Biotechnology bingo modularity, knowledge processes, and the collaborative experience

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Biotechnology Bingo
Modularity, Knowledge Processes, and the Collaborative Experience

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CERTIFICATION

I, Desiree A. Monty, declare that this thesis, submitted in fulfillment of the requirements for the award of Doctor of Philosophy, in the Department of Management, Marketing, and Employment Relations, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. The document has not been submitted for qualifications at any other academic institution.

Desiree M. Monty

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ABSTRACT

This thesis examines collaborative relationships between university scientists and private biotechnology firms. Using the concepts of *modularity*, *boundary objects*, and *articulation*, I demonstrate that these relationships are structured in a modular fashion. How knowledge is used, reused, and valued in an alliance is dependent upon the structure of that alliance. Knowledge is seen to exist in two forms – *migratory*, being mobile and combinable, and *ingrained*, being personally idiosyncratic and intertwined with specialization. In examining these forms of knowledge and the way that they are used by members of a collaboration, I use an interpretive methodology to analyze the data derived from four case studies of university-industry collaboration. One case study is based on an alliance in the United States and the other three cases present evidence from collaborations in Australia. I explore the appropriateness of applying the concepts of modular design to interorganizational collaborations, the production and use of knowledge within the boundaries of these structural arrangements, and the role of the university and firm scientists in the endeavour to develop therapeutics through the application of biotechnology. I argue that the movement of knowledge is dependent upon the structure through which knowledge processes are operationalized. In addition, I submit that knowledge based collaborations in biotechnology must be analyzed with respect to the larger contextual framework of the biopharmaceutical industry, with consideration of both the competitors of an alliance and the ill patients who stand to benefit from the work within an alliance.

Chapter 1 Commencement

As a student of management during the previous decade, I was taught that there is an insurmountable barrier between management theory and the actual practice of management. Management researchers were portrayed as uninformed, inexperienced scholars who operated at such a distance from the mainstream empirical activities of management that there was no way for them to actually understand and explain what it meant to practise management. Furthermore, the environment in which a manager operates is rapidly changing and unpredictable, and a theory is just the opposite – stagnant and steady. Aligning the two, then, was perceived and conveyed to be an impossible task.

As a budding management researcher, I have learned that a well-crafted theory is often the best defense to this type of criticism. Despite the existence of a plethora of business schools and flourishing commerce faculties that dot the landscape of tertiary education across the globe, there are many managers at work today who do not hold formal management credentials, who have moved up the ranks of an organizational structure and gained their knowledge of the duties of management through experience alone. These types of practitioners do not read the theoretical literature on how to manage, but rather rely on what they have seen, what makes sense, and they follow the almighty indicator of capital returns. A theory of management that takes this into account should be capable of providing an empirically valid, practice-relevant explanation of the activity of management.

Moreover, management is a fairly new discipline, particularly when compared to psychology or sociology, two disciplines on which management is based. Management must be considered a multi-disciplinary art or science (depending on one's preferred terminology of management) in itself. An acceptable theory of management, then, would need to consult

different perspectives and draw from various discourses. The theory presented in this thesis attempts to do just that. Not only does it fuse together different social science disciplines, but it also crosses the social science-natural science boundary.

The type of managerial activity considered in this report is the management of collaborations between university and industry in the area of biotechnology. The managers in these types of arrangements are scientists. They often have years of experience in management positions, but they are trained scientists, holding doctoral degrees in areas such as chemistry, microbiology, and virology. In developing a theory pertaining to the activities of these scientists-cum-managers, I seek not to cover the already navigated waters of alliance governance, the closely associated investigations of risk and interorganizational collaboration, or the highly applicable notion of networks. I do, however, aim at generating a theoretical explanation of what it is that these managers do (or try to do). In my effort to cultivate this explanation, I use empirical data to describe and define their activities, and I utilize the concepts of knowledge resources and modularity to place this explanation in the existing literatures – to give it a home.

In this chapter, I provide the reader with an introduction to this theory and the research that supports it. The first section, Situating the Research, deals with some of the existing literature, serving both to position the report within the relevant bodies of literature and to highlight the main sources used to generate the theory. The Significance of the Research is the second section of this chapter. It aims to preview and explain the significance of the forthcoming findings, as they are presented in this thesis. The final section of this chapter, Surveying the Report, is a brief overview of the contents of each of the following chapters.

1.1 Situating the Research

"Reliance on strategic alliances and interfirm relationships has grown considerably in recent years, while partnerships with external actors have become a central strategy for many organizations in a wide range of industrial contexts" (Lorenzoni & Lipparini, 1999, p1). While

many management scholars have demonstrated the existence and implications of strategic alliances within a variety of *industries*, including Albino, Garavelli, and Schiuma's (1999) study of the leather sofa district in Italy, Avadikyan et al's (2001) work in the energy field, Chung, Singh, and Lee's (2000) investigation of investment banking, and Stuart's (2000) evidence drawn from the semiconductor industry, other researches have tended to be more specific in the *types* of alliances they study. For example, there is a segment of the interorganizational collaboration literature devoted to research and development alliances (cf. Barnes, Pashby, & Gibbons, 2003; Turpin & Garrett-Jones, 1997). On an even more defined scope, there is a strand in the strategic alliance discourse dedicated to collaborations involving biotechnology.

The work of W. W. Powell and his colleagues, the stream of publications by Lynne Zucker and colleagues, and the comparative studies done by Wendy Faulkner and Jacqueline Senker, and by Bruce Kogut and associates, among others, have opened up a niche literature base for the investigation of collaborations in the area of biotechnology. This niche, of course, is intertwined with and feeds into and from the literatures on innovation and human or knowledge capital.

Some of the scholars contributing to this niche agree on certain central tenets. For example, researchers agree that biotechnology has originated primarily in university laboratories. Powell (1996) notes that, "[t]he science underlying biotech has its origins in university laboratories and research institutes" (p199). And, Zucker, Darby, and Brewer (1998) suggest that, "…the innovations which underlie biotechnology are properly analyzed in terms of naturally excludable knowledge held by a small initial group of discoverers, their co-workers, and others who learned the knowledge from working at the bench-science level with those possessing the requisite know-how" (p291). Both of these articles also point to the significance of venture capital in the establishment and growth of dedicated biotechnology firms. In addition, Powell, Koput, and Smith-Doerr (1996) agree with Faulkner and Senker (1995) in pointing to the exploratory nature of public-private R&D collaboration.

There are also conflicting findings. Powell (1996) argues that in the "biotechnology industry", there are severe limitations to market transactions, while Zucker, Darby, and

Armstrong (1998) contend that their findings demonstrate the market exchange of rivalrous and excludable goods, namely knowledge. Powell (1996), however, focuses on a reputation for collaborative capability as a vital signaling tactic in the industry, while Zucker, Darby, and Brewer (1998) concentrate on the importance of intellectual capital as the impetus for collaborative endeavours.

There is, then, a nicely packaged, easily identifiable niche of the interorganizational collaboration literature that deals specifically with alliances in biotechnology. I seek to contribute to this literature base, and in the process, contest some of the presumptions and assertions that exist within it. The collaborations investigated in this report are aimed at a specific outcome, rather than being exploratory, as is suggested in the literature. University-industry collaborations in biotechnology are directed towards the resolution of specific technological problems. Furthermore, while much of the niche literature base is centred on knowledge, it fails to engage the work of the philosophers and sociologists of knowledge that has long preceded management theory. The work of philosophers and sociologists of knowledge offers precedence for discussion on the role, use, and value of knowledge in social engagements. As such, I draw from this work in discussing collaborations as social engagements.

The research presented in this thesis conceptualizes knowledge as a resource, in accord with much of the management literature. Unlike the work of Albino, Garavelli, and Schiuma (1999), Argote and Ingram (2000), Cummings and Teng (2003), Gilbert and Cordey-Hayes (1996), and Yli-Renko, Autio, and Sapienza (2001), however, this resource is seen as multi-faceted and does not necessarily "flow" or diffuse in an unsystematic manner. As it is conceptualized in this report, knowledge exists in two forms, namely ingrained, as a correlate of Polanyi's (1958) tacit knowledge, and migratory, as a form of knowledge that moves, and more importantly, can be absorbed and accumulated. There is, however, not a clear distinction between these two forms in that the existence of one form is tightly intertwined with the existence of the other. Migratory and ingrained knowledge are complementary, not juxtaposed.

The concept of migratory knowledge draws on the work of Aadne, von Krogh, and Roos (1996), Berger (1967), Latour (1987), and Rescher (1997), in addition to other influential sources. Migratory knowledge is very similar to the common conceptualization of knowledge that reigns throughout the knowledge and strategic management literatures. It assumes similar cognitive bases of senders and receivers of messages.

Ingrained knowledge, on the other hand, stems from a biological depiction of knowledge, following Maturana and Varela (1980), Varela (1992), and von Krogh, Roos, and Slocum (1996). This type of knowledge is inseparably linked to the actions of the beholder of knowledge. Ingrained knowledge is presented as being convertible to migratory knowledge, which can then be reused.

This process of conversion differs from Nonaka and Takeuchi's (1995) knowledge spiral in that migratory knowledge is not necessarily codified knowledge. The process of converting ingrained knowledge into migratory knowledge, or what I refer to as objectified knowledge, occurs within the structure of a collaboration between university and industry, or in a knowledge value alliance. Once converted, it rests in "things" (Latour, 1987), including objects and techniques, which are absorbed and utilized by members of an alliance. In developing the description of the process of transforming ingrained knowledge into objectified, migratory knowledge, readying it for accumulation, I draw from Knorr-Centina (1981, 1983), Langlois (2001), and Latour (1987). The purpose of the processes of transformation and accumulation is to reuse the objectified knowledge.

The arguments presented throughout this thesis are based on Sussland's (2001) observation that, "[r]esources can be traded or exchanged. For example, money can be spent to strengthen the value of the brand, or time can be spent to increase human capital. However, one of the peculiarities of intangible resources is that they may actually strengthen in use rather than depreciate" (Sussland, 2001, p2). Knowledge, as an intangible resource, becomes more valuable when it can be reused. Reuse of knowledge is possible because collaborations between university and industry are part of a social level of a larger hierarchical arrangement of actors and institutions. The knowledge created within these collaborations is useful and has value

beyond the level at which the collaborations exist, given the appropriate connections between the levels of the hierarchical system.

Following this line of reasoning, alliances between university and industry are conceptualized as partially modular arrangements. They are characterized by distinct divisions of labour, which operate as silos, or modules within the framework of the alliance. This conceptualization draws from the scholars of modularity, including Baldwin and Clark (1997, 2000, 2003), Langlois and Robertson (1995, 2003), Sanchez (1999, 2000), and Simon (1962, 1976). I attempt to apply the principles of modularity, including architectures, design rules, and interfaces, to elucidate the structure of collaborations. I also draw from and mingle the theory of modularity with the theories of the sociology of science developed by Fujimura (1987, 1996) and Star and Griesemer (1989).

My aim in doing so is to overcome the deficiencies of the discussion that runs through the knowledge management literature, in which knowledge processes such as flows (Gibbons et al, 1994), socialization, externalization, combination, and internalization (Nonaka, Reinmoeller, & Senoo, 2000), and the management of the resource itself (Blumentritt & Johnston, 1999) are discussed with little attention to the structure through which the processes are operationalized. Structure is a crucial analytical construct in the examination of knowledge related to biotechnology because, as noted by Woodward (1971), "…different technologies impose different kinds of demands on individuals and organizations…" (p65). Thus, the technology used in an alliance will ultimately affect its structure and its knowledge processes.

These aforementioned authors, however, show minimal concern for the technological or structural mechanisms that can enhance or hinder knowledge processes. Nonaka, Reinmoeller, and Senoo (2000) introduce the concept of *ba*, or the place or platform for knowledge creation and emergence, but their discussion of place and platform is much different from the type of organizational structure addressed in Woodward (1965), Chandler (1966), and Burns and Stalker (1961). According to Nonaka, Reinmoeller, and Senoo (2000), *ba* comes in four forms, which include where knowledge creation begins, individual reflection of mental modes and skills, a place of monologue, and participative activities. Structure, in accordance with Burns

and Stalker (1961), Galbraith (1977), and Woodward (1965), is the organization of activities and tasks to accomplish a specific purpose. There is no mention of purpose in the conceptualization of *ba*. *Ba* is a general place or platform applicable to an array of activities. Conversely, different structures are required in different circumstances. For instance, Burns (1963) suggests that a mechanistic structure is suitable to stable conditions and an organismic structure is appropriate in changing conditions.

If the purpose of a firm or an alliance is research and development, the organizing of the structure of such endeavours is not only difficult, but also likely to impact on the knowledge processes that are crucial to the success of such activities. Following Burns and Stalker (1961), the difficulties of organizing research and development stems from the co-existence of the many different scientific languages and skills that are part of the research and development process. These authors note that organization in research and development laboratories is centred on two things:

> *(i)* the relating of everything that happens to the production of designs which will meet precisely and economically the requirements of the users, and *(ii)* the support of the individual engineer by a network of communication with others which ensures that the technical resources of the whole staff of the establishment are readily available to him, and which yet does not require or encourage him to dissipate too much time or effort merely in communication with others (Burns & Stalker, 1961, p160).

This type of arrangement is indeed difficult to pin down, and the very act of pinning it down has implications for the levels of communication and exchange that occur within the structure. As Burns and Stalker (1961) suggest, "…lines are drawn across the continuous flow, and the average level of each resulting section of the process [of research and development] thereafter represents a separate kind of activity which requires a different kind of skill and training, a different language" (p156).

There are, indeed, some management scholars who address the importance of structure in relation to knowledge "flows". For example, Santoro and Gopalakrishnan (2000) report findings that depict knowledge transfer as a "multi-staged process, consisting of knowledge creation, knowledge acquisition, and knowledge integration" (p312). They contend that mechanistic organizational structures facilitate knowledge acquisition through the institutionalization of the

acquisition process and that organic structures are required for knowledge creation and knowledge integration. While these authors rightfully acknowledge the importance of structure to the pattern of knowledge processes, their focus is on the structure of industry firms in industry-university collaborative ventures. In this thesis, the structure I refer to is the structure of the alliance itself, not the structure of one or the other alliance constituents. I submit that the alliances presented in this thesis are characterized by a modular structure.

Modularity is one type of structure for organizing research and development activities. In this thesis, I attempt to identify and illustrate the modular structures of university-industry alliances and the implications that this type of structure has on the knowledge processes of the collaborative participants. Modularity, however, is only one type of structure and there could quite possibly be an assortment of structures appropriate for the organization of research and development activities and interorganizational relationships. Indeed, a structure should allow for people to get the information they need without being overloaded and this should be done with the expenditure of the least possible resources. I build my theory around this notion of structure.

Because I intend the theory presented in this thesis to be empirically valid and practice-relevant, I make a considerable effort to engage with the scientific content of the theory. As I strive to accurately explain the activities of the scientist-cum-manager, I also aim to offer the social scientist-cum-management scholar a detailed understanding of the scientific techniques and tangible artifacts of the collaborative endeavours investigated in this study. The result is a reciprocal relationship of theories and behaviour. I apply the concepts of modularity and the sociology of knowledge to the work performed in university-industry collaborations in biotechnology, and what I get in return, and what is presented here to the reader, is a translation of the practices of biotechnology in the language of these concepts.

The theory presented and illustrated in the forthcoming chapters can be said to bring together interorganizational relationships, modularity, the sociology of knowledge, and science-oriented practices. These elements are combined in a metaphor that serves to enliven and disentangle the complexity that could potentially result from the combination of these various discourses. The game of Bingo is used to explain the activities that occur within a collaboration

between university and industry, providing a metaphor for the alignment of the tasks of various collaborative participants in cases of task complexity and uncertainty. The context in which these collaborations dwell is characterized as unpredictable and science-dependent. The role of the scientist-cum-manager, who is often in control of the direction of such alliances, is that of an architect, or a broker of knowledge (Snow, Miles, & Coleman, Jr., 1992). As noted by Snow, Miles, and Coleman, Jr. (1992), "[b]usinesses such as fashion, toys, publishing, motion pictures, and biotechnology may require or allow firms to outsource extensively. In such circumstances, the lead firm identifies and assembles assets owned largely (or entirely) by other companies" (p14).

The lead firm in the biopharmaceutical industry (the industry in which collaborations between university and industry in biotechnology exist and operate) is argued to be the dedicated biotechnology firm. The scientists-cum-managers of this type of organization assemble and accumulate the resources of outside parties, with the main outside parties in this report being universities and their scientists. The goals of such activity are to achieve the desired output of a collaborative endeavour and embark on the journey of getting pills into a bottle for those on the other side of the equation, the ill patients who stand to benefit from the application of biotechnology.

The work presented in this thesis is cross-disciplinary, explanatory, and employs an interpretive methodology. A multiple case study design (Eisenhardt, 1989b; Herriott and Firestone, 1983; Lennick-Hall, 1992; Yin, 1994) is used to investigate the activity inherent in university-industry alliances in biotechnology. The evidence from these cases is evaluated and analysed in accordance with the concepts of Klein and Myers (1999) and follows a hermeneutical approach.

The pages of this report, then, present a theory that is uniquely my own. They tell a story of the activities of scientists-cum-managers, which aims to provide a significant contribution to the discourses on interorganizational collaboration, modularity, and the sociology of knowledge. The next section of this introductory chapter previews the significance of the study.

1.2 Significance of the Research

The arguments presented in this thesis are developed with the intention of contributing to the existing literatures from which this report draws. There are two core contributions around which the many smaller findings of this research revolve. The first contribution is the thoroughly argued, illustrated point in this thesis that university-industry collaborations in biotechnology are structure-based entities, and it is the structure of these alliances that most importantly influences how knowledge is created and used. Secondly, this thesis offers the contribution of conceptualising collaborations as inherently social engagements, not in terms of the interactivity of the two sides of an alliance (although such activity is undeniably social), but in relation to the larger context in which these alliances dwell.

Interorganizational collaboration has been conceptualised as and investigated through, inter alia, the paradigms of developmental processes (Ring & Van de Ven, 1994), as mechanisms for technology transfer (Lynskey, 1999; Steensma, 1996), as conduits for efficiency and profitability (Contractor & Lorange, 1988), but there has been little work done to explore or explain the social organization of strategic alliances. The transaction cost scholars have concentrated on coordination, governance, and asset specificity (Amit & Schoemaker, 1993; Klein, 1980; Williams, 1983, 1985). Other researchers have centred their work on competitiveness (Porter & Fuller, 1986) and the absorption of extramural knowledge (Hamel, Doz & Prahalad, 1989; Kogut, 1988). And, indeed, Arora, Fosfuri, and Gambardella (2001) explore in detail the division of innovative labour in high technology industries. In my view, however, there is an insufficient amount of work that focuses on the division of labour within collaborative arrangements, and in doing so, applies the concepts of modularity. Tackling collaborations in this fashion allows for the application of modularity to process designs, rather than products or artifacts, and allows for a novel conceptualisation of complementary resource-based alliances.

With this contribution, attention is turned to the structure of the alliance, with implications for how knowledge is generated, valued, and used within the structure. This line of

reasoning stands in direct contrast to Gibbons et al's (1994) proposal of Mode 2 knowledge, or the transdisciplinary knowledge that they claim is inherent to current research and development endeavours. These authors state that, "Mode 2 creates a novel environment in which knowledge flows more easily across disciplinary boundaries, human resources are more mobile, and the organization of research more open and flexible" (p20). It is my contention that the structure-based interpretation of alliances, as supported by the evidence in this thesis, suggests otherwise. In the modular structures characteristic of the alliances presented here, knowledge remains fixed in disciplinary boundaries, human resources are combinable, but are also firmly attached to and entrenched in the organizational boundaries of firms and universities, and the organization of research is premised on a division of labour. In the process of attempting to achieve the desired output of an alliance, knowledge is integrated in the structure of an alliance by various design rules and interfaces.

In a manner similar to the arguments of Gibbons et al (1994), the Australian Government also describes the importance of knowledge "flows" in research and development efforts.

> It is now recognized that the generation of knowledge and its development into new technologies for commercialization can only be considered in terms of the national innovation system and that the key to successful innovation is the flow of creativity, ideas, skills and people between players in the innovation system, namely the universities, public research institutes (primarily CSIRO) and private enterprise. Understanding this system can help identify leverage points for enhancing innovative performance and competitiveness (Australian Research Council, 1998, p1).

I argue in this thesis that it is not only the flow within the structure that is the key to success, but the structure of the system itself. Surely, knowledge does flow among the components of a system in many cases. The interesting question, though, is how the rate, quality, efficiency, etc. of the flows change according to the structure of an alliance. More importantly, one has to ask if the structure is conducive to the flows that are necessary to achieve a desired outcome.

This is where the second major contribution of this work comes into play. Collaborations between university and industry are presented as social engagements, requiring the appreciation and acknowledgement of the activities of competitors and the needs of intermediate and ultimate consumers, namely large pharmaceutical firms (as intermediate consumers) and ill patients (as ultimate consumers). Although an alliance operates at varying degrees of distance

from these social constituents, it is imperative that an awareness of these social actors and their activities and needs is facilitated and nurtured. The social engagement between the participants of an alliance and the agents of the larger social system in which the alliance is situated is premised on a cycle of accumulation, following Latour (1987).

The significance of the social engagement contribution comes from the movement away from viewing alliances between university and industry in biotechnology as some sort of activity that occurs in the isolation of some secret laboratory or hidden corner of the biopharmaceutical industry. Under the terms of a social engagement approach, alliances are initiated and conducted for specific purposes that go well beyond their own existence. The lead firm, or the dedicated biotechnology firm, accumulates knowledge in order to affect the constituents of the larger social system in different ways. The process of accumulating knowledge is carried out with the purposes of displacing competitors, generating profits, and benefiting ill patients. This transcends the typical approach to studying research and development collaborations in terms of technology transfers aimed at spawning innovation. The purposes of an alliance between university and industry are much broader than the technology transfer and innovation discourses warrant.

I only offer a preview of these contributions here, though. I extend these arguments and take on the proposals, assertions, and findings of a variety of scholarly research throughout this thesis. My aim in doing so is not only to highlight these significant contributions, but to also provide a framework for future research.

1.3 Surveying the Report

This report is composed of three sections, namely the Grafted Theory section, the section titled Grounding the Theory, and the Grand Finale. Within these sections are chapters devoted to a common purpose. The Grafted Theory section incorporates chapters two, three, and four, in which I develop and present the theory that I call Biotechnology Bingo. These chapters contain a literature review and theoretical framework wrapped in an argumentative presentation. The

second section of this report, Grounding the Theory, contains chapters five, six, seven, and eight. Chapter five depicts the methodology used in developing this theory, while chapters six, seven, and eight are presentations of the cases that illustrate the theory. The Grand Finale, the final section of this report, is composed of a cross-case analysis, chapter nine, and the conclusion, chapter ten.

Chapter two provides the background and context of the investigation. In this chapter, I attempt to acclimate the reader to the setting and concepts associated with the research. I provide a preliminary overview of the history and practices of biotechnology and examine its infiltration into the traditional pharmaceutical industry, demonstrating how biotechnology impacted the arrangement of this industry and why collaborations between university and industry have come to be such a vital part of the existence of what I call the biopharmaceutical industry. In this chapter, I conceptualize these types of collaborations as knowledge value alliances, following Rogers and Bozeman (2001), with the aim of these endeavours being value cultivation. The final portion of chapter two introduces the metaphor of Biotechnology Bingo.

In chapters three and four, this metaphor is developed into a theory of task alignment and knowledge integration in university-industry collaborations. The game of Biotechnology Bingo is premised on the concepts of modularity, and therefore the rules of the game revolve around design rules, interfaces, and most importantly, the architecture. Following Sanchez (1999) the architecture in this application of modularity is a knowledge architecture. This architecture comprises people, knowledge, design rules, interfaces, and what Star and Griesemer (1989) call boundary objects. Chapter three characterizes the knowledge architecture in relation to these elements. It provides a detailed conceptualization of the types of knowledge inherent to the architecture and an account of how these types of knowledge are used by the collaborative participants to solve technological problems. In addition, it covers the concept of a modular structure.

Chapter four is based on the notion that while knowledge value alliances are indeed modular arrangements, they are only partially modular. There is a certain amount of interdependency that exists within these structures. With this in mind, there is a need to address

the issues created by the culture and communication within the architecture. I aim to satisfy this need in chapter four. Chapter four provides an account of university-industry alliances as social engagements and introduces the concept of displacement. The culture beyond the collaborative level is discussed to demonstrate how the work within an alliance is impacted by the culture outside of it, and more importantly, how the work within the alliance affects the constituents beyond the knowledge architecture. With the conclusion of chapter four, the theory is complete. The agenda then turns to illustrating the theory.

Chapter five discusses the methodology used in this study. It details the interpretative process of the research. This chapter highlights the original assumptions made in planning the research. I cover the guiding methodologies and the reasons for their selection. My interpretation of university-industry collaborations and the generation and use of knowledge that occurs within them changed significantly in the process of investigation, and chapter five details this change and the resulting interpretation of the data. I rely on the principles of interpretive research, as depicted by Klein and Myers (1999), and the hermeneutical circle to convey my process of interpretation. Emphasizing the ability of data to tell their own story, I demonstrate how this occurred in the research presented in this thesis.

Chapters six, seven, and eight are the empirical grounding of the theory of Biotechnology Bingo. In each case, the basic principles of the theory are applied, including the use of design rules, interfaces, and boundary objects. Each case has something different to say about collaborations between university and industry in biotechnology. In analyzing the findings of each case, I draw from the originality of each case to further elaborate on the theory in the later chapters of this thesis.

Chapter six presents the findings from the first case study I conducted. This case covers an alliance between the Center for Marine Biology and Biotechnology (CMBB) at the University of California, San Diego and Nereus Pharmaceuticals, a dedicated biotechnology firm that is also located in San Diego, California (United States of America). Interestingly, the director of CMBB is also the co-founder of the industry firm. The highlights of this case include a trajectory of luck created by the continued collaboration between the two partners and the

ability of the collaboration to procure large government research grants that have been renewed throughout the life of the collaboration.

Chapter seven is focused on the alliance between the Institute for Biomolecular Science (IBS) at the University of Wollongong and amrad[1] Corporation Limited, a small biotechnology firm from Richmond, Victoria (Australia). This collaboration involves three projects, and the application of design rules, interfaces, and boundary objects occurs at the inter-project level, or across projects. This case illustrates what may happen when there are considerable differences in the knowledge bases of the two segments of the alliance. The elements of modularity that provide for integration and connection in a product architecture are shown to also induce integration and connection in a process (or knowledge) architecture. This case also offers evidence of the reuse of knowledge across different projects.

Chapter eight is the final full-length case study presented in this report. This case is the alliance between the Institute for Glycomics (IG), Griffith University, located in Brisbane, Queensland, and Progen Industries Limited, a biotechnology firm in Darra, Queensland (Australia). The members of this alliance use similar design rules to the ones found in the case presented in chapter seven, the IBS-amrad alliance. This case differs from the others in that after three years of existence, the members of the alliance have not been able to reach their desired output. They have, however, agreed to further investigation. The implications of this case are found in the notion that collaborations in biotechnology take time to produce results. The types of collaborations presented in this report are science-dependent, and no matter what types of rules, interfaces, or milestones are attached to a collaborative agenda, the uncertainty of the science cannot be overcome.

Chapter nine builds on the findings from the three cases presented in chapters six, seven, and eight. Chapter nine is a cross-case analysis, with the inclusion of a fourth case, the alliance between the Institute for Biomolecular Science (IBS) at the University of Wollongong and Novogen, a dedicated biotechnology firm in North Ryde, New South Wales (Australia). The

[1] The company's name is spelled in all lower case letters, and thus it appear in this form throughout the thesis.

discussion aims to extract the key findings of the four cases to further refine the theory of Biotechnology Bingo. The rules of the game are presented, with an emphasis on manipulating these rules in a bid to win the game. This chapter comprises a discussion of the applicability of modularity to these cases, a depiction of the processes of knowledge production and function that occur in the alliances presented in this report, and a qualification of the operation of displacement that serves as one of the purposes of the game.

Chapter ten concludes this thesis. It aims to provide an overview of the findings of the research. A considerable effort is made to address these findings in terms of the practice of biotechnology, so that the findings are not only relevant to management scholars, but also to the work of the scientist-cum-managers of the types of collaborations investigated in this study.

SECTION I

GRAFTED THEORY

Chapter 2 Context, Collaboration, & Complexity

> "Revolutionary technological innovation is an inherently dynamic and coevolutionary process requiring considerable care in research design" (Hamilton, 2001, p162).

This chapter provides the necessary preparation for the arguments presented in this thesis. The following four sections, 1) Biotechnology as a "Design for Purpose Affair", 2) The Infiltration of Biotechnology into the Pharmaceutical Industry, 3) Knowledge-Based Collaboration in the Biopharmaceutical Industry as a Method of Value Cultivation, and 4) Biotechnology Bingo, not only contextualize the wellspring of discussion and analysis found in the forthcoming chapters, but also shed a new light on what it really means to practise biotechnology research. Stepping outside of the box that rigidly defines biotechnology as the utilization and advancement of the technological breakthroughs of the past century, the approach inherent to this argument is grounded in the conjecture that biotechnology represents a range of practices, draws from an agglomeration of knowledge bases, and thus, cannot be appropriately explained by a core set of technological procedures. As Bud (1993) asserts, as the potency of biotechnology became apparent in the 1980s, "the clarity of local visions was replaced by a cacophony of dissonant interests, speaking each in their own tongue. This, rather than any single philosophy, became the striking characteristic of 'biotechnology'" (p189).

As argued in the following sections, biotechnology, whether yielding products such as the bionic ear or the latest treatment for cancer, is centred on a "design for purpose" strategy. This strategy comes to fruition in, among other places, collaborations between industry and academia, where various knowledge bases are integrated, and, as a result, the strengths of each type of institution are aggregated. Collaborative ventures between industry and academia rely

on a task-performance matrix to cull the knowledge and capabilities of the different types of organizations. If successful, these cooperative endeavours are akin to a game of Bingo, in which the winner prevails by gaining possession of a sequence of intersections between the alphabetical row and the numerical squares. Similarly, therapeutics in the biopharmaceutical industry are derived from finding the appropriate intersection between the tasks that must be accomplished in designing the therapeutic and those individuals best suited to perform those tasks.

2.1 Biotechnology as a "Design for Purpose Affair"

Biotechnology, with the emergence of its current form in the early 1970s, was both a new paradigm in the Kuhnian sense (Kuhn, 1970) and a Schumpeterian wave of creative destruction in the commercial arena (Schumpeter, 1942), particularly in industries such as pharmaceuticals, agriculture, and chemicals. With the initial technological breakthroughs of Boyer and Cohen in 1973 and Köhler and Milstein in 1975, and the development of protein engineering in the 1980s, biotechnology supplanted traditional practices of treating human disease, developing fertilizer, and producing fuels and plastics. Such disruption and redefinition of scientific and technological practice has been associated with biotechnology since its evolution from zymotechnology in the late 19th century[2], during which a movement from brewing as a hit-and-miss convention to a procedure with a particular emphasis on science, including microbiology,

[2] Bud (1993) contends that modern-day biotechnology can be traced back to the nineteenth century practice of zymotechnology, which, in addition to brewing, represented all types of industrial fermentation. "Because of the new ability to control a wide range of applications, from the curing of leather to the manufacture of citric acid, it was widely commended as the future superstar of the economic stage by 1900" (Bud, 1993, p6). Like biotechnology, zymotechnology was closely allied with the practice of chemistry. Bud (1993) goes on to suggest that, "[z]ymotechnology as an ensemble of several disciplines and skills was a phenomenon characteristic of the last century. It was also clearly descended from German chemistry of the Age of Enlightenment, the eighteenth century. Whether one looks to institutional roots, intellectual content, or the aspirations with which zymotechnology came to be attached, chemistry's promise to both explain and control provided a reliable precedent for the new dispensation" (p8). There are authors, however, that trace the history of biotechnology, going back as far as 3000 BC. Rehm and Präve (1987), for example, begin their "Information on the Historical Development of Biotechnology" (Table 1-1, p5) with proving bread with leaven, fermentation of juices to alcoholic beverages in almost all natural populations, and knowledge of vinegar formation from fermented juices, all said to have occurred in the prehistoric period, "before 3000 BC".

bacteriology, and biochemistry, created a distinct formula for the methodical conversion of inputs into outputs and the investment in purposeful engineering and design.

Although commonly referred to by some as an industry, biotechnology remains just what its name implies – a technology. Some sources appropriately recognize this distinction. For example, Powell and Brantley (1992) emphasize that biotechnology is strictly a technology, not an industry. Hamilton (2001) characterizes biotechnology as a "set of powerful technologies (e.g., Recombinant DNA and hybridoma technologies) with potential applications in a variety of industries…" (p158). The Victorian Government defines biotechnology as "the application of knowledge about living organisms and their components to make new products and to develop new industrial processes. Biotechnology is often referred to as an 'enabling' technology…" (Department of Innovation, Industry and Regional Development, 2002). The following sections discuss the history of this technology and the purpose behind the practice of it.

2.1.1 The History of Biotechnology

While the literature from the past decade credits the discoveries in the early 1970s and 1980s as the beginning of biotechnology (cf. Barley, Freeman, & Hybels, 1992; Hamilton, 2001; Powell & Brantley, 1992; Russell, 1999; Zucker, Darby, & Brewer, 1998), there is evidence to suggest that the practices and motives of 19th century zymotechnologists and even the 20th century evolutionary theorists relate to the action manifested in modern scientific and industrial activities in biotechnology. Bud (1993) credits the 1828 term "biotechnie" as it was used by Virey, to explain man's need to develop technology to counteract the loss of natural instincts as the first, true surfacing of biotechnology. It is in the definition of biotechnology as a practice of manipulating man's external environment and tinkering with the very substance of man's composition that allows one to make a connection between what we call biotechnology today and the scientific and technological activities of the 19th and 20th centuries.

The social hygiene theory of Goldscheid and the description of man as *Homo faber* (man the maker) by Bergson (Bud, 1993) are some of the first indications of how biotechnology could and would be used. As we witness the spread of biotechnology in a plethora of industries across

the globe today, we do so with the understanding that the technology is ostensibly employed to benefit humanity through treating diseases, growing agriculturally superior products, and avoiding the depletion of some of our most valuable natural resources.

This is not to say, however, that the application of biotechnology is uncontested. One only has to look at the considerable debate surrounding stem cell research or the outrage expressed by traditional farmers (and consumers) in relation to the growing of genetically modified crops to grasp the extent of opposition to a new technology that claims to prolong life and benefit humankind. For example, the "golden rice" story (Eyck, Thompson, & Priest, 2001) that circulated through the realms of different policy makers, scientists, and farmers in the U.S. demonstrates the differences in opinion that exist among these groups, in addition to demonstrating the various types of opposition to products produced via biotechnology. "Golden rice" is rice that is transformed through biotechnological procedures to contain increased contents of vitamin A. "The product was widely touted as a response to nutritional deficiencies among the poorest of the poor. Advocates of biotechnology argued that opponents of the technology were putting forth an elitist view that was contrary to the interests of people in the developing world" (Eyck, Thompson, & Priest, 2001, p310). A report by seven different science academies, however, argued that although current trends in biotechnology could be an important tool for increasing the world's food supply, the technology did little for the concerns of poor farmers (Eyck, Thompson, & Priest, 2001).

2.1.2 Biotechnology as Teleological Activity

Overshadowing both the hope and the debate linked to biotechnology is the shared notion that those individuals immersed in the biotechnology game play with a passionate purpose. In 1925, Alfred Wagner made the point that *biotechnik* is "only an idea, a word, but one of those which unifies an entire world", but unlike the idea of elementary mechanics, it embodies the idea of *design for a purpose* (cited in Bud, 1993, p61 – emphasis added). Indeed, such an ideology of "design for purpose" was evident in Massachusetts Institute of Technology's (MIT) 1936 inauguration of the School of Biological Engineering, aptly named to denote the home of

subjects teaching "the art of organizing and directing men and of controlling factors and materials of nature for the benefit of the human race…with the aid of physics, chemistry and other allied sciences (Bud, 1993, p86). The "design for purpose" mantra has become one of the foundations of biotechnology that has raised the technology to the status of a tool for future development in both Third World and wealthy nations, and as a dynamo in the international economically competitive context.

Biotechnology as a general technological praxis, with its inherent teleological trajectory, confers a specific focus on a company's work and creates the opportunity for an organization to surpass market boundaries. Indeed, very influential economists such as Dosi (1988b) and Freeman (1989) contend that biotechnology represents a technological paradigm, or a sequence of "selected technoeconomic problems based on highly selected principles derived from natural sciences, jointly with specific rules aimed to acquire new knowledge and safeguard it, whenever possible, against rapid diffusion to the competitors" (Dosi, 1988b, p1127). Biotechnology, like its ancestor, zymotechnology, indicates "a technological skill that [is] rooted in a variety of sciences but [has] a practical character transcending mere applied science" (Bud, 1993, p26).

The development of the recombinant DNA, monoclonal antibody, and protein engineering technologies of the last century that most scholars cite as the first instances of the infiltration of biotechnology into the academic and industrial arenas, merely extended the merging of science and technology that biotechnology had demonstrated in the past. More importantly, however, these discoveries opened up the door for wider applications and process refinement, indicating, and leaving many anticipating, the arrival of new products and methodologies, and the benefits of technological revolution. Following Orsenigo (1989), Russell (1999) states that the new practice of biotechnology extends the possibilities in terms of the number and scope of potential applications and generates distinct and surpassing technological opportunity. As Barley, Freeman and Hybels (1992) note,

> …by 1982 recombinant DNA and hybridoma technology were widely viewed as having opened a vast commercial frontier where genetically engineered microorganisms would be used to degrade wastes and manufacture medical and industrial products. Some entrepreneurs even dreamed of directly manipulating the genetic code of higher organisms, including humans. The promise of

> spectacular profits was particularly acute in the areas of new drugs, new diagnostics, waste treatment, new plants, and even genetically altered livestock. As a result, interest in commercializing the technologies rapidly spanned traditional industries and organizational populations (p315).

It is important to note that the discoveries of the 1970s and early 1980s did not represent an entirely new set of technologies, as much as they did a new form of an existing set, in that they carried with them the "design for purpose" approach already associated with the term *biotechnology*. For example, the recombinant DNA technology allowed scientists to act like editors of a text, by "cutting" human genes and "pasting" them into bacteria to produce substances of medical and economic value, which, in the case of the initial development of recombinant DNA, was insulin (Biotechnology Industry Organization, 1989). The technology allowed scientists to *design* substances for the *purpose* of creating value.

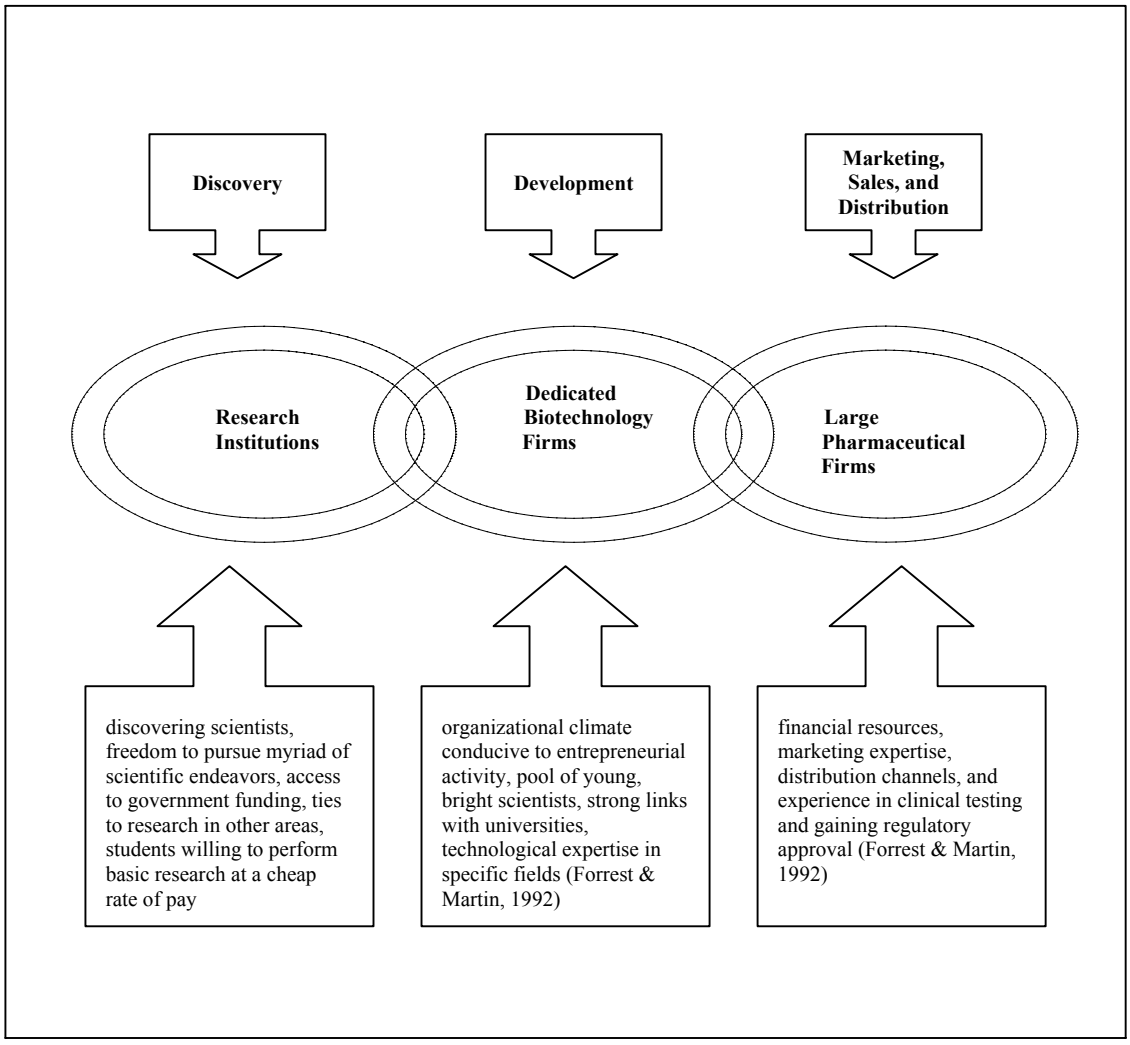
One result of this "design for purpose activity" is that scientists can do more and expect more, but often times, they can't do it alone. Processes have changed, with search processes becoming more routinized than random. Different outcomes can be expected, particularly in relation to the search for new therapeutics. Task complexity is also increased, however. So, with this processural change and hope for advanced drugs, comes the need for industry and academia to unite forces under the umbrella of taking basic discoveries, usually made in an academic setting, and putting them on the pathway to development. Therefore, the next portion of this chapter is devoted to portraying the biopharmaceutical industry as a facilitator of collaboration.

2.2 The Infiltration of Biotechnology into the Pharmaceutical Industry

As a result of advancements in biotechnology and its adoption in the pharmaceutical industry, the search for new drugs is becoming more scientific. With a traditional focus on organic chemistry, the pharmaceutical industry was devastated by the introduction of biotechnology as a tool to identify therapeutic targets and, subsequently, to design and test drugs for these targets. Over time, however, as Hamilton (2001) details, significant technical and strategic complementarities have emerged, creating an industry where there are three dominant types of players – research institutes, dedicated biotechnology firms (DBFs –

Teitelman, 1989), and traditional, large pharmaceutical companies. Each type of industry player possesses unique skills and capabilities that spawn the complementary nature of the industry and create an impetus for collaboration. The following diagram signifies the types of firms in the industry and the definitive capabilities associated with each.

Diagram 2.1 Industry Players



The "biopharmaceutical industry" (Hamilton, 2001) is very much an environment conducive to the development and conglomeration of complementary skills and resources. The

large pharmaceutical firms are particularly adept at taking a developed therapeutic and bringing it to market. By contrast, research institutions, including universities, are versed at conducting basic and applied research, yielding candidates for development. Dedicated biotechnology firms, or DBFs, play an intermediary role, usually assessing the potential of university discoveries and developing university findings to the point of clinical evaluation or, in very rare instances, readiness for market.

2.2.1 Collaboration in the Biopharmaceutical Industry

Collaboration in drug design has long been a feature of the pharmaceutical industry, even before the introduction of biotechnology. It has always been centred on acquiring access to new and innovative knowledge. For example, in the time of Japanese industrialization, Texan Professor Jackson Foster played an influential role in bringing the Japanese discovery of fermenting amino acids to American industry (Bud, 1993). As it is practised today, international collaboration in biotechnology sees nations such as Australia outsourcing the later stages of drug development to places like the United States of America. While much of the international collaboration is still geared toward accessing novel knowledge, it is also attributed to the extreme costs of drug development[3].

Early on in the formulation of the biopharmaceutical industry, collaboration resulted from the recognition that there were few scientists knowledgeable in the area of biotechnology. The discoveries of recombinant DNA and the process of creating monoclonal antibodies were made in the U.S.A. and Britain, respectively. Therefore, tapping into these technologies meant forming an alliance with those scientists possessing the requisite knowledge for employing the technologies[4]. When looking at the first ten to fifteen years in the field, biotechnology can only be analyzed "in terms of naturally excludable knowledge held by a small initial group of discoverers, their co-workers, and others who learned the knowledge from working at the

[3] The process of bringing a drug from discovery to market is estimated to be between US$100 million and US$250 million (Powell, 1996).
[4] This statement portrays a particularly marginalized view of the university scientists, where in fact, the key scientists were also keen to establish collaborations with parties capable of developing new discoveries, in the hope of reaping some of the profits associated with developing new findings.

bench-science level with those possessing the requisite know-how" (Zucker & Darby, 1996, cited in Zucker, Darby, & Brewer, 1998, p291).

2.2.2 Methodological Change in the Pharmaceutical Industry

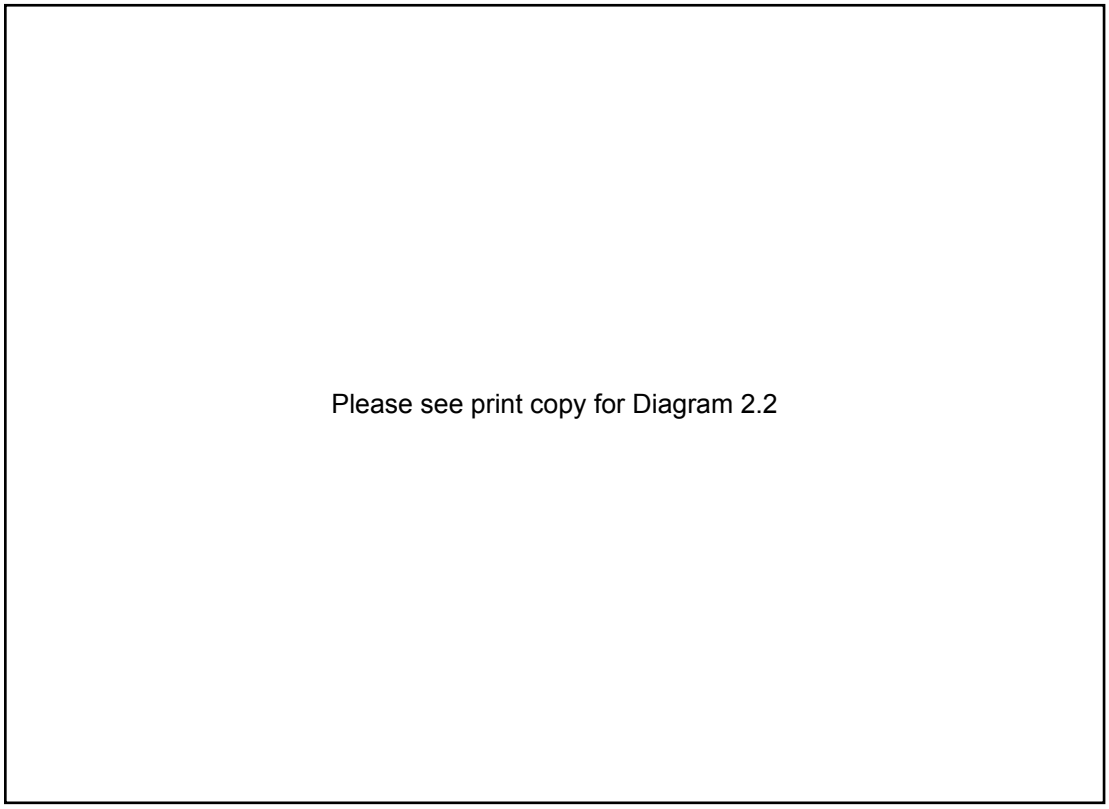
The infiltration of biotechnology into the pharmaceutical industry brought new screening techniques (Henderson, Orsenigo, & Pisano, 1999) and methods of fermentation (Primrose, 1987). Access to these techniques initially required collaborating with the scientists who knew how to perform them. The pharmaceutical industry was traditionally based on random screening techniques for therapeutics. Although there was considerable tacit knowledge and explicit routines involved in such processes, it was limited by the fact that the testing of potential drugs typically took place within animal models (Henderson, Orsenigo, & Pisano, 1999). Biotechnology has allowed for the production and purification of proteins associated with diseases. Therapeutic candidates can now be tested against these proteins in specific assays (rather than animals), thus providing more precise information about activity. With the techniques of random screening, it was often the case that drug companies did not know exactly how the drug worked, only that it worked. For example, it is not known how the drug thalidomide works[5]. Through the practice of biotechnology, scientists can begin with a target disease and, with the knowledge about that disease and the function of the proteins implicated in it, develop a drug to effectively target the disease. This process is known as rational drug design.

As Primrose (1987) notes, "[m]uch of biotechnology centers around the large-scale cultivation (10- 500,000 l[liters]) of microbes for the production of cells themselves, e.g. biomass, or the production of useful metabolites and proteins" (p49). The methods of extracting,

[5] Thalidomide has recently re-entered the market for the treatment of leprosy, cancer, and human immunodeficiency virus (HIV) after being proven to have severe toxicity in the early 1960s. Indeed, it was originally prescribed for the treatment of nausea and morning sickness in pregnant women, until it was shown to cause alarming birth defects in their children. The discovery of the drug resulted from random screening processes, which were ineffective in both identifying how the drug worked and how toxic it was (WHO/LEP, 2003). Following this disaster, amendments were passed in the United States in 1962 that established regulatory controls over the testing of drug candidates and introduced proof-of-efficacy for approval of new drugs (Henderson, Orsengio, & Pisano, 1999).

purifying, and fermenting proteins made possible by biotechnology have allowed for the production of enzymes, proteins, and other substances on a significantly large scale. As a result, enzymes can now be crystallized into a stable state, which can be studied to determine the functionality of the enzyme itself and the efficacy of compounds against the enzyme. According to Henderson, Orsenigo, and Pisano (1999), the application of biotechnology in the pharmaceutical industry originally followed two distinct technical trajectories that have now merged to make the practice of biotechnology the leading process of drug production. Diagram 2.2 demonstrates these trajectories and their merger.

Diagram 2.2 Biotechnical Trajectories



Source: Henderson, Orsenigo, and Pisano (1999, p283, Figure 7.1)

The cases presented in this thesis make use of the advances in biotechnology in varying ways. The first case is premised on the search for new therapeutics that are derived from marine

microbes. Scientists in this case have made use of biotechnology through fermenting the microbes and growing them on a large scale, identifying the chemicals found in the microbes, and testing them in assays for efficacy against different diseases. The second case employs biotechnology through extracting an HIV enzyme, integrase, from the human body, purifying it, and creating testing assays from it. This second case, along with cases three and four use rational drug design to develop drugs. Similar to case two, the third case uses rational drug design and biotechnology in the areas of isolating and purifying the target enzyme, and attempting to elucidate the three-dimensional structure of the enzyme through x-ray crystallography[6]. The fourth case makes use of advances in science by extracting plant cells from the red clover plant and synthesizing the chemistry produced by these cells in the scientists quest for new therapeutics. Much of the science used in these alliances is so advanced that one team of scientists cannot be expected to have the requisite breadth of knowledge or to know all the necessary techniques required to develop a drug. As such, collaboration with other scientists is necessary.

2.2.3 The Rise of DBFs and University-Industry Collaboration

After the spread, adoption, and adaptation of the discoveries of the 70s and 80s, the birthrate of new, small research and development organizations devoted to the magnum opus of biotechnology increased in an astounding fashion. Much of the hype surrounding biotechnology came not only from the possibilities accorded to the new forms of technology, but also from the reception that the firms claiming to operate in biotechnology received from financial markets. Genetech, established in April, 1976 by Herbert Boyer, was the first dedicated biotechnology firm (DBF) to go public, doing so in October, 1980 (Bud, 1993; Elkington, 1985). Some $60

[6] X-ray crystallography, or diffraction analysis, is a technique aimed at high-resolution structural analyses of a protein. It is used to provide the "…underlying native protein structure that will be the target for specific change, bring into focus those regions of the macromolecule [the protein] that can tolerate change in a structural sense, or provide grounds for desired changes through recombinant DNA techniques. Subsequentlly, crystallography is the tool that allows the genetic engineer to examine the altered polypeptides or protein and see directly the structural consequences of the changes he has introduced" (McPherson, 1995, p170).

billion were invested in biotechnology over the course of the next decade and a half (*The Economist*, 1994).

With the arrival of the multitude of new companies and the great financial interest in the area, the traditional pharmaceutical industry metamorphosed into the biopharmaceutical industry. According to Powell (1996), a new premium was placed on innovation. This stemmed from the combination of various factors, including competition from less expensive generic drugs, more sophisticated biotech products, and cost-effectiveness pressures from health-care providers. While the timeframe for drug development in pharmaceuticals ranged from seven to eleven years, biotech had proven instances of bringing new medicines to market in four years (Powell, Smith, & Koput-Doerr, 1996).

The redefinition of the industry spawned new forms of interaction. Guided by the new premium on innovation, collaborative engagements ensued between the large pharmaceutical firms and the emerging biotech organizations. In the late 1970's, Eli Lilly, the pharmaceutical leader in the insulin segment of the industry, took out a licence on its key product from a biotech organization less than three years old (Bud, 1993). Since that time, many large, traditional pharmaceutical firms have jumped on a bandwagon of outsourcing research and development to small biotechnology firms. "Firms such as Ciba-Geigy, Glaxo, Lilly, and Roche each have more than twenty collaborative ventures with biotechs – a recognition that no matter how large their budgets, R&D can no longer be done internally" (Powell, 1996, p204). The premium on innovation that was responsible for the restructuring of the industry impelled the pharmaceutical giants to tap into the entrepreneurial spirit of the young dedicated biotechnology firms. In addition, the pharmaceutical giants were seeking facilitated access to the DBFs' knowledge bases and ties with university scientists.

Fulfilling their intermediary role, the dedicated biotechnology firms had formed tight links with the key scientists in the field of biotechnology. These key university scientists, or "star" scientists as they are referred to by Zucker, Darby, and Armstrong (1998, 2002), were, and continue to be, renowned for their academic prestige and usually have a host of research projects and publications in specific biotechnology niches. Some of these links were fortified by

the fact that a portion of the DBFs owed their very existence to star university scientists, who were starting small research and development organizations dedicated to the niche in which the scientists and their core group of researchers specialized. These DBFs were formed with two intentions: to make the university scientists more attractive collaborators (Hamilton, 2001) and to ensure that the university scientists' discoveries were put on the pathway to development, thus creating the potential for substantial monetary rewards. Over the years, the founding scientists have remained connected to the firms either via consultancy, research grants, or as members of scientific advisory boards[7]. As Powell (1996) notes,

> [m]ost biotech firms have been started by scientists, with the assistance of either venture capitalists, law firms specializing in high tech, or ex-pharmaceutical executives. Because their focus was on science, and a firm's reputation was tied to its R&D prowess, the scientists 'contracted out' many of the financial and managerial aspects of the business. An organizational model developed in which biotech firms possessed an 'open architecture', a fluid structure in which some of the key functions were provided by 'outsiders' and key projects were pursued jointly with external collaborators (p200).

In contrast to the bureaucratic cultures of the large pharmaceutical firms that despised risk[8], the new biotechnology firms had, and still do have, scientists from a variety of disciplines, thus furnishing the necessary scientific knowledge to allow for the absorption of new knowledge from collaboration with university scientists[9]. In addition, the DBFs possessed the requisite technical know-how to identify and evaluate novel drug candidates. The technology-driven cultures of the dedicated biotechnology firms provided a close match to the environments in which academics comfortably operated (Hamilton, 2001).

Government also had a hand in priming the environment to make the biopharmaceutical industry a context conducive to collaboration, specifically for instances of cooperation between

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[7] While this practice has proved to be an economically valuable endeavour for many university scientists, it has also created a considerable amount of debate over the scientists' conflict of interest (where the research results could be forced in order to reap monetary benefits). In addition, the phenomenon of university-industry collaboration, in general, has also prompted legal and ethical battles over who has the right to publish research results and what material can actually be published (cf Wells, 1999).

[8] Large pharmaceutical organizations have been criticized for their resistance to biotechnology and their inclination to make low-risk improvements to existing drugs, rather than opting for new and innovative medicines (Powell, 1996).

[9] See Cohen and Levinthal (1989, 1990) for a detailed explanation of absorptive capacity, which is essentially the necessary knowledge base for understanding and deciphering the knowledge gathered from an external source. The evidence attesting to similarities in knowledge bases between university staff and industry scientists is drawn from Deeds (2001), who utilizes the number of papers co-authored by university staff and industry practitioners as a proxy of absorptive capacity.

universities and DBFs[10]. Lucas (2001) observes that policy makers have tried to connect "sites of knowledge production with sites of commercial innovation by creating financial incentives and organizational structures to promote research collaboration between universities and firms" (p1). In Australia, the government introduced the 150% Tax Concession Scheme and the Grants for Industry Research and Development (GIRD) Scheme, which provided a catalyst for collaboration between industry and academia (National Board of Employment, Education and Training, 1993, pxv).

In the United States, Congress passed the Bayh-Dole Act in 1980. This piece of legislation was designed to remove the restrictions on licensing, creating a uniform patent policy across federal agencies and giving universities the privilege of maintaining ownership of patents that arise from federal research grants. The hope was that university ownership of intellectual property would induce the commercialization of new technologies, and elevate entrepreneurial activity and economic development (Siegel et al, 2003). Mowery et al (2001), however, present evidence that suggests "…the Bayh-Dole Act itself has had little impact on the content of academic research" (p100), noting that, "…it is a fallacy to think of U.S. university research as traditionally 'basic' and conducted with no attention to practical objectives" (p101). Henderson, Orsenigo, and Pisano (1999) suggest that it was the passage of Public Law 98-620 in 1984[11] that provided additional leeway for universities in the kinds of inventions that they could own and their right to assign property rights to other parties. The passage of this law provided additional impetus for collaborations between university and industry in the United States.

[10] Etzkowitz and Leydesdorff (1997) offer a triple helix model of public, private, and academic relationships focused on the capitalization of knowledge. Their work provides a more in-depth account of the role of government in innovation. The basis of their theory is that the intersection between academia, state, and industry is best represented as a spiral movement in which the different institutions serve distinct functions in the production and transfer of knowledge.

[11] This law amended the Bayh-Dole Act, allowing contractors to receive patent royalties, laboratories to make decisions regarding licensing, private companies of any size to obtain exclusive licensing, the retention of some invention titles by laboratories run by nonprofits and universities, and "the Government to retain the right to a worldwide, nonexclusive, irrevocable, paid license to pratice the invention elected by the management and operating contractor" (The Environment Technology Commercialization Center, 2003).

The various players in the industry, in conjunction with the industry's profound heterogeneity, have raised the level of cooperation to unprecedented heights. Moreover, the structural heterogeneity of the industry is the cumulative product of the distinct strategies of the individual firms[12] (Kogut, Shan, & Walker, 1992). The technology at the heart of the industry, namely biotechnology, has surged, affecting all constituent firms. As a result, there is an obvious interdependency among these firms, whereby the products of a certain type of firm, for example, a dedicated biotechnology firm, are the goods demanded by another type of organization, for instance, a large pharmaceutical company. Similarly, the discoveries of the universities scientists are the intermediate good required by the dedicated biotechnology firms.

It is here, in the relationship between the university scientist and the DBF, that the following insight and analysis are couched. This thesis is dedicated to deciphering how knowledge is used and integrated in the relationships between these two patrons of the biopharmaceutical industry. With this agenda at the forefront of investigation, particular attention is paid to the knowledge structure in which the entities dwell, where their similarities and differences interlace, and where their similarities and differences unravel. The next section, therefore, intensifies the focus on collaboration between industry, specifically DBFs, and university, with an underlying emphasis on the pertinence of knowledge-based collaboration.

2.3 Knowledge-Based Collaboration as a Method of Value Cultivation

According to Chung, Singh, and Lee (2000), firms engage in interorganizational collaboration for a variety of reasons, including to solve market failure problems caused by asset specificity (Williamson, 1985), to buttress competitiveness (Porter & Fuller, 1986), and to absorb extramural knowledge (Hamel, Doz, & Prahalad, 1989; Kogut, 1988). In the case of the biopharmaceutical industry, collaboration between DBFs and universities is viewed as an extension of the reasoning put forward by Hamel, Doz, & Prahalad (1989) and Kogut (1988).

[12] It is important to note here that Powell and Brantley (1992) argue that many young, dedicated biotechnology firms lack the relevant managerial expertise to plot the strategic direction of their organizations.

University-industry collaboration is ventured with the intent of absorbing extramural knowledge, but central to this intent is the expectation that the extramural knowledge will *complement* what knowledge already exists internally. As Powell and Brantley (1992) suggest, "external ties should be viewed as complementary; that is, one agreement would serve as a means to enhance a configuration of skills and products that a firm is developing" (p373). Stated otherwise, "internal expertise and external collaboration are not substitutes for each other but complementary. Internal capability is indispensable in order to evaluate research done outside, while external collaboration provides access to 'news' and resources that cannot be generated internally" (Powell, 1996, p208).

2.3.1 University-Industry Alliances & Complementary Resources

I make the claim regarding the complementary nature of collaboration in the biopharmaceutical industry not only as an argument in alignment with the theories of other scholars[13], but also with careful consideration of other explanations for collaboration and their pertinence to the types of cooperation indicative of the investigative context. For example, the complementary resource conceptualization of collaboration differs significantly from that put forth by transaction cost scholars[14]. As Grant and Baden-Fuller (2000) note, "[t]ransaction cost analysis provides incisive analysis of the factors influencing the relative efficiencies of firms and markets in organizing economic activity. However, it is less successful in its analysis of interfirm collaboration: a characteristic feature of industrial organization in the advanced economies of the world" (p113).

Transaction cost economics suggests that collaboration is particularly avoided in cases of high asset-specificity and intensified risk (Williamson 1975, 1985). As Church and Ware (2000) contend, "[i]f the costs of writing complicated contracts and the inefficiencies associated with incomplete contracts – especially underinvestment in specific assets – are relatively large, the

[13] Shan and Hamilton (1991) attest to the logic of complementary resources as a motive for strategic alliance in the biotechnology industry.
[14] Powell (1996) also contests the appropriateness of applying the transaction cost explanation for collaboration to alliances in the area of biotechnology.

firm might want to consider internalizing the transaction" (p76). One lesson that has emerged from the biopharmaceutical industry is that the incumbent firms cannot neglect the need for or prosperity of collaboration[15]. The sheer vastness of the amount and types of knowledge necessary for discovering new drugs and bringing them to market makes it difficult for one organization to make the discovery-to-development journey on its own. In the case of collaboration between university and industry, assets may be specific to the collaborative project, transcending organizational boundaries, and intensified risk is routinely featured in all projects. The transaction cost explanation for collaboration simply does not suffice.

Perhaps this is due to the fact that not only are immense variations in types of knowledge required for bringing a drug to market, but the different mechanisms for collaboration in the area of biotechnology are numerous as well. While several scholars have commented on the types of collaborative relationships evident in the pursuit of drug development via biotechnology (cf Forrest & Martin, 1992; Powell, 1996), one body of work that serves to exemplify the range of cooperative endeavours is that expounded by Barley, Freeman, and Hybels (1992). Table 2.1 is a representation of their work.

Table 2.1 Types of Relationships

Please see print copy for Table 2.1

Source: Barley, Freeman, & Hybels (1992, p322, Table 12-2)

[15] Recall Powell's (1996) observation that with the infiltration of biotechnology into the pharmaceutical industry came recognition that R&D could not longer be conducted on a solely internal basis.

Clearly, potential collaborators have a number of different options for coordinating and governing the cooperative relationship. In-house capability, asset-specificity, and risk can be juggled in an array of different ways. Equity holdings, however, tops the list of mechanisms for collaboration, lending credibility to the transaction cost account of collaboration[16]. It is important to note, though, that the category of equity holdings represents only 23% of the collaborations. As the empirical work of Colombo and Delmastro (2001) demonstrates, when collaborations are premised on a technology component, bilateral contractual modes are more likely than equity joint ventures or unilateral quasi-market agreements. Their work also shows that where there is an overlap in technological specialization between the collaborators, non-equity bilateral forms of governance are more frequently utilized.

The other 77 per cent of the biopharmaceutical industry's collaborations call for an alternative explanation of collaboration. The categories of "licensing agreement", "development agreement", "research agreement", and "R&D agreement" particularly demand an alternative explanation. In these types of collaboration, organizations (dedicated biotechnology firms and universities) are providing each other with valuable information pertaining to key assets, if not sharing the assets entirely, coordinating decisions and actions, and in many cases, collectively facing benefits and risks[17]. They do so with the ambitions of a) testing and expanding competencies (Powell 1996) and b) employing a "design for purpose" approach to set university discoveries on a pathway for development (and simultaneously offer DBFs material for development).

The relationships are recursive and their complementary nature is based on the knowledge possessed by each of the collaborating parties. Collaborations between dedicated biotechnology firms and university scientists are premised on reaping value from amalgamating the knowledge bases of the collaborative constituents. These types of collaborations can only be conceptualized as endeavours to absorb extramural knowledge, but a key factor is that this

[16] The theory of transaction costs states that when collaboration is necessary, firms may need to protect themselves from the opportunistic behaviour of others by retaining control via equity positions (Church & Ware, 2000).
[17] See Appendix A for a table detailing types of collaboration, amount of interdependency between the organizations engaged in collaboration, and the durability of the different types of collaboration.

knowledge must complement internal knowledge bases and aid in the process of creating value from knowledge.

2.3.2 The Collaborative Knowledge Environment

The knowledge environment that hosts this type of collaboration is characterized by an array of structural elements. The knowledge exists in the minds of geographically dispersed scientists, but the mechanisms for combining the knowledge and the forces that impinge upon the combinatory process are multifarious. Santos (2003) defines this knowledge environment as being:

- dependent on the set of technologies, tools, and work practices that translate scientific knowledge into useful products,
- influenced by the institutional and organizational mechanisms for the production of new knowledge and for the training of professionals,
- influenced by the institutionalized mechanisms for the dissemination of new and existing knowledge,
- affected by the regulatory systems that determine the possibilities of appropriating new knowledge and by the interactions with other fields of scientific knowledge, and,
- affected by the sources of funding and incentive mechanisms for the production of new knowledge and innovation.

These forces have served to segment the biopharmaceutical industry into communities of technological similarity, while simultaneously creating common value schemes across the range of communities.

Indeed, as Powell (1996) suggests, "[t]he cross-traffic between universities and biotech companies is so extensive and reciprocal that it is appropriate to consider them part of a

common technological community[18]" (p200). It would be quite far-reaching, though, to describe all collaborations in biotechnology between university and industry as indicative of one giant technology community, particularly considering the earlier argument that biotechnology represents a range of technologies premised on the design for purpose credo. Instead, technological communities are formed around university scientists, DBFs, and specific collaborative projects between the two entities that solve similar problems.

Each technological community can be thought of as a knowledge value collective (KVC), in which producers and users of knowledge pursue common goals, but to diverse ends (Rogers & Bozeman, 2001). Each collective contains knowledge value alliances (KVA)[19], originated via a knowledge compact (a formal alliance agreement) and terminated when the resources once devoted to the alliance are diverted or depleted (ibid). A knowledge value collective is a group of alliances or research teams pursuing similar goals, whereas a knowledge value alliance is one collaboration.

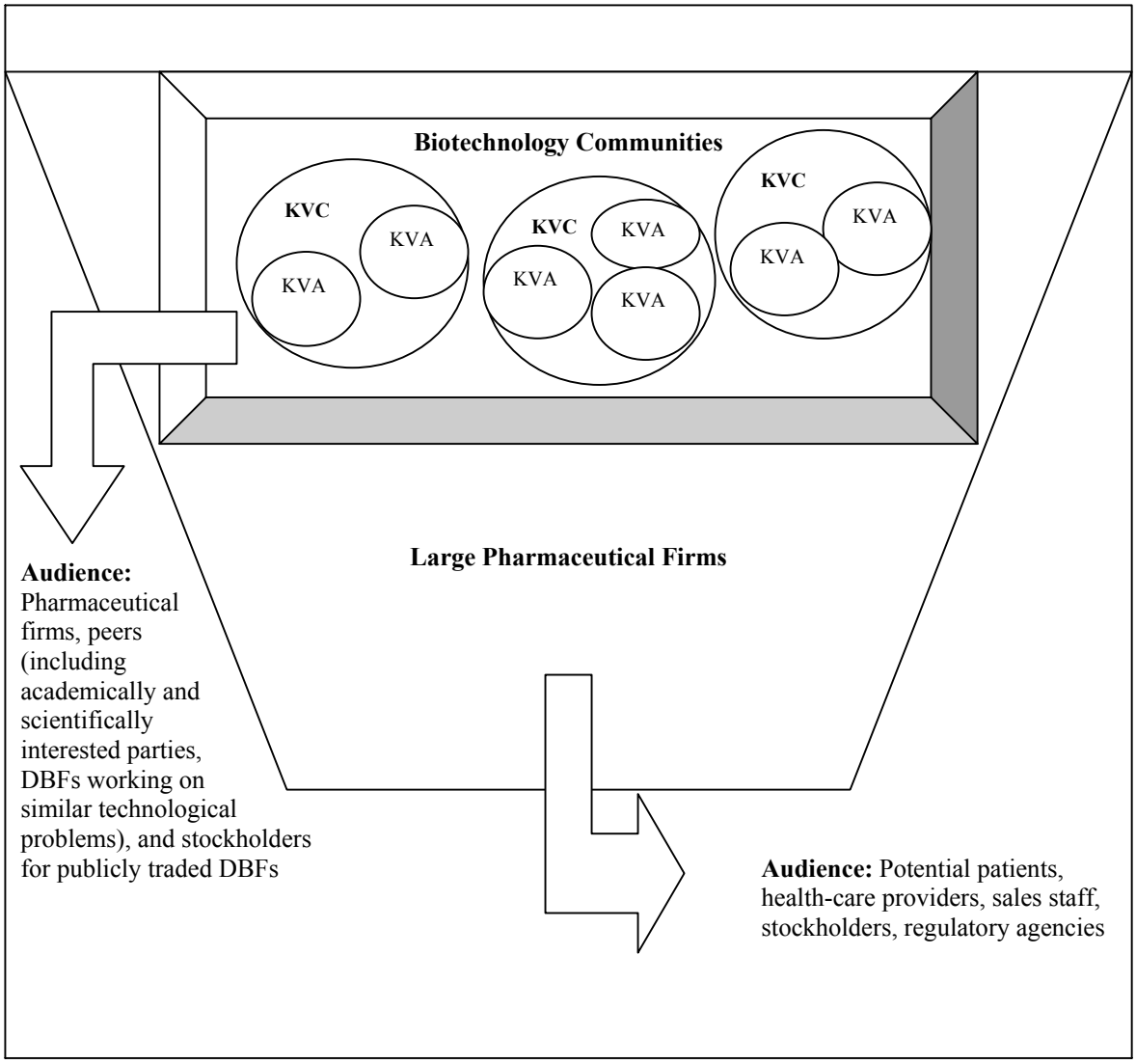
Distinct levels of competition and tension exist within each particular collective. Members of the KVC speak to a common audience and, therefore, they compete for the audience's attention and respect. Often times, members of the collective will be in a race to see who can solve a particular problem first. There is a certain amount of tension or anxiety that

[18] A technological community, as defined by Rappa and Debackere (1992), is a geographically or organizationally dispersed group of scientists and engineers working on an interrelated set of technological problems

[19] The concept of a knowledge value alliance is favoured in this research agenda over the commonly used project unit of analysis to allow for the view that collaborations can often be comprised of several overlapping and concurrent projects. In addition, as Rogers and Bozeman (2001) proffer, "one major difference between project evaluation foci and a focus on knowledge value interactions is that the latter gives consideration to persons who are not scientists or engineers and who are not officially parts of projects or work groups (but who nonetheless affect the interpretation and use of scientific work)" (p26). As it will be argued in chapter four, there are people outside of the collaboration who will inevitably have an affect on the interpretation and use of the work produced within the collaboration. As a preview, these people include members of the other collaborations who stand to be displaced by another collaboration's success in solving a technological problem, the venture capitalist and government funding agencies that support university-industry collaborations, and the ill patients who may potentially benefit if a knowledge value alliance is successful in solving a particular problem (and developing a novel therapeutic). What should also be noted, here, however, is that Rogers and Bozeman (2001) also contend that the concept of a KVA should be employed to focus on the sustained interactions and relations between collaborative parties rather than the outputs resulting from those interactions. And, clearly, as evidenced in this chapter, there is considerable focus placed on the output of the collaboration. Therefore, the concept of a knowledge value alliance, as used in this thesis, complies with Rogers and Bozeman (2001) prescription for its use in some ways, but not in others.

rests within the technological community because of this. Those working on a problem, knowing that there are other researchers attempting the same or a very similar problem are always looking over their shoulder, attempting to gauge their position in the race. The researchers who succeed at solving the problem first stand to acquire a significant amount of social prestige, or value. There is also a tremendous amount of economic value that is expected to come from the resolution of the problem. The value on offer exists within a determinate space of the biopharmaceutical industry – a space characterized by the following diagram.

Diagram 2.3 The Biopharmaceutical Industry



The lists of audiences depicted in the diagram are not intended to be all-inclusive, but rather to portray the audience differentials between a specific biotechnology community and the large pharmaceutical firms. Each KVC will have its own distinct audience, consisting of different members of the biotechnology communities' audience groups displayed in the diagram. Within a KVC, scientists from the DBFs write research papers, university scientists publish the results of research conducted with or on behalf of DBFs[20], and the scientists from the two types of organizations co-author papers. They speak to a common audience. The publication of research results serves both as a signifier of the technological field that defines the collective and as a deterrent to other firms and collaborations pursuing similar technological problems. Powell (1996) states that, "pressures to publish, and thus reveal the latest advances, are intense in this field. Thus discovery is open to all to evaluate" (p211).

Differences do exist, however, between the members of a KVC. There are particular audience segments of a collective that are more pertinent to one portion of the community than the other. For instance, university scientists are typically ignorant of or indifferent to the interests of the DBF's stockholders. Another difference comes in the form of risk. Dedicated biotechnology firms, although much more willing to engage in risky endeavours than large pharmaceutical firms, are more risk adverse than university scientists. In the case in which the DBF fronts the funding for scientific and technological quests in a collaborative endeavour, the sharing of risk is not evenly split between the firm and the university scientists. If the project fails, the money invested in the project becomes a sunk cost for the DBF, whereas, the university scientists can usually write the failure off as an impossible scientific task, still having gained funding for trying. Or, if another team solves the problem first, the DBF again stands to lose (in monetary terms) considerably more than the university scientists.

[20] One important aspect pertaining to the publication of research results by university scientists, and even DBF scientists for that matter, is that publication usually does not occur until patents have been procured on any valuable knowledge resulting from the research.

2.3.3 The Value on Offer in the Knowledge Environment

Nonetheless, the systemic factors of the biopharmaceutical knowledge environment identified by Santos (2003) have created a convergence in value between the two constituents of the various knowledge value collectives. The possible rewards from collaboration between university and industry are embodied in both social and economic value.

A social value results from the interdependency of the collaborators. The mechanisms for the production and dissemination of new knowledge, the regulatory systems that determine the possibilities of appropriating new knowledge (such as technology transfer and patent laws), and the interactions with other fields of scientific knowledge (such as the need to combine both chemistry and microbiology in the search for new drugs), have generated a need for DBFs to work with star scientists from universities. Zucker, Darby, and Armstrong (1998, 2002) provide evidence that research collaborations between DBFs and university star scientists have a significant impact on firm performance. Reciprocally, relationships between university scientists and industrial firms, namely DBFs, have created a new identity among university ranks. The "scientist-entrepreneur" is now increasingly seen as a title or description that is both legitimate and desirable (Powell, 1996). Here, the sources of funding and incentive mechanisms for the production of new knowledge and innovation have facilitated the link between DBFs and university scientists. The incumbents of the biotechnology community need each other in a socio-structural way. They bestow value upon one another through their collaborative relationships.

Value is also manifested in a vision of a final product that is expected to result from the collaborative endeavour. It is anticipated that this product will confer economic value. The product may be a lead compound that has superior activity when put into a biological assay, it may be the crystallization of the structure of an enzyme, or it may be intellectual property in the form of a microbial library that offers future testing potential for the DBF. The end product may be a multitude of things, but it is the systemic dependency "on the set of technologies, tools, and

work practices that translate scientific knowledge into useful products" (Santos, 2003, p688) that makes economic value a possibility. Value stems from this process of translation.

The translation process requires that the collaboration be built upon the appropriate knowledge bases to solve a specific technological problem that, in turn, can be used in the pursuit of commercial value. University-industry collaboration, then, is seen as a process of value cultivation, through which value accrues via the combination of complementary know-how. The basic scientific know-how (usually a possession of the university scientist) and the development know-how (typically residing among the staff members of the DBF) are integrated and the "set of technologies, tools, and work practices that translate scientific knowledge into useful products" (Santos, 2003, p688) is the integrating factor.

The potential of knowledge produced in a university setting is made evident by the numerous success stories detailing the transformation of a university scientist's discovery into a valuable, novel product[21]. In the form of a discovery, the new knowledge produced in a university setting offers less value than if it were to be developed to the point of commercialization. In such a form, it is little more than a "potential" product to the general public[22] (which in the case of a drug would be the ill patients standing to benefit from the product once commercialized). The failure to at least attempt to capitalize on this potential, though, is an opportunity cost. Parker and Zilberman (1993) recognize a narrowing gap between scientific knowledge and application of this knowledge through technological innovation, and comment, that "failure to get technology out of the laboratory constitutes a social loss" (p100).

The possibility of mitigating this loss lies in the combination of knowledge bases through collaboration and the deployment of the necessary tools, technology, and work practices to bring the collaborative goals to fruition. Most academic discoveries in biotechnology are the product of intelligent scientific minds that do not have the experience or know-how to develop

[21] The value of discoveries made in a university setting is also confirmed by University Technology Transfer Offices (UTTO). Incidentally, UTTOs are accused of overvaluing technology to the extent of dissuading potential industry partners to collaborate. They tend to focus on the potential of the discovery with little consideration of market uncertainty or the incalculability of actually converting the discovery into a commercial product (Seigel et al, 2003).

[22] University discoveries may, however, be viewed as products in the eyes of industry partners or technology transfer offices.

discoveries to the point of commercial viability. Complementary to the scientific brilliance of the university scientist is the know-how to develop the discovery, which exists among the ranks of many DBFs (provided the industrial scientists have enough knowledge of the scientific area pertaining to the discovery). The synthesis of complementary knowledge bases by way of a strategic alliance between the two entities, namely the university scientists and the DBF, is a cogent response to the need to create value by taking a discovery through the process of development.

Penrose (1959), Richardson (1972), and Teece (1986)[23] suggest that resource complementarity and co-specialized assets are catalysts for collaboration that allow for value creation from pooled resources. "By engaging in strategic alliances, firms expect to enhance their performance and create value" (Chung, Singh, & Lee, 2000, p3). Under the auspices of complementary collaboration, a firm seeks a partner with the know-how and capabilities that it lacks. In return for the provision of the necessary competencies, the seeking firm will provide capabilities that the providing firm lacks. If executed properly, the collaboration can amount to a mutually rewarding, valuable endeavour.

There are several factors involved in extracting the value from a complementary collaborative relationship. These factors are: selecting partners with appropriate knowledge bases, sufficiently aligning project goals, allocating tasks, coming to agreement on the value of the anticipated outcome(s), and marshalling the right tools, technologies, and work practices to get the job done. Devising a way to effectively exercise all of these requirements is a schematic task. The next section offers a preliminary discussion on this exercise. It is a discussion that is resumed in the later chapters of this dissertation.

[23] As noted in Langlois and Robertson (1995), these authors all use different terminology. Penrose (1959) was probably the first to suggest viewing the firm as a "pool of resources". Richardson, building on the work of Penrose, introduced the concept of capabilities, which referred to the knowledge, skills, and experience of a firm. In addition, Richardson contended that "activities need not be *complementary*, that is synergistically related; rather, they must be *similar*" (cited in Langlois & Robetson, 1995, p15 – emphasis their own).

2.4 Biotechnology Bingo

Knowledge-based collaboration, even if executed properly, using the relevant and necessary resources to their fullest potential, does not always yield the desired result. Collaborators aim to design a product that meets specific functional demands. This functionality has an estimated and anticipated value. The output of the collaboration, then, is mentally comprehensible in terms of function and value, but requires articulation of both social worlds and task production to reach fruition (Fujimura, 1987). The articulation process, like the output, is mentally conceivable, but faces the possibility of never coming to fruition.

> Researchers usually do not know what will be necessary to carry their research to some point of completion before they begin the research. But they do know that they need, in addition to a novel problem, some basic elements including interested audiences who will publish or use their work, sponsors or clients who will provide funding, institutional infrastructure to support their work, skilled staff to assist in getting the work done, and basic research materials and equipment and their suppliers (Fujimura, 1996, p187).

The possibility of not obtaining desired results is a collective derivative of the uncertainty associated with the desired product (the output) and the tools, technologies, and work practices used to bring the product into existence (the input).

2.4.1 The Uncertainty of the Design Process

As Clark (1985) states, the design itself is the search for understanding about what an object is and what it ought to be in terms of the context in which it must function. There are, then, unpredictable factors associated with both the output itself and the design process for producing the output. The precariousness of both the output and the input is partially attributable to the novelty of the desired output. Typically, the collaboration is based on highly experimental scientific principles, and the anticipated outcome is hoped to make a significant contribution to both science and medicine. In the instance in which the collaboration is centred on drug-design, the aim is to produce a novel therapeutic, offering new mechanisms for killing bacteria and/or viruses (in addition to the other things that drugs do). As a result of this novelty, there are several unanswered, critical considerations to be taken into account in the design

process. Some of these aspects are the toxicity of the drug, the metabolic life of the drug's chemistry, and the capital requirements for producing the drug on a mass scale. With few precedents to follow, it is difficult to say if the underlying science is even achievable, which creates a considerable amount of uncertainty and complexity for the designers.

Not all collaborations between dedicated biotechnology firms and university scientists in the biopharmaceutical industry are geared toward drug development, though. Some collaborative endeavours are aimed at producing viable leads for further scientific analysis. Other cooperative engagements may be focused on mapping out the basic science of a disease and coming up with hypotheses for what impact biotechnology can have in terms of curing or alleviating the ailment. Nevertheless, uncertainty and complexity still prevail. There is a multitude of forms of collaboration (as identified in section 2.3) and the collaborative agendas among the large number of collaborations in existence today are enormously varied, but in spite of the variations in form and direction, all collaborations between university and industry in biotechnology face a certain amount of complexity and uncertainty because of their novel aims and their footing in highly experimental science.

2.4.2 The Structure of the Design Process

Although it cannot be entirely avoided, the uncertainty and complexity resulting from the novelty and revolutionary scientific nature of the desired output, can be mitigated by carefully designing the processes of collaboration. The design process can be constructed in a manner that acknowledges the interdependencies in the relationship and attentively selects the appropriate tools, technologies, and work practices to facilitate these interdependencies. As Baldwin and Clark (2000) argue,

> [w]hen the [output's] complexity exceeds one mind's capacity…assigning all the tasks to one person will not be feasible and the design tasks must then be divided up among different people, meaning that the design process must allow for *connections* between them. In practice, designers whose [design specifications] are dependent must be aware of and must communicate with one another. They must transfer and share relevant knowledge and coordinate their final [design] selections. Should they not do so, the design effort as a whole could well fail (p46 – emphasis their own).

In instances of collaboration in high-technology industries, like the biopharmaceutical industry, however, total interdependency between the collaborators cannot be expected. The inherent complexity of biotechnology, in conjunction with the distinct areas of knowledge necessary to produce the desired result, provide evidence that the collaborative agenda is a compilation of multiple tasks to be performed by key specialists. While some of these tasks may be closely interwoven, others will be disparate. The design of the desired project, then, is not just an interdependent one, but also a modular one[24].

Modularity, according to Baldwin and Clark (1997), is the breaking up of product or processes into subsystems[25], or modules, which allows designers and producers increased flexibility in their endeavours. The subdivision of particular systems serves to reduce the complexity of the system. It follows the premise of decomposability proffered by Simon (1962). As Garud, Kumaraswamy, and Langlois (2003) note, if a project is organized in a non-decomposable fashion, "…then interdependency will be high, meaning that each development team will need to constantly receive and use information about what all the other development teams are doing" (p2). To the extent that drug development involves an array of different scientific disciplines – which could include synthetic chemistry, computational chemistry, microbiology, virology, glyco-biochemistry, marine microbiology, oncology, in addition to many other types of science – it is feasible to decompose a drug development project into specific silos, each centred on the practice of a specific type of science that contributes to the process of drug development. This type of decomposition requires a division of scientific or innovative labour.

Some scholars, however, see the process of innovation as much more interdependent than this. For example, Leonard and Sensiper (1998) discuss three specific types of tacit knowledge

[24] I use Baldwin and Clark's (2000) definition of modularity as a construct based on structures that has two subsidiary connotations, including interdependence within and independence across modules and the use of modular division to reduce complexity.

[25] Modularity has been generally applied to products rather than processes. This can be split into the application of modularity to product design and product use. For example, Baldwin and Clark (1997, 2000) apply the concept to modular product designs in the computer hardware industry. Langlois and Robertson (1992) focus on modularity in use by consumers of the products of the microcomputer and stereo component industries. While these two examples are not the limit of the application of modularity to products, this type of application is more widespread than the application used here – modularity in processes.

that need to be managed in the process of innovation. These include overlapping specific knowledge, collective knowledge, and guiding knowledge. The overlapping specific knowledge represents the common ground between collaborative parties. Collective knowledge and guiding knowledge are task specific, being co-developed and providing a common vision for partners of an interdependent task such as innovation. Taking these three breeds of knowledge as a sweeping explanation of the types of tacit knowledge used in innovation does not specifically address the complementary nature of the collaborative relationships inherent to the biopharmaceutical industry, particularly the relationships between university scientists and their industrial counterparts. Nor does it provide much room for a division of labour among innovators.

The knowledge employed in collaborations between university scientists and dedicated biotechnology firms is both vast (coming from a multitude of sources) and technologically specific. Despite the specificity, the vastness precludes a complete knowledge overlap between collaborative partners. In the practice of biotechnology, scientists start with a focused target. Knowing, then, what they are aiming for, scientists "attempt to 'design' a drug to affect either a target or a biological interaction they wish to alter" (Powell, 1996, p152). As a collaborative effort between university scientists and industrial practitioners, this process requires, at the very minimum, knowledge of the target, knowledge of the chemical engineering necessary to modify a molecule to have a desired effect on the target, knowledge relevant to designing drugs (including knowledge of toxicity indicators and metabolic rates), measures for testing the effect of the drug on the target, and tools and technologies to further develop a promising lead. There are clearly areas here that will overlap and areas that are mutually exclusive. For instance, knowledge of chemical engineering may overlap with knowing how to design drugs. Knowledge of the target, however, is a completely different knowledge base than knowing how to design drugs.

Interdependency and modularity coexist in this ambiance of knowledge overlap and simultaneous knowledge distance[26]. Where the overlap exists, the exchange of knowledge can occur freely because both parties have the necessary knowledge bases to understand one another (Dougherty, 1992), although different levels in states of knowing may be the result[27]. Interdependency dwells here. On the other hand, the knowledge distance that created the commitment to complementary knowledge collaboration calls for modular segmentation, where design rules would be required to ensure the knowledge bases and the work performed using these bases are in alignment. A gap between the knowledge of the two parties is the fuel for the collaboration and the distinct knowledge bases of the collaborators, if combined effectively, are the competitive weapon in the production battle. Without an ability to bridge the gap, however, the collaborative goals will not be met.

The desired output that is the goal of the alliance provides for some coordination. Following March and Simon (1958), Galbraith (1988) notes that "[a]s the uncertainty of the [alliance's] task increases, coordination increasingly takes place by specifying outputs, goals or targets" (p119). To the extent that alliance partners are different in knowledge bases and independent social organizations in their own right, coordination via the specification of desired outputs will not be enough to align the work in the collaboration. As such, additional tools for alignment are necessary.

2.4.3 Using Modularity for Alignment

Bridging the gap, according to Baldwin and Clark (1997), requires three interrelated elements of visible information, that simultaneously serve to create and guide many different and potentially rewarding avenues of independent exploration and to decentralize control over the entire collaborative agenda (Baldwin & Clark 2000). Visible design information is the set of rules that link together different "black boxes", or modules. Following Baldwin and Clark

[26] Knowledge distance is the degree to which the knowledge possessed by the source and the knowledge possessed by the recipient varies. In the context of R&D collaboration, knowledge transfer may prove to be particularly difficult because the R&D environments of the source and the recipient may by quite dissimilar (Cummings & Teng, 2003).

[27] This concept is discussed in more detail in the next chapter.

(2000), modules are units whose structural elements are intensely connected among themselves and weakly connected to elements in other units. Within modules, there are hidden design rules, or hidden information, that affect the work within the module, but not beyond the module. The hidden design rules "…can be changed without triggering any changes in distant parts of the system. They invite tinkering, which can lead to improvements in performance[28]" (Baldwin & Clark, 2000, p75). The visible information is "visible" to everyone in the alliance. The hidden information is "visible" only to task level scientists – it is "hidden" from those beyond a specific task domain. The visible information elements correspond with the three stages of the design process identified by Baldwin and Clark (2000). The following chart summarizes this correspondence.

Table 2.2 Elements and Stages of the Design Process

Visible Information Elements	Stages of Design Process
An architecture-specifying what modules will be part of the system and what their functions will be	Establishing design rules to guide performance throughout the entire collaboration
Interfaces – describing in detail how the modules will interact, including how they will connect and communicate	Performing parallel work on hidden modules, where decisions do not effect the design beyond the local module
Standards – defining testing procedures to assess modules' conformity to design rules	Testing and integrating the work done in each module

[28] Modularity is typically used to define objects, not processes. One example is the IBM PC introduced in 1981 (Langlois and Robertson, 1992). Unlike the previously bundled portable computers, the new PC "was a system, not an appliance: it was an incomplete package, an open box ready for expansion, reconfiguration, and continual upgrading" (Langlois & Robertson, 1992, p307). Different components of the PC were manufactured by companies other than IBM. These companies followed their own hidden design rules in product development and production, which allowed them to be innovative in their designs. The compatability between what they produced and the IBM components came from the S-100 open architecture standard, or the visible design rule. In this thesis, I use the concept of modularity in a design process, rather than in application to a product. The collaboration and its specified design process is a system. Tasks in a collaboration are likened to the components of a modular product. Visible design rules link these tasks, but the work within each task domain is guided by hidden design rules. As such, hidden information does not mean that scientists in a task domain beyond the one where a specific set of hidden rules are in place *cannot* have access or know this information. It means that they do not *need* to know this information for the purposes of their own task work.

Through the implementation of these design rules, the knowledge alliance, consisting of university scientists and employees from a DBF, pursues and controls various unique "mini-projects" that support the collaborative agenda. These so called "mini-projects" are modules that are defined by the architecture, interconnected by the interfaces, and amalgamated and validated by the standards that compose the design rules. Production of knowledge is occurring within each module, but articulation, or the work needed to consolidate the various levels of production, is necessary to generate the desired output (Fujimura, 1987).

This process of articulation, which is required for the team to be successful in its collaborative agenda, encompasses four essential factors. These requirements include having a common purpose, establishing goals and individual and collective accountability, agreeing on a common approach to getting the work done, and having complementary skills (Katzenbach & Smith, 1992, cited in Sharifi & Pawar, 2002, p659). The design rules identified above – the architecture, interfaces, and standards – allow for the realization of these requirements. A common purpose is established in the "architecture" through defining collective goals and delegating the tasks necessary to accomplish these goals to the individuals best equipped to complete the tasks. Although the individual work is performed within each module according to hidden design parameters, individual modules are held accountable by the "standards". Approaches to getting the work done, then, are agreed upon within modules (by hidden design parameters) and across modules (by the visible design rules). And, the complementary skills are connected by the "interfaces".

The architecture of a university-industry collaboration in biotechnology can be thought of as a knowledge architecture. Borrowing from Sanchez (1999), a knowledge architecture is defined as the collective knowledge held by the members of the collaboration and the mechanisms through which people with the individual knowledge bases interact in the collaborative process of creating the desired output. Knowledge architectures are arranged and initiated in a variety of ways. A university scientist may approach a DBF with a newfound discovery, hoping for funding and complementary knowledge in advancing the discovery through the stages of development. Alternatively, a DBF may have knowledge relating to a

particular target, for instance, an enzyme, and may actively seek out university scientists with the knowledge required for developing a drug capable of altering the target. There is no set procedure for creating a knowledge architecture.

Similarly, the technologies, tools, and work practices that fashion the standards and interfaces of the design rules are unique to each collaboration. For example, the process of rational drug design, explained by McPherson (1995)[29], is a standard that is used in many collaborations in biotechnology aimed at drug development. It is used in three of the four cases presented in this thesis. It is, however, not the only type of standard available to collaborating scientists. The other case presented in this report uses a simple specification of "novelty and activity" as a standard, having developed a technology for capturing and testing marine microbes to determine their novelty and activity against types of cancer specifically and other diseases more generally. Collaborators can draw from an array of different mechanisms as standards and interfaces to suit the collaborative agenda. They do so, however, with no guarantee that the mechanisms which they choose to serve as interfaces and standards will achieve the intended effect.

2.4.4 The Luck of the Draw

Therefore, as mentioned previously, the input required to fulfill the goals of a collaborative arrangement is mentally conceivable, but is not easily translated into a realized method of design. The design process is often plagued by a considerable amount of uncertainty, which can be attributed to the fact that those seeking a complementary knowledge collaborator must not only find the most appropriate party with the pertinent knowledge and skills, but the collaboration must also be premised on specific design rules that effectively split the necessary

[29] McPherson (1995) explains the process of rational drug design as being inclusive of the following steps: determining the structure of an enzyme, analyzing the structure-function, modeling the protein (or enzyme) with candidate drug molecules, and diffusing molecules into protein crystals or co-crystallizing the drug molecule and protein. He notes that, "[t]his idea of rational drug design based on a clear picture of the target's structure, is not particularly novel or clever; what is exciting and intriguing is that we are now in a position to actually apply the procedure in practice. We now have the analytical tools at our disposal to determine at the atomic level of detail the structures of enzymes and their active and regulatory sites, and to exploit this knowledge in the design of new and potentially useful drugs" (p164).

tasks among the collaborators, and provide a means for amalgamating the knowledge developed in each module. Compounding the uncertainty is the fact that the scientific experiments being attempted in a collaborative endeavour may not be achievable, but this cannot be determined without actually attempting the experiment(s).

Furthermore, Baldwin and Clark (2003, p168) contend that design rules "…support efficient, repeated plays for valuable market positions", and these plays can occur in rapid sequence or in parallel, with the structure created by modularity reducing complexity, enabling parallel work, and permitting adaptive responses to market developments. I, however, contend that the design rules exemplified in some of the cases presented in this thesis actually restrict rather than permit adaptation to market developments.

These design rules call for methodical processes of drug discovery and development with minimal room for maneuvering in response to market development. In fact, in the way that some of the design rules are applied in the cases studied for this investigation, there is no room at all for response to market developments. Once a development in the market becomes apparent, such as the resolution of a specific technological problem, or say the crystallization of an enzyme, collaborators who are working in the area in which the development is made face the possibility of having to terminate the project or abandon the current design process. Those scientists successful at solving the problem first typically acquire the rights to all work in the area specific to the problem. This is accomplished either via patents or the hoarding of intellectual property to avoid appropriation of the knowledge related to their findings. Rational drug design in particular does not allow for the consideration of the potential influences, contingencies, and effects seen in an open system, such as the impact on a group of researchers of the resolution of the technological problem specific to their research agenda (prior to their ability to do so). Some of these collaborative endeavours are essentially races with the competition to solve a technological problem, and while a rule or strategy for behaviour in a race that does not take the competition into account may get one to the finish line, it will not ensure that one gets to the finish line first.

Conceding the uncertainties and contingencies associated with university-industry collaborations in biotechnology, it is possible to argue that there is a certain amount of skill and luck involved in getting the design process right. With this in mind, the process of designing a collaboration between university and industry in biotechnology can be likened to a game of Bingo.

2.4.5 The Game

The Bingo card represents the knowledge architecture of the collaboration, in which a match between a specific task and the appropriate person, team, or firm to accomplish the task scores a mark. And, as any devoted Bingo player knows, the key to a winning Bingo system is card selection[30]. The word "TASKS" written across the top of the card, where the word "BINGO" would normally appear, signifies the various tasks that belong to the knowledge architecture[31]. The numbers on the bingo card are the teams of scientists that could potentially perform the necessary and desired tasks. Each box, then, where there is an intersection between tasks and people, is a module. The gridlines on the Bingo card represent the interfaces and the forces that arrange the marks into a line (diagonal or horizontal) can be matched to the standards of the design rules. Playing the game involves drawing the appropriate people to perform the required tasks, developing the appropriate interfaces, and utilizing the relevant standards to make the marks appear in a row. Like the real game of Bingo, the play continues until a player claims bingo.

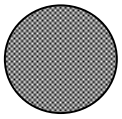
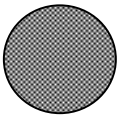
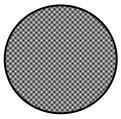
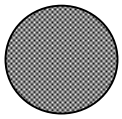
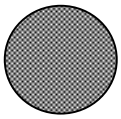
Diagram 2.4 represents a winning Biotechnology Bingo card. For entertainment purposes, I have added the numbers that were not selected and the numbers' signature bingo calls (or the

[30] Joseph E. Granville, the well-known mathematician who has devoted his career to developing stock market strategies, has also spent some time studying Bingo. He contends that there are crucial relationships between winning numbers and the master board. Following Blanchard (2003), Granville's strategy for Bingo suggests that one can greatly improve his or her chances of winning by selecting a card having different digit endings because the laws of probability predict different digit endings. According to Granville (1977), there are two general strategies to embrace in the game of Bingo: the management of money that a player spends and the selection of cards to be played.

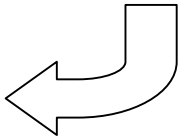
[31] This concept is similar to "the arc of work" concept introduced by Strauss (1985), which refers to the totality of tasks arrayed both sequentially and simultaneously along the course of a project.

saying generally associated with a given number in a game of Bingo) as detailed on Online Bingo (2003).

Diagram 2.4 The Biotechnology Bingo Card

T	A	S	K	S
 Appropriate team of scientists to perform task "T"	5 Man Alive	34 Ask For More	82 Straight On Through	53 Stuck In The Tree
26 Pick And Mix	 Appropriate team of scientists to perform task "A"	39 Steps	45 Halfway There	85 Staying Alive
9 Doctor's Orders	89 Nearly There	 Free cell -- firm's own knowledge and capabilities required for task "S"	71 Bang On The Drum	58 Make Them Wait
75 Strive And Strive	23 Thee And Me	6 Tom's Tricks	 Appropriate team of scientists to perform task "K"	81 Stop And Run
79 One More Time	4 Knock At The Door	13 Unlucky For Some	7 Lucky	 Appropriate team of scientists to perform task "S"

BINGO
(Desired Output)



There are inherent similarities between the real Bingo game and Biotechnology Bingo. As with the real game of Bingo, the centre space usually represents a free space that counts towards winning. In the game of Biotechnology Bingo, the free space represents one of the collaborator's own knowledge bases and that knowledge counts towards the final product. In the real game of Bingo, there is a minimum buy-in. Similarly, in the Biotechnology Bingo game, there is a minimum buy-in, known as the costs of engaging in research and development. In the traditional game of Bingo, players know what they need to win, but they may not be able to get what they need. Biotechnology Bingo also features players that know what they need to win, but often times the players cannot find what they need (in terms of concrete task definitions, appropriate people capable of performing the tasks, or molecules that do what the scientists want them to do[32]). The randomness of the numbers being called in a normal game of Bingo represents the chances that the architect, the research manager of a DBF or a university scientist, will be able to attract and convince the most suitable collaborators to participate in the alliance, although there are admittedly distinct differences in levels of probability here[33].

There are also differences between the traditional game of Bingo and Biotechnology Bingo. Unlike the real game of Bingo, the tasks change with each new knowledge architecture, whereas in the real game of Bingo, "BINGO" is always featured on the top of every card. In the real game of Bingo, players can win by getting diagonal, horizontal, or vertical lines. In the game of Biotechnology Bingo, players can only win by getting diagonal or horizontal lines, as a vertical line would be just a series of similar tasks performed by different people.

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[32] There is, in fact, no guarantee that the molecules produced in a collaborative endeavour will be suitable or potent enough to appropriately act against a given disease. Indeed, as a repondent from one of the cases suggested, the uncertainties of the project include whether or not the compounds will be "sufficient to afford the biological outcomes that [they] all want" (von Itzstein, 29 September 2003 – personal interview). Similarly, Callon (1986) provides an account of nature being difficult to align with other elements of a research project. In Callon's account, scallop larvae proved to be one of the most formidable obstacles in carrying out a research project to restock a particular body of water with scallops. The molecules in an alliance between university-industry may well be as equally stubborn.

[33] The numbers being called in a game of Bingo are called in the purest form of randomness. The chances of attracting suitable and willing collaborators, while there is a certain amount of chance involved in this process, is not purely random. There is a general pool of scientists from which the most suitable would be selected. Architects can look at potential collaborators' track records to determine their suitability. Because there is a mutual need among collaborators for a potential partner's resources, the chances of the suitable collaborator agreeing to collaborate are also less than random.

Like Joseph E. Granville, the noted mathematician who has studied Bingo and highlighted the key patterns in the game (Online Bingo, 2003), I also seek to identify patterns in the game of Biotechnology Bingo. I am specifically looking for patterns in the standards and interfaces that exist in the different types of collaboration between university and industry in biotechnology. In addition, I am attempting to explain the knowledge architecture of these cooperative endeavours, including the production and use of knowledge within this architecture. I embark on this journey with the aim of further reducing the complexity of the collaborative process. While a modular design can reduce a certain amount of the complexity that is part of the process, getting the design process right also requires skill (and a bit of luck). An explanation and devolution of common interfaces and standards, and the identification of a pattern in the production and use of knowledge, therefore, can only serve to clarify the intricacies of collaboration.

2.5 Conclusion

Biotechnology is not just the utilization of specific technologies to produce drugs, but rather the deployment of particular designs with the purpose of deriving a desired outcome. The term biotechnology may allow university scientists and industrial practitioners to capitalize on the claim of practising "biotechnology", but the merits of their claims are measured by their engagement in design for purpose activities. These types of activities are prevalent in the biopharmaceutical industry, where knowledge alliances between university scientists and industrial players serve to cultivate value. Value cultivation occurs via the integration of the knowledge bases that belong to the collaborative constituents and the application of the relevant knowledge in tasks that are indicative of the design and connected to the purpose.

While there are several guidelines for amalgamating the knowledge bases, including both articulation and design rules, the process still faces inherent uncertainty. This uncertainty is the product of both the scientific nature of collaborations in biotechnology and the inevitable choice of which tools, technologies, and work practices will best serve the agenda. Getting it right is

not a common occurrence. Indeed, there are a number of dedicated biotechnology firms that have spent the last five years trying to "get it right". And, as more and more university scientists enter the collaborative arena, either willingly or by force, they bring new uncertainties, which result from their inexperience in the game.

As Fujimura (1987) contends, there are "[m]any different kinds of worlds involved in constructing scientific knowledge in numerous and diverse ways" (p168). Aligning these worlds and the knowledge produced within them to achieve a desired purpose is not an easy feat. While the veterans of the game may have their own individual prescriptions for success, it remains to be seen whether these prescriptions are always applicable. I argue here that, as with the game of Bingo, there is the necessity for both luck and skill. The luck cannot be controlled. The skill, however, can and it involves an understanding of the rules of the game, and, as will be seen in the forthcoming chapters, the ability to manipulate these rules to one's advantage.

The next chapters explore these types of alliances in more detail. From there, I proceed to identifying my role as researcher in the game. After doing so, I offer the findings from three case studies to illustrate the theory which I have developed to represent the collaborative experience. In addition, I use the data from the case studies to investigate the interfaces and standards inherent in the design mechanisms of the various collaborations, and develop a rich explanation of the rules of Biotechnology Bingo.

Chapter 3 Characterizing Knowledge & the Modular Structure

> "In everyday language we use the word *knowledge*…We speak of having acquired *much knowledge*, and we also speak of *having knowledge* of this or that. But if *knowledge* means both what we know and our state of knowing it, we might have to say that we *have knowledge of much knowledge*" (Machlup, 1980, p27 – emphasis added).

The purpose of this chapter is to characterize the knowledge architecture in terms of the knowledge, people, and processes that comprise it, and the modular arrangement through which these architectural constituents are operationalized. I begin by discussing the nature of knowledge. Utilizing two philosophical depictions of knowledge, this section offers a perspective on knowledge that attempts to incorporate objectivity, subjectivity, and relativism. In some of the current management literature, knowledge is often discussed as if it were a newly discovered, cutting-edge construct. In reality, though, knowledge has been the subject of scrutiny for many centuries, with scholars from an array of disciplines analyzing it. Developing a discourse on knowledge without consideration of the work of these scholars is inadequate. The findings and perspectives of philosophers, sociologists of knowledge, philologists, and cognitive theorists must be taken into account.

In an attempt to integrate the work of these various types of theorists, I provide detailed accounts of two forms of knowledge in this chapter – a mobile form that can move among people and a private form that is encapsulated in the mind of an individual. Typically, management theorists *assume* that knowledge can indeed move, or "flow" as it is often termed in the literature, from individual to individual, across contexts, and between minds. Alterations

to the original bit of knowledge do occur, but these scholars contend that knowledge retains enough of its original form and that individual recipients are like-minded enough to interpret the intended meaning of the information, transforming the message into a form that resembles the original bit of knowledge. Furthermore, many management theorists assume that movement is necessary to coordinate work activities and knowledge processes.

Invoking the findings of current analysis of cognition and the discourse from the sociology of knowledge, however, it becomes apparent that the notion of knowledge movement and its ability to remain stable in the process is not an agreed upon conceptualization. Some management researchers have embraced this point of ambiguity in assessing knowledge exchange. For example, Kim and Nelson (2000) postulate a perspective in which the transfer of knowledge is seen as the re-creation of a source's knowledge in the recipient (cited in Cummings & Teng, 2003), where information flows, but the formulation of knowledge is dependent upon the recipient. Knowledge, however, is still seen as something that has to move between various parties in order to make work processes effective.

While I do not attempt to solve the unanswered questions on the nature of knowledge in this thesis, I do seek to address how the movement of knowledge occurs and/or possibly varies under different structures. Knowledge movement can be seen as unproblematic, a process in which knowledge is stable and objective, or problematic, being centred on interpretation and subjective elements. The structure through which knowledge movement is operationalized will enhance or hinder the ability of and need for knowledge to move, in addition to influencing its stability in the process. For example, if the structural arrangement of an alliance dictates that people with quite different scientific backgrounds and languages work in the same vicinity, then knowledge mobility and particularly stability may well be problematic because of the probability that mutual interpretation of information will be less likely than if the people were similar in terms of scientific background and language.

Therefore, when addressing knowledge it is essential to also discuss the people, processes, and structure that impinge upon its character. Using the concept of modularity, it can be shown that the people that make up a knowledge architecture do not necessarily have to be

fully informed about the knowledge and practices of their fellow collaborators. When there is a modular structure in place, the knowledge processes that occur within the architecture do not have to be fully disclosed to all those participating in the collaboration, as long as there is a workable connection (an interface) between the members of the alliance. Modularity as a structure follows the purpose of limiting knowledge exchange to the levels of absolute necessity and viability.

This chapter first examines two approaches to knowledge: one that is inherently philosophical and sociological, and one that begins with a biological account of knowledge and moves into philosophical and sociological frameworks. The conclusion of the first section of this chapter is that knowledge processes, including knowledge use and movement, are best described by adopting elements of both views. In the second section of this chapter, the two views of knowledge are unified under the auspices of a modular structure. The third section discusses how technological problems are solved in a knowledge architecture.

3.1 Migratory Knowledge & Ingrained Knowledge

Philosophy and the sociology of knowledge provide several distinct characterizations of knowledge that specify where knowledge resides, its defining qualities, and its relationship with reality. Two of these characterizations, as depicted in von Grogh and Roos (1996a), provide varying degrees of focus on the individual and his or her relationship with knowledge. Different terminologies and theories are aligned in the depiction of these two views. Table 3.1 provides clarification of the different terminologies used in the discussion of knowledge.

Table 3.1 Knowledge Terminology

View One	View Two
Migratory Knowledge	Ingrained Knowledge
Cognitivist Theory (Varela, 1992)	Autopoiesis Theory (Maturana & Varela, 1980)
Representationist Approach (von Grogh & Roos, 1996a)	Anti-Representationist Approach (von Krogh & Roos, 1996a)

The first view postulates the existence of mobile knowledge, or knowledge that "flows" and remains stable in form and content. Knowledge is seen as migratory. Based on this, knowledge is created and utilized under the auspices of bounded universalism[34] and, therefore, can be passed from one person to another. Objectivity and the existence of a pre-given world play central roles in the transfer of knowledge. The alternative view of knowledge, informed by autopoiesis theory (Maturana & Varela, 1980), maintains that knowledge is re-created from person to person; it is ingrained in an individual's mind. The concept of knowledge flows has no grounding. Individualized cognition and the lack of existence of a pre-given world fortify this perspective.

In presenting these two views, I engage Machlup's (1980) distinction between knowledge as "that which is known" and knowledge as "a state of knowing". The cognitivist perspective is harmonized with the view that knowledge is "that which is known". I aim to show that this view paints a picture of knowledge that is mobile and stable in meaning. Knowledge is "migratory". The second view of knowledge lends its introspective quality to assessing knowledge as a private state of knowing, or as knowledge that is "ingrained" in the mind of the individual.

[34] I use the term "bounded universalism" to represent the fashionable understanding of knowledge as a commodity available to all members of a group with common beliefs, worldly lenses, and understandings. Knowledge is universal to a given group of individuals. This concept is discussed in more depth later in the chapter when referring to Rescher's (1997) conceptualization of first person plural groups.

The following section presents both views. Due to the anticipated novelty of these concepts to the reader, both perspectives are covered in detail. In addition and probably more importantly, knowledge is a central construct in this thesis, with considerable attention being paid to knowledge processes. Because knowledge is a central tenet in these processes, a comprehensive conceptualization of knowledge is required. The first portion synthesizes the literatures on the cognitivist and representationist approaches to knowledge. The concepts presented in the literature are buttressed with theories from the discourses on the philosophy and sociology of knowledge. The second section outlines the basic principles of autopoiesis theory and the anti-representationist paradigm. While this perspective remains a less frequently explored and adopted concept than its cognitivist cousin, it is nonetheless convincing. Each view is given equal credibility in the line up for creating a unified view.

3.1.1 From the Cognitivist Perspective to Migratory Knowledge

The nature of knowledge is couched in a variety of forms, all specifically geared to fit the way that it is employed. Drucker (1993) defines knowledge as *the* basic economic resource. His definition emphasizes the role of knowledge in post-industrialist society. Many authors adhere to this scheme of a broad conceptualization of knowledge. Faulkner (1994) defines knowledge as a composite of knowledge, expertise, skills, and information, intimately related to questions of who possesses it and how specific groups access and make use of it. Rothwell, Prescott, and Taylor (1998) refer to knowledge capital, including elements such as institutional memory, the talent pool, and creativity. These definitions, in line with many others, are reflective of what Varela (1992) has called the "cognitivist" perspective and which Aadne, von Krogh, and Roos (1996) have termed "representationism".

The representationist paradigm follows the premise established by cognitive science in the 1950s and has provided the foundation for organizational theory and strategic management developed by such seminal writers as Simon, March, and Cyert (von Krogh & Roos, 1996). As von Krogh and Roos (1996) suggest, the cognitivist framework is the background of such constructs as expertise, skills, and information (Faulkner, 1994), core competencies (Hamel &

Prahalad, 1990), distinctive competencies (Andrews, 1971; Ansoff, 1965; Hofer & Schendel, 1978), core capabilities (Stalk, Evans & Schulman, 1992), underlying capabilities (Williams, 1992), capability for effective search (Nelson, 1982), and valuable heuristic processes (Shoemaker, 1990). These concepts are used interchangeably with the concepts of know-how and knowledge. Arguably, activities such as acquiring expertise and skills, developing competence, and building heuristics play a pivotal role in learning, and indeed, in the accumulation of knowledge. These activities also, however, shed light on the notion that the *object* of the knowledge in question determines the reality of *what is known.*

For something to be known, its existence and the validity of its intellection must be acknowledged by one or more individuals. As a philosophical reflection, this statement follows the fastidious[35] contention of the philosophers of knowledge that the consignment of knowledge status to a claim depends solely on the claim's ability to be verified by others. It engages the metaphysical realists' assertion of an objective reality that can be witnessed and agreed upon by several individuals.

Aadne, von Krogh, and Roos (1996) explain that cognition is seen as a representative apprehension of the real world. "This implies that reality, be it objects, events, or states, resides outside the cognizing subject, and is objectively given for everyone. Further, in multiple ways the mind has the ability to create inner representations, which more or less correspond to this given reality. Thus, knowledge can be seen as a mirror of reality" (p11). Inquiry guided by the representationist perspective presupposes that knowledge is centred on objective reality. In sharing or transferring knowledge, individuals rely on their cognitive capacities to develop parallel or congruent interpretations of the real world.

3.1.1.1 Objectivity

The process of creating this shared sense of reality is called "objectivation of knowledge" (Berger, 1967; Schutz & Luckmann, 1973; von Krogh & Roos, 1996), or the process of

[35] The term "fastidious philosophers of knowledge" is taken from Machlup (1980) and signifies those philosophers of knowledge who distrust all direct knowledge if it cannot be objectively verified by others (p99).

objectifying subjective experience to create a standardized perception of reality; a process entailing the social construction of knowledge (Latour & Woolgar, 1979; Semin & Gergen, 1990). Objective knowledge is contrasted with personal, unique perceptions and understandings, or subjective knowledge (Berger & Luckmann, 1967; Hayek, 1945, 1975; Habermas, 1984). The two can be contrasted but not compared. It is "confirmed that [one] cannot compare subjective knowledge (in B) with objective knowledge, except in judging B's beliefs from the point of view of [ones' own] beliefs" (Polanyi, 1958, p306). It is possible, though, to use subjective understanding as the beginning or basis for further refinement into objective knowledge.

An understanding of the process of objectivation is imperative because, as demonstrated in this thesis, this process is fundamental in the production and function of knowledge in a modular structure. This process entails turning the subjective understanding and the individual application of knowledge into a tangible "thing" (Latour, 1987)[36] that all members of the collaboration can access and validate.

As John Locke's representative realist approach to knowledge states, the subjective is the individual formulation of ideas relative to the external environment. "Ideas are [the] ways of subjectively reacting to the influences which bodies bring to bear on [the individual]" (Gallagher, 1982, p73). These ideas, as they are held subjectively by individuals, are used in the production of knowledge, including techniques, artifacts, and knowledge claims in general, that, once produced, are verified in relation to other individuals' ideas. This act of refinement relies on information processing capabilities and the unanimous depiction of the reality or object under scrutiny. Objectivity is achieved via this act of refinement.

Rescher (1997) confers two modes of objectivity, which serve both in the process of objectifying knowledge and as requirements for objectivity. The first principle is object-oriented, relating to whether a claim deals with a concretely realized object in the real world,

[36] Latour (1987) defines 'things' as new objects, tools, or techniques that, through a process of routinization and reification, become a 'black box', whereby their inner workings are no longer a matter of controversy or inquiry. He offers examples such as polonium, an ultracentrifuge, and a can opener.

which different individuals can physically observe. The second mode relates to the appropriateness of a claim of knowledge, "addressing the question of whether a claim is impersonally and generically cogent rather than personal and idiosyncratic (Rescher, 1997, p4). Impersonal claims to knowledge based on physicality facilitate objectivation. Objectivity, then, is a form of human cognition that is attained through intersubjective agreement on something that is known.

Objectivation and objectivity never connote the abandonment of human perspective. Indeed, in the valuation of the discoveries made in the collaborations presented in this thesis, the use of one's own perspective plays a vital role. As Polanyi (1958) notes, the real and objective truth still exist, but as a rational human being, one cannot avoid having a personal lens through which cognitive perceptions of truth and reality are filtered.

> …if [one] decided[s] to examine the universe objectively in the sense of paying equal attention to portions of equal mass, this would result in a lifelong preoccupation with interstellar dust, relieved only at brief intervals by a survey of incandescent masses of hydrogen…It goes without saying that no one – scientists included – looks at the universe this way, whatever lip-service is given to 'objectivity'… For, as [a] human being, [one] must inevitably see the universe from the centre lying within [oneself] and speak about it in terms of a human language shaped by the exigencies of human intercourse. Any attempt rigorously to eliminate [the] human perspective from [the] picture of the world must lead to absurdity (Polanyi, 1958, p3).

In the case of objectivity, several individuals try to negotiate common lenses for the filtration of reality.

The filtration lens adopted by a group of individuals, while it still resonates with personal experience and subjectivity, becomes a universal standard for the group, resulting in bounded universalism. This standard can be anything from a technique for mining marine microbes, which can later be cultured and tested as therapeutics for disease, or beliefs in the value of such activity and the objects that it produces. As Polanyi (1958) argues, "the act of knowing includes an appraisal; and this personal coefficient, which shapes all factual knowledge, bridges in doing so the disjunction between subjectivity and objectivity. It implies the claim that man can transcend his own subjectivity by striving passionately to fulfill his personal obligations to universal standards" (p17). Grene (1974) maintains that our sensemaking is fundamentally dependent on the universal standards and common beliefs that we hold; "…we make sense of

experience only through subsumption under universals, and that such universals act as standards for the evaluation of experience, or rather that we act in submission to these standards as judges of experience…" (p169). The goal then becomes to adopt the universal standards or judgmental criteria of a like-minded group. Through this process, objectivity is seen as an achievement.

Adopting and committing to the universal standards of a group with similar circumstances and similar beliefs allows personal knowledge to be objectified through rationality and generality. While generality suggests that what is objectively so holds independently of personal idiosyncrasies, rationality implies that different people in similar circumstances judge cognitive representations without significant variation between the various interpretations (Rescher, 1997). Environment and context, then, play a critical role in establishing objectivity.

As Fuller (2002) states, the universalists' policy of attributing differences in the cognitive dispositions of disparate reference groups in relation to context, understanding, or other cognitive impositions "explains away differences between what the observer would ideally expect and what the alien [the outsider] actually does as the result of mitigating circumstances in the [outsider's] environment" (p92). Where one group might find extreme value in researching the efficacy of chemicals produced by marine microbes against disease, another group might believe that a more viable route is to explore plant cells and their ability to inhibit and affect specific diseases. It is the environment, though, that creates these differences in value.

The scientists who believe in the significance of marine microbes for drug discovery have built their careers on such a belief, and have been rewarded with prestige and economic returns for their efforts in substantiating their beliefs. They have recruited other scientists to work in an institution premised on the belief that "marine microbes are the next great source of drug discovery" (Nereus Pharmaceuticals, 2002). The same holds for the scientists who concentrate on the role of plant cells in fighting disease. Their beliefs are validated in a given context by producing "things" (Latour, 1987) that are tangible to other scientists (general to them) and rational (make sense to the other scientists in accordance with their own subjective knowledge).

Together, the principles of generality and rationality create a platform for the metamorphosis of personal knowledge into objective knowledge via the common confidence in the reliability of knowledge held by a group. Knowledge becomes relative and enslaved to bounded universalism. The crucial component in the function is the group to which one seeks affiliation so that beliefs and standards can be shared.

Rescher (1997) speaks of the "first-person plural" (FPP) group and identifies two types of groups. The first affiliation group is the one an individual belongs to by destiny or fate – for example, a gender group or a racial group. The second sort of group is the one with which an individual chooses to identify. This type of group is representative of groups like academics or members of a political party. These groups represent the core of the bounded universalism that is intimately connected to objectivism. As the core radiates beyond one single group and different groups adopt similar standards, the universality that is a fundamental correlate of objectivism is strengthened. Cognitive objectivity results from postulating claims to knowledge with a concern for rationality and generality related to the universal standards of the predicated FPP group(s).

3.1.1.2 That Which Is Known

Using Machlup's (1980) definition of knowledge as "that which is known", it is possible to arrive deductively at the cognitivist interpretation of knowledge as it results from a series of facts or objects that are fiercely dependent on the values and techniques that are commonly held, communicated, and employed across a group of "knowledge seekers".

To view knowledge as "that which is known" is to rely on a combination of Aristotelian certainty and the representationist reflection of reality. Viewing knowledge in this manner demands an acknowledgement of the objects in the world as enduring objects and an appreciation of the human cognitive capacity to accurately and consistently interpret those objects. The role of facts in the relationship between the objective world and the cognitive understanding of it is centred on commonality, both between the two realms and between individuals in the cognitive realm.

Following Turner (1987), Fulop and Linstead (1999) explain the concept of facticity as a "presumption that individuals in social interactions share things in common" (p278). Through facticity (Berger, 1967; Turner, 1987; Ring, 1997) and conversational exchanges (Garfinkel, 1967; Fulop & Linstead, 1999), objectivation occurs, creating a realm of connectedness and shared meanings. *Objectivity is the collective validation of objects and techniques, and the social negotiation of beliefs.* That which is known is objective knowledge. It is knowledge that is held in common by a group of individuals. It is mobile across individuals and stable in meaning.

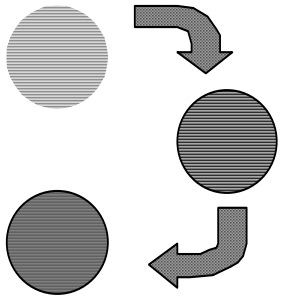
The representationist perspective of knowledge, then, as it draws from the basic premises of cognitive objectivity and the bounded universalism paradigm, adheres strictly to the assertion that knowledge is solely an interpretation of the objective artifacts and natural objects that are encountered. This paradigm allows for inquiries based on the premise that knowledge is a mirror of reality that becomes clearer through the creation of congruent interpretations. Perceptions of the world gain magnitude through consensus and, in the process, knowledge that originated in one becomes the belief of many. The tunnel sculptured by the cognitivist paradigm is supported by objectivation, merging personal judgment into the ranks of universal standards. The adherence to a cogntitivist framework supports the assertion that knowledge can indeed "flow" from one person to another and remain stable in the process. As summarized by Aadne, von Krogh, and Roos (1996), representationsim is based on five general assumptions about knowledge:

- Knowledge represents a pre-given world.
- Knowledge is believed to be objective.
- Knowledge results from information processing.
- Knowledge is transferable.
- And, knowledge enables problem solving.

The following figure provides a representation of the cognitivist perspective.

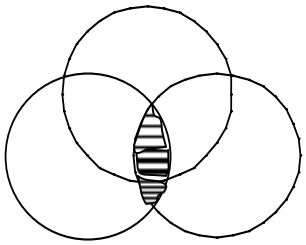
Diagram 3.1 The Cognitivist View of Knowledge

Figure A



This diagram represents the process of three individuals transferring knowledge. Each circle represents an individual. The arrows represent the transmission of information via conversation and other methods. The patterns in each circle, being different, symbolize the subjectivity of each individual. While not the same, the patterns are similar, which serves to represent the individuals' like-mindedness.

Figure B



This diagram represents the cognitivst interpretation of the result of the process depicted in Figure A. Each circle is indicative of an individual. The area intersecting all three circles is the shared understanding (between the individuals) *of that which is known* (on a particular topic or about an object). The three different patterns in the intersection represents the fact that the shared bit is collectively validated and socially negotiated.

3.1.2 From Autopoiesis Theory to Ingrained Knowledge

While the cognitivist paradigm is far-reaching and undoubtedly explanatory, there is another metasystemic (Beer, 1980) approach to the study of knowledge. Informed by neurobiology's observation that in cellular reproduction, cells reproduce themselves and simultaneously replicate their own capacity to reproduce (Maturana & Varela, 1980), autopoiesis theory has emerged as a general theory of systems, living, psychic, and social systems, all inherently self-referential (Varela, 1979; Luhmann, 1986, 1990; van Twist and Schaap, 1991; von Krogh, Roos, & Slocum, 1996)[37]. Autopoiesis theory, drawing from epistemology and biology, depicts cognition as both a function – the defining of a domain of interactions in which a cognitive system can act with relevance to the maintenance of itself – and a process – the actual inductive acting or behaving in this domain (Maturana and Varela,

[37] While much of the application of autopoiesis theory in the social sciences has been in social systems, I use the theory as Maturana and Varela (1980) prescribe it – as an interpretation of the individual as a system.

1980) – with the main premise being that cognition, and consequently its product, knowledge, are dependent upon human kind's classification as an "individual" living system.

At the heart of this theory is the observer, a living system that remains self-referential and circular in organization. The observer is capable of both description and cognition, which occur on a hierarchical scale, with description proceeding as a characterization of the conditions in which an object exists and cognition resulting from the establishment of a "meta-domain" in which observer and object are interrelated, but only in a phenomenological sense. Therefore, rather than speaking of a universal world where objects dwell and provide recourse for parallel interpretations (as is presupposed in the representationist perspective), the anti-representationist paradigm connotes self-referenced worlds (meta-domains), in which the object of knowledge is created in the descriptive domain of the observer.

Investigation informed by this paradigm focuses on the degree to which knowledge is reconstructed by its recipient, with time and history playing influential roles. Knowledge is not transmitted from one person or entity to another in its explicit or tacit forms. Instead, it is recognized that the capacity to know is reliant upon previous experiences and the temporal medium (past and present) as it is exclusively held in the cognitive domain of the observer. Maturana and Varela (1980) explicitly state that while the past does not participate in the inductive process of cognition itself as it occurs in the present, it serves as a deterministic function in the process of cognition because of the historical transformation of the nervous system that results from past experience and previous confrontation with the external environment. Cognition, then, is a recursive process that produces knowledge based on individual experiences.

3.1.2.1 The Role of Experience

Maturana and Varela (1980) highlight the relevance of spatio-temporal orientation to the cognitive function that exists as the dynamic, internal wiring of the system, namely the spatio-temporal configuration of afferent nerve cell activity. The reactions in the nervous system of the observer form a unidirectional ordering of experiences that result from whether or not the

collector areas and effector areas recognize the "perturbation" from the external environment (an experience). If the "perturbation" is recognized, the observer will biologically react in the same manner as the reaction to the initial experience that is recognized as synonymous to the current perturbation. If the experience is new, the observer will undergo an emotional reaction of uncertainty, which will reorganize the spatial relationship of the observer's afferent influences (the nerves that convey sensory information to the brain) so that next time, when the experience is encountered again, the collector and effector areas will have a predefined relationship[38], which will have a deterministic effect on the activity and behavior assumed by the observer. This explanation of the interconnectivity of the neural network of the system is representative of the neo-connectionist approach to cognition (Varela, 1992).

Cognition is not the recovery of a pre-given outer world (realism), nor is it the projection of a pre-given inner world (idealism). It is what Varela, Thompson, and Rosch (1991) term embodied action. Through this terminology, Varela, Thompson, and Rosch (1991) emphasize the link between perception and action, a bind that signifies the fundamental inseparability of sensory and motor processes in lived cognition. In this sense, knowledge is conjoined with action. Embarking on this pragmatic approach to knowledge, particularly employing the notions of Dewey, we see the amalgamation of knowledge and action creating a situation where "ideas are not privileged glimpses into transcendent standards; they are facets of […] *action*" (Gallagher, 1982, p189 – emphasis his own). This interpretation of knowledge accords with a convincing explanation of expertise, where an expert is seen as someone who is capable of doing the right thing at the right time (cf Dörner & Schölkopf, 1991).

Autopoiesis theory evokes a view of knowledge in which the object of knowledge becomes subservient to action and reality becomes the domain of individual descriptions. "There is no object of knowledge. To know is to be able to operate adequately in an individual or cooperative situation. [One] cannot speak about the substratum in which [one's] cognitive

[38] This concept can be linked to the notion of absorptive capacity á la Cohen and Levinthal (1990). Indeed, if one is to be able to "absorb" knowledge, he or she must have the appropriate nerve configurations to do so. That is, his or her brain must be adequately structured and the incoming data must be appropriately chocked to be recognized and made sense of within the mind.

behavior is given…This silence, however, does not mean that [one] fall[s] into solipsism…It means that [individuals], as thinking systems, live in a domain of descriptions…" (Maturana & Varela, 1980, p53). This is the domain where judgments are formulated. And, as Gallagher (1982) reasons in a pragmatic fashion, a judgment is true if the results of acting upon that judgment are "useful and beneficial", but a judgment is false if the activity predicated on that judgment proves to be disadvantageous.

Knowledge, as it is defined in reference to autopoiesis theory, is a product of the individual, a product that derives from experience and is inextricably linked to action. "Moreover, at the individual level, knowledge is not abstract but rather is embodied in the individual" (von Krogh, Roos, & Slocum, 1996, p163). It is descriptive conduct relative to the cognitive domain of the knower (Maturana & Varela, 1980). It is not the result of communication or social construction, but is the product of individual experience and response to external stimuli.

It must be stressed, however, that the embodiment of knowledge in the individual does not imply that it is identical with brain activity (MacKay, 1984). The individual living system has a consciousness that is essential for the process of cognition (Varela, Thompson, & Rosch, 1991). In a conscious state of mind, one does not merely react to perturbations from the external environment. Instead, "the ability to *evaluate and modify [one's] priorities in the light of experience* is one of the chief distinguishing characteristics of [one's] conscious agency…" (MacKay, 1984, p307 – emphasis his own). While conscious thinking and reflex mechanisms are both neurophysiological processes, they differ in that with conscious thinking, the chain of nervous interactions begin with a state of activity of the nervous system itself and with reflex mechanisms, the chain of nervous interactions begins with a state of activity at the sensory surfaces (Maturana & Varela, 1980). How one "evaluates and modifies his or her priorities" is contingent upon both processes, what is perceived at the sensory level as an experience *and* the inter-activity of the nervous system itself to create meaning from this experience.

MacKay (1984) postulates a "supervisory activity" that is the specific correlate of conscious experience. This supervisory activity exercises control of planning, representation,

and evaluation, so that it essentially controls the ordering of experience. In the context of autopoiesis theory, this supervisory activity is the circular organization of the individual. For, as Maturana and Varela (1980) contend, the self-referring circular organization of every living system "specifies a closed domain of interactions that is its cognitive domain, and no interaction is possible for it which is not prescribed by this organization" (p49).

3.1.2.2 Distinctions in Data and States of Knowing

This cognitive domain of a living system is simultaneously opened and closed (Maturana & Varela, 1980; von Krogh and Roos, 1995). The closed domain of interactions specified by the circular organization of the system is closed to new information and knowledge. It is, however, open to data that occur in the form of perturbations from the external environment. "Perturbations can trigger knowledge development processes in the receiving, autopoietic system" (Vicari et al, 1996, p186). It is important to note, though, that, "perturbations are interpreted according to the distinction tree (knowledge system) of the receiving system. This means that when a scientist reads a journal article or hears about a recent discovery, he or she evaluates this material as data, not knowledge, and does so in accordance with his or her own knowledge framework.

The links among knowledge, individual cognitive capacity, and experience are further ingrained by the production of knowledge also being dependent upon the individual's "personal construct", as it is called in psychology (cf Neimeyer & Neimeyer, 2002). An individual possesses the ability to make unique distinctions in the data he or she encounters based upon his or her established personal constructs. For example, a scientist with considerable experience in drug design will be able to determine what type of features are necessary in a chemical compound to make it drug-like. This scientist will be able to observe a given compound and determine what features need to be modified to reduce toxicity or increase efficacy.

It is through this type of process that new knowledge is created and existing knowledge is applied; a process which is neurologically pre-programmed and inextricably linked to the individual, so that no two individuals have the same processing pattern and therefore, cannot be

similarly cognizant of the same thing. Duly noted is the argument by Maturana and Varela (1980) that the nervous system does not code descriptions that the observer makes of an environment, rather, it codes "processes that specify series of transformations from initial states, which can be decoded only through their actual implementation" (p53). Although two individuals may have identical descriptions of an environment, these elements of their cognitive domain are not what are coded as reference for later consultation. In addition, the likelihood that they have identical or even similar initial states which will be changed by their interaction with the environment or that the process of decoding via implementation will occur simultaneously in both individuals without further interrupting perturbations is equivalent to an airplane being able to fly under water. No two individuals, conceding the definition of cognition in terms of a biological function, can possess congruent "states of knowing".

Machlup (1980) presents thirteen elements that serve to characterize an individual's "state of knowing": being acquainted, being familiar, being aware, remembering, recollecting, recognizing, distinguishing, understanding, interpreting, being able to explain, being able to demonstrate, being able to talk about, and being able to perform. He also suggests that, "it is possible for a state of knowing to emerge from creative thinking, observing, experimenting, intuiting, speculating, theorizing, inventing, discovering, etc" (Machlup, 1980, p57). With many possible elements capable of representing the state of knowing and many possible ways of arriving at that state, it becomes paramount to acknowledge that these possibilities are constrained by the individual's path to arriving at that state. As it has been argued in this section, an individual's state of knowing is history dependent, resulting from experience. The state of knowing reflects how the individual attributes meaning to experience, what distinctions are made in the course of observation, and how an individual's personal construct influences this process. And, in the light of autopoiesis theory, this path is demarcated by the self-referential, circular organization of the individual.

The process of moving from distinctions in data to a state of knowing is contingent upon the parallel interactions of the many elements in the neural network, as professed by Hebb (1949). Contrary to the overlay paradigm for building intelligent tutoring systems, where a tutor

should augment a student's knowledge base in a step-wise fashion, (Carr & Goldstein, 1997, cited in Holyoak 1991), skilled performance depends on the parallel integration of multiple sources of information (Holyoak, 1991). Yet, information, as presupposed in autopoiesis theory, is strictly held in the cognitive domain of the individual and, therefore, "parallel integration of multiple sources of information" is only possible as a uniquely individual cognitive activity. Therefore, to view knowledge as state of knowing is to say that outright agreement on that which is known is a fallacy. Two or more individuals may have similar conceptions of a fact or an object, but by way of autopoiesis theory, their states of knowing cannot be completely congruent because of the direct impact of the history of the individual, the uniqueness of the individual system itself, and the various influences for the external environment that impinge upon one's ability to know.

3.1.2.3 Specialization as a State of Knowing

An individual, however, can have different states of knowing in different areas or disciplines, and indeed, the knowledge compiled in one area will directly influence the distinctions an individual makes in another area[39]. Holyoak (1991) points to the following reports of knowledge transfer across domains. Nisbett and his associates (Cheng et al, 1986; Fong, Krantz, & Nisbett, 1986; Nisbett et al, 1987) provide evidence that training in statistics can improve performance on novel problems. Dörner and Schölkopf (1991) convey findings that experienced executives demonstrated more success than college students in solving non-programmed problems associated with managing a dynamic environment. These findings follow Descartes' testimony that knowledge is undiversified and as Grene (1974) states in her interpretation of Descartes, "practice in geometry will not stop a man from understanding medicine, it will, in Descartes' view, aid him in doing so…" (p80).

It should be noted, however, that due to the pressures of social forces in shaping the process of knowledge development, narrow focuses and applications of compiled knowledge, or

[39] As a reader of this dissertation, your knowledge, in conjunction with your experiences, will impinge upon your interpretation of this argument. Your knowledge in a particular area will undoubtedly lead you to credit or discredit the assertions made here.

specialization, have become a common feature of knowledge endeavours. Society and market forces have been influential in producing specialization, affirming William James' argument that the validity of a proposition is in its "cash value" (Gallagher, 1982). This is in accordance with Laudan's (1981) "zweckrational", or ends-rational, interpretation of scientific activity, in which scientists are seen to follow the scientific method (if one can assert that such a thing does exist) to facilitate certain extrascientific interests (cited in Fuller, 2002). As Beer (1980) declares, "a man that can lay claim to knowledge about some categorized bit of the world, however tiny, which is greater than anyone one else's knowledge of that bit, is safe for life: reputation grows, paranoia deepens" (p64).

The notion that a social force can impinge upon an autopoietic system, as evidenced by the existence of specialization, can be explained via the theory of structural coupling. Varela, Thompson, and Rosch (1991) point to the early recognition by philosophers such as Merleau-Ponty that the organism and environment must be seen as bound together in a reciprocal fashion. While both the living, autopoietic system and the contextual medium operate independently in each interaction, they do not operate in mutually exclusive realms and as a result, the potential for structural change in one to induce a structural change in the other remains (Maturana & Varela, 1980). This process is the "conservation of adaptation", as Maturana and Varela (1980) have defined it. With the recurrent interactions between system and context, a structural change in the system can ensue.

Due to the circular organization of the system, however, "the configuration of constitutive relations that remain invariant in the adapted [living system], determines the matrix of possible perturbations that the [living system] admits at any instant, and, hence operates as a reference for the selection of the path of structural changes that take place in its history of interactions" (Maturana & Varela, 1980 pxxi). The contextual medium may provide an inductive force for change, but the actual change that occurs is resultant of and determined by the self-referential, circular nature of the system. Thus, specialization can be viewed as a conscious choice made by the individual that is triggered by the individual's contextual medium (society and market forces). The process of knowledge development, however, that comprises

the act of specialization occurs in a system that must first seek to fulfill the criteria set down by its circular organization. The selection of structural change takes place within this system.

The second view of knowledge, while it acknowledges that external forces can have an influential effect in the form of structural coupling on the formulation of knowledge, presupposes knowledge as a product of the cognitive domain of the observer. This product is not derived in the form of inputs and outputs (the system that produces knowledge is mechanically closed), but rather is a result of the self-referential, circular organization of an individual living system. Changes in the relationship between nervous system components ensue from the impact of perturbations from the external environment, but the system continues to operate independently and maintains its circular organization. Through this process, knowledge is developed and action is enlisted. Conceding the anti-representationist approach to knowledge equates to viewing knowledge as a state of knowing, kindred to experience and inseparable from meaning, where data are interpreted based on personal constructs. Combining the depictions of autopoiesis theory provided by both Maturana and Varela (1980) and Varela (1992), it is possible to summarize knowledge in the following manner:

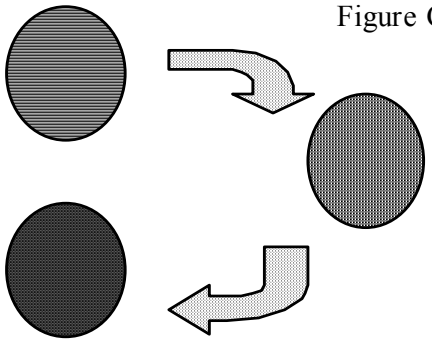
- Knowledge represents a world that is brought forth.
- Knowledge is effective action.
- Knowledge results from distinctions made in data.
- Knowledge is embodied.
- And, knowledge enables problem definition[40].

The diagram below serves to visually represent the anti-representationist approach.

[40] Ingrained knowledge, as it arises from the anti-representationist approach and autopoiesis theory, is also crucial in problem resolution. Individuals use their ingrained knowledge to solve sub-problems in the knowledge architecture. The larger technological problem(s) that members of an alliance seek to solve requires the resolution of several sub-problems, which are integrated through articulation mechanisms as discussed in the following sections. Defining the sub-problems that are crucial to the resolution of the larger technological problem can only occur through the application of the individual scientists' ingrained knowledge.

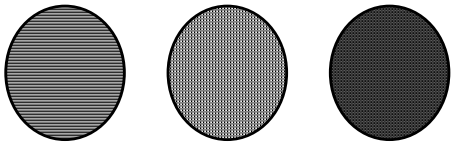
Diagram 3.1 The Anti-Representationist View of Knowledge

Figure C



This diagram represents the attempted transference of knowledge between three individuals. Each circle represents an individual. The patterned areas signify the knowledge developed within each individual as he or she intercepts the data from the primary source. The arrows correspond to the act of data transmission. (Notice that the arrows are patterned the same, indicating that the data remain in their original form.)

Figure D



This diagram represents the result of the process depicted in Figure C, as it is conceptualized under the anti-representionist approach. Each circle represents an individual's *state of knowing*. The pattern within the circle represents the unique knowledge formulated in reference to a given set of data, common to each individual.

3.1.3 Unifying the Two Views

The two approaches, the cognitivist and the anti-representationist, each prescribe a distinct praxis for the examination of knowledge. The presumptions that underlie the cognitivist view vindicate the hypothesis that knowledge is produced by interacting individuals and can be transferred between and shared among individuals. Knowledge is seen as migratory. The beliefs that fortify the anti-representationist paradigm put forth an understanding that bars individuals from simultaneously being in equivalent states of knowing. Knowledge is ingrained in the mind of individuals, and as no two minds are identical, no two individuals can be in possession of congruent states of knowing. The two perspectives, however, do share a common assumption.

The main commonality between the two provisions is that all statements, whether viewed in terms of the cognitivist or anti-representationist paradigms, have a subjective element. As Grene (1974) argues, "there can be no *purely* factual statements, i.e., statements which do not even presuppose evaluation, because there can be no intelligible discourse except on the ground of evaluation or appraisal" (p160 – emphasis her own). In recognition of the arguments developed under the cognitivist theory, subjective understanding is the basis of all knowledge. Employing Locke's representative realist approach to knowledge, subjective understanding is indicative of the ideas developed in response to external stimuli. It is only through interaction and conversation with others that these ideas become objectified and even through participation in the objectivation process, the subjective nature of knowledge is not altogether obliterated. Similarly, under the anti-representationist conceptualization of knowledge, knowledge maintains its subjective character, as under this theory, knowledge never ventures beyond the individual. It can be communicated to another individual, but in this form, it is only data to the recipient and must undergo the interpretation process to regain the status of knowledge, thus aligning with a new subjective filter.

The difference between the two theories is a matter of focus. The cognitivist interpretation of knowledge focuses on the social aspect of knowledge, whereas the anti-representationist approach examines knowledge from the perspective of the individual. A knowledge architecture is comprised of both a social arrangement between a group of individuals and the individuals themselves. Therefore, both perspectives are necessary to adequately explain knowledge processes. Doing so, however, requires a consolidation of the two theories. The next section embarks upon this enterprise of unification with the aim of showing how the two types of knowledge operate in a modular structure.

3.2 Operationalizing Knowledge in a Modular Structure

Inherent to the literature on strategic management is the assumption that knowledge exists outside of the individual (Argote & Ingram, 2000; Galbraith, 1990; Levitt & March,

1988; Starbuck, 1992; Walsh & Ungson, 1991; Zander & Kogut, 1995). For example, Walsh and Ungson (1991) declare that there are five internal sources of knowledge within an organization, including individuals, culture, transformations (or tasks), structures (or roles), and the ecology (physical structure) of the organization. In addition, these authors postulate that knowledge in reference to the organization also exists outside of the organization itself in the form of archives. This position is indicative of the cognitivist approach to knowledge and provides a cogent grounding for the advancement of the argument that, because of the existence of knowledge in these various repositories, individuals within the context of the organization can effectively share knowledge.

This assumption is in direct contradiction to the proposition of the anti-representationist approach, which asserts that knowledge resides strictly in the individual, and specifically in the cognitive domain of the individual. The anti-representationist theory posits the self-referential, circular organization of the individual, creating a footing for the notion of knowledge as self-referred. And, as von Krogh, Roos, and Slocum (1996) point out, "self-referentiality means that new knowledge refers not only to past knowledge but *also* to potential future knowledge" (p164 – emphasis their own). Under this presumption, knowledge does not exist without the individual, without the individual's past, and without the individual's intended use for the knowledge.

So, where does knowledge exist? The answer to this question depends on which approach to knowledge is preferred. I have already stipulated, however, that both approaches are necessary for explaining knowledge processes. This question is best answered, then, by stating that knowledge exists in a structure – be it an organizational structure shaped by divisions, products, or cross-functional teams, or a collaborative structure shaped by modularity – and both views of knowledge are relevant to any given structure. And, for the purposes of this thesis, structure is defined as the internal differentiation and patterning of relationships and/or connections between segments of an alliance (Thompson, 1967).

Objective knowledge, or migratory knowledge, exists within this type of structures and the mobility and need for movement of such knowledge is dependent on the structure itself. The

type of knowledge made evident in the anti-representationist approach to knowledge, or ingrained knowledge as I will call it, resides in individuals, but these individuals are also part of a structure.

Three ways of thinking about knowledge are useful in clarifying my point. These include: tacit versus articulated knowledge (Polanyi, 1958), knowledge-of and knowledge-about (Grote, 1865; James, 1885), and knowing how (Ryle, 1949). The discussion of these ways of thinking about knowledge is supplemented with an analysis of common knowledge bases and knowledge "flows".

3.2.1 Tacit and Articulated Knowledge

The first and most widely cited distinction in the various literatures on knowledge is that between tacit and articulated knowledge (Polanyi, 1958). Serving as the building block for several current theories of knowledge, Polanyi's (1958) dichotomous model of knowledge has been reinvented and particularized to various contexts. Many of the authors, however, remain in disagreement as to whether there is a definitive division between explicit and tacit knowledge, with some authors proclaiming the existence of a knowledge spiral, in which explicit knowledge becomes tacit through internalization and tacit knowledge becomes explicit via externalization (Nonaka & Takeuchi, 1995). Von Krogh and Roos (1996b) make a distinction between thematized and non-thematized knowledge. They acknowledge the consistency of classification between thematized knowledge with Nonaka's (1991) notion of explicit knowledge, Badaracco's (1991) depiction of migratory knowledge, and Itami's (1987) explication of articulated knowledge. Parallels are drawn by von Krogh and Roos (1996b) between the idea of non-thematized knowledge and Nonaka's (1991) and Badaracco's (1991) tacit and embedded conceptualizations, respectively. The following table serves to clarify these classifications.

Table 3.2 Classifications of Migratory and Ingrained Knowledge

	MIGRATORY	INGRAINED
THEORY	Cognitivist	Autopoiesis
TYPES OF KNOWLEDGE	Articulated	Tacit
	Thematized	Non-thematized
	Explicit	Embedded[41]

There are, however, two problems with presenting knowledge in these nicely packaged categories. The first is that many management scholars use the terms embedded, non-thematized, or tacit knowledge to refer to the knowledge of an individual *and* the knowledge of a firm. As such, the anti-representationist approach to knowledge has been used to define and describe the knowledge of a system that goes beyond the individual. Von Krogh and Vicari (1993) talk about the autopoietic firm. Luhmann (1986) refers to autopoietic social systems. Gibbons et al (1994) write that, "[t]he distinction between codified and tacit knowledge can be complemented by a parallel distinction between migratory and embedded knowledge. The former is mobile and can move rapidly across organizational boundaries, while the latter is less so because its movement is constrained in a given network or a set of social relations" (p24).

My contention is that knowledge in firms and interorganizational relationships can only exist in a migratory form. Members of firms or alliances can erect boundaries to stop the knowledge from moving beyond the organizational (or interorganizational) setting. The knowledge, however, does not exist in companies or collaborations because they produce and use knowledge themselves. A firm may house routines that faciliate these processes, but it is the people within the firm that enact the processes.

As I see it, ingrained knowledge resides in individuals, not firms. Indeed, if the anti-representationist approach is accepted, knowledge does not move beyond the individual at all,

[41] One could certainly raise the question here as to whether or not embedded knowledge is the same as tacit knowledge. Should they be organized in the same column, under the same heading? My response is that the way knowledge is viewed in much of the management literature, where the firm is said to be in possession of knowledge without due mention of the people within the firm, allows for the terms to be used interchangeably. Embedded knowledge is knowledge that is tacit to the firm. Tacit knowledge is embedded in the firm. I, however, contend this line of thought and argue against it in this section.

but remains tacit. So, while I do not wish to solve the problems related to the nature of knowledge here, I would like to argue against the theme running through the management literature that a firm has the ability to do anything with respect to knowledge. I do not believe that a firm has a brain or the impetus to do things without the people that are part of the firm. When people leave a firm, it has no will.

There are several management theorists whose choice of language reflects a belief that firms have knowledge and decide how to use knowledge. I submit that the firm cannot do this without the people who comprise a firm. For example, while Badaracco (1991) rightfully acknowledges the potency of structure in stating that "[t]he boundaries of firms can either impede or hasten the slow movement of embedded knowledge[42]", he also claims that a knowledge link "is a way in which companies can learn embedded knowledge from other organizations and work with them to create it" (p79). Is it the companies that do this, or is it the people within the companies?

Logically, it is the people that perform the types of activities to which Badaracco (1991) refers. Indeed, as Granovetter (1985) suggests, "…the overlay of social relations on what may begin in purely economic transactions plays a crucial role" in economic life (p498). Badaracco (1991) has this much right – conceding his definition of embedded knowledge – specialized, social relationships are important. People and their interactions cannot be eliminated from the picture, whether the picture is painted in economical terms, scientific terms, or otherwise. The important part here, though, is that it is the people[43], not the firms that act in knowledge processes.

Embedded knowledge is not created in relationships between firms, rather it forms from relationships among people. Migratory knowledge can move between the constituents of two firms, but it is already objectified knowledge in at least one firm and must be evaluated from the

[42] Badaracco (1991) defines embedded knowledge as knowledge that "resides primarily in specialized relationships among individuals and groups in the particular norms, attitudes, information flows, and ways of making decisions that shape their dealings with each other" (p79).

[43] I acknowledge here that people act in social relationships. My argument about the importance of people should not be misconstrued to the point of viewing people as "atomized individuals", to use the words of Granovetter (1985). The people are indeed important, but there interrelationships are equally worthy of attention.

framework of the ingrained knowledge of the recipients. People from two companies can work together to objectify knowledge. That is, the ingrained knowledge of people within firms can be aggregated by using mechanisms to extract the ingrained knowledge from the mind of the individual, such as using it in a process or scientific practice.

This type of activity, however, is operationalized in the structure of the organization or collaborative endeavour. If the structure of an alliance is thought of as modular, with prescribed design rules for action and precise ways of connecting (interfaces), not only are the activities of the collaborative participants focused on the purpose dictated by the rules, but the movement of knowledge is limited to what is needed to achieve the desired output of the collaboration.

The second problem with categorizing knowledge as is done in Table 3.1 is that these categories gather support from the sharp partition between explicit and tacit knowledge. This becomes a problem when considering that there are authors who adhere more rigidly to Polanyi's (1958) assertion that all knowledge has tacit dimensions (Leonard & Sensiper, 1998; Wong & Radcliffe, 2000). Where all knowledge is thought to have tacit dimensions, knowledge can only be conceptualized as a spectrum. As such, most knowledge falls in the middle of the range (Leonard & Sensiper, 1998). Slotting different categories of knowledge into a table such as the one above becomes increasingly difficult if all knowledge is thought to have tacit dimensions. The line that separates the migratory knowledge from the ingrained knowledge loses relevance.

As defined in both of the views of knowledge presented in this chapter, subjectivity is never totally abandoned. Therefore, all knowledge does indeed have tacit dimensions (assuming tacitness involves subjectivity), whether this comes through in negotiated understandings (as would be the case under representationism) or in the creation of knowledge in the mind of the individual (as the anti-representationist approach would suggest). If a chemical compound is produced using the ingrained (tacit) knowledge of a synthetic chemist, that compound is composed of the ingrained knowledge of the scientist. The production of the compound does not shed this ingrained knowledge. Instead, the process of producing the compound changes the ingrained knowledge of the scientist into a new form, migratory knowledge, or the compound

itself. In this form, it is objectified and evaluated by other scientists. It can move between the scientists and remain in a stable form[44]. The compound's usefulness, value, and even the acknowledgement of its very existence are made possible through validation by other scientists, who have the requisite ingrained knowledge, viewing the compound and assessing its potency or efficacy. Migratory knowledge, then, is only relevant to people with overlapping ingrained knowledge bases.

3.2.2 Common Knowledge Bases and Knowledge Flows

This is consistent with a theme that runs through the knowledge and innovation literatures, suggesting the necessity of a common knowledge base between the source and the recipient of knowledge (Cohen & Levinthal, 1990; Cummings & Teng, 2003; Dixon, 2000, Dougherty, 1992; Hamel, 1991; Teece, 1977). For example, Lane and Lubatkin (1998) argue that a firm's[45] ability to assimilate and utilize external knowledge depends on the similarity between the exchange partners, including correspondence between their knowledge bases, dominant logics, and systems. The type of common knowledge bases I refer to in this thesis are individual scientific knowledge bases that allow members of an alliance to critically evaluate the work performed in a specific task domain and participate in the activities of that domain. I do not contend that all members of a collaboration must have similar knowledge bases, however, as many of the scholars in the management literature do.

In fact, in chapter two, I put forth the argument that university-industry collaborations in biotechnology are complementary in nature and this complementarity comes from the knowledge held by the diverse members of the knowledge value alliance (KVA). Where, though, is the similarity between the collaborators that allows them to absorb each other's knowledge that is put forth as being vital to the success of an alliance in the knowledge

[44] The form of a compound will remain stable only if the laws of chemistry are obeyed. That is, if the compound is not subjected to extreme temperatures and pressures, or if it is kept away from various liquids, among other things.

[45] I must point out here the abilities of assimilation and utilization being discussed as the actions of a firm. I maintain my earlier argument here that these abilities do not actually belong to the firm, but rather to the people who work in a firm. This view is also supported by the work of Nonaka and Takeuchi (1995).

management literature? If knowledge is taken to be migratory, as is the case with articulated knowledge and its corresponding classifications, the similarity is a necessity. If knowledge is conceptualized as ingrained knowledge, the similarities may indeed exist, but not to the extent that one person's knowledge can be transposed in exact form into the mind of another. It is "things" (Latour, 1987) that are moving, and these "things" contain the ingrained knowledge of their producers. The complementary knowledge of the collaborative partners must be operationalized in a structure that appropriately integrates their knowledge bases and provides specific channels for the movement of "things".

The sentiment that knowledge does move and does so in a "flowing fashion", however, is all too common in the knowledge management literature. Take for instance, the Gibbons et al (1994) account of knowledge production and diffusion. Knowledge, or what these authors have coined as Mode 2 knowledge, is knowledge developed via collaborative action. Gibbons et al. (1994) describe Mode 2 knowledge as:

- Carried out in a context of application,
- Transdisciplinary,
- Heterogeneous,
- Heterarchical,
- Socially accountable,
- Reflexive,
- And, temporary with a heterogeneous set of practitioners, collaborating on a problem defined in a specific and localized context.

The results of knowledge generated in Mode 2 fashion are transmitted to those who participated in the course of its generation, "so, in a sense, the diffusion of the results is initially accomplished in the process of their production" (Gibbons et al., 1994, p5).

The problem with this line of reasoning is that it takes into consideration neither the abilities of the people involved in the collaborative action to interpret the results in a meaningful

manner nor the structure through which the diffusion process is operationalized (if a diffusion process can even be said to occur).

While members of the knowledge value alliance may be privy to the results of the collaboration and the associated knowledge, they will certainly not all be in equivalent states of knowing regarding those results. The results may be migratory, making the respective knowledge migratory, but the knowledge as it is ingrained in the participants, remains ingrained. The denominations of articulated, thematized, migratory, or explicit knowledge fortify the assumption that knowledge can indeed be shared and these types of knowledge lend credibility to the instance in which all members of the collaboration *have access* to the results.

This is not to say, however, that *having access* to the results or associated knowledge is synonymous with knowing and understanding. The problem with the migratory argument is that the assumptions are providing validity to the concepts, rather than the other way around. This type of problem stems from the theory, specifically the theory of migratory knowledge, being severed from the elements it ties together (Latour, 1987)[46]. Armed with the ammunition of the anti-representationist paradigm, it becomes apparent that knowledge may indeed move throughout the collaboration in the form of results (among other things), but whether or not the knowledge becomes part of the cognitive repertoire of those who have access to the knowledge is another question, as is whether or not different people interpret the results as meaning the same thing.

Moreover, the process of transforming ingrained knowledge into migratory knowledge (in the form of compounds, results, etc.) is operationalized within the structure of a collaborative endeavour. In a modular structure, the design rules will dictate what needs to be produced to achieve the desired outcome, who should produce it, and how the objects that are produced should be handled (i.e., who should they be sent to, who needs to see them, how will they be tested, etc.). In this type of structure, ingrained knowledge and migratory both have a role to fulfill. If a compound is thought of as the end result of one task, and the testing of the

[46] According the Latour (1987), this type of situation, in which the theory becomes an abstraction and is severed from the objects it ties together, is synonymous "with doing a history of hammers without considering the nails, the planks, the houses, the carpenter and the people who are housed" (p242).

compound is the activity of another task, the unity of the two tasks comes from the compound moving from one task domain to another, making ingrained knowledge crucial for task completion and migratory knowledge essential to task progression.

Whether or not collaborative participants must be similar in terms of knowledge is dependent upon the structure chosen to organize the alliance. If a modular structure is chosen, tasks can be conducted simultaneously without the need for the scientists performing one task to know how to perform the activities of other scientists in another task domain. A modular structure will dictate the forms of migratory knowledge to be generated in a task domain and the direction of movement for such knowledge once it has been produced. Knowledge does not diffuse in a collaborative relationship, spreading freely to all those who are part of the alliance as Gibbons et al (1994) contend that it does. Where the collaboration is organized modularly, distinct pathways for the movement of migratory knowledge are created. In the instance of modularity, the amount of knowledge overlap necessary for the desired output of a collaboration to be achieved will be designated by the design rules. In turn, such overlap will be the guiding factor in who receives information in an alliance and how that information is interpreted. Thus, shared knowledge can be said to exist, but only on a "need-to-know" basis.

3.2.3 Knowledge-Of and Knowledge-About

The categories of knowledge-of and knowledge-about, as explicated by Grote (1865) and James (1909) respectively, help to demonstrate how varying levels of knowledge overlap between collaborative participants and predetermined directions for the movement of knowledge can be structured into interorganizational relationships. Machlup (1980) conveys knowledge-of as acquaintance or familiarity with a subject matter and knowledge-about as the result of systematic study and reflection. The distinction between knowledge-of and knowledge-about exists only as different levels in a state of knowing, with the state of knowing being an individual (anti-representationist) conceptualization of knowledge. With access to the results and associated knowledge of a collaboration, one can have knowledge-of, but only if one can understand and explain those results, can one be said to have knowledge-about those results.

These two states of knowing, knowledge-of and knowledge-about, in conjunction with the array of other states of knowing listed by Machlup (1980)[47], demonstrate a sense of inadequacy of knowing – a contention that current knowledge is never enough, one can always progress to another state and indeed, one needs to progress. Using Rescher's (1989) description of man as *Homo quarens* and the associated definition of man as as dependent on knowledge as he is on his basic physiological needs[48], it can be said that one is severely limited in relying on his or her own knowledge, particularly in areas like biotechnology where there are a variety of techniques that could be of valuable use with any given agenda. The complementary nature of the knowledge in a knowledge value alliance and the act of collaboration itself allow this inadequacy to be overcome, but only if the appropriate tools, technologies, and work practices are chosen to integrate the knowledge of the collaborative participants.

The structure of the collaboration must be chosen to effectively utilize the ingrained knowledge of the members of the alliance. In addition, the tasks designated as essential to the attainment of the desired output in an alliance must be organized in a structure that efficiently brings about the production of the requisite migratory knowledge and channels such knowledge in the relevant directions.

The person responsible for arranging this structure is the "architect" of the alliance. As Snow, Miles, and Coleman, Jr. (1992) suggest, in network firms "…certain key managers operate *across* rather than *within* hierarchies, creating and assembling resources controlled by outside parties. These managers, therefore, can be thought of as brokers" (p15 – emphasis their own). The role of an architect is to broker the knowledge of collaborators, seeking out individuals with the necessary ingrained knowledge to perform the tasks that are deemed to be essential to achieving a desired output and organizing these people into a structure that appropriately facilitates the purpose of the research agenda.

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[47] See section 3.1.2.2 for a reiteration of the various states of knowing.

[48] Rescher (1989) writes that, "[m]an has evolved within nature into the ecological niche of an intelligent being. In consequence, the need for understanding, for 'knowing one's way about', is one of the most fundamental demands of the human condition. Man is *Homo quarens*. The requirement for information, for cognitive orientation within our environment, is as pressing a human need as that for food itself. We are rational animals and must feed our minds even as we must feed our bodies" (p6 – emphasis his own).

The architect will need to have knowledge-of, á la Machlup (1980), the tasks required to achieve the desired output in order to organize the tasks into a coherent structure and delegate them to the appropriate teams of scientists. There need not be significant knowledge overlap between the architect and the scientists working in any given task domain, as long as there are design rules to articulate task work and interfaces to facilitate connection. The architect will need to know enough of the knowledge of each task domain to conceptualize how the tasks fit together, choose the appropriate design rules to effect this fit, and determine the direction in which migratory knowledge needs to travel in order to achieve the desired output. Such knowledge is a state of knowing of the architect and is usually acquired via experience.

The architect, however, as noted by Snow, Miles, and Coleman Jr. (1992), will have only a vague idea of the necessary inputs required to attain the desired output. There are, of course, uncertainties that the architect and the other members of the alliance will have to face in the process of design, which will impact on the conceptualization and definition of these inputs. Furthermore, the architect cannot be expected to have knowledge-about, as it is defined by Machlup (1980), of all the types of scientific tasks necessary to complete the research agenda. It is for this reason that complementary based knowledge collaboration is a useful practice. If the knowledge of others can be successfully integrated and aligned, the alliance can achieve its desired output, thus overcoming the inefficiencies of one scientist's knowledge. As such, the architect need not "know how" to perform all the tasks necessary to achieve a desired output.

3.2.4 Knowledge How

In a modular structure, it is essential that the people most qualified to perform the desired tasks, the people with the appropriate "know-how" (Ryle 1949), are enlisted. An alliance is structured around the know-how of teams of scientists with the purpose of achieving the desired output. This type of knowledge is undoubtedly individual. It is ingrained knowledge. To be sure, more than one individual can know-how to perform a certain task or activity such as typing, cooking, or making chemical compounds, but in order to be effective, the knowledge

has to reside in the individual, which is an argument comparative to the anti-representationist theory of knowledge.

Machlup (1980) offers four types of knowing how:

- knowing how something looks, sounds like, feels, smells, and tastes
- knowing how something happened
- knowing how something (a cause or antecedent) is generally connected to something else (a subsequent, an effect)
- knowing how to perform a certain task

On closer examination, it becomes evident that all of these types of knowing how are relative only to the cognitive domain of the individual. For example, knowing how something looks is a description made by *an* observer; knowing how something happened is contingent upon the individual's experience; knowing the relationship between two things is a connection between two observations in the cognitive domain of the individual; and, knowing how to perform a task is the procedural knowledge possessed by the individual. These activities are intuitive and experiential.

A technique, such as mining marine microbes, can be considered a type of know-how. In order to be used, it must reside in the mind of an individual scientist. It can, however, also be considered a form of migratory knowledge if the technique has been objectified. That is, if the technique has been shown to other scientists and they have collectively validated the technique, it can be considered to be a mobile form of knowledge among those scientists. This is not to say, though, that all those scientists using the technique will be in similar states of knowing how to use or employ the technique. Some scientists may be adept at being able to explain the technique, demonstrate it to others, and use it in several different circumstances. Other scientists may be able to modify the technique to make it more effective or efficient.

There can, then, be two or more individuals who know how to perform a task, but they do so with varying degrees of knowing how. They may also know different parts of a complicated process. For instance, there are a plethora of trained synthetic chemists in this world who all know how to perform the task of chemical synthesis. The states of knowing how to perform

chemical synthesis, however, may vary between individuals. One synthetic chemist may have over 30 years experience with such a task, while another may have less than three. It would, therefore, be illogical to think that these two synthetic chemists have similar states of knowing how to perform the task of synthesis. Even if two chemists who each have 30 years of experience are compared, it is difficult to say that their states of knowledge are similar. States of knowing differ not just by amount of experience, but also by type of experience, and the individual's capacity to accumulate and create new knowledge.

A certain amount of luck, then, enters the picture when considering the architect's need for choosing the appropriate scientists to perform a given task. Ingrained knowledge is extremely difficult to assess, with only previous experience, reputation, and prior production of migratory knowledge (such as journal articles and compounds) serving as indicators of know-how or ingrained knowledge. Gauging performance and a scientist's know-how is an enigmatic process best done after the scientist has already performed the specified task. For the architect, however, this needs to be done prior to attempts to complete a task. Thus, the architect calls on a bit of luck to make an accurate assessment of one's ability to perform.

Moreover, scientists can be classified as "routine" or "adaptive" experts (Holyoak, 1991; Hatano & Inagaki, 1986; Hatano, 1988). Routine experts are able to solve familiar types of problems efficiently and effectively, but endure grave difficulties when confronted with a novel situation. They do not have the appropriate representations upon which to draw to solve the ill-programmed problem. "Adaptive" experts, as defined in Holyoak (1991), are able to use non-specific domain knowledge to invent new procedures to handle the novel problem. At the heart of these concepts is the notion that expertise is not so much what someone knows, but what that someone can do with what he or she knows. A scientist can be both a routine expert in one instance, and an adaptive expert in another.

Each new scientific problem, though, is novel. Although the ingrained knowledge applied to the problem may be routine, the material in each new problem is unique, which may require adaptive expertise. For example, in one alliance x-ray crystallographers may be working toward uncovering the three-dimensional structure of the enzyme integrase, whereas in another

collaboration the same scientists may be working on the structure of 5-α-reductase. Where these scientists may have been successful at defining the three-dimensional structure of integrase, they may have severe difficulties with uncovering the structure of 5-α-reductase. Their difficulties may be attributed to the uncertainties associated with the science of x-ray crystallography or the lack of adaptive expertise. Nonetheless, assessing the ability of the scientists to perform is gravely difficult and becomes even more so in the face of scientific uncertainties.

A modular structure can do little to eliminate these problems. While there may be rigid testing mechanisms that allow a product to be determined to fit into a modular system, this is not necessarily so when people are organized modularly. A modular structure can serve to organize people, or scientists, so that their work coalesces and the desired output of a given alliance can be achieved. It also certainly reduces the uncertainties that would be faced if one team of scientists tried to tackle a technological problem on its own. As Quinn, Baruch, and Zien (1997) suggest, "[i]n an increasing number of innovations…complexity is so high (as in advanced physics, aerospace, communications, or biotechnology projects) that teams, as they are ordinarily defined, cannot cope as well as collaboration among a large number of relatively independent units" (p107, cited in Langlois & Robertson, 2003, p105). The modular structure, however, is ineffective against scientific uncertainties. A modular structure is only effective against the uncertainties created by complexity.

With the complementary nature of a knowledge value alliance, there will undoubtedly be various types of know-how at work within the knowledge architecture. For example, one group of scientists may know how an enzyme is extracted from a host of other substances. Another team of scientists may know how the enzyme functions in the body or the effect of a newly developed compound on the enzyme. While still yet, another group of scientists in the knowledge value alliance may know how to construct the compound that has the desired effect. Bringing these types of knowledge together is not a matter of teaching one scientist the practice

of another[49], but instead requires a modular structure that is centred on the purpose of the collaborative endeavour. Along side differentiation, however, is the need for integration and coordination across sub-teams and sub-projects (Langlois & Robertson, 2003). If the alliance is aiming to produce drug leads via rational drug design, the structure of the alliance should appropriately allow for the integration of the know-how of the collaborative participants to achieve this output.

These ways of thinking about knowledge – tacit versus articulated knowledge (Polanyi, 1958), knowledge-of and knowledge-about (Machlup, 1980), and knowledge how (Ryle, 1949) – help to demonstrate how both migratory and ingrained knowledge are utilized in a modular structure. There is, of course, an abundance of other classifications of knowledge[50]. The requirement to continue to develop new categories and classifications of knowledge, however, is obsolete. One has to ask when is the right time to stop describing knowledge and start reflecting upon how it moves from one state to another, how it moves from one individual to another, or if it even *moves* at all? If it does move, what are the structural mechanisms through which movement is operationalized and how do they impact on this movement? If biologists contented themselves with describing plant cells, would they have ever discovered osmosis?

As a simple, summary classification, then, knowledge, for the purposes of this investigation, is seen as both migratory and ingrained. Migratory knowledge depicts an objectified form of knowledge that may exist in the form of results of a collaborative effort – for instance, in a compound or a patent. It resides outside of the individual. Ingrained knowledge, on the other hand, resides within the individual. Typically, arriving at the desired output of a collaborative endeavour requires the utilization of many different kinds of migratory and ingrained knowledge, which can be organized in a modular structure. The work within an

[49] This would eventually eliminate the need for collaboration, as one scientist would then be able to perform the full gamut of tasks on his or her own. Such a process of teaching and learning, however, would be quite cumbersome and extensive.

[50] For instance, Collins (1993) offers the classifications of symbolic type knowledge, embodied knowledge, embrained knowledge, and encultured knowledge. Winter (1987) and Dosi (1988a) use continuums of knowledge such as tacit versus articulated, nonobservable versus observable, complex versus simple, elements of a system versus independent, and specific versus general. Faulkner (1994) details five types of knowledge used in innovation: knowledge related to the natural world, knowledge related to design practice, knowledge related to experimental research and development, knowledge related to the final product, and knowledge related to knowledge.

alliance is centred on solving a technological problem and therefore, the design rules and interfaces that support this structure must be chosen to facilitate the purpose of resolving the specified technological problem. The next section of this chapter examines the design rules of a modular structure.

3.3 Knowledge, Technological Problems, & Modular Structures

Problem solving in a modular structure occurs through the use of both migratory knowledge and ingrained knowledge. The problem that a knowledge value alliance seeks to solve defines the purpose of the alliance and this purpose must be supported by the structure of the alliance. Recall that the representationist approach to knowledge is said to enable problem solving (Aadne, von Krogh, & Roos, 1996) and the anti-representationist approach is defined as enabling problem definition (von Krogh, Roos, & Slocum, 1996). As such, migratory knowledge is used in solving the problem of a collaborative endeavour and ingrained knowledge is used to define the problem. These types of knowledge must be used as such in a modular structure of an alliance to target the purpose of the research agenda.

3.3.1 Solving Technological Problems

Recall the argument made in chapter two concerning the use of modularity in a design process to reduce the uncertainties created by complexity. "Modularity reduces uncertainty and increases doability[51] [of the problem], because scientists construct a circumscribed subproblem which makes sense *vis-à-vis* a larger umbrella problem to one or more social worlds" (Fujimura, 1987, p277 – emphasis her own). Using migratory knowledge, members of a knowledge value alliance seek to solve the larger "umbrella problem". Compounds and three-dimensional structures of enzymes, both forms of migratory knowledge, are produced in a bid to solve the technological problem that defines the purpose of a collaborative engagement. Journal articles and the patent literatures are searched to see how scientists may have approached similar

[51] Fujimura (1987) conceptualizes "doability" as the alignment of several levels of work organization.

problems in the past and to see what existing knowledge can be used in the process of problem resolution.

This larger problem, as Fujimura (1987) notes, is decomposed[52] into smaller problems that are solved through the use of the specialized knowledge of the scientists. Von Hippel (1994, 1998) suggests that greater efficiency can be achieved by portioning the overall problem-solving efforts into tasks.

> In doing so, one can reduce one fundamental source of inefficiency, notably that actions in one particular innovation stage or activity may require information or even changes of actions in several other innovation stages or activities. This is a source of inefficiency because of the extensive coordination and information flows that this process requires and the potential disruptions that may be brought about by these interdependencies (Arora, Fosfuri, & Gambardella, 2001, p105).

Once a task has been designated to a group of scientists, these scientists use their specialized, ingrained knowledge to determine what needs to be accomplished in order to complete the task. In this sense, they define the problem. Completing the task, however, may also require the use of migratory knowledge, such as compounds produced in another module of the alliance or relevant literature to determine the features necessary in a compound to effectively target an enzyme.

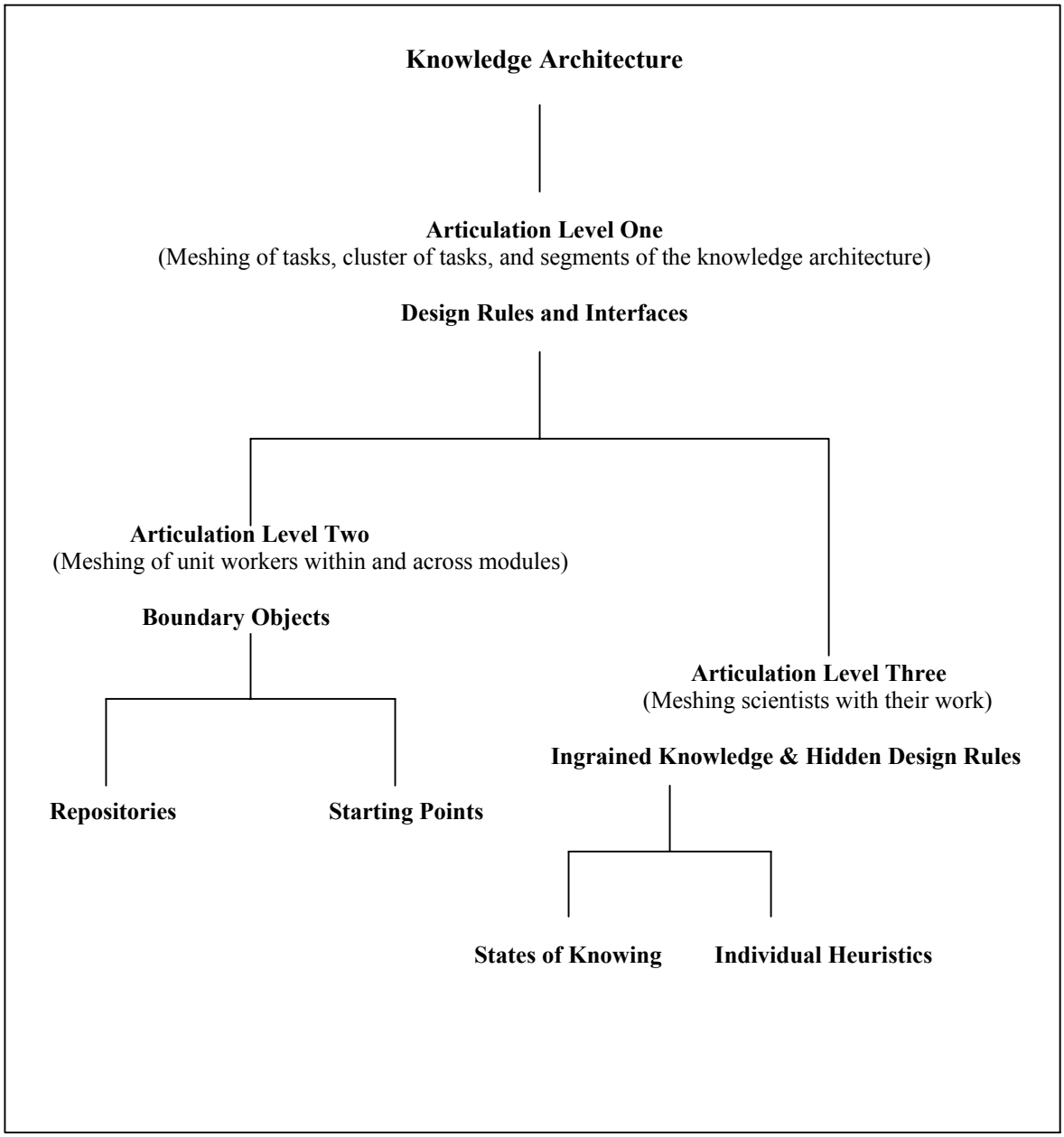
3.3.2 Articulation

The modular structure of a knowledge value alliance is centred on a simultaneous division of labour, and articulation of the tasks and work performed in each division to serve the purpose of the alliance. "The process of constructing a doable problem can be conceptualized as the art of articulation" (Fujimura, 1996, p187). Following Strauss (1985), this process of articulation involves: 1) the meshing of the various tasks, clusters of tasks, and segments of the knowledge architecture, 2) the meshing of unit-workers, and 3) the meshing of actors with their types of work and designated tasks. In chapter two, I argued that it is the design rules and tools, technologies, and work practices used in the collaboration that accomplishes the first type of

[52] This term is taken from Simon (1962). It reflects the fact that a larger system, hierarchical, social, biological, or otherwise, can be segregated and segmented off into smaller sections, which makes the system easier to understand and modify.

articulation (the meshing of the various tasks, clusters of tasks, and segments of the knowledge architecture). In light of the two views of knowledge presented in this chapter, the articulation processes required for the meshing of unit-workers and the meshing of actors with their types of work and implicated tasks are made possible by the use of boundary objects (Star & Griesemer, 1989) and ingrained knowledge, respectively. Diagram 3.3, which is inspired by Strauss' (1985) three levels of articulation, displays the various mechanisms that serve the processes of articulation. Each of these mechanisms is discussed in detail following the diagram.

Diagram 3.3 Levels of Articulation



The specific design rules used to accomplish Strauss' (1985) first level of articulation include standards and interfaces. These are the basic visible elements identified by Baldwin and Clark (2000). These elements of the knowledge architecture are established at the beginning of an alliance and are communicated broadly to all collaborative participants (Baldwin & Clark, 1997). The process of rational drug design is an example of a standard, or a design rule as I will refer to it, and the areas of overlapping knowledge between collaborative participants are

interfaces. These visible elements of the architecture coordinate the tasks performed in an alliance. For instance, if the standard of an alliance is rational drug design, the tasks will methodically include determining the three-dimensional structure of an enzyme, crystallizing the enzyme, building compounds to specifically target that enzyme, and modeling the compounds with the enzyme or co-crystallizing the compound and the enzyme (McPherson, 1995). Each task within an alliance will be delegated to the teams of scientists most qualified to perform the given task. The standard of rational drug design, however, creates relevancy between the tasks, allowing them to be synthesized into a coherent attempt at solving the designated technological problem. Where members of an alliance have overlapping knowledge, although there need not be large amounts of overlap between the collaborative participants, interfaces are created that allow for communication and connection between the scientists in the alliance.

Strauss' (1985) second level of articulation, meshing unit-workers, is achieved via the use of boundary objects (Star & Griesemer, 1989). Even people from different social worlds, beyond one specific unit, are harmonized (to a certain extent) through the creation and use of boundary objects. In a study of the translation between viewpoints of amateurs and professionals in the establishment of the Museum of Vertebrate Zoology in California, Star and Griesemer (1989) conclude that there are four types of boundary objects that serve to produce a common representation of nature that can be subscribed to by a range of actors from a variety of social worlds. These so called boundary objects include: standardized forms, coincident boundaries, repositories, and ideal types.

Standardized forms are essentially equivalent to the standards defined by Baldwin and Clark (2000). They represent the methodologies chosen to guide the work in a knowledge value alliance. Rational drug design is an example of a standardized form. This type of boundary object does not make knowledge migratory, somehow allowing it to move between the alliance constituents. Instead, it allows different orders of ingrained knowledge to be integrated in the larger framework of the knowledge architecture and creates the pathway for the movement of migratory knowledge.

Coincident boundaries are representative of the interfaces between various modules in an alliance. This type of boundary object, such as work in the area of marine microbiology or synthetic chemistry, offers a conduit for the flow of migratory knowledge. With a coincident boundary, or an interface as I will call it, members from both sides of an alliance are able to evaluate the forms of migratory knowledge that exist within the knowledge architecture. If a compound is produced, for example, it is a form of migratory knowledge that can move between the modules of an alliance and be evaluated within a synthetic chemistry interface.

I use modularity terminology, namely design rules and interfaces, in lieu of these two boundary objects. As such, their role in an alliance is to accomplish Strauss' (1985) first level of articulation, meshing tasks and clusters of tasks in the knowledge architecture.

The remaining two types of boundary objects, repositories and ideal types, however, can be argued to provide tools for meshing unit-workers both within and across task domains. I will continue to use the word repository to represent journal articles, patents, and compound libraries that may be used in a knowledge value alliance (KVA).

An ideal type is defined by Star and Griesemer (1989) as an object that is abstracted from all domains and is fairly vague. "[I]t is adaptable to a local site precisely because it is fairly vague; it serves as a means of communicating and cooperating symbolically – a 'good enough' road map for all parties" (p410). Indeed, the term ideal type is used by other authors as well, and thus carries other connotations. Burns (1971) discusses his attempts to define and describe the concerns of organizations in the electronics industry, which were confronted with rapid technological change. He states that he found it necessary to posit "…two 'ideal types' of working organization, the one mechanistic, adapted to relatively stable conditions, the other, 'organismic', adapted to conditions of change" (p47). Weber (1948) also uses the term "ideal types". According to Gerth and Mills (1948), Weber uses "ideal types" in the construction of certain elements of reality into logically precise conceptions. For example, Weber uses rationality as an "ideal type" for different forms of God-willed action in various religions (1948, chapter 13).

While the concept of ideal types is perfectly valid and common in usage, it does not accurately describe the connection mechanisms found in the cases investigated for this thesis. Therefore, I introduce a fifth type of boundary object – starting points. As it is used in this thesis, a starting point may be something like a first generation drug, or a compound that was discovered through random screening techniques, where the exact functionality of the compound may be unknown. If the goal of an alliance is a second generation drug, or a drug discovered and developed via rational drug design so that its efficacy and functionality are specified and known, the first generation drug is a starting point for such an endeavour. A starting point, then, is an initial lead for one or more projects. If it is used as a boundary object between two projects, the directions from the starting point onward and the methods that facilitate such directions may vary between the projects (which undoubtedly suggests a high degree of path dependency).

Repositories and starting points are forms of migratory knowledge that mesh the unit workers in a KVA. The meshing effect of these boundary objects comes from their ability to act as a thread between different task domains. A repository can be accessed by two different scientists (and perhaps many others) for specific purposes, without having "to negotiate differences in purpose" (Star & Griesemer, 1989, p410). They are a link between workers within a given task domain, between task domains, and indeed a link between a knowledge alliance and the social sphere beyond the collaboration. A starting point meshes unit workers in a similar fashion. It provides an interstice between two modules. If a starting point is thought of as a compound that has been identified as efficacious against a certain disease, but needs to be more potent, thus requiring the application of synthetic chemistry, this compound can be thought of as a starting point between a testing module and a synthetic chemistry module in a knowledge value alliance. As such, the work in each module begins with the compound, but the way the compound is dealt with in each module will differ.

Strauss' (1985) third level of articulation, the meshing of actors with their various types of work and designated tasks, is accomplished via the use of hidden design rules and ingrained knowledge. This is the level where production (Fujimura, 1987) occurs and individuals engage

their knowledge-about and know-how to perform specific tasks and solve the sub-problems specific to the agenda of the KVA. Hidden design parameters, or decision rules that apply only to the local module (Baldwin and Clark, 2000), guide the work in a module and mesh the actors with their work. By acting as coordination mechanisms within the module, hidden design parameters are the cords surrounding individual work. They tell the individual scientists what to do. In addition, scientists within a module rely on their ingrained repertoires of knowledge, or heuristic patterns (Liao, 2002) and states of knowing, to define the task level problem and navigate the intermediate states between problem definition and problem resolution. This activity serves to mesh the individual scientist with his or her work by engaging the ingrained knowledge of the scientist to solve the modular level problem(s).

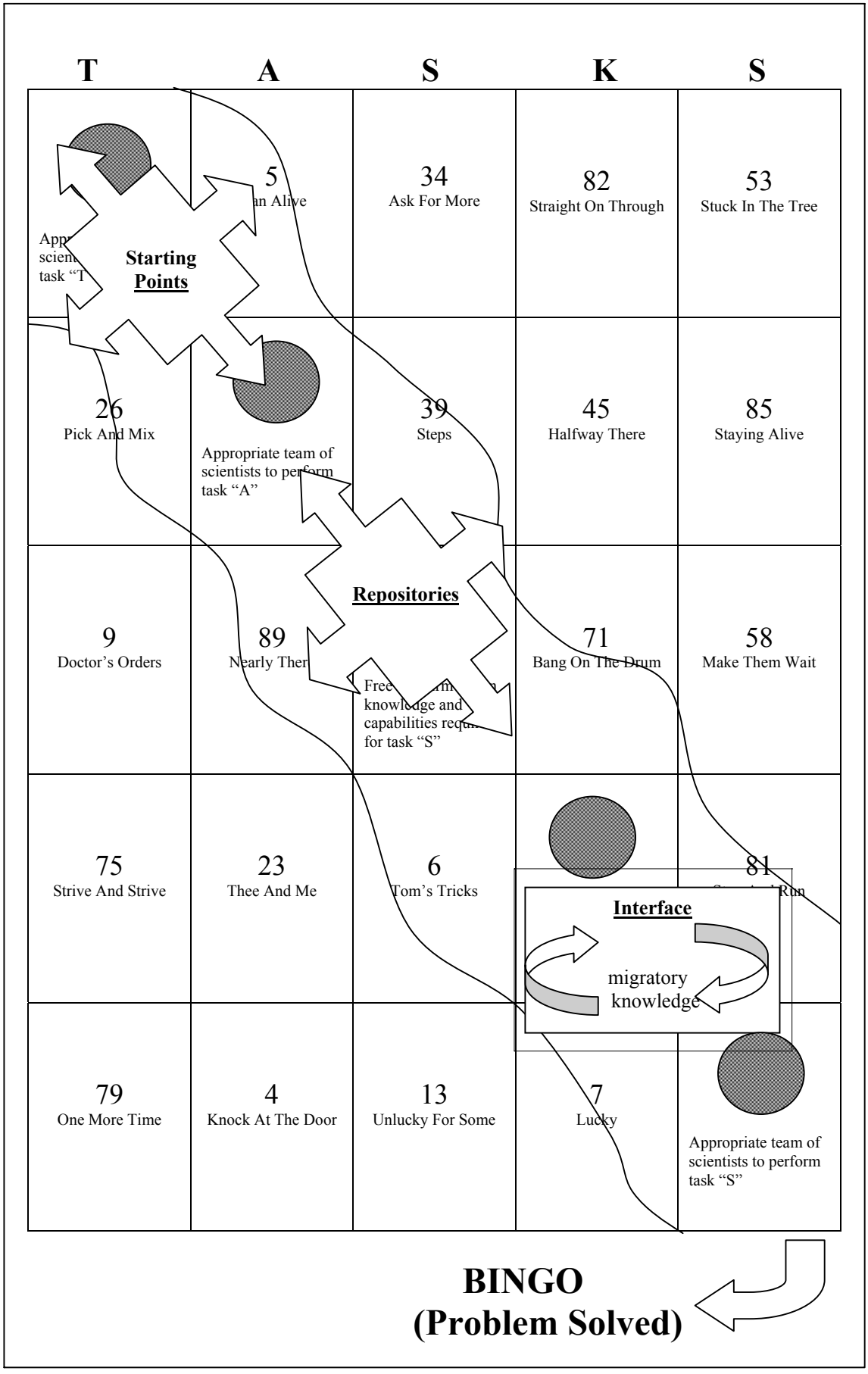
3.3.3 Modular Structures

Together, the mechanisms chosen for articulation will have a determining effect on the structure of the alliance. The specific design rules chosen for an alliance will govern how the other mechanisms, including interfaces, repositories, and starting points, are fashioned and employed within this structure. For example, if rational drug design is chosen as a design rule, the structure of the collaboration can be argued to be functional, where the modules in an alliance are centred on the different functions of rational drug design. An enzyme purification module may be present. An x-ray crystallography module may be present. A synthetic chemistry module may be present, as well as a testing module. In this type of arrangement, the movement of knowledge is predetermined by the design rules. Synthesized compounds will move between the synthetic chemistry module and the testing module, as will test results. Starting points may connect modules and move between them. A computer-generated model of a compound that is hypothesized to effectively target an enzyme may connect a computational chemistry module and a synthetic chemistry module.

The modular structure of an alliance provides a foundation for the knowledge architecture of that alliance. Engaging the Biotechnology Bingo metaphor offered in the previous chapter, the mechanisms for articulation are represented in a knowledge architecture in the following

manner. Interfaces, repositories, and starting points appear at the intersections of modules. The interfaces and starting points used in a collaboration are specific to that alliance, whereas repositories (with the exception of compound libraries) and design rules are not necessarily specific to the collaboration and, therefore, may move beyond the confines of the architecture to be applied to and used in other knowledge value alliances and research agendas. The design rules amount to a force, which appears in the diagram below as parallel squiggly lines, that reduces the risk of the marks on the card falling out of alignment. Design rules are used in an attempt to position all marks on the card into a diagonal or horizontal line. Together, these mechanisms provide for alignment in complex conditions.

Diagram 3.4 Articulation Mechanisms and the Knowledge Architecture



While these various articulation mechanisms provide a means through which architects can attempt to ensure that the knowledge bases of the members of a KVA are connected and appropriately integrated, they do not take into consideration how the sub-problems are solved at each modular level. This is, as stated previously, the role of ingrained knowledge and hidden design rules. This type of activity can be thought of as occurring within a group of scientists that are located in a given module, which could be module "T", "A", "S", "K", or "S", as is presented in Diagram 3.4

Nevertheless, all of the activities discussed in this section, including the act of coordination seen at articulation level one, the act of meshing unit workers evident in articulation level two, and the meshing of individual scientists with their work that is the core of articulation level three, occur within the modular structure of the alliance. The modular structure is found in varying degrees in the cases presented in this thesis, and the design rules differ between some of the cases. All the alliances in this thesis have a modular structure, but the design rules determine if the modules are split by product or function. That is, a modular structure is centred on the division of labour around specializations, but this does not limit the specializations being based on products or functions. Rational drug design is an example of a function-oriented structure, where modules are split between the functions of enzyme purification, structure elucidation, crystallization, synthesis, and testing. This function-oriented division of labour has implications for the process of knowledge production and movement. The task of structure elucidation will require the input of enzyme purification. The task of synthesis will depend on structure elucidation. Thus, there is a hierarchical arrangement among the structure of an alliance, the design rules, and the knowledge processes.

Does this destroy the modularity of the alliance? My argument is that it doesn't totally destroy it. It may increase the interdependencies of the alliance, but the alliance is still partially modular. These arrangements are modular because the firm and the university research centres operate independently of each other. Without the collaboration, they would still exist. The alliance can be separated or split and the modules composed of the firm and the research centre can be recombined with other institutions. The tasks performed within the modules that make-

up each side of the alliance can also be performed in other alliances. For instance, if the task of determining the three-dimensional structure on an enzyme (structure elucidation) is completed, that task module can be "plugged" into another arrangement where tasks consist of synthesizing compounds to target that enzyme and modeling the structure of the enzyme with those compounds. In pointing out the function-oriented structure of the alliance that is established by rational drug design, I am mainly suggesting the role of design rules in the implementation of a structure and the role of the structure in the production and function of knowledge.

3.4 Conclusion

Knowledge, then, is seen as both migratory and ingrained. The two views are not mutually exclusive. Knowledge, as it is conceptualized for the purposes of this research agenda, carries with it characteristics of both paradigms. It comes in the form of objectified knowledge, including repositories, compounds, techniques, structures of enzymes, etc., and it resides in the minds of individual scientists. Problem solving in the knowledge architecture is not possible unless knowledge is considered to be both migratory and ingrained.

The two types of knowledge coexist. Migratory knowledge allows for problem resolution. In addition, certain forms of migratory knowledge, namely repositories and starting points, mesh the efforts of various unit-workers, both across and within modules. Ingrained knowledge, on the other hand, meshes the specific actors of the architecture with their work, permitting the identification and resolution of sub-problems at the modular level.

The knowledge processes that make use of these types of knowledge, however, are operationalized through the modular structure of the alliance. The processes necessary to accomplish the purpose of the alliance, and how and in which directions knowledge should move to accomplish the desired output of the collaboration are determined based on the structure of the alliance. The design rules govern the knowledge processes that occur within the modular structure of the alliance. While such a modular organization of activities serves to

reduce the complexities associated with a collaborative endeavour in highly experimental science, it does not reduce the uncertainties of the science itself.

The knowledge architecture, along with the modular structure that is its bedrock, is more that just knowledge, people, and processes that are governed by design rules. Because this modular arrangement is composed of people and interdependent elements, further examination is necessary in relation to the ecological context of the architecture and the communication practices that create this context. The next chapter embarks on this agenda.

Chapter 4 Cultural Ecology & Communication

> "…knowledge used in innovation does not come in watertight boxes but is mutable and multidimensional, precisely because of the complex social processes by which it is generated and utilized" (Faulkner, 1994, p449).

In the previous chapter, I put forth an argument made by Latour (1987) that highlighted the inseparability of a theory and the elements that a theory seeks to explain[53]. Hence, while progress has been made in terms of developing a theory of knowledge synthesis and task alignment in university-industry collaborations in biotechnology, this theory remains incomplete without the consideration of the people, the holders and seekers of knowledge, and the context in which these people work. Addressing concepts such as the movement of knowledge or the use of ingrained knowledge to solve problems requires an explanation of where and how these events occur.

Another conjecture introduced in a previous chapter, specifically in chapter two, is the conceptualization of collaborations between university and industry as knowledge value alliances, which take place in the larger context of knowledge value collectives. In turn, these knowledge value collectives dwell within the biopharmaceutical industry. This expansion of domains may appear to blur the picture painted thus far by the thesis. In the words of Latour (1987), however, "all the distinctions one could wish to make between domains", whether they are between the knowledge value alliance and the knowledge value collective, between the collective and the biopharmaceutical industry, between the biopharmaceutical industry and other systems of society, or between academia and industry, "are less important than the unique

[53] A footnote was presented in section 3.2.2, following the argument made by Latour (1987) that stresses the deficiencies associated with doing a history of the hammer without considering the nails, planks, houses, etc. that are closely intertwined with the concept of a hammer.

movement that makes all these domains conspire towards the same goal: a cycle of accumulation that allows a point to become a *centre* by acting at a distance on many other points[54]" (p222 – emphasis his own).

The tools, technologies, and work practices, as has been argued in the previous chapters, may allow for the knowledge inherent in the knowledge architecture to be integrated, but by what means and with what amount of potency does the knowledge generated in a knowledge value alliance contribute in the grander scheme of things? Does a KVA play a role in Latour's "cycle of accumulation"? If the Biotechnology Bingo game is won, does it matter to anyone else but the winner(s) and the loser(s)? These issues obviously take the discussion beyond the context of one knowledge value alliance, and even beyond the context of one knowledge value collective.

The journey beyond these realms requires the application of certain concepts, namely Latour's (1987) concepts of mobility, stability, and combinability. Latour (1987) defines these concepts as the ability to move (mobility), the quality of being able to avoid distortion, corruption, or decay in the process of movement (stability), and the attributes of being susceptible to accumulation and aggregation, and being useful to people in other contexts (combinability) (p223). These concepts are used to further define the knowledge architecture, relate current understandings from the sociology of knowledge to the research agenda, and further classify the collaborations under scrutiny in terms of modularity and interdependency.

This agenda is pursued in the following sections. The concepts of mobility, stability, and combinability resonate throughout the chapter. The goal of furthering the definition of the knowledge architecture is tackled in the first section, The Cultural Ecology of the Knowledge Architecture. Linking current ideas in the sociology of knowledge with the research agenda is the subject of the second section. The final section of this chapter deals with communication and, in doing so, argues that while modularity is certainly associated with the knowledge value

[54] As I understand and apply Latour's (1987) quotation, the focus is on a domain's (a group of scientists, a firm, a knowledge value collective, etc.) efforts to accumulate enough knowledge to become essential in anyone else's desires or needs to use that knowledge. In addition, the cycle of accumulation is a competitive endeavour, whereby accumulating more knowledge than competitors allows for displacement of those competitors.

alliances presented in this thesis, the modularity described here is not so extreme that it completely precludes interdependency.

4.1 The Cultural Ecology of the Knowledge Architecture

It is essential to address the contextual elements in any discussion on knowledge. Both the cognitivist and anti-representationist approaches to knowledge recognize the significance of context in the conceptualization of knowledge. As a result, an understanding of knowledge as both migratory and ingrained carries with it the acknowledgement that context is important. This is a virtue, for as Howells & Roberts (2000) note:

> Although much innovation, and indeed new knowledge, comes from purposeful study, learning and action by economic agents in a market-oriented and mediated context, much important knowledge does not. Serendipity and non-market situations are still highly important; social interaction and embeddedness, past historical actions, geographical proximity, trust and chance all play a significant role in knowledge processes (p21).

With this in mind, it becomes particularly important to address the nature of relationships within the knowledge architecture, given that these arrangements are not completely modular and there is room for interdependency. In addition, the particular physicalities and systematic routines that make up the architecture must also be examined in order to determine the role that they play in the interactions between the collaborative participants. The relationships that exist between members of the collaboration, the physicalities that shape these relationships, and the systematic routines are what I call the *cultural ecology* of the knowledge architecture.

The cultural ecology of the architecture can best be described by socio-psychological constructs, such as trust and openness[55], the use of "things" (Latour, 1987)[56] to alter usual patterns of human conduct, and a social organization centred on division of labour. Following

[55] Trust and openness are classified here as elements of the cultural ecology of the knowledge architecture because of the phenomenological nature of the knowledge architecture itself. Cultural ecology suggests the formation of a culture pertaining to how individuals interact with their environment. If the environment itself is phenomenological, then it is logical to think of elements of that environment as being phenomenological too. Therefore, trust can be conceptualized as a feature of a phenomenological environment in the same manner that landscape is conceived of as a feature of a physical environment.

[56] Recall here that Latour (1987) defines "things" as new objects, tools, or techniques that, through a process of routinization and reification, become a "black box", whereby their inner workings are no longer a matter of controversy or inquiry. He offers examples such as polonium, an ultracentrifuge, and a can opener.

Barney and Hansen (1994), trust and openness are conceptualized as characteristics of the interpersonal relationships inherent in the knowledge architecture. They determine the ambiance of the architecture. The concept of "things" is used to demonstrate how particular objects, tools, routines, or technologies can mediate and modify human interaction. The social organization of the architecture provides the platform for knowing and understanding the material world through the social world, which, as Freidson (1976) contends, is the only way one can come to know the material world[57]. Conceptualizing the social worlds of these knowledge value alliances in terms of a division of labour allows one to develop a better understanding of the material world, namely the world pertaining to the knowledge, as knowledge is the central material that is produced and packaged in the collaborations investigated in this study. Together, these constituents help to further define the knowledge architecture and the relationships that exist within it.

It must be remembered that, in chapter two, the argument was made that interdependency and modularity are both features of the knowledge architecture (interdependency within modules, modularity across the scope of the architecture, and even certain levels of interdependency between modules in cases where the tasks of the knowledge architecture form an iterative or sequential process). As a result of the interdependency inherent to these alliances, actors in the collaboration will indeed interact in a bid to align their social worlds, and attempt to share knowledge, mainly in the form of migratory knowledge. Therefore, a distinct culture, stemming from the interaction and knowledge sharing activities of the members of the knowledge value alliance, will emerge in the architecture.

4.1.1 The Social Ambiance of the Knowledge Architecture

Wathne, Roos, and von Krogh (1996) define three key factors relevant to the knowledge sharing process that relate specifically to the actors involved and help to define the ambiance of the knowledge architecture. These factors are: openness, prior experience, and trust. Using the

[57] In his discussion on the division of labour as social interaction, Freidson (1976) suggests that the division of labour can be analyzed on a wholly social level, "independently of the material world of technology and production…but only on the basis of understanding that the material world is known and assessed through the social world" (p312).

metaphor of the game of Biotechnology Bingo, these factors come into play when considering whether all parties involved in the game are working towards winning. I use this idea, and subsequently elaborate on it, in the following discussion to define the concepts of openness and trust. The actions of the actors partaking of the game can be further defined by Knorr-Cetina's (1981) first aspect of indexicality[58], opportunism.

The opportunism defined by Knorr-Cetina (1981) is different from the opportunism that is normally referred to in the management and interorganizational literature[59]. The common conceptualization of opportunism is centred on one party's inclination to take advantage, for its own benefit, of another party. For example, Williamson (1985, p47) defines opportunism as, "self-interest seeking with guile. This includes but is scarcely limited to more blatant forms, such as lying, stealing, and cheating…More generally, opportunism refers to the incomplete or distorted disclosure of information, especially to calculated efforts to mislead, distort, disguise, obfuscate, or otherwise confuse" (cited in Hill, 1990, p500).

Knorr-Cetina's (1981) version of an opportunist is quite different. It engages the concept of tinkering (Knorr, 1979) and suggests that scientists are constantly involved in "producing and reproducing some kind of workable object[60] which successfully meets the purpose they have temporarily settled on" (p34), seizing the various *opportunities* in the production process that allows them to accomplish a specified goal. Opportunism, as defined by Knorr-Cetina, is taking advantage of various opportunities, rather than people, to meet the requirements of a specified

[58] Knorr-Centina (1981) defines indexicality as indexical logic, or the contingency and contextuality of scientific action, which demonstrates that the products of science are hybrids, bearing the mark of the mode by which they are produced (as opposed to a special scientific rationality) (p33). She suggests that the hybrid nature of scientific products comes from the input of different areas of science (and the ingrained knowledge of the producing scientists) and the process of production does not somehow shed these different inputs. This is contradictory to the account of Mode 2 knowledge offered by Gibbons et al (1994). Mode 2 knowledge is conceptualized as being transdisciplinary and does not contribute to individual areas of science used in its production. These two different views of knowledge and whether or not the advancement of cross-disciplinary knowledge contributes to individual disciplines are discussed in more detail in chapter nine.

[59] Knorr-Cetina's definition of opportunism is used in alignment with the precedent set in chapter two, in which the transaction costs account of collaboration was argued to be inappropriate for alliances between university and industry in biotechnology. Opportunism is indeed a construct of the transaction costs scholars, and therefore, to adopt such a construct now would contradict the argument made in chapter two.

[60] The production of a particular object to fulfill the requirements of a specific purpose is similar with Latour's (1987) conceptualization of "things", which is elaborated on later in this section of the chapter.

purpose, thereby demonstrating a commitment to the achievement of the purpose. This definition is, of course, more consistent with an emphasis on environmental uncertainty and luck.

In chapters two and three, I argued that the purpose of the alliance is to solve a particular technological problem, which can be solved by the participants of the collaboration via migratory knowledge and the appropriate articulation process to integrate various casts of ingrained knowledge. Knowing, then, what they are working towards, the members of the knowledge value alliance can determine what must be accomplished at the modular level to achieve the goal of problem resolution – to see how their specific tasks fits into the larger scheme of things, although it is their ingrained knowledge that is ultimately used to solve the task. As an opportunist (in the Knorr-Centina sense of the word), a collaborative participant would take advantage of all opportunities in performing the designated task, and make every effort to work toward the completion of the desired output.

The ecology of the knowledge architecture is characterized by openness when all parties involved in the collaboration are honestly working towards succeeding at solving the problem. It is important to note that members of a collaborative alliance often have other collaborative engagements that create a certain amount of competition for the scientists' resources. Being open about these other commitments allows for the adoption of realistic goals in terms of the timeframe set out for discovery and development. In addition, because of the difficulties associated with performing the type of science inherent to these collaborations, the possibility remains that the experiments designed to make progress toward the desired outcome could fail. Again, here, it is essential that those attempting experiments, particularly in cases where the experiments fail, are open about the outcomes of such endeavours so that alternative arrangements can be made for the pursuit of the desired output.

Admitting to a failure of an experiment, however, may be problematic for two reasons. Often times there are large amounts of money riding on the success of the experiment and scientists may be ashamed to admit failure because it makes them appear fallible, and in the end, it could have a detrimental impact on their reputations. With this in mind, assessing a

scientist's inclinations for openness can be difficult, as can evaluating a scientist's ability to tackle a novel problem or experiment. Architects of an alliance often seek collaborators with a reputation for success and quality performance. Their reputations can be judged by the outcomes of other collaborations, performance track records, or social standing. Following Merton (1968) and Podolny (1994), Stuart (2000) notes that, in the event of uncertainty about the quality of someone, evaluations are strongly influenced by the social standing of the actor.

The architects and other members of the knowledge value alliance can make a more reliable judgment of fellow participants' openness and ability to perform based on prior experience[61] (whether or not the participants of the collaboration have worked together in the past), but neither prior experience nor a reputation for high-level performance are complete indicators of one's ability to succeed in current endeavours[62]. There is inherent difficulty in assessing ingrained knowledge and determining whether this knowledge is sufficient for the task at hand. Furthermore, when novel problems are to be solved, proven track records of performance may not be a valid indicator of ability to solve the problem.

Trust, then, becomes a central feature in the cultural ecology of the knowledge architecture. The type of trust specified here is a characteristic of interpersonal relationships and in the context of a knowledge architecture, it can be thought of as collective trust[63]. As Lewis and Weigert (1985) suggest, "[b]eing a collective attribute, trust is applicable to the relations among people rather than to their psychological states taken individually[64]" (p968). Therefore, collective

[61] Zollo, Reuer, and Singh (2002) report findings that "partner-specific-experience" influences the performance of collaborative agreements in the biotechnology industry.

[62] This is illustrated in Case C, Chapter Eight, whereby the collaborators on both sides of the alliance boasted a track record of performance in the work pertaining to the collaborative agenda. Despite their proven abilities, the collaboration under investigation has not been able to attain the desired output in the time frame specified by the first contractual arrangement.

[63] This type of specification is necessary because trust, probably more than any other construct, remains immeasurable and, consequently, the variations in types and descriptions of trust are vast. As Hosmer (1995) contends, "there appears to be a widespread agreement on the importance of trust in human conduct, but unfortunately there also appears to be equally widespread lack of agreement on a suitable definition of the concept" (p380).

[64] The argument can also be made that psychological states must be taken into account because there may be members of an alliance who will deliberately cheat others or who have been exposed to such cheating. The context in which these alliances operate is characterized by high levels of uncertainty and thus the contracts to guard against such "cheating" are necessarily incomplete. Nevertheless, as is discussed in more detail later in this chapter and demonstrated in chapter nine, members of an alliance go to great lengths to protect valuable knowledge (usually through the practice of secrecy), even to the extent of

trust can be used to define the cultural ecology of the knowledge architecture. In this sense, trust is the collective confidence (which can be supported by reputational assessments, evaluations of performance track records, or a reliance on social standing, but doesn't necessarily have to rely on any of these ex ante proxies) in the ability of members of an alliance to complete their designated tasks.

Following Cummings and Bromiley (1996), collective trust is a shared belief of a group of individuals that another individual or group 1) makes constructive efforts to behave in accordance with any commitments, 2) is honest in whatever negotiations preceded such commitments, and 3) does not engage in opportunism even when the risk of being discovered is minimal (cited in Jarvenpaa, Knoll & Leidner, 1998, p3). While the third aspect rigidly adheres to the mainstream definition of opportunism, the first two attributes reflect opportunists in the Knorr-Cetina fashion. The cultural ecology of the knowledge architecture, then, can be said to be characterized by collective trust when the members of the knowledge value alliance believe in fellow participants' efforts to work towards the goal of problem resolution and their honesty in negotiating the commitments[65], which serve in meeting that goal.

These three elements of the social ambiance of the knowledge architecture, openness, prior experience, and trust, can have a beneficial impact on the alignment of the social worlds of the actors involved in the alliance. I do not wish to paint the picture that what we have here is an instance of extreme modularity, with little or no interaction between members of the alliance, and therefore, a case in which the social and cultural backgrounds of the collaborative participants can be ignored; or that the level of modularity that does exist in these types of collaborations is enough to completely mesh the social worlds of the members of the alliance. I would contend exactly the opposite, stating that the complete alignment of social worlds is close to impossible,

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excluding some members of the alliance from access to potentially useful knowledge. Thus, trust can really be addressed as both a collective attribute and a psychological state. Members of an alliance do not always "trust" their fellow collaborators with potentially valubale knowledge, which can be viewed from the standpoint of trust as a psychological state. But there is also a "collective trust" in the other members of the alliance and their abilities to at least work toward the desired output.

[65] These negotiations may refer to the allocation of specific tasks and the work to be performed within each module, or the amount of money required to perform the task in cases where funding is being pursued.

but through the application of appropriate principles of interaction, namely, openness, prior experience and trust, alignment of social worlds can be achieved to the extent that it makes the technological problem of the alliance doable. And, indeed, because of the distinct levels of interdependency in the collaborations discussed in this thesis, considerable effort in achieving this state of alignment is warranted.

4.1.2 The Use of "Things" to Mediate and Modify Behaviour

Clashes of social worlds and cultural values can be mitigated (and I maintain my earlier thought here that they cannot be altogether eliminated, but they can be considerably reduced) through the use of "things" (Latour, 1987) to mediate or modify social interaction. Expanding upon this logic, it can be argued that the cultural ecology of the knowledge architecture can be further defined by elements ("things"), such as the use of electronic communication, the production of compounds, or the use of specific techniques.

For instance, Kristensen and Vinding (2001) offer evidence of a "thing" mediating human interaction. This study investigates the exchange of employees, the exchange of prototypes, and the use of electronic media as mechanisms supporting the transmission of knowledge in new product development. In this study, particular "things", such as prototypes and electronic media, are used to mediate human interaction. Essentially, they represent a form of migratory knowledge that remains stable through the process of transmission so that different parties may utilize their ingrained knowledge to evaluate the legitimacy of a knowledge claim. Without these "things", the members of the development team would be relegated to traditional forms of communication that could not ensure the stability in meaning of the migratory knowledge and conflict could ensue as a result of different interpretations of the migratory knowledge based on different cultural backgrounds.

"Things" can also serve to characterize the ecology of the knowledge architecture by modifying human interaction. The object, which scientists aspire to create (that was alluded to earlier in this section), once created, can replace the scientists' verbal commitment to solving the larger problem of the knowledge value alliance. In such a sense, the object would be a more

tangible contribution to the process of problem resolution and may represent a modification of a credible commitment (de Laat, 1997)[66], which is typically based on modes of and guidelines for interaction, from the form of a protocol or specified work arrangement to a "thing". For example, the production of compounds in an alliance where the desired output is a drug lead would be a much more credible commitment than signing the contract to produce the compounds that may eventually result in a drug lead. If an object is produced that demonstrates progress toward the desired outcome, then that object is indeed a much more solid commitment to the collaborative agenda that could replace the contract or verbal commitment to the attainment of desired outcomes, in addition to demonstrating ability to perform in relation to these outcomes.

Alternatively, "things" may have the effect of altering the third level of articulation discussed in chapter three (the meshing of the actors with their various types of work and implicated tasks). Knorr-Cetina (1981) provides an account in which a task that would normally be performed by a scientist was, instead, executed by a service lab.

> I saw a paper on functional properties of proteins based almost exclusively on chemical determinations supplied by one of the institute's specially designed 'service' laboratories. The scientist who wrote the paper made it clear to me that, if he had been forced to perform (or even supervise) the work himself, he would have selected an entirely different series of tests from those available at the service lab; but given the techniques available, he would prefer to use the service lab whenever possible (Knorr-Cetina, 1981, p35).

Here, the "thing", the technique for defining the functional properties of proteins, was not an activity in which the scientist was meshed with his task of defining the properties. Instead, the "thing", the technique for defining the functional properties of proteins, served as a modifier of human interaction in creating a dependency between the scientist and his associated institute's "specialized service lab". Given that the technique was fairly routine, that there were most likely established rules for defining the functional properties of proteins, and that the results of employing the technique were both mobile and stable, the scientist could count on the

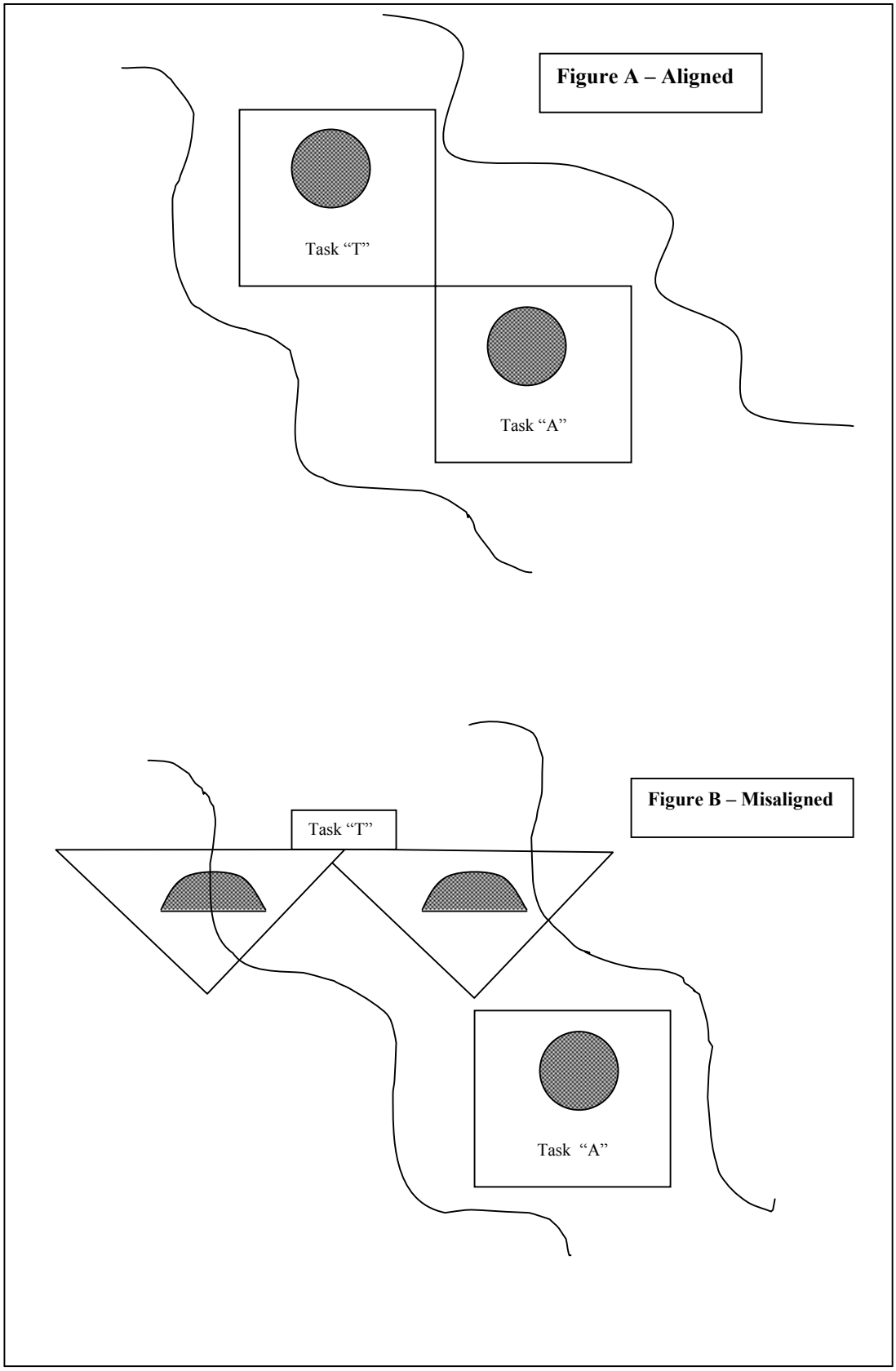
[66] De Laat (1997) offers the idea of a credible commitment, which may be in the form of a contract or a verbal pledge, as a mechanism to open up the gate between collaborative partners where there would normally be a dam to the flow of valuable knowledge. This term, however, can also be traced back to the work of Williamson (1983), in which he defines a credible commitment as an undertaking to support alliances and to promote exchange (the opposite of a credible threat).

validity of the findings from the service lab. In such an instance, the "thing" shapes the cultural ecology of the knowledge architecture referred to in Knorr-Cetina's example (not to mention the number and types of players in the architecture).

4.1.3 The Social Organization of the Architecture

In essence, the "thing", in the above case, is impacting on the division of labour, or the social organization of the architecture. The consequences of such an impact must be considered because, in the words of Blumer (1969, p87-88), "[s]ocial organization is a framework inside of which acting units develop their actions…It sets conditions for their action but does not determine the actions…It shapes situations in which people act, and…it supplies fixed sets of symbols which people use in interpreting their situations" (cited in Freidson, 1976, p311). With the revision of the social organization of an architecture comes the associated alterations to the cultural ecology of the organization, impacting how the members of the knowledge value alliance interact and who interacts with whom. As a result, new design rules, or new tools, technologies, and work practices, are required to ensure the alignment of the work being conducted in the knowledge architecture after a change in social organization. Taking an excerpt from Diagram 3.4, this effect is demonstrated in the following series of figures.

Diagram 4.1 Misalignment after Change in Social Organization



In Diagram 4.1, a change in the division of labour concerning task "T" causes the design rules (represented by the squiggly lines) to cut directly across the activities that represent task "T" (as seen in Figure B). This type of change is common in university-industry alliances where, for instance, the university module may be required to perform the task of synthetic chemistry. This task, however, may be split[67] between the university scientists and the research assistants or PhD students because the technique for synthesis (the "thing") is routine and shared among the members of the module. As a result of such a split, the alignment originally provided by the design rules, which is represented by Figure A in the diagram, is no longer ensured. Some activities of task "T" may occur outside of the boundaries of the original design rules, and therefore, the meshing of the various tasks, clusters of tasks, and segments of the knowledge architecture (the first part of the articulation process) may not be attained[68].

In the face of the revision of the social organization of the architecture, which may result from the modifications of human interaction inspired by "things" or through other various mechanisms, existing design rules will have to be revised or new design rules pertaining to the knowledge architecture will have to be devised and implemented. In the example provided here, these design rules will need to force alignment between task "T" and task "A", so that the tasks become part of a diagonal line and the game of Biotechnology Bingo can still be won.

This can be accomplished in one of two ways, depending on whether the split portion of task "T" is part of what Baldwin and Clark (1997, 2000) refer to as visible or hidden information

[67] Splitting is one of the six modular operators defined by Baldwin and Clark (2000). "Splitting takes a single-level design [process] with interdependent parameters and converts it into a hierarchical design [process] with a core set of independent modules. After the split, however, each module will constitute a separate design in its own right…" (p133). While Baldwin and Clark (2000) detail other modular operators and suggest that the operators can be used in conjunction with one another to create design options, they do not address the need for new design rules in the use of splitting. They do note, however, that design options can only be pursued within the limits set by the design rules. Inversion, their fifth modular operator, is the one that dictates the need for new design rules. "The opertor *inversion* describes the action of taking previously hidden information and 'moving it up' the design hierarchy so that it is visible to a group of modules" (p138 – emphasis their own). The example above, however, is clearly an instance of splitting, not inverting, and it is my submition that new design rules are necessary in the case of splitting.

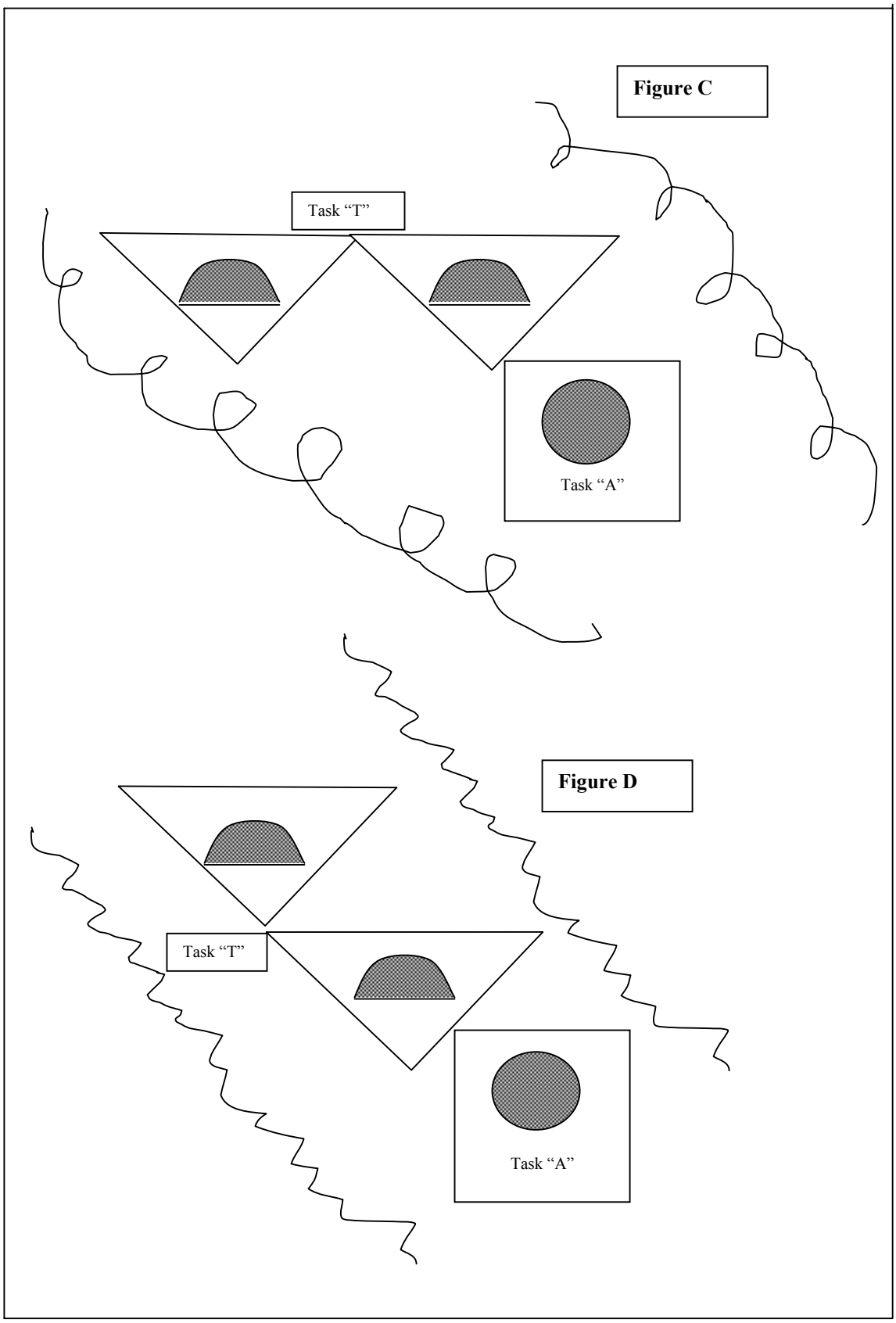
[68] It can be argued that attainment of articulation is achieved in cases of successful delegation or outsourcing. In such instances, however, there are still rules to be adhered to; each time a task is delegated or outsourced these rules must be checked and/or communicated to ensure alignment between the delegated or outsourced task and the related tasks. It does not matter who performs the task. The important aspect is that the task work is aligned with the other tasks required to resolve the larger problem to which they all contribute.

in the design process[69]. If the portion of task "T" that has been split is part of the visible information in the design process, the design rules will have to be revised to ensure the alignment between both portions of task "T" and task "A", in addition to the other tasks in the architecture, because visible information affects all modules. This could be accomplished by revising existing design rules to restore the alignment or implementing new design rules to create an entirely new alignment, as indicated in Figure C of Diagram 4.2. If, on the other hand, the portion of task "T" that has been split is part of what Baldwin and Clark (1997, 2000) refer to as the hidden information in the design process, the split will only affect the task "T" module and new design rules will only be necessary for the module represented by task "T". The aim here would be to bring the split portion of task "T" into alignment with the remainder of the work being performed in the task "T" module. The result of drafting and implementing new hidden design rules in this manner is demonstrated in Figure D in Diagram 4.2[70], in which the split portion of task "T" that sat adjacent to the remainder of task "T" in Diagram 4.1 is forced into the diagonal line formed by the remainder of task "T" and task "A".

[69] The visible information affects subsequent design decisions and, therefore, is communicated to all those involved in the design process; whereas, hidden information does not affect decisions beyond the local module and, therefore, does not have to be communicated to anyone beyond the modular level (Baldwin and Clark, 1997).

[70] This portion of the diagram could also serve to represent the revision of existing design rules in response to a split relating to the visible information of the design process, whereby alignment is restored. As demonstrated in Diagram 4.1, the alignment originally produced a diagonal line. When task "T" was split, however, that alignment was destroyed. If the design rules were revised to restore alignment in response to a split in relation to the visible information in the design process, the re-establishment of alignment would appear in the same manner it does in Figure D of Diagram 4.2.

Diagram 4.2 Realignment after Change in Social Organization



The need to restore alignment is increased when the tasks are iterative. For example, in some cases, the tasks performed in a collaboration may follow a sequence of testing, synthesis of compounds, additional testing, and further synthesis, until the desired outcome has been achieved. The arrangement is still modular in the sense that there is a division of labour and testing of compounds can be performed concurrently in one module, while the synthesis of compounds that have already been tested is occurring in another module. As Fujimura (1996) contends, "[p]roblem structures are set in mud, not stone. They are rarely if ever purely generative or purely modular[71]" (p172). Because they are "set in mud" (and not stone) problem structures are open to revision. With this revision, however, comes the need to attempt to ensure the articulation of the relevant task work. If there is a split in the synthesis module, it becomes particularly important for not only hidden design rules to provide alignment within the module, but for these hidden parameters to be in line with the visible design rules.

In the case of the iterative and reiterative tasks, a visible design rule might stipulate increased activity of a compound with each iteration. If the hidden design parameters do not specify how this increased activity can be achieved, and thus the hidden design rules do not support the visible rules, the iteration between tasks is likely to continue for an unnecessary period of time, and consequently threaten the attainment of the desired outcome of the alliance.

In the preceding diagram, the design rules, represented again by the squiggly lines, provide for the realignment of the various task modules in the knowledge architecture, representing a case where the hidden design parameters support the visible ones. Without this process of realignment, the knowledge value alliance would be confronted with the possibilities of not being able to achieve the desired output and not being able to solve the designated technological problem because of a lack of task articulation. What must be remembered here, though, is that the need for this realignment was sparked by a change in the cultural ecology of the architecture, namely by a "thing" modifying the cultural ecology and consequently changing

[71] Fujimura (1996) defines modular problem structures as problems in which it does not matter which order scientists solve their designated sub-problems. She defines generative problem structures "…as necessarily serial, because the 'subsequent' problem is dependent on the 'previous' problem's solution" (p172).

the social organization of the structure. Therefore, an architect of a knowledge value alliance must not only be aware of the tools, technologies, work practices, and types of knowledge specific to the knowledge architecture, but also of the cultural ecology of the architecture and the impact of changes in the cultural ecology on the arrangement and activities within that architecture.

The specific elements of the cultural ecology of the knowledge architecture that an architect should be concerned with include the social ambiance of the architecture, or the openness, levels of prior experience, and trust; the "things" being employed in the architecture and their various effects; and, the social organization of the architecture. Adhering to the premise that a knowledge architecture is characterized by both interdependency and modularity, a concept presented in chapter two, implies the existence of social interaction and a simultaneous division of labour amongst the members of the knowledge value alliance, both of which are subject to alteration.

The cohesion within the architecture can also be affected by an agitation from beyond the knowledge architecture. To use the metaphor of a Bingo game, a person sitting at a shared table may abruptly shake the table in a rage of excitement (or frustration), causing the marks on other players' cards to become misaligned. In other words, influences from the cultural ecology *beyond* the knowledge architecture may disrupt the arrangements *in* the knowledge architecture and, therefore, the context beyond the architecture must also be investigated. Furthermore, the cultural ecology beyond the knowledge architecture should also be assessed to determine whether or not the work performed in the architecture has significance beyond the knowledge value collective. These are the topics visited in the next section.

4.2 The Cultural Ecology Beyond the Knowledge Architecture

The cultural ecology beyond the knowledge architecture is one that has been characterized by tremendous change over the course of the past two decades, especially in the area of the biopharmaceutical industry. Some of these changes were revealed in chapter two in

the discussion relating to the infiltration of biotechnology into the pharmaceutical industry. There are, however, additional changes that have occurred and have impacted how individuals handle knowledge. These changes include the natural excludability (Zucker, Darby, & Armstrong, 1998), general excludability, and appropriability (Liebeskind et al, 1994) of knowledge relating to biotechnology. Natural excludability occurs because not everyone is able to decipher and utilize knowledge related to biotechnology. General excludability occurs because patents and the efforts of scientists to keep some knowledge secret impede others in their attempts to access and use the protected knowledge. Appropriability, on the other hand, occurs because those that are qualified to decipher and utilize knowledge relating to biotechnology may use it to their own benefit at the exlusion or expense of others. The impact of these changes in the cultural ecology beyond the knowledge architecture can be seen in the way in which new knowledge is dealt with inside of the architecture and in the potential effect that the knowledge value alliance can have in the broader scheme of things.

The past half-century has brought new understanding in the sociology of scientific knowledge. The traditional view depicted stability in meaning and free flowing knowledge, which moved unhindered between various domains to anyone who desired to learn from the knowledge creator, regardless of context (Merton, 1957; Stark, 1958). The assumptions behind this view were based on equivalent social strength among knowledge producers and knowledge seekers, invariable access to knowledge across the broad range of society, and unwavering ability to interpret new knowledge. Indeed, this is the conviction that, for a long time, has helped to define the role of the academic scientist[72].

The work of Michael Mulkay, among others, popularized the view that the variance in social position and intellect, and the political influences that exist in society had to be taken into account in assessing the diffusion or transference of knowledge among members of society. In

[72] It is also the view that has fueled the argument against collaboration between the academy and industry. This argument is premised on the notion that such types of collaboration will only serve to hinder the "free flow of knowledge" because of the need for industry to protect and hoard knowledge in a bid to reap monetary rewards from its commercial application. Along this line of thought, Florida and Cohen (1999) contend that, "[f]or universities, the key issue has to do with the trade-off between the quest for eminence and the pursuit of funding support from industry" (cited in Ranga, 2001, p6).

accordance with Mulkay's (1992) revision of the standard view of the sociology of knowledge, value and meaning are direct attributions of the recipients of knowledge, representing a structure where actors take centre stage. "Knowledge claims move through a sequence of phases, within which their content and their meaning are continually reinterpreted in accordance with the demands of different interpretative and social contexts" (Mulkay, 1992, p57).

While the revised view has undoubtedly made headway in how the sociology of scientific knowledge is understood, there is still work to be done[73], for, as Latour (1983) argues,

> [s]ociology of science cannot always be borrowing from sociology or social history the categories and concepts used to reconstruct the 'social context' inside which science should be understood. On the contrary, it is time for sociology of science to show sociologists and social historians how societies are *displaced* and *reformed* with and through the very contents of science (p160 – emphasis added).

Fortunately, some sociologists of science have managed to produce empirical findings that answer Latour's (1983) call. Zucker et al (1996) are an example. In an investigation showing how trust can produce organizational boundaries, these authors conclude that, when scientific discoveries (whether from the academic or commercial arena) carry a significant value, those responsible for or closely associated with the discovery methodically exclude potential competitors from the information pertaining to the discovery. This finding is the backbone of the concepts of the general excludability and appropriability of knowledge in biotechnology. Other groups of people designing drugs are indeed displaced and reformed because of the general excludability and appropriability of knowledge related to biotechnology.

[73] This is not to say that the view put forth by Mulkay (1992) is not credible. There are, indeed, numerous reports to suggest that context plays a deterministic role in how knowledge is interpreted and applied. Brannen, Liker, and Fruin (1998) argue that knowledge is so context-oriented that it must undergo a process of de-contextualization before being transferred and must additionally be re-contextualized by the recipient seeking meaning in the knowledge (cited in Cummings & Teng, 2003). Similarly, in a recent case study reported by Garrety, Robertson, and Badham (2004) and Garrety and Badham (2000), a new manufacturing technology developed in a research laboratory was trialed in a manufacturing plant with established operating mechanisms. The pitfalls of the technology could not be realized in advance, thus requiring the re-contextualization of the technology and related knowledge in alignment with the established procedures of the manufacturing plant. There are also a host of other studies that reflect the notion that knowledge must be re-contextualized by its recipient (Argote, 1982; Nonaka, 1994; Dixon, 1994; von Hippel & Tyre, 1995; Yeung et al, 1999). Rather than reiterating the findings from these studies, the approach taken here is centred on a more macro-sociological account of knowledge. That is, the approach in this thesis is premised on demonstrating how knowledge produced and utilized in one context, namely a collaborative context, can displace members of another context. I aim to show how the activities in one collaboration can "cancel-out" the activities of another collaboration or firm.

The types of knowledge to which this applies include knowledge that is deemed to be valuable or potentially useful to a group of scientists. It refers to scientific discoveries, which, according to Zucker, Darby, and Brewer (1997), vary in the degree to which someone can make use of them. Anyone wishing to make use of the knowledge must have both access to it and the requisite ingrained knowledge to apply it. Knowledge related to biotechnology that is naturally and generally excludable, and appropriable is hoarded by its possessors and coveted by the possessor's competitors.

4.2.1 Appropriability and Displacement as an Effect

If the contents of science are thought of as the findings produced within the knowledge architecture, it can be argued that these findings can actually displace other members of "society", or groups of scientists designing drugs. Recall the line of reasoning in chapter two that centred on a knowledge value collective being characterized by a common technological problem. Once one knowledge value alliance within the collective manages to solve the technological problem, the other members of the collective are displaced in terms of recognition and financial gain[74]. This has had a profound effect on how members of a knowledge value alliance deal with valuable knowledge.

Following Eisenberg (1987), Zucker, Darby, and Armstrong (1998) detail the result of recent litigation and legislation, whereby biotech inventors, in lieu of disclosing valuable information relating to a patent, can place a culture in a recognized public depositary as evidence of the patentable knowledge. This practice allows inventors, who can also be conceptualized as members of a knowledge value alliance, to protect particular techniques used in deriving the patentable knowledge and, therefore, to avoid the risk of displacement and inherent difficulties that would arise if another KVA could access the information pertaining to the technique and use that information to replicate the new knowledge. It allows inventors to generally exclude other

[74] Liebeskind et al (1994) highlight this conjecture in their discussion of the "extreme payoff structure engendering patent races". They note that, "competition in the biotechnology industry is characterized by a "win or lose" payoff structure. A firm which succeeds in being first in terms of patenting a new product or process gets the right to monopoly profits for a period of seventeen years; firms which are followers in the discovery process get nothing in return for their investment" (p5).

scientists from access to that knowledge. In this manner, elements from the cultural ecology beyond the knowledge architecture influence the activities within the architecture.

Similarly, members of an alliance may be unwilling to be completely open and forthcoming with all knowledge related to the collaborative agenda. This is because of the fear and the risk that other members of the alliance could appropriate such knowledge, claiming it was their own or original idea, thus threatening the potential future returns of the rightful holder of the knowledge. Typically, contracts and intellectual property agreements would forbid this from happening with the knowledge specific to the collaborative agenda, but peripheral knowledge (i.e., knowledge that is connected to the knowledge used in the collaborative agenda, that is not yet covered by a patent, but not directly used in the design process specific to the collaboration) is not protected in the same manner.

The need to protect knowledge – whether via patenting or secrecy, or general excludability as I refer to it – results from the appropriability of knowledge in relation to biotechnology. As Liebeskind et al, (1994) argue, "[b]iotechnology knowledge is potentially very valuable: single discoveries can result in drugs which can generate billions of dollars in sales over their lifetime. This enormous potential value provides a strong incentive for appropriating biotechnology knowledge which is not protected by patent laws" (p6). I have argued previously, however, (in chapter three), that knowledge is both migratory and ingrained and that migratory knowledge can be represented by repositories (including journal articles and patents), starting points, techniques, or objects, and ingrained knowledge is descriptive of individual know-how. To suggest, then, that knowledge derived via individual know-how is appropriable may seem illogical.

So, from where and how is knowledge appropriated? The practice of submitting a culture in place of a detailed description of how a particular piece of patentable knowledge was derived implies that if the technique for generating the knowledge were known and a person capable of performing that technique were enlisted, the process could be duplicated or imitated, and the knowledge reproduced. Knowledge produced in biotechnology, then, is naturally excludable to those individuals that do not have the requisite ingrained knowledge to understand or utilize

what has been produced. This can be seen in the willingness of this study's participants to allow me to observe their meetings and investigate their collaborative endeavours. They were comfortable with the fact that I am fairly scientifically illiterate and I would, therefore, not be able to appropriate the knowledge that I encountered in the process of inquiry. This answers the question of who can appropriate knowledge. It does not, however, shed any light on the person, place, or form from which knowledge can be appropriated.

The answer to that question is that knowledge can be appropriated by individuals with the requisite know-how from repositories and through the process of verbal disclosure. Patent laws offer one mechanism for guarding against appropriation. Many academics and dedicated biotechnology firms, however, are inexperienced in obtaining patents and the process is very expensive. Furthermore, patenting a discovery too early can limit the areas in which a firm or alliance can patent at a later date (Coates, 20 May 2003 – personal interview). Therefore, often times, the patenting process is stalled, leaving valuable knowledge open to appropriation, particularly in cases where collaborative partners are interacting in scientific realms that border on or are related to the not yet patented knowledge and this knowledge is not being specifically used in the alliance. This risk of knowledge being appropriated in such circumstances is further compounded by the fact that members of an alliance often have multiple partners and, should the valuable (not yet patented, not collaborative specific) knowledge be disclosed within the alliance, there is always the chance that it could be inadvertently leaked to secondary partners and, thus, appropriated by them.

4.2.2 Managing Appropriability and Displacement

There are two ways in which this dilemma is managed in a collaborative setting: 1) prohibiting publication at early stages of discovery and development prior to patenting, and 2) making a verbal agreement, or contractual commitment, to not discuss peripheral knowledge in the alliance. In many cases, academics involved in an alliance with industry are restricted from publishing the data that result from the collaboration until patents have been secured. This is in spite of the academics' need to do so for the purposes of their profession. Lucas (2001)

reiterates that, despite the fact that university-industry interaction has increased, significant differences remain between academic research and those involved in the firm's R & D process. "The most frequently mentioned distinction is the academic's desire to publish in internationally respected journals and the firm researcher's desire to contribute to the local innovation of new technology" (p9). A way of overcoming this is by obscuring the new knowledge in literary reports, particularly the techniques used to generate the knowledge, a practice that is common in scientific activity (Knorr-Cetina, 1981)[75]. This practice could substantially limit the appropriability of knowledge from journal articles, and in the process, allow academics engaged in alliances with industry to meet their publication needs[76].

Members of an alliance may also agree not to discuss or disclose findings and knowledge that is related to the collaborative agenda, but not necessary for the attainment of the desired output of the alliance. For instance, if an industry partner is pursuing a project in-house, and this project is similar to the one being attempted within the knowledge value alliance, the knowledge produced by or relating to the in-house project may be explicitly made off limits to the university partner. This is in spite of the fact that there may be a great deal of congruency between the in-house and collaborative endeavours, and the in-house knowledge may be of some benefit to the achievement of the collaborative aims. The industry partner would be simply unwilling to share that knowledge because of the potential for appropriation, and the ultimate loss of the time and monetary support invested in the in-house project should the appropriator be able to solve the related problem first.

The practices engendered by members of knowledge value alliances that demonstrate the natural and general excludability of knowledge and shield against the appropriability of

[75] Knorr-Cetina (1981) emphasizes that there is a long history of sociologists who point out the discrepancies between what is done in laboratories and what is written in scientific papers. "…Merton traces the questions raised by these discrepancies back to Bacon and Leibniz, and Medawar is famous for his observation that the conventions of the research paper not only 'conceal, but actively misrepresent' what happens in the laboratory" (1969, p169, cited in Knorr-Cenita, 1981, p95).

[76] It may, at first glance, seem that knowledge cannot be appropriated from journal articles because the very act of publishing serves to grant rights of ownership to the author. In the case of knowledge related to biotechnology, it is not the actual appropriation of the knowledge that one must be concerned with, but rather the appropriation of the techniques used in the production of the knowledge, that, given the requisite ingrained knowledge, could be creatively duplicated so as to not completely overlap with the original technique, but to be useful enough to reproduce the knowledge with subtle differences and use it to one's own benefit.

knowledge suggest that those partaking in the generation of knowledge in biotechnology presume that the knowledge is mobile, stable, and combinable[77]. I have suggested that, as a result of various repositories, this type of knowledge can indeed be both mobile and stable. Ingrained knowledge, however, is required to combine the contents of these repositories. In this manner, immutable and combinable mobiles (Latour, 1987) are produced. These immutable and combinable mobiles, or collections of data (and knowledge)[78] that require the application of ingrained knowledge to be combined, allow a knowledge value alliance to participate in Latour's (1987) cycle of accumulation that was introduced at the beginning of this chapter[79].

Having brought together the necessary ingrained knowledge to perform the required tasks in a knowledge value alliance, the architects of the alliance, in conjunction with its members, attempt to solve a specific technological problem and, as suggested above, protect the solution to the problem from poaching by competitors (which, as described previously, can be accomplished by submitting cultures instead of detailed documents in the patenting process, stalling patenting, obscuring techniques in written reports, and withholding peripheral knowledge from collaborative partners). In doing so, the members of a KVA hope to accumulate enough knowledge to become a centre, and thus, "act at a distance on many other points" in a specific domain (Latour, 1987, p222). If a KVA is successful in doing so, and solves a certain technological problem before others can generate a solution, it displaces other

[77] This presumption has also given rise to the construct of knowledge spillovers (Jaffe, 1986, Jaffe, Trajtenberg & Henderson, 1993).

[78] Latour (1987) discredits the conjecture that *what* is accumulated should be termed "knowledge" (or power, money, profit or capital, for that matter) because there are a host of other elements, including events, people and places that are part of the accumulation process. Knowledge, however, is a central construct in this thesis, and because I have attempted to thoroughly define knowledge and have done so with the inference that knowledge does also refer to people and places, I will continue to use knowledge in the discussion on accumulation. To this, I would like to add that what is also accumulated is support from a variety of sources. As discussed in the third section of this chapter, members of an alliance also engage in activities and interaction with constituents from beyond the knowledge architecture to gather support for their collaborative endeavours.

[79] This concept follows the line of reasoning that no matter what distinctions are made between various domains, all domains aspire toward a process of accumulation that will allow them to become a "centre" and to command a significant influence over other domains.

members of the collective and the knowledge value alliance becomes a recognized authority in a specific technological arena[80].

Displacement occurs because of the acknowledgement of authority. This happens in two forms. Other members of the collective will disengage activities aimed at solving the technological problem. It has already been solved, and if those successful at solving it have appropriately hoarded and protected their relevant knowledge, they may very well have won the patent race (and most likely have established a first mover advantage). And, as the authoritative theory of knowledge tells us, "thinking for oneself diminishes as society's knowledge gathering activities expand to the point of requiring a division of cognitive labour into autonomous expertises" (Fuller, 2002, p278). Rather than thinking for oneself, one will be more inclined to consult those recognized as solving the problem first should another individual or group need knowledge relating to the area encompassed by the problem. In addition, this consultation may be the only way to access the knowledge because usually, at the point of problem resolution, the knowledge is protected by a patent. General excludability has come into effect.

In this sense, the displacer becomes an obligatory passage point (Latour, 1987), whereby those who want or need to know about the solution to the technological problem can only fulfill these wants or needs by consulting the displacer. If the knowledge value alliance-cum-displacer is thought of as a module in the larger knowledge value collective (or even if the knowledge value collective is thought of as a module in the larger realm of biotechnology communities), then, with this title of obligatory passage point comes interfaces between the KVA-cum-displacer and those that need the knowledge it possesses. To be more explicit, if a knowledge value alliance succeeds at solving a particular technological problem, arriving at a desired outcome of a drug lead, and this is done prior to all competitors solving the problem, that alliance becomes an obligatory passage point for all pharmaceutical firms that want to work with the lead compound (and attempt to develop it to the point of marketability). The

[80] Other domains, including collectives and academic circles, also engage in this type of behaviour. Collectives use the process of accumulation to establish themselves as legitimate technological communities. Academics partake in this kind of conduct to both gain recognition in their field and establish certain research disciplines as recognized fields of study.

knowledge of the compound itself becomes an interface between the two constituents of the biopharmaceutical industry.

This natural and general excludability and appropriability of knowledge (tenets of the cultural ecology beyond the knowledge architecture) have a profound effect on activities within the architecture and on how the resolution of problems within the architecture can impact on constituents in the broader scheme of things. While these two constructs do not necessarily impact on the alignment within the architecture, they certainly influence behaviour within the architecture, specifically how new knowledge is handled in the patenting process and how knowledge is dealt with prior to patenting, if it is even patented at all.

Alignment is, however, affected by the needs of the different actors of various modules. For as Fujimura (1987) asserts, doable problems are the result of alignment of tasks as well as social worlds. If one module is composed of academics that need to publish and that need is overlooked and ignored, the actors of that module would be less inclined to act as opportunists in the Knorr-Cetina (1981) conceptualization of the term. Alignment is required to facilitate the process of accumulation that, if conducted appropriately, can result in a KVA becoming an authoritative centre.

For this process of accumulation to be appropriately executed, communication both within the architecture and with other constituents of society must become an effective routine of all those involved. Communication is required within the architecture to facilitate the interdependency that may exist in modules, and in some cases, across modules. Communication between the KVA and the constituents beyond the architecture is necessary to enlist allies in the process of playing the game of Biotechnology Bingo, signify when a technological problem has been solved, and establish the authority that results from such resolution. These issues surrounding communication are addressed in the next section.

4.3 Communication Within & Beyond the Knowledge Architecture

Communication comes in many forms and can be accompanied by any number of intentions. According to Habermas (1998), the act of communicating, or communicative action, is the task of mutual interpretation, which aims to achieve a definition of a situation that all participants can share. Verbal, non-verbal, and written forms of communication are used in a knowledge architecture, with the main purposes being to organize and signify opportunistic behaviour (again, in the Knorr-Cetina meaning of the term), bridge the differences between members of an alliance, and facilitate cohesion among them. Members of a KVA also engage in communication to enlist allies and signify their stance in relation to problem resolution to the constituents beyond the borders of the knowledge architecture. In the process of engaging in these types of communication, alliance members have several communicative aids from which to choose. Two of these aids, value and tact, are addressed in the following discussion.

4.3.1 Social Systems and Modularity

I have argued thus far that the knowledge value alliances being conceptualized in this thesis are characterized by both modularity and interdependency. To this, I would like to add that, while each participant in an alliance is distinct in terms of cognitive framework and scientific background, the members of an alliance are homophilous (Rogers, 1995)[81]. That is, they are considerably more similar than say members of an alliance and members of a knowledge value collective, or for that matter, members of a knowledge value collective and constituents of the larger biopharmaceutical industry[82]. One can say that as an interactive context becomes broader, heterophily increases.

Social systems can be conceptualized as systems such as a knowledge value alliance, the biopharmaceutical industry, or the larger system in which these sub-systems dwell. If these

[81] "Heterophily is the degree to which pairs of individuals who interact are different in certain attributes. Heterophily is the opposite of homophily" (Rogers, 1995, p287).
[82] Recall that in chapter two, Diagram 2.3 detailed how members of the biotechnology communities speak to different audiences than members of pharmaceutical firms.

types of systems are thought of as being nearly decomposable and hierarchical[83], as Simon (1962) contends that they are, it is possible to conceptualize a continuum of modularity and interdependency, on which the movement to the higher levels of a social system represents increased modularity and expanding heterophily.

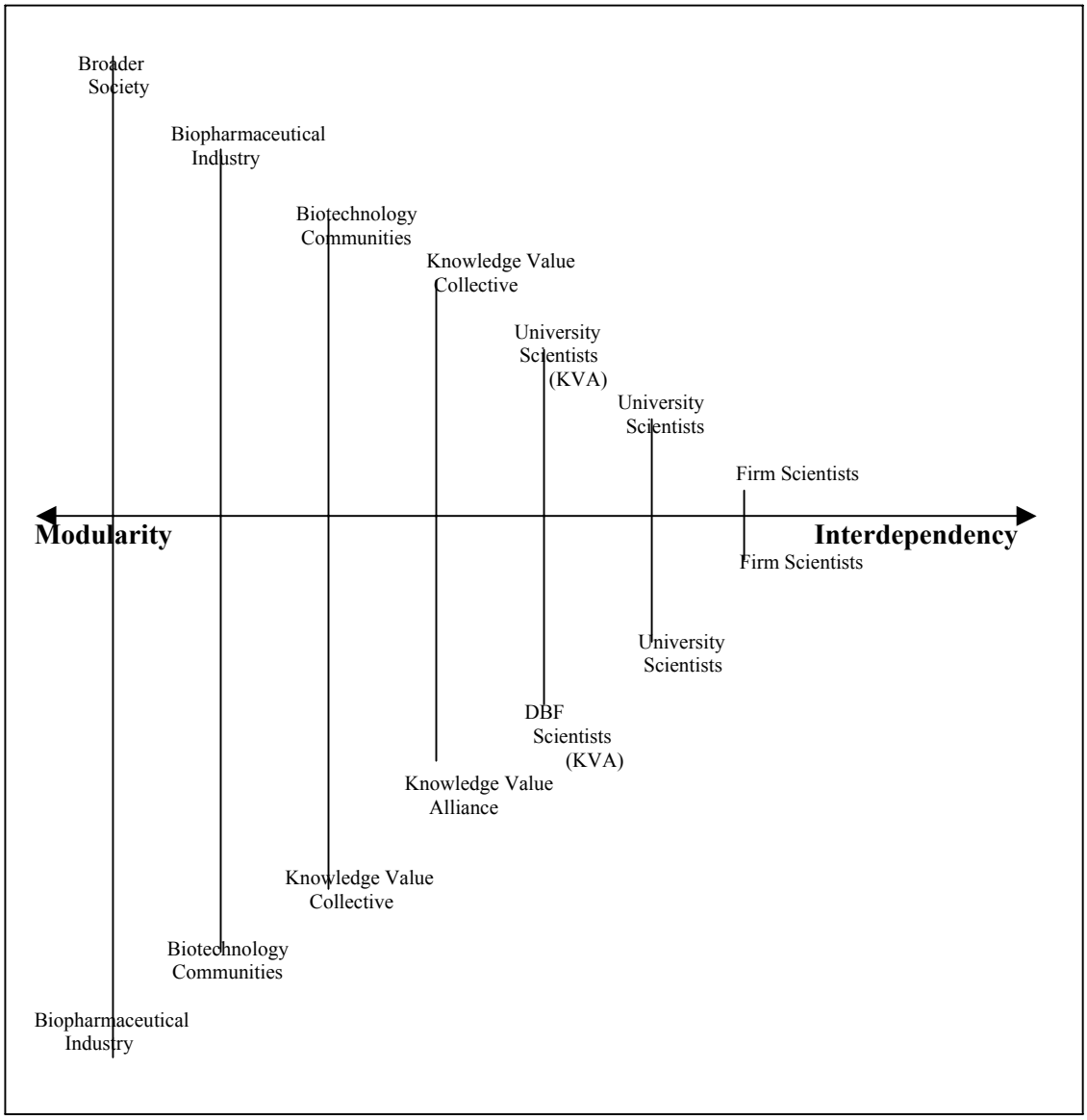
This would suggest that as one moves closer to extreme modularity, communication becomes more difficult because of the differences in the cognitive frameworks (in addition to other differences) and the diminishing frequency of interaction. Viewed from the paradigm of modularity, however, this is not a problem because there are standard interfaces and design rules that virtually eliminate the need for detailed communication, making coordination and cohesion possible without interaction. In acknowledging this role of interfaces, it is important to note that the degree of modularity varies, depending on whether interfaces are standardized within only a single relationship (in a subsystem) or throughout a conglomeration of relationships (across the entire set of subsystems) (Garud & Kumaraswamy, 1995).

Using the social arrangement that spans from knowledge value alliances at the lower level of the hierarchy to broader groups within society, say shareholders of pharmaceutical firms, at the upper end of the hierarchical arrangement, it becomes apparent that knowledge value alliances are less modular (and more customized) than relationships between pharmaceutical firms and their shareholders. It would be expected, then, that interfaces are not standardized across the conglomeration of knowledge value alliances. The interfaces between members of a knowledge value alliance are dependent upon the alliance itself and the agenda being pursued in that alliance. On the other hand, the interfaces between pharmaceutical firms and their shareholders are much more standardized; these interfaces are the money invested by shareholders and the return on investment that they receive from the firms.

[83] Simon (1962) refers to a hierarchical system as a system that is hierarchical in nature, composed of interrelated subsystems, and decomposable into elementary subsystems. He offers examples of social systems, biological and physical systems, and symbolic systems, where each of these types of systems is composed of smaller sub-systems. Simon (1962) notes that the immediate behaviour of each of the subsystems is "approximately independent" of the immediate behaviour of the other components. That is, the system is "nearly decomposable". The concept is applied to organizations, among other systems. As Simon (2000) contends, the near decomposability of organizational structures allows for the benefits of coordination, while minimizing costs through the division of labour among subunits (cited in Augier & Simon, 2003).

Diagram 4.3 serves to visually clarify the modularity-interdependency continuum and the increasing heterophily that occurs with the movement toward extreme modularity. The vertical lines represent the amount of heterophily (or the weakening ties) between various groups depicted in the diagram. Essentially, the longer the line, the greater the amount of heterophily. The similarities in ingrained knowledge between two parties are increased in the movement toward interdependency. While "broader society" is listed at the top of the hierarchy of the system presented in the diagram, this category can be further decomposed into groups of society such as "ill patients needing drugs", "shareholders of pharmaceutical firms", or "state or federal research grant agencies".

Diagram 4.3 Modularity, Interdependency, and Heterophily



From the diagram, it is possible to conclude that there is a great deal of heterophily between the biopharmaceutical industry and any group of the broader community, particularly when compared to the level of heterophily within a knowledge value alliance. This works, as stated previously, because of the extreme modularity in the system at that point on the continuum[84]. Indeed, if the broader society category is characterized in terms of "ill patients

[84] For example, the application of drug regulations set by the Therapeutic Goods Administration (TGA) in Australia and the Food and Drug Administration (FDA) in the U.S. work because of modularity. There is little need for interaction, in most cases, between producers of drugs and the TGA or FDA, or producers of drugs and ill patients because they are parts of different modules in a system where the

needing drugs", it is simply a matter of throwing the drug over the wall that stands between the biopharmaceutical industry and the patient needing the drug. It could be argued that the patient will most likely not be interested in how the drug was discovered and developed, who was involved in that process, what rules governed that process, or probably even how the drug works. The patient cares only that it does work.

I am talking about exchanges between people here, though, not about compatibility between products or modular artifacts. And, as Langlois and Robertson (2003) point out,

> …the use of modular systems must take into account not only technical but also human factors. Because they have broader ranges of characteristics than artifacts, people are often not susceptible to being treated as possessors of 'interfaces' that can be standardized. Moreover, these human characteristics may be subject to frequent and arbitrary autonomous changes. To the extent, therefore, that people are important parts of technological systems, they may substantially limit the usefulness of principles of modularity, or even render them counterproductive (p104).

With this in mind, I revisit the modularity-interdependency continuum from a systems theory approach.

4.3.2 The Need for Communicative Aids

Following Langlois' (1982) application of systems theory[85] to the information and knowledge discourse, it can be argued that the meaning of information or knowledge is determined by the system, or the subsystem for the purposes of the proceeding discussion. Following this line of thought and combining it with the limitations of modularity addressed in Langlois and Robertson (2003), I postulate that interfaces between groups of people cannot always be relied on to have a standardized meaning. It is the people within the group that give

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regulations act as design rules. Modularity, however, is not always applicable to packages of people, and so, we end up with situations like AIDS activist groups putting pressure on the FDA (Epstein, 1997) and the FDA becoming an active participant in the R&D process itself, which occurred after the thalidomide disaster in the early 1960s (Henderson, Orsenigo, & Pisano, 1999).

[85] There are several scholars who have made extensive headway in the development and application of systems theory. Two, for instance, are von Krogh and Roos (1996) in their edited text, *Managing Knowledge*, and Maturana and Varela (1980). Indeed, I draw heavily from these two sources in the conceptualization of ingrained knowledge presented in chapter three. Others include Katz and Kahn (1996), Luhmann (1982, 1986), and van Twist and Schaap (1991). Systems theory is also congruent with the concept of indexicality of social action used by ethnomethodologists to suggest that, "a sign may have different meanings in different contexts, and that the same meaning may be expressed by different signs" (Knorr-Cetina, 1981, p33). For the purpose of succinctness, however, I rely on Langlois' explanation and application here.

the interface meaning. There are, however, certain communicative aids that can be used to ensure that an interface serves its intended purpose.

While there are probably numerous types of communicative aids one could think of to discuss in relation to this argument, I introduce here two aids that have particular relevance to the interactions among members of a knowledge value alliance, and also to the exchange and interaction that are likely to occur between members of a KVA and constituents of the other levels of the system. These communicative aids are value and tact, with value connoting meaning or worthiness, and tact being defined as "[t]he ability to say and do the right thing at the right time" (Roget's II, 1988, p485). Value is a communicative aid that becomes increasingly important as one moves toward extreme modularity, while tact is a useful aid the closer one comes to interdependency. In saying this, I do not claim that value is not a useful communicative aid in interdependent relationships, or that tact could not be beneficial in cases of extreme modularity. Indeed, if it is possible to use them in combination with one another, the more powerful they will be.

There are reasons, however, why I say that value is more applicable as a communicative aid at levels of increased modularity, and tact is more appropriate in cases of higher interdependency. Value is a more general communicative aid. If attached to an interface, it can subsidize the much-needed interconnection that an interface typically provides in instances of modular products. It is a communicative aid that serves well in cases of increased heterophily, whereas tact is more applicable in less heterophilous circumstances. The use of tact as a communicative aid requires that the individuals engaged in interaction are homophilous enough to arrive at a mutual interpretation – that there is enough of a common framework (whether this comes from the background provided by their respective sub-systems or through the institutionalization of mechanisms that serve this purpose) for them to build a mutual understanding.

Examples of each type of communicative aid may help to clarify my point. If the interface between a biopharmaceutical firm and "ill patients needing drugs" is thought of as a drug produced by the firm, members of the two collectives do not have to agree on an

interpretation of what that drug actually is; they do not have to come to a mutual interpretation of that drug as an interface between the two of them. If value, used as a communicative aid, is attached to that interface, the interface is more likely to have its intended impact, which is affording a connection between the two sub-systems[86]. Importantly, though, the constituents of the two sub-systems, "ill patients needing drugs" and the biopharmaceutical industry, do not even have to agree on what the value is (for, this would be particularly difficult considering the heterophilous relationship between the two[87]), as long as they find value attached to the interface. To the group, "ill patients needing drugs", the value could come in the form of a cure for their ailment. The value ascribed to the drug by the members of the biopharmaceutical industry could be in the form of financial return on their investment in the process of developing the drug. The result, then, is almost market-like. Despite the two different interpretations of value, the interface still fulfills its intended purpose and it is ensured of doing so.

Value can be used within an alliance as well, and indeed, it often is. If an interface in an alliance is the realm of synthetic chemistry, value can be attached to that interface to ensure that both sides of the alliance see the benefits of the work in synthetic chemistry. To members of industry, it may be an efficacious compound that demonstrates the potential for commercialization. For university scientists, it may be the ability to produce publications based on that compound. The collaborative participants on both sides of the alliance must recognize the value, but the value they see does not have to be consistent with that of their counterparts.

The process of attaching value to an interface, however, requires that the attacher have some sort of preconception of what members at the other side of the interface *might* find valuable. The attacher need not have an interpretation of this value identical to that of the other party, but must have an idea of what the value might be. For instance, the value of a drug as an

[86] This follows Knorr-Cetina's (1983) observation that relationships between scientists and members of systems beyond the scientist's community are symbolic relationships. "These symbolic relations are not primarily determined by characteristics held in common by its members as in the case of a logical class. The social integration which emerges from this picture is based not upon what is shared, but upon what is *transmitted* between agents" (Knorr-Cetnia, p133 – emphasis her own). In applying this concept, I contend that the value is what is transmitted in the use of an interface between heterphilous parties. This value does not have to be mutually interpreted by both parties of the exchange (although both parties have to recognize some sort of value) to be useful.

[87] Besides, most of the work relating to the value of a drug is done by the regulatory agencies. The TGA and the FDA determine the "value" of the drug, i.e. whether it is a legitimate treatment or not.

interface may be known to the attacher of value as a cure, a temporary relief of symptoms, or a limitation on the spread of a disease. On the other side of the picture, however, the value may come in the form of seeing one's children grow up, being able to go to the grocery store and perform daily routines, or saving a limb from amputation. With a drug as an interface, the idea of what one might value in the drug is simple. It is known from the early stages of discovery right through the process of development.

Taking an interface between two other groups, say a member of a knowledge value alliance and a reader at a government research grant committee, the preconceived notion of value that the attacher needs may be more difficult to formulate. This can be achieved, however, through the process of what Latour (1987) calls translation[88]. Latour's (1987) second basic principle of scientific method suggests that members of a knowledge alliance may engage in a very political game of showing how their work in a particular scientific or technological arena will meet the needs of others beyond their domain. He contends that, "scientists and engineers speak in the name of new allies that they have shaped or enrolled" (p90), and do so through the first mode of translation, which he describes as "I want what you want" (Latour, 1987, p108).

Typically, research grant agencies will have goals or objectives that define their reason for being. Take a grant application as an interface between a group of research scientists and the granting agency. If the applying scientists can attach value to a grant application that shows how the proposed outcome of the research described in the application coincides with the agency's objectives, the applicants will be more likely to get the grant. In addition, the knowledge value alliance of which the scientist is a part will be enlisting a new ally. And, in turn, this ally will provide support to the KVA that will propel the collaboration along its journey to problem resolution, and aid in the ultimate goal of becoming an obligatory passage point[89].

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[88] Although Latour (1987) uses the act of translation to show how scientists acquire support for what they believe to be facts, thus making the fact a more formidable force, this activity also works in the process of synthesizing values and interfaces.

[89] I must emphasize that considerable care should be used in the process of translation and attempting to preconceive what others may value in an interface, for this is the same process that saw stem cell researchers acquire anti-abortionist activists as opponents. This example was, in fact, a *failure* to translate. Anti-abortionists are not convinced by the argument that stem cell research will cure disease(s). Therefore, not only must considerable caution be used in the process of translation and attempting to

The act of completing a grant application also involves a considerable amount of tact, the other communicative aid introduced previously, which was argued to be more appropriate in cases of interdependency. This would suggest, then, that the relationship between a state or federal grant agency and scientists in a knowledge value alliance would be more interdependent (and possibly more homophilous) than the relationship between 'ill patients needing drugs' and constituents of the biopharmaceutical industry (the other example that was provided in the discussion on value as a communicative aid). For, tact is much more useful and appropriate in relationships involving interdependency. Using tact in conjunction with an interface requires that parties to a relationship are similar enough that they have a common conception of the tact, that is, they agree that the right thing has been done at the right time.

If an interface between two parties of a knowledge value alliance is taken to be a particular field of science that is relevant to the pursuance of the collaborative agenda, and this science is brought in or employed at a certain time in the journey to problem resolution, the interface becomes an increasingly potent link between the university scientists and the firm scientists (which is the designated role of an interface) if both sides of the alliance agree that the interface was the appropriate field of science to use in the problem resolution and it was used at the right time. If the firm scientists and the university scientists do not agree that the interface was appropriate, tact can be used in combination with, or maybe in lieu of, the interface to maintain the link between the collaborative participants[90].

It should be noted, though, that in the context of a knowledge value alliance (as it is presented in this thesis) there is a level of modularity that sees the institutionalization of design rules, repositories, and starting points that would reinforce or negate whether the right thing has been done at the right time. This level of modularity is one that calls for particular amounts of overlap between the collaborative participants. Overlap in ingrained knowledge allows the scientists to be critical of the work on the other side of the alliance and have an opinion on when

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preconceive what others may value in an interface, but translators must make a point to see things from others' points of view and find a way to reach a middle ground that is suitable to both parties.

[90] There are, however, other communicative aids that could be used including coercion. There is also the option of ignoring the opinion of others. For the purposes of this discussion, though, I focus only on tact as a communicative aid because it connotes a sense of good intentions among the interactive parties.

certain work should be carried out, terminated, or augmented with different procedures. Divisions of labour do exist, but knowledge overlap is necessary (as discussed in chapter three) to avoid instances where work in a particular division may be inefficient or, worse, ineffective. Scientists are using their own ingrained knowledge to solve problems within the architecture of the alliance, and although the application of their ingrained knowledge is guided by the design rules, and aided by repositories and starting points, there is a degree of freedom that would allow for them to make a wrong choice. Tact would, then, be a useful communicative aid in such instances. In this type of situation, it could be argued that the use of value as a communicative aid could also play a pivotal role in maintaining the link between the members of the alliance.

These communicative aids, value and tact, are relevant to the knowledge value alliances discussed in this thesis because these types of interorganizational collaborations are not completely modular. Although there is a specific degree of modularity that characterizes these relationships, they are also composed of interdependent elements. This mid-range modularity is supported by the members of an alliance being somewhat heterophilous, which is what makes the resources that they bring to the table complementary, and not mutually overlapping, and allows for the division of labour characteristic of these alliances.

The relationships formed by university and industry scientists are also part of a larger social system that is decomposable and hierarchical. Following Gibbons et al (1994), one could say that the transdisciplinary knowledge that is used in these collaborative endeavours spawns an increasing density of communication between levels of this system, namely between science and society. Science is undertaken by actors performing scientific tasks, while society is made-up of individuals engaged in a plethora of different behaviours. These two sets of actors are quite heterophilous, particularly compared to the actors within a KVA. As a result, it becomes pertinent that communicative aids are used in this increasing density of communication. For without them, it cannot be ensured that a viable link can be provided between the communicators of various sub-systems.

4.4 Conclusion

This chapter highlights the notion that the activities performed in the architecture aim for a purpose that transcends the alliance boundaries. This purpose is to become an obligatory passage point through the displacement of other alliances seeking to solve an equivalent or similar technological problem. Doing so, however, requires not only the design rules, interfaces, repositories, and starting points discussed in the last chapter, but also specific attention to the cultural ecology within and beyond the knowledge architecture. Factors such as the social ambiance, the use of "things", and the social organization within the architecture, as well as the natural and general excludability, and appropriability that characterize knowledge in biotechnology all play a pertinent role in shaping the activities within the architecture.

In addition, it is important to acknowledge the levels of interdependency within the architecture of the alliance. Without this acknowledgement, it is not even possible to consider factors like social ambiance. With this acknowledgement comes the realization that members of an alliance are indeed heterophilous and that constituents beyond the knowledge alliance are even more heterophilous to those within the architectural arrangement. This requires the institutionalization of specific communicative aids, namely value and tact, to ensure that the interfaces (along with other mechanisms employed for the purposes of alignment) have their intended effect. Moreover, value as a communicative aid becomes critical in communication attempts with actors beyond the alliance.

With these constructs in mind and with the conclusion of this chapter, a theory has been grafted. Attention is turned now, in the second section of this thesis, to grounding the theory in empirical cases. I begin with a consideration of my role as researcher and proceed to providing illustrations of the theory that has been developed and presented throughout the last three chapters. Before doing so, I present the reader with a pointed summary of chapters two, three, and four.

Section I Summary

Here, a summary of chapters two, three, and four is provided. Chapter two is concerned with examining the context of the collaborations presented in this thesis and explaining the practice of biotechnology. Chapter three moves on to the conceptualization of knowledge and to characterizing the modular structure of university-industry alliances in biotechnology. Acknowledging that these alliances are not entirely modular, chapter four explores the social aspects and organization of a knowledge architecture, the environment beyond the architecture, and the role of communication in these endeavours.

In chapter two, I argued that biotechnology is not just the utilization of specific technologies to produce drugs via advanced techniques, but rather the deployment of particular designs with the purpose of deriving a desired outcome. Following Clark (1985), a "[d]esign is a search for understanding of what an object…is, and ought to be given the context in which it must function" (p241). "The search for understanding" is complicated by an array of factors, including the complexity of the design, the uncertainties inherent in the highly experimental scientific practices used in the design, and the differences in ingrained knowledge that come to bear on the design process. Desired outcomes are pursued in collaborations between university and industry called knowledge value alliances (Rogers & Bozeman, 2001). As is demonstrated in the later chapters of this thesis, the rules chosen for design have an impact on the way labour is divided in the process of collaboration and the way knowledge processes are enacted. In addition, while several collaborations may be premised on drug leads as desired outcomes, there are different design rules that can be used to attain this type of output.

The design rules may differ, but the alliances are aimed at cultivating value through the use of design rules. Collaborative participants combine complementary knowledge bases to

solve a technological problem and arrive at a desired output that would often times be unattainable to one or the groups of collaborators on their own. This becomes important when considering that analysis of the four cases presented in this thesis shows that, if the knowledge bases are combined in a manner that is in line with the contingencies of the external environment, the effectively and appropriately combined resources (knowledge bases) can create a competitive advantage for the collaborative participants.

Collaborative relationships are often under heavy pressure to solve their specified technological problem before other researchers manage to do so. They are essentially in a race with other members of their knowledge value collective (Rogers & Bozeman, 2001), that is, with the entire body of scientists attempting the same or a similar problem(s). There is no guarantee, however, that the technological problem is even solvable. There are many uncertainties associated with the science practised in biotechnology and the complexity of the activities typical in an alliance is overwhelming. Design rules can reduce the complexities, but do not serve to eliminate the scientific uncertainties.

Therefore, there is a certain amount of luck associated with these alliances. The social worlds of the collaborative participants must be meshed (Fujimura, 1987). Uncertainties will inevitably be faced. Yet, the alignment of tasks is a skill that contributes to success. Considering these factors – the luck, the skill, and the alignment necessary to achieve the desired output of any given alliance – the activities of a university-industry collaboration in biotechnology can be likened to a game of Bingo. Success in this game depends on the understanding of the rules of the game, and, as will be seen in the forthcoming chapters, the ability to manipulate these rules to one's advantage.

It also requires the effective and appropriate use of knowledge processes. This was the subject of chapter three. Knowledge, as conceptualized in this thesis, is both migratory and ingrained. Migratory knowledge is objectified knowledge that comes in the form of compounds, techniques, journal articles, patents, and intellectual property just to name a few. Ingrained knowledge exists in the mind of the individual, but it can be transformed into migratory

knowledge through the process of objectification. Problem solving in the knowledge architecture is not possible unless knowledge is considered to be both migratory and ingrained.

The two types of knowledge coexist. Migratory knowledge allows for problem resolution. In addition, certain forms of migratory knowledge, namely repositories and starting points, mesh the efforts of various unit-workers, both across and within modules. Ingrained knowledge, on the other hand, meshes the specific actors of the architecture with their work, permitting the identification and resolution of sub-problems at the modular level. I submit that the knowledge processes evidenced in the cases here do not, for the most part, involve the codification of knowledge. Knowledge is produced in the minds of individuals and objectified in the process of, inter alia, developing techniques, synthesizing compounds, testing these compounds, and writing journal articles. While this notion is evidenced in the individual cases, it is strongly argued in the cross-case analysis.

The knowledge processes in an alliance are articulated at three levels, following Strauss (1985). The first level of articulation involves meshing or coordinating tasks across the entire architecture. This is accomplished through the use of design rules. The second level of articulation is the meshing of unit workers, which occurs through the use of boundary objects (Star & Griesemer, 1989). Two specific types of boundary objects, repositories and starting points, connect modules and the scientists within them. Repositories are "piles of objects" that are migratory in nature and are often used for the purposes of problem resolution. Starting points are initial leads into the task work of the scientists. They connect unit workers both within modules and across modules, as do repositories. The third level of articulation is meshing scientists with their own tasks. Level three articulation is the result of using hidden design parameters, or design rules specific to a given module that do not affect the work beyond the module (Baldwin & Clark, 1997, 2000), and ingrained knowledge. These articulation mechanisms are found in each of the full-length cases presented in this thesis.

There are two consequences of the implementation of these articulation mechanisms beyond the integration of knowledge and tasks within the alliance. The design rules used at the first level of articulation will result in a product-oriented or function-oriented modular structure.

Obviously, this affects the way knowledge is handled in the knowledge architecture. In addition, as will become apparent in the analysis of the cases, the articulation mechanisms used at level one do not always have their desired effect because the collaborations are undertaken by groups of people, and do not involve just artifacts and/or products. This applies particularly to the interfaces used in these alliances. While interfaces may provide for routine connection and communication in product architectures, people are less susceptible to being treated as routine processors of interfaces (Langlois & Robertson, 2003). The use of value and tact as specific communicative devices is evidenced in the interactions between collaborative participants and constituents from beyond the knowledge architecture, and among collaborative participants in this thesis.

The alliances presented in this thesis are, indeed, not entirely modular. There are particular interdependencies that are peculiar to each alliance. The interdependencies stem from people (rather than just products) being organized modularly and from the design rules chosen for the alliance. For example, if rational drug design is chosen as a design rule, there will be sequential steps of chemical synthesis and testing that are repetitive and interdependent.

Because this modular arrangement is composed of people and interdependent elements, chapter four explores the cultural ecology of a knowledge architecture and the use of communication within it. An explanation is also provided of the cultural ecology beyond the knowledge architecture and the impact that the elements of this environment have on the activities in a knowledge value alliance.

The cultural ecology of a knowledge architecture is defined by the social ambiance of the architecture, how "things" (Latour, 1987) are used to mediate and modify human behaviour, and the social organization, or structure, of the alliance. The social ambiance is characterized by trust, openness, and prior experience. If the scientists in an alliance are deemed to be taking advantage of every opportunity that comes their way in order to solve task level problems in an effort to attain the desired output of the alliance, they are considered to be opportunists, as defined by Knorr-Centina (1981). Particular "things" like electronic communication, compounds, or techniques can alter the way that people interact in an alliance. They can change

the levels of modularity or interdependency in an alliance and the relationships within various modules. Thus, they can impact on the social organization of the alliance, or the division of labour.

These are vital elements for the architect of an alliance to attend to and be aware of because new design rules may be necessary to maintain alignment of tasks. Moreover, the architect needs to be certain that he or she is acting as an opportunist (in the Knorr-Cetina sense of the word), in that every opportunity must be taken to ensure that the right people for the task are performing the work. This situation is discussed in chapter seven, where analysis is provided in relation to a modular level task being split. Junior level scientists are performing the task work and I pose the question as to whether or not the manager(s) of the alliance is acting as an opportunist (again following Knorr-Cetina) in allowing this to occur.

The way knowledge is handled within an alliance is also affected by the cultural ecology beyond the knowledge architecture. Elements from the cultural ecology beyond the knowledge architecture include the natural excludability (Zucker, Darby, & Armstrong, 1998), general excludability, and appropriability (Liebeskind et al, 1994) of knowledge related to biotechnology. The natural excludability of the knowledge comes from the notion that one must possess the requisite ingrained knowledge in order to produce or make use of the knowledge related to biotechnology. As will be argued in this thesis, knowledge related to biotechnology is abstruse, being difficult for someone from outside of the knowledge area to understand.

The general excludability and appropriability of knowledge stems from the fact that one who does have the requisite ingrained knowledge can make use of the knowledge for his or her own benefit. Sometimes, this is to the detriment of the initial knowledge producer. Therefore, the knowledge must be protected. Scientists may seek to use the construct of general excludability and protect the knowledge through the use of secrecy or patenting. The potential appropriability of knowledge has a profound impact on the amount of knowledge that is shared among collaborative participants. In chapter nine, I demonstrate that firm scientists often see the need to hide knowledge from other members of the collaboration for fear of (mis)appropriation.

While what is done within the knowledge architecture is important in its own right, the activities performed in the architecture aim for a purpose that transcends the alliance boundaries. This purpose is to become an obligatory passage point through the displacement of other alliances seeking to solve an equivalent or similar technological problem. Answering Latour's (1983) call for social scientists to show how societies or portions of society are "displaced" via the use of scientific knowledge, I argue that the types of alliances illustrated in this thesis are part of a larger social arrangement and that the activities of a dedicated biotechnology firm can result in the displacement of its competitors. This occurs through firms accumulating knowledge via the process of collaboration for the purposes of solving technological problems and getting drugs to market.

The alliances depicted in this thesis are modular in that there is a distinct division of labour that is evident in them and each side of the alliance is independent in its own right. A firm is a firm without the collaborative endeavour, and a research centre is a research centre without being engaged in an interorganizational relationship. They respond to different institutional mechanisms that guide their work. This becomes particularly relevant in the discussion in chapter nine that is premised on the industry practitioners being the appropriators and accumulators of knowledge. In this discussion, I argue that the university scientists are positioned in a system that encourages them to contribute to alliances where they can, and to tolerate the displacement they endure after they have produced the knowledge pertinent to the attainment of the collaborative goals.

Nonetheless, the structure that combines these two types of entities in a university-industry collaboration is modular. I contend that this type of organization has unavoidable implications for the "flow" of knowledge in an alliance. The way that knowledge is used, reused, and valued in an alliance is determined in accordance with the structure of the alliance. In this thesis, I contend that "flows" cannot be analyzed independent of the structure of an alliance. I do not wish to paint a picture of the analysis being centred on "flows" *versus* structure, but rather to position my argument in terms of "flows" *and* structure. The structure I

refer to is a modular one, and the "flows" of knowledge (along with the other knowledge processes evidenced in the cases presented here) are impacted by this arrangement.

Being modular, however, does not preclude the recognition that these relationships are part of a larger system. They do not occur in some isolated corner of the biopharmaceutical industry that can be studied in its own right without the acknowledgement of the constituents beyond the alliance. The work performed in an alliance is significant within and beyond the borders of the alliance.

Having provided a pointed summary of the previous three chapters, I now move on to illustrating the theory that has been detailed in chapters two, three, and four. The next portion of this thesis contains four chapters. Chapter five offers an explanation of the methodological and epistemological approaches used in this research. Chapters six, seven, and eight are the case studies that underpin the theory of Biotechnology Bingo.

SECTION II

GROUNDING THE THEORY

Chapter 5 Considering the Researcher's Role

> "One must want to learn in order to be able to ask the right questions – those questions that still 'reach into the sphere of the truly open' – and this desire can only exist when one is aware of one's own ignorance. Mastering the art of asking questions, then, is not a matter of learning some *method*, but rather of cultivating a readiness to see what remains to be shown" (Bontekoe, 1996, p115 – emphasis his own).

In building this theory of knowledge synthesis and alignment in collaborations between university and industry in biotechnology, it is pertinent that I explain my role as researcher in the development of the theory, as well as the techniques employed in the research process. This requires a declaration of my experiences and assumptions, and an examination of the methodologies used to formulate a research agenda, collect and analyze data, and generate a theoretical argument. The research process spanning the formulation of an agenda to the generation of a theory was an interpretive enterprise. Using various methodologies and epistemological stances, including case study guidelines, hermeneutical suppositions, and a version of grounded theory analysis techniques, I maneuvered my way through the literatures relevant to my research, solicited the opinions of university and industry collaborators, observed some of their activities, and developed an interpretation of how knowledge is managed in alliances between university and industry.

Along the way, my interpretation was informed by different sources. In the process of formulating a research agenda, I relied on the evidence presented in the literature to develop an understanding of university-industry collaborations and came to the realization that these types of interorganizational relationships are centred on knowledge. I eventually came to the conclusion that, in my research endeavour, I would be asking the question, how does knowledge flow in university-industry collaborations in biotechnology? I built a research agenda around

this question and solicited participants who I thought were suitable and capable of making a valid contribution to the inquiry. Upon analyzing the data that I collected, however, I realized that knowledge does not necessarily "flow" in these bilateral alliances. The data were telling a story that did not directly answer the question I had posed. As a result, my interpretation of the knowledge management process in university-industry collaborations changed with the movement from literary informants to social informants. This, however, required an appreciation of my own ignorance and a "readiness to see what remains to be shown", to use Bontekoe's words from the introductory quotation.

This chapter traces my process of interpretation and the changes that occurred along the way. There are three sections in this chapter, 1) The Original Interpretation and the Research Strategy, 2) The Processes of Reconstructive Interpretation and Data Analysis, and 3) The Final Interpretation and Theory Construction. Each section offers a description of my interpretation process that is accompanied by specific methodological and epistemological approaches. This combined formula of descriptive interpretation and prescriptive methodology aims to legitimize my position as interpreter of the game of Biotechnology Bingo, while conferring validity and reliability on the interpretive insights that are offered throughout this dissertation. In addition, this chapter attempts to avoid what Janesick (1998) defines as "methodolatry", or the "preoccupation with selecting and defending methods to the exclusion of the actual substance of the story being told" (p48).

5.1 The Original Interpretation & the Research Strategy

Following the recommendation of my advisors in the Faculty of Commerce at the University of Wollongong, the practices of my peers, and the numerous books I read in preparation for PhD candidature, I began the research process by investigating the literature. I did so with the intention of devising a research project on university-industry collaborations. My investigation of the literature began with a thorough reading of the work done by W. W. Powell and his associates and, immediately, I was drawn to collaborations in the area of

biotechnology. Through the research of Powell (1996), Powell and Brantley (1992), and Powell, Koput, and Smith-Doerr (1996), I came to the realization that biotechnology was a powerful impetus for interorganizational collaborations, particularly between university and industry, and that I would be able to find a plethora of potential participants for my research in this area. For as Hamilton notes, "[c]ollaboration is not optional in the early stages of technological revolution" (2001, p163). While the current biotechnology revolution was already into its second decade of existence, there would be a substantial number of university scientists and industry practitioners that either had engaged in collaboration or were currently involved in an alliance.

The stage was set, but I still needed to determine what I wanted to know about these collaborative endeavours. I was inspired by Basri's (2001) observation that, "from the early 1980s, [technological linkages] began to be closely studied, and quickly moved from a focus on strictly technological linkages to studies of the nature, organisation and content of collaboration and 'interactive learning' between firms" (p145). In addition, Badaracco's (1991) theory of creating competitive advantage through knowledge alliances fueled my original conceptualizations. Badaracco suggests that, "many firms are creating knowledge links – alliances that give them access to the skills and capabilities of other organizations and sometimes enable them to work with other organizations to create new capabilities"[91] (1991, p107). After additional reading, I came to the understanding that the interorganizational relationships between university and industry in biotechnology revolved around the utilization and combination of knowledge for the purposes of product development and competitive advantage.

[91] Badaracco (1991) goes on to say that, "[k]knowledge links can be tactical or strategic" (p107). A tactical link is a single knowledge link that can help a company build new skills in a limited area of its operations. A strategic link occurs when a company creates a multitude of knowledge links with customers, suppliers, universities, etc., which serve to strengthen the company's long-term objectives. As I would later uncover, the firms chosen for investigation in this study engage in both tactical and strategic alliances. Both university scientists and firms participate in tactical alliances for the purposes of combining complementary resources to reach a desired output. In addition, these university scientists and firms are involved in an array of other collaborations with different scientists, dedicated biotechnology firms, and large pharmaceutical firms in order to advance their own long-term objectives.

5.1.1 The Original Interpretation

My original interpretation of the knowledge utilization and combination process was based on findings from the knowledge management literature that suggested there was a fluid exchange of knowledge between members of a knowledge alliance. This presumption was based on the research, publications, and theoretical insights of Albino, Garavelli, and Schiuma (1999), Decarolis and Deeds (1999), Gilbert and Cordey-Hayes (1996), Nonaka (1991, 1994), Nonaka and Takeuchi (1995), Santoro and Gopalakrishnan (2000), Steensma (1996), and Yli-Renko, Autio, and Sapienza (2001). These articles are premised on the assumption that knowledge does indeed flow and that it flows in specific patterns of acquisition, communication, application and assimilation (Gilbert & Cordey-Hayes, 1996) or via knowledge spirals (Nonaka & Takeuchi, 1995). Much of the knowledge management literature converged on the assumption that knowledge "flows"[92], and, therefore, I was inclined to adopt a similar view of knowledge.

I was not content, however, to explore knowledge and its "fluidity" without investigating perspectives of knowledge from other disciplines. I read the work of philosophers and sociologists of knowledge, including Berger (1967), Berger and Luckmann (1967), Bruner (1973), Gallagher (1982), Knorr-Cetina (1981), Latour (1987), and Polanyi (1958), and became entangled in the viscosity and complexity of knowledge. I was intrigued by the monograph, *Managing Knowledge*, edited by von Krogh and Roos and settled on two conceptualizations of knowledge based on that piece of work: namely, what I have termed migratory and ingrained knowledge throughout this thesis[93].

This settlement, however, did not get me any closer to a research question and this was a crucial obstacle to overcome. For, as Eisenhardt (1989a) stipulates, "[a]n initial definition of the

[92] There are, however, exceptions to this perceived bandwagon. One example is the work of Szulanski (1996), in which he discusses the major barriers to the transfer of knowledge within a firm as being the recipient's lack of absorptive capacity, casual ambiguity, and an arduous relationship between the source and the recipient.

[93] While these characterizations of knowledge are informed by several sources, including Rescher (1997), Polanyi (1958), and Maturana and Varela (1980), among others, my idea for characterizing knowledge in this fashion was inspired by my reading of von Krogh and Roos (1996).

research question, in at least broad terms, is important in building theory from case studies" (p536)[94]. And, indeed, it was my intention to build an explanatory theory of how knowledge flows. After considerable amounts of reading, writing, mentally debating, and conversing with my supervisors, I concluded that I would seek to answer the question, how does knowledge flow in university-industry collaborations in biotechnology?[95]

The next step was to find a methodology applicable to this type of question. I deliberately set my sights on a qualitative methodology because I knew that answering the research question would require close interactions between myself and potential respondents. Furthermore, I did not know that much about biotechnology. I would need to rely on the detailed explanations of the research participants and be able to interactively ask for clarification during the process of inquiry, which would not be possible if I selected a quantitative methodology.

I set out to define a research strategy that would lend itself not only to arriving at an answer to the research question, but also to gathering, analyzing, and interpreting data in a meaningful, illuminating manner. Obviously, the determination of what is "meaningful" requires some sense of understanding regarding the research goals and objectives (Yin, 1981b). And so, the process of devising the research agenda, including its goals and objectives, began.

The purpose of the research, which, at the time, I was conceptualizing as determining how knowledge flows in university-industry collaborations in biotechnology, had to be strategically aligned with specific data collection procedures and types of evidence that would, through the process of analysis, yield answers to the question being asked. Arriving at the desired strategic alignment between research aims and research conduct required selection of appropriate design mechanisms. Following Yin (1981b), there were four levels of planning that needed to be materialized prior to investigation, including the research strategy, the types of

[94] Eisenhardt goes on to explain that, "[t]he rationale for defining the research question is the same as it is in hypothesis testing research. Without a research focus, it is easy to become overwhelmed by the data" (1989a, p536).

[95] Appleyard (1996) asks the same question of interfirm relationships in the semiconductor industry. She compares knowledge sharing activites in the semiconductor and steel industries, and draws another comparison between knowledge sharing in Japan and the United States. The results of her study demonstrate that both public and private mechanisms are used for interfirm knowledge sharing, with the benefits of refined strategic plans, inclusion in professional networks, and coordination of industry standards.

collection methods, sources of evidence, and the plot for analysis. This planning took place in the construction of a detailed case study protocol[96], which provided background on the investigation, outlined the research strategy, conveyed the questions to be asked of the study participants, linked these questions with the literature, and described the techniques to be used in the analysis of the data.

5.1.2 The Research Strategy Leading up to Investigation

The case study method was chosen as the appropriate strategy for the proposed research project. This decision is based on Yin's (1994) provisions for case study methodology. "In general, case studies are the preferred strategy when "how" or "why" questions are being posed, when the investigator has little control over events, and when the focus is on a contemporary phenomenon within some real-life context" (Yin, 1994, p1). These three conditions specified by Yin (1994) can be matched with characteristics inherent to the research agenda. The key focus of the research project is determining "how" knowledge flows in university-industry R&D collaborations. The specific social context of inquiry for this project is centred on R&D collaboration between university scientists and their respective partners from biotechnology firms. These endeavours are clearly unavailable for manipulation or experimentation by the investigator. And, as Basri (2001) notes, interorganizational collaboration is a contemporary phenomenon that is the subject of many research projects.

The objective of the research strategy was to develop an *explanation* of how knowledge flows in university-industry collaborations. Using the multiple-case-comparative method[97], the

[96] Yin (1994) claims that the protocol is the major tactic in increasing the reliability of the case study and it is intended to convey the procedures and general rules that should be followed in the process of empirical investigation. He contends that, "[h]aving a case study protocol is desirable under all circumstances, but it is essential if [one] is using a multiple-case design" (p63). Excerpts from my case study protocol, including the questions used in interviews and the Table of Principles for Interpretive Research are found in appendices B and C, respectively.

[97] Yin (1994) defines the multiple-case-comparative method as a research design that can potentially yield evidence that is more compelling than a single-case approach. He cautions, however, that the multiple-case study method is not intended to yield the same type of generalizability that a survey would, but instead, the multiple-case study method should target a replication logic (rather than a sampling logic), whereby similar results are sought from all cases in the investigation. Similar multiple-case design strategies are also presented in Eisenhardt (1989b), Herriott and Firestone (1983), and Lennick-Hall (1992).

ultimate research aim is what Yin (1994) calls replication logic. This is a process wherein "each individual case study consists of a 'whole' study, in which convergent evidence is sought regarding the facts and conclusions for the case; each case's conclusions are then considered to be the information needing replication by other individual cases" (Yin, 1994, p49). The cases were not chosen because they represent a larger population, but because they offered the potential to build an explanation of knowledge flows. They were "instrumental case studies" (Stake, 1998) chosen to provide insight into the issue of knowledge and its ability or inability to "flow". I anticipated, at the time of designing the research strategy, that the cases selected for investigation would yield similar patterns in the flow of knowledge, despite different contextual influences.

Four cases were chosen for investigation, with the intention of being able to build a sufficiently complex theory, but without a being swamped by data. Eisenhardt (1989a) claims that between four and ten cases works well in terms of providing enough evidence to generate a theory and avoiding the complexity that can often be difficult to navigate. This complexity is said to come from the fact that the context is a major part of the study and, in employing a case study methodology, "the number of variables exceeds the number of data points" (Yin, 1993, p32). The potential for a large number of variables becomes apparent when considering that the four cases that were chosen for this investigation varied in national and regional context, physical distance between the collaborators, area of biotechnology, numbers of participants in the collaboration, strength of the ties between the collaborative parties and their prior experience with one another, duration of the collaborative venture, desired output of the alliance, and the outcomes achieved by the alliance partners at the time of investigation.

The explanation of how knowledge flows was expected to be the product of analyzing the data accumulated from these varied cases through several different collection methods. While my interpretation would change, moving away from the view that I had adopted through reading the relevant literature, the type of data prescribed by the research strategy remained the data that were indeed collected and analyzed in the investigative process. These data are described in terms of the source of evidence and the factors affecting access to that source. Three sources of

evidence were used in the collection of data. These include direct observations, document review, and interviews, both open-ended and semi-structured. Each case study was initiated by telephone or face-to-face contact, at which time a written, formal research brief (a copy of which can be found in Appendix D) was presented to the key informant. Once the key informant agreed to participate in the study, the depth of investigation was negotiated, confidentiality agreements were signed, and informal direct observation of the physical environment was conducted[98].

5.1.3 The Research Strategy During Investigation

Although I was able to arrange inquiries into four cases[99], the depth of investigation varied with each case. This was due to both the limitations placed on me by time, distance (between the respondents and myself) and financial resources, and the unwillingness, in some cases, of the study participants to let me delve deeply into matters relating to their most valuable asset, namely their knowledge, and the practices that they consider to be fruitful in creating and utilizing that knowledge. This is not to say that the respondents concealed a tremendous amount of information from me, but rather to point out that some respondents were more agreeable to my research agenda than others. For instance, in investigating one collaboration, the university scientist only allotted thirty minutes for his interview and was relatively hasty in his responses, although he had agreed to participate without any pressure or pestering[100]. The difficulties in this case were further compounded by the fact that the collaboration was between university scientists and industrial practitioners in Brisbane, Queensland and I was in Wollongong, New South Wales, about 1050 kilometers (652 miles) in distance between the two locations. I did not have the financial resources to travel to either of the collaborative member's sites, and therefore, had to resort to conducting this inquiry via telephone interviews and investigation of the

[98] In the instances in which contact was made by phone, the research brief was later sent to the potential informant via e-mail, with negotiation proceeding after he or she responded.
[99] Three of these cases are presented in detail in chapters six, seven, and eight. The fourth case is presented in vignettes throughout chapter nine, the cross-case discussion.
[100] I did not, in any of my efforts to attract participants, pressure or pester the informants into cooperating. This sentence is meant to merely reflect that I did not "coerce" the respondent into participating in my study.

participants' information that was available on the Internet. In an effort to ensure reliability in this case, I tape recorded the interviews with the scientists and/or managers from each side of the collaboration.

This case stands in contrast to the collaboration between the Institute for Biomolecular Science at the University of Wollongong and amrad Corporation Limited. The director of the Institute for Biomolecular Science allowed me to observe the meetings between his staff members for a period of five weeks, which amounted to thirteen hours of observation. He arranged for me to observe the collaborative meetings, introduced me to his staff members and presented to them, in his own view, my research agenda, and even suggested that I investigate one of his other collaborations, which I eagerly accepted. He was a voice of persuasion in enlisting participants for the purposes of my investigation from both his research team and his collaborative partners[101].

The other two cases, the collaboration between the Center for Marine Biology and Biotechnology at the University of California, San Diego (CMBB) and Nereus Pharmaceuticals, and the alliance of the Institute for Biomolecular Science (IBS) at the University of Wollongong and Novogen, fell between these two extremes in terms of the cooperation and enthusiasm demonstrated by the study participants. Respondents from the CMBB-Nereus alliance made ample time for interviewing and attempted to arrange times for observation, although each time I arrived in California to observe meetings, the meetings were cancelled[102]. In addition, they were keen to introduce me to other members of the collaboration for the purposes of interviewing. The collaboration between IBS and Novogen was the final case that I investigated. And, in a fashion similar to the reception I received from the CMBB-Nereus team, I was given plenty of time for interviewing, the respondents suggested other members of the

[101] The generosity was evident in the conduct of his collaborators as well. The Chief Scientific Officer at amrad provided me with cab charge vouchers to cover my travel fare from the airport and back again, which totaled more than $100.

[102] This happened twice, once, prior to the interviewing process in December 2002, and the second time in July 2003.

alliance for me to interview, even going as far as contacting them for me, and generally displayed eagerness in their participation[103].

I was able to collect a sufficient amount of data and to reach a point of saturation (Glaser & Strauss, 1967), where I was beginning to notice similarities in the tools, technologies, and work practices being used in different collaborations. I realized I was near a point of saturation when I interviewed the Director of Research at Novogen and he began to tell me that his scientists use a "QSAR" methodology, although he could not remember what that acronym represented[104], and I was able to tell him that it was a structure-activity relationship methodology, which clued him into the "Q" signifying "quantitative". The only reason I knew what "QSAR" meant was because it was a tool that over 50 per cent of my other study participants had discussed in detail.

In total, I conducted sixteen interviews, sixteen hours of observation[105], and analyzed a variety of documents. Interviews were conducted with, at a minimum, the Director of Research and the Head of a particular department that was involved in the collaboration from the industry partner and the principal investigator from the university side of the alliance. The collaborations varied in terms of the weight held in the overall portfolio of each industry firm, and, therefore, the number of participants in the collaboration also varied. Interviewing members from both sides of the collaboration not only yielded multiple perspectives, but it also created embedded units of analysis[106] (Yin, 1998) in the research design. The collaboration was, of course, the main unit of analysis. Each side of the collaboration, namely the firm and the university research centre, was also a unit of analysis, or an embedded unit of analysis. Table 5.1 reports

[103] The Director of Research at the firm offered a meeting time within the same week that I had contacted him to assess his willingness to participate in my study.
[104] His reason, as he claimed, for not knowing what this represented was that not only is his background in pathology and immunology and the QSAR methodology is used mainly in relation to chemistry, but he oversees the research direction of Novogen and is not involved in the daily activities of constructing and testing compounds.
[105] Thirteen of these hours were spent observing the meetings between members of the Institute for Biomolecular Science and three of these hours were spend observing meetings between the Institute for Biomolecular Science and amrad Corporation Limited.
[106] Yin (1998) explains embedded units of analysis being more than one unit of analysis existing in a single case. In this study, the collaboration was the key unit of analysis and the two sides of the alliances were "embedded" in the collaborative unit. The result is a hierarchical arrangement of the units of analysis, where the collaboration is the top tier and the two sides of the alliance fall into the second tier.

the number of interviews conducted in each case, along with the other sources of evidence gathered in investigating each case. A diary of my own thoughts and interpretations that arose throughout the research process supplemented these sources.

Table 5.1 Account of Data Sources

Case	Number of Interviews and Sources	Observation Hours	Documents Collected
Center for Marine Biology and Biotechnology and Nereus Pharmaceuticals	4 Research Center Principal Investigator Head of Microbiology Research Firm Vice President of R&D and Chief Scientific Officer Chemist involved in the collaboration*	0	• Information from both parties' websites • Journal articles written by study participants • Grant proposals • Brochure from CMBB • News articles on the Center for Marine Biology and Biotechnology
Institute for Biomolecular Science and amrad Corporation Limited	7 Research Center Principal Investigator (project 1) Principle Investigator (project 2) Professor Research Fellow PhD Candidate Firm Chief Scientific Officer Head of Virology	16	• Information from both parties' websites • Journal articles written by study participants • Reports prepared for collaborative meetings
Institute for Glycomics and Progen Industries	3 Research Center Principal Investigator Firm R&D Manager Chemist involved in the collaboration*	0	• Information from both parties' websites • Journal articles written by study participants
Institute for Biomolecular Science and Novogen	3 Research Center Principal Investigator PhD Candidate Firm Research Director	0	• Information from both parties' websites • Journal articles written by study participants

* denotes respondents who opted for anonymity

Permission to investigate was initially sought from the director of each university research centre[107]. These directors of the university research centres, if they agreed to participate in my study, were considered the key informants in each case. These participants played a vital role in creating avenues of access for me, suggesting data sources, and paving the way for the entire investigation. Following Bouma's (2000) snowballing technique, the key informants nominated other members of the collaboration as points of contact for my investigation, even going as far, as mentioned previously, as arranging interviews for me. The key informants' importance is reiterated in Yin's (1994) comment that, "[k]ey informants are often critical to the success of a case study. Such persons not only provide the case study investigator with insights into a matter but also can suggest sources of corroboratory evidence and initiate the access to such sources" (p84). In this investigation, the key informants were not necessarily the respondents that offered the most information, and certainly not the ones that offered the most controversial information. Rather, the key informants were the ones that made the inquiries possible through providing links to other participants.

My interview style varied between the key informants and the remainder of the participants. The interviews I conducted with the key informants were very general, as opposed to the interviews with the remainder of the study participants that were focused interviews (Merton, Fiske, & Kendall, 1990). The interviews with the other participants were still open-ended, but more focused on the questions outlined in the case study protocol (as previously noted, these questions are listed in Appendix B). My aim in the interviews with the key

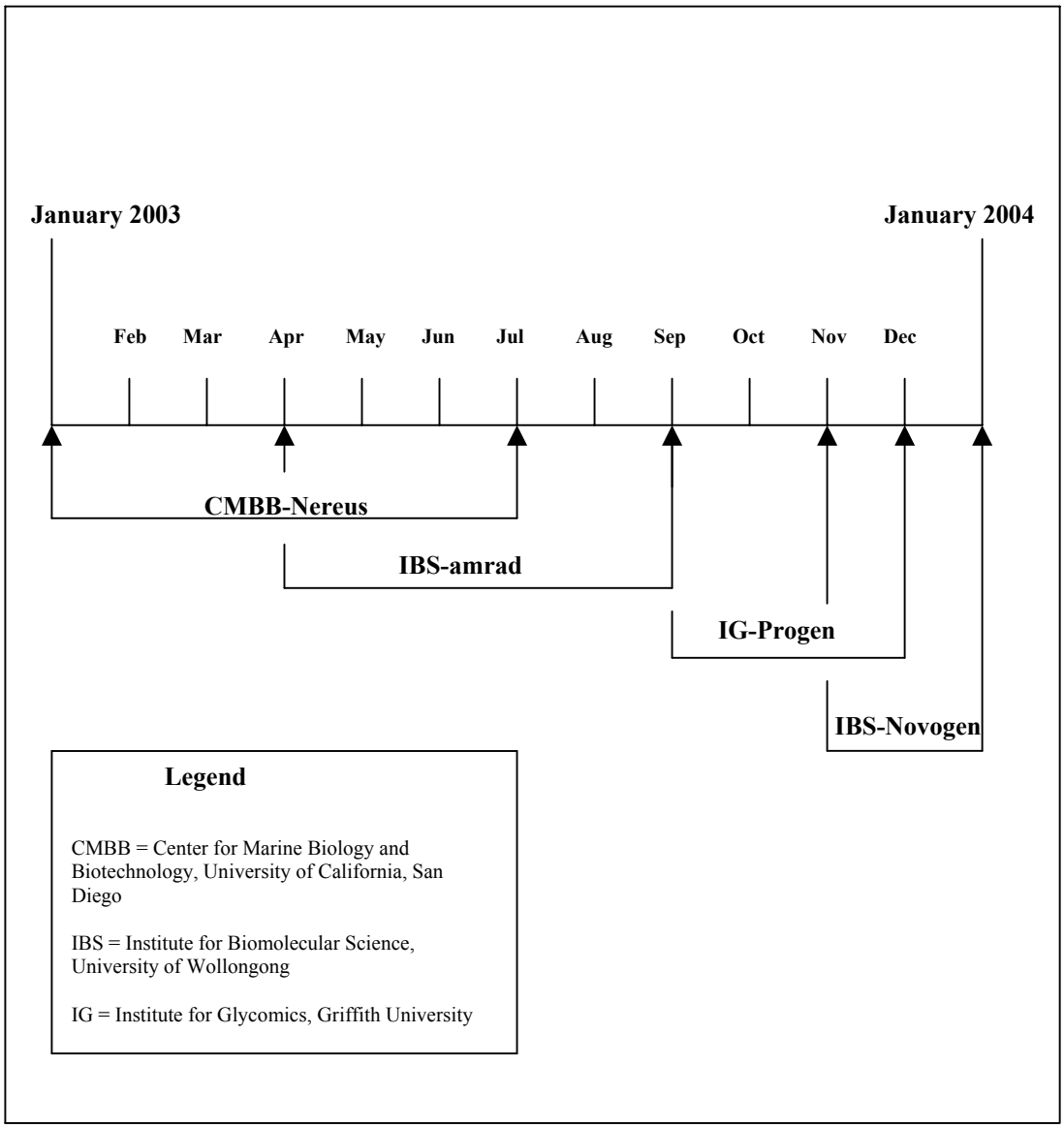
[107] This plan proceeded without interruption, except in the case of the collaboration between the Institute for Glycomics and Progen Industries. I had originally selected a case between scientists at the University of California, San Fransisco (UCSF) and Progen. When I contacted the lead scientist at UCSF, he responded to my plea for permission to investigate the alliance by directing me to contact the R&D Executive at Progen to request her permission to study the collaboration, which I did. She replied to me, stating that the collaboration between UCSF and Progen had finished and that the details of the collaboration were confidential. To my surprise, however, she listed collaborations between Progen and the Australian National University, and Progen and Griffith University and said that she would be happy to arrange for me to investigate one of these collaborations should I choose to have her do so. After an initial look at the collaborations, I decided to have her arrange interviews for me in relation to the collaboration between Progen and the scientists at the Institute for Glycomics because both organizations were located in the same state and the other Australian collaboration that I already had lined-up was an inter-state alliance. (I had originally intended to compare the flow of knowledge in collaborations where the participants were co-located, with alliances in which there was a significant geographical distance between the collaborators.)

informants was to develop an initial overview of the collaboration, which included gathering data pertaining to the history of the alliance, the collaborative goals, the number of participants, and the weight of the collaboration in terms of the university scientists' (and research centres') total load of research. I remained in contact with the key informants throughout the investigation of each case. In two cases, specifically the collaborations between the Center for Marine Biology and Biotechnology and Nereus Pharmaceuticals, and the Institute for Biomolecular Science and amrad alliance, I followed the procedures discussed in Yin (1981a) and contacted the key informants after formally concluding the investigation to arrange more interviews and times for observation.

There was an overlap in the investigative time frames of each case, which allowed me to return to previous cases in a bid to find data that would correspond to or contradict data that were being found in current cases. The total time spent collecting data amounted to one year, with the amount of time dedicated to each case varying with the geographical distance between the study participants and myself, the willingness of the participants to comply with my requests for inquiry, and the length of time it took me to acquire the information and insight necessary to draw conclusions about the case. As I came to know more about the general practice of biotechnology and its associated sciences, my ability to apprehend the basic activities used in each alliance accelerated[108]. Diagram 5.1 is a chronology of the fieldwork, serving to delineate the length of each single case investigation and demonstrate the specific overlaps in investigative time frames.

[108] I was able to conduct the investigation of the collaboration between the Institute for Biomolecular Science and Novogen relatively quickly, in comparison with the time frames of other cases, because I had already studied the Institute for Biomolecular Science in detail. The activities performed by IBS in collaboration with amrad were similar to the activities performed by IBS in collaboration with Novogen. They varied only as a result of the peculiarities of the collaborative context and the relationships between the scientists in the collaboration. And, this is one reason why I have chosen to present the findings from the IBS-Novogen case as vignettes in the cross-case discussion.

Diagram 5.2 Investigative Timeframe



5.1.4 The Beginnings of Interpretive Change

It was over the course of this year of study that my interpretation of how knowledge was managed in collaborations between university and industry in biotechnology began to change. My dependency on the literature for insight and answers diminished with the acquisition of empirical data. Through the process of analyzing the data, I started to notice that knowledge

was not exactly "flowing" between collaborative constituents. There were, indeed, types of knowledge, such as journals and databases, to which all members of the collaborations had access, but most of the alliance participants retained their own ingrained knowledge bases and there was not a lot of evidence to suggest that these collaborations were aimed at one party obtaining the specific scientific knowledge of the other members of the alliance. In fact, as the analysis advanced, specific evidence surfaced that elucidated legitimate reasons for knowledge not to be fluidly shared and exchanged in these collaborations[109]. The evidence was pointing to the collaborations being geared toward the procurement of a product that could only be achieved by corralling the requisite ingrained knowledge of the scientists involved in the collaborative endeavour.

It should be noted, though, that this assumption was only the result of preliminary analysis. It was, however, disturbing in terms of my ability to answer the question of how knowledge flows in university-industry collaborations in biotechnology. Could my answer be, "it doesn't"? And, if so, what would this say about my planning process? If I was to believe my data, and if the data were really saying that knowledge did not flow, I would need to revise my conceptualization of knowledge management considerably, not to mention the research agenda. I obviously needed to investigate the matter further. The next section of this chapter details how I proceeded with this investigation and the epistemological parameters that guided the process.

5.2 The Processes of Reconstructive Interpretation & Data Analysis

When I initiated the research process, I did so under the auspices of a theoretical framework that drew on two paradigms of knowledge that, while not being mutually exclusive, offered accounts of knowledge with disparate focuses. One view relied heavily on the

[109] In analyzing the data from the collaboration between the Institute for Glycomics and Progen, it became clear to me that there are certain instances in which knowledge is deliberately kept secret from a collaborative partner. Dr. Robert Don, the R&D Manager at Progen, highlighted that, "[o]ne of the issues in working under confidentiality [is] if you share knowledge, in essence, the other group can claim that they held that idea as well. So, it means that your hold in IP is not as strong. So, ideally, if your knowledge is not public, you really don't want to tell anyone else who is working in similar areas…We agreed to the boundaries beforehand, and if we have something new or [our collaborator] has something new that doesn't relate to the project, then we simply will not discuss it" (8 December 2003 – personal interview).

sociological and philosophical accounts that depicted knowledge as a product of social construction. It was this approach that yielded the construct of migratory knowledge. The other approach commenced under the influence of a biological interpretation of how knowledge is generated in the brain and, consequently, allowed for the development of the ingrained knowledge construct.

My original plan was to gather data with these two meta-theories of knowledge, (the representationist approach or migratory knowledge versus the anti-representationist approach or ingrained knowledge) as the theories to be tested by the data. I chose this course of action because the general sentiment from the knowledge management literature, as I perceived it, was based on the assumption that knowledge "flowed". As von Krogh and Roos (1996) suggest, labels of knowledge from this discourse include "explicit knowledge" (Nonaka, 1991), "migratory knowledge" (Badaracco, 1991), and "articulated knowledge" (Itami, 1987). These types of knowledge fortify the assumption that knowledge can be shared. Or perhaps, the assumption lends credibility to the concepts. Because there are types of knowledge that cannot be shared, for instance Polanyi's (1958) tacit knowledge and Maturana and Varela's (1980) autopoietic knowledge, it is vitally important to consider how knowledge that cannot be shared impacts on the interactions between individuals, specifically in cases of collaboration.

Scholars of knowledge management do indeed attempt to analyze this consideration. Nonaka (1991) examines tacit knowledge. Badaracco (1991) provides an account of embedded knowledge. These authors do so, however, with little attention to the discussion of knowledge that dates back many decades. The philosophy and sociology of knowledge are disciplines that preceded knowledge management and it is unwise to neglect the findings and main claims of the scholars in these areas. In my book, knowledge is cumulative, and treating it as such requires delving into the literatures that existed prior to the discourse on knowledge management. The representationist approach to knowledge matched the constructs I found in the knowledge management literature. The anti-representationist approach offered a way into the work of the philosophers and sociologists of knowledge. I thought that by taking these two theories into account in the process of investigation and comparing the data from the cases I

proposed to study with these two meta-theories of knowledge, I would be overcoming the pitfalls that I found to be prevalent in the knowledge management literature.

Following Yin (1994), I had planned to "iterate[110]" between the data collected and the theories, whereby one theory would more adequately describe the nature of knowledge, albeit with some modification. I had prepared a 40-page conceptualization of the theories for this purpose. The end result would be a position that dictated whether or not knowledge flowed on the basis of an account of knowledge depicted as socially constructed (the representationist approach) *or* an understanding of knowledge as a product of the individual mind that was incapable of being directly transferred to another being (the anti-representationist approach).

Perhaps I had an illegitimate conceptualization of the research process. Perhaps I had paved the road for inquiry with an impassible barrier: asking philosophical questions and seeking empirical answers. Wherever the fault lay in my original plan, I, fortunately, found my stumbling ground to be a springboard to enlightenment. Upon analyzing the data, it became apparent to me that the story being told was centred not on knowledge being migratory *or* ingrained, but on it being both. With that insight came the revelation that it did not, in fact, need to diffuse to al members of the collaborations under investigation, but that there needed to be specific mechanisms for integrating it together in a coherent, usable, valuable manner. Indeed, the data exemplified distinct divisions of labour, which created partitions between the scientists that I was studying and impermeable boundaries that blocked the flow of knowledge, namely the cultural divides between academic and industry scientists, and the silos created by divergent scientific knowledge bases.

5.2.1 The Turning Point

The turning point in my interpretation came in the analysis of the data acquired from the Institute for Biomolecular Science and amrad alliance. I had been following a strict pattern of

[110] Yin (1994) describes a process of iteration for explanation-building. He writes that, "…the case study evidence is examined, theoretical positions are revised, and the evidence is examined once again from a new perspective, in this iterative mode" (p111).

concurrent data collection and analysis[111]. During the interview process, I had taken copious notes, taking the time to write down direct quotes during interviews[112]. I recall the moment of reconstructive interpretation beginning with analysis of my interview with Dr. Jonathan Coates from amrad. I had conducted the interview on May 20, 2003. I analyzed the data from the interview, in conjunction with the notes from my observations of the meetings at the Institute for Biomolecular Science and several other secondary sources, including a co-authored paper from members of the collaboration and information from amrad's website, on May 21, 2003. Coates had said that he didn't need to learn synthetic chemistry (his background knowledge is in virology and immunology), but yet the collaboration was aimed at finding the most active compounds, a practice that requires the use of advanced knowledge in synthetic chemistry.

There was clearly no "flow" of knowledge in the area of chemistry from the scientists at the Institute for Biomolecular Science to the staff at amrad. Amrad did not even have any chemists at the time. The actual compounds that were shipped from IBS in Wollongong, NSW to amrad in Richmond, VIC via that Australian Post System were the elements that could be considered to be "flowing" in the alliance. I forced myself to answer the question, does knowledge flow through the Australian Post? My answer was both yes and no. Certain forms of knowledge could be sent in the mail, namely journal articles and reports – migratory knowledge. Other forms of knowledge, specifically the knowledge used to make the compounds that constituted the rationale for the IBS-amrad alliance – ingrained knowledge – could not be sent in the mail. And, these were indeed the constructs, migratory and ingrained knowledge, which I had developed in my original research agenda.

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[111] Eisenhardt (1989a) suggests that "[o]verlapping data analysis with data collection not only gives the researcher a head start in analysis but, more importantly, allows researchers to take advantage of flexible data collection" (p539), a practice which proved to be useful when I returned to the key informants from the CMBB-Nereus and IBS-amrad collaborations to uncover more data.

[112] I had chosen to take notes during my interviews rather than use a tape recorder because I did not foresee myself having the time or equipment to transcribe the contents of the tape. And, as Yin (1994) notes, "…the interviews should always be considered verbal reports only. As such, they are subject to the common problems of bias, poor recall, and poor or inaccurate articulation…a reasonable approach is to corroborate interview data with information from other sources" (p85). In an effort to mitigate the possible bias and inaccurate articulations, I sought data from both other members of the collaboration and from secondary sources. I also attempted to reduce the harm caused by poor recall on my part, by adopting Eisenhardt's (1989b) 24-hour rule, in which the notes from the interviews, along with the subjective notes in my field diary, were reviewed, analyzed, and written into a summary report within 24 hours of conducting each interview.

My interpretation changed. The constructs endured. The durability of these constructs has provided validity in the generation of my final theory. For, as Eisenhardt (1989a) argues, constructs that are specified a priori and demonstrate significance as the study progresses provide a "firmer empirical grounding for the emergent theory" (p536). But of what emergent theory am I speaking?

5.2.2 Data Analysis

Along with the reconstruction of my interpretation arose the need to temporarily put aside my prior assumptions and allow the data to become the sole source of illumination. While the methodological approach to this research cannot be classified as a grounded theory approach, á la Glaser and Strauss (1967) and Strauss (1987), particularly because there were intentionally focused questions used in the interview process, grounded theory tactics were applied in searching for patterns in the data and the overall meaning of the data. These tactics included coding strategies, the constant-comparative method, and theoretical conceptualization.

If theory is taken to represent "interpretations made from given perspectives as adopted or researched by researchers" and consists of "*plausible* relationships proposed among *concepts* and *sets of concepts*" as Strauss and Corbin contend (1998, p171 and p168, respectively – emphasis their own), then chapters two, three, and four of this thesis may be regarded as a theory grafted from my interpretation of the findings from the multiple-case investigation that is enmeshed with the "concept" of modularity and the related "set of concepts" known as boundary objects. This theory emerged inductively, as opposed to the deductive theory that I had planned to arrive at by beginning with the general principles of the representationist and anti-represenationist persuasions of knowledge and deducing a theory from the data's correspondence with one or the other of these theories.

In arriving at this theory, once I had gathered enough evidence to persuasively conclude that there was a distinct division of labour within the alliances under investigation (which was achieved via a process of review, analysis, and coding of the data), I adopted modularity as the core code in my analysis and the four specific types of boundary objects (standardized forms,

coincident boundaries, repositories, and starting points) as the axial coding concepts[113]. This allowed me to use the constant-comparative method, in which I compared the data with the literature, and the data with the data, seeking "patterns of actions and interaction between and among various types of social units" (Strauss & Corbin, 1998, p169). The patterns of action detailed in the data amounted to the use of specific design rules, interfaces, repositories, and starting points to amalgamate the ingrained knowledge of the collaborative participants. This pattern was repeated across the four contexts defined by the alliances, resulting in a cross-situational generalization (Miller, 1997).

5.2.3 Guiding Principles

Throughout this process of analysis, I gauged my interpretation on the seven principles of interpretive research, as described by Klein and Myers (1999). While a table of these principles and their proposed function in the research agenda, as it was conceived during the planning phase of this multiple-case inquiry, can be found in Appendix C, I also list them here as a prelude to a discussion based on their application in the process of analysis. The seven principles include: 1) the fundamental principles of the hermeneutic circle, 2) the principle of contextualization, 3) the principle of interaction between the researcher and the subjects, 4) the principle of abstraction and generalization, 5) the principle of dialogical reasoning, 6) the principles of multiple interpretations, and 7) the principle of suspicion. Each of these principles played a role in the reconstruction of my interpretation and the process of analysis. These principles are not addressed in any specific order, but instead, are discussed in relation to the thought patterns I followed in arriving at the interpretation of the data that is presented in this thesis.

That the collaborations under scrutiny exist in social worlds composed by "power structures, vested interests, and limited resources to meet the goals of various actors who

[113] This, admittedly, is not in the traditional form of grounded theory. But, what is the traditional form? (Even the originators of the method can't seem to agree on it.) And, this application of coding was valid in the sense that it allowed me to draw from the literature and compare data with data, and the emerging conceptual categories with the concepts of modularity and boundary objects (Melia, 1997).

construct and enact this social world" (Klein & Myers, 1999, p78) is arguably a foundational precept in understanding their order, function and, most importantly, their fragility. Many of these collaborations, and many scientific endeavours in general, fail to accomplish their goals because of the inability of the involved actors to appropriately align their social worlds (Fujimura, 1987). As mentioned in chapter two, in cases where the industry partner is funding the work performed in the alliance, that partner has considerably more to lose than a university partner who can merely write-off a failure as a scientific problem that cannot be solved under the existing circumstances. With these considerations in mind, it became paramount for me to analyze the data I collected through an application of the principle of suspicion.

One example from the data may help to clarify my point. In the process of interviewing the participants from one alliance, one respondent was very hasty with his answers to my questions. I pondered whether his hastiness was a result of my intrusion on his hectic work schedule. In an interview with a second respondent from this case, however, I was informed that the collaboration was not meeting the established expectations and that a portion of the cause of the less than desirable performance, according to the second respondent, was the first respondent's inability to perform to the level to that this scientist (first respondent) was contracted to perform[114]. Thus, I had a plausible explanation for the first respondent's hastiness: the collaboration was not going to plan and it was potentially his fault. But, this explanation for the first respondent's rashness could not be taken at face value, nor could the firm respondent's claim that the collaboration was not meeting expectations. (Nor was there any reason to doubt that the university respondent was hasty simply because he was pressed for time.)

There could perhaps be a rivalry between the two interviewees. The failure to reach the collaborative goals, if there was indeed a failure, may have been a result of inefficiencies of the industry partner, and the industry partner may have been ashamed to let this come out in the interview. I also had to keep in mind the fact that the industry firm was sponsoring the entire project and a failure to achieve the collaborative goals would be much more detrimental, at least

[114] According to the second respondent, this was due to both scientific uncertainties and insufficient levels of work.

in the short term, to the firm, as opposed to the consequences that the university research centre would face. Therefore, the members of the firm may be more sensitive to failure. The failure could possibly be attributed to the failure of the experiment, and have nothing to do with the capabilities of the scientists. One could think of a number of reasons why the second interviewee may have pinpointed a failure to accomplish the agenda of the alliance and blamed some of this failure on the first respondent. I, however, first needed to find evidence that the collaboration was indeed not meeting expectations, uncover the expectations that needed to be met, and then, if the alliance was on a failing trajectory, find triangulated evidence of the reasons for failure.

I first looked at the length of time that the collaboration had been in existence. I sought evidence from other interviewees regarding the aims of the alliance and came up with a triangulated answer. The alliance was initiated and funded to create a drug lead to target a specific enzyme. Nearing the end of the contractual term, the desired drug lead had not been attained.

The principle of multiple interpretations came into play, however, with the interview of a third respondent from the collaboration. The third interviewee was less pessimistic about the collaboration than the second interviewee had been. He expressed a hope for the collaborative project and a sense of respect for the abilities of the university scientists working on the collaborative agenda.

In continuing to strive for a resolution and final interpretation of the performance of the alliance, I applied the principle of abstraction and generalizaton. I compared the three year time frame of the collaboration with the amount of time it had taken other collaborations in my study to produce the desired outcome, specifically in the cases where the desired outcome was a drug lead. I engaged the principle of contextualization, considering the notion that I was seeking to understand a moving target and that relationships between people, organizations, and the technology that they use are constantly changing (Klein and Myers, 1999). I considered that these types of endeavours take time to reach their desired output. Recall one of the arguments made in chapter two relating to the context of these collaborations that was premised on the

highly experimental nature of the scientific work and the contextual factors that typically co-exist with this type of work, and how they amount to a great deal of complexity and uncertainty. Three years is not a lot of time considering the nature of the work, the need for the collaborative partners to get to know one another (this was their first time working together), and the fact that all parties involved had other work related commitments that distracted them from the collaborative agenda. While the answer I eventually arrived at was that there was indeed a lack of success in the collaboration at the time of interviews, the collaboration had not yet ended.

The process of interpretation detailed above utilizes several of the seven principles of interpretation dictated by Klein and Myers (1999). These principles, along with the remainder of the seven guidelines for interpretive research, were applied in the process of interpreting the other cases under investigation as well. One principle that pervaded the analysis phase of investigation was the principle of interaction between the researchers and the subjects[115]. It is important to note that, upon embarking on this research, I was virtually scientifically illiterate. I knew what the periodic table was, but I had never heard of an assay. I had studied biology, but never microbiology. I had never even thought about the methodologies, outcome considerations, or the uncertainty associated with developing a drug.

Conversely, the interviewees in my study were scientists and, although some of them had made their way into the upper echelons of the organizations of which they were members, achieving managerial status, they were by no means trained managers. They had not studied management. As Fryxell and Judge (1995) note,

> …R&D managers get very little exposure to management training. R&D managers are nearly always promoted into their positions from dynamic technical specialties. Given their hectic schedules and struggle to maintain some semblance of expertise, the choice between technological currency or managerial training is readily reconciled in favor of the former (p35).

The senior scientists from the firms in my study, although they currently held management positions such as Chief Scientific Officer and R&D Manager, were unfamiliar with the

[115] Interestingly, the use of tact (one of the communicative aids introduced in chapter four) became important in my interactions with the research subjects. Standardized methodological and ethical approaches were sometimes ineffective and needed to be modified to fit the situation at hand. I needed to be seen as "doing the right thing at the right time", particularly in instances of political sensitivity.

terminology of management and they needed to be seen as interpreters of their own environment. Many of them had never critically analyzed their work environment to the extent required for them to appropriately respond to the research questions.

I, of course, had to consume and digest a considerable amount of scientific knowledge, which I did by reading various texts on the methodologies used by the interviewees, talking to them in detail about their work, and, probably most influentially, observing the meetings during which they discussed their hypotheses, the rationale for their ways of thinking, and the implications of their assumptions. This endeavour required me to "study-up"[116]. In turn, I had to inform my participants of the purpose of the research and introduce them to the theoretical concepts being probed in the investigation. I became considerably more adept at doing so as I gained a better understanding of the work that the scientists performed. "The term *reflexivity* (Hammersley & Atkinson, 1983) is often used for this unavoidable mutual influence of the research participants and the researcher on each other" (Maxwell, 1998, p86 – emphasis his own).

[116] This is a term taken from Laura Nader as she is quoted in Charlesworth et al (1989). With her usage of the term, "study-up", she, according to Charlesworth et al, advocates the sociological investigation of high social status, professional groups, rather than the deviant, marginalized groups and communities, such as criminals, prostitutes, etc., that she contends to be typically studied in anthropological inquiries. While the study being reported in this thesis is not an anthropological investigation, whereby researchers observe their "subjects" in their natural setting and, then, make their best attempt at accurately interpreting and depicting that setting and the interactions of their subjects within it, management is a social science and I, for the purposes of my investigation, had to develop a detailed understanding of the world of the scientists that participated in my research project. These scientists can be described as high-social status individuals that make-up a professional group of biotechnologists, or university-industry collaborators. And, in carrying out this research project, I was "studying-up". This notion of "studying-up" in terms of investigating a high-social status group becomes particularly pertinent when considering that several of my participants conveyed their belief in the inferiority of management studies in relation to the natural sciences. While most of my participants demonstrated that I had achieved a valid understanding of their scientific management activities (one interviewee, when asked at the end of our conversion whether he thought there was anything glaringly missing from my line of questioning, said that I had pretty much covered the central aspects of his job and appropriately targeted his role as Director of Research), several of them would consistently refer to my work as a "study in scientific communication" or "research into how knowledge is generated", deliberately avoiding the term "management", even though I used the phrase "knowledge management" quite frequently in my conversations with them. This may have been influenced by the fact that I was increasingly fascinated with their work, particularly in the cases of the CMBB-Nereus investigation, where the scientists often traveled to exotic locations to extract mud from the bottom of the ocean, to later turn it into a potential therapeutic for breast cancer, and the IBS-amrad study, where during my observation of their meetings they would put large, colorful computer-modeled images of an enzyme up on the wall and debate the functionality of it. I had several informal conversations with my key informants about how much more interesting their work was than what I was studying for the purposes of my PhD.

5.2.4 Hermeneutics and the Research Process

This was essentially a hermeneutic experience. It involved a process of language acquisition, by both my study participants (becoming accustomed to the language of the research agenda) and myself (learning the basic scientific concepts associated with the work being performed by the scientists). And, as How (1995) notes, "[l]anguage is not just a particular social-historical artifact, it is that medium through which we have a 'world', and thus nothing that is intelligible remains outside of it" (p160). In the later stages of collecting and analyzing data (remember that this was an overlapping process), I developed a more concrete interpretation of the research world that pertained to my investigation, both in terms of my own framework and the social worlds of my participants. As a result, I was better prepared to share that world with and define it to those individuals who were part of my investigation.

Creating this "research world" required application of the principle of dialogical reasoning[117], whereby I was notably sensitive to the contradictions between the theoretical preconceptions guiding the research design and the actual findings. As noted previously, my interpretation changed with the analysis of the data to the extent that my original plan for testing the two preset theories represented by the representationist and anti-representationist approaches to knowledge against the data had to be scrapped. The data, rather than my preconceived notions of knowledge and its role and function in university-industry collaborations, were what corresponded to the world I was investigating. The data, then, were a much more credible source.

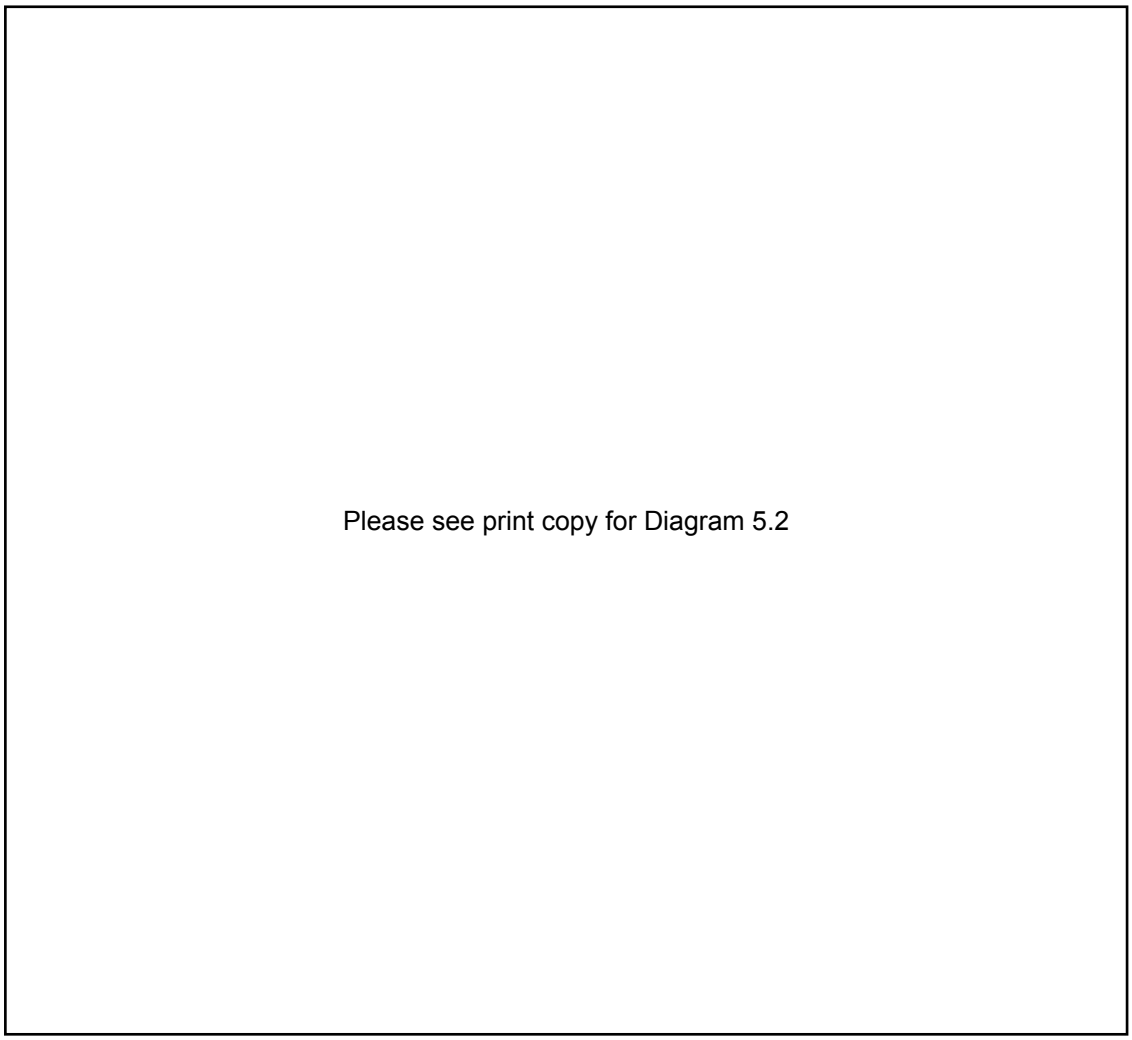
In a traditional Gadamerian[118] fashion, my interpretation of the research world came from finding myself affected by something questionable, namely the way knowledge was dealt with in university-industry collaborations in biotechnology. My interpretation was the result of

[117] The principle of dialogical reasoning "[r]equires sensitivity to possible contradiction between the theoretical preconceptions guiding the research design and actual findings…with subsequent cycles of revision" (Klein & Myers, 1999, p72, Table 1).

[118] Hans-Georg Gadamer produced one of the most influential texts in the field of hermeneutics, *Truth and Method* (1989). This text provides a profound discussion on the implications for the arts and humanities of the historical conditionedness of all human understanding (Bontekoe, 1996). Moreover, Gadamer's debates with Jurgen Habermans are an engaging pathway into understanding the role of language in social action and the process of self-discovery (cf How, 1995).

concluding that I did not know how knowledge was handled or how it functioned in these contexts, and of realizing that I must question this handling and functioning in a certain way that went beyond my familiar assumptions (How, 1995). Following the principle of the hermeneutic circle, my interpretation resulted from several parts of the study, including my own preliminary understandings, those of the study participants, the social interaction between the participants and myself that reformulated those preliminary understandings, the input from the various sources, literary, social and secondary, and the discussion of my research with my peers and supervisors. These pieces of the research represent a continuous stream of information that is represented in the hermeneutic circle of my interpretive process, shown figuratively in Diagram 5.2.

Diagram 5.2 The Hermeneutic Circle of the Research Project



Source: Adapted from Bontekoe (1996)

"[T]he hermeneutic circle merely reflects the way in which the structure of human understanding is dictated by the temporal nature of…experience. It is *because* information becomes available to us only serially that it must be incorporated piecemeal into the synthetic vision which illuminates the meaning of the object of comprehension" (Bontekoe, 1996, p4 – emphasis his own). The order in which the various parts of the whole meaning of my interpretation were presented shapes the construction of my entire research experience. I have stated previously that I underwent a process of reconstructive interpretation. The tools of

reconstruction are the parts of the hermeneutic circle. The final interpretation, while it may not appear to fit into a circular pattern that continues to "circulate", stands to be revised as I receive feedback from the examiners of this thesis and as I continue to conduct research into the area presented here and other contexts as well. Stated otherwise, I will continue to re-evaluate this experience in the light of my future experiences.

The reader of this thesis is not presented with the parts in the same order as I encountered them. Chapters two, three, and four of this thesis are both a literature review and a presentation of a grafted theory. Some of the elements that contributed to my conceptualization, the first block in the hermeneutic circle, are presented in these chapters, others are not. These chapters, however, also contain literature that was not reviewed prior to investigation because the parts, block two of the hermeneutic circle, called for an integration of additional literature. The combination of the original literature review, the story that was told by the data, my interpretation of the activities of the study participants, and the additional literary elements added during the process of analysis are what is encountered by the reader in chapters two, three, and four. This is what I call grafted theory. The contents of chapters two, three, and four are a theoretical argument that provides an explanation of how knowledge is managed, integrated, and aligned, in university-industry collaborations in biotechnology[119].

That the reader encounters these parts in both a different form and a different order than I did may lead to the reader having a different interpretation of the research than I do. Using the concepts of migratory knowledge and ingrained knowledge that were presented in chapter three, it can be said that this thesis is a form of migratory knowledge, and both my interpretation of the research and the reader's interpretation of the research are types of ingrained knowledge. The result, then, may be that the reader and I have different states of knowing relating to the research. And, this is to be expected considering that the reader and I have encountered the data in different forms and been confronted with the parts of the research in different orders.

[119] Here, in chapter five, the reader is presented with an account of the development of my interpretation and the methodologies used in the process of that development. The following chapters offer my interpretation of the data. And, the final chapters detail the implication and impact of my investigation.

Nonetheless, if the argument that I am making in this thesis is strong, if I am presenting myself as a credible researcher, if my interpretation is valid and reliable, then the reader and I should diverge only in terms of states of knowing and not in terms of that which is known. Essentially, we should agree on that which is known, but with an allowable dissonance in states of knowing because, unless the reader conducts the research on his or her own, confronting the data head-on and in the same temporal pattern as I did, our states of knowing cannot converge.

Let me reiterate, though, that attempts have been made to ensure the validity and reliability of my interpretation. Validity has been achieved through using multiple sources of evidence and having the reports of each case, as they appear in this report, reviewed by study participants. Internal validity has been secured using a pattern-matching approach to data analysis (Yin, 1994). The development of a case study protocol and the codification of the operational aspects of the research in this chapter have aided in generating reliability. And, throughout the research process, from data collection to analysis, to the integration of the various parts into a coherent whole, the seven principles of interpretive research have been applied in a bid to make the "research story more plausible and convincing" to the reader (Klein & Myers, 1999, p79).

The result of these efforts is, of course, a final interpretation and a theory that is subject to the reader's judgment. While the final interpretation is my own conclusive understanding of knowledge synthesis and alignment in university-industry collaborations in biotechnology, the theory comes from grafting the principles of modularity and boundary objects, and applying these principles to create an effective argument about how knowledge synthesis and alignment are achieved. This argument is metaphorically based, centred on the similarities between the game of Bingo and the inherent activities of collaboration between university and industry with a design for purpose rationale. The next section of this chapter details how this theory arose from my final interpretation.

5.3 Final Interpretation & Theory Construction

"An essential feature of theory building is comparison of the emergent concepts, theory, or hypotheses with the extant literature. This involves asking what is this similar to, what does it contradict, and why. A key to this process is to consider a broad range of literature" (Eisenhardt, 1989b, p544). My original preconceived ideas were that collaborations between university and industry revolved around the sharing and exchange of knowledge between the collaborative participants. The story being told by the data indicated that knowledge "flowed" in certain forms, but the structure of the alliance also had to be considered because it is through the structure that the "flows" are operationalized. Elements such as choosing the right individuals to perform the tasks, appropriately matching those individuals to the tasks necessary to accomplish the goals, and utilizing the correct tools, technologies, and work practices to integrate the task level performances also had to be considered. It was not a matter of "flows", but a matter of "flows" *and* structure. There was an obvious contradiction between my original interpretation and the story being told by the data. In order to overcome the barrier imposed by this contradiction, I needed to find literature that offered a story similar to the one being told by the data. The literature on modularity and boundary objects provided that story, but why? And, what are the benefits of using these literature bases to explain how knowledge is managed in university-industry collaborations?

5.3.1 Applying Exogenous Literature

The similarity resulted from the division of labour that was evidenced in the data and the notion that the participants in collaborations between university and industry were from different social worlds. The concept of modularity is premised on a nearly decomposable system (Simon, 1962), or a complex system that is composed of interrelated subsystems that in turn have their own micro-systems (Sanchez & Mahoney, 1996). Modularity as an explanation for the design process correlated rather well with the activities of the scientists under investigation and their loosely-coupled architectural context because of the unifying principle of

a division of labour that, in order to be effective, had to be controlled by specific orchestrating mechanisms. The concept of boundary objects, in addition to the three main components of a modular design process, namely an architecture, design rules, and interfaces, was a convincing and applicable set of constructs that helped to define these orchestrating mechanisms. Like Star and Griesemer (1989), I was interested in how actors from heterogeneous social worlds could cooperate and align their activities to accomplish an encompassing goal, and the boundary objects defined by these authors were a way of achieving this, that was both empirically grounded and suitable to the contexts under scrutiny. In my search of exogenous literatures, I also found Latour's (1987) concept of "things" to be relevant to and descriptive of some of the elements of the data. The concept of "things" is used by Latour (1987) to demonstrate how abstruse articles of science become routine in nature and use, and this was precisely the pattern evidenced by the data.

Moving beyond the contradiction between my preconceived ideals and the story being told by the data, I was able to find similarity in different literature bases, specifically within the discourse on modularity, the literature utilizing the theoretical constructs of boundary objects, and the STS (science and technology studies) literature. The similarities between these literary informants and the story being told by the data became even more apparent as I proceeded with analyzing the data in a constant-comparative method[120]. There were indeed similarities between the cases, and these congruencies corresponded with the concepts in the literature. These similarities set the tone for the emerging theory because, as Maxwell (1998) notes,

> [a] useful theory helps you to organize what you see. Particular pieces of data that otherwise might seem unconnected or irrelevant to one another or to your research questions can be related if you can fit them into the theory. A useful theory also illuminates what you are seeing in your research. It draws your attention to particular events or phenomena, and sheds light on relationships that might otherwise go unnoticed or misunderstood (p78).

As Eisenhardt (1989a) suggests, literature that discusses findings similar to those encountered through the analysis of current data links underlying similarities in phenomena not

[120] The constant comparative method was discussed in section 5.2, The Process of Reconstructive Interpretation and Data Analysis. This technique for analysis is cited in Strauss and Corbin (1998). It entails "constantly comparing" data with other data, and data with the concepts in the literature during the process of analysis.

normally associated with each other. This becomes apparent when considering that interorganizational relationships have been conceptualized from the viewpoint of developmental processes (Ring & Van de Ven, 1994), as mechanisms for the acquisition of technological competencies (Steensma, 1996), as means for avoiding the administrative costs of performing an in-house set of virtually integrated activities (Williamson, 1985), and as the forerunner to efficiency and profitability (Contractor & Lorange, 1988), but few attempts have been made to incorporate the concept of modularity into the discourse on collaborative relationships. While Beer, Eisenstat, and Spector (1990) point to the necessity of coordination for innovation and competitive success in cooperative endeavours (Smith, Carroll, & Ashford, 1995), this coordination has typically been discussed in terms of contracts, values (trust, reputation, etc.), and prior experience with one another.

Through the application of the concept of modularity and the acknowledgement of a division of labour among cooperators with complementary resources, new instruments for coordination are introduced. These instruments include the design rules, interfaces, repositories, and starting points taken from the literature on modularity and boundary objects and transposed into the realm of interorganizational collaboration. The result of embracing the literature that is not generally applied to a given phenomenon, that is, applying the concepts of modularity and boundary objects to the phenomenon of interorganizational collaboration, "is often a theory with stronger internal validity, wider generalizability, and higher conceptual level" (Eisenhardt, 1989a, p544).

The representational form that I have chosen to demonstrate the application of the concepts of modularity and boundary objects to collaborations between university and industry in biotechnology, and the resultant theory from the process of this application, is metaphor. "Metaphor, a literary device, is the backbone of social science writing. Like the spine, it bears weight, permits movement, is buried beneath the surface, and links parts together into a functional, coherent whole" (Richardson, 2000, p926). In developing the metaphor of Biotechnology Bingo, I was inspired by the work of Baldwin and Clark (1997, 2000) and their description of the task-performance matrix. Upon exploring the traditional game of Bingo in

detail, I found inherent similarities between the game and the practices subsumed under the heading of university-industry collaboration in biotechnology.

These similarities spawned the use of the metaphor of Biotechnology Bingo to explain the activities of alliance participants and shed light on their interworkings. The adoption of this metaphor not only provided an avenue for coherency in the report on the research findings, but it also created channels for analysis and theorizing. As Richardson (2000) contends, the metaphor frames the actions taken in theorizing and what is believed to constitute theory. The metaphor of Biotechnology Bingo has structured the theorizing in the sense that I have focused on successfully playing the game and winning, as opposed to an analysis of the simple rules of conduct in the game[121]. If the metaphor of Biotechnology Bingo is taken as the form of the theory, the foundation of the theory is the various literary informants used in the process of theory construction, my interpretation of the strategies necessary to win the game, and, most importantly, the data that were used in the development of my interpretation. The theory has been crafted from all of these sources.

5.4 Conclusion

The contents of this chapter detail how the material presented throughout this thesis was produced. The production process had as inputs: an initial literature review that resulted in my preconceived ideas of the contexts that I would be investigating; information from the participants in my study; the secondary sources that both corroborated and negated this information; the observation periods that informed by interpretation; my interpretation in its initial and reconstructed states; the many conversations and debates I had with my peers and supervisors; the research strategy; the literature bases that were added in the process of data analysis; the grounded theory techniques used in this process of analysis; and, the hermeneutic principles that guided my thought processes. The very process of writing this report is also an

[121] While the prior chapters have only focused on the basic elements required to finish the game, chapter nine develops a discussion on the best strategies for winning the game, that is, finishing ahead of the other players. And, the conclusions drawn from this research project highlight the differences between finishing and winning the game.

input into the production process. As Marshall and Rossman (1989) note, by choosing "particular words to summarize and reflect the complexity of the data, the researcher is engaging in the interpretive act, lending shape and form – meaning – to massive amounts of raw data" (p119)[122]. In addition, the metaphor of Biotechnology Bingo used to structure the theory that resulted from the production process must also be considered an input.

The output of the production process is not just the theory, cases, and conclusions that comprise this thesis, but the eventual meaning that the reader extracts from it. While the production process was cumbersome, consuming, and mind altering, it is anticipated that the output will be all of these packed into a much shorter period of time. The reader will approach this report with his or her own repertoire of knowledge that will add complexity to the output. Thus, the reader's own knowledge should be viewed as an input into the production process as well. The final output, however, the meaning that is imposed upon this report by the reader, very much like the desired output of the collaborations that I investigated, is intended to be both novel and valuable. And, this novelty and value, if conferred upon the thesis by the reader, will create a common ground between the reader and myself.

I wish not to explicitly define my conceptualization of the novelty and value of this research here. This is a discussion that was first hinted on in the introduction of this report and a line of thought that will be expounded in the concluding chapters. I will, however, say that I have attempted to tell a story, albeit a story that has been pumped and prodded throughout the production process, which provides novelty and value. If the reader is able to find evidence of novelty and value within the pages of this report and wrap his or her meaning of the investigation in this evidence, I have a successful thesis and we, the reader and I, have common ground.

The next chapters – chapters six, seven, and eight – present the first three cases of this investigation and, in making this presentation, I am attempting to construct this common ground. Chapter five has provided the reader with an account of the processes I have used in

[122] Stake (1998) and Richardson (2000) also contend that the writing process is a source of input into the production of the final interpretation.

arriving at the interpretation of these cases. The cases are illustrative of the theory introduced in the chapters two, three, and four. With this in mind, my aim is not only to create a common ground between the reader and myself, but also to relay a coherent story that intrigues the reader from beginning to end.

Chapter 6 Case A CMBB-Nereus

The Knowledge Value Alliance between the Center for Marine Biology and Biotechnology (CMBB) and Nereus Pharmaceuticals

> "The cycles of synthesis and decomposition in creating a modular […] architecture begin with a synthesis of technology and market forecasts whose objective is the identification of the new kinds of functionalities to be developed and delivered to the market in future product concepts. This synthesis is followed by a decomposition of the desired functionalities into new (or perhaps existing) functional components that can provide the functionalities desired in future product concepts" (Sanchez, 2000, p621).

The case presented in this chapter provides for a detailed application of the theoretical concepts developed in chapters two, three, and four. The alliance between the Center for Marine Biology and Biotechnology (CMBB) at the University of California, San Diego and Nereus Pharmaceuticals, a small biotechnology firm in San Diego, California is characterized by varying levels of interdependency and modularity that have evolved with the passage of time. This collaboration, however, from the beginning and throughout its evolution, has been premised on the "future product concept" (to use Sanchez's terminology, as stated in the quotation above) of pharmaceuticals derived from marine microbial sources. In order to research and develop this "future product concept", the activities or tasks of the alliance have to be decomposed and delegated to relevant expert members of the architecture, creating the various modules in the architecture. Once the tasks have been performed, the work resulting from this delegation process has to be synthesized to reach the desired output of the

collaboration, namely the "future product concept", or, in the language of Nereus Pharmaceuticals, the "high quality lead".

The discussion in the first section is an overview of the case, the tasks, and the areas of expertise of the collaborative participants. Drawing from the data yielded in the interview, observation, and document review phases of the research, the description of the case is designed to provide material for further analysis in relation to the theory generated in the earlier chapters of this thesis. This first section merely aims to provide a rough sketch of the knowledge architecture, identifying the players and their prescribed roles.

The next section, the analysis, sharpens the view of the architecture. Beginning with a description of how the architecture works, the concept of boundary objects, and migratory and ingrained knowledge are illustrated in terms of the work performed within the alliance and these constructs are positioned within the architecture. The implications of the functionality of the architecture are also discussed in an attempt to build the foreground for chapter nine, the cross-case analysis. As will become apparent, each case highlights important aspects in developing a modular approach to university-industry collaborations in biotechnology. In the alliance between CMBB and Nereus, the significant findings include a distinct transfer of the work produced in one module to the members of the following module, which occurs in the form of a patent, and an obvious overlap in ingrained knowledge that allows this process of transference to occur smoothly.

6.1 Case Description

The collaboration between the staff members from the Center for Marine Biology and Biotechnology (CMBB) at the University of California, San Diego (UCSD) and Nereus Pharmaceuticals is representative of the types of strategic alliances found among the Californian biotechnology communities. The availability of venture capital (Kenney, 1986) and the level of intellectual human capital (Zucker, Darby, & Brewer, 1998) have both played significant roles in the birth of new biotechnology firms, specifically in regions such as San Francisco and San

Diego. Figures reveal that one in three U.S. biotechnology companies is within 56 kilometers (35 miles) of a University of California (UC) campus, one in four Californian biotechnology companies has been founded by UC scientists, and 85% of the biotechnology companies in California employ UC alumni with graduate degrees (Industry-University Cooperative Research Program, 2003). As Zucker, Darby, and Brewer (1998) note, the commercialization of the underlying science in biotechnology is dependent on the flow of knowledge between those that know how to perform the techniques characteristic of the basic or underlying science and those with the capabilities to develop the findings from the initial discoveries.

The alliance between CMBB and Nereus illustrates the importance of geographical proximity between UC scientists and Californian biotechnology firms and the role of intellectual capital in the founding of these organizations. CMBB is located at the Scripps Institute of Oceanography in La Jolla, California and Nereus is located less than 32 kilometeres (20 miles) away in a business park area of Sorrento Valley. One respondent from Nereus noted that, "the geographical proximity is pertinent to the transfer of materials and allows for the creation of trust and teamwork, and aids in building relationships" (Vaughn[123], 17 January 2003 – personal interview).

Nonetheless, findings from the investigation of the relationship between the two parties elucidate the disparate types of knowledge and scientific practices particular to each constituent of the collaboration. The effects of discrepancies and gaps in knowledge and scientific practices are, however, lessened by a common technological bond, in which the needs and uses for knowledge are united.

The following sections discuss the relationship between the two parties, including the discovery, development, and transference processes, and the variations in types of knowledge, scientific methods used, and focus among the collaborators. After addressing these disparities, the needs and uses for knowledge that define the collaboration are revealed. Finally, the technology that creates the coalescence of the various knowledge bases is explored.

[123] This respondent requested anonymity. Therefore, the name of the respondent has been changed and the respondent's title has not been disclosed.

6.1.1 The Collaborative Relationship

Nereus Pharmaceuticals was founded in 1998 by Dr. Bill Fenical (the director of CMBB) and Dr. Michael Palladino (now the VP of Technology Assessment and Development at Nereus). Together, these two individuals aggregated over ten years of world-renown academic research in marine microbiology (Fenical) and cell biology (Palladino). Fenical boasts over 300 refereed publications in the area of marine microbiology. Indeed, as the Chief Scientific Officer (CSO) of Nereus, Dr. Ken Lloyd, commented in an interview, "Bill [Fenical] spent 10 to 12 years of trial and error, logic and intelligence doing this [marine microbiology]. Nereus saved a good decade of work learning from Bill" (18 July 2003 – personal interview). Palladino, a cell biologist specializing in the role of cytokines in the development of inflammatory disease and cancer, contributed experience in cancer drug development, in-licensing, and pre-clinical testing. While Palladino remains on the executive team at Nereus, Fenical still calls CMBB (the Center at the university) his home. Fenical remains connected to Nereus via collaborative grants, being a member of the scientific advisory board of the organization, and providing consultation and contracted services. CMBB and Nereus are also united by the work of Paul Jensen, a leading microbiologist at CMBB[124].

Under the auspices of the Industry-University Cooperative Research Program (IUCRP), CMBB and Nereus seek to discover new compounds with drug potential from marine microbes. IUCRP is a three-way partnership between UC, the State of California, and industry sponsors. According to the program's website (Industry-University Cooperative Research Program, 2003), the interaction focuses on feedback, collaboration, and support, yielding potential results to all three parties[125], including:

- For UC researchers and students
    - New curricula
    - New research centres

[124] While Jensen is not a founder in the legal sense (incorporation documents, etc.), he was an important part of the CMBB team that developed the technology shared by CMBB and Nereus.
[125] Interestingly, this list does not account for the economic, medicinal, or social benefits associated with the discovery of drugs or the "future product concepts" that I contend to be the aim of this collaboration.

  - Student research opportunities
  - New research explorations
  - Up to four years funding
- For industry sponsors
  - Access to UC talent
  - Strengthening of R&D programs
  - Leveraged R&D investments
  - Intellectual property rights
  - Tax credits
- For the State of California
  - Expanded R&D enterprise
  - More competitive companies
  - Increased employment
  - Increased tax revenue
  - Improved quality of life

A project funded by the IUCRP, titled "Marine Actinomycetes as a Resource for Drug Discovery", awarded Fencial US$420,139. Nereus made an equivalent contribution to CMBB's research agenda under the grant, in exchange for the first right of refusal on discoveries resulting from the research. The grant proposal, prepared by Fenical, was reviewed by the Head of Microbiology and the Head of Research at Nereus. There is, however, as Jensen from CMBB reminded me, no collaboration in the formal sense. "We do not do research for Nereus" (7 July 2003 – personal interview). "There is no commitment, no contract. Like any other research grant, the Center is not obligated to follow the original research agenda. The sponsoring company can make suggestions, but the Center does not have to follow these suggestions" (Jensen, 15 January 2003 – personal interview). In corroboration, Vaughn acknowledged the importance of academic freedom, particularly as a factor leading to discoveries.

The members of CMBB retain their publishing rights on the discoveries they make from research funded by the grant, but the discoveries must pass through the Office of Technology at the University of California, San Diego first. Information is free to flow outside of the CMBB-Nereus relationship based on publication. Publication is necessary to keep the Center up and running (Jensen, 15 January 2003 – personal interview).

The relationship was described as "reciprocal" by Lloyd and "synergistic" by Jensen. Lloyd defined the relationship as Nereus working in conjunction with Fenical and his group of researchers. The reciprocity inherent to the relationship between CMBB and Nereus, in addition to the overlap in knowledge necessary for the transference and utilization of the discoveries made at CMBB, illuminates a common ground between the collaborators. Each party's goals, however, are distinct. As will be addressed in the following discussion, the fundamental knowledge and methodologies employed by each group are also quite different (a quality to be expected considering the two sides of the alliance have divergent goals to fulfill and that the knowledge of the individuals that comprise each organization is considered to be complementary). "At Nereus, the emphasis is on novel chemistry and at CMBB the emphasis is on novel organisms" (Lloyd, 18 July 2003 – personal interview).

Nereus is premised on developing compounds derived from marine microbes to combat infectious disease, cancer, and inflammation. Combining the scientific realms of chemistry, microbiology, biology, pharmacology, and oncology, the company seeks to identify and produce biologically active compounds from its microbial library. In an effort to achieve this goal, the company employs 45 individuals (at the time of interviewing), including nine chemists, ten microbiologists, eight screening scientists, and the remaining 18 employees in informatics and personnel. Well beyond discovering sources of drugs from marine microbes, the scientific area that links the two parties together, the Nereus scientists' know-how and capabilities lie in the methodologies combining "cutting-edge purification and structure elucidation with state of the art high-throughput screening" (Nereus Pharmaceuticals, 2002). Aiming to identify high quality leads through the development of novel chemical structures to

produce clinical candidates[126], Nereus' focus is on enhancing and developing its screening methods to diagnose the specificity, selectivity, and toxicity of the chemicals in a manner that surpasses the capabilities provided by traditional screening techniques. Diagram 6.1 depicts Nereus' research agenda.

[126] The marine microbes discovered, cultured, and tested at the Center for Marine Biology and Biotechnology provide the core structures of some of the compounds that have been developed at Nereus. The outer regions of these compounds are usually modified to make the molecules more drug-like. At this time, most of the marine microbes leading to novel chemistry at Nereus have been discovered by Nereus scientists.

Diagram 6.1 Nereus' Research Agenda

Please see print copy for Diagram 6.1

Source: Nereus Pharmaceuticals (2002)

* TNF-alpha/IL-1 is a small organic molecule that Nereus is developing for the treatment of rheumatoid arthritis, inflammatory bowel disease, and psoriatic arthritis.

The work done at CMBB is centred on the development of new methods and the discovery of new organisms. A recent discovery made by Fenical's group at CMBB, the Salinospora genus, resulted from the discovery of new methods for working with marine

microbes. These new methods entailed the sifting through samples that contain one billion microorganisms per cubic centimeter, culturing the microorganisms, using genetic methods to identify them, and screening the metabolic products for medicinal properties (Scripps News, 2003). Straddling the fence of applied research, CMBB's work is focused on microbial distributions, microbial diversity, methodologies for culturing microbes, and identifying new microbes (Jensen, 7 July 2003 – personal interview).

6.1.2 Discovery and Development

Lloyd detailed two ways in which Nereus collaborates with the Center for Marine Biology and Biotechnology, one in basic discoveries (but not all of these can be licensed to Nereus because there are at times other people involved, such as the National Cancer Foundation and the Cancer Center at UCSD), and the second on a service basis, in which Fenical grows organisms in large amounts or performs large-scale fermentation for Nereus.

The basic discoveries are also found in two forms. "There are different types of discoveries, including new organisms where the knowledge is rudimentary. If it is a new organism, then it probably produces new compounds. And, then there are the type that Bill [Fenical] performs, where Bill's group discovers new compounds and Nereus takes them over" (Lloyd, 18 July 2003 – personal interview). When presented with 15 discoveries recently made at CMBB, the scientists at Nereus chose to license three of those discoveries. Once a discovery has been made and Nereus decides to license it, there is basically a handover of the finding(s). "The disclosure pertaining to the discovery is written up, containing the foundation of knowledge and the knowledge is transferred as a patent" (Jensen, 7 July 2003 – personal interview). According to Jensen, the discoveries come from asking what microbes make molecules and what can these microbes make to fight diseases?

Once in the hands of Nereus, these discoveries can be modified, advanced, developed, or discarded. The discoveries are based on a scaffold or core structure, but there is the

possibility of the loss of the original derivative[127]. After Nereus takes over the discovery, the scientists at the firm probe the scaffold and open up the possibility of finding a new molecule with less toxicity or increased efficacy that is different to the original derivative (Jensen, 7 July 2003). In addition, Nereus has to prioritize its resources.

> The goal is to discover drugs…the company must decide what to do with the discoveries, which ones look best. Nereus starts off with 100% and transfers some resources so that there are fewer new discoveries as older ones are brought forward. If only the newer ones are transferred forward, it is no good from a medical point of view, just to continue to make new discoveries and never advance them (Lloyd, 18 July 2003 – personal interview).

While the relationship is based on a common mission to discover and develop marine microbes with the potential to fight human diseases, the goals that make up this mission are varied between the two parties. "CMBB's goals are to gain knowledge and train students and Nereus' goals are to discover drugs and add to the body of knowledge. The technologies are the same between us, but training a PhD student is not in Nereus' immediate corporate goals – the knowledge has to be new and applicable" (Lloyd, 18 July 2003 – personal interview). "The Center works on culturing metabolites from the ocean, a process called second metabolite discovery. Nereus works on the commercial aspect of the findings" (Jensen, 15 January 2003 – personal interview).

This relationship has evolved over time. "When Nereus started off and it was only about five or six people, the company depended on Fenical. Now our goals are different." Now, most of the discoveries are done at Nereus, the percentage done by Fenical has fallen dramatically (Lloyd, 18 July 2003 – personal interview). The relationship is expected to continue to change. "Nereus knows that it needs the [CMBB] lab right now. There is a very good relationship between us and it is important that it remains that way. It would not look very good if there were no relations between us, particularly with one party being the co-founder. But, I expect that there may come a time when Nereus does not need us anymore" (Jensen, 7 July 2003 –

[127] This means that the molecules licensed to Nereus initially have a core structure. Typically, synthesis concentrates on modifying the outer regions of a compound, leaving the core structure intact. There is, however, no reason why the core could not be changed or why the molecule could not be modified so much that it is not a recognizable development of the original derivative. "Unique chemistry is discovered from marine microbes. However, individual compounds are made via commercially viable chemical synthesis" (Nereus Pharmaceuticals, 2002).

personal interview). The evolving relationship is also demonstrated by a comment that Jensen made in his first interview. "The Center is just starting to learn more from the company. In the beginning, the company was so new, it didn't know much about the industry. We [CMBB] knew more about the industry because of our past relationships. Now that the company has been established for a few years, it is establishing partnerships with other firms and is starting to give the information to the Center" (15 January 2003).

Beyond the level of information pertaining to industry, there are certain interdependencies that serve to characterize the relationship in more definitive terms. Vaughn pointed out that the work at Nereus depends on a certain number of samples from CMBB. These samples, along with topics relating to grants, sediments from the ocean, upcoming expeditions, new microorganisms, new methodologies, and recent findings in the literature, are discussed in the bi-monthly meetings between the two parties. The close geographical proximity allows staff members from Nereus to go to CMBB or vice versa. For example, a student of Fenical's recently spent some time at Nereus looking for biological activity because of the lack of the proper equipment for such a task at CMBB.

The two sides of the alliance also share a microbial library. The microbial library is the intellectual property of Nereus, but because of the contribution that the CMBB scientists make to this library and the substantial amount of trust between the researchers at CMBB and the staff at Nereus, members from both sides of the alliances are allowed access to the database. It was developed by the Head of Medicinal Chemistry at Nereus, and "is specific to chemistry and microbiology and hosts a rich source of evidence on the compounds produced at Nereus" (Vaughn, 17 January 2003 – personal interview). Vaughn indicated that there is one person at CMBB working with the database and one scientist spending 50% of his time on the relevant materials supplied by CMBB.

6.1.3 Knowledge Needs and Knowledge Uses

The interviews conducted with members from both sides of the collaboration reveal heterogeneous knowledge bases, particularly in relation to the knowledge and methods on each side of the collaboration. The following table is designed to demonstrate these differences.

Table 6.1 Types of Knowledge Used at CMBB and Nereus

CMBB SCIENTISTS' KNOW-HOW	NEREUS SCIENTISTS' KNOW-HOW
Sampling methodologies	Screening methodologies
Microbial distribution	Fermentation
Microbial diversity	Attrition (chemical synthesis)
Culturing microbes	Commercializing cultured microbes

Although the Head of Nereus is a microbiologist, "Nereus can't go study microbial distribution" (Jensen, 7 July 2003 – personal interview). In relation to Nereus' methods and know-how, Lloyd accentuated the company's commercializing capabilities. As the third step in the treatment of a discovery (following identification as a novel structure and attrition), the staff members at Nereus possess the ability to select one potential candidate from a series of compounds, based on a feeling for potential, activity, ability to be metabolized (but not too quickly), and toxicity levels. "Bill's group doesn't have the methods to perform [this] task and that is not the definition of an academic group anyway" (Lloyd, 18 July 2003 – personal interview).

The differences in knowledge and methodologies existent between the two sides of the collaboration are unified by a common need and use for knowledge. "There is a reason why Bill and Paul were the founders of Nereus, which is to have their discoveries put down a pathway of development" (Lloyd, 18 July 2003 – personal interview). The discovery process, as pioneered and refined by Fenical and Jensen, and the development of discoveries, a process in which

Nereus is advanced, are linked together by a common need to seek out and advance novel sources for fighting human health afflictions.

> Microbes isolated from terrestrial sources have been one of the major foundations for drug discovery. In fact, today, over 120 important drugs used clinically have been derived from terrestrial microbes. The evidence that marine microbes can also yield novel biologically-active compounds is substantial. Nereus believes that these marine microbes will be the next great source of drug discovery for the pharmaceutical industry (Nereus Pharmaceuticals, 2002).

The discovery of Salinosporamide A by the CMBB scientists illustrates the connection between the Center and Nereus. The IUCRP grant, "Marine Actinomycetes as a Resource for Drug Discovery", supported a quest for knowledge that yielded a new compound proving to be "a potent inhibitor of cancer growth, including human colon carcinoma, non-small cell lung cancer, and most effectively, breast cancer" (Scripps News, 2003). The scientists at CMBB discovered the source and the scientists at Nereus sought out to develop the findings, but both CMBB and Nereus were, and still are for that matter, focused on how to kill cancer cells in new ways.

In addition to the exchange of personnel and the shared microbial database discussed previously, there is considerable exchange involved in channeling the collective focus. This exchange serves to fortify the link between CMBB and Nereus, as each party learns and gains an understanding of the knowledge and methodologies employed by the other. According to Lloyd (18 July 2003 – personal interview), Bill's group learns drug discovery and development techniques from the interaction between CMBB and Nereus. And, Nereus has excellent fermentation capabilities (Jensen, 7 July 2003 – personal interview), the basics of which are taught to the CMBB staff in exchange for knowledge on culturing microbes.

Know-how is exchanged in the form of training. On a training expedition to Guam, the staff members from CMBB trained Nereus staff members in capturing and isolating microbes from the ocean. The training consisted of CMBB scientists showing the Nereus trainees how to do the process and providing guidelines. Interestingly, the Nereus scientists maintained their own lab space at the University of Guam, used their own methods for collection (based on what

was demonstrated by the CMBB staff), and isolated their own microbes. Jensen was unaware of whether Nereus found anything during that excursion.

The training and exchange practices that characterize the collaborative relationship between CMBB and Nereus have produced a technological bond. As Nereus has grown, its scientists have acquired a tremendous amount of knowledge from the staff members at CMBB. As part of its description and overview, Nereus claims an "exclusive worldwide license to the technology" used by Fenical (Nereus Pharmaceuticals, 2002). Indeed, Nereus is now capable of embarking on solo collection expeditions. For example, a group of trained divers, chemists, and microbiologists went to Puerto Rico to collect marine samples. The excursion resulted in the collection of over 1000 samples. Fenical agreed to have his group test twelve of these samples[128].

The scenario in which the Nereus scientists assume the role of collecting microbes and the CMBB scientists undertake testing activities, in spite of their divergent goals and knowledge bases, is made possible by the analogous technology employed by the two parties. This technology is centred on how to work with marine microbes and accommodates both parties' needs to discover microbial compounds that have a novel structure and are sufficiently interesting. As Lloyd emphasized during his interview, "the two most important things are that the discovery has a novel structure and interesting biological activity" (18 July 2003). The recipe for establishing novelty in structure and interesting activity follows a five-step process developed by Fencial and his staff and adopted by Nereus:

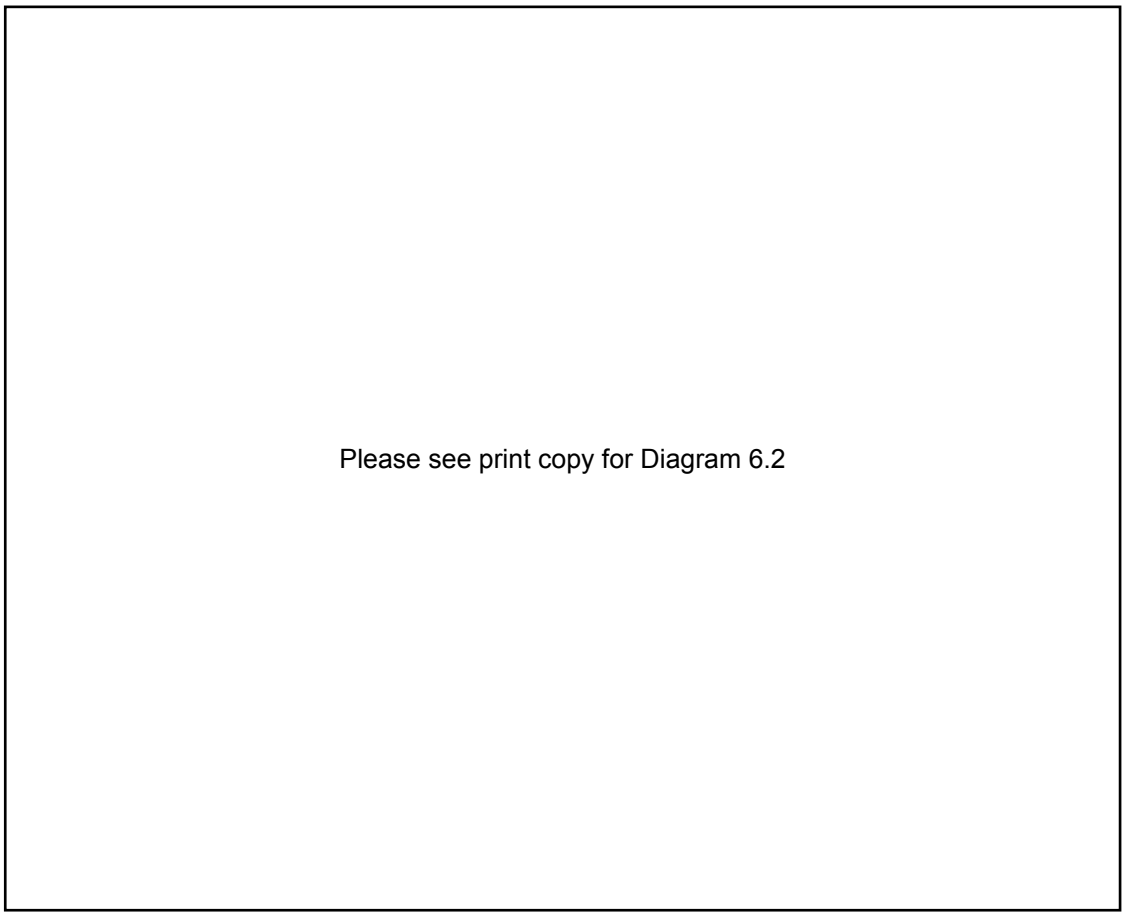
1. grow microbes (from trees, sponges, algae, etc.)
2. isolate the compounds to purify and put into pure columns
3. grow them under different conditions to develop the chemistry (fermentation)
4. extract, dry, and take-in solvent and test to see if they kill cancer cells

[128] If discoveries result from the testing performed by Fenical and his staff, they must still pass through the Office of Technology at UCSD prior to being licensed by Nereus (even though Nereus was responsible for the collection of the samples).

5. if the compound is active, but not novel, the question is, is it expanding (is it potentially more efficacious than current therapeutics)?
    a. what is its breadth (one cancer cell, two to five cancer cells?)
    b. does it have the capability of killing cancer cells in humans?

A diagram from Nereus Pharmaceuticals (2002) illustrates the role this technology plays in the overall drug discovery platform at Nereus.

Diagram 6.2 Nereus' Drug Discovery Platform



Source: Adapted from Nereus Pharmaceuticals (2002)

The dashed line that runs diagonally across the diagram signifies the limits of the technology developed at CMBB. The technology developed by the researchers at CMBB, shown on the upper left hand side of the dashed line, enables the collection of strains, the culture of collected microbes, the growth of the cultures, the drying and extraction of the cultures, and the preliminary testing for biological activity. The processes shown on the lower right hand side of the dashed line, including screening, fractionation, dereplication, and structure elucidation, are part of the unique technological capabilities of the Nereus scientists. The technological capabilities of the CMBB scientists, however, produce the product (the discovery), which provides a substance for the technological processes of the Nereus scientists (the development).

Reflecting back on the IUCRP grant that funded Fenical's discovery of actinomycetes, (the Salinospora genus), the division of technological capacity can be defined in functional terms. The non-technical abstract of the grants reads:

> The group we have discovered is only found in the ocean, requires seawater for growth, and is clearly distinct from all currently described bacteria. We have initiated preliminary studies of a few strains from this group and they are clearly a good source of potent antibiotics and anticancer agents. We now propose to isolate large numbers of these bacteria from diverse marine sediments and to thoroughly explore their biomedical potential. These bacteria will be cultured and extracted at Scripps Institute of Oceanography and the extracts tested in sophisticated biomedical assays performed at Nereus Pharmaceuticals, Inc., the corporate sponsor of this program (Funded Projects, 2003a).

While the know-how and technological capability of each party are clearly distinct, the integration of these realms of knowledge and understanding is crucial to fulfilling the need to find and develop new sources of drugs from marine microbes for combating human diseases. Nereus and CMBB have created an intricate web of various types of knowledge to conquer the goal of discovering new medically useful compounds from marine microbes. Each member of the collaboration continues to practise and progress a distinct area of scientific knowledge, with obvious overlaps and delicate connections between the various arenas. The technology that dictates how each entity works with marine microbes transforms the fragile interlace into a secure connection. The vast types of knowledge necessary for the collaborative agenda are

metamorphosed into an alignment of both tasks and knowledge, linking together the collaborative partners and their research agendas.

The next section takes a closer look at the alignment of the tasks and knowledge inherent to the collaboration between CMBB and Nereus in terms of the game of Biotechnology Bingo. The constructs of migratory knowledge and ingrained knowledge are explored in relation to the activities within the architecture. Additionally, the functionality of the architecture and its implications are addressed in order to draw attention to the uniqueness of this case in relation to the other cases presented in this thesis, and to further develop the depiction of the game of Biotechnology Bingo in chapter nine, the cross-case analysis.

6.2 Case Analysis

As mentioned in chapter two, the game of Bingo is used in this thesis as a metaphor for both alignment in conditions of complexity and as a map of the activities performed in knowledge value alliances between university and industry in biotechnology. Similarities between the traditional game of Bingo and Biotechnology Bingo exist because of the requirement for alignment and the amount of luck often associated with getting the design process right. Whenever luck is a factor, there is also risk. As a result, particular attention must be devoted to the known, controllable aspects of the game, namely the architectural planning, including interfaces and design rules, and the employment of migratory and ingrained knowledge in order to reduce the risk and to attempt to ensure alignment in the work performed within the knowledge architecture. Attention is also warranted by the use of trust and "things" in the knowledge architecture, and the communicative aids used to supplement the interface between the CMBB-Nereus alliance and potential allies.

The alliance between the Center for Marine Biology and Biotechnology and Nereus Pharmaceuticals differs from other collaborations between university and industry, particularly from the ones presented in this report, because of its origin and driving forces. While the other collaborations presented in this thesis are based on scientists from university and industry

coming together to pursue a specific goal (which could be anything from developing compounds to crystallizing enzymes), the alliance between CMBB and Nereus is designed as a long term endeavour aimed at discovering and developing compounds from marine microbial sources with the potential to kill various types of cancer cells. This agenda does not stop once the desired output is achieved. The alliance is designed so that the process is repetitive. Even after the alliance has produced a compound and sent the compound on its way down the path of development, the scientists at CMBB continue to discover new promising marine microbes and the Nereus scientists continue to enact the role of developing novel compounds.

6.2.1 A Trajectory of Luck

The luck or uncertainties that the architects of many alliances face stems from the notion that they must attract and enroll the appropriate people, and make use of the adequate tools, technologies, and work practices to appropriately solve a technological problem. In the case of the collaboration between CMBB and Nereus, *the people are already enlisted*. The university scientists, Fenical and Jensen, started Nereus Pharmaceuticals with the intention of having a pathway of development for the discoveries made at CMBB and, therefore, the decision of whom to solicit and enroll in relation to the development process is, in effect, already made. There is no need for the university scientists to search for the appropriate people to develop their findings. Development of the most promising findings of the CMBB scientists is the designated role of Nereus Pharmaceuticals[129].

Members of the CMBB-Nereus knowledge value alliance are part of the same elected first-person plural group (Rescher, 1997) that operates in the areas of marine microbiology and chemistry[130]. This first-person plural group is identified by the belief held by its members that, "marine microbes are the next great source of drug discovery for the pharmaceutical industry"

[129] What must be noted here, though, is that this is the case with each repetition of discovery and development that the alliance pursues. Prior to the collaboration and the establishment of Nereus, the appropriate people for the task of development had to be found and enlisted. The scientists thought to be most appropriate for this task have subsequently become the staff at Nereus.

[130] As discussed later in this analysis, marine microbiology and chemistry are the interfaces between the two parties.

(Nereus Pharmaceuticals, 2002). Within this group, claims to knowledge (that which is known) are based on the bounded universalism of the collaborative members and these claims are solidified by the technology that both sides of the collaboration use to collect, culture, and identify the potency of compounds derived from marine microbes. The tie between CMBB and Nereus is a strong one (Granovetter, 1973)[131]. Members of the collaboration exchange materials (including access to Nereus' microbial library, not to mention the contribution that both sides of the alliance have made to building this library). They work in each other's labs and have a sense of teamwork. With this tie comes a particular "luck trajectory".

In establishing Nereus Pharmaceuticals, Fenical, Palladino, and Jensen searched for the candidates they thought would be most suitable to commercializing the findings made at CMBB. The candidates were selected on the basis of their ability to perform screening methodologies, fermentation techniques, and chemical synthesis, with all of these activities being conducive to the development and commercialization of findings. Whether or not the right people were selected is a matter of perspective and hindsight. One could argue that if the results are forthcoming, if the alliance has been successful in producing a high quality lead, then the right people were selected. One could also argue that different people could have been selected who would have sped up the process of producing a high quality lead, or made the process more efficient. The members of the alliance will inevitably say that the correct people were indeed selected, while someone who considers herself to be particularly skilled at one or more of the areas listed above might argue that she should have been made a member of the Nereus team, and consequently a participant in the knowledge value alliance. The fact of the matter is, however, the original decisions made in regards to the composition of the Nereus staff

[131] According to Granovetter (1973), the strength of a tie can be calculated on the basis of the amount of time, emotional intensity, intimacy, and reciprocal services that serve to characterize the tie. As evidenced in the description of the CMBB-Nereus case, there is a considerable amount of time and intensity devoted to the alliance by both parties. In addition, the two parties are intimate and are engaged in reciprocal services as demonstrated by their exchange of techniques, their switching of roles, and their sharing of the microbial library.

were a one-time attempt at "getting it right". The initial decision then becomes a trajectory of luck[132] as each new process of discovery and development is commenced[133].

Along with the trajectory of luck is an associated set of tools, technologies, and work practices used in the alliance. The people originally selected for the alliance came to the setting experienced in the use of specific tools and technologies, and accustomed to particular work practices. These may or may not have been adapted into the alliance, but they certainly are a part of the ingrained knowledge of the participants of the collaboration and, thus, have an effect on how problems are solved in each module. In addition, as the processes of discovery and development are embarked upon again and again in the alliance, the tools, technologies, and work practices used in the initial processes become a feature of each new process. The concepts of technological trajectories (Dosi et al, 1988) and asset stock accumulation (Dierickx & Cool, 1989) suggest that the future activities of each module are predicated on what has been used in the past.

6.2.2 The Application of Design Rules

These tools, technologies, and work practices become the defining activities of each module. For example, in the modules[134] comprised of the university scientists, the tools, technologies, and work practices are routinely made up of developing new methods for sifting through marine soil samples, culturing microorganisms, using genetic methods to identify them, and screening the metabolic products for medicinal properties. The research focus in the Center is on novel organisms. In the module composed of the firm's (Nereus') staff, where the focus is on novel chemistry, the process of development conventionally includes:

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[132] Although commentary is offered here in relation to the notion of a trajectory of luck, it would obviously require a comparative, longitudinal study to investigate the consequences of collaborations building an enduring team and the results of these types of collaborations in comparison to those that assemble a team with each new endeavour.

[133] In the instances of the other cases reported in this thesis, the luck inherent to the design process is encountered with each new approach to a technological problem. A new team may be put together based on "weak ties" (Granovetter, 1973) and the alliance is not solidified into the arrangement where there is a preset pathway for the following round of discovery and development.

[134] Recall here that a module can be conceptualized as a side of an alliance, but there are also modules within modules. For instance, the CMBB module may contain modules consisting of sampling, culturing, identification, and screening. This argument is evidenced in the following discussion.

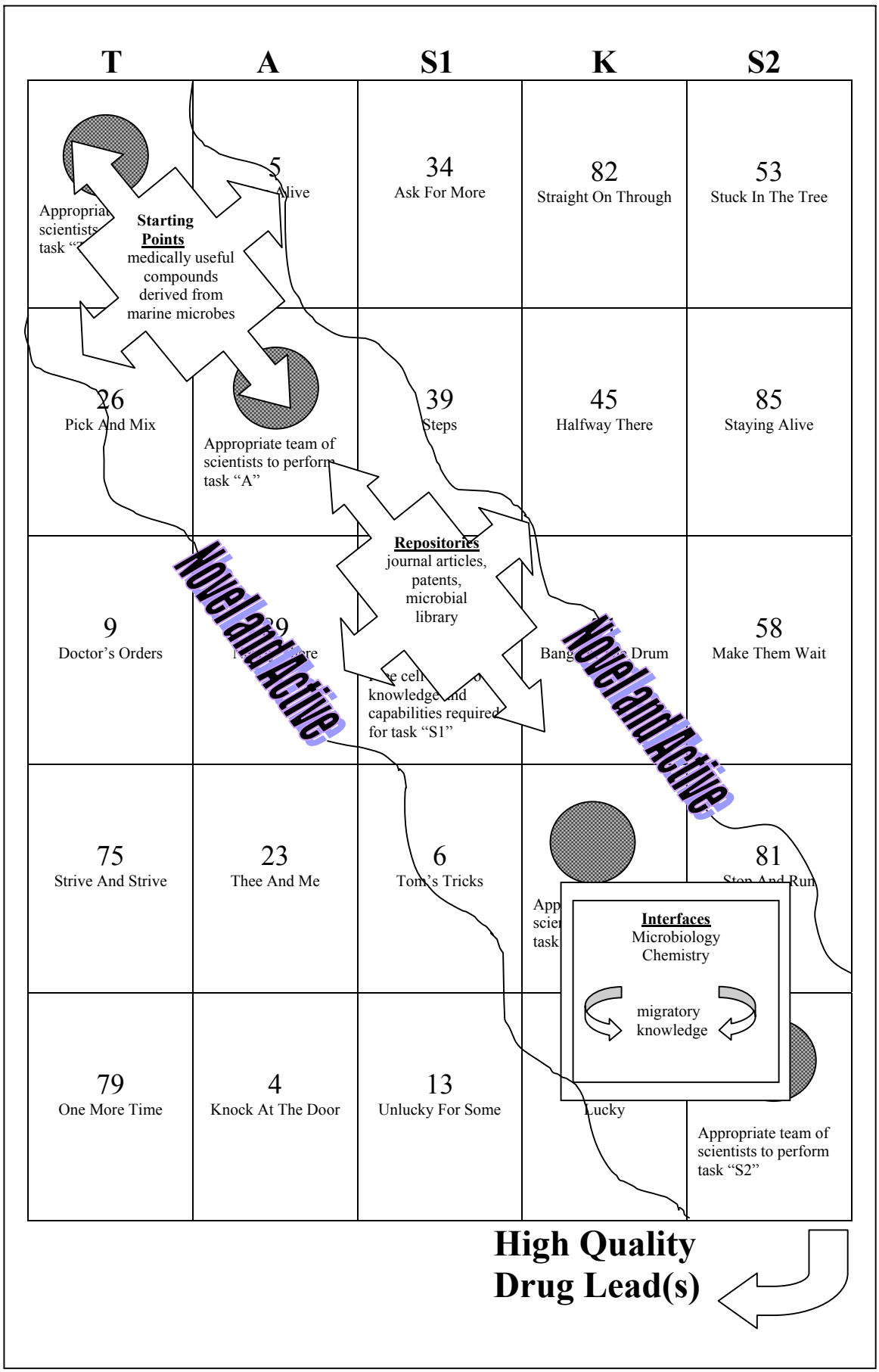
1. identification as a novel structure (via in vitro screening activity)
2. attrition (chemical synthesis)
3. selection from a series of compounds (based on feeling for potential activity, ability to be metabolized and levels of toxicity) (Lloyd, 18 July 2003 – personal interview).

These activities are guided by specific design rules and the integration of these activities is made possible by not only the design rules, but also by the interfaces. The design rules characteristic of this knowledge value alliance are centred on all activities yielding organisms and compounds that are *novel and active*. The interfaces in the CMBB-Nereus architecture are chemistry and microbiology. The repositories and starting points that mesh unit workers within and across modules include: patents, journal articles, the microbial library, and medically useful compounds from marine microbes.

The design rules, interfaces[135], and boundary objects used to induce alignment and knowledge integration within the architecture can be diagrammatically represented on the Biotechnology Bingo card. The "tasks" featured across the top of the card can be interpreted as follows: task "T" is sampling, task "A" is culturing, task "S1" is identification and screening, task "K" is attrition, and task "S2" is advancement of a high quality lead, with the first two tasks performed at CMBB, the third task an activity that can be performed in either organization, and the final two tasks the type of work carried out at Nereus. Diagram 6.3 serves to detail these features of the CMBB-Nereus knowledge architecture. A discussion on each of these features follows the presentation of the diagram.

[135] Although the microbiology and chemistry interfaces are featured between tasks "K" and "S2", they should be thought of as moveable boundary objects that are conduits for migratory knowledge and interfaces between all modules of the knowledge architecture.

Diagram 6.3 The CMBB-Nereus Knowledge Architecture



6.2.2.1 Design Rules

The design rules are grounded in the technology shared by the two entities, CMBB and Nereus. This technology dictates the way in which the collaborative parties work with marine microbes. As identified by Lloyd, there is a distinct procedure that embodies this technology. It includes, as previously identified, growing microbes, isolating compounds, fermenting them, extracting them, and testing the compounds for activity. When employed in the collaboration, the design rules create alignment between the two parties. In addition, the design rules allow for the individual needs of both parties to be fulfilled by the work performed within the alliance. Novel microorganisms make for unique and original knowledge that can be the subject of a journal article (meeting one of the needs of the academics) and provide the requisite starting point for developing a high quality lead (meeting the need of the firm). The picture becomes clear, then, that, in spite of Jensen's claim that the CMBB scientists do not "do research for Nereus", alignment still persists because of the design rules.

The communicative aid of value is used in this instance to insure connection between the CMBB and Nereus modules in this alliance. The connection mechanisms, starting points, repositories, and interfaces (which are discussed later on in this report) provide connection between these modules, but this connection is fortified by the value attached to novel microorganisms. The value each constituent of the alliance sees in these objects, or "things" (Latour, 1987), is simultaneously different and overlapping. Both parties see value in novel microorganisms as "future product concepts", or therapeutics derived from marine sources. In addition, both parties stand to benefit from this value. Both parties attach differing value to the "thing". This value is, as mentioned previously, new and interesting knowledge that can meet the publication requisites of the CMBB staff and a valuable starting point for the Nereus scientists.

Despite this connection provided by value and the various other connection mechanisms, and the coordination provided by the design rules, it is important to note that the design rules do not ensure that patentable knowledge is produced. The compounds produced at CMBB adhere

to the principle of being novel and active, but the scientists at Nereus assess the value of these compounds. Recall the scenario in which the Center for Marine Biology and Biotechnology recently made 15 discoveries and Nereus decided to license three of these. Once this decision was made, the discoveries were patented, if a patent had not already been procured[136]. Nereus then commenced the development of these compounds. Although the 15 discoveries made at CMBB were all novel and active, the decision as to whether or not these discoveries were worthy of development came from the application of Nereus' know-how. Lloyd emphasized that the staff members at Nereus possess the ability to select one potential candidate from a series of compounds, based on a feeling for potential, activity, ability to be metabolized (but not too quickly), and toxicity levels (18 July 2003 – personal interview). Developing these discoveries selected for advancement, however, requires that the compounds synthesized in development are also novel and active.

So, while the design rules do not ensure patentable knowledge, they do guide the work in the knowledge architecture and align the various tasks ranging from sampling to the advancement of a high quality lead. Without the design rules, the work performed at CMBB would be less likely to meet the needs of Nereus. CMBB operates within its own module, where the scientists follow their own hidden design rules. Without the visible design rules of novelty and activity, however, the material produced at CMBB would not mesh with the work performed at Nereus.

The hidden design rules used at CMBB include the rules that guide the work of sampling, culturing, fermenting, and extracting microbes. The hidden design rules used at Nereus include the rules that govern identification of a chemical structure, attrition, and selection of a compound for advancement. There are hidden design parameters that guide the process of sampling in the sampling module. There are hidden design parameters that govern the work in the culturing modules. Each module has its own set of rules, or hidden design parameters, that dictate how the work within the modules should be performed. These rules are not necessarily

[136] It is important to note here that CMBB via the patent office at UCSD may well have submitted a patent application prior to this point. This would occur in instances were patent officers at UCSD's Office of Technology Transfer deemed the discoveries to be valuable and worthy of patenting.

hidden from the members on either side of the alliance as they would be in a modular product. Indeed, Nereus is capable of and does perform the activities of sampling, culturing, fermenting, and extracting microbes. The rules that govern these activities, as with the rules that govern the work at Nereus, are hidden in the sense that they do not affect the work performed in other modules.

6.2.2.2 Interfaces

The alignment of the work and the articulation of various activities performed at the modular level within the architecture are also the result of various interfaces. The members of the collaboration exchange knowledge within the confines of two specific interfaces, marine microbiology and chemistry. Scientists from Nereus participating in discovery diving expeditions must be trained and certified, and "a rudimentary knowledge of microbiology is required" (Lloyd, 18 July 2003 – personal interview). There are general scientific advisory meetings between the two parties, where chemists and microbiologists are present to talk about how to stimulate growth in particular development projects. So, while the work across the modules may be disparate, encompassing knowledge related to sampling and screening methodologies, microbial distribution and fermentation, and microbial diversity and attrition, communication and interdependencies are developed in the areas of marine microbiology and chemistry. Profoundly, these interfaces also relate to the design rules, whereby the novelty of an organism and the potency of its associated chemical activity can only be assessed via the necessary ingrained knowledge in marine microbiology and chemistry.

6.2.2.3 Repositories and Starting Points

Specific types of migratory knowledge, including repositories and starting points, move within the interfaces of marine microbiology and chemistry. The firm, in conjunction with the members of the Center for Marine Biology and Biotechnology, holds patents pertaining to novel marine organisms that produce unique chemical structures with the ability to fight diseases.

Once a discovery is made at CMBB, the knowledge pertaining to that discovery is passed on to the scientists at Nereus in the form of a patent. The members of the collaboration browse patents in the areas of microbiology and chemistry to assess the novelty of their findings. Journal articles are written that disclose the discovery of new organisms, including the techniques used to capture the microorganisms, their classifying strain, the year and location in which they were captured (right down to the habitat description and depth), and their taxonomic designation (cf Mincer et al, 2002). It is important to note, however, that much of this information is of little value or clarity to someone who does not possess the requisite ingrained knowledge in marine microbiology and chemistry. As Faulkner and Senker (1995) note,

> …the experience of technology transfer reveals that ownership of intellectual property on its own is inadequate, since additional tacit knowledge and skills are generally needed in order to effect the transfer. Tacit knowledge cannot be transferred in written form, unlike articulated knowledge, and so requires on the hoof of 'person embodied' mechanisms of transfer[137] (p37).

There is also evidence of another repository in the alliance between the Center for Marine Biology and Biotechnology and Nereus Pharmaceuticals that depends on the interface of marine microbiology and chemistry as conduits for movement. The microbial library established by the Head of Medicinal Chemistry at Nereus is a repository of the compounds derived in the processes of discovery and development. The library is accessible to both sides of the collaboration and hosts the compounds created by both sides. In the words of Vaughn, the library "is specific to chemistry and microbiology" (17 January 2003 – personal interview). As with the patents and journal articles, the microbial library is also of little interest or use to someone who does not possess the requisite ingrained knowledge to interpret and understand its contents.

As mentioned in the introduction to this chapter, the collaboration is based upon the "future product concept" of pharmaceuticals derived from marine sources. Scientists from both

[137] This quote is meant to emphasize that the migratory knowledge moving within the architecture cannot be understood without the necessary ingrained knowledge of the recipient. This notion is corroborated by other findings and it also has application to the transfer of CMBB's technology for sampling and culturing marine microbes to the Nereus staff members. Recall that in the description of the case, members from the two sides of the alliance attended an expedition in Guam, during which the scientists from CMBB demonstrated how to use the technology to the Nereus staff members, which, in the words of Faulkner and Senker (1995) is a "person embodied" transfer of the technology.

sides of the alliance are attuned to the fact that terrestrial microbes have been a pharmaceutical source for many decades, but they are also of the belief that the returns from such sources are diminishing.

> Historically, microbes isolated from terrestrial sources have been a premier source for commercially successful drugs. Recently, however, there have been diminishing returns from attempts to further exploit terrestrial sources. Nereus believes that the production of new biologically active compounds from marine microbes will meet or exceed that previously developed from terrestrial sources and published trends support this belief (Nereus Pharmaceuticals, 2002).

Medically useful compounds derived from marine microbes are used as a starting point within the architecture. The marine actinomycetes discovery project produced novel actinomycetes never seen before on land (Lloyd, 18 July 2003 – personal interview). The discovery of novel actinomycetes, however, was the end point of the discovery task. The starting point was the goal of finding medically useful compounds from marine microbes.

The CMBB-Nereus knowledge architecture is unique in its inherent tools, technologies, and work practices used to combat the uncertainty associated with the highly experimental science practised in this collaboration. The repositories, starting points, the marine microbiology and chemistry interfaces, and the design rules dictating novelty and activity provide the mechanisms for accomplishing Strauss' (1985) first and second levels of articulation. These levels include the meshing of the various tasks, clusters of tasks, and segments of the knowledge architecture, and the meshing of unit-workers.

The third level of articulation, the meshing of actors with their types of work and implicated tasks, is accomplished by individuals at the modular level using their ingrained knowledge to interpret, analyze, and create knowledge based on the interception of migratory knowledge, and by applying their ingrained knowledge to solve modular level problems. In addition, scientists from both sides of the alliance follow the hidden design rules discussed previously. For example, at CMBB, individual scientists may use their ingrained knowledge to study and investigate microbial distribution and diversity. They may also apply their ingrained knowledge in a heuristic pattern to develop new sampling methodologies. At Nereus, individual scientists use their ingrained knowledge to practise fermentation and attrition. The scientists at

the firm may also use their ingrained knowledge and develop a heuristic approach to employing and advancing screening methodologies.

6.2.3 Cultural Ecology

There are two important things to note about the use of ingrained knowledge in the CMBB-Nereus alliance. It is expected that the ingrained knowledge of the collaborative participants will be applied in an appropriate, viable manner. This expectation stems from the social ambiance of the knowledge architecture. Issues of trust, openness, and prior experience all play a role in this expectation. Furthermore, there are particular mechanisms that exist within this architecture, which allow for the production of objectified knowledge. Certain "things" (Latour, 1987), such as technologies and methodologies used in this alliance are not just objectified knowledge themselves, they are also means for producing additional objectified knowledge.

Recall Jensen's comment that the CMBB scientists do not do research for Nereus. Yet, Nereus matched the funds that CMBB received through the IUCRP grant. In return for the funding, Nereus receives the first right of refusal on any discoveries made at CMBB that result from the use of the funds. The collective trust[138] in this alliance allows Nereus to operate in acceptance of CMBB's honesty in negotiating this agreement. It also allows Nereus to be concerned with its own agenda and less concerned about the behaviour of the CMBB scientists. Lloyd commented that there is a substantial amount of trust between the members of each side of the alliance, which results in the sharing of information between the two parties. At collaborative meetings they share things that Fenical is just beginning to develop. "Nereus agrees not to tell about the development and not to perform the development on its own" (Lloyd, 18 July 2003 – personal interview). And, the relationship is reciprocal. "What goes on

[138] Collective trust, as defined in chapter four, can be said to be present when the members of the knowledge value alliance believe that fellow participants "make constructive efforts to behave in accordance with commitments", and that fellow participants were "honest in whatever negotiations preceded such commitments" (Cummings & Bromiley, 1996, cited in Jarvenpaa, Knoll, & Leidner, 1998, p3).

at Nereus is also shared and [Fenical] keeps it confidential" (Lloyd, 18 July 2003 – personal interview).

There is, then, a large degree of openness among the collaborative participants, which results from two things. The first factor is that the alliance is a repeat affair. Producing a high quality lead does not signify the end of the collaboration. Therefore, the two sides of the alliance can be said to have prior experience with one another. The second aspect that allows for the openness within the relationship is that Fenical and Jensen are the co-founders of the firm, and Fenical holds a position on Nereus' scientific advisory board. As a result, there is a great deal of exchange that happens between the two sides of the alliance because neither side has to worry about the risk of appropriation.

CMBB's technique for capturing marine microbes was shared with Nereus. Nereus shares its microbial library with CMBB. And, there are other types of exchange mentioned in the description of this case. This exchange is made possible not only by the collective trust that exists in the knowledge architecture, but also by the interfaces that exist within the architecture. Significantly, though, as CMBB's techniques for capturing and culturing marine microbes are shared with Nereus, the knowledge of the CMBB scientists becomes objectified. The technique no longer rests solely in the mind of the CMBB scientists. It metamorphoses from ingrained knowledge to objectified knowledge as the Nereus scientists pick up the technique and practise it themselves.

Furthermore, the technology for working with marine microbes that is shared between the collaborative participants is also a means for producing additional objectified knowledge. As this technology is applied in the practice of sampling marine soils, culturing microbes from these soils, growing microbes, and testing them, it allows for the production of novel chemicals that are themselves a form of objectified knowledge. Once a testing report showing particular chemicals' efficacy on cancer cells has been produced, the knowledge of these chemicals ability to act against cancer cells is no longer just ingrained. It becomes not only a state of knowing in the mind of an individual scientist, but it also becomes a form of objectified knowledge that can be shared with members of the alliance and accumulated by different parties to the alliance.

6.2.4 The Structure of the Alliance

While there is overlap in the ingrained knowledge of the collaborative participants, there are clear areas of specialization among the members of the alliance. The focus at CMBB is on novel organisms and the emphasis at Nereus is on novel chemistry (Lloyd, 18 July 2003 – personal interview). The structure of this alliance, while still modular, is premised on products. Modules are divided according to the products of marine microorganisms and developed compounds, and linked together by the design rules, interfaces, repositories, and starting points discussed in this analysis.

Product structures allow for the maximum use of personal skills and specialized knowledge, and facilitate the use of specialized capital (Koontz & O'Donnell, 1959, cited in Walker & Lorsch, 1996, p221). In the CMBB-Nereus alliance, the scientific skills and specialized knowledge are grouped into modules centred on sampling marine microbes, culturing them, screening them for activity, chemical attrition, and advancement of leads. Funds dedicated to discovering marine microorganisms, such as the ones appropriated by the Industry-University Cooperative Research Program, are used in the microorganism product modules and the funds from Nereus (not specific to the IUCRP grant) are used in the compound product modules. Sampling and culturing marine microbes is the role of the CMBB scientists in this alliance. Chemical attrition and advancement of leads is the responsibility of the Nereus scientists. Screening occurs in both CMBB and Nereus depending on project specifications[139]. Products leave the CMBB modules as novel marine microorganisms with interesting chemical activity and enter Nereus in this form. Products leave Nereus as chemical compounds with promising drug-like efficacy against target diseases.

Take for instance the Salinospora genus discovered by the CMBB scientists. This is the typical product produced at CMBB. This discovery was licensed by Nereus and the scientists at

[139] Recall that this alliance is representative of repeat projects in which the same set of tasks occur repeatedly.

the firm embarked upon the task of making chemical analogs[140] of the molecules produced by the recently discovered microorganisms, thus producing the product definitive of the Nereus modules, compounds. Nereus, however, can change the compound so drastically in a bid to increase its activity that there is a loss of the original derivative, as mentioned previously.

The product structure has clear implications for the movement of knowledge in the alliance. Clearly, ingrained knowledge has become objectified in at least two forms in this alliance: the techniques for capturing and culturing microbes from the ocean have been demonstrated to the scientists at Nerues, thus objectifying the ingrained knowledge of the CMBB scientists, and the novel marine organisms discovered at CMBB are patented when deemed to be valuable by the Nereus scientists, making the ingrained knowledge of the discovering scientists objectified[141]. The former, however, is less a function of the product structure of the alliance than the strength of the tie between the two sides of the collaborative relationship. The strong tie between the two parties permits considerable amounts of exchange. Showing the Nereus scientists how to capture and culture marine microbes does not further the collaborative agenda, but increases the chances of success for the firm in which Fenical and Jensen hold a vested interest.

The latter is, though, a result of the product structure of the alliance. While the modules in the alliance are divided according to product, the integration occurs because CMBB's product is a starting point for Nereus. As such, the structure of the alliance specifies that knowledge must move from CMBB to Nereus in the form of patented novel marine microorganisms with novel and interesting chemistry. Nereus may voluntarily inform the staff at CMBB of their work on the organism and the advances in the chemistry that it makes, but this information is neither

[140] A chemical analog is a structural derivative of a parent compound that differs from the parent in small elements.

[141] Note this does not imply that the ingrained knowledge of the CMBB scientists is not objectified if there is no patent. Indeed, if there is a discovery made by the CMBB scientists, and that discovery is validated by the culturing and testing of the marine microbes at CMBB, then the ingrained knowledge of the discovering scientist(s) is objectified. Recall that the argument has been made in chapter three that ingrained knowledge is embedded in the products, techniques, and repositories that represent forms of migratory knowledge. As such, ingrained knowledge is objectified by its manifestation in migratory knowledge that can be collectively validated. I discuss this line of reasoning in more detail in chapter nine.

necessary nor dictated under the product structure of the alliance. It may, however, occur because of Fenical and Jensen's vested interest in the future of Nereus.

The products produced in this structure are integrated by the goal of a "future product concept" (Sanchez, 2000). As Thompson (1967) notes, the term goal refers

> …only to some imagined state of affairs which may conceivably be attained or approached (if not infinite) at some future time…It seems reasonable to consider goals *for* an organization as *intended future domains* for the organization. Goals for the organization will usually be multiple and may be held by individuals or categories having no affiliation with the organization (p127 – emphasis his own).

While the goals of CMBB and Nereus differ, their work is brought together under the intention of inhabiting the future domain of therapeutics sourced from marine microorganisms. The products of both CMBB and Nereus are necessary to arrive at this future domain.

This may suggest a particular amount of interdependency in the alliance. Indeed, I have tried to make it clear that these arrangements are not entirely modular. Both sides of the alliance, however, function individually. CMBB is a research centre affiliated with the Scripps Institute for Oceanography. Nereus is a privately held corporation. The two entities come together in a modular organization for the purposes of upgrading the standings of each organization (and discovering and developing compounds from marine microbes). As such, the alliance can be said to be "idiosyncratically synergistic" (Langlois & Robertson, 1995), whereby the outcome of the alliance is more than the organizations could expect to achieve on their own.

6.2.5 Enlistment of Allies

The use of specialized funds in each of the product modules is made possible, in part, by the enlistment of allies, or various supporters of the alliance agenda. The collaboration is co-sponsored by the Industry-University Cooperative Research Program (as mentioned previously). Over the past four years, Fenical has been granted US$651,966 from the state sponsorship

program[142] for his work in the collaboration with Nereus (Funded Projects, 2003a, 2003b, & 2003c).

This has been possible because of Fenical's ability to translate his needs into the needs of his sponsor and attach value to the grant applications. The State of California articulates its benefits from sponsorship of the IUCRP as: 1) expanded R&D enterprise, 2) more competitive companies, 3) increased employment, 4) increased tax revenues, and 5) improved quality of life (UC Discovery Grant, 2001). Excerpts from Fenical's grant proposal abstracts demonstrate how the intended outcomes of his proposed projects meet these needs. The excerpts state that:

> This program will help realize the biomedical importance of a new group of marine bacteria and help establish Nereus as a major new pharmaceutical company in the San Diego area. Goals of this program are also to help train students to fill a growing void in the biotechnology workforce, to foster economic competitiveness by increasing the rate of technology transfer from the University of California to the private sector, and to enhance collaboration between industry and university researchers (Funded Projects, 2003a).

> The techniques developed will prove in principle that marine fermentation is a reliable discovery and production method and set the stage for a commercial fermentation industry to be established in Southern California (Funded Projects, 2003b).

The State's needs and benefits in terms of expanded R&D enterprise, more competitive companies, and increased employment are obvious in Fenical's abstracts.

If the actual proposals represented by these abstracts are thought of as interfaces between CMBB and the State of California, then the value attached to the grant proposals aids in Fenical's translation efforts. With the attainment of these grants, Fenical is able to accumulate power in the form of monetary support. The accumulation of such support allows CMBB and Nereus to become more formidable players in the game of Biotechnology Bingo. And, as Powell, Koput, and Smith-Doerr (1996) suggest, "…a firm grows by being a player; it does not become a player by growing" (p122).

[142] Fenical has been granted at total of $983,138 from the IUCRP, however, two grants, one for $135,802 and one for $195,370, are for work with other companies (SeaTech Inc and AgraQuest, repectively). It is important to note, though, that the work performed under these grants is still in the area of marine microbial biotechnology.

Similarly, Nereus, upon its establishment and through its endeavours to raise much needed financial capital, was able to enlist a host of venture capitalists as allies. In the first and second rounds of financing, Nereus raised US$8.6 million and US$23.6 million, respectively. The support from venture capitalist allies can be seen in the comment made by Jean Deleage, Managing Partner at Alta Partners. "Alta Partners is excited to back a new biotechnology company from San Diego. Nereus will be in a position to provide its pharmaceutical partners an entirely new source of chemical diversity to replace the conventional soil samples that have provided such a rich supply of novel pharmaceuticals in the past…" (cited in Nereus Pharmaceuticals, 2002). In a similar display of support, Annette Bianchi, Partner at Pacific Venture Group stated, "Nereus is developing a cutting-edge drug discovery program based specifically on marine microbiology and we believe this new source of chemical diversity could deliver medicinally-relevant, marketable products" (cited in Nereus Pharmaceuticals, 2002).

With the assistance of these allies, the collaboration between CMBB and Nereus increases its chances of success. These allies, however, are only one part of the picture. The movement from discovery to development, which is the keystone of the knowledge value alliance, would not be possible without the migratory knowledge that moves throughout the architecture, the ingrained knowledge of the members of the alliance, and the tools, technologies, and work practices that integrate the knowledge, people, and tasks inherent to the collaboration.

Discovery of marine microbes and development of chemical compounds are pursued under the auspices of the novel and active design rules. Once the scientists at CMBB have made a discovery, it is proven that the discovery meets the standards set by the design rules, and it is deemed to be valuable by the scientists at Nereus, the knowledge becomes migratory in the form of a patent. Development, then, is initiated under the very same standards by which the discovery was guided. Without the ingrained knowledge of the recipients of the patented knowledge, however, the process of discovery and development would remain plagued by an inability of the collaborators in the development phase to unlock the patented knowledge and

put it to valuable use[143]. The interfaces of marine microbiology and chemistry and the medically useful compounds derived from marine microbes starting point provide conduits for comparison, communication, and connection between the modules of the alliance.

It should be remembered, though, that it is still the ingrained knowledge of the alliance participants that makes discovery and development possible. Migratory knowledge, design rules, and interfaces do not produce discoveries or carry out development, *people do*. Individuals rely on their own states of knowing to produce discoveries and incite developments. (They are, however, supported by various types of migratory knowledge along the way.) It is these individuals who are responsible for the problem solving at the modular levels, but with the aid of boundary objects, design rules, and interfaces in the architecture, the resolution of modular level problems can become coalesced into the desired output of the alliance, which in this case, is a high quality lead.

6.3 Conclusion

Has this alliance won the game of Biotechnology Bingo? It has certainly been successful in accomplishing its desired output, namely a high quality lead[144]. And, in the words of the CEO of Nereus, Kobi Sethna, "Nereus has distinguished itself as a leader in the discovery and development of novel drugs from marine microorganisms" (Nereus Pharmaceuticals, 2002). This leadership would not be possible without the alliance with Fenical and Jensen and their associates at CMBB[145]. In turn, the alliance would not be successful without the tools,

[143] Recall the comment made by Jensen that the discoveries are based on a scaffold, but there is the possibility of the loss of the original derivative. Once Nereus takes over the discovery, the scientists at the firm probe the scaffold and open up the possibility of finding a new compound with less toxicity or increased efficacy that excludes the original derivative. This would not be possible without the ingrained knowledge of the receiving scientists, and the interfaces of marine microbiology and chemistry.

[144] Nereus is currently conducting pre-clinical trials on two patented compounds derived from marine microbial sources. U.S. Patent No. 6,358,957, titled, "Phenylahistin and The Phenylahistin Analogs, A New Class of Anti-tumor Compounds" is a high quality lead on a new compound with the ability to fight breast cancer. U.S. Patent No. 6,096,146, is an exclusively licensed patent from the University of California, San Diego dealing with the "Halimide" compound and its anti-tumor functionality (Nereus Pharmaceuticals, 2002).

[145] Recall the comment made by Vaughn that Nereus depends on a large number of samples from CMBB. "Nereus' library of marine obligate microorganisms is in excess of 10,000 unique strains and is growing

technologies, and work practices that fuse the various tasks, clusters of tasks, and segments of the knowledge architecture. Together, the people, knowledge, and tools, technologies, and work practices used in the collaboration created winning conditions for the playing of Biotechnology Bingo and have effectively reduced the complexity of the practice of biotechnology.

This particular knowledge value alliance, however, is set apart from the other cases presented in this thesis by the fact that Fenical is a scientific co-founder of the collaborating firm and holds a seat on the firm's scientific advisory board. He, therefore, has a certain amount of influence on the research direction of Nereus Pharmaceuticals. Is this conducive to winning the game of Biotechnology Bingo? Obviously, Fencial and the host of other scientists on the west coast of the United States who have founded spin-off ventures based on their scientific enterprises would argue that this *is* a successful strategy. One interviewee, however, from a biotechnology firm in Victoria (Australia), cited a phenomenon of "founder's syndrome" and suggested that this type of arrangement dispels the creativity necessary for success in the practice of biotechnology.

Perhaps it is the case that there is a host of strategies for winning the game of Biotechnology Bingo, with the main theme of each strategy being the adoption of the appropriate tools, technologies, and work practices to adequately align the work performed across the various modules of the collaboration. These tools, technologies, and work practices may, indeed, vary between alliances. And, a certain amount of luck is still associated with the game because the architects of these alliances are faced with bounded rationality (Simon, 1976) in their quest to solicit and enlist the most suitable people for the alliance. In addition, there is no guarantee that the marine microbes will continue to be sufficient sources of promising therapeutics. The important aspect (and the most controllable factor), however, is that these tools, technologies, and work practices create an articulation of the people and their work within the alliance. Following this line of reasoning, it would not matter whether the members of the collaboration are part of the founding team of the organization, sit on the scientific advisory

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at a rate of 4,000-5,000 strains a year" (Nereus Pharmaceuticals, 2002), and CMBB has played a vital role in this accumulation of strains.

board, or are solicited only to solve a particular technological problem. Winning the game of Biotechnology Bingo would essentially require matching the tools, technologies, and work practices to the people and their respective supplies of ingrained knowledge.

Nevertheless, the conditions external to the alliance vary and it is not incomprehensible to think that different strategies may be more or less applicable in different conditions. The institutionalization of the appropriate tools, technologies, and work practices may also be viewed as the rules to the game and not the means for winning. The next three chapters – chapters seven, eight, and nine, the cross-case analysis – seek to explore this matter in more detail.

Chapter 7 Case B IBS-amrad

The Knowledge Value Alliance between the Institute for Biomolecular Science (IBS) and amrad Corporation Limited

> **"T**he discovery of drugs and drug molecules has always been the aim of pharmaceutical sciences and, in particular, of medicinal chemistry, which evolved from pharmaceutical chemistry…Drug design in its broad sense and structure-activity relationship studies are essential and at the heart of medicinal chemistry, and it is the progress and development of this field of research that has made medicinal chemistry the modern and enormously productive science it has become in recent decades (Testa, 1992). Today, studies on structure-activity relationships and their influence on the design of new drugs have rendered them one of the most useful and thus important activities of pharmacochemistry, a modern component science in the group of pharmaceutical sciences" (Kourounakis & Rekka, 1994a, p1).

As with chapter six, this chapter is illustrative of the theoretical constructs introduced in chapters two, three, and four. Evidence of design rules, interfaces, boundary objects, migratory knowledge, and ingrained knowledge are presented in the description of the collaboration between the Institute for Biomolecular Science at the University of Wollongong and amrad Corporation Limited. These constructs are scrutinized in more detail in the analysis section of this chapter. Unlike the other cases, this case presents a knowledge value alliance, which is comprised of more than one knowledge architecture.

Various component activities of the process of drug design occur across the different knowledge architectures, namely work in the area of medicinal chemistry, biological testing functions, and the production of structure-activity relationships, which, as described by Kourounakis & Rekka (1994a) in the introductory quotation, is one of the most useful activities

of pharmacochemistry. Interestingly enough, the structure-activity relationships produced in the collaboration between IBS and amrad are also a sub-component of the design rule that serves to align some of the work in the various modules of the alliance. The first section of this chapter, while providing a summary of the findings from the research conducted on the collaboration between the Institute for Biomolecular Science and amrad, aims to emphasize the centrality of the use of structure-activity relationships in the alliance.

The analysis section of this chapter evaluates the findings in terms of the theory developed in chapters two, three, and four. In analyzing this case, I focus on the three distinct knowledge architectures inherent to the alliance and the resultant social organization of the collaboration. The alliance between the Institute for Biomolecular Science and amrad Corporation Limited is similar to two of the other collaborations presented in this thesis (Case C and Case D), in that there is no tie in the form of ownership or founding status between the academic members of the alliance and the firm. In addition, this case is similar to the following two cases in its use of the structure-activity relationship methodology to pursue the desired output, which one respondent cited as being "getting pills in bottles" (Keller, 19 June 2003 – personal interview). This case also exemplifies how and why chemistry is being unified with biology. The practice of biotechnology often takes the form of the combination of these two previously distinct fields of science, with the intention of "designing (a compound) for a known purpose"[146].

[146] During the observation of a joint meeting between IBS and amrad, I was asked if I had any questions. I conveyed my limited understanding of the discussion that I had just witnessed to be exchanges in traditional pharmaceutical chemistry and queried as to where biotechnology came into the picture. Members of the collaborative meeting responded by saying that biotechnology is a host of sciences, including chemistry and biology, and the way in which the compounds produced by IBS are tested at amrad is a practice in biotechnology, along with how the biological material used in the testing is extracted at amrad. In addition, the IBS website states that, the research centre "brings together a large multidisciplinary team of chemists and biologists from the Departments of Chemistry and Biological Sciences, with exciting research programs focussed in three key areas: anti-microbial agents…, age-related diseases…, and cancer. These programs are underpinned by crucial core expertise in drug discovery, design and synthesis, together with the discovery and structural characterisation of biological targets. The long term goals are to develop new drug leads to address problems of drug resistance in infectious disease and to tackle in a new and more effective way diseases associated with ageing", making the IBS a "*regional centre of expertise in biotechnology*" (Institute for Biomolecular Science, 2003 – emphasis added).

7.1 Case Description

The alliance between amrad Corporation Limited and the Institute for Biomolecular Science (IBS) at the University of Wollongong began five years ago when Professor John Bremner (Director of IBS) approached amrad, a dedicated biotechnology firm in Richmond, Victoria, with a proposal he had for developing and designing compounds to overcome vancomycin-resistant bacteria. Bremner had prepared a three-page proposal for the company to review. The company agreed to fund Bremner's research agenda, and since that time, the alliance between the Institute for Biomolecular Science and amrad has been reshaped into a new form. At the time of the inception of the alliance, amrad did not, and still to this day, does not, have any chemical labs. The company is essentially outsourcing a portion of its medicinal chemistry to the Institute for Biomolecular Science.

The collaboration has been rewarding in that in its sixth year of existence, there has been a patent obtained on the compounds developed by the IBS staff. These compounds have reached the level of pre-clinical trials. As Dr. Jonathan Coates, the Chief Scientific Officer (CSO) at amrad, stated, the collaboration was infecund at first, "then the anti-bacterial compounds started to improve. They [the IBS chemists] started putting their theories to work" (20 May 2003 – personal interview). This alliance is well on its way to reaching its ultimate goal of "getting pills in bottles", but it must be stressed that it is estimated that it can take between 10 and 12 years to take a compound from discovery to market (amrad Corporation Limited, 2002), not to mention the millions of dollars consumed in the process. Therefore, decisions must be made with a future focus and current projects must be continuously evaluated for potential and alignment with company goals (specifically in cases where the industry firm is funding the research). The amrad-IBS collaboration has survived changes to the amrad project team, the re-focus of the company and, most interestingly, the addition of other projects.

Throughout this process, each side of the collaboration has continued to invest in its core scientific area, with one party's knowledge of the other's practices extending only to the

fundamental techniques necessary for the collaboration[147]. On each side of the collaboration, certain individuals have developed knowledge-of what the practices of the other side entail, but not detailed knowledge of how to perform the activities on the other side of the alliance. This is not necessary, however, because the work performed in this alliance is unified by the structure-activity relationship methodology and the ultimate goal of getting "pills in a bottle".

The following discussion details the various changes in the alliance since its beginning, along with the concurrent shifts in the focus and project team composition at amrad. In this discussion, I examine the structure-activity relationship methodology and its role in the collaboration. The various types of knowledge used in the alliance are introduced, culminating in an argument that provides a clear indication of three knowledge architectures. The summary of findings from the case concludes with an overview of the collaborative agenda and a preliminary judgment of how the breadth of knowledge employed in the alliance is combined to advance toward the goal of drug development.

7.1.1 The Genesis of the Alliance

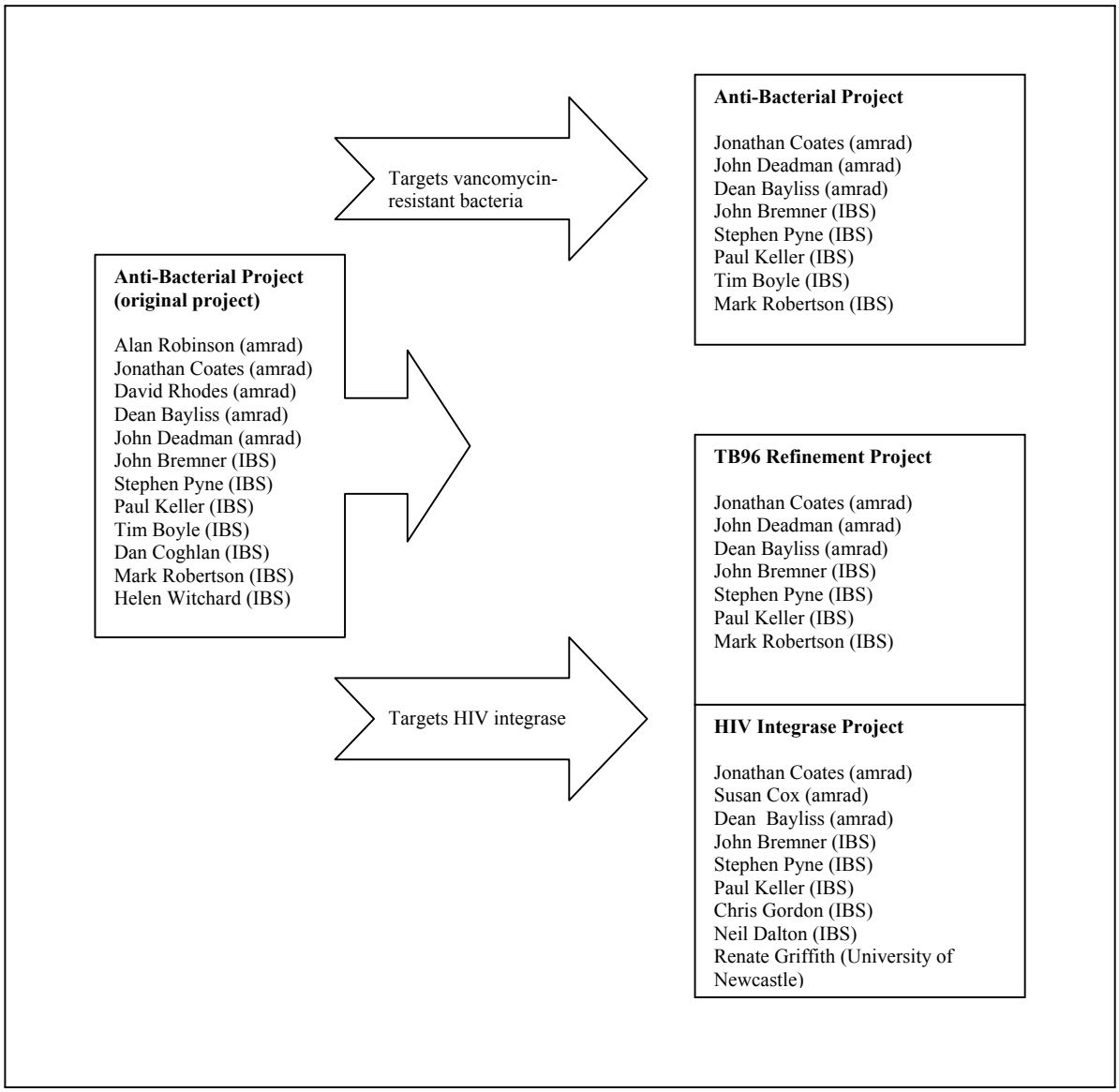
Five years ago, the collaborative project was initiated as an anti-bacterial project. Over the years, it has attracted the devotion of, among others, three full-time, permanent IBS chemists, two research assistants (RA), three PhD students, three honours students (all from the University of Wollongong), and a computational chemist from the University of Newcastle. These members meet once a week to discuss the progress of the project and initiate plans for the upcoming week. The RAs, the PhD students, and the honours students perform most of the lab work, with the full-time IBS faculty members providing guidance and liaising between the amrad staff members. Production of the first significantly active compound took three years. Helen Witchard, a PhD student who has now graduated, took three years to synthesize the molecule. Since then, Tim Boyle, a current participant in the collaboration and a PhD candidate, has developed a second compound, TB96, originally intended to be an anti-bacterial agent.

[147] Members of the alliance from amrad know that the IBS module synthesizes compounds and, conversely, the IBS collaborators know that amrad tests the compounds.

Coates described the collaborative project as a "network connection of facilitated contact" (20 May 2003 – personal interview). Among the several collaborations in which amrad participates is a cooperative endeavour between amrad and the Victorian College of Pharmacy, focusing on HIV (human immunodeficiency virus) integrase (one of three viral enzymes associated with HIV). As a result of this "network connection", TB96 was tested at amrad as an inhibitor of HIV integrase. "Never before would [TB96] have been put into an HIV integrase assay at the Institute for Biomolecular Science without the Victorian College of Pharmacy and amrad" (Coates, 20 May 2003 – personal interview). The compound proved to be very promising as an anti-viral agent and has since been synthesized for this purpose.

Dr. Paul Keller, one of the IBS chemistry faculty members, who was originally involved in the anti-bacterial project, has initiated another project dealing with HIV. The original anti-bacterial project between amrad and IBS has branched off and now ventures in two distinct directions. Several interviewees commented on the deviation from the original agenda. "The original project has [branched off] in different directions, with HIV targets being pursued and computer modeling being performed" (Robertson, 17 June 2003 – personal interview). "There are currently three projects including the anti-bacterial project, the TB96 refinement project, and the modeling project, involving Chris [Gordon], [Paul Keller] and Renate [Griffith]. Knowledge flows through all three projects, with huge overlaps in knowing what all parties are talking about" (Keller, 19 June 2003 – personal interview). Diagram 7.1 serves to represent the extent of the collaboration between the Institute for Biomolecular Science and amrad.

Diagram 7.1 Projects in the IBS-amrad Alliance



7.1.2 Changes in Focus and Project Team Membership at amrad

The new directions in the alliance have occurred in conjunction with some changes at amrad. When the anti-bacterial project was pitched to amrad five years ago, the project leader from amrad (Alan Robinson) had a medicinal chemistry background. In 2001, Coates became the CSO at amrad. Joining amrad in 1996, Coates had previously been the virology project director. His background is in virology and immunology. During his interview, he expressed the

view that there is a lack of virologists with drug discovery experience and because he has knowledge in both areas, he was headhunted for the position at amrad (Coates, 20 May 2003). After Coates became the CSO, he recruited Susan Cox as the Head of Virology. Amrad now employs eight virologists. There is currently 15% of an equivalent full-time employee in virology at amrad devoted to the collaborative project with the Institute for Biomolecular Science (Cox, 20 May 2003 – personal interview).

Amrad has clearly refocused, undergoing both internal and external reviews. The company now focuses on R&D with a five to ten year vision (Coates, 20 May 2003 – personal interview). After Coates assumed the role of lead scientist at amrad and the company underwent a cycle of internal and external review, the decision was made to divest some land and re-examine the firm's research agenda. The reviews described the company as promising and prepared to succeed, and the collaborative project with the Institute for Biomolecular Science as an interesting project with significant potential (Coates, 20 May 2003 – personal interview). The strategic focus at amrad is now on anti-infectives. While amrad's research and development (R&D) portfolio fails to mention anti-bacterial research, it does reveal HIV integrase as the target of current research efforts (amrad Corporation Limited, 2002). Anti-bacterials are, however, anti-infectives. Furthermore, the alliance has recently applied for and been granted an NH&MRC[148] award for the development of anti-bacterials. IBS will procure the services of two more post-doctoral scientists to work on the anti-bacterial project during the next few years.

Amrad's policy is to assess the viability of current projects and terminate them when it is deemed that they will not be able to reach their anticipated goals or are not in line with the research directions of the company. This mechanism is known as portfolio management. Portfolio management deals with compounds (not projects) and seeks to identify the limitations of compounds as quickly and as cheaply as possible. As Coates suggested (16 January 2004 –

[148] NH&MRC stand for the National Health and Medical Research Council of Australia. The Council provides "competitive grants awarded by the Commonwealth Government to an individual and small teams of researchers undertaking biomedical, public health and health services research in Australian universities, medical schools, hospitals and other research institutions" (Macquarie University, 1999).

personal communication), the type of skill required in industry allows for the recognition of the possibilities of and the appropriate time for cross testing. As such, TB96 has not been determined to be a limited compound by amrad, but just the opposite – a very useful compound in the area of HIV integrase.

During the last year, amrad's board decided to cut costs, which amounted to the hold on all contract renewals for a specified period of time. During that time, the IBS-amrad contract was up for renewal. IBS, however, continued to pursue work on the alliance agenda, synthesizing compounds and drawing from their own funds to do so, which demonstrated their dedication to the agenda and their sentiments about the value of it. During a meeting that I observed, Coates expressed his appreciation for the dedication and perseverance of the IBS staff members. The collaborative anti-bacterial contract has since been renewed (and as mentioned previously, additional funding has been secured from the NH&MRC).

7.1.3 The Structure-Activity Relationship Methodology

Across all of the projects, the collaborative relationship remains centred on finding the most potent compounds (Coates, 20 May 2003 – personal interview). "The project began with the goal of developing active compounds and it is still following along this same pathway" (Robertson, 17 June 2003 – personal interview). "The goal of the collaboration is to develop new compounds or improve the activity of existing ones to be more active than the competitor's" (Pyne, 4 June 2003 – personal interview). The difference between the various projects of the alliance is the target of the compounds. In one project, the target is vancomycin-resistant bacteria and in the other projects, it is HIV integrase, as depicted in Diagram 7.1.

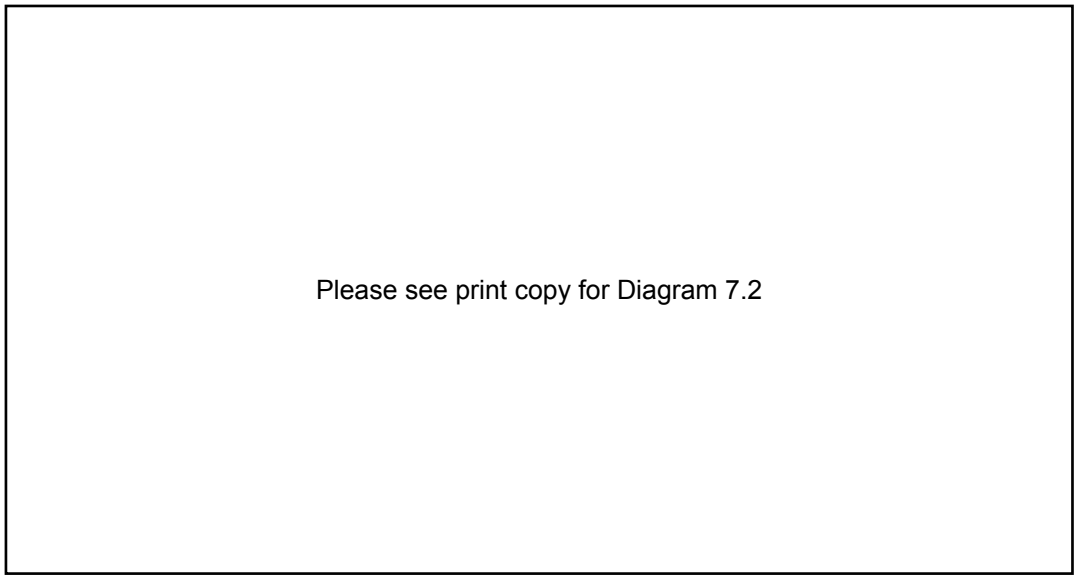
The adjoining factor in the alliance (both between two of the projects and between the collaborative members) is the structure-activity relationship methodology, which is a methodology used in attempts to uncover the compound (the "structure") with the most optimal activity against a specified target. The structure-activity relationship is a methodology that guides the activities of each party. It entails the following steps:

1. developing compounds (performed at IBS)

2. sending the physical compounds to amrad
3. testing the compounds (performed at amrad)
4. recording the results in an excel spreadsheet (performed at amrad)
5. transmitting the results to Bremner via e-mail (in a document formatted by excel)
6. discussing the results at the IBS weekly meetings (performed at IBS)
7. deciding on how to make the compounds more active (performed at IBS)

The alliance is centred on designing compounds through the use of synthetic chemistry. "It is an interactive collaboration with the virologists from amrad doing the in-house testing of the compounds produced at IBS – a medicinal chemistry project involving amrad" (Pyne, 4 June 2003 – personal interview). The effort culminates in the structure-activity relationship profile, which integrates the results of the two parties' scientific activities. The chemists from the Institute for Biomolecular Science synthesize the compounds and the amrad scientists perform the testing for biological activity. This methodology is portrayed in Diagram 7.2.

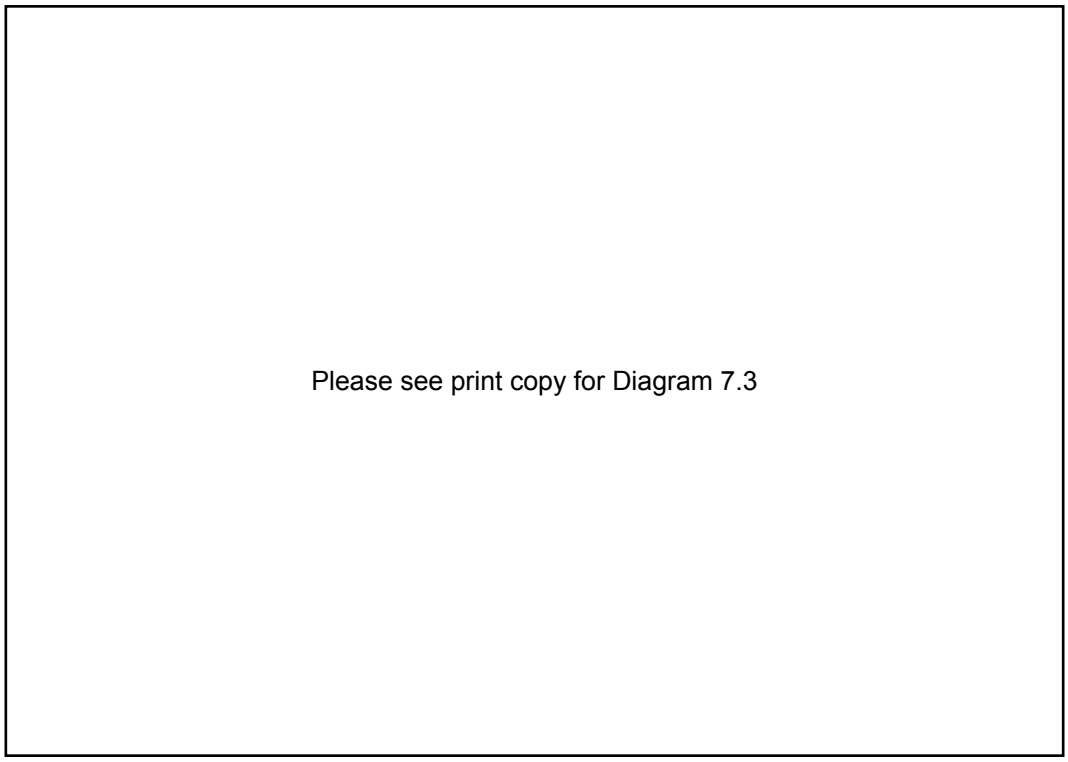
Diagram 7.2 The Structure-Activity Relationship Methodology



Source: Pyne (4 June 2003 – personal interview)

Coates explained the process of developing a structure-activity relationship profile as a roadmap. He said that each part is important. The methodology is reciprocal, with the results obtained at one end impinging on the activity at the other end. "Both parties are driving to get a drug. Amrad informs John [Bremner] of the activity of the compounds produced at IBS and it may cause John [Bremner] to vary his chemistry" (Coates, 20 May 2003 – personal interview). The structure-activity relationship is reported in the manner presented in Diagram 7.3.

Diagram 7.3 The Structure-Activity Reporting Format (An Example)



Source: Coates (20 May 2003 – personal interview)

In Diagram 7.3, the structure of the compound is detailed in the right column and the activity of the compound in the left column. The smallest value represents the highest activity. The IBS chemists generally decide on how to increase the activity of the compound, once they have received the results from testing.

7.1.4 Knowledge Used in the Alliance

Based on my observation of the meetings, the PhD students and research assistants develop a plan on how to enhance the activity of the compound, and the three supervisors (Bremner, Keller, and Pyne) comment on the plan, either corroborating the plan or offering suggestions for improvement. Spectra reports are produced by the students and research assistants as proof of production, purification, and synthesis and are reviewed by the supervisors, who use their ingrained knowledge to interpret the reports and gain an understanding of what the results signify in terms of the direction of the project. Keller commented that, "looking at the spectra reading is like looking at a bit of information." The knowledge used by Keller represents his "understanding of what the spectra is telling him and what it means to the overall picture of the project" (Keller, 19 June 2003 – personal interview).

Normally, synthesizing the compounds is the task of the IBS chemists and the changes to make as a result of the testing are decided upon at the Institute for Biomolecular Science. The molecular design is the responsibility of IBS, but it occurs with input from the scientists at amrad. After TB96 was identified as an anti-viral candidate, the scientists at amrad suggested the production of four similar compounds. When TB96 was discovered, the scientists from amrad came back with four compounds for IBS to make (Keller, 19 June 2003 – personal interview). During his interview (11 June 2003), Boyle (from IBS) revealed that the collaboration between amrad and the Victorian College of Pharmacy (VCP) had resulted in a molecule that was docked into an enzyme[149]. Following this achievement, Boyle was asked to produce four specific compounds, which were suggested by David Rhodes from amrad[150].

[149] This refers to the binding between a molecule (a compound) and an enzyme in a computer generated model.

[150] Note here that the compounds suggested by Rhodes were compounds that would be different in structure to that of TB96. The compounds that Boyle was asked to make, however, were compounds that would not dock appropriately in the enzyme, if the theory that the scientists from AMRAD and the Victorian College of Pharmacy had developed – with the aid of computer modeling – was correct. While the VCP and AMRAD scientists had the knowledge to work with computer modeling of compounds and enzymes, the synthetic chemistry knowledge was held by the scientists at IBS. Therefore, Boyle was asked to use his knowledge in synthetic chemistry to make the suggested compounds, which subsequently did not target the enzyme appropriately and served to prove the theory of the VCP and AMRAD scientists to be correct.

As Keller stated in his interview, "everyone always can do with more knowledge, but there is a limit to how much one person can do by himself. If he wants to do things properly, he brings in expertise" (19 June 2003). Keller explained that the IBS team gives two-dimensional structures of compounds to Coates and he understands these because of what he studies himself. In turn, Keller has knowledge of virology from his experience with HIV projects. During the meetings that I observed, Keller displayed confidence in matters relating to HIV and virology. His level of knowledge is supported by Coates' comment that Keller certainly has enough knowledge in these areas to make the IBS-amrad collaboration work (20 May 2003 – personal interview).

7.1.4.1 The Division of Labour and Knowledge Differences

Due to the division of labour in the alliance, however, there is a distinct difference in the knowledge bases used by the collaborative participants in their endeavours to succeed at achieving the collaborative goals. For example, when probing about Coates' level of knowledge relating to synthetic chemistry, several sources contended that his understanding and capabilities are limited, but they also stressed the fact that he did not need this knowledge to perform his role in the collaboration. Robertson said that Coates doesn't know how to synthesize compounds, but he doesn't need to (17 June 2003 – personal interview). Keller said that Jonathan cannot read spectra reports and that he doesn't need to be able to read them, "it is a matter of trust" (19 June 2003 – personal interview). Even Coates himself said that he didn't need to learn any in-depth knowledge of synthetic chemistry, but he did claim to possess the ability to interpret Bremner's results. During the interview with Coates (20 May 2003), he said that if Bremner sent him a number of compounds and some were active but more potency was required, he might be able to suggest a course of action for improving activity. He contended that this was so even with his limited understanding of synthetic chemistry. The possibility of Coates being able to suggest appropriate changes can be attributed to his significant experience with the structure of drugs.

Other interviewees were more restrained in claiming to understand or have knowledge-of the practices of the other party of the alliance. This did not impact on their own activities or roles in the project because of the division of labour in the alliance. For instance, Boyle said that he doesn't know much about virology and he is not interested in that area of science (11 June 2003 – personal interview). Robertson said that he doesn't know much about virology either, but his lack of knowledge in that area does not impact on his job (17 June 2003 – personal interview).

There is even a clear division of labour within the IBS team, particularly between the synthetic and the computational chemists. The synthetic chemists are responsible for physically making the compounds more active, while the computational chemists concentrate on the interaction between compounds and the target enzyme, HIV integrase. Pyne stated that Keller possesses more knowledge in relation to HIV and that he "takes [Keller's] word for it" on matters relating to the HIV project (4 June 2003 – personal interview). Gordon, one of the PhD students, is studying the design of compounds and how the designs work through modeling them on the computer. "This is an unnecessary project for John [Bremner] and Steve [Pyne]. They do not have expertise in this area" (Keller, 19 June 2003 – personal interview).

This evidence provides a concise depiction of the specific types of knowledge employed by each group and an explicit delineation between the capabilities of the collaborative parties. "Amrad's in-house pharmaceutical expertise is focused on three key areas: infectious diseases, neurological disease, and allergy and inflammation", with R&D targets aimed at the clinical development of compounds for the treatment of chronic severe pain, infertility, cardiovascular disease, neuromuscular disease, and stroke (amrad Corporation Limited, 2002). In relation to the collaboration, the activities at amrad are focused on biological testing of the compounds produced at IBS, and drug design and development.

Complementarily, the research teams at IBS engage in areas of research relating to medicinal chemistry, organic chemistry, peptide chemistry, and computational chemistry. The practices of the IBS chemists involve methodology development and synthesis of compounds, which, as Robertson asserted, requires the employment of tacit knowledge and an understanding

of the basic blocks used in developing compounds. "This requires knowledge-how-to and a hands-on approach" (17 June 2003 – personal interview). In his explanation of the structure-activity relationship methodology, Pyne stated that "the decision regarding which modifications to make [synthesis] are [sic] based on the structure activities. If there was 10mm of X used, 1mm of Y used, and 100mm of Z used, medicinal chemistry knowledge can be used to tinker with the levels of X to manufacture a compound that will hopefully lead to increased activity" (4 June 2003 – personal interview). As evidenced in Pyne's explanation, the activity of the Institute for Biomolecular Science research team is iterative and systematic, based on the structure-activity relationships.

The IBS researchers also engage in modeling of the compounds to test possible designs. The scientists at amrad do not perform this kind of work and do not have the facilities to do so (Keller, 19 June 2003 – personal interview). Together, with Gordon and Griffith (the chemist from the University of Newcastle), Keller is working on understanding and furthering knowledge related to the HIV enzyme, integrase, and determining how that knowledge will be put to use. "The knowledge comes through actually doing the work" (Keller, 19 June 2003 – personal interview). The computer aided design activities, in addition to the literature searches performed by Gordon and Dalton (an honours student at IBS), help to educate everyone on the existing knowledge relevant to the project.

7.1.4.2 Knowledge Provision

The role of education is not limited to the learning by the members of the Institute for Biomolecular Science research teams. While the IBS research teams are trying to fill knowledge gaps, they also try to explain things and satisfy the curiosity of the amrad staff (Keller, 19 June 2003 – personal interview). And, the chemists at IBS have been successful in doing so. Cox acknowledged a sense of satisfaction with the knowledge provided by the IBS researchers, in terms of both practicality and provision (20 May 2003 – personal interview). But, the relationship is reciprocal. Coates mentioned his endeavour to educate Bremner and his staff on what it is that amrad is trying to achieve. "Academics can be reticent to learn from industry

sometimes. Their discovery is like their baby and it totally offends them if you tell them that it may not be practical" (Coates, 20 May 2003 – personal interview).

Through the processes of educating and learning, the collaborators on each end of the relationship have laid the foundation for unified expectations. As Coates (20 May 2003 – personal interview) said, the members of the collaboration "have identical expectations: developing a drug safe enough to give to people to cure diseases" and illnesses, whether they are caused by vacomycin-resistant bacteria or HIV. The education offered by Coates has been fruitful in the sense that Keller claims to be working in the area of drug design and development and even Coates avowed that, "John [Bremner] has learned significantly about drug development and he is an expert in medicinal chemistry." John knows the value of knowledge and Coates trusts him enough to make decisions that will benefit the project (Coates, 20 May 2003 – personal interview).

"The scientific area common to the UOW scientists and amrad staff members is multifaceted. It involves drug design and development, and key methodologies. In addition, it includes synthesis, computer aided design, and biological testing" (Keller, 19 June 2003 – personal interview). The common area cannot be summed up or described by one specific type of science. Each party contributes to the goal of developing a drug by practising a specific type of science and applying expert knowledge in crucial phases of the structure-activity relationship methodology. Each group fulfils a specific role. "We are all striving to get pills in bottles. The role of the IBS researchers is to find out why the activity is the way it is, but the team can't deviate too much from its scientific base" (Keller, 19 June 2003 – personal interview). Amrad's role is based on early drug target identification, late stage compound optimization, and drug candidate characterization (amrad Corporation Limited, 2002).

The tasks within the alliance are target-specific and, as such, the process of discovery and development begins with an aim (Coates, 20 May 2003 – personal interview). This aim is facilitated by the interwoven roles of the collaborators, and specifically, by the structure-activity relationship methodology. Although there is considerable variance in the types of knowledge used in the alliance, sufficient harmony is created by the goal of drug development. Large

amounts of knowledge overlap are not necessary because of the structure-activity relationship methodology. There is clearly a division of scientific labour inherent to the alliance, which serves to create modular divides between the collaborative parties.

For the concept of modularity to work, as has been argued in the earlier chapters of this thesis, there need to be design rules, interfaces, repositories, and starting points, and these articulating features must adequately integrate the ingrained knowledge and task work of the members of the alliance. Do these essential elements exist in the alliance between the Institute for Biomolecular Science and amrad? It has been argued thus far that the structure-activity relationship plays a vital role in amalgamating the work performed in the alliance. The two parties, the Institute for Biomolecular Science and amrad, also agree on the desired output of the collaboration. They have the common goal of "getting pills in bottles". But, do the structure-activity relationship methodology and the existence of a common goal amount to the essential elements stated previously? What sort of structure is created in this arrangement and how is the flow of knowledge affected by it? The next section engages this line of questioning.

7.2 Case Analysis

As revealed in a footnote in chapter two, the concept of a knowledge value alliance was suited to this thesis because it allowed for the conceptualization of collaborations as hosts for multiple projects. Indeed, the case between the Institute for Biomolecular Science and amrad Corporation Limited is one such example. The knowledge value alliance between IBS and amrad consists of three distinct knowledge architectures (three separate Biotechnology Bingo cards): the anti-bacterial knowledge architecture, the TB96 refinement knowledge architecture, and the HIV integrase knowledge architecture. This chauffeurs in a comparison between the traditional game of Bingo and Biotechnology Bingo, whereby there is a similarity in a traditional Bingo player's motive for playing multiple cards in one game, and a dedicated biotechnology firm's and academic's motives for playing more than one architecture (three in

the case the IBS-amrad alliance) in the game of Biotechnology Bingo. This similarity can be thought of as the common motive to increase the chances of winning the game.

Following Rosenberg (1992) and Nelson (1982), Faulkner (1994) suggests that companies are bounded in their ability to totally know in advance what it is they should be searching for and that corporate expenditure on basic research "…enhances the productivity of applied research and development by helping companies to establish where they should be looking" (p441). Amrad's sponsorship of the research conducted at IBS, however, is strategic in nature, and the research conducted in the alliance is applied research. As mentioned previously, it is target-specific.

Playing more than one Biotechnology Bingo card is an effort to avoid putting "all eggs in one basket" and an undertaking to develop an extensive breadth of knowledge that can effectively guide the future research directions of the dedicated biotechnology firm[151]. It is an effort, however, that is directed at expanding search alternatives (á la Rosenberg, 1992) *and* simultaneously solving a designated technological problem. The instance in which the amrad scientists tested the previously anti-bacterial compound (TB96) as an anti-viral compound and found that it was an even more promising lead in that area (specifically in relation to HIV integrase) demonstrates that breadth in research and application can be a rewarding endeavour.

How, though, is alignment achieved when there is more than one project within the knowledge value alliance? Is alignment necessary across all three projects, or simply within each individual project?

[151] Dedicated biotechnology firms and academics alike do not usually limit themselves to collaborations with one or two of their respective types of collaborators, but instead usually engage in multiple alliances. For example, amrad has three specific projects with IBS (as demonstrated in this chapter) and a host of projects with other collaborators, including the Victorian College of Pharmacy, the Queensland Institute of Medical Research, the Ludwig Institute for Cancer Research, Monash University, and University of Queensland. Similarly, the Institute for Biomolecular Science has collaborations with Sydney University, the Victor Chang Cardiac Research Institute, NSWAg (New South Wales Government, Department of Agriculture), Johnson and Johnson, and Novogen. While this polydemic approach to collaborations may indeed provide dedicated biotechnology firms with a number of options to pursue and academics with a host of funding mechanisms, the problem with the arrangement lies in the fact that it is virtually impossible to ascertain whether or not a collaborator will inadvertently leak secret knowledge to a third party. And, while the commonly used protection mechanism to prevent this from happening is the use of contracts, the notion that many of these collaborative agendas are based on the reusable ingrained knowledge of collaborative participants makes it increasingly difficult to altogether avoid "the inadvertent leak" of valuable or potentially valuable knowledge.

7.2.1 The Application of Design Rules

From the description of the case offered in section 7.1, it seems that the structure-activity relationship methodology is the design rule used in both the anti-bacterial project and the TB96 refinement project. In the HIV integrase project, work is centred on developing an understanding of and furthering knowledge related to the HIV enzyme, integrase, and determining how that knowledge will be put to use (Keller, 19 June 2003 – personal interview). There are no predetermined design rules in this type of activity, other than the methods of computational chemistry that suggest gathering as much data on a target as possible. Once a three-dimensional structure of an enzyme has been developed and is modeled with different candidate compounds, the scientists' ingrained knowledge and individual heuristics become the main source for pinpointing the active site of the enzyme, along with its "hydrophobic valleys and electrostatic landmarks, the chemical hooks and eyes that endow it with its unique biochemical properties" (McPherson, 1995, p164). The work in this area demonstrates particular interdependencies between the scientists engaged in this project[152].

This alliance can be viewed in terms of three large modules. I have been using modules as a tool to conceptualize work done at the task level – modules, thus far, have represented task domains. In this case, they are found to represent not only task domains, but also projects. Module I is the Anti-Bacterial Project. Module II is the TB96 Refinement Project. Module III is the HIV Integrase Project. Within each module, however, there are sub-modules, or different task domains specific to the goals of each project.

The TB96 Refinement Project (Module II) and the HIV Integrase Project (Module III) are both dedicated to a common desired output, a drug lead for HIV. The Anti-Bacterial Project (Module I) aims for the production of a drug lead for illnesses created by vancomycin-resistant bacteria. The alignment *between* Module II and Module III is achieved through the

[152] Recall the argument made in chapter three that work within a module can be characterized as either interdependent, with effective levels of communication, or modular, with specific hidden design parameters. The notion of the HIV integrase project being interdependent is examined in more detail further on in this analysis.

implementation of rational drug design procedures[153], of which the structure-activity relationship methodology is a component practice. The alignment *within* Module I is achieved by the structure-activity relationship methodology.

If the process of rational drug design is thought of as the following four steps, as outlined by McPherson (1995), it is obvious that Modules II and III are fulfilling a role in the process. McPherson's steps include:

1. Determining structure
2. Analyzing structure-function[154]
3. Modeling the protein with candidate drug molecules
4. Diffusing drug molecules into protein crystal **or** co-crystallizing drug molecule and protein

Clearly, Module I and Module II are in line with step two of the rational drug design process. The structure-activity relationship methodology is used in both of these projects, detailing the structure of specific compounds and the function of the compounds in relation to vancomycin-resistant bacteria and HIV integrase, respectively. The third project, Module III, is operating in step three of the rational drug design process, where the scientists are modeling the integrase enzyme and docking the developed compounds and hypothetical compounds into the model to determine their impact.

When this is analyzed in conjunction with the acknowledgement that there is an interface of synthetic chemistry and a starting point, TB96, between the projects, it becomes apparent that

[153] Recall the brief discussions in chapters two, three, and four that highlighted the use of rational drug design as a design rule in some of the collaborations presented in this thesis. Rational drug design is the advent of modern structural analytical approaches, whereby the target of a disease (viral, bacterial, or otherwise) is examined in extraordinary chemical detail, creating a relatively precise indication of what small molecules should be designed to interact with the target in specified and controlled ways. This new approach to drug discovery, utilizing systematic and directed drug design, "has assumed an important place in the biotechnology revolution that has emerged over the past 15 years" (McPherson, 1995, p161).

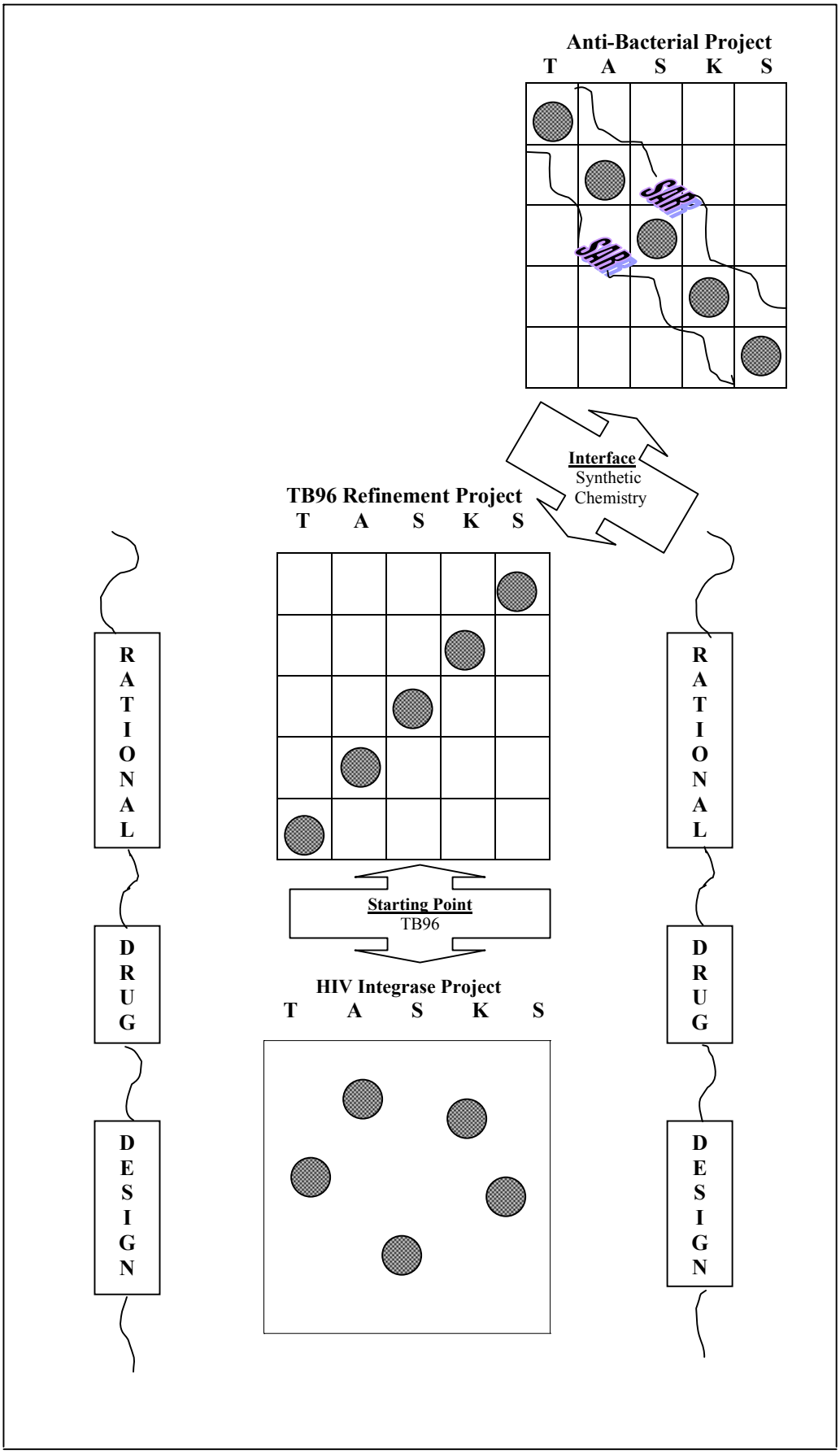
[154] McPherson's second step is intended to represent identifying the structure and function of the macromolecular target. If, however, the evaluation and investigation of the macromolecular target is occurring concurrently with the development of compounds, as is the case in the alliance between IBS and AMRAD, this step can also be interpreted as the application of the structure-activity relationship methodology. For, as McPherson himself notes, "…in practice, the application of rational design to drug discovery and development requires not only determination of the native enzyme structure [the macromolecular target], but many cycles of drug synthesis, [testing], further synthesis and review, and ultimately optimization of the stereochemical parameters that govern the event" (1995, p165).

there are connections between the projects, but alignment is only necessary across two of the projects. Considering that synthetic chemistry is used in both Module I and Module II, it can be considered to be an interface between the two projects, providing a means for connection and communication. TB96 was developed in Module I using synthetic chemistry. In Module II, synthetic chemistry is being used to make the compound more efficacious against HIV integrase. Within Module III, computer models are being built using computational chemistry to conceptually assess the impact of TB96 on the enzyme and to predict what modifications can be made to the compound in order to have the desired effect on the enzyme. Therefore, TB96 is a starting point[155] between Module II and Module III. It is a boundary object between the two projects that is simultaneously applicable to both, but how it is used in each project differs.

A snap shot of the three projects in the knowledge value alliance is portrayed in Diagram 7.4. Each project is presented as a module in the alliance with a starting point and an interface providing connection between the projects. The HIV integrase project is illustrated in terms of an interdependent arrangement, rather than a modular one, as has been suggested (and the rationale behind this depiction is discussed later in the chapter). The dots or markers in the HIV Integrase Project are presented in a circular arrangement without divisions between them in order to signify this interdependency. The other two projects are modular in arrangement, where there is less interaction and exchange (than there is in the HIV integrase project) between the collaborative participants. The markers in the Anti-Bacterial Project and the TB96 Refinement Project appear in opposing directions to demonstrate that the TB96 Refinement Project branched off from the other and the two are going in different directions. The rational drug design process is depicted as the design rule, serving to align all the work performed within Modules I and II.

[155] As defined in chapter three, a starting point is a boundary object that provides an initial lead for one or more projects, however, the directions from the starting point onward and the methods that facilitate such directions may vary between the projects.

Diagram 7.3 The IBS-amrad Architectural Arrangement



Rational drug design serves as a coordination mechanism in the alliance. The testing of TB96 as an anti-viral candidate came about because of the amrad scientists' knowledge of features necessary in a compound to effectively target HIV integrase, which could only be developed through the type of analysis dictated by rational drug design. The scientists at amrad know when cross testing is appropriate and when there is a likelihood that a compound may work as an inhibitor of HIV integrase. This knowledge stems from the work that the amrad scientists have done with the scientists at the Victorian College of Pharmacy, in which knowledge of HIV integrase has been developed. Thus, this knowledge allowed the scientists at amrad to recognize the features of TB96 as potentially efficacious against HIV integrase.

Within Module I, the Anti-Bacterial Project, the structure-activity relationship methodology provides alignment between the tasks in that module. This design rule dictates that synthesized compounds must be tested and advanced in the direction of increased potency. As a result, the activity within each task domain is centred on increasing the potency of the compound. The directional flow of knowledge under the guidance of this design rule comprises compounds from the synthetic chemistry domain being sent to the testing domain, and testing results from the testing domain being sent to the synthetic chemistry domain. The synthetic chemists, however, do not need detailed knowledge-about the work in the testing domain (i.e., how testing is performed) and the testing scientists do not need to know how to synthesize compounds. The structure-activity relationship design rule allows for the coordination of the task work in a manner that mitigates the necessity for large amounts of knowledge overlap among the scientists in Module I.

The synthetic chemistry interface and the TB96 starting point provide connections *between* the projects. Synthetic chemistry as an interface allows for communication and connection between the members of Module I and Module II. The connection that is provided between Module II and Module III comes from TB96 as a starting point. The way TB96 is dealt with in each project differs though. In Module II, the compound is physically modified. In Module III, the compound is used in the modeling of HIV integrase. It is modified in a computer program to determine the effect of changes to the compound and their impact on the

compound's ability to accurately and appropriately target HIV integrase. Following rational drug design, the computer program will eventually, with enough added information, be able to predict the precise modifications to be made to TB96 (or one of its already modified successors) in order for it to have the desired effect on the target. In turn, these predicted modifications become another starting point in the synthetic chemistry module, Module II, or the TB96 Refinement Project.

7.2.2 Internal Project Arrangements

Connections *within* the projects are achieved via different mechanisms. Indeed, Coates has extensive knowledge of drug development and virology, whereas the scientists from the IBS side of the different projects boast knowledge in synthetic and computational chemistry. There are clear differences in knowledge bases here, but the alignment within the projects is achieved as a result of the structure-activity relationship methodology. The knowledge of virology or synthetic chemistry does not need to "flow" per se between the two sides of the alliance because of the use of this methodology. Rather, the knowledge produced by each side, in the form of compounds and testing results, is integrated by the structure-activity relationship methodology, allowing for a modular divide between tasks and a division of labour.

Where the projects are modular, such as in Module I and Module II, the interfaces are the knowledge of the structure of drugs and synthetic chemistry. Coates, Bremner, Keller, and Pyne all have experience in drug development and knowledge of the molecular features necessary in a compound to make it drug-like. With the addition of Dr. John Deadman, the Head of Medicinal Chemistry at amrad[156], a synthetic chemistry interface has been established between IBS and amrad. Prior to the addition of the synthetic chemistry interface, the interface created by the common knowledge of the structure of drugs was supplemented by the trust between the two parties. Coates commented that he trusts Bremner and has significant faith in his ability as a

[156] While AMRAD has had the intention of hiring a medicinal chemist for a while now, the search for an appropriate scientist ended in mid 2003 with the hiring of Deadman as the Head of Medicinal Chemistry at amrad.

scientist, thus he knows that Bremner would never deliberately stall or misdirect the project (20 May 2003 – personal interview).

In the HIV Integrase Project, the arrangement is much more interdependent than modular. In this module, various levels of collaborators participate, communicate, and offer input based on their ingrained knowledge, and, most importantly, they share the knowledge generated on both sides of the alliance. The HIV integrase was modeled at the Victorian College of Pharmacy, giving the staff at amrad an understanding of the structure and function of the enzyme. Similarly, the enzyme was also modeled by the team consisting of Gordon, Keller, and Griffith, giving them an understanding of the structure and function of the enzyme. At the time of my investigation, the collaborative effort was aimed at modeling the enzyme with candidate drug molecules (stage three of McPherson's steps) and attempting to assess where the important activity sites are in the modeled enzyme. There is a significant amount of knowledge overlap in this project and the interdependencies are evidenced in the amount of exchange among the parties. According to Keller (19 June 2003 – personal interview), the HIV Integrase Project is trying to fill mutual knowledge gaps, and develop an explanation of HIV integrase and the impact of specific types of compounds on this target for both IBS and amrad.

7.2.2.1 The Use of Migratory and Ingrained Knowledge

Both migratory and ingrained knowledge played a role in these aims and the process of trying to achieve them. Migratory knowledge was used when the members of the HIV Integrase team frequently combed the literature to see what compounds had been used previously by other scientists outside of the collaboration to successfully target HIV integrase. From the literary repositories, namely journal articles, the IBS and amrad scientists were able to make a preliminary judgment regarding the features of molecules to pursue in the effort to find an efficacious molecule capable of appropriately targeting HIV integrase.

Interestingly, during one period of observation it became apparent to me that the reports of scientists, specifically in journal articles, do indeed accord with the suppositions of Merton, Bacon and Leibniz, and Medawar discussed in Knorr-Cetina (1981 – discussed in chapter four)

that suggest the purposeful concealment and distortion of results in the write-up of scientific findings. The members of the IBS team had found some desired information relating to compounds that could potentially be used in targeting HIV integrase in a journal article produced by chemists at the University of California, San Diego. The information, however, was concealed to the point that the chemists from the Institute for Biomolecular Science could not adequately decipher the information that they desired to know about the compounds. During the meeting that I observed, the chemists from IBS considered writing to the scientists who produced the paper to request more information.

Ingrained knowledge was also an important feature in the processes involved in modeling the enzyme and in gauging its important areas of activity. During another meeting I observed (9 May 2003), Gordon, one of the PhD students involved in the project, was making a presentation that demonstrated six catalytic cores in the three-dimensional structure of the enzyme. Keller interrupted Gordon's presentation to suggest that, for the purposes of their drug design, the "looped region" is and should be the area of focus. Keller emphasized the importance of the role of the "flexible loop". When I presented Coates and Cox with this observation, they agreed that if Keller had formulated a hypothesis that pointed to the important area of the enzyme, they would test his hypothesis because they respected his opinion. There are, then, in the case of this module, various states of knowing[157] in relation to where the active area of the HIV integrase is. The scientists from IBS and amrad (and the Victorian College of Pharmacy) have been using their ingrained knowledge in an attempt to accurately identify the region of activity.

The levels of interaction and communication between Gordon, the PhD student, Keller, the full-time IBS faculty member, and the staff at amrad suggest that the HIV Integrase Project is not premised on a division of labour. Members of this project are using similar areas of

[157] These states of knowing vary among the members of the project. Following Machlup's (1980) thirteen states of knowing – including being acquainted, being familiar, being aware, remembering, recollecting, recognizing, distinguishing, understanding, interpreting, being able to explain, being able to demonstrate, being able to talk about, and being able to perform – it can be said that Keller's state of knowing the active region of the enzyme is somewhere between recognizing and being able to explain. He has indeed been involved in other projects concerning HIV where he acquired additional ingrained knowledge about the disease and how certain types of compounds act on the enzymes implicated in it. Gordon's state of knowing is in the range of being aware to recollecting. In his presentation, he was in fact drawing from the literature and other sources that have helped him to form a belief about the important and active areas of the enzyme.

knowledge and there is considerable knowledge overlap among them, suggesting an interdependent arrangement, rather than a modular organization.

In contrast, the TB96 refinement project is organized in a more modular fashion. There is a clear division of labour between the scientists at amrad, who develop the material for testing and perform the testing, and the scientists at IBS, who synthesize the compounds. Work occurs independently in each side of the collaboration and is aligned by the structure activity relationship methodology. The IBS module in this project, however, has been split by the routinization of the process of chemical synthesis[158].

7.2.2.2 Splitting the IBS Modules

There is a clear division of labour in the Anti-Bacterial Project and TB96 Refinement Project. The laboratory work in both projects is performed by Boyle, PhD candidate, and Robertson, research fellow. The three full-time faculty members from IBS act as supervisors to the work performed by Boyle and Robertson, supporting their efforts and suggesting alternative approaches to their work. Within the IBS task domains of Modules I and II, then, there is a split caused by the routinizaiton of the procedures for chemical synthesis.

Pharmacochemistry, the modern expression of pharmaceutical chemistry, originated half a century ago as a science whose main interest is the design of new pharmacomolecules (Kourounakis & Rekka, 1994a, p1). Synthetic design, the activity performed in pharmacochemistry, then, has had a significant amount of time to become substantially developed, widespread, and essentially routinized. When Boyle and Robertson accepted their respective positions (PhD candidate and research fellow), they did so with the intention of mastering the process of design synthesis. They have been developing this technique and

[158] Recall the discussion in chapter four centred on the ability of "things" (Latour, 1987) to modify and mediate human behavior and interaction. An example taken from Knorr-Centina (1981) demonstrated how the routinized technique for defining the functional properties of proteins caused a split in a module. The practice of defining functional properties of proteins would have been a meshing of an actor with a task, but instead, because the technique was a routine procedure, the task was outsourced to a lab and a split was conceived in the module, requiring new design parameters to bring the module into alignment.

learning from the three IBS supervisors and other students in the supervisors' labs[159]. This technique, however, is standard and routine in the eyes of the supervisors, and, therefore, can performed adequately and appropriately by Boyle and Robertson. (It is not worth the supervisors' time to perform the task, and, in addition, the task should rightfully be performed by PhD students and research assistants during their apprenticeships). As Henderson, Orsenigo, and Pisano (1999) note, chemistry and chemical engineering

> …have existed in academia and industry since the 18th century and…there is a long history of basic scientific research [in these disciplines]. As a result much of the relevant theoretical knowledge has been codified in scientific journals and textbooks, and in searching for and selecting alternative chemical processes for the development of small molecular drugs, [the scientist] has at [his or her] disposal a wealth of scientific laws, principles, and models which describe the structure of relationships among different variables (e.g., pressure, volume, temperature) (p285)[160].

The division of labour within the synthesis domains of Modules I and II requires the use of hidden design parameters, which should help to ensure that the work of the synthetic chemists is in line with the work of the other scientists. The hidden design rules present in the synthesis module can be thought of as agent-practice, which describe and guide the agent's actions "without a detailed reference to his or her thoughts" (Koppl & Langlois, 2001, p287). These are the rules that tell the synthetic chemist what to do in the process of synthesis, picked up in years of study. They are rules that govern the synthetic chemistry commons. To be a member of the synthetic chemistry community, one must have a command of these procedures. They exist in migratory forms, for example in textbooks or manuals.

The hidden design parameters can also be thought of as agent-theory, or the rules that describe the agent's possible actions with detailed references to his thoughts and ideas (Koppl & Langlois, 2001). They exist as ingrained knowledge in the mind of the synthetic chemist, acting as a heuristic in the process of chemical synthesis. As Robertson conveyed during his interview

[159] During his interview, Keller professed that knowledge exists within his lab and it is important not to let there be a significant time lapse between when students are graduating from the lab and new students are coming into the lab. Having an overlap of graduating and new students in the lab, according to Keller, ensures the transfer of knowledge between the two types of students (19 June 2003 – personal interview).
[160] Henderson, Orsenigo, and Pisano (1999) contrast the amount of codified information in chemical engineering and synthesis with the level of uncodified knowledge that is used in biotechnology process development. They contend that, "[t]here has been very little basic research conducted on the problems of engineering larger-scale biotechnology processes. Thus process developers in biotechnology have little theory to guide them in the development of new manufacturing processes" (p285).

(17 June 2003), synthetic chemistry involves peptide chemistry and the creation of peptide bonds, where the synthetic chemist changes the molecules on either end of the compound. This practice requires "knowledge-how-to and a hands-on approach".

While these rules may be standardized and familiar to all synthetic chemists, there are still differences in the states of knowing and what is known among synthetic chemists. For example, in the meeting I observed on the 24 September 2003, amrad's newly appointed Head of Medicinal Chemistry, Deadman, was reviewing the work of the IBS chemists. To his surprise, he discovered that the IBS chemists had been using double bonds in their compounds. Deadman communicated his knowledge of double bonds to the IBS scientists, suggesting that double bonds can pose problems for drug metabolism; they often create an extended exposure of the chemical when ingested. Using his ingrained knowledge, Bremner from IBS offered the solution of using hydrogination to replace the double bonds with single bonds. Coates concluded the debate by saying that amrad would test Deadman's hypothesis about double bonds to find out more about their metabolic status. So, despite the agent-practice and agent-theory design rules that govern the synthetic chemistry modules, differences in states of knowing and what is known do exist[161].

The hidden design parameters of the synthesis modules are concealed from the scientists in the testing modules of the projects, but the testing scientists do not need to know about or know of these design rules. The members of the testing module are concerned only that the product from the synthesis module is in line with the structure-activity relationship methodology, whereby the compounds produced in the synthesis module show heightened activity in the testing process, and that the results of synthesis and testing meet the standards

[161] This brings the notion of luck back into the discussion. Architects of an alliance inevitably would like to enlist the scientists most suitable for the task, however, ingrained knowledge is difficult to gauge, and therefore, there is a certain amount of luck involved in actually enrolling the person(s) who have the requisite ingrained knowledge to perform a specific task. What this suggests too, is that, with the agent-practice being a derivative of Wittgenstein's language-games, language predicated as rules "does not consist of neutral propositions which correspond to an independent reality" (How, 1995, p87) and, therefore, various states of knowing agent-practice rules will exist because reality is individually (and socially) constructed.

prescribed by the rational drug design design rule (specifically in Module II, or the TB96 Refinement Project).

In the cases in which the modules are divided in terms of labour and knowledge, there is a clear hierarchy of requirements. The work must meet the demands of the hidden design parameters. It must also meet the design rules of the project (ie. the standards set by the structure-activity relationship methodology). In conjunction, the work performed at the modular level must meet the design rules that govern Modules II and III, namely the rational drug design rule. The HIV Integrase Project must adhere to the standards set by the structure-activity relationship methodology and the requisites of the rational drug design parameters. All three sets of design rules, the hidden ones, the modular ones, and the one at the alliance level are, however, subsets of each other. Meeting the lower level ones, then, automatically conditions the work to be in line with design rules at the higher levels.

7.2.3 The Structure of the Alliance

The application of rational drug design in this collaboration creates a functional structure within and across the modules of the alliance. The functional structure is seen in the clustering of projects around specific scientific specializations and goals. The TB96 Refinement Project, for instance, is centred on using synthetic chemistry and testing, with the goal of developing a compound to target HIV integrase. The HIV Integrase Project is centred on the use of computational chemistry to develop a theory, aided by computer design, of the necessary features in a compound to appropriately target HIV integrase. Within the projects, the structure is also functional. When looking at the Anti-Bacterial Project and the TB96 Refinement Project, it becomes apparent that the modules within each project are split according to function. The testing module is based on the function of testing. The synthesis module is based on the function of synthesizing compounds.

Across modules, the structure is also divided according to products. The Anti-Bacterial Project is centred on producing a drug lead to combat vancomycin-resistant bacteria. The other two projects are geared toward deriving a drug to act against HIV integrase. This division of

labour based on products has specific implications for the movement of knowledge within the alliance. Indeed, the Anti-Bacterial Project is connected to the TB96 Refinement Project by a synthetic chemistry interface. Communication can occur among members of the two projects because of this interface. The desired outputs differ between the two projects, however. As such, the level of migratory knowledge needing to flow between the two projects (or the Anti-Bacterial and the HIV Integrase Projects, for that matter) is relatively insignificant.

The functional structure of the alliances has implications for the way knowledge is handled in the collaboration too. Only migratory knowledge in the form of compounds, testing reports, and various repositories (i.e. journal articles) moves between functional divisions. The ingrained knowledge does not, and does not need to move because the design rules integrate the knowledge of the collaborative participants in such a way that the virologist does not need to learn synthetic chemistry, and vice versa.

The work performed at the modular level is also facilitated by the existence of specific boundary objects, including starting points and repositories. These two elements align agents within units and across units, providing conduits for communication and mechanisms for social configuration. Ingrained knowledge does play a vital role in this alliance, but it is a role that is fulfilled at the level of the scientists within modules. In turn, however, with the use of the design rules and boundary objects, the application of ingrained knowledge becomes the driving force in moving the alliance between the Institute for Biomolecular Science and amrad closer to its goal of "getting pills in bottles".

The modular structure of the alliance is premised on the performance of specialized tasks within modules. As Gulick (1917 cited in Walker & Lorsch, 1996, p220) states, a structure based on function and specialization "…guarantees the maximum utilization of up-to-date technical skill and…makes it possible in each case to make use of the most effective divisions of work and specialization…[It] encourages coordination on all of the technical and skilled work of the enterprise…". Indeed, the functional modular structure of the IBS-amrad alliance takes advantage of the specialized expertise of the collaborative participants. Even within modules, work is coordinated and scientists are meshed with their tasks via hidden design

parameters and the use of ingrained knowledge. But what of the split in the IBS synthetic chemistry module?

The split does not impact on the flow of migratory knowledge between modules, but it does cause ripples in the use of specialized labour and advanced expertise. The compounds produced in this module still move straight to the testing module as they would if the module had not been split. While a PhD student and a research fellow are advanced in the knowledge of their area of specialization, their levels of ingrained knowledge are not thought to be equivalent to a professorial synthetic chemist with over 20 years of experience. As such, the split in the module could be thought of as diminishing the utilization of all possible expertise. In allowing the split, the architect of the alliance could be conceived of as a non-opportunist in the Knorr-Cetina translation of the term.

Yet, with the arrangement of the IBS synthetic chemistry module, the veteran synthetic chemists still have input into the processes of the junior synthetic chemists (the PhD student and research fellow). The junior chemists may make the decisions on how to approach the chemistry, but their work is supervised by the veteran chemists who either support or veto the compound trajectories[162] of the junior chemists' work. This is made possible by the adherence of all the chemists in that module to the agent-practice guidelines found in the module's hidden design parameters. Recall three things here: the agent-practice does not make reference to one's thought patterns, but simply tells one what to do; there are two mechanisms – hidden design rules and ingrained knowledge – for the third level of articulation (meshing an individual with a task); and, migratory knowledge is said to include the ingrained knowledge used to produce it. As such, the veteran chemists are in theory the agent-practice that links the ingrained knowledge of the junior chemists with the hidden design parameters. Where the ingrained knowledge of the junior chemists is insufficient to effectively increase the potency of a compound, where these chemists are unaware of the rules (agent-practice or hidden parameter) that tell them how to do this, the veteran chemists assume the role of "rule communicator".

[162] I use this term to represent the fact that the compounds produced by the synthetic chemists are usually small modifications of a previous compound. The compound generally retains its core structure, with modifications only made to the outer portions in a bid to increase the potency of the compound.

With the architect's trust in the veteran chemists, then, the architect can indeed be considered an opportunist (as defined by Knorr-Cetina) because he or she has faith that the required expertise is being embedded into the migratory knowledge. It is not necessarily just the junior chemists' knowledge that comes forth in the compound, but the knowledge of the veteran chemists as well via their translation of the rules.

The modular structure of this alliance is functional in that it groups task work around the distinct areas of expertise necessary to reach the desired output. It is also product-oriented in that there are two separate products being pursued in the alliance. Coordination and the meshing of individuals with their tasks are achieved via ingrained knowledge and hidden design parameters. Unit workers, both within modules and across modules, are meshed by the use of repositories to aid in problem resolution and starting points that provide connections between different modules. The articulation of tasks across the entire alliance is achieved by the rational drug design design rule. The three projects that are structured in this alliance are amalgamated via the use of this design rule and the synthetic chemistry interface.

7.3 Conclusion

The fact that all parties to the collaboration have a common goal of "getting pills in bottles" is an added bonus in the attempts to align the work performed in the alliance. The common goal, however, is it necessary for alignment. As Koppl and Langlois (2001) note, "[m]uch of the literature on knowledge management takes it for granted that coordination of knowledge within a firm [or in this case, within a collaboration] requires that everyone in the firm has the same interpretation of the firm, its goals, and its procedures" (p296). The concept of modularity suggests that this type of shared mental representation is not necessary. Knowledge management can be effective, rather than through a fluid exchange between all parties, by implementing the appropriate design rules, interfaces, and boundary objects to integrate the ingrained knowledge of collaborative participants in a suitable structure.

This can be accomplished in one knowledge architecture, as seen in the case of the CMBB-Nereus alliance, or across several knowledge architectures, as demonstrated in the case presented in this chapter. While achieving alignment within the alliance is quite an achievement and goes a long way toward winning the game of Biotechnology Bingo, particularly when alignment can be achieved across a host of projects, it does not ensure that the alliance has appropriate allies outside of the collaboration, a practice which also contributes to winning in the game of Biotechnology Bingo.

The alliance between IBS and amrad has not been as successful as the alliance between the Center for Marine Biology and Biotechnology and Nereus Pharmaceuticals at enlisting allies from the environment beyond the alliance. Most of funding for the three projects that comprise the IBS-amrad knowledge value alliance comes from amrad[163] (as opposed to the substantial amount of funding that Fenical from CMBB has been able to procure from the California State Government)[164]. The IBS-amrad alliance has, however, recently applied for and been granted an NH&MRC grant. The current arrangement of the alliance is meeting the needs of the members on both sides of the collaboration. To seek additional allies could well be unnecessary at this time, and to let other researchers in on the IBS-amrad game could certainly diminish any future returns that may accrue to the current alliance participants.

Nonetheless, the alliance between the Institute for Biomolecular Science and amrad provides evidence of the increasingly common practice of unifying chemistry and biology under the auspices of a "design for purpose mantra". As Kourounakis and Rekka (1994b) contend, "[t]he impact of the combination of chemistry with biology goes further than synthetic, preparative methods for the production of bioactive macromolecules. It extends to the conferring of drug selectivity and to drug delivery processes" (p138). The union of the ingrained knowledge of the chemists at IBS with the ingrained knowledge of the virologists, immunologists, and biologists at amrad is a purposeful endeavour aimed at drug delivery. The

[163] One respondent suggested that the funding for this alliance amounted to AMRAD contributing $200,000 per year for a total of six years.
[164] This, however, could also be attributed to a difference in funding policies between the Australian context and funding standards and mechanisms in California.

activity of integrating these knowledge bases is a design process that requires the implementation of the appropriate tools, technologies, and work practices to be effective.

Chapter 8 Case C IG-Progen

The Knowledge Value Alliance between the Institute for Glycomics (IG) and Progen Industries Limited

> "The creation of relational rents is often contingent on a firm's ability to find a partner with (1) complementary strategic resources and (2) a relational capability (i.e., a firm's willingness and ability to partner)" (Dyer & Singh, 1998, p672).

In chapter two, I put forth the argument that collaborations in biotechnology between university and industry are premised on the notion of complementary resources. There is, however, as Dyer and Singh (1998) note, another dimension to consider, the relational capability of a potential collaborative partner. Following Eisenhardt and Schoonhoven (1996), Larson (1992), Gulati (1995), and Mitchell and Singh (1996), these authors highlight the risks of potential partners lacking the relational capability to employ effective governance mechanisms, make relation-specific investments, or develop knowledge sharing routines. They suggest that, in a bid to avoid these risks, potential partners with collaborative experience should be sought. While these are all very relevant concerns, complete with possibly serious consequences (i.e., failure to generate value or relational rents) and mechanisms for avoidance (i.e., seek partners with a proven track record of collaborative endeavours), the dimension of relational capability is deeper than suggested.

As demonstrated in the case that is the subject of this chapter, even with the application of the appropriate tools, technologies, and work practices, and the investigation and approval of

a potential partner's track record, collaborations are still not guaranteed the attainment of their specified outputs. There is, as has been argued throughout this thesis, an element of luck involved in getting these alliances right. The luck associated with the alliances discussed in this thesis can be attributed to a number of things, including the fact that collaborations in biotechnology are based on innovative and highly experimental science, in which there is no guarantee that experiments will work, or that, in many cases, members of a collaboration have multiple priorities to attend to and cannot always devote sufficient attention and resources to the successful attainment of the alliance's desired outcome.

The collaboration between the Institute for Glycomics, Griffith University and Progen Industries, a small biotechnology firm located in Darra, Queensland, is interesting because it has not attained the desired outcome initially specified at the commencement of the alliance, despite the application and use of relevant design rules, interfaces, repositories, starting points, and ingrained knowledge. In addition, both sides of this collaboration have proven track records of success in previous collaborations and in taking a drug through the stages of discovery and development. In line with the cases of the last two chapters, this one is illustrative of the theory developed in chapters two, three, and four via the existence of a division of labour among the collaborators, the functioning of the concepts of modularity and boundary objects, and the relevance of ingrained knowledge.

This collaboration, however, makes evident the notion that even in the face of modularity, it takes a considerable amount of time to get things working. Members of a collaboration must get to know each other and find mechanisms for facilitating the relationship. Results often don't come until the final stages of a collaborative endeavour, and articulation mechanisms alone will not keep the relationship between members of an alliance stable and strong when results and movement toward the desired output are not seen in a steady stream. In such circumstances, the institutionalization of tact, an element of interaction that has not surfaced in the presentation of the previous cases, is necessary to facilitate the relationship.

8.1 Case Description

The alliance between the Institute for Glycomics (IG), Griffith University, and Progen Industries, also located on the Gold Coast of Queensland, began in March 2001. A contract was drafted that stipulated the funding of the project by Progen for three years and the exclusive licensing rights by Progen of the material produced in the collaboration, should the firm foresee potential value in this material. The total dollar amount Progen was to invest over the course of the three year period was over AU$1,000,000. This amount was appropriated for the use of equipment (and possible purchase of equipment if necessary), the purchase of materials, and the salaries of the IG scientists working on the project.

As a follow-on project from the collaboration between Progen and scientists at the Australian National University (ANU), the work performed in the IG-Progen collaboration is based around heparanase, an enzyme implicated in a range of diseases, including inflammatory diseases (multiple sclerosis and inflammatory bowel disease) and cancer[165]. The collaboration was put together after a conversation between Dr. Mark von Itzstein, the Director at the Institute for Glycomics, and Dr. Robert Don, the R&D Manager at Progen. In an effort to get some more value added from the intellectual property (IP) that was derived from Progen's collaboration with the scientists from ANU, Don devised a collaborative agenda whereby Progen would provide the enzyme to the Institute for Glycomics and von Itzstein would use his resources to develop drugs based on that enzyme (Vance[166], 29 September 2003 – personal interview). The respondents agreed that the collaboration is premised on solid ground. "The strength of the project is that the concept is a good one. It has a good target. It is potentially new and exciting" (Vance, 29 September 2003 – personal interview).

[165] "Heparanase is an enzyme which acts to degrade the natural 'glue' (or extracellular matrix) which holds cells together in the human body" (Progen Industries, 2002). In the collaborations with the Institute for Glycomics and the Australian National University, Progen's goals have been and continue to be discovering and developing compounds capable of inhibiting this enzyme. "By inhibiting heparanase, the expectation is that various inflammatory and cancer disease processes can be disrupted" (Progen Industries, 2002). The ANU has procured a patent on detecting heparanse activity and purifying the enzyme, on which Progen holds an exclusive worldwide licence.

[166] Vance is a pseudonym for one of the respondents in this case. He expressed his desire to remain anonymous, and therefore, his name has been altered and his position has not been disclosed.

In addition, all interviewees conveyed similar conceptualizations of the goals of the alliance. The project started "with the aims of the development of potential, novel small molecules", stated von Itzstein (29 September 2003 – personal interview), "that would inhibit the enzyme and an elucidation of the structure of the enzyme". The contract called for von Itzstein and his staff of scientists to crystallize the enzyme, get the structural information on it, and turn that into drug leads. "Von Itzstein was to deliver a structure by x-ray crystallography and use it to design drug leads" (Vance, 29 September 2003 – personal interview). "The goal of the project is to make a drug like molecule that inhibits the protein target that we have, heparanase. There are a couple of approaches we are taking, but the goal is the drug…modeling is a central part of it, but not the goal…in its own right" (Don, 8 December 2003 – personal interview).

The design and synthesis of a drug to inhibit heparanse, however, was not the only desired outcome of the alliance. Von Itzstein pointed to the staff at Progen wanting to upskill (29 September 2003 – personal interview). Vance suggested that the reason for the collaboration was twofold. "Obviously, Progen wanted something marketable, something we could on-sell further as IP. We were looking for a commercial benefit, but we also wanted to develop an in-house structure-based drug design group and we felt if we worked with someone who had a reputation in that area, then we could tap into that expertise" (29 September 2003 – personal interview). "In designing the collaboration, we looked at the skills we wanted, but also looked at the crossover of IP. We made sure that it was clearly defined as well, so we had a very good goal of where we were heading" (Don, 8 December 2003 – personal interview).

The desired outcome of the alliance was clearly specified at the onset of the collaborative endeavour. There is a division of labour that has existed from the beginning of the collaboration, which, if the work performed within the modules were to be adequately and appropriately integrated, would potentially lead to the desired outcome. With the commencement of the alliance, there were also disparate knowledge bases in the two entities. One goal of the collaboration, as disclosed by the respondents in the case, was to minimize this disparity. This was to be accomplished not by the direct transference of expertise from one party

to another, but by the scientists at Progen witnessing the practice of rational drug design technology and acquiring their own group of experts in the field of rational drug design to perform the technology. While this goal has been achieved, the collaboration has yet to produce the desired drug lead(s). The collaboration, however, is not yet over.

8.1.1 Knowledge Used in the Collaboration

The scientific realms that define this alliance include sugar chemistry and rational drug design (Don, 8 December 2003 – personal interview). According to von Itzstein (29 September 2003 – personal interview), the project is specific to mammalian glyco-biochemistry. Analysis of the data pointed to five core scientific areas pertinent to the collaborative agenda. The first two areas are synthetic chemistry and microbiology. The third core scientific area, glyco-biochemistry, is concerned with carbohydrate recognizing proteins that are important in mammalian disease. Structural glycobiology and computational chemistry are one combined area, namely the fourth type of science used in this collaboration, that would allow for the definition of the three-dimensional structure of heparanase and the identification of the features necessary in a molecule to effectively target that enzyme. The final area of science, or perhaps more in the area of technology, is the use of protein x-ray crystallography techniques.

The two main areas that define this alliance, sugar chemistry and rational drug design, can be split into the other scientific and technological areas that were identified in the interviews. The realm of sugar chemistry consists of the sciences of synthetic chemistry, microbiology, and glyco-biochemistry. It deals with how to work with sugars, and specifically with synthetic sugars, or glycomimetics[167]. Both IG and Progen have scientists who are experienced in this type of work.

The realm of rational drug design includes the practices of structural glycobiology, along with computational chemistry, synthetic chemistry, and x-ray crystallography. Rational drug design is often thought of in terms of a lock and key arrangement, whereby if one can tell how well the key (the drug) fits in the model of the enzyme (the lock), then based on that

[167] Glycomimetics are small molecule drugs that mimic the action of carbohydrates in the human body.

information, one can refine the key to make a better fit, and logically, a more effective drug can be produced[168] (Don, 8 December 2003 – personal interview). The scientists at Institute for Glycomics have experience in taking a drug to market via the rational drug design approach. Progen has only within the last three years hired-in the expertise in order to apply the rational drug design approach.

The expertise of the scientists at the Institute for Glycomics and Progen overlaps in the following areas. The focus at IG, as a general institute of research, is on sugars and their role in diseases (Don, 8 December 2003 – personal interview). The scientists at the Institute work on the development of enabling glycotechnologies[169] (Griffith University, 2003). The IG scientists have specific expertise in synthetic chemistry, glyco-biochemistry, structural glycobiology, and x-ray crystallography. The focus at Progen is on screening natural carbohydrates and the synthesis of glycomimetics (Progen Industries, 2002). In addition, the work at Progen is centred on understanding how sugars work in the body (Don, 8 December 2003 – personal interview). Upon initiating the IG-Progen alliance, the scientists at Progen were experienced in synthetic chemistry, microbiology, and glyco-biochemistry. With the addition of a drug development group, Progen has also acquired expertise in computational chemistry. There is, then, a significant overlap in the knowledge between the two entities.

Despite this overlap, there is an obvious division of labour in the collaboration. "The scientists at Progen are responsible for production of the enzyme (heparanase) as well as looking at the biological evaluation through enzyme assays of the chemicals that the Institute produces" (von Itzstein, 29 September 2003 – personal interview). The scientists at the Institute for Glycomics are doing the synthesis of glycomimetics (Vance, 29 September 2003 – personal interview). "From a chemistry perspective, this entails designing and synthesizing compounds

[168] It should be noted here, however, that as McPherson (1995) argues, the lock and key relationship "…is extremely demanding in that supplementary or improperly placed atoms on the substrate, like an additional tooth on a key, immediately excludes its binding at the active site. A substrate too small leaves the active site exposed to invasion by water, imperfect bonding distances, and multiple nonproductive orientations" (p163).

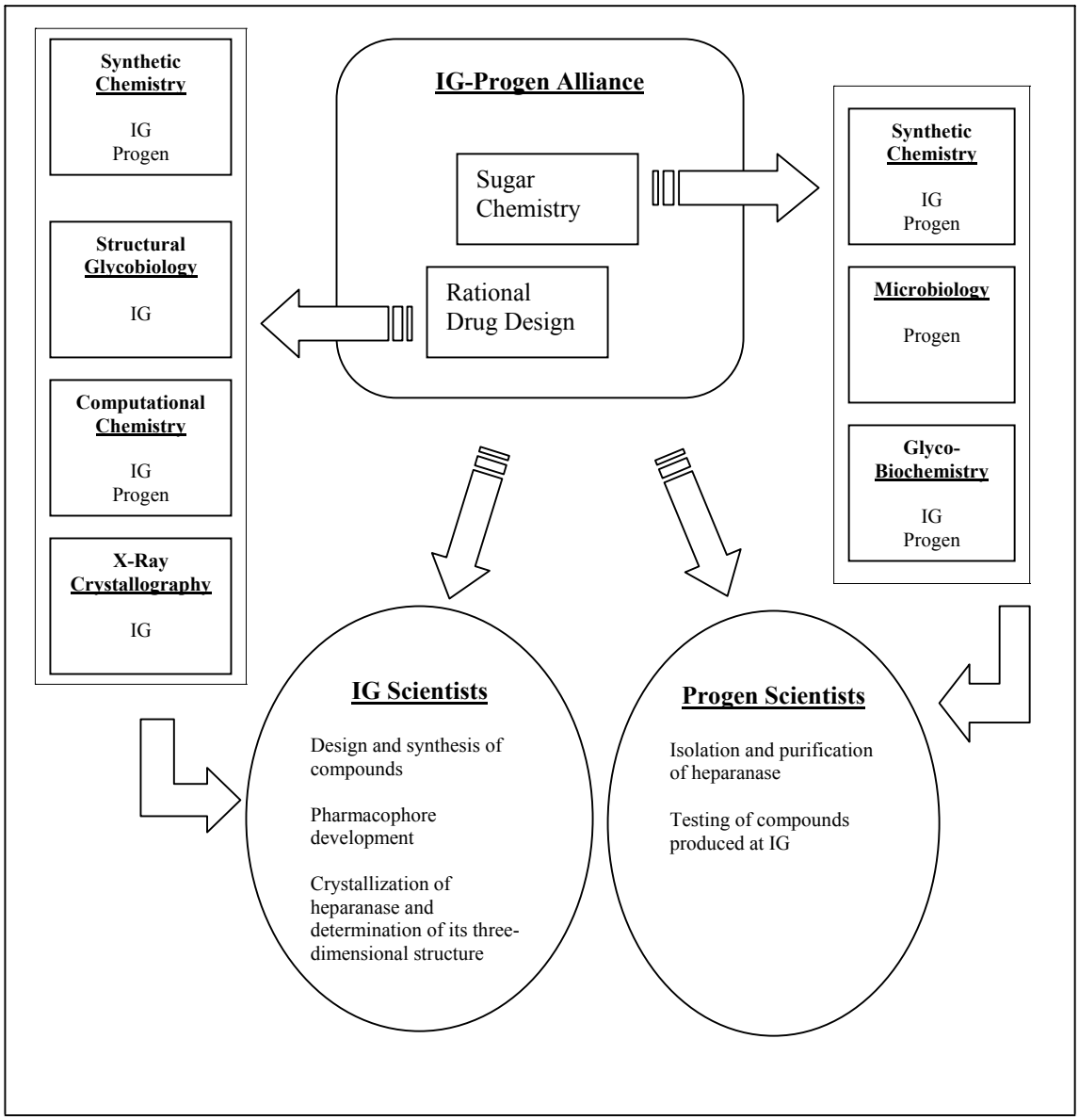
[169] This process was explained to me in the interviews for this project as developing and standardizing methodologies or technologies for working with sugars.

to develop a pharmacophore[170], a pharmacophore patent, of the catalytic domain of the enzyme, which requires the crystallization of the protein and the use of structural biology to determine the 3D structure, which has great relevance to a more rational drug design approach" (von Itzsetin, 29 September 2003 – personal interview). In the collaboration, the staff at Progen perform the purification and isolation of large quantities of the enzyme, which is provided to the crystallographer at IG to solve the enzyme structure (Vance, 29 September 2003 – personal interview).

The details of the preceding discussion, namely the scientific realms specific to the collaboration, the expertise of the collaborative partners, the overlap in knowledge bases, the division of labour, and the specific scientific disciplines relevant to this work, are represented in Diagram 8.1. The scientific realm is characterized by sugar chemistry and rational drug design. The different types of expertise of the collaborative partners are found in the peripheral boxes that are specified according to scientific disciplines. The overlap in knowledge bases can be seen where both members of the collaboration are listed in one scientific discipline box. The work required to fulfill the desired outcome is shown in the circles at the bottom of the diagram. The connection between this work and the contributing sciences is signified by the arrows between the multi-disciplinary boxes and the ovals that represent the work to be performed by members from each side of the alliance.

[170] A pharmacophore is a list derived by computational chemistry of the features necessary in a molecule to ensure that the molecule binds appropriately with an enzyme (Faragalla, 9 January 2004 – personal interview). (Faragalla is a respondent from another case.)

Diagram 8.1 Contributing Sciences and the Division of Labour



8.1.2 Knowledge Re-use and Knowledge Restriction

The expertise that exists within each institution has the potential for re-use. The crystallizing of the enzyme and development of a compound to target the enzyme, which, as von Itzstein noted, would be a glycopharmaceutical, is to be performed by the staff at the Institute for Glycomics, following a rational drug design approach. This approach utilizes the expertise of the IG scientists in the characterization of the target protein, heparanase, and the

design of a carbohydrate-based therapeutic to interfere in the biological process of the diseases (cancer or inflammatory diseases) (Griffith University, 2003). This knowledge can be reused across several different projects. As von Itzstein pointed out, there is the possibility for the sharing of IP across projects.

> The background knowledge with respect to the chemistry domain is applied to other projects. The potential to reuse the technology itself is also possible. There is some scope for overlap in knowledge between projects. If a breakthrough is made in one project that may have little relationship if any [to another project], it may [come to] have relevance in another project, such as using a particular synthetic method to generate a particular functional entity. And, that's the beauty of having the appropriate critical mass in the Institution: you can leverage and transfer technology into other programs (29 September 2003 – personal interview).

Progen's in-house knowledge relevant to the collaboration relates to the specific know-how associated with handling heparanase. This know-how is used to fulfill the firm's roles of purifying and isolating the enzyme, and testing the compounds produced at IG in enzyme assays. Vance said that,

> [w]e know how to purify heparanase. Someone could work out how to do that, but they would have to go through lots of experiments. We know how to acquire it from a particular source and purify it in such a way that it is useful for the study. We know a few tricks and things that aren't written in publications. But in order to tackle the study, each person must have a grasp of the broader subject (29 September 2003 – personal interview).

As with IG, there is also a reuse of knowledge within the organizational borders of Progen. When molecules are discovered that don't effectively meet the standards for becoming a drug candidate, rather than simply getting rid of them, the scientists at Progen use them in research probing how molecules interact (Don, 8 December 2003 – personal interview).

The work performed within the borders of each organization, although it may overlap and be complementary to the collaborative partner's work, is, in certain instances, not made available to all members of the collaboration. As mentioned in chapter five, difficulties may arise where both parties of a collaboration are working in similar scientific areas not specific to the collaborative agenda. Sharing knowledge in the area of similarity may lead to instances where one party can unrightfully claim the discoveries of another. A policy of secrecy can be used to avoid such conflicts. As Don (8 December 2003 – personal interview) stated,

> [w]e have other projects where we're making related types of molecules with

> fairly unique chemistry, and we've agreed, as has Mark, that we won't tell him about the chemistry that we're using. We can test those molecules without telling him what they are. If we tell him the chemistry, then he's in the awkward position that, if he comes up independently with a similar sort of chemistry, we can always claim that it was our idea, even if it wasn't. We agreed to the boundaries beforehand and if we have something new or Mark has something new that doesn't relate to project, then we simply will not discuss it…Mark looks at other kinds of sugars that we aren't privy to and we look at ones that he isn't privy to.

The academic, trade, and patent literature, however, is a means by which members of the collaboration can assess what other groups are doing, but only in terms of what is in the public domain. Moreover, the literature allows for, in conjunction with the practical experience of the collaborative participants, a conceptualization of the subject matter pertaining to the alliance agenda. Von Itzstein stated that, "when you start any science project, you pick up the literature about any known chemicals that inhibit the enzyme, as well as retrieval of any ongoing or recent information that comes out" (29 September 2003 – personal interview). Similarly, Don suggested that it would be foolish "not to take into account what has been done in science leading up to where we are now. We have automatic searches, where everyone reads and subscribes to journals in the area, and we stay up-to-date with what is happening with other research groups" (8 December 2003 – personal interview).

In addition, as Vance pointed out, a lot of the knowledge about heparanase is already public knowledge (29 September 2003 – personal interview). Being in the public domain, heparanase is also a target in other scientific endeavours. Other collaborations, other firms, and other academic groups are working on heparanse as a target in drug development.

As a result, the literature plays a vital role in the alliance between the Institute for Glycomics and Progen as a source of information on other research groups' achievements in relation to the enzyme. There are particular research groups working in the same area as the members of the IG-Progen alliance and "we feed off each other, so that a central part of research is not working in isolation" (Don, 8 December 2003 – personal interview). Vance (29 September 2003 – personal interview) provided a much more competitive point of view in relation to the other research groups working in the same scientific area of the alliance,

suggesting that the alliance is under competitive pressures and is essentially in a race to achieve its desired output.

Within the collaboration, there is a literary source that keeps both sides of the alliance up-to-date on the progress toward the desired outcome. The staff from the Institute for Glycomics and Progen meet quarterly to discuss performance. At the time of these meetings, von Itzstein produces a quarterly report and the contents are re-hashed at the meetings between the collaborative members. The meetings are where the Progen scientists ask questions about the report and discuss the strategy of the alliance with the IG scientists. The scientists at Progen provide intellectual input into the project and guide the direction of it as well (Vance, 29 September 2003 – personal interview). "The information in this project is exchanged formally in the quarterly report, where IG breaks down what they've achieved in the previous quarter and how that tracks against the milestones" (Don, 8 December 2003 – personal interview).

8.1.3 Coordination and Control Mechanisms

Along with the rational drug design approach used to guide and define the work done in the alliance, specific milestones were agreed upon at the commencement of the collaboration. While von Itzstein detailed his role as principal investigator of the project, and his associated duties of overseeing the program of research and its direction, he also conceded that there are milestones that the industry partner desires. "There are milestones built into the contract", stated Don (8 December 2003 – personal interview),

> that Mark is expected to reach and perform to. They are reviewed formally on a quarterly basis and more regularly on an informal basis, where we meet with the scientists to discuss what is happening. The milestones are flexible, we can change them if we need to, but both parties have to agree. The expectations and time frame for those expectations are well defined (Don, 8 December 2003 – personal interview).

The rational drug design approach employed in the collaboration fits in with the milestones. "Progen expects certain numbers of first and second generations of drugs to be synthesized and analyzed in certain periods of time" (Don, 8 December 2003 – personal interview). Don also suggested that the milestones are gaugeable. The scientists at Progen are responsible for the testing of the compounds produced at IG, "…so we can quite clearly gauge what they're saying

they're doing. So, we know that they're making what they're making and we can feedback how effective those potential drugs are" (Don, 8 December 2003 – personal interview).

The ability to gauge the progress in terms of the milestones has increased with the addition of a drug development group to Progen's line-up. The level of in-depth evaluation has changed since Progen put together its own drug design group. Vance (29 September 2003 – personal interview) communicated that he's become more informed in finding out what's involved in the specific science and technology drug design areas where Progen has only recently acquired expertise. Now that Progen has acquired people with expertise in rational drug design in-house, the sections of the quarterly report prepared by von Itzstein are passed on to those people to evaluate. Progen's drug development scientists then analyze the report, asking questions and making judgments about the work performed at IG. This input allows the staff at Progen to ask more in-depth questions relating to the science being performed at IG.

With this in mind, however, von Itzstein's group, as all interviewees agreed, has been given a considerable amount of leeway in how the science is conducted. During his interview, von Itzstein emphasized that he is in control of the project from a scientific point of view. He oversees the program of research and its direction. Don (8 December 2003 – personal interview) stated that von Itzstein is given "free rein in terms of the approaches he takes. We do review and suggest directions if we are not pleased with the way it is going though". It is a matter of allowing IG the freedom to do what they are contracted to do. There is a certain amount of trust involved in granting this freedom. One has to be seen as understanding and not too critical (Vance, 29 September 2003 – personal interview).

The trust bestowed in the IG scientists by the staff at Progen is a result of von Itzstein's track record. Indeed, both sides of the alliance have experience in drug development. Progen has taken PI-88, the compound discovered at the Australian National University, through Phase I and Phase II trials. Von Itzstein is credited with the discovery and development of Relenza, an anti-influenza drug. This achievement has made IG "the only research group in Australia to bring a carbohydrate based designer drug to market. Its discovery earned Institute director, Professor Mark von Itzstein, the Australian Prize in 1996" (Griffith University, 2003). During

his interview, von Itzstein commented that one of the impetuses behind the formation of the alliance was that the staff at Progen recognized the expertise within the Institute for Glycomics. Corroborating von Itzstein's statement, Vance said that von Itzstein's group sells itself as a drug design group, and that when von Itzstein established the Institute, he "brought with him a reputation in structure-based drug design based on his previous work…" (29 September 2003 – personal interview). "Mark has a high-profile in the Australian research community and has been involved with other biotech companies" (Don, 8 December 2003 – personal interview).

The two entities' expertise in drug development became apparent during the interviews. When questioned as to whether or not von Itzstein considers things like the toxicity of the molecule at the early stages of discovery, he commented that, "[t]here are some general rules that guide the development of compounds, like the thoughts about the types of molecules one would want in a drug…We are conscious about those things that are particularly nasty, but until you go through a full tox-screen, you won't know the outcome" (29 September 2003 – personal interview). One of the reasons von Itzstein's group was chosen for the collaboration was because he has an appreciation of the rules relating to toxic molecules and compounds. "Mark has been involved in taking a drug through to market and is aware of these things" (Don, 8 December 2003 – personal interview).

Despite the agreed upon milestones and the reputation for success of both organizations in the alliance, at the time of interviewing, the alliance had yet to attain its aim of a drug lead to target heparanase. Von Itzstein mentioned that there have been no patents or journal articles based on the collaboration (29 September 2003 – personal interview). The alliance has succeeded in developing a database of compounds specific to the collaboration, "but it is small because the output in terms of compounds has been small" (Vance, 29 September 2003 – personal interview).

The sentiments of the respondents from Progen were that the project would have been more controllable if it had been conducted in-house. These reflections were *not* based on the failure of the scientists from either side of the alliance to perform their tasks; the uncertainties associated with the type of science being performed in this collaboration were acknowledged in

the interviews with scientists from both IG and Progen. The instances where the project went in directions that were less than fruitful and the amount of time spent in these directions, however, could have been better controlled in-house, according to the respondents from Progen. "There have been occasions where we've pursued areas longer than would have been necessary or than we would have done in-house…But, given the resources, it probably would have been better in-house…I think it is all just the ability to turn the research around quickly, if we knew we were going in the wrong direction" (Don, 8 December 2003 – personal interview). Vance (29 September 2003 – personal interview) suggested that ideally, Progen would have liked to take this project on in-house. At the time of initiating the project, however, the Progen scientists did not have the requisite knowledge to do so, and thus made the decision to outsource part of the project.

Despite these sentiments, the collaborative scientists have determined that there is a large amount of potential value to be reaped from continuing the collaboration. The contract between the two parties has recently been re-negotiated and extended. The deployment of resources from each side of the alliance has been re-examined. Both parties are of the impression that it takes considerable time to get these types of endeavours up to speed. Vance (19 January 2003 – personal communication) commented that von Itzstein, with his considerable experience in collaborative relationships, suggested up front that, in most instances, results are not seen until the latter stages of the contractual life cycle.

According to the respondents, the achievement of results generally takes a considerable amount of time for two reasons. First, the cultural differences between university and industry have to be acknowledged and ways of dealing with these differences have to be intermittently built into the collaborative relationship. Second, the uncertainties of science cannot be predicted in advance.

For example, Vance's point of view was that, in industry, decisions are strictly based on cost, whereas in academia, decisions about the direction and time spent on a project can sometimes be influenced by the appeal of the project and how intrigued scientists are by the work involved in a given project (29 September, 2003 – personal interview). In industry,

however, one has to be accountable to shareholders and justify the costs to the investors in an organization. The staff at Progen has to maintain some control of the project because of the amount of money Progen has invested. "We can't let it be a research grant that we don't manage or control effectively" (Don, 8 December 2003 – personal interview).

Beyond the costs of the project, however, one has to also consider that this type of work is based on highly experimental science with unknown outcomes, and as discussed in chapter two, there is a tremendous amount of uncertainty associated with these types of endeavours. Indeed, von Itzstein (29 September 2003 – personal interview) suggested that one of the uncertainties associated with the project is the same uncertainty that one would find with any drug discovery program, "the unknown quantities". This entails asking the question, "will the small molecules be sufficient to afford the biological outcomes that we all want?" (von Itzstein, 29 September 2003 – personal interview). Vance echoed von Itzstein's discussion of uncertainty. "I can certainly appreciate that when you do an experiment, there is no guarantee it is going to work, because there could be an inherent problem of the particular science you're trying to do" (29 September 2003 – personal interview).

In addition, the uncertainty also stems from the fact that the desired outcome is novel. The pathway for arriving at the desired outcome is unchartered. The scientists of this collaboration have been successful in developing other drugs, in arriving at the desired outcome associated with other targets, but not in the case of heparanase. Although PI-88, the compound discovered at the Australian National University, acts against heparanase, it was discovered via a random screening process. It was not created through rational drug design, as is intended in the IG-Progen alliance. It was a first generation drug. "The drug to be produced by Mark [von Itzstein] is to be a second generation drug" (Vance, 29 September 2003 – personal interview). The uncertainty resulting from using a different process, namely the rational drug design process, to develop a compound to target heparanase was made clear in the interview with Vance (29 September 2003). He suggested that things are never just black and white in these types of endeavours. While the alliance is aiming for drug leads, satisfaction can come from arriving at the structure of the enzyme, crystallizing it, or being able to conclude that with the

current provisions of science, the goal is not attainable. The goal may be specified up front, but the contract remains open-ended.

8.1.4 Connectivity

The inability to reach the desired outcome by the end of the first contract period, which is compounded by the differences in culture between IG and Progen, or more generally between academic groups and industry firms, and the uncertainty associated with the type of design for purpose affairs found in this alliance, has spawned a need for tact in the interactions between the collaborative participants. Vance highlighted the problem of finding a way to remain on good terms with any partner when there is the need to be critical (29 September 2003 – personal interview). He noted that it is important not to apportion blame to any side of the alliance, but instead to focus on the difficulties of the science and try to mutually find ways to overcome them. Tact is essential in such efforts.

Tact becomes particularly important when considering the size of Progen, the number of collaborations it has with other institutions, both academic and industrial, and the notion that the interactions from this alliance will inevitably effect the reputation of the parties involved. Don stated that, "Progen doesn't have that many projects. Rather than walking away from projects that are not working, it is more in our benefit to work out why it's not working and bring it back on line, as long as we agree the potential is there" (8 December 2003 – personal interview).

The scientific problems to be solved in the collaboration (that were defined at the time of initiating the alliance) took the form of clearly defined goals that were supported by predetermined milestones. The alliance was based on solid ground, both in terms of these goals and the concept of developing a drug lead to target heparanase, at least in the view of the collaborative participants. The soundness of the concept is validated, though, by the notion that there are other groups working on this target and that there is a literature base, which is consulted by the members of the alliance, relating to the research agenda.

As with any other collaboration between university and industry in biotechnology, however, there are inherent uncertainties that come into play. These uncertainties include the capability of the members of the alliance to align their different social worlds, the ability of the scientists to perform the required tasks specific to the collaborative agenda, and the unknowns associated with the novelty of the desired outcome. These uncertainties have played a role in the Institute for Glycomics-Progen alliance, evidenced by the fact that the desired output has not yet been achieved.

Questions remain as to whether or not the desired output was attainable, or is the failure to achieve the set aims really a failure to appropriately manage the inherent uncertainties? Clearly, a policy of tact has been implemented in this case as a response to the situation created by the effect of the uncertainties. All tact can do, though, is tidy-up the frail ends of an alliance. This is probably necessary though, considering that both parties wish to have future engagements with the constituents of their knowledge value collective, and more importantly, with each other. Recall that recently, the contract has been amended, resources have been re-negotiated, and the length of the collaboration has been extended.

With the agreement to continue collaboration comes the need to evaluate the effectiveness of the tools, technologies, and work practices used in the alliance. An analysis of these aspects includes looking at the design rules, interfaces, repositories, and starting points used in the collaboration between the Institute for Glycomics and Progen. Additionally, the ingrained knowledge of the collaborative participants is also a pertinent analytical construct, and one that undoubtedly featured prominently in the alliance. These concepts are addressed in the following section.

8.2 Case Analysis

The luck inherent in the game of Biotechnology Bingo is exemplified in the knowledge value alliance between the Institute for Glycomics and Progen. Despite a well-scouted choice in alliance partner and the institutionalization of specific design rules, namely rational drug design

and the milestones specific to the collaborative agenda, this project has not yet produced the desired outcome. There are many things that could be at the root of this, including insufficient task articulation, the disability inflicted by not creating a "doable problem" (to use the terminology of Fujimura, 1987), and the misadventures that are always a possibility when tackling novel scientific problems.

Thus, it becomes paramount to assess the knowledge architecture of the alliance in terms of three key areas: 1) the application of the design rules, interfaces, repositories, and starting points; 2) the ingrained knowledge of the participants; and, 3) the cultural ecology of the knowledge value alliance. I have argued in this thesis that the selection of the appropriate tools, technologies, and work practices is a crucial element in playing the game of Biotechnology Bingo. I have also suggested that it is the ingrained knowledge of the collaborative participants that makes the resolution of scientific problems possible. In addition, because these types of collaborations are not extreme cases of modularity, there is a certain amount of interdependency that exists within an alliance. This interdependency can be characterized in terms of the use of tact to supplement the interfaces that exist within the architecture, and the notion that both parties to the alliance are committed to other projects and collaborations, which may reduce their ability to be fully committed to the IG-Progen agenda.

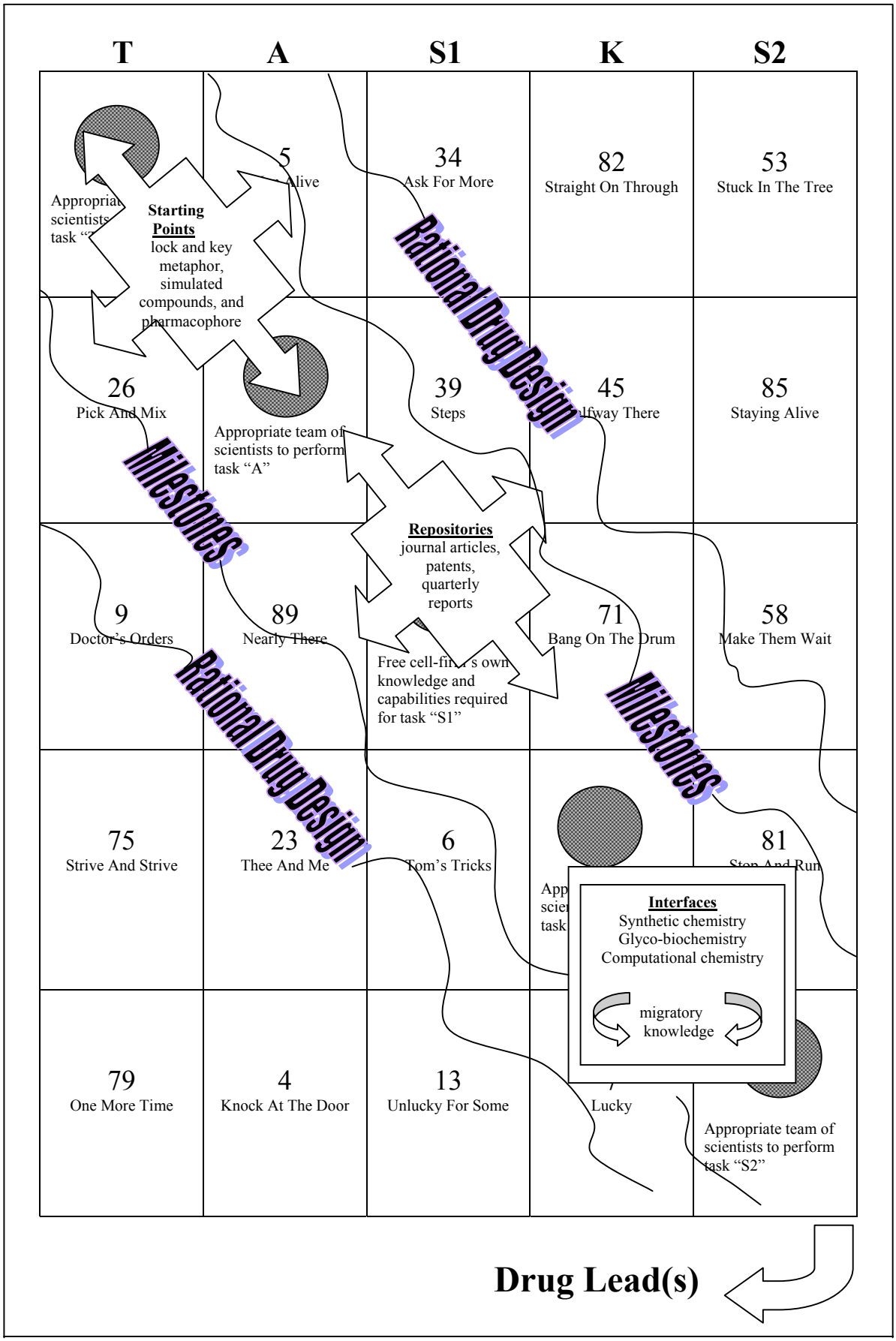
8.2.1 Application of Design Rules

Analyzing the architecture in terms of the design rules, starting points, interfaces, and repositories results in the realization that most of these elements appear in the knowledge architecture. While these elements are discussed in detail in the following sections, a brief introduction to them is provided here. The scientific realm of the knowledge value alliance was characterized by Don (8 December 2003 – personal interview) as consisting of sugar chemistry and rational drug design. It can be argued, however, that rational drug design is a design rule, which provides the necessary meshing of the tasks, clusters of tasks, and segments of the knowledge architecture. Rational drug design is supported by the milestones that guide the collaborative agenda. Hence, there are two design rules used in this alliance – rational drug

design and the milestones. There are three specific starting points inherent in this collaboration, including the lock and key metaphor, the compounds produced via computer modeling, and the pharmacophore. The other elements, including interfaces and repositories appear in the architecture as well.

Each of these tools for articulation is represented in Diagram 8.2. The tasks of the architecture are: task “T” is the isolation and purification of heparanase, task “A” is the crystallization of the enzyme and the determination of its structure, task “S1” is the design of candidate compounds, task “K” is the testing of the compounds, and task “S2” is the synthesis of the compounds. Tasks “S1”, “K”, and “S2” are repetitive tasks.

Diagram 8.2 The IG-Progen Knowledge Architecture



Each of the features of Diagram 8.2 – the design rules, starting points, repositories, and interfaces – has a role to fulfill in creating alignment within the architecture and in moving forward in the direction of the desired output of the knowledge value alliance. The design rules force the tasks into alignment, articulating tasks across the entire architecture. The role of starting points is to provide the scientists with an initial lead into their task work. The repositories from beyond the boundaries of the architecture aid in the collaborative participants' resolution of the larger problem to be solved by the members of the knowledge value alliance. The repositories within the knowledge architecture, the quarterly reports, track the progress on the resolution of this problem in terms of the design rules. The interfaces allow collaborative participants to gain an understanding of how specific tasks fit into the larger framework of the research agenda. The functions of each of these features are addressed in the following discussion.

Rational drug design is not a science, but a technology that is comprised of an array of scientific practices used to accumulate information to facilitate the understanding of the functionality of a protein, enzyme, or nucleic acid, and the development of drugs to have a desired effect on that functionality. Several sources suggest that increased amounts of information relating to a target enzyme allows for a more precise design of the therapeutic. Don (8 December 2003 – personal interview) stated that, "[r]ational drug design is based on computer simulation, so the more data you have to feed into that simulation, the better". Mukherjee and Miele (1995) suggest that, when detailed information is available on a protein or enzyme from x-ray diffraction or x-ray crystallography, the design of peptides is greatly facilitated. Similarly, in his interview, Vance discussed the functions of drugs in relation to an enzyme and the importance of knowing as much information as possible about the target enzyme.

> Drugs interact with things such as enzymes in the body to turn them off, turn them on, or to give an effect against the disease. You need information about the enzyme to use in developing the drug…The process by which [a] second generation drug is to be produced is called rational drug design because you take the information about the target and use that to create a drug that fits the target. It is like a lock and key. You use the information about the lock to design the key, as opposed to giving out keys and seeing if they fit (29 September 2003 – personal interview).

Rational drug design is the technology that dictates the collection of information on the target and the design of the compounds to deliberately have the desired effect on the target. "If you have a 3D structure of the molecule that you're targeting with a drug, you're trying to get the drug to interact with, it helps to design the drug by modeling the 3D model of the drug with the 3D model of the protein and seeing how they interact" (Don, 8 December 2003 – personal interview). While rational drug design may be the realm that defines the collaborative agenda, it is strictly a technology that provides a strategy on how to develop drugs, rather than a science. This strategy entails certain steps that include determining the structure of the target; designing, testing, and synthesizing compounds (which is a repetitive process); and modeling these compounds with the target to get a clear idea of how they work[171]. Drugs produced prior to the modeling of the compound are first generation drugs, whereas the drugs produced with the knowledge of the structure of the target are second generation drugs, and the synthesis of the second generation compounds would result in third generation compounds, and the process continues (Vance, 29 September 2003 – personal interview; Don, 8 December 2003 – personal interview).

The milestones specific to this knowledge value alliance, as they were conveyed by Don in his interview (8 December 2003 – personal interview), support the process of rational drug design. The steps of the rational drug design process correlate with the milestones set forth for the collaborative agenda. "Progen expects certain numbers of first and second generations of drugs to be synthesized and analyzed in certain periods of time" (Don, 8 December 2003 – personal interview) and the rational drug design approach lays out the steps of producing first and second generations of drugs. These two elements are design rules in their own right, as depicted in Diagram 8.2. They integrate and set boundaries for the work performed by the two groups of scientists in the alliance. The staff at Progen provide the enzyme to the scientists at

[171] Recall that rational drug design was also the technique employed in the knowledge value alliance between the Institute for Biomolecular Science and AMRAD. In that case, it was shown that rational drug design created alignment across two of the projects in the alliance for the specific reason that each project was dedicated to a specific step of the rational drug design process. The specific steps of the process, as detailed by McPherson (1995), were disclosed in chapter seven, and these are the same steps that constitute the rational drug design process employed in the IG-Progen alliance.

the Institute for Glycomics, who then attempt a crystallization of the enzyme and develop compounds to target the enzyme, which are tested at Progen. The cycle of synthesis and testing continues to ultimately arrive at potential drug leads. All along, these tasks follow the rational drug design approach and are guided by the prescribed milestones.

8.2.1.1 Starting Points

The lock and key metaphor associated with rational drug design can be thought of as a starting point for the scientists in the knowledge architecture. This metaphor is general in its applicability, but still provides a lead for the work to be performed at the task level. When assessing the goals of the alliance and the use of the rational drug design approach, the tasks required to be performed for the attainment of those goals becomes apparent in the view of having the lock, heparanase, and having to develop the key, the candidate compounds. Through this starting point, the tasks can be split, defined, and delegated to the scientists most capable of performing each task. According to McPherson (1995), the lock and key metaphor suggests that, "there must be instances where the inviolable specificity of enzyme substrate interaction breaks down and other molecules that closely resemble the natural substrate or effector molecules bind in their place" (p163). The fit between the lock and the key is the interaction or binding spoken of in McPherson's statement, and this fit can be used to guide the direction of the tasks. The work inherent in each task must aim for the best fit between the lock and the key.

To discuss the binding of the enzyme and the compound, one would need to carry out the simulation and modeling processes used in rational drug design to provide a 3D portrait of the binding and interaction. Advanced knowledge in simulation and modeling, or computational chemistry and structural glycobiology to put the practice in scientific terms, allows one to use the technology to predict compounds that should be made in order to have the desired effect on the target enzyme. As Don noted,

> [y]ou simulate the structure on a computer and then you relate that back to the activity you see in the laboratory. What you're trying to do is make changes in computer modeling that will predict what you see in the laboratory, hence the structure versus activity. Changing it in the laboratory and going back and changing it in the computer predicts it correctly, but as you get more and more confidence in the computer and the

> particular system you are working in, you get to a point, theoretically, where the computer will tell you what sort of molecule you should be making. So, it can define a structure that will give you the function you want (8 December 2003 – personal interview).

Each change in the compound is a next generation drug candidate. The molecules simulated and predicted by the computer program are a starting point for future generations of drugs, or the actual, physical compounds yet to be produced.

Following this line of thought, earlier generation drugs *should* be a starting point for future generations of drugs in that they provide the baseline from which progress needs to ensue. PI-88, the compound discovered by the scientists at the Australian National University in their collaboration with Progen, could then be considered a starting point for the work being performed by IG. Yet, as Vance commented, "[t]he information on PI-88 isn't really relevant to Mark's [von Itzstein] work (29 September 2003 – personal interview). The irrelevancy of PI-88 to the agenda being pursued in the IG-Progen alliance can be approached in two ways: first, by considering that PI-88, although it is the object of most of the development work occurring at Progen, is not an ideal drug; and second, PI-88 was discovered through a random screening process and IG is attempting to develop a drug through rational drug design.

Although PI-88 is Progen's bread and butter, so to speak, and it does possess a variety of desirable qualities[172], it was developed as an inhibitor of heparanase in its role in cancer. The alliance between IG and Progen is aimed at developing an inhibitor of heparanase in its role in inflammatory diseases, namely multiple sclerosis and inflammatory bowel disease. The explanation of PI-88 provided by Don serves to indicate why PI-88 may, in fact, not be a relevant starting point for the work being performed in the IG-Progen alliance.

> …PI-88 is a complex sugar. It is not an ideal drug in its structure, but this is not an issue for us because we are using it in cancer, which is a disease where you have a population of people who are willing to take variations of drugs that are not ideal. And, by that I mean PI-88 has to be administered by injection and it is just like insulin. The patients

[172] Progen has an extensive patent position on PI-88. The compound demonstrates the following desirable qualities: it is inexpensive and straightforward to manufacture; it has a well understood and novel mode of action; it is a qualified glycopharmaceutical capable of inhibiting heparanase; it demonstrated efficacy in preclinical trials; it has improved performance when used in combination with cytotoxic drugs and other angiogenesis inhibitors; it has made it through Phase I and II clinical evaluations; and, it has 100% bio-availability via subcutaneous administration (Progen Industries, 2002).

> inject themselves once a day. Now, if you were looking at a headache drug, it would be unlikely that someone would go down to the chemist and buy a needle to give [herself] a shot for a headache. But, people with cancer, where the drug offers them considerable potential and the only discomfort they're going to have is being like a diabetic, basically it is a choice of facing a disease that is fatal or taking a small discomfort to take a quality of life and keeping them alive longer (8 December 2003 – personal interview).

Someone with inflammatory bowel disease would probably also be unwilling to inject the drug, making PI-88 an irrelevant starting point for drugs developed to inhibit heparanase in this disease. An individual afflicted with multiple sclerosis, however, may be more likely to inject a drug, and thus PI-88 cannot be entirely disqualified as a starting point in the alliance between the Institute for Glycomics and Progen. PI-88, however, is not currently serving this role. The scientists at IG are following a totally different approach to drug design.

The approach IG is following in the aim to develop a drug as an inhibitor of heparanase is, of course, rational drug design. Under this strategy, the simulated compounds and the pharmacophore developed in the alliance would certainly be starting points for the tasks to be performed at the Institute for Glycomics. The simulated compounds provided by computational chemistry would provide a synthetic chemist not only with a starting point, but also a direction in his or her task of synthesizing. Based upon the simulated compound, the scientists would be able to decipher which areas of the molecule, or candidate compound, need manipulation and what the aims of that manipulation would be. Similarly, the pharmacophore, or the list of features necessary in a given molecule to effectively target the enzyme, would also be a valid starting point for the synthetic chemist.

PI-88, however, does not offer this same degree of definition or direction for the synthetic chemist, and therefore, it cannot be qualified as a valid starting point. During his interview, Vance (29 September 2003) suggested that the scientists at IG need to be given the freedom to do what they are contracted to do, which is to develop a novel drug lead via the application of rational drug design. Perhaps it is the case that using PI-88 as a starting point would impinge upon this freedom. Rational drug design, with its inherent steps of determining the structure and function of a target and then developing a compound to appropriately impact on that function, is

a much different process than developing a compound and randomly screening it against a target, although the two processes can be complementary.

What is important to note here, though, is that it is nearly impossible to foresee what information will be needed in drug design or how specific types of information will impact on the process. The argument can be made that the consequence of limiting information may be the loss of the game. Limiting information or restricting a player from specific information can be likened to taking a number out of the box of numbers to be called in the game of Bingo. If the information on PI-88 is represented by a number on the Biotechnology Bingo card, say S1-28, and it turns out that S1-28 is needed to win the game, taking S1-28 out of the box of possible numbers that can be called will preclude the player who needs S1-28 from winning. It will restrict a player from reaching the desired output of the alliance. Looking at the issue in this manner suggests that the firm acts in the role of the caller in the game of Biotechnology Bingo.

Progen does claim, however, to have shared all information relevant to the project with IG, though. Where the Progen scientists have seen the potential for information on PI-88 to be of use to the IG scientists, they have divulged that information. The only information that has been deliberately withheld is market sensitive information, such as the results of clinical trials. Furthermore, the Progen scientists have actually made a considerable effort to share additional relevant information with the IG scientists. For example, the scientists from Progen have provided the IG scientists with the results of an extensive literature search performed in-house (at Progen) on the known inhibitors of heparanase. This literature search was more extensive than ones done at IG and the staff members at Progen were happy to provide this information to IG because it potentially played a role in furthering the research agenda (Vance, 19 January 2004 – personal communication). With this type of exchange, Progen is still playing the role of the caller in the game of Biotechnology Bingo, but is creating more favorable odds for the alliance than would be the case if information were deliberately concealed.

8.2.1.2 Interfaces and Repositories

Evaluation of the starting points and their use within the knowledge architecture is only one part of the picture. Certainly, there are other features of the knowledge architecture deserving of attention, and the analysis of the mechanisms for articulation and alignment in this alliance would not be complete without discussing them. These features include the interfaces and repositories utilized in this knowledge architecture that have helped create a path toward arriving at the desired outcome of drug leads.

The interfaces created by the knowledge overlap between IG and Progen in the areas of synthetic chemistry, glyco-biochemistry, and computational chemistry are a common ground between IG and Progen that allows for not only the exchange of information, but also the critical evaluation of the work performed by various task members. Glyco-biochemistry frames the entire research agenda, in that an understanding of heparanase requires a more general understanding of the role of sugars in mammalian diseases, and glyco-biochemistry makes this possible. Moreover, an understanding of rational drug design, while it is more of a design rule than an interface, is also required to conceptualize the research agenda. This understanding is made possible by experience in and application of the sciences that constitute rational drug design, namely synthetic chemistry, computational chemistry, and x-ray crystallography.

The evaluation of task work in the architecture becomes possible with this understanding. Indeed, as Vance (29 September 2003 – personal interview) pointed out, Progen has always been able to critically evaluate the synthetic chemistry being performed in the collaboration, but it has only been with Progen's acquisition of a computational chemist that more in-depth analysis of the work being performed by the scientists at IG has been possible. This insight has allowed a conceptualization of what is actually involved in performing the tasks (Vance, 29 September 2003 – personal interview). The critical evaluation and exchange of ideas and information made possible by the interfaces facilitate the production process through the input of more than one scientist and by providing a general framework for the research agenda.

It should be noted that if a scientist is working in isolation, practising only the science necessary to perform a designated task, and this scientist has little knowledge-of the overall framework and how the task contributes to that framework, it would be difficult for that scientist to see how the project should be moving forward and what he or she needs to do to make that happen. The scientists need not have knowledge-about how to perform all the tasks in the alliance, but they need to have knowledge-of the other task domains in the alliance[173]. One marker on the Biotechnology Bingo card will obviously not win the game. It must be the "right" marker that fits in line with the rest of the markers. Interfaces, then, allow for the connection and communication that is necessary to see how one task fits in line with the others.

Repositories are another mechanism that serves this purpose. The quarterly reports (as repositories which exist within the alliance) detail the work that is performed by each module and how this work fares in relation to the milestones. An evaluation of this work is only possible with an understanding of the science used in the work. Furthermore, an evaluation of how the work tracks against the milestones is only possible via an appreciation of the overarching science. This understanding of the overarching science is also crucial in assessing whether or not the milestones are even viable, let alone if they have been achieved. This assessment comes from a particular scientist's understanding of and experience with the science that frames the research (i.e., the scientist's ingrained knowledge relating to the overarching science) and the internal repositories that provide a directional account of the work performed in different task domains.

The repositories that exist beyond the architecture of the alliance can also be used effectively to pursue the target within the alliance. With the requisite ingrained knowledge, a scientist can piece together various findings in the literature to further the research agenda. Members of the IG-Progen alliance have used the external literature in this manner. The scientists from Progen performed an extensive literature search on all known inhibitors of

[173] Following Machlup (1980), I defined knowledge-of as the knowledge resulting from access to scientific results that is represented by a limited understanding and knowledge-about as a detailed understanding of a particular task or piece of knowledge that allows for the practice and explanation of a particular task.

heparanase. This information was then turned over to the staff at IG who used it in developing a pharmacophore of the heparanase inhibitors, or a list of the features required in a compound to target the enzyme. Building a pharmacophore is, however, what one does in absence of a three-dimensional structure of the enzyme. As such, progress was made toward arriving at drug leads, but not in the manner originally stipulated by the contractual agreement.

8.2.1.3 Ingrained Knowledge

What should be noted here, as has been echoed in the other cases presented in this thesis, is that the ingrained knowledge of any member of a collaborative relationship is essential not only to understanding the research agenda and seeing how tasks fit into that agenda, but also to actually performing the tasks. The collaborative partners were chosen on the basis of their speculated ingrained knowledge. From the description of the case, it becomes apparent that the Institute for Glycomics was chosen by Progen as a collaborative partner because the administrators at Progen making this decision believed that the IG scientists had the necessary ingrained knowledge to perform the tasks required to solve the research problem. Their judgment was based on the reputation of the scientists at IG and their experience in taking Relenza from discovery and development, through to the market. Similarly, Progen was deemed to be a suitable and desirable collaborative partner because of the Progen scientists' work in developing PI-88 and taking that compound through both Phase I and II of clinical evaluation. Progen holds an exclusive worldwide licence on ANU's patent for purifying heparanase. Therefore, the staff at IG had reason to believe that Progen could fulfill this role in the IG-Progen alliance.

While reputation and prior experience may usually provide valid measures of ability to perform, it is inherently difficult to assess scientists' ingrained knowledge and their ability to use this knowledge to solve novel problems. Indeed, as Holyoak (1991) contends, there are routine experts and adaptive experts. Routine experts are able to solve familiar problems efficiently and correctly, but only have a modest ability to deal with novel problems; whereas,

adaptive experts may be able to invent new procedures derived from their expert knowledge to solve novel problems (p310).

Assessing whether or not the scientists involved in the collaboration are routine or adaptive experts (or, it may even be the case that some are routine experts and others are adaptive, rather than a black and white categorization of all of the collaborative scientists fitting into one framework or the other) is quite a difficult task that involves allowing the experts to attempt the resolution of a novel problem, and then and only then, evaluating the scientists in terms of being routine or adaptive experts. This was the only option for the architects of the alliance, and it points to the luck associated with designing these types of collaborations. One can definitively say with hindsight whether or not someone is qualified to perform a task, but if that judgment must be made without testing the ability to perform a novel task, there is a considerable amount of luck in judging the ability correctly.

The types of technologies and methodologies being applied in this alliance are both routine and novel. Rational drug design is a routine technology for IG. Isolating and purifying heparanse is a well-developed procedure for Progen. The material used in the process of rational drug design and the way that the scientists at Progen must apply their know-how related to the purification of heparanase are novel, though. The scientists from IG obviously gained expertise in applying rational drug design effectively in developing Relenza, evidenced by their success in the matter. Working with heparanase and developing compounds to target this enzyme is, however, a set of tasks that involves using rational drug design (the routine technology) to solve a novel problem.

Similarly, while the scientists at Progen have licensed the technology for purifying heparanase from ANU and developed large-scale purification techniques based on this knowledge, these scientists are using these techniques for the first time in the IG-Progen alliance. The crystallization process requires abundant amounts of the enzyme. Although the scientists at Progen have routine knowledge on how to purification the enzyme, they are applying this knowledge in a novel problem of finding and funding the cost of acquiring

sufficient quantities of platelets from which to extract and purify the enzyme in the amount necessary for the IG-Progen research agenda.

The reputations of IG and Progen that are premised on the successes of Relenza and PI-88, respectively, demonstrate the scientists' abilities to achieve success in isolated cases, but they may not be a general indication of their ability to be repeatedly successful in novel situations. If they had to solve the problems associated with research agendas of Relenza and PI-88 again, they would probably have no problem in doing so. These scientists, however, can only be qualified as adaptive experts if they can use the knowledge gained in the experiences with Relenza and PI-88 to solve the novel problem of crystallizing heparanase and developing an inhibitor for it in inflammatory diseases.

Even in the instance of prior experience and a reputation for success, then, it is difficult to assess a team of scientists' ability to perform a novel task, unless of course the prior experience yielded evidence of adaptive expertise. It should be noted, however, that IG and Progen did not have prior experience in collaborating with one another. All that the architects (Don and von Itzstein) had to rely on was the previous performance of the potential partner in other collaborations, that is, the potential partners' reputations of ability to produce a quality product and to collaborate with other members of the biotechnology community. Reputation is strictly based on past performance and does not always give a clear indication of ability to perform in uncertain circumstances, but it is the only type of indicator that architects of this knowledge value alliance had. In the absence of this indicator, the luck associated with getting the right people to enlist in the alliance becomes an even more formidable obstacle. Furthermore, even if the collaborators have been identified as adaptive experts, this does not eliminate the possibility that luck will be a major factor in implementing the highly experimental science in discovery.

Following Hatano and Inagaki (1986), Holyoak (1991) suggests that,

> …the key to adaptive expertise is the development of deeper conceptual understanding of the target domain. Such understanding…is heavily dependent on the conditions under which learning takes place. Understanding is more likely to result when the task is variable and in some degree unpredictable, rather than stereotyped, and when *the task is explored freely without heavy pressure to achieve an immediate goal* (p310 – emphasis added).

The rational drug design approach used in this collaboration lends itself appropriately to the emergence of adaptive experts, should the scientists have the potential to become such, because it is a tool to develop a "deeper conceptual understanding" of the target domain, namely heparanase. In addition, an avenue for the emergence of adaptive experts is also evident in the tasks inherent to the research problem being variable and unpredictable. Recall the comment that Vance made during his interview (29 September 2003) describing this collaboration as open-ended, with the ultimate outcome being difficult to specify. As a result, trust is a necessary characteristic of the cultural ecology of the knowledge architecture. Indeed, Vance suggested that, "[t]here is a bit of trust involved. If they say they can do it, then we trust them to do it" (29 September 2003 – personal interview)[174]. The fact that there is a "heavy pressure to achieve an immediate goal" (a quotation taken from the argument made in Holyoak, 1991) found within the architecture of the alliance, however, mitigates the effects of the elements conducive to the emergence of adaptive experts.

8.2.2 Alignment of Social Worlds

Revisiting the sentiments of Vance (29 September 2003 – personal interview) and Don (8 December 2003 – personal interview), it becomes apparent that the pace of the project, as it has been in the collaborative environment, might have been much different if the project had been conducted in-house at Progen. Vance contended that, in industry, decisions in regards to the pace and progress of a specific project are made in relation to costs and commercial reality, and that there is a certain amount of urgency in making progress on a project[175]. Don reiterated that there have been instances where the collaboration has lingered in areas longer than Progen felt

[174] Das and Teng (1998) comment on trust as a moderator between control mechanisms and control level. They go on to note that formal control tends to be especially relevant in strategic alliances, due to high degrees of goal incongruence and performance ambiguity. In the IG-Progen alliance, the inability to specify in advance whether or not the desired outcome is achievable and the associated uncertainty of the science being used in the project require the use of trust as a moderator between the milestones (control mechanisms) and the freedom granted to the scientists at IG to pursue the work in the manner they see to be most appropriate (control level).

[175] This is especially true when considering that there are other groups working in the same area that have the potential to solve the problem inherent to the research agenda, and that this may occur prior to the IG-Progen alliance's resolution.

was necessary. If the project had been conducted in-house, it could have been turned around quickly, if there was a belief that it was going in the wrong direction. These thoughts are echoed in the work of Fujimura (1987). "Experiments often fail, and presidents of companies get impatient when a product is not ready by established deadlines. Colleagues may disagree with interpretations of results. In sum, a project – that is, the development of a problem from inception to solution – rarely runs smoothly" (p271).

There are certainly heavy pressures to achieve fairly immediate goals in this alliance, but these pressures are necessary because of the race that the knowledge value alliance finds itself in, in terms of the competition to solve the research problem before other members of the knowledge value collective do. This is a pressure that should be felt by both sides of the collaboration. It is, however, a pressure that puts more weight on the industry partner, because not only do IG and Progen stand to be displaced if the problem is solved by another research group prior to the arrival at a resolution by IG and Progen, but should this occur, or should the scientists involved in the IG-Progen alliance never achieve the collaborative aims, Progen stands to lose the AU$1,000,000[176] plus that it has invested in this endeavour.

The fact that the pressures to resolve the research problem are felt by the two sides of the alliance in unequal proportion creates a barrier to the amalgamation of the social worlds of each entity[177]. This is a barrier that must be overcome, according to Fujimura (1987), if the problem is to be considered doable. An explanation of these different social worlds, or cultures, was provided by Vance (29 September 2003 – personal interview) and presented in the description of the case. There are, however, methods to breach this barrier.

The members of the alliance have instituted a policy of tact to ease the tensions resulting from the misalignment of social worlds. They have used tact as a communicative aid, supplementing the various interfaces, to maintain the link between the two sides of the

[176] This includes the salaries for at least three IG scientists, the cost of equipment use, and the costs of purchasing materials or any additional equipment.

[177] It should be noted here that this is not the only contributing barrier to the alignment of the social worlds of the collaborative participants. Other factors would include the differing scientific backgrounds of the members of the alliance, the current social influences felt by each side of the alliance beyond issues of cost, and the prior experiences, which can quite literally never be eradicated as a barrier to alignment of social worlds.

knowledge value alliance. For example, when results have not been as expected, scientists from both sides of the alliance say that they prefer to focus on what went wrong and how such tribulations can be overcome in the future, rather than apportioning blame. In addition, if those in control of the project from the side of Progen have a problem with a lower level IG scientist, the concerns of the Progen staff are always directed to von Itzstein, the Director of the Institute for Glycomics (Vance 29 September 2003 – personal interview).

Another method that can be applied in such cases is the notion of credible commitments that was introduced in chapter four. Following de Laat (1997), a credible commitment can be a contract or a verbal pledge that signifies a participant's commitment to a collaborative endeavour. Strong commitments to a collaborative arrangement should serve to mitigate the barrier created by differences in social worlds through easing the tension of one party's doubts that may arise in relation to whether or not the desired output will materialize (and soothing the friction that can result when the possibility of not materializing comes to light and there are substantial losses to be encountered). Credible commitments provide reassurance that a party is committed to the completion of the tasks necessary to reach the desired output. In chapter four, I argued that the production of "things" (Latour,1987), or objects, could supplant the contracts or verbal pledges deemed to be credible commitments to the collaborative agenda. The production of such objects, which, in this case could be the compounds produced at IG, signifies that not only is this production possible, but that the party is committed to production for the purposes of attaining the desired output of the collaborative arrangement.

In the collaboration between the Institute for Glycomics and Progen, the use of objects to demonstrate IG's commitment to the collaboration has been insufficient to replace the contract. According to the respondents from Progen, however, von Itzstein warned the Progen team up-front that production takes time and the results would probably not come until the later stage of the collaborative life cycle. In his interview, Von Itzstein stated that, in the process of discovering compounds for a target, "the total number of entities produced would be in the hundreds over a period of time, and that's not final compounds, just the novel chemical entities produced along the pathway of chemical synthesis. The final target is about 50 to 60

compounds" (29 September 2003). The number of compounds tested at Progen over the life of the collaboration as potential candidates has been between six and 12 (Vance, 23 December 2003 – personal conversation).

Development of compounds is a later stage of the discovery and development process in rational drug design[178]. There are highly experimental scientific and technological procedures that come before the development of compounds under the strategy of rational drug design, including crystallizing the enzyme and/or elucidating its three-dimensional structure. A drug lead is dependent upon one of these two initial developments. There are uncertainties associated with both developments. Moreover, there are other reasons why the scientists at IG may have not been able to produce the number of compounds necessary for reaching the desired output, a drug lead.

8.2.3 Uncertainties and Reasons for Lack of Success

The inability of the scientists in the IG-Progen alliance to arrive at the specified desired output can be attributed to a number of things. There are, of course, uncertainties associated with the type of science being conducted in this collaboration. These uncertainties include the difficulty of crystallizing an enzyme. Interference or distractions from other collaborations could have impinged upon the ability of the collaborative participants to reach the desired output. As one would appreciate, both segments of the alliance are also playing other Biotechnology Bingo cards with different collaborators. In addition, the contribution made by Progen in terms of financial support could have been less than was needed to accomplish the desired output.

The alliance is premised on rational drug design, which stipulates the crystallization and three-dimensional structural analysis of the enzyme prior to the development of compounds to target that enzyme. According to Mukherjee and Miele (1995, p240), there are "arduous

[178] In traditional screening methods, the building and synthesis of compounds is one of the initial procedures. In rational drug design, there is more emphasis on trying to gather information about the target, a protein or nucleic acid, so that when compounds are actually developed and synthesized, there is more knowledge on how the compounds should affect the target and what needs to be done to ensure that this functionality is built into the candidate compounds.

technical and conceptual problems" that are typical of the work in this area. The problems stem from both the unavailability of high-quality protein structures for high-resolution diffraction studies (the studies necessary to determine the three-dimensional structure of a protein), and the requirement for a large amount of purified native proteins, which can often be too unstable or too scarce to allow for large-scale purification. They contend that, "although the primary structures of tens of thousands of proteins have been determined, mostly deduced from their cDNA[179] sequences, the three-dimensional structures of only a few hundred have been resolved" (Mukherjee & Miele, 1995, p240).

Vance, in defining the know-how used in this alliance that is possessed by the Progen scientists, claimed that the scientists at Progen are adept at isolating and purifying heparanase in quantities large enough for crystallization. Sources of the enzyme, however, have to be located and purchased in order to apply this know-how. The source of the enzyme is purchased from the Red Cross, but Progen only budgeted a certain amount of money for this purpose. Once these funds were depleted, the amount of enzyme available for the IG scientists to work with in their efforts to crystallize the enzyme dropped. This has obviously been an impediment to the achievement of the desired output.

Even with the sufficient provision of enzymes, there are still considerable difficulties associated with its crystallization and the determination of its three-dimensional structure. As the design and synthesis of compounds is expected to follow the determination of the 3D structure of the enzyme, the production of only a minimal number of compounds could be justified by the difficulties faced in solving the three-dimensional structure of the enzyme. As Faragalla (a respondent from another case) (9 January 2004 – personal interview) put it, in order to get a valid, workable crystal of an enzyme, it has to stack properly. Enzymes aren't like pieces of Lego. They are moveable structures. The crystallization process could change the

[179] The term cDNA refers to complementary DNA, or a "single stranded DNA that is formed from a mRNA (a form of RNA that transfers the coding information for protein synthesis from the nucleus to the ribosome) template by the enzyme reverse transcriptase. Using radioactive nucleiotides, cDNAs can be obtained in a highly radioactive form and used as probes in hybridization assays to determine the number and location of genes in a chromosome, to construct physical maps of different genomes, to study the organization of eukaryotic genes, and to locate coding sequences in a portion of DNA" (Coombs, 1986, p50).

structure of the enzyme significantly. The compound might bind with the enzyme in one spot in its natural state, but that spot might be different or less detectable when the enzyme is in a different shape (when it is crystallized). Thus, there must be considerable time and resources devoted to this task.

With this in mind, it becomes important to consider von Itzstein's comment that IG has a number of other projects on which they are producing papers (29 September 2003 – personal interview). The milestones and expectations placed on IG could, perhaps, be too stringent, considering that IG is committed to other engagements beyond the IG-Progen alliance. These milestones, according to Don (8 December 2003 – personal interview), were open to negotiation, though. Perhaps it is the case that the scientists at IG are not acting as opportunists in the Knorr-Centina (1981) sense of the word. Her conceptualization of an opportunist, as discussed in chapter four, is that one takes advantage of all opportunities available in order to succeed in terms of a desired outcome. With the distraction of other alliances, the IG scientists cannot be complete opportunists, á la Knorr-Cetina, because of the requirement to attend to these other engagements. They may be opportunists (Knorr-Cetina) is a different sense though – trying to run multiple projects (to maximize funding) and producing just enough work to keep collaborators hanging on.

In consideration of Progen's work on taking PI-88 through clinical trials, many of the firm's resources would also be occupied. The scientists at Progen could also be precluded from being considered total opportunists (in the Knorr-Cetina meaning of the word) in relation to the IG-Progen agenda. Certainly, the decision to only budget a particular amount of money to the purchase of platelets from the Red Cross would suggest that resources are being appropriated to other concerns. Unfortunately, this is a reality in most university-industry alliances.

Considering these possible contributions to the inability of the collaborative participants to reach their desired output under the terms of the initial contractual agreement, it becomes clear that the inability of the scientists to achieve the specified desired output could also be due to under-sourcing. Conceptually, AU$1m spread over three years and across at least three scientists does not allow much room for maneuvering or extra input. This becomes particularly

true when considering that the funding provided by Progen probably needed to cover not only the IG scientists' salary, but also the use of expensive equipment and the purchase of necessary materials. It could be the case that the alliance has been hindered by a shortage of funds.

In summary, there are several reasons why the members of the alliance may not have been able to achieve their desired output. These reasons include: the inherent problem of aligning the social worlds of the two segments of the alliance; the uncertainties of the highly experimental science being practised in this collaborative endeavour and the luck of the game of Biotechnology Bingo; and the possible failure to appropriately manage and/or fund this alliance.

Although the alignment of social worlds is crucial to creating a doable problem, the ability to completely align social worlds is plagued by the notion that the individuals in the alliance do not leave their social worlds behind in the formation of a knowledge value alliance. As Garrety (1997) notes, social worlds "…are characterized by a commitment to common assumptions about what is important, and what should be done" (p730). Where an industry practitioner may think that costs and efficient decisions are important, an academic may think that interesting and potentially useful findings are significant. This is precisely what makes the work between the two simultaneously complementary and conflicting.

The social worlds of the two different kinds of actors are brought to bear in the cultural ecology of the knowledge architecture, and must clash, mesh, or do something in between. While there are ways to push toward the side of meshing, the influence of these means can be mitigated by barriers to their attainment. In the collaboration between the Institute for Glycomics and Progen, the unpredictability of the science inhibited the production of sufficient numbers of compounds to replace the contractual credible commitments. Indeed, the difficulty, uncertainty, and novelty associated with highly experimental science will accompany, and potentially threaten, any collaboration utilizing the sciences inherent in the IG-Progen knowledge value alliance.

No one could guarantee that a solution would be found under the circumstances surrounding the alliance. In fact, the odds of producing a three-dimensional structure of heparanase are indeed very small. Recall Mukherjee and Miele's (1995, p240) claim that

scientists know the primary structures[180] of tens of thousands of proteins, but "the three-dimensional structures[181] of only a few hundred have been resolved". As these authors note, "[a]lthough the past decade has seen tremendous progress in molecular biology, which is still continuing at a very rapid pace, the advances in our understanding of protein folding and structure-function relationship have not bee as striking" (p240).

If it can be believed that scientists know 20,000 primary structures and 300 three-dimensional structures, then it is possible to say that there are 20,000 known structures of proteins because, as I presume, the known three-dimensional structures are also known primary structures. This would suggest that only 1.5 percent of the known structures of proteins are three-dimensional structures. As such, the odds of obtaining the three-dimensional structure of heparanase are very small[182]. The underlying science is still, indeed, cutting-edge, with advanced biotechnology firms (such as Progen) just now acquiring expertise in this area. This is a technique that has originated and been advanced in university laboratories and it may well be the case that scientists have not yet tried to find the 3D structures of 20,000 known proteins. To the extent, though, that determining the three-dimensional structure of an enzyme was a prerequisite for building and developing compounds to target the structure, as is the case under a rational drug design approach, the lack of success in this case could be attributed to overzealous expectations.

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[180] A primary structure is the structure of a molecule (protein, compound, etc.) that depends on covalent bonding. "For example, the primary structure of a nucleic acid or protein is defined in terms of the sequence of bases or amino acids" (Coombs, 1986, p250).

[181] A three dimensional structure of an enzyme is the elucidation of the structural elements of the enzyme achieved through x-ray crystallography. Rather than relying on amino acid bases, as is the case with a primary structure, a three-dimensional structure allows a scientist to visualize the structure of the enzyme at the atomic level of detail. In turn, the active and regulatory sites of the enzyme can be identified.

[182] The figure of 1.5 percent was derived by taking an estimated 300 known three-dimensional structures and dividing it by an estimated 20,000 known structures (both primary and three-dimensional). Considering that Mukherjee and Miele made their claim in 1995, however, it is also important to note that additional primary and three-dimensional structures may have been discovered since the publication of their work, and the process for obtaining three-dimensional structures of enzymes may have been significantly refined or advanced. Even if the number of known primary structures has grown to 30,000 and the number of known three-dimensional structures has grown to 500, the percentage of known three-dimensional structures is still only 1.7 percent. Or, if the number of known-three dimensional structures has grown to 1000 and the number of known primary structures is estimated to be 30,000, the percentage of known three-dimensional structures is 3.3 – still a relatively small amount. These estimations are complicated by the fact that not all proteins are enzymes. Hence, the odds of being able to determine the 3D structure of the enzyme may be slightly different than suggested here. For example if 15,000 of the known protein structures are enzymes and 280 of the known 3D structures are enzymes, the known 3D structures of enzymes would be 1.87 percent of all known structures.

The majority of the factors that have been identified as possible causes of the inability of the scientists in this alliance to attain their desired output are perhaps unavoidable, but not all of them. The collaborative partners really had no way of assessing the adaptive expertise of their respective partners, and thus, the only option was to allow them to attempt the problem. In addition, the uncertainties of the highly experimental science could not be avoided. Over-commitment to other endeavours on behalf of either side of the alliance, however, could have certainly been reduced, if not avoided. The project may have also suffered from lack of financial resources, and this too is something that could have been controlled if not avoided. Indeed, the members of the alliance have recently amended the original contract, passing a portion of the responsibility for acquiring and purifying the enzyme to the scientists at the Institute for Glycomics.

8.2.4 The Structure of the Alliance and Success

Nonetheless, decisions have to be made up front in any alliance to appropriate resources. What this may suggest is that the modular structure of the alliance, as it was specified under the original contract, was not appropriate for its purpose. The recent amendment to the contract and the reduction of functional divisions in the alliance points to a more interdependent arrangement. Under the original contract, tasks were split according to the different steps of rational drug design. In this organization of tasks, migratory knowledge was to move in the order of the tasks to the scientists who needed the knowledge to perform their task work. With the new arrangement, knowledge will move less systematically as there is a less definite division of labour, with the scientists at IG also working on purification of the enzyme.

Only time will tell if the new organization of tasks is more appropriate than the original. It depends on the IG scientists' ability to solve not only the technological problems relating to the structure and crystallization of heparanase, but also their ability to find new sources conducive to isolating and purifying the enzyme. The amendment of the contract has specified that the IG scientists assume some of the responsibility for locating sources of the enzyme and developing new ways to isolate and purify it. As they are in a race to solve this problem, it is

wise that they have decided to continue the alliance. They may have the opportunity to develop "idiosyncratic synergies" (Langlois & Robertson, 1995)[183] that could benefit them in the race.

Success is not only measured in this type of endeavour by the ability to solve a problem, but also by return on investment. Having invested over AU$1,000,000, the scientists and administrators at Progen are hoping for considerable returns, no doubt. This is, after all, an industry in which the constituents talk about a burn-rate rather than a profit (Vance, 29 September 2003 – personal interview), and all efforts must be made to ensure that the rate of burn is supported by a claim on future earnings. In an effort to protect both the reputations and futures of the parties involved in the IG-Progen alliance, and reap rewards from the resources invested, the decision to continue the collaboration has been made. As many of the decisions in the game of Biotechnology Bingo are based on a bit of luck, this one is too. On one side of the picture of the future there sits IG and Progen with the patent on an efficacious inhibitor of heparanase, and on the other is a very rich description of the problems associated with being unable to do so.

The collaboration between the Institute for Glycomics and Progen, while it has not been successful in meeting its desired outcome, is not yet over. Indeed, at the time of interviewing, von Itzstein commented that the scientists would want to start publishing their findings within the next five months (29 September 2003 – personal interview), which implies that work is forthcoming. The collaboration has been successful in getting Progen close enough to the process of rational drug design to afford the scientists who work there an understanding of it. In addition, the Progen scientists have been able to build their own drug design group, which was, indeed, one of the stated aims of the alliance. The project has also highlighted the problems associated with developing a compound via rational drug design to target heparanase, which may help the collaborative participants to find success in the future. Rather than saying this project is a failure, it would be wise to consider the comments of von Itztein and Don. Von Itzstein suggested that every project has its own life span (29 September 2003 – personal

[183] According to Langlois and Robertson (1995), idiosyncratic synergies are enhanced outcomes or outputs attributable to particular resources that are being combined, particularly where substitutes are not available.

interview). Don claimed that, "[w]hen you enter into collaborations, you make a lot of prejudgments based on previous collaborations you've had, and you always find that there are different cultures and different ways of dealing with each group that have to be taken into account" (8 December 2003 – personal interview).

Furthermore, several scholars emphasize the need for a tolerance for failure or support for overreach failures in managing R&D (Cummings & Teng, 2003; Peters & Waterman, 1982; Pinchot, 1985). With the considerable amount of pressure to succeed in these types of collaborative endeavours, which is brought to bear by the race to solve the particular technological problem that the alliance is attempting, and the amount of money that Progen has invested in this project, the prospect of accepting failure becomes increasingly difficult. As Fryxell and Judge (1995) suggest, the requisite virtues of direction and intervening in projects that appear to be failing are sacrificed with the emphasis on tolerance for failure. The tolerance is still necessary because of the difficulties associated with the science being utilized, but in turn, this tolerance needs to be balanced against the progression toward the desired output. This has been accomplished in the alliance between IG and Progen via the firm's managers' appreciation for the tribulations of the science, and simultaneously, the implementation of milestones and the negotiated efforts between the collaborative participants to redirect the work within the project when necessary.

8.3 Conclusion

For the most part, the IG-Progen knowledge value alliance has followed the rules of Biotechnology Bingo. The collaboration has institutionalized relevant design rules, interfaces, repositories, and starting points. It has come as far as tuning into the cultural differences created by members belonging to different social worlds. They have institutionalized a policy of tact to mitigate the friction created by the clashing of different social worlds. Members of the alliance were chosen based on the best proxy available to determine their ability to perform, namely their reputation. The inability of the members of the alliance to achieve the desired output can

be attributed, then, (in part) to the luck involved in playing the game. It can also be said to have resulted from the "systematic uncertainty[184] (Bonaccorsi & Pammolli, 1996 cited in Arora, Fosfuri, & Gambardella, 2001, p109) of the alliance.

The result of this case could have easily been similar to the two alliances discussed previously, as there are inherent similarities between this case and the others. The IBS-amrad alliance utilized rational drug design as the mechanism for alignment, as has been done in this case. The IG-Progen alliance is similar to the CMBB-Nereus alliance in that it has been able to enlist allies. While not specific to the project discussed here, IG and Progen also collaborate on another project that is supported by an industry-government co-funded grant.

The next chapter, the cross-case analysis, takes a closer look at these similarities, in addition to the contrasts among the various cases. Although there is an undeniable amount of luck associated with these types of collaborative endeavours, there is also a reasonable amount of skill that needs to be incorporated into the management of them. In an attempt to highlight the strategies that effectively reduce the luck and optimize the skill, chapter nine pieces together the findings from all three cases, along with presenting evidence from a fourth case.

[184] "Systematic uncertainty means that even if one knows and has perfectly tested the functions performed by the different modules, there is still uncertainty about whether the system as a whole will perform as expected" (Arora, Fosfuri, & Gambardella, 2001, p109).

SECTION III

GRAND FINALE

Chapter 9 Cross-Case Analysis & Discussion

> "I would submit, I think, that it is only by imparting 'casually fertile' propositions or generic codes that general education in the broad range of human knowledge is made possible. General education does best to aim at being generic education, training [humankind] to be good guessers, stimulating the ability to go beyond the information given to probable reconstructions of other events" (Bruner, 1964, p67).

The game of Biotechnology Bingo involves both luck and skill. The luck comes from the bounded rationality that affects architects attempting to find scientists who are both willing and able to be part of a proposed knowledge value alliance. Scientists are typically engaged in numerous activities, collaborative or otherwise, and even if they are deemed suitable or qualified to perform the task(s) necessary to attain the desired output of a proposed alliance, they may not have the time or the resources to participate. Furthermore, reputation and prior experience are usually all an architect has to gauge one's ability to perform, and, as has been argued in chapter eight, these proxies are not always valid indicators of performance ability and outcomes, particularly when a novel problem needs to be solved. Compounding the uncertainty, the problem itself may not be doable, but this cannot always be determined prior to attempting to solve it. The social worlds of the collaborative participants need to be aligned. The highly experimental nature of the science involved in these types of collaboration yields a tremendous amount of uncertainty, and, as a result, the science itself is a tribulation in the trot toward the desired outcome. An architect is also faced with having to select the appropriate tools, technologies, and work practices to effectively integrate the ingrained knowledge of the collaborative participants.

With this in mind, it becomes paramount that an architect has and applies the requisite skills to see the alliance through from commencement to completion. These skills, like the

ingrained knowledge of the scientists attempting to solve the technological problem specific to a collaborative agenda, are unique to each individual. They can, however, be informed or guided by certain precedents and parameters. These guidelines allow an architect to "go beyond the information given", to use Bruner's terminology, in a bid to effectively use his or her ingrained knowledge to plot the course of a knowledge value alliance.

These principles include: guidelines for the applicability of modularity, a paradigm for the process and intricacies of the production and function of knowledge, and a pattern that reflects the operation of displacement. A discussion of each of these principles follows. This discussion is presented in the form of a cross-case analysis, drawing additional evidence from a fourth case, which appears as a series of vignettes throughout the chapter. This chapter aims to convey that Biotechnology Bingo is a game that cannot be won by simply following the rules. Winning the game requires the ability to manipulate the rules, but there are certain contingencies associated with this, which are revealed throughout the chapter.

9.1 The Applicability of Modularity

The types of collaborations presented in this thesis consist of architectural arrangements whose elements are both modular and interdependent. Because of the hybrid nature of these alliances, there are particular aspects of modularity that apply to these collaborative arrangements that, if applied appropriately, can be effective strategies in the game of Biotechnology Bingo. These aspects or strategies, however, cannot always be counted on to pan out as anticipated, and this is due mostly to the fact that knowledge value alliances are modular packages that include people (and not just products or artifacts). Nonetheless, an understanding of these strategies can prepare architects, and members of an alliance alike, to manipulate the rules of the game. These strategies are: the recombinability of modules, mechanisms for combating the urgency in the contexts in which these alliances dwell, the upgradibility of modular architectures, and tools to address the limitations of design rules and interfaces. Two of

these strategies, namely recombinability and upgradibility, make use of Baldwin and Clark's (2003) modular operators.

9.1.1 Recombinability

Schilling (2000) notes that modularity, at its most basic level, refers to the degree to which a system's components can be separated and recombined. Clearly, because the knowledge value alliances discussed in this report are only temporary, they can be separated. University scientists are part of a faculty or research centre at a university, which provides them with an income and a stable professional work residence. This is the case, too, with scientists from a dedicated biotechnology firm. Knowledge value alliances can be separated and partitioned into the university modules and firm modules. But can they be recombined?

The easy answer to this question would be 'yes'. And, in theory, these modules are separated and recombined all the time. Once a collaboration ends, whether the desired output has been achieved or not, a new one typically takes its place, either furthering the collaborative agenda (or still trying to complete it, as could also be the case[185]) or endeavouring to solve a new technological problem. In addition, members of an alliance are often involved in various alliances simultaneously, which would suggest that university and industry modules are, in fact, recombinable. Vignette one offers evidence of the possibilities afforded to architects in combining and recombining various modules in pursuit of a desired output.

[185] In instances where an initial alliance is unable to complete the collaborative agenda or attain the desired output, one module from the original alliance may combine with a different module (which was not part of the original alliance) to attempt a completion of the original agenda.

Vignette One

Case D
The Knowledge Value Alliance
between
the Institute for Biomolecular Science (IBS)
and
Novogen

The Institute for Biomolecular Science (IBS), University of Wollongong and Novogen Ltd., Sydney, formed a knowledge value alliance four years ago. The collaboration is aimed at developing an inhibitor of the 5-α-reductase (5AR) enzyme implicated in a range of diseases and ailments, including benign prostate hyperplasia, prostate cancer, hirsutism, acne, and male patterned baldness. Professor Alan Husband of Novogen noted that the collaboration was initiated by Andrew Heaton, a senior chemist at Novogen and a colleague of Professor John Bremner, the Director of the Institute for Biomolecular Science (11 December, 2003 – personal interview). According to Husband, Novogen was seeking to inhibit the enzyme that creates an imbalance in the male reproductive tract and the firm didn't have time to do it alone, so Heaton recommended that Bremner and his staff be consulted for the job. A recent paper by Jane Faragalla et al (2003), reporting the findings of one aspect of the project, contends that inhibitors of 5AR are of therapeutic interest for prostate cancer, which is cited as "the most common non-cutaneous cancer among men in most western countries and the second most deadly cancer" (p83). The broad policy of the project is controlled by the research manager at Novogen. The day-to-day decision-making and implementation of the project are handled by Faragalla (a PhD student at IBS) and Bremner (Faragalla, 9 January 2003 – personal interview). Heaton, the senior chemist at Novogen, guides the direction of the collaborative agenda (Husband, 11 December, 2003 – personal interview). As Faragalla commented, everyone is holding the reins, which adds direction to the overall project (9 January 2003 – personal interview).

The work at Novogen is based on the discovery of plant chemicals that are involved in regulating cell processes, including ones relating to survival or death, and growth or non-growth. "These chemicals are known as isoflavonoids - these are plant's signal transduction regulators." When human cancer cells are exposed to these chemicals, the result is an immediate stoppage to the multiplication of the cell and eventual death of the cell (Marshall Edwards, Inc., 2001). Novogen has developed and advanced an array of synthesized compounds based on this discovery, with all of the compounds being modifications of the isoflavonoid core. As one might imagine, Novogen has put together an extensive library of isoflavonoid compounds, and the method of synthesis used in developing these compounds is protected by an international patent. The company has recently collaborated with scientists at Yale to test one particular compound from its isoflavonoid library, Phenoxodiol, which has excitingly been shown to kill ovarian cancer cells.

Vignette One (continuation)

The core molecules that the scientists at IBS are synthesizing are also based on the isoflavonoid drug scaffold. The work follows the premise of the structure-activity relationship methodology that has been identified as a design rule in two other cases presented in this thesis, with the structure-activity relationship methodology being a key tool in the process of rational drug design. As stated in Faragalla et al (2003), the three-dimensional structure of 5-α-reductase is unavailable, and thus, one way of designing a compound to inhibit the enzyme is to use a ligand-based strategy that looks at the structure and activity of the compound and enzyme. The IBS scientists have focused on building a pharmacophore, or a list of the features necessary in a compound to appropriately bind with the enzyme (5AR). A pharmacophore is derived through the application of computational chemistry (Faragalla, 9 January 2004 – personal interview). IBS has been enlisted in the discovery program at Novogen to find a compound with a higher activity profile via substitutions to the molecule (Husband, 11 December, 2003 – personal interview). Novogen is responsible for the testing of the compounds produced at IBS (Husband, 11 December, 2003 – personal interview). Faragalla has been heavily involved in the discovery of 5AR inhibitors. She has also spent some time at Novogen developing the enzyme assay to be used in this project (Bremner, 12 February 2004 – personal communication). The scientists from the Institute for Biomolecular Science are able to publish their findings, and have done so, in consultation with Novogen because of a patent that Novogen holds on Trinovin, a non-prescription product discovered and developed by Novogen for the maintenance of prostate health and urinary function in men (Husband, 11 December, 2003 – personal interview; Novogen, 2003). The patent held by Novogen covers the use of isoflavonoid compounds in target diseases such as prostate cancer, and as such, the synthesis of isoflavonoid compounds performed at IBS is covered under this patent. The project, however, is set to finish because the PhD student will be finishing and Novogen is not interested in continuing this endeavour with another PhD student. In addition, the collaborative agenda is a low-profile project at Novogen (Husband, 11 December, 2003 – personal interview).

The recombinability of different modules of a knowledge value alliance can scarcely be argued against. The Institute for Biomolecular Science featured in Vignette One is the same Institute involved in the collaboration with amrad, which was presented in chapter seven. Some of the same people are involved in both alliances: Bremner from IBS and Griffith from the University of Newcastle. Novogen has chosen scientists from Yale to create a testing module for one of the company's promising compounds. Novogen's own in-house chemistry department is being substituted by IBS in the knowledge value alliance presented in Vignette One. Interviewees from Progen (the industry firm from Case C) indicated that the collaborative project may have been more cost-effective if the project had been conducted in-house, suggesting that the work performed at the Institute for Glycomics could have been substituted

with work performed by Progen scientists. The act of substitution, the replacement of one module with another, is one of Baldwin and Clark's (2000) modular operators[186].

Following Schilling (2000), modularity allows for heterogeneous inputs to be recombined to produce a variety of heterogeneous outputs. Indeed, taking knowledge value alliances to be modular, it can be seen that the heterogeneous inputs, the various scientific disciplines and associated ingrained knowledge of the collaborative participants, are often recombined to produce a variety of heterogeneous outputs. Recombinability raises a question, however. If there is a combination between "A" and "B" and "A" and "C", is "A" identical in character in both instances? I would argue that "A" takes on different aspect of character with each new combination to meet specific combinatorial needs. As Fujimura (1996) suggests, "[m]aterials and technologies can at one time, in one place, be a tool for solving a research problem and at another time or place become the problem itself…They can be objects acted upon by scientists, and agents acting upon science" (p66). With this in mind, the heterogeneity of "A", whether it is considered to be the ingrained knowledge of a collaborative participant or a chemical in a chemical compound[187], is all the more increased.

The input for the IBS-amrad alliance consists of several scientists from the Institute for Biomolecular Science and additional scientists from amrad combining to produce anti-bacterial agents, a model of integrase, and therapeutic compounds to inhibit integrase. Some of the scientists from the Institute for Biomolecular Science are also, however, dedicated to the collaboration with Novogen. These scientists, namely Bremner and Griffith, operate as the synthetic chemistry and computational chemistry modules in the IBS-Novogen alliance, along with Faragalla, and their heterogeneous input is expected to result in an inhibitor or inhibitors of 5-α-reductase, an output quite different to the output desired in the IBS-amrad alliance.

[186] Modular operators, as defined by Baldwin and Clark (2000), are a set of tools an architect can employ to manipulate modular arrangements in the search for value. Modular operators "…can be applied at many points in a large design, and in many combinations and sequences. Hence they define a very large number of potential paths, which can be used to explore a very large space of designs" (Baldwin & Clark, 2000, p346).

[187] I submit here that an individual scientist has a large repertoire of ingrained knowledge that can be considered to be combinatorial component "A". Different areas of his or her ingrained knowledge will be necessary and useful in different collaborations. Similarly, a given chemical will bind differently in different compounds, depending on the other characteristics of those compounds.

9.1.1.1 The Effectiveness of Recombinability

While the recombination of various modules to produce heterogeneous outputs is obvious in the cases presented in this thesis, the effectiveness of such a strategy is not. In the IBS-Novogen alliance, Novogen boasts an isoflavanoid library of over 100 compounds, of which IBS has contributed five or six[188] (Husband, 11 December 2003 – personal interview). Re-examining the alliance between the Institute for Glycomics and Progen, IG has contributed somewhere between six and 12 compounds (Vance, 23 December, 2003 – personal communication), nowhere near the 50 or 60 that von Itzstein suggested would be desirable for producing a drug lead. This is so despite the Institute for Glycomics' reputation of being among Australia's finest laboratories in the discovery and development of glycopharmaceuticals. The five or six compounds produced in the IBS-Novogen alliance were produced over the course of the last four years. The six to 12 compounds produced in the IG-Progen alliance were produced over the course of the last three years. This is in striking contrast to the number of compounds discovered at the Center for Marine Biology and Biotechnology in its alliance with Nereus.

In the last year alone, CMBB presented Nereus with 15 discoveries that met the design rules of being both novel and active, and Nereus decided to license three of these for further development. Interestingly, the knowledge value alliance between CMBB and Nereus always consists of the same two core modules, namely the scientists from CMBB at one end and the Nereus scientists at the other end. The architectural alliance is often augmented, with different modules from the Chemistry Faculty and Cancer Center at the University of California, San Diego. The architectural arrangement, however, never excludes or substitutes either of the two core modules[189]. Analytically, this says something very distinct about the functionality and effectiveness of the recombination strategy. The CMBB-Nereus collaboration may be on

[188] It should be noted, however, that the scientists at IBS have produced other compounds that have not yet been submitted for testing, and that there are other dimensions to the project, including molecular modeling and developing new synthetic methodologies (Bremner, 12 February 2004 – personal communication).

[189] Augmenting, excluding, and substituting are all modular operators defined by Baldwin and Clark (2000). Augmenting is the act of adding a new module to a system. Excluding is the removal of a module from a system. And, as mentioned previously, substituting is replacing one module with another.

trajectory of luck, stuck with the scientists of the two core modules whether they are the most suitable and qualified agents for the purpose or not, but the evidence suggests that, while the alliance is still separable (CMBB and Nereus would both continue to function if separated), it is not following a pattern of recombination, at least in relation to the two core modules. To put it colloquially, it may just be a matter of "if it ain't broke, don't fix it". The members of the CMBB-Nereus alliance are getting what they need from the collaboration and both parties are benefiting.

Contrasted with the other alliances presented in this report, the CMBB-Nereus knowledge value alliance has been quite successful in discovering compounds for development. This could, perhaps, be due to what Langlois and Robertson (1995) call "idiosyncratic synergy", which is the "…enhanced outcome [that] is specific to the particular resources that are being combined…" (p13)[190]. The uniqueness of the way that CMBB and Nereus combine their resources may be the defining factor in the ability of the CMBB-Nereus alliance to "out-produce" the other alliances presented in this thesis. As Dyer and Singh (1998) suggest, "idiosyncratic interfirm linkages" may be a source of competitive advantage[191]. The consequence of idiosyncratic synergy, however, is that a degree of recombinability is forfeited (Schilling, 2000). Splitting the CMBB-Nereus alliance and substituting one of the modules (CMBB or Nereus) would eliminate the idiosyncratic synergy that exists between CMBB and Nereus.

[190] The differences in levels of production may also be due to different design rules. The CMBB-Nereus alliance uses a design rule based on novelty and activity, whereas the other three cases presented here use rational drug design. Under rational drug design, fewer compounds are to be expected because there is generally more time spent on understanding the target (enzyme) and producing compounds to have a specific effect on the target. Under the novelty and activity design rules used in the CMBB-Nereus alliance, the focus is on producing more chemicals and screening them for effects. I would submit, though, that because CMBB and Nereus are repeatedly involved in their collaborative endeavour with the recurring aim of discovery and development of novel compounds derived from marine microbes, the members of the alliances have become adept at their roles in the collaboration. This has allowed the collaboration to become idiosyncratically synergistic, which could potentially allow it to outperform other alliances using similar design rules.

[191] Zollo, Reuer, and Singh (2002) also report findings that affirm the role of repeated experience between collaborative partners in instances of high levels of performance. They argue that, "[p]artner-specific experience facilitates the development of interorganizational routines, or stable patterns of behavior aimed at the interaction and cooperation across the two organizations. These routines may contribute to the performance of the alliance by facilitating the information gathering, communication, decision making, conflict resolution, and the overall governance of the collaborative process" (p709).

So, is recombinability an effective strategy for knowledge value alliances in biotechnology? Answering this question requires consideration of the sense of urgency that defines the context in which these alliances exist. Where an alliance (or a side of an alliance) does not hold a patent in the area under investigation, there is a considerable sense of urgency associated with solving the technological problem prior to any competitor's announced resolution.

The levels of urgency differed between the cases presented in this thesis. As mentioned in Vignette One, a patent held by Novogen protects the work being performed in the alliance between IBS and Novogen. Recall, however, that the IBS-amrad alliance is comprised of three projects. The Anti-Bacterial Project is protected by a patent jointly held by the members of the alliance. The TB96 Refinement Project is unprotected, as is the Integrase Modeling Project. Similarly, the discovery work performed at CMBB is also unprotected until Nereus decides to license a discovery, at which time a patent is acquired. The work performed in the IG-Progen alliance is unprotected too, and importantly, members of the alliance are aware of research groups attempting problems similar to the one they are pursuing.

If recombinability hinders an alliance's ability to perform quickly (note this says nothing about an alliance's ability to perform effectively or accurately), as is demonstrated in the contrast between the CMBB-Nereus alliance and the other three cases under scrutiny in this investigation, it would make considerable sense to aim for the idiosyncratic synergy exemplified in the CMBB-Nereus alliance in cases where the work being performed is not protected by a patent. Where organizations are able to effectively combine their resources in an alliance to create idiosyncratic synergy, they have an added advantage in a patent race, in that the synergy between the members of the alliance may very well allow the alliance to find a resolution to a specific technological problem before their competitors are able to do so. Substitution in the process of recombination demands that time is allotted to finding suitable partners, and the recombination of modules may not provide the "enhanced outcome" of which Langlois and Robertson (1995) speak.

If there is sufficient time, however, to complete the technological problem without the threat of displacement[192] by competitors, then the strategy of recombinability may be effective. It may allow for more creative input and not constrain or limit scientists in terms of input into the process of design. If the work necessary to complete a desired output is already covered by a patent, alliances should be able to effectively utilize the recombination strategy because there is a reduced sense of urgency.

Schilling (2000) suggests that the primary factors inducing urgency in a system's context are technological change and competitive intensity. As Schilling (2000) notes, these external factors increase the likelihood that a system will respond by becoming more modular. Indeed, the context in which the knowledge value alliances discussed in this thesis exist is defined by rapid technological change and competitive intensity. I am arguing, however, that where competitive intensity is high, modularity, at least in terms of recombinability, should be avoided. In instances of competitive intensity, knowledge value alliances should aim for modularity within themselves, but should not seek to substitute or exclude core modules, for pursuing these two types of modular operators threatens the idiosyncratic synergy that an alliance can use as a weapon in the race to solve a technological problem. This, however, assumes that the combination is currently effective. Obviously, if idiosyncratic synergy is apparent, the alliance is effective. When it is not, though, other options should be pursued.

Those alliances operating in a patent protected area can benefit by utilizing the recombination strategy. The alliance, if protected by an international patent, can work for up to 17 years on the collaborative agenda without being threatened by another scientist, firm, or research group. This is, however, an industry where large amounts of money are invested in discovery and patenting, and alliances would be ill-advised not to attempt to reap the rewards of their jewel as quickly as possible.

[192] As defined in chapter three, displacement occurs with the resolution of a specific technological problem. Within a knowledge value collective, there will typically be several groups (teams or alliances) of scientists who are seeking to solve the same or a similar technological problem. Once one group of scientists has been successful at solving the problem, the others are displaced in terms of time, effort, and financial investment.

9.1.1.2 Upgradability

Realizing these rewards requires that the alliance components be upgradable. The alliance must remain open to augmenting the architecture in an effort to move the product from late discovery, early development stages through the clinical testing phases, and into the areas of sales, marketing, and distribution, and must ensure that the modules are portable[193]. Firms and alliances have several options in doing so, which include licensing the product to other entities or engaging in a collaborative endeavour to upgrade the product. It is important to note, however, that compatibility between different modules, should the collaborative approach be chosen, is essential. Upgradability creates competency-enhancing knowledge (Tushman and Anderson, 1986) as designers realize which aspects of a technological platform will lead to future improvements, which aspects will lead to dead ends, and how lower-order components[194] can be materialized or developed (Garud and Kumaraswamy, 1995). These types of realizations, typical of an alliance upgrading and moving from discovery toward marketability, require that different members of the various modules in an alliance are compatible and agree on these realizations.

Knowledge value alliances are packages of people, albeit with some artifacts, and therefore, mechanisms to ensure compatibility and coordination are more complex than those operating in a product architecture. The IG-Progen alliance is an excellent example of modular mechanisms' failure to ensure compatibility and the attainment of a desired output. The

[193] Porting is another of Baldwin and Clark's (2000) modular operators. Porting makes a module compatible with two or more systems.

[194] Following Clark (1985), Hughes (1987), and Simon (1962), Garud and Kumaraswamy (1995) define lower order components as those components that exist at the lower end of a hierarchy in a technology system (where the hierarchy ranges from dependent components to independent components). Movement up a hierarchy requires advancement and development of the independent components. The speed of a microprocessor is offered as an example in their definition. In applying this concept to the cases in this thesis, the lower-order components could be conceptualized as the type of testing used in drug development. Traditional screening methods would be considered a lower-order component, where the advancement of the system of drug development would be dependent upon the advancement of such components. For example, the use of *in vitro* testing (testing an enzyme reaction in artificial conditions) is an advancement upon *in vivo* testing (testing within a living organism where the reaction cannot be observed) and the movement to *in vitro* would allow for an advanced system of drug development. Drugs, however, still have to be tested in humans because *in vitro* tests cannot include all relevant variables. Thus, there is still room for advancement, where *in vitro* tests would be considered the lower-order components in the system.

members of this alliance were unable to align their social worlds to produce the desired output in the time allotted to the project. This is in spite of the institutionalization of adequate design rules and interfaces in the alliance, which highlights the notion that there are particular limitations associated with the application and usefulness of visible information when a modular arrangement consists of people. This becomes even more apparent considering that the IG-Progen alliance had two design rules (rational drug design and supporting milestones) and three interfaces, more than any of the other alliances presented in this report. The matter was also compounded by the uncertainties associated with the highly experimental nature of the science being performed in the alliance. So, while modularity may serve to reduce complexity, it clearly cannot resolve the problems of scientific uncertainty.

9.1.2 The Pitfalls of Design Rules and Interfaces

The design rules do not necessarily ensure the production of patentable material. They merely allow for the alignment of tasks across a modular arrangement and they should only be used for such purposes[195]. This is seen in Case A, Case C, and Case D. In Case A, the CMBB-Nereus knowledge value alliance, the 15 most recent discoveries were produced in accordance with the design rules that dictate novelty and activity. Only three of the 15 discoveries were determined to be worthy of a patent, however. The IG-Progen collaboration has been even less successful in producing patentable or publishable material, despite adherence to the rational drug design rules. The same holds for Case D, although IBS has been able, in conjunction with the scientists from Novogen, to produce a paper underpinning the design of the compounds discovered in the collaboration, the alliance has not produced material that requires immediate patenting, even with the use of the structure-activity relationship design rule. In Case B, there have been patents procured on the work done in that alliance, but this cannot necessarily be

[195] Rational drug design, for instance, is useful in aligning tasks. It does not, however, necessarily lead to the production of patentable knowledge. It can indeed, but only through the application of relevant ingrained knowledge to produced objectified knowledge, including compounds, (a concept that is addressed in the next section) that meet the demands of the rational drug design rule(s).

attributed to the design rules. It could also be explained by the enlistment of the appropriate scientists to perform the appropriate tasks and the members of the alliance being "lucky".

Taking a closer look at the design rules illustrated in this thesis, it can be argued that they create a product-oriented structure and a function-oriented structure in alliances. Rational drug design, for instance, creates a functional division of labour where it is used. This type of social organization sees each task performed in response to information received. Each task involves altering or recomposing things – compounds, enzymes, etc. – and ends with the transmission of the altered thing to the performers of another task[196]. Under the coordination of rational drug design, the structure of the enzyme is determined, compounds are specifically designed to have the desired effect on this structure, the enzyme and the candidate compounds are modeled together, and/or co-crystallized, and the compound is synthesized to be more efficacious. The division of labour within an alliance using rational drug design is centred on each of these tasks and the necessary ingrained knowledge to perform them.

Is this a modular arrangement? Although I admit to particular interdependencies in such an arrangement, I do contend that the functional structure created by rational drug design "provides the materials for individual level rationality" (Stinchcombe, 1986, p7). And, as I see it, "individual level rationality" is the basis of modular design. Each product component, task in a design process, or level of a hierarchy is individually rational in modularity. Each component, task, or level operates independently and, given the appropriate design rules or interfaces, each component, task, or level is compatible with others in the system and in other relevant systems. Under rational drug design, each task is independent, but also compatible with other tasks in the alliance.

The process of rational drug design may not necessarily be rational[197], but it does provide for a functional structure where it is used. The problem is, though, that rational drug design,

[196] I take this line of thought from Burns and Stalker (1961, p78). They use it to refer to the similarities in organizations practising a wide array of activities. I use it here to demonstrate the interdependency created by the application of rational drug design.

[197] Rational drug design is also termed structure-based drug design because some practitoners do not believe that it is all that rational (Don, 8 December 2003 – personal interview). This, however, is not the

with all of the advancement it provides beyond the traditional screening techniques, is a standard rule that has to be applied to dynamic task environments. Rational drug design is an "intensive technology" (Thompson, 1967) that is used to achieve change in an object, such as the activity of a compound or the state of an enzyme as it moves from its natural state to a crystallized state. This type of technology operates to near perfection in a closed system, or a system that remains closed to influences from the external environment.

Alliances, however, are very much open systems, and, as such, the task environment in an alliance is dynamic. The science is unpredictable. The threat of competition is very real. "Scientists solve innovative problems in open systems" (Fujimura, 1996, p156). Therefore, rational drug design as a standard response to drug design is limited by these conditions. As Thompson (1967) states, "[w]hen the task environment becomes dynamic rather than stable, new complications arise…Standardized response rules are inadequate, for the [alliance or other type of organization] faces contingencies as well as constraints. It must determine when and how to act, and its cues must be taken from the task environment" (p73). Simply taking the approach of determining the structure of an enzyme, developing compounds to target that enzyme, modeling the two together, and following the other steps of rational drug design cannot occur without a consideration of the dynamics of the task environment and the contingencies[198] and constraints provided by the openness of the alliance. "[A]n important function of any system is adaptation to what goes on in the world outside" (Lawrence & Lorsch, 1967, p7). Indeed, practitioners in a dynamic environment must "go beyond the information given", á la Bruner (1964), to assess the implications of their current state and pace of work in relation to competitors.

The effect of interfaces is also altered when used in relation to people (rather than products) in a dynamic environment. While interfaces are supposed to "detail how modules will

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reason why I contend that it provides for structural organization. I am referring to the structure of the alliance and not the structure of compounds or enzymes as the name structure-based drug design implies.

[198] As Fujimura (1996) contends, these contingencies can be viewed in terms of "…roadblocks to ongoing action or new opportunities to the work of the laboratory" (p157). I submit that when a technological problem is solved by scientists beyond the knowledge value alliance it is certainly a roadblock to ongoing action for the members of the alliance that were unable to solve the problem before the competitor's ability to do so. It may also be viewed, however, as an opportunity for new collaborations.

interact, including how they will fit together, connect, and communicate" (Baldwin & Clark, 2003, p151), this cannot be guaranteed in human interaction. In such instances, social worlds need to be intertwined and connected, not material worlds. The act of aligning social worlds remains a formidable obstacle, even with the use of interfaces. Take, for example, the interfaces of synthetic chemistry, glyco-biochemistry, and computational chemistry that exist in the IG-Progen alliance. Despite these interfaces, there are still flaws in the connection and communication between the two sides of the alliance. One party is disappointed in the collaborative participants' inability to achieve results. Call it a failure to align social worlds. Blame it on the uncertainty of the science involved. The fact remains that the interfaces used in the alliance have shortcomings because they are being applied to people operating in a dynamic and uncertain environment.

In acknowledgement of these shortcomings, there is a specific tool that can be used in combination with an interface in modular arrangements comprised of people that can supplement the intended link of an interface. This tool is tact, a specific communicative aid identified in chapter four. The synthetic chemistry, glyco-biochemistry, and computational chemistry interfaces did not provide the link between IG and Progen. Instead, it has been Progen's use of tact, in doing and saying the right thing at the right time, that has afforded the connection between the two sides of the alliance and allowed them to continue the collaboration. With the institutionalization of tact, the members of the alliance have acknowledged their differences and, rather than writing-off the project, are reassessing the division of labour in the alliance – amending and extending the contract. Tact, then, is a pertinent communicative aid that can be used in conjunction with interfaces to increase the likelihood that two modules of humans connect and communicate in a manner appropriate for the pursuit and achievement of a desired output.

Knowledge value alliances are arrangements of complementary resources that are both modular and interdependent in composition. Many of the concepts used in a modular product architecture are applicable to these types of arrangements; many, however, are not. The applicability of modular strategies can provide benefits that could not be achieved without the

integration of the various knowledge bases of collaborative constituents. In applying these strategies, one must pay particular attention to the external context, beyond the knowledge architecture, and the levels of interdependency that exist within the architecture. Focus on modular strategies should not outweigh attention to the production and function of knowledge within the alliance.

9.2 The Production & Function of Knowledge

One of the reasons why modular strategies are limited in applicability is that knowledge does not function in the same manner as physical artifacts. Because it is a product of the human mind, there is little consistency or controllability associated with its production process[199]. Some scholars even argue that there need not be external input into the knowledge production process, which diminishes any hope of defining and managing it. "Any kind of experience – accidental impressions, observations, even 'inner experience' not induced by stimuli received from the environment – may initiate cognitive processes leading to changes in a person's knowledge. Thus, *new knowledge can be acquired without new information being received*" (Machlup, 1983, p644 – emphasis his own, cited in Langlois, 2001, p81).

Implementing rules and guidelines to control the process of knowledge production would seem, then, to be an unattainable task. The design rules and interfaces that work quite well to guide production in product architectures are what Avadikyan et al (2001) call coordination function rules, or rules that bring together individual actions to meet a defined set of goals. These types of rules are not as efficient, however, in guiding or governing the production of knowledge. They merely function to coordinate and amalgamate the knowledge once it has been produced.

Indeed, coordination is achieved via design rules and interfaces when employed in knowledge value alliances. This is demonstrated throughout the cases presented in this thesis. But these rules do not solve technological problems – *people do*. People may follow hidden

[199] Physical artifacts are at one point also a contrivance of the human mind, but once produced, there tends to be a consistent, controllable process delineated for their future production and use.

design parameters or their own individual heuristic patterns in resolving the many sub-problems that lead to the completion of the desired output. The sub-problems are coordinated by the design rules, but without the completion of the sub-problems, the larger technological problem remains unresolved. Following this line of reasoning, I argue here that knowledge production occurs in the mind of individuals. Once produced, the knowledge functions through the individual's use of it in the process of patenting, the publication of journal articles, and the creation of "things", namely compounds and methodologies or techniques. The use of individual knowledge in this manner amounts to a process of objectification, not codification. There is a considerable difference between objectification and codification, which will be elaborated on in the next section. Following objectification, the knowledge is susceptible to reuse.

9.2.1 The Objectification of Knowledge

Following Rescher's (1997) two modes of objectiveness, knowledge can be said to be objectified when it consists of a concretely realized object, which different individuals can observe, and it must be impersonally and generically cogent. The compounds produced in all four cases meet these criteria. So, too, does the technique for capturing marine microbes in the CMBB-Nereus case. The methodologies, while they are objectified knowledge themselves, become "things", in the Latour sense of the word[200], that aid in the objectification of other material. The method of collecting marine microbes used in the CMBB-Nereus alliance is an objectification of the ingrained knowledge of Fenical and Jensen who invented the process. By sharing the process and demonstrating it to others, Fenical and Jensen objectify their ingrained knowledge. Through the application of the method, new objectifiable material, marine microbes suitable for the alliance's purposes are produced. Objectification, then, is the social validation of knowledge.

[200] "Things", as defined by Latour (1987), are new objects, tools, or techniques that, through a process of routinization and reification, become a "black box", whereby their inner workings are no longer a matter of controversy or inquiry.

Much as the production of the marker in the game of Bingo occurs without being witnessed or understood by the Bingo player, so too does the knowledge that eventually amounts to the marker in Biotechnology Bingo. After production, the marker is objectified as a marker (that is, players observe that it is a marker and use it for such purposes). This does not guarantee, however, that it is a marker that will fall in line with others. Moreover, through this process of production and objectification, the marker becomes available for use in many Bingo games, and may one day even be a marker in a winning game.

Knowledge in Biotechnology Bingo functions in a very similar manner. The ingrained knowledge of members of an alliance is produced, accumulated, modified, and put to use in experiences prior to, during, and after the collaborative endeavour. This knowledge is used to solve task level problems, the solution to which must fall in line with the prescription laid down by the design rules. "Problems and possible solutions do not come to systems (with a system being an individual mind, á al Maturana and Varela, 1980) from an outside world, but are generated within the system itself" (van Twist & Schaap, 1991, p40). An individual scientist uses his or her own ingrained knowledge to define the task level problem and devise possible solutions. Knowledge, in this sense, is embodied action (Varela, Thompson, & Rosch, 1991).

Although it is not possible to directly observe the processes of developing ingrained knowledge and using it to define both a task level problem and the method(s) of resolution, some alliance members have been witness to and involved in the experiences that shaped the knowledge development or production processes of their colleagues. This is particularly true in cases like the IBS-amrad alliance and the IBS-Novogen collaboration, where PhD students, along with their supervisors, are members of the university side of the alliance. In my observation of the IBS faculty meetings, during which the PhD students would present the results of one week of synthesizing compounds, the supervisors were very much a part of the PhD students' experience of presenting their knowledge. The supervisors either corroborated their work, supporting their findings, or suggested alternative methodologies. While the supervisors were obviously not privy to the internal process of knowledge production from these experiences, they were at least there to witness and partake in the experience itself. They

were, in the words of Maturana and Varela (1980), a "perturbation" from the external environment.

Partaking in the experiences that resulted in knowledge production also occurred in the CMBB-Nereus alliance, when members from both sides of the collaboration attended a joint expedition to Guam. The scientists from Nereus were shown the technique for capturing marine microbes. The CMBB scientists provided a perturbation, which the Nereus scientists could make use of for the purposes of producing ingrained knowledge. The Nereus scientists were then left to their own resources to apply the ingrained knowledge. The intention was, however, that, based on the demonstration of the technique for capturing marine microbes, the Nereus scientists would be able to produce something objectifiable: marine microbes that could be used for the purposes of drug discovery and development[201].

There was a clear cycle of knowledge production and function evident in the cases investigated during this study. Scientists use their own ingrained knowledge, applying their states of knowing, to produce something that can be objectified, to create that which is known. Both the marine microbes and the technique used to capture them are instances taken from the CMBB-Nereus case that exemplify how ingrained knowledge is objectified. This cycle featured in the other cases as well. When scientists from the IBS-amrad alliance produced compounds for testing, they used their ingrained knowledge to create objectifiable material, the compounds. The same thing occurred in the IG-Progen collaboration.

9.2.1.1 How Knowledge is Objectified

The various activities used in these collaborations to objectify ingrained knowledge include the production of compounds, the development of methodologies and techniques, the publication of journal articles, and the procurement of patents. The process of objectification allows the ingrained knowledge of the individual to be verified by others. In each of the cases presented in this report, scientists use their ingrained knowledge to produce something, an

[201] It is important to note here that marine microbes exist without the collection technique. The technique yields a particular kind of marine microbe that can be used for the purposes of the alliance.

object, a tool or technique, a written description of the product of their work, which serves to demonstrate that the ingrained knowledge really does exist, for without it, that "something" could not be produced. Surely, someone with quite insufficient levels of knowledge can, by chance, piece together various materials to produce "something", but the likelihood of that "something" being recognizable as a chemical compound capable of inhibiting a specific enzyme, or as a three-dimensional structure of an enzyme stable enough for evaluation, is very small. Furthermore, people with the "right" (ingrained) knowledge are needed to recognize these "somethings" as useful for the project.

The process of objectifying knowledge is illustrated in the sequence of using ingrained knowledge to produce compounds, testing these compounds for activity, and, if interesting and significant activity is found, publishing the findings on these compounds. As demonstrated in the cases presented in this thesis, the production of compounds and the testing of compounds are usually performed in two different modules. First, the actual production of a compound is the initial objectification of a scientist's ingrained knowledge. When a second scientist tests the compound for activity, not only is his or her ingrained knowledge objectified in the process, specifically with the production of test results, but the compound being tested is further objectified through the handling of it by another person.

This process takes place within the framework of a first-person plural group (Rescher, 1997) composed of biotechnology scientists, and, even narrowly, in the context of the strong tie provided by the knowledge value alliance[202]. Thus, the original objectivity bestowed on the knowledge that has been objectified is based on the bounded universalism[203] of the collaborative participants. If the findings pertaining to the production and testing of the compounds are published or patented, the bounded universalism of the knowledge value alliance members

[202] All knowledge value alliances can be characterized as manifestations of relatively strong ties, but the strength of the tie may vary between different alliances depending on the level of interaction and amount of exchange occurring between the members of the collaboration.

[203] As defined in chapter three, bounded universalism is the belief among a group of individuals, say a knowledge value alliance, in the validity of a piece of knowledge. As such, the validity of that piece of knowledge is universal to the members of the knowledge value alliance, but this universalism is bounded by those members. The piece of knowledge does not transcend this bounded universalism until it is validated by someone beyond the knowledge value alliance.

gradually expands toward more general universalism as the findings circulate to other scientists. As the knowledge becomes more universal, the members of the alliance form weak ties with other scientists and research groups that make use of the material found in the publications or patents that have diffused beyond the knowledge architecture.

9.2.1.2 Objectification versus Codification

There are two things that I would like to discuss in relation to this line of reasoning. The first point of contention revolves around this process being termed objectification rather than codification. I draw on the following two definitions in my argument: objectification is defined as the social validation of knowledge, and codification, following Cowan and Foray (1997), is defined as "the process of conversion of knowledge into messages which can be then processed as information" (p596). In this process, "[k]nowledge becomes transferable *independently of the transfer of other things*…" (Cowan & Foray, 1997, p597 – emphasis added). Where objectified knowledge may be transferable, it is not transferable independently of other things.

The second point, while it may not be as contentious as the first, certainly deserves elucidation. I must clarify that the process of objectification is an activity that retains, rather than obliterates, the ingrained knowledge it serves to represent. The two points are, indeed, intertwined (i.e., one cannot be explained without the other).

In showing how the process of making ingrained knowledge objectified is not the same as codifying that knowledge, I use Langlois' (2001) three positions that explain why codified knowledge is not necessary for knowledge reuse, or even necessarily conducive to economic activity. Following Boisot, (1995) and Saviotti (1998), Langlois (2001) defines codified knowledge as "…knowledge that has been (or can be) converted into symbols for easy transmission, replication, and storage" (p78). He argues that the literature praising knowledge codification misses three crucial points:

1. Generality and abstractness[204] does not always require codifiability.
2. Knowledge can be externalized and made more mobile in ways that do not necessarily involve codification.
3. Social institutions are often valuable precisely because they circumvent the process of codification.

Each of these points is supported by evidence presented in this thesis.

Position One: Generality and abstractness do not always require codifiabililty

The design for purpose work that comprises the craft of biotechnology requires the utilization of distinct skills and fields of science. Biotechnology is, indeed, a highly specialized area of work. And, as Gulbrandsen (1997) contends, "[s]pecialized factors involve narrowly skilled personnel, knowledge bases in particular fields, and other factors with relevance to a limited range of or [in] a single industry…An important development in most industries is the increasing importance of advanced and specialized factors" (p122). Significantly, however, much of the knowledge used biotechnology is abstract[205], being abstruse and difficult for someone from outside of the area to understand (Lexico Publishing Group, LLC, 2004), but it is also quite general in its applicability.

The practice of rational drug design is applicable across an array of agendas. It depends to a large extent on the theories generated via computational chemistry. To the extent that computational theory and informatics has invaded the practice of biotechnology, the practice itself can be said to be general and abstract. For instance, the theories derived via the use of

[204] Langlois (2001) discusses generality and abstractness in terms of tacit knowledge not being idiosyncratic. He notes that knowledge of the Chinese language is a tacit skill, but it is highly abstract in nature, general in applicability, and far from idiosyncratic (being shared by over a billion people).
[205] This becomes particularly evident when considering three definitions of "abstract" offered by Lexico Publishing Group, LLC (2004). Abstract is defined as: 1) not applied or practical, but theoretical, 2) thought of or stated without reference to a specific instance, and 3) difficult to understand. Indeed, there are many university courses offered on the theoretical aspects of biotechnology, one can think of biotechnology without application to a specific instance (a discussion on gene manipulation does not have to involve what genes are being manipulated or for what purposes, but may only be centred on how the technique is done), and biotechnology can be difficult to understand, particularly for people without the requisite ingrained knowledge. To the extent that the process of knowledge production itself, as it occurs in the mind of an individual, is difficult to define (as discussed in section 9.2), it is also abstract.

computational chemistry are indeed abstract, needing the production of physical compounds in order to be proven to be correct. Fujimura and Fortun (1996) detail a related story about the division between two branches of biology intimately related to the practice of biotechnology, which demonstrates the generality and abstractness of the technology.

> Computational theoretical biologists use computers in their "dry labs" to construct theories of nature. Since they use the sequences submitted by molecular biology and biochemistry laboratories, they are often viewed as "feeding off" the detailed labors of "wet lab" researchers. In one case, theoretical computational biologists submitted a paper to a journal arguing for a functional relationship between two proteins on the basis of some computer work and "thinking". The biochemical researchers who refereed the paper rejected it on the grounds that there was no experimental "wet lab" work to support the "speculation" (Fujimura & Fortun, 1996, p165).

The division between computational chemistry and synthetic chemistry is no different than that in the story told by Fujimura and Fortun. Courses on computational chemistry are taught at the theoretical level in universities. Computational chemistry is central to the application of rational drug design. Rational drug design is a common, general, abstract practice in biotechnology. Hence, the knowledge used in biotechnology can be considered to be abstract.

With this type of knowledge in mind, it becomes apparent that knowledge value alliances can be separated and recombined as modular architectures because of the generic applicability of the knowledge associated with biotechnology. Take for instance the various sciences discussed in this report, with one being synthetic chemistry. This type of science involves abstract knowledge, but it is applicable in any modular arrangement attempting drug design, rational or otherwise. And, indeed, it is useful in a range of other endeavours not specific to drug design. It was used in all four cases studied during this investigation. Furthermore, the knowledge pertaining to this science does not *have to be* codified to be reused. It does not *have to be* written down anywhere, although it usually is (scientists use recipes). *It simply has to exist in the mind of the performing scientists*.

The knowledge does, however, have to be objectified[206]. A scientist's ability to contribute in a knowledge value alliance is gauged on previous objectification, in which the scientist used

[206] For example, a scientist can produce monoclonal antibodies without the recipe, provided he or she is experienced enough to do so. The monoclonal antibodies produced are objectified knowledge. They are available for others to see and examine. The process, although it may not have been dependent upon

his or her ingrained knowledge to produce objectified material (methodologies, drugs, drug leads) that was available for evaluation by an architect, or other potential collaborator, searching for that scientist's specific capabilities. A scientist's ability to contribute is also judged by current objectification, whereby the scientist uses his or her ingrained knowledge in a current endeavour to produce material that progressively moves the alliance toward the desired outcome of the collaboration.

These types of objectified material, however, are still evaluated from the framework of ingrained knowledge. In addition, following objectification, the material or knowledge is still reflective of the ingrained knowledge by which it was produced. A three-dimensional structure of an enzyme is evaluated by x-ray crystallographers and computational chemists, and the structure itself reflects the ingrained knowledge of the scientists who produced it. As Knorr-Cetina (1981) suggests, "…the products of science are hybrids which bear the mark of the very *indexical logic* which characterizes their production" (p33 – emphasis her own).

This conflicts with the Gibbons et al (1994) model of Mode 2 knowledge, in which knowledge developed in a transdisciplinary context, like that of a knowledge value alliance, is proposed to be a contribution to knowledge in general, but not to disciplinary knowledge. The evidence presented here, in the cases in this report, suggests otherwise. The high quality leads produced in the CMBB-Nereus alliance can be seen as contributions to the fields of chemistry and marine microbiology used in their production. Drug leads from the application of rational drug design offer contribution and advancement to the fields of enzymology, x-ray crystallography, computational chemistry, biochemistry, and the other various scientific disciplines that were drawn upon in the production of the lead. This is so because the final product, as Knorr-Cetina contended quite some time ago, bears the mark of the indices, or scientific logic, used in its production.

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codification, results in codification as it still involves a lot of writing to record results along the way. This is a legal requirement in most laboratories. Codification is not necessary, though, for the process to occur. For, as Henderson, Orsenigo, and Pisano (1999) suggest, the exploitation of biotechnology requires the mastery of a large body of tacit knowledge that cannot be easily acquired from the literature, but rather must be developed through "learning by doing". (Zucker, Darby, & Brewer, 1998; Pisano, 1996).

As Langlois (2001) suggests, "[b]ecause abstract knowledge can be applied widely, innovation is no longer tied to trial-and-error learning in particular concrete circumstances. And individuals can increasingly *specialize* in the production of new knowledge..", whereby this specialization is the ability to combine the most distant and dissimilar objects (p82 – emphasis his own). Take for instance, the testing of TB96 (the anti-bacterial compound produced in the IBS-amrad alliance) as an anti-viral agent[207]. This cross-testing came about because of the amrad scientists' abstract and general knowledge of virology, cross-testing, and drug design. The results from the test, however, are contributions to these areas of knowledge, contrary to the Gibbons et al (1994) argument. The knowledge used to produce the test results, or the resulting objectified knowledge, may have been abstract and general in applicabililty, but the test results themselves are contributions to the specific areas of science used in the production of the knowledge.

Position Two: Knowledge can be externalized and made more mobile in ways that do not necessarily involve codification

It is here that Langlois' second rule comes to fruition. The scientist's ingrained knowledge is made explicit, in the circumstances discussed above, not necessarily through codification, but via the production of an object tangible to others. It is also made explicit through the development of technology that is made available to other scientists through demonstration, as in the CMBB-Nereus case, while still "bearing the mark" of the science by which it was produced. It is not, as it would be if codified, converted into messages that are transferable independently of the transfer of other things, including techniques or compounds.

Even when patents or publications are taken into account, the knowledge is not always codified in these repositories, but rather, is sometimes objectified. In writing a journal article, a scientist does not script the ingrained knowledge used in the production of a compound or a

[207] Recall that TB96 was developed as a compound to act against vacomycin-resistant bacteria, but because of the ability of the amrad scientists to recognize the potential of TB96 as a potentially active anti-viral compound, thus connecting "distant and dissimilar objects" (Langlois, 2001), it is being pursued as a promising compound capable of targeting HIV integrase.

three-dimensional structure of an enzyme. The main purpose behind publication is to signify that the compound, three-dimensional structure, or other drug-related element exists. For example, in the work pertaining to the IBS-Novogen alliance, Faragalla et al (2003) produced a paper on their findings that reads, "[w]e have developed pharmacophores to aid inhibitor design for both human types I (preliminary) and type II 5-α-reductase isozymes and also the rat type II isozyme" (p83), emphasizing that the pharmacophores exist.

In the case of patenting, ingrained knowledge can also be objectified, instead of codified. A patent provides a mechanism for objectification by claiming the existence of the knowledge and allowing one or more scientists to lay claim (and potentially earn returns) on that knowledge. This is particularly evident in recent laws that have allowed biotechnology inventors to place a culture in a designated repository in lieu of detailing the process used in developing the patentable knowledge (cf. Eisenberg, 1987; Zucker, Darby, and Armstrong, 1998), thereby objectifying the knowledge without codification.

A patent can also create an instance where knowledge is codified, particularly when the technique being patented is described in detail. The passage of the law in which patenting scientists can provide a culture instead of a description of the relevant knowledge provides a mechanism through which scientists can build a more substantial shield against appropriation and creative replication of their potentially valuable knowledge. Even when knowledge is protected by a patent, whether the patent was awarded after submission of a culture or a detailed explanation of the knowledge production process, scientists still seek to safeguard it from appropriation via creative replication[208]. Knowledge can indeed by made mobile and externalized in ways that do not involve codification, but once codified, the appropriability alarm bells start to ring.

[208] A scientist with the requisite ingrained knowledge can reproduce a patented bit of knowledge in a manner that avoids patent infringement, but still allows the knowledge to be employable. As Zucker, Darby, and Waguespack (2001) note, "[s]ignificant parts of knowledge are difficult to protect through formal mechansism, being too new to codify easily…or better protected through secrecy of some kind, as in cases where it is easy to find a 'work around' way to duplicate a product using a different set of procedures than is specified and protected in a patent" (p10).

Position Three: Social institutions are often valuable precisely because they circumvent the process of codification

Where knowledge is codified, rather than objectified, the knowledge value alliances practising codification risk their most prized possession, the basis of their future potential returns, the material that many collaborations have invested upwards of AU$1,000,000 in creating – the knowledge resulting from the amalgamation of the complementary resources of the collaborative participants. As Langlois (2001) notes, "…social institutions are often valuable precisely because and to the extent that they *obviate* the codification of knowledge" (p83 – emphasis his own).

If knowledge is codified, rather than objectified, thus becoming easily replicated and transmitted independent of other things, it opens the door for appropriation. And, as evidenced in the cases presented in this thesis, members of a knowledge value alliance will go to great lengths, even to the extent of the exclusion of fellow members of the collaboration, to prevent this from happening. Recall the PI-88 incident in the IG-Progen alliance. PI-88 was a first generation drug developed in the collaboration between Progen and scientists at the Australian National University. Some of the information on PI-88 (particularly market-sensitive information like the results of clinical testing), although it was potentially related to the work of the IG-Progen research agenda and may have possibly served to steer the IG scientists in different directions, was not shared with IG. Vignette Two paints a similar picture.

Vignette Two

Case D
The Knowledge Value Alliance
between
the Institute for Biomolecular Science (IBS)
and
Novogen

The technology platform specific to the industry partner in the IBS-Novogen alliance is known as the Novogen Isoflavonoid Technology Platform (Novogen, 2003). The company maintains an extensive library of synthesized and semi-synthesized isoflavonoid compounds, which, according to Husband (11 December 2003 – personal interview), holds over 100 compounds. IBS has contributed five or six of these compounds over the last four years. There are, however, other contributions made by IBS.

Renate Griffith is involved in the computer assisted design aspect of the alliance. She also performs this same role in the IBS-AMRAD alliance. Her duty includes collecting little bits of information that are put into a computer program, which enables the prediction of structures of compounds that will effectively target the desired part of the enzyme. Bremner is involved in synthesizing the compounds, and Faragalla is also engaged in this type of activity, while supplementing it with testing procedures that she developed while spending time at Novogen. Novogen has also tested Faragalla's compounds in cell-based anti-tumor assays (Bremner, 12 February 2004 – personal communication). Faragalla's role in the project is centred on determining what structures are important and making compounds (Faragalla, 9 January 2004 – personal interview). The alliance aims to discover novel molecules with useful biological activity. Bremner sees the results of the compounds developed at IBS and tested at Novogen, but does not see all the results of other molecules in the isoflavonoid library.

Bremner recently asked for access to the database, but Novogen declined his request. Novogen is considered to be an IP company and the value of Novogen is in making new discoveries. Consequently, it has to control its IP. IBS had wished to access the database to use Novogen's compounds in the development of a pharmacophore, which would make the pharmacophore more valid (because of the inclusion of additional compounds into the computer program) and more applicable to isoflavonoid compounds. Instead, IBS searched the literature for existing compounds to include in the development of the pharmacophore (Faragalla, 9 January 2004 – personal interview). Following the need to control IP (and avoid the overlap in activities performed in IBS and Novogen), the scientists at IBS have been asked not to use certain synthetic chemistry methods that Novogen uses. While this may limit the scientists at IBS, it also serves to make them better scientists because they have to find new ways of doing things (Faragalla, 9 January 2004 – personal interview).

The value of the alliance comes from the confirmation that it is possible to make molecules to target 5-α-reductase, which was the topic of the paper produced by Faragalla et al (2003). At the moment, Novogen is not planning to develop any of the compounds discovered at IBS. Husband commented that, even if Novogen never uses 5-α-reductase, the information may allow Novogen to develop another drug. "That is what science is all about, you never know where the important bits are" (11 December 2003 – personal interview). As Faragalla suggested, 5-α-reductase "is a good starting point, but there are better targets" (9 Janauary 2004 – personal interview).

Novogen is unwilling to share its intellectual property[209] with the scientists at IBS for fear of appropriation, not by the IBS scientists themselves, but by IBS' other collaborators who may inadvertently come across Novogen's IP. It is difficult to assess whether or not it would make any difference to the research direction of Bremner and his team of scientists if they were allowed access to the isoflavonoid library. Novogen, however, is willing to forsake the potential benefits afforded by such access in order to protect the company's IP.

9.2.2 The Reuse of Knowledge

What is also discernible from Vignette Two is that once objectified, knowledge can be reused. Husband's suggestion – that the compounds developed at IBS have no immediate value, but it is difficult to say whether they may be of use in the future – indicates that the compounds produced in the collaboration that are shown to inhibit 5-α-reductase or have anti-cancer activity may be reused for other purposes at a later point in time. Such reusability of objectified knowledge was also found in the three other cases. The technology for capturing marine microbes, culturing them, and growing them for testing that was used in the CMBB-Nereus alliance is reused repeatedly. TB96, the compound developed as an anti-bacterial agent in the IBS-amrad collaboration, is being reused and developed as an anti-viral agent. The testing technique amrad developed in its collaboration with the Victorian College of Pharmacy allowed TB96 to be tested as an anti-viral agent. In the investigation of the IG-Progen alliance, interviewees from both sides of the collaboration detailed instances in which objectified knowledge is reused. Von Itzstein suggested that synthetic methods for generating a particular functional entity may be reused in different projects (29 September, 2003 – personal interview). Don noted that the large molecules produced at Progen that are not suitable for inclusion in a drug are reused in research into how molecules interact (8 December, 2003 – personal

[209] Note here that intellectual property can be in the form of either objectified or codified knowledge. If it exists as a compound or a technique of which the mechansisms for production reside only in the mind of practising scientists, it is objectified. If there is a detailed written description of the mechanisms for production existing in a patent or elsewhere, it is codified.

interview). Objectified knowledge, then, in the form of technology, compounds, or synthetic methodologies, is reused in knowledge value alliances.

In addition, the ability of various modules of scientists to be separated and recombined suggests that the scientists' ingrained knowledge is also reusable. And, as Tsoukas (1996, p13 – emphasis his own) contends, "the more practitioners *invent* new ways of using their resources (themselves included), the more services they can potentially derive" (Soros, 1987; Tsoukas & Papaoulias, 1996). This reuse of knowledge through the invention of new ways of combining resources allows for the creation of economies of scope, whereby gains accrue from the repeated configuration of the same technologies and skills in various ways to meet the demand of the market (Gibbons, et al, 1994).

It is important to note here that knowledge value alliances are producers of intermediate goods, drug leads that are usually licensed to large pharmaceutical firms for further development. It is these large pharmaceutical firms, in conjunction with the ill patients, that are creating the demand for the products produced by knowledge value alliances. In meeting these demands, public standards, like rational drug design that can be used across various alliances to amalgamate the variegated knowledge bases of different scientists, allow for the creation of external economies of scope, much like the ones discussed in Langlois and Robertson (1995). Not all alliances utilize rational drug design as a design rule[210], however. To the extent that more alliances adopt this approach to drug design, external economies of scope may become a more prominent feature in the biopharmaceutical industry.

Within the current external context of the knowledge value alliances, there still exists a fiercely competitive climate that sees certain alliances and firms effectively participate in a cycle of accumulation (Latour, 1987) to displace other firms and alliances. Under the auspices of this cycle of accumulation, displacement occurs within alliances. This type of displacement was illustrated in Novogen's restriction on IBS' access to the company's (Novogen's)

[210] The CMBB-Nereus alliance does not employ rational drug design. The four cases studied in this investigation are not necessarily representative of the entire population of knowledge value alliances (i.e., I did not use statistical sampling methods to pick them). Further work would indeed be necessary to determine the extent of use regarding rational drug design in knowledge value alliances.

isoflavonoid library. Displacement also occurs across alliances. These acts of displacement appear to be an influential feature in the game of Biotechnology Bingo, and are thus worthy of additional discussion and analysis. This is the subject of the third section of this chapter, The Operation of Displacement.

9.3 The Operation of Displacement

The ability to reuse knowledge allows for displacement. Displacement occurs with the resolution of a specific technological problem. It appears in two forms. Within a knowledge value alliance, it is the eradication of the need to continue to work with those who contributed to the resolution of the problem because, once resolved, the knowledge relating the problem is appropriable. Within a knowledge value collective, it is the competitive elimination of those scientists from the game who are seeking to solve the same or a similar technological problem.

Displacement within the knowledge architecture occurs as a result of the reusability of knowledge produced in the knowledge value alliance. It is premised on the dispensability of university scientists. Displacement of other alliances and firms, or external displacement, occurs through a cycle of accumulation (Latour, 1987) and the resolution of one or more technological problems. External displacement, however, is usually achieved by the industry partner alone, without the university scientists, and is dependent on one of Baldwin and Clark's (2000, 2003) modular operators, namely porting. In a rare link between modular processes and the sociology of knowledge, porting allows for Latour's (1987) fifth mode of translation: becoming indispensable.

9.3.1 Displacement within an Alliance

Displacement within the knowledge alliance occurs because knowledge has been objectified and made into a form that is mobile, stable, and, most importantly, combinable (Latour, 1987). Although, under Cowan and Foray's (1997) definition of codification, codified knowledge is mobile, stable, and combinable, knowledge does not have to be codified to meet

these standards. Under this definition, however, it moves freely and independently of other things, or objects. In the case of objectified knowledge, it is the actual object that moves, remaining stable and combinable. Objectified knowledge, as argued previously, contains the ingrained knowledge of its producer. It is a "thing" (Latour, 1987), a black box from the standpoint of those who use it. Once produced, it becomes possible (with the possession of and rights to objectified knowledge), to displace, or eradicate the need for, the producer of the objectified knowledge.

Displacement in knowledge value alliances refers to the fate of university scientists after their production of objectified knowledge, and there seems to be a tolerance for it among some of the university scientists investigated during this study. While it is difficult to say how entrenched this tolerance is, where it stems from, or whether or not the scientists even have a sense of being displaced, the act of displacement is apparent in the cases. Vignette Three provides an example of the type of displacement found within a knowledge value alliance.

Vignette Three

Case D
The Knowledge Value Alliance
between
the Institute for Biomolecular Science (IBS)
and
Novogen

The IBS-Novogen alliance was described by Husband (11 December, 2003 – personal interview) as a structured, controlled relationship that involves frank discussion and exchange of information between the members of the alliance. Husband has not worked with IBS in the past, and accepted Heaton's (the senior chemist at Novogen) word of trust in relation to Bremner's ability to perform. In nearing the end of the collaboration, Husband has adopted a view of Bremner as a "well regarded and clever scientist" (11 December, 2003 – personal interview).

The collaborative agreement is actually between the University of Wollongong and Novogen, not IBS and Novogen, or Bremner and Novogen. Bremner, under this arrangement, has agreed to assign all rights to the intellectual property developed in this alliance to Novogen. In return, Bremner receives publishing rights (Husband, 11 December, 2003 – personal interview). As Husband explained during his interview, "It takes experience to know how to structure these things so that both parties are protected" (11 December, 2003).

Faragalla, the PhD student from IBS involved in the alliance, is bound by the same agreement as Bremner. Faragalla has to assign the work of her thesis to the company, Novogen in this case. "Novogen will only collaborate if the Institution [the company] owns the IP" (Husband, 11 December, 2003 – personal interview). There are, however, particular stipulations involved with working in a collaboration that involves PhD students. Husband (11 December, 2003 – personal interview) stated that these stipulations amount to the signing of agreements up front regarding the ownership of intellectual property and the moral obligation of being sensitive to students' needs, recognizing that they need to finish in a reasonable period of time. "The student has to present the work in a thesis, and must be allowed the freedom to do so. Agreements must be signed up front, otherwise it can hold up the publication of work" (Husband, 11 December, 2003). In discussing these matters, Husband reiterated that there is a difference between what should be kept secret and what is intellectual property. "Faragalla can't sell the information [or rather knowledge that she has produced under the collaborative agreement] for commercialization, but it is not secret because Novogen has a patent" in this area of knowledge (Husband, 11 December, 2003). And, indeed, the information or knowledge is not secret considering the publication of Faragalla et al (2003).

Once intellectual property, which can be conceptualized as a form of objectified knowledge (as I have been calling it), is produced, the university scientist is no longer needed. Once the IBS staff members produced objectified knowledge in the form of compounds that effectively targeted 5-α-reductase, they become dispensable. They are set to be displaced and left with publication rights when the collaborative contract expires. With the ownership of

intellectual property rights, whether this is through a patent or contractual agreement, the firm can effectively make use of the objectified knowledge without the university scientist.

Even in the case where a patent has been taken out, and the patent is jointly held by university scientists and the industry partner, the university scientist is typically precluded from further work after the objectification of his or her knowledge, with the result of compensation usually being royalty or licensing fees being paid to the university, which may eventually trickle down to the university scientist(s). A similar incident of displacement is occurring in the IBS-amrad alliance. Boyle, the PhD student from IBS, has assigned all of the intellectual property pertaining to his thesis to amrad and the University of Wollongong. His name is on the patent of compounds discovered by the IBS scientists. Upon completing his thesis, however, he will move on to a new endeavour and amrad, possibly, but not necessarily, with the help of IBS, will continue to work on these compounds.

The firm then embarks on a cycle of accumulation, using the recombinability principle of modularity, because the work is now protected by a patent, to collaborate with other university scientists, testing laboratories, and eventually, pharmaceutical firms in the final stages of refinement, clinical evaluation, and if all goes well, large scale production, marketing, sales, and distribution. Through this process, the various collaborators of the firm are displaced, while the firm itself becomes more indispensable, particularly in the eyes of large pharmaceutical firms who want to work with the compound or drug lead on which the firm is accumulating knowledge, and even more so in the eyes of the patients needing the drug. Indeed, this process is very similar to the common story of appropriability. Scientists and other contributors tolerate displacement because the alternative is having no input at all. The scientists and other contributors are not in a position to carry out the process from discovery to development alone. They are, however, situated in a system that creates an impetus for them to offer input where they can.

One method to avoid displacement that is evidenced in this report is the strategy utilized by Fenical and Jensen at CMBB, not to mention a host of other university biotechnologists in the United States, particularly in California. The possibility of the displacement of the CMBB

scientists (and the University of California, San Diego, for that matter) was evident in Jensen's suggestion that the discoveries made at CMBB are based on a scaffold, but there is the possibility of the loss of the original derivative. Once Nereus takes over the discovery, the scientists at the firm probe the scaffold and open up the possibility of finding a new molecule with less toxicity or increased efficacy that excludes the original derivative (Jensen, 7 July 2003 – personal interview). By founding Nereus and retaining ownership in the company, however, Fenical and Jensen avoid displacement. They become *part of* the firm's cycle of accumulation, rather than being dispensed by it[211]. In other words, they increase their ability to appropriate the rewards flowing from their scientific activities.

9.3.2 Displacement of Competitors

Through this cycle of accumulation, firms aim to displace rival firms. They do so by solving technological problems first. This type of competition was illustrated in Vance's comments that,

> It could've happened that six months after we started, some company published on or patented a drug strictly for the enzyme, so you've been blown out of the water before you even start. Or, someone publishes that they've already solved the structure of the enzyme, and if it's an academic group, they could well have put that in the public domain, and then, that would blow you out before you've even started (29 September 2003 – personal interview).

Solving a technological problem prior to the announcement of a competitor's successful resolution allows a firm, or alliance, to procure a patent on the resolution, effectively making the owners of the patent an obligatory passage point in the further development of a drug. The resolution of technological problems and the patenting of the knowledge pertaining to the resolution commence the cycle of accumulation.

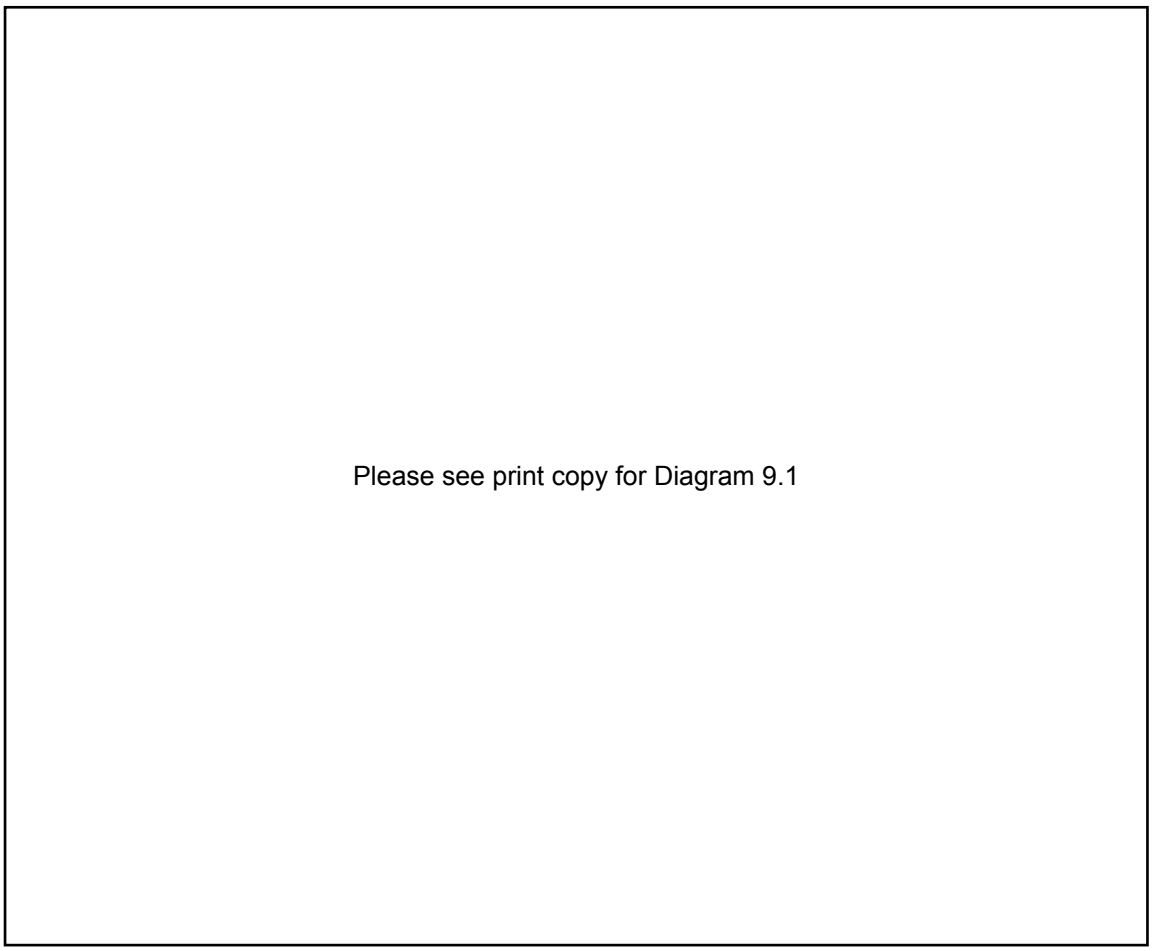
There are, however, several technological problems to be solved, multiple testing phases, and a plethora of regulatory hurdles to endure in the process of developing an actual therapeutic, which represents the need for additional accumulation of knowledge. Many dedicated

[211] In addition, they open the door to an endless debate on their conflict of interest in being part owners of the firm and, simultaneously, doing research on behalf of the firm, although Jensen did stress that the CMBB scientists do not do research for Nereus (7 July 2003 – personal interview).

biotechnology firms are not equipped to go this road alone. This is due not only to the extreme financial costs of the journey, but also to the lack of expertise in many organizations to do so. Firms, then, in the cycle of accumulation are forced into additional collaborative endeavours.

The firm, as a module in itself, must adopt Baldwin and Clark's (2000, 2003) sixth modular operator, porting. Porting amounts to the compatibility of a module with two or more systems made possible through the introduction of new visible apexes, translator modules, and overlapping systems (Baldwin & Clark, 2000, p346; 2003, p168). That is, a module becomes compatible with other systems through porting, and the requirement for such activity is the use of appropriate visible design rules (new visible apexes) and interfaces (overlapping systems). The key to this, though, is that the central module, the firm, remains central, yet compatible. The centrality of the firm comes from its patent ownership, while the compatibility of the firm with other collaborating modules is realized by the implementation of appropriate design rules and interfaces. Following Latour's (1987) fifth mode of translation, centrality in combination with compatibility creates the situation in which one must pass through the firm's position and help it to further its interests. This arrangement is exemplified in Diagram 9.1.

Diagram 9.1 The Firm as an Obligatory Passage Point



Source: Adapted from Latour (1987)

In Diagram 9.1, the firm is represented as the circle in the middle. The wavy lines are the collaborators that offer contributions in the form of objectified knowledge to the firm's cycle of accumulation, and the dark arrow signifies the therapeutic that can be derived from such a process. The firm, then, is indispensable in producing the therapeutic, or drug. The centrality and compatibility of the firm allow it to become the obligatory passage point in the route to drug development. The centrality is seen in all contributions passing through the firm, whereby the passage is the result of overlapping systems or interfaces. The ability of these contributions to fall through the passage point created by the firm, and not miss the target, falling off to the

left or right of the circle, can be attributed to the use of design rules (or visible apexes, following Baldwin and Clark, 2000) in the collaborations with the contributors.

Like the displaced university scientists whose objectified knowledge was used in the initiation of this process, contributors are also displaced. Their objectified knowledge is absorbed into the firm through the passage point, and they too are discarded. The firm appropriates their knowledge. This becomes apparent when considering that when a drug goes to market, there is usually one company's name associated with that drug. Although one could readily generate a list of all the contributors and collaborators that made the drug possible, the firm that successfully activated and completed the cycle of accumulation to the extent of becoming an obligatory passage point sees its name on the bottle of pills. This is partly how the game of Biotechnology Bingo is won. A collaboration or contribution has to be bought, though. Whether the firm wins the game also depends on how much it has had to pay for its inputs. As Granville (1977) notes, there is a big difference between winning on the one hand, and coming out ahead on the other. "The first rule of good money management for [B]ingo players is: DON'T SPEND MORE THAN YOU CAN POSSIBLY WIN" (Granville, 1977, p17- capitalization his own).

9.4 Conclusion

The rules of Biotechnology Bingo are to use the principles of modularity (including design rules, interfaces, repositories, and starting points) within a knowledge architecture to align the tasks and synthesize the knowledge of collaborative participants, aiming for a production and application of suitable and qualified knowledge to win the game. The manipulation of the rules follows a course of applying modularity where most appropriate, mediating through the production and function of knowledge as it moves from an ingrained state to an objectified state in order to effect displacement. An architect must have an understanding of the rules to manipulate them.

The basic principles of modularity, including the use of design rules, interfaces, repositories, and starting points, are always applicable. Interfaces, though, sometimes need to be supplemented with tact to ensure connection and communication between human modules. Strategies of modularity, such as recombinability, while applicable in some cases, are not always the right way to go. The strategy of recombination should only be utilized if a patent has already been secured on the work being performed within an alliance.

The game of Biotechnology Bingo is not merely about producing and applying knowledge. Rather, it is about the metamorphosis of ingrained knowledge into objectified knowledge via the production of journal articles, compounds, and technologies, and through the procurement of patents. Of course, it is also possible to retain intellectual property without patenting. This process of metamorphosis, whether it results in patents or not, allows knowledge to be reused and accumulated.

In the process of accumulation, dedicated biotechnology firms become the key accumulator, shedding collaborators and absorbing the objectified knowledge developed in collaborations. This cycle of accumulation involves the displacement of various collaborators and allows for the displacement of competitors. The result, if the cycle of accumulation is appropriately effected, is the indispensability of the firm in getting a drug to market.

An understanding of the basic tenets of Biotechnology Bingo, namely the use of a modular design process to produce and apply the necessary knowledge to win the game, offers a player the generic code that allows him or her to go beyond the information given, as Bruner (1964) puts it. Going beyond the information given entails the manipulation of the rules of the game to align plays with predicted future outcomes. Those who can successfully do so, tip the odds in their favour.

Chapter 10 Conclusion

Biotechnology Bingo is a game that is played at many levels. The "architecture as a Bingo card" structure that has been utilized throughout this thesis can be thought of as the knowledge architecture of a single knowledge value alliance. Conversely, it can be conceptualized as the process architecture of drug development as a whole, which involves many alliances. The former has been illustrated in a variety of ways in this report. The latter would entail each box on the Biotechnology Bingo card being considered a new collaboration or new step in the road to development[212]. That this works in both circumstances emphasizes the applicability and relevance of the metaphor of Biotechnology Bingo.

The theory that underwrites the metaphor is multi-faceted, drawing from a range of discourses and disciplines. Support for this theory, in terms of both development and explication, comes from the literature on modularity, the philosophy and sociology of knowledge, and all those scholars who have ventured to address teleology (or talked about purpose in general). Indeed, the theory of Biotechnology Bingo is about conceptualizing university-industry alliances as partially modular structures in which the industry firm is the dominant player, seeking and accumulating knowledge for the purpose of winning the game. The game ends (with the architecture perceived to be at the alliance level) when the collaborative goal has been achieved and when the benefits associated with reaching the goal outweigh the costs of doing so. When the architecture is conceptualized as the process of drug development, the game ends with regulatory approval and marketing of a drug developed through the application of biotechnology. In both conceptualizations, – that is, whether the goal

[212] As Arora, Fosfuri, and Gambardella (2001) contend, "…a natural degree of task partitioning exists among the various facets of pharmaceutical innovation" (p162).

is a promising drug lead or a fully developed drug entering the market – winning the game entails the ultimate displacement of those who could not keep pace with the leader, in addition to the displacement of those who sell their knowledge. These aspects of the theory were covered in detail in chapter nine.

The theory is also about the design for purpose nature of biotechnology. The design entails the production and use of knowledge, which occurs in different structures that are made possible by modularity. The purpose is composed of both explicit and implicit elements. In concluding this thesis, I re-address the "design for purpose mantra" in light of the findings of the research. This final piece of summative commentary is followed by a brief discussion of the limitations of the study, suggestions for future research directions, and the implications of the findings.

10.1 Design For Purpose & the Game of Biotechnology Bingo

Players in the game of Biotechnology Bingo are from different social worlds in the biopharmaceutical industry – universities, dedicated biotechnology firms, and large pharmaceutical firms. There are very distinct roles for each type of player in the game, with university scientists making valuable contributions at the beginning of the game, and large pharmaceutical firms offering the services necessary to bring a drug with significant potential to market. Dedicated biotechnology firms, however, play a central role. University scientists perform the applied or strategic science that gives the other players something to work with. Large pharmaceutical firms are adept at late stage development, gaining regulatory approval, and marketing and distribution. The dedicated biotechnology firm is the industry constituent, however, that packages objectified knowledge and mediates between discovery and development. Taking the work of all three constituents into account, the game of Biotechnology Bingo is a design for purpose affair.

10.1.1 The Design Process

Interestingly, I originally thought that the design process was centred on streams of knowledge that flowed among the various constituents of a knowledge value alliance. This conceptualization was based on the work of Albino, Garavelli, and Schiuma (1999), Decarolis and Deeds (1999), Gilbert and Cordey-Hayes (1996), Nonaka (1991, 1994), Nonaka and Takeuchi (1995), Santoro and Gopalakrishnan (2000), Steensma (1996), and Yli-Renko, Autio, and Sapienza (2001). Following Aadne, von Krogh, and Roos (1996), Berger (1967), Latour (1987), and Rescher (1997), I reformulated this conceptualization of "flowing" knowledge in a manner that acknowledged the mobility of a certain type of knowledge, that is, knowledge that has been objectified. The notion of the design process being premised on "flows" of knowledge led to the conceptualization of migratory knowledge offered in chapter three of this thesis.

There was, however, another view of knowledge proffered in chapter three, namely ingrained knowledge. This view centres on knowledge as structure, rather than as a fluid, transmissible commodity. Drawing mainly from the work of Maturana and Varela (1980), Varela (1992), and von Krogh, Roos, and Slocum (1996), ingrained knowledge was defined as embodied action – a type of knowledge that exists within the mind of the individual and is inherently and inseparably connected to and manifested in the thoughts and actions of the individual.

These two takes on knowledge, migratory and ingrained, were allied with Machlup's (1980) conceptualizations of knowledge as "that which is known" and knowledge as a "state of knowing", respectively. The result of this was the acknowledgement that the two forms of knowledge are not mutually exclusive. The design process encompasses and makes use of both migratory and ingrained knowledge. In the process of design, the basic principles of modularity, including design rules, interfaces, repositories, and starting points, are used to synthesize ingrained knowledge bases and articulate the task work of scientists in a knowledge value alliance.

10.1.2 The Importance of Structure

Findings from the research suggest that these knowledge value alliances are not only centred on the flow of knowledge, but are also structure-based, science-dependent endeavours. In the larger scheme of things, both knowledge value alliances and the game of Biotechnology Bingo itself are about reusing knowledge. A knowledge value alliance revolves around the transformation of ingrained knowledge into objectified knowledge, and the game of Biotechnology Bingo is won by the players who best and most appropriately accumulate the objectified knowledge and reuse it at the least possible cost.

The research supports and validates the constructs of ingrained and migratory knowledge. Ingrained knowledge is shown to be the substance that is at the base of the design process. It is the possession of requisite ingrained knowledge by collaborative participants that allows modular level tasks to be solved, with resolution of these tasks being integrated to achieve the desired output of the alliance. Migratory knowledge is found to be many things. It is objectified knowledge that can be seen in patents, publications, compounds, techniques, and so on. In the form of repositories and starting points, it aids collaborative participants in solving the technological problem specific to an alliance. It is the material that is accumulated by dedicated biotechnology firms that seek to win the game of Biotechnology Bingo.

The research presented in this thesis suggests that absorbing knowledge, accumulating, and reusing it are dependent on the flow of knowledge *and* the structure of the alliance. This is contrary to what Gibbons et al (1994) propose. These authors contend that,

> [i]mmediate access to knowledge is now more a function of networking and less of institutional position…Here again, *flows are more important than structures*, and the challenges for institutions now is to find new ways of supporting ever more complex and changing communication channels rather than to invest in costly, heavy, and inevitably rigid forms of institutionalization (p146 – emphasis added).

Based on the evidence presented in this thesis, I contend that what kind of flows one gets is dependent upon the structure through which the flows are operationalized.

In considering knowledge value alliances as partially modular arrangements, immediate access to knowledge is facilitated by the elements comprising the alliance. It is, indeed, about position and function within networks, but it is about the structure of the alliances too. Structure is a crucial analytical construct because the structure of the system, whether conceived of as an interorganizational form or individual minds, determines not only the meaning of data from the external environment, but also what is allowed into the system (Langlois, 1982; Maturana & Varela, 1980).

The structures of the knowledge value alliances presented in this report are premised on a division of labour. Different types of expertise and ingrained knowledge are necessary to solve the specified technological problem(s) of a collaboration, and consequently, achievement of the desired output of an alliance comes via the articulation of the work performed in different divisions, or modules. Because all knowledge, migratory, objectified, or otherwise, is evaluated with the types of ingrained knowledge and expertise existent within a knowledge value alliance, only data permissible by the system will be allowed to enter. Other data may enter, but they may also induce a restructuring of the system. This restructuring could come in the form of a recombination, substitution, exclusion, or augmentation of existing modules. Hence, *structures are at least as important as flows*.

Communication still plays a role because of the strength of the ties (Granovetter, 1973; Rogers, 1995) in any given alliance. Modularity, with its use of interfaces and design rules, mitigates the need for communication, but does not completely diminish it. What modularity does accomplish in full force is the avoidance of the investment in the "costly, heavy, and inevitably rigid forms of institutionalization" of which Gibbons et al (1994) speak. The modular knowledge architectures used in collaborations between university and industry are separable, recombinable, and temporary.

10.1.3 The Uncertainties of the Process

Nonetheless, architects of an alliance cannot avoid the costly aspect of research and development that is inherent to the collaborations in this study. Initiation of the game of

Biotechnology Bingo demands this investment. With industry usually footing the bill, at least in the cases I investigated (although many projects are also co-funded by government entities), the industry player (a dedicated biotechnology firm) is granted the title of central player in the game.

Even with considerable amounts of money being plugged into the design process, however, there are still specific hurdles of luck to be encountered. Architects of an alliance must find and retain suitable and willing participants for a potential collaboration (and the search costs of doing so may outweigh the benefits). Reputation and previous experience cannot always accurately predict ability to perform. Moreover, the problem to be solved in an alliance might not be doable in terms of the science and/or the requisite alignment of social worlds (Fujimura, 1987), but this cannot be determined prior to attempts to solve the problem.

The type of science being practised in the design process, which I have termed highly experimental, is cutting edge. The design process is about the resolution of novel problems, with very few precedents serving to demonstrate how the problem should be tackled or whether it is even resolvable at all. This creates a tremendous amount of uncertainty in the game of Biotechnology Bingo in terms of both input and output in the design process. Scientists cannot be sure of what types of input are required and thus, the output can be quite elusive.

Severe difficulties in trying to align the social worlds of industry and university scientists participating in a collaborative endeavour are the result of not knowing up front whether a particular scientific problem can be executed to plan. With industry partners providing the financial capital in many of these alliances, return on investment is a given expectation. With the achievability of a target scientific endeavour being uncertain, the return on investment cannot be guaranteed. The loss to a capital sponsor in the cases where the scientific problem proved not to be doable is of greater immediate significance than to the scientists who attempt the problem, but do not pay for the costs of executing it[213]. In such cases, the gap between the

[213] Sooner or later, however, the unsuccessful university scientists (those who have not been able to solve the particular technological problems that they hoped to or said that they could) will find themselves in a position of being unable to attract industry sponsorship and other research grants. Thus, they too have an

social worlds of the sponsoring partner and the performing partner remains entrenched. This is a problem that was identified in the work of Fujimura (1987) and it continues to plague scientific enterprises a decade and a half later.

10.1.4 The Purpose of the Process

When the purpose of the design process is considered, however, the social worlds of industry scientists and university scientists seem to be aligned. With the aid of various repositories (mainly patents and publications) and the use of ingrained knowledge, design rules, interfaces, and starting points, members of an alliance may be able to solve a specified technological problem. The different parties to an alliance can have disparate goals (such as in the CMBB-Nereus alliance), but the implementation of design rules and interfaces allows collaborative participants to work toward a unifying problem, which may resultantly fulfill the different goals of the members of the knowledge value alliance. The act of unification comes from the existence of a common purpose for the alliance. This common purpose has both explicit and implicit features. Table 10.1 displays the general classification of explicit and implicit purposes that are associated with a knowledge value alliance.

Table 10.1 Explicit and Implicit Purposes of a Knowledge Value Alliance

Explicit Purpose	Implicit Purpose
Solve technological problem	Gain social and economic value
Provide drug for ill patients	Displace competitors

As Gaskell and Bauer (2001) note, biotechnology is living up to its description as a strategic technology and many of us today are able to see the progress of biotechnology and

incentive to achieve, which is to avoid being reduced to teaching drudges, or such, with the consequent loss of reputation, power, and other trimmings of success.

pass judgment on the implications of such advancement[214]. The design for purpose activities employed in collaborations between university and industry in biotechnology are a social engagement. They entail not only the collaborative participants, but the ill patients who may potentially benefit should a drug be discovered in an alliance and subsequently brought to market. They also involve the competitors of the alliance who stand to be displaced should the alliance find success in attaining its desired output. The shareholders of dedicated biotechnology firms and the universities to which the scientists belong who hold reserves of economic and social value for the collaborative participants if they are successful in their collaborative endeavour should also be considered as part of the social engagement.

In addition, as Gaskell and Bauer (2001) note, the social engagement of a knowledge value alliance also sees the activation of special interest groups, the stirring of politicians in political and ethical debates that relate to the practice of biotechnology, and the sometimes naïve, sometimes well-informed commentary of laypeople offering their opinions. These latter social elements are not included in the immediate purpose of a knowledge value alliance, but they affect profits for a company and access for ill patients (and, indeed, profits and ill-patients are two immediate concerns of a knowledge value alliance).

It is with respect to the ill patients, competitors, shareholders, and universities that a knowledge value alliance directs its attention, and more importantly, how it defines its purpose. The design activities that circumscribe a collaborative relationship centre on a strategic initiative to accomplish a set of purposes. In the case of the knowledge value alliances investigated in this study, the set of purposes is divided into four elements, as indicated in Table 10.1 The explicit elements include solving a technological problem and bringing a drug to market. These elements are correlated with the implicit purposes of gaining economic and social

[214] These authors point out that, "[t]he pace of biotechnological R&D and the developing range of applications continues to accelerate. With the completion of the sequencing of the human genome, proteomics is now the focus of basic research. The breakthrough of nucleic transfer for cloning that led to the first cloned mammal, Dolly the sheep, has been found to be inefficient and new techniques of stem-cell cloning have been developed. Genetic testing is bringing the genetic information society closer as forensic, insurance and other uses of gene banks are identified. Transgenic animals are now ready for xenotransplantation and, in the pharmaceutical and agricultural areas, modern biotechnology continues to challenge traditional methods" (Gaskell & Bauer, 2001, p3).

value, and displacing competitors. The implicit elements, while they may define the purpose of a knowledge value alliance, are actually consequences or results of satisfying the requirement set at the explicit purpose level. Players in the game of Biotechnology Bingo, however, win by succeeding in the fulfillment of all of these purposes.

Some of the technological problems identified in this thesis are the collection and testing of compounds derived from marine microbes to determine their efficacy against cancer cells, the identification of a three-dimensional structure of an enzyme, and the discovery and development of compounds to target an enzyme. As explicit purposes of a knowledge value alliance, these types of technological problems are identified at the commencement of collaboration, or even in the process of negotiating the alliance. From the start, collaborative participants know what their aims are. They may not specifically know how to reach those aims, but they know that the aims exist, and that they define the work being performed within the alliance.

Resolution of a specific technological problem allows for the acquisition of economic and social value, the first implicit purpose of a knowledge value alliance. With the resolution of a technological problem, particularly if the problem is significant, comes the procurement of patents. Patents create economic value in two ways. First, they entitle the owner to licensing and royalty fees. Second, they are mechanisms for standardizing the resolution to a technological problem, whether the patenting process calls for codification or objectification. And, as Langlois (2001) argues, standardization is the key source of increasing returns. Once standardized, the solution to a technological problem can be reused in other collaborations and throughout the effort to get the drug to market, increasing the economic value of the resolution along the way. Economic value, in the case of dedicated biotechnology firms, also comes from increased shareholder interest when a future earning potential is communicated to the investment community via patent awards.

Social value is also bestowed on the members of an alliance who successfully solve a technological problem. Constituents of the social worlds to which the collaborative participants belong offer potential value for the collaborative scientists. Constituents of the academic arena

(including both administrators who provide promotional opportunities and peers who confer reputational status), grant social value to university scientists in the instance that a technological problem is resolved. This was witnessed in the cases presented in this thesis. For example, in the IG-Progen alliance, von Itzstein had gained a persuasive reputation from his discovery and development of Relenza, not to mention his reward of an Australian Federation Fellowship[215]. Similarly, Fenical from CMBB was well known and highly regarded for his work in marine biotechnology by many of the Australian researchers I interviewed.

It is important to note, though, that social and economic value are not always seen to be pursued in conjunction with one another. There is a tremendous amount of criticism that surrounds the activities of drug companies. Underlying the criticism is the belief that drug companies tend to pursue economic value in an unrelentless fashion, often to the detriment of social value. Barlett and Steele (February 2, 2004) suggest that,

> [p]artly because of EXTRAORDINARILY generous tax breaks but mostly because of high prices guaranteed by Congress, the U.S. pharmaceutical industry, year in and year out, ranks as the country's richest. Pfizer which for 2002 reported profits of $9.1 billion [U.S.$] on revenue of $32.4 billion [U.S.$], earned a return on revenue of 28%, a rate more than twice that of General Electric, nine times that of Wal-Mart and 31 times that of General Motors (p47 – capitalization authors' own).

The drug companies' favor for economic value over social value is demonstrated in the recent GlaxoSmithKline scandal (GSK). Early last year the president of the AIDS Healthcare Foundation (AHF) filed a complaint with the Competition Commission of South Africa against the British pharmaceutical company. Weinstein, president of the AHF, contended that "GSK's stranglehold on key AIDS drug patents and their unfettered monopoly pricing on these life-saving medications means thousands of deaths daily" (cited in Biotech Week, February 26, 2003, p11). Even more recently, the Australian Pharmaceutical Benefits Scheme (PBS) has come under attack in the free trade negotiations between Australia and the United States of

[215] Von Itzstein was awarded a Federation Fellowship following his work on the development of Relenza. "The fellowships are designed to attract and retain Australia's leading researchers, and outstanding international researchers, in key positions to lead world-class research teams in work that benefits Australia – economically, environmentally and socially. Under the Fellowship scheme each recipient receives a salary of around $1.125 million over five years. The Fellowship was awarded to further Professor von Itzstein's research into carbohydrates and carbohydrate-recognising proteins as drug discovery targets" (Griffith University, 2003).

America. The Australian Financial Review (September 4, 2003) reports that, "[t]he U.S. government has already received submissions from the U.S. pharmaceutical companies calling for deregulation of drug pricing in Australia…And this could create an Australian health system where the chronically ill and elderly will be forced to pay higher prices to fund a greater return to pharmaceutical manufacturers" (p14)[216].

In this thesis, I am, however, talking about the firms that are the intermediaries between large drug companies and university scientists. To the extent that these intermediary firms, or dedicated biotechnology firms, advance in their ability to take drugs closer to market, they may fall prey to the same criticisms directed at the large pharmaceutical firms. That is, once dedicated biotechnology firms have mastered the requirements for taking a drug through the phases of testing, regulatory approval, mass production, and marketing, as many of them aspire to do, they may need to find new ways to project the image of pursuing both economic and social value.

Nevertheless, many drug companies – and specifically many alliances between drug companies and university scientists – claim to operate under the auspices of the second explicit purpose identified in Table 10.1. They endeavour to bring drugs to ill patients, albeit at a substantial cost, as some the companies' critics suggest. Many of the researchers I interviewed, were familiar with and understood, to some extent, (that is, they had knowledge-of) the target disease they were seeking to control, inhibit, or cure. Indeed, the advances provided by the biotechnology discoveries of the past 15 years have allowed scientists to develop a drug to combat a specific disease, which is the target of the scientific endeavours from their very onset. Not only do firms stand to reap tremendous economic and social value should a drug be developed, marketed, sold, and consumed, but in the process, they also are helping people to live longer, healthier lives.

[216] Canadian pharmacies have also recently come under attack by U.S. drug companies and their political agents. Barlett and Steele (February 2, 2004) report that, "Pfizer is aggressively seeking a pharmaceutical blacklist, warning Canadian pharmacies that if they sell drugs to Americans, Pfizer will halt supplies of all its products" (p45). The Food and Drug Administration (FDA) is supplying pressure as well. "The FDA, charged with assuring the safety of the nation's prescription drugs, has sided with the [pharmaceutical] industry, coming down hard on the Canadians" (Barlett & Steele, February 2, 2004, p45).

Many drug companies do operate with the intentions of getting drugs to market as quickly as possible to presumably benefit ill patients. While this may be seen by some as the continued relentless pursuance of profits, for some activitist groups, such as the AIDS Treatment Activist Group (TAG), it is the answer to a quest for access to new drugs (cf Epstein, 1997). In fact, many drugs are brought to market with the ability to only stabilize a disease or inhibit a side effect of another therapeutic. The drug is actually made available to ill patients prior to developing it to the point of maximum efficacy. This is for the purpose of offering some immediate benefit to needy patients (in addition to gaining more immediate economic value). This is the case with Novogen's drug, Phenoxodiol. Novogen intends to continue work on Phenoxodiol after its development and release to market to make it more efficacious against ovarian cancer, the disease it is believed to target best (Husband, 11 December 2003 – personal interview).

Fast track drug approval is made possible by the U.S. Food and Drug Administration's 1997 early and expedient approval policy, whereby a drug development program – considered to be a "continuum from early preclinical and clinical studies through submission of a marketing application" (U.S. Department of Health and Human Services Food and Drug Administration, 1998, p1) – can be designated for accelerated approval. The requirements for such approval include a drug with proven potential to treat serious or life-threatening conditions by way of:

- Having an effect on a serious manifestation(s) or serious symptom(s) of the condition
- Having the ability to improve diagnosis or detection of the condition, with scientific data providing a strong basis for a presumption that the improvements in diagnosis or detection of the condition will lead to improved outcomes
- Having the ability to prevent the condition, with scientific-based reasons to assume that prevention of the condition would prevent its serious consequences

- Having the ability to treat a condition while avoiding the side effects of currently accepted treatments of the condition, if such side effects are considered serious (U.S. Department of Health and Human Services Food and Drug Administration, 1998, p5).

This program allows drug companies to offer immediate benefits to ill patients and fulfill the second explicit purpose identified in Table 10.1.

While the explicit purpose of bringing a drug to market early and quickly is ostensibly to benefit ill patients, the implicit purpose is the displacement of competitors. As discussed in this thesis, displacement occurs via the accumulation of objectified knowledge and the ability to reuse that knowledge. Although the displacement I have been referring to is the displacement of competitors using similar techniques and sciences to target a specific disease, there are multiple types of therapies in combating serious illness. Take for example Progen's approach to combating prostate cancer with isoflavonoid-based molecules. Cytopia Inc., a small biotechnology firm in Melbourne, Victoria (Australia) has also recently developed and advanced compounds for the treatment of prostate cancer, but they are not based on the isoflavonoid scaffold. Thus, it becomes apparent that the implicit purpose of displacement will continue to be on the agenda of those involved in the game of Biotechnology Bingo until these serious and life-threatening illnesses have been cured. Where one firm or alliance may be successful in treating the symptoms of a disease, another firm or alliance may be able to prevent or cure the disease. The race, then, turns to favor the biotechnologists who can create and develop the most efficacious drug. And, indeed, we may see more alliances where parties with complementary therapeutics team-up to target diseases in multiple ways.

The game of Biotechnology Bingo is unpredictable. Playing the game requires awareness of the rules and an ability to manipulate the rules when necessary. It also necessitates having a contingency plan to fall back on should displacement by a competitor occur. It is a game that promises to benefit humankind, but beneath all of the promises and hoopla are enormous rewards for the winners. As one respondent stated, "you can invest AU$25 to AU$35 million on research and if only one molecule is successful, you are looking at the possibility of AU$100

millions in return each year. You only need one hit, but until you get that hit, it is still speculative" (Husband, 11 December 2003 – personal interview).

So, who plays this game? One would be inclined to say risk-takers – probably the same people who, if they weren't stuck in a laboratory all the time or behind a desk worrying about the company's "burn-rate", would be at the top of Mount Everest. This type of question, however, can only be answered by additional research. The next section of this chapter, which includes the discussion of the limitations of the study, suggestions for future research directions, and the implications of the findings, aims to provide a footing for and inspire future research in the area of collaboration involving biotechnology.

10.2 Limitations, Future Research Directions, & Implications

The generalizability of the theory presented in this thesis is limited because of the case study approach used in this research. As a result, there is work still to be done. Future research directions should involve different methodologies, including both qualitative and quantitative, and cross-disciplinary work. The implications of the findings from the current study, although limited to what Yin (1994) calls analytical generalization, are two-fold and contentious.

The multiple case study methodology employed in this project followed a replication logic (Yin, 1994), seeking to find similar results across the four cases studied. The study generated a considerable amount of data, which supported the theory of Biotechnology Bingo. The data collected in this study allowed for a formulation of the rules of Biotechnology Bingo, a means for the manipulation of the rules, and the strategies for winning the game. Moreover, the application of the principles of modularity in knowledge value alliances was demonstrated and a concrete explanation of the production of knowledge was developed.

This work, however, is limited in three distinct ways. I cannot definitively determine the applicability of this theory on a larger scale until it is tested in additional cases. Furthermore, there was a variation in depth of investigation among the four cases presented in this thesis. Ideally, I would have liked to observe the meetings of all four alliances, but time and financial

constraints prohibited me from doing so. Additional data that could have supported the theory, or alternatively provided counter points to the theory, may have been yielded by such observations.

As a final limitation, it is important to reiterate that I am not a scientist. I do not claim to be one, although I do purport to have developed an understanding of the practice of biotechnology for the purposes of drug development. My limited insight into the scientific practices discussed in this thesis could have hindered or helped this study. I may be misinterpreting some of the scientific activities described in this thesis due to my lack of knowledge in the area of science, although the reports appearing in this thesis were reviewed by respondents for the purposes of reliability. My lack of knowledge in science is, however, what got me through the door of many of the respondents. They did not feel threatened in telling me about their work. Nonetheless, it would be interesting to see if someone with more knowledge in the area of science than myself would arrive at similar findings.

This is not the most important area for future research pertaining to collaborations between university and industry in biotechnology though. Longitudinal research on the discovery of a drug through to marketability would provide evidence of the numbers and types of collaborations necessary to complete the cycle, while also affirming or discrediting my theory about the dedicated biotechnology firm being the obligatory passage point in such activity. Future research should also include comparative studies of modular recombinability versus idiosyncratic or synergistic specificity – or firms and university scientists that frequently separate and recombine with other parties versus collaborations that maintain core partners – to assess the efficacy of the different strategies. I also call for comparative studies of the type of support a collaboration receives, including industry versus government funding, and the implications of using broad-based goals, such as the ones found in the CMBB-Nereus alliance, or strict, milestone-guided goals, like the ones found in the IG-Progen collaboration.

The use of different methodologies and cross-disciplinary research are also in order. Quantitative work could be performed to assess the frequency of alliances using rational drug design as a standard, which would allow a researcher to explore the existence of external

economies of scope and the impact that these have on the notion of displacement. It would also be interesting and rewarding to incorporate management, finance, and communications in a bid to look at how publicly traded dedicated biotechnology firms fare in getting a drug to market, with variables such as the price of their stock and media publicity.

With the conclusion of the current study and the suggested possibilities for future research, it is necessary to review the implications of the findings from the current investigation. This work has shown that in a time of increasing focus on knowledge, with theories and terms like the knowledge-based view of the firm, the knowledge economy, and knowledge capital pervading the literature on knowledge management, it is important to consider that the use of knowledge is not only about how it flows, from where or to whom it flows, but it is also about the structure and forms in which it exists. It is the structure that makes knowledge usable, reusable, and valuable. This goes against the grain of a lot of the recent work in the study of knowledge and interorganizational collaborations, however.

The implications of this study also include the acknowledgement that knowledge value alliances in biotechnology are not simply a matter of integrating complementary resources for the benefit of collaborative parties. They are, according to the theory of Biotechnology Bingo, a social engagement, requiring awareness of the actions of competitors and the needs of intermediate (pharmaceutical firms) and ultimate consumers (ill patients). Collaborations do not occur in some isolated and disconnected corner of the biopharmaceutical industry. They, instead, constitute a social level of the hierarchical arrangement of that industry, and thus, will impact not only the constituents of the biopharmaceutical industry, but on social actors beyond the industry as well.

Winning the game of Biotechnology Bingo, then, is about appropriately accumulating and using knowledge, and recognizing and reacting to the social influences that shape the game. It requires the utilization of a strategy that is conducive to the conditions of an unpredictable, uncertain context. Players need to be adept, skilled, and armed with a contingency plan, for it is not inconceivable that they will endure the downside of the luck associated with the game.

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APPENDIX A

Collaboration, Interdependency, & Length of Relationships

Table A.1 Types of Collaborations, Interdependency, and Length of Relationships

Type of Collaboration (Forrest & Martin, 1992)	Definition (Forrest & Martin, 1992)	Degree of Organizational Interdependency (Hagedoorn & Lundan, 2001)	Type of Long Lasting Relationship (Borzeda & Rizopoulos, 2001)
operating joint venture	an independent third enterprise formed by two firms, combining economic interests, profits, losses, assets and risks	highest	alliance
equity investment	an investment in a firm by a large established company	highest	alliance
client sponsored research contract	the small company is paid to conduct research on particular products or processes for another organization	medium	cooperation
Marketing/distribution agreement	an agreement whereby another company will market and distribute the firm's products	medium	explicit interaction
manufacturing agreement	an agreement whereby another company agrees to manufacture products for firms	low	explicit interaction
University agreement	an agreement with a university whereby the firm pays the university to conduct research on its behalf	medium	cooperation
Research institute agreement	similar to an university agreement, but with a research institute	medium	cooperation
collaborative R&D	an agreement between the firm and another company to collaborate on the development of specific products or processes	high	alliance
research and development limited partnership	a tax advantage investment vehicle which provides funding for new product R&D at no cost to the company	medium	implicit interaction
technology licensing (inward)	a contractual agreement by which the firm is granted access to another company's patents or technology for a fee	lowest	explicit interaction
technology licensing (outward)	the reverse of an inward technology licensing agreement, in which the firm receives the fee	lowest	explicit interaction

APPENDIX B

Study Questions

QUESTIONS TO BE ASKED OF THE STUDY PARTICIPANTS (UNIVERSTIY)

- How did the project come about?
- Was there a knowledge preparation process prior to project initiation (addressing who knows what, collaborators' expertise, what type of knowledge is needed for the project, where the knowledge is located-communication)?
- What is participant's background?
- What is participant's role in the project?
- What types of knowledge are used in the project (what are the sources of knowledge, any sources outside of project-journal articles, other projects, etc.-address appropriability-assimilation and exploitation)?
- Are there PhD students involved in the project (are they sponsored by the project, do they spend time at the company)?
- How does participant contribute to the development and flow of knowledge?
- Is participant aware of what happens to data, information or knowledge once it is sent/transferred/shared to/with industry partner (exploitation)?
- Where does knowledge exist?
- Does the participant internalize knowledge (can he appropriate his learning derived from the project for other purposes; does he keep his knowledge to him self/willingness to share knowledge)?
- What role does trust play in the flow of knowledge? (When knowledge is relayed to interviewee, does he take it as face value or judge it in relation to his own knowledge scheme)?
- What is learned in the process of collaboration in this project?
- Who does participant interact with regularly (both at university and at industry)? (This question entails the number of visits to the partner's site, the types of communication, communication language (lay-terms, scientific terms, etc.) and the regularity of contact.)
- What is the common scientific territory (equivocality and social capital) between the two parties (university and industry), if any (address goals, norms, expectations and common versus diversified knowledge)?
- Is the discovery process (basic R&D, scientific expeditions, etc) carried out jointly?
- Are functional aspects such as marketing or product toxicity considered in university participant's research endeavors (discuss time frame for awareness of commercial applicability)?
- What are the strengths and weaknesses of the project?
- Are there any communication deficiencies in the relationships between the two parties (use of common software)?
- Who is in control of the project (who makes decisions, who recognizes and evaluates pertinent knowledge, who defines problems)?
- What weight does the project hold in the overall R&D portfolio of the company?

QUESTIONS TO BE ASKED OF THE STUDY PARTICIPANTS (INDUSTRY)

- How did the project come about?
- Was there a knowledge preparation process prior to project initiation (addressing who knows what, collaborators' expertise, what type of knowledge is needed for the project, where the knowledge is located)?
- What is participant's background?
- What is participant's role in the project?
- What types of knowledge are used in the project (what are the sources of knowledge, any sources outside of project-journal articles, other projects, etc.- address appropriability)?
- Are there PhD students involved in the project (are they sponsored by the project, do they spend time at the company)?
- How does participant contribute to the development and flow of knowledge?
- Is participant aware of any knowledge needs or desires existing on behalf of university actors?
- Where does knowledge exist?
- Does the participant internalize knowledge (can he appropriate his learning
- derived from the project for other purposes; does he keep his knowledge to him self/willingness to share knowledge)?
- What role does trust play in the flow of knowledge? (When knowledge is relayed to interviewee, does he take it as face value or judge it in relation to his own knowledge scheme)?
- What is the learning culture of the organization (supporting overreach failures, environmental scanning, future focus versus past focus, knowledge more important than job title) (address knowledge viscosity and knowledge velocity)?
- What is learned in the process of collaboration in this project?
- What does the university partner learn from the collaboration?
- Who does participant interact with regularly (both at university and at industry)? (This question entails the number of visits to the partner's site, the types of communication, communication language (lay-terms, scientific terms, etc.) and the regularity of contact.)
- What is the common scientific territory (equivocality and social capital) between the two parties (university and industry), if any (address goals, norms, expectations and common versus diversified knowledge)?
- Is the discovery process (basic R&D, scientific expeditions, etc) carried out jointly?
- Are functional aspects such as marketing or product toxicity considered in university participant's research endeavors (discuss time frame for awareness of commercial applicability)?
- What are the strengths and weaknesses of the project?
- How satisfied is participant with the knowledge that is received (in terms of both provision and practicality)? Is knowledge targeted towards the industry partner's needs?
- Are there any communication deficiencies in the relationships between the two parties (use of common software)?
- Who is in control of the project (who makes decisions, who recognizes and evaluates pertinent knowledge, who defines problems)?
- What weight does the project hold in the overall R&D portfolio of the company (how does the CEO feel about the project)?

APPENDIX C

Principles of Interpretive Research

Table A.2 Principles of Interpretive Research

PRINCIPLE	INTENDED FUNCTION
1. The Fundamental Principle of the Hermeneutic Circle Dictates that all human understanding is achieved by iterating between considering the interdependent meaning of parts of the whole that they form. This principle of human understanding is fundamental to all other principles.	Two cycles of the hermeneutic circle are to be employed. The first cycle leads to a consideration of the role each data source plays in the construction of the entire case story, including the significance of the contribution, the validity of the contribution, and the meaning of the contribution. Each data source is considered a part in the whole perspective of the case context. The cycle flows directly into the second principle (the principle of contextualization). The second cycle relates to the preliminary understandings of the research, in terms of both agenda and theoretical outlay, of both the researcher and the participants. While it is not intended that the questions posed at level one be leading questions, it is recognized that participants may appropriate ideas from the researcher and vice versa and it is important to identify where this has occurred. This cycle feeds into principle number three (dealing with the interaction between the researcher and the subjects).
2. The Principle of Contextualization Requires critical reflection and detailed demonstration of the social and historical background of the research setting, so that the intended audience can see how the current situation under investigation emerged.	The research seeks to understand a moving target. As a result, it is crucial to communicate the dynamic relationship between people and institutions as part of the description of the context. The participants are simultaneously both producers of knowledge and members of distinct institutions, which must be reflected in the depiction of the context of each individual case to place the object of study, knowledge, in a context.
3. The Principle of Interaction Between the Researchers and the Subjects Requires contemplation and illumination of how the data were socially constructed through the interaction between the researchers and participants.	Recognizing that participants must be seen as both interpreters and analysts, the research agenda adopts an attitude that the data are not just sitting there waiting to be collected. Instead, the participants must act as interpreters and be informed of the purpose of the research and the underlying theoretical concepts that are being probed in the investigation to yield an accurate response to the focus questions. The participants are also analysts of their own context, as most of them will have never critically scrutinized their work as required by the research agenda. In addition, the researcher will need to embrace the contexts of each case and both document and follow her changing understanding of the contexts and the participants as the research proceeds.
4. The Principle of Abstraction and Generalization Involves relating the ideographic details manifested by the data through the application of principles one and two to theoretical, general concepts that describe the nature of human understanding and social action.	Following Walsham (1993 cited in Klein & Myers, 1999), it is acknowledged that the validity of the inferences drawn from the cases will not depend on the representativeness of the cases to a larger population, but instead on the vigor and integrity of the reasoning used in developing conclusions. There is a clear need for a link between the data, conceptual framework, and the ideographic findings. Two of the four types of generalizations relevant to case research proffered by Walsham (1995 cited in Klein & Myers, 1999) will be used in the case conclusions of this specific research endeavor. These generalizations include drawing specific implications and contributing rich insight.
5. The Principles of Dialogical Reasoning Demands sensitivity to possible contradictions between the theoretical preconceptions guiding the research design and actual findings with subsequent cycles of revision.	The researcher will need to confront any preconceptions that guided the research design. Following the hermeneutic rule that these prejudgements are a necessary starting point of understanding, the key is to decipher between true prejudices and the false ones that lead to a misunderstanding (Gadamer, 1976 cited in Klein & Myers, 1999).

6. The Principle of Multiple Interpretations Requires awareness of possible differences in interpretations among the participants as are typically expressed in multiple accounts of the same events under study.	It is expected that multiple interpretations of the contextual setting, the relationships between participants, and the role and identity of each participant will result from the investigation. This expectancy stems from the recognition that human actions are conditioned by a social context in which multiple agents interact. In examining these multiple interpretations, the researcher must explore the social influences on the participants, peruse the conflicts related to the values of the participants, and revise her own understanding of the cases based on the discrepancies in interpretations. The multiple interpretations will provide a source of data triangulation.
7. The Principle of Suspicion Directs attention to possible biases and systematic distortions in the narratives collected from participants.	The process of data interpretation will entail discovering any false preconceptions that exist in the attitudes and offerings of the participants. Going well beyond a mere understanding of the meaning of the data, the researcher will be required to read the social world of the actor, where influences such as power structures, vested interests, and limited resources to meet the goals of the actors who participate in this world are all a part of the participants' responses.

Adapted from Klein and Myers (1999)

APPENDIX D

Research Brief

Research Brief
Title: How Does Knowledge Flow in University-Industry Collaborations?
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Overview:

Building on the framework provided by two contrasting theories of knowledge, namely the cognitivist perspective (Varela, 1992; Aadne, von Krogh, & Roos, 1996) and the anti-representationist paradigm (Maturana & Varela, 1980), the proposed research seeks to provide an explanation of how knowledge flows in university-industry R&D alliances. The cognitivist theory offers the conjecture that based on interpersonal trust and a pre-given world, knowledge is transferable. Standing in direct opposition to this notion is the anti-representationist's supposition of knowledge as embodied action, bringing forth a world resulting from unique distinctions made by each individual in his encounter with data.

Biotechnology has been chosen as the environment for investigating this research agenda because of the overwhelming evidence provided in the literature on the importance of collaboration in this technological community. "The cross-traffic between universities and biotech companies is so extensive and reciprocal that it is appropriate to consider them part of a common technological community" (Powell, 1996, p200). The constituents of this community, including large pharmaceutical companies, dedicated biotechnology firms, and university research centres, remain diverse in their range of skill and their role in product development. These constituents are dependent on the networks to which they are attached and product development is a result of the ability to not only situate oneself in the appropriate network structure, but also to absorb and apply the knowledge inherent in the network. As pointed out by Gibbons et al (1994), the new production of knowledge, which these authors call Mode 2, presents a unique situation based on transdisciplinarity and embeddedness, where access to knowledge requires participation in its generation.

This project will expound upon the construct of situational *context* by examining how knowledge is exchanged in various collaborative settings, including one R&D alliance in Australia and one in American that are closely geographically co-located and one venture in each country that is not closely located. While the mere mention of the word *knowledge content* may seem like an infringement upon the core of which collaborative parties build their competitive advantage, especially in an arena such as biotechnology where knowledge is so valuable, it should be noted that the proposed research does not seek to invade scientific *content*. Rather, the knowledge categories used in this project will utilize the framework offered by various philosophers, including Polanyi (1958), Grote (1965), James (1909), and Ryle (1949). These knowledge categories include: a) tacit versus articulated knowledge, b) knowledge-of and knowledge-about and, c) knowledge how.

Based on this brief introduction to the research agenda, it should be inferred that an explanation of *how* knowledge flows is the aim of the proposed project. It is anticipated that the researcher will be able to synthesize the data obtained in accordance with the prescribed framework to produce an account of knowledge transference in university-industry R&D alliances that both protects the valuable knowledge base of the study participants and simultaneously provides a rich explanation of the knowledge dissemination process.

Significance:

In an effort differentiated from the common prescriptive project found in the field of management, where self-proclaimed gurus offer their unilateral advice, this project seeks significance via its explanatory power. The researcher anticipates making a novel contribution to the field based upon the investigation of how knowledge transfer differs in regard to co-location (or the absence thereof) and a unique argument that knowledge transfer in these types of endeavors is bi-directional. Existing studies focus more specifically on the transfer of technology from public sector research to industry, without critically acknowledging that

university research centers and their staff are also gaining knowledge in the process of collaboration. An additional contribution stems from the novel theoretical framework adopted for the study. A widespread assumption inherent in the strategic management literature is based on the premise that knowledge can indeed be shared (a purely cognitivist thought). This research attempts to test this assumption by posing an alternative theory of knowledge (the anti-representationist approach) and focusing on participants with diverse knowledge bases engaged in a collaborative endeavor that requires a synthesis of various types of knowledge.

Methodology:

The proposed project will employ an explanatory case study methodology (Yin, 1994). Performing a within case analysis and a cross-case analysis, this project will build its explanatory base by answering the following research questions:

1. Is knowledge able to be directly transferred, or is it re-created from person to person?
2. How does the diffusion process differ between projects whose
3. members are located near one another and those projects whose participants are dispersed?
4. What modes of communication are used to transmit knowledge?
5. Do different types of knowledge have different patterns of exchange, both in terms of media and direction?
6. What patterns emerge in the flow of knowledge between project members (uni-directional, bi-directional, feedback loops, etc)?
7. Is knowledge appropriated to or from constituents external to the project (members of academic groups not specific to the collaboration, members of the firm that did not partake in the project)?

These questions are at the overall research project level. Data will be gathered at the project level and it will be culled and compared to address these questions. The modes of inquiry set forth for this investigation include in-depth interviews and direct observation of meetings where possible. A list of the questions that will be asked of study participants during the interviews is attached. Study participants will also be asked to review the case descriptions, once they are compiled, to ensure that the report reflects their commentary and that valuable knowledge is not included in the report.

The proposed methodology also provides a measure for the protection of valuable knowledge and participant anonymity where requested. Prior to interviews or observation, a confidentiality agreement can be signed and identity can be obscured in the research report.