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Additive BIO Fabrication: Impact, Opportunities and Challenges

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Additive BIO Fabrication: Impact, Opportunities and Challenges

Abstract

In recent years we have outrun our ability to fabricate structures from the amazing materials that we can now create. While this can be said of many areas of materials research it is particularly so in the area of biomaterials. Here, we are often confronted with delicate compositions with nano- to microscopic features that will not survive the traditional (*hammer and chisel*) approach to fabrication. There is good reason why nature "grows" complex, highly functional structures. Such structures with functionality determined by the spatial distribution of composition with nanodimensional resolution can not be *chiselled* from a slab of material.

Additive fabrication (AdFab), often referred to as 3D Printing, involves layer-by-layer deposition and fusion of materials to create customised structures. The structure to be produced can be conceptualised, manipulated and defined within a growing array of modelling environments; from conventional parametric Computer-Aided Design (CAD) solutions such as Solidworks™ or ProE™, through to free-form animation toolsets such as Autodesk 3ds Max™, and even free web-based applications like Tinkercad™ (www.tinkercad.com). Once a design is completed, a file that describes the structures' surface geometry is generated and a set of digitised instructions then drives the printer to create the required structure layer by layer.

The fabrication process can involve several deposition modes. In fused deposition modelling / extrusion printing, a molten build material is deposited and solidified on cooling. For higher resolution structures (layer thicknesses as low as 16 μm), a fluid material precursor is ink-jetted onto a substrate and simultaneously transformed into a solid structure via a chemical reaction (UV induced polymerisation). Metal structures can be fabricated through a physical micron-scale welding process known as selective laser melting.

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Article for ATSE Magazine

Additive BIO Fabrication: Impact, Opportunities and Challenges

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In recent years we have outrun our ability to fabricate structures from the amazing materials that we can now create. While this can be said of many areas of materials research it is particularly so in the area of biomaterials. Here, we are often confronted with delicate compositions with nano- to microscopic features that will not survive the traditional (*hammer and chisel*) approach to fabrication. There is good reason why nature "grows" complex, highly functional structures. Such structures with functionality determined by the spatial distribution of composition with nanodimensional resolution can not be *chiselled* from a slab of material.

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The Impact

The recent race to embrace AdFab has had significant wide-ranging impact on those of us involved in biomaterials and biodevices research. For example:-

In Wollongong, we have established Additive Biofabrication capabilities within a dedicated Processing and Devices Facility (Figure 1). Equipment housed here includes commercial additive fabrication systems like the Objet Connex 350™ and Relaizer SLM50™, commercial bio-fabrication systems such as the EnvisonTec Bioplotter™, and customised printing systems such as the KIMM SPS1000, a Reactive Ink-jet Printer and an Extrusion Printer. A more detailed description can be found at http://www.electromaterials.edu.au/equipment/index.html

Figure. 1. The Processing and Devices Building located at the Innovation Campus, North Wollongong, houses the ACES-ANFF Bio Fabrication Facility.

The ability to create customised 3D polymeric or metallic structures in the laboratory accelerates experimental design by enhancing the realisation of material components that facilitate experimentation. Additive fabrication provides an in-house capability to design and realise unique set ups in a minimal period of time.

One case in point was the development of an experimental procedure to electrically stimulate cells *in vitro* on organic conducting polymer surfaces (a study in the field of "Organic Bionics"[1]). Off-the-shelf chamber wells were removed from their original substrate and bonded to a conducting polymer coated gold Mylar substrate to act as a media reservoir. A custom platinum counter electrode mount was produced by additive fabrication (see Figure 2). The mount allows accurate placement of the platinum mesh electrodes in the media reservoir and ensures a repeatable electrode orientation. A proprietary bio-compatible material, Objet MED610™, was chosen as the build material. Production of these components by conventional machining would have been relatively expensive and would not have easily facilitated the small dimensional features of the component.

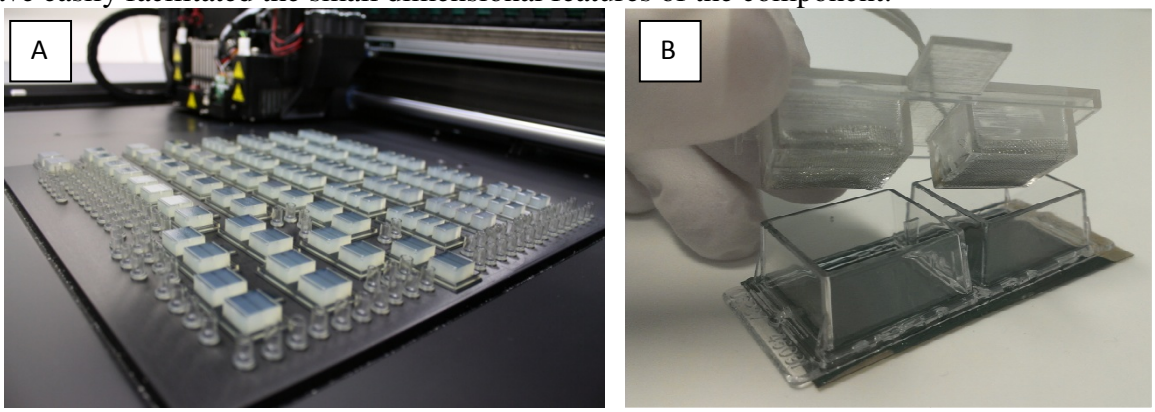

Figure. 2. Batch production of biocompatible components using Objet MED610™ for use in biological experiments (Fig. 2.A). Platinum mesh electrode mount as used to provide repeatable spacing between electrode surfaces during cell stimulation trials (Fig. 2.B).

Another example of experimental tool production involved the development of a device to enable studies related to the alleviation of eye pressure arising from glaucoma; a study led by Prof. Michael Coote at the Centre for Eye Research Australia. Concept outline sketches were provided and translated into 3D CAD models. Graphical representations of the implant design allowed for revisions and modifications to be easily communicated and implemented before fabrication (Figure 3).

Batch production of an array of design permutations was achieved in a single build tray printing cycle. Design iterations were simply undertaken without any concern for re-tooling of the hardware.

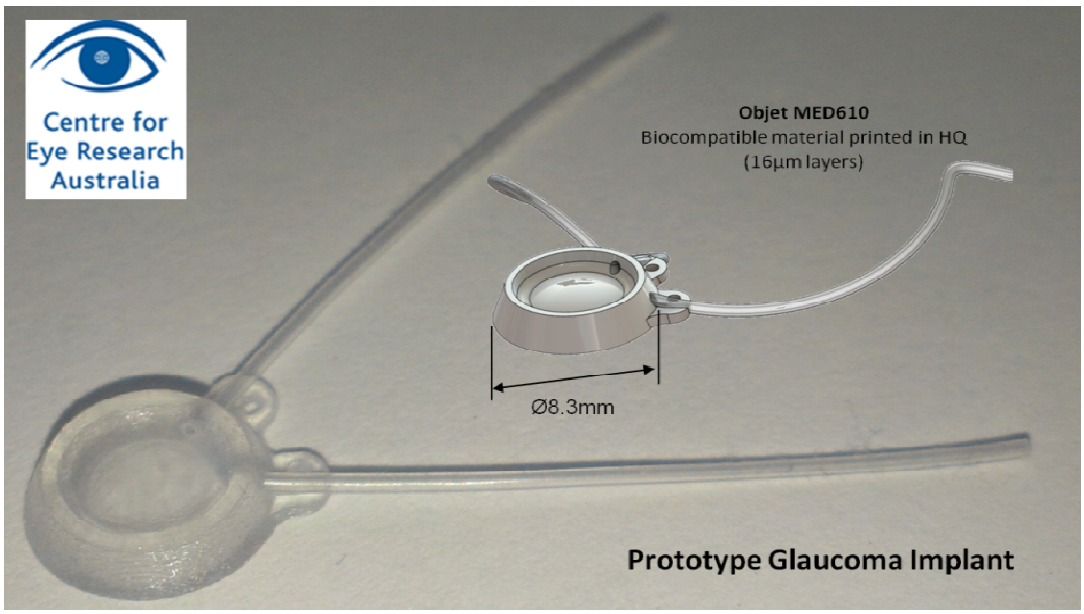

Figure 3: Illustration depicting concept glaucoma implant as developed within Solidworks™ 2012 and highlighting external dimensions. Completed device as produced using Objet MED610™, after addition of 700 µm OD silicone tubing.

These examples illustrate what can be achieved with commercially available machinery and materials. In other aspects of our work within the ARC Centre of Excellence for Electromaterials Science (ACES), we are concerned with the fabrication of structures containing biopolymers, organic conductors and even living cells within new structures for bionics[1].

Existing commercially available equipment can not handle such materials. Consequently we have been involved with the Korean Institute of Machinery and Materials (KIMM) and the company M4T, who have supplied a customised Scaffold Plotting System (SPS1000™) that is capable of extrusion printing biopolymers; including synthetic biodegradables such as polycaprolactone, or naturally occurring biopolymers such as chitosan. Using this system, we have printed 3D scaffolds (Figure 4(a)). The lower feature size is limited to about 200 µm and is determined by the rheological properties of the bio-ink. Such structures have previously proven useful as scaffolds for tissue regeneration. More recently we have modified this extrusion printer to enable co-axial printing. This required the design and fabrication of a dual reservoir system and a co-axial print head (Figure 4(b)). These components were designed and fabricated *in-house* – the printhead itself was produced using a 3D metal printer – the era of printing printers is upon us! Co-axial structures with an inner

core diameter range of 200 to 500 µm and an outer core of 600 to 1200 µm diameter were produced. This customised co-axial printing system has already proven useful for the creation of alginate / polycaprolactone co-axial 3D structures and even the creation of structures containing living cells[2].

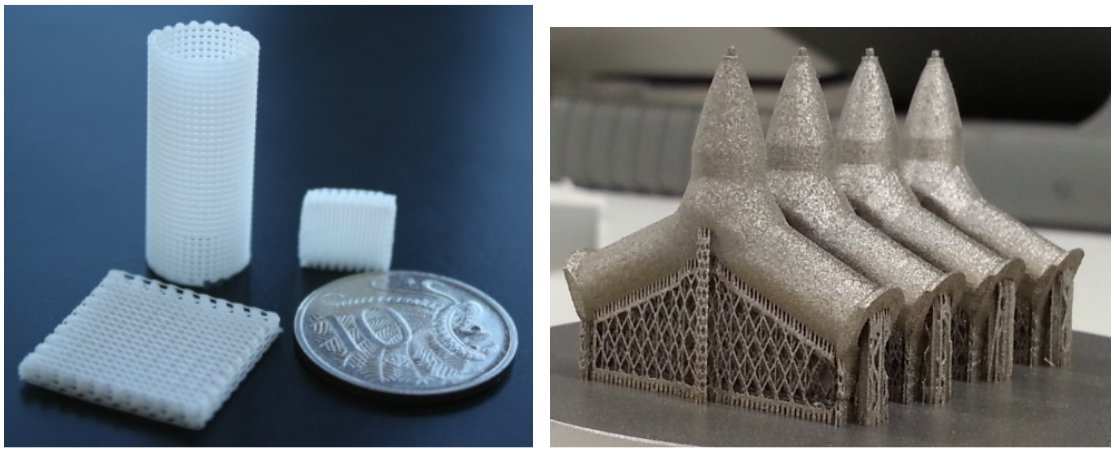

Figure 4 (a): Porous polycaprolactone (PCL) structures produced through hot-melt extrusion printing in an array of structure geometries based on geometric .stl data and user defined grid spacing parameters. (b): A batch of co-axial extrusion tips, before final finishing and polishing, produced in Stainless Steel 316L with a Realizer SLM50™ operating with layer slice thickness of 25µm

Using a commercially available ink-jet printer from Dimatix™ and a customised ink using organic conducting polymer nano-particles, we have printed features as small as 20 µm that have been used as bionic guidance tracks to control the direction of nerve growth[3]. Another addition to our printing armoury is a custom built multi-head ink-jet printer that allows printing of multiple components to create new material structures during fabrication, so called reactive printing, wherein the individual components react to form a more mechanically robust structure. For example, this has been used to form biopolymer hydrogel structures that are ionically cross-linked during printing.

With minimal modification, we have also found these print heads to be useful in allowing for the effective delivery of living cells during the printing process; delivering both nerve and muscle cells to create unique biofunctional structures. The cells are maintained using a biopolymer suspension with optimised rheological properties that enable effective delivery through the ink-jet head. The formulation used is multi-purpose and multi-functional, in that it maintains the cells in a healthy state in suspension for many hours, protects cells during delivery and sustains cell viability after printing[4].

AdBioFab – Changing the way we teach, commercialise and do research

After a number of decades wherein advances in materials science have often been limited by our inability to fabricate effectively, we have now entered a new era. Biomaterials researchers have been empowered with the ability to fabricate customised structures using hardware that can be accommodated in most research laboratories at reasonable cost.

The convergence of advances in biomaterials, AdBioFab, Information technology, Nano technology and Bio technology is set to move us forward in biomedical science at an

unprecedented rate. Our ability to convert data into knowledge and to effectively disseminate that knowledge has been outrun by our ability to create the primary data!

The knowledge dissemination gap continues to grow wider and this has implications for:

- Schools and Universities: those responsible for skilling the next generation of researchers.

- Regulatory authorities: who require information and an understanding of the implications of advances occurring on a number of technological fronts simultaneously.

- The commercialisation sector: these advances are challenging traditional commercialisation models that are based on mass-manufacturing / cost reduction / sales targets. With additive biofabrication, localised manufacture using exotic materials will deliver the most effective solutions.

- The community: social acceptance of advances in the medical sector is obviously critical to success. We must develop innovative approaches to present understandable chunks of knowledge.

Now we in materials science can be bold, even audacious. We can develop materials not amenable to current processing and fabrication approaches with the knowledge that we can print-printers; creating the fabrication machinery of the future in tandem with breakthroughs in materials science!

Advances in AdBioFab will have a staggering impact because it not only accelerates the thought-to-thing process, delivering practical solutions sooner, but it also empowers us to make unprecedented fundamental advances. For example, the ability to arrange living cells in 3D within naturally occurring or synthetic biomaterial structures will give insights into environmental effects on cell behaviour – insights hitherto unavailable.

Acknowledgements

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