Biocompatible/Biodegradable Materials for Implantable Mg-Air Batteries

Xiaoteng Jia

University of Wollongong

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Biocompatible/Biodegradable Materials for Implantable Mg-Air Batteries

Xiaoteng Jia
B.Sc., M.Sc.

This dissertation is presented as part of the requirements for the Award of the Degree of Doctor of Philosophy of The University of Wollongong

October 2017
With profound affection for my great parents
Certification

I, Xiaoteng Jia, declare that this dissertation, submitted in fulfilment of the requirements for the award of Doctor of Philosophy, at the Australian Institute for Innovative Materials, University of Wollongong, is wholly my own work except where specific references or acknowledgements are made. The dissertation has not been submitted for a degree to any other university or institution.

Xiaoteng Jia

October, 2017
Publications


ABSTRACT

Biodegradable implantable medical bionics can be used to diagnose and/or treat disease and eventually disappear without surgical removal. If an “external” energy source is required for effective operation, then a biocompatible/biodegradable battery would be ideal.

This thesis is focused on the development of biocompatible/biodegradable air cathode materials and polymer electrolytes for implantable Mg-air batteries. Bioreabsorbable Mg alloy serves as the anode because of its benign biological function and high theoretical capacity. Polypyrrole with excellent electroactivity and biocompatibility satisfies the requirements for cathodes. To obviate its inherent non-biodegradability, a biopolymer component affording biodegradability is introduced in forming a composite. Polymer electrolyte is desirable to fabricate miniaturized Mg-air batteries. The biopolymer-ionic liquid polymer electrolyte can achieve both high ionic conductivity and biodegradability.

A biodegradable cathode material is prepared by embedding silver nanowire into silk fibroin film, followed by the electrodeposition of polypyrrole thin-film. This composite shows no major cytotoxic effects as evidenced by conventional cell viability and imaging assays. Such cytocompatible composite is used as a potentially implantable cathode for constructing a Mg-air bioelectric battery with phosphate-buffered saline electrolyte.

A bilayer structured film is prepared by chemically depositing PPy on the silk substrate. It demonstrates a rapid degradation rate ascribed to the low β-sheet content in silk. A
high discharge capacity is achieved because of high polypyrrole content in the air cathode. The Mg-air bioelectric battery is also discharged in protease XIV solution at 37 °C to estimate the battery performance upon enzyme exposure.

In consideration of a miniaturized biocompatible battery, a polymer electrolyte-enabled compact Mg-air battery is fabricated. The biocompatible electrolyte is made of choline nitrate embedded in chitosan. The conductivity and mechanical property of the polymer electrolyte are investigated. The discharge performance of Mg-air batteries is investigated using the polymer electrolyte and phosphate-buffered saline electrolyte for comparison.

To further reduce the battery thickness and impart a soft nature, an encapsulated Mg-air battery is developed. It is made of thin-film electrodes with sputter coated Mg alloy and gold on silk films as anode and cathode, respectively. The whole device degradation is achieved in the protease XIV solution. A modulated lifetime of an encapsulated battery is obtained via controlling the packaging material: silk film.

Biocompatible/biodegradable cathode materials and polymer electrolytes are critical components for implantable Mg-air batteries. This type of Mg-air battery system may power the biodegradable implantable medical bionics with further optimization in terms of power output and biodegradation profile.
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I am sincerely grateful to my supervisors, Professor Gordon G. Wallace and Dr. Caiyun Wang, who provided an excellent platform and resources to undertake this PhD. I would like to especially thank them for their patience, trust and encouragement to engage in activities outside the lab, such as overseas research visits, media work, competitions and seminars.

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I would like to thank Professor Douglas R. MacFarlane, Professor Maria Forsyth, and Dr. Vijayaraghavan Ranganathan for their collaboration within the ARC Centre of Excellence for Electromaterials Science. Furthermore, I would also like to thank Professor Fiorenzo G. Omenetto for giving me the opportunity to work in the Silklab at Tufts University.

Finally, I would like to thank my parents and brother, all of whom never seemed to have a doubt that one day I would successfully become a PhD. Thank you!
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<tr>
<td>IMBs</td>
<td>Implantable medical bionics</td>
</tr>
<tr>
<td>BIMBs</td>
<td>Biodegradable implantable medical bionics</td>
</tr>
<tr>
<td>Bio-battery</td>
<td>Bioelectric battery</td>
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<tr>
<td>ORR</td>
<td>Oxygen reduction reaction</td>
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<tr>
<td>PBS</td>
<td>Phosphate-buffered saline</td>
</tr>
<tr>
<td>AgNW</td>
<td>Silver nanowire</td>
</tr>
<tr>
<td>DI</td>
<td>Deionized</td>
</tr>
<tr>
<td>SS</td>
<td>Stainless steel</td>
</tr>
<tr>
<td>AZ31</td>
<td>Mg-Al-Zn alloy (wt%: Mg, 96; Al, 3; Zn, 1)</td>
</tr>
<tr>
<td>IL</td>
<td>Ionic liquid</td>
</tr>
<tr>
<td>[Ch][NO₃]</td>
<td>Choline nitrate</td>
</tr>
<tr>
<td>CPs</td>
<td>Conducting polymers</td>
</tr>
<tr>
<td>PPy</td>
<td>Polypyrrole</td>
</tr>
<tr>
<td>PTh</td>
<td>Polythiophene</td>
</tr>
<tr>
<td>PEDOT</td>
<td>Poly(ethylenedioxythiophene)</td>
</tr>
<tr>
<td>PANI</td>
<td>Polyaniline</td>
</tr>
<tr>
<td>pTSA</td>
<td>p-toluenesulfonic acid</td>
</tr>
<tr>
<td>pTS</td>
<td>Sodium p-toluenesulfonate</td>
</tr>
<tr>
<td>B. mori</td>
<td>Bombyx mori</td>
</tr>
<tr>
<td>SF</td>
<td>Silk fibroin</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>CS</td>
<td>Chitosan</td>
</tr>
<tr>
<td>hADSCs</td>
<td>Human adipose-derived stem cells</td>
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<tr>
<td>calcein AM</td>
<td>Calcein acetomethoxy</td>
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<tr>
<td>PI</td>
<td>Propidium iodide</td>
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<tr>
<td>SHE</td>
<td>Standard hydrogen electrode</td>
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<tr>
<td>EIS</td>
<td>Electrochemical impedance spectroscopy</td>
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<tr>
<td>FTIR</td>
<td>Fourier transform infrared spectra</td>
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<tr>
<td>LSV</td>
<td>Linear sweep voltammetry</td>
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<tr>
<td>SEM</td>
<td>Scanning electron microscopy</td>
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<tr>
<td>OCV</td>
<td>Open-circuit voltage</td>
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<tr>
<td>ATR</td>
<td>Attenuated total reflectance</td>
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<tr>
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<tr>
<td>Rct</td>
<td>Charge transfer resistance</td>
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<tr>
<td>Rs</td>
<td>Bulk resistance</td>
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<tr>
<td>A</td>
<td>Ampere</td>
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<td>M</td>
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<td>Hz</td>
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<tr>
<td>mV</td>
<td>Millivolt</td>
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<td>mA</td>
<td>Milliampere</td>
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<td>Nanometre</td>
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<td>Centimetre</td>
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<tr>
<td>µ</td>
<td>Micro</td>
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<tr>
<td>k</td>
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1. Introduction

Implantable medical bionics (IMBs) have been widely used for therapies serving as functional devices to detect, prevent and cure many diseases challenging human life.\textsuperscript{1-3} Various types of IMBs are designed to be implanted within the human body, such as drug delivery system, cardiac rhythm management devices, neurological stimulation devices, and the like (Figure 1.1). They can help manage a broad range of ailments, such as cardiac arrhythmia, diabetes, and Parkinson’s disease. The first and most important requirement for IMBs is biocompatibility, which is defined as the ability to be in contact with a living system without producing an adverse effect.\textsuperscript{4} IMBs should not bring toxicity or be rejected by the organisms where they are implanted.\textsuperscript{5}

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure1.png}
\caption{Demonstrated examples of commercial implantable medical bionics.}
\end{figure}
According to the final states after their function in vivo, medical devices can be broadly classified into two types: chronic implants and transient implants (i.e. biodegradable implants). Chronic IMBs, typically designed to be permanent, are susceptible to evoking complex biological responses and increase the risk of complications. These devices necessitate secondary surgery to retrieve or replace them once the desired functional outcome has been achieved. Biodegradable implants, in contrast, can physically disappear in a controlled manner after a stable period of operation. This approach enables the devices to be gradually dissolved, absorbed, consumed or excreted while releasing biologically benign products in the body. Biodegradable implantable medical bionics (BIMBs) are desirable in monitoring and treating transient biological processes, such as wound healing, bone fracture and drug delivery, in which the devices would be needed only for a transient period. In this respect, BIMBs preserve sophisticated capabilities of electric systems while eliminating secondary surgical retrieval and reducing chronic inflammation.

1.1 Implantable Power Sources for Implantable Medical Bionics

The proper functionality of IMBs relies heavily on a power supply. Clinical diagnosis and therapy commonly require an electrical energy capable of generating relatively low current pulse inside the human body without any adverse response. These power sources are implanted into the body as part of the medical device and are housed within a sealed case. Demonstrated power sources include mechanical energy harvesters, wireless power transmission modules and energy storage devices. However, wearing of an external power transferring coil is uncomfortable for patients. The energy harvesting methods commonly produce very low instant energy output with
poor efficiency. In other words, these technologies are not yet free from energy storage systems that are needed to compensate for their intermittency since they are not so constant. Commercialized batteries provide a viable solution for active chronic implants due to their high energy densities.\textsuperscript{16} To realise BIMBs, a biocompatible and biodegradable battery would be ideal. These batteries would satisfy device power requirements during the lifetime of BIMBs and then, wholly or in part, harmlessly degrade into non-toxic products.

1.1.1 Basics in Electrochemical Batteries

An electrochemical battery (\textit{i.e.} battery) is an energy storage device that can convert chemically stored energy of a material into electrical energy through oxidation/reduction (redox) reactions. Electrochemical batteries are categorized into two types: primary (single use) or secondary (rechargeable) according to different working principles. Primary batteries are suitable for low-power applications that require low current drain; secondary batteries are used in devices with high energy and power consumptions. A battery is composed of three key components as follows:

(1) A negative electrode (anode) which gives up electrons and undergoes oxidation reaction during discharge. (2) A positive electrode (cathode) which accepts electrons and undergoes reduction reaction during discharge. (3) An electrolyte which facilitates the flow of ions between the electrodes and ultimately influences the kinetics of the electrode reaction. An ion-conducting separator keeps the electrodes isolated electronically from each other to prevent short circuit.
In primary batteries, the redox reactions result in inactive reaction sites at one electrode. As discharge proceeds, more and more reaction sites become unavailable until the battery becomes completely not dischargeable. In secondary batteries, the redox reaction is reversible and the battery can be recharged by an electric source. Take lithium-ion (Li-ion) battery for example (Figure 1.2), during discharge an oxidation reaction occurs at the anode/electrolyte interface. This produces positively charged ions (i.e. Li\(^+\)) that are moving from anode to cathode while the electrons pass via the external circuit into the cathode. The reduction of positively charged ions (i.e. Li\(^+\)) is carried out at the positive electrode. On the contrary, when the battery is charged, the oxidation-reduction will occur in a reverse direction to the discharging process.

**Figure 1.2** Schematic representations of processes during discharging (a) and charging (b) of a Li-ion battery (adapted from reference [17]).

### 1.1.2 Typical Power Sources for Commercial Implantable Medical Bionics

Local electrochemical batteries are the most common source of energy for chronic medical devices. This is mainly because of their reliable, safe and robust operation, which is essential for medical devices. The choice of battery system for medical
devices depends on several factors, such as size, power consumption and lifetime. The power requirements and energy sources of some representative existing commercial IMBs are summarized in Table 1.1.18

Table 1.1 Power requirements and power sources of some commercial IMBs.

<table>
<thead>
<tr>
<th>Implanted device</th>
<th>Power requirement</th>
<th>Power source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pacemaker</td>
<td>30-100 µW</td>
<td>Li-I₂ primary battery</td>
</tr>
<tr>
<td>Cardiac defibrillator</td>
<td>30-100 µW</td>
<td>Li-SVO primary battery⁴</td>
</tr>
<tr>
<td>Neural stimulator</td>
<td>1-100 mW</td>
<td>Li-SOCl₂ primary battery</td>
</tr>
<tr>
<td>Retinal implant</td>
<td>40-250 mW</td>
<td>Inductive power</td>
</tr>
<tr>
<td>Drug pump</td>
<td>100 µW-2 mW</td>
<td>Li-CFₓ rechargeable battery</td>
</tr>
<tr>
<td>Cochlear implant</td>
<td>10 mW</td>
<td>Zn-air rechargeable battery</td>
</tr>
</tbody>
</table>

Note: SVO is referred to as silver vanadium oxide.

Currently, Li batteries are the predominant power sources for various types of IMBs.¹⁹ Li batteries are selected mainly due to their high energy density, low self-discharge rate and long shelf life. Several battery chemistries based on Li have been developed, such as Li-iodine primary battery for pacemakers,²⁰ Li-thionyl chloride batteries for neurostimulator and Li-MnO₂ batteries for cardioverter-defibrillators.²¹ Inevitably, Li
batteries contain toxic chemicals which require an absolute encapsulation and thus limits their shapes, size and flexibility.

Metal-air batteries such as zinc-air and magnesium-air are promising because they use oxygen as one of the battery’s main reactants, reducing the weight of the battery and freeing up more space devoted to energy storage. Metal-air batteries have higher energy densities than most types of commercialized batteries (Figure 1.3).22

**Figure 1.3** Gravimetric energy density of some representative primary/rechargeable batteries, metal-air batteries, hydrogen-air fuel cells and gasoline (adapted from reference [22]).

Metal-air batteries are usually of an open cell structure to allow oxygen to pass through the cathode and consequently participate in the electrochemical reactions. This feature makes them akin to a fuel cell, with the ‘fuel’ being a metal. Metal-air batteries generate electricity through the redox reactions between the metal anode and oxygen.
The major applications of metal-air batteries include Zn-air battery for hearing aid device, Mg-air and Al-air battery for marine lifejacket lights, and undersea power supplies.23

1.2 Bioelectric Battery

Batteries to drive IMBs need to meet the strict clinical dimension constraints.24 In fact the size of active IMBs is determined by the battery component as it occupies the largest volume of the whole device. A strong case is required to contain toxic/harmful chemicals, which prevents their contact with the body.25 A promising way to realize a miniaturized battery is to utilize body fluid directly as the electrolyte. The body fluid is mainly composed of water, dissolved ions (sodium, potassium, calcium, chloride, phosphate and hydrogen carbonate ions), small molecules, and large water-soluble molecules (such as proteins).26 The pH of body fluid is around 7.0-7.4. The concentration of dissolved oxygen in body fluid is 0.15-0.45 mL/L.27 In this dissertation, we use 1 M phosphate-buffered saline (PBS) solution as the electrolyte (pH=7.4) in aqueous metal-air bioelectric batteries. PBS is a commonly used electrolyte in the biological research area.

This type of primary metal-air battery that may use body fluid as the electrolyte is often called bioelectric battery (denoted as ‘bio-battery’ for simplification herein). It was first reported in the 1970s.28 It is a galvanic cell composed of two metallic electrodes with different electrochemical potentials. The bio-battery has advantages of small size, low cost and long lifetime, and can be utilized as a low power source for IMBs. Generally, the bio-battery provides power in the order of 100 μW, which may be sufficient to power many types of IMBs.9 Due to the small foot-print and
biocompatibility of all components, the bio-battery could be implanted in the body (e.g., neck, pectoral cavity or superior vena cava etc.). In 2006, Adam Heller proposed a potentially harmlessly subcutaneously implantable Zn-O$_2$ microcell. He found that a foreseen battery composed of a bioinert hydrogel-shielded wired bilirubin oxidase-coated carbon cathode worked well for about two weeks in pH 7.4 physiological saline buffer at 37 °C.

1.2.1 Configuration of a Metal-Air Bioelectric Battery

The configuration and working mechanism of a metal-air bio-battery is relatively simple. It can be explained using the schematic diagram in Figure 1.4. It contains a sacrificial anode, a biocompatible cathode and a body fluid electrolyte. The anodes normally are biocompatible and bioresorbable metals, such as magnesium (Mg), zinc (Zn) and their alloys, and will be used up during the course of electrochemical reactions. The cathode is a non-consumable material and serves as a catalyst for the reaction. The oxygen reduction reaction (ORR) on the cathode provides hydroxyl ions which are the key reactant for the liquid/solid interface reaction of the metal anode. Therefore, the key issue of an air cathode is to enhance ORR efficiency. As oxygen is presented in the body in plentiful supply, the lifetime of a bio-battery is determined by the corrosion rate of the anode.
1.2.2 Magnesium Anode

Mg element offers a unique combination of mechanical, electrochemical, electrical and physiological properties that are attractive for biomedical applications. Mg is the fourth most abundant cation in the human body and an essential mineral nutrient with recommended daily intake values in the range of 300-400 mg per day.\textsuperscript{30} For example, adenosine triphosphate, the main energy source in biological cells, requires a bound Mg ion to be biologically active. Mg also plays a critical role in stabilizing polyphosphate compounds involved in DNA and RNA synthesis.\textsuperscript{31} Mg and their alloys are normally used for bioresorbable implants, due to their combination of biocompatibility, acceptable degradation rate, and non-toxic soluble dissolution product.\textsuperscript{32-33} Moreover, Mg is an electronegative element metal with a standard
electrode potential of -2.34 V (vs. SHE), and a high theoretical capacity of ca. 2200 mAh g\(^{-1}\) (3833 mAh cm\(^{-3}\)). Mg-air batteries show promising properties, such as a high theoretical voltage of 3.09 V (in practice, the open circuit voltage is about 1.7-1.8 V in aqueous electrolyte) and an energy density of 2840 Wh kg\(^{-1}\). The reaction chemistry of a Mg-air battery in an aqueous electrolyte is described as follows:\(^{22}\)

\[
\text{Anode}: \ 2\text{Mg} + 4\text{OH}^- \rightarrow 2\text{Mg(OH)}_2 + 4e^- \ (E = -2.69 \text{ V vs. SHE}) \\
\text{Cathode}: \ \text{O}_2 + 2\text{H}_2\text{O} + 4e^- \rightarrow 4\text{OH}^- \ (E = 0.40 \text{ V vs. SHE}) \\
\text{Overall reaction}: \ 2\text{Mg} + \text{O}_2 + 2\text{H}_2\text{O} \rightarrow 2\text{Mg(OH)}_2 \ (E_{cell} = 3.09 \text{ V vs. SHE})
\]

Mg, due to its chemical properties, is susceptible to a rapid and uncontrolled degradation. In the presence of oxygen or water, Mg will form a passivation layer in the body fluid or blood plasma.\(^{34}\) The formation of hydrogen gas can be problematic.\(^{35}\) This can lead to the formation of gas pockets, an undesirable complication that can cause blood clotting and tissue necrosis. The major solution to reduce the hydrogen evolution reaction is to alloy Mg with other elements such as aluminum (Al), and Zn.\(^{36}\) The alloying can prevent the Mg enriched phase from crack corrosion or pitting corrosion and therefore stabilise the interface reaction between the anode and aqueous electrolyte.\(^{37}\) It is this rationale that has led to the choice of the anode used in this thesis work: which is Mg-Al-Zn (AZ31) alloy (wt\%: Mg, 96; Al, 3; Zn, 1).

### 1.3 Biocompatible and Biodegradable Air Cathode Materials

Compared with the studies on the Mg anode, more research work has been focused on the oxygen reduction catalyst for the air cathode. In a metal-air alkaline battery, a
A typical air cathode consists of three components; a catalyst layer, a gas diffusion layer and a current collector. A gas diffusion layer is an integration of several types of carbonaceous materials bound together by polytetrafluoroethylene followed by a burning off which results in a porous structure. The carbon nature and porous structure of the gas diffusion layer promotes air transport and prevents electrolyte from penetrating it through the pores. The catalyst layer coated onto the gas diffusion layer is the most essential component of an air cathode. ORR is very complex and involves multiple molecular adsorption-desorption processes.

Metal-air bio-batteries share similar working principles with traditional metal-air alkaline batteries. When designing a metal-air bio-battery operating at physiological conditions and body temperature, some basic requirements need to be considered. The implanted air cathode materials should be biocompatible in the body fluid. In early studies of metal-air alkaline batteries, the most studied air cathode materials are noble metals (e.g. Pt and Pt-Ru alloy), which have been proven to be one of the best solutions to reduce oxygen efficiently and are still being widely used in industry today. However, Pt is an extremely rare metal, with projected concentrations of only 0.003 ppb in the Earth’s crust. Recently, numerous efforts have been devoted to finding Pt-free alternatives; such as transition metal oxides (e.g. MnO₂) and carbon based nanomaterials. Neither of these traditional air cathode materials is safe for implantation due to their toxicity to the human body.

As alternatives to these traditional catalysts, conducting polymers (CPs) with good electrical conductivity and electrocatalytic behaviour have aroused wide interest as cathode materials for ORR. The main advantage of CPs over inorganic catalysts is
their mechanical flexibility, essentially required for biomedical implants interfaced with curved surfaces and moving parts. In addition, CPs exhibit inherent fast redox switching, high conductivity, and easy processability. Their biomedical applications have also been considered including biosensors and cell growth substrates. The latter application is made more appealing by using biologically functional macromolecules (e.g. proteins, polysaccharides and even whole living cells) as dopants during the polymerization process. Furthermore, with recent evidence uncovering important physiological roles for in vivo electrical stimulation of cells, in order to provide wound healing for instance, CPs may offer new advantages as biomaterials. With these characteristics, CPs are promising air cathode materials for bio-batteries.

1.3.1 Conducting Polymers

During the last few decades, CPs have been gathering great interest in academia and industry by affording the merits of combining the electrical properties of a semiconductor or metals with mechanical properties of conventional polymers together with easy processability and low cost. After the discovery made by MacDiarmid and co-workers in 1977 that polyacetylene can gain the conductivity of a metal by doping with either I₂, Br₂ or AsF₅, many aromatic conjugated polymers have been studied. There are many classes of organic CPs, the most fascinating ones are the polyheterocycles such as polypyrrole (PPy), polyaniline (PANI), polythiophene (PTh), poly(3,4-ethylenedioxythiophene) (PEDOT) and their derivatives (Figure 1.5). They typically exhibit good environmental stability and reach electrical conductivity in the range from 0.01 to 500 S cm⁻¹.
1.3.1.1 Conductivity and Doping of Conducting Polymers

Conductivity in conjugated polymers is attributed to the unique alternating double and single bonds that form the \( \pi \) conjugated system (delocalised 2p\( _z \) orbitals). Along the backbone of CPs, \( \sigma \)-bonds hold each carbon atom together by concentrating electrons between them.\(^{48}\) The \( \pi \)-bonds, which constitute the second bond in each double bond, strengthen the connection between their atoms by attracting electrons above and below the plane of the molecule. This forms delocalised 2p\( _z \) orbitals which allow the generation and movement of charge carrier entities.\(^{49}\) Nevertheless, delocalization is limited and the conductivity is affected by doping. Prior to doping, these systems are insulating (~10\(^{-10}\) S cm\(^{-1}\)); however, the electrical conductivity of polyheterocyclic films can be augmented by up to 12 orders of magnitude (~10\(^2\) S cm\(^{-1}\)) depending on the polymer system and the type and extent of doping.

---

**Figure 1.5** Chemical structures of typical conducting polymers (A\(^-\) represents the doping counting ions).
Figure 1.6 (a) Formation of the bipolaron state in PPy or PTh upon oxidation: During charging of the polymer chain, the ionized states are stabilized by a local geometrical distortion from a benzoid-like to a quinoid-like structure. (b) Band structures in conjugated polymers upon doping as proposed in the bipolaron model, and optical transitions for the polaron and the bipolaron state (adapted from reference [52]).
These polymer systems are only conducting when doped, and the electrical conduction depends on the extent of doping. Doping is the process of oxidising (p-doping) or reducing (n-doping) a neutral polymer and providing a counter-anion or -cation (*i.e.*, dopant), respectively.\(^{50}\) Upon doping, a conjugated polymer becomes a conducting system and a net charge of zero is produced due to the close association of counter-ions with the charged polymer backbone.\(^{51}\) This process introduces charge carriers, in the form of charged polarons, *i.e.*, radical ions, or bipolarons, *i.e.*, dications or dianions, into the polymer, as shown in Figure 1.6a.

The creation of these charge carriers is affiliated with the appearance of midgap states, which, in essence, facilitate the movement of electrons from the valence band to the conductance band. The attraction of electrons in one repeat unit to the nuclei in neighbouring units yields charge mobility along the chains and between chains, often referred to as "electron hopping" (Figure 1.6b). The ordered movement of these charge carriers along the conjugated CPs backbone gives rise to electrical conductivity.\(^{52}\)

### 1.3.1.2 Synthetic Methods

CPs can be synthesized by chemical or electrochemical oxidative polymerization, and doped with negatively charged counter-ions during the polymerization process to maintain their charge neutrality.\(^{53}\) Chemical polymerization is a more-cost-effective method for mass production of CPs. The oxidants used for chemical polymerization mainly include \(\text{H}_2\text{O}_2\), \((\text{NH}_4)_2\text{S}_2\text{O}_8\), and salts containing transition metal ions. Selecting proper dopants is one of the main research directions to achieve high electrical conductivities or unique redox properties.\(^{54}\) Various types of nanostructured CPs have
been synthesised using soft-templates or hard templates, such as nanofibers, nanotubes and nanoparticles.\textsuperscript{55}

Electrochemical polymerization is preferable to produce a thin layer of clean polymer with controlled thickness on conductive electrodes. The electrochemical preparation of CPs is usually carried out through oxidative polymerization of their corresponding monomers via constant current, constant potential, or cyclic voltammetry.\textsuperscript{56} The electropolymerization is performed in a solution which contains solvent, electrolyte salt, and monomer. There are many factors influencing the electropolymerization processes, such as solvents, supporting electrolyte salts, concentration of monomers, and pH value, as well as the polymerization potential, current, and temperature.\textsuperscript{57-58}

The most significant difference between electrochemical and chemical methods of CP synthesis is that very thin CP films of the order of 20 nm can be produced using the electrochemical technique, whereas powders are typically produced with chemical polymerization. All CPs can be synthesized chemically, but electrochemical synthesis is limited to those systems in which the monomer can be oxidized in the presence of a potential to form reactive radical ion intermediates for polymerization.

\subsection*{1.3.2 Polypyrrole}

PPy is one of the most interesting CPs and has been investigated intensively over the past decades due to its ease of synthesis, environmental stability, and striking electronic and optical properties.\textsuperscript{59} PPy is a typical p-type conjugated polymer with a very low oxidation potential in the range of \textit{ca.} -0.6 to 0.3 V vs. SCE,\textsuperscript{60} which makes the p-doped conducting PPy stable, and the reduced PPy is easily oxidized to its p-
doped state. The electrochemical properties of conducting PPy are therefore usually inferred from the reduction (dedoping)/re-oxidation (doping) of the p-doped PPy. With a relatively small monomeric mass, PPy has a theoretical specific charge capacity of 136 mA h g$^{-1}$, assuming a typical doping level of 0.33. Its straightforward synthesis procedure and compatibility with a variety of substrates, has led to a high interest for using PPy as active materials for energy storage electrodes.

1.3.2.1 **Biocompatibility of Polypyrrole**

The biocompatibility of PPy prepared from both chemical and electrochemical means was thoroughly evaluated by Wang et al. They carried out a series of systematic toxicity tests according to ISO 10993 and ASTM F1748-82 standards by applying a solution of extracts from PPy powder to cell cultures and animal models. They found that extract solutions did not have adverse effects on cell cultures or on the animals tested. PPy has been demonstrated to be cytocompatible with fibroblasts cells, neuroblastoma, osteogenesis and marrow-derived stem cells. In the case of animal models, this includes the absence of body temperature change, red cell haemolysis, allergic response or mutagenesis. PPy is also compatible with hypodermis tissues, brain tissue and peripheral nerve in the *in vivo* tests. PPy implants were implanted in the cerebral cortex of the rat (Figure 1.7). Neural tissue and glial cells were grown on PPy surfaces. No signs of toxicity or abnormality in the surrounding tissues were observed. The presence of PPy did not cause any undesirable inflammatory response.
**Figure 1.7** PPy implants at six weeks post-surgery: (a) a stained slice with neurons (blue) and glia (green), scale bar: 100 μm; (b) a fluorescently stained slice around the implant site showing glial and neuronal cell bodies (blue) with the neurons highlighted (red) (adapted from reference [66]).

In addition, PPy can support cell adhesion and growth of a number of different cell types, including endothelial cells,^{67} rat pheochromocytoma cells,^{68} neurons and support cells.^{69} It has also been demonstrated that introduction of PPy into a biological system has the potential to not only provide a physical substrate for cell growth and tissue repair, but also allow the local delivery of an electrical stimulus to a specific site to foster cell growth and repair damaged tissue.^{70} This implied that if PPy could modulate cellular reactions then it could be possible to limit the toxicity of implantable devices by incorporating biomolecules to influence biocompatibility, opening up new vistas for PPy in biomedical applications.

1.3.2.2 *Catalytic Activity for Oxygen Reduction Reaction*

Apart from biocompatibility, electrocatalytic activity is required for air cathodes in a bio-battery. In 2005, V.G. Khomenko *et al.* discussed the mechanism and feasibility
of various types of CPs as ORR catalysts in acid and neutral electrolytes. They proposed an “oxygen absorption” theory of PPy, hypothesizing that molecular oxygen can be absorbed by the carbon atoms on the polymer chain to form an “oxygen-conductive polymer” bridging complex (Figure 1.8). The bridging complex could weaken the O-O bond of oxygen and lower the activation energy for reduction, leading to the electrocatalytic activity. It is worth noting that oxygen can interact only with PPy in the reduced state (close to fully-dedoped state). In other words, the reduced PPy is very easily oxidized by oxygen, and they can be utilized as electrocatalysts towards oxygen in the metal-air bio-batteries.

![Figure 1.8](image_url) The “oxygen-conductive polymer” bridging complex of PPy formed during oxygen reduction reaction (adapted from reference [71]).

The general redox chemistry of a Mg-air bio-battery using PPy cathode can be explained by the scheme shown in Figure 1.9. The Mg anode with lower electrochemical potential is first oxidized to Mg$^{2+}$ and donates electrons when discharged. The cathode, oxidized PPy, takes up electrons and releases small mobile dopant anions into the electrolyte and is reduced concomitantly. PPy in the reduced state after discharge could be re-oxidized (‘recharged’) by oxygen. These reactions are
fast and highly reversible, and thus make PPy a highly promising electrode material as an ORR catalyst.

Anode:

$$\frac{1}{2} \text{Mg} + \text{OH}^- \rightarrow \frac{1}{2} \text{Mg(OH)}_2 + e^-$$  \hspace{1cm} (1.4)

Cathode:

$$\text{PPy}^+ + e^- \rightarrow \text{PPy}^0$$  \hspace{1cm} (1.5)

$$\text{PPy}^0 + \frac{1}{4} \text{O}_2 + \frac{1}{2} \text{H}_2\text{O} + \text{A}^- \rightarrow \text{PPy}^+ + \text{OH}^-$$  \hspace{1cm} (1.6)

**Figure 1.9** General redox chemistry of a Mg-air bioelectric battery using PPy cathode (A⁻ represents small mobile charge balance anions) (Adapted from reference [73]).

### 1.3.3 Biodegradable Conducting Polymer-Biopolymer Cathodes

The main drawback in using CPs as the cathode material for a biodegradable battery is their non-biodegradability under physiological conditions. This property is inherent to all traditional CPs. CPs cannot be degraded via hydrolysis or by enzymatic processes resulting from the action of cells.

This limitation has motivated researchers to explore different approaches to synthesize biodegradable CPs. The first way to achieve biodegradability is to synthesize a block copolymer that contains conjugated oligomers and chemically degradable subunits. As model compounds of CPs, conjugated oligomers with well-defined structures have
been heavily investigated due to their good electroactivity, enhanced solubility and excellent processability. Schmidt’s group have synthesized a series of biodegradable and conductive block copolymers composed of degradable ester linkers and conjugated oligomers, including oligopyrroles, oligothiophenes and oligoanilines. The incorporation of conjugated oligomers into aliphatic polyesters backbones is ideal for applications in electrochemically-triggered drug delivery and neural cell growth. However, the electronic conductivity is impeded by the limited dopant used and low extent of π-conjugation in the polymer backbone.

Another popular strategy is to form CP-biopolymer composite/blend. To enhance the biodegradability of conductive blends, natural biopolymers and synthetic biodegradable polymers, such as polyesters, polyanhydrides and polycarbonates, have been introduced into small amounts of PPy. Unlike bio-stable materials, these synthetic polymers undergo hydrolytic degradation. Although the polymer degradation mechanism varies with the chemical composition, the mechanism of hydrolytic degradation can be broadly classified into two types: bulk erosion and surface erosion. For example, synthetic biodegradable hydrophilic polymers such as polyesters are known to undergo bulk erosion whereas hydrophobic polyanhydrides degrade through surface erosion. This conductive composite/blend is usually prepared by emulsion polymerization of nanoparticles in the polymer solution. Low content of PPy nanoparticles is dispersed in the resulting composite/blend, and thus unable to form a conductive network within the polymer matrix.

Generally, these biodegradable conductive copolymers and CP-biopolymer composite/blend usually suffer from low conductivity (10⁻⁷-10⁻³ S cm⁻¹) and poor
electrochemical activity, making them unsuitable as air cathodes for Mg-air batteries. When designing biocompatible/biodegradable CP-biopolymer compositeblend for Mg-air batteries, there are two key issues need to be considered: (1) introducing a thin-film of PPy and preserving its electrocatalytic activity; (2) identifying a suitable biopolymer that affords a controllable degradable profile.

1.3.3.1 Biodegradation of Biopolymers

Biopolymers are defined as biologically derived polymers and their attractiveness is due to their availability, biocompatibility, and biodegradability. Biopolymers can be divided into three main groups depending on their source:\textsuperscript{84}

- Polymers that are directly extracted from biomass, in other words natural polymers. Polysaccharides such as starch and cellulose, and proteins like casein and gluten belong to this group.

- Polymers that are produced through classical chemical synthesis using renewable bio-based monomers, such as polylactic acid.

- Polymers produced by microorganisms or bacteria, like polyhydroxyalkanoates and bacterial cellulose.

A variety of biopolymers have been used for medical care including preventive medicine, clinical inspections, and surgical treatments of diseases.\textsuperscript{85} Among the biopolymers employed for such purposes, a specified group of polymers are called polymeric biomaterials when they are used in direct contact with living cells or tissues of human body. The development of a polymeric biomaterial that is used as a
polymeric support must fulfil three key characteristics, namely biocompatibility, mechanical robustness and biodegradability. First and foremost, the material must be biocompatible in order to avoid any unfavourable immune system responses and possible implant rejection from the host. This would prevent the need for expensive and risky immunosuppressant therapy, which is a common complicating factor in organ transplantation.

Biodegradation of biomaterials takes place through the action of enzymes and/or hydrolysis process in the human body. This event occurs through a number of stages, the first being the breakdown of polymeric biomaterial into smaller, less complex fragments by solubilisation, hydrolysis, or through the biological action of enzymes. The second stage involves removal of the degradation products from the site of implantation. This can occur via bioresorption, whereby the degradation products are eliminated from the patient’s body through natural pathways (i.e. metabolism excretion). Alternatively, the removal of degradation products could potentially occur via an absorptive process (i.e. bioabsorption). This process occurs when the degradation products are too large to be removed through a simple diffusion mechanism, and therefore the products are transported from the initial site of implantation and stored in various organs.

Biodegradability depends not only on the origin of the polymer but also on its chemical structure, polymer morphology, and molecular weight. Some general rules are applicable in estimating the evolution of biodegradability; and these include an increase in hydrophobic character, molecular weight, and crystallinity. The use of naturally occurring polymeric biomaterial is advantageous as they are composed of
molecules that are able to promote favourable interactions with the surrounding tissues, thus enhancing their biocompatibility. Proteins (natural biopolymers) differ from synthetic polymers in the sense that proteins do not have equivalent repeating units along the peptide chains. The irregularity results in protein chains being less likely to crystallize, and this is attributed to the biodegradability.93

1.3.3.2 Silk Fibroin

Among a variety of natural biopolymers, silk fibroin (SF) has garnered increasing interest as a prime candidate spanning the field of bioelectronics and biomedicine. SF is a biocompatible, naturally occurring protein fiber. Natural silk fibers (*Bombyx mori*) are about 10-25 mm in diameter and consist of two proteins: a fibroin core and a sericin coating. Fibroin consists of a repetitive heavy chain (~390 kDa) and a light chain (~26 kDa) which is present in a 1:1 ratio and linked by a single disulfide bond.94 SF is generally composed of β-sheet structures due to the dominance of hydrophobic domains consisting of short side chain amino acids in the primary sequence. These structures permit tight packing of stacked sheets of hydrogen bonded anti-parallel chains of the protein.

A number of silk polymorphs have been reported, including the glandular state prior to crystallization (silk I), the spun silk state which consists of the β-sheet secondary structure (silk II), and an air/water assembled interfacial silk (silk III, with a helical structure).95 The silk I structure is observed *in vitro* in aqueous conditions and converts to a β-sheet structure when exposed to methanol or potassium chloride (Figure 1.10).96 The silk II structure imparts the protein-based materials with high mechanical strength and toughness.
Figure 1.10 Transition of silk fibroin secondary structures (adapted from reference [96]).

The raw silk cocoons are treated first to remove sericin and then boiled in an alkaline solution. The resulting silk fibers can be dissolved into an aqueous solution, which can then be used as the building block and processed into different materials ranging from gels and sponges to blocks and films. Figure 1.11 shows the recent breakthrough in silk technology that allows the ancient material to successfully tap into various high-tech biomedical fields. Among various forms, SF film shows robust mechanical strength, facile control of materials properties and programmable degradation lifetime (from minutes to years). SF films have oxygen and water vapour permeability that are dependent on the content of silk I and silk II structures, which is favourable for CP to interact with oxygen molecules. Efforts have also been made to use silk film as biologically active substrates for deposition of CPs.
Figure 1.11 Examples of materials that can be fabricated from silk in various shapes and forms, leading to functional devices and technology platforms for various research fields (adapted from reference [98]).

SF is reported to be biocompatible and induce minimal inflammatory responses when implanted. As a Food and Drug Administration approved biomaterial, silk has been used most extensively as sutures for wound ligation in the biomedical industry. Silk is able to degrade via the action of proteases, with the peptides generated metabolized by cells. B. mori yarns have been incubated in protease XIV solution up to 12 weeks.
The enzyme cleaves SF at multiple locations along the chains. The overall enzymatic degradation is mediated by surface erosion.\textsuperscript{102} In addition, the degradation rate of SF can be altered by different forms, as well as post-processing treatments, related to the content of β-sheet crystals and degree of organization of the non-crystalline domains. In general, the degradation rate decreases with an increase in overall β-sheet content.\textsuperscript{98}

1.4 Biocompatible and Biodegradable Polymer Electrolytes

An electrolyte plays a significant role in transmitting ions during the discharge process. It affects the battery’s performance such as energy density, power density and rate capability.\textsuperscript{103-104} Acting as both a separator and an ionic conductor, polymer electrolytes allow lightweight designs. It enables the entire cell components (anode, cathode, and electrolyte) to be integrated into a single contiguous unit. Such integration has potential advantages of allowing devices to be fabricated in a more functional manner of thin film with mechanical flexibility. Polymer electrolytes are emerging to attract much attention because of their advantages over their liquid counterparts, such as flexibility in battery shape/design and high safety.\textsuperscript{105}

Research efforts into developing polymer electrolytes are centred on achieving high ionic conductivity at room temperature, large electrochemical window, and good mechanical stability.\textsuperscript{106} The first ion conducting polymer electrolyte: polyethylene oxide complexes with alkali metals salt, was discovered by Wright \textit{et al.} in 1973.\textsuperscript{107} Solid polymer electrolytes can be divided into two different categories\textsuperscript{108}: (1) Dry solid polymer electrolytes in which ion conduction is coupled to segmental and structural motions of polymer chains at temperatures higher than the glass transition of the
polymer. (2) Plasticized polymer electrolytes in which the ion conduction occurs through the liquid solvent upheld within the polymer structure. Dry solid polymer electrolytes usually constitute of a precursor solution of salt in a polymer. The major drawback of dry solid polymer electrolytes is their low ionic conductivity ($10^{-5}$ S cm$^{-1}$) at ambient temperature, since the high degree of crystallinity (~65% in polyethylene oxide) in the polymer matrix hinders their ability for ionic conduction.

### 1.4.1 Plasticized Polymer Electrolyte

Despite the large number of studies on dry solid polymer electrolytes, their low ionic conductivity limits their practical applications. Increasing the amorphous nature of the polymer electrolyte can be achieved by addition of plasticizing agents, enhancing the dissociation of ion pairs of the salt. Plasticized polymer electrolytes provide ionic conductivities as high as $10^{-3}$ S cm$^{-1}$ at room temperature.$^{109}$ A typical solid polymer electrolyte consists of a polymer matrix, an ionic conductor, and additives.

A polymer network should immobilize the ionic conductor while providing conduction paths with a low barrier to ionic motion. Crystallinity and electrochemical stability of the polymer matrix are main factors that influence the overall performance of the polymer electrolyte.$^{110}$ Polymers with a low glass transition that provide flexibility to the polymer electrolyte is preferred. Meanwhile, the polymer needs to provide sufficient mechanical integrity to process thin-film polymer electrolytes. A promising strategy to develop biocompatible and biodegradable polymer electrolyte with high ionic conductivity is to incorporate the plasticizing fragment into a host biopolymer.
Ionic conductors are the source of the charge carriers in polymer electrolytes and responsible for the electrochemical properties. The additives, such as polar organic solvents act as a plasticizer. They can lower the glass transition temperature of the polymer matrix and facilitate segmental motions of the polymer chains, thus improving ion conduction in the system. Therefore, ion conduction in a plasticized polymer electrolyte occurs through segmental motions of polymer chains combined with the solution.

1.4.2 Polymer Electrolyte Containing Ionic Liquids

So far, the approach of plasticization has been the conventional way to reduce the crystallinity of a polymer matrix, resulting in an increase in amorphous phase content of polymer electrolytes. Room temperature ionic liquids (RTILs) can act as both ionic conductor and plasticiser that can substantially decrease the crystallinity of a polymer matrix. Compared to classical aqueous and organic electrolytes that are obtained by dissolution of salts in solvents, ILs are salts composed of organic cations and organic or inorganic anions with a relatively low melting point (<100 °C). The first scientific report about ILs was in 1914 on the preparation of ethylammonium nitrate. The structures of common IL cations and anions are shown in Figure 1.12.
Figure 1.12 Examples of cations and anions used in the formation of ionic liquids, together with changes in hydrophilic-hydrophobic properties associated with anion type (adapted from reference [115]).

ILs have received attention as electrolytes due to the advantages such as non-flammability, negligible vapour pressure, high ionic conductivity and high thermal, chemical and electrochemical stability. A broad and stable amorphous region is increased and creates free-volume, facilitating ion conduction. The improvement of conductivity requires low viscosity and high dielectric constant IL to increase the flexibility of polymer electrolytes and to promote the dissociation of paired ions. ILs are “designable” or “fine-tunable” to meet the requirements of specific applications. In addition to electrochemical characteristics, their high thermal stability plays an important role in the safety issue of energy storage devices. Different classes of ILs have been prepared for various applications, not only in electrochemical devices such as Li-ion batteries, electrochemical capacitors, fuel cells, but also in diverse synthetic reactions, separations and extractions as well as electrodeposition, and
biotechnological processes. Recently, it was reported that a polymer electrolyte can be obtained by incorporation of ILs into polymer solutions for high performance batteries (Figure 1.13).

Figure 1.13 Preparation of polymer electrolytes containing ionic liquid (compatible binary systems between polymer networks and ionic liquids). The flexibility of molecular design of ionic liquids can facilitate various interesting applications of ion-conducting polymer electrolytes (adapted from reference [121]).

Amongst a variety of ILs, choline-based ILs are considered to be of low toxicity, holding promise for ILs for a variety of biomedical applications. This is mostly due to the fact that choline is a naturally occurring cation that shows very low toxicity and it can work as a cell signaling agent. Choline salts have also been used recently in IL-gel systems for cancer therapy delivery. Another interesting feature of this IL is that it has a stable plastic crystalline phase. These organic plastic crystals are attractive
proton-conducting materials that can be used as solid-state solvents for fuel cell electrolytes.

1.5 Recent Developments in Implantable Biodegradable Batteries

As a recent emerging technology, biodegradable implantable medical bionics (BIMBs) offer great promise in the field of smart controlled release and tissue regeneration. They provide the ability to influence biological processes in a controlled fashion. Transistors being the building blocks of modern electronic technology have attracted attention in their development for biodegradable electronics. Christopher et al. successfully demonstrated an entirely degradable transistor deposited on resorbable biomaterial substrate. In vitro degradation of this organic transistor is shown (Figure 1.14). The time-line suggested that device integrity was intact up to 40 days with total device resorption at 70 days. BIMBs systems involve the use of electrical stimulation to perform their function. Current demonstrations have typically been limited by the use of an external power source or a wireless powering system. An on-board biodegradable battery to BIMBs is a crucial challenge in the design scheme of devices because of the limited size and material restrictions. The field of implantable biodegradable energy storage is relatively unexplored compared with the advances in the bioelectronics field. According to different energy storage materials used, including redox active biopolymers and bioresorbable metals, two types of biodegradable batteries will be summarized in the following sections.
Figure 1.14 Organic electronics and biodegradable materials have the potential to be integrated to create a new class of electronic devices for use in biomedical and environmental applications (adapted from reference [125]).

1.5.1 Biologically Derived Redox-Active Biomolecule Electrodes in Rechargeable Batteries

Melanin is a broad term for a group of natural pigments found in most organisms. In humans, melanin is the primary determinant of skin colour. It is also found in hair, the pigmented tissue underlying the iris of the eye, and the stria vascularis of the inner ear. Melanin pigments are intriguing electrode materials, owing to their ability to reversibly bind many cations during a redox process. Melanin pigments can serve as both anode and cathode materials depending upon the initial oxidation state. Melanin anodes (600-mg active material) coupled with manganese oxide cathodes can supply 5 mW of power for up to 20 h, while pre-oxidized melanin cathodes (600-mg active material) coupled with sodium-titanium phosphate anodes can supply 18 mW of power for up to 16 h. Bettinger and coworkers developed melanin cathodes that use aqueous Mg²⁺ electrolytes (Figure 1.15). These batteries satisfy the power requirements of many existing medical devices including sensors and drug delivery pumps. The required volume of active electrode material is compatible with standardized form factors commonly used in wireless capsule endoscopy. Additionally,
melanin electrodes may disintegrate and biodegrade to reduce the risk of long-term complications associated with device retention.\textsuperscript{131}

\textbf{Figure 1.15} (a) Pre-oxidized biologically derived melanin pigments serve as a suitable cathode material for aqueous Mg\textsuperscript{2+} batteries. (b) Melanin nanoparticles can be packaged into cathodes. (c) Discharged and (re)charged melanin using Mg\textsuperscript{2+} with a voltage hysteresis of 0.83 V (adapted from reference [129]).

Another type of biodegradable and redox-active endogenous biomolecule, dopamine, plays several important roles in the human body. In the brain, dopamine functions as a neurotransmitter, a chemical released by neurons to send signals to other nerve cells.\textsuperscript{132} Dopamine can be broken down into inactive metabolites by a set of enzymes. As an energy storage material, dopamine-hyaluronic acid, was prepared entirely from endogenous biomolecules via one-step carbodiimide conjugation of dopamine to
hyaluronic acid (Figure 1.1). The composite can be electropolymerized to create a pseudocapacitive biopolymer that exhibits catechol-quinone interconversion, stability, and long-term electroactivity for 400 cycles. A bio-battery with an operating voltage of \( \sim 0.85 \) V was fabricated when coupled with an implantable Ag/AgCl electrode. Recently, polydopamine was synthesized via oxidation by electron transfer as electrode material for a sodium-ion rechargeable battery. Through precisely controlling the redox state of carbonyl groups, an optimization between conductivity and capacity was achieved. The optimized polydopamine endowed the sodium-ion battery with a high capacity of 500 mAh g\(^{-1}\) and 100% capacity retention after 1024 cycles.

**Figure 1.16** Bioelectronic energy storage: a pseudocapacitive hydrogel composed of endogenous biomolecules (adapted from reference [133]).
1.5.2 Bioresorbable Metal Primary Batteries

Bioresorbable metal primary batteries can also serve as an on-board power source. This simple strategy utilises biocompatible and bioresorbable metals as electrodes to generate a voltage. The electrochemical cell in the ingestible component of a Proteus Discover system utilizes thin-film Mg anodes (8 μm thick; 0.0079 mg) and Cu cathodes (7 μm thick; 0.0071 mg), which produce open circuit voltages of 1.85 V at 0.1 mA for ~4 min.\textsuperscript{135} The amounts of Mg and Cu used are well below the maximum allowable daily limit.

Rogers and coworkers reported on a fully biodegradable primary battery using Mg coupled with other cathode materials including Mo, W, and Fe.\textsuperscript{136} The operating voltages of Mg-Mo, Mg-W, and Mg-Fe are 0.75 V, 0.65 V, and 0.45 V, respectively. This battery utilized biodegradable polyanhydrides as a packaging material and connected in series to increase output voltage (Figure 1.1). Recently, Allen and coworkers demonstrated a biodegradable Mg-Fe battery featured with an electroplated Mg anode.\textsuperscript{137-139} Electroplated Mg thin-film performs better than commercial Mg foil in terms of crystal orientation, electrical resistivity and corrosion behaviour. A completely biodegradable Mg thick-film (up to 50 μm) battery exhibited a capacity and power of up to 2.85 mAh and 39 μW, respectively.\textsuperscript{140} Another type of Mg primary battery with sputter coated Fe cathode has demonstrated a maximum power and capacity of 67 μW and 5.2 mAh, respectively.\textsuperscript{141}
Figure 1.17 (a) Configuration of a battery pack that consists of four Mg-Mo cells in series. (b) Discharging behaviour (0.1 mA cm$^{-2}$). (c) Dissolution of the battery (adapted from reference [136]).

Jimbo et al. reported a swallowable micro-battery based on Zn and Pt electrodes and ceramic porous separator using gastric fluid as electrolyte. A maximum potential of 0.42 V and a current of 2.41 mA were achieved. Another recent advance in this field employs gastric juices in the digestive tract and a Zn anode in combination with a Pd cathode for powering a wireless endoscopy capsule (Figure 1.18). For a surface area of 15 mm$^2$, 1.25 mW is generated with output voltage of 0.25 V.
Figure 1.18 (a) Structure of a Zn-Pd battery using gastric juices inside the stomach as an electrolyte. (b) Photograph of a microfabricated battery. (c) Output voltage and power as a function of discharge current densities (adapted from reference [143]).

Implantable biodegradable batteries are recently emerging. To date, all reported biodegradable batteries have limitations, including uncompetitive potential (less than 0.7 V), low discharge current (lower than 0.1 mA), short shelf-life (shorter than one week), and lack of degradation control (Table 1.2). This is mainly stemmed from the battery chemistries: semiconducting nature of melanin (poor redox activity and conductivity) and low theoretical cell voltage in metal primary batteries (low ORR activity).
Table 1.2 Projected characteristics of potentially implantable biodegradable batteries

<table>
<thead>
<tr>
<th>Battery</th>
<th>Cathode</th>
<th>Capacity</th>
<th>Plateau</th>
<th>Power</th>
<th>Time</th>
<th>Energy</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na ion</td>
<td>MnO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>16 g&lt;sup&gt;-1&lt;/sup&gt; 0.60</td>
<td>5 g&lt;sup&gt;-1&lt;/sup&gt; 20</td>
<td>100 g&lt;sup&gt;-1&lt;/sup&gt;</td>
<td>[128]</td>
<td></td>
<td></td>
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<tr>
<td>Mg ion</td>
<td>Melanin</td>
<td>61.6 g&lt;sup&gt;-1&lt;/sup&gt; 0.70</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>[129]</td>
</tr>
<tr>
<td>Na ion</td>
<td>Poly-dopamine</td>
<td>500 g&lt;sup&gt;-1&lt;/sup&gt; -</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>[134]</td>
</tr>
<tr>
<td>Mg-Mo</td>
<td>Mo</td>
<td>2.4 cm&lt;sup&gt;2&lt;/sup&gt; 0.75</td>
<td>75 cm&lt;sup&gt;2&lt;/sup&gt; 24</td>
<td>1.8 cm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>[136]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mg-Fe</td>
<td>Fe</td>
<td>2.9 cm&lt;sup&gt;2&lt;/sup&gt; 0.65</td>
<td>39 cm&lt;sup&gt;2&lt;/sup&gt; 22</td>
<td>1.9 cm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>[140]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mg-Fe</td>
<td>Sputter coated Fe</td>
<td>6.5 cm&lt;sup&gt;2&lt;/sup&gt; 0.27</td>
<td>84 cm&lt;sup&gt;2&lt;/sup&gt; 13.2</td>
<td>1.1 cm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>[141]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zn-Pt</td>
<td>Pt</td>
<td>2.41 cm&lt;sup&gt;2&lt;/sup&gt; 0.42</td>
<td>1 cm&lt;sup&gt;2&lt;/sup&gt; 0.67</td>
<td>0.10 cm&lt;sup&gt;2&lt;/sup&gt;</td>
<td>[142]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zn-Pd</td>
<td>Pd</td>
<td>- 0.25</td>
<td>125</td>
<td>-</td>
<td>-</td>
<td>[143]</td>
<td></td>
</tr>
</tbody>
</table>
1.6 Goals for This Dissertation

Despite the recent breakthroughs achieved in implantable biodegradable batteries, a demonstration of miniaturized biodegradable batteries with high performance is still lacking. The battery system accounts for a large volume of the implantable medical bionics device. Its miniaturization limits the development of these devices. Biodegradable high performance batteries would support the operation of biodegradable implantable medical bionics with greater functionality over longer times. A Mg-air battery is promising because of its benign biological function, acceptable dissolution rate and high energy density afforded. In addition, a particular challenge exists in the controlling of battery lifetime and correlating it with medical devices. To cater for various transient medical applications with different lifetimes, a modulated degradation process in energy storage materials and even the whole device is in high demand.

The following characteristics are highly desirable for implantable biocompatible/biodegradable battery systems: (1) a high capacity can be generated; (2) battery components should induce attenuated immunogenicity to the tissues/organs; (3) electrochemical storage system can be degraded in the body fluid; (4) end products during degradation process are nontoxic nor accumulated in the tissues/organs; (5) degradation process can be programmed; (6) battery should have an appropriate size.

This thesis aims to fulfil the above stated requirements by developing two critical components of an implantable biodegradable Mg-air battery, namely biocompatible/biodegradable cathode materials and polymer electrolyte. The battery
miniaturization can be achieved by using either PBS electrolyte (bio-batteries) or polymer electrolytes (solid-state battery). Four representative experimental works are developed in this thesis, which include:

(1) Partially biodegradable cathode materials are prepared by introducing PPy as the oxygen reduction catalyst onto biodegradable silk film by either electrochemical or chemical deposition method.

(2) Biodegradable polymer electrolytes are fabricated by embedding biocompatible ionic liquid into a biopolymer as host matrix.

(3) Enzymatic degradation of the whole encapsulated battery is achieved by engineering thin-film electrodes on silk film substrates.

(4) A controllable battery degradation profile is demonstrated via packaging material: silk film.
1. references


2. Experimental Methods

In this Chapter, chemicals and materials used in this thesis are summarized. A brief introduction of materials preparation and a general description of characterization methods are presented. Detailed preparation procedures and the specific experimental works are included in the following chapters.

2.1 Chemical Reagents and Materials

Table 2.1 List of chemical reagents and materials used in this thesis.

<table>
<thead>
<tr>
<th>Reagents and Materials</th>
<th>Grade</th>
<th>Company</th>
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</thead>
<tbody>
<tr>
<td>Glacial acetic acid</td>
<td>Analytical Reagent</td>
<td>Sigma-Aldrich</td>
</tr>
<tr>
<td>Sodium hydroxide</td>
<td>Analytical Reagent</td>
<td>Sigma-Aldrich</td>
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<td>Hydrochloric acid</td>
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</tr>
<tr>
<td>Chitosan</td>
<td>Medium molecular</td>
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</tr>
<tr>
<td>Sodium carbonate</td>
<td>Analytical Reagent</td>
<td>Sigma-Aldrich</td>
</tr>
<tr>
<td>Iron (III) chloride</td>
<td>Analytical Reagent</td>
<td>Sigma-Aldrich</td>
</tr>
<tr>
<td>PBS tablet</td>
<td>Analytical Reagent</td>
<td>Sigma-Aldrich</td>
</tr>
<tr>
<td>Substance</td>
<td>Purity/Concentration</td>
<td>Supplier/Details</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>----------------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>Sodium chloride</td>
<td></td>
<td>Ajax Fine Chemicals</td>
</tr>
<tr>
<td>Sodium p-toluenesulfonate</td>
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<td>Sigma-Aldrich</td>
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<td>p-toluenesulfonic acid</td>
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<td>Lithium bromide</td>
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<td>Human adipose-derived stem cells</td>
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<td>Lonza company</td>
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<td>Life Technologies, Australia</td>
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<tr>
<td>Calcein acetomethoxy</td>
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<td>Life Technologies, Australia</td>
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</tbody>
</table>
Propidium iodide  >94%  Life Technologies, Australia

*Bombyx mori* silkworm cocoons  -  Peaceful Silkworms, Australia

Protease type XIV from *Streptomyces griseus*  >3.5 units mg\(^{-1}\)  Sigma-Aldrich

Stainless steel mesh (316 type)  -  Shijiazhuang Yunchong Trading Co., Ltd

Dialysis tubing cellulose membrane  molecular weight cut-off=9000  Sigma-Aldrich

### 2.2 Synthesis and Preparation

Chapter 3 and Chapter 4 describe the preparation of biocompatible/biodegradable cathode materials composed of SF and PPy. Chapter 5 involves the preparation of biocompatible polymer electrolyte by embedding choline nitrate into chitosan. Chapter 6 illustrates the development of an encapsulated thin-film Mg-air battery. The general preparation and characterization techniques are described as follows.

#### 2.2.1 Preparation of Regenerated Silk Fibroin Aqueous Solution

The silk aqueous solution was used as the building block to prepare silk films for application as substrate for cathode and polymer matrix for polymer electrolyte in Chapter 3, Chapter 4 and Chapter 6. The silk fibroin extraction from silkworm cocoons was according to the procedures as described in the literature (Figure 2.1).\(^1\) Briefly, 5 g cocoons from *B. mori* silkworm were cut into small pieces and boiled in 0.02 M Na\(_2\)CO\(_3\) solution (1 L) for 30 min. The degummed silk fiber was rinsed with distilled
(DI) water for three times, and then dried at room temperature for 24 hours. The resulting silk fiber was dissolved in 9.3 M LiBr at 65 °C for 4 hours to obtain a 20% (w/v) silk solution. The solution was dialyzed against 2 L DI water for 3 days to remove the salt. After removal, the silk solution was further purified by centrifugation twice at 9000 rpm (Eppendorf Refrigerated Centrifuge 5702) for 20 min. The final solution typically had a concentration of 7-8% (w/v) and was stored at 4 °C. The silk aqueous solution was stable for one month.

**Figure 2.1** Schematic of the silk fibroin extraction procedure (adapted from reference [1]).
2.2.2 Preparation of Water Insoluble Silk Film

Silk films were prepared by casting 1.5-2.5 mL of aqueous silk solution onto a Teflon mould and dried at room temperature for 24 hour. The thickness of the silk film can be controlled by adjusting the volume and concentration of silk solution. The as-cast silk film is water soluble.

To render amorphous silk films insoluble in water, three methods were used to engender crystallinity in silk films. (1) Methanol annealing (for producing silk-silver nanowire composite, Chapter 3): The soluble silk films were immersed in 99% methanol solution for 5 min to 3 h to increase β-sheet content within the films. (2) Water annealing (for producing silk substrates on which PPy was chemically deposited, Chapter 4): The silk films were placed in a water-filled vacuum desiccator. The vacuum pump was switched on for ~5 min to fill the desiccator chamber with vapour. The vacuum was then turned off to let the homogeneous water vapour anneal the silk films. A minimum of 3 h vapour annealing was used to ensure the silk films would not dissolve in water any more. Longer annealing time increases the crystallinity within the films, resulting in slower degradation once implanted. (3) Thermal annealing (for device encapsulation using silk films, Chapter 6): The soluble silk films were thermal-treated using an embosser. The embossing time, pressure, and temperature profile determined the crystallinity of the silk films, which would influence the lifetime of the as-encapsulated devices. These annealing methods may endow silk with different β-sheet contents, affording tunable enzymatic degradation times.
2.2.3 Oxygen Plasma Treatment

Plasma activation is the process by which a material is treated to improve its ability to be painted or printed on. Oxygen plasma treatment can be used to modify the surface properties of polymers. The surface of a polymer becomes more hydrophilic after oxygen plasma treatment because of the formation of high energy groups between the surface groups of the polymer and the plasma. The enhanced hydrophilicity can be used to improve the adhesion of metal coating on polymers. In this work, crystallized silk substrates and silk-silver nanowire conductor were treated with oxygen plasma before metal deposition and electropolymerization. The treatments were done in a Harrick plasma cleaner PDC-002 equipped with a PlasmaFlo PDC-FMG gas flow mixer (Figure 2.2). The substrates were treated with oxygen plasma for 5-10 min with high energy level at a chamber pressure of ~1000 mTorr.

Figure 2.2 Photograph of plasma activation equipment.
2.2.4 Sputter Coating

Magnetron sputtering is a physical vapour deposition process which involves ejecting particles from a solid target that is bombarded by energetic particles. Those ejected particles collide with argon and move diffusively; reaching the substrates and growing. The sputter coating was processed in an Edwards Auto 306 Sputter Coater. The silk substrate was placed underneath an acrylic shadow mask (thickness 2 mm) prepared by laser cutting. When the pressure became lower than 0.01 mPa, the chamber was sealed and refilled with Ar to adjust the pressure to around 2.0-2.5 mPa. When the pressure was stable, the power supply was turned on to start the sputtering. First, a thin layer of Ti was deposited as an adhesion promotor. The deposition powers were 30 W and 40 W for Au and AZ31 targets, respectively. Those conditions minimized delamination. The growth and microstructure of sputtering layer can be controlled by the Ar pressure in the chamber and power applied.

2.2.5 Chemical Deposition of Polypyrrole on Silk Film

The experimental setup for chemical polymerization of pyrrole on silk film is shown in Figure 2.3. To achieve a bilayer structure, the bottom side of the silk film was sealed with polyimide film (Kapton tape, Ted Pella) and then adhered onto the container wall to avoid reaction solution reaching the back side. Oxidants were added drop-wised to initiate the polymerization. The reaction was performed in an ice-bath with constant stirring. The detailed synthesis process is described in Chapter 4.
**Figure 2.3** The setup used for PPy deposition only onto one side of a silk film.

### 2.2.6 Electrochemical Polymerization of Pyrrole

The electrochemical polymerization of pyrrole was carried out in a three-electrode system with a working electrode (where PPy was deposited), a stainless steel mesh counter electrode and a reference electrode, as shown in Figure 2.4. The reference electrode was either a silver/silver chloride (Ag/AgCl) electrode in aqueous solution or Ag/Ag⁺ in non-aqueous solution. In this work, PPy was deposited at a constant current density of 0.5 mA cm⁻². The silk-silver nanowire conductor (Chapter 3) and stainless steel mesh (Chapter 5) were used as the working electrodes. PPy was electrochemically deposited from a solution containing 0.1 M pyrrole and 0.1 M dopant (p-toluenesulfonic acid in Chapter 3 or sodium p-toluenesulfonate in Chapter 5). In chapter 3, acetonitrile was used as the solvent to prevent any distortion of silk film in water, while the solvent was Milli-Q water in Chapter 5.
2.3 Characterization

The physicochemical characterization techniques employed mainly include: (1) scanning electron microscopy, (2) optical microscopy, (3) thermogravimetric analysis, (4) Raman spectroscopy, (5) Fourier transform infrared spectroscopy, (6) sheet resistivity, (7) mechanical properties, and (8) enzymatic degradation test. The electrochemical characterization methods used include: (1) cyclic voltammetry, (2) electrochemical impedance spectroscopy, and (3) galvanostatic discharge tests.
2.3.1 Physicochemical Characterization

2.3.1.1 Scanning electron microscopy

A scanning electron microscope (SEM) is a type of electron microscope that produces images of a sample by scanning it with a focused beam of electrons. The most common SEM mode is detection of secondary electrons emitted by atoms excited by the electron beam. For conventional imaging in the SEM, specimens must be electrically conductive at the surface and electrically grounded to prevent the accumulation of electrostatic charge at the surface. Low conductive or non-conductive samples are usually coated with a 10 nm thick conductive layer such as gold or platinum for use. All the SEM images in this work were taken by using a JEOL JSM7500 FA cold-field-gun scanning electron microscope. Films were froze and fractured in liquid nitrogen to visualize cross sections, and all samples were mounted with carbon tape on aluminium stubs. Films were sputter coated with 15 nm Au using an Edwards Auto 306 Sputter Coater.

2.3.1.2 Optical microscopy

The optical microscope uses light and a system of lenses to magnify images of samples. It was used to observe the surface and cross-section of silk fibroin-polypyrrole bilayer film and the integrated solid-state Mg-air battery. The images were captured using a CCD camera and recorded by a computer. The optical microscope system used in this work was a Leica M205A.
2.3.1.3  **Raman spectroscopy**

Raman spectroscopy is a spectroscopic technique used to observe vibrational, rotational, and other low-frequency modes. Raman is commonly used to provide a fingerprint by which molecules can be identified. In Raman spectroscopy, the energy of the incident photon is much greater than the molecular vibrational quantum energy. The photon loses part of its energy to the molecular vibration and the remaining energy is scattered as a photon with reduced frequency. In this thesis, Raman spectra were obtained using a JOBIN YVON HR800 Confocal Raman system with 632.8 nm diode laser excitation on a 300 lines/mm grating at room temperature.

2.3.1.4  **Fourier transform infrared spectroscopy**

Fourier transform infrared spectroscopy (FTIR) is a technique which gives information on the vibrational and rotational modes of motion of a molecule. It is used to obtain an infrared spectrum of absorption or emission of a solid, liquid or gas. An FTIR spectrometer simultaneously collects high spectral resolution data over a wide spectral range. This confers a significant advantage over a dispersive spectrometer which measures intensity over a narrow range of wavelengths at a time. The instrument used in this thesis was a Shimadzu AIM8000 spectrometer with attenuated total reflectance mode (ATR). ATR has advanced to become the standard FTIR sampling technique, providing excellent data quality combined with high reproducibility. In this thesis, samples were measured over the range 600 cm\(^{-1}\) to 4000 cm\(^{-1}\).
2.3.1.5  *Thermogravimetric analysis*

Thermogravimetric analysis (TGA) is a method of thermal analysis in which changes in a material’s weight is measured as a function of ascending temperature. TGA is commonly used to determine mass change due to decomposition, oxidation, or loss of volatiles (such as moisture). TGA was conducted by heating the samples from room temperature to 600 °C at a heating rate of 5 °C min\(^{-1}\) under nitrogen flow (90 mL min\(^{-1}\)) using a Q500 TGA analyser (TA Instruments, UK).

2.3.1.6  *Sheet Resistivity*

Electrical resistivity is an intrinsic property that quantifies how strongly a given material opposes the flow of electric current. A low resistivity indicates a material that readily allows the flow of electric current. Sheet resistivity is a measure of resistivity of thin films. It is commonly used to characterize materials made by semiconductor doping, metal deposition, resistive paste printing, and conducting polymer coating.\(^5\) Sheet resistivity was measured with a Jandel RM3 Conductivity Meter using a four-point probe method (Figure 2.5). Sheet resistivity was calculated based on the current-voltage relationship according to the following equation:\(^6\)

\[
R = 4.532 \times \frac{V}{I} \quad (2.1)
\]

Where \(R\) is the sheet resistivity (\(\Omega\ sq^{-1}\)), \(V\) (volt) is the voltage measured across the two inner electrodes, and \(I\) (amperes) is the current passed between the two outer electrodes.
Electrical conductivity is the reciprocal of sheet resistivity, and measures a material’s ability to conduct an electric current. The electrical conductivity was calculated according to the following equation:

$$\sigma = \frac{1}{Rd}$$  \hspace{1cm} (2.2)

Where $\sigma$ is the electrical conductivity (S cm$^{-1}$), $R$ is the sheet resistivity (Ω sq$^{-1}$), and $d$ (cm) is the thickness of polymer coating which is obtained by evaluating film cross-sections with a light microscope or SEM.

**2.3.1.7 Mechanical properties test**

Mechanical properties test is a test in which a sample is subjected to a controlled tension and speed until failure. From the measurements, tensile strength, maximum
elongation, Young’s modulus, Poisson’s ratio, yield strength, and strain-hardening characteristics can be determined. In this dissertation, the mechanical properties of polymer electrolyte were evaluated using a Shimadzu EZ mechanical tester with a 500 N load at an elongation rate of 10 mm min⁻¹.

2.3.1.8 Enzymatic degradation of silk materials

Silk fibroin degrades via the action of proteases, including α-chymotrypsin and collagenases. The protease type XIV from *Streptomyces griseus* was dissolved in PBS solution to prepare the enzyme solution (1.0 mg mL⁻¹). Before incubation, silk sample films were dried under vacuum at 50 °C for 24 h. Three samples per time point were immersed in individual 5 mL buffered protease XIV solutions. Samples were incubated in the enzyme solution at 37 °C. Enzyme solutions were refreshed daily. At the designated times, samples were taken out, washed with DI water, dried under vacuum at 50 °C for 24 h and weighed. The degradation rate of the samples was calculated as the ratio of weight after digestion to the initial weight. Samples in PBS solution were used as controls following the same procedures.

2.3.2 Electrochemical Characterization

2.3.2.1 Cyclic voltammetry

Cyclic voltammetry (CV) is one of the most useful and widely applied techniques in electrochemistry. It involves sweeping the applied potential between two potential limits at a constant scan rate and the resulting current is monitored (Figure 2.6). In this thesis, it was used to evaluate the redox behaviour and electrocatalytic activity of cathode materials. A conventional three-electrode cell configuration was used in a
typical CV experiment, *i.e.* working electrode, counter electrode and reference electrode. An Ag/AgCl reference electrode was used. All potentials in this work are quoted against this reference electrode. The counter electrode was a stainless steel mesh. Before experiments, the counter electrode was sonicated in ethanol and finally rinsed with distilled water. The CV measurements were conducted using a CHI 650D electrochemical workstation (CHI Instruments, USA).

![Figure 2.6 A classical triangular waveform used in cyclic voltammetry.](image)

2.3.2.2 Electrochemical impedance spectroscopy

Electrochemical impedance spectroscopy (EIS) is used to characterize the electrochemical interface properties of electrodes. The impedance is measured by applying a single-frequency voltage or current to the interface between electrodes and electrolyte and monitoring the phase shift and amplitude of the current response at that frequency. EIS scans through this response as a function of frequency. Normally a small excitation signal is used to make sure that the response is pseudo-linear. In this
thesis, EIS tests were performed using a Gamry EIS 3000TM system in the frequency range of 100 kHz to 0.01 Hz with AC amplitude of 10 mV at open circuit potential.

Ionic conduction is the movement of an ion from one site to another through defects in the crystal lattice of a solid or aqueous solution. The ionic conductivity of an ionic liquid or a polymer electrolyte was determined with AC impedance in the frequency range of 100 kHz to 1 Hz. The polymer electrolyte or the ionic liquid saturated filter paper was sandwiched between two stainless steel plates. The ionic conductivity (S cm\(^{-1}\)) was estimated using the following equation:

\[
\sigma = \frac{d}{R_s A}
\]  \hspace{1cm} (2.3)

Where d is the thickness of the film (cm), \(R_s\) is the bulk resistance (\(\Omega\)) obtained from the first intercept on the x-axis of the impedance data in the complex plane, and \(A\) is the contact area (cm\(^2\)).

2.3.2.3 **Open-circuit voltage of PPy electrode**

Open-circuit voltage (OCV) is the difference of electrical potential between two terminals of a device. In OCV experiments the “free” potential of the cell is monitored as a function of time. The effect of oxygen on the reduced PPy electrode was investigated by monitoring OCV of the PPy electrode in oxygen saturated, air saturated and normal PBS solutions (no gas disturbance), similar to the work reported by Wu et al.\(^9\) In detail, PPy electrode was used as the working electrode. A platinum wire was used as the counter electrode. An Ag/AgCl electrode was used as the reference electrode. The electrolyte used was PBS (Figure 2.7). The PPy electrode was
first reduced at -0.8 V (vs. Ag/AgCl) until a stable potential was reached. Then the change of OCV with time upon bubbling gas was monitored and recorded using a CHI 650D electrochemical workstation.

**Figure 2.7** Experiment configuration for investigation of gas effect on PPy electrode (adapted from reference [9]).

### 2.3.2.4 **Battery discharge test**

The battery was constructed using a Mg alloy (AZ31) anode and a biocompatible/biodegradable air cathode. Mg alloy was first polished with sandpapers (three different grit sizes P400, P800 and P1200), followed by sonication in acetone and ethanol prior to use. The discharge performance of batteries was tested using a battery test system (Neware Electronic Co., Ltd). The system was equipped with
software that allowed multi-step discharge processes setup at different currents and cut-off potentials. The testing current densities were in the range of 5-100 μA cm$^2$. 
2.4 References


3. Cytocompatible/Biodegradable Silk Fibroin-Silver Nanowire-Polypyrrole Composite as an Air Cathode Material for Mg-Air Bioelectric Battery
3.1 Introduction

Biodegradable implantable medical bionics (BIMBs) has gained more exposure spanning from biomedicine to microelectromechanical systems.\(^1\),\(^2\) These devices could gradually degrade and disappear after their use in a programmed fashion, thereby eliminating secondary surgery retrieval and chronic inflammation associated with permanent implants.\(^3\)\(^-\)\(^5\) These biodegradable electronic systems may cater for various medical applications, such as wound healing monitoring, disease progression tracking, drug release and cardiovascular stimulators.\(^6\)

A biocompatible and biodegradable power source is ideal for their operation. Implantable Mg-air bioelectric batteries (bio-batteries) provide a feasible solution because of their benign biological function and high energy density available.\(^7\) They can rely on the oxygen in the body fluid to produce a voltage between the anode and cathode. The cathode material serves as a catalyst for oxygen reduction reaction (ORR). The key challenge to achieve a high performance biodegradable Mg-air bio-battery is the realisation of a biocompatible and biodegradable air cathode material with desired electrochemical properties.

Silver (Ag), as a bioinert noble metal, is widely considered nontoxic and utilized as electrodes for electronic devices.\(^8\) Ag(Hg) amalgam has been used for many years to fill dental cavities due to their non-reactive and corrosion resistant properties. Implantable Ag electrode is widely applied as a biosensing material for continuous glucose monitor and determination of zinc in cell cultivation medium.\(^9\) Silver nanomaterials have the added benefit of being a broad-spectrum anti-microbial agent, and are extensively used in wound care products and coatings for medical devices.\(^{10,11}\)
Silver nanowires (AgNWs) network can form a reliable, stretchable and transparent conductive layer that can be buried in various materials.\textsuperscript{12} AgNW-biopolymer composite could improve biocompatibility. Trapping AgNW into a biocompatible matrix has shown to reduce the \textit{in vitro} and \textit{in vivo} toxicity dramatically.\textsuperscript{13} Recently, AgNW embedded in collagen and polydimethylsiloxane have been developed as bioelectrodes and electroactive scaffolds for electrical stimulation of cells.\textsuperscript{14,15}

In this chapter, a cytocompatible conductor was prepared by burying AgNW network into silk fibroin (SF) film for constructing air cathodes. SF is a naturally occurring biodegradable protein fiber.\textsuperscript{16} Silk film has been used as a biological substrate for the fabrication of bio-integrated electronics,\textsuperscript{17} implantable therapeutic device\textsuperscript{18} and transient silicon electronics\textsuperscript{19}. To enhance the electrochemical activity, a thin-film of polypyrrole (PPy) is electrodeposited onto the silk fibroin-silver nanowire (SF-AgNW) conductor. PPy possesses the joint merits of biocompatibility\textsuperscript{20,21} and electrocatalytic activity to ORR\textsuperscript{22}. It is also a suitable substrate for cell attachment and proliferation.\textsuperscript{23} The coverage of PPy onto SF-AgNW composite could further enhance biocompatibility and limit the toxicity. This novel SF-AgNW-PPy composite can be degraded in the protease XIV solution and offer a discharge capacity of 2.91 mA\textit{h cm}^{-2} when coupled with Mg alloy in phosphate-buffered saline (PBS) electrolyte.

\section{3.2 Experimental}

\subsection{3.2.1 Preparation of SF-AgNW-PPy Composite}

AgNW film was prepared by spin-coating the AgNW dispersion in isopropanol (0.25 mg mL\textsuperscript{-1}) onto glass slides. Prior to use, these glass slides were cleaned with deionized water.
water, acetone and isopropanol, followed by a UV-ozone treatment (PSD Pro Series) for 30 min. These slides were dried at room temperature and then annealed at 150 °C for 30 min to reduce the resistance. Regenerated SF aqueous solution (4 wt%) was prepared from B. mori silkworm cocoons as previously reported. The SF solution (2 mL) was dropped onto the AgNW-coated glass slides. AgNW was embedded into the silk film after water evaporation. Dried SF-AgNW composites were then treated with 99% methanol for 2 h to induce formation of a silk II (β-sheet) structure. The film thickness is in the range of 50-60 μm.

SF-AgNW conductor was firstly treated with oxygen plasma (Harrick plasma cleaner PDC-002) for 10 min to produce a hydrophilic surface. A typical electrochemical deposition of PPy onto SF-AgNW conductor was carried out. PPy with dopant of p-toluenesulfonic acid (pTSA) was galvanostatically electrodeposited onto the SF-AgNW conductor from the solution containing 0.1 M pyrrole and 0.1 M pTSA in acetonitrile at 0 °C at a current density of 0.5 mA cm\(^{-2}\) for 30 min. The PPy content in the composite was calculated as the ratio of weight after electrodeposition to the initial SF-AgNW composite weight. SF-AgNW-PPy composite was washed with deionized water to remove the dopant and loosely bound PPy particles, and dried under vacuum at 50 °C for 24 h. PPy film was synthesized on a stainless steel mesh using the same conditions as above.

3.2.2 Characterization of SF-AgNW-PPy Composite

Cyclic voltammetry (CV) of SF-AgNW composite and SF-AgNW-PPy composite were conducted using an electrochemical workstation (CHI 650D). The specific
capacitance of electrodes can be calculated according to the following equation from CV curves:\textsuperscript{25}

\[
\mathcal{C} = \frac{A}{2s\Delta V}
\]

(3.1)

Where \(\mathcal{C}\) is the specific capacitance (F cm\(^{-2}\)), \(A\) is the area of the CV loop, \(s\) (V s\(^{-1}\)) is the scan rate, and \(\Delta V\) is the voltage window (V).

### 3.2.3 Cell Culture

Silk film, SF-AgNW composite and SF-AgNW-PPy composite were treated by soaking in sterile PBS supplemented with 500 Unit mL\(^{-1}\) penicillin-streptomycin for 20 h. They were placed into 24-well polystyrene cell culture plates and soaked overnight with culture medium, followed by rinsing with PBS twice. Human adipose-derived stem cells (hADSCs) were seeded on the samples at a density of \(2\times10^4\) cells cm\(^{-2}\), and cultured in Gibco Dulbecco’s Modified Eagle’s Medium media supplemented with 10\% Fetal bovine serum for seven days. Then cells were visualized using live/dead staining with 2 \(\mu\)M calcein acetomethoxy (calcein AM) and 4 \(\mu\)M propidium iodide (PI) in PBS. Images were obtained using a ZEISS Axio Imager microscope (Carl Zeiss).

### 3.2.4 Battery Assembly

The battery was fabricated with a Mg alloy (AZ31) anode (10 mm \(\times\) 10 mm) and SF-AgNW-PPy composite cathode (10 mm \(\times\) 10 mm) in a one compartment cell with 20 mL of PBS electrolyte, and tested using a battery-testing device (Neware Electronic
Co.). It was discharged galvanostatically to a cut-off cell voltage of 1.0 V at room temperature.

3.3 Results and Discussions

3.3.1 Preparation and Characterization

Figure 3.1 illustrates the fabrication procedure of SF-AgNW conductor. It started with the spin-coating of AgNW dispersion onto a cleaned glass slide, followed by an annealing process at 150 °C forming a fused interconnected network.26 The thickness and hence resistance of AgNW films can be controlled by adjusting the amount of AgNW. When the silk solution was dropped onto the AgNW-coated glass slide, it penetrated into the AgNW network. After water evaporation, the fused percolating AgNW networks were embedded in the silk film. The as-cast SF-AgNW film can be completely dissolved in deionized water within 3 min. To program its solubility in water, a methanol annealing process was employed to treat SF for 2 hours. After the treatment, SF-AgNW composite was peeled off from the glass slides with a thickness of 50-60 μm. The strong adhesion between SF and AgNW networks lead to the formation of a free-standing robust SF-AgNWs film.27,28 This fabrication process created a smooth conductive surface only on one side of the silk film. The contained silver in the composite was approximately 27 μg cm$^{-2}$, an amount that was expected to be well-tolerated by the human body (350 μg/day for a 70 kg person).29
The oxygen plasma treatment on SF-AgNW conductor ensured that pyrrole monomer could completely wet the conductive surface with a uniform distribution. The chronopotentiogram (Figure 3.2a) for PPy growth exhibited an initial spike due to charging of the double layer and oxidation of monomer, followed by a slow potential decrease as polymer growth proceeded, approaching a steady potential of 0.76 V. The PPy component composed about 1.2% of the total mass of SF-AgNW-PPy composite.

The SF-AgNW-PPy composite structure was investigated by Fourier-transform infrared spectra equipped with attenuated total reflectance accessory (ATR-FTIR). The as-cast SF film exhibited prominent peaks at 1650 cm\(^{-1}\) and 1540 cm\(^{-1}\) (Figure 3.2b), characteristic of silk I conformation (random coils and \(\alpha\)-helices). The methanol treated SF-AgNW composite showed a typical silk II structure with strong peaks at 1620 cm\(^{-1}\) and 1525 cm\(^{-1}\). The conductive side of SF-AgNW-PPy composite showed characteristic broad absorptions of PPy comprising various stretching modes at about 1288 cm\(^{-1}\) (C-N), and different C-H bending modes at around 1152 and 1016 cm\(^{-1}\). SF-AgNW-PPy composite clearly displayed both the typical bands of PPy and silk II conformation.

**Figure 3.1** Schematic fabrication sequence of SF-AgNW composite.
Figure 3.2 (a) Chronopotentiogram recorded during the growth of PPy-$p$TSA on a SF-AgNW conductor at a current density of 0.5 mA cm$^{-2}$. (b) Fourier-transform infrared spectra of as-cast silk film (1), methanol treated SF-AgNW composite (2), the conductive side of SF-AgNW-PPy composite (3), and PPy film (4).

The AgNWs were randomly distributed on the SF surface or buried inside the matrix forming an inter-connected AgNW networks (Figure 3.3a). These nanowires showed an average diameter of 50-60 nm and length of 10-20 μm (Figure 3.3b). After
electrochemical polymerization of pyrrole, the AgNW networks became much thicker and denser (Figure 3.3c). PPy nanoparticles not only wrapped around the AgNW, but also filled in the open space between AgNW networks (Figure 3.3d), as previously reported. The hydrophilic surface of SF-AgNW conductor readily accommodated and anchored freshly deposited PPy. Continuous electrons supplied from the negative voltage promoted lateral growth and uniform coverage across the whole conductor surface.

![Image of scanning electron microscopy images](image)

**Figure 3.3** Scanning electron microscopy images of SF-AgNW composite (a) and (b), and SF-AgNW-PPy composite (c) and (d).

The thermal stability of SF-AgNW-PPy composite was investigated using thermogravimetric analysis (TGA) (Figure 3.4). All the samples exhibited a mass loss
of 5.8-7.4% before the temperature reached 150 °C, attributed to the bound water in the film. The rapid weight loss above 240 °C represented the thermal degradation of SF. The content of AgNW in the SF-AgNW composite was only 0.6%. Such a tiny amount did not impact on the thermal stability of SF. After PPy deposition, no obvious decomposition step corresponding to PPy can be observed because of the low content of PPy in the composite. However, a slightly higher weight retention at 600 °C was observed, 45.6% for SF-AgNW-PPy compared to that (42.1%) for SF-AgNW composite. This can be explained by the high thermal stability of PPy.

![Thermogravimetric analysis curves](image)

**Figure 3.4** Thermogravimetric analysis curves of silk film, SF-AgNW composite, SF-AgNW-PPy composite, and PPy film.

### 3.3.2 Electrochemical and Electrocatalytic Properties

Sheet resistivity was measured with a four-point resistivity probe. The sheet resistivity of SF-AgNW conductor was 36±4 Ω sq⁻¹ at room temperature, and it was decreased
by 53% (16±2 Ω sq⁻¹) after annealing at 150 °C due to the result of fusion at the contact of nanowires, thus reducing contact resistance between nanowires. SF-AgNW-PPy composite showed a sheet resistivity of 306±12 Ω sq⁻¹.

The electrochemical properties were evaluated using cyclic voltammetry (CV) (Figure 3.5). It was conducted in nitrogen-saturated PBS solutions at a scan rate of 20 mV s⁻¹. In the SF-AgNW composite, only the surface AgNW layer was active for the electrochemical reactions while the embedded AgNW functioned as the conducting layer. The SF-AgNW composite presented well defined redox peaks centred at -0.23 V and 0.22 V, which could be ascribed to the formation and reduction of silver chlorides (0.14 M Cl⁻ contained in PBS):

\[
Ag + Cl^- \leftrightarrow AgCl + e^-
\]  

(3.2)

After electrodeposition of PPy, a new couple of broad redox peaks appeared around -0.45 V and -0.06 V, which was related to the electrochemical activity of PPy. The absence of AgNW redox peaks was attributed to the complete coverage with PPy. The SF-AgNW-PPy composite exhibited a 455% increase in the specific capacitance (68 F cm⁻²) compared with that (15 F cm⁻²) of SF-AgNW composite. The enhanced specific capacitance was due to the high capacitive activity of PPy. PPy exhibited broad redox peaks, which can be explained by the reason that the charge carriers in conducting polymers were highly delocalized and strongly affected each other.  

33
Electrochemical impedance spectroscopy (EIS) is used to gain a deeper insight into electrochemical systems. The Nyquist plots mainly included a semicircular region lying on the real axis, which was followed by a straight line. It can be seen that SF-AgNW conductor (Figure 3.6a) exhibited a lower intersecting point with the X-axis at high frequency than the SF-AgNW-PPy composite (Figure 3.6b); demonstrating a smaller uncompensated bulk resistance. In addition, a smaller semicircle was observed for SF-AgNW conductor, indicative of its smaller charge transfer resistance. An equivalent circuit model was employed to quantitatively analyse the impedance spectra (Figure 3.6c). In the circuit, Rs is the bulk resistance; Rct is the charge transfer resistance. A constant phase element, CPE, is associated with the double-layer capacitance across the electrode/electrolyte interfaces; Wo corresponds to the Warburg impedance resulting from the semi-infinite diffusion of ions within the electrode at low frequency. A good fitting result was shown for both electrodes. The
fitting values of the equivalent circuit elements are listed in Table 3.1. SF-AgNW conductor showed a Rs and Rct of 12.4 Ω and 14.4 Ω, respectively. The bulk resistance and charge transfer resistance of SF-AgNW-PPy composite was about 36.7 Ω and 96.2 Ω, respectively. These values are on par with the recently reported results for poly(glycerol-co-sebacate)-cinnamate-AgNW composite bioelectrode used in self-deployable power sources.34

![Figure 3.6](image)

**Figure 3.6** Electrochemical impedance spectra of SF-AgNW composite (a), SF-AgNW-PPy composite (b) in PBS solution; (c) the equivalent circuit used for the simulation.
Table 3.1 Resistance of the equivalent circuit elements obtained from the Nyquist plot.

<table>
<thead>
<tr>
<th></th>
<th>Rs</th>
<th>Rct</th>
<th>CPE</th>
<th>W1</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-AgNW</td>
<td>12.4</td>
<td>14.4</td>
<td>0.79</td>
<td>14.99</td>
</tr>
<tr>
<td>SF-AgNW-PPy</td>
<td>36.7</td>
<td>96.2</td>
<td>0.64</td>
<td>298.9</td>
</tr>
</tbody>
</table>

To verify if the reduced PPy can be used as an ORR electrocatalyst, SF-AgNW-PPy composite was firstly reduced by applying a constant potential of -0.8 V for 10 min. The open-circuit voltage of SF-AgNW-PPy composite increased immediately after the applied current was removed (Figure 3.7), due to the re-oxidation of reduced PPy. It can be seen a potential of -0.15 V, -0.10 V, -0.03 V and 0.04 V was detected after 25 min with no gas bubbling, bubbling with N₂, air, and O₂, respectively. It was higher in the solution with more oxygen available. Thereby a conclusion can be made that the SF-AgNW-PPy at the reduced state was re-oxidized by oxygen, that is, it can function as catalyst to oxygen reduction.
Figure 3.7 Potential response of SF-AgNW-PPy composite from the reduced PPy in PBS solution with air, oxygen, nitrogen or no gas bubbling after the applied potential (-0.8 V vs. Ag/AgCl) was removed.

3.3.3 Discharge Characteristics of Mg-Air Bioelectric Batteries

The Mg-air bio-batteries were discharged galvanostatically to a cut-off cell voltage of 1.0 V at various current densities (Figure 3.8a). In this Mg-air battery system, PPy functioned as the catalyst towards oxygen reduction. It involves Mg oxidation, oxygen reduction and anions insertion into PPy matrix processes. The main discharge reactions are as follows:\textsuperscript{35}

Anode:

\[
\frac{1}{2} \text{Mg} + \text{OH}^- \rightarrow \frac{1}{2} \text{Mg(OH)}_2 + e^- \quad (E = -2.69 \text{ V})
\]

Cathode:

\[
(\text{PPy})^+ + p\text{TS}^- + e^- \rightarrow (\text{PPy})^0 + p\text{TS}^-
\]
(PPy)$^0 + \frac{1}{4} \, \text{O} + \frac{1}{2} \, \text{HO} + A^- \rightarrow (\text{PPy})^+ / A^- + \text{OH}^- \, (E = 0.40 \, \text{V})$

Overall reaction:

$\frac{1}{2} \, \text{Mg} + \frac{1}{4} \, \text{O}_2 + \frac{1}{2} \, \text{H}_2\text{O} \rightarrow \frac{1}{2} \, \text{Mg(OH)}_2 \, (E_{\text{cell}} = 3.09 \, \text{V})$

Where $A^-$ represents anions in PBS electrolyte, including $\text{Cl}^-$, $\text{H}_2\text{PO}_4^-$, $\text{HPO}_4^{2-}$ and $p\text{TS}^-$.

The open-circuit voltage for the battery was in the range of 1.80-1.72 V just after the cell was assembled. The cell voltage dropped immediately when the discharge current was applied and soon reached a flat discharge plateau. The assembled Mg-air bio-batteries exhibited a discharge capacity of up to 2.91 mAh cm$^{-2}$ at a current density of 10 $\mu$A cm$^{-2}$ in PBS solution, offering a specific energy density of $\sim 3.92$ mWh cm$^{-2}$. This bio-battery satisfied the power requirements of many existing medical devices including sensors and drug delivery pumps.$^{36}$

To further support that PPy cathode in this battery system served as a catalyst for O$_2$ reduction, a blank stainless steel (SS) mesh was used as control. Upon discharge the cell voltage sharply decreased to around 1.0 V, in sharp contrast to a high plateau voltage of 1.35 V offered from the cell with PPy cathode at the same discharge current of 10 $\mu$A cm$^{-2}$ (Inset of Figure 3.8a). Even at a very low cut off voltage of 1.0 V the cell with SS can only be discharged for 42 hr, much lower than that 290 h using PPy electrode. It clearly demonstrates that PPy plays a catalytic role in oxygen reduction. SS mesh mainly acted as a current collector in this battery system.

Plots of power density vs. current density were obtained (Figure 3.8b). The plateau voltages ranged between 1.35 V and 1.05 V with an applied discharge current density in the range of 10-100 $\mu$A cm$^{-2}$. Due to the high ORR efficiency of SF-AgNW-PPy composite, this Mg-air bio-battery delivered much higher plateau voltages and slightly
higher specific capacity than those (0.4-0.7 V, 2.4 mAh cm$^{-2}$) recently reported of fully biodegradable primary Mg-Mo battery.$^{37}$

Figure 3.8 (a) Galvanostatic discharge curves of Mg-air bio-batteries composed of SF-AgNW-PPy composite in PBS electrolyte at various current densities. (Inset: discharge curve of Mg-air battery using SS mesh cathode as control). (b) Plateau voltage and the corresponding power density of Mg-air bio-batteries as a function of discharge current densities.
The areal energy and power densities were used to build Ragone plots in comparison with other reported biocompatible implantable energy storage systems (Figure 3.9). The Mg-air bio-battery stated in this work delivered an areal energy density of 3.91 mWh cm\(^{-2}\) at an areal power density of 13.5 µW cm\(^{-2}\), while an areal energy density of 1.64 mWh cm\(^{-2}\) could still be delivered at a high areal power density of 105 µW cm\(^{-2}\). The areal energy density reported in this work was higher than the reported biocompatible implantable energy storage devices, including Mg-Mo battery reported (1.8 mWh cm\(^{-2}\)),\(^{37}\) Mg-Fe battery (1.9 mWh cm\(^{-2}\)),\(^{38,39}\) Zn-Pt battery (0.1 mWh cm\(^{-2}\))\(^{40}\) and melanin-based supercapacitor (0.07 mWh cm\(^{-2}\))\(^{41}\). It clearly demonstrates that our device can provide remarkably high energy densities.

![Figure 3.9 Ragone plot of a Mg-air battery based on SF-AgNW-PPy electrode in comparison to the reported biocompatible implantable energy storage devices.](image-url)
3.3.4 Cytocompatibility

The integration of AgNW into biopolymers shows great promise for the next generation of bioelectronics and biosensors. However, serious concerns remain about the safety issues they may pose, especially for implantable devices. The cytotoxicity of SF-AgNW composite and SF-AgNW-PPy composite was evaluated using human adipose-derived stem cells (hADSCs) and silk film as a control (Figure 3.10). hADSCs were seeded and cultured on those samples over seven days. Cells grew and proliferated well on all the samples. The Live/Dead staining hardly showed any dead cells, noted by the lack of red emission of PI. All the samples showed an obvious cell proliferation during the seven days culture, indicative of low cytotoxicity. The toxicity of silver nanomaterials was mainly derived from the release of silver ions. The low dose of AgNW (27 μg cm⁻²) resulted in a low local concentration of silver ions. The trapping of AgNW in the silk matrix and coverage of PPy further hindered the release of silver ions.
Figure 3.10 Live/dead imaging of hADSCs on silk film, SF-AgNW composite and SF-AgNW-PPy composite with live (green, calcein AM) and dead (red, PI) staining. Scale bars: 100 μm.

3.3.5 Enzymatic Degradation

As the enzyme-mediated degradation was a surface phenomenon, the protease would readily adsorb on the silk substrate of SF-AgNW-PPy composite, giving a partially biodegradable conductive composite. To assess its biodegradation, SF-AgNW-PPy composite and silk film as a control were exposed to protease XIV solution (1 mg mL$^{-1}$) (Figure 3.11a). All the samples degraded in the enzyme solution as evidenced by the continuous weight loss. Specifically, weight loss of the SF-AgNW-PPy composite was 13%, lower than that of silk film (21%) in the first 24 h. At this stage, the weight
loss may be caused by the degradation of silk I and non-crystalline region in SF.\textsuperscript{43} The silk film had completely fallen apart and unable to be collected for analysis after 8 days. The weight loss of SF-AgNW-PPy composite was 71\% after 20 days incubation. It was much higher than that reported of 8\% over 10 days for SF-PPy composite with PPy chemically coated on both sides of the silk films.\textsuperscript{44} As PPy was stable in the protease solution, SF contributed to the overall biodegradation of the composite. The mass loss of the composite exhibited a significantly longer time compared with that of silk film, demonstrating the coverage of PPy could slow down the biodegradation rate of SF.

Figure 3.11b showed images of SF-AgNW-PPy composite after incubation in the protease XIV solution. The composite membrane kept its structural integrity and the PPy layer was not delaminated from the SF-AgNW composite up to 10 days incubation. Small irregular debris was generated after 20 days degradation as a result of the SF degradation. Further degradation of the composite into several hundred nanometer pieces may result in their elimination by renal excretion, phagocytosis and/or endocytosis.\textsuperscript{45}
To investigate the effect of biodegradation on the electrochemical properties of SF-AgNW-PPy composites, the CV curve was probed during the incubation period. Samples were adhered with copper tape encapsulated with Kapton tape prior to incubation in the protease solution. SF-AgNW-PPy composites still preserved their electrochemical response throughout the enzyme exposure period (Figure 3.12). A slight shift in the reduction potential from -0.45 V to -0.53 V and a 66% decrease in reduction current were observed after three days. The decrease in electrochemical
activity may be caused by the protein accumulation on the surface affecting the ability of ions to flow in and out of films. Nevertheless, the SF-AgNW-PPy composite did retain its electrochemical activity over three days of incubation. After five days of incubation, the SF-AgNW-PPy composite showed a current response of 20 µA cm⁻², which was 100 times lower than the original current. The current decrease may be attributed to the disruption of the continuous conductive PPy framework caused by the degradation of silk substrate.

**Figure 3.12** Cyclic voltammograms of the SF-AgNW-PPy composite during incubation in 1.0 mg mL⁻¹ protease solution for five days. Cyclic voltammetry was performed in PBS electrolyte at a scan rate of 20 mV s⁻¹.
3.4 Conclusions

In this chapter, a cytocompatible and biodegradable air cathode material with PPy electrodeposited on a SF-AgNW conductor has been developed. SF-AgNW-PPy composite shows a high conductivity and a mild catalytic activity towards oxygen reduction. It supports the adhesion and proliferation of hADSCs and degrades in a concentrated buffered protease XIV solution, with a weight loss of 71% after 20 days. The composite preserves its electrochemical activity over three days of incubation in the enzyme solution. The assembled Mg-air bio-battery exhibits a discharge capacity of up to 2.91 mAh cm$^{-2}$ at a current density of 10 µA cm$^{-2}$ at room temperature, offering a specific energy density of $\sim$3.92 mWh cm$^{-2}$. These materials may find future applications as biocompatible/biodegradable bioelectrodes and soft scaffolds for electrically stimulated tissue regeneration.
3.5 References


4. Towards Biodegradable Mg-Air Bioelectric Batteries Composed of Silk Fibroin-Polypyrrole Film

This chapter is adapted from the article, “Towards biodegradable mg-air bioelectric batteries composed of silk fibroin-polypyrrole film”, by Xiaoteng Jia, Caiyun Wang, Chen Zhao, Yu Ge, Gordon G. Wallace, which was published in Advanced Functional Materials, 2016, 26, 1454-1462. (Adapted with permission from WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim)
4.1 Introduction

The major challenge to achieve a biodegradable Mg-air bio-battery is to prepare a biocompatible/biodegradable cathode material. As a promising air cathode material, conducting polymers (CPs) are very stable in physiological conditions. They cannot degrade via hydrolysis or by enzymatic process resulting from the action of cells.

A possible solution to this problem involves the fabrication of CP-biopolymer composites in which the biopolymer component provides controllable degradability. Silk fibroin (SF) is a sustainable biopolymer and a promising candidate for advanced implantable electronic devices interfaced with the body. A biocompatible silk-PPy composite with a conductivity of 1 S cm$^{-1}$ has been recently reported for use as electromechanical actuators. A degradation profile of 8% mass loss after 10 days incubation in protease XIV solution was reported.

As described in Chapter 3, the author prepared a cytocompatible conductor by incorporating AgNW into silk film, followed by the electrodeposition of PPy onto the composite. In this chapter, to further enhance the bio-battery capacity, a biocompatible/biodegradable SF-PPy bilayer film was prepared. In this SF-PPy film, the PPy layer was chemically coated onto one side of the silk film substrate. Compared with the electropolymerization method used in Chapter 3, chemical polymerization is favourable for the mass production of PPy. The resultant device provided a capacity and energy density of up to 3.79 mAh cm$^{-2}$ and 4.70 mWh cm$^{-2}$, respectively. The battery performance is better than that (2.91 mAh cm$^{-2}$ and 3.91 mWh cm$^{-2}$) achieved in Chapter 3. The operation of the Mg-air bio-battery in the enzyme solution at 37 °C was also evaluated. In addition, as reported in this chapter, a water-annealing process
was employed to enable SF-PPy film to be water stable. This treatment could endow
a low content of β-sheet conformation in SF, resulting in a rapid enzymatic
degradation. An 82% weight loss was observed after 15 days when incubated in the
protease solution, faster than that (71% after 20 days) reported in Chapter 3.

4.2 Experimental

4.2.1 Preparation and Characterization of SF-PPy Bilayer Film

The as-cast silk films were subjected to a water-vapour annealing process for 24 h to
induce the formation of silk I and silk II structures. A PPy layer was chemically
deposited on silk film. Films were exposed to a 45 mL aqueous solution containing
pyrrole and α-TPS, where, in addition, 5 mL of ethanol was added to improve the
wettability of the silk film. The solution was kept stirring in an ice bath for 30 min,
followed by addition of 5 mL pre-cooled FeCl₃ solution drop-wise to initiate the
polymerization. The reaction was performed in an ice-bath for 4 h. The concentration
of pyrrole, FeCl₃ or α-TS was 0.1 M. The obtained film was washed with abundant
deionized (DI) water, followed by sonication in DI water for 30 min to remove any
loosely bound PPy. Finally, the film was dried at room temperature overnight. PPy-
α-TS powder was synthesized using the same conditions as above. After 4 h
polymerization, black precipitate was formed. PPy-α-TS powder was collected by
filtration and rinsed with DI water several times. It was dried overnight at room
temperature.

The PPy content in the SF-PPy film was determined using the same method as
described in Chapter 3. The tilted cross-sectional view (approximately 20°) of SF-PPy
film was characterized using an optical microscope (Leica DM6000). The chemical structure of SF-PPy film after biodegradation was determined by ATR-FTIR. Morphological changes during biodegradation were observed using SEM.

4.2.2 Cell Construction and Testing

The cell was fabricated with a Mg alloy anode (10 mm × 10 mm) and SF-PPy film cathode (10 mm × 10 mm) in a one compartment cell with 20 mL of PBS electrolyte. For rate capability testing, the cell was discharged for 8 hours at various current densities without a cut-off voltage applied. An idle time of 0.5 hour (no applied current) was used between each step. The cell discharge performance was also investigated at 37 °C in 20 mL of 1.0 mg mL⁻¹ protease XIV PBS solution or PBS only electrolyte as controls at a current density of 20 µA cm⁻².

4.3 Results and Discussion

4.3.1 Preparation and Characterization

The silk film was prepared using a simple casting method from a 7.5 wt% SF solution. The water-vapour annealing procedure allows the fibroin chain to self-assemble into a structure with reduced β-sheet content, thus resulting in a rapid biodegradation rate. SF-PPy film prepared by chemically coating a PPy layer only onto the top side of the silk support showed a bilayer structure with a total thickness of ~60 µm (Figure 4.1a). The glossy black PPy coating was composed of particles/aggregates (Figure 4.1b). The thickness of the PPy layer was about 7 µm (Figure 4.1c). The film substrate (referred to the back side of SF-PPy film) retained a smooth and uniform morphology after the
polymerization; no obvious PPy product can be observed (Figure 4.1d). The SF-PPy film contained 3.9% (w/w) PPy. The PPy content was higher than that (1.2%) achieved for the SF-AgNW-PPy composite in Chapter 3. The sheet resistivity of SF-PPy film doped with pTS was in the order of $1 \times 10^3 \ \Omega \ \text{sq}^{-1}$. This value was on par with other biodegradable conductive composites with similar PPy content. The SF-PPy film demonstrated a conductivity of $\sim 1.1 \ S \ cm^{-1}$ measured by the four-point probe method.

![Image](image.png)

**Figure 4.1** (a) Optical image of the cross-sectional view (20° tilted) of SF-PPy film; scanning electron microscope images of PPy-modified side (b), cross-section (c) and back side (d) of SF-PPy film.

Fourier-transform infrared spectra equipped with attenuated total reflectance (ATR-FTIR) and Raman spectroscopy were used to further characterize the SF-PPy film.
structure. The characteristic absorbance bands in FTIR spectra for silk secondary structures include 1650∼1630 cm\(^{-1}\) for amide I (C=O stretching), 1540∼1520 cm\(^{-1}\) for amide II (secondary N-H bending) and 1270∼1230 cm\(^{-1}\) for amide III (C-N stretching) (Figure 4.2a).\(^7\) The bare silk film and film substrate exhibited similar absorption bands. They both showed a strong peak at 1650 cm\(^{-1}\), corresponding to the silk I structure. In the amide II region, one peak at 1540 cm\(^{-1}\) (silk I) appeared, with a shoulder at 1520 cm\(^{-1}\) (silk II). In the amide III region a peak at 1236 cm\(^{-1}\), generally assigned to random coil-structures, was observed.\(^8\) These results indicated that SF-PPy film was dominated by the silk I structure (random coils and \(\alpha\)-helices) over silk II (\(\beta\)-sheets). They were consistent with the previously reported water-annealed silk films.\(^9\) The PPy-modified side of SF-PPy film showed only characteristic peaks of PPy due to its complete coverage on the silk substrate. It exhibited absorption peaks of C-N absorption at around 1293 cm\(^{-1}\), PPy ring breathing at 1150 cm\(^{-1}\) and C-H in plane bending modes at about 1025 cm\(^{-1}\). The band at 965 cm\(^{-1}\) was assigned to a fraction of PPy free from the influence of the dopant.\(^10\)

Raman spectroscopy also provides a powerful tool to study surface composition. No significant differences were observed among the spectra collected for the bare silk film and film substrate (Figure 4.2b). They both showed a prominent peak at 2940 cm\(^{-1}\) ascribed to the C-H stretching. The amide I band appeared at 1665 cm\(^{-1}\), and the amide III range showed a complex structure at 1277 and 1243 cm\(^{-1}\).\(^11\) This was a characteristic spectral pattern of SF with a prevailing silk I conformation, in good agreement with the IR results. After PPy deposition, the typical bands of PPy located at 1570 and 1324 cm\(^{-1}\), assigned to C=C backbone stretching and ring-stretching were
observed. The bands at 1046 and 927 cm\(^{-1}\) were attributed to C-H out-of-plane and in-plane deformation of PPy, respectively.\(^{12}\)

**Figure 4.2** Fourier-transform infrared spectra (a) and Raman spectra (b) of bare water-annealed silk film (1), the film substrate (2), PPy-pTS powder (3) and PPy-modified side of SF-PPy film (4).
The thermal behaviour of silk film was affected by the PPy layer, as evidenced from the thermogravimetric analysis (TGA) results (Figure 4.3). PPy-\(\rho\)TS powder showed a high thermal stability. The weight loss was 5% at temperatures up to 150 °C due to water evaporation. It was stable up to 290 °C, and 52% of the weight remained at 600 °C. The silk film underwent a nearly 10% weight loss at 150 °C, indicating a strong water-silk interaction in a silk I predominant structure. Then it underwent a rapid decomposition from 250 °C, and had 37% weight remaining at 600 °C. For SF-PPy film, the decomposition of the polymer backbone moved to a higher temperature compared to silk film, from 250 to 262 °C. Weight retention at 600 °C increased as well, from 37% to 42%. These results suggested that the PPy layer acted as a protective layer against thermal degradation.

![Thermogravimetric analysis curves of silk film, SF-PPy film and PPy-\(\rho\)TS powder.](image)

**Figure 4.3** Thermogravimetric analysis curves of silk film, SF-PPy film and PPy-\(\rho\)TS powder.
4.3.2 Electrochemical and Electrocatalytic Properties

The electrochemical property of SF-PPy film was evaluated using cyclic voltammetry (CV) in oxygen-saturated or nitrogen-saturated PBS electrolyte at a scan rate of 5 mV s\(^{-1}\) (Figure 4.4a). In N\(_2\)-saturated solution, a pair of redox peaks appeared at around -0.70 V and 0.30 V. These are related to the redox activity of PPy. In O\(_2\)-saturated solution, the cathodic peak increased in magnitude. The cathodic current increase can be ascribed to the enhanced redox properties of PPy in the presence of O\(_2\). The reduced PPy (close to the fully dedoped state at -0.7 V) can be re-oxidized by oxygen (and oxygen is reduced concomitantly), and the conductivity of reduced PPy was enhanced resulting in an increased cathodic current density.\(^{13}\)

To verify the electrocatalytic activity of SF-PPy film electrode, it was first reduced by applying a constant potential of -0.85 V for 600 s. After removal of the applied potential, the open-circuit voltage (OCV) increased immediately. A higher potential increase could be observed in oxygen-rich solution (Figure 4.4b). After 10 min of bubbling oxygen, the potential increased from -0.41 V to 0.03 V, compared to -0.14 V with no bubbling.
Figure 4.4 (a) Cyclic voltammograms of SF-PPy film in nitrogen or oxygen saturated PBS electrolyte at a scan rate of 5 mV s\(^{-1}\). (b) Voltage response of reduced SF-PPy film in PBS electrolyte with air, oxygen or no gas bubbling after the applied potential (-0.85 V vs. Ag/AgCl) was removed.

The Nyquist plots obtained using electrochemical impedance spectroscopy (EIS) (Figure 4.5a) revealed a semicircular region lying on the real axis, which was followed by a straight line. An equivalent circuit model was used to analyse the impedance spectrum (Figure 4.5b). In this circuit, Rs is the bulk resistance; Rct is the charge
transfer resistance. The constant phase elements CPE, is associated with the double-layer capacitance across the film/electrolyte solution interfaces; $W_0$ corresponds to the Warburg impedance resulting from the semi-infinite diffusion of ions at the electrode at low frequency.\textsuperscript{14} Electrochemical parameters were simulated using Z-view software, and a good fit between the experimental results and the simulated equivalent circuit was shown. The bulk resistance was about 82 $\Omega$ cm$^{-2}$ and SF-PPy film showed a charge transfer resistance of 15 $\Omega$ cm$^{-2}$. Despite the insulating nature of the silk substrate, the charge transfer resistance reported here was comparable to the PPy-$p$TS electrode (9.4 $\Omega$ cm$^{-2}$) on stainless steel (SS) mesh in PBS electrolyte, suggesting good conductivity and redox activity.\textsuperscript{15}

**Figure 4.5** (a) Electrochemical impedance spectroscopy spectrum and the simulated spectrum (lines) of SF-PPy film in PBS electrolyte; (b) the equivalent circuit used for the simulation.
4.3.3 Discharge Characteristics of Mg-Air Bioelectric Batteries

Galvanostatic discharge profiles of batteries at various current densities were investigated in PBS electrolyte at room temperature (Figure 4.6a). In this Mg-air battery system, PPy functions as the catalyst towards oxygen reduction. The limiting factor of battery performance is the corrosion rate of the Mg anode. The capacity normalized in terms of areal unit is more suitable and chosen in this work. The cell voltage was in the range of 1.72-1.79 V just after being assembled. This dropped immediately when a discharge current was applied and soon reached a flat discharge plateau. The voltages at the middle point of the discharge curves ranged between 1.24 V and 1.10 V at the current density range of 10-100 µA cm\(^{-2}\). The assembled Mg-air bio-batteries exhibited a discharge capacity ranging from 0.64 to 3.79 mA h cm\(^{-2}\), offering a specific energy density of up to \(~4.70\) mW h cm\(^{-2}\). This bio-battery exhibited slightly lower middle point voltages and capacities (1.29-1.06 V, 4.42-0.93 mA h cm\(^{-2}\)) than the previously reported result with electrodeposited PPy-pTS cathode on SS mesh. Nevertheless, it delivered a much higher stable voltage and specific capacity than those (0.4-0.7 V, 2.4 mA h cm\(^{-2}\)) from recently reported biodegradable Mg-Mo battery.

Compared with Chapter 3, the capacity and energy generated were higher than those (2.91 mAh cm\(^{-2}\) and 1.72 mWh cm\(^{-2}\), respectively) of the SF-AgNW-PPy composite; ascribed to the high PPy loaded in the air cathode. Further studies were done on the rate capability (Figure 4.6b) within the range of 5 to 100 µA cm\(^{-2}\). SF-PPy film delivered relatively stable discharge plateaus at all these current densities, indicative of good stability as cathode material for bio-batteries.
Figure 4.6 Galvanostatic discharge curves (a), rate capabilities (b) of Mg-air bio-batteries composed of SF-PPy film at various current densities in PBS electrolyte at room temperature.

Plots of power density vs. current density were obtained (Figure 4.7). The voltage used was obtained at the 4th hour during the 8 hours of discharge. This bio-battery delivered a maximum power density of 64.6 µW cm\(^{-2}\) at a current density of 80 µA cm\(^{-2}\). This power output was higher than that (39 µW cm\(^{-2}\)) reported for biodegradable
electroplated Mg battery. This battery could drive some types of commercial chronic IMBs, such as cardiac pacemakers or bio-monitoring systems. Generally, the power requirements for these IMBs fall within the level of micro- to milliwatts.20

![Graph](image.png)

**Figure 4.7** Plateau voltage and the corresponding power density of Mg-air bio-batteries composed of SF-PPy film at various current densities in PBS electrolyte at room temperature.

### 4.3.4 Enzymatic Degradation

To assess the biodegradation of SF-PPy film, it and silk films were exposed to a buffered protease XIV solution (1.0 mg mL⁻¹) (Figure 4.8a). After 24 h exposure, the weight loss of SF-PPy film was 24%; lower than the 42% for a pure silk film. In this stage, the weight loss can be attributed to the degradation of silk I and/or non-crystalline regions in SF. The weights of both samples decreased slowly afterwards. The silk film was disintegrated after 5 days. SF-PPy film exhibited a much smaller
weight loss, suggesting that the PPy layer could slow down the degradation rate of SF. After 10 days, SF-PPy film lost 65% of its original weight, much higher than that (8%) previously reported for PPy coatings on both sides of the silk substrate. The degradation obtained can be attributed to the low β-sheet content in SF obtained via water annealing treatment and the unique bilayer structure of SF-PPy film, which facilitated the enzyme to attack the silk film with cleavage sites available on the surface. After 13 days of incubation, SF-PPy film could not keep its original form and crumbled into small fractions due to the degradation of the silk substrate. This water-annealing treated SF-PPy film degraded faster than that (71% weight loss in 20 days) methanol treated SF-AgNW-PPy composite developed in Chapter 3, due to the low sheet β-content in SF. Through tailoring the properties of silk film, we can achieve a biodegradable air cathode material with programmable degradation time.

Figure 4.8b provides the images of SF-PPy film or film debris on the filter paper after degradation in the protease XIV solution. The SF-PPy film kept its structural integrity and the PPy layer was not delaminated from the silk substrate during 10 days incubation. Small irregular debris was present on the filter paper after 15 days degradation. All of the residual materials accounted for 18% of its starting weight. If SF-PPy film could be further degraded into several hundred nanometer pieces under optimized enzyme treatment, this material may eventually be eliminated by renal excretion, phagocytosis and/or endocytosis. It should be mentioned that both the silk films and SF-PPy film incubated in only PBS were stable throughout the whole incubation period.
Structural changes after enzymatic degradation were investigated by ATR-FTIR. As demonstrated in Figure 4.9, the dominant structure of the film substrate was basically unchanged, but with some slight increase of β-sheet crystalline region probably due to
the digestion of silk I and/or non-crystalline region in the silk substrate.\textsuperscript{23} With the increased incubation time, the intensity of the amide I shoulder at 1630 cm\textsuperscript{-1} increased, indicating an enhancement in the degree of crystallinity.\textsuperscript{24} After 10 days incubation, an interesting feature was observed that the film substrate showed a combined pattern of PPy and silk. This can be attributed to the degradation of silk substrate resulting in the exposure of PPy layer. The amide III (C-N stretching) band at 1236 cm\textsuperscript{-1} decreased gradually, which was considered markers for the amorphous structure of SF.\textsuperscript{25} This band finally disappeared after 15 days incubation, whereas a new broad band for C-N stretching from PPy appeared at 1303 cm\textsuperscript{-1}.

![Fourier-transform infrared spectra](image)

**Figure 4.9** Fourier-transform infrared spectra of the pristine film substrate (1), after incubation in the protease XIV solution for 5 days (2), 10 days (3) and 15 days (4) in the protease XIV solution.
To further understand the enzymatic degradation process, the surface morphologies were observed by SEM. Figure 4.10 shows representative images of SF-PPy film during the degradation as a function of time. Before incubation, both sides appeared to be even and uniform. After 5 days degradation, the film substrate experienced a rapid weight loss, resulting in cracks, whereas the PPy particles/aggregates on the SF-PPy film became smaller. After 15 days of continued surface corrosion, the residual sheets/debris were carefully collected by filtration and used for examination. The film substrate showed the presence of larger surface stripping region and increased surface roughness associated with the extensive degradation (Figure 4.10c), confirming that the enzyme could penetrate and diffuse inside the swollen film matrix toward available cleavage sites. Several cavities were also observed on the SF-PPy film owing to the delamination of PPy particles from the substrate (Figure 4.10f). These results demonstrate that the overall enzymatic degradation of the silk component was mediated by surface erosion.26
Figure 4.10 Scanning electron microscope images of the film substrate (a-c) and SF-PPy film (d-f) after cultivated in buffered protease XIV solution at various stages of degradation.

To evaluate the effect of enzyme exposure, the electrical resistance was monitored during the incubation period in buffered protease XIV solution or PBS as controls (Figure 4.11a). The sheet resistivity increased from 0.6 to ~5.4 kΩ sq⁻¹ upon 10 days exposure to the enzyme solution, roughly 9 times higher compared with its original value. The resistivity increase may be attributed to the disruption of the continuous
conductive PPy framework or the decreased affinity of the PPy to the silk substrate. Electrodes soaked in PBS electrolyte exhibited a much smaller increase (~0.8 kΩ sq\(^{-1}\)) during that period. These results demonstrated that SF-PPy film still retained electrical functionality throughout the 10 days of enzyme exposure. However, after 15 days incubation, the resistivity was hard to measure because of the physical disintegration of SF-PPy film.

To give a preliminary estimate of battery performance upon enzyme exposure, experiments were conducted on galvanostatic discharge tests in buffered protease XIV solution or PBS electrolyte at 37 °C (Figure 4.11b). The battery in the protease solution exhibited a discharge plateau (middle point of the discharge curve) of 1.14 V; lower than that (1.19 V) in PBS electrolyte at 37 °C. The protein molecules adsorbed on the electrode’s surface can retard the electron/charge transfer process and thus slow down the redox reactions.\(^{27}\) Therefore, a lower cell voltage and faster potential drop were observed. This battery maintained a steady output at 1.14 V at a current density of 20 µA cm\(^{-2}\) after exposure to the enzyme solution for 19.3 h. The power density offered (22.8 µW cm\(^{-2}\)) may fulfil the requirements for average consumption of published wireless implantable sensing systems (<0.5 V, <0.5 µW).\(^{28}\) It was also noted that the battery in PBS electrolyte at 37 °C demonstrated a much lower capacity too, only ~21 % of that obtained at room temperature. This can be ascribed to the accelerated Mg dissolution rate and significant increase of hydrogen evolution induced at high temperature.
Figure 4.11 (a) Electrical resistance (R) of SF-PPy film incubated in buffered 1.0 mg mL$^{-1}$ protease XIV solution or PBS over 10 days with respect to their original values ($R_0$), n=3, bars represent standard deviation. (b) Discharge performance of Mg-air bio-batteries composed of SF-PPy film at a current density of 20 µA cm$^{-2}$ in buffered 1.0 mg mL$^{-1}$ protease XIV solution or PBS electrolyte at 37 °C.
4.4 Conclusions

This study demonstrates the development of a novel air cathode material, PPy fabricated on a biodegradable silk film. Silk film functions as a substrate to support the catalytic material (PPy) and provides controllable biodegradability. PPy was deposited only on one side of the silk substrate, thus providing the cleavage sites for the enzyme to attack. SF-PPy film undergoes degradation with an 82% weight loss after 15 days incubation in buffered protease XIV solution. Degradation of the silk substrate leads to fracture and disintegration of the SF-PPy film, thereby offering the possibility to be eliminated by renal excretion, phagocytosis and/or endocytosis without surgical removal. These results highlight the feasibility of realizing a biodegradable battery when coupled with bioresorbable Mg alloy, which could provide appropriate power coupled with the required degradation profile. Developments in the area of biodegradable battery structures, together with implantable medical devices, will open up new possibilities for biomedical research and clinical care.
4.5 References


5. Biocompatible Ionic Liquid-Biopolymer Electrolyte Enabled Thin and Compact Biocompatible Magnesium Air Batteries

This chapter is adapted from the article, “Biocompatible ionic liquid-biopolymer electrolyte enabled thin and compact biocompatible magnesium air batteries”, by Xiaoteng Jia, Yang Yang, Caiyun Wang, Chen Zhao, R. Vijayaraghavan, Douglas MacFarlane, Maria Forsyth, Gordon G. Wallace, which is published in ACS Applied Materials and Interface, 2014, 6, 21110-21117. (Adapted with permission from American Chemical Society)
5.1 Introduction

With the surge of interest in miniaturized implanted medical bionics (IMBs), implantable power sources with small dimensions and biocompatibility are in high demand.\textsuperscript{1} However, miniaturization of IMBs remains a challenge that is hampered by battery size. Batteries normally account for a large volume of the overall IMB, and are typically constructed with a strong case that encapsulates toxic/harmful chemicals to prevent their contact with the body.\textsuperscript{2,3} Batteries could be easily miniaturized if all of the components are biocompatible and integrated into one single, continuous unit without the need for packaging.

In Chapter 3 and Chapter 4; PBS solution was employed as a biocompatible aqueous electrolyte to assemble the Mg-air bio-batteries. To date, the author is not aware of any report on using biocompatible polymer electrolytes for this application. The use of a polymer electrolyte enables the components to be integrated to form a thin, compact configuration that is easy to implant.\textsuperscript{4} In addition; a whole flexible and even stretchable solid-state energy storage device can be achieved when coupled with flexible electrodes.

Hence the main objective of this chapter is to develop a biocompatible polymer electrolyte based on a biocompatible ionic liquid embedded in a host biopolymer, chitosan (CS). CS is a versatile, abundant, and naturally occurring cationic polyelectrolyte, that has been extensively studied for pharmaceutical and biomedical applications.\textsuperscript{5-7} Room temperature ionic liquids (ILs) are promising electrolytes because they possess negligible vapour pressure, low flammability, high ionic...
conductivity and high electrochemical stability.\textsuperscript{8,9} Choline nitrate, [Ch][NO\textsubscript{3}], is chosen in this chapter due to its low viscosity, high conductivity and biocompatibility.\textsuperscript{10-12} CS hydrogels incorporated with choline chloride and choline dihydrogen phosphate have demonstrated their utility in biocompatible multi-responsive drug delivery systems.\textsuperscript{13}

This chapter also demonstrates the development of a compact battery system with the use of this polymer electrolyte, chitosan-choline nitrate. Bioresorbable Mg alloy and biocompatible polypyrrole-sodium \textit{p}-toluenesulfonate (PPy-\textit{p}TS) served as anode and cathode, respectively. The Mg-air battery performance is compared between this polymer electrolyte and PBS aqueous electrolyte.

## 5.2 Experimental

### 5.2.1 Fabrication and Characterization of Polymer Electrolyte

This polymer electrolyte was prepared by a simple casting method. CS was dissolved in an acidic solution (1\% v/v glacial acetic acid) to a concentration of 2 wt\% and stirred overnight until a clear solution was obtained, followed by addition of choline nitrate ([Ch][NO\textsubscript{3}]). The weight ratios of CS to [Ch][NO\textsubscript{3}] used were 1:1, 1:5 and 1:9. The mixtures were stirred continuously for 4 h and then cast onto a Teflon mould and dried at room temperature for two days. The formed films were dipped into an aqueous 0.1 M NaOH solution to remove any remaining acetic acid and washed several times with deionized water. They were dried for 24 h at room temperature and peeled off the substrate. Their thickness was in the range of 60-100 µm. They were cut into 10×10 mm\textsuperscript{2} squares for testing.
The ionic liquid component may potentially separate from the polymer electrolyte due to lack of long term compatibility with CS when it is directly exposed to air. As a result, the conductivity of electrolyte will decrease and affect the Mg-air battery performance. An IL leaching test was carried out by leaving the polymer electrolyte in open air under ambient conditions. The liquid released from the film was absorbed with Kimwipes until a constant weight was reached, and it was monitored every 24 h. The ionic liquid loss was calculated according to the following equation:

\[
\text{IL loss (\%)} = \frac{W_I - W_L}{W_{IL}} \times 100\% \quad (5.1)
\]

Where \(W_I\) is the initial weight of film, and \(W_L\) is the film weight during the leaching test. \(W_{IL}\) is the initial weight of IL in the film. The ionic conductivity change was also monitored and its loss was calculated according to the following equation:

\[
\text{Ionic conductivity loss (\%)} = \frac{\sigma_I - \sigma_L}{\sigma_I} \times 100\% \quad (5.2)
\]

Where \(\sigma_I\) is the initial conductivity of the polymer electrolyte, and \(\sigma_L\) is the conductivity of polymer electrolyte during the leaching test.

### 5.2.2 Battery Assembly and Testing

The integrated solid-state battery was fabricated with a PPy cathode (11×10×0.04 mm\(^3\)), Mg alloy anode (11×10×0.2 mm\(^3\)) and CS-[Ch][NO\(_3\)] polymer electrolyte (10×10×0.06 mm\(^3\)). This electrolyte functioned as both electrolyte and separator. Two such electrodes with polymer electrolyte were pressed together face-to-face to form a sandwich structure. During the assembly process, a thin layer of CS-[Ch][NO\(_3\)]...
solution was dropped onto the electrode surface to hold all the device components together like a glue, improving the mechanical integrity. The tilted cross-sectional view (approximately 20°) of the solid-state battery was characterized using an optical microscope (Leica DM6000). In addition, batteries were assembled with the same size electrodes in a one component cell with 5 mL of PBS solution for comparison. Polarization curves of Mg alloy foils were obtained with the CHI workstation (CHI 650D) after being immersed in PBS solution and contacted with polymer electrolyte for 6 h under ambient conditions. They were performed at a scan rate of 1 mV s⁻¹ using Mg alloy as the working electrode and a stainless steel mesh as the combined counter and reference electrodes.

5.3 Results and Discussion

5.3.1 Characterization and Properties of Polymer Electrolyte

Within the weight ratio range investigated, 1:1, 1:5, 1:9 (chitosan to [Ch][NO₃]), it was found that free standing polymer electrolyte films can be formed. These films were robust and, for instance, the film formed at a ratio of 1:5 could withstand large mechanical deformation (Figure 5.1a).

The weight loss in TGA curves (Figure 5.1b) over the temperature range up to 150 °C was attributed to water vaporization. It was 9%, 13%, and 11% for the CS film, [Ch][NO₃] and CS-[Ch][NO₃] polymer electrolyte (1:5), respectively. The decomposition of the CS backbone occurred mainly at 230-350 °C due to the depolymerisation of glucosamine units. The ionic liquid was stable up to 260 °C and decomposed at 320 °C. The CS-[Ch][NO₃] polymer electrolyte showed a similar
thermal stability up to 230 °C as CS, followed by a sharp weight loss as IL, proving that its thermal stability was affected by these two components.

Figure 5.1 (a) Digital image of a CS-[Ch][NO₃] (1:5) polymer electrolyte demonstrating its mechanical robustness. (b) Thermogravimetric analysis curves of chitosan film, ionic liquid and CS-[Ch][NO₃] polymer electrolyte (1:5).

The mechanical properties of these polymer electrolytes are shown in Figure 5.2a. The CS substrate exhibited a tensile strength of 27 MPa, being able to withstand a 32% elongation at break. When the weight ratio was 1:5 (CS:[Ch][NO₃]), the mechanical
strength decreased to 4.5 MPa and a 82% elongation at break was observed. After the introduction of [Ch][NO₃] into the CS matrix, the hydrogen bonding interactions between polymer chains were reduced due to the plasticizing effect. When the CS:[Ch][NO₃] ratio was 1:9, the mechanical strength was lowered to 0.4 MPa and the elongation to break slightly reduced to 66%. At higher choline nitrate content, film formation was not possible due to insufficient CS.

The pure CS film did not present any measurable ionic conductivity (<10⁻⁸ S cm⁻¹) (Figure 5.2b). Upon addition of [Ch][NO₃], the ionic conductivity was significantly enhanced to 0.73 mS cm⁻¹ when the weight ratio was 1:1 (CS:[Ch][NO₃]). This is attributed to the joint influence of the strong plasticizing effect of ionic liquid along with the inherent ionic conductivity introduced by the IL ions. The ionic conductivity of a polymer electrolyte is related to the polymer chain motion which increases with increasing plasticizer and continuously creates free volume into which the ions migrate. With an increase in concentration of choline nitrate (ratio of 1:5), the conductivity increased to 6.2 mS cm⁻¹, one order of magnitude higher than films with a ratio of 1:1. At a ratio of 1:9, the conductivity reached 8.9 mS cm⁻¹. The limitation on conductivity increase with a large amount of IL may be related to the formation of ion aggregates, which decreased the number of effective charge carriers. Interestingly, the ionic conductivity of CS-[Ch][NO₃] polymer electrolyte (1:5 and 1:9) is higher than that of pure ionic liquid [Ch][NO₃] (4.9 mS cm⁻¹). This may be attributed to the increasing “ionicity” of the ionic liquid induced by the presence of chitosan, which has highly polarizable substituents such as amino and hydroxyl groups. This phenomenon was also observed for chitosan-based gel electrolytes containing an imidazolium based ionic liquid.
Figure 5.2 (a) Stress-strain curves, and (b) AC impedance spectra of polymer electrolyte containing different amounts of ionic liquid (inset, expanded view at high frequency region).

In this CS-[Ch][NO₃] gel polymer electrolyte system, the polymer CS provides mechanical support and dimensional stabilization, and the ionic liquid functions as a charge carrier and plasticizer for the polymer matrix. The mechanical and electrochemical properties of the polymer electrolyte are summarized in Table 5.1.
CS-[Ch][NO₃] (1:5) polymer electrolyte was selected for further tests due to its robust mechanical properties and high conductivity.

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Resistance (ohm)</th>
<th>Conductivity (mS cm⁻¹)</th>
<th>Thickness (mm)</th>
<th>Strength (MPa)</th>
<th>Elongation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n/a</td>
<td>-</td>
<td>0.077</td>
<td>27.0</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>1:1</td>
<td>10.31</td>
<td>0.73</td>
<td>0.113</td>
<td>5.10</td>
<td>59</td>
</tr>
<tr>
<td>1:5</td>
<td>1.279</td>
<td>6.2</td>
<td>0.118</td>
<td>4.46</td>
<td>82</td>
</tr>
<tr>
<td>1:9</td>
<td>0.896</td>
<td>8.9</td>
<td>0.121</td>
<td>0.38</td>
<td>66</td>
</tr>
</tbody>
</table>

a. Weight ratio is referred to CS to [Ch][NO₃].

It has previously been reported that the ionic liquid leakage from the polymer matrix reduces ionic conductivity.²¹ To evaluate the IL retention ability in the polymer electrolyte during long-term operation, an IL leaching test was carried out by leaving the polymer electrolyte in open air under ambient conditions.

It was observed that liquid was expelled from the polymer matrix onto the polymer surface. Such liquid exhibited the same characteristic peaks in the FTIR spectra as that of [Ch][NO₃] (Figure 5.3a), indicating the released liquid is the IL ([Ch][NO₃]) or an aqueous solution of it. The percentage of IL leached out from the polymer electrolyte during one-week is shown in Figure 5.3b. It can be seen that the film weight remained nearly steady after a 120 h testing period. The weight loss was 13.4% after 168 h. The IL leakage from the film reflects the fact that the IL is not anchored to the polymer.
chain via strong hydrogen bonds and can easily partition into an IL-water phase on the surface. The ionic conductivity decreased to 4.9 mS cm\(^{-1}\) (21.5% loss) after 168 h (Figure 5.3b). This conductivity is still high enough to maintain battery operation.

**Figure 5.3** (a) Fourier-transform infrared spectrum of the released liquid from CS-[Ch][NO\(_3\)] (1:5) polymer electrolyte and pure ionic liquid [Ch][NO\(_3\)]. (b) The weight loss (%) and ionic conductivities change of the polymer electrolyte during the ionic liquid leaching test at ambient condition.
5.3.2 Electrocatalytic Properties of PPy-pTS Electrode

In a typical metal-air battery system, the ORR occurs at the cathode electrode/air electrode.\(^{22}\) Noble metal Pt is a biocompatible electrocatalyst for ORR. However, the high cost limits its use. A PPy cathode would be reduced by the action of the electrochemical cell when coupled with a Mg anode and in the presence of oxygen would be re-oxidised to create a catalytic cycle. To verify if the reduced PPy-pTS can be used as an ORR electrocatalyst, it was firstly reduced by applying a constant potential of -0.8 V for 10 min. The OCV of such reduced PPy increased immediately after the applied current was removed (Figure 5.4a), due to the re-oxidation of reduced polypyrrole. It is also noticed that a much higher potential increase can be produced with the introduction of air or O\(_2\) stream. A potential of 0.04 V, -0.03 V and -0.27 V was measured after 10 min with O\(_2\), air, and no gas bubbling, respectively. The high potential observed in the oxygen-rich solution demonstrates the effective re-oxidation of reduced PPy induced by oxygen reduction.

The ORR on PPy was also investigated using cyclic voltammetry in oxygen-saturated or nitrogen-saturated PBS solutions at a scan rate of 10 mV s\(^{-1}\) (Figure 5.4b). In N\(_2\)-saturated solution, the influence of oxygen could be excluded and the redox peaks can be attributed to PPy only. In O\(_2\)-saturated solution, the cathodic peak became more pronounced, with a higher current response. The cathodic current increase can be attributed to the enhanced redox properties of polypyrrole in the presence of O\(_2\). The reduced PPy (close to the fully-doped state) can be re-oxidized by oxygen (and oxygen is reduced in that process). For the anodic peak, a slightly reduced current compared to that in N\(_2\)-saturated solution was observed. This can be attributed to the
decrease of dedoped PPy leading to a less electrons involved in the electrochemical oxidation. This is consistent with previous reports.\textsuperscript{23,24} It is believed that the carbon atoms on the pyrrole ring could supply an active site for oxygen chemical adsorption, which could weaken the O-O bond of oxygen and lower the activation energy for reduction according to the mechanism proposed by Khomenko et al.\textsuperscript{25}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure5}
\caption{(a) Voltage response of the reduced PPy-\textit{p}TS electrode in PBS solution with oxygen, air, or no gas bubbling after the applied potential (-0.8 V vs. Ag/AgCl) was removed. (b) Cyclic voltammogram of a PPy-\textit{p}TS electrode in nitrogen or oxygen saturated PBS solution at a scan rate of 10 mV s\textsuperscript{-1}.}
\end{figure}
5.3.3 Battery Performance Using Polymer Electrolyte or PBS Aqueous Electrolyte

The integrated solid-state batteries were fabricated with the CS-[Ch][NO₃] film sandwiched between PPy-pTS cathode and Mg alloy anode, as shown schematically in Figure 5.5a. Thus the polymer film functioned both as the electrolyte and separator. During the assembly process, the polymer electrolyte could hold all the device components together like a laminating adhesive, improving mechanical integrity. The PPy polymer (doped with toluene-4-sulphonic acid (pTS)) was grown on the stainless steel substrate using conditions described in the experimental section. The whole thickness of the solid-state battery was about 300 µm as shown in Figure 5.5b.

Figure 5.5 Schematic configuration (a), and optical image of cross-sectional view (20° tilted) (b) of the integrated solid-state Mg-air battery.
The discharge characteristics of cells at various current densities were investigated using a polymer electrolyte and PBS solution electrolyte for comparison (Figure 5.6). The open circuit voltages for the integrated solid-state batteries were in the range of 1.80-1.71 V just after the cell was assembled. The cell voltage dropped immediately when the discharge current was applied and soon reached a flat discharge plateau. At low current density, batteries using the polymer electrolyte delivered a slightly higher discharge plateau than that with PBS solution electrolyte.

Specifically, at a current density of 10 µA cm\(^{-2}\), the Mg[CS-[Ch][NO\(_3\)]|OH|O\(_2\)(aq)|PPy cell displayed a voltage of 1.33 V (middle point of the discharge curve) for up to 160 h, 40 mV higher than that of Mg|PBS|O\(_2\)(aq)|PPy cell (1.29 V). However, when the current density increased to 50 µA cm\(^{-2}\), the Mg[CS-[Ch][NO\(_3\)]|OH|O\(_2\)(aq)|PPy cell could only sustain a voltage of 1.13 V for 35 h, 60 mV lower than that of Mg|PBS|O\(_2\)(aq)|PPy cell (1.19 V). The main cause for the lower discharge voltage of the solid-state battery at higher discharge current is likely due to the lower ion mobility in the polymer electrolyte. This creates a potential drop, the size of which depends on the resistivity of the electrolyte.

To further support the hypothesis that this battery system involves processes involving Mg oxidation and O\(_2\) reduction, a blank stainless steel (SS) mesh cathode was used in a control experiment. With a plain SS mesh as the cathode, this cell could only be discharged for 0.5 h to a cut off voltage of 1.0 V (Figure 5.6a inset), in sharp contrast to that of 88.7 h using PPy electrode at the same discharge current of 20 µA cm\(^{-2}\). This supports the proposal that PPy plays a catalytic role in oxygen reduction. The
contribution from SS mesh is negligible. SS mesh acts as an underlying conductive substrate material for PPy electropolymerization and as a current collector in this work.

Figure 5.6 Discharge curves of Mg-air batteries with PPy cathode and Mg alloy anode at various discharge current densities using CS-[Ch][NO₃] (1:5) polymer electrolyte (a) and PBS solution electrolyte (b). (Figure 5.6a inset: discharge curve of Mg-air battery using stainless steel mesh cathode as control).
In order to evaluate the practical battery performance, the volumetric power density was calculated. The plateau voltages ranged between 1.33 V and 1.13 V with an applied discharge current density in the range of 10-100 µA cm$^{-2}$ (Figure 5.7a). Compared with the recently reported biodegradable Mg-Mo primary battery,$^{26}$ this novel battery structure exhibited a much higher voltage than previously reported (0.4 V-0.7 V) and had a longer lifetime of up to 160 h compared to 24 h.

**Figure 5.7** Plateau voltage and the corresponding power density of Mg batteries as a function of discharge current densities using CS-[Ch][NO$_3$] (1:5) polymer electrolyte (a) and PBS solution electrolyte (b).
This battery system also delivered a maximum volumetric power density of 3.9 W L\(^{-1}\) (Figure 5.7b), which is almost 200 times higher than that (0.02 W L\(^{-1}\)) from the same size electrode in 5 mL PBS. This was attributed to the large dead volume when PBS electrolyte was used. Nevertheless, a maximum energy density of 72 Wh L\(^{-1}\) could be generated from this solid-state battery, much higher than that (2.2 Wh L\(^{-1}\)) of the flexible thin-film lithium-ion battery reported previously.\(^{27}\) Generally, the power requirements of active IMBs fall in the level of \(\mu W - mW\).\(^{2}\) This integrated solid-state battery could thus become a power source for some IMBs, such as cardiac pacemakers or bio-monitoring systems. A higher power output can be achieved using devices connected in series.

The electrochemical impedance spectra for both the solid-state and liquid electrolyte batteries were acquired before and after 6 hours of discharge. They exhibited similar Nyquist plots with a compressed semicircle in the high to medium frequency range. This semicircle was associated with the charge transfer reaction at the electrolyte/electrode interface.\(^{28}\) The charge transfer resistance, \(R_{ct}\), was 1175 ohm with polymer electrolyte and 243 ohm in PBS, respectively (Figure 5.8a). After the discharge (6 h), this \(R_{ct}\) of the cell with PBS electrolyte was 577 ohm, much lower than that of solid-state battery (3968 ohm) (Figure 5.8b). The large resistance of the solid-state battery can be mainly ascribed to a low ion migration rate in the polymer electrolyte. The low ion movement can decrease the ion exchange rate at the interface and consequently deteriorate the catalytic efficiency of the cathode. The greatly increased resistance of polymer electrolyte during discharge was the main cause for the lower discharge voltage of the solid-state battery at higher discharge current.
Figure 5.8 Electrochemical impedance spectra of Mg-air batteries before and after discharge at a current density of 20 µA cm\(^{-2}\) for 6 h using CS-[Ch][NO\(_3\)] (1:5) polymer electrolyte (a) and PBS solution electrolyte (b).

To determine the corrosion behaviour of the Mg anode, its polarization behaviour was investigated in these two electrolytes with a stainless steel mesh serving as both counter and reference electrode (Figure 5.9). Prior to the scan, the Mg anode was left at open circuit voltage in both electrolytes for 6 h until a steady, free corrosion
potential value was recorded. The corrosion potential shifted towards more positive potential from -2.12 V using PBS solution to -1.72 V with the polymer electrolyte. The anodic and cathodic current densities decreased by nearly an order of magnitude. These results clearly demonstrated that the anodic dissolution of Mg was hindered by the use of polymer electrolyte, and a better discharge performance may be obtained. This may explain the higher discharge plateau obtained at low current density (10 µA cm\(^{-2}\)) using the polymer electrolyte. However, the reduced ionic mobility also limited the battery performance at higher discharge current.

**Figure 5.9** Polarization curves of AZ31|electrolytes|SS at a scan rate of 1 mV s\(^{-1}\).

After the discharge experiment, the Mg anode surfaces were examined. Mg alloy was treated in an ultrasonic bath (H\(_2\)O) for 5 min, followed by rinsing with deionized water. Much less cracks were observed with the polymer electrolyte (Figure 5.10a). In contrast, a great number of cracks were formed on the Mg alloy electrode after use in
PBS solution (Figure 5.10b) because of the hydrogen evolution associated with the rapid oxidation of Mg. This can be used to explain the reduced corrosion rate of Mg alloy using the polymer electrolyte.

Figure 5.10 Scanning electron microscopy images of AZ31 surfaces after the discharge experiment at a current density of 20 µA cm$^{-2}$ using CS-[Ch][NO$_3$] (1:5) polymer electrolyte (a) and PBS solution electrolyte (b).
5.4 Conclusions

The results presented in this work indicate a promising approach to the fabrication of compact biocompatible batteries employing a bioresorbable metal anode, biocompatible conducting polymer cathode and biocompatible polymer electrolyte. This polymer electrolyte functions as an electrolyte and separator and as the “glue” to hold all the device components together. With a whole device volume of 30 mm$^3$, the integrated solid-state battery can generate an open circuit voltage of 1.80 V and a maximum output power of 72 Wh L$^{-1}$, which could be sufficient to drive some low power IMBs such as cardiac pacemakers or bio-monitoring systems. In contrast to conventional aqueous bio-batteries, this integrated solid-state battery would occupy minimal space. However, its performance declines at higher discharge currents, due to the low ion motilities. Given its small device dimensions and biocompatibility, this battery may be a promising power source for miniaturized implantable medical devices.
5.5 References


6. A Biodegradable Thin-Film Magnesium Primary Battery Using Silk Fibroin-Ionic Liquid Polymer Electrolyte

This chapter is adapted from the article, “A biodegradable thin-film magnesium primary battery using silk fibroin-ionic liquid polymer electrolyte”, by Xiaoteng Jia, Caiyun Wang, Vijayaraghavan Ranganathan, Bradley Napier, Changchun Yu, Yunfeng Chao, Maria Forsyth, Fiorenzo G. Omenetto, Douglas R. MacFarlane, Gordon G. Wallace, which is published in ACS Energy Letter, 2017, 2, 831-836. (Adapted with permission from American Chemical Society)
6.1 Introduction

In Chapter 5, a biocompatible polymer electrolyte was prepared by embedding [Ch][NO₃] into chitosan matrix. The efficacy of this polymer electrolyte was demonstrated in a solid-state battery with a whole device thickness of 300 µm. The assembled battery was not degradable with PPy on a stainless steel substrate as cathode. To obtain a fully biodegradable battery, thin-film electrodes were fabricated by sputtering AZ31 and gold onto silk film to serve as anode and cathode, respectively. Such thin-film electrode could minimize mechanical injury associated with implantation and chronic use. The development of thin-film batteries can offer integration compatibility with the electronic systems (sensors and bioelectronics) within BIMBs.¹

This Chapter describes the development of a biodegradable thin-film Mg-air battery using a silk fibroin-choline nitrate (SF-[Ch][NO₃]) polymer electrolyte. Silk fibroin (SF) is a naturally occurring biodegradable protein fiber and is a promising candidate for electronic implants interfaced with the human body.²,³ The use of regenerated SF lies in the fact that it possesses the ability to entrap or stabilize chemical or biologically active molecules, allowing the addition of a new function.⁴,⁵ Drugs, fluorescent dyes and metallic nanoparticles have been previously embedded into SF for thin-film biocompatible electronic and photonic devices.⁶,⁷ ILs are ambient temperature molten salts that are currently being used as solvents or additives for macromolecules.⁸ When used as electrolytes they possess the following advantages: a wide and stable electrochemical potential window, high ionic conductivity and in some cases good biocompatibility. Degummed silk fibers can be dissolved in ILs and processed into
different forms after the extraction of IL\(^9\). Here is demonstrated the use of SF to immobilize an IL to form a free-standing membrane, harnessing both the biological activity of SF and the ionic conductivity of the IL.

In addition, the whole battery device was encapsulated in silk films by a hot-press process. The outer crystallized silk protection layer could extend the battery lifetime when exposed to PBS. Through controlling the layer numbers of silk films, a modulated lifetime of the encapsulated battery has been demonstrated.

### 6.2 Experimental

#### 6.2.1 Polymer Electrolyte Preparation and Characterization

The polymer electrolyte was prepared by adding [Ch][NO\(_3\)] into silk solution with weight ratios of 1:1, 1:3 and 1:5 (SF to IL). The mixture was stirred continuously for 4 h and cast onto a Teflon mould, followed by drying in air for 24 h. The thickness of the polymer electrolyte obtained was in the range of 55-80 \(\mu\)m. Linear sweep voltammetry (LSV) was carried out using SS as the working electrode and AZ31 as both the counter and reference electrodes at a scan rate of 5 mV s\(^{-1}\).

#### 6.2.2 Electrode and Battery Fabrication, Electrochemical Measurements

Silk film (50-60 \(\mu\)m) was crystallized by heating at 120 °C and 80 psi for 30 s, followed by a treatment in oxygen plasma for 2 min. A thin-film anode (1 \(\times\) 0.5 cm\(^2\)) composed of a 100-500 nm AZ31 and a 30 nm Ti adhesive layer was deposited by magnetron sputtering (Edwards 306 Sputter Coater) through a shadow mask onto a
crystallized silk film. Similarly, a crystallized silk film with 100 nm gold and 10 nm Ti coating was fabricated and used as cathode. Polymer electrolyte with a very thin layer of IL coating was used for easy assembly of batteries. The unsealed battery was fabricated with a polymer electrolyte sandwiched between an Au-SF cathode and an AZ31 foil anode. Specific volumetric power density (P) of the battery was calculated from the discharge curves using the following equation:

\[ P = \frac{UI}{V} \]  

(6.1)

Where P is the volumetric power density (W L\(^{-1}\)), V (volt) is the plateau voltage at the middle point of discharge curve, I (A) is the discharge current, and V (L) is the whole device volume.

The encapsulated battery was assembled by stacking Au-SF cathode, polymer electrolyte, amorphous adhesive silk frame (30 μm) and AZ31-SF anode. Only the edges were laminated using a thermal-process (120 °C and 130 Psi for 30 s). A platinum wire contact was pasted onto each electrode. The in situ OCV changes were recorded for encapsulated batteries affixed to an acrylic well with 1 mL of PBS using silicone adhesive sealer (Permatex).

6.2.3 Enzymatic Degradation of Encapsulated Battery

The encapsulated battery was incubated in 1.0 mg mL\(^{-1}\) buffered protease XIV solutions at 37 °C. The enzyme solutions were refreshed daily. At designated times; the battery was taken out and photographs taken (Sony α6000 digital camera).
6.3 Results and Discussions

6.3.1 Preparation and Characterization of Polymer Electrolyte

Different amounts of [Ch][NO$_3$] were introduced into SF aqueous solution, the weight ratios of SF to [Ch][NO$_3$] used were 1:1, 1:3 and 1:5. At all ratios investigated, the [Ch][NO$_3$]/SF solutions were miscible during long-term (up to six weeks) storage (Figure 6.1a). The chemical structures of the polymer matrix and ionic liquid used in the polymer electrolyte are shown in Figure 6.1b.

**Figure 6.1** (a) Fabrication procedures and digital images of silk-ionic liquid solution and polymer electrolyte (SF:[Ch][NO$_3$], weight ratio of 1:3). (b) Molecular structures of silk fibroin and choline nitrate.

The FTIR of polymer electrolyte (Figure 6.2a) exhibited the expected absorbance bands at 1650 cm$^{-1}$ and 1236 cm$^{-1}$, corresponding to the silk I structure, as well as bands at 1330 cm$^{-1}$ (vibration of NO$_3^-$) and 954 cm$^{-1}$ (vibration of C-C-OH) due to the presence of IL. As the content of [Ch][NO$_3$] was increased, the intensity of the amide I shoulder at 1630 cm$^{-1}$ increased, indicating a crystallinity enhancement.$^{11}$ A protein conformation transition from random coil and/or helical structure to β-sheet can be
ascribed to IL binding to the protein surface and increasing surface tension.\textsuperscript{12} This behaviour is similar to that observed for SF interacting with metallic cations.\textsuperscript{13} The coordination of cations to the carbonyl and/or OH group of SF could affect the hydrogen bonding interactions in SF and consequently its secondary structure. TGA (Figure 6.2b) revealed the amount of water confined in the polymer electrolyte was 5-9\% (w/w). This acted as a proton source to support the ORR at the cathode.\textsuperscript{14}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure6.2}
\caption{(a) Fourier-transform infrared spectra, and (b) thermogravimetric analysis curves at a heating rate of 5 °C min\textsuperscript{-1} under nitrogen atmosphere of polymer electrolyte containing different amounts of [Ch][NO\textsubscript{3}].}
\end{figure}
The silk film exhibited a tensile strength of 21 MPa with an 8% elongation to break (Figure 6.3a). Addition of IL to obtain a polymer electrolyte composition of (SF:[Ch][NO$_3$], weight ratio of 1:3) resulted in decreased mechanical strength (2.0 MPa) but an enhanced ductility, producing a 98% elongation to break. The inclusion of [Ch][NO$_3$] weakens the hydrogen bonding interactions between glycine and alanine in the crystalline region and enhances segmental motion, thereby increasing the overall flexibility of the material.$^{15}$ The plasticizing effect was also observed by the addition of glycerol in SF because of the formation of hydrogen bonds between the hydroxyl (OH) group of glycerol and the hydrophilic polar groups present in some amino acids.$^{16}$ However, when the [Ch][NO$_3$] content was further increased to a weight ratio of 1:5 (SF:[Ch][NO$_3$]), the mechanical strength was lowered to 1.2 MPa and the elongation to break was also reduced to 81%.

The effect of [Ch][NO$_3$] addition on ionic conductivity was also determined (Figure 6.3b). The conductivity was 0.85 mS cm$^{-1}$ for the 1:1 composite, and increased to 3.4 mS cm$^{-1}$ for a 1:3 composite. This is attributed to the strong plasticizing effect of the IL and the inherent high ionic conductivity of the IL.$^{17}$ A further increase of [Ch][NO$_3$] to 1:5 resulted in an even higher ionic conductivity of 7.4 mS cm$^{-1}$. 
Figure 6.3 (a) Stress-strain curves, and (b) AC impedance spectra of polymer electrolyte containing different amounts of [Ch][NO₃] (Inset of Figure 6.3b, expanded view at high frequency region).

However, some IL component may potentially separate from the polymer electrolyte when contained in such high amounts.¹⁸ Thus SF-[Ch][NO₃] (weight ratio of 1:3) was chosen for further studies for its combination of ionic conductivity and mechanical properties (Table 6.1).
### Table 6.1 Basic properties of SF-[Ch][NO₃] polymer electrolytes.

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Resistance (ohm)</th>
<th>Conductivity (mS cm⁻¹)</th>
<th>Thickness (μm)</th>
<th>Strength (MPa)</th>
<th>Elongation (%)</th>
<th>Water (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF</td>
<td>n/a</td>
<td>n/a</td>
<td>37±3</td>
<td>21.0</td>
<td>8.0</td>
<td>10.2</td>
</tr>
<tr>
<td>1:1</td>
<td>12.96</td>
<td>0.85</td>
<td>55±5</td>
<td>4.61</td>
<td>74</td>
<td>4.5</td>
</tr>
<tr>
<td>1:3</td>
<td>4.02</td>
<td>3.4</td>
<td>69±2</td>
<td>2.02</td>
<td>98</td>
<td>7.3</td>
</tr>
<tr>
<td>1:5</td>
<td>2.18</td>
<td>7.4</td>
<td>81±6</td>
<td>1.23</td>
<td>81</td>
<td>9.4</td>
</tr>
</tbody>
</table>

a. Weight ratio is referred to SF to [Ch][NO₃].

b. The water content was estimated from the TGA curves, i.e. weight loss between 20 and 150 °C.

#### 6.3.2 Enzymatic Degradation of Polymer Electrolyte

Biodegradation of the SF-[Ch][NO₃] film was investigated in a buffered protease XIV solution, with PBS solution as a control. The weight loss was 68% in PBS after a 24 h exposure (Figure 6.4a). The polymer electrolyte retained 22% of its initial weight after 5 days, close to the content of SF component (23%). The weight loss was mainly attributed to IL migrating from the polymer matrix into solution. This is a reflection of [Ch][NO₃] not being tightly bound to the SF host matrix, but being highly mobile, which was also evidenced by the concomitantly sharp decrease in ionic conductivity from 3.4 to 0.03 mS cm⁻¹ after incubation in PBS for 12 h (Figure 6.4b). In the enzyme solution, the weight loss was 89% after 24 h, much higher than that (68%) in PBS. In
this case, the degradation of silk I and/or amorphous structure was involved.\textsuperscript{19} The polymer electrolyte disintegrated after 2 days.

![Graph](image.png)

**Figure 6.4** (a) Mass loss in protease XIV solution and PBS (bars represent standard deviation, n=3); the dashed line represents the content of SF in polymer electrolyte. (b) Conductivity change upon 12 h exposure in PBS.

Structural changes after 24 h degradation in the enzyme and PBS were investigated by FTIR. The characteristic peaks from [Ch][NO\textsubscript{3}] were not observed for these two samples (Figure 6.5a), a clear demonstration of the disappearance of IL, thus matching the biodegradation results. The polymer electrolyte retained the structure of silk I in
PBS, whereas the intensity of the amide I shoulder at 1630 cm\(^{-1}\) increased after exposure in enzyme solution. This slight increase in the \(\beta\)-sheet crystalline region was probably due to the digestion of silk I and/or non-crystalline region of silk component by the action of protease.\(^{20}\) To further understand this degradation process, changes in the surface morphologies were monitored. The polymer electrolyte was of smooth and uniform surface (Figure 6.5b). After 24 h of degradation, a textured, microporous structure created by IL leaching was developed in PBS (Figure 6.5c); whereas the film was degraded into small fragments in the enzyme solution (Figure 6.5d).

**Figure 6.5** (a) Fourier-transform infrared spectra of polymer electrolyte before and after exposure in PBS and enzyme solution for 24 h; scanning electron microscopy images before exposure (b), after exposure in PBS (c) and enzyme (d) solution for 24 h.
6.3.3 Electrochemical Properties of Polymer Electrolyte

The linear sweep voltammetry (LSV) recorded for the SS|SF-[Ch][NO₃]|Mg cell showed the electrolyte was stable up to 2.3 V (Figure 6.6a). This electrochemical potential window was sufficiently high for use in a Mg primary battery. To evaluate the efficiency of this polymer electrolyte, it was deployed in a magnesium-air battery. Mg or its alloys, including AZ31, have been suggested as the sacrificial anodes for biodegradable batteries because of a high theoretical capacity, acceptable dissolution rate and favourable biocompatibility.²¹ As a bio-inert noble metal and catalyst toward ORR,²² a 100 nm layer of gold nanoparticles was physically deposited onto a crystallized silk film (Au-SF).

The role of Au-SF in this solid-state battery was then evaluated. The battery using a stainless steel (SS) mesh cathode displayed a significantly decreased performance in plateau voltage and discharge time (0.75 V, 9 h), compared to those (0.86 V, 61 h) for Au-SF cathode at the same current density of 20 μA cm⁻²; confirming the catalytic role of the Au-SF cathode (Figure 6.6b).
Figure 6.6 (a) Linear sweep voltammetry of a SS|SF-[Ch][NO₃]|AZ31 cell at a scan rate of 5 mVs⁻¹. (b) Discharge performance of a AZ31|SF-[Ch][NO₃]|Au-SF and a AZ31|SF-[Ch][NO₃]|SS cell at a current density of 20 µA cm⁻².

This battery system, AZ31|SF-[Ch][NO₃]|Au-SF, is a metal-air battery. The main discharge reactions of this encapsulated Mg-air primary battery are as follows:\(^\text{23}\)

Anode: \(2\text{Mg} + 4\text{OH}^- \rightarrow 2\text{Mg(OH)}_2 + 4\text{e}^- \ (E = -2.69 \text{ V}) \) \hspace{1cm} (6.2)

Cathode: \(\text{O}_2 + 2\text{H}_2\text{O} + 4\text{e}^- \rightarrow 4\text{OH}^- \ (E = 0.40 \text{ V}) \) \hspace{1cm} (6.3)
Overall reaction: $2\text{Mg} + \text{O}_2 + 2\text{H}_2\text{O} \rightarrow 2\text{Mg(OH)}_2$ $(E_{\text{cell}} = 3.09 \text{ V})$ (6.4)

The anion in the polymer electrolyte may also participate in the reaction with Mg alloy, forming magnesium nitrate and results in a decreased conductivity after discharge.

The open circuit voltages (OCV) for the AZ31|SF-[Ch][NO$_3$]|Au-SF battery were in the range of 1.58-1.45 V just after the cell was assembled (Figure 6.7). The cell voltage dropped immediately when a discharge current was applied and soon reached a flat discharge plateau. At a current density of 5 $\mu\text{A cm}^{-2}$, the battery displayed a capacity of 2.2 mAh cm$^{-2}$ with a plateau voltage of ~1.03 V (middle point of the discharge curve). This battery could deliver a maximum volumetric power density of 1.07 W L$^{-1}$ and an energy density of 70.9 Wh L$^{-1}$ based on the dimensions of the whole device (1×1×0.032 cm$^3$).

![Figure 6.7 Galvanostatic discharge profile of AZ31|SF-[Ch][NO$_3$]|Au-SF batteries (unsealed) using SF-[Ch][NO$_3$] (weight ratio of 1:3) polymer electrolyte at various current densities.](image-url)

Figure 6.7 Galvanostatic discharge profile of AZ31|SF-[Ch][NO$_3$]|Au-SF batteries (unsealed) using SF-[Ch][NO$_3$] (weight ratio of 1:3) polymer electrolyte at various current densities.
6.3.4 Modulated Functional Time of Encapsulated Mg-Air Battery

To impart a soft nature to the anode as well, they were fabricated by sputtering AZ31 onto crystallized silk films (AZ31-SF) to substitute for the stiff AZ31 foil. This silk-based battery was further encapsulated by a thermal processing method (Figure 6.8).\textsuperscript{24} To avoid the mechanical stress on electrodes and polymer electrolyte, only the outer edges around the battery were laminated with an amorphous silk adhesive frame between the electrodes.\textsuperscript{25} This frame was of the same size as the silk substrate, far larger than that of electrodes and electrolyte. This process could create a small air pocket, providing air for the cathode reaction.

![Figure 6.8 Schematic of an encapsulated battery with a silk pocket.](image)

Figure 6.9a shows the evaluation of the effect of AZ31 thin-film thickness on the performance of encapsulated batteries. As expected, batteries with thicker AZ31 thin-films displayed longer discharge times. The battery with a 500 nm AZ31 layer could deliver a specific capacity of 0.06 mAh cm\textsuperscript{-2} at a current density of 10 µA cm\textsuperscript{-2}, which is significantly lower than that from an unsealed battery with an AZ31 foil anode (1.43 mAh cm\textsuperscript{-2}). The rapid depletion of the active AZ31 coating and the limited oxygen available may be the main reasons for this discrepancy. The encapsulated battery achieved a Coulombic efficiency of 27%. Nevertheless, the power afforded (8.7 µW
cm²) may fulfil the requirements for average consumption of published wireless implantable sensing systems (<0.5 V, <0.5 μW). This air pre-loaded strategy was advantageous for batteries when implanted in the sites with limited availability of oxygen. The encapsulated battery exhibited a bulk resistance of ~11.5 ohm (Figure 6.9b), indicating good contact and low resistance in the cell.

**Figure 6.9** (a) Effect of AZ31 thin-film thickness on the discharge performance of an encapsulated battery at a current density of 10 μA cm². (b) Electrochemical impedance spectroscopy of an encapsulated thin-film Mg battery (AZ31 thickness 500
nm) over the frequency range of 100 kHz to 0.01 Hz (Inset, expanded view at high frequency region).

The battery lifetime can be extended by adding an additional crystallized silk film on top of an encapsulated battery (Figure 6.10a). Crystallized silk films can serve as non-immunogenic diffusion barriers for water influx.27 In between each crystallized silk layer, a 30 μm amorphous silk adhesive frame was stacked. The stacks were then laminated together using the above method with pressure applied only to the outer edges around the battery. An acrylic well was affixed on top of the additional silk protection film with silicone adhesive sealer.

The modulated degradation profile of encapsulated batteries via multilayer silk films is demonstrated in Figure 6.10b. An encapsulated battery (single protection layer) showed a stable OCV (1.21 V) in air with 11% of self-discharge loss after 180 min, likely due to the corrosion of the AZ31 layer at the interface with the polymer electrolyte. When exposed to PBS, a two-stage transient behaviour was observed: a stable OCV above 1.21 V for 64 min (i.e. same discharge profile as in air), followed by a rapid functional degradation in 22 min. This discharge profile can be explained by the protection afforded by the crystallized silk film; the silk film absorbed water and began to swell, with liquid water being held within the swollen film. Thus, the device behaved as it would in the absence of water. In the second stage, the water penetration through the hydrated silk films led to fast degradation as the AZ31 thin-film rapidly dissolved and IL leached from the polymer electrolyte. An additional silk protection layer over the encapsulated battery resulted in an extension of the stable operating period to 109 min and the functional degradation to 68 min. These results clearly demonstrate that the device degradation profile can be simply modulated by
the silk protection layer/layers. It can be envisioned that control over silk film thickness and its crystallinity (e.g., β-sheet content) can further tune the degradation profile.\textsuperscript{28}

Figure 6.10 (a) Schematic of an encapsulated battery with an additional silk protection layer for \textit{in situ} degradation test. (b) \textit{In situ} open-circuit voltage changes of an encapsulated battery (AZ31 thickness 500 nm) and with an additional silk protection layer exposed to air and 1 mL of PBS.

6.3.5 Enzymatic Degradation of Encapsulated Mg-Air Battery

A biodegradation study was performed to demonstrate that this whole battery system can indeed decompose (Figure 6.11). The biodegradation process of an encapsulated
battery is determined by the slow SF degradation by proteolytic activity, which can be regulated by changing crystallinity and molecular weight.\textsuperscript{29} A thin-film AZ31 dissolution process via hydrolysis also occurred forming mainly Mg(OH)\textsubscript{2}, at a rate of 0.02-0.1 µm h\textsuperscript{-1} in simulated body fluids.\textsuperscript{30} In this encapsulated battery, AZ31 thin-film (500 nm thickness) completely disappeared in 4 h, whereas the overall encapsulated battery (170 µm thickness) nearly totally degraded after 45 days. The Au component (0.09 mg/230 mg device) was physically fragmented in the solution because of the degradation of the silk substrate. Au nanoparticles was considered to be safe owing to its inert nature, extreme resistance to oxidation and considerable biocompatibility.\textsuperscript{31} If SF-Au film could be further degraded into several hundred nanometer size pieces under optimized enzyme treatment, gold nanoparticles may be eventually cleared by renal excretion, phagocytosis and/or endocytosis.

\textbf{Figure 6.11} Optical images demonstrating the biodegradation profile of an encapsulated battery (device size of 3.6×2.7×0.017 cm\textsuperscript{3}) in buffered protease solution at 37 °C.
6.4 Conclusions

In summary, demonstration of a silk-based compact Mg battery entirely made of biocompatible and biodegradable materials has been achieved. By introducing a biocompatible IL into a silk solution, the formed polymer electrolyte (SF-[Ch][NO₃] (1:3)) composite shows an ionic conductivity of 3.4 mS cm⁻¹ coupled with a two-day degradation profile in concentrated buffered protease solution. The encapsulated thin-film battery offers a capacity of 0.06 mAh cm⁻² at a current density of 10 μA cm⁻², and an almost full-degradation profile of 45 days when incubated in the protease solution. The battery lifetime upon exposure to PBS can be tuned using silk protection layers.
6.5 References


7. Conclusions and Outlook

7.1 Conclusions

In summary, the author has achieved promising results showing the potential of biopolymer-PPy cathode materials and biopolymer-ionic liquid polymer electrolytes for implantable miniaturized Mg-air batteries. The combination of silk fibroin and PPy provides both controllable biodegradability and electrochemical activity. The approach to fabricate a composite film with a bilayer structure is feasible to achieve a partially biodegradable cathode material by providing cleavage sites for the enzyme to attack. The enzymatic degradation profile can be programmed through tailoring the \( \beta \)-sheet content of silk using different annealing methods, including methanol immersion and water-vapour treatment. Biopolymer-choline nitrate polymer electrolyte is selected to fabricate a miniaturized solid-state Mg-air battery. The polymer electrolyte enables a more flexible and robust battery design. It could also reduce the corrosion rate of Mg alloy compared with PBS electrolyte. Using thin-film electrode on silk film enables a fully degradable encapsulated Mg-air battery. All these results would provide useful information for designing future biocompatible/biodegradable Mg-air batteries.

Implantable Mg-air bioelectric batteries developed in this thesis could generate stable plateau voltages of 1.05-1.35 V affording a discharge capacity of up to 4.4 mAh cm\(^{-2}\). Compared with traditional energy storage systems for implantable medical devices, additional features are introduced in such batteries; such as biocompatibility and/or
biodegradability. There is a trade-off between device performance and biodegradable behaviour, so it is important to find an appropriate balance. Future research opportunities lie within the materials optimization, device designs, and manufacturing methods that can accelerate translating this emerging technology into clinical practice. In the following section, two research directions are summarised in the context of enhancing battery performance and engineering the battery package.

## 7.2 Outlook

The first important research direction is to improve the battery performance with respect to energy and power density for practical applications. The limiting factor that determines Mg-air battery performance is the electrocatalytic activity of the air cathode. In this thesis, PPy is employed as the preferred electroactive component. The electrochemical properties of PPy can be adjusted via molecular structure design affording high energy density and power density. Their “soft” nature facilitates tuning the properties by containing (as dopant) or modifying (through covalent attachment) with molecules. In addition, nanoscale design of PPy can provide both large surface area and shortened pathways for charge/mass transport, which are beneficial for electrocatalytic activity enhancement. For example:

- Incorporation of redox-active anions as dopants.

One approach is to introduce biocompatible redox-active dopant. The enhanced electrocatalytic activity can be attributed to the more favourable kinetics and electron transport environment in the presence of PPy matrix and redox-active dopants.\(^1\) The incorporation of redox-active anions can contribute to additional oxygen reduction
reaction, leading to an improved capacity. A lignin derivative (lignosulfonate) which contains quinone groups has been applied as dopant for fabrication of PPy electrodes.\(^2\) The quinone system of lignosulfonate can be electrochemically reduced from its Q form (quinone) to its QH\(_2\) form (phenol) along with the reduction of PPy in aqueous electrolyte. Another redox-active anion, anthraquinone sulfonate (Figure 7.1), has been co-doped with reduced graphene oxide into PPy via a facile electrochemical route, and used as a novel cathode material for Mg-air batteries.\(^3\)

\[\begin{array}{c}
\text{O}_2 \quad \text{O}_2 \\
\text{O}_2 \quad \text{O}_2 \\
\end{array}\]

**Figure 7.1** Electrochemical-chemical mechanism of anthraquinone sulfonate (adapted from reference [3]).

The dopant makes up a large percentage of the composition of a conducting polymer and hence affects its inherent chemical/biological properties. The biocompatibility of PPy/redox-active dopant composites needs to be evaluated. Nevertheless, PPy can be rendered “biological” in nature through the incorporation of biological molecules or polyelectrolytes.\(^4,5\) A future research direction is to find an appropriate biologically derived redox-active dopant that can achieve both high electrochemical activity and excellent biocompatibility.
- Synthesis of a fully bio-erodible conducting polymer.

Alternatively, bio-erodible CPs which could retain its electroactivity and ensure full disappearance can be used for this application. These polymers do not degrade into smaller non-toxic components by breaking chemical bonds. They are simply water soluble polymers within the molecular weight threshold appropriate for renal clearance (30-50 kDa).\(^6\) The \(\beta\)-substituted pyrrole monomers containing ionisable/hydrolysable side groups were successfully polymerized (Figure 7.2).\(^7\) The slightly water-soluble polymer showed a weight loss of 27% after 80 days incubation in water at 37 °C. The resistance of polymer thin films was 300 Ω, and increased to 700 Ω after incubation for 2 days. It supported the growth, proliferation, and differentiation of primary human cells. The conjugated backbone endows these polymers with a doping-dedoping capability as required for cathode materials. The great structure diversity and synthetic tailorability creates a rich range of slightly water-soluble conducting polymers for further development and deployment as cathode material.

![Figure 7.2 Chemical structures of bio-erodible polypyrrole derivatives by electrochemical polymerization (adapted from reference [7]).](image)

1: \(R = H\)  
2: \(R = CH_3\)  
poly-1  
poly-2
• Fabrication of nanostructured PPy materials.

It is well-recognised that nanostructure can significantly improve the performance of materials. The derived high surface area facilitates oxygen reduction by providing easier access for electrolyte and oxygen. Different structured PPy nanomaterials have been synthesized for energy storage applications, such as the one-dimensional nanowires/nanotubes, two-dimensional nanostructured film and three-dimensional nanostructured polymers and composites. Among them, the gel-like structure is fascinating because ions would transport as in a liquid rather than a solid, leading to more accessible dopants that involve in the electrochemical reactions. Recently a cytocompatible robust hybrid PPy/PEDOT hydrogel has been demonstrated for use in a Mg-air bioelectric battery. Their 3D interconnected porous structure with gel-like mechanical properties make them highly suitable for tissue engineering. Future work would turn to developing conducting polymer hydrogels with hydrolysable crosslinking bonds which can undergo biodegradation in physiological conditions. Hydrogels are formed through different gelation mechanisms where polymer chains are crosslinked by covalent, ionic, or physical bonds. Covalently crosslinked hydrogels offer tunability in mechanical properties and biodegradation through radical chain polymerizations and chemical crosslinking.

Another critical consideration is to package the battery properly for in vivo application. Despite the fact that the Mg-air battery system developed in this thesis uses a bioreabsorbable anode, biocompatible/biodegradable cathode, and biocompatible/biodegradable electrolyte, a conformal biocompatible oxygen-permeable encapsulation layer is recommended for practical applications. The
encapsulation material introduces a protection layer to ensure the efficacy of the battery for a desired duration before degradation. In Chapter 6, the author has achieved preliminary results of modulated lifetime of encapsulated Mg-air battery upon exposure to PBS solution. It is anticipated that tailoring the properties of silk layers can further modulate the degradation profile and lead to a predictable battery lifetime. The degradation rate of silk film can be altered by the film thickness and crystallinity (e.g., β-sheet content). This approach may provide additional avenues for on-board energy storage systems on a single chip of silk for the next generation of biodegradable medical devices, such as a system required for tissue regeneration.
7.3 References

1. Zhang, G.; Yang, F., Direct electrochemistry and electrocatalysis of anthraquinone-
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