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## Organic bionics

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### Abstract

Bionic technology involves the efficient integration of biology and electronics and is providing the basis for significant improvements in a number of medical treatments. The use of organic conducting polymers to provide a compatible multifunctional platform to interface the world of biology and electronics has attracted an increasing amount of attention over the past 15 years. This paper will discuss advances being made in the development of organic bionics and their application to improved health strategies. © 2010 Copyright SPIE - The International Society for Optical Engineering.

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# Organic Bionics

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## ABSTRACT

Bionic technology involves the efficient integration of biology and electronics and is providing the basis for significant improvements in a number of medical treatments.

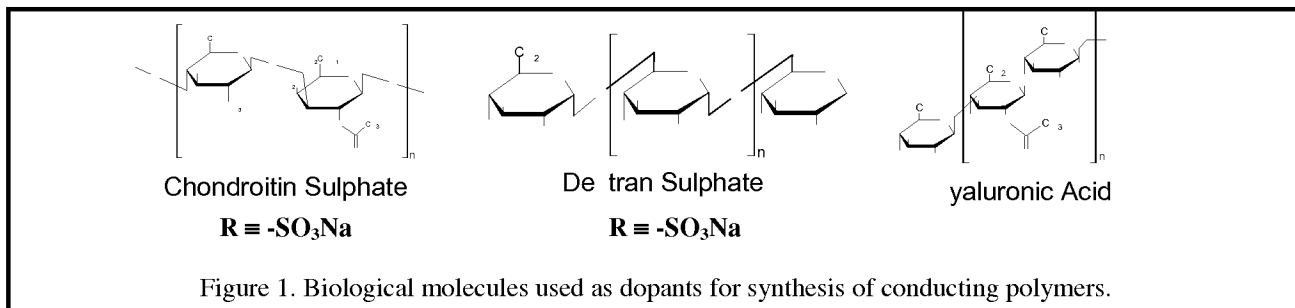
The use of organic conducting polymers to provide a compatible multifunctional platform to interface the world of biology and electronics has attracted an increasing amount of attention over the past 15 years. This paper will discuss advances being made in the development of organic bionics and their application to improved health strategies.

## 1. INTRODUCTION

The ability to communicate across the biology – electronics interface (**bionics**) has fascinated biologists and medical engineers for some time. Successes in the field include the cochlear ear implant, the heart pacemaker and more recently the emerging field of neural prostheses enabling communication with limb replacements. These are examples of bionic devices that need to function effectively for a long period of time (several decades). Another emerging area is that of regenerative bionics wherein the bionic device is required to facilitate repair of the biological system, only over a period of weeks or months. However, all of these bionic devices require the ability to communicate effectively across an “electrode” - cellular interface. This places strict and onerous requirements on the candidate materials<sup>1</sup>.

Inherently conducting polymers (ICPs) have emerged<sup>2,3</sup> as materials of promise in recent years. These organic conductors provide a versatility in composition hitherto unavailable with conducting materials. The most studied of the ICPs are the polypyrroles, polythiophenes and polyanilines. The ability to produce the polypyrroles at neutral pH from aqueous media has meant that, to date at least, the use of this organic conducting backbone has attracted most attention from those interested in the development of new materials for medical bionics.

Using polypyrrole a significant proportion of the material can be rendered “biological” in nature through the incorporation of appropriate biomaterials such as biological polyelectrolytes or even living cells<sup>4</sup>. Some of the biological polyelectrolytes incorporated into conducting polymers during synthesis are shown in Figure 1. In all cases electronically conductive polymers are produced. An interesting and beneficial consequence of incorporating polyelectrolytes as the dopant is that often gel-like (high water content) electronic materials are formed spontaneously upon formation of the conducting polymer.

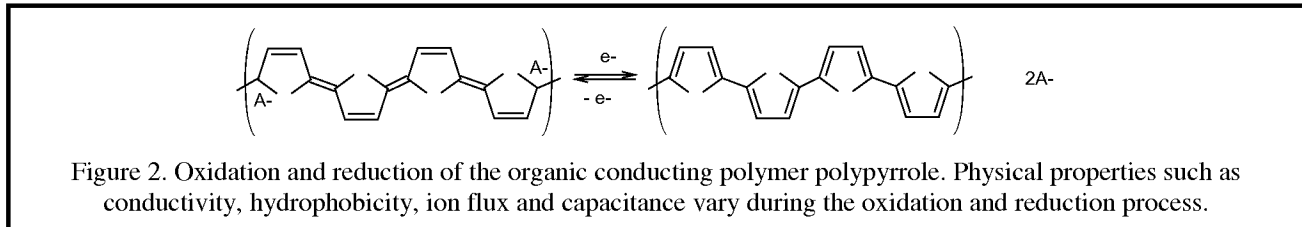


Another exciting feature of the organic conductors is the ability to create the electrode assembly under physiological conditions, permitting fabrication in the presence of living cells. Wallace *et al*<sup>5</sup> employed facile polymerisation

conditions to incorporate red blood cells into a polypyrrole matrix, while more recently Martin and co-workers developed an ingenious protocol that allows formation of a conducting polymer in the presence of living cells (neuroblastoma-derived cells) *in vitro*<sup>6</sup>. These novel approaches enable, for the first time, the seamless integration of an electrode with living cells.

So, the electronic conductivity of these organic materials and a composition biological in nature provide a somewhat unique platform for bionic applications. This is a significant step forward, however, organic conducting polymers such as polypyrrole provide further dimensions in our desire to create more effective electro-cellular interfaces.

These further dimensions arise from the inherent electroactivity of the structures (see Figure 2).



This somewhat simplistic depiction of the redox processes involved belies the complexity of the system. Each transfer of electrons to/from the conducting polymer imparts a change in the chemical and physical properties of the material that effect subsequent charge transfer. The most obvious effect is the decrease in electronic conductivity observed as the conducting polymer backbone is reduced. For most conducting polymers electrochemical reduction will also cause an increase in hydrophobicity affecting the electrochemical double layer since polymer-solvent interactions will be influenced. Reduction also causes an expulsion of anions (A<sup>-</sup>) resulting in a decrease of volume often accompanied by a decrease in the materials modulus. The molecule expelled can be chosen to have selected biological properties for particular applications.

This ability to control the properties of organic conducting polymers *in-situ* via manipulation of the oxidation state provides further dimensions in the design of the electrode-cellular interface. The ability to release bioactive molecules, to control surface energy and even mechanical properties are all possibilities not previously available in a conducting material. It has also been established that the nanostructured forms of these organic conducting materials take on properties that significantly enhance their performance in the field of bionics with a dramatic effect on the physical, chemical and biological properties of these materials being observed<sup>4</sup>.

### Cell Studies

Early *in-vitro* studies with living cells indicated that polypyrroles are not cytotoxic<sup>7,8</sup> and subsequently the use of polythiophene based structures has also been successful<sup>9</sup>.

It has now been demonstrated that polypyrroles are compatible with a range of mammalian cells including endothelial<sup>10</sup>, nerve<sup>11</sup> and muscle<sup>12</sup>. More recently the nerve growth factor (NT3) has effectively been incorporated into and released from a Ppy polymer via electrical stimulation<sup>13</sup>. Significantly, this controlled release of NT3 was seen to have a positive effect on neurite outgrowth from Spiral Ganglion Neuron (SGN) explants<sup>14</sup>. The therapeutic effects of NT3 release has also been demonstrated *in-vivo* with an increase in SGN growth being observed upon NT3 release compared to the control<sup>15</sup>. Based on earlier studies by Clark and coworkers who demonstrated a synergistic beneficial effect used two neurotrophins: Brain Derived Neurotrophic Factor (BDNF) combined with NT3 we developed procedures to incorporate both of these bioactive molecules into polypyrrole. We also demonstrated the ability to provide effective controlled release of these two neurotrophins by electrical stimulation<sup>16</sup>.

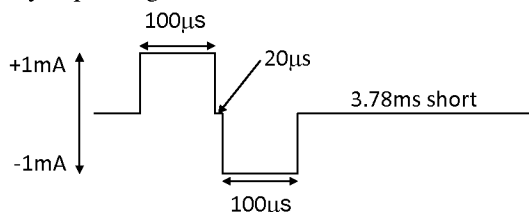
The composition of the polymer is determined by the dopant A<sup>-</sup> selected plays an important role in determining the ability of the polymer to support cell adhesion and proliferation. Given that the dopant used also influences the electronic and physical (e.g. nanotopography) of the materials produced the influence of dopant on the “bionic” performance is somewhat complex.

Our recent studies demonstrate that this compatibility is dependent on the inherent nanostructure of ICP surfaces<sup>17</sup>. Furthermore, the introduction of nanostructure via templates has been shown to enhance the ability of ICPs to provide electrically stimulated release of bioactive molecules at the interface<sup>18</sup>.

A wide range of cell types have been cultured and studied on OCPs. Schmidt et al<sup>19</sup> evaluated the *in vitro* cell compatibility of PC-12 cells on a Ppy polymer that contained the extracellular matrix component hyaluronic acid. In a parallel study we demonstrated that even incorporation of a synthetic polyelectrolyte (polystyrene sulfonate) could inverse electronic hydrogel properties and provide a platform to support PC-12 cell growth.<sup>20</sup> These early findings showed that this OCP was a suitable substrate to support a neural like cell line. In a subsequent study they showed that the use of electrical stimulation (constant current of 10 $\mu$ A for 2hr) during protein adsorption increased fibronectin adhesion which in turn resulted in longer neurite growth from PC-12 cells compared to controls. More recently<sup>11</sup> we showed that using a biphasic charge balanced current pulse to stimulate a Ppy substrate it was possible to accelerate nerve growth and increased Schwann cell migration when compared to non-stimulated OCP substrates.

More recently OCPs have been used to culture muscle cells<sup>12,20,21</sup>. Rowlands and Cooper-White cultured vascular smooth muscle cells (SM) on PPy and showed an increase in proliferation and expression of SM phenotype markers (smooth muscle  $\alpha$ -actin and smooth muscle myosin heavy chain) when the cultures were stimulated with 50 $\mu$ A sinusoidal AC current at 5 and 500 Hz. Razal et al showed the beneficial effects of combining Ppy with degradable (PLGA) fibres to culture and direct the growth of partially differentiated muscle (ROSA) cells<sup>12</sup>. In this study aligned degradable fibres were used to direct the growth of aligned myotubes. These fibres were deposited onto a PPy surface which can facilitate the use of electrical stimulation to compliment the fibres in assisting aligned myotubes growth. As with other cell types the role of the dopant is critical in optimising the performance of conducting polymers as a new bionic platform<sup>21</sup>.

Early studies with living cells highlighted that the *modus operandi* in using organic polymer electrodes to interface with cells would be diverse and multifunctional. For example, Schmidt<sup>22</sup> and co-workers utilized their inherent electronic conductivity to deliver direct electrical stimulation to cells either by applying a constant potential across two electrodes or by directly passing a current through the conducting film. This is in contrast to techniques used by Supronowicz *et al*<sup>23</sup> how used a pulsed current stimulation protocol (10 $\mu$ A at 10Hz) to stimulate osteoblasts cultured on polylactic acid/carbon nanotube composite films. In our laboratories the electrical stimulation protocol is based around applying a charge balanced pulse (Scheme 1) directly to the conducting polymer and involves biphasic current pulse trains with varying current amplitude and varied frequency depending on the cells we wish to stimulate.



Scheme 1 Electrical stimulation waveform.

### Energy Requirements

Obviously bionic devices, even those more temporary in nature, as used for regenerative bionics, require energy. A power supply and/or energy generation system is required. The general power source requirements include safety, reliability, high energy density with low weight and small size, predictability of performance and low self-discharge<sup>24</sup>. For rechargeable systems, the batteries should not significantly raise the body tissue temperature while charging<sup>25</sup>.

Consider the example of using electrical stimulation with conducting polymers to facilitate nerve regeneration. As discussed above we have shown that the stimulation could significantly increase the extent of Schwann cell migration and axonal growth. The clinically relevant electric stimulation protocol applied was 1.0 mA amplitude with biphasic pulses at a frequency of 250 Hz, 100  $\mu$ s pulse width, 3.78 ms interphase gap, and a 20  $\mu$ s short circuit (Scheme 1). To drive the nerve regeneration stimulation for 7 days assuming 8 hours stimulation per day, the charge consumed would be 10.08C or 2.8 mAh. In terms of the all-polymer batteries we have developed<sup>26</sup>, the discharge capacity (at a 0.5 mA cm<sup>-2</sup> drain) was found to be 20.9 mAh g<sup>-1</sup> (based on the mass of anode active material only). Given battery configuration composed of one anode layer (10 mg mass) and one cathode layer (1 cm<sup>2</sup> in size) electrical stimulation, using the

waveform shown in Scheme 1, can be applied for approximately 4 hours. In this battery configuration it is the anode material (functionalised polyterthiophene) that limits the performance. This battery system is far from being considered implantable and as such development of sustainable power supplies for autonomous and portable systems is being developed.

A number of other biopolymer based implantable battery systems are being pursued in our laboratories. In addition, we have been investigating the use of new electrode materials for the development of implantable biofuel cells to generate energy. Biofuel cells harness the power generated from energy sources of the body, and the energy capacity would not be limiting in a cell utilizing glucose and O<sub>2</sub> available in the blood supply as fuels<sup>27</sup>.

### Processability and Device Fabrication

Most OCPs are not amenable to traditional processing and fabrication options. However, the advent of nanotechnology in the OCP world has had a dramatic effect on processing capabilities and this is critical for creating appropriate bionic interfaces. The ability to provide stable nanodispersions means that inkjet printed tracks<sup>28,29</sup> with micron resolution are now readily attainable. The same dispersions are also amenable to wet spinning approaches<sup>30,31</sup> to provide long lengths of fibres again with micron resolution.

### Conclusion

Having established the feasibility of using the dynamic properties of organic conductors in bridging the biology electronics interface, there is work to be done in terms of understanding and optimizing the synergistic effects that the multi dimensional control of this interface might provide. Already it is obvious that the modern bionic engineer is endowed with a materials inventory Luigi Galvani may have given one of his frog's legs for.

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