APPLIED PHYSICS

Electrode-Cellular Interface

Electrode materials that facilitate interaction with living cells are crucial for the development of next-generation bionic devices.

G. G. Wallace, S. E. Moulton, G. M. Clark

Pacemakers and bionic ears (cochlear implants) (*1*) were the first medical bionic devices to be used successfully in humans. On the horizon there is the prospect of a neural prosthesis capable of operating prosthetic limbs (*2*), a bionic eye (*3*), as well as other devices for the restoration of body function. These developments are crucially dependent on successfully connecting the device to cellular tissue. The development of organic polymer conductors is contributing to achieving that success.

In a bionic ear, sound is coded as electrical pulses via a speech processor (see the figure) This temporal pulse pattern stimulates nerve cells in specific areas of the cochlea (the auditory portion of the inner ear) that correspond to different frequencies. The transmission of the pulses is critically dependent on the efficacy of the electrode-cellular interface. The electrode structure must be biologically compatible, not be prone to infection, and be stable for a time appropriate to the application. Control over the electrode's composition and its physical and mechanical properties—including surface roughness, porosity, and modulus—is therefore required. Because the electrode must be integrated into a package suitable for implantation, processability and fabrication methods are also important considerations.

For effective transmission of charge from electrodes to cells, the interface created by implantation must have low electrical impedance. However, the impedance inevitably increases after implantation because of tissue scarring—the process that attempts to separate the implant from the body. An in vitro model has been developed to investigate the factors, such as cell type, that influence the impedance changes (*4*). The model mirrors results obtained in vivo in that electrical stimulation of a cell-covered electrode initially reduced the impedance, followed by recovery to prestimulation levels during inactive periods (*4*).

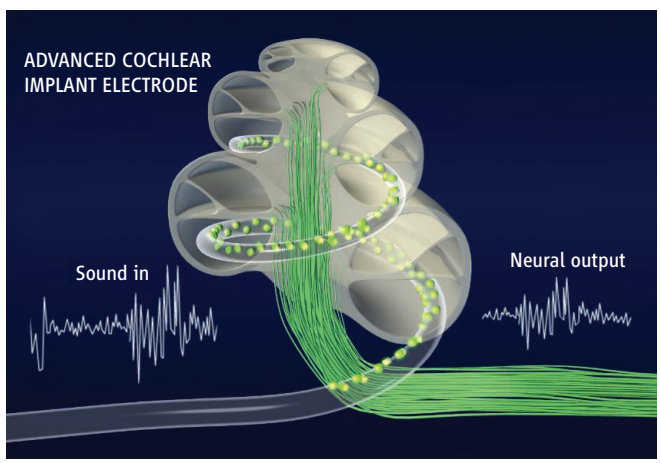
Since the pioneering frog's leg experiments conducted by Luigi Galvani in 1783, the electrodes of choice for bionic applications have been based on inert metals. These include platinum and iridium oxide (*5*). Platinum and iridium alloys have been used in deep brain stimulator electrodes (*6*). Nanostructuring of such electrodes improves performance by reducing impedance and influencing cell compatibility. Organic conducting polymers have also been used for electrode-cellular interfaces. These electrodes are compatible with biological molecules such as enzymes and antibodies (*7*), and may also act as reservoirs for biologically active molecules and drugs that could then be released in response to electrical stimuli (*8*, *9*). In vitro studies with living cells indicate that polypyrroles are not toxic to cells (*10*). Polythiophene-based structures have also been used successfully (*11*).

Studies with living cells also indicate that using organic polymer electrodes to interface to cells would be diverse and multifunctional. For example, Schmidt *et al.* (*12*) have electrically stimulated cells either by applying a constant potential across two electrodes or by directly passing a current through the conducting film. As the field has progressed, materials with improved mechanical, electrical, and biological properties have emerged. In parallel, material processing and fabrication approaches that enable organic conductors to be produced in useful forms have also been developed. Organic conducting polymer electrodes can now be produced with numerous approaches including electroplating, electrospinning to produce nanofibers, wet spinning of long length microfibers, and even inkjet printing of tracks or patterns with micrometer dimensions.

These advances have led to a flurry of activity addressing more specifically targeted applications and have helped define the electrical stimulation that can be acceptably applied. For example, when using such materials to communicate with spiral ganglion cells in a cochlear implant, the stimulation must be charge balanced and restricted to charge densities below 75 $\mu C/cm^2$. Despite these limitations on the stimulation parameters, beneficial effects (in terms of neurite outgrowth) are obtained by direct electrical stimulation; furthermore, that same stimulation can be used to release nerve growth factors (*13*) just where they are needed.

Another exciting feature of organic conducting polymers is the ability to create the electrode under physiological conditions, which permits fabrication in the presence of living cells. Campbell *et al.* (*14*) used facile polymerization conditions to incorporate red blood cells into a polypyrrole matrix, and another protocol allowed formation of a conducting polymer in the presence of living cells in vitro (*15*). These approaches enable the integration of an electrode with living cells, and should facilitate improvements in the performance of electrode-based biomedical devices.

Other organic electrode structures to emerge are those based on nanostructured carbons: carbon nanotubes and graphene. Both provide an inherently electrochemically stable organic interface. Carbon nanotube–based interfaces produce electrodes with high capacitance and low impedance. These materials have been used to accelerate the growth of osteoblasts (cells important in bone regrowth) (*16*). Providing electrical stimulation to neurons via a carbon nanotube–based platform (*17*) has led to the formation of a functional neural network of neural stem cells (*18*). The ability to separate and assemble sheets of graphene into electrode substrates has created new bionic electrode possibilities. Graphene sheets are not toxic to cells (*19*), and electrical stimulation facilitates osteoblast proliferation (*20*).



Wiring up cells. The fabrication of organic conducting polymers that can deliver neurotrophic factors and promote the survival of auditory spiral ganglion neurons is being developed in conjunction with the advanced cochlear electrode fabrication.

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The inherent strength of carbon nanotubes and graphene (or nanocomposites containing them) make them well suited to use in bone regrowth, where matching the mechanical properties of an implant with that of the bone to be regrown is critical. Another attractive feature is that they can be processed at high temperature, enabling composites to be formed with melt-extrudable materials that are known to be biocompatible.

The bionic materials store is well and truly stacked, and many tools are available to characterize and use the contents. The challenge lies in determining the most appropriate electrode materials for a particular application. For medical bionic applications involving tissue engineering—such as implants for peripheral nerve, spinal cord repair, or muscle regeneration—the ability to produce biodegradable and bioabsorbable materials with appropriate function and lifetime profiles will be critical. For bionic prosthetics, challenges include reducing power requirements, finding natural (biological) power supplies, and extending device lifetime. In the case of bionic repair systems, devices should be biodegradable. Our increasing understanding of the properties of new electrodes and of how to design and control the electrode-cellular interface promises exciting advances in medical bionics.

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