A Non-Invasive Approach to the Bionic Eye

N. Grossman
Imperial College London, UK

H. Yang
Imperial College London, UK

E. Drakakis
Imperial College London, UK

K. Nikolic
Imperial College London, UK

P. Degenaar
Imperial College London, UK

C. Toumazou
Imperial College London, UK

INTRODUCTION

According to the World Health Organisation definition for blindness, that is, visual acuity bellow 3/60 for the best eye on the Snellen scale, there are thought to be 38 million blind people worldwide (Delbeke et al., 2004). This figure is expected to double over the next 25 years due to combination of an increasing population and aging worldwide. There are additionally 110 million people who have severely impaired vision and are high risk of becoming blind. The most common causes of blindness are: cataract, trachoma, glaucoma, diabetic retinopathy, age related macular degeneration (AMD) and retinitis pigmentosa (RP). In the west countries, cataract and glaucoma make up only 11% of the total causes of blindness. In these regions AMD and RP are prevalent eye diseases. AMD increases dramatically with age, so that (with about 2million cases in the USA) it is the leading cause of blindness among Americans of European descent (Friedman et al., 2004).

The AMD and RP result in the loss of photosensitivity primarily due to destruction of the rod and cone photoreceptors. Medical intervention to date has been disappointing. There is no known mechanism by which the eye can self-repair. Anti-angiogenesis drugs can significantly slow down the progression of wet type AMD, but in most cases there is very little treatment. Even more significantly, none of the drugs are capable of restoring lost vision. The idea of using stem cells in therapies is still complex and may be many decades away from potential treatment. Prosthetic implants are therefore the only method at present by which we can offer a return of some of the lost vision. Here we present a special type of vision restoration based on the optical stimulation of retinal ganglion cells (RGCs), which remain operational.

BACKGROUND

Most of current concepts for a visual prosthesis are based on neuronal electrical stimulation. Several different locations along the visual pathways have been proposed and examined so far for visual prosthesis:

- Retinal implant (which is either epiretinal or subretinal)
- Optic nerve implant and
- Visual cortex implant

A nice historical perspective regarding electrical visual prosthesis can be found in Lovell et al. (2007). There is a number of very good reviews of the artificial vision and visual prosthesis, such as Dowling (2005), Loewenstein, Montezuma, and Rizzo (2004), Margalit et al. (2002), Zrenner (2002), and so forth. The most favoured approach is the intraocular electrode array, since the retinal implant seems to be the most convenient

for surgical intervention and it is easier to retinotopically map individual pixels on the light sensing array with points on the retina.

In most forms of retinal dystrophy, the photoreceptors are lost, but the RGCs, the output neurones of the retinal network, survive and project to the retinorecipient areas of the visual cortex. There have been numerous attempts to stimulate these cells as a prosthetic strategy. The implants to date have come in two forms: subretinal and epiretinal. Subretinal implants are placed underneath the retinal layers and usually consist of a microphotodiode array which attempts to stimulate the remaining signal processing layers in the retina (U.S. Patent No. 5,024,233, 1991). The epiretinal chips are positioned on the surface of the retina, and try to stimulate the retinal ganglion cell layer (U.S. Patent No. 5,935,155, 1999). In this case, additional image processing is required to replicate that of the bypassed retinal layers.

The retinal prosthetics that have been implanted to date have several problems (Dowling, 2005). Both types of implants have to be implanted inside the eyeball (and subretinal structures need to be placed under the retina, requiring more delicate surgery) and the stimulating electrodes have to be in good physical contact with the cells which they stimulate. The invasive electrodes can cause further degradation of remaining functional tissue. The curved nature of the eye makes it very difficult to cover any significant portion of the retina, though there have been attempts at more flexible substrates. Furthermore, power consumption issues are highly significant. Introduction of power cables is difficult, and power transmission through an RF link, for example, does not always provide sufficient power to power a significant quantity of stimulation points. Additionally, the position of the electrodes is fixed once they are inserted, and precise positioning on the micrometer scale is hard to control.

To date, epiretinal implants have used small numbers of electrodes and thus the patient has seen light flashes known as phosphenes. It has been possible for patients to interpret some basic shapes from these phosphenes (Humayun et al., 2003). However, if the stimulation matrix is to be scaled to allow detailed analysis of the visual scene, then the image processing component will become increasingly important.

There has been substantial progress toward an electronic retinal prosthesis, but fully functional, long-lasting devices are presently limited largely by power consumption issues.

PHOTONIC RETINAL PROSTHESIS

Optical Stimulation of Neuron Cell

Recent advances in biochemistry have generated a novel neuronal stimulation technology that is based on light. Using light to stimulate neuronal signals has many advantages. First, in contrary to electrode based stimulation, light does not require mechanical contact and can enable noninvasive remote control on the cell activities. Second, since light beams can be easily scanned, the stimulating point is flexible and does not require a prior decision on the stimulation location. Third, using conventional optics light can be focused to very high spatial resolution.

The feasibility of using light instead of electricity to trigger neuronal signals was first demonstrated in 1971 by Richard Fork who used high power laser to stimulate action potentials in the abdominal ganglion of the marine mollusk Aplysia California (Fork, 1971). Since then scientists have been exploiting developments in Nanotechnology and Genomics to realize various photostimulation tools that would revolutionize biology and neuroscience. The impartment of light sensitivity, also known as photosensitization, is achieved by either:

1. Photolysis of blocking moiety attached to neurotransmitters
2. Expression of natural photosensitive proteins and ion channels
3. Attachment of a photoisomerizable switch next to the active site of ion channel or membrane receptor.

Photolysis of Caged Neurotransmitter

The photolysis of caged neurotransmitter approach is based on disabling the neurotransmitter activity by attaching a photoremoveable blocking compound. This idea was first introduced in 1978 by Kaplan, Forbush, and Hoffman (1978), but the utility of the caged compounds tool became widely apparent to the neuroscience world just in 1986 when an NB-caged-acetylcholine agonist, carbamoylcholine, was used to study the kinetics of nicotinic acetylcholine receptors (Walker, McCray, & Hess, 1986). Since then photolysis of caged molecules has gained a wide use as a remote control means of stimulating cellular responses. Since