

## Chapter 1

# Introduction to Bioelectronic Vision

As everyone would certainly agree, vision is the most crucial sense; it provides the primary means of gathering information from the surrounding environment starting from birth. During our lifetimes, vision is the sense through which most of the information is perceived and, in many ways, is responsible for and affects who we are. For example, it is through vision that human beings perceive art. In everyday life, vision is an indispensable resource used in performing the most simple tasks. People who unfortunately lost their vision can become very dependent upon others, which in most cases represents a social problem.

Blindness is a severe impairment, since for the blind, it is very difficult to recognize other people, landscapes, and objects of daily life. In addition, they usually have severe motion restrictions, since they are depending on others to move safely. People who have been able to see for years lose an essential contributor to their quality of life due to blindness. Loss of vision is not only an enormous psychological burden, but it can also cause severe handicaps and cause tremendous difficulties in moving in strange, and even in formerly familiar, environments.

In 2002, it was estimated that more than 161 million people were visually impaired, of whom, 124 million people had low vision and 37 million were blind. However, refractive error as a cause of vision impairment was not included in these figures, which implies that the actual global magnitude of vision impairment is greater [World Health Organization (2004)].

Human vision disabilities are of different types and have different geneses. Thus, depending on the nature of the disability, different approaches have to be used to circumvent the dysfunction. Impairments in the eye's optical system, which is responsible for transmitting and focusing light as a sharp image on the retina, usually are easily overcome with the use of an

external corrective optical system. Optical lenses (glasses) are a typical optical choice to remedy this problem; another option is surgical intervention, like in the case of cataracts, where an eye lens transplant can be performed.

The current challenge is to circumvent retinal and other superior vision center damages that frequently lead to what is designated *profound blindness*. The hope in these cases is to combine the increasing knowledge we have about the biology and the anatomy of our vision system with the amazing advances in science and technology, to set up a new field that can be designated as *BioElectronic Vision*. This book is about this emergent field, with the final goal of achieving components that substitute for these damaged vision centers. The remainder of this chapter identifies the main causes of blindness, discusses the primary concepts of *Bioelectronic Vision*, and references the research efforts around the world to design visual neuroprostheses.

## 1.1 Main Causes of Blindness

The impairments of profound blindness may have origins in degenerative retinal diseases or in brain injuries that affect the superior vision centers due to accidents or to direct surgical intervention (e.g. for a tumor removal). Figure 1.1 shows the distribution of the principal causes of blindness in the world, and their prevalence based on data collected from the World Health Organization, authority for health within the United Nations Organization, in 2002 [World Health Organization (2004)].

One of the major causes of vision impairments in the world is cataract. Cataract is normally related to the aging process and is characterized by opacity of the eye's lens, which impedes the regular flow of light. The actual treatment for this disease consists of a surgical intervention to replace the opaque lens with an artificial intraocular lens.

The second major cause of blindness is glaucoma. Glaucoma occurs when the aqueous humor does not drain out correctly and the pressure within the eye becomes too high, compromising the blood vessels of the optic nerve's head, and eventually the axons of the ganglion cells, which results in the death of these vital cells. The reduction of intraocular pressure is imperative to avoid total blindness. This disease affects the retinal nervous system and can cause permanent damage.

The third cause of blindness worldwide is the age-related macular degeneration (AMD). In some persons, the macula, which is responsible for

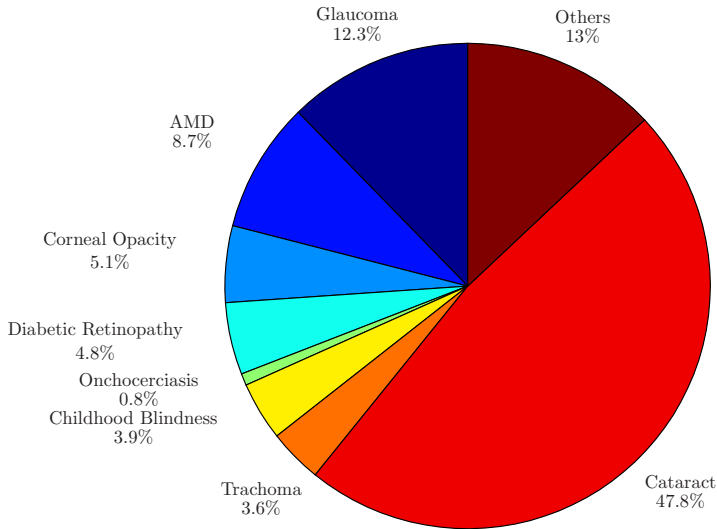


Fig. 1.1 Causes of blindness in the world in 2002 (data from [World Health Organization (2004)]).

the perception of fine detail in the center of the visual area, degrades with age for unknown reasons. The pigment epithelium behind the retina degenerates, forming drusen, and leaks fluid behind the foveal macular area. The cones in the fovea then die, which causes central vision loss and makes it impossible to read or see fine details. The AMD is a major cause of blindness in developed countries due to the high number of people above 70 years of age.

The graphic in Fig. 1.1 shows that the next cause of blindness is corneal opacity, which occurs when the cornea becomes scarred, preventing light from passing through the cornea to the retina, and causing, in some cases, the cornea to appear white or clouded. Corneal opacity can be caused by infections like conjunctivitis, or by the herpes virus, measles, injury, or inflammation of the eye caused by a stroke or a chemical agent. In many cases, it can be reversed by adequate treatment, which may include surgery.

Trachoma, another cause of blindness, is an infection caused by an organism (*Chlamydia trachomatis*) that can be treated with antibiotics. It is a common cause of blindness worldwide, but rare in developed countries.

A significant percentage of blindness is caused by diabetes, which is a serious problem in industrialized countries. Approximately 90% of all diabetic patients have retinopathy after twenty years. Diabetic retinopathy is characterized by anomalies in the blood vessels that get blocked and leak, or multiply in an uncontrolled manner, leading to irreversible blindness.

A major cause of blindness among children is the deficiency of vitamin A, particularly in children under 5 years. Included in this percentage is blindness caused by premature birth, infant retinopathy and cataracts. Blindness among children is a major problem due the length of time they will have to contend with the disability. It is estimated that 1.4 million children below age 15 are blind.

Onchocerciasis is responsible for blindness particularly in African and Latin America countries. Onchocerciasis is a disease transmitted by a parasite spread by flies in riverside areas.

The remaining causes of blindness are grouped in the general class "others". This includes a terrible disease called retinitis pigmentosa (RP), which presently has no cure. RP is an inherited disease that causes degeneration of the retina and pigment excess. First, it provokes night blindness, then tunnel vision and, as more of the peripheral retina becomes damaged and the rods die, progresses gradually to total blindness.

The blindness distribution is not geographically uniform. About 90% of visually impaired people live in developing countries. Statistics suggest that females have a higher risk of being visually impaired. In terms of age, it is estimated that about 82% of visually impaired people are more than 50 years old. "Vision 2020: The Right to Sight" is a global initiative for the elimination of avoidable blindness, launched jointly by the United Nations World Health Organization (WHO), the International Agency for the Prevention of Blindness (IAPB) and international eye care institutions and corporations. One of the largest and most productive eye care facilities in the world is the Aravind Eye Care System, which was established in 1976 in Madurai, India. It has treated over 2.3 million outpatients and performed over 270,000 surgeries. They mainly serve people living in rural India, and they were the recipient of the first edition of the António Champalimaud <sup>1</sup>

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<sup>1</sup>The Champalimaud Foundation (<http://www.fchampalimaud.org>), which is based in Lisbon, was created in 2004 at the bequest of the late Portuguese industrialist and entrepreneur António Champalimaud, to support individual researchers and research

Vision Award in 2007.

At the same time, several projects involving multidisciplinary research groups have been promoted to develop and demonstrate the feasibility of artificial vision systems. There are a handful of initiatives around the world devoting significant resources and attention to the research and development of visual neuroprostheses. The huge challenge of artificially restoring vision to the blind poses several engineering and biological problems that are difficult to overcome and also requires clinical human testing. The challenge is being addressed primarily by those in academia, but the effort comes from all over the world, as it can be seen in Fig. 1.2. Due to the initial cost of such prostheses, people who live in industrialized countries are expected to be the initial beneficiaries of this research. Thus, blind people affected by diabetes (AMD) and RP could be the first to take advantage of those neuroprostheses.

## 1.2 Main Components of a Bioelectronic Vision System

As will be seen later in this chapter and in Chap. 6, bioelectronic vision systems are supported on two main classes of visual neuroprostheses: *i*) retina neuroprostheses are suitable when the front end of the retina is functioning properly, while *ii*) a cortical neuroprosthesis is the last hope when the retina, including the optic nerve, is not functional at all, and only the brain vision centers remain (see Fig. 1.3). In this latter case, the neuroprosthesis directly interfaces with the visual processing center in the brain, the area (V1) of the visual cortex. In the profoundly blind, the optical signaling pathways are irreversibly damaged. Thus, the neuroprosthesis is a substitute for these patients' entire vision system. The concept and components of a bioelectronic vision system supported on a complete visual neuroprosthesis that directly interfaces with the brain is depicted in Fig. 1.3 and in Fig. 1.4.

The first component of the visual system is the eye. The eye is responsible for transducing light into neural signals, consisting of electrical impulses, that are then transmitted to the brain for further information extraction. Roughly speaking, the eye is composed of an optical system that focuses light on the retina, a neuronal tissue. Light patterns are encoded into electrical signals and the neuronal processing starts in the retina, as the retina is, in fact, an extension of the brain. A visual neuropros-

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teams working in medical science, and particularly in the field of neuroscience.



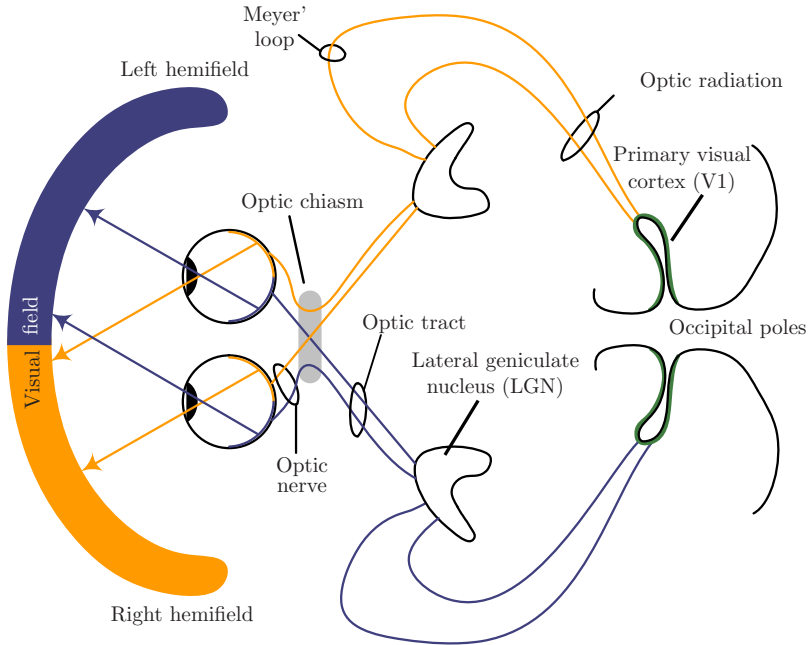


Fig. 1.3 Diagram of the human visual system.

thesis must model the optical eye system, which currently does not pose major technological difficulties, and the neuronal processing occurring in the retina, which is where the true challenge lies. Therefore, a significant step in the development of any visual prosthesis is the selection and evaluation of the adopted retina model. Two different approaches have been proposed for these models: the structural models try to mimic the biological systems based on knowledge about its physiological composition and operation, while the functional models attempt to replicate the functions performed by the retina but are not motivated by the characteristics of the biological systems themselves [Wulf (2001)]. Images in the visual field are mapped according to these models into a set of discrete signals that are then used to stimulate the visual cortex in the brain.

As can be seen in Fig. 1.4, a bioelectronic vision system includes a set of components which, depending on the class of visual neuroprosthesis, can be biological structures or their electronic circuit counterparts. For example, an external video acquisition device is usually required for capturing the visual field image and converting the light patterns into electrical sig-

nals. However, when an array of stimulation electrodes is placed in the subretinal space, the image falling on the retina and its light impulses are converted into electrical currents by microphotodiodes that directly replace and function in the place of the damaged photoreceptors.

The digital signal processing system transforms the visual space image into a set of discrete signals, according to the retina model and taking into account the visuotopic organization of the target structure (retina or cerebral cortex). A module to transmit power and control signals to the implanted electronics is usually required. This module provides energy and controls the stimulator that interfaces with the nervous system to induce the perception of phosphenes, which is an entoptic phenomenon characterized by the sensation of seeing light. The implemented electronics, based on integrated circuits and (micro)electrodes, will ultimately replace the function of their biological counterpart elements. Let us zoom in on the components represented in Fig. 1.4.

Image acquisition is currently a common task in engineering. For cortical or optic nerve neuroprostheses, a general, small and fully functional digital camera is well-suited for a visual prosthesis in terms of dynamic range, sensitivity and depth of field and it is aesthetically pleasing. In a retinal neuroprosthesis, the image encoder can be integrated into the neural interface, and can reside at the plane of the retina, with the advantage that the eye optics are used to project the image onto the encoder.

In the signal processing block, the biggest challenge is the visuotopic mapping of the visual space onto the target visual structure, particularly the visual cortex. This is a somewhat complicated task due to the uniqueness of this map among individuals and because it is conformal only at a low resolution; for high spatial resolutions, this mapping seems to be locally random. Therefore, parameterizable models have to be developed for implementing this module and properly stimulating individuals. This is a somewhat more complicated task due to the plasticity of the visual pathways and the different possible combinations between electrodes and phosphenes elicited. Based on the developed models, the electronics of this

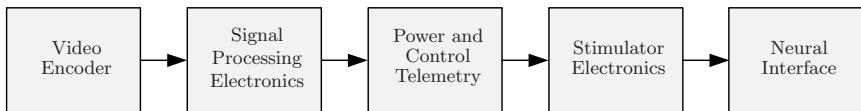


Fig. 1.4 Main components of a visual neuroprosthesis.

module transform the image into a discrete set of signals that drive the stimulators. To adapt the intensity of the incoming light signals into the range level of the neurons being stimulated, an automatic gain control (AGC) can function similarly to the photoreceptors. The first two components of the visual neuroprosthesis can be combined into a single device attached to a set of eyeglasses, while the elements of the visual neuroprosthesis described in the following are likely to be located inside the patient.

The information from the visual scene must be conducted to the implant, but a retinal neuroprosthesis and a cortical neuroprosthesis accomplish this via different methods. There are two main ways to transmit signals through the skin: percutaneous connectors [Dobelle (2000)] or using radio frequency (RF) telemetry [Piedade *et al.* (2005)]. On one hand, the percutaneous connectors have the advantage of being more robust and obviate the use of multiplexers, but on the other hand, they have the drawback of being a source of infections. A radio frequency link also has the challenge of communicating both power and control signals and the requirement that it must be bidirectional. In a retinal neuroprosthesis, a percutaneous connection would have to pass to the outside of the eye through the sclera. For the case of a retinal neuroprosthesis, a laser can also be used to transmit power and information to the implanted circuits used to stimulate the target cells [Weiland *et al.* (2005)]. All types of connections have a series of constraints such as bandwidth, which increases with the number of electrodes in the neural interface, and the transmitted power must also be limited to avoid causing damage to the tissues by heating.

The next component in the chain of Fig. 1.4 is the neural stimulator that must be capable of exciting multiple electrodes at the same time in order to evoke consistent phosphenes. It receives power and data through a telemetry sub-system, and must be capable of controlling the amount of power delivered to avoid damaging neighboring tissues. Furthermore, it should be able to circumvent malfunctioning electrodes. The implementation of this module on chips involves a trade-off between the processing capabilities and power consumption; increasing the process capabilities of the chip diminishes the required link bandwidth, but increases power consumption and potential failures [Maynard (2001)]. The most appropriate technology today, based on size and power consumption, is a digital VLSI circuit [Warren and Normann (2003)].

The last element in a vision prosthesis is the interface with the nervous system. The neural interface establishes the bridge between the nervous system and the external electronics. It mediates the transduction between

the electrical currents generated by the electronic device into ionic currents that flow inside the human body. For the retinal neuroprosthesis, the neural interface options range from silicon chips to specific developed ceramic materials [Wu (2006)]. For cortical interfaces, oxidized iridium is a candidate material because it has shown good biocompatibility and acts as a good electronic to ionic current transducer. There are also other compatibility issues related to the neural interface that must be taken into account [Warren and Normann (2003)].

In conclusion, before reaching the ganglion cell layer in the retina or the visual cortex, the visual signal has already been subjected to a series of processing stages. When the interface with the visual stimulus is made at the level of the ganglion cell layer, as in the case of an epiretinal neuroprosthesis, the output information must be identical to the output produced by a healthy retina; the transformation of information about the visual space to the retinotopic space is done by modeling the neural processing of the retina. For the case of a cortical neuroprosthesis, the signal processing occurring along the visual pathway should take place such that an adequate stimulus for the neural interface is generated.

### 1.3 Classification of Visual Prostheses

The effort to provide the profoundly blind with some kind of vision has led to some results [Rizzo III and Wyatt (1997)]. Throughout the world, several research groups and consortia dedicate their efforts to designing vision prosthesis capable of conveying to the blind "some kind" of vision. The words "some kind" are used frequently by scientists when referring to this goal and reflect the huge extension of this task framed by the complexity of the human visual system, ranging from the retina's neural circuitry to the deep brain processes involved.

Some unconventional approaches and electronic devices have been proposed to convey vision to visually impaired people. In some of these devices, the visual information is converted to auditory [Arno *et al.* (1999)] or tactile signals and is afterwards communicated to the brain. One somewhat curious device is one that consists of a flexible cable with a matrix of electrodes at the end that is placed against the patient's tongue, and a pattern of electrical impulses stimulates its sensitive nerves [Weiss (2001)].

Bioelectronic visual systems are supported on visual neuroprostheses that interface with the following neural structures: *i*) the photoreceptor

layer of the retina; *ii*) the ganglion cell layer of the retina; *iii*) the optic nerve, and *iv*) the visual cortex [Warren and Normann (2003)]. Thus, there are three types of prostheses that still uses some part of the human visual system: retinal and optic nerve neuroprostheses at the eye level, and cortical neuroprostheses at the brain level. The retinal neuroprostheses use the remaining functioning parts of the retina to send the visual signals to the brain, the optic nerve neuroprostheses stimulate what is left of the optic nerve, and the objective of the cortical neuroprostheses is to inject the visual signals directly into the visual cortex.

The type of approach used in a visual prosthesis is related to the type of blindness. In one extreme, the blindness may be caused by damage to the superior retina layers as a consequence of the early stages of diseases like RP. Such blindness may also stem from some kinds of macular degeneration, where the principal injuries occur at the photoreceptor layer, but the ganglion cell layer remains mostly intact, which allows for the (re)usage of these cells. In this type of blindness, a retinal neuroprosthesis can be used. At the other extreme, there is what is called *profound blindness*, where the ganglion cell layers and the optic nerve are irreversibly injured and incapable of transmitting any kind of nervous signals. In this case, the re-establishment of some sort of vision can only be done by the circumvention of the optic nerve, and the remaining option is to stimulate the visual cortex directly with an electronic device. This is where the cortical neuroprostheses come into play.

An intermediate situation is the utilization of the optic nerve to conduct the visual signals to the brain. Some of the retinal diseases leave a significant number of intact ganglion cells dispersed along the retina, whose axons converge to form the optic nerve. The strategy here is to induce the visual signals in this great bunch of ganglion cells at the optic nerve, expecting conductive axons to be excited by the stimulus.

In the remainder of this chapter, we present the main characteristics of the prostheses that interface with the retina and directly with the visual cortex. The signal processing modules associated with these neuroprostheses will be discussed in the next chapters. All this information will be put together in Chap. 6, where the design and the implementation of bioelectronic vision systems will be discussed.

### 1.3.1 *Retinal Neuroprosthesis*

There are the two kinds of retinal implants, depicted in Fig. 1.5. In a *subretinal* implant, the prosthesis is placed between the pigment epithelial layer and the outer layer of the retina, which contains the photoreceptors cells. In contrast, the *epiretinal* device is placed directly against the ganglion cells and their axon layer, bypassing the rods and cones, and directly stimulating the inner retina; this is a more invasive technique.

Unlike the subretinal implant, the *epiretinal* implant does not use any remaining network of the retina for information processing. Thus, the epiretinal sensor has to encode visual information as trains of electrical impulses that are then conveyed by an electrode array directly into the ganglion cell axons, which converge to form the optic nerve. This spatiotemporal stimulation pattern of electrical impulses must represent the visual information in such a way that it can be understood by the brain's visual cortex. On the other hand, the information-transfer characteristics of the epiretinal implant are more amenable to external control, while the subretinal implant requires intact original optics [Zrenner (2002)]. A relevant example of the development and testing of a subretinal implant is reported in [Chow *et al.* (2004)], and an example of an epiretinal implant can be found in [Rizzo III and Wyatt (1997); Humayun *et al.* (1999)].

Nevertheless, retinal neuroprostheses require the presence of viable cells in the inner retina. Therefore, diseases limited primarily to the outer retina are potentially treatable with a retinal neuroprosthesis. Margalit *et al.* references [Margalit *et al.* (2002)] and Weiland *et al.* [Weiland *et al.* (2005)] present an extended overview of retinal neuroprostheses.

One of these prostheses, entitled the "Bionic Eye", uses a new ceramic material to replace the retina's photoreceptors, which acts as an optic detector that transduces light into electrical impulses by means of the photo-ferroelectric effect [Wu (2006)]. This material is directly implanted in the patient's eye and, under optic illumination, generates a photo-current that directly excites the retinal ganglion cells. It seems to be bio-compatible, and it can be used in retinal dystrophies, where the optic nerve and retinal ganglia are intact. For example, for RP, the ceramic material is used to directly stimulate the retinal ganglia.

Another example of a retinal neuroprosthesis is the artificial silicon retina (ASR) microchip [Chow *et al.* (2004)], which uses well-known silicon technology [Optobionics Corporation (2006)]. The ASR microchip is a silicon-based device with a diameter of 2 mm that contains approximately

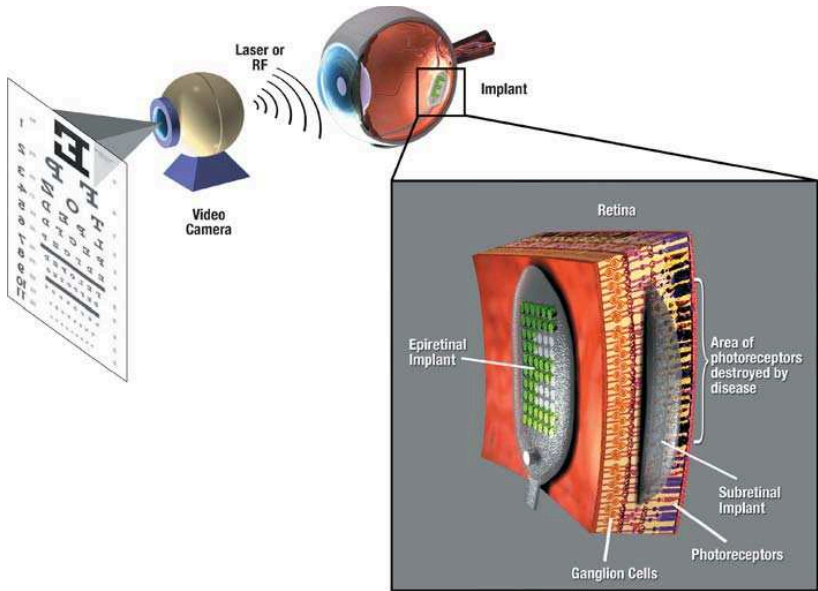


Fig. 1.5 Main components of epiretinal, retinal and subretinal prostheses. (From [Weiland *et al.* (2005)])

5000 microelectrode-tipped microphotodiodes and is powered by incident light. The ASR microchip was implanted in the eyes of patients with retinitis pigmentosa. Patients did not show signs of implant rejection or infection, and all of them demonstrated improved visual function.

There are other examples of subretinal implants. For example, one consists of a chip ( $3 \times 3 \times 0.1$  mm, 1500 microphotodiodes, amplifiers and electrodes of  $50 \times 50 \mu\text{m}$ , spaced  $70 \mu\text{m}$ ) and a  $4 \times 4$  array of identical electrodes, spaced  $280 \mu\text{m}$  apart, for direct stimulation. These were chronically implanted next to the foveal rim of two blind retinitis pigmentosa patients [Zrenner *et al.* (2006)]. The implant was removed in one patient after 4 weeks, but the other patient decided to keep the implant. Patients reported small, yellowish or greyish phosphenes for individual electrode stimulation and they were able to differentiate spatial patterns such as lines, angles and bright squares.

There is a second type of approach at the level of the visual system whose functional principle is to directly stimulate the optic nerve, circumventing the retinal layers entirely, which may be damaged. These devices are implanted around the optic nerve to stimulate the fibers electrically [Brélen

*et al.* (2005)]. This type of prosthesis also requires the development of a retina model.

### 1.3.2 *Cortical Visual Neuroprosthesis*

Cortical visual neuroprostheses are bioelectronic systems that use the visual cortex in the brain as the interface between the electronics components and the biological visual pathway. A last resource for blind individuals who cannot benefit from a retinal neuroprosthesis is the direct stimulation of the visual cortex. This is the last hope when the retina is not functioning at all (including optic nerve failure) because retinal neuroprostheses rely on the optic nerve to transmit electrical signals from the eye to the visual cortex. The visual cortex is a brain vision processing center, and it is well positioned for direct stimulation. This kind of neuroprosthesis includes all the electronic components presented in Fig. 1.4 to substitute the biological counterparts, shown in Fig. 1.3.

The first permanent device developed and applied for chronic stimulation of neural tissue was accomplished in 1968 [Brindley and Lewin (1968)]. The device had 80 electrodes, each with its own controlling unit (receiver). Using this system, the feasibility of a permanent cortical vision neuroprosthesis was demonstrated as the electrical stimulation of the occipital lobe of the human cortex caused subjects to perceive phosphenes.

Despite this initial success [Dobelle and Mladejovsky (1974)], the surface electrodes have a number of drawbacks. The electrical current necessary to induce a phosphene is relatively high (on the order of a milliamperere); consequently, the distance between the electrodes must be considerable in order to minimize their interactions due to current spread. Unfortunately this degrades the spatial resolution. Moreover, current injections can produce short term and long term complications depending upon the levels of the currents that are injected [Agnew and McCreery (1990)].

Two main groups worked during the 1990's towards a cortical vision prosthesis. One was based at the National Institute of Health (NIH) in Washington, D.C., and the other at the John Moran Laboratories in Applied Vision and Neural Sciences at the University of Utah. Both groups tried to overcome the problems mentioned above by employing penetrating microelectrodes instead of using surface electrodes on the visual cortex. One example of such a microelectrode array was manufactured using semiconductor technology [Maynard (2001)] and was developed at University of Utah; it is known as the Utah Electrode Array:  $10 \times 10$  microelectrodes,

each 1.0 – 1.5 mm long, dispersed in a square grid contained in a package with dimensions  $4.2 \times 4.2$  mm [Maynard *et al.* (1997); Normann *et al.* (1999)]. The silicon micromachining and micromanufacturing technologies allow the fabrication of small arrays with a large number of microelectrodes capable of stimulating only the neurons nearest to the electrode with a small amount of current (on the order of dozens of  $\mu\text{A}$ ). The major concerns with the microstimulation are related to the biocompatibility and long term functioning of the inserted microelectrode array.

Research is ongoing to design and develop cortical visual neuroprostheses through intracortical stimulation, but none of these prostheses has been permanently applied for chronic stimulation. A European research project, CORTIVIS, has been conducted over the last few years to design and develop a complete visual neuroprosthesis designed to restore useful vision to profoundly blind people [Project CORTIVIS (2006)]. It performs intracortical microstimulation through one or more Utah Electrode Arrays implanted into the primary visual cortex. The system is composed of a primary unit located outside the body and a secondary unit, implanted inside the body, that communicate with each other using wireless communication technology. A prototype of the proposed system is presented in detail in Chap. 6.

## 1.4 Conclusions and Further Reading

In 2002, it was estimated that more than 161 million people were visually impaired, of whom 124 million people had low vision and 37 million were blind. However, refractive error as a cause of visual impairment was not included in these figures, which implies that the actual global magnitude of visual impairment is greater [World Health Organization (2004)].

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retina's photoreceptors, acting as an optical detector, transducing light into electrical impulses via the photo-ferroelectric effect [Wu (2006)]. Another example of a retinal neuroprosthesis is the artificial silicon retina (ASR) microchip [Chow *et al.* (2004)], which uses the well-known and dominant silicon technology [Optobionics Corporation (2006)].

There are other examples of subretinal implants, namely the one that consists of a chip, 16 direct stimulation (DS) electrodes, and a power line implanted subdermally, connecting the chip to an external energy supply [Zrenner *et al.* (2006)].

The effort to provide some kind of vision to the profoundly blind already has some history [Rizzo III and Wyatt (1997)]. The first permanent device developed and applied for chronic stimulation of neural tissue was accomplished in 1968 [Brindley and Lewin (1968)]. Although it was observed that the electrical stimulation of the occipital lobe of the human cortex causes a subject to perceive phosphenes, it was also concluded that current injection can produce short term and long term complications [Agnew and McCreery (1990)].

Some of the experiments conducted at the Dobbelle Institute, when cortical neuroprostheses were initially proposed in 1974 [Dobbelle and Mladejovsky (1974)], involved implantation of prototypes in blind people [Dobbelle (2006)] and demonstrated that focal epileptic activity can be induced by electrical stimulation. Therefore, penetrating microelectrode arrays manufactured using semiconductor technology [Maynard (2001)], such as the microelectrode array, were developed at the University of Utah, and are now known as Utah Electrode Arrays. These microelectrodes are deeply inserted into the virtual cortex, using a pneumatic insertion technique, to allow for intracortical stimulation with low currents and without provoking major injuries [Maynard *et al.* (1997); Normann *et al.* (1999)]. The silicon micromachining and micromanufacturing technologies allow the fabrication of small arrays with a large number of microelectrodes capable of stimulating only the neurons nearest to the electrode with a small amount of current (on the order of dozens of micro amperes). Donoghue [Donoghue (2002)] provides a general perspective of cortex electronic interfaces.

A European research project, CORTIVIS, has been conducted in the last few years to develop a visual cortical neuroprosthesis based on the Utah Electrode Array [Project CORTIVIS (2006)]. A prototype of the proposed system has been developed. More detailed technical information can be found in Chap. 6 and in [Piedade *et al.* (2005)].

Table 1.1 summarizes the main pros and cons of the different approaches

described in this chapter to develop visual neuroprostheses. In the next chapter we will present the main features of the human visual system which are important to introduce, in Chap. 3 and in Chap. 4, the signal processing tools and the retina models adopted to design bioelectronic vision systems.

## Exercises

- 1.1. *Identify the main components of the human visual system represented in Fig. 1.3 and enumerate their main functions and characteristics.*
- 1.2. *Based on the 2002 world population of 6 thousand million, predict the relative percentages of people who were visually impaired and who were blind at that time.*
- 1.3. *Enumerate the main classes of visual neuroprostheses referred to in the text.*
- 1.4. *By taking as a reference the main classes of visual neuroprostheses presented in the text and enumerated in the previous section,*
  - 1.4.1 *associate the different classes of neuroprostheses with the types of vision impairments they would be used to treat;*
  - 1.4.2 *identify to which class of visual neuroprostheses the "Bionic Eye" and the ASR microchip belong;*
  - 1.4.3 *identify the class of visual neuroprosthesis targeted in the CORTIVIS project.*
- 1.5. *List the main components of a bioelectronic vision system and the main electronic components associated with visual neuroprostheses. Comment on the main challenges for the implementation of these prostheses.*
- 1.6. *Elaborate on the advantages and disadvantages of the different approaches to develop visual neuroprostheses, starting with the information provided in Table 1.1.*
- 1.7. *Identify the main advantages of the penetrating microelectrodes, such as the Utah Microelectrode Array, compared to the surface electrodes used, for example, by Dobbelle.*
- 1.8. *Enumerate the two main approaches used to develop retina models, referring to their main differences.*
- 1.9. *Choose three research groups on the world map shown in Fig. 1.2,*

*from different continents, participating in this kind of research. Consult the internet and describe the research they have performed and their achievements in the field of visual neuroprosthesis development.*

Table 1.1 Main pros and cons of visual prostheses approaches.

Advantages	Disadvantages
<b>Visual Cortex</b>	
<p>Only approach for non-functional retinas and/or optic nerves</p> <p>Implant site robust and protected by skull</p> <p>Easy surgical access</p> <p>High density electrode implantation</p> <p>Phosphene thresholds are low (1-10 <math>\mu\text{A}</math>)</p>	<p>Stimulation far from photoreceptors</p> <p>Possibly poor visuotopic organization</p> <p>Multiple feature representations in V1 (color, lines, motion, ocular dominance)</p> <p>Societal phobias about "brain implant"</p> <p>Consequences of surgical complications</p>
<b>Epiretinal</b>	
<p>Stimulating close to photoreceptors: uses native processing in thalamus and cortex</p> <p>Fewer surgical complications than cortical implants</p> <p>Saccadic eye motions cause sheer loads on implanted arrays</p> <p>Difficult to adhere electrode array to retina</p>	<p>Requires functional optic nerve pathway</p> <p>May stimulate optic nerve fibers – greatly complicates visuotopic organization</p>
<b>Subretinal</b>	
<p>Stimulating closest to photoreceptors – uses retinal, thalamic and cortical processing</p> <p>If bipolar cells can be directly stimulated, retinotopic organization should be preserved</p> <p>Fewer surgical complications than cortical implants</p>	<p>Requires functional retina and optic nerve pathway</p> <p>Blockage of nutrients from choroid by the implant</p> <p>Very complex surgical access</p> <p>Cannot stimulate cells passively with microimplants (requires external power)</p>
<b>Optic Nerve</b>	
<p>Fewer surgical complications than cortical implants</p>	<p>Requires functional optic nerve pathway</p> <p>Visuotopic organization requires placing electrodes at many closely spaced regions of the optic nerve</p> <p>Complex electrode array to provide patterned vision</p> <p>Very difficult surgical access</p>