

Artificial epi-Retinal Prosthesis (AeRP)

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There are several research projects going on around the world, which are attempting to develop a prosthetic device to restore sight to the blind. This paper describes the efforts of Second Sight of New York, Inc. The device being developed is called an Artificial epi-Retinal Prosthesis (AeRP), which is basically a small optical computer that fits into the intraocular space of the eye. The AeRP is designed to draw light into the device by specially designed fibre optics. The light is 'digitized' by the fibre optic system and then directed to individual photodiode cells making up concentric cylinders thus providing several hundred photodiode cells in the device. The produced electrical stimulation from each cell is then delivered to the retinal ganglion cells by a specially designed delivery system utilizing electrically conducting polymer strands (ECP), which sit on an 'umbrella' at the back of the device. The retinal ganglion cells receive the electrical stimulation, which would then be transmitted through the visual system of the brain. There are several innovations in this approach as compared to the other projects. They include, first the design, which will allow for a high number of PC to produce electrical stimulation that will stimulate multiple RGC per PC; the use of the ECP strands has not been used in such an approach before this. Tests have revealed that nerve cells have a good affinity for the material of the ECP. The use of the ECP as well as the fact that the AeRP is completely photovoltaic, with no external power sources, implies that there will not be high heat build-up in the back of the eye, which might damage RGC. A smaller version of the AeRP called the Mini epi-Retinal Prosthesis (MeRP) is the subject of a complimentary paper. It is being built now and will be tested in cell culture studies to determine the efficacy of the design and materials. No actual implants have been performed yet.

1. Introduction

In this paper is presented an artificial eye implant which could help to restore some semblance of vision to people who suffer blindness from retinal diseases such as macular degeneration (AMD), retinitis pigmentosa (RP), as well as some genetic diseases that can cause blindness. This implant is called an Artificial epi-Retinal

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†Dedicated to restoring sight to the blind!

Prosthesis (AeRP). It is actually an artificial photoreceptor-ganglion stimulator (APRGS).

The human retina is an extremely delicate and thin structure (~0.4mm) composed of several layers of: photoreceptors and different types of nerve cells such as amacrine cells, horizontal cells and ganglion cells. When light impinges upon the retina, the photoreceptors hyperpolarize the cell, in effect stopping the flow of neurotransmitters. When a cell depolarizes it initiates the release of neurotransmitters to stimulate the nerve cells to send a signal back to the areas of the brain responsible for vision. These areas are the lateral geniculate nucleus (LGN) and the occipital lobe.

Diseases such as age related macular degeneration (AMD) cause loss of vision with age. Retinitis pigmentosa also causes blindness. Several genetic conditions also lead to blindness, and the AeRP may help in these conditions as well.

Research has shown that in patients blinded by diseases, such as retinitis pigmentosa, between 30% and 80% of the retinal ganglion cells, and cells of the inner nuclear layer, respectively, are still viable [1]. What this means is that if the nerves in the retina are useful, then blindness may be repaired to some degree. If only the photoreceptors are damaged but the nerves are not affected, then they could possibly be stimulated in other manners in order to allow the resumption of the signalling to the visual pathway in the brain and therefore the resumption of some semblance of sight.

What is proposed is to duplicate as much as possible, the natural process of vision. But how can this be done if the light cannot trigger the photo-electro-chemical reaction? Logically, then, we must try and replace the damaged link in this 'circuit'. The most logical 'replacement' in this circuit of vision is to replace the photoreceptor-ganglion connection. If the photoreceptor process can be duplicated and good portions of the nerves are viable then sight may be restored to some degree because the process of getting a nerve signal to the LGN and the occipital lobe is restored. It is in the brain where vision actually takes place. When the retina receives different wavelengths of light from the outside world, then corresponding electrical currents are produced and sent to the visual system. A process of hyperpolarization-depolarization sets up the 'circuit'. The LGN and occipital lobe receive these different currents and then reassemble their signal into a 'picture' of the object, which has reflected the light to the eye.

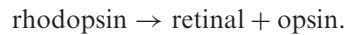
Contrast is an important mechanism in the process of 'seeing' [2]. Different wavelengths will cause a ganglion cell to fire if it falls on its 'on-centre receptive field' or it will not fire if it falls on its 'off-centre receptive field' [3]; or it may be a combination of both [2], thus initiating contrast.

When retinal disease interferes with the process of producing corresponding electrical currents per colour then this is the process which must be replaced. The photoelectric effect is a process whereby light strikes a metal surface and releases an electron, producing an electric current is therefore possible. By a process of electrical induction, electrical currents corresponding to particular wavelengths will stimulate the retinal ganglion cells, which are unmyelinated until they reach the optic disc [4].

1.1 *The human retina*

The human retina is one of the most fascinating structures of the body, especially since it is a readily accessible part of the brain. The retina is extremely thin, about 0.4mm, and yet it is composed of several layers. Among these layers we have: the pigment epithelium layer, the layer in close contact to the rods and cones (the photoreceptors); the outer nuclear layer, the layer containing the rods and cones; the outer plexiform layer, the region of connection between the rods and cones and the region containing the retinal neurons (the inner nuclear layer): the bipolar cells, horizontal cells and amacrine cells; the inner plexiform layer, again a connecting layer between the inner nuclear layer and the ganglion cell layer [5]. There is also the outer limiting membrane, a sort of covering [6]. See figure 1.

Now, when light enters the retina it first bypasses the ganglion cell layer, which is closest to the lens and penetrates the entire retina until it strikes the photoreceptors where the light triggers the photo-electro-chemical reaction. The rods are structures, which are very sensitive to low-level light and allow for vision at night. The cones are colour sensitive in brighter light. The rods use a substance called rhodopsin which, when light is absorbed, cause a chemical reaction such as:



Opsin is a protein and retinal is a substance formed by oxidation of vitamin A. The photodissociation of rhodopsin is what triggers the beginning of sight.

The cones contain a pigmented substance, which is more colour specific. Specifically, the cones absorb red, green and blue wavelengths. They are basically light filters.

Once the process begins, the photo-electro-chemical process then triggers the neurons of the retina. The bipolar cells, connected to the cones, form direct contact with the ganglion cells, which ultimately form the optic nerve. The bipolar cells from the rods must first stimulate the amacrine cells. The amacrine and horizontal cells are the 'messenger-cells' from the light receiving photoreceptors to the ganglion cells. 'Amacrine (axon-less) cells, together with another type of inter-neuron, the horizontal cells, serve to modulate the visual information as it is transmitted from the receptor cells to the ganglion cells' [5].

Finally, the photo-electro-chemical process reaches the ganglion cells, which are unmyelinated until they reach the optic disc. There are 100 million photoreceptors to one-million ganglion cells. The ganglion cells come in several varieties, which stimulate different parts of the LGN along the visual pathway. Ganglion cells come in 'midget' ganglion cells which are small, densely packed dendrite cells which lead into the parvocellular pathway of the lateral geniculate nucleus (LGN). They vary in size from 1.0 to 5.6mm in diameter; that is measuring the entire cell: body plus dendrites.

Ganglion cells also come in 'parasol' ganglion cells, which range in size from about 1.0 to 5.8mm in diameter. Again, this measurement encompasses the cell body plus dendrites. In the parasol cells, the dendrites are more sparsely concentrated.

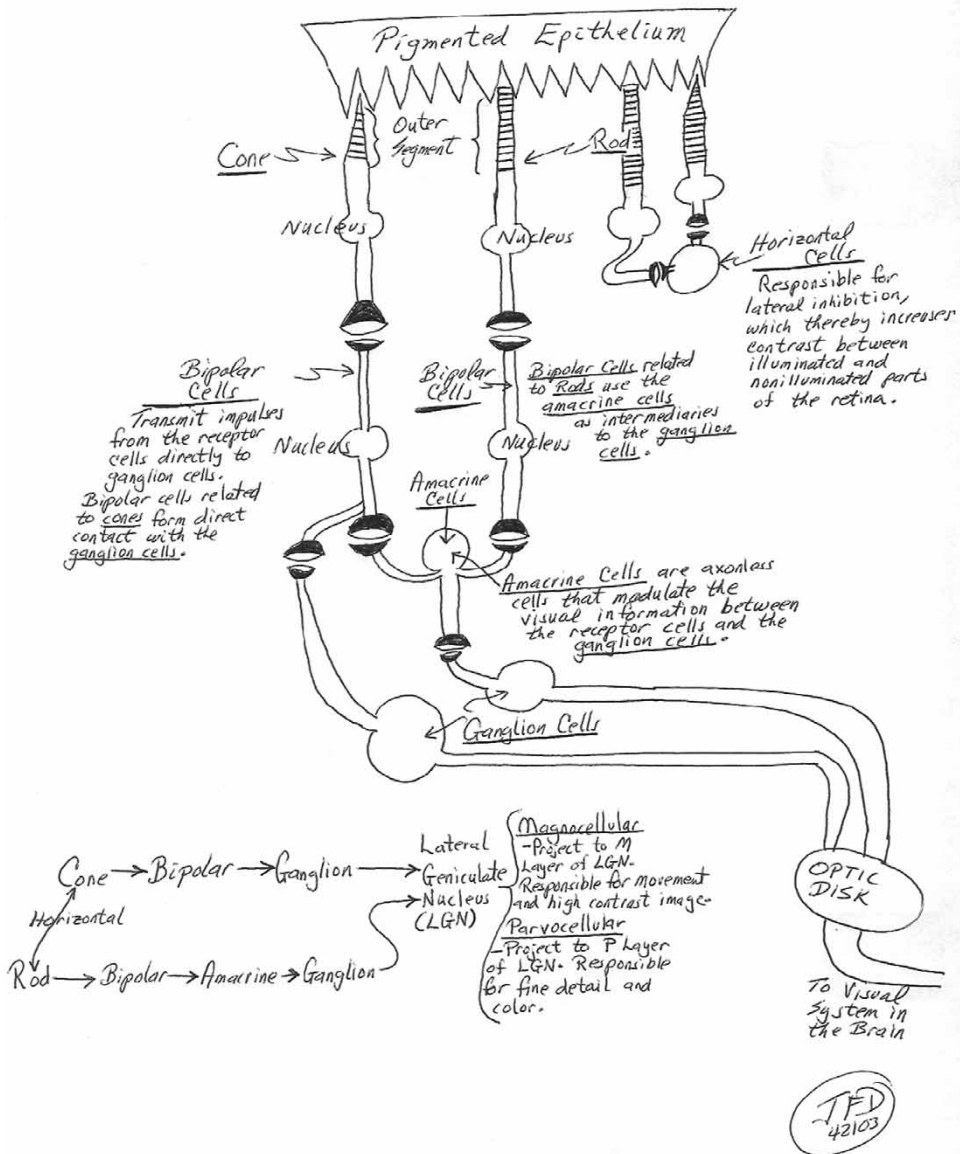


Figure 1. The human retina.

The parasol cells terminate in the magnocellular layer of the LGN. It seems that the dendrite field spreads out for all cell types the further away from the fovea you get.

Thus, the retina helps to deliver visual information from the outside world to the brain where it is reassembled into vision. For a general description of the visual system see Heimer [5]; and, for a more detailed description of vision see the text by Wandell [7].

1.2 Retinal pathologies

It is not specifically the intention of this paper to discuss, in detail, the diseases of the human retina. For that, there are many articles and texts, such as Garner [8] and Sideman [9]. However, we are concerned with diseases such as retinopathy or maculopathy.

For instance, when a retinal ischemia, that is, a blockage of the blood vessels to the retina causes a decreased blood flow to the retina, the result is basically a proliferative retinopathy. The ischemia is caused by the closure of the retinal capillaries, which become diseased ultimately by the death of the endothelial cells. As a result of this ischemia a sort of ‘anemia’ results, and to compensate, the eye produces new vascular connections. This is a process called neovascularization. This process extends from the capillary bed within the retina to the inner limiting membrane, which is eventually penetrated and the new vessels grow along the anterior surface of the retina. As these vessels adhere to the retina, the vitreous body may detach. The pressure of the detachment causes the process of retinal detachment and can cause haemorrhage in the vitreous body.

A treatment of laser surgery is used to destroy the ischemia and halt the neovascularization and therefore the haemorrhaging. Unfortunately, this treatment, together with the problem it seeks to alleviate, leave the retina permanently damaged. As a result, a loss of sight ensues.

Since the retina is damaged the incoming light cannot stimulate the retina and trigger the visual pathway. The implantation of a small device to mimic the damaged portions of the retina may take advantage of the photoelectric effect and restore some sight to the patient.

2. Building a first generation prototype (FGP) for laboratory tests

How can the photoelectric effect [10, 11]—an effect very similar in nature to the photoreceptors of the eye—fit into the concept of a device which can stimulate the retina? Taking full advantage of the photoelectric production of electrons, electricity can be produced to directly stimulate the visual system.

If a device is built small enough to be implanted in the eye, then that device must be able to convert light which passes through the lens of the eye into useful stimulation for the retina. To this end the photoelectric effect is fully utilized. In order to test an initial design for the AeRP in a laboratory setting, we constructed the following FGP.

The photodiodes are placed behind a coloured filter, in order to mimic the natural cones of the retina. Since the natural photoreceptors are ‘colour coded’ [12] to receive specific wavelengths, the artificial devices should mimic them as closely as possible. Of course, filterless optics allow for a greater amount of light absorption by the photodiode cells. By this means the device will produce a current, based on a specific colour, which will be transduced through the optic nerve.

This artificial device seeks to allow the visual system to ‘see’ at least contrast. A study of the reception of brightness in the primary visual cortex [2] indicates what

happens at the neural level when light of various brightness is received by the visual system. This is a process termed brightness induction. This ultimately leads to the concept that contrast is an important factor in vision. 'By contrast, changes in luminance ratios...are indicative of reflectance changes. These are, of course, the conditions that lead to brightness induction' [13]. Thus, it seems logical to build a device, which imitates, as closely as possible, the natural colour-coded photoreceptor stimulation process.

Contrast is actually a condition of the brightness of one colour as opposed to another colour. The traditional view of vision was one in which, when one photoreceptor cell sensitive to a particular wavelength was stimulated (its 'on-centre receptive field' was stimulated) it was inhibited by a different wavelength. Thus a ganglion cell would fire under red light but not under green light. This is termed spectral opponency. However, Dacey *et al.* [14] point to a different or alternate theory.

In their work, they indicate that as a cell is stimulated by one wavelength, it is not necessarily inhibited by another wavelength. The region of the retina, over which light of a stimulating wavelength falls, is called the cell's receptive field centre and is smaller than the region over which an inhibitory wavelength falls, which is called the surround. The surrounds may not be entirely sensitive to the inhibitory wavelengths, but rather is mixed with both wavelengths. Thus, the ganglion cell is stimulated by say, a red light while the surround may not necessarily be inhibited by a green light but is rather a mixture of red and green [15].

This could bring about a sense of contrast in the visual pathway.

As Rossi *et al.* [2] point out: two key elements in vision are form and the colour and brightness of the form. Any artificial device must be able, to some degree, to perceive these two elements. The research performed by Rossi *et al.* [2] indicates that neurons in the primary visual cortex are able to respond to perceived brightness. This means, basically, that vision begins even before the signals reach the higher cortical areas associated with vision. The neurons studied were also responsive to stimuli from orientation and spatial frequency. The cells seemed to process information from several, seemingly different, stimuli.

This is a very important finding because it allows any artificial device to be rather simple because the brain performs the bulk of the work. Once the retina is stimulated by electrical signals, which correspond, to specific wavelengths and, at least theoretically, contrast signals are sent to the LGN and then to the occipital lobe, then vision should be restored to some degree.

Other research performed by Bradley *et al.* [16] has found neurons, which seem to be involved in directed locomotion. They are part of the visual system. If these neurons can have any communication with the cells studied for brightness by Rossi *et al.* [2], then vision may be 're-routable'. That is, if an artificial device can stimulate the retina with proper current so that the signal does in fact pass through the optic nerve and into the visual pathway, then it may be possible that both types of neurons—those responsible for contrast and those responsible for direction of self-motion—may 'assist' each other to bring about a new pathway for vision to reach the higher cortical areas.

Thus the brain performs the bulk of vision whereas the eye is more of a filtering system, allowing selective stimuli to reach the visual system. Once this ‘filtering’ takes place in the retina, and the corresponding currents reach the proper brain locations, a ‘picture’ of the outside world is formed.

Work being done at the University of Utah by Norman and colleagues, has shown that the neural plasticity (adaptation) of the visual system ‘should allow ever-improving correlation between the physical world and evoked phosphenes’ [17]. The human visual system is expertly designed to adapt to new and varied incoming information. A retinal prosthesis that can deliver ‘adequate’ information to the visual system should be sufficient to allow the brain to adapt well enough so that the person can begin to ‘see’. Now, in order to build the FGP of the AeRP, we used the following basic design for the laboratory tests.

2.1 First generation prototypes and tests

The design of the AeRP is based upon several tests performed on a first generation prototype (FGP) (see figure 2) built between 1995 and 1996 in the authors’ former laboratory at Columbia University.

A retinal prosthesis that can deliver ‘adequate’ information to the visual system should be sufficient to allow the brain to adapt well enough so that the person can begin to ‘see.’ Now, in order to build the FGP of the AeRP, we used the following basic design for the laboratory tests.

This FGP–AeRP was basically a reduced efficiency device (RED), which was designed to produce picoamps current. A photodiode under direct light can produce up to milliamp currents and could therefore damage retinal ganglion cells. The design called for the efficiency of the photodiode to be reduced. This was accomplished using an infrared (IR) coupled system. The photodiode produced power to stimulate the IR emitter, which was attached to an IR receiver and produced current in the picoamps range.

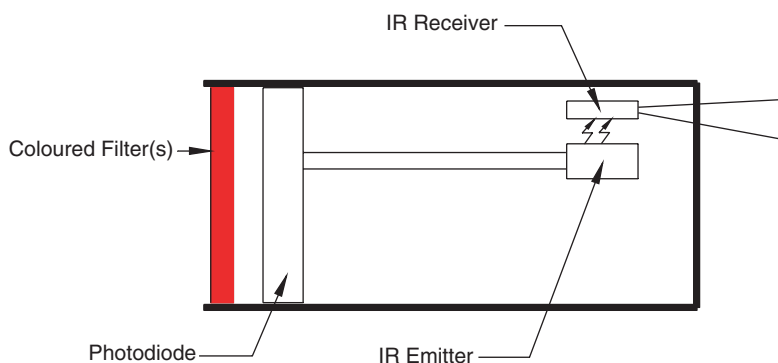


Figure 2. Basic design of the first generation prototype of the AeRP. (The colour version of this figure is included in the online version of the journal.)

Four such devices (modules) were built: one without filters and one each with a red, green and blue filter to simulate the colour coding of the natural photoreceptors of the human eye. The filters were basic 'paper-thin' colour filters.

The photodiodes used were obtained from Hamamatsu Corporation. They were photodiodes that peaked in the red wavelength of 640 nm and had a spectral response range of 300 to 680 nm. They were item numbers G1115. Their photosensitivity at the peak wavelength is 0.3 A W^{-1} , without filters.

The IR emitter/receiver set was obtained from an 'off-the-shelf' Radio Shack unit (item number 276-142).

Under direct light, the photodiode produced about 1.25 V and the IR emitter was pumped with 1.07 V. Thus, the photodiode was sufficient to pump the IR emitter. The IR receiver picked-up the IR signal which was then registered on an ammeter.

2.2 AeRP FGP tests

Here is detailed a design, based upon patent number 5,836,996 [18]. This design, or first generation prototype (FGP), was based on light reception via a photodiode system as opposed to a fibre optic system. Basically, we built several FGP-prototypes based upon this design. All these tests took place in a physics laboratory setting.

The basic concept of this early design consisted of a first photodiode, which received light reflected from an object being observed. The light triggered the photodiode to produce up to 1.25 V and milliamp (mA) current. This voltage was used to light up a small light emitting diode (LED) in the infrared (IR) range. This LED would then stimulate an IR receiver that was sensitive to IR radiation. This second photodiode would produce a lower voltage and current than the first photodiode. The current range of the second photodiode was on the order of picoamps (pA). See Patent Number 5,836,996 [18] for the basic design of this type. In these physics laboratory tests, the 'retina' was a common ammeter. Several FGP-prototypes based upon this design were built.

2.2.1 Test set one. The following three, single celled, prototypes were built during the Spring and Summer of 1996. By 'single-celled' we mean a device consisting of one first electrical producing device such as a photodiode, one LED, in the IR range, one second IR receiver and one set of wire leads to deliver the current.

Summer to the End of 1996: During the Summer to the end of 1996, four 'modules' (i.e. the FGP of the AeRP) were built based upon the design described above. Again, they were 'single celled' devices.

Current readings were made using a CENCO (30736) current meter (with a 10 000 times amplifier) that was powered by a Universal Power Supply (Science Kit, Inc.). The meter contained an amplifier, which amplified pA current to 10^{-8} and 10^{-9} A, as read on the meter, depending on the light reception. This system was designed to study the photoelectric effect (see figure 3 and tables 1 to 3). Experiments (23 September 1996) on FGP prototypes were performed using a small ($\sim 30 \text{ W}$) light source.

2.2.2 Test set two. On 8 October 1996, the following experiment in contrast was performed. It tested whether or not the modules; clear and colour-coded;

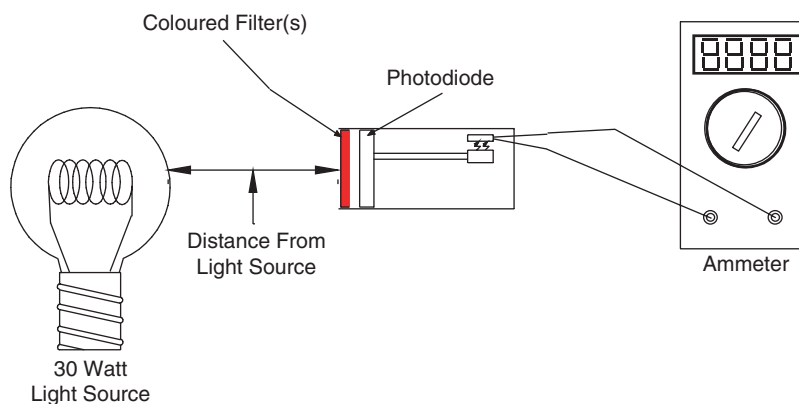


Figure 3. Setup for tables 1, 2 and 3. (The colour version of this figure is included in the online version of the journal.)

Table 1. Current (pA) produced by modules about 3–4 inch from light.

Red module	Blue module	Green module	Clear module ^a
5.00	1.25	2.25	2.00

^a Clear module is one without a filter.

Note: It would be expected that the clear module, which contained no filter should have produced a higher current output than the red, green or blue filtered modules. However, the photodiodes used, peaked in the red wavelength, therefore the red module would have produced a higher current. It is not certain why the green module produced higher current than the clear module.

Table 2. Current (pA) produced by modules about 6 inch from light.

Red module	Blue module	Green module	Clear module ^a
1.00–1.50	0.00	0.80	6.50

^a Clear module is one without a filter.

Note: It seems unusual that further from the light source, the clear module produced more than three times the current than it did at closer range. It is assumed that the ambient light in the lab added significantly to the stimulation. The filtered modules produced a lower current further from the light source.

Table 3. Current (pA) produced by modules using magnifying lens—about 6 inch from light.

Red module	Blue module	Green module	Clear module ^a
2.50	0.70	2.00	7.70

^a Clear module is one without a filter.

Note: The magnifying lens produced a greater reception of light upon the modules, especially in the clear module. Although the photodiodes peaked in the red wavelength, the magnified light reception was higher than in table 2.

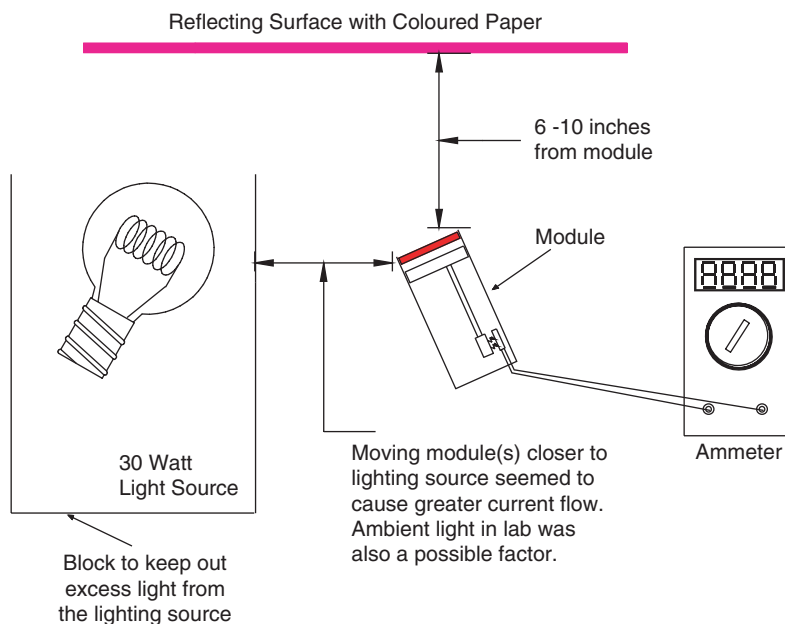


Figure 4. This setup shows how the modules registered corresponding currents as each measured reflected light from coloured surfaces lying upon the reflecting surface. The three coloured surfaces were red, green and blue. Light from a 30 W bulb was shown on the coloured surfaces and measurements were taken from each module (see table 4). (The colour version of this figure is included in the online version of the journal.)

would distinguish between colours and produce corresponding currents, indicating contrast reception.

This experiment tested how well the modules ‘see’ colour variation. Sheets of colour paper were glued to a white background and the modules were held in front of them as a 30 W light bulb was used to illuminate the paper. Modules were varied in distance from the coloured paper from 6 to 10 inch. As the modules were held closer to the reflecting surface, the current produced, increased (see figure 4).

The clear module was one that did not contain a filter. In table 4, the readings were taken as the modules were moved from the coloured paper to the white paper thus providing a sense of contrast, in trials C and D. This test seems to indicate that the modules were able to ‘see’ the shape via the contrast of the coloured paper observed.

Now, as each module was held 12 inch from the direct light source, we get the following readings of current (I):

- Red module: $I = 0.2 \text{ pA}$,
- Green module: $I = 0.05 \text{ pA}$,
- Blue module: $I = 0.075 \text{ pA}$,
- Clear module: $I = 0.60 \text{ pA}$.

Table 4. Current produced per module in a test to determine contrast (modules were moved 6–10 inch from coloured paper.)

Test number	Clear module (pA)	Red module (pA)	Green module (pA)	Blue module (pA)
A: White paper (modules moved perpendicular to coloured paper)				
	1.00	0.100–0.200	0.075	0.100
B: Coloured paper: (modules moved perpendicular to coloured paper)				
Red:	0.25–0.50	0.150	0.040–0.050	0.050
Green:	0.75–1.00	0.150	0.075	0.075–0.10
Blue:	0.40–0.50	0.100–0.200	0.075	0.050–0.20
C: Coloured paper against white paper: (modules moved parallel (sideways) across coloured paper)				
Red:	0.60	0.100–0.150	0.050	0.090
Green:	0.50–0.75	0.125	0.050	0.060
Blue:	0.40	0.300	0.300	0.200
D: Borders of coloured paper against white paper:				
Red:	0.40–0.50	0.100–0.200	0.000–0.125	0.000–0.15
Green:	0.25	0.100–0.200	0.000–0.150	0.000–0.10
Blue:	0.25–0.40	3.00–3.50	0.150–0.400	0.200–0.40

(Notice how the current increases as the module is moved across the borders from the coloured paper to the white paper. Obviously, the white paper reflects more light into the module.)

The readings on the previous data table (table 4) imply contrast; the measurements of the colour paper, using the different modules (both clear and colour coded) fall in the range of the borders.

The tests performed on these FGP modules were of a similar nature to the tests conducted in 1975 by Judd and Wysecki [19]. These tests were designed to test colour matching, a basic ability of the retina to discriminate colours and therefore how the cones operate.

2.3 Discussion and conclusion

These tests led to the final design incorporating a fibre optic system, described in patent number 5,865,839 (issue date of 2 February 1999 [20]). This system will be described in a following paper.

The modules used in these tests would be too large to be of any real use in an eye, the design has to be refined. This information has led to the final design. The designs described have led to a more sophisticated engineering system comprising a specially designed system of concentric cylinders of photodiode sheets interlinked with a specially designed fibre optic system. Each module described herein would have to be shrunk to the size of several millimetres and multiplied by the hundreds to be of real use.

3. Design of the Artificial epi-Retinal Prosthesis (AeRP)

In order to stimulate the retina, the ganglion cells must receive an electrical signal. The device should be completely implantable in the human eye. Therefore it must be small and rather simple in structure. Assuming the vitreous body is spherical, and the distance between the posterior of the lens and the anterior of the retina, is about 14.6 mm gives a volume of:

$$V(\text{vitreous body}) = (4/3)\pi r^3,$$

where r is the radius of the vitreous body: $r = d/2 = 7.3$ mm. Then the vitreous body has an approximate volume of 1629.5 mm^3 . This means that for an artificial device to be fully implantable in the eye, it must be no longer than 14.6 mm (unless the natural lens is removed to give more space) and less than about 10 mm in diameter in order to fit directly behind the lens. Bulk wise, it must be very light and have a volume much less than 1629.5 mm^3 . In other words, it must be able to fit into the space of the vitreous body. To ensure safe surgical implanting techniques, the device should be about 7 to 8 mm in diameter. It must also be able to be secured, to the inside of the eye; the desired method is at the retina, surgical tacks which would hold the device steady as possible and also allow the stimulating leads to touch the retina in a safe manner, while at the lens, the front of the device will be hooked into the sulcus of the lens. It must have the primary light receiving device placed in front of the lens and the electrical charge device to stimulate the retina, facing the retina. After implantation, a fluid of non-ionic chemistry will be placed in the eye, since a complete vitrectomy was initially performed. This will help buoy-up the device and, at the same time press it closer to the retina.

To avoid toxicity of the eye, the device must be 'housed' in a material, which is completely harmless to the eye. A possible solution is to use the same material that is used for a cataract replacement lens.

The device would have filters, in front of the photodiodes to select proper wavelength reception; or, there may be no filter to allow the maximum amount of light to the photodiodes. A photodiode will receive light of all wavelengths within a specified range of design; for our purposes it must be in the visible spectrum; and peak at a particular wavelength, say about 670 nm for red; but as close to the peak reception of the human retina. That is, about 555 nm. A simpler design could use filterless diodes.

Thus, what is needed is a device, which is sensitive to red, green, and blue the primary colours of the human visual system. The filter is placed in front of the photodiodes, in a fibre optic system, which is directed to an individual photodiode cell, and, then produces a corresponding current per colour (wavelength). We will call each corresponding current per colour: red current, green current and/or blue current. The current will be relayed to the retina by electrically conducting polymers.

A device such as this would be internal, lightweight and safe. It would be entirely photovoltaic. It would therefore avoid any excess heat buildup in the back of the eye. The front of the device would include a lens system and a fibre optic strand system that is colour-coded. The fibre optic strands would comprise a fibre optic

plate on the side facing the lens and it would have fibre optic strands in bunches directed to the individual photodiode cells. Then each cell would produce a corresponding electrical stimulation. That is, as the AeRP views an object, the image is transferred through the lens system and strikes the fibre optic plate which is used to direct parts of the image to individual photodiode cells to produce corresponding electrical stimulation. This stimulation is sent to the retina via leads of electrically conducting polymer (ECP) strands, that are held in place on an 'umbrella' shaped polymer sheet that rests up against the retina. The device would be attached to the front of the eye in a manner similar to a cataract replacement lens and it would be surgically tacked to the back of the eye with the 'lead umbrella' opened up to lie against the retina in a gentle fashion. Lying upon the lead umbrella are the ECP strands that are biphasic leads from each of the photodiode cells.

3.1 AeRP design

In this section is described the second generation prototype (SGP) of the Artificial epi-Retinal Prosthesis (AeRP) that was suggested in the previous section. Here we include computer aided design (CAD) drawings.

The design of the SGP is described in detail in United States patent number 5,865,839 (issue date 2 February 1999 [20]). In this section, we show several CAD drawings of the AeRP.

The SGP of the AeRP allows images to be mapped upon the fibre optic plate (FOP) in a manner similar to the way Nature maps images upon the retina. As each section of the image is mapped onto a particular section of the FOP, the illumination is transmitted through its own individual fibre optic strand (FOS) to stimulate its individual photodiode cell. The produced current per photodiode cell is transmitted to the retinal ganglion cells (RGC) via biofriendly, ECP, which lie upon the lead umbrella.

The photodiodes comprise two concentric cylinders in order to take advantage of the limited space in the eye. Each photodiode cell is one-square millimetre, instead of micro-photodiode cells, as is used in other artificial retina projects. The reason for this is that the bigger the cell collecting area, the more light it can collect, especially under dim light conditions. Microcells, while possibly using microlenses to increase light gathering ability, since they are less efficient at collecting light, also require more expensive manufacturing techniques. Also, very small pixel size requires more expensive resolution techniques. This would increase costs to the patients. Thus, it seems logical to use larger cells.

The photodiode cylinders can be made of standard silicon or they can be manufactured by advanced techniques using a polymer substrate to hold the cells and form the photodiode cylinders.

The umbrella will take the basic shape of the retina upon implantation, due to inertia. After implantation an artificial vitreous solution will be replaced and help to force the umbrella against the retina. The fluid also gives a buoyant effect to the AeRP.

3.1.1 CAD sketches (figures 5–8) detailing the structure of the AeRP. Figure 5 shows the lens system. In order to collimate the light coming through the eye and entering the AeRP a lens is necessary. A cataract replacement lens will be placed in front of the fibre optic plate.

Figure 6 shows the fibre optic plate system. Placed immediately behind the lens system is a fibre optic plate (FOP). A FOP consists of millions of individual fibre optic strands (FOS) with diameters measured in microns. This particular FOP will be a conventional FOP facing the lens but groups of FOS coming out the back end of the FOP will be directed to individual cells of the photodiode cylinders. Each group of FOS will be held in place against an individual photodiode cell by a plastic holder, which contains holes through which the FOS will be directed.

The FOS will transmit a particular part of the image being observed to a particular cell and produce a corresponding electrical current. When all groups of FOS transmit their individual images to their respective photodiode cells and corresponding current is produced, the retina will be stimulated with current which represents the image coming in through the lens system.

Figure 7 shows the photodiode system. The photodiode system (PS) will be the mechanism to produce corresponding electrical stimulation produced by the reception of light from the object being observed and directed to it via the fibre optic system. To take advantage of the small space in the vitreous cavity, the PS will be built in ‘concentric’ cylinders (figure 8). A large photodiode cylinder (PC) will contain strips of 15 photodiode cells and there will be about 24 strips built in cylindrical shape. A small PC will consist of about 6 strips of 15 photodiode cells. The FOS will be placed between the two PC and FOS will be directed to each individual photodiode cell to stimulate them with the particular part of the image they receive. This gives 450 stimulating cells, which will have leads to carry the stimulating current to the retina.

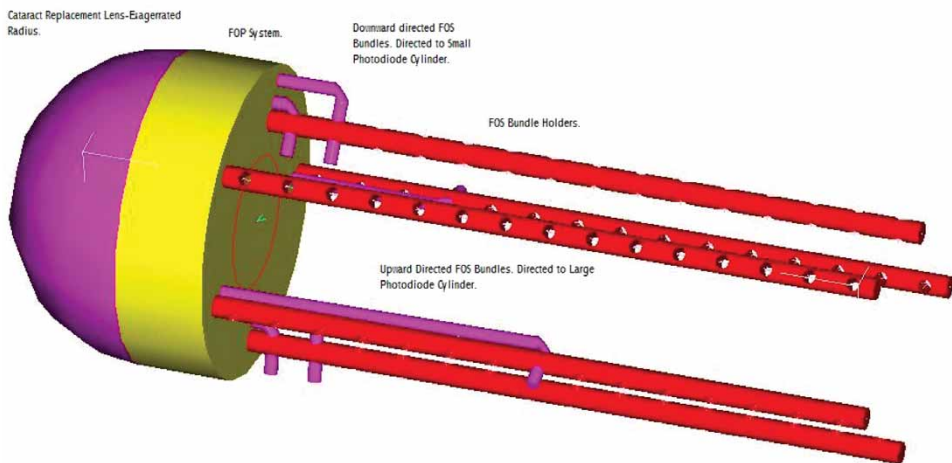


Figure 5. The lens system. (The colour version of this figure is included in the online version of the journal.)

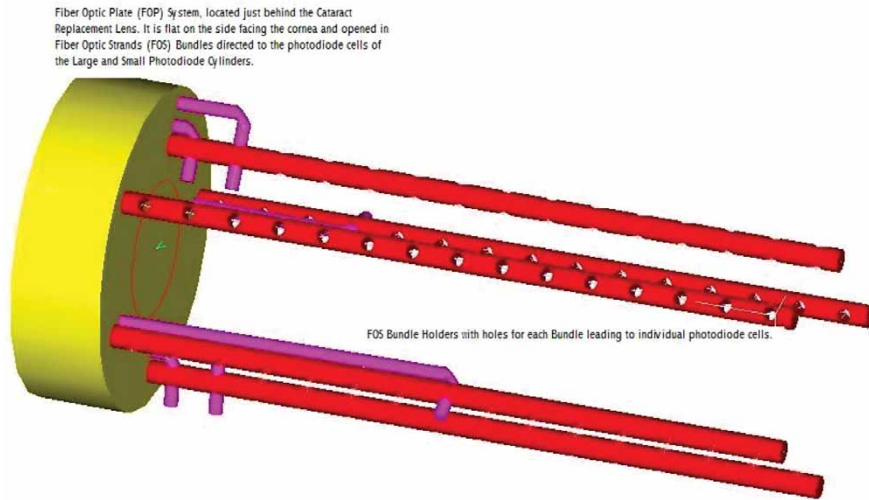


Figure 6. The fibre optic plate system. (The colour version of this figure is included in the online version of the journal.)

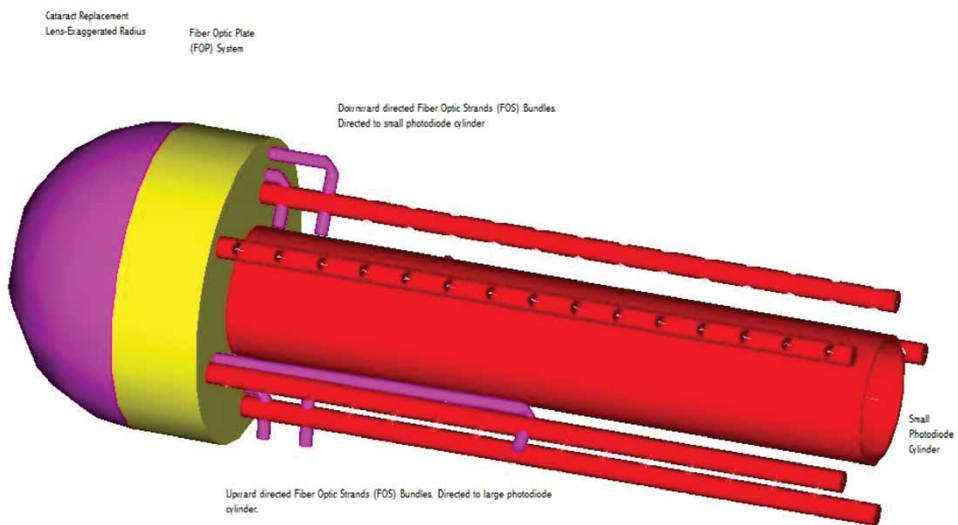


Figure 7. The photodiode system. (The colour version of this figure is included in the online version of the journal.)

Figure 9 shows the AeRP lead umbrella system. The leads from each cell in the PC will be bipolar (biphasic) and directed to the retina. The leads will lie upon an ‘umbrella’ structure composed of a biofriendly non-electrically conducting polymer, which will open up against the retina. This will allow the leads, which will be separated by about 10–20 μm distance, to supply descent resolution. The leads will lie up against the retina or the inner limiting membrane (ILM). The ganglion

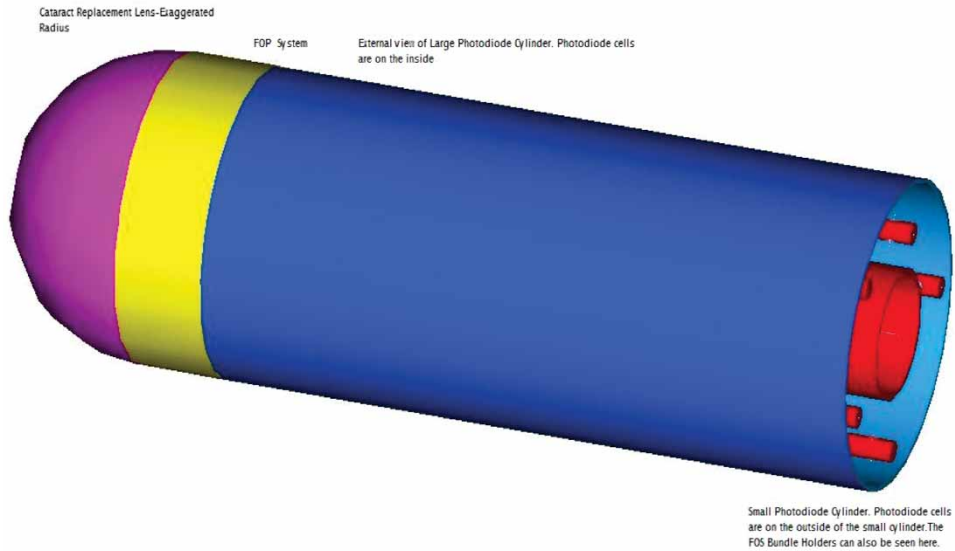


Figure 8. AeRP showing large photodiode cylinder and small photodiode cylinder, lens and FOP. (The colour version of this figure included in the online version of the journal.)

cells are located approximately $50\mu\text{m}$ below the ILM and the ILM is not very resistive. Opinions vary on whether or not it is logical to remove the ILM.

4. Basic calculations on the photometry of the AeRP

For a very detailed discussion of the topics mentioned below, see work by Doorish [25].

4.1 Fibre optic plate (FOP) system leading to the photodiode cells

Now, from the previous CAD drawings and sketches, some basic calculations for fibre optics and photodiode cells can be obtained. In the following calculations the total current output of all the cells of the AeRP under light are considered. Of course, this is an ideal situation, but useful for an understanding of how the AeRP could help to stimulate retinal ganglion cells of the retina.

If the FOP of the AeRP is structured in such a manner as to bring light intensity to each of the photodiode cells in the device, then it must be composed of separate strands. Thus, the FOP, which is approximately 8 mm in diameter, has a surface area of πr^2 which equals 50.27mm^2 . In the AeRP, the cylinders contain 450 photodiode cells, and the fibre optic strands (FOS) comprising the FOP lead to each photodiode cell. This means that the number of cells per FOS is equal

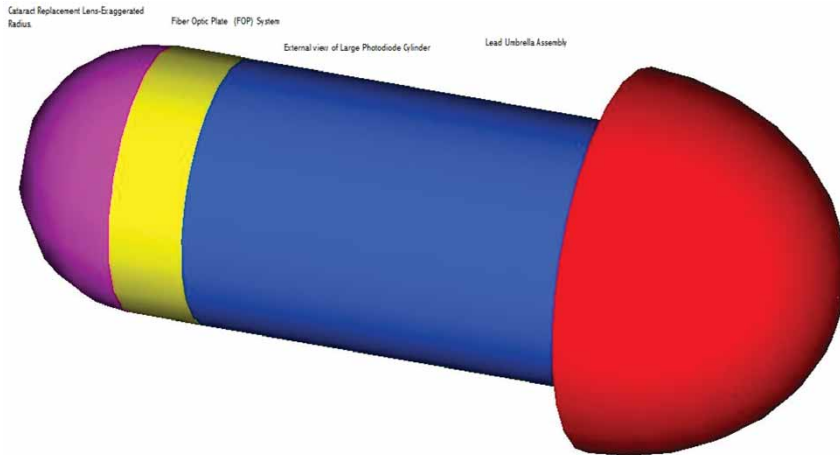


Figure 9. AeRP in whole structure showing lead umbrella system. (The colour version of this figure is included in the online version of the journal.)

to 450 photodiode cells divided by 50 (which is approximately equal to the area of the FOP) which results in 9 cells per FOS.

Thus, each fibre optic strand bundle in the fibre optic plate must feed light to nine photodiode cells (see figure 7).

Thus:

$$\frac{\text{photodiode cells}}{\text{FOS}} = \frac{450 \text{ photodiode cells}}{50 \text{ strands}} = \frac{9 \text{ photodiode cells}}{\text{FOS}}.$$

This means that each bundle of FOS comprising the FOP, must feed light to 9 photodiode cells. There are 50 FOS comprising the face plate of the FOP since they are each one-millimetre in diameter at the face plate and branch off into nine separate strands to feed the nine prescribed photodiode cells. In this way, an image, which is laid upon the FOP, is therefore digitized.

Now, using basic photometric quantities, to first calculate the illuminance onto the FOP from light being reflected off of an object being observed, the light is then transmitted to each photodiode cell.

Assume that the AeRP is outdoors on an average cloudy day with about 5000 lux of light present. A lux is equal to one lumen per square metre of surface. A lumen is equal to 1.464×10^{-3} W at a wavelength of 555 nm. This is where photopic (that is, cone functioning in the retina) and scotopic (that is, where rod functioning in the retina) sensitivities meet. Thus, one watt at 555 nm is equal to 683 lumens. Then, the amount of light incident upon the FOP, in lux, is:

$$I_i = I_o[(R/\Omega)(\pi/4)((T/f\#)^2)], \tag{1}$$

where I_o is the illuminance in lux onto the object being observed, R is the reflectance of the object (between 0 and 1), Ω is the solid angle in steradians, T is

the transmittance of the lens and fibre optic strand (between 0 and 1) and $f\#$ is the f-number of the lens (focal length/diameter) (see [21]).

Now, in general, assume that $R = 0.5$; $T = 0.5$; $f\# = 1.00$; and:

$$\Omega = \text{Area}/r^2 = (\pi r^2)/(ar)^2 = \pi/a^2,$$

where 'a' is merely a number, a multiple, or a fraction of r . Simply by varying the solid angle, Ω , to smaller values we get the following form of equation (1):

$$I_i = I_o[0.0625a^2]. \quad (2)$$

The smaller the solid angle, the more efficiently the AeRP produces current, because more light is directly entering the device. Then, I_i can be calculated for the AeRP.

For example, for a solid angle of $\pi/4$ for $a=2$ and for I_o of 5000 lux, or a bright sunny day, we obtain I_i equal to 1250 lux incident upon the FOP. For a solid angle of $\pi/25$ for $a=5$, I_o of 5000 lux, we get I_i equal to 7812.5 lux. In an office environment which might have about 300 lux and for a solid angle of $\pi/4$, we get I_i equal to 75 lux. And so on.

This, then, is the light reflected onto the FOP from an object being observed with the AeRP. Now, if there are about 50 FOS comprising the FOP, then:

$$\delta = \frac{I_i}{\text{FOS}} = \frac{I_i}{50}.$$

This is the amount of light, which enters each fibre optic strand in order to stimulate the photodiode cells. This is assuming equal light falling on the entire surface of the FOP. This is of course not a realistic or even necessarily useful situation, since light reflected off of an object being observed will fall on the FOP differentially to stimulate the photodiode cells differentially.

Then for δ , considering a sunny day (with 5000 lux), we have 1250 lux/50 FOS equal to 25 lux/FOS, which falls onto each FOS and is directed to its corresponding photodiode cell (pc). If each strand thus feeds light to nine photodiode cells, then we have the illuminance at each cell of:

$$I_{pc} = \delta/9 \text{ photodiode cells},$$

which here would equal (25 lux/FOS)/9 pc, or 2.78 lux/FOS/pc.

According to engineers at PerkinElmer (private correspondence, 13 July 2000) each typical photodiode cell generates about $0.01 \mu\text{A mm}^{-2} \text{lux}^{-1}$. This gives the current output of each photodiode cell (I_{pc}), which in the situation just mentioned would produce about:

$$(I_{pc}) = (I_{pc})(0.01 \mu\text{A mm}^{-2} \text{lux}^{-1}),$$

which here is equal to $0.0278 \mu\text{A}$. The values will change depending upon how much light actually falls onto the FOP of the AeRP, as well as the solid angle considered. In the AeRP with a total of 450 photodiode cells designed into the device, this would produce an average current of $12.51 \mu\text{A}$ for the entire device.

The size of the photodiode cell is important (see [22]).

Direct sunlight usually produces about 100 000 lux or more. This would mean that the ARP would have I_o equal to this value and therefore the total current output ($O_{c_{pc}}$) of the device would be higher.

4.2 Photodiode cylinders

The two concentric photodiode cylinders are cylinders composed of strips of photodiode cells.

Photodiode cells come in different sizes and functions for different purposes. Cells that are large enough to produce sufficient power for received photon energy, which ultimately produce enough current to stimulate the ganglion cells are used. To this end are used not micro-photodiode cells, as is the choice of other artificial retina projects, but rather cells that have a surface area of 1 mm^2 . Such cells are capable of producing proper physiological current depending upon the amount of light absorbed.

The choice of photodiode cells is such that it produces enough current when the proper range of wavelengths of light falls upon it. There are two basic types of cells: a planar diffusion silicon type and a Schottky type.

The planar diffusion cell 'has an improved response for wavelengths longer than 8000 \AA ' [23], whereas 'the Schottky (cell) has a considerably improved response for wavelengths shorter than 8000 \AA ' [23]. The relative response to light reception of these cells differs greatly at the specified wavelengths. The wavelength region of interest for the AeRP is in the visible range, i.e. wavelengths between about 400 and 700 nm (4000 to 7000 \AA). The human retina has peak wavelength sensitivity for scotopic (that is, for the rods of the retina) at 507 nm; while, peak wavelength sensitivity for photopic (that is, for cones in the retina) at 555 nm [7].

For a sketch of the relative response for these two types of cells see [23], figure 7.30.

There is also a third type of cell called an avalanche photodiode. This type of cell will multiply the electrical current by a gain factor, which could be relatively high. However, the internal noise of the cell is also multiplied.

Therefore, a Schottky cell is a cell of choice for the AeRP photodiode cylinders, considering the wavelength region and spectral response desired. The quantum efficiency of a Schottky cell is better than the planar diffusion cell.

The current output of the cells is given by:

$$\text{Current } (i) = \frac{(A_d^{1/2} \Delta f) R}{D^*}.$$

This formula shows the basic dependence of the current (i) upon the surface area of the photodiode cell, not to mention the responsivity. Here D^* is the normalized detectability of the photodiode cell which is dependent upon the surface area of the cell; A_d is optically active detector area, Δf is the noise equivalent electrical bandwidth, NEP is the noise equivalent power $= i/R$, R is the responsivity of the photodiode cell in units of A W^{-1} and i is the current output in units of A.

According to calculations by Doorish [25] the size of the ECP strands will be sufficient to stimulate multiple cell structures, such as soma, axons and dendrites.

The strands are grown to 10–20 μm thickness, which in a bi-phasic configuration will cover an area on the retina of about 60–70 μm in width coverage of the retinal surface. With cathodal stimulation, the leads are thicker in order to cover similar area.

For a detailed description of the matrix algebra of the AeRP see [25]. This paper details a smaller version of the AeRP called the MINI AeRP, or the MeRP. Here will be found detailed calculations on the ECP stimulation of the retinal ganglion cells (RGCs) and the interface of the AeRP (MeRP) with the human retina.

4.3 Lead umbrella and electrically conducting polymers (ECPs)

The lead umbrella is a non-electrically conducting polymer upon which sit bi-phasic leads of electrically conducting polymer (ECP) strands. A chemistry company supplied these strands. The cells will each have their own bi-phasic leads coming off of them and lying upon the umbrella. The lead umbrella is of the contour similar to that of the retina. The bi-phasic leads therefore rest upon the retinal ganglion cells (which may be laid bare by the removal of the inner limiting membrane (ILM), during a complete vitrectomy). Some ophthalmologists would rather not remove the ILM, but has recently been shown to be of some advantage in macular hole surgery [24]. At least it appears to do no harm to the retina [6, 24].

Two types of electrically conducting polymers were tested in the laboratory. They had the following properties:

Sample 1: thin strands with a linear resistance of $7 \times 10^7 \text{ ohm cm}^{-1}$.

Sample 2: thin strands with a linear resistance of $2 \times 10^4 \text{ ohm cm}^{-1}$.

The strands are grown in the laboratory to specification. Strands with greatly reduced resistance are used in the AeRP. They are basically polyaniline fibres.

Some basic tests were run on these polymers in which varying voltages were run through them with voltages up to five volts for up to two weeks. The polymers were simply connected by alligator clamps to a power source and to an ammeter. The strands were treated rather roughly; certainly more roughly than they would be inside the intraocular space. Current readings were taken. The strands were able to carry between picoamp and milliamp currents for the duration.

The strands were also connected to the first generation prototypes of the AeRP [1]. They carried the current in an efficient manner from the modules to the ammeter. Current was registered in the picoamp range, due to the design of the FGP.

5. The AeRP—retina interface

The AeRP will interface with the retina via the ECP strands. Cell culture studies have been accomplished in which nerve cells were grown upon the ECP sheets. The cells proved to have an affinity for the polymer. They grew to a length of 5 cm [25].

The AeRP will have nerve cells grown upon the umbrella before implantation on the retina, so that there is a ‘wet–wet’ situation. In other words, the

retina will have similar material laid upon it. There will also be attempts that will implant the AeRP without the cells grown upon it. This will show to the retina, the ECP strands directly. Cell culture tests will determine the proper mode of implantation.

6. Conclusion

In this paper an eye implant has been described which is termed an Artificial epi-Retinal Prosthesis (AeRP); a small optical computer, for lack of a better term, that fits into the intraocular space of the eye. The dimensions of the AeRP are large compared to some other projects' implants, but it has done so, in order to take advantage of the small space in the eye, while at the same time providing as many stimulating cells of a large enough photonic surface area as possible. This would provide adequate electrical stimulation for the retinal ganglion cells.

The dimensions of the human eye are 14.3 mm from the posterior of the lens to the retina. The AeRP is therefore the same dimensions, with the fibre optic plate system facing the lens and the lead umbrella facing the retina. The diameter of the AeRP is 8 mm. This is a large device to implant in the eye but not beyond surgical abilities. It is designed to be surgically tacked to the back of the eye and hooked into the sulcus in the front. Since a complete vitrectomy is performed before implantation, an artificial vitreous will be replaced after implantation. The artificial vitreous will also give a buoyant effect to the device, helping to stabilize it.

The second generation prototype is being built in collaboration with an engineering company. A smaller version of the AeRP, called the MINI AeRP (MeRP) is also being designed and built; see paper by Doorish [25].

An interesting and useful question has been raised regarding this design. 1) What about the concern that there is a loss of stimuli as there are no multiple levels of processing involved?

There are actually multiple levels of processing involved in the design. Since different structures of the retinal ganglion cells (RGCs) are stimulated by the electrical current produced at different values, there will be multiple levels of processing. That is, depending on where the leads are placed, in relation to the naturally random layout of the RGCs, they may stimulate soma, axons, and/or dendrites correspondingly. Thus, when light from an object observed in the outside world impinges upon the MeRP, a photodiode cell(s) will be triggered. The electrical current will be carried via the electrical conducting polymer (ECP) strands to the RGCs. The appositioning of the leads will be such that they will stimulate multiple RGCs and their corresponding structures. The brain will then process the information in a logical manner.

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