62.2: A Biomedical Smart Sensor for the Visually Impaired

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Abstract

In this paper, we describe the current version of the artificial retina prosthesis and cortical implant that we are developing. This research project will require significant advances in a variety of disciplines. We have assembled a multidisciplinary team of researchers in Ophthalmology, Neurosurgery, Computer Networking, VLSI, and Sensors to develop the novel solutions needed to make artificial vision for the visually-impaired a reality. This paper describes the novel approach that we have adopted to providing a complete system for restoring vision to visually-impaired persons – from the signals generated by an external camera to an array of sensors that electrically stimulate the retina via a wireless interface.

Keywords

Sensor systems, biomedical sensors.

INTRODUCTION

In this paper, we describe the current version of the artificial retina prosthesis and cortical implant that we are developing. This research is a multidisciplinary project involving researchers in Ophthalmology, Neurosurgery, Computer Networking, Sensors, and VLSI. Restoring vision to the blind and visually impaired is possible only through significant progress in all these research areas.

In the future, artificial retina prostheses may be used to restore visual perception to persons suffering from retinitis pigmentosa, macula degeneration, or other diseases of the retina. In patients with these diseases, most of the rods and cones are destroyed, but the other cells of the retina are largely intact. It is well known that the application of electrical charges to the retina can elicit the perception of spots of light. By coupling novel sensing materials with the recent advances in VLSI technology and wireless communication, it is now feasible to develop biomedical smart sensors that can support chronic implantation of a significant number of stimulation points. Although the development and use of artificial retina prostheses is still in the early stages, the potential benefits of such technology are immense.

Similarly, the use of cortical implants has promise for the visually impaired. Unlike the retina prosthesis, a cortical implant bypasses most of the visual system, including the eye and the optic nerve, and directly stimulates the visual cortex, where information from the eyes is processed. Therefore, in addition to overcoming the effects of diseased or damaged retina tissue, a cortical implant could circumvent many other problems in the visual system, including the loss of an eye.

The smart sensor package is created through the backside bonding of an array of sensing elements, each of which is a set of microbumps that operate at an extremely low voltage, to a integrated circuit for a corresponding multiplexed grid of transistors that allows individual voltage control of each microbump sensor. The next generation design supports a 16 × 16 array of sensors and is being fabricated by MOSIS based on the circuit design created in our Smart Sensors and Integrated Devices (SSID) research lab. Our earlier circuit design, which has been fabricated and tested, supports a 10 × 10 array of sensors. The package is encapsulated in inert material except for the microbumps, which must be in contact with the retina.

The long-term operation of the device, as well as the difficulty of physically accessing a biomedical device implanted in the eye, precludes the use of a battery-powered smart sensor. Because of the high volume of data that must be transmitted, the power consumption of an implanted retinal chip is much greater than, for example, a pacemaker. Instead, we plan to power the device using RF inductance. Because of the difficulties of aligning the two coils – one being within the body and the other one outside the body – for RF power transmission, a low frequency is required to tolerate misalignment of the coils. On the other hand, a relatively high frequency is required to operate in the unlicensed ISM band. For this reason, we have adopted the novel approach of using two frequencies: RF inductance using a frequency of 5 MHz and RF data transmission using a frequency in the range of either 900 MHz or 2.4 GHz. The FCC regulations for low-power non-licensed transmitters are explained in [1].

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RETINAL AND CORTICAL IMPLANTS

Proposed retina implants fall into two general categories:

- Epiretinal, which are placed on the surface of the retina.
- Subretinal, which are placed under the surface of the retina.

Both approaches have advantages and disadvantages. The main advantages of the sub-retinal implant are that the implant is easily fixed in place, and the simplified processing that is involved, since the signals that are generated replace only the rods and cones with other layers of the retina processing the data from the implant. The main advantage of the epi-retinal implant is the greater ability to dissipate heat because it is not embedded under tissue. This is a significant consideration in the retina. The normal temperature inside the eye is less than the normal body temperature of 98.6^{o} Fahrenheit. Besides the possibility that heat build-up from the sensor electronics could jeopardize the chronic implantation of the sensor, there is also the concern that the elevated temperature produced by the sensor could lead to infection, especially since the implanted device could become a haven for bacteria.

There are also two options for a cortical implant. One option is to place the sensors on the surface of the visual cortex. At this time, it is unknown whether the signals produced by this type of sensor can produce stimuli that are sufficiently localized to generate the desired visual perception. The other option is to use electrodes that extend into the visual cortex. This allows more localized control of the stimulation, but also presents the possibility of long-term damage to the brain cells during chronic use. It should be noted, however, that although heat dissipation remains a concern with a cortical implant, the natural heat dissipation within the skull is greater than within the eye.

Given the current state of the research, it is unclear which of these disadvantages will be most difficult to overcome for a chronically implanted device. Therefore, different research groups are investigating different solutions. Here we describe our proposed solution.

An implantable version of the current ex-vivo microsensor array, along with its location within the eye, is shown in Figure 1. The microbumps rest on the surface of the retina rather than embedding themselves into the retina. Unlike some other systems that have been proposed, these smart sensors are placed upon the retina and are small enough and light enough to be held in place with relatively little force. These sensors produce electrical signals that are converted by the underlying tissue into a chemical response, mimicking the normal operating behavior of the retina from light stimulation. The chemical response is digital (binary), essentially producing chemical serial communication. A similar design is being used for a cortical implant, although the spacing between the microbumps is larger to match the increased spacing between ganglia in the visual cortex.

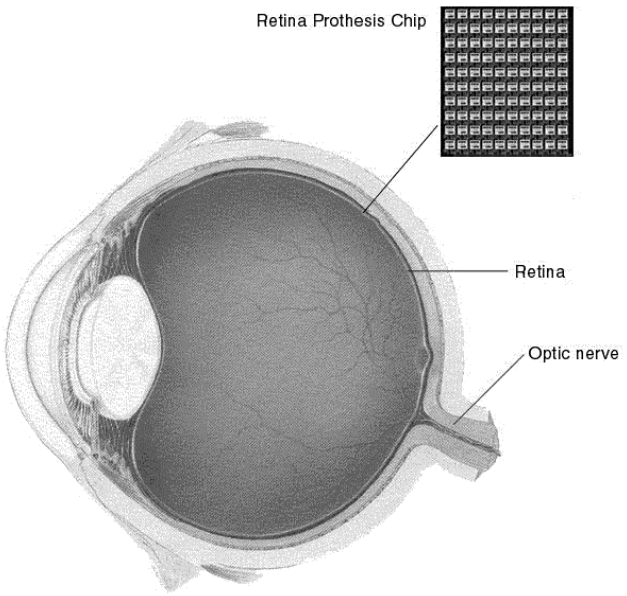

Figure 1. Location of the Smart Sensor within the Eye

As shown in Figure 1, the front side of the retina is in contact with the microsensor array. This is an example of an epiretinal implant. Transmission into the eye works as follows. The surface of the retina is stimulated electrically, via an artificial retina prosthesis, by the sensors on the smart sensor chip. These electrical signals are converted into chemical signals by the ganglia and other underlying tissue structures and the response is carried via the optic nerve to the brain. Signal transmission from the smart sensors implanted in the eye works in a similar manner, only in the reverse direction. The resulting neurological signals from the ganglia are picked up by the microsensors and the signal and relative intensity can be transmitted out of the smart sensor. Eventually, the sensor array will be used for both reception and transmission in a feedback system and chronically implanted within the eye. Although the microsensor array and associated electronics have been developed, they have not yet been tested as a chronic implant. Another challenge at this point is the wireless networking of these microsensors with an external processing unit in order to process the complex signals to be transmitted to the array.

SMART SENSOR CHIP DESIGN

Figure 2 shows a close-up of the smart sensor shown in figure 1. Each microbump array consists of a cluster of extrusions that will rest on the surface of the retina. The small size of the microbumps allows them to rest on the surface of the retina without perforating the retina. In addition, the slight spacing among the extrusions in each microbump array provides some additional heat dissipation capability. Note that the distance between adjacent sets of microbumps is approximately 70 microns.

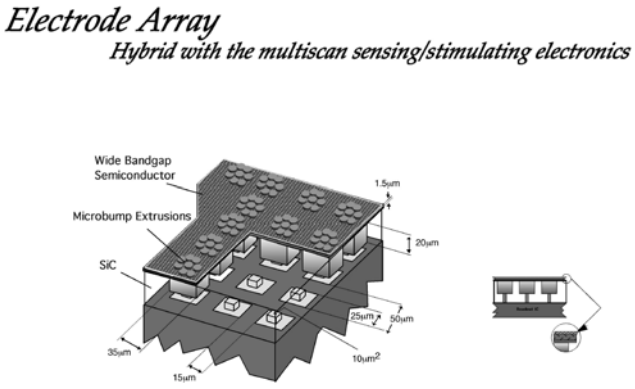

Figure 2. Illustration of the Microbump Array

These sensors are bonded to an integrated circuit. The integrated circuit is a multiplexing chip, operating at 40KHz, with on-chip switches and pads to support a grid of connections. Figure 1 shows a 4 × 4 grid for illustrative purposes, although the next generation of sensor chip has a 16 × 16 array. The circuit can the ability to transmit and receive, although not simultaneously. Each connection has an aluminum probe surface where the micromachined sensor is bonded. This is accomplished by using a technique called backside bonding, which places an adhesive on the chip and allows the sensors to be bonded to the chip, with each sensor located on a probe surface. Before the bonding is done, the entire IC, except the probe areas, is coated with a biologically inert substance.

The neural probe array is a user-configured 1:100 demultiplexer/ 100:1 multiplexer, where an external switch controls the configuration. The neural array is a matrix of 100 microelectrodes constructed as bi-directional switched-probe units that will stimulate or monitor the response state of an aggregate of neurons, more specifically, bipolar cells, which are two-poled nerve cells. When the array is configured as a demultiplexer, the switched-probe units serve to stimulate the corresponding aggregate of neurons; thus, the array functions as a neurostimulator. When the array is configured as a multiplexer, the units serve to monitor the evoked response of the aggregate of neurons in the visual cortex; thus, the array functions as a neural response monitor. The array has an additional bi-directional port called the signal carrier, where the direction of the signal flow to and from this port depends on the configuration of the array. As a neuro-response monitor, the neural signals from each aggregate will be relayed through the signal carrier port on a single line. As a neurostimulator, the external signal, whose magnitude will depend on the intensity of the signal required to revive the degenerate neurons, will be injected into the circuit through the signal carrier (bypassing the amplifier) to be distributed to each aggregate through the corresponding unit. Each switched-probe unit consists of a neural probe and two n-channel MOSFETs, whose W/L ratio is 6/2. The W/L ratio defines the behavior of the transistor, where W is the width of the active area of the transistor and L is the length of the polysilicon used for the gate channel. For each unit, the probe is a passive element that is used to interface each aggregate of neurons to the electronic system and the transistors are the active elements that are used to activate the units.

The second-generation prototype adds the decoder with its outputs connected to the row and to the column ports of the array. The addition of the decoder reduces the number of required contact pads from 22 to 5 (Set, master clock, V_{DD}, V_{SS}, and the signal carrier port) and enhances the reliability of the Scanner with the configuration of 2 inputs, rather than the external connections of 20 inputs. The configuration of the Set and clock cycles will enable the decoder to sequentially activate each unit by sending +5V pulses to the corresponding row and column ports. To establish the required Set and clock cycles, further neural analysis on the periodic stimulation of the bipolar cells must be conducted. The Set signal initiates the scanning of the probe from left to right and from top to bottom.

COMPUTER COMMUNICATION

It is not feasible to do the processing internally using the capabilities of only the sensor arrays. Thus, work on interconnecting these smart sensors with an external processing system is a fundamental aspect of realizing the potential of an artificial retina. On-going diagnostic and maintenance operations will also require transmission of data from the sensor array to an external host computer. These requirements are in addition to the normal functioning of the device, which uses wireless communication from a camera embedded in a pair of eyeglasses into the smart sensor arrays. The research challenges in providing wireless networking solutions for smart sensors is described in [4].

The processing steps from external image reception to transmission to the retina prosthesis are as follows. A camera mounted on an eyeglass frame could direct its output to a real-time DSP for data reduction and processing (e.g., Sobel edge detection). The camera would be combined with a laser pointer for automatic focusing. The DSP then encodes the resultant image into a compact format for wireless transmission into (or adjacent to) the eye for subsequent decoding by the implanted chips. The setup could use a wireless transceiver that is inside the body, but not within the retina, and a wire to the retina chip.

Our ultimate research goal is to support an array of 1600 smart sensor chips, each with a 25 × 25 grid of electrodes. The rods and cones fire at an approximate interval of 200 – 250ms. Therefore, the processing will be performed periodically in a 200 – 250ms processing loop. Hence, data will be transmitted four or five times per second. Although the actual rods and cones in the eye operate in an analog manner (variety of possible values), our initial system will operate in a strictly on/off mode. In other words, one bit of data per sensor every 200 – 250ms. We plan on eventually moving to multiple-level stimulation.

The investigations into understanding the visual processing of the brain will indicate whether or not the sensor arrays will be implanted with uniform distribution. Functionally, electrode arrays within the center of the macula (the central retina) will have to stimulate the retina differently than peripherally placed electrode arrays, since the functions of these various parts of the retina are very different.

Centrally, in the macula, we perceive our high-resolution detail vision, while in the periphery, the retina is better at detecting motion or illumination transients. (For example, most persons can perceive their computer monitor's vertical refresh when looking at the monitor using peripheral vision, since the peripheral retina has better temporal resolution, but poorer spatial resolution than the macula.) Thus, a multi-electrode array visual prosthesis will have to encode the visual scene slightly differently, depending upon where on the retina each electrode array is placed. The peripherally placed electrodes need to generate signals based on lower spatial resolution with greater emphasis on temporal events, while centrally placed sensor arrays upon the macula need to encode more spatially oriented information. Each array will have to transmit some common information such as the overall luminosity of the visual scene. So, each smart sensor will have to be coordinated with other smart sensors based on an image processing algorithm designed to control a set of smart sensor arrays, each separate, sending input to functionally different retinal areas.

In order to achieve the envisioned functionality, two-way communication will be needed between an external computer and cortical implant so that we can provide input to the cortical implant and determine if the desired image is "seen". We also need two-way communication with the retinal implant so that we can determine that the sensors in the retina are operating as expected. Besides input from the camera, we also need the ability to provide direct input to the retinal implant to determine if the patient sees what is expected from that input pattern. This will validate our understanding of the signaling between the camera and the smart sensor array as well as the operation of the wireless communication protocols.

Our main objective is to design a communication system that is energy efficient and performs satisfactorily under interfering sources. For very low power transmitter applications, reducing the power consumed in the transmitter architecture and an ideal modulation technique produces the best energy efficiency. Many energy efficient transmitter architectures have been developed [2] and can be used for low power applications. Comparison of various digital modulation techniques have been done in terms of SNR/bit and bandwidth efficiency for a known BER and fixed data rate [2][3].

The power must be carefully controlled to avoid damage to the retina and surrounding tissue. Each sensor array operates with less than one microampere of current. The *power* can be provided in different ways. One option is to use wires to provide the power, although we would still require wireless data communication to limit the number of wires. Implanting a battery near the eye could provide the power. A second option is to use inductance, provided by RF or IR signals. A third option is a photo-diode array, which converts light to power. It is important to note that even if the power source is wired, the data communication needs to be wireless in order to minimize the number of wires and improve the flexibility of the system. After considering all factors, the decision has been made to use radio frequencies for both power inductance and data transmission

RELATED WORK

The goal of artificially stimulating the retina to produce vision is currently being investigated by seven large, multidisciplinary research teams worldwide, including four groups in the United States, two in Germany, and one in Japan. Table 1 describes the location of the other six groups and the design approach used. In addition, to the large groups listed below, efforts toward a visual prosthesis via cortical stimulation are being made by Richard Normann of the Utah Visual Prosthesis Project and the NIH Visual Prosthesis Project Lab of Neural Control/NINDS with Schmidt, Heetderks, and Hambrecht.

Table 1: Summary of other retina implant research labs

Investigators	Location	Stimulus Site
DeJuan/Humayan	North Carolina State	Epiretinal
Rizzo/Wyatt	Mass. Eye and Ear/MIT	Epiretinal
Chow/Peyman	Optobionics/ LSU	Subretinal
Eckmiller	Duisburg, Germany	Subretinal
Zrenner	Bonn, Germany	Subretinal
Yagi	Nagoya, Japan	Unknown

Each group has directed their efforts toward the design of an implantable device. The Massachusetts Eye and Ear/MIT program, as well as the North Carolina State groups have been independently working on an epiretinal, electrically based retinal stimulator. Groups designing an electrical subretinal device include Chow/Peyman, Zrenner, and Eckmiller. The Yagi group at the University of Nagoya is attempting to hybridize cultured neurons with a silicone-based stimulator, borrowing from work pioneered by the Pine lab at Cal-Tech.

The North Carolina State group and the Massachusett's Eye and Ear/MIT group share common design approaches. Both implants are intended to stimulate the retina using electrical current, applied to the inner retina by a two dimensional, multiple-electrode array. Although the intended target cell was believed to be the retinal ganglion cells, the doctoral dissertation of Robert Greenburg, at Johns Hopkins, demonstrated that the retinal bipolar cells were the predominant cell population stimulated. These data were derived through an analysis of the temporal dynamics of neuron responses after epiretinal electrical stimulation in the frog.

In addition to an epiretinal electrode array, both groups have designed VLSI (very large scale integration) chips intended for ocular implantation. Both of these integrated circuits are

designed to accept an electrical signal that encodes visual information. This signal is formatted as an electrical representation of a visual scene, provided by an external solid-state camera, or computer. The VLSI chip is designed to decode this signal and produce a graded electrical stimulation in the appropriate electrodes, re-creating a spatially structured electrical stimulus to the retina. The North Carolina State group has borrowed from work done with the cochlear implant. A radio-frequency (RF) receiver has been integrated into the VLSI design to permit the RF transmission of the visual signal into the chip. The MARC IV is an improvement over previous versions because it is capable of measuring the electrode contact impedance with the retina, automatically compensating for fluctuations by altering the stimulus voltage.

The Massachusett's Eye and Ear/MIT group in Boston powers their VLSI implantable silicone chip using a specially designed silicon photocell array. The array is capable of delivering sufficient energy to power the VLSI chip. This photocell array is mounted within a posterior chamber intraocular lens. It consists of an array of sixteen parallel sets of twelve linear photodiodes. A two-watt, 820 nanometer laser is used to power the photodiode array. By modulating the laser output energy according to the pulse stream of a CCD sensor, visual information may be transmitted into the VLSI chip, digitally. This information is then decoded in a similar manner to the MARC IV to generate a stimulus voltage, corresponding to the level of illumination for a given pixel at the appropriate stimulus electrode site.

Worldwide, three groups are working on the design of a subretinal electrode array implant. Alan Chow and associates at Optobionics Corporation conducted the first work in this area. Their design has much inherent strength with some additional technical issues. For patients with hereditodegenerative retinal disease, the outer retina is most commonly affected. Rods and cones are dysfunctional or missing. These disease states often leave the inner retina somewhat less affected. Therefore, the true goal of a retinal implant in these cases is to replace the missing functionality of rods and cones. This involves stimulating the bipolar/horizontal/amacrine systems of the retina. Those groups working with subretinal electrode arrays hypothesize that these cell populations are most accessible from the subretinal space. Although this may be true, the North Carolina State group has shown that the bipolar cells are stimulated by an epiretinal implant. The inherent design of the subretinal electrical implants is vastly different from those groups working on the epiretinal approach.

The epiretinal implants are designed to derive their power from a source that is independent from the electrode array. The NC State group derives their power from an inductive transformer. Energy from this source is then switched to the appropriate electrodes, according to the visual data input signal. The Massachusetts Eye and Ear/MIT group uses a silicon photodiode array placed within a posterior chamber intraocular lens for power. Energy from this array is then switched by the VLSI implant to the appropriate epiretinal electrode, based upon the input of a CCD camera.

Subretinal implants are inherently simpler by design and mimic the modular organization of individual rods and cones. Power is generated at the site of sub-retinal electrical stimulation, using photosensitive microphotodiodes (MPDs). When arranged two-dimensionally, these microphotodiode arrays (MPDAs) provide spatially organized electrical stimulation to the retina. Thus, their design is inherently much simpler. Incident light falls upon the MPDA, generating an electrical stimulus with identical spatial organization. No cameras or encoding/decoding circuitry is needed. In addition, the power supply is integrated within the implant. Although these are great benefits in design simplicity, other factors may complicate their use. These include the need for optically clear media and also assume that an adequate amount of stimulation current can be generated by an MPD for each stimulation point. Further, since the implant is within the subretinal space, metabolic issues concerning adequacy of oxygen and nutrient delivery to the outer retina become considerations. A report at ARVO by the Eckmuller group, 1998, noted that microholes had to be made through the MPDA to permit prolonged viability within the rabbit retina.

Both epiretinal and subretinal approaches have thus far been based upon electrical stimulation of the retina. The North Carolina State group use platinum electrodes, while the MIT/Mass. Eye and Ear group uses a platinum/iridium alloy. Using platinum electrodes, current densities for epiretinal stimulation have been reported between 2.98 (bullfrog) and 11.9 (adult rabbit) microcoulombs/cm2. Reported current densities from the MIT/Mass. Eye and Ear group for 25 micrometer platinum wire is 16 microamperes while a five micrometer platinum/iridium electrode requires 0.4 microamperes in the adult rabbit.

Electrical stimulation of the retina through injection of current dissipates power and heat. In patients with degenerative retinal disorders, the choriocapillaris, which normally provides heat dissipation in the retina, is markedly pathologic. Therefore, any study regarding the energy dissipation requirements must be performed to account for the compromised outer retinal blood flow/heat dissipation system. In addition to the thermodynamic issues introduced by electrical stimulation, ionization of electrodes does occur at physiologic pH and temperature within saline media. Thus, chronically implanted electrodes oxidize, diminishing their effectiveness over time.

CONCLUSION

In this paper, we have described our initial approach to an artificial retina prosthesis and cortical implant, which will be refined further as testing and development continue. The creation of a smart sensor implant to restore vision to persons with diseased retinas or suffering from other damage to the visual system has tremendous potential for improving the quality of the life for millions.

It also presents a number of challenging research problems that require the involvement of a multidisciplinary research team. The eventual goal of this research is a chronically implanted visual prosthesis that provides significant visual functionality.

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