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Visual Prostheses: Current Progress and Challenges

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INTRODUCTION

Vision is arguably the most important sense that we possess. Diseases that cause an impairment of this sense result in a debilitating condition. Additionally age-related causes of blindness, such as age-related macular degeneration (AMD), are exacerbated by the increase in average lifespan especially in developed countries. It is imperative then, that a means of restoring a useful level of vision to these patients who have become blind be pursued. Three main questions naturally arise and must be addressed at the outset 1) What are the diseases that will be amenable to restoration by an engineering approach 2) Where is the ideal placement of this device? 3) What are the strategies that one could use to restore vision?

The retina is often referred to as an approachable part of the brain [1] and is composed of exquisite neural circuitry that performs an amazing level of processing. Hence, the greatest chance of building a successful retinal prosthesis is to start with diseases that leave much of the retinal architecture intact. There are two such diseases that affect only the sensory transduction layer, the photoreceptor layer, of the retina. The first is AMD and the second is retinitis pigmentosa (RP), both these diseases result in a loss of photoreceptors, see figure 1.

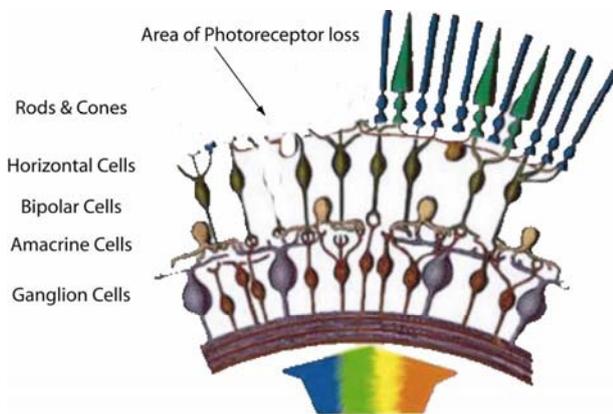


Figure 1: Schematic showing retinal degeneration due to diseases such as AMD and RP.

The answer to the second question needs careful consideration of the pros and cons of placing the device in a specific location. There are three logical placements of the device 1) The retina, which can be further be divided into epi-retinal and sub-retinal. The epi-retinal referring to the side that faces the vitreous and the sub-retinal to the side that is adjacent to the choroid. 2) The visual cortex and 3) the optic nerve. If the device were placed in the retina, and if we are able to harness much of the processing capability of the remaining intact neural tissue, it offers the most seamless and natural method. This is mainly due to the fact that it does not bypass the natural flow of information. However, it also places the most stringent demands on the prosthesis. The retina is an extremely delicate tissue with the consistency of wet tissue paper, placing a device here is a daunting

surgical challenge. As to epi-retinal versus sub-retinal, the epi-retinal approach is easier from a surgical point of view but the mechanical anchoring of the implant to the epi-retinal surface is difficult[2]. This can be partially alleviated by placing the device subretinally[3], though the surgery becomes more difficult.

Cortical implants offer another means of restoring visual function by placing a device that interfaces directly with the brain. This is advantageous since it does not require an intact optic nerve and hence has a wider range of diseases that can be treated. However, the columnar organization of the visual [5] and the fact that much of the preprocessing that occurs in the retina and the lateral geniculate nucleus is bypassed, makes the conversion of the visual image into a meaningful cortical stimulus rather difficult. The optic nerve [4] is another possible location, this has the advantage of easy surgical access but the bundle organization makes the spatiotemporal mapping onto the optic nerve rather challenging. Though it is partially this author's bias, the placement of the prosthesis in the retina seems to be the best choice. Furthermore, since the mechanical anchoring seems to be the more difficult than the surgical task, subretinal implantation is preferred to epi-retinal implantation.

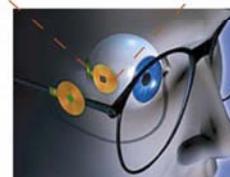
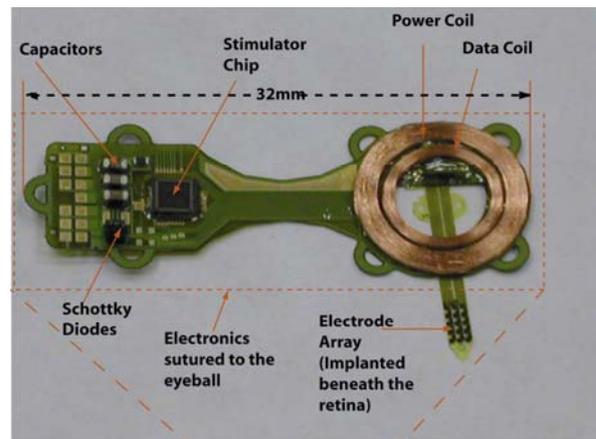


Figure 2: Schematic representation of the minimally invasive ab-externo approach. The transmitter coils are placed outside on a pair of eyeglasses and the receiver coils and the stimulator chip are placed on the eyeball. The electrode array is placed in the subretinal space through a scleral flap.

ELECTRONIC VISUAL PROSTHESES

When current is injected in the vicinity of the neural membrane, some of this current will charge the membrane via the membrane capacitance. Current flowing out depolarizes the membrane and

current flowing in membrane hyperpolarizes it. Hence for a patch that depolarizes there will be another patch nearby that will hyperpolarize due to the change in the current direction [6]. For electrical stimulation to be highly effective the electrode must be fairly close to the neuron. The other problem is that the low resistivity of the surrounding electrolyte compared to the neural membrane will also shunt much of the current away from the nerve if the electrode is not very close. The goal of an artificial retinal prosthesis is to stimulate the remaining healthy layers of retinal neurons using brief biphasic pulses of current. These current pulses produce a sensation of vision in the brain, which is termed a phosphene. We hope that over time that the patient will be able to integrate these phosphenes into useful vision. A key step toward this goal is the development of a chronic implant. Our design philosophy is based on the following requirements: 1) the implant must be powered via an external source (i.e. no batteries). 2) Ability to communicate wirelessly with the implant via external commands. 3) Allow for parameter tuning i.e. current amplitude, duration and interpulse timing. The first and second constraints were met by using an inductively coupled power and data link. The third was enabled by implementing a flexible stimulator chip architecture as discussed below.

can be safely transmitted to the secondary 3) Larger physical space in which the implant resides which allows for larger secondary coils.

The basic architecture of the stimulator chip is shown in Fig. 3. The chip is powered via an inductive link; the power signal is rectified and filtered using off-chip diodes and capacitors with the nominal supply voltage being $\pm 2.5V$. The data is received through a separate coil placed concentric to the power coil. The digital data is transmitted using as an amplitude shift keyed (ASK) waveform. The carrier frequencies of the power and data are 125 KHz and 13.56 MHz respectively. The front-end decouples the power and data signals, demodulates and restores the data signal to digital levels. The symbol is encoded as a pulse width modulated signal, a 50-50% duty cycle encodes a 0 and 30-70% duty cycle encodes a 1. The data and clock are recovered by the delay locked loop and fed to a control logic block. The signals from the control block control the current driver array that outputs biphasic current pulses to the electrode array. The specific circuit details of the stimulator chip have been reported in detail [7]. The fabricated stimulator chip that has been used in the retinal implant is shown in Fig. 4. The chip contains roughly 30,000 transistors and consumes about 1.2mW at a data rate of 25 kb/s and 3.2mW at 700 kb/s.

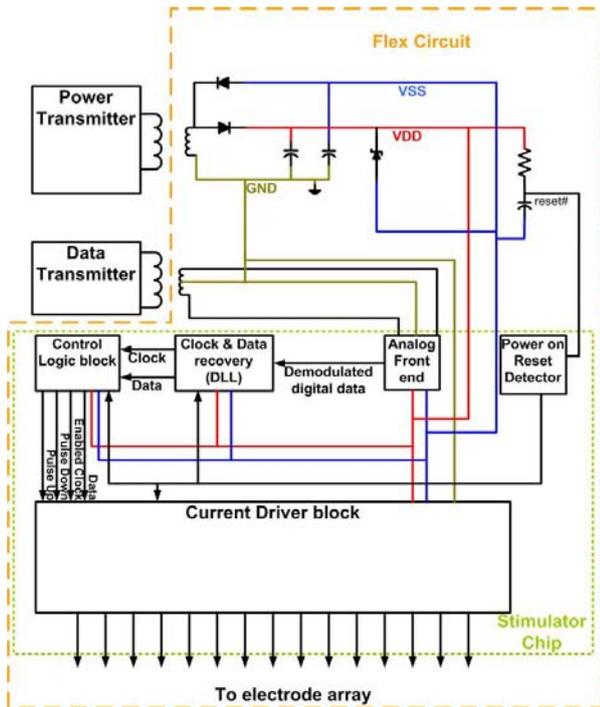


Figure 3: Architectural overview of the current retinal implant. The blocks that correspond to the stimulator chip are outlined in green. The chip receives data and power through two separate inductive links, demodulates the signal, recovers the data and the clock and outputs biphasic current pulses upon receiving the appropriate commands.

Our physical implant design is based on a minimally invasive *ab-externo* approach, which is schematically shown in Fig. 2. In this approach only the electrode array is placed in the sub-retinal space (underneath the retina), while the secondary coils and stimulator chip are placed outside on the eyeball. This technique minimizes the number of components that are placed in these retinal space which provides the following key advantages: 1) Minimizes the risk of infection due to the implant 2) Increases the amount of power that

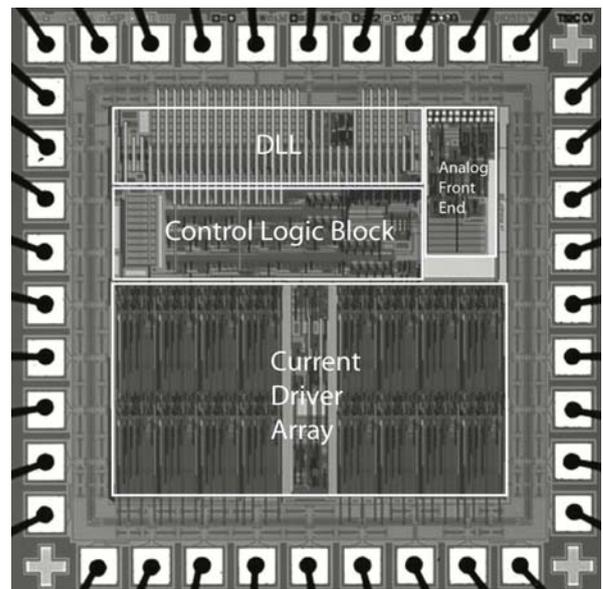


Figure 4: Microphotograph of the complete stimulator chip, the chip has a total area of 5.612 mm² and contains approximately 30,000 transistors.

The control sequence crucially controls the entire working of the chip and the experimental results from this block are shown in Fig 5. Complete details of the command sequence can be found elsewhere [7]. The first was to test the reliably serial data transfer following the reception of the command word. The chip was configured so that the input data stream could be read out from the registers on the following configure command cycle, using this procedure the data integrity was tested. The 170 clock cycle burst that clocks the data registers is shown in Fig. 5. The Pulse-Down command, followed by a stop (this controls the pulse width of the current pulse without the use of clock dividers) was transmitted and then the transmit sequence was repeated for the Pulse-Up command. The command sequence,

the assertion and deassertion of this experiment can be clearly seen in Fig 5. The pulse width commanded and obtained were within the accuracy of experimental error as shown in Fig 5.

The next step was to see if the implantable retinal stimulator chip would function as designed when powered wirelessly while driving a 400 μ m diameter iridium oxide electrode immersed in saline. The results of this experiment are shown in Fig 6, the separation between the primary and secondary coils are 15mm and the current driven was 90 μ A. The data from the register was additionally recorded to ensure data integrity.

We have recently implanted our retinal prosthesis in a Yucatan minipig and the results from the animal experiments are shown in Fig. 7. Basic implant function was tested by measuring the stimulus artifact by commanding up-down current pulses from the implant via wireless commands.

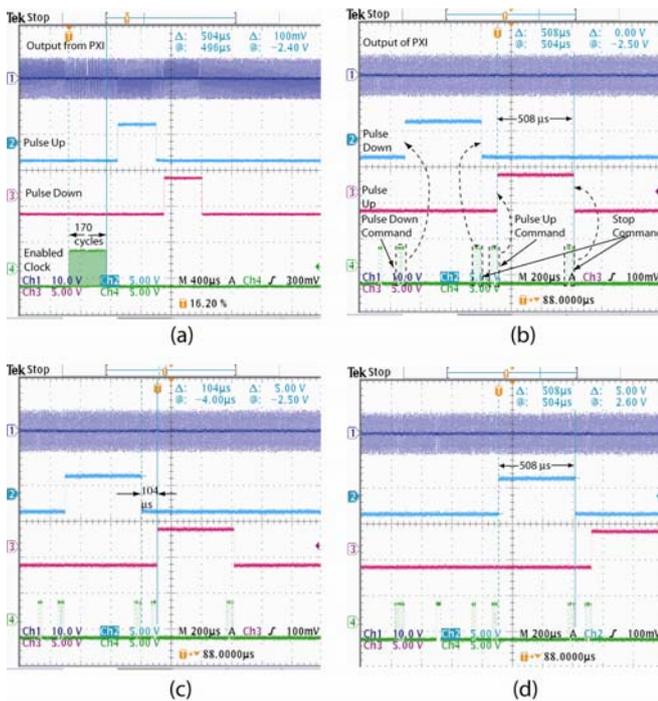


Figure 5: For these tests a LabView PXI system output was fed into a transformer and the secondary connected to the input of the chip. a) Successful decoding of Pulse Up, Pulse Down and Stop commands is evidenced by the Pulse Up and Pulse Down signals. The 170 clock cycle burst shows that the Configure command has been decoded successfully. b) Pulse Up and Pulse Down durations are generated by the arrival of the Pulse Up, Pulse Down and Stop commands. The width of the Pulse Down signal was 508 μ s (pulse width commanded by the software was 506 μ s). c) Measurement of the interpulse interval (commanded=105 μ s, measured=10 μ s). d) Measurement of the Pulse Up signal duration (commanded = 506 μ s, measured = 506 μ s). Minor discrepancies in the numbers arise from measurement errors rather than functional errors

CHALLENGES

Though we have successfully demonstrated the design, fabrication and implantation of a preliminary visual prosthesis much remains to be done. The first major challenge that stands out is the number of electrodes in the current implant. For investigative

purposes we had designed a 15-channel implant. However, for a successful human implant we envision that we would need at least 100 electrodes or more. A reasonable estimate that compromises between high visual acuity and power would probably be around a 1000 electrodes. From earlier human studies by our group and others [8,9], suggests that a current level of at least 200 μ A and pulse widths of 4ms are needed for effective stimulation. Additionally we need a minimum supply voltage of 5V, provided the electrodes are large (~400 μ m in diameter), to meet the required compliance voltage. This gives us 500 μ W/electrode for a swing that is symmetrical about ground. This in turn implies that we need 500mW for a 1000 electrode array, which is of course impossible to achieve while maintaining cell viability due to the amount of heat dissipation. Of course things are not quite this bleak since all electrodes are not switching at the same time. If we assume that we limit the array to a 0.3 activity factor we still need 150mW, this still exceeds the safety limit, which is around 10-50mW[17]. The use of a switched supply design using capacitor banks can mitigate some of the power losses [16] and thereby lower the power required.

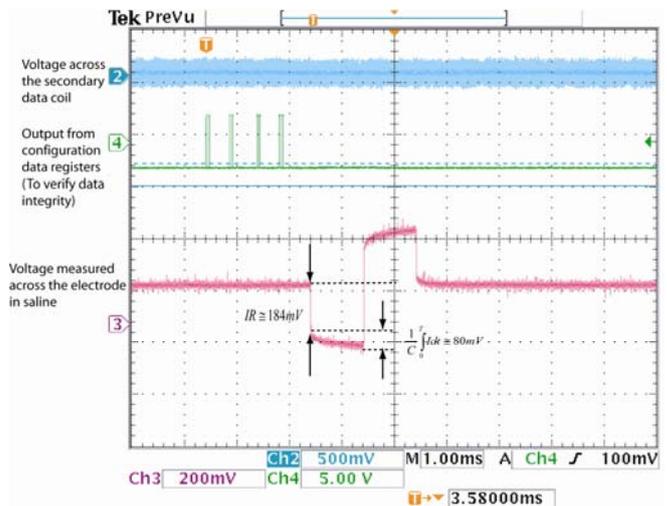


Figure 6: Output of the wirelessly driven and powered stimulator chip driving an electrode immersed in saline. The separation between primary and secondary coils is 15mm.

An alternative way of approaching the problem is to design better electrode architectures that can be placed closer to the retinal tissue and thereby lowering the current required for stimulation. An encouraging note is that routinely in the lab we use 1-10 μ A to stimulate retina in-vitro [11] where the stimulating electrode is placed very close to the cell. Another approach to enhance proximity is to induce neurons to grow towards the electrode by using drug eluting electrodes [12].

The next major challenge is biocompatibility of the retinal implant. Though, polymer coatings such as paralyene, polyimide and polysiloxanes are currently being used in neural prosthesis [13] they degrade over time. Metal encapsulation such as titanium packaging is another possibility though this may make the implant bulky and surgically hard to handle. Apart from general biocompatibility there is also the issue of tissue encapsulation of the electrodes, which increases the access resistance of the electrodes. Use of special coatings near the vicinity of the electrode array may overcome this [13].

From a VLSI design and test stand point of view many improvements can be made. Currently many transmission schemes

have been investigated such as ASK, FSK and DPSK [7,14,15] each having its own advantages. As electrode counts increase data rate increases and advanced low-power, high data-rate transmission schemes need to be investigated. However, the bigger obstacle is efficient power transmission, which is severely impeded by the low coupling between primary and secondary. One approach might be to use a rechargeable battery to wireless recharge it[10], though battery lifetime becomes an obstacle. Instead of using a fixed current level that is imposed from the outside, it may be better to use a closed loop feedback system where the output of the neuron is coupled to the stimulator and the current necessary to elicit a neural response is determined by this loop. The overall viability of the implant must be continuously monitored to ensure safety and efficacy of the implant. One important parameter that needs to be regularly monitored is the impedance of the electrode.

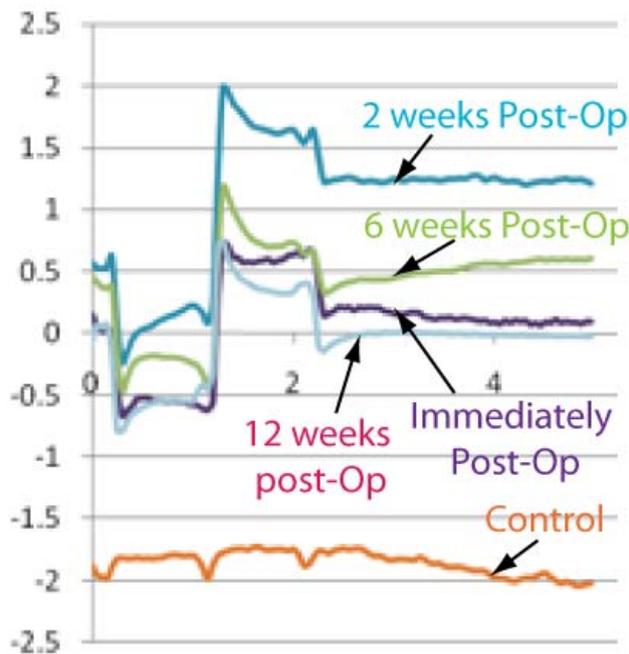


Figure 7: Stimulus artifacts recorded from an implanted Yucatan minipig while the implant was powered wirelessly and commanded wirelessly to output biphasic current pulses.

We have only addressed, albeit briefly, the challenges from a design standpoint of view. There remains numerous challenges in the areas of behavioral studies, brain plasticity and patient training that need to be addressed and is outside the scope of this paper.

CONCLUSION

We have recently designed, fabricated and implanted a visual prosthesis. Animal studies show that the implant remains viable post-op. There exist numerous challenges to move the implant from the bench to the bedside and requires a concerted effort from scientists in different disciplines to come together. We hope that in the future that we will eventually take the important step being able to perform human studies to understand the efficacy of a chronic retinal implant.

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