Design Considerations for High-Density Fully Intraocular Epiretinal Prostheses

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***Abstract*—Retinal prostheses have successfully proven to be a viable treatment for advanced stages of retinal degenerative diseases such as retinitis pigmetosa. However, current implementations have critical limitations that affect their functionality and resolution. This paper reviews design challenges of the electronics considering the biology of the eye and discusses new approaches for future high-density fully intraocular prostheses. An origami retinal implant that has the potential to alleviate the size, power and cost constraints of such systems is proposed. Measured results of enabling technologies are also discussed.**

I. Introduction

Retinal degenerative diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD) affect primarily the photoreceptor cells (rods and cones) and damage the ability of the retina to sense light, resulting in severe vision loss. However, the majority of inner neurons in the retina remain functional and can be electrically activated [1], [2]. Retinal prostheses (Fig. 1) aim to partially restore vision in such patients by bypassing the damaged photoreceptors and directly stimulating the remaining healthy neurons.

Recent work on retinal prostheses has shown significant progress over the past years and has led to the development of commercialized products. One of them is the FDA-approved Argus II retinal prosthesis system which features 60 electrodes and a visual acuity of up to 20/1260 [2]. However, similar to previous work, it uses an extraocular implant with a trans-sclera trans-choroid cable to connect the electrode array to the retina [4], [5]. Not only does having a cable across the eye wall increase the risk of infection and lower the normal eye pressure, but it also leads to unpredictable and difficult to control forces on the electrode array that results in malpositioning of the electrodes relative to the retina.

To avoid the use of such cable, a fully intraocular implant is desired. In this paper we discuss design challenges of the electronics and our proposed solutions for a fully intraocular epiretinal implant. Implementation of such device is extremely difficult due to the limitations imposed by the anatomy and biology of the eye as well as desired features such as waveform programmability and large number of electrodes. Sections II and III of this paper are dedicated to these challenges, and will cover critical building blocks of an implant with large number of stimulation channels and wireless power/data telemetry. In order to have a minimally invasive surgery and guarantee self-healing, the intraocular device needs to be implanted through a small incision of less than 5 mm. In section IV we will discuss the possibility of using multiple chips instead of a single chip to reduce the size of the implant while achieving high performance. To enhance the efficiency of the stimulation it is also crucial that all the electrodes be placed uniformly

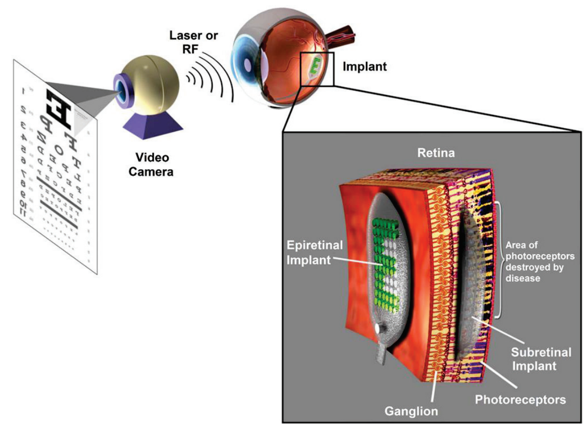

Fig. 1. Retinal Prosthesis (Image courtesy of annual review of biomed. eng).

close to the retina without damaging the tissue. In current implants [2], a single surgical tack at one end of the electrode array is used to fix the position of the electrodes. However, this approach does not guarantee a uniform placement, and the other end of the array can lift. In section V we discuss a new approach that can alleviate this problem and thus reduce the stimulation current and total power consumption of the implant.

II. Electrical Stimulation in Epiretinal Prosthesis

In an epiretinal implant, the prosthesis stimulates the retina via an electrode array placed in front of it as shown in Fig. 1. The electric charge is then delivered to the tissue in a precisely controlled fashion to initiate a functional response (i.e. action potential) by depolarization of the membrane of retinal neurons. The electrode-retina interface, shown in Fig. 2(a)-(b), presents an impedance that depends on the electrode size and the distance from the retinal tissue [3], [4]. This impedance is relatively large due to the small size of the electrodes and properties of retinal tissue.

Of special interest is the perceptual threshold in the retina, since this stimulus threshold together with the electrical properties of the electrode-retina interface will define the output load and voltage compliance of the implant. To ensure stimulation of retinal cells, initial designs targeted current levels up to 1 mA. For those designs, an output compliance of $>$10V was required, and high-voltage (HV) technologies were used at the expense of area and power consumption [4], [5]. Human clinical trials have recently revealed that the stimulus threshold of a single biphasic pulse with 1 ms duration at each phase can be as low as 20 μA for a 260 μm diameter electrode implanted in the macular region [6]. In addition, advances in implant

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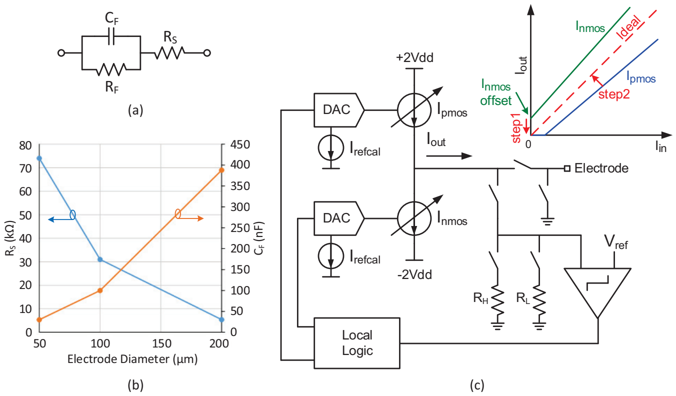

Fig. 2. (a) Simplified model of the electrode-retina interface, where C_F represents the double-layer capacitance, R_F the Faradaic charge transfer, and R_S the solution impedance. (b) Estimated values for R_S and C_F based on measurements of Pt electrodes implanted in cadeveric porcine eye (from [3]). (c) Model of calibration scheme proposed in [7].

technology promise close placement of the electrode array and retinal tissue, which can further decrease the required current. This creates an opportunity for highly scaled low-voltage (LV) technologies to reduce area and power, and to support hundreds of flexible channels for fully intraocular implants.

We have implemented such system in 65 nm CMOS [7]. It features dual-band telemetry for power and data, clock recovery, and a 512-channel stimulator array. To enable robust operation with high output voltage, core transistors were used extensively, and I/O transistors were used only for protection. A 5 V output stage was designed with 1.2 V core and 2.5 V I/O transistors using stacking and dynamic biasing.

It is important to note that recent studies suggest that near term retinal implants must be able to deliver higher currents, but future implants, with advanced electrode array technology, may be able to use lower stimulus and still elicit perception [2]. In section V, we present a promising approach that can pave the way to achieve this important goal.

A. Waveform Programmability and Biphasic Stimulation

Several studies have shown that more complicated stimulation waveforms such as high-frequency pulse trains, asymmetric biphasic pulses, or non-rectangular shapes (Gaussian, linear and exponential), present advantages over biphasic pulses [4], [8]. A recent work [8] has proved that the required voltage compliance can potentially be reduced by 10%-15% if a step-down current pulse shape is used. Thus, having a highly flexible stimulation waveform is desired and allows further studies in stimulation efficiency, color perception and parallel stimulation [4]. In order to achieve this flexibility, our chip is designed to produce independent arbitrary waveforms with 4 bits of resolution at about 100 μs time-steps.

Another important design consideration in retinal prosthesis is matching the current or charge of biphasic stimulation, since any remaining charge beyond tolerable limits can result in tissue damage and electrode corrosion. Analog techniques to sample correction currents require large area and have to run for every stimulation. In addition, they rely on a constant output current that limits them to biphasic pulses. Instead, as shown in Fig. 2(c), we have proposed a digital calibration method to match biphasic currents that reduces area and power. It needs to run only once when the implant is turned on (e.g. daily), and is compatible with arbitrary output waveforms. This technique achieves a current mismatch with μ=1.12 μA and σ=0.53 μA (2.24%).

B. Number of Channels

Clinical trials have proven to successfully provide visual restoration to blind patients suffering from retinal degeneration [2]. To restore functional visual perception to a degree that will enable reading and face recognition, simulation studies in normally sighted subjects have predicted that hundreds of channels are required [1]. Although the number of channels has increased considerably, most of previous work have used extraocular implants due to their large size and high power consumption [4], [5]. In order to have a fully intraocular design, the area of the chip, and therefore the area of the stimulator, should be minimized. In our design, control logic and calibration circuitry are shared among several channels to reduce the chip size and power consumption. To further reduce the area of the stimulator, circuit-under-pad technique has been used. This design achieves a pixel size of 0.0169 mm^2, improving the state-of-the-art by 35%.

III. Dual-Band Telemetry

A. Power Telemetry

Fully intraocular implants require the use of coils that can fit inside the eye. Such intraocular coil is placed in the anterior chamber of the eye after the crystalline lens is removed. This imposes hard constraints on its size (<10 mm outer diameter) and weight (<46 mg in saline). Due to these limitations, the efficiency of traditional 2-coil inductive link reduces drastically ($\approx$7% with 1 inch separation). By using a high-efficiency MEMS foil coil and a 3-coil power transmission scheme as shown in Fig. 3, our power delivery link achieves 36% of efficiency at 10 MHz [10].

The power management circuitry also needs to have very high efficiency and should be optimized for the frequency at which the coil has its maximum quality factor (Q). In order to reduce the number of off-chip components, an on-chip rectifier is desired to avoid external diodes used in previous work [5]. Our rectifier design utilizes transistor-based diodes and unidirectional switches to prevent reverse conduction loss in the power transistors, improving its efficiency to more than 80% while delivering 25 mW. A feed-forward ripple cancellation LDO regulator is also used to generate the analog supply, enhancing its PSRR. Both circuits are shown in Fig. 4. The power management achieves a total combine efficiency of 65%.

B. Data Telemetry

As mentioned in the previous section, hundreds of channels are required to restore functional visual perception, and arbitrary stimulation waveforms present advantages over traditional biphasic pulses. Thus, high-data rate communication is required in order to have independent channels that generate high-resolution waveforms. As an example, for a 1000-channel retinal implant with a resolution of 4-bit at 100 μs time-steps, a data rate of 40 Mb/s is required. Such data rates need a carrier

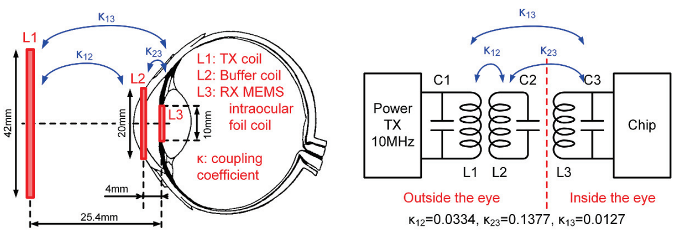

Fig. 3. Three-coil inductive power transmission [7].

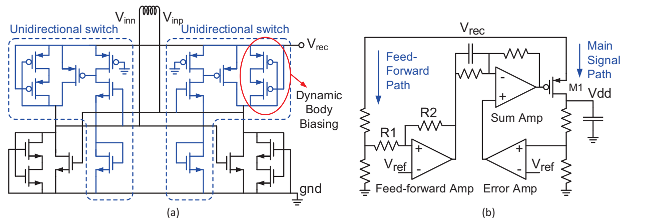

Fig. 4. (a) Full-wave rectifier and (b) feed-forward ripple cancellation LDO regulator [7].

frequency in the order of hundreds of MHz. A PSK modulation scheme and a communication protocol with error-detection capabilities can be used to provide robust data transmission while minimizing the interference from the power telemetry.

Fig. 5(a) shows the electrical characteristics of the vitreous humor. It can be seen that the optimal frequency range is located between 100 MHz to 1 GHz because of the approximately constant relative permittivity (i.e. low distortion) and low tissue absorption. Our design implements a PSK demodulator at 160 MHz as shown in Fig. 5(b). The on-chip PLL synthesizes the clock from the power signal and removes the need for an external crystal oscillator used in previous designs [5], [9].

IV. Multiple-Chip Approaches

Recent developments in retinal prosthesis design have increased the number of electrodes achieving more than 1000 channels [9]. As discussed before, the prosthesis should have a number of extra features such as programmable stimulation waveforms, current calibration and charge balancing [4], [7]. Such increase in capabilities requires the development of specialized system-on-chip designs. In a conventional approach, a single chip manages all major tasks of the implant (wireless power and data telemetry, power management, digital processing and electrical stimulation) and gets connected to the electrode array via a dense cable. Even with a highly integrated solution, the size of such system can be around 8×8 mm^2 [4] requiring a large incision, which can pose an implantation challenge in a small and delicate organ like the eye.

Retinal prostheses can be implemented using either HV or LV process. HV technologies allow us to have a high output voltage compliance, but increases the size and power consumption of the chip and limits its functionality. On the other hand, LV technologies reduce the area and power consumption and offer advantages for digital design, data telemetry and waveform programmability. However, the output current of such systems may be limited depending on the impedance of the electrode-retina interface.

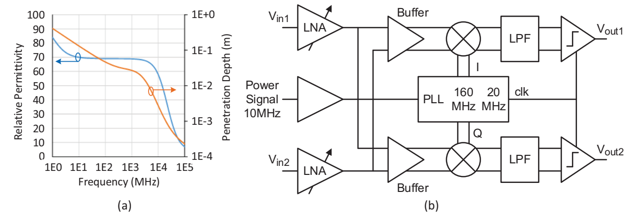

Fig. 5. (a) Electrical characteristics of the vitreous humor [13]. (b) Schematic of the data telemetry and clock recovery [7].

A possible approach involves a hybrid 2-chip solution using HV and LV technologies. In such a scheme, stimulator array and part of power management are designed in the HV process while data telemetry, clocking, synchronization and control logic are designed using a LV process. A possible design strategy to minimize the area and power consumption of the implant for a 2-chip system is as follow:

1) HV Chip: Simplify the architecture of the stimulator array by extensive use of digitally-assisted analog design and time-multiplexing of electrodes (i.e., only anodic and cathodic current DACs, muxes, level shifters, and registers).

2) LV Chip: It includes a low-power high-data rate data telemetry, a frequency synthesizer with adjustable phase, and control logic for self-calibration and adaptation of both chips. The size and power of this chip will be extremely small.

Another possible but completely different approach that can alleviate the size problem of implants involves miniaturization through folding and unfolding. Not only folding offers an efficient technological solution for size reduction and minimal surgical cut, novel origami designs can improve mechanical matching with retinal tissue enhancing the overall performance of the implant. In the next section we discuss this approach.

V. Origami Implants with Distributed Electronics

Our proposed origami design is a 3D integration technique that addresses the size and cost constraints of biomedical implants. Large systems can be split into many smaller chips and connected using 3D integration techniques to be folded compactly for implantation, and then deployed inside the body.

Retinal prostheses can particularly benefit from this approach given their challenging requirements. Instead of a single large chip, many micro-size low-cost chips are distributed over a flexible biocompatible thin film substrate along with the electrodes. Electrodes are micro-manufactured on the top surface of the film in a sub-array fashion. Each sub-array is connected to a microchip by parallel micro-manufactured electrical wires on the film. Power and ground are distributed via such wires avoiding sharp folds. The origami design will place chips facing each other across the fold and wireless (proximity) chip-to-chip communication can be used to reduce reliance on electrical wires [11]. As shown in Fig. 6(a), when inside the eye, the origami implant will take a curved shape to conform to the shape of the retina improving electrode contact for effective stimulation [12]. The location of the chips and electrodes can be optimized through the design of the origami structure. This high-performance system will achieve the following goals: allows minimally invasive surgery, closely

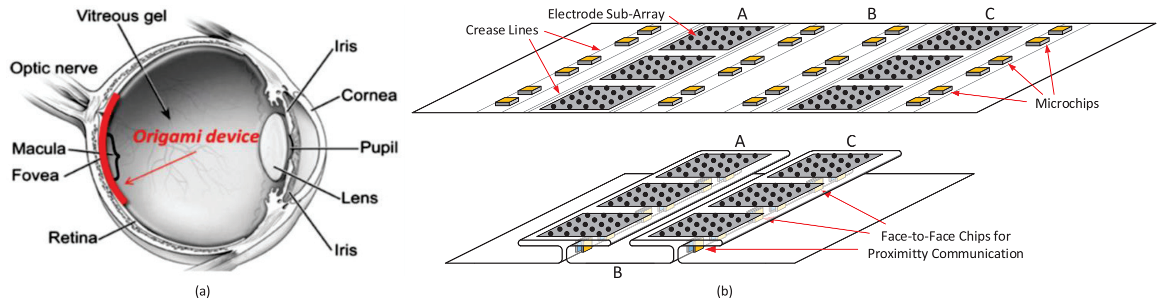

Fig. 6. Origami retinal prosthesis: (a) position in the eye and (b) Configuration of microchips and electrode sub-arrays before (top) and after (bottom) folding.

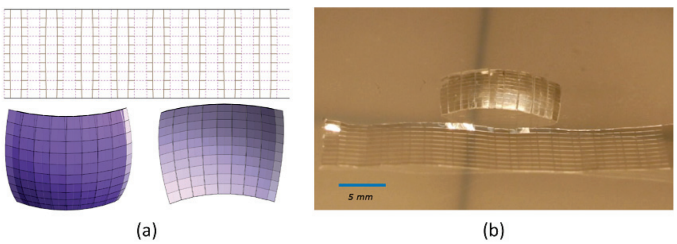

Fig. 7. (a) Crease pattern (top) and outer and inner views of curved surface (bottom). (b) Fabricated origami structure [12].

apposes electrodes to the retina, places all components within the eye, reduces the interconnect cable density, and enhances the yield and reliability of the system.

The flat film is designed to be folded in two different ways. First, it has to change shape from flat to spherical by creasing along a set of curved fold lines. Then it has to be folded or rolled into a cylindrical shape with a diameter of 1-2 mm to fit inside the surgical tool. Once inside, the design will be unfolded (or unrolled) to go back to the origami spherical shape. Fig. 7(a) shows a possible origami pattern and design for retinal prosthesis suitable for AMD patients. Starting from a flat sheet, the folded design conforms to the shape of the macular region (5-6 mm in diameter). Fig. 7(b) shows a prototype based on these crease patterns using parylene-C [12].

Proximity communication provides a compelling way to achieve wireless communication between the chips, as many of the chips can be placed close to each other and face-to-face. Because of its high sensitivity and ability to sense alignment, capacitive proximity coupling has been adopted. It provides a compact solution which supports high-data rates at extremely low power. In addition, it enables straightforward adaption of the link to changes in the alignment conditions as well as monitoring of the deployment status of the implant. A prototype of such scheme has been implemented in 65 nm CMOS and achieves data rates from 10-60 Mb/s with a power efficiency of 0.18 pJ/bit [11].

VI. Conclusion

Although retinal prostheses have successfully restored vision in patients suffering from advanced stages of retinal degeneration, their traditional implementation presents critical limitations that need to be solved for future generation devices. Fully intraocular implants are emerging as promising solutions to reduce area and power consumption and to avoid the use of a trans-sclera cable. However, as the number of electrodes increases, the size, power and cost of a single chip solution increase dramatically. Multiple-chip approaches provide means to work around such problems. In particular, origami implants have the potential to generate a high-performance system that is fully suitable for retinal prostheses. Enabling technologies such as capacitive proximity interconnect and parylene origami MEMS technolgy support the feasibility of this approach.

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