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Microelectronic Retinal Prosthesis: I. A Neurostimulator for the Concurrent Activation of Multiple Electrodes

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Abstract—**An application specific integrated circuit (ASIC) capable of delivering charge to multiple electrodes in unison has been developed. The ASIC is designed to function as part of an epi-retinal prosthesis driving an array of electrodes in a hexagonal mosaic. This unique organization of electrodes and the use of current sources and sinks is implemented to reduce the electrical cross-talk that occurs when many electrodes are activated in unison. Due to the large numbers of electrodes needed to provide useful vision to implantees, the interleaving strategies used in cochlear implants will not suffice for a vision prosthesis, where the "frame rate" is important for acceptable perceptual outcomes. This paper describes the design, and architectural approaches and performance testing of the developed ASIC.**

I. INTRODUCTION

IT has long been determined that electrical stimulation of the spiral ganglia in patients deafened by sensorineural loss can elicit auditory sensations. Similarly, stimulation of the retinal ganglion cells in select visually impaired patients can elicit visual sensations. The cochlear implant and its analogy in the visual system, have naturally followed from these discoveries with the prior having significantly improved the quality of life of many hearing impaired implantees. On the other hand, the current state-of-the-art vision prosthesis is as yet to realize a commercially available device capable of restoring "useful" vision, in large part due to the increased complexity of the visual system compared to the auditory system.

The majority of current cochlear implants operate by providing neural stimulation in a serial manner, in which a single stimulator is multiplexed across a small number of electrodes [1]. The use of a single stimulator allows for simplified electronic designs and removes the effects of electrical cross-talk between multiple stimulation sites [2], [3]. This cross-talk reduces the ability of an implant to accurately target neural elements and has been linked to decreased speech recognition in cochlear implant recipients [4], [5]. To overcome this, stimulation strategies such as Continuous Interleaved Sampling (CIS) have been developed that multiplex stimulation events at high frequencies (over 18000 pulses/second [6]) across a few electrodes, so that the implantee perceives sounds as if they occurred simultaneously [1].

The majority of vision prostheses have followed the lead of cochlear implants with the use of serial stimulators, but if future prostheses are to provide useful vision, multiple stimulators will be required to adequately drive a large numbers of electrodes. The critical observation to be made is that the channel numbers needed to restore vision (over 500) are far beyond those of cochlear implants (below 30). In simulations, Cha *et al.* found that a 25x25 array of pixels allows reading rates of approximately 100 words/min [7], [8]. Further studies by Hallum *et al.* have shown that by increasing the number of phosphenes in simulated vision from 100 to 525, a subject's facial recognition abilities increase from 63.8±11.5% accuracy to 90.7±6.8% accuracy [9]. In addition to this, stimulations need to occur above a certain rate, to convey continuous images that do not flicker, the critical flicker fusion (CFF) frequency. This CFF frequency has reported to be 40-50Hz for electrical stimulation of the retina [10]. If the vision prosthesis is to provide good clinical outcomes, one of two things must occur; serial stimulation rates must increase to the order of 26250 pulse trains per second (525 electrodes x 50Hz), or serial stimulation must be replaced by parallel stimulation. Multiple stimulators operating in unison can be used to allow sufficient electrodes to be stimulated at a rate in which conveyed images appear continuous and without flicker.

This paper describes an ASIC neurostimulator for an epi-retinal prosthesis that can drive 16 electrodes (14 bipolar electrodes and two monopolar return electrodes). This system can be scaled to drive 100 electrodes (98 bipolar electrodes and two monopolar return electrodes), using simultaneous stimulation of up to 14 electrodes, when up to seven ASICs are connected together. The ASIC is powered and controlled by a radio frequency (RF) link and contains features which have been shown to reduce the effects of cross-talk.

II. METHODOLOGY

The following section provides a brief overview of the main features of the ASIC and the driving forces behind their inclusion.

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A. Simultaneous Stimulation

The stimulation strategy that is proposed in this paper is a novel integration of the aforementioned serial and parallel methods. A fully parallel stimulation system in which each pair of electrodes is assigned a dedicated stimulator would allow for stimulation rates much higher than the required CFF frequency but would also result in increased cross-talk. Instead this ASIC contains a single stimulator for every seven electrodes. Each of the electrodes in these groups of seven are then stimulated in a sequential interleaved fashion. Due to their only being seven electrodes in a group, it allows the effective stimulation rate to be maintained above the CFF frequency. The design scales as for every addition of seven electrodes, only one additional stimulator is required.

The choice of one in every seven may seem arbitrary at first glance, but it allows the electrodes to be organized in a hexagonal fashion with an electrode in the centre acting as the stimulating electrode. This hexagon organization enables large electrode numbers to be tiled together seamlessly and more importantly, the surrounding electrodes effectively electrically guard individual stimulation sites from others, thereby reducing cross-talk substantially.

Fig. 1 illustrates a 49 electrode mosaic in which seven stimulators simultaneously inject charge into seven groups of hexagons. It is convenient to think of a set of seven electrodes (one stimulating, six return) as a functional unit. This functional unit can be moved such that the stimulating electrode is centered on any one of seven unique positions. When a stimulating electrode moves to the edge of the array less than six guard electrodes are available. This effect has been modeled (in unpublished work) with results showing that the remaining guard electrodes still significantly reduce electrical cross-talk compared to paired electrodes.

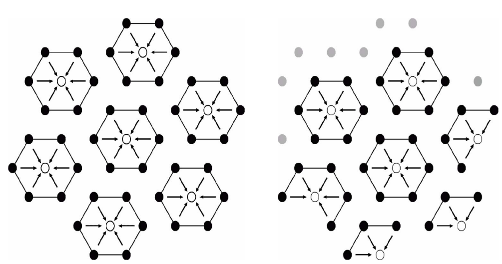

Fig. 1. (Left panel) The cathodic phase of a biphasic stimulation with 49 electrodes organized into seven hexagons. Current enters the surrounding black electrodes and returns through the centre white stimulating electrodes. (Right panel) The stimulation position and associated hexagon guard electrodes move to the bottom right electrodes of the initial hexagons. The stimulation position may be moved to seven unique positions. In the second, anodic phase of stimulation (not illustrated) current enters the white electrodes and returns through the surrounding black electrodes. The gray electrodes are unused and remain at a floating potential.

B. Pull, Push, and Push-Pull Stimulation

Conventional stimulation techniques inject current into a system by connecting the return electrode to the highest electrical potential in the neurostimulator, in this ASIC V_{stimulus}, and connecting the stimulating electrode to a current sink. The authors refer to this method of stimulation as "pull-mode" stimulation. The alternative to this is to connect the stimulating electrodes to the lowest potential and to connect a current source to the return electrode(s), referred to "push-mode" stimulation. For simplicity, the following discussion will refer to pull-mode stimulation only but the concepts are applicable to push-mode as well.

When multiple current sinks are active during simultaneous stimulation, each return electrode may provide current to any one of the current sinks. That is, there exists cross-talk between the active channels. In the example of Fig. 2, the filled circles denote stimulating electrodes connected to current sinks and the unfilled circles denote the return electrodes connected to V_{stimulus}. The top two electrodes are an active/return pair set to deliver 1mA of current and the bottom two are an active/return pair set to deliver 0.5mA, as indicated by the solid black lines. However, a scenario likely to occur for the top right electrode, is that the 1mA of current that it draws, will comprise of 0.75mA from its paired electrode, and 0.25mA from the bottom left electrode as indicated by the dotted line.

This cross-talk can ultimately lead to charge imbalance and damage across the target neural tissue. Cross-talk also reduces the ability to provide focused neural stimulation. While the exact response of a subject to a stimulation such as that of Fig. 2 is unknown, intuitively the ability of the neurostimulator to elicit closely packed phosphenes of differing intensities is reduced. If it is desired to convey a pattern composed of a bright phosphene superior to a dimmer phosphene, cross-talk may affect the delivered currents to the extent that an implant can only convey two phosphenes of equal brightness. When electrode numbers (in the form of active and return pairs) are extended to the hundreds, cross-talk will become much more complex and an image comprised of phosphenes of many differing levels of brightness may no longer be accurately conveyed in a parallel manner.

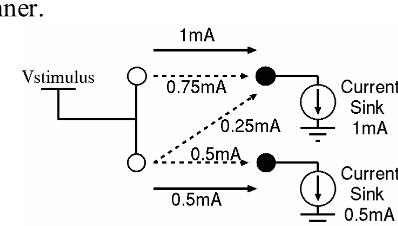

Fig. 2. A simple example of channel cross-talk in pull-mode stimulation. In contrast to the desired 1mA driven between the top electrode pair and 0.5mA between the bottom electrode pair (solid arrows), current shunting between the pairs (dotted arrows) may result. This is ultimately a consequence of the shared V_{stimulus}.

To create what the authors refer to as "push-pull-mode" stimulation, the return electrodes are connected to a current source set to deliver the same amount of current as the current sink, instead of V_{stimulus}. This is illustrated in the right panel of Fig. 3. The push-pull mode may not reduce the number of current paths between the electrodes but will control where the current is injected and recovered from.

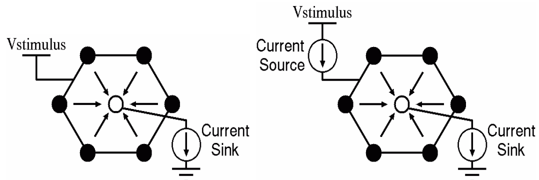

Fig. 3. (Left panel) Conventional pull-mode stimulation where a current sink is attached to the stimulating electrode with the guard electrodes connected to $V_{stimulus}$. (Right panel) Push-pull mode stimulation where a current sink is connected to the centre stimulating electrode and a current source is connected to the guard electrodes. The cathodic phase of a biphasic stimulation is illustrated. To recover the injected charge in the anodic phase, the return and stimulating connections are reversed.

C. Current Levels

The ASIC neurostimulator has three configurable stimulation current ranges, 20µA – 620µA, 40µA – 1.24mA (default), and 130µA – 4.03mA. The two lower current ranges have been implemented due to the relative uncertainty surrounding the charge needed to evoke a psychophysical response in both animal models and humans, and to allow a wide range of choices of electrode sizes and geometries. The highest current range has been implemented to allow the neurostimulator to be used for other functional electrical stimulation purposes. To ensure the upper current range is not inadvertently used in a visual prosthesis application, which risks destroying viable neural tissue, this range can only be activated by connecting an external pin on the ASIC to the logic power supply voltage.

D. Charge Recovery and Electrode Shorting

An accumulation of residual charge due to unbalanced biphasic stimulation can result in the damage of neural tissue [11]. To minimize the chance of this occurring, a balanced biphasic stimulation waveform is used. Unfortunately, (no matter how careful a neurostimulator is designed), imbalances in the waveform are inevitable, caused by slight differences in anodic and cathodic stimulation durations and current levels (even by a few ns or nA). By shorting all the electrodes to a common potential, a path is provided for this residual charge to be dissipated. Shorting the electrodes together also defines the pre-stimulus implant-tissue potential and if the electrodes are shorted to an appropriate potential, it ensures that the voltage at the output of the current source or sink is sufficient for them to operate in.

The electrodes can be shorted to the lowest electrical potential in the ASIC, V_{SS}, the highest potential $V_{stimulus}$ or to the "tissue reference potential", (a potential set midway between $V_{stimulus}$ and V_{SS}). For push-pull stimulation, the electrodes are shorted to the "tissue reference potential".

E. ASIC Control

The ASIC is fully configured and powered through a radio-telemetry link. The RF stream from this link is in the form of a fixed communications protocol that once received by the ASIC is decoded into data which sequentially set up internal registers required for a single, simultaneous event of stimulation. These registers are cleared at the end of every stimulation sequence. The use of a fixed protocol and minimum state across stimulations helps guard against corrupted data which may result in unwanted stimulations. Each stimulation protocol must begin with a "synchronization" sequence; if this is not received or too many or few RF pulses are received, the ASIC will reset and wait for a correct RF sequence to arrive. Power is obtained from the rectified RF stream.

F. Monopolar Stimulation

Drennan and Pfingst reported that monopolar stimulation provides better current level sensitivity in cochlear implants than bipolar stimulation [12]. Bipolar stimulation has been chosen as the default stimulation method as it has been reported to provide better localized current injection. In the current ASIC implementation, two monopolar electrodes have been implemented to allow investigation into the effects of a monopolar electrode on phosphene perception.

G. Anodic Scaling

Anodic scaling refers to a longer anodic phase of stimulation at a lower current setting than the initial cathodic phase. The same amount of charge is recovered, however as it is recovered at a lower current level, the likelihood of eliciting a second, unwanted action potential is reduced [13]. The ASIC can be configured to reduce the anodic current by a factor of two, four, eight, or 16 with the anodic stimulation phase time increased accordingly in real time, through the controlling RF data stream. Sharing the average injection current between the six hexagonal guard electrodes during the anodic phase should also limit the likelihood of unwanted action potential generation in the vicinity of the guard electrodes.

III. Results

A. Concurrent Stimulations

The ASIC was used to inject charge into a resistor mesh which allowed current to flow between any combinations of electrodes. The push-pull stimulation mode was chosen. In this resistor mesh, each electrode is connected to a common point through a 1kΩ resistance. Forty-two electrodes were analyzed and the current injected or returned through each electrode was measured and plotted in Fig. 4. To simplify figures only two out of the possible seven stimulators were set to a non-zero value. The injected current was 1.13mA into the right stimulation site, with 0.645mA being injected into the left stimulation sites. In all cases, full hexagon guards of electrodes, partial guards and single return electrodes, the injected current is returned equally through all the available return electrodes.

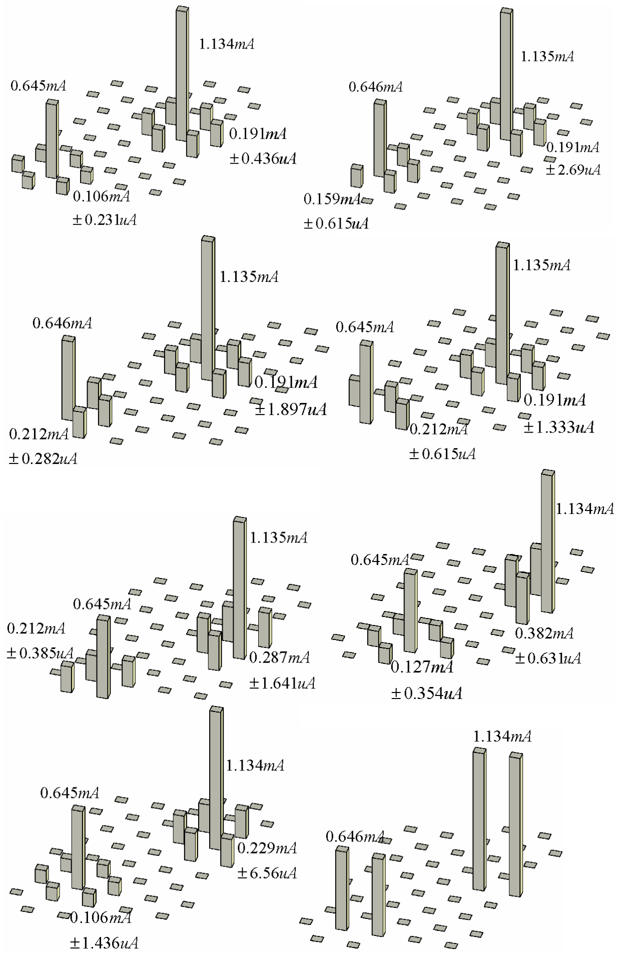

Fig. 4. Injected and returned current for a neurostimulator activating a resistor mesh using push-pull mode stimulation. For each of the eight mosaics shown, 1.134mA and 0.645mA are injected into two stimulating electrodes and returned through numerous proximal electrodes – full and partial guard electrodes. The bottom right panel illustrates the same current injection with only a single return electrode.

IV. Discussion

The injection of currents into a resistor mesh allows the ASIC's ability to inject and recover charge to be tested. The resistor mesh does not however, take into account the complexity of the electrode-tissue interface, the introduction of capacitive effects, and the multiple current paths that occur when injecting current into saline and neural tissue. The authors aim to further investigate the effects of parallel stimulation on saline and neural tissue with this device.

The following section will consider the psychophysical effects of parallel stimulation over serial stimulation. In normal human vision, millions of parallel pathways present information to the vision processing centers to allow perception to operate "at a glance". Serial stimulators would effectively paint an image in the implantee's visual field one phosphene at a time. This would place demands on the human visual system comparable to cognitive tasks such as piecing together a nine or ten letter word being presented one letter after another. While this task can be accomplished with mild concentration, the recognition of a visual scene is vastly more complex and will put a large amount of stress on an implantee's working visual memory. A parallel stimulator would better utilize the native parallel pathways of the visual system and hence provide implantees with better object perception through phosphenized vision.

V. Conclusion

An ASIC neurostimulator system capable of driving 100 electrodes (but scalable to many hundreds of electrodes) has been developed. Fourteen unique electrode sites can be stimulated simultaneously each surrounded by six guard electrodes to reduce electrical cross-talk. The ASIC is a first step towards understanding the effects of simultaneous stimulation on neural tissue, and the eventual therapeutic use of multiple-channel epi-retinal implants.

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