DEVELOPMENT OF THE ELECTRONICS AND ELECTRODES FOR A SAFE DIRECT CURRENT STIMULATOR

by
Patrick Ou

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ABSTRACT

Currently available commercial neuroprostheses are limited in their functionality by the necessity of biphasic pulsatile stimulation. Direct current (DC) has the capability both excite and inhibit neural activity; however, direct current cannot be applied directly to neurons due to the charge injection thresholds of electrode-electrolyte interfaces that when violated result in harmful, corrosive faradaic reactions. We are developing a Safe Direct Current Stimulator (SDCS) that safely applies ionic direct current (iDC). The design of the SDCS uses a series of eight valves in conjunction with four alternating current electrodes to rectify ionic current in microfluidic channels. The rectified iDC can then be directly applied to neural tissue without the issues associated with conventional direct current.

Although previous work has shown a functional proof of concept, the next generation of the device must be miniaturized to be viable as an implantable device. I designed and assembled the electronics of the device on a 23-mm circular printed circuit board (PCB). I then designed tests to confirm proper operation of the device. Analysis of the outputs confirmed the ability to cycle through the different valve and electrode configurations and provide a constant current level that is robust to changes in impedance.

The alternating current electrodes must be designed to ensure the rate of faradaic reactions are kept to a minimum. I fabricated electrodes with varying lengths of PtIr wire. I then designed and conducted preliminary experiments to verify their stability. These voltage waveforms were then analyzed and parameters related to the rate of faradaic reactions were extracted. The results of the experiments suggest that electrodes fabricated
from 30 cm of PtIr wire not only exhibited the lowest rate of faradaic reactions, but also did not experience significant changes over the course of 24 hours of constant stimulation.

Although this work outlines significant steps made towards the development of the SDCS device, aspects of the device such the accompanying microfluidic layer and ionic electrodes must be developed before a functional device can be assembled and tested. Upon completion, the device will then be tested for efficacy and longevity.

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CHAPTER 1

1.1 NEURAL STIMULATION THEORY

The nervous system facilitates communication between different regions of the body through the transmission of electrochemical signals. The main functional unit of the nervous system is the neuron, a specialized cell that is electrically excitable. The nervous system is composed of large, complex networks of interconnected neurons that communicate with each other in the form of action potentials. From a high level perspective, the nervous system is responsible for controlling the body: sensing of external stimuli, processing stimuli to determine an appropriate response, and coordination of muscle groups to enact the response [1].

![Diagram of a neuron and its interface to a second neuron.](image)

Figure 1: Diagram of a neuron and its interface to a second neuron. The neuron that is sending information along its axon is known as the presynaptic cell while the postsynaptic cell receives the information through either its dendrites or soma. [58]

Although multiple types of neurons exist, a typical neuron is composed of three structures: the cell body or soma, an axon, and dendrites. Dendrites and axons are extrusions from the soma, which houses the nucleus of the cell. Axons serve as the output to other neurons while dendrites serve as the inputs. The connection between the axon of
one neuron and the dendrite or soma of another is known as the synapse. When referring to the synapses, the neuron that is sending information through its axon is known as the presynaptic cell, while the neuron receiving the information through its dendrite is known as the postsynaptic cell [2]. The structure of a typical neuron and its interface with a neighboring neuron is shown in Figure 1.

Information in the nervous system is encoded in the form of action potentials, which are events during which a neuron’s transmembrane potential rises and falls in a predetermined manner. The transmembrane potential of a cell is defined as the voltage difference between its interior and exterior. A plot of transmembrane potential with respect to time during an action potential is shown in Figure 2. In the event of sufficient excitation of the soma or dendrites, this transmembrane potential can change, causing it to deviate from its resting potential (typically -70 mV). When the transmembrane potential reaches a threshold of approximately -55 mV, an action potential is generated. The beginning of an action potential is characterized by an initial period of rapid depolarization, followed by a period of rapid repolarization. The repolarization period causes the membrane potential to drop below the resting potential. This refractory period reduces the likelihood of any

![Diagram of an action potential](image.png)

Figure 2. Diagram of an action potential [3]
additional stimulation to evoke an additional action potential within a short period after the action potential is initiated. The transmembrane potential then returns to its resting potential of -70 mV [3].

The transmembrane potential of a neuron is not uniform, but varies between regions of the cell. Action potentials do not affect an entire neuron at once, but the depolarization of one region causes the depolarization of neighboring region, allowing the action potential to propagate from one region to another. Typically, action potential propagation begins at the soma of the neuron and propagates outwards along the axon. When the action potential reaches the synaptic terminals at the end of the axon, the axon of the presynaptic neuron releases neurotransmitters. The uptake of neurotransmitter of the postsynaptic neuron results in either hyperpolarization or depolarization of the soma of the postsynaptic neuron [2]. Sufficient depolarization results in an action potential being generated in the postsynaptic neuron. In networks of neurons, action potentials can be chained until the signal is ultimately received at the intended cell.

One of the primary characteristics of an action potential is its “all or nothing” nature. Changes in transmembrane potential that fail to reach the threshold level do not induce an action potential. Similarly, stimulation far past the threshold potential will yield the same amplitude action potential as stimulation that just reaches the threshold (This statement is only true up to a point, as extremely positive transmembrane potentials result in inactivation that render a neuron unable to generate an action potential). This property allows the system to be robust to noise, while also discretizing the information sent by neurons and simplifying information transfer between neurons [3].
Although neurons typically fire action potentials in response to the presence of neurotransmitter, action potential firing can also be induced through electrical stimulation. Neuromodulation, according to the International Neuromodulation Society, is “the alteration of nerve activity through targeted delivery of a stimulus, such as electrical stimulation or chemical agents, to specific neurological sites in the body.” [4] In this work I will be focusing on neuromodulation through electrical stimulation. This involves the manipulation of the transmembrane potential of a neuron, influencing the pattern of action potential firing. Current through electrodes influences the extracellular potential by the equation:

\[ V_e = \frac{I}{4\pi \sigma r} \]

where \( V_e \) is the extracellular potential, \( I \) is the current from the electrode, \( \sigma \) is the conductivity of fluid nearby the area of stimulation, and \( r \) is the distance from the electrode [5]. When this stimulation current is applied at an extracellular point source, a distribution of potential along the axis of the nerve forms, as shown in Figure 3a. According to classical cable theory, the induced extracellular potential results in regions of hyperpolarization and depolarization of the transmembrane potential along the axis of the nerve, depending on whether the current is anodal or cathodal [6]. The change in the transmembrane potential can be approximated by the activating function, which is the second derivative of the extracellular voltage with respect to the distance along the axis of the neuron from the site of stimulation. The activating function resulting from anodal and cathodal current is shown in Figure 3b and 3c as a function of distance from the stimulation site. If the electrode is passing anodic current, the region closest to the point of stimulation is hyperpolarized,
forming a real anode, while regions to the side of this central portion (referred to as side lobes) are depolarized to form virtual cathodes. In the case of cathodal stimulation, the central region forms a real cathode while the side lobes form virtual anodes [7].

Figure 3. a) The shape of the extracellular potential along the axis of an axon induced by an electrode passing current. b) The shape of the activating function from anodal current. c) The shape of the activating function from cathodal current. d) The transitions between the side lobes and main lobe occur 70 degrees apart from the point of stimulation. Shaded regions indicate depolarization, which results in a lowered threshold for action potential firing. Adapted from [6].

Depolarization brings the transmembrane potential closer to the threshold for action potential firing, while hyperpolarization brings the transmembrane potential further away from threshold. Therefore, anodal current, which hyperpolarizes the transmembrane potential, suppresses firing of action potentials, while cathodic current, which depolarizes the transmembrane potential, excites action potential firing. The presence of side lobes caused by virtual anodes and cathodes complicates these effects. When strength of the side
lobes, which is dependent on the distance from the electrode and amplitude of the current applied, reaches a certain threshold, the virtual anodes and cathodes present in the side lobes dominate the neural response, as opposed to the real anodes and cathodes [7].

1.2 EARLY NEUROMODULATION HISTORY

The use of electrical stimulation in the human body is not a modern occurrence, as the idea has been explored before the concept of electricity was fully understood. The earliest known recording of neural stimulation is from 46 AD, where Scribonius Largus advocated for the use of electric eels as a treatment of conditions such as gout, headache, and hemorrhoids [8]. Claudius Galen, a Greek physician and philosopher in the 2nd century, noted that electric fish produced no pain relief when eaten, but produced a numbing sensation when applied to patients while still alive. The use of electric fish for pain relief continued until the 19th century, and is still used today in certain non-Western cultures [9].

The 18th century saw a significant increase in the understanding of electricity and its effect on neural tissue. The invention of the Leyden jar, the first electrical capacitor, in 1745 allowed for charge to be stored, resulting in the proliferation of the use of electricity for medical purposes [10]. Luigi Galvani, known as the father of bioelectricity, discovered that direct current induced movement in the legs of a dead frog [11]. His contemporary and intellectual rival, Alessandro Volta discovered that current could be created through the use of two dissimilar metals. His discovery eventually led to the development of the voltaic pile, the first battery. In 1800, he connected two terminals from one of his batteries into both of his ears, reportedly hearing “a kind of crackling, jerking or bubbling as if some dough or thick stuff was boiling.” His experiment is the first known electrical stimulation of the human auditory system [12].
In 1831 Michael Faraday discovered the relationship between electric and magnetic fields. His research led to the invention of the induction coil, a type of electrical transformer which produced high voltage pulses from a direct current supply [13]. The induction coil became the basis of early neural stimulation devices. In 1863, French scientist Gaiffe developed a low voltage transcutaneous electrical nerve stimulation (TENS) device, using the induction coil as the pulse generator, that is considered a precursor to modern stimulation devices [14].

The modern era of electrical stimulation was preceded by a phase in which marketing took precedence over efficacy. In 1882, the Boston Globe advertised the Faradic Electrifier, another TENS device that stemmed from the development of the induction coil, as a miraculous cure-all device: “All cases of Rheumatism, Diseases of the Liver, Stomach and Kidneys, Lung Complaints, Paralysis, Lost Vitality, Nervous Disability, and Female Complaints are cured with the Electrifier! [14]” In 1919, the Electreat, another TENS device, was advertised to be used as a treatment of pain, but was also marketed for the “return of sleep, increase of strength and vital energy.” Eventually in 1938 the passage of the Food, Drug, and Cosmetic Act expanded the powers of the Food and Drug Administration in the US, placing medical devices under its jurisdiction [15]. After regulations were introduced, makers of TENS devices had to limit their claims about the efficacy of their devices to pain relief alone.

The invention of the transistor in 1947 at Bell Labs led to an explosion of technological advancement. The silicon transistor replaced the previously bulky and power inefficient vacuum tube technology that proceeded it. The invention of the transistor changed the scale at which electronics were developed, allowing electronics to be
developed orders of magnitude smaller than possible previously. The ability to miniaturize allowed for the development of fully implantable neuromodulation devices, ushering in the modern era of neuromodulation technology [16].

1.3 MODERN NEUROMODULATION TECHNOLOGY

1.3.1 Artificial Pacemaker

One of the most well-known neuromodulation technologies is the artificial cardiac pacemaker. According to a 2009 survey, over one million implantable pacemakers were in use worldwide [17]. Although external pacemakers did exist as early as 1950, the first implantable artificial cardiac pacemaker was implanted at the Karolinska Institute in Sweden in 1958 [18]. The purpose of an artificial pacemaker is to treat arrhythmias, which are irregularities in heart rate due to malfunctioning of the heart’s natural pacemaker. These irregularities can occur if the heart beats too slowly in the case of bradycardia, beats too quickly in the case of tachycardia, or has issues with the proper conduction of electrical signals in the case of heart block [19].

The device consists of a battery, an implantable pulse generator, and wires containing electrodes. The electrodes are fed through a large vein into the chambers of the heart that require stimulation, while the pulse generator and battery are typically implanted underneath the collarbone [20]. Two stimulation categories for pacemakers exist: asynchronous and synchronous. Synchronous pacemakers detect when a heartbeat has not occurred within a certain period of time after the previous heartbeat. If this condition is satisfied, the device will stimulate the heart with a pulse to cause contraction. This type of device is suitable for patients who possess normal heart function with some irregularities. Asynchronous pacemakers by contrast are always stimulating at a preset rate, regardless of
the patient’s normal heart rate. This type of stimulation is suitable for patients with consistent issues with heart rate such as permanent heart block [21][22]. Pacemakers can also be divided into categories based on the area of stimulation; single-chamber pacemakers stimulate either the right atrium or ventricle, while dual-chamber pacemakers stimulate both areas [23].

Figure 4 shows an example stimulation waveform of an artificial pacemaker. After an initial period of cathodic stimulation to induce a heartbeat, a delay occurs before switching to a recharge phase to avoid tissue damage. This anodic recharge phase occurs when the heart is in non-excitable state [24].

![Stimulation waveform](image)

Figure 4. Example stimulation waveform of an artificial pacemaker. The graph shows voltage as a function of time. Adapted from [24].

1.3.2 Cochlear Implants

One of the most prominent examples of modern neuromodulation technology is the cochlear implant. Cochlear implants are devices that electrically stimulate areas of the cochlea, an organ in the inner ear that converts vibrations resulting from sound waves into
action potentials. The cochlea is tonotopically organized, meaning that different regions of the cochlea correspond to different frequencies of sound. By stimulating different regions of the cochlea based on incoming sound, these implants enable deaf individuals with damaged portions of the outer and middle ear to partially regain a sense of hearing. The device bypasses the natural mechanisms for hearing of the outer, middle, and inner ear, stimulating the auditory nerves directly, as opposed to hearing aids that amplify the sounds while still utilizing the outer portions of the ear [25]. The first single electrode device was implanted in 1961 by William House and John Doyle in Los Angeles [10]. The first commercially successful cochlear implant was developed by Graeme Clark at the University of Melbourne in 1978 [10]. Since then, the technology has improved and its use became widespread, although the fundamental mechanisms behind its operation remain unchanged. In 2012, the National Institute on Deafness and Other Communication Disorders estimated that approximately 324,200 registered devices were currently implanted worldwide [26].

The device is composed of two modules: an external module and internal module. The external module houses a microphone that converts sound vibrations into electrical signals that are input to a signal processing block. This block converts the information into a digital representation of the cochlear stimulation pattern that corresponds to the input sound. The output of this block is transmitted through the skin into the implanted portion through an inductive link, which also serves as the mechanism for providing power. The internal module of the device decodes the information sent through the inductive link and coordinates the activity of electrodes to stimulate the cochlea in the desired temporal and spatial pattern [25].
Figure 5 depicts two examples of current waveforms applied to regions of the cochlea. The waveforms are charge balanced to avoid issues with tissue damage and electrode corrosion [25].

![Figure 5](image)

Figure 5. Two types of current waveforms applied by cochlear implants. Both example waveforms have both cathodic and anodic phases that pass the same amount of charge to avoid tissue and electrode damage. Adapted from [25].

1.3.3 Deep Brain Stimulation

Deep Brain Stimulation (DBS) is another application of neuromodulation that developed in the late 20th century. After Alim Benabid of the University of Grenoble discovered high frequency stimulation of the ventral intermediate thalamic nucleus had similar results to lesioning regions of the brain for the treatment of movement disorders, DBS became the preferred method of treatment for Parkinson’s disease [27]. Benabid’s research in 1987 prompted further exploration of the modality for the treatment of other diseases. Currently, DBS is used to treat a wide variety of conditions such as chronic pain, obsessive-compulsive disorder, and depression but is officially approved by the FDA for the treatment of essential tremor, Parkinson’s disease, dystonia, and obsessive-compulsive
disorder. While the exact mechanisms of action behind DBS are currently not fully understood, the benefits, at least for Parkinson’s disease and dystonia, are undisputed [28].

Deep Brain Stimulators are similar to pacemakers in that they possess electrodes that stimulate a certain region of neural tissue which varies depending on the intended treatment. The device is composed of similar components: an implantable pulse generator, a battery and the electrode with corresponding extension wire. The electrodes are placed deep within the brain through a small hole drilled in the skull, while the pulse generator is generally implanted below the collarbone. The implantable pulse generator generates a charge balanced biphasic pulsatile waveform (typically between 120-180 Hz with 60-200 μs pulse duration) that is delivered to the electrodes to stimulate the areas of interest [27]. In the case of Parkinson’s disease, the stimulation is thought to replace the inhibitory function of the substantia nigra to the subthalamic nucleus and globus pallidus interna [29].

An example a DBS waveform is shown in Figure 6. As with the other neural prostheses presented, the charge balanced nature of the waveform is necessary to avoid tissue death and premature electrode corrosion.

![Figure 6. Charge balanced biphasic stimulation waveform of a Soletra implantable pulse generator used for deep brain stimulation. Adapted from [59].](image)

1.3.4 Spinal Cord Stimulator
In 1965 Ronald Melzack and Patrick Wall introduced the gate control theory of pain, which asserts that activation of large diameter nerve fibers that carry non-nociceptive (non-painful) signals inhibit the transmission of pain signals. Soon after, C. Norman Shealy implanted the first spinal cord stimulator in 1967 for the treatment of chronic pain. The intended mechanism for spinal cord stimulation (SCS) was to stimulate the dorsal column, activating nerve fibers associated with non-painful stimuli to “close the gate” to pain signals [30]. Currently, approximately 34,000 new spinal cord stimulators are implanted each year [31]. The device is commonly used to treat neuropathic pain (resulting from damage to nerve fibers) associated with failed back surgery and ischaemic pain due to insufficient oxygen to tissue [31].

Although Shealy intended for spinal cord stimulation to function through gate control mechanisms, spinal cord stimulators are now thought to function through several mechanisms, not all of which are completely understood. The mechanism that Shealy proposed involved the stimulation of large diameter A-β nerve fibers associated with non-painful stimulation. The stimulation of these afferent neurons indirectly inhibits the activation of the A-δ and C nerve fibers associated with painful stimuli [32]. Animal studies have shown that the spinal cord stimulation also results in the activation of gamma-amino butyric acid and adenosine receptors, resulting in a reduction in pain [33]. Additional studies also suggest suppression of dorsal horn wide dynamic range neuron activity [34].

The most common type of SCS is comprised of four components: a pulse generator, a battery, a lead wire containing the electrodes for stimulation, and a form of external remote control. The entire device is implanted, with the electrodes placed in the epidural space above the spinal cord [35]. A non-rechargeable spinal cord stimulator generally has
a battery life of between 2 to 5 years, however newer rechargeable systems possess a longevity of 10 to 25 years [32].

Figure 7 shows an example of two types of commonly used SCS waveforms. The first waveform depicts tonic stimulation, which involves a constant set of pulses spaced evenly apart. A charge recovery phase follows each pulse to prevent tissue damage and electrode corrosion. The second waveform depicts the newer burst stimulation, which more closely mimics natural neuronal firing. Burst stimulation involves phases of higher frequency, lower amplitude (compared to tonic) pulsatile stimulation followed by phases solely dedicated to charge recovery. Both forms of stimulation are reported to result in similar reductions in pain perception, but the newer burst stimulation is less likely to induce paresthesia, which is a tingling, burning sensation that affects the areas in which pain is suppressed [36].

![Figure 7. Tonic and Burst stimulation waveforms typically used by spinal cord stimulators. The voltage is plotted with respect to time. Adapted from [36]]
1.4 SAFE DIRECT CURRENT OVERVIEW

Examination of the stimulation waveforms of the neuroprostheses presented in the previous section reveal a core characteristic of current neuromodulation technology: the reliance on biphasic pulsatile stimulation, in which electrodes have both a cathodic phase and an anodic phase to pass charge in both directions. This form of stimulation, while useful considering the success of current neuroprosthesis, possesses drawbacks that limit its usefulness in certain applications. Inhibition, a reduction in action potential firing, is difficult to achieve with these devices, as biphasic pulsatile stimulation necessitates both anodic and cathodic phases. At lower frequencies, the switching between these phases generates action potentials, making direct inhibition impossible at the site of stimulation. As a result, prostheses such as deep brain stimulators and spinal cord stimulators function through lateral inhibition, exciting neurons that have inhibitory projections to the neuron of interest rather than directly inhibiting the target neuron itself [37], [38]. If these inhibitory projections do not exist, inhibition is not possible. This methodology also results in phase locking to the stimulation frequency, as seen in Figure 8, which can be an issue if the natural firing pattern of the neuron needs to be preserved. At higher frequencies of approximately 1-30 kHz, biphasic pulsatile stimulation can result in neural block, in which action potentials cannot propagate across the blocked region of the axon. Neural block

Figure 8. Recording of action potential firing in a zebrafish neuron (top) as a result of pulsatile stimulation (bottom). The firing pattern clearly shows evidence of phase locking to the stimulation frequency. Adapted from [60].
originating from high frequency stimulation occurs after an initial excitatory phase ranging from 50 milliseconds to as long as 30 seconds [39]. Ultimately, the capabilities of biphasic pulsatile stimulation are limited to excitation and neural block. The reliance on biphasic pulsatile stimulation limits the capabilities of currently commercially available neuroprostheses, creating a gap in the applications in which these devices can be applied.

Using direct current (DC) as a means of neuromodulation possesses several advantages over biphasic pulsatile stimulation. The primary advantage is the capability to directly inhibit action potential firing. At low charge densities, anodic DC reduces neural sensitivity and spontaneous firing rate, while cathodic DC increases sensitivity and firing rate [40][41]. This capability allows for a graded response, as the amount of inhibition or excitation can be controlled by changing the amplitude of stimulation. At higher charge densities, DC is capable of producing a complete neural block[42]. Additionally, by modulating the chance of an action potential firing as opposed to directly inducing an action potential, DC produces an arguably more natural firing pattern that is not phase locked to a stimulation frequency (DC inherently does not possess a frequency). Ultimately, DC offers more versatility than biphasic pulsatile stimulation; direct excitation, inhibition, and neural block are possible within the same stimulation paradigm. Given these advantages, DC has the potential to augment the capabilities of current neuroprostheses that rely solely on biphasic pulsatile stimulation.
The primary drawback of applying DC to neurons is safety. When an electrode is placed in contact with tissue, as is the case with electrical stimulation, an electrode-electrolyte interface is formed. At these interfaces, charge moving from one phase to another must be balanced by charge moving in the opposite direction to avoid faradaic current. If this reversal does not occur, electrolysis occurs, resulting in issues such as bubbling, electroplating, corrosion of electrodes, and pH changes [5]. Figure 9 depicts the application of DC directly to electrode-electrolyte interfaces.

The amount of charge that can be passed in one direction through an electrode-electrolyte interface without causing faradaic reactions is known as the charge injection limit. DC violates this limit because charge always flows in one direction. Neurons cannot survive in the presence of the reactions caused by faradaic current, and thus neuromodulation has primarily revolved around the use of biphasic charge balanced stimulation in which the direction of current constantly changes. Unfortunately, the charge

![Figure 9. A diagram of the process of electrolysis. Application of DC across electrode-electrolyte interfaces results in oxidation and reduction reactions occurring at these interfaces. [61]](image-url)
injection limits of electrodes have made DC for the purposes of neuromodulation unusable outside of acute experiments. A 1 cm² platinum iridium electrode will start to cause significant faradaic reactions after passing 200 μA DC (value chosen from stimulation amplitudes used in our lab) for approximately 1.5 seconds. Figure 10 depicts the consequences of prolonged DC application to biological tissue.

If the safety concerns were addressed, direct current could potentially be used either by itself or in conjunction with biphasic pulsatile stimulation to allow neuroprostheses to be used in a wider range of applications. For example, DC has been used in combination with high frequency biphasic pulsatile stimulation to eliminate issues with onset activation typically associated with high frequency stimulation [43]. The potential utility of DC has
spurred development of methods for its safe application [44], [45]. For example, one method involves cycling stimulation patterns applied to multiple electrodes passing charge balanced waveforms such that the electrodes are only in contact with the nerve of interest during the anodic phase of the waveform. A complete DC nerve block, in which all action potentials were blocked, was achieved using this carousel configuration [45].

We are currently developing the technology for a direct current stimulator that can safely apply DC to neural tissue without violating the charge injection limits of electrode-electrolyte interfaces. We accomplish this through passing alternating current through an isolated fluid network and rectifying the resulting ionic current. The ionic direct current (iDC) can then in principle be applied directly to tissue without causing harmful electrochemical reactions at the metal electrode interfaces. Previous work has shown a proof of concept in a large-scale implementation using a series of tubes and hand operated valves. Figure 11 shows the results from previous designs, the SDCS1 (first generation) and SDCS2 (second generation) [46], [47]. SDCS1 demonstrated that rectification of ionic direct current using valves was possible; however, non-ideal valves (not instantaneously switching) produced interruptions in the current. SDCS2 compensated for valve actuation times by using one system to deliver the current while the second system switches its valve states. SDCS2 was successful in producing uninterrupted iDC. Following the development SDCS2, the focus of our work has shifted from presenting a proof of concept to designing a miniaturized functional prototype, with the eventual goal of creating an implantable neural prosthesis. In chapter 2, I will describe the development, implementation, and testing of the electronics of the SDCS device. In chapter 3, I will describe the design and
testing of the electrodes used to deliver alternating current waveforms to the microfluidic portion of the device.

Figure 11. (A-B) Proposed work from SDCS1 which uses two electrodes and four valves to rectify ionic current. Part A shows two states of the same device. The individual electrodes change polarity to achieve charge balance at the electrode-electrolyte interfaces, but the current that the tissue remains constant due to the changing configuration of the valves. Part B shows the output current from SDCS1 that possessed artifacts due to valve actuation time. (C-D) Proposed work from SDCS2 which uses four electrodes and eight valves to rectify ionic current. Part C shows one of the 12 states of the device. One side of the device provides the current while the other side of the device changes valve configurations. Part D shows the electrode configuration and current output from SDCS2. With proper operation, output no longer shows the artifacts present in SDCS1’s current waveform. Adapted from [46] and [47].
2.1 PRINCIPLES BEHIND IMPLANTABLE SAFE DIRECT CURRENT STIMULATION

The primary obstacle for non-pulsatile neuromodulation is inability of electrodes to pass current in the same direction without causing harmful faradaic reactions. The threshold after which these electrochemical reactions occur is known as the charge injection limit. Before this threshold is reached, the direction of current must be reversed. Our proposed method of bypassing this charge injection limit is to pass alternating current through the electrode-electrolyte interfaces, thus not violating the charge injection limit. Once in the form of ionic current, the alternating current can then be rectified into ionic direct current. This ionic direct current can be applied to tissue without risk of adverse faradaic reactions because there are no longer any electrode-electrolyte interfaces involved.

Multiple mechanisms for the rectification of ionic current exist, but the restrictions of implantable devices limit the viable options. One method of rectification of ionic current that was considered involves the use of ionic diodes to construct the ionic equivalent of a full bridge rectifier. Unfortunately, ionic diodes are only functional for current levels much lower than what is needed for neural stimulation. It was determined that a system utilizing valves that open and close to ionic current would be the simplest to implement effectively.

The exact mechanism of actuation for these valves is important for the viability of the device. While the original SDCS prototypes utilized hand operated valves, an implantable device must utilize a miniaturized solution. Mechanisms for actuation such as microelectromechanical systems (MEMS) and electroactive polymers were explored as potential solutions. MEMS solutions were determined to be unnecessarily complicated and
unsuitable for the amount of current we were looking to apply (up to 200 μA). Electroactive polymer valves generally require extremely high voltages to operate, making them unsafe for use in implantable devices. Nitinol wires were eventually chosen as the actuation mechanism for their simplicity and potential longevity. Although nitinol wire actuators are not power-efficient, the level of power consumption was determined to be acceptable for the purposes of an implantable device.

The size constraints placed on the device depend on the specific intended applications. Currently, we are exploring the use of safe DC in pain suppression, improvement of vestibular prostheses, and treatment of asthma attacks. Of these applications, augmentation of vestibular prostheses imposes the strictest size requirements on our device, as vestibular prostheses currently in clinical trials are designed to be implanted in the head outside of the skull [48]. These size constraints of these vestibular prostheses were derived from those of cochlear implants, which are implanted in a similar manner [48]. We decided to base the size constraints of the SDCS on the size of a commercially available cochlear implant.
In the interest of modularity, we have divided our device into four functional layers that are outlined in Figure 12. The power layer provides the power for the rest of the device. While the design of the layer has not been finalized, the layer will either contain the circuitry for providing power wirelessly or a rechargeable battery. The contents of the application specific electronics layer will depend on the desired application. For example, a vestibular prosthesis may require gyroscopes for sensing head rotations. This layer will output the amplitude of iDC needed for the specific application. The microfluidics layer contains channels filled with saline to provide a medium for ionic current. This layer will also possess valves that are actuated by nitinol wires to facilitate the rectification of the ionic current. The design of the nitinol valves have been adapted from the work of Vyawahare et al [49]. The microfluidics layer interfaces with the electronics layer, which contains all the circuitry necessary to operate the valves and pass alternating current to the electrodes. The electronics layer also contains circuitry to monitor and adjust current levels. This chapter will focus on the implementation of the electronics layer.
The proposed device uses a set of four electrodes and eight valves to produce rectified iDC. Although each individual electrode will pass a charge balanced waveform, the valves will control the path of the ionic current in such a way that the current the tissue experiences will always be in the same direction. The specific pattern of valve and electrode activation required to achieve iDC is outlined in Figure 13.

![Diagram of state machine implementation](image)

**Table 1.** State machine implementation for the SDCS. Ionic direct current is produced by cycling the electrodes and valves through the states listed in the table above. No matter the state, the direction of the current indicated by the red arrow remains the same. A primary goal of the SDCS is to reproduce this state machine implementation. Adapted from [47].

### 2.2 REQUIREMENTS

The overall goal of our work is to produce a device that can safely provide constant uninterrupted iDC to tissue. This section will cover the requirements of the electronics and the reasoning behind them.

#### 2.2.1 Power
The exact mechanism for power delivery will depend on the application. For convenience, we set a goal for the device to be capable of being powered by 3.7 V. This voltage corresponds to the voltage provided by rechargeable lithium ion batteries, which we intend to use for the initial in-vivo animal studies.

2.2.2 State Machine Implementation

To produce iDC, the device must be able to reproduce the state machine implementation described in Figure 13. This requirement encompasses being able to control the sequence of both switching of the active electrodes and operation of the valves.

1) Switching Active Electrodes

To reproduce the states described by Figure 13, the device must be able to switch which two of the four electrodes (E1, E1’, E2, E2’) are actively passing current. This switching must not disrupt current flow. The inactive electrodes must be disconnected from the rest of the circuit to prevent current from passing through them.

2) Valve Controllers
The requirements for the valve controllers (indicated by A, B, C, and D in Figure 10) stem from the design of the valves themselves. We chose nitinol wires for the actuation mechanism of our valves due to their long-term reliability and small footprint. When current passes through a nitinol wire, the wire contracts by 4% of its length [50]. When no current flows through the wire, it returns to its original length. These wires loop around portions of the microfluidic channels. When a wire is activated with current, it constricts the channel, reducing its cross-sectional area and therefore increasing its impedance. A sufficiently high impedance channel is considered a closed valve, while a low impedance channel is considered an open valve. A diagram of the intended function of these valves is shown in Figure 14.

![Diagram of the nitinol wire valve mechanism. A cross sectional area of the channel is shown. When current passes through the wire, it contracts, reducing the cross-sectional area of the channel and increasing its impedance.](image)

The device must be able to deliver current to the nitinol wires in the microfluidic layer to control the actuation of the valves. The manner in which the current is delivered to these wires is particularly important, as the nitinol wires have stress and strain requirements that are outlined by the manufacturer. From the viewpoint of the electronics, adhering to these stress and strain requirements mainly involves controlling the amount of current...
passing through the wires. Depending on the diameter of the wire, the manufacturer specifies a recommended current for a 1 second contraction time [50]. If the current is too high, the longevity of the wires suffers and power is wasted. If the current is too low, the wire will not contract optimally. Previous work in our lab suggest that if we follow this requirement for 1 second contraction time, the nitinol wires can withstand at least 500,000 cycles of expansion and contraction without degradation in functionality [51]. When using higher currents, a significantly degraded lifespan of 10,000 cycles was reported [49].

3) **Microcontroller**

A microcontroller must be used to control the sequence of valve operations and the switching of the active electrodes. The speed at which the device switches states is limited by the valve actuation time of approximately 1 second. As microcontrollers typically operate at time scales many orders of magnitude smaller than 1 second, any microcontroller with a small form factor and the necessary number of outputs should be suitable.

### 2.2.3 Current Feedback Mechanism

While the state machine implementation results in ionic current flowing in the same direction, it does not guarantee that the current provided will be of a constant amplitude. It is difficult to guarantee that every channel in the device will possess the same impedance, or that every valve will be able to close with the same effectiveness. When switching between the different current pathways associated with each state, one pathway could potentially have a slightly higher impedance than another, resulting in a different resistance and therefore different current for each state. Depending on the degree of these differences,
unwanted action potentials could be generated at every state transition, making the device unsuitable for neural control.

Ultimately, the variance in path resistance may be insignificant in the final design of the microfluidic layer. In the interest of having a robust design, the electronics of the device should ideally be able to compensate for these potential variances. The device should be current controlled such that the current to the tissue will remain unchanged regardless of the changes in the resistance of the channels. Unfortunately, the nature of iDC makes current control difficult. Typical current controlled circuitry relies on the use of a sense resistor placed in series with the current path to measure current flow; however, this is not possible with our device, as the non-ideal nature of our valves would make this measurement inaccurate. To illustrate this concept, we refer to the top portion of Figure 13, which shows the gate and electrode configuration for S1. In this state, most of the current will travel from E1’ to E1 through the tissue, but a small portion will instead leak through the closed A and C valves, which have a high but non-infinite impedance. To get an accurate measurement of the current going to the tissue, we must measure the current at a position either immediately before or after it has been applied to the tissue. To accomplish this, we require a mechanism to measure ionic current flow. This ionic current measurement can then be used to implement current control.

2.2.4 Form Factor/Miniaturization

To facilitate implantation, the device must be made as small as possible while still meeting the other requirements. We set a goal of having the PCB of the device be smaller than 25-mm by 25-mm (2 inch square). These dimensions are comparable to the MED-EL Synchrony cochlear implant, which has a 25-mm by 46-mm footprint [52].
2.3 CIRCUIT DESIGN

2.3.1 Block Diagram

![Block Diagram of Electronics and Microfluidics](image)

Figure 15. A block diagram of the electronics layer and its interfaces to other layers of the device. Layer 4 provides the input voltage that powers the entirety of the device, while Layer 3 provides a command regarding the amplitude (through \(V_{CTRL}\)) of iDC needed for the specific application. The electronics also receive a measurement of the iDC amplitude through the F+ and F- signals.

A block diagram of the electronics layer and its interface with the microfluidics layer is shown in Figure 15. The device is controlled by a PIC18F240 microcontroller programmed to cycle through the states described in Figure 13. This microcontroller controls the function and timing of the valve controllers and the current driver to produce the necessary outputs. The electronics layer takes in a measurement of the ionic current being generated through the F+ and F- inputs (complete mechanism for measuring ionic current described in section E of the circuit design) and adjusts the electrode voltages to produce a constant current.

2.3.2 Power Regulation

The power regulation block takes in the input voltage from the power layer referenced in Figure 12. Multiple step up and step down converters scale the input voltage to the appropriate voltages for the operation of the different integrated circuits. The input
voltage is first passed through a TPS61202 step-up converter, which can scale a wide variety of input voltages up to 5V, allowing the device to be powered by a 3.7 V lithium ion battery, while also providing some flexibility for other power sources. The 5V signal is scaled up with a RT8580 step-up converter to 25 V for use in the switching current driver.

The voltage that drives the current across the nitinol wires is provided by a variable step-down converter in the form of a RT5795A chip. The 5V signal is scaled down to an appropriate voltage, designated $V_{\text{Gate}}$, that is fed directly to the nitinol wires. We can adjust the exact voltage needed using a potentiometer, allowing fine tuning of the current through the wires to meet the stress and strain requirements. The 50 μm diameter nitinol wires in our valves require 85 mA for a 1 second contraction time, which corresponds to a $V_{\text{Gate}}$ of approximately 0.85 V for the 10-mm wires used in the microfluidic valve design.

2.3.3 Valve Controllers

A diagram of the valve design is shown in Figure 16. The current through each of the individual nitinol wires is controlled by the microcontroller using a transistor. $V_{\text{Gate}}$ is connected to one end of the nitinol wire, while the other end is connected to the drain of a

**Valve Controller**

![Diagram of Valve Controller](image)

Figure 16. A diagram of the valve controller circuitry. The nitinol wire functions similarly to a resistor. When a digital high is sent from the microcontroller, current can pass through the wire to cause it to contract. When digital low is sent, no current can pass through and the wire will expand to its original length.
transistor. The source of the transistor is connected to ground. When the output of the microcontroller is low, no current can flow from the drain to source of the transistor, and therefore no current can pass through the nitinol wire. When a digital high signal is sent to the transistor, current can pass through the wire allowing it to contract and close the channel.

2.2.4 Switching Current Driver

The final design of the switching current driver relies primarily on two multiplexors (implemented with a MAX14753 dual MUX) controlled by the same signal $S$, which is composed of two digital outputs from the microcontroller. The $S$ signal determines which electrode is connected to the high line (25 V) and which electrode is connected to the path to ground. The remaining electrodes form open circuits so no current can pass through them, making them inactive. For example, when the microcontroller sends a 0 to the multiplexors, the E1 electrode is connected to the high line while the E1’ electrode is connected to the path to ground. Although the E1 electrode is also connected to the 3rd output of MUX2, no current passes through that path because that output is currently not selected.

![Switching Current Driver](image)

Figure 17. (Left) Schematic of the switching current driver. The microcontroller sends a digital signal to two multiplexors to determine which electrodes are connected to the high and low lines. Note that every electrode is attached to an output capacitor connected to ground to prevent current interruptions due to MUX switching times. (Right) Depictions of the different electrode states due to different signals from the microcontroller.
Every electrode output is connected to a 0.01 μF capacitor attached to ground. The purpose of these capacitors is to filter the electronic noise associated with switching MUX states. A diagram of the entire switching current driver implementation is shown in Figure 17.

2.2.5 Current Feedback Mechanism

The device must utilize some sort of feedback to ensure a constant current. To implement this feedback, there must be an accurate measurement of the current being applied to the tissue. Normally this would involve placing a sense resistor in series with the tissue and measuring the voltage drop across this resistor; however, for our device, the measurement must be done while the current is still in the form of ions. To accomplish this, we placed a fixed length of tube filled with saline agar in series with the current path to the tissue. The tube has a fixed impedance (which can be calibrated based on the concentration of saline used) which allows it to function as an ionic sense resistor that we refer to as a current sensing element (CSE). Similarly to a sense resistor, we can measure the voltage

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![Diagram of the current feedback mechanism.](image)

Figure 18. Diagram of the current feedback mechanism. $V_{CTRL}$ is adjusted to control the current passing through the tissue. $R_{SENSE}$ refers to the resistance of the CSE. The feedback transistor and multiplexors are the same components referenced in Figure 14.
drop between the two ends of this tube to get a measurement of the current [46]. The ends of the CSE are terminated with small regions of metal tubing to provide soldering points for wiring. With this measurement, the rest of the feedback can be implemented on the PCB.

Figure 18 shows the full design of the current feedback circuit we implemented. The voltage signal from the CSE is connected to the F+ and F- signals and amplified by an AD8421 instrumentation amplifier. The output of this stage is limited to 5 V by a Zener diode to prevent damage to further stages (the output of the instrumentation amp can reach as high as 25 V).

This amplified signal is connected to a MCP6002 comparator that compares this signal to a control voltage \( V_{CTRL} \). The output of the comparator is passed through a low pass filter with a time constant of 100 ms. The output of the filter connects to the gate of a transistor in series with the overall current.

\( V_{CTRL} \) is an adjustable voltage that is used to control the amplitude of the current. If the current is too high the output of the instrumentation amplifier will be higher than \( V_{CTRL} \). The comparator will output a low voltage to the transistor to lower the current passing through it until the output of the instrumentation amp matches \( V_{CTRL} \). If the current is too low the output of the instrumentation amplifier will be lower than \( V_{CTRL} \). The comparator will output a high voltage to the transistor to increase the current, again until the output of the instrumentation amp matches \( V_{CTRL} \). This transistor is the same feedback transistor mentioned in the switching current driver in Figure 17. This configuration results in the output current scaling linearly with \( V_{CTRL} \). The low pass filter with the 100 ms time constant keeps the output of comparator from changing too quickly (which causes
oscillations in the output current) while also ensuring that the circuit will be able to respond appropriately to changes in resistance caused by valve state switching (which takes between 0.5 to 1 sec to occur). For the full implementation of the device, $V_{\text{CTRL}}$ is meant to be an input signal originating from layer 3, but in this iteration the signal was simulated using a voltage divider.

The maximum current that can be applied to the tissue, assuming 25V is sufficient for the impedance of the path, is described by the equation:

$$I_{\text{max}} = \frac{5V}{A \times R_{\text{CSE}}}.$$  \hspace{1cm} (1)

$R_{\text{CSE}}$ is the impedance of the CSE and $A$ is the amplification factor of the instrumentation amplifier. The relationship between $V_{\text{CTRL}}$ and the output current is described by the following equation:

$$I_{\text{out}} = \frac{V_{\text{CTRL}}}{A \times R_{\text{CSE}}}.$$  \hspace{1cm} (2)

For our testing, we kept $A$ at 1, while the impedance of the CSE was calibrated to approximately 5 kΩ.

2.2.6 Microcontroller Programming

The PIC18F2420 microcontroller is programmed to generate an interrupt approximately every 1 millisecond. Each state configuration described in the state machine implementation in Figure 13 is saved in the code that is uploaded to the microcontroller.
At every interrupt, the microcontroller checks its current state and sends the corresponding digital signals to both the gates and the dual MUX of the current switching driver.

State switching is implemented using a counter that is incremented every interrupt. When this counter reaches a certain threshold (which can be adjusted depending on the length of time we want the SDCS to remain in each state) the microcontroller switches to the next state in the sequence and this counter is reset to 0.

2.3 METHODS

This section will cover testing the electronics layer for proper functionality. We could not test the electronics layer with the full microfluidics layer because the microfluidics layer is still in development; however, we tested the capability of the electronics layer to provide the necessary outputs that when interfaced with the microfluidics layer will be able to produce iDC. Where necessary, we simulated parts of the microfluidics layer with tubes filled with saline agar to facilitate ionic current. The testing of the electronics layer was divided into two modules: the state machine implementation testing and the current output testing.

2.3.1 State Machine Implementation Testing

Proper functionality of the finite state machine was confirmed by monitoring the outputs of the device and constructing a timing diagram based on the resulting waveforms with the states described in Figure 13. For the valve controllers, the metric of interest is the current through nitinol wires. For our testing, the 10 mm long, 50 μm diameter nitinol wires used in our valve design were simulated with 10 Ω resistors. The differential voltage across each individual valve resistor was measured and converted to current. For the switching current driver, 6 kΩ sense resistors were placed in series with each electrode output. Every
electrode was then immersed in a 0.9% saline to simulate the interconnections between the electrodes in the microfluidic layer. For every electrode, the voltage across the sense resistor was measured and converted to a discretized measurement (the magnitude of the current is unimportant for the purposes of the timing diagram). A 1 indicated that the electrode was connected to the high line, a 0 indicated that the electrode was disconnected, and a -1 indicated that the electrode was connected to the path to ground.

The output measurements were taken over a period of 25 seconds, with the phase transitions programmed to occur every second, to ensure all 12 states were captured. These measurements were taken using a Measurement Computing 1608G DAQ sampling at a rate of 1000 samples per second.

2.3.2 Current Output Testing

The current output of the electronics was tested to ensure that our device will not produce any interruptions in current flow that could potentially generate unwanted action potentials in the target neural population. During normal operation, these interruptions occur during the state transitions. We divided our initial state machine implementation described in Figure 13 into two types of state transitions. The first transition type occurs when the active electrodes remain the same, but the configuration of the gates changes. States 2, 3, 5, 6, 8, 9, 11 and 12 fall under this classification. These transitions can potentially cause a change in resistance in the microfluidic channels, which must be compensated for by the current feedback mechanism. The second transition type occurs when the gate configurations remain the same, but the electrode configuration switches. States 1, 4, 7, and 10 fall under this classification. These transitions can potentially cause interruptions if the non-instantaneous switching time of the MUX is not properly accounted
for using output capacitors. A series of two experiments were designed to test the capability of our device to produce uninterrupted iDC despite changes caused by these transitions.

The first experiment was designed to test the current response to a changing resistance path. The microfluidic path (tissue resistance + microfluidic circuit resistance) was simulated using a tube filled with 1M saline agar. The CSE was implemented as a small length of the agar filled tube with electrodes placed a fixed distance apart such that there was a constant resistance between the two electrode sites. The resistance of the path

![Diagram](image.png)

Figure 19. (Top) Diagram of the experimental setup for testing the changing resistance current. A tubing clamp is used to vary the resistance of the tube, while the CSE acts as an ionic sense resistor. (Bottom) Diagram of the experimental setup for testing the electrode switching current. The high line electrode switches between E1 and E2.
(outside of the region used as the sense resistor) was changed by using a tubing clamp to change the cross-sectional area of the tube. We varied the resistance path using the tubing clamp at a time scale similar to the valve actuation time of approximately 0.5 seconds. The voltages were measured across the CSE and across the region of tubing with the tubing clamp. The top panel of Figure 19 shows a diagram of the experimental setup.

The second experiment was designed to test the current response to switching the active electrodes. The E1 and E2 electrodes are submerged into a petri dish filled with 3M saline (Lower concentrations will be used in the final design. High concentration was used here to ensure conductivity for testing purposes, as the focus of the experiment was the electronic noise due to MUX switching). One end of the CSE, implemented in the same manner as the first experiment, was connected to the petri dish, while the other end was connected to a 5 kΩ sense resistor used to calibrate the impedance of the CSE. The other end of the sense resistor was connected to both the E1’ and E2’ electrodes. The voltage was measured across the CSE, which was tuned to have an impedance of approximately 5 kΩ, to determine the current. The output was recorded both with and without the output capacitors to both ensure that the transition artifact exists and that they have been removed from the final waveform. The bottom panel of Figure 19 shows a diagram of the experimental setup.

The measurements for the first current output experiment were taken using the Measurement Computing 1608G DAQ. Due to the limitations of the sampling rate of the DAQ, the measurements for the second current output experiment were taken using a Tektronix TDS 1001B oscilloscope.

2.4 RESULTS
2.4.1 Form Factor/Miniaturization

The current design is assembled on a circular PCB approximately 23 mm in diameter. An image of the assembled electronics layer can be found in Figure 20.

![Image of the assembled SDCS electronics layer compared to a U.S. quarter. The electronics were assembled on a 23-mm diameter circular printed circuit board.]

2.4.2 Timing Diagram

Figure 21 shows the timing diagram of the outputs of the valve controllers and the switching current driver. The results are consistent with the state machine implementation described in Figure 13.
2.4.3 Current Output Measurements

Figure 22 shows the response of the circuit to changes in resistance. The blue line shows the voltage across a sense resistor in series with the tissue path (and therefore the current) while the red line shows the voltage across the simulated tissue path. Despite the
changes in the resistance of the path indicated by the red line, the current through the path (blue line) remains constant.

Figure 22. Current response to changing resistance. The red line corresponds to the differential voltage across the entire current path, while the blue line shows the differential voltage across the CSE. Despite the changes in the resistance path, the current through the CSE remains constant.

Figure 23 shows the current output of the electronics layer in response to the switching electrodes. In the first panel, the output capacitors are removed intentionally to contrast the otherwise stable output. The resulting current waveform shows a disruption in the current flow caused by the switching of the active electrodes. The bottom panel of Figure 23 shows the current output with the output capacitors implemented. The resulting waveform no longer shows evidence of interruptions caused by the electrode switching.
2.5 DISCUSSION

Our design was successful in producing the necessary outputs required to produce iDC. The circuit we have constructed can reproduce the necessary states described in the state machine implementation. We show that the system can produce a constant current amplitude despite changes in the gate configuration of the electrode configurations. The footprint of the electronics has been reduced to a 23-mm diameter circle. Ultimately our design for the electronics has met our requirements for developing the miniaturized prototype.
CHAPTER 3

3.1 INTRODUCTION: ELECTRODE OVERVIEW

The prevalence of biphasic pulsatile stimulation in electrical stimulation stems from the properties of current flow through electrode-electrolyte interfaces. An electrode-electrolyte interface can be modeled as capacitor and a resistor in parallel. When a voltage is applied across this interface, current flows through both components at different rates. Current through the capacitive component corresponds to charge redistribution, in which no electron transfer between the electrode and electrolyte occurs. Current through the resistive component corresponds to faradaic reactions in which the electrode either reduces or oxidizes the ions in the electrolyte, eventually leading to electrode corrosion and tissue death. When current is passed in one direction through such an interface, initially the current primarily flows through the capacitive component, charging the capacitor by increasing the voltage difference between the electrode and electrolyte. As the voltage difference increases, the current flow transitions from charging the capacitive component

![Figure 24. A simplified model of an electrode-electrolyte interface. Current through the capacitive component can be considered charge storage, while current through the resistive component can be considered charge dissipation. From [5].]
to being dissipated through the resistive component [5]. To minimize faradaic reactions, the direction of current must change to discharge the capacitive component. Exactly how quickly the change in current direction must occur is dependent on the characteristics of the electrode, the amplitude of current, and the desired longevity of the electrodes.

The SDCS functions by passing a charge balanced biphasic waveform through a set of electrodes and rectifying the resulting ionic current, avoiding the issues with faradaic reactions due to DC at the electrode-electrolyte interfaces. However, simply passing a charge balanced waveform does not prevent the occurrence of significant faradaic reactions. The electrodes and current waveform must be designed such that the level of faradaic reactions does not result in premature electrode corrosion. For the SDCS, the current waveform is predetermined by the state machine implementation described in the previous chapter. As the waveform cannot be changed, ensuring that minimal faradaic reactions occur at these electrode-electrolyte interfaces primarily involves optimizing the design of the electrodes.

When designing the electrodes for an implantable device, it is important to determine what level of faradaic reactions is considered acceptable. Unfortunately, it is impossible to ensure that no faradaic reactions occur, as any charging of the capacitive component of the electrode-electrolyte interface will result in faradaic reactions. What is important in electrode design is not the prevention of faradaic reactions altogether, but rather ensuring that the faradaic reactions do not result in electrode corrosion in the time scale of the desired application. To be viable as an implantable neural prosthesis, the SDCS must possess electrodes capable of passing the predetermined current waveform for a time
period on the order of years. The rate of faradaic reactions must be low enough such that any changes in the electrodes occur at a time scale on the same order of magnitude.

Much of the analysis of an electrode’s characteristics can be condensed into one parameter: the charge storage capacity also known as the charge injection limit. The charge storage capacity refers to the amount of charge that can be passed through an electrode in one direction without causing large amounts of faradaic reactions [5]. The charge storage capacity is an intrinsic property of a material, usually given in the form of charge per unit area. Although this measurement is not all encompassing, particularly because there is no time component, the metric is widely regarded as a starting point for electrode design.

An ideal electrode for the SDCS would be fabricated from a material with a high storage capacity per unit area. In terms of the shape of the electrode, geometries possessing high surface area to volume ratios without compromising structural integrity are preferred. In terms of size, smaller electrodes are preferable to larger electrodes; as the electrode size grows larger the microfluidic channels that accommodate them must also increase in size. The optimal electrode would be large enough to possess an adequate charge storage capacity while small enough such that final dimensions of the device are still appropriate for the intended applications.

Properly functioning electrodes are essential to the viability of the SDCS. This chapter will focus on the design, fabrication, and preliminary testing of these electrodes.

3.2 DESIGN CONSIDERATIONS
The design of the electrodes involves the manipulation of factors such as the size, shape, and material to reach an adequate charge storage capacity. This section will outline the electrode design process.

3.2.1 Charge Storage Capacity

The first step we took in designing the electrode was determining the necessary charge storage capacity. The charge storage capacity required for the SDCS is determined by the current waveform the electrodes must pass. In its current implementation, the electronics of the device remain in each of the 12 states for approximately 0.5 seconds, chosen to correspond to the actuation time of the nitinol wires in the microfluidic valves. Each current configuration lasts for three states, and there are four current configuration phases total. Assuming no leakage currents, the active electrodes will alternate between passing cathodic and anodic 200 μA, with a pause between the two phases during which no current is passed. Each electrode therefore experiences the periodic waveform shown in Figure 25.

![Charge balanced waveform for the electrodes. 200 μA are passed for 1.5 seconds in both the anodic and cathodic phases of the waveform.](image)

From this waveform, we can determine the amount of charge passed during one phase before reversing the polarity. Both the anodic and cathodic phases require 200 μA for 1.5 seconds, necessitating a charge storage capacity of 300 μC.

3.2.2 Electrode Material
The choice of electrode material greatly influences its charge storage capacity. As previously mentioned, the charge storage capacity is an intrinsic characteristic of a material. Ideally, the SDCS electrodes would be made of a material that has the highest charge injection limit possible without sacrificing usability. Unfortunately, many materials possessing high charge storage capacities also possess undesirable properties. For example, tantalum, while having a high charge injection limit of approximately 700 uC/cm^2[53], cannot be reverse biased, and thus cannot be used as our electrode material. Other materials such as copper cannot be used due to their toxicity to biological tissue [5].

Platinum iridium (PtIr) wire was chosen for the electrode material because of its high intrinsic charge storage capacity per area and its widespread use in electrical stimulation due to its biocompatibility and safety. PtIr wire possesses a charge injection limit of approximately 300 uC/cm^2 [54].

Other potential materials do exist that may be well suited for use in the electrodes. Activated iridium oxide possess a higher charge injection limit than PtIr and is also used extensively in electrical stimulation. Surface coatings with a high surface area material known as platinum black can also increase the charge injection limits of electrodes. However, the preliminary nature of these experiments combined with the prohibitive cost of these materials led us to focus solely on PtIr until the experimental procedures a finalized. Further exploration of the electrode design will include alternative materials to PtIr.

3.2.3 Shape

Using the charge injection limit of platinum iridium, the appropriate length of wire to use was determined using the equation
\[ \text{CSC} \cdot l \pi d = I \cdot t \quad \text{or} \quad l = \frac{I t}{\pi d \text{CSC}} \quad , \] (3)

where \( l \) is the length of the platinum iridium wire, \( \text{CSC} \) is the charge storage capacity of platinum iridium, \( t \) is the amount of time spent in one phase, \( I \) is the current amplitude during that phase, and \( d \) is the diameter of the wire. Assuming a \( \text{CSC} \) of 300 \( \mu \text{C/cm}^2 \) and a wire diameter of 0.127 mm, a length of 25 cm was calculated to be the necessary length to pass 200 \( \mu \text{A} \) for 1.5 seconds.

The SDCS electronics layer, which interfaces with the microfluidics layer that houses these electrodes, is assembled on a 23-mm diameter PCB. The microfluidics layer will have similar dimensions. In order to have electrodes made from 25 cm of wire, some modification of the wires must be done in order to have all four electrodes fit into the microfluidic layer. We decided to coil the wire tightly around a 1.5 mm diameter rod to minimize the required volume for each individual electrode while preserving the surface area.

3.3 METHODS

The electrodes were designed primarily through the analysis of the charge storage capacity. However, as previously mentioned, charge storage capacity does not encompass every aspect of electrode design; an electrode can obey the charge storage capacity criteria and still produce extensive faradaic reactions and undergo rapid corrosion. The charge storage capacity parameter does not include a time component, which will be important for the purposes of the SDCS as the current waveform has long period relative to the waveforms used in other forms of stimulation [25]. Additionally, tightly coiling the electrode may decrease the effective surface area for the electrode when compared to a cylindrical wire. For these reasons, we deemed it necessary to test a variety of electrode
wire lengths and assess their performance under typical SDCS operating conditions.

It is important to note that typically, design of electrodes involves the use of cyclic voltammetry, in which the current passing through an electrode is measured as a function of the applied voltage. Conventional cyclic voltammetry linearly sweeps through the water window, the range of voltages in which no reduction or oxidation of water occurs [5]. Through analysis of the resulting graph of current vs voltage, certain characteristics such as the charge injection limit and the presence of irreversible faradaic reactions can be ascertained [55]. We chose not to use cyclic voltammetry for the preliminary experiments, as we wished to test the electrodes in conditions closer to operating conditions. Cyclic voltammetry will be added in future testing stages.

3.3.1 Fabrication

The electrodes were fabricated with 36 AWG (0.1270 mm diameter) PtIr wire. The desired length of wire was tightly coiled around a 1 mm diameter rod to produce a low volume, high surface area electrode. An excess of wire was left at one end of the coil to facilitate soldering to normal copper wire. Only the PtIr portion of the wire was in contact with the electrolyte.

Although we calculated that the necessary electrode wire length was 25 cm, we wanted to optimize the electrode length to ensure minimal faradaic reactions. We fabricated electrodes of 5, 10, 15, 20, 25, and 30 cm length PtIr wire. These lengths were chosen to provide a distribution of electrode lengths within the same order of magnitude as the calculated value. Additionally, one 5 cm copper electrode pair was added to the electrode array as a control.
3.3.2 Testing

The overall goal of the electrode testing is to ensure that our electrodes will be suitable for use with the SDCS. For this reason, the testing conditions should emulate the operating conditions as closely as possible. A test chamber made from polydimethylsiloxane (PDMS) was designed to reproduce microfluidic layer conditions. The PDMS test chamber possessed three channels with each channel containing two regions at each end for electrode placement. Each channel contains a region for saline to
provide an ion path between the two electrode sites. The outer edge of the device has a raised lip to facilitate the addition of a layer of mineral oil over the channels to prevent evaporation.

Two electrodes were submerged in the one of the three channels of the PDMS testing layer such that only the PtIr portion would be submerged in electrolyte. The channel was filled with 3M saline to facilitate conduction (The impedance of the fluid is irrelevant for a current controlled system if adequate voltage is applied). A thin layer of mineral oil was administered to the top of the PDMS testing structure to impede evaporation. The PDMS testing chamber was then placed into a petri dish with 3M saline such that the saline surrounded the PDMS but did not come into contact with the mineral oil layer or the saline in the channels. The surrounding saline was introduced to increase the humidity of the system to further impede evaporation of water inside the test channel. The top of the petri dish was used to enclose the experimental setup and parafilm was used to seal the container.

The charge balanced waveform described in Figure 25 was continuously applied for 24 hours to both electrodes such that when one electrode was in its anodic phase the other was in its cathodic phase. A 5 kΩ sense resistor was placed in series with the current

![Diagram](image)

Figure 28. Diagram of the experimental setup for the electrode testing. The voltage across the two electrodes and the voltage across the sense resistor is measured.
path to ensure the proper amplitude was being applied. The voltage difference across the electrodes was measured for a 10 second window every hour for 24 hours using a Measurement Computing USB 1608G DAQ interfaced with LABVIEW software. Additionally, pictures of the experimental setup were taken at the time of measurement for some of the experiments to capture any bubble formation or visible changes.

3.3.3 Metrics of Interest

The determination electrode efficacy is dependent on two factors: the rate of faradic reactions and stability over time. The presence of excess faradaic reactions was determined through analysis of the voltage waveform corresponding to either the cathodic or anodic phase of the electrode. Figure 29 illustrates the different voltage responses to a current controlled waveform. If the current is purely capacitive, the voltage measurement across the electrodes should change linearly with time, as all the charge contributes to the change in voltage of the capacitive component. If there is a significant portion of the current causing faradaic reactions, either reversible or irreversible, the voltage measurement will deviate from a linear measurement with respect to time.

![Figure 29](image_url)

Figure 29. a) The voltage response that corresponds to purely capacitive charging. b) The voltage response in the presence of capacitive charging and reversible faradaic reactions. c) The voltage response in the presence of irreversible faradaic reactions. Although the current waveform applied is different than that of the SDCS, the basic principle expressed is that if the voltage response is straight, no faradaic reactions occur. Adapted from [5].
We assessed the quality of the electrodes through analysis of the degree of linearity of the voltage waveform. We defined a metric called the linear ratio, which is the ratio of the length of the voltage waveform for one phase to the length of the straight line the beginning and end points of the voltage waveform. It is important to note that “length” is not defined by default, so we must transform the x and y axis of the voltage vs time graph into a Euclidean space. We defined one volt as one unit in the y-direction and one second as one unit in the x-direction. To calculate the length of the waveform, we summed the Euclidean distance between each sample of the waveform. To determine the ideal line length, we calculated the Euclidean distance between the first and last sample. Waveforms that are close to linear will have a ratio of approximately one, while waveforms with deviations from linearity will have linear ratios higher than 1.

The second metric we used to assess electrode quality was the voltage envelope. In general, a smaller voltage envelope is more desirable than a larger envelope, as the rate of faradaic reactions is heavily influenced by the overpotential of an electrode, which is defined as the difference between the electrode’s potential and its potential at equilibrium (with no current passing between the electrode-electrolyte interface) [56]. Current causes the capacitive component of the electrode to charge, increasing the magnitude of its overpotential. The voltage envelope was calculated by determining the maximum and minimum voltages within one period of the current waveform, which are the voltages across the electrodes at the end of the anodic and cathodic phases. As the electrodes
increase in length, we expected the voltage envelope to decrease due to higher capacitance from increased surface area.

Not only is the size of the voltage envelope important, but also its change over time. An unstable electrode will produce unstable voltage envelopes, as the changes in the electrode such as pitting can affect parameters such as an electrode’s effective surface area. For this reason, we will also consider the percentage change in the voltage envelope in our assessment of electrode quality. We expected longer electrodes to exhibit less change over time. Ideally, the electrodes used for the SDCS will either not change over time or change very slowly such that frequent replacements will not be required.

The images taken of the experimental setup at the time of recordings were visually inspected for changes. Any bubble formation, visual changes in the electrode, or discoloration of the surrounding saline indicated the presence of significant amounts of faradaic reactions.
3.4 RESULTS AND DISCUSSION

Figures 30 and 31 depict the resulting voltage waveforms (across the electrodes) of the copper, 10 cm PtIr, 20 cm PtIr, and 30 cm PtIr electrodes after 0, 12, and 24 hours of stimulation with the current waveform described previously. The blue lines indicate the
voltage difference across the electrodes while the orange lines show the voltage drop across a 5 kΩ sense resistor in series with the current path through the electrodes. Note that there is a small spike in the current flow when the electrodes go from the resting phase to passing
either positive or negative 200 μA. We deemed these spikes to be insignificant because they did not produce disruptions in the voltage waveforms.

The electrodes made of normal copper wire produced results that were consistent with the symptoms of faradaic current. The voltage waveform changed significantly over the course of 24 hours. Additionally, the voltage waveforms for the copper electrodes showed significant deviations from a linear change in voltage with respect to time for both the anodic and cathodic phases. During testing, the copper electrodes exhibited bubble formation and a blackening of the surrounding fluid (see Figure 32). These results indicate that, as expected, significant faradaic reactions occurred, resulting in changes in the electrodes over time.

For the PtIr electrodes, the shapes of the voltage waveforms suggested a correlation between electrode length and quality. From visual inspection of the three PtIr electrodes shown above, the longer electrodes exhibit less change over time in the shape of the voltage waveforms.
waveforms. Additionally, the longer electrodes exhibit voltage responses that are more linear with respect to time during the cathodic and anodic phases of stimulation.

Figure 33. Plot of the linear ratio vs time. We have defined linear ratio as the ratio between the length of one phase of the voltage waveform vs the ideal electrode waveform length.

Figure 34. Plot of the final % change of the linear ratio vs the electrode length. The asterisk on the y axis refers to the linear ratio value of the copper electrodes.
Figure 35. Voltage Envelope across the electrodes vs. time. Smaller voltage envelopes are considered better than larger voltage envelopes.

Figure 33 shows the linear ratio with respect to time of all the electrodes included in the study. All the electrodes except for the 30 cm PtIr exhibit a change in their linear ratios that improves over the course of 24 hours, suggesting a change in capacitance due to corrosion. At the end of 24 hours, longer electrodes had linear ratios closer to 1. The 30 cm

Figure 36. The percentage change of the voltage envelope. The percentage change is defined as the absolute value of \((V_{E\text{original}} - V_{E\text{final}})/V_{E\text{original}}\). The asterisk on the y axis refers to the voltage envelope value of the copper electrodes.
electrode did not exhibit significant change over time, suggesting that 30 cm of PtIr wire is necessary for to ensure stability.

The change in linear ratio is also important, as any changes in the electrode characteristics suggest corrosion. Figure 34 shows the final percentage change of the linear ratio after 24 hours. Note that the asterisk data point on the y axis denotes the copper electrode value. The data suggests that longer electrodes have a lower final percentage change, which is expected as shorter electrodes should exhibit higher rates of corrosive faradaic reactions. All electrodes exhibited a significant change in their linear ratios after 24 hours except for the 30 cm PtIr electrodes, which exhibited a final change of less than 1 percent.

Figure 35 shows the voltage envelope of the electrodes over 24 hours. Although the initial values of the voltage envelope did not follow a clear trend, the final values showed longer electrode lengths corresponded to lower voltage envelopes. Again, only the 30 cm PtIr electrode did not change appreciably over the course of 24 hours.

Figure 36 shows the final percentage change of the voltage envelope after 24 hours. The graph does suggest some correlation between length and final percentage change, however the final percentage for the 25-cm electrode does not follow this trend. The graph does show that the voltage envelope of the 30 cm PtIr electrode does change slightly over time, but the change for the other electrodes is much more significant.

3.5 CONCLUSION

Our findings suggest that the originally calculated length of 25 cm PtIr was insufficient to produce stable electrodes with minimal faradaic reactions. Significant changes in the voltage envelope as well as the linear ratio were observed over the course
of 24 hours. The shorter electrodes as well as the copper electrodes performed similarly. Ultimately, the data suggests that only the 30 cm PtIr electrodes are capable of passing the desired waveform for 24 hours without undergoing significant changes.

Despite the short time scale, these preliminary experiments were successful in providing metrics that disqualify electrode designs in a relatively short amount of time. An electrode that changes over the course of 24 hours is obviously unsuitable for long term implantation. The experimental setup will be useful as a short-term diagnostic tool for filtering potential electrode designs before they undergo long term testing.

Future experimentation will be necessary to fully optimize the design of the electrodes and determine their longevity. In retrospect, the addition of longer electrode lengths of platinum iridium wire will be necessary to provide information about the stability of electrodes greater than the calculated required length. The current experiments, while sufficient for determining change occurring on the time scale of days, is insufficient for the time scale of an implantable device, which will be on the order of years. The current experimental design must be expanded to a longer time scale to match the time scale required for an implantable device. The use of other materials must also be explored; iridium oxide has a much higher charge storage capacity than platinum iridium but its cost was too prohibitive to be used in initial experiments. Currently planned expansions to the study include the addition of cyclic voltammetry as well as analysis of the chemical composition of the electrode and electrolyte before and after stimulation.
CHAPTER 4: CONCLUSIONS

The reliance on biphasic pulsatile stimulation limits the ability of currently available neural prostheses to inhibit neural activity. Direct current has the capability to both excite and inhibit action potential firing, but safety issues concerning toxic electrochemical reactions at electrode-electrolyte interfaces have prevented its use as a viable neuromodulation modality for implantable devices. The aim of the SDCS is to safely apply ionic direct current through the rectification of ionic alternating current. The development of the SDCS will expand the range of applications in which implantable neural prostheses can be applied.

I presented the design, implementation, and testing of the electronics for the next generation of the SDCS device. The footprint of the PCB on which the electronics are assembled was reduced to a 23-mm diameter circle: a size suitable for implantation. Testing of the electronics demonstrated proper functionality of the finite state machine that, when interfaced with the microfluidic layer, will be able to produce rectified ionic current. The current output of the circuit was shown to be robust to changes in impedance. Overall, the electronics of the device are ready to be interfaced with the microfluidic layer to create a functional prototype capable of delivering iDC.

I presented the design and preliminary testing of the electrodes that pass an alternating current waveform through the microfluidic layer of the SDCS. Although the required length of platinum iridium wire necessary to fabricate a stable electrode was calculated to be 25 cm, testing suggests that 30 cm of wire was necessary to produce electrodes capable of passing the desired waveform without changes to its characteristics over the course of 24 hours. Overall, the tests were successful in quickly identifying
unsuitable electrodes, but longer term testing will be necessary to truly ascertain electrode stability. In the future, these preliminary studies will be expanded upon with chronic studies on a wider variety of electrodes to ensure the safety of the device.

While the implementation of the electronics is a large step towards a working SDCS prototype, significant challenges for the creation of a functional prototype remain. The SDCS is a complex device that requires multiple pieces to function properly to produce iDC. The development of the microfluidic layer is particularly challenging, as fabricating eight valves reliably has proven to be difficult. The development of the electrodes that deliver the iDC to the tissue (as opposed to the electrodes that interface with the microfluidic layer) is a key component of the device that has not yet been explored. The completion of the electronics will allow us to focus our efforts in these areas.

The development of the microfluidic layer is an area of focus for the immediate future. The SDCS requires eight valves that are capable of adjusting the impedances of the channels to direct the direction of current, ideally with a large difference (10 to 1 ratio) in impedance between the off and on states. The difficulties in the fabrication of the valves stem from the properties of nitinol wires; while these nitinol wires do possess the longevity required for long-term implantation, only 4% contraction of these wires can be expected if operating under reversible conditions [50]. The low degree of contraction introduces difficulties with the current design of the valves, which rely on contraction to constrict the microfluidic channels. Testing of the preliminary valve design presented in chapter 2 suggest that the changes in impedance for that particular design are insufficient. Research is currently underway to optimize the design of these valves with the goal of increasing the change in impedance while still maintaining a small form factor.
As previously mentioned, the design of electrodes responsible for delivering the current to neural tissue have not yet been explored. These electrodes are arguably less straightforward to design than conventional electrodes due to the delivery of ionic current. Although the delivery of ionic current removes the charge storage capacity limitations, the risk of the electrodes degrading from factors such as loss of moisture is introduced. Unfortunately, ionic electrode designs in existing literature focus on their use for acute studies[57]. Current ideas for the implementation involve a strip of PDMS with two channels filled with agar saline embedded in the interior of the strip. Two of the endpoints would be connected to the microfluidic layer, while the other two endpoints will serve as the anode and cathode for stimulation. The anode and cathodes will require a mechanism that would allow for the flow of ions but would block the agar and any water from escaping. Implementation and testing of these ionic electrodes is necessary for the assembly of a functional SDCS prototype.

When a functional prototype is developed, further exploration into the safety and efficacy of safe DC as a neuromodulation modality will be possible. Ongoing experiments are currently underway to explore the usefulness of safe DC in applications such as pain suppression and vestibular system modulation. In these studies, DC is applied to neural tissue through pipette tips filled with agar saline (0.9 %), distancing the electrode-electrolyte interfaces from the neural tissue to delay the effects of the toxic electrochemical reactions. The completion of a functional miniaturized SDCS prototype will pave the way for chronic experiments, allowing a full exploration of long-term iDC safety and effectiveness in in-vivo experimentation. Ultimately, we hope to establish safe direct current as a viable neuromodulation modality for implantable devices.
BIBLIOGRAPHY


APPENDICES

FILE LOCATIONS

Eagle File Location:
C:\Users\Fridman Lab\Documents\eagle\SDCS v1
This includes the Schematics and PCB Layout. Rev D is the most updated version of the schematic/layout. Note that rev D does not have the output capacitors implemented.

MPLABX IDE Code Location:
C:\Users\Fridman Lab\Desktop\SDCS_Controller
The most updated file used as the source file is SDCS_Timing_Diagram.c

General Files:
C:\Users\Fridman Lab\Desktop\Patrick Ou Thesis Stuff

Labview Files: In the microfluidics room computer
C:\Users\MouthLabStudy\Documents
The main file of interest is automatedtesting2, which is used for the electrode testing.

Matlab Files:
C:\Users\Fridman Lab\Documents\MATLAB

danalyses.m is the script used to analyze all of the excel files from Labview.

ElectrodeData is the function that elecanaalysis uses to process each file.
GENERAL SDCS BOARD OPERATION

Power is currently provided to the board using two leads attached to the bottom of the board. The bottom right lead is connected to the input voltage while the bottom left lead is connected to ground. In the event the step-up converter fails, it is possible to attach a 5V line directly to the 2\textsuperscript{nd} pin from the left on the top connector to bypass the converter.

Two 10 pin connectors are found at the top and left sides of the board. These connectors are intended to connect to the PCB associated with the microfluidic layer. Additionally, five of these pins connect to the microcontroller for programming.

The connections are as follows:

Left Connector from top to bottom:
F+, F-, I1, I1’, I2, I2’, RA5, RA4, RA3, RA2

Top Connector from left to right:
Microcontroller pins(1 through 5), VGATE, RB3, RB2, RB1, RB0

To connect program the microcontroller, the ICD3 puck is used to interface the board and the computer. The puck connects to the computer through USB. The connection to the board goes through a series of adapters. The direct output of the puck is an ethernet cable. An adapter is used to convert the ethernet connection into a 5 pin connector. This 5 pin connector must be connected to the board using a final adapter that uses the 1-mm pitch connectors that the SDCS board uses. When looking at the final adapter with the plastic flap beneath the pins and the pins pointing away, plug in the 5 pin connector such that the blue wire is on the left and the black wire is on the right. This 1-mm pitch connector can then be connected to the top of the board.
ELECTRODE TESTING NOTES

The electrode testing involves the use of the automatedtesting2 Labview file on the laptop in the microfluidics room. The dt on upper left of the Labview block diagram controls the amount of time between each recording. The integer that feeds into the = comparator block on the bottom of the block diagram controls the number of iterations to perform.

On the front panel, the rate and number of samples/channel menus control the amount of time for each individual recording. The physical channels menu determines which channels of the DAQ are being recorded from. The front panel also shows a preview of the image that is being taken. It is important to note that the camera that was used was not Labview compatible. We used a workaround in which Labview takes a screenshot of what is currently on the screen. Labview also has issues correctly taking screenshots if Labview is not the currently active window on the desktop. If pictures are important for the experiment, ensure that Labview is the main panel and the camera software is also displayed on the screen.

In the current experimental setup, the older, 30 by 30 mm SDCS board was used to deliver the current waveform. I would recommend moving away from the previous waveform and simply using a function generator with current control, as the tuning the amplitude of the current waveform on the old SDCS electronics relies on an extremely sensitive potentiometer.
PCB LAYOUT

Top Layer
CIRRICULUM VITAE

Patrick Ou
(650) 892-9109 | pou1@jhu.edu

EDUCATION

Johns Hopkins University
Baltimore, MD
Masters of Science and Engineering in Biomedical Engineering
Graduation in May 2017
• GPA: 3.8
• Relevant Coursework: Mechatronics, Computer Vision, FPGA Synthesis, Audio Signal Processing, Neural Systems

University of California, Berkeley
Berkeley, CA
Bachelor of Science in Bioengineering
May 2015
Minor in Electrical Engineering and Computer Science
• GPA: 3.9
• Honors: magna cum laude, Deans List 2013-2014, Tau Beta Pi member
• Relevant Coursework: Engineering Physics, Multivariable Calculus, Linear Algebra and Differential Equations, Matlab Programming for Engineers, Biophysical Chemistry, Organic Chemistry, Data Structures, Structure and Interpretation of Signals and Systems, Microfabrication Technology

RESEARCH EXPERIENCE

Research in Gene Fridman Lab
Baltimore, MD
Masters Student Researcher
2015 to 2017
• Designed the control electronics for safe Direct Current Stimulator (SDCS)
• Implemented the control electronics design using EagleCad software
• Assembled and designed test fixtures for the SDCS
• Designed experiments to test electrode stability/corrosion for the safe direct current stimulator using a Metrohm Potentiostat

Microfluidic Circuit Research in Liwei Lin Lab
Berkeley, CA
Undergraduate Researcher
2013 to 2015
• Involved in design of novel microfluidic devices (Not gates, If gates, bridge rectifiers, diodes, etc) with Solidworks
• Post processed new devices in preparation for characterization
• Characterized physical properties of newly designed microfluidic devices through testing with Fluigent Maesflo software and Sensiron flow sensor
POSTERS
Conference Posters
Developing a Microfluidic Device for Safe DC Stimulator
Annie Mao, Patrick Ou, Kevin King, Gene Fridman
2016 Minnesota Neuromodulation Symposium

Safe Direct Current Stimulation for the Treatment of Chronic Peripheral Pain
Fei Yang, Yun Guan, Patrick Ou, Gene Fridman
2016 Minnesota Neuromodulation Symposium

TEACHING EXPERIENCE

Biomedical Engineering Modeling and Design
Teaching Assistant

SKILLS, ACTIVITIES & INTERESTS
Activities: Tennis
Languages: Proficient in Cantonese and French
Technical Skills: Xilinx ISE, Eagle, DesignSpark, MATLAB, MultiSim, Java, COMSOL, SolidWorks, Labview, Microsoft Word, Excel, Maesflo, Pymol
Interests: Audio engineering, Computer hardware, Arduino