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Safe Direct Current Stimulator 2: Concept and Design

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***Abstract*— Essentially all neuroprostheses use alternating biphasic current pulses to stimulate neural tissue. While this method can effectively excite neurons, it is not very effective for inhibiting them. In contrast, direct current (DC) can excite, inhibit, and modulate sensitivity of neurons. However, DC stimulation is biologically unsafe because it violates safe charge injection criteria. We have previously described the concept of a safe direct current stimulator (SDCS) that overcomes this constraint. The SDCS drives DC ionic current into the tissue by switching fluid valves in phase with biphasic current pulses delivered to the metal electrodes within the device. The original prototype of this device, SDCS1, could both suppress and excite the vestibular nerve with DC stimulation delivered by the device. In the process of building the SDCS1 we identified several problems that must be addressed to further develop this technology. Consequently, we designed the SDCS2, which eliminates periodic interruptions in stimulation current flow observed in the original SDCS1 design and is small enough for head-mounted use in chronic animal studies.**

I. Introduction

Pacemakers, cochlear implants, and essentially all other chronically implanted neuroelectronic prostheses used in clinical settings rely on charge-balanced, biphasic pulses or other forms of alternating current (AC) to excite neural or muscular activity without driving electrochemical reactions that would otherwise liberate toxic substances at the electrode-saline interface [1;2]. All of these devices are constrained to excite the neural tissue in which they are implanted. Inhibition is difficult to achieve with these devices, because the need to avoid a net charge flow above a small threshold (e.g., ~100 μC/cm^2 geometric area for platinum electrodes) mandates the use of brief, charge-balanced pulses for which the cathodic, excitatory phase dominates the neural response[3-5]. When the target neural tissue is spontaneously active and the therapeutic goal is to inhibit activity, AC neuroelectronic prostheses must work indirectly, by exciting a set of neurons that then trans-synaptically inhibit the actual target or by hyper-exciting a set of neurons to engender downstream adaptive changes that result in effective inhibition when the stimulus intensity is reduced.

Many neurologic deficits would be treated most optimally by prostheses that can both excite *and inhibit* neural tissue. For example, prostheses to assist micturition require both excitation of sacral nerves to activate the detrusor muscle and simultaneous inhibition of lumbar nerves to relax the urethral sphincter[6]. Similarly, inner ear vestibular afferent fibers require not only excitation to encode head motion toward the stimulated side of the head but also inhibition to encode head motion in the opposite direction[7]. Furthermore, highly prevalent disorders characterized by uncontrolled neural firing rates such as tinnitus[8], chronic pain[9], and epilepsy[10] could be effectively treated by an implantable prosthesis capable of neural inhibition.

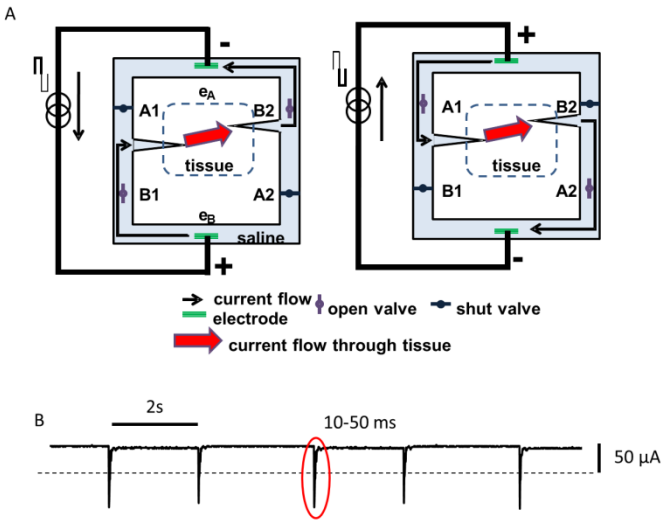

Figure 1. (A) SDCS concept. The two panels represent two states of the same device. (Left) Current flows from the lower electrode to the upper electrode. (Right) Current reverses direction, but because valves change state along with the electrical current direction, the ionic DC current (indicated by thick red arrow) still flows through the electrode tubes from left to right through the tissue. Valve A1 is always in the same state as valve A2 and valve B1 is always in the same state as valve B2, and all switch in synchrony with changes in electrode polarity. (B) Output current when the system is fully operational.

In contrast to the anodic phase of a brief biphasic stimulus pulse, continuous anodic *direct current* (DC) delivered by an extracellular electrode is very effective at inhibiting neural activity. Continuous cathodic DC can excite neural activity in a graded, stochastic fashion unlike the phase-locked, more artificial behavior elicited by pulsatile stimuli. Given these advantages, DC has long been a mainstay of laboratory experiments, in which the charge-balance constraints imposed on medical devices can be ignored (at the expense of eventual neuronal death) or overcome through the use of electrodes that are incompatible with chronic implantation. Unfortunately, DC stimulation protocols have not been available to implantable medical device designers during most of the 54 years since the first successful demonstration of a chronically implanted pacemaker.

An elegant solution to this dilemma was initially described for treating sensorineural hearing loss by Spelman *et al.*, who created a switching network that effectively

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delivered DC flow of ions into target tissue by switching mechanical valves in phase with AC square waves applied to metal electrodes immersed in a saline bridge[11;12]. This approach achieves DC ionic current through the tissue while ensuring that both metal electrodes always operate within classic "safe charge injection" thresholds. Based on this idea, we built a Safe DC Stimulator (SDCS) prototype, the SDCS1, using standard laboratory equipment[13].

Conceptually, the first SDCS we developed, SDCS1, delivers alternating current pulses to electrodes suspended at the opposite ends of a torus filled with ionic solution (termed "saline" in Fig.1). With each change in stimulation polarity the valves on either side of each electrode change from open-to-closed and closed-to-open, effectively modulating the path for ionic flow through each valve between low impedance and high impedance. Two extension tubes connected to the sides of the torus are directed into the body to complete the ionic current circuit. Fig. 1 demonstrates this concept, comparing two states of the apparatus. In both panels of the figure, ionic current flows from left to right through the stimulated tissue. In this way, a continuous AC square wave controlling the apparatus will deliver DC ionic current through the tissue from left to right. This system also addresses the problem of ionic buildup, by creating a closed-circuit path for the ions to flow, so that the anions that flow into the electrode tube on the right are replaced by the anions that flow out of the electrode tube on the left.

To confirm that a SDCS can deliver ionic DC current as intended, we built and bench-tested a prototype of the SDCS, the *SDCS1*. We used normally-closed valves from Ehcotech International Inc., San Diego, CA Model DDB-CD-12VDC interconnected with laboratory tubing filled with saline. The operation of the valves was synchronized to the electrode polarity changes because the valve operation was controlled from the same square wave AC signal applied to the electrodes e_A and e_B. An isolated oscilloscope was connected between sensing electrodes placed at the output of the device to sense the output current of the SDCS1. The system's current output is shown in Figure 1B.

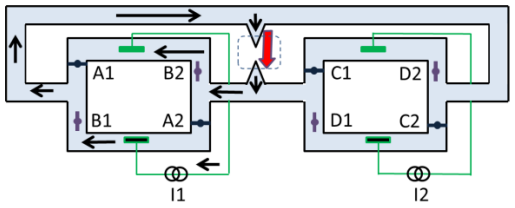
The fidelity of SDCS1's output was degraded by periodic interruptions in current flow due to non-ideal behavior of the valves (Fig. 1B red oval). Interruptions occurred because ionic current bypasses the tissue when valves are temporarily and simultaneously both open during valve transitions. For example, if A1 and B1 are both temporarily open during a transition, the short circuit causes a shunt through the system and no current flows through the tissue. This artifact can last as long as 50 ms. The degraded fidelity of the DC flow produced by SDCS1 was acceptable for acute studies of the SDCS principle of operation (effectively resulting in DC plus a ~1 Hz pulsatile stimulus) [14;15], but smooth flow of DC (or low frequency analog waveform) current without interruptions is required for continuous excitation or inhibition of the target tissue.

II. Safe Direct Current Stimulator 2 Design

To eliminate DC current flow interruptions and miniaturize the device, we engineered the SDCS2, which uses two SDCS systems in the arrangement shown in Figure 2. One system drives current through the tissue while the other closes all valves and then opens the next set of valves in sequence. The intermediate step of closing all valves on the system undergoing valve transitions prevents current shunts.

A. Artifact Elimination

In the system state indicated in red in the table and shown in Figure 2 (*S1), I1 drives the current through the tissue while I2 is shut off. In order to switch valves from



	I1	A1	A2	B1	B2	C1	C2	D1	D2	I2
*S1	-	0	0	1	1	0	0	1	1	0
S2	-	0	0	1	1	0	0	0	0	0
S3	-	0	0	1	1	1	1	0	0	0
*S4	0	0	0	1	1	1	1	0	0	-
S5	0	0	0	0	0	1	1	0	0	-
S6	0	1	1	0	0	1	1	0	0	-
*S7	+	1	1	0	0	1	1	0	0	0
S8	+	1	1	0	0	0	0	0	0	0
S9	+	1	1	0	0	0	0	1	1	0
*S10	0	1	1	0	0	0	0	1	1	+
S11	0	0	0	0	0	0	0	1	1	+
S12	0	0	0	1	1	0	0	1	1	+

I1, I2:
+ Current Left to Right
- Current Right to Left
0 Current Source Shut Off

A, B, C, D valves:
1 Open Valve
0 Shut Valve

State Numbers:
Si State Number

*Si State with current change, but no valve transition

Figure 2. SDCS2 consists of two SDCS systems. One state of the system shown in the figure is also indicated in first row in the table and highlighted in red. Each row of the table indicates system state. The columns show the open/close orientation of each valve and the current flow direction delivered by I1 and I2 current sources. The system is designed to eliminate interruption in ionic current flow through the target tissue (indicated by dashed square) independent of the speed of valve transitions. The states are intended to proceed from S1 to S12 sequentially and cycle back to S1 after state S12 is reached.

open-to-closed and closed-to-open in the right system (I2) from the state depicted in Figure 2, we first close the D valves as indicated in state S2. Because C valves remain shut during this operation, closing D valves will not cause any interruption in current flow even if D valves are relatively slow to close or they do not close at the same instant. Next, we open C valves as indicated in state S3. This transition does not cause any interruption in current flow, because D valves are now closed. Finally, we transition current control to the right system (I2), and simultaneously shut off the left system (I1) by transitioning to the state *S4. Since this transition is electronic rather than mechanical, it is very fast and does not cause interruption in current flow. In the table, we indicate the system states in which only the current sources change without the valve transitions with an asterisk. The procedure is then repeated for the left (I1) system, first closing B valves and then opening A valves, while the right (I2) system drives current through the tissue. These system states are designated by states S5 and S6 respectively. In this way, SDCS2 avoids all valve transition artifacts, even when the valves are slow. The system state cycles back to *S1 after S12.

B. Size Reduction

We established a layered 3D printer prototype construction for this device that can serve as a template for a future version that is fully implantable and miniaturized using micro-electro-mechanical (MEMS) and microfluidic technology. Figure 3A-C shows the computer-aided-design (CAD) model of this design. Four layers are assembled in a stack. The first layer has a vertical post that is used as a guide to accurately position the other three layers. Layer 1 contains fluid channels, each of which corresponds to the channels depicted in Figure 3A between the valves. The two

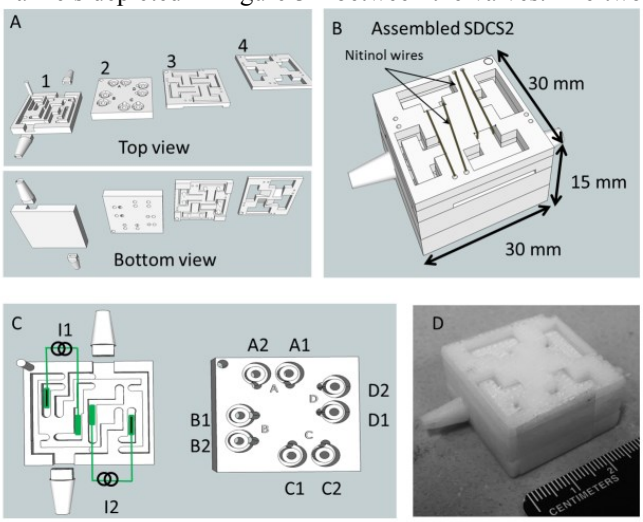


Figure 3. SDCS2 construction. A. design components. B. assembled device. Two of the four valve controllers are depicted with NiTi actuation wires. Each valve controller operates one pair of valves: (A1 and A2), (B1 and B2), (C1 and C2), and (D1 and D2). C. close-up of design layers 1 and 2 indicating the location of the metal electrodes and valves. D. Photograph of first 3D-fabricated SDCS2.

hollow ports emanating from the sides of Layer 1 provide the output of the device and are intended to connect to saline-filled catheters that deliver electrical current to target tissue.

Layer 2 adds valves to the design as shown in Figure 3C. Each valve (A1, A2, B1, B2, C1, C2, D1, and D2) contains two holes that connect to the appropriate channels in Layer 1. The center hole is surrounded by a solid ring that is recessed approximately 1 mm from the top of Layer 2. When Layers 1 and 2 are assembled and saline is allowed to fill the channels, there is a direct electrical conduction path between the center and the side hole. This conduction path is broken when the center hole is plugged to shut off the valve.

The valves are open or shut using lifters shown in Layer 3. Each lifter is equipped with two plungers that are positioned directly over the valve rings of Layer 2. A thin sheet of silicone is placed between Layer 2 and Layer 3 to prevent saline from leaking out of Layers 1 and 2 and also to provide a gasket between each valve plunger in Layer 3 and the corresponding ring in Layer 2. The plungers are normally pushing down on the rings to keep the valves shut. Each lifter operates two valves at a time (A, B, C, or D valves).

100 µm diameter Ni-Ti alloy (a.k.a. "Nitinol" or "Muscle") wires are used to open the valves. The wires contract approximately 5% of their length when activated with 180 mA of current (or heated to ~90 °C). When activated, they contract with force equivalent to 150 g. When current is turned off, they extend back to their original shape under a tensile force equivalent to 28 g. At room temperature, they can be cycled between extended and contracted states at approximately 2 Hz for >1M lifetime cycles. The wires are attached to the lifters in Layer 3 using the support structure provided by Layer 4 (Fig. 3B). When a wire is electrically activated with constant current, it pulls the corresponding lifter to open the two valves controlled by that lifter. These valves close when the wire activation stops, and the lifter naturally returns to its original position and extends the wire back to its original shape. Although we anticipate that Nitinol actuators must eventually be changed to a faster actuation means that is more compatible with MEMS system fabrication, the SCDS2 design is sufficient to aid in animal experimentation of the SDCS technology.

Figure 3C also shows the location of the metal electrodes internal to the device. Assuming 100 µC/cm^2 charge density safety limit[3-5] Pt/Ir electrode area should be ≥50 mm^2 to deliver 100 µA for 500 ms.

III. Methods

To test if the system concept is sound in its design to eliminate current flow interruptions, we constructed a bench prototype of the SDCS2 using laboratory tubing, two AM2100 (A-M Systems, Carlsborg, WA) isolated current sources and manually operated clamps in place of A,B,C, and D valves. The current sources were set to switch control in 20s intervals to allow time to manually open and close the valves. We then operated the system according the state transitions described in Figure 3. Occasionally, A and B valves were intentionally momentarily pulsed into closed position at an inappropriate time to test that the system was indeed sensitive to improper valve transitions.

IV. Results

Figure 4 shows the results of the bench experiment in which we tested the current interruption concept of SDCS2 with laboratory tubing. The figure shows the time-dependent states of the current sources I1 and I2, and the corresponding state changes that occur during each phase of the current sources. The first 20 second epoch of the Output Current shows that the test system is indeed sensitive to the current interruption when the valves A and B were operated *improperly* (indicated with downward arrows). When the system is operated as designed, interruptions in current flow disappear, successfully eliminating SDCS1 glitches shown in Figure 1B.

V. Conclusion

We showed a solution for the next generation prototype of the SDCS technology that eliminates interruptions in output current flow that were unavoidable in the original design of this device. We offered a practical construction for the

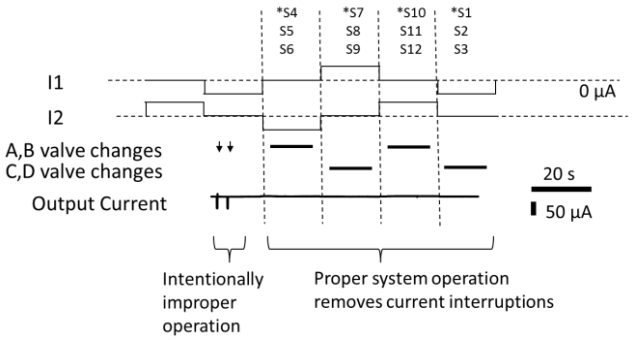


Figure 4. The behavior of a bench SDCS2 prototype. A and B valves are intentionally momentarily pulsed into closed position (indicated with arrows) to demonstrate the sensitivity of the system to improper valve operation. When the system is operated as designed, the output current interruptions seen with SDCS1 operation disappear.

SDCS2 that should allow chronic animal testing of the SDCS neural stimulation technology. While the lifetime of each prototype device is limited to approximately a month of operation by the maximum Nitinol wire operational cycles; the layered design establishes a path toward miniaturizing this device further for an implantable solution using MEMS fluidic or similar approaches. In addition to the miniaturization of this technology for permanent implantation, further work toward developing the SDCS technology should address safety and effectiveness limitations of using chronic ionic-DC current to modulate neural behavior in a variety of neural prosthetic applications.

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