A Wireless Implantable Switched-Capacitor Based Optogenetic Stimulating System

Hyung-Min Lee, Ki-Yong Kwon, Wen Li, and Maysam Ghovanloo

***Abstract*—This paper presents a power-efficient implantable optogenetic interface using a wireless switched-capacitor based stimulating (SCS) system. The SCS efficiently charges storage capacitors directly from an inductive link and periodically discharges them into an array of micro-LEDs, providing high instantaneous power without affecting wireless link and system supply voltage. A custom-designed computer interface in LabVIEW environment wirelessly controls stimulation parameters through the inductive link, and an optrode array enables simultaneous neural recording along with optical stimulation. The 4-channel SCS system prototype has been implemented in a 0.35-µm CMOS process and combined with the optrode array. *In vivo* experiments involving light-induced local field potentials verified the efficacy of the SCS system. An implantable version of the SCS system with flexible hermetic sealing is under development for chronic experiments.**

I. Introduction

Electrical neural stimulation has been widely utilized in neuroscience, electrophysiology, and also clinical study to substitute sensory modalities or alleviate neurological diseases, such as Parkinson's, epilepsy, and depression [1]. However, electrical stimulation has several limitations such as electrical artifacts, unpredictable current path, and limited selectivity of target neurons [2]. Optical stimulation of genetically-modified neurons, known as optogenetics, has become an effective way to selectively generate neural activity using various light-delivery schemes because of its fast, spatially controlled, and potential for minimally invasive modulation of target cells [3]. The optical stimulation is also capable of eliminating electrical artifacts, while enabling extended lifetime by hermetic sealing of light sources [4].

There are several light-delivery schemes for optogenetic experiments on freely behaving subjects, such as a laser-coupled optical fiber and single light-emitting diode (LED). However, they suffer from poor spatial resolution and tethering effects through wires and optical fibers. Recently, a multichannel 3-D optrode array, integrating micro-LEDs with micro-needle waveguides, has been demonstrated, which can minimize light scattering in the tissue and achieve high spatial resolution for implantable optogenetics [5].

Inductive power transmission across the skin has been a viable solution to provide sufficient power to the implantable medical devices (IMDs), while overcoming size, cost, and longevity constraints of embedded primary batteries [6]. Light sources, however, typically require high instantaneous power to emit sufficient light for optical neural stimulation, which can be a significant limiting factor in conventional IMDs [7]. Fig. 1 shows the conceptual block diagram of a conventional inductively-powered array of LEDs for wireless optogenetics, where a rectifier and a regulator convert AC voltage across a secondary coil, L_2, to DC output voltage to supply an LED driver. Power losses in these stages result in poor overall power efficiency from L_2 to the LED. Moreover, high instantaneous power that flows to the LEDs when they are on leads to large load variation, which affects the impedance matching with the inductive link, significantly increasing the required inductive power level, affecting a safety issue, and degrading the inductive link power efficiency as well as supply voltage for the rest of the IMD.

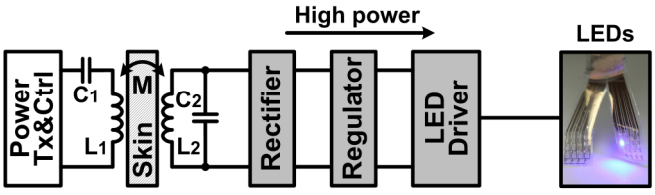

Fig. 1. Simplified block diagram of a conventional inductively-powered device combined with an array of LEDs for wireless optogenetics.

To address these limitations in implantable optogenetics, we have utilized a switched-capacitor stimulating (SCS) system, proposed in [8], for power-efficient wireless optical stimulation. The SCS system efficiently charges a small array of storage capacitors directly from the inductive link and periodically discharges them into the micro-LED array, providing high instantaneous current without burdening the inductive link and system supply. To control stimulation parameters, a custom-designed PC interface wirelessly sends data to the SCS system through the inductive link, while a commercial neural recording system simultaneously detects the evoked neural signals from the same 3-D optrode array. Moreover, the proposed hermetic sealing method and *in vitro* test results verified the functionality and reliability of the chronic implant prototype, which will be used to prepare the SCS system for implantable optogenetics.

II. Wireless Optogenetics with the SCS System

Fig. 2 shows the simplified block diagram of the SCS system for power-efficient wireless optogenetics. In the inductively-powered SCS system, a power transmitter (Tx) drives the primary coil, L_1, at the power carrier frequency, f_C. This signal induces current in the secondary coil, L_2, through the inductive link, generating an AC voltage, V_{COIL}, across the resonance circuits, L_2 and C_2. The SCS system efficiently

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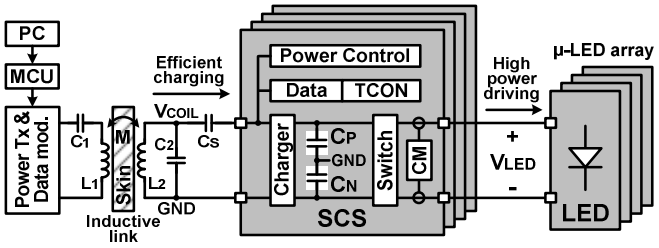


Fig. 2. Simplified block diagram of the switched-capacitor stimulating (SCS) system architecture for power-efficient wireless optogenetics.

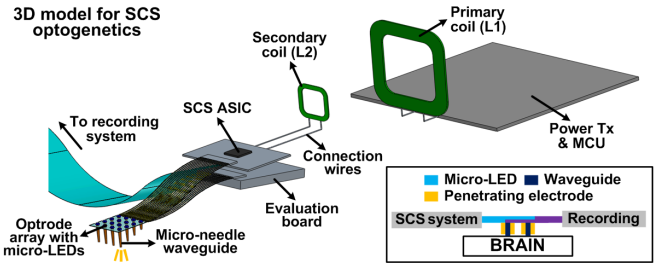


Fig. 3. 3-D model for *in vivo* optogenetics experiments with the SCS system. Inset: Optrode array with micro-LEDs for optical stimulation and penetrating electrodes wrapped around the waveguides for neural recording.

charges a bank of storage capacitors, C_P and C_N, directly from V_{COIL} through a series capacitor, C_S, and an inductive charger without using any rectifiers and regulators [9], improving the capacitor charging efficiency. The charge stored in capacitors is delivered to the load through switches, efficiently creating stimulation pulses. In addition, a charge monitoring (CM) circuit measures the amount of injected charge to enable charge-balanced stimulation. For power-efficient wireless optogenetics, the SCS system periodically discharges the storage capacitors into an array of micro-LEDs to emit sufficient light and evoke the neural activity. After charging, C_P and C_N pairs are connected in series to provide higher LED voltage, V_{LED}, for optical stimulation.

The forward data telemetry utilizes the same inductive link to wirelessly set stimulation parameters in the system, and the on-chip timing controller (TCON) generates timing signals for capacitor charging and LED driving. Hence, the SCS system can be chronically implanted for experiments with freely behaving animal subjects. The power control unit generates supply voltages for the rest of the system and prevents the systems against overvoltage due to sudden strong coupling.

Fig. 3 shows the 3-D model for *in vivo* wireless optogenetics with the SCS system, which receives wireless power and data through the inductive link. The SCS ASIC drives the 3-D flexible optrode array, which consists of micro-LEDs for optical stimulation, penetrating electrodes for neural recording, and micro-needle waveguides to enable precise and efficient light delivery to the target tissue with high spatial resolution [5]. Neural signals are recorded from the penetrating electrodes wrapped around the waveguide core and only exposed at the tips of the waveguides, through an independent recording setup. In this setup, the wireless SCS system with slanted optrode arrays enables simultaneous optical stimulation and electrical neural recording to test an untethered bi-directional neural interface.

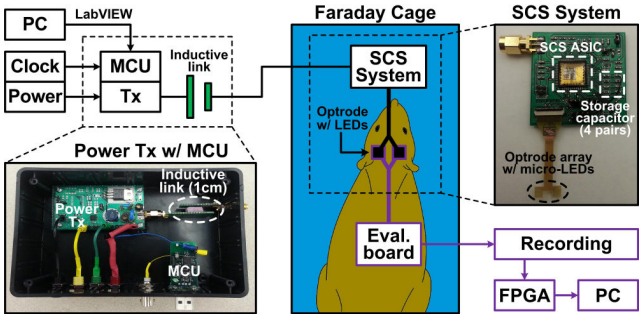


Fig. 4. Block diagram of animal experiment setup for optogenetics with the wireless SCS system.

III. *In Vivo* Wireless Optogenetic Experiments

In order to verify the feasibility of power-efficient wireless optogenetics with the SCS system, *in vivo* acute animal experiments were conducted using the optrode array and the recording setup, rendered in Fig. 3. Sprague-Dawley rats were virally-transfected with channelrhodopsin-2 (ChR2) to enable light sensitivity. In the optrode array, each surface-mount micro-LED chip (TR2227TM, Cree Inc., Durham, NC), which occupies 220 × 270 × 50 μm^3 area and has a wavelength that peaks at 460 nm, was coupled with a 1.2 mm waveguide made of SU8 core with the gold electrode wrapped around it [5].

Fig. 4 shows the block diagram of animal experiment setup for optogenetics with the wireless SCS system. The power Tx drives the inductive link to transfer wireless power, while the computer interface provides data packets through a USB cable to a microcontroller unit (MCU) (CC2510, Texas Instruments, Dallas, Tx), which modulates the coil voltage amplitude to send wireless data through the same inductive link. The power Tx module including its MCU and an inductive link with 1 cm coil spacing occupies 15 cm (L) x 8 cm (W) x 5 cm (H).

The SCS system receives wireless power and data through the inductive link and drives micro-LEDs in the optrode array. The SCS prototype, on the upper right side of Fig. 4, occupies 3.9 x 3.9 cm^2 on PCB, and includes off-chip components for testing and optrode connectors. The key parts of this prototype are the SCS chip (5 x 2.4 mm^2) and 4 pairs of 1 ~ 5 μF off-chip storage capacitors (SMD-0402, 1 x 0.5 mm^2 each). The SCS system can be further shrunk using a single flex-PCB that can directly connected to the LED array and include the receiver coil, L_2, without connectors or testing components. The storage capacitors can also be placed on the opposite side of the SCS chip, minimizing the PCB size for implantable optogenetics. The neural signals were recorded simultaneously from the penetrating electrodes on the same optrode array through an evaluation board and commercial hardwired recording setup (RHD2132, Intan Technologies, Los Angeles, CA).

A graphical user interface (GUI) has been implemented in the LabVIEW environment to send data packets from the PC to the MCU of the power Tx module, as shown in Fig. 5. Several parameters of the LED driving signal can be adjusted in this setup: 1) stimulation frequency, 0.5 ~ 2 Hz, 2) LED total turn-on time, 10 ~ 100 ms, 3) LED peak voltage, 2.5 ~ 3.45 V, 4) pulse period, 2 ~ 16 ms, 5) pulse width, 512 μs, 6)

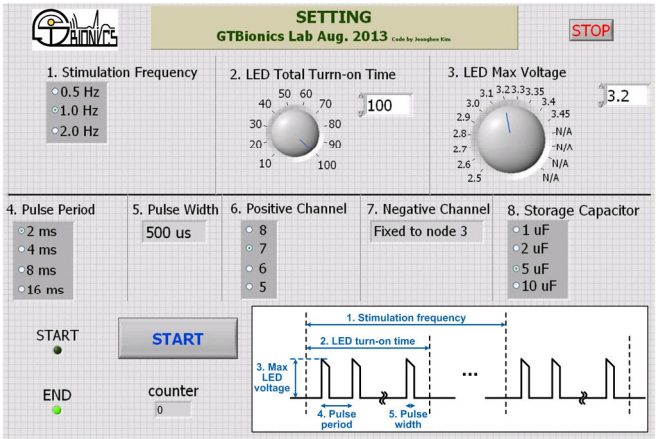


Fig. 5. SCS system GUI in LabVIEW to wirelessly control the SCS parameters. Inset: LED driving voltage waveform and its controllable parameters.

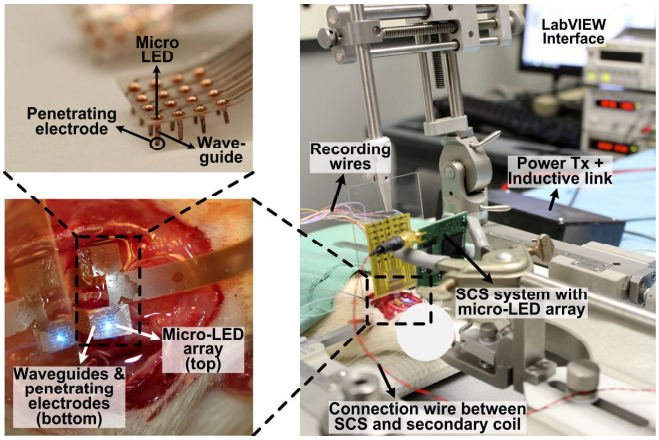


Fig. 6. *In vivo* experiment setup for wireless optogenetics on an anesthetized viral-transfected rat with the SCS system.

positive output connections, 4 channels, 7) negative output connections, fixed, and 8) storage capacitance, 1 ~ 10 µF. While the pulse train periodically turns the LEDs on and off, the effective turn-on time can be simply calculated as total turn-on time x (pulse width / pulse period).

Fig. 6 shows the *in vivo* experiment setup for optogenetic stimulation of the primary visual cortex (V1) in the brain of the anesthetized rat. The receiver L_2C_2 tank provides the SCS-PCB with AC power and data via a twisted pair of wires. The SCS chip on the PCB provides high instantaneous power to the LEDs, which in turn generate light and deliver it to the target area in the brain via slanted micro-needle waveguides. The recording setup simultaneously measures local field potentials (LFP) from the same optrode array through its penetrating electrodes.

Fig. 7 shows the LED driving voltage, V_{LED}, for optical stimulation with SCS and light-induced *in vivo* LFP results. The LFPs below 500 Hz were recorded using an optrode array with waveguides in the brain of the rat when the SCS system drove micro-LEDs with a 512 µs pulse train for 100 ms at 1 Hz and V_{LED} = 2.7 V_{peak} and 3.2 V_{peak}, as shown in Fig. 7a. While no significant neural modulation was observed at V_{LED} = 2.7 V_{peak}, the higher V_{LED} = 3.2 V_{peak} resulted in higher light intensity from micro-LEDs that provided sufficient irradiance through the micro-needle waveguide for light-evoked neural

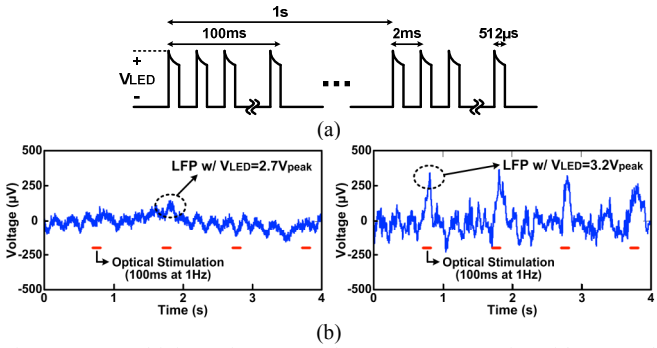


Fig. 7. (a) LED driving voltage, V_{LED}, for *in vivo* optogenetics with SCS and (b) light-induced local field potentials (LFP) with V_{LED} = 2.7 V_{peak} and 3.2 V_{peak}.

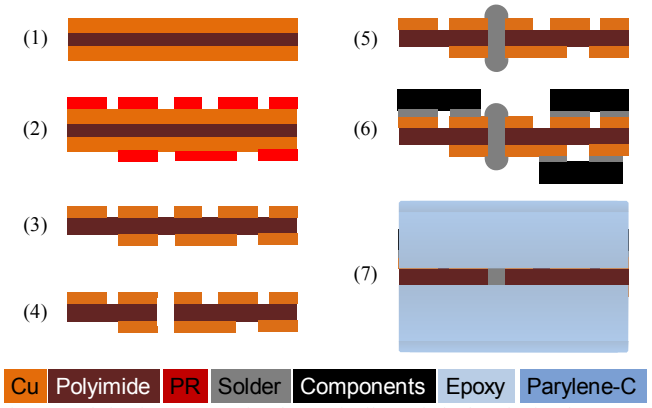


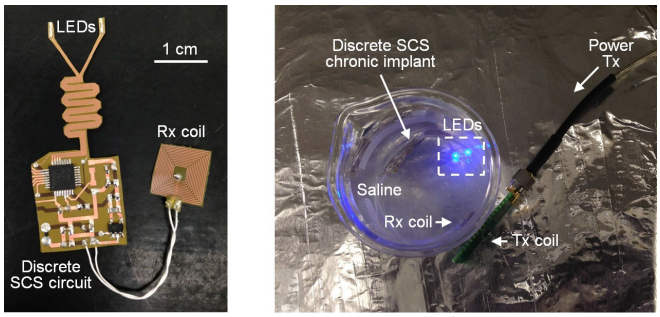
Fig. 8. Fabrication steps of a hermetically-sealed chronic implant on a flexible polyimide circuit.

response in the selective target tissue, leading to larger LFP variations, as shown in Fig. 7b. This experiment verified the feasibility of wireless optical stimulation via the SCS system.

IV. Hermetic Sealing for Chronic Implants

Fig. 8 shows the fabrication steps of a hermetically-sealed chronic implant on a flexible polyimide circuit for experiments using freely behaving animals. The flexible polyimide circuit was fabricated using Pyralux®AP (AP7163E, DuPont) with the following steps: 1) A 3-inch Pyralux® wafer was cut and cleaned, and a 3-µm thick photoresist (PR) layer was spin coated. 2) The circuit design was transferred on to the PR using a lithography technique. 3) The circuit was patterned by wet etching of copper. 4) Through holes were made by a laser cutter. 5) Vias were made by filling the through holes with solder. 6) Solder paste was applied on the contact pads and the SCS chip, and other surface mount devices (SMDs) were populated on the pads. The circuit was baked at 200 °C for 5 min, and extra flux was applied for reflow soldering, if necessary. 7) Once all components were populated, a thick layer of epoxy (200 ~ 500 µm) was applied followed by 10-µm Parylene-C coating as a biocompatible package.

In order to evaluate the performance of epoxy-Parylene-C packages and the possible electrical failure of the chronic implant, active accelerated-lifetime soak testing was performed in saline at a higher than body temperature. For the soak testing, a discrete version of the SCS circuit was designed using a MCU (MSP430, Texas Instruments, Dallas,



(a) (b)

Fig. 9. (a) Discrete SCS chronic implant and (b) accelerated soak testing in saline with wireless power and data transfer.

TX), as shown in Fig. 9a. This circuit was programmed to mimic SCS stimulation patterns, once it received wireless power and data through the inductive link. Dimensions and fabrication process of the discrete circuit were identical to the SCS system. Four LEDs (LB QH9G, blue 466 nm, OSRAM, Germany) were integrated on the flexible PCB, and each LED was individually controlled by the MCU. Spring structured interconnects were utilized to reduce mechanical stress caused by stretching and twisting movements in the neck and shoulder area of the animal. A MEMS-based receiver (Rx) coil was fabricated separately to be placed on the back of the animal and connected to the SCS with flexible wires (392 F high-flex miniature wire, 36 AWG, McMaster-Carr. OH).

Five discrete SCS devices were prepared and immersed in saline at 75 °C, as shown in Fig. 9b. Each device was activated by coupling the Rx and Tx coils, and the samples were visually inspected on a daily basis to monitor possible device failure. No delamination or major physical corrosion occurred after 14-days in accelerated lifetime testing conditions, while the long-term stability experiment is still ongoing at the time of this publication. Using the Arrhenius relationship, the preliminary results show that the implant lifetime can be equivalent to 3.5 years at body temperature of 37 °C, which is sufficient for one-year duration of our animal study [10]. Further improvements can be achieved by optimizing the temperature and duration of heat treatment for the Parylene/metal thin-film skin or by using additional chemical treatments.

The discrete SCS system on the flexible circuit with the integrated LED array was chronically implanted to assess the feasibility and stability of the chronic SCS implant. The SCS board and Rx coil were coated with a thin layer of Polydimethylsiloxane (PDMS) to protect the surrounding tissue against damages caused by sharp edges. The virally-transfected rat was anesthetized and placed in a stereotaxic apparatus. Using sterile surgical procedures, a 2 ~ 3 cm incision was made in the skin overlying the skull, and the skin was detached from the skull using a scalpel blade. Once bregma and lambda sutures were clearly exposed, a hemostat was inserted under the skin of dorsal area, detaching the spinotrapezius muscle and skin to make a reservoir for the discrete SCS implant. The Rx coil was inserted on the center of dorsal area through the channel, and the flexible circuit was placed around the shoulder of the rat.

After both Rx coil and SCS circuit were in place, the Tx coil was inductively coupled with the Rx coil through the skin, and the discrete SCS system was tested to verify possible damages during insertion. Once functionality was confirmed, a small craniotomy was made to expose V1 using a micro drill (Ideal Micro-Drilltm, Roboz Surgical Instrument Co., MD). With the LED array in place, dental cement was applied to secure the array in position. A piece of gel foam was placed on top of the exposed V1 to cover the dental cement. The skin overlying the skull was sutured closed. After two days of recovery the rat was brought to the lab and slightly anesthetized with a mixture of oxygen and isoflurane. The discrete SCS implant was tested daily by visual inspection of the LED light through the skin. The implant was verified for 14 days, while no behavioral changes were observed.

V. Conclusion

We have demonstrated a switched-capacitor stimulating (SCS) system for implantable wireless optogenetics, which provides high instantaneous power through the inductive link to emit sufficient light and evoke neural activities. The LabVIEW PC interface and custom-designed power Tx module provide wireless power and data to the SCS system, while electrodes embedded in the optrode array enable simultaneous neural recording. Our self-assembled LED array on a single substrate can reduce the manufacturing cost. Acute *in vivo* experiments with optical stimulation and LFP recording have verified the efficacy of the SCS system for wireless optogenetics. Moreover, the hermetic sealing method for chronic implantation is under development to enable implantable optogenetics with the SCS system.

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