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Intraspinal Stimulation with Light Activated Micro-Stimulators

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Abstract— **Chronic tissue response to microelectrode implants stands in the way as a major challenge to development of many neural prosthetic applications. The long term tissue response is mostly due to the movement of interconnects and the resulting mechanical stress between the electrode and the surrounding neural tissue. Wireless microstimulators are a potential solution to the problem. As a method of energy transfer to the microstimulator, we propose to use a laser beam at near infrared (NIR) wavelengths. Microstimulators of various sizes were fabricated with two cascaded GaAs PIN photodiodes. The voltage field of the device was measured in saline solution as a response to an NIR laser source. The voltage in medium had a peak of around 190 mV above the cathodic contact and stayed flat for the duration of 0.2 ms pulse. In rats, microstimulators were inserted into the ventral horn of cervical spinal cord. A train of NIR pulses (0.2 ms, 100 Hz) were applied to wirelessly activate the devices. The forces generated due to stimulation of the motor neurons were measured from the ipsilateral forelimb with a force transducer. The largest force generated was around 0.9 N. The volume conductor and force measurements suggest that the floating light activated micro-electrical stimulator (FLAMES) approach is feasible for intraspinal stimulation.**

Key Words: **neural microstimulation, wireless microstimulators.**

I. INTRODUCTION

Neural micro-stimulation offers a possibility of treating disorders of the central nervous system. One of the obstacles in these applications is the breakage of wire interconnects, causing the device to fail [1]. Having a chronically implantable microelectrode array that can last for a life time is in great demand. The interconnect longevity in the feline spinal cord is rarely more than one year [2]. Mushahwar *et al.* has implanted arrays of individual microwires in the cat lumbar spinal cord where stimulation thresholds remained stable for months [3].

Having a wireless system in the CNS is important to eliminate the mechanical stress and the resulting chronic tissue response induced by the movement of the electrode and the tethering of interconnects. Our group is investigating the feasibility of a floating light activated micro-electrical stimulator (FLAMES) powered wirelessly using an NIR light beam. Elimination of interconnects should improve device longevity by solving the wire breakage problem [4]. The tethering forces due to interconnects, which is the primary source of chronic tissue reaction [5], [6], should also be eliminated.

In the envisioned paradigm, the micro stimulator is implanted into the spinal cord at the targeted site. The devices are activated using NIR light that is transferred through a multi-mode optical fiber. The tip of the optical fiber is secured through a hole into the vertebrae. The location of the optical fiber is just above the micro-stimulator but outside the dura mater. Therefore, the distance the light has to penetrate into the targeted tissue and activate the device is in the order of a few millimeters.

In this study, we fabricated various sizes of floating light activated micro-electrical stimulators (FLAMESs) with integrated gallium arsenide (GaAs) PIN photodiodes. The gold contacts were coated with Poly 3,4-ethylenedioxythiophene (PEDOT) to improve the charge injection capacity [7]. The stimulation voltage levels were tested by placing the device in a volume conductor and measuring the voltage field near the surface. The FLAMES were also tested for intraspinal stimulation in rats.

II. METHODS

A. Device Fabrication

Gallium arsenide FLAMES containing PIN photodiodes were fabricated in different sizes. A selective wet etching technique was used to reach the doped p and n layers by utilizing the AlAs etch stops. After patterning the photoresist, a 10:1 citric acid/H_2O_2 solution was used to wet etch GaAs and $Al_xGa_{1-x}As$ layers and stop at the AlAs etch stop layer. Before etching, it is very important to remove a thin surface oxide layer of the cap layer, which was achieved by dipping the device in 15:1 DI H_2O/ buffered oxide etch solution for 10 seconds. The etch rate was characterized with a 1 M citric acid / 30% wt H_2O_2 solution and an etch rate of approximately 100 nm/minute was measured. Then, a short dip in 15:1 H_2O/buffered oxide etch (BOE) was used to remove the AlAs layer. After the p and n layers were reached, metal was deposited for each layer. The n metal deposition consisted of Ge/Au/Ni layers of 26 nm/54 nm/15 nm, respectively. The n metal was deposited first since it required to be annealed at a high temperature (420° C). The p metal layer was deposited with 10nm of Ti as a sticking layer, followed by 100 nm of Au. Finally a 600-700 nm silicon dioxide layer was deposited with PECVD and then patterned. The top oxide layer was then etched with BOE to expose the contacts. A thick gold overlay (300-400 nm) was then deposited to make uniform and low-ohmic contacts. The devices were released using a rotary dicing saw. A sketch of the device is shown in Figure 1.

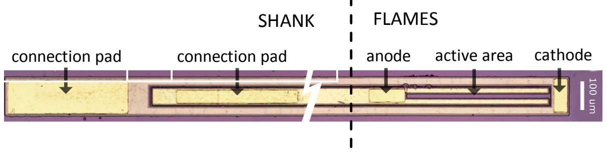

Fig. 1 A sketch showing the device layout at the tip of a 4 mm shank with connection pads.

B. *Volume Conductor Measurements*

Device contacts (Au) were coated with PEDOT using electrochemical method with constant current [7]. The voltage field generated by the FLAMES was measured in normal saline (0.9%) solution diluted ten times to simulate neural tissue impedance while being pulsed with an NIR laser beam. The device was secured at the bottom of a petri dish. A tungsten micro-electrode and a large Ag/AgCl reference were utilized to record the voltage field generated by the device, in response to a laser beam at 830 nm, pulsing at 10 Hz (PW= 0.2 ms). The laser source (DLS-500-830FS-100, StockerYale, Canada, 74 mW) and acquisition of the signals into the computer were controlled by a custom LabVIEW program (National Instruments, TX). The laser beam size and power were sufficiently large to saturate the photodiodes during each pulse. The voltage field generated inside the solution was recorded with the tungsten electrode placed immediately above the cathode (~10 µm) without making direct contact, and a high impedance buffer amplifier (TLC2274, Texas Instrument).

C. *In Vivo Testing*

Five Sprague-Dawley rats (400-500 g) were used for in vivo testing. Anesthesia was induced with sodium pentobarbital (50 mg/kg) and maintained with further doses as needed. Marcaine (0.2 mL) was injected at the site of incision. The body temperature was continuously monitored and maintained between 36-37 ^{O}C using a temperature regulated heating pad. Laminectomy was performed at C5-C7 level and the dura was removed. The spinal cord was kept moist using warm saline or mineral oil. All experimental procedures were approved by the Animal Care Committee at Rutgers University.

Two devices were tested in this study; Devices A (cathode and anode areas ~20,300 µm^2 each, active area ~35,000 µm^2, and total device size 200×700 µm) and B (cathode and anode areas ~8,500 µm^2 each, active area ~25,500 µm^2, and total device size 170×600 µm). Figure 2 shows the preparation used for the intraspinal stimulation. The FLAME stimulator was inserted into the cervical spinal cord at an angle of 30 degrees entering from the dorsal side near the dorsal entry zone and reaching the ventral horn on the ipsilateral side using a 3-axis micromanipulator. The laser was placed 13.5cm above the cord using another micromanipulator and aimed at the photodiode from above (Fig. 2). A train of NIR pulses (0.2 ms pulse width, 1000 ms duration, 100 Hz) were sent to the device with a circular footprint of 1 mm in diameter at the cord surface. The force generated due to activation of the ventral horn neurons was measured with a force transducer attached to the ipsilateral hand.

The total laser output power was measured directly using a powermeter. The control signal was varied from 0 (maximum power) to 4.5 V (0 mW) in steps of 0.05 V. The power output increased linearly with the control signal (data not shown). The power density in mW/cm^2 was calculated accordingly for a train of pulses using the equation below:

$$powerdensity = \frac{P}{A} \times PW \times f \qquad (1)$$

where P is the power of the laser source (mW), A is the beam cross-sectional area (cm^2), PW is the pulse width (sec), and f is the frequency (Hz).

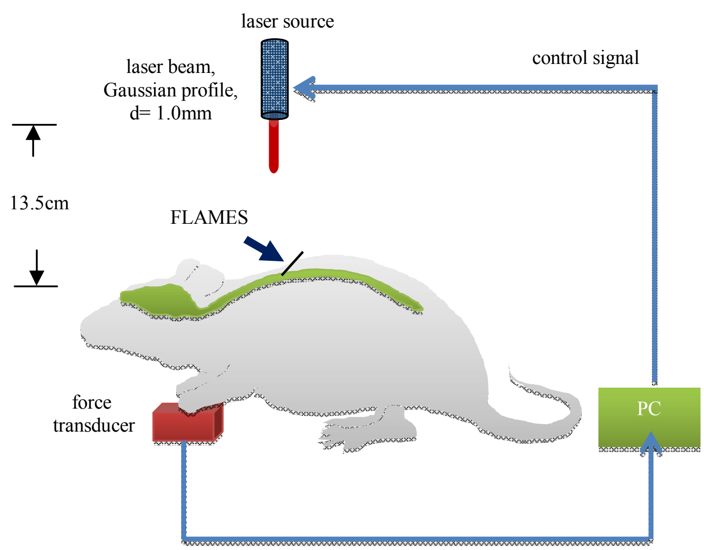

Fig. 2 The setup used for in vivo testing.

III. RESULTS

A. *Volume Conductor Measurements*

Open circuit voltages of both devices were measured as 700 mV at saturation. Figure 3 shows the voltage field generated in saline immediately above the cathode of Device A. The voltage in medium near the cathodic contact was around 190 mV in peak and sustained around this value for the duration of the 0.2 ms pulse, indicating a high charge injection capacity for the contact-medium interface. The test at 10 Hz (Figure 3B) suggests that the interface is discharged completely during the off cycles through the leakage currents of the photodiodes. A parallel resistor maybe included in the design to ensure a pathway for the discharge current.

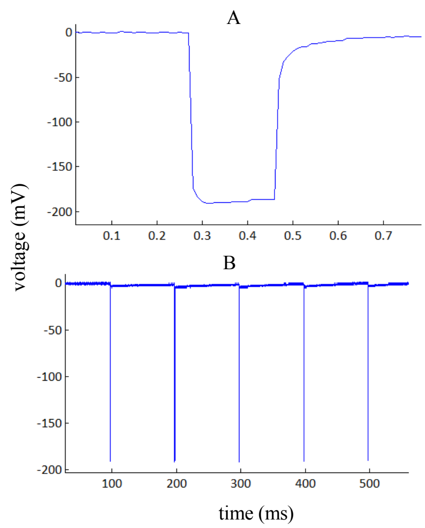

Fig.3 Volume conductor measurements. (A) The waveform recorded immediately above the center of the cathode as a response to a single laser pulse and (B) a train of pulses at 10 Hz.

B. *In Vivo Testing*

A point of stimulation was searched in the gray matter to obtain elbow extension, which primarily generated downward forces. The device tip and thus the cathodic contact was located about 2.5 mm below the dorsal pia surface to generate this forelimb movement in C6. Figure 4 shows the force signal recorded in a rat. Figure 4.A is a raw force data showing the stability of the generated force during a 1s on-1s off cycle for 50 s. The force in each cycle is fused and stable without any signs of fatigue (Fig. 4.B) at this stimulation frequency (100 Hz).

Figure 5 shows the peak forces generated as a function of power density in all rats and for both devices. The plots look different because the devices were implanted at slightly different anatomical locations in each animal. The largest forces produced with Devices A and B were around 0.9 N and 0.3 N respectively. The cathodic contact impedances at 1 KHz were 7 and 20 kΩ for Devices A and B respectively. The current injected by the microstimulators into the tissue was calculated to be about 5-60 µA.

IV. Discussion

In this study, we tested prototype FLAMES activated by an NIR laser beam. Volume conductor and force measurements suggest that the FLAMES approach is feasible for neural stimulation. The differential voltage generated between the two contacts seems sufficiently large to activate nearby nerve cells.

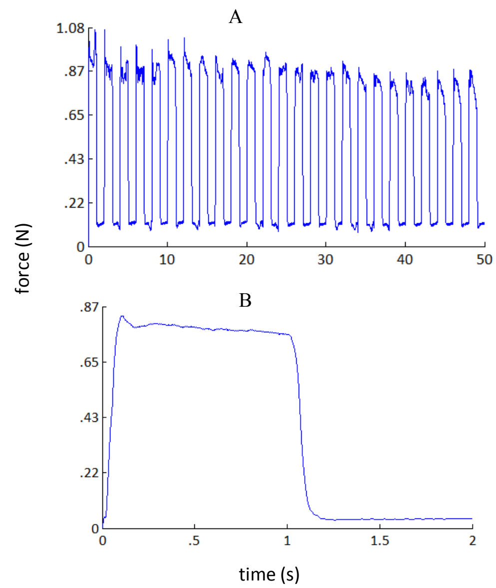

Fig. 4 Force signal recorded from a force transducer attached to the ipsilateral hand to the stimulated side in rat 3. (A) Forelimb force data for a series of 1s ON-1s OFF cycles. Each tetanic force increase is generated by a train of 100 Hz, 0.2 ms pulses. (B) A sample tetanic force pulse on a larger time scale.

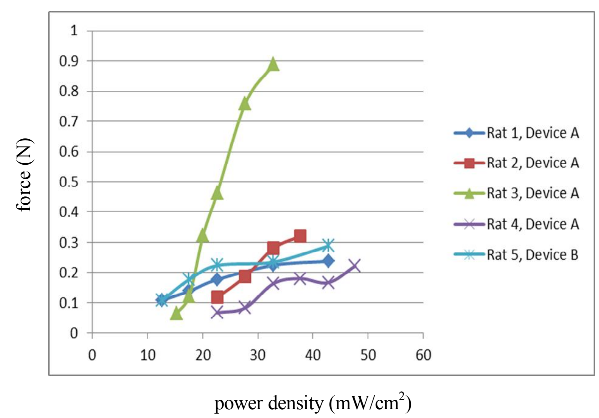

Fig. 5 Forelimb forces generated by intraspinal microstimulation at 100 Hz (Pulse width=0.2 ms) as a function of laser power density using Devices A and B.

The force generated from the rat arm was sufficiently large to be considered functional. John Stanford *et. al.* reported a maximum force of 0.46 N from rats as they extend their forelimb through a rectangular slot to press on a lever [8]. In this study, the average force from four trials (Rat 1, 2, 4, and 5) was 0.27 N. The largest force was 0.9 N (Rat 3) where the electrode tip might have been at a low threshold area in the spinal cord. Minimal laser power was used for generating the observed arm movement to avoid fatigue. The force increased as the power increased monotonously except in rat 4. The relation between the force and power density look different in each rat, which is possibly due to slightly different implant locations in the spinal cord. Therefore, different spinal circuits were probably involved in generating the movement.

Two different device sizes were used in this study. One of the goals of this research is to minimize the device size while safely generating sufficient current for stimulation. The power density range used in this report was from 13 to 48 mW/cm^2. The safe level of NIR exposure is given only for the skin (~300 mW/cm^2) and retina by American National Standards for Safe Use of Lasers (ANSI Z136.1-2007). Our simulations suggested NIR exposure limits of 325 and 250 mW/cm^2 for gray and white matter respectively in order to keep temperature elevation under 0.5 ºC in the neural tissue [9]. The power density range used in this study represents only 7-19% of our predicted maximum allowable exposure. The maximum charge density used was 140 $\mu C/cm^2$. Xinyan Tracy Cui *et. al.* reported a charge injection limit of 2.3 mC/cm^2 for PEDOT [10]. A parallel resistor will be included in the future device designs to ensure a discharge path for the double-charge layer capacitors of the contacts during the off periods of the current.

Electrical stimulation of the CNS is being developed as a new treatment technology for a number of neurological disorders. A floating, wireless micro-stimulator can be an important step towards the development of such a system that can be implanted in humans. The human spinal cord experiences substantial translational and rotational displacements that make chronic implantation of microwire electrodes nearly impossible. FLAMES approach can facilitate clinical implementation of intraspinal cord microstimulation where only a few channels of stimulation can produce functional results [11]-[13].

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