A FLEXIBLE ORIGAMI OPTO-ELECTRO ARRAY FOR IN VIVO OPTOGENETIC STIMULATION AND ELECTROPHYSIOLOGY RECORDINGS FROM DORSAL ROOT GANGLION

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ABSTRACT
In this study, a thin-film, three-dimensional (3D) opto-electro array with 4 addressable microscale light-emitting diodes for surface illumination of dorsal root ganglions (DRGs) and 9 penetrating electrodes for simultaneous recordings of light-evoked DRG activities is described for Developing a tool to better understand the relationship between spindle length-sensitive afferents from hip muscles and both interlimb coordination and gait selection. Importantly, using the origami design concept, the array can be fabricated directly on a silicon wafer in a two-dimensional (2D) configuration, which can transform into a 3D structure by folding.

KEYWORDS
Thin-Film, Opto-Electro Array, Origami, Optogenetic.

INTRODUCATION
Developing a tool to better understand the relationship between spindle length-sensitive afferents from hip muscles and both interlimb coordination and gait selection is an active area of biomedical microelectrochemical systems research. Future tools must be flexible and configurable, given the evolving understanding of both neuroscience mechanisms and clinical outcomes. We describe a thin-film, three-dimensional (3D) opto-electro array (Fig.1) with 4 addressable microscale light-emitting diodes for surface illumination of dorsal root ganglions (DRGs) and 9 penetrating electrodes for simultaneous recordings of light-evoked DRG activities. Inspired by origami concept [1], a trench structure combined with magnetic material to form a hinge structure on a flexible polymer substrate, The opto-electro array can rely on this hinge structure to automatic raising up to achieve the function of 2D to 3D conversion. Compared with the traditional 3D array fabrication, this origami folding technique can reduce the probe fabricating difficulty and cost, especially in the production of relatively long probes (>1mm). Moreover, fabricating a 2-dimensional opto-electro array by photolithography enables independently control the shape, and the length of individual microneedles, thereby forming an array of different lengths to meet the requirements of optogenetic stimulation and electrophysiology recording.

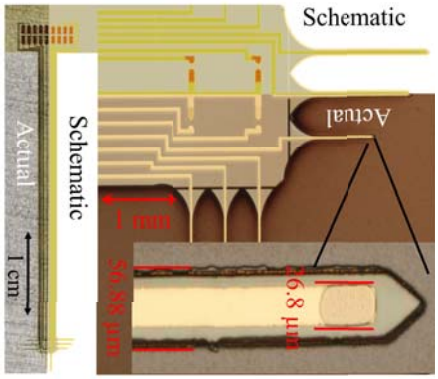

Fig. 1. Schematic diagram of the flexible origami opto-electro array vs. images of the fabricated array.

METHOD
In this study, polyimide was chosen as the substrate and packaging material. Particularly, PI-2600 low stress polyimide (PI, HD MicroSystem™, Parlin, NJ, US) is used, because its high-temperature stability (up to 400 °C) [2], and high bendability [3]. While using flexible materials as probe array, compared to solid materials, low stress polyimide material provides a certain degree of mechanical buffering that avoids damaging the soft tissue [4]. Fig.2 depicts the core fabrication process flow of the opto-electro array. Specifically, (Fig.2-1) A 1μm thick layer of silicon dioxide as a sacrificial layer was deposited on the wafer by PECVD. Etching the sacrificial layer at the last step ensured that the probe can be released from the wafer smoothly. PI was spun on the adhesion promoter (VM652), and the thickness of PI was about 5μm. After PI was cured, 200nm copper layer was thermal evaporated on PI layer as hard mask, followed by a reactive ion etching processing. (Fig.2-2) Gold was selected as the electrode material, and the designed circuit was patterned by photolithography. (Fig.2-3) Another PI layer was fabricated by same way to encapsulate the probe and define the detection windows and mounting pads. (Fig.2-4) Next, a 500nm copper layer was thermal evaporated on the designated location that can reinforce the gold layer to prevent the metal peel off due to soldering. (Fig.2-5) flexible arrays were released from wafer. (Fig.2-6) LEDs were soldered on the device. Meanwhile, the simulation results (Fig.3) show that after bending, the stress points are concentrated in the preset trench structure. The design purpose is to reduce the force applied to the wire as much as possible, and to safely increase the force applied to the substrate to ensure its deformation. Ideally, a part of the thickness of the cantilever structure will "sit" on the bottom structure to keep the bent state stable.

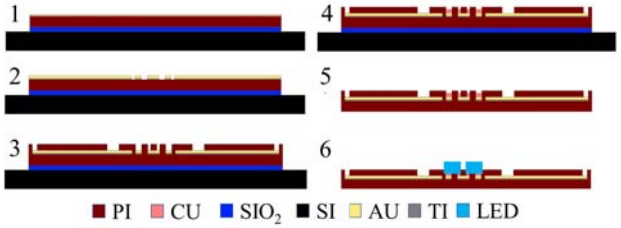

Fig. 2. Fabrication process flow of the opto-electro array.

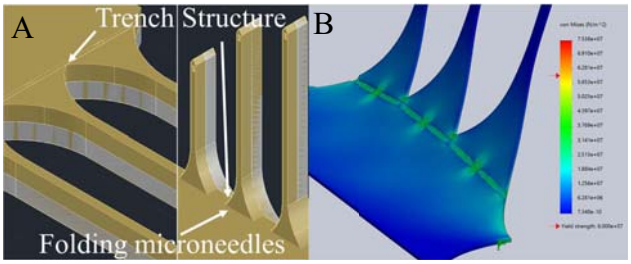

Fig. 3. (A) Schematic diagram of the trench structure. (B) FEM Simulation of the force distribution on the trench area.

DISCUSSION

Although the results from the current stage are relatively preliminary, they still demonstrate the feasibility of the flexible origami opto-electro array. The optical and thermal properties of the probe after implantation were also investigated by in vitro experiments (Fig.4 and 5). Fig. 4 shows that the LEDs installed on the probe are sufficient to affect the target area with a light intensity of 1mw/mm^2 at 1mm away from the LEDs, suitable for activating channelrhodopsin [5,6]. Fig. 5 shows that the temperature rise caused by continuously powered LEDs in 30 minutes is less than 1.5ºC, which would not cause severe damage to the nerves in a short term. The average impedance of the electrophysiological recording probe by EIS measurement is 239 KΩ (n=3) at 1000Hz (Fig.6). Furthermore, the maximum brain tissue force is known to be 1000 μN and based on buckling force calculation formula [7], the theoretical yield strength of a single probe in our array is 993 μN. This means that the probe cannot penetrate brain tissue smoothly, and this calculation result is consistent with the actual insertion experiment results. It means that Polyethylene glycol (PEG) coating technique will be further introduced to enhance the strength of the microneedle to penetrate the tissue [8,9]. In the future, the device will be assembled with an external electronic head stage [10] and tested in cat models to validate its capability for optogenetic stimulation and electrophysiology recordings from DRGs.

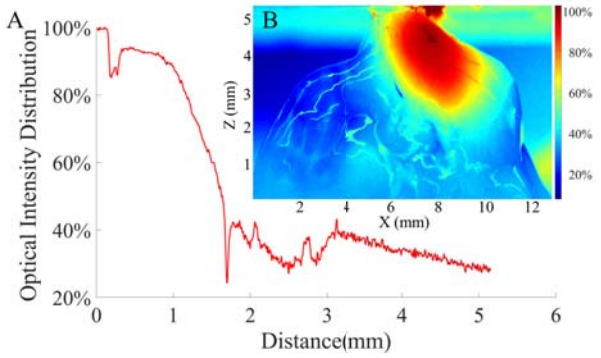

Fig. 4. (A) Optical intensity distribution measured from the μ-LED to the surrounding mouse brain. (B) Photo image of the optical intensity distribution around the μ-LED in the mouse brain (input power = 15mW/optical power =3.85mW)

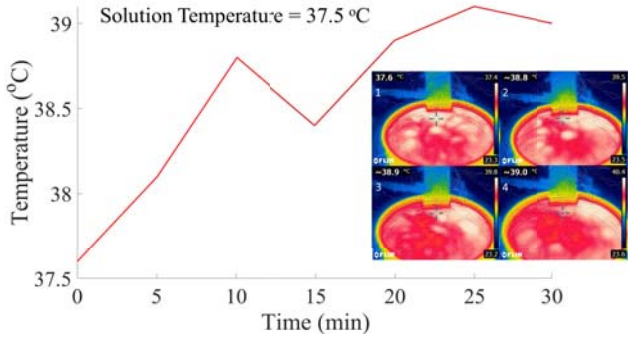

Fig. 5. Time-dependent temperature fluctuation of the LED (input power = 10mW), measured in PBS solution with a FLIR infrared thermal imaging camera at 10 cm distance. Inset shows the infrared images taken (1) at 0 min, (2) at 10 min, (3) at 20 min and (4) at 30 min.

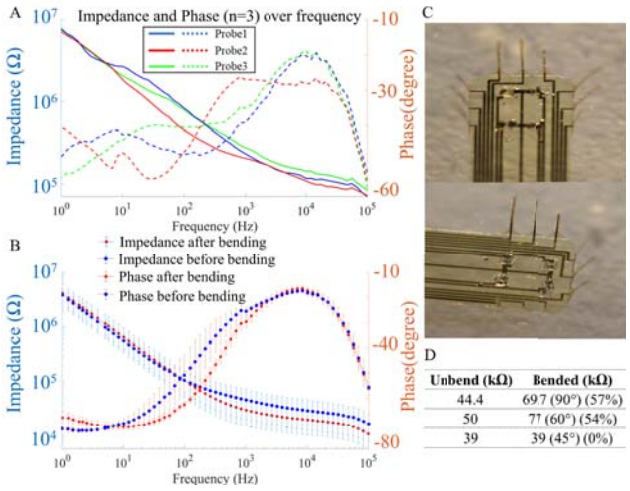

Fig. 6. (A) Electrochemical impedance of the electrodes measured over a broad frequency range from 1-100 kHz. (B) Comparison of the broad-band impedance of the electrodes (n=4) before and after bending. (C) Photo images of the bent probes. (D) Impedance of the bent probes measured at different bending angles.

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