A 16-SITE NEURAL PROBE INTEGRATED WITH A WAVEGUIDE FOR OPTICAL STIMULATION

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ABSTRACT

In this paper, we report a neural probe which can selectively stimulate target neurons optically from an integrated optical waveguide and also monitor extracellular neural signals in electrical recording sites. The waveguide is composed of SU-8 core and oxide cladding layer to guide a light from optical source. A U-groove has been formed at the end of the waveguide for easy alignment with an optical fiber. The coupling loss between the optical fiber and waveguide has been measured below -3.7 dB with a waveguide loss of -0.22 dB/mm. We have successfully transmitted a light of 470nm in wavelength through the integrated polymer waveguide on the neural probe.

1. INTRODUCTION

There have been numerous efforts to understand nervous systems and develop treatments for its disorders. Patch clamp has been explored as an effective tool to record intracellular neural signals with high signal-to-noise ratio but the simultaneous access of multiple neurons is limited due to manual operation of single electrode. Various MEMS neural probes have been introduced to simultaneously record as well as stimulate multiple-sites for studying central nervous system at the cellular level [1-3]. Although massive-parallel access of single neuron activities has been realized in three-dimensional probe shanks for both recording and stimulation, the area of monitoring neural activities are still more than 100μm around each site and specific target neurons cannot be selectively screened. Electrical stimulation injects a large amount of current into the tissue to stimulate neurons in the vicinity of stimulating sites. This electrical stimulation may damage the neurons and also suffers from poor spatial resolution limited by the propagation of electrical pulse through the solution and thus all the neurons within the vicinity of the stimulation electrode are potentially excited.

Recently, optical stimulation has been widely investigated to selectively stimulate the specific neural cells which are genetically modified to express channelrhodopsin-2 (ChR2) responding to a light illuminated at a specific wavelength [4]. Several methods have been tried to stimulate genetically modified neurons using an external light source such as laser coupled optics [5] or LED (light emitting diode) [6]. In these methods, neurons are directly stimulated from an external light source implemented in a separate device by optically focusing to target locations. This makes it difficult to record neural signals close to the stimulating location because the close positioning of the electrical recording probe to the optical stimulating device is a major challenge. In order to monitor neural signals in the vicinity of the stimulated neuron, an optical fiber (~200 μm diameter) was directly attached to the probe shank [7-8]. However, this makes the probe dimension bulky, damaging the neurons during insertion of the probe and the manual assembly makes it difficult to accurately control the location of stimulation sites. A recent report on optical stimulation still has a large gap between the stimulation and recording sites more than 0.4mm [9].

In this paper, we report a new approach of

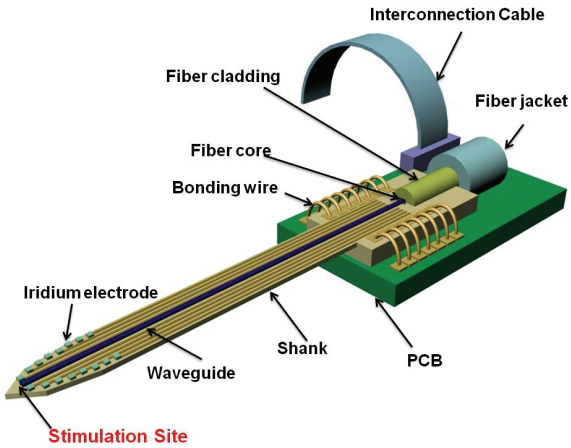


Fig. 1 Proposed neural probe structure integrated with optical waveguide for optical stimulation and the iridium electrode array for electrical recording.

optical neural probe by directly integrating a polymer optical waveguide on the shank where multiple recording electrode sites are located. The distance between the stimulation and recording sites can be accurately controlled within the tolerance of misalignment of photolithography. In this probe, effects of signal propagation with and without optical stimulation can be monitored from the integrated multiple recording sites.

2. OPTICAL PROBE DESIGN

Figure 1 shows the schematic diagram of the proposed neural probe structure. The optical waveguide is integrated on top of the shank and connected to an optical fiber which introduce a light to the waveguide from an external light source. The optical fiber and waveguide should be accurately aligned to minimize a coupling loss. A U-groove is formed on the silicon substrate to secure a room for of the optical fiber. The process has been modified from the standard Michigan probes [10] in order to incorporate a bottom cladding layer under the waveguide core to minimize propagation loss in the waveguide. We used silicon dioxide as the cladding layer because it has a lower refractive index of 1.44 smaller than that of the SU-8 core (1.53).

There are total 16 iridium electrodes in the vicinity of the stimulation site to monitor extracellular neural signals during optical stimulation. Polysilicon interconnection lines are defined from the iridium electrodes to boning pads on the probe body. In this proposed structure, the shank body is

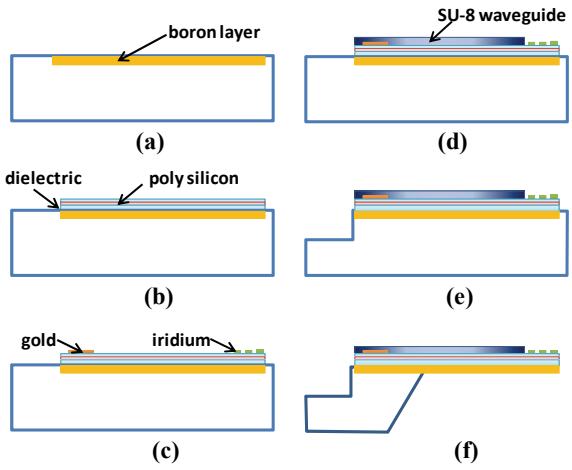
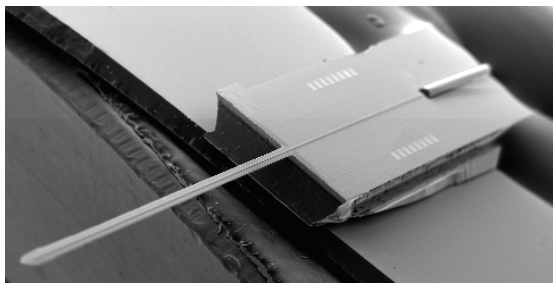
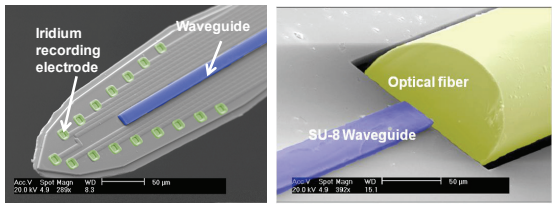


Fig. 2. Fabrication process flow: (a) boron diffusion, (b) 1st dielectric layer, poly-silicon and 2nd dielectric deposition, (c) iridium electrodes and gold pad deposition and patterning, (d) SU-8 waveguide patterning, (e) U-groove for mounting optical fiber, (g) Release by DRIE etching and EDP etching.



(a)



(b) *(c)*

Fig. 3. SEM pictures of the fabricated neural probe (a) Overview of the neural probe with optical fiber mounted at the end of the waveguide, (b) Iridium electrode array around stimulation site, and (c) Coupling between optical fiber and waveguide

composed of boron doped silicon layer of 12 µm, oxide/nitride/oxide stress compensation layer of 3 µm and the waveguide of 5 µm, respectively. The total thickness of the shank is maintained below 20 µm, which is comparable to conventional Michigan probe dimension and does not induce any additional cell damage during implantation.

3. FABRICATION

The Fabrication of the proposed neural probe is illustrated in Fig.2. First, deep-boron diffusion is performed to form a layer for the probe shank. Next, a composite layer of oxide/nitride/oxide layer is deposited for electrical isolation and stress compensation. Poly-silicon is deposited and patterned for interconnections. On top of the patterned poly-silicon layer, the second dielectric layer is deposited for electrical insulation. Next, iridium electrode sites are formed and gold pads are patterned. SU-8 is patterned on the cladding oxide layer to define an optical waveguide and a U-groove is patterned at the end of the waveguide using DRIE. Finally, the probe is release by wet etching in EDP by using a boron layer as an etch stop.

The SEM pictures of the fabricated neural probe are shown in Fig. 3. The length of the shank which will be inserted into a brain is 5 mm and the width is 80 µm. The thickness of the shank is 12 µm, which is determined by the boron diffused silicon

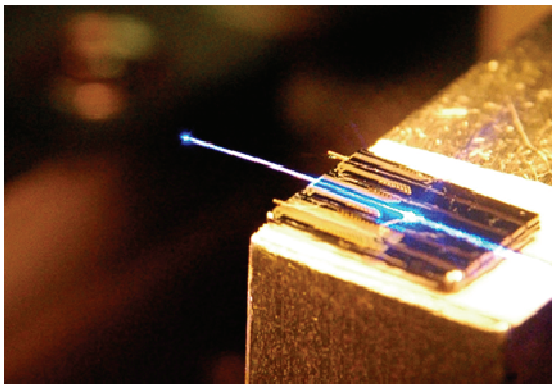


Fig. 4. Light transmission through an optical waveguide integrated on the neural probe.

layer and it can be adjusted by boron diffusion time. Fig. 3(b) shows an enlarged view of the shank. There are total 16 iridium recording electrodes around the optical stimulating site at the end of the waveguide. The distance between the recording electrodes and optical stimulation site is exactly controlled in the range from 20 μm to 160 μm. The optical fiber is mounted in the U-groove at the end of the SU-8 waveguide as shown in Fig. 3 (c). The width of U-groove was determined by the optical fiber diameter (62.5 μm) for accurate alignment between the optical fiber and the waveguide.

4. MEASUREMENT RESULTS

For optical characterization of the fabricated probe, the optical fiber is connected to an external light

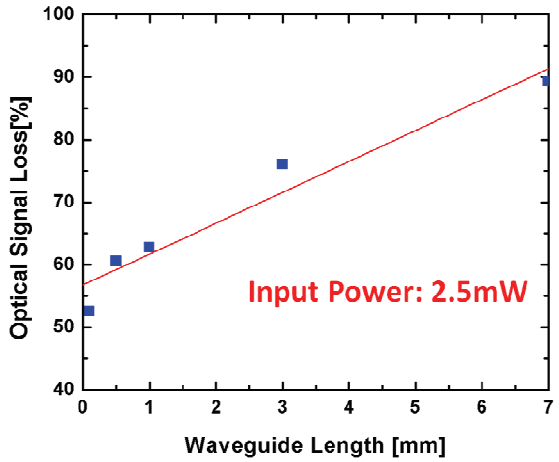


Fig. 5. Total optical signal loss as a function of waveguide length. From the slope, transmission loss can be estimated.

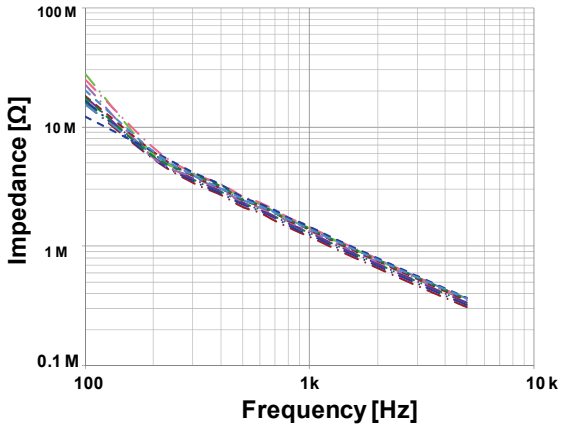


Fig. 6. Impedance measurement of the 16 iridium electrodes in a saline solution.

source with a wavelength of 475 nm and the light has been successfully transmitted to the end of the shank for optical stimulation as shown in Fig. 4. The wavelength (blue light) was chosen to effectively stimulate channelrhodopsin-2 (ChR2) expressed neurons [5].

Optical loss of the waveguide has been measured using optical power meter. To separately characterize the coupling and transmission loss, different lengths of waveguides have been fabricated. By assuming that the coupling loss is almost same, transmission loss has been calculated by measuring a slope from the plot of total loss for different waveguide lengths as shown in Fig. 5. The coupling loss is estimated to be -3.7dB (57%) and the waveguide loss as -0.22 dB/mm (4.9%).

In this experiment, we have successfully demonstrated the light transmission through the waveguide integrated on the shank by using a light source of 2.5 mW. The output power measured at the end of the waveguide was measured to be 0.31 mW, which is sufficient to optically stimulate neurons [3].

The electrical characteristics of the iridium electrode array have been measured as shown in Fig. 6. The fabricated neural probe is packaged on the PCB with bonding wires connected for measurement as shown in Fig. 7. The probe shank has been loaded in a saline solution and the electrode impedance has been measured as a function of frequency. The average impedance was 1.49MΩ with a small variation between 1.3 MΩ and 1.6 MΩ at 1 kHz.

5. CONCLUSIONS

We have integrated an optical waveguide on the probe shank to add optical stimulation capability in

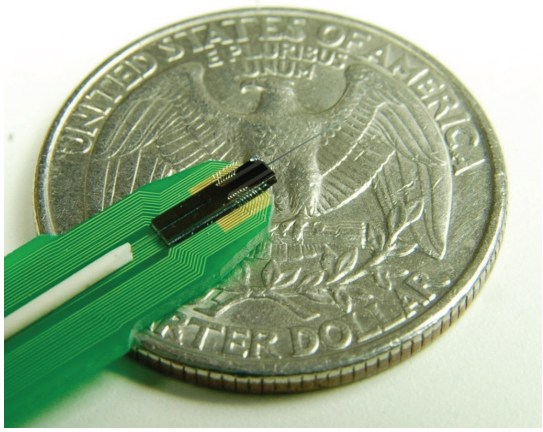


Fig. 7. Neural probe attached on the PCB with electrical and optical connections for in-vivo test.

addition to electrical recording of single neuron activities. The proposed neural probe can maintain the shank thickness below 20 μm which is comparable to the conventional Michigan probe and does not induce any additional cell damage during implantation. The distance between the stimulation site and the recording electrodes can be precisely controlled to monitor neuronal behavior before and after optical stimulation. The coupling loss between the optical fiber and the waveguide was measured as -4.3 dB and the waveguide transmission loss as -0.22 dB/mm. In the fabricated neural probe, we have successfully transmitted a light to the stimulation site through the waveguide from an external optical source.

REFERENCES

[1] K. D. Wise, Amir M. Sodagar, Ying Yao, M. N. Gulari, Gayatri E. Perlin and K. Najafi, "Microelectrodes, Microelectronics, and Implantable Neural Microsystems," *Proceesings of the IEEE*, vol. 96, No. 7, July 2008.

[2] P. T. Bhatti, Sangwoo Lee, K. D. Wise, "A 32-Site 4-Channel Cochlear Electrode Array," *IEEE J. Solid-State Circuits*, pp. 2965-2973, 2008.

[3] Patrick J. Rousche, Richard A. Normann, "Chronic recording capability of the Utah intracortical electrode array in cat sensory cortex", *Journal of NeuroSCience Methods*, vol. 83, pp1-15, 1998.

[4] E.S. Boyden, F. Zhang, E. Bamberg, G. Nagel, and K. Deisseroth, "Millisecond-Timescale, Genetically Targeted Optical Control of Neural Activity," *Nature Neuroscience*, vol. 10, pp. 663-668, May 2007.

[5] L. Petreanu D. Huber, A. Sobczyk, and K. Svoboda, "Channelrhodops in-2-assisted Circuit Mapping of Long-Range Callosal Projections," *Nature Neuroscience*, vol. 10, pp. 663-668, May 2007.

[6] V Poher, N Grossman, G T Kennedy, K Nikolic, H X Zhang, Z Gong, E M Drakakis, E Gu, M D Dawson, P M W French, P Degenaar and M A A Neil, "Micro-LED Arrays: A Tool for Two-Dimensional Neuron Stimulation," *Journal of Physics*, vol. 41, 094014, 2008.

[7] Alexander M Aravanis, Li-Ping Wang, Feng Zhang, Leslie A Meltzer, Murtaza Z Mogri, M Bret Schneider and Karl Deisseroth, "An Optical Neural Interface: *In Vivo* Control of Rodent Motor Cortex with Integrated Fiberoptic and Optogenetic Technology," *Journal of Neural Engineering*, vol. 4, S143-S156, 2007.

[8] V. Gradinaru, K. R. Thomson, f. Zhang, M. Mogri, K. Kay, M. B. Schneider, and K. Deisseroth, "Targeting and Readout Strategies for Fast Optical Neural Control *In Vitro* and *In Vivo*," *Journal of Neuroscience*, vol. 27, pp. 14231-14238, 2007.

[9] Jiayi Zhang, Farah Laiwalla, Jennifer A. Kim, Hayato Urabe, Rick Van Wagenen, Yoon-Kyu Song, Barry W. Connors and Arto V. Nurmikko, "A Microelectrode Array Incorporating an Optical Waveguide Device for Stimulation and Spatiotemporal Electrical Recording of Neural Activity," *Proceeding of EMBC*, pp. 2046-2049, 2009.

[10] Qing Bai, K. D. Wise, D. J. Anderson, "A high yield microassembly structure for three-dimensional microelectrode arrays", *IEEE Transactions on Biomedical Engineering*, vol. 47, NO.3, 2000