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A Dual-Shank Neural Probe Integrated with Double Waveguides on Each Shank for Optogenetic Applications

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***Abstract*—This paper presents a dual-shank neural probe integrated with double-waveguides on each shank, which enables both optical stimulation and electrical recording. Two 15-μm-thick polymeric (SU-8) waveguides on each neural probe shank have been precisely defined by photolithography with a width of 24 μm and a spacing of 10 μm. The waveguides transmit a light coupled from optical fibers which are placed in the grooves located at the neural probe body. Each shank has 8 iridium recording electrodes which have the area of 11 μm × 13 μm. In front of each waveguide, four recording sites are deployed with a pitch of 100 μm. Blue light (473 nm in wavelength) has been successfully transmitted to the stimulation sites located at the end of the fabricated neural probe tips.**

I. Introduction

THE electrical stimulation of the nervous system has been extensively studied with various micro-devices [1-4], particularly, for the treatment of most debilitating brain diseases such as Parkinson's disease, epilepsy, and depression [4, 5]. Probes for deep brain stimulation are commercially available by Medtronic for clinical applications [6].

Despite the tremendous amount of studies and commercial success, the electrical stimulation of neurons has serious drawbacks [7]. It has relatively poor spatial and temporal resolutions, sometimes possibly over-activates the neurons, is susceptible for electrical noise, and does not provide specificity. Recently, neuroscientists have developed an optical stimulation method which specifically targets a group of selected neurons that are genetically engineered to be sensitive to a light of specific wavelength [8-10]. They utilized a light-sensitive positive ion channel protein, e.g., *Channelrhodopsin-2* (*ChR2*), to make neurons selectively excited by blue light [8]. On the other hand, activity of neurons can be inhibited by another wavelength after introducing another type of molecule, e.g., *Halorhodopsin* (*NpHR*), to make neurons responsive to yellow light [11]. Since the optical stimulation method can give high temporal and spatial resolutions [8-10] in addition to specificity without any possible neuronal damage often observed in electrical stimulation [12], it has drawn a wide attention from neuroscientist community over the past few years.

Rather than the direct insertion of optical fibers into the brain in animals [8], neuroscientists manually attached a chemically-thinned optical fiber on a probe shank [11]. However, this method provides neither accurate control in positioning of optical stimulation site, nor reproducibility in multiple attachments. Moreover, it is very challenging to place closely two or more optical fibers on the same probe shank. In order to monitor neuronal activities with simultaneous light illumination at multiple stimulation sites and of different wavelengths such as blue and yellow, it is desirable to deliver various different wavelengths on a single shank with accurate position control. Even though a multi-waveguide probe had been recently reported [13], it seems difficult to be implanted in living animals because its shank thickness is thicker than 600 μm.

In this paper, we report an 18-μm-thick dual-shank neural probe with integrated with double waveguides on each shank for chronic optogenetic studies. Using micro-fabrication technologies, multiple waveguides composed of photodefinable polymer (SU-8) are precisely formed on a neural probe shank, as shown in Fig.1.

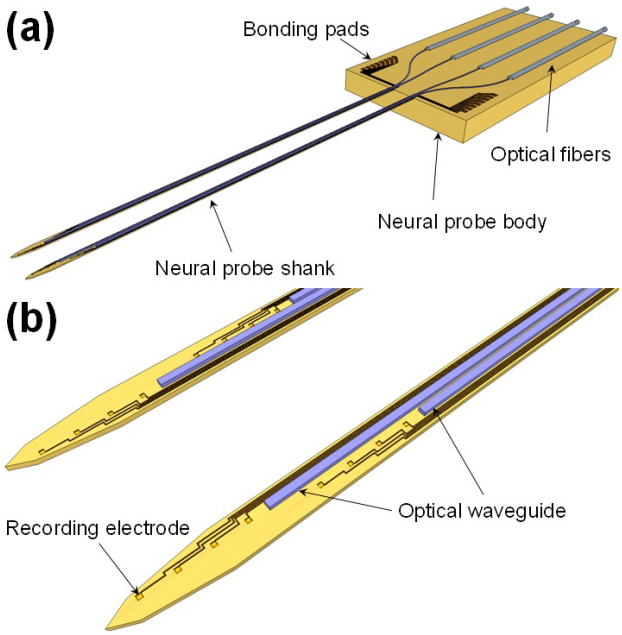

Fig. 1. (a) Schematic diagram of the proposed dual-shank neural probe integrated with double waveguides, (b) Magnified view of the neural probe shank showing two waveguides on each shank with recording electrodes.

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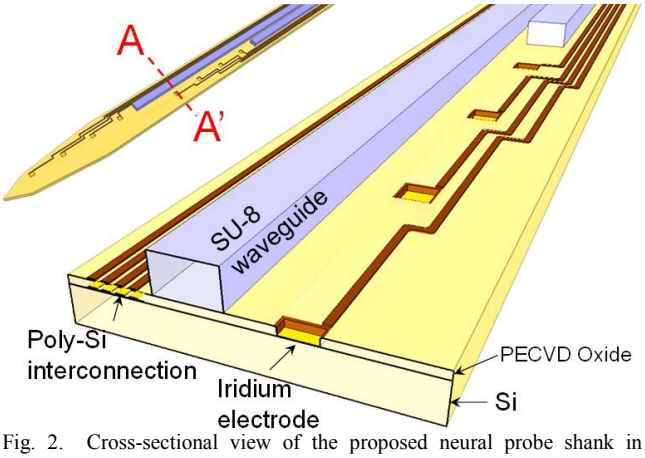

Fig. 2. Cross-sectional view of the proposed neural probe shank in direction of AA'

II. Structure Design and Fabrication Process

A. Structure of Neural Probes with Double Waveguides

In the neural probe shown in Fig. 1, two 5-mm-long probe shanks are designed to be 430 µm apart from each other. On a 110-µm-wide shank, dual stimulation sites at two different/same wavelengths can be simultaneously illuminated through the 15-µm-thick and 24-µm-wide SU-8 waveguides with 10 µm spacing. Geometrical parameters such as thickness, width, and spacing of the SU-8 waveguides can be lithographically defined. This is the main advantage of the proposed neural probes with SU-8 waveguides.

The recording electrode closest to the waveguide is 50 µm apart from the waveguide. All the recording electrode sites have an area of 11 µm × 13 µm in a pitch of 100 µm. Interconnection lines with a width of 3 µm and a spacing of 2 µm are formed along the shank and connected to the bonding pads on the probe body. At the end of the probe body, there are four deep grooves where optical fibers are positioned and coupled to each SU-8 waveguide, respectively.

B. Fabrication Process of the Proposed Neural Probe

The fabrication process of the proposed neural probes was reported by our group [14]. In this work, we incorporated the structural optimization to integrate the double waveguides for multi-site stimulation in different wavelengths. Fig. 2 shows a cross-sectional view of the proposed neural probes in the direction of AA'.

The final thickness of the fabricated neural probes will be accurately defined by the top silicon thickness (15 µm) of a silicon-on-insulator wafer, instead of a bulk silicon wafer used in the previous work [15]. After thermal oxidation of the wafer for electrical isolation of interconnection lines, a 500-nm-thick poly-silicon layer was deposited and doped with boron for low-resistivity. The poly-silicon layer was patterned by dry etching to form electrical interconnection lines and was insulated again with another thermal oxidation. After etching the oxide for contact holes, Ti/Ir (30 nm/300 nm) and Cr/Au (30 nm/300 nm) were deposited and patterned by lift-off for recording sites and bonding pads, respectively.

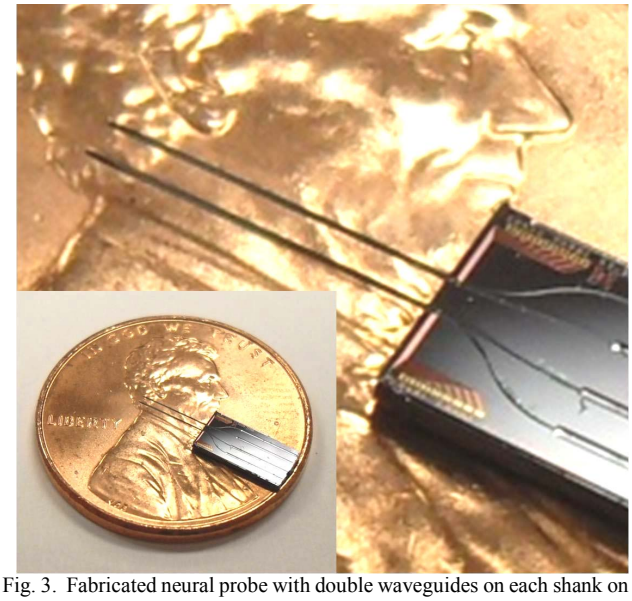
Fig. 3. Fabricated neural probe with double waveguides on each shank on a U.S. penny

Next, an additional oxide layer of 3 µm in thickness was deposited by plasma-enhanced chemical vapor deposition (PECVD) as a bottom cladding layer as well as a thick insulation layer on top of poly-silicon interconnection lines as shown in Fig. 2. This thick PECVD oxide layer was etched for Ir recording electrodes and Au bonding pads exposed. So the Ir electrodes were recessed as described in Fig. 2.

A photodefinable polymer, SU-8 2010 (MicroChem Corp., Newton, MA), was patterned with a thickness of 15 µm to form waveguides on the neural probe shanks. On the probe body, deep grooves were etched for optical fibers by deep reactive ion etch (DRIE). Finally, probes were released by two DRIE steps: one for defining the top silicon from the frontside, and the other for removing the silicon body and 2-µm-thick buried oxide from the backside.

C. Fabricated Neural Probes

Fig. 3 shows a fabricated neural probe on a U.S. penny for relative size comparison of the device. Four curved SU-8 waveguides begin from the probe body and are running through the two probe shanks. In the grooves etched on the probe body, four optical fibers can be butt-coupled to four SU-8 waveguides.

Scanning electron microscopy (SEM) images are shown in Fig. 4. Lithographically defined SU-8 waveguides are well defined on the probe shank. Fig. 4(c) clearly shows the rectangular shape of the SU-8 waveguide cross section. As described in the previous section, Ir recording electrode sites are recessed from the probe surface by 3 µm, which is the thickness of PECVD oxide. This recessed electrode structure did not show significant signal degradation in *in-vivo* recording of neural activities from animal experiments (data not shown).

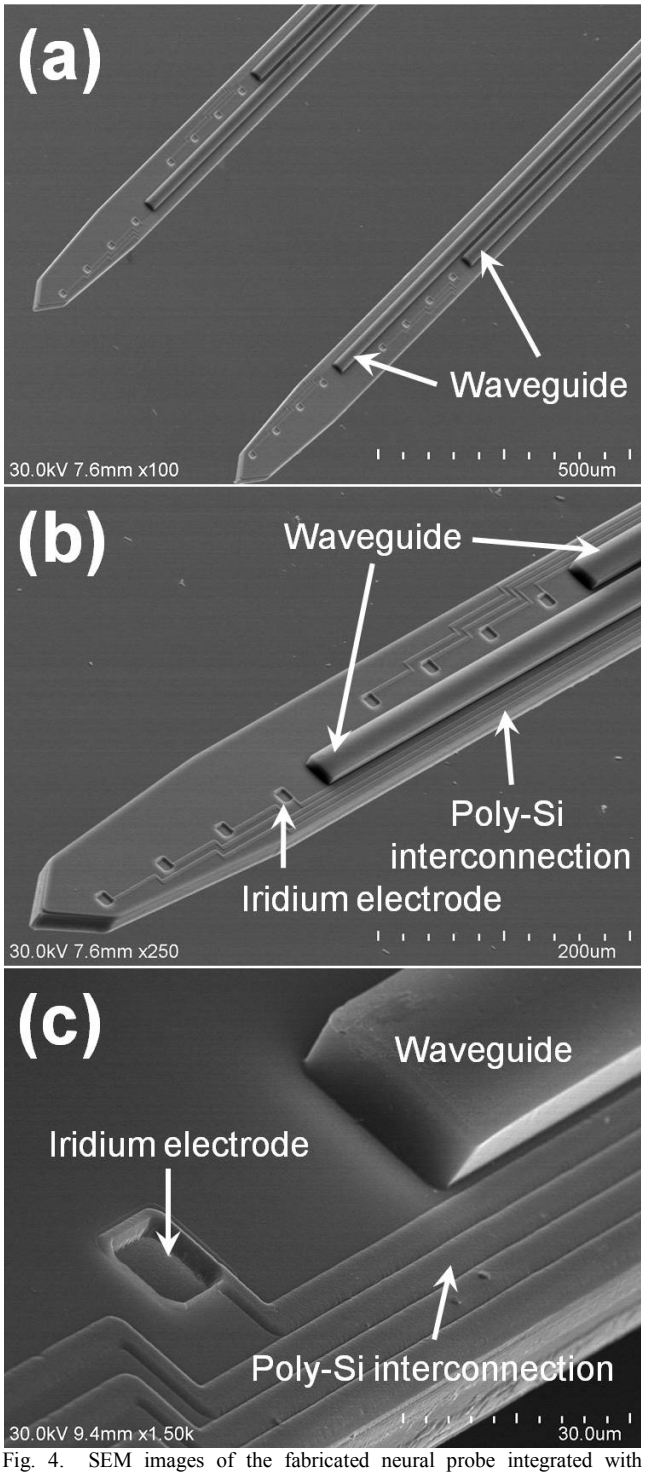

Fig. 4. SEM images of the fabricated neural probe integrated with double-waveguides on a shank: (a) Top view of dual shank showing double waveguides on each shank; (b) Tilted view of a single shank; and (c) Magnified view near the end of the integrated waveguide

III. Experimental Results

In order to demonstrate the capability of light transmission through the fabricated waveguides, a multi-mode optical fiber was coupled to each waveguide in the fabricated device. A multi-mode optical fiber with a core diameter of 10 µm was used for light transmission, and the outer diameter of the

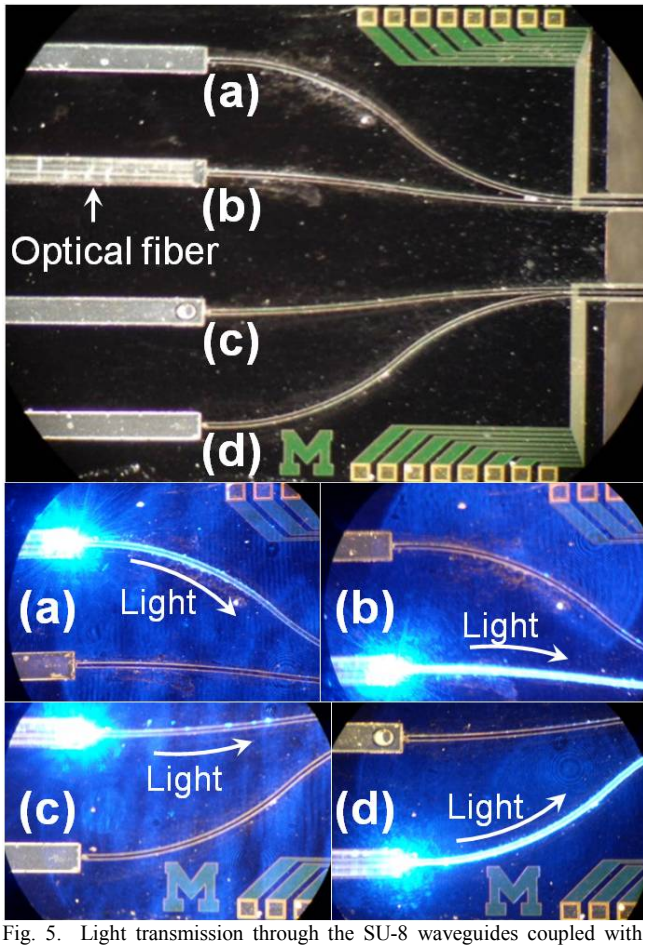

Fig. 5. Light transmission through the SU-8 waveguides coupled with optical fibers. Upper microscope image is showing an optical fiber placed in the groove for the second waveguide from the top.

optical fiber was 125 µm including the cladding layer. The groove was etched precisely for accurate vertical alignment of the optical fiber core to the center of waveguides. For maximum optical output power at the end of the waveguide, the optical fiber placed in the groove was aligned vertically as well as horizontally using a micromanipulator (561 Series ULTRAlign™, Newport, Irvine, CA). As shown in Fig. 5, four waveguides successfully transmitted a blue light (wavelength 473 nm), which is known to stimulate *ChR2*-modified neurons [8].

Fig.6 also demonstrates blue light transmission through one of the waveguides to the end of probe shank. Transmitted light is clearly visible in the dark field microscope in Fig. 6(b). At the end of the cleaved facet, the multi-mode optical fiber delivered 7.5 mW light power from the laser source (FC-473-005-SM-PC-0-1, RGBLase LLC, Fremont, CA).

For accurate measurement of the light intensity at the waveguide end, UV-curable black epoxy (EPO-TEK OG147, Epoxy Technology, Inc., Billerica, MA) was applied to block the scattered light from the junction of the optical fiber and the waveguide. (Images were taken before application of the epoxy to clearly visualize the light transmission along the waveguide.) Since the epoxy used is optically opaque at 473 nm with less than 6% of transmission [16], it can effectively

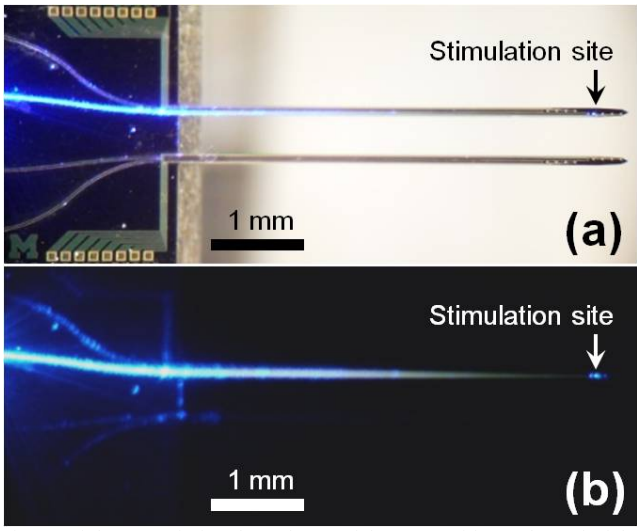

Fig. 6. Light transmission through one of the waveguides to the end of the waveguide: (a) a bright field microscope image; and (b) a dark field microscope image.

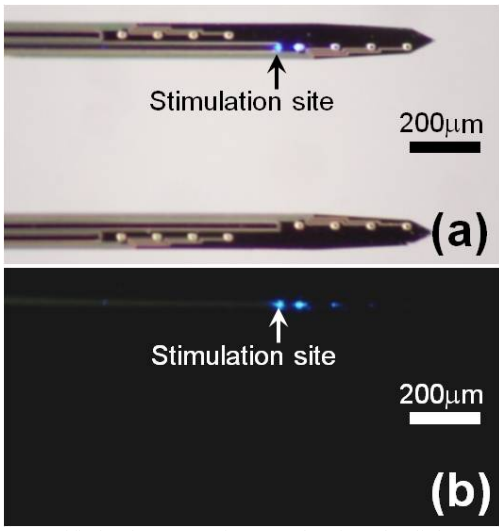

Fig. 7. Magnified microscope images showing the light transmission through one of the waveguides: (a) a bright field microscope image; and (b) a dark field microscope image.

prevent the scattered light at the junction from being detected. Light intensity at the end of the SU-8 waveguide was measured to be approximately 50 μW with an optical meter (1936-C, Newport, Irvine, CA); this power is enough to stimulate *ChR2*-engineered neurons [10, 11]. Fig. 7 illustrates transmitted light at the end of the waveguide with a higher magnification of the microscope.

IV. Conclusion

In this work, the double waveguides incorporated in a single neural probe shank has been reported. The presented probe has a dual-shank with 16 recording channels and 4 waveguides for optical stimulation. The shank thickness is 18 μm in thickness and the two 15-μm-thick SU-8 waveguides have been lithographically defined on top of each shank with the precise control of distance between the waveguides and recording sites. Light has been successfully delivered to the end of the SU-8 waveguides from a multi-mode optical fiber coupled in the probe body.

The neural probe with double waveguides can be used in stimulation/inhibition of genetically targeted neurons by selectively switching the wavelength of light at a close distance to each other.

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References

[1] S.-H. Cho, L. Cauller, W. Rosellini, and J.-B. Lee, "A MEMS-based fully-integrated wireless neurostimulator," in *Proc. MEMS 2010 Conference*, Hong Kong, China, January 24-28, 2010, pp.300-303.

[2] J. Coulombe, M. Sawan, and J. Gervais, "A highly flexible system for microstimulation of the visual cortex: Design and implementation", *IEEE Trans. Biomed. Circuits Syst.*, vol. 1, no. 4, pp. 258-269, Dec. 2007.

[3] M. Ghovanloo, and K. Najafi, "A wireless implantable multichannel microstimulating system-on-a-chip with modular architecture", *IEEE Trans. Neural Syst. Rehabil. Eng.,* vol. 15, no. 3, pp. 449-457, Sep. 2007.

[4] A. A. Fomani, M. Moradi, S. Assaf, and R. R. Mansour, "3D microscopes for deep brain stimulation and recording," in *Proc. 32nd Annu. Int. Conf. IEEE EMBS*, 2010, pp.1808-1811.

[5] J. S. Perlmutter, and J. W. Mink, "Deep brain stimulation," *Annu. Rev. Neurosci.*, vol. 29, pp.229-257, Mar. 2006.

[6] http://www.metronic.com

[7] M. Williams, (2010, Feb. 24). A brain implant that uses light. Available: http://www.technologyreview.com/biomedicine/24644/page1/?a=f

[8] E. S. Boyden, F. Zhang, E. Bamberg, G. Nagel, and K. Deisseroth, "Millisecond-timescale, genetically targeted optical control of neural activity", *Nat. Neurosci.*, vol. 8, no. 9, pp. 1263-1268, 2005.

[9] F. Zhang, L.-P. Wang, M. Brauner, J. F. Liewald, K. Kay, N. Watzke, P. G. Wood, E. Bamberg, G. Nagel, A. Gottschalk, and K. Deisseroth, "Multimodal fast optical interrogation of neural circuitry", *Nature*, vol. 446, pp.633-639, 2007.

[10] X. Han, X. Qian, J. G. Bernstein, H.-H. Zhou, G. T. Franzesi, P. Stem, R. T. Bronson, A. M. Graybiel, R. Desimone, and E. S. Boyden, "Millisecond-timescale optical control of neural dynamics in the nonhuman primate brain", *Neuron*, vol. 62, pp. 191-198, 2009.

[11] S. Royer, B. V. Zemelman, M. Barbic, A. Losonczy, G. Buzsaki, and J. C. Magee, "Multi-array silicon probes with integrated optical fibers: light-assisted perturbation and recording of local neural circuits in the behaving animal", *Eur. J. Neurosci.*, vol. 31, pp. 2279-2291, 2010.

[12] D. B. McCreery, W. F. Agnew, T. G. H. Yuen, and L. A. Bullara, "Comparison of neural damage induced by electrical stimulation with faradaic and capacitor electrodes", *Ann. Biomed. Eng.*, vol. 16, no.5, pp. 463-481, 1988.

[13] A. N. Zorzos, E. S. Boyden, and C. G. Fonstad, "Multiwaveguide implantable probe for light delievery to sets of distributed brain targets," *Opt. Lett.*, vol. 25, no. 24, pp.4133-4135, Dec. 2010.

[14] M. Im, I.-J. Cho, F. Wu, K. D. Wise, and E. Yoon, "Neural probes integrated with optical mixer/splitter waveguides and multiple stimulation sites," in *Proc. MEMS 2011 Conference*, Cancun, Mexico, January 23-27, 2011, pp. 1051-1054.

[15] I.-J. Cho, H. W. Baac, and E. Yoon, "A 16-site neural probe integrated with a waveguide for optical stimulation", in *Proc. MEMS 2010 Conference*, Hong Kong, China, January 24-28, 2010, pp. 995-998.

[16] Datasheet of EPO-TEK OG147. Available: http://www.epotek.com