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Development of Optical Waveguiding Neural Probe with Upconversion-Nanoparticle Light Emitter for Optogenetics

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Abstract

Upconversion nanoparticles (UCNP) can emit visible light with NIR irradiation. Opto-neural probe with UCNP (UC probe) can perform optical stimulation wirelessly. Therefore, the UC probe can reduce the invasiveness to the neuron and keep animals moving freely during the experiment. Although NIR light penetrates body tissues, it is difficult to obtain sufficient light intensity for the upconversion in deep brain areas due to the attenuation of NIR light in the body tissues. In this study, to avoid the light's attenuation, we fabricated a new opto-neural probe having an optical waveguiding structure and UCNP light emitter (WG-UC probe). This probe can optically stimulate the deep brain area with visible light where NIR light does not reach from the outside body.

1. Introduction

Optogenetics has recently attracted much attention in neuroscience. Optogenetics can control activities of neurons with optical stimulation by expressing light-sensitive proteins, such as a channelrhodopsin-2 (ChR2), C1V1, and ACR1, in the cell membrane of the neuron. It is possible to perform both excitation and inhibition of cells by using different light-sensitive proteins. Currently, optogenetics can be considered as one of the most effective methods to investigate brain functions. In general, optical fibers, optical waveguides, and LEDs-embedded neural probes are used to optically stimulate brain tissues [1]-[3]. However, these neural probes need optical or electrical wires to interconnect between the neural probe and the external devices. Wired connections may induce serious damages to the neuron and disturb the moving of animals [4]. Therefore, wireless opto-neural probes are strongly required for advanced optogenetics.

We have been focusing on upconversion nanoparticles (UCNP) and proposed opto-neural probe using UCNP (UC probe) [5]. UCNP can emit visible light with a particular wavelength by absorption of near-infrared (NIR) light, where the absorption and emission wavelengths can be controlled by both types and ratios of the elements of the UCNP. As shown in Fig. 1(a), we can wirelessly stimulate nerve cells expressing light-sensitive proteins using the UC probe and NIR light irradiation from outside the body, which leads to lower invasiveness and free moving of animals during experiments.

Although NIR light used to excite UCNP has a relatively high transmittance, it is attenuated in body tissues. Therefore, it is difficult to irradiate deep brain areas with NIR light with sufficient intensity. In this study, we proposed an optical waveguiding neural probe with UCNP light emitter to avoid the NIR light attenuation.

2. Proposal and design of WG-UC probe

Figure 1(b) shows the proposed WG-UC probe. The WG-UC probe has UCNP light emitter at the position close to the body surface. Thus, attenuation of NIR due to the body tissue can be suppressed. The visible light emitted from UCNP propagates through the probe and reaches the tip, because of the optical waveguiding structure. Then, the deep part of the brain is stimulated by visible light.

Figure 2(a) shows the schematic illustration of the WG-UC probe. The widths of the UCNP light emitter, W, were 500 and 900 μm. The angles from the light-emitter to the shank (θ) were 5° and 10°. The width and length of the probe shank were 200 μm and 10 mm, respectively. By designing the angle of the probe tip to be 45°, light propagating through the probe is reflected and irradiated along the lateral direction. Fig. 2(b) shows the FDTD simulation results of green-light propagation in the WG-UC probe. The simulation results indicated that most of the light generated by the UCNP light emitter entered the shank and was reflected at the probe tip.

3. Fabrication of WG-UC probe

We fabricated the opto-neural probe using UCNP-mixed photosensitive resin. We used SU-8 as photosensitive resin. The UCNP used in this study consisted of ytterbium (Yb) and erbium (Er). The particle size was 1-3 μm. It has an excitation wavelength of 980 nm and an emission peak wavelength of 540 nm (green). As SU-8 has high flexibility compared with Si, the SU-8 based opto-neural probe can reduce the damages to brain cells. And since SU-8 has a high refractive index, the SU-8 probe can work as the core of the optical waveguide.

Figure 3 shows the fabrication process of the WG-UC probe. First, we deposited SiO_2 on a 2-inch Si wafer by plasma-enhanced chemical vapor deposition (PE-CVD). Then, the UCNP light emitter was formed by lithography using UCNP-mixed SU-8. Next, we formed the probe shanks with SU-8. Finally, WG-UC probes were released from the Si wafer by dipping in an aqueous hydrofluoric acid solution. Fig. 4(a) shows the photograph of the fabricated WG-UC probe with four light reflection planes. Figs. 4(b) and 4(c) show the photographs of the tip of the fabricated WG-UC probe with NIR irradiation. By forming multiple reflection planes at the tip of the probe, it is possible to perform multiple optical stimulations to the neuron simultaneously. Also, this WG-UC probe has the potential to perform stratified stimulation of the cerebral cortex.

4. Experimental results and discussion

Figure 5 shows a measurement setup to evaluate the upconverted visible light intensity. A neural probe was inserted into an agarose gel, and the emission part was irradiated with NIR light. Then, a photodetector measured the intensity of green-light emitted from the probe tip. Agarose gel created an environment like that in which a neural probe is inserted into the brain. We measured the light intensity for four WG-UC probes with different W and θ shown in Fig. 2 and a conventional UC probe.

The measurement results are shown in Fig. 6. All WG-UC probes showed higher emission intensities than conventional UC probe. In the case of the conventional UC probe, the NIR light was attenuated before reaching the light-emitting part buried deeply in the gel. On the other hand, in the WG-UC probe, since green-light propagated with little attenuation in the probe, the light emission intensity at the probe tip was high. Consequently, the WG-UC probe can optically stimulate the deeper area in the brain compared with the conventional UC probe. Among the fabricated WG-UC probes, the probe with the width of 900-μm and the slope of 5° exhibited the highest light emission intensity. It is considered that large width increases the initial luminance intensity, and lower θ helps to propagate the upconverted light to the shank efficiently.

5. Conclusions

In this study, we proposed and fabricated the optical waveguiding UC probe for optogenetics with deep stimulation. WG-UC probes enable deep brain optical stimulation that is difficult with conventional UC probes. WG-UC probes have the potential to be very useful tools for optogenetics and neurophysiology.

References

[1] E. G. R. Kim *et al.*, *LoC*, 2015, Vol. 15, 2939-2949

[2] I. J. Cho *et al.*, *IEEE 23rd ICMEMS*, 2010, 995-998

[3] F. Wu *et al.*, *Neuron*, 2015, Vol. 88.1136-1148

[4] J. Thelin *et al.*, *PLoS ONE*, 2011, Vol. 6, e16267.

[5] S. Urayama *et al.*, SSDM, 2019, 41-42.

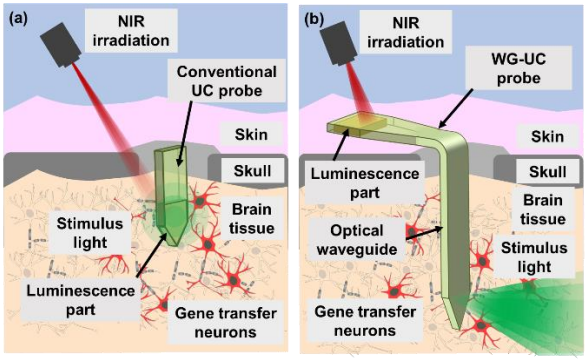

Fig. 1. Schematic illustrations of optical stimulation with (a) conventional UC probe and (b) proposed WG-UC probe.

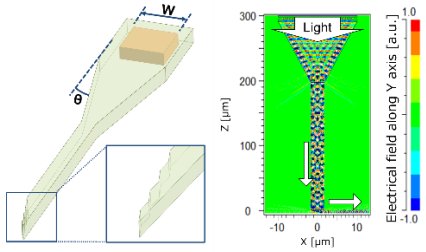

Fig. 2. (a) Schematic illustration of WG-UC probe and (b) FDTD simulation result.

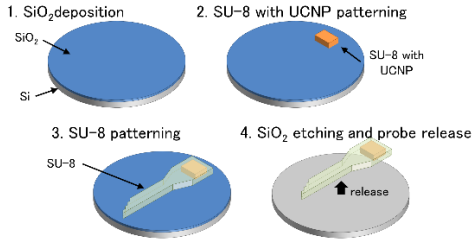

Fig. 3. Process flow of the WG-UC probe.

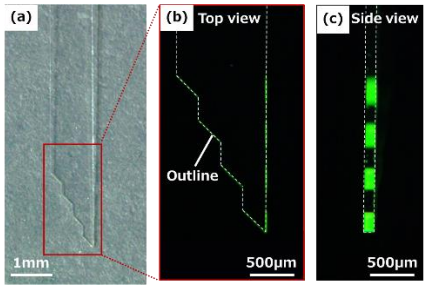

Fig. 4. Photographs of the WG-UC probe. (a) Top view without NIR light irradiation, (b) Top view with NIR light irradiation, and (c) Side view with NIR light irradiation. Green-light was emitted with NIR light irradiation.

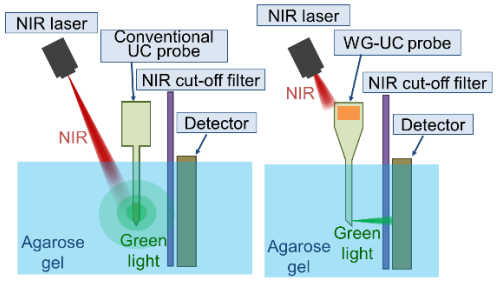

Fig. 5. Measurement setup for the evaluation of the upconverted visible light intensity with the conventional UC probe (left) and the proposed WG-UC probe (right).

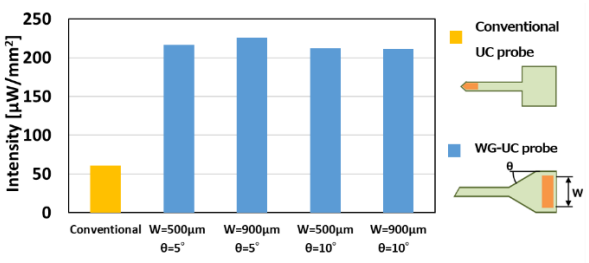

Fig. 6. Upconverted visible light intensity comparison among the fabricated probes.