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A 1μm Diameter Tip Fiber-based Surface Plasmon Resonance System for Single Unit Optical Neural Recording

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Abstract — **A gold-deposited optical fiber sensor system based on surface plasmon resonance (SPR) was developed for optical measurement of neuronal activity. To enhance the sensitivity of localized SPR and to make a precise and safe contact with the cellular membrane, we designed a tapered optical probe of 1μm diameter at the tip of the fiber. By wet etching and gold evaporating processes, pencil-shaped optical probes were successfully fabricated. The SPR system with the sharp optical probe was integrated with a conventional patch clamping system to realize a simultaneous optical and electrical recording on a single neuron. Although the shape of optical signal is not clear due to tiny change of intrinsic optical properties on the neuron, optical and electrical signals were simultaneously changed by capsaicin stimulation. Furthermore, our designed fiber probe can be applicable to localized optical stimulation as well as in vivo optical neuroprosthetic devices.**

I. Introduction

NEURAL signal recording is an important technique to interpret neural behaviors in the neuroprosthetic devices. In general, electrophysiological approaches have been applied using various shaped microelectrodes, but the approaches entail stimulation artifacts [1]. To exclude the problem, optical recording methods have been recently developed and applied in the neuroscience and neuroporsthesis researches. However, extrinsic optical recording which is using fluorescent dyes, have some shortcomings: measurement time limit, additional labeling process, and photo-bleaching [2]. Therefore, ideally, intrinsic optical recording is desirable and has been widely studied as an alternative to electrical neural recording.

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Surface Plasmon Resonance (SPR) is induced by excitation of surface plasmon, which is the surface electromagnetic wave which propagates in a direction parallel to the metal and the dielectric interface. SPR sensor has been widely used as an intrinsic optical sensor to detect various biochemical reactions because of its high sensitivity. In the previous study, we proved that SPR sensor is also effective to detect neural signals from ex-vivo rat sciatic nerve with a conventional Kretschmann SPR scheme [3]. In the present study, to advance the SPR technique for neural recording and to verify the origin of SPR neural signals, the single neuron-based SPR recording was attempted. We proposed a 1μm diameter tip fiber probe for single cell SPR recording system and applied it to single neuron recording with the conventional patch clamping system.

II. Method

A. Optical fiber tip tapering

Various types of fiber-type SPR system have been designed as a sensor. Among those systems, the design with tapered optical fibers is the most versatile geometry used in laboratories. Tapered geometry can increase the evanescent electromagnetic wave magnitude and the penetration depth. We fabricated the pencil-shaped tapered fiber tip by chemical etching with hydrofluoric (HF) acid [4].

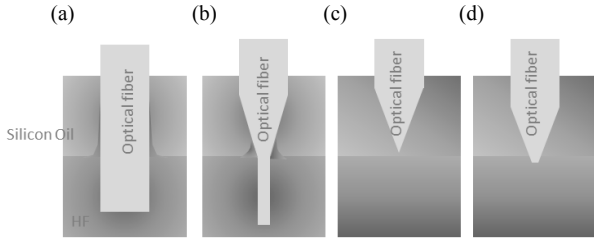

Fig. 1. Tapering process of the optical fiber. (a) Optical fiber immersed into HF/Oil interface, (b) meniscus decreases as the cladding etched by HF acid, (c) very sharp pencil-shaped fiber tip, (d) smoothing tip by dipping in HF acid.

Fig.1 shows the fabrication process for tapering optical fibers. First, the buffer and the jacket of one end of the single-mode fiber coupler (Thorlabs, FC632-50B-FC) were stripped off. Then, cladding was tapered by etching at the interface between HF acid (49%) and silicone oil. The meniscus was formed at the interface, and the height of the meniscus decreased as the cladding becomes thin due to the HF etching [5]. Approximately after 40 minutes, the very sharp pencil-shaped fiber tip is formed. However, if the apex

of the tip is too sharp, the cell membrane can be penetrated or pierced by the fiber. To prevent these destructions of cell membrane, the optical fiber tip was smoothed by 2 minutes HF acid dipping. Etch rate of the core in HF acid is 3.3μm/min, which is little higher than that of cladding 3μm/min, thus the fiber tip can be flattened about 1μm.

B. Fiber-based SPR system

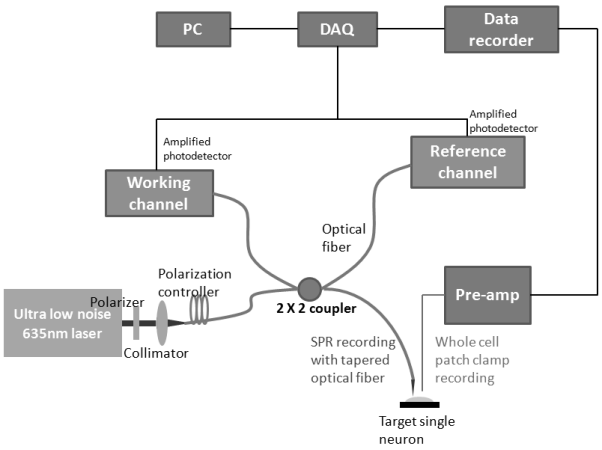

Fig. 2. Fiber based SPR system with tapered tip probe of single mode optical fiber.

The experimental setup is shown in Fig.2 [6]. The 635nm laser beam is collimated to optical fiber and divided by passing a 2 x 2 coupler (50: 50). Half of light reached at the photodetector with 60dB amplification which is named as a reference channel, and another half goes to the SPR probe and excites the surface plasmon waves. The reference channel is used to compensate intrinsic noise of the laser source. The reflected light from the probe tip is divided again by coupler and half of it is detected by 60dB amplified photodetector, which is labeled as a working channel. The data from the two detectors is sent to an analog to digital converter and monitored by LabVIEW-based software.

C. Stimulation and recording of neuron cell

To compare optical signals with electrical signals, a current clamping method is used to measure action potentials or other voltage changes of excited cell. Glass pipettes were pulled and the tip resistance was measured about ~3MΩ for whole-cell recordings. Depolarization of dorsal root ganglion (DRG) neurons were induced by the capsaicin agonist and blocked by the capsazepine antagonist [7]. Detected electrophysiological signals were amplified, low-pass filtered at 5kHz, and exported to a personal computer in a sampling rate of 500Hz.

III. Result and Discussion

A. Fabricated optical fiber tip

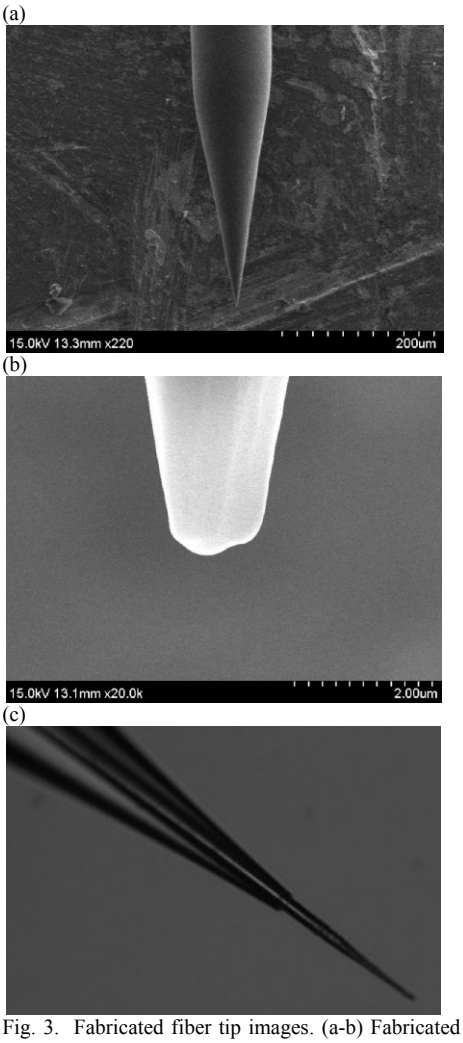

Fig. 3. Fabricated fiber tip images. (a-b) Fabricated pencil-shaped optical fiber tip images by scanning electron microscopy (SEM), (c) microscopic image of the fiber tip with glass conduit.

Fig.3 (a) and (b) show the images of the fabricated pencil-shaped probe taken by scanning electron microscope. The apex diameter was measured about 1.2μm. A solid glass conduit was used to protect the slender fiber probe tip as shown in Fig.3 (c). After that, the cleaning sequences with acetone, ethanol solution and radiating UV light for 10 minutes was done.

B. Sensitivity test

Different distributions of localized evanescent field coupling of the flat and the tapered fiber tip make the sensitivity of two fiber systems different. Ethanol test was performed to test the sensitivity of each fiber system. The amount of ethanol (n=1.362) in the water (n=1.333) was increased gradually while the voltage change from the SPR sensor was being monitored. Voltage change per refractive

index change ($\Delta V/\Delta n$) was 2.1×10^{-4} for the flat fiber system and 2.8×10^{-4} for the tapered fiber system. The system noise n_s was about 676μV, and the sensitivity or the minimum measurable refractive index change of the system can be calculated by following equation.

$$S = \frac{\Delta V}{\Delta n} n_s \quad (1)$$

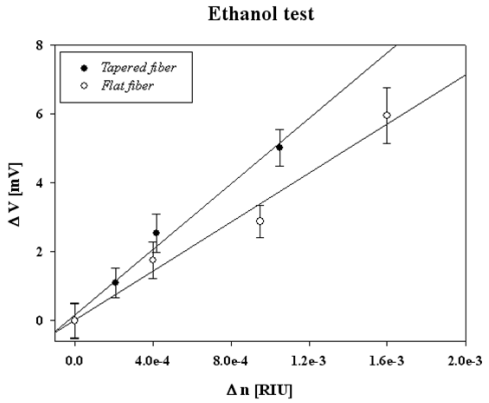

Fig. 4. Sensitivity test of the flat and tapered tip fiber-based SPR sensors.

$S_{flat}=1.92\times10^{-4}$ RIU and $S_{tapered}=1.42\times10^{-4}$ RIU, thus the sensitivity of the tapered fiber system is 34.9% improved than that of the flat fiber system.

C. Preliminary neural recording experiment

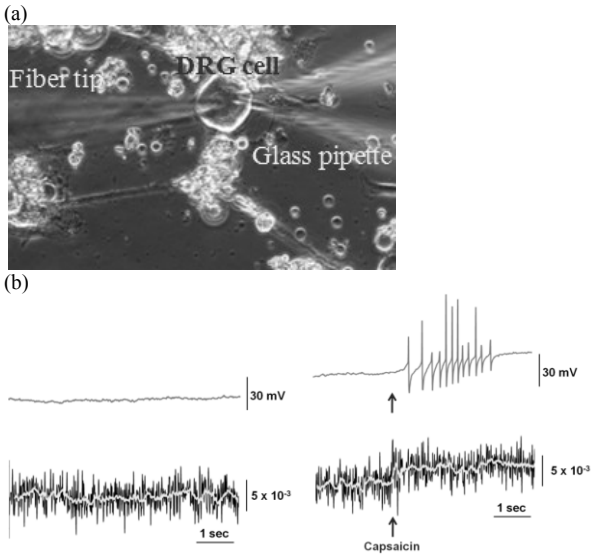

Fig. 5. (a) Microscopic image of bimodal recording on sing DRG cell and (b) recorded signals at resting (left) and activated (right) stage.

Fig.5 (a) shows a microscopic image of single neuron recording [6]. As shown here, our tapered optical probe resembles in size and shape compared with a glass pipette of the patch clamp system. The results with optical (black lines) and electrical (gray lines) recordings were shown in Fig.5 (b) [6]. Resting state is illustrated in the left side, and activated state by capsaicin stimulation is shown in the right side. SPR responses are expressed by differential reflectance (ΔR/R) and their sectional averaged data in every 0.02msec is plotted by white line. Here, we can see the evoked electrical potential changes and slight different optical responses (about 2×10^{-3} RIU) after the 5μM capsaicin injection.

As shown in Fig. 5(b), the shape of optical response is different from electrical firing signals. However, it was proven that the small optical change was oriented to cellular changes by capsaicin. When the DRG cell was not attached at the end of the optical probe, the reflectance shift was not observed after the capsaicin injection in the culture media. The optical responses were not so distinguishable as those from sciatic nerve recording. The sensitivity of the system will be improved systemically by implementing noise reduction and/or optimization of LSPR effect.

Finally, our fiber-based SPR sensor can be widely used for other applications. This system is used to verify the mechanism of intrinsic optical recording, considering several factors (cellular volume change, ionic exchange, dipole reorientation, membrane potential change, and so on) which are known to induce the change of intrinsic optical properties. We also expect to use our system to employ the localized optical stimulation system as well as in vivo optical neuroprosthetic devices.

IV. Conclusion

We developed a tapered fiber based SPR system for single unit neural recording. Fiber tip was tapered with wet etching to increase the sensitivity of SPR and to make a precise and safe attachment to the cell. This fiber SPR system was combined to the patch-clamp method system. Preliminarily, we recorded electrical and optical signals simultaneously from single dorsal root ganglion cells, and expect that this system can be used for various applications.

References

[1] F. O. Morin, Y. Takamura, and E. Tamiya, "Investigating neuronal activity with planar microelectrode arrays: achievements and new perspectives**",** *Journal of Bioscience and Bioengineering*, vol. 100, Issue 2, pp.131-143, 2005.

[2] T. J. Ebner and G. Chen, "Use of voltage-sensitive dyes and optical recordings in the central nervous system*", Progress in Neurobiology*, vol. 45, Issue 5, pp/463-506, 1995.

[3] S. A. Kim, K. M. Byun, J. Lee, J. H. Kim, D. A. Kim, H. Baac, M. L. Shuler, and S. J. Kim, " Optical Measurement of Neural Activity Using Surface Plasmon Resonance", *Optics Letters*, vol. 33, no. 9, pp. 914-916, 2008.

[4] S. Mononobe and M. Ohtsu, "Fabrication of a pencil-shaped fiber probe for near-field optics by selective chemical etching", *Journal of Lightwave Technology*, vol. 14, no. 10, 1996.

[5] P. K. Wong, T. H. Wang, and C. M. Ho, "Optical Fiber Tip Fabricated By Surface Tension Controlled Etching", *Technical Digest, Solid State Sensor and Actuator Workshop*, pp. 94-97, 2002.

[6] S. A. Kim, "Surface Plasmon Resonance Biosensors for Optical Neural Recording and Avian Influenza Detection ", Ph.D. Thesis, School of Electrical Engineering and Computer Science, Seoul National University, February 2011.

[7] S. W. Hwang, H. Cho, J. Kwak, S. Y. Lee, C. J. Kang, J. Jung, S. Cho, K. H. Min, Y. G. Suh, D. Kim, and U. Oh, "Direct activation of capsaicin receptors by products of lipoxygenases: Endogenous capsaicin-like substances", *Science Signaling: Signal Transduction Knowledge Environment*, vol.97, p.6155, 2000