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Performance improvement and functionalization of an electrode array for retinal prosthesis by iridium oxide coating and introduction of smart-wiring technology using CMOS microchips

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ABSTRACT

The improvement of an electrode array for retinal prosthesis is described. Two elements of fundamental technology required in next-generation retinal prosthesis, the miniaturization of and wiring of a stimulus electrode, were investigated. To miniaturize the stimulus electrode without performance degradation, surface coating by iridium oxide (IrOx), a high performance material, was introduced. The electrochemical properties and durability of an IrOx coated electrode were evaluated through *in vitro* and *in vivo* experimentation. Results showed that IrOx coating delivers a higher performance with sufficient durability and contributes to the miniaturization of the electrode without degrading the stimulus capability. Smart-wiring technology using CMOS microchips was also investigated. A prototype electrode array with CMOS microchips was fabricated to clarify the concept. A dedicated CMOS microchip was hybrid-integrated into a stimulus electrode array. Results of *in vivo* experiments showed that the fabricated array stimulated retinal cells effectively. Miniaturized electrodes with an IrOx coating and smart-wiring technology enable the fabrication of a super-multi-channel (*i.e.*, more than 1000) electrode array, which is required for next-generation retinal prosthesis.

1. Introduction

In recent years, neural interface devices, including brain machine interface devices, have been the subject of much research interest [1–9]. Target applications of these devices include the clinical treatment of functional diseases of the brain, prosthesis of a sensory organ, rehabilitation, control of an artificial arm or hand, and so on. Some applications require a neural interface device that is miniaturized and has a high density electrode array. Using CMOS and/or MEMS technology is one approach to fabricating such devices [4–9]. Retinal prosthesis is emerging as one of the most promising applications of highly functional electrode arrays based on CMOS technology.

In the case of age-related macular degeneration (AMD) and retinitis pigmentosa (RP), although photoreceptor cells are degenerated, some of the retinal cells that include ganglion cells remain. In such cases, retinal prosthesis technology enables blind patients to partially regain their vision by stimulating these remaining cells. The primary target of retinal stimulation is the ganglion cells. There are three approaches to stimulating them. One of them, epi-retinal stimulation [10–13], has a low stimulation threshold obtained by the close configuration of ganglion cells and stimulus electrodes. However, fixing an electrode array by tacking is not ideal. In the case of the second one, sub-retinal stimulation [14–19], photo detection in the eyeball is possible, but surgically inserting an electrode array in the sub-retina is difficult. In addition, interference of nutrition flow from the choroid to the retina is a serious issue that needs to be resolved. The third approach, suprachoroidal-transretinal stimulation (STS) [20–23], is the approach that we focus on in this study. A retinal stimulator is advantageous because it does not directly touch the retina, surgical operation is easy, and the invasiveness is lower than with the other approaches. However, a higher stimulus current is required because of the larger

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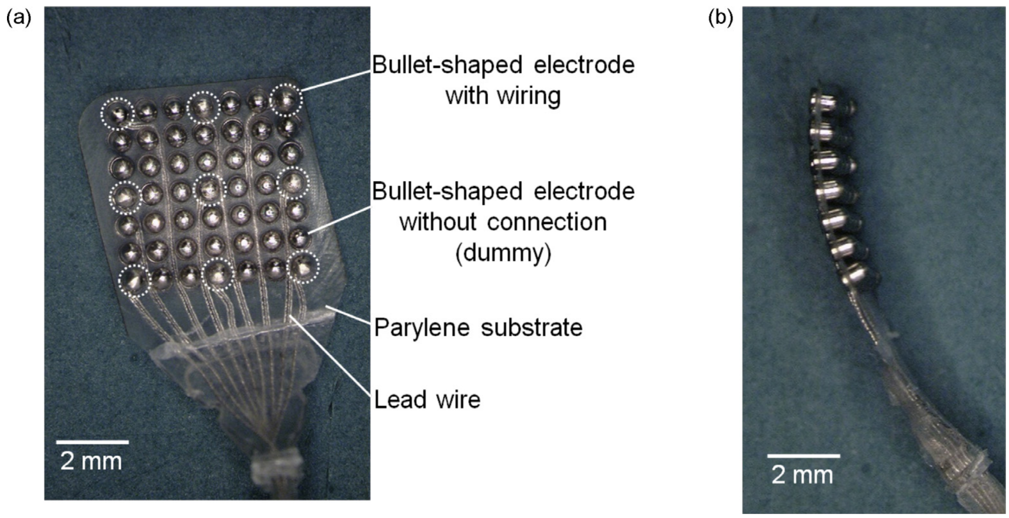

Fig. 1. Photographs of the stimulus electrode array utilized in clinical trial: (a) top view; (b) side view.

gap between ganglion cells and stimulus electrodes. For safe stimulation, this higher current requires a larger surface area of electrodes, *i.e.*, larger electrodes. Bullet-shaped electrodes of bulk Pt have been utilized for the STS approach to increase the surface area of stimulus electrodes [24]. This makes the stimulus current density at the electrode surface lower, and the maximum current allowable at the inside range of the potential window becomes larger due to the increased surface area. A retinal prosthesis system with bullet-shaped electrodes was implanted semi-chronically in two patients [25]. The system was safe and the stimulus function maintained operation for at least four weeks.

A bullet-shaped electrode array (Fig. 1) was utilized for the clinical trial [25]. Bullet-shaped electrodes were mounted onto a parylene substrate in a 7×7 array. Although the clinical trial was performed successfully, the number of electrodes and stimulus points was limited due to the size of the electrodes and the difficulty of wiring. We feel that a super-multi-channel (*i.e.*, 1000+ channels) electrode array is required for next-generation retinal prosthesis, so we have to miniaturize electrodes to integrate 1000 or more electrodes into the same array size, which must still be small enough to implant in an eyeball. Moreover, all electrodes in the super-multi-channel electrode array have to be driven to stimulate retinal cells with high definition. In the case of the array utilized in the clinical trial (Fig. 1), only 9 electrodes of the 49-channel electrode array were connected to an implanted stimulator because of the difficulty of the wiring. The other 40 electrodes were not active and were mounted onto a flexible substrate as dummy electrodes. The difficulty of wiring is an issue that needs to be solved in order to increase the number of stimulus points. For an electrode array intended for utilization in next-generation retinal prosthesis, a miniaturized electrode and smart-wiring technology are necessary.

In this paper, we propose and clarify two elements of fundamental technology for utilization in next-generation retinal prosthesis. Miniaturized bullet-shaped electrodes were fabricated and the effects of surface coating were investigated. The properties of the miniaturized electrodes were evaluated through *in vitro* and *in vivo* experimentation. As a smart-wiring technology, we introduced CMOS technology to a stimulus electrode array. Dedicated CMOS microchips were designed and hybrid-integrated to the stimulus electrode array of the bullet-shaped electrode. A prototype of the electrode array was fabricated and characterized through *in vivo* animal experiments.

This paper is organized as follows: first, in Section 2, we introduce the two technology elements that are required for next-generation retinal prosthesis. In Section 3, we describe the first technology element, which is the high performance electrode, and discuss its fabrication and evaluation. In Section 4, we describe the other technology element, which is the smart-wiring technology, and discuss our fabrication of the prototype of an electrode array with a CMOS microchip as a demonstration. *In vivo* animal experiments were performed as a functional validation of the array.

2. Technology elements required for next-generation retinal prosthesis

The miniaturization of the stimulus electrode and the establishment of smart-wiring technology are the two key issues that we are focused on solving. As described in Section 1, large bullet-shaped electrodes of bulk Pt have been utilized for the STS method. When stimulus electrodes are miniaturized, their stimulus capability decreases along with the decrease of surface area. This is problematic because the stimulus capability should be maintained even if the electrodes are miniaturized. Utilizing a higher performance material is one of the solutions to this. We have been considering iridium oxide (IrOx) as such a material [26,27]. In this study, we coated bullet-shaped electrodes with IrOx and then investigated the stimulus capability through *in vitro* experiments in an electro-chemical evaluation. The durability of the coating was also evaluated through *in vitro* and *in vivo* experiments.

We previously proposed a smart-wiring technology for a stimulus electrode array [28–31] with built-in CMOS microchips. High-resolution retinal prosthesis requires an increase in the number of electrodes used. However, a large number of wires to connect a large number of electrodes are not suitable for implantation. The reduction in the number of wires by introducing the CMOS technology is useful in increasing the number of electrodes because the multiplexer function can be integrated into the CMOS microchip. However, the CMOS microchips are composed of Si, which is a rigid material. We therefore have proposed a multichip architecture in order to design a CMOS-integrated electrode that is flexible. The smart-wiring technology, which is the integration of individual microchips into the electrode, realizes a reduction in the number of wires used. A smart electrode array device using the smart-wiring technology was successfully fabricated, and functional validations through animal experimentation were performed [31]. The stimulus function was successfully operated. However, the margin of performance was insufficient in the stimulus electrode required for STS because small-sized Pt electrodes were used in the device.