

Development and In Vivo Evaluation of Conductive Polymer (PEDOT) Stimulus Electrodes for Fully Implantable Retinal Prosthesis

Chikashi Kigure¹, Hideki Naganuma², Yuichiro Sasaki¹,
Hiroshi Tomita³, and Tetsu Tanaka^{1,2}

¹Department of Biomedical Engineering, Graduate School of Biomedical Engineering, Tohoku University
6-6-01 Aza-Aoba, Aramaki, Aoba-ku, Sendai 980-8579, Japan

Phone: +81-22-795-6258, Fax: +81-22-795-6908, E-mail: link@lbc.mech.tohoku.ac.jp

²Department of Bioengineering and Robotics, Graduate School of Engineering, Tohoku University

³Department of Chemistry and Bioengineering, Faculty of Engineering, Iwate University

1. Introduction

Recently, a lot of studies for retinal prostheses have been reported for blind patients to restore visual sensations by electrical stimulation to remaining retinal cells with stimulus electrodes [1, 2]. We have been developing a fully implantable retinal prosthesis with 3D stacked retinal prosthesis chip to achieve low power and small size artificial retina which gives a high quality of life (QOL) to patients [3]. To realize visual restoration with high resolution, we need to miniaturize stimulus electrodes. As we miniaturize them, however, their electrochemical impedances (EI) become higher and their injection charges in amount become smaller. Therefore, we need superior electrodes that have low EI and large charge injection capacities (CIC). In this study, we fabricated three kinds of implantable flexible cables with electrodes made of Pt, IrOx, and poly(3,4-ethylenedioxythiophene) (PEDOT), respectively, and evaluated their EI and CIC. In addition, we performed *in vivo* experiments with the electrodes using a rabbit. We electrically stimulated the retina and measured electrically evoked potentials (EEPs) from visual cortex of the rabbit. We succeeded in measuring EEPs and showed possibilities of visual restoration by retinal prosthesis.

2. Fabrication and Evaluation of Pt, IrOx and PEDOT electrodes

We fabricated flexible cable electrodes using conventional LSI processes. Figure 1 shows the fabricated flexible cable with 100 stimulus electrodes. Figure 2 shows EI behaviors for various electrode materials. The impedance magnitude of IrOx and PEDOT electrodes are significantly lower than that of Pt electrode, which means that we can stimulate the retina with lower voltages using IrOx and PEDOT electrodes. We also measured CIC values with cathodal-to-anodal pulses having the pulse width of 1msec. CIC indicates the maximum injection charge density that keeps electrode potential within potential window. Table 1 summarizes CIC of Pt, IrOx and PEDOT electrodes. It is clearly demonstrated that PEDOT electrode can supply thirty times larger electric charges than Pt and IrOx electrodes with single stimulation. Considering these results, PEDOT is one of the most suitable materials for retinal stimulation.

3. In vivo evaluation using PEDOT stimulus electrodes

We performed *in vivo* experiment using PEDOT stimulus

electrodes. Figure 3 shows a setup of *in vivo* experiment, where we used Japanese white rabbits (2-3kg) and PEDOT stimulus electrodes implanted in the rabbit eyeball. All procedures adhered to the Association for Research in Vision and Ophthalmology (ARVO) Resolution on the Use of Animals in Research. A recording electrode and a reference electrode were implanted in the rabbit brain. We applied subretinal stimulations and measured EEPs from the visual cortex. We used a cathodic stimulus current pulse with 600 μ A and 3ms. In this study, we used only cathodic pulses because the major target of this work was to obtain fundamental information on the electrical stimulation of retinal cells. We also measured visually evoked potentials (VEPs) when the rabbit retina was stimulated by a light pulse. VEP is the reaction in the visual cortex for optical stimulations to the retina. The light intensity was 1000lx with the duration of 10ms. We compared waveforms for VEP, EEP, and control conditions in Figure 4. The control waveform was measured with no optical/electrical stimulations. All measurements were done in a dark room. As results, similar waveforms were observed in comparison between EEP and VEP, unlike control condition. It is shown that we can successfully stimulate the retina by electrical stimulation with PEDOT electrodes. In addition, we performed other experiments in order to examine the relationships between electrical stimulation and EEPs in detail. We measured EEPs with stimulation currents having various amplitudes and durations. Figure 5(a) shows the relationship between the amplitude of measured EEP and the amplitude of stimulus current. The pulse width was 3 ms. There is a positive relationship between the amplitude of stimulus current and the amplitude of measured EEP. Figure 5(b) shows the relationship between the amplitude of measured EEP and the pulse width of stimulus current. The pulse amplitude of 600 μ A was used. There is also a positive relationship between the pulse width of stimulus current and the amplitude of measured EEP. From these results, it becomes clear that EEP depends on both the amplitude and pulse width of the stimulus current. By adjusting the amplitude and pulse width of the stimulus current, visual restoration will be realized with PEDOT stimulus electrodes.

4. Conclusion

We fabricated flexible cables with Pt, IrOx, and PEDOT electrodes, and measured their electrochemical impedances and charge injection capacities. We showed that PEDOT electrode had the most superior characteristics among them. In *in vivo* experiment, we successfully elicited a reaction in the visual cortex by electrical stimulation to the retina.

Furthermore, we confirmed that the amplitude of measured EEP depended on the amplitude and pulse width of the stimulus current. It becomes possible to obtain a reaction like VEP by adjusting the amplitude and pulse width of the stimulus current. There is a high probability that visual restoration will be realized with PEDOT stimulus electrodes.

Acknowledgements

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References

- [1] E. Zrenner, KU. Bartz-Schmidt, H. Benav, D. Besch, A. Bruckmann, VP. Gabel, F. Gekeler, U. Greppmaier, A. Harscher, S. Kibbel, J. Koch, A. Kusnyerik, T. Peters, K. Stingl, H. Sachs, A. Stett, P. Szurman, B. Wilhelm and R. Wilke: The Royal Society (2010) 2280.
- [2] T. Fujikado, M. Kamei, H. Sakaguchi, H. Kanda, T. Morimoto, Y. Ikuno, K. Nishida, H. Kishima, T. Maruo, K. Konomi, M. Ozawa, and K. Nishida: Investigative Ophthalmology & Visual Science (2011) 4726.
- [3] T. Tanaka, K. Sato, K. Komiya, T. Kobayashi, T. Watanabe, T. Fukushima, H. Tomita, H. Kurino, M. Tamai and M. Koyanagi: International Electron Devices Meeting Technical Digest (2007) 1015.

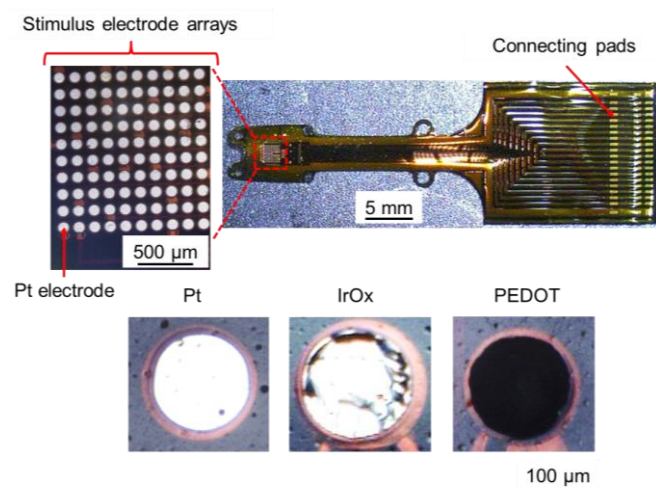


Fig. 1 Photographs of the fabricated flexible cable and Pt, IrOx, PEDOT electrodes.

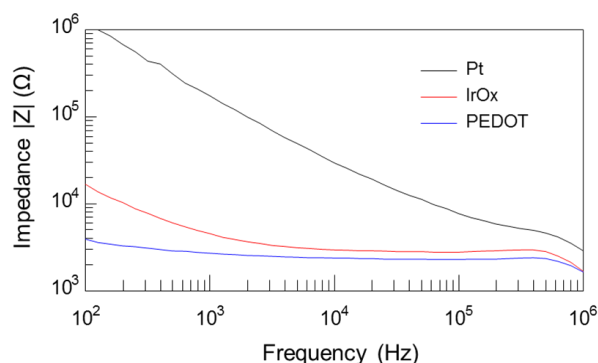


Fig. 2 Impedance spectra of Pt, IrOx, and PEDOT electrodes.

Table 1 CIC values of Pt, IrOx, and PEDOT electrodes.

Material	CIC (mC/cm ²)
Pt	0.23
IrOx	0.35
PEDOT	11.38

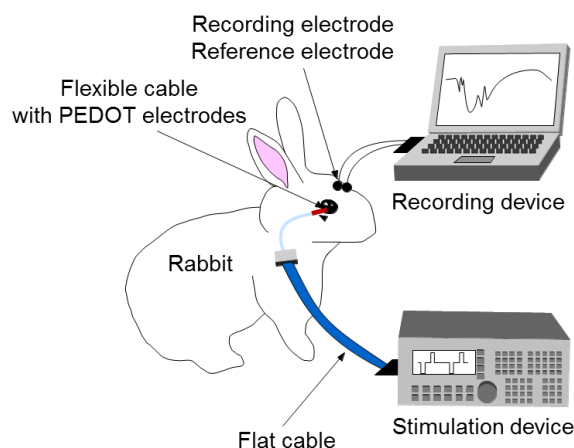


Fig. 3 Setup of *in vivo* experiment.

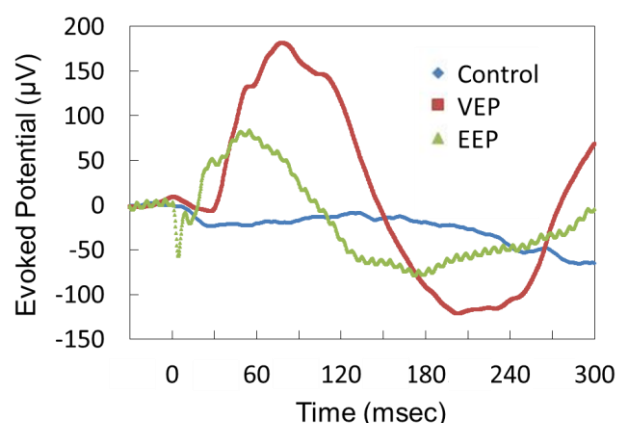


Fig. 4 Comparison among VEP, EEP and control waveforms measured from the visual cortex of the rabbit.

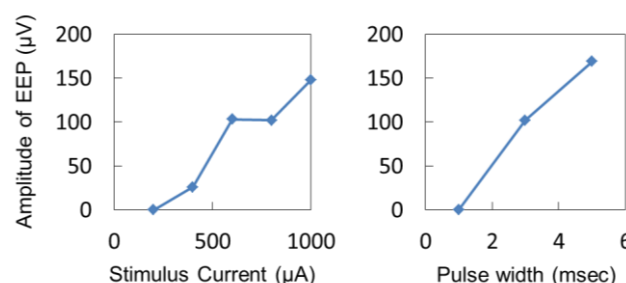


Fig. 5 (a) Relationship between the measured EEP amplitude and the stimulus current. (b) Relationship between the measured EEP amplitude and the pulse width of stimulus current.