# Fully Implantable Retinal Prosthesis Chip with Photodetector and Stimulus Current Generator

| | |
|---|---|
| 著者 | 福島 誉史 |
| journal or publication title | IEEE International Electron Devices Meeting, 2007. IEDM 2007 |
| volume | 2007 |
| page range | 1015-1018 |
| year | 2007 |
| URL | http://hdl.handle.net/10097/46419 |

doi: 10.1109/IEDM.2007.4419127

# Fully Implantable Retinal Prosthesis Chip with Photodetector and Stimulus Current Generator

T. Tanaka, K. Sato, K. Komiya, T. Kobayashi, T. Watanabe,
T. Fukushima, H. Tomita*, H. Kurino, M. Tamai*, and M. Koyanagi

Department of Bioengineering and Robotics, Graduate School of Engineering, Tohoku University
6-6-01 Aza-Aoba, Aramaki, Aoba-ku, Sendai 980-8579, JAPAN
Phone: +81-22-795-6906, Fax: +81-22-795-6907, E-mail: ttanaka@sd.mech.tohoku.ac.jp
* Tohoku University Biomedical Engineering Research Organization

**Abstract**

To recover visual sensation of blind patients, we have fabricated a fully implantable retinal prosthesis chip that includes photodetector and stimulus current generator. For the first time, we successfully implanted the retinal prosthesis chip bonded on the flexible cable with stimulus electrode array into a rabbit eyeball. Moreover, we recorded and analyzed electrically evoked potential (EEP) elicited from a rabbit brain by current stimulation to retina.

## Introduction

Recently, a number of patients are suffering from retinitis pigmentosa (RP) and age-related macular degeneration (AMD). Several million patients become blind due to these diseases in the world. The RP and AMD result from impairment of photoreceptor cells that convert light signals to electrical signals in retina. Indeed, effective medical treatments for RP and AMD have not been established yet. While the photoreceptor cells degenerate with RP and AMD, many other retinal cells (bipolar, horizontal, amacrine, and ganglion) remain normally [1]. Accordingly, it will be possible to recover one's vision with stimulating the remaining retinal cells. Many studies for retinal prosthesis are in progress worldwide at the present time [2]-[4].

Figure 1 shows a conventional retinal prosthesis configuration. There are three indispensable components such as photodetector, signal processing circuit, and stimulus current generator with stimulus electrode array. The photodetector receives optical signals from the outside world and converts these optical signals into electrical signals. After that, processing circuits perform image processing such as edge extraction and motion detection. Next, the stimulus current generator placed on the surface of retina generates appropriate patterns of electrical current. Finally, stimulus electrode array stimulates remaining retinal cells. When the remaining retinal cells are activated by the stimulus current, blind patients would perceive a dot of light at each stimulating point.

In the conventional retinal prosthesis, only the stimulus current generator with tens of stimulus electrodes is implanted in the eyeball, which is due to a small retinal area of approximately 3mm$^2$ suitable for retinal chip implantation. As the photodetector and processing circuits are placed outside the eyeball, the conventional retinal prosthesis is large, heavy, and complicated system. Moreover, the patients cannot use saccadic effects based on high speed eye movement. These disadvantages lead a low quality of life (QOL) to the patients.

We have been developing a three-dimensional (3-D) stacked retinal prosthesis chip fabricated using the 3-D integration technology [5], [6]. Figure 2 shows a conceptual drawing of our 3-D stacked retinal prosthesis, where all key components are vertically stacked into one chip and completely implanted on the surface of retina, unlike other group's retinal prosthesis. By implanting the 3-D stacked retinal prosthesis chip into the eyeball, the patients can employ their own lens and cornea and can shift a gaze point by moving the eyeball, leading to high speed visual information processing by using saccadic effects. As the 3-D stacked retinal prosthesis chip has layered structure similar to human retina, photodetectors with more than 1000 pixels can be fabricated in the retinal chip (Fig. 3). This leads to small chip size, light weight, large fill-factor, high resolution, and the resultant high QOL.

## Design of retinal prosthesis chip

Figure 4 shows biphasic current pulses which are usually used to stimulate retinal cells. Cathodic current pulses activate retinal cells while anodic current pulses keep charge balance. It is very important for the patients to optimize parameters of stimulus current individually. Therefore, we designed pixel circuits so that we can adjust current pulse waveforms with BIAS voltages, as shown in Figure 5. In this work, we fabricated the 2-D retinal prosthesis chip as a prototype for 3-D retinal prosthesis chip by using 0.35μm double poly-Si and triple metal CMOS process. There is no functional difference between 2-D and 3-D designs except area size of a pixel circuit. Figure 6 shows a photograph of fabricated retinal prosthesis chip with

1-4244-0439-X/07/$25.00 

16 pixels and pixel circuit layout. Each pixel has the photodetector circuit, biphasic pulse control circuit, and stimulus current generator circuit.

## Fabrication and evaluation of retinal prosthesis module

In order to implant the retinal prosthesis chip into the eyeball, the chip needs to be attached on the flexible cable with stimulus electrode array. Figure 7 shows fabrication process of retinal prosthesis module that is composed of stimulus electrode array, flexible cable, and retinal prosthesis chip. Biocompatible polyimides were employed as the flexible substrate of the cable. Pt and Au/Cr are employed for stimulus electrodes and wiring materials connected to power supply, respectively. The retinal prosthesis chip was bonded on the cable with epoxy resin, and electrically connected with Au/Cr wiring by using wire bonding technique. The bonded chip was encapsulated by silicone for protection from corrosive biological fluid. Figure 8 illustrates both the flexible cable and stimulus electrode array used for animal experiments. An array of 4×4 Pt stimulus electrodes was formed at the end of flexible cable. The stimulus electrodes were placed at a pitch of 200μm. Three rings were formed and used for module fixation on the retina. One ring was inserted by a retinal tack inside the eyeball and the other two rings were sewn on the sclera outside the eyeball. At the other end of flexible cable, connection pads to a power supply were formed. The photograph of the fabricated retinal prosthesis module was shown in Figure 9.

In order to confirm chip functions after module fabrication process, electrical characteristics were evaluated. Figure 10 shows that the anodic pulse duration and the interphase delay of stimulus current pulses can be sufficiently adjusted by using BIAS voltages. Moreover, current pulse frequency changes in proportion to incident light intensity, as shown in Figure 11. We confirmed that proportional relationships don't degrade after encapsulation process. To verify usability of the retinal prosthesis module and to optimize parameters of stimulus current pulse, it is very significant to perform fundamental animal experiments. All procedures on animal experiments in this work adhered to the Association for Research in Vision and Ophthalmology (ARVO) Resolution on the Use of Animals in Research and the guidelines of the University of California at San Francisco Committee on Animal Research. Japanese white rabbits (2-3Kg) were anesthetized with ketamine hydrochloride (66mg/kg) and xylazine hydrochloride (33mg/kg) and maintained at a surgical anesthetic level by additional injections of the mixture. Figure 12 shows photographs for implantation of retinal prosthesis module into the rabbit eyeball. The retinal prosthesis chip was completely implanted into the eyeball and fixed on the surface of retina. It becomes obvious that our module has sufficient endurance for implantation into the eyeball. Figures 13 and 14 show a recording apparatus and waveforms of recorded EEP, respectively. Stimulus current pulses to elicit EEP from the rabbit brain were applied by using implanted stimulus electrode array. Because there is no EEP amplitude after axotomy, the EEP waveform before axotomy indicates that some visual signal was transferred to the primary visual cortex through the visual pathway. As results, the rabbit would perceive the light by the retina stimulation. Figure 15 investigates effects of both duration and amplitude of stimulus current pulse on the recorded EEP amplitude. The amplitude of stimulus current pulse is more effective than the duration in spite of the same electrical charge quantity of stimulus current.

## Conclusions

We successfully fabricated the fully implantable retinal prosthesis chip with photodetector and stimulus current generator. Our chip shows excellent electrical characteristics even after module fabrication process. For the first time, we completely implanted the retinal prosthesis chip bonded on the flexible cable with stimulus electrode array into the rabbit eyeball. In animal experiments, the recorded EEP behaviors indicate that the rabbit would perceive the light by the electrical current stimulation to retina, and that there would be threshold current to elicit the EEP from the brain.

## References


[1] N. E. Medeiros and C. A. Curcio, "Preservation of ganglion cell layer neu-rons in age-related macular degeneration," Investigative Ophthalmology & Visual Science, Vol. 42, pp. 795-803, 2001.

[2] M. S. Humayun, E. Juan Jr., J. D. Weiland, G. Dagnelie, S. Katona, R. Greenberg, and S. Suzuki, "Pattern electrical stimulation of the human retina," Vision Research, Vol. 39, pp. 2569–2576, 1999.

[3] W. Liu, K. Vichienchom, M. Clements, S. C. DeMarco, C. Hughes, E. McGucken, M. S. Humayun, E. de Juan, J. D. Weiland, and R. Greenberg, "A Neuro-Stimulus Chip with Telemetry Unit for Retinal Prosthetic Device," IEEE Journal of Solid-State Circuits, Vol. 35, pp. 1487-1497, 2000.

[4] J. Ohta, N. Yoshida, K. Kagawa, and M. Nunoshita, "Proposal of application of pulsed vision chip for retinal prosthesis," Japanese Journal of Applied Physics, Vol. 41, pp. 2322-2325, 2002.

[5] H. Kurino, K. W. Lee, T. Nakamura, K. Sakuma, K. T. Park, N. Miyakawa, H. Shimazutsu, K. Y. Kim, K. Inamura, and M. Koyanagi, "Intelligent image sensor chip with three dimensional structure," International Electron Devices Meeting Technical Digest, pp. 879-882, 1999.

[6] M. Koyanagi, Y. Nakagawa, K. W. Lee, T. Nakamura, Y. Yamada, K. Inamura, K. T. Park, and H. Kurino, "Neuromorphic vision chip fabricated using three-dimensional integration technology," International Solid-State Circuit Conference Digest of Technical Papers, pp. 270-271, 2001.

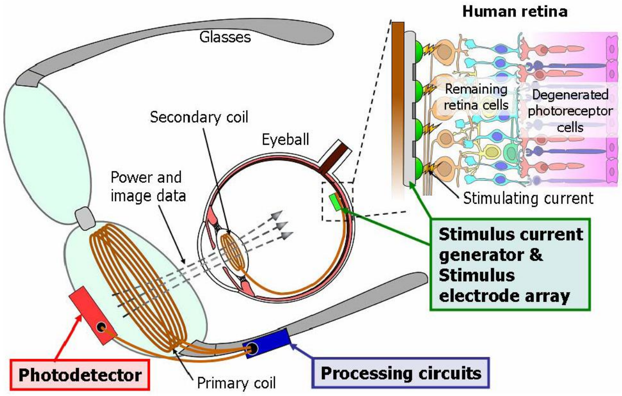


Fig. 1. Configuration of conventional retinal prosthesis. There are key components such as photodetector, processing circuits, and stimulus current generator with stimulus electrode array.

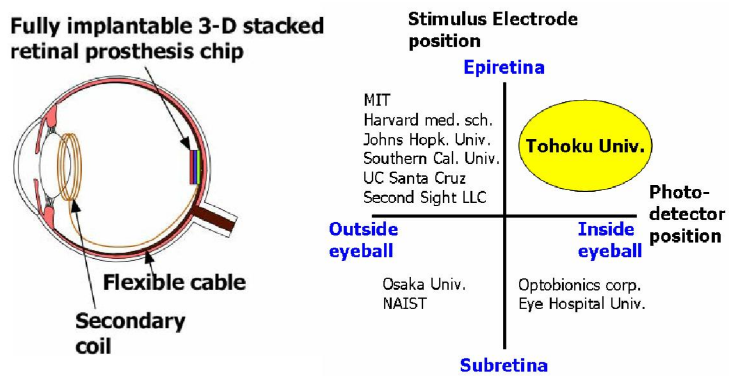


Fig. 2. Conceptual drawing with fully implantable 3-D stacked retinal prosthesis chip and classification of retinal prostheses in accordance with stimulus electrode position and photodetector position.

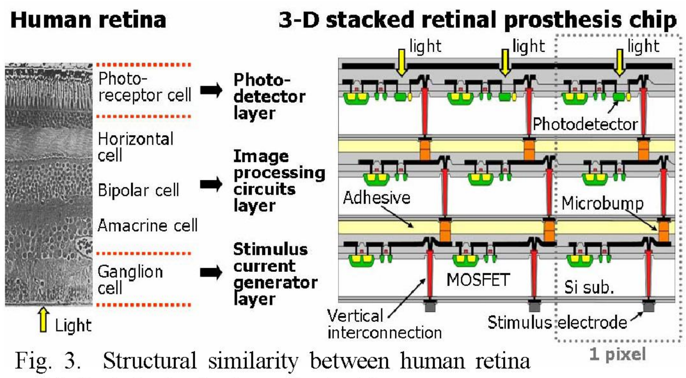


Fig. 3. Structural similarity between human retina and 3-D stacked retinal prosthesis chip.

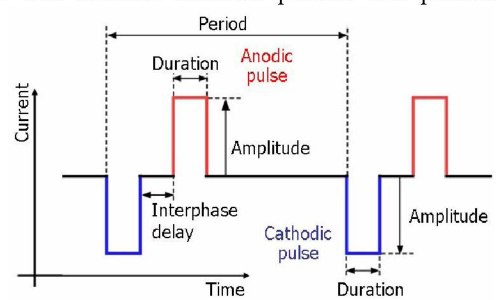


Fig. 4. Bipahsic current pulse waveform for retinal stimulation. Cathodic current pulses activate retinal cells. Anodic current pulses balance charge quantity.

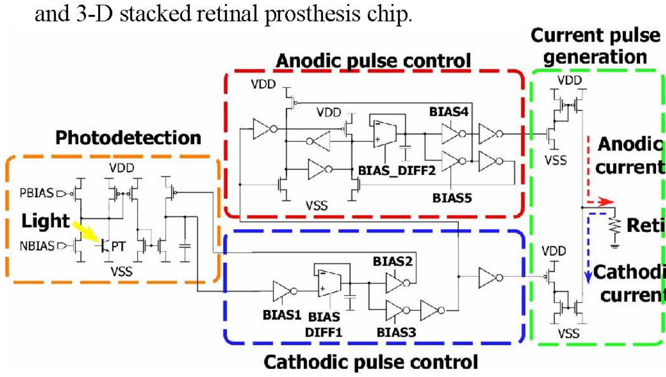


Fig. 5. Pixel circuit diagram of retinal prosthesis chip.

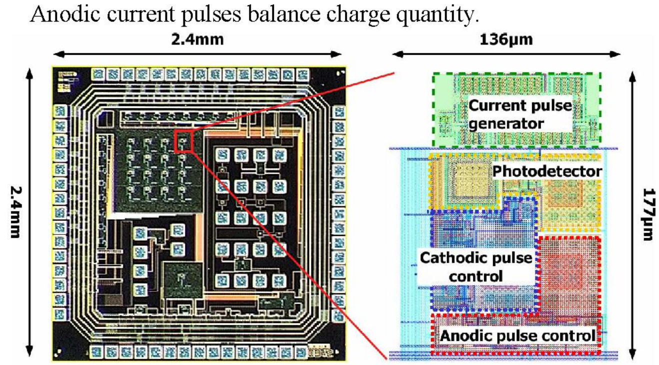


Fig. 6. Photograph of fabricated retinal prosthesis chip and pixel circuit layout. 0.35μm CMOS with double poly-Si and triple metal process was used.

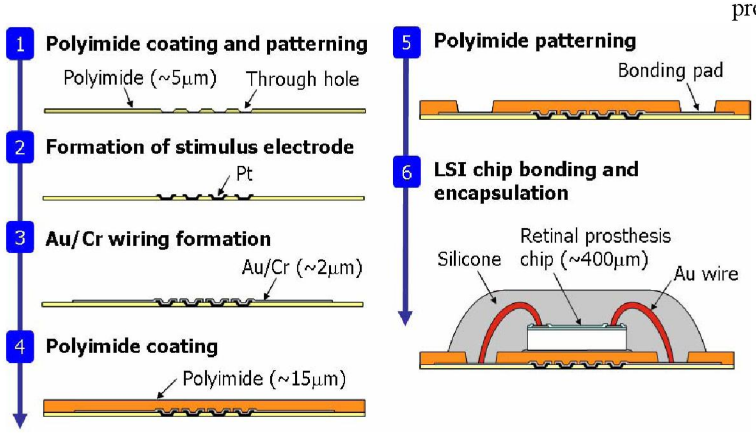


Fig. 7. Fabrication process of retinal prosthesis module consisting of flexible cable, stimulus electrode array, and retinal prosthesis chip.

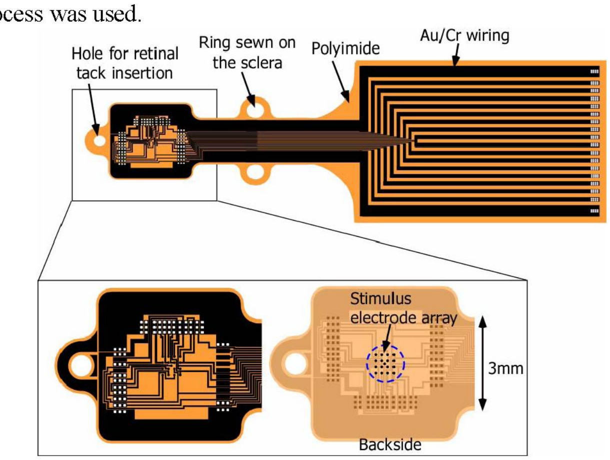


Fig. 8. Structures of flexible cable and stimulus electrode array.

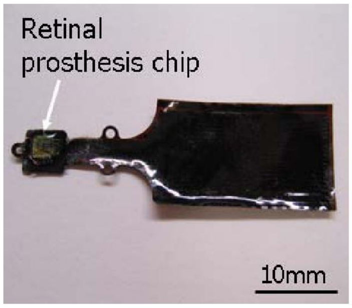


Fig. 9. Photograph of retinal prosthesis module.

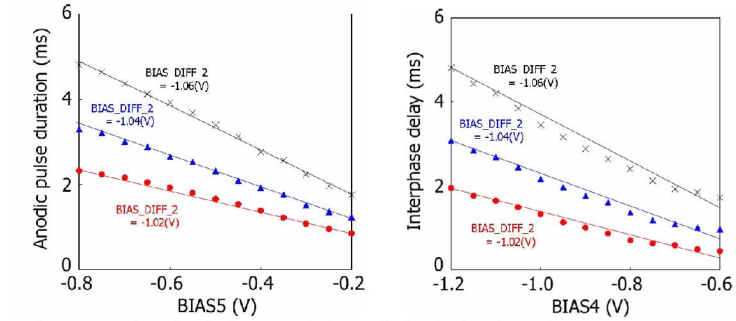


Fig. 10. Electrical characteristics of pixel circuit. [Plots: measurement, Lines: SPICE simulation]

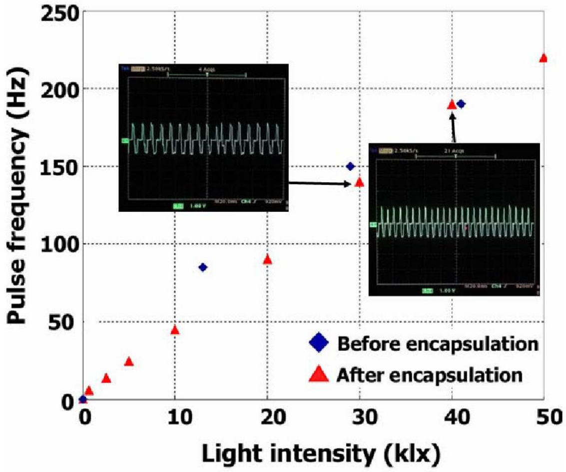


Fig. 11. Relationships between incident light intensity and generated current pulse frequency.


Fig. 12. Photographs for implantation of retinal prosthesis module into the rabbit eyeball. (Left: before implantation, Right: after implantation). The end of retinal prosthesis module was completely implanted and fixed on the retina.

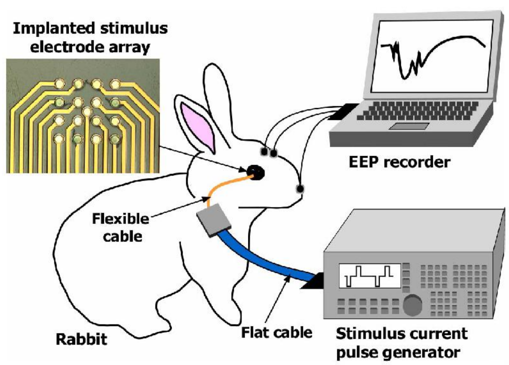


Fig. 13. Recording apparatus for electrically evoked potential (EEP) of rabbit. The stimulus electrode array was implanted into the rabbit eyeball. The EEP was recorded from the rabbit brain.

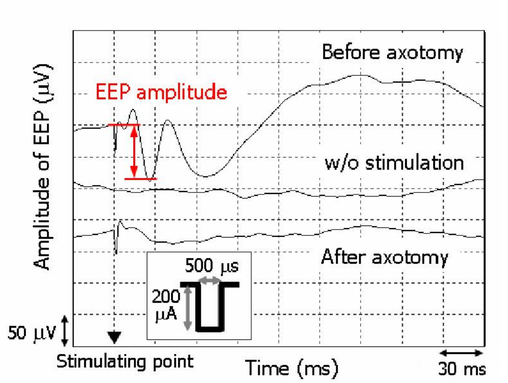


Fig. 14. EEP waveform comparison between before and after axotomy. The inset is the stimulus current pulse waveform used for EEP recording experiments.

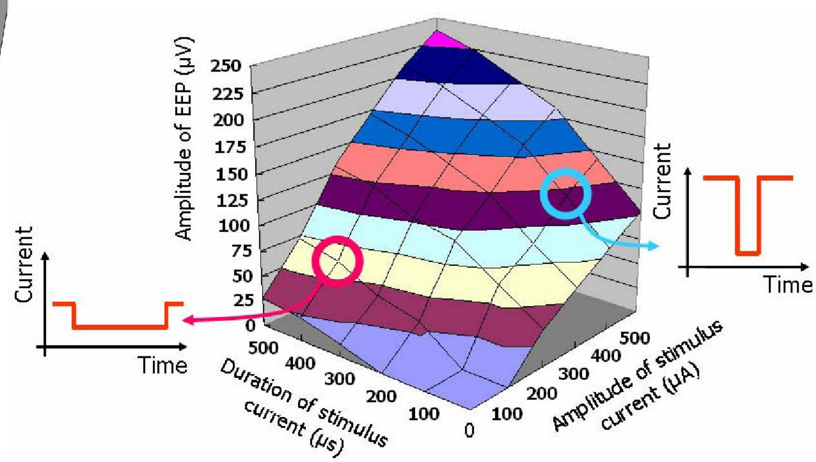


Fig. 15. Effects of both duration and amplitude of stimulus current pulse on the recorded EEP amplitude. The amplitude of stimulus current pulse is more effective than the duration in spite of the same electrical charge quantity of stimulus current.