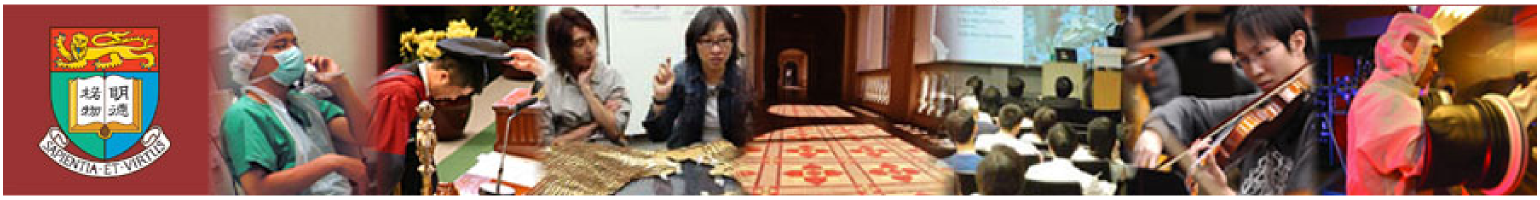

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Wide Field Epiretinal Micro-electrode-Design and Feature Test *

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Abstract—**This study was aimed to design and fabricate a wide field implantable epi-retinal microelectrode array for the purpose of retinal repair, and to perform electrochemical test on the array. With parylene as flexible substrate material and Pt as electrode and route material, microelectrode array prototypes was designed and fabricated, and electric characteristics of the array was tested with the three-electrode test system. The feature analysis showed that morphological and electrical properties of the array well met the requirements of implantation and electrical stimulation of retina. The microelectrode array can be put in the in vivo electrophysiological experiments on animal and can perform reliably.**

I. Introduction

Blindness from retinal diseases, including age-related macular degeneration (AMD) and retinitis pigmentosa (RP), usually causes a significant decline in quality of life for affected patients. Currently there is no cure for these conditions. However, over the last decade, several groups have been developing retinal prothesis which hopefully will provide some degree of improved visual function to these patients [1]. For those who suffered from AMD and RP, photoreceptor degeneration started and progress, parts of the inner layers of the retina, including bipolar and ganglion cells, remain [2,3]. To activate the dystrophic retina, different approaches have been proposed. Sub-retinal stimulation with implants at the original site of photoreceptors aims at activating bipolar cells [4], whereas epi-retinal stimulation with implants in the vitreous body on the inner limiting membrane aims at stimulating retinal ganglion cells[5,6].

Mobility is a process involving navigation and orientation; it enables one to correctly recognize one's position with respect to the immediate environment and move safely from one location to another. Difficulty with mobility has been reported in a variety of ocular diseases including AMD and RP. As the visual field decreases the mobility performance declines. Studies have shown a significant correlation between the visual field and mobility performance in low vision patients [7].

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To improve the visual field in patients implanted with a retinal prosthesis two approaches may be taken. Capturing a wide field image and presenting it to a small area of the retina through current size electrode arrays. The problem with this approach is that the visual field is increased at the expense of image size and visual acuity, as such a system would inherently be associated with minification of the perceived image. However, implantation of a large electrode array brings on new challenges. Most importantly, as the size of the electrode array increases, the conformity of the array to the curvature of the eye becomes more imperative. One potential solution to tackle this problem could be pre-curving the electrode arrays during the Fabrication. Nevertheless, the curvature of the eye varies among individuals and a fixed curvature may not fit every individual eye. Ideally, the curvature of the array should be customized to the curvature of each individual eye [8]. Also, it involves complicated fabrication.

A wide field electrode array that may increase the field of vision in patients implanted with a retinal prosthesis. The purpose of this paper was to present a wide field electrode array that may improve mobility performance, and perhaps visual acuity, especially in horizontal direction. We designed and fabricated a wider range (in horizontal direction) epi-retinal microelectrode array, and conducted electrochemical characteristics analysis of the electrode array so as to provide the basis for electrophysiological experiments on animals.

II. Design and Fabrication of the Micro-electrode Array

A. Micro electrode array design

A wide view implantable epi-retinal electrode array was designed and fabricated in this study. Based on our knowledge of the retina prothesis and epi-retinal implantation, we proposed an epi-retinal electrode array with width of 3mm in vertical and 5mm in horizontal, in the concept of providing wider view in horizontal direction.

The microelectrode array consisted three parts: 1) implantable stimulating electrode array which was intended to be inserted into the inner surface of retina, with each electrode's diameter of 150μm and the separation of each two electrodes of 100μm. The implantable stimulating electrodes were designed in the arrangement of a rectangular array, with each two electrodes separated in equal distance. 2) Metal routes which connect the stimulating electrode array and tail pads. The width of the route was 15μm, and the distance of each two routes was 10μm. 3) Tail pads which allowed the connection to outer electric signal from a voltage to current signal generator.

B. Micro electrode array material

In terms of microelectrode array material choice, consideration of the biocompatibility of material would be the first, since the implantation of the electrode makes the contact with biological tissues and fluids forms friction, this will easily cause corrosion on electrode surface. In order to conform to the curvature of the eye, the substrate material of the electrode should be flexible. Based on the above considerations, we chose parylene, which is commonly used as neural microelectrode array substrate, as substrate material. Besides having good biocompatibility, parylene can be fabricated at room temperature, uniform coating thickness with no pinhole could easily to be achieved, and it has good flexibility and excellent electric insulation, as well as good mechanical properties. Stability and good biocompatibility of the electrode and route material are another key part to be taking into consideration in order to ensure long-term implantation into the retina and the overcoming of rejection phenomenon occur during their stay in the retina tissue. Also, excellent electrical conductivity and corrosion resistance are required. Also, there need to have very strong binding force [9] between electrodes and substrate material. We chose platinum Pt as the material of stimulating electrodes and Al as routes material.

C. Fabrication and feature test of the array

The fabrication of the electrode array was as follow: 1) Deposition on silicon parylene layer of 20μm. 2) Spin coating photoresist, exposure of the substrate after development to give the desired thickness. 3) Sputtering metal Al. 4) Using lift-off process to form patterned route layer. 5) Using oxygen RIE etching technique to form metal Al route layer. 6) Spin coated with photoresist, then by exposure to give the desired micro-electrode pattern. 7) Sputtering TI/Pt electrode materials. 8) Using lift-off process was performed to get micro-electrode array, and the flexible microelectrode array was peeled off from the silicon substrate.

Since the microelectrode was designed to be implanted in tissues where a certain concentration of electrolyte ions, mainly components are Na^+ and Cl exist, we constructed a bionic environment to carry out the electric feature test. We used three-electrode electrochemical testing system shown in Fig.1 to simulate physiological fluid and performed electrochemical characteristics test on the electrode array [10]. In the diagram, EA was the electrode array to be tested, Ag/AgCl was reference electrode, Pt was the pair electrode, and the solution was 0. 9% NaCl saline used as physiological fluid.

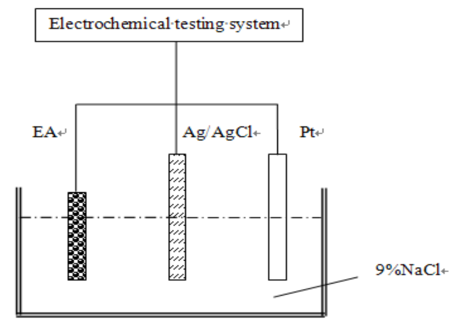
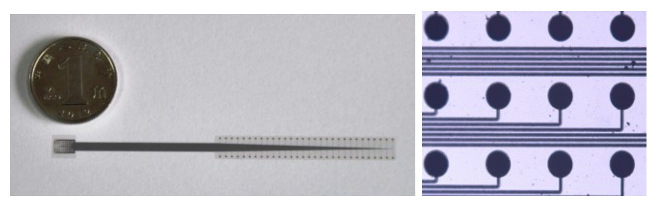


Fig.1 Schematic diagram of electrochemical testing system

III. RESULT

A. Electrode morphology test

Fig.2 shows the appearance of the electrode (a) and morphology observation by microscope (b). The observation showed that the stimulating electrodes were clear with smooth edge; routes that connecting the electrodes were clear and well paralleled, with no short out. The end tail pads were also clear edged, and all connections between stimulating electrodes were tightly bonded. Each route and end pad also joined in good condition. Also, the electrode array had good flexibility, well met the requirements of design.



(a) (b)

Fig.2 The microelectrode array (a) .The close-up of part of the electrode array (b).

B. Electrical properties test

Fig.3 (a) and (b) are logarithmic impedance change with frequency and impedance phase change with frequency, respectively, of the test electrode. In Fig.5 (a) it can be seen that with the increase of frequency, the impedance of the electrode gradually reduces, the electrode present good high-pass characteristics. Fig. 3 (b) shows that within the frequency range of 100Hz to 10 KHz (10^2 Hz - 10^4 Hz), impedance phase shows a relatively stable trend, and the electrode can work stably. When the frequency was higher than 10 KHz, the absolute value of impedance phase gradually decreases. The test results of electrode impedance and phase show that at high frequency the electrode perform resistance characteristics, while at low frequency capacitance characteristic.

Fig.3 (a)

Fig.3 (b)

Fig. 3 Test result of impedance change with frequency (a) and impedance phase change with frequency (b).

IV. DISCUSSION

A. Electrode safety

Regarding the electrical conductivity of the retina, there may be a difference in values between the degenerated and healthy retina. In this study we have used values available in the literature for the healthy retina. However, retinal prostheses are eventually used to restore function in the cases of degenerated retina. After photoreceptors' death, the bipolar layer thickness decreases and the limiting inner membrane become thicker [11]. We took into consideration when designing the parameter of the electrode so as it can not only be implanted in normal retinal for electrophysiological study but also endure the higher electrical stimulation necessary for the degenerated retina.

Once implanted in retina, the electrode–electrolyte interface is operating in a mode of reversible electrochemistry, which implies that charge injection per unit area is limited. When design the electrode, we took into consideration of the interface, so the plane on the surface can well protect the electrode.

According to Beebe and Rose's research, Platinum can safely deliver 0.35–0.4 mC cm^{-2} and iridium oxide has been shown to have a safe stimulation limit of up to 3–4 mC cm^{-2} [12], and thus the cover layer of iridium oxide was introduced in our study in order to avoid parts of the metal with high current density (e.g. hot spot on return electrode in the panel).

B. Electrode size

In a experimental implantation, the size of the stimulating electrode has direct relationship with visual resolution, as long as the electrodes are closer to the cell than the electrode size, smaller stimulating electrode sizes are also preferable in terms of reducing cell activation threshold [13]: that means, if a pixel activates too few cells, its effect may not be perceived and thus visual perception may require multiple neighboring pixels stimulation [14]. Thus, the small electrode size does not guarantee improved resolution.

The maximal number of electrodes will also depend on the tracks connecting each individual electrode to the electronic stimulator. Each lead must have a minimum width that needs to be taken into account when designing the implant.

Eventually, the electrodes will have to adapt to the human retina where the size of the cells will be comparable to the implant electrode size. Electrode parameters with reference to the cones, enables the electrode stimulation to cause the reaction of cones, resulting in the visual cortex of the image can be up to a certain resolution, stimulating electrode design was 150 µm in diameter in our study.

C. The property of the electrode

Technically, the electrode arrays should conform to the inner curvature of the eye. One potential solution to tackle this problem could be pre-curving the electrode arrays during the Fabrication. Nevertheless, the difficult part of the job is that the curvature of the eye varies among individuals and a fixed curvature may not fit every individual eye. Ideally, the curvature of the array should be customized to the curvature of each individual eye, while the very complicated fabrication of the array involves.

Parylene was used as the substrate material due to its flexibility and the satisfactory adaption to natural radian of the retina. So the microelectrode array can contact with the retina properly and to stimulate more effectively; In addition, parylene was to widely used as nerve stimulation, implantable sensor, blood analysis sensor and other fields, its good performance has been widely recognized.

According to the related research, the projected visual field for every 1 mm of the retina is about 3.35°[15]. For instance, if the implanted epi-retinal electrode array is 3 × 3 mm, it would provide a central vision with a field of view of about 10°× 10°. In our study, the horizontal view provided by the electrode will be 16.75°, wider than the vertical view of 10.05°.

From Fig.3 (a), with the increase of frequency, the impedance of the electrode gradually reduces, the microelectrode present good high-pass characteristics. From fig.3 (b), within the frequency range of 100Hz to 10 KHz(10^2 hz - 10^4 hz), impedance phase present a trend of relatively stable, while the absolute value of impedance phase decrease gradually when the frequency was higher than 10 KHz, The test results of electrode impedance and phase show that at high frequency the electrode perform its resistance characteristics, while at low frequency it perform its capacitance characteristic, this result is in consistant with the results from electrode-tissue equivalent circuit model [16, 17].

V. Conclusion

In this study, we designed and fabricated and implantable epi-retinal electrode array with the concept of providing wider view in horizontal direction.

We used parylene with flexibility as substrate material, in light of the material will easily conform to the natural curvature of the retina. Then we conducted electrochemical test on the electrode array. Impedance spectrum of the microelectrode array showed that the electrode perform a high-pass characteristic in mid-frequency band. This flexible array with low impedance value, small phase delay will be suitable for retinal implantation.

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