

Flexible Microfabricated Parylene Multielectrode Arrays for Retinal Stimulation and Spinal Cord Field Modulation

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ABSTRACT

The first flexible parylene-based multielectrode arrays (MEAs) designed for functional electrical stimulation (FES) in retinal prostheses, and the extension of this technology toward enabling reflex-arc neuromodulation in cases of spinal cord damage or transection, are presented. A single metal layer 16×16 retinal electrode array of 125 μm -diameter thin-film Ti/Pt electrodes and lines of 12 μm -pitch has been fabricated as a demonstration of this technology. To allow for even higher density arrays, a novel dual-layer process has also been implemented that enables leads to pass under overlying electrodes without making electrical contact to them. A biomimetic parylene-based electrode array consisting of 1024 electrodes of highly variable spacing, 60 of which have been connected in this manner, has been fabricated according to this paradigm. A parylene-parylene annealing process has also been developed to increase device longevity under accelerated-lifetime saline soak conditions. Surgical tests of novel anatomically-conformal geometries that enable such parylene-based electrode systems to interact with their neuronal targets of interest while causing minimal mechanical damage to tissues or to the implants are also presented. The use of these flexible electrode arrays in spinal cord stimulation experiments in animal models has proven their efficacy in stimulating neurons.

Keywords: BioMEMS, Dual-layer, Electrode array, Neural prosthesis, Parylene, Retinal prosthesis

1 INTRODUCTION

Prototypical hand-made retinal prostheses have shown great promise, enabling subjects blind from such diseases as retinitis pigmentosa and age-related macular degeneration to perceive visual data [1]. The next-generation retinal prosthesis (Fig. 1), however, requires a high-density flexible electrode array and a high lead-count cable to allow for high resolution vision. We are developing parylene-based technologies that use microfabrication techniques to increase the electrode densities by more than an order of magnitude over the state-of-the-art 16-electrode implant being used in such studies. These technologies include parylene-based electrode arrays and flexible cables, radiofrequency (RF) coils for power and data transmission, and scalable interconnect packages for connecting prefabricated application-specific integrated circuits (ASICs) and discretes with the other system components [2]. We are adapting these technologies to enable modulation of innate reflex-arcs through FES from MEAs of a different geometry, with the aim of facilitating locomotion in cases of spinal cord damage. It has been shown that such reflexes are preserved even in cases of complete spinal cord transection [3]. Because our low-profile flexible architectures obviate the positioning problems associated with traditional wire-based electrode technologies, these MEAs should minimize tissue damage while enabling chronic electrical field modulation of multiple lumbosacral segments through a single point of entry. The advantages of the use of parylene C as the bulk-material for such neuroprostheses, when compared with technologies based on the use of other materials such as polyimide [4] and silicon [5], include

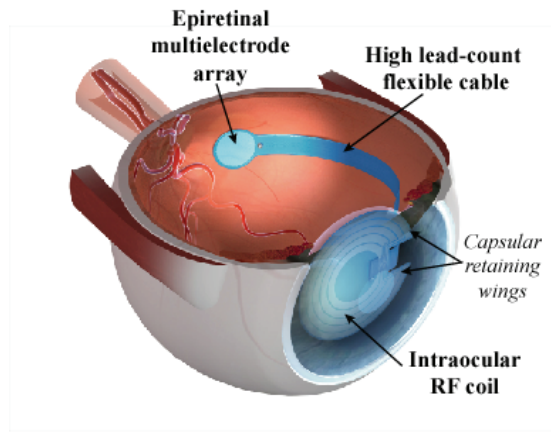


Figure 1. Intraocular retinal prosthesis components.

parylene's pinhole-free conformality, its low water permeability, its United States Pharmacopeia (USP) Class VI biocompatibility, and its flexibility and mechanical strength (Young's modulus ~ 4 GPa).

In this work, we present electrode arrays fabricated using a single metal-layer process. Building on this, a dual-layer process has also been devised and implemented that enables these electrode arrays to overcome the wire-routing and electrode-crowding problems typically encountered in such high lead-count applications. Novel anatomically-conforming geometries have also been developed and tested for both the intraocular retinal prosthesis and spinal cord applications, and demonstrate

the implantability of these parylene-based technologies. Finally, preliminary stimulation experiments have demonstrated that these electrode arrays are efficacious for neuronal stimulation.

2 FABRICATION

2.1 Single-layer process

The process flow for the fabrication of single-layer multielectrode arrays is given elsewhere [6]. Briefly, $\sim 8 \mu\text{m}$ of parylene C is vapor-deposited on a standard silicon wafer (a sacrificial photoresist precoat is optional). A subsequent thin-film metal deposition and liftoff forms the contacts, conductive lines, and electrodes. A second layer of parylene C is then deposited, and oxygen plasma is applied through a photoresist mask to remove the parylene covering the electrodes and contacts, as well as to form the overall array geometry. The electrodes are finally peeled from the wafer in an acetone or water bath.

2.2 Dual-layer process

Dual-layer electrode arrays are fabricated as shown in Fig. 2. Again, an optional sacrificial photoresist is spun on a standard silicon wafer. A first parylene deposition on the entire wafer forms the underside of the electrode array. A metal liftoff pattern is exposed and developed into a photoresist mask using a 10X reduction stepper. A subsequent 200 Å titanium and 2000 Å platinum deposition and liftoff forms the first metal layer, creating the traces that will underlie the metal electrodes. A second parylene deposition ($\sim 1 \mu\text{m}$) forms the insulation layer between the two metal layers. 6 $\mu\text{m} \times 6 \mu\text{m}$ vias are patterned in this parylene layer using a photoresist mask in an oxygen plasma reactive-ion etc. After stripping the photoresist, a second liftoff pattern is exposed and developed in photoresist. Another metal deposition of 200 Å titanium and 2000 Å platinum and subsequent photoresist strip forms the second layer of metal, and coats the via sidewalls due to the slightly isotropic nature of the via parylene etch [7]. The final parylene coating creates the top insulation. To expose the electrodes and fabricate the overall geometry, this parylene layer is then patterned with another photoresist mask and reactive-ion etching in oxygen plasma. Finally, the photoresist is stripped and the electrodes are peeled from the wafer in a water bath or released through removal of the sacrificial photoresist in acetone.

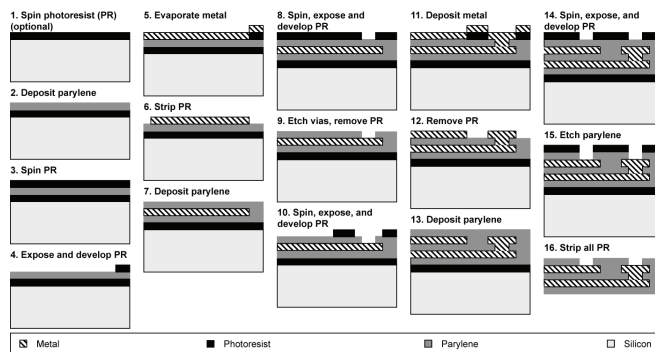


Figure 2. Fabrication process for parylene-based dual-layer multielectrode arrays.

2.3 Parylene-parylene annealing

These electrodes ideally undergo post-processing to prepare them for implantation or any electrochemical or accelerated-lifetime saline soak testing. It has been found that, in samples that have not undergone post-processing, parylene-parylene delamination can be observed sometimes in a matter of hours under accelerated-lifetime conditions in 77°C saline. This failure time depends on the processes performed on the underlying layer of parylene before deposition of the overlying layer. However, if the parylene stack is annealed in a vacuum oven with nitrogen backfill at elevated temperatures for a short time (usually 200°C for 2 days) before soaking, a sample that would fail can be converted into one that remains stable under identical conditions for more than one year. This parylene-parylene annealing process is now routinely performed on our devices prior to any further testing with excellent results.

3 BIOMIMETIC DESIGN

The dual-layer electrode fabrication process obviates the usual concerns over wire routing and electrode crowding, because more incoming traces can be on two separate layers, and because the first layer of traces can pass under overlying electrodes. The traces would not have to be unreasonably narrow (thus, high impedance) to route lines to all of the electrodes in a 1024 electrode array. As an added benefit, it facilitates electrode connections in arrays of multiple geometries and with varying electrode-electrode spacing. In order to demonstrate this, an electrode array was fabricated in which the electrode spacing was designed to more closely match (when compared with arrays in the traditional grid arrangement) the topography of the ganglion cells in the macula of the human retina with respect to radial density [8] (Fig. 3).

Single layer retinal electrode arrays were also designed and fabricated to simulate the geometry of a fully-implantable intraocular retinal prosthesis, comprising an RF coil region designed for placement in the crystalline lens capsule, a flexible cable that exits the posterior capsule, coursing through the vitreous cavity to the point of attachment of the electrode array with a retinal tack on the macula. These took into account results from previous surgical testing in which such problems as cable length and traction of the RF coil region into the vitreous cavity due to the point of attachment of the cable were noted. In addition to shortening the cable, capsular retaining-wings were added to the design so as to enable the flexible cable and electrode array to bend away from the lens capsule while retaining a tether to a stably-situated RF coil region. These modifications were designed to enable the retinal prosthesis to more closely conform to the anatomy of the eye while remaining

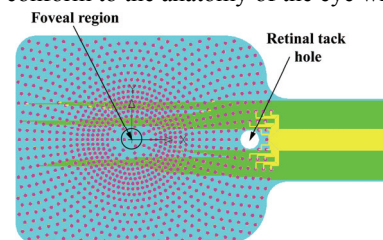


Figure 3. Biomimetic retinal microelectrode array layout.

securely anchored in place. Electrodes were added to these surgical test structures to determine their resilience to the implantation techniques. Each test structure contained a set of 4 electrodes, with each electrode connected by two traces to contact pads in the RF coil region (two facilitate continuity testing). The metallization of thin-film platinum in these test devices was of comparable thickness to that envisioned for the metallization in the final device (~2000 Å to 3000 Å).

The electrode array designed for implantation and electrical field modulation in spinal cord prostheses has been designed according to similar biomimetics considerations (Fig. 4). The small width of the array (1.2 mm) enables its insertion through a small incision under the dura mater and threading along the spinal cord so as to be in close contact with multiple spinal segments. Suture holes and tabs for manipulation with forceps facilitate surgery and anchoring without excessive damage to the traces or electrodes. The flexibility of the array is ultimately its greatest attribute, in that it is bioconformal. The stiffness of parylene is such that the material is neither too limp nor too rigid when compared with other materials such as PDMS or polyimide, respectively, while remaining robust under surgical conditions.

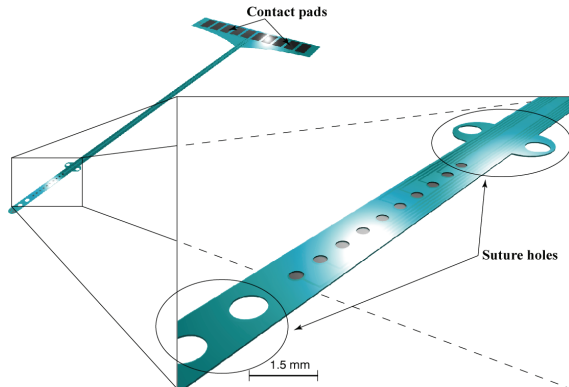


Figure 4. Graphical depiction of bioconformal spinal cord MEA.

4 TESTING AND RESULTS

A fabricated single-layer electrode array, with 256 electrodes of 125 μm diameter in a traditional 5 mm-square 16 × 16 square grid arrangement with traces of 12 micron pitch is shown in Fig. 5a, and a scanning electron micrograph (SEM) depicting the morphology of the electrode and the parylene opening is shown in Fig. 5b. Energy dispersive spectroscopy (EDS) and electrochemical tests have confirmed the lack of contamination of the exposed platinum in these structures.

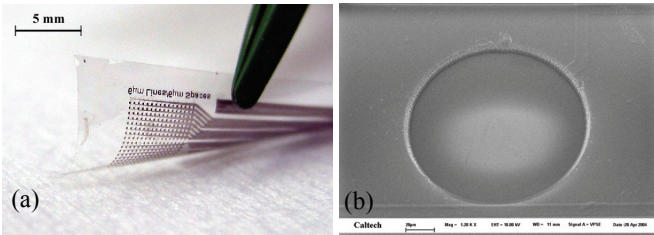


Figure 5. (a) A 16 × 16 Ti/Pt electrode array and (b) SEM micrograph detailing electrode geometry.

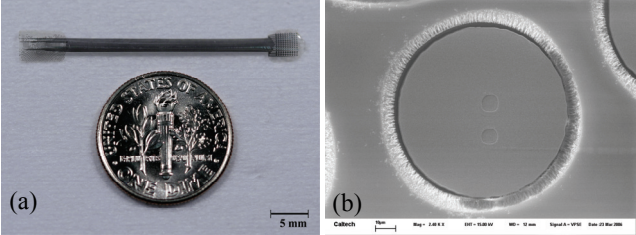


Figure 6. (a) Fabricated dual-layer electrode array and (b) SEM micrograph detailing electrode geometry (note vias in center).

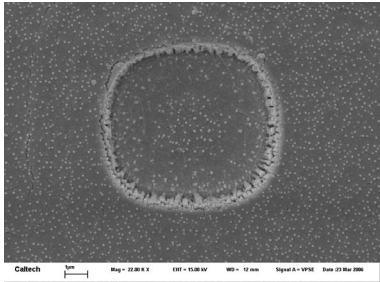


Figure 7. Magnified view of 6 μm × 6 μm via forming connection between metal layers.

Fig. 6 shows a fabricated dual layer electrode array and a scanning electron micrograph of a typical electrode in this array. A magnified view of a via making contact between the overlying metal and the underlying trace in such an electrode is shown in Fig. 7, demonstrating the metal step coverage over the parylene sidewall. Electrical testing between the contacts connected to each of the incoming traces has demonstrated a typical impedance in the range of 5 kΩ, including the two 8 μm wide traces of 20 mm length as well as the via step junction. The junction itself has been shown to have an impedance of less than 12.5 Ω. Additional testing has shown that traces are not shorted to other electrodes under which they pass, and that second-layer traces are not shorted to those underneath, indicating that there are no pinholes in the parylene insulation layer. Electrochemical testing of these dual-layer electrode arrays is now underway.

A fabricated single-layer surgical test structure with embedded traces is shown in Fig. 8. Pad-electrode-pad impedances were measured prior to surgical implantation of this device using the anticipated procedures in an *ex vivo* porcine eye and an *in vivo*

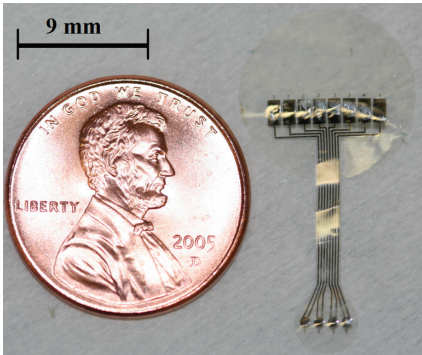


Figure 8. Surgical test structure for mechanical and electrical characterization.

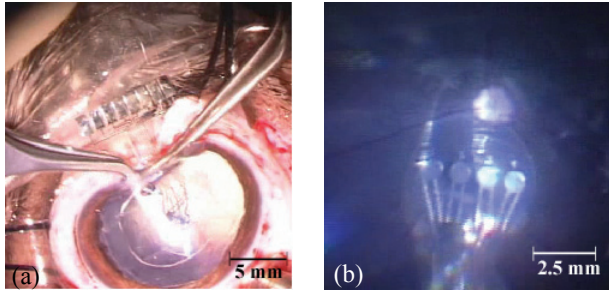


Figure 9. Surgical implantation under (a) anterior and (b) intravitreal illumination.

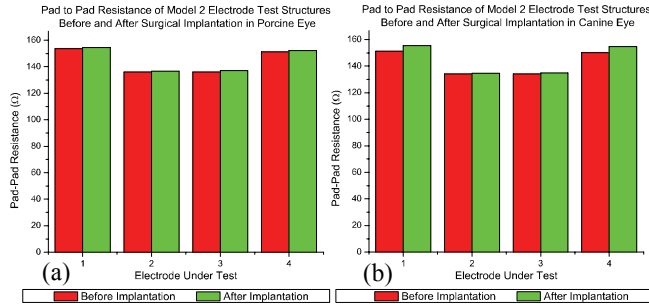


Figure 10. Pad-electrode-pad circuit resistances before and after surgical implantation in (a) porcine eye and (b) canine eye.

canine eye (surgical photographs under anterior (a) and intravitreal (b) illumination are shown in Fig. 9). After explantation, the line impedances were measured and compared with those done prior. The results graphed in Fig. 10 show that the pre-surgical coil-electrode-coil circuit impedances fell into two groups based on the physical lengths of these circuits, the shorter having a mean impedance of 135 Ω and the longer having a mean impedance of 152 Ω . Post-surgical testing of the electrical characteristics of the circuits revealed mean impedances of 136 Ω and 154 Ω for the short and long circuits, respectively, with no lines having been broken during the surgical procedures. These results indicate that the embedded thin-film metal wires are robust under surgical conditions.

Structural prototypes of parylene-based electrode arrays were fabricated implanted on the spinal cords of two mice with excellent results. Based on these results, spinal cord electrode arrays were fabricated as shown in Fig. 11. One of these electrode arrays was implanted in contact with the spinal cord of a mouse, and stimulation with simultaneous electromyogram recordings demonstrated their efficacy in neuronal stimulation over the testing period of several hours.

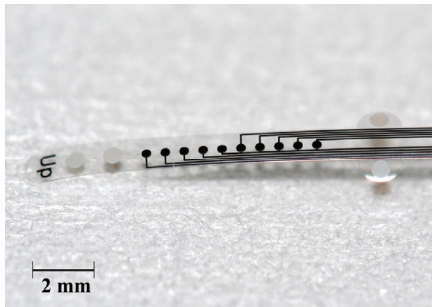


Figure 11. Fabricated spinal cord flexible electrode array.

5 CONCLUSION

Parylene-based flexible MEAs for retinal and spinal cord prostheses are being developed to solve such problems as blindness from photoreceptor loss and locomotor dysfunction due to spinal cord injury. Single-layer electrode arrays have been tested and implanted in animals to demonstrate that these technologies are robust under surgical conditions and efficacious in stimulating neurons. A new dual-layer process has been devised that significantly increases the possible electrode densities possible in such arrays. It is of note that this technology is not restricted to two layers of metal. Indeed, it is a simple task to add additional alternating layers of metal and parylene to enable even more complicated wire routing if necessary. In addition, this fabrication technology is not restricted to the use of parylene, however the conformality and uniformity of the parylene deposition process facilitates the fabrication of such multilayer neural prosthetic devices.

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