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Flexible parylene-based multielectrode array technology for high-density neural stimulation and recording

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Abstract

Novel flexible parylene-based high-density electrode arrays have been developed for functional electrical stimulation in retinal and spinal cord prosthetics. These arrays are microfabricated according to a single-metal-layer process and a revolutionary dual-metal-layer process that promises to meet the needs of extremely high-density stimulation applications. While in many cases thin-film platinum electrodes in parylene C would be sufficient, high surface-area platinum electroplating has been shown to extend the lifetime of stimulated electrodes to more than 430 million pulses without failing. Iridium electrode arrays with higher charge delivery capacity have also been fabricated using a new high-temperature stabilized parylene variant, parylene HT. In addition, a new heat molding process has been implemented to conform electrode arrays to approximate the curvature of canine retinas, and a chronic implantation study of the mechanical effects of parylene-based electrode arrays on the retina over a 6-month follow-up period has provided excellent results. Retinal stimulation from these parylene-based electrode arrays in an isolated tiger salamander preparation was shown to be comparable to light stimulation in terms of generation of action potentials in the inner retina. Finally, electrode arrays have also been implanted and tested on the spinal cords of murine models, with the ultimate goal of facilitation of locomotion after spinal cord injury; these arrays provide a higher density and better spatial control of stimulation and recording than is typically possible using traditional fine-wire electrodes. Spinal cord stimulation typically elicited three muscle responses, an early (direct), a middle (monosynaptic), and a late (polysynaptic) response, classified based on latency after stimulation. Stimulation at different rostrocaudal levels of the cord yielded markedly different muscle responses, highlighting the need for such high-density arrays.

Keywords: Artificial vision; BioMEMS; Biomimetic; MEA; Neural prosthesis; Parylene C; Parylene HT; Retinal prosthesis

1. Introduction

Low-electrode-density neural prostheses have shown incredible promise, enabling those with severe hearing impairments to recognize speech [1] and those blind from such devastating outer retinal diseases as retinitis pigmentosa (RP) (where the photoreceptors are damaged but the remaining inner retinal circuitry remains largely intact [2]) to perceive visual data [3]. Subjects with prototype sixteen-electrode retinal prostheses can even distinguish between objects such as plates, cups, and knives, and perceive directions of movement in high-contrast environments far better than would be possible by chance alone [4]. However, there exists a need for a multielectrode array (MEA) technology that is capable of increasing the density of neural stimulation beyond its current limits, while ensuring biocompatibility and device longevity. In fact, for retinal stimulation in particular, it has been shown that room navigation could be significantly improved with an electrode array comprising one thousand or more electrodes, and furthermore such an array would likely enable facial recognition and large type reading [5]. The next-generation retinal prosthesis for patients with diseases like RP and age-related macular degeneration (AMD) (Fig. 1), then, requires a high-density flexible electrode array

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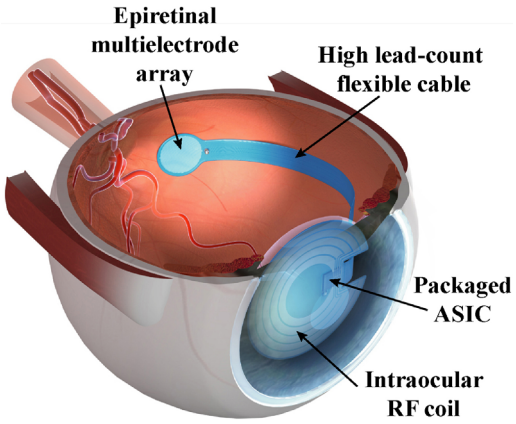

Fig. 1. Placement and components of envisioned next-generation intraocular retinal prosthesis.

capable of stimulating the inner retina and a high-lead-count cable to allow for high-resolution vision. We present the first flexible parylene-based MEAs designed for functional electrical stimulation in retinal prostheses, and the extension of this technology to enable stimulation of central nervous system structures after spinal cord injury. In addition to presenting a high surface-area electroplating technology that extends stimulation electrode longevity to at least 430 million pulses, which is ample for many applications, we address the importance of a novel parylene-enabled dual-metal-layer fabrication methodology that permits complex electrode arrangements while alleviating the traditional problems of electrode crowding and electrode size restrictions caused by wire routing. Promising chronic biomechanical stability results in canine eyes and acute neural recording and stimulation results in an *in vitro* retinal preparation and *in vivo* in murine spinal cords are presented, demonstrating the ability of these parylene-based arrays to both record from and stimulate the neuronal targets of interest. All animal procedures conformed to the ARVO Statement on the Use of Animals in Ophthalmic and Vision Research.

The advantages of using parylene C as the structural material for such neuroprostheses, when compared with technologies based on the use of other materials such as PDMS, polyimide [6] and silicon [7], include parylene's pinhole-free conformality due partly to its unique room-temperature chemical vapor deposition process, its low water permeability, its chronic implantability as an ISO 10993, United States Pharmacopeia (USP) Class VI material (highest biocompatibility class for plastics in the United States), and its high flexibility and mechanical strength (Young's modulus ~4 GPa). Since parylene is deposited at room temperature (we have verified this using Temp-Plate irreversible temperature recorders traceable to NIST (Wahl Instruments, Inc., Asheville, NC, USA)), the coating process is post-integrated-circuit (IC) compatible. Parylene C is also optically transparent, enabling the anatomy to be seen through the cable and the array during ophthalmic surgery, post-implantation examination, and follow-up. While many groups use parylene C as a coating of their arrays for many of these reasons, we have chosen to use it as the main substrate for our devices [8,9], a paradigm that leverages these advantages to the greatest extent. A new high-temperature stable [10] and ISO 10993 biocompatible [11–13] fluorinated variant of parylene, parylene HT, that is similar in many respects to parylene C, has also been used to fabricate iridium electrode arrays. We show that while evaporation and patterning of iridium was unsuccessful on parylene C due to the high melting temperature of iridium, parylene HT lends itself to such a process, and we present this as another possible technology for ensuring good charge delivery to neural tissue.

2. Fabrication methods

2.1. Single-layer process

Single-metal-layer parylene C-based electrode arrays are fabricated as shown in Fig. 2. A photoresist sacrificial layer is optionally spun on a standard silicon wafer. Approximately 8 μm of parylene C is then vapor-deposited in a PDS2010 system (Specialty Coating Systems, Indianapolis, IN, USA) on the entire wafer. An LOR3B photoresist layer (Microchem Corporation, Newton, MA, USA) and an AZ1518 layer (AZ Electronic Materials, Branchburg, NJ, USA) are spun on top of the parylene, exposed in a 10× reduction GCA Mann 4800 DSW wafer stepper (General Signal Corporation, Stamford, CT, USA) or a Kasper 2001 contact aligner (Kasper Instruments, Inc., Sunnyvale, CA, USA) depending on the required resolution of the electrode array, and developed to achieve a liftoff pattern consisting of contacts, conductive traces, and electrodes. After hard-bake, approximately 2000–5000 Å of platinum, with or without a 200 Å titanium layer, is then e-beam evaporated (SE600 RAP, CHA Industries, Fremont, CA, USA) on the wafer. The subsequent photoresist strip generates the desired single-layer metallization pattern. An approximately 7-μm-thick coating of parylene C is then deposited, followed by a spin coating of photoresist. This photoresist etch mask is exposed over the areas of the electrodes and contact pads and to pattern the overall array geometry, and the entire wafer is then subjected to a reactive-ion etch in oxygen plasma, removing the parylene insulation over the electrodes and the parylene surrounding the array. The photoresist mask is then removed with solvent. Finally, if a sacrificial photoresist layer was used, the array is released from the substrate in an acetone bath. If no sacrificial layer was used, it is peeled from the silicon in a water bath. Ultimately, for most cases, the sacrificial photoresist layer is unnecessary.

Due to the higher thermal stability of parylene HT (long-term stability at 350 °C, intermittent exposures up to 450 °C [12]), it was surmised that the material would be better suited to iridium array fabrication than would parylene C (the melting temperature of iridium is 2447 °C whereas that of platinum, for which a parylene C substrate works well, is 1772 °C [14]). Consequently, a minor modification of this process is made to fabricate iridium electrode arrays. A thin parylene C layer (~2.4 μm) is deposited on the silicon wafer followed by a thicker layer of parylene HT (~5.7 μm) in a PDS2035 system (Specialty Coating Systems). The parylene C layer facilitates fabrication and subsequent release, whereas the HT layer provides the necessary thermal stability. The dual photoresist layer is spun and patterned, and the