Fabrication of Flexible, Implantable Probes for *in vivo* Recording of Neural Activity

Brianna Thielen
Engineering, Harvey Mudd College

NNIN iREU Site: Centre Microélectronique de Provence, Ecole Nationale Supérieure des Mines de Saint Etienne, France
NNIN iREU Principal Investigator: Professor George Malliaras, Department of Bioelectronics, Centre Microélectronique de Provence, École Nationale Supérieure des Mines de Saint-Etienne, France
NNIN iREU Mentor: Marc Ferro, Department of Bioelectronics, Centre Microélectronique de Provence, École Nationale Supérieure des Mines de Saint-Etienne, France
Contact: bthielen@hmc.edu, malliaras@emse.fr, ferro@emse.fr

Introduction:

In order to study the brain activity of living organisms, electrode arrays can be implanted into a rat brain and can determine the source of an electrical signal down to the firing of a single neuron. Commercial probes containing these arrays are available; however, most of these probes contain an inflexible silicon backbone. Because of the large discrepancy in flexibility between the silicon probe and the brain tissue, the probe is seen as a foreign object and is encapsulated during the body's immune response.

In order to perform long term neural recordings, flexible materials that better match the Young's modulus of brain tissue (approximately 100 kPa) [1] must be used as the probe backbone. In addition, a conducting polymer coating made of poly(3,4-ethylenedioxythiophene) doped with poly(styrene sulfonate) (PEDOT:PSS) can be coated on top of the electrodes to improve the performance of the probe.

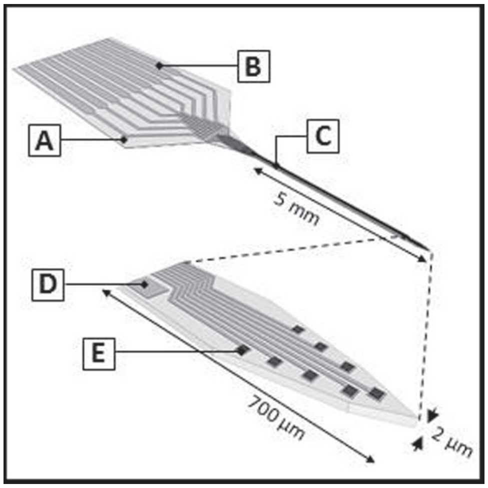

Figure 1: The configuration of the neural probe with PaC probe backbone (A), metal contacts (B), probe shank (C), temperature control pad (D), and the PEDOT:PSS coated electrodes (E).

Probe Configuration:

In this study, flexible neural probes (with the configuration shown in Figure 1) were fabricated. The probe backbone (Figure 1-A) was made of a Parylene-C film. On top of the backbone, metal contacts to interface with a data acquisition device (Figure 1-B), electrodes to collect the neural signals (Figure 1-E), a temperature control pad to adjust for thermal drift (Figure 1-D), and the wires connecting all of the components were patterned. A layer of PEDOT:PSS was coated on top of the electrodes, then a layer of DE1 permanent photoresist (Orthogonal, Inc.) was added on top of the probe to insulate everything except for the electrodes and metal contacts.

Materials and Fabrication:

Probe Backbone: Parylene-C. Parylene-C (PaC) is an FDA approved biocompatible polymer that is electrically insulating, durable, and conformable to most surfaces, while having a relatively simple fabrication process [2]. Using a PDS 2010 Labcoater (Specialty Coating Systems), PaC dimer can be vaporized and deposited as a uniform film onto a surface at room temperature. The film thickness is controlled by the amount of dimer loaded into the instrument. For this project, four grams of dimer were deposited onto silicon wafers, resulting in a film thickness of approximately 2 μm.

Electrodes, Contacts, and Wires: Metal. Metal was patterned by spin-coating photoresist onto the PaC-coated wafers, exposing the pattern using an MJB4 mask aligner (SUSS Microtech), coating the surface of the substrate with metal using an Auto500 metal evaporator (BOC Edwards), then lifting off in an acetone bath. The acetone dissolved the remaining photoresist and removed the metal above it, leaving only the patterned metal (as shown in Figure 2-1).

Electrodes (Conducting Polymer): PEDOT:PSS. Poly(3,4-ethylenedioxythiophene):poly(styrenesulfonate) (PEDOT:PSS) is an electrochemically stable conductive polymer that is able to translate ionic signals into electronic signals by moving holes in the polymer structure. When coated on an electrode, the "fuzzy" polymer structure increases the surface area, thus decreasing the impedance (due to better contact with the target tissue) and improving the performance of the electrode [1].

Rather than using a traditional PaC lift-off technique to pattern the PEDOT:PSS, a subtractive technique was used in order to prevent damage to portions of the probe fabricated in prior steps while also significantly reducing fabrication time. The fabrication process began by spin-coating a layer of PEDOT:PSS on top of the substrate (a silicon wafer coated in PaC with the metal patterned on top). The electrode pads were then masked using a layer of OSCoR 4000 photoresist (Orthogonal, Inc.) (Figure 2-2). The substrate was then etched in an Oxford Plasmalab 80^+ reactive ion etcher (RIE) to remove the unprotected PEDOT:PSS (this process is shown in Figure 2-3). Finally, the remaining OSCoR 4000 photoresist was stripped off the surface using a fluorinated stripper (Orthogonal, Inc.), leaving only the PEDOT:PSS on the electrode pads (Figure 2-4).

Insulating Coating: DE1 Photoresist (Orthogonal, Inc.). DE1 photoresist from Orthogonal, Inc. is a permanent, biocompatible photoresist. It was used as an insulating layer for the probe (to prevent damage and expose only the electrodes to the brain tissue) and was patterned via standard photolithography (result shown in Figure 2-5).

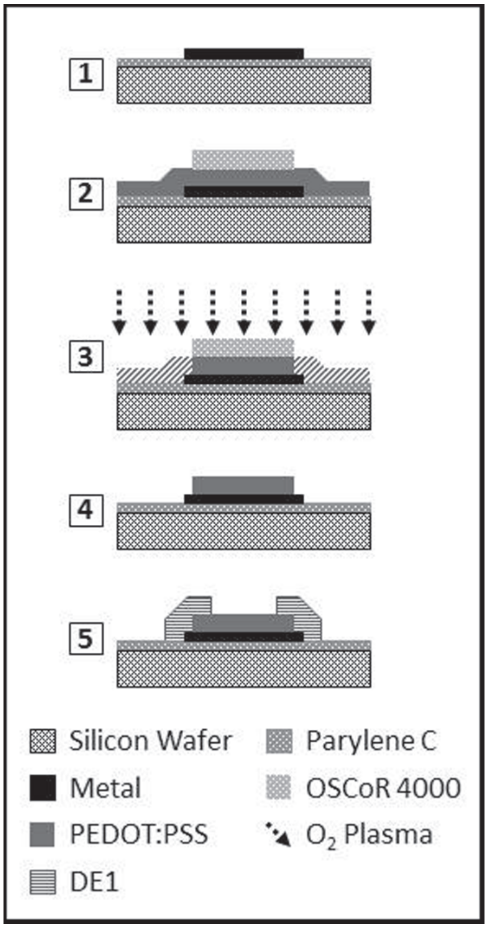

Figure 2: A process flow diagram of the PEDOT:PSS patterning and probe insulation processes, beginning with a silicon wafer coated in PaC and patterned with metal (1), followed by PEDOT:PSS coating and OSCoR 4000 patterning (2), etching in an RIE (3), stripping remaining OSCoR 4000 (4), and insulating the probe using DE1 (5).

Results and Future Work:

Each component of fabrication was tested and optimized; however several steps must be taken prior to the completion of the electrode and probe production process. First, a stiff "shuttle" layer must be added to aid in the insertion of the probe into the rat brain. The shuttle must attach to the probe, minimize insertion damage to the brain, maintain flexibility of the probe, and must allow for accurate insertion (a flexible, removable, or dissolvable shuttle). After the shuttle is completed, the probes must be tested *in vivo* by implanting into a rat brain and recording neural signals over time. A successful probe will not be walled off or otherwise damaged in the immune response and will not wear over time.

Acknowledgements:

This work was sponsored by the National Science Foundation and the NNIN iREU Program. The bioelectronics department, specifically Professor George Malliaras and Marc Ferro, provided the equipment, materials, training, and all other necessary support for this project.

References:

[1] D.H. Kim, et al., Soft, Fuzzy and Bioactive Conducting Polymers in W.M. Reichert, Indwelling Neural Implants: 165-207 (2010).

[2] C. Hassler, et al., Polymers for Neural Implants, Polymer Science Part B: Polymer Physics 49.1, 18-33 (2011).