ADVANCED NEURAL IMPLANTS USING THIN-FILM POLYMERS

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ABSTRACT

BioMEMS devices can be designed to provide viable neural interfaces for long-term, high-density, two-way communication with selected areas of cerebral cortex. Prototype thin-film polymer implantable microelectrode arrays were developed to extend the microelectrode design space in several ways, including enhanced flexibility, engineered surfaces and coatings, and new types of microchannels. Prototype MEMS silicon microdevices were developed as microsurgical tools for reliably inserting the flexible polymer electrodes into the cerebral cortex. Hybrid polymer microdevices were also developed for neural recording and stimulation combined with micro-drug delivery.

1. INTRODUCTION

Increasingly more sophisticated neural implant technologies have the potential to advance neuroscience and neurosurgery applications. This fertile area of research and development is driven on one side by steady advances in diverse technologies (e.g., MEMS, nanotechnology, materials science, communications) and on the other side by steady advances in cellular and molecular biology, and systems neuroscience. While silicon-based microelectrode arrays have been under development for many years, complementary polymer-based microdevices are in the early development stages. Silicon-based devices available for implantation into the brain today are chronically implantable with multiple recording sites and can include electronics for signal processing [1].

The objective of this paper is to briefly report recent results concerning three aspects of neural implant development: (i) implantable microelectrode arrays using thin-film polymers, (ii) prototype silicon microknives used as microsurgical tools for handling the polymer microelectrodes, and (iii) prototype hybrid polymer microdevices for neural recording and micro-drug delivery.

2. THIN-FILM POLYMER IMPLANTABLE MICROELECTRODE ARRAYS

An emerging idea in neural implant research is that electrode design should be driven more by the neural tissue structure and the chronic tissue-electrode interface rather than the ability of the electrodes to reliably penetrate the membranes (meninges) that enclose the brain and spinal cord [2], [3]. As such, one of the goals is to keep the microelectrodes thin and flexible, with site geometries designed for specific neural areas (e.g., cerebral cortex, basal ganglia, etc.). Electrode flexibility is hypothesized to be a critical factor minimizing the effects of micromotion of the brain relative to the implanted electrode.

An initial version of a polymer-based intra-cortical microelectrode array was recently reported by our group [3]. This device uses a thin-film microfabrication process with a polyimide substrate (Figure 1). It is designed for neural sensing and stimulation. This device continues to be refined by our group at the University of Michigan [4].

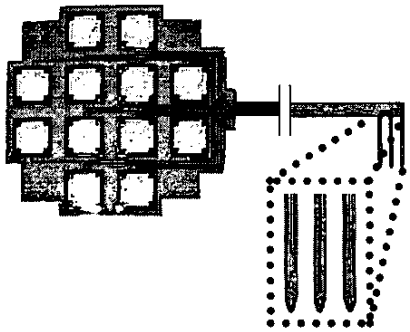

Figure 1. Photograph of a representative polyimide implantable microelectrode array. The inset shows the three shafts with exposed sites. Each of the outer shafts has 4 recording sites separated by 250μm. The center shaft has only a single large ground plane. The bond pads (left) mate to a commercial 12-pin mini-connector (Microtech, Inc.) using conductive epoxy. An integrated flexible polyimide ribbon cable (1 cm x 0.5 mm) connects the shanks to the bond pads. The microdevice is 0.015 mm thick.

The current fabrication process uses three photolithographic masks to pattern two photo-definable polyimide layers and a conductive gold/chrome embedded

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layer. The upper polyimide layer is patterned to expose the conductive metal layer at recording sites and at connector bonding areas.

The recording sites are typically ~400 μm^2 (Figure 2). The holes in the substrate near the recording sites are designed to be filled with selected bioactive molecules that diffuse into the neuropil immediately around the electrode shank.

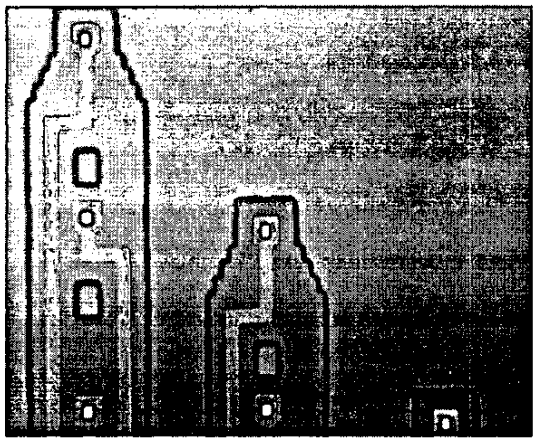

Figure 2. Magnified view of recording sites and chemical seeding holes near the tips of three shanks of a polyimide electrode. The exposed recording sites are 20x20 μm^2. The metal traces connecting the exposed recording sites and the bond pads (not shown) are insulated by the upper and lower layers of polyimide.

At present, the manufacturing process uses photo-definable polyimides. One disadvantage of the currently available photo-definable polyimides is their tendency towards moisture uptake. Several methods are under investigation to minimize this process. One method is CVD deposition of moisture impermeable dielectrics such as parylene-C or a composite of stress-reduced low temperature oxides and nitrides. A second method is CVD of engineered photo-definable polyimide precursors to serve as drop-in replacements for the photo-definable polyimides. Non-photo-definable polyimides, which tend to be more moisture-resistant, are a third potential method.

The basic microfabrication process can be elaborated upon to increase device functionality. The gold recording sites have been electroplated with platinum black to reduce impedance and improve recording characteristics. Several additional enhancements are under active investigation, including using activated iridium for stimulation sites, selective laser micromachining of recording sites and shank locations to modify electrode surfaces and shapes, and including front-end electronic circuits using bump-bonding of silicon chips to the polyimide structure.

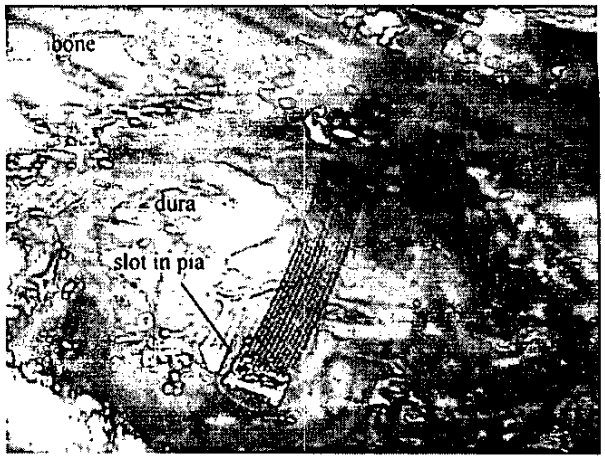

Figure 3. Polyimide electrode implanted into rat brain. The electrode is shaped into a conformal position prior to implant. The shafts penetrate approximately 0.8 mm into the cortex. The polyimide interconnect lies along the brain surface, minimizing tethering forces on the implanted portion of the electrode

The polyimide microelectrodes have been implanted in small animal models for periods up to 14 days. An aseptic surgical procedure is used to expose a small section of cerebral cortex. The shanks are then carefully inserted into the brain. The percutaneous connector is cemented to the exposed skull and the polyimide interconnect is made to lie along the brain surface to result in minimal tethering forces on the implantable aspects of the electrode (Figure 3). The brain area around the electrode is closed with a polymer sealant. All animal procedures were approved by the Institutional Animal Care and Use Committee at Arizona State University.

3. SILICON MICROSURGICAL TOOLS

Implanting these thin, flexible microelectrodes has proven to be a difficult task. For chronic implants, flexibility provides a compatible interface for micromotion of the brain relative to the skull, but during the insertion process the electrodes tend to buckle before enough force has been generated to penetrate the cortex. In addition, the devices are relatively blunt (see Figure 2), which also makes it difficult for them to penetrate through even the inner meninges (pia mater) and into the brain. A surgical insertion tool of some fashion is required to streamline and make consistent the surgical insertion procedure.

Several materials and methods were considered for manufacturing and using the required microsurgical tools. Bulk micromachined silicon and wire EDM machined metal foils provide two possible solutions. The tool must

be as small and thin as the electrode to minimize surgical trauma, but it must also be stiff enough to penetrate target tissues easily. The device should also be biocompatible, relatively easy to fabricate, and be relatively inexpensive. It must also provide a place to hold the electrode during the surgical insertion procedure and allow the microelectrode to remain in the brain while the insertion tool is removed.

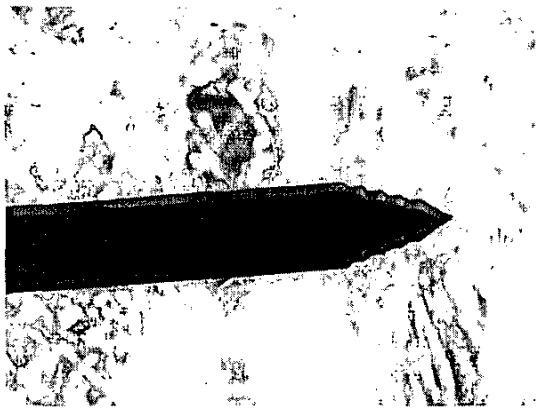

Figure 4. Close-up of the sharp, stiff tip of a bulk micromachined silicon tool for inserting flexible polymer electrodes. The tool is slightly wider than electrode. The electrode will be held on to the tool with a polymer that dissolves upon contact with biological fluids.

Prototypes of bulk micromachined silicon insertion tools were developed and tested in animal studies (Figure 4). The devices were made from 4" silicon wafers by a two step KOH etch process. An initial etch was used to thin the silicon wafers. Next, a silicon nitride masking layer was patterned onto the wafer into the final device shape. A second anisotropic KOH etch was used to complete shaping the device and to release it from the rest of the wafer.

Several methods of reversible attachment of the electrode to the tool were investigated. Two examples of hold-and-release systems are the vacuum method, and the dissolvable polymer method. For the vacuum method, a small channel for routing a vacuum line was etched into the insertion tool. A hole on the face of the tool connects the vacuum chamber to the surface of the electrode. Enough force was generated by the vacuum to hold the electrode to the tool during insertion. After the insertion, the vacuum was released, allowing the tool to be withdrawn, leaving the electrode in the tissue.

Dissolvable polymers were an alternative hold-and-release method. Poly-ethylene glycol (PEG) is a stiff biocompatible polymer that dissolves quickly upon contact with biological fluids. Initially, we tried coating the electrode with only PEG and inserting it directly, but the layer of PEG required for a successful implant was much thicker and rounder than the electrode itself, resulting in excessive surgical trauma. PEG worked best when it was used as a thin adhesive layer between the surgical tool and the electrode. Figure 5 shows an electrode attached to a bulk micromachined silicon knife with PEG. This photograph was taken during the insertion of a polyimide electrode into a rat brain.

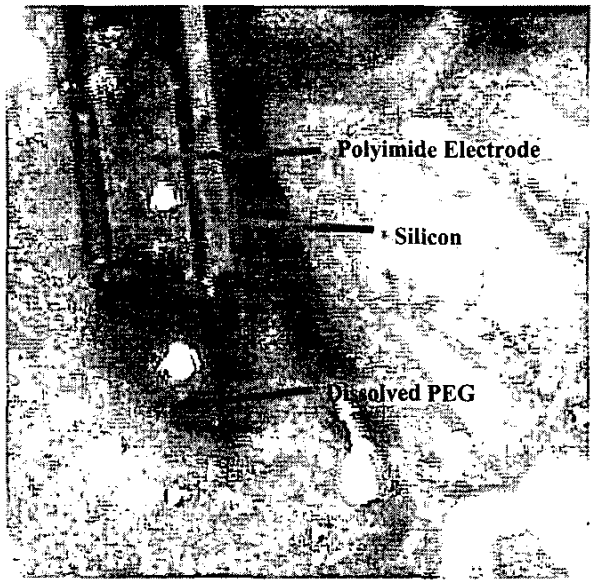

Figure 5. Polyimide electrode backed by a silicon insertion tool during insertion into rat brain. The shiny pools at the electrode/brain interface are dissolved PEG.

4. HYBRID NEURAL IMPLANTS

In addition to a polymer electrode's enhanced flexibility and the ease with which polymers can be modified for the inclusion of engineered surfaces and coatings, polymers can extend the design space of microelectrode arrays by the addition of new types of microchannels. We are currently developing prototype hybrid polymer microdevices for neural recording and micro-drug delivery.

An effort to understand the electrochemical function of the brain is a strong driving force behind ongoing studies of intracerebral chemical/drug delivery into the CNS [5]. Also, recent advances in protein and peptide chemistry are providing neuro-active compounds having therapeutic potential as neuro-protective treatments. The ability to deliver these molecules systemically is hampered by degradation and metabolism prior to reaching the CNS [6]. The method used in the past has been to give large doses of medication, so large that the

patient may experience serious damage elsewhere. In addition, the blood-brain barrier poses a significant obstacle for the delivery of many neuro-active factors. Hybrid neural implants circumvent these problems by bypassing the blood-brain barrier.

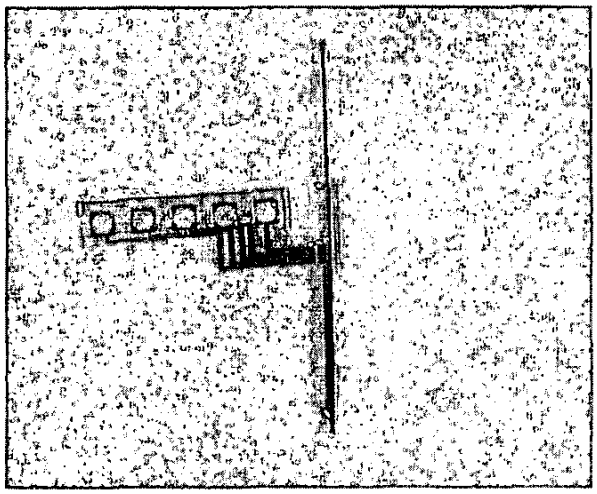

Figure 6. Five site neural recording electrode with integrated commercial polyimide tubing for drug delivery. The bond pads (left) mate to a commercial 12-pin mini-strip-connector (Microtech, Inc.) using conductive epoxy. The recording sites (not shown in detail) are spaced around the fluid outlet of the electrode.

The first generation of polymer recording array with a microchannel is shown in Figure 6. The device consists of a commercially available small diameter polyimide tube integrated into a five recording site electrode array.

The next generation of drug delivery micro-neural recording electrode is currently being designed. The microchannel is being created by a sacrificial process with a combination of photoresist, polyimide, parylene and metallization. Methods to control flow via hydrophobic/ hydrophilic patches, electrostatics, and other non-mechanical means are part of this research activity.

5. DISCUSSION AND CONCLUSIONS

This paper briefly describes a new class of implantable microelectrode arrays that are fabricated using a thin-film polymer process. This technology is amenable for application areas involving advanced brain implants. Prototype polymer implantable microelectrode arrays are currently being used to extend the microelectrode design space in several ways, including enhanced flexibility, engineered surfaces and coatings, and microfluidic drug delivery capabilities.

There are, however, important problems that have to be overcome before flexible polymer microelectrode arrays can be used to their full potential. Insertion difficulties arising from the inability of the devices to independently penetrate tissue have to be solved. Also, the ability of polymers to withstand long term contact with biological systems has to be improved, either with modifications to the polymer structure itself, or the use of sealant layers such as parylene-C, or CVD nitride/oxide stacked layers.

6. ACKNOWLEDGEMENTS

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7. REFERENCES

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