Design and fabrication of neuroelectronic device containing gold pyramid electrodes

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Abstract. A neuroelectronic device containing an electrochemically deposited multi-walled carbon nanotube (MWCNT) sensitive layer was designed, fabricated and characterized. The neuroelectronic device consists of a flexible polyimide substrate bearing four shanks with 16 gold rectangular pyramid electrodes per shank and MWCNT sensitive layer. Each of the 16 gold pyramid electrodes with a top active area of 6 μm x 60 μm and depth of 750 μm are positioned with a vertical separation distance of 100 μm on a shank width of 40 μm. Gold rectangular pyramid electrodes are selected as the recording electrodes to enhance the electroactive surface area. Electrochemical impedance spectroscopy (EIS) analysis of the resulting 16 gold pyramid electrodes on one of the shanks of the neuroelectronic device was characterized at the physiological relevant frequency of 1 kHz. The experimental results show that the gold electrodes are uniformly coated with MWCNTs sensitive layer. With no MWCNT coating, the impedance response at 1 kHz could reach as high as 17.16 MΩ on average. Additionally, the MWCNT coated gold pyramid electrodes exhibited a significant reduction in electrode impedance at 1 kHz to 45.73 kΩ on average demonstrating MWCNT ability to lower the impedance of the electrodes by roughening the electrode surface.

Keywords: Microfabrication, polyimide, flexibility, neural probes, electrochemical impedance spectroscopy.

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1 Introduction

Neuroelectronic devices used for the integration of neurons with electrodes in neurological studies have enabled a better understanding of the complex neurological processes in animals and in humans. Electroencephalography (EEG), electrocorticography (ECoG), local field potential (LFP) and single-unit recordings are the four main technologies employed to stimulate and record electrical signal from targeted neural tissues, and are particularly useful for elucidating the complex processes that contributes to the onset of neurodegenerative diseases[1,2]. However, these technologies suffer from a number of limitations such as relatively low resolution and are not suitable for use in recording brain activity from multiple sites deep within

the brain. The application of micro- and/ or nano-electromechanical systems (MEMs) or (NEMs) to the fabrication of LFPs or single-units recording electrodes have led to the development of minimally-invasive high density neuroelectronic devices that are designed to penetrate the pia and maintain intimate contact with neurons. Electrode characteristics such as size, electrical impedance, and the electrode's ability to achieve intimate contact with a neuron play a key role in differentiating LFPs from single-units recordings[3].

The current metal stereotrodes, tetrodes and microwire arrays employed are only capable of recording activity at their exposed distal tips and the number of recording electrodes that can be incorporated in these devices are limited[4]. A key challenge that remains to be addressed is the reduction in the probe size while maintaining a large density of recording electrodes in order to minimize tissue damage, scarring and device encapsulation. An advantage of using silicon based microelectronics and/ or MEMs based fabrication techniques is that it can effectively reduce the probe size and address the limitations of conventional metal microwire based neuroeletronic devices[5] in addition to the fact that it can be batch processed and yield reproducible planar or three-dimensional electrode geometries[6]. However, these silicon-based electrodes are also prone to host immune responses[7,8] that eventually cause the recording signal to degrade during the operation of the electrodes. Neuroelectronic devices based on polymers have been recently demonstrated to offer an alternative to silicon based devices due to their mechanical (flexibility) and chemical (biocompatible)[9] properties. These devices can easily conform to the surrounding brain tissue[10], thus minimizing inflammation due to micromotion and tissue damage and improve the device overall biocompatibility[11,12].

In order to acquire high quality signal when implanted, it is important that the impedance of the recording electrode is optimal for the recording and stimulation of brain cells or tissues.

Neuroelectronic devices that exhibit high electrode impedance increases the electrode noise profile, which further obscures recorded neuronal signals[13]. Therefore, it is important to employ neuroelectronic devices with electrode sites that have low electrical impedances and high signal-to-noise ratio to enable the acquisition of high quality recording signals from targeted neural cells or tissues. Xiang et al demonstrated the reduction of gold electrode impedance characteristics via the electrochemical deposition of multi-walled carbon nanotubes (MWCNTs)[14]. The deposited MWCNTs provided a roughened sensitive layer that have been shown to detect dopamine via cyclic voltametry[14,15] and improve the quality of neuronal cell to electrode adhesion[16].

In this paper, we took advantage of the flexibility and biocompatibility of polymers to design and fabricate polyimide based neuroelectronic device. Thin MWCNT coated gold pyramid electrodes were employed to reduce the electrode impedance. The detailed design, development and fabrication of such fully integrated neuroelectronic device is described and discussed.

2 Experimental Results and Discussion

2.1 Flexible Neuroelectronic Probe Design

The flexible polyimide neurotronic probes are designed to use silicon substrate to provide initial mechanical support, from which the flexible probe substrate is released and integrated with interconnect cable. The 64-site flexible multi-shank neuroelectronic probes are constructed by sandwiching the electrical interconnect traces in between two polyimide layers. These interconnect traces connect the small electrodes sites to the large bond pads and is made from chromium (Cr) thin film and gold (Au) thin film. The two polyimide layers consist of 1) an

insulating layer of HD-4104 (HD Microsystems, USA) polyimide (PI1) to structurally connect the electrodes sites and bond pads, but electrically isolate them and 2) a final passivation layer of HD-8820 polyimide (PI2) to serve as the final structural material and passivation for the interconnect traces. Figure 1 presents the probe architectural design where four shanks are protruding from the wider base platform. The multi-shank probe is made up of two metallization layers: the first metallization layer forms the exposed 64 electrode sites and bond pads and the second metallization carries the insulated interconnect traces. The metallization layers are separated by a thin PI1 film. This architecture enables the packing of 16 electrodes per shank. The shank width is 40 μm, widening to 250 μm at the base platform. The probe thickness is approximately 8 μm. The shank length is 3 mm and the shanks are spaced at 7750 μm with 16 electrode sites on each of shanks. The electrode sites have top area of 6 μm x 60 μm and thickness of 750 μm and distributed with 100 μm pitch. Additionally, the key design elements of the probe structure are: the fine tip pyramidal shaped electrodes, 30° tapered polyimide shanks for penetration into neural tissue, and the narrowly spaced gold interconnect traces.

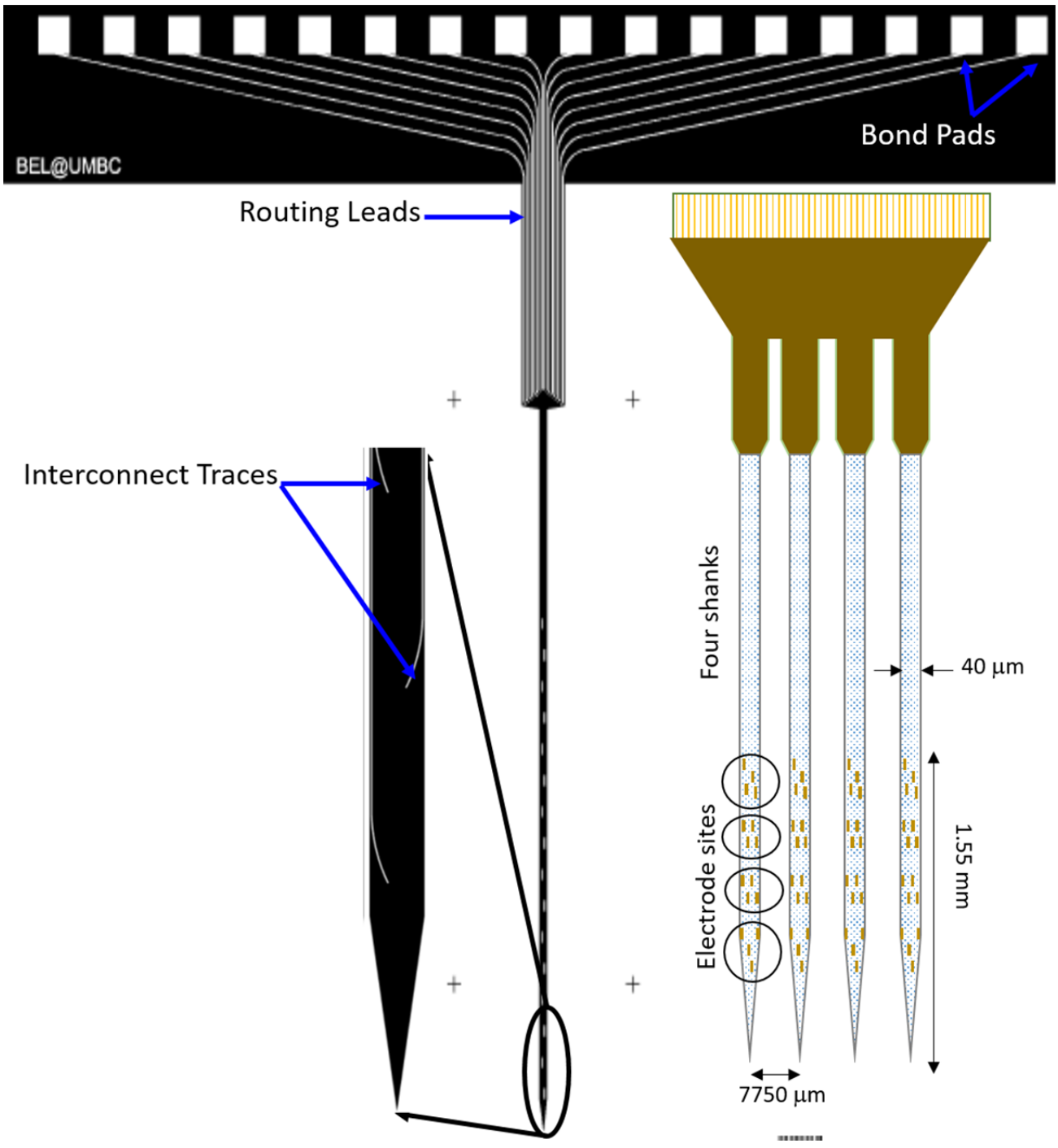

Figure 1. Schematic design of the flexible neuroelectronic probe structure and CAD layout showing the electrode sites, interconnect traces and bond pads.

2.2 High-Density Electrode and Probe Fabrication

A flexible gold rectangular pyramid neuroelectronic probe platform is fabricated using flexible biocompatible polyimide[17]. Figure 2 illustrates the fabrication sequence employed to translate the gold pyramid electrodes into a flexible multi-shank neural probe in a cross-sectional view. Five photolithographic masks are used to fabricate the probes on a 4-inch silicon wafer. The p-type (100) silicon wafer is purchased from WRS Materials. The electrodes contain two metallization layers. The first metallization forms the gold pyramid recording electrodes and bond pads and the second metallization defines the interconnection traces. Polyimide (HD-4104) is used as the insulation layer for the electric interconnection traces on the front side and are necessary to block ionic current flow due to HD-4104 high electrical resistivity ($\sim 10^{16}$ Ωcm)[18,19]. Both negative (HD-4104) and positive (HD-8820) polyimide are used as the dielectric and structural material respectively for the probe manufacturing because together they provide better mechanical stiffness and flexibility for probing neurons.

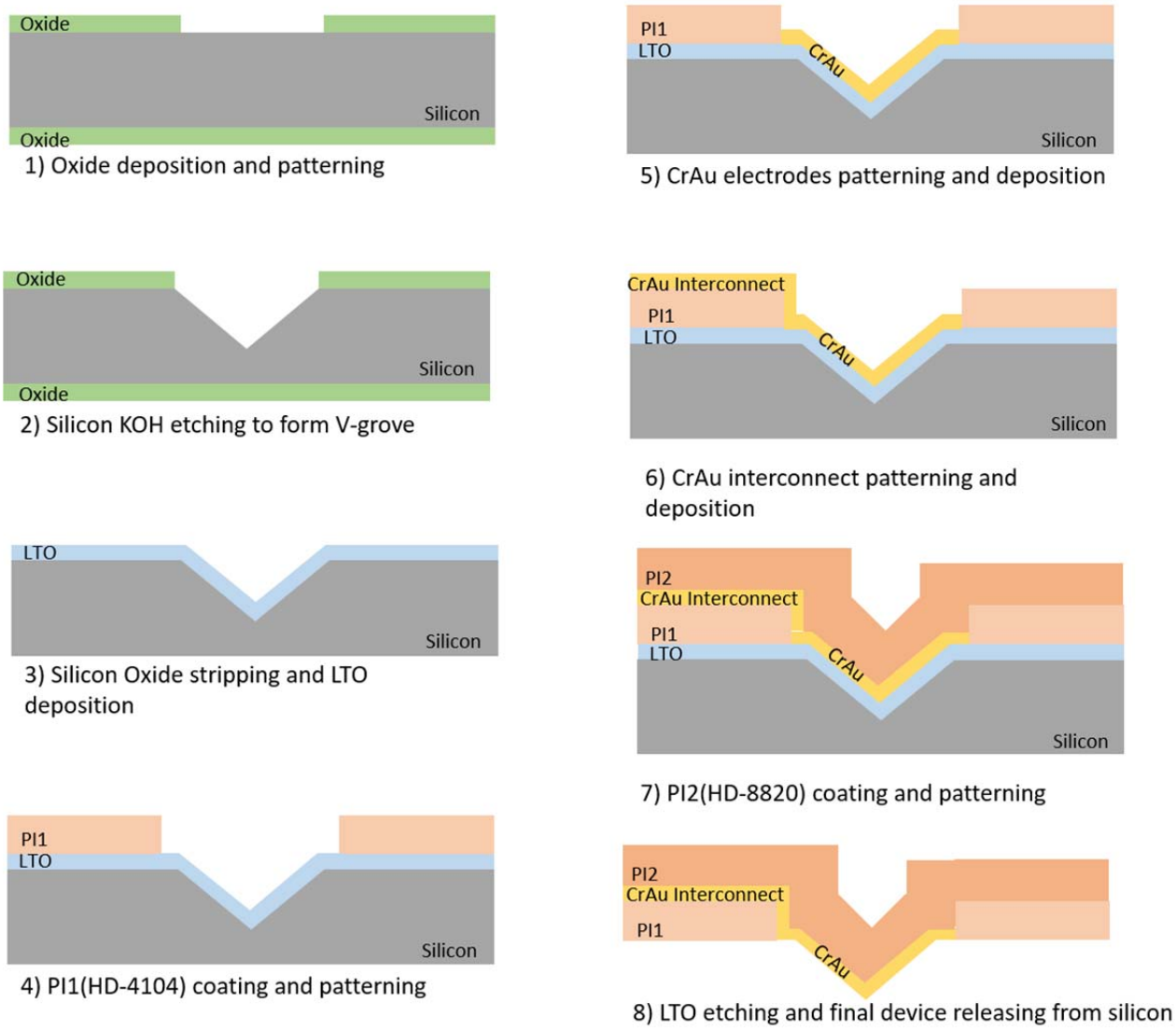

Figure 2. Schematic illustration of the major processing steps in the fabrication of the 64-site probe.

A 200 nm thermal oxide is grown on the silicon wafer to serve as a mask for anisotropic etching of silicon using potassium hydroxide (KOH). Photoresist patterning (standard S-1813 recipe using MA6/MA8 mask aligner) is employed to create a mask for etching the SiO_2 with buffer oxide etchant. The silicon is then etched with KOH to form the inverted rectangular pyramid cavity to enable the molding of the gold rectangular electrode sites inside the inverted pyramid cavity. Upon stripping the SiO_2 layer, a blanket 600 nm LTO is deposited and serves as the

sacrificial layer for final release of the probe. HD-4104 is photolithographically patterned on the silicon substrate to expose the inverted pyramid cavity and to define the bond pads as well as serve as the insulation layer for the second metallization layer. After curing the polyimide, the polyimide film measures approximately 2-4 μm thick depending of the curing processing details. NR9-6000PY is photolithograpically patterned on top of the polyimide to expose the electrodes and associated bond pads. The first metallization layer composed of 20 nm chromium and 750 nm is then deposited. The chromium layer is designed to provide adhesion between gold and LTO. The gold electrodes and associated bond pads are e-beam evaporated to a thickness of 750 nm from a 99.99% pure gold target. Gold (Au) is selected as the electrode material due to its chemical inertness, and compatibility with brain tissue[20,21]. The second metallization layer of Cr/Au (20 nm/ 250 nm) is e-beam evaporated and designed for the interconnection traces. The interconnect traces are photoresist patterned and etched via ion milling to connect the electrode sites to the bond pads. After interconnect traces fully patterned, a second polyimide layer HD-8820 is spin coated, patterned to define the outer geometry of the devices and insulate the interconnect traces as well as serve as the structural material. This is then followed by the complete etching of the 600 nm LTO layer in buffer oxide etchant for the final release of the flexible neuroelectronic probe. The chrome surfaces on the electrode sites and bond pads are then removed by carefully dipping the probe in a chromium etchant solution while monitoring the etch process under a microscope. The chromium etched probes are cleaned with Isopropanol and DI water.

2.3 Process development and integration challenges

The polyimide based neuroelectronic probe fabrication was carried out on a 4-inch silicon substrates. Polyimide serves as structural, insulating, and passivating layers for the device. Both

144 negative and positive polyimides selected provide mechanical flexibility, chemical stability, and
145 biocompatibility. In addition, they both exhibit the lowest moisture uptake of 0.5% and are
146 expected to provide excellent biostability by minimizing possible failure due to moisture
147 absorption. As for the metallization layers, gold was chosen for its biocompatibility and process
148 compatibility. The characteristic pyramid profile of the electrode was achieved via anisotropic
149 etching of 5 μm x 50 μm features patterned on the silicon wafer with KOH. The bias introduced
150 by KOH in these features and the alignment marks resulted in several process challenges
151 downstream, wherein subsequent features were not perfectly aligned. To resolve this challenge,
152 it was important that the mask used (Step 1; Figure 2) was aligned flush with the wafer during
153 UV exposure to ensure minimum KOH bias. Additionally, the first polyimide layer PI1 (Step 4;
154 Figure 2) was designed to create a larger 6 μm x 60 μm openings to account for this bias in the
155 electrode features and any undercutting that may occur during the wet-chemical etch process.
156 The 10 μm routing leads, bond pads and electrode sites were formed on a single metallization
157 layer (Step 5; Figure 2). However, the wet etching of Cr/Au resulted in an interface-activated
158 undercutting of the resist film and openings between some of the routing leads and the bond
159 pads. Although the use of 10 μm routing leads with a wider opening toward the bond pads were
160 found to eliminate the openings observed between these features, the electrode site features were
161 still defective. To circumvent this problem, we employed e-beam lift-off process using negative
162 resist to eliminate the undercut problem.

163 Moreover, the thick polyimide/metal stack posed challenge for process integration. In
164 order to ensure continuous electrical flow between the pyramid gold electrode and bond pad,
165 blanket Cr/Au deposition follow by ion milling was developed over the thick polyimide to form
166 the interconnect traces (Step 6; Figure 2). The interconnect traces were designed to overlap the

10 μm routing leads and the electrode sites. During the initial ion milling process development, complete etching of the Cr/Au was not achieved, thereby impacting the functionality of the final device. A descum step using reactive ion etching (RIE) was adopted to remove any residual photoresist thus enable the Cr/Au to be fully etched. As a result, the ion milling process produced interconnect traces with a width and spacing as narrow as 1 μm on certain portions of the shank. Final device was formed by releasing shanks from the silicon substrate using buffer oxide etching. The final shank formed has thickness of 8 μm and width of 40 μm. These shanks are tapered at angle of 30° and exhibit flexible properties. Thereby, flexible gold pyramid electrode probes with a Young's Modulus of 8.5 GPa are realized. The flexibility afforded by the probe enables the shanks to bend when in contact with neural tissue, thus minimizing neural tissue damage.

Scanning electron microscopy (SEM) micrographs of the 16-site electrodes per shank are shown in Figure 3. A shank width of approximately 40 μm accommodates16 channels. The thickness of the shank varied from 6-10 μm. The shank length of 3 mm is necessary to allow access to specific target of neural clusters within the brain tissue. The probe tip has a sharp angle of 30° to enable easy penetration where the insertion force is concentrated at the end of the probe. The shanks are placed 7750 μm apart and all the electrode sites are positioned within a 1.55 mm vertical coverage in order to increase the probability of recording neural signals from multi-target neural clusters. The insert of Figure 3 depicts a close up view of the tip of the shank and subsequently the electrode site, rectangular pyramid structure. This pyramidal structure increases the conductive surface available for signal acquisition similar to that observed for nano-composite surfaces [13].

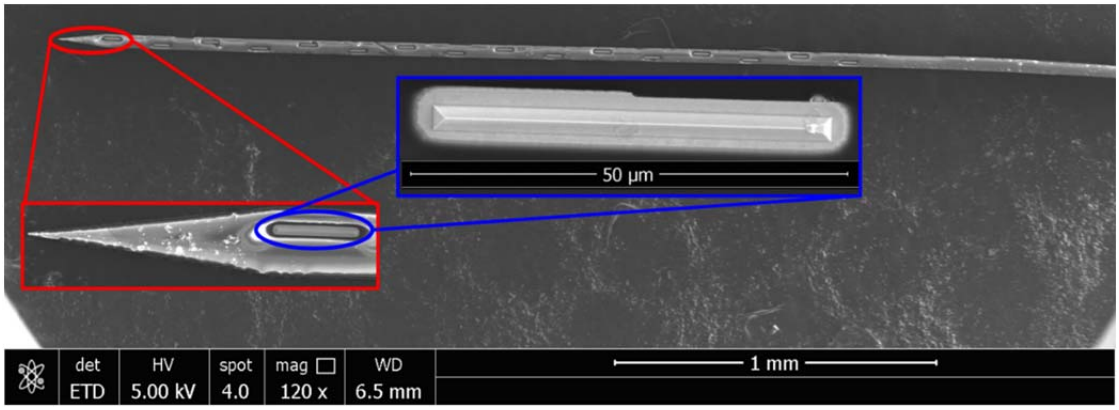

Figure 3. SEM micrographs of neuroelectronic probe shank with 16 recording electrode sites and submicron interconnect traces sandwiched between two polyimide layers and insert views of shank tip and rectangular pyramid shaped electrode.

The probes that are acceptable for testing are identified by visual inspection under a microscope, and by electrochemical impedance spectroscopy (EIS) to assure electrical isolation of the electrode sites. Optical images of the fabricated probes are shown in Figure 4. To isolate the interconnect traces of the device from the aqueous environment, the traces were sandwiched between two biocompatible polyimide layers with low liquid permeability. The polyimide layers show very good adhesion. No visible delamination or defect due to adhesion is found between the first polyimide (HD-4104) layer and the second polyimide (HD-8820) layer, nor between the two polyimide layers and the gold electrode sites, interconnect traces and bond pads. The present yield indicates that about 90% of the fabricated probes pass these initial tests and can be suitable for impedance characterization and neural recording. As shown in Figure 4, the surface of the gold interconnect traces and electrode sites are smooth and reflective, whereas the polyimide surface appears dark due to light absorption by the polymer resin.

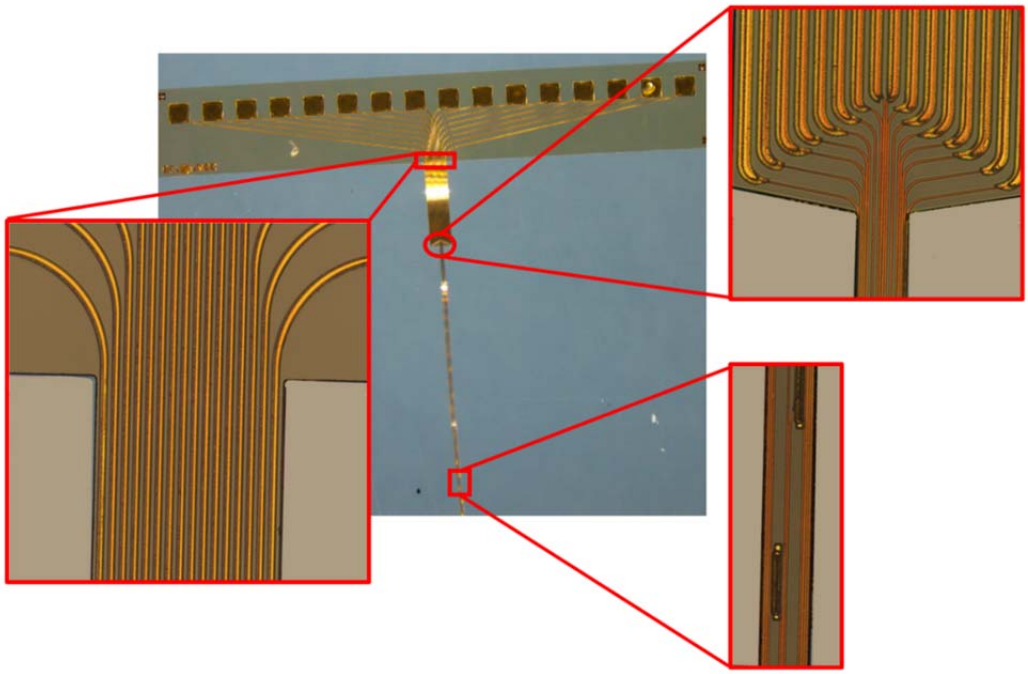

Figure 4. Flexible and optically transparent polyimide neuroelectronic probe accommodates associated bond pads, interconnect traces 10 µm to 1 µm in two distinct metallization layers, and the traces are connected to the electrode sites.

2.4 Device Packaging

The optical image in Figure 5 displays a clear view of the fabricated interconnects, bonding pads and electrode sites on a single shank equipped with 16 gold recording electrode sites. For ease of interfacing the flexible polyimide neuroelectronic probe to the measurement equipment, a printed circuit board (PCB) consisting of interconnect lines is fabricated and connected to the probe contact pads via tungsten wires ($\phi \approx 200$ µm). The tungsten wires were manually affixed with conductive silver wire glue to the bonding pads in order to create a secure electrical connection. Finally, a group of jumper wires were soldered to the distal end of the PCB for further wire extension.

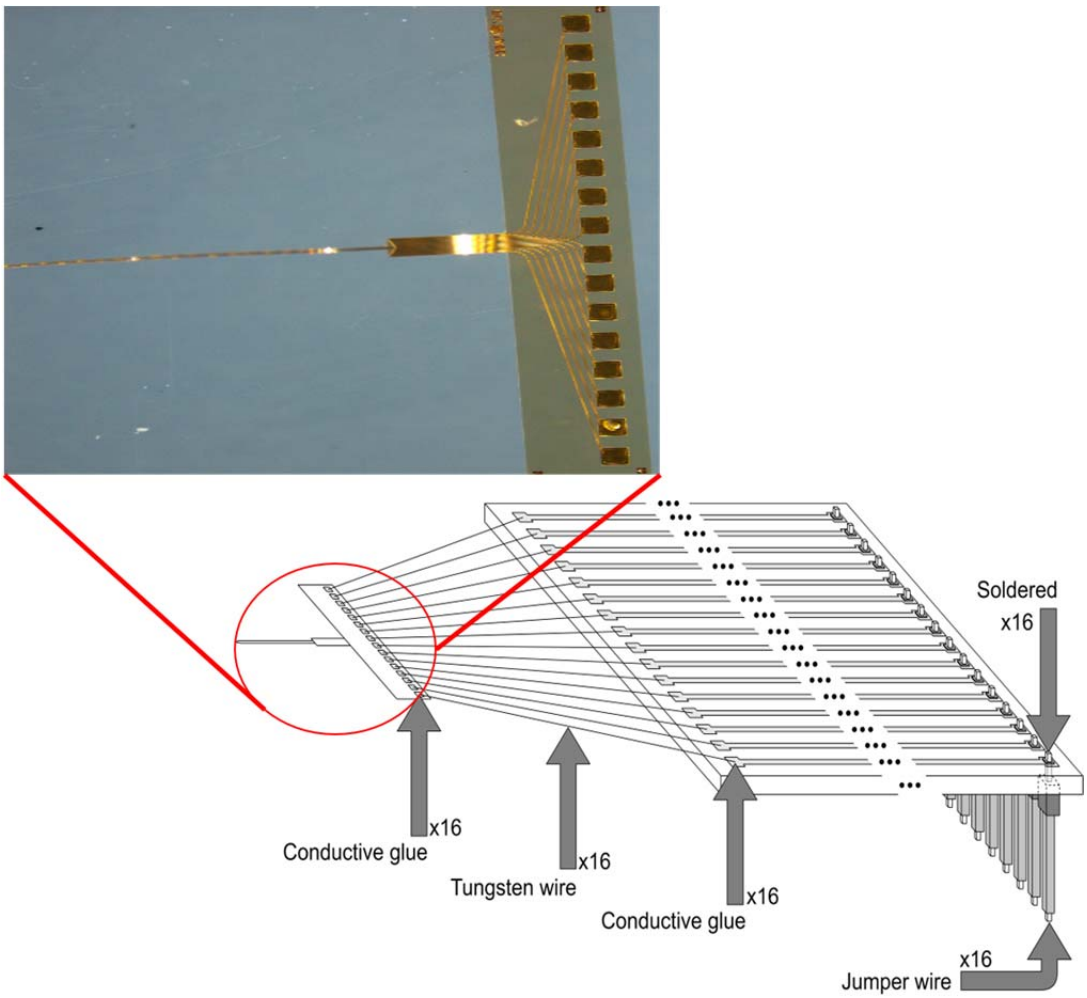

Figure 5: Flexible and optically transparent polyimide neural probe packaging.

2.6 Electrochemical Impedance Spectroscopy

The shank of probe was mounted in a test fixture and the probe was then immersed beyond the uppermost electrode site in a phosphate buffer saline (PBS) to mimic the physiologic environment at 37 °C and pH 7.4. The EIS experiment was performed with a potentiostat PGSTAT204, Metrohm Autolab to determine the electrode site impedance before and after MWCNT deposition. A three-electrode cell configuration with a Ag/AgCl electrode as the reference electrode and platinum electrode as the counter electrode was used. The probe was left in solution for 45 minutes before acquiring each impedance recording in triplicates. The

electrochemical impedance measurements were taken with a frequency range between 0.1 Hz – 10 kHz using a 10 mV peak-to-peak waveforms in order to identify stabilized probe site impedances. The electrode impedance was observed to be on average approximately 135 kΩ (n = 24) at 1 kHz. In addition, the impedance was observed to gradually increases with decreasing frequency. The impedance values obtained for the gold electrode sites are attributed to the pyramidal geometry of the recording site electrode. The impedance value is well below most values reported for non-surface treated neural probes[22]. Moreover, observed failed sites (impedance out of range) are usually due to open interconnect traces or over etched traces. Post failure SEM micrograph of probes appear to indicate open interconnect traces caused by fabrication as the major cause for the failed sites.

2.5 Multi-walled carbon nanotube (MWCNT) deposition

The gold recording pyramid electrode surfaces were roughened with MWCNT in order to increase the electrocatalytic surface area for cell adhesion and sensing, in addition to lowering the overall electrode impedance. MWCNTs concentration of 1mg/mL was prepared using gold sulfite electrolyte solution. The prepared solution was sonicated for 1 hour prior to electrochemical deposition. The probe shank was assembled in a test fixture and to isolate the gold bond pads of the device from the liquid test fixture environment, the tungsten wires and the upper section of the probe were encapsulated with a biocompatible epoxy low water permeability. MWCNT were deposited on six electrodes subsequently using each of the recording electrodes as the cathode. A platinum wire electrode was used as the anode. The anode and cathode were then connected to a function generator (Agilent 33250A). A monophasic voltage pulse of 1.2 V, 10 Hz, at 50% duty cycle was applied for 1 minute. After the deposition cycles, multiple layers of MWCNTs with gold nanoparticles were deposited on each of the gold

recording electrode sites on the shank. The optical images of the flexible polyimide probe shank tip pre and post-MWCNT deposition are shown in Figure 6. The surface of the rectangular gold electrode appears smooth and reflective, whereas the MWCNTs coated electrode surface appeared rough and dark.

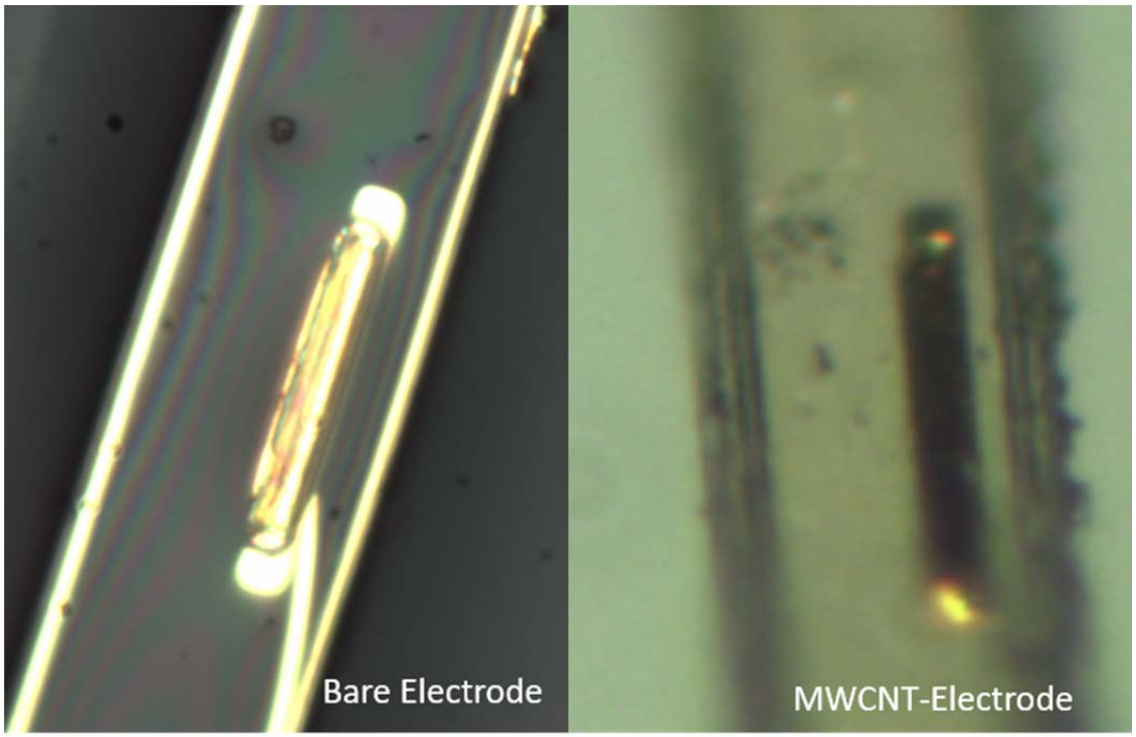

Figure 6: Recording electrode site before (left) and after (right) MWCNT deposition.

Figure 7 shows the comparison of the electrode impedance before and after MWCNT deposition. The relatively large impedance value of 17.16 MΩ at 1 kHz on average is attributed to the electrode area being covered by a small amount of the biocompatible epoxy used to affix the flexible probe shank to the borosilicate glass during the construction of the test fixture chamber. The 60 seconds long deposition of MWCNTs resulted in a significant decrease in the overall impedance. The average impedance at 1 kHz after MWCNT deposition was 45.73 kΩ. Clearly, the MWCNTs contribute to the decrease of the electrodes electrical impedance. Thereby

resulting in an enhancement of charge storage capability[23]. The observed average impedance after MWCNT deposition is an acceptable impedance value for electrochemical sensing of dopamine[14].

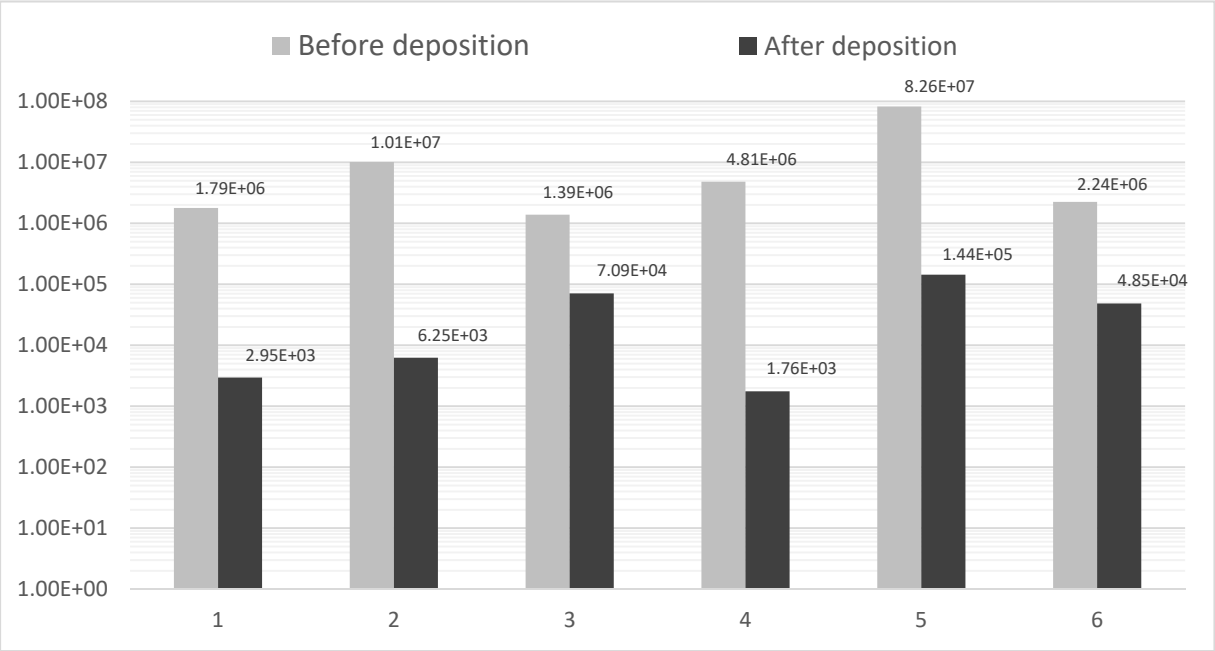

Figure 7. EIS measurement of six electrodes on a single probe shank before and after MWCNT deposition on a logarithmic scale.

This work is the first to demonstrate the use of standard microfabrication processes to fabricate multi-site neural probes with polyimide as supporting/structural and insulating/protective layers. Polyimide is an excellent alternative because it exhibits high electrical resistivity, mechanical flexibility, and biocompatibility properties. In addition, polyimide is known to not hydrate over time, which will eventually improve the probes' usefulness for chronic neural recording. The flexible neuroelectronic probe as described herein contains two polyimide layers as the insulting and structural material. The probe is approximately 8 μm thick and contains 64 pyramidal shaped electrode sites. The device was successfully integrated and the process development challenges were overcome by employing lift-off process to eliminate metal undercut, ion milling process to

create good step coverage of Cr/Au layer over the thick polyimide, and RIE descum process to remove resist residual and resolve thin interconnect traces. The polyimide probe structure is fabricated using standard microfabrication technology and does not require advanced CMOS processing techniques. The flexibility afforded by the probe should increase the ruggedness of the probe in various chronic neural recording applications. Additionally, we successfully demonstrated the reduction of the gold recording electrodes' impedance via the electrochemical deposition of MWCNTs. The observed impedance values at physiologically relevant frequency 1 kHz were on average 45.73 kΩ), which is suitable for electrochemical sensing.

Disclosures

The authors have no conflicts of interest.

Acknowledgments

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Biographies and photographs for the other authors are not available.

Caption List

Fig. 1 Schematic design of the flexible neuroelectronic probe structure and CAD layout showing the electrode sites, interconnect traces and bond pads.

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Fig. 3 SEM micrographs of neuroelectronic probe shank with 16 recording electrode sites and submicron interconnect traces sandwiched between two polyimide layers and insert views of shank tip and rectangular pyramid shaped electrode.

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Fig. 5 Flexible and optically transparent polyimide neural probe packaging..

Fig. 6 Recording electrode site before (left) and after (right) MWCNT deposition.

Fig. 7 EIS measurement of six electrodes on a single probe shank before and after MWCNT deposition on a logarithmic scale.

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