31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Titanium-Based Multi-Channel, Micro-Electrode Array for Recording Neural Signals

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Abstract— **Micro-scale brain-machine interface (BMI) devices have provided an opportunity for direct probing of neural function and have also shown significant promise for restoring neurological functions lost to stroke, injury, or disease. However, the eventual clinical translation of such devices may be hampered by limitations associated with the materials commonly used for their fabrication, e.g. brittleness of silicon, insufficient rigidity of polymeric devices, and unproven chronic biocompatibility of both. Herein, we report, for the first time, the development of titanium-based "Michigan" type multi-channel, microelectrode arrays that seek to address these limitations. Titanium provides unique properties of immediate relevance to microelectrode arrays, such as high toughness, moderate modulus, and excellent biocompatibility, which may enhance structural reliability, safety, and chronic recording reliability. Realization of these devices is enabled by recently developed techniques which provide the opportunity for fabrication of high aspect ratio micromechanical structures in bulk titanium substrates. Details regarding the design, fabrication, and characterization of these devices for eventual use in rat auditory cortex and thalamus recordings are presented, as are preliminary results.**

I. Introduction

MULTI-CHANNEL, micro-electrode arrays, also referred to as neural probes, are brain-machine interfaces (BMI) used to record from or stimulate neurons. BMIs have contributed a great deal to the understanding of the nervous system. In particular, multi-channel, micro-electrode arrays have proven to be critical in better understanding the relationship between brain cells and other neural networks by providing simultaneous recording of several sites of neurons [1-2]. Recent studies have also shown the potential of BMIs for restoration of neurological functions lost to stroke, injury, and disease [3].

However, despite this promise, clinical translation of such devices may be hampered by the inherent limitations associated with the materials used in their fabrication. Owing to the reliance upon fabrication techniques adopted from the semiconductor industry, most microelectrode array devices developed thus far have been fabricated using silicon as a structural backbone [1,4-5]. While use of silicon provides opportunity for monolithic integration of signal processing circuitry [6], its intrinsic brittleness limits structural reliability and compromises safety, due to potential for catastrophic fracture and fragmentation [7]. The large modulus mismatch between silicon and neural tissues may also promote glial encapsulation of the device, thus reducing chronic recording reliability [7-8]. Finally, its biocompatibility in chronic neurological implant applications is still unproven.

More recently, efforts targeted towards addressing the brittleness of silicon have explored use of polymeric materials, such as SU-8, parylene, and polyimide [9-11]. While these offer significant improvement in toughness relative to silicon, their low moduli do not provide sufficient stiffness for reliable insertion and/or positioning of recording sites within the vicinity of neurons of interest [11]. Efforts have been made to improve the stiffness of polymeric devices, but often at the expense of added complexity, which can complicate fabrication and use [9-10]. Finally, the long-term biocompatibility of these polymeric materials in neural implantation is still unproven as well.

In order to develop a neural probe that has the stiffness needed for successful insertion, as well as the toughness to avoid fracture, we have undertaken the development of titanium-based BMI devices. This effort is fundamentally enabled by recently developed techniques that allow, for the first time, fabrication of high aspect ratio micromechanical devices within bulk titanium substrates [12]. Titanium's intrinsic toughness provides opportunity for mechanically robust probes that fail gracefully (i.e. by plastic deformation) rather than catastrophically (i.e. by fracture), thus enhancing safety by preventing fragmentation. Moreover, while titanium's modulus is greater than polymeric materials used thus far, its moderate modulus relative to silicon could possibly reduce potential for gliosis, due to decreased modulus mismatch with cortical tissues, while still enabling reliable insertion. Finally, titanium's

Manuscript received April 7, 2009. This work was supported by a Cordier Fellowship, the Purdue Research Foundation, and Showalter Research Trust, Purdue University.

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The authors would like to thank the Center for Neural Communication Technology for providing the silicon microelectrode arrays (NIH/NIBIB P41-EB002030)

well-proven biocompatibility in various other chronic implantation applications (e.g. cardiac pacemakers, orthopedic implants, dental implants, etc.) suggests similar potential for success in neurological applications although thorough evaluation will be required to verify this, due to the unique needs and constraints of neural recording and stimulation.

II. Design and Fabrication

A. Design

The neural probes produced in this effort were designed to study the auditory responses within a rat model. As such, short probe lengths (2 mm) were fabricated to record electrical signals in the auditory cortex. Longer probes (4.9 & 5.4 mm) were also designed to penetrate into the auditory thalamus. To date, study of the auditory thalamus has been hampered by the brittleness of silicon-based probes, which are more prone to buckling-induced fracture, due to the added length required to access these deep structures [13]. Both device types were modeled on commercially-available "Michigan" type electrode arrays (e.g. A1 x 16 – 5 mm 100 - 413, NeuroNexus Technologies, USA; Shank Length – 5 mm, Recording Site Diameter – 23 μm, Recording Site Pitch – 100 μm) [14].

Each titanium device contained 16 independently addressable circular recording sites, and 18 distinct design variants were developed with differing shank length (2, 4.9, & 5.4 mm) recording site diameter (23 & 40 μm), and pitch (50, 75, 100, & 150 μm). Since optimal designs for the intended applications have yet to be defined, the given variation of the latter two parameters was reflective of the desire to eventually determine the most favorable combination of recording site size and pitch that ensures consistent sampling of discrete neurons with high signal to noise ratio.

Figure 1 shows a schematic representation of one of the multi-electrode array device design variants developed in this effort. In all devices, recording sites were connected by 5 μm wide traces (with 9 μm pitch) to remote 100 μm x 100 μm contact pads (with 150 μm pitch) arrayed at the distal end of the device. In devices with 23 μm diameter recording sites, this resulted in shanks with width that tapered from 48 μm at the recording site closest to the proximal end of the device (i.e. near the sharp tip) to 192 μm at the base. In the 40 μm diameter recording site devices, shank width ranged from 65 – 209 μm.

B. Fabrication

The titanium-based microelectrode arrays were fabricated from 25 μm thick Ti foil substrates (Gr 1 Ti, 99.7% Ti, Fine Metals Corp, USA). The as-received foils were first solvent cleaned by ultrasonic agitation in acetone and isopropanol, respectively, followed by DI rinsing and N_2 drying. Next, as shown in Fig. 2, the first 0.6 μm SiO_2 dielectric layer was deposited by plasma-enhanced chemical vapor deposition (PECVD) to insulate the subsequent electrical structures from the substrate (Benchmark 800 CVD, Axic Inc, USA; Process conditions SiO_2: Pressure - 230 mT, RF Power - 26

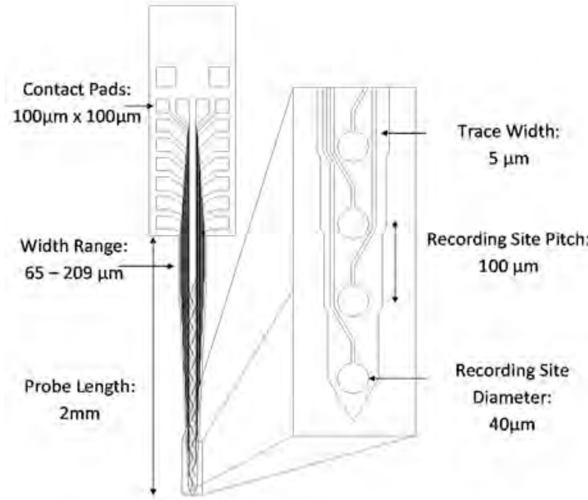

Fig. 1. Schematic representation of a typical titanium-based microelectrode array device.

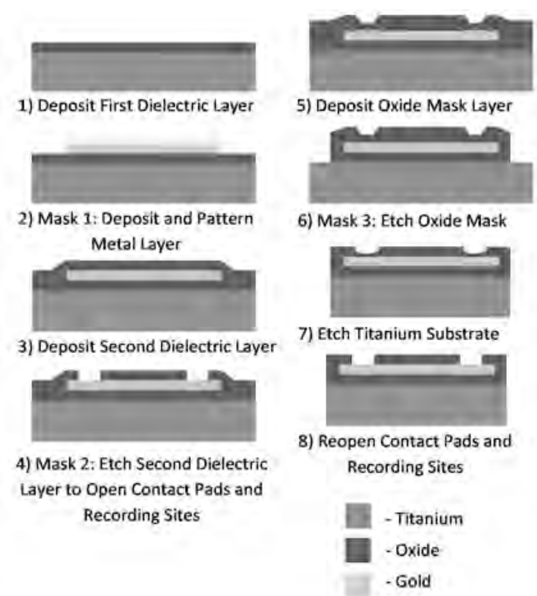

Fig. 2. Process flow for titanium-based neural probes.

W, 200 sccm N_2O, 35 sccm 5% SiH_4, Temp – 300 ^oC). The substrates were then subjected to solvent cleaning, and mounted to 100 mm Si carrier wafers with thermally conductive adhesive tape (9882, 3M Electronics, USA). Recording sites, traces, and contact pads were then patterned via standard photolithographic liftoff techniques with electron beam depositions of 20 nm Ti/500 nm Au (CHA SE-600, CHA Industries, USA; Process conditions Ti: 1.0 x 10^{-6} T, 1 Å/s; Process conditions Au: 1.0 x 10^{-6} T, 1 Å/s).

Following metal deposition, the samples were soaked in acetone to release the Ti foils and then solvent cleaned. The second dielectric layer, composed of 0.2 μm Si_3N_4 followed by 0.8 μm of SiO_2, was then deposited by PECVD to provide insulation from the surrounding environment (Process conditions Si_3N_4: Pressure - 400 mT, RF Power - 100 W, 100 sccm NH_3, 120 sccm 5 % SiH_4, Temp – 300 ^oC). This dual layer stack was chosen to promote adhesion to the underlying Au patterns and minimize stress-induced curvature of the devices arising from intrinsic stresses and thermal expansion mismatch between the deposited film and the underlying Ti substrate.

After completion of the second dielectric layer deposition, the Ti foils were again mounted to 100 mm carrier wafers with thermally conductive tape. The contact and recording site windows were then opened via photolithographic patterning and dry etching of the second dielectric layer (E620 R&D, Panasonic Factory Solutions, Japan: Process conditions: Pressure – 1.00 Pa, RF Source Fwd Power – 500 W, RF Bias Fwd Power – 400 W, 40.0 sccm CHF_3). The photoresist was then stripped and the samples soaked in acetone to release the Ti foils from the carriers.

The third dielectric layer, composed of 0.2 μm Si_3N_4 and 2.75 μm SiO_2, was then deposited by PECVD to serve as an etch mask for the subsequent deep etch of the underlying Ti substrate. The samples were re-mounted to carrier wafers, and the shank profiles were patterned and transferred into the third dielectric layer via dry etching (Process conditions: Pressure – 0.25 Pa, RF Source Fwd Power – 900 W, RF Bias Fwd Power – 200 W, 40.0 sccm CHF_3). The photoresist was then stripped and the shank profiles were transferred through the underlying Ti substrate using the Titanium Inductively Coupled Plasma Deep Etch (TIDE) process (Process conditions: Pressure – 2.0 Pa, RF Source Fwd Power – 400 W, RF Bias Fwd Power – 100 W, 100 sccm Cl_2, 5 sccm Ar). The samples were then subjected to a final short dry etch to remove the remaining thin dielectric layer protecting the contact pads and recording sites, and released from the carrier by soaking in acetone. An SEM image of a typical titanium probe is shown in Fig. 3. The smooth vertical sidewalls resulting from the TIDE process are clearly evident, as is the integrity of the dielectric and metal layers deposited on the titanium substrate.

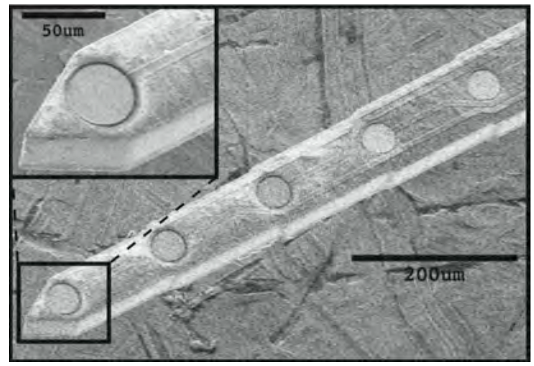

Fig. 3. SEM image of Titanium probes.

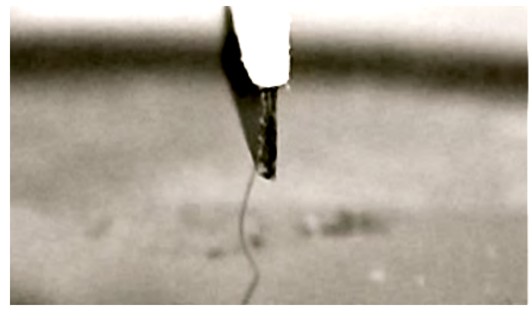
Fig. 4. Elastic buckling of 5.4 mm titanium probe under uniaxial compression.

III. Device Testing Procedures

A. Mechanical Testing

Buckling and failure forces were measured for 2 mm and 5.4 mm length titanium probes with width range of 65 – 209 μm. Also tested were 5 mm commercially-available silicon probes with 15 μm thickness, width range of 33 – 200 μm, and half elliptical cross-sectional shapes. Forces exerted by the tips of the probes during longitudinal uniaxial compression were recorded using a microbalance (AB54-S/FACT, Mettler Toledo, USA) [11]. The probes were mounted to a silicon carrier chip using cyanoacrylate adhesive (Pacer Technology, USA). The mounted probes were then attached to a micromanipulator (M3301R, World Precision Instruments Inc., USA), which was used to manually load the probe tips against the microbalance scale, as seen in Fig. 4. The probes were carefully observed for buckling and fracture via a CCD with magnifying optics.

B. *In vitro* Electrical Testing

Electrochemical impedance spectroscopy (EIS) and cyclic voltammetry (CV) measurements were collected for the titanium-based neural probes using an Autolab potentiostat PGSTAT12 (EcoChemie, Utrecht, The Netherlands) and frequency analyzer (Brinkmann, Westbury, NY) [15]. Titanium probes (both 2 & 5.4 mm length) with recording site diameters of 40 μm were bonded to printed circuit boards (a1x16, NeuroNexus Technologies, USA) via cyanoacrylate adhesive. The probes were gold wire-bonded to the printed circuit boards (PCBs) using a manually-operated wire bonder (7400A, West-Bond, USA). *In vitro* testing was performed utilizing a three-electrode setup. A calomel electrode (Fisher Scientific, Waltham, MA) was used as the reference electrode with a platinum wire as the counter electrode. Measurements were taken in 1X Phosphate Buffered Saline (PBS) at room temperature within an electrically-isolated copper mesh “Faraday” cage. A 25 mV RMA sine wave was applied to electrode sites for EIS tests with frequencies ranging logarithmically from 0.1 to 10 kHz. CV testing was performed using a linear voltage sweep from -0.2 V to 0.75 V with a scanning rate of 50 mV/s.

IV. Results & Discussion

Measured elastic buckling loads for the titanium probes varied from 39.7 to 60.8 mN for 5.4 & 2 mm length probes, respectively, while subsequent failure via gross plastic deformation was observed at loads as high as 84.3 mN. Measured elastic buckling loads for the commercially-available silicon probes varied from 1.96 mN to 3.33 mN, and subsequent failure by fracture occurred at loads as high as 3.92 mN. Although the titanium probes demonstrated greater load bearing capability than silicon probes of similar length (due to greater cross section moment of inertia), both Ti and Si probes demonstrated sufficient buckling strength to withstand the ~1 mN insertion forces reportedly required for insertion into rat cortex [16]. However, the wedge-like

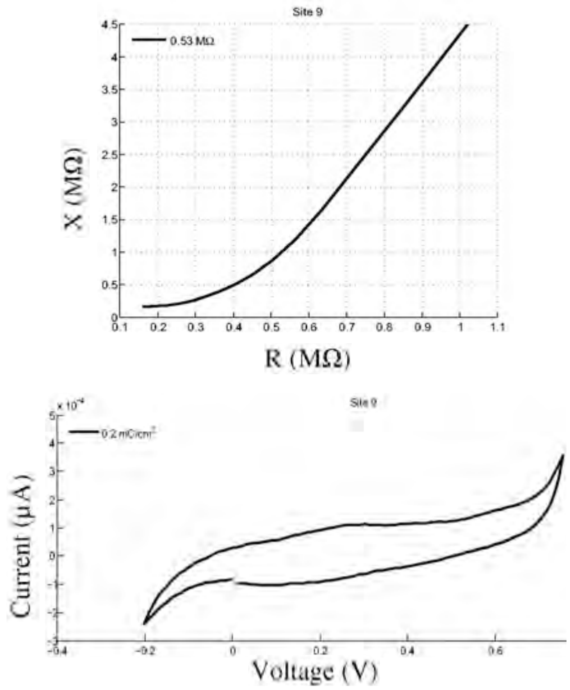

Fig. 5. EIS and CV plots for a 5.4 mm titanium probe with 40 μm diameter recording sites tested in 1x PBS at room temperature.

tip geometry of the current Ti probes may require greater insertion forces and produce greater trauma, thus motivating future efforts to develop probes with sharper pointed tips. Nevertheless, the current test data clearly demonstrate the potential for greater mechanical reliability and safety of the Ti probes, since graceful, plasticity-based failure minimizes the potential for catastrophic fragmentation observed in the Si probes.

Measured EIS results for the Ti probes indicated impedance values between 0.27 and 0.79 MΩ at 1 kHz frequency, while CV tests revealed maximum current carrying capacities ranging from 0.1 to 0.2 mC/cm^2. Fig. 5 displays the resulting plots for a typical recording site. Commercially-available silicon probes have an impedance range of 0.5 – 3.0 MΩ depending on the recording site diameter (NeuroNexus Technologies, USA). Since our recording site areas are large, our impedance values look very promising. Also, current literature suggests that the charge carrying capacities of our gold receptor sites are within reason [17]. It is important to note, however, that many recording sites on the Ti probes were observed to be non-functional, thus further efforts are needed to refine the fabrication processes to produce devices with greater recording site yield. Finally, while the current device fabrication process is reliant upon capital-intensive infrastructure, the inherent scalability provided by this infrastructure suggests the opportunity for eventual transition to high-volume/low-cost manufacturing.

V. Conclusion

Initial results from the design, fabrication, and testing of titanium-based "Michigan" type multi-channel, micro-electrode array BMIs have been presented for the first time. Mechanical testing results demonstrate potential for greater mechanical reliability and safety of these probes relative to current commercially-available silicon probes. *In vitro* electrical testing results demonstrate adequate functionality, but also highlight continuing need for fabrication process optimization to improve device yield and performance.

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