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Improving Mechanical Stiffness of Coated Benzocyclobutene (BCB) Based Neural Implant

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Abstract— **We briefly report recent results of a simple alternate method to improve mechanical stiffness of BCB polymer neural implant for surgical insertion into brain tissue, which uses coatings dissolvable in bio-fluids. We have studied three different coating materials such as thermo-reversible gel Poloxamer 407, glucose ($C_6H_{12}O_6$) and regular table sugar that were applied by dip coating onto the implant surface. The preliminary results of this study have shown that coating BCB probes with Poloxamer 407 polymer, a thermo-reversible gel, or table sugar significantly improves the buckling strength. However, the table sugar coating provides the greatest increase in stiffness, which is sufficient to penetrate both the preserved and live brain tissues without buckling.**

Keywords—**flexible polymer electrodes, neural implant, bioactive coating, surgical technique, neuroprostheses**

I. Introduction

Advancements in neural interfacing technology have increased our understanding into the operation of neural circuits by providing simultaneous recording from large numbers of neurons. Amongst all the different materials investigated, silicon has been the most interesting and widely used material for neural interfacing. There have been successful applications in chronic recording of cortical signals in rats and primates from some laboratories. However, the stable and long-term performance of silicon based neural interface devices has been limited due to the inability to effectively and chronically interface them with the neurons of the brain. After a few weeks, the probe to tissue electrical resistance typically increases to levels that reduce effectiveness of the devices, and conventional histology shows a compact cellular sheath surrounding the insertion site [1]. Polymers, which are flexible and have comparable young's modulus with brain tissues, provide conformal coverage when placed on curved surfaces and therefore are less likely to induce adverse tissue reaction at the neuron electrode interface. The polymer flexibility is highly desirable to minimize tissue damage at the brain-tissue/implant interface and various surface modifications can also be applied to improve biocompatibility. Another advantage is the ease for surface modification on polymer materials.

Researchers at Arizona State University reported the first successful fabrication of a polyimide-based flexible multi-channel neural interface and recorded the neural activities from the barrel cortex of a rat's brain [2]. Recently, we have shown the first successful fabrication [3] and neural recording capability of Benzocyclobutene (BCB) polymer based neural interface [4].

BCB is a new class of polymer developed by Dow under the trade name Cyclotene™ with unique properties that we believe is suitable for chronic implant application if proven long-term biocompatibility. A serious drawback with polymer based neural interfaces is: they have virtually no mechanical stiffness, and hence easily buckle during insertion and therefore cannot penetrate the pia or the brain tissue. A penetrating electrode must have sufficient mechanical stiffness to withstand the forces associated with surgical insertion into the brain without buckling or fracturing. When the insertion force exceeds the microelectrode's buckling strength, the probe will buckle along its shaft. Thus additional methods or tools have been developed to insert flexible polymer microelectrodes into the brain. Polymer and hydrogel coatings were used to increase the buckling strength of silicon microelectrodes [5]. A silicon based micro-surgical tool was also attempted to assist the insertion procedure for polyimide microelectrodes [6]. In this case, silicon is micromachined such that it is slightly wider than the electrode to be inserted. A polymer electrode is reversibly attached onto the silicon surgical tool by applying a thin coating of poly-ethylene gel (PEG) which acts as an adhesive between the surgical tool and the polyimide electrode and dissolves quickly upon contact with biological fluids. The disadvantage with this approach is the excessive surgical trauma during insertion due to the additional thickness that is added to the electrode. Recently we have succeeded in improving the buckling strength of BCB microelectrodes by micromachining a thin layer of silicon 5-10 μm onto the BCB electrode. However, the fabrication process is long and not cost effective because the starting wafer is SOI, which is many times more costly than silicon.

The objective of this paper is to briefly report recent results of a simple alternate method, which uses coatings dissolvable in bio-fluids, to improve mechanical stiffness of BCB polymer neural implant. We have studied three different coating materials such as thermo-reversible gel Poloxamer 407, glucose ($C_6H_{12}O_6$) and regular table sugar that were applied by dip coating onto the implant surface.

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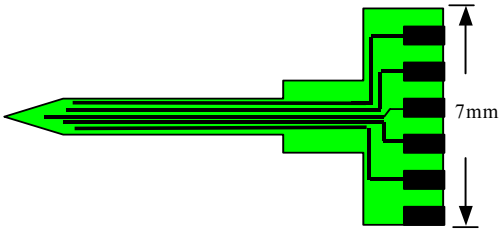

Fig. 1. Schematic diagram of the BCB based neural implant

II. Methodology

Electrode Fabrication: BCB microelectrodes without a silicon backbone layer were fabricated on a 4 in silicon substrate with 1.0 μm thermally grown silicon dioxide layer. The microfabrication process details are reported in our previous papers [3]. The schematic diagram of the BCB neural implant is shown in Fig 1. The portion of the tip inserted in the brain is 1.5 mm in length and 0.16 mm in width. It is then followed by a 9.5 mm flexible shank, which is interfaced with a connector to external circuitry. Typical thickness after fabrication is 12 – 14 μm.

Coatings: To temporarily increase the mechanical (buckling) strength of the electrode, a thin coating of either thermo-reversible gel, glucose or regular table sugar was applied to the surface of the electrode by a dip coating technique. Poloxamer 407, a thermo-reversible gel, was chosen based of its physicochemical properties and biocompatibility. Poloxamer 407, a block copolymer made of polyoxyethylene and polyoxypropylene, is known for its excellent compatibility with other chemicals, high solubility capacity for different drugs, and good drug release characteristics [7]. The polymer in aqueous solution (10-20% w/v) is a colloidal liquid solution at temperatures below 25°C and forms a stiff hydrogel at 37°C. The mechanical properties (modulus of elasticity) of the gel can be adjusted by varying the amount of poloxamer formulation. BASF Corp (N.J.) made Pluronic F-127 available. A 100 ml coating solution was prepared by mixing 20 % or 50 % Pluronic polymer in a bath held at 0 C. The solution was mixed in a mechanical stirrer for 10 hrs. The clear liquid was refrigerated before use. Glucose ($C_6H_{12}O_6$) was obtained from Sigma Chemicals. A saturated solution of glucose was prepared by mixing glucose at 45^0 C until the liquid became viscous. It was stored at ambient temperature. Similarly, a near saturated solution of regular table sugar was prepared at 40^0 C until the solution became viscous at ambient temperature. It was stored at ambient temperature and showed no sign of crystals appearing for several weeks. Care was taken not to make a fully saturated solution because crystals would start to appear at ambient temperature.

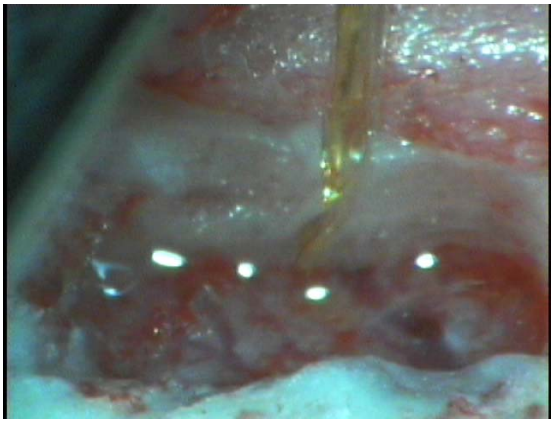

Fig. 2. BCB electrode (yellow) buckling during insertion into the brain.

Surgical Procedure: A rat was anesthetized with a Ketamine-Xylazine-Acepromazine cocktail and placed into a stereotactic frame to immobilize the skull. A craniotomy was performed, as described in our earlier paper [4], to access the targeted implant site over the rat's right barrel cortex (approximately 2 mm posterior and 5 mm lateral to bregma). All procedures were performed in compliance with the protocol for use of laboratory animals, which was reviewed and approved by the IACUC.

Brain Tissue: The animal was perfused and fixed with 4% paraformaldehyde in physiological saline as per the protocol by Turner and Shain [1]. After perfusion, the entire rat skull was allowed to soak in the perfusative (4% paraformaldehyde) for an additional 24-48 hours. Then the brain was removed from the skull and the brain tissue was returned to a solution of Hank's buffer for storage until use.

III. Results

A BCB microelectrode on its own cannot penetrate the brain tissue. The electrode always buckles under the insertion force, as shown in Figure 2.

To test the effect of coatings on improving buckling strength, we first dip coated 2 mm of the tip of the electrode several times in the thermo-reversible gel, which was refrigerated prior to bringing to ambient temperature. The temperature of the coated electrode was raised to 37^0 C under a lamp. At this temperature the coating forms a stiff gel. An attempt was made to insert the coated electrode into the barrel cortex. The electrode quickly lost its stiffness when it came in contact with the CSF (biofluid) around the craniotomy site, due to quick absorption of the gel by the CSF.

We also tried to insert the coated electrode in preserved brain tissue, which is stiffer than the live brain. It was found that the increase in the electrode stiffness was not sufficient to penetrate the preserved or live brain tissues. Similar results were obtained with glucose-coated electrodes. A near-saturated solution of glucose showed crystallization

Fig. 3. Optical micrograph showing full penetration of the electrode tip in preserved brain tissue. The electrode tip is coated with regular sugar film.

and the films dissolved quickly when they came in contact with the CSF.

Promising results were obtained with near-saturated regular table sugar solution, which was found to be stable at ambient temperature. An electrode tip 2 mm in length was dip-coated several times and left to dry at room temperature for several hours. The coated electrode was found to penetrate the preserved brain without buckling under the insertion force, as shown in Figure 3. However it failed to penetrate in the case of live tissue. The coating quickly dissolved when it came in contact with the CSF.

To protect the dissolvable coating we dip coated the sugarcoated electrode with mineral oil that is used for human consumption. Figure 4 shows penetration without buckling in live brain.

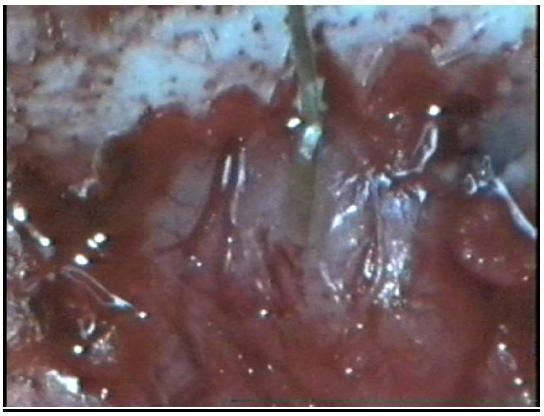

Fig. 4. Optical micrograph of sugarcoated BCB electrode after penetration into live brain tissue.

IV. Discussion

The maximum penetration stress experienced by the probe in penetrating the dura mater and pia is an important parameter. Experimentally it has been measured by Najafi that the maximum penetration stress is 4 x 10^8 and 2 x 10^9 dynes / cm^2 to penetrate rat pia and dura respectively for a silicon probe of 30 μm thickness and 80 μm in width [8]. The buckling strength of BCB can be increased significantly by micro-machining a thin layer of silicon onto the electrode [3]. Similar studies have shown that applying a thin coating of polymer can increase the buckling strength of silicon probes [6]. We have noticed that applying a thin coating of thermo-reversible gel or table sugar significantly increases the buckling strength. We are currently in the process of obtaining quantitative data on buckling strength using a Micro-Force Thermo-Mechanical tester.

V. Conclusion

The preliminary results of this study have shown that coating BCB probes with Poloxamer 407 polymer, a thermo-reversible gel, or table sugar significantly improves the buckling strength. However, the table sugar coating provides the greatest increase in stiffness, which is sufficient to penetrate both the preserved and live brain tissues without buckling. Dip coating the probe in mineral oil overcomes the problem of the coatings being dissolved too quickly in CSF.

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