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Neural Recordings from a Benzocyclobutene (BCB) Based Intra-cortical Neural Implant in an Acute Animal Model

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Abstract—**Multi-channel micro-electrode arrays provide unmatched spatio-temporal resolution for assessing the activity of populations of neurons. These neural implants provide a powerful tool for developing a better understanding of cortical processing, as well as provide an intimate interface for neuroprosthetic applications. Over the years, micro-wire based devices that are manufactured by hand, have allowed researchers to record for several months, and in rare cases up to a year or more. Devices based on microelectro-mechanical systems (MEMs) offer more controlled designs with the added benefit of batch fabrication. Polymer-based MEMs interfaces offer exciting promise over traditional silicon arrays due to their mechanical flexibility and excellent biocompatibility. In this paper we microfabricated a neural interface using a new class of polymer known as Benzocyclobutene (BCB), developed for microelectronics under the trade name Cyclotene™. This polymer has properties that we believe make it an attractive candidate for chronic implant applications. We provide for the first time a quantitative assessment of its recording capability in an acute animal model. Continuous recordings of neural signals (100 μV) from barrel cortex of a rat were successfully demonstrated. These results are encouraging for further development of a long term implant based on BCB.**

Keywords—**Benzocyclobutene (BCB), polymer-based microelectrode array, neural interface, neuroprostheses**

I. Introduction

Advancements in neural interfacing technology have provided an exciting view into the operation of neural circuits by providing simultaneous recording from large numbers of neurons. This technology has ranged from hand-made microwire arrays [1] to more sophisticated micro-electro-mechanical systems (MEMs)-based structures [2, 3]. However, if this technology is to have clinical impact in the form of such devices as direct brain-machine interfaces and/or neuroprostheses, the interface must yield stable communication channels for years. This is not usually possible with current state-of-the-art neural interfacing technology. Typically, the quality of the neural recordings can be excellent initially, but over time (weeks, months) decays. This is largely attributed to the foreign body response that walls off the implant making it difficult for the small currents created during neuron action potentials to make contact with the recording sites. Furthermore, there is thought that the interface degradation may also be partially caused by micro-motion between the rigid recording interface and the extremely soft brain tissues.

Polymer-based interfaces offer exciting promise due to their mechanical flexibility as well as the potential for applying various surface modification techniques to improve biocompatibility. Recently, researchers at Arizona State University reported the first successful fabrication of a polyimide-based multi-channel intracortical device and recorded the neural activities from the barrel cortex (whisker representation area) of a rat's brain [4]. Polyimide material has many attractive features: biocompatibility, flexibility for moving with the brain, and ease of manufacture using existing microfabrication technology. However, polyimide has relatively high moisture uptake (4-6 wt%) which leads to a rapid fall in the electrode impedance and therefore may not be suitable for chronic application.

Benzocyclobutene (BCB) is a polymer widely used in the microelectronics industry for packaging but has not been studied for biomedical applications. We believe, BCB's unique properties of very low moisture uptake (0.12 %) and low dielectric constant (2.64) over polyimide suggest that this class of polymer will be a strong candidate for chronic implant application. In the companion paper, we have reported on the details of the microfabrication process of BCB implants as well as *in vitro* testing for cytotoxicity [5, 6]. These preliminary studies suggest good biocompatibility of the BCB-based neural implant, but the true test for any neural implant is demonstrating recording functionality.

This paper describes *in vivo* functional tests of a BCB-based neural implant and provides quantitative assessment of its recording capability in an acute animal model. For this study, a single-shaft BCB implant was inserted into barrel cortex (whisker representation area) of a rat. Continuous recordings were then made during contralateral whisker stimulation. We successfully obtained neural recordings with the device that contained multi-unit activity, modulated by external stimulation of the whiskers. These findings suggest that BCB is a suitable material for the development of intracortical recording electrodes, and spurs further study aimed at creating a functional chronic interface.

II. Methodology

Electrode Fabrication. BCB electrodes were fabricated on a 4-in silicon-on insulator (SOI) substrate with varying top device silicon thickness from 2 to 10 μm and buried

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oxide thickness of 1 μm. Top device silicon is (100) oriented n-type silicon with resistivity of 10~25 Ω-cm. SOI wafer provides easy thickness control for stiff segments and excellent etching control during backside etch process. The first layer of photosensitive BCB (Cyclotene 4026™ from Dow Chemical) was spin-coated, exposed, and then developed. The BCB layer was then partially cured for 40 minutes at 210°C in N_2 gas. Gold was evaporated and patterned to form traces for the recording sites. A second layer of BCB then encapsulated it. It was exposed and developed to expose the recording sites. There were 5 – 6 recording sites, each 20 x 20 μm in size, per shank. The fabrication details are given elsewhere [5]. The schematic diagram of the electrode and the SEM close-up view of the recording sites are shown in Fig. 1.

Surgical Procedure. The rat was anesthetized with a Ketamine-Xylazine-Acepromazine cocktail and placed into a stereotactic frame to immobilize the skull. A craniotomy was made to access the targeted implant site over the rat's right barrel cortex (approximately 2 mm posterior and 5 mm lateral to bregma). Using a 27 gauge hypodermic needle, a small hole was made in the dura through which the implant was inserted into the cortex. The implant and connector were fixed in a custom made holder that was lowered near the implant site with a micromanipulator. With the aid of Teflon™ coated forceps, the single shaft was guided through the hole just made in the dura and inserted approximately 1 mm into the cortex. A stainless steel reference wire was placed under the skin near the jaw muscle on the side contralateral to the implant. Saline was then injected over the implant site to help maintain the brain tissue over several hours of recording.

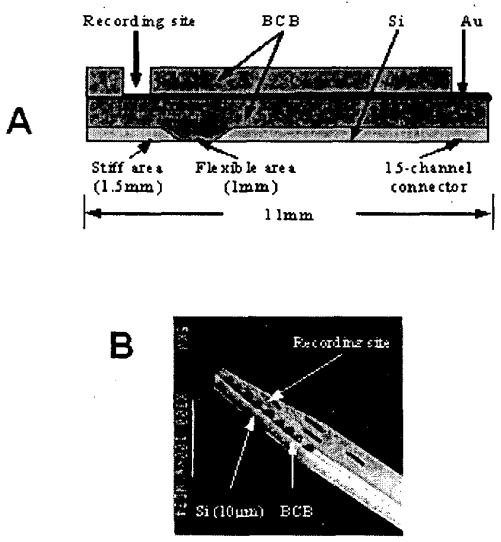

Fig 1 (a) Schematic diagram of the electrode; (b) SEM micrograph showing individual recording sites

Recording Protocol. A commercial multi-channel amplifier system was used to collect simultaneous neural recording data (Tucker-Davis Technologies Inc.). At the connector site, small FET head stage amplifiers (unity gain) provided high input impedance matching and current level amplification to preserve signal-to-noise ratios along the cable to the amplifier. The amplifier digitized the signals (25kS/s) with low-noise 16-bit A/D converters (+/- 7mV operating range; 5-6 μV rms noise floor; 0.2 μV resolution) and then multiplexed the recorded signals on one 10-meter fiber-optic cable to the rack-mounted analysis system. Tucker-Davis Technologies' OpenEx software environment was used to create a custom graphical user interface to provide visual feedback of the ongoing recordings, and control neural spike detection/classification details. Signals were band-pass filtered from 300-5000 Hz, and neural spikes were detected by manually setting the threshold above the estimated noise floor, or by automatically setting the threshold to 3 deviations of the estimated mean-RMS of the noise (1-s calculation window). In addition spike waveforms, continuous A/D recordings from all 6 electrodes were also obtained and analyzed offline to determine signal-to-noise ratio and assess recording quality.

Stimulation. The cortex exhibits rhythmic bursting activity while under anesthesia. In order to verify that the recordings were indeed neural activity originating from barrel cortex, the contralateral whiskers were stimulated. This was done by taking a small plastic rod and brushing it by the whiskers near their base. Several stimulation rates were tried (~1, 2, 5 Hz).

III. Results

A. Neural recording assessment

The implanted BCB-based electrode yielded recordings of neural activity on all functional channels of the implant. A representative example of the neural recordings obtained during 1-Hz whisker stimulation is shown in Fig. 2. The recordings contain both the rhythmic bursting induced by anesthesia as well as stimulus elicited bursts. Peak responses were in the neighborhood of 100 μV in amplitude, while the smaller spontaneous bursts were around 50 μV.

At high temporal resolution (Fig. 3), the neural recordings were observed to contain mostly multiunit activity from clusters of neighboring neurons although occasionally a single unit could be discerned. This figure also shows the low level of background noise (~10 μV) when bursts of neural activity were not present. The signal-to-noise-ratios obtained were around 20 dB.

B. Varying the stimulation details

In order to further validate the recordings and help to discriminate between the spontaneous, rhythmic bursting

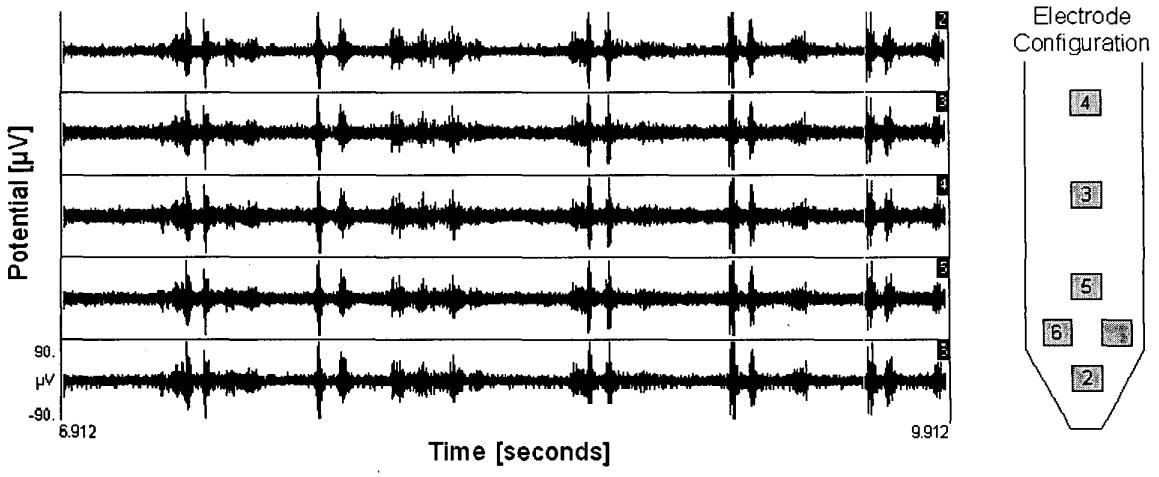

Fig. 1. Representative neural recordings from five channels of a BCB implant inserted in barrel cortex of rat. Contralateral whiskers manually stimulated at approximately 1 Hz. Electrode configuration shown at right.

and the stimulus induced bursting, several stimulation rates were utilized. A summary of responses obtained for each stimulation rate as well as for 'no stimulation' is provided in Fig. 4. The spontaneous rhythmic bursting oscillated with a frequency on the order of 2 Hz, and smaller amplitude (50 μV) as compared to the stimulus driven burst which usually included a onset peak on the order of 100 μV. As the stimulation frequency increased from 2 Hz to 5 Hz, the spontaneous bursts were virtually eliminated as the cortex became entrained to the higher stimulation rate. In fact, in some instances the entrained oscillation appeared to continue for several seconds after the stimulus was removed (not shown here). The fact that varying the stimulation rate induced a proportional modulation in the bursting rate provided confidence that the responses were originating from neural activity in barrel cortex. Furthermore, stimulation of the ipsilateral whiskers induced no observed bursting modulation (data not shown) providing additional assurance.

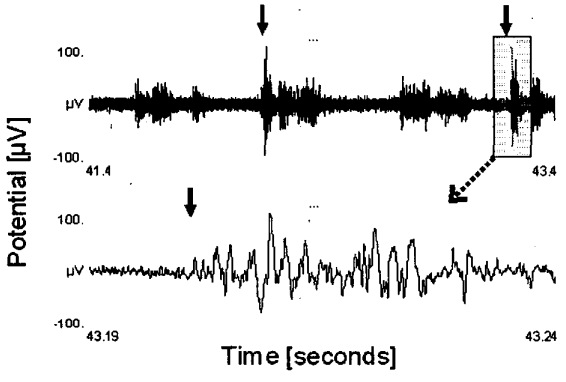

Fig. 2. Recording from one electrode (ch 2) during contralateral whisker stimulation (downward pointing arrows). *Top*: 2-s recording block. *Bottom*, a 50-ms block at higher temporal resolution.

C. Insertion trauma

The overall insertion trauma for the silicon-backed BCB implant appeared minimal. During the smooth insertion very little, if any, bleeding occurred around the implant site. It also appeared to stay in position during the duration of the recordings (approximately 2 hours). At the end of the recording session, the implant was removed by hand with forceps. No bleeding was observed after this and virtually

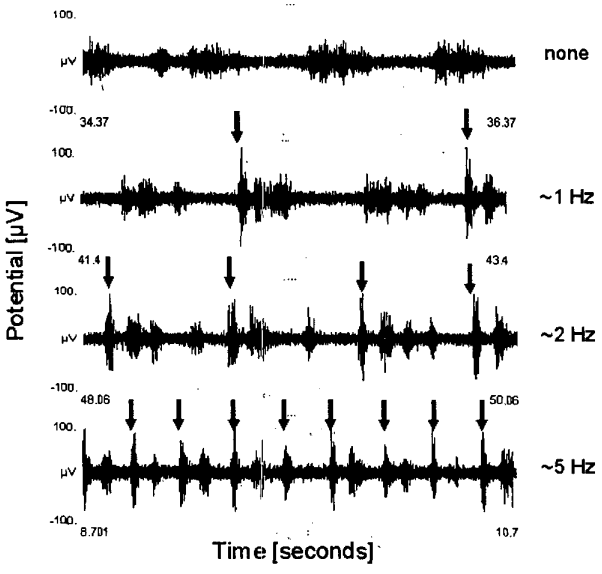

Fig. 3. Recordings obtained from one electrode site (ch 2) for different whisker stimulation conditions as indicated at right: 'none' indicates no stimulus was applied while 1, 2, and 5 Hz was the approximate rate of stimulation of contralateral whiskers.

no visible damage (except that caused by the dura opening) could be identified. This suggests that these electrode dimensions may allow for easy implantation and minimal insertion trauma. Further studies must be conducted to determine if the implant will be viable chronically, but these preliminary results are promising.

IV. Discussion

We have demonstrated the functional recording capability for the first time with a BCB-based neural implant fabricated using a traditional MEMs approach. Typical bursts of multiunit activity contained peaks around 100 μV yielding signal-to-noise-ratios upwards of 20 dB. These results and the small insertion footprint caused by these implants suggest that they may be well suited for chronic implantation.

Our observation of rhythmic neural bursting in the barrel cortex was consistent with the findings of other investigators for rats under anesthesia [7, 8]. We also observed that the burst amplitudes varied despite consistent stimulation. This was also noted in [7], who found that when the stimulation coincided with one of the spontaneous bursts, the amplitude of the driven activity was greatest. These findings, along with our ability to modulate the bursting pattern frequency provide a control that verifies that the recordings were multiunit neural activity originating from neurons in barrel cortex.

Our recorded signal amplitudes of 100 μV peak (200 μV peak-peak) were also comparable to the 150 μV peak-peak signals previously reported with polyimide electrodes [4]. This suggests that the BCB-based implant should be able to provide an adequate recording interface without the problems of water uptake that occurs with polyimide as mentioned above. Future studies are currently being pursued to observe the chronic recording capabilities of BCB-based electrodes.

V. Conclusion

We have demonstrated acute neural signals recorded from barrel cortex of a rat using BCB polymer based neural interface. The recorded signal amplitudes of 100 μV peak (200 μV peak-peak) were comparable to the 150 μV peak-peak signals previously reported with polyimide electrodes. These findings provide support for developing a chronic device based on BCB.

Acknowledgment

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