Proceedings of the 25th Annual International Conference of the IEEE EMBS
Cancun, Mexico • September 17-21, 2003

Benzocyclobutene (BCB) Based Intracortical Neural Implant

A. Singh[1], K. Lee[2], J. He[1], G. Ehteshami[1], S. Massia[1], and G. Raupp[3]
[1]Department of Bioengineering, [2]Electrical Engineering, and [3]Chemical Engineering
Arizona State University, Tempe, AZ 85287, USA

Abstract—**Photosensitive benzocyclobutene (photo-BCB) is a class of photoimagable polymers developed for microelectronics under the trade name Cyclotene™ with properties that we believe make it an attractive candidate for chronic implant applications. We report for the first time a complete microfabrication process of BCB polymer-based intracortical neural implant for chronic application. The new design of the implant provides flexibility for micro-motion compliance at the brain/implant interface and the necessary stiffness for better surgical handling. We have demonstrated that the implant with a silicon backbone layer of 5~10μm is robust enough to penetrate the pia without buckling, a major drawback with polymer. The averaged impedance value at 1KHz was ~250 KΩ.**

Keywords—Benzocyclobutene, bio-MEMS, micromotion, neural interface, neuroprosthetics.

I. Introduction

Recently, researchers at ASU reported the fabrication of polyimide-based multichannel intracortical interface and recorded the neural activities from the auditory cortex of a rat's brain [1,2]. Polyimide material has many attractive features. First it is biocompatible, second it provides much needed flexibility for conformal coverage, and thirdly the manufacturing process using existing microfabrication technology can be easily implemented. The intended flexibility is highly desirable to minimize tissue damage at the brain-tissue/implant interface. Unfortunately, there are two key problems associated with the flexible polyimide electrodes. First due to the lack of stiffness, polyimide electrodes easily buckle during insertion and therefore, cannot penetrate the pia during surgery. Second, polyimide has relatively high moisture uptake (4-6 wt%), which leads to the rapid fall in the electrode impedance and therefore unsuitable for chronic application.

We report for the first time the microfabrication process of benzocyclobutene (BCB) polymer-based intracortical neural implant for chronic application. Photosensitive benzocyclobutene (photo-BCB) is a class of photoimagable polymers developed by the Dow Chemical Company under the trade name Cyclotene™ with properties that we believe make it an attractive candidate for chronic implant applications. BCB resin is currently the established material of choice for many applications in the microelectronics [3] but has largely been ignored for biomedical application as there is no reported data on biocompatibility, the prime requirement that needs to be satisfied before this material can be considered for such application. We have recently reported the cytotoxicity and cell adhesion behavior of Cyclotene 4026™ coatings and found, BCB to have no adverse effect on cell adhesion and cell growth [4]. We believe, BCB's unique properties (Table I) of very low moisture uptake (0.12 wt%) and low dielectric constant (2.64) over polyimide suggest that this class of polymer will outperform polyimide for chronic implant application.

This paper describes the new design that will provide flexibility for micro-motion compliance at the brain/implant interface and stiffness for better surgical handling (holding and insertion), microfabrication process, and initial performance evaluation of the first prototype BCB-based intracortical implant. Figure 1 shows a schematic diagram of the neural implant.

TABLE I
ELECTRICAL PROPERTIES OF BCB AND POLYIMIDE (PI)

Properties	BCB	PI
Photo acting type	Negative	Negative
Dielectric constant	2.65	3.5
Volume resistivity (ohm-cm)	1×10^{19}	10^{16}
Breakdown voltage (V/cm)	3×10^{6}	3×10^{6}
Glass temperature (°C)	> 350	430
Water uptake (wt%)	0.12	4
Planarization level	Excellent	Poor
Volume shrinkage after cure (%)	< 5	30 - 40

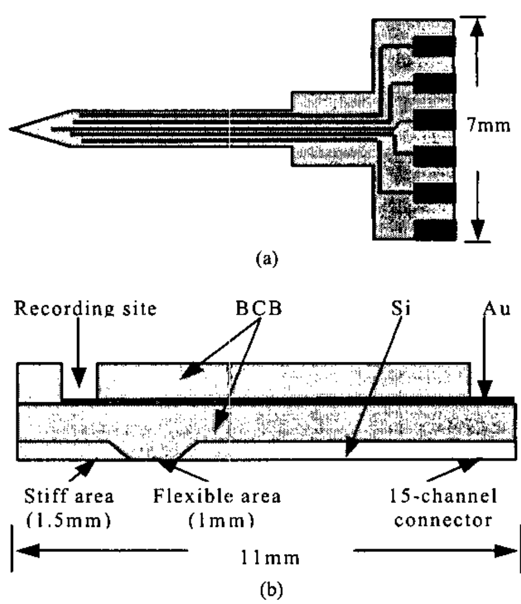


Fig. 1. Simple schematic diagram of the BCB based neural implant: (a) Top view and (b) cross-sectional view.

II. Design and Fabrication

Pure BCB-based electrode has buckling problem during insertion. To facilitate penetration of the pia during surgery, a 5~10μm thick silicon backbone layer, from SOI substrate, is attached onto the desired regions of the electrode to increase the stiffness (Young's modulus). By changing the thickness of the silicon backbone layer, we can increase the stiffness at the tip and the connection regions while leaving the middle region flexible. The length of the tip is 1.5 mm in length and 0.2 mm in width that remains inside the brain. It is then followed by 1 mm of flexible part of the electrode without silicon backbone layer designed to absorb stress from any micro-motion between the brain tissue and the electrode. There are 5 to 6 recording sites, 400 μm^2 each, per shank which are positioned near the end of the shank to increase the probability of recording neural signals from a target volume of tissue. The recording sites are interfaced to the external circuitry via a zero force 15-channel connector, which is especially designed to facilitate processing of neural signals to the external circuitry.

Fabrication starts with a 4-in silicon-on insulator (SOI) substrate with varying top device silicon thickness from 2 to 10μm and buried oxide thickness of 1μm. Top device silicon is (100) oriented n-type silicon with resistivity of 10~25Ω-cm. SOI wafer provides easy thickness control for stiff segments and excellent etching control during backside etch process. Figure 2 shows schematic diagrams for fabrication procedure. Top device silicon layer was selectively etched away to form flexible segment using a 2000Å thick gold masking layer (Fig. 2(a)). To make smooth transition between flexible and stiff portions, silicon wet etching in 7% Tetra Methyl Ammonium Hydroxide (TMAH) was performed at 80°C. The silicon-etching rate depends on crystal planes in TMAH. The (100) crystal plane showed 20 times faster etching rate than that of (111) plane. The resulting post etch angled slope of the silicon removes a step problem in next metallization process for recording sites (Fig. 3) [5]. After removing gold masking layer, the SOI wafer was cleaned and etched in an 80°C, 4:1 solution of H_2SO_4 and H_2O_2. A reactive ion etch (RIE) was used to clean and micro-roughen the top device silicon surface prior to depositing the first BCB layer.

The first layer of photosensitive BCB (Cyclotene 4026™ from Dow Chemical) was spin-coated, exposed, and then developed as shown in Fig. 2(b). Then the BCB layer was partially cured for 40 minutes at 210°C in N_2 gas environment to protect the developed pattern from subsequent processing steps and provide a suitable surface for metal deposition. Excellent planarization of the underlying topography and a flat plane for subsequent metal deposition were observed (Fig. 3). A reactive ion etch (RIE) was used to clean and micro-roughen the base BCB surface. After RIE, a 2000Å thick gold layer was deposited for recording sites, followed by wet etching (Fig. 2(c)). Gold was used for recording site because it has excellent surface inertness, and it provides no native oxide. However, gold is a soft material, so long-term corrosion issues should be examined. The upper BCB layer was spun, exposed, and developed to encapsulate or reveal the desired conducting surfaces (Fig. 2(d)). The electrode was then fully cured for 1hour at 250°C in N_2 gas environment. Partial cure of base BCB layer and full cures of the upper BCB layer terminates any route for water transmission through the boundary between the base and upper BCB layers.

Compared to polyimide (Durimide 7510™ from Arch Chemicals) electrode, BCB had less shrinkage during the curing process (~5% shrinkage during cure) and is likely to introduce less stress. The final BCB structure thickness is 20μm, where there is no silicon backbone layer. After the second exposure it was found that the recording sites were not completely opened, probably due to a lateral penetration of UV light. These residues hamper signal recording and electrical contact with a 15-channel connector. RIE was used to etch away the BCB residues on the gold surface using a 10μm thick photoresist-masking layer. A CF_4 and O_2 mixture was used for RIE (100W, 100mTorr, 10sccm CF_4, and 40sccm O_2) [6].

Wafer was flipped over for backside silicon etching in RIE. A top device surface was protected from plasma heat and RF power on the ground plane with photoresist and another dummy silicon wafer. Backside silicon etching was performed for 10 hrs in RIE with SF_6 (25sccm SF6, 5sccm O_2, 100mTorr, at 120W power). Clean and uniform silicon backside etching was obtained (Fig. 2(e)). Silicon etching exactly stopped on the buried SiO_2 layer due to the high differential etching rate between Si and SiO_2. After complete removal of backside silicon, the buried SiO_2 was etched away in 49% HF acid solution (Fig. 2(f)). Finally top-protecting photoresist was dissolved in microstrip for 2 hr at 50°C. Several rinses with de-ionized water were performed to remove any unwanted etchant products.

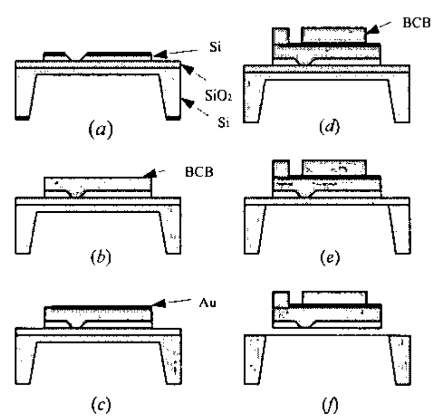
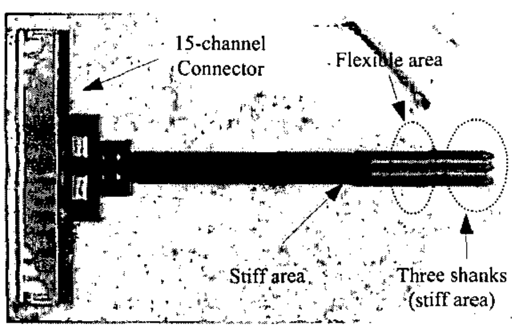


Fig. 2. Fabrication procedure of the BCB electrode with flexible region. (a) Selectively etched top device silicon layer for flexible region using a gold masking layer, (b) the first layer of BCB, (c) gold deposition for recording sites and gold traces, (d) the upper layer of BCB to encapsulate or reveal the desired conducting surfaces, (e) backside silicon etching, and (c) buried SiO_2 etching and lifted final device.

III. Results

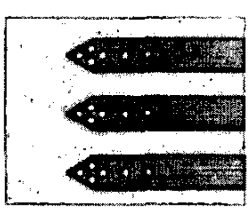
The fabricated device was visualized through an optical microscope and a scanning electron microscope (SEM). Figure 3 is a SEM micrograph depicting the cross-sectional view of the electrode after spin coating an SOI wafer with the first layer of BCB. The angled slope after TMAH etch and high degree of planarization that BCB offer are clearly visible. Silicon backbone layer is 5μm. The fabricated implants are tri-shanks with 5 recording sites (20μm x 20μm) and 2 vias (40μm x 40μm) per shank (Fig. 4). The tip with silicon backbone layer is 1.5 mm in length and 0.2 mm in width and remains inside the brain. Flexible portion without silicon backbone layer is 1mm in length. The thickness was approximately 20μm. The connecting pads of the completed electrode were interfaced with a 15 channel commercially available connector (Fig. 5).

Fig. 3. Cross-sectional SEM view of boundary between flexible and stiff regions.

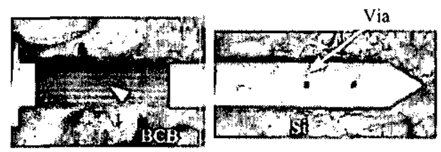


(a)

(b)



(c)



(d)

Fig. 4. Optical microscope and SEM images of the fabricated electrode: (a) Entire view of the electrode, (b) angled view of recording sites, and (c) top view of the shanks, and backside view of the electrode.

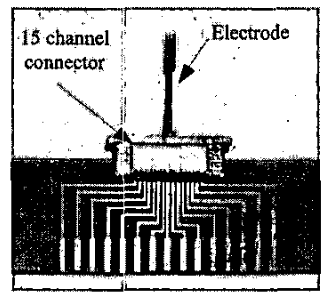


Fig. 5. Microscope image of the connector and electrode. The connector portion of the completed probe was exactly fitted into the commercial connector with 15-channel metal pads.

A. *In vitro biocompability test*

Devices intended for long-term implant in the nervous system must first meet a strict biocompatibility standard. We for the first time have verified the biocompatibity of BCB Cyclotene 4026 films [4]. Here we report the biocompatibility results on a complete functional electrode. The cytotoxicity and cell adhesion behavior of a functional BCB electrode exposed to monolayers of 3T3 fibroblasts cell line in vitro was studied using a *Live/Dead* Viability/Cytotoxicity Kit (L-3224, Molecular Probes) and previously described methods [4]. The morphology of 3T3 cells showed conformal coverage over the BCB electrode surface over a period of 24 hrs as shown in Fig. 6. The results indicated that 3T3 cell viability was not significantly different from positive control values (cells cultured on tissue culture plastic). Thus the functional electrode was considered not toxic for cultured fibroblasts cells.

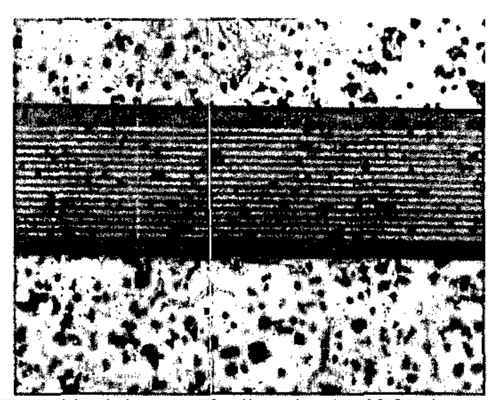


Fig. 6. Morphology of 3T3 cells on functional BCB electrode.

B. Electrical test

Electrical impedance testing was performed using HP 4284A precision LCR meter. All the recording sites were immersed into a 0.9% saline solution at room temperature. When an alternating current source is passed through one of the recording sites in the saline solution, a potential develops at the electrode-electrolyte interface. This potential determines the recording site impedance. The area of the recording site was $400\mu m^2$. Two prototype BCB implant devices were tested at 1 KHz frequency.

Table II shows the averaged impedance values from 6 recording channels. The averaged impedance value at 1KHz was ~250 KΩ. Furthermore the value of θ was negative and remained stable. Value of $\theta > -80°$ is capacitive in nature. We believe the observed impedance data is somewhat low but acceptable for recording [7]. Usually it is anticipated to be 1~2 MΩ [1, 2]. It is likely that after RIE the recording area may have been increased.

C. Mechanical test

We have reported the mechanical stiffness test on polyimide electrode using a micro-force thermo-mechanical tester [2]. A small force is applied and changes in the length are monitored. The Young's modulus is the slope of the stress-strain curve in the elastic region and it is the measure of the stiffness. For a 5μm thick silicon backbone polyimide electrode, the stiffness was improved to 31GPa, a 10 times increase. Since BCB's Young's modulus is comparable with polyimide we can infer that similar increase in the stiffness will be observed. The penetration test confirms this.

Penetration test into rat's brain was performed to check whether the microprobe could penetrate the pia without any surgical tool. First, rat was anaesthetized. Heart rate and oxygen saturation were monitored. Skull and dura were removed and the electrode was lowered to the surface (pia) by hand. Great care was made to encourage post implant recovery. Enough force was applied using a Teflon tweezers. Stiff electrodes with 5μm and 10μm thick silicon backbone penetrated the pia of rat without buckling (Fig. 7). However, a 2μm thick silicon backbone electrode fractured and failed during insertion (Table III).

IV. CONCLUSION

We have presented for the first time a complete fabrication process of BCB polymer-based multichannel intracortical neural implant for stable long-term chronic application. We have also demonstrated that our electrode design with a silicon backbone layer of 5 - 10μm is robust enough to penetrate the pia without buckling, a major drawback with polymer material. The averaged impedance value at 1KHz was ~250 KΩ which is acceptable for recording. Electrodes were able to record neuron signals. The details are presented elsewhere.

TABLE II
IMPEDANCE DATA (Z, -θ)

Channel	1	2	3	4	5	6
Z (KΩ)	210	206	290	295	240	255
θ (degree)	-63	-64	-58	-62	-63	-61

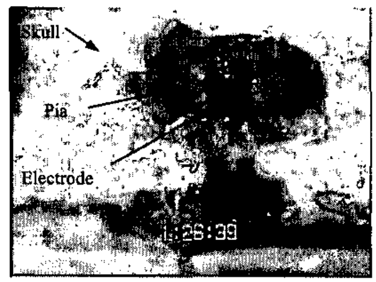


Fig. 7. Optical microscope picture of the penetration test into rat's pia. 5μm thick silicon backbone layer electrode penetrates pia without buckling.

TABLE III
MEASURED MECHANICAL STIFFNESS (YOUNG'S MODULUS) VALUES

	Rat pia penetration
Pure BCB electrode	No
2μm Si backbone electrode	No
5μm Si	Yes
10μm Si	Yes
Bulk Si	Yes

REFERENCES

[1] P. Rousche, D. Pellinen, D. Pivin, J. Williams, R. Vetter, and D. Kipke, "Flexible polyimide-based intracortical electrode arrays with bioactive capability," IEEE Trans. Biomedical Eng., Vol. 48, No. 3, 361-371 (2001).

[2] K. Lee, J. He, A. Singh, S. Massia, G. Ehteshami, B. Kim, and G. Raupp, "Polyimide based intracortical neural implant with improved structural stiffness", J Micromechanics & Microeng. (unpublished).

[3] M. Mills, P Townsend, D Castillo, S Martin and A Achen, "BCB polymer as an interlayer dielectric (ILD) Material," Microelectronic Packaging 33, 327-334 (1997).

[4] G. Ehteshami, A. Singh, S. Massia, , G Coryell, J. He and G. Raupp, "Glial cell and fibroblast cytotoxicity study on 4026-Cyclotene photosensitive Benzocyclobutene (BCB) polymer films", J Biomat Res.-Polymer Ed. (unpublished).

[5] O. Tabata, "Anisotropic Etching of Si in TMAH solutions," Sensors and Materials, Vol. 13, No. 5, 271-273 (2001).

[6] C. Korman, T. Chow, and D. Bower, "Etching characteristics of polysilicon, SiO_2 and$MoSi_2$ in NF_3 and SF_6 plasmas," Solid State Tech., 115-124, January (1983).

[7] N. Blum, B. Carkhuff, H. Charles, R. Edwards, and R. Meyer, "Multisite microprobes for neural recordings," IEEE Trans. Biomedical Eng., Vol. 38, No. 1, 68-74 (1991).