A NEW NEURAL PROBE USING SOI WAFERS WITH TOPOLOGICAL INTERLOCKING MECHANISMS

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Abstract – **A new method of fabricating multielectrode arrays on undoped single-crystal silicon for use in electrical stimulation and recording of nerve signals has been developed. The microscale topological design of grooves and dimples in the surface of the probes minimize differential movement in response to external stress by mechanical anchoring. The key function of topological controls is to promote the integration of microelectrodes with neural tissue in order to improve the effective electrical stimulation and signal-to-noise ratio. An adhesion peel test between PDMS and silicon is used as a simple model of this interface. Results show a 2 – 5 times increase in adhesion between the polymer and silicon surface when a patterned area was compared to a plain unpatterned area. This significant increase in adhesion strength without chemical modification indicates a robust mechanism by which neural tissue can bind to neural probes. The probes fabricated here are tested in an animal model.**

I. INTRODUCTION

An implantable microelectrode is an essential tool in the study of neuronal responses to sensory stimuli [1]. Neural probes which allow simultaneous stimulation and recording of electrical nerve signals at the cellular level will contribute to the understanding of how visual stimuli and other sensory information are processed in the brain to build a representation of the environment [2]. Multielectrode arrays that are used to record electrical nerve signals must be capable of being batch fabricated reproducibly. They must also be as small as possible for minimal disruption of the surrounding neural tissue [3]. Biocompatibility is an important issue in the fabrication of microelectrodes since such a recording/stimulation system should not evoke significant tissue reaction *in vivo*. The use of topographical patterning and biopolymer thin film coatings can increase biocompatibility and improve the interaction of living cells with these devices [4].

This work, which incorporates micro- and nano- scale topological designs, presents a new method of fabricating neural probes using silicon-on-insulator (SOI) wafers. A robust mechanical anchoring mechanism is achieved through this topological design, and is designed to enhance high-resolution signals and the long-term stability of implantable neural probes.

A. Single Crystal Probe Fabrication using SOI wafers

Our new microfabrication process, which is based on SOI technology, gives excellent control over the final probe thickness without the use of a wet etch and a boron etch stop. Although SOI wafers are costly, this simplified process eliminates the photolithographic steps and the expensive ion implantation steps associated with other fabrication methods.

In addition, the fabrication of neural probes using undoped single crystal silicon gives added strength to the multielectrode array. At 190 GPa, the Young's modulus of single crystal silicon is higher than that of boron-doped silicon, which can range from 150 to 180 GPa [5], [6]. At the high concentration of boron needed to effect an etch stop (greater than 5×10^{19} cm^{-3}, the solid solubility limit) in KOH or ethylene diamine pyrocatechol (EDP), the silicon is placed under tension as the smaller boron atoms enter the lattice. This residual stress can contribute to the breakage of probes during experiments. The use of undoped single crystal silicon may produce a sturdier neural probe.

B. Topological interlocking mechanism

Sometimes during the recording of electrical responses from cells in the cerebral cortex, the cortex does not remain absolutely motionless. There is a slight pulsation, perhaps due to motion in the cat while breathing. While silicon-based microelectrodes have an elastic modulus on the order of 100 GPa, the stiffness of neural issue is on the order of 0.1 MPa. This million-fold difference in stiffness can cause significant differential movement in response to external stress. Another explanation might be that the removal of the tough dura covering that area of the brain leaves the tissue more susceptible to motion since the cerebral spinal fluid, which circulates around the brain and spinal cord, is not stationary. The influence of topographical cues on cell behavior has been widely studied [7]. In general, studies have shown that cells align to grooves, with cytoskeletal elements such as actin and microtubules organizing in some cases along the walls and edges. Microtubules form in as soon as 30 minutes and are the first to align to grooves,

followed by actin. Thus, the patterning of surface topology on the multielectrode arrays might offer the surrounding neural cells a robust mechanism of attachment and stabilization during such recording sessions, which can span several hours. This mechanical anchoring mechanism can be attained without a complicated chemical surface treatment, which can produce a nonuniform result.

C. A simple adhesion test model

Since it is difficult to quantify the level of a cell's interaction with probes that have topological patterning, we are using polydimethylsiloxane (PDMS), a polymer, as a first study of adhesion. The ease with which the cured polymer can be removed from a silicon mold wafer will give an indication of the ability of a biocompatible coating (or living tissue) to interlock with the neural probe surface. This property is related to the aspect ratio of the surface features; the probes fabricated here have minimum feature size 4 μm width and 4 μm depth.

D. Testing in the cat visual system

In order to gain understanding of how the spiking of individual neurons and, more importantly, how the activity of a group of neurons are used to code information in the nervous system, our multielectrode array will be used to collect electrical data from neurons in the cat lateral geniculate nucleus (LGN). Since the focus of this work is to improve the biocompatibility of neural probes and the surrounding tissue, we present only data showing the ability of these probes to record electrical signals in animal tests.

II. FABRICATION

A. Fabrication of multielectrode arrays

The neural probes were fabricated on 25-μm SOI wafers. A 1.0 μm thick layer of thermal oxide was first grown on the wafer to provide electrical insulation. Electrode areas were patterned using standard photolithographic techniques. A thin sputtered layer of chrome served as an adhesion layer for the 1000 Å thick platinum which was sputtered on top of the chrome. The electrodes were then defined through a lift-off process in acetone. A 3500 Å layer of PECVD silicon nitride was deposited on top of the entire wafer. Contact areas to the platinum electrodes were etched through the nitride in an SF_6 reactive ion etch (RIE). The surface topology (rectangular grooves and square dimples) was patterned on the wafer, then etched in CF_4 and CHF_3 through the nitride and oxide layers. A short RIE in SF_6 drives the surface features into the silicon. The outline of the probes was then etched through the entire thickness of the silicon device layer on the SOI using a deep reactive ion etch (DRIE), stopping on the buried oxide layer. The back side of the SOI wafer was then patterned with the probe outline. Using a back-side DRIE that stopped on the buried oxide layer, the multielectrode arrays were defined so that only the thin surface silicon layer would remain where the actual probes were. In contrast, the contact pad area was unetched and remained at the original wafer thickness. Finally, the finished probes were released from the wafer in HF and acetone.

The finished multielectrode arrays were glued to a custom-made circuit board using epoxy. Using aluminum wire, the contact pads on the electrodes were wirebonded to the copper lines on the circuit board. The copper lines were soldered to pins so that the entire package could be connected to a standard DIP connector for ease in data acquisition.

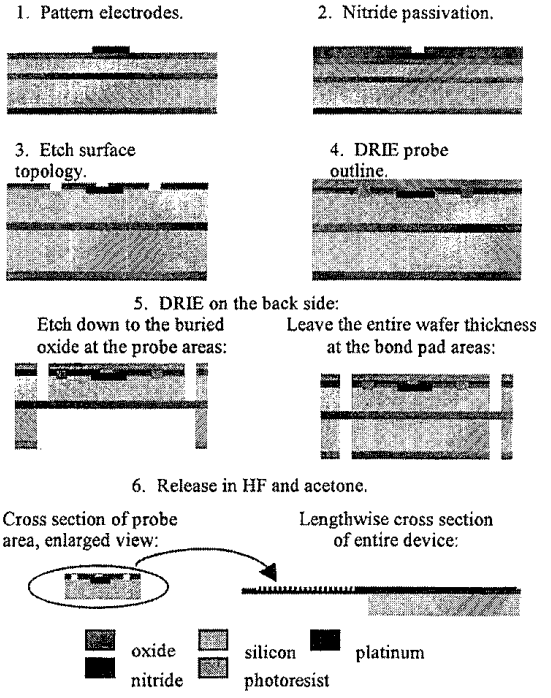

Fig. 1. Cross-sectional view of process flow for the fabrication of neural probes on SOI wafers.

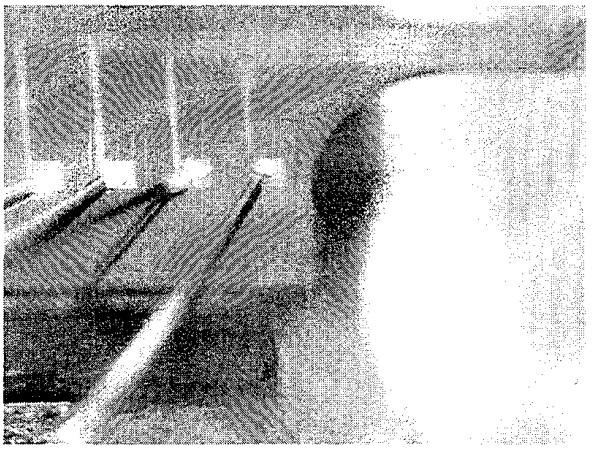

Fig. 2.. Oblique view showing the contrast between the thickness of the probes and the thickness of the bond pad area. Electrodes are wirebonded to the circuit board.

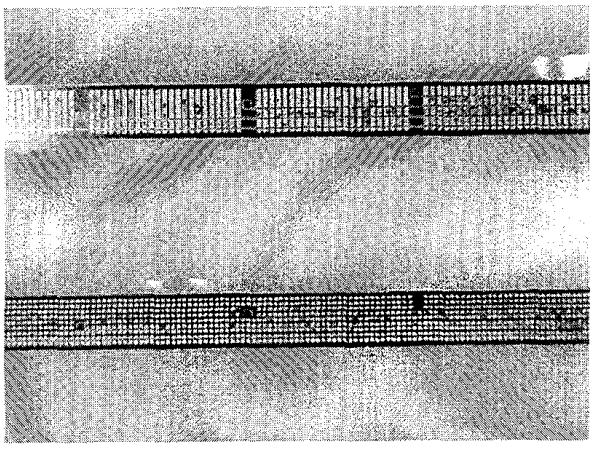

Fig. 3. Surface topology.
Top : 4 μm wide rectangular grooves etched 5 μm deep into the surface of the probes. Bottom : 4 μm squares etched 5 μm into the surface.

In this fabrication method, the thickness of the top silicon device layer on the SOI wafer determines the thickness of the finished probes. The use of SOI wafers obviates the need for using a timed KOH etch or using boron implantation areas as an etch stop to define the probe thickness. This new scheme gives precise control over the final probe thickness, and also permits parts of the probes (under the contact pads) to remain at the original wafer thickness. This is especially convenient since it gives ease in handling and wirebonding.

Here the probes are 25 μm thick while the electrode pad area remains at the thickness of the entire SOI wafer (~550 μm). Since these SOI wafers were made by fusion bonding a thin double-polished silicon wafer to an oxidized handle wafer, the backs of the probes are very smooth.

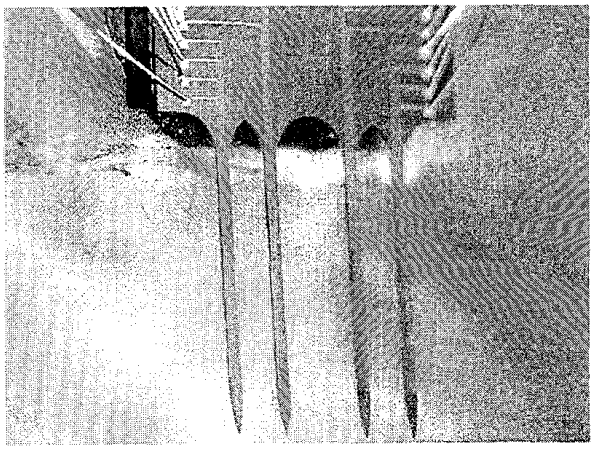

Fig. 4. Completed and packaged multielectrode array.
The probe shafts extend beyond the edge of the circuit board. There are four electrodes along the length of each shaft. The allows simultaneous recordings from 16 different sites.

B. Fabrication of wafers for the adhesion tests

In order to determine the adhesive strength between patterned silicon features and a PDMS layer in the 90° peel test, plain silicon wafers were patterned with the same features as those on the neural probes. Each patterned area was a 0.25 cm^2 square. The areas included horizontal rectangular grooves, vertical rectangular grroves, and arrays of square dimples.

The wafer was then baked at 120°C for 1 hour. The patterns were etched into the silicon in a Cl_2 and HBr RIE. Wafers were etched for varying times to produce several aspect ratios.

After removing the photoresist, a thin layer of PDMS was spun onto the wafer at 500 rpm for 30 seconds. It was then heated on a 90°C hot plate for 5 minutes to cure the polymer. This results in a polymer thickness of 200 μm.

III. Experimental Methods

A. Adhesion tests

In order to study how surface topology affects bonding strength, a model system using a surface-modified silicon wafer and a polymer layer was used.

The polymer was cut into strips on the wafer so that each individual pattern (horizontal lines, vertical lines, and square arrays) could be tested separately. During the 90° peel test, the each polymer strip was first removed from a plain, unpatterned area of the wafer and then from the patterned area of the wafer. The strips were peeled away from the silicon substrate at 5 mm/min using an Instron. Data was passed to a personal computer and recorded.

B. Testing in the cat visual system

In order to test the functionality of the new multielectrode array design, cats ranging from 2 to 3 kg in weight were used in the experiments. The cat was first anesthetized with isofluorane and then with sodium pentobarbitol; lidocaine, a local anesthetic, was injected before all incisions. A tracheostomy was performed to allow artificial respiration. The cat was then put on a Horsley-Clarke stereotaxic frame.

A craniotomy (approximately 0.25 cm^2) was performed over the LGN, and the underlying dura was removed. Pupils were dilated with a topical application of atropine sulfate. The eyes were fitted with contact lenses and focused on a tangent screen. The cats were paralyzed and artifically respirated. The core body temperature was monitored and maintained at 38°C, while the electrocardiogram and electroencephalogram were also monitored continuously during the experiment. The eye positions were mechanically stabilized by glueing the sclerae to metal posts attached to the stereotaxic apparatus.

Geniculate cells were recorded with the multielectrode array. Visual stimuli were created on a PC. The stimuli consisted of parallel black and white bars that moved across the screen. In order to find the orientation axis of the cells'

receptive fields, these gratings were rotated around 360°. The cells' responses to the moving gratings were measured, and the frequency of action potentials was recorded as a function of the orientation of the bars. Recorded signals were amplified, filtered, and passed to a personal computer.

IV. Results and Discussion

A. Adhesion tests

The patterns used in the 90° peel tests were the same as the patterns on the multielectrode arrays. These included 4 μm horizontal lines/4μm spaces, 4 μm vertical lines/4μm spaces, and arrays of 4 μm squares.

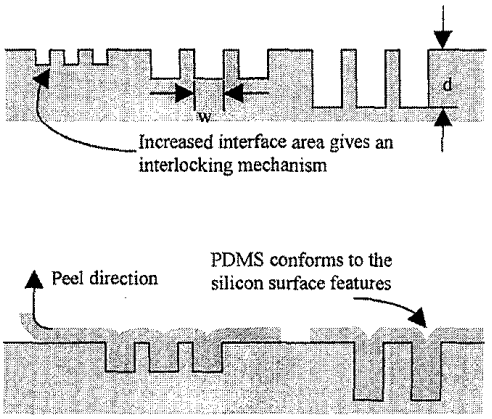

Fig. 5. Schematic of 90° peel test. The peel strength required to remove the polymer from the silicon substrate is measured. Once the peel test reaches the patterned area, there is more surface area between the PDMS and silicon, thus requiring more force to remove the PDMS from the silicon and providing an anchoring mechanism. The width w and depth d of the patterns were varied to give different aspect ratios ; w ranged from 500nm to 4 μm, and d ranged from 0.5 to 10 μm.

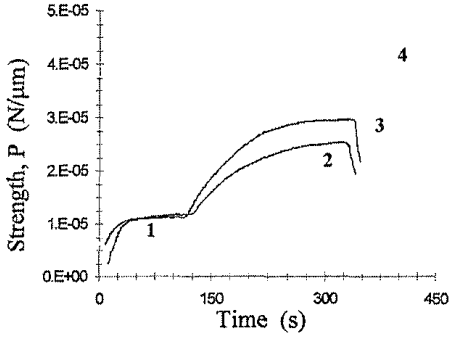

Fig. 6. Results of the 90° peel test.
1 : plain, unpatterned area on the silicon wafer
2 : rectangular groove pattern, 5 μm depth
3 : square dimple pattern, 5 μm depth
4 : square dimple pattern, 10 μm depth

As expected, the areas patterned with a square array required more force to peel the polymer film from the silicon surface, since the square array patterns have more interface area between the polymer and silicon. There is a 200 – 500 percent increase in the force required to remove the polymer from the patterned area as compared with the force required to remove the polymer from the plain unpatterned area. Also as expected, an increase in aspect ratio (the ratio of pattern depth to pattern width) also required an increase in strength to peel the polymer from the wafer.

This trend in the data indicates that increasing the aspect ratio of the grooves and other surface topological features will increase the stability of the probes in neural tissue if the cells attach to the walls and edges of the surface features. The more area there is available for cell attachment, the more force will be required to separate the probes from the tissue.

B. Testing in the cat visual system

The new multielectrode arrays showed good durability and did not break during insertion into the LGN.

The figure below shows the response strength of a cell to different moving gratings on the monitor screen. The data was taken from a single electrode on a multielectrode array that did not have topological patterning.

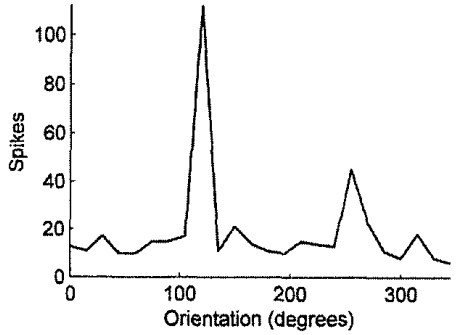

Fig. 7. Data from a single electrode on the multielectrode array. This plot shows the number of action potentials in response to different moving gratings on the monitor screen. This cell has a particularly sharp direction tuning at 120°. The secondary peak might be attributed to a nearby cell that also fired action potentials in response to gratings at 250°.

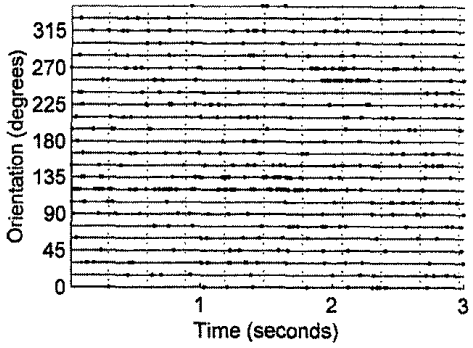

Fig. 8. Individual spike times during all orientations of the grating sets.

V. CONCLUSION

The 90° peel test demonstrated a 2 to 5 times increase in adhesion between the polymer and silicon surface when a patterned area was compared to a plain unpatterned area. This significant increase in adhesion strength indicates a robust mechanism by which cells can bind to neural probes if they attach to the walls and edges of the patterned grooves and dimples. Our next experiments will be a comparison study of patterned and unpatterned microelectrode arrays, examining stability and signal enhancement.

In future designs, we will combine topological patterning with chemical patterning on the surface of the neural probes. Certain fragments of laminin have been shown to promote neuronal cell attachment by interaction with cell membrane receptors [8]. The covalent attachment of chemical signals to the mechanical surface modification could improve biocompatibility even more than either mechanical or chemical modification alone.

Future designs will also include a biocompatible polymer coating on the probes. Polymers such as parylene, a member of the poly-*p*-xylylene family of polymers, have demonstrated minimal gliosis and tissue reaction in implants [9]. Since they are vapor-deposited at room temperature, parylene films are stress-free and extremely conformal. Also, in order to better understand neuron interaction, the fabrication of closed channels running along the shaft of the needles will allow the injection of desired neurotransmitters or other molecules at highly localized positions around the recording site. Work is in progress to fabricate probes that have a polymer thin film passivation layer for improved biocompatibility and closed parylene channels for selective chemical delivery.

ACKNOWLEDGMENTS

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