Neural Interface with a Silicon Neural Probe in the Advancement of Microtechnology

Seung Jae Oh, Jong Keun Song, and Sung June Kim*

School of Electrical and Computer Engineering, Nano Bioelectronics and Systems Research Center, Seoul National University, Seoul 151-744, Korea

Abstract In this paper we describe the status of a silicon-based microelectrode for neural recording and an advanced neural interface. We have developed a silicon neural probe, using a combination of plasma and wet etching techniques. This process enables the probe thickness to be controlled precisely. To enhance the CMOS compatibility in the fabrication process, we investigated the feasibility of the site material of the doped polycrystalline silicon with small grains of around 50 nm in size. This silicon electrode demonstrated a favorable performance with respect to impedance spectra, surface topography and acute neural recording. These results showed that the silicon neural probe can be used as an advanced microelectrode for neurological applications.

Keywords: silicon neural probe, neural prosthesis, neural recording, neural interface

INTRODUCTION

One of the biomedical applications for silicon-based micro-machined devices is a silicon neural probe for neurophysiological studies or prosthetic applications [1-3]. The use of a silicon neural probe for the study of the central nervous system, at the cellular level, has produced considerable understanding of neural networks in many sensory regions of the brain [4-6]. In these studies, simultaneous recording from many spatially-distributed sites is requires, as well as external signal analysis. The greatest advantage of a silicon neural probe is that they can sample many sites in a small tissue area. These silicon neural probes can be as small as 30 μm thick by 100 μm wide, and can have approximately 8 recording sites [7] (Fig. 1). An additional advantage is their ability to more accurately know the distances between recording sites. They can be used for the simultaneous recording of electrical activity at a large number of specific tissue locations with conventional metal wire or pulled glass microelectrodes. Therefore, more precise information about the spatial relationships between the recorded neuron is more readily available than with conventional electrodes [8]. The scale of these spatial dimensions can range from a few microns, to centimeters, across the brain. Seeing these advantages, Wise *et al.* [9] described the first photoengraved microelectrodes formed by high temperature boron diffusion, with wet etching to define the probe shape. However, this method only gives a probe thickness limited range below about 15 μm. In this paper, using a combination of dry (plasma) and wet etch, we were able to obtain over a 30 μm probe thickness, well beyond that readily obtainable by boron diffusion [7].

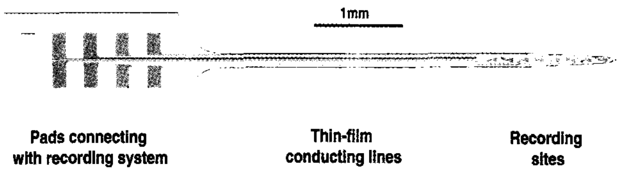

Fig. 1. A micromachined silicon neural probe. This is a single shank, 8-channel recording array. The thickness and width of the electrode are about 30 μm and 100 μm, respectively. Features of the silicon neural probe can be modified to a given application.

The most important feature of a silicon neural probe is that they show promise for their integration with CMOS (Complementary Metal Oxide Semiconductor) circuitry, such as preamplifiers and multiplexers, for on-site signal conditioning [10]. Generally, noble metals, such as gold, platinum and iridium, are widely used. Unfortunately however, these metals are considered contaminating impurities in industrial CMOS processes [11]. For this reason, we explored polycrystalline silicon (poly-Si) as a new site material for use in standard CMOS lines [12]. We employed a standard poly-Si as the site material, and proved that this material can be successfully used for neurological applications, and presented the material, electrical and neurobiological characteristics of such fabricated microelectrode.

***Corresponding author**
Tel: +82-2-880-1812 Fax: +82-2-882-4158
e-mail: kim@helios.snu.ac.kr

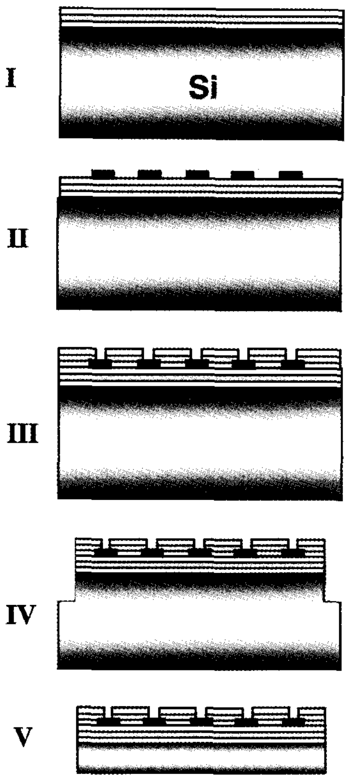

Fig. 2. Schematic process flow for fabrication of the silicon neural probe. I - Deposition of triple dielectric layer; II - Patterning of conducting layer; III - Site opening; IV - Deep-Si dry etching; V - Wet etching on backside of the wafer.

MATERIALS AND METHODS

Fabrication Process

The silicon neural probe was fabricated from <100> oriented, p-type silicon, polished on both the front and back. Fig. 2 shows the overall process flow developed. A system of triple dielectric layers (SiO_2 100 nm/Si_3N_4 200 nm/SiO_2 500 nm) was used as the underlying insulating layer. The middle nitride layer plays an important part as a diffusion barrier against alkali ions. Poly-Si was deposited using a Low Pressure Chemical Vapor Deposition (LPCVD) method, at 625°C and 300 mTorr, to a thickness of 300 nm. This layer was then doped, in a furnace at 950°C, with $POCl_3$ to a concentration of 10^{21} cm^{-3}, and patterned for recording sites and interconnections. The same types of triple dielectric layers, as described above, were then deposited on top. Subsequently, a masking layer for deep-silicon etching was deposited and patterned. The deep-silicon etching was performed using the Bosh process, to a depth of 30 μm. This etch depth determines the final shank thickness of the neural probe. The wafer was then placed in a 30 wt% KOH solution at 65°C, with the front side protected with silicon nitride. The silicon on the backside was etched until the structure was finally released. After the final probe shaping, the completed probes was mounted, and wire-bonded, to a printed circuit board, which was designed for easy connection to an external recording system.

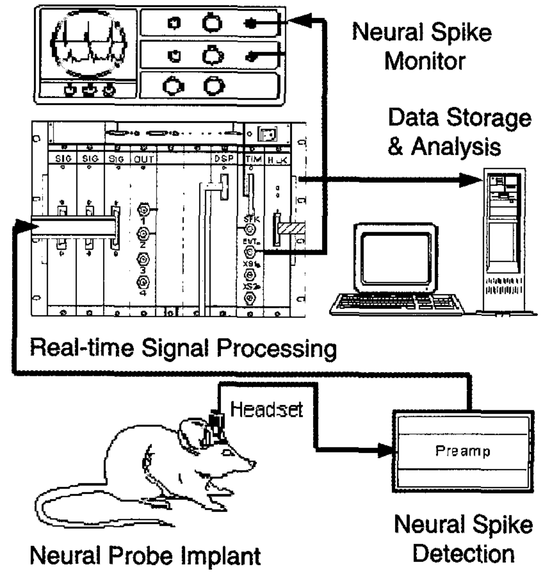

Fig. 3. A diagram of the typical set-up for neural recording *in vivo*.

Impedance Measurements

The impedance spectra of the electrodes were measured using a PC-driven potentiostat. All electrochemical measurements were performed in 0.1 M phosphate buffered saline (pH=7.4) using the electrolyte in a three-electrode cell. An Ag/AgCl electrode was used for the reference electrode, and a platinum rod for the counter electrode. The measurements were performed with a 5 mV AC signal between the counter electrode and a poly-Si electrode used as the working electrode. The frequency was cycled between 300 Hz and 20 kHz in 10 steps per decade.

Surface Topography

Scanning Electron Microscopy (SEM) and Atomic Force Microscopy (AFM) were used to investigate the surface morphology and structure of the electrode. The SEM was used to study of the shank structure with a voltage of 25 kV. The surface roughness was obtained from an AFM image consisting of 512 × 512 arrays of height data over 5 × 5 μm^2 scan sizes.

Acute Neural Recording *In Vivo*

Neural recording experiments were used to verify the electrophysiological performance of the silicon neural probe. Fig. 3 shows a diagram of the *in vivo* set-up for the neural recording from a rat. Sprague-Dawley rats (250 g) were anaesthetized with urethane (1 g/kg, i.p.).

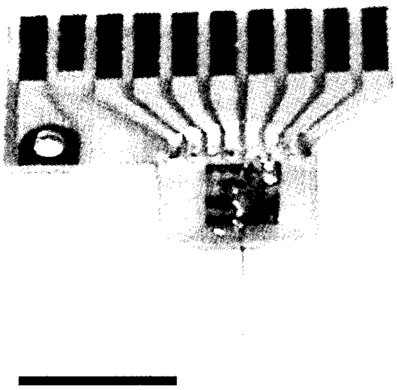

Fig. 4. A view of the whole depth-type poly-Si neural probe mounted on a printed circuit board.

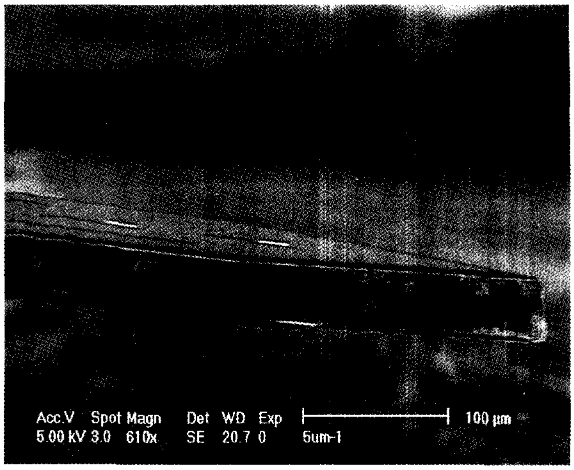

Fig. 5. A view of the probe tip using scanning electron microscopy.

The animals were mounted in a stereotaxic frame (David Kopf Inst.), and a craniotomy (2-3 mm diameter) was performed over the primary somatosensory (SI) cortex, using the bregma as the initial point of reference. All animals used in neural recording were treated in accordance with academic animal research guidelines of Seoul National University. The silicon neural probe was driven into the forepaw area of the SI cortex (0.5~1.0 mm anterial from bregma; mediolaterally, 3.5~4.5 mm; 0.5~1.2 mm from the brain surface) with a micromanipulator. Stainless steel wire, used as a reference electrode, was located in the lateral region of the brain [13]. The cutaneous receptive fields were identified by listening to the recorded signal through an audio speaker, while using a fine brush to tap the forepaw lightly, until the zones responding most intensely and reliably were defined. The electrical stimulation was provided by a bipolar concentric stimulating electrode (100 µm tip, 0.5 mm tip separation, A-M System), consisting of monophasic square pulses (pulse width 0.1ms, frequency 1 Hz) passed through a stimulator (Model 1830, World Precision Instr.), with an isolation unit to provide a constant current (50~500 µA). A multichannel acquisition system (Plexon Inc., Dallas, TX, USA) was used to carry out the extracellular neural recording in vivo. Responses were amplified for a gain of 1,000; bandpass filtered at 150 Hz to 5 kHz, and passed for storage and analysis to a personal computer.

RESULTS AND DISCUSSION

The silicon neural probe was fabricated to consist of micromachined silicon shanks, with gold or poly-Si sites on their surface. Fig. 4 shows the depth-type silicon neural probe fabricated, and bonded to a printed circuit board. The range of the shank thickness obtainable using the combination of plasma and wet etch processes is estimated to be from 5 to 200 µm [7]. While the new combination method etches 30 µm of silicon in about an hour, the boron diffusion process will take about 60 h to reach the same depth. If an even thicker shank is required, the etch time required with the newly developed process increases linearly with the required etch-depth, but the diffusion time increases as a square function of the required shank thickness. Fig. 5 shows the SEM picture of the probe tip after the dry etching of the silicon to a thickness of 30 µm. The silicon neural probe is fabricated by deposition of a thin-film onto a thick substrate. Therefore, silicon electrodes can be bent, by stress, between dielectrics and substrate [14]. With a combination of thermal oxide and LPCVD nitride film, a nearly stress-free condition in silicon shank can be achieved.

Impedance spectroscopy involves measuring an electrode's impedance over a spectrum of frequencies. Information about the system under test is obtained by comparing the input and output signals. The magnitude and phase information are measured directly. Using these data, we can get qualitative and quantitative information about the electrical properties of a system over a large range of frequencies, as well as the morphology of the electrode-medium interface [15]. Fig. 6 shows the magnitude of impedance of poly-Si measured using a potentiostat, as mentioned in the methods. The area of the electrode site was 30 × 20 μm^2, and 0.1% phosphate buffered saline was used as the electrolyte. The impedance of the 600 μm^2 doped poly-Si electrode was 1.96 ± 0.18 MΩ (n=13) at 1 KHz, which is slightly lower than the impedance of a gold site in the same area. This impedance data was encouraging, but even lower values may be obtained if the surface can be treatment to remove the native oxide layer formed on the poly-Si surface [11]. The measured phase was -87.2±3° at 1 KHz (n=13). This result indicates that the doped poly-Si was dominated by its capacitive component. A capacitive characteristic of an electrode is helpful when the microelectrode serves in the recording of neural signals. As the

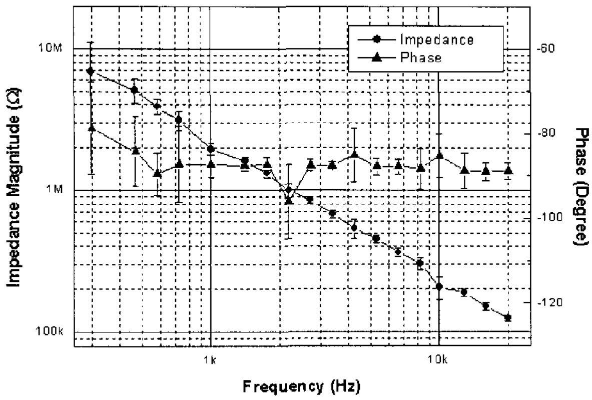

Fig. 6. The impedance and phase of the poly-Si silicon neural probe (n=13). The site area is 20 × 30 μm².

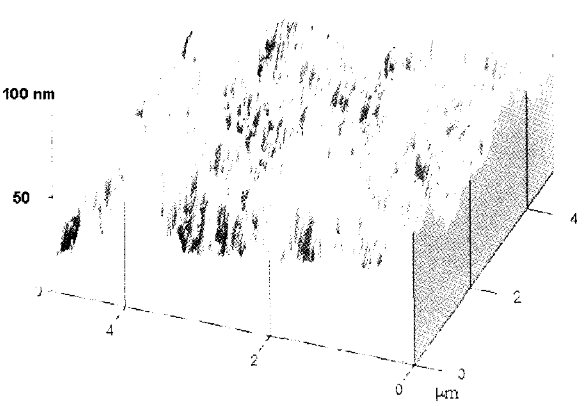

Fig. 7. An AFM image of the doped poly-Si site of electrode. The surface roughness of the site was measured as 6.5 nm RMS.

capacitance value is directly related to the surface area of the electrode, increasing the surface area will increase the double-layer capacitance, thus improving the characteristics of the electrode [16].

To investigate the surface morphology of the electrode, AFM was used. Fig. 7 shows an AFM image of a poly-Si site of the electrode. The surface appeared to be composed of small grains around 50 nm in size. The intrinsic roughness of the doped poly-Si surface was determined to be 6.5 nm RMS, which measured six times larger than a gold surface deposited by the evaporation method. If the dimensions of an electrode site are limited to the micron-scale for recordings from individual neurons, the electrode impedance may be influenced by the surface roughness of the site [16].

To ensure that the electrode interfaces well with the external recording system, simultaneous recordings of evoked neural activity from a rat's somatosensory cortex were obtained using the silicon neural probe, and are shown in Fig. 8. Four sites, each with an area of 600 μm^2 and separated from each other by 150 μm, were located perpendicularly through the cortex, as shown in Fig 8.

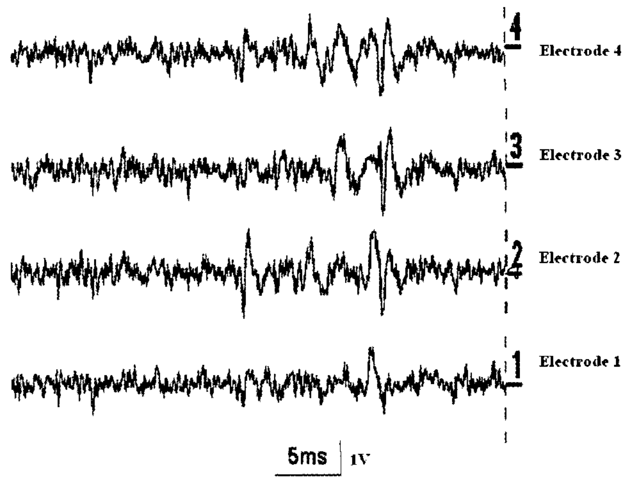

Fig. 8. Evoked action potentials recorded in the somatosensory cortex of a rat with the silicon neural probe.

The recording sites can be determined *in vivo* by monitoring the unit activity, and the amplitude versus the depth distribution of the evoked potentials [17]. The action potentials being recorded at the different sites are shown to be independent. The recording sites residing in cell body layers provide units with very large signal-to-noise ratios (SNR) [7]. We recorded the action potentials for about three hours with each animal. During these periods, we observed no deterioration of the SNR of the recorded signals.

CONCLUSION

In conclusion, we have developed a silicon neural probe with doped poly-Si, using plasma and wet etching, which allowed for a wide range of shank thickness. In this study, we describe a silicon neural probe, which shows a favorable performance with respect to impedance spectra, surface topography and acute neural recording. These results demonstrate that a silicon neural probe can be used as an electrode for neural interface. While this characterization of the silicon-based neural probe is continuing, the emphasis in the near future will be on the development of chronic implants capable of long-term stable use within the central nervous system. Work is also underway to extend these results to a novel, three-dimensional probe, with flexibility. We strongly believe that these studies will lead to advances in our understanding of neural network in the brain, and to the realization of micromachined neuroprostheses in the advancement of micro/nano technology.

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