DEVELOPMENT OF MULTISITE MICROELECTRODES FOR NEUROSCIENCE

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Abstract

Neural probes with a 32-site electrode array have been fabricated using an all-dry Si-etch based micromachining process. The fork-like probe shafts were formed by double-sided deep reactive ion etching (DRIE) of a silicon-on-insulator (SOI) substrate, with the buried SiO_2 layer acting as an etch stop. The probe shafts typically had the dimensions of 4-15 mm (length), 25 µm (width), 20-30 µm (height) and a tip taper angle of 4°. An array of electrodes, each 100 μm^2, as well as Au conductor traces were formed by e-beam evaporation. Both Ir and Pt were used as electrode material and focused ion beam (FIB) studies, as well as electrical measurements, showed differences between these materials. Also a post process cleaning procedure was developed to remove process residues from the electrode surface. SEM studies showed well defined straight probe shafts with sharp probe tips. The function was verified in bench-top measurements and probes have been successfully used by neuroscientists in brain preparations. The next generation of probes, with 64-sites, have already been designed and are under way in the manufacturing process.

1. Introduction

Until recently, neurobiologists have largely relied on sequential analysis of single-unit recordings. Such a method limits the throughput and complexity of experiments. It has become clear that a key to the understanding of the neural system is to make *simultaneous* observations of the activity of a *large number* of neural cells. The cell activity is measured as an *action potential*, typically 50–500 µV in amplitude [1]. Probes that can penetrate neural tissue and insert a large number of recording sites without damaging the neurons or tissue are thus needed. Micro System Technology is well suited to this end, and several MST based neural probe concepts have been presented over the years.

For example, a wet Si etch based process, where the probe shape is defined by a p^{++} diffused etch stop was demonstrated early on [2]. In a later approach, a combination of patterned deep reactive ion etching (DRIE) of the wafer front side, and blank wet Si etching of the back side was used to form the probe shapes [3].

Nevertheless, there is still room for improvement on previous processes and designs, in order to optimize the trade off between different requirements, such as: the possibility to independently tailor the shape of the probe tips for reduced tissue dimpling; the inclusion of a thicker support structure to facilitate handling of the thin probes after processing; process uniformity; yield; complexity; manufacturability; electrical connection as well as cost.

In this work we introduce an all-dry Si-etch based process where the buried oxide layer of an silicon-on-insulator (SOI) substrate acts as an etch stop, thus avoiding visual end point conditions, which should improve upon uniformity and manufacturability. Double-sided lithography and etching allows a thicker base plate to be part of the design.

2. Design

2.1 General

One of the most important issues in the design of recording microprobes is size, which should be comparable to or smaller than the neurons, usually 50 µm or less in diameter. The cross section of the shaft should be as small as possible to facilitate entry and movement through tissue but also to allow the shaft to approach and couple to the target cells as closely as possible to improve the signal-to-noise ratio of recorded activity [1]. But there is always a trade-off between electrode array size, number of electrodes, conductor line-width, mechanical stability and shaft width.

Referring to figure 1, the main design elements of the probe structure are: (a) Si shafts for penetration and insertion into neural tissue. (b) Micro electrode sites distributed over the outermost section of the shafts. (c) Au conductor traces from each electrode ending in (d) Au contact pads for external electrical connection (via a flexible printed circuit, FPC) using wire bonding. (e) A thicker Si base plate as a support for the contact pads, and to allow easy handling of the probes.

Two generations of probes have been designed, one with 32 [4] and one with 64 electrodes. Both have their own FPC design due to differences in base plate size. There are eight different models (all custom designed) in the 32-channel design as well as the 64-channel design. All probes have 10 × 10 μm^2 electrodes symmetrically distributed in an array like scheme and a tip taper angle of 4°. The shaft thickness is targeted to 20 μm but can be varied with the SOI wafer specification. Other parameters can be found in figure 2. In the second generation of probes the number of channels is increased in order to get more measurement sites or to use the stereotrode effect. Compared to the 32-channel design, the 64-channel probes have doubled their number of shafts or have decreased their conductor line width to find room for additional sites.

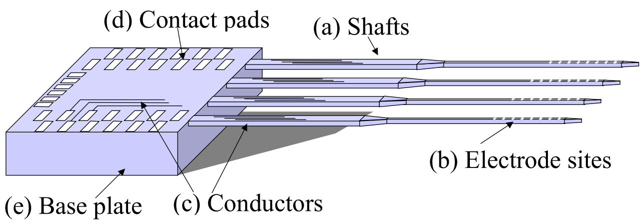
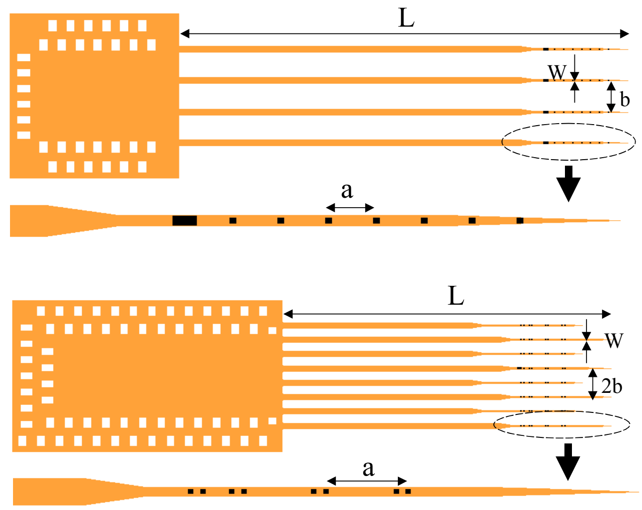


Figure 1. *Schematic 3D drawing of the probe structure (not to scale).*



Parameter	Design 32	Design 64
Base plate	2,2x1,9 mm	2,1x3,3 mm
N:o of shafts	1 - 8	2 - 8
L	4 - 15 mm	4 - 10 mm
b	ca 400 μm	200-600 μm
w (at active area)	25 μm	38 μm
w (at base plate)	75-200 μm	75-300 μm
a (single electrode)	100 μm	50 μm
a (stereotrode)	-	100 μm
Inter stereotr. pitch	-	30 μm
Conductor width	1 - 3 μm	1 - 1,5 μm
Conductor spacing	1 - 3 μm	1 - 1,5 μm
Tip taper angle	4°	4°

Figure 2. *Top: 32-channel and Middle: 64-channel CAD layout with close ups of active shaft areas. Note the four stereotrodes in the 64-channel design. Bottom: Design parameters, typical values.*

2.2 Stereotrode model

The 32-channel probes are designed to do simultaneous recordings at 32 different positions. Thus, each position has only one single electrode for this recording. To record simultaneous activities from multiple neurons, the data must be sorted by some kind of algorithms (in a data acquisition system). However, sorting algorithms based on recordings from single electrodes tend to have high error rates [5]. In an effort to avoid these errors the *stereotrode* recording technique was developed [6]. A stereotrode consists of two electrodes close to each other. Using algorithms based on the stereotrode model you are able to separate different recordings with less error rates than using the ones based on single electrodes.

3. Fabrication process

So far, two batches (*i* and *ii*) have been fabricated. Both *i* and *ii* have the 32-channel design but they differ in some process steps as described below. The silicon probe fabrication process is outlined in figure 3 and is indicated by bold lettering.

(**a**) The probes were manufactured on SOI substrates from Shin Etsu, 100 mm ϕ with specifications (*i*) 525/1.5/20 µm and (*ii*) 525/2.0/30 µm for Si/SiO_2/Si. (**b**) In (*i*) a PECVD Si_3N_4 was deposited as an isolation layer. In (*ii*) this film was replaced by thermal SiO_2 for stress reduction. Ti/Au (≈500/2500 Å) was e-beam evaporated and patterned with a photo-resist lift off process, to form conductor traces. Step-and-repeat projection lithography was used. (**c**) Another Si_3N_4 layer was deposited as an intermediate dielectric. Via holes were opened to the Au-layer using reactive ion etching (RIE) through a resist mask. (**d**) In (*i*) Ti/Ir (≈300/3500 Å) and in (*ii*) Ti/Pt (≈300/3100 Å) was e-beam evaporated and patterned with lift-off, to form electrode sites. (**e**) A final Si_3N_4 layer was deposited as a protective layer. Windows were opened to the Au bond pads and to the electrode sites using RIE. The Si_3N_4 covers the edges of the sites for increased reliability in wet working environments. (**f**) With a resist mask the remaining dielectric layer was first RIE etched, after which the top silicon layer was etched down to the buried SiO_2 in an inductively coupled plasma deep RIE equipment (ICP DRIE, Surface Technology Systems). (**g**) A thick resist was spun on the wafer front side for protection. Double-sided mask alignment was used to pattern a thick resist on the wafer backside. The backside was then etched 525 µm down to the buried SiO_2 in the ICP DRIE. (**h**) Before a final resist strip the shafts were released by etching the SOI buried SiO_2 in (*i*) buffered HF or by (*ii*) a dry oxide etch. Figure 4 shows a SEM of a test wafer after this release.

Post process cleaning procedures have also been tried out to remove process residues from the electrode surface. Four different cleaning procedures were investigated.

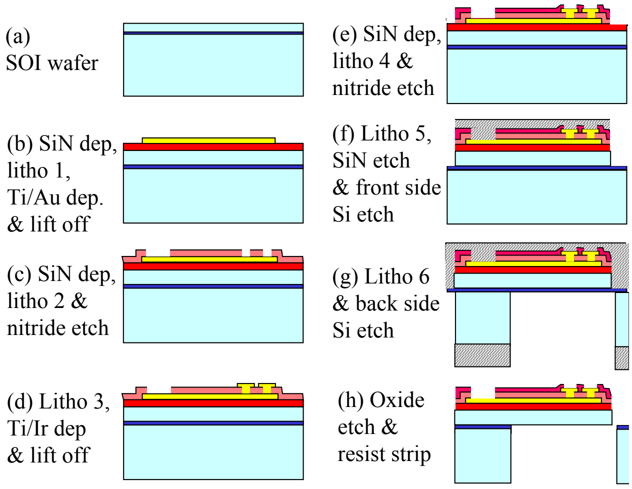


Figure 3. *Schematic cross section of the fabrication process (not to scale).*

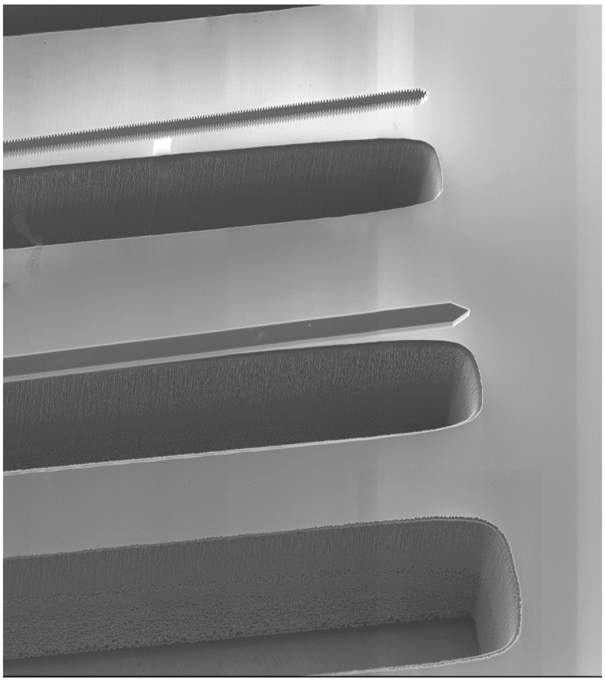


Figure 4. *SEM of test shafts after etch of buried oxide. Three deep trenches, etched from the backside in an ICP DRIE, can also be seen.*

4. Experimental results

Figures 5 and 6 show scanning electron micrographs of the results of the micromachining process.

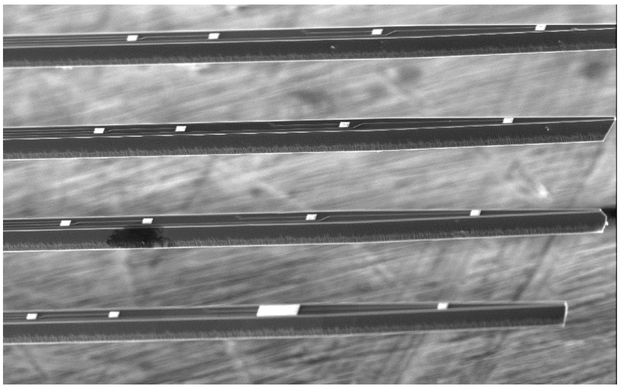


Figure 5. *Close up of four probe shafts, active region.*

Bench-top measurement setups were used to verify the electrical functionality of the probes after processing. We have been able to verify a satisfactory process yield. The electrode impedance is a parameter of prime interest, since it influences the thermal noise and the ability to record small neural signals. Impedance measurements were carried out in a 0.9 % saline solution with a Pt counter electrode. 224 Ir recording sites had an average impedance of 0.79 MΩ (standard deviation of 0.30 MΩ) at 1 kHz, see figure 7. The Pt sites had about 5.5 MΩ at the same frequency. The electrical measurements also showed that the impedance of the Ir electrodes were more unstable than the impedance of the Pt electrodes.

As post process cleaning, the detergent Decon 90 (Decon Laboratories Ltd.) turned out to be the best. We also noticed that the electrode impedance for both Ir and Pt was reduced after this cleaning, to about 0.4 MΩ and 2.3 MΩ respectively. SEM-micrographs (see figure 8) showed how process residues, probably resist residues or polymers from RIE, were removed after cleaning, which explains the effect.

These results are comparable to those of needle electrodes suitable for single unit recording. Neuroscientists have successfully used probes with both Ir and Pt electrodes for recordings in neural tissue.

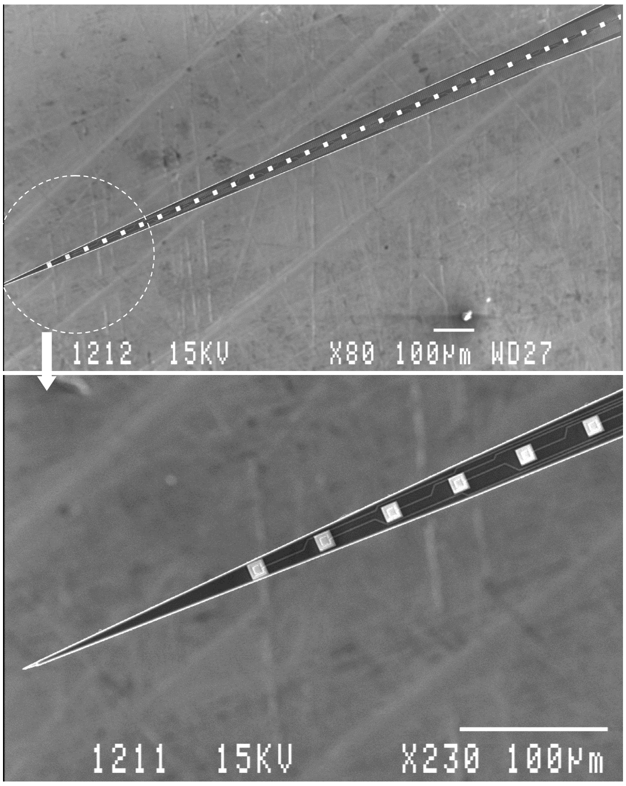


Figure 6. *SEM of a probe shaft with 32 electrodes.*

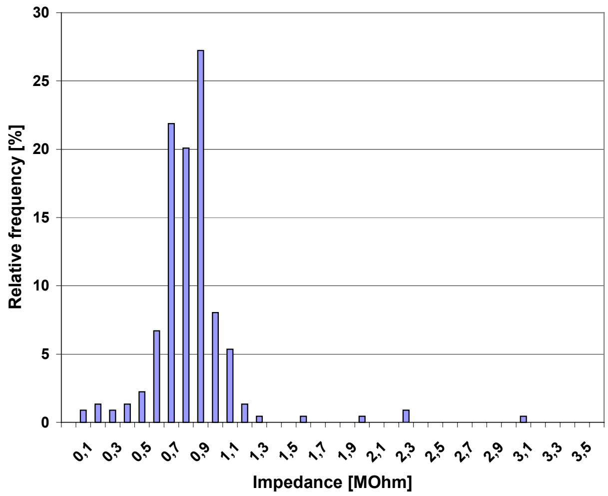


Figure 7. *Impedance distribution of 224 measured Ir electrodes at 1 kHz.*

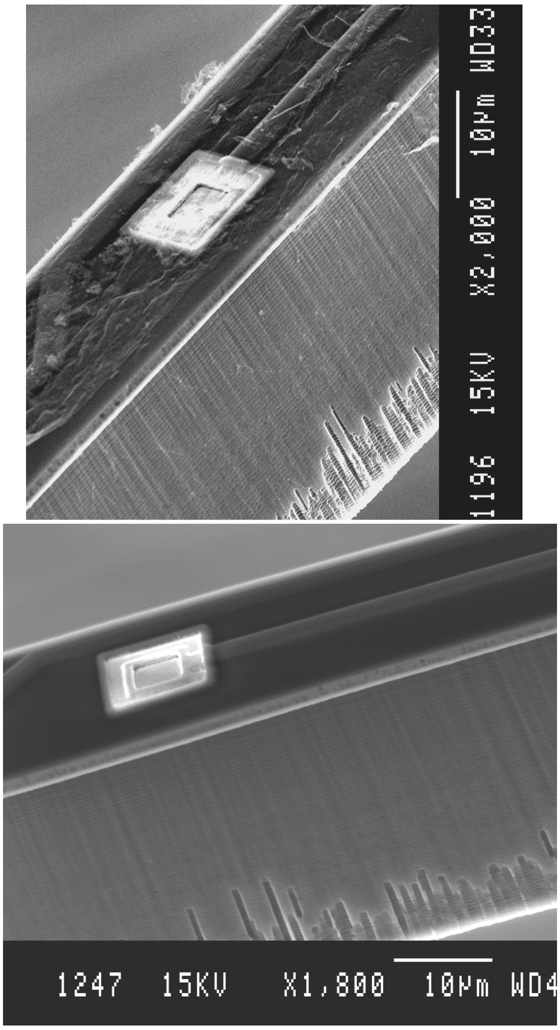


Figure 8. *SEM of a probe shaft before and after cleaning in Decon90.*

Focused ion beam (FIB) studies showed a difference in appearance between Ir and Pt. Ir has a smoother but also more brittle surface than Pt and tends to crack easily. Pt has a more grain like surface, see figure 9.

Three layers of standard PECVD Si_3N_4 resulted in shaft bending, which may cause insertion problems for the neuroscientists using long shafts. Stress reduction by thermal SiO_2 was successful. Measurements showed that the probe shafts were flat and straight.

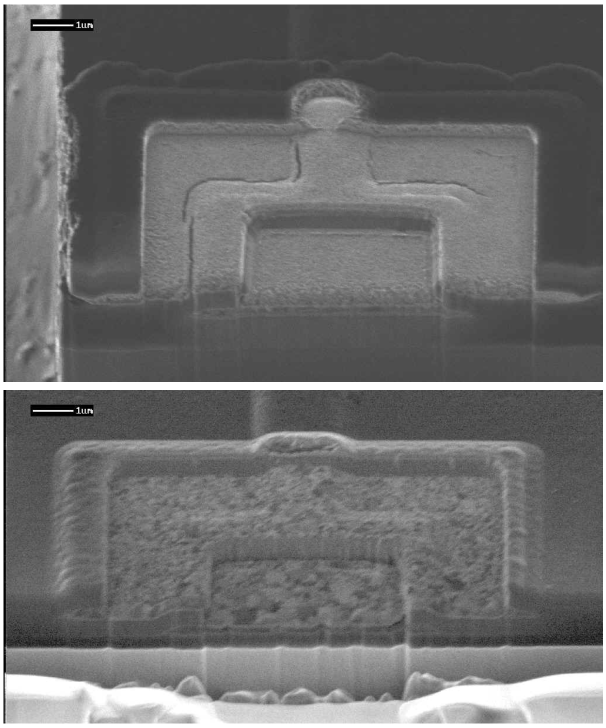


Figure 9. *FIB studies of Ir (top) and Pt (bottom) electrodes.*

5. Conclusions and outlook

A novel manufacturing process for micromachined neural probes, based on double-sided DRIE of SOI substrates was presented. Two batches with 32 recording electrodes distributed on one to eight fine and pointed Si shafts were fabricated. The electrical yield was verified and the magnitude of the electrode impedance was shown to be consistent with neural recordings. The process appears attractive with respect to complexity, process uniformity and manufacturability. Using a combination of thermal SiO_2 and PECVD Si_3N_4 as dielectric layers was a successful method to reduce intrinsic stress. Flat (indicating low stress) and more easy-to-use probe shafts were obtained by this technique. Yet another method, employing mixed frequency PECVD Si_3N_4 dielectrics, have been carried out as an alternative for stress reduction in the shafts. This concept will be integrated in the next batch which is already under way. In addition, the next generation of probes will have up to 64 electrodes distributed on 2 – 8 shafts. Some of the 64-channel probe models will rely on the stereotrode effect to improve separations of signal recordings.

What Acreo AB delivers to cooperating neuroscientists is shown in figure 10. The probe is mounted and wire bonded on the FPC and the probe shafts can be seen in the corner up to the right. On top of the probe's base plate there is an epoxy glob top.

Figure 10. *Shows ZIF connector, a flexible printed circuit and a probe on FPC ready for delivery.*

Furthermore, this work is part of a larger effort to develop a complete system for neural recordings, and to demonstrate the system in different application experiments [7], see figure 11. The name of the project consortium is VSAMUEL and there are three main system developers; (#1) Institute of Signal Processing *Medical University of Lübeck,* Germany (Ulrich Hofmann), (#2) *Acreo AB* and (#3) *Uwe Thomas Recording*, Germany (Dirk Hoehl). The three main experiments going on are: (#4) studies of the functional properties of the cerebellum at the Laboratory of Theoretical Neurobiology *University of Antwerp,* Belgium (Erik de Schutter), (#5) studies of extracellular field responses at the cortex of an isolated guinea pig brain at the Istituto Nazionale Neurologico *Carlo Besta*, Italy (Marco de Curtis) and (#6) studies of recordings from acute and chronic peripheral nerve implants at the Center for Sensory-Motor Interaction, *Aalborg University*, Denmark (Ken Yoshida). The systems approach as well as the collaboration between several hardware developer groups and neuroscience user groups is expected to bring added value to the neural probe concept.

Acknowledgements

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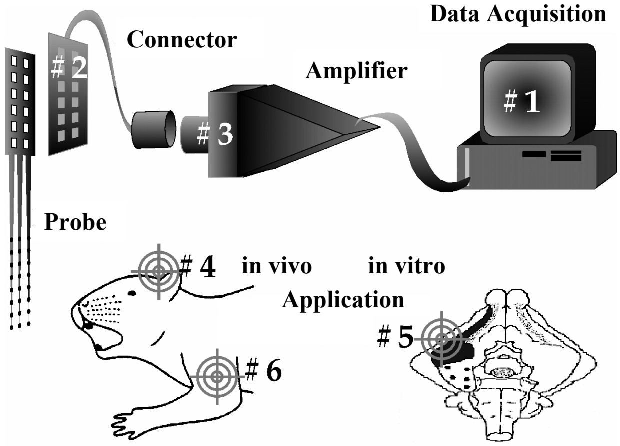

Figure 11. *Overview of a complete recording system (#1-3) and areas of application experiments (#4-6).*

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