

HIGH-ASPECT RATIO SUBMICROMETER NEEDLES FOR INTRACELLULAR APPLICATIONS

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Abstract

Presented is a processing technology to produce high aspect ratio submicrometer needles. This processing technique is required to create single or arrays of needles suited for intracellular interfacing. Pillars are created using deep reactive ion etching. The sharpening of the pillars is achieved by reactive ion etching. 200-300 μm tall needles with a 200 nm wide tip have been produced. Integration with flexible electrical interconnects is described.

Keywords: silicon needle, intracellular recording, DRIE, RIE, neuronal electrodes

I. INTRODUCTION

Intracellular sensing probes have a great potential in understanding the physiology and processes of single living cells.

A major challenge in producing probes for intracellular sensing is the tip geometry. Intracellular probes must have tips in sub-micrometer dimensions and the length needs to be longer than $\sim 100 \mu\text{m}$ (assuming cells with sizes in the hundreds of micrometers, as opposed to mammalian cells). These characteristics are necessary for effective bending and penetration of the flexible cell membrane (figure 1). The probe cannot penetrate the cell membrane if it is too dull, or too short to compensate for the bending of the membrane.

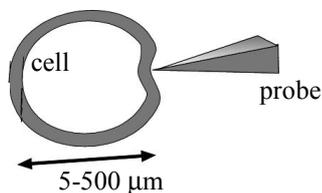


Figure 1. Schematic drawing of the bending of the cell membrane during insertion of a sharp probe.

Standard techniques for intracellular recording consist of glass capillaries [1] and fine insulated conducting wires [2]. Pulled glass micro-capillaries can be transformed into intracellular neuronal probes by filling them with an electrolyte and placing a Ag/AgCl electrode in the electrolyte. The

glass walls provide ionic insulation and ensure low leakage current. Both techniques are widely used and were developed in the past few decades.

However, these techniques lack in a number of categories. Among them are their overall large dimensions and the limited ability to integrate them with other components, such as amplifiers, memory and power source. Therefore, a very challenging task in bio-MEMS is the development of tools for intracellular sensing (electrical or chemical) for single living cells. The advantages of MEMS devices are the small dimensions, the ease with which multi-site devices can be produced and the ability to integrate the probes with additional components, as mentioned above.

The need for intracellular MEMS probes is quite evident in the discipline of field neurobiology. The information gathered by extracellular sensing is not exclusive to a single cell. Rather, it is an average over several cells located at the vicinity of the probe. For example, in the case of neuronal recording, extracellular probing does not provide the critical information about the DC state of a cell, which is associated with synaptic interactions, nor can it be used to easily identify the behavior of single cells or the interaction of cells in successive order. Therefore, intracellular recording is of great advantage for understanding heterogeneous living cell populations that make up dynamic systems such as neural networks.

While several extracellular MEMS devices have been presented [3-7], only one MEMS approach for intracellular recording has been presented so far [8, 9]. We have recently shown that by using silicon micro-fabrication techniques it is possible to realize needles with geometry close to the conventional pulled glass capillaries mentioned above. Measurements obtained with these devices confirm the qualities of the electrodes as extremely localized bio-sensors. The overall aim of the project is to record intracellular signals from a freely behaving animal (*Tritonia diomedea* – sea

slug). The signals obtained with the needle will be connected to a silicon chip containing the necessary electronics and memory. The power will be supplied by a small battery. Both, the silicon chip with the needle and the battery are implanted into the animal, which is then set free. First experiments show that the *Tritonia diomedea* survives for about two weeks after the implantation. These experiments would not be possible with the traditional sensing techniques as here, the animal needs to be fixed permanently under a microscope.

Similar probes can be used not only for this specific application with the *Tritonia diomedea* but also for studying the physiology and the process of other living cells.

The original fabrication procedure of the probes presented before [8] is cumbersome as the pillars ($70 \times 70 \mu\text{m}^2 \times 350 \mu\text{m}$) are created by a wafer saw. The pillars are then sharpened in an RIE (reactive ion etching) process to create needles. Replacing the sawing procedure gave the motivation to produce DRIE (deep reactive ion etching) fabricated pillars.

In this paper we describe a new DRIE based fabrication process of sub-micrometer needles. The process consist of pillars formed using DRIE followed by a RIE sharpening. These DRIE/RIE fabricated needles can be implemented into a flexible polyimide-based interconnect scheme, which we have recently presented [10].

II. DRIE PROCESS

To fabricate needles suited for intracellular recording, a highly conducting $500 \mu\text{m}$ thick p-type silicon wafer is used. The masking material is $12 \mu\text{m}$ thick positive photoresist (Clariant AZ4620). The resist was softbaked before exposure at 70 degC for 5 min and at 95 degC for 5 min on a hotplate. After developing, the resist is not hardbaked as this would re-flow the pattern. Then the wafer is placed in an Oxford Instruments DRIE to etch $300 \mu\text{m}$ tall pillars as shown in figure 2. The etching rate is $\sim 3.5 \mu\text{m}/\text{min}$.

For the DRIE (Bosch process), the distances of the needle-pillar ($\varnothing 70 \mu\text{m}$) to the protection-pillars ($\varnothing 30 \mu\text{m}$) have been varied. Pitches of $250 \mu\text{m}$ (figure 2) and $750 \mu\text{m}$ diameter (figure 3) of

protection-pillars with the needle-pillar in the center have been designed. The results after etching show that the pillars within the small pitch have a vertical sidewall, whereas the needle-pillars with a greater distance from the protection-pillars have a negative profile as can be seen in figure 3.

When the process parameters were changed to favor a more positive profile for the $750 \mu\text{m}$ pitch design, the unwanted formation of silicon-grass (black silicon) begins. This is due to polymer build up during the deposition stage, which is not completely etched away during the etching stage and also due to the limitations of the Oxford Instruments DRIE equipment in obtaining a reproducible, vertical profile.

The DRIE process can be used to create single needles or a whole array of needles as shown in figure 4.

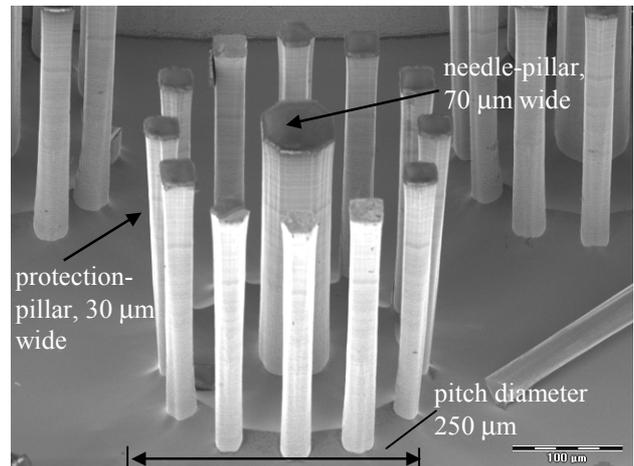


Figure 2. DRIE etched pillars; pitch diameter $250 \mu\text{m}$. The pillars are about $300 \mu\text{m}$ tall. The use of protection pillars ensures a straight profile.

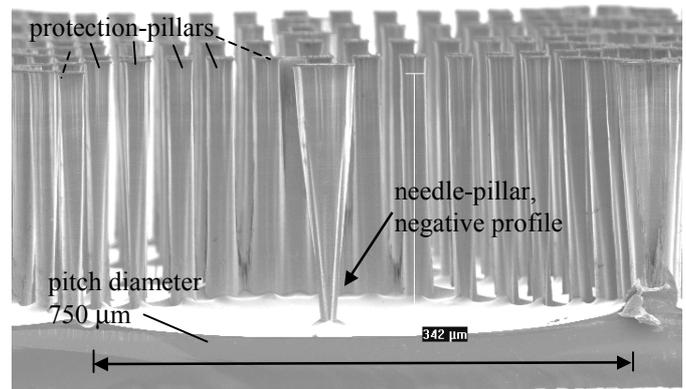


Figure 3. DRIE etched pillars; pitch diameter $750 \mu\text{m}$. The pillars are about $340 \mu\text{m}$ tall. Large distances between needle pillar and protection pillars results in a negative profile.

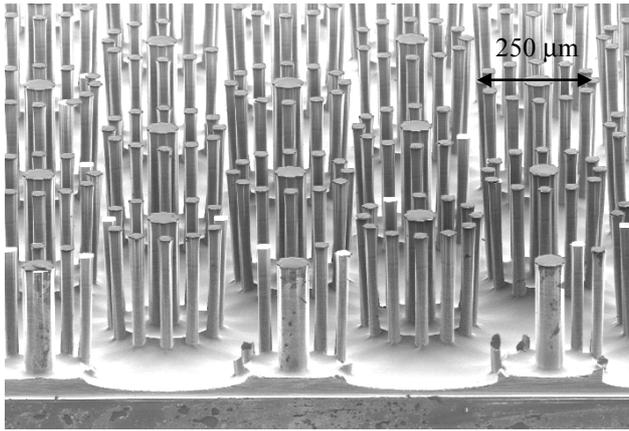


Figure 4. Array of DRIE fabricated pillars. The pillars are about 300 μm tall. The distance between the center pillars is 400 μm .

III. RIE PROCESS

After the DRIE process the resist is stripped with acetone. Then the wafers were cleaned in EKC830 solution (EKC Technology Inc.) to remove the DRIE residual polymer. Without EKC830 cleaning, a white residue would remain after the RIE process. The wafer is then placed into an RIE (Trion) to form the needles out of the 70 μm diameter pillars. This is a robust, self-sharpening process using SF_6 , which is optimized in order to obtain long tips with high aspect ratio. At the same time the 30 μm protection-pillars are completely etched away leaving a $\sim 230 \mu\text{m}$ tall single needle per pitch (figure 5). The processing time is about 25 min. The tip of the sharpened needle is 200 nm wide (figure 6), which reaches the goal of producing long submicrometer silicon micro needles.

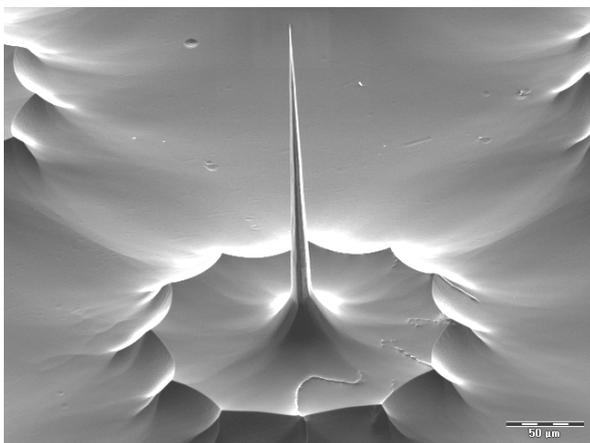


Figure 5. RIE sharpened silicon needle. The needle is 230 μm tall and etched from the needle shown in figure 2. The protecting pillars are eliminated during the sharpening process.

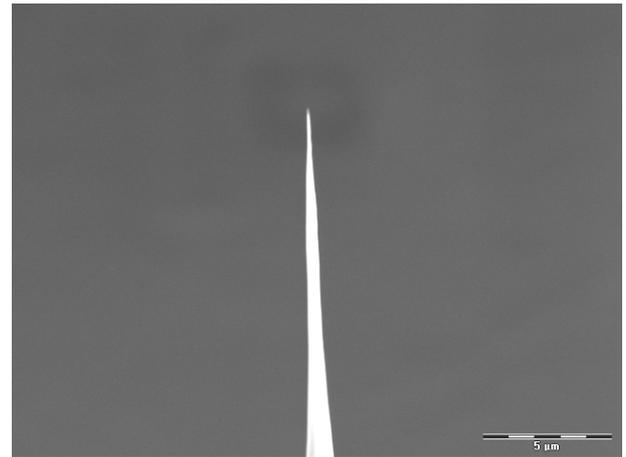


Figure 6. Submicrometer tip of an RIE sharpened needle. The tip is 200 nm wide.

IV. FLEXIBLE POLYIMIDE BASED INTERCONNECTION

A flexible polyimide-based interconnect scheme was developed to connect isolated needle-like microelectrodes and is described in detail in [10]. A simple fabrication approach allows the integration of micro-machined silicon needles with a larger silicon base designed to carry elements such as amplifiers, battery or memory. The interconnecting scheme uses two polyimide layers to sandwich a metallic layer. The metal layer forms the electrical connection between the silicon base and the needle, while the polyimide layers provide flexible insulation. A schematic of the device is shown in figure 7.

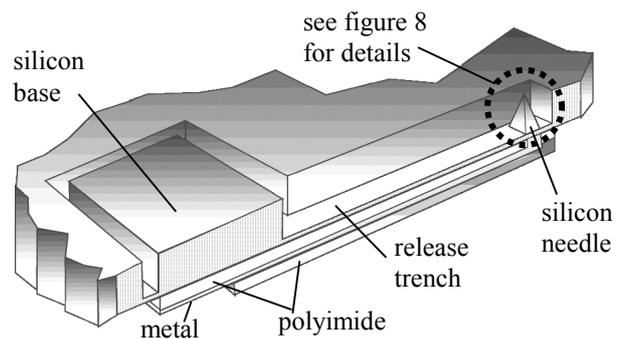


Figure 7. Schematic of the flexible neural implant device. The device consists of a large silicon base, a metallic wire encapsulated between two polyimide layers and silicon needle.

The above described DRIE process is applied to the fabrication process of the flexible interconnects (figure 7). SEM photographs of the 480 μm long pillars, which form the needle after

RIE sharpening, can be seen in figure 8. Again, for the same reasons as described above, protecting pillars are used (figure 8a). Single pillars result in a negative profile (figure 8b).

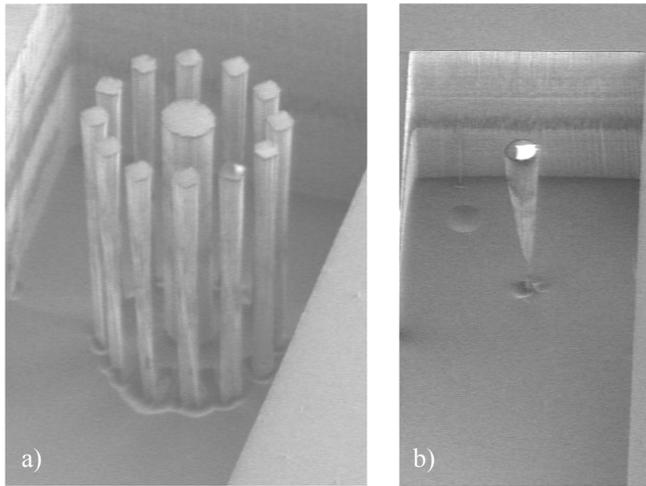


Figure 8. DRIE fabricated 480 μm tall pillars, which are part of the flexible polyimide based interconnection scheme. The trench is 500 μm wide. a) A straight profile is obtained with protecting pillars around the center pillar. b) Using the center pillar only results in a negative profile.

V. CONCLUSION

A technique to produce submicrometer high aspect ratio silicon needles has been presented. Arrays of 230 μm long and 200 nm wide needles were fabricated. Also, 480 μm long single needles have been integrated into the fabrication process of flexible interconnection devices.

Additional advantage of replacing the dicing saw with the DRIE process is the possibility of versatile design of needle arrays.

The long term goal of our research is to build stand-alone implantable sensing units made of probes, amplifiers, and memory components, with the specific goal to allow intracellular recording from freely behaving animals.

For intracellular recording, the silicon needles need to be covered with metal and nitride as described in [8]. This is necessary to enhance the electrical properties of the metal-electrolyte interface (needle and fluid within cell) and to insulate the stump of the needle to obtain electrical signals from the inside of the cell only. Integrating these processes with the flexible interconnection device is our goal for the near future.

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REFERENCES

- [1] K. T. Brown, and D. G. Flaming, New microelectrode techniques for intracellular work in small cell, *Neuroscience*, 2 813-827 (1977).
- [2] D. A. Robinson, The electrical properties of metal electrodes, *Proceedings of the IEEE*, 56, 1065-1071 (1968).
- [3] D.J. Anderson, K. Najafi, S.J. Tanghe, D.A. Evans, K.L. Levy, J.F. Hetke, X. Xue, J.J. Zappia, K.D. Wise, Batch fabricated thin-film electrodes for stimulation of the central auditory system, *IEEE-Transactions-on-Biomedical-Engineering*, 36, 693–704 (1989).
- [4] P.K. Campbell, K.E. Jones, R.J. Huber, K.W. Horch, and R.A. Normann, A silicon-based, three-dimensional neural interface: manufacturing processes for an intracortical electrode array, *IEEE-Transactions-on-Biomedical-Engineering*, 38, 758-768 (1991).
- [5] G. Ensell, D. J. Banks, D. J. Ewins, W. Balachandran, P. R. Richards, 'Silicon based microelectrodes for neurophysiology fabricated using a gold metallization/nitride passivation system', *Journal of Microelectromechanical Systems*, Vol. 5, pp. 117-121, 1996.
- [6] G.T.A. Kovacs, C.W. Storment, M. Halks-Miller, C.R. Jr. Belczynski, C.C.D. Santana, E.R. Lewis, N.I. Maluf, Silicon-substrate microelectrode arrays for parallel recording of neural activity in peripheral and cranial nerves, *IEEE-Transactions-on-Biomedical-Engineering*, 41, 567–577 (1994).
- [7] P.J. Rousche, D.S. Pellinen, D.P. Jr. Pivin, J.C. Williams, R.J. Vetter, D.R. Kirke, Flexible polyimide-based intracortical electrode arrays with bioactive capability, *IEEE-Transactions-on-Biomedical-Engineering*, 48, 361–371 (2001).
- [8] Y. Hanein, U. Lang, J. Theobald, R. Wyeth, K.F. Böhringer, T. Daniel, D.D. Denton, and A.O.D. Willows, Intracellular recording with high aspect ratio MEMS neuronal probes, *Proceedings of the International Conference on Solid-State Sensors and Actuators (Transducers)*, 2001, Munich, Germany.
- [9] Y. Hanein, K.F. Böhringer, R.C. Wyeth, and A.O.D. Willows, Towards MEMS Probes for intracellular recording, *Sensors Update* 10, 1-29 (2002).
- [10] G. Holman, Y. Hanein, R. C. Wyeth, A. O. D. Willows, D. D. Denton, K. F. Böhringer, 'Silicon micro-needles with flexible interconnections', *Proceedings of the 2nd Annual International Conference On Microtechnologies in Medicine and Biology*, Madison, Wisconsin, USA, pp. 255-260, 2002.