FLEXIBLE MICRONEEDLE ELECTRODE ARRAY BASED-ON PARYLENE SUBSTRATE

Renxin Wang[1], Zewen Wei[2], Wei Wang[1], Zhihong Li[1]

[1] *National Key Laboratory of Science and Technology on Micro/Nano Fabrication, Institute of Microelectronics, Peking University, Beijing, China ,*

[2]*National Center for Nanoscience and Technology, Beijing, China*

ABSTRACT

We present a parylene-based microneedle electrode array (MNEA). The silicon microneedle electrode array is formed on the glass substrate, packaged by parylene and released from glass substrate. This structure combines the flexibility of parylene substrate and the rigidity of silicon needle. The impedance and penetration tests validate that the flexible MNEA is promising in transdermal drug delivery and electroporation applications.

KEYWORDS

Microneedle, Flexible, Electrode array, Parylene, Transdermal

INTRODUCTION

Recently, MNEAs are applied in transdermal drug delivery and electroporation [1]. However, most of these MNEAs are based on rigid substrate that could not conform to natural shape of target objects. In contrary, flexible chips with flat electrodes afford low invasiveness and good conformation but are lacking in physically transdermal capability [2]. To address these problems, S. Choi presented a flexible MNEA with Ni electrode to enhance the strength of needle [3], but Ni was not biocompatible. In our previous work, a 3D flexible MNEA with silicon needle was presented [4], but the needles are too short for transdermal application. In this paper, we have designed, fabricated and characterized a flexible parylene-based MNEA for transdermal electroporation application.

FABRICATION

The fabrication process is schematically presented in Figure 1. A 400 µm-thick Silicon wafer with 100 nm SiO_2 and 100 nm Si_3N_4 on the front was bonded with glass. SiO_2/Si_3N_4 was patterned using lithography and reactive ion etching to form the KOH mask. Then 320 µm-deep silicon was etched by KOH (Figure 1.1). Silicon was diced with remained thickness of 80 µm (Figure 1.2). The 80 µm-deep silicon was etched by KOH and independent silicon microneedle array was formed (Figure 1.3). The metal was deposited and patterned by lift-off process to cover the silicon needles and form the connection lines. Then 4µm gold was electroplated on the metal layer. Sequentially, 10 µm-deep glass was isotropically etched by HF. Therefore, 10 µm-wide undercut beneath silicon needles and metal lines was formed. Here, rigid MNEA without parylene was obtained (Figure 1.4). The 8 µm-thick parylene was deposited and patterned using lithography and oxygen plasma. Here, rigid MNEA with parylene was obtained (Figure 1.5). Finally, the glass substrate was removed by HF. Meanwhile, silicon needles and metal lines were packed by parylene layer and released along with the whole chip. Thus flexible MNEA was obtained (Figure 1.6).

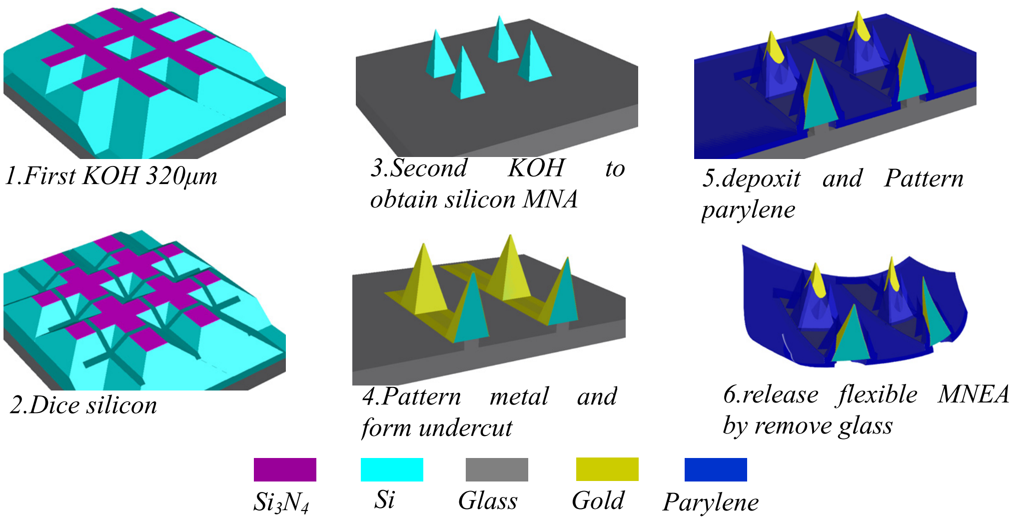

Figure 1: Schematic fabrication process

RESULTS AND DISCUSSIONS

Figure 2 shows the profile of diced silicon array and independent silicon microneedle array with height of 190 µm. Here, the interval of silicon needles was 340 µm, whereas 500-µm interval would be required if just square mask was utilized to get the same height [5]. By the introduction of dicing process, the interval of needles could be reduced, which meant the density of microneedles could be increased. Moreover, the height and interval could be adjusted to meet versatile needs.

As shown in Figure 3, after lift-off and electroplating, the electrode metal conformed to the tips array well. The thick gold layer was electroplated for two purposes: one was to make the metal line stronger to accomplish the final releasing; the other was to afford large current which was required in electroporation application.

The SEM micrograph of the front side in Figure 4 shows that parylene was patterned. The bright area indicates the exposed electrode, whereas the dark area indicates the covering parylene.

The SEM micrograph of the backside in Figure 5 shows that silicon needles and metal lines were packed by parylene and released along with the chip after the glass was removed. The red arrows indicate the positions of silicon needles and metal lines respectively.

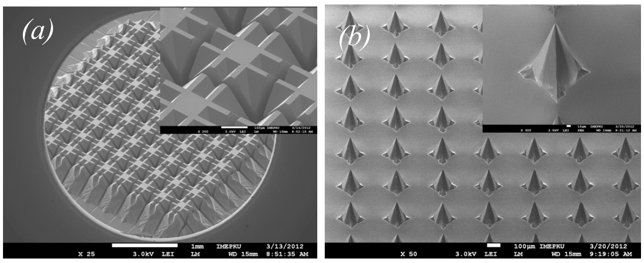

Figure 2: (a) diced silicon array; (b)Silicon microneedle array

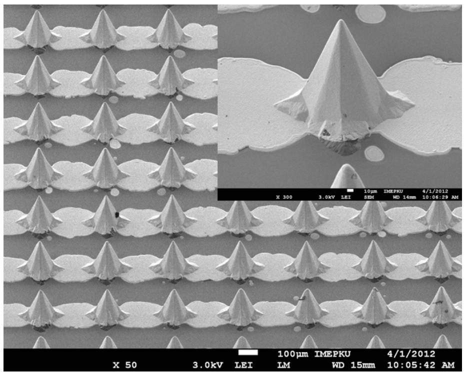

Figure 3: SEM of MNEA without Parylene

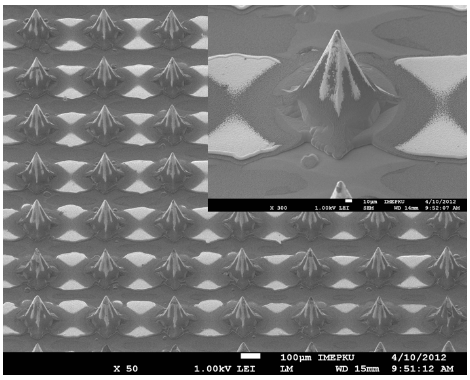

Figure 4: Front of flexible MNEA: Parylene was patterned.

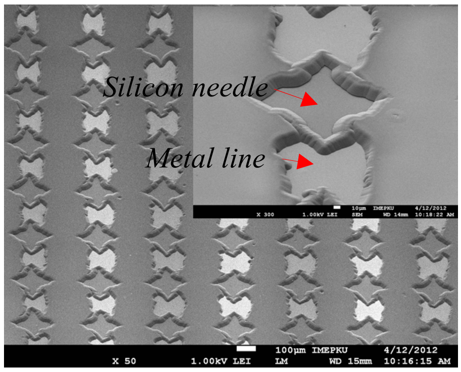

Figure 5: Backside of flexible MNEA

Photos of rigid MNEA with parylene and flexible MNEA chip are shown in Figure 6. The MNEA consisted of 9×9 microneedle electrodes, which were divided into two ports as shown in Figure 6.a. The flexible MNEA could be distorted easily without damage due to good extensibility of gold as shown in Figure 6.b. The microneedles are clearly demonstrated in the magnifying image.

The impedance of rigid MNEA without parylene, rigid MNEA with parylene, and flexible MNEA in PBS were characterized, and the magnitude were 118 Ω, 430 Ω and 146 Ω respectively, at the typical frequency of 1 KHz (Figure 7). Flexible MNEA showed significantly lower impedance than rigid MNEA with parylene, probably due to the conducting backside, which could be insulated by another parylene layer if necessary.

Flexible MNEAs with naked dye were pressed on the muscle of the pig. The result (as shown in Figure 8.a) indicated that flexible MNEA penetrated into the tissue with spots left. Figure 8.b shows MNEA retained previous structure and profile without observable damage.

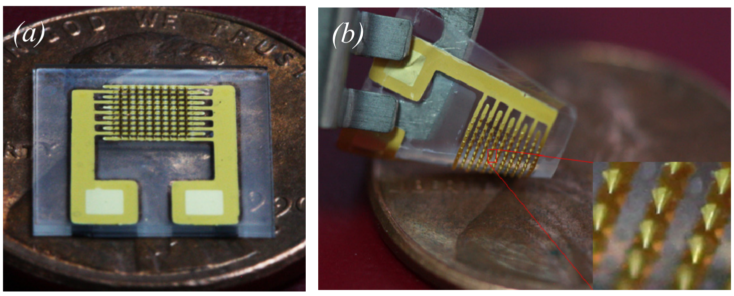

Figure 6: Photos of rigid and flexible MNEA: (a)Rigid MNEA with parylene; (b)Flexible MNEA

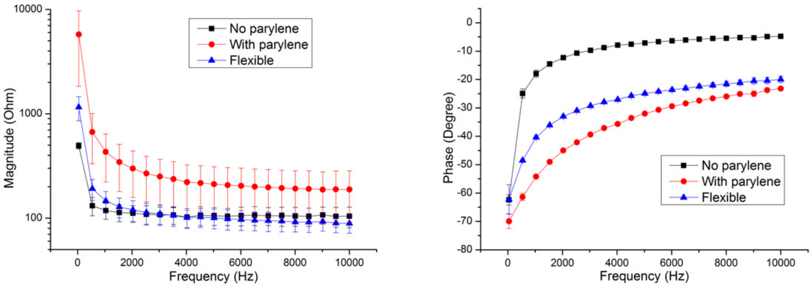

Figure 7: Impedances contrast of rigid and flexible MNEA

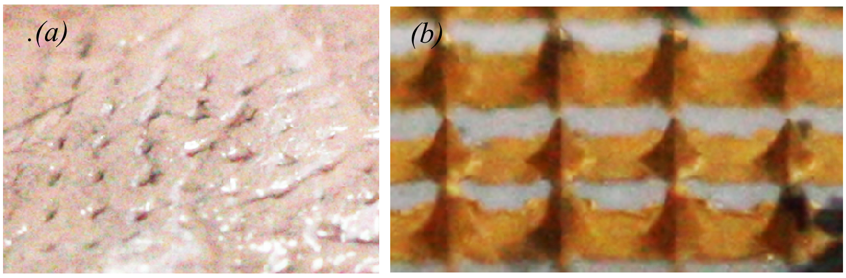

Figure 8: Penetration test of flexible MNEA:(a) spots indicated that flexible MNEA penetrated into tissue;(b)After penetration, MNEA retained previous structure and profile without obvious damage

CONCLUSION

A flexible microneedle electrode array for use of transdermal electroporation was successfully fabricated, which had flexible parylene substrate and rigid silicon microneedles. The impedance spectroscopy indicated good conductivity of the flexible MNEA. The MNEA was penetrated successfully into pig muscle, and maintained the electrical functionality necessary after penetration.

ACKNOWLEDGEMENT

This work was supported by the National Basic Research Program of China (Grant No. 2011CB707505) and the National Natural Science Foundation of China (Grant No. 61176111). The authors would like to thank the stuff in the National Key Laboratory of Science and Technology on Micro/Nano Fabrication in Peking University for their valuable assistance in fabrication process. The authors would also like to thank Huaiqiang Yu in Peking University for his helps in impedance test.

REFERENCES

[1] N.Wilke *et al.*, *Silicon microneedle electrode array with temperature monitoring for electroporation*, Sensors and Actuators A 123–124, Elsevier Science, pp. 319–325, (2005)

[2] Z. Wei *et al.*, *A parylene-based flexible electroporation chip applicable for in vivo gene and sirna delivery*, Transducers2011, IEEE, pp,1942-1945, (2011)

[3] Seong-O Choi *et al.*, *A polymeric electroporation microneedle array for enhanced intracellular delivery*, μtas2008, RSC Publishing, pp.1263-1265, (2008)

[4] Z. Li *et al.*, *Fabrication and properties of 3d flexible parylene-based microelectrode array with silicon tips*, MEMS2011, IEEE, pp.253-256, (2011)

[5] N. Wilke *et al.*, *Process optimization and characterization of silicon microneedles fabricated by wet etch technology*, Microelectronics Journal 36, IEEE, pp.650–656, (2005)

CONTACT

Zhihong Li Tel:86-10-62752536 Email: zhhli@pku.edu.cn