LOCALIZED STIMULATION OF AND RECORDING FROM NEURAL CELLS WITH FLUID INJECTABLE NEURONAL MICRONEEDLES

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ABSTRACT

A neuronal microneedle, a single-crystalline silicon microneedle with fluidic microchannels and microelectrodes, is developed for localized stimulation of and recording from neural cells. The neuronal microneedle delivers drugs such as excitatory amino acids at the cellular level as well as electrically records neural signals from neural cells. The fluidic behavior, the mechanical stability, and the electrode-electrolyte interface impedance of the fabricated neuronal microneedle were characterized, respectively. Then, the neural cell responses of a brain of a male Sprague-Dawley rat to a 25μM kainic acid (KA) stimulus were acutely monitored by using the developed neuronal microneedle.

Keywords: Kainic acid, Microchannel, Microelectrode, Neuronal microneedle

1. INTRODUCTION

Miniaturized medical and biomedical instruments from the MEMS technology allow the precise control of the depth and location of the device and the amount of fluid to be injected or extracted due to their small feature size [1]. Microneedles are used to deliver agents through the skin, into a blood vessel, or into a cell, or to extract fluids. Microneedles are also useful tools for introducing pharmaceutic solutions at the cellular level. In this paper, the neuronal microneedle is designed and fabricated on the basis of the silicon microneedle [2] and the microelectrode on a roughened polysilicon film [3]. The microneedle with both fluid microchannels and electrical microelectrodes injects chemical agents and records the extracellular response of neural cells in a localized region.

2. EXPERIMENTAL

The processes for the neuronal microneedle are performed with only one double-polished (100) silicon wafer. The schematic of the neuronal microneedle and process flow are shown in figure 1. The buried microchannel in the neuronal microneedle is fabricated by using the processes of anisotropic dry etching, sidewall passivation, isotropic dry etching, and trench-refilling with a LPCVD polysilicon film. Because the microchannel fabrication process uses the isotropic dry etch, the direction of microchannels can be oriented to any crystallographic direction in-plane. Afterward, the gold microelectrodes are fabricated top of a polysilicon film which is deposited on top of a SiO_2 film. Finally, a fluid reservoir, a handling body, and a microneedle shank of the neuronal microneedle structure is defined and released from the silicon substrate by using the anisotropic dry etch. Figure 2

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shows fabricated neuronal microneedles, next to 23 and 26 gauge needles and a Korean 100 Won coin.

The pressure drop of the microchannel in the neuronal microneedle is measured by using a syringe pump and a pressure sensor, and then the product of the Reynolds number and the Darcy friction factor of the microchannels is calculated. For the mechanical stability of the neuronal microneedle, in-plane buckling tests, out-of-plane bending fracture tests, and in-plane bending fracture tests are performed with a load cell. The electrode-electrolyte interface impedance of the roughened microelectrode is measured with an impedance analyzer (ZAHNER-electrik IM6e, Germany).

The neuronal microneedle is used to acutely monitor the neural cell response to a 25 μM KA stimulus in the somatosensory cortex of a male Sprague-Dawley rat. The KA is injected into the somatosensory cortex through the microchannel in the neuronal microneedle.

3. RESULTS AND DISCUSSION

The SEM pictures of the fabricated neuronal microneedle are shown in figure 3. The width and the thickness of the shank are 200 μm and 150 μm, respectively. The length of the shank is 3.3 mm, which was determined in consideration of the location of the somatosensory cortex of the rat. The dimension of the microelectrode is square-shaped 30 μm × 30 μm, and the distance between microelectrodes is 200 μm. The average roughness of the microelectrode is 31.4 nm. The significantly roughened polysilicon film on top of the SiO_2 film increased the effective surface area of the microelectrodes.

From the pressure difference of microchannels, the product of the Reynolds number and the Darcy friction factor of the microchannel results in 99.56. The critical buckling load of the microneedle shank is measured as 9.43 N. The neuronal microneedle shank is strong enough to endure 1.142 mN·m of out-of-plane bending moment and 0.865 mN·m of in-plane bending moment, respectively. The impedances of microelectrodes are measured in a 1 × phosphate buffered saline (1×PBS) solution, and the magnitude and the phase of the average impedance of 23 microelectrodes are 328 kΩ and - 83.5º at 1 kHz as shown in figure 4, respectively. The electrode-electrolyte interface impedance is significantly lowered without additional processes such as electroplating of platinum black and activation of iridium oxide.

The injected KA evoked neural cell responses, then the neural signals were recorded with the neuronal microneedle. As shown in figure 5, just after injection of the KA, the neural discharges from four recording microelectrodes reduce because the bulk flow of the injected KA produces mechanical effects such as pushing cells away from microelectrodes. Then, after the injected drug is spread, the neural discharges increase to about 600 spikes/min.

4. CONCLUSIONS

The neuronal microneedle which combines buried microchannels and microelectrodes is developed and demonstrated for neurophysiologic electrical recording with real time chemical stimulation at the specified brain region of a rat. Since the injection volume of drugs and the position of the microelectrode can be precisely controlled, the neuronal microneedle will enhance the functionality for the diagonistic and therapeutic applications.

ACKNOWLEDGEMENTS

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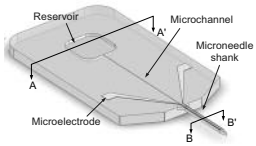
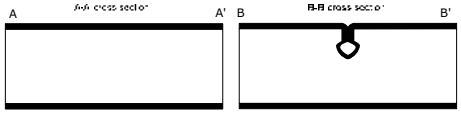
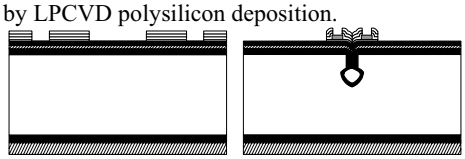


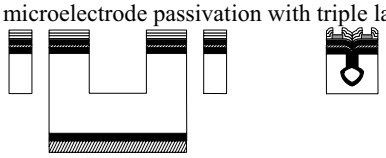
(a) schematic of a neuronal microneedle.



(b) microchannel fabrication using trench refill by LPCVD polysilicon deposition.



(c) gold microelectrode definition on a roughened polysilicon on a SiO_2 film and microelectrode passivation with triple layer.



(d) structure release with anisotropic dry etch processes.

Figure 1. Schematic and process flow of the single-crystalline silicon neuronal microneedle (not to scale).

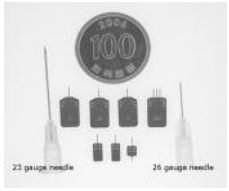
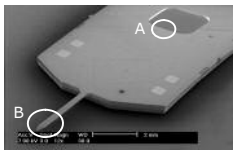
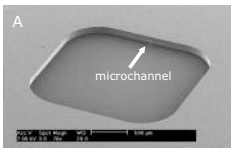


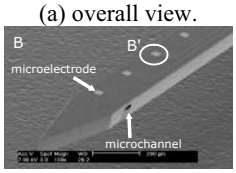
Figure 2. Photography of neuronal microneedles next to the 23 gauge and 26 gauge needles and a Korean 100 Won coin.



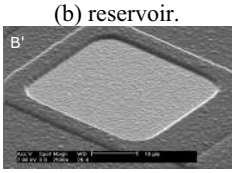
(a) overall view.



(b) reservoir.

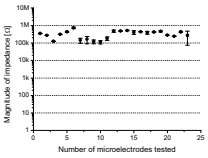


(c) end of a shank.

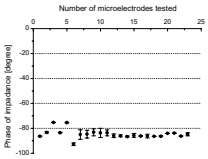


(d) microelectrode.

Figure 3. SEM of a neuronal microneedle.



(a) magnitude.



(b) phase.

Figure 4. Electrode-electrolyte interface impedance at 1 kHz.

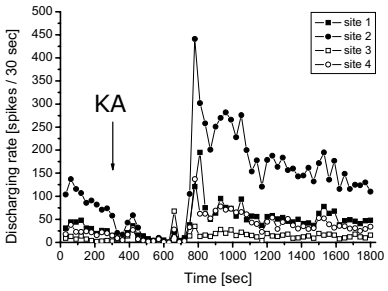


Figure 5. Neural discharges from four recording microelectrodes in the somatosensory cortex of the rat.