NOVEL PIEZOELECTRONIC MICRODEVICE FOR ELECTRICAL CELL STIMULATION

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Abstract

This paper reports a bioelectronic microdevice for electrical cell stimulation using ultrasound signals within the predefined medical frequency range. The microdevice size is comparable to a common human cell (around 1000 µm3). It is able to generate a local electric potential due to the actuation of a piezoelectric resonator that provides high-spatial resolution for the electrical stimulation. The electrical field generated by these microdevices is enough to open the voltage-gated calcium channels on the cell membrane, and therefore, electro-stimulate cells for future therapeutical applications.

Background

Our previous work related to cell stimulation was reported in various articles in the last years [1], [2]. The fabrication of piezoelectric microdevices was presented in MEMS 2021[3]. This paper shows the design, simulation and on-going fabrication of novel cell-sized piezoelectric microdevices.
Previous attempts at electro-stimulating cells using piezoelectric materials in bone cells are reported using 2D ZnO nanosheets [1] and BNNTs in osteosarcoma cells (SaOS-2) using ultrasounds signals. The results show an enhanced expression of collagen type I (COL1). BNNTs also have been used in neuronal-like and human neuroblastoma cells with ultrasounds signals as mechanical stimuli. These results presented neurite sprout 30% greater than control [4]. Furthermore, using millimeter-sized piezoelectric devices and a neural interface platform, other authors have obtained promising results on neural activity monitoring and stimulation on in-vivo rodent models [6-8]. Lastly, the usage of ZnO nanosheets has also been studied in smooth and skeletal muscle cells demonstrating stimulation triggered by the nanogenerators only on smooth muscle cells [5].

Methodology

Using silicon on insulator (SOI) wafers, the fabrication of the biomedical microdevices is divided in four stages. First, the deposition and etching of electrodes and piezoelectric material using sputtering and wet etching techniques. Then, the microdevices membrane is created using reactive ion etching (RIE) on the handle side of the wafers and, finally, the microdevices are released from the substrate using a patented procedure (WO2010112532A1). In the last step, the released microdevices are suspended in a biocompatible solution, ready to be applied to cell cultures or tissues as Figure 1 shows.

Experimental Results

Using Finite Elements Modeling (FEM) software, COMSOL Multiphysics, the expected voltage output of the microdevices under biological media is ~40 V at 1.47 MHz as shown in Figure 2. A change on the dimensions of the microdevice will allow tunability in frequency spectrum. The fabrication process and device liberation is schematically shown in Figure 3. Previous work on microfabrication of piezoelectric devices is shown in Figure 4, showing the feasibility of the on-going fabrication process. The fabricated devices will be characterized by using a medical-frequency range ultrasound generator. The resonant frequency used to design the microdevices are in the range of 1 to 3 MHz. A cell culture of Saos-2 cells will be used in combination to the released microdevices to demonstrate the stimulation of the voltage-gated ion gates of the cell membrane.

References

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[4] Ciofani, G. et al., ACS Nano 4, (2010) 6267-6277
[5] Blanquer, A. et al., Int J Mol Sci 2, (2021) 432

Figures

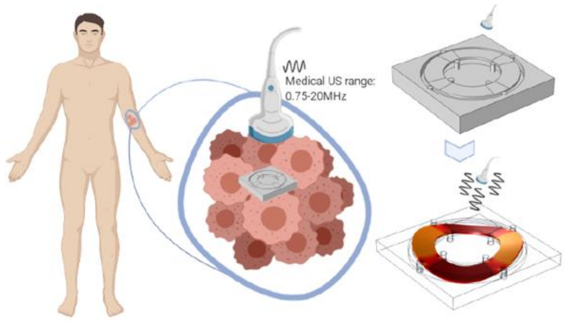

Figure 1. Final application of the presented novel microdevices for electrical cell stimulation.

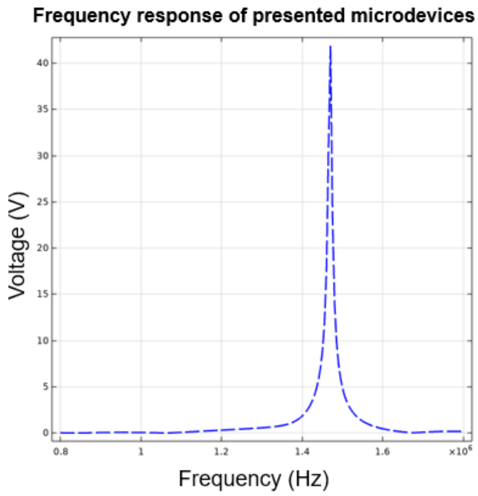

Figure 2. Simulated voltage frequency response of the novel proposed microdevices under biological media.

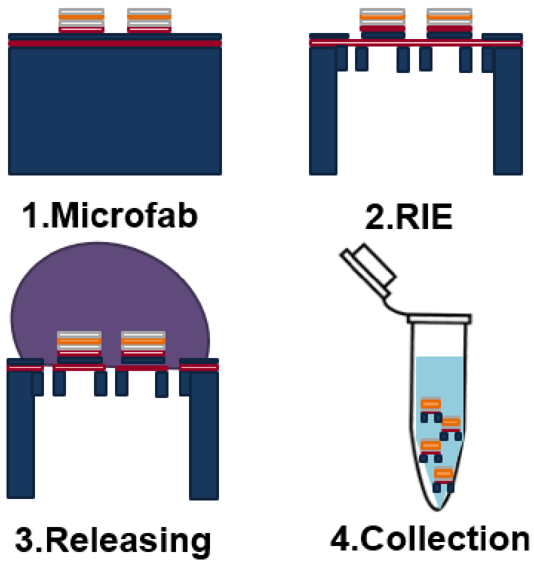

Figure 3. Simplified fabrication scheme of the novel piezoelectric bioelectronic microdevices.

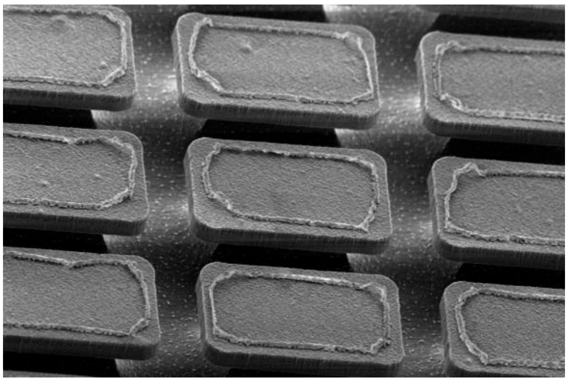

Figure 4. SEM of previous microfabrication work of piezoelectric bioelectronic microdevices.