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SELF CONTROL OF CELL ELECTROPORATION BY DIELECTROPHORESIS TRANSITION

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This paper deals with the transition of the dielectric properties of cells as a marker of their permeabilization. A demonstration of the transition between positive and negative DiElectroPhoresis (DEP) as a reaction to electroporation pulses is achieved in a microfluidic device.

Electropermeabilization of cell membrane is broadly used in cell biology for electrotransfert of genes and other molecules in vitro and in vivo [1] or for electrofusion [2]. The success rate of this technique is nevertheless highly variable, depending on the type of cells, its status in the cell cycle and on the method used. In the case of the use of conventional electroporation cuvet, the electroporation rate remains unsatisfying (if we apply an electric field for which 90% of the cells survive, the efficiency remains below 20% [3]). Several attempts to propose biochips dedicated to the electroporation have been proposed to address this issue [4]. The advantages of using a dedicated microfluidic device are i) the capability to control precisely the electrical field at the scale of the single cell [4] ii) the possibility to parallelize ([5], [6]) or serialize [7] the single cell electroporation function in order to achieve the high number of cells with a good ratio of permeabilization.

We present in this paper a novel method, implemented on a microfluidic device, that permits to control automatically and independently the level of electropermeabilization of cells. The cells are disposed in successive traps, using DEP force. Once the membrane permeabilization occurs, the dielectrical properties of cells change. If the electric field is maintained, the cells are automatically and separately expelled from the high electrical field zone. In that way, the cells are self-controlling their permeabilization level, prior to further utilization.

Fabrication of the device

The microfabrication of the device is performed on a quartz substrate. Electrodes (10 nm Ti/ 240 nm Pt) are patterned on this substrate thanks to the lift-off of a Titanium/Platinum layer sputtered on a negative resist. Channels are defined in 25µm thick SU8 thanks to photolithography. The device is packaged using a membrane of PDMS bounded irreversibly after silanization. The several steps of the fabrication process are shown on figure 1.

The figure 2 shows the simulation within the device that includes insulating SU8 structures that generate the field gradients necessary for the cell handling.

Experiment and results

The mouse fibroblast cells NIH3T3 were injected within the fluidic channel (buffer conductivity= 272µS/cm). A sinusoidal field excitation applied on the electrodes ($f=1\text{MHz}$, $V=30\text{V}$) permitted the trapping of cells by positive DEP (figure 3.a). Buffer was injected to eject untrapped cells. Electroporation pulses (10 pulses, duration 100µs, $V=75\text{V}$) were superposed to the DEP excitation. Maintaining the same level and frequency of excitation, the permeabilized cells moved progressively to the low electric field areas thanks to negative DEP (as shown on figure 3.b).

Acknowledgements

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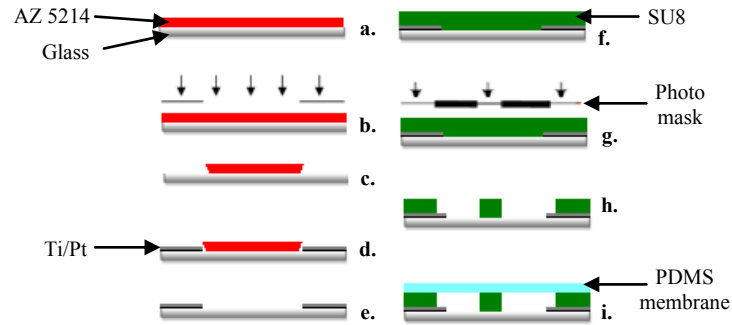


Figure 1: Process of fabrication: (a,b,c).photolithography of negative resist AZ 5214, d. Ti and Pt sputtering, e. lift-off,(f,g,h). SU8 photolithography, i. silanization and packaging with PDMS

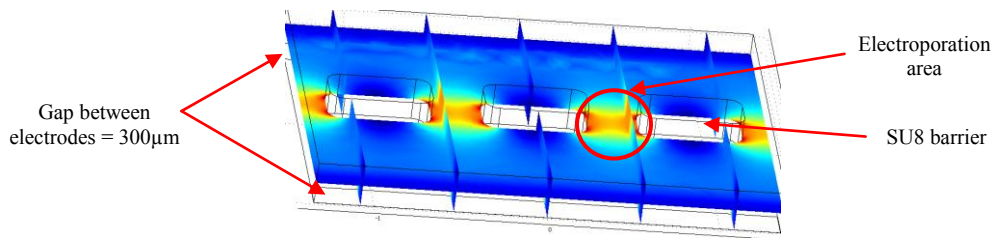


Figure 2: Simulation of the electric field

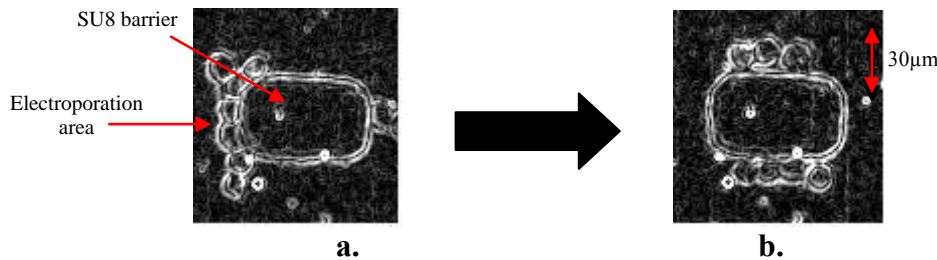


Figure 3: **a.** Before electroporation: Cells are trapped by positive DEP, **b.** Once electroporated, cells are ejected from the electroporation area by negative DEP (contour detection with Image J ©)

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