Single Cell Poly e-caprolacton (PCL) Membrane Electroporation Device for Gene Delivery

Hyunchul Jung[†], Brian E. Henslee*, Xin Hu*, L. James Lee*, and Wu Lu[†] (lu@ece.osu.edu)
[†]Department of Electrical and Computer Engineering, The Ohio State University, Columbus, OH 43210
*Department of Chemical and Biomolecular Engineering, The Ohio State University, Columbus, OH 43210

Electroporation is a widely used non-viral gene transfer method for cell transfection. Bulk electroporation techniques require a high electric field and suffer from a non-uniform electrical field distribution to cells causing poor transfection efficiency and cell viability. We have demonstrated that the transfection efficiency and uniformity can be greatly improved using membranes with micropore arrays for cell imbobilization. To more accurately probe the extracellular activities for a better understanding of electroporation process, in this study, a poly (e-caprolacton) (PCL) membrane with a single micro-pore providing localized electroporation is used for cell immobilization and gene delivery to a single cell. For device fabrication, the PCL membrane films are replicated from patterned SU-8 structure. A 5 μm diameter hollow in SU-8 with 15 um in height is transferred to a PDMS (Polydimethylsiloxane) film by soft lithography. The PDMS film with transferred circular pillar pattern is used as the mold for another replication of uniform PCL thin polymer films with a thickness of 5 to 8 um. For electroporation experiment, Opti-MEM ITM reduced-serum medium is filled into the channels of the device and the center reservoir before the DNA sample is loaded into the inlet reservoir. Figure 1 shows the cross section diagram of (a) PCL device and (b) a cell on PCL membrane. Electroporation is carried out followed by a cell culture process to check the transfection effect with dyed plasmid DNAs. Figure 2 (a) shows immobilization of single NIH 3T3 cell on the PCL membrane by vacuum. The fluorescence image of single NIH 3T3 cell after DNA delivery by electroporation in a PCL device is shown in Fig. 2 (b). Numerical simulations are performed to study the transmembrane potential distribution by solving the conductive DC mode. The single cell is modeled as a three-layer model consisting of cytoplasm, medium, and the cell membrane, respectively [1]. As shown in Fig. 3(a), the electric field becomes very strong at the center of micropore and therefore, more genes can be delivered to the cell to enhance the transfection efficiency. The transmembrane potential distribution as a function of θ, the polar angle of the electric field to the cell, is shown in Fig 3 (b). The concentrated electric field by micropore produces higher transmembrane potential which results in higher transfection efficiency. The discussion on impedance spectroscopy of the single cell PCL device before and after electroporation will be presented at the conference.

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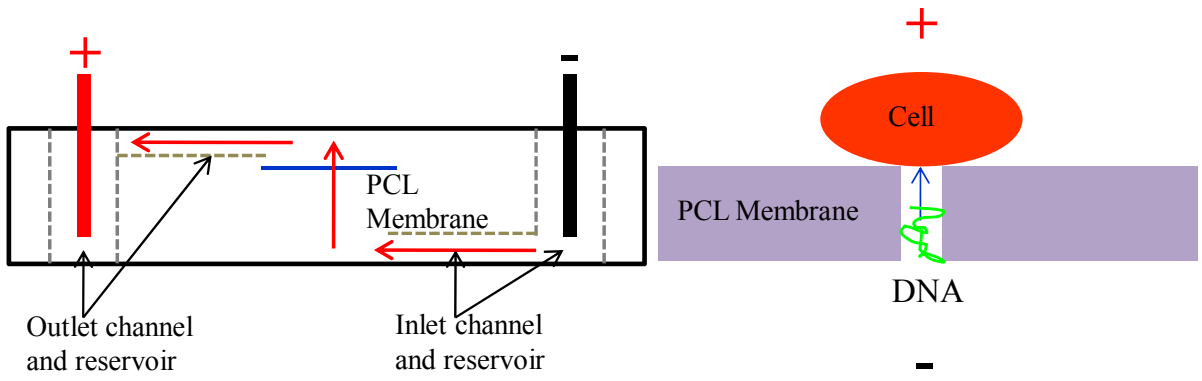
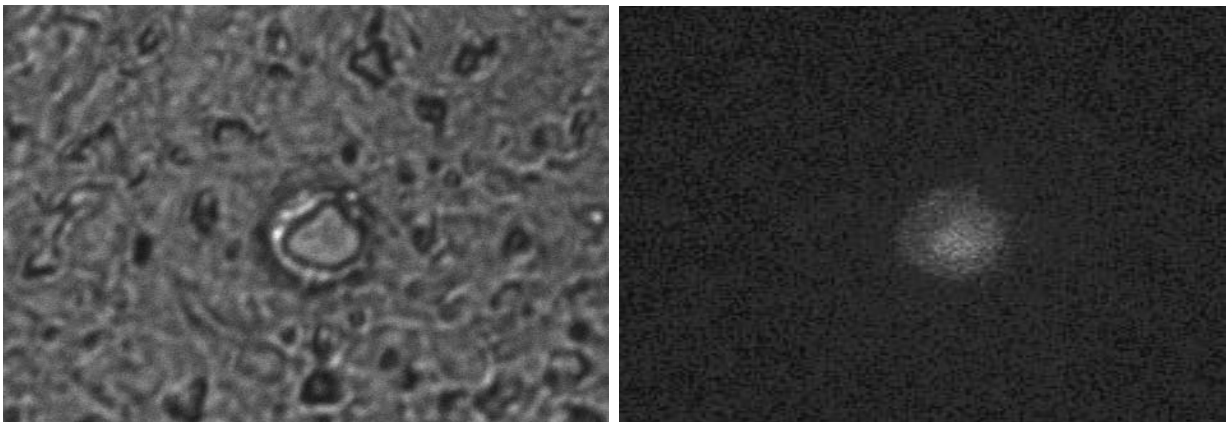
[1] Z. Fei, X. Hu, H. W. Choi, S. Wang, D. F. Farson, and L. J. Lee, *Anal. Chemistry* **82**(1), 353-358 (2010).



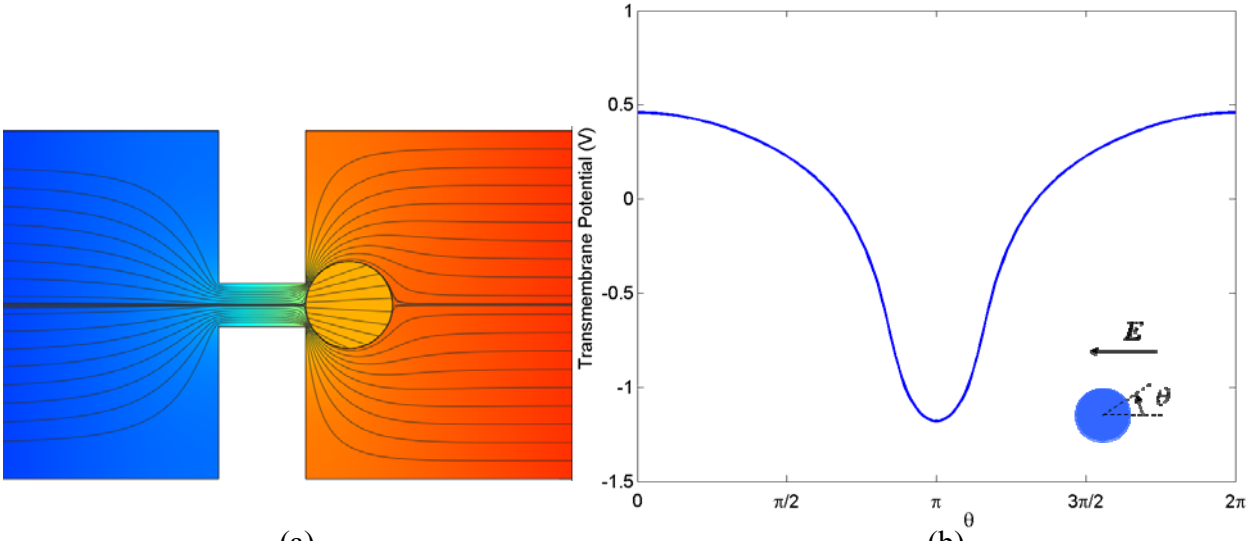
(a) (b)

Fig 1. Cross section diagram of (a) PCL device and (b) NIH 3T3 cell on PCL membrane.



(a) (b)

Fig 2. (a) Optical image of NIH 3T3 cell immobilized on the PCL membrane and (b) Fluorescence image of the cell after electroporation.



(a) (b)

Fig. 3. Simulation results of the single cell by the COMSOL software: (a) electric potential distribution and electric lines across/around single cell and (b) transmembrane potential distribution.