Cell Electroporation – A Diffusion Process or A Drive-In Process?

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Various attempts have been made in the past to develop micro-fluidic devices for cell electroporation for drug and gene delivery. Such devices, generally through vacuum for cell trapping, however, have poor control of cells and introduce deformation of cells during electroporation [1]. In this work, we employ an optical tweezer to facilitate the control of cell position at micro/nano-channels instead of using a pressure difference and apply the electric field across the cell for localized drug/gene delivery. We focus on the mechanism of electroporation of cells at nature state in devices with different scales.

For device fabrication, SU-8 negative tone resist is coated with the intention to attain variable thicknesses ranging from 100 nm to 5 μm thickness on Si substrates. Optical and ebeam lithography are used to pattern 100 nm to 5 μm wide and high lines. After that, a higher viscous SU-8 resist is coated to have 25 μm thickness on top of the lines. After aligning and exposure using a photo mask, 40 μm wide and 25 μm high patterns are connected to the lines. Using SU-8 patterns on Si as a mold, PDMS-based micro/nanochannels are replicated. These micro/nanochannels are sealed with a 160 μm thickness cover slide. For electroporation experiment, Opti-MEM ITM reduced-serum medium is filled into the channels of the device and then a cell is positioned by the optical tweezers at the micro/nano-channels shown in Fig. 1. After that, a short electric pulse is applied to the cell for drug/gene delivery. The time series video capture (Fig. 2) fluorescent images of single K562 cell showed the Propidium iodide (PI) dye predominantly entering the cell by electroporation through a 5 μm and 1 μm micro-channels. As can be seen in Fig. 2, two scales of micro-channels exhibit different drug/gene transfer mechanisms at their critical electric fields. The 5 μm device shows a diffusion dominant process while the 1 μm device shows a drive-in process at the beginning and becomes diffusion dominant through the cell. The critical electric strength and drug/gene transfer mechanism for single cell electroporation with PI dyes and DNAs are characterized in electroporation devices with different channel sizes (100nm to 5μm). The experiments are coupled with simulation studies on electric field distribution and transmembrane potential distribution by solving conductive DC mode at different device scales. Comparing simulation results to experiment results, we show how the scaling of devices could affect the cell electroporation.

This work is supported by NSF Grant EEC-0914790.
[1] Michelle Khine, Adrian Lau, Cristian Ionescu-Zanetti, Jeonggi Seo and Luke P. Lee, Lab on a chip, Vol.5, 38-43 (2005).

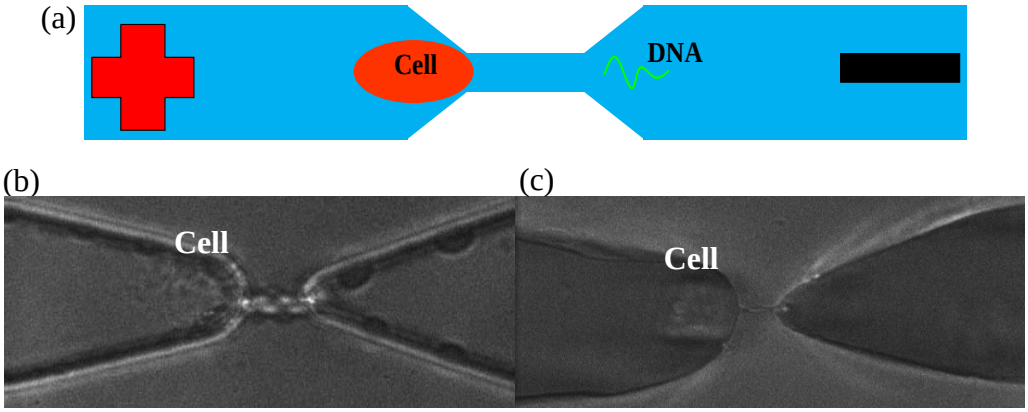

Figure 1: (a) Schematic of the device set-up and Optical image of K562 cell positioned by optical tweezer at (b) 5 µm and (c) 1 µm channel.

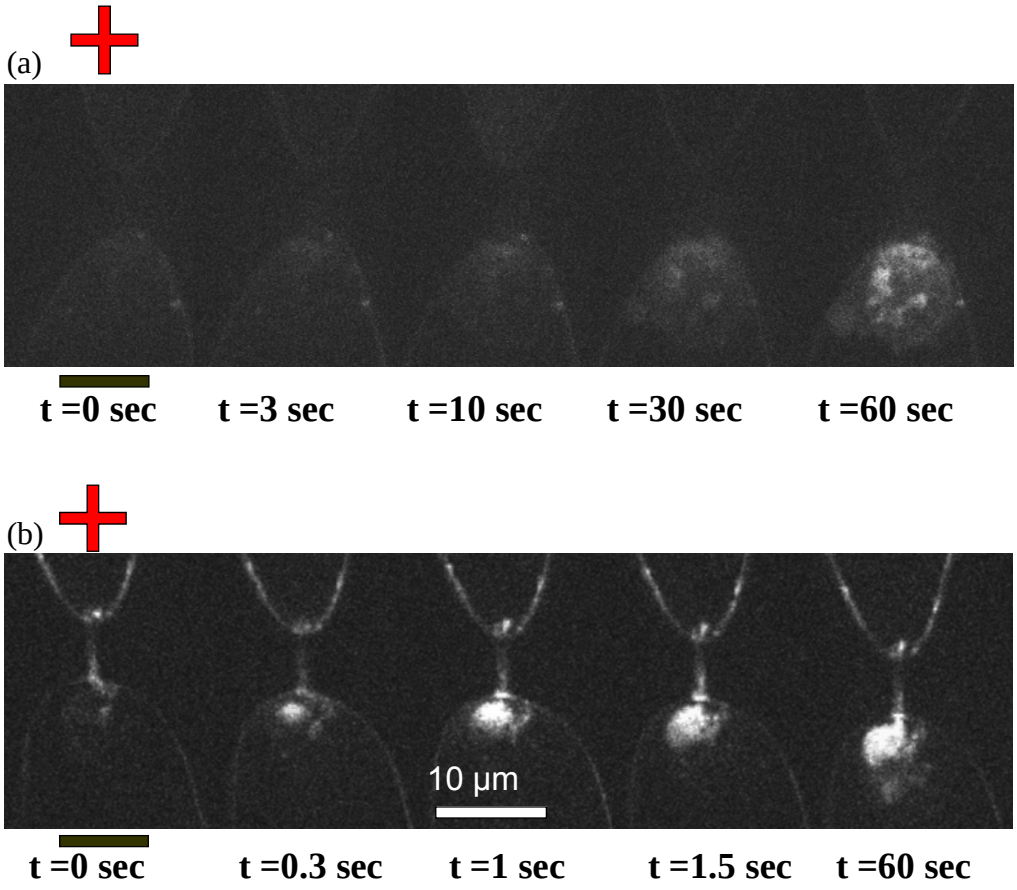

Figure 2: Time series dye entrance: (a) 5 µm and (b) 1 µm devices.