Measurement and Analysis of Joule heating in localized cellular micro/nanochannel electroporation

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Abstract: Localized Electroporation by nano/microchannels has various advantages over bulk electroporation (BEP) because of its minimized cell perturbation and controllable cargo delivery. Joule heating and the temperature rise inside the microfluidic device induced by the electric field affect the cell viability and protein denaturation. Recently, the heat shock to the cell caused by localized electroporation was found to be an important factor that stimulates the cell to secrete more exosome which showed profound impact on exosome-based therapy[1]. However, a comprehensive quantification and analysis of Joule heating on a cellular level during localized cellular electroporation have not been yet explored.

In this study, we fabricated a localized electroporation device by the process described in our previous work[2]. In brief, a silicone mold with arrays of small sub-micron wires in between two large micron wires was first processed. The patterns on Si mold was replicated to PDMS and the final device was obtained by bonding the PDMS layer with a glass slide (Fig.1a&b). The localized electroporation was performed on a fluorescence microscope with EMCCD camera (Fig.1c). The fluorescence images were taken by every 10 ms during electroporation and analyzed by MATLAB. Fig. 1d showed the real-time analysis of a fluorescence labeled oligonucleotides being injected into the cell by localized electroporation.

Rhodamine B (RhB) was used as a temperature sensitive dye for fluorescently labeling the cell[3]. A calibration curve that converts the fluorescence intensity to the temperature was generated by heating the whole microfluidic device to a stabilized temperature while recording the fluorescence intensity and the temperature simultaneously (Fig.2a). The fluorescence intensity decreased with increasing temperature. The heat shock of the cell was observed during the cargo delivery by localized electroporation (Fig.2b). The temperature of the cell membrane close to the small channel increased much higher than that far away from the small channel. Also, the heat dissipated rapidly after electroporation stopped. The Finite Element Analysis (FEA) showed that the localized heating of the cell was because due to the concentrated heat generation inside the small channel (Fig.2c). This study provides a method to further understand the impact of Joule heating on exosome production during localized cellular electroporation.

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[1] Yang, Z. et al. Nat Biomed Eng 4, 69–83 (2020).
[2] Zhao, X. et al. Adv. Sci. 2, 1500111 (2015).
[3] Moreau, D.et al. Biomed. Opt. Express 6, 4105 (2015).

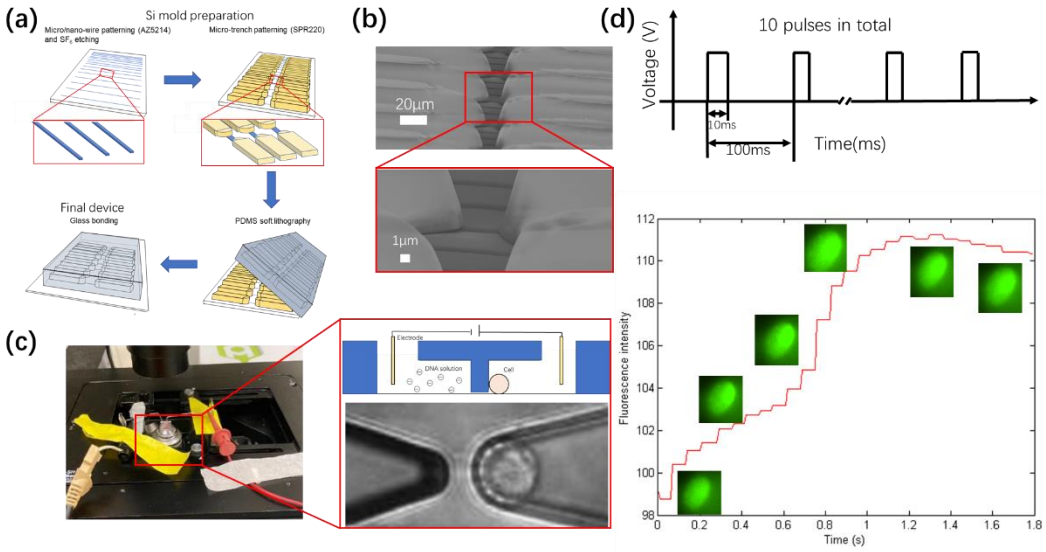

Figure 1: *Micro/nano fabrication and experimental setup of localized electroporation:* (a) fabrication process; (b) SEM images of the Si mold; (c) set-up of electroporation on a fluorescence microscope; (d) Delivery of a fluorescence-labeled oligonucleotides (FAM-ODN) into a single cell.

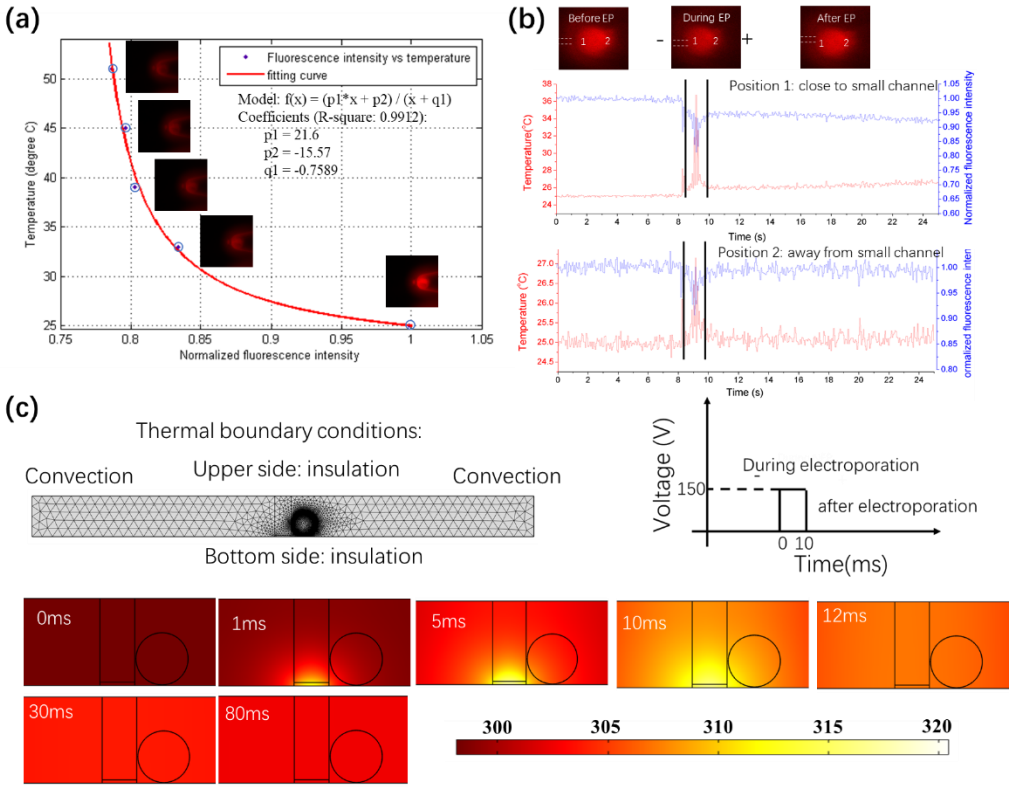

Figure 2: Experimental measurement and FEM analysis of Joule heating when localized electroporation happened to the cell: (a) Calibration curve for converting fluorescence intensity to temperature; (b) localized heat shock of the cell before, during and after electroporation; (c) FEA of the Joule heating when a single pulse of square wave is applied.