DEP Cell-patterning for Controlling Cellular Organization

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The ability to place cells at specific locations on a substrate is a useful tool to study and engineer interactions between cells [1], perform image-based cell selection [2], and create cell-based biosensors [3]. The ability to pattern with single-cell resolution is necessary in order to perform studies of single-cell physiology in which these cells are interacting with other cells. We have previously created nDEP-based traps that were used to hold single micron-size beads at chosen locations on a substrate [4]. We have recently extended this work by modifying the design to allow us to manipulate and pattern single cells. We accomplished this modification by adding interdigitated electrodes to minimize non-specific cell adhesion and determining operating parameters that minimized heating and electric field exposure. The resulting structures are termed nDEP microwells to reflect that fact that they present an electrical microwell to incoming cells, allowing only cell-substrate attachment inside the DEP trap. With these nDEP microwells we have been able to place non-adherent cells and pattern adherent cells (Figure 1). Additionally, we have demonstrated that our cell-patterning technique does not affect gross cell phenotype as measured by morphology and proliferation. Finally, we have developed a method that combines pressure-driven and convective flows to manipulate cells in two dimensions (Figure 2).

Figure 1: Phase and fluorescent images of GFP-expressing HeLa cells trapped in an nDEP microwell array, showing that they exhibit normal morphology and proliferation over 4 days after being trapped at 1 Vpp and 10 MHz. Arrows in the Day 1 figure (top, right) show the displacement of cells that moved out of the trap. The scale bar represents 100 µm.

Figure 2: Top: Schematic of operating procedure. In the "Fill" step, orange lines show the motion of the fluid while red lines show the motion of (two) untrapped cells. The flow must be kept slow enough (< 5 µm/s) so that cells do not get lifted with the flow. Bottom: Use of convective flow to pattern cells. (a) → (b): Convective flow pushes untrapped cells towards the center of the electrode array (not shown at this scale) when electrodes are driven at 2.5 Vpp. Blue arrows show the movement of cells between frames. This flow is used to align cells with the trap. (b) → (c): Transition is made to pressure-driven flow using a syringe pump. All untrapped cells move in the same direction, along the array. The pressure-driven flow is used to push aligned cells into the traps. The scale bar represents 25 µm.

REFERENCES