Design and Optimization of High-throughput Cell Pairing Chip for Cell Fusions

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High-throughput single cell-cell pairing is strongly desired for the study of intercellular communications and cell fusion [1]. For example, precise single cell–cell pairing could drastically improve the cell fusion efficiency. Dielectrophoresis (DEP) is an approach that can manipulate cells with label free character, and it is compatible with live cells and easy to operate [2]. In our previous work, we proposed and fabricated a novel planar DEP-based microfluidic chip for high-throughput single cell-cell pairing (74.2% single cell-cell pairing efficiency) [3]. The microchip had numerous cell trapping and pairing microwells within a 1×1.5 cm working area and could be bonded with a PDMS microfluidic channel (Fig. 1a). By appropriate ac signal input to a two-pair interdigitated array electrode, two cells in array could be trapped and paired in proximity by p-DEP (Fig. 1b). Single cell-cell contact was further accomplished in a microbaffle structure. To further improve chip performance, such as the cell trapping, pairing and contact efficiencies, device optimizations are needed.

In a DEP-based cell pairing microchip, we use two neighboring DEP electrode pairs to trap two cells in proximity (Fig. 2a). When ac signal is applied on the chip for p-DEP cell trapping, it is important to understand the electric field distribution in the electrodes. Because two different types of cells are trapped consecutively in close proximity, it is critical to avoid interferences when biasing the DEP electrode pairs for high throughput and efficiency in cell-cell pairing. Electromagnetic simulation was performed with COMSOL Multiphysics® to calculate the electric field distribution during p-DEP trapping process (see an example in Fig. 2b), and the simulation results were used to guide the electrode design and biasing scheme.

The baffle structure in the device is also critical for cell contact after cell trapping. We optimized the microbaffle structure to improve the single cell-cell contact efficiency (Fig. 3). The cell fusions after cell-cell contact were induced by in-situ heating (Fig. 4) under the presence of polyethylene glycol. A conductive and transparent ITO heating film was placed under the chip and a temperature of 37.2 °C on the working area was obtained by adjusting the input power. The design, optimization, fabrication, and characterization of this cell fusion chip will be discussed in detail.

References

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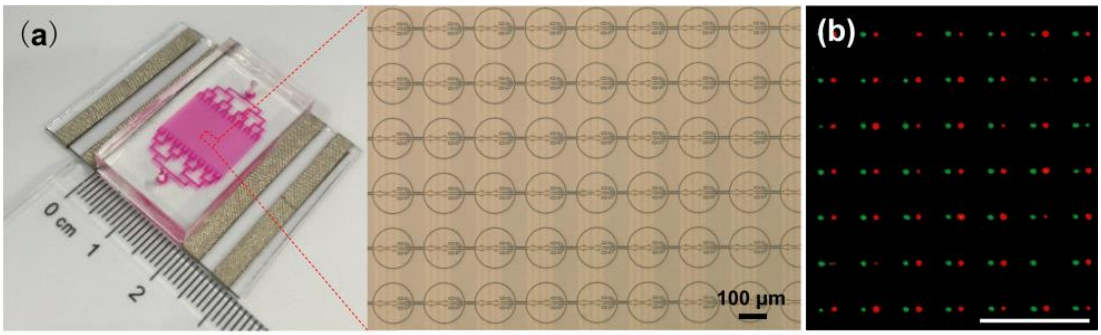

Fig. 1 (a) Photo and optical images of the planar DEP-based microfluidic chip for high-throughput single cell-cell pairing. (b) Merged fluorescence image of high-throughput cell pairing. Scale bar: 500 μm. [3]

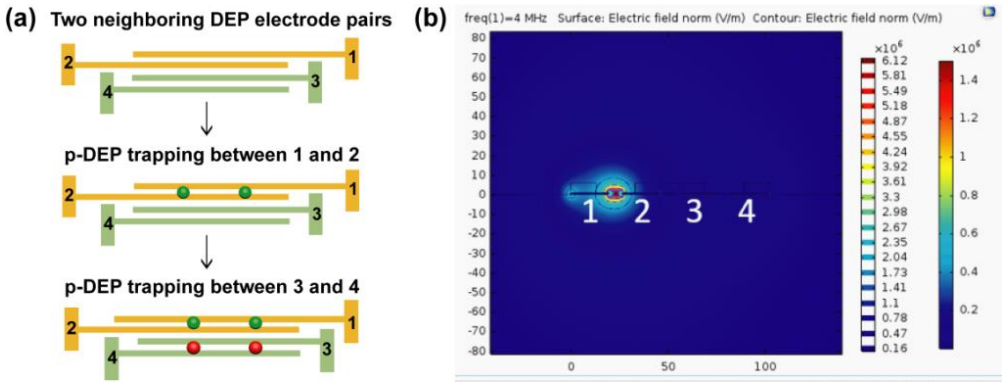

Fig. 2 (a) Scheme of a DEP-based cell pairing process. (b) Simulation results of electric field distribution. (When electrode 1 was applied to an ac signal, and 2, 3, 4 were grounded together.)

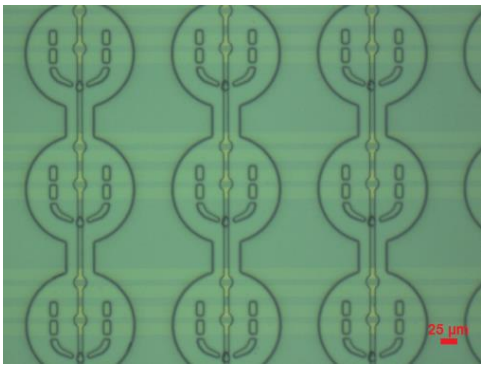

Fig. 3 Optical image of a fabricated device with optimized structure.

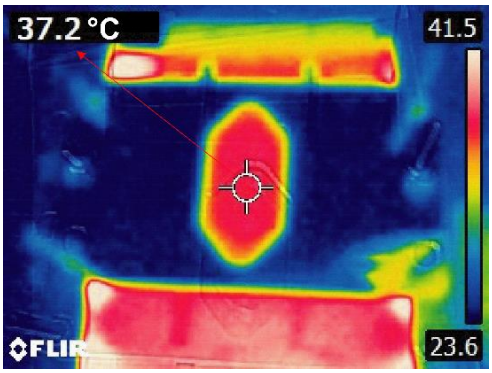

Fig. 4 Infrared thermal image of the chip with underlayer heating electrodes.