Development of a Single Cell Trapping Microfluidic Device

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Abstract

Array-based technologies are important for many applications in drug discovery, microbiology and cell biology. A large-scale array of single cells allows high-throughput monitoring of characteristics or behaviors of individual cells in parallel, avoiding the lack of cell specificity inherent to traditional bulk measurement methods. In this study, we designed a passive-pumping microfluidic device for trapping single cells in an array (Figure 1), and used the CFD module in the COMSOL Multiphysics® software to simulate the velocity and pressure fields of the laminar flow within the device. We also studied the effect of trapped cells on the surrounding velocity field. Figure 2 shows the geometry of the single-layer flowing channels (35 μm in height) and the dual-layer trapping array. To increase the trapping efficiency, we designed a 10 μm central gap for each pair of trapping posts, and a 2.5 μm gap between the trapping posts and the cover glass. The velocity fields obtained from the COMSOL simulation are shown in Figure 3. The maximum velocity between different pairs of traps is up to 800 μm/s, compared to ~300 μm/s in the central gap (Figure 3C). When a cell is trapped, it partially occludes the gap and reduces the velocity through the central gap to less than 150 μm/s. As a result, the probability of cells entering an occupied trap is significantly decreased. The average shear stress applied to the trapped cell is about 0.04 Pa. Figure 4 shows representative microscopic images of our device trapping patient cultured circulating tumor cells. On average, 93.5% of the traps designed in the device were occupied by cells and 71.0% of all the traps captured only a single cell. Cell clusters captured within individual traps were observed to enter the device as pre-formed clusters, rather than forming clusters within the trap. We suggest that enlarged bottom gaps and gentle trypsin treatment will further improve single-cell trapping efficiency. The single cell trapping microfluidic device developed in this study can be useful in experiments requiring monitoring of single cells, due to its high efficiency and the ease of operation.

Figures used in the abstract

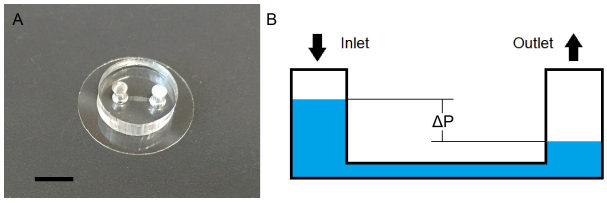

Figure 1: Figure 1. A: The single cell trapping microfluidic device with featured polydimethylsiloxane (PDMS, 3 mm in thickness) bonded to a cover glass (15 mm in diameter) using plasma treatment (Scale bar: 5 mm); B: The device is passive-pumping based on the mechanism of communicating vessels, where the fluid flow is driven by the pressure difference (ΔP=24.5 Pa) between the inlet and outlet reservoirs.

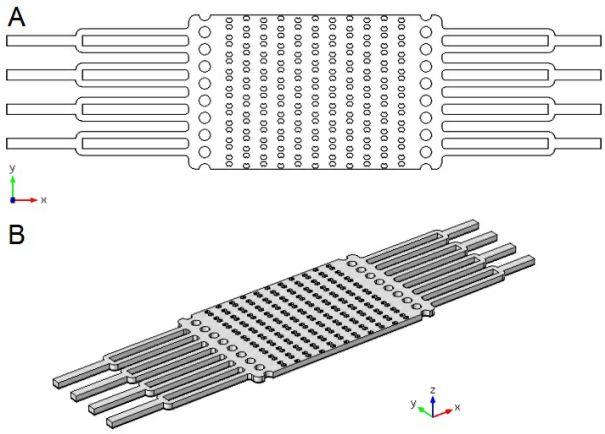

Figure 2: Figure 2. The geometry of the channels and the cell trapping array. A: The orthogonal projection on x-y plane; B: The three dimensional view.

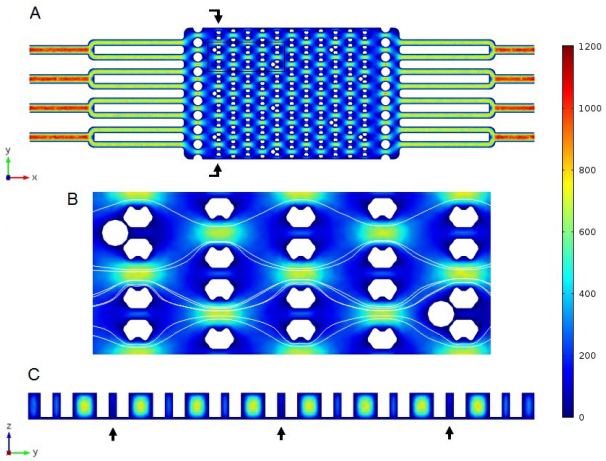

Figure 3: Figure 3. The velocity field in the cell trapping microfluidic device obtained from the COMSOL simulation. A: The x-y plane at z=14 µm (The cell suspension flows from left to right); B: The zoomed-in view of the velocity field and streamlines surrounding trapped cells; C: The y-z plane at x=969 µm as indicated by the pair of arrows in A. The three arrows in C indicate the positions where the traps are partially occluded by cells. (The velocity unit is µm/s.)

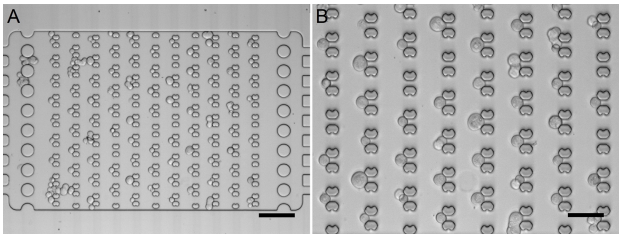

Figure 4: Figure 4. Representative micrographs of the microfluidic device trapping patient cultured circulating tumor cells (A: 10X and B: 20X). The diameter of the cells ranges from 8.8 µm to 28.6 µm. (Scale bars: 100 µm)