High spatial efficiency single-particle trapping array based on a microfluidic device

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Abstract. High-throughput single cell trapping is critical for cell biology research. In this paper, a microfluidic device with micro-cup array is designed to achieve high-throughput single-particle trapping. Microspheres were aspirated in the micro-cup array and immobilized in site by hydrodynamic force generated by the flow. Design of micro-cup is optimized based on “least flow resistance path” principle showing that higher volume flow ratio leads to better capturing efficiency. The result showed 100% capturing efficiency with flow ratio of 1.744. Also, by placing the micro-cup structure side-by-side in the channel, high-throughput of the microfluidic device is realized. 35 microspheres can be captured in the trapping area of 160×510 μm² which is a promising tool for high-throughput single cell analysis.

1. Introduction

Single cell trapping plays an important role in single cell analysis especially for morphology, genomics, proteomics and metabolomics study at single cell level[1]. Microfluidic devices which are widely used for single cell immobilization inherit many advantages including low reagent consumption, low risk of device contamination, and controllable device dimension[2]. Precise single cell analysis requires a large number of single cells for statistical analysis where high-throughput function is essential in microfluidic device design. Single cell isolation methods have been widely studied based on different mechanism. Optical method[3] which can precisely control cell movement in 3D direction demonstrated low throughput due to the large scale of integrated laser-based systems. Mechanical and electrophoresis methods[4-5] can achieve high throughput, but require large device dimension which prevent the real-time high-resolution observation of all cells under the same field of view.

Hydrodynamic method has been widely applied in single cell analysis in microfluidic devices[6]. By taking advantage of dynamic flows in the microchannel, cells can be fixed in specific designed microstructures by hydrodynamic force. To evaluate the effective throughput, spatial efficiency which is defined by the number of trapping cells in unit area (cm²) of functional structure in the microfluidic channel has been proposed recently[7].

In this work, we propose a hydrodynamical microfluidic device with high spatial efficiency by using side-by-side micro-cup array. 100% microsphere was captured by the micro-cup structure with a spatial trapping efficiency of 41600/cm². With proper treatment of microsphere, single cell can be bonded on the microsphere and hold in the micro-cup array which demonstrate the potential application of high throughput single cell trapping and analysis on our microfluidic device.
2. Device Design
The schematic of the microfluidic device is shown in figure 1(a). A 6 mm long inlet channel was designed to stabilize the flow before they reach the micro-cup structure. Also, instead of injecting microspheres-mixed suspension from top side, we integrated the inlet/outlet in the whole device fabrication process. The opening dimension of the inlet is 110×110 μm² which can precisely insert a capillary tube with inner diameter of 40μm. With this flow injection setup, single microsphere was guaranteed to move in the inlet channel so that avoiding the clogging of the microfluidic device during trapping process.

The core component of the device is micro-cup array which is located in the microfluidic channel side-by-side. The trapping mechanism is based on the flow pattern driven by fluid dynamics around micro-cup as shown in figure 1(b). The flow around the micro-cup is divided into two paths which are going along the main microfluidic channel or rotating into the micro-cup leading to the aspiration of microspheres. Through the size design of the main and branch channels, flow resistance in main channel is higher than that in branch channel. Based on the least flow resistance path principle, most of the fluid will flow into branch channel, so that the cells are directed to the trapping structure. The volume flow between branch channel (Q') and main channel (Q) can be expressed as

\[
\frac{Q'}{Q} = \frac{C(\alpha)}{C(\alpha')} \cdot \left(\frac{L}{L'}\right) \cdot \left(\frac{W + H'}{W' + H'}\right)^2 \cdot \left(\frac{W' \cdot H'}{W \cdot H}\right)^3
\]  

(1)

Where \(C(\alpha)\) is laminar friction constant, \(L\) and \(L'\), \(H\) and \(H'\), \(W\) and \(W'\) denote the length, height, and width of the corresponding channel. From equation (1), to obtain higher capturing efficiency, higher \(Q'/Q\) is desired. However, higher \(Q'/Q\) factor leads to larger device dimension, therefore, optimized design parameters which can balance capturing efficiency and spatial efficiency of our device are listed in table 1.

![Figure 1. Schematic of the microfluidic device (left) and the micro-cup design for cell trapping (right)](image)

Table 1. Design Parameters of microfluidic channel.

| Parameters     | Main Channel | Dam Interval | Branch Channel |
|----------------|--------------|--------------|----------------|
|                | Length       | Width        | Length         |
| Symbol         | (μm)         | (μm)         | (μm)           |
| Value          |              |              |                |
| \(L\)          | 6            | 30           | 720            |
| \(W\)          | 5            |              | 22.5           |
| \(H\)          | 20           |              | 20             |
| \(D\)          |              |              | 1.744          |
3. Fabrication and Experiment Result

The device was fabricated by soft-lithography and replica template process as shown in figure 2(a). We adopted two types of negative photoresist, SU-8 2010 spin-coated at 1200 rpm for 30 seconds with a thickness of about 20μm which defined the microfluidic channel in the center of the device, and SU-8 2050 spin-coated at 1000 rpm for 30 seconds with a thickness of about 100μm which were used for insertion of capillary tube at the inlet. To ensure clear peel off the PDMS chip from SU8 mold, we deposited a monolayer of 1H, 1H, 2H, 2H-perfluorooctyltrichlorosilane (FOTS) on the surface of the mold at 80°C for 1 hour. The fabricated device was shown in figure 2(b).

![Fabrication process of the microfluidic device](image1)

**Figure 2.** Fabrication process of the microfluidic device (top) and micrography of the fluidic channel with micro-cup array (bottom)

![Experiment setup of the microfluidic device](image2)

**Figure 3.** Experiment setup of the microfluidic device
The experiment was performed under the microscope and observed under a 20-fold objective as shown in figure 3. The force on injection syringe was applied by self-assembly stepping motor. By using polystyrene (PS) microsphere with a diameter of 15μm and the applied running step speed of 0.1mm·min⁻¹, we achieved the capturing efficiency of 100%, and 7×5 microspheres were arrayed within the area of 160μm×510μm sequentially as demonstrated in figure 4. It corresponds to 46000/cm² of the spatial efficiency.

![Figure 4](image-url)

**Figure 4.** PS microsphere capture experiment on microfluidic device. Microspheres were captured by the micro-cup array sequentially at: (a)t=4s; (b)t=5s; (c)t=6s; (d)t=10s; (e)t=11s; (f)t=15s; (g)t=34s; (i)t=93s

**4. Conclusion and Discussion**

In this paper, we fabricated a microfluidic device with high single cell trapping efficiency and spatial efficiency through side-by-side micro-cup structure. Design parameter of the micro-cup was optimized based on least flow resistance path principle and the result showed 100% microsphere trapping efficiency and 41600/cm² spatial efficiency. This demonstrate a large potential on high throughput single cell analysis in biomedical application.

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