Study of a microfluidic chip with converse fluid

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Abstract. The current microfluidic chip design generally forms a stagnation point in the exit flow area of the microfluidic chip. The presence of the stagnation area can cause problems such as choke of channel and sample purity degradation. For this problem, a microfluidic chip with converse fluid was designed. The converse sheath liquid can avoid the adverse effects caused by the presence of the stagnation point. It can prevent the cells from contacting the wall surface, and avoid the blocking problem of cell. At the same time, the introduction of the converse sheath liquid can also focus the sample flow in the sorting channel and the waste channel again, which is convenient for the detection of the sorted sample. The fluid flow state in this microfluidic chip was also simulated, and it verified the benefit of introducing converse sheath fluid, which has reference value for the design of microfluidic chip for cell analysis and sorting.

1. Introduction

A microfluidic chip [1, 2] is a multifunctional integrated system for studying the detection and sorting of particles in microscale fluids in biology and chemistry at the micron and submicron scale. It is also called “chip laboratory” as an integrated system. In such a microfluidic chip, it can not only focus [3, 4] the sample, but also has the function of analysis and sorting [5, 6] of the cell. Compared with the traditional experimental operation, the use of microfluidic technology can reduce the volume of reagents required for the experiment and achieve the analysis and sorting of microscale particles. At the same time, considering multiple functions are integrated in a small size, the micro-fluidic chip has the advantages of portability and full operation automation.

Since the introduction of microfluidic chips, people are paying more and more attention to it in many fields such detection [7, 8, 9] of microbial, medical sorting analysis [10], and bacterial detection [11, 12]. The characteristic size of the microfluidic system is in the same order with cells and microbe. In such a system, not only can the cell microenvironment be effectively simulated in vitro, but also the analysis and sorting of individual cells can be achieved. Specifically, in the field of cell analysis, many people have made progress in the interaction of cells, the construction and simulation of vitro cell microenvironments, single cell manipulation and analysis [13, 14], which have boosted the development of modern biomedicine greatly.

Generally, the microfluidic chip applied to flow cytometry includes one sorting channel and one waste channel for the outlet channel. However, a stagnation point of flow will emerge in the intersection of the two outlet channels. The existence of this stagnation point causes cells or particles to adhere to it, thereby causing the aggregation of cells or particles, and the changing of flow state, which has problem of the worse accuracy of analysis or sorting, the congestion of channel and sample pollution.
In this paper, a sheath fluid inlet is added in the region between the sorting outlet and the waste outlet in microfluidic chip. The sheath fluid is a converse flow because it flows in the opposite direction of the main channel. With the help of countercurrent, the cells can be prevented from contacting the wall surface in the stagnation point region, thereby the cells won’t agglomerate and block in the flow channel. This paper also simulated the flow field in the chip, and it will contribute to the optimize of chip's fluid structure.

2. Principle and Methods

In a specific fluid model, Reynolds number is a dimensionless parameter related to the ratio of viscous and inertial forces. It is usually represented by $Re$, and its calculation formula is

$$Re = \frac{\rho D v}{\mu}$$

$\rho$ is the density of liquid, $D$ is hydraulic diameter; $v$ is the average flow velocity of cross section; $\mu$ is viscosity coefficient of liquid. The Reynolds number reflects the contrast between the viscous force and the inertial force during the flow of the fluid, and its size is the basis for judging the flow state of the fluid. There is a relation between $Re$ and flow state:

1. $Re < 1$, peristaltic flow;
2. $2000 < Re < 4000$, transitional flow;
3. $Re > 4000$, turbulent flow.

According to the fluid theory, in consideration of the average flow velocity of the fluid section and the design parameters of the chip, the Reynolds number of the microfluid in the microfluidic chip is very small. In the low Reynolds number’s flow rule, adjacent multilayer fluids in the microchannel can flow adjacent without mixing with each other. This is the basic principle of hydraulic focusing.

At the same time, according to the principle of fluid continuity, for incompressible steady flow

$$\rho_1 A_1 V_1 = \rho_2 A_2 V_2 = Q$$

If the sheath fluid and the sample are loaded with the same cross-sectional area, the area of cross section in mainstream channel becomes 1/3 of the original area when the sheath fluid and the sample enter the main-stream channel in same flow rate. According to the principle of continuity, the sample flow velocity will increase as the area of cross section decreases, and then a focusing effect emerged.

3. Model and boundary conditions

Figure 1 shows a typical microfluidic chip structure which is a two-dimensional model with the function of refocusing. It mainly includes an injection port with a width of 100um; two sheath fluid inlets with a width of 100um; two outlets with a width of 100um. The sample flow velocity is $v_1$, the sheath fluid velocity is $v_2$, and the converse sheath fluid velocity is $v_3$.

![Figure 1. A two-dimensional model of microfluidic chip](image)

4. Results

4.1. Analysis of flow state in microfluidic chip

Figure 2 simulates the distribution of the sample fluid in the main stream with the primary focus of the sample stream under the sheath fluid on both sides and the distribution of the sample fluid in the terminal area with the converse sheath fluid to refocus. In a normal experiment, a sheath fluid is firstly introduced
to exhaust air bubbles inside the chip, and then a sample is introduced. In order to simulate the experiment condition, it is assumed that the initial state of the microfluidic chip is full of sheath fluid. In Figure 2, it is assumed that the velocity of sample stream is 0.02 m/s, the velocity of sheath fluid is 0.03 m/s, and the velocity of counter-current sheath fluid is 0.1 m/s.

![Figure 2. Volume fraction of sample stream with or without refocusing](image)

It can be known from Figure 2 that the flow state of the sample stream focused initially is basically similar in the presence or absence of a converse sheath fluid. That is, the sample stream slowly converges and gets focused under the action of the sheath fluid on both sides. This can be explained from two aspects. First, affected by the wall, velocity of the laminar flow in the microchannel is different at different position, showing a parabolic law with a higher speed at middle and lower at sides, so the flow rate of the sample flow must be faster than both sides of the sheath fluid, and the sample flow will be slimmer; on the other hand, according to the principle of fluid continuity, the sample flow and the sheath flow enter the same channel. That is, the cross-sectional area of the flow channel becomes smaller than the inlet. Further considering that the sheath fluid and the sample flow can be considered as incompressible flows, therefore the velocity of the fluid will inevitably be increased. According to the continuity principle, the cross-sectional area of the fluid inevitably will be narrowed.

Compared with the microfluidic chip without converse sheath fluid, the sample flow is full at the junction of both outlets of the microfluidic chip, forming a significant stagnation point. In this circumstance, the cells or microspheres of sample flow easily adhere to the wall surface at the stagnation point area, and then the flow channel is blocked. However, when there is a converse sheath fluid, the cells or microspheres in the stagnation point area will be driven away from the wall surface and flow to the outlets on both sides, preventing the cells from blocking and reducing the effects of the stagnation point on cells or particles; at the same time, it can be known from Figure 2-b that the sample flow will be focused again with the converse sheath fluid and flows to the two outlets, increasing the stability of the sample flow.

4.2. Analysis the sample flow focused firstly.

Figure 3 shows the flow state of sample focused firstly at different flow rates of sheath fluid and the same sample flow rate. It can be seen from the figures that at different flow rates of the sheath fluid, the sample stream will begin to focus firstly under the action of the sheath fluid on both sides, and the width of the sample stream will gradually decrease as the focus progresses. However, the width of the sample stream is different at different flow rates of sheath fluid changing from 0.01 to 0.04 m/s, as shown in Figure 3. In Figure 3, v1 = 0.02 m/s and v3 = 0.1 m/s. With the changing of flow rate, the ratio for the velocity of sheath fluid to the velocity of sample flow is from 1 to 4, the width of the sample flow gradually becomes smaller. This is because with the increasing of the sheath fluid on both sides, the fluid flow speed increases. According to the principle of fluid continuity, if the cross-sectional area of the fluid is further reduced, the sample flow will be further focused. We can conclude that as the ratio of sheath fluid flow to sample flow gradually increases, the width of the sample flow gradually decreases.
4.3. Analysis of the sample flow focused secondly

It can be seen from Figure 4 that as the flow velocity of the converse sheath fluid decreases, the width of sample stream refocused gradually increases, which is similar to the sample focused firstly. At the same time, the center position of the sample stream gradually shifts to the right. Specifically, under the action of the converse sheath fluid, the sample flow is far away from the wall at the junction area of two out channel; it can be seen from Figure 4 that with the increasing of the velocity of the countercurrent sheath fluid, the sample flow is farther from the wall and the probability of cell adhesion is smaller. It also can be seen that with the increasing of the flow velocity of the countercurrent sheath fluid, the width of the sample flow refocused is smaller, and the flow state is more stable, which facilitates the detection and verification of sample after being sorted.

Figure 3. Volume fraction of sample stream with or without refocusing

Figure 4 shows the flow state with different sheath fluid velocity which is converse at same sample flow velocity and sheath fluid velocity. In Figure 4, v1 is 0.02 m/s and v2 is 0.01 m/s. As we all know, the flow velocity of channel is parabolic under the influence of sheath liquid. We also can conclude that, as the velocity of the converse flow increases, the velocity ruled by the parabolic law gradually increases.
Figure 4 shows that the larger the converse flow rate is, the smaller the width of the sample stream focused secondly is. The larger the converse flow rate is, the greater the distance between the sample and the other side wall surface is, and the less likely it is to become blocked.

5. Conclusion

This paper presents a new type of microfluidic chip. Refocused by a converse sheath fluid can prevent cell aggregation from blocking the flow channel, and make the sample flow more stable after sorting. For this new chip, we also simulated the flow field in this microfluidic chip, which verified the feasibility of introducing a countercurrent sheath fluid, and also provided a reference for the next experiment.

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