Recent advances in active and passive microfluidic sorters

Haoran Wang*
Kunshan High School of Jiangsu, Kunshan, Jiangsu, 215316, China
hgcj@kshytech.com.cn

Abstract. Due to the fast development in biology and chemistry, scientists find that it is important to get a suitable sorter since it can enhance the accuracy and speed of the cell sorting application. For instance, researchers in the biological field need precise sorters to help them separate different kinds of components. The need for micro-fluidic based sorting, a useful technique in medicine or biology, has promoted the development of microscale sorters. This paper reviews two types of sorters, including active and passive sorters. The principles, mechanisms, merits and demerits, avenues for improvement, and application in the future of those two sorters are summarized. In conclusion, this paper could be a useful reference for those who would like to know the microfluidic sorter's overall knowledge.

1. Introduction
Sorter is a tool to separate particles in the fluid by varying sizes of particles and different inertial cohesive forces [1-5]. Moreover, it allows continuous separation based on complex hydrodynamic forces only by going through a curved channel axisymmetric. It is helpful for scholars who mainly focus on biological, medical, and physical research. Researchers usually divide these sorters by sources of power, namely as active or inactive sorters [2,3]. The development of sorters has increased rapidly in recent years because an efficient microfluidic device provides higher efficiency, accuracy, and less time to finish for research and becomes a preparatory step for further study [6-9]. The main idea of the active sorters is usually identical. Because they all use the idea of force which acts at various angles to the hydrodynamic flow, but they lead to the separation of the fluid by different external forces, such as acoustic waves or force generated by the magnetic field. However, the conceptions and techniques of passive sorters are different: one only uses the idea of the different sizes of particles. The other one utilizes the special adhesion of microorganisms and cells.

This paper aims to provide a mini review of the recent advances of the two different types of sorters. The mechanism and application of typical sorters are covered. Moreover, the pros and cons of the two types of sorter are summarized. Section 2 summarizes typical active and passive sorters. Conclusions are drawn in Section 3.

2. Main body
According to the mechanism of the sorter, they can be classified as active and passive sorters. In this section, typical active and passive sorters are introduced.

2.1. Active sorters
Interdigital transducers (IDTs) were deposited on a transparent piezoelectric substrate [1]. Polydimethylsiloxane (PDMS) microchannel, three inlets, and three outlets, was positioned and
bonded between these two IDTs. The sorting principles of SSAW and PDMS are illustrated in Figure 1(a) and (b), respectively.

A mixture solution of different particles was injected through the side inlets, and a sheath flow was injected through the central inlet, which can form a laminar flow of three liquid streams.[1] Applying acoustic (AC) signals to the IDTs can generate two types of surface acoustic waves (SAWs) with identical frequency, which helped in opposite directions toward the channel. When the SAW encountered the liquids, which were put in an encapsulant in the microfluidic channel, it generated longitudinal leakage waves to lead to pressure fluctuations inside the liquids [1]. These pressure fluctuations caused acoustic radiation forces later on in the suspended particles, which drives them to either minimum pressure amplitude or maximum pressure amplitude, depending on the relative density and the ability to press between the particles and the medium. For advantages, it has high efficiency because two openings in the PDMS were fabricated on each side of the channel, and they also reduced propagation loss of the SAWs. Moreover, this high separation efficiency would only yield great accuracy in sample detection and analysis, which makes this method attractive for various biochemistry applications where experimental performance is highly based on the purity of samples. Compared to other platforms, it has the greatest accuracy and highest efficiency. For disadvantages, although it is no doubt that it acts well on big particles, many small particles cannot be separated well during the process, and the efficiency of it can be enhanced by increasing the flow speed and applied power. However, the method cannot provide such a noteworthy accuracy when it is used for other objects, except sample detection and analysis. Moreover, the cost of making such a platform is expensive because of the solvent in flow and mass customization of the tools.

The separation of the cell is made possible by an array of very thin magnetized “wires” which are put at an angle to the direction of the net hydrodynamic flow [2]. When there are no magnetic monopoles, force is led by field gradients that act on magnetic dipole moments, which is a permanent magnetic:

$$\mathbf{F} = (\mathbf{\mu} \cdot \nabla) \mathbf{B}$$  \hspace{1cm} (1)

where $\mathbf{F}, \mathbf{\mu}, \mathbf{B}$ denotes forces result from field gradients acting on magnetic dipole moments, a permanent magnetic moment, beads attached to the cells, respectively [2]. A paramagnetic object with magnetic susceptibility will feel a force given by:

$$\mathbf{F} = (\chi \mathbf{B} \cdot \nabla) \mathbf{B}$$  \hspace{1cm} (2)

where $\chi$ represents magnetic susceptibility. These two formulas can be defined as the two most important things in this work. With a special hydrodynamic path and the distinctive design of wires, the device works well to separate small particles [2].
For advantages, the extremely thin layer forces the spin system to be the only domain with resultant very high magnetic fields. Because of the small length scale of the wires, such small structures have large magnetic field gradients at their edges. Since magnetic force is based on field gradients, the path of such a paramagnetic object exposed to this way of wires will be altered. Moreover, compared to other devices with external forces, the device does not cost much and is easy to use when it is established. For disadvantages, the device should try to find a better way for scientists to use this device in micro-scale experiments. Because of its limited size, it is unreasonable for scientists to do a series of experiments and record the data.

Their main problem is how they can get a more precise separation with lower energy for active sorters. The work about SSAW clearly shows its high efficiency and low-power quality, which means that it is one of the most wonderful sorters. However, the design of a microfabricated magnetic cell separator still has many not perfect enough processes, and it really costs time. Nevertheless, the design of this separation is important to determine how to utilize the hydrodynamic force produced by the magnetic forces. From my perspective, scientists should try to minimize the price of its platform and broaden the application of this sorter.

2.2. Passive sorters

The mechanism of separation is based on inertial focusing. The inertial focusing requires lift and drag forces acting on particles inflows with high velocity to interact, creating an equilibrium position for particles dependent on their particle size. A design of the passive sorter [3] is illustrated in Figure 2(a) and (b), respectively.

![Figure 2. A design of the passive sorter [3]](image)

According to the study, I concluded five formula to help us understand the mechanism of the device, which are listed as:

\[ F_i = \frac{\mu^2}{\rho} R_c^2 f_c \left( R_c x_i \right) \]

\[ R_y = \frac{\rho U_m a^2}{\mu D_h} = R \frac{a^2}{D_h^3} \]

\[ U_h = \frac{\rho U_m^2 a^3}{3 \pi \mu D_h^3} f_i \left( R_c x_i \right) \]

\[ F_{10} \sim \rho U_m^2 a D_h^2 / r \]

\[ r \frac{a_{12}^3}{D_{h2}^3} = r \frac{a_{12}^3}{D_{h1}^3} \]

\[ D_{h2} = D_{h1} \left( \frac{a_{12}}{a_{11}} \right)^{3/4} \]
where $F_l, \mu, \rho, R, f, R, x$ denote the lift forces, viscosity, density, the particle Reynolds number, the lift coefficient, the channel Reynolds number, the particle within the cross section of the channel, respectively; $U_m, a, D_h$ is the maximum velocity of the fluid, acceleration, hydraulic diameter, respectively; $U_p$ represents the potential the speed need to separate the particles, respectively; $F_D, r$ denote dean drag, the channel radius of curvature, respectively; $r_1, r_2$ means the different radius of curvatures; subscript 1, 2 denote the parameters at the inlet and outlet.[3] In short, the five formulas use various factors in the flow to get the answer to what it needs. In their previous work, the five formulas that described asymmetric curving geometries are useful for reducing the four inertial focusing equilibrium positions in channels to a single position and separate particles with different sizes and different focusing forces. This system is designed to focus on rapid separation and filtration of rigid particles, emulsions, and blood components. For advantages, the device successfully separates small particles without using any external forces, and the application of these devices is not so limited. Moreover, it has different kinds of choices to separate small particles. For disadvantages, the device does not work precisely, and most of its part is still based on the experiments. Thus, people do not know whether the device is good or bad since it is not perfectly completed. However, such a device is even not easy to use without an external force to power it. From my perspective, this device should improve its accuracy and try to make its cost lower. Furthermore, using it should be decreased because it is too difficult for common citizens to use and do not help people too much in their daily lives.

Figure 3 present the mechanism of another passive sorter [10]. The paper does not clearly introduce the mechanism of the sorter. Still, it tells us two aspects of the device: immobilization of IgG on microchannels surface and surface bio-functionalization and cell adhesion. Each objection is connected closely with the idea of biology, and the target of the two experiments are all studying the molecules. For advantages, it is no doubt that the device has a great influence on biology since it is precise and cheap and easy. For disadvantages, it is not useful because it only applies to biological fields.

![Figure 3. Principle of a passive sorter](image)

From my perspective, the researchers should develop its application. For passive separators, their main problem is quite clear since they only want to own a technique that can separate fluid or particles accurately without power. The paper [3] mainly discusses the force that can help the researchers to achieve their goal instead of having some true examples. Nonetheless, it is pointed out that these separations cannot do some precise work because of lacking power, and they may have good achievements in bio-analysis, cell sorting, and cell culture.

3. Conclusions and prospects
This paper summarized the recent advances of the two different types of sorters, namely the active and passive sorters. The mechanisms of typical sorters are surveyed, and there is some advice on applying these sorters. The defects and advantages of those sorters are analyzed. For active sorters, it is found that they are more complicated and precise. Hence its application is limited. Besides, it is a little
expensive. While for passive sorters, they show a better performance in learning and using, but they are not precise enough. The sorter designer/producer should try to decrease its price and make it easier to be used in the future.

References
[1] Bergerl M., Castelino J., Huang R., Shah M., Robert H. A. (2001) Design of a microfabricated magnetic cell separator, Electrophoresis 22:3883–3892
[2] Shi J., Huang H., Stratton Z., Huang Y., Huang J. (2009) Continuous particle separation in a microfluidic channel via standing surface acoustic waves, 09:3354-3359
[3] Carlo D. D., Edd J. F., Irimia D., Tompkins R. G., Toner M. (2008) Equilibrium Separation and Filtration of Particles Using Differential Inertial Focusing, Analytic Chemistry, 80:2204-2211
[4] Andersson H, Van den Berg A. (2003) Microfluidic Devices for Cellomics: A Review. Sensors and Actuators, B: Chemical, 92(3): 315–325.
[5] Chen C C, Zappe S, Sahin O, et al. (2004) Design and Operation of a Microfluidic Sorter for Drosophila Embryos. Sensors and Actuators, B: Chemical, 102(1): 59–66.
[6] Sun Y, Lim C S, Liu A Q, et al. (2007) Design, Simulation and Experiment of Electroosmotic Microfluidic Chip for Cell Sorting. Sensors and Actuators, A: Physical, 133(2 SPEC. ISS.): 340–348.
[7] Chen C H, Cho S H, Tsai F, et al. (2009) Microfluidic Cell Sorter with Integrated Piezoelectric Actuator. Biomedical Microdevices, 11(6): 1223–1231.
[8] Yin H, Marshall D. (2012) Microfluidics for Single Cell Analysis. Current Opinion in Biotechnology, 23(1): 110–119.
[9] Pritchard R H, Zhukov A A, Fullerton J N, et al. (2019) Cell Sorting Actuated by a Microfluidic Inertial Vortex. Lab on a Chip, 19(14): 2456–2465.
[10] Zhang Z.L., Crozatier C., Berre M.L., Chen Y. (2005) In situ bio-functionalization and cell adhesion in microfluidic devices, 78:556-562