ISSN (e): 2250 – 3005 || Volume, 12 || Issue, 4|| Jul. - Aug. – 2022 ||
International Journal of Computational Engineering Research (IJCER)

An overview on fluid micromixing and particle separation

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ABSTRACT
The applications of microfluidic systems are observed in a broad range of scientific fields, such as biology, engineering, etc. Two significant microfluidic devices are micromixers and the ones utilized for particle separation. Both systems are divided into passive and active ones. The present review article describes the techniques of micromixing and particle separation and presents some advances in these fields and explains the mechanisms govern the mixing and particle isolation in microfluidic systems. Active techniques, such as electroosmotic, electrokinetic, magnetic, acoustic, etc. are explained for these two utilizations.
KEYWORDS:*Microfluidics, Micromixing, Particle separation, Active, Passive.*
AMS Subject Classification: 05C12.

Date of Submission: 05-07-2022 Date of acceptance: 20-07-2022

I. INTRODUCTION

Microfluidic devices have numerous applications in biological and chemical systems, food industries, environmental equipment, etc. Two major microfluidic devices are micromixers and the ones utilized for particle separation. Both systems are divided into passive and active ones [1-3]. Passive devices do not employ external actuators while active ones use external energy sources. Since the fluid flow velocity is very low in microfluidic systems, the fluid regime is laminar flow with the Reynolds number of less than unity. Hence, in passive devices, molecular diffusion plays a dominant role in micromixing and particle separation.Passive microfluidic devices have relatively more complicated structures than active ones because their geometries are designed to enhance their performance. Active systems can be more easily controlled due to their simpler structure compared to passive ones.

The mixing efficiency and separation efficiency are utilized to quantify the performance of the microfluidic devices. This review paper briefly describes the techniques of micromixing and particle separation and presents some advances in these fields published during 2017 and 2022.The rest of paper is organized as follows: section 2 describes various kinds of micromixers, including active and passive ones. Section 3 presents the characteristics of passive and active devices used to separate microparticles. Conclusions are provides in section 4.

II. MICROMIXING

Active and passive micromixers have been analyzed by many investigators. In this section, several advances in the field of micromixing are introduced and discussed. Agarwal et al. [4] examined an electroosmotic micromixer by changing the electric frequency and number of electrodes (Figure 1). It was found that the micromixing process can be performed better when the fluid flow rate is low, i.e., small Reynolds numbers because the impact of electrophoretic forces is higher. They also demonstrated that the maximum mixing efficiency can be achieved by using four electrodes on the channel walls.Ansari et al. [5] numerically and experimentally evaluated the micromixing process in a T-shaped vortex micromixer and revealed that the vortex micromixer has higher efficiency than a simple one for the Reynolds number ranging from 1 to 80.They also integrated the vortex T-shaped micromixer with a serpentine one and calculated the mixing efficiency at Reynolds numbers of 20 and 40 and reached the mixing index of about 40%.Bagherabadi et al. [6] considered an electrokinetic micromixer to assess the impacts of diffusion, electro-migration, and convection on the micromixing process. It was reported that these mechanisms have a dominant role when AC electrodes are utilized. They achieved a mixing efficiency of 96.2% in 1.8 seconds by mounting electrodes vertically and horizontally. Balasubramaniam et al. [7] evaluated the performance of spiral microchannels by changing their aspect ratio to generate secondary flows and enhance mixing quality.It was found that the mixing index of >

90% can be obtained for the Reynolds numbers of 20. They showed that lower pressure drop and higher mixing quality are achieved by changing the hydraulic diameter of the microchannels.

RazaviBazaz et al. [8] examined the operation of a hybrid micromixer containing Tesla, nozzle, and barrier units to improve its performance for low and moderate Reynolds numbers (Figure 2). They utilized the Taguchi method to diminish the number of experiments to 25. They finally introduced an optimal hybrid micromixer containing a unit of nozzle and pillar, two Tesla units, and three obstacle-based ones. Besides, a critical point was reported by the authors for the Reynolds number, i.e. Re = 2. Bordbar et al. [9] analyzed the mixing of glycerol and water as high-viscosity liquids in a micromixer by creating slug flow in the main channel. They reached a mixing efficiency of more than 90% and 80% for the liquids with viscosities about 54% and 160% higher than that of water. It was demonstrated that the length of slugs and Reynolds number have a major influence on the mixing process in their proposed micromixer.

Chen et al. [10] compared two types of Koch fractal micromixers numerically and experimentally and demonstrated that the secondary one results in better mixing quality compared to the primary Koch fractal micromixer. It was revealed that the pressure drop is reduced considerably when the corners of the secondary Koch fractal mixer are rounded. For instance, at Reynolds number of 100, the pressure drop was reduced from 21295 Pa to 12789 Pa; however, the mixing index was also reduced. They reported that for the secondary Koch fractal micromixer with rounded corners, the pressure drop is reduced, and mixing efficiency is not changed significantlyas the Reynolds number is enhanced.

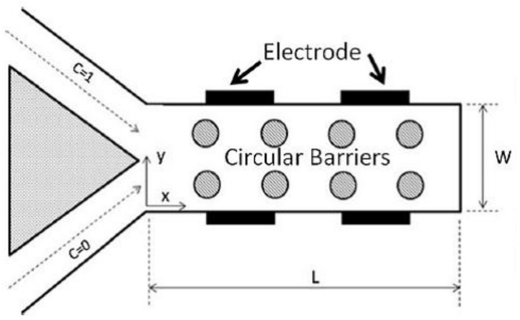

Figure 1: Schematic of an electroosmotic micromixer proposed by Agarwal et al. [4].

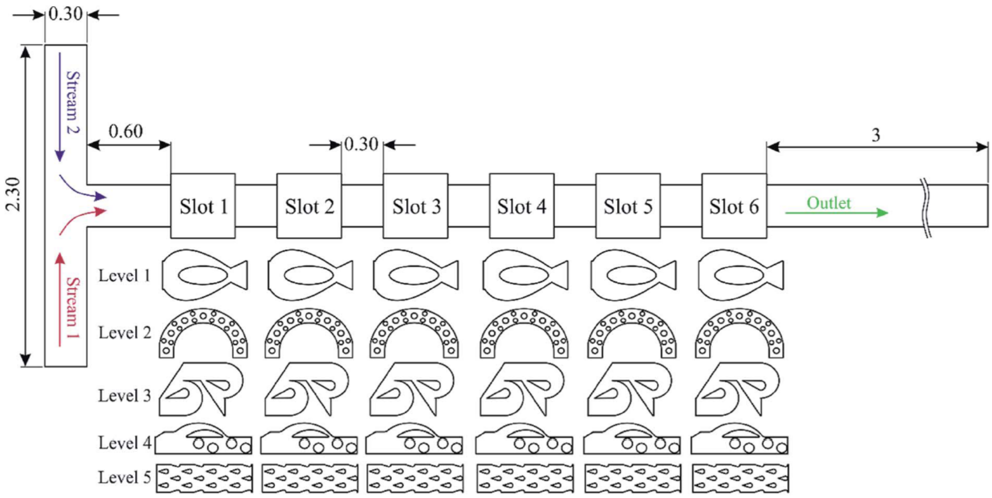

Figure 2: Schematic of a hybrid micromixer proposed by RazaviBazaz et al. [8].

Clark et al. [11] utilized non-rectangular cross-sections for a serpentine micromixer and changed the channel direction between each unit to improve the mixing quality. They reached a maximum mixing index by employing four units when the Reynolds number was 20. Compared to a simple serpentine micromixer, their proposed one experienced higher performance, especially at lower Reynolds numbers, i.e., Re = 1 and 20.Gidde et al. [12] utilized COMSOL Multiphysics software to evaluate the mixing process in two types of split and recombine micromixers (Figure 3). The Reynolds number varied between 0.1 and 70. They showed that diffusion plays a major role in the mixing process when the Reynolds number is less than 5. Both micromixers exhibited a higher performance for higher Reynolds numbers (Re > 5) due to the creation of secondary flows and the formation of separation vortices. They also demonstrated that the pressure drop is enhanced with the Reynolds number and the micromixer with circular elements shows a higher pressure drop for a given Reynolds number.

Hama et al. [13] examined the mixing process in a reverse-staggered herringbone micromixer (Figure 4) numerical and experimentally. It was reported that the Reynolds number has a small impact on the mixing distribution due to the existence of a laminar flow regime. Besides, the diffusion coefficient has a slight influence on the process due to the small amount of residence time of fluids in the micromixer.

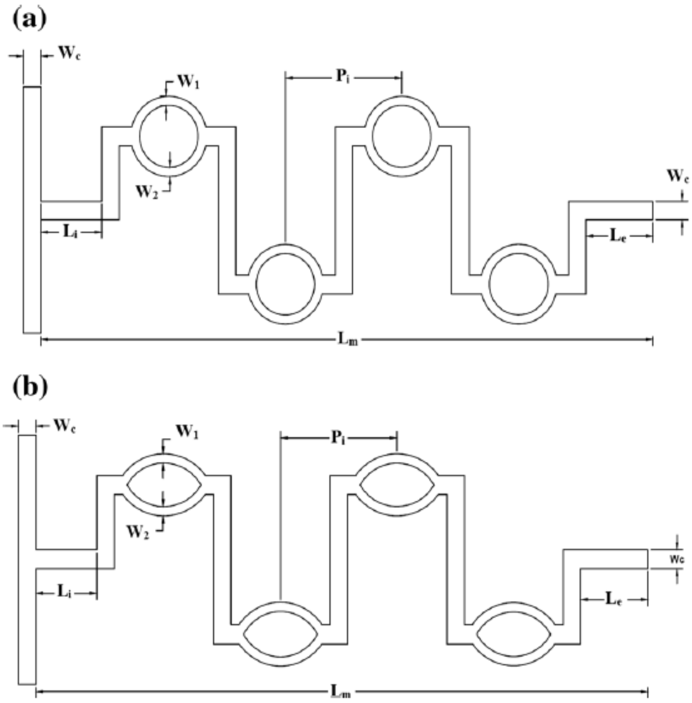

Figure3: Schematic of two types of split and recombine micromixer proposed by Gidde et al. [12]: (a) circular elements, and (b) elliptical elements.

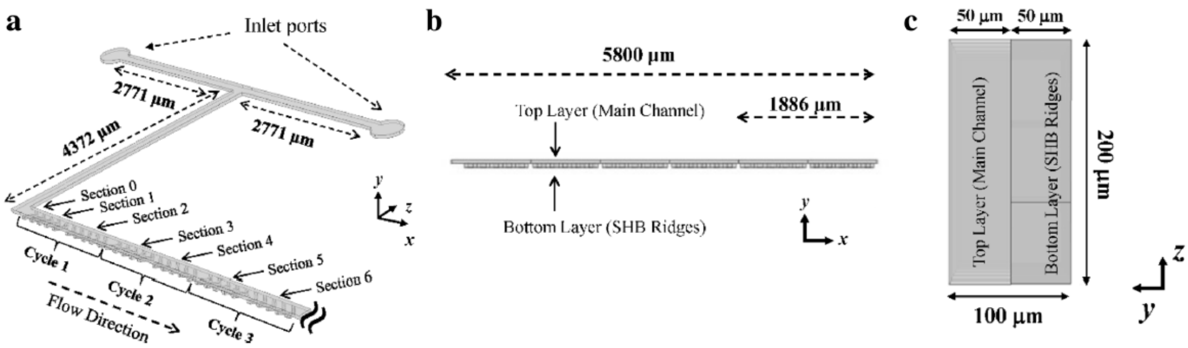

Figure4: (a) Schematic of two types of a reverse-staggered herringbone micromixer, (b) side view, and (c) lateral view [13].

Table 1 summarizes main characteristics andfindings of several investigations presented in recent years. It should be pointed out that artificial errors must be considered in the simulation of micromixing [14].

Table 1: Active and passive micromixers.

Active /Passive	Re	Mixing efficiency	Materials	Year	Reference
Passive	1-80	95%	Numerical simulation	2018	[15]
Active	-	88%	PDMS	2017	[16]
Active	-	83%	PDMS	2019	[17]

Active	0.78-1.56	98%	Numerical simulation	2019	[18]
Passive	9-75	100%	PDMS	2020	[19]
Active	5-50	96%	Numerical simulation	2019	[20]
Active	-	96%	PDMS	2019	[21]
Active	-	98%	Numerical simulation	2019	[22]
Active	-	91%	Numerical simulation	2020	[23]
Passive	1-100	99.11%	PDMS	2021	[24]
Passive	0.01-100	95%	Numerical simulation	2022	[25]
Active	0.1-0.7	98%	Numerical simulation	2022	[26]
Passive	0.01-100	99.89%	PDMS	2022	[27]
Passive	0.1-10	94.44%	Numerical simulation	2021	[28]
Active	-	-	Numerical simulation	2022	[29]

III. PARTICLE SEPARATION

The second application of microfluidic devices is the isolation of microparticles/cells. Like micromixers, passive and active techniques are employed to separate or sort particles. In this section, several advances in the field of particle separation are presented and discussed. Berendsen et al. [30] utilized a pinch flow fractionation to separate spermatozoa from erythrocytes and reached separation efficiencies of 95% and 90% for spermatozoa and erythrocytes, respectively.Shiriny and Bayareh [31] collected two kinds of circulating tumor cells (CTCs) from whole blood using a single-loop spiral channel (Figure 5). The Reynolds number was between 30 and 120 and it was demonstrated that the separation efficiency of 100% can be obtained when the Reynolds number ranges from 90 to 110.

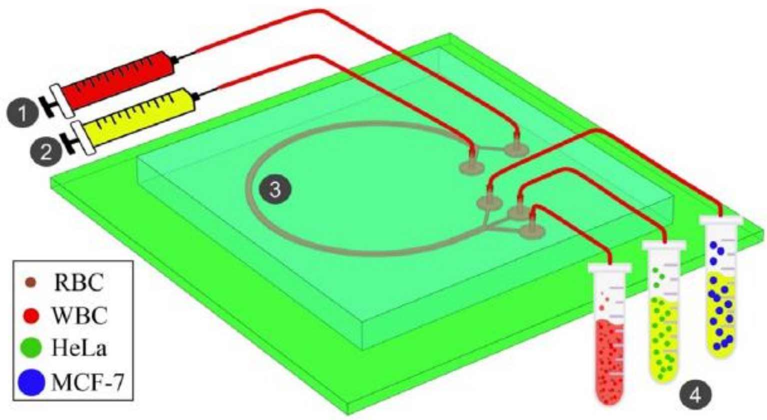

Figure5: Schematic of a spiral channel utilized to separate CTCs from blood cells [31].

Lee et al. [32] utilized a multi-stage geometry to separate microparticles using ANSYS Fluent software (Figure 6). They also conducted experiments to validate the numerical results. Their findings revealed that microparticles can be separated better when the curved angle is 60° compared to the curved angle of90°. They reached a separation efficiency of 90.1% for polystyrene microparticles with diameters of 8 and 25 micrometers and obtained a separation efficiency of 88% for polystyrene microparticles with diameters of 3, 12, and 25 micrometers. Fan et al. [33] used a sheath-free microfluidic device to separate microparticles suspended in Newtonian and viscoelastic fluids (Figure 7).To distribute the elastic force symmetrically, they utilized contraction-expansion geometry on one side of the channel and found that this structure creates strong vortices in channel cross-sections for the Newtonian case. They assessed the impact of fluid velocity, particle diameter, the concentration of viscoelastic fluid, and the geometry of the channel on the separation mechanism.

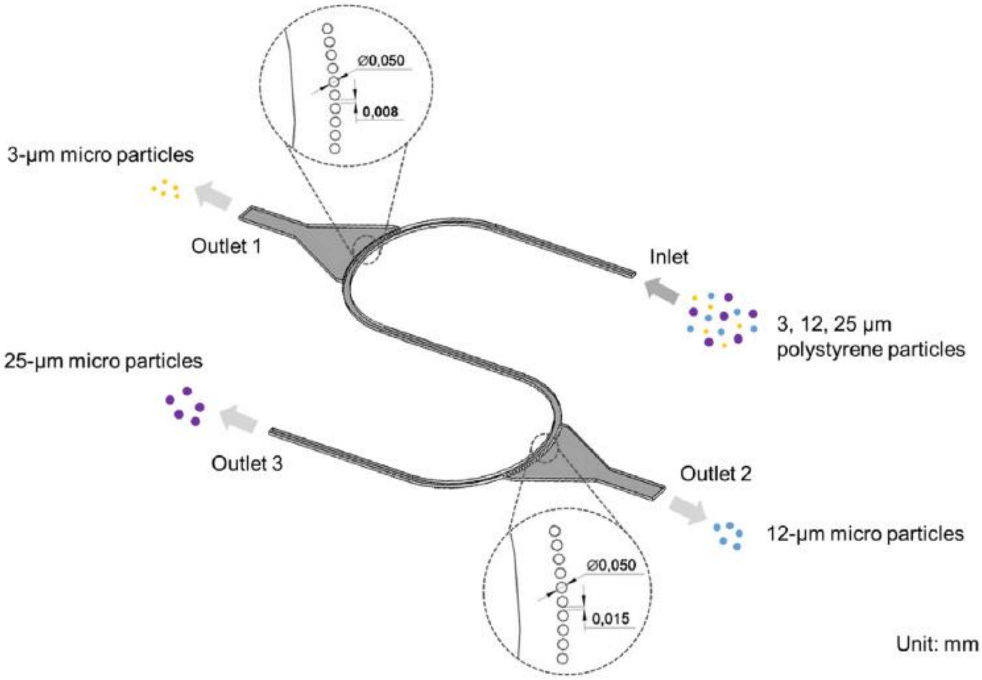

Figure6: Schematic of a microchannel utilized to separate polystyrene microparticles [32].

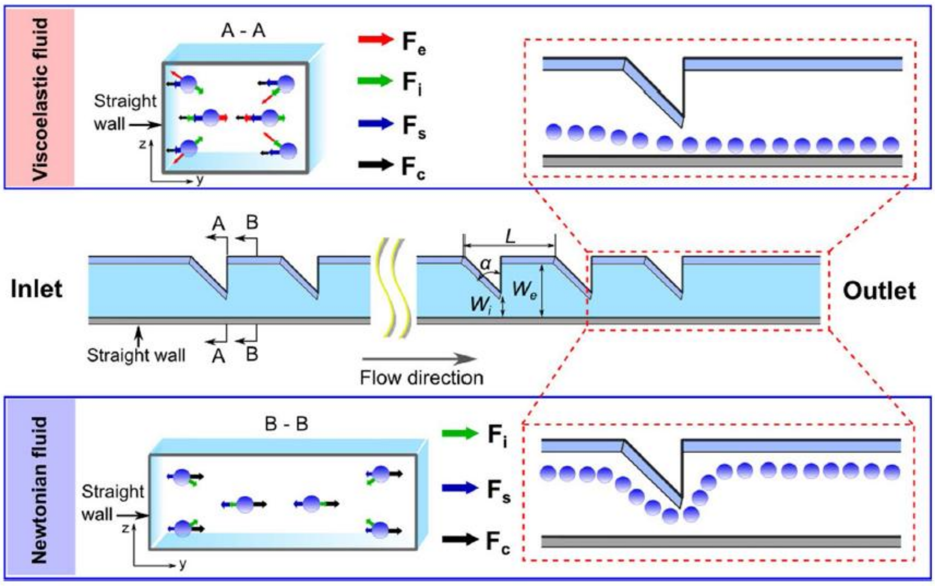

Figure7: Schematic of a sheath-free microfluidic device to separate microparticles suspended in Newtonian and viscoelastic fluids [33].

Gao et al. [34] separated CTCs from blood cells by employing a hydrodynamic microfluidic device (Figure 8). They used multi-stage microchannels and inertial lift force for the separation of human brain glioma cells from red and white blood cells. Their experiments demonstrated that a separation efficiency of more than 90% can be achieved using an optimized device. It was revealed that the maximum recovery of CTCs and red blood cells corresponds to the fluid velocity of 9 microliters per minute.

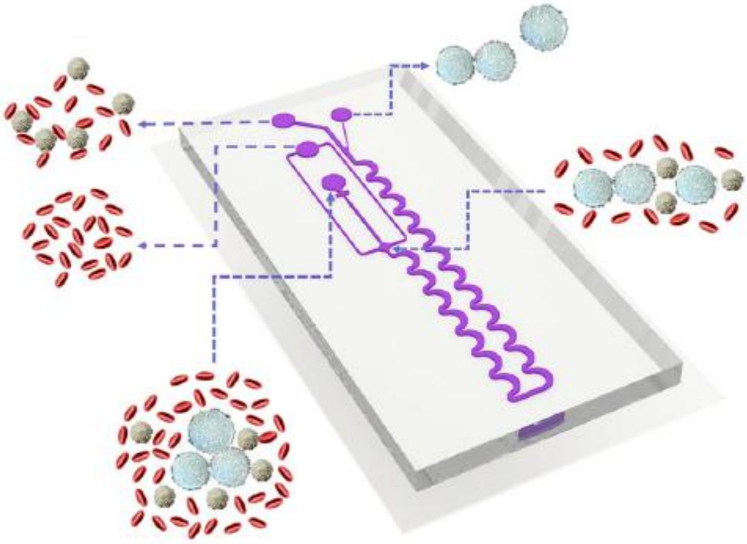

Figure8: Schematic of a hydrodynamic microfluidic device to separate CTCs from blood cells [34].

Table 2 summarizes the main characteristics andfindings of several investigations on particle/cell separation presented in recent years.

Active /Passive	Separation efficiency	Material of channel	Year	Reference
Passive	-	PDMS	2018	[35]
Passive	90%	PDMS	2017	[36]
Passive	-	PDMS	2017	[37]
Passive	90%	PDMS	2017	[38]
Passive	-	PDMS	2017	[39]
Passive	90%	PDMS	2018	[40]
Passive	-	PDMS	2019	[41]
Passive	96%	PVC	2019	[42]
Active	100%	Numerical simulation	2020	[43]
Active	100%	Numerical simulation	2021	[44]
Passive	100%	Numerical simulation	2022	[45]
Active	95%	Numerical simulation	2021	[46]

IV. CONCLUSIONS

Microfluidic devices have numerous applications in biological and chemical systems, food industries, environmental equipment, etc. Two major microfluidic devices are micromixers and the ones utilized for particle separation.This review paper briefly describes the techniques of micromixing and particle separation and presents some advances in these fields published during 2017 and 2022. The analysis of the paper considered micromixing and particle separation demonstrates that hybrid microfluidic devices can be utilized to improve the performance of these devices. Besides, scientists and engineers should attempt to explore cost-effective ways to commercialize them. Different models should be modified for the simulation of non-Newtonian fluids, including viscoelastic ones.

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NastaranFaraji. "An overview on fluid micromixing and particle separation." *International Journal of Computational Engineering Research (IJCER*), vol. 12, no.4, 2022, pp 01-08.