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Cells and Model Particles in Lateral Focusing Microfluidics

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Summary:

In the field of medical diagnostics, the microfluidic devices are widely applied for implementation accelerated sample handling steps although reliable and reproducible results are to be achieved. In many cases, the medium must be pre-filtered to extract the target before analysis. In this work the aim was to gain better understanding of particle and cell behaviour in special lateral focusing systems, dedicated for size dependent separation and lateral positioning the target above the sensor zone. Fluorescent polystyrene beads in the size range of Ø = 0.5 -16.5 µm were injected into the asymmetrically curved microfluidic system, and their size dependent trajectories and lateral positions were recorded. A particle map was defined according to their lateral positions and compared to the behaviour of real cell-types (Escherichia coli, Red Blood Cell, Saccharomyces cerevisiae, HeLa), considering their morphology and size. The results highlight the importance of living cell's morphology significantly affecting the cell movement in microfluidic channels compared to the rigid, spherical beads.

Keywords: microfluidics, dean flow, hydrodynamic lift, lateral focusing, cell manipulation

Background, Motivation an Objective

Among the suitable particle separation methods, a passive, label-free solution, the lateral focusing technique was analysed for comprehension the micro-scale hydrodynamic processes governing the cell movements in such microfluidic systems. In continuous Poiseuille flow, inertial lifting forces (shear-gradient lift force, wall-effect induced lift force) are acting on the extended shells and influencing their lateral migration. In terms of particle size, larger beads settle sooner, approaching their equilibrium position, although the sorting of small particles is quite challenging, while their lateral migration occurs more slowly. By varying the geometry of the microfluidic system as channel cross-section, the number and pattern of the particle size specific equilibrium positions in the channel cross-section can be tuned.

In an asymmetric curvilinear channel, the focusing nodes can be reduced to a single sheet or point. Due to the curvature of the geometry, a secondary flow is formed to generate counter rotating Dean-vortices in the channel cross-section. In this flow the particles experience an evolving Dean-drag-force, which further helps focusing them to a certain extent. Dino Di Carlo et. al. [1] was a pioneer in the topic and defined a focusing criteria (*Eq. 1*) based on the ratio of bead diameters (a) and hydraulic diameter of the channel (D_h):

$$\frac{a}{D_h} > 0.07, \qquad \textit{(Eq. 1)},$$

where $D_h = \frac{2wh}{w+h}$, w and h are channel width and height, respectively.

Microfluidic System applied

The particle-size-dependent lateral focusing phenomenon was examined in our study by intensive variation of geometrical parameters (height and critical width) of the asymmetrically curved serpentine channel. The measurements were implemented in a ~35 mm long channel consisting a periodic sequence of 23 curvatures. The lateral positions of the fluorescent beads and the biological cells were recorded at the end of the channel in the major curvature having 300 µm width. The applied flow rates were varied between 0.5 and 2 µL and the minimal flow rates required for efficient lateral focusing at a given channel size were also determined. [2]

Results and discussion

We proved that in the channel characterised with 25 µm height and 50 µm critical width (H25_W_{cr}50), the focusing of rigid particles having diameters of Ø 15.8 and 4.8 µm is successful

at 0.5 µL/s flow rate, although the focusing positions were determined at 1 µL/s flow rates for several particle sizes as presented in Fig. 1. In the designed curvilinear channel the size dependent focusing positions of the rigid, spherical polystyrene beads were represented by a precise bead map and compared to the behaviour of multi-dimensional, deformable cells (see Fig. 2 and Table 1). [3] In this microfluidic system the later focusing was possible theoretically above the diameter of 2.4 µm.

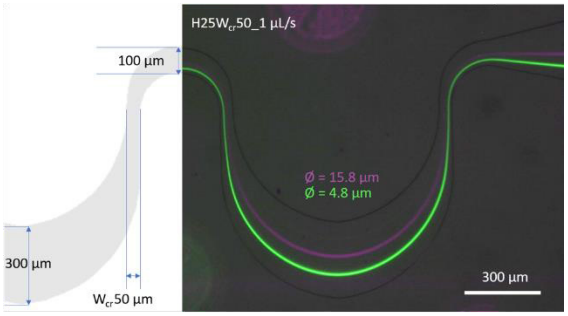

Fig. 1. Lateral focusing fluorescent beads (Ø 5.8 and 4.8 µm) at 1 µL/s flow rate in H25_W$_{cr}$50 type curvilinear microchannel.

The lateral focusing phenomena of Escherichia coli bacteria, Red Blood Cells, Saccharomyces cerevisiae yeast and HeLa cancer cells were characterised and compared to the behaviour of rigid polystyrene beads falling in the diameter range of 0.5 - 16.5 µm as presented in Table 1.

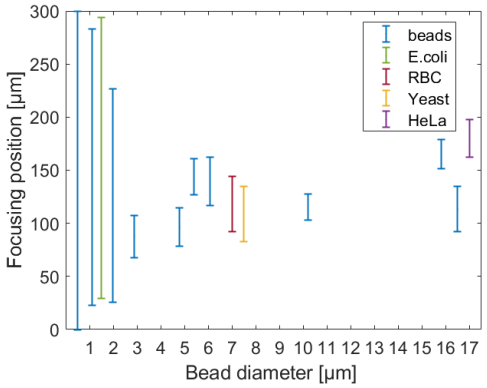

Fig. 2. The focusing positions or concentration ranges of rigid beads and target cells in H25_W$_{cr}$50 type channel at 1 µl/s flow rate.

Conclusion

Our experiences (see Fig. 2 and Table 1) project that the stick-shaped cells presumably take up oscillatory motion in the flow, they are not focused in a single point and their degree of concentration best matches with the 1.1 µm beads. RBC cells may adopt a tumbling motion, they were focused according to their larger dimension and their lateral position can be mostly represented by the 6.08 µm diameter beads. The spherical yeast cells characterised by an average diameter of 9.75 µm could be modelled by 10.2 µm diameter beads. The inhomogeneous, deformable cancer cells can be typified by variable sizes with the mean of 24 µm. In our microfluidic system the 15.8 µm beads were the most capable model regarding their lateral position.

Table 1: Size-dependent lateral focusing of beads and cells (see Fig. 2)

	Particle diameter (a) [µm]	$\frac{a}{D_h}$	*Focused position / range [µm]*
Polysterene beads	0.5	0.015	[0–300]
	1.1	0.033	[22.6–283]
	1.97	0.059	[25.5–226.4]
	2.9	0.087	[67.9–107.5]
	4.8	0.144	[78.6–114.3]
	5.4	0.162	[126.8–160.8]
	6.08	0.182	[117–162]
	10.2	0.306	[103.03–127.3]
	15.8	0.474	[151.5–178.6]
	16.5	0.495	[91.8–134.7]
E. coli	0.5	0.015	[28.37–294.3]
	2.0	0.060	
RBC	2.5	0.075	[91.8–143.9]
	8.0	0.240	
Yeast	5.0	0.150	[82.7–134.7]
	10.0	0.300	
HELA	16.0	0.480	[162.4–197.9]
	29.0	0.870	

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