MICROFLUIDIC DRIFTING: THREE DIMENSIONAL HYDRODYNAMIC FOCUSING OF MICROPARTICLES
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ABSTRACT
In this work we present numerical simulation and experimental validation of a three-dimensional (3D) hydrodynamic microparticle focusing method based on “microfluidic drifting” technique recently developed in our group. Microfluidic drifting utilizes Dean vortical flow induced in a microfluidic curve to realize 3D hydrodynamic focusing in a single-layer planar microfluidic device. Here we show this principle can be effectively adapted to focus microparticles with size and density close to those of lymphocytes.

KEYWORDS: Microfluidic Drifting, 3D Hydrodynamic Focusing, Dean Flow, Microparticle

INTRODUCTION
Three dimensional hydrodynamic focusing is the key to develop microfluidics-based flow cytometry system. In conventional flow cytometry, 3D hydrodynamic focusing is achieved using a co-axial structure. However, such structures are difficult to implement using the standard soft-lithography technique, which only facilitates the 2D planar fluidic structures. Recently, our group introduced a novel 3D hydrodynamic focusing technique named “microfluidic drifting” to enable the 3D hydrodynamic focusing in a single-layer two dimensional (2D) planar microfluidic structure. Previously we have demonstrated this technique for 3D hydrodynamic focusing of a fluorescent dye solution [1]. Recently we have expanded our previous work by investigating the possibilities to use the same principle for the 3D focusing of discrete microparticles, such as lymphocytes which are routinely screened in HIV diagnosis using flow cytometry.

THEORY
The “microfluidic drifting” based 3D hydrodynamic focusing is a two step process as detailed in our previous publication [1]. The first step involves the focusing of sample in vertical direction using the transverse dean flow, and the second focusing step is the focusing of fluids in horizontal plane using the sheath flows (Figure 1a). Small molecules such as fluorescein usually follow the streamlines (Figure 1b) and can be effectively focused. However whether this technique can be used for 3D focusing of larger microparticles such as biological cells were not clearly, as larger microparticles with density different from that of carrier fluids tend to migrate across the streamlines and render the 3D focusing ineffective.
In the cross-sectional plane of curve channels, forces acted on suspended particles include (i) Dean viscous (stoke) drag due to the secondary rotational Dean flow ($F_D$), (ii) apparent centrifugal force ($F_{cfg}$), and (iii) apparent gravitational force ($F_G$) [2]. $F_D$ accelerates particles transversely to ensure the particles to stay on course of streamlines. $F_{cfg}$ and $F_G$, on the other hand, cause particles to deviate from the streamlines. $F_D$ increases with the 1st order of the particles size while the $F_{cfg}$ and $F_G$ increase with the 3rd order. Therefore for large microparticles such as cells centrifugal and gravitational effects may be significant enough to cause particles to deviate from streamlines and resulting in failure of the 3D focusing.

RESULTS AND DISCUSSION

We first compared the relative magnitudes of these three forces as follows:

\[ F_D = 6\pi\mu U_D \]
\[ F_c = \frac{4}{3}(\rho_P - \rho_L)g r^3 \]
\[ F_{cfg} = \frac{4}{3}(\rho_P - \rho_L)\rho_P^3 U_P^2 / R \]

where $\mu$ is the dynamic viscosity of the carrier fluid, $r$ is the radius of the particle, $\rho_P$ and $\rho_L$ are the densities of particles and carrier fluid, respectively, $R$ is the radius of curvature of the curved channel, $U_P$ is the particle velocity and $U_D$ is the rotational dean flow velocity scale as

\[ U_D \sim De^2 \mu / D_h \rho_L \]

$De$ is the Dean number defined as

\[ De = \text{Re}(D_h / 2R)^{1/2} \]

where $D_h$ is the hydraulic diameter, $Re$ is the Reynolds number. We calculated three forces experienced by the particles (lymphocyte, $r_p = 3.5$ $\mu$m, $\rho_P = 1.09 \times 10^3$ kg/m$^3$) using water ($\rho_L = 1.09 \times 10^3$ kg/m$^3$) as carrier fluids. We found $F_G$ and $F_{cfg}$ are several orders lower than $F_D$, indicating the dean drag is the dominate factor and centrifugal and gravitational effect are not likely to affect the 3D focusing result.

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We further conducted a numerical simulation of microparticle focusing process using a finite-volume (FV) based multi-physics package, ESI-CFD+ (ESI-CFD, U.S.A). The “flow module” and “spray module” were employed to simulate the motion of discrete solid particles in 3D focusing process. The simulation result is shown in Figure 2a. Particle sources were uniformly distributed at the particle inlet. The color of each particle represents its height (Z direction). In X-Y plane, it is clearly visualized particles are lined up in the main channel. The color of the particles changes from rainbow colors to uniform color, representing the particles are focused vertically to the center plane of the channel.

Finally we experimentally characterized the 3D particle focusing process with fluorescent polystyrene microparticles with size and density similar to lymphocyte cells. The flow pattern in both fluorescent image (Figure 2b) and bright field image (Figure 2c) shows the “drifting” behavior of the particles in the curved channel which matches the flow pattern obtained using the fluorescent dye previously reported [1], suggesting a successfully 3D particle focusing.

![Figure 2. (a) CFD simulation of 3D particle focusing process, and fluorescent (b) and bright field (c) images of 3D particle focusing.](image)

CONCLUSIONS

In summary, we have shown our “microfluidic drifting” technique can be effectively used in focusing not only the small molecules but also larger microparticles such as biological cells. “Microfluidic drifting” is readily applicable for 3D hydrodynamic focusing of biological cells for microfluidics based flow cytometry devices.

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REFERENCES
