Inertial blood plasma separation in a contraction–expansion array microchannel

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Continuous inertial blood plasma separation is demonstrated in a contraction–expansion array microchannel with a low aspect ratio (AR). The separation cutoff value of the particle size can be controlled by modulation of the force balance between inertial lift and Dean drag forces. The modulation is achieved by changing the channel AR at contraction region, which causes the change in magnitudes of the inertial lift forces on the particles. The presented blood plasma separator provides a level of yield and throughput of 62.2% and 1.2 ml/h (≈1.0×10^8 cells/min), respectively. © 2011 American Institute of Physics. [doi:10.1063/1.3601745]
of the particle migration across the channel depending on the particle size. At a low AR (width $\gg$ height) of the contraction region, higher shear rate between the top and bottom of the channel is induced than between the left and right of the channel, which results in strong inertial lift forces that drive the particles toward the top and bottom of the channel wall. As changing the channel AR, modulation of separation cutoff value can be achieved due to inertial lift force changed by high-shear rate being induced between the top and bottom channel wall. Figure 1(b) shows the principle of inertial migration of the particles in the CEA microchannel with a different AR. The force balance between $F_{FL}$ and $F_{FD}$ is a determining factor for particles to occupy equilibrium position by inertial lift forces or entrain in Dean flow by Dean drag forces. At an AR of 1, the injected particles (red, RBCs model) and fluorescent dye (green, blood plasma model) influenced by dominant Dean drag force, thereby, migrating toward sidewall 2 (s2) ($F_{FL} < F_{FD}$). However, at a low AR, the particles migrate toward the top and bottom of the microchannel due to high-shear induced inertial lift force and then entrain in Dean flow, thereby, migrating toward sidewall 1 (s1) ($F_{FL} \geq F_{FD}$). Fluorescent dye still migrates toward s2 under the dominant Dean drag force being induced by Dean flow ($F_{FL} < F_{FD}$). Using the change in channel AR of the contraction region, the direction and magnitude of migration of the particles can be modulated.

The CEA microchannel was fabricated in poly(dimethylsiloxane) using soft lithography techniques (see Ref. 21, Experimental). The device was 350 $\mu$m wide, with contraction regions of 50 $\mu$m wide and 300 $\mu$m long. The contraction regions were formed with six rectangular structures in the microchannel. The interval between contraction regions was 700 $\mu$m. The heights of the CEA microchannel were fabricated with 20 and 50 $\mu$m at each device for investigation of particle migration. We defined AR as the ratio of the channel height to width (AR=$H/W$, $W$: channel height, $W$: contraction channel width). The AR of the fabricated CEA device is 0.4 and 1, corresponding to channel height of 20 $\mu$m and 50 $\mu$m, respectively. Reynolds number (Re) is defined as: Re=$\rho UD_{h}/\mu$, where $\rho$ is the fluid density, $U$ is the x-axial velocity (as the total flow rate at the expansion region), $D_{h}$ is the hydraulic diameter defined as $2wh/(w+h)$ ($w$: expansion channel width, $h$: channel height), and $\mu$ is the viscosity. Particles and cells in the CEA microchannel were investigated through a fluorescence microscope (see Ref. 21, Experimental).

Figure 2 shows the lateral migration of the 4 and 10 $\mu$m polystyrene particles and fluorescent dye at Re of 12.5. The 10 $\mu$m particles were observed near to s1 due to occupying their equilibrium position by dominated inertial lift forces ($F_{FL} > F_{FD}$) at AR of 0.4 and 1. However, the opposite direction of the 4 $\mu$m particles migration was observed due to the modulation effect of the force balances, resulting in migration toward s1 and s2 at AR of 0.4 and 1, respectively. Even though strong streaks of particle trajectory were observed near to s1 for the 4 $\mu$m particles at AR of 0.4, the other weak streaks were also observed near to channel center (see Ref. 21, Fig. S1). It means that the 4 $\mu$m particles are influenced by superposition effect between strong inertial lift and Dean drag forces ($F_{FL} \geq F_{FD}$). Induced high-shear rate between the top and bottom of the channel causes strong inertial lift forces acting on particle migrating toward the top and bottom of the channel wall. The 4 $\mu$m particles migrate toward the top and bottom of the channel due to the dominance of inertial lift force; and simultaneously entrain in Dean flow. From this mechanism, the most of 4 $\mu$m particles migrate the top and bottom of the channel and then toward s1 by Dean flow directed to s1; and some particles which still located in the middle of the channel migrate toward s2 by Dean flow directed to s2. On the other hand, the lateral positions of fluo-

![FIG. 1.](image1.png)  
![FIG. 2.](image2.png)
The particle (with a diameter of $a_p$) focusing by influence of dominant inertial lift force is strongly dependent on the ratio of inertial force ($a_p/D_b$). From the calculated $a_p/D_b$ of 4 μm particles, we also expect that the RBC separation from blood plasma is accomplished at the CEA device under 20 μm height in the regime above $Re$ of 12 (see Ref. 21, Ratio of inertial force and Fig. S2).

For the blood plasma separation, we designed the CEA device with 18 μm height which connected with bifurcation outlet for separation and collection of the RBCs and blood plasma. In order to achieve high flow rate and high yield blood plasma separation, we introduced the whole blood and phosphate buffered saline (PBS) with a total flow rate of 13.2 mL/h ($Re = \sim 19.9$). After passing through the CEA microchannel, most of RBCs dominated by inertial lift forces were wasted in the upper outlet and blood plasma dominated by Dean flow was substantially collected in the bottom outlet. RBC rejection ratio and yield of blood plasma separation was calculated with a level of 60% and 62.2%, respectively (Fig. 3). The collected blood plasma were substantially diluted by PBS focusing flow in the separation process. Even though the RBC rejection ratio was relatively low, it might increase after a second round of separation with collected blood plasma at the first round.

In conclusion, we have demonstrated a continuous blood plasma separation by using inertial microfluidics with a level of throughput of 1.2 mL/h ($\sim 1.0 \times 10^8$ cells/min) and high yield (62.2%). The CEA microchannel offers advantage, in that simple scaling of the channel AR allows the modulation of the force balance between the inertial lift and Dean drag forces, thereby controlling the particle migration.

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