Three-dimensional particle focusing under viscoelastic flow based on dean-flow-coupled elasto-inertial effects

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ABSTRACT

Based on dean-flow-coupled elasto-inertial effects, 3D particle focusing in a straight channel with asymmetrical expansion-contraction cavity arrays (ECCA channel) is achieved. First, the mechanism of particle focusing in both Newtonian and non-Newtonian fluids was introduced. Then particle focusing was demonstrated experimentally in this channel with Newtonian and non-Newtonian fluids using three different sized particles (3.2 μm, 4.8 μm, 13 μm), respectively. The influences of flow rates on focusing performance in ECCA channel were studied. Results show that in ECCA channel particles are focused on the cavity side in Newtonian fluid due to the synthesis effects of inertial and dean-drag force, whereas on the opposite cavity side in non-Newtonian fluid due to the addition of viscoelastic force. Compared with the focusing performance in Newtonian fluid, the particles are more easily and better focused in non-Newtonian fluid. A further advantage is three-dimensional (3D) particle focusing in non-Newtonian fluid is realized according to the lateral side view of the channel while only two-dimensional (2D) particle focusing can be achieved in Newtonian fluid. Conclusively, this Dean-flow-coupled elasto-inertial microfluidic device could offer a continuous, sheathless, and high throughput (>10000 s⁻¹) 3D focusing performance, which may be valuable in various applications from high speed flow cytometry to cell counting, sorting, and analysis.

Keywords: Microfluidic, Dean-flow-coupled elasto-inertial effects, 3D particle focusing

1. INTRODUCTION

Three-dimensional (3D) particle focusing is essential for separating¹, sorting, counting², detecting and analysis in numerous biological and chemical applications, such as the flow cytometers used for the detection and enumeration of bio-particles.

The manipulation of particles is based on their intrinsic physical characteristics such as particle size, shape, density, polarizability and magnetic susceptibility. Focusing techniques can be classified to two categories: active methods and passive methods. Active methods are based on the application of external force fields, such as dielectrophoresis (DEP)³⁻⁶, magnetophoresis⁷⁻⁸, surface acoustic wave (SAW)-induced streaming⁹, and optical tweezers¹⁰. Passive methods are based on the microchannel geometrical effects and hydrodynamic forces¹¹, such as pinched flow fractionation (PFF)¹², hydrodynamic filtration¹³, Dean-flow coupled inertial effects¹⁴⁻¹⁵, deterministic lateral displacement (DLD)¹⁶. Most of particle focusing methods are performed in Newtonian fluid. Active methods can provide precise control of target bio-particles, however, they have a low throughput and require extra, expensive device components for the external forces. Passive methods are relatively simple, effective and have a high throughput, but some of the channel design are still very complex and lack flexibility. Moreover, either the active or the passive methods are difficult to realize 3D focusing in Newtonian fluid, however, in non-Newtonian fluids, with the aid of elasto-inertial effects, 3D sheathless particle focusing can be easily achieved in a simple square or rectangular channel by properly adjusting the flow rate. Recently, particle manipulation including focusing and separation have gained significant attention in non-Newtonian fluids. The positive first normal stress difference (N₁) arising in pressure driven flows of dilute polymer solutions can lead suspended particles or cells to migrate to the mid-plane of the channel¹⁷⁻¹⁹, Leshansky, et al²⁰ observed that the particles migrate toward the centreline due to the imbalance in the first normal stress difference between the centreline and the walls in a slit channel. These particles are two-dimensionally focused under the conditions.
A. Particle focusing in Newtonian and non-Newtonian fluids

In Newtonian fluids, the shear gradient lift force and wall lift force are the two dominant forces to govern the particle migration, and an equilibrium position is created by the balancing the two lift forces. The sum of the two inertial lift forces, which is called the net inertial lift force, was first derived by Asmolov\textsuperscript{24}, and later simplified by Di Carlo\textsuperscript{25} as following:

\[ F_L = \rho_L \frac{U_m a^4}{h^2} f_L(R_c, x_c) \]  
\[ R_c = \frac{\rho L U_m a}{\mu L} = \frac{2 \rho L Q}{\mu L (w+h)} \]  

where \( \rho_L, U_m \) and \( \mu_L \) are the fluid density, mean velocity, and dynamic viscosity, respectively; \( a \) is the spherical diameter of the particles; \( D_h = 2wh/(w+h) \) is the hydraulic diameter for a rectangular channel with \( w \) and \( h \) the width and height of the channel cross section. The lift coefficient of net inertial lift force \( f_L(R_c, x_c) \) is a function of the position of the particles within the cross section of channel \( x_c \) and the channel Reynolds number \( R_c \).

Particle migration and focusing in non-Newtonian viscoelastic fluid is different with that in Newtonian fluids. In non-Newtonian viscoelastic fluid, the elastic force is determined by the intrinsic properties of the medium. The elastic effects of a non-Newtonian fluid in the channel flow can be characterized by \( W_e \), which is defined as the ratio between two time constants:

\[ W_e = \frac{\tilde{\lambda}}{\tilde{t}_f} = \lambda \tilde{\gamma} = \lambda \frac{2V_m}{w} = \frac{2 \lambda Q}{hw^2} \]  

where \( \lambda \) is the relaxation time of the fluid and \( t_f \) is the characteristic time of the channel flow. The characteristic time is approximately equal to the inverse of the average (characteristic) shear rate, \( \tilde{\gamma} \), which is \( 2V_m/w \) or \( 2 \lambda Q/hw^2 \) in a rectangular channel. \( V_m \) is the average velocity and \( w \) and \( h \) is the channel width and height, respectively.

Figure 1 is the simulation results of velocity magnitude in the cross section of a rectangular channel 100 \( \mu m \times 50 \mu m \) (Width \( \times \) Height) using COMSOL. (As the shear viscosity in non-Newtonian fluid is considered constant, there is no difference between Newtonian and viscoelastic flows in the velocity distribution within a cross-section at the same flow rate\textsuperscript{25,26}.) The color bar represents the magnitude of the velocity. The magnitude of velocity increases from the bottom of
the bar (dark blue) to the top of the bar (dark red). It can be seen from the simulation results that the maximum velocity occurs in the central part of the rectangular channel, and decreases gradually from the centre line to the channel wall, which validates that the velocity profile is a parabolic curve. Figure 2 is the simulation results of the shear rate, which is the differential of the flow velocity. The centreline and the corners of the channel are low shear rate regions, which also correspond to the low first normal stress $N_1$ regions and particles tend to migrate towards the channel centreline and corners under pure elastic effects. The elastic force $F_E$ can be assumed to stem from the imbalance in the distribution of $N_1$ over the size of the particle,

$$F_E = a^3 \nabla N_1 = a^3 (\nabla \tau_x - \nabla \tau_y) = 2a^3 (1 - \beta) W_t \nabla \dot{\gamma}^2$$

where $a$ is the particle radius, $\beta$ is the ratio of the solvent to solution viscosity and $\nabla \dot{\gamma}$ is the non-dimensional local shear rate.

The number of multiple equilibrium positions can be reduced to one at the centreline by properly adjusting the flow rate due to the synergetic effect of inertia and viscoelasticity. The competition between the elasticity and the inertia determines the particle migration. Since the elasticity and inertia is represented by $W_t$ and $Re$, respectively, the elasticity number (the ratio between these two numbers ($W_t/Re$)) can be used to measure the relative importance of elastic forces to inertial effects, which is defined as:

$$EI = \frac{W_t}{Re} = \frac{2 \pi \mu (w+h)}{\rho \mu^2 \eta h}$$

If the medium does not yield apparent shear-thinning viscosity, $EI$ is independent of the flow rate and only dependent on fluid viscosity and relaxation time in a specific channel.

**B. Principle of Dean-flow-coupled elasto-inertial particle focusing**

In the ECCA channel with non-Newtonian fluid, three kinds of forces are harmonized: Lift force $F_L$, including the shear-gradient lift force ($F_{LS}$), wall-repulsion force ($F_{Lw}$); the Dean drag force $F_D$ resulting from the curved channel geometry; and elastic force $F_E$ induced by the nature of the viscoelastic medium. Figure 3 shows the simulation results of the flow field in the cross section 100 $\mu$m away from the cavity along the x direction at the outlet in the ECCA channel using COMSOL and the schematic illustration of the focusing mechanism in Newtonian (a) and non-Newtonian (b) fluid. When particles flowing in the ECCA channel with a Newtonian fluid, the effects of inertial migration and secondary flow act in superposition on the particles, thus the four equilibrium positions induced by Lift force $F_L$ in rectangular channels are destroyed by the dean drag force $F_D$ and particles become stable in two modified equilibrium positions, Figure 3(a). The arrows represent the magnitude and direction of the secondary flow field induced by the abrupt contraction of the channel. When particles flowing in ECCA channels with a viscoelastic non-Newtonian fluid, the
elastic force $F^E$ should be considered, which is directed away from the wall and decays with increasing distance from the wall. In a straight rectangular channel with non-Newtonian fluids, the particles tend to migrate to the centreline of the channel by the synergetic effect of inertia and viscoelasticity. In the ECCA channel, the particles become unstable when an additional secondary flow drag is exerted on the particles. Subsequently, a new equilibrium position can be achieved near the channel wall by the combined effects of lift force $F^L$, elastic force $F^E$ and the dean drag force $F^D$ as shown in Figure 3(b). Finally, 3D particle focusing is realized in an ECCA channel with the combined effect of Dean-flow-coupled elasto-inertial forces.

![Figure 3](image_url)

Figure 3 Simulation results of the flow field in the cross section 100 µm away from the cavity along the x direction and the schematic illustration of the focusing mechanism in Newtonian (a) and non-Newtonian (b) fluid. (a) The red circles represent two equilibrium positions that resulted from a balance between the inertial lift force $F^L$ and secondary flow drag $F^D$, and (b) The red circle represents the single equilibrium position by the synergetic effect of inertia, secondary flow and viscoelasticity. The dashed circles are the unstable equilibrium positions. The arrows represent the magnitude and direction of the secondary flow field induced by the abrupt contraction of the channel.

![Figure 4](image_url)

Figure 4 Schematic diagrams of particle focusing in Newtonian and non-Newtonian fluids in the ECCA channel. Particles are randomly injected to the inlet, and finally focused in a single line on the opposite cavity side at the outlet in non-Newtonian fluid in Dean-coupled elasto-inertial effects, while focused to two equilibrium positions on the cavity side at the outlet in Newtonian fluid in the combination of Dean and inertial effects.
Figure 4 shows the schematic diagram of particle focusing in Newtonian and non-Newtonian fluids in the ECCA channel. There are 26 repeated expansion-contraction triangular cavities in this channel, while only the inlet and outlet section of the channel is illustrated here. Particles are randomly injected to the inlet, so from the top view, cross section view and side view in the amplified inlet section the particles are dispersed. As the particle suspension flows, particles are driven into a single line along the channel wall on the opposite cavity side in non-Newtonian fluid with the Dean-flow-coupled elasto-inertial effects described above. However, in a Newtonian fluid, because there is no elastic effect induced by the polymers, particles are focused to two equilibrium positions on the cavity side at the outlet in a Newtonian fluid as result of Dean and inertial effects.

3. EXPERIMENTS

A. Design and fabrication of the microfluidic device

Figure 5 The schematic geometry of the microfluidic channel with triangular expansion-contraction cavity arrays, \( L_0 = 48 \) mm, \( L_1 = 900 \) μm, \( L_2 = 900 \) μm.

The right angled isosceles triangular cavities are patterned on one side of a straight channel. The channel has a cross section of 100 μm x 40 μm (width x height). The longest edge of the triangle is \( L_1 = 900 \) μm, and the space between two adjacent cavities is uniform at \( L_2 = 900 \) μm. The total length of the straight channel is \( L_0 = 48 \) mm, including 26 repeated expansion-contraction triangular cavities. Its schematic geometry is shown in Figure 5.

The device was fabricated by standard photolithography and soft lithography techniques. The fabrication included rapid prototyping on a silicon master, polydimethylsiloxane (PDMS) replica moulding, and sealing through plasma oxidation. Briefly, photoresist (SU-8 2025, MicroChem Co., Newton, MA) was spun on a silicon wafer at 2000 rpm to a thickness of 40 μm, and then exposed to UV light through a designed mask using a mask aligner system (ABM, San Jose, CA). After that the photoresist on the silicon wafer was developed in an SU-8 developer solution and rinsed by isopropylalcohol (IPA) to create a positive replica of channel geometry. A PDMS mixture with a 10:1 ratio of base to agent (Dow Coming, Midland, MI) was poured over the silicon master, degassed to remove bubbles in a vacuum oven, and cured at 100°C for 45 min. After the PDMS was cured and taken out of silicon master, the inlet and outlet holes were punched with a custom needle tip. Finally, the PDMS slide was bonded with another PDMS slide after exposure to oxygen plasma (PDC-002, Harrick Plasma, Ossining, NY) for 3 minutes.

B. Suspending fluid and particles

In this work, two kinds of fluids were prepared: Newtonian fluid (deionized water), and Non-Newtonian fluid (moderate elasticity fluid). For the moderate elasticity fluid, PEO (poly (ethylene oxide), \( M_w = 2 000 000 \), Sigma-Aldrich) was added to deionized water in 500 ppm. The density of the fluid matches with the polystyrene (PS) particles (1.05 g cm\(^{-3}\)). The PEO solution is considered to have a constant shear viscosity of 3.12 x 10\(^{-2}\) Pa s under the present experimental conditions and its relaxation time is 9.1 x 10\(^{-3}\) s. The viscosities for deionized water is 1.0 x 10\(^{-3}\) Pa s. Tween 20 (0.01 wt%, Sigma-Aldrich) was added to all the solutions to prevent particle-particle adhesion. Internally dyed fluorescent polystyrene microspheres were purchased from Thermo Fisher Scientific., USA. A particle suspension was prepared by diluting 3.2 μm (product no.G0300, CV<5%), 4.8 μm (product no.G0500, CV < 5%), and 13 μm (product no.G1000, CV < 5%) particles to the concentration of ~10\(^7\) particles ml\(^{-1}\) by deionized water and PEO solution respectively. This concentration was considered to be low enough to neglect any interaction between particles in the micro-channel. Before the experiment, the particles were shaken by a vortex device to guarantee a good suspension.
C. Experimental setup

The particle suspensions were transferred to a 1 ml syringe, and then introduced into the microfluidic chip through a silicon tube by a syringe pump (Legato 100, Kd Scientific). The outflow of the particle suspension was collected in a glass bottle. The microfluidic chip was placed on an inverted microscope (CKX41, Olympus, Japan), and illuminated by a mercury arc lamp. The images of the fluorescent particles were observed and captured by a CCD camera (Rolera Bolt, Q-imaging, Australia) which had a maximum capturing speed of 50 frames per second. The fluorescent images were then post-processed and analysed with the software Q-Capture Pro 7 (Q-imaging, Australia). The flow rate in the experiment was increased from 10 µl min⁻¹ to 300 µl min⁻¹, which corresponds to an average fluid velocity from 0.04 m s⁻¹ to 1.2 m s⁻¹. A profile of the fluorescent intensity was taken from the outlet of the last cavity to examine the focusing performance of this microfluidic device in both Newtonian and non-Newtonian fluid.

4. RESULTS AND DISCUSSION

A. Effects of elasticity on particle migration

Figure 6 shows the fluorescent images of 3.2-µm, 4.8-µm, 13-µm particles at the outlet under the flow rate of 60 µl min⁻¹ in both Newtonian and non-Newtonian fluids, respectively, and corresponding intensity profiles for each particle type along the width of the channel. In the 500-ppm PEO dissolution, three particle types were focused very well at the flow rate of 60 µl min⁻¹ (Re = 4.62, We = 45.48, El = 9.84) and in a specific range of flow rate around 60 µl min⁻¹ as well. The particles experience the lift force $F_L$, the dean drag force $F_D$ and the elastic force $F_E$ at the same time, and an equilibrium position was observed on the opposite of cavity side due to the combined effects of the three forces. In a Newtonian fluid, however, no obvious particle focusing is observed at the outlet under 60 µl min⁻¹ flow rate with the 3.2-µm, 4.8-µm particle size. The 13-µm particles begin to focus from 60-µl µl min⁻¹ flow rate under the effects of the lift force $F_L$, the dean drag force $F_D$. It can also be seen from the fluorescent intensity profile (Figure 6 d,e,f) that the particles in DI water are mostly dispersed, while in PEO solution the particles are tightly focused. The width of the focusing line (derived from the difference of lateral position in the fluorescence intensity profile at 70% intensity peak) in PEO solution is similar to the diameter of the particles. It’s concluded that single-particle focusing is achieved in the x-y plane. Compared with particle focusing in a Newtonian fluid, the elasticity in a non-Newtonian fluid accelerates the particle focusing, improves the focusing performance, and finally focuses particles on the opposite side of cavity.

(a) 3.2 µm particle in PEO
(b) 3.2 µm particle in DI water
(c) 13 µm particle in PEO
(d) 13 µm particle in DI water
(e) 3.2 µm particle in PEO
(f) 3.2 µm particle in DI water

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Figure 6 The fluorescent images of 3.2-μm, 4.8-μm, 13-μm particles at the outlet under the flow rate of 60 μl min⁻¹ in Newtonian and non-Newtonian fluids, respectively, and corresponding fluorescent intensity profiles for each particle type along the width of the channel.

B. Effects of different flowing conditions.

As the inertial lift force, secondary force and elastic force are all related to the flow rate. Under different flowing conditions, the particles will experience different dominant forces, which will lead to different particle distributions. Take 4.8-μm particle as an example, the 4.8-μm particles distribution was observed under different flowing conditions in 500ppm PEO fluid and DI water, as is shown in Figure 7. The flow rate Q varies from 10 μl min⁻¹ to 300 μl min⁻¹, which corresponds to the levels of Re ranging from 0.77 to 23.10, Wr ranging from 7.58 to 227.4, and EI 9.84 which is independent of the flow rate. In DI water, Wr and EI are both zero since Newtonian fluid does not exhibit elastic properties. When the flow rates are relatively low (<30 μl min⁻¹, Re = 2.31, Wr = 22.74, EI = 9.84) with 500ppm PEO solution, the inertial effect and the Dean effect are negligible, while elastic force is dominant, and the particles are randomly distributed. As the flow rate increases, the inertial and Dean drag force being exerted on a particle competes
with elastic force, and the particles gradually migrate to the opposite side of the cavity in the channel and focused tightly (as shown in Figure 7 at 60-μl min⁻¹ flow rate in PEO (Re = 4.62, Wi = 45.48, EI = 9.84)) due to the balance of the lift force \( F_L \), Dean drag force \( F_D \) and elastic force \( F_E \). The focusing range is approximately from 30 μl min⁻¹ to 120 μl min⁻¹. When the flow rate reaches 120 μl min⁻¹ (Re = 9.24, Wi = 90.96, EI = 9.84), another focusing line occurs on the cavity side. This is partly because inertia and secondary flow effects begin to dominate the particle migration. Consequently, the elastic force was eventually overwhelmed by the inertial force all the particles migrate and focus on the cavity side when the flow rate reaches 240 μl min⁻¹ (Re = 18.48, Wi = 181.92, EI = 9.84). In DI water, the particles are dispersed until the flow rate reaches 120 μl min⁻¹, then the particles are focused on the cavity side of the channel under the combined effect of the lift force \( F_L \) and the Dean drag force \( F_D \). The minimum focusing flow rate in a Newtonian fluid is higher than that in a non-Newtonian fluid and the focusing performance in a Newtonian fluid is not as good as in a PEO solution. That is to say, the elastic force accelerates and improves the particle focusing performance. It can also be seen from the fluorescent intensity profiles of particles flowing with different flow rates in 500ppm PEO and DI water. A further advantage is that in ECCA channel the flow rate that allows particle focusing is dozens of or even hundreds of microlitre per minute, which is much higher than that in a straight channel (several microlitres per minute)²¹, resulting in a higher throughput (>10000 s⁻¹).

![Image](image_url)

**Figure 7** The fluorescent images of 4.8μm particle at the outlet at the flow rate of 30 μl min⁻¹, 60 μl min⁻¹, 120 μl min⁻¹, 240 μl min⁻¹ in 500ppm PEO and DI water fluids, respectively, and corresponding fluorescent intensity profiles for different flow rates along the width of the channel.

**C. Side view of the channel**

Figure 8 (a) is the side view of the channel when particles flowing in 500ppm PEO solution at a flow rate of 60 μl min⁻¹. It is verified that the particles flowing in non-Newtonian fluid are not only focused in the x-y plane, but also form a single line in the centreline of the channel in the x-z plane. That means, the 3D particle focusing in non-Newtonian fluid...
in this ECCA channel is realized by properly balancing the effects of inertia, secondary flow and elasticity. This phenomenon was not observed for the case of a Newtonian fluid when particles focused in DI water in x-y plane as shown in Figure 8 (b) in 240 µl min⁻¹. Instead, the particles in DI water are focused in two lines along the two channel walls in the x-z plane due to the synergetic effect of inertia and secondary flow, which is not suitable for practical applications such as one-by-one particle counting or sorting. It is confirmed that the equilibrium positions are reduced to single one by the additional elasticity effect in PEO solution in ECCA channel. It’s also obvious from the corresponding fluorescent intensity profiles in PEO and DI water, respectively. In a PEO solution, only one fluorescence intensity peak exists in the middle of the lateral side view, while there are two peaks in DI water.

![Figure 8](image)

Figure 8 Fluorescent images of the side view of the channel when particle focusing in 500ppm PEO solution and DI water, respectively, and corresponding fluorescent intensity profiles.

5. CONCLUSION

To summarize, 3D particle focusing was demonstrated in an ECCA channel by exploiting the Dean-flow-coupled elasto-inertial effects. By properly controlling the flow rates to harmonize the inertial force, viscoelastic force and Dean-drag force, 3D particle focusing in non-Newtonian fluid along the opposite side of cavities was achieved. Particle focusing under Newtonian and non-Newtonian fluids using three different sized particles (3.2 µm, 4.8 µm, 13 µm) were demonstrated. The particles were focused on the cavity side in a Newtonian fluid by the composition of inertial and Dean-drag force, whereas on the opposite cavity side in a non-Newtonian fluid due to the addition of the viscoelastic force. Compared with particle focusing in Newtonian fluid in an ECCA channel, it can be concluded that particles in non-Newtonian fluid are more easily and better focused. In the ECCA channel, the flow rate that allows particle focusing is dozens of or even hundreds of microlitre per minute, which is much higher than that in a straight channel (several microlitres per minute)², resulting in a higher throughput (>10000 s⁻¹). This Dean-flow-coupled elasto-inertial microfluidic device could offer a continuous, sheathless, and high-throughput (>10000 s⁻¹) 3D focusing performance, which may be valuable in various applications from high speed flow cytometry to cell counting, sorting, and analysis.

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