HIGH-RESOLUTION DEAN FLOW FRACTIONATION (HiDFF): A NOVEL DEAN MIGRATION PHENOMENON FOR SMALL MICROPARTICLE SEPARATION

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Herein, we introduce a novel Dean migration phenomenon in spiral microchannel, termed High-resolution Dean Flow Fractionation (HiDFF), for separation of small microparticles based on differential Dean migration profiles. Inertial microfluidics is an emerging class of passive size-based sorting technique for cell separation [1,2]. However, inertial focusing of small microparticles (particle size, a_p < 1-2 μm) remains a huge technical challenge as channel dimensions have to be scaled down (hydraulic diameter, D_h ~10 μm) for them to experience significant inertial forces (F_L) and undergo lateral migration. Our group previously developed a spiral microfluidics sorter (Dean Flow Fractionation, DFF) which enables well-controlled, Dean-induced lateral migration of small particles including bacteria [3], nanoparticles [4] and biomolecules [5] to channel outer wall while target cells (>10 μm) focus near inner wall for separation. However, it cannot further size-fractionate small particles (1 μm vs. 2 μm) as they would recirculate continuously due to Dean vortices. Using HiDFF, we were able to demonstrate efficient separation of 1–3 μm microbeads mixture, and then apply the technology to size-fractionate different small biological components including bacteria and nanoparticles.

The 2-inlet, 2-outlet spiral microdevice (60×300 μm (H×W)) is fabricated using polydimethylsiloxane (PDMS) (Fig. 1A). Small particles (a_p/ D_h <0.07) introduced at channel outer wall experience Dean drag forces (F_D) due to Dean vortices and migrate laterally towards inner wall (Fig. 1B). Near the inner wall, particles occupy different innermost transient positions under influence of size-dependent wall-induced inertial lift force (F_{WL}) (Fig. 1C). Hence, smaller particles are positioned closer to inner wall and separated into the inner outlet (outlet 1) while larger particles are sorted into outer outlet (outlet 2).

We first used 50 nm fluorescent polystyrene microbeads to study the lateral migration of small particles at different channel positions. Particles migrated along the channel top and bottom towards inner wall, and recirculated outwards as a tight band along the channel midline (Fig. 2A). Interestingly, the innermost transient particle position moved further away from inner wall with increasing particle size at same flow conditions, which led to distinct transient positions for each particle size (50 nm–3 μm) (Fig. 2B). We next characterized the separation efficiencies of different binary bead mixtures including 2 and 3 μm, and 1 and 2 μm beads (Fig. 3). Approximately 20% of the smaller particles were sorted into outlet 1 which resulted in a ~10 to 30–fold enrichment. Lastly, we used the developed HiDFF technology to size-fractionate *Escherichia coli* (*E. coli*) and Poly(lactic-co-glycolic acid) nanoparticles (PLGA NPs) into 2 different size groups (Fig. 4), and verified the particle size distribution using optical imaging and scanning electron microscope (SEM).

Currently, there is a critical need for small particle sorting which is important in applications ranging from material sciences, environmental bio-sampling to bacterial/exosomes clinical diagnostics. The developed HiDFF technology represents an important progress towards this goal, as it enables high throughput (~100 $\mu L min^{-1}$) membrane-free separation of small particles (<1 μm), and can be easily integrated to existing point-of-care platforms for small biological targets purification and detection.

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Figures captions

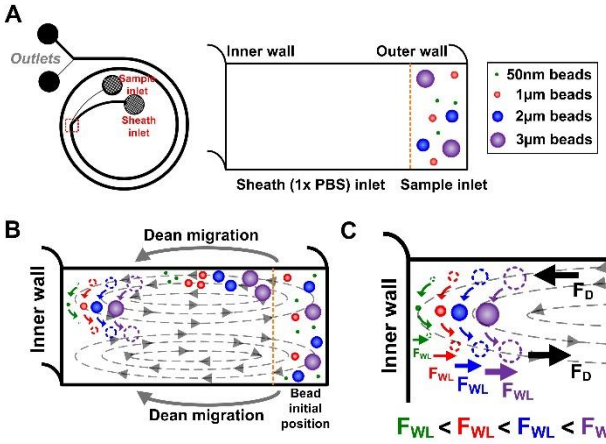

Figure 1 *(**A**) Device schematic of the High-resolution Dean Flow Fractionation (HiDFF) microdevice for small particle separation. (**B**) Under the influence of Dean vortices in spiral microchannel, small particles (particle size (a_p) to channel height (h), a_p/h <0.07) migrate laterally towards inner wall. Larger particles experience greater Stoke's drag and move slower than smaller particles during Dean migration. (**C**) Near the inner wall, the innermost transient positions of the particles are determined by size-dependent wall-induced inertial lift forces (F_{WL}) acting on the particles, which can be exploited for small particle separation with superior resolution.*

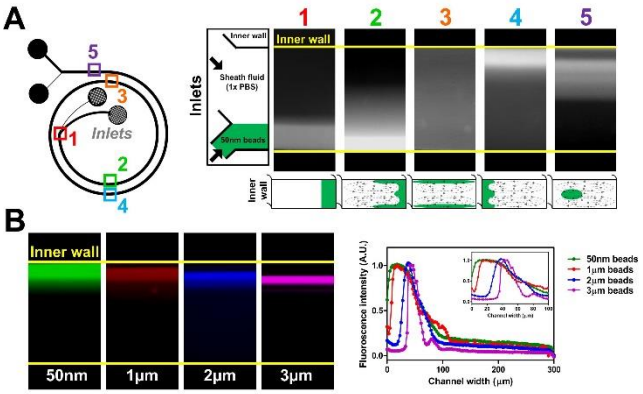

Figure 2 *(**A**) Average fluorescent composite images and cross-sectional channel schematic illustrating Dean migration trajectory of 50 nm particles along the channel. Particles at the outer wall (position 1) migrate laterally across the top and bottom channel (position 2 and 3) towards the inner wall (position 4). It will continue to recirculate as a tight band (position 5) towards the outer wall along the channel mid-plane. (**B**) Average fluorescent composite images and intensity linescans of the innermost transient particle positions at the same flow conditions. Inset plot highlights the distinct equilibrium positions for particles of different sizes.*

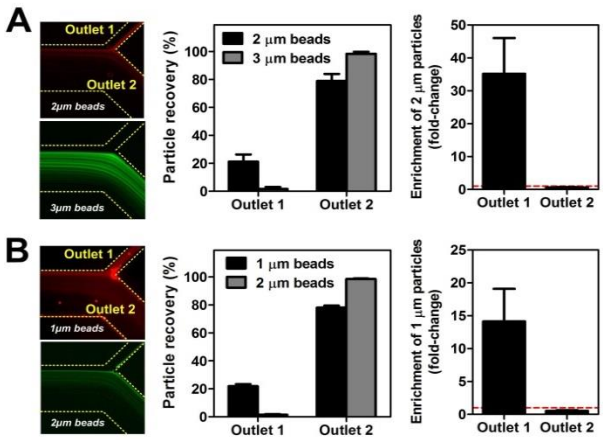

Figure 3 *Average fluorescent composite images and flow cytometry analysis for small particle separation between (**A**) 2 and 3 μm, and (**B**) 1 and 2 μm bead mixture using the HiDFF microdevice at optimized conditions. Smaller particles are sorted and highly enriched at the smaller inner wall outlet (outlet 1).*

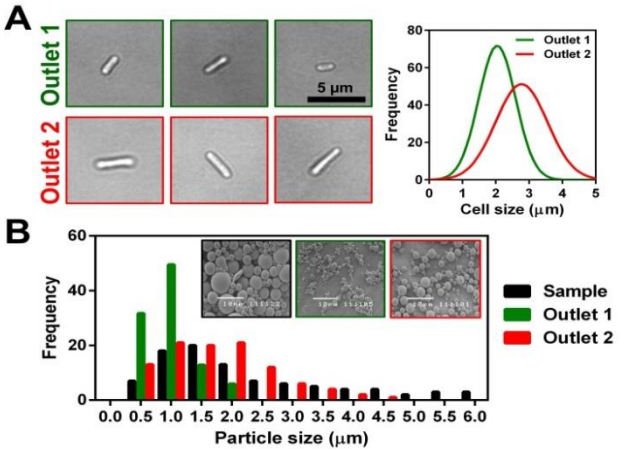

Figure 4 *(**A**) Size fractionation of bacteria population (E. coli) using HiDFF. Smaller E. coli are enriched in outlet 1. Size distribution is obtained from ~80-100 measurement in each outlet. (**B**) Size fractionation of PLGA nanoparticles. Inset SEM images highlight distinct size differences between sample (inlet) and different outlets.*

References

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