# CENTRIFUGE-ON-A-CHIP: SELECTIVE CELL TRAPPING WITH RAPID SOLUTION EXCHANCE IN MICROVORTICES

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# ABSTRACT

Here, we present a novel mechanism for cell trapping using microscale laminar vortices containing stable and predictable recirculating fluid flow. Particles larger than the critical size cut-off migrate laterally through fluid streamlines and orbit within the vortex while smaller particles follow fluid streamlines and travel out of the device. Larger particles were measured to experience shear gradient lift forces of up to  $0.21\mu$ N while entering the vortex. We envision this technique as a method for on-chip rapid exchange of various solutions around cells, that yields a result identical to centrifugation and may prove useful for flow cytometry at the point-of-care.

KEYWORDS: Laminar Microvortices, Cell Trap-and-Release, Rapid Solution Exchange

## **INTRODUCTION**

Cell trapping in localized regions of microfluidic systems are essential for many cell-based assays. Typically, cell trapping is performed with geometric traps, sieve filters, or external fields [1]. However, these systems have difficulty in releasing cells from the respective traps and may not be suitable for off-chip and downstream cell-based applications. Here, we present a new method for the trapping of particles and cells using laminar microvortices with a simple trap-and-release function. Previously, laminar microvortices were studied for their high radial acceleration and ability to aggregate platelets within the vortex [2,3]. Here we investigate for the first time how particles migrate into and orbit within the vortex traps. We also identify the hydrodynamic forces responsible for the particle trapping phenomenon, determine the critical particle size required for trapping in specific geometries, and present potential biological applications.

## THEORY ON PARTICLE TRAPPING

Microscale vortices are generated using high fluid flow rates where a sudden channel expansion creates a detached boundary layer with a region containing recirculating fluid. When inertia is important and a particle with diameter *a* is introduced into a straight channel of width *d*, the particle experiences two lateral lift forces, namely shear gradient and wall-effect (Fig. 1A)[4]. The shear gradient lift directs particles towards the wall while the wall-effect lift directs particles away from the wall focusing particles to equilibrium positions,  $X_{eq}$ , determined by particle size (Fig. 1B). As particles approach the expansion (channel width D=11d), larger shear gradient lift induces larger particles to migrate laterally across streamlines and into the vortex, since the balancing wall-effect lift is no longer significant immediately after the expansion. Smaller particles are maintained in streamlines that flow out of the device because they experience less shear gradient lift–scaling with  $a^3$  (Fig. 1C)



Figure 1: Particle trapping mechanism. (A) Schematic of sudden channel expansion where large (red) and small (green) particles are introduced randomly into the channel. (B) Particles migrate to respective equilibrium positions based on size, where larger particles are focused closer to the channel center. (C) Large particles migrate through fluid stream-lines into the laminar vortex while smaller particles follow streamlines and are flushed out of the device.

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Figure 2. Critical particle size cutoff. (A) Trajectory of a PDMS particle (a/d=0.6) migrating through fluid streamlines and orbiting within the vortex at a stable position. (B) Average trajectories of particles overlaid on fluid direction vectors derived from COMSOL modeling. Small particles begin their migratory path closer to the channel wall and migrate into the vortex farther downstream while large particles occupy equilibrium positions closer to channel center and migrate closer to the vortex center.

#### **RESULTS AND DISCUSSION**

Polydisperse PDMS particles with sizes (a/d=0.1-1.0) were injected (flow rate = 450 µL/min) into the straight channel device with a sudden expansion region. Using high-speed video microscopy, individual particle trajectories were mapped and overlaid onto fluid streamlines computed using FEM modeling (Fig. 2A). We observed that the critical particle size cut-off was a/d>0.3 for the tested system (Fig. 2B).

Particle migration into the vortex is made possible through decoupled lift forces where the shear gradient provides the driving force to move particles across fluid streamlines. The shear rate was mapped over the expansion region (Fig. 3A,B). The shear rate within the vortex was found to be significantly lower than in the straight channel upstream of the expansion (Fig. 3B). Additionally, the magnitude of shear gradient lift force,  $F_L$ , was determined from the transverse velocity of particles assuming lift balanced Stokes drag  $F_L=3\pi\mu av_t$  where the force is dependent on the particle size *a* and transverse velocity  $v_t$ . This velocity is derived from the mismatch in particle and fluid element trajectories as the particle migrates across streamlines (Fig. 3C). The lift force for larger particles (a/d>0.8) was calculated to be up to 0.21µN (Fig. 3D) and lift force decreased as expected with decreasing particle size.

The lower shear rate at the vortex center provides a gentle environment for cell trapping. This may be useful for applications which require trapping and enrichment of larger cells above a desired size from a heterogeneous sample. As a proof of concept, we loaded blood spiked with MCF-7 cancer cells and demonstrated selective trapping of MCF-7 cells (20  $\mu$ m) spiked within blood (cell sizes 2-15  $\mu$ m) (Fig, 4B). Further, we utilized this trapping phenomenon as a micro-scale "centrifuge" where cells initially suspended in one solution were washed and suspended within another solution (Fig. 4C-D).



Figure 3. Shear gradient lift force. (A) Using COMSOL finite element simulations, downstream slices (orange) were analyzed to determine shear rate and gradient. (B) The shear gradient decreases as the fluid flows downstream in the expansion. Note that the shear rate inside the vortex is significantly lower than that of the channel center. (C) The calculation of the lift force requires a transverse velocity based on the mismatch in particle velocity and fluid velocity. (D) Particles with sizes a/d > 0.3 experience enough shear gradient lift force to migrate through fluid streamlines.



Figure 4. Biological applications with microvortices. (A) Using a two-inlet system with an expansion-contraction array, one syringe was filled with cell solution while another syringe was filled with PBS washing solution. (B) To demonstrate selective size-based trapping of MCF-7 breast cancer cells, we isolated MCF-7 cells (20  $\mu$ m) in the low shear vortex, and separated them from human blood cells (2-15  $\mu$ m), which are flushed out of the device. (C) The ability to trap cells in vortices allows for continuous washing of cells and the resuspension of the cells in a different solution. To demonstrate this capability, we obtained fluorescent images of trapped MCF-7 cells labeled with Calcein AM in rhodamine solution and (D) PBS wash. The cells can be released from the vortex traps by decreasing the flow rate, and can be collected separately.

## CONCLUSION

This novel cell-trapping phenomenon with microvortices holds promise for high density trapping with an expansioncontraction array. We demonstrate two biological applications with microvortices including selective size-based isolation of cancer cells from blood and rapid exchange of solution for vortex-trapped cells. The latter technique creates opportunities for on-chip centrifugation and cell labeling techniques where these labeled cells can be released on demand for downstream cell-based assays.

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