Cavity-Induced Microstreaming for Simultaneous On-Chip Pumping and Size-Based Separation of Cells and Particles

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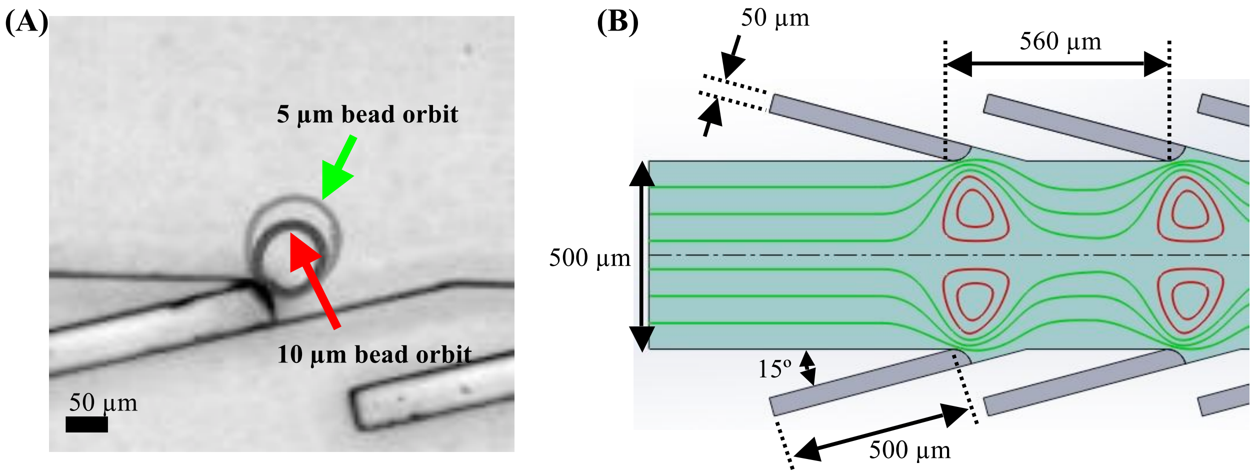
ESI Figure 1: Size dependent particle orbits and LCAT array dimensions



ESI Figure 1 – (A) Size dependent particle trajectories in angled LCATs. Larger 10 µm particles are trapped within a smaller orbit, while smaller 5 µm particles are trapped within a larger orbit. (B) Dimensions of LCATs and microchannels.

ESI Video 1: Oscillating interface motion

This movie shows a high speed video of the LCAT interface while undergoing periodic oscillations followed by how it is simulated as a time varying velocity profile. The high speed video (220,000 fps) shows that the interface oscillates such that a traveling wave starts at the PDMS tip and travels across the LCAT interface. To approximate this interface motion the inlet is set to a have a time varying velocity profile that resembles a traveling wave originating at the tip and moving towards the other wall.

ESI Video 2: LCAT Separator in operation

This movie shows the LCAT separator device in operation. For an applied voltage of 3 V_{pp}, both particle sizes are being trapped within the microstreaming vortices. Upon closer inspection, size-dependent particle trajectories are also distinguishable in the videos. The larger particles within the center of the vortex flow represent the orbits of 10 µm particles, while the smaller particles around the outside of the vortex represent the trajectories of 5 μm particles. As the voltage is increased to 4 V_{pp}, smaller particles are observed to travel forward within the flow from one LCAT pair to the next. Although there is still some trapping of 5 μm particles occurring within each microstreaming vortex, there is also release of a significant amount of beads that eventually reach the outlet reservoir.

It is important to note that as the voltage is increased from 3 V_{pp} to 4 V_{pp} there was an increase in the size of the vortex traps. Orbits of 5 μm and 10 μm beads still maintain their size dependent trajectories relative to one another. When the applied voltage is increased to 5 V_{pp} we observe a larger degree of 5 μm particles being released to the outlet. We also observe that the orbits of the larger 10 μm beads are at their maximum compared to 3 V_{pp} and 4 V_{pp}. The symmetry of the vortices previously observed begins to break down at 5 V_{pp}. Voltages higher than 5 V_{pp} caused cavitation nucleation within the microchannel walls.

ESI Method 1: Simulation model setup details

2-dimensional CFD simulations were conducted using CFD-ACE+ v2011 (ESI Group, Inc., France) using the fluid flow and spray modules on a single angled LCAT pair. The microchannel was 250 µm wide and 2200 µm long with a structured grid of 10 µm x 10 µm throughout as shown in Figure M1.

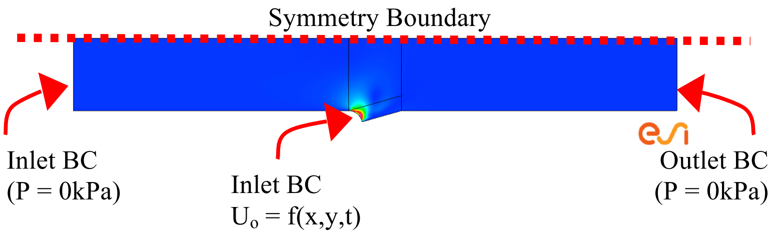


Figure M1 – LCAT separator simulation setup. 2D model with the oscillatory motion of the interface modeled as an inlet with a time varying velocity profile.

The air/liquid interface of the LCAT oscillates as a traveling wave which originates from the tip of the LCAT to the opposite wall on the other side of the air/liquid interface. This was modeled in the simulation as a time varying velocity profile at the inlet resembling a traveling wave as shown in Figure M2.

The equation used to describe this motion is as follows:

$$U_o = \omega d * \cos\left(\frac{D\pi}{w} - \omega t\right) \qquad \text{(M-1)}$$

where U_o is the magnitude of the time varying velocity profile at the inlet, ω is the angular frequency of the acoustic field ($\omega = 2\pi * 50$ kHz), d is the interface displacement amplitude, D is the distance from the tip of the LCAT to a specific location on the interface, w is the half-wavelength of the traveling wave and t is the time. A value of w = 33.5 µm was used because through high speed imaging it was observed that approximately three-quarters of a full wavelength was present on the interface on a given frame (i.e. $0.75*2*w \approx 50$ µm). Because the angle of the cavity is 15° with respect to the microchannel, the X and Y component of the time varying velocity profile at the inlet were described by the following equations:

$$U_x = U_o \cos\left(\frac{15\pi}{180}\right) \quad \text{(M-2)}$$

$$U_y = U_o \sin\left(\frac{15\pi}{180}\right) \quad \text{(M-3)}$$

where U_x represents the velocity of the oscillating flow field in the X-direction and U_y represents the velocity of the oscillating flow field in the Y-direction.

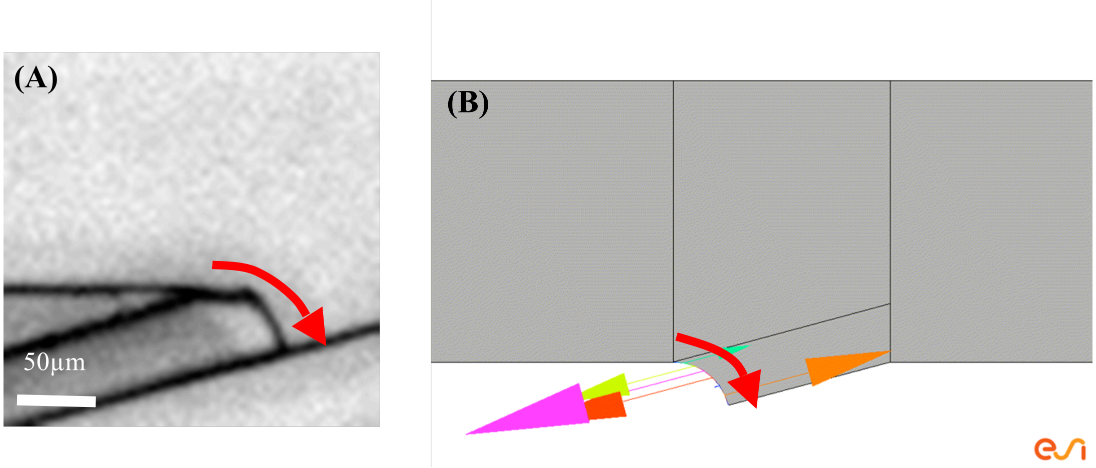


Figure M2 - Simulating angled LCAT interface oscillation. (A) High speed videos of the oscillating LCAT interface showed that the interface oscillates as if a traveling wave originates from the tip of the LCAT and travels towards the other wall as shown by the red arrow. (B) In simulations, this type of interface oscillation was simulated by creating an inlet with a time varying velocity profile. The traveling wave originates from the tip of the LCAT towards the other wall as shown by the red arrow.

To determine the impact of the additional force terms on the trajectories of particles, 10 nm and 5 μm particles were tracked in the vicinity of the LCAT interface. The simulation was solved using constant time steps of 1.25 μsec, resulting in 16 time steps per oscillation cycle of the air/liquid interface. The reference pressure throughout the control volume was set to 0kPa and the reference temperature was set to 300 K. The inlets were treated as walls and the particles were set to stick to the walls in the event that they collided with the boundaries of the control volume. The maximum iteration per time step was set to 40 with a convergence criterion of

0.0001 and a minimum residual of $1\text{x}10^{-18}$. An upwind spatial differencing method was used for the velocity and the inertial relaxation for velocity was set to 0.2, while the linear relaxation was set to 1 for pressure, density and viscosity. The simulation was run for at least 80 oscillation cycles of the air/liquid interface. The density of the fluid matched the density of the polystyrene beads (ρ = 1050 kg m^{-3}) and the dynamic viscosity was $\mu = 1.28\text{x}10^{-3}$ Pa*sec as measured in ESI Method 3.

ESI Method 2: Total Volumetric Flow – LCAT Separator Characterization

Experiments were conducted to determine the total volume of fluid that flows through a LCAT separator device during a 5 µm and 10 µm bead separation experiment. The protocol followed was from Materials and Methods – LCAT Separator Characterization, except videos of the bulk flow from the inlet to the outlet were captured with at least 15 second intervals between each video. These experiments were conducted at an applied voltage of $4.5V_{pp}$ to the piezoelectric transducer on a total of 3 devices ($n = 3$). The mean velocity of particles flowing through the device was measured. The maximum measured mean velocity was used along with the total experimental run time of each device and the measured cross-sectional area of the microchannel (487 µm width X 93 µm height) to determine the total volume of fluid that flows through the device during a single experiment. The data is in Table 1. The total volume of fluid that flows through the device is 83 µL ± 2 µL (SEM). These results are slightly higher than the total volume pipetted into the inlet well during a single experiment which is 80 µL (40 µL of bead solution followed by 40 µL of wash solution). Therefore, in the experimental results for LCAT Separator Characterization, 83 µL ± 2 µL and the total run time of the device was used to calculate the mean velocity of bulk flow, U_b, throughout a single experiment.

Table 1 - Measured mean velocity of particles. The mean velocity of particles, U_b measured within the microchannels. The total volume of fluid that flows through the device during an experiment can be calculated using the total run time, U_b and cross-sectional area of the microchannel.

	Device 1	Device 2	Device 3
Video 1, U_b	0.0061 m/sec	0.0073 m/sec	0.0107 m/sec
Video 2, U_b	0.0065 m/sec	0.0082 m/sec	0.0117 m/sec
Video 3, U_b	0.0068 m/sec	0.0088 m/sec	0.0122 m/sec
Video 4, U_b	0.0078 m/sec	0.0105 m/sec	0.0129 m/sec
Video 5, U_b	0.0077 m/sec	0.0097 m/sec	0.0125 m/sec
Maximum U_b	0.0078 m/sec	0.0105 m/sec	0.0129 m/sec
Total Run Time	240 seconds	179 seconds	135 seconds
Total Volume	85 µL	85 µL	79 µL

Mean Total Volume	83 µL
Standard Error of the Mean	2 µL

ESI Method 3: Viscosity of Ficoll-Paque Plus and PBS w/ 6mM EDTA

In order to determine the viscosity of the 2:1 ratio of Ficoll-Paque PLUS to PBS with 6mM EDTA solution a falling ball type viscometer (Thermo Scientific, USA) was used. The viscometer tube was first filled with DI H_2O and a glass ball provided with the viscometer was used for calibration purposes. The calibration constant was calculated using the following formula provided with the viscometer.

$$K = \frac{\mu}{(\rho_p - \rho_f)t} \tag{M-4}$$

Where K is the viscometer constant, μ is the dynamic viscosity of the fluid in centipoise (0.949 centipoise for DI H_2O), ρ_p is the density of the ball in g/mL (2.53 g/mL for the glass ball), ρ_f is the density of the fluid (0.998 g/mL for DI H_2O), and t is the time of descent in minutes. The time of descent was measured 3 times and with an average descent time of 0.0395 minutes, the viscometer constant was calculated to be 15.68.

The viscometer was thoroughly cleaned and filled with the 2:1 ratio of Ficoll-Paque PLUS to PBS with 6mM EDTA solution. The time of descent was measured 3 times and the average descent time was 0.0550 minutes. Based on these results and K = 15.68, the dynamic viscosity of the 2:1 Ficoll-Paque PLUS to PBS with 6mM EDTA solution was calculated to be $\mu = 1.28$ centipoise or $\mu = 1.28\text{x}10^{-3}$ Pa*sec. This value was used throughout this manuscript as the viscosity of the 2:1 ratio of Ficoll-Paque PLUS to PBS with 6mM EDTA solution.