Microfluidic Cell Sorter

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ABSTRACT

- Current microfluidic chips move cells too fast past the detector
  - Goal is to design a microfluidic plate that will sufficiently slow cells down
  - Need to consistently hold an x, y, z location for cells
- Two designs selected for additional testing
  - Funnel Design
  - Inertial Ordering (AKA Snake Design)
- Flow simulations utilizing SolidWorks
- Results:
  - Funnel shows promise, further experimentation needed
  - Snake design demonstrates reasonable centering at low input pressures
- Future:
  - Increased physical testing and prototype development

BACKGROUND

Skala Lab

- Run by Dr. Melissa Skala
- Research focuses on studying cancer via photonics-based technology
- Developed new cell sorting tech with aid of the Morgridge Institute

Cell Sorting

- Process of separating cells by size or type for further analysis
- Usually accomplished via an innate system of size identification or vi labeling/tagging
- Often important as a source of cell identification and for stem cell research

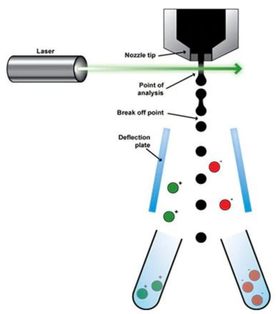

Figure 1. Fluorescence Activated Cell Sorting (FACS)[1].

DESIGN CRITERIA

- Sufficiently slow cells down
- Should allow for 100's of ms integration time on the detector
- Single-file cell flow through interrogation window
- Flow in PBS (Phosphate-Buffered Saline)
- Cells held in a fixed x, y, z location
- Flow cell has to fit the microscope stage insert
- Bottom side of the flow cell would need to have ~150 micron glass thickness and accommodate the ~1 inch wide objective lens with a working distance of 0.2 mm.

FINAL DESIGNS

The Funnel

- Based on previous in-lab designs
- 3D cone-shaped cellular inlet
- Allows sheath flow to surround cell injection site
- Cell centering is more consistent

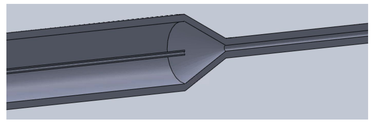

Figure 2. Cross sectional view of the the funnel design.

Inertial Ordering (The Snake)

- Cells laterally focus themselves
- The sum of inertial lift forces encourages cells to line up as they take the path of least resistance[2]
- Can test for alterations in width and input pressure on the designs ability to adjust output velocity and focusing capabilities

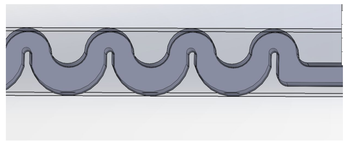

Figure 3. Lateral view of the 100 um wide Inertial Lift Design (the Snake).

TESTING AND RESULTS

The Funnel

Pressure Vs. Velocity

- Cell pressure is always 5 mBar more than sheath pressure
- Changing cell pressure has no effect on velocity.
- Cell velocity is linearly related to the input pressure

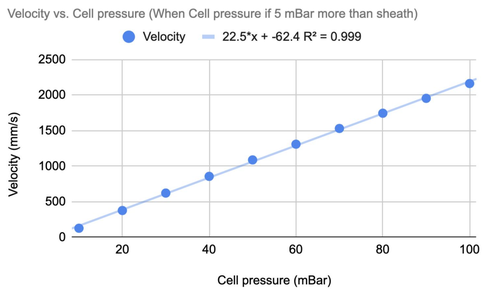

Figure 4. Graph of particle velocity in mm/s in relation to the pressure of the cell input.

Y/Z Focusing

- The spread of the particles, measured by standard deviation decreases as the pressure increases.
- The change in spread levels out
- Figure 6 shows the difference in the spread of cells at 10 mBAr and 100 mBar

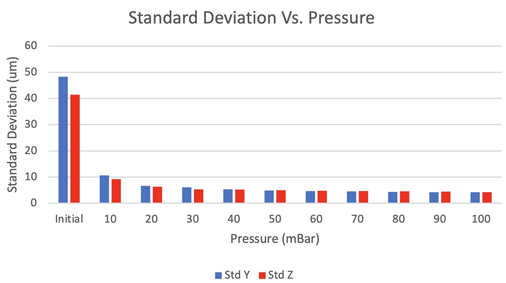

Figure 5. Graph of the standard deviation of the Y and Z spread of particles at each pressure.

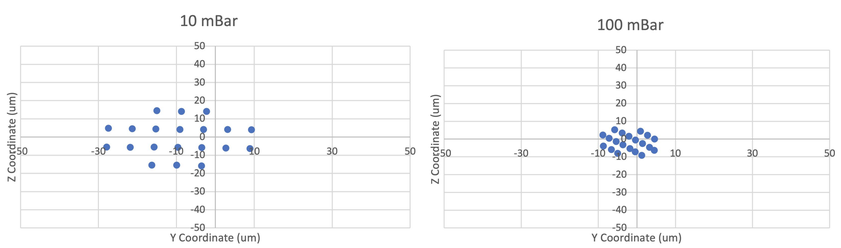

Figure 6. Graphs of the particle positions at the end of the funnel design for 10 mBar (left) and 100 mBar (right). The origin of the graph is the center of the output channel.

RESULTS (Snake Design)

The Snake

Altering Channel Width

Velocity

- Using 30 mBar as a constant pressure
- Output particle speed was measured to be:
  - 17 mm/s for a 50 um channel width
  - 40 mm/s for a 100 um channel width
  - 46 mm/s for a 150 um channel width
- Small channel ~ slower speed
- Affected by core flow velocity

Changing Input Pressure

Velocity

- Using 100 um channel as constant
- At low speeds, for every 1 mBar of pressure, the speed of the particle increases by 1.3 mm/s
- At increased speeds, the slope declines until the particle stream splits in two
- This slope decreases again near 200 mBar when the velocity of the particles stabilizes to the average velocity of flow

Y/Z Focusing

- For a 100 um channel, 30 mBar of pressure provides lowest Y and Z standard deviations with ~4 um of clearance in the Y direction and ~0.5 um of clearance in the Z direction

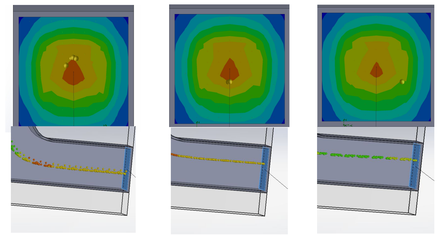

Figure 7. Cross-sectional flow velocity with side-view displayed below. Images are taken from 100um wide Snake channel at input pressures of 1, 30, and 100 mBar.

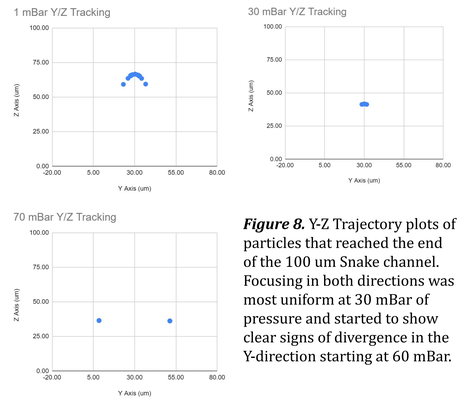

Figure 8. Y-Z Trajectory plots of particles that reached the end of the 100 um Snake channel. Focusing in both directions was most uniform at 30 mBar of pressure and started to show clear signs of divergence in the Y-direction starting at 60 mBar.

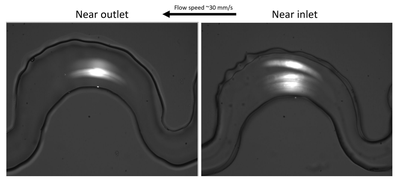

Figure 9. Tests run by the Skala Lab using a 100 um device designed by Emmanuel Contreras and operated by Kayvan Samimi. White flashes correspond to cells.

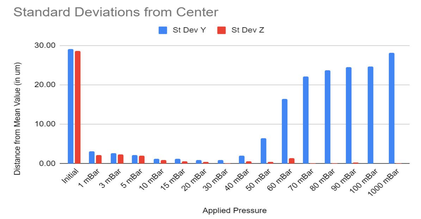

Figure 10. Standard deviations for Y and Z positions of the relevant input pressure simulations. Focusing reached its optimal level for both directions at 30 mBar (0.86 and 0.16 um in the Y and Z directions respectively).

CONCLUSIONS/FUTURE WORK

- Both Funnel and Snake designs are capable of generating centered particles at reasonable speeds
- Further fabrication and testing with physical designs would be ideal
- Clients are working with the 100 um inertial design to further experiment with its physical capabilities

ACKNOWLEDGEMENTS

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- Kayvan Samimi

REFERENCES

[1] D. D. Carlo, D. Irimia, R. G. Tompkins, and M. Toner, "Continuous inertial focusing, ordering, and separation of particles in microchannels," *PNAS*, vol. 104, no. 48, pp. 18892–18897, Nov. 2007, doi: 10.1073/pnas.0704958104.

[2] "facs-live-cells1.jpg 472×500 pixels." https://a.static-abcam.com/CmsMedia/Media/facs-live-cells1.jpg (accessed Dec. 04, 2020).