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Microfluidic Cell Sorter

Advisor:
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Client: Skala Lab - Melissa Skala, Emmanuel Contreras Guzman

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Client Background

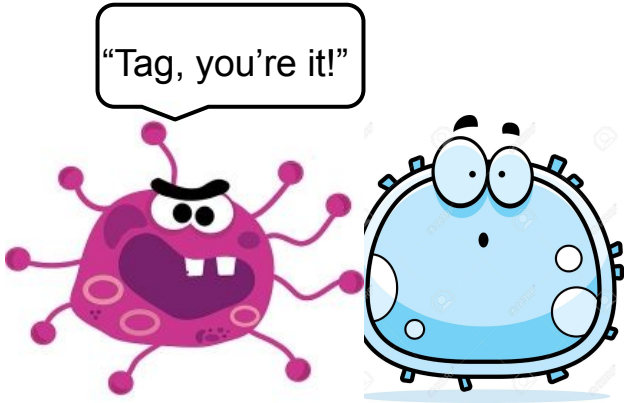
- Dr. Melissa Skala
  - Department of Biomedical Engineering
  - Morgridge Institute for Research
- Emmanuel Contreras
  - Morgridge Institute for Research

Problem Statement

- Skala lab has developed label-free optical signals to sort T cells by activation state with high accuracy
- 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
  - Should allow for 100's of ms integration time on the detector

Background - Cell Sorting

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



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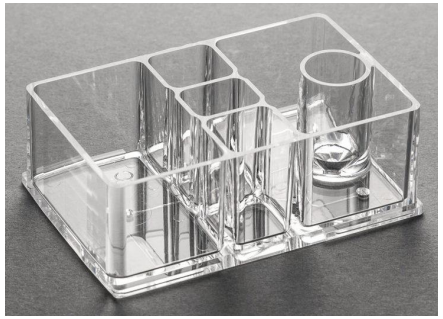
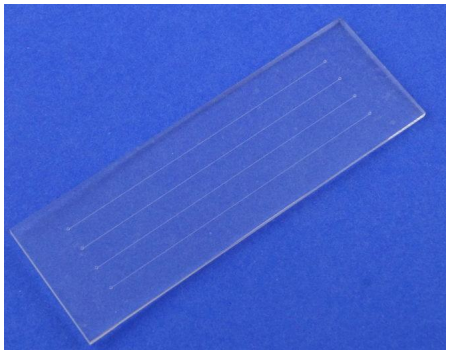
Background - Competing Designs



Microfluidic Cell sorter: On-chip Sort[3]

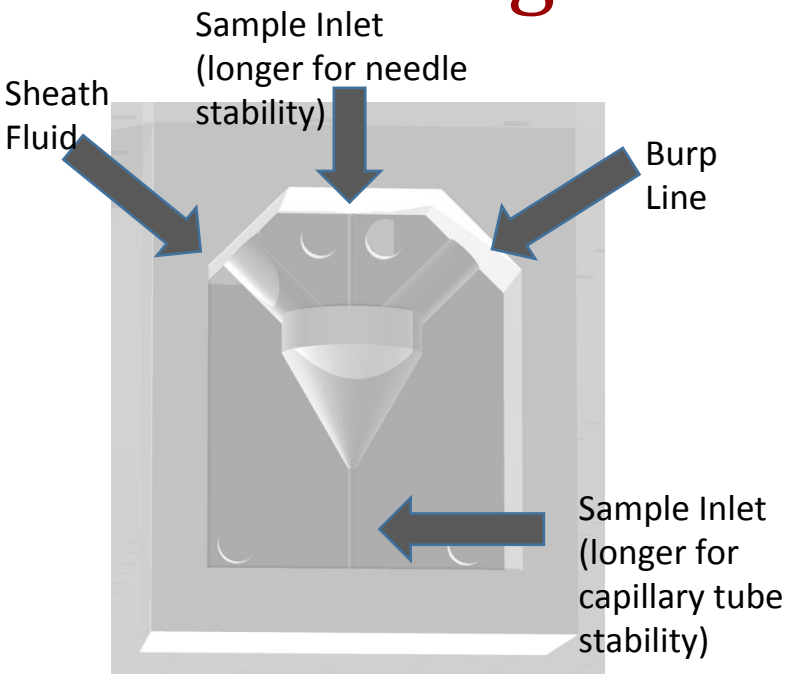
- Cell sorting and Flow Cytometers
- Expensive
- All-in-one device
- Unable to detect decay time which is not standard

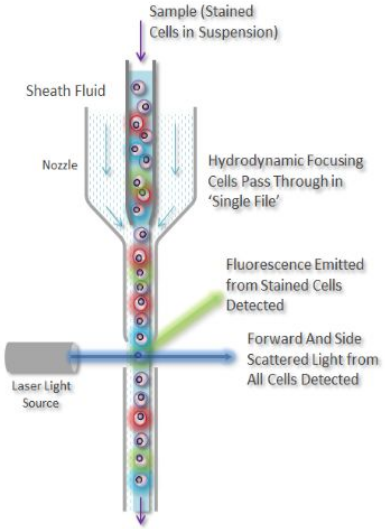


Microfluidic ChipShop[4]

- A straight channel chip from Microfluidic ChipShop
- Cells are not focused

Background - Previous Designs





Flow Cytometry fluidics[5]

Clients initial design

- Uses sheath flow to center cells
- Same methods used in Flow Cytometry

Cons

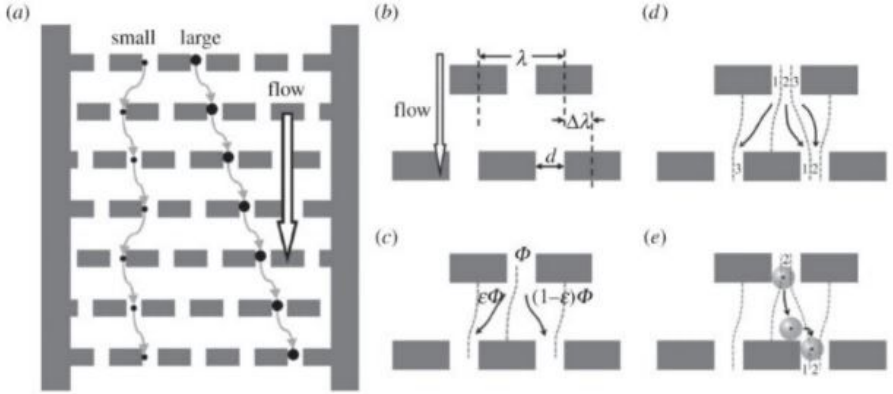
- Currently too fast
- Too crowded to read each cell individually
- Created bubbles in the line

PDS Summary

- Design/Source a flow cell for a flow cytometer given the following constraints:
  - Single-file cell flow through interrogation window
  - Stable core diameter (20 um to 50 um) (stability in Z more important than X and Y)
  - Flow speed of ~1 mm/s
  - Flow in PBS (Phosphate-Buffered Saline)
  - 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.
  - Entire flow cell would have to fit the microscope stage insert.
- CFD simulations for various designs

Design 1: Plinko

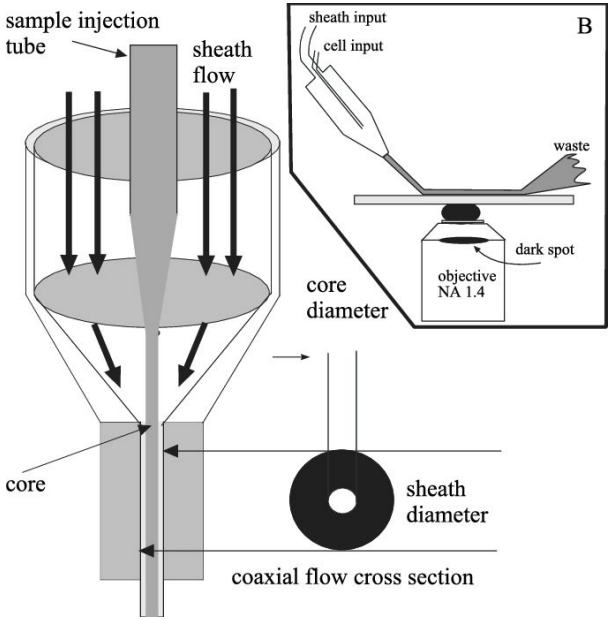
- Cell centering through seemingly random motion
- Allows for relatively precise cell centering
- Potential to slow flow down by widening channel



Sturm *et al.*, *Interface Focus*, **2014**;4(6):20140054. doi:10.1098/rsfs.2014.0054.

Design 2 - Funnel

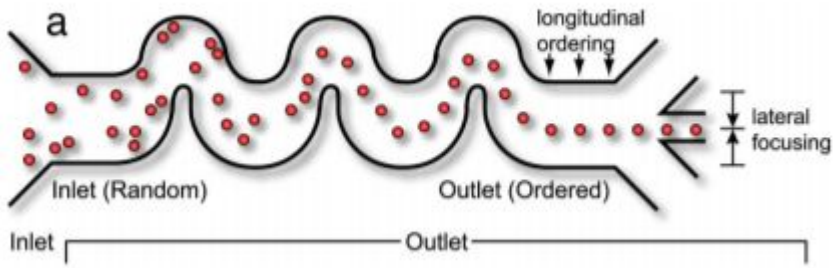
- Based on previous in-lab designs
- 3D cone-shaped cellular inlet
- Allows sheath flow to surround cell injection site
- Cell centering is more consistent



https://www.researchgate.net/figure/Shown-here-is-the-basic-structure-of-a-typical-flow-cell-Sheath-fluid-flows-through-a_fig1_230745384

Design 3 - Snake

- Relies on properties of entry and diffusion
- Cells laterally focus themselves
- Potential to reduce flow via outlets



https://www.pnas.org/content/pnas/104/48/18892.full.pdf

Design Matrix

Design Criteria	**Plinko**		**Funnel**		**Snake**	
Speed Reduction (25)	5/5	25	3/5	15	4/5	20
Positioning (25)	3/5	15	3/5	15	4/5	20
Ease of Fabrication (20)	3/5	12	5/5	20	4/5	16
Reusability/Sterility (15)	4/5	12	5/5	15	5/5	15
Manufacturing Cost (10)	5/5	10	5/5	10	5/5	10
Safety (5)	5/5	5	5/5	5	5/5	5
Total (100)	79		80		**86**	

Future Work

- Complete computer modeling and flow simulations
- Fabricate a larger-scale model of the chosen device
  - Investigate flow patterns
- Test the device using beads to simulate cells

Acknowledgements

- Professor Justin Williams
- Skala Lab members: Melissa Skala, Emmanuel Contreras, Kayvan Samimi

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8. "Continuous inertial focusing, ordering, and separation of particles in microchannels" https://www.pnas.org/content/pnas/104/48/18892.full.pdf

Questions / Comments?