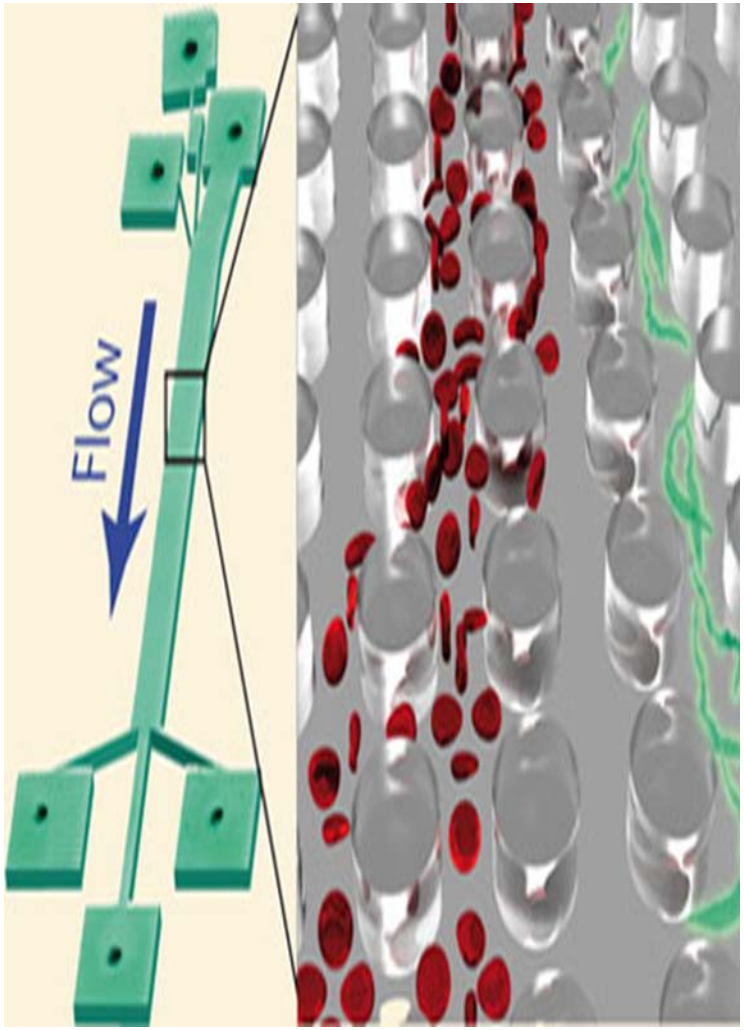
Particle Separation Using Deterministic Lateral Displacement

Design Objective

- Design a microfluidic device capable of separating particles of varying sizes
- Should be small
- Easy to fabricate
- Durable for multiple usage and possible high throughput applications

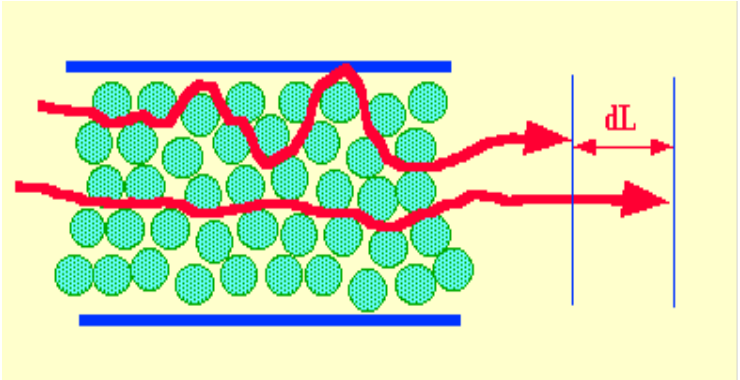


Current Methods

1. **Hydrodynamic Chromatography**

PROS

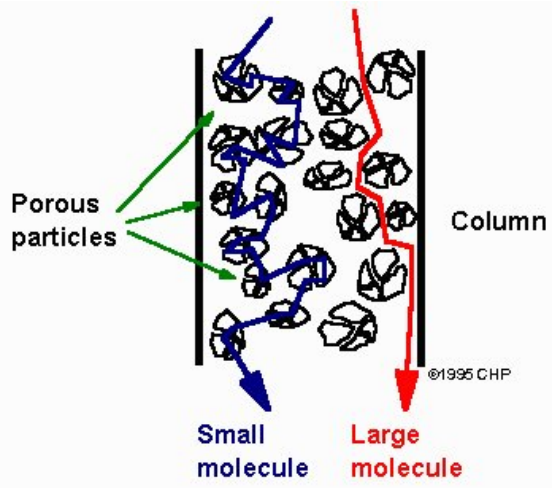
- Efficient with high sensitivity
- No sample loss
- Well defined separation times



http://www.chemistry.adelaide.edu.au/external/soc-rel/content/size-exc.htm

CONS

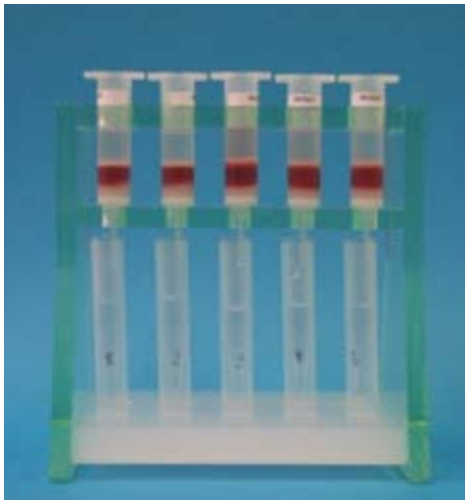
- Multipath effect – reduces resolution
- High diffusion effect
- Large scale set up



[4]Blood Cell Classification Utilizing Hydrodynamic Filtration.

Current Methods

2. mAECT- mini Anion Exchange Centrifugation Technique

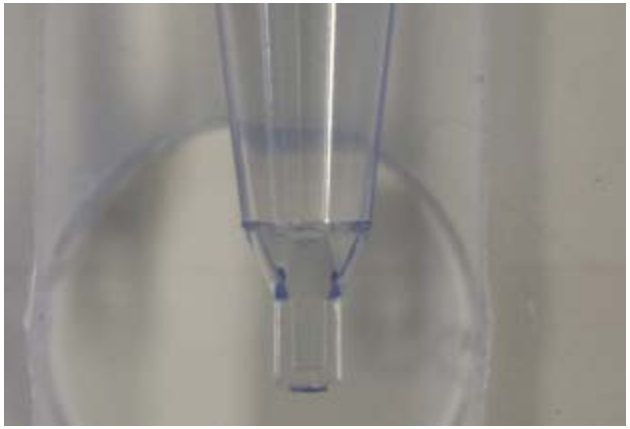


PROS

- high selectivity, detection limit ~ 100 trypnasomes /ml
- Works on charge difference in cells

CONS

- Large scale experiment set up.
- Difficulty to view under microscope.
- Requires pre-treatment to increase concentration of trypnasome



Current Methods

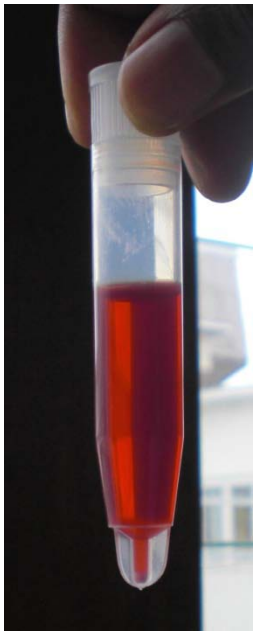
3. **Cell lyses**

PROS –

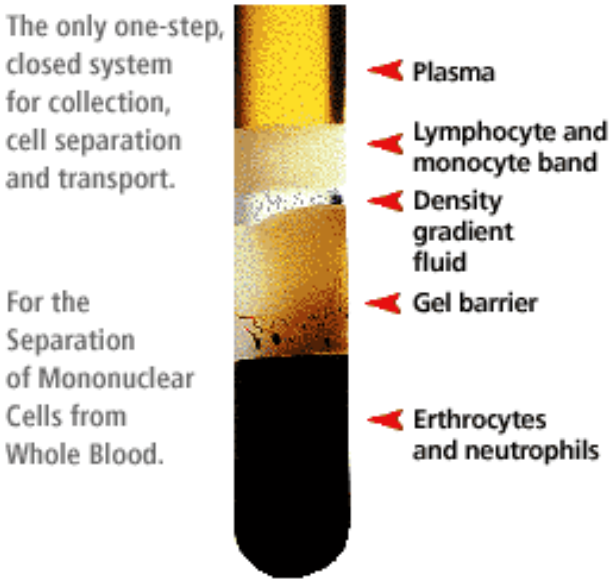
- Simple and fast method of concentration RBC.
- Detection limit of ~ 500 trypnasomes/ml blood.
- Sensitivity increased by 20%

CONS-

- Pretreatment, Centrifugation of blood required before detection.

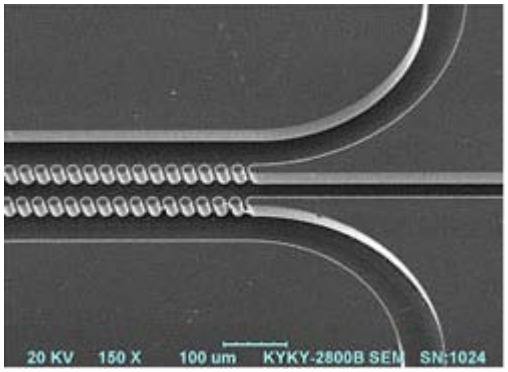


The sediment at the bottom contains both parasites and white blood cells



Current Methods

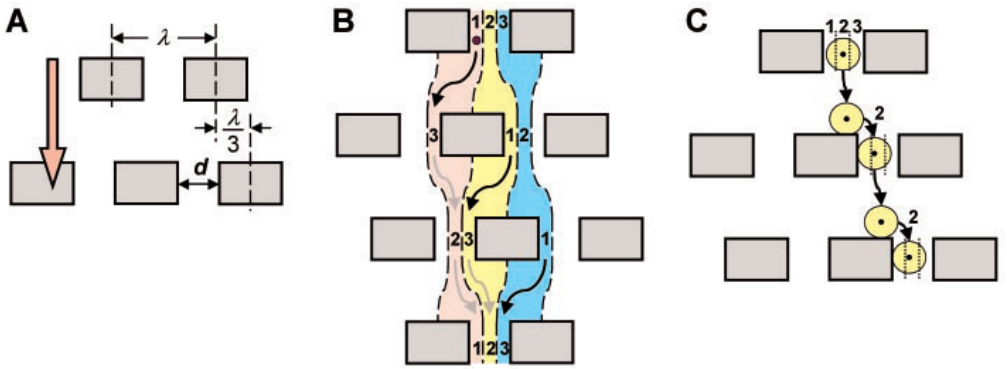
- There are several on-chip methods used, but they all have limitations.
  - Physical features are easy to implement but are very limited.



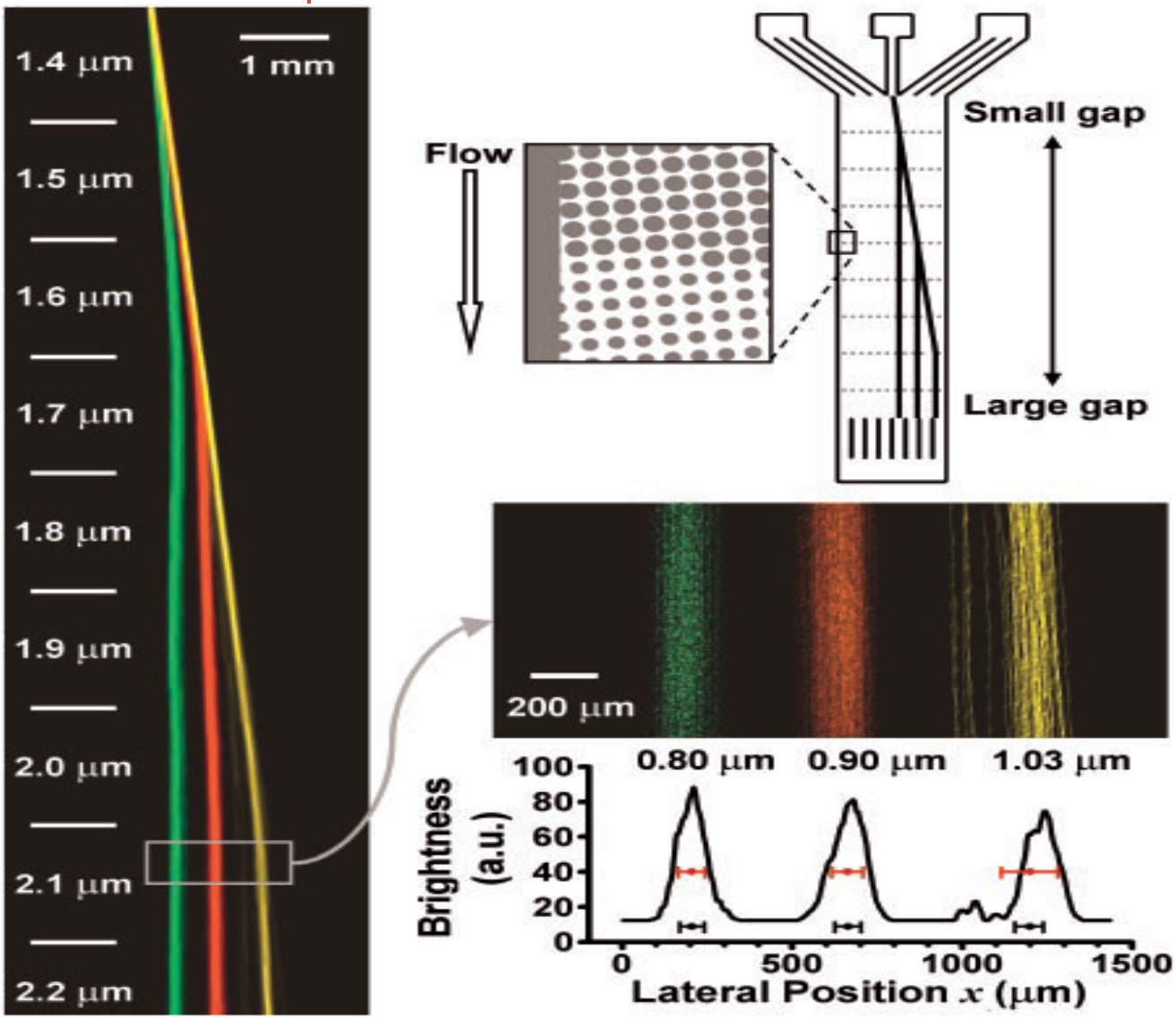
  - Dielectrophoresis
  - Magnetic
  - Deterministic lateral displacement

Theory

- Deterministic lateral displacement
  - Works by using the mechanism of laminar flow past an array of posts.
  - The array of posts divide the flow into several different streams.
    - Since the flow is very low Reynolds number there is very little diffusion and mixing between streams.
    - If the particle is smaller than the stream, it will travel within it.
    - If the particle is larger than the stream, it will pushed laterally by the posts.



Theory


1.4 μm
1 mm
1.5 μm
1.6 μm
1.7 μm
1.8 μm
1.9 μm
2.0 μm
2.1 μm
2.2 μm
Flow
Small gap
Large gap
200 μm
0.80 μm
0.90 μm
1.03 μm
Brightness (a.u.)
100
80
60
40
20
0
0
500
1000
1500
Lateral Position x (μm)

Theory

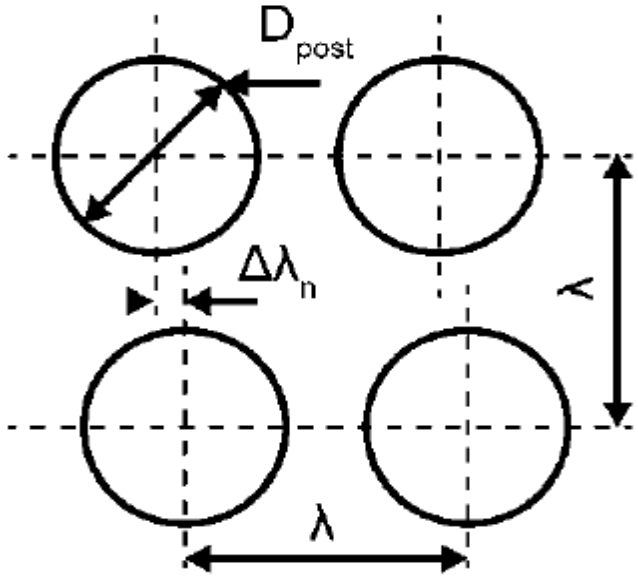
- The size of particle to be separated (critical diameter) is dependent on 3 variables.
  - The diameter of the posts
  - The distance between the posts
  - The offset of the posts

- The following equations can be used to estimate the size of the particles that will be separated.

$$D_{c,n} = 1.4dN_n^{-0.48}$$

$$N_n = \lambda/\Delta\lambda_n$$

$$d = \lambda - D_{post}$$



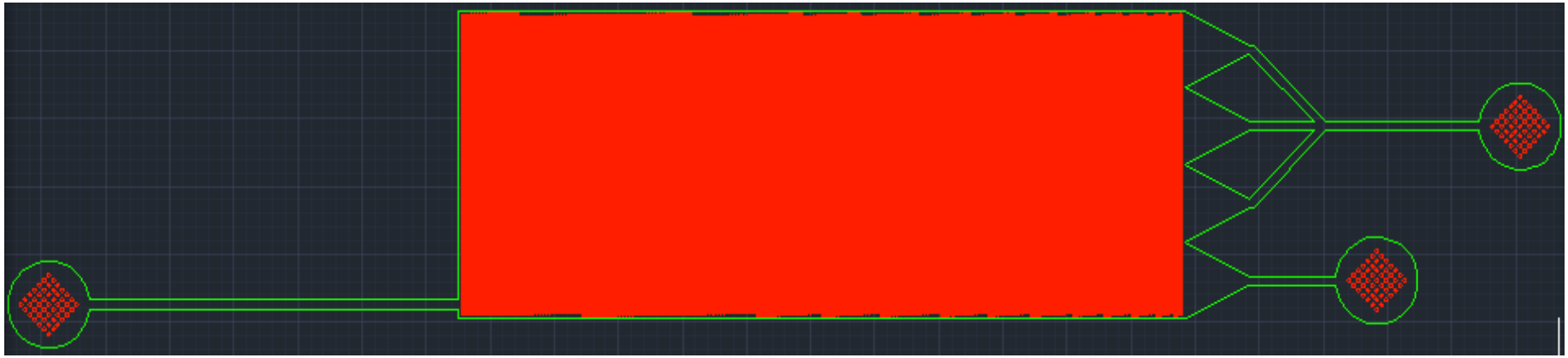
Determination of Design Parameters

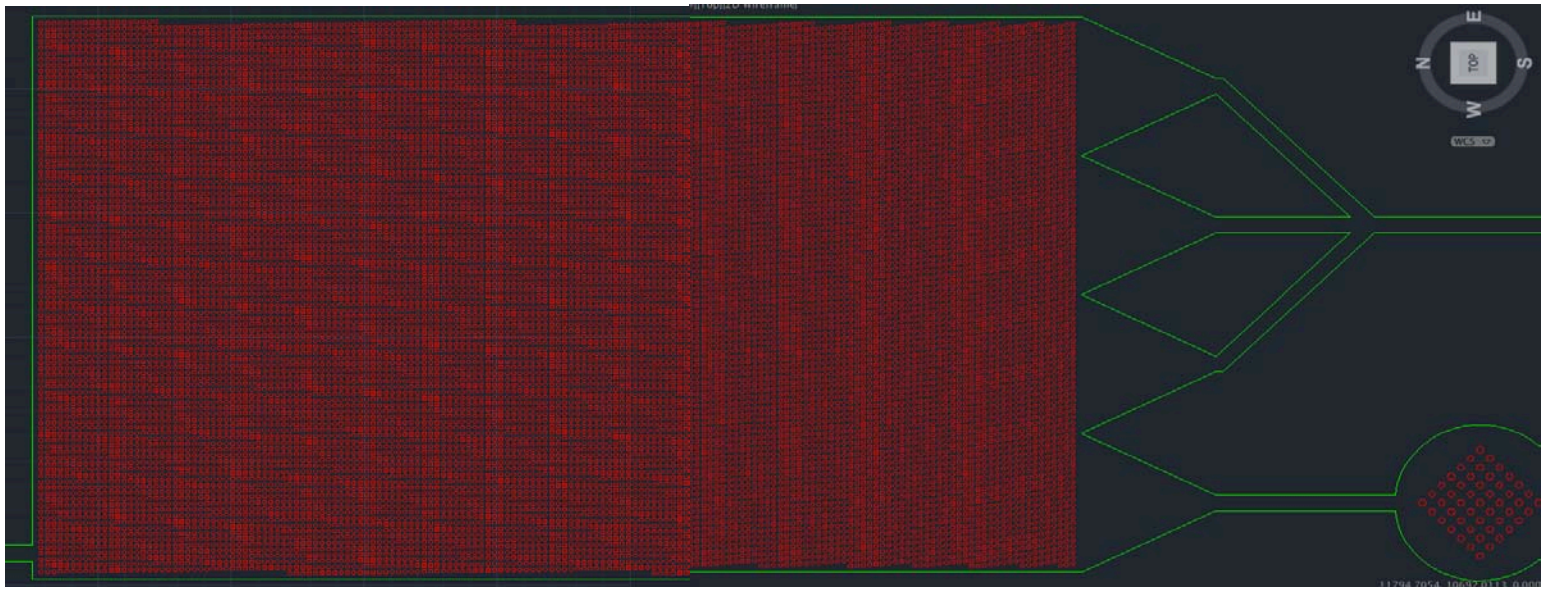
Section	Row Shift	Critical Diameter
	µm	µm
1	0.8	3.95
2	1.6	5.52
3	2.6	6.97
4	3.8	8.36
5	5.2	9.72
6	6.8	11.06
7	8.8	12.52

- Posts are 50µm in diameter, and have 25µm spacing.
- Using the previous equations we designed our system to have 7 sections, each capable of separating different sized particles.
- The smallest size particle our system can separate is theoretically 4µm

Apparatus

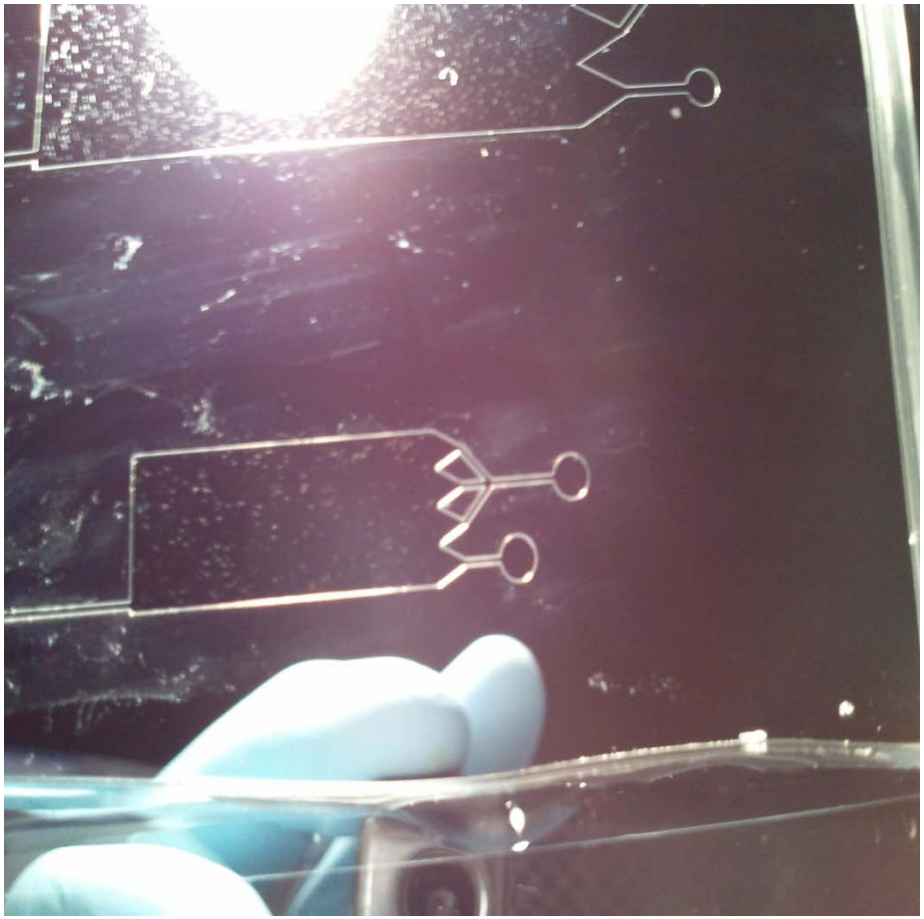
- Utilized AutoCAD to create mask design





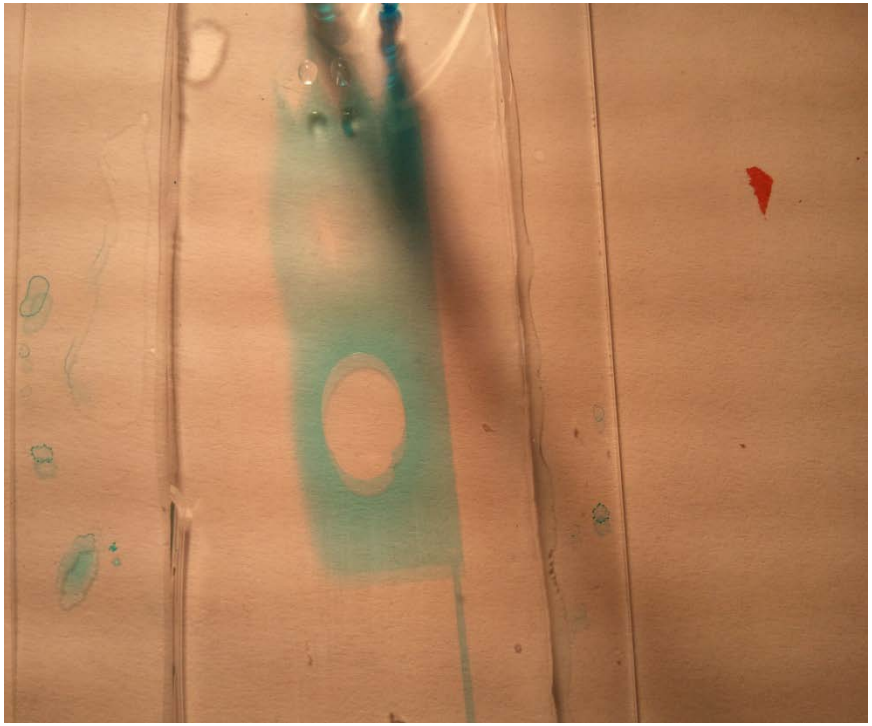
Fabrication

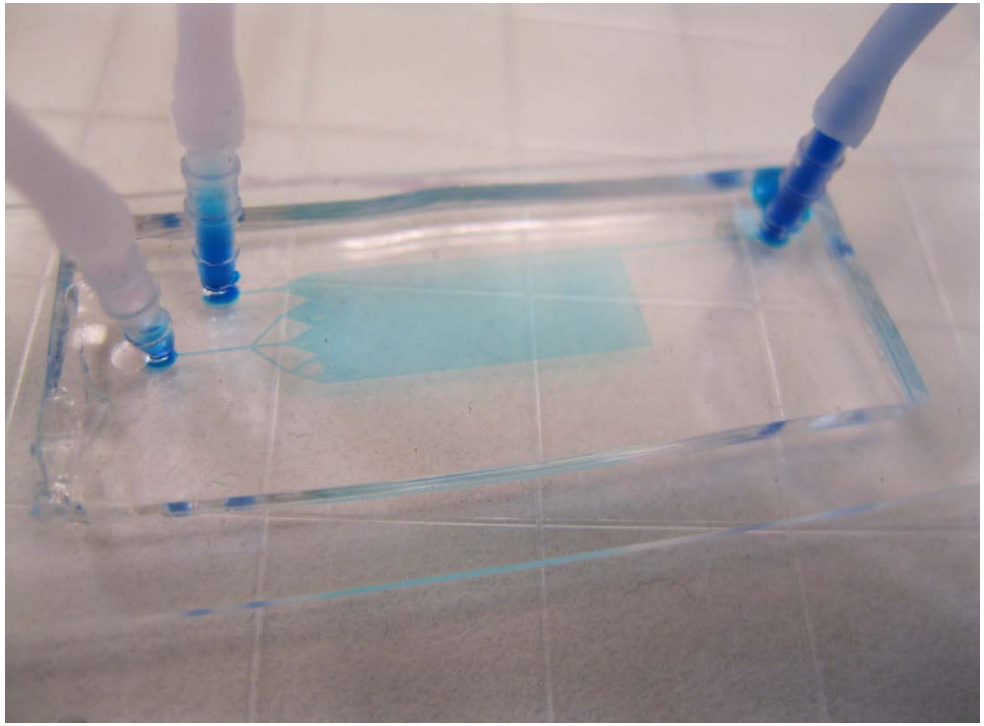
- Master Mold
  - SU-8 photoresist, 30 µm thickness
  - Spin speed 3,000 rpm for 2025 resist
  - UV lamp energy 2 mJ/cm
  - Exposure time was 75 seconds
- PDMS
  - 10:1 PDMS to curing agent ratio
  - 3 mm thick
- Glass Substrate



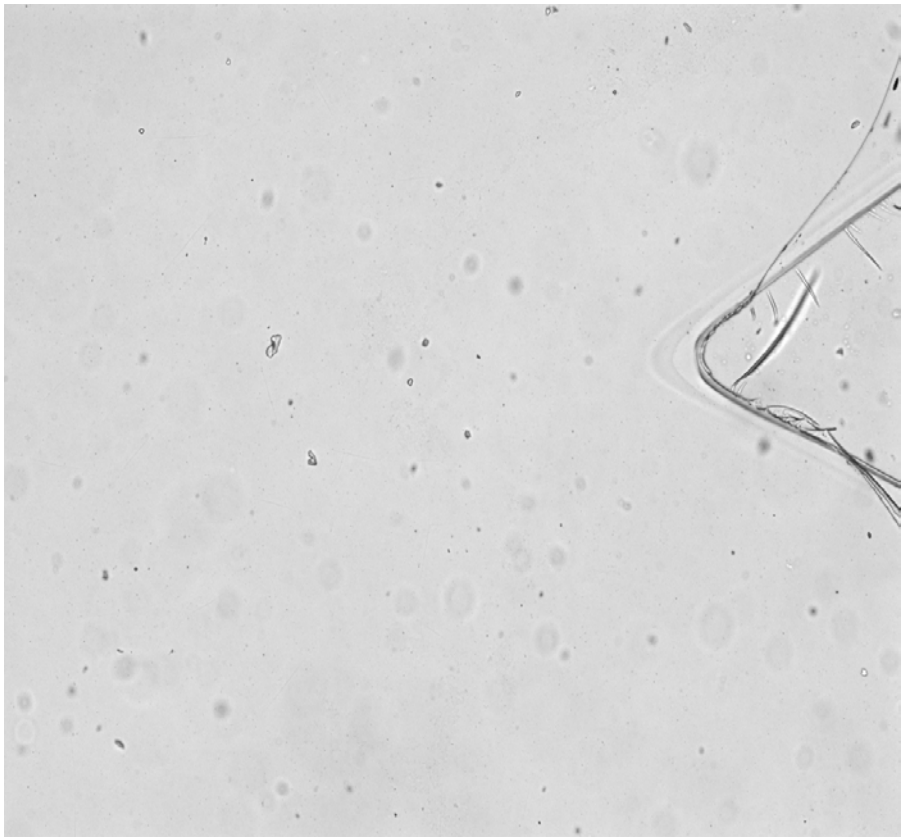
Final Device

- Initial fabrication resulted in a device with no posts causing the main chamber to collapse
- The second fabrication used more sensitive photolithography equipment and resulted in better definition of the posts

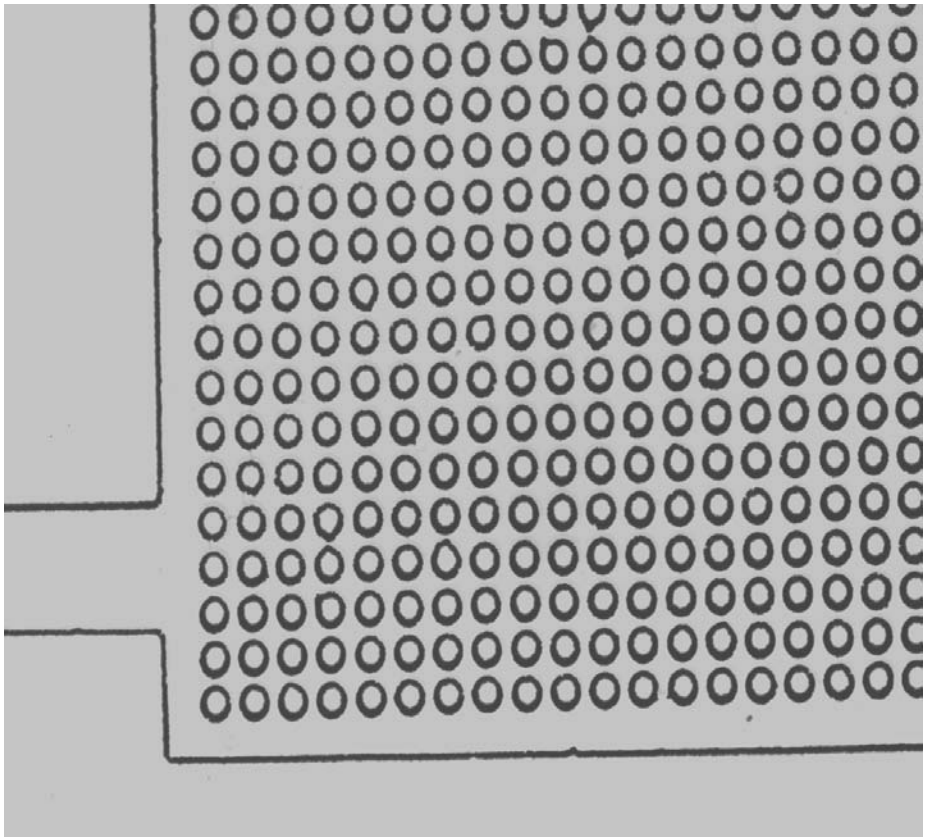




Final Device



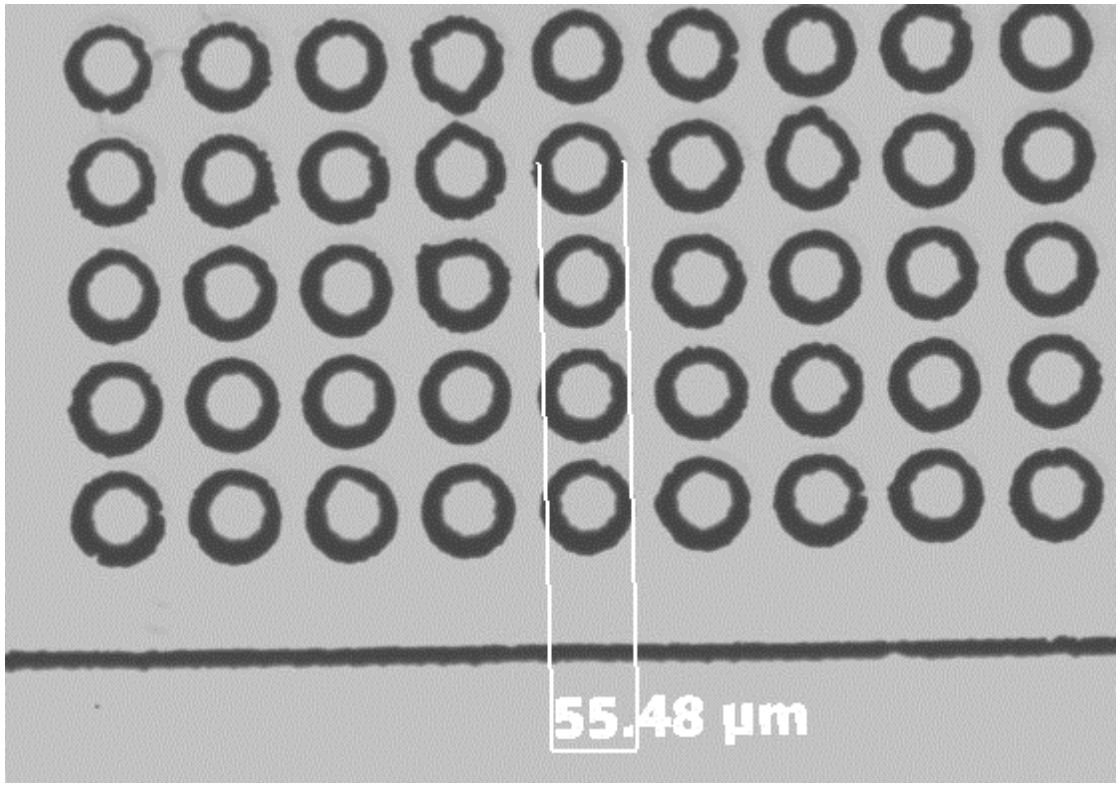
Fabrication 1



Fabrication 2

Final Device

- The post size came out to ~55 µm within 10% of our original design parameters



Experimental Set-up

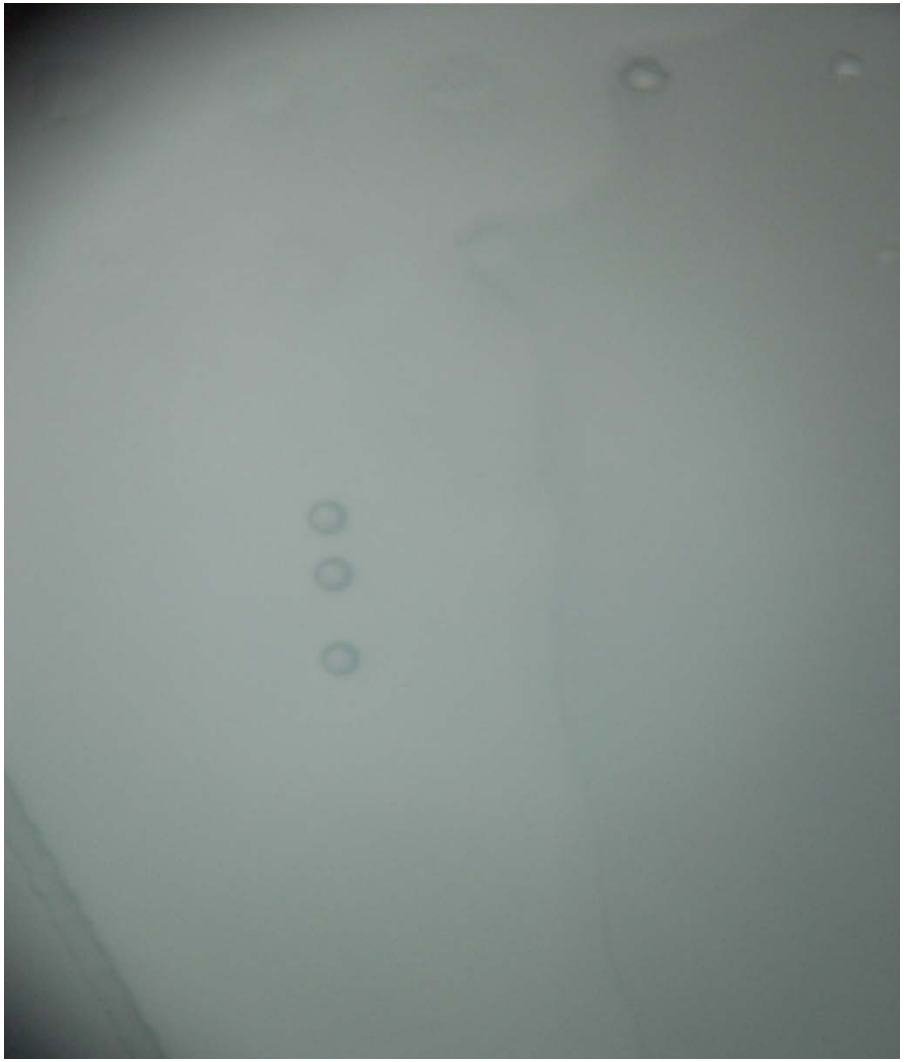
- Testing the separation between two different particle sizes, 2.8µm and 15µm
- Flow induced by syringe pump and varied between 2 and 200 µL/min
- Both beads were first pushed through the device separately to observe any possible flow patterns

Results

- Small beads were too small to record their flow on video
- Most of the particles aggregated around posts near the inlet even though some did reach the correct outlet well

Results

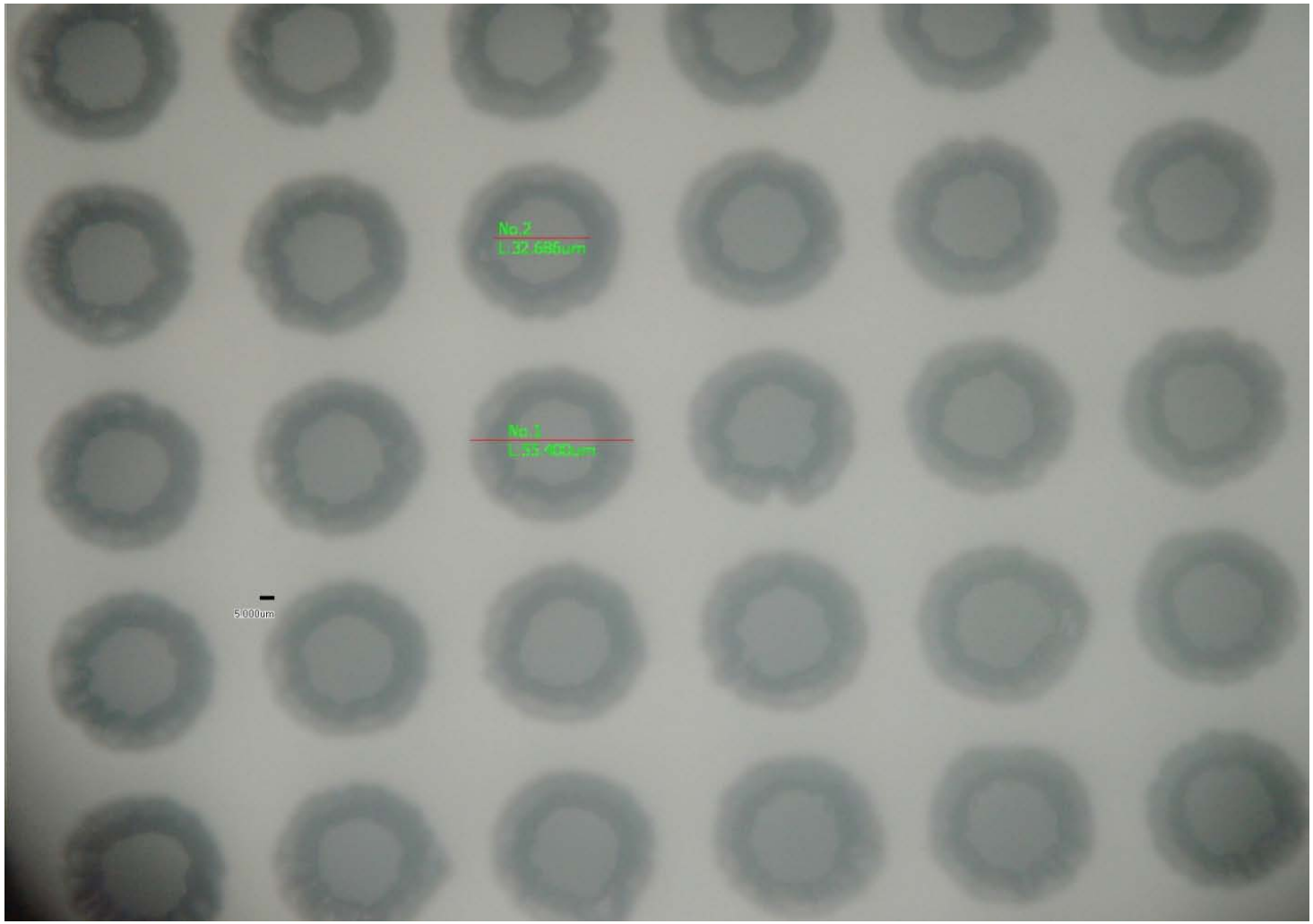
- Were able to inject large beads but flow was inhibited
- Several beads moved to the outlet but the majority were stuck near the inlet



Design Issues

- Lithography
  - Our design was very sensitive to any lithography limitations.
  - Mask
    - Rough edges on the mask led to imperfect circles
  - Exposure
    - Over exposure could lead to no or non-uniform posts
- PDMS
  - Small post diameters led to some breaking off in master mold

Design Issues

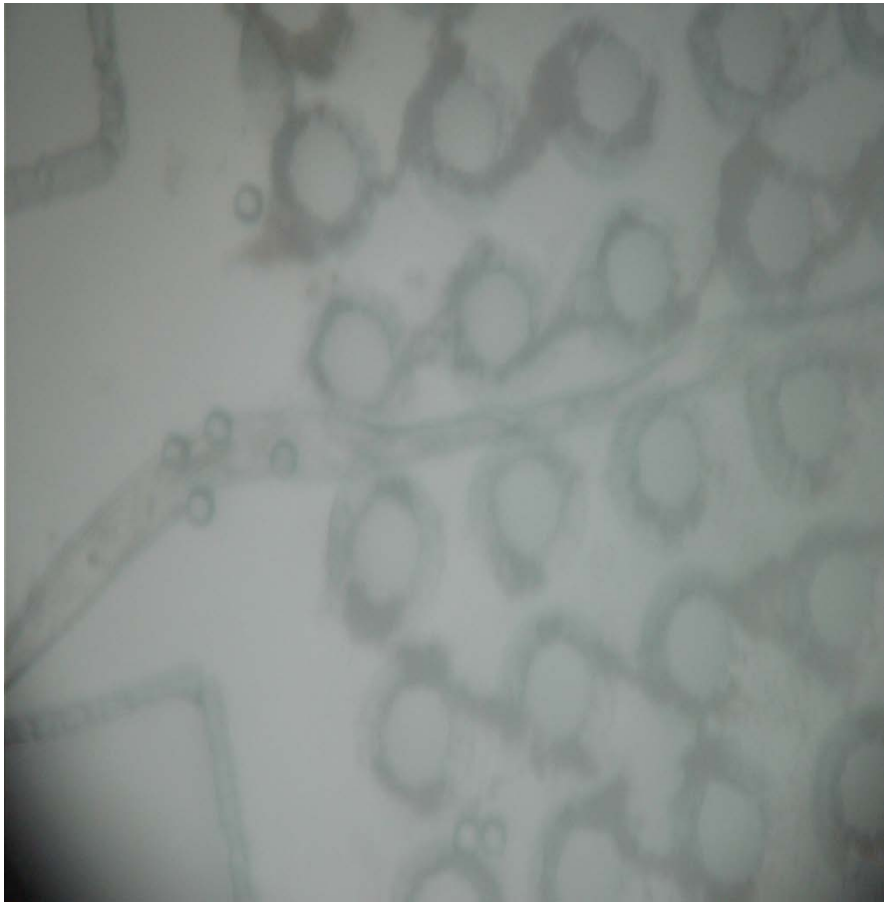


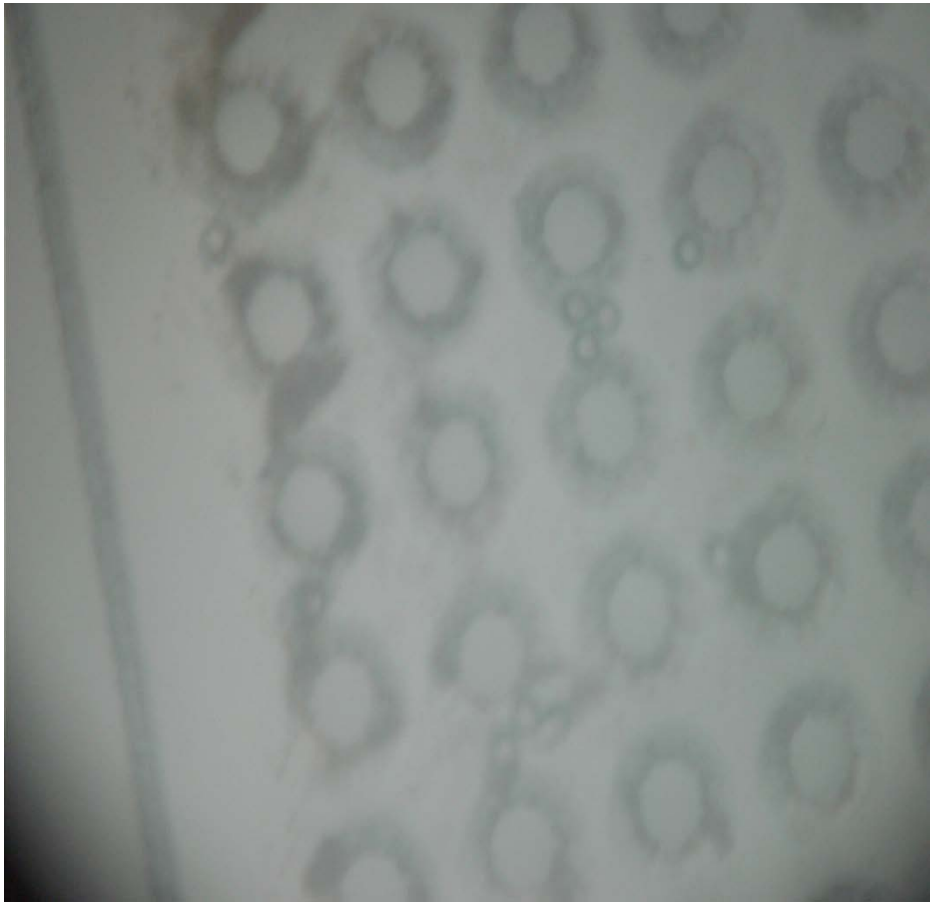
Post diameter varied from 55µm at PDMS surface to 33µm at glass surface

Design Issues

- Areas where we left out partial posts became traps for beads.
- Beads stuck to posts.
  - Could be cause by surface roughness of posts

Design Issues





- Dust particles obstructed flow patterns forcing beads to aggregate
- Larger particles also adhered to the posts

Conclusions

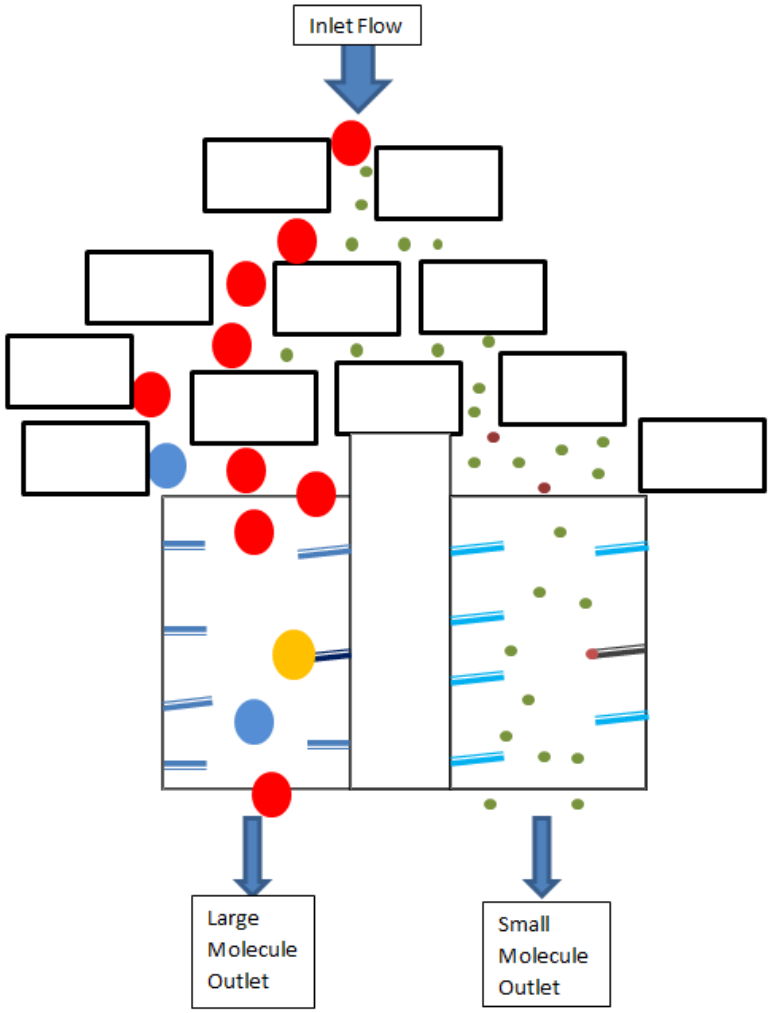
- Posts for the second fabrication were more defined due to more accurate photolithography process
- Lifetime of device was limited due to outside contamination
- Were able to determine bead flow in the device but couldn’t demonstrate proper separation

Future Work / Recommendations

- More sensitive photolithography will lead to more uniform posts
- Treatment of PDMS beforehand to minimize particle adhesion and aggregation
- Operation under a hood or in a clean room would be ideal to limit contamination
- Modify design to allow ample space for microscope to view inlet flow of particles

Future Work / Recommendations

- After testing lateral displacement for particle sizes, design appropriate outlet spacing
- Possible addition of antibody ligands to better capture and sort particles in each flow stream



QUESTIONS?

References

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