A Membraneless High-throughput Micro-separator

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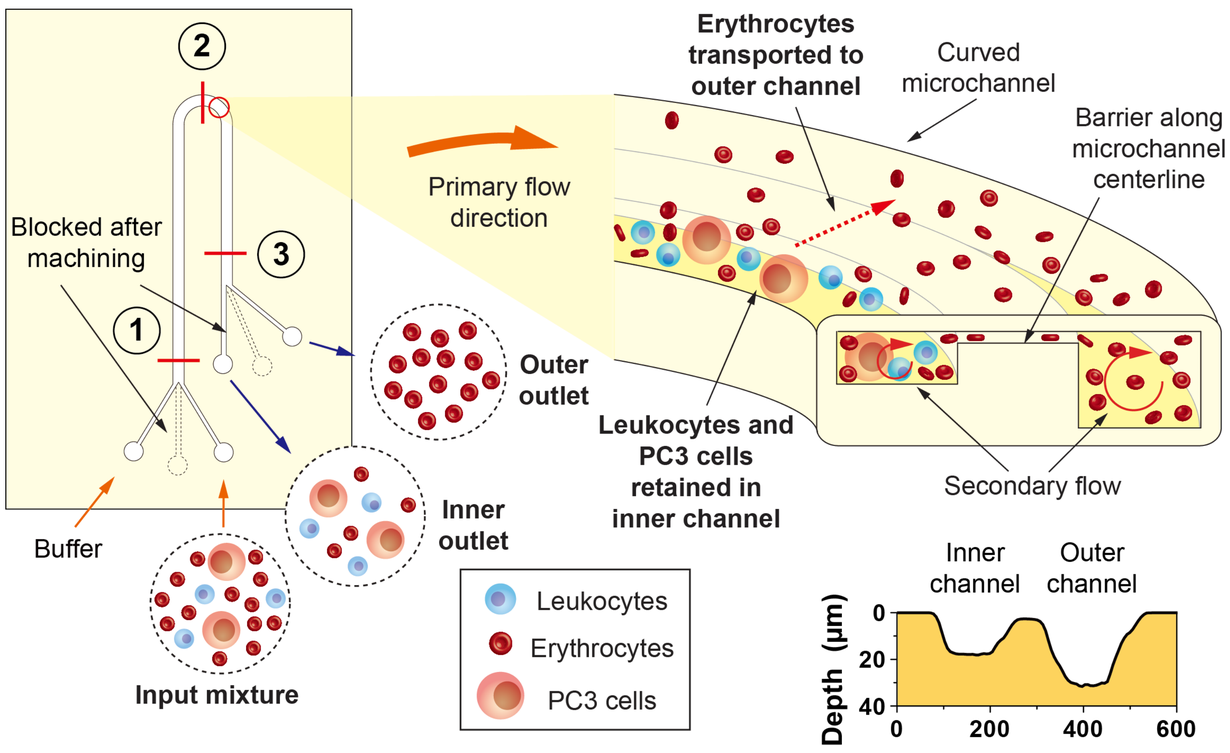
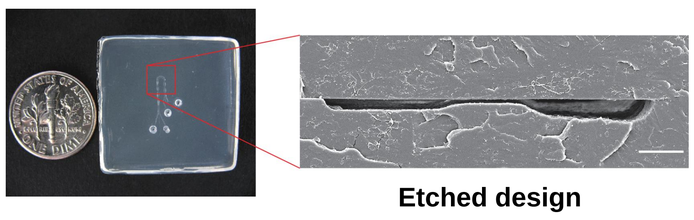
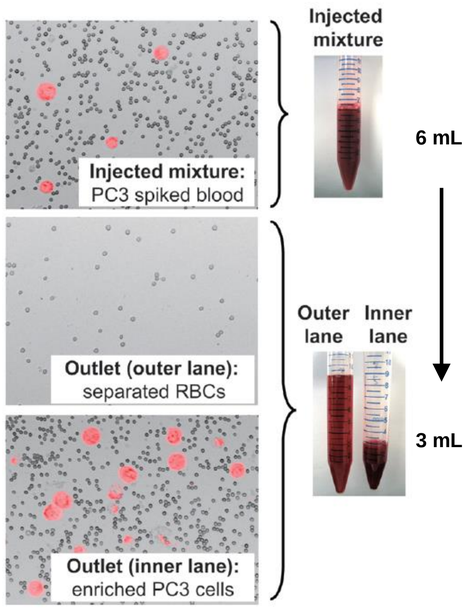
We have developed a microfluidic platform capable of enabling rapid size-based separations of micron-scale species (particles, cells)

- **Embedded weir-like barrier** separates two lanes with unequal depths, oriented parallel to the flow direction and extending along the entire centerline length
- Merges high selectivity of a physical membrane barrier with ability to operate at high flow rates (mL/min), making it possible to process large volumes with no clogging





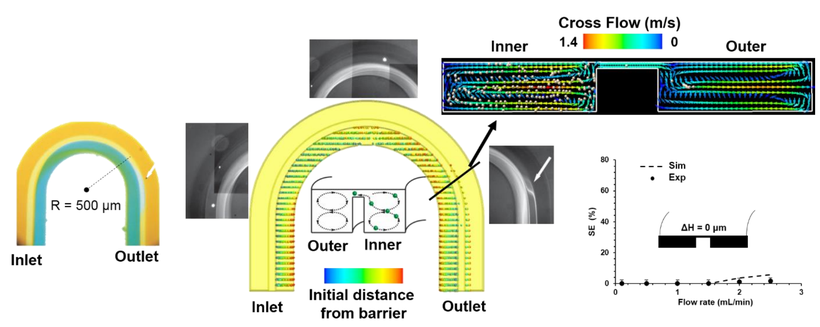
- PC3 cells (20 – 30 μm dia.) spiked into whole blood diluted 1:5 with PBS to equalize viscosities
  - PC3: 1.43 x 10^6 cells/mL
  - WBC: 1.45 x 10^6 cells/mL
  - RBC: 8.12 x 10^8 cells/mL
- PC3 spiked blood injected into the inner inlet at 1 mL/min
- PBS co-injected into the outer inlet at the same flow rate (20-3-35 μm depths)
- **PC3 cells separated with > 99% efficiency and enriched by 2.2x**
- **6 mL sample processed in 6 min**



Method	Flow Rate (reported)	Dilution Factor	Normalized Throughput (mL min^{-1})	CTC recovery	Comments
This work	**1 mL min^{-1}**	**5**	**0.2**	**99 %**	**• Optimal operation at high flow rates**
Immunoselection (bead-based)	10 mL h^{-1}	> 1*	unknown*	90 %	• Antibody-based
	240 μL min^{-1}	> 1*	unknown*	85 %	• Additional washing
Immunoselection (micropost array)	1 mL h^{-1}	1	0.017	65–80 %	• Antibody-based • Low volume capacity
	1 mL h^{-1}	1	0.017	95 %	
	2 mL h^{-1}	1	0.03	92 %	
Dielectrophoresis	1.5 ml min^{-1}	40,000	3.75 x 10^{-5}	90 %	• Special buffer conditions
	126 μL min^{-1}	400	3.15 x 10^{-4}	75 %	
Physical barrier					• Dilution and/or low flow rate operation needed to avoid clogging
• Pool-dam	0.1 mL min^{-1}	5,000	2 x 10^{-5}	99 %	
• Isolation wells	0.7 mL h^{-1}	3	3.9 x 10^{-3}	80 %	
Hydrodynamics					• Dilution and/or low flow rate operation needed to avoid clogging
• Expansion/ contraction	0.4 mL min^{-1}	20	0.02	80 %	
• Microvortex trapping	4.5 mL min^{-1}	40	0.11	85 %	

Separation Performance

Particle-based experiments, 3D simulations (STAR-CCM+)



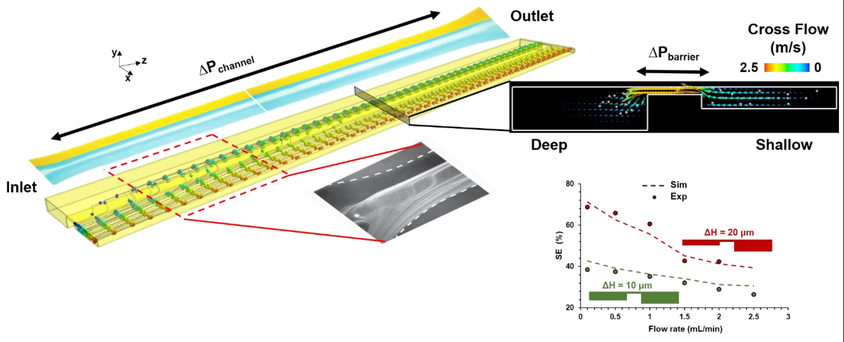
Curved, equal depth

- inner and outer lanes: 40 μm
- centerline barrier gap: 5 μm
- radius of curvature: 500 μm

Particle size: 2 μm

Flow rate: 2 mL/min

Dean vortices in curved region transport a few small particles across gap to the outer lane



Straight, unequal depth

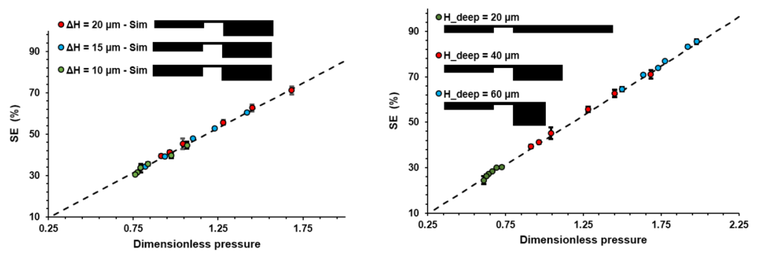
- Lane 1: 40 μm
- Lane 2: 20 μm
- centerline barrier gap: 7 μm

Flow rate: 2 mL/min

Pressure difference at entry drives particle migration from shallow lane into deep lane

Particles in the deep region remain concentrated near the barrier and are able to cross back into the shallow region

Ratio of transverse to lateral pressures governs transport across barrier



Curved, unequal depth

- Inner lane: 20 μm
- Outer lane: 40 μm
- centerline barrier gap: 7 μm
- radius of curvature: 500 μm

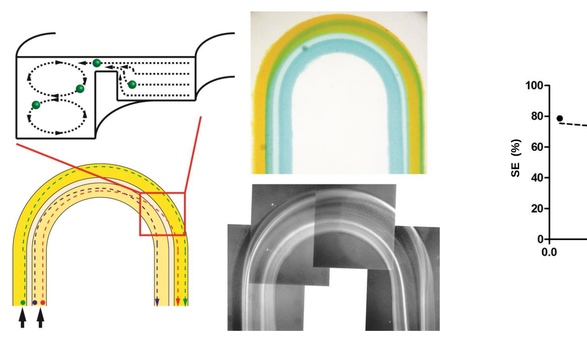
Flow rate: 2 mL/min

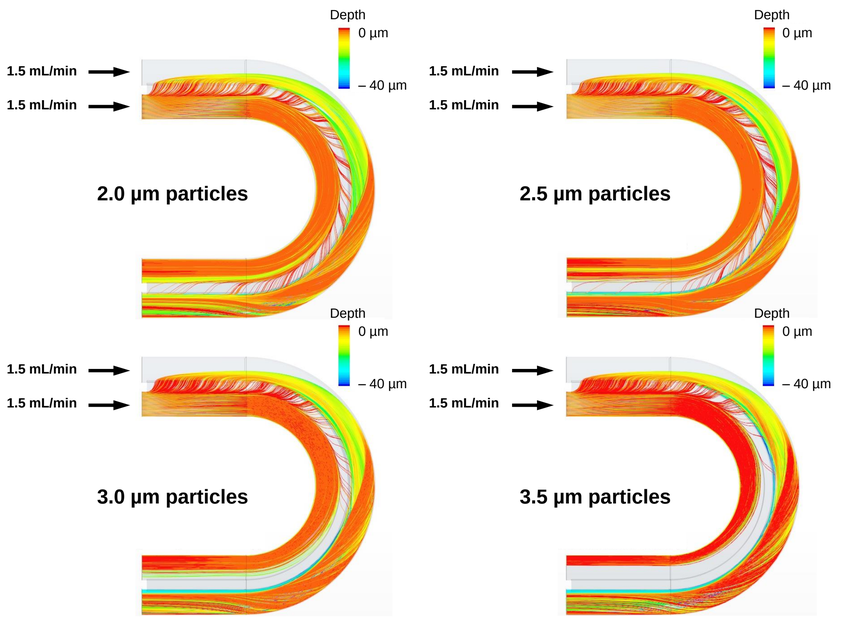
Dean vortices coupled with entry pressure difference

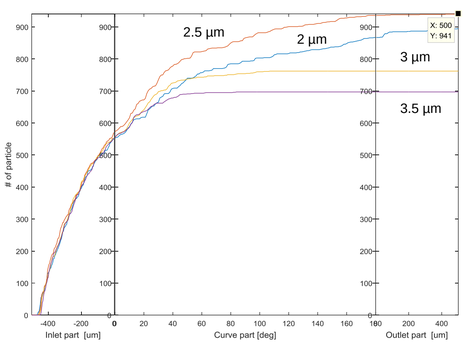
Particles cross to outer lane due to pressure difference at entry

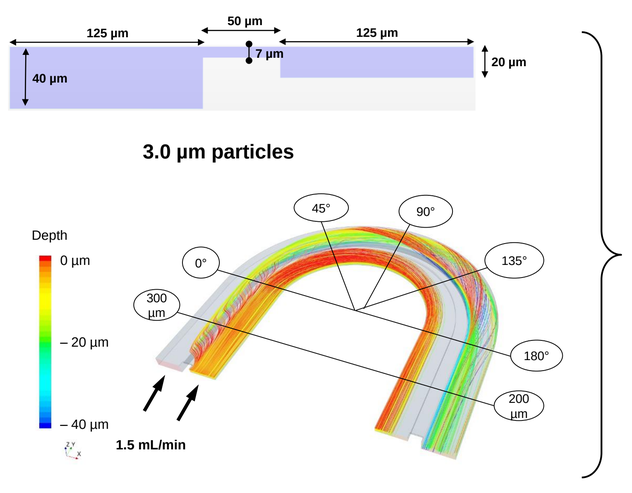
After crossing the barrier, transverse circulation in the curved region keeps particles in the outer lane

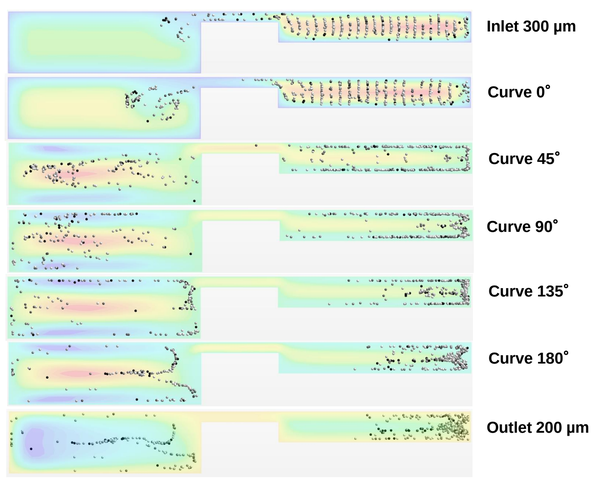
Size selectivity can be further tuned by manipulating inertial effects in curved segment











High separation efficiencies can be maintained across flow rates from 0.1 – 2.0 mL/min, making this approach ideal for high-throughput processing

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