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Ultrasonic radiation forces for cell sorting and characterisation

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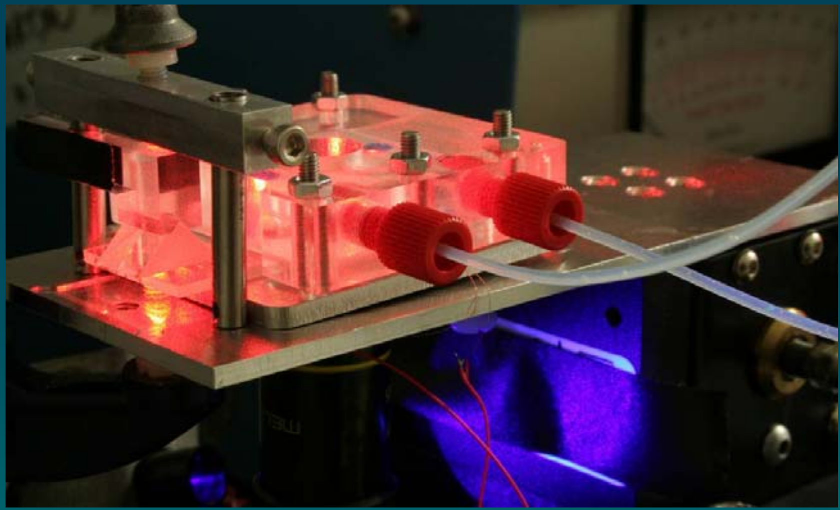

Acoustic Particle manipulation
- a **Half-wave** (λ/2) device

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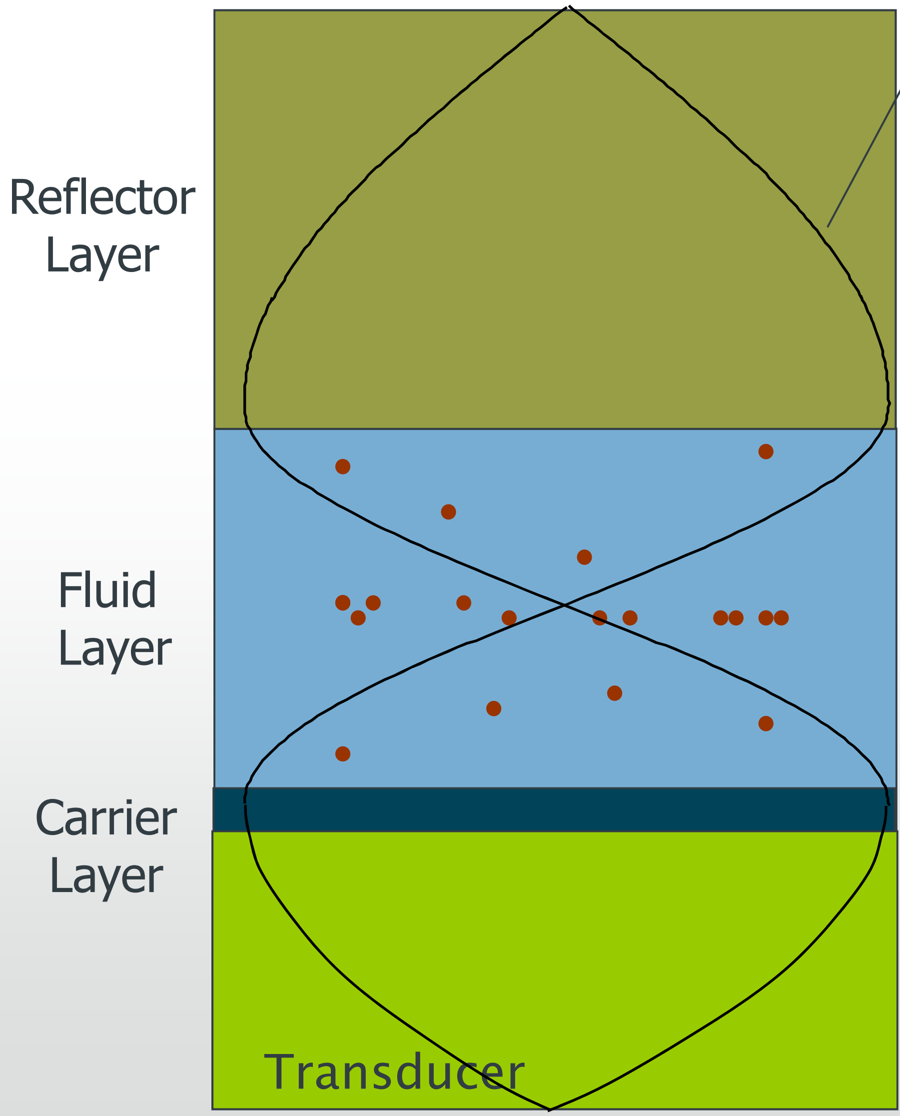
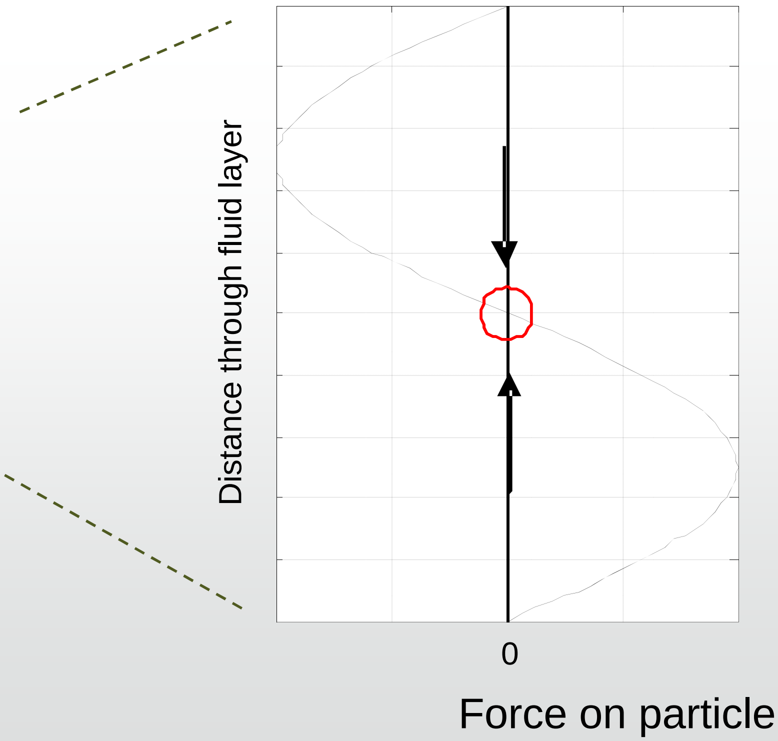
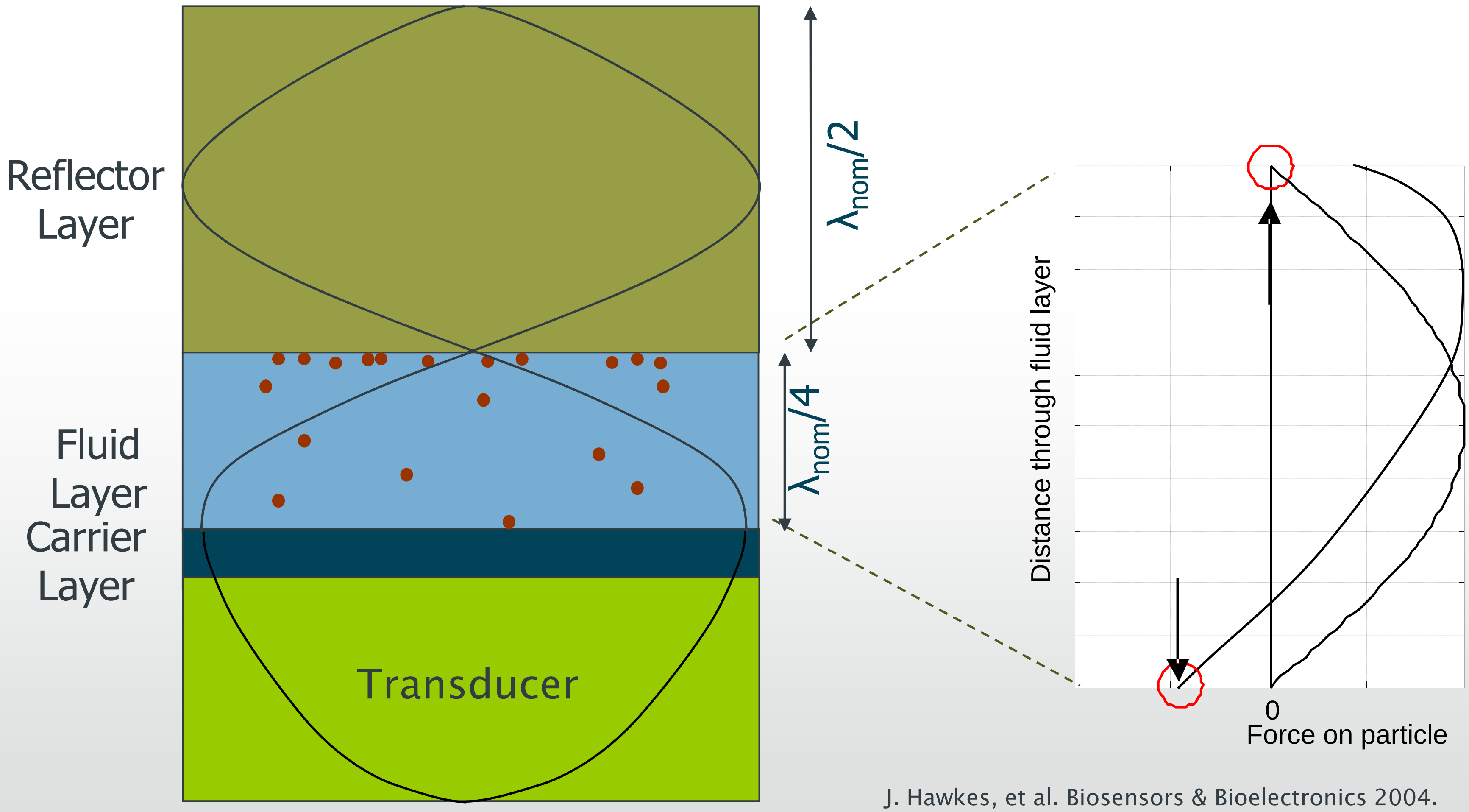




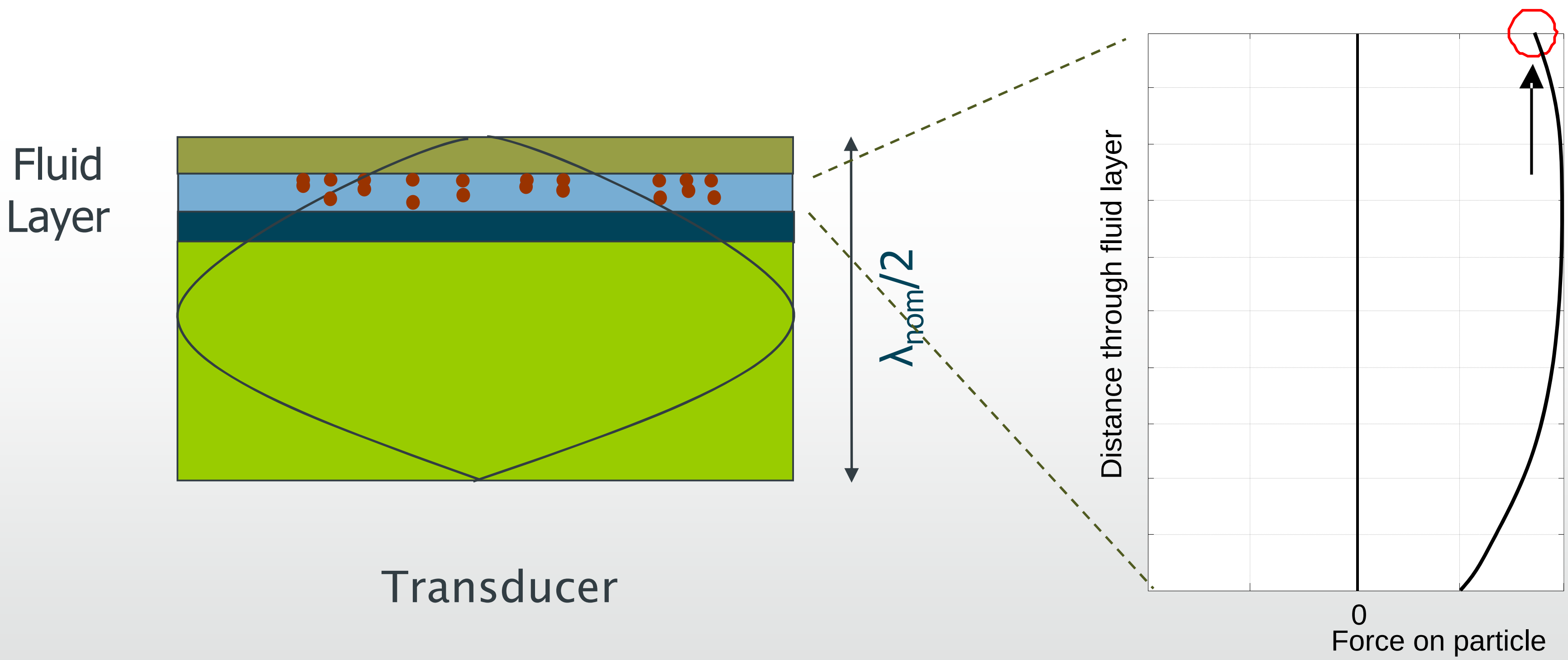
A **Quarter-wave** (λ/4) device



J. Hawkes, et al. Biosensors & Bioelectronics 2004.

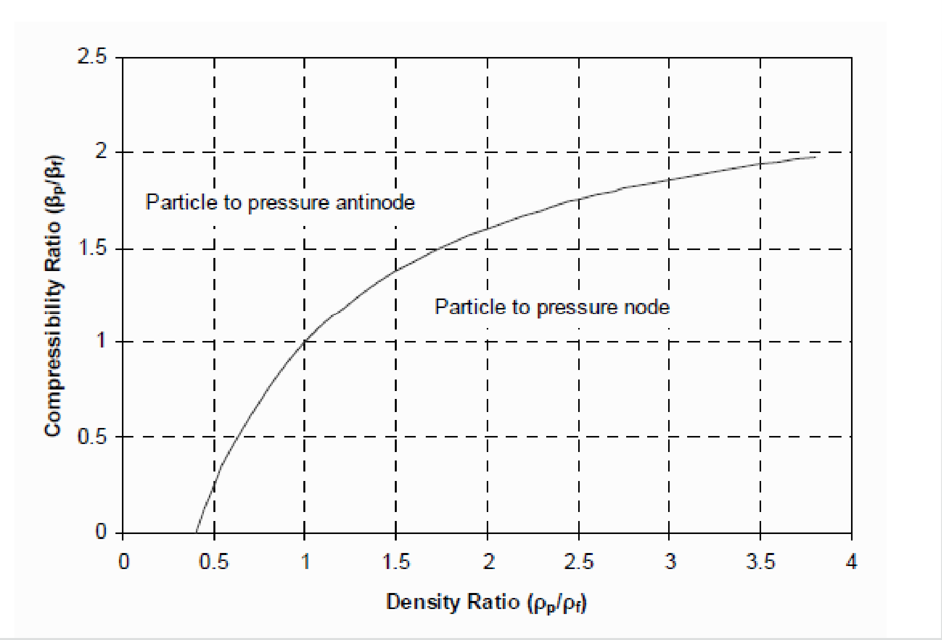
M. Hill, J. Acoustical Society of America, 2003.

The thin-reflector device

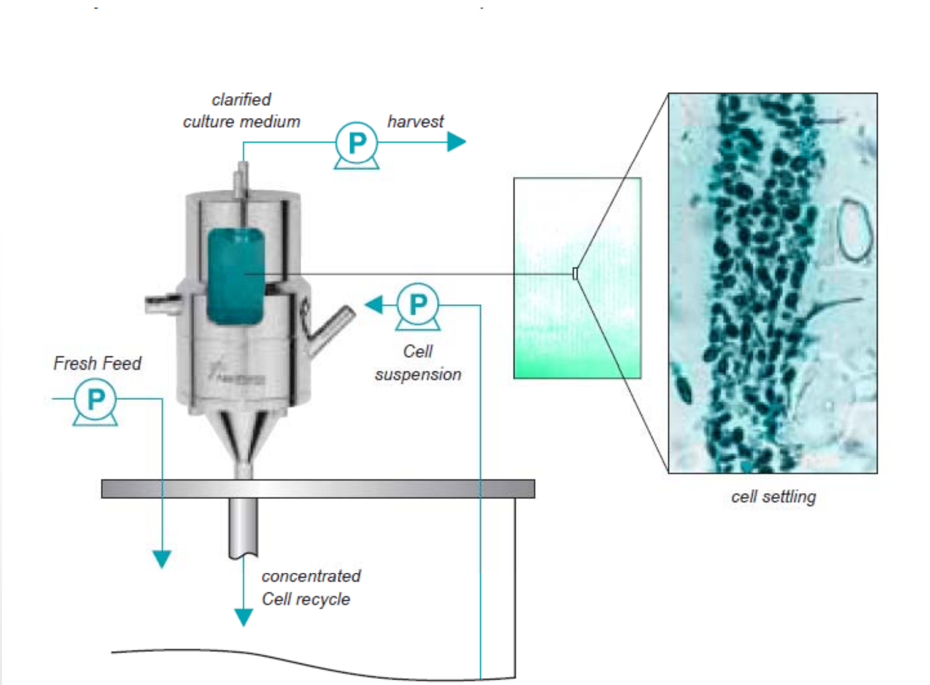


Acoustic Radiation Force

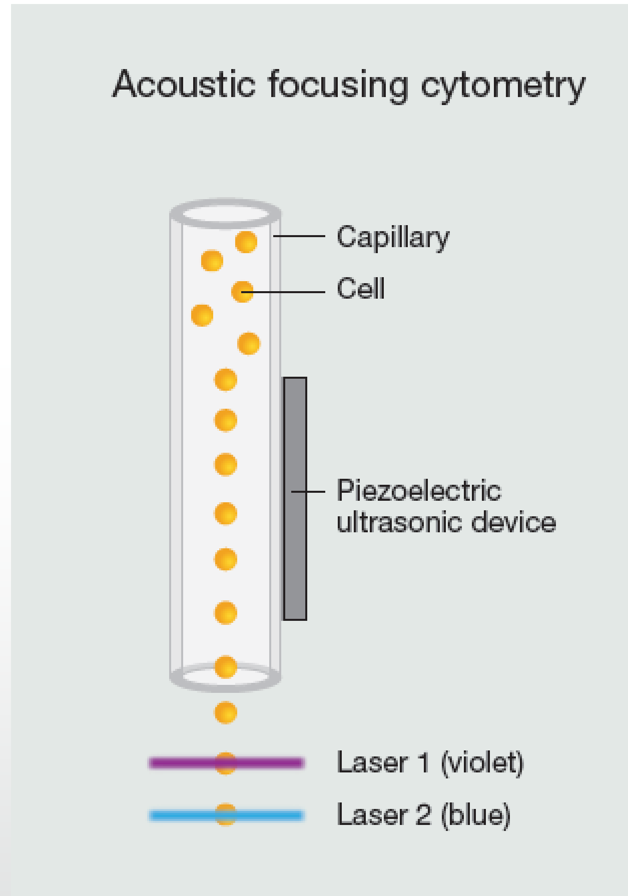
$$F_{max} = 4\pi k * \text{Energy density} * \text{Particle volume} * \text{Acoustic contrast}$$



Existing Commercial applications

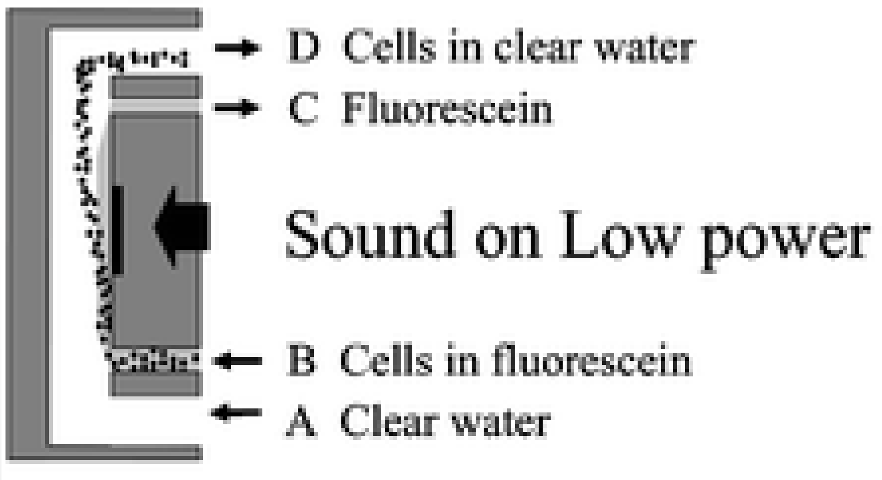


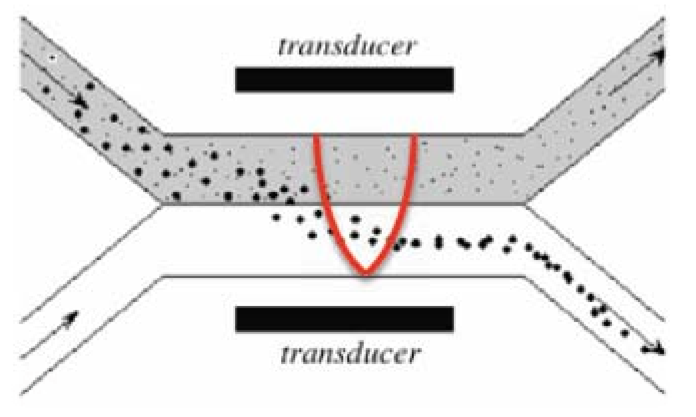
Biosep cell washing / filtration



Applied Biosystems acoustic focussing cytometry

Cell medium exchange

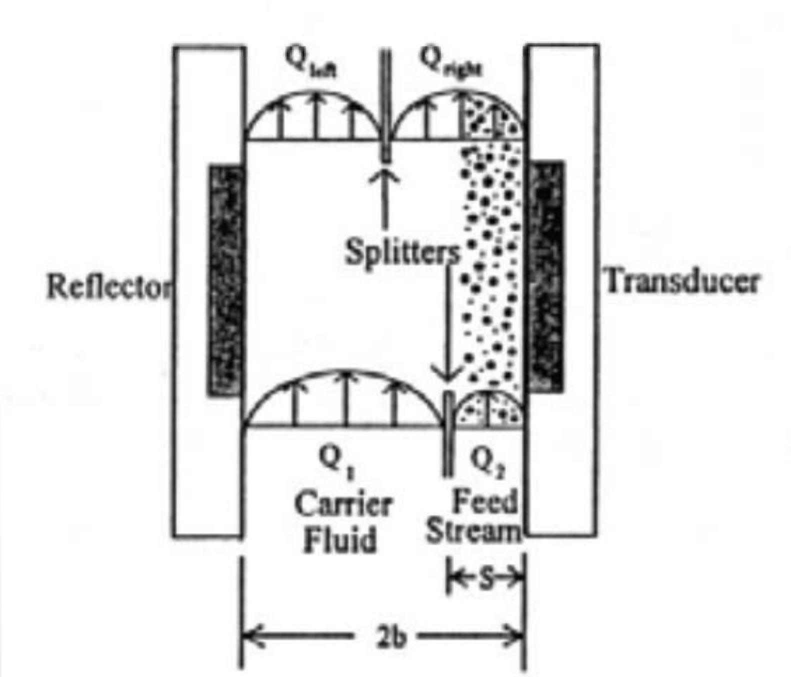




SU-based channel
Kapishnikov, J. Stat. Mech. , 2006

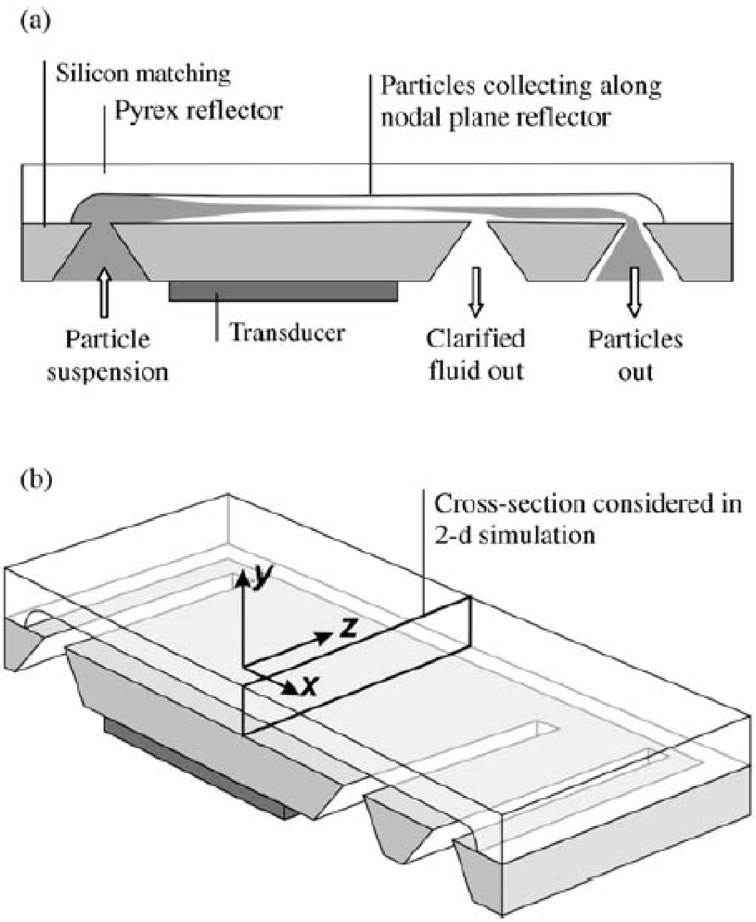
Hawkes et asl, Lab on chip, 2004

Particle sorting



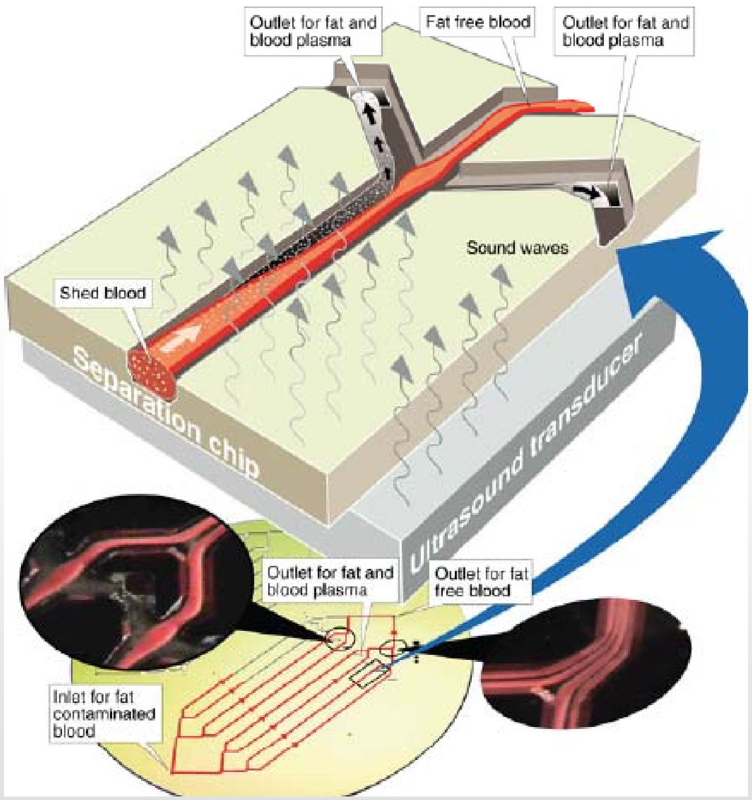
- Feke, Separations Technology, 1995

Particle sorting



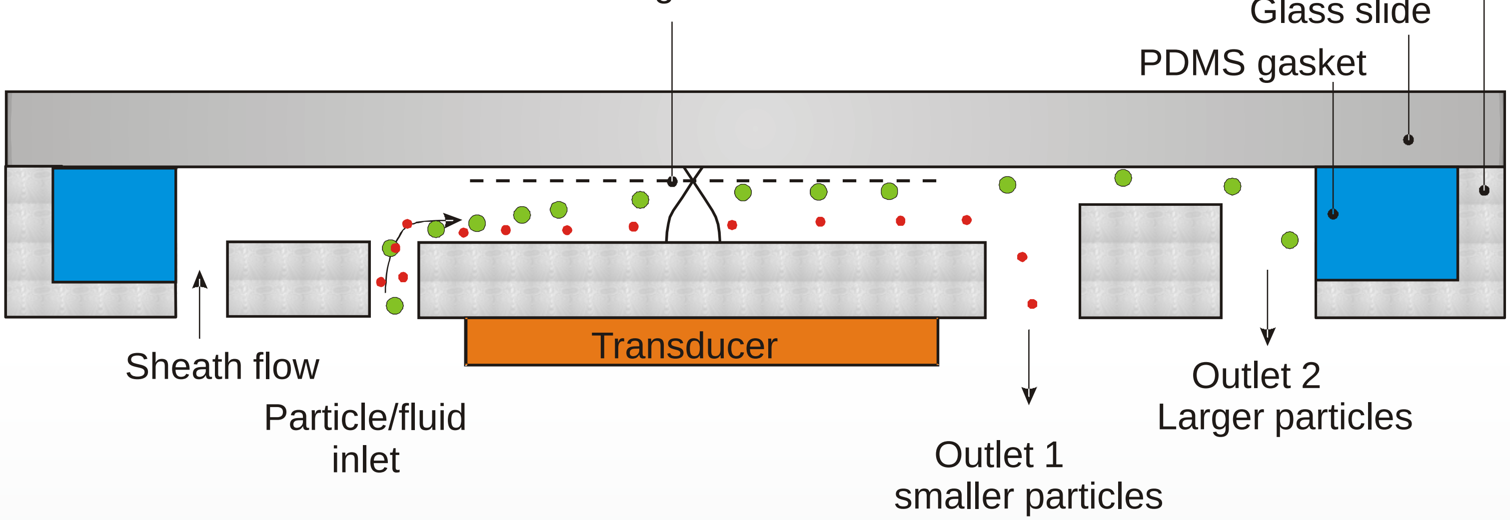
Townsend et al, Ultrasonics, 2006

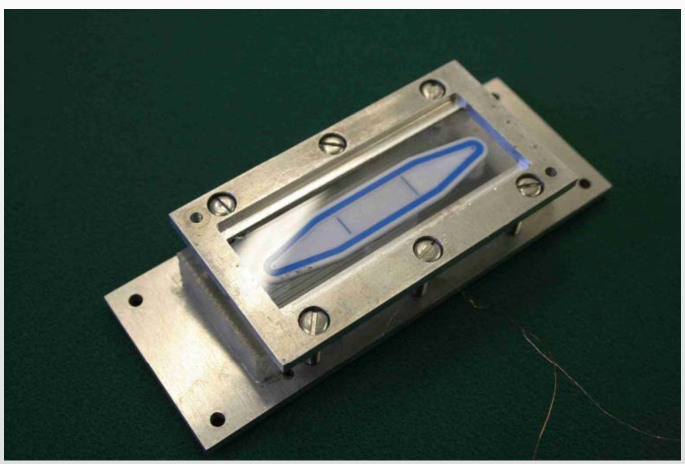
Particle sorting: Separation of blood cells from lipids

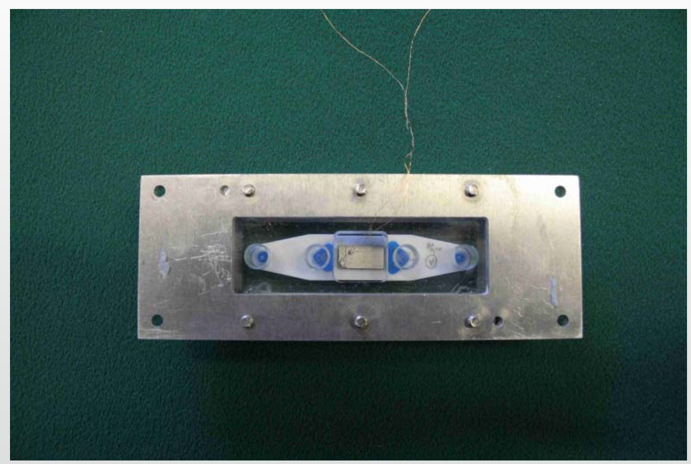


Petersson et al., Analyst, 2004 / microTAS 2002

Sorting device



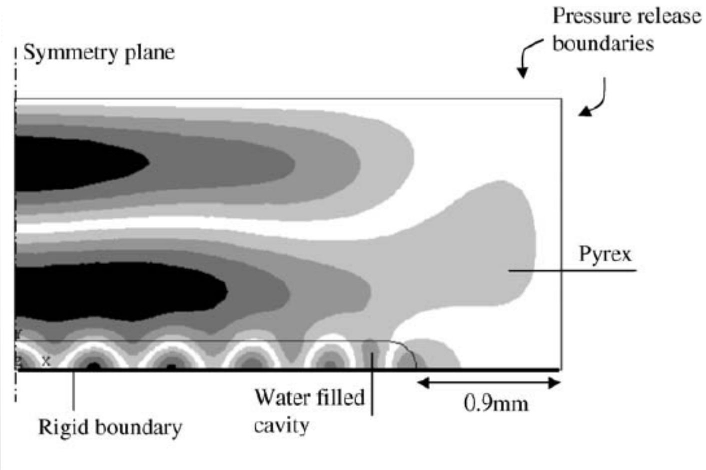




Bead sorter

Challenges for cell sorting

- Do cells have significantly different acoustic properties?
  - Size often dominates
- Can we overcome lack of uniformity in the acoustic field?
  - Lateral fields especially troubling
  - Flow based averaging helps in the flow direction
- Stable fluidics
  - Replacing the sheath flow with another USW stage could enhance reliability, and reduce sample dilution.



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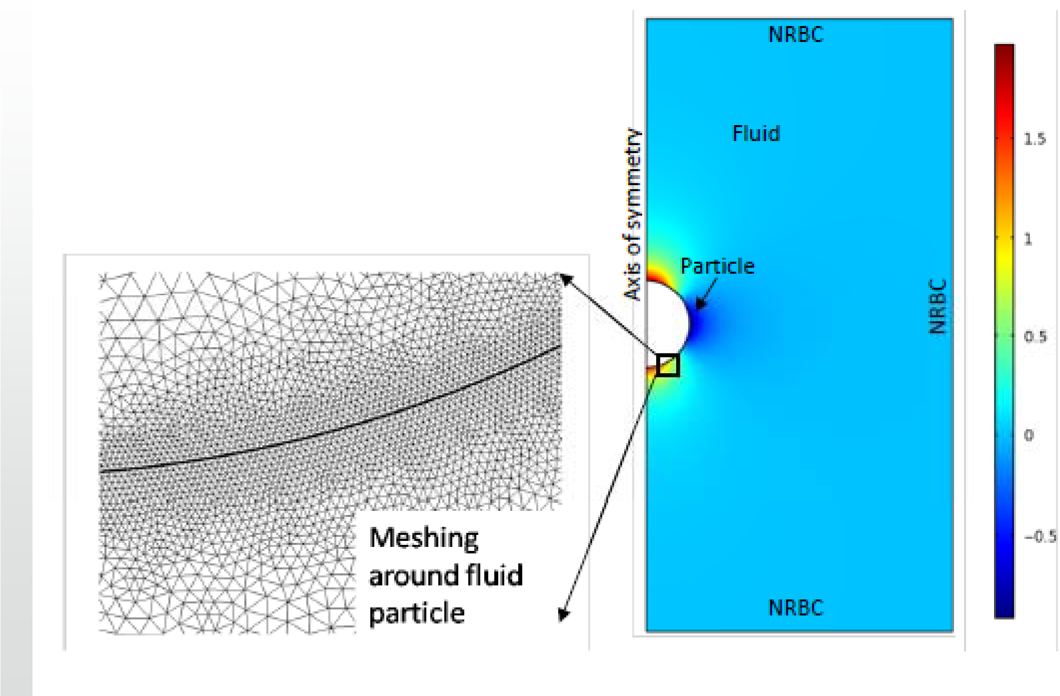
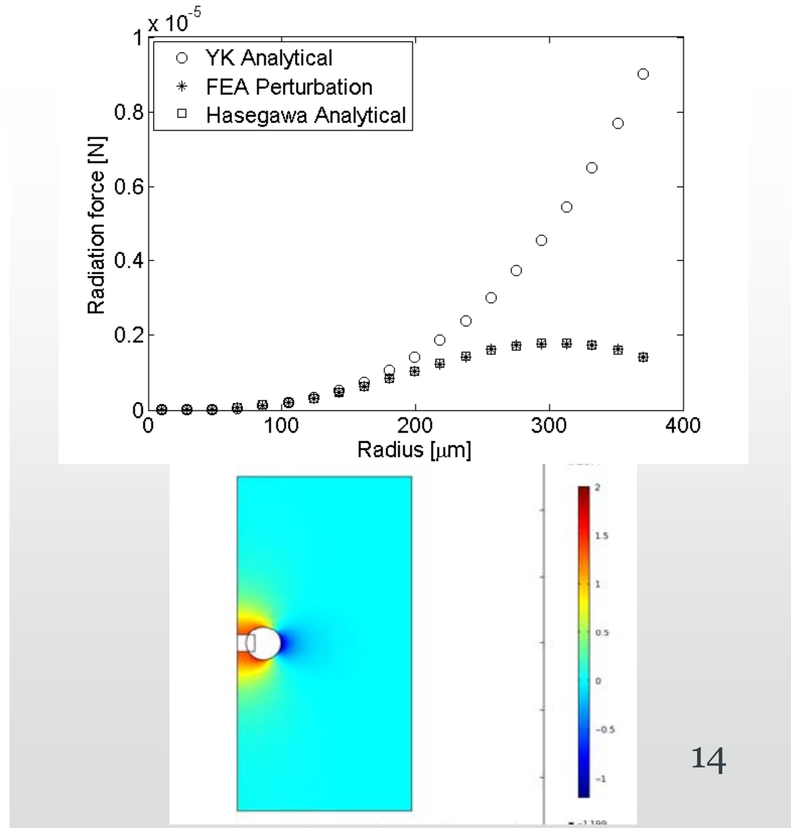
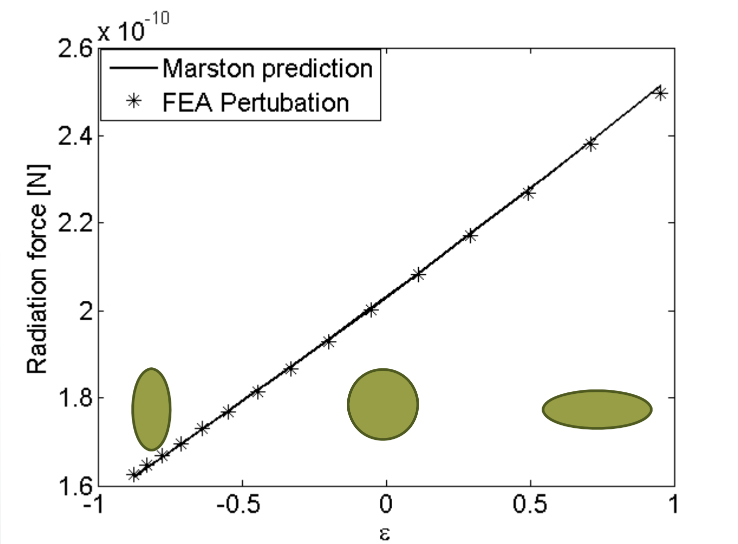
Modelling Forces on arbitrary particles

- Finite element modelling method
  - includes composite, multilayer and elastic structures

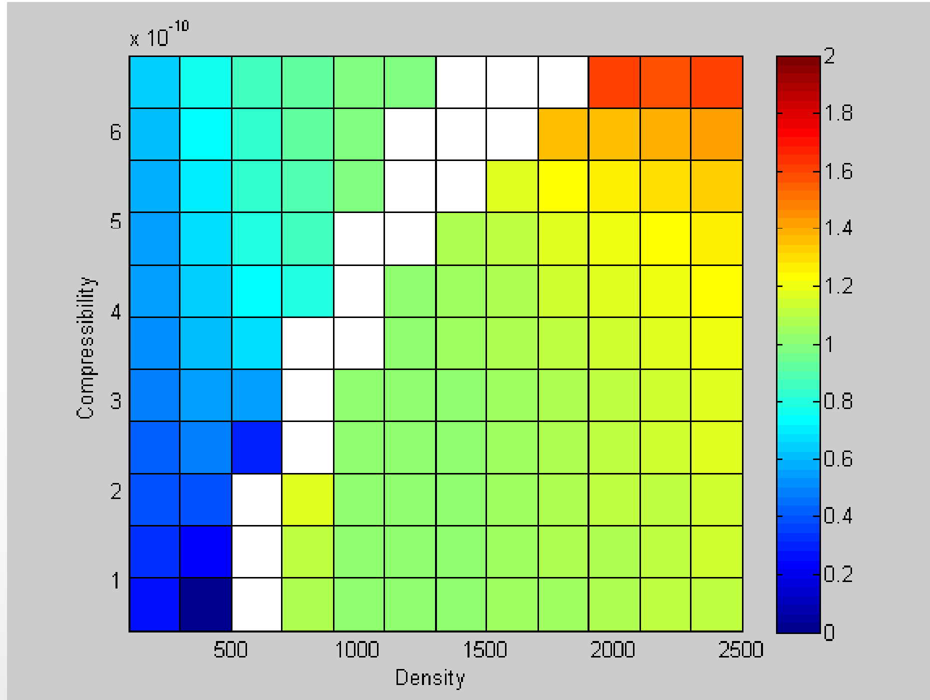




Effect of shape on force



Force vs shape parameter for dense spheroid

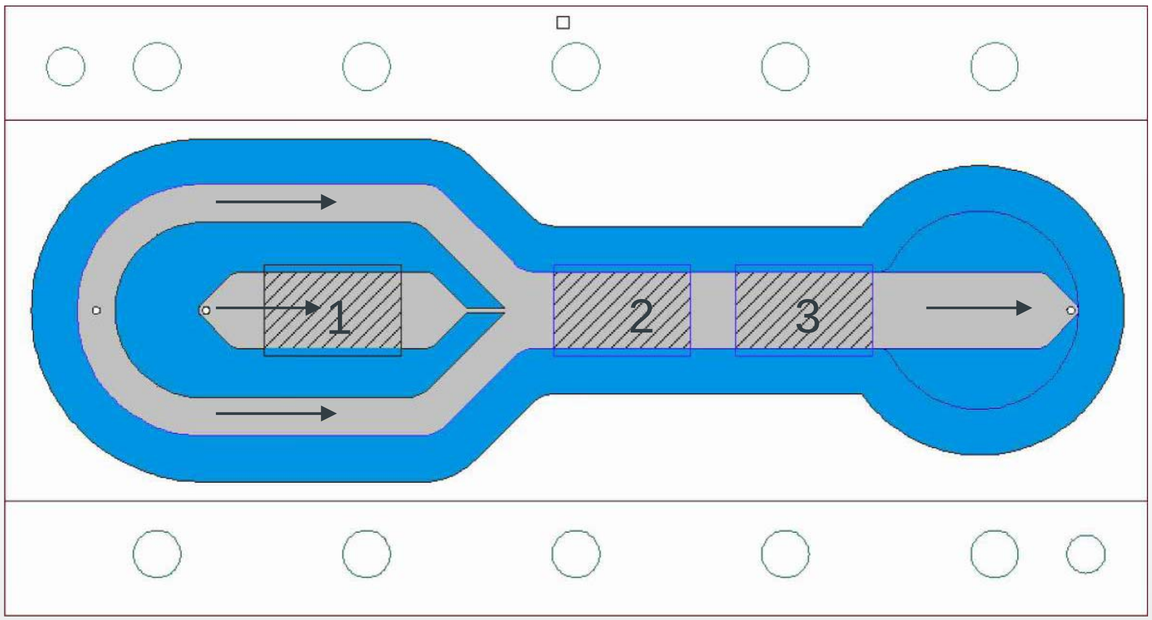


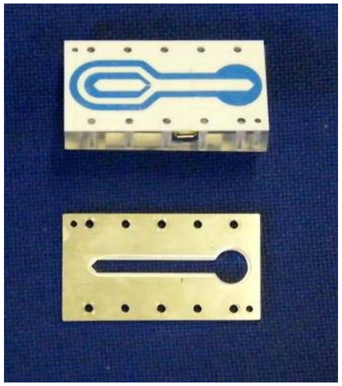
Force on oblate spheroid for range of material properties

For neutrally buoyant objects such as cells the force is less influenced by shape. However such objects still exeprience acoustic torque.

Acoustic cytometer

- Device for measuring acoustic force on a stream of cells

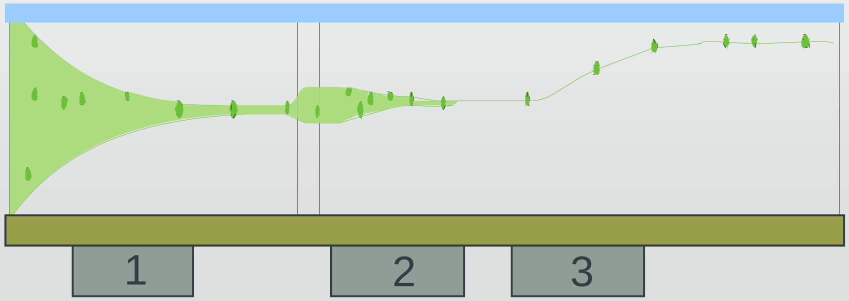




1: half-wave pre-focus

2: half-wave correction

3: Thin mode deflection

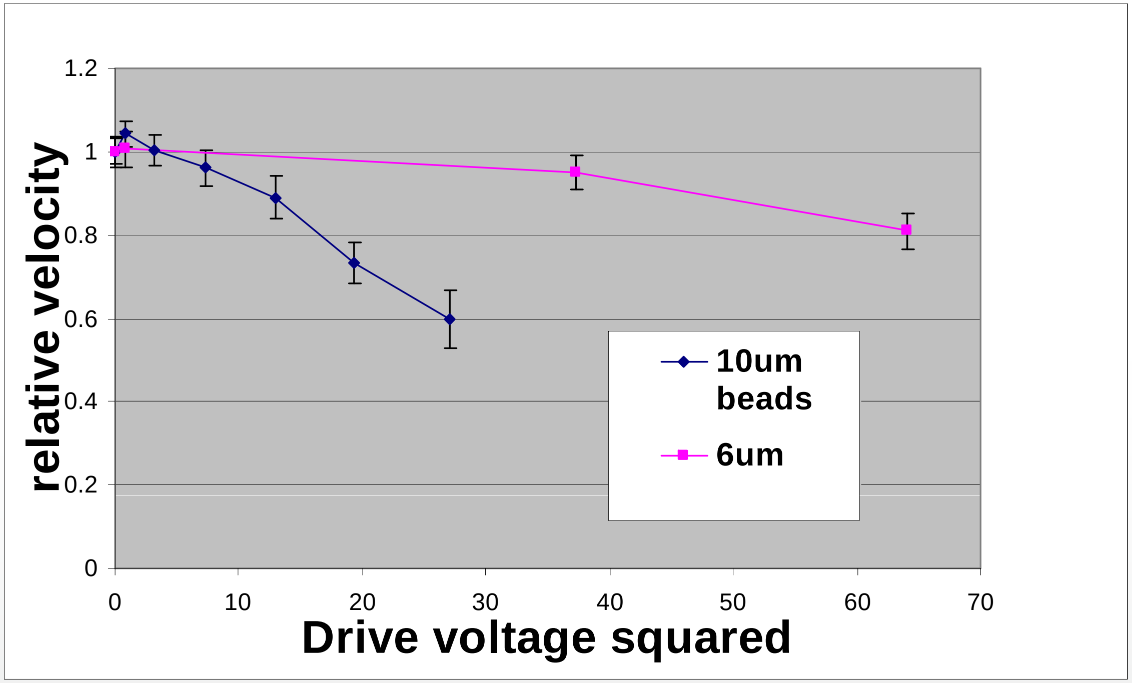


Particle position in device x-section

Results: 10 and 6μm beads

Larger beads are deflected into the slower moving parts of the flow.

Error bars show variation within bead population (diameters vary by ~2%).



- Issues: complexity (3 xdrs, 2 pumps), flow uniformity, non-linear, surface effects, visualisation / detection.

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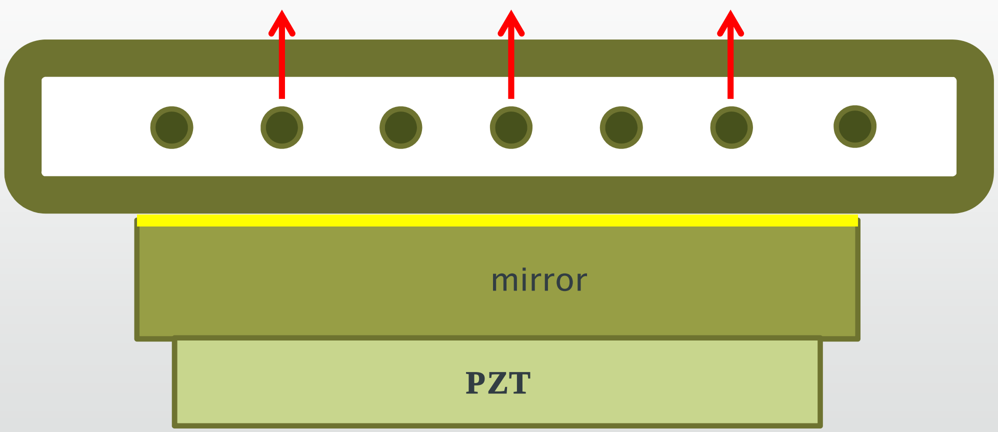
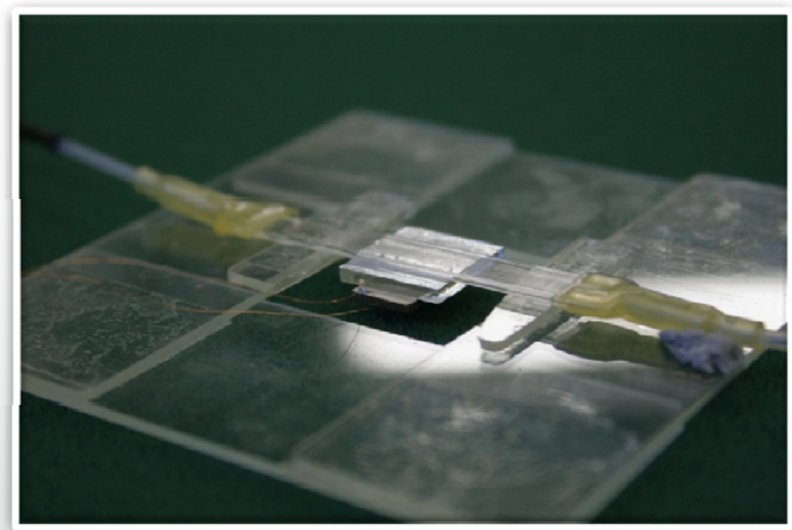
Static force measurement

- A mirror between the transducer and capillary provides darkfield imaging of particles in the chamber.
  - Axial displacement is measured using focus tracking



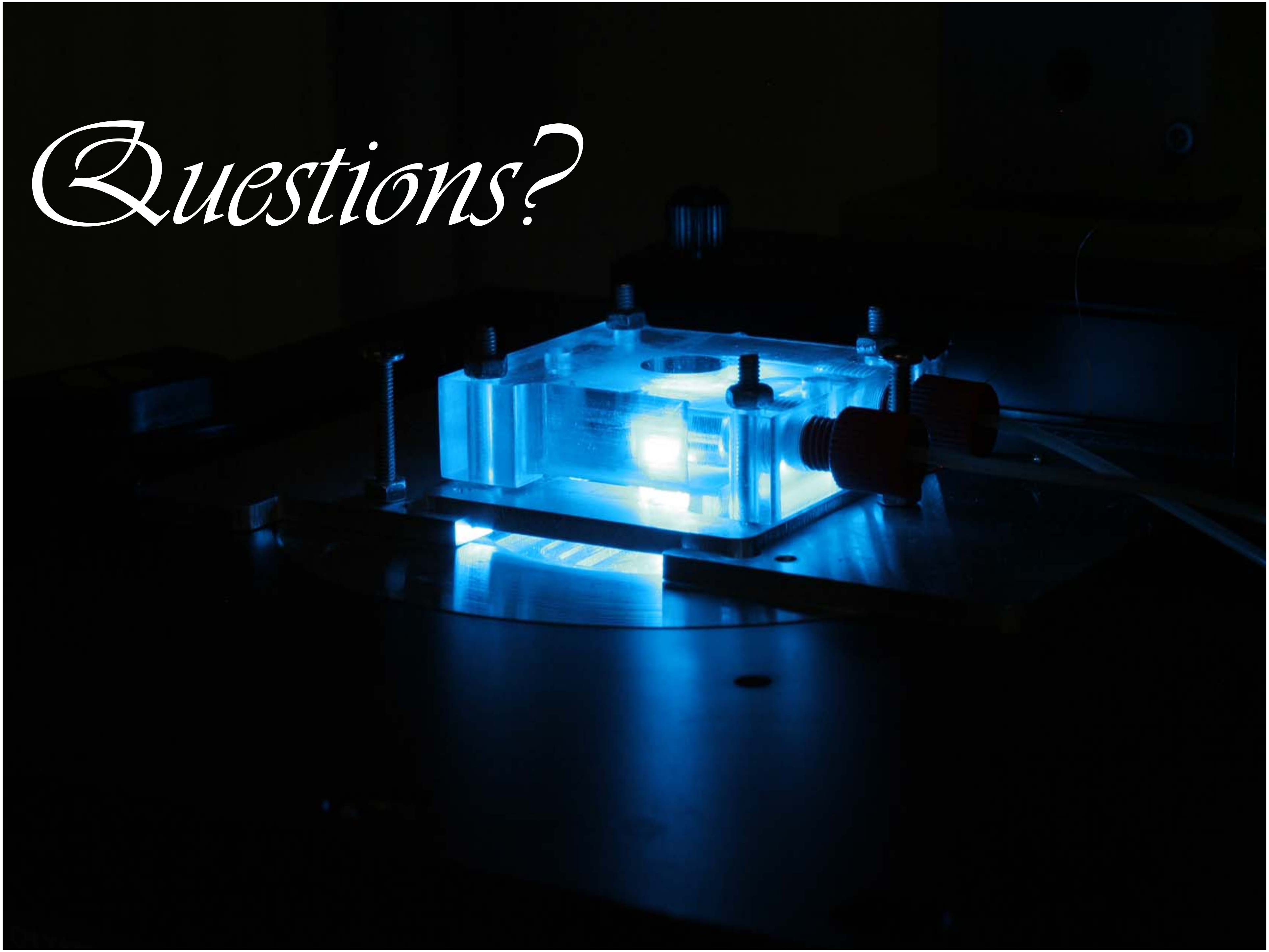


Scaling towards higher throughputs

- Current devices tend to be limited to a flow rate of order $\boldsymbol{ml/min}$, consuming 10's of $\boldsymbol{mW}$ of power.
- Some applications require much higher rates: e.g. water pathogen detection, various filtration systems.
- Planar designs offer higher flow
- $Dilema$: The wavelength limits chamber height (and hence flow rate). Solving this by decreasing frequency allows higher chambers, but lowers the force, requiring longer dwell times (lower flow rates)

Possible future applications

- Sorting live and dead cells
  - Sorting on more subtle differences?
- Commercialised cell medium exchange
- Non-contact bio-reactors for cell sheets and pellets


Questions?