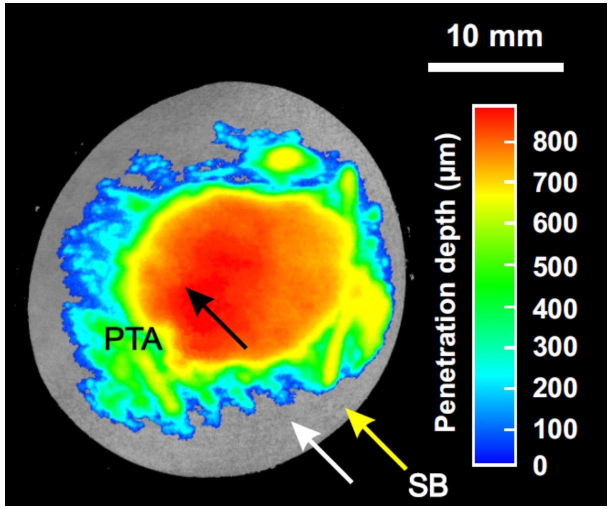
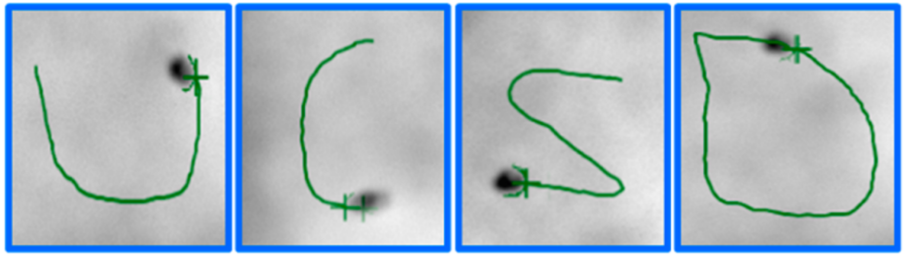
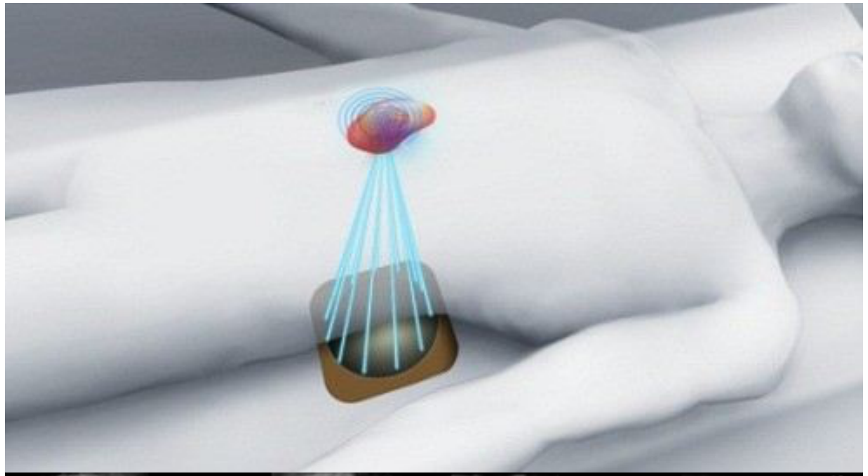
Biomedical Ultrasonics, 5 cr

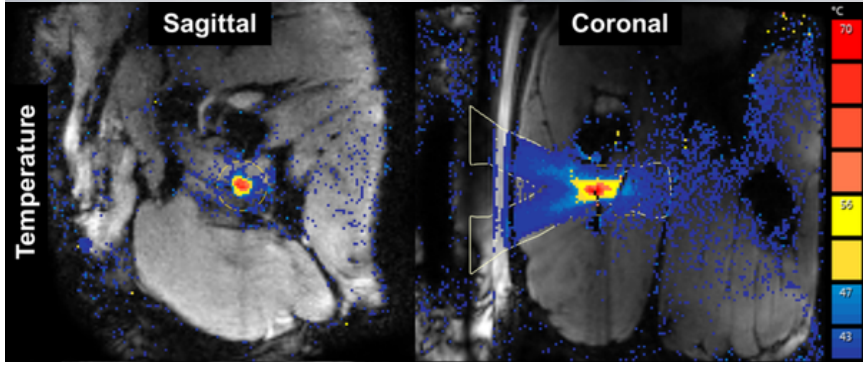
Heikki Nieminen

7.1.-31.5.2019

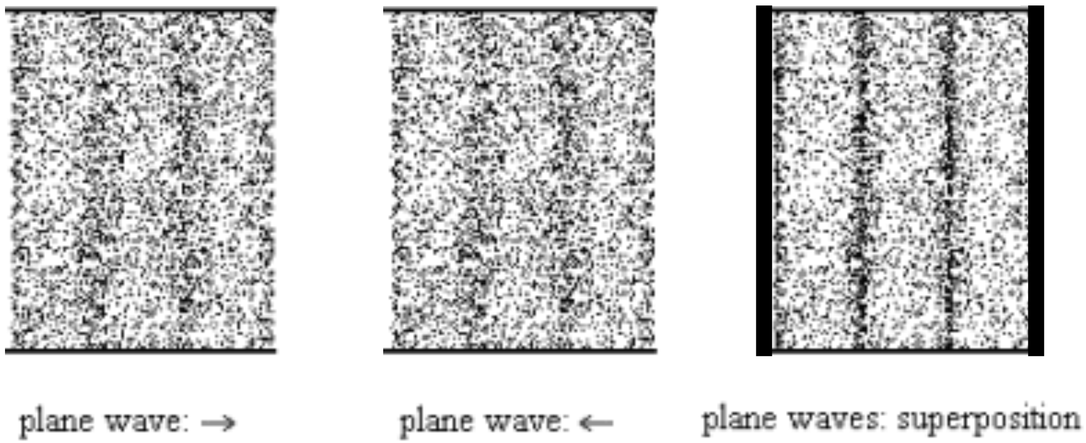








Standing wave

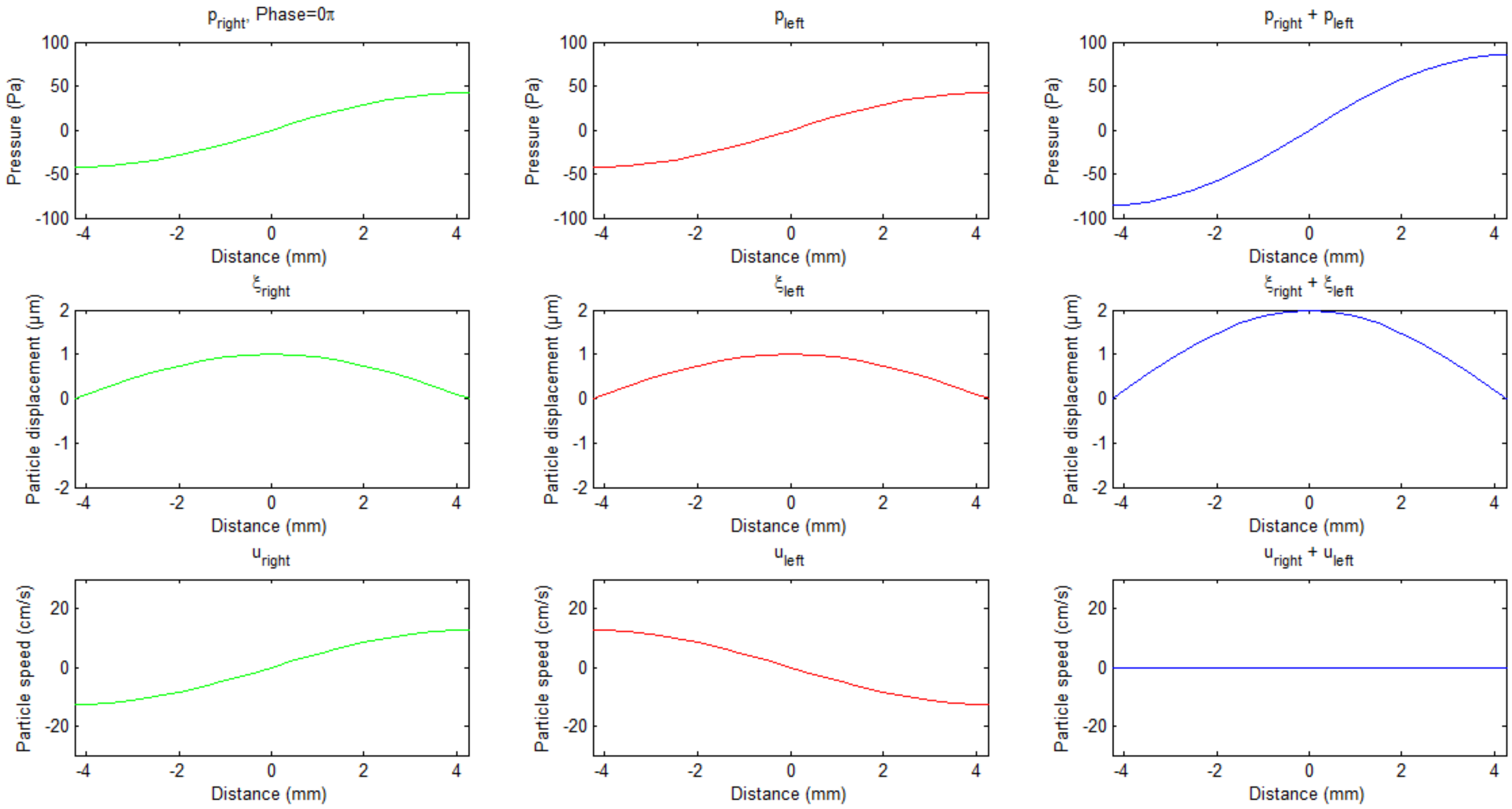


Where are the pressure nodes/anti-nodes?

Where are the displacement nodes?

Matlab demo

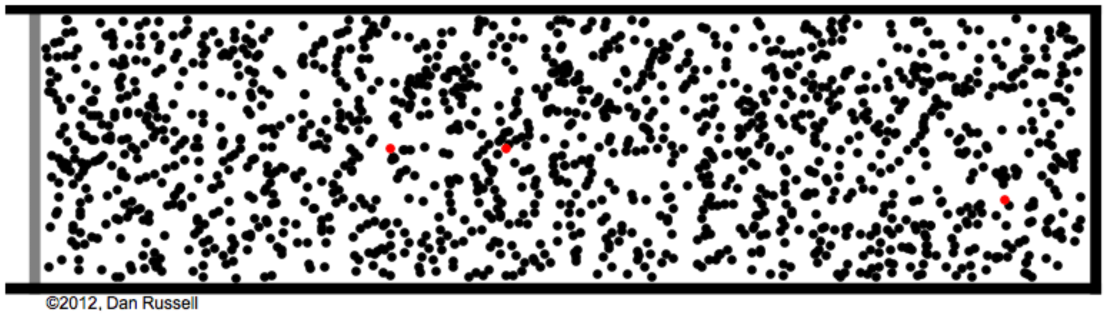
λ/2 resonator c = 340 m/s, f = 20 kHz



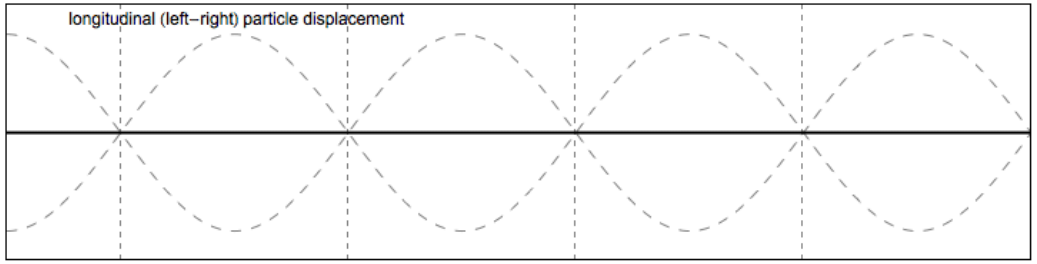
Standing wave

Where is the energy density the lowest?

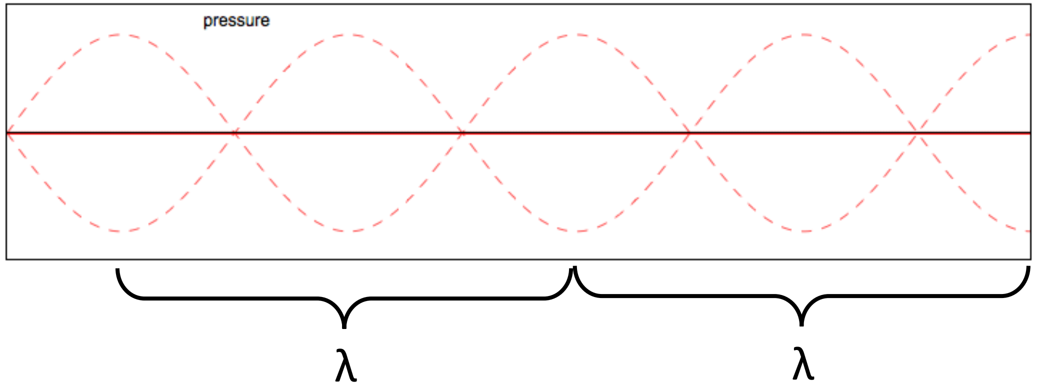
Where is the energy density the highest?



Particle displacement:



Pressure:



Acoustic radiation force on a sphere within a standing wave

- A linear one-dimensional stationary standing wave the time-averaged radiation force applied to a sphere can be expressed as

$$F = -\left(\frac{\pi \hat{p}^2 V_s \beta_m}{2\lambda}\right)\phi \sin(2kx) = -\underbrace{\frac{4\pi}{3}R^3}_{V_s}\frac{k}{2}\underbrace{\frac{\hat{p}^2}{2\rho_m c_m{}^2}}_{\text{Maximum energy density}}\phi \sin(2kx)$$

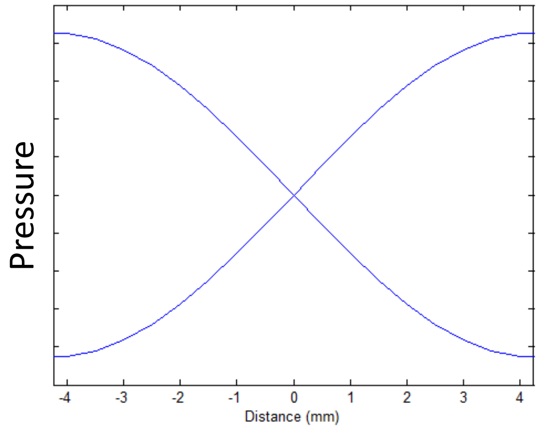
k = wavenumber = $2\pi/\lambda$

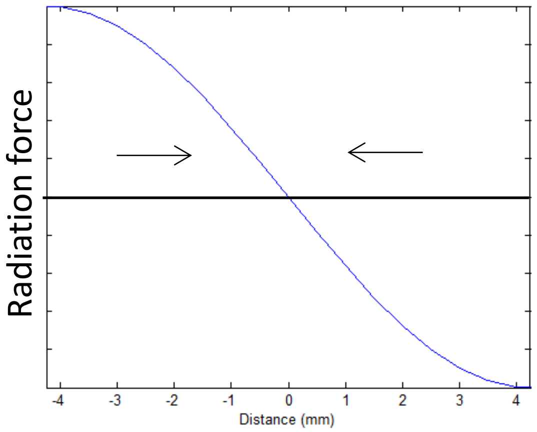
ϕ: Contrast factor

where
- R = sphere radius
- x = distance from the pressure node
- $\hat{p}$ = peak pressure amplitude of the standing wave
- β_m = 1/K = compressibility
- ϕ = is a contrast factor, *i.e.* $\phi = \frac{5\Lambda-2}{2\Lambda+1} - \frac{1}{\Lambda\sigma^2} = \frac{5\Lambda-2}{2\Lambda+1} - \frac{\beta_s}{\beta_m}$, where $\Lambda=\rho_s/\rho_m$, $\sigma = c_s/c_m$, and s = sphere, m = medium.

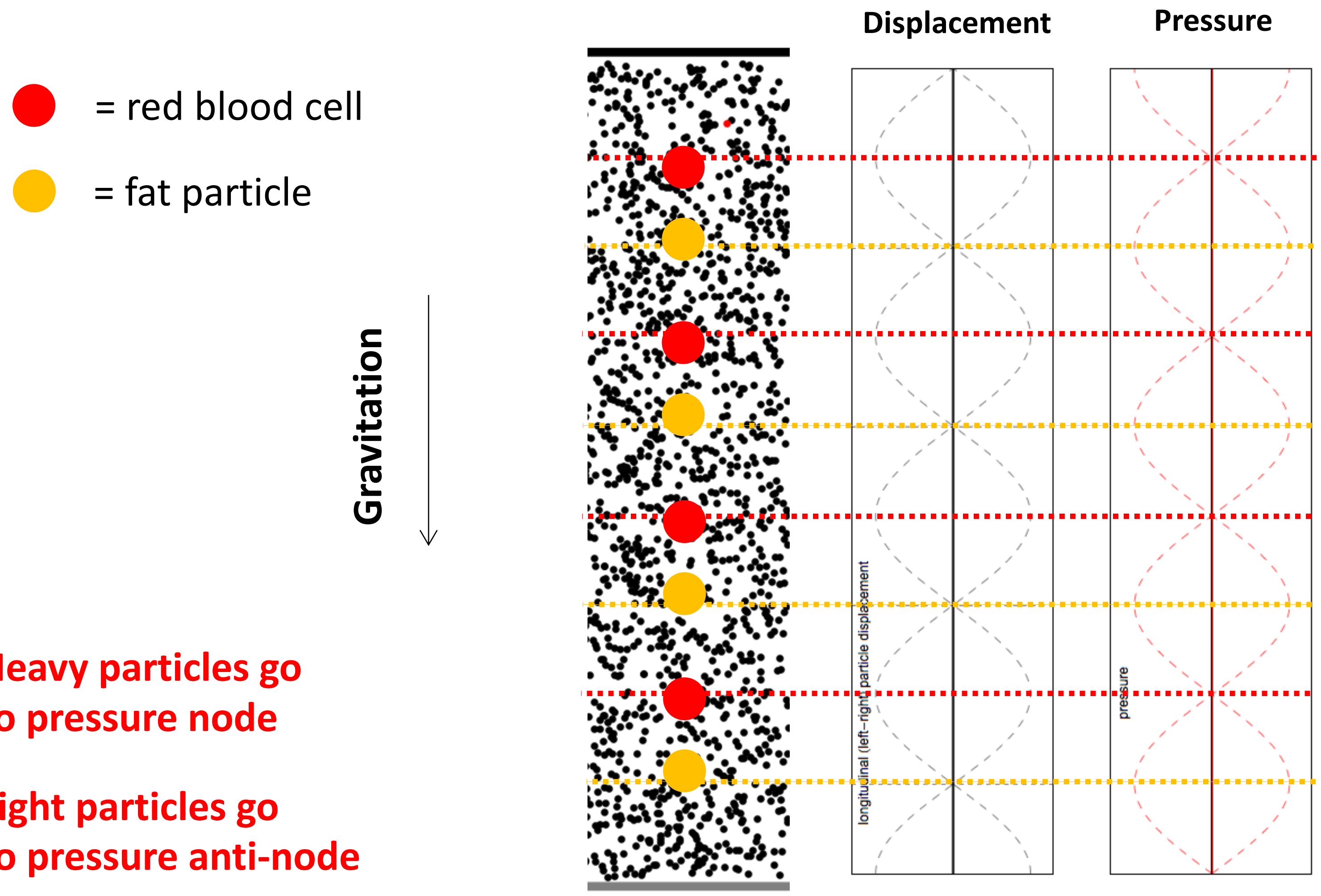
When $\phi > 0$, the sphere travels towards the pressure node. When $\phi < 0$, the sphere travels towards the pressure antinode.

λ/2 resonator





Where does the particle want to go?
Acoustic trap with blood

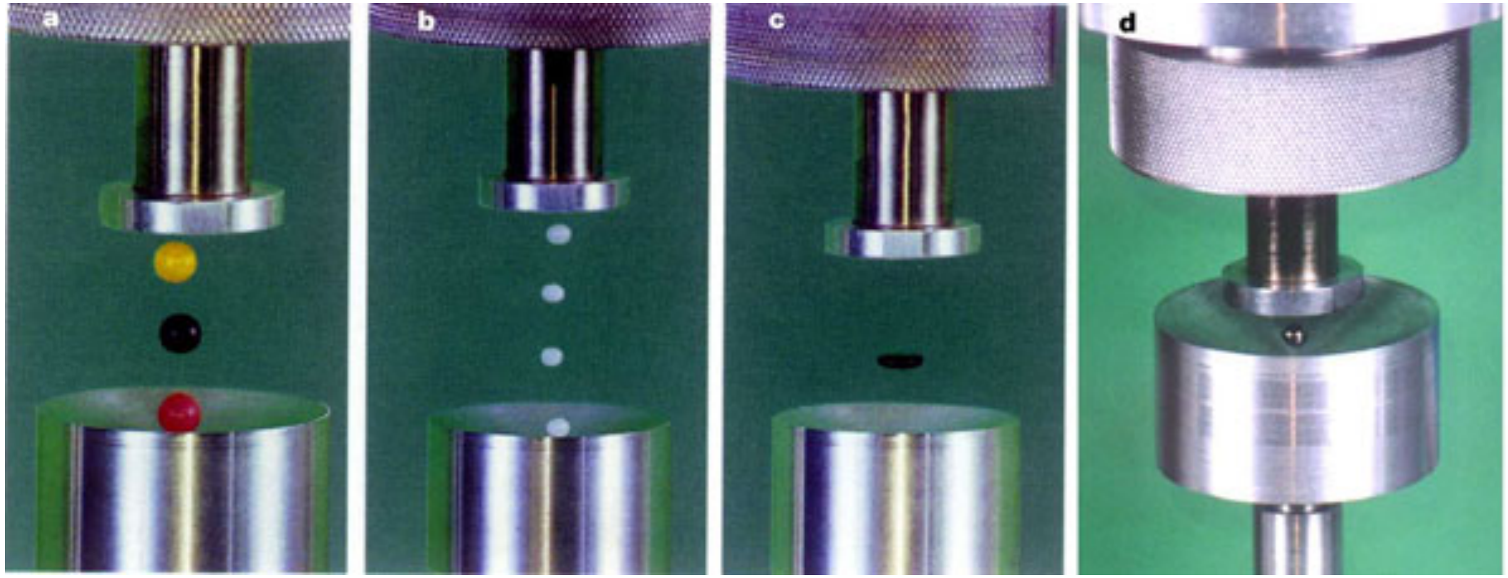


Heavy particles go to pressure node

Light particles go to pressure anti-node

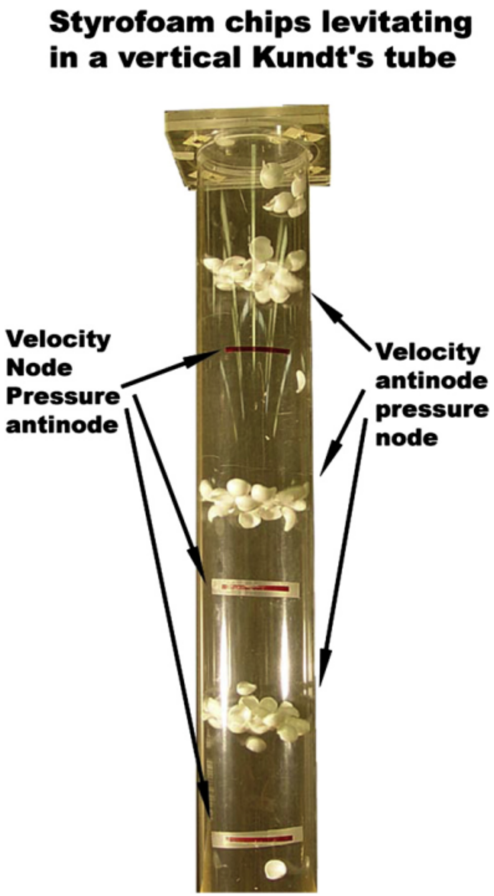
Wall-less chemistry by acoustic levitator

Multiple polystyrene spheres | **Multiple liquid droplet** | **Liquid compressed to a pancake** | **Heavy Tungsten sphere**



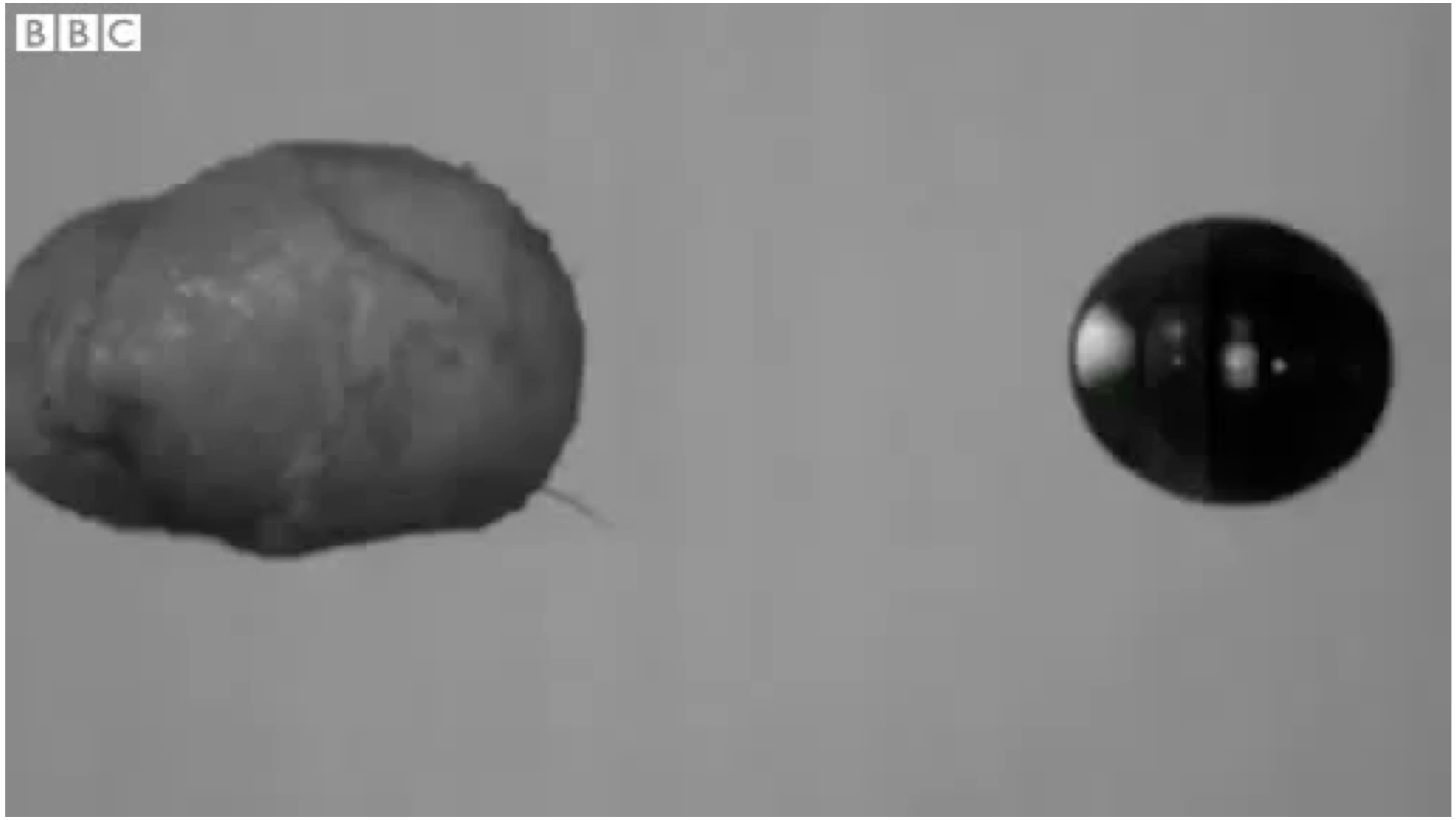
Brandt et al. 2001: http://www.nature.com/nature/journal/v413/n6855/fig_tab/413474a0_F1.html

Acoustic levitator



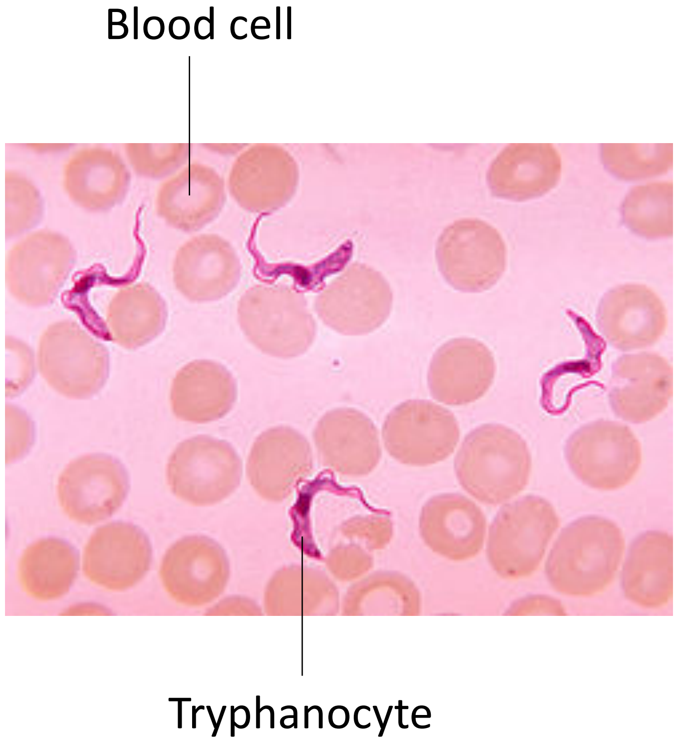
Acoustic levitator

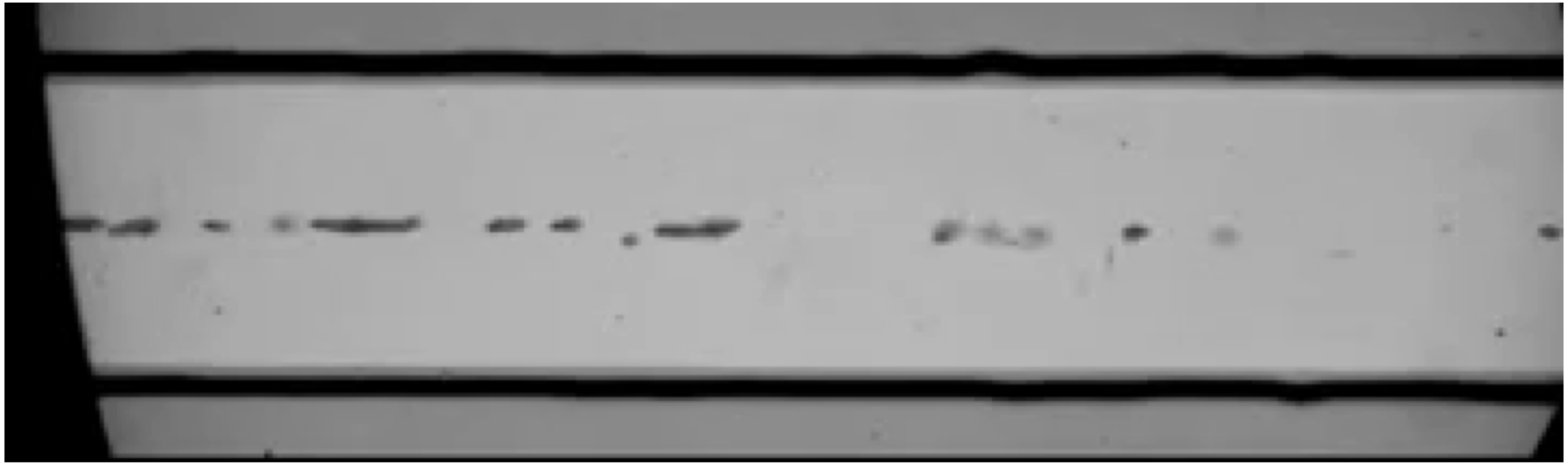
- Wall-less chemistry:



Acoustic levitator

- Separation of blood cells and tryphanocytes:



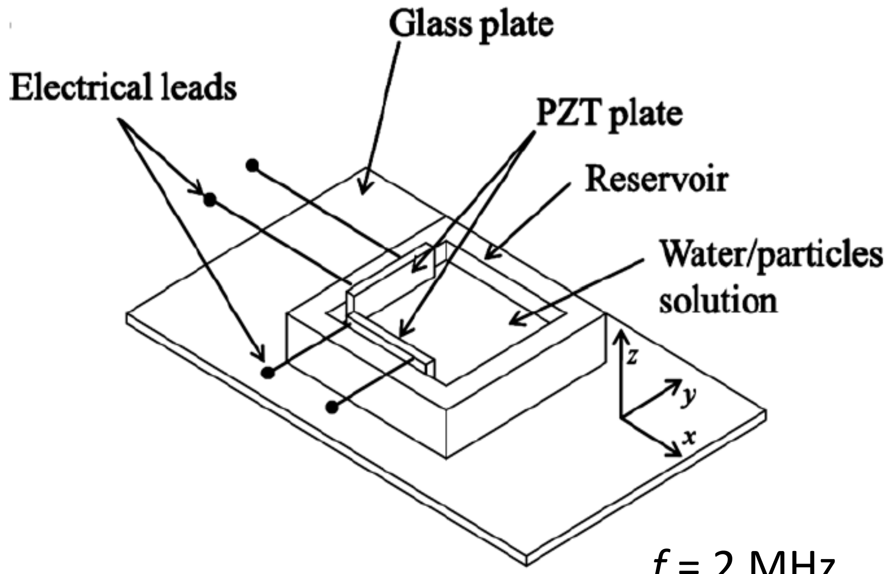


Advantages of acoustic levitators

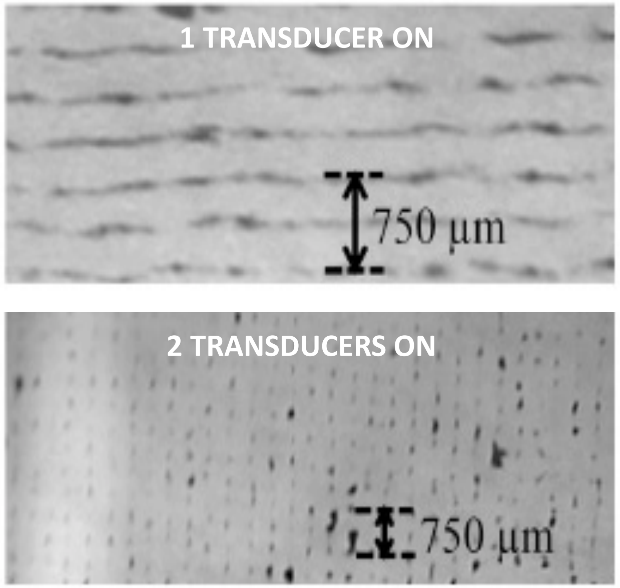
- Wall-less chemistry, bio-chemistry
- Remote forces ➔ non-touching platform
- Trapping of entities in blood stream
- However, not yet applied in human *in vivo*

Separation of diamond nanoparticles

- **Radiation force**
- **Collecting 5nm diamond spheres using radiation force in standing waves**



f = 2 MHz



Raeymaekers *et al. J. Appl. Phys.* (2011)
doi:10.1063/1.3530670

f = 2 MHz
p_0 = 50.2 kPa

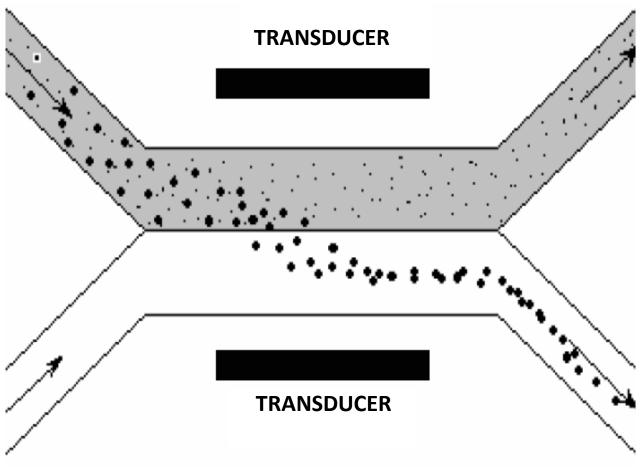
Radiation force – standing wave

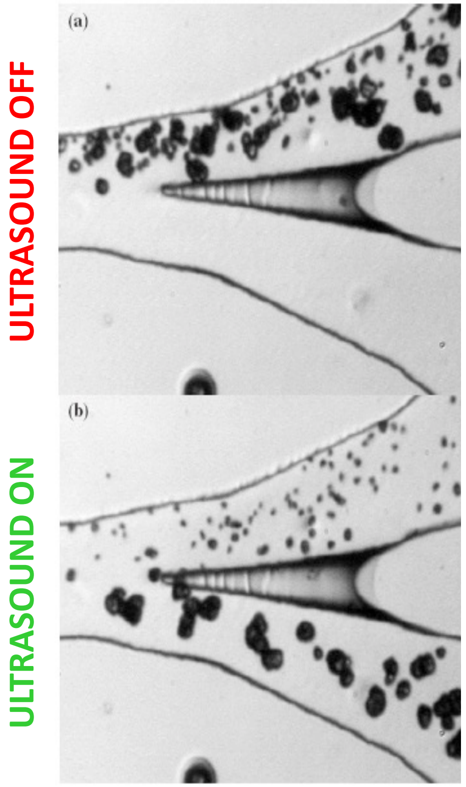
- **Separation of blood cells: standing waves in microfluidic channel**

Why are big particles moved and not small ones?

EXPERIMENTAL SETUP

E = 0.1J/m^3

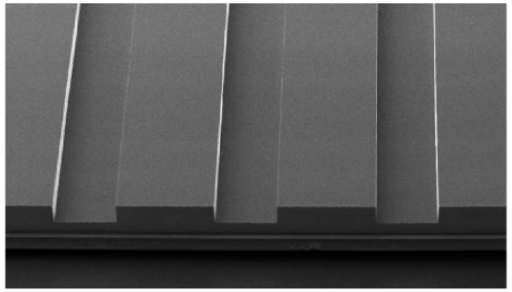




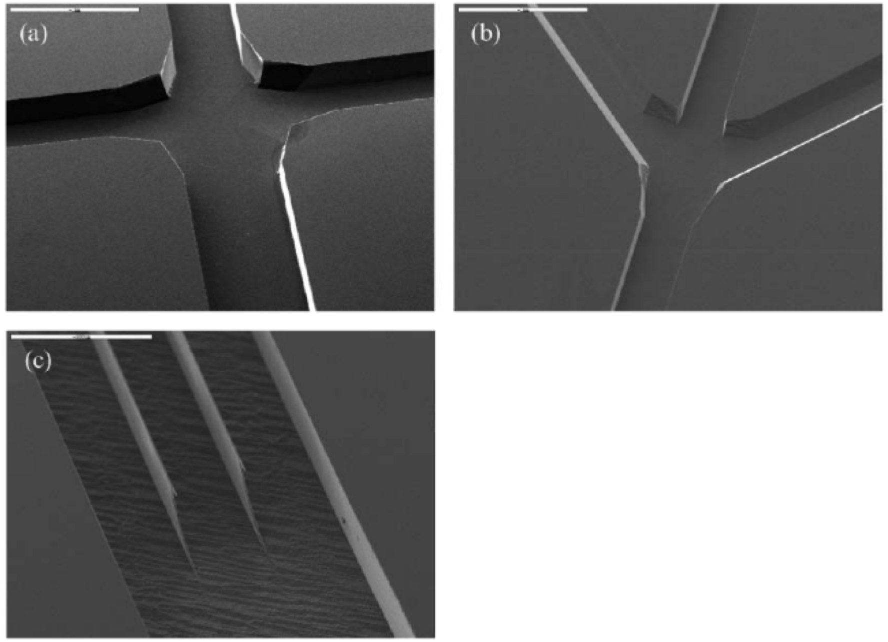
Kapishnikov *et al. J. Stat. Mech.* (2006)
doi:10.1088/1742-5468/2006/01/P01012

Cell separation with ultrasound

Single channel in silicon wafer

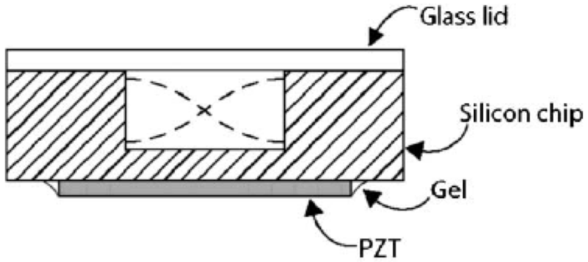


Complex channels in silicon wafer



[Laurell et al 2006: http://pubs.rsc.org/en/content/articlepdf/2007/cs/b601326k](http://pubs.rsc.org/en/content/articlepdf/2007/cs/b601326k)

750 um wide channel



Cell separation principle

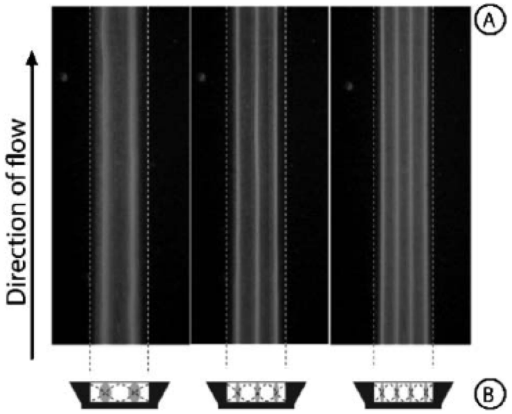
Fat

Red blood cells

Fat

Separation in single channel

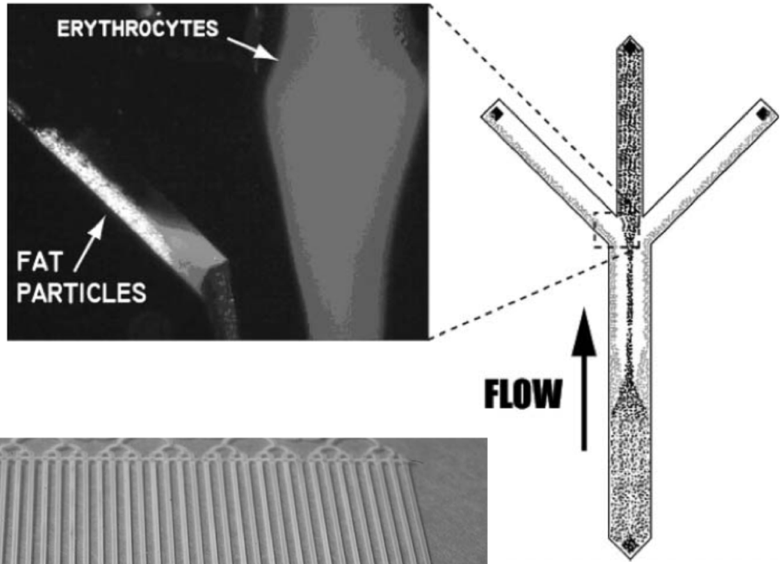
Separation at different harmonics



~2 MHz ~3 MHz ~4 MHz

Cell separation with ultrasound

Cell separation in action



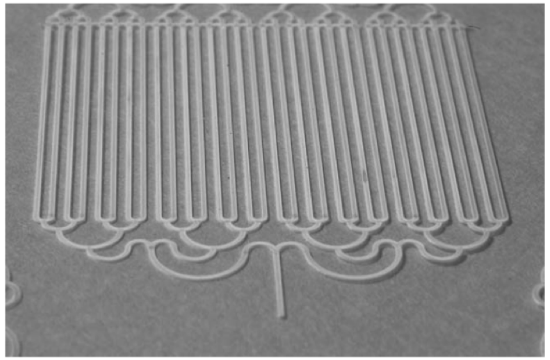


Fig. 20 2^5 bifurcation channel tree holding 32 parallel ~400 µm channels realised by micromilling in a polycarbonate sheet. It is possible to realize separation channels in polymers but due to acoustic losses in the bulk material this is less preferential.

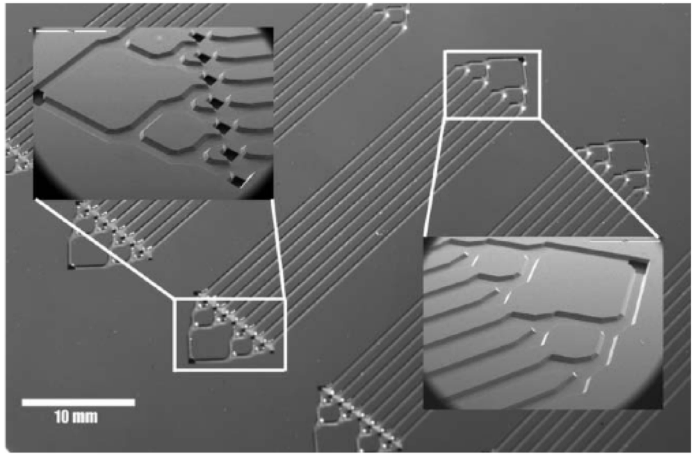


Fig. 21 Picture of eight channel separation structures with scanning electron micrographs showing details of the bifurcation channel outlets (left) and inlet (right). The row of black diamond-shaped structures are the waste outlets. These are connected to a common waste outlet on the back side of the chip. The single outlet at the far left is the enrichment outlet.

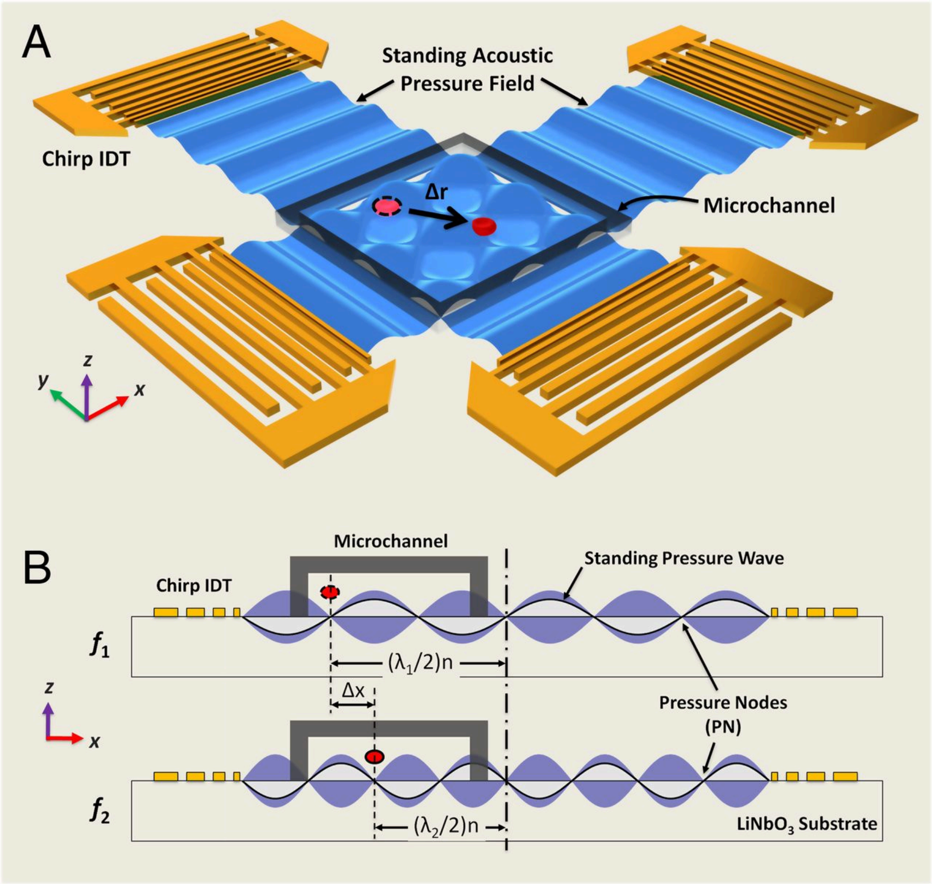
Bifurcation enables:

- More efficient particle separation
- Higher concentration of the end product
- Less contaminants in the end product

Laurell et al 2006: http://pubs.rsc.org/en/content/articlepdf/2007/cs/b601326k

Radiation force
(standing SAWs)

Surface acoustic wave (SAW) tweezers



IDT = interdigital transducers

Movement of an organism using SAW tweezers

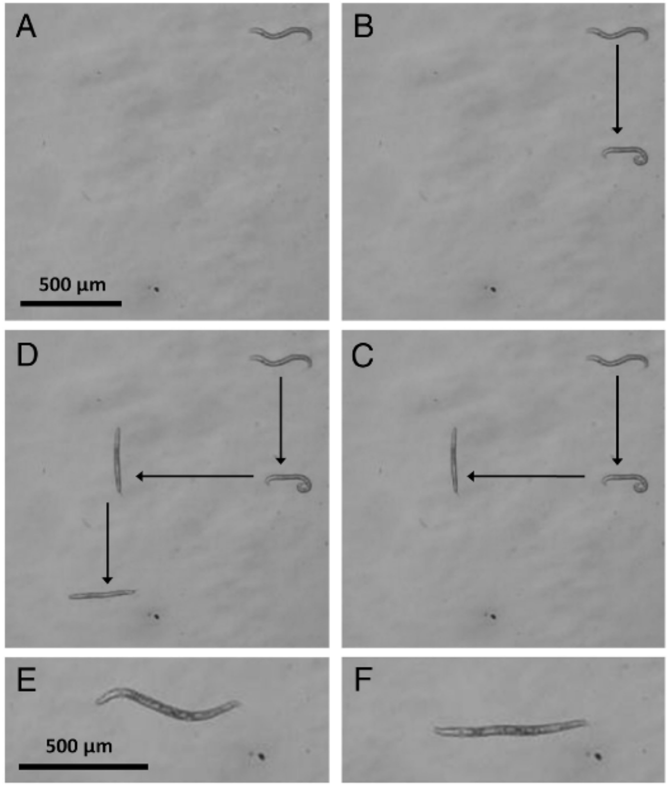


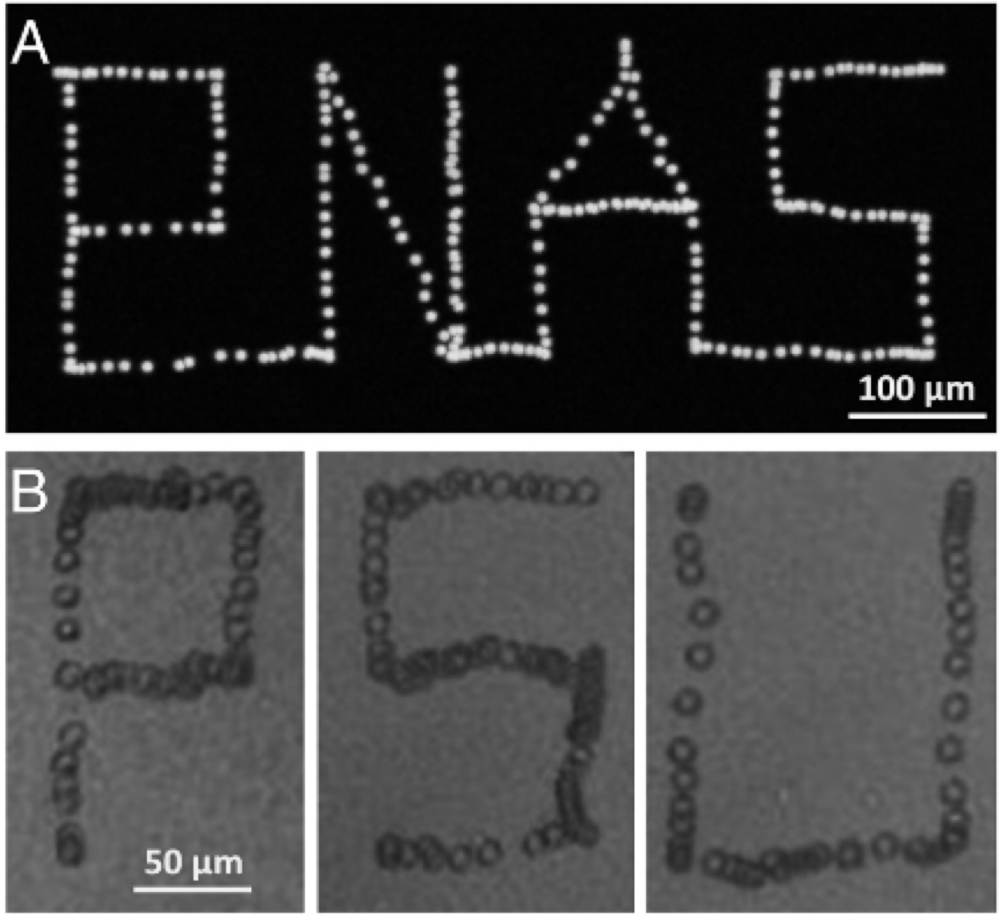
Fig. 5. Single *C. elegans* manipulation. One single *C. elegans* was (*A*) trapped, (*B*) moved in *y* direction, (*C*) moved in *x* direction, and (*D*) moved in *y* direction again and released, with the average velocity of approximately 40 µm/s. An optical image of *C. elegans* (*E*) before and (*F*) after being fully stretched. C. elegans = Caenorhabditis elegans

Ding et al 2012: http://www.pnas.org/content/109/28/11105.full.pdf+html

Track generated by surface acoustic wave tweezers

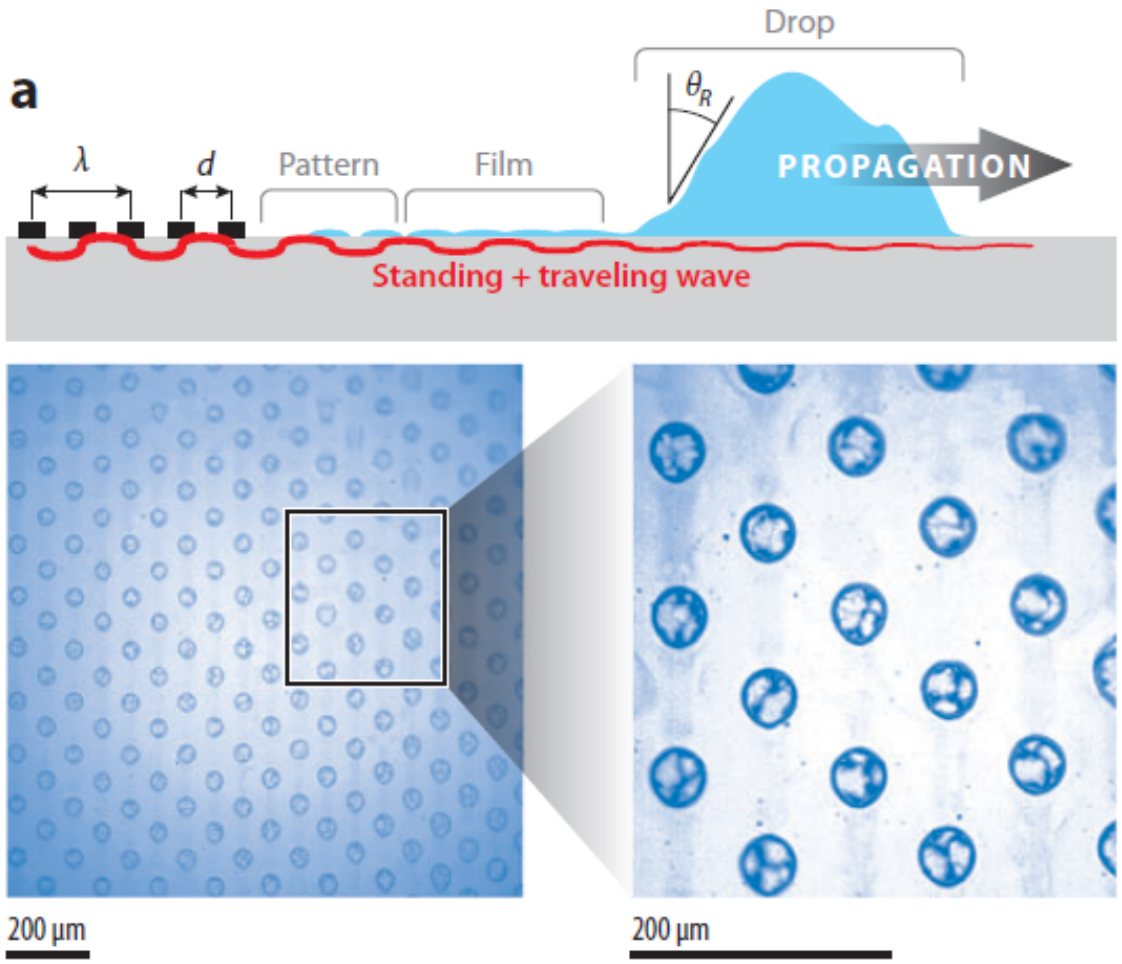
Path drawn by

A. Polystyrene spheres
B. Bovine red blood cells



Ding et al 2012: http://www.pnas.org/content/109/28/11105.full.pdf+html

Droplet matrix generation



Yeo et al 2012: http://www.annualreviews.org/doi/pdf/10.1146/annurev-fluid-010313-141418

Biological responses to radiation force

Table 3.3. *Summary of pulsing regimes required to generate acoustic bio-responses apparently caused by radiation pressure.*

Effect	Pulse length	Number of pulses
Choroid blanching (Lizzi)	100 μs	1
Tactile sensation (Daleki)	1 ms	repetitive
Cardiac response in frog (Daleki)	5 ms	1
Fluid movement (Starritt)	0.5 μs	1

Drug delivery & standing waves

- How would you apply standing wave radiation force for drug delivery?
  - IOP?
  - Melanoma?
  - Meniscus tear?
  - Other ideas?

Summary: Radiation force

- Radiation force (travelling wave):
  - Can move tissue and tissue interfaces
    - Secondary streaming near a moving interface?
  - Can translate particles (and gas voids)
    - Translation of drug or drug vehicle
    - Contribution to drug localization/deposition/release
  - Depends on material properties:
    - Absorption
    - Reflection
    - Scattering
    - Speed of sound