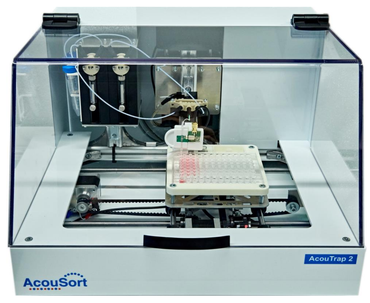
Moving Cells with Sound

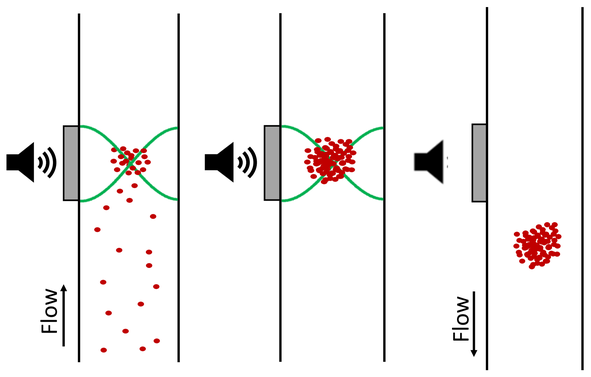
Jay Mallinson, Oskar Linander, Jessica Congiu, Mikael Evander, Lars Løjkner; AcouSort AB

Particle Trapping

In the AcouTrap platform it is possible to capture, enrich and stain

- Micro-vesicles and exosomes
  - (directly from plasma)
- Cells
- Bacteria



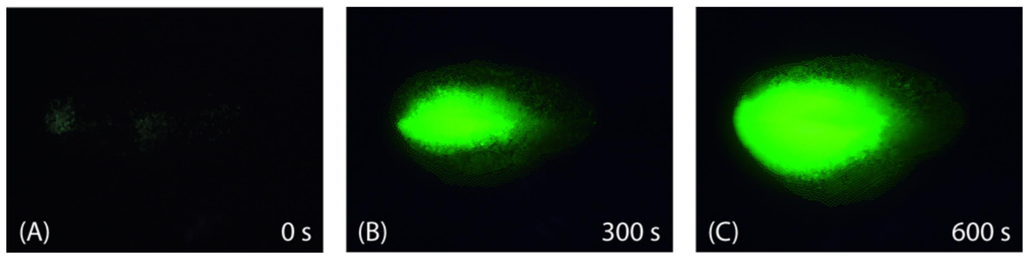


left: Trapping of particles from a sample
Center: As more particles are trapped, a very concentrated sample is obtained.
Right: The ultrasonic field is turned off and sample is released

Sample is aspirated in a capillary and an ultrasonic standing resonance wave is applied and automatically tuned for the optimal frequency.
Large particles can be directly captured in the trap, whereas for smaller particles like micro-vesicles or exosomes, it is required to use seed particles.

Once the particles are trapped they can be concentrated, washed and stained directly in the trap.

Bacteria trapping



GFP-producing *Escherichia coli* are captured in a seed particle cluster (1)

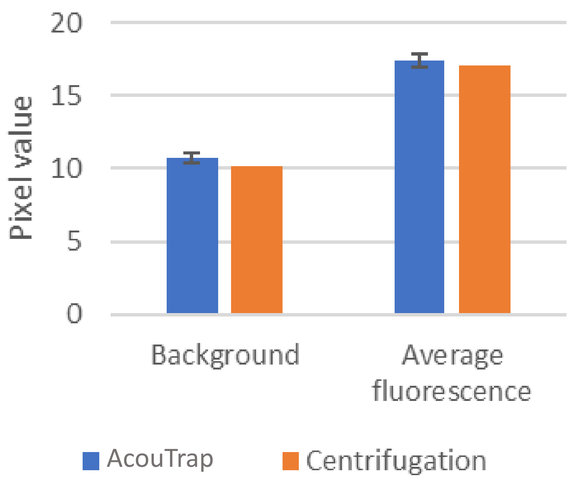
To capture bacteria and particles smaller than 2 µm, a seed cluster is required. In seed trapping, large polystyrene particles are first captured and the bacteria sample is then infused into the trapping unit. The bacteria will be captured in the spaces between the seed particles by secondary acoustic forces. Once the ultrasound is turned off, the seed particles and bacteria will disperse from each other and can be released for further analysis.

Staining of platelet derived microparticles

Platelet derived micro particles are often obtained via ultra-centrifugation protocols, followed by staining and then ultra-centrifugation.

All of this can be directly done in the AcouTrap, starting from plasma and ending with a stained, concentrated sample of plasma micro particles ready for analysis, with less time, less manual handling and less antibodies used.

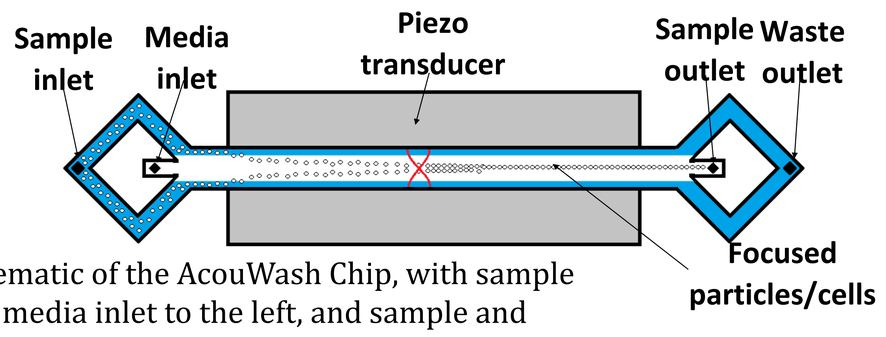
The stained micro particles are compared in an Amnis ImageStream.



ImageStream particle intensity of stained micro particles. AcouTrap incubation time is 1 minut.

Acoustic Washing

In acoustic washing and separation, the force applied upon the particles is used to move them from one laminar flow stream to another, with low carry-over of the initial solvent, being very gentle and with a very high recovery.



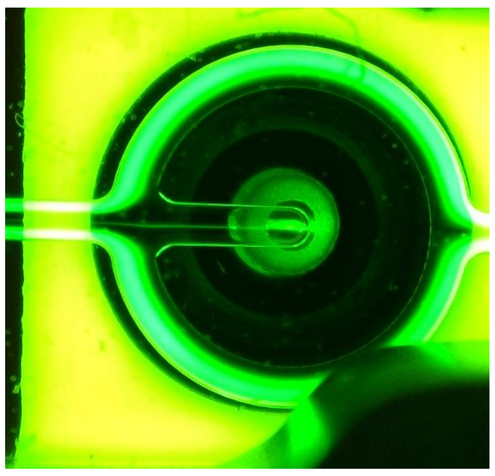
Schematic of the AcouWash Chip, with sample and media inlet to the left, and sample and waste outlet to the right.

Since particles have various acoustic properties (density, compressibility, size), some particles will move towards the edge of the capillary while other will migrate towards the centre.

The technique allows for:

- Cell wash and concentration
- Blood/plasma separation
- Separation of cell types.

Acoustic Washing



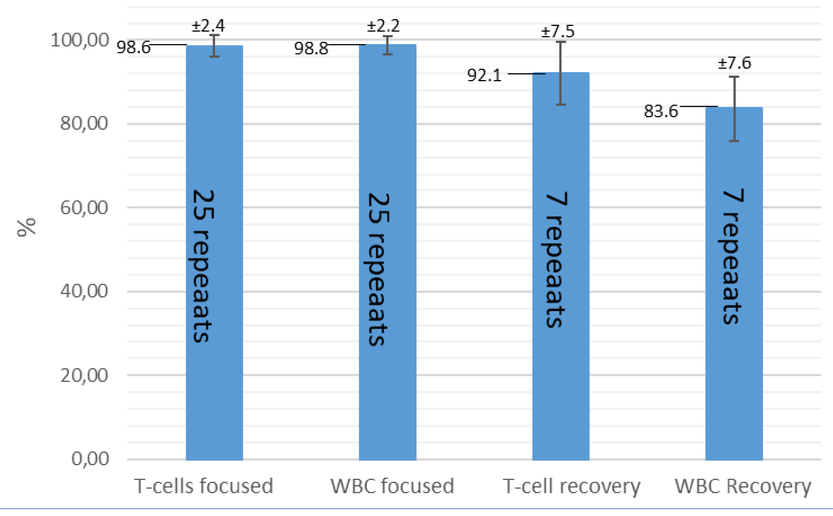
Picture of the 3 um beads being separated from fluorescein

3 µm beads in fluorescein solution are moved by the acoustic forces from the outer flow-stream into the centre flow stream at high recovery, while the fluorescein is not affected.

The input and output samples are measured in a plate-reader,
and after just one wash, the bead recovery is > 99,9% and the fluorescein concentration in the output sample is reduced >5.000 times.

Lymphocyte wash

Human blood samples were depleted of red blood cells and stained(A-HUMAN CD45 APC and CD3 PE(SK7) CE 100T) for differentiating T-cells and white blood cells during cell counting. The marked cells were washed from a protein rich media into PBS using the AcouWash system. It was possible to focus ~99% of the cells, and recover 92% of the T-cells and 84% of the WBCs overall as the system was tuned for the T-Cells.



AcouSort

(1) Integrated acoustic separation, enrichment and microchip PCR of bacteria from blood for rapid sepsis diagnostics
Ohlsson, P.*,Evander, M.*, Petersson, K.*, Mellhammar, L., Lehmusvuori, A., Karhunen, U., Soikkeli, M., Seppä, T., Tuunainen, E., Spangar, A., von Lode, P., Rantakokko-Jalava , K., Otto, G., Scheding, S., Soukka, T., Wittfooth, S., and Laurell, T.
Analytical Chemistry, 2016, 88 (19), pp 9403–9411, DOI: 10.1021/acs.analchem.6b00323