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Acoustic reconcentration or separation of cells

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By using an acoustic field in a cavity, we create a standing wave composed of one pressure node. A pressure gradient is created in the cavity, which allows us to manipulate micron-size objects like particles or living cells. Thanks to a force called the Acoustic Radiation Force (ARF) [1], these objects will move toward the nodal plane at mid-height of the cavity where they will be trapped in acoustic levitation. Each type of cells has mechanic properties (size, density, compressibility), which define their reaction to the acoustic force. Larger, denser, stiffer cells will undergo larger ARF. It is then possible to separate two types of cells in a micro-channel using their relative response to the ARF. This non-intrusive method (no contact, no marker) has a lot of potential and can become a useful alternative to classic separation methods like centrifugation or immuno-magnetism.

In this study, we firstly characterize our micro-channel to know the position of the nodal plane depending on the frequency [2]. We show that a small shift of the frequency can change the position of aggregation of cells from the bottom to the top of the channel. We also observed that the medium (plasma or cell culture medium) could react to the acoustic force. A shift in frequency is measured depending on the medium used for cells culture.

The first and easiest application is to increase the concentration of a cell suspension. In this case, we force the cells to reach the nodal plane to be collected in the central outlet.

The second, more challenging application is separation. First, we measure the focalisation velocity toward the nodal plane of cells we want to separate. If two types of cells are mixed, each type will have a focalisation velocity different from the other. Like the position of the nodal plane, this velocity will vary depending the frequency. Knowing these two parameters, we apply the adequate flow rate and acoustic parameters to separate the two populations. Cells with higher acoustic contrast factor reach the nodal plane faster and can be collected in the central outlet while cells with a lower acoustic contrast factor stay on the borders of the channel and be can collected in the lateral outlets. For example, if we use, total blood, Red Blood Cells (RBC) will focus to the central outlet and be separated from platelets which will be collected in the lateral ones.

Different set-ups, using different combinations of transducers, with or without gravity, have been tested. We already achieved reconcentration of HepaRG cells where we increased significantly the concentration rate. We also showed that we can choose in which outlet we want to collect the cells just by moving the nodal plane with the frequency. We also achieved first separation experiments between red blood cells (RBC) and platelets in plasma. We succeeded to double the initial concentration of RBC in one outlet.

References

- [1] K Yosioka and Y Kawasima. Acoustic radiation pressure on a compressible sphere. *Acta Acustica united with Acustica*, 5(3) :167-173 (1955)
- [2] O. Dron and J.-L. Aider. Varying the agglomeration position of particles in a micro-channel using Acoustic Radiation Force beyond the resonance condition *Ultrasonics* 12, 4617-4627 (2013).

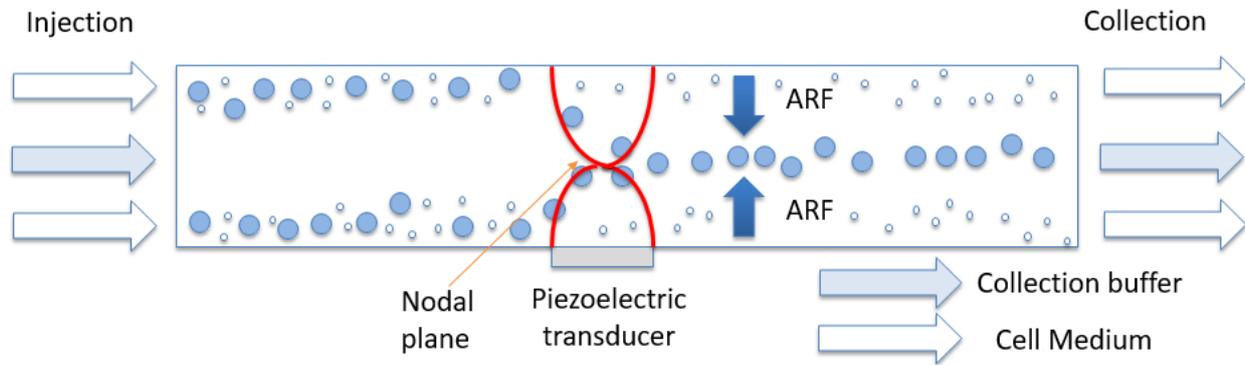


Figure 1. Micro-channel view from the side. Cells to separate are injected from the lateral inlets. A piezoelectric transducer creates a stationary wave in the channel inducing a nodal plane at mid-height. Thanks to the ARF, cells will move to the nodal plane. Big cells will move faster than small cells authorizing a separation. Small cells are collected in the lateral outlets while big cells are collected in the central outlet with a buffer for collection.

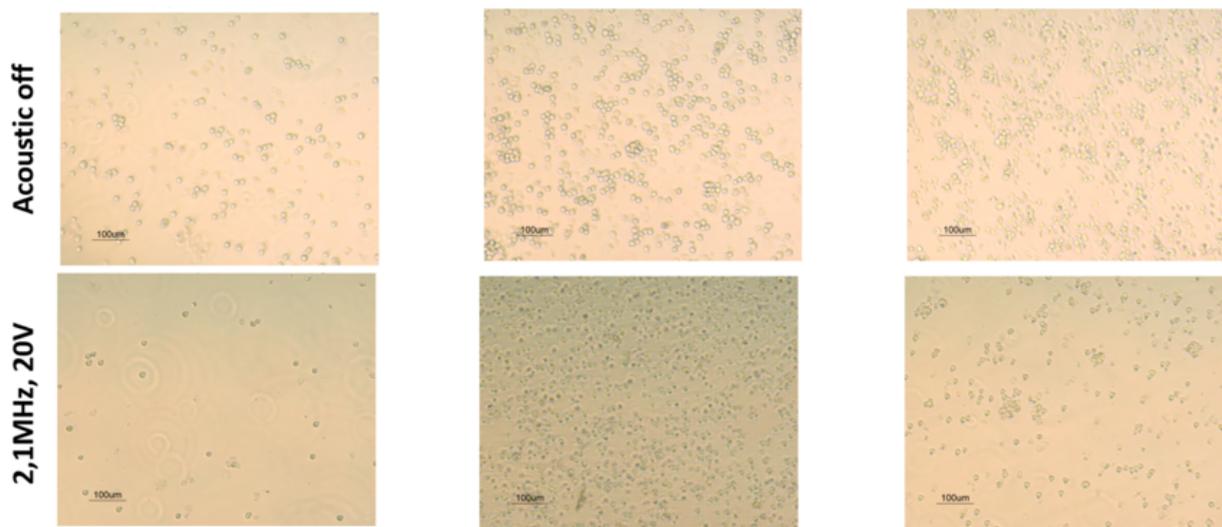


Figure 2. Concentration of HepaRG cells in the outlet opposed to the transducer, central outlet and the outlet adjacent to the transducer (from left to right). The three top images are observation without acoustic field while the three bottom images are observation after passed the channel under acoustic. Frequency: 2.1MHz, Voltage: 20V, Flow rate: 1.5 mL/min
A major part of cells have been collected in the central outlet.