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Ultrasonic standing wave manipulation of cells in microfluidic systems

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Recent developments of microchip integrated manipulation and separation of cells using ultrasonic standing wave forces in lab-on-a-chip devices will be overviewed. Acoustic standing wave technology offers a label free and non-contact mode of cell manipulation in microfluidic systems[1]. The most common mode of acoustic standing wave operation in microfluidic channels is at the λ/2 resonance[2]. In this case the excitation frequency is matched to the channel width to support a half wave length resonance. Under these conditions particles in aqueous media with higher density than water will experience an acoustic force, eq 1, that drives them to an equilibrium position in the centre of the channel, Fig1.

$$F_{Ax} = -\left(\frac{\pi P^2 V_c \beta_w}{2\lambda}\right) \cdot \phi(\beta,\rho) \cdot \sin(2kx) \qquad (1)$$

$$\phi(\beta,\rho) = \frac{5\rho_p - 2\rho_f}{2\rho_p + \rho_f} - \frac{\beta_p}{\beta_f} \qquad (2)$$

Where V_c is the volume of the particle, P is the acoustic pressure amplitude and ϕ is defined by eqn. (2). The density of the medium and particles are denoted ρ_f and ρ_p respectively and the corresponding compressibilities β_f and β_p.

The low mechanical strain that is imposed on the cells in this process thus opens the route to a wide range of clinical applications. Recent developments describe whole blood plasmapheresis based on acoustophoresis, which subsequently has been coupled to protein micro arrays for PSA (prostate specific antigen) analysis in undiluted plasma[3]. Further more, two modalities of microchip acoustophoresis will be outlined – free flow acoustophoresis and affinity acoustophoresis.

Since the acoustic primary radiation force is dependent of the particle size this opens the possibility to design systems that enables separation of different particles sizes from a complex mixture. This separation modality is called free flow acoustophoresis (FFA) and relies on the different velocities that particles of different size traverse the flow channel on their way towards the pressure node. By providing the FFA separation channel with multiple outlet channels, defined particle sizes can be collected at each outlet.

Continuous flow fractionation of mixed particles suspensions or multiplex cellular speciation has been obtained utilizing FFA (free flow acoustophoresis) where a key target was blood component fractionation[4]. Separation of mixed particle suspensions and erythrocytes, leukocytes and platelets in a buffy-coat will be demonstrated. An optional modality is to perform FFA in a binary mode of operation where cells are separated based on their acoustic contrast factor and where the composition of the carrier buffer media is tuned such that two normally non-separable species can be separated[4]. The density media is selected such that particle type A displays a positive contrast factor and the particle type B a negative contrast factor. Thereby the two particle types will migrate to the pressure node (in the centre) and the pressure antinode (along the side walls) and can thus be colleted from different outlets of the chip. This

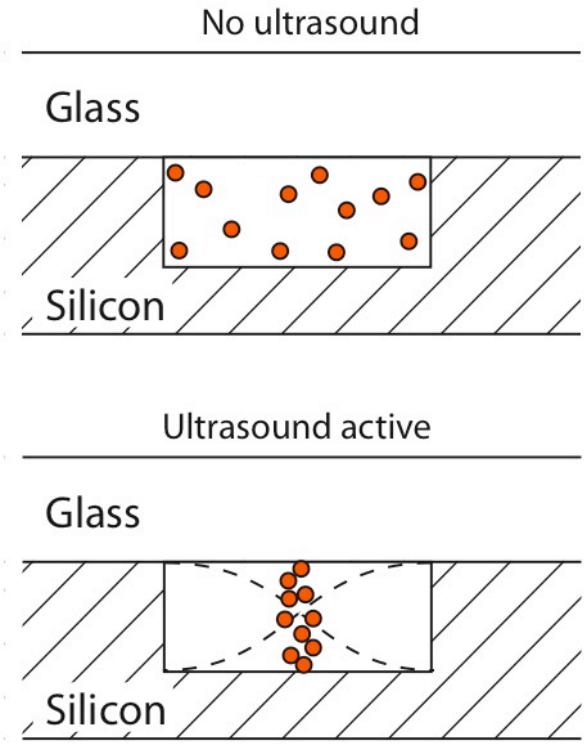

Fig. 1. Schematic cross-section of acoustic particle focusing in a λ/2 standing wave generated in a silicon microfabricated microchannel

mode of operation can be regarded as an analogue to conventional density media centrifugation. This principle opens up for the development of a wide variety of protocols for very specific on-chip cell separations, yet to be explored.

As a further extension of FFA, an acoustophoretically driven buffer exchange modality has been developed, utilizing affinity specific microbeads (affinity acoustophoresis). The ability to extract targeted species from complex mixtures using affinity acoustophoresis will be demonstrated, where affinity acoustophoresis has been used in decomplexing proteomic samples, prior to mass spectrometry readout[5]. This mode of operation will also be demonstrated in its ability to extract viral particles from complex solutions, where an example given is the extraction of specific bacteriophages from a phage library[6], demonstrating an optional and improved modality as compared to magnetic bead based phage display selection.

By operating the microchannel at higher harmonics improved conditions for on-line sample preparation has recently also been demonstrated. Examples of raw milk separation for direct quality analysis regarding protein and lactate content as well as lipid content will be presented[7].

References

[1] T. Laurell, F. Petersson, and Nilsson A., *Chip integrated strategies for acoustic separation and manipulation of cells and particles*, Chemical Society Reviews, 2007, 36, 3, 492 – 506

[2] Nilsson A., Petersson F., Jönsson H. and Laurell T., *Acoustic Control Of Suspended Particles In Micro Fluidic Chips*, Lab On A Chip, 2004, 4, 131 – 135

[3] Lenshof, A. Ahmad-Tajudin, K. Järås, A.-M. Swärd-Nilsson, L. Åberg, J. Malm, H. Lilja and T. Laurell, *Acoustophoresis based extraction of plasma from whole blood for micro chip PSA-analysis*, Analytical Chemistry, in press.

[4] Petersson F. T., Åberg L. B., Swärd-Nilsson A.-M. S. and Laurell T., *Free flow acoustophoresis (FFA) – A new microfluidic based mode of particle and cell separation*, Analytical Chemistry, *Accelerated article*, 2007, 79, 14, 5117-5123.

[5] P. Augustsson, J. Persson, S. Ekström, M. Ohlin and T. Laurell; *Decomplexing biofluids using microchip based acoustophoresis*; Lab-On-A-Chip, 2009, 9, 810–818

[6] Persson J., Augustsson P., Laurell T. and Ohlin M., *Acoustic microfluidic chip technology to facilitate automation of phage display selection of specific binders from protein libraries*, FEBS J, 2008, 275, 5657-5666

[7] Carl Grenvall, Per Augustsson, Jacob Riis Folkenberg and Thomas Laurell, *Harmonic microchip acoustophoresis – A route to on line raw milk sample precondition in protein and lipid content quality control*, Analytical Chemistry, 2009, DOI 10.1021/ac900723q

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