



CrossMark
click for updates

Cite this: *Lab Chip*, 2015, 15, 1000

Spatial tuning of acoustofluidic pressure nodes by altering net sonic velocity enables high-throughput, efficient cell sorting

Seung-Yong Jung,^{ab} Timothy Notton,^{ac} Erika Fong,^{de} Maxim Shusteff^{*d} and Leor S. Weinberger^{*abcf}

Received 11th November 2014,
Accepted 23rd December 2014

DOI: 10.1039/c4lc01342e

www.rsc.org/loc

Particle sorting using acoustofluidics has enormous potential but widespread adoption has been limited by complex device designs and low throughput. Here, we report high-throughput separation of particles and T lymphocytes (600 $\mu\text{L min}^{-1}$) by altering the net sonic velocity to reposition acoustic pressure nodes in a simple two-channel device. The approach is generalizable to other microfluidic platforms for rapid, high-throughput analysis.

Biological fluids, particularly clinical samples, are complex, inherently heterogeneous mixtures that contain particles with highly variant shapes and sizes. Precise analysis of the constituent particles from these fluids often requires separation and enrichment of the specific target particles from this complex mixture. When these targets exist at low concentrations, such as in the early stages of disease, high-throughput approaches (that are biocompatible) are necessary. One attractive approach is acoustophoresis—manipulating suspended analyte particles with ultrasonic standing waves. This gentle (*i.e.* contactless) and label-free approach sorts particles based on their physical properties, such as size, density, and compressibility.^{1,2} Acoustophoresis has been adapted for a wide range of applications that require well-controlled conditions provided by laminar flow, such as sorting or synchronizing cells,³ manipulating single cells,⁴ enriching circulating tumor cells,⁵ and separating cells from virus.⁶

In acoustophoresis, particle separation occurs due to acoustic radiation forces that arise from an acoustic sound-pressure field acting upon particles suspended in fluid.⁷ These forces are proportional to particle volume, making particle size the most accessible separation parameter. When the

acoustic contrast factor, a number depending on a particle's density and compressibility in relation to the suspending fluid, is positive, which is the case in most applications, the forces transport particles toward the pressure minima (nodes) of the standing wave, with larger particles moving rapidly, while smaller particles or dissolved species remain on their original laminar streamlines.

In microfluidic separation applications, an ultrasonic standing wave can be generated by attaching a piezoelectric actuator to the back of a silicon etched channel structure. The piezo driving frequency can then be tuned to match the width or height of the microfluidic channel. These dimensions set the harmonic resonance modes in the fluid, which predict the number and positions of nodal planes. The most common mode is the half-wave resonance, with the nodal plane at the center of the channel. However, these predetermined and symmetric nodal positions are not easily adjustable, which limits the flexibility of the device. For example, modulating only the axial distance from the input streamline to the focal position could be insufficient to achieve the required throughput for samples where volumes of several milliliters must be rapidly processed. Other studies examined acoustophoretic devices with asymmetric or adjustable locations for nodal planes,^{8–12} and while these devices are exceptionally elegant and exhibit impressive separation efficiency, unfortunately, they are limited by low sample throughput, with separation channel flow rates limited to $\leq 10 \mu\text{L min}^{-1}$.

Here, we present an approach to maintain total flow rates of over $200 \mu\text{L min}^{-1}$ while allowing adjustable node positioning. We utilize our previously reported device,⁶ with a two-channel geometry comprising a main sample separation channel and a secondary “bypass” (or “echo”) channel separated from the main channel by a thin silicon wall. These

^a Department of Biochemistry and Biophysics, University of California, San Francisco, CA 94143, USA. E-mail: leor.weinberger@gladstone.ucsf.edu; Fax: +415 355 0855; Tel: +415 734 4857

^b Gladstone Institutes (Virology and Immunology), 1650 Owens Street, San Francisco, CA 94158, USA

^c Joint Graduate Group in Bioengineering, University of California, Berkeley and University of California, San Francisco, CA 94158, USA

^d Lawrence Livermore National Laboratory, Livermore, CA 94550, USA. E-mail: shusteff1@llnl.gov

^e Department of Biomedical Engineering, Boston University, Boston, MA 02215, USA

^f QB3: California Institute for Quantitative Biosciences, University of California, San Francisco, CA 94158, USA