

**MICROFLUIDIC ULTRASONIC PARTICLE
SEPARATORS WITH ENGINEERED NODE
LOCATIONS AND GEOMETRIES**

CROSS-REFERENCE TO RELATED
APPLICATIONS

The present application is a Divisional of pending U.S. application Ser. No. 14/246,981 filed Apr. 7, 2014, which is a Divisional of U.S. application Ser. No. 13/571,640 filed Aug. 10, 2012, now issued as U.S. Pat. No. 8,727,129 on May 20, 2014, which is a non-provisional application of U.S. Provisional Patent Application No. 61/524,020 filed Aug. 16, 2011, now expired, the entire contents and disclosures of which are specifically incorporated by reference herein.

STATEMENT AS TO RIGHTS TO INVENTIONS
MADE UNDER FEDERALLY SPONSORED
RESEARCH AND DEVELOPMENT

The United States Government has rights in this invention pursuant to Contract No. DE-AC52-07NA27344 between the United States Department of Energy and Lawrence Livermore National Security, LLC for the operation of Lawrence Livermore National Laboratory.

BACKGROUND

1. Field of Endeavor

The present invention relates to microfluidic particle separators and more particularly to microfluidic ultrasonic particle separators with engineered node locations and geometries.

2. State of Technology

The article, "Chip integrated strategies for acoustic separation and manipulation of cells and particles," by Thomas Laurell, Filip Petersson, and Andreas Nilsson in *Chem. Soc. Rev.*, 2007, 36, 492-506, states: "Chip integrated strategies for acoustic separation and manipulation of cells and particles," by Thomas Laurell." The article includes the state of technology information quoted below and drawing FIGS. 1A, 1B, and 1C are copies of Fig. 5, 6 and 7 from the article. The article, "Chip integrated strategies for acoustic separation and manipulation of cells and particles," by Thomas Laurell, Filip Petersson and Andreas Nilsson in *Chem. Soc. Rev.*, 2007, 36, 492-506, is incorporated herein in its entirety for all purposes.

"Fig. 5 Schematic cross-section of separation chip utilizing the Lund method. The silicon separation channel is sealed by a boron silica glass lid and is actuated from below using a piezoelectric ceramic." [FIG. 1A]

"Fig. 6 Illustrated cross-section (along the dashed line in Fig. 7) of a separation channel showing negative w-factor particles (e.g. lipid particles) collected in the pressure antinodes by the side walls and positive w-factor particles (i.e. red blood cells) in the pressure node." [FIG. 1B]

"Fig. 7 Illustration of separation of negative w-factor particles (black—centre outlet) and positive w-factor particles (grey—side outlets) in 45u design chip." [FIG. 1C]

"The Lund-method for acoustic separation of suspended particles from their medium is based on a laminar flow micro-channel that is ultrasonically actuated from below, using a piezoelectric ceramic (Fig. 5). The width of the channel is chosen to correspond to half the ultrasonic wavelength, thereby creating a resonator between the side walls of the flow channel in which a standing wave can be formed. The induced standing wave is thus generated orthogonal to the incident ultrasonic wave front. As suspended particles with a positive

w-factor perfuse the channel they are moved, by means of the axial PRF, towards the pressure nodal plane along the channel centre, while those with a negative w-factor are moved towards the anti-nodal planes close to the side walls (Fig. 6)."

"The end of the separation channel is split into three outlet channels, thus allowing the positive w-factor particles to exit through the centre outlet and the negative w-factor particles to exit through the side outlets, provided that all outlet flow rates are alike (Fig. 7). The separation efficiency of positive and negative w-factor particles is defined as the fraction of particles exiting through the centre and side outlets respectively."

SUMMARY

Features and advantages of the present invention will become apparent from the following description. Applicants are providing this description, which includes drawings and examples of specific embodiments, to give a broad representation of the invention. Various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this description and by practice of the invention. The scope of the invention is not intended to be limited to the particular forms disclosed and the invention covers all modifications, equivalents, and alternatives falling within the spirit and scope of the invention as defined by the claims.

The present invention provides high-throughput sample processing of biological material. The system of the present invention separates out cell-sized particles from a background solution containing other biological materials (viruses, proteins, nucleic acids, etc.) in order to allow uncontaminated analysis of either the background sample or the separated cells. The present invention uses the vibrations of a piezoelectric transducer to produce acoustic radiation forces within microfluidic channels. Whereas other investigators have demonstrated technologies that position a single stream of concentrated particles on the center-line of a fluid channel, or multiple streams of particles, such that some of them are off-center, the system of the present invention positions a single stream of concentrated particles off-center in the fluid channel. This is highly advantageous for achieving improved separation between the two sample fractions, and greater purity within each fraction. In one embodiment, the stream of concentrated particles is positioned off-center in the separation channel by means of subdividing the channel with one or more thin acoustically transparent walls. In another embodiment the stream of concentrated particles is positioned off-center in the fluid flow with the aid of a polymer gel structure positioned adjacent to the fluid channel. In these embodiments, or in any other, the pressure field resulting from the acoustic waves can be optimized by driving the piezoelectric transducer at multiple frequencies on a single device. Additionally, in these embodiments, or in any other, the separation channel can be routed in a serpentine fashion to pass multiple times (3, 5, etc.) through the ultrasound region, thereby providing a longer residence time for the sample in the acoustic field, increasing separation efficiency.

The present invention provides an ultrasonic microfluidic system for separating smaller particles from larger particles suspended in a sample fluid. This sample fluid flows down a separation channel, side-by-side with a "recovery buffer," which is typically a fluid into which the larger particles of interest are to be transferred. The two fluid streams are in contact with each other, but mixing is limited only to diffusion due to the low Reynolds number of microfluidic flows. An acoustic transducer in contact with the microfluidic chip produces an ultrasound pressure field throughout these fluids.