SYSTEMS AND METHODS FOR PARTICLE FOCUSING IN MICROCHANNELS

RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Application No. 60/923,609 filed on Apr. 16, 2007 and entitled "Methods and Devices for Separating and Focusing Particles," U.S. Provisional Application No. 60/923,837 filed on Apr. 17, 2007 and entitled "Methods and Devices for Separating and Focusing Particles," and U.S. Provisional Application No. 60/999,131 filed on Oct. 16, 2007 and entitled "Methods and Devices for Separating and Focusing Particles," all three of which are expressly incorporated herein by reference in their entireties.

BACKGROUND OF THE INVENTION

[0002] Particle separation and filtration has been applied for numerous technological solutions in industry, medicine, and research. Industrial applications include chemical process and fermentation filtration, water purification for the microelectronics industry, and wastewater treatment. Biomedical applications focus around counting, sorting and filtering various components of blood and preparing safely sized micro-bubble ultrasound contrast agents. Applications in basic and applied research include concentrating colloid solutions, purifying colloidal reaction products, and purifying and concentrating environmental samples.

[0003] Various macroscale techniques have been developed for particle separation to address these applications. Centrifugation and filter-based techniques are most common in current industrial applications because of the large scale of material that can be processed, but these systems are bulky, expensive, and may contain complex moving components. More recently, techniques based on the concept of field-flow fractionation (FFF) have been developed for a variety of applications. In these techniques, particle separation is due to either varied equilibrium positions within a channel in an applied force field or different transport rates. Various external fields have been implemented including gravitational, electrical, magnetic, and centrifugal, allowing successful separation of blood components, emulsions, and various colloids. A closely related technique, hydrodynamic chromatography, is also widely used in analytical separations and depends on size-dependent variation in the ability of particles to access low-drag regions of the flow. In most cases, the maximum flow through these systems is limited since sufficient time for forces to interact with particles or particles to sample the flow field is required. Flow cytometers are often used in sorting applications and allow sorting based on different parameters than other techniques (e.g., protein content, granularity); however, they have higher complexity than most sorting systems.

[0004] Microscale techniques offer advantages, in that scaling down allows the use of unique hydrodynamic effects and intensifies electromagnetic separation forces. Dielectrophoretic forces have been used to discriminate particles based on size or some dielectric tag. Other techniques for continuous separation rely on the laminar flow profile and different intersected cross sections of the flow for particles of varied sizes aligned at a wall. Further microscale techniques involve precisely designed filters or post arrays that create a bifurcation in particle direction based on size. These techniques can produce very accurate separations based on size or the dielectric properties of particles. For example, for deterministic displacement by asymmetrically aligned obstacles, a resolution of less than 20 nm is reported for particles of ~1 μm in diameter. Additionally, complexity can be low in these systems.

[0005] A disadvantage of current microscale separations is that scaling usually limits the throughput of these techniques. In most cases, particle volume fractions are maintained well below 1%, since particle-particle interactions can drastically affect performance. Additionally, small volumetric flow rates can lead to large average fluid velocities in microchannels leading to insufficient time for separation forces to act on particles. Flow rates usually range from 1 to 50 μL/min for these systems, insufficient for many preparative applications (e.g., concentration of rare cells in large volumes of blood, filtration of ultrasound contrast agents, or preparation of large amounts of colloids/emulsions). In these applications, it would be beneficial to process volumes of 3-20 mL within several minutes. For example, 2-6 mL of micro-bubble contrast agent is often injected for ultrasound imaging.

[0006] Accordingly, there is a need for a continuous particle sorting, separation, enumerating, or separation system that can take advantage of microscale physics but with throughput comparable to macroscale systems.

SUMMARY OF THE INVENTION

[0007] The invention described herein includes a number of systems, devices, apparatus, and methods that result in and use the self-ordering of particles suspended in a fluid traveling through a microfluidic channel. In a first aspect, a system is provided for focusing particles suspended within a moving fluid into one or more localized stream lines. The system includes a substrate and at least one channel provided on the substrate having an inlet and an outlet. The system further includes a fluid moving along the channel in a laminar flow having suspended particles and a pumping element driving the laminar flow of the fluid. The fluid, the channel, and the pumping element are configured to cause inertial forces to act on the particles and to focus the particles into one or more stream lines.

[0008] In another aspect, a method is provided for focusing particles in a moving fluid and includes providing particles suspended in a moving fluid into a channel and flowing the fluid through the channel under conditions such that inertial forces acting on the particles result in the localization of a flux of particles in the channel.

[0009] In a further aspect, an apparatus is provided for focusing particles of a predetermined size suspended within a moving fluid into one or more localized stream lines. The apparatus includes a substrate and at least one channel provided on the substrate having an inlet and an outlet wherein moving a fluid suspension having particles of a predetermined size from the inlet to the outlet in a laminar flow focuses the particles of a predetermined size into one or more localized stream lines.

[0010] In a still further aspect, a system is provided for sorting particles from a group of particles suspended in a fluid and includes a tagging system for tagging particles that are to be selectively sorted from a group of particles. The system further includes a substrate having at least one channel provided on the substrate having an inlet and an outlet. Moving the fluid suspension having particles, at least some of which have been tagged, from the inlet to the outlet in a laminar flow focuses the particles into one or more localized stream lines.