

focusing corresponds to filled squares, focusing to two streams corresponds to open triangles, focusing to a single stream is represented by open circles, and more complex behavior is shown as filled triangles. Data for this graph was collected using various size particles (2-17 μm) as well as 4 different channel geometries.

[0220] The results shown in FIG. 21 apply universally for any diameter ratio and Dean number falling within a specific region independent of the specific geometry. For example a 2 μm particle in a 10 μm channel should focus to the same extent as a 200 nm particle in a 1 μm channel. In addition, the lateral distance traveled in a straight rectangular channel at constant R_c can theoretically be shown to increase with a/D_h cubed, yielding kinetic separations. In particular, FIG. 22 illustrates the dependence of particle focusing on a/D_h . Streak images at the outlet are shown 3 cm downstream of the inlet for a flow at $R_e=100$. The image is shown at the recombination of two branches to illustrate the uniformity of the flow profile from channel to channel. Focusing becomes more diffuse as a/D_h decreases indicating a shallower potential well at the face in the y direction. This follows from the limiting case of an infinitely wide channel where no y force is present and focusing occurs only at the channel bottom and top. In fact, as the diameter ratio for particles in a square channel decreases, the channel starts to show characteristics of a circular channel with focusing in a modified annulus (note the high intensity at the edges for $a/D_h=0.04$). At a given distance focusing becomes more defined as R_p increases following the dependence of F_z on R_p^2 .

[0221] For an asymmetric system, the additional effects due to Dean flow act along with inertial lift to shape the allowable range of particles and channel dimensions for successful focusing of particles into single streams. From the experimental data and theoretical calculations a large region for successful particle focusing can be defined where $a/D_h > 0.07$. Below this value two effects scaling with a/D_h may result in a loss of focusing: (i) inertial migration (scaling with $(a/D_h)^3$ is slower than what is required for complete focusing in the given length of the channel); or (ii) Dean drag becomes much larger than inertial lift for all values of R_c as a/D_h becomes small. Another limit is seen for $D_e > 20$; above this level, drag from Dean vortices is larger than the inertial lift forces for most particle sizes and leads to particle mixing. Still, sufficient Dean flow is necessary to bias particular equilibrium points (a line of constant average Dean drag is drawn with the value $F_D=0.5$ nN). Last, a practical limit is seen for $a/D_h=0.5$, where particle obstruction of the channels may occur.

[0222] The data plotted in FIG. 21 appear similar to a phase diagram and are critical for determining the correct design conditions. In particular, a vertical movement on the diagram corresponds to changing particle size if channel geometries are held constant. To effect a separation, one must choose a region in the phase diagram (i.e., a specific geometry) where a small change in particle size leads to a change from a focused to an unfocused stream. Thus, one particle size is focused to a particular streamline and can be collected as an enriched fraction, whereas the other, smaller, particles are unfocused.

Example 6

[0223] In other embodiments, high-throughput separations are possible with these systems because of the high R_c at which they operate, an example of which is shown in FIGS.

23A-23C. For a flow rate of $1.5 \text{ ml}\cdot\text{min}^{-1}$ of 1% particle solution a mass sorting rate of $\sim 1 \text{ g}\cdot\text{hr}^{-1}$ can be achieved for an unoptimized device that covers an area of 1.6 cm^2 . Particles close in size (4 and 7 μm) can also be separated by tuning the asymmetric channel geometry, as shown in FIG. 23A, although with slightly less throughput. In these systems there are no externally applied forces other than the pressure to drive the flow, and therefore it is straightforward to cascade and parallelize these design elements, as shown in FIG. 23C, to enhance enrichment and throughputs to very high levels, or combine elements with different hydraulic diameters to separate across more than one size threshold. Ideally pure fractions can be collected through the use of multiple outlets as shown in FIG. 23A in which streak images show at the left, focusing is shown in the middle frame, and four collection channels are shown at the outlet demonstrating the feasibility of the separation in a channel 1 and 3. FIG. 23B further illustrates such a separation. The inlet is shown having a random distribution of particles therein. One type of particle can be focused and separated out from the rest of the sample and three different outlets 1, 2, and 3 can be provided as shown. The focused particles can be directed into outlet 1 and collected in a reservoir as shown, while the rest of the sample is collected in outlets 2 and 3. Typical of most microfluidic systems, a throughput of $30 \text{ mg}\cdot\text{hr}^{-1}$ was described for deterministic displacement with a device area of 15 cm^2 . In applications dealing with rare cell cytometry and purification or industrial filtration, however, increased throughput is essential.

Example 7

[0224] Referring to FIG. 24, rapid (1 mL/min) separation and filtration of rigid particles, emulsions, and blood components is also provided. In one embodiment, flow conditions in the system were tuned to achieve the best particle focusing with the highest possible flow rates. Streak images of 10 μm fluorescent beads are shown at various controlled flow rates in the system described herein. As shown in FIG. 24, for low channel Reynold's numbers, particles are seen to be distributed randomly throughout the channel width. As R_p increases, there is a gradual change to one focused streakline near the outer edge of the larger width channel. For R_p larger than ~ 2 , the particle stream again becomes more diffuse. It is also observed that the position of the focused streakline moves out from the wall of the larger turn increasing particle Reynold's number. Using this data, an optimal flow rate of, for example, 0.9 mL/min ($R_p=1.53$) can be used to operate the systems described herein for exemplary separation applications.

Example 8

[0225] Referring now to FIGS. 25-27, a flow rate of 0.9 mL/min, 20 mL of a mixture of 9.0- and 3.1- μm diameter polystyrene beads can be introduced into the system. As shown in FIG. 25, fluorescent streak images reveal essentially uniformly distributed particle positions at the input for both particle sizes. At the outlet of the device, 9.0- μm -diameter particles can be observed in a focused streakline, while 3.1 μm particles remained unfocused. In one embodiment, five fractions were collected from the system and were labeled according to the scheme in FIG. 25. Particle diameter distributions were obtained by Coulter Counter for the input solution and various outlet fractions, a distribution of which is shown in FIG. 26A. The size distribution for 3.1 μm particles