

moderate  $D_e < 75$  observed in the microfluidic systems described herein, the secondary rotational flow, or Dean flow, consists of only two vortices. The velocity magnitude of the Dean flow scales as  $U_D \sim \rho D_e^2 / (\mu D_h)$  and therefore, Stokes drag on suspended particles due to this secondary flow becomes significant for large  $D_e$ . In particular, the Dean flow velocity dependence on Dean number can be seen in FIG. 6B. FIG. 6B illustrates a simulation of Dean flow at an average streamwise velocity of 1 m/s, corresponding to a Dean number of  $\sim 10$ . The geometry in FIG. 6B is 50- $\mu\text{m}$  in width at the smaller turn and 80- $\mu\text{m}$  at the larger turn. The main flow is coming out of the page. FIG. 6C is a graph further illustrating average secondary flow (vortex) velocity magnitude as a function of changing Dean number for a single geometry. A quadratic relationship between  $D_e$  and average vortex velocity is observed for a constant geometry and agrees with theory.

[0157] In general, the drag due to Dean flow, or Dean drag ( $F_D$ ) scales as

$$F_D \sim \frac{\rho U_m^2 a D_h^2}{r}$$

[0158] Equilibrium separations can be conducted considering the balance of these two forces, Dean drag 64 and inertial lift 66, as shown in FIG. 7. In particular, FIG. 7 illustrates the cross-section of any asymmetric curved channel depicting the superposition of the four stable positions 68a, 68b, 68c, 68d due to inertial lift forces with the Dean flow. A possible mechanism for biasing a single minimum is also presented. The dominant viscous drag due to the Dean flow acts strongly at the channel mid-line, directing particles to one side of the channel over the other (for the opposite turn this force is of less magnitude in the opposite direction, and does not surpass the inertial force). Once a particle 70 is trapped in this minimum, it can remain because the viscous drag 64 at the split point of the two vortices is less in magnitude than the shear gradient-induced lift 66. Particles at the top and bottom minimum may not remain trapped because the viscous drag acts strongly here as well, and in the direction of a weaker shear gradient.

[0159] The ratio of lift to drag forces,  $R_f$  scales as  $R_f \sim \delta^{-1} (a/D_h)^3$  for a constant  $R_c$ . Separations are ideal when  $R_f \geq 1$  within the channel cross section for a particle of a given size and less than 1 for a particle of another size. For  $R_f$  lift forces that push particles to an equilibrium position dominate, while for  $R_f < 1$ , dominant Dean drag overwhelms these equilibrium positions and leads to mixing of particles. The dependence on particle diameter cubed suggests effective separation of particles with small size differences. The  $R_f$  relation also suggests that the separation can be tuned to separate particles over a range of diameters by modification of the geometry  $D_h$  and curvature ratio ( $\delta$ ).

[0160] Theory predicts a limit to the speed of equilibrium separations. Previously, the dependence of the lift/drag ratio,  $R_f$  on  $R_c$  was neglected. When this dependence is taken into account, velocities higher than optimum are predicted to lead to defocusing. This is because the inertial lift force scales with the channel velocity squared ( $U_m^2$ ) and the lift coefficient ( $f_c$ ), where the lift coefficient decreases with increasing  $U_m$ . Therefore, the inertial lift force increases at a rate less than  $U_m^2$ . This can be compared to the drag force due to Dean flow

which scales with  $U_m^2$ . This leads to the ratio of these forces,  $R_f$  decreasing with increasing  $U_m^2$ .

[0161] Therefore, three flow regimes can be considered: (1) At low fluid velocities,  $R_f$  may be larger than 1 over the majority of the channel cross section; however, the magnitudes of  $F_z$  and  $F_D$  are too low to create focused streams within the length of channel. (2) At intermediate fluid velocities,  $R_f$  may be greater or equal to 1 over a limited region of the channel cross section, and the magnitude of forces is large enough to create focusing to one or more streams. (3) For high fluid velocities,  $R_f$  is less than 1 over the entire channel cross section, and Dean drag is dominant, leading to particle mixing.

[0162] Using  $R_f$  one can predict the particle size cutoff below which focusing does not occur.  $R_f$  varies in magnitude across the channel cross section due to variation in  $F_D$  and  $F_z$  over this region. The functional form of this variation, however, is not currently known and thus it is difficult to predict a priori a particle size cutoff for a given geometry (i.e., for what particle size does  $R_f$  initially become  $< 1$  throughout the channel cross section). Thus, empirically determined cutoffs can give unknown parameters in  $R_f$ . The known geometry and cutoff can then be inserted into the equation  $R_f = 1$  to find the scaling of unknown positional dependent factors. This is because the particle diameter below which the ratio,  $R_f$  first becomes less than 1 over the entire channel cross section corresponds to the size cutoff in that channel geometry. In other words, with decreasing particle diameter,  $R_f$  decreases to less than 1, resulting in particle mixing due to Dean drag forces dominating.

[0163] A semi-empirical relationship is provided quantitatively as follows: First, the condition  $R_f(x_{c1}) = k(r a_c^3 / D_h^4) = 1$  is produced, where  $x_{c1}$  are the coordinates of the final position to become less than 1 within the channel cross section and  $k$  is a scaling factor. The empirical parameters are the channel radius of curvature ( $r$ ), the cutoff size ( $a_c$ ), and the channel hydraulic diameter. Solving for  $k$  for one or more experimental systems allows the development of a relationship that can be applied to an unknown system and size cutoff:

$$r_2 \frac{a_{c2}^3}{D_{h2}^4} = r_1 \frac{a_{c1}^3}{D_{h1}^4}$$

[0164] This treatment assumes that both systems are operated at a constant  $R_c$  and that particle sizes are small compared to the flow field, since  $x_{c1}$  is assumed to remain independent of particle size.

[0165] A simplified expression that dictates the geometry of a new channel to separate at a new cutoff can then be developed. If the same radius of curvature is maintained, then an empirical relation for  $D_h$  as a function of the cutoff diameter can be written as:

$$D_{h2} = D_{h1} \left( \frac{a_{c2}}{a_{c1}} \right)^{3/4}$$

[0166] If height is the dominant factor in determining the inertial lift force and channels with large widths are considered, such that  $h$  is the dominant dimension for Dean flow, the equation for  $D_{h1}$  above can be rewritten as  $h_2 = h_1 (a_{c2}/a_{c1})^{3/4}$ . In general, particles close to the center and outer wall will