Long-range forces affecting equilibrium inertial focusing behavior in straight high aspect ratio microfluidic channels

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The controlled and directed focusing of particles within flowing fluids is a problem of fundamental and technological significance. Microfluidic inertial focusing provides passive and precise lateral and longitudinal alignment of small particles without the need for external actuation or sheath fluid. The benefits of inertial focusing have quickly enabled the development of miniaturized flow cytometers, size-selective sorting devices, and other high-throughput particle screening tools. Straight channel inertial focusing device design requires knowledge of fluid properties and particle-channel size ratio. Equilibrium behavior of inertially focused particles has been extensively characterized and the constitutive phenomena described by scaling relationships for straight channels of square and rectangular cross section. In concentrated particle suspensions, however, long-range hydrodynamic repulsions give rise to complex particle ordering that, while interesting and potentially useful, can also dramatically diminish the technique's effectiveness for high-throughput particle handling applications. We have empirically investigated particle focusing behavior within channels of increasing aspect ratio and have identified three scaling regimes that produce varying degrees of geometrical ordering between focused particles. To explore the limits of inertial particle focusing and identify the origins of these long-range interparticle forces, we have explored equilibrium focusing behavior as a function of channel geometry and particle concentration. Experimental results for highly concentrated particle solutions identify equilibrium thresholds for focusing that scale weakly with concentration and strongly with channel geometry. Balancing geometry mediated inertial forces with estimates for interparticle repulsive forces now provide a complete picture of pattern formation among concentrated inertially focused particles and enhance our understanding of the fundamental limits of inertial focusing for technological applications. *Published by AIP Publishing.* [<http://dx.doi.org/10.1063/1.4946829>]

INTRODUCTION

Inertial focusing is a phenomenon that occurs at low but finite Reynolds numbers in straight microfluidic conduits. Initially observed in cylindrical channels,¹ inertial focusing is understood to be the product of a force balance between opposing radial hydrodynamic lift forces. At critical, geometry-dependent Reynolds numbers, a wall-induced lift force pushes particles towards the channel centerline, while an opposing shear-gradient force pushes particles away from it.¹⁻⁷ The balance of these two opposing forces creates predictable and precise particle equilibrium positions, while interacting Stokes' wakes^{8,9} surrounding rotating particles induce consistent interparticle spacing. The number and orientation of lateral particle focusing positions is determined by microchannel geometry.^{1,8,10,11} As first observed in channels with circular cross sections,¹ particles migrate to

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an annulus of equilibrium focusing positions within the channel. Manipulating cross sectional symmetry decreases the number of equilibrium focusing positions.^{8,10} These optimizations have allowed microfluidic inertial focusing to be applied to a broad spectrum of particle separation,^{8,12–16} encapsulation,^{17–19} and filtration^{20–22} challenges. These applications, in turn, place heavy emphasis upon an accurate description of the hydrodynamic forces responsible for functional inertial focusing behavior.^{9,23–26}

Cross sectional channel geometry is the fundamental basis of design for most straight channel inertial focusing microfluidic applications and is of interest to particle analysis^{27–29} and separations technologies.^{8,12,13,15} Straight, high aspect ratio channels have shown to be particularly effective at concentrating particles, which can subsequently be isolated as a concentrated fraction.³⁰ Under certain conditions, however, lateral conformity is broken and particles assume more complex orientations.³¹ This observation has been speculated to be the result of elevated linear particle concentration.³² In this paper, we examine the effects of both high aspect ratio rectangular channel geometry and extremely high particle concentration on particle focusing behavior. We have found that high aspect ratio rectangular channels alone can induce the onset of non-linear particle orientations in which focused particles buckle laterally out of the equilibrium focusing plane as a result of a weakened wall-induced lift force. We demonstrate that this particle buckling phenomenon depends upon channel geometry by not only increasing the linear particle concentration³² but by altering the relative magnitude of inertial and hydrodynamic forces that define equilibrium focusing behavior.

MATERIALS AND METHODS

Standard soft-lithography techniques were used to fabricate microfluidic devices within polydimethylsiloxane (PDMS)^{33,34} (Sylgard 184, Dow Corning). PDMS microchannel replicas were sealed to standard glass slides following exposure to oxygen plasma. Fluorescent polystyrene microparticles (Thermo Scientific) with an aqueous suspension of 1% solids by volume, a density of $\rho = 1.05 \text{ g/cm}^3$, and a diameter of $a = 9.9 \text{ }\mu\text{m}$ were used. In order to achieve desired particle suspension volume fractions, microparticles were dispersed into deionized water and iodixanol (Optiprep, Sigma Aldrich). At the required Optiprep concentration, the solution viscosity was approximately 1 cP. Microparticle suspensions were pumped (neMESYS, cetoni GmbH) into microchannels using a 3 ml plastic syringe coupled to Tygon tubing (0.01 in. ID). Particle behavior was observed and recorded via fluorescent and high speed microscopy (Olympus IX71 inverted microscope and a VisionResearch Phantom v310 camera). Long-exposure fluorescent streak images were taken of focused fluorescent microparticles and behavior was quantified using image processing and analysis software (ImageJ, National Institutes of Health).

At microchannel inlets, particles were randomly distributed, but after a short distance, focusing could be readily observed. After reaching their equilibrium positions, particles continue unperturbed throughout the remainder of the channel. Inertial focusing was consistently observed to be fully developed by one quarter of the total channel length. This observation was confirmed by measuring consistent full width-half maximum (FWHM)/ a for all channel widths at one, two, and three quarters of the channel length. All experimental data were collected at approximately three-quarters length, corresponding to the lowest absolute pressure of the three positions examined for optimal focusing to equilibrium positions.⁶ Experiments were designed to systematically examine particle focusing behavior over a range of rectangular channel aspect ratios, w/h . Experiments were conducted using a series of thirteen straight wide rectangular microfluidic channels with a constant channel height of $h = 25 \text{ }\mu\text{m}$ and channel widths varying from $w = 40 \text{ }\mu\text{m}$ to $w = 280 \text{ }\mu\text{m}$, increasing by widths of $\Delta w = 20 \text{ }\mu\text{m}$. The overall length of the channel measured 6 cm. Each microchannel was fabricated with a constant cross section spanning its entire length. The initial concentration of the polystyrene microparticle solution used was $1.5 \times 10^6 \text{ beads/ml}$, corresponding to a bead volume fraction of $\phi = 8.8 \times 10^{-4}$. Following initial experiments, concentration effects were further examined using polystyrene microparticle solution concentrations of

1.0×10^6 beads/ml, 6×10^6 beads/ml, 11×10^6 beads/ml, and 16×10^6 beads/ml with corresponding bead volume fractions of $\phi = 6.0 \times 10^{-4}$, $\phi = 3.5 \times 10^{-3}$, $\phi = 6.4 \times 10^{-3}$, and $\phi = 9.3 \times 10^{-3}$, respectively. The average velocity of the solution flowing through the channels ranged from $u = 0.02$ m/s to $u = 0.4$ m/s and was increased stepwise by increments of $\Delta u = 0.0016$ m/s, with optimal focusing conditions occurring at and beyond an average velocity of $u = 0.4$ m/s. We used a dimensionless parameter, the particle Reynolds number (Re_p), which accounts for both particle and channel size, to quantify the inertial forces experienced by a single particle in a given flow. The particle Reynolds number⁸ is defined by $Re_p = U_m a^2 / \nu D_h$, where U_m is the maximum channel velocity, a is the particle diameter, ν is the kinematic viscosity, and D_h is the hydraulic diameter where $D_h = 2wh/(w + h)$. To maintain constant Re_p for varying channel geometries, solution flow rates were scaled by channel cross sectional area. PDMS channel deformation was considered for the range of channel geometries and flow rates used in these experiments.³⁵ Sollier *et al.* describe the deformation of PDMS-glass devices under a range of flow rates. At equivalent pressures, they report a 2%-3% increase in channel height, which corresponds to a deflection of less than one micron for our geometry. Our experimental conditions remained within the region in which PDMS deformation is minimal as reported by Sollier *et al.*; therefore, channel height was assumed to remain constant and pressure variation linear for the constant cross section channels used in this study.³⁵

RESULTS AND DISCUSSION

As the channel geometric aspect ratio was increased, an increase in the width of the equilibrium particle focusing streak was observed. At a threshold aspect ratio of 5.6, focused particles began to buckle laterally, orthogonal to the equilibrium focusing plane, resulting in a wider focusing streak. It was also observed that the lateral distance particles were displaced from the channel centerline became more exaggerated as the channel aspect ratio was increased past the 5.6 aspect ratio threshold, as shown in Figs. 1(a)-1(c).

FIG. 1. [(a)-(c)] Fluorescent streak images of focusing behavior at rectangular aspect ratios. Channel widths: (a) $w = 40 \mu\text{m}$, (b) $w = 140 \mu\text{m}$, and (c) $w = 280 \mu\text{m}$. (d) Intensity profile displays variance in particle focusing behavior at increasing rectangular aspect ratios represented in (a)-(c). The Re_p of these experiments ranged from 0.1 to 1.5. Particles flowed through channels with a constant height $h = 25 \mu\text{m}$, volume fraction $\phi = 8.8 \times 10^{-4}$, and at an average velocity of $u = 0.4$ m/s for all data shown.

To quantify this observed behavior, one-dimensional Gaussian distributions of fluorescent streak images were measured at each channel width represented in Figs. 1(a)-1(c). It was found that as aspect ratio increased, maximum fluorescent intensity was reduced as a result of an increase in the volume of the channel occupied by the buckled particle stream. Physically, this implies that in higher aspect ratio channels, focused particles are distributed over a larger proportion of the channel cross section as opposed to being tightly focused to a single particle width. Intensity distributions measured from fluorescent streaks created by focused particles of the same volume fraction and Re_p are depicted in Fig. 1(d).

We postulate this transition in particle position, from tightly focused to buckled, is the result of a new geometry-induced equilibrium between the wall-induced lift force and coupled viscous dissipation forces⁹ between particles. An increase in the rectangular channel aspect ratio equates to a greater lateral distance over which the wall-induced lift force must act to achieve centerline focusing. We have shown elsewhere²⁶ wall induced-lift forces decay according to $F_L \propto r^{-2}$, where F_L is the wall-induced lift force and r is the distance from the wall to the particle center. Eventually, a threshold is crossed beyond which the dominant focusing force is insufficient to overcome the viscous repulsive interactions⁹ resisting that resist focusing. As a result, particle buckling occurs and optimal particle focusing is compromised as schematically illustrated in Figs. 2(a) and 2(b).

To further assess the particle buckling phenomenon, relationships between Re_p , geometric aspect ratio, and particle buckling were examined. $FWHM$ values of Gaussian fluorescent intensity distributions were measured from focused particle streaks and found to decrease as Re_p was increased. Theoretically, the $FWHM$ of an optimal particle focusing streak should be equivalent to that measured from the intensity distribution of a single fluorescent particle. Consequently, measured $FWHM$ values were normalized by dividing the streak $FWHM$ by the $FWHM$ measured from a single particle of diameter $a = 9.9 \mu\text{m}$. Therefore, optimum equilibrium focusing behavior should collapse to one constant asymptote at a value of $FWHM/a = 1$. Data collected in lower aspect ratio channels all collapsed to a value of $FWHM/a$ value of approximately 1, indicating tight focusing with little experimental variance. However, at aspect ratio values exceeding 5, focusing collapsed to a second asymptote at a value of $FWHM/a$ equal to about a value of 1.4. At a larger aspect ratio of 8, a stable streak formed at high Re_p with a $FWHM/a$ value of 2.1. These trends in asymptotic focusing behavior with increasing channel geometric aspect ratios are shown in Figs. 3(a) and 3(b).

Throughout the experiments summarized by Figure 3, a constant particle concentration was maintained to establish particle buckling as a function of geometry and magnitude of the inertial lift force. To further establish the onset of particle buckling, particle concentration was next varied. The following concentration experiments were conducted using channel parameters consistent with those of our previous experiments: straight microfluidic channels with a constant height $h = 25 \mu\text{m}$ and a continuous rectangular cross section bridging the entire length of the channel. Examined channel widths included $w = 100 \mu\text{m}$, $w = 120 \mu\text{m}$, $w = 140 \mu\text{m}$, and $w = 160 \mu\text{m}$, which were selected in order to focus on channels with aspect ratios immediately above and below the threshold at which buckling was previously observed. The following solution concentrations were used: 1×10^6 beads/ml, 6×10^6 beads/ml, 11×10^6 beads/ml, and 16×10^6 beads/ml. These concentrations correspond to volume fractions $\phi = 6.0 \times 10^{-4}$, $\phi = 3.5 \times 10^{-3}$, $\phi = 6.4 \times 10^{-3}$, and $\phi = 9.3 \times 10^{-3}$, respectively. The average fluid velocity ranged from $u = 0.02$ m/s to $u = 0.4$ m/s and increased by increments of $\Delta u = 0.0016$ m/s. Velocity was scaled by channel cross sectional area to maintain consistent velocity and Re_p within varying channel aspect ratios. Over this flow rate span, Re_p ranged from 0.4 to 1.6.

These experiments, isolating for the influence of concentration on particle buckling, revealed that particle focusing behavior exhibited similar asymptotic relationships to those observed previously [Figs. 3(a) and 4(a)-4(d)]. At a rectangular aspect ratio of 5.6, previously established as the geometry-induced buckling threshold for $\phi = 8.8 \times 10^{-4}$ (or 1.5×10^6 beads/ml), particle streak width increased at both high and low particle concentrations as shown in Fig. 4(e). Although particle buckling occurs at both high and low concentrations, it is amplified at higher concentrations but most pronounced in high aspect ratio channels [Fig. 4(e)]. Figure 4(f) illustrates the most exaggerated particle buckling witnessed in these experiments occurred at high geometric aspect

FIG. 2. [(a)-(b)] Schematics contrasting inertial focusing of particles in low and high aspect ratio rectangular channels. (a) illustrates tight particle focusing in a low aspect ratio rectangular channel. High-speed micrograph of particle streams in low aspect ratio rectangular channel with a constant width $w = 40 \mu\text{m}$, height $h = 25 \mu\text{m}$, volume fraction $\phi = 8.8 \times 10^{-4}$, and velocity of $u = 0.4 \text{ m/s}$. (b) demonstrates particle buckling as a result of a weakened wall lift force in a high aspect ratio rectangular channel. High-speed micrograph of particle streams in high aspect ratio rectangular channel with a constant height $h = 25 \mu\text{m}$, width $w = 140 \mu\text{m}$, volume fraction $\phi = 8.8 \times 10^{-4}$, and velocity of $u = 0.4 \text{ m/s}$.

ratios, high particle concentrations, and low Re_p . Figure 4(f) clearly depicts the coupled effects of both concentration and geometry where particle buckling scales weakly with concentration and strongly with channel geometry. An examination of these observations requires the consideration of exogenous factors, such as channel deformation,³⁵ that could contribute to the observed focusing behavior. Figure 4(f) demonstrates that dilute bead solutions are focused within tight position distributions. In identical channels and under the same flow conditions, more concentrated solutions displayed buckling, characterized by broadening of the focused stream. If channel deformation was responsible for diminished focusing, stream broadening would be evident at lower bead concentrations. In fact, we observe focusing that is optimal, as quantified by a normalized streak width of unity. Deviation of particles from their expected position at the channel centerline is readily explained by a shifting balance between the inertial and hydrodynamic forces in increasingly high aspect ratio channels. This observation indicates that although particle buckling can be amplified by particle concentration, particle buckling is predominantly a geometry-dependent phenomenon at high aspect ratios. Particle buckling is amplified at high concentrations in high aspect ratio

FIG. 3. (a) Particle focusing behavior at constant geometric aspect ratios and variable Re_p . Dotted lines connect points as a guide for the eye only. (b) Particle focusing behavior at constant Re_p and variable geometric aspect ratios. The width of particle focusing streamlines expressed presented as a particle-normalized $FWHM$. The Re_p of these experiments ranged from 0.1 to 1.5. Particles flowed through channels with a constant height $h = 25 \mu\text{m}$, volume fraction $\phi = 8.8 \times 10^{-4}$, and at an average velocity of $u = 0.4 \text{ m/s}$ for all data shown.

rectangular channels by viscous repulsive forces acting in opposition to a weakened wall-induced lift force.

To distinguish the effects of channel geometry from situations in which particle concentration alone is sufficient to promote buckling, the cumulative physical effects of these two variables must be established. We begin by defining two dimensionless parameters that account for channel features: the effective volume fraction (ϕ_{eff}), which describes the volume fraction of focused particles residing strictly within the effective volume of a given channel occupied by tightly focused particles (Equation (1)), and the maximum effective volume fraction (ϕ_{max}), which describes the maximum volume fraction of inertially focused particles that can occupy a channel's effective volume (Equation (2))

$$\phi_{eff} = \frac{\phi_0 W_c}{a} \quad (1)$$

and

$$\phi_{max} = \frac{nV_p}{h_c l_m a}, \quad (2)$$

where ϕ_0 represents the initial volume fraction of the particle solution, W_c is the channel width, V_p the volume of the particle, h_c the height of the channel, and l_m is the measured length of the channel. The variable n is the maximum number of inertially focused particles that can occupy the channel volume defined by $h_c * W_c * l_m$ within the length of the channel measured and

FIG. 4. (a)-(d) Particle focusing behavior at constant geometric aspect ratios and concentrations with variable Re_p . Re_p ranged from 0.4 to 1.6. (e) Particle focusing behavior at constant Re_p and concentrations with variable geometric aspect ratios. (f) A closer look at particle focusing behavior of (a)-(d) at a constant Re_p of 1.28. All channels used in experiments had a height $h = 25 \mu\text{m}$ and channel widths of $w = 100 \mu\text{m}$, $w = 120 \mu\text{m}$, $w = 140 \mu\text{m}$, $w = 160 \mu\text{m}$. Solution contains particles with a diameter $d = 9.9 \mu\text{m}$ and was pumped through channels at an average velocity of $u = 0.4 \text{ m/s}$.

was determined empirically. Both dimensionless groups depend upon the diameter of the particle, a . To establish a parameter that combines both geometry and concentration, we have developed a normalized effective volume fraction parameter ($\phi_{n,eff}$), which is a single dimensionless variable

$$\phi_{n,eff} = \frac{\phi_{eff}}{\phi_{max}} \quad (3)$$

that is a function of both geometry and concentration (Equation (3)).

In inertial focusing, particles are collapsed to the channel centerline by inertial forces and the majority of the channel volume is devoid of particles. It therefore follows that $\phi_{n,eff}$ establishes the optimal focusing carrying capacity for a given inertial focusing channel, which is reached at lower volume fractions for higher aspect ratio channels. Buckling subsequently results as the maximum number of particles that can physically occupy the effective volume of the channel under ideal conditions is exceeded. Figures 5(a) and 5(b) illustrate this principle schematically. The effective volume of the channel that contains inertially focused particles remains constant and is independent of channel size, provided that inertial forces are sufficient to achieve equilibrium focusing. When inertial forces are insufficient to achieve equilibrium, the effective channel volume becomes dependent upon channel geometry, as illustrated in Figure 5(c). Figure 5(c) displays data for solutions of increasing volume fraction, scaled against the occupied fraction of the dimensionless channel carrying capacity. Within data sets for discrete solution volume fractions, ϕ_0 increasing values of $\phi_{n,eff}$ are due solely to increasing channel aspect ratio. As $\phi_{n,eff}$ approaches and exceeds a value of 1.0, a sharp increase in streak width is observed. At higher solution volume fractions, normalized streak widths exceed 1.0, even for low aspect ratio channels. The observation that a transition

FIG. 5. [(a) and (b)] Schematics contrasting particle behavior at a normalized effective volume fraction less than and greater than one. (c) Comparison of particle focusing behavior at each normalized effective volume fraction used in our experiments: $\phi_0 = 6.0 \times 10^{-4}$ (red), $\phi_0 = 8.8 \times 10^{-4}$ (orange), $\phi_0 = 3.5 \times 10^{-3}$ (green), $\phi_0 = 6.4 \times 10^{-3}$ (blue), $\phi_0 = 9.3 \times 10^{-3}$ (black). Channel width is increasing as one moves from left to right within a concentration series. The width of particle focusing streamlines expressed as the full width half maximum (FWHM) of the Gaussian distribution of experimental data, divided by a , the microparticle diameter. All channels used in experiments had a height $h = 25 \mu\text{m}$ and channel widths of $w = 100 \mu\text{m}$, $w = 120 \mu\text{m}$, $w = 140 \mu\text{m}$, $w = 160 \mu\text{m}$. Solution contains particles with a diameter $d = 9.9 \mu\text{m}$ and was pumped through channels at an average velocity of $u = 0.4 \text{ m/s}$.

FIG. 6. (a) A schematic representation of the force profile exhibited by the exponentially decaying wall-induced lift force. High-speed micrographs at the three regimes of particle focusing behavior represented in (a). Channel widths at aspect ratios: 1.60 $w = 40 \mu\text{m}$, 5.60 $w = 140 \mu\text{m}$, and 11.2 $w = 280 \mu\text{m}$. Images taken in channels with a constant height $h = 25 \mu\text{m}$, volume fraction $\phi = 9.3 \times 10^{-3}$, and average flow speed $u = 0.4 \text{ m/s}$.

from tightly focused to buckled particles appears at $\phi_{n,eff}$ values of less than 1.0 indicates that particles are not uniformly distributed along the channel length and that trains³¹ of focused particles have local $\phi_{n,eff}$ values exceeding 1.0. This analysis recapitulates the observation that the transition from tightly focused to buckled particle streams is more pronounced in wider channels, while also capturing the concept that geometry-induced buckling occurs at diminished inertial lift, mediated by geometry can induce buckling at both low and high particle concentrations.

Particle focusing behavior for a constant volume fraction solution is displayed in Figure 6. A schematic of the ratio of forces F_L/F_R experienced by particles is illustrated as a function of lateral channel position, where F_L is the exponentially decaying²³ wall-induced lift force and F_R is the isotropic viscous repulsive force⁹ between particles, assumed to be isotropic. While F_L decays rapidly as particles are translated away from the channel wall, there is a sufficient force acting at the channel center to counteract interparticle forces and conserve the zero point force responsible for maintaining optimal particle focusing at low aspect ratios. In Figure 6, this is indicated by a net positive force ratio. As channel aspect ratio is increased, F_L decays further and F_L/F_R travels through one. When F_L no longer exceeds F_R , particles buckle laterally to positions offset from the channel centerline. As geometric aspect ratio is further increased, F_L/F_R occurs further from the channel centerline and particle buckling becomes more exaggerated.

CONCLUSION

We have investigated the effects of high aspect ratio rectangular channel geometries on particle focusing and contrasted our observations with the effects of high particle concentrations. We show that the onset of buckling is both a nuanced concentration effect that is governed by solution concentration and compounded by geometry in multiple ways. We have found that the lateral displacement of particles from the channel centerline in particle buckling behavior is dependent on both channel geometry and particle concentration and can be introduced by either variable, independently. The relative magnitude of the inertial force and hydrodynamic interactions dictates both the onset and magnitude of buckling. Geometry-induced particle buckling was observed for both low and high particle concentrations, whereas concentration-induced particle buckling is most pronounced in high aspect ratio channels. Therefore, particle buckling scales weakly with concentration and strongly with channel geometry. Our explanation for this buckling effect is based upon extended empirical observations and provides a framework by which experimental and device design may be conducted. A dimensionless parameter, the normalized effective volume fraction, was introduced to quantify the combined effects of geometry and concentration in microfluidic inertial focusing systems that account for the constraints associated with inertial focusing phenomena. This allows us to couple mechanism to the onset of buckling and therefore provides a useful guide that will predict focusing for given solutions, geometry, and flow conditions. This parameter and the insight that it provides is useful in a variety of inertial focusing contexts including particle concentration, filtration, and focusing applications.

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¹ G. Segre and A. Silberberg, "Radial particle displacements in Poiseuille flow of suspensions," *Nature* **189**, 209 (1961).

² D. Leighton and A. Acrivos, "The shear-induced migration of particles in concentrated suspensions," *J. Fluid Mech.* **181**, 415 (1987).

³ J. A. Schonberg and E. J. Hinch, "Inertial migration of a sphere in Poiseuille flow," *J. Fluid Mech.* **203**, 517 (1989).

- ⁴ E. S. Asmolov, "The inertial lift on a spherical particle in a plane Poiseuille flow at large channel Reynolds number," *J. Fluid Mech.* **381**, 63 (1999).
- ⁵ J.-P. Matas, J. F. Morris, and E. Guazzelli, "Inertial migration of rigid spherical particles in Poiseuille flow," *J. Fluid Mech.* **515**, 171 (2004).
- ⁶ D. Di Carlo, "Inertial microfluidics," *Lab Chip* **9**, 3038 (2009).
- ⁷ J. Zhou and I. Papautsky, "Fundamentals of inertial focusing in microchannels," *Lab Chip* **13**, 1121 (2013).
- ⁸ D. Di Carlo, D. Irimia, R. G. Tompkins, and M. Toner, "Continuous inertial focusing, ordering, and separation of particles in microchannels," *Proc. Natl. Acad. Sci. U. S. A.* **104**, 18892 (2007).
- ⁹ W. Lee, H. Amini, H. A. Stone, and D. Di Carlo, "Dynamic self-assembly and control of microfluidic particle crystals," *Proc. Natl. Acad. Sci. U. S. A.* **107**, 22413 (2010).
- ¹⁰ B. Chun and A. J. C. Ladd, "Inertial migration of neutrally buoyant particles in a square duct: An investigation of multiple equilibrium positions," *Phys. Fluids* **18**, 031704 (2006).
- ¹¹ D. R. Gossett and D. D. Carlo, "Particle focusing mechanisms in curving confined flows," *Anal. Chem.* **81**, 8459 (2009).
- ¹² N. Pamme, "Continuous flow separations in microfluidic devices," *Lab Chip* **7**, 1644 (2007).
- ¹³ A. A. S. Bhagat, S. S. Kuntaegowdanahalli, and I. Papautsky, "Continuous particle separation in spiral microchannels using Dean flows and differential migration," *Lab Chip* **8**, 1906 (2008).
- ¹⁴ E. Sollier, H. Rostaing, P. Pouteau, Y. Fouillet, and J.-L. Achard, "Passive microfluidic devices for plasma extraction from whole human blood," *Sens. Actuators, B* **141**, 617 (2009).
- ¹⁵ J. M. Martel and M. Toner, "Inertial focusing dynamics in spiral microchannels," *Phys. Fluids* **24**, 032001 (2012).
- ¹⁶ E. Ozkumur, A. M. Shah, J. C. Ciciliano, B. L. Emmink, D. T. Miyamoto, E. Brachtel, M. Yu, P.-I. Chen, B. Morgan, J. Trautwein, A. Kimura, S. Sengupta, S. L. Stott, N. M. Karabacak, T. A. Barber, J. R. Walsh, K. Smith, P. S. Spuhler, J. P. Sullivan, R. J. Lee, D. T. Ting, X. Luo, A. T. Shaw, A. Bardia, L. V. Sequist, D. N. Louis, S. Maheswaran, R. Kapur, D. A. Haber, and M. Toner, "Inertial focusing for Tumor antigen-dependent and-independent sorting of rare circulating tumor cells," *Sci. Transl. Med.* **5**, 179ra47 (2013).
- ¹⁷ J. F. Edd, D. Di Carlo, K. J. Humphry, S. Koster, D. Irimia, D. A. Weitz, and M. Toner, "Controlled encapsulation of single-cells into monodisperse picolitre drops," *Lab Chip* **8**, 1262 (2008).
- ¹⁸ A. R. Abate, C.-H. Chen, J. J. Agresti, and D. A. Weitz, "Beating Poisson encapsulation statistics using close-packed ordering," *Lab Chip* **9**, 2628 (2009).
- ¹⁹ E. W. M. Kemna, R. M. Schoeman, F. Wolbers, I. Vermes, D. A. Weitz, and A. van den Berg, "High-yield cell ordering and deterministic cell-in-droplet encapsulation using Dean flow in a curved microchannel," *Lab Chip* **12**, 2881 (2012).
- ²⁰ J. Seo, M. H. Lean, and A. Kole, "Membrane-free microfiltration by asymmetric inertial migration," *Appl. Phys. Lett.* **91**, 033901 (2007).
- ²¹ D. Di Carlo, J. F. Edd, D. Irimia, R. G. Tompkins, and M. Toner, "Equilibrium separation and filtration of particles using differential inertial focusing," *Anal. Chem.* **80**, 2204 (2008).
- ²² A. J. Mach and D. Di Carlo, "Continuous scalable blood filtration device using inertial microfluidics," *Biotechnol. Bioeng.* **107**, 302 (2010).
- ²³ D. Di Carlo, J. F. Edd, K. J. Humphry, H. A. Stone, and M. Toner, "Particle segregation and dynamics in confined flows," *Phys. Rev. Lett.* **102**, 094503 (2009).
- ²⁴ H. Amini, E. Sollier, W. M. Weaver, and D. Di Carlo, "Intrinsic particle-induced lateral transport in microchannels," *Proc. Natl. Acad. Sci. U. S. A.* **109**, 11593 (2012).
- ²⁵ D. R. Gossett, H. T. K. Tse, J. S. Dudani, K. Goda, T. A. Woods, S. W. Graves, and D. Di Carlo, "Inertial manipulation and transfer of microparticles across laminar fluid streams," *Small* **8**, 2757 (2012).
- ²⁶ J. McConnell and J. Oakey, "Observed and predicted particle dynamics driven by inertial flows within high aspect ratio microfluidic channels," *Microfluid. Nanofluid.* **20**, 1 (2016).
- ²⁷ E. Racila, D. Euhus, A. J. Weiss, C. Rao, J. McConnell, L. W. M. M. Terstappen, and J. W. Uhr, "Detection and characterization of carcinoma cells in the blood," *Proc. Natl. Acad. Sci. U. S. A.* **95**, 4589 (1998).
- ²⁸ S. C. Hur, H. T. K. Tse, and D. Di Carlo, "Sheathless inertial cell ordering for extreme throughput flow cytometry," *Lab Chip* **10**, 274 (2010).
- ²⁹ J. Oakey, R. W. Applegate, E. Arellano, D. D. Carlo, S. W. Graves, and M. Toner, "Particle focusing in staged inertial microfluidic devices for flow cytometry," *Anal. Chem.* **82**, 3862 (2010).
- ³⁰ A. E. Reece, K. Kastrup, H. D. Sikes, and J. Oakey, "Staged inertial microfluidic focusing for complex fluid enrichment," *RSC Adv.* **5**, 53857 (2015).
- ³¹ J.-P. Matas, V. Glezer, É. Guazzelli, and J. F. Morris, "Trains of particles in finite-Reynolds-number pipe flow," *Phys. Fluids* **16**, 4192 (2004).
- ³² K. J. Humphry, P. M. Kulkarni, D. A. Weitz, J. F. Morris, and H. A. Stone, "Axial and lateral particle ordering in finite Reynolds number channel flows," *Phys. Fluids* **22**, 081703 (2010).
- ³³ D. C. Duffy, J. C. McDonald, O. J. A. Schueller, and G. M. Whitesides, "Rapid prototyping of microfluidic systems in poly(dimethylsiloxane)," *Anal. Chem.* **70**, 4974 (1998).
- ³⁴ J. C. McDonald and G. M. Whitesides, "Poly(dimethylsiloxane) as a material for fabricating microfluidic devices," *Acc. Chem. Res.* **35**, 491 (2002).
- ³⁵ E. Sollier, C. Murray, P. Maoddi, and D. Di Carlo, "Rapid prototyping polymers for microfluidic devices and high pressure injections," *Lab Chip* **11**, 3752 (2011).