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Citation: Appl. Phys. Lett. **99**, 044101 (2011); doi: 10.1063/1.3608115
View online: http://dx.doi.org/10.1063/1.3608115
View Table of Contents: http://apl.aip.org/resource/1/APPLAB/v99/i4
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Inertial focusing of non-spherical microparticles

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(Received 18 May 2011; accepted 10 June 2011; published online 29 July 2011)

We have investigated the focusing and dynamics of non-spherical polymeric particles in microfluidic flows at finite Reynolds number. The rotational diameter, D_{max}, of a particle, regardless of its cross-sectional shape, was found to determine the final focused position, except for the case of asymmetric disks. Additionally, elongated particles with larger D_{max} exhibited longer residence times in a horizontal orientation than those with smaller D_{max}. These findings inform approaches to hydrodynamically control shaped and barcoded particles for multiplexed biochemical assays. © *2011 American Institute of Physics*. [doi:10.1063/1.3608115]

Despite rapid advancements in the field of molecular biology, fast and information-rich identification and quantification of minute analytes remains challenging for various applications. Increase in demand for such techniques has lead to development of innovative multiplexed planar and suspension biochemical assays.[1,2] Particularly, suspension assays utilizing multifunctional encoded microparticles as an active analyte-binding substrate[3,4] were reported to be more advantageous than current time- and labor-intensive planar assays (e.g., microarray and Enzyme-Linked ImmunoSorbent Assay (ELISA)), owing to their higher sample throughput and probe-set flexibility. Unlike spectral encoding, spatial barcoding techniques eliminate the need for a complex optical detection setup and enable an almost limitless number of encoding combinations. Recently, barcoded microparticles, synthesized using stop flow lithography, were used to demonstrate multiplexed biochemical assays with high-throughput.[3,5,6] However, despite success in automated detection and manipulation of such particles, the requirements of sheath flow and active guiding techniques[7,8] limit the further improvement of throughput desired for clinical applications. Hence, a method of particle manipulation in a high-throughput manner without sheath-flow or active guiding is needed.

Inertial focusing allows manipulation and separation of microparticles/cells in such a manner utilizing only intrinsic hydrodynamic forces.[9] An increase in overall processing speed can be attained with inertial focusing due to its intrinsically high operational flow rate combined with its sheath-less focusing ability, allowing massive parallelization.[10] For particle-based assays, the orientation, the position, and the rotational behavior of focused flowing particles are all important parameters to determine. Particularly, the effect of inertial lift forces on nonspherical particles is important to understand for future high throughput barcode detection applications, since they would inevitably require high operational flow rates. Thus far, however, only spherical or discoid shapes have been examined in inertial flows.

In addition to the barcoding application, inertial focusing of nonspherical particles will be of interest to other research areas. There are many arbitrarily shaped particles widely studied in biology and industrial processing[11] that would be important to either separate or focus for counting purposes. Therefore, how particle shape affects focusing position in a channel is important to investigate.

In this study, we investigate inertial effects on nonspherical particles with various size, cross-sectional shape, and asymmetry using single-layered straight rectangular microchannels over a wide flow rate range. Various anisotropic particles were synthesized by an optofluidic maskless lithography setup[12] combined with the stop-flow lithography technique[13] (Figures 1(b)–1(d)). Spheres and doublets were synthesized by emulsifying polydimethylsiloxane in deionized water with surfactant, followed by thermal curing.[14] Detailed experimental procedures can be found in supplementary material.[15]

Inertial focusing of the created microparticles was assessed by injecting particle suspensions through a

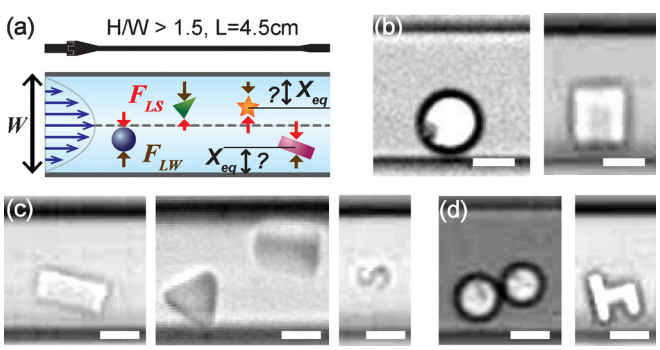

FIG. 1. (Color online) (a) Device design and schematic showing inertial forces, namely, the wall effect, F_{LW}, and the shear-gradient lift, F_{LS}, acting on microparticles, resulting in different average lateral equilibrium positions, X_{eq}. High-speed microscopic images of (b) spheres and symmetric disks, (c) cylinders with various cross-sections and aspect ratios, and (d) an asymmetric doublet and h-shaped disk.

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microchannel at an overall flow rate, Q, ranging from 25 to 1400 μl/min. Our initial studies with cylindrical particles suggested that the behavior of flowing non-spherical particles could be very complex and drastically varied with the channel Reynolds number, $R_C = \frac{\rho U_m D_h}{\mu}$. Here, ρ, U_m, and μ are the density, the maximum velocity, and the kinematic viscosity of the fluid, respectively, whereas D_h is the hydraulic diameter of the channel, defined as $D_h = \frac{2WH}{W-H}$, where W and H is the channel width and height, respectively. Multiple particles flowing with a periodically consistent motion were grouped together and categorized as "focused," "bouncing," and "translating," respectively, while the remaining individual particles without a motion in common were classified as "Other." The "translating" mode (i.e., particles flowing at the channel centerline without a tumbling motion) was found to be very unstable since the behavior was observed for only a few particles flowing at low flow rate ($R_c = 14$), and quickly dissipated downstream with increasing fluid inertia. At moderate flow rates ($14 < R_c < 28$), the majority of cylindrical particles (>81%) exhibited a "bouncing" motion[15] (i.e., particles periodically translated back and forth across the channel centerline, see Figure 2(a)). The cause of this periodic cross-streamline migration, however, is still unclear and further investigation would be important to identify what leads to a transition from bouncing to focusing and rotating. As the fluid inertia increases ($R_c > 43$), however, particles begin to inertially focus at two streamlines (i.e., "focused" mode) and, finally, at $R_c = 200$, all particles were inertially focused and rotating at two lateral distinct locations near the channel walls and at the middle vertical plane[15], similar to that observed for spheres in rectangular channels.[10] Thus, further empirical investigations on inertial focusing of nonspherical particles were conducted only at $R_c = 200$.

The experimental results conducted at $R_c = 200$ revealed distinct rotational orientations for disks and cylinders, which agreed well with previous computational analysis.[16] As discussed in the previous study, the vorticity direction (the z-axis for the current study) was the stable orbital axis, and regardless of their aspect ratios (ARs) or cross-sectional shapes, cylinders and disks exhibited "tumbling" and "log-rolling" motion, respectively.[15] Importantly, for possible separations based on particle shape, the rotational diameter, D_{max}, was found to be the important dimension for nonspherical particles that determines the lateral equilibrium position, X_{eq}, among many other dimensionless parameters.[15] All tested particles, except disks with an "h-shaped" cross-section (referred to as h-particles hereafter), followed the similar focusing trend of spheres when X_{eq} was plotted versus D_{max} (Figure 2(b)). The h-particle was identified as an outlier since both the coefficient of determination for the linear regression, R^2, and Cook's distance,[17] C_i, predicted it as the most influential data point.[15]

In order to investigate whether this dissimilar behavior of h-particles originated from its reduction in symmetry, we evaluated X_{eq} for doublets with various rotational diameters,

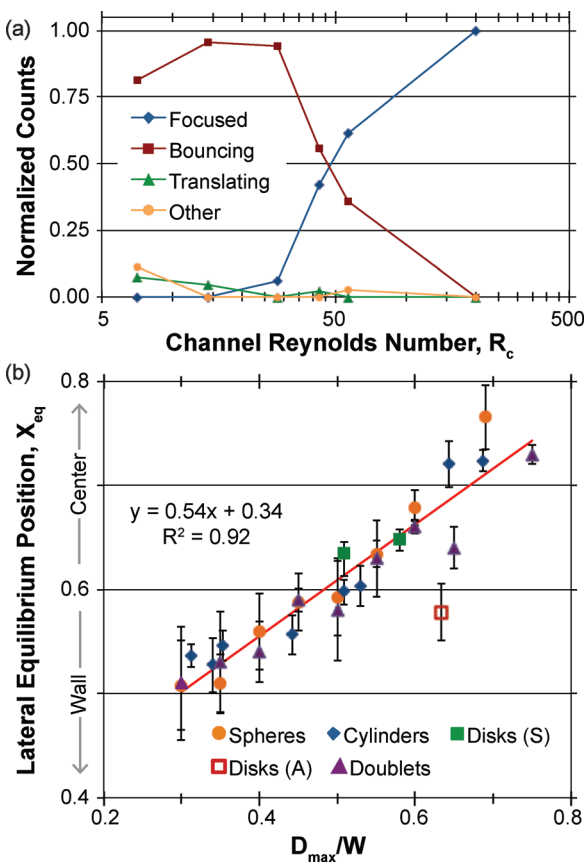

FIG. 2. (Color online) Flow rate and rotational diameter affect inertial focusing. (a) Behavior of flowing cylindrical particles at 4.5 cm downstream varied as flow rate increased. (b) Microparticles with various shapes can be inertially focused at uniform lateral and vertical locations at $R_c = 200$. Regardless of cross-sectional shape or aspect ratio, all particles followed the focusing trend of spheres with similar D_{max} except for asymmetric disks with an h-shaped cross-section.

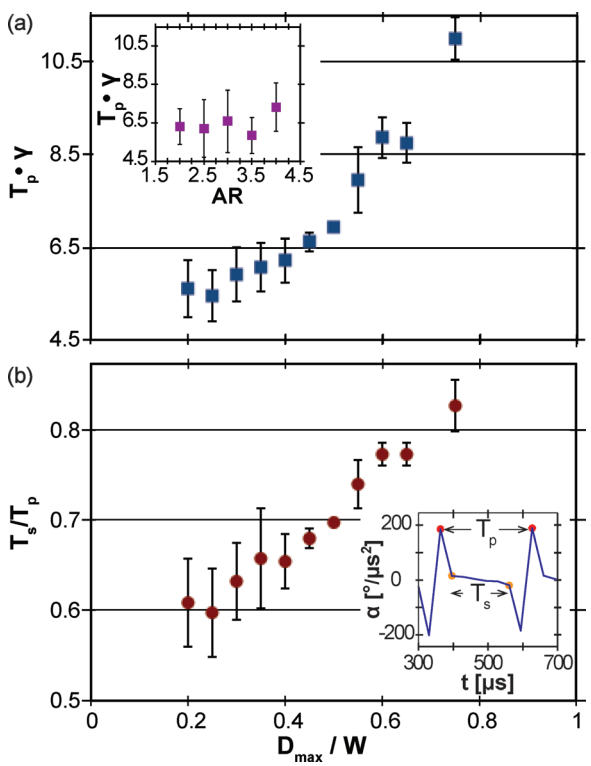

FIG. 3. (Color online) Rotational behavior of doublets with various size and asymmetry. (a) Nondimensionalized rotational period of doublets, $T_p \cdot \gamma$, and (b) the period ratio, T_s/T_p, were strongly dependent on D_{max} and independent of AR (inset (a)). Inset (b): definition of T_s/T_p. Here, α is the magnitude of the angular acceleration of the doublet.

$D_{max} = D_1 + D_2$, $AR = D_{max}/D_1$, and diameter ratios, $DR = D_1/D_2$. Here, D_1 and D_2 are diameters of spheres comprising the doublet and $D_2 <= D_1$. Slight fluctuations in the doublet center of mass, CM_D, were observed as doublets rotate,[15] and the magnitude of deviation in lateral equilibrium positions, ΔX_{eq}, was found to increase with D_{max}. Thus, an average value of CM_D was taken to be X_{eq} for a doublet with a given D_{max}. Still, for these particles a similar trend for X_{eq} as that of spheres with similar diameters was observed (Figure 2(b)).

In contrast to D_{max}, a clear correlation between X_{eq} of doublets and AR and DR was not found[15] (Figure 3(a)), suggesting that the asymmetry in shapes would not significantly contribute to the variation in X_{eq}. Hence, one can creatively design various particles with large surface area promoting chemical reactions or with easily distinguishable shapes, but still accurately predict their X_{eq} as long as D_{max} is controlled carefully. The ability to synthesize particles with shapes having distinctive and predictable X_{eq} can also lead to accurate and passive purification of such particles based on X_{eq} differences.[14,18,19]

The origin of dissimilar behavior between the asymmetric disk (h-particle) and cylinder (doublets) is still not clear. Presumably, however, it can be attributed to (i) even greater asymmetry of h-particles compared to asymmetric doublets, (ii) different lift forces that rod-like and plate-like particles would experience, and/or (iii) additional complex flows in asymmetric void areas of an h-particle's cross-section, introducing additional lift force. Further study would be required to clarify this discrepancy.

Finally, rotational behavior of anisotropic particles in shear flow was investigated using doublets. Doublets resided longer at the horizontal orientation and least at the vertical orientation during the course of rotation. This behavior greatly resembles the classic Jeffrey orbits.[20] Figure 3(a) shows that the nondimensionalized rotational period, $T_p \cdot \gamma$, increased with D_{max}, but was independent of AR (inset). Here, $\gamma = \frac{u_m}{W/2}$ is an average shear rate of the channel flow. This trend agreed well with the previous numerical analysis, reporting an increase in Jeffrey orbit period with increasing length of rod-like fibers in shear flow.[21] Moreover, the ratio between the time that the doublet spent at horizontal orientations, T_s, and T_p was found to be proportional to D_{max}, suggesting that the cylinders with larger D_{max} would reside longer at a horizontal orientation and recover that orientation more rapidly than the smaller particles. This longer residence time and rapid recovery of preferred orientation would particularly benefit applications, requiring accurate orientation control for encoded shape- or pattern-recognition. Furthermore, the sheathless particle manipulating ability should have great potential to enable high-throughput multiplexed particle-based bioassays by integrating a massively parallel focusing system[10] with a wide-field of view optical detection technique.[22]

In conclusion, we have found that inertial effects can be utilized to focus nonspherical microparticles at uniform lateral and vertical locations. For most cases, the cross-sectional shape does not significantly contribute to differences in X_{eq}. Instead, among many other particle dimensions, we found that D_{max} determines X_{eq} and can be used to predict the behavior of the flowing particles. Thus, particles with various shapes (e.g., shapes that have large surface areas allowing rapid chemical reaction) can be designed, passively focused, and used for high-throughput multiplex bioassays. Furthermore, it is found that elongated particles preferred the horizontal orientation as they rotate, suggesting that the particles with larger D_{max} would be more useful for applications requiring accurate orientation control for reading of patterns on the particle surface.

The authors thank Henry Tse, Mahdokht Masaeli, Wook Park, and Richard Yau for their help. This work is partially supported by National Science Foundation (Grant No. 0930501) and by the Korea Science and Engineering Foundation (Grant No. 2010-0017860) funded by the Korea government (MEST).

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