Gravity Driven Deterministic Lateral Displacement for Particle Separation in Microfluidic Devices

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ABSTRACT: We investigate the two-dimensional continuous size-based separation of suspended particles in gravity-driven deterministic lateral displacement (g-DLD) devices. The suspended particles are driven through a periodic array of cylindrical obstacles under the action of gravity. We perform experiments covering the entire range of forcing orientations with respect to the array of obstacles and identify specific forcing angles that would lead to vector separation, in which different particles migrate, on an average, in different directions. A simple model, based on the lateral displacement induced on the trajectory of a particle by irreversible particle–obstacle interactions, accurately predicts the dependence of the migration angle on the forcing direction. The results provide design guidance for the development of g-DLD devices. We observe directional locking, which strongly depends on the size of the particle and suggests that relatively small forcing angles are well suited for size-fractionation purposes. We demonstrate excellent separation resolution for a binary mixture of particles at relatively small forcing angles, that is, forcing angles that are close to but smaller than the first transition angle of the larger particles in the mixture.

A number of standard separation technologies have been scaled down to microfluidic devices, seeking faster processing times, reduced consumption, multidimensional and continuous operation, and the potential for integration into microtot-al-analysis systems.1–5 Successfully miniaturized techniques include electrophoretic and dielectrophoretic methods, hydrodynamic and size-exclusion chromatography, and various flow-field-fractionation systems.6–19 There has also been a growing number of novel separation strategies that aim to exploit the specific advantages of microfluidic platforms, such as the possibility to design topographic structures to act as the stationary phase, which could be tailored for specific applications.20–27 In this case, available microfabrication methods offer unprecedented control on the geometry and surface chemistry of the stationary phase. Periodic arrays of obstacles, for example, can be fabricated with characteristic length scales that are comparable to the size of the different components present in many applications, such as DNA fragments, blood constituents, and other biological materials.28–33 Deterministic lateral displacement (DLD) is one such novel method in which different components of a mixture migrate in different directions as the suspension flows through an array of cylindrical posts.32 Among the most important advantages of DLD separation devices, are the two-dimensional and continuous character of the separation3 and the potential for high-throughput due to the proven deterministic nature of the underlying separation mechanism.33 DLD separations have been successfully implemented in a variety of applications, including the fractionation of a number of different biological samples.34–41

Recently, we have used theoretical models, simulations, and macroscopic experiments to show the potential of an alternative operation mode for DLD, namely the use of a constant force to drive the suspended components through the obstacle array in a quiescent fluid.42–45 Here, we demonstrate for the first time, the separation of microparticles using such force-driven deterministic lateral displacement (f-DLD) in a microfluidic device. Specifically, we use gravity as the driving force moving the particles through a square array of cylindrical obstacles and therefore call this method gravity-driven deterministic lateral displacement (g-DLD). We performed experiments that span the whole range of force orientations relative to the obstacle array and were able to identify specific forcing angles that would lead to high separation efficiency. In fact, we show that several forcing angles induce vector chromatography, in which different particles migrate, on an average, at different angles. The results are in excellent agreement with a simple collision model based on short-range hard-core repulsive interactions between the particle and the cylindrical obstacles that can be attributed to surface roughness or other irreversible effects.42,43

EXPERIMENTS

Materials and Microfabrication. Silica particles with a density of 2 g/cm³ and average diameter 4.32 μm (Bangs Laboratories, Inc., CA) and 10, 15, and 20 μm (Corpuscular Inc., NY) were used. The stationary phase consisted of a square array of cylindrical posts, with their diameter (and the spacing between them) comparable to the largest particles used in the experiments (see Figure 1). The post arrays were written on a photomask (FineLine Imaging Inc., CO) and transferred to a photoresist (SU8 3025, Microchem Corp., MA) spun coated...
on a microscope glass slide (Fisher Scientific, Inc., PA), using standard photolithographic techniques in a clean room. The thickness of the photoresist and, as a result, the height of the resulting posts, were approximately 40 \( \mu m \). The profile of a fabricated array of obstacles obtained with the 3D Laser Scanning Microscope VK-X100/X200 (Keyence Corp., Japan) is shown in Figure 1. The measured diameter of the obstacles is \( 2R = 17.5 \mu m \) and the lattice size is \( l = 40 \mu m \).

**Experimental Setup and Imaging.** A well surrounding the array of obstacles is created using a double sided adhesive tape (Grace Bio-Labs, Inc., OR), as schematically shown in Figure 2. The well area includes both the array of obstacles as well as obstacle-free regions. The height of the well is set by the adhesive tape and is approximately 120 \( \mu m \). The suspensions of \( \mu m \) particles ranging between 0.3 and 5 \( \mu m \) are introduced into the well area without creating disturbances. A calibration scale was used to track particles moving through the array of obstacles without disturbing the system. A calibration scale was used to track particles in the desired size range in each of the experiments. For each forcing angle, we track approximately 20–30 different particles of the same size both in the obstacle-free region as well as inside the array. We only consider particles that travel at least 100 \( \mu m \) in the forcing direction to reduce fluctuations in the average migration angle measured in each trajectory. Finally, we use the trajectories inside the obstacle array to calculate the average migration angle relative to the obstacle array, \( \alpha \), as well as its standard deviation. The definition of the migration and forcing angles (as well as the coordinate axes) are shown in Figure 1. The forcing angle is the angle between the applied force (gravity) and the matrix of obstacles (x-axis in Figure 1).

The migration angle is defined as the angle between the average direction of motion of the particles and the matrix of obstacles.

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**RESULTS AND DISCUSSION**

**Gravity Driven Migration and Directional Locking.** In Figure 3, we present the average migration angle, \( \alpha \), as a function of the forcing angle, \( \theta \), for all the particle sizes and the entire range of forcing directions. Let us mention that each migration angle is obtained from independent experiments at a given forcing angle, and both average angles are determined from the motion of the particles inside and outside the array of obstacles, respectively. Furthermore, the different experiments performed for a given particle size are not performed in any particular order of the forcing angle. In all cases, except for the smallest particles, we notice that there are intervals of constant migration angles connected by sudden transitions. In fact, the migration angles exhibit directional locking into lattice directions (represented in the figure by horizontal solid segments). The lattice directions are labeled according to their lattice vector \( [p,q] \), which also indicates the periodicity. The transitions between locking directions in the migration angle are generally sharp, which result in a structure similar to the Devil’s staircases characteristic of analogous phase-locking systems.\(^4^4\)

We note that the Peclet number in the experiments, calculated using the average velocity of the particles in the obstacle-free region and the theoretical bulk diffusivity, ranges from \( O(10^2) \) to \( O(10^3) \), with the average velocity of the particles ranging between 0.3 and 5 \( \mu m/s \). Interestingly, the locking behavior is analogous to that observed at significantly higher Peclet numbers in macroscopic experiments.\(^4^3\) On the other hand, writing the Peclet number in terms of the external force acting on the particles, \( \text{Pe} = Fa/kT \propto a^3 \) (where \( F \) is the...
force acting on the particles, $a$ is the radius of the particle, $k$ is the Boltzmann constant, and $T$ is the absolute temperature), it becomes clear that $a \ll 1 \mu m$ would lead to diffusion dominated transport and low separation resolution, unless a larger external force drives the separation, e.g., using larger fluid-particle density contrasts or centrifugal methods.\textsuperscript{46} Furthermore, the results also suggest that for a forcing direction $\theta$ particles from the rest at a number of forcing directions. This is indicative of the potential to separate these small particles,\textsuperscript{3,1} but the largest, 20 $\mu m$ particles, would move very close to the forcing direction after a sequence of independent particle—obstacle encounters or collisions.\textsuperscript{42}

We model these collisions by approximating the effect of all the short-range non-hydrodynamic interactions between the particle and the obstacle with a hard-core repulsive potential. Therefore, in this model there is a single parameter $\varepsilon$, which corresponds to the effective range of the repulsive potential. A particle that moves past a fixed obstacle would experience this repulsive force only if the separation between the two surfaces reaches the size of the repulsive core, $\varepsilon$. The minimum separation between the surfaces during a particle—obstacle collision is dictated by the initial offset (or impact parameter) of the particle with respect to a line parallel to the external force that goes through the center of the obstacle. There is a one-to-one correspondence between the range of the repulsive potential $\varepsilon$ and the value of the offset that results in a minimum separation that is exactly $\varepsilon$, i.e., the critical offset, $b^\ast$.\textsuperscript{42}

Then, all possible particle—obstacle collisions can be classified into reversible and irreversible (touching) collisions. Reversible collisions correspond to initial offsets that are larger than the critical value. In this case, the particle trajectories are symmetric and there is no net lateral displacement resulting from the collision. Touching or irreversible collisions occur when the initial offset is smaller than the critical value. In this case, the collisions lead to a net lateral displacement due to the hard-core repulsive interaction between the particle and the obstacle. The presence of a critical offset and the resulting net lateral displacement from touching collisions leads to the observed directional locking, as schematically shown in Figure 4. Specifically, we represent the motion of particles of two different sizes. Both types of particles are locked with a

Separation Mechanism and Deterministic Model. In order to describe the gravity driven motion of particles through an array of obstacles we use a simple model in which a suspended particle is assumed to interact with a single obstacle at a time (dilute approximation), and its trajectory is obtained as

![Figure 3. Average migration angle as a function of the forcing direction for particles of different size. The solid segments show the migration angle corresponding to the indicated lattice directions. The diagonal dashed line represents $\alpha = \theta$.](image)

![Figure 4. Schematic trajectories of 4.32 $\mu m$ (green, left) and 15 $\mu m$ (red, right) particles colliding with two consecutive cylindrical posts (black) of 20 $\mu m$, separated center to center by a distance $l$. The driving angles are $\theta = 5^\circ$ (a), $\theta = 10^\circ$ (b), and $\theta = 20^\circ$ (c). The dotted circles show the trajectories of the particles in the absence of obstacles. The two particles have two different values of the impact parameter, $b_0$. Initially, both particles move with $a = 0^\circ$. Each particle then transitions out of this locking direction when $b_0 < l \sin(\theta)$. Transitions occur at different $\theta$. The middle cartoon is representative of a separative case.](image)
migration angle $\alpha = 0^\circ$ for forcing angles below the first transition angle $\theta_c$ at which $b_c = l \sin(\theta_c)$, where $l$ is the center to center distance between the obstacles. Figure 4 also illustrates the separation of such a binary mixture at intermediate angles, when the components have different critical offsets. Figure 4 also shows the case in which the larger particles have a larger critical angle, as observed in the experiments. Therefore, there is a range of intermediate angles for which only the larger particles are still locked moving along a line of obstacles with $\alpha = 0^\circ$. This simple model was successfully used to explain the deterministic motion of large particles both in model macroscopic experiments as well as in pinched geometries. It is the cumulative action of these touching collisions and the corresponding lateral displacements that lead to an average migration angle that is different from the direction of the driving force.

Let us mention that small inertia effects (including both particle and fluid inertia) could also lead to irreversible collisions with a net lateral displacement. However, the Reynolds number in the experiments reported here is $Re \lesssim 10^{-5}$, and therefore, inertia effects are expected to be negligible. In addition, the simple collision model described above could implicitly incorporate inertia effects into the irreversible collisions and the corresponding critical offset. In fact, this simple model accurately described the behavior of the migration angle in previous macroscopic experiments with $Re \sim 1$.

In Figures 5–8, we present the average migration angle as a function of the orientation of the driving force for 4.32, 10, 15, and 20 $\mu$m particles, respectively. We compare the experimental results with the migration angles predicted by the proposed model. The value of the critical impact parameter in each case is obtained by fitting the experimental data. The dashed lines in the figures represent the uncertainty in the fitted value of the critical impact parameter.

Figure 5. Average migration angle as a function of the forcing angle for 4.32 $\mu$m particles. The solid line corresponds to the model discussed in the text, with the critical impact parameter $b_c = (5.64 \pm 0.04) \mu$m obtained as a fitting parameter. The diagonal dashed line represents $\alpha = \theta$. Error bars show the uncertainty in the average forcing and migration angles.

Figure 6. Average migration angle as a function of the forcing angle for 10 $\mu$m particles. The solid line corresponds to the model discussed in the text, with the critical impact parameter $b_c = (8.4 \pm 0.35) \mu$m obtained as a fitting parameter. The diagonal dashed line represents $\alpha = \theta$. Error bars show the uncertainty in the average forcing and migration angles.

Figure 7. Average migration angle as a function of the forcing angle for 15 $\mu$m particles. The solid line corresponds to the model discussed in the text, with the critical impact parameter $b_c = (11.2 \pm 0.1) \mu$m obtained as a fitting parameter. The diagonal dashed line represents $\alpha = \theta$. Error bars show the uncertainty in the average forcing and migration angles.
In all cases, we observe excellent agreement between the model and the experimental data. Moreover, we observe that the measured migration angles show larger fluctuations (variance) close to the transition angles, which is consistent with the discontinuous nature of these transitions as predicted by the collision model. Let us mention that $b_c$ is the only fitting parameter for each particle size, and therefore, all the locking directions predicted by the model (for a given particle size), as well as the angles at which the migration angle transitions between two lattice directions, are determined once the value of the critical impact parameter is obtained. We observe that the values obtained for the critical impact parameter increase with the size of the particle. The sharp transitions in the migration angle observed at specific forcing directions and the fact that the critical impact parameter depends on the size of the particle, indicate the potential for size-based separation.

Separation Resolution. We have also investigated the separation resolution in a binary mixture of 4.32 and 15 μm particles. In Figure 9, we present the average migration angles for the two components in the mixture, together with their standard deviation (error bars). We note that the migration angles are in close agreement with those obtained in the single component experiments corresponding to these particles, shown in Figures 5 and 7. The solid lines in Figure 9 correspond, in fact, to the critical impact parameters obtained by fitting the data of the single component experiments. These experiments with a binary mixture also allow us to quantify the separation resolution and to identify favorable forcing angles.

In Figure 10 we present the angular resolution of the binary mixture, $R_\theta$ defined by

$$R_\theta = \frac{\Delta \alpha}{2(\sigma_1 + \sigma_2)}$$

where $\Delta \alpha = |\alpha_1 - \alpha_2|$ is the difference in migration angles between the two components and $\sigma_1$, $\sigma_2$ are the standard deviations measured for the corresponding migration angles.

We observe excellent separation resolution for forcing angles $\theta \approx 14^\circ$. This corresponds to angles close to but smaller than...
the first transition angle of the larger particles ($\theta_c \approx 16^\circ$, as discussed before). These results demonstrate the high resolution that is possible using g-DLD.

**Separation of a Multicomponent Mixture.** Finally, we performed a proof-of-concept separation experiment using a multicomponent suspension including all the particles discussed above. We select a forcing angle of $15^\circ$ based on the first transition angles observed in the single-component experiments. In Figure 11, we show a typical example of the migration trajectories observed for the different particles in the experiment. The $4.32 \mu m$ particle, as well as the 10 $\mu m$ particle, moves close to the forcing direction, as expected for these small particles from the single-component experiments. A larger particle, which is approximately 15 $\mu m$ in size also moves close to the forcing direction, but exhibits some degree of locking, in that we observe only one event in which the particle is able to move across a line of obstacles oriented along the $x$ direction. Finally, the largest particle, 20 $\mu m$ in diameter, is clearly locked into the $[1,0]$ direction, corresponding to $\alpha = 0^\circ$, as evidenced by the fact that it moves along a line of obstacles in the $x$ direction. This indicates the potential of g-DLD for high resolution separation of multicomponent mixtures.

**CONCLUSIONS**

We demonstrated that it is possible to operate deterministic lateral displacement devices and induce size-based separation by driving the particles with a uniform external force, in this case, using gravity (g-DLD). We performed microfluidic experiments at relatively large Peclet numbers and measured the average migration angle of particles of different size, covering the entire range of forcing orientations relative to a square array of cylindrical obstacles. We observe the presence of directional locking, in which the particles migrate at selected lattice directions for finite intervals of the forcing angle. We identified sharp, size-dependent transitions between consecutive locking directions of the migration angle, thus demonstrating the potential for high resolution size-based continuous separation of particles.

We described the migration angle as a function of the forcing direction using a simple model, based on the lateral displacement that occurs during the collision of a single particle with a fixed obstacle, in the presence of a short-range hard-core repulsive interaction. The model accurately predicts the migration angle over the entire range of forcing directions, which exhibits a Devil’s staircase type of structure characteristic of phase-locking systems. Also consistent with the proposed model are the large uncertainties observed in the migration angle close to the transition angles. The proposed model predicts discontinuous jumps in the migration angle, and large fluctuations are expected close to the transition.

We demonstrated a high resolution of separation in binary mixtures using g-DLD. We further showed that the method can also be used to fractionate multicomponent suspensions. The results presented here also provide design guidance for the development of g-DLD devices. We observed that the first transition angle depends strongly on the size of the particle, and hence, we suggest that the region of relatively small force orientations, where the critical transition angles for the different particles occur, is well-suited for separation purposes. In fact, we demonstrate excellent separation resolution for a binary mixture of particles for forcing angles that are close to but smaller than the first transition angle of the larger component. We also observe differences in the average migration speed (not presented here), which would add to the resolution capacity of the method. Finally, we point out that according to the collision model used here, and the size-dependent value of the critical transition angles observed from the experiments, a single line of obstacles would be able to fractionate a binary mixture of particles. Specifically, a single line of obstacles oriented at an angle $\theta$ with respect to the driving force would deflect those particles with a larger first critical angle $\theta_c > \theta$, but particles with a smaller first critical angle would simply pass through the line of obstacles. Therefore, a complex multicomponent mixture could be fractionated using a series of such single lines oriented at successively smaller angles with respect to the forcing direction.

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