Directional locking in deterministic lateral-displacement microfluidic separation systems

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We analyze the trajectory of suspended spherical particles moving through a square array of obstacles, in the deterministic limit and at zero Reynolds number. We show that in the dilute approximation of widely separated obstacles, the average motion of the particles is equivalent to the trajectory followed by a point particle moving through an array of obstacles with an effective radius. The effective radius accounts for the hydrodynamic as well as short-range repulsive nonhydrodynamic interactions between the suspended particles and the obstacles, and is equal to the critical offset at which particle trajectories become irreversible. Using this equivalent system we demonstrate the presence of directional locking in the trajectory of the particles and derive an inequality that accurately describes the “devil’s staircase” type of structure observed in the migration angle as a function of the forcing direction. We use these results to determine the optimum resolution in the fractionation of binary mixtures using deterministic lateral-displacement microfluidic separation systems as well as to comment on the collision frequencies when the arrays of posts are utilized as immunocapture devices.

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I. INTRODUCTION

One of the essential unit operations in micro-total-analysis-systems (μTAS) is the separation of species for downstream analysis. Early microfluidic separation strategies involved miniaturization of different macroscopic separation methods, e.g., size exclusion [1] and hydrodynamic chromatography [2]. However, current microfabrication techniques enable the design and fabrication of precisely controlled microstructures to act as separation media, in contrast with the random microstructure common in conventional separation media. For example, in “entropic trapping,” a channel with alternating thick and thin regions was used to separate DNA molecules by size based on the time they spend in the entropic traps (thick regions) [3]. In “pinched flow fractionation,” species entering a constriction and exiting into a sudden expansion experience a lateral displacement from their trajectories that is a function of their size [4]. Deterministic lateral displacement (DLD) employs a periodic array of solid obstacles, through which species of different sizes migrate in different spatial directions in the presence of the same driving force [5]. This effect can also be achieved with a periodic array of optical traps (soft potentials instead of solid obstacles, [6,7]). Although DLD systems have been studied extensively [5,8–11], the understanding of the underlying mechanism is presented only heuristically and lacks a theoretical framework for their analysis.

We have performed numerous detailed computational and experimental studies of DLD-like systems [13–18]—where the experiments include microfluidic as well as macroscopic platforms at low Reynolds number—and have established that directional locking dictates the particle trajectories in such systems. In the context of dynamical systems, directional locking is exhibited by (and results in a dynamically rich behavior of) driven vortex lattices through periodic energy landscapes [19], electrons being transported through a periodic array of scatterers [20], simulations of colloidal particles being driven through localized array of other colloidal particles [21], simulated vortices and/or particles moving on random, quasiperiodic, and periodic substrates [22–24], as well as experimentally observed colloidal monolayers driven on quasiperiodic substrates [25].

In this work, we employ directional locking to explain the mechanism underlying separations in the DLD systems. Specifically, we present a theoretical analysis of DLD systems, involving the motion of a particle of arbitrary radius in a square array of obstacles of circular cross section. We assume a “dilute limit” for the obstacles, such that the interobstacle spacing is sufficiently large and a particle interacts with a single obstacle at a time. The field driving the particle (either a constant force, or a flow field) is assumed to be at an arbitrary angle (henceforth, the forcing angle) with respect to the principal lattice directions of the square array. We assume negligible particle as well as fluid inertia, and infinite Péclet number (non-Brownian particles, deterministic trajectories). We show that under the dilute approximation, the particle-obstacle interaction can be replaced by a point particle moving in straight lines past an obstacle with an effective radius equal to a critical offset. The critical offset is the offset at which particle-obstacle collisions become irreversible and can be interpreted as a length scale that characterizes the effect of short-range repulsive nonhydrodynamic interactions between the particles and the obstacles. (Previous work presents a detailed discussion of the critical offset, both computationally [14] and theoretically [26].)

Using this equivalent representation of the system under the dilute approximation, the problem of calculating the particle trajectories reduces to simple geometric manipulations. We derive a periodicity criterion for particle trajectories in terms of

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the design parameters of the system, namely, the critical offset, the forcing angle, and the interobstacle spacing in the square array. The periodicity criterion yields the experimentally and computationally observed directional locking behavior.

Further, we show that the same framework can be used to determine the properties of arrays of posts operated as immunocapture devices to collect rare cells. Unlike DLD, an immunocapture device uses particle-obstacle binding events to capture cells. Therefore, the optimal strategy is to maximize the frequency of particle-obstacle collisions. We show that the frequency of particle-obstacle collisions emerges naturally from our analysis and is in agreement with recent calculations by Kirby and co-workers [12].

The article is organized as follows: In Sec. II we introduce the system under consideration, the system variables, and the dilute approximation. We also explain the model for short-range repulsive nonhydrodynamic interactions leading to the definition of the critical offset \( b_c \), and establish an abstract model for the particle-obstacle pair. In Sec. III A, we use the abstract model to derive a periodicity condition for particle trajectories. We apply the periodicity condition to derive expressions for the simplest locking directions in Secs. III B 1 and III B 2 . In Sec. IV A, we use the periodicity condition corresponding to particles exhibiting the simplest directional locking behavior. We comment on the resolution of separation attained by the particle from the obstacle is denoted \( b_{in} \) and \( b_{out} \), respectively. The dimensionless minimum surface-to-surface separation attained by the particle from the obstacle is denoted by \( \xi_{min} \) in the figure. The functional relationship between \( b_{in} \) and \( \xi_{min} \) explicitly incorporates the hydrodynamic mobility

II. SYSTEM DESCRIPTION, ASSUMPTIONS, AND ABSTRACTIONS

Figure 1 depicts the system under investigation. We consider a suspended spherical particle of radius \( a \) negotiating a square array of obstacles with circular cross section of radius \( b \), under the action of a driving field \( F \) (either a constant force or a uniform flow away from the lattice). The field is oriented at an angle \( \theta \) with respect to one of the principal axes of the array (say, the \( X \) axis as shown in the figure). The lattice spacing is \( \ell \). The domain of the “forcing angle” is restricted to \( \theta \in [0, \pi] \), since the system possesses a reflection symmetry in the \( X = Y \) line.

We work in the Stokes regime, i.e., we neglect fluid inertia (vanishingly small Reynolds number) and particle inertia (vanishingly small Stokes number). We consider the deterministic limit (infinitely large Péclet number, non-Brownian limit). Further, in DLD microdevices, the enclosing walls perpendicular to the \( Z \) axis (i.e., walls parallel to the plane of the paper) screen the hydrodynamic interactions between the particle and distant obstacles. Therefore, we assume that the lattice spacing \( \ell \) is sufficiently larger than the \( Z \) spacing between the walls, such that, to a good approximation, we can consider the interaction between the particle and only the closest obstacle (Fig. 2, dilute approximation). Figure 2 depicts the variables of the problem; the incoming and outgoing offsets are denoted by \( b_{in} \) and \( b_{out} \), respectively. The dimensionless minimum surface-to-surface separation attained by the particle from the obstacle is denoted by \( \xi_{min} \) in the figure. The functional relationship between \( b_{in} \) and \( \xi_{min} \) explicitly incorporates the hydrodynamic mobility

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**FIG. 1.** (Color online) (a) A spherical particle of radius \( a \) negotiating a portion of a square array of obstacles of circular cross section with radius \( b \) (adapted from [14]): the length of a unit cell is \( \ell \), the driving field \( F \), oriented at an angle \( \theta \) as shown, drives the particle through the array. The principal lattice directions are indicated with Cartesian axes \( X \) and \( Y \). (b) A few example particle trajectories exhibiting directional locking (adapted from [14]): results of Stokesian dynamics simulations with \( a = b, \ell = 5a \) and the range of nonhydrodynamic interactions \( \epsilon = 10^{-3} \) (see Sec. II for a discussion on nonhydrodynamic interactions). Counterclockwise, from \( X \) axis to \( Y \) axis, the trajectories can be seen to be locked in directions \([1,0],[3,1],[1,1],[2,3],[1,2]\) (the inset shows the migration directions). The dot-dashed lines are to guide the eye and highlight \([3,1] \) and \([2,3] \) locking directions.

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of the particle around the fixed obstacle, thereby taking into consideration the hydrodynamic interactions [26].

Apart from the hydrodynamic interactions between the particle and the obstacle that arise from their finite size, we also take into account the effect of short-range repulsive non-hydrodynamic interactions such as solid-solid contact due to surface roughness, electrostatic repulsion, steric repulsion, etc. A simple and effective model for these nonhydrodynamic interactions is to treat them as leading to a hard-wall potential with a given dimensionless range \( \epsilon \), such that it creates a hard shell around the obstacle, and the particle surface cannot approach the obstacle surface closer than \( \epsilon \). We have shown elsewhere that the presence of such nonhydrodynamic repulsion leads to the occurrence of a critical trajectory that corresponds to \( \xi_{\text{min}} = \epsilon \), where the particle grazes the obstacle and defines the critical trajectory; and (c) the trajectories that would correspond to \( \xi_{\text{min}} < \epsilon \) in the absence of nonhydrodynamic interactions. However, in this last case, the particles are forced to circumnavigate the obstacle by maintaining a constant separation equal to \( \epsilon \) on the approaching side due to the hard-core potential. The last group of trajectories collapse onto the critical trajectory downstream of the obstacle, breaking their fore-aft symmetry. Thus, the critical trajectory [of type (b) described above] defines the critical offset \( b_c \) and the range of the interactions \( \epsilon \), such that the corresponding minimum separation is the range of the nonhydrodynamic interactions (i.e., \( \xi_{\text{min},c} = \epsilon \)). Therefore, in the presence of short-range repulsive nonhydrodynamic interactions, the relationship between \( b_{\text{in}} \) and \( \xi_{\text{min}} \) is equivalent to the relationship between the critical offset \( b_c \) and the range of the interactions \( \epsilon \).

Using the hard-wall model for the nonhydrodynamic interactions combined with the dilute assumption, we can thus replace the physical particle-obstacle system with an equivalent abstract system shown in figure 3(b). The obstacle radius \( b \) can be replaced by \( b_c \) and the particle can be reduced to a point particle. As shown, since the particle trajectories with incoming impact parameter \( b_{\text{in}} < b_c \) remain fore-aft symmetric, one can replace them with straight lines uninfluenced by the obstacle. The trajectories with \( b_{\text{in}} < b_c \) (that would intersect the new, abstract obstacle), get laterally displaced by \( (b_c - b_{\text{in}}) \), and continue as tangents to the obstacle parallel to the forcing direction. It is interesting to note that both the hydrodynamic and nonhydrodynamic interactions are incorporated in the single parameter \( b_c \).

III. MATHEMATICAL DESCRIPTION OF DIRECTIONAL LOCKING

The defining feature of deterministic lateral displacement is directional locking of particle trajectories [see Fig. 1(b)]. In a square array of obstacles (e.g., DLD devices), the particle follows a periodic trajectory with a periodicity of (say) \( p \) lattice units in the \( X \) direction and \( q \) lattice units in the \( Y \) direction for a range of values of \( \theta \), and some integers \( p \) and \( q \). In such a case, the trajectory is said to be locked in the \( [p,q] \) direction for that range of values of \( \theta \). The migration angle \( \alpha \) is
FIG. 4. (Color online) Schematic depicting three possibilities leading to periodic trajectories (see text). In (a) and (b), the trajectories repeat after $p$ obstacles along the $X$ axis and $q$ obstacles along the $Y$ axis. In (c), the period along the $X$ axis is $(p_1 + p_2)$ and that along the $Y$ axis is $(q_1 + q_2)$.

defined by

$$\tan \alpha = \frac{q}{p}.$$ 

Note that $\tan \alpha$ is synonymous with “winding number” in the parlance of nonlinear dynamical systems [40].

Equipped with the abstraction of the particle-obstacle pair described in the previous section, we now consider a square array of such obstacles with radius $b_c$, separated by the lattice spacing $\ell$. Figure 4 shows a schematic of the equivalent system with straight-line trajectories between two successive particle-obstacle collisions that occur $p$ lattice units apart in the $X$ direction and $q$ lattice units apart in the $Y$ direction, thereby representing a $[p,q]$ periodic trajectory. The figure shows two coordinate systems, the $XY$ system with its axes parallel to the principal axes of the lattice as well as the $xy$ system with $x$ axis parallel to the direction of the driving field $F$. Since we have a point-particle traversing in a straight line parallel to the direction of the driving field, it is evident that a particle-obstacle interaction (a collision) is possible only if the particle trajectory intersects the obstacle, i.e., only if the distance $d$ to the obstacle center from the trajectory is less than the obstacle radius. Note that, as shown in Fig. 4, $d$ is the same as the initial offset $b_{in}$ for the corresponding obstacle. It is evident that there are only two kinds of collisions with respect to the sign of the $y$ coordinate of the point of collision, $\text{top} (y > 0)$ and $\text{bottom} (y < 0)$ ones. Therefore, a given periodic trajectory can exhibit periodicity in exactly three distinct modes: (a) all successive collisions satisfy $y > 0$ [top-top collisions, Fig. 4(a)], (b) all successive collisions satisfy $y < 0$ [bottom-bottom collisions, Fig. 4(b)], or (c) collisions alternately satisfy $y > 0$ and $y < 0$ [top-bottom-top collisions or equivalently, bottom-top-bottom collisions, Fig. 4(c)].

As shown in Fig. 4, we choose an arbitrary obstacle, which has undergone a collision, as the origin of the $XY$ system. In the case of top-top and bottom-bottom collisions [Figs. 4(a) and 4(b)], we assume that the period is $p$ in the $X$
direction, and $q$ in the $Y$ direction, for some integers $p$ and $q$. Hence the coordinates of the center of the next obstacle are $(p\ell,q\ell)$ in Figs. 4(a) and 4(b). In the case of periodic trajectories arising from top-bottom-top (equivalently, bottom-top-bottom) collisions [Fig. 4(c)], we assume that $p_1$ and $p_2$ are the alternate periods in the X direction, while $q_1$ and $q_2$ are the periods in the Y direction, again for some integers $p_1, p_2, q_1, q_2$.

A. Periodicity condition

For a top-top collision, the equation of the trajectory in the $XY$ system is

$$Y = X \tan \theta + b_c \sec \theta.$$  

Since the center of the next obstacle $(p\ell,q\ell)$ lies in the lower half-plane of the trajectory, it satisfies $q\ell < p\ell \tan \theta + b_c \sec \theta$. Therefore, the normal distance between the obstacle center and the trajectory in the case of top-top collisions is

$$d_{TT} = \frac{p\ell \tan \theta - q\ell}{\sqrt{1 + \tan^2 \theta}} = p\ell \sin \theta - q\ell \cos \theta + b_c.$$  

(1)

For a top-bottom collision, in the $xy$ system centered on the second obstacle, the initial offset must satisfy $0 \leq b_{in} = d_{TT} < b_c$. Therefore, Eq. (1) yields $0 < q\ell \cos \theta - p\ell \sin \theta \leq b_c$. This inequality can be rephrased as

$$0 < |\sin(\alpha - \theta)| \leq \frac{b_c}{s\ell},$$  

(2)

where $s([p,q]) = \sqrt{p^2 + q^2}$. The same critical offset $b_c$ is used in both cases, which corresponds to a particle of the same size as the obstacle $(a = b)$ and a range of nonhydrodynamic interactions $\epsilon = 10^{-3} a^2$ (the interobstacle spacing is $\ell = 5 a$). The same figure also shows an agreement between data from microfluidic experiments [18] and theory (the ratio $b_c/\ell$ corresponding to the experimental data shown in the figure is approximately equal to that used in theoretical calculations).

B. Transitions from and to periodicities

The transition forcing angles from one locked migration direction to the next as well as the migration angle itself can be computed by treating Eqs. (2) and (4) as equalities. We have noted earlier that for each periodicity $[p,q]$ corresponding to a migration angle $\tan \alpha = q/p$, two distinct transition angles $\theta_1$ and $\theta_2$ can be obtained from the equalities corresponding to Eqs. (2) and (4), by solving $\sin(\alpha - \theta) = b_c/s\ell$ and $\sin(\theta - \alpha) = b_c/s\ell$, respectively. Then, consider two consecutive locking directions $[p',q']$ and $[p,q]$, with the primed direction representing the lower step in the staircase (i.e., $\alpha' < \alpha$), as shown in schematic in Fig. 6. If the periodicities do not

In the above double inequalities, only one side becomes relevant depending on the relative magnitudes of $\theta$ and $\theta_c$. If $\theta < \theta_c$ we have $\sin(\alpha - \theta) > 0$, and inequality (2) is relevant, whereas in the case of $\theta > \theta_c$, the inequality (4) is the appropriate choice.

Thus, Eqs. (2) and (4) together describe the periodic behavior of the particle trajectories in the lattice. Both can be combined into a single inequality as

$$|\sin(\alpha - \theta)| \leq \frac{b_c}{s\ell}.$$  

(5)

We observe that the values of $\theta$ satisfying inequality (5) are symmetric about $\theta = \theta_c$. Which means, if $\theta_1$ and $\theta_2$ satisfy the equalities corresponding to Eqs. (2) and (4), respectively, then

$$\alpha = \frac{\theta_1 + \theta_2}{2}.$$  

Further, note that Eqs. (2) and (4) are necessary conditions for periodicity of a trajectory in a strict mathematical sense, but they are not sufficient conditions. Which means, if a trajectory is known to exhibit $[p,q]$ locking, then the pair $[p,q]$ must satisfy Eq. (2) or Eq. (4) depending upon the relative magnitudes of $\alpha$ and $\theta_c$. Conversely, there may exist many integer pairs $[p,q]$ which satisfy Eq. (2) or Eq. (4) for a given forcing angle $\theta$ and parameters $b_c$ and $\ell$. However, physically, the trajectory would become periodic after a collision with the obstacle closest to the one at the origin, i.e., only if the pair $[p,q]$ is the closest possible pair to the origin $[0,0]$ satisfying the inequalities. Thus, the converse problem of finding the periodicity $[p,q]$ lies in the domain of mixed-integer minimization problems, stated as minimize $\sqrt{p^2 + q^2}$ for integers $p$ and $q$ subject to the constraints $p > 0$, $q \geq 0$, and the inequalities (2) and (4).
satisfy either of the two inequalities (2) and (4) simultaneously.

\[
\alpha > \theta \\
\alpha < \theta
\]

simultaneously satisfy the inequalities (2) and (4), then there is no overlap between the two steps as shown in Fig. 6(a). Therefore, the transition from \([p', q']\) to \([p, q]\) takes place at the end of the lower step, given by \(\theta = \theta_c\) (‘*’ point in the figure). But since there is no overlap between the steps, this has to be the angle at the beginning of the \([p, q]\) step, given by \(\theta = \tilde{\theta}_c\) (‘o’ point in the figure). Therefore, this is the case when both critical angles are equal \(\tilde{\theta}_c = \theta_c\), and either equality corresponding to Eq. (2) or (4) gives the same result.

An example of such a transition is seen in Fig. 5 from [3, 1] periodicity to [2, 1] periodicity. Although \(s([2, 1]) = \sqrt{5} < s([3, 1]) = \sqrt{10}\), there is no forcing direction \(\theta\) for which both inequalities are satisfied, and there is no overlap between the corresponding steps. If there is an overlap between the steps as shown in Fig. 6(b), the two inequalities are satisfied for the forcing directions \(\theta\) in the overlap region. Then in the region of overlap, the step with a smaller \(s\) is realized, thus satisfying the physical requirement that the trajectory becomes periodic with the shortest period. An example of this type of transition is that from [4, 1] periodicity to [3, 1] periodicity, shown in Fig. 5. In this case, since \(s([3, 1]) = \sqrt{10} < s([4, 1]) = \sqrt{17}\), the transition occurs before \(\theta = \theta_c([4, 1])\) (the end of the [4, 1] step). Therefore, in the case of an overlap between the steps,

(1) if \(s < s'\), then the transition occurs at the beginning of \([p, q]\) [equality in Eq. (2)] at the ‘o’ point [in Fig. 6(b)];

(2) otherwise, the transition occurs at the end of \([p', q']\) at the “*” point in the figure.

We apply the above argument to the transitions from and to [1, 0] and [1, 1] directions, respectively, the simplest possible locking directions:

The transition from [1, 0]: Since [1, 0] gives the smallest possible \(s\) value (\(s = 1\)), the transition always occurs at the end of [1, 0] step, i.e., using the equality in Eq. (4),

\[
\sin(\theta_F - 0) = \sin(\theta_F) = \frac{b_\ell}{\ell},
\]

where \(\theta_F\) is defined as the first transition angle.

The transition to [1, 1]: The final locking direction [1, 1] gives the second smallest possible \(s\) value (\(s = \sqrt{2}\)). Therefore, the transition to the [1, 1] direction always occurs at the beginning of the [1, 1] step, i.e., using the equality in Eq. (2),

\[
\sin\left(\frac{\pi}{4} - \theta_L\right) = \frac{b_\ell}{\sqrt{2}\ell},
\]

where \(\theta_L\) is the last transition angle. The only exception to Eq. (7) is when there is a direct transition from [1, 0] to [1, 1], which is the case of a one-step staircase. In this case, \(s = 1 < s = 2\), the transition takes place at \(\theta = \theta_c(\ell)\) (the end of the [1, 0] step), which may or may not be the same as \(\theta = \theta_L\) (the beginning of the [1, 1] step).

1. First locking direction after [1, 0]

If the locking direction after the first transition is \([p_F, q_F]\), then

\[
|q_F \cos \theta_F - p_F \sin \theta_F| \leq \frac{b_\ell}{\ell}.
\]

However, from Eq. (6), \(\sin(\theta_F) = b_\ell/\ell\). Also, increasing \(\theta\) counterclockwise from the X to the Y axis, the first transition should be from a locking direction along the zeroth row of obstacles along the X axis (i.e., [1, 0]) to the first row of obstacles along the X axis (i.e., \([p, 1]\) for some integer \(p\)). Therefore, \(q_F = 1\) [see Fig. 10(b)]. Thus, \(|\cot \theta_F - p_F| \leq 1\). Since \(p_F\) is an integer, we get

\[
p_F = \lfloor \cot \theta_F \rfloor \ldots \lfloor . \rfloor \equiv \text{floor function}.
\]

Thus, the locked direction after the first transition is \(\tan \alpha = q_F/p_F = 1/\lfloor \cot \theta_F \rfloor\), where \(\theta_F\) is given by Eq. (6) above.
PHYSICAL REVIEW E 90, 012302 (2014)

DIRECTIONAL LOCKING IN DETERMINISTIC LATERAL-

2. Last locking direction before [1,1]

If the locking direction before the final transition is \([p_L, q_L]\), then

\[|q_L \cos \theta - p_L \sin \theta| \leq \frac{b_c}{\ell}.\]

From Eq. (7), \(\cos \theta_L - \sin \theta_L = b_c/\ell\). Further, increasing \(\theta\) counterclockwise from the X to the Y axis, the last transition from \([p_L, q_L]\) to \([q_L, q_L]\) (i.e., \([1,1]\)) should satisfy \(p_L = q_L + 1\). Thus, the above inequality becomes \(|(\frac{\sin \theta_L}{\cos \theta_L} - \sin \theta_L) - q_L| \leq 1\). Since \(q_L\) is an integer,

\[q_L = \left[\frac{\sin \theta_L}{\cos \theta_L - \sin \theta_L}\right] = \left[\tan \frac{\theta_L}{1 - \tan \theta_L}\right]. \quad (9)\]

Therefore, the locked direction before the final transition to \([1,1]\) is given as

\[\tan \alpha = q_L/p_L = \left[\frac{\tan \theta_L}{1 - \tan \theta_L}\right] + 1,\]

where \(\theta_L\) is the solution of Eq. (7). We note again that the only exception to the calculation leading to Eq. (9) is the case when the transition to \([1,1]\) occurs from \([1,0]\). In this case, the transition occurs at the corresponding \(\theta_F\) instead of \(\theta_L\).

IV. DESIGN RULES: LATERAL DISPLACEMENT (SIZE-BASED SEPARATION) AND COLLISION FREQUENCY (IMMUNOCAPTURE)

A. Simplest staircase structures

We first derive the constraints on the ratio \(b_c/\ell\) for a particle to exhibit exactly one transition \([\text{Fig. 7(a)}]\) and exactly two transitions \([\text{Fig. 7(b)}]\), based on Eq. (5) and the discussion in Sec. III. We have shown in Sec. III B that the first transition angle is given by \(\sin \theta_L = b_c/\ell\) corresponding to the transition from \([1,0]\) locking direction. Further, we noted earlier that \(\theta_L\) from Eq. (9) is not necessarily equal to \(\theta_F\), since the transition to \([1,1]\) from \([1,0]\) is an exception. Therefore, applying the constraint in Eq. (2) for \(\theta_F\) we get

\[\sin \left(\frac{\pi}{4} - \theta_F\right) \leq \frac{b_c}{\ell \sqrt{2}} \Rightarrow \tan \theta_F \leq \frac{1}{2}. \quad (10)\]

![FIG. 7. (a) One-step staircase with transition \([1,0] \rightarrow [1,1]\) at \(\theta_F\). (b) Two-step staircase \([1,0] \rightarrow [2,1] \rightarrow [1,1]\) with transitions at \(\theta_F\) and \(\theta_L\).](012302-7)

Thus, for a fixed particle radius \(a\), obstacles of size \(b\), and a range \(\epsilon\) of nonhydrodynamic interactions (i.e., for a fixed \(b_c\)), a square lattice with \(\ell \geq \sqrt{5}b\) can be constructed in which the particle exhibits a one-step staircase structure.

In the case of a two-step staircase \([\text{Fig. 7(b)}]\), the locking direction after the first transition from \([1,0]\) is \([2,1]\), which is the same as the locking direction before the final transition to \([1,1]\). Using Secs. III B 1 and III B 2,

\[\tan \alpha = \frac{1}{2} = \frac{1}{\left[\cot \theta_F\right]} = \frac{\left[\frac{\tan \theta_F}{1 - \tan \theta_F}\right]}{1 + 1} \Rightarrow \sin \theta_F = b_c/\ell.\]

The first set of equations above yields \(\left[\cot \theta_F\right] = 2\) and \(\left[1 - \tan \theta_F\right] = 1\). Thus, using \(\sin \theta_F = b_c/\ell\), we obtain

\[\frac{1}{3} < \tan \theta_F < \frac{1}{2} \leq \tan \theta_L < \frac{5}{2}, \quad (12)\]

Thus, if a square lattice satisfies Eq. (13) for a particle of radius \(a\), a critical parameter \(b_c\) (a function of \(a\), \(b\), and \(\epsilon\)) and unit cell \(\ell\), then the particle exhibits locking with a two-step staircase structure with the corresponding two transition angles satisfying Eq. (12).

B. Design constraints and separation resolution in DLD

In pairwise size-based separation, two particles of different sizes, say, \(a\) and \(a'\) (and perhaps different length scales corresponding to the range of nonhydrodynamic interactions, say \(\epsilon\) and \(\epsilon'\)) exhibit two distinct critical parameters, viz., \(b_c\) and \(b'_c\). Separation is possible at forcing angles such that the migration directions \(\tan \alpha = q/p\) and \(\tan \alpha' = q'/p'\) are distinct. Further, a larger difference between the migration directions is synonymous with a higher resolution. Thus, a simple design strategy is to maximize \(|\alpha - \alpha'|\).

By rearranging Eq. (5) as

\[|\sqrt{q^2 + p^2} \sin(\alpha - \theta)| \approx |\sqrt{q^2 + p^2} (\alpha - \theta)| \leq \frac{b_c}{\ell}, \quad (14)\]

where the last inequality results from the small angle approximation \(\sin(\alpha - \theta) \approx (\alpha - \theta)\), since \(0 < \alpha\) and \(\theta \leq \pi/4\). Similarly, a good approximation for \(|\alpha - \alpha'|\) can be obtained by combining Eq. (14) for both particles \(a\) and \(a'\),

\[|\alpha - \alpha'| \leq \frac{b_c}{(\sqrt{p^2 + q^2}) \ell} + \frac{b'_c}{(\sqrt{p'^2 + q'^2}) \ell}. \quad (15)\]

As an immediate consequence of Eq. (14), we note that the largest difference between the migration direction and the forcing direction (i.e., \(|\tan \alpha - \tan \alpha'\| \approx |(\alpha - \theta)|\) occurs before the first transition from \(\alpha = 0\) (locking \([1,0]\)) and when \(p^2 + q^2 = 1\), and it is always equal to \(|(\alpha - \theta)\| \leq b_c/\ell\). Furthermore, along with Eq. (15), we infer that the largest separation resolution between two species can be obtained when one of the species has undergone its first transition, while the other is still locked in the \([1,0]\) direction (for
example, $\theta_F < \theta < \theta_L$). This observation supports our earlier experimental inference that it is the most beneficial strategy to set the forcing angle between the first transitions ($\theta_F$ and $\theta_L$) of the two species undergoing separation [13,17,18]. The inequality, i.e., expression (15), not only gives an upper bound on the resolution, but also gives design constraints on the obstacle radius $b$ and the lattice spacing $\ell$ through the ratio $b_c/\ell$ for known locking directions $\{(p,q)\}$ and $\{(p',q')\}$, a fixed forcing angle $\theta$ and known radii of particles ($a$ and $a'$).

In the following, we illustrate this result for particles with simple staircase structures, viz., only one transition from $[1,0]$ to $[1,1]$ and two transitions $[1,0] \mapsto [2,1] \mapsto [1,1]$.

For a mixture of two species, both exhibiting one-step staircases with different transitions $\theta_F$ and $\theta_L$ satisfying Eqs. (10) and (11), it is readily understood that the forcing angle needs to be between these two values if any separation is desired. The separation resolution $|\alpha - \alpha'|$ is always $\pi/4$ in this case, since one species is always locked in $[1,0]$ periodicity, while the other is locked in $[1,1]$ periodicity for a forcing angle between $\theta_F$ and $\theta_L$.

For a mixture of one species exhibiting a one-step staircase (say, for particles of radius $a'$) and another species exhibiting a two-step staircase (say, for particles of radius $a$), Eqs. (10) and (12) permit only one possible scenario depicted in Fig. 8(a). After appropriate algebra corresponding to this case, we get

$$\frac{1}{2} < \tan \theta_F \leq \frac{1}{2} < \tan \theta_L \leq \tan \theta_L < \frac{2}{\pi}.$$

Similarly, for a mixture of particles exhibiting a two-step staircase, Eqs. (6), (7), and (12) permit only two cases, depicted in Figs. 8(b) and 8(c), which correspond to the two cases $b_c > b'_c$ or $b_c < b'_c$, respectively. Again, applying these constraints we get

$$\frac{1}{2} < \tan \theta_F < \tan \theta_F' \leq \frac{1}{2} < \tan \theta_L < \tan \theta_L' < \frac{2}{\pi},$$

or

$$\frac{1}{2} < \tan \theta_F < \tan \theta_F' < \frac{1}{2} < \tan \theta_L < \tan \theta_L < \frac{2}{\pi}.$$

In terms of separation, it is evident from the figure that separation between primed and nonprimed species is possible only if the forcing angle satisfies

(i) $\theta \in [\theta_F, \theta_F'] \cup [\theta_L, \theta_L']$ corresponding to Fig. 8(a),
(ii) $\theta \in [\theta_F', \theta_F] \cup [\theta_L, \theta_L']$ for Fig. 8(b), and
(iii) $\theta \in [\theta_F, \theta_F'] \cup [\theta_L', \theta_L]$ in the case of Fig. 8(c).

Further, the figure also indicates that $[\pi/4 - \arctan(1/2)]$ and $\arctan(1/2)$ are the only two separation resolutions ($|\alpha - \alpha'|$) corresponding to these cases.

Thus, the maximum separation resolution between species corresponding to the three cases shown in Fig. 8 is $\arctan(1/2) \approx 26.56^\circ$ since it is greater in magnitude than $[\pi/4 - \arctan(1/2)]$, and it occurs if $\theta \in [\theta_F, \theta_F]$ for Fig. 8(a), $\theta \in [\theta_F', \theta_F]$ for Fig. 8(b), and $\theta \in [\theta_F, \theta_F']$ for Fig. 8(c). As highlighted in the context of Eq. (15), this conclusion is consistent with our experimental observation that the forcing angle between the first transition angles of the species to be separated achieves the best resolution [13,17,18].

C. A note on per-row collision frequency from an immunocapture perspective

Obstacle arrays are also used as immunocapture devices by fabricating obstacles that exhibit adhesion specificity toward components of interest in the suspension flowing through the array [e.g., due to antibody coating on the obstacles specific to rare cells like circulating tumor cells (CTCs)][41]. As noted by Kirby and co-workers, the parameter to be optimized in this application is the collision frequency of particles with obstacles (number of collisions per row of obstacles) [12]. Assuming sufficiently high adhesion specificity, higher collision frequency would lead to increased capture efficiency for the device.

The calculations in the previous section as well as Figs. 4(a) and 4(b) indicate that a particle undergoes one collision per $q$ rows of the array in the case of top-top or bottom-bottom modes. This yields the corresponding per-row collision frequency of $1/q$. On the other hand, a particle undergoes two collisions every $q$ rows in the case of top-bottom-top or bottom-top-bottom modes. In this case, the per-row collision frequency is $2/q$. These results agree with those presented in [12]. Therefore, maximum per-row frequency is obtained for the smallest possible value of $q$. This leads to the conclusion that $[p,1]$ periodic trajectories exhibit the maximum per-row collision frequency. Finally, we note that our analysis assumes a steady state for the periodicity of particle trajectories and ignores the initial aperiodic transients as the particles enter the array [12].

V. SUMMARY

In summary, we have presented a theoretical analysis of the directional locking phenomenon exhibited by particles navigating through a square array of obstacles, in the limit of negligible particle and fluid inertia. In the dilute limit for the array (i.e., a sparse array), interactions between a single obstacle and a particle are sufficient for trajectory analysis. Coupled with the dilute assumption, we have used a critical parameter (incorporating both hydrodynamic and short-range repulsive nonhydrodynamic particle-obstacle interactions) to replace the physical particle-obstacle system with its kinematically equivalent abstraction. Within the abstract model, the particle is replaced by a point particle, while the obstacle radius is scaled to be equal to the critical parameter. Due to the model, a simple geometric analysis suffices to derive the periodicity condition, both necessary and sufficient for the
particle trajectory. The periodicity condition directly leads to the devil’s-staircase-like behavior of the migration direction as a function of the forcing direction. Using this framework, we have also computed the per-row collision frequency of particles, which is the relevant optimization parameter in the context of obstacle arrays used as immunocapture devices. Finally, using the periodicity condition, we have computed the design constraints on the ratio of the critical parameter to the lattice spacing of the square array, and commented on the resolution of deterministic separations, when the particle exhibits simple staircase structures.

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