Partition-induced vector chromatography in microfluidic devices

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1. Introduction

Separation of the different constituents of a complex sample has long been of paramount relevance in many fields of engineering and science. The ubiquity of particle separation, for example, has led to the development of a vast number of different techniques [1]. The manipulation of chemical and biological species at the micro and nanoscale has also received special attention in the ongoing effort toward process miniaturization, with nearly every advance in our understanding of the effects that are dominant at these scales leading to novel separation devices, as surveyed in recent reviews [2–4]. An ideal technique would be able to discriminate particles based on small differences in any of a wide range of physicochemical properties, thus allowing the fractionation of intricate mixtures. In addition, continuous operation is generally preferred over a batch process because of the ease of operation and higher yields. To facilitate operation and portability it is also desirable that the device be autonomous, thus eliminating the need for external components. In contrast, most techniques discriminate particles based on a specific physicochemical property, are inherently batch-processes, or require external fields to drive separative displacement.

One of the most versatile separation methods is field-flow fractionation (FFF) [5], a family of techniques in which a variety of force fields can be used to induce separation based on different physicochemical properties, with subtechniques including gravitational, sedimentation, flow, thermal, and electrical FFF [6,7]. In FFF, particles are typically transported by a parabolic flow between two parallel plates and, at the same time, externally forced in the direction perpendicular to the flow toward one of the walls. The velocity of the particles is thus governed by their equilibrium particle-wall distance, which results in the separation of the sample into bands of particles moving in the direction of the flow at different speeds. Dielectrophoretic methods [8,9] are also versatile since differences in a broad spectrum of properties result in different dielectric signatures allowing, similarly to FFF, the separation of multifarious mixtures.

Despite the breadth of FFF techniques, they share the common drawback of being fundamentally a batch process. A technique as wide-ranging as FFF that allows for continuous operation is split-flow lateral-transport thin (SPLITT) fractionation [10]. In this technique, particles are streamed near one of the walls of the SPLITT channel and, at the same time, an external force drives particles selectively in the direction perpendicular to the carrier flow into different streams which can then be continuously collected. On the other hand, SPLITT only allows bi-modal separation in a single stage. Other methods also allowing continuous operation have been developed by acoustic and optical means. Acoustic forces have been used to separate particles according to their density and compressibility into two streams at the pressure node and antinode created by a standing wave between two parallel walls [11]. Optical forces have allowed the sorting of nano and...
microparticles of different materials and sizes, as recently reviewed [12]. These continuous methods, however, require the integration with external components.

Continuous separation methods that do not require the presence of external fields include pinched flow fractionation (PFF) [13–15], hydrodynamic filtration (HF) [16], Hydrophoresis [17–19], and inertial focusing [20–22]. In PFF particles of different size initially aligned to one of the walls of a channel exit with different trajectories after passing through a pinched flow region. Similarly, in HF particles are first aligned along the walls of a main channel and then sequentially collected according to their size by controlling the flow rate in side channels. Hydrophoresis, on the other hand, does not require precise flow focusing of the particles. Hydrophoretic separation is achieved using an array of obstacles to induce a pressure field responsible for the selective displacement of particles of different size. More recently, inertial lift forces and Dean flows in curved conduits have been used to stream particles in precise locations within a flow channel. However, hydrophoresis and inertial focusing methods are difficult to implement for the simultaneous collection of particles in polydispersed samples.

Two dimensional (2D) separation is another approach that allows for continuous fractionation. The spatial resolution that allows continuous operation in 2D methods could be achieved by a combination of transport in one direction with selective displacement in the perpendicular direction resulting in greater resolving power compared to 1D techniques [23]. An extension of FFF, for example, combines radial and tangential carrier flows between two parallel disks to allow for the continuous collection of separated bands in different locations of the fractionation cell [26]. Other examples of 2D fractionation use a flow field and an external force applied in the direction perpendicular to the flow as the selective displacement. In magnetophoresis [27], for instance, particles are sorted according to their magnetic susceptibility and size. Another paradigm that allows 2D separation relies on a periodic potential to cause selective displacement of particles. In particular, a periodic dielectrophoretic potential has been shown to result in a force that selectively opposes one of the components of the driving force acting on different particles, thus causing them to move in different average directions [28–30]. These methods fall in the category of vector chromatography (VC) techniques [24,25], where the fractionation relies on differences in the average direction in which different species move.

A promising trend in VC exploits the interactions between the species being separated and features intentionally designed in the separation media to drive separative displacement without the need of an external component (force field). For example, deterministic lateral displacement [31–36] (DLD) is carried out in devices patterned with a 2D sieving matrix in which particles of different sizes move at different angles, thus enabling the simultaneous fractionation and collection of multiple components in a polyporous sample with very high resolution. However, the underlying mechanism leading to separation in these sieving devices is not completely clear, which has led so far to ad hoc designs that are difficult to optimize [37–39]. In the context of VC, Dorfman and Brenner [24] considered the illustrative case of a periodic system consisting of repeating layers of two immiscible fluids. They showed that differences in the partition ratio of the particles, due to differences in affinity between the particles and each of the layers of fluid, results in vector chromatography when the particles are animated by a constant external force. Unfortunately, as noted by the authors [24], such a two-fluid layer system cannot be easily implemented in practice.

In this study we demonstrate the potential of planar microfluidic devices as a platform to achieve partition-induced vector chromatography (PIVC), a technique that combines the versatility of FFF with the multiple advantages of continuous 2D vector separation. The high surface-to-volume ratio characteristic of microfluidic devices makes it possible to induce partition by means of surface interactions. In fact, it has been shown that the spontaneous partition of different species into regions of low and high concentration can be controlled by means of the potential energy landscape created by a chemical or physical pattern on one of the surfaces of a channel [40,41]. In particular, we consider cases in which partition is induced via Van der Waals forces and 1-g gravity, both approaches resulting in autonomous devices. In addition, external fields could also be used to cause or enhance partition. We show that partition results in diffusive fluxes that are responsible for the migration of particles at angles different from the angle of the driving field.

The content of this work is structured as follows. First, we derive the equation governing the probability density for a spatially periodic potential following the macrotransport paradigm [42]. In the subsequent sections, we solve this governing equation under the Fick-Jacobs (FJ) approximation for the cases in which the particle is animated either by a constant external force or by a fluid flow and obtain closed-form solutions for the particle trajectory angle in a slit geometry for an arbitrary two-dimensional potential. These general solutions are evaluated to obtain analytical expressions for a piece-wise constant potential. Then, we show how such a potential can be achieved by patterning chemically or physically one of the surfaces of a microfluidic device with an array of rectangular stripes. Finally, we look at experimentally accessible systems and validate the results obtained under the FJ approximation with Brownian dynamics simulations, and show that particles exhibiting different partition ratios can be fractionated via vector chromatography.

### 2. Particle transport in patterned microfluidic devices: macrotransport theory

In this section we derive the equations governing the transport of suspended particles in the periodic system shown in Fig. 1. The particles are confined between two infinite parallel walls separated a distance $d$. We shall assume that the physicochemical properties of the walls of the channel render the system $l_x$ and $l_y$ periodic in the $x$ and $y$ directions, respectively. Let $N(R,t;R_0)$ be the conditional probability density of finding the particle center, modeled as a stochastic variable, at location $R$ at time $t$, given the initial position $R_0$ at time $t=0$. This conditional probability density is governed by the following convection-diffusion equation,

$$\frac{\partial P}{\partial t} + \nabla \cdot J = \delta(R - R_0)\delta(t).$$

(1)

The flux $J$ is composed of a convective and a diffusive contribution, the latter assumed to have a Fickian form.
\[ J = U P - D \cdot \nabla P, \] (2)

where \( U \) is the net convective velocity of the particle due to both flow and applied forces, and \( D \) is the diffusion tensor. Due to the periodicity of the system, \( P(\mathbf{r}, t \mid \mathbf{r}_0) \) can be written in the equivalent functional form \( P(\mathbf{r}, t \mid \mathbf{r}_0) \), where \( \mathbf{r}_0 = j, k \mathbf{i}_j + l \mathbf{i}_k \), represents the location of the \( j, k \)th unit cell with respect to some arbitrary origin, and \( r = (x, y, z) \) is the intracellular position vector. In addition, both \( U \) and \( D \) are periodic and dependent on the intracellular position \( r \). Therefore, the probability distribution function \( P \) is not a function of \( \mathbf{r}_{nm} \) and \( \mathbf{r}_{nm} \) independently but of their difference, \( \mathbf{r}_{nm} = \mathbf{r}_{nm} - \mathbf{r}_{nm} \), \( t \mid \mathbf{r}_0 \). Then, the zeroth order moment of the distribution,

\[ P_0(\mathbf{r}, t \mid \mathbf{r}_0) = \sum_{n,m} P(\mathbf{r}_{nm} - \mathbf{r}_{nm}, \mathbf{r}, t \mid \mathbf{r}_0), \] (3)

represents the conditional probability density that the particle will be found in the local, intracellular position \( \mathbf{r} \) at time \( t \), given that it was introduced at the location \( \mathbf{r}_0 \) at time \( t = 0 \). \( P_0(\mathbf{r}, t \mid \mathbf{r}_0) \) satisfies the equation

\[ \frac{\partial P_0}{\partial t} + \nabla \cdot J_0 = \delta(r - \mathbf{r}_0) \delta(t), \] (4)

where the flux \( J_0 \) follows Eq. (2). This governing equation for the probability distribution corresponds to the Smoluchowski equation describing the stochastic motion of a particle in the limit of negligible inertia [43].

The steady state solution,

\[ P_0^s(\mathbf{r}) = \lim_{t \to \infty} P(\mathbf{r}, t \mid \mathbf{r}_0), \] (5)

is then governed by the equation

\[ \nabla \cdot J_0^s = 0, \] (6)

with periodic boundary conditions,

\[ P_0^s(x, y, z) = P_0^s(x + l, y, z), \] (7a)

\[ P_0^s(x, y, z) = P_0^s(x, y + l, z), \] (7b)

and the no-flux condition on the impermeable walls confining the particle in the \( z \) direction. Finally, the standard normalization condition requires that

\[ \int_{\tau} P_0^s(\mathbf{r}) dV = 1, \] (8)

where \( \tau \) is the volume of the unit cell.

The asymptotic flux of probability density can be written in our case as

\[ J_0^s = u P_0^s + M \cdot F P_0^s - M \cdot \nabla P_0^s - D \cdot \nabla P_0^s, \] (9)

where \( u(\mathbf{r}) \) is the velocity of the particle when convected by a flow field, \( F(\mathbf{r}) \) is a constant external force acting on the particle, \( V(\mathbf{r}) \) is the potential energy landscape in which the particle moves, and \( M(\mathbf{r}) \) is the mobility tensor. Note that all quantities are assumed to be periodic. Given the symmetry of the geometry considered here, it is convenient to write the mobility and diffusion tensors as

\[ M = I_i I_j M_{ij} + (I - I_i I_j) M_1, \] (10a)

\[ D = I_i I_j D_{ij} + (I - I_i I_j) D_1, \] (10b)

The mobilities and diffusivities follow the Stokes–Einstein relation,

\[ D_1 = k_B T M_1, \] and \( D_1 = k_B T M_1 \), where \( k_B \) is the Boltzmann constant and \( T \) the absolute temperature.

Knowledge of \( P_0^s \) yields the mean particle velocity from the quadrature

\[ \mathbf{U} = \int J_0^s dV. \] (11)

The orientation angle of \( \mathbf{U} \) is the relevant parameter in vector chromatography, termed hereafter the chromatographic trajectory angle, more simply the trajectory angle [24], or the migration angle.

In the following sections we derive analytical expressions for the migration angle, under the Fick–Jacobs approximation, for the cases in which the particle is driven either by an externally applied force or by a fluid flow.

2.1. Non-equilibrium transport: the Fick–Jacobs approximation

The three-dimensional problem posed in the preceding section can be solved numerically for a particular system and driving fields. In this section, we focus on 2D problems that capture the fundamental mechanisms leading to PIVC, and which are amenable analytically. Specifically, we consider the \( x \)-invariant case whereby \( u(\mathbf{r}), M(\mathbf{r}), V(\mathbf{r}) \) and \( P_0^s(\mathbf{r}) \) depend on \( y \) and \( z \) only. In addition, we study 2D driving fields in which the external force and the fluid-flow velocity are in the \( x \)-\( y \) plane. Under these conditions the asymptotic flux, Eq. (9), takes the form

\[ J_0^s = (u P_0^s + M_{10} F P_0^s) \mathbf{i}_x + \left( u P_0^s + M_{10} F P_0^s - M_{11} \frac{\partial N}{\partial y} P_0^s - k_B T M_1 \frac{\partial P_0^s}{\partial y} \right) \mathbf{i}_y, \] (12)

where we have used the fact that at low Reynolds number \( u_y = 0 \) for the 2D flow field considered here. The equation governing the asymptotic probability density Eq. (6) then becomes

\[ 0 = \frac{\partial}{\partial y} \left( u P_0^s + M_{10} F P_0^s - M_{11} \frac{\partial N}{\partial y} P_0^s - k_B T M_1 \frac{\partial P_0^s}{\partial y} \right) \mathbf{i}_y + \frac{\partial}{\partial z} \left( -M_{12} \frac{\partial N}{\partial z} P_0^s - k_B T M_1 \frac{\partial P_0^s}{\partial z} \right). \] (13)

A heuristic approach first introduced by Jacobs [44,45] allows solving Eq. (13) approximately assuming local equilibrium in the transverse direction. This approximation, termed by Zwanzig the Fick–Jacobs (FJ) approximation, has been shown to provide accurate results in narrow channels [46–48]. Under this local equilibrium assumption, and given that the system is \( x \)-invariant, the asymptotic probability distribution conditioned to a given intracellular position \( y \) can be written as

\[ \rho(x, z | y) \approx \rho(x, z | y)_{eq} = e^{-N(z)/k_B T} / I(y), \] (14)

where

\[ I(y) = \int e^{-N(z)/k_B T} dz. \] (15)

Therefore, the probability distribution takes the form

\[ P_0^s(\mathbf{r}) = P(y) \rho(x, z | y) \approx P(y) \rho(x, z | y)_{eq} = P(y) e^{-N(z)/k_B T} / I(y), \] (16)

where

\[ P(y) = \int P_0^s(\mathbf{r}) d\mathbf{r} \] (17)

is the marginal probability density. We apply this approximation to the cases in which the particle motion is driven either by a constant external force or by a fluid flow in what follows.

2.1.1. External force

When the particle is animated solely by a constant external force, Eq. (13) reads

\[ 0 = \frac{\partial}{\partial y} \left( M_{10} F P_0^s - M_{11} \frac{\partial N}{\partial y} P_0^s - k_B T M_1 \frac{\partial P_0^s}{\partial y} \right) + \frac{\partial}{\partial z} \left( -M_{12} \frac{\partial N}{\partial z} P_0^s - k_B T M_1 \frac{\partial P_0^s}{\partial z} \right). \] (18)
Nondimensionalizing with the variable changes \( x \to x/l_p, y \to y/l_p, z \to z/d, M_1 \to M_1/l_p, \) and \( M_0 \to M_0/l_p \) with \( M_0 \) being the bulk mobility, \( V \to V/k_r T, \) and \( P_0^* \to \tau P_0^* \) substituting the FJ approximation for \( P_0^* \), integrating in \( x \) and \( z \), and rearranging the terms yields

\[
\frac{\partial}{\partial y} \left( \int_{l_0^y} \mathcal{M}_y(r)dzdx \right) - \frac{\partial}{\partial z} \left( \int_{l_0^z} \mathcal{M}_z(r)dx \right) = -\left( \int_{l_0^x} \mathcal{M}_x(r)dy \right),
\]

where the only dimensionless parameter is the Péclet number, \( Pe = U_i/k_r T \). The total dimensionless flux in the \( y \) direction, \( J \), is clearly constant and can be written as

\[
J = \int \int_{l_0^y} \mathcal{M}_y(r)dzdx = l(y) \mathcal{M}_y \left[ Pe \frac{\partial \mathcal{M}}{\partial y} - \frac{\partial \mathcal{M}}{\partial y} \right],
\]

where \( \mathcal{M}_y = \int M_1(y,z) e^{-V(y,z)} dz \) is the local average of the mobility in the FJ approximation, and \( \mathcal{P}(y) = \mathcal{P}(y)/l(y) \). The general solution for the marginal density is given by

\[
\mathcal{P}(y) = e^{\mathcal{P}(y)} \left[ - \int_0^y \frac{dy'}{e^{\mathcal{P}(y')}} I(y') \mathcal{M}_y(y') + N \right] I(y).
\]

The flux \( J \) and the constant \( N \) are obtained by solving simultaneously the periodicity and normalization conditions:

\[
N = \frac{1}{\Sigma} \int_0^1 \frac{dy'}{e^{\mathcal{P}(y')}} I(y') \mathcal{M}_y(y'), \quad J = \frac{1}{\Sigma} \int_0^1 \left( 1 - e^{-\mathcal{P}(y)} \right), \quad \Sigma = \int_0^1 I(y') \mathcal{M}_y(y')
\]

The total flux in the \( z \) direction is identically equal to zero. Thus,

\[
J_z = U_i^y + U_i^z = \int_{l_0^y} \mathcal{M}_y dy + \int_{l_0^z} \mathcal{M}_z dx
\]

Employing Eqs. (22)–(24), we obtain one of our main results, a chromatographic trajectory angle that depends in general on the properties of the particle through the potential \( V \) and the external force \( F \):

\[
\tan \theta^0 = \frac{U_i^y}{U_i^z} = \tan \theta_0 \frac{Pe}{1 - e^{-\mathcal{P}(y)}} \int_0^1 I(y') \mathcal{M}_y(y') \int_0^{y+1} \frac{dy'}{I(y') \mathcal{M}_y(y') e^{\mathcal{P}(y)}},
\]

where \( \theta_0 = \arctan(F_y/F_z) \) is the orientation angle of the external force.

2.1.2. Entrainment in a fluid flow

When the particle is convected by a fluid flow, Eq. (13) governing the asymptotic probability density reduces to

\[
0 = \frac{\partial}{\partial y} \left( u_y P_0^n - M_1 P_0^n - k_r T M_0 \frac{\partial P_0^n}{\partial y} \right) + \frac{\partial}{\partial z} \left( -M_0 \frac{\partial P_0^n}{\partial z} - k_r T M_1 \frac{\partial P_0^n}{\partial z} \right)
\]

Nondimensionalizing with the same change of variables as those used for Eq. (18) in addition to \( u_y \to u_y/\mathcal{U}_i \), where \( \mathcal{U}_i \) is the average velocity of the particle-free flow in the \( y \) direction, substituting the FJ approximation for \( P_0^n \), integrating in \( x \) and \( z \), and rearranging the resulting terms we obtain the (constant) total flux in the \( y \) direction

\[
J = \int \int_{l_0^y} \mathcal{M}_y(r)dzdx = l(y) \mathcal{M}_y \left[ Pe \frac{\partial \mathcal{M}}{\partial y} - \frac{\partial \mathcal{M}}{\partial y} \right].
\]

In this case, the Péclet number is \( Pe = U_i/k_r T \), and \( \mathcal{U}_i \) analogously to \( \mathcal{M}_y \), is the local average of the particle velocity \( u_y \) in the FJ approximation. We can then define a local effective hydrodynamic force as the ratio of the local average velocity to the local average mobility,

\[
\Phi(y) = \frac{\mathcal{U}_i(y)}{\mathcal{M}_y(y)}.
\]

Then, the general solution for the marginal probability distribution under the FJ approximation can be expressed as

\[
\mathcal{P}(y) = e^{\mathcal{P}(y)} \left[ - \int_0^y \frac{dy'}{e^{\mathcal{P}(y')}} I(y') \mathcal{M}_y(y') + N \right] e^{-V(y)},
\]

where

\[
\Phi(y) = \int_0^y \phi(y')dy'.
\]

The flux \( J \) and the constant \( N \) are obtained, as in the external force case, by solving the periodicity and normalization conditions simultaneously:

\[
N = \frac{1}{\Sigma} \int_0^1 I(y') e^{\mathcal{P}(y')} \mathcal{M}_y(y') I(y') \mathcal{M}_y(y') dy', \quad J = \frac{1}{\Sigma} \int_0^1 [1 - e^{-\mathcal{P}(y)}], \quad \Sigma = \int_0^1 I(y') \mathcal{M}_y(y')
\]

Lastly, the chromatographic trajectory angle is given by

\[
\tan \theta^0 = \frac{U_i^y}{U_i^z} = \tan \theta_0 \frac{Pe}{1 - e^{-\mathcal{P}(y)}} \int_0^1 I(y') \mathcal{M}_y(y') \int_0^{y+1} \frac{dy'}{I(y') \mathcal{M}_y(y') e^{\mathcal{P}(y)}},
\]

where \( \theta_0 = \arctan(F_y/F_z) \), with \( F_y \) and \( F_z \) being the component of the average velocity in the \( y \) direction and the orientation angle of the particle-free flow, respectively. Eqs. (25) and (32) are valid for an arbitrary two dimensional potential, under the FJ approximation. We use these expressions in the next section to obtain analytical results for an interaction potential resulting from surface modifications to a channel in a microfluidic device.

3. Vector chromatography in microfluidic devices: stripe patterns

Using standard microfabrication techniques, a parallel plate channel in a microfluidic device can be modified to create a periodic system by patterning one of the surfaces of the channel with an array of rectangular stripes as shown in Fig. 2. We assume that the interfaces between the stripes are sharp, which results in an interaction potential that, for particles in close proximity to the wall, can be approximated as a piece-wise function of the form

\[
V(r) = \begin{cases} V_1(z) & 0 < y < \varepsilon, \\ V_2(z) & \varepsilon < y < \varepsilon, \end{cases}
\]

The migration angles can then be calculated by substituting this potential into the general expressions given by Eqs. (25) and (32). It is worth mentioning that the transition potentials do not contribute to
the trajectory angle whenever the transition regions are much narrower than the stripes, and therefore their explicit inclusion in Eq. (33) is not necessary. This simple approximation provides analytical expressions that facilitate the understanding of the physics underlying the separation process, and shows that separation is feasible.

### 3.1. Interaction potential

In general, the potential on each stripe includes the Van der Waals and electrostatic forces between the particle and the surface and, for non-neutrally buoyant particles, it has a gravitational contribution as well,

\[ V(h) = V_{\text{edl}}(h) + V_{\text{vdw}}(h) + V_{\text{grav}}(h), \]

where \( h \) is the particle-wall separation (see Fig. 1). The electrostatic double-layer potential for the case of a \( z \sim z \) electrolyte has the form [40]

\[ V_{\text{edl}}(h) = aB \exp(-\kappa h) \]

with

\[ B = 64\pi \epsilon_m \left( \frac{k_B T}{2e} \right)^2 \tanh \left( \frac{e\psi_p}{4k_B T} \right) \tanh \left( \frac{e\psi_s}{4k_B T} \right). \]  

where \( \epsilon_m \) is the dielectric permittivity of the medium, \( e \) is the charge of an electron, \( \psi_p \) and \( \psi_s \) are the Stern potentials of the particle and the wall, respectively, and

\[ \kappa^{-1} = (2e^2z^2CN_A/\epsilon_m k_B T)^{-1/2} \]

is the Debye length, where \( C \) is the bulk electrolyte concentration, \( z \) is the valence of the ions, and \( N_A \) is Avogadro’s number.

The Van der Waals potential can be rigorously computed via Lifshitz theory and fit for convenience to a power law expression of the form [40]

\[ V_{\text{vdw}}(h) = -a\kappa h^{-p}. \]

These surface potentials have been referenced to zero at an infinite particle-wall separation. The gravitational potential is given in terms of the buoyant weight of the particle

\[ V_{\text{grav}}(h) = \frac{4}{3} \pi a^3 \Delta \rho g (h + h_{\text{ref}}) k_B T, \]

where \( \Delta \rho = \rho_p - \rho_m \) is the density difference between the particle and the medium (or buoyant density), \( g \) is the acceleration due to gravity, and \( h_{\text{ref}} \) is the height of the channel wall with respect to an arbitrary reference. Fig. 3 shows the total potential for particles with a radius of 2 \( \mu m \) as a function of the particle-wall separation for two values of the buoyant density, calculated using parameters representative of the experimental values reported by Wu et al. [40]. Specifically, Stern potentials of \(-60 \text{ mV}\), and Van der Waals affinity prefactor and exponent of 2 \( \text{nm} \) and 2, respectively, are representative of the experimental values corresponding to a silica particle suspended above a bare glass surface in a 1 mM aqueous solution of a 1:1 electrolyte. In this case the surface interactions are important within a few hundred nanometers from the wall with gravity dominating for larger separations. We also use the same Van der Waals and electrostatic forces to calculate the interaction potential of a less dense particle. It is clear from Fig. 3 (see panels (a) and (b)) that the less dense particle explores a broader range of separations and is, on average, farther away from the wall than the highly confined denser particle. Fig. 4 shows the average...
particle-wall separation and the standard deviation as a function of particle radius for different buoyant densities. The particles are on average closer to the wall and more narrowly confined as the particle buoyant density and size increase, with the excursions of the heavier particles restricted to within tens of nanometers from their equilibrium position. This degree of confinement makes the FJ approximation valid and in fact accurate even at relatively large Péclet numbers, as we shall show later by comparison with Brownian dynamics simulations.

### 3.2. Inducing partition via physical and chemical patterns

In the absence of a driving field, the concentration of particles undergoing Brownian motion over a stripe pattern, as that shown in Fig. 2, follows the Boltzmann distribution. In this case, the marginal distribution is given by

$$
\mathcal{P}(y) = \begin{cases} 
\frac{1}{e^{\frac{y}{\epsilon}} - 1} & 0 < y < \epsilon, \\
\frac{1}{\epsilon(1 - e^{-\epsilon})} & \epsilon < y < 1.
\end{cases}
$$

with the partition ratio, $K$, defined as

$$
K = \int e^{-\frac{V_z}{\epsilon}} dz / \int e^{-\frac{V_y}{\epsilon}} dz.
$$

(41)

It is clear that differences between the potential energy of the particle in the two regions would result in partition, $K$ being a measure of the relative affinity of the particle with each of the stripes.

Patterning the stripes chemically would result in different surface potentials while physically modifying the topography of the channel surface into parallel stripes of different heights would result in different sampling of the gravitational potential. Fig. 5 shows partition ratios predicted from Eq. (41) with the electrostatic and Van der Waals potentials based on the experimental values reported by Wu et al. [40]. Specifically, we first show the partition ratio induced by gravity in a pattern of chemically identical stripes as a function of the height difference between them for (Fig. 5a) different values of the buoyant density, ranging approximately from that of polystyrene particles to that of silica particles, and (Fig. 5b) for different values of the particle radius. In this case, in which the surface properties of both stripes are the same, Eq. (41) for the partition ratio simplifies to

$$
K = \frac{e^{\frac{\Delta h}{\epsilon}}}{1 + \epsilon}.
$$

(42)

where $\Delta h$ is the height difference between the stripes. The partition ratio increases with the height difference between the stripes, the buoyant density and the size of the particle. It is worth mentioning that the average particle-wall separation is larger than the largest $\Delta h$ considered (see Fig. 4), and therefore the particles do not experience physical hindrance at the transition regions. In panels (c) and (d) of Fig. 5 we present partition induced via Van der Waals interactions by increasing the particle affinity, parameter $A$ in Eq. (38), with one of the two (otherwise identical) stripes. Specifically, we consider $p = 2$ and values of $A$ between 2 and 10 nm, which are representative of the range spanned in the case of a silica particle in a 1 mM aqueous solution of a 1:1 electrolyte interacting with a glass substrate coated with a gold film of thickness between 0 and 30 nm [40]. In this case the Van der Waals-induced partition ratio increases as the affinity ratio, the buoyant density, and the size of the particle increase.

### 3.3. Non-equilibrium transport

We now consider the cases in which the particle is either driven by a spatially uniform external force $F$ oriented at an angle $\theta_0$ with respect to the $y$ axis (see Fig. 2), or convected by a flow field that far from the particle is oriented at an angle $\theta_0$ with respect to the $y$ axis. The migration of particles at angles that differ from the forcing direction can be explained qualitatively by considering the normal flux at the transition between the stripes. Consider the equilibrium marginal probability density shown in Fig. 6a for a partition ratio $K = 2$. In the presence of a driving field, the convective flux on each side of the interfaces between the stripes would differ due to the concentration differences. Thus, for the system to reach steady state the corresponding continuity of the total flux, concentration gradients and the ensuing diffusive fluxes must compensate for the differences in the convective fluxes. As can be seen in Fig. 6b–d, the diffusive fluxes augment (reduce) the flux in the region of lower (higher) concentration and convective transport. The average diffusive flux on each stripe is proportional to the concentration difference across them (height of the shaded regions shown in Fig. 6). Therefore, the average diffusive fluxes differ by a factor $K$. The net result is a diffusive component of the flux normal to the stripes that reduces the total flux in this direction, the effect being stronger for increasing partition ratios. As a consequence, the trajectory angle of the particle is different from the orientation angle of the field and strongly depends on the partition ratio. This is the basis for the separation of particles exhibiting different partition ratios.

Evaluating the general expression for the chromatographic trajectory angle, Eq. (25), for the piece-wise potential given by Eq. (33), we obtain the trajectory angle in terms of the partition ratio for the case in which the particles are driven by an external force

$$
\tan \theta^* - \tan \theta_0 = \frac{(1 - \lambda K)^2}{\lambda K} \left[ \frac{1 - e^{-\frac{\lambda K}{\epsilon}}}{1 - e^{-\frac{\lambda}{\epsilon}}} \right] \frac{1}{Pe}.
$$

(43)

where $\lambda = M_{11} / M_{12}$, with $M_{ij}$ the local average of the mobility over stripe $i$ as defined by Eq. (21). In the limit of vanishing $Pe$ the above expression reduces to

$$
\tan \theta^* - \tan \theta_0 = \frac{(1 - \lambda K)^2}{\lambda K} \epsilon (1 - \epsilon).
$$

(44)

while in the convection dominated case the trajectory angle tends to the forcing angle.
Analogously, replacing the piece-wise potential into Eq. (32) yields the migration angle for the case in which the particle is convected by a fluid flow
\[
\tan \theta' = \tan \theta_1 \left\{ 1 + \frac{(1-jK)(1-\Pi LK) \left[ 1-e^{-\Phi_0(1-\epsilon)} \right] \left[ 1-e^{-\Phi_0(1-\epsilon)} \right] \frac{1}{jK} \epsilon + \Pi(1-\epsilon) \right\} \right.
\]
where \( \Pi = \phi_2/\phi_1 \), with \( \phi_i = \bar{u}_i/M_i \) being the effective hydrodynamic force acting on the particles moving on stripe \( i \).

In the limit as \( \text{Pe} \) tends to zero the above expression simplifies to
\[
\tan \theta' = \tan \theta_1 \left\{ 1 + \frac{(1-jK)(1-\Pi LK) \left[ 1-e^{-\Phi_0(1-\epsilon)} \right] \left[ 1-e^{-\Phi_0(1-\epsilon)} \right] \frac{1}{jK} \epsilon + \Pi(1-\epsilon) \right\} \right.
\]
and as in the external force case, the migration angle converges to the forcing angle in the high \( \text{Pe} \) limit.

3.4. Brownian dynamics simulations

The expressions for the migration angle in the case of stripe patterns, Eqs. (43) and (45), are valid under the FJ approximation, i.e., under the assumption of instantaneous equilibrium in the transverse direction. This assumption is clearly valid when the particle has ample time to equilibrate in the direction perpendicular to the patterned surface via diffusion as it is convected across the stripes by either an external force or a fluid flow. Therefore, the relevant parameter is the ratio between the diffusive time in the transverse direction and the convective time along a single cell, i.e., \( \text{Pe}^{FJ} = \text{Pe}(\sigma/l)^2 \), where \( \sigma \) is the width of the confinement region. The particles could be physically constrained to move in a narrow channel or, alternatively, a highly confining potential could restrict the vertical motion of the particles to a narrow region regardless of the height of the channel. In either case, if the particles are narrowly confined to the vicinity of the patterned surface the FJ approximation could be valid even for relatively large values of \( \text{Pe} \). Therefore, we performed Brownian dynamics (BD) simulations in order to determine the full range of validity of the results presented in the preceding section. Specifically, we considered the case in which the particle is convected by a fluid flow. Using the Ermak and McCammon algorithm [49], the dimensionless equations of motion for a suspended particle are

\[ \frac{d^2 \vec{x}}{dt^2} = -\gamma \vec{v} - \nabla U(\vec{x}) \]
\[ \gamma = \frac{6 \pi \eta R_D}{M} \]

where \( \gamma \) is the friction coefficient, \( \eta \) is the viscosity of the solvent, \( \eta = 0.01 \text{ poise} \), and \( R_D \) is the hydrodynamic radius of the particle.
\[
\Delta x = \xi \tan \theta_y Pe u_y \Delta t + \xi \sqrt{2M_1^0 \Delta t} \psi
\]  
\[
\Delta y = Pe u_y \Delta t - M_1^0 \left( \frac{\partial V}{\partial y} \right) \Delta t + \sqrt{2M_1^0 \Delta t} \phi
\]  
\[
\Delta z = \gamma^2 \left( \frac{dD_1}{dz} \right) \Delta t - \gamma^2 M_1^0 \left( \frac{\partial V}{\partial z} \right) \Delta t + \gamma \sqrt{2M_1^0 \Delta t} \omega
\]

The characteristic scales used to nondimensionalize the equations are \(l_x, l_y,\) and \(d\) for the displacements in the corresponding directions, the unbounded mobility \((M_{1\omega})\) and diffusivity \((D_{1\omega})\) for the corresponding quantities both parallel \((//)\) and perpendicular to the wall \((\perp)\), the y component of the average velocity of the particle-free flow \(u_\parallel\) for the particle velocity, \(k_B T\) for the interaction potential, and \(l_y/D_{1\omega}\) for the time step. In the above equations \(\xi = l_y/l_x,\) \(\gamma = l_y/d, u_y\) is the dimensionless particle velocity in the y direction due to the flow, \(Pe = u_\parallel l_y/D_{1\omega}, \phi\) is the orientation angle of the particle free flow, and \(\psi, \phi,\) and \(\omega\) are independent random numbers chosen from a symmetric distribution of zero mean and unit width. Lastly, the superscript indicates that the quantities are evaluated at the beginning of the time step.

In order to carry out the simulations it is necessary to specify transition potentials. As the particle moves from one stripe to the other it experiences a force toward the stripe of higher affinity. The magnitude of this force is dictated by the imbalance in the particle-substrate affinity between the anterior and posterior regions of the particle. The exact form of the transition potential would depend on the physicochemical properties of the transition region and these, in turn, would depend on the specific way in which the pattern was created. Simple, analytical expressions are not available for the electrostatic and Van der Waals potentials in the case of a sphere interacting with a heterogeneous semi-infinite medium, even in the case in which the properties of the semi-infinite solid change discontinuously, representing two homogeneous materials in contact. Thus, we model the transition potential either as a linear function constructed to satisfy the continuity of the total potential at every height or as an s-shape curve given by a third degree polynomial in \(y\) constructed to both, satisfy continuity of the total potential, and yield a vanishing force at the edges of the transition regions at every height. As will be seen in the following section, the results of the BD simulations are insensitive to the shape of the transition potential for the case in which the transition region is much narrower than the width of the stripes.

Fig. 6. Marginal probability density for different Pécel numbers for a partition ratio \(K = 2\). The differences in the convective fluxes at the interface between the stripes due to partition result in compensating diffusive fluxes to satisfy continuity of the flux. The shaded areas represent the concentration difference across the stripes, which differ by a factor of \(K\). The net diffusive flux opposes the total flux in the direction normal to the stripes.
3.5. PIVC in microfluidic devices

To show the potential of PIVC we consider different separation scenarios for a mixture of particles carried by a pressure-driven flow over the stripe pattern shown in Fig. 2 and compare the predictions based on the FJ approximation with the results of BD simulations. The geometry considered is a slit channel with a height of 10 μm. The bottom wall is patterned with 10 μm stripes, oriented 45° with respect to the forcing angle of the undisturbed flow ($\theta_f = 45^\circ$). To predict the migration angles from Eq. (45) and to carry out the simulations from Eq. (47c) we use the analytical approximation given by Pawar and Anderson [50] for the in-plane motion of a particle confined between two parallel walls, the analytical expression for the out-of-plane mobility of a particle in the vicinity of a plane wall [51] along with the linear superposition approximation [52] to account for the presence of the other wall, and interpolate the numerical results tabulated by Staben et al. [53] for the velocity of a particle confined between two parallel walls in Poiseuille flow. Let us note that in the case of physical patterns we neglect the effect of the steps in the hydrodynamic force and resulting velocity of the particle. Fig. 7 presents the discrimination angle, i.e., the difference between the trajectory angle and the forcing angle, for different pairs of particles as a function of the average velocity of the carrying flow. Specifically, each of the systems and pair of particles considered in panels (a)–(d) in Fig. 7 correspond to a system and particles for which the partition ratio is shown in panels (a)–(d) in Fig. 5, respectively. In Fig. 7a and b particles of the same (different) size are separated according to their mass with partition induced by gravity. Panels (c) and (d) in Fig. 7 show the separation of particles based on their Van der Waals interaction with chemically different stripes. Specifically, Fig. 7c shows the separation of particles of the same size but with different affinity with one of the stripes. The separation of particles of the same material but of different size is shown in Fig. 7d. Separation is readily accomplished for all cases considered; one of the particles only marginally departs from the forcing angle owing to weak partition, while the other particle has a high affinity to one of the stripes resulting in strong deviations from the forcing angle. The data points in panels (c) and (d) correspond to the results obtained by BD simulations. The error bars correspond to the standard deviation of 128 realizations of BD simulations tracking an individual particle for 50 units of dimensionless time. These simulations have

Fig. 7. Discrimination angles as a function of the average velocity of the underlying flow with partition induced by gravity, (a) and (b), and Van der Waals interactions, (c) and (d), for particles of the same and different sizes. The solid curves correspond to the results of the Fick-Jacobs approximation while the data points in panels (c) and (d) correspond to Brownian dynamics simulations.
a transition region with a width of two-hundredth the length of the unit cell in the y direction (let us call this dimensionless width of the transition region). In order to validate our analytical results obtained with a piece-wise potential ($\delta = 0$) we have carried out simulations for a linear and an s-shape transition potential for decreasing values of $\delta$. We found that as $\delta$ decreased the results of the simulations approach the analytical results and become independent of the shape of the transition potential. More specifically, the components of the average velocity of the particle for $\delta = 0.005$ and $\delta = 0.025$ differ by less than 5%.

The FJ approximation and the simulation results are in excellent agreement over the whole range of flow velocities due to the narrow confinement of the particles by the potential (see Fig. 4). Note that $Pe = 47.14$ for the highest velocity considered in the simulations. However, the particle with the largest excursions, corresponding to the lower curve (and data points) in Fig. 7d, is confined to a region of about 10 nm around the equilibrium particle-wall separation, resulting in $Pe^{35} = Pe(a/l_y)^2 = 0.001$.

4. Conclusions

We showed that vector chromatography in planar microfluidic devices is feasible by harnessing surface interactions that lead to the spontaneous partition of different species. First, we derived analytical solutions for the trajectory angle of a particle driven by an external force or convected by a flow field in a slit geometry. These results were obtained for an arbitrary two-dimensional periodic potential with the Fick–Jacobs approximation. We showed that the migration angle depends on particle properties, thus providing the basis for vector chromatography of different species. We then considered the case of a piece-wise constant periodic potential, which could be created by chemically or physically patterning one of the surfaces of a microfluidic device with an array of rectangular stripes, that causes the spontaneous partition of suspended particles. We showed that partition results in diffusive fluxes that oppose the convective transport that drives the system out of equilibrium and reduce the velocity component in the direction normal to the stripes. As a result, the particles migrate at angles that differ from the orientation angle of the driving field, the effect being stronger with increasing partition ratios. Specifically, we considered the fractionation of particles of the same and different size using both physically patterned channels where partition is induced by 1-g gravity as well as chemically patterned channels in which partition is induced by Van der Waals interactions. We validated our results by means of BD simulations that agree well with the results obtained by means of the FJ approximation. We observe good agreement even at relatively large values of Pe due to the highly confining nature of the particle-wall interaction. Thus, we demonstrated that partition-induced vector chromatography (PIVC) of particles exhibiting different partition ratios is feasible in microfluidic devices. In addition to continuous operation, another promising feature of PIVC is its potential versatility that stems from the vast range of physicochemical properties that can be employed to induce partition. Furthermore, separation can be achieved in an autonomous device without the need for external components, thus facilitating its portability and integration with other lab-on-a-chip components. In addition, partition can also be induced or enhanced by means of externally applied fields. As in FFF, different subtechniques are envisioned depending on the nature of the forces leading to partition. Further work is needed to explore different pattern geometries besides the stripe case considered here in order to optimize the sensitivity of the discrimination angle to the partition ratio and extend the range of operation to higher Péclet numbers. Future work will also explore the effects that the shape of the periodic potential and its magnitude, relative to thermal energy, have on the trajectory angle. Lastly, it is interesting to note that the results presented here suggest the possibility of inducing vector chromatography by exploiting the dependence of the trajectory angle on the velocity and mobility of the particles over each stripe through the parameters $\lambda$ and $\Pi$ in Eq. (45).

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References