Spatially dependent diffusion coefficient as a model for pH sensitive microgel particles in microchannels

S. Pieprzyk,^{1,a)} D. M. Heyes,^{2,b)} and A. C. Brańka^{1,c)}

¹*Institute of Molecular Physics, Polish Academy of Sciences, M. Smoluchowskiego 17, 60-179 Poznań, Poland*

²*Department of Physics, Royal Holloway, University of London, Egham, Surrey TW20 0EX, United Kingdom*

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Solute transport and intermixing in microfluidic devices is strongly dependent on diffusional processes. Brownian Dynamics simulations of pressure-driven flow of model microgel particles in microchannels have been carried out to explore these processes and the factors that influence them. The effects of a pH-field that induces a spatial dependence of particle size and consequently the self-diffusion coefficient and system thermodynamic state were focused on. Simulations were carried out in 1D to represent some of the cross flow dependencies, and in 2D and 3D to include the effects of flow and particle concentration, with typical stripe-like diffusion coefficient spatial variations. In 1D, the mean square displacement and particle displacement probability distribution function agreed well with an analytically solvable model consisting of infinitely repulsive walls and a discontinuous pH-profile in the middle of the channel. Skew category Brownian motion and non-Gaussian dynamics were observed, which follows from correlations of step lengths in the system, and can be considered to be an example of so-called “diffusing diffusivity.” In Poiseuille flow simulations, the particles accumulated in regions of larger diffusivity and the largest particle concentration throughput was found when this region was in the middle of the channel. The trends in the calculated cross-channel diffusional behavior were found to be very similar in 2D and 3D.

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I. INTRODUCTION

An important feature of biomicrofluidic devices^{1–7} is that the fluid flow is laminar.^{8,9} Adjacent flow streams translate by advection without significant mixing, and solutes in the adjacent streams only intermingle via the process of diffusion, which is therefore an especially important mechanism of particle transport on the microscale.^{10,11} Volumes of fluid do not mix to any significant extent except by boundary diffusion around its borders and, if required, mixing of the solutes can be enhanced by the introduction of zig-zag channel geometries (“mixers”).^{1,2} It is important to understand the intermixing process of biomolecules between liquid layers, of possibly different chemical constituency, as it has an impact on the effectiveness of assay-related activity, and consequently microfluidic device geometry design. This has received relatively little theoretical analysis in the context of microfluidics, which we redress in this work. The results of this work could eventually be used to assist in optimising the design and functionality of biomolecular microfluidic devices, which may include converging channels, valves, pumps, and mixers within the flow network.

Spatial variations of the diffusion coefficient can arise through the action of confinement, surface coatings, and external stimuli (e.g., temperature gradient, electric and magnetic fields),

^{a)}Electronic address: slawomir.pieprzyk@ifmpan.poznan.pl

^{b)}Electronic address: david.heyas@rhul.ac.uk

^{c)}Electronic address: branka@ifmpan.poznan.pl

and the ability of the particles to navigate around bends and other distortions of the channel geometry can combine to govern the particle flow profiles and mean speeds in a non-trivial way.¹² A potential consequence of medium inhomogeneity is that the diffusion coefficient of the dispersed particle is not a constant but becomes a space-dependent quantity. The position dependence of diffusivity can also significantly influence properties of the dispersion, such as viscosity and the mixing facility of multicomponent systems. In fact, inhomogeneity can lead to fundamentally new behavior such as anomalous diffusion (super- or subdiffusion), nonergodic effects,^{13,14} and the occurrence of multiplicative noise.¹⁵ Therefore, when describing the system dynamics and explaining related experimental results, it is important to consider any diffusion inhomogeneity effects and their potential interplay with any imposed flow profiles, as this will affect the spatial distribution of the particles along the channel with time and hence the flux of particles.

The diffusion coefficient of the suspended particle can be changed through variable chemistry and particle size (which follows directly from the Stokes-Einstein equation). Soft colloidal particles such as core-shell systems with grafted polymer coats and microgel particles have been used in this capacity. Microgel particles (MG) are crosslinked macromolecules of colloidal size that swell or shrink to varying extents in solvents depending on the constituent chemistry, crosslinked density, and external stimuli such as temperature or pH.^{16,17} This allows the thermodynamic and physical property state to be controlled *in situ* through the imposition of external conditions. The MG have found use in medical applications as potential cartilage replacement¹⁸ and as friction and antiwear modifiers.^{19,20} Dispersions of MG exhibit the characteristics of colloids in general, such as an increase of viscosity with volume fraction, progressing eventually at sufficiently high densities to a jammed or glassy nonequilibrium state with non-zero shear modulus and a yield stress required to initiate flow.^{21,22}

Biomolecular systems in solution have been modelled numerous times using the computer simulation technique of Brownian Dynamics (BD), which is based on the Langevin formulation of Brownian motion. This treats the solvent as a continuous background. The dispersed particles are followed explicitly through time and space in the simulation, subject to their interparticle forces and solvent drag and Brownian forces. The BD technique has also been exploited for biomolecular systems in model biomicrofluidic devices. For example, Hsieh and Lin²³ examined by BD two conformational preconditioning approaches to improve DNA stretching in a microcontraction in direct gene analysis. Jain and Dorfman²⁴ calculated by BD the Kirkwood (short-time) diffusivity and long-time diffusivity of DNA chains from free solution down to channel confinement in the de Gennes regime.

The situation becomes more complicated if the self-diffusion coefficient is spatially varying in the system, as it can be in biomicrofluidic devices. In the Langevin formulation of Brownian motion, the position-dependent diffusion coefficient leads to, for example, multiplicative noise and different particle position update formulas.^{25–29} The overdamped Langevin equation (OLE) depends explicitly on the convention of the noise evaluation and there has been much discussion on the physical meaning and role of some of the terms, in particular, the one usually referred to as “spurious drift” which results from taking into account the spatial gradient of the diffusion coefficient. Recently, this fundamental issue has been revisited in Refs. 15, and 30–32 and it has been shown that the OLE is uniquely determined. It has been proved that there is no controversy concerning the interpretation of multiplicative noise and no preferred physically favorable representation exists.

The problem of Brownian motion with a position-dependent self-diffusion coefficient has also been a subject of intensive theoretical and mathematical investigation in relation to particle transport and tracking in heterogeneous media with discontinuous interfaces, where so-called “skew Brownian motion,” which is a stochastic process in which the skewness of the transition probability is nonzero, is realized.^{33–35} The effective position-dependent diffusion coefficient has an impact on dispersed particle motion in channels with various 2D geometries including, for example, narrow bottlenecked channels and random wall configurations.^{36,37} The physical origin of a position-dependent self-diffusion coefficient, $D(\underline{R})$, where $\underline{R}$ is the coordinate of the dispersed particle in a liquid can arise in different ways. Causes include hydrodynamic

interactions mediated by boundary walls, a spatial temperature variation,³⁸ and a pH spatial variation.^{39–41} We focus here on the latter type as the variation of MG size with pH can be well controlled. This is an important stimulus for MG as they are used as biosensors^{5–7} and as drug delivery agents whose function depends on pH.⁴²

A microgel particle subject to a pH gradient, $\text{pH}(\underline{R})$, can cause its diameter, σ , to be $\underline{R}$ -dependent, reflecting the local pH value. Consequently the spherical microgel self-diffusion coefficient can be taken to be inversely proportional to its diameter, according to the Stokes-Einstein formula.⁴³ Therefore, in the case of a pH sensitive microgel particle, it is possible to introduce a corresponding spatial pattern of the diffusion coefficient through the design of the space dependence of $\text{pH}(\underline{R})$ or pH-field. Different pH distributions can be achieved readily in microchannels within microfluidic devices. For example, a constant pH gradient across a microchannel can be established during laminar flow in Y-type microchannels.^{44,45} Also the sharpness of the interface can be varied by design, and more complex pH-fields can be achieved by varying the size, shape, and the structure of the confining walls or introducing special constrictions (so called “mixers”) into the device.^{46–48}

Therefore, a dispersion of stimuli-active microgel particles in a microchannel with inhomogeneous solvent composition is a practical realization of particle Brownian motion with a varying diameter and position-dependent diffusion in a confined space. There are three elements to this class of system. It is an example of an “advection dispersion” model, which is characterized by (a) a stationary inhomogeneity in the diffusion coefficient, (b) confinement effects through the microchannel geometry, and (c) a superimposed flow field, of the Poiseuille type, here. The spatially varying pH causes two changes simultaneously; it introduces diffusional inhomogeneity and changes the interaction between the particles through the variable particle diameter and hence alters the thermodynamic state of the system.

In this work, various aspects of this general and relatively little studied configuration are investigated. The model and the equations of motion are described in Sec. II. In Sec. III, a one dimensional (1D) model of particle diffusion across the channel in the z -direction is studied, which may be considered to be a simple model for the motion of a Brownian particle moving between repulsive walls subject to a given $D(z)$ -profile. The next case studied, in Sec. IV, is the flow along the x -direction of N dispersed particles of various concentrations in a 2D channel with a $D(z)$ -profile of different analytic forms. Finally, some aspects of the corresponding 3D Poiseuille flow (PF) model are reported.

II. MODEL

An example of the pH dependence of a microgel spherical particle of diameter, σ , is shown in Fig. 1, which can be represented well by

$$\sigma(\text{pH}) = c_1 + c_2 \arctan(c_3 \text{pH} + c_4), \quad (1)$$

where c_1, c_2, c_3 , and c_4 are four adjustable constants. The three experimental examples given in the figure show typical pH sensitive behavior.^{39–41} There are two examples of a MG which increases in diameter as the solution becomes more acidic, and one example (shown as triangles) where there is an decrease. In both cases, the change in size can range by a factor of 2 – 5 over the accessible pH range.

A schematic diagram of the basic system 3D geometry used in this work is shown in Fig. 2. It consists of a channel with a square cross-section of dimensions, $2w \times 2w$, and a length, L , along the x -direction with periodic boundary conditions in that direction. The pH decreases from bottom to top of the channel in the z -direction according to the profile function, $\text{pH}(z)$

$$\text{pH}(z) = b_1 \tanh(b_2 z) + b_3, \quad (2)$$

where the transition range and pH bounds are determined by the three constants, b_1 , b_2 , and b_3 . Therefore, the pH-profile function acts as an external stimulus which causes the size of the microgel particle diameter to change according explicitly to z as,

FIG. 1. Examples of the pH dependence of the microgel particle diameter for three types of experimentally realizable microgel system. PEGMA/PDPA,³⁹ poly(2-vinylpyridine-co-styrene),⁴⁰ and poly(EA/MAA/BDDA).⁴¹ The PEGMA/PDPA MG is a combined monomethoxy-capped poly-(ethylene glycol) methacrylate macromonomer (PEGMA) and a poly(2-(diisopropylamino)ethyl methacrylate) (PDPA) microgel. The poly(EA/MAA/AM) microgel particle contains MAA (methacrylic acid), where EA and AM are ethyl acrylate and allyl methacrylate. The solid lines are produced from the expression in Eq. (1) with different sets of the constants, c_1 , c_2 , c_3 , and c_4 . A microgel particle in two different diameter states is sketched schematically in the figure.

$$\sigma(z) = c_1 + c_2 \arctan(c_3 [b_1 \tanh(b_2 z) + b_3] + c_4), \quad (3)$$

obtained by substituting Eq. (2) in Eq. (1). The position-dependent self-diffusion coefficient $D(z)$ is then calculated from the Stokes-Einstein relation $D(z) = \text{const}/\sigma(z)$, where $\sigma(z)$ is taken from Eq. (3).

In this work, the channel width is of order of 20 minimal diameters or the diameter of a particle in the unswollen “reference” state. An inverse power force with exponent, m , of the form, $F_{zi}^{\text{wall}} = m\epsilon(\sigma_i/(z_i + w))^m/(z_i + w) + m\epsilon(\sigma_i/(z_i - w))^m/(z_i - w)$ acts between the i -particle and the walls placed at $z = \pm w$. The interaction F_{yi}^{wall} with the walls at $y = \pm w$ is defined in the same way. The interparticle interactions, $\mathbf{F}_{ij}^{\text{int}} = 4n\epsilon(\sigma_{ij}/r_{ij})^n \mathbf{r}_{ij}/r_{ij}^2$, are also purely repulsive, where the stiffness exponent is n . This form has been used previously to represent microgel particles for not too dense suspensions.⁴⁹ In this interaction, r_{ij} denotes the separation

FIG. 2. A schematic diagram of the basic system geometry. The swelling of the particle diameter going from the bottom of the channel to the top in the z -direction is shown.

distance between particles i and j , ϵ is the unit of energy, and $\sigma_{ij} = (\sigma_i + \sigma_j)/2$ is derived from the two different particle values which as noted above are in general a function of z .

The Brownian Dynamics equations of motion of N particles in the microchannel geometry of Fig. 2 are

$$\dot{x}_i = \frac{D(z_i)}{T} F_{xi} + g(z_i) \xi_{xi}(t) + v_x(y_i, z_i), \quad (4)$$

$$\dot{y}_i = \frac{D(z_i)}{T} F_{yi} + g(z_i) \xi_{yi}(t), \quad (5)$$

$$\dot{z}_i = \frac{D(z_i)}{T} F_{zi} + \frac{\partial D(z_i)}{\partial z_i} + g(z_i) \xi_{zi}(t), \quad (6)$$

where the notation $\dot{X} \equiv (dX/dt)$ as usual and the Ito convention³² has been adopted. The force Cartesian components on particle i are, $F_{xi} = \sum_{j \neq i}^N F_{xij}^{int}$, $F_{yi} = F_{yi}^{wall} + \sum_{j \neq i}^N F_{yij}^{int}$ and $F_{zi} = F_{zi}^{wall} + \sum_{j \neq i}^N F_{zij}^{int}$. Note the walls are smooth so there is no x -component to the wall-particle force. $\xi_{xi}(t)$ is the Gaussian white noise that satisfies $\langle \xi_{xi}(t) \rangle = 0$ and $\langle \xi_{xi}(t) \xi_{\beta j}(t') \rangle = \delta_{ij} \delta_{\alpha\beta} \delta(t - t')$. The z -dependent amplitude of the noise is $g(z) = \sqrt{2D(z)}$. The imposed flow profile, $v_x(y_i, z_i)$, takes the Poiseuille flow form.

In this work, the following reduced units are used. Temperature is in ϵ/k_B where k_B is Boltzmann's constant, length in σ_0 , energy in $k_B T$, force in ϵ/σ_0 , and time in σ_0^2/D_0 , or τ_B the Brownian relaxation time, which is the time it takes the particle to diffuse a distance of order its own diameter. The length, σ_0 , in real units is taken to be the average diameter of the poly-(ethylene glycol) methacrylate (PEGMA)/poly(2-(diisopropylamino)ethyl methacrylate) (PDPA) microgel particles treated in Ref. 39, which is equal 600 nm, and $D_0 = 0.8 \times 10^{-12} \text{ m}^2/\text{s}$ is the Stokes-Einstein derived self-diffusion coefficient of that particle in the bulk. In the calculations, the parameter, n , in the interparticle interactions was maintained at the value of 12, and for the particle-wall interaction different values, $m \geq 12$, were used. This study focuses on low density dispersions and slow laminar flow characterized by a Peclet number, $Pe = \sigma_0 v_0 / D_0 < 5$, where v_0 is the maximum velocity of the flow and the characteristic length scale in the shear gradient direction is taken to be the particle diameter. Water is the usual host fluid in microfluidic experiments, with v_0 experimentally being typically in the range $10^{-6} - 10^{-2} \text{ ms}^{-1}$, with a typical channel half-width of $ca. w = 100 \mu\text{m}$, which gives a Reynolds number, Re , ($\sim v_0 w / \mu$, where μ is the kinematic viscosity) in the range between $10^{-4} - 1$.⁹ The flow is not turbulent therefore. The corresponding experimental Pe range is from $ca. 1 - 10^4$, and these simulations are therefore at the lower end of the experimental scale.¹² In this region, the effects of diffusion and diffusional inhomogeneity are more important than convection, which is the focus of this part of our study. The reduced temperature was $T = 1$. The channel geometry was $2w = 20$ and $L = 40$. The number of particles in the 2D channel varied from 9 to 64, and in 3D from 32 to 256. The equations of motion were integrated with a time step of $\Delta t = 0.0001$. After equilibration, the time averages were calculated from 10 independent simulations of length each at least of 5×10^7 time steps.

The parameters chosen for the model are within the experimental range for microgel particles in microfluidic devices. The MG swelling (deswelling) or "lag" time, τ_s , is typically in the range $10^{-3} - 10^{-1} \text{ s}$.^{50,51} A swelling theory based on a stress balance on the solid network predicts $\tau_s \leq \tau_B$,⁵⁰ which indicates that the reversible swelling-deswelling transition can take place on a time scale less than the time it takes the model particle to diffuse a distance equal to its diameter, which justifies the imposition of sharp diffusion coefficient boundaries in the present computer model. Typical microfluidic channel widths are from a few to hundreds μm across,^{44-46,52} which correspond to from several to hundreds of particle diameters, or approximately the same number of τ_B to diffuse across the system channel. The simulations were carried out for the same order of magnitude number of τ_B as experiment, which is sufficient time

for the particles to come to equilibrium in one stripe, cross between stripes (“residence time”), and explore the whole system. Typical experimental flow rates in the channels range between 10^{-1} – 10^4 $\mu\text{m/s}$ ^{53–56} or 10^{-1} – 10^4 τ_B^{-1} for ~ 1 μm diameter MG, the lower end of this range being the flow rates used in the BD simulations, when converted to reduced units. This ensures that our computations were in the Newtonian flow regime for the particle volume fractions considered (see below).

The Brownian Dynamics computer model used here does not include hydrodynamic interactions between the particles nor hydrodynamic coupling between each particle and the confining walls. The model also does not include the effects of the forces on the colloidal particles on the host fluid velocity which is formally present in the basic fluid mechanics equation (for example, see Eq. (1) in Ref. 9), which can be important, for example, for polarizable sub-micron particles in traveling wave dielectrophoresis.⁵⁷ The velocity profile of the solvent in the present study is an input function which in this study has the Poiseuille flow analytic form. These other effects could be introduced in future studies, but here the most basic (and standard) model of Brownian motion was adopted, to act partly as a reference system, and to facilitate in a more analytically tractable way an understanding of the relationship between the particle properties and diffusional behavior.

First, the case where the particle trajectories are confined to a line along the z -direction is considered. This focuses just on some of the cross-channel aspects of the microchannel behavior. In particular, the influence of inhomogeneity on dynamics of a diffusing particle and the role of confinement are studied. The results from the 1D case are important to understand the behavior of the corresponding 2D and 3D models in which the gradient of the pH-field is still only in the z -direction.

III. THE 1D CASE

The variation in the pH-profile is along the z -direction and the Brownian motion of the model microgel particle is confined to a line between the two repulsive walls in that direction.

The z -dependent diffusion coefficient, $D(z)$, is obtained from the particle diameter formula from Eq. (3) but otherwise the particle diameter is not required and for the wall-particle interaction the prescription, $\sigma(z) = \sigma_0$, is chosen for model simplicity. In this section, to obtain quantities with sufficient accuracy, an ensemble of 10^6 noninteracting Brownian particles was evolved simultaneously for 5×10^7 time steps.

Integration of Eq. (6) for the 1D case and then application of a standard iterative procedure (see, e.g., the Appendix in Ref. 15), the particle displacement to first order in Δt in the Ito convention is derived to be

$$\Delta z = \frac{D(z)}{T} F_z \Delta t + \frac{\partial D(z)}{\partial z} \Delta t + g(z) \Delta W, \quad (7)$$

where $F_z = F_z^{\text{wall}}$, Δz is the particle displacement in a time step and $\Delta W(t) = \int_t^{t+\Delta t} \xi(t') dt'$ is the Wiener increment.

A. Mean square displacement (MSD)

It is of interest to establish how the inhomogeneity introduced by the position-dependent diffusion coefficient affects basic physical properties. In Fig. 3, the time-dependent mean square displacement obtained for different $D(z)$ functions and walls of different softness or m -values is shown. It may be seen from the figure that the form of $D(z)$ does influence considerably this basic dynamical quantity. The influence of the wall softness in the case of the steeply repulsive walls considered is marginal. All curves obtained with the same $D(z)$ and for $m > 12$ are hardly distinguishable. Also it can be seen from the figure that the time dependent mean square displacement, $\text{MSD}(t)$, is mainly determined by the magnitude of $D(z)$ in the two extreme z -limits (see Fig. 3(b)) and not by its shape (see Fig. 3(a)).

At long times, irrespective of the form of $D(z)$, the function, MSD , must tend to a constant value because the system is confined. The rate at which this constant value is reached depends

FIG. 3. The time-dependent mean square displacement (MSD) for different $D(z)$ -profiles and wall softness parameters, $m = 12$ and 36 . The symbols are the BD data, the solid lines represent the long time limit for the hard walls (i.e., $m \rightarrow \infty$), and dashed and dashed-dotted lines represent the soft walls. In the insets, the long time behavior is enlarged and the applied profiles denoted as P1 and P2 are drawn. The results in frame (a) are for the sharp and extended shape $D(z)$ -profiles, and in frame (b) for the sharp function, $D(z)$ -profiles with different plateau values.

on the form of $D(z)$, however. The limiting value $\text{MSD}(t \rightarrow \infty)$ is determined mainly by the channel width ($2w$) and the wall interaction parameters. For the steeply repulsive walls, as would be expected and may be seen in the figure, the limit tends to the known hard wall limit value, $2w^2/3$,⁵⁸ which is given in the figure as a solid line. Straightforward numerical calculations show that for $m > 12$ the limiting value, $\text{MSD}(t \rightarrow \infty) = 2w^2/3 - C/m$, where C is a constant for a given w . Thus, the limiting value scales simply with m , which may be used to define an effective channel width, $w^* = (w^2 - 3C/2m)^{1/2}$.

In addition to the limiting value, the estimation of MSD at other times is not a trivial task either. Below a scheme is proposed which allows some insight into the $D(z)$ -dependence of the MSD in the short-time regime to be obtained for steep $\text{pH}(z)$ -profiles. Note first that the model of a Brownian particle trapped between hard walls can be solved analytically.⁵⁹ Also, Brownian motion through step function interfaces with opened space boundaries has been studied intensively and the transition probabilities are known.^{34,60} The present system has features of both these two cases which need to be combined to develop an appropriate model for the present system description. The difference is that the walls are not hard and the pH -profile is defined

by a differentiable function, which is the physically realizable situation. It is reasonable to expect that for large m and a steep $D(z)$ -profile, so that the variance, δ_{var} , of $D'(z)$ is small, such a superposition might yield the correct short-time behavior of the particle MSD.

We consider the following “Wall-Interface-Wall” (WIW) specifications to explore the physical processes determining the behavior of the MSD of our BD modeled system. There are reflecting hard walls at $-w$ and w , the (discontinuous step function) interface is at $z=0$, the stationary distribution is $P_{st}(-w < z < w) = 1/2w$, and the definitions $D_1 = D(-w < z < 0)$ and $D_2 = D(0 < z < w)$ are used. The procedure is to consider the transition probability, $p(z, t; z_0)$, where z_0 denotes the initial position, separated into four regions, $-w < z_0 < -w/2$, $-w/2 < z_0 < 0$, $0 < z_0 < w/2$, and $w/2 < z_0 < w$. At short times, the Gaussian transition probability in the first region is affected mainly by particle reflection from the bottom wall at $z = -w$, the second and third regions are dominated by the $D(z)$ interface, and in the fourth region the transition probability must take into account the reflection from the top wall at $z = w$. The mean square displacement is then calculated according to its definition from integrals of the form, $\int dz \int dz_0 P_{st}(z_0) p(z, t; z_0) (z - z_0)^2$. There are ten double integrals defining the short-time MSD which are given in the [Appendix](#). Importantly, each of these integrals can be calculated analytically which results in the sum of a large number of terms involving polynomials, exponentials, and Gaussian error functions. In the small time limit, most of these terms are negligible and the following simple overall formula for $\langle [z(t) - z(0)]^2 \rangle$ is obtained

$$\begin{aligned} \langle [z(t) - z(0)]^2 \rangle &= (D_1 + D_2)t - \frac{4}{3w\sqrt{\pi}} \left(2D_1^{3/2} - D_1\sqrt{D_2} - \sqrt{D_1}D_2 + 2D_2^{3/2} \right) t^{3/2} \dots \\ &= 2C_1t - C_2t^{3/2} \dots, \end{aligned} \quad (8)$$

where C_1 and C_2 are the linear and second term time coefficients which both depend on D_1 and D_2 , and both are positive. The second term is due to the presence of the confining walls, which becomes negligible for $w \rightarrow \infty$. As $C_2 > 0$, the presence of the reflecting walls lowers the short-time MSD, and for $D_1 = D_2 = D$ the function $\langle [z(t) - z(0)]^2 \rangle$ simplifies to $2Dt(1 - (4/3w\sqrt{\pi})\sqrt{t})$.

A comparison between the BD simulation results and the above formulas for this WIW model is made in Fig. 4, and WIW is shown to represent very well the MSD for all systems in which $D(z)$ is sufficiently sharp (more specifically, $\delta_{var} < 0.03$ of its derivative) and $m \geq 12$. Importantly for all of these systems, the agreement extends to about $t=4$, which is sufficient time for the $D(z)$ form dependence of the MSD to be clearly evident. The close agreement obtained suggests that the physical system of interest here, that is, a microgel particle in a microchannel with a sharp pH(z)-profile, is a system where skew Brownian motion³⁵ can be evident. This behavior may have an influence on MG diffusional transport across interfaces in experimental microfluidic devices as discussed in Refs. 34 and 61.

The expression in Eq. (8) not only provides the initial behavior of the MSD but also helps to reveal some consequences of the positional dependence of the diffusion coefficient. It indicates, for example, that the linear term is just an average or effective diffusion $C_1 = 2D_{av}t$, where $D_{av} = \int_{-w}^w dz D(z)/2w$, which allows us to calculate it for any $D(z)$ function. Using the known value of C_1 , the coefficient C_2 can be obtained unequivocally from the short-time MSD which can be determined from BD simulations or by experiment using, for example, the incoherent intermediate scattering function.⁶² Also the coefficient C_2 can be used to determine D_1 and D_2 and hence the transition probability factor, $T_r = (\sqrt{D_1} - \sqrt{D_2})/(\sqrt{D_1} + \sqrt{D_2})$. Thus, the determination of C_2 may reveal relevant information about the effect of the buffer region interface. Similar conclusions have been made by Sen,⁶³ who studied the time-dependent diffusion coefficient behavior as a probe of the permeability of cell membranes.

A closer inspection of $C_2(D_1, D_2)$, represented in contour form shown in Fig. 5, reveals a new feature of the inhomogeneous system. Figure 5 indicates that this coefficient possesses a minimum along the line, $D_2 = kD_1$ for $D_2 > D_1$ and $D_2 = k^{-1}D_1$ in the case of $D_2 < D_1$, where the constant k is $18/(4 + \sqrt{7}) \approx 2.7085$. This means that for a given D_1 , there are particular

FIG. 4. The mean square displacement (MSD) at short times for the same $D(z)$ -profiles as in Fig. 3 (the insets) and $m = 12$. The symbols represent the BD data and the solid lines are for the calculated expression for that quantity from Eq. (8) for the WIW model. The dashed line in frame (a) is a fit to the BD data, $2D_{av}t - 0.0635t^{3/2}$.

values of D_2 , which are about three times larger and three times smaller, for which the short-time MSD is mainly dominated by the first or linear term in Eq. (8). Therefore, the values of D_1 and D_2 where the MSD is closest to being linear at short times have been identified.

B. Non-Gaussian parameter

Following the same procedure as for the MSD, it is possible to calculate for the WIW model the short-time behavior of the fourth moment of the displacement distribution (see the [Appendix](#)), and the resulting expression is

$$\begin{aligned} \langle [z(t) - z(0)]^4 \rangle &= 6(D_1^2 + D_2^2)t^2 \\ &- \frac{32}{5w\sqrt{\pi}} \left(4D_1^{5/2} - D_1^2\sqrt{D_2} - D_1^{3/2}D_2 - D_1D_2^{3/2} - \sqrt{D_1}D_2^2 + 4D_2^{5/2} \right) t^{5/2} \dots \quad (9) \end{aligned}$$

FIG. 5. Contour plot of the second term, $C_2(D_1, D_2)$ in the short-time analytical MSD function, given in Eq. (8). This coefficient possesses a minimum at $D_2 = kD_1$ for $D_2 > D_1$ (the upper solid line) or $D_2 = k^{-1}D_1$ in the case of $D_2 < D_1$ (the lower solid line), where $k = 18/(4 + \sqrt{7}) \approx 2.7085$. The dashed line is for $D_2 = D_1$.

The fourth moment is therefore predicted to have the form, $B_1 t^2 - B_2 t^{5/2}$, and it was confirmed that the range of its applicability is comparable to that of the MSD given in Eq. (8) and Fig. 4.

The results for the second and fourth moments enable deviations from simple diffusive motion to be assessed via the non-Gaussian parameter, $\alpha_2(t) = \langle (\Delta z)^4 \rangle / 3 \langle (\Delta z)^2 \rangle^2 - 1$. This frequently used indicator of non-Gaussian behavior is expected to vanish in the short time limit as the dynamics are Gaussian there. Indeed, for the homogeneous case of $D_1 = D_2$, then $\alpha_2(t \rightarrow 0) \rightarrow 0$, but for the inhomogeneous cases, $\alpha_2(t \rightarrow 0)$ tends to a value of $\alpha_{20} = (D_1 - D_2)^2 / (D_1 + D_2)^2$. This is confirmed in Fig. 6, where the analytical form for $\alpha_2(t)$ calculated from Eqs. (8) and (9) is compared with the BD simulation results for several combinations of D_1 and D_2 . Thus, the calculated $\alpha_2(t)$ for the WIW system indicates that inhomogeneity in the local diffusion coefficient can introduce departures from the classical Gaussian behavior.

FIG. 6. The non-Gaussian parameter, α_2 , as a function of time for different D_1 and D_2 values given in the graph. The symbols are the BD data and the solid lines represent the analytical expression obtained from the quantities defined in Eqs. (8) and (9) for the WIW model. The black dots at $t=0$ are for $\alpha_2(t=0)$, which is equal to $\alpha_{20} = (D_1 - D_2)^2 / (D_1 + D_2)^2$.

C. Displacements distribution

The departure from classical Gaussian behavior is also observed in the probability distribution functions (PDFs) of particle displacements Δz , or $P(\Delta z, \tau)$, for a time interval, τ , obtained for different $D(z)$ -profiles. The displacements $z(\tau) - z(0)$ were calculated from $N = 10^6$ equally spaced initial positions, $z(0)$, across the channel. Examples of the calculated distributions are shown in Fig. 7 for a fixed one interval $\tau = 0.05$. For sharp $D(z)$ -profiles represented well by the WIW model, this PDF can be expressed by a sum of two Gaussian distributions. Comparison with the effective Gaussian distribution, $G_{av} = \exp(-(\Delta z)^2/4D_{av}\tau)/\sqrt{4\pi D_{av}\tau}$, shown in the figure, demonstrates that $D(z)$ enhances both small and large particle displacements (see Fig. 7(a)). In the homogeneous case (where $D_1 = D_2$), it was observed that the PDF is a Gaussian distribution (as it must be). In general, for arbitrary $D(z)$, the PDF is not a simple

FIG. 7. The probability distribution functions, PDF, or $P(\Delta z, \tau)$ of particle displacements, Δz , for time interval $\tau = 0.05$. Frame (a) is for a sharp $D(z)$ -profile, and frame (b) is for a more gradual continuous function profile. Note the log-lin scale. The $D(z)$ -profiles used are plotted in the frame insets. The BD results are indicated by the symbol, ($\circ$), for $D(z)$ -profiles with the D_1, D_2 bounding values given in the figure. Results for the homogeneous $D_1 = D_2$ case are represented by the ($\times$) symbols. The lines are for models denoted in the plot, where G_1 , G_2 , and G_{av} are the Gaussian distributions with variances, D_1 , D_2 , and D_{av} , respectively. For the soft profiles in frame (b) the bold solid line represents the expression given in Eq. (10). In the central insets on both frames the distributions are plotted vs. $(\Delta z)^2$ to demonstrate any non-Gaussian behavior.

function (see Fig. 7(b)) which cannot be represented by conventional distribution forms. The general expression for the PDF can be deduced to be

$$P(\Delta z, \tau) = \frac{1}{2w} \int_{-w}^w \frac{ds}{\sqrt{4\pi D(s)\tau}} \exp\left(-\frac{(\Delta z)^2}{4D(s)\tau}\right). \quad (10)$$

This equation comes from the observation that in the case of the sharp $D(z)$ -profile (which is characterized by D_1 and D_2) this distribution is expressed as the sum of two Gaussians. Therefore, for the more gradual profile (see Fig. 7(b)) the distribution is the sum of more Gaussians and in the limit this sum goes over to an integral. The formula for $P(\Delta z, \tau)$ in Eq. (10) represents very well the simulation data for different $D(z)$ and is plotted in Fig. 7(b) as a bold solid line.

It is not immediately obvious why the displacement distribution is non-Gaussian if displacements are sampled from the Gaussian distributions of different variances, $2D(z)\Delta t$. A possible explanation is that as we are dealing with a heterogeneous system, and although the step directions are uncorrelated, there are correlations of the step lengths. The issue of correlations of step magnitudes without correlations of step directions, named *diffusing diffusivity*, has been investigated recently by Chubynsky and Slater,⁶⁴ in order to explain the problem of the normal linear time dependence of the MSD accompanied by a non-Gaussian displacement distribution. As these authors noticed, if there are regions of different diffusivity a long step, Δz , is more likely to be associated with a region of high diffusivity, and subsequent steps of the same particle are also likely to be longer than average. Such a situation would appear to take place in the case considered here of a Brownian particle confined between walls and subject to an imposed $D(z)$ -profile. For the WIW model or the infinitely sharp $D(z)$ -profiles, the strength of the step length correlation, in accordance with the a_{20} , increases with the difference $|D_2 - D_1|$. In conclusion, it is the diffusivity memory without directional memory that leads for different $D(z)$ to a non-Gaussian PDF of particle displacement. Thus, microgel particles in a microchannel with a pH-field may constitute a practical realization of the *diffusing diffusivity* behavior. Now we consider the model MG flow in 2D and 3D microchannels as a function of concentration.

IV. 2D AND 3D MICROCHANNELS

In this section, 2D and 3D channels containing a finite density of particles is considered. The basic features of the BD simulations reported above are maintained. The effect of particle concentration on the effective viscosity is neglected. Volume fractions up to *ca.* 10% are considered (experimental concentrations can be much smaller).⁵³ According to Einstein's viscosity formula,⁶⁵ the relative viscosity should be 1.25 at this concentration. This should not produce a significant qualitative effect, especially as there are no bends or constrictions in this channel configuration which could lead to a local build up of particles.

In what follows, three types of pH-field which may be introduced in a 2D microchannel are considered, which are illustrated schematically in Fig. 8. The channel axis is along the x -direction and z is the direction across the channel. The three variants in frames from top to bottom in the figure are referred to as models, M1, M2, and M3, respectively. Variants of M2 and M3, defined by different width values of the central stripe (H) in the figure, were also studied. In all of these cases, a sharp interface is assumed which yields a well defined pH stripe along the x -direction. The corresponding position-dependent diffusion coefficients are defined in the case of M1 via $\sigma(z)$ from Eq. (3). In the M2 and M3 cases, the diffusional inhomogeneity is represented by $D(z) = (D_1 - D_2) \exp(-(2z/H)^\gamma) + D_2$ and $D(z) = -(D_1 - D_2) \exp(-(2z/H)^\gamma) + D_1$, respectively, where γ is a constant determining its steepness. These $D(z)$ -profiles can be largely distinguished by their minimum and maximum values, which we denote, as for the WIW case above, by the symbols, D_1 and D_2 . Specifically, M1 is a two region (D_1, D_2) model, while M2 and M3 consist of three regions with diffusion coefficient orders arranged as (D_2, D_1, D_2) and (D_1, D_2, D_1) , respectively. Additionally, another model labeled M0, with the homogeneous situation $D_1 = D_2$, was simulated as a reference for comparison purposes.

FIG. 8. The three types of pH-field in the microchannel denoted by M1, M2, and M3 and the corresponding $D(z)$ -profiles and $\sigma(z)$ -profiles on the right hand side of the figure. The different pH(z) induce size particle differences which are illustrated schematically in the figure. The grey area indicates the D_1 defined region and the white area is for the D_2 specified diffusion coefficient region. The M2 and M3 models have variants defined by different values of the H value, the width of the central stripe.

The N model dispersed particles moved according to an imposed Poiseuille flow (PF) profile which is the prototype type of flow in microchannels.⁶⁶ The PF in 2D is characterized by a parabolic velocity profile of the form, $v_x(z) = v_0(1 - (z/w)^2)$, where v_0 is the maximum velocity of the flow. Details of the influence of the channel walls on the parabolic profile⁶⁷ are not included in our model. In fact, taking into account the other conditions of a wide channel and low Peclet number employed here, they are expected to be insignificant anyway, and the main focus here is on the role of $D(z)$. This simplified treatment allows us to capture some significant features of microgel particle flow in the confined space with a position-dependent diffusion coefficient. Also, the $D(z)$ -profiles of M1, M2, and M3 models in Fig. 8 are close to the idealized WIW and WIIW models (for W-hard wall, I-discontinuous interface) where as previously found these boundary conditions may be the subject of some rigorous mathematical treatments.^{34,35}

The steady-state behavior of the microgel suspension in the microchannel flow is determined in general by a large number of parameters and conditions. In the present model with a given microchannel geometry and type of particle-particle and wall-particle interaction, the response is determined mainly by three factors. These are the analytic form of $D(z)$, the value of v_0 which defines the flow strength, and the particle number density, $\rho = N/V = N/2wL$. BD simulations using the equations of motion given in Eqs. (4) and (6) were employed to explore the role of these three factors for dilute particle assemblies. The basic structural and dynamic

properties, the particle distribution, the MSD, and the particle flux J_x in the microchannel were calculated. Because of the channel symmetry, the microstructure of the suspension is well characterized by the position density distribution, $p(z)$, which is shown in Fig. 9 for the three $D(z)$ patterns. The figure shows that $p(z)$ is significantly influenced by the form of $D(z)$ and the average density, ρ . In the considered range of flow strength, the flow has a marginal effect on the calculated $p(z)$ and is therefore not presented in Fig. 9. For the three $D(z)$ cases (M1, M2, and M3),

FIG. 9. The position density distribution, $p(z)$, for different particle number densities, and for the models, M1, M2, and M3 given in frames (a), (b), and (c), respectively. The central stripe width is $H=4$. The sharp $D(z)$ -profiles are characterized by D_1 (grey area) and D_2 (white area).

the particle number density is enhanced in the higher diffusivity region(s), a tendency which increases with average particle density. The particles tend to move to a region where they are smaller in size (see Fig. 9(a)). This qualitative trend may be due to lower excluded volume repulsions between the smaller particles compared to the large particles, allowing more of them to be accommodated in that region. The distance decaying density maxima near the walls are known structural effects caused by the repulsive confining walls.^{68,69}

However, the particular form of $p(z)$ is the result of a nontrivial competition between entropic effects from the particle packing, the influence of the walls, and the imposed position dependence of particle diameter and diffusion coefficient which mimics the effects of the pH spatial variation in an experimental system. A convenient order parameter which can quantify this non-uniform distribution and tendency of the smaller particles to accumulate in a given region of space is the (relative) excess density quantity or the accumulation parameter defined by

$$\lambda = \left(\frac{\rho_1 - \rho_2}{\rho} \right) \frac{V_1}{V} = \frac{N_1}{V_1} - \frac{N_2}{V_2} \bigg/ \frac{N}{V}, \quad (11)$$

where N_1 and $N_2 = N - N_1$ denote the average number of particles in the two regions determined by D_1 and D_2 , respectively. The average particle number densities in the two domains are ρ_1 and ρ_2 , respectively, and V_1 and V_2 are the volume (area in 2D) of these regions. If all of the particles are in the V_1 region, there is maximum accumulation and $\lambda = 1$. In contrast, $\lambda = 0$ signifies that no particle accumulation takes place in either type of region (i.e., the particles are uniformly distributed across the whole volume, V). The Brownian Dynamics calculations performed here show that apart from in the very dilute region (where $\rho \rightarrow 0$), this measure of small particle accumulation increases linearly with overall density, so, $\lambda \approx K\rho$, where K is the constant of proportionality. The $\lambda(\rho)$ dependence is shown in the inset of Fig. 10. This figure also shows that the constant, K , depends markedly on the $D(z)$ models. In the main part of Fig. 10, the quantity λ is plotted as a function of v_0 for the three $D(z)$ -profile classes and at one density. An increase of the flow strength causes a noticeable increase of λ which depends on the given $D(z)$ model. Therefore, the accumulation effect as measured by λ can also be controlled by using different flow strengths and $D(z)$ patterns. These results suggest that the steady state structure of pH sensitive microgel particles flowing in a microchannel could be substantially modified by the form of the implemented pH-field.

FIG. 10. The particle number density accumulation parameter, λ , defined in Eq. (11) and plotted as a function of the flow strength v_0 for density $\rho \approx 0.07$. Results for the three models M1, M2, and M3 are presented. In the inset λ for different densities without applied flow is shown. The open symbols are the BD data and lines are linear regression fits to these data.

Perhaps even more significant is an observed influence of the pH heterogeneity on particle transport efficiency along the channel, which can be estimated from the particle flux. The particle flux is the net number of particles which flow per unit area per unit time and was calculated in the present simulations from the following expression:

$$J_x = \frac{1}{At} [N_L - N_R], \quad (12)$$

where A is the cross-sectional area or channel width in 2D, N_L is the total number of particles which moved from left to right, and N_R is the number of particles which moved from right to left in time t across an arbitrarily positioned plane. This measure of the rate of transfer of particles through a unit area quantifies particle transport efficiency through the microchannel.

The particle flux calculated for different densities, v_0 , and $D(z)$ models is shown in Fig. 11, which shows J_x/ρ plotted as a function of v_0 . The results obtained show that the flux increases almost linearly with v_0 and ρ in the considered range, which is the expected dependence. The influence of the $D(z)$ -profile is significant and seems to be well quantified by the average diffusion coefficient, $D_{av} = \int_{-L/2}^{L/2} dx \int_{-w}^w dz D(z) / 2wL$ as shown in the inset of Fig. 11. It is evident from the figure that the variation of H in the M2 and M3 models produces only small changes in the flux value. This indicates that the particle flux is determined mainly by the arrangement of the D_1 and D_2 domains which define M2 and M3. Figure 11 shows that the most efficient particle transport can be achieved with the M2, i.e., where the central domain has the larger diffusivity, as might have been expected.

From its definition, the mean square displacement is the sum of the MSD in the wall parallel and orthogonal directions, $\langle [\mathbf{r}(t) - \mathbf{r}(0)]^2 \rangle = \langle [x^*(t) - x(0)]^2 \rangle + \langle [z(t) - z(0)]^2 \rangle$, where $x^* = x(t) - v_x(z)\Delta t$, to subtract off the advected component of the displacement. At long times, this quantity exhibits the expected dependence, $2Dt + C$, where the constants D , C depend on the particle density. At short and intermediate times, the form of the MSD, as for the previously investigated 1D case, depends considerably on the $D(z)$ -profile. The complicated character of the dependence is well reflected in the non-Gaussian parameter, $\alpha_2 = \langle (\Delta \mathbf{r})^4 \rangle / 2 \langle (\Delta \mathbf{r})^2 \rangle^2 - 1$, which is shown as a function of time in Fig. 12(a) for the different $D(z)$ -profile cases. As may be seen diffusional inhomogeneity causes a nonzero value of this property as $t \rightarrow 0$. These results as well as being direct observations of the BD trajectories indicate that the magnitudes of the step sizes are correlated. The apparent similarity of these results with those of the 1D case in Fig. 6 suggests that the Brownian motion in the z -direction preserves its own character in 2D flow. This is consistent with a conclusion proved by Ramirez *et al.* in Ref. 33 that in the

FIG. 11. The normalized particle density flux, J_x , as a function of v_0 for different $D(z)$ -profiles denoted in terms of the different 2D models. The symbols are BD data and are linear regression fits to these data. In the inset the influence of different $D(z)$ -profiles is expressed using the D_{av} as the variable.

FIG. 12. The non-Gaussian parameter, α_2 , as a function of time. Frame (a) is for the 2D system at $\rho = 0.1$ with α_2 defined as $\langle(\Delta\mathbf{r})^4\rangle/2\langle(\Delta\mathbf{r})^2\rangle^2 - 1$. Frame (b) is for the 3D system at $\rho = 0.01$, where α_2 is defined as $3\langle(\Delta\mathbf{r})^4\rangle/5\langle(\Delta\mathbf{r})^2\rangle^2 - 1$. The results for different $D(z)$ -profiles denoted in the graph are presented. The symbols represent the BD data for 2D and 3D models.

direction transverse to the flow and across an interface where the diffusion coefficient is discontinuous, the stochastic particle trajectory is given by skew Brownian motion.

Finally, the role of a spatially dependent diffusion coefficient was investigated for a 3D microchannel using the same type of $D(z)$ -profiles as in the 2D case of Fig. 8. The BD simulations using Eqs. (4)–(6) were performed for a square channel geometry with Poiseuille flow of the form

$$v_x(y, z) = v_0 \sum_{n, \text{odd}} \frac{1}{n^3} \left[1 - \frac{\cosh\left(n\pi \frac{y}{2w}\right)}{\cosh\left(\frac{n\pi}{2}\right)} \right] \sin\left(n\pi \frac{z+w}{2w}\right). \quad (13)$$

The above velocity profile is an analytical solution of the Navier-Stokes equation for laminar flow in a rectangular microchannel.⁶⁶ In fact, the series given in Eq. (13) converges quickly and in the simulations only the first three terms were needed to represent $v_x(y, z)$ to sufficient accuracy. The flow strength v_0 stands for $16w^2\Delta p/\pi^3\mu L$, where $\Delta p/L$ denotes the pressure gradient, w and L are geometry of the microchannel (in Fig. 2), and μ is the fluid viscosity.

FIG. 13. Normalized particle density flux, J_x , as a function of v_0 for different $D(z)$ -profiles denoted in the figure for different 3D models. The symbols are the BD data and the lines are linear regression fits to these data. In the inset, the influence of different $D(z)$ -profiles is expressed through D_{av} .

The BD simulations carried out revealed that most of the trends observed in the 2D case (see Figs. 9–12) take place also in the 3D microchannel. In particular, a non-Gaussian character of the time-dependent MSD was also observed. This can be seen in Fig. 12 where the non-Gaussian parameter is compared for 2D (frame a) and 3D (frame b). Note that the overall 3D behavior is similar to that manifested by the 2D case. The results indicate that the Brownian motion in the z -direction preserves the same characteristics in 2D and 3D flow.

Figure 13 shows that the particle flux, again calculated using Eq. (12), displays most of the same features as those seen in the 2D case. The higher dimensionality causes a slight decrease in the value of J_x at a given v_0 . Also the influence of the different $D(z)$ models on the flux appears to be slightly less strong than in the 2D case. As found in 2D, this can be quantified via the average diffusion coefficient as is shown in the inset of Fig. 13.

An important result from the 3D model is that of the considered models the most efficient particle transport in a square cross-section channel is as for 2D the M2 model, i.e., when the central stripe domain has the largest particle diffusivity.

V. CONCLUSIONS

Simple models which cast light on the diffusive and flow characteristics of a low particle number density dispersion of pH sensitive microgel particles in a microchannel with spatially varying pH have been explored. The pH affects both the local diffusion coefficient and the thermodynamic state through the pH dependence of the particle diameter. Brownian Dynamics (BD) simulations were used to solve the overdamped Langevin equations of motion for particles manifesting this location dependent diffusion constant, D , term. Simulations were carried out in 1D to represent some of the cross flow (z -direction) issues, and in 2D and 3D to include the effects of flow for slow flow (small Peclet number) and typical stripe-like D inhomogeneities which could be realized in the microchannels experimentally. Because of the system symmetry the spatial inhomogeneities are entirely specified through the $D(z)$ -profile.

In the 1D model, the mean square displacement and particle displacement probability distribution function obtained by BD was compared with an analytically solvable WIW model consisting of infinitely repulsive walls and a discontinuous pH-profile. The WIW model describes very well the BD system with a sharp $D(z)$ -profile and steep confining walls and gives explicit formulas for the short time expansion of the MSD, which reveals a nontrivial influence of the local diffusion coefficient on the system parameters, called “skew-Brownian motion” or “diffusion diffusivity” which results from a correlation of the particle step lengths.⁶⁴ This behavior is characterised by a short time mean square displacement which is not linear in time, and which is accentuated as the channel becomes thinner. The displacement probability

distribution function could be expressed entirely in a (generalised) Gaussian form given in Eq. (10), which reduces to the sum of two Gaussians in the WIW case. Although an exponential plus Gaussian representation of the PDF was found for another occurrence of this behavior for swimming microorganisms.⁷⁰ The Brownian Dynamics particle based approach is an appropriate technique to model microfluidic particle transport because it automatically produces this behavior and the various factors which may contribute to determine a spatially dependent diffusion coefficient.

Simulations of flowing Brownian particles through a 2D channel show that the steady state structure and particle transport efficiency depend significantly on the $D(z)$ -profile form. Accumulation of particles in regions of larger diffusivity was observed, an effect which increased with density and flow rate, and is mainly connected with the position dependence of the particle size. The particle flux along the channel displays substantial sensitivity to different $D(z)$ -profiles even at low densities and for very weak flows, which may be quantified by an effective diffusion coefficient. Of the several inhomogeneity profiles investigated, the one with a central strip of high diffusivity and corresponding largest accumulation tendency gave the most efficient particle transport. This is physically reasonable as a larger number of small particles are then found in the region where the fastest part of the Poiseuille velocity arises. Therefore, maximum particle throughput could be achieved in practical microfluidic devices by using three stripes, in which the stimuli-sensitive particles are smallest in the central stripe and within which the peak of the Poiseuille flow velocity profile will be present.

The 2D short time dynamics displays features similar to the 1D case, in particular, it is non-Gaussian and sensitive to the $D(z)$ -profile. Also a correlation of step lengths was found which indicates that the particle dynamics in the direction transverse to the flow preserves its 1D characteristic features and that skew Brownian motion may be expected to occur in a 2D channel. The BD calculations performed for the square 3D microchannel exhibited qualitatively similar behavior to those carried out in 2D. Within the studied range of densities and flow strengths similar trends caused by the various $D(z)$ -profiles were obtained for structural and dynamic properties.

Thus, it may be concluded that pH sensitive microgels flowing in a microchannel with a given pH-field constitute an example of physical system which displays a number of novel and unique features. Combined theoretical and simulation treatments of the type explored here could potentially be used to improve the design of microgel carrying microfluidic devices.

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APPENDIX: SHORT-TIME MEAN SQUARE DISPLACEMENT (MSD) EXPRESSION

In this [Appendix](#), the integrals used to obtain the formula in Eqs. (8) and (9) for the WIW model are presented.

For short-times, the $2k$ -moments of the displacement distribution can be expressed as

$$\langle [z(t) - z_0]^{2k} \rangle = \sum_{i=1} \int_{a_i}^{b_i} dz \int_{c_i}^{d_i} dz_0 P_{st}(z_0) p_i(z, t; z_0) (z - z_0)^{2k}, \quad (\text{A1})$$

where $p_i(z, t; z_0)$ is the transition probability which has a dominant contribution for short-times in the range, $a_i < z < b_i$, $c_i < z_0 < d_i$. The stationary distribution is $P_{st}(-w < z < w) = 1/2w$ and $k = 1, 2$.

The transition probability for the interface with a discontinuous diffusion coefficient at $z = 0$ is known and given by^{34,60}

$$p^\omega(z, t, z_0) = \begin{cases} \frac{1}{\sqrt{4\pi D_2 t}} \left[\exp\left(-\frac{(z-z_0)^2}{4D_2 t}\right) + \frac{\sqrt{D_2} - \sqrt{D_1}}{\sqrt{D_1} + \sqrt{D_2}} \exp\left(-\frac{(z+z_0)^2}{4D_2 t}\right) \right] & \text{for } z_0 > 0, z > 0, \\ \frac{1}{\sqrt{4\pi D_1 t}} \left[\exp\left(-\frac{(z-z_0)^2}{4D_1 t}\right) - \frac{\sqrt{D_2} - \sqrt{D_1}}{\sqrt{D_2} + \sqrt{D_1}} \exp\left(-\frac{(z+z_0)^2}{4D_1 t}\right) \right] & \text{for } z_0 < 0, z < 0, \\ \frac{2}{\sqrt{D_2} + \sqrt{D_1}} \frac{1}{\sqrt{4\pi t}} \exp\left(-\frac{(z\sqrt{D_1} - z_0\sqrt{D_2})^2}{4D_1 D_2 t}\right) & \text{for } z_0 \leq 0, z \geq 0, \\ \frac{2}{\sqrt{D_2} + \sqrt{D_1}} \frac{1}{\sqrt{4\pi t}} \exp\left(-\frac{(z\sqrt{D_2} - z_0\sqrt{D_1})^2}{4D_1 D_2 t}\right) & \text{for } z_0 \geq 0, z \leq 0. \end{cases} \quad (\text{A2})$$

The stochastic process generated by this transition probability set is an example of so-called “skew Brownian motion,” which is defined by the skewness parameter, $\omega = \sqrt{D_2}/(\sqrt{D_2} + \sqrt{D_1})$. For the homogeneous case, $\omega(D_1 = D_2) = 1/2$ and normal Brownian motion is then recovered.

The transition probability $p^\omega(z, t, z_0)$ yields six p_i which have a dominant contribution near the interface for $-w/2 < z_0 < w/2$ and are defined as follows:

$$p_1 = \frac{1}{\sqrt{4\pi D_2 t}} \exp\left(-\frac{(z-z_0)^2}{4D_2 t}\right) \quad \text{for } 0 < z < w, 0 < z_0 < w/2, \quad (\text{A3})$$

$$p_2 = \frac{1}{\sqrt{4\pi D_2 t}} \frac{(\sqrt{D_2} - \sqrt{D_1})}{(\sqrt{D_1} + \sqrt{D_2})} \exp\left(-\frac{(z+z_0)^2}{4D_2 t}\right) \quad \text{for } 0 < z < w, 0 < z_0 < w/2, \quad (\text{A4})$$

$$p_3 = \frac{1}{\sqrt{\pi t}(\sqrt{D_1} + \sqrt{D_2})} \exp\left(-\frac{(\sqrt{D_2}z - \sqrt{D_1}z_0)^2}{4D_1 D_2 t}\right) \quad \text{for } -w < z < 0, 0 < z_0 < w/2, \quad (\text{A5})$$

$$p_4 = \frac{1}{\sqrt{4\pi D_1 t}} \exp\left(-\frac{(z-z_0)^2}{4D_1 t}\right) \quad \text{for } -w < z < 0, -w/2 < z_0 < 0, \quad (\text{A6})$$

$$p_5 = -\frac{1}{\sqrt{4\pi D_1 t}} \frac{(\sqrt{D_2} - \sqrt{D_1})}{(\sqrt{D_1} + \sqrt{D_2})} \exp\left(-\frac{(z+z_0)^2}{4D_1 t}\right) \quad \text{for } -w < z < 0, -w/2 < z_0 < 0, \quad (\text{A7})$$

$$p_6 = \frac{1}{\sqrt{\pi t}(\sqrt{D_1} + \sqrt{D_2})} \exp\left(-\frac{(\sqrt{D_1}z - \sqrt{D_2}z_0)^2}{4D_1 D_2 t}\right) \quad \text{for } 0 < z < w, -w/2 < z_0 < 0. \quad (\text{A8})$$

The p_i which have a dominant contribution near the top $w/2 < z_0 < w$ and bottom $-w < z_0 < -w/2$ hard reflecting walls are defined as follows:

$$p_7 = \frac{1}{\sqrt{4\pi D_2 t}} \exp\left(-\frac{(z-z_0)^2}{4D_2 t}\right) \quad \text{for } 0 < z < w, w/2 < z_0 < w, \quad (\text{A9})$$

$$p_8 = \frac{1}{\sqrt{4\pi D_2 t}} \exp\left(-\frac{(z-2w+z_0)^2}{4D_2 t}\right) \quad \text{for } w/2 < z < w, w/2 < z_0 < w, \quad (\text{A10})$$

$$p_9 = \frac{1}{\sqrt{4\pi D_1 t}} \exp\left(-\frac{(z-z_0)^2}{4D_1 t}\right) \quad \text{for } -w < z < 0, -w < z_0 < -w/2, \quad (\text{A11})$$

$$p_{10} = \frac{1}{\sqrt{4\pi D_1 t}} \exp\left(-\frac{(z + 2w + z_0)^2}{4D_1 t}\right) \quad \text{for } -w < z < -w/2, -w < z_0 < -w/2. \quad (\text{A12})$$

The integrals in (A1) can be calculated analytically using the transition probabilities in Eqs. (A3)–(A12). The final expression obtained is cumbersome and consists of hundreds of terms. However, most of these terms are negligible for small t and the final results for $k = 1, 2$ are presented in Eqs. (8) and (9).

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