DNA Dynamics in a Microchannel

Richard M. Jendrejack,^{1,*} Eileen T. Dimalanta,² David C. Schwartz,² Michael D. Graham,^{1,†} and Juan J. de Pablo^{1,‡}

¹Department of Chemical and Biological Engineering, University of Wisconsin–Madison, Madison, Wisconsin 53706, USA

²Department of Chemistry and Laboratory of Genetics, University of Wisconsin–Madison, Madison, Wisconsin 53706, USA

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An extended Brownian dynamics simulation method is used to characterize the dynamics of long DNA molecules flowing in microchannels. The relaxation time increases due to confinement in agreement with scaling predictions. During flow the molecules migrate toward the channel center line, and thereby segregate according to molecular weight. Capturing these effects requires the detailed incorporation of solvent flow in the simulation method, demonstrating the importance of hydro-dynamic effects in the dynamics of confined macromolecules.

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Emerging technologies for single-molecule analysis of DNA in micron and nanometer scale devices (e.g., [1-6]) have fueled considerable interest in the structure and dynamics of solutions of DNA in confined geometries. Predictive methods capable of describing the conformation and motion of polymer chains in micro- and nanofluidic geometries would be of considerable significance for the conception and design of such devices. The longest time scales of interest for confined solutions of DNA are accessible to coarse-grained, Langevin models [7,8]. The central challenge is to consider polymer and solvent motion simultaneously and self-consistently, with the solvent motion satisfying the no-slip boundary condition on the surfaces of the confining geometry. In this Letter, we develop a computationally tractable formalism to address this challenge, and use it to generate the first predictions of the dynamics of long (> 1μ m) DNA molecules flowing in channels of micrometer dimensions. In particular, hydrodynamic interactions in confined, flowing systems are shown to give rise to a pronounced, molecular-weightdependent depletion layer, thereby providing a basis for separation processes for DNA.

The equilibrium properties of polymer molecules in confined solutions have been studied extensively [9,10]. Their dynamics, both at equilibrium and under flow, have also been the subject of a considerable amount of research [11]. Nevertheless, previous computational studies of the dynamics of long, flexible polymer molecules in confined geometries have either ignored hydrodynamic interactions between polymer segments, or have considered these in a highly approximate manner (see, e.g., [12]). Even simple scaling arguments, however, show the limitations of these studies. Because of hydrodynamic screening by the walls [13], Rouse rather than Zimm scaling is expected for the chain diffusivity [17], a result supported by analyses with equilibrium-preaveraged hydrodynamic interactions [18,19]. More importantly, as shown in this Letter, fluctuating hydrodynamic interactions play a dramatic role in the dynamics of confined polymer solutions, especially under flow, and their correct treatment is essential to capture much of the physics relevant to descriptions of microfluidic systems.

In the present Letter, we extend to the microchannel situation a coarse-grained molecular model and simulation method that we have previously shown to provide an accurate representation of experimental data for DNA in bulk solution [20,21]. In that model, a dissolved double-stranded DNA molecule is represented by N_b interaction sites (beads) connected through $N_s = N_b - 1$ entropic connectors (springs). A force balance on this chain leads to a stochastic differential equation

$$d\mathbf{R} = \left[\mathbf{U} + \frac{1}{k_B T} \mathbf{D} \cdot \mathbf{F} + \frac{\partial}{\partial \mathbf{R}} \cdot \mathbf{D}\right] dt + \sqrt{2} \mathbf{B} \cdot d\mathbf{W}, \quad (1)$$

where k_B is Boltzmann's constant, T is absolute temperature, and $\mathbf{D} = \mathbf{B} \cdot \mathbf{B}^T$ is the diffusion tensor, described below. The vector \mathbf{R} contains the N_b positions, \mathbf{r}_i , of the interaction sites; subscript *i* denotes a specific site. The vector \mathbf{F} contains the non-Brownian, nonhydrodynamic forces \mathbf{f}_i acting on each site. The vector $\mathbf{U}_i = \mathbf{v}(\mathbf{r}_i)$ is the unperturbed velocity field (i.e., the velocity field in the absence of the polymer) at site *i*. The components of $d\mathbf{W}$ are obtained from a real-valued Gaussian distribution with mean zero and variance dt.

As it moves, a segment of the macromolecule exerts a force on the solvent, which creates a velocity field that in turn affects the motion of the entire macromolecule. In an unbounded domain, the Stokes flow velocity field due to a point force **f** located at \mathbf{x}_j is given by $\mathbf{v}'_{OB}(\mathbf{x}) = \mathbf{\Omega}^{OB}(\mathbf{x} - \mathbf{x}_j) \cdot \mathbf{f}(\mathbf{x}_j)$, where $\mathbf{\Omega}^{OB}$ is the free-space Green's function, or Oseen-Burgers tensor [7,15]. These hydrodynamic interactions (HI) enter the chain dynamics through the $3N_b \times 3N_b$ diffusion tensor, **D**, where

$$\mathbf{D}_{ij} = k_B T [(6\pi\eta a)^{-1} \mathbf{I} \delta_{ij} + \mathbf{\Omega}_{ij}].$$
(2)

Here η is the solvent viscosity and *a* is the bead hydrodynamic radius. In an unbounded fluid, $\Omega_{ij} = (1 - \delta_{ij}) \Omega^{OB}(\mathbf{r}_i - \mathbf{r}_j)$ [7,22]. A number of groups have incorporated HI at this level of description into

Brownian dynamics studies of unconfined chains [20,21,24–29].

Recent work has provided experimental validation of the use of point-particle hydrodynamics to describe the motion of a pair of Brownian particles near a surface [30]. In view of those findings, we assume that the pointparticle hydrodynamic formalism just described can continue to be used to study the confined motion of a chain in solution. In a general flow domain, the velocity perturbation $\mathbf{v}'(\mathbf{x})$ due to a point force **f** acting at \mathbf{x}_j is given as

$$\mathbf{v}'(\mathbf{x}, \mathbf{x}_i) = \mathbf{v}'_{\text{OB}}(\mathbf{x} - \mathbf{x}_i) + \mathbf{v}'_{\text{W}}(\mathbf{x}, \mathbf{x}_i).$$
(3)

Here $\mathbf{v}'_{W}(\mathbf{x}, \mathbf{x}_{j}) = \mathbf{\Omega}^{W}(\mathbf{x}_{i}, \mathbf{x}_{j}) \cdot \mathbf{f}(\mathbf{x}_{j})$ is the solution to an incompressible Stokes flow problem subject to $\mathbf{v}'_{OB} + \mathbf{v}'_{W} = 0$ at the walls. We solve this problem numerically with a finite element method, determining $\mathbf{\Omega}^{W}(\mathbf{x}_{i}, \mathbf{x}_{j})$ at a grid of points \mathbf{x}_{i} [31]. Then, $\mathbf{\Omega}_{ij}$ in Eq. (2) is given by

$$\mathbf{\Omega}_{ij} = (1 - \delta_{ij})\mathbf{\Omega}^{\text{OB}}(\mathbf{r}_i - \mathbf{r}_j) + \mathbf{\Omega}^{\text{W}}(\mathbf{r}_i, \mathbf{r}_j).$$
(4)

During a Brownian dynamics simulation, Ω_{ij}^{W} and its divergence are obtained by finite element interpolation [32].

The model is completed by specification of the spring and excluded volume forces. (We consider the high ionic strength case where electrostatic interactions are screened out.) For the spring we use the wormlike spring (WLS) model [33] used in many bulk studies of DNA dynamics [19,21,33–38]. As in our earlier work [19,21], a Gaussian excluded volume potential between any two sites of the chain is used [39].

Using $N_s = 10$ ($N_{k,s} = 19.8$) for 21 μ m stained λ -phage DNA at room temperature, in previous work [21] we determined, by direct comparison to available bulk experimental data, that suitable parameter values are Kuhn length $b_k = 0.106 \ \mu m$ [32], bead hydrodynamic radius $a = 0.077 \ \mu m$, and excluded volume parameter $v = 0.0012 \ \mu m^3$ [38]. With these values, the model reproduces the experimentally observed bulk relaxation time, diffusivity, and equilibrium coil size. It also gives results in quantitative agreement with transient and steady-state behavior of 21 μ m DNA in both simple shear and planar extension over a wide range of strain rates. The model also agrees with experimental diffusivity data for chains ranging from 21 to 126 μ m, underscoring its predictive capability. Therefore, after appropriate modifications to the hydrodynamics, as described above, the model should provide useful predictions of DNA behavior in microfluidic devices, particularly in the limits $N_s \gg 1$ and $H \gg a$, where H is a characteristic dimension of the device.

In this Letter, we consider the behavior of individual DNA molecules, at room temperature in a 1 cP solvent, in an infinitely long microchannel with square cross section. The center line of the channel is oriented along the x axis, with the cross section lying in the yz plane. A simple bead-wall repulsive potential confines the chain within the channel [40]. Molecules ranging from 4.2 μ m ($N_s = 2$) to 420 μ m ($N_s = 200$) were simulated in channels having widths H of 0.636 to 21.2 μ m. We define the "stretch" X of a chain as the absolute length of the molecule in the x direction. The longest relaxation time λ_1 is calculated by allowing an ensemble of chains that are initially fully stretched along the center line of the channel to relax to equilibrium; the tail of the relaxation curve of $\langle X^2 \rangle$ is fit to an exponential. ($\langle \rangle$ denotes ensemble average.) The (ensemble average) radius of gyration is denoted by S. The subscript b on a quantity denotes that it is evaluated in the bulk.

Figure 1(a) shows the dimensionless equilibrium stretch, $X^* = \langle X \rangle_{eq} / \langle X \rangle_b$, as a function of the inverse dimensionless channel width, $1/H^* = S_b/H$. Simple scaling arguments [9] and Monte Carlo simulations [10] give $\langle X \rangle \propto N_k H^{-2/3}$ for a chain in a good solvent. Our results are consistent with this scaling, and show that the transition from bulk to confined behavior is fairly sharp, and centered about the point $1/H^* \approx 0.4$.

Unlike static equilibrium properties such as stretch, dynamic properties such as relaxation time are affected by hydrodynamic interactions, as are transient processes like the dynamics of a chain in flow. Figure 1(b) shows the reduced relaxation time, $\lambda_1^* = \lambda_1/\lambda_{1,b}$ as a function of $1/H^*$ for chains up to 126 μ m. We observe a crossover region centered about $1/H^* \approx 0.1$ followed by a power law region which is fully developed at $1/H^* \approx 0.5$. A scaling theory [17] puts the power law exponent at 1/3, which agrees well with our results. In contrast, if hydrodynamic interactions with the wall



FIG. 1. Scaled stretch (a) and relaxation time (b) for DNA of various lengths. Symbols correspond to $L = 4.2 \ \mu m$ (\bigcirc), $L = 10.5 \ \mu m$ (\square), $L = 21 \ \mu m$ (\diamondsuit), $L = 42 \ \mu m$ (\bigtriangleup), $L = 84 \ \mu m$ (\triangleleft), $L = 126 \ \mu m$ (\bigtriangledown), $L = 210 \ \mu m$ (\triangleright), and $L = 420 \ \mu m$ (+).



FIG. 2. Scaled steady-state stretch as a function of channel width for chains lengths of 42 μ m (white), 84 μ m (gray), and 126 μ m (black). Symbols types represent values of $\dot{\gamma} = 3.98 \text{ s}^{-1}$ (\bigcirc), $\dot{\gamma} = 30.8 \text{ s}^{-1}$ (\bigcirc), $\dot{\gamma} = 308 \text{ s}^{-1}$ (\diamondsuit).

are neglected, the relaxation time is unaffected by channel size.

Bakajin *et. al* [41], in qualitative experiments with \sim 74 µm DNA chains confined to a slit, estimated that the relaxation time roughly doubled when the slit width was decreased from 5 to 0.3 µm, and again when it was decreased to 0.09 µm. We estimate $S_b \approx 1.6 \mu m$ for 74 µm chains, which puts their data into the confined scaling regime (the exponents for slit and channel are expected to be the same), and their data is consistent with the $H^{*-1/3}$ dependence.

We turn now to the single-molecule dynamics in a pressure-driven flow. The flow strength is characterized by an effective shear rate, $\dot{\gamma} = 2v_{\text{max}}/H$, where v_{max} is the imposed velocity at the center line of the channel (in the absence of a DNA molecule). Figure 2 shows the steady-state stretch as a function of H (scaled with its equilibrium value at the same H) for various chain lengths and flow strengths. At small H, the chain is cigar shaped at equilibrium. The first effect of the flow is to compress the chain slightly in the axial direction. As the confinement decreases, a channel size is reached where the flow strength is sufficient to stretch the chain away from its equilibrium value. A simple "blob" picture (cf. [9,17,42]) predicts that the chain will begin to stretch at a critical shear rate $\dot{\gamma}_c \sim \lambda_{blob}^{-1}$, where λ_{blob} is the blob longest relaxation time, which depends on H but not chain length. This prediction is in good agreement with the simulation results of Fig. 2.

At equilibrium, or when $\lambda_{blob}\dot{\gamma} \ll 1$, a molecule uniformly samples the entire cross section of the channel, aside from the obvious *static* depletion layer near the wall. Once $\lambda_{blob}\dot{\gamma} \ge 1$ and the chains begin to stretch, a quite dramatic *dynamic* depletion layer can form. Figure 3 shows a sample cross-sectional center of mass distribution. Figure 4 shows the distance traveled by DNA mole-



FIG. 3 (color online). Steady-state center-of-mass probability distribution vs cross-sectional position in the channel for 42 μ m chains in 10.6 μ m wide channels, $S_b/H = 0.11$. (a) $\dot{\gamma} = 0 \text{ s}^{-1}$, (b) $\dot{\gamma} = 308 \text{ s}^{-1}$.

cules of various lengths through the channel: the longer the chain, the more pronounced the localization to the center line. Distinct "bands" can be observed for DNA chains of 10.5, 21, 42, and $84 \,\mu\text{m}$, indicating that this phenomenon might be used to separate DNA molecules in small channels.

Migration of macromolecules and deformable particles away from walls in flow fields with nonuniform velocity gradient is a well-known phenomenon [11,43]. No previous theoretical study, however, has addressed the importance of confinement for this phenomenon — we find that at the scales studied here, the hydrodynamic effect of confinement dominates. If the wall contribution Ω^{W} to the diffusion tensor is turned off, the migration effect is much weaker, and is *toward* the wall. If hydrodynamic interactions are turned off entirely, there is no migration at all. A detailed examination and mechanism of this phenomenon will be presented elsewhere.



FIG. 4 (color online). Axial distance traveled by individual chains versus axial distance traveled by a fluid element at the center line of the channel. Results are for a 10.6 μ m channel at a flow strength of $\dot{\gamma} = 308 \text{ s}^{-1}$. Top to bottom bands correspond to 84, 42, 21, and 10.5 μ m chains, respectively. Twenty trajectories from each molecular weight are shown.

In this Letter we have presented a computationally tractable formalism for Brownian dynamics studies of dissolved polymers in confined geometries. We have confirmed equilibrium scaling predictions and established the importance of hydrodynamic confinement in the migration of polymer chains under flow. To the best of our knowledge, the hydrodynamic confinement effects put forth here have not previously been quantitatively predicted or studied experimentally. We hope that the availability of these detailed results will stimulate quantitative experiments aimed at verifying the predictions of this Letter.

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*Permanent address: 3M Corporation, St. Paul, MN 55144-1000, USA.

[†]Electronic address: graham@engr.wisc.edu

[‡]Electronic address: depablo@engr.wisc.edu

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$$\mathbf{f}_{ij}^{s} = \frac{k_B T}{2b_k} \left[\left(1 - \frac{|\mathbf{r}_j - \mathbf{r}_i|}{N_{k,s} b_k} \right)^{-2} - 1 + \frac{4|\mathbf{r}_j - \mathbf{r}_i|}{N_{k,s} b_k} \right] \frac{\mathbf{r}_j - \mathbf{r}_i}{|\mathbf{r}_j - \mathbf{r}_i|}.$$

Here, b_k is the Kuhn length for the molecule and $N_{k,s}$ the number of Kuhn segments per spring.

[39] The excluded volume potential is

$$U_{ij}^{ev} = \frac{1}{2} v k_B T N_{k,s}^2 \left(\frac{3}{4\pi S_s^2}\right)^{3/2} \exp\left[\frac{-3|\mathbf{r}_j - \mathbf{r}_i|^2}{4S_s^2}\right],$$

where v is the excluded volume parameter, and $S_s^2 = N_{k,s} b_k^2/6$.

- [40] The wall potential is $U_i^{\text{wall}} = A_{\text{wall}} b_k^{-1} \delta_{\text{wall}}^{-2} (h \delta_{\text{wall}})^3$ for $h < \delta_{\text{wall}}$, where *h* is the the distance of site *i* from the nearest wall. We use $A_{\text{wall}} = 25k_BT/3$ and $\delta_{\text{wall}} = b_k N_{k,s}^{1/2}/2 = 0.236 \,\mu\text{m}$. Results were insensitive to the wall parameter δ_{wall} , provided $\delta_{\text{wall}} = O(a)$.
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