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Kirkwood diffusivity of long semiflexible chains in nanochannel confinement

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Abstract

We compute the axial diffusivity of asymptotically long semiflexible polymers confined in square channels. Our calculations employ the Kirkwood approximation of the mobility tensor by combining computational fluid dynamics (CFD) calculations of the hydrodynamic tensor in channel confinement with pruned-enriched Rosenbluth method (PERM) simulations of a discrete wormlike chain model. Three key results emerge from our study. First, for the classic de Gennes regime, we confirm that Brochard and de Gennes' blob theory correctly predicts the scaling of the axial diffusivity, contrary to the conclusions of previous analyses. Second, for the extended de Gennes regime, we show that a modified blob theory, which has been used to incorporate the effect of local stiffness on DNA diffusion in nanoslits, explains the deviation from the prediction of classic blob theory for diffusion in nanochannels. Third, we provide a calculation similar to the modified blob theory to explain the relative insensitivity of the diffusivity to channel size for channels between the extended de Gennes regime and the Odijk regime, which is the most relevant regime for experiments and technological applications of DNA confinement in nanochannels. Our results are not only relevant to the dynamics of confined semiflexible polymers such as DNA, but also reveal interesting analogies between confinement in channels and slits.

Graphical abstract

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Supporting Information Available

Molecular weight dependence of the mobility in the classic de Gennes regime, contour length dependence of the mobility in the classic Odijk regime, calculation of prefactor for eq 20, normalized mobility plotted as a function of dimensionless channel size and a brief description of estimation of error in mobility. This material is available free of charge via the Internet at <http://pubs.acs.org/>.

1 Introduction

The dynamic properties of polymers in dilute solution are strongly coupled to their static properties due to long-ranged intramolecular hydrodynamic interactions (HI).^{1,2} For a polymer chain confined in a channel, the range of these hydrodynamic interactions is greatly restricted, due to the screening of HI induced by the walls.³ However, the presence of walls complicates accurate calculation of the frictional forces on the confined chain. The walls not only alter the distribution of monomers of the confined chain,¹ but also affect the motion of the solvent in the channel.³ The dynamic properties of confined chains, therefore, are a function of the coupling between the monomer conformations and the motion of the solvent, both of which depend on the cross-sectional dimensions of the channel.⁴

The dependence of the near-equilibrium diffusivity of channel-confined single molecules on the confinement size has been the subject of various studies^{5–7} since the seminal work of de Gennes and coworkers almost 35 years ago.^{1,8} The results of these studies, however, were interpreted in the context of the knowledge of the static properties at the time. Renewed interest in the problem of nanochannel-confined DNA⁹ has brought new insights into the static properties of semiflexible polymers in channel confinement.^{10,11} For a semiflexible polymer of persistence length, l_p , effective width, w , and contour length, L , confined in a square channel of size, H , the dependence of static properties such as the extension of the molecule, the variance of extension, and the confinement free energy on the channel size is now reasonably well understood.^{10–15} Indeed, the behavior of the static properties can be categorized into various regimes depending on the value of the channel size, H , relative to the persistence length, l_p and width, w .

For a wide channel, whose channel size is much bigger than the persistence length ($H \gg l_p$), the static properties of confined semiflexible polymers can be explained by blob theory.^{1,10,16} When $H \gtrsim 2l_p$, de Gennes' blob theory has been shown to correctly predict the scaling of the average extension.^{11,13,14,17} However, other properties including the variance of extension and confinement free energy exhibit a scaling different from de Gennes' blob theory for $2l_p \lesssim H \lesssim l_p^2/w$, while the blob theory scaling is recovered for $H \gtrsim l_p^2/w$.¹⁴ A modified blob theory that accounts for the effect of stiffness,¹⁰ however, can be applied to explain this deviation from de Gennes' theory, which does not account for local stiffness of the chain.¹ Accordingly, the range of channel sizes where de Gennes' theory is satisfied on all counts ($H \gtrsim l_p^2/w$) is termed the 'de Gennes regime' or the 'classic de Gennes regime', while the region where the modified blob theory is applicable is called the 'extended de Gennes regime'.^{14,15}

In contrast, if $H \ll l_p$, Odijk suggested that the confined chain forms repeating units of deflection segments, which are linearly ordered, giving rise to an extension close to the contour length.¹⁸ The scaling of static properties in this 'classic Odijk regime' has been extensively studied, so much so that the prefactors in these scaling relations are known to multiple decimal places.^{19,20} Our recent work confirmed the existence of a universal backfolded Odijk regime, wherein the deflection segments can form hairpins inside the

channel.^{10,13} Indeed, our calculations of the static properties in the backfolded Odijk regime¹³ showed excellent agreement with Odijk's theory.¹⁰

The lack of experimental data for single molecule diffusivity in channel confinement means much of our understanding of the scaling of the diffusivity comes from theory and simulation.^{1,5-8} Although this problem has been the subject of attention for several decades, there are three key open questions surrounding the diffusivity of channel-confined semiflexible polymers.

The first of these questions concerns the scaling of the diffusivity in the classic de Gennes regime. Employing blob theory, Brochard and de Gennes⁸ predicted that the diffusivity of a polymer parallel to the axis of the channel, D , scales with the channel size as $D \sim H^{2/3}$ for $H \gg l_p$. Using the contemporary value of the Flory exponent, 21 this scaling law would translate to $D \sim H^{0.701}$. Harden and Doi argued that the diffusivity has a slightly weaker scaling, $D \sim H^{0.61}$.⁵ They attribute this deviation from the scaling theory prediction to a transverse correlation length that arises in their variational calculation, which is based on self-consistent field theory. More recently, Brownian dynamics simulations of a bead-spring model by Jendreck et al.⁷ found that $D \sim H^{0.5}$ in the de Gennes regime. Subsequent simulations of a touching bead model by Tree et al.⁶ appear to show a scaling that is closer to the one predicted by Harden and Doi,⁵ albeit with limited amount of data. While the scaling of the static properties of channel-confined polymers in the classic de Gennes regime has been well established for many decades, a definitive answer for the scaling of the diffusivity still remains elusive.

A related question pertains to the scaling of the diffusivity in the extended de Gennes regime. Several authors have proposed that blob theory can also be applied to estimate the diffusivity in the extended de Gennes regime, which would result in a predicted scaling of $D \sim H^{0.701}$.^{6,12} However, recent work²² on DNA diffusion in slits suggests otherwise. To summarize briefly, early experiments on DNA confined in slits²³ suggested that the scaling of the in-plane diffusivity is much weaker ($D \sim H^{0.5}$) than the scaling predicted by blob theory ($D \sim H^{2/3}$).⁸ Interestingly, this anomalous behavior was observed in the range of channel sizes where DNA exhibits the blob theory prediction of the extension parallel to the slit walls, $R_{||} \sim H^{1/4}$. Subsequent Monte Carlo simulations demonstrated that this deviation in the scaling of the diffusivity from the blob theory prediction arises from the semiflexible nature of DNA, even though semiflexibility does not appreciably affect the scaling in extension.²² Given the similarity of the behavior of properties of confined semiflexible polymers in slits and channels,^{13,24} one would expect stiffness to affect the diffusivity in the extended de Gennes regime for channel confinement. The behavior of the diffusivity in the extended de Gennes regime remains an open question, primarily due to lack of sufficient data.

Finally, a preliminary simulation study from our group recently by Tree et al.⁶ revealed a "Rouse-like" diffusion regime in between the Odijk and the extended de Gennes regimes, where the diffusivity is inversely proportional to the contour length of the chain but independent of its characteristic size (i.e., the extension of the chain). The diffusivity in this regime not only increases with stiffness, but the range of fractional extension spanned by

this Rouse-like regime widens with increasing monomer anisotropy, l_p/w .⁶ These conclusions need to be treated as tentative, as the results from these simulations correspond to only 3 values of l_p/w and are limited to relatively low molecular weights. Although at the time of the study⁶ the range of channel sizes for such Rouse-like behavior was thought to be a sharp transition between the Odijk and the blob regimes,⁶ it is now clear that this range of channel sizes is characterized by the backfolded Odijk regime, particularly for molecules with large values of l_p/w .¹³ The behavior of the static properties of a chain in the backfolded Odijk regime remain unconnected to these observations about chain diffusivity, in particular why the diffusivity appears to increase with stiffness.

Despite the fact that simulations have contributed to much of the progress in understanding the physics of static properties, the available simulation data on diffusivity of channel-confined chains are limited and indeed conflicting,^{6,7} owing to the challenges involved in simulation methodology arising from the disparity in the relevant length scales of the molecule such as contour length, persistence length and width, and juxtaposition of other length scales such as the confinement size.²⁵ Often, bead-spring models have been used to simulate the dynamics of such polymers in confinement via Brownian Dynamics (BD) simulations, both with^{7,26,27} and without hydrodynamic interactions (HI).²⁸ The coarse-grained nature of these models allows simulation of experimentally relevant molecular weights with a small number of beads for a sufficiently long time.²⁹ Because such bead-spring models do not have the necessary resolution when the confinement size is of the order of the persistence length of the polymer, finer models have been used recently for Metropolis Monte Carlo^{6,22} and lattice Boltzmann-based simulations³⁰ of semiflexible chains in confinement. Models with adequate resolution used in conjunction with these methods, however, require hundreds or even thousands of beads to reach the length scales relevant to scaling theories and experiments, making such simulations infeasible.

In this contribution, we compute axial diffusivity of long semiflexible polymers over the entire range of channel confinement from the classic de Gennes regime to the classic Odijk regime. We achieve this by combining pruned-enriched Rosenbluth method (PERM) simulations^{31,32} of a discrete wormlike chain model with computational fluid dynamics (CFD) calculations of the hydrodynamic tensor. We account for the effect of HI through the pre-averaging approximation in Kirkwood-Riseman theory,³³ which has recently been shown to provide reliable estimates of diffusivity in channel confinement.³⁴ By computing the diffusivity for asymptotically long chains for several values of l_p/w , we show that the blob theory proposed by Brochard and de Gennes⁸ is valid in the classic de Gennes regime. We further develop a modified blob theory inspired by the work of Dai et al.²² for the scaling of diffusivity in the extended de Gennes regime, and demonstrate that this theory captures the deviation of our simulation data from blob theory in this regime. Finally, we propose a simple model for the backfolded Odijk regime, which is consistent with the Rouse-like regime proposed by Tree et al.⁶ Our simulations and corresponding theoretical analysis address the three key open questions surrounding the diffusion of semiflexible polymers in channels.

2 Methods

Our objective here is to calculate the axial diffusivity or mobility of the center of mass of semiflexible polymers confined in square channels. The mobility tensor, $\boldsymbol{\mu}_{\text{CM}}$, of the center of mass of a chain under an external force $\mathbf{F}_{\text{CM}}$, with a resultant drift velocity of the center of mass $\mathbf{v}_{\text{CM}}$, is defined by

$$\mathbf{v}_{\text{CM}} = \boldsymbol{\mu}_{\text{CM}} \cdot \mathbf{F}_{\text{CM}} \quad (1)$$

Note that the diffusivity tensor, $\mathbf{D}_{\text{CM}}$, is related to the mobility tensor by the Einstein-Smoluchowski relation, $\mathbf{D}_{\text{CM}} = \boldsymbol{\mu}_{\text{CM}} k_{\text{B}} T$, where k_{B} is the Boltzmann constant and T is the absolute temperature. For our case of a polymer confined in a square channel, we cast the problem as a one-dimensional analogue along the axis of the channel. We are interested in the motion of the confined chain parallel to the x -axis, which points in the direction of the axis of the channel. Accordingly, the velocity of the chain in the x direction, v_x , due to a force parallel to the x axis, F_x , is determined by the xx component of the mobility tensor, μ , as

$$v_x = \mu F_x \quad (2)$$

Since we are only concerned with center-of-mass diffusion, we drop the subscript ‘CM’ from this point forward. As μ and the xx component of the diffusion tensor, D , differ only by a factor of $k_{\text{B}} T$, we use μ and D interchangeably in the rest of the paper. Additionally, in the subsequent discussion we confine ourselves to the diffusion of polymer chains near equilibrium. In other words, we assume that the conformations of the molecule are unperturbed on an average by the forces exerted by the solvent.

2.1 Model

To calculate the diffusivity and other thermodynamic properties of confined chains in PERM simulations, we use a variant of the discrete wormlike chain model that we employed previously for diffusivity calculations of DNA in free solution.⁶ In our model, the chain is discretized as a string of N_b touching beads of diameter d . This length scale corresponds to the local hydrodynamic diameter, d . The corresponding radius is a ($d = 2a$), which measures the distance between the center of the backbone and the surface of shear on the molecule. Our model, therefore, is essentially a more flexible analogue of the ‘shish-kebab’ model that is often used to model rod-like polymers.³⁵ A bending potential quantified by

$$\beta U_{\text{bend}} = -\kappa(1 - \cos\theta_i) \quad (3)$$

is imposed on all contiguous triplets of beads along the chain, where κ is the bending constant of the chain. The quantity $\cos\theta_i = (\mathbf{r}_{i+2} - \mathbf{r}_{i+1}) \cdot (\mathbf{r}_{i+1} - \mathbf{r}_i)$ for $i = 1, \dots, N_b - 2$. From the bending potential, we can derive the average of $\cos\theta$ as $\langle \cos\theta \rangle = \coth(\kappa) - 1/\kappa$. Therefore the persistence length, $l_p = d/(1 - \langle \cos\theta \rangle)$,^{36,37} is related to the bending constant κ by

$$\frac{l_p}{d} = \frac{\kappa}{\kappa - \kappa \coth(\kappa) + 1} \quad (4)$$

We associate a hard-core width, w , commensurate with the excluded volume strength of the segments of the chain. Furthermore, we assume that the width for intramolecular interactions is the same as the width for the polymer-wall interaction. This renders the size of the channel accessible to the center of the backbone to be $H_{\text{eff}} = H - w$. For simplicity, we assume $d = w$. However, the two quantities are not necessarily identical as w corresponds to the length scale for excluded volume, while d represents the length scale for the friction due to the solvent. For instance, we recently found that a value of $d = 2.94$ nm, which is smaller than the value $w = 4.6$ nm from Stigter's theory for DNA,³⁸ yields the best agreement between simulation results and experimental data for diffusivity of DNA in bulk solution.³²

2.2 Kirkwood mobility

We adopt the Kirkwood preaveraging approximation^{25,33,36} to estimate the effect of HI on the diffusivity of confined molecules. In this approximation, the center of mass mobility of a chain of N_b beads is³⁹

$$\mu_{N_b} = \frac{1}{N_b^2} \left\langle \sum_{i=1}^{N_b} \sum_{j=1}^{N_b} \left(\frac{\delta_{ij}}{6\pi\eta a} + \Omega_{ij}^{xx}(\mathbf{r}_i, \mathbf{r}_j) \right) \right\rangle, \quad (5)$$

where $\langle \dots \rangle$ denotes an ensemble average over an equilibrium ensemble of chain configurations. The second term in eq 5 is the xx component of the hydrodynamic interaction tensor in confinement,

$$\mathbf{v}_i = \boldsymbol{\Omega}_{ij}(\mathbf{r}_i, \mathbf{r}_j) \cdot \mathbf{F}_j, \quad (6)$$

which measures the velocity perturbation in the solvent, $\mathbf{v}_i$, at a point $\mathbf{r}_i$ due to the point force, $\mathbf{F}_j$, applied on the solvent by a bead at $\mathbf{r}_j$. Note that the first term on the right hand side of eq 5, which accounts for self diffusivity, is required to capture the diffusivity at low molecular weights. However, the HI term dominates as $N_b \rightarrow \infty$, making the long-chain diffusivity insensitive to the choice of a .⁴⁰

The Kirkwood approximation is known to introduce errors in the estimates of the diffusivity for polymers in dilute solution, as it neglects intramolecular dynamic correlations.^{39,41–43} For this reason, the Kirkwood diffusivity is also sometimes referred to as the “short-time” diffusivity. However, recent work from our group indicates that the deviation in the value of the Kirkwood diffusivity from the “long-time” diffusivity given by Einstein's theory is suppressed in channel confinement.³⁴ This result is encouraging in hindsight, as the Kirkwood approximation has been used extensively in scaling theories for polymer diffusion in confinement.^{1,6,8,22}

2.3 CFD methodology

While our PERM simulations generate the configurations needed to compute the ensemble average in eq 5, we also need to evaluate the hydrodynamic tensor Ω_{ij} , which we carry out via a CFD solution of the Stokes equation for the solvent in the channel. To solve the Stokes equations, we use a method similar to that of Jendrejack et al.⁷

We employ a three-step process to obtain the hydrodynamic tensor in the channel. First, we construct a three-dimensional, uniformly-spaced, staggered grid in the channel, consisting of pressure, x -velocity, y -velocity and z -velocity nodes, thus circumventing the need to explicitly specify the boundary conditions for pressure.⁴⁴ The pressure grid points also serve as grid points to compute the velocity perturbations due to point forces in the channel. A unit force applied at one of these grid points $\mathbf{r}_j = (x_j, y_j, z_j)$ generates a velocity perturbation at another grid point $\mathbf{r}_i = (x_i, y_i, z_i)$, which can be quantified by the hydrodynamic tensor Ω_{ij} . In free solution, the hydrodynamic tensor is the Oseen tensor,

$$\Omega_{\text{free}}(\mathbf{r}_i - \mathbf{r}_j) = \frac{1}{8\pi\eta} \left(\frac{\mathbf{I}}{|\mathbf{r}_i - \mathbf{r}_j|} + \frac{(\mathbf{r}_i - \mathbf{r}_j)(\mathbf{r}_i - \mathbf{r}_j)}{|\mathbf{r}_i - \mathbf{r}_j|^3} \right), \quad (7)$$

which can be used to evaluate the velocity perturbation, $\mathbf{u}_{\text{free}}(x_i, y_i, z_i)$. To compute the velocity perturbation in the channel, $\mathbf{u}(x_i, y_i, z_i)$, the calculation method⁷ exploits the linearity of the Stokes equations by splitting the velocity field as $\mathbf{u} = \mathbf{u}_{\text{free}} + \mathbf{u}_{\text{walls}}$. Here, $\mathbf{u}_{\text{walls}}(x_i, y_i, z_i)$ is the correction to the free solution velocity field that arises due to the presence of the channel walls. We obtain $\mathbf{u}_{\text{walls}}$ by numerically solving the Stokes equations

$$\begin{aligned} -\nabla p + \eta \nabla^2 \mathbf{u}_{\text{walls}} &= 0, \\ \nabla \cdot \mathbf{u}_{\text{walls}} &= 0, \end{aligned} \quad (8)$$

subject to no-slip boundary conditions at the walls, i.e.,

$$\mathbf{u}_{\text{free}} + \mathbf{u}_{\text{walls}} = 0 \quad \text{at the walls.} \quad (9)$$

We compute the boundary velocities at grid points on the boundaries by calculating the flux of $-\mathbf{u}_{\text{free}}$ over each cell at the boundaries and then dividing by the total surface area of the cell. This method ensures mass conservation, which is not necessarily satisfied if one naively computes $-\mathbf{u}_{\text{free}}$ exactly at the boundary grid points.

Due to translational symmetry along the channel axis, the wall correction $\Omega_{\text{walls}}(\mathbf{r}_i, \mathbf{r}_j) = \Omega_{\text{walls}}(|x_i - x_j|, y_i, y_j, z_i, z_j)$. Therefore, the hydrodynamic tensor that determines the velocity perturbation at $\mathbf{r}_i$ due to a point force at $\mathbf{r}_j$ is given by

$$\Omega_{ij}(|x_i - x_j|, y_i, y_j, z_i, z_j) = \Omega_{\text{walls}}(|x_i - x_j|, y_i, y_j, z_i, z_j) + (1 - \delta_{ij}) \Omega_{\text{free}}(\mathbf{r}_i - \mathbf{r}_j) \quad (10)$$

We determine Ω_{ij} for all pairs of grid points by successively solving eq 8 for point forces at each grid point $\mathbf{r}_i$, using a finite-difference method (FDM) with boundary conditions

obtained from eq 9. Our FDM formulation uses forward differences for first derivatives and second-order central differences for second derivatives in eq 8.⁴⁴ Although in principle the channel is infinitely long along its axis, the length of the channel was fixed at $10H$ in these calculations.⁷ This box size is sufficient to obtain all the relevant information about Ω_{ij} because of the rapid decay of the magnitude of the hydrodynamic tensor Ω_{ij} with $|x_i - x_j|$. In all our calculations, the domain is divided such that there are 72 grid points in the x direction and 18 grid points each in the y and z directions, regardless of the channel size. As a result, the total number of grid points in the domain is 23 328. The resulting set of linear equations generates a sparse matrix, which we solve using GMRES via an incomplete LU factorization. Thereafter, we compute each element of Ω_{walls} following the method outlined in previous work.^{7,25}

With the knowledge of Ω_{walls} and Ω_{free} , we compute Ω_{ij} for all combinations of $\mathbf{r}_i$ and $\mathbf{r}_j$ on our grid. We store the computed elements of the tensor Ω_{ij} in a lookup table, which is in turn used in our PERM simulations. Figure 1 shows a typical result from our CFD calculation. In particular, it illustrates the behavior of the magnitude of the xx component of the tensors, $\Omega_{\text{free}}^{xx}$, $\Omega_{\text{walls}}^{xx}$ and Ω^{xx} for a point force applied at $(0, 0, 0)$. The relatively low magnitude of Ω^{xx} in comparison to $\Omega_{\text{free}}^{xx}$ and $\Omega_{\text{walls}}^{xx}$, particularly for $|x/H| > 1$, points to the screening of HI as one traverses away from the perturbing force along the channel.³

2.4 Integrating CFD with PERM

We employ PERM, a biased chain growth method, to generate configurations of confined chains.^{13,45,46} We start with a single bead placed randomly inside the channel and grow chains by adding a bead at a time, suitably enriching (branching) or pruning the growth as per Prellberg's algorithm.³¹ Because we bias the chain growth to achieve growth of long chains, each configuration at each growth step is associated with a statistical weight based on the amount of bias. To compute a chain property, such as the Kirkwood diffusivity in eq 5, the bias is undone by weighting each configuration appropriately. Unlike Grassberger's original algorithm,⁴⁷ we do not need to set upper and lower threshold weights to guide the chain growth towards long chains. Prellberg's algorithm does not use any such parameters; the target weights for chain growth are obtained from performing preliminary PERM simulations. We use exactly the same algorithm as in previous work from our group and we refer the reader to earlier publications from our group for more details on PERM methodology.^{13,24,45,46} Starting from a single bead, we grow the chain until it reaches a preset maximum number of beads or gets pruned with no more branches to grow. Such an excursion that starts from a single bead and grows till the end is known as a tour. In this work, we used PERM to grow chains up to 10 000 beads for a total of 50 000 tours in each simulation for a specific combination of (l_p, w, H) for calculations of diffusivity.

We compute the center-of-mass axial mobility from a given configuration by

$$\Omega_{\text{CM}, N_b}^{xx} = \frac{1}{N_b^2} \sum_{i=1}^N \sum_{j=1}^N \left(\frac{\delta_{ij}}{6\pi\eta a} + \Omega_{ij}^{xx}(|x_i - x_j|, y_i, y_j, z_i, z_j) \right). \quad (11)$$

The average axial mobility of the chain over the total number of tours, N_{tours} , is calculated on the fly during PERM chain growth as

$$\mu_{N_b} = \langle \Omega_{\text{CM}, N_b}^{xx} \rangle = \frac{\sum_{k=1}^{N_{\text{tours}}} W_{N_b, k} \Omega_{\text{CM}, N_b, k}^{xx}}{\sum_{k=1}^{N_{\text{tours}}} W_{N_b, k}}, \quad (12)$$

where $W_{N_b, k}$ is the weight of a chain with N_b beads in the k th tour. For the purpose of comparing our simulation results for diffusivity with scaling theory, employing the Kirkwood approximation does not imply any loss of generality, as the theoretical predictions themselves are based on the preaveraging approximation. Since the values of $\Omega_{ij}^{xx}(|x_i - x_j|, y_i, y_j, z_i, z_j)$ computed from our CFD simulations are tabulated only for grid points, we use multi-linear interpolation to estimate Ω_{ij}^{xx} for arbitrary values of $\mathbf{r}_i$ and $\mathbf{r}_j$. Given that we use the same number of grid points for all channel sizes, we restrict the channel sizes in our calculations to values between $H/d = 5$ and $H/d = 100$. The largest channel size, $H/d = 100$, is large enough that we can reach the classic de Gennes regime for chains with sufficiently low l_p/w , but does not introduce significant interpolation errors between the grid points. The double-sum in eq 11 makes our method $O(N_b^2)$ in computational time. We are able to run simulations for a confined chain of 10 000 beads for 50 000 tours on 60 processors within a span of 3 days. We only need to calculate the pairwise HI tensor for monomers within a cutoff length of $10H$ along the channel, which significantly reduces the computational time.

3 Summary of existing theories

As we discussed at the outset, our goal is to compare the results for diffusivity obtained from our PERM simulations to existing theories. Here, we briefly summarize these theories to facilitate our subsequent discussion.

3.1 Blob theory

Blob theory was originally proposed to describe the properties of confined polymers in the classic de Gennes regime.^{1,8} In the classic de Gennes regime, the chain conformation consists of a series of linearly ordered compression blobs, each of which has a size proportional to the channel size, H . Figure 2(a) shows a typical conformation in the classic de Gennes regime. One can use the blob argument and write the scaling of the average extension in the classic de Gennes regime as^{13,45}

$$\frac{X}{L} \simeq \left(\frac{H}{l_p} \right)^{1-1/\nu} \left(\frac{w}{l_p} \right)^{2-1/\nu}, \quad (13)$$

where $\nu = 0.58\,97(7)$ is the Flory exponent.²¹ Because the the inter-segmental HI in confinement is screened beyond a length scale of H inside the channel,³ one can estimate the axial mobility via the Kirkwood preaveraging approximation as^{1,8}

$$\mu \simeq \frac{1}{L} \int_0^{H/2} \Gamma(r) \Omega^{xx}(r) dr, \quad (14)$$

where $\Omega^{xx}(r)$ is the angle-average of the xx component of the Oseen tensor. Note that $\Omega^{xx}(r) = 1/6\pi\eta r$ is identical to the angle-average of the whole Oseen tensor, $\Omega(r)$. The function $\Gamma(r) = 4\pi^2 l_p g(r)$ is a dimensionless form of the pair correlation function, $g(r)$, of Kuhn segments of the chain. In other words, the function $\Gamma(r)$ measures the average contour length of the chain present in a shell enclosed by radii r and $r + \Delta r$ as $\Delta r \rightarrow 0$. It turns out that the length scale for screening of HI, the hydrodynamic blob, also scales linearly with the channel size H (Figure 1). Note that the hydrodynamic blob and the compression blob are length scales that arise from different physical phenomena. In the classic de Gennes regime, however, both these length scales are proportional to H as shown in Figure 2(a).

In blob theory, the pair correlation function is estimated as if there is a gas of monomers within each blob, neglecting correlations along the backbone of the chain. In particular, we assume that the blob size is such that the local stiffness of the chain has very little effect on the pair correlation function inside a blob. Therefore, the pair correlation function is simply the concentration of monomers inside a blob, which is given by^{6,45}

$$g(r) \sim r^{1/\nu-3} l_p^{2-2/\nu} w^{1/\nu-2} \quad (15)$$

Using eqs 14 and 15, the mobility in the classic de Gennes regime can be written as

$$\mu \simeq \frac{1}{6\pi\eta L} l_p^{3-2/\nu} w^{1/\nu-2} H^{1/\nu-1}. \quad (16)$$

In terms of the mean extension, the scaling of μ becomes

$$\mu \simeq \frac{1}{6\pi\eta X} \text{ or } 6\pi\eta L \mu \simeq \left(\frac{X}{L}\right)^{-1}, \quad (17)$$

where we have used the well established scaling relation for the mean extension in the de Gennes regime given in eq 13. If we use the classical value of the Flory exponent, eq 16 assumes the form $6\pi\eta L \mu \simeq (H/l_p)^{2/3} (l_p/w)^{1/3}$.

An equivalent way to determine the scaling law in eq 17 is by estimating the friction constant of the confined chain.¹² The use of eq 15 for the pair correlation implicitly assumes that sub-chain inside the blob is a swollen coil. Given that the subchain inside a blob is non-draining (eq 14), the friction of a blob scales with blob size as $\zeta_{\text{blob}} \simeq 6\pi\eta H$. Due to screening of HI, the friction of the chain is the product of the friction of each blob and the number of blobs: $\zeta_{\text{chain}} \sim 6\pi\eta H(X/H)$ or $\zeta_{\text{chain}} \sim 6\pi\eta X$, where X/H is the number of blobs in the confined chain. The resultant scaling of the mobility, which is the inverse of the friction on the chain, is indistinguishable from that in eq 17.

It has been proposed that the blob theory outlined above can also be applied to the extended de Gennes regime.^{6,12} Here, the static properties of the chain are described by a series of anisometric compression blobs each having a length proportional to $(Hl_p)^{2/3} w^{-1/3}$, as shown in Figure 2(b). The other two orthogonal dimensions of the blob are still proportional to H , because of the constraints imposed by the cross section of the channel. Accordingly, the extension scales exactly like eq 13,¹⁰ with a recent theory¹⁵ suggesting that $\nu = 3/5$ gives the right scaling in the extended de Gennes regime. Nonetheless, one can distinguish between the two blob regimes using the fact that they exhibit dissimilar scaling in properties such as the variance of extension and the confinement free energy^{13,14}

The scaling of the concentration of the monomers in the extended de Gennes regime is identical to that in the classic de Gennes regime owing to the similarity in the scaling of extension. Naively, we can then write the pair correlation in the extended de Gennes regime as the concentration of monomers within a blob, giving rise to $g(r) \sim r^{1/\nu-3} l_p^{2-2/\nu} w^{1/\nu-2}$, which is again indistinguishable from eq 15. Figure 2(b) indicates that while the compression blob in the extended de Gennes regime is anisotropic, the size of the hydrodynamic blob is unchanged, as it only depends on the boundary conditions on the solvent. Application of blob theory now leads to the scaling for the axial mobility given by eqs 16 and 17. We thus see that blob theory for the extended de Gennes regime predicts the same diffusivity as the classic de Gennes regime, i.e. that the diffusivity scaling is “extended” from large channels into the smaller ones characterizing the extended de Gennes regime.

3.2 Classic Odijk regime

In the classic Odijk regime, the chain consists of rod-like deflection segments linearly ordered in the channel.¹³ To estimate the total friction on the chain, we need to estimate the friction of the sub-chain in the screening volume H^3 , which is shown in red in Figure 2(c). To do so, recall that the translational friction constant of a rod of length l and hydrodynamic diameter d for motion parallel to its axis is³⁵

$$\zeta_{\parallel}^{\text{rod}} = \frac{2\pi\eta l}{\ln(l/d)}. \quad (18)$$

Owing to tight confinement in the Odijk regime, the motion of the polymer is roughly that of a string of rods moving parallel to their axes. A scaling law for the friction constant for the chain can be obtained by summing up the friction on each of these rods of length H contained in the screening volume. Accordingly, the friction is⁴⁸

$$\zeta_{\parallel} \simeq \frac{2\pi\eta X}{\ln(H/d)}. \quad (19)$$

Therefore, the axial diffusion coefficient in the Odijk regime scales as

$$\mu \simeq \frac{\ln(H/d)}{2\pi\eta X}. \quad (20)$$

Note that L is often used instead of X in eqs 19 and 20.^{6,12} This does not affect the scaling relations as X and L are related to each other by a factor of almost unity.²⁵

3.3 Backfolded Odijk regime

Recently, we showed¹³ that the “transition regime” that bridges the Odijk and the de Gennes blob regimes is the backfolded Odijk regime predicted by Odijk.¹⁰ Here, the chain contains deflection segments that can form hairpins as long as the chain is sufficiently long to overcome the bending penalty, and excluded volume interactions between deflections segments are weak enough to allow for backfolding, as shown in Figure 2(d).

Our recent work also indicated that the upper limit in channel size for the backfolded Odijk regime is $H/l_p \approx 2$.¹³ While this limit in H is fixed, the lower limit in fractional extension corresponding to this channel size depends on l_p , w , and H . Specifically, the average fractional extension in this regime is given by

$$\frac{X}{L} \simeq c\xi^{1/3}, \quad (21)$$

where the scaling variable ξ is defined as

$$\xi \simeq \frac{g}{l_p} \left(\frac{l_p}{H} \right)^{5/3} \left(\frac{w}{l_p} \right). \quad (22)$$

and $c = 0.92$ is a prefactor obtained from simulations.¹³ Here, g is the global persistence length, which is a measure of the average contour length between two hairpin turns along the chain.^{13,49} The upper limit in fractional extension for this regime is determined by $\xi \approx 1$, which translates to a fixed upper limit in fractional extension, $(X/L)_{\max} \approx 0.92$ (eq 21), irrespective of the value of l_p/w . However, because g/l_p is a function of H/l_p only,¹³ the lower limit in fractional extension corresponding to $H/l_p = 2$ scales as $(X/L)_{\min} \sim (w/l_p)^{1/3}$. In other words, the lower limit in X/L for the backfolded Odijk regime decreases with increasing l_p/w , although the upper limit is more or less fixed regardless of the value of l_p/w . Consequently, the range in fractional extension occupied by the backfolded Odijk regime increases with monomer anisotropy.

Previous work from our group by Tree et al.⁶ revealed a Rouse-like scaling for the axial diffusion coefficient in this regime. The premise behind the model was that the number of monomers in this regime is not high enough for substantial HI within the screening volume.⁶ This Rouse-like behavior inside the screening volume leads to a Rouse-like behavior for the whole chain, with a diffusion coefficient that scales as

$$\mu \sim \frac{1}{\eta L}. \quad (23)$$

An alternate way to write eq 23 is⁶

$$\mu \eta L \sim \left(\frac{X}{L}\right)^0, \quad (24)$$

which explicitly expresses that the mobility is independent of the extension of the molecule. This is of course contrasting behavior to that of the blob regimes, where the mobility is inversely proportional to the average extension (eq 17).

4 Results and Discussion

All of the theories discussed above apply to long chains. PERM natively produces data as a function of chain length via eq 12. A necessary, but not especially interesting, first step in our analysis is to confirm that the data we are analyzing indeed correspond to the long-chain limit. In the Supporting Information, we provide data and explanatory text confirming that the data presented here correspond to $\mu \sim 1/L$ regardless of the regime of confinement for long enough chains. In what follows, we restrict ourselves to examining the scaling of the asymptotic, long-chain diffusivity with respect to other quantities such as the channel size and fractional extension.

4.1 Blob regimes

Figure 3(a) shows the dimensionless mobility plotted against the fractional extension, X/L , which is also obtained from simulations, for channel sizes $H_{\text{eff}}/l_p > 3$. This is the range of channel sizes where we observe agreement with the extension scaling from blob theory (eq 13).¹³ Note that each data point for each value of l_p/w corresponds to a distinct channel size. For the plot of normalized mobility against dimensionless channel size, we refer the reader to the Supporting Information. Our data in Figure 3(a) show good agreement with the prediction from blob theory (eq 17) for $X/L < 0.1$ for the range of l_p/w values used in our simulations. However, for higher fractional extension values (narrower channels), we observe a deviation from the predicted -1 slope. For a given value of fractional extension, this deviation grows with increasing monomer anisotropy, suggesting that blob theory fails to explain the diffusivity for relatively stiff chains. Indeed, the departure of our data from the blob theory prediction for stiff chains is consistent with diffusivity studies of DNA confined in slits.^{22,23}

To ascertain whether blob theory produces the correct prediction in the classic de Gennes regime, we plot the subset of our data that correspond to the scaling of the classic de Gennes regime with respect to static properties such as extension and confinement free energy. To identify this subset, we use the condition furnished by Dai et al., $H_{\text{eff}} > 2.24l_p^2/w$.¹⁴ Figure 3(b) shows the collapse of mobility when plotted against fractional extension in the classic de Gennes regime. A fit indicates an exponent of -0.995 , which is extraordinarily close to the exponent from blob theory (eq 17). Instead, if we plot the same data against H_{eff}/l_p as

shown in the inset of Figure 3(b), we obtain a fit that suggests $\mu\eta L \sim (H_{\text{eff}}/l_p)^{0.68}$, again showing agreement with the 0.70 exponent from blob theory (eq 16).

Our results for diffusivity show excellent agreement with blob theory provided that the confinement corresponds to the classic de Gennes regime. This means that the data points inconsistent with blob theory in Figure 3(a) correspond to the extended de Gennes regime, as we have plotted only data points with $H_{\text{eff}} > 3l_p$. To explain the behavior of mobility in the extended de Gennes regime, we propose an alternate theory along the lines of the modified blob theory for DNA in slit confinement.²² This modification to blob theory²² supposes that the difference between the mobility and the prediction from the classic blob theory arises from the neglect of the stiffness of semiflexible polymers in describing the pair correlation function in eq 15 for short distances along the contour length. We use the modified form of the dimensionless pair correlation function proposed by Dai et al.²²

$$\Gamma(r) = \begin{cases} 2 & \text{if } r \leq l_p/2, \\ \alpha r^{1/\nu-1} l_p^{3-2/\nu} w^{1/\nu-2} & \text{if } l_p/2 < r < H_{\text{eff}}/2, \end{cases} \quad (25)$$

where α is the proportionality constant for the scaling of the pair correlation function. The factor of 2 ensures that the contour length inside a sphere of radius $r = l_p/2$ is $\int_0^{l_p/2} 2dr = l_p$. For channel sizes $H_{\text{eff}} > l_p$, the modified blob theory now yields

$$\mu \simeq \frac{1}{L} \left[\int_0^{l_p/2} \frac{2}{6\pi\eta r} dr + \int_{l_p/2}^{H_{\text{eff}}/2} \frac{\alpha r^{1/\nu-1} l_p^{3-2/\nu} w^{1/\nu-2}}{6\pi\eta r} dr \right]. \quad (26)$$

In the latter, we have assumed the concentration of monomers as an approximation to the pair correlation function, and employed the angle-averaged Oseen tensor to account for HI. This is acceptable because the orientational order parameter, which measures the alignment of the chain along the axis of the channel, is nearly zero for channels with $H \gtrsim l_p$.¹³ Furthermore, as noted by Dai et al.,²² this modification to the pair correlation does not affect the scaling of extension significantly,¹³ but leads to an appreciable change in the scaling of diffusivity. This behavior of the diffusivity can be explained by the factor of $1/r$ in the integral in eq 26, which amplifies the effect of correlations arising from stiffness at short distances along the chain.²²

Computing the integrals in eq 26 results in

$$\mu = \frac{1}{6\pi\eta L} \left[2\beta \ln(l_p/a) + \delta \left(l_p^{3-2/\nu} w^{1/\nu-2} H_{\text{eff}}^{1/\nu-1} - l_p^{2-1/\nu} w^{1/\nu-2} \right) \right], \quad (27)$$

where we have regularized the first integral in eq 26.²² Notably, Dai et al.²² used a single constant δ in their work on slit confinement. Considering the approximations involved, it is not obvious that the modified blob theory leads to an exact prefactor in the logarithmic term in eq 27. Accordingly, we use the two constants β and δ as fitting parameters to correct for the approximations such as the sharp crossover of $\Gamma(r)$ and the use of the free-solution Oseen

tensor. As a result, these constants are not universal and are functions of l_p/w . Note that modified blob theory for slits²² was only developed for a single value of l_p/w corresponding to DNA, so the universality (or lack thereof) of the constants was speculated upon but not addressed in the latter work. Figure 3(a) shows that eq 27 satisfactorily captures the essential physics giving rise to the deviation of mobility away from blob theory for $l_p/w = 4.65, 8.95, 17.70$. The second term in the sum present in eq 27 is identical to the result from blob theory, and it is the only term dependent on H (eq 16). In contrast, the other two terms in eq 27 originate from the stiffness of the chain; the first term, $2\beta \ln(l_p/a)$, is greater than the third term, $\delta l_p^{2-1/\nu} w^{1/\nu-2}$. The relative values of these terms elucidate why chains with higher l_p/w exhibit bigger deviation from the blob theory value. Furthermore, eq 27 also indicates that we eventually recover the scaling expected from blob theory for sufficiently wide channels (i.e., in the classic de Gennes regime), as the second term dominates for $H \gg l_p$.

Having explained the deviation from the blob theory prediction in the extended de Gennes regime, let us turn our attention again to the scaling in the classic de Gennes regime and compare our results to previous studies of chain mobility in this regime. In Figure 3(b), we find that

$$6\pi\eta\mu = 1.2/X \quad (28)$$

is a good fit for our simulation data. The prefactor furnished by our simulations allows us to compare with the prefactor one would expect from scaling theory. Recall that the diffusivity for real flexible chains in the bulk, D_{bulk} , is

$$D_{\text{bulk}} = \frac{1}{12.07} \frac{k_B T}{\eta R_g}, \quad (29)$$

where R_g is the radius of gyration in free solution.⁵⁰ Therefore, the friction constant in bulk is given by $\zeta_{\text{bulk}} = 12.07 \eta R_g$. de Gennes' blob theory suggests that the sub-chain inside the blob behaves as if it is a chain in bulk, unperturbed by the presence of walls. If this theory was quantitatively correct, the friction constant for a blob is $\zeta_{\text{blob}} = 12.07 \eta (H_{\text{eff}}/2)$. Now the total friction of the confined chain can be written as

$$\zeta = \frac{12.067\eta X}{2} = 6.03\eta X, \quad (30)$$

by multiplying the friction of the blob by the number of blobs. Therefore, the rescaled mobility of the chain from eq 30 is $\mu\eta X = 0.17$. In comparison to the fit obtained in our simulations in eq 28, $\mu\eta X = 0.064$, the prefactor estimated from bulk behavior is remarkably close. Indeed, if we write the actual friction of the chain as $\zeta = c(6.03\eta X)$, c is just a $O(1)$ prefactor that presumably accounts for the errors due to chain-wall friction and the approximations in the bulk diffusivity calculation by Oono and Kohmoto.⁵⁰ The existence of these $O(1)$ prefactors for both dynamic and static properties,^{45,46} points to the extraordinary

accuracy of de Gennes' blob theory applied to confinement of flexible chains in the classic de Gennes regime.

The inset of Figure 3(b) reveals a dependence on H_{eff} given by $D\eta L \sim H^{0.68}$. However, previous studies have questioned this scaling of D with H citing the effect of polymer-wall interactions. Using a coarse-grained bead-spring model, Jendrejack et al.⁷ found that $D \sim H^{1/2}$, although their data for mean extension reveals that $X \sim H^{-2/3}$, in agreement with blob theory. This discrepancy was attributed to the finite value of the ratio a/ℓ , where a is the segment hydrodynamic radius and ℓ is the length-scale for polymer-wall interactions. Their claim was further substantiated by a comparison of their results with that of Harden and Doi,⁵ who suggested that $D \sim H^{0.61}$, a slightly weaker scaling as opposed to de Gennes' blob theory (eq 16). Harden and Doi obtained this scaling by combining the Kirkwood preaveraging approach to estimate transport properties, with the self-consistent field method to calculate the monomer distribution in the presence of excluded volume.⁵

In our work, which produced mobility data for very long chains with very high spatial resolution of the chain configurations and without any self-consistent field approximations, we find no evidence supporting the conclusions of Jendrejack et al.⁷ or Harden and Doi⁵ concerning the scaling of D with H . In the case of the work of Jendrejack et al.⁷ on diffusivity of DNA, one could argue that the exponent of 1/2 observed in their simulations might indicate an apparent exponent for the extended de Gennes regime. Yet it is unlikely that their model captures the physics of the extended de Gennes regime as the springs in their bead-spring model are about 40 persistence lengths long.⁷ Rather, this points at a possible shortcoming in the resolution of such bead-spring models especially when they are employed in problems where stiffness effects are important. With respect to the results from Harden and Doi,⁵ we note that the applicability of self-consistent field theory (SCFT) for obtaining monomer distributions in channel confinement has been called into question recently.⁵¹ Thus, we believe that the recent objections on the application of SCFT⁵¹ and a superior high-resolution model used in our work in comparison to the highly coarse-grained model of Jendrejack et al.,⁷ explains the aforementioned discrepancies with respect to the scaling of diffusivity in the classic de Gennes regime.

4.2 Backfolded and classic Odijk regimes

We now examine the behavior of diffusivity outside the blob regimes. Figure 4(a) shows dimensionless mobility plotted against fractional extension. To begin, we observe that the data points in Figure 4(a) approach the blob theory prediction for $X/L \lesssim 0.1$, as we discussed in section 4.1. However, the points on the extreme right of Figure 4(a) for $X/L \gtrsim 0.8$ correspond to the classic Odijk regime,¹³ as the curve generated using eq 20 passes right through the data points in this region. Our results thus confirm the scaling relation in the classic Odijk regime given by eq 20. Our simulations also allow us to study the contour length dependence of mobility, in addition to the calculation of the prefactor in eq 20 (see Supporting Information).

For large values of l_p/w , the region between the extended de Gennes regime and the classic Odijk regime in Figure 4(a) is characterized by a value of the dimensionless mobility that is almost independent of fractional extension (or channel size). The dependence of the mobility

on channel size is shown in the Supporting Information. Our results are therefore consistent with the observation of Tree et al.⁶ However, the crossover point in X/L from the de Gennes scaling depends on the l_p/w ratio. Chains with low l_p/w values (flexible chains) exhibit the de Gennes scaling out to higher values of X/L , while chains with high l_p/w transition into the $\mu\eta L \sim (X/L)^0$ scaling quickly. This insight was not possible using the data from Tree et al.,⁶ as they only considered 3 relatively flexible values of l_p/w .

We posit that the backfolded Odijk regime^{10,13} can explain the insensitivity of the data to channel size for this range of channel sizes. Noting that the confined chain in the backfolded Odijk regime consists of a one-dimensional random walk of deflection segments of length $\lambda \simeq H^{2/3}l_p^{1/3} \approx l_p$ for $H \approx l_p$, we can write the diffusivity of the chain as

$$\mu \simeq \frac{1}{L} \int_0^{H/2} \Gamma(r) \Omega^{xx}(r) dr \approx \int_0^{l_p/2} \frac{2}{6\pi\eta r} dr \approx \frac{1}{3\pi\eta L} \ln(l_p/a), \quad (31)$$

along the same lines of the modified blob theory for the extended de Gennes regime. Note that using the angle-averaged Oseen tensor is still justified as the alignment is minimal when $H \approx l_p$, indicated by the relatively modest value of the order parameter.¹³ Indeed, the region around $H \approx l_p$ corresponds to the range of channel sizes where there is a steep change in fractional extension from about 0.2 to 0.8 for the l_p/w values considered here.¹³ However, we should bear in mind that the angle-averaged Oseen tensor will become a poor approximation as we approach channels with $H \ll l_p$. We know from our previous work that chains with a moderate value of l_p/w , such as DNA ($l_p/w \approx 10$), exhibit backfolded Odijk behavior for a very narrow range of channel sizes between $1 \lesssim H_{\text{eff}}/l_p \lesssim 2$.¹³ Only chains with extremely high l_p/w values, such as actin and microtubules ($l_p/w = 2375$ and 9600 respectively) could backfold substantially for $H_{\text{eff}} \ll l_p$, if they are available at a sufficiently high molecular weight.¹³ As a result, the expression in eq 31 is not a universal scaling law for the backfolded Odijk regime, as chains with very high values of l_p/w still show behavior characteristic of this regime even for $H \ll l_p$. In such cases, the mobility will scale more like the classic Odijk regime (eq 20), as the alignment of the chain along the channel dictates the hydrodynamics. However, for readily available semiflexible polymers such as DNA and actin, for which the backfolded Odijk regime corresponds to channels with $H \approx l_p$, we expect eq 31 to be a reasonable explanation for the behavior of diffusivity.

We verify our prediction in eq 31 for channels with $H_{\text{eff}} \approx l_p$, by plotting the subset of our data for $H_{\text{eff}} < 2l_p$ in Figure 4(b) as this roughly represents the upper limit for the backfolded Odijk regime.¹³ Note that the lower limit in channel size for the backfolded Odijk regime corresponds to $\xi \approx 1$ (eq 21), whereupon there is a transition to the classic Odijk regime for narrower channels. To make this clear, we also plot the data from the classic Odijk regime in Figure 4(b) to show the crossover between the two Odijk regimes. We observe that data points for chains with different l_p/w ratios fall essentially on the same horizontal line for $0.2 \lesssim X/L \lesssim 0.8$. Additionally, our data in this region indicate that

$$6\mu\eta L \approx 1.75 \ln(l_p/a) \quad (32)$$

suggesting that the simple scaling arguments used to derive eq 31 give rise to nearly accurate prefactors. Because of the approximate nature of eq 31, we do not expect absolute collapse of the data in Figure 4(b), in contrast to the classic de Gennes regime (Figure 3). Along the same lines, the plateau in Figure 4(b) is not perfectly horizontal. But the model in eq 31 is a simple and useful explanation of diffusivity for highly stiff chains when $H \approx l_p$.

We further observe that range of X/L spanned by the plateau of the normalized mobility in Figure 4 widens with increase in l_p/w . Recall from section 3.3 that the range of fractional extension spanned by the backfolded Odijk regime widens with increasing monomer anisotropy. Thus the window of fractional extension spanned by the mobility plateau in Figure 4 is consistent with what we would expect in the backfolded Odijk regime.

5 Conclusion

By computing the Kirkwood diffusivity of semiflexible chains for molecules over many decades of l_p/w confined in channels spanning a wide range of sizes, we mapped out the diffusion behavior from the Odijk regime of strong confinement to the classic de Gennes regime of weak confinement as summarized in Table 1. We were able to show conclusively that blob theory correctly predicts the diffusivity in the classic de Gennes regime ($H \gtrsim l_p^2/w$). However, we find that blob theory needs to be modified to account for local stiffness of the chain in order to explain the scaling of the diffusivity in the extended de Gennes regime. Thus, the behavior of diffusivity in the blob regimes mirrors the behavior in slits for commensurate confinement sizes.

Likewise, we also demonstrated that a similar theory predicts the insensitivity of the diffusivity to channel size (or fractional extension) in the backfolded Odijk regime when $H \approx l_p$. Although this regime spans a very narrow range in channel size for most practical circumstances like channel-confined DNA, it is extremely important in practice due the steep change in fractional extension from about 0.2 to 0.8 for molecules such as DNA. Our previous work has shown that this steep change in extension is due to the exponential dependence of the global persistence length on the channel size.¹³ Based on the successful analogies between diffusion in the extended de Gennes regime in channels and the corresponding slit heights in slits,²² we expect to observe similar Rouse-like diffusion behavior for slit heights $H \approx l_p$, where the diffusivity is insensitive to the channel size. Nonetheless, we do not expect this region to be very important in terms of the range of fractional extension spanned for slits. Explicitly, the range of fractional extensions when $H \approx l_p$ should be extremely narrow, because unlike the case of channels, the global persistence length in a slit does not vary exponentially with slit height and has an upper bound of $2l_p$ in slits.^{13,24} Taken together, we believe our work will prove useful in further understanding the dynamics of confined semiflexible polymers and serve as a valuable reference when single molecule experimental data become available for DNA diffusivity in nanochannels.

From a methodological standpoint, combining PERM simulations with CFD calculations of the hydrodynamic tensor demonstrates the capability of PERM in estimating the diffusivity of polymers in confined geometries. Due to the general nature of our method, it can be extended to compute the dynamic properties of single molecules confined in other

geometries such as nanoslits²² and triangular channels.⁵² Certainly, another area of interest would be to adopt this method in rectangular channels,⁵³ where the ‘regime mixing’ observed with respect to static properties,⁵⁴ in combination with the asymmetric nature of hydrodynamics, will lead to complicated behavior in the dynamic properties. Furthermore, the asymptotic friction factor obtained in our simulations can be used in conjunction with the variance of extension to obtain estimates of the longest relaxation time of confined molecules using the dumbbell model.⁵⁵

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

Magnitude of the xx component of the dimensionless hydrodynamic tensor due to a point force in the x -direction at $(x, y, z) = 0$ on the plane $z = 0$ in logarithmic scale: (a) free solution term, $6\pi\eta H|\Omega_{\text{free}}^{xx}|$, (b) wall correction, $6\pi\eta H|\Omega_{\text{walls}}^{xx}|$ and (c) resultant channel confinement term, $6\pi\eta H|\Omega^{xx}|$.

Figure 2.

Schematic showing the conformation of the chain in different regimes. The red part of the chain in each of the channels represents the sub-chain within a hydrodynamic screening volume, which is shown as a red sphere. The black dashed lines are a representation of compression blobs in the blob regimes.

Figure 3.

Mobility data in the blob regimes versus fractional extension. The l_p/w values of the molecules shown here are 2.54 (purple +), 4.65 (green x), 8.95 (blue), 17.70 (red □). The standard error of the mean for all the data points is smaller than the symbol size (see Supporting Information). (a) Comparison to the slope predicted from blob theory and modified blob theory to account for stiffness. The dashed lines are best fit curves using eq 27 with $\beta = 0.54$, $\delta = 1.12$ (green curve); $\beta = 0.62$, $\delta = 1.01$ (blue curve); $\beta = 0.71$, $\delta = 0.87$ (red curve). There is no purple dashed line because all of the data for $l_p/w = 2.54$ correspond to the classic de Gennes regime. (b) Power law fits to the data points belonging to the classic de Gennes regime. Data in the main panel can be fit to the expression, $6\pi\eta\mu L = 1.2(X/L)^{-0.995}$. The inset shows the same data against H_{eff}/l_p , for which a fit yields $6\pi\eta\mu L(w/l_p)^{-0.298} = 1.23(H_{\text{eff}}/l_p)^{0.68}$.

Figure 4.

Normalized mobility as a function of fractional extension. The l_p/w values are 2.54 (violet +), 4.65 (purple ×), 8.95 (blue *), 17.70 (green □), 35.54 (gold ■), 71.85 (orange ○), 145.8 (red ●), 296.5 (black △) and 603.2 (gray ▲), 1228 (dark-green ▽), 2500 (brown ▼). The standard error of the mean for all the data points is smaller than the symbol size (see Supporting Information). (a) The dotted lines show the expected behavior in the classic Odijk regime. The dashed line shows the -1 slope expected in the classic de Gennes regime. (b) Subset of the data for channels with $H_{\text{eff}} < 2l_p$ showing collapse of mobility data in the backfolded Odijk regime. The black dashed line represents $6\pi\eta\mu L = 1.75(X/L)^0$.

Table 1

Summary of the behavior of axial diffusivity of semiflexible polymers in channel confinement. Prefactors from simulations are also included.

Regime	$6\pi\eta L$
Classic de Gennes ($H \gtrsim l_p^2/w$)	$\approx 1.2 \left(\frac{H}{l_p}\right)^{1/\nu-1} \left(\frac{w}{l_p}\right)^{1/\nu-2}$
Extended de Gennes ($H \lesssim l_p^2/w$)	$\approx 2\beta \ln(l_p/a) + \delta \left(l_p^{3-2/\nu} \omega^{1/\nu-2} H^{1/\nu-1} - l_p^{2-1/\nu} w^{1/\nu-2} \right)$
Backfolded Odijk ($H \approx l_p$ and $\xi \ll 1$)	$\approx 1.75 \ln \left(\frac{l_p}{a} \right)$
Classic Odijk ($H \ll l_p$ and $\xi \gtrsim 1$)	$\approx 2.44 \left(\frac{l_p}{\lambda} \right) \ln \left(\frac{H}{d} \right)$