MULTISCALE SIMULATIONS OF DILUTE-SOLUTION MACROMOLECULAR DYNAMICS IN MACROSCOPIC AND MICROSCOPIC GEOMETRIES

By

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To my wife, Kristine

For your love, your support, your patience,
and three wonderful children.

To my eldest son, Jonathan

For your curiosity, from which I benefit daily.
For your readiness to challenge, which I admire daily.

To my daughter, Sarah

For your enthusiasm and love of life, which brightens my life.
For your quiet persistence – never give up.

To my youngest son, Thomas

For your fearless attitude and ready laughter.
For your stubbornness, which always brings a smile to my face.
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Summary

This thesis is concerned with the development of techniques which enable the accurate simulation of dilute-solution macromolecular dynamics. We develop a coarse-grained kinetic theory model for linear polymers in general, and for DNA in particular. It is demonstrated, through direct comparison with experimental data, that the model is both quantitative and predictive. Methods are developed which allow for efficient simulation of macromolecular dynamics in each of the following three cases:

Homogeneous flows. We use these viscometric flows to develop models and numerical techniques which enable predictive simulations of dilute-solution macromolecular dynamics. A fast, accurate method of calculating the Langevin forces on the molecule is presented, as well as a semi-implicit stochastic integration scheme which allows for the use of reasonable time steps. Also, a Brownian model of DNA is developed and shown to give results in quantitative agreement with available equilibrium and non-equilibrium experimental data.

Macroscopic flows. In these flows, the length scale of the confining geometry is much larger than the length scale of the microstructure (i.e. polymer molecule) – conditions typically encountered in traditional polymer processes such as extrusion. In this area, we develop and critique a new method for the simulation of polymer dynamics in macroscopic devices. The method involves a splitting of the diffusion equation into internal configuration and convective fluxes. The internal configuration of the microstructure is evolved via stochastic simulation to give a $\delta$-function representation of the distribution function. The convective update of the distribution function is performed in an orthogonal polynomial representation, taking advantage of the natural hierarchy of length scales.
present in the problem. We find that convective update can performed accurately by considering only the large length scale (slow mode) contributions.

*Microfluidic devices.* In these flows, the length scale of the microstructure is on the order of the length scale of the confining geometry. Macromolecular dynamics in confined spaces is central to many natural and technological processes, and has taken on renewed importance because of new and developing technologies for single molecule manipulation and analysis of DNA. We develop and critique a general method for dynamic simulations of macromolecules in confined geometries. We also investigate the dynamics of DNA in microchannels with $0.1 < H/S_b < 100$, where $H$ is the channel width and $S_b$ is the equilibrium free-solution radius of gyration of the molecule.

At equilibrium (no flow), we examine the stretch, diffusivity and relaxation time of DNA as a function of channel width and molecular weight. The ratio of these properties to their free-solution values form master curves when plotted against $S_b/H$. Scaling laws are obtained for highly confined chains.

In pressure-driven flow the DNA chains migrate toward the channel centerline in agreement with well-known experimental observations. The thickness of the resulting hydrodynamic depletion layer increases with molecular weight at constant flow strength; higher molecular weight chains therefore move with a higher average axial velocity than lower molecular weight chains. In contrast, when the hydrodynamic effects of the confining geometry are neglected, depletion of concentration is observed in the center of the channel rather than at the walls, contradicting experimental observations. The mechanisms for migration are illustrated using a simple kinetic theory dumbbell model of a confined flexible polymer. The simple theory correctly predicts the trends observed in
the detailed simulations. We also examine the steady-state stretch of DNA chains as a function of channel width and flow strength. The flow strength needed to stretch a highly confined chain away from its equilibrium length is shown to increase with decreasing channel width, independent of molecular weight; this is fairly well-explained using a simple blob picture.
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Chapter 1

INTRODUCTION

New and developing technologies for single molecule manipulation and analysis of DNA in micron and nanometer scale devices (Andersen, 1999; Chou et al., 2000; Lim et al., 2001; Perna et al., 2001; Sauer et al., 2001; Hinz et al., 2001) have fueled considerable interest in the structure and dynamics of solutions of DNA in confined geometries. Consider for example the device shown in Figure 1. This photo was contributed by a research group1 that uses microchannels to manipulate the conformation of individual DNA molecules absorbed to a wall for use in the physical mapping of DNA. In certain other implementations of exonucleolytic sequence analysis it is desirable to link an individual long DNA strand to a bead without manual intervention (Hinz et al., 2001; Stephan et al., 2001). 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. As we discuss below,

1D. C. Schwartz, Department of Chemistry and Laboratory of Genomics, University of Wisconsin – Madison
the long-time dynamics of these DNA molecules are out of reach of atomistic simulations. However, they are accessible to coarse-grained, Langevin models (Bird et al., 1987; Fixman, 1978). A significant portion of this thesis is concerned with developing a general method for dynamic simulations of macromolecules in confined geometries. This is achieved by modifying the Langevin (Brownian) model to account for confinement in an efficient, self-consistent manner.

Coarse-grained models have long been used to investigate the dynamics of complex solutions. These complex fluids may be polymer solutions or melts, fiber or particle suspensions, or any fluid consisting of a complex microstructure. The presence of the microstructure incorporates additional time and length scales into the problem. For example, a simple process involving a dilute solution of monodisperse linear polymer contains time and length scales of the solvent, polymer, fluid deformation, and, of course, the process. The polymer molecule itself contains a spectrum of time and length scales.

There are many levels of description which one may employ when simulating the flow of complex fluids. For example, one may choose molecular dynamics in which the solvent, microstructure, and process are all treated explicitly. In principle, one can then resolve the entire solution space of the system. These methods provide valuable information regarding the physical interactions of the microstructure with the solvent, process walls, and external fields. Currently, atomistic methods can only resolve short time and length scales; resolution of the macroscopic fields (i.e. macroscopic velocities and stresses) of realistic systems are still out of reach of these methods.

Alternatively, one may choose to “coarse-grain” the microstructure via kinetic theory. In the kinetic theory of macromolecules (Bird et al., 1987), the solvent is treated as a viscous continuum which acts on the microstructure through thermal fluctuations
and viscous drag. The microstructure in turn acts on the solvent through the microscopic contribution to the stress tensor. In the case of infinite particle Peclet number (fiber suspensions, for example) thermal fluctuations become negligible compared to hydrodynamic effects and the coarse-grained microstructural representation is no longer considered “Brownian”. At the heart of kinetic theory is the diffusion equation which governs the evolution of the configurational probability distribution function for the microstructure. From this distribution, one can obtain all configurational information about the microstructure, including the microscopic contribution to the overall stress in the fluid. In general, there is no exact analytical solution for the probability distribution function; there is no closed-form expression for the microscopic stress tensor that one may insert into the fluid conservation equations (mass, momentum, and energy). If one wishes to retain the level of physical description chosen for the microstructure, one must preserve the intimate coupling between the solvent and microstructure, as well as any direct coupling of the microstructure with the process itself (walls, external fields, etc.). Simulation methods which attempt to preserve these couplings are termed “micro-macro” or “multi-scale” simulations.

In this thesis, we present some contributions which we have made developing models and numerical solution techniques for use in simulating dilute-solution macromolecular dynamics in various cases. As mentioned in the abstract, these flow fields may be microscopic (flow through microfabricated geometries) or macroscopic. We consider macromolecular dynamics in the absence of electrostatic effects, focusing to a large degree on the hydrodynamic interaction between the macromolecule, solvent and confining geometry. The long hours of work spent in attaining these contributions have primarily served to convince the author of the need for further investigation into the coupling between
macromolecule, solvent and process geometry. This is particularly true in microfluidic applications in which charge distributions in both the macromolecule and fluid are common. In microfabricated devices, the material properties of the confining geometry will also affect the dynamics of the macromolecule and fluid.

In Chapter 2, we present the conservation equations which govern the flow of a dilute solution of monodisperse polymer. Connectivity, solvation effects and hydrodynamic interactions are introduced in Chapter 3. In Chapter 4 we present the conservation equations in stochastic form and discuss the solution of these ordinary stochastic differential equations. In Chapter 5, we develop and validate a method for the efficient calculation of the Langevin forces in stochastic simulations. In that chapter we also present simulation results for DNA dynamics in homogeneous flows and compare those results to available experimental data. Macroscopically inhomogeneous flow fields are considered in Chapter 6, where we present and critique a new Eulerian solver for use in multiscale simulations of complex fluids. In Chapter 7, we present numerical techniques for the solution of kinetic theory problems in microfluidic devices. In that chapter, we present simulation results for DNA dynamics in microchannels of molecular dimension; we consider the dynamics of DNA in equilibrium and in pressure-driven flow through these microchannels. Ongoing and future work is briefly summarized in Section 8.

The different sections in Chapters 5 through 7 correspond to different publications. Those sections are therefore fairly self-contained, and some repetition should be expected.
Figure 1: Flow of a solution of fluorescent stained 21 µm λ-phage DNA through a microchannel. Contributed by E. T. Dimalanta and D. C. Schwartz of the Department of Chemistry and Laboratory of Genomics at the University of Wisconsin – Madison.
Chapter 2

PROBLEM STATEMENT

In this work, we consider a complex fluid consisting of a dilute solution of monodisperse linear polymer immersed in an incompressible Newtonian solvent. The polymer is modeled as a sequence of $N_b$ “beads” connected by $N_s = N_b - 1$ “springs”. The contour length of the molecule is given by $L = b_k N_k$, where $b_k$ is the Kuhn length and $N_k$ denotes the number of Kuhn segments in the molecule. Each spring represents a section of the overall molecule (a sub-molecule) with contour length $q_o = b_k N_{k,s}$, where $N_{k,s} = N_k/N_s$ is the number of Kuhn segments per sub-molecule. The $3N_b$ Cartesian coordinates of the beads in configurational space are represented by the vector $\mathbf{r}$, with the vector $\mathbf{r}_i$ denoting the position of the $i^{th}$ bead in physical space $\mathbf{x}$.

For the system described above, the microstructural configurational probability distribution function, $\Psi(t, \mathbf{r})$, is a function of time and the configurational space of the molecule. The evolution of $\Psi$ is described by the diffusion equation (Bird et al., 1987;
\[
\frac{\partial \Psi}{\partial t} = - \nabla_r \cdot \left( \left[ \omega + \frac{1}{k_B T} D \cdot f - D \cdot \nabla_r \right] \Psi \right) = - \nabla_r \cdot j_r, \tag{1}
\]

where \( k_B \) is Boltzmann’s constant, \( T \) is the absolute temperature, and \( \nabla_r \equiv \partial / \partial r \) is the gradient in configuration space. The vector \( \omega \) of length \( 3N_b \) contains the components of the imposed solvent velocity field at each of the \( N_b \) interaction sites. That is, \( \omega_i = v_s^*(t, r_i) \), where \( v_s^*(t, x) \) represents the imposed solvent velocity field in physical space; \( v_s^*(t, x) \) is the solution to the incompressible Navier-Stokes equations in the absence of the polymer molecules. Motion of the polymer molecule gives rise to perturbations, \( v'(t, x) \), to the solvent velocity field. These hydrodynamic interactions enter Equation 1 through the off-diagonal elements of the positive-definite \( 3N_b \times 3N_b \) diffusion tensor, \( D(r) \). The vector \( f(r) \) contains the \( 3N_b \) components of the total non-hydrodynamic, non-Brownian forces acting on the polymer chain; it is this force that defines our molecule by providing connectivity and excluded volume interactions, as well as wall interactions and external fields. We will present and discuss \( D \) and \( f \) in Section 3.

Rather than using \( r \), one may represent the microstructure by the 3 coordinates of the center-of-mass, \( r_c \), and the \( 3N_s \) coordinates of the connector vectors, \( q_i \), with \( q_i \) representing the vector \( r_{i+1} - r_i \). This coordinate transformation can be expressed as

\[
\begin{pmatrix}
q
r_c
\end{pmatrix}
= \begin{pmatrix}
W
C
\end{pmatrix}
\cdot
\begin{pmatrix}
r
\end{pmatrix}, \tag{2}
\]

where the \( 3N_s \times 3N_b \) matrix \( W \), and the \( 3 \times 3N_b \) matrix \( C \) are defined as

\[
W_{ij} = -I \delta_{ij} + I \delta_{i,j-1} \tag{3}
\]
and

\[ C_{1j} = \frac{1}{N_b} I, \] (4)

respectively, and \( I \) is the \( 3 \times 3 \) identity matrix.

Expressed in terms of \( r_c \) and \( q \), the microstructural configurational probability distribution function, \( \Psi(t, r_c, q) \), is a function of time, position of the center of mass of the molecule, and the internal configuration of the molecule, and the diffusion equation becomes

\[
\frac{\partial \Psi}{\partial t} = - \nabla_{r_c} \cdot \left( \left[ C \cdot \omega + \frac{1}{k_B T} C \cdot D \cdot f - C \cdot D \cdot C^T \cdot \nabla_{r_c} \right] \Psi \right)
- \nabla_{q} \cdot \left( \left[ W \cdot \omega + \frac{1}{k_B T} W \cdot D \cdot f - W \cdot D \cdot W^T \cdot \nabla_{q} \right] \Psi \right)
= - \nabla_{r_c} \cdot j_x - \nabla_{q} \cdot j_q, \] (5)

where \( \nabla_{r_c} \equiv \partial / \partial r_c \) and \( \nabla_{q} \equiv \partial / \partial q \) are gradients with respect to the polymer center of mass and internal configuration, respectively.

In the incompressible Stokes flow regime, the total fluid velocity field, \( v(t, x) = v^s(t, x) + v'(t, x) \), and the total hydrostatic pressure, \( p(t, x) = p^s(t, x) + p'(t, x) \), are the sum of the imposed fields and the fields which arise due to motion of the polymer molecules. In cases where the length scale of the molecule is much smaller than the other relevant length scales of the process, perturbations to the solvent velocity and pressure fields are typically accounted for through the polymer contribution, \( \tau^p(t, x) \), to the overall fluid stress, \( \tau(t, x) \), which is taken to be the sum of the Newtonian and polymer stress tensors. That is, \( v(t, x) \) and \( p(t, x) \) are obtained by requiring overall conservation of mass and linear momentum. For the system described above, the resulting Navier-Stokes
and continuity equations are

\[ \rho \frac{\partial \mathbf{v}}{\partial t} + \mathbf{v} \cdot \nabla \mathbf{x} \mathbf{v} = -\nabla \mathbf{x} \cdot \left[ \rho \mathbf{I} + \tau^p \right] + \mu \nabla^2 \mathbf{x} \mathbf{v} + \rho \mathbf{g}, \]

(6)

\[ \nabla \mathbf{x} \cdot \mathbf{v} = 0, \]

(7)

where \( \nabla \mathbf{x} \equiv \partial / \partial \mathbf{x} \) is the gradient in physical space, \( \eta \) is the solvent viscosity, and \( \rho \) is the density of the fluid. The polymer contribution to the stress tensor, \( \tau^p(t, \mathbf{x}) \), can be expressed (Bird et al., 1987) as functionals of \( \Psi \), summed over all bead contributions,

\[ \tau^p(t, \mathbf{x} = \mathbf{r}_c) = n \sum_{i=1}^{N_b} \int \Psi(t, \mathbf{r}) \left[ (\mathbf{r}_i - \mathbf{r}_c) \mathbf{f}_i \right] d\mathbf{r} + nN_s k_B T \mathbf{I}, \]

(8)

where \( n \) is the total number density of polymer molecules. Note that \( \Psi \) can also be expressed as

\[ \Psi(\mathbf{r}_c, \mathbf{q}, t) = C(\mathbf{r}_c, t) \hat{\Psi}(\mathbf{r}_c, \mathbf{q}, t), \]

(9)

\[ C(\mathbf{r}_c, t) = \int \Psi(\mathbf{r}_c, \mathbf{q}, t) d\mathbf{q}, \]

(10)

and \( nC(\mathbf{r}_c, t) \) is then the local number density of polymer at \( \mathbf{x} = \mathbf{r}_c \).

Simultaneous solution of Equations 6 through 8, along with the diffusion equation, yields the complete evolution of the fluid flow and microstructural configuration in cases where the length scale of the polymer is much smaller than the smallest relevant length scale of the process.

In this work we consider the solution of the diffusion equation for three general cases:

1. Cases in which \( \omega, f, \) and \( D \) are independent of \( \mathbf{r}_c \). These cases are referred to as \textit{homogeneous} flows, and will be treated in Chapter 5.

2. Cases in which the length scale of the confining geometry is much larger than the length scale of the polymer. These \textit{micro-macro} simulations are treated in Chapter
6. Micro-macro simulations typically assume that \( f \) and \( D \) are independent of \( \mathbf{r}_c \), and that \( \omega \) can be linearized about \( \mathbf{r}_c \) – the local velocity gradient is assumed to be linear over the length scale of the polymer.

3. Cases in which length scales of the confining geometry are on the order of the length scale of the polymer. These microfluidic devices are discussed in Chapter 7.

In each of these cases we will be interested in ensemble averages of \( \Psi \). One is generally concerned with ensemble averaged properties as a function of position of the center of mass of the chain(s) in physical space. The ensemble average (or expectation) of a property of the polymer configuration, \( A(\mathbf{x}, q) \), is defined as

\[
\langle A \rangle_q(t, \mathbf{x}) \equiv \int \Psi(t, \mathbf{x}, q)A(\mathbf{x}, q)dq, \tag{11}
\]

where integration is over all internal degrees of freedom of the polymer. The stress tensor defined in Equation 8 is an example of an ensemble average property of \( \Psi \). In some cases one is interested in an average of \( \langle A \rangle_q(t, \mathbf{x}) \) over all or part of physical space. For example, the average of \( \langle A \rangle_q(t, \mathbf{x}) \) over all physical space is given by

\[
\langle A \rangle_r(t) \equiv \int \Psi(t, \mathbf{r})A(\mathbf{r})d\mathbf{r} \equiv \int \langle A \rangle_q(t, \mathbf{x})d\mathbf{x}, \tag{12}
\]

where integration is over all polymer degrees of freedom in the first integrand, and over all physical space in the second. The ensemble averages will be redefined in subsequent chapters in a nomenclature appropriate for the particular chapter.
Chapter 3

INTRAMOLECULAR INTERACTIONS

The behavior of the polymer molecule within a process is defined by intramolecular and intermolecular interactions, as well as interactions with the process walls and other external fields. In this chapter we discuss molecular connectivity (spring forces), excluded volume interactions, and the form of the hydrodynamic interaction tensor in unbounded domains. Wall potentials and hydrodynamic interactions in confined geometries are discussed in Chapter 7.

3.1 CONNECTIVITY

Consider a free-draining linear polymer molecule of contour length $L = b_k N_k$ at equilibrium in a theta solvent. For an infinite number of Kuhn segments, the probability distribution for the end-to-end distance of the molecule is given by a Gaussian with variance $2b_k^2 N_k / 3$. That is, the molecule is in a coiled state at equilibrium. We assume here
that the change in energy of the chain upon stretching is purely entropic; the chain uncoils upon stretching, but bond and bending energies remain constant. For small deformations, one finds that the effective “entropic” potential between two ends of the molecule is given by a Hookean spring potential, with spring constant $3k_B T/b_k^2 N_k$. Extending this idea to a submolecule (represented by a “spring”), we obtain the connector force acting on bead $i$ due to tension in the $i^{th}$ spring,

$$f_i^H = \frac{3k_B T}{b_k} \tilde{q}_i,$$

(13)

where $\tilde{q} \equiv q_i/q_o$. This force implies that the chain is infinitely extensible, which is, of course, physically unrealistic, and due to the assumption of an infinite number of Kuhn segments. When one considers the probability for the end-to-end distance of a freely-jointed Kramer’s chain with finite $N_k$, one arrives at the inverse Langevin model,

$$f_i^L = \frac{k_B T}{b_k} \tilde{L}^{-1}(\tilde{q}) \frac{\tilde{q}}{\tilde{q}},$$

(14)

where $\tilde{q} \equiv |\tilde{q}|$, and

$$\tilde{L}(\beta) = \tilde{q} = \coth \beta - \frac{1}{\beta},$$

(15)

is known as the Langevin function. To obtain the force at a given extension, one must solve a non-linear equation. This shortcoming can be circumvented by using either the Finitely Extensible Non-linear Elastic (FENE) model,

$$f_i^F = \frac{3k_B T}{b_k} \frac{\tilde{q}}{1 - \tilde{q}^2} \frac{\tilde{q}}{\tilde{q}},$$

(16)

or the Padé approximation to the inverse Langevin model,

$$f_i^P = \frac{k_B T}{b_k} \frac{3 - \tilde{q}^2}{1 - \tilde{q}^2} \frac{\tilde{q}}{\tilde{q}}.$$

(17)
We note here that the inverse Langevin, FENE, and Padé models all linearize to the Hookean model in the limit of small extension. In addition, both the FENE and Padé models have singularities of \((1 - \tilde{q})\); the singularity in the inverse Langevin model can not be expressed as a polynomial.

The above finitely extensible models have been used successfully in the prediction of material properties. Until recently, the ability of kinetic models to accurately portray molecular behavior had to be inferred from the ability of the model to reproduce material or optical properties. In the 1990’s, fluorescence microscopy was used to visualize large DNA molecules in proscribed flow fields. With visualization of individual polymers now possible, it was found that the FENE and Padé chain models were incapable of predicting the non-equilibrium configurational properties of DNA molecules, particularly at higher extensions (> 70%). This was confirmed by Bustamante et al. (1994), who used Atomic Force Microscopy to measure the tension in a DNA molecule as a function of extension.

Rather than start with a Kramer’s chain representation of the molecule, one may chose the worm-like chain as a starting point. The asymptotics of the resulting Worm-Like Spring (WLS) model were developed by Marko and Siggia (Marko and Siggia, 1994, 1995) and match the underlying worm-like chain in both the small and large force limits. The final functional form of the WLS force was obtained by fitting the intermediate region to the experimental DNA data of Bustamante et al. (1994). The result can be expressed as

\[
\mathbf{f}_{W}^{t} = \frac{k_{B}T}{b_{k}} \left[ \frac{1}{2(1 - \tilde{q})^2} - \frac{1}{2} + \frac{\tilde{q}}{\tilde{q}} \right] \tilde{q}
\]

This model has been used successfully in the simulation of rheological and configurational properties of DNA (Larson et al., 1997; Hur et al., 2000; Larson et al., 1999; Marko and Siggia, 1995; Ladoux and Doyle, 2000). We again note that the WLS model
linearizes to the Hookean model in the limit of small extension, with the singularity at large extension given by \((1 - \tilde{q})^2\). The success of the WLS model in predicting the configurational properties of DNA is primarily due to this second order singularity (as opposed to the first order singularity of the FENE and Padé models).

### 3.2 EXCLUDED VOLUME INTERACTIONS

The choice of solvent can have a large impact on the configurational and rheological properties of dilute solutions of polymers. In kinetic theory, solvents are usually grouped into three broad categories – good solvents, theta solvents, and bad solvents. These categories can be understood qualitatively in the following manner.

In a good solvent, the polymer-solvent interactions are energetically more favorable than polymer-polymer interactions. This causes the chain to swell in a good solvent, since the polymer prefers to be surrounded by solvent molecules. In kinetic theory, good solvent effects are realized through repulsive bead-bead potentials.

In a theta solvent, polymer-solvent and polymer-polymer interactions are energetically indistinguishable. This causes the polymer to behave as a “phantom chain”, since at large length scales the polymer does not “feel” itself. In kinetic theory, theta solvents are realized by omitting solvation potentials (by doing nothing).

In a bad solvent, polymer-polymer interactions are more favorable than are polymer-solvent interactions. This causes the polymer to contract, since it prefers to be solvated with its own monomers. This effect is accounted for in kinetic theory by incorporating attractive bead-bead potentials.

In this work, we are concerned only with good solvents and theta solvents. Since
no action is required to accommodate theta solvents, the remainder of this section will
deal only with repulsive potentials. There are 3 commonly used forms for these repulsive
interactions – power law, decaying exponential, and Gaussian. The power representation
is generally cast in the form of a Lennard-Jones potential (Cifre and de la Torre, 1999),

\[ U_{ij}^{LJ} = 4\epsilon \left[ \left( \frac{\sigma}{r_{ij}} \right)^{12} - \left( \frac{\sigma}{r_{ij}} \right)^6 \right], \quad (19) \]

where \( r_{ij} \equiv |r_j - r_i| \), and \( \epsilon \) and \( \sigma \) are model parameters with dimensions of energy and
distance, respectively. Often, the attractive term is neglected, or the potential is shifted
and truncated to give only repulsive interactions. Also, the exponent on the repulsive
term can be adjusted for computational efficiency. The decaying exponential excluded
volume potential is generally written as (Cifre and de la Torre, 1999),

\[ U_{ij}^{EXP} = Ak_B T \exp \left( -\frac{r_{ij}}{\hat{\sigma}} \right), \quad (20) \]

where \( A \) and \( \hat{\sigma} \) are again model parameters. The Gaussian excluded volume potential can
be written in the form (Öttinger, 1996)

\[ U_{ij}^G = \hat{v} k_B T \frac{1}{(2\pi \alpha^2)^{3/2}} \exp \left( -\frac{1}{2} \frac{r_{ij}^2}{\alpha^2} \right), \quad (21) \]

where \( \hat{v} \) and \( \hat{\alpha} \) are model parameters with dimensions of volume and distance, respec-
tively. These excluded volume potentials have all been used successfully. In fact, the
choice of the excluded volume potential is arbitrary – the parameters simply need to be
fit to give the correct static properties at equilibrium. The expected molecular weight
scaling of properties for good solvent conditions can be realized for any reasonable form
of excluded volume potential, with the strength of the potential dictating the molecular
weight at which the transition from theta to good solvent scaling occurs. The disadvan-
tage of using arbitrary excluded volume potentials is that once a set of parameters has
been determined at a given level of molecular discretization ($N_{k,s}$), molecular weight must be increased at the same $N_{k,s}$. That is, the dependence of the model parameters on $N_{k,s}$ is unknown.

From neutron scattering data (Strobl, 1997) for dilute solutions of linear polymer in a good solvent, one finds ideal chain behavior at small distances along the chain, and good solvent behavior at large distances. In this spirit, Jendrejack et al. (2002a) considered the increase in energy due to the overlap of two sub-molecules, each consisting of $N_k$ Kuhn segments. Each sub-molecule is considered to be ideal with a (Gaussian) probability distribution with second moment $S^2_s = b_k^2 N_{k,s}/6$. Considering the energy penalty due to overlap of two Gaussian coils (Doi and Edwards, 1986), one arrives at the following expression for the excluded volume potential between two beads of the chain

$$U_{ij}^C = \frac{1}{2} \tilde{v} k_B T N_{k,s}^2 \left( \frac{3}{4\pi S^2_s} \right)^{3/2} \exp \left[ -\frac{3}{4} \frac{r_{ij}^2}{S^2_s} \right], \quad (22)$$

where $\tilde{v}$ is the excluded volume parameter (Doi and Edwards, 1986). This potential simply states that the energy due to the overlap of two Gaussian coils with second moment $S^2_s$ is proportional to a Gaussian distribution with second moment $2S^2_s$. Integration over all space gives a constant total excluded volume energy proportional to $N_{k,s}^2$ with proportionality constant $\tilde{v} k_B T/2$. We feel that this potential removes some of the arbitrariness often associated with excluded volume interactions in Brownian dynamics simulations. Although this potential is not self-consistent (we have ignored any deformation of the coil caused by the overlap), Jendrejack et al. (2002a) demonstrated that Equation 22 does provide the correct dependence on $N_{k,s}$ in the scaling regime. The results of Jendrejack et al. (2002a) will be presented in Chapter 5.
3.3 HYDRODYNAMIC INTERACTIONS

Motion of a polymer molecule in a solvent generates a perturbation in the solvent velocity field. In the kinetic theory of macromolecules, this velocity perturbation, $v'$, is generally taken to be due to a chain of point forces acting in the fluid – $v'$ is the solution to the incompressible Stokes flow problem

\[ \mu \nabla^2 v' = \nabla p + \sum_{i=1}^{N_b} f_i \delta(x - r_i), \]

\[ \nabla \cdot v' = 0, \]  

(23) (24)

subject to appropriate boundary conditions. The velocity field at point $i$ due to a point force at $j$ can in general be represented as

\[ v'_i = \Omega_{ij} \cdot f_j, \]

(25)

where $\Omega_{ij}$ is referred to as the hydrodynamic interaction tensor, or Green’s function. In dilute solutions, these velocity perturbations cause the polymer molecule to behave in a non-draining manner; at equilibrium the polymer coil diffuses through the fluid according to the Stokes-Einstein relation (Doi and Edwards, 1986),

\[ D = \frac{k_B T}{6 \pi \eta R_H}, \]

(26)

where $R_H$ is the hydrodynamic radius of the chain, which is proportional to the “size” of the polymer coil. Equation 26 states that a polymer coil at equilibrium behaves as a large solid Brownian particle of radius $R_H$, rather than as a collection of $N_b$ smaller non-interacting Brownian particles. The diffusion tensor, $D$, appearing in the diffusion equation, is related to $\Omega_{ij}$’s by

\[ D_{ij} = \frac{k_B T}{\zeta} I \delta_{ij} + k_B T \Omega_{ij}, \]

(27)
where $\zeta$ is the bead friction coefficient. In a free-draining model, the $\Omega_{ij}$'s are set to zero, and the molecule diffuses as a collection $N_b$ non-interacting beads, with $D = k_B T/(N_b \zeta)$. This is in contradiction to the experimentally confirmed non-draining behavior characterized by Equation 26.

The far-field velocity perturbation due to a point force in an infinite domain is given by the Oseen-Burgers tensor,

$$
\begin{align*}
\Omega_{ii}^{OB} & = 0 \\
\Omega_{ij}^{OB} & = \frac{1}{8\pi \eta r_{ij}} \left[ I + \frac{r_{ij} r_{ij}}{r_{ij}^2} \right].
\end{align*}
$$

The diffusion tensor obtained from using Oseen-Burgers hydrodynamics is not guaranteed to be positive-definite for all chain configurations. This unphysical artifact arises from the assumption of point forces in the Oseen-Burgers treatment. This assumption was eliminated to first order in the Rotne-Prager-Yamakawa (RPY) tensor (Rotne and Prager, 1969), which can be written as

$$
\begin{align*}
\Omega_{ii}^{RP} & = 0 \\
\Omega_{ij}^{RP} & = \frac{1}{8\pi \eta r_{ij}} \left[ C_1 I + C_2 \frac{r_{ij} r_{ij}}{r_{ij}^2} \right] \quad \text{if } i \neq j \text{ and } r_{ij} \geq 2a, \\
\Omega_{ij}^{RP} & = \frac{1}{\zeta} \left[ (1 - \frac{9}{32a}r_{ij}) I + \frac{3}{32} \frac{r_{ij} r_{ij}}{ar_{ij}} \right] \quad \text{if } i \neq j \text{ and } r_{ij} < 2a,
\end{align*}
$$

$$
\begin{align*}
C_1 & = 1 + \frac{2a^2}{3r_{ij}^2}, \\
C_2 & = 1 - \frac{2a^2}{r_{ij}^2},
\end{align*}
$$

where parameter $a$ represents the bead hydrodynamic radius, and the relation $\zeta = 6\pi \eta a$ has been assumed. The correction for $r_{ij} < 2a$ takes hydrodynamic overlap of the beads into account.
In the early work of Kirkwood and Riseman, and later in the Zimm theory, fluctuations of the equilibrium hydrodynamic interaction tensor were ignored in the interest of constructing a tractable analytical theory; $D$ was taken to be its value with the structure fixed at equilibrium. A “consistently averaged” (Öttinger, 1996) (CAHI) model is obtained by replacing $D$ by its instantaneous ensemble average, $\langle D \rangle$.

We note here that the Oseen-Burgers and Rotne-Prager-Yamakawa representations of the velocity perturbations are derived for particles in an infinite domain, and are therefore only valid in cases where hydrodynamic interactions with walls can be ignored (cases in which the length scale of the geometry is much larger than that of the confining geometry). These cases are investigated in Chapters 5 and 6. In the case of microfluidic devices, hydrodynamic interactions with walls can not be ignored, and the calculation of the hydrodynamic interactions becomes much more complicated. The importance of hydrodynamic interactions in microfluidic devices is discussed in Chapter 7, as well as methods for evaluating the $\Omega_{ij}$’s in these cases. We also note here that, contrary to the case of an infinite domain, $\Omega_{ii} \neq 0$ in confined geometries.
Chapter 4

STOCHASTIC INTEGRATION

Integrating Equation 44 over \([t, t + \Delta t]\) yields,

\[
(\Psi^{n+1} - \Psi^n) = -\int_t^{t+\Delta t} \nabla_r \cdot j_r \, dt. 
\]  

(35)

In order to solve Equation 35, we must first choose a representation, or basis, for \(\Psi\). Typically, a stochastic representation of \(\Psi\) is chosen, and Equation 35 is recast as (Öttinger, 1996)

\[
r(t + \Delta t) - r(t) = \int_t^{t+\Delta t} \left[ K \cdot (r - r_c) + \frac{1}{k_B T} D \cdot f + \nabla_r \cdot D \right] dt' \\
+ \sqrt{2} \int_{w(t)}^{w(t+\Delta t)} \mathbf{B} \cdot d\mathbf{w}',
\]

(36)

\[
D \equiv \mathbf{B} \mathbf{B}^T, 
\]

(37)

where each component of \(w(t)\) is a random Gaussian, or Wiener process with mean zero and variance \(t\). Each \(w(t)\) chosen in this manner will generate one microstructural realization, \(r(t)\). A set of \(N_t\) such realizations will provide a \(\delta\)-function representation
of $\Psi$, with accuracy $O(N_t^{-1/2})$. When free-solution hydrodynamic interactions is used, $\nabla_r \cdot D \equiv 0$. This is not true in confined geometries, as we shall see in Chapter 7.

In a stochastic simulation, $\Psi$ is represented as the sum of $\delta$-functions,

$$\Psi(t, r) \approx \frac{1}{N_t} \sum_{i=1}^{N_t} \delta (r(t) - r_i(t)),$$

and ensemble averages in the stochastic representation are obtained by inserting Equation 38 directly into Equation 11 to give

$$\langle A \rangle(t) \approx \frac{1}{N_t} \sum_{i=1}^{N_t} A(r_i(t)).$$

Steep gradients in excluded volume and spring potentials require the use of small time steps when an explicit Euler scheme is used to integrate Equation 36. Jendrejack et al. (2000) developed a semi-implicit method that scales as $N^2$ and allows stable integration for reasonable time step sizes. They used an explicit Euler scheme on the second integral in Equation 36, and an semi-implicit Euler scheme on the first integral, treating $D(t)$ as constant over the time integration. Using $\nabla_r \cdot D \equiv 0$, this semi-implicit method is written as

$$r(t + \Delta t) - r(t) = [K(t) \cdot (r(t) - r_c(t)) + D(t) \cdot f(t + \Delta t)] \Delta t + \sqrt{2} B(t) \cdot \Delta w,$$

and maintains the requirement that Equation 37 be satisfied at each time step. Note that this is equivalent to using a pure implicit Euler scheme on the right-hand side of (36), and then ignoring the quantity

$$E_{iex} = [K(t + \Delta t) \cdot r(t + \Delta t) - K(t) \cdot r(t)] \Delta t$$

$$+ [D(t + \Delta t) - D(t)] \cdot f(t + \Delta t)] \Delta t$$

$$+ \sqrt{2} [B(t + \Delta t) - B(t)] \cdot \Delta w,$$

(41)
which we expect to be $o(\Delta t)$ as $\Delta t \to 0$, resulting in a first order scheme. Equation 40 is similar to a semi-implicit scheme proposed by Öttinger (1996) in that portions of the drift term are treated implicitly, while the diffusion term is treated explicitly. Our semi-implicit method, which treats $f$ implicitly, provides the desired increase in stability, and we expect (and confirm in Chapter 5) that first order accuracy is maintained.

Equation 40 represents a system of $3N_b$ nonlinear equations, which can be solved by Newton iteration. The key to Newton iteration is the construction of the $3N_b \times 3N_b$ Jacobian matrix (which in this case can be determined analytically), and subsequent solution of the system to get a correction $\delta r$. With hydrodynamic interactions, the Jacobian is a full matrix, but with proper preconditioning, the iterative solver GMRES (Saad and Schultz, 1986) solves the system rapidly in $O(N_b^2)$ operations.

To improve the computational efficiency of the semi-implicit integration scheme, the singularity in the spring force is removed by linearizing the spring force about a specified extension, $q_m$. Above $q_m$, the modified form of the spring force is then

$$f^s_{ij} = \left[ f^s(q_m) + \left( \frac{df^s}{dr_{ij}} \right)_{q_m} (r_{ij} - q_m) \right] \frac{r_{ij}}{r_{ij}}, \text{ for } r_{ij} > q_m.$$  \hfill (42)

We used $q_m = 0.99q_o$ (99% extension) for all runs. Note that we always verify that this modification is only accessed during intermediate Newton iterations of the semi-implicit method: configurations at the end of a time step always have $|q_i| < q_m \forall i = 1, N_s$.

This method described in this chapter is implemented and validated in Chapter 5. For cases in which HI was included, the semi-implicit integration scheme resulted in a code that was about ten times faster for a given accuracy than that of the explicit Euler, as well as properties that were somewhat smoother in time.
Chapter 5

SIMULATION OF
DILUTE-SOLUTION POLYMER
DYNAMICS IN
HOMOGENEOUS FLOWS

In this chapter, we will consider the solution of the diffusion equation in special homogeneous flow fields. Homogeneous flows are the starting point for validation of kinetic theory models. For example, experimental viscometric flows such as simple shear and planar extension are easily represented in the diffusion equation as homogeneous flows. In these special flows, we are interested in the internal configuration and the thermal diffusivity of the polymer under the influence of a constant imposed velocity gradient. In this case, it convenient to linearize the unperturbed solvent velocity field about the center
of mass,
\[
\omega(t, r) = \nu(t, r_c) + K \cdot (r - r_c). 
\] (43)

Inserting this expression into the diffusion equation gives
\[
\frac{\partial \Psi}{\partial t} = -\nabla_r \cdot \left( \left[ K \cdot (r - r_c) + \frac{1}{k_B T} D \cdot f - D \cdot \nabla_r \right] \Psi \right) 
\]
\[
= -\nabla_r \cdot \mathbf{j}_r 
\] (44)

where the constant (and arbitrary) velocity at the center of mass of the molecule has been set to zero.

In Section 5.1 we develop a method for the efficient calculation of the Langevin forces in stochastic simulations. In Section 5.2, present simulation results for DNA dynamics in homogeneous flows and compare those results to available experimental data.

5.1 HYDRODYNAMIC INTERACTIONS IN LONG-CHAIN POLYMERS: APPLICATION OF THE CHEBYSHEV POLYNOMIAL APPROXIMATION IN STOCHASTIC SIMULATIONS

5.1.1 ABSTRACT

We have simulated Brownian bead-spring chains of up to 125 units with fluctuating hydrodynamic and excluded volume interactions using the Chebyshev polynomial approximation proposed by Fixman [M. Fixman, Macromolecules 19, 1204 (1986)] for the

\footnote{Jendrejacks et al. (2000)}
square root of the diffusion tensor. We have developed a fast method to continuously determine the validity of the eigenvalue range used in the polynomial approximation, and demonstrated how this range may be quickly updated when necessary. We have also developed a weak first order semi-implicit time integration scheme which offers increased stability in the presence of steep excluded volume potentials. The full algorithm scales roughly as $O(N^{2.25})$ and offers substantial computational savings over the standard Cholesky decomposition. The above algorithm was used to obtain scaling exponents for various static and zero shear rate dynamical properties, which are found to be consistent with theoretical and/or experimental predictions.

5.1.2 INTRODUCTION

The inclusion of hydrodynamic interactions in the simulation of dilute polymer solutions is necessary if one wishes to capture the basic physics of non-free-draining polymer molecules (Petera and Muthukumar, 1999). Hydrodynamic interactions have been studied extensively by analytical methods, stochastic simulations and, to some extent, by numerical solution of the probability distribution function (Jendrejack et al., 2000). There has been recent interest in the rheological and conformational properties of dilute solutions of DNA and other proteins (Kwan and Shaqfeh, 1999; de Gennes, 1999; Zimm, 1998; Haab and Mathies, 1999; Larson et al., 1997, 1999). The treatment of hydrodynamic interactions in these systems, particularly in microfabricated geometries (Haab and Mathies, 1999) and near walls, is essential if one wishes to understand their microstructural behavior and subsequently predict their transport properties.

Stochastic simulations of polymers in a dilute solution with fluctuating (i.e. not preaveraged) hydrodynamic interactions have been limited to relatively short chains (Cifre and
de la Torre, 1999). Studies of the behavior of these systems in the long-chain limit have been hindered due to the computational demands associated with the calculation of the hydrodynamic interactions. Such interactions involve the decomposition of the diffusion tensor that appears in the stochastic form of the Fokker-Planck equation. In 1986, Fixman (1986) presented a polynomial approximation to this decomposition which considerably reduced the required computations. At that time, long chains were still out of range, even using Fixman’s method. Even with the introduction of fast, inexpensive workstations, Fixman’s method has never been applied to long chain polymers, probably due to the lack of an effective means of assuring that polymer configurations remain within the valid range of the approximation.

It is imperative that fast, practical methods of accurately dealing with hydrodynamic interactions be developed if realistic simulations of long chain polymer solutions are to be realized. This is particularly true if one wishes to include fluctuating hydrodynamic interactions in coupled microscopic/continuum calculation schemes, such as the Brownian Configuration Fields (BCF) (Öttinger et al., 1997) or Operator-Splitting Cumulant-Matching (OSCM) (Bell, 1998; Jendrejack et al., 2000) methods. In this work we propose one such method.

The outline of this paper is as follows. In Section 5.1.3, we present the governing equations, polymer model, and our choice of parameters. In Section 5.1.4, we discuss the Chebyshev polynomial expansion and present a rapid method of assessing the validity of the polynomial expansion. The scaling properties of interest are defined in Section 5.1.5. Details of the simulation are given in Section 5.1.6; the results are presented and discussed in Section 5.1.7.
5.1.3 MODEL

In a Lagrangian frame of reference, the dimensionless \(^2\) governing equation for the probability distribution function of an isolated “bead-spring” polymer chain in the presence of a velocity gradient \(\nabla v\), can be expressed as (Doi and Edwards, 1986; Bird et al., 1987; Öttinger, 1996)

\[
\frac{\partial \Psi}{\partial t} = - \frac{\partial}{\partial R} \cdot [(K \cdot R + D \cdot F) \Psi] + \frac{\partial}{\partial R} \cdot D \cdot \frac{\partial}{\partial R} \Psi. \tag{45}
\]

Here \(N\) is the number of beads in the chain, \(R\) is a vector containing the \(3N\) spatial coordinates of the beads that constitute the polymer chain, \(D\) is a \(3N \times 3N\) diffusion tensor, \(F\) is a force vector of length \(3N\) acting on the chain. The \(3N \times 3N\) matrix \(K\) is block diagonal with diagonal components \((\nabla v)^T\).

Equation (45) can be expressed as a stochastic differential equation in the \(3N\) spatial coordinates:

\[
dR = [K \cdot R + D \cdot F] \, dt + \sqrt{2}B \cdot dw, \tag{46}
\]

\[
D = B \cdot B^T. \tag{47}
\]

The components \(dw\) are obtained from a real-valued Gaussian distribution with mean zero and variance \(dt\).

Hydrodynamic interactions enter Equation (46) through the diffusion tensor. In this work we take \(D\) to be the Rotne-Prager-Yamakawa (RPY) tensor (Rotne and Prager, \(^2\))

\(^2\)The quantities used for nondimensionalization throughout this paper are \(\sqrt{k_B T/H}\) for distance, \(\zeta/(4H)\) for time, \(k_B T\) for energy, \(\sqrt{k_B T H}\) for force, and \(nk_B T\) for the stress tensor. The parameter \(k_B\) is Boltzmann’s constant, \(T\) is temperature, \(H\) is Hooke’s spring constant, \(n\) is the number density of polymer, and \(\zeta\) is the bead friction coefficient.
which, in dimensionless form, is

\[
D_{ii} = \frac{1}{4} I,
\]

\[
D_{ij} = \frac{3a}{16 R_{ij}} \left[ C_1 I + C_2 \frac{R_{ij} R_{ij}}{R_{ij}^2} \right] \text{ if } i \neq j \text{ and } R_{ij} \geq 2a,
\]

\[
D_{ij} = \frac{1}{4} \left[ (1 - \frac{9 R_{ij}^2}{32a}) I + \frac{3}{32} \frac{R_{ij} R_{ij}}{a R_{ij}} \right] \text{ if } i \neq j \text{ and } R_{ij} < 2a,
\]

where

\[
C_1 = 1 + \frac{2a^2}{3 R_{ij}^2},
\]

\[
C_2 = 1 - \frac{2a^2}{R_{ij}^2},
\]

and \( R_{ij} \equiv R_j - R_i \). The vector \( R_i \) contains the 3 coordinates of the position vector of the \( i^{th} \) bead. The RPY tensor is positive-definite for all chain configurations, but exact only as \( R_{ij} \to \infty \). Parameter \( a \) represents the dimensionless hydrodynamic radius of each bead, and \( I \) is the \( 3 \times 3 \) identity matrix.

The beads of the polymer chain are connected by Finitely Extensible Non-Linear (FENE) springs, with total potential energy

\[
\phi^{(c)} = \sum_{|i-j|=1} \frac{1}{2} b \ln \left[ 1 - \frac{R_{ij}^2}{b} \right],
\]

where \( R_{ij} \equiv \sqrt{R_{ij} \cdot R_{ij}} \), and where \( b \) is the square of the maximum dimensionless bond length. For excluded volume interactions, we use a soft exponential repulsion with total energy

\[
\phi^{(v)} = \sum_{i<j} A \exp \left[ -\alpha R_{ij} \right].
\]

The force appearing in Equations (45) and (46) is given by

\[
F_i = -\frac{\partial}{\partial R_i} (\phi^{(c)} + \phi^{(v)}).
\]
As far as scaling laws are concerned, the type or strength of the excluded volume inter-
action should only serve to shift the point at which long-chain behavior is realized. A
soft potential satisfies the purpose of this paper, which is to demonstrate the practical
application of Fixman’s method for long chains, and to generate results for the scaling of
static and dynamic chain properties with molecular weight in the presence of fluctuating
hydrodynamic interactions. In this paper we used $b = 56.25$, $A = 75.0$, and $\alpha = 4.0$. A
cutoff of $R_{ij} = 2.5$ was used for $\phi^{(v)}$. The values of $A$ and $\alpha$ are similar to those used by
Rey et al. (1991). We used $a = 0.4$ for the dimensionless bead hydrodynamic radius.

5.1.4 FIXMAN’S METHOD

As the length of the polymer chain increases, the calculation of $B$ from Equation (47)
becomes the computational bottleneck of the stochastic simulation. This operator is not
unique; any $B$ satisfying Equation (47) is valid for the determination of ensemble av-
erages (Öttinger, 1996). Nevertheless, there are two natural choices for $B$. One is the
square root matrix, which satisfies

$$D = S \cdot S,$$

with

$$S = S^T,$$

for symmetric $D$. The other arises from the Cholesky decomposition of $D$, which gives
$B$ as an upper (or lower) triangular matrix. This decomposition scales as $N^3$, and we
are not aware of faster methods for the calculation of $B$ (Fixman, 1986). The exact
computation of $S$, on the other hand, requires solution of an eigenvalue problem, also an
$O(N^3)$ process. The Cholesky decomposition is the preferred method in the literature.
Fixman, however, was able to exploit two important facts. First, $S$ can be approximated and, second, it need not be constructed explicitly. Rather, it is the vector $S \cdot dw$ that is required, and computation of its polynomial approximation scales roughly as $N^{2.25}$. For a detailed discussion on the vector approximation, we refer the reader to Fixman’s original work (Fixman, 1986). Here we present the algorithm, and discuss some key issues that arise in the use of Fixman’s method.

Let $s^{(d)}$ be the Chebyshev polynomial approximation (Canuto et al., 1988) of the scalar function $\sqrt{d}$ over the range $[\lambda_{min}, \lambda_{max}]$. Then $s^{(d)}$ can be expressed as

$$s^{(d)} = \sum_{l=0}^{L} a_l C_l,$$

(58)

where

$$C_0 = 1,$$

(59)

$$C_1 = d_a d + d_b,$$

(60)

$$C_{l+1} = 2(d_a d + d_b)C_l - C_{l-1},$$

(61)

(these follow from the recursion relations for the Chebyshev polynomials) with

$$d_a = \frac{2}{\lambda_{max} - \lambda_{min}},$$

(62)

$$d_b = -\frac{\lambda_{max} + \lambda_{min}}{\lambda_{max} - \lambda_{min}},$$

(63)

and $L$ is the order of the polynomial approximation. For the calculation of the Chebyshev coefficients, $a_l$, we refer the reader to Canuto et al. (1988).

Using the properties of functions of matrices (Wylie and Barrett, 1995), generalization of the above scalar case gives $S^{(D)}$, the Chebyshev polynomial approximation of the matrix function $D^{1/2}$:

$$S^{(D)} = \sum_{l=0}^{L} a_l C_l,$$

(64)
where

\[ C_0 = I, \quad (65) \]

\[ C_1 = d_a D + d_b I, \quad (66) \]

\[ C_{l+1} = 2(d_a D + d_b I)C_l - C_{l-1}. \quad (67) \]

The \( a_l \) are the same Chebychev coefficients as obtained in the scalar case and the eigenvalues of \( D \) are bounded by \([\lambda_{\text{min}}, \lambda_{\text{max}}]\). The explicit calculation of \( S^{(D)} \) is not necessary, because the quantity of interest is \( S \cdot dw \), whose polynomial approximation \( y \) may be obtained by a series of matrix-vector multiplications

\[ y = S^{(D)} \cdot dw = \sum_{l=0}^{L} a_l x_l, \quad (68) \]

\[ x_0 = dw, \quad (69) \]

\[ x_1 = [d_a D + d_b I] \cdot dw, \quad (70) \]

\[ x_{l+1} = 2[d_a D + d_b I] \cdot x_l - x_{l-1}. \quad (71) \]

The Chebyshev approximation can be calculated to any desired accuracy, provided \( \lambda_{\text{max}} \) and \( \lambda_{\text{min}} \), of \( D \) are known. The explicit calculation of these eigenvalues for each configuration, coupled with a Chebyshev polynomial expansion at each configuration, would result in little or no savings in computational time (compared to the exact Cholesky decomposition). Fixman had partially circumvented this difficulty by using preaveraged Rotne-Prager hydrodynamic interactions to obtain approximations for the upper and lower limits of the eigenvalues. There is, however, no guarantee that during a simulation the eigenvalues will remain within the preaveraged limits for all configurations. We show now how to efficiently maintain an accurate polynomial approximation.

The Chebyshev expansion is only valid within the chosen eigenvalue range; we have developed a rapid method to evaluate the error which results from a violation of the
eigenvalue limits. Using Equations (56), (57), and (68) we have

$$\lim_{L \to \infty} [y \cdot y] = d\mathbf{w} \cdot \mathbf{D} \cdot d\mathbf{w},$$

(72)

assuming that we are using a valid eigenvalue range. We now define a relative error $E_f$ according to

$$E_f = \sqrt{\frac{|y \cdot y - d\mathbf{w} \cdot \mathbf{D} \cdot d\mathbf{w}|}{d\mathbf{w} \cdot \mathbf{D} \cdot d\mathbf{w}}}.$$  

(73)

If the polynomial approximation given by Equation (68) were exact, $E_f$ would be identically zero for any choice of $d\mathbf{w}$ and Equation (56) would be satisfied. In other words, $E_f$ measures the extent to which the Fluctuation-Dissipation Theorem is violated. Strictly speaking, $E_f$ should be small for all possible $d\mathbf{w}$. However, the probability that an arbitrary $d\mathbf{w}$ coupled with an erroneous $\mathbf{S}^{(D)}$ will result in small $E_f$ is vanishingly small, as we have verified by performing trial simulations using both the Cholesky decomposition and Fixman’s method. The two methods showed identical time series for all ensemble averaged properties.

In practice, the polynomial approximation $y$ and corresponding $d\mathbf{w}$ can be used to calculate $E_f$ for each configuration at each time step with negligible computational cost. If $E_f$ proves to be unacceptable, a new eigenvalue range can be computed for the given configuration, and this new range used until another violation of $E_f$ occurs. In our work, we use the free software package ARPACK, which is capable of rapidly solving for only the upper and lower eigenvalues of $\mathbf{D}$ by the Arnoldi method in $O(N^2)$ operations (Lehoucq et al., 1997).

A few more words on the polynomial approximation are in order. The number of terms (or collocation points) that must be retained to achieve a desired accuracy depends on the condition number ($C_n = \lambda_{\text{max}}/\lambda_{\text{min}}$) of $\mathbf{D}$. We found this dependence to scale
roughly as $C_n^{0.5}$ for accuracy of $O(10^{-3})$, which is consistent with the findings of Fixman (1986). This relatively weak dependence makes the computational savings (over Cholesky factorization) increase with chain length.

Excluded volume potentials facilitate implementation of Fixman’s method. Aside from the loss of physical meaning of the RPY hydrodynamic approximation in cases where overlaps between beads is are common, it is useful to note that Fixman’s method itself becomes impractical in the absence of excluded volume. The RPY tensor achieves positive-definiteness by ignoring the overlap volume during integration of the viscous dissipation (recall that the RPY tensor is the result of seeking an upper limit to the true viscous dissipation). While ignoring the overlap volume assures us of a positive definite $D$, it also tends to drive $\lambda_{min}$ down with increasing overlap. In the limit of complete overlap, $\lambda_{min}$ approaches zero, and $C_n$ tends to infinity. For example, consider a pair of tangent beads oriented along the x-axis, and let $C_n^0$ be the condition number at that orientation. With our choice of the hydrodynamic radius, we find $C_n/C_n^0 = (2.23, 12.08, 24.38)$ for overlaps of 50%, 90%, and 95% respectively. Here, a 0% overlap corresponds to tangent beads of radius $a$, and 100% overlap indicates complete superposition of the beads. Recall that the number of collocation points needed to achieve a given accuracy increases with increasing $C_n$. Once the number of collocation points used approaches $3N$, the Cholesky decomposition becomes faster than the polynomial approximation.

### 5.1.5 SCALING PROPERTIES

The physical properties investigated in this paper include the diffusion coefficient $D$, the radius of gyration $R_g$, the end-to-end distance $R$, the shear viscosity $\eta$, and first normal stress coefficient $\Psi_1$. 
The radius of gyration and end-to-end distance are given by

\[ R_g^2 = \frac{1}{2N^2} \sum_{i,j} \langle R_{ij}^2 \rangle, \quad (74) \]

and

\[ R^2 = \langle R_{1N}^2 \rangle. \quad (75) \]

The theoretical scaling for these static properties is (Doi and Edwards, 1986)

\[ R_g^2 \propto R^2 \propto N^{2\nu}. \quad (76) \]

In a good solvent, as \( N \to \infty \), the scaling exponent has a theoretical value of \( \nu \cong 0.588 \) from a perturbation analysis, and an experimental value of \( \nu \cong 0.6 \) (Strobl, 1997; Li et al., 1995).

The diffusion coefficient can be calculated from the center of mass trajectory

\[ \langle \Delta R_c^2 \rangle = 6Dt. \quad (77) \]

We also computed the diffusivity by the approximate Kirkwood formula (Bird et al., 1987)

\[ D^{(Kirkwood)} = \frac{1}{3N^2} \sum_{i,j} \text{tr}(\langle D_{ij} \rangle). \quad (78) \]

The two results were indistinguishable within the error of the simulation. In the non-free-draining limit, \( D \propto R_g^{-1} \), and we have

\[ D \propto N^{-\nu}. \quad (79) \]

The non-isotropic polymer contribution to the stress tensor can be expressed in dimensionless form as (Bird et al., 1987)

\[ \tau_p = \sum_{i=1}^{N} \langle R_i F_i \rangle + (N - 1)I \quad (80) \]
The steady shear properties of concern in this paper are the dimensionless viscosity and first normal stress coefficient defined by (Bird et al., 1987),

\[ \eta = \frac{-\tau_{12}}{\dot{\gamma}}, \quad (81) \]

and

\[ \Psi_1 = -\frac{\tau_{11} - \tau_{22}}{\dot{\gamma}^2}, \quad (82) \]

where \( \dot{\gamma} \) is the non-dimensional shear rate. The Zimm model predicts in the limit of zero shear (Doi and Edwards, 1986)

\[ \eta \propto N^{3\nu}, \quad (83) \]

and

\[ \Psi_1 \propto N^{6\nu}. \quad (84) \]

5.1.6 SIMULATION DETAILS

All simulations were equilibrated without hydrodynamic interactions, then restarted with hydrodynamic interactions and again allowed to equilibrate. The semi-implicit integration scheme outlined in Chapter 4 was used with a dimensionless time step of \( \Delta t = 0.1 \). This time step is small enough to give good performance of the semi-implicit method (average convergence rate of 2–3 Newton iterations), and trial simulations with various \( \Delta t \) show that it gives accurate results. Chains ranging from 20 to 125 beads were simulated at equilibrium and in shear flow at a \( We = 1.0^{3} \), at which point the transition to

\[ \text{In our non-dimensionalization, the Weissenberg number is defined as } We = \dot{\gamma} \tau_1, \text{ where } \tau_1 = \frac{2}{[\sin(\pi/(2N))] \text{ is the longest Rouse relaxation time, and } \dot{\gamma} \text{ is the shear rate (non-dimensionalized with } \zeta/(4H)).} \]
<table>
<thead>
<tr>
<th>number of beads</th>
<th>ensemble size</th>
<th>averaging period ($\lambda_R$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>200</td>
<td>38</td>
</tr>
<tr>
<td>40</td>
<td>100</td>
<td>38</td>
</tr>
<tr>
<td>60</td>
<td>50</td>
<td>38</td>
</tr>
<tr>
<td>80</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>100</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>125</td>
<td>14</td>
<td>15</td>
</tr>
</tbody>
</table>

Table 1: Sizes and lengths of simulations. $\lambda_R$ refers to the longest non-dimensional Rouse relaxation time.

zero shear rate dynamic properties is approximately complete. At $We = 1.0$, we found \( \langle Q^2 \rangle / \langle Q^2 \rangle_{eq} < 1.02 \) for all chain lengths, where \( \langle Q^2 \rangle \) is the average square bond length for a given chain. We also found \( \langle S_{yy} \rangle_{eq} / \langle S_{yy} \rangle < 1.2 \) for all chain lengths, where \( \langle S_{yy} \rangle \) is the component of the radius of gyration tensor in the gradient direction. Ensemble sizes and averaging times are given in Table 1.

Variance reduction by parallel processes (Öttinger, 1996) was used for all simulations, which resulted in improvement over the non-variance reduced properties, albeit not to the extent that would occur in the absence of excluded volume and non-linear springs.

5.1.7 RESULTS AND DISCUSSION

The molecular weight dependence of the physical properties defined in Section 5.1.5 is illustrated in Figures 2, 3, and 4. The slopes of the linear fits and the values of the exponent $\nu$ extracted via the scaling of Section 5.1.5 are presented in Table 2. The errors bars on $D$ in Figure 3 are not shown as they are smaller than the symbols. The error bars on $\eta$ and $\Psi_1$ in Figure 4 are large relative to those of the other properties. This is primarily due to the inefficiency of variance reduction for long chains with excluded volume, and
Table 2: Summary of values of slopes and corresponding $\nu$ as obtained from various physical quantities.

<table>
<thead>
<tr>
<th>Physical Quantity</th>
<th>Slope</th>
<th>$\nu$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R^2$</td>
<td>1.224</td>
<td>0.612</td>
</tr>
<tr>
<td>$R_g^2$</td>
<td>1.226</td>
<td>0.613</td>
</tr>
<tr>
<td>$D_c$</td>
<td>-0.609</td>
<td>0.609</td>
</tr>
<tr>
<td>$\eta$</td>
<td>1.913</td>
<td>0.638</td>
</tr>
<tr>
<td>$\Psi_1$</td>
<td>3.825</td>
<td>0.637</td>
</tr>
</tbody>
</table>

also because of the relatively short simulation time and small ensembles.

The ratio $R^2/R_g^2$ was also calculated and was found to be independent of molecular weight. We determined $R^2/R_g^2 = 6.3 \pm 0.3$, in excellent agreement with the value of $6.2539 \pm 0.0078$ from recent Monte Carlo simulations reported by Li et al. (1995). We also calculated the ratio $R_h/R_g$, where $R_h$ is the effective chain hydrodynamic radius from the Stokes-Einstein equation for the diffusivity

$$D = \frac{k_BT}{6\pi\eta_sR_h}.$$  \hspace{1cm} (85)

In dimensionless form, $R_h$ is given by

$$R_h = \frac{a}{4D}.$$ \hspace{1cm} (86)

We found $R_h/R_g = 0.62 \pm 0.03$ for all molecular weights. This compares favorably to the theoretical value of 0.64 (from renormalization group theory) (Oono and Kohmoto, 1983), but less favorably to the value of $\sim 0.67$ from the Kirkwood-Riseman theory (Kirkwood and Riseman, 1948). The latter prediction relies on preaveraging of the hydrodynamic interaction tensor. The renormalization group calculation does not make this approximation. Both of these theories assume $N \to \infty$.

The scaling exponent for the static properties $R^2$ and $R_g^2$ is $\sim 4\%$ higher than the
Figure 2: Molecular weight scaling for $R^2$ and $R_g^2$. 
Figure 3: Molecular weight scaling for $D$. 

- $D$ 
- **linear fit**
theoretical limit of $\nu = 0.588$, and $\sim 2\%$ higher than the accepted experimental value of 0.6 (Strobl, 1997). The scaling exponent for $D$ is closer to the predicted values but still slightly high. The calculated scaling exponents for $D$ and $R_g^2$ agree to within 0.7%, indicating that the non-free draining assumption is realized for our choice of parameters. The exponents derived for the dynamic properties $\eta$ and $\Psi_1$ are nearly indistinguishable and overpredict experimental and theoretical values by 6.3% and 8.5%, respectively.

The predicted scaling exponent in all cases lies above the theoretical limit of $\nu = 0.588$. This is consistent with the Monte Carlo simulations of Li et al. (1995), which show that the effective scaling exponents corresponding to $R^2$ and $R_g^2$ approach the theoretical value from above. We attribute part of these discrepancies to the fact that we have not reached the infinite chain length limit in our simulations.

Table 2 demonstrates the internal consistency of our simulations, and in all cases agreement to within $\sim 6\%$ of experimental values provides an external validation of both our implementation of Fixman’s method and our semi-implicit integration scheme.

These simulations, all of which were performed on simple workstations, demonstrate the ease with which Fixman’s method can be applied to stochastic processes. The method presents a considerable savings in computational time over the standard Cholesky factorization, and the semi-implicit time integration scheme further improves efficiency by about a factor of ten. More importantly, it offers the opportunity to include fluctuating hydrodynamic interactions in studies of the dynamics of long polymers in complex flows.
Figure 4: Molecular weight scaling for $\eta$ and $\Psi_1$. 
5.2 STOCHASTIC SIMULATIONS OF DNA IN FLOW: DYNAMICS AND THE EFFECT OF HYDRODYNAMIC INTERACTIONS⁴

5.2.1 ABSTRACT

We present a fully parameterized bead-spring chain model for stained λ-phage DNA. The model accounts for the finite extensibility of the molecule, excluded volume effects and fluctuating hydrodynamic interactions (HI). Parameters are determined from equilibrium experimental data for 21 μm stained λ-phage DNA, and are shown to quantitatively predict the non-equilibrium behavior of the molecule. The model is then used to predict the equilibrium and non-equilibrium behavior of DNA molecules up to 126 μm. In particular, the HI model gives results that are in quantitative agreement with experimental diffusivity data over a wide range of molecular weights. When the bead friction coefficient is fit to the experimental relaxation time at a particular molecular weight, the stretch in shear and extensional flows is adequately predicted by either a free-draining or HI model at that molecular weight, although the fitted bead friction coefficients for the two models differ significantly. In shear flow, we find two regimes at high shear rate (\(\dot{\gamma}\)) that follow different scaling behavior. In the first, the viscosity and first normal stress coefficient scale roughly as \(\dot{\gamma}^{-\frac{6}{11}}\) and \(\dot{\gamma}^{-\frac{14}{11}}\), respectively. At higher shear rates, these become \(\dot{\gamma}^{-\frac{2}{3}}\) and \(\dot{\gamma}^{-\frac{4}{3}}\). These regimes are found for both free-draining and HI models and can be understood based on scaling arguments for the diffusion of chain ends.

⁴Jendrejack et al. (2002a)
5.2.2 INTRODUCTION

The ability to directly visualize individual DNA molecules via fluorescent staining allows one to obtain experimental data on the behavior of individual polymer molecules (Han and Craighead, 2000; Smith et al., 1999, 1996, 1992; Smith and Chu, 1998; Bustamante et al., 1994; Perkins et al., 1997; Larson et al., 1997). Recent work (Hur et al., 2000; Larson et al., 1999; Hur et al., 2001) has shown that simple bead-spring or bead-rod models can reproduce some of the non-equilibrium properties of \( \lambda \)-phage DNA. That work has also demonstrated that, provided the friction coefficient is determined from the experimental relaxation time, these simple models can reproduce some properties of non-dilute solutions (Hur et al., 2001). As important as that work has been, the models employed in these references have not included excluded volume effects or hydrodynamic interactions, and therefore cannot be used as predictive tools for molecules of differing sizes. Furthermore, experimental evidence (Smith et al., 1996) indicates non-free-draining behavior for DNA molecules as short as \( 3 \mu m \). Recent studies (Jian et al., 1997, 1998; Schlick et al., 2000) have considered both excluded volume and hydrodynamic interactions in stochastic simulations of DNA. However, that work only considered chains of less than a micron in length and simulation times of less than a second. For simulations of transport in microfluidic devices which involve external fields, such as those proposed for DNA separation (Han and Craighead, 2000; Jendrejack et al., 2002a), a sound treatment of hydrodynamic interactions is essential.

In this work we present a fully parametrized bead-spring model for DNA which includes finite extensibility, excluded volume effects and hydrodynamic interactions. The parameters in the model are inferred from available experimental data for \( 21 \mu m \) \( \lambda \)-phage DNA. The model satisfies all the molecular weight scaling laws for dilute solutions of
linear polymers, and therefore is expected to provide a useful predictive tool at higher molecular weights.

In Section 5.2.3, we present the model and governing equations. In Section 5.2.4, we define properties of interest in this paper, and, in Section 5.2.5, we present details of the simulation and parameter selection. In Section 5.2.6, we validate our model by quantitative comparison to available experimental data, and, then, in Section 5.2.6 we use the model to predict the behavior of DNA molecules up to 126 µm in length. High shear rate scaling results are presented in Section 5.2.6 for 84 µm chains. In Section 5.2.6, we examine the dependence of the model on the degree of molecular discretization (number of Kuhn segments per spring). We conclude in Section 5.2.7 with a summary of our results.

### 5.2.3 MODEL

We consider here a linear molecule represented by \( N_b \) beads connected by \( N_e = N_b - 1 \) springs. The model described here does not contain any mechanism for helical structuring or other sub-Kuhn length phenomena. It does, however, contain the most relevant physics for rheological properties and conformational properties which occur on longer length scales (gyration tensor and diffusivity tensor, for example). The governing stochastic differential equation for an isolated bead-spring chain immersed in a thermal solvent is given by (Jendrejack et al., 2000)

\[
\begin{align*}
\frac{d\mathbf{R}}{dt} & = \left[ \mathbf{K} \cdot \mathbf{R} + \frac{1}{k_B T} \mathbf{D} \cdot \mathbf{F} + \frac{\partial}{\partial \mathbf{R}} \mathbf{D} \right] dt + \sqrt{2} \mathbf{B} \cdot d\mathbf{W}, \\
\mathbf{D} & = \mathbf{B} \cdot \mathbf{B}^T.
\end{align*}
\]

\( (87) \)  
\( (88) \)
Here $k_B$ is Boltzmann’s constant, and $T$ is the absolute temperature. The vector $\mathbf{R}$ contains the $3N_b$ spatial coordinates of the beads that constitute the polymer chain, $\mathbf{D}$ is a $3N_b \times 3N_b$ diffusion tensor, and $\mathbf{F}$ is a force vector of length $3N_b$. The $3N_b \times 3N_b$ matrix $\mathbf{K}$ is block diagonal with diagonal components $(\nabla \mathbf{v})^T$, with $\mathbf{v}$ being the unperturbed solvent velocity. The components of $d\mathbf{W}$ are obtained from a real-valued Gaussian distribution with mean zero and variance $dt$.

Hydrodynamic interactions enter Equation (87) through the off-diagonal components of the diffusion tensor. In this work, we take $\mathbf{D}$ to be the Rotne-Prager-Yamakawa (RPY) tensor (Rotne and Prager, 1969), which can be written as

\[
\mathbf{D}_{ii} = \frac{k_B T}{\zeta} \mathbf{I},
\]

\[
\mathbf{D}_{ij} = \frac{k_B T}{8\pi \eta R_{ij}} \left[ C_1 \mathbf{I} + C_2 \frac{\mathbf{R}_{ij} \mathbf{R}_{ij}}{R_{ij}^2} \right] \quad \text{if} \quad i \neq j \quad \text{and} \quad R_{ij} \geq 2a,
\]

\[
\mathbf{D}_{ij} = \frac{k_B T}{\zeta} \left[ (1 - \frac{9}{32a}) \mathbf{I} + \frac{3}{32} \frac{\mathbf{R}_{ij} \mathbf{R}_{ij}}{aR_{ij}} \right] \quad \text{if} \quad i \neq j \quad \text{and} \quad R_{ij} < 2a,
\]

where $R_{ij} \equiv \sqrt{\mathbf{R}_{ij} \cdot \mathbf{R}_{ij}}$, and $\mathbf{R}_{ij} \equiv \mathbf{R}_j - \mathbf{R}_i$, where the vector $\mathbf{R}_i$ contains the 3 cartesian coordinates of the position vector of the $i^{th}$ bead. Parameter $a$ represents the bead hydrodynamic radius, $\zeta \equiv 6\pi \eta a$ is the bead friction coefficient, and $\mathbf{I}$ is the $3 \times 3$ identity matrix. For the RPY tensor, the term $\partial / \partial \mathbf{R} \cdot \mathbf{D}$ appearing in Equation 87 is zero.\(^5\) In the early work of Kirkwood and Riseman (1948), and later in the Zimm (Bird et al., 1987; Doi and Edwards, 1986) theory, fluctuations of the equilibrium hydrodynamic interaction tensor were ignored in the interest of constructing a tractable analytical theory; $\mathbf{D}$

---

\(^5\)In a previous paper (Jendrejack et al., 2000), we also used the RPY tensor, but omitted the divergence term without comment.
was taken to be its value with the structure fixed at equilibrium. A “free-draining” (FD) approximate model is obtained by neglecting hydrodynamic interactions \( D_{ij} = 0 \) for \( i \neq j \). A “consistently averaged” (Öttinger, 1996) (CAHI) model is obtained by replacing \( D \) by its instantaneous ensemble average, \( \langle D \rangle \), in Equations 87 and 88. In this work, we will compare the “exact” (HI) model with the FD model. Although not presented in this work, simulations using the CAHI model were in good agreement with the HI model.

The connectivity between adjacent beads is described by means of a worm-like spring (WLS) model. Marko and Siggia (1994, 1995) proposed a simple expression that matches the asymptotics of the exact worm-like chain model in both the small and large force limits, and fits the experimental DNA data of Bustamante et al. (1994). The result can be expressed as

\[
F_{ij}^s = \frac{k_B T}{2b_k} \left( 1 - \frac{R_{ij}}{R_o} \right)^{-2} - 1 + \frac{4R_{ij}}{R_o} \frac{R_{ij}}{R_{ij}},
\]

where \( b_k \) is the Kuhn length of the molecule. Letting \( N_k \) represent the number of Kuhn segments in the molecule and \( N_{k,s} \) the number of Kuhn segments per spring, \( R_o = N_{k,s} b_k \) is the maximum spring length, or the contour length of the portion of the molecule represented by one spring in our model. The contour length of the chain is then \( L = N_s R_o \).

This model has been used successfully in the literature. (Larson et al., 1997; Hur et al., 2000; Larson et al., 1999; Marko and Siggia, 1995; Ladoux and Doyle, 2000)

To complete the model, we now describe our treatment of the non-bonded interactions. From neutron scattering data (Strobl, 1997; Farnoux et al., 1978) for dilute solutions of linear polymer in a good solvent, one finds ideal chain behavior at small distances along the chain, and good solvent behavior at large distances. In this spirit, we consider the increase in energy due to the overlap of two sub-molecules (i.e. beads). Each sub-molecule is considered to be ideal with a (Gaussian) probability distribution with second
moment $S_{s}^{2} = N_{k,s}b_{k}^{2}/6$. Considering the energy penalty due to overlap of two Gaussian coils (Doi and Edwards, 1986), one arrives at the following expression for the excluded volume potential between two beads of the chain

$$U_{ij}^{\text{ev}} = \frac{1}{2}v k_B T \left( \frac{3}{4 \pi S_{s}^{2}} \right)^{3/2} \exp \left[ \frac{-3R_{ij}^2}{4S_{s}^{2}} \right],$$

where $v$ is the excluded volume parameter. Although this potential is not self-consistent (we have ignored any deformation of the coil caused by the overlap), Equation 95 does provide the correct parameter dependence in the scaling regime. That is, for a specified $v$ we obtain good solvent scaling for static properties by either fixing $N_{s}$ and varying $N_{k,s}$, or by fixing $N_{k,s}$ and varying $N_{s}$. We demonstrate this in Section 5.2.6. Strictly speaking, the number of Kuhn segments per bead ($N_{k,b}$), rather than $N_{k,s}$, should have been used in developing this excluded volume potential. However, $N_{k,s}/N_{k,b} \sim 1$ for most systems of interest.

Note that, as with most Brownian dynamics approaches to coarse-grained polymer dynamics, ours does not rigorously prevent chain-crossing. We make two comments regarding this point. First, Kumar and Larson (2001) have recently addressed the issue of chain-crossing with a model that, rather than imposing bead-bead repulsions, imposes “spring-spring” repulsions acting along the shortest line segment between nearby connector vectors. Nevertheless, with a soft potential, they find results essentially identical to those with bead-bead repulsions, while with a singular ($r^{-12}$) potential the time step required becomes prohibitive. Second, we also performed simulations in which a harder inner core was also imposed in the form of Equation 95 with $v_{\text{inner}} = 2v$ and $S_{s,\text{inner}}^{2} = S_{s}^{2}/2$, and no change in chain properties was observed.

The Gaussian form of the excluded volume potential has been discussed by Öttinger (1996) in the context of renormalization group theory. Although other excluded volume
potentials (hard-sphere, Lennard-Jones, soft exponential) have been used extensively in Brownian dynamics simulations, it is not obvious how the parameters in these models should vary with molecular discretization. This was the motivation for the development of Equation 95, which explicitly contains the dependence on $N_{k,s}$.

### 5.2.4 PROPERTIES

The measure of chain size most easily obtained from fluorescence microscopy experiments is the “stretch”. The stretch of molecule $m$, $X_m$, is defined as the distance between the upstream-most portion of the molecule and the downstream-most portion,

$$X_m = \max_i (R_{i,x})_m - \min_i (R_{i,x})_m,$$

and the ensemble average stretch is then simply

$$\langle X \rangle = \frac{1}{N_t} \sum_{m=1}^{N_t} X_m,$$

where $N_t$ is the number of molecules, or trajectories, in our ensemble. The end-to-end distance, $R$, the radius-of-gyration tensor, $S$, and the radius of gyration, $S$, are defined as usual:

$$R = \left\langle tr \left( [(R_{N_b}) - (R_1)][(R_{N_b}) - (R_1)]^{\frac{1}{2}} \right) \right\rangle,$$

$$S = \left\langle \frac{1}{N_b} \sum_{i=1}^{N_b} [(R_i) - (r_c)][(R_i) - (r_c)] \right\rangle,$$

$$S = tr(S)^{\frac{1}{2}}.$$
where \((r_c)\) is the center of mass of the molecule. The diffusivity tensor, \(D_{tr}\), and diffusivity, \(D\), are given by

\[
D_{tr} = \frac{1}{2\Delta t} \langle \Delta(r_c - v_c \Delta t) \Delta(r_c - v_c \Delta t) \rangle, \tag{101}
\]
\[
D = \frac{1}{3} tr(D_{tr}), \tag{102}
\]

where \(v_c\) refers to the velocity of the solvent at the center of mass of the molecule.

In this work, the relaxation time was obtained by the same method as in the experiments (Smith and Chu, 1998) from which we determined our model parameters. A stretched chain was allowed to relax to equilibrium. Near equilibrium (e.g. final 10% of decay), the longest relaxation time, \(\lambda\), was determined from a fit to

\[
\langle X^2 \rangle = A \exp \left( -\frac{t}{\lambda} \right) + B. \tag{103}
\]

Relaxation times determined from the decay of the equilibrium autocorrelation function for the end-to-end vector gave essentially identical results.

The microstructural contribution to the stress tensor, \(\tau^p\) is given by:

\[
\tau^p = n \sum_{i=1}^{N_b} \langle (R_i - r_c)F_i \rangle + nN_b k_B T I, \tag{104}
\]

with \(n\) being the number density of molecules (Bird et al., 1987). In this work, we are interested in two types of flows: planar extension and simple shear. In planar extension, \(\nabla v\) is given as

\[
(\nabla v)_p = \begin{pmatrix}
\dot{\epsilon} & 0 & 0 \\
0 & -\dot{\epsilon} & 0 \\
0 & 0 & 0
\end{pmatrix}, \tag{105}
\]
while, in simple shear, we have

\[
(\nabla \mathbf{v})_s = \begin{pmatrix}
0 & 0 & 0 \\
\dot{\gamma} & 0 & 0 \\
0 & 0 & 0
\end{pmatrix}.
\] (106)

Alternatively, one can represent the strength of the flow field through the Weissenberg number \( (We) \), which represents the ratio of the time scale of molecular relaxation to the that of solvent deformation. For planar extension and simple shear, we have \( We_p \equiv \dot{\epsilon} \tau \) and \( We_s \equiv \dot{\gamma} \tau \), respectively.

In the case of simple shear, the shear viscosity, \( \eta \), and the first normal stress coefficient, \( \Psi_1 \), are obtained from \( \tau^p \) and the shear rate \( \dot{\gamma} \) by

\[
\eta = -\frac{\tau_{xy}^p}{\dot{\gamma}},
\] (107)

\[
\Psi_1 = -\frac{\tau_{xx}^p - \tau_{yy}^p}{\dot{\gamma}^2}.
\] (108)

The longest relaxation time obtained from the Rouse theory (i.e. Hookean springs, free-draining, theta solvent) is

\[
\lambda_R = \frac{\zeta b_s^2 N_{k_s}}{24k_B T \sin^2 \left( \frac{\pi}{2N_b} \right)}. \] (109)

Throughout this work, we use the abbreviations HI and FD to refer to the non-free-draining and free-draining models, respectively.

### 5.2.5 SIMULATION

Equations 87 through 95 define our model for Brownian dynamics simulations of \( \lambda \)-phage DNA. The parameters appearing in the HI model are \( \{ L, N_s, b_k, a, v \} \). For YOYO-1 stained \( \lambda \)-phage DNA we have \( L = 21 \mu m \) (Smith and Chu, 1998). The parameter \( N_s \)
defines the level of discretization of the molecule, and we choose \( N_s = 10 \) for 21 \( \mu m \) \( \lambda \)-phage DNA. The remaining three parameters \((b_k, a, v)\) were chosen so that our model reproduces available experimental data. For YOYO-1 stained 21\( \mu m \) \( \lambda \)-phage DNA in a 43.3cP solvent at 23C, we have available experimental values (Smith and Chu, 1998) of the equilibrium stretch \((1.5 \mu m)\), and relaxation time \((4.1 s)\). We also have available diffusivity data for native DNA fragments \((< 1 \mu m)\) obtained from light-scattering data (Sorlie and Pecora, 1990) and diffusivity data for TOTO-1 stained fragmented and concatenated \( \lambda \)-phage DNA \((2-140 \mu m)\) in a 0.95cP solvent (Smith et al., 1996). The diffusivity data for the stained DNA can be scaled to correspond to native DNA in an solvent of arbitrary viscosity, \( \eta \), by the scaling \( D \sim \eta^{-1} \), and correcting for the change in persistence length due to dye intercalation. Smith et al. (1996) found that the diffusivity of TOTO-1 stained DNA needed to be scaled by \((1.75)^{2/5}\) to bring it into line with the with native DNA fragments of Sorlie and Pecora (1990). They also reported that this correction factor decreased to \((1.32)^{2/5}\) when YOYO-1 stain was used (Smith and Chu, 1998). Using the data of Smith et al. (1996), we can therefore estimate the diffusivity of YOYO-1 stained 21\( \mu m \) \( \lambda \)-phage DNA in a 43.3cP solvent at 23C to be 0.0115\( \mu m^2/s \).

The parameters \({b_k, a, v}\) were then determined so that the model reproduced experimental values of the equilibrium stretch \((1.5 \mu m)\), relaxation time \((\lambda = 4.1 s)\), and the estimated diffusivity \((0.0115 \mu m^2/s)\). This gave \({b_k = 0.106 \mu m, a = 0.077 \mu m, v = 0.0012 \mu m^3}\). This value of \(a\) corresponds to a bead diffusivity of \(k_B T/\zeta_{HI} = 0.065 \mu m^2/s\), and hydrodynamic interaction parameter (Bird et al., 1987), \(h^* = 0.16\). The relaxation time was determined in the same way as was done in the experiment (Smith and Chu, 1998); a fully stretched chain was allowed to relax to equilibrium, and the tail of the curve was fit to Equation 103. We note here that Smith et al. (1996) reasoned, using
the scaling \( D \sim b_k^{-2/5}L^{-3/5} \), that the Kuhn length of TOTO-1 stained DNA increased by a factor of 1.75 relative to the native DNA value of \( b_k = 0.106 \mu m \), while, for YOYO-1 stained DNA, the Kuhn length increased by a factor of 1.32. In our simulations, however, we found that that we needed \( b_k = 0.106 \mu m \) (the native DNA value, by coincidence) to reproduce both the experimental relaxation and diffusivity of YOYO-1 stained DNA.

For the FD model, we again used \( v = 0.0012 \), and \( b_k = 0.106 \mu m \), which left the simulation equilibrium stretch unchanged. The free-draining friction coefficient was chosen so that the FD model reproduced the experimental relaxation time \( (\lambda = 4.1s) \). This resulted in a bead diffusivity of \( k_B T/\zeta_{FD} = 0.084 \mu m^2/s \), indicating a 23% decrease in the bead friction coefficient relative to the HI model. This is consistent with previous findings (Hatfield and Quake, 1999).

A first order semi-implicit scheme described in an earlier paper (Jendrejack et al., 2000) was used to integrate Equation 87. A time step of \( 0.1 \min \{\zeta S^2_\zeta/k_B T, [(\nabla v) : (\nabla v)^T]^{-1/2}\} \) was used in all simulations. The quantity \( \zeta S^2_\zeta/k_B T \) represents the time scale for diffusion of the sub-molecule, while \( [(\nabla v) : (\nabla v)^T]^{-1/2} \) represents the flow time scale. The decomposition of the diffusion tensor (Equation 88) was performed using Fixman’s method (Fixman, 1986) as described in earlier work (Jendrejack et al., 2000). Here we simply note that Fixman’s method involves a fast polynomial approximation to the square root of the diffusion tensor, and we required \( \sim 5\% \) relative accuracy in the decomposition for all simulations. A method for accurately determining the error in the decomposition is discussed in detail in our earlier work (Jendrejack et al., 2000).

We performed both HI and FD simulations for chains of length 21 \( \mu m \) \((N_s = 10)\), 42 \( \mu m \) \((N_s = 20)\), 84 \( \mu m \) \((N_s = 40)\), and 126 \( \mu m \) \((N_s = 60)\) in extensional and shear flow. In all computations except those in Section 5.2.6, the level of molecular discretization
$N_{k,s} = 19.8$ was kept constant as the molecular weight was increased. In Section 5.2.6, both $N_k$ and $N_{k,s}$ are varied to determine the effect of molecular discretization on model predictions.

Most of our results are presented in terms of Weissenberg numbers. These Weissenberg numbers are based on the relaxation time, $\lambda$, of the model in question (HI or FD). Therefore, a comparison at equal Weissenberg numbers does not indicate equivalent strain rates at a given molecular weight, with the exception of the 21 $\mu$m chains. For longer chains, at a given Weissenberg number, the FD strain rate is always less than that of the HI case.

5.2.6 RESULTS AND DISCUSSION

COMPARISON TO EXPERIMENT: $\lambda$-PHAGE DNA

Figure 5 shows the mean steady-state fractional extension versus Weissenberg number from experiment (Smith et al., 1999) and our simulations. Results are shown for 21 $\mu$m DNA in both shear and planar extension. We find good agreement between our simulations and experiment. At this molecular weight, the HI and FD models give practically identical results for steady-state stretch. As molecular weight is increased, discrepancies appear between the two models. These discrepancies are discussed in Section 5.2.6.

Figure 6 shows the transient mean fractional stretch from experiment (Smith and Chu, 1998) and our simulations, plotted in real time. Results are shown for startup of planar extension at $We = 2$, and $We = 48$. In the experimental plot, the thin lines are individual molecular trajectories, while the symbols are the mean fractional extension at the indicated point in time. A few individual trajectories are also shown from the
Figure 5: Mean fractional stretch versus Weissenberg number. Our simulation results for the HI (dashed lines) and FD (dot-dashed lines) models superimposed on the experimental data of Smith et al. (1999). The solid lines were provided with the experimental data and serve to guide the eye only.
Figure 6: Mean stretch versus time. Comparison of our simulations with the experimental data of Smith and Chu (1998). The data points are ensemble averages, while the thin lines correspond to individual molecular trajectories (in the simulations, these are HI trajectories). All simulations were started from random equilibrium configurations.
simulations. As has been noted in the literature (Hur et al., 2000; Larson et al., 1999), the average stretch does not appear to be significantly affected by neglecting hydrodynamic interactions, provided the friction coefficient is fit to the experimental relaxation time.

In the $We = 48$ simulations (top right in Figure 6), transient plateaus appear in some molecular trajectories. As discussed by Smith and Chu (1998) and Larson et al. (1999), these plateaus occur when molecules form folded configurations during the unraveling process.

Figure 7 shows the equilibrium scalar diffusivity, $D$, as a function of molecular weight. Results are shown from the experiments of Smith et al. (1996), as well as our simulations. All data have been scaled to a solvent viscosity of $1cP$, and adjusted (as described in Section 5.2.5) for dye intercalation to give native DNA results. As expected, the molecular weight scaling of the HI model matches that of experiment, while the FD model does not. Also shown are the predicted scaling exponents from the Rouse ($D \sim L^{-1}$) and Zimm ($D \sim L^{-0.588}$) theories. Zimm scaling is observed in the experimental data for DNA starting at around $3 \mu m$. As seen in Figure 7, all of our HI simulation results follow Zimm scaling.

**PREDICTIONS FOR LONGER CHAINS**

In this section, we predict and examine various dynamic and static properties of DNA for a range of molecular weights. Having fit both the HI and FD models to the same experimental data for $21 \mu m$ DNA, we can quantify the error in these properties that arises when hydrodynamic interactions are ignored.

Figure 8 shows the mean steady-state fractional stretch for $126 \mu m$ DNA. Ignoring hydrodynamic interactions leads to a slightly lower stretch for planar extension, and a
Figure 7: Diffusivity as a function of molecular weight for the FD and HI models. Experimental data is from Smith et al. (1996). All data has been scaled to native DNA in 1cP solvent (see text). The solid and dashed lines are the theoretical scalings for the HI and FD models, respectively.
Figure 8: Mean steady-state fractional stretch versus Weissenberg number. Simulation results for 126 $\mu m$ DNA in planar extension and simple shear.
higher stretch in simple shear. This is expected: in simple shear, hydrodynamic interactions attenuate the relative motion of the beads, thereby damping the dynamic tumbling motion of the chain (which involves beads sliding past one another). The same trend was also found by Petera and Muthukumar (1999) for bead-rod chains. In extensional flow, this tumbling is absent. Recall that we determined the bead friction coefficient so that the simulation relaxation time matched that of the actual chain. The result was that the bead friction coefficient in the FD model was 23% less than that of the HI model. When the chain is stretched, hydrodynamic interactions are diminished as the beads become further separated, and the chain becomes “more free-draining”. Therefore, for planar extension the steady-state stretch is higher when we include hydrodynamic interactions ($\zeta_{HI} > \zeta_{FD}$).

Figure 9 shows the transient mean fractional stretch as a function of real time for 21 $\mu m$ and 126 $\mu m$ DNA, respectively, in planar extension. As molecular weight increases, the calculated approach to steady-state for the FD model becomes retarded due to its inability to correctly capture the relaxation time. In a FD model, the diffusivity tensor, $D_{tr}$, is isotropic and independent of molecular configuration. In reality, due to hydrodynamic interactions, $D_{tr}$ is anisotropic and dependent on the molecular configuration. Figure 10 illustrates the anisotropic diffusivity of 21 $\mu m$ and 126 $\mu m$ DNA molecules in planar extension and simple shear. Steady state values of the trace components of $D_{tr}^{HI}$ are shown as a function of Weissenberg number. Also shown are the “free-draining” diffusivities of the HI and FD models. For the HI model, this asymptotic limit is never reached; these finitely extensible chains cannot achieve the bead-bead separation necessary to approach $D_{tr}^{HI} = k_B T/N_b \zeta_{HI}$. The free-draining model, having always $D_{tr}^{FD} = k_B T/N_b \zeta_{FD}$, is, of course, unable to capture the highly anisotropic behavior.
Figure 9: Mean fractional stretch versus time. Simulation results for 21 µm and 126 µm DNA in planar extension.
Figure 10: Diagonal components of the diffusivity tensor for the HI model as a function of Weissenberg number. Simulation results for 21 µm DNA and 126 µm DNA. Both planar extension (open symbols) and simple shear (solid symbols) are shown. The dashed lines correspond to the “free-draining” diffusivities of the HI and FD models. All data have been scaled to correspond to native DNA in a 1cP solvent (as described in Section 5.2.5).
WEISSENBERG NUMBER SCALING OF SHEAR RHEOLOGY

To examine the dependence of \( \eta \) and \( \Psi_1 \) on Weissenberg number, we performed simulations of \( N_s = 40 \) over a wide range of Weissenberg numbers. Both the HI and FD models were investigated. The results are shown in Figure 11, along with the transverse component of the gyration tensor, \( S_{yy} \). In these runs, the Weissenberg numbers are based on the longest Rouse relaxation time, as we are here only concerned with scaling laws. The parameters used in the simulations presented in this section (and in Section 5.2.6) were \( b_k = 0.14 \, \mu m, v = 0.0027 \, \mu m^3 \), and \( a = 0.138 \, \mu m \).

The results in Figure 11.A suggest the existence of two distinct scaling regimes in the shear rheology of chains in flow. In this section, we analyze these results in the light of relatively simple scaling arguments (Doyle et al., 1997; Grassia and Hinch, 1996). A steady-state balance between entropic and hydrodynamic forces leads to an expression for the \( x \)-component of the tensile force in a molecule in shear flow:

\[
F_x \sim \zeta \dot{\gamma} \delta_y,
\]

where \( \delta_y \) represents the length scale of chain fluctuations transverse to the flow direction. Examination of the polymer contribution to the stress tensor at high Weissenberg number, assuming that the characteristic chain length in the flow direction is roughly constant (at some fraction of the contour length), gives

\[
\eta \sim \delta_y^2
\]

\[
\Psi_1 \sim \delta_y / \dot{\gamma}.
\]

Taking \( \delta_y \) to be proportional to the transverse distance a chain end diffuses during one flip of the chain, a balance of streamwise convective transport \( \dot{\gamma} \delta_y \) and transverse diffusive
Figure 11: A) The shear viscosity (open symbols) and first normal stress coefficient (solid symbols) versus Weissenberg number for various models of 84 µm DNA. B) The $S_{yy}$-component of the gyration tensor versus Weissenberg number for the various models. In both A and B, the Weissenberg numbers are based on the Rouse relaxation time, and properties are reduced by their $We = 10$ values. Local scaling exponents are shown for two regions of the curves.
transport $D / \delta_y^2$, with $D$ being the (constant) bead diffusivity, leads to

$$\delta_y \sim \dot{\gamma}^{-\frac{\alpha}{2}}.$$  \hfill (113)

This is essentially the classical Graetz-Leveque result for the thickness of a concentration boundary layer in shear flow (Deen, 1998; Doyle et al., 1997). Using the result in the expressions for the viscometric properties gives that $\eta \sim We^{-2/3}$, $\Psi_1 \sim We^{-4/3}$, in good agreement with the results in Figure 11.A for $We \gtrsim 10^4$. In this regime, the computed value of $S_{yy}$ is also in agreement with this simple argument: $S_{yy} \sim \delta_y^2 \sim We^{-2/3}$. These results are also recovered for a wide variety of simple dumbbell or chain based constitutive equations (e.g. the FENE-P and FENE-PM), essentially because of the generic nature of the Graetz-Leveque argument made above (Wedgewood et al., 1991).

At intermediate shear rates, $10^2 \lesssim We \lesssim 10^3$, the simulations do not follow the above simple scaling, but rather give exponents close to $-1/2$ and $-5/4$. Similar scalings were observed by Doyle et al. (1997) for simulations of bead-rod chains. They argued that these “non-classical” exponents could be explained by arguments based on anomalous diffusion. In chain relaxation simulations, they found that $\delta_y^2 \sim t^\alpha$, with $\alpha \approx 3/4$. This subdiffusive response is related to the connectivity constraint (Grassia and Hinch, 1996), and translates into a diffusivity that depends on position as $D \sim \delta_y^{-2/3}$. Substituting this relation into the flux balance above gives that $\delta_y \sim \dot{\gamma}^{-3/11}$, yielding $S_{yy} \sim We^{-6/11}$, $\eta \sim We^{-6/11}$ and $\Psi_1 \sim We^{-14/11}$. The corresponding slopes are shown on Figure 11 and are seen to be in good agreement with the simulation results. At very high shear rates, Doyle et. al observed a leveling off of $\eta$, when $\delta_y$ approaches the (fixed) bond length. As described above, we see no such leveling off, but rather a reversion to a classical result. This can be explained by the fact that, in contrast to the bead-rod chains, here there is no bond length constraint to fix a small length scale.
PARAMETER DEPENDENCE

In Section 5.2.3, we stated that the excluded volume potential given by Equation 95 should give the correct parameter dependence in the scaling regime. To illustrate this point, we performed equilibrium simulations for a range of molecular weights \( N_k \) and molecular discretizations \( N_{k,s} \). In the simulations presented in this section, we used \( b_k = 0.14 \, \mu m \), and \( v = b_k^3 = 0.0027 \, \mu m^3 \). We also let each submolecule (spring) obey Zimm scaling, \( a = C \alpha b_k (N_{k,s}/6)^{\alpha'}/k_B T \), giving \( \zeta = 6\pi \eta a = \zeta' N_{k,s}^{1/2} \). The constant of proportionality was taken to be \( C \alpha = 0.64 \).

Figure 12.A shows the molecular weight dependence of \( S \) for different \( N_s \). Our simple excluded volume potential clearly contains the correct dependence on \( N_{k,s} \). Once \( v \) is specified, \( N_s \) can be changed at constant \( N_k \), and no significant change in \( S \) is observed. Molecular weight can be increased by increasing \( N_k \) at constant \( N_{k,s} \) or \( N_s \), and the correct scaling is observed. Also shown in Figure 12.A is the theoretical good-solvent scaling.

Figure 12.B shows the molecular weight dependence of \( D\zeta'/k_B T \) for different \( N_s \). We find that at fixed \( N_s \) we can increase molecular weight and obtain the correct theoretical scaling. We already demonstrated in Figure 7 that we can obtain the correct scaling by fixing \( N_{k,s} \) and increasing molecular weight. Also, increasing \( N_s \) at constant molecular weight does not significantly affect the diffusivity.

To summarize, if we assume ideal, non-draining behavior at the spring (submolecule) level, the HI model presented in this work provides the correct dependence on molecular discretization (for equilibrium properties). That is, once \( \{b_k, \alpha', v\} \) have been determined, molecular weight can be changed by varying \( N_{k,s} \) or \( N_s \), with static properties
Figure 12: Molecular weight dependence of A) the radius of gyration and B) the diffusivity for the HI model at various levels of molecular discretization ($N_s$). The solid lines correspond to the theoretical scalings, $S \propto N_k^{0.588}$ and $D \propto N_k^{-0.588}$. 
and diffusivity scaling correctly with molecular weight. Also, $N_s$ can be changed at constant molecular weight (and constant $\{v, k_B T / \zeta', a'\}$) with very little change in static properties or diffusivity.

5.2.7 CONCLUSIONS

We have presented a fully parameterized non-draining (HI) bead-spring model for DNA with parameters determined from experimental data for 21 µm DNA, and demonstrated that the model predictions are in quantitative agreement with available experimental data. In addition, we examined a free-draining (FD) model in which hydrodynamic interactions are ignored. In order to obtain equivalent relaxation times at the experimental molecular weight, the FD bead friction coefficient needed to be 23% lower than that of the HI model. Both models adequately predict the configurational properties of 21 µm DNA in simple shear and planar extension. At higher molecular weights, however, the approach to steady state for the FD model lags behind that of the HI model. This lag increases considerably with increasing molecular weight, and is mainly due to the inability of the free-draining relaxation time to scale properly with molecular weight. By comparison to experimental data, we have shown that the HI model correctly predicts the diffusivity of longer DNA, while the FD model does not.

The high Weissenberg number scaling behavior of $\eta$ and $\Psi_1$ is independent of solvent quality and hydrodynamic interactions. For $We \gtrsim 10^4$, $\eta$ and $\Psi_1$ scale as $We^{-2/3}$ and $We^{-4/3}$, respectively, consistent with classical arguments balancing convection and diffusion of chain ends. For $10^2 \lesssim We \lesssim 10^3$, these properties scale as $We^{-6/11}$ and $We^{-14/11}$, consistent with anomalously slow diffusion due to the connectivity constraint.

For the HI model, all molecular weight scalings are in good agreement with expected
values. Using consistently averaged hydrodynamic interactions gives static and dynamic results in quantitative agreement with fluctuating hydrodynamics. The excluded volume potential presented in this work provides the correct dependence on molecular discretization (Kuhn segments per spring): *i.e.* at fixed molecular weight, a change in molecular discretization does not significantly affect static properties, and good solvent scaling is obtained by either varying the number of springs at constant molecular discretization, or by varying the molecular discretization at constant number of beads.
In this chapter, we consider the solution of complex fluid flow problems over a macroscopic domain. In these cases, diffusion of the center-of-mass of the polymer is ignored, and the solvent velocity is linearized about the center-of-mass of the polymer. This linearization implies that the velocity field is homogeneous on the length scale of the molecule, and inhomogeneous on the length scale of the confining geometry (the velocity gradient is a function of time and position in physical space). This is generally a valid assumption for cases in which the length scale of the process is much larger than the length scale of the polymer. With these assumptions, Equation 5 becomes

\[
\frac{\partial \Psi}{\partial t} = -\nabla_x \cdot (\mathbf{v} \Psi) - \nabla_q \cdot \left( \left[ \mathbf{K} \cdot \mathbf{q} + \frac{1}{k_B T} \mathbf{W} \cdot \mathbf{f} - \tilde{\mathbf{D}} \cdot \nabla_q \right] \Psi \right) = -\nabla_x \cdot \mathbf{j}_x - \nabla_q \cdot \mathbf{j}_q,
\]  

(114)
\[ \tilde{D} \equiv W \cdot D \cdot W^T. \] (115)

In the following section, we briefly review a few common methods of solving Equation 114 over macroscopic domains. We also present a new method developed by us (Jendrejack et al., 2002b) which resolves the diffusion equation in a dual basis (stochastic and orthogonal polynomial).

6.1 A METHOD FOR MULTISCALE SIMULATION OF FLOWING COMPLEX FLUIDS\(^1\)

6.1.1 ABSTRACT

The Brownian Configuration Fields (BCF) method provides an attractive approach to simultaneous solution of flow and microstructure problems in complex fluids. At the continuum level, it is implemented in an Eulerian reference frame (i.e. on a stationary computational mesh), which makes it amenable to standard computational approaches for convection problems, and at the microstructural level it simply involves adding a convective term to the evolution of individual Brownian dynamics trajectories. We present here a variation on BCF that may hold advantages over the original formulation. It uses a hybrid representation of the configurational distribution function (CDF), splitting a time step into two parts: (1) a standard Brownian dynamics step (here the CDF is implicitly represented as a superposition of delta-functions) and (2) a convective step, where the distribution is projected onto an orthogonal polynomial basis and convection problems are

\(^1\) Jendrejack et al. (2002b)
solved for the generalized Fourier coefficients, then “lifted” back to the delta-function basis. This approach, which we call OSCM (operator-splitting coefficient-matching) allows the solution of fewer convection problems per time step than BCF and guarantees spatial smoothness of the convected properties – in some sense it is a filtered version of BCF. We present comparisons of accuracy and computational efficiency of BCF and OSCM for a simple model problem involving bead-spring dumbbells and chains. The efficiency of the two methods is comparable, and in situations where the finite extensibility becomes important, BCF can lose accuracy, due to a loss of correlation between trajectories at different point in the flow domain, where OSCM does not.

6.1.2 INTRODUCTION

In this work we are concerned with the solution of complex fluid flow problems over a macroscopic domain, where the underlying microstructure is represented through kinetic theory (Bird et al., 1987; Doi and Edwards, 1986). In the kinetic theory of macromolecules, the solvent is treated as a viscous continuum which acts on the microstructure through thermal fluctuations and viscous drag. At the heart of kinetic theory is the diffusion equation which governs the evolution of the configurational probability distribution function of the microstructure (Bird et al., 1987; Doi and Edwards, 1986; Öttinger, 1996). In general, there is no exact analytical solution for the probability distribution function. A great deal of numerical work has been done for spatially homogeneous flows. In these cases, the diffusion equation is most often replaced by an equivalent stochastic differential equation and solved via Brownian dynamics – in this approach the distribution function is implicitly represented as a sum of $\delta$-functions centered at the instantaneous positions of the various trajectories. In the language of numerical analysis, Brownian dynamics is
a “particle method”. Chaubal et al. (1997) recently provided a brief critique of methods of density estimation in the context of particle methods, as well as an application of a smoothed particle method to the dynamics of liquid crystals.

Methods designed to treat macroscopically inhomogeneous flows are termed “micro-macro” techniques. There are three commonly used micro-macro simulation techniques. In the first two, CONNFFESSIT (Laso and Öttnger, 1993) (Calculation of Non-Newtonian Flow: Finite Element and Stochastic Simulation Technique) and LPM, (Lagrangian Particle Method) (Halin et al., 1998; Gallez et al., 1999; Wapperom et al., 2000), one solves stochastic realizations of the probability distribution in a Lagrangian frame; that is, particles (CONNFFESSIT) or ensembles of particles (LPM) move with fluid elements. Use of the Lagrangian frame results in an “easy” stochastic simulation, in that each particle (or ensemble) is decoupled from the rest of the system. However, the continuum momentum and continuity equations are usually most easily solved in an Eulerian reference frame, in which case the microstructural information (e. g. the polymer contribution to the stress tensor) must be transmitted to a stationary mesh, leading to a slight artificial stress diffusion. In general, Lagrangian formulations may lead to areas of high or low concentrations of particles (or packets), so additional techniques have been developed to “redistribute” the microstructure over the physical domain (Gallez et al., 1999). Both CONNFFESSIT and LPM have been used successfully in micro-macro simulations of a variety of viscoelastic flows (Wapperom et al., 2000; Cormenzana et al., 2001; Hua and Schieber, 1998; Bell et al., 1997).

In the third method, Brownian Configuration Fields (BCF) (Hulsen et al., 1997; van Heel et al., 1999; Somasi and Khomami, 2000; Fan et al., 2000; Somasi and Komami, 2001), stochastic realizations of the probability distribution function are treated as fields
in physical space, and the system is then evolved in an Eulerian frame. There are no grid deformation or interpolation issues in this Eulerian method – it is a general and powerful approach. One specific advantage of the approach is its suitability for linear stability analysis of steady flows with a stochastic microstructural model (Somasi and Khomami, 2000; Somasi and Komami, 2001). However, one must now solve a convection problem (over all physical space) for every degree of freedom of every stochastic realization. Also, individual trajectories in a stochastic simulation contain a large amount of noise, and the BCF method (in general) convects both noise and signal. As we will show, for strong flows the BCF method can suffer from a degradation of smoothness of the configuration fields in physical space, i.e. a loss of correlation between the stochastic trajectories at neighboring spatial points, unless a fine mesh is used.

In this work, we present a new Eulerian frame multiscale method, which does not require spatial correlation of individual trajectories. It involves a splitting of the diffusion equation into internal configuration and convective fluxes. The internal configuration of the microstructure is evolved via stochastic simulation to give a \( \delta \)-function representation of the distribution function. The convective update of the distribution function is performed in an orthogonal polynomial representation, taking advantage of the natural hierarchy of length scales present in the problem. The method is called the Operator-Splitting, Coefficient-Matching (OSCM) method. After describing the approach, we present comparisons of OSCM and BCF for a simple model problem and assess the relative advantages and disadvantages of the two approaches.
6.1.3 POLYMER MODEL

In this paper, we consider a dilute, homogeneous solution of monodisperse linear polymer immersed in an incompressible Newtonian solvent. The polymer is modeled as a sequence of $N_b$ beads connected by $N_s = N_b - 1$ springs. The contour length of the molecule is given by $L = b_kN_k$, where $b_k$ is the Kuhn length and $N_k$ denotes the number of Kuhn segments in the molecule. Each spring represents a section of the overall molecule (a sub-molecule) with contour length $q_o = b_kN_{k,s}$, where $N_{k,s} = N_k/N_s$ is the number of Kuhn segments per sub-molecule. The $3N_b$ Cartesian coordinates of the beads in configurational space are represented by the vector $\mathbf{r} = \{r_1, r_2, \ldots, r_{N_b}\}$, with the vector $\mathbf{r}_i$ denoting the position of the $i^{th}$ bead. Position within the flow domain is denoted by $\mathbf{x}$.

The connectivity between adjacent beads of a molecule is described by means of a worm-like spring (WLS) model. The asymptotics of this model were developed by Marko and Siggia (1994, 1995) and match the underlying worm-like chain in both the small and large force limits. The final functional form of the WLS force was obtained by fitting the intermediate region to the experimental DNA data of Bustamante et al. (1994). The result can be expressed as

$$f_{ij}^s = \frac{k_BT}{2b_k} \left[ \left( 1 - \frac{r_{ij}}{q_o} \right)^{-2} - 1 + \frac{4r_{ij}}{q_o} \right] \frac{r_{ij}}{r_{ij}} \left( \delta_{i,j-1} - \delta_{i,j+1} \right), \quad (116)$$

where $f_{ij}^s$ represents the force on bead $i$ due to bead $j$, $r_{ij} \equiv \sqrt{\mathbf{r}_{ij} \cdot \mathbf{r}_{ij}}$, and $\mathbf{r}_{ij} \equiv \mathbf{r}_j - \mathbf{r}_i$.

This model has been used in the simulation of the rheological properties of DNA. (Larson et al., 1997; Hur et al., 2000; Larson et al., 1999; Marko and Siggia, 1995; Ladoux and Doyle, 2000; Jendrejack et al., 2002a)

The excluded volume potential is obtained by considering the energy penalty due to
overlap of two Gaussian coils of \( N_{k,s} \) Kuhn segments (Jendrejack et al., 2002a). The result is given by

\[
U_{ij}^{ev} = \frac{1}{2} v k_B T N_{k,s}^2 \left( \frac{3}{4 \pi S_s^2} \right)^{3/2} \exp \left[ \frac{-3r_{ij}^2}{4S_s^2} \right], \tag{117}
\]

and

\[
f_{ij}^{ev} = -\frac{\partial U_{ij}^{ev}}{\partial r_{ij}}, \tag{118}
\]

where \( S_s^2 = \frac{b_{k,s}^2 N_{k,s}}{6} \), and \( v \) is the excluded volume parameter (Doi and Edwards, 1986).

The solvent acts on the microstructure through convection of the center-of-mass, and through the \( 3N_b \times 3N_b \) deformation tensor \( K(t,x) \), which is block diagonal with elements \((\nabla_x v)^T; \nabla_x \equiv \partial/\partial x\). Motion of the polymer molecule gives rise to perturbations in the macroscopic velocity field. These hydrodynamic interactions (HI) enter the dynamics through the off-diagonal elements of the positive-definite \( 3N_b \times 3N_b \) diffusion tensor, \( D(r) \), which we take to be the Rotne-Prager-Yamakawa tensor (Rotne and Prager, 1969; Jendrejack et al., 2000). We will also consider the free-draining (FD) case in which the off-diagonal components of \( D \) are set to zero.

Rather than using \( r \), one may represent the microstructure by the 3 coordinates of the center-of-mass, \( r_c \), and the \( 3N_s \) coordinates of the connector vectors, \( q = \{ q_1, q_2, \ldots, q_{N_b} \} \), with \( q_i \equiv r_{i+1} - r_i \). This coordinate transformation can be expressed as

\[
\begin{pmatrix}
q \\
r_c
\end{pmatrix} = \begin{pmatrix}
W \\
C
\end{pmatrix} \cdot \begin{pmatrix} r \end{pmatrix}, \tag{119}
\]

where the \( 3N_s \times 3N_b \) matrix \( W \) (the Kramers matrix), and the \( 3 \times 3N_b \) matrix \( C \) are defined as

\[
W_{ij} = -I \delta_{ij} + I \delta_{i,j-1} \tag{120}
\]
and

\[ C_{1j} = \frac{1}{N_b} I, \quad (121) \]

respectively, and \( I \) is the \( 3 \times 3 \) identity matrix.

For the system under consideration, the microstructural configurational probability distribution function, \( \Psi(t, x, q) \), is a function of time, position in physical space, and the internal configuration of the molecule. In an Eulerian frame, \( \Psi \) is described by the equation

\[
\frac{\partial \Psi}{\partial t} = -\nabla_x \cdot (\nu \Psi) - \nabla_q \cdot \left( \left[ K \cdot q + \frac{1}{k_B T} W \cdot D \cdot f - \tilde{D} \cdot \nabla_q \right] \Psi \right)
\]

\[ = -\nabla_x \cdot j_x - \nabla_q \cdot j_q, \quad (122) \]

where

\[ \tilde{D} \equiv W \cdot D \cdot W^T, \quad (123) \]

and diffusion of the center of mass of the molecule has been neglected (Bird et al., 1987; Doi and Edwards, 1986). Parameter \( k_B \) is Boltzmann’s constant, \( T \) is the absolute temperature, and \( \nabla_q \equiv \partial / \partial q \) is the gradient with respect to internal configuration. The vector \( f(r) = \{ f_1, f_2, \ldots, f_{N_b} \} \) contains the \( 3N_b \) components of the intramolecular spring and excluded volume forces.

The microscopic contribution to the stress in the fluid, \( \tau_p(t, x) \), can be expressed as functionals of \( \Psi \), summed over all bead contributions,

\[
\tau_p = n \sum_{i=1}^{N_b} \int (r_i - r_c) f_i \Psi d\mathbf{r} + n N_s k_B T \; I, \quad (124)
\]

where \( n \) is the number density of molecules. Simultaneous solution of Equations 122 and 124, along with the equations for conservation of fluid mass and momentum, yields the complete evolution of the macroscopic flow field and microstructural configuration.
In Section 6.1.6, we will compare the BCF and OSCM methods to an exact solution for dumbbells, 5-spring chains, and a 10-spring model of 21\(\mu\)m \(\lambda\)-phage DNA. The properties of interest will be the average spring length,

\[
\langle q^2 \rangle^{\frac{1}{2}} = \left( \frac{1}{N_s} \sum_{i=1}^{N_s} q_i \cdot q_i \right)^{\frac{1}{2}},
\]

(125)

and the radius-of-gyration of the chain,

\[
\langle S^2 \rangle^{\frac{1}{2}} = \left( \frac{1}{N_b} \sum_{i=1}^{N_b} (r_i - r_c) \cdot (r_i - r_c) \right)^{\frac{1}{2}}.
\]

(126)

With the exception of the DNA results, the longest relaxation time of the chain was taken to be \(\lambda = \lambda_R\), where

\[
\lambda_R = \zeta \frac{b^2_N k_{s, k} N_b^2}{24 k_B T \sin^2 (\pi/2N_b)}
\]

(127)

is the longest Rouse relaxation time of the chain in question, and \(\zeta\) the bead friction coefficient. For the DNA results, the longest relaxation time was obtained by direct comparison of the HI model with experimental data. The parameters for the DNA model are discussed in Section 6.1.6.

### 6.1.4 THE OSCM METHOD

As indicated at the beginning of Section 6.1, we wish to develop a “smooth” variant of the BCF method. This approach will involve a dual representation of \(\Psi\) (\(\delta\)-function and modal), and it is worth discussing these representations in a simple context.

Consider \(\Psi(q)\), where \(q\) is a scalar which has been scaled to lie on \([-1, 1]\). In a stochastic representation, \(\Psi\) is given as the sum of \(\delta\)-functions centered on the individual trajectories, \(q\):

\[
\Psi(q) = \frac{1}{N_t} \sum_{t=1}^{N_t} \delta (q - q_t)
\]

(128)
where $N_t$ is the number of stochastic realizations used (the level of the approximation). Alternatively, we can represent $\Psi$ in an orthogonal polynomial basis, such as a Legendre series (Pozrikidis, 1997)

$$\Psi(q) = \sum_{i=0}^{p} A_i L_i(q), \quad (129)$$

where $p$ represents the order of the series, and $L_i(q)$ is a Legendre polynomial of order $i$ (Pozrikidis, 1997). Each generalized Fourier coefficient, $A_i$, is simply the ensemble average of its respective polynomial.

$$A_i = \int \Psi L_i \, dq. \quad (130)$$

Now, suppose that we have a $\delta$-function representation of $\Psi$, and we wish to obtain a Legendre polynomial representation. All that is needed are the coefficients, $A_i$, which are obtained by inserting Equation 128 into Equation 130 to give

$$A_i = \frac{1}{N_t} \sum_{t=1}^{N_t} L_i(q_t). \quad (131)$$

The coefficients are still just the ensemble averages of their respective polynomials, now with the averages taken in the $\delta$-function representation. Figure 13 illustrates the process of moving from a $\delta$-function representation of $\Psi$ to a Legendre polynomial representation.

Now suppose we slightly perturb $\Psi$ to obtain $\Psi + \Psi'$ in the Legendre polynomial representation, and wish to transform or “lift” back to the $\delta$-function representation, $q + q'$. This is easily done by performing a Taylor expansion of Equation 129 about the realizations $q$ and equating coefficients to give

$$A_i' = \frac{1}{N_t} \sum_{t=1}^{N_t} \left( \frac{\partial L_i(q_t)}{\partial q_t} \right)_{q_t} \cdot q'_t + O(\|\Psi'\|^2). \quad (132)$$
Figure 13: Three representations of a Gaussian distribution (cut off at \( \|x\| = 1 \), where the function is exponentially small). The top figure shows the Gaussian distribution, the middle shows the distribution in a \( \delta \)-function representation using 500 trajectories, and the bottom figure shows a 20\(^{th}\) order Legendre series representation. The coefficients of the Legendre series were determined from the \( \delta \)-function representation of the Gaussian distribution. For visual clarity, the \( \delta \)-functions in the middle figure have been plotted as narrow Gaussians.
Equation 132 should be satisfied for all $A_i$. For an order $p$ Legendre polynomial expansion, this results in a set of $p$ equations in $N_t$ unknowns. We consider only the case $p \ll N_t$, so Equation 132 is underdetermined and has infinitely many solutions. A reasonable way around this nonuniqueness is to seek the minimum-norm solution, i.e. $||q'||_2$ is minimized such that Equation 132 is satisfied. We make no claim that this is the “best” approach in the current context.

Having illustrated how to move back and forth between the dual representations of $\Psi$, we return now to the multidimensional problem. From Equation 122 we see that the evolution of $\Psi$ naturally decomposes into two parts – a term involving the flux in physical space ($j_x$), and a term involving the flux in internal configuration space ($j_q$). This natural decomposition motivates our proposed method. Before discussing the method in detail, we first present a general outline for a single time step of the simulation. Beginning with the distribution function at step $n$, $\Psi^n$, we

1. Perform a regular Brownian dynamics step, ignoring convection in physical space.
   This gives a $\delta$-function representation of $\Psi^*$, the intermediate distribution function.

2. Switch – “restrict” – from a $\delta$-function representation of $\Psi^*$, to a Legendre polynomial representation with $N_p$ terms – hopefully $N_p \ll 3N_bN_t$ is sufficient to capture the smooth part of $\Psi$. The truncation of Legendre series is discussed below.

3. Solve $N_p$ convection problems to obtain the Legendre polynomial representation of $\Psi^{n+1}$.

4. Switch – “lift” – from a Legendre polynomial representation of $\Psi^{n+1}$ to a $\delta$-function representation, as described above, at each nodal point in the flow domain.
Note that all operations except Step 3 are decoupled in physical space.

As noted above, the Legendre polynomial representation is a representation in terms of ensemble averages. One might call this a “coarse” or macroscopic representation, while the δ-function representation is a “fine” or microscopic one. Independently, but in a spirit similar to that of the present work, Kevrekidis and coworkers have used coarse and fine representations and restriction and lifting operators to demonstrate that complete bifurcation diagrams, including unstable states, can be computed from particle-level simulations (Theodoropoulos et al., 2000).

We now pause briefly to compare and contrast the stochastic and Legendre polynomial representations of the distribution function over the internal configuration space of the molecule. The degree of an orthogonal polynomial expansion determines the smallest length scale in configuration space which can be captured. The δ-function representation, on the other hand, is very rough. Moving from a δ-function basis to a Legendre polynomial basis can be thought of as a filtering process, in that fluctuations on length scales shorter than the spacing between the collocation points of the basis polynomials are smoothed out. In the dynamics of \( \Psi \), sufficiently short length scales will be rapidly damped by diffusion in configuration space.

When the polymer molecule is represented as a chain, additional length scales, corresponding to variations along the chain backbone, are incorporated into the problem. The Rouse modes provide a natural hierarchy of these length scales (Bird et al., 1987). The \( m^{th} \) Rouse mode, \( \mathbf{q}_m' (\mathbf{q}) \), is defined as

\[
\mathbf{q}_m' = \left( \frac{2}{N_b} \right)^{1/2} \sum_{i=1}^{N_v} \sin \left( \frac{mi\pi}{N_b} \right) \mathbf{q}_i.
\]  

For the special case of the Rouse model (Bird et al., 1987), internal motion of the molecule decouples in terms of the Rouse modes, with the \( m = 1 \) contribution corresponding
to the longest length scale (slowest motion). In general, motion of the microstructure does not decouple in terms of the Rouse modes. Nevertheless, the longer Rouse modes (lower \(m\)) still correspond to slower motion of the molecule, and thus the Rouse modes do provide a hierarchy of length scales in the problem. A complete polynomial representation of the distribution function for the \(3N_s\) internal coordinates of a chain would have the form:

\[
\Psi(t, x, q) = \sum_{i_1=0}^{\infty} \sum_{j_1=0}^{\infty} \sum_{k_1=0}^{\infty} \ldots \sum_{i_{N_s}=0}^{\infty} \sum_{j_{N_s}=0}^{\infty} \sum_{k_{N_s}=0}^{\infty} A_{i_1,j_1,k_1\ldots,i_{N_s},j_{N_s},k_{N_s},}(t, x) \\
\times \prod_{m=1}^{N_s} L_{i_m}(q'_{m,x}) L_{j_m}(q'_{m,y}) L_{k_m}(q'_{m,z}),
\]

(134)

where \(q'_{m,x}, q'_{m,y},\) and \(q'_{m,z}\) are the 3 Cartesian components of \(q'_m\), and the coefficients are defined as in Equation 130. The size and complexity of this expansion is the reason that Galerkin methods are not used to solve the diffusion equation for chain models. The polynomial expansions of the contracted distribution functions for each Rouse mode, however, are tractable, since each of these functions is only 3-dimensional in configuration space and can therefore be approximated as:

\[
\Psi_m(t, x, q'_m) \approx \sum_{i+j+k=0}^{i+j+k=p} A_{m,ijk}(t, x) L_{ijk}(q'_m),
\]

(135)

with

\[
L_{ijk}(q'_m) = L_i(q'_{m,x}) L_j(q'_{m,y}) L_k(q'_{m,z}),
\]

(136)

and the approximation becoming exact as the polynomial order \(p \to \infty\). In the present work, we assume that these contain sufficient information about the microstructure that properly accounting for their convection captures the essential features of the overall distribution function; we will solve convection equations for the \(A_{m,ijk}\). In other words, our
use of the contracted distribution functions corresponds to a Galerkin method for the convective step with a very specific, and arguably severe, truncation of the series, Equation 134. Further details of the truncation are given below. Despite the apparent severity of the truncation, it yields reasonably good results, as shown below. The successful use of these contracted distributions implies that coupling of the Rouse modes is not important when considering the convective flux of $\Psi$. Using these contracted distribution functions in the convective portion of the algorithm will allow us to take advantage of the natural hierarchy of length scales in the polymer. That is, we can require higher accuracy (more terms in the series) for the longer wavelengths, and lower accuracy for shorter wavelengths. Note that the Legendre polynomials require that each component of the Rouse modes be scaled to lie on $[-1, 1]$. This was achieved by scaling each component of the $m^{th}$ Rouse mode by

$$\xi_m = \left( \frac{2}{N_b} \right)^{\frac{1}{2}} \sum_{i=1}^{N_s} \left\| \sin \left( \frac{m_i \pi}{N_b} \right) \right\|. \quad (137)$$

Integrating Equation 122 over $[t, t+\Delta t]$, and splitting the update into pieces involving the flux in physical space and the flux in internal configuration space yields,

$$\begin{align*}
(\Psi^* - \Psi^n) &= -\int_t^{t+\Delta t} \nabla q \cdot j_q \, dt', \\
(\Psi^{n+1} - \Psi^*) &= -\int_t^{t+\Delta t} \nabla x \cdot j_x \, dt' = -\int_t^{t+\Delta t} v \cdot \nabla x \Psi \, dt'. \quad (139)
\end{align*}$$

where incompressibility of the solvent has been used to obtain the last term in Equation 139. Choosing to solve Equation 138 in its stochastic form (Öttinger, 1996), we obtain the stochastic representation, $q^*(t, x)$, of the intermediate distribution function, $\Psi^*$,

$$q^* - q^n = \int_t^{t+\Delta t} \left[ K\cdot q + \frac{1}{k_BT} W\cdot \nabla \cdot f + \nabla q \cdot D \right] \, dt' + \sqrt{2} \int_{w(t)}^{w(t+\Delta t)} B \cdot dw', \quad (140)$$
\[ \mathbf{D} = \mathbf{B} \cdot \mathbf{B}^T, \]  

where each component of \( w(t) \) is a Wiener process (Öttinger, 1996), with mean zero and variance \( t \). A set of \( N_t \) such realizations will provide a \( \delta \)-function representation of \( \Psi^* \), with weak accuracy \( O(N_t^{-1/2}) \). In the OSCM method the Wiener process could also have been chosen to be uncorrelated in space, but this is more computationally expensive and makes no difference to the results. In the BCF method, the Wiener process must be the same at each point or spatial smoothness of the configuration fields, which is necessary for the convective term to be well-defined, cannot be maintained.

Substituting Equation 135 into Equation 139, and equating coefficients, leads to a convection equation for each of the Legendre coefficients of the \( m^{th} \) Rouse mode

\[ (A_{m,ijk}^{n+1} - A_{m,ijk}^*) = - \int_t^{t+\Delta t} \mathbf{v} \cdot \nabla A_{m,ijk} dt'. \]  

(142)

The intermediate values of the coefficients, \( A_{m,ijk}^* \), are obtained as ensemble averages of their respective polynomials with respect to the stochastic representation of the intermediate distribution function, \( \Psi^* \) (see Equation 131).

Having obtained the polynomial representations of the \( \Psi_m^{n+1} \), we need to update the \( \delta \)-function representation of the microstructure (to begin a new time step). We obtain this update by performing a linear expansion of Equation 131 about the intermediate state at each node in the flow domain. Letting \( \theta \) be a vector containing all \( N_t \) of the stochastic realizations of \( q \), and \( \alpha \) be a vector containing all \( N_p \) of the \( A_{m,ijk} \) at a particular node, the linear expansion can be expressed as

\[ (\alpha^{n+1} - \alpha^*) = \left[ \frac{\partial \alpha}{\partial \theta} \right]_{\theta^*} \cdot (\theta^{n+1} - \theta^*). \]  

(143)

The Jacobian, \( \partial \alpha / \partial \theta \), has dimension \( N_p \times 3N_sN_t \). In general, \( N_p \ll 3N_sN_t \) and Equation 143 is solved in a least-squares sense via singular value decomposition; i.e. we
solve \( \| \alpha^{n+1} - \alpha^* \| = \min \), subject to Equation 143. The Jacobian in Equation 143 is generally very ill-conditioned, and the cutoff in the singular value decomposition should be chosen to filter out numerical noise, while keeping as much information as possible. A cutoff of \( 10^{-3} \) times the largest singular value gave consistently good results for all cases considered in this work. In the least-squares mapping back to the stochastic representation, it is, in principle, possible to obtain configurations that violate the finite extensibility of the springs. For the cases studied here that was not the case (we always checked that our spring lengths were within bounds). If violation of finite extensibility becomes an issue, it is a straightforward matter to recast equation 143 as a constrained least-squares problem, requiring all \( ||q_i|| < q_o. \)

The last remaining issue is the truncation of the series, Equation 135. Taking symmetry of the distribution function into account \( (i. e. \quad \Psi_m(q'_m) = \Psi_m(-q'_m)) \), there are

\[
N_{m,p} = \sum_{n=2,4,...}^{p} (n + 2)(n + 1)/2
\]

(144)
nonzero coefficients in the 3-dimensional Legendre polynomial expansion of order \( p. \) In determining which of the coefficients to keep, it is helpful to divide the coefficients into 2 sets. Terms in the expansion which depend on only one component of the Rouse mode will be termed “decoupled”. Terms which involve more than one component will be referred to as “coupled”. The number of decoupled and coupled terms in a \( p^{th} \) order expansion is \( 3p/2 \) and \( N_{m,p} - 3p/2 \), respectively.

We have performed numerous simulations testing the importance of these decoupled and coupled terms in the expansion, and the following guidelines give good results. For the first Rouse mode \( (m = 1) \), all 6 of the \( 2^{nd} \) order terms are retained \( (i. e. \quad \{ A_{1,200}, A_{1,020}, A_{1,002}, A_{1,110}, A_{1,101}, A_{1,011} \}) \). For higher orders of \( \Psi_{m=1} \), only the
decoupled terms are kept. For all other Rouse modes \((m > 1)\), only the 3 decoupled 2\(^{nd}\) order terms are retained. This gives a total of \(3(p/2 + N_s)\) terms which are kept for a chain consisting of \(N_s\) Rouse modes. The low order truncation of the \(m > 1\) Rouse modes is in line with our postulation that the convective update can be adequately achieved by considering “slow” properties of the microstructure.

Finally, note that, although we have chosen to use a Legendre series, other bases can be used within the OSCM method. For example, a Chebyshev series concentrates collocation points at the boundaries of the configurational domain, which may be desirable in strong flows.

We now consider the CPU scaling of the OSCM method. For the semi-implicit stochastic step (Section 6.1.5) we expect

\[
(CPU)_{\text{stoch}} = \alpha N_b^2 N_t N_g,
\]

where \(N_g\) is the number of grid points in the physical domain. The convection problem scales as

\[
(CPU)_{\text{conv}} = \beta N_p N_g,
\]

assuming that an order \(N_g\) algorithm is available, while the least-squares update (determined with a direct method) goes as

\[
(CPU)_{ls} = \gamma N_p^2 N_b N_t N_g.
\]

The predicted scalings for the CPU time required for the OSCM and BCF methods are then

\[
(CPU)_{\text{OSCM}} = \alpha N_b^2 N_t N_g + \beta_1 N_p N_g + \gamma N_p^2 N_b N_t N_g \quad (148)
\]

\[
(CPU)_{\text{BCF}} = \alpha N_b^2 N_t N_g + \beta_2 N_b N_t N_g. \quad (149)
\]
This scaling is for a direct solution of the least-squares problem; with iterative methods, which have not been explored here, it is possible in principle to lower the exponent on $N_p$ from 2 to 1 (Björk, 1996).

### 6.1.5 SAMPLE PROBLEMS

We will apply the OSCM method to two sample problems. In both cases, we consider a one-dimensional flow domain $0 < x < X$, in which the chains are initially at equilibrium. Starting at $t = 0$, chains begin to travel through the domain with constant $x$-velocity, $v_x$, while experiencing a constant velocity gradient in the $yz$-plane. At $x = 0$, the inlet to the domain, the ensemble of trajectories is in an equilibrium distribution. In essence, the flow is a spatial step change of deformation rate at $x = 0$ and temporal step change at $t = 0$ (for $x > 0$). One sample problem will involve planar extension in the $yz$-plane (see Figure 14), while the other will involve simple shear in the $yz$-plane. The macroscopic velocity field is then

$$v_p = R \cdot \begin{pmatrix}
  v_x \\
  \dot{\epsilon} y \\
  -\dot{\epsilon} z
\end{pmatrix},$$  

(150)

for the case of planar extension, and

$$v_s = R \cdot \begin{pmatrix}
  v_x \\
  \dot{\gamma} z \\
  0
\end{pmatrix},$$  

(151)
Figure 14: Schematic of a sample flow problem involving convected planar extension. There is a constant velocity in the $x$-direction, with a constant velocity gradient in the $yz$-plane.
for the case of simple shear. The rotation matrix

$$R = \begin{pmatrix}
0 & 0 & 0 \\
0 & \cos \theta & -\sin \theta \\
0 & \sin \theta & \cos \theta
\end{pmatrix}. \tag{152}$$

was added as a check to ensure that our truncation of the Legendre series was not dependent on the orientation of the velocity gradient tensor. No dependence on the orientation was observed; therefore, for the results presented in this paper, $\theta = 0$ was always used.

We define a Deborah number, $De = v_2 \lambda / X$, and Weissenberg number, $We_\epsilon = \dot{\epsilon} \lambda$ or $We_\gamma = \dot{\gamma} \lambda$, where $\lambda$ is the longest relaxation time of the molecule. The advantage to using these simple flow fields is that we can easily obtain an “exact” solution by a simple Lagrangian Brownian dynamics simulation. That is, we solve Equation 140 with an equilibrium condition at $t = 0$, and relate time and position in physical space through $x = v_x t$.

In addition to the exact and OSCM results, we will present results using the BCF method. Like the OSCM method, the BCF method can also be expressed in the form of Equations 138 and 139. In the BCF method, however, both portions of the diffusion equation are solved in a stochastic representation. That is, one solves Equation 140 for the stochastic representation of the intermediate distribution function, $\Psi^*$, and then solves

$$\left( q^{n+1} - q^* \right) = \int_t^{t+\Delta t} \left[ \mathbf{v} \cdot \nabla x q \right] dt', \tag{153}$$

to obtain the stochastic representation of $\Psi^{n+1}$.

In all stochastic simulations we used a semi-implicit time integration scheme described in a previous paper (Jendrejack et al., 2000). To improve the computational efficiency of the semi-implicit integration scheme, the singularity in Equation 116 was
removed by linearizing the spring force about a specified extension, \( q_m \). Above \( q_m \), the modified form of the spring force is then

\[
f_{ij}^s = f^s(q_m) + \left( \frac{df^s}{dr_{ij}} \right)_{q_m} (r_{ij} - q_m) \frac{r_{ij}}{r_{ij}}, \quad \text{for } r_{ij} > q_m.
\]  

(154)

We used \( q_m = 0.99q_o \) (99% extension) for all runs. Note that this modification was only accessed during intermediate Newton iterations of the semi-implicit method: we checked to confirm that configurations at the end of a time step always had \( |\mathbf{q}_i| < q_m \) \( \forall \) \( i = 1, N_s \).

Spatial discretization was performed using quadratic finite elements with streamwise-upwind Petrov-Galerkin weighting functions (Baaijens, 1998; Brooks and Hughes, 1982; Marchal and Crochet, 1987). We used an upwinding parameter of \( \alpha = \Delta x/(2v_x) \), where \( \Delta x \) represents the grid spacing. Note that, for the velocity fields described above, discretization of physical space is required only in the \( x \)-direction. The convection problem was solved using an implicit Euler integration scheme, with the resulting linear system solved using the iterative solver GMRES (Saad and Schultz, 1986). In all cases, a time step of \( 0.1 \min\{\zeta S_s^2/kT, [(\nabla \mathbf{v}) : (\nabla \mathbf{v})^T]^{-\frac{1}{2}}, \Delta x/v_x\} \) was used.

### 6.1.6 RESULTS

**DUMBBELLS**

Time-averaged steady-state results for the RMS end-to-end distance are shown in Figure 15 for dumbbells \( (N_k = 30) \) in \( We = 2 \) planar extension and \( We = 10 \) simple shear. Focusing first on the OSCM results in planar extension, we find fairly good accuracy by 8\(^{th}\) order in the polynomial expansion \( (i.e. i+j+k \leq 8) \), with a slightly premature approach
Figure 15: Time-averaged steady-state spring length of a free-draining dumbbell model ($N_k = 30$) in a theta solvent as a function of position in physical space. Comparison of the BCF and OSCM methods to the exact solution. Stochastic ensemble sizes are $N_t = 10,000$ for the exact solution, and $N_t = 1,000$ for the OSCM and BCF methods. The Deborah number for both flows is $De = 1/8$. The details of the flow fields are given in Section 6.1.5.
to the asymptotic value of the average chain length; it is this approach to the plateau region where OSCM has the most difficulty. At this level of approximation, OSCM is about twice as fast as BCF. By order $p = 20$ order in the expansion, the approach to the asymptotic average chain length is substantially improved. In the case of simple shear, convergence of the OSCM method is achieved by 8th order in the expansion.

Figure 16 shows an instantaneous “snapshot”, randomly chosen from the time-averaging sequence which produced Figure 15. Note that the plateau region in planar extension is completely free of fluctuations for the OSCM method. The BCF results of Figure 15 are in good agreement with the exact solution for simple shear. In planar extension, however, the BCF method fails to capture the asymptotic value of the average chain length. Recall that the BCF method convects every degree of freedom of every stochastic realization. The use of spatially correlated noise helps to maintain spatial smoothness of the trajectories. However, as illustrated in Figure 17, for strong flows in which the springs approach full extension, this spatial correlation is destroyed, resulting in discontinuities of the trajectories which are intermittently generated throughout the course of the simulation – they are not a transient effect – and convect through the physical domain like a shock wave. Figure 18 shows the asymptotic offset of BCF from the exact solution (i.e. the error on the plateau region of Figure 15) as a function of grid refinement and/or time step reduction for $We = 2$ planar extension. The BCF method does converge to the correct limiting value as the spatial grid is refined. Note that as the grid is refined, the time step is decreased as discussed in Section 6.1.5. However, as illustrated, a simple decrease in time step does not result in convergence of the BCF method; the asymptotic offset is dependent on grid spacing.

This effect is related to the failure of variance reduction by parallel process simulation
Figure 16: An instantaneous “snapshot” of the steady-state data presented above in Figure 15.
Figure 17: The transient behavior of a single BCF trajectory of the flow considered in Figure 15. The trajectory is shown at three points in time, separated by $\delta t = 0.28 \lambda_R$, where $\lambda_R$ is the Rouse relaxation time of the dumbbell.
Figure 18: Plateau value (e.g. the value at $x = X$ in Figure 15) of the average spring length of a free-draining dumbbell model ($N_k = 30$) undergoing convected planar extension in a theta solvent as a function of grid refinement. Stochastic ensemble sizes are $N_t = 10,000$ for the exact solution, and $N_t = 1,000$ for the BCF methods – the result from OSCM is indistinguishable from the exact and is not shown. The details of the flow field are given in Section 6.1.5.
(Öttinger, 1996) for chains with non-linear forces in homogeneous flows (Öttinger et al., 1997; Jendrejack et al., 2000). In nonlinear kinetic theory models, applying the same random forcing to two trajectories simulated under different conditions does not keep the dynamics of the two trajectories correlated. While variance reduction in a Lagrangian frame requires correlation with an equilibrium trajectory over all time, the BCF method only requires correlation over the grid spacing, $\Delta x$ (Öttinger et al., 1997). This results in good performance of the BCF method for chains in weak flows, but for strong flows a very fine mesh may be required.

**CHAINS**

The results of the OSCM and BCF methods are shown in Figure 19 (average spring extension), and Figure 20 (radius-of-gyration) for 5-spring, FD chains in a theta solvent ($N_k = 150, v = 0$). Results are shown for both $We = 2$ planar extension and $We = 10$ simple shear, and are similar to those from the dumbbell model (Figure 15). For planar extension, we again find good agreement by $8^{th}$ order in the expansion, with the approach to the asymptotic values nicely captured by $16^{th}$ order in the expansion. The BCF method again shows a deviation from this asymptotic value. As with the dumbbell model, the behavior of the chain in simple shear is well-captured by $8^{th}$ order in the expansion. Recall that, in the OSCM method, most of the information we keep corresponds to motion of the first Rouse mode, with only 3 terms being kept for each of the $N_s - 1$ shorter modes. For an $8^{th}$ order representation of a 5-spring chain, we are convecting 30 Legendre coefficients (18 of which correspond to the longest Rouse mode), rather than the $18N_s$ stochastic degrees of freedom. As seen from Figures 19 and 20, both the long and short length scale behavior is well-captured at $8^{th}$ order.
Figure 19: Time-averaged steady-state spring length of a free-draining 5-spring model ($N_k = 150$) in a theta solvent as a function of position in physical space. Comparison of the BCF and OSCM methods to the exact solution. Stochastic ensemble sizes are $N_t = 1,000$ for the exact solution, and $N_t = 100$ for the OSCM and BCF methods. The Deborah number for both flows is $De = 1/8$. The details of the flow fields are given in Section 6.1.5.
Figure 20: Time-averaged steady-state radius-of-gyration of a free-draining 5-spring model ($N_k = 150$) in a theta solvent as a function of position in physical space. Comparison of the BCF and OSCM methods to the exact solution. Stochastic ensemble sizes are $N_t = 1,000$ for the exact solution, and $N_t = 100$ for the OSCM and BCF methods. The Deborah number for both flows is $De = 1/8$. The details of the flow fields are given in Section 6.1.5.
Figure 21: An instantaneous “snapshot” of the steady-state data presented above in Figure 19.
Figure 22: An instantaneous “snapshot” of the steady-state data presented above in Figure 20
Figures 21 and 22 show instantaneous “snapshots” from the time-averaging sequences which produced Figures 19 and 20, respectively. As in the case of dumbbells, the plateau region in planar extension is completely free of fluctuations for the OSCM method. In a Brownian simulation, there are always transient fluctuations in an ensemble averaged chain property (the amplitude of which decrease with ensemble size). Generally, the OSCM method produces fluctuations of longer wavelength than those produced by BCF.

Finally, we consider a model for DNA, incorporating HI and excluded volume (Jendrejack et al., 2002a). From experimental data for 21µm λ-phage DNA in a 41cP solvent, for which \( b_k = 0.14\mu m \), and \( N_k = 150 \), parameters for a 10-spring chain were determined to be \( v = b_k^3 \), \( a = b_k \), and \( \zeta b_k^2/k_B T = 0.196 \). In this solvent, the longest relaxation time of the DNA molecule is \( \lambda = 4.1 \) s. Figures 23 and 24 show the average spring length and radius-of-gyration of the DNA molecule from the OSCM and BCF methods as well as the exact solution. Again, results are shown for both \( We = 2 \) planar extension and \( We = 10 \) simple shear. As with the earlier results, we find good convergence of the OSCM method by 16th order in the polynomial expansion. At the Deborah number considered in Figures 23 and 24, the chains do not reach their asymptotic configurations before exiting the domain. When the DNA chains are allowed to reach their asymptotic configurations, the BCF method again shows an offset from the exact and OSCM methods.

For these 10-spring chains, OSCM begins to have difficulty in capturing the approach to the plateau region in planar extension. We mentioned in Section 6.1.6 that this was the area of greatest difficulty for OSCM. The Legendre series approximates \( \Psi \) on a stationary grid, and is expected to become less efficient as the size of the domain (Equation 137) increases or as \( \Psi \) becomes very sharply peaked. We note problems with convergence at
Figure 23: Time-averaged steady-state spring length of a non-free-draining 10-spring model ($N_k = 150$) of DNA in a good solvent as a function of position in physical space. Comparison of the BCF and OSCM methods to the exact solution. Stochastic ensemble sizes are $N_t = 1,000$ for the exact solution, and $N_t = 100$ for the OSCM and BCF methods. The Deborah number for both flows is $De = 1/5$. The details of the flow fields are given in Section 6.1.5, and the DNA parameters are given in Section 6.1.6.
Figure 24: Time-averaged steady-state radius-of-gyration of a non-free-draining 10-spring model ($N_k = 150$) of DNA in a good solvent as a function of position in physical space. Comparison of the BCF and OSCM methods to the exact solution. Stochastic ensemble sizes are $N_t = 1,000$ for the exact solution, and $N_t = 100$ for the OSCM and BCF methods. The Deborah number for both flows is $De = 1/5$. The details of the flow fields are given in Section 6.1.5, and the DNA parameters are given in Section 6.1.6.
higher Weissenberg numbers in strong flows ($We = 5$ planar extension, for example) using the polynomial approximation. However, for weak to moderately strong flows, OSCM performs quite well at rather low order in the Legendre polynomial expansion.

Figures 25 and 26 show instantaneous “snapshots” from the time-averaging sequences which produced Figures 23 and 24, respectively. The same behavior as for the dumbbells and 5-spring chains is observed for the DNA model.

### 6.1.7 CONCLUSIONS

We have presented a new Eulerian solver which we call OSCM (operator-splitting, coefficient-matching). The method splits the Smoluchowsky equation into a portion involving the flux in internal configuration space ($j_q$) and a portion involving the flux in physical space ($j_x$). The portion involving $j_q$ is solved in a stochastic representation, corresponding to a $\delta$-function representation of the configurational distribution function, $\Psi$. We then project this $\delta$-function representation onto a Legendre polynomial series. The portion of the Smoluchowsky equation involving $j_x$ is then solved in the polynomial representation. Finally, at the end of the time step, $\Psi$ is transformed from the polynomial representation back to the stochastic representation. Results for non-linear chains of various lengths in convected planar extension and in convected simple shear demonstrated good performance of the OSCM method, even for 10-spring chains with hydrodynamic interactions in a good solvent. Results of the OSCM method were compared to “exact” Lagrangian solutions as well as the BCF results. Compared to the BCF method, this approach allows the solution of fewer convection problems per time step and guarantees spatial smoothness of the convected properties. The efficiency of the two methods is comparable, and in situations where the finite extensibility becomes important, BCF was shown to lose
Figure 25: An instantaneous “snapshot” of the steady-state data presented above in Figure 23
Figure 26: An instantaneous “snapshot” of the steady-state data presented above in Figure 24.
accuracy, while OSCM does not. The failure of the BCF method is due to loss of correlation of individual stochastic trajectories in physical space. The OSCM method accounts for spatial convection in a polynomial basis, the coefficients of which are obtained as ensemble averages of the distribution function; therefore, OSCM does not rely on spatial correlation of the individual trajectories.

The Legendre polynomial approximation of $\Psi$ gave fairly good results for the cases studied here. However, the Legendre series approximates $\Psi$ on a stationary grid, and is expected to become less efficient as the size of the configuration space domain (Equation 137) increases or as $\Psi$ becomes very sharply peaked. We note problems with convergence at higher Weissenberg numbers in strong flows ($We = 5$ planar extension, for example) using the polynomial approximation. BCF appears to behave roughly the same for all Weissenberg numbers in strong flows. For weak to moderately strong flows, OSCM performs quite well at rather low order in the Legendre polynomial expansion, and is faster than BCF for the cases studied here. The computational bottleneck for the current implementation of OSCM is the $O(N_p^2)$ scaling of the SVD algorithm for the final microstructural update. An $O(N_p)$ solution to this problem, or a faster strategy for the update, would allow for more accurate Galerkin approximations to the convective update and improve the accuracy of OSCM in strong flows.
Chapter 7

SIMULATION OF DILUTE-SOLUTION DNA DYNAMICS IN MICROFLUIDIC DEVICES\(^1\)

In this chapter, we consider the solution of complex fluid flow problems in microfluidic devices. In these cases, diffusion of the center-of-mass of the polymer cannot be ignored, and the solvent velocity field is in general non-linear on the length scale of the molecule. In microfluidic devices, the diffusion equation is most conveniently solved in the full configuration space of the molecule (Equation 1), rewritten here as

\[
\frac{\partial \Psi}{\partial t} = - \nabla_r \cdot \left( \left[ \omega + \frac{1}{k_B T} \mathbf{D} \cdot \mathbf{f} - \mathbf{D} \cdot \nabla_r \right] \Psi \right). \tag{155}
\]

\(^1\)Jendrejack et al. (2003a,b)
We will solve Equation 155 in a stochastic basis,

\[ r(t + \Delta t) - r(t) = \int_{t}^{t+\Delta t} \left[ \omega + \frac{1}{k_B T} D \cdot f + \nabla_r \cdot D \right] dt' + \sqrt{2} \int_{w(t)}^{w(t+\Delta t)} B \cdot dw', \quad (156) \]

\[ D = B \cdot B^T, \quad (157) \]

This is similar to the form given in Section 5, except that the solvent velocity has not been linearized about the center of mass of the molecule, and the \( \nabla_r \cdot D \) term is not zero.

In Section 7.1, we present a model for the simulation of DNA in microchannels, including a method for the treatment of hydrodynamic interactions in arbitrary, confined geometries. In Section 7.2, the model is used to study the equilibrium dynamics of DNA in microchannels, and in Section 7.3 to study the behavior of DNA in pressure-driven flow through microchannels.

### 7.1 MODEL AND SIMULATION APPROACH FOR CONFINED POLYMER DYNAMICS

#### 7.1.1 BULK SOLUTION MODEL

In the present work, 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 structural and dynamical experimental data for DNA in bulk solution (Jendrejack et al., 2000, 2002a). A linear molecule dissolved in a viscous solvent 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 the stochastic differential
equation (Jendrejack et al., 2002a; Bird et al., 1987; Öttinger, 1996; Jendrejack et al.,
2000)
\[ dr = \left[ u + \frac{1}{k_B T} D \cdot f + \frac{\partial}{\partial r} \cdot D \right] dt + \sqrt{2} B \cdot dw, \]  \hspace{1cm} (158)
\[ D = B \cdot B^T. \]  \hspace{1cm} (159)

Here, \( k_B \) is Boltzmann’s constant, and \( T \) is the absolute temperature. The vector \( r \) contains the \( 3N_b \) spatial coordinates of the beads that constitute the polymer chain, with \( r_i \) denoting the three Cartesian coordinates of bead \( i \). The vector \( f \) has length \( 3N_b \), with \( f_i \) denoting the total non-Brownian, non-hydrodynamic force acting on bead \( i \). The vector \( u \) of length \( 3N_b \) represents the unperturbed velocity field (i.e. the velocity field in the absence of the polymer), with \( u_i = v(r_i) \) denoting the unperturbed velocity field at the location of bead \( i \). The components of \( dw \) are obtained from a real-valued Gaussian distribution with mean zero and variance \( dt \).

The motion of a segment of the macromolecule creates a velocity field in the fluid, which in turn affects the motion of the entire macromolecule. The velocity field generated by motion of the macromolecule is taken to be due to a chain of point forces acting on the fluid. These hydrodynamic interactions (HI) enter the chain dynamics through the \( 3 \times 3 \) block components of the \( 3N_b \times 3N_b \) diffusion tensor, \( D \), which can be expressed as
\[ D_{ij} = k_B T \left( \frac{1}{6\pi \eta a} I \delta_{ij} + \Omega_{ij} \right), \]  \hspace{1cm} (160)
where \( \eta \) is the solvent viscosity, \( a \) is the bead hydrodynamic radius, and \( \Omega_{ij} \) is the hydrodynamic interaction tensor (Pozrikidis, 1997; Bird et al., 1987), which relates the velocity perturbation at point \( r_i \) to a point force at \( r_j \). The Brownian forces (Fixman, 1986), which
appear in the last term of Equation 158, are intimately coupled to these velocity perturbations through the fluctuation-dissipation theorem (Eq. (159)).

In an infinite domain (no walls), the Stokes flow velocity field due to a point force located at $x_j$ is given by $v'(x) = \Omega^{OB}(x - x_j) \cdot f(x_j)$, where $\Omega^{OB}$ is the free-space Green’s function, or Oseen-Burgers tensor (Bird et al., 1987; Pozrikidis, 1997),

$$\Omega^{OB}(x - x_j) = \frac{1}{8\pi\eta|x - x_j|} \left[ I + \frac{(x - x_i)(x - x_i)}{|x - x_j|^2} \right],$$  

(161)

The tensor, $\Omega_{ij}$, appearing in Eq. (160) is then given by

$$\Omega_{ij} = (1 - \delta_{ij}) \Omega^{OB}(r_i - r_j).$$  

(162)

In Brownian dynamics simulations (Jendrejack et al., 2002a, 2000, 2002b) of polymers, $\Omega^{OB}$ is typically replaced with the Rotne-Prager-Yamakawa (RPY) tensor (Rotne and Prager, 1969),

$$\Omega^{RPY}(x - x_j) = \begin{cases} \frac{1}{8\pi\eta|x - x_j|} \left[ C_1 I + C_2 \frac{(x - x_i)(x - x_i)}{|x - x_j|^2} \right] & \text{if } |x - x_j| \geq 2a, \\ \frac{1}{6\pi\eta a} \left[ C_1' I + C_2' \frac{(x - x_i)(x - x_i)}{|x - x_j|^2} \right] & \text{if } |x - x_j| < 2a, \end{cases}$$  

(163)

$$C_1 = 1 + \frac{2a^2}{3|x - x_j|^2}, \quad C_2 = 1 - \frac{2a^2}{|x - x_j|^2}, \quad C_1' = 1 - \frac{9|x - x_j|}{32a}, \quad C_2' = \frac{3|x - x_j|}{32a}.$$  

(164)

(165)

A diffusion tensor generated using RPY hydrodynamics is guaranteed to be positive-semidefinite for all chain configurations (it is positive definite unless $x_i = x_j$ for some pair of beads). Oseen-Burgers and RPY hydrodynamics, $\Omega_{ij} = 0$ for $i = j$, and $\partial/\partial r_i \cdot \Omega_{ij} = 0$ for all $i, j$. In Section 7.1.2 we describe how the above discussion is modified for bounded domains.
The spring force between adjacent beads is described by means of a worm-like spring (WLS) model (Marko and Siggia, 1994, 1995) which has been shown to be appropriate for molecules such as DNA having stiff backbones (Jendrejack et al., 2002a,c,b; Marko and Siggia, 1995; Larson et al., 1997; Hur et al., 2000; Larson et al., 1999; Ladoux and Doyle, 2000).

\[ f_{ij} = \frac{k_BT}{2b_k} \left[ \left( 1 - \frac{|r_j - r_i|}{q_o} \right)^{-2} - 1 + \frac{4|r_j - r_i|}{q_o |r_j - r_i|} \right] \frac{r_j - r_i}{|r_j - r_i|}. \]  

(166)

Here, \( f_{ij} \) is the force exerted on bead \( i \) due to connectivity with bead \( j \), and \( b_k \) is the Kuhn length of the molecule. Letting \( N_k \) represent the number of Kuhn segments in the molecule and \( N_{k,s} \) the number of Kuhn segments per spring, \( q_o = N_{k,s} b_k \) is the maximum spring length, or the contour length of the portion of the molecule represented by one spring. The contour length of the chain is then given by \( L = N_s q_o \).

Following our previous work (Jendrejack et al., 2002a,c,b), for the excluded volume potential between two beads of the chain we use

\[ U_{ij}^{ev} = \frac{1}{2} \nu k_BT N_{k,s}^2 \left( \frac{3}{4\pi S_s^2} \right)^{3/2} \exp \left[ \frac{-3|r_j - r_i|^2}{4S_s^2} \right], \]  

(167)

where \( \nu \) is the excluded volume parameter, and \( S_s^2 = N_{k,s} b_k^2 / 6 \) is the radius of gyration of an ideal chain consisting of \( N_{k,s} \) Kuhn segments.

Using \( N_s = 10 \) for 21 \( \mu \)m stained \( \lambda \)-phage DNA at room temperature in a 43.3 cP solvent, in previous work (Jendrejack et al., 2002a,c) we determined, by direct comparison to available bulk experimental data, that suitable parameter values are \( b_k = 0.106 \) \( \mu \)m, \( \alpha = 0.077 \) \( \mu \)m, \( \nu = 0.0012 \) \( \mu \)m\(^3\). With these values, the model outlined above was able to reproduce the experimentally observed bulk relaxation time, diffusivity and equilibrium stretch (size) of DNA. The model also gives results in quantitative agreement with transient and steady-state behavior of 21 \( \mu \)m DNA in both simple shear and planar
extension over a wide range of Weissenberg numbers. In contrast to other available treatments for DNA in solution, the model discussed here also produces diffusivity results in quantitative agreement with experimental data for chains ranging from 21 μm to 126 μm, underscoring its predictive capability. After appropriate modifications to account for confinement, the model should provide useful predictions of DNA behavior in microfluidic devices.

7.1.2 CONFINEMENT

As mentioned above, simple arguments predict that the dynamics of a dissolved macromolecule confined to a channel comparable to its equilibrium coil size (\(\sim 1 \mu m\) for viral DNA) are different from those in free solution, largely as a consequence of the no-slip boundary condition on the fluid motion. Available analytical work (Happel and Brenner, 1991; Pozrikidis, 1997, 1992) has concentrated on resolving particle-wall interactions for a few special geometries (i.e., a spherical particle near an infinite plane or located between two infinite planes, and a particle at the centerline of a cylindrical channel). The long-range effect of the wall on the mobility of a particle decays slowly as \(1/h\), where \(h\) is the distance from the wall. Hydrodynamic interactions between confined particles decay as \(1/r^2\) for particles near an infinite plane and exponentially in a channel (Pozrikidis, 1997, 1992). Dufresne et al. (2000) recently considered the hydrodynamic coupling of two Brownian particles near a plane wall. Those authors compared their experimental results to analytical predictions for point particles near an infinite plane – i.e., keeping only the leading order far field effects – and found good agreement with experimental observation provided \((h/a) > 2\), where \(a\) is the radius of the particle. That study represents the first
direct experimental validation of the use of point particle hydrodynamic interactions between Brownian particles near a surface. The findings of Dufresne et al. are particularly relevant to dynamical studies of polymers in confined geometries (microfluidic devices), where the velocity field generated by motion of the macromolecule is generally taken to be due to point forces acting on the interaction sites, or “beads” that constitute the chain.

We now present a method for the numerical evaluation of the hydrodynamic interaction tensor for general geometries. The level of treatment of HI in a bounded domain considered here is similar to that employed by Dufresne et al. (2000) in their work. Note however, that closed form solutions only exist for Oseen-Burgers hydrodynamics in a few special cases (i.e. point particles between infinite planes or in straight channels with constant cross-section); for general geometries the problem must be solved numerically.

The Green’s function for Stokes flow in an arbitrary device can be expressed as

$$\Omega = \Omega^{\text{OB}} + \Omega^W,$$  \hspace{1cm} (168)

where $\Omega^{\text{OB}}$ is the free-space Green’s function (Eq. (161)) and $\Omega^W$ is a correction which accounts for the no-slip constraint on the walls. The velocity perturbation due to a point force acting at $x_j$ is then given as

$$v'(x, x_j) = v'_{\text{OB}}(x - x_j) + v'_{\text{W}}(x, x_j) = \left[ \Omega^{\text{OB}}(x - x_j) + \Omega^W(x, x_j) \right] \cdot f(x_j).$$  \hspace{1cm} (169)

Thus, $v'_{\text{W}}(x, x_j)$ can be obtained as the solution to the incompressible Stokes flow problem

$$-\nabla p + \eta_s \nabla^2 v'_{\text{W}} = 0, \quad \nabla \cdot v'_{\text{W}} = 0,$$  \hspace{1cm} (170)

subject to

$$v'_{\text{OB}} + v'_{\text{W}} = 0 \quad \text{at the walls.}$$  \hspace{1cm} (171)
The wall Green’s function, \( \Omega^W(x, x_j) \), can be obtained by the following procedure. First, one takes \( \mathbf{v}'_{\text{OB}}(x - x_j) \) to be due to a point force \( (f_1) \) acting in the \( x_1 \) direction, located at the point \( x_j \). The Stokes flow problem can be solved numerically to obtain \( \mathbf{v}'_W(x, x_j) \). This gives the first column of \( \Omega^W(x, x_j) \) by

\[
\begin{pmatrix}
   \Omega^W_{11} \\
   \Omega^W_{21} \\
   \Omega^W_{31}
\end{pmatrix} = \frac{1}{f_1} \mathbf{v}'_W.
\]  

(172)

Similarly, the second and third columns of \( \Omega^W(x, x_j) \) are obtained by applying point forces in the \( x_2 \) and \( x_3 \) directions, respectively. Now, \( \Omega_{ij} \), in Eq. (160) is given by

\[
\Omega_{ij} = \Omega^W(r_i, r_j) + (1 - \delta_{ij}) \Omega^\text{OB}(r_i - r_j).
\]  

(173)

In contrast to the case of unbounded flow, here \( \Omega_{ij} \neq 0 \) for \( i = j \). Furthermore, \( \partial / \partial r_i \cdot \Omega^W_{ij} \) is non-zero for \( i = j \), resulting in a non-zero drift term in Eq. (158).

As in the bulk case (Section 7.1), use of the Green’s function in the above formulation leads to non-positive-semidefinite \( D \) for some chain configurations. However, a diffusion tensor constructed by the above-outlined method using \( \Omega^\text{RPY} \) in place of \( \Omega^\text{OB} \) results in a non-symmetric \( D \); this violates the reciprocity relation

\[
\Omega(r_i, r_j) = \Omega^T(r_j, r_i),
\]  

(174)

which follows from self-adjointness of the Stokes operator (Pozrikidis, 1997). This violation is analogous to that which would occur if RPY hydrodynamic interactions were used naively for spheres of unequal size (Felderhof, 1977; Beenakker, 1986; Hase and Powell, 2001). For that situation, Felderhof (1977) performed a multipole expansion of the free-solution hydrodynamic interaction tensor. To order \( 1/r^3 \), the resulting hydrodynamic interaction tensor is identical (for \( |r_{ij}| \geq 2a \)) to the symmetrized RPY tensor.
\( \Omega_{ij}^{\text{MP}} = (\Omega_{ij}^{\text{RPY}} + \Omega_{ji}^{\text{RPY}})/2 \). By analogy with this result, we obtain a symmetric, positive-semidefinite diffusion tensor as follows. First, \( \Omega_{ij}^{\text{OB}} \) is replaced by \( \Omega_{ij}^{\text{RPY}} \) in Equations 171 and 173, giving a wall correction \( \Omega_{ij}^{\text{W}} \neq (\Omega_{ji}^{\text{W}})^T \). Then, a symmetric, positive-semidefinite diffusion tensor is calculated according to

\[
\Omega_{ij}^{\text{W}} = \frac{\Omega_{ij}^{\text{W}} + (\Omega_{ji}^{\text{W}})^T}{2}.
\] (175)

We note here that we account for hydrodynamic interactions at the point force level \( (i.e. \) Oseen-Burgers in a confined geometry); the Rotne-Prager-Yamakawa formulation is employed only to maintain positive-semidefiniteness of the diffusion tensor. While the use of Eq. (175) to obtain a symmetric \( \Omega \) is not rigorous, it is essentially a near-field regularization, and introduces an error in the point force hydrodynamics of order \( a/H \ll 1 \). Our treatment of hydrodynamic interaction may be considered as an approximate Rotne-Prager-Yamakawa formulation for confined geometries. For the special case of particles above an infinite plane wall, our treatment of the hydrodynamic interaction can be worked out analytically. We have done this and verified that our method is indeed a well-behaved near-field modification of the near-wall point-force solution. We have included a demonstration of this in Appendix A.

The evaluation of the Green’s function is performed once, in a pre-processing step, for a given device or geometry; \( \Omega^{\text{W}}(x_i, x_j) \) is obtained numerically on a grid using a finite element method\(^2\). During a Brownian dynamics simulation, \( \Omega_{ij}^{\text{W}} \) and its divergence are obtained by finite element interpolation\(^3\). Figure 27 shows a typical mesh used.

At first glance, it may appear that one needs \( O(N_G^2) \) of the \( \Omega_{mn}^{\text{W}} \)'s, with \( N_G \) being the number of grid points in the microfluidic domain. However, in confined geometries,

\(^2\)We used a quadratic velocity, linear pressure formulation. The resultant sparse, symmetric system of equations was solved using GMRES with a partial LU decomposition preconditioner.

\(^3\)3D quadratic interpolation functions are used.
Figure 27: Green’s function meshing for a $63.6 \mu m \times 6.36 \mu m \times 6.36 \mu m$ channel. Also shown is the $v_x = 0.01/\zeta$ (red) and $-0.01/\zeta$ (blue) contours due to a point force in the $x$-direction of magnitude 1, located at the center of the channel. The inset is a close up view of the velocity contours.
the Green’s function decays rapidly (exponentially, in a channel (Happel and Brenner, 1991)), and in practice one only needs to keep the \( \Omega_{mn}^W \)’s for \( |x_n - x_m| < x_o \), where \( x_o \) is a cutoff distance which depends on the proximity of the point \( x_j \) to the device walls. Thus, in practical applications, one needs \( O(N_G) \) of the \( \Omega_{mn}^W \)’s, with the coefficient of proportionality depending on the details of the computational domain.

In addition to the detailed “HI” model described above, we consider two approximate models. In the reduced mobility (RM) model, hydrodynamic interactions between particles are neglected, while modifications to the bead mobility due to the wall are maintained. In that case the diffusion tensor (Eq. (160)) becomes block-diagonal,

\[
\mathbf{D}_{ij}^{RM} = k_B T \delta_{ij} \left( \frac{1}{6 \pi \eta a} \mathbf{I} + \Omega_{ij}^W \right). \tag{176}
\]

In the free-draining (FD) model, which has been favored in many literature studies of DNA, both hydrodynamic interactions and modifications to the bead mobility are neglected, resulting in a position-independent, isotropic diffusion tensor,

\[
\mathbf{D}_{ij}^{FD} = \delta_{ij} \frac{k_B T}{6 \pi \eta a} \mathbf{I}. \tag{177}
\]

In this work, we consider the behavior of individual DNA molecules in an infinitely long microchannel with square cross-section. The centerline of the channel is oriented along the \( x \)-axis, with the cross-section lying in the \( yz \)-plane. The imposed velocity field in the channel is given by (White, 1991)

\[
v(x, y) = \frac{4H^2}{\eta \pi^3} \left( -\frac{dp}{dx} \right) \sum_{k=1,3,5,...}^{\infty} (-1)^{(k-1)/2} \left[ 1 - \frac{\cosh(k\pi z/H)}{\cosh(k\pi/2)} \right] \frac{\cos(k\pi y/H)}{k^3}, \tag{178}
\]

where \( p \) is the pressure. The strength of the flow is defined through an effective shear rate, \( \dot{\gamma}_{eff} = 2v_{max}/H \), where \( v_{max} = |v(y = 0, z = 0)| \) is the imposed velocity at the centerline of the channel.
Figure 28: A chain of 7,920 Kuhn segments (bulk radius of gyration = 36.3 Kuhn lengths) confined to a channel 30 Kuhn lengths wide.
The physical confinement of the molecule is taken into account through a simple bead-wall repulsive potential of the form

\[ U_{i}^{\text{wall}} = \begin{cases} \frac{A_{\text{wall}}}{\delta_{\text{wall}}^{2}} (h - \delta_{\text{wall}})^{3} & \text{for } h < \delta_{\text{wall}} \\ 0 & \text{for } h \geq \delta_{\text{wall}}, \end{cases} \]  

(179)

(180)

where \( h \) represents the distance of bead \( i \) from the wall in the wall-normal direction (into the fluid). Throughout this work, we take \( A_{\text{wall}} = 25k_{B}T \) and \( \delta_{\text{wall}} = bN_{k_{s}}^{1/2}/2 = 0.236 \mu m \).

### 7.2 EFFECT OF CONFINEMENT ON DNA DYNAMICS IN MICROFLUIDIC DEVICES

#### 7.2.1 ABSTRACT

The dynamics of dissolved long-chain macromolecules are different in highly confined environments than in bulk solution. A computational method is presented here for detailed prediction of these dynamics, and applied to the behavior of \( \sim 1-100 \mu m \) DNA in micron-scale channels. The method is comprised of a self-consistent coarse-grained Langevin description of the polymer dynamics and a numerical solution of the flow generated by the motion of polymer segments. Diffusivity and longest relaxation time show a broad crossover from free-solution to confined behavior centered about the point \( H \approx 10S_{b} \), where \( H \) is the channel width and \( S_{b} \) is the free-solution chain radius of gyration. In large channels, the diffusivity is similar to that of a sphere diffusing along

\(^{4}\text{Jendrejjack et al. (2003a)}\)
the centerline of a pore. For highly confined chains \( H/S_b \ll 1 \), Rouse-like molecular weight scaling is observed for both translational diffusivity and longest relaxation time. In the highly confined region, the scaling of equilibrium length and relaxation time with \( H/S_b \) are in good agreement with scaling theories. In agreement with the results of Harden and Doi [J. Phys. Chem. 96, 4046 (1992)], we find that the diffusivity of highly confined chains does not follow the scaling relation predicted by Brochard and de Gennes [J. Chem. Phys. 69, 1527 (1978)]; that relationship does not account for the interaction between chain and wall.

### 7.2.2 INTRODUCTION

The behavior of a dissolved polymer chain in a confined space is central to many natural and technological processes, and has taken on renewed importance because of new and developing technologies for single molecule manipulation and analysis of DNA (Andersen, 1999; Chou et al., 2000; Lim et al., 2001; Perna et al., 2001; Sauer et al., 2001; Hinz et al., 2001; Stephan et al., 2001). For instance, in certain implementations of exonucleolytic sequence analysis it is desirable to link an individual long DNA strand to a surface (e.g. a bead) without manual intervention (Hinz et al., 2001; Stephan et al., 2001). The ability to engineer such tasks will be greatly improved by predictive computational tools for polymer chains in microfluidic geometries. In this work, we present a general method for dynamic simulations of macromolecules in confined geometries.

The equilibrium properties and conformations adopted by a confined chain in solution have been studied extensively (Wall et al., 1978; van Vliet and ten Brinke, 1990). Much less theoretical or computational work is available on the dynamics of confined chains, either in equilibrium or flow, in spite of their practical importance (Schwartz and...
Cantor, 1984; Schwartz and Koval, 1989; Viovy, 2000; Kantor et al., 1999; Shrewsbury et al., 2001, 2002). Qualitatively, one might envision two effects of confinement on the dynamics of a dissolved chain. First, the change in equilibrium conformation brought on by confinement may change the molecular motion. Second – and more important, as we shall see – the solvent flow in the confining geometry will also influence the polymer segment dynamics. More precisely, the mobility of an individual segment decreases while hydrodynamic interactions between segments are screened, leading to Rouse rather than Zimm scaling of the diffusivity for small channels (Brochard and de Gennes, 1977). The resulting dependence of diffusivity on channel width has been predicted from scaling arguments by Brochard and de Gennes (1977) and from self-consistent mean field theory and the Kirkwood approximation by Harden and Doi (1992). Both studies predict power law behavior of the diffusivity in terms of channel width, but the predicted exponents are different. The results of those two studies will be discussed below in more detail.

Progress beyond scaling or quasistatic results has been slow. In principle, the time scales of interest in many cases are accessible to coarse-grained, or Brownian models (Bird et al., 1987; Fixman, 1978). Existing simulations (Chopra and Larson, 2002) of chain models in confined geometries have not accounted for changes in the hydrodynamics brought on by confinement. The central challenge is to consider polymer and solvent motions simultaneously, with the solvent motion satisfying the no-slip boundary condition on the surfaces of the confining geometry. In this work, we address this challenge with an approach that combines techniques from computational fluid dynamics and polymer physics. This method is then used to generate computational predictions of the dynamics of long DNA molecules in a channel of micrometer dimensions. Our results represent the first self-consistent Brownian dynamics treatment of polymer dynamics and
hydrodynamics under confinement. We find that confinement begins to affect the equilibrium configuration of the molecule when the channel width \( (H) \) is on the order of the free-solution radius of gyration \( (S_{\text{bulk}}) \). Significant changes in the equilibrium relaxation time and diffusivity are observed at much larger widths.

### 7.2.3 SIMULATION

In this work, we consider the behavior of individual DNA molecules in an infinitely long microchannel with square cross-section (Figure 28). The centerline of the channel is oriented along the \( x \)-axis, with the cross-section lying in the \( yz \)-plane. In the limit of infinite channel length, a point force acting on the fluid generates no net flow even if the channel ends are open; for there to be a net flow the force would need to be infinite. For the numerical evaluation of the hydrodynamic interaction tensor, the infinitely long channel is therefore approximated by a closed channel of length \( 10H \), at which the results are insensitive to further increase in length. Figure 27 shows the mesh and \( v_x = 0.01/\zeta \) (red) and \( -0.01/\zeta \) (blue) contour surfaces for a unit point force in the \( x \)-direction, located at the center of a 6.3 \( \mu \text{m} \) wide channel.

\[
D_{ij}^{\text{FD}} = \delta_{ij} \frac{k_B T}{6\pi \eta a} \mathbf{I}. \tag{181}
\]

The physical confinement of the molecule is taken into account through a simple bead-wall repulsive potential of the form

\[
U_{i,\text{wall}} = \frac{A_{\text{wall}}}{\delta_{\text{wall}}^2} (y - \delta_{\text{wall}})^3 \text{ for } y < \delta_{\text{wall}} \tag{182}
\]

\[
= 0 \text{ for } y \geq \delta_{\text{wall}}, \tag{183}
\]

where \( y \) represents the distance of bead \( i \) from the wall in the wall-normal direction.
(into the fluid). Throughout this work, we take $A_{\text{wall}} = 25k_B T$ and $\delta_{\text{wall}} = b_N k_{s}^{1/2}/2 = 0.236 \mu m$.

Eq. (158) was evolved in time using a semi-implicit integration scheme described in our previous papers (Jendrejack et al., 2002a, 2000). The range of the hydrodynamic interaction is proportional to the channel width, $H$; all components of $D$ less than $0.001 \max(D_{ii})$ were neglected. The decomposition of $D$ (Eq. (160)) is computationally demanding, and was achieved using a fast algorithm proposed by Fixman (1986) and implemented as described in our earlier work (Jendrejack et al., 2000). A time step of $\Delta t = 0.01(6\pi \eta a_s S_s^2)/(k_B T)$ was used in all simulations. All simulations here were performed without an imposed velocity field ($v = 0$). All results are presented for DNA at room temperature in a 1 cP solvent. Chains ranging from $4.2 \mu m$ ($N_s = 2$) to $420 \mu m$ ($N_s = 200$) were simulated in channels having widths in the range of $0.636 - 21.2 \mu m$. Note that the level of molecular discretization was kept constant at $N_{k,s} = 19.8$. We investigated the effect of molecular discretization on the full model by using $N_{k,s} = 13.2$ in simulations of $42 \mu m$, $126 \mu m$ and $210 \mu m$ chains in $1.6 \mu m$ channels; the results were within a few percent of the coarser representation, lending credence to the predictive capabilities of the model. The results were also found to be fairly insensitive to the wall parameter $\delta$, provided $\delta = O(a)$.

### 7.2.4 PROPERTIES

The following properties are considered in this work. The instantaneous “stretch” of the chain $X$ is defined as the absolute length of the molecule in the channel direction

$$
\bar{X} = \max_i (r_{i,x}) - \min_i (r_{i,x}),
$$

(184)
where \( r_{i,x} \) is the \( x \)-component of the position vector of bead \( i \). The steady-state stretch of the molecule is defined as

\[
X = \langle \bar{X} \rangle_n,
\]

where

\[
\langle A \rangle_n = \frac{1}{N} \sum_{n=1}^{N} A_n,
\]

represents a steady-state average over \( N \) observations and \( A_n \) is the value of \( A \) at observation \( n \). The equilibrium diffusivity of a chain in the channel direction, \( D_x \), is determined by

\[
D_x = \lim_{t \to \infty} \frac{1}{2t} \langle [r_{c,x}(t) - r_{c,x}(0)]^2 \rangle_n
\]

where \( r_{c,x} \) is the \( x \)-component of the center-of-mass of the chain. The approximate Kirkwood diffusivity tensor is given by

\[
D^K = \left\langle \frac{1}{N_b} \sum_{i,j=1}^{N_b} D_{ij} \right\rangle_n.
\]

The Kirkwood diffusivity in the channel direction is \( D^K_x = D^K_{11} \). We have compared the Kirkwood diffusivity to the center-of-mass diffusivity calculated by Eq. (187), and found them to be in quantitative agreement for all channels considered in this work. Figure 29 shows a comparison between the Kirkwood diffusivity and that obtained by Eq. (187) for a 21 \( \mu m \) DNA chain in a 1.59 \( \mu m \) wide channel.

The longest relaxation time of a chain, \( \lambda_1 \), is calculated by allowing a chain that is initially fully stretched along the centerline of the channel to relax to equilibrium. Near equilibrium, the relaxation time is determined by a fit to an exponential decay,

\[
\langle \bar{X}^2 \rangle_n(t) = \left( \bar{X}^2(0) - \langle \bar{X}^2 \rangle_{n,eq} \right) \exp \left( -\frac{t}{\lambda_1} \right) + \langle \bar{X}^2 \rangle_{n,eq},
\]
Figure 29: Comparison between the mean-squared displacement of the chain center of mass (solid line) in the axial direction and that predicted by the Kirkwood diffusivity (dashed line). Results are for a 21 $\mu m$ chain in a 1.59 $\mu m$ wide channel. The mean-squared displacement was averaged over 80 trajectories.
where $\langle \rangle_{n,eq}$ indicates an equilibrium average. The radius of gyration of the chain, $S$, is defined through

$$S^2 = \left\langle \frac{1}{N_b} \sum_{i=1}^{N_b} |r_i - r_c|^2 \right\rangle_n,$$

(190)

We also define $X_b$, $D_{x,b}^K$, $\lambda_{1,b}$ and $S_b$ as the equilibrium bulk values of the stretch, Kirkwood diffusivity in the channel direction, longest relaxation time and radius of gyration, respectively.

### 7.2.5 RESULTS

We first present results on the equilibrium stretch of DNA molecules in microchannels. Simple scaling arguments (Wall et al., 1978) give $\langle X \rangle \propto N_k H^{-2/3}$ for a chain in a good solvent; this scaling has been previously verified by Monte Carlo simulations (Wall et al., 1978; van Vliet and ten Brinke, 1990). Figure 30 shows the dimensionless equilibrium stretch, $X^* = \langle X \rangle_{eq}/X_b$, as a function of the inverse dimensionless channel width, $1/H^* = S_b/H$. Chains ranging from 4.2 $\mu$m ($N_s = 1$) to 420 $\mu$m ($N_s = 200$) are considered. Also shown is the predicted scaling, $X^* \propto (H^*)^{-2/3}$. As found previously (van Vliet and ten Brinke, 1990), static confinement effects appear here at $1/H^* \approx 0.3$, while the scaling regime is realized for $1/H^* \gtrsim 0.5$. The transition from free-solution to confined behavior is centered about the point $1/H^* \approx 0.4$. For $1/H^* \gtrsim 0.4$, we refer to the chains as strongly confined, while below the transition we refer to the chains as weakly confined.

Although static equilibrium properties such as the stretch can be obtained through Monte Carlo simulations, dynamic properties such as relaxation time and diffusivity require the resolution of solvent motion, as do transient processes like the dynamics of a
Figure 30: Stretch as a function of inverse channel width for various lengths of DNA. Symbols correspond to $L = 4.2 \, \mu m$ (○), $L = 10.5 \, \mu m$ (□), $L = 21 \, \mu m$ (◇), $L = 42 \, \mu m$ (△), $L = 84 \, \mu m$ (▷), $L = 126 \, \mu m$ (▽), $L = 210 \, \mu m$ (⊿), and $L = 420 \, \mu m$ (+). The solid line corresponds to the scaling $X^* \propto (1/H^*)^{2/3}$. 
relaxing chain. Figure 31 shows the dimensionless Kirkwood diffusivity, $D^* = D^K_x / D^K_{sb}$, as a function of $1/H^*$ for chains ranging from 4.2 $\mu m$ to 420 $\mu m$. For $a \ll H$, $a \ll S_b$, and $N \gg 1$, dimensional analysis leads one to expect $D^* = f(H^*)$. This will be discussed in more detail below. The results shown in Figure 31 were obtained by FD simulation, with the diffusion tensor and corresponding Kirkwood diffusivity periodically evaluated from an instantaneous realization of the static equilibrium configuration.

Figure 31 shows a broad crossover from free-solution behavior. In the weakly confined region ($1/H^* \lesssim 0.4$), the molecule might be expected to behave as a sphere diffusing in a large channel. The special case of a sphere diffusing along the centerline of a circular channel has been solved to varying degrees of accuracy (Happel and Brenner, 1991). The asymptotic solution of Faxen (1923) is given by

$$D^* = 1 - 2.104 \left( \frac{r_s}{r_p} \right) + 2.09 \left( \frac{r_s}{r_p} \right)^3 - 0.95 \left( \frac{r_s}{r_p} \right)^5 + O \left( \frac{r_s}{r_p} \right)^7,$$  (191)

where $r_s$ and $r_p$ are the sphere and cylinder radii, respectively. From our bulk simulations, we determined the hydrodynamic radius ($r_h$) of our chains to be 0.55 $S_b$. The dashed curve in Figure 31 represents Eq. (191) with $r_s = r_h$ and $r_p = H/2$. We find that Faxen’s solution matches well our results for chain molecules when $1/H^* < 0.1$. In comparison, for solid spheres in a circular channel, Faxen’s expression is relatively accurate out to $r_s/r_p = 1/2$, which would correspond to $1/H^* \approx 0.45$. Our results lie slightly below Faxen’s expression for small $1/H^*$, probably because we do not force the chains to remain centered in the channel. The good agreement with Faxen’s expression indicates that in the region $1/H^* < 0.1$ the molecule behaves as a non-draining chain with the decrease in mobility due to channel walls affecting the entire chain uniformly. In the region $0.1 \lesssim 1/H^* \lesssim 0.4$, the chain can no longer be represented as sphere diffusing in a channel, and the mobility becomes higher than predicted by the Faxen result; hydrodynamic
screening due to channel walls causes a transition towards free-draining behavior. This transition from non-draining to free-draining behavior begins at \( H \approx 10S_b \), well before the transition to strongly confined behavior (\( H \approx 2S_b \)) in Figure 30.

Before discussing our results for larger \( 1/H^* \), it is of interest to review several experimental investigations in the region \( 1/H^* < 0.5 \). All available experiments on porous materials measure an effective diffusivity (\( D_{\text{eff}} \)). This quantity is related to our reduced diffusivity by (Satterfield et al., 1973)

\[
D_{\text{eff}} = D_b \theta K_p D^*/\tau,
\]

where \( D_b \) is the bulk diffusivity, \( \theta \) is the volume fraction of the pores, \( \tau \) is the tortuosity, and \( K_p \) is the equilibrium partition coefficient. In 1973, Satterfield et al. (1973) reported on the diffusion of low molecular weight paraffins, aromatic hydrocarbons, and sugars through homogeneous microporous silica-alumina bead catalyst. For \( r_s/r_p < 1/2 \), they found their data could be fit to the expression

\[
D^* = \exp(-4.6r_s/r_p).
\]

This relation is shown as the dashed-dotted curve in Figure 31. In that work they noted that this exponential dependence on \( r_s/r_p \) had also been observed in other systems. In 1975, Colton et al. (1975) reported on the diffusion of proteins and monodisperse polystyrene (molecular weights up to 670,000) through borosilicate glass. They found that \( D^* \) for the proteins was in qualitative agreement with the exponential fit given above, but that \( D^* \) for the polystyrene chains was independent of \( H^* \). In 1980, Cannell and Rondelez (1980) considered the diffusion of monodisperse polystyrene chains (molecular weights up to 600,000) through porous membranes. For \( 0.1 < r_s/r_p < 0.5 \), they found their data followed the Renkin equation (Renkin, 1953)

\[
D^* K_p = (1 - \frac{r_s}{r_p})^2 \left[ 1 - 2.104 \frac{r_s}{r_p} + 2.09 \left( \frac{r_s}{r_p} \right)^3 - 0.95 \left( \frac{r_s}{r_p} \right)^5 \right],
\]  

(192)

provided they set \( r_s = 1.45r_h \), where \( r_h \) was the Stokes-Einstein hydrodynamic radius of the molecules as determined from light-scattering experiments. The Renkin equation combines Ferry’s equilibrium partition coefficient (Ferry, 1936; Satterfield et al., 1973),
Figure 31: Kirkwood diffusivity as a function of inverse channel width for various lengths of DNA. Symbols correspond to $L = 4.2 \mu m$ (○), $L = 10.5 \mu m$ (□), $L = 21 \mu m$ (◇), $L = 42 \mu m$ (△), $L = 84 \mu m$ (⊙), $L = 126 \mu m$ (◇), $L = 210 \mu m$ (▷) and $L = 420 \mu m$ (●). Line styles correspond to $D^* \propto (1/H^*)^{-2/3}$ (solid), Faxen’s expression (dashed), the curve fit of the data of Cannell and Rondelez (1980) (dotted) and the curve fit of the data of Satterfield et al. (1973) (dot-dashed). The solid symbols are the RM model results for the 420 μm chains.
\( K_p^F = (1 - r_s/r_p)^2 \), with Faxen’s expression for the diffusion of a sphere along the centerline of a channel. The dotted curve in Figure 31 represents Faxen’s expression with \( r_s = 1.45r_h \). The Renkin equation has been used with varying success to describe rigid solute diffusion through biological and artificial membranes (see Satterfield et al. (1973) for references).

We note that the curve representing the experimental study of the diffusion of long flexible polymers through membranes lies below our simulation results (the other study (Colton et al., 1975) concluded no dependence on \( H^* \)). Our simulations provide a direct measurement of \( D^* \), unlike the experimental studies which inferred \( D^* \) from indirect estimates of \( \tau, \theta, \) and \( K_p \). In addition, our simulations are performed at infinite dilution, while the experimental investigations, although performed at finite concentrations, assumed \( D^* \) (and \( K_p \)) to be independent of solute concentration within the pores. This is in contrast to the study of Cannell and Rondelez (1980), who observed a large change in \( K_p D^* \) when the (dilute) concentration was increased by a factor of 3. Also, in our simulations, there is no adsorption of the solute to the pore walls. In the experiments of Colton and Satterfield, preferential solute adsorption was estimated from equilibrium studies, and the estimated corrections to the pore diameters were made when necessary. Cannell and Rondelez measured the flow rate of polystyrene solutions through their membranes as a function of time and concluded that adsorption did not occur. Furthermore, all of the experiments discussed above were obtained from membranes having pore radii on the order of nanometers; the diffusivity determined from those experiments may include effects of potential wells.

We now turn our discussion to the “strongly confined” region of Figure 31 (\( 1/H^* > 0.5 \)). In 1977, Brochard and de Gennes (1977) used a modified blob theory to obtain
the scaling relation $D^* \propto (1/H^*)^{-2/3}$, provided that $a \ll H \ll S_b$. In developing this relation, they assumed that the highly confined molecule could be represented as a sequence of blobs which do not interact hydrodynamically. This assumption imposes the scaling $D \propto N_k^{-1}$. In fact, if $a \ll H$, $D \propto N_k^{-1}$ and $D^* \propto (H^*)^m$, then dimensional analysis and good solvent bulk molecular weight scaling are sufficient to arrive at $m = 2/3$.

More recently, Harden and Doi (1992) combined an analytical-series solution for the Stokes flow due to point forces in a capillary (circular cross-section) with a self-consistent mean field calculation for the equilibrium configuration of the confined chain. They obtained $D \propto N_k^{-1}$ for highly confined chains, but found that transverse averaging of the Kirkwood diffusion coefficient results in $D^* \propto (H^*)^{0.61}$. Note that the results of Harden and Doi indicate that the reduced variable $D^*$ will not display a master curve in $1/H^*$ for highly confined chains. But as mentioned above, if the scale $a$ does not enter the problem, the exponent must be $2/3$. However, in the work of Harden and Doi and in our work presented here, there is an additional ratio of length scales $a/\delta$ that comes into play, where $\delta$ is the length scale associated with polymer-wall interactions. The ratio $a/\delta$ is order unity, which suggests that the $2/3$ scaling proposed by Brochard and de Gennes cannot be realized; the magnitude of the exponent will depend on the magnitude of $a/\delta$.

The fact that Harden and Doi’s exponent of $0.61$ persists for $H/a > 10^2$ is consistent with this reasoning, as are our results, which we now discuss.

Our results collapse onto a master curve in $D^*$ versus $H^*$ in the weakly confined region. This master curve extends beyond the region represented by Faxen’s expression, all the way to the transition to strongly confined behavior. However, in the strongly confined region ($1/H^* \gtrsim 0.4$), we observe some scatter in the data ($D^*$ lower for longer
chains) as well as a deviation from the predicted scaling for the diffusivity data; we find $D^* \sim (1/H^*)^{-1/2}$ from a fit of the data in this region, rather than $D^* \sim (1/H^*)^{-2/3}$. As discussed above, this deviation indicates that additional length scales (i.e., the ratio $a/\delta$) are coming into play that were not accounted for in the simple scaling theory of Brochard and de Gennes.

As the level of chain confinement increases, the hydrodynamic interactions between beads become weaker due to the solvent boundary condition on the walls of the device. To quantify this effect, we performed simulations using the RM model (Eq. (176)), which assumes complete screening of inter-bead hydrodynamic interactions. The diffusivity of $420 \mu m$ DNA chains using the RM model are shown as solid circles in Figure 31. The RM model results converge to those of the full model at $S_b \gtrsim 5H$. In general, the point at which the RM results match those of the full model is a function of the level of molecular discretization ($N_{k,s} = 19.8$, for the results reported in this work). When $H$ is on the order of the equilibrium spring length ($\approx b_k N_{1/2}^{1/2}$), hydrodynamic interactions between beads are screened. However, at that level of confinement, a finer molecular model (smaller $N_{k,s}$) should be used, at which point screening will again no longer be complete. The RM model is thus of limited value.

We next consider the relaxation of DNA chains in microchannels. Individual chains, initially $99\%$ stretched along the axis of the channel, were allowed to relax to equilibrium. Figure 32 shows the transient stretch of $126 \mu m$ DNA chains, averaged over 10 trajectories, for various channel widths. Both the HI and FD model results are shown. Recall that model parameters were chosen so that relaxation times of both the HI and FD models matched the experimental bulk relaxation time for $21 \mu m$ DNA chains. In order to provide a more reasonable comparison between the two models, the time axis of the
Figure 32: Relaxation of 126 $\mu$m chains, initially 99% stretched along the centerline of the channel. Results for both the HI and FD models are shown. The time axis for the FD case has been scaled so that the two model have equivalent bulk relaxation times (see text). Each data set represents an average over 10 trajectories. Line colors correspond to channel widths of $H \to \infty$ (black), $H = 10.6 \mu m = 4.8 S_{\text{bulk}}$ (red), $H = 6.36 \mu m = 2.9 S_{\text{bulk}}$ (green), $H = 3.18 \mu m = 1.5 S_{\text{bulk}}$ (blue), $H = 1.59 \mu m = 0.73 S_{\text{bulk}}$ (orange), $H = 0.636 \mu m = 0.29 S_{\text{bulk}}$ (brown).
FD results was scaled by $\lambda_{126}^{\text{HI,b}} / \lambda_{126}^{\text{FD,b}} \approx 0.6$, where $\lambda_{126}^{\text{HI,b}}$ and $\lambda_{126}^{\text{FD,b}}$ are the bulk relaxation time of 126 $\mu$m chains as determined by the HI and FD models, respectively. The HI relaxation dynamics are strongly dependent on channel width, while the relaxation dynamics of the FD model are virtually unaffected by confinement. The RM model (results not shown) overpredicts the relaxation times; the HI and RM relaxation results converge at the same point as the diffusivity results in Figure 31.

Longest chain relaxation times were determined by the method leading to Eq. (189) for various chain lengths and channel widths. Figure 33 shows the reduced relaxation time, $\lambda_1^* = \lambda_1/\lambda_{1,b}$ as a function of $1/H^*$ for chains up to 126 $\mu$m. We observe a crossover region centered about $1/H^* \approx 0.1$ followed by a power law region which is fully developed at $1/H^* \approx 0.5$. We note two sources of scatter in the $\lambda_1$ data obtained in the crossover region. First, chains in this region may be fully relaxed before they have had time to sample the cross-section of the channel; the relaxation time obtained by Eq. (189) in this region is not a true equilibrium average (such as that obtained from the autocorrelation function for the end-to-end vector). Second, there is significantly more noise in the relaxation trajectories in this region.

The only existing theoretical prediction for the longest relaxation time is for highly confined chains, and again comes from the scaling analysis of Brochard and de Gennes (1977). By assuming complete screening of blob-blob hydrodynamic interactions, they predicted $\lambda_1 \propto N_k^2 H^{-1/3}$. As in the case of diffusivity, dimensional analysis for the case of weak confinement leads to a master curve in the reduced variables $\lambda_1^*$ and $1/H^*$. If no new length scales come into play in the highly confined region, we again expect a master curve in the reduced variables. Since Rouse-like scaling ($\lambda_1 \propto N_k^2$) is also expected in this region, one obtains (using bulk good solvent scaling, $\lambda_{1,b} \propto N_k^{9/5}$ and $S_b \propto N_k^{3/5}$)
Figure 33: Chain relaxation time as a function of inverse channel width for various lengths of DNA. Symbols correspond to $L = 10.5 \, \mu m$ ($\bigcirc$), $L = 21 \, \mu m$ ($\square$), $L = 42 \, \mu m$ ($\bigtriangleup$), $L = 84 \, \mu m$ ($\bigtriangleleft$), $L = 126 \, \mu m$ ($\bigtriangledown$). The solid line corresponds to the scaling $\lambda^* \propto (1/H^*)^{1/3}$. 
a power law in the reduced variables $\lambda^* \propto (1/H^*)^{1/3}$. This prediction is shown as the solid line in Figure 33, which is in good agreement with our results. As anticipated by Brochard and de Gennes (1977), for strongly confined chains the relaxation time shows a weaker dependence on channel width than does the stretch or diffusivity.

The relaxation of a stretched chain in a narrow slit has been observed experimentally by Bakajin et al. (1998). In that work, fluorescently dyed DNA molecules were allowed to relax to equilibrium after being stretched in an electric field. Those authors found that confinement significantly increased the time required for individual molecules to relax to equilibrium. For $\approx 74 \mu m$ chains, Bakajin et. al estimated that the relaxation time roughly doubled when the slit width was decreased from 5 $\mu m$ to 0.3 $\mu m$, and again when the slit width was decreased to 0.09 $\mu m$. We estimate $S_b = 1.6 \mu m$ for 74 $\mu m$ chains, which gives $1/H^* = 0.32, 5.3$ and 17.8 for the 5, 0.3 and 0.09 $\mu m$ slits, respectively. Figure 33 indicates that $\lambda^*$ does increase by about a factor of two in going from $1/H^* = 0.32$ to $1/H^* = 5.3$ in agreement with the observations of Austin et. al. From the power law scaling (for which the exponents for slit and channel are expected to be the same), one expects that $\lambda^*$ will increase by a factor of 1.5 as $1/H^*$ increases from 5.3 to 17.8.

7.2.6 CONCLUSIONS

We have performed self-consistent Brownian dynamics-hydrodynamic simulations of DNA in microchannels, using a method that simultaneously resolves both macromolecular and solvent motion in microfluidic devices. For diffusivity in the axial direction ($D^K_x$) and longest relaxation time ($\lambda_1$), we observe a cross-over region from free-solution
dynamics centered about the point \( H \approx 10S_b \), where \( H \) is the width of the square channel and \( S_b \) is the free-solution radius of gyration of the chain. For \( H \gtrsim 10S_b \), we find that the molecule diffuses in a manner similar to a solid sphere with radius equal to the free-solution hydrodynamic radius of the molecule. At \( H \approx 10S_b \) the molecule begins a transition to free-draining behavior, which is complete at \( H \approx 2S_b \). For \( H \lesssim 2S_b \), the chains may be considered strongly confined and Rouse-like. In the strongly confined region we find the equilibrium length \((X)\) and \(\lambda_1\) to be well-represented by the scaling relations \( X \propto N_k H^{2/3} \) and \( \lambda_1 \propto N_k^{-2} H^{-1/3} \) as predicted by Brochard and de Gennes (1977). The computed diffusivity in the strongly confined region does not follow the predicted scaling of Brochard and de Gennes (1977), \( D^K_x \propto N_k^{-1} H^{-2/3} \). While we do observe Rouse-like behavior (\( D^K_x \propto N_k^{-1} \)), we find \( D \propto H^{-1/2} \). Our diffusion results, as well as those of Harden and Doi (1992), suggest that the diffusivity scaling exponent also depends on the ratio \( a/\delta \), where \( a \) is the segment hydrodynamic radius and \( \delta \) is the length scale associated with polymer-wall interactions.
7.3 SHEAR-INDUCED MIGRATION IN FLOWING POLYMER SOLUTIONS: SIMULATION OF LONG CHAIN DNA IN MICROCHANNELS

7.3.1 ABSTRACT

We simulate dilute solution dynamics of long DNA molecules \( (O(10 - 100 \, \mu m)) \) in pressure-driven flow through micron-scale channels using, a self-consistent coarse-grained Langevin description of the polymer dynamics and a numerical solution of the flow generated by the motion of polymer segments. During flow, the chains migrate toward the channel centerline in agreement with well-known experimental observations. The thickness of the resulting hydrodynamic depletion layer increases with molecular weight at constant flow strength; higher molecular weight chains therefore move with a higher average axial velocity than lower molecular weight chains. In contrast, when the hydrodynamic effects of the confining geometry are neglected, depletion of concentration is observed in the center of the channel rather than at the walls, contradicting experimental observations. The mechanisms for migration are illustrated using a simple kinetic theory dumbbell model of a confined flexible polymer. The simple theory correctly predicts the trends observed in the detailed simulations. We also examine the steady-state stretch of DNA chains as a function of channel width and flow strength. The flow strength needed to stretch a highly confined chain away from its equilibrium length is shown to increase with decreasing channel width, independent of molecular weight; this is fairly well-explained using a simple blob picture.

\(^5\text{Jendrejack et al. (2003b)}\)
7.3.2 INTRODUCTION

New and developing technologies for single molecule manipulation and analysis of DNA in micron and nanometer scale devices (Andersen, 1999; Chou et al., 2000; Lim et al., 2001; Perna et al., 2001; Sauer et al., 2001; Hinz et al., 2001) 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. In this work, we investigate the dynamics of DNA molecules of contour length $10.5-126\ \mu m$; the free-solution radii and relaxation times (in a 1cP solvent) of these molecules are $\approx 0.5-2\ \mu m$ and $\approx 0.03-2.4\ s$, respectively.

The long-time dynamics of these DNA molecules are out of reach of atomistic simulations. However, they are accessible to coarse-grained, Langevin models (Bird et al., 1987; Fixman, 1978). 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. We have previously developed a computationally tractable formalism to address this challenge, and used it to investigate relaxation and diffusion of DNA in micron-scale channels (Jendrejack et al., 2003a). Here, we apply the method to generate the first predictions of the pressure-driven flow behavior of long DNA molecules in channels of micrometer dimensions. Hydrodynamic interactions in confined, flowing systems are shown to give rise to a pronounced, molecular-weight-dependent depletion layer toward the walls, thereby providing a basis for separation processes for DNA. As we will show, the depletion layer arises from polymer-wall hydrodynamic interaction.
Molecular migration in flowing dilute polymeric solutions is a well-known phenomenon that has received a fair amount experimental and theoretical investigation. Much of this was recently reviewed by Agarwal et al. (1994), who examined various experimental and theoretical studies and concluded:

We find a disagreement between different theories, even with regard to their prediction of the direction of polymer migration during simple flows. While we have seen that these mechanisms can explain many indirect implications of the flow-induced polymer migration phenomena, they are able to explain only some and not all of the direct experimental results, even qualitatively.

Spatial variations in polymer concentration arise from symmetry-breaking contributions to the steady-state mass flux of polymer. In inhomogeneous rectilinear channel flow of dilute linear polymers, general considerations from polymer kinetic theory point to two sources of migration:

a) Coupling of hydrodynamics with spatial variations in the polymer conformational distribution function lead to Brownian migration (Agarwal et al., 1994; Sekhon et al., 1982; Brunn and Chi, 1984; Brunn, 1984), and

b) in the presence of a wall, symmetry of the hydrodynamic interaction is broken, leading to deterministic migration (Jhon and Freed, 1985).

The deterministic contribution to migration is present even in homogeneous flows such as simple shear over a wall. In inhomogeneous flows, the wall hydrodynamic interaction also contributes additional terms to the Brownian migration. Note that if one ignores wall contributions, the point-force (Oseen-Burgers) hydrodynamic interaction is anisotropic.
but symmetric, and deterministic migration is not predicted. The above discussion assumes that the hydrodynamics of the polymer molecule are adequately represented by a chain of point forces. Past studies (Agarwal et al., 1994; Sekhon et al., 1982; Brunn and Chi, 1984; Brunn, 1984) have almost universally neglected wall hydrodynamic interaction. The kinetic theory predictions for migration in the absence of wall hydrodynamic interaction have been mixed. For example, the use of preaveraged bulk hydrodynamic interactions for a polymer in a parabolic velocity profile predicts a weak depletion of polymer at the wall, while using non-preaveraged bulk hydrodynamic interactions predicts depletion at the centerline of the channel. Jhon and Freed (1985) used a kinetic theory dumbbell model of a polymer near an infinite plane wall with approximate wall hydrodynamic interactions and concluded that this contribution to migration was away from the wall. In this work, we review and extend the kinetic theory. Fan et al. (2003) used dissipative particle dynamics (DPD) (Españo and Warren, 1995; Ripoll et al., 2001) to study the behavior of flexible polymers in rectilinear flow through microchannels, and predicted very weak hydrodynamic depletion at the walls. However, for their choice of DPD parameters, diffusion was artificially fast relative to momentum transport; the Schmidt number for the solvent was $O(1)$. At a Schmidt number of $O(1)$, hydrodynamic interactions are still developing on the time scale of polymer motion, and the consequences of this for the polymer dynamics is yet unknown (Groot and Warren, 1997). In any event, the DPD results appear rather different than the results presented in this work, which do not suffer from the Schmidt number problem and indicate a very strong depletion of polymer near the walls.

Migration is also observed for solutions of rigid Brownian fibres in inhomogeneous flows. Recent theoretical studies by Nitsche and Hinch (1997) as well as Schiek and
Shaqfeh (1997) predict weak migration toward the walls for (rectilinear) parabolic flow between flat plates; wall hydrodynamic interaction and steric effects were not considered. Earlier, de Pablo et al. (1992) had considered steric effects but not hydrodynamic interactions and found a decrease in the thickness of the static wall depletion layer – again, migration toward the wall.

Finally, deterministic migration of droplets immersed in flowing fluids has also received a fair amount of attention (Leal, 1980). Starting with a rigid particle in a Newtonian fluid at zero Reynolds number, Chan and Leal (1979) systematically examined the perturbative effects of inertia, droplet deformability, and non-Newtonian fluid character. For a slightly deformable drop in a Newtonian fluid in zero Reynolds simple shear flow near a wall, wall hydrodynamic interaction is the sole contribution to droplet migration. Chan and Leal, using far-field wall hydrodynamic interaction found that drift was always away from the wall (in agreement with experiment). For inhomogeneous flows, they found that the first order contribution was interaction with the gradient of the local shear rate, provided the shear rate changed significantly over the length scale of the droplet. They found that the direction of migration depended on the ratio of solvent and droplet viscosities; for the range of viscosity ratios used in experiments, migration was always toward regions of lower local shear rate (toward the “center”). For circular Couette flow, they found that the final position of the droplet was determined from a competition between the streamline curvature effect and wall hydrodynamic interaction. Related to droplet migration in unbounded inhomogeneous flows are the deterministic studies on migration of fairly rigid cyclic bead spring models (Nitsche, 1996) and the dumbbell model of Brunn (1983), which treated the beads as solid finite-sized spheres. Those model particles are predicted to migrate deterministically toward regions of lower
local shear rate in unbounded (no wall hydrodynamic interaction) inhomogeneous flows.

In this work, we present results on dilute solution behavior of DNA in pressure-driven flow through square micron-scale channels, accounting for hydrodynamic interactions in the confining geometry, steric effects and excluded volume (good solvent) interactions. Migration of DNA is a central theme of this study, and in Section 7.3.4 we employ a simple dumbbell model (within the context of kinetic theory) to elucidate the various mechanisms contributing to variations in the steady-state concentration of polymer mass.

SIMULATION

In the limit of infinite channel length, a point force acting on the fluid generates no net flow even if the channel ends are open; for there to be a net flow the force would need to be infinite. For the numerical evaluation of the hydrodynamic interaction tensor, the infinitely long channel is therefore approximated by a closed channel of length $10H$, at which the results are insensitive to further increase in length. Figure 27 shows the mesh and $u_x = 0.01/\zeta$ (red) and $-0.01/\zeta$ (blue) contour surfaces for a unit point force in the $x$-direction, located at the center of a 6.3 $\mu$m wide channel.

Eq. (158) was evolved in time using a semi-implicit integration scheme described in our previous papers (Jendrejack et al., 2002a, 2000). The range of the hydrodynamic interaction is proportional to the channel width, $H$; all components of $D$ less than $0.001 \max(D_{ij})$ were neglected. The decomposition of $D$ (Eq. (159)) is computationally demanding, and was achieved using a fast algorithm proposed by Fixman (1986) and implemented as described in our earlier work (Jendrejack et al., 2000). For general robustness, we also implemented the method outlined in Appendix B to ensure that $D$ remained positive semidefinite. A time step of $\Delta t = 0.1 \min \left[ (6\pi \eta a_s^2) / (k_B T), \dot{\gamma}_{\text{eff}} \right]$. 
was used in all simulations. All results are presented for DNA at room temperature in a 1 cP solvent. Chains ranging from 10.5 µm ($N_s = 5$) to 126 µm ($N_s = 60$) were simulated in channels having widths in the range of 0.636 – 10.6 µm. Note that the level of molecular discretization was kept constant at $N_{k,s} = 19.8$. We investigated the effect of molecular discretization on the full model by using $N_{k,s} = 13.2$ in simulations of 42 µm, 126 µm and 210 µm chains in 1.6 µm channels; the results were within a few percent of the coarser representation, lending credence to the predictive capabilities of the model. The results were also found to be fairly insensitive to the wall parameter $\delta$, provided $\delta = O(\alpha)$.

**PROPERTIES**

The following properties are considered in this work. The instantaneous “stretch” of the chain $\bar{X}$ is defined as the absolute length of the molecule in the channel direction

$$\bar{X} = \max_i (r_{ix}) - \min_i (r_{ix}),$$

(193)

where $r_{ix}$ is the $x$-component of the position vector of bead $i$. The steady-state stretch of the molecule is defined as

$$X = \langle \bar{X} \rangle_n,$$

(194)

where

$$\langle A \rangle_n = \frac{1}{N} \sum_{n=1}^{N} A_n,$$

(195)

represents a steady-state average over $N$ observations and $A_n$ is the value of $A$ at observation $n$. 

Table 3: Equilibrium bulk radius of gyration and bulk relaxation time from simulation for different chain contour lengths.

<table>
<thead>
<tr>
<th>$L$ ($\mu m$)</th>
<th>$S_b$ ($\mu m$)</th>
<th>$\lambda_{1,b}$ ($s$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.5</td>
<td>0.52</td>
<td>0.03</td>
</tr>
<tr>
<td>21</td>
<td>0.76</td>
<td>0.09</td>
</tr>
<tr>
<td>42</td>
<td>1.14</td>
<td>0.3</td>
</tr>
<tr>
<td>84</td>
<td>1.73</td>
<td>0.9</td>
</tr>
<tr>
<td>126</td>
<td>2.19</td>
<td>1.9</td>
</tr>
</tbody>
</table>

The longest relaxation time of a chain, $\lambda_1$, is calculated by allowing a chain that is initially fully stretched along the centerline of the channel to relax to equilibrium. Near equilibrium, the relaxation time is determined by a fit to an exponential decay,

$$
\langle \bar{X}^2 \rangle_n(t) = \left( \bar{X}^2(0) - \langle \bar{X}^2 \rangle_{n,eq} \right) \exp \left( -\frac{t}{\lambda_1} \right) + \langle \bar{X}^2 \rangle_{n,eq},
$$

where $\langle \rangle_{n,eq}$ indicates an equilibrium average. The radius of gyration of the chain, $S$, is defined through

$$
S^2 = \left\langle \frac{1}{N_b} \sum_{i=1}^{N_b} |\mathbf{r}_i - \mathbf{r}_c|^2 \right\rangle_n,
$$

where $\mathbf{r}_c$ is the center of mass of the molecule. We also define $X_b$, $\lambda_{1,b}$ and $S_b$ as the equilibrium bulk values of the stretch, longest relaxation time and radius of gyration, respectively. Table 3 gives the simulation predictions for the bulk equilibrium radius of gyration and relaxation time for different chain contour lengths.

The steady state center of mass distribution in the cross section of the channel is given by

$$
P_c(y, z) = \langle \delta(y - y_{c,n}) \delta(z - z_{c,n}) \rangle_n,
$$

where $y_{c,n}$ and $z_{c,n}$ are the $y$ and $z$ coordinates of the center of mass of the molecule at observation $n$. The second moment of the center of mass distribution in the cross-section
of the channel is

\[ w^2 = \int (y^2 + z^2) \ P_c(y, z) \ dy \ dz. \]  \hspace{1cm} (199)

The quantity \( w/w_{eq} \) gives a measure of the width of the center of mass distribution relative to the equilibrium value. The intramolecular mass distribution in the axial direction is given by

\[ g(x - x_c) = \left\langle \frac{1}{N_b} \sum_{i=1}^{N_b} \delta \left( |x - x_c| - |x_{i,n} - x_{c,n}| \right) \right\rangle_n, \]  \hspace{1cm} (200)

where \( x_{i,n} \) and \( x_{c,n} \) are the axial positions of bead \( i \) and the chain center of mass at observation \( n \).

### 7.3.3 RESULTS

**ONSET OF FLOW-INDUCED STRETCHING**

We first present results on the steady-state stretch of DNA chains in pressure-driven flow through square microchannels. Figure 34 shows the steady-state stretch as a function of channel width for various chain lengths and flow strengths. Consider, for example, the results for a 126 \( \mu m \) chain at a flow strength of \( \dot{\gamma}_{eff} = 30.8 \ s^{-1} \) (triangles in Figure 34.b).

At small \( H \), the chain is elongated or cigar-shaped at equilibrium. The first of effect of the flow is to compress the chain slightly in the axial direction and push the “cigar” along the channel (compression of the chain will be demonstrated more clearly below). As the level of confinement decreases, a channel size \( (H_c) \) is eventually reached where the flow strength is sufficient to cause the chain to stretch away from its equilibrium value. Figures 34.a - 34.c indicate that the value of \( H \) at which the chain stretches away from its equilibrium value is independent of molecular weight and decreases with increasing
Figure 34: Steady-state stretch reduced by the equilibrium stretch as a function of channel width. (a) $\dot{\gamma}_{eff} = 3.98 \text{ s}^{-1}$, (b) $\dot{\gamma}_{eff} = 30.8 \text{ s}^{-1}$, (c) $\dot{\gamma}_{eff} = 308 \text{ s}^{-1}$. Symbols refer to chains lengths of 21 $\mu m$ (○), 42 $\mu m$ (□), 84 $\mu m$ (◊) and 126 $\mu m$ (△). These chain lengths have equilibrium free-solution radii of gyration of 0.76, 1.14, 1.73 and 2.19 $\mu m$, respectively.
flow strength. For example, in Figure 34.a ($\dot{\gamma}_{\text{eff}} = 3.98 \text{ s}^{-1}$) all chain lengths (symbols) stretch at the same value of $H$. This is also true for the stronger flows (Figures 34.b and 34.c), although the value of $H_c$ decreases. Using a simple “blob” model (Daoud and de Gennes, 1977; Brochard and de Gennes, 1977; Wall et al., 1978), one expects that, in homogeneous simple shear with shear rate $\dot{\gamma}$, the chain will begin to stretch away from its equilibrium value when the blob Weissenberg number $\text{We}_{\text{blob}} = \dot{\gamma} \lambda_{\text{blob}}$ is order unity, where $\lambda_{\text{blob}}$ is the blob longest relaxation time. In a good solvent, $H = b_k N_{\nu}^{\nu}$, where $N_{\nu}^{\nu}_{\text{blob}}$ is the number of Kuhn segments per blob, and the exponent $\nu \approx 3/5$.

The Zimm longest relaxation time of such a blob is approximated by (Doi and Edwards, 1986) $\lambda_{\text{blob}}^{\nu} \approx (\eta_s b_k^2)/(k_B T) N_{\nu}^{\nu}_{\text{blob}} = (\eta_s H^3)/(k_B T)$. Note that the stiffness of the chain does not appear explicitly in this expression for the relaxation time of a blob; this is for $H \gg b_k$. The Weissenberg number based on the blob good solvent Zimm relaxation time is $\text{We}_{\text{blob}} = \lambda_{\text{blob}}^{\nu} \dot{\gamma} \approx (\eta_s H^3 \dot{\gamma})/(k_B T)$, and the chain is expected to stretch when

$$H^3 > H_c^3 \approx \frac{k_B T}{\eta_s \dot{\gamma}}.$$  \hspace{1cm} (201)

Equation 201 gives two interesting results. First, the critical shear rate is independent of molecular weight; our simulations (Figure 34) agree with this; for a given $\dot{\gamma}_{\text{eff}}$, all chain lengths stretch away from the equilibrium value at the same value of $H$. Second, Equation 201 predicts $H_c \propto (\dot{\gamma}_{\text{eff}})^{-1/3}$. Although our simulations show a definite decrease in $H_c$ with increasing $\dot{\gamma}_{\text{eff}}$, the relation between the two does not appear to satisfy the power law relation in Eq. (201). This discrepancy is not surprising since the scaling argument assumed simple shear, while we have a non-uniform velocity gradient.

The internal structure of the chain is illustrated in Figure 35, which shows the $\dot{\gamma}_{\text{eff}} = 308 \text{ s}^{-1}$ steady-state intramolecular axial mass distribution (relative to equilibrium) for
Figure 35: Steady-state intramolecular mass distribution (relative to equilibrium) as a function of distance from the chain center-of-mass. Results are for a 42 $\mu m$ chain in various channels at a flow strength of $\dot{\gamma}_{\text{eff}} = 308$ s$^{-1}$. Line styles correspond to channel widths of 0.636 $\mu m$ (solid), 1.06 $\mu m$ (dotted), 1.59 $\mu m$ (dashed) and 3.18 $\mu m$ (dot-dashed). The corresponding $H/S_b$ values are 0.56 (solid), 0.93 (dotted), 1.39 (dashed) and 2.79 (dot-dashed). These results are from the same simulations as the square symbols in Figure 34.c.
a 42 $\mu m$ chain in various channel sizes. The dotted line in Figure 35 shows the intramolecular axial mass distribution in a channel size which is a little bit too small to allow the chain to stretch (at this flow strength). The dashed line shows the intramolecular axial mass distribution in a channel size which is large enough to allow the chain to stretch. From the dotted line we see that just prior to stretching there is a redistribution of monomer density – there is an increase in monomer concentration near the center of mass (at small $|x - x_c|$) and a decrease in monomer concentration at large $|x - x_c|$. This redistribution of monomer density may be interpreted as an effective compression of the chain in the axial direction just before stretching.

**CROSS-SECTIONAL DISTRIBUTIONS: CROSS-STREAM MIGRATION AND ITS CONSEQUENCES**

The effect of flow on the chain center of mass distribution in the cross-section of the channel is illustrated in Figure 36 for a 42 $\mu m$ chain in a 10.6 $\mu m$ channel ($H/S_b \approx 9.3$ – a weakly confined chain). At equilibrium, the distribution is fairly uniform across the channel, with a static depletion layer of size $S_b \approx 1.14 \mu m$ near the walls. As flow strength increases, a hydrodynamically-induced depletion layer (dark blue areas) forms near the walls. The effect of flow on the chain stretch distribution in the cross-section of the channel is illustrated in Figure 37 for a 42 $\mu m$ chain in a 10.6 $\mu m$ channel. The dark blue areas in Figure 37 represent regions where no chains were observed at large times. At equilibrium, the chain stretch is fairly uniform across the channel. Chains within the static depletion layer are more highly stretched due to steric constraints. At higher flow strengths the distribution becomes highly non-uniform, with chains away from the centerline more stretched due to a higher local velocity gradient. A comparison between
Figure 36: Steady-state center-of-mass distribution $P_c(y, z)$ in the cross section of the channel for a 42 µm chain in a 10.6 µm wide channel. a) $\dot{\gamma}_{\text{eff}} = 0 \text{ s}^{-1}$, b) $\dot{\gamma}_{\text{eff}} = 3.98 \text{ s}^{-1}$, c) $\dot{\gamma}_{\text{eff}} = 30.8 \text{ s}^{-1}$, d) $\dot{\gamma}_{\text{eff}} = 308 \text{ s}^{-1}$. Grid line spacing is 2 µm in the $yz$-plane and 0.2 for $P_c(y, z)$. 
Figure 37: Steady-state stretch $X(y, z)$ as a function of location of chain center-of-mass in the cross section of the channel. Results are for a 42 $\mu$m chain in 10.6 $\mu$m wide channel. a) $\dot{\gamma}_{\text{eff}} = 0$ s$^{-1}$, b) $\dot{\gamma}_{\text{eff}} = 3.98$ s$^{-1}$, c) $\dot{\gamma}_{\text{eff}} = 30.8$ s$^{-1}$, d) $\dot{\gamma}_{\text{eff}} = 308$ s$^{-1}$. Grid line spacing is 2 $\mu$m in the $yz$-plane and 4 $\mu$m for $X(y, z)$. Values of zero (dark blue area) represents regions where chains were not observed (see Figure 36 and corresponding discussion). The data around the edges are noisy due the small number of observations (small probability of finding a chain there).
the stretch and center of mass distributions indicate that although chains are much more highly stretched where the local velocity gradient is higher, it is much less likely to find the chain in those regions. Figure 38 shows the chain center of mass distribution for a longer chain (84 µm) at a flow strength of $\dot{\gamma}_{\text{eff}} = 30.8 \, s^{-1}$ in various channel sizes. We remind the reader that these are dilute-solution results (single-molecule simulations).

The non-equilibrium, steady-state center of mass distributions in Figures 36 and 38 indicate a non-monotonic concentration profile in the cross-section of the channel. There is a shallow local minimum at the centerline, a maximum off the centerline, then a monotonically decreasing concentration toward the walls, with substantial depletion of polymer near the walls. This non-monotonic concentration profile is due to a competition of Brownian migration (due to coupling of hydrodynamics with spatial variations in the the polymer conformational distribution function) away from the centerline and deterministic migration (due to asymmetry in the wall hydrodynamic interaction) away from the walls. These mechanisms will be discussed in detail in Section 7.3.4.

One way of quantifying the depletion effect is to consider the width, $w$ (Equation 199), of the center of mass distribution. Figure 39 shows $w$, reduced by the equilibrium value $w_{\text{eq}}$, as a function of channel width for various molecular weight chains and flow strengths. Using as an example the diamond symbols in Figure 39.b (84 µm chain, flow strength $\dot{\gamma}_{\text{eff}} = 30.8 \, s^{-1}$), we identify three regions of interest. As mentioned above, for small $H/S_b$ one of the first effects of the flow is to compress the chain slightly in the axial direction. This effective increase in monomer density reduces the transverse fluctuations of the chain center of mass resulting in $w/w_{\text{eq}} < 1$. As channel width increases, the flow is eventually able to stretch the chain, allowing the chain center of mass to sample closer
Figure 38: Steady-state center-of-mass distribution $P_c(y, z)$ in the cross section of the channel for an 84 $\mu m$ chain at a flow strength of $\dot{\gamma}_{\text{eff}} = 30.8$ s$^{-1}$ in channel widths of a) 10.6 $\mu m$, b) 7.95 $\mu m$, c) 6.36 $\mu m$ and d) 4.77 $\mu m$. Grid line spacing is 2 $\mu m$ in the $yz$-plane and 0.2 for $P_c(y, z)$. 
Figure 39: Width of the steady-state center-of-mass distribution (relative to equilibrium) as a function of channel width for chain lengths of 21 $\mu m$ ($\bigcirc$), 42 $\mu m$ ($\Box$) and 84 $\mu m$ ($\Diamond$). (a) $\dot{\gamma}_{\text{eff}} = 1.98 \, s^{-1}$, (b) $\dot{\gamma}_{\text{eff}} = 30.8 \, s^{-1}$, (c) $\dot{\gamma}_{\text{eff}} = 308 \, s^{-1}$. The equilibrium free-solution radius of gyration of the 21, 42 and 84 $\mu m$ chains is 0.76, 1.14 and 1.73 $\mu m$, respectively. Note the different scales on the vertical axis.
to the walls, which results in $w/w_{eq} > 1$. As channel width is increased further, hydrodynamic depletion effects become important and $w/w_{eq}$ again decreases below unity.

As mentioned in the introduction, it is well known that deformable particles in this type of flow experience a hydrodynamic driving force toward the centerline of the channel (Leal, 1980; Agarwal et al., 1994). To clarify the origin of this driving force for our case of long flexible chains, we performed non-Brownian simulations by “turning off” the Brownian contributions (the $\partial/\partial r \cdot D$ and $B \cdot dw$ terms) in Eq. (158), for a 42 $\mu m$ chain in a 10.6 $\mu m$ channel ($H/S_b = 9.3$) at various flow strengths, with the chain initially located away from the centerline of the channel. The results are illustrated in Figure 40. There is clearly a deterministic hydrodynamic driving force toward the centerline of the channel, and this force increases with increasing flow strength. Migration occurs while the chain is flipping – this is apparent from the “steps” in the 30.8 $s^{-1}$ results (square symbols in Figure 40). This effect is not captured using a free-draining diffusion tensor, bulk hydrodynamic interactions or the reduced mobility model. This suggests that for long flexible non-Brownian chains, the hydrodynamic depletion effect is due to hydrodynamic interactions between confined chain segments. The thin lines in Figure 40 represent Brownian trajectories for a flow strength of $\dot{\gamma}_{eff} = 308 s^{-1}$ (the same flow strength as for the diamond symbols). For Brownian chains, the width of the steady-state center of mass distribution is ultimately determined by a balance between hydrodynamic drift and chain diffusion. As mentioned in the introduction, for Brownian chains there is an additional contribution to the hydrodynamic drift. We will discuss these depletion mechanisms in more detail in Section 7.3.4. Note that the time required to reach steady-state in Figure 40 is more than an order of magnitude longer than the relaxation time of the chain.
Figure 40: Hydrodynamic drift of a 42 µm non-Brownian chain in pressure-driven flow through a 10.6 µm channel ($H/S_b \approx 9.3$). All trajectories were started from the same equilibrium configuration with center of mass located at $(y, z) = (-1.9, -4.5) \mu m$. Symbols correspond to $\dot{\gamma}_{\text{eff}} = 3.98 \, s^{-1}$ (○), $\dot{\gamma}_{\text{eff}} = 30.8 \, s^{-1}$ (□) and $\dot{\gamma}_{\text{eff}} = 308 \, s^{-1}$ (♦). The dotted lines represent several Brownian trajectories for $\dot{\gamma}_{\text{eff}} = 308 \, s^{-1}$, all started from the same initial configuration. The bulk equilibrium relaxation time of a 42 µm chain is $\approx 0.3 \, s$. 
Figure 41: Width of center-of-mass distribution as a function of chain contour length for various flow strengths in a 10.6 μm channel. Symbols correspond to flow strengths of $\dot{\gamma}_{\text{eff}} = 0 \, s^{-1}$ (○), 1.98 $s^{-1}$ (□), 30.8 $s^{-1}$ (◇) and 308 $s^{-1}$ (△).
We next examine the molecular weight dependence of the depletion effect. Figure 41 shows the steady-state width of the center of mass distribution in a 10.6 \( \mu m \) channel as a function of molecular weight for various values of \( \dot{\gamma}_{\text{eff}} \). For all flow strengths (and also at equilibrium), the width of the distribution decreases with increasing molecular weight. At equilibrium, this is due entirely to excluded volume effects between the equilibrium DNA coil and the channel walls; for large \( H/S_b \) at equilibrium, \( w/H \sim f(H/S_b) \). As discussed earlier, at higher flow strengths, the width of the distribution decreases significantly below its equilibrium value. At all flow strengths considered here, \( w \) decreases with increasing molecular weight, indicating that a higher molecular weight chain will on average spend more time in regions of higher axial fluid velocity than a lower molecular weight chain. This leads one to imagine that a microchannel could be used as a crude separation device. Figure 42 illustrates this capability for a flow strength of \( \dot{\gamma}_{\text{eff}} = 308 \ s^{-1} \) in a 10.6 \( \mu m \) channel, showing the axial distance traveled by a chain center of mass as a function of distance traveled by a fluid element at the center of the channel \( (v_{\text{max}}t) \). Results are shown for 20 unique trajectories for various molecular weight chains. The fact that distinct “bands” can be observed for different length DNA chains indicates that this phenomenon can be used to separate DNA molecules in small channels. We have also performed dilute multiple-chain simulations using a 10.6 \( \mu m \) square channel of (periodic) length 84 \( \mu m \) containing four 42 \( \mu m \) chains and eight 21 \( \mu m \) chains at a flow strength of \( \dot{\gamma}_{\text{eff}} = 308 \ s^{-1} \). This corresponds to a volume fraction of 0.004 based on the free-solution radius of gyration of the DNA chains. The results of these simulations were identical to the results in Figure 42; dilute chain-chain interactions do not appear have a noticeable impact on the average velocity of the chains. Note that in one of these dilute multiple-chain simulations, a 42 \( \mu m \) chain will pass by a 21 \( \mu m \) chain \( \approx 600 \) times in
Figure 42: Axial distance traveled by individual chains versus axial distance traveled by a fluid element at the centerline of the channel. Results are for a 10.6 µm channel at a flow strength of $\dot{\gamma}_{\text{eff}} = 308$ s$^{-1}$. Colors correspond to 84 µm (black), 42 µm (red), 21 µm (blue) and 10.5 µm (green) chains. Twenty trajectories from each molecular weight are shown. The solid and dashed orange lines are the result one would obtain if a chain moved at the maximum or average fluid velocity, respectively.
generating results such as those in Figure 42.

The slope of the results in Figure 42 gives $v_c$, the average chain velocity in the axial direction. Figure 43 shows the average chain velocity (reduced by $v_{\text{max}}$) as a function of channel size for various chain lengths and flow strengths. Note the non-monotonic behavior of $v_c/v_{\text{max}}$ for the $\dot{\gamma}_{\text{eff}} = 308\ s^{-1}$ flow. The data in Figure 43 collapses at small $H$ because the chains are highly confined and have not yet stretched away from their equilibrium configuration. These highly confined chains move at a velocity greater than the average imposed fluid velocity because they are excluded from regions near the walls. After the initial decrease for small $H$, the $v_c/v_{\text{max}}$ begins to increase due to hydrodynamic depletion effects. Since the local shear rate is proportional to $\dot{\gamma}_{\text{eff}}/H$, as $H \rightarrow \infty$, we expect $v_c$ to again decrease and approach the average imposed axial fluid velocity, $v_{\text{ave}} = 0.47707v_{\text{max}}$. There will be a local maximum in $v_c/v_{\text{max}}$ at some value $H = H_{\text{max}}(\dot{\gamma}_{\text{eff}}, L)$, although Figure 43 suggests that $H_{\text{max}}$ may be independent of chain contour length, $L$. An accurate determination of $H_{\text{max}}(\dot{\gamma}_{\text{eff}}, L)$ through simulation may provide a useful blueprint for the design of microcapillary hydrodynamic chromatography devices.

Above, we have presented simulation results for DNA chains in pressure-driven flow through micron-scale channels incorporating full hydrodynamic interactions. In the next section we will discuss the migration mechanisms within the context of a simple dumbbell model. Before entering that discussion we first present a brief comparison between our full hydrodynamic model and some approximate models. Figure 44 shows the steady-state center of mass distribution for a 42 $\mu m$ chain in a 10.6 $\mu m$ channel ($H/S_b = 9.6$) at a flow strength of $\dot{\gamma}_{\text{eff}} = 308\ s^{-1}$. Results are shown for our full model (Figure 44.a) and three approximate formulations: bulk hydrodynamic interactions model (Figure 44.b), a reduced mobility model (Figure 44.c), and a free-draining model (Figure 44.d). The bulk
Figure 43: Average chain axial velocity (reduced by the maximum fluid velocity) as a function of channel size. Symbol colors correspond to flow strengths of $\dot{\gamma}_{\text{eff}} = 3.98$ s$^{-1}$ (white), $\dot{\gamma}_{\text{eff}} = 30.8$ s$^{-1}$ (red) and $\dot{\gamma}_{\text{eff}} = 308$ s$^{-1}$ (blue). Symbol types correspond to chain lengths of 21 $\mu$m ($\bigcirc$), 42 $\mu$m ($\Box$) and 84 $\mu$m ($\bigdiamond$). The dashed line represents the average imposed axial fluid velocity.
hydrodynamic interaction model predicts a minimum in concentration at the centerline of the channel followed by a monotonically increasing concentration toward the walls (with the expected steric depletion at the walls); the direction of migration in the bulk hydrodynamic interaction model is opposite that of the full model, and the magnitude is significantly less. The reduced mobility predicts a very slight increase in concentration at the centerline, while the free-draining models predict no migration at all. Note that all three of the approximate models show a slight narrowing of the steric depletion effect (relative to equilibrium) because the stretched chains can sample nearer the walls (de Pablo et al., 1992). It turns out that the behavior of all these models can be qualitatively explained using a simple kinetic theory dumbbell model of a confined polymer, as we now show.

7.3.4 THEORY OF POLYMER MIGRATION IN RECTILINEAR FLOW: DUMBBELL MODEL

GENERAL FRAMEWORK

In the previous section we demonstrated that hydrodynamic interactions in a polymer solutions flowing through channels of molecular dimension give rise to significant migration effects. We also showed in Figure 44 that different approximations lead to qualitatively different cross-sectional concentration profiles. Here, we look at the migration effect within the context of a simple kinetic theory dumbbell representation of the confined polymer. The polymer is modeled as a simple dumbbell – two beads connected by a spring. The level of description is the same as we have been using in previous sections,
Figure 44: Steady-state center-of-mass distribution $P_c(y, z)$ in the cross section of the channel for 42 $\mu m$ chains in a 10.6 $\mu m$ channel at a flow strength of $\dot{\gamma}_{\text{eff}} = 308$ $s^{-1}$. a) Full hydrodynamic interactions, b) Bulk hydrodynamic interaction, c) Reduced mobility model, d) Free-draining model. Grid line spacing is 2 $\mu m$ in the $yz$-plane and 0.2 for $P_c(y, z)$. 
except that excluded volume interactions are ignored (for simplicity). The configurational probability distribution function ($\Psi$) for the polymer is a function of time ($t$), the position of the center of mass ($r_c = [r_1 + r_2]/2$) in physical space and the connector vector ($q = r_2 - r_1$). The governing equation for $\Psi(r_c, q, t)$ is (Bird et al., 1987)

$$\frac{\partial \Psi}{\partial t} = -\frac{\partial}{\partial r_c} \cdot (\dot{r}_c \Psi) - \frac{\partial}{\partial q} \cdot (\dot{q} \Psi),$$  \hspace{1cm} (202)

where the momentum-space averaged velocity of the center of mass of the dumbbell is given by (Bird et al., 1987)

$$2 \dot{r}_c = \sum_{i=1}^{2} v_i + \frac{1}{k_B T} \sum_{i,j=1}^{2} D_{ij} \cdot f_j^s - \sum_{i,j=1}^{2} D_{ij} \cdot \frac{\partial}{\partial r_j} \ln \Psi,$$  \hspace{1cm} (203)

and the time rate of change of the connector vector by (Bird et al., 1987)

$$\dot{q} = [v_2 - v_1] + \frac{1}{k_B T} \sum_{j=1}^{2} (D_{2j} - D_{1j}) \cdot f_j^s - \sum_{j=1}^{2} (D_{2j} - D_{1j}) \cdot \frac{\partial}{\partial r_j} \ln \Psi.$$  \hspace{1cm} (204)

Integrating Eq. (202) over $q$ and defining

$$\Psi(r_c, q, t) = C(r_c, t) \hat{\Psi}(r_c, q, t),$$  \hspace{1cm} (205)

$$C(r_c, t) = \int \Psi(r_c, q, t) \, dq,$$  \hspace{1cm} (206)

gives the governing equation for the center of mass probability distribution, $C(r_c, t)$,

$$\frac{\partial C}{\partial t} = -\frac{\partial}{\partial r_c} \cdot \langle \dot{r}_c \rangle = -\frac{\partial}{\partial r_c} \cdot \langle \dot{r}_c \rangle C,$$  \hspace{1cm} (207)

where $\langle \dot{r}_c \rangle = \langle \dot{r}_c \rangle C$ is center of mass flux integrated over the internal degrees of freedom of the molecule, and the angle brackets are defined through

$$\langle \langle A \rangle \rangle = \int A \Psi \, dq = C \langle A \rangle,$$  \hspace{1cm} (208)

$$\langle A \rangle = \int A \hat{\Psi} \, dq.$$  \hspace{1cm} (209)
Defining \( f^s = f^s_1 = -f^s_2 \) and using Eq. (160) along with

\[
\frac{\partial}{\partial r_1} = \frac{1}{2} \frac{\partial}{\partial r_c} - \frac{\partial}{\partial q}, \tag{210}
\]
\[
\frac{\partial}{\partial r_2} = \frac{1}{2} \frac{\partial}{\partial r_c} + \frac{\partial}{\partial q}, \tag{211}
\]

we can express Eq. (203) as

\[
\dot{r}_c = v_c + \frac{1}{2} \Omega \cdot f^s + \frac{1}{2} \hat{D} \cdot \frac{\partial}{\partial q} \ln \Psi - \frac{1}{4} \hat{D} \cdot \frac{\partial}{\partial r_c} \ln \Psi, \tag{212}
\]
\[
\Omega = (\Omega_{11} - \Omega_{22}) + (\Omega_{21} - \Omega_{21}^T), \tag{213}
\]
\[
\hat{D} = k_BT\Omega, \tag{214}
\]
\[
\hat{\Omega} = (D_{11} + D_{22}) + (D_{21} + D_{21}^T), \tag{215}
\]
\[
v_c = \frac{1}{2} (v_1 + v_2), \tag{216}
\]

where we have made use of Eqs. (160) and (174). Multiplying Eq. (212) by \( \Psi \) and integrating over the internal coordinates, one can show that

\[
\langle \langle \dot{r}_c \rangle \rangle = \frac{1}{2} \left[ 2 \langle v_c \rangle + \langle \Omega \cdot f^s \rangle \right] C
\]
\[
- \frac{1}{4} \left[ 2 \left( \frac{\partial}{\partial q} \cdot (D_{11} - D_{22}) \right) - \left( \frac{\partial}{\partial r_c} \cdot (D_{11} + D_{22}) \right) + \frac{\partial}{\partial r_c} \cdot \langle \hat{D} \rangle \right] C
\]
\[
- \frac{1}{4} \langle \hat{D} \rangle \cdot \frac{\partial C}{\partial r_c}. \tag{217}
\]

The steady-state solution (\( \langle \langle \dot{r}_c \rangle \rangle = 0 \)) of Eq. (207) using Eq. (217) and appropriate boundary conditions gives the steady-state mass distribution \( C(r_c) \) in physical space. Note that the center of mass distributions presented in Section 7.3.3 represent numerical solutions to this same problem for a much more complicated model of the molecule.

Eq. (217) is a general dilute solution result for a dumbbell representation of a Brownian molecule in an arbitrary flow field and geometry. We refer to the terms proportional to \( C \) as “drift” contributions and the term proportional to the gradient of \( C \) as a “diffusive”
contribution. The first line in Eq. (217) represents a deterministic contribution to the drift term, while the second line is a Brownian contribution to the drift term. The last line represents standard Fickian diffusion – note that $\langle \hat{D} \rangle / 4$ is the Kirkwood diffusivity (Bird et al., 1987), averaged over the internal coordinates of the molecule. Eq. (217) indicates that a Brownian molecule in rectilinear flow in a confined geometry can experience a drift normal to the imposed streamlines, and this drift can have both deterministic and Brownian contributions. Both of these mechanisms have been discussed in the literature, which we will review shortly. First we give a brief physical explanation of the drift terms appearing in Eq. (217).

For rectilinear flow, the $\langle v_c \rangle C$ term represents pure convection along imposed streamlines. The $\langle \hat{\Omega} \cdot f^s \rangle C$ term indicates that a molecule in tension (or compression) near a solid boundary can experience a deterministic drift which is not necessarily along the imposed streamlines. The three drift terms appearing in second line of Eq. (217) are Brownian in nature and arise from spatial variations in the hydrodynamic interactions. The first two of these terms are due to spatial variations in bead mobility, and vanish when wall contributions to the hydrodynamic interaction tensor are ignored. The third is due to spatial variations in bead mobility as well as spatial variations in bead-bead hydrodynamic interactions. For the special case of homogeneous rectilinear flow, Eq. (217) becomes

$$\langle (\dot{r}_c) \rangle_{\text{homo}} = \frac{1}{2} \left[ 2 \langle v_c \rangle + \langle \hat{\Omega} \cdot f^s \rangle \right] C - \frac{1}{2} \left( \frac{\partial}{\partial q} \hat{D} \right) C - \frac{1}{4} \left( \hat{D} \right) \cdot \frac{\partial C}{\partial r_c}.$$  (218)

In the absence of wall hydrodynamic interactions, Eq. (218) predicts no migration for homogeneous rectilinear flow.

Eq. (207) has been the starting point for many investigations into migration effects in flowing dilute solutions of long flexible polymers. Although some investigations (Sekhon
have employed bulk hydrodynamic interactions (Oseen-Burgers), many have ignored hydrodynamic interactions altogether. We are aware of only one qualitative discussion (Jhon and Freed, 1985) considering a simple first-order account of wall hydrodynamic interaction for a flexible polymer chain.

**CHAIN MIGRATION NEGLECTING WALL HYDRODYNAMIC INTERACTION**

The use of Oseen-Burgers (OB) free-solution hydrodynamics allows considerable simplification of Eq. (217). In free-solution $\Omega_{ii} = \text{constant}$ and $\Omega_{ij}$ is symmetric, yielding (Sekhon et al., 1982)

$$\langle \langle \dot{r}_c \rangle \rangle^\text{OB} = \left[ \langle v_c \rangle - \frac{k_B T}{2} \frac{\partial}{\partial r_c} \cdot \langle \Omega_{12}^\text{OB} \rangle \right] C - \frac{k_B T}{2 \zeta} \langle I + \zeta \Omega_{12}^\text{OB} \rangle \cdot \frac{\partial C}{\partial r_c}.$$  \hfill (219)

Deterministic cross-stream migration in rectilinear flow is not predicted by this model, although there is cross-stream Brownian drift due to coupling of hydrodynamics with spatial variations in the distribution of polymer configurations.

Sekhon et al. considered the case of bulk hydrodynamic interactions (Eq. (219)) in rectilinear slit flow, $v_x(y_c) = f(y_c)$, where $y_c$ is the distance from the centerline. In this case $\langle \Omega_{12}^\text{OB} \rangle$ can be written in the general form

$$\langle \Omega_{12}^\text{OB} \rangle(y_c) = \begin{pmatrix} a_{11}(y_c) & a_{12}(y_c) & 0 \\ a_{12}(y_c) & a_{22}(y_c) & 0 \\ 0 & 0 & a_{33}(y_c) \end{pmatrix}. \hfill (220)$$

At steady-state $C$ is a function of $y_c$ only, and the steady-state wall-normal component of
\( \langle \dot{r}_c \rangle \) is given by
\[
\langle \dot{r}_c \rangle_y = -\frac{k_B T}{2} \frac{\partial a_{22}(y_c)}{\partial y_c} C(y_c) - \frac{k_B T}{2\zeta} (1 + \zeta a_{22}(y_c)) \frac{\partial C(y_c)}{\partial y_c} = 0, \tag{221}
\]
from which Sekhon et al. concluded that cross-stream migration is possible. Although Sekhon et al. stopped here, we can continue the analysis a bit further. We rewrite Eq. (221) as
\[
\frac{\partial \ln C}{\partial y_c} = -\zeta (1 + \zeta a_{22})^{-1} \frac{\partial a_{22}}{\partial y_c}, \tag{222}
\]
and note that for free-solution Oseen-Burgers hydrodynamic interactions \( a_{22} \propto q^{-1}(1 + q_0^2/q^2) \), where \( q = |q| \). Considering the flow to be parabolic, one can readily deduce that \( a_{22} \) is always positive and decreases monotonically from a maximum at the centerline.

The use of bulk hydrodynamic interactions therefore predicts migration toward the walls leading to a minimum in \( C(y_c) \) at the centerline of the channel (note that \( \partial a_{22}/\partial y_c = 0 \) at the centerline of the channel). \( C(y_c) \) increases monotonically toward the channel walls. This prediction compares well to the center of mass distribution in Figure 44.b, obtained from our detailed chain simulations using bulk hydrodynamic interactions. Brunn and Chi (1984); Brunn (1984) numerically solved for the steady-state \( C(y_c) \) for a dumbbell through a first order perturbation analysis using Oseen-Burgers free-solution hydrodynamic interactions and also found migration toward the walls. Interestingly, Brunn also found that using preaveraged Oseen-Burgers hydrodynamics predicted depletion at the walls.

Ignoring hydrodynamic interactions altogether \( (\Omega_{ii} = \Omega_{ij} = 0) \), but assuming a configuration dependent friction coefficient (CDFC) (Hinch, 1977), \( \zeta = \zeta_0 g(q) \) gives (Fuller and Leal, 1981)
\[
\langle \dot{r}_c \rangle_{\text{CDFC}} = \left[ \langle v_c \rangle - \frac{k_B T}{2\zeta_0} \frac{\partial}{\partial r_c} \cdot \langle g^{-1}(q) \rangle \right] C - \frac{k_B T}{2\zeta_0} \langle g^{-1}(q) \rangle \cdot \frac{\partial C}{\partial r_c}, \tag{223}
\]
and the steady-state concentration is determined from

\[
\frac{\partial \ln C}{\partial y_c} = -\frac{1}{\left\langle g^{-1}(q) \right\rangle} \frac{\partial \left\langle g^{-1}(q) \right\rangle}{\partial y_c}.
\] (224)

Since the friction factor \( g \) is positive and generally (Hinch, 1977) taken to be proportional to \( q \), \( \left\langle g^{-1} \right\rangle \) is again a maximum at the centerline and decreases toward the wall, giving the same qualitative results as obtained from the use of bulk hydrodynamic interactions. This is not a coincidence; if we ignore wall hydrodynamic interaction in Eq. (217), the steady-state mass flux in the wall-normal direction results in

\[
\frac{\partial \ln C}{\partial y_c} = -\frac{1}{\left\langle \hat{D}_{yy} \right\rangle} \frac{\partial \left\langle \hat{D}_{yy} \right\rangle}{\partial y_c},
\] (225)

where \( \hat{D}(q) \) is proportional to the Kirkwood diffusivity of the dumbbell. The diffusivity of the dumbbell decreases with increasing \( q \) whether we use bulk hydrodynamics or the CDFC model. We note here that Seo et al. (1996) used a preaveraging for the configuration-dependent friction coefficient model and predicted the opposite – depletion at the wall. Note also that if one uses a friction coefficient that decreases with increasing \( q \) (as would be appropriate for a model of a concentrated solution or melt), Eq. 225 predicts depletion near the wall.

Finally, ignoring hydrodynamic interactions altogether and assuming a constant bead friction coefficient, gives the free-draining (FD) model result

\[
\left\langle \left\langle \dot{r}_c \right\rangle \right\rangle^{FD} = \langle \dot{v}_c \rangle C - \frac{k_B T}{2\zeta} \frac{\partial C}{\partial r_c},
\] (226)

which predicts no cross-stream migration in rectilinear flow. This prediction is consistent with the results of Figure 44.d, which shows the mass distribution for a free-draining chain.
CROSS-STREAM MIGRATION WITH WALL HYDRODYNAMIC INTERACTION

We now turn our attention back to the general expression for the center of mass flux (Eq. (217)), and incorporate the effect of walls on chain migration. For rectilinear channel flow, the deterministic (DET) portion of $\langle \langle \dot{\mathbf{r}}_c \rangle \rangle$ in the wall-normal direction is given by

$$
\langle \langle \dot{\mathbf{r}}_c \rangle \rangle_{y}^{DET} = \langle \mathbf{\Omega} \cdot \mathbf{f}^s \rangle_y(y_c) \, C(y_c).
$$

(227)

Recall that $\mathbf{\Omega}$ (Eq. (213)) is proportional to the difference in bead mobilities and also proportional to the asymmetric portion of the hydrodynamic interaction between the two beads, $\Omega_{12} - \Omega_{12}^T$. Recall also that $\mathbf{\Omega} = 0$ when wall hydrodynamic interaction is ignored. Now suppose for the moment we ignore the Brownian drift terms in Eq. (217) and allow the deterministic and Fickian terms to balance at steady-state yielding

$$
\frac{\partial \ln C}{\partial y_c} = \langle \mathbf{\Omega} \cdot \mathbf{f}^s \rangle_y.
$$

(228)

To get an idea of the magnitude and sign of the deterministic contribution to migration, we consider rectilinear shear flow over a single infinite plane wall. As mentioned in Appendix A, for the case of point force hydrodynamics near an infinite plane wall, an analytical expression is available for the hydrodynamic interaction tensor, $\mathbf{\Omega} = \mathbf{\Omega}_{pw}^{PF}$. We can use the simple dumbbell model along with $\mathbf{\Omega}_{pw}^{PF}$ to gain some insight into the origins of the wall-normal drift. The Green’s function for a point force located at $\mathbf{x}_j = (x_j, y_j, z_j)^T$ a distance $y_j$ above an infinite plane wall can be expressed as (Pozrikidis, 1997)

$$
\mathbf{\Omega}_{pw}^{PF}(\mathbf{x}, \mathbf{x}_j) = \mathbf{\Omega}_{pw}^{PF}(\mathbf{x} - \mathbf{x}_j) - 2y_j \mathbf{\Omega}_{SD}(\mathbf{x} - \hat{\mathbf{x}}_j) + 2y_j^2 \mathbf{\Omega}_{PD}(\mathbf{x} - \hat{\mathbf{x}}_j),
$$

(229)

where $\hat{\mathbf{x}}_j = (x_j, -y_j, z_j)^T$ is the position of the “image” of particle $j$. The first two terms on the right are the point force solutions for the particle and its image in free solution,
Figure 45: Model system used to obtain the results in Figure 46.
while the last two terms involve the image Stokeslet doublet $\Omega^{SD}$ and image potential dipole $\Omega^{PD}$ in free solution. The hydrodynamic interaction tensor is then given by

$$
\Omega_{ij} = \begin{cases} 
\Omega_{ij}^{PF}(r_i, r_j) & \text{for } i \neq j, \\
\Omega_{ij}^{PF}(r_i, r_j) - \Omega_{ji}^{PF}(r_i, r_j) & \text{for } i = j.
\end{cases}
$$

(230)

Jhon and Freed (1985) have also considered the deterministic contribution to the drift of a dumbbell in rectilinear flow near a wall. Those authors used the first two terms of Eq. (229) (the point force and its image) to obtain a qualitative picture of the hydrodynamic drift of the dumbbell center of mass. Ignoring the last two terms in Eq. (229) gives a “Green’s function” that violates the reciprocity requirement for the Green’s function of a self-adjoint operator ($\Omega_{ij} \neq \Omega_{ji}^T$). This is in essence an artificial symmetry breaking, whose consequences are unknown. The work presented here for a dumbbell near an infinite plane wall (as well as the general method outlined in earlier sections) does satisfy the identity $\Omega_{ij} = \Omega_{ji}^T$. Jhon and Freed (1985) did qualitatively state that drift away from the wall was possible, but did not give specific examples of how this drift depended on intramolecular configuration and position relative to the wall. Here, we address these issues directly.

In simple shear, the flexible polymer stretches and “flips” repeatedly. For the case of an infinite plane wall, the wall-normal drift of our dumbbell model can be characterized by three variables – the magnitude of the connector vector ($q$), the angle ($\theta$) that the connector vector makes with the wall, and the distance ($y_1$) of bead 1 from the wall. This representation is illustrated in Figure 45.

Using this crude model, we can easily compute how the magnitude and sign of $(\hat{\Omega} \cdot f^*)_y$ depends on molecular extension, orientation relative to the wall, and distance from the wall. The results are illustrated in Figure 46, which shows $v_{c,y} = (\hat{\Omega} \cdot f^*)_y$ as a function
Figure 46: Wall-normal center of mass drift as a function of distance from the wall for various values of molecular extension and orientation. (a) $\theta = 0$, (b) $\theta = \pi/8$, (c) $\theta = \pi/4$, (d) $\theta = \pi/2$. The arrow indicates direction of increasing $q$; values of $q = \{0.3, 0.4, 0.5, 0.6, 0.7\}q_o$ are shown. For this model, $q_o = 2.1 \mu m$ and $\langle q^2 \rangle^{1/2} \approx 0.225q_o$. 
of $y_1$ for various molecular orientations and extensions. We only show results for values of $0 \leq \theta \leq \pi/2$ due to symmetry; $v_{c,y}(q, \theta, y_1) = v_{c,y}(q, \pi - \theta, y_1)$ for the dumbbell model. In these results the dumbbell corresponds to one spring from our DNA model (spring contour length $q_o \approx 2.1 \mu m$) with no excluded volume. Figure 46.a shows $v_{c,y}$ as a function of $y_1$ for a dumbbell oriented parallel to the wall for different values of $q$. For this particular orientation, the drift is always away from the wall. Figures 46.b through 46.d show results for increasing values of $\theta$. As $\theta$ increases, drift towards the wall is observed for dumbbells close enough to the wall. When $\theta$ becomes large enough, the drift is always toward the wall. Recall that $\bar{\Omega}$ (Eq. (213)) is proportional to the mobility difference between the two beads of the dumbbell (this contributes a drift toward the wall), and also proportional to the non-symmetric portion of the hydrodynamic interaction between the two beads (this contributes a drift away from the wall); the direction of the deterministic migration is determined from a competition between these two terms. The orientations that give rise a negative $v_{c,y}$ are not particularly relevant for the case of simple shear near a plane wall, as $\langle \theta \rangle$ is fairly small for $\dot{\gamma}_{\text{eff}} \lambda_1 > 1$ ($\langle \theta \rangle \to 0$ as $\dot{\gamma}_{\text{eff}} \to \infty$). Even during the flipping process when $\theta$ passes through $\pi/2$ (orientation perpendicular to the wall), the magnitude of $q$, and therefore $f^*$, is small; the magnitude of $v_{c,y} \to 0$ as $|f^*| \to 0$.

From the preceding paragraph it it clear that for rectilinear channel flow $(\bar{\Omega} \cdot f^*)_y$ is positive near the wall and decreases toward the centerline of the channel, and from Eq. (228) we conclude that deterministic migration will be toward the centerline when full wall hydrodynamic interactions are considered. The results of Section 7.3.3 demonstrate that for the channel sizes and chain lengths considered in this study, the deterministic migration is the dominant contribution and is directed away from the wall.
Figure 47: The wall-normal component of the velocity field due to a point force located at $(x, y) = (-5a, 4a)$ acting in the positive $x$ direction. The red and blue areas indicate regions where the wall-normal velocity is positive (away from wall) and negative (towards the wall), respectively. Also shown is a “bead” of radius $a$ located at $(x, y) = (5a, 4a)$ – this can be thought of as the other end of a relaxing dumbbell oriented parallel to the wall.
The last model we will analyze with the simple dumbbell model is the reduced mobility (RM) model (Eq. (176)). For this model Eq. (217) can be written as

\[
\langle \dot{\mathbf{r}}_{c}^{RM} \rangle = \frac{1}{2} \left[ 2 \langle \mathbf{v}_{c} \rangle + \langle (\mathbf{\Omega}_{11} - \mathbf{\Omega}_{22}) \cdot \mathbf{f}^s \rangle \right] C \\
+ \frac{1}{4} \left[ 2 \left( \frac{\partial}{\partial r_1} \cdot \mathbf{D}_{11} \right) + 2 \left( \frac{\partial}{\partial r_2} \cdot \mathbf{D}_{22} \right) - \frac{\partial}{\partial r_1} \cdot \langle \mathbf{D}_{11} \rangle - \frac{\partial}{\partial r_2} \cdot \langle \mathbf{D}_{22} \rangle \right] C \\
- \frac{1}{4} \langle \mathbf{D}_{11} + \mathbf{D}_{22} \rangle \frac{\partial C}{\partial r_c}.
\]

We already know that deterministic migration due to differences in bead mobility is always toward the wall. However, near the wall the local shear rate is high and the difference in bead mobilities is therefore small; deterministic migration to the wall is weak. Since bead mobilities decrease toward the wall, the first two terms in the Brownian contribution to migration in Eq. (231) yield migration toward the centerline, while the last two terms yield migration toward the wall. If one assumes that \(|\langle \partial/\partial r_i \cdot \mathbf{D}_{ii} \rangle| \approx |\partial/\partial r_i \cdot \langle \mathbf{D}_{ii} \rangle|\) then if migration occurs at all, it should be toward the centerline. This simple analysis agrees qualitatively with the mass distribution in Figure 44.c, obtained from our detailed simulations of a reduced mobility chain. The weak migration effect in Figure 44.c indicates that spatial dependence of the bead mobilities plays a minor role in migration of flexible polymers in rectilinear channel flow.

Recognizing that the main contribution to Brownian migration comes from hydrodynamic interaction between beads (the last term in the second line of Eq. (217)), one concludes that Brownian migration is toward the wall; this was demonstrated in Section 7.3.4. From this one concludes finally that migration of long flexible polymers away from the walls is “deterministic” (aside from the entropic origin of the spring force) and is due to asymmetry in the hydrodynamic interaction between different portions of the confined
polymer. This asymmetry is illustrated in Figure 47, which shows the wall-normal component of the velocity field due to a point force acting parallel to an infinite plane wall. This can be interpreted as the wall-normal flow set up by one end of a relaxing dumbbell oriented parallel to the wall. The other end of the dumbbell (illustrated as a white circle of radius $a$) experiences a drift away from the wall because it lies in a region where the flow has a component away from the wall.

7.3.5 CONCLUSIONS

We have performed simulations of DNA (contour length $\approx 10 - 126 \mu m$) using a model which includes excluded volume and hydrodynamic interactions in a confined geometry. The behavior of these DNA chains was examined in pressure-driven flow through micron-scale channels (channel width $\approx 1 - 10 \mu m$).

The steady-state stretch of DNA chains was examined as a function of channel width and flow strength. The flow strength needed to stretch a chain away from its equilibrium length was shown to increase with decreasing channel width. This is fairly well-explained using a simple blob picture.

The mass distribution of the DNA chains in the cross-section of the channel was examined as a function of molecular weight, channel width and flow strength. A significant hydrodynamically-induced depletion of DNA was observed toward the wall. The thickness of the depletion layer was shown to increase with increasing molecular weight. The result is that higher molecular weight chains are more concentrated in the center of the channel where the imposed axial fluid velocity is higher. This causes higher molecular weight chains to move with a higher average axial velocity than lower molecular weight chains, resulting in separation based on molecular weight.
From the simple analysis of a kinetic theory dumbbell model of a confined polymer and simulations of the more complex multi-bead model, we draw the following qualitative conclusions for dilute flexible polymer solutions in inhomogeneous rectilinear channel flow:

1. There is a “deterministic” hydrodynamic drift away from the walls due to asymmetry of hydrodynamic interactions between different portions of the confined polymer. This asymmetry is due to wall contribution to the hydrodynamic interactions. This effect is expected to be strongest near walls due both to proximity to the wall and high local shear rate (and therefore polymer extension).

2. There is a Brownian drift (due to coupling of the hydrodynamic interactions with spatial variations in the distribution of polymer configurations) away from the centerline.

3. The balance of these two effects, along with Fickian diffusion, determines the steady-state concentration profile. This balance in general leads to a non-monotonic concentration profile across the channel.

Our full model results indicate that, for our chain lengths and channel widths, the competition between deterministic drift (wall hydrodynamics) and Brownian drift result in a minimum in concentration at the centerline, a maximum in concentration near the centerline, followed by a monotonically decreasing concentration toward the walls with substantial depletion of polymer concentration occurring toward the walls. The depletion layer grows with increasing flow strength and increasing molecular weight.
Chapter 8

CURRENT AND FUTURE WORK

We have presented a systematic investigation into the numerical solution of complex fluid flow problems in homogeneous flows, macroscopic flows, and flows in microfluidic devices. A key goal of this research group is the development of software capable of exploratory design of microfluidic devices involved in the transport of macromolecules. Simulation techniques have been already been extended to multi-chain simulations in microchannels with adsorbing/desorbing surfaces. This includes the ability to simulate the flow macromolecular solutions through microchannels with polymer chains adsorbed to the surface (polymer brushes). Related work in the group includes

1. Hongbo Ma is looking at the flow of DNA into a small pore from a large reservoir. This has biological applications as well as a potential for DNA sequencing. Parameters include flow strength, pore size and molecular weight. Simulations are used to examine effect of flow on molecular configuration as a function of distance from pore entrance. Simulations also enable one to predict which portion of the chain is most likely to enter the pore first, and the probability of entering the pore for a
given flow strength.

Hongbo is also continuing simulations of DNA chains in microchannels. He is currently looking at how pulsing the flow on and off affects migration of DNA molecules. The idea here is to periodically shut off the flow and allow the molecules to begin to diffuse back to their (uniform) equilibrium concentration profile. Since the smaller ones will diffuse faster, this could in principle lead to enhanced separation of different molecular weight chains.

2. Chris Stoltz has developed methods to study electrostatic effects on macromolecular dynamics in free-solution. He has incorporated counterions and full periodic hydrodynamic interactions between both chain segments and counterions. Electrostatics play an important role in biological systems, including condensation of DNA for packaging in viruses. Chris is currently examining the effect of charge distribution and strength on relaxation dynamics of DNA. Also under investigation is the effect of discretization on the static and dynamic properties of DNA. For example, suppose one has a charge $q$ on one “bead” of the DNA chain. Should the counterions which correspond to this section of the DNA molecule also be modeled as a single bead with charge $q$, or should they be modeled as $N_{ion}$ beads each with charge $q/N_{ion}$? What should be the size ratio of DNA “bead” to a counterion “bead”?

Future work may include

- Effect of concentration. The code is already set up for binary systems with an arbitrary number of chains of either molecular weight. However, it could get quite expensive to try to maintain constant concentration in larger channels.
- Effect of microchannel curvature on macromolecular dynamics. This is a fairly straightforward next step. It would be interesting to see how migration due to wall hydrodynamics balances with migration due to streamline curvature in these microchannels.

- Modeling of concatenation reactions – parameter dependence of the distribution of end-to-end distances between different chains, perhaps of different molecular weight.

- Surface absorption/desorption.

- Intramolecular and intermolecular entanglement, as well as entanglements with micro-structures.

- Electrostatic/counterion effects in microchannels, including wall electrostatics.

- It would be interesting to examine other methods for solving the kinetic theory diffusion equation in microfluidic devices. Are there other particle methods (Smoothed Particle Hydrodynamics, for example) that would work, or a deformable mesh method?
Appendix A

APPROXIMATE RPY HYDRODYNAMICS NEAR AN INFINITE PLANE WALL

As discussed in the text, the use of point force hydrodynamics can lead to non-physical behavior, in particular non-positive-semidefiniteness of the diffusion tensor. This occurs when “beads” (which represent many monomer units) of the chain overlap. The overlap itself is not unphysical, and in free solution the point force, or Oseen-Burgers, formulation is typically replaced by Rotne-Prager-Yamakawa (RPY) hydrodynamics. The free solution RPY formulation contains a near field “fix” which guarantees positive-semidefiniteness of the diffusion tensor for all chain configurations. The method presented in this work meets this practical requirement as well as satisfying the reciprocity
requirement $\Omega(x_1, x_2) = \Omega^T(x_2, x_1)$, and can be considered as an approximate RPY formulation for confined geometries. We will now give an example of our formulation for the special case of infinite plane wall.

For non-overlapping beads, the free-solution RPY tensor can be written as

$$\Omega^{\text{RPY}} = \Omega^{\text{PF}} - \frac{2a^2}{3} \Omega^{\text{PD}}, \tag{232}$$

where $\Omega^{\text{PF}}$ and $\Omega^{\text{PD}}$ are the hydrodynamic interaction tensors for a point force (Oseen-Burgers) and potential dipole, respectively (Pozrikidis, 1992). In the presence of an infinite plane wall, we can write

$$\Omega^{\text{RPY}}_{\text{PW}} = \Omega^{\text{PF}}_{\text{PW}} - \frac{2a^2}{3} \Omega^{\text{PD}}_{\text{PW}}, \tag{233}$$

where the subscript PW indicates that these hydrodynamic interaction tensors are now evaluated in the presence of a single infinite plane wall; $\Omega^{\text{RPY}}_{\text{PW}}$ can be considered an approximate RPY hydrodynamic interaction tensor for a particle near an infinite plane. Note that our method is a generalization of this to arbitrary geometries. There are analytical solutions (Pozrikidis, 1992) for both $\Omega^{\text{PF}}_{\text{PW}}$ and $\Omega^{\text{PD}}_{\text{PW}}$. The $\Omega^{\text{PF}}_{\text{PW}}$ term satisfies the reciprocity requirement, but the potential dipole term does not (it is not a point force solution). However, the effect is weak. Consider a point force located at $r_1 = (0, 2a, 0)$ above an infinite plane (plane at $y = 0$), and another point $r_2 = (x, 4a, 0)$, as illustrated in Figure 48. Figure 49.a compares the $yy$-component of $\Omega^{\text{RPY}}_{\text{PW}}(r_1, r_2)$, $(\Omega^{\text{RPY}}_{\text{PW}}(r_1, r_2) + [\Omega^{\text{RPY}}_{\text{PW}}(r_2, r_1)]^T)/2$ (enforcement of reciprocity using Eq. (175)) and $\Omega^{\text{PF}}_{\text{PW}}$ as a function of $x$. Likewise, Figures 49.b and 49.c show the $yx$ and $xx$ components. Two things are clear from Figure 49. First, the potential dipole term is a near field modification of the point force solution. Second, the “non-reciprocal” portion ($[\Omega(x_1, x_2) - \Omega^T(x_2, x_1)]/2$) of the potential dipole
term is short-ranged and very weak (it is difficult to tell the difference between the solid and dotted lines).

Our development of the general method outlined in the text was guided by the observations described above for a particle near an infinite plane. It worth pointing out that we could satisfy the reciprocity requirement by getting the higher order terms from a multipole expansion for two spheres near an infinite plane satisfying no-slip on the spheres and the plane. However, since we are interested in a method which is applicable to general geometries, we choose the approximate RPY formulation described in this paper. Note also that a multipole expansion would not address the issue of “bead”-”bead” overlap, which is accounted for in our approximate RPY formulation.
Figure 48: Example system from which the results in Figure 49 were obtained.
Figure 49: Comparison between $\Omega_{\text{RPY}}^{r1, r2}$ (solid line), $(\Omega_{\text{RPY}}^{r1, r2} + [\Omega_{\text{PRW}}^{r2, r1}]^T)/2$ (dotted line), and $\Omega_{\text{PRW}}^{r1, r2}$ (dashed line). a) $yy$ component, b) $yx$ component, c) $xx$ component.
Appendix B

POSITIVE-SEMIDEFINITENESS OF THE DIFFUSION TENSOR

The formulation presented in Appendix A for a particle near an infinite plane wall ensures a positive-semidefinite diffusion tensor for all chain configurations provided the bead “surfaces” do not overlap with each other or with the wall. When the the free solution portion (Pozrikidis, 1992) of $\Omega^{RPY}_{pw}$ is replaced with the equivalent RPY near field modification (Eq. (163) with Eq. (165)), the resulting diffusion tensor is guaranteed to remain positive-semidefinite for all chain configurations, provided the bead surfaces do not penetrate the wall. In contrast, the general method outlined in the text generates a positive-semidefinite diffusion tensor for all chain configurations (provided, of course, that the interaction sites of the chain remain within the proscribed geometry). However, positive-semidefiniteness is only guaranteed to level of accuracy of the Stokes flow problem which generated the hydrodynamic interaction tensor. In the work presented in Section 7.2 and 7.2, all entries in the diffusion tensor which were less then 0.1% of the
maximum diagonal component of the diffusion tensor were set to zero, which seemed to keep the accuracy of the diffusion tensor consistent with the accuracy of the Stokes flow problem (for our choice of parameters). For robustness, one may wish to guarantee positive-semidefiniteness of the diffusion tensor even in the event that accuracy of the Stokes flow problem is insufficient. In the following we address this issue.

As mentioned above, the Oseen-Burgers formulation is not guaranteed to remain positive-semidefinite for all chain configurations. The reason for this is that the Green’s function for a point force (in any geometry) is a “far-field” solution. For example, the velocity field at \( x^\nu \) due to a point force acting at \( x^\mu \) is given by

\[
 v^\nu_\mu = \frac{1}{k_B T} D^{\nu\mu} \cdot f^\mu ,
\]

which diverges as \( |x^\nu - x^\mu|^{-1} \) in free-solution; in the Oseen-Burgers formulation, the velocity is infinite at the location of the point force. However, the velocity of the bead located at \( x^\nu \) is defined through the Stokes drag

\[
 v^\nu = \frac{1}{k_B T} D^{\nu\nu} \cdot f^\nu .
\]

In free solution, the velocity of bead \( \mu \) is a constant for a given force (independent of position). Note that for two beads close enough together, the use of Oseen-Burgers hydrodynamics results in \( |v^\nu_\mu| > |v^\nu| \); the motion of bead \( \mu \) generates a solvent velocity greater than the velocity of bead \( \mu \). This unphysical “negative viscous dissipation” leads to a non-positive-semidefinite diffusion tensor. As we now demonstrate, it is fairly simple to check if hydrodynamic interaction between two particular beads results in negative viscous dissipation.

The velocity of bead \( \mu \) is given by Eq. (235), while the velocity at the location of bead \( \nu \) due to motion of bead \( \mu \) is given by Eq. (234). The magnitude squared of these
velocities is given by

\[(k_B T)^2 |v_\mu^\mu|^2 = f^\mu \cdot (D^{\mu\mu})^2 \cdot f^\mu \quad (236)\]

\[(k_B T)^2 |v_\mu^\nu|^2 = f^\mu \cdot (D^{\nu\mu})^2 \cdot f^\mu, \quad (237)\]

where \(v_\mu^\mu\) is the velocity of bead \(\mu\) due to a point force on bead \(\mu\), and \(v_\mu^\nu\) is the solvent velocity at bead \(\nu\) due to the point force at bead \(\mu\). Taking the difference and requiring positive viscous dissipation, we obtain

\[(k_B T)^2 \left( |v_\mu^\mu|^2 - |v_\mu^\nu|^2 \right) = f^\mu \cdot \left[ (D^{\mu\mu})^2 - (D^{\nu\mu})^2 \right] \cdot f^\mu \geq 0, \quad (238)\]

This is the definition of positive-semidefiniteness for the \(3 \times 3\) matrix \((D^{\mu\mu})^2 - (D^{\nu\mu})^2\).

We can easily check for positive-semidefiniteness (eigenvalues of a \(3 \times 3\) matrix), and determine if \(D^{\nu\mu}\) (the hydrodynamic interaction tensor for a point force at \(\mu\)) needs to be modified. If \((D^{\mu\mu})^2 - (D^{\nu\mu})^2\) is not positive-semidefinite, the simplest modification is to simply set \(D^{\nu\mu} = D^{\mu\mu}\). Physically, this means that in the absence of any other force acting on bead \(\nu\), bead \(\nu\) moves with the velocity of bead \(\mu\). Note that this gives a symmetric hydrodynamic interaction tensor. For computational efficiency, if \((D^{\mu\mu})^2 - (D^{\nu\mu})^2\) is not positive-semidefinite, one may set \(D^{\nu\mu} = cD^{\mu\mu}\), where \(c < 1\).

The procedure outlined above is fairly straightforward, but there is a sticking point. We can repeat the above argument for a point force acting on bead \(\nu\), rather than bead \(\mu\). The result is

\[(k_B T)^2 \left( |v_\nu^\nu|^2 - |v_\nu^\mu|^2 \right) = f^\nu \cdot \left[ (D^{\nu\nu})^2 - (D^{\mu\nu})^2 \right] \cdot f^\nu \geq 0, \quad (239)\]

and we find that \((D^{\nu\nu})^2 - (D^{\mu\nu})^2\) must also be positive-semidefinite. Since \(D^{\mu\nu} = (D^{\nu\mu})^T\) through reciprocity of the Green’s function (Pozrikidis, 1997), the hydrodynamic
interaction tensor must be chosen such that Eqs. (238) and (239) are satisfied simultaneously. There are many ways to do this. For example, one simple scheme is:

1. If Eq. (238) is not satisfied, set $D^{\nu\mu} = cD^{\mu\mu}$, and $D^{\mu\nu} = (D^{\nu\mu})^T$.

2. If Eq. (239) is not satisfied, set $D^{\mu\nu} = cD^{\nu\nu}$, and $D^{\nu\mu} = (D^{\mu\nu})^T$.

3. Re-check Eq. (238). If not satisfied set $D^{\nu\mu} = cD^{\nu\mu}$, and $D^{\mu\nu} = (D^{\nu\mu})^T$.

4. Re-check Eq. (239). If not satisfied set $D^{\mu\nu} = cD^{\mu\nu}$, and $D^{\nu\mu} = (D^{\nu\mu})^T$.

5. Loop over steps 3 and 4 until Eqs. (238) and (239) are both satisfied.

Note that this is a rather general requirement, which means that one should be able to use this with straight Oseen-Burgers hydrodynamics. This may be advantageous, since there are analytical series solutions for point force hydrodynamics in some geometries. If one were to apply this to point force hydrodynamics, care should be taken that $D^{\mu\mu}$ also be positive-semidefinite for beads very near a surface.
Bibliography


