Macromolecules in Microdevices: Multiscale Simulation of DNA Dynamics in Model Microfluidic Geometries

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ABSTRACT

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 quite different from those in free solution, because of the no-slip boundary condition on the fluid motion. Nevertheless, detailed, predictive computations have not been previously performed. We have incorporated a Brownian dynamics model of DNA into a fully self-consistent computational scheme that simultaneously resolves the macromolecular and fluid (i.e. solvent) dynamics of DNA in a microfluidic channel. The key novel feature of this scheme is the numerical computation of the Green's function for the flow problem, enabling a stochastic solution method that incorporates detailed hydrodynamics and respects the fluctuation-dissipation theorem. With this methodology we study a number of important confinement effects, focusing here on the retardation of relaxation of a chain in small channel.

Keywords: DNA, microfluidic, hydrodynamic interactions, Brownian dynamics, polymer solutions

1 INTRODUCTION

Microfluidic devices rely for their effectiveness on the ability to control the flow and transport of fluids and macromolecules through micron and nanometer scale geometries. In particular, DNA is a sufficiently large and stiff molecule that its dimensions can easily reach the micron scale, thus overlapping with the size regime in which microfluidic devices are made. The work described here forms part of a large-scale computational approach to predicting the transport of complex fluids in microdevices.

We begin by presenting a fully parameterized bead-spring chain model for stained λ-phage DNA flowing in free solution [1], [2]. This model accounts for the finite extensibility of the molecule, excluded volume effects, and fluctuating hydrodynamic interactions (HI) – this last effect is particularly important, because it must be properly included for the model to be predictive in a microfluidic geometry. Parameters are determined from equilibrium experimental diffusion and size data for 21 μm stained λ-phage DNA [4], [5], and are shown to quantitatively predict the longest relaxation time, shear and extensional flow behavior (Figure 1) of that molecule. The model, along with an efficient Brownian Dynamics simulation method [1] is then used to predict the equilibrium and non-equilibrium behavior of DNA molecules up to 126 μm. In particular, the model matches experimental diffusivity data and reproduces known molecular-weight scaling relations (see Figure 2), and can therefore be confidently used to predict the dynamics of DNA of arbitrary molecular weights.

We then incorporate the DNA model described above into a fully self-consistent computational scheme that simultaneously resolves the macromolecular and fluid (i.e. solvent) dynamics of DNA in a microfluidic channel. The key novel feature of this scheme is the numerical computation of the Green's function for the flow problem. This is performed once in a preprocessing step; during the simulation, values are retrieved by finite element interpolation, enabling a stochastic solution method that incorporates detailed hydrodynamics, respects the fluctuation-dissipation theorem and does not require the solution of a flow problem at each time step. With this methodology we present results for the relaxation of a chain in small channel. Other work is in progress regarding the influence of flow and confinement on DNA adsorption to boundaries, and the influence on rates of ligation reaction between DNA strands.

2 DNA MODEL

Motion of a macromolecule in a solvent creates a velocity field in the fluid, and this velocity field in turn affects the motion of the macromolecule. These hydrodynamic interactions (HI) enter the chain dynamics through the Green's function, or hydrodynamic interaction tensor [8], [9], $\mathbf{\Omega}$. For example, the velocity field due to a point force, $\mathbf{f}$, located at $\mathbf{x}_j$ in an infinite domain (no walls) is given by $\mathbf{v}(\mathbf{x}) = \mathbf{\Omega}_{\mathrm{OB}}(\mathbf{x}-\mathbf{x}_j)\cdot\mathbf{f}(\mathbf{x}_j)$, where $\mathbf{\Omega}_{\mathrm{OB}}$ is the Oseen-Burgers hydrodynamic interaction tensor [8], [9]. In this work we replace $\mathbf{\Omega}_{\mathrm{OB}}$ with the Rotne-Prager-Yamakawa (RPY) tensor [1]–[3], [7], $\mathbf{\Omega}_{\mathrm{RPY}}$.

A bead-spring chain model for DNA incorporating HI has been described in previous work [1], [2]. The physical parameters appearing in this model are the con-

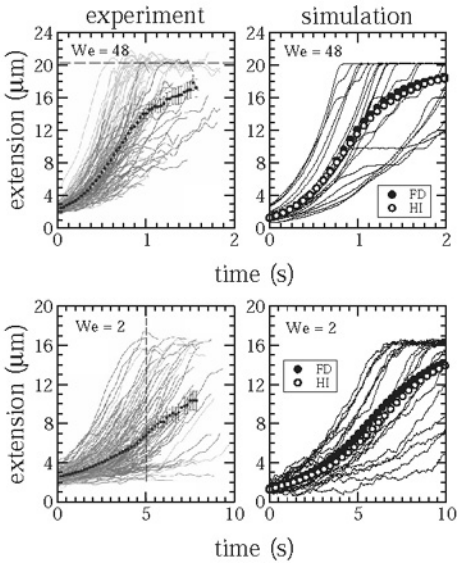

Figure 1: Mean stretch versus time for startup of planar extension. Comparison of our simulations with the experimental data of Smith and Chu (D. E. Smith and S. Chu, Science, **281**, 1335 (1998)) . The thin lines correspond to individual molecular trajectories, while the data points are ensemble averages of these trajectories. All simulations were started from random equilibrium configurations.

tour length, L, the Kuhn length, b_k, the bead hydrodynamic radius, a, and the excluded parameter, v. For stained λ-phage DNA ($L = 21\mu m$), model parameters were determined [2] so that the model produced results which matched available experimental data for the relaxation time [5], λ, the equilibrium stretch [5], X, and the diffusivity [4], D. Details of the simulation, including parameter values, can be found in previous work [1], [2].

Figure 1 shows a comparison of our model with available experimental data [4] on $21\mu m$ DNA in transient planar extension. Simulation results are shown for both the complete (HI) model, and an approximate "free-draining" (FD) model, which neglects hydrodynamic interactions. In these bulk flows (in which wall interactions can be ignored), both the HI and FD models show good agreement with experiment, provided that the friction coefficient for each model is chosen so that that the given model (FD or HI) gives the correct relaxation time [2].

Figure 2 shows the center of mass diffusivity of DNA as a function of molecular weight (MW) obtained from experiment [5] and from our simulations. The HI model shows good agreement with experimental data and theoretical scaling, underscoring the predictive ability of the model. Again, both experiments and simulations were performed in the bulk, where wall interactions could be

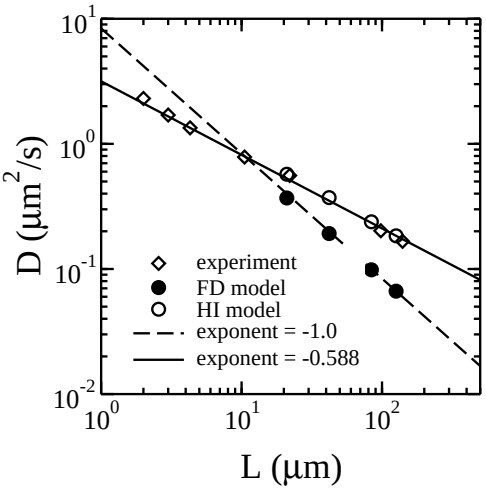

Figure 2: Diffusivity as a function of molecular weight for the FD and HI models. Experimental data is from Smith, Perkins, and Chu (D. E. Smith, T. T. Perkins and S. Chu, Macromolecules, **29**, 1372 (1996)). All data have been scaled to native DNA in $1cP$ solvent (see text). The solid and dashed lines are the theoretical scalings for the HI and FD models, respectively.

ignored.

3 HYDRODYNAMIC INTERACTIONS IN MICROFLUIDIC DEVICES

In microfluidic devices, the velocity field due to motion of the macromolecule must also satisfy the no-slip condition on the walls of the device. For example, consider the velocity field due a point force located at $\mathbf{x}_j$ near a plane wall. As the distance of the point force from the wall decreases, two interesting phenomenon arise as a direct result of the no-slip constraint. The magnitude of the velocity perturbation at the location of the particle *increases*, while the range of the velocity perturbation *decreases*. That is, hydrodynamic interactions between particles are screened, while the mobility the particle is decreased. For general microfluidic devices, the velocity field due to a point force located at $\mathbf{x}_j$ can be written as $\mathbf{v}(\mathbf{x}) = \mathbf{\Omega}(\mathbf{x}, \mathbf{x}_j, \text{geometry}) \cdot \mathbf{f}(\mathbf{x}_j)$, where the Green's function now depends on the absolute position of the point force and details of the geometry.

We can express the Green's function for an arbitrary device as the sum of a bulk solution and a regular solution, $\mathbf{\Omega} = \mathbf{\Omega}_{\text{RPY}} + \mathbf{\Omega}_{\text{R}}$, where we have again used $\mathbf{\Omega}_{\text{RPY}}$ in place of the Oseen-Burgers tensor. The regular solution, $\mathbf{\Omega}_{\text{R}}$, is obtained as the solution to the incompressible Stoke's flow problem with $\mathbf{v} = 0$ on the walls of the device (no-slip on the walls). We use a finite element method to solve the incompressible Stoke's flow problem.

The Green's function for an arbitrary device is obtained on a grid; the physical domain is discretized, and a Green's function, $\mathbf{\Omega}_{mn}$, is constructed relating the velocity field at grid point m due to a point force at grid point n. Now, let point $\mathbf{x}_i$ be located in the volume element associated with grid points $\{m_1, m_2, \ldots, m_p\}$, and let point $\mathbf{x}_j$ be located in the volume element associated with grid points $\{n_1, n_2, \ldots, n_p\}$. Then the Green's function relating the hydrodynamic interaction at point $\mathbf{x}_i$ due to an arbitrary point force at point $\mathbf{x}_j$ is given by the dual interpolation

$$\mathbf{\Omega}(\mathbf{x}_i, \mathbf{x}_j) = \sum_{m=m_1}^{m_p} \sum_{n=n_1}^{n_p} N_m(\mathbf{x}_i) N_n(\mathbf{x}_j) \mathbf{\Omega}_{mn}, \qquad (1)$$

where N_m and N_n are the interpolation functions associated with grid points m and n, respectively. Note that the numerical evaluation of the Green's function is performed only once, in a preprocessing step, for a given microfluidic device.

At first glance, it may appear that one needs $O(N_G^2)$ of the $\mathbf{\Omega}_{mn}$'s, with N_G being the number of grid points in the microfluidic domain. However, in confined geometries, the Green's function decays rather quickly, and in practice one only needs to keep the $\mathbf{\Omega}_{mn}$'s for $|\mathbf{x}_n - \mathbf{x}_m| < x_o$, where x_o is a cutoff distance which depends on the proximity of the point $\mathbf{x}_j$ to the device walls. Thus, in practical applications, one needs $O(N_G)$ of the $\mathbf{\Omega}_{mn}$'s, with the coefficient of proportionality depending on the details of the computational domain.

4 SIMULATION OF DNA IN MICROCHANNELS

We performed simulations of the relaxation of $126\mu m$ DNA in square microchannels of widths $1.6\mu m$, $3.2\mu m$, and $6.4\mu m$. Individual DNA molecules were initially stretched (99% extended) along the centerline of the channels, and allowed to relax to their equilibrium configurations. The stretch (or length) of the molecule in the channel direction was measured as a function of time, and the results are shown in Figure 3. We note three important points.

1. At channel widths beginning at $\sim 1.5\, S_{bulk}$, the equilibrium configuration of the molecules become elongated in the channel direction. S_{bulk} is the bulk equilibrium radius of gyration of $126\mu m$ DNA from simulation.

2. The relaxation of the FD model is virtually unaffected by the physical confinement of the molecule. Even for the smallest channel (width $= 0.7\, S_{bulk}$), where the equilibrium configuration is elongated considerably in the channel direction, the relaxation to the equilibrium stretch is basically the same as for the case of relaxation of the FD model in the bulk.

3. The HI model shows a considerable increase in the relaxation time of the molecule as channel width is decreased. For the smallest channel (width $= 0.7\, S_{bulk}$), the relaxation time of the chain is more than twice that of the bulk value. Note that this decrease in relaxation time is due solely to hydrodynamic interactions – the physical confinement of the molecule does not alter the relaxation time from the bulk value, as can be seen from the results of the FD model.

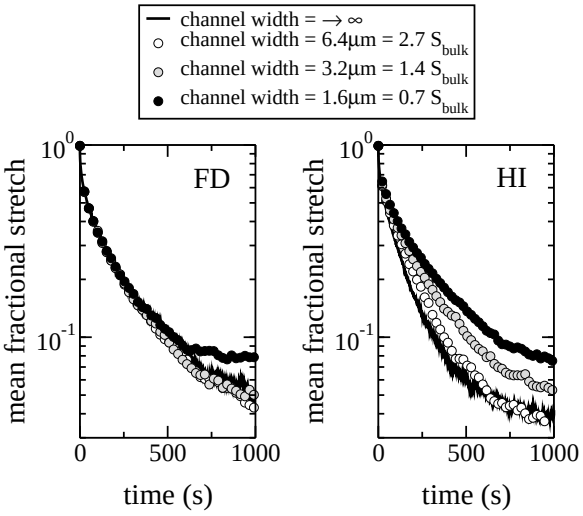

Figure 3: Relaxation of 126 μm DNA molecules in square channels. The bulk data were averaged over 14 molecules. Channel data were averaged over 10 molecules. Channel widths are given in units of μm and in units of the bulk equilibrium radius of gyration (S_{bulk}).

5 CONCLUSIONS

We have incorporated a quantitative Brownian dynamics model of DNA into a fully self-consistent computational scheme that simultaneously resolves the macromolecular and fluid (i.e. solvent) dynamics of DNA in a microfluidic channel. The key novel feature of this scheme is the numerical computation of the Green's function for the flow problem. This is performed once in a preprocessing step; during the simulation, values are retrieved by finite element interpolation, enabling a stochastic solution method that incorporates detailed hydrodynamics, respects the fluctuation-dissipation theorem and does not require the solution of a flow problem at each time step. Simulations were performed on the relaxation of 126 μm DNA molecules in square microchannels. It was found that the relaxation was retarded, relative to the bulk relaxation, even for channel

widths greater than twice the bulk equilibrium radius of gyration. This effect is due to modification of the hydrodynamic interactions, necessary to satisfy the constraint of zero solvent velocity on the walls of the channel.

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