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Effect of internal viscosity on Brownian dynamics of DNA molecules in shear flow

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Abstract

The results of Brownian dynamics simulations of a single DNA molecule in shear flow are presented taking into account the effect of internal viscosity. The dissipative mechanism of internal viscosity is proved necessary in the research of DNA dynamics. A stochastic model is derived on the basis of the balance equation for forces acting on the chain. The Euler method is applied to the solution of the model. The extensions of DNA molecules for different Weissenberg numbers are analyzed. Comparison with the experimental results available in the literature is carried out to estimate the contribution of the effect of internal viscosity.

Keywords: Effect of internal viscosity; Dumbbell model; Brownian dynamics; DNA molecules in shear flow

1. Introduction

Along with the progress in study of biological properties of polymer (such as DNA) molecules, their mechanical features in solutions have also been investigated recently (Smith et al., 1999). Modeling the macromolecules is a key in studying the dynamics of single molecules or solutions. The bead–spring chain model is a widely used model to simulate the chain molecules. If the entropic springs connecting the beads are assumed nonlinear, the governing equations of the system cannot be solved analytically. The development of efficient numerical procedures becomes then necessary. Indeed, the increasing numbers of beads in the molecule chain makes the numerical simulation difficult and time-consuming. However, the dumbbell model with only two beads is known to be computationally efficient. Furthermore, it can yield good results if appropriate factors, such as internal viscosity, hydrodynamic interactions, are considered.

There are two main approaches in investigating polymers in solutions: one is to study the bulk rheology of polymeric solutions (Larson, 2005) and the other is to chase the dynamics of a single molecules in detail (Shaqfeh, 2005). With the ability to examine dynamics of macromolecule chains by fluorescence microscopy measurement developed in recent years, the research on the deformation and dynamics of single molecules has progressed substantially.

In the study of bulk rheology of polymer solutions, the dynamics of the flow of start-up or sudden cessation have been discussed theoretically (Prabhakar et al., 2005; Hua and Schieber, 1995) and experimentally (Smith and Chu, 1998; Goff et al., 2002; Goshen et al., 2005). Hua and Schieber (1995) studied the finitely extensible nonlinear elastic (FENE) dumbbell model with internal viscosity (IV). They discussed the contribution of IV to the bulk rheology of polymer solutions.

On the other hand, by video fluorescence microscopy method, Smith et al. (1999) experimentally studied the fractional extension of λ-phage DNA molecules in steady shear flow for different Weissenberg numbers that denote the dimensionless shear rates. They also calculated the probability distribution of the extension by a statistical method. Although the bulk rheology can be obtained by further computation of the extension of the dumbbell model molecules, the analysis of the extension and its distribution for specific polymers analytically is still limited in the literature (Hur and Shaqfeh, 2000).

In this paper, the FENE dumbbell model with IV proposed by Hua and Schieber (1995) is employed to study the extensions of λ-phage DNA molecules in steady shear flow. After numerical computation, the results of molecule extension and

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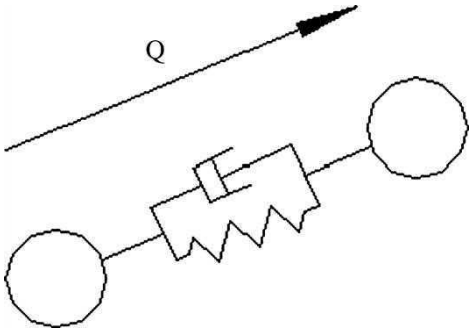

Fig. 1. The dumbbell model with IV.

probability distribution are compared to that obtained in experiment by Smith et al. (1999). The plot of fractional extension for different Weissenberg numbers is also superimposed by that of different models, e.g., the bead–spring model with wormlike spring by Jendrejack et al. (2002) and classical FENE dumbbell model by Hur and Shaqfeh (2000). We show that the FENE dumbbell model with IV can yield good agreement in simulation of λ-phage DNA molecules.

In Section 2, we give a brief description of the dumbbell model with IV and its governing stochastic differential equation. In Section 3, the details of the algorithm to solve the governing equation and the values of parameters are given. The numerical results are presented and discussed in Section 4, followed by concluding remarks.

2. Model for the dynamics of DNA molecules

From classical physics viewpoint, the mass points, beads of the dumbbell model are assumed to be subjected to three forces: (1) a hydrodynamic force, which describes the resistance to motion of the bead bathing in the solvent, (2) a connector force, which is denoted by the spring between the beads, and (3) a Brownian force, which is caused by the rapidly bombarding of the beads by small solvent molecules. The second force is due to the entropic force leading the molecules to their statistical equilibrium positions. It is natural to think that there exists, a forth force, the resistance to motion experienced during changes in the molecule conformation. In what follows, the internal viscosity force is introduced to reflect such intramolecular resistance effect.

We start our consideration with the bead–spring–bead dumbbell model of a single DNA molecule in a Newtonian solvent with viscosity η_s. It is assumed that there is no interaction among the beads of different dumbbells and the viscous drag coefficient is due to the resistance of the flow denoted further by ζ.

For the dumbbell model with internal viscosity, we use a schematic representation of Fig. 1 where $\mathbf{Q}$ is the connector vector of the two beads. The spring force is a function of the configuration vector and configuration velocity. This force is the combination of connector force and the IV force mentioned in the first paragraph of this section. If we consider the finitely extensible model, we get a force law of the following form:

$$\mathbf{F}\left(\mathbf{Q}, \frac{\mathrm{d}\mathbf{Q}}{\mathrm{d}t}\right) = \frac{H\mathbf{Q}}{1-(Q/Q_0)^2} + K\left(\frac{\mathbf{QQ}}{Q^2}\right)\frac{\mathrm{d}\mathbf{Q}}{\mathrm{d}t}, \tag{1}$$

where extension Q defined by $\sqrt{\mathbf{Q}\cdot\mathbf{Q}}$. In Eq. (1), Q_0 is the maximum spring extension, and when the extension of the dumbbell approaches this value, the spring force tends to be infinite; H and K are Hookean constant and interval viscous coefficient, respectively. The second moment tensor $\mathbf{QQ}$ is a key to study the dynamics of the molecules. The first term of the right side of Eq. (1) denotes the FENE spring force proposed by Warner (1972). Considering the forces described above, the equation of one bead's motion can be obtained if the inertial term is neglected. According to the phase-space theorem (Bird et al., 1987), the equation of motion can be given in the form of the equation of the dumbbell configuration vector $\mathbf{Q}$:

$$\frac{\mathrm{d}\mathbf{Q}}{\mathrm{d}t} = \left(\boldsymbol{\delta} - \frac{1}{(\zeta/2K)+1}\frac{\mathbf{QQ}}{Q^2}\right) \cdot \left([\boldsymbol{\kappa}\cdot\mathbf{Q}] - \frac{2kT}{\zeta}\frac{\partial}{\partial\mathbf{Q}}\ln\psi - \frac{2}{\zeta}\frac{H}{1-(Q/Q_0)^2}\mathbf{Q}\right), \tag{2}$$

where ψ is the configuration distribution function of $\mathbf{Q}$ changing with time. The fluid velocity is given by specifying transpose of imposed fluid velocity gradient $\boldsymbol{\kappa} = (\nabla\mathbf{v})^{\mathrm{T}}$, and $\boldsymbol{\delta}$ is unit matrix.

Now we introduce dimensionless parameters:

$$\bar{\mathbf{Q}} = \frac{\mathbf{Q}}{\sqrt{kT/H}}, \qquad \bar{t} = \frac{t}{\lambda} = \frac{4Ht}{\zeta}, \tag{3}$$

so that Eq. (2) could be cast into the dimensionless form:

$$\frac{\mathrm{d}\bar{\mathbf{Q}}}{\mathrm{d}\bar{t}} = \left(\boldsymbol{\delta} - \frac{1}{(\zeta/2K)+1}\frac{\bar{\mathbf{Q}}\bar{\mathbf{Q}}}{\bar{Q}^2}\right) \cdot \left([\lambda\boldsymbol{\kappa}\cdot\bar{\mathbf{Q}}] - \frac{1}{2}\frac{\partial}{\partial\bar{\mathbf{Q}}}\ln\psi - \frac{1}{2}\frac{\bar{\mathbf{Q}}}{1-(\bar{Q}/\bar{Q}_0)^2}\right), \tag{4}$$

where $\lambda = \zeta/4H$ is the relaxation time of the molecules and $\sqrt{kT/H}$ is the root-mean-square average size of Hookean dumbbell in one dimension at equilibrium. For convenience, the bars over the dimensionless parameters are omitted thereafter without confusions.

Before we get the governing stochastic differential equation, the Smoluchowski equation for this dumbbell model should be deduced, which can be obtained by substituting Eq. (4) in equation of continuity (Bird et al., 1987):

$$\frac{\partial\psi}{\partial t} = -\frac{\partial}{\partial\mathbf{Q}}\cdot\left[\left(\boldsymbol{\delta} - \frac{1}{\varepsilon+1}\frac{\mathbf{QQ}}{Q^2}\right) \cdot \left(\lambda\boldsymbol{\kappa}\cdot\mathbf{Q} - \frac{1}{2}\frac{\mathbf{Q}}{1-(Q/Q_0)^2}\right)\psi\right] + \frac{1}{2}\frac{\partial}{\partial\mathbf{Q}}\left(\boldsymbol{\delta} - \frac{1}{\varepsilon+1}\frac{\mathbf{QQ}}{Q^2}\right)\cdot\frac{\partial}{\partial\mathbf{Q}}\psi, \tag{5}$$

where the internal viscosity parameter is defined as $\varepsilon = 2K/\zeta$.

With the Ito interpretation we can obtain the equivalent stochastic differential equation of Eq. (5) (see, e.g., Hua and

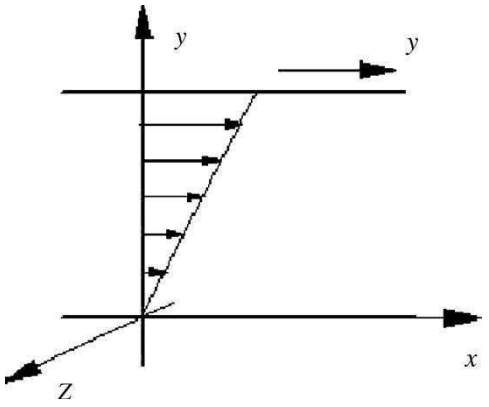

Fig. 2. The shear flow.

Schieber, 1995):

$$\mathrm{d}\mathbf{Q} = \left[\left(\boldsymbol{\delta} - \frac{\varepsilon}{\varepsilon+1}\frac{\mathbf{QQ}}{Q^2}\right)\cdot\left(\lambda\boldsymbol{\kappa}\cdot\mathbf{Q} - \frac{1}{2}\frac{\mathbf{Q}}{1-(Q/Q_0)^2}\right) - \frac{\varepsilon}{\varepsilon+1}\frac{\mathbf{Q}}{Q^2}\right]\mathrm{d}t + \left[\boldsymbol{\delta} - \left(1-\sqrt{\frac{1}{\varepsilon+1}}\right)\frac{\mathbf{QQ}}{Q^2}\right]\mathrm{d}\mathbf{W}_t, \tag{6}$$

where

$$\langle \mathrm{d}\mathbf{W}_t\rangle = \mathbf{0}, \qquad \langle \mathrm{d}\mathbf{W}_t\,\mathrm{d}\mathbf{W}_t\rangle = \delta(t-t')\delta\,\mathrm{d}t. \tag{7}$$

If $\varepsilon = 0$ in Eq. (6), the stochastic differential equation degenerates to case for the classical FENE dumbbell case as in the references by Hur and Shaqfeh (2000) and Ottinger (1996).

In the next section, the algorithm and the specific parameter values will be presented in detail for λ-phage DNA in steady shear flow.

3. Computational implementation

The steady state simple shear flow in the Cartesian coordinate system has the velocity vector $\mathbf{v}$ in three dimensions, with elements $\upsilon_x = \dot{\gamma}y$, $\upsilon_y = 0$, $\upsilon_z = 0$ and where $\dot{\gamma} = \mathrm{d}\upsilon_x/\mathrm{d}y$ is the shear rate (see Fig. 2). In such flow, $\boldsymbol{\kappa}$ can be expressed in linear function of shear rate $\dot{\gamma}$:

$$\boldsymbol{\kappa} = \begin{pmatrix} 0 & \dot{\gamma} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}. \tag{8}$$

So we can adjust the parameter $\lambda\boldsymbol{\kappa}$ in Eq. (6) by tuning Weissenberg number W_i defined by $W_i = \lambda\dot{\gamma}$:

Based on Euler's method, Eq. (6) can be discretized as

$$\mathbf{Q}_{t+\Delta t} = \mathbf{Q}_t + \left[\left(\boldsymbol{\delta} - \frac{\varepsilon}{\varepsilon+1}\frac{\mathbf{Q}_t\mathbf{Q}_t}{Q_t^2}\right)\cdot\left(W_i\cdot\mathbf{Q}_t - \frac{1}{2}\frac{\mathbf{Q}_t}{1-(Q_t/Q_0)^2}\right) - \frac{\varepsilon}{\varepsilon+1}\frac{\mathbf{Q}_t}{Q_t^2}\right]\Delta t + \left[\boldsymbol{\delta} - \left(1-\sqrt{\frac{1}{\varepsilon+1}}\right)\frac{\mathbf{Q}_t\mathbf{Q}_t}{Q_t^2}\right]\Delta\mathbf{W}_t, \tag{9}$$

where Δt is the constant time step and the components of increments $\Delta\mathbf{W}_t = \mathbf{W}_{t+\Delta t} - \mathbf{W}_t$, which are all independent real-valued random variables with mean 0 and variance Δt.

To solve Eq. (9) numerically, we need to give the values of Weissenberg number, W_i, and the maximum spring extension, Q_0. For convenience of comparison with the experimental results of Smith et al. (1999), Weissenberg number, decided by shear rate of the solvent and relaxation time of DNA molecules, is chosen in the range between 0 and 80. Further, the contour length of λ-phage DNA is chosen as the extensibility parameter. So, the maximum spring extension can be expressed as $Q_0 = (N-1)a$, where N and a are the number of beads and the length of a rod of the corresponding bead–rod chain, respectively. All the parameters used in our computation can be found in Table 1. In the computation, the initial values of extension are chosen randomly as Gaussian distribution.

For the FENE dumbbells, there is a certain probability that the maximum allowed spring extension Q_0 is exceeded for any finite time steps. To avoid this problem, we adopt the rejection method that all moves larger than a fixed big value are rejected. Because the extension that is very close to the maximum allowed value will bring bad results, as proposed by Ottinger (1996), we reject all moves which lead to a value of Q^2 larger than

$$(1-\sqrt{\Delta t})Q_0^2, \tag{10}$$

and note that all the variables we use are in dimensionless form.

After giving the initial position, the connector vector will be calculated by the algorithm stated above. Fig. 3 shows the flow chart of the procedure. To obtain a good valuation of the mean extension, 1000 molecules or more should be considered, that

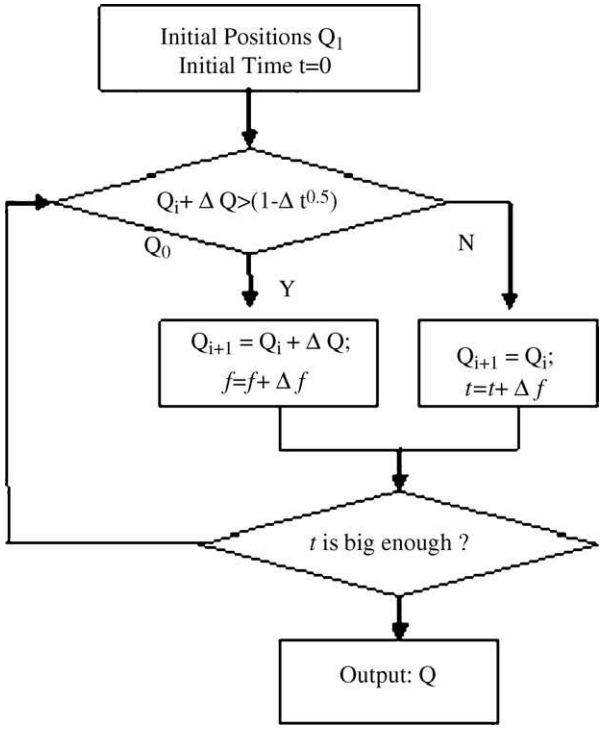

Fig. 3. Flow chart of the simulation.

Table 1
The values of parameters

Parameters	Values	Parameters	Values
Weissenberg number, W_i	0–80	Number of bead–rod chain, N	150
Contour length of λ-DNA, L	22 μm	Length of rod, a	0.147 μm
Time step, Δt	10^{-5} to 10^{-3}	Internal viscosity, ε	0.001

is, the procedure will be performed repeatedly to yield more accurate mean value of the molecule extension.

4. Numerical experiments

In this section, the computational method described in Section 3 will be applied to the solution of Eq. (9) to obtain the extension distributions of the dumbbell of λ-phage DNA molecules for different Weissenberg numbers. Simulation results will be compared with the experimental data by Smith et al. (1999) and the simulation results of FENE model (Hur and Shaqfeh, 2000), as well as with the wormlike spring model with hydrodynamic interactions (Jendrejack et al., 2002).

First, we study the extension's fluctuations along time. After the numerical experiments with the parameters listed in Table 1 for 2×10^6 dimensionless time steps with $\Delta t = 10^{-4}$, we obtained the time history of one DNA molecule extension at $W_i = 6.3$, as demonstrated in Fig. 4. The fractional extension means the ratio between extension of one molecule with its contour length, Q/Q_0. It can be found out from the raw data that there are large fluctuations in the extension of the molecules even at low shear rates.

Next, we study the mean extension of 1000 molecules for different Weissenberg numbers. In the simulation, the molecular extension is projected in the $x-y$ plane to match Smith's experimental data obtained by fluorescence microscopy with intensified video camera perpendicular to the flow-vorticity plane. Every simulation with different W_i has given a specific mean extension value after 10^6 time steps when the average molecular extension appears steady.

In Fig. 5, we compare our simulation obtained with the FENE dumbbell model accounting for internal viscosity with the experimental data by Smith et al. (1999). The dumbbell model without IV (Hur and Shaqfeh, 2000) and the wormlike model with hydrodynamic interactions (Jendrejack et al., 2002) are also superimposed in the plot. The classical FENE dumbbell model cannot predict the extension result when Weissenburg number is high. Our dumbbell model and wormlike model have given better values at high Weissenberg numbers.

When $W_i = 0$, that is, the shear rate of the solvent vanishes, the fluctuations of molecular extension are only caused by the Brownian force bombarding on DNA molecules of small solvent molecules. When W_i increases, the extension reaches an asymptotic plateau as found by Smith et al. (1999) and Hur and Shaqfeh (2000). Our simulation results have better agreement with the experimental data compared to the other two simulations presented in Fig. 5, especially when the value of Weissenberg number is high. We remark that this agreement with available experimental data is obtained with a relatively simple mathematical model where the internal viscosity effects were taken into account.

Finally, we study the probability distribution of extension with the numerical methodology described in Section 3. As shown in Fig. 4, from every snapshot of one DNA molecule we can get different values of extension. Further, every molecule at the same time shows us different extension. Now, we investigate the probability distribution of the extension of DNA molecules for some specific Weissenberg numbers. After sampling 1000 DNA molecules during steady state, we plotted the probability distribution function (PDF) of the dimensionless extension in Fig. 6. The PDF looks Gaussian in shape at small Weissenberg number ($W_i = 1.3$). Note further that when the Weissenberg

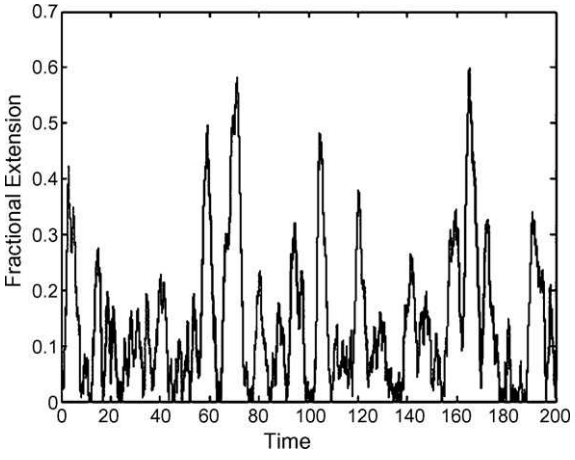

Fig. 4. Dimensionless extension vs. time.

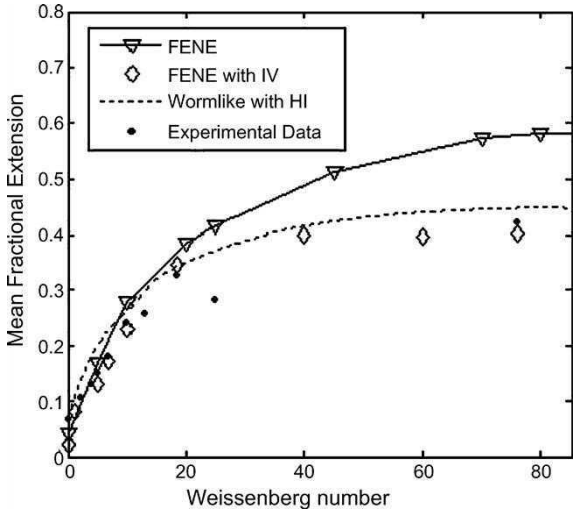

Fig. 5. Dimensionless extension of DNA molecules vs. W_i.

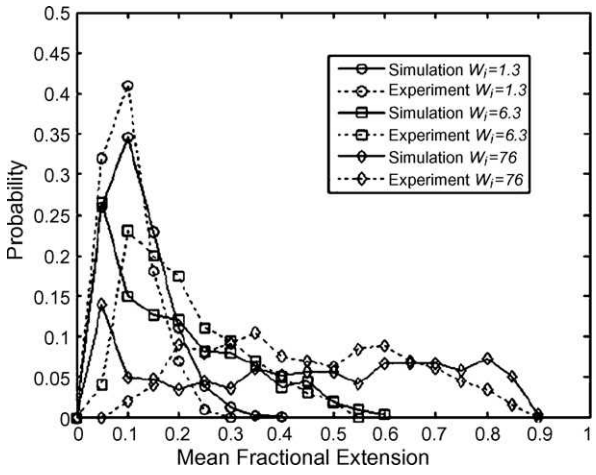

Fig. 6. The probability distribution function (PDF) of the dimensionless extension.

number increases, the peak of the PDF decreases and the distribution broadens. At large Weissenberg numbers ($W_i = 76$), the PDF appears like white noise. For comparison, the experimental results by Smith et al. (1999) were superimposed in Fig. 6. As seen, the simulation results have good qualitative and quantitative agreement with the experimental results.

The demonstrated agreement with the experimental results is remarkable, given relative simplicity of the dumbbell model with IV and its computational efficiency. The model and the developed computational implementation provide a tool for the analysis of extension and rheology properties.

5. Conclusion

In this paper, we focussed our analysis on the FENE dumbbell model with internal viscosity for the single DNA molecule in shear flow. The Brownian dynamics simulation was used to study the extension between the two beads of the dumbbell. The results are in agreement with the experimental data, which is especially important for high Weissenberg numbers. The probability distribution functions of the extension were also presented and the qualitative and quantitative agreement with available experiment data was demonstrated.

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