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RADIAL MIGRATION OF DNA MOLECULES IN CYLINDRICAL FLOW.
III. Circles and the effect of non-gaussian polymer statistics

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We have previously shown that DNA will migrate radially inward in a concentric-cylinder shear flow apparatus. We assumed gaussian chain statistics, and we considered only linear molecules. In this paper, we extend the analysis to closed circular molecules, and we consider non-gaussian statistics for both linears and circles. We find that, in good solvents, the inward radial migration velocity is more sensitive to the molecular weight than $M^{5/2}$, which we previously reported for gaussian chains. Furthermore, linears migrate radially inward 8 times faster than do circles of the same molecular weight. This suggests the possibility of separating linear from circular DNA in solution.

1. Introduction

In the preceding two papers [1,2], referred to as I and II, respectively, a theoretical description of the behavior of long chain molecules in concentric cylinder flow was presented. The calculations, based on gaussian polymer statistics, showed a radial migration of linear, non-draining molecules toward the inner cylinder at a rate proportional to the $\frac{5}{2}$ power of the molecular weight. In this paper, we extend the calculations to closed circular molecules and also consider the effects of non-gaussian polymer statistics.

2. Method of calculation

We consider steady Couette flow in the annular gap between two concentric cylinders. The inner cylinder has radius R_1, the outer cylinder has radius R_2. The inner cylinder rotates with a constant angular velocity Ω rad/sec. The details of the coordinate system for the migrating molecule and the (unperturbed) solvent velocity field can be found in I. We consider a dilute solution of bead-spring molecules in that solvent. Each molecule consists of $N+1$ beads connected by N hookean springs, each spring with a force constant $3k_BT/b^2$, where b^2 is the mean square length of a spring, k_B is Boltzmann's constant, and T is the absolute temperature. Interaction with the solvent occurs at each bead, characterized by a frictional coefficient ρ. Hydrodynamic interaction is included by using the equilibrium-averaged Oseen tensor [3] as follows:

$$T_{ij} = \frac{1}{6\pi\eta}\langle R_{ij}^{-1}\rangle, \tag{1}$$

where R_{ij} is the distance between the ith and jth beads, η is the solvent viscosity, and the brackets denote the equilibrium average. T_{ij} is a mobility operator which transforms the forces on each bead to the velocity of each other bead.

It is easy to show that, for a gaussian distribution, the following relation is true,

$$\langle R_{ij}^{-1}\rangle = (6/\pi)^{1/2}\langle R_{ij}^{2}\rangle^{-1/2}. \tag{2}$$

Also, for a gaussian distribution we have, for straight chains,

$$\langle R_{ij}^{2}\rangle = b^{2}|i-j| \tag{3}$$

and for circular chains [6]

$$\langle R_{ij}^{2}\rangle = b^{2}|i-j|(N-|i-j|)/N. \tag{4}$$

Following Bloomfield and Zimm [5] and others [7], we assume that the deviation from gaussian statistics in describing the equilibrium properties of a real chain molecule can be represented by a uniform expansion parameter ϵ such that eq. (3) becomes

$$\langle R_{ij}^{2}\rangle = b^{2}|i-j|^{1+\epsilon} \tag{5}$$

and eq. (4) becomes [5]

$$\langle R_{ij}^{2}\rangle = b^{2}\,\frac{|i-j|^{1+\epsilon}(N-|i-j|)^{1+\epsilon}}{|i-j|^{1+\epsilon}+(N-|i-j|)^{1+\epsilon}}. \tag{6}$$

Calculations are reported below for values of ϵ between 0.0 and 0.4. For native DNA in 0.195 M Na^{+} neutral buffers, ϵ has a value of 0.1 [10].

For the various cases described above in eqs. (3)–(6), we define a matrix:

$$(\mathbf{H})_{ij} = \rho T_{ij}, \quad i \neq j, \tag{7a}$$

$$(\mathbf{H})_{ii} = 1. \tag{7b}$$

We also define an operator $(3kT/b^{2})\,\mathbf{A}$ which transforms the position vector of the beads into a force vector of the intramolecular springs. As described previously [1,4], the resulting equations of motion in the y-direction are:

$$\dot{y} = V_{y} - D\mathbf{H}\cdot(\partial/\partial y)\ln\psi - \sigma\mathbf{H}\cdot\mathbf{A}\cdot y, \tag{8}$$

where the circular chain dynamics differ from the straight chain dynamics in both $\mathbf{H}$ and $\mathbf{A}$ [5], but the non-gaussian character is incorporated only in $\mathbf{H}$. This oversimplifies the non-gaussian behavior of the model, in that we have neglected any non-linearity in the springs.

3. Calculation of radial velocity

Following Shafer et al. [1,2], we transform the equations of motion to normal coordinates, then we consider only the zeroth component, i.e., the translational motion of the center of resistance of the whole molecule. The result is

$$\langle \dot{y}_{\mathrm{cr}}\rangle = -N^{-1/2}\gamma_{2}\langle \boldsymbol{\beta}_{0}^{\mathrm{T}}\cdot xy\rangle, \tag{9}$$

where $\langle \dot{y}_{\mathrm{cr}}\rangle$ is the average radial migration velocity, in the y-direction, of the center of resistance of the molecule; γ_{2} is a geometrical factor describing the Couette geometry and the coordinate system [1]; N is the number of springs; and $\boldsymbol{\beta}_{0}^{\mathrm{T}}$ is the zeroth row vector of matrix $\mathbf{Q}^{-1}$ [1,4].

We first consider circles. Due to the translational invariance of circles, the eigenvectors are sines and cosines, independent of any hydrodynamic interaction (see ref. [5] for actual demonstration of this). The effects of hydrodynamic interaction, and non-gaussian behavior in this model, enter only in the eigenvalues for circles. Thus, $\mathbf{Q}$ is orthogonal,

$$\mathbf{Q}^{-\mathrm{T}}\cdot\mathbf{Q} = \mathbf{Q}\mathbf{Q}^{-\mathrm{T}} = \mathbf{1},$$

where $\mathbf{1}$ is the identity matrix. It then follows that

$$\boldsymbol{\beta}_{0} = (1/N)^{1/2}\begin{pmatrix}1\\1\\1\\ \cdot\\ \cdot\\ \cdot\\ 1\end{pmatrix}, \tag{10}$$

where we assume $N \simeq N+1$ for large N. Eq. (9) then becomes

$$\langle \dot{y}_{\mathrm{cr}}\rangle = -N^{-1}\gamma_{2}\langle x^{\mathrm{T}}\cdot y\rangle, \tag{11}$$

or

$$\langle \dot{y}_{\mathrm{cr}}\rangle = -N^{-1}\gamma_{2}\sum_{k}\langle \xi_{k}\eta_{k}\rangle. \tag{12}$$

Eq. (12), identical to eq. (41) of I, applies to both free-draining and non-draining circles.

To proceed further, we must evaluate the average value of the product of normal coordinates, $\langle \xi_{k}\eta_{k}\rangle$. Following II, we assume the shear rate K to be constant over molecular dimensions. Then the distribution function ψ for Couette flow can be replaced by the distribution function for simple shear flow, with the results for steady flow [4]

$$\begin{aligned} \langle \xi_k \eta_k \rangle &= KD/(2\mu_k \lambda_k \sigma^2), \quad k \neq 0, \\ \langle \xi_0 \eta_0 \rangle &= \langle \xi_k \eta_l \rangle = 0 \qquad k \neq l. \end{aligned} \tag{13}$$

With these results, eq. (12) becomes

$$\langle \dot{y}_{cr} \rangle = -N^{-1} \gamma_2 (KD/2\sigma^2) \sum (\mu_k \lambda_k)^{-1}. \tag{14}$$

For free-draining circles, the eigenvalues, doubly degenerate except for $k = 0$, are [5]

$$\lambda_k = 4\pi^2 k^2/N^2, \quad k = 0, 1, 2, \ldots . \tag{15}$$

Since the α_k are sines and cosines, $\mu_k = \lambda_k$, and we obtain

$$\langle \dot{y}_{cr} \rangle = K\gamma_2 \rho b^4 N^3/12{,}960 k_B T. \tag{16}$$

Comparison of eq. (16) with eq. (10) of II shows that free-draining circles migrate inwards eight times more slowly than the corresponding free-draining straight chain. This is approximately the radial velocity of a straight chain one-half as large. This is to be expected since a circle has a smaller linear dimension, i.e., smaller radius of gyration, than the straight chain and thus will not "sense" as much of the curvature as the straight chain will.

In the non-draining limit, the eigenfunctions are modified by the hydrodynamic interaction. They are given by

$$\lambda_k = [4h(\epsilon)/N^2]\lambda'_k, \tag{17}$$

where $h(\epsilon)$ is the draining parameter, [5]

$$h(\epsilon) = 2^{\epsilon/2} N^{(1-\epsilon)/2} \rho/(12\pi^3)^{1/2} b\eta \tag{18}$$

and the numbers λ'_k are tabulated in ref. [5]. Eq. (14) then becomes

$$\langle \dot{y}_{cr} \rangle = -(\gamma_2 K\eta/k_B T)\, A(\epsilon) \langle R^2 \rangle_0^2 \langle R^2 \rangle_\epsilon^{1/2}, \tag{19}$$

where

$$A(\epsilon) = 0.977\, [2^\epsilon \alpha(\epsilon)]^{-1/2} \sum_k (k^2 \lambda'_k)^{-1}, \tag{20}$$

$\langle R^2 \rangle_\epsilon$ is the mean square radius of gyration, $\langle R^2 \rangle_\epsilon = \alpha(\epsilon) b^2 N^{1+\epsilon}$, $\langle R^2 \rangle_0 = b^2 N/12$, the mean square radius of gyration when $\epsilon = 0$, and $\alpha(\epsilon)$ is tabulated in ref. [5]. Values of $A(\epsilon)$ are presented in table 1.

The calculation for non-draining straight chains and $\epsilon \neq 0$, is somewhat more complicated. In this case, the quantity required to calculate the radial migration is

Table 1
Numerical results for non-draining models

ϵ	$A(\epsilon)$ circles	$B(\epsilon)$ straight	$\langle \dot{y}_{cr} \rangle_s / \langle \dot{y}_{cr} \rangle_c$
0	0.568	0.749	7.46
0.1	0.450	0.595	7.58
0.2	0.358	0.471	7.65
0.3	0.280	0.369	7.78
0.4	0.218	0.284	7.85

$$\begin{aligned} \langle \beta_0^T \cdot xy \rangle &= \frac{2\Gamma(\frac{1}{4}[\epsilon + 5])}{N^{1/2} \Gamma(\frac{1}{2}) \Gamma(\frac{1}{4}[\epsilon + 3])} \\ &\quad \times \sum_k \langle \xi_k \eta_k \rangle \int_{-1}^{+1} \frac{\alpha_k^2(r)}{(1 - r^2)^{(1-\epsilon)/4}} \mathrm{d}r, \end{aligned} \tag{21}$$

where $\Gamma(x)$ is the gamma function of argument x. This is the appropriate form of eq. (4) in II, obtained by applying the results of Auer and Gardner to extend the calculation of $\beta_0(r)$ [9] to include the effect of $\epsilon > 0$. The integrals in eq. (21) were solved by expanding the eigenfunctions in a Fourier series, as in II.

As done in refs. [5,7], we assume the required normal coordinate averages are still given in eq. (13). Now, however, the values of both μ_k and λ_k depend on ϵ. Again, the eigenvalues are written as in eq. (17) and the λ'_k are given in ref. [5]. The μ_k are calculated from the expression [8]

$$\mu_k = (4/N^2) \int_{-1}^{+1} [\alpha'_k(r)]^2 \,\mathrm{d}r. \tag{22}$$

Then the expression for the radial migration rate is

$$\langle \dot{y}_{cr} \rangle = -(\gamma_2 K\eta/k_B T) B(\epsilon) \langle R^2 \rangle_0^2 \langle R^2 \rangle_\epsilon^{1/2}, \tag{23}$$

where

$$\begin{aligned} B(\epsilon) &= \frac{2^{-\epsilon/2} (12)^{1/2} \Gamma(\frac{1}{4}[\epsilon + 5]) (6 + 5\epsilon + \epsilon^2)^{1/2}}{\pi \Gamma(\frac{1}{4}[\epsilon + 3])} \\ &\quad \times \sum_k (\mu'_k \lambda'_k)^{-1} \int_{-1}^{+1} \frac{\alpha_k^2(r)}{(1 - r^2)^{(1-\epsilon)/4}} \mathrm{d}r. \end{aligned}$$

where $\mu'_k = \Sigma_m (m\, {}^k a_m)^2$, ${}^k a_m$ are the Fourier coefficients of α_k (see II) and $\langle R^2 \rangle_\epsilon$, the mean square radius of gyration, is $(6 + 5\epsilon + \epsilon^2)^{-1} b^2 N^{1+\epsilon}$. $\langle R^2 \rangle_0$ is this expression evaluated at $\epsilon = 0$. Values of $B(\epsilon)$

as a function of ϵ are given in table 1.

6. Discussion of results

In both eqs. (19) and (23), the radial velocity is proportional to the $\frac{1}{2}(5 + \epsilon)$ power of the molecular weight, as compared to the $\frac{5}{2}$ power dependence found in II for the ideal gaussian non-draining model. Thus the effect of the non-gaussian statistics is to increase the sensitivity of the radial migration rate to the molecular weight. It is assumed that ϵ is independent of the molecular weight, a good assumption for large molecular weights. This general result is to be expected, since the non-gaussian statistics lead to larger polymer dimensions, allowing the polymer to sense more of the curvature of the flow field. As discussed in II, this will lead to a greater radial velocity.

In the final column of table 1, we present the ratio of radial velocities of straight chains to those of closed circles as a function of ϵ. For $\epsilon = 0$, this ratio, 7.46, is slightly less than the same ratio for the free-draining model, 8. We also see that the ratio increases slowly as ϵ increases.

The large difference in radial migration rates for circles and straight chains can provide a simple means of separating these two species. In addition, the effects of non-gaussian statistics result in the radial migration rate having a greater sensitivity to molecular weight than in the ideal gaussian model discussed in I and II. This increased sensitivity further enhances the potential for fractionating large DNA molecules in solution, as discussed in II.

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