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Electrophoretic Behavior of Polyelectrolytes in Gel and Polymer Solutions

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Electrophoresis using gel and uncrosslinked polymer solutions is widely used to separate DNA chains by chain length. We studied the electrophoretic behavior of chains using Brownian dynamics with an anisotropic friction tensor. We show the anisotropic-friction model proposed by Curtiss and Bird is an effective method to describe dynamics of polyelectrolyte chains under an electric field in gel and polymer solutions. With a low anisotropy of friction (dilute polymer solutions), a chain fluctuates between elongated and compact states with no periodicity under a steady electric field. On the other hand, with a high anisotropy of friction (gel or entangled polymer solutions), a chain oscillates periodically: Polyelectrolyte chain is trapped by gel fibers with a U-shaped conformation, stretches out, and re-acquires a compact conformation. The above results agree well with experiments on DNA electrophoresis.

Key words: DNA, electrophoresis, anisotropic friction, Brownian dynamics, entangled polymer solution

1. INTRODUCTION

Sieving media such as gel and polymer solutions are used for separation of DNA by electrophoresis, because the mobility of linear polyelectrolytes is independent on their chain length in free solution. To find better conditions for separation, the dynamics of DNA electrophoresis using gel [1-5] and polymer solutions [5-9] have been extensively studied. Some authors [1-5], using simulation, as well as direct observation, have revealed that DNA migrates in a gel matrix under a steady field with oscillation between elongation and contraction: DNA is trapped by gel fibers to show U-shaped conformation, and then stretches out and re-acquires a coiled conformation. The oscillation period under a steady field reportedly corresponds to the antiresonance period, at which the mobility of DNA is minimal in field-inversion gel electrophoresis.

In the past decade, a linear uncrosslinked polymer solution has been used instead of a slab gel in capillary electrophoresis based on advantages such as a higher resolution and rapid separation [6]. Long DNA fragments (*ca.* 20 kilo base pairs) can be separated even in ultradilute solutions by steady-field electrophoresis [6]. Some studies [7,8] using direct observation have described the conformational dynamics of DNA, *i.e.*, the formation and deformation of a U-shape, under a steady field in linear-polymer solutions both above and below the overlap concentration c*. Ueda *et al.* [8] reported that DNA migrates in a linear conformation, which they called an I-shaped motion, in 6-10% polyacrylamide solutions, which is *ca.* 10 times more concentrated than c*. In the I-shaped motion, DNA is not fully stretched and has high segment-density regions, which remain at the same positions in space during migration of the entire chain.

Some theories [2-4] on gel electrophoresis are based on a tube model [9]. On the other hand, another theory [10] on electrophoresis using dilute polymer solutions is based on a transient entanglement coupling mechanism: DNA drags solvent polymers after collision.

In Refs. 11-13, we showed that the anisotropic-friction model proposed by Curtiss and Bird [14] is applicable to electrophoresis using both gel matrix and polymer solutions. We used two models: segments corresponding to 8λ in Ref. 11 (model I) and $\lambda/4$ in Refs. 12, 13 (model II), where λ is the persistence length. The following types of migration behavior are shown. With low anisotropy of friction, chains of both models fluctuate with no periodicity between elongated and compact states. With high anisotropy of friction, chains of model I oscillate periodically between elongated and compact states and chains of model II migrate with linear conformation with high segment-density regions. The segment size of model should correspond to the mesh size of polymer solutions or a gel matrix. An increase in anisotropy should correspond to an increase in the length of solvent polymers with constant monomer concentration.

The purpose of our study is to examine the mechanism of the migration of DNA in a gel matrix in comparison with the migration in polymer solutions. We simulated model I (1 segment = 8λ) using Brownian dynamics in a three-dimensional space.

2. MODEL

As detail numerical procedure has been de-

scribed in Ref. 11, here we would explain the method only briefly. A DNA chain is modeled using $N+1$ beads tethered by elastic joints. The motion of the i-th bead follows the underdamped Langevin equation with a leapfrog algorithm:

$$m\frac{d^2\boldsymbol{r}_i}{dt^2} = -[\zeta_0\boldsymbol{u}_i\boldsymbol{u}_i + \zeta_n(\boldsymbol{I}-\boldsymbol{u}_i\boldsymbol{u}_i)]\frac{d\boldsymbol{r}_i}{dt} + \boldsymbol{g}_i(t) + \boldsymbol{f}_{\rm bond}(\boldsymbol{r}_i-\boldsymbol{r}_{i+1}) + \boldsymbol{f}_{\rm bond}(\boldsymbol{r}_i-\boldsymbol{r}_{i-1}) + \boldsymbol{f}_{\rm ex}, \quad (1)$$

where m is the mass of a bead and $\boldsymbol{u}_i$ is the vector tangential to the chain. $\boldsymbol{g}_i(t)$ is the Gaussian white noise and obeys the fluctuation-dissipation theorem. ζ_0 and ζ_n represent friction for motion parallel and normal to the chain, respectively. We set $\zeta_n/\zeta_0 = \Lambda$ at $2 \le i \le N$ and $\zeta_n/\zeta_0 = \Lambda/2$ at $i = 1, N+1$, since the end segments are affected less by entanglement with solvent polymers than the middle segments.

The neighboring beads along the chains are connected with the bond force $\boldsymbol{f}_{\rm bond}(\boldsymbol{r})$,

$$\boldsymbol{f}_{\rm bond}(\boldsymbol{r}) = Ak_{\rm B}T\left(-\frac{1}{4(1-r/l)^2} + \frac{1}{4} - \frac{r}{l}\right)\frac{\boldsymbol{r}}{r}, \quad (2)$$

where $k_{\rm B}$ is the Boltzmann constant and T is the temperature. l is the maximum stretched length. The force $\boldsymbol{f}_{\rm bond}(r)$ asymptotically corresponds to an analytical solution of a wormlike chain at large and small force limits in the case of $l >> 1$ [15]. We choose the values $A = 1.7$ and $l = 2$, which indicate $l = 8\lambda$. We set the external force as $\boldsymbol{f}_{\rm ex}$ =($f_{\rm ex}$, 0, 0).

We used $l/2$ as the unit length, $k_{\rm B}T$ as the unit energy, and $\zeta_0(l/2)^2/k_{\rm B}T$ as a unit time step. In this paper, N is fixed 64 (corresponding to 90 kbp of DNA) and $f_{\rm ex} = 0.125, 0.25, 0.5, 1, 2, 4$, and 8 (corresponding to the electric field $E = 0.3 - 20$ V/cm in a typical experiment). We changed the anisotropy parameter $\Lambda = 10, 20, 100$, and 1000.

3. RESULTS AND DISCUSSION

Figure 1 shows snapshots of a polyelectrolyte chain at $\Lambda = 10$. A chain forms a U-shaped or W-shaped conformation. These conformation is induced by the external force and the anisotropy of friction, and is not stable without the external force. The x coordinate of the apex of the U-shape is not fixed and moves 25 units from Fig. 1(b) to (c) and 23 units from (c) to (d). These snapshots agree with fluorescence images of T4DNA in dilute (c<c*) or semidilute (c ~ c*) polymer solutions [7,8].

Figure 2 shows snapshots of a chain at $\Lambda =$ 1000. A chain forms a stretched U-shaped conformation in Fig. 1(a), (b), and (c). The x coordinate of the apex of the U-shape almost fixed and moves only 4 units from Fig. 1(a) to (b). The chain becomes the compact conformation as soon as the apex of U-shape vanishes at the chain end. Though the leading end stretches at U-shaped conformations by pulling force along the chain, the end unorients in x-direction by thermal fluctuation at

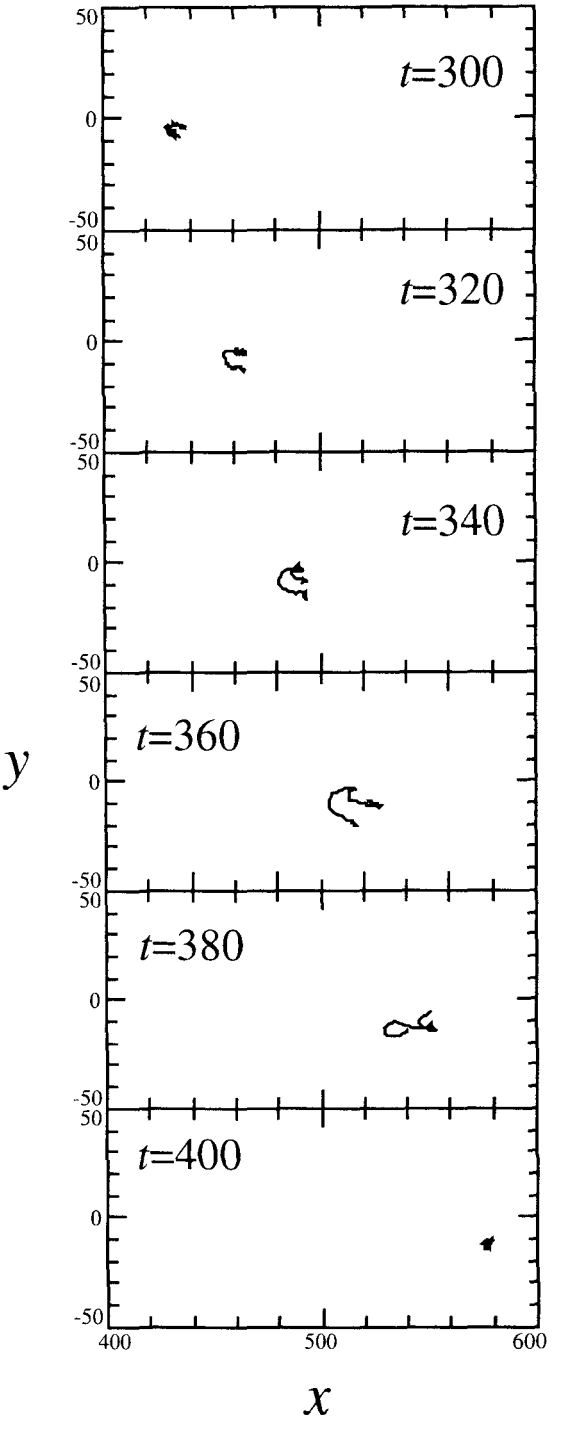

Fig. 1 Chain conformation at anisotropy parameter $\Lambda = 10$ in steady-field electrophoresis. The snapshots are displayed as projections to the xy plane. Chain length is $N = 64$ and the external force is $f_{\rm ex} = 4$ in the x direction.

the linear shaped conformation, and is caught by the back segments. Similar conformational changes have been reported in simulations [1,2], where a polyelectrolyte chain migrates on a plane of dotted obstacles, and in direct observations of DNA in

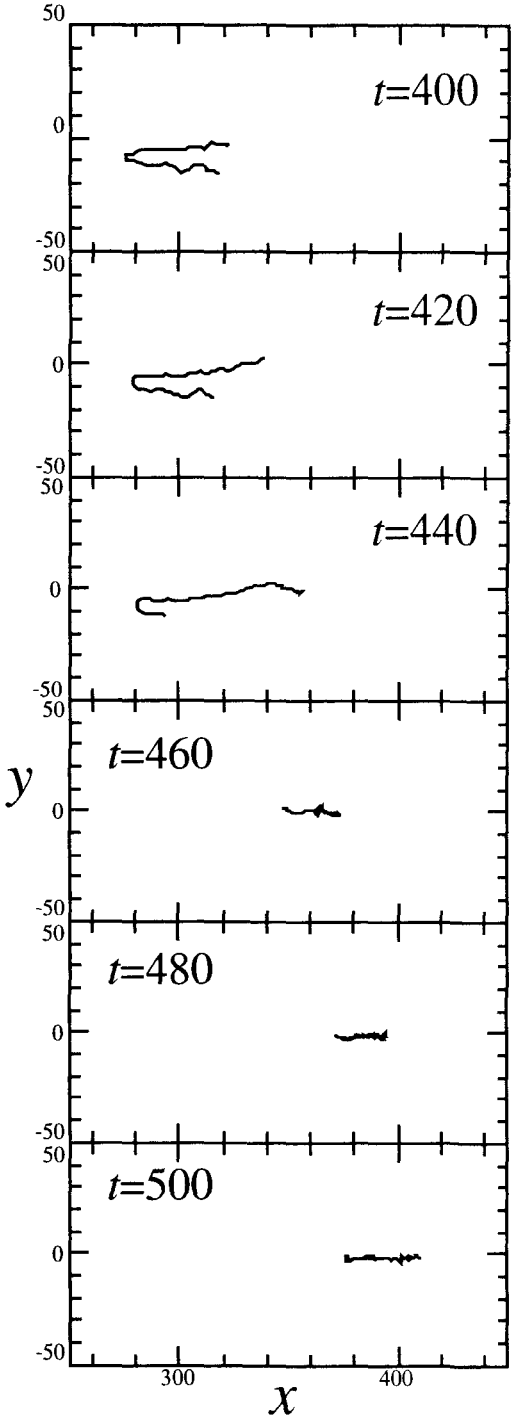

Fig. 2 Chain conformation at anisotropy parameter $\Lambda = 1000$ in steady-field electrophoresis. Snapshots are displayed as projections to the xy plane. The other parameters are the same as those shown in Fig. 1.

gel [3,4] or in entangled polymer solutions (c>c*) [7]. As anisotropy of friction increases, the chain has more stretched U-shaped conformation. Figure 3 shows the time development of the end-to-end distance R_{end} for the same examples as in Figs. 1

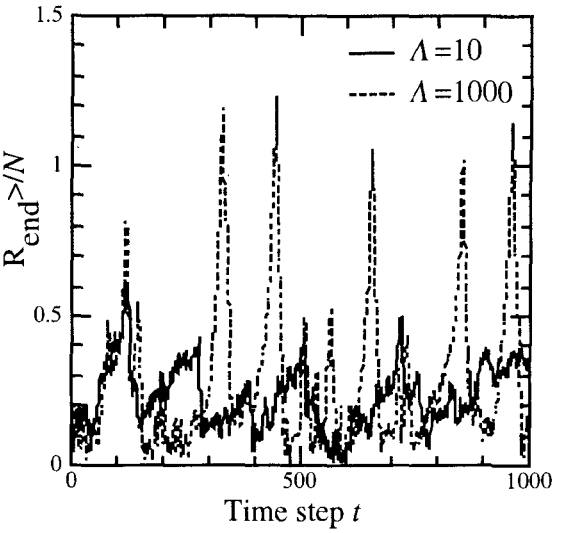

Fig. 3 Time development of the end-to-end distance R_{end} at $\Lambda = 10$ and 1000 from the same data shown in Figs. 1 and 2.

and 2 at $\Lambda = 10$ and 1000. These conformational dynamics are not dependent on initial states. A large fluctuation of R_{end} is seen for both $\Lambda = 10$ and 1000. That at $\Lambda = 1000$ looks more periodic than that at $\Lambda = 10$.

To evaluate periodicity, We calculate the autocorrelation functions of physical quantities, such as the end-to-end distance, the radius of gyration, and the velocity of the center of mass calculated from three runs with 160000 time steps (see Fig. 6 in Ref. 11). All of them have very similar shape. At $\Lambda = 10$, the autocorrelation function decreases as a single exponential function of time with no periodicity. At $\Lambda = 100$ and 1000, the autocorrelation functions are oscillatory. The period of oscillation is 170($\pm$30) and 100($\pm$30) at $\Lambda = 100$ and 1000, respectively. The increase in anisotropy of friction induces the periodicity of conformation change. This trend is caused by faster growth to U-shaped conformation at higher anisotropic friction. At $\Lambda = 10$, R_{end} increases slowly from a coiled to U-shaped conformation, and U-shaped conformation often deforms at small R_{end} as shown in Fig. 3. On the other hand, at $\Lambda = 1000$, R_{end} increases faster from a coiled to U-shaped conformation. Since the duration of coiled conformations is short, the chain conformation is U-shape at most of the time. Thus, the duration of U-shaped conformation equals almost the period of the autocorrelation function.

The period of oscillation is proportional to N [11]. As the chain becomes shorter, the periodicity of chain becomes weaker and disappears at $N = 8$. This suggests that a sufficient chain length is needed to generate periodicity. These period in steady field corresponds to the antiresonance period in field-inversion gel electrophoresis [11]. These results agree with experimental results [1-4].

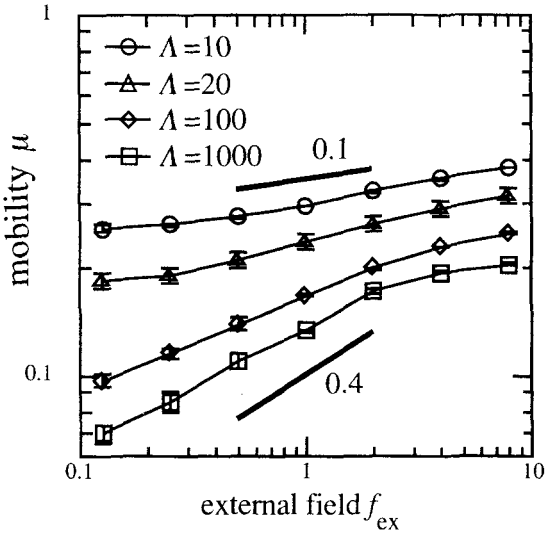

Fig. 4 Dependence of mobility μ on steady field strength f_{ex} at $N = 64$ and $\Lambda = 10, 20, 100$, or 1000. Thick lines represent slopes of 0.1 and 0.4.

Figure 4 shows that mobility $\mu =< V_x > /f_{ex}$ is proportional to f_{ex}^{α} under a steady field at $\Lambda = 10, 20, 100$, and 1000, where V_x is the x-component of the velocity of the center of mass. As Λ increases, α increases from 0.1 to 0.4. This agrees with an experiment on CE using polymer solution by Mitnik *et al.* [16]. They estimated that α was 0.07, 0.27, 0.3, and 0.4 for 0.1, 0.2, 0.4, and 1% hydroxypropylcellulose (HPC) solutions, respectively (c*= 0.37%). $\Lambda = 10$ agrees with 0.1 – 0.2% dilute HPC solutions. $\Lambda = 1000$ agree with entangled HPC solutions (c>c*), and the exponent in gel electrophoresis [4] is 0.4–0.5. As anisotoropy of friction increases, the mobility μ has larger f_{ex} dependence. Thus, the high exponent 0.4 in gel and entangled polymer solutions is generated by the strong confinement of high anisotropy of friction.

We show that the chain fluctuates between elongated and compact states with no periodicity at low anisotropic friction and oscillates between elongated and compact states at high anisotropic friction. The former corresponds to dilute polymer solutions, and the latter corresponds to gel or entangled polymer solutions. Periodic oscillation between elongated and compact states causes an antiresonance of mobility in field-inversion gel electrophoresis. U-shaped conformations accompany such periodic oscillation. For a shorter chain or a lower concentration of gel fibers, the U-shaped conformation disappears as periodicity disappears. We have found that in dilute polymer solutions the periodicity disappears whereas U-shaped conformation exists.

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