DIFFUSION COEFFICIENT IN AN ELECTROPHORETIC ASYMMETRICALLY TILTING RATCHET*

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Dedicated to Professor Andrzej Fuliński on the occasion of his 70th birthday

We use the cellular-automaton Duke–Rubinstein model to simulate gel electrophoresis of DNA in periodically changing electric field. The field is dichotomic and its time average is zero. We observe non-vanishing current of molecules, what is known as the ratchet effect. We calculate the drift velocity and the diffusion coefficient for large field amplitude, where nonlinear effects can be observed. The results indicate that tuning the amplitude and frequency of the applied field for a given range of the molecule length can improve the resolving power of the separation of DNA.

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1. Introduction

Separation of molecules of DNA is of current interest in biophysics, because of existing and new applications in genetic technology. For this purpose, the gel electrophoresis (GE) is a standard technique [1]. The resolving power of GE depends on the velocity v of the investigated molecules and on the bandwidth [2], which in turn can be expressed by the mobility μ and the diffusion coefficient D. From an experimental point of view, these quantities can be modified by the gel concentration and the field intensity. They are known to depend also on the molecule length.

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Here we are interested in GE in the presence of electric field which periodically varies in time pulsating between two field intensities E_+, E_-, each of duration t_+, t_-, respectively. The motivation for this kind of studies is twofold: First, additional parameter which is the frequency of the applied field allows for a better tuning of the experimental values of the steady-state velocity [2]. Second, it can be used to control the diffusion coefficient of the moving molecules and a resolution ratio for the GE separation. The latter is due to the fact that the unbiased but asymmetrical electric field pulses are responsible for building a ratchet-type mechanism which stands behind the efficient isolation of various conformational forms of the same polymer [3,4]. The process investigated is of great interest and a special challenge for nanotechnology, as it serves for a design of molecular Brownian machines and rectifying devices that transport small (micrometer- to millimeter-sized) particles [5–7]. In the case discussed in this study, simulations of the tilting ratcheting device [4] are performed by use of the cellular-automaton model. Its feasibility for the purpose of the ratchet-modeling and applications of the methodology in bio-materials research and engineering have been discussed elsewhere [8]. Here we report the results of our cellular automata simulations of the GE and demonstrate ratcheting efficiency of the diffusion of DNA molecules in the presence of applied ac field with zero time average. To allow for the non-zero current, the field has to be large enough to include nonlinear effects. For low field intensity, the mobility $\mu = v/E$ does not depend on E and the net current is zero by symmetry. The simulations are performed within the Duke–Rubinstein model [9,10], with additional tricks adopted after Ref. [11]. More detailed description of the algorithm can be found in [11–14]. Except Ref. [13], all those works are devoted to situations with the external field constant in time. Some preliminary results of the simulation for time-varying field have been presented in [13]. There, the velocity v and diffusion D of moving DNA fragments have been investigated as dependent on the field frequency. In this work we present a more detailed and complete study of the case.

2. Calculations

The simulation of an electrophoretic ratchet is similar to that one, at constant field described in [12]. However, now we have two values ε_- and ε_+ proportional to intensities of the applied field in two directions. Durations of the appropriate pulses are t_- and t_+, hence we can define field frequency f as $f = 1/(t_+ + t_-)$. There, the time unit, 1MCs, is defined as a time in which every repton realizes $\exp(-\varepsilon/2)$ trials of movement in field direction and $\exp(\varepsilon/2)$ trials of movement in the opposite direction, where ε is the electric to thermal energy ratio [11]. In order to keep the time average value of the field equal to zero, we require that $\varepsilon_- t_- = \varepsilon_+ t_+$. A course of

simulation for a single DNA chain is as follows: first we apply the constant field ε_+ allowing the molecule to reach a stationary state (constant velocity) and then, after switching the pulsing field on, we wait again until the mean velocity is constant. Next we let the molecule move in the varying field for some time to get good statistics, writing its position x and x^2 every 100 MCs. The long-time drift velocity v and the diffusion coefficient D are obtained by averaging over 2000 molecules in stationary states.

The parameters of the simulation are: the molecule length expressed by the number N of reptons in a molecule, the electric to thermal energy ratio ε_1 and ε_2 for both field intensities E_1 and E_2, and the frequency f of the changing field. The output is v and D, both in arbitrary units. An attempt to a quantitative comparison with experiment for the field constant in time is described in Ref. [14].

3. Results

In Fig. 1 the average velocity of molecules is shown as dependent on the applied field frequency for three values of the amplitude of the applied field, $\varepsilon_- = 0.1$, 0.6 and 0.9. The amplitude ε_+ is kept constant, $\varepsilon_+ = 0.3$. We note that for $\varepsilon_- = 0.3$, the average velocity vanishes identically by symmetry for any value of the field frequency. For $\varepsilon_- = 0.1$, we observe a nontrivial inverse point (not implied by the up–down symmetry of the applied field), for which again $v = 0$. Moreover, at $\varepsilon_- = 0.6$, the process is characterized by a non-monotonous velocity dependence on the field frequency with an apparent maximum of v at values $f \approx 10^{-6}$. The functional dependence of the diffusion coefficient D *versus* field frequency f is displayed in Fig. 2 for $\varepsilon_- = 0.1$. We note that the plot does not show any particular variation at the inverse point; as a rule, D decreases with the field frequency except

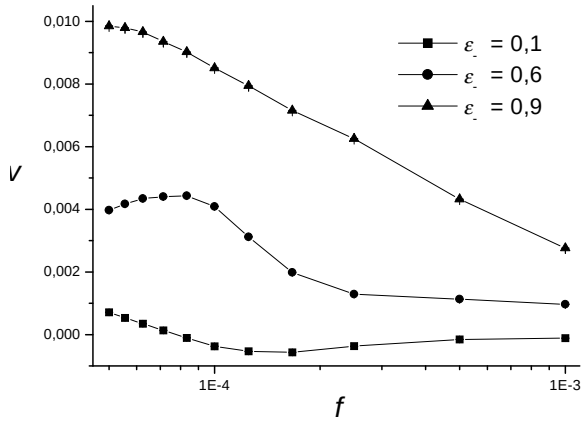

Fig. 1. Average velocity v against the field frequency f, for $N = 60$.

irregularities at low frequencies, which are due to numerical errors. It is rather obvious, that in the limit of small f, D achieves its value typical for a constant field ε, averaged over ε_- and ε_+ with times t_-, t_+ as weights. As found from Ref. [13], for constant field $\varepsilon = 0.1$ and $N = 60$ we get $D = 0.01$, that is much less than $D = 0.18$ for $\varepsilon = 0.3$. The weight expressing time ratio is $t_+/(t_+ + t_-) = 0.25$ and gives the average $D(f = 0)$ about 0.045, *i.e.* two times larger than $D = 0.025$ for $f = 4 \times 10^{-5}$, read from Fig. 2. As we see, D decreases rather sharply with f at small frequencies.

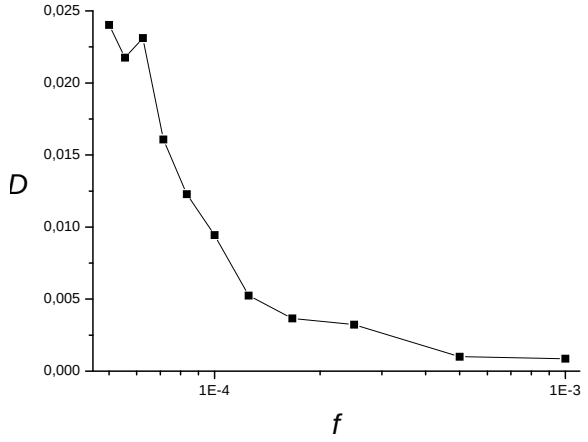

Fig. 2. Diffusion coefficient D against the field frequency f, for $N = 60$.

Fig. 3 shows the velocity v in function of the field amplitude ε_-. The results have been obtained for $N = 60$, $\varepsilon_+ = 0.2$, $t_+ = 2500$. The plot is characterized by two zeros, at $\varepsilon_- = 0.03$ and $\varepsilon_- = 0.2$. As a rule, v is small in this range of relatively small fields showing that we are almost in

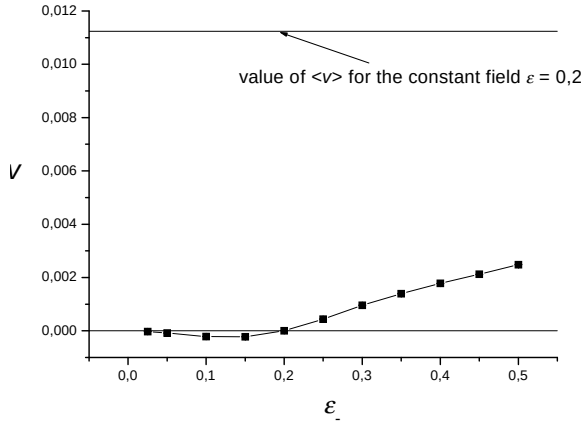

Fig. 3. Average velocity v against ε_-, for $N = 60$ and $f = 0.77 \times 10^{-4}$.

the linear regime. The second zero follows from the up–down symmetry. We note that the velocity is not constant for this plot, but it varies from 0.44×10^{-4} till 2.8×10^{-4} as ε_- increases. This is because t_- depends on ε_- through the condition $\varepsilon_- t_- = \varepsilon_+ t_+$.

As we see in Fig. 4, the diffusion coefficient D increases remarkably with ε_- in the same range of parameters. This is in accordance with the experimental rule that D increases with ε in the nonlinear regime [14].

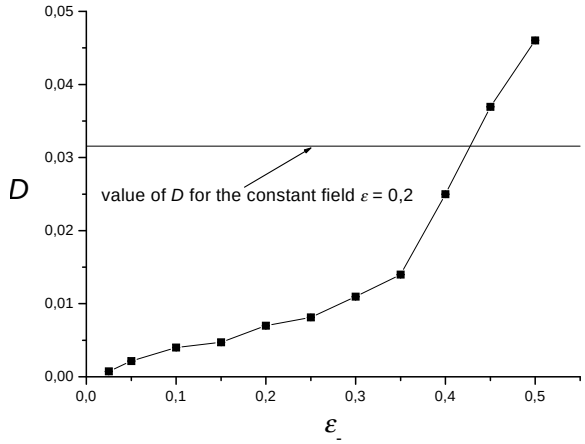

Fig. 4. Diffusion coefficient D against ε_-, for $N = 60$ and $f = 0.77 \times 10^{-4}$.

In Figs. 5 and 6 we show the steric effects of v and D as dependent on the molecule length N, for $f = 0.77^{-4}$. We note that for $N < 10$, both quantities display an unexpectedly sharp behavior. In particular, the maximum in the

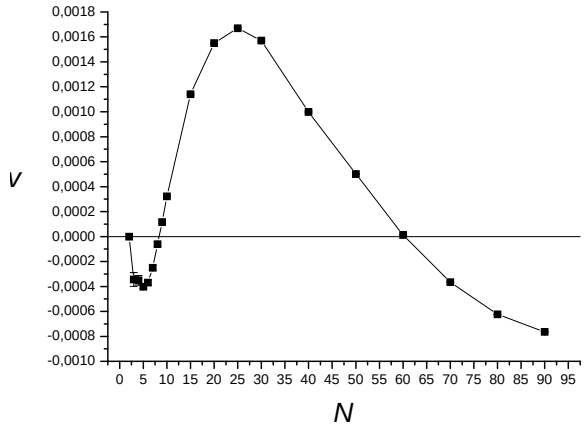

Fig. 5. Average velocity v against the molecule length N, for $t_+ = 2500$ and $\varepsilon_+ = 0.2$. Inverse point at the right side is the same as the one in Fig. 1 for $\varepsilon_- = 0.1$.

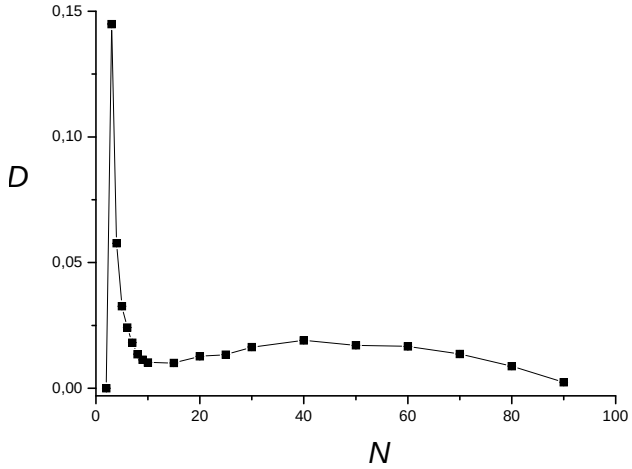

Fig. 6. Diffusion coefficient D against the molecule length N, for $t_+ = 2500$ and $\varepsilon_+ = 0.2$.

function $D(N)$ at $N = 3$ is due to the fact that quite frequently, the molecule is trapped in a symmetric configuration, hooked on the "gel fiber" exactly at its centre. Such a configuration restricts, therefore, the motion of the molecule along the applied field. This effect, however, is not of particular interest for sufficiently long molecules whose length exceeeds $N = 10$. In fact, above $N = 10$, the diffusion coefficient varies rather slowly. On the contrary, v shows a maximum near $N = 30$ and a nontrivial inverse point at $N = 60$. This means that the efficiency of the separation has a maximum at $N = 30$. We have checked that the position of this maximum does depend on the applied field amplitude and frequency.

4. Conclusions

Our numerical results indicate, that the velocity v of simulated motion of DNA molecules is a complex function of the field amplitude and frequency, it depends also strongly on molecular length. For field intensities $\varepsilon_- = \varepsilon_+$ and arbitrary f and N values, the velocity function is zero by symmetry. Besides that, some other inverse points are found and are not implicated by the above symmetry requirement. Between the zeros, some maxima of v appear, as the one in Fig. 5. This behavior is of particular interest for the resolving power of the GE technique. Best conditions can be achieved if the velocity varies smoothly with the molecular length and, when simultaneously, the diffusion coefficient is small to provide narrow electrophoretic bands. The results obtained so far do not allow to formulate general rules for the velocity. In a directed GE polymer motion, the frequency and ampli-

tude of the applied field should be tuned relevantly by taking into account the desired length-range of separated molecules. As suggested by the results presented in Figs. 2, 4, and 6 best experimental results may be expected for low external field-values, high frequencies and not too short molecules. That scenario should provide small values of the diffusion coefficient, which results in a relatively narrow electrophoretic bands.

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