Electrostatic/entropic macromolecule manipulation in nanochannel. Swapping of macromolecule locations

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Abstract

Evolution of a polyion and an electrically uncharged macromolecule in confined environment, represented by a tight nanopore, induced by external electric field, is investigated. The motion of the uncharged macromolecule is forced by the polyion. In suitably selected conditions, the collision between macromolecules, compression of the uncharged macromolecule, and finally the swap of positions of macromolecules in the nanochannel are observed by means of the nonequilibrium Monte Carlo method on the lattice. The exemplary trajectories of macromolecules, their geometry, and energetics are analyzed. The dependence of the time of swapping on the number of macromolecule beads is described by scaling laws.

Keywords Molecular modeling · Monte Carlo simulation · Polyelectrolytes

Introduction

The single-macromolecule manipulations have been of growing interest in the last two decades due to the development of new techniques allowing specific operations like trapping, moving, and sorting of particular objects in the nanoscale systems [1]. The manipulation techniques are based on a variety of physical laws and inventions [1, 2]. They include the glass microfiber micromanipulation [3], the magnetic beads used as the force probes controlled by optical microscopy (magnetic tweezers) [4], the atomic force microscopy allowing measurements of mechanic properties of single macromolecule such as the force needed for stretching its conformation or for the rupture of a covalent bond [5, 6], and the optical tweezers which can catch and drag nanosize dielectric objects, and also some macromolecules [7]. These techniques have been developed mainly for biophysical applications, but their use has quickly spread to other domains, such as the study of Brownian motors [8]; untangling, unknotting, and unlinking of DNA molecules [1]; sorting of microscopic particles by size or by refractive index [9]; and microrheological measurements in small volumes and on short length scales,

including the interior of cells and prestretching and stabilizing of DNA before threading through a nanopore [10]. These very advanced methods can be supplemented by innovative applications of electrokinetic phenomena, i.e., electrophoresis [11] and electroosmosis [12] often assisted by optical effects such as optoelectronic tweezers [13], optically induced dielectrophoresis [14], methods based on thermally induced gradients of permittivity and conductivity of fluids [15, 16], alternating current electroosmosis [17, 18], optically induced electrokinetic effect [17], and dielectrophoresis [19] to list a few. The nonzero energy of interaction between polymer beads and walls of the tight slit can produce jumps of macromolecule from one surface to the other [20].

Spontaneous motion of macromolecules can be also induced by the particular geometry of tight cavities. This motion—the entropophoresis—is an emerging nanofluidic method using nanoscale confinement to control the spontaneous transport and separation of macromolecules and other nanoscale objects [21]. The free energy landscapes of macromolecules in tight confinement [22] can be designed to entropically manipulate their random diffusion, e.g., the asymmetry of 3-branched star macromolecule can induce its spontaneous motion [23].

Recent progress in chemical modification and technology of material conversion having a molecular-scale porous structure with well-controlled pore diameters and interlayer distances has led to construction of a variety of tight nanocavities including complex channels, slit matrices, or labyrinths, in which motions and locations of particular species can be

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controlled. An example is a graphene oxide membrane [24–28], for which high-speed water flow [29] and ion transports [30] across nanochannels and nanoslits stacking sheets have been observed. Such a transport of ions or polyions can be controlled using voltage-gated channels [31, 32].

Combinations of the methods mentioned above have opened a new approach to the application of thermodynamically controlled processes to automate the operation of lab-on-a-chip technology, for both practical applications and fundamental investigation [21]. Such methods would allow controlled displacement of individual macromolecules or polyions, their forced translocation in nanopores and ion-switched nanochannels, and their segregation or trapping. Nevertheless, the physical backgrounds of certain techniques are still not fully understood.

A very interesting method for micromanipulation of macromolecules is a superposition of two effects—the external electrostatic field and the tight nanoscopic confinement, leading to the electrophoretic and entropophoretic effects, especially in systems containing a pair of uncharged macromolecules and/or macromolecules bearing functional ionogenic groups. An example of the phenomena occurring in such systems is the spontaneous segregation of genetic material, chromosomes, after replication accompanying the cell division in some bacteria [33]. This entropy-driven process seems to be strongly influenced by electrostatic interactions in the electrolyte solution [34].

Polymer molecules under nanoconfinement show unique dynamical properties different from those of free macromolecules in the bulk [35], altered by both the statics [36] and dynamics of a polymer chain [37, 38]. Some approaches to the description of chains in nanoconfinement are based on the excluded volume effects and elasticity of chains (both governed by conformational entropies of chains) influence on their behavior. The models concern SAW (self-avoiding walk) chains with different stiffness and confinement limits [39–41]. Numerous studies have been performed on segregation of macromolecules [42, 43], polymer translocation through narrow pores [44, 45] and chamber-pore system [46], prestretching and stabilizing of DNA before threading through a nanopore [10, 47], etc.

The main idea of the current study is to use one of the macromolecules—a polyion—as a tool for micromanipulation of the position of another one—an electrically neutral macromolecule, by means of electrophoretic and entropophoretic effects. The study concerns the tight nanoconfinement represented here by a nanochannel. Thus, the objective of the study is to perform a numerical experiment in attempt to answer the question whether the macromolecule endowed with electric charge can be used for induction of controlled movement of the electrically neutral one and which mutual interactions between macromolecules will be observed, taking into account the possibility of translocation, interpenetration/segregation of macromolecules, or their

swapping. The scheme of processes of potential interest is shown in Fig. 1. The paper concentrates on the swapping process; however, other processes shown in the figure are also observed in the study.

The paper is organized as follows: in “[Model and simulation method](#),” the details of the simulation technique applied are described including the model representation of polymer chains, simple electrolyte ions, and geometry of the systems. The results of single simulation and the analysis of evolution of geometric and thermodynamic properties of migrating chains are gathered in “[Details of motions of the polyion and uncharged macromolecule](#).” Finally, some generalizations based on formulation of some scaling laws describing the influence of chain bead number and the nanochannel width are presented in “[Generalization of the system behavior—some scaling laws](#).”

Model and simulation method

The study was performed by means of simply and relatively fast nMC (nonequilibrium Monte Carlo) method [48]. The method was chosen because of the ease of its implementation.

The simulations were performed on the three-dimensional cubic lattice of the lattice constant b . The confined space of the studied process was a rectangular nanochannel with one end open and the other end closed. The length of the nanochannel was $600b$ and the width D was equal from $3b$ to $11b$ (depending on the simulation, in most simulations $D = 5b$). The choice of geometry of the nanochannel was determined by the fact that the simulation performed in the nanochannel with both ends open lasted very long as a result of pushing of neutral macromolecule by polyion over long distances.

The polymer chains are represented by SAWs embedded in the lattice. Each monomer is identified by the site on the lattice (B bead), so each chain is an ensemble of N consecutive sites occupied by B beads. The beads succeeding along the chain are located in adjacent lattice sites at the distance b . Two different polymer chains were considered: one (C1) made of two types of beads: electrically neutral and bearing elementary electric charge, and the other (C2) consisting only of electrically uncharged beads located at equal distances along the chain. A single charged bead, bearing an electric charge q_p/e equal to $+1$ (where e is the elementary charge), was assumed to interact electrostatically with all other charges in the system. Since the general athermal conditions were assumed, all other intermolecular interactions were neglected, except the excluded volume effects. Both studied chains consisted of N beads. The simulations were performed for a constant electric charge of the polyion determined by the constant density of electrically charged beads equal to σ (the ratio of the number of charged beads to the total number of beads in the chain, usually $\sigma = 0.2$). Positions of charged beads along the chain were

Fig. 1 Scheme of mutual motions of positively charged polyion (C1) and uncharged macromolecule (C2) in the electrostatic field: **a)** motion of C2 forced by C1, **b)** interpenetration of C1 and C2 and **c)** capturing of C1 in the end of nanochannel and free diffusion of C2 ($N=200$)

fixed. The nearest neighboring lattice sites of these beads were assumed to be unavailable to the other charged beads, mimicking thus the ion solvation effect. Simulations were performed for the SAW chains using the Verdier-Stockmayer algorithms [49, 50].

The dispersion medium was represented by a solution of monovalent electrolyte molecules. Ions were treated as lattice nodes containing the electric charges q_i/e equal to -1 or $+1$. Individual ions (I beads) occupied lattice nodes surrounded by empty nodes corresponding to solvent molecules constituting the ion solvation shell. The lattice sites forming the solvation shell were assumed to be unavailable to charged beads. This mode of accounting for ion solvation, similar to solvation of polymer-charged beads, is similar to that proposed by Ruckenstein et al. [51]. The assumed excluded volume around a single charged bead corresponded roughly to that estimated by Paunov et al. [52] to account for the hydration of ions, which is six times the volume of the ion. The shell thickness exceeded the Bjerrum length for the relative dielectric permittivity of the medium used in the study ($\epsilon = 80$), thus allowing the neglect of the Manning condensation [53]. The adopted value of ϵ corresponds to the aqueous bulk phase.

Numbers of positively and negatively charged beads I in the simulation box (n_+ and n_- respectively) were determined by the ionic strength I_s of the solution which was defined as:

$$I_s = \frac{1}{2} \left(\frac{(n_+ + n_-) q_1^2}{e^2 V} \right) \quad (1)$$

where V represents the volume of the microchannel. The numbers n_+ and n_- were calculated taking into account the charges of the polymer to ensure electroneutrality. The initial positions of beads I were random as generated by using a pseudorandom number generator, taking into consideration the effects of the excluded volume of the chains and previously randomly generated I beads together with their solvation shells.

Relaxation of the system was achieved by random micromodifications of positions of beads I made with steps

that have a length b in any lattice direction. Numbers of charged beads I in the simulation box were adjusted by assuming the ionic strength ($I_s = 0.001$) and the electric charge carried by polyion C1.

At both ends of the channel, the periodic boundary conditions were applied for the motion of simple ions. Since in the course of the simulation, the ions move to the opposite charged electrodes outside of the box, the boundary conditions guarantee the electroneutrality of the system. At the closed end, the membrane impermeable for macromolecules but permeable for simple ions was applied. The model membrane mimics the real semipermeable membrane or the electrode surface on which the ion creation and annihilation by the electrode reactions take place. There are no additional constraints applied on the other end of the nanochannel since both types of macromolecules do not cross it: C1, because it moves in the opposite direction; and C2, because the simulation stops before reaching the nanochannel end.

The external electric field E was applied in the direction parallel to the nanochannel. Its polarization forced the motion of C1 chain towards the closed end and motions of ions in directions specified by their signs. Initial locations of both chains are shown in Fig. 1a.

In the course of simulation, the components of the free energy of the system were calculated. Since the internal energy of nonionic intra- and intermolecular interactions for the polymer chains was equal to zero as a result of the assumption of athermal conditions, the only energy component of the system was the energy of electrostatic interaction. All the constituent average energies of electrostatic interactions occurring between the beads representing charged monomers and ions, and the total energy of electrostatic interactions in the system, were determined from Coulomb's equation, assuming that all the objects were point electric charges:

$$U_M = \frac{b}{4\pi\epsilon_0\epsilon} \sum_i \sum_j \frac{q_i q_j}{e^2 r_{i,j}} \quad (2)$$

where ε_0 is the permittivity of vacuum and ε denotes relative permittivity of the medium, whereas q_i and q_j represent electric charges of the currently analyzed charged objects located at the distance r_{ij} . The computation was performed using the minimum image convention and the cutoff radius equal to half box length ($300b$) in the direction parallel to the nanochannel. In most simulations ($N = 50$, $\sigma = 0.2$), the radius applied guarantees that only long-range ionic interactions of the energy smaller than 0.03 the elementary interaction between neighboring charged polymer beads were neglected.

Within the framework of the model, it was assumed that $\varepsilon_0 b/e$ was equal to $8 \cdot 10^{-4}$, which ensured that the energy of interactions between two monovalent point charges located at the distance b (i.e., in the immediate vicinity determined by the lattice constant) was equivalent to $100 k_B T$ (since for so small distance $\varepsilon = 1$). The energy of charged beads in the external electric field was calculated from the equation:

$$U_E = \frac{E}{\varepsilon_0 \varepsilon} \sum_i \frac{q_i x_i}{eb} \quad (3)$$

where E is the external electric field directed in the same way in all unit boxes (usually, $E(eb/k_B T) = 0.1$) and x_i is the distance of the i -th charged bead from the bottom of the nanochannel. The influence of dielectric nanochannel walls on the movements of electrically charged species was neglected.

Calculations of the conformational entropy of the chains were performed using the modified SCM (statistical counting method) [54] from the equation:

$$\frac{S_N}{k_B} = \sum_{i=1}^{N-1} \ln(\omega_i) \quad (4)$$

where N denotes the number of beads in the chain, k_B is the Boltzmann constant, and ω_i is the effective coordination number of each succeeding bead in the chain, which is simply equal to the number of lattice sites occupied by the solvent molecules. The modification consists in application of the “phantom chain”; initially the whole chain was removed from the simulation space, than—following the chain path—the ω_i value was calculated step-by-step. After each step, the succeeding bead was put back to the chain structure.

The entropy contribution S_E due to the rearrangement of ions (B_1 beads) in the nanochannel was calculated as the difference between the mixing entropies of beads I in the simulation box in the presence and in the absence of the polymer chains:

$$\frac{S_E}{k_B} = -4\pi \sum_{i=1}^{R_S} i^2 (\rho_- \ln(\rho_-) + \rho_+ \ln(\rho_+) - \rho_0 \ln(\rho_0)) \quad (5)$$

where ρ_- and ρ_+ denote densities of anions and cations, respectively, along the channel, whereas ρ_0 stands for the

density distribution of the corresponding kind of beads I in the box without charged chains, assuming that at each point of the simulation the stationary state of counterion cloud is reached. The densities are defined as the ratios of the number of nodes occupied by ions to the total number of nodes in layers around the center of C1 macromolecule and in the empty channel. The summation radius R_S was equal to $300b$ and satisfied the minimum image convention requirement.

The Helmholtz free energy A of the system was calculated as the sum of (i) energetic contributions U_M and U_E associated with the mutual electrostatic interactions between all charged species in the system and their interaction with the external electric field and (ii) entropic contributions S_P and S_E associated with the chain conformations and the distribution of ions near polymer chains, respectively:

$$A = U_M + U_E - T(S_P + S_E) \quad (6)$$

The nMC [48] method was applied for the study of macromolecule translocation and ion migration. The elementary micromodification applied in the simulation consists of (i) random selection of the object to be moved (a polymer bead of one of macromolecules or a simple ion), (ii) a shift of the object to a new position (using elementary Verduer-Stockmayer algorithms which include the kink-jump, crankshaft (two segments), reptation (bilocal), or end movements [49, 50] of a polymer bead or a single jump to one of the neighboring lattice sites of a simple ion), (iii) checking whether the new position does not violate the topological constraints or excluded volume condition, and finally (iv) the Metropolis criterion. In the criterion, umbrella sampling [48] based on the entropies of macromolecules and ions (Eqs. 4 and 5) was applied as a measure of the probability of state of the system, whereas the system energy defined by Eqs. 2 and 3 was used to calculate the Boltzmann factor in the standard Metropolis algorithm at a constant reduced temperature $T = 1$. All types of elementary micromodifications were employed with the frequency proportional to the number of objects to which they can be applied because such a procedure provided the correct time scale of the simulation [55, 56].

Each simulation started with the macromolecules initially equilibrated and then located at the initial distance between their mass centers approximately equal to $50b$. As a result of the equilibration, the coordinates of mass centers and the distances between them in general were not integers but this uncertainty did not matter since the time from the start of simulation to the moment of macromolecules collision was not essential in the study. The polyion was located always at the opposite side relative to the attractive electrode. Then, the electrical field was switched on and directed movement of polyion (C1) started.

All the results presented in the paper are averages of at least 500–5000 trajectories of pairs of migrating chains. The

number of beads in both chains tested was $N = 10 \div 200$ (in most simulations $N = 50$). Each single simulation is a result up to 10^5 nMC steps (one nMC step corresponds to the number of shifts needed to give each of the beads the possibility to move once, i.e., 100 elementary macromolecule micromodifications of two macromolecules of $N = 50$). The actual number of steps was limited by reaching the bottom of the nanochannel by molecule C1. The unit of the corresponding time period was defined as one nMC cycle.

The data collected from the simulation contain the following: positions of mass centers of coils, all components of free energy of the system including internal energy of electrostatic interaction between all charged species—ions and charged segments, the electrostatic interaction of the species with the external electric field, conformational entropy of polyion and uncharged macromolecule, and configurational entropy of ions of a simple electrolyte in a dispersion medium. Since the athermal conditions were assumed, the study neglects all other intermolecular interactions as well as interaction with nanochannel walls except for the excluded volume effect. It should also be stressed that the studied system represents a damping dynamic model, holding only the activation aspect of diffusion and neglecting of the inertia effects [57].

Results

Details of motions of the polyion and uncharged macromolecule

The studies of the behavior of macromolecular pairs, consisting of a polyelectrolyte and a nonionic polymer confined in a nanopore, have shown that the translocation of the polyion caused by electric field may induce the collision between macromolecules, their mutual movement, compression of neutral macromolecule, and finally swapping of positions of both macromolecules. The exemplary trajectories of both macromolecules are presented in Figs. 2 and 3.

Figure 2 presents evolution of the system composed of two linear macromolecules in a nanochannel and subjected to an external electric field. One of the macromolecules is electrically charged (C1), while the other is neutral (C2). The trajectories of the centers of mass of both macromolecules can be divided into a few sections corresponding to the stages of the processes taking place in the nanochannel: (1) mutual approach of C1 and C2 ended with a collision, (2) stage of contact and permeation of C2 by C1 (induction time), (3) swapping of positions of C1 and C2 centers, (4) segregation of both macromolecules, and (5) diffusion of the released C2 into the bulk of nanochannel. The main parameters determining the rate of the whole process studied here are the time of swapping induction t_S , i.e., the time period between the collision (t_1) and exchange of coils' positions (t_2) and the time of

segregation t_R , i.e., the time between swapping (t_2) and final release (t_3) of macromolecules. The moment of collision of the macromolecules (t_1) was assumed to be the time when the mass centers of both macromolecules approach each other to a distance equal to the double radius of gyration (more specifically to the radius of gyration of the uncharged macromolecule in the bulk, R_{g0}). The moment of swapping (t_2) was precisely specified by the change in the sign of the vector projection on the axis parallel to the channel, representing the distance between the positions of macromolecules' centers, namely it is a moment of passing by the centers of mass. The moment of macromolecule release (t_3) was taken as the time when they cross-up the distance of R_{g0} moving away from each other.

The evolution of macromolecules can be more complex than that shown in Fig. 2. When the stimulus of the process, the electric field strength, is small, the swapping becomes a reversible process and “oscillations” of both macromolecules in the course of their travel along the nanochannel occur. Figure 3 presents the visualization of collision events in the course of migration of molecules. The collisions may result in bouncing when the chains come close to each other and then return in the direction they came from or in the swapping of their positions. In most simulations presented in the study (at $E(eb/k_B T) = 0.1$), the bouncing and multiple swapping events were negligible.

The evolution of molecule conformation is well illustrated by the ratio of the x component of the radius of gyration to the nanochannel width $2R_g(x)/D$ (Fig. 4). As shown, initially both conformations are usually elongated along the x -axis and undergo strong fluctuation. The initial elongation of C1 molecule is relatively large and rather constant as a result of electrostatic repulsion. C2 molecule structure is less stiff and undergoes stronger fluctuation. After the collision, the fluctuations of elongation of both macromolecules are much weaker since the number of available lattice nodes is reduced by beads of the other chain. The elongation of C1 molecule along the nanochannel is still somewhat larger than that of C2 because of the electric repulsion that stretches the conformation, which is not screened by any species and only slightly influenced by the counterion cloud. The values of $2R_g(x)/D$ of C2 molecule after collision are close to 1, which indicates that it forms a plug clogging the nanochannel and pushed by C1 molecule. Near the swapping moment, the spectacular changes in the conformations of interpenetrating molecules are observed—C2 molecule collapses whereas the C1 polyion takes more elongated structure. Finally, in the course of segregation and the conformation releasing stage, both molecules are heavily stretched along the nanochannel. After the separation stage, in the course of the following free diffusive expansion, a significant increase in the elongation of C2 molecule takes place whereas C1 undergoing the electric interaction remains compressed at the bottom of the nanochannel.

Fig. 2 Exemplary trajectories of two macromolecules (the distances of both macromolecules from the bottom of the nanochannel versus the number of nMC steps I), a polyion and an electrically neutral macromolecule, confined in a nanopore and subjected to an electric field. The figure presents the stages of motion of the neutral macromolecule C2 induced by translocation of the polyion in the electric field: diffusion, collision with macromolecule C1 (1), forced translocation, compression, swapping position with C1 (2), segregation to the distance of the radius of gyration (3), and finally free diffusion ($N = 50$, $D = 5b$)

The evolution of the conformational entropy of both molecules is shown in Fig. 5. As shown, the initial entropies of C1 and C2 are quite large. The C2 entropy undergoes higher fluctuations since the molecule conformation is more chaotic and not stretched by the electrostatic repulsion. The entropy of C1 is rather constant, which corresponds to a constant shift of the whole practically undeformed molecule induced by the external force. After collision, both entropies dramatically decrease. The entropy of C1 is larger than that of the compressed C2 molecule. In this stage, both molecules interpenetrate each other, so the available space is reduced by neighbors. The separation following the swapping of molecules produces an increase in the conformational entropy of both of them. The increase in entropy of C2 is much higher—the final entropy

is similar to that at the beginning of the process. The entropy of C2 is reduced by the compression induced by electrostatic attraction to the bottom of the nanochannel.

As shown in Fig. 6, the energy of interaction of the polyion with the external electric field, which dominates in both the energy and the entropy components of the free energy of the system, can be approximately represented by straight lines whose slopes are determined by the location of C1 molecule in the course of the whole process. Initially, a fast decrease in free energy results from the relatively fast electrophoresis of the polyion. The collision with C2 molecule breaks this fast motion—both molecules in the course of interpenetration move very slowly or even stop until the moment of swapping, when the C1 molecule velocity

Fig. 3 Difference between mass center coordinates of migrating macromolecules versus the number of nMC steps at the weak electric field ($N = 50$, $D = 5b$, $E(eb/k_B T) = 0.1$)

Fig. 4 Evolution of the ratio of the x component of the diameter of gyration to the nanochannel width ($2R_g(x)/D$) of both macromolecules in the course of migration specified by the number of nMC steps, I , accompanying the evolution shown in Fig. 2 ($N = 50$, $D = 5b$)

increases. This stage of the C1 motion is the fastest since the electrophoresis of macromolecule is assisted by entrophoresis caused by the increase in the conformational entropy of C1 and C2. Finally, the free energy of the system takes a minimum value when C1 molecule touches the nanochannel bottom. The position of molecule C2 does not bring a direct contribution to the free energy of the system because it is represented by electrically uncharged chain in athermal solution.

The exemplary results presented in Figs. 2, 3, 4, 5, and 6 were obtained by means of single simulations. Further results are averages of independent 500–5000 simulations.

Figure 7 shows the time distributions of particular steps of the studied process. The wide distribution of the time needed for macromolecule collision is not very representative of the macromolecule properties since its width depends on the arbitrarily assumed initial positions of both molecules. The time distributions of the following stages—the incubation time of swapping (interpenetration C2 by C1) and the time of final segregation shown in Fig. 7—are much narrower and can be well approximated by the logarithmic normal distribution. The process of mutual releasing of molecules (segregation) is faster than interpenetration since it is

Fig. 5 Dependence of conformational entropies of both macromolecules on the number of nMC steps in the course of migration accompanying the evolution shown in Fig. 2 ($N = 50$, $D = 5b$)

Fig. 6 The decrease in the total free energy of the system on the number of nMC steps in the course of migration accompanying the evolution shown in Fig. 2 ($N = 50$, $D = 5b$)

triggered by two consistent phenomena: electrophoresis and entropophoresis.

Generalization of the system behavior—some scaling laws

The results collected below are the attempt at quantitative description of characteristic time or rate of selected stages of the studied process. According to the relaxation of single macromolecules [48, 58, 59] or segregation of pairs of macromolecules [33, 35] in the tight confinement, we postulated the universal scaling law linking

the time of the stage t with the number of beads in the polymer chain N and the width of the nanochannel D :

$$t = aN^{\nu}D^{\mu} \quad (7)$$

where a is the proportionality coefficient.

As shown in Fig. 8a, an increase in the chain length causes an increase in the incubation time t_S . The relation between t_S and the number of beads is linear in the logarithmic system of coordinates. The mean value of the slope at $E(eb/k_B T) = 0.1$ is $\nu = 1.50 \pm 0.12$, which seems to be close to the time of relaxation of a single macromolecule in a confining channel ($\nu = 1.6 \pm 0.04$ or 1.33 [48, 60]). However, the process presented

Fig. 7 Distributions of time (expressed by the number nMC steps) needed for macromolecule swapping and releasing ($N = 50$, $D = 5b$). The fitted log-normal distributions are marked in blue

Fig. 8 The mean swapping induction time (a) and segregation time (b) versus the number of beads in the chain ($D = 5b$)

here is not a pure segregation nor a relaxation on the individual macromolecule, but it is a superposition of the pushing and interpenetration of macromolecule C2 by C1. The results obtained for weaker external electric field ($E(eb/k_B T) = 0.01$ and 0.001) are slightly biased producing a higher slope ($\nu \approx 1.6$, marked in dashed line). However, the longer swapping induction time results from repeated bouncing of macromolecules before swapping (as shown in Fig. 3).

The time of segregation process t_R versus number of beads scales approximately with the exponent $\nu = -0.3 \pm 0.1$ (see Fig. 8b) showing the increase in mutual velocity of macromolecules with the number of their beads. This dependence seems to be the opposite of that observed for the systems with no external electric field applied ($\nu = 0.3$ [33, 35]) and should be related to the relatively large electrostatic force pulling out C1 macromolecule from the C2 coil.

Dependencies of characteristic times of swapping and segregation processes on the nanochannel width are presented in Figs. 9a and 10a. As shown, both times t_s and t_R scale well with D , however with different exponents: $\mu = 1.5 \pm 0.09$ (for swapping) and $\mu = 2.0 \pm 0.11$ (for segregation). The difference is due to the fact that the swapping and segregation processes differ in some aspects: while swapping is influenced by two opposite forces induced by electrical field and the decrease in the conformational entropy, in the segregation both forces cooperate. However, these phenomena are not symmetrical since the relaxation of the C1 structure is often influenced by an additional confinement—the bottom of the nanochannel.

The unexpected increase in the incubation time of swapping with D can be explained if one takes into account that

Fig. 9 The mean swapping induction time (a) and the mean mutual velocity of chains in the time period between collision and swapping (b) versus the nanochannel width ($N = 50$)

Fig. 10 The mean segregation time (a) and the mean mutual velocity of chains in the time period between swapping and releasing of the chain C2 (b) versus the nanochannel width ($N = 50$)

not only the time but also the distance covered by macromolecules in the course of pushing of C2 molecule by C1 and simultaneous interpenetration of C2 by C1, depend on the pore diameter. The mutual velocity (the velocity of C1 relative to molecule C2) v_S versus D shown in Fig. 9b, although slightly irregular, illustrates a more intuitive trend—an increase in nanochannel width induces an increase in v_S .

The dependence of the segregation time on the nanochannel width presented in Fig. 10a is less controversial and generally agrees with the relationship obtained for pure segregation reported in [33, 35] (where $\mu = 0.3$) since the t_R is an increasing function of D , however with the exponent $\mu = 2.0$. The increase in D exerts a diminishing effect on conformational entropy; therefore, the entropic force causing the expansion of macromolecules decreases and the relaxation time increases. However, the electrostatic force pulling C1 macromolecule can affect t_R . Moreover, one should take into account that the distance covered in the segregation stage can be influenced by the bottom of nanochannel which stops the motion of C1 polyion. These additional effects are probably responsible for the difference in the μ exponents observed here and in [33, 35]. Finally, the more adequate relationship of the mutual segregation velocity versus pore width (Fig. 10b) shows that the diminishing trend disappears at large nanochannel widths.

In all simulations presented in the study, the persistent length of chains [61] ($\sim 2b$) was smaller than D , whereas the radius of gyration in the bulk exceeded D and varied from $8b$ to about $25b$. It implies rather the de Gennes or transition regime of confinement than the Odijk one [60]. Figures 8, 9, and 10 seem to present reasonable dependencies similar to the results presented for segregation or relaxation of macromolecules in similar circumstances [33–35]. However, the dependencies deal with the special case when the diffusion and

forced motion occur at the same time and cannot be compared directly with available experiments and theories.

Conclusions

It was shown that the polyion moving in the external electric field in the tight channel is able to force the motion of an uncharged macromolecule. After the moment of collision of both molecules, the pushing of the neutral macromolecule accompanied by its interpenetration by the polyion takes place. The interpenetration is associated with changes in conformation of the macromolecules as well as in their entropies and internal energies. In the course of interpenetration, the swapping of mass centers occurs and then, when the electric external field is strong enough, the unidirectional segregation takes place, in which the uncharged macromolecule diffuses to the bulk of the nanochannel. The induction time of swapping scales with the number of beads in polymer chains in the way independent of the density of electric charges on the macromolecule and the strength of electric field.

The results presented permit designing new methods for manipulation and control of individual macromolecules subjected to external electric field. The hypothetical system of nanochannels and/or microswitches consisting of a labyrinth of crossing patches switched on by electrophoretic or entropic gradients seems to be able to be used for the segregation/isolation of macromolecules of assumed properties. The system can be controlled by the external electric field, pH, and the ionic strength of dispersion medium.

However, it should be noted that since the simulations concern a relatively small number of ionic beads, the presented results are applicable only to the systems containing an electrolyte solution of extremely small ionic strength.

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