Noise effects in polymer dynamics

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The study of the noise induced effects on the dynamics of a chain molecule crossing a potential barrier, in the presence of a metastable state, is presented. A two-dimensional stochastic version of the Rouse model for a flexible polymer has been adopted to mimic the molecular dynamics and to take into account the interactions between adjacent monomers. We obtain a nonmonotonic behavior of the mean first passage time and its standard deviation, of the polymer centre of inertia, with the noise intensity. These findings reveal a noise induced effect on the mean crossing time. The role of the polymer length is also investigated.

Keywords: Polymer dynamics, metastability, noise enhanced stability, DNA translocation.

I. INTRODUCTION

Many important biological processes are governed by the transport of molecules across membranes. In cellular systems proteins translocate from the cytosol into the endoplasmatic reticulum [Hu et al., 2005; Chiam et al., 2006], or into mitochondria or chloroplasts [Frappat et al., 2003]; RNA molecules are transported across a nuclear membrane after their synthesis [Schatz & Dobberstein, 1996]; in infections from bacteria resistant to antibiotics, alternative therapy uses bacteriophages which push a long chain of DNA molecules through the pores of a membrane [Adhya & Merril, 2006]. The study of the dynamics of translocation of individual polymers across nanometer-scale pores is essential to help the understanding of how biological systems work and it also represents a powerful instrument to investigate the structural characteristics and conformational changes of chain molecules, their interactions with the walls of the pore and specific folding or unfolding processes related to the crossing event. A fundamental work on polymer translocation was carried out by Kasianowicz et al. [1996]. In their experiments, single-stranded DNA molecules are forced by an applied electric field to move through a 2.6-nm diameter ion channel in a voltage-biased lipid bilayer; during the passage across the pore, the polymer significantly reduces the single-channel ion current. By measuring the duration time of each current drop - blockade -, they have demonstrated that the crossing time linearly increases with the polymer length. By using a similar experimental setup, Meller et al. [2002] have also shown that the time-length relationship depends on the number of adenines in the polymer, concluding that the translocation time is heavily influenced by specific interactions between the DNA and the nanopore walls. They also suggest stronger interactions at lower temperatures because of the longer measured translocation times [Meller et al., 2000]. On the other hand, very interesting experimental results by Han et al. [1999] show longer crossing times for shorter DNA molecules, suggesting the existence of a quasi-equilibrium state of the polymer after being trapped for a time. Theoretical studies have demonstrated that the translocation time of a long N-segments chain molecule, diffusing across a membrane, scales as $N^3$ if there is no free energy bias between the two sides, or as $N^2$ in case of adsorption [Sung & Park, 1996; Park & Sung, 1998]. Strong interactions between the polymer and the pore modify the dynamics of the portion of the chain inside the channel, mak-
ing linear the relationship between the crossing time and $N$ [Lubensky & Nelson, 1999]. In the presence of an externally applied potential, the linear dependence of the crossing time on the length of the polymer is confirmed only for the case of a hairpin crossing mechanism of translocation [Schatz & Dobberstein, 1996; Sebastian & Paul, 2000]. The dependence of the crossing time on the length of the polymer chain, as reported in different experimental works, may be influenced by the different geometrical and physical characteristics of the pore-channel device, the adopted polynucleotides, the intensity of the driving electric fields. We are convinced that, in some cases, a special condition for the polymer travelling across a nanometer-scale channel can be realized to make it temporarily trapped into a metastable state, as already suggested by Han et al. [1999]. For this reason, we decided to start a theoretical study of the dynamics of polymers in a state out of equilibrium under the influence of a noisy environment. In this paper, we firstly describe the model and the mathematical framework adopted to simulate the polymer dynamics and, finally, we comment our results.

II. THE MODEL

Stochastic modelling of polymer dynamics starts with the choice of a model for the chain molecule. In the simplest model of a polymer, monomers are freely-jointed rigid rods of a fixed length (Kuhn length) and any kind of interactions among them is neglected. For our studies, we have adopted the Rouse model for a flexible polymer [Rouse, 1953; Doi & Edwards, 1986]. This model describes the molecule as a chain of $N$ monomers connected by harmonic springs (Fig. 1).

At this stage, we have neglected the excluded-volume effect and any hydrodynamic interaction between monomers and solvent, as modelled by the Zimm theory [Zimm, 1956]. In a recent experiment, a fluorescent correlation spectroscopy technique has been applied to monitor the stochastic motion of individual monomers within isolated DNA molecules [Shusterman et al., 2004]. By comparing the observed time dependence of the mean-squared displacement of the fluorescent monomer with that predicted by the available models, Shusterman and coworkers assert that double stranded DNA (dsDNA) behaves like a semiflexible coil following the Rouse model, while in the case of single stranded DNA (ssDNA) the monomers show a Zimm-type kinetics. A similar analysis of the short-time dynamics demonstrates that intramolecular hydrodynamic interactions in dsDNA chains cannot be ruled out [Tothova et al., 2005; Petrov et al., 2006], suggesting the application of a mixed Rouse-Zimm model [Lisy et al., 2005]. We have decided to start our investigation by using a relatively simple bead-spring model in order to avoid any secondary effect of metastability induced by the combination of an excessive number of parameters.

The translocation of a long molecule through a narrow pore is caused by a forced process of unfolding by which the coil is stretched across the channel, returning in its native folded state again at the exit only. Within the pore region, the free energy per segment of the polymer is higher, representing a barrier for the motion of the molecule [Sung & Park, 1996]. In the present work, we study the effect of the temperature fluctuations on the dynamics of a chain polymer escaping from a metastable state through a potential barrier in a two-dimensional domain. The polymer motion is modeled as a stochastic process of diffusion in the presence of a time-independent potential having a profile described by the following equation:

\[ U(x) = ax^2 - bx^3, \]

with parameters $a=0.3$ and $b=0.2$, as already adopted by Fiasconaro et al. [2003] for the unidimensional single-particle case. The corresponding 2D-surface is shown in Fig. 2. The drift of the $i$-th monomer of the chain is described by the
following coupled Langevin equations [Gardiner, 1993]:

\[ \frac{\partial x}{\partial t} = -\frac{\partial U(x)}{\partial x} + F_{\text{int}}(x) + \sqrt{D} \xi_x(t), \]  
\[ \frac{\partial y}{\partial t} = F_{\text{int}}(y) + \sqrt{D} \xi_y(t), \]

where \( F_{\text{int}}(x) \) and \( F_{\text{int}}(y) \) are the \( x \) and \( y \) components, respectively, of the harmonic forces between adjacent monomers and \( \xi_x(t) \) and \( \xi_y(t) \) are white Gaussian noise modeling the temperature fluctuations, with the usual statistical properties, namely \( \langle \xi_i(t) \rangle = 0 \) and \( \langle \xi_i(t) \xi_j(t + \tau) \rangle = \delta_{ij}(\tau) \) for \( (i, j = x, y) \). We have numerically solved the above system of equations by performing a set of \( 10^5 \) simulations for 22 different values of the noise intensity \( D \) and 5 different polymer length configurations. In this study, we put the starting distance \( L_0 \) between two adjacent monomers of the molecule chain equal to the rest length of the ideal spring connecting them. We have chosen \( L_0 = 0.01 \) and the harmonic constant equal to 1.0 (in arbitrary unit). The number \( N \) of monomers changes between 2 and 10. The initial position is set to \( x_0=1.3 \) for all monomers; every simulation stops when the \( x \) coordinate of the center of mass of the chain reaches the final position at \( x_f=2.2 \). Then, the Mean First Passage Time (MFPT) and its standard deviation are calculated.

III. RESULTS

First results of this study suggest the presence of the noise enhanced stability (NES) effect [Mantegna & Spagnolo, 1996; Agudov & Spagnolo, 2001; Fiasconaro et al., 2003; Fiasconaro et al., 2005] for a short polymer escaping from a potential barrier. In the left panel of Fig. 3 we show how the MFPT changes with the noise intensity at different polymer lengths. Assuming identical unstable initial conditions we find that: (i) the NES effect is more relevant for shorter chains (lower number of monomers); (ii) the maximum of the MFPT rapidly decreases at increasing polymer length and its position shifts towards higher levels of noise.

The dynamics of shorter chains is much more similar to that of a single particle escaping from the potential well. As a consequence shorter chains show more pronounced NES effect, with higher maximum values of the MFPT. Moreover, the shift of the position of this maximum is directly connected with the polymer length. In fact, longer polymers need higher noise intensity values to move the centre of mass back into the metastable state, starting from initial unstable states. Longer chain polymers experience more than shorter ones the effect of the potential slope in the unstable region. It is important to note that the behavior of MFPT at very low noise intensities \( (D \leq 5 \cdot 10^{-2} \), in Fig. 3a) should have divergent trend because the initial unstable states used in our simulations are in the divergent dynamical regime (detailed analysis on the divergent dynamical regime can be found in Fiasconaro et al. [2005]). To find this behavior we need very long computer simulation times, which become greater as the polymer length increases. In fact the probability that the entire sequence of \( N \) monomers experience the potential well is much lower than the single particle, and so more difficult to see in a finite time computer simulation.

The plot of the standard deviation of the first passage time as a function of the noise intensity \( D \) is shown in Fig. 3b. An increasing of the standard deviation means a spread of the passage time distribution and this represents a direct evidence of the noise-induced capture effect.

FIG. 2 Potential surface of the two-dimensional barrier. Inset: projection of the potential surface on the plane \( y = 0 \).
FIG. 3 (a): Mean first passage time vs. noise intensity for five different numbers $N$ of monomers in the polymer. The starting distance between adjacent monomers coincides with the rest distance $L_0 = 0.01$. The initial condition $x_0 = 1.3$ is the same for all the monomers. The dashed line indicates the shift of the maximum of the MFPT. (b): Standard deviation of the passage time vs. noise intensity for different polymer configurations.

of the barrier. In Fig. 4 we report the probability density function (PDF) of the passage time of the polymer center of mass for the case of $N=4$ and four values of the noise intensity, namely $D = 0.01, 0.1, 1.0$ and $10.0$. The PDFs obtained with lower noise intensities are characterized by a strong asymmetry and high long tails. In this figure we can clearly see that, while the most probable value follows a monotonic decreasing trend with increasing noise intensity, the MFPT is strongly affected by the rare events of trapped particles giving the long tail of the distribution at high values of the passage time (see inset in Fig. 4). The shape of the tail significantly influences the mean crossing time by increasing its value with respect to the mode. For the case of $N=10$, the plot of MFPT vs. $D$ does not show any evidence of a NES effect, but not the standard deviation, which shows a non-monotonic behavior.

The plot of the MFPT as a function of the polymer length (Fig. 5a) at different noise intensities shows that: (i) the quasi-deterministic MFPT (noise level $D = 0.01$) does not depend on $N$; (ii) for $D > 0.01$, the dependence of MFPT on the polymer length shows a non-monotonic trend with the noise intensity: differences of MFPT are very sensitive to the number of monomers when the noise level is low, while they are reduced at higher noise intensities. In Fig. 5b it is interesting to note the capture effect also for the polymer with $N=4$ and the low level of noise $D = 0.03$.
FIG. 5 (a): Dependence of the MFPT on the number $N$ of monomers at different noise intensities. Initial conditions are the same as in Fig. 3. Red lines are used to discriminate the ascending trend of MFPTs with the decreasing of the noise intensity with respect to the opposite behavior at extremely low noise intensity (blue lines). (b): Standard deviation of the passage time vs. $N$ for different levels of noise.

IV. CONCLUSIONS

Experimental and theoretical studies on the translocation time, taken by a chain molecule to cross a membrane, show a strong dependence of this time with the length of the polymer. In this work we propose a possible reason of this dependence by investigating the stochastic dynamics of a polymer, with different lengths, surmounting a potential barrier. After being trapped for a while, the molecule leaves the top of the barrier exhibiting an enhancement of the mean crossing time as a function of the temperature fluctuations. This is a typical signature of the presence of a metastable state in the system investigated. Our analysis shows a clear effect of noise-enhanced stability on the mean first passage time of short polymers for initial unstable conditions. Our simulations demonstrate that longer polymers can travel the same channel distance faster than shorter chains. This result is in agreement with the experimental measurements of DNA mobility carried out by Han et al. [1999], but a deeper analysis on the role of initial conditions on the translocation time is necessary. Our findings are also in accordance with the experimental results of Meller et al. [2000], that is the longer translocation times measured at lower temperatures, as we have found near the maxima of MFPTs (see Fig. 3a).

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