

New and Notable

How Polymers Translocate Through Pores: Memory is Important

Anatoly B. Kolomeisky

Department of Chemistry, Rice University,
Houston, Texas

Many biological processes, such as DNA and RNA transport across nuclear pores, injections of viral DNA, gene swapping, and protein transport across cellular membranes, involve the motion of polymer molecules across narrow channels (1). Translocation through nanopores is also one of the most important and powerful methods for analyzing properties of single biopolymer molecules and for investigating different biophysical phenomena (2,3). The polymer translocation is generally viewed as an effective one-dimensionally activated process that involves overcoming the entropic barriers. These barriers appear due to the decrease in the number of available polymer configurations in the translocating molecule in comparison with the free polymers. External fields and chemical interactions significantly accelerate transport across the channels. In biological systems, the motion of DNA, RNA, and proteins through the pores is assisted by specific chemical interactions with membranes or other molecules (1). In experiments, charged polymer molecules are driven through nanopores with the help of electric fields (2,4).

The polymer translocation is well-studied experimentally using biological channels (α -hemolysin proteins) and solid-state synthetic nanopores. However, theoretical understanding of the transport mechanism of polymer molecules is still limited. The situation is especially controversial when external

fields are weak and the translocation dynamics is mainly controlled by entropic factors. Phenomenological theories, which assume that during the translocation, the polymer quickly relaxes to an equilibrium state (5,6), predict that in this regime, the mean translocation time τ is a function of the polymer's size N , which is $\tau \propto N^\alpha$ with $\alpha = 2$. However, this result is unphysical (7), since the translocating polymer chain cannot move faster than the free polymer, which has a relaxation time of $\sim \tau \propto N^{1+2\nu}$, where $\nu \approx 0.59$ is an exponent for real polymers in three-dimensional systems (7,8). It was suggested that the mean translocation time-scales exactly as $\tau \propto N^{1+2\nu}$, which corresponds to neglecting polymer-pore interactions (7). It was also argued that the polymer translocation shows anomalous dynamic behavior (9), although the origin of this phenomenon was not explained. Since the weak forces regime is not easily accessible experimentally, extensive Monte Carlo computer simulations have been performed (8,9). But the results of computer studies led to more confusion, yielding values of the exponent α that are between 2.18 and 2.59, and underscoring the complexity of polymer translocation processes. An article by Panja and Barkema in this issue of *Biophysical Journal* provides a comprehensive theoretical description of mechanisms of driven polymer translocation, and it is supported by high-precision, extensive Monte Carlo computer simulations.

A theoretical model by Panja and Barkema focuses on dynamics of polymer segments at the immediate vicinity of the pore. Entry of a monomer into the channel or moving out of the pore affects the chain tension, which leads to an adjustment of the translocation velocity as well. However, the change in the tension is not instantaneous, and there is some delay in the response for the translocation velocity. This leads to an important observation that memory effects are critical for polymer translocation. The delay is determined by the

properties of a polymer chain near the hard wall, and it is shown that for weak forces, the Rouse time $\tau_{\text{Rouse}} \simeq N^{1+2\nu}$ and for large forces, the time $\tau_F \simeq N^2$ separates regimes of anomalous translocation dynamics and simple diffusive behavior. Theoretical calculations also show that the mean translocation times for weak forces scales as $\tau \simeq N^{2+\nu}$ as a function of the polymer length, while for large external forces F , the dependence is $\tau \simeq N^2/F$. The most striking result of this work is the fact that translocation velocity is not a constant, and it generally depends on time as a direct consequence of the dynamics of polymer segments near the pore.

Although the theoretical picture of polymers threading through pores presented by Panja and Barkema provides a significant advancement in our understanding mechanisms of translocation, it still leaves many questions unanswered. The theoretical analysis has been performed for a local application of the external force at one of the polymer ends. In cells, chemical interactions that assist in the polymer moving across the channels are typically localized in or near the membrane pores. In experiments, the external fields influence many monomers inside and around the pore. External forces might also change significantly the distribution of polymer segments near the pore. Probably, the most important question is related to the effect of hydrodynamic forces and interactions during the polymer translocation. It is not at all clear how hydrodynamics might affect memory. Another question is what the mechanisms of translocation are when the polymer moves through the channel not like a single linear chain but in a folded configuration (10). The work by Panja and Barkema presents an excellent example of how complex biophysical processes can be analyzed via a combination of theoretical and computational approaches that provide guidance for future experiments.

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Address reprint requests to Anatoly B. Kolomeisky, Tel.: 713-348-5672; E-mail: tolya@rice.edu.

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