Polymer translocation in solid-state nanopores: Dependence on hydrodynamic interactions and polymer configuration

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ARTICLE INFO

ABSTRACT

We present a Brownian dynamics investigation of 3-D Rouse and Zimm polymer translocation through solid-state nanopores. We obtain different scaling exponents α for both polymers using two initial configurations: minimum energy, and 'steady-state'. For forced translocation, Rouse polymers (no hydrodynamic interactions), shows a large dependence of α on initial configuration and voltage. Higher voltages result in crowding at the nanopore exit and reduced α. When the radius of gyration is in equilibrium at the beginning and end of translocation, $\alpha = 1 + \upsilon$ where υ is the Flory exponent. For Zimm polymers (including hydrodynamic interactions), crowding is reduced and $\alpha = 2\upsilon$. Increased pore diameter does not affect α at moderate voltages that reduce diffusion effects. For unforced translocation using narrow pores, both polymers give $\alpha = 1 + 2\upsilon$. Due to increased polymer–pore interactions in the narrow pore, hydrodynamic drag effects are reduced, resulting in identical scaling.

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1. Introduction

One of the most significant advances in the single-molecule analysis of polymers is the use of nanopore devices to obtain information on individual biopolymer chains as they translocate through the nanopore. Such nanopores typically have diameters in the 1–10 nm range and have been fabricated using ion channel proteins [1–5] or solid-state materials such as silicon oxide [6–9] and silicon nitride [10–19]. Nanopore devices are one of the potential 'next-generation' single-molecule analysis devices, due the possibility of obtaining both high resolution and throughput [20]. One example of the use of nanopore devices is in the determination of DNA chain lengths (Supporting Information, Figure S1). Because DNA possesses an inherent negative charge, it can be driven through a nanopore with the aid of an applied voltage. When placed in an aqueous electrolyte solution, a current flows through the nanopore. At the beginning of the experiment, when the DNA is on the 'cis' side of the nanopore (corresponding to the electrode with negative voltage) and not blocking the pore, the current is at its maximum value. When the DNA chain begins to thread through the nanopore, a large fraction of the electrolyte ions will be blocked and hence the current decreases to a minimum value.

Once the DNA has fully translocated and reaches the 'trans' side of the nanopore, the ionic current returns to its original maximum value. Based upon the duration of current blockage, theoretically, the length of the DNA chain can be determined. This experiment, which is orders of magnitude faster than conventional gel electrophoresis [20], is referred to as a translocation time measurement [3,20,21]. It should be noted that currently, due to the interactions between the DNA and the nanopore, translocation times can have very large distributions making it difficult to know the exact length of the DNA chain [21]. However, it may be possible to control DNA-nanopore interactions by changing the nanopore surface composition with either atomic layer deposition [15,22] or coating the surface with an organic material [23] thus reducing the stochasticity of the translocation process. Further research is needed to find the perfect nanopore composition that will provide optimum results.

Unfortunately, the underlying mechanisms of biopolymer translocation through a nanopore are far from well-understood. Several authors, including ourselves, have studied a number of aspects of biopolymer translocation with coarse-grained dynamical simulation techniques [24–51]. One primary issue, that has yet to be completely resolved, is the scaling law behavior of translocation time vs. chain length [24]. In fact, as we will discuss, the scaling exponent is heavily dependent upon applied force, pore diameter, and initial polymer configuration. In the first studies involving unforced polymer translocation, Sung and Park [52] and Muthukumar [53], using a derived free energy equation involving polymer

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translocation through a narrow hole, found the translocation time scales as $\tau \sim N^2$ where N is the number of monomers in the chain. Chuang et al. [25] later found an inconsistency in this scaling law in relation to self-avoiding polymers, in which the radius of gyration scales as $R_g \sim N^{\upsilon}$, where υ (the Flory exponent) is 0.588 in three dimensions [54]. By estimating the distance a polymer travels during the translocation process as R_g and noting that the center-of-mass diffusivity of a Rouse polymer (i.e. no hydrodynamic interactions) is D_o/N (where D_o is the diffusion coefficient of a single monomer), Chuang et al. [25] estimated the unforced translocation time scaling law as $\tau \sim (R_g)^2/(D_o/N) \sim N^{1+2\upsilon}$, which is the same scaling behavior of the Rouse relaxation time [54], estimated as the time required for a polymer to diffuse its radius of gyration [25,33]. Thus, for self-avoiding polymers, a scaling exponent of $\tau \sim N^2$ would indicate translocation being much faster than the polymer relaxation time, which is not possible. Hence, $\tau \sim N^{1+2\upsilon}$ could be seen as a better estimate. Unfortunately, as Chuang et al. [25] points out, one would assume that a polymer would diffuse through a pore much slower than in the bulk. As a result, this scaling exponent could be seen as a lower bound. Panja et al. [26] modified the expression to $\tau \sim N^{\upsilon+2}$ to account for memory effects, due to a local change in monomer concentration on both sides of the pore during the translocation process, which was also observed by Dubbeldam et al. [50] and Gautheir et al. [55]. In addition, de Haan and Slater [46] found the scaling exponent is heavily dependent on the pore diameter varying from $\tau \sim N^{1+2\upsilon} \sim N^{2.2}$ for a diameter of σ up to a value of $\tau \sim N^{2.93}$ for a diameter of 10σ, where σ is the diameter of each monomer. This increase in scaling exponent is due to the fact that for pore diameters larger than 1.5σ, the monomers do not translocate in a single-file fashion but rather the polymer folds inside the nanopore during the translocation process.

When translocation is aided with an applied force, the scaling laws will change. For example, Kantor and Kardar [27] derived a scaling law expression for a long polymer chain traversing a short pore with an applied force F, viz. $\tau \sim R_g/(F/N) \sim N^{\upsilon+1}/F$. A limitation of this scaling law is the assumption that the polymer is in equilibrium throughout the translocation process. This may not always be correct, especially in the presence of high driving forces. Vocks et al. [28] derived a new scaling law, $\tau \sim N^{(1+2\upsilon)/(1+\upsilon)}/F$, including the memory affects due to local tension in the polymer chain when a monomer translocates from one side of the pore to the other. Another factor that greatly affects scaling law behavior is the applied force strength. In some previous simulations it was found that the scaling exponent increased with increasing force [29–31], while in others the scaling exponent decreases with increasing force [32–34,56].

One proposed explanation for these differing observations is that during forced translocation, the polymer is driven out of equilibrium [32,33,35,36]. At first, as was demonstrated in previous simulation studies, extreme monomer crowding on the *trans* side of the nanopore [29–34,36], a clear indication that the polymer has not had ample time to equilibrate once it has passed through the nanopore, was thought to be responsible for scaling laws differing from the value predicted by Kantor and Kardar [27]. However, in more recent studies involving tension propagation theory [31,56–65], it has been proposed that non-equilibrium effects are solely based on changes to the polymer on the *cis* side of the nanopore rather than any *trans* side effects. As discussed by Lehtola et al. [30], in the presence of a moderate driving force, the translocation time process can be thought of as a force balance between the applied driving force and the drag force due to the monomers on the *cis* side moving towards the nanopore. When the force used to drive the polymer through the nanopore is applied to monomers inside the nanopore, a tension in the chain is created. This tension propagates along the backbone of the chain creating a "tension front" or boundary in which monomers influenced by the tension move towards the nanopore, and thus contribute to the overall drag force, while the other monomers beyond the front do not. This tension in the chain, depending upon the strength of the applied force, will alter the initial equilibrium shape of the polymer. Weak forces ($N^{-\upsilon} < F < 1$) will result in a "Trumpet" shape, moderate forces ($1 < F < N^{\upsilon}$) will result in a "Stem–Flower" (or "Stem-Trumpet") shape, whereas strong forces ($F > N^{\upsilon}$) will result in "Strong stretching" (or "Stem") shape [31,59]. These changes in polymer shape are potential reasons for scaling law deviations.

One of the goals of tension propagation theory is to predict the movement of the tension front as a function of time during the translocation process. Using the conservation of mass relating the tension front and the number of monomers experiencing the chain backbone tension, Saito and Sakaue [58,59] and Dubbeldam et al. [31], predicted that the total translocation time is the sum of three individual time components with different scaling laws. The first component, τ_{ini}, is the time that it takes to create an initial blob state before monomer translocation. This term, in both the research of Dubbeldam et al. [31] and Saito and Sakaue [59], has been hypothesized to be force, not length dependent and, in recent Brownian Dynamics Tension propagation theory [56], has been questioned to even exist. Hence, we will omit it from our discussions here. The second component, τ_1, is the time required for the tension in the chain (generated by the pulling force) to propagate to the end of the polymer. This term dominates for longer chains. Once the tension reaches the end of the chain, the polymer then moves with a constant velocity for a time period τ_2, which is the dominant term in short chains. For moderate to strong forces, the range at which most simulations and experiments are performed at [59], Dubbeldam et al. [31] concluded the translocation time $\tau = \tau_1 + \tau_2$, where $\tau_1 \sim N^{1+\upsilon}/F$ and $\tau_2 \sim N^{2\upsilon}/F$. In addition, they also proposed a scaling law transition from $\tau \sim N^{2\upsilon}$ to $\tau \sim N^{1+\upsilon}$ as the applied force is increased, thereby indicating a lower bound exponent of $\alpha = 2\upsilon$, also proposed by Vocks et al. [28]. Slight differences were obtained for these scaling laws in the research of Saito and Sakaue [59]. For example, for moderately applied driving forces, the second translocation time component was found to scale as $\tau_1 \sim N^{\alpha}/F$, where $\alpha = ((z-1)(1+\upsilon) - (1-\upsilon))/(z-1)$. For a Rouse polymer, $z = (1+2\upsilon)/\upsilon$, which results in $\tau_1 \sim N^{1.43}/F$, which is smaller than the values obtained by Kantor and Kardar [27] and Dubbeldam et al. [31]. On the other hand, for strong forces, Saito and Sakaue [59] obtained $\tau_1 \sim N^{1+\upsilon}/F$, agreeing with the previous results. Finally, for both moderate and strong forces, Saito and Sakaue [59] obtained the third time component to scale as $\tau_2 \sim N^{2\upsilon}/F$, which agrees with the results obtained from Dubbeldam et al. [31].

Most recently, using the same mechanisms described in the tension propagation theory discussed above, Ikonen and coworkers [56,62,63], beginning with the energy balance equations initially derived by Sung and Park [52] and Muthukumar [53], developed a method for computing the Brownian dynamics motion of the translocation coordinate (length of the chain that has translocated to the *trans* side of the nanopore) in the high damping limit known as the Brownian Dynamics Tension Propagation (BDTP) theory. As shown in previous simulation results [30,42,66,67], the velocity of a polymer translocating through a nanopore is not constant, but rather varies with time. Using this observation, instead of assuming a constant drag coefficient throughout the translocation time simulation, Ikonen and coworkers [56,62,63] instead assumed a drag coefficient that varied in time. Interestingly, from their results, not only did they find good agreement between their predictions and results from MD simulations, but they also discovered that the translocation time scaling exponent is dependent upon length, only