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Abstract – We derive a scaling ansatz for the mean first passage time (MFPT) τ of a driven polymer chain through a nanopore as a function of the chain length N, the external bias f, and the effective pore-polymer friction η, and demonstrate that the pore-polymer interaction, which we introduce as a correction term to asymptotic scaling, is responsible for the dominant finite-size effect. This ansatz provides a simple procedure to extract the asymptotic τ in the large-N limit from a finite chain length data (obtained either from experiment or simulation) by eliminating the correction-to-scaling term. We validate the ansatz applying it on a large set of data for τ obtained using Brownian dynamics (BD) and Brownian dynamics tension propagation (BDTP) simulation results (IKONEN T. *et al.*, *Phys. Rev. E*, **85** (2012) 051803; *J. Chem. Phys.*, **137** (2013) 085101) for a variety of combination for N, f, and η. As an important practical application we demonstrate how the rescaling procedure can be used to quantitatively estimate the magnitude of the pore-polymer interaction from simulations or experimental data. Finally, we extend the BDTP theory to incorporate Zimm dynamics and find that the asymptotic results for τ (or the translocation exponent) remains unaltered with the inclusion of the hydrodynamics interactions (HI), although the convergence is slower than what we observe for Rouse dynamics. Using the rescaling ansatz we find that these new findings are in good agreement with the existing experimental results as well as with lattice Boltzmann results for driven polymer translocation (PT) for small N.

Introduction. – The transport of a polymer through a nano-sized pore occurs in many biological processes and functions, including DNA and RNA translocation through nuclear pores, protein transport across membrane channels and virus injection [1]. The translocation process is also envisioned to have several biotechnological applications in gene therapy, drug delivery and rapid DNA sequencing [2–4]. Naturally, polymer translocation (PT) problem (for reviews, see, *e.g.*, refs. [5,6]) has attracted considerable attention among broad scientific disciplines [2–44]. Of particular interest is the case of driven PT where the segment of the polymer inside the pore is driven by an electric field, in which case one asks the

central question as to how the MFPT τ depends on the chain length N, characterized by the translocation exponent α ($\tau \propto N^{\alpha}$). A large number of experimental groups have been exploring different variations of this method for fast, portable and inexpensive DNA sequencing device. To date, many aspects of driven PT has remained elusive and offers theorists a number of unresolved issues to be settled.

Unlike unbiased translocation where the threading polymer through the nanopore can be considered as a one-dimensional diffusion across an entropic barrier [9,10], the driven PT is essentially a non-equilibrium process [18–21] which makes this apparently innocuous problem intrinsically harder. A true non-equilibrium

treatment was given first by Sakaue, using a phenomenological picture of tension propagation (TP) along the chain backbone at the *cis* side [34]. Using force balance, mass conservation, and self-similarity of the polymer [34–37], Sakaue's theory is analytically solvable but only in the asymptotic limit of long chains when local effects, such as, friction inside the pore, small variations of pore width etc., become negligible. Therefore, this theory as such cannot be used to compare results obtained from many simulation studies and experiments on finite chains where non-universal effects can be large and can play a significant role. Indeed for the case of driven PT, translocation exponents obtained from different simulation and theoretical studies are scattered in a broad range and often underscore the theoretical prediction which has not been understood [23]. Therefore, a theory which will account for these effects for finite chain lengths and yet will smoothly interpolate to the infinite chain limit is something which is thus far missing and badly needed to understand and elucidate the role of different contributing factors to the translocation process.

One of the main purposes of this letter is to find a reason for the scattered values of the scaling exponents reported in the literature. We derive a scaling ansatz for the MFPT $\langle \tau \rangle$ of a driven polymer chain through a nanopore as a function of the chain length N, the external bias f, and the pore-polymer interaction (friction) η, and demonstrate that the pore-polymer interaction, which we introduce as a correction term to asymptotic scaling is responsible for the dominant finite-size effect. This ansatz i) provides a simple procedure to extract the asymptotic $\langle \tau \rangle$ in the large-N limit from a finite chain length data (obtained either from experiment or simulations) by eliminating the correction-to-scaling term, and ii) allows to exploit the rescaling procedure to quantitatively estimate the magnitude of the pore-polymer interaction from simulations or experimental data which can be of immense practical value.

Having established rather conclusively (from a huge set of simulation data that we gathered from BD and BDTP studies as explained later in the text) we naturally became ambitious to address the role of hydrodynamic interactions (HIs) in this context. Our third significant result in this letter is the iii) incorporation of Zimm dynamics into the BDTP model that we introduced earlier and iv) showing that in the presence of HIs the asymptotic behavior of MFPT of driven PT remains unaltered, although the finite chain effect is more acute. The existing lattice Boltzmann (LB) simulation study by Fyta *et al.* [33] and experimental results for driven PT by Storm *et al.* [8] agree well with our theory. Thus, we believe that these novel results apart from resolving some of the long-standing issues will promote further work on PT. We provide some of the possible extensions of these new results in the "Conclusions" section.

Theory. – A thorough account of the TP theory for the driven PT is given in [34,35,41,42] in the asymptotic N limit, here we present some central results using relatively simple arguments. To find the mean translocation time τ (or the mean translocation velocity $\langle v \rangle$), for a chain of length N, one needs to consider the force balance between the driving force f and the drag force, as suggested, *e.g.*, in ref. [8]. In principle, the total drag has three contributions: the friction due to the *cis* side subchain and the solvent, the corresponding friction for the *trans* side subchain and the friction of the chain portion inside the pore. For driving forces typically used in experiments and simulations, the *trans* side has an almost negligible contribution to the overall friction [42,43]. Therefore, the effective friction Γ can be approximately written as $\Gamma(t) = \eta_{\text{cis}}(t) + \eta_p$, where η_{cis} is the friction of the *cis* side subchain and η_p is the (effective) pore friction. If the length of the pore, l_p, is small compared to the contour length of the chain, $l_p \ll aN$ (with a the segment length), the number of segments occupying the pore and thus the pore friction η_p can be regarded as constant during the translocation process.

The friction due to the *cis* side subchain, on the other hand, depends explicitly on the number of mobile monomers on the *cis* side. Due to the non-equilibrium nature of the problem, this number depends not only on the chain length N but also on time t [17,18,32, 34,36,37,40–43]. Solved as a function of time, $\eta_{\text{cis}}(t)$ shows non-monotonic behavior that suggests the division of the translocation process into two stages: the tension propagation stage of increasing friction, and the post propagation stage of decreasing friction [42,43]. However, averaged over the whole process, the time-averaged η_{cis} is approximately given as $\langle \eta_{\text{cis}} \rangle \sim N^\nu$, leading to the asymptotic ($N \to \infty$) scaling of the mean translocation time as $\tau \sim N^{\nu+1}$ [40–43].

The full solution of $\eta_{\text{cis}}(t)$ is rather involved (cf. refs. [42,43]). Here we show that the result $\langle \eta_{\text{cis}} \rangle \sim N^\nu$ can be obtained with a relatively simple argument, based in part on the work of DiMarzio *et al.* [45]. In equilibrium, the polymer assumes a configuration comprising several loops. Before the driving force can be transmitted to any given chain segment, the preceding loops need to be straightened. Only then can the tension propagate along the chain backbone. Therefore, the effective friction $\langle \eta_{\text{cis}} \rangle$ is dominated by the motion of the unraveling loop closest to the pore, with the chain segments further away from the pore remaining essentially immobile. To estimate the average length of the loop, we note that for large N, the end-to-end distance of the polymer is given by the usual Flory scaling form $R \sim aN^\nu$. To estimate the number of times the chain intersects a plane of thickness dR parallelly to the membrane (see fig. 1), we note that the number of segments within the plane, dN, is proportional to the average line density of monomers, N/R, giving $dN \sim N^{1-\nu} dR$. This is proportional to the number of times the chain intersects the plane and also proportional to the average number of loops in the chain (for large N). The average length of one loop is thus proportional to $N/N^{1-\nu} = N^\nu$. The number of mobile monomers at
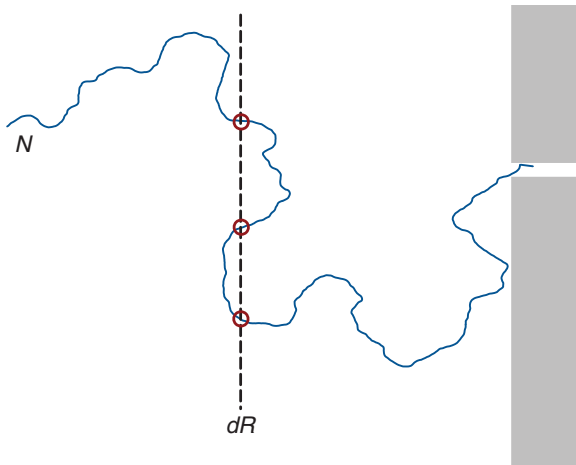
Fig. 1: (Color online) A schematic illustration showing the configuration of the *cis* side subchain of the polymer, with one end confined inside the pore. Intersections of the polymer with an imaginary plane of thickness dR oriented parallelly to the wall are indicated by the red circles. The average number of times a polymer of length N intersects the plane is proportional to $N^{1-\nu}$.

any given time is therefore proportional to N^{ν}, and the friction due to the drag on the *cis* side is $\langle \eta_{\mathrm{cis}} \rangle \sim \eta N^{\nu}$, where η is the solvent friction per chain segment. The total effective, time-averaged friction is thus of the form $\langle \Gamma \rangle \approx C \eta N^{\nu} + \eta_p$, with C an N-independent constant.

For a sufficiently strong driving force f, one can express the mean translocation time in terms of the average translocation velocity $\langle v \rangle$. In a dissipative system, force balance implies $\langle v \rangle = f/\langle \Gamma \rangle$. Since the driven translocation proceeds via gradual uncoiling of the whole chain, the relevant length scale of the process is the chain's contour length, aN (note that this is in contrast with the assumption of ref. [8], where the uniform contraction of the *cis* side chain suggests the radius of gyration as the relevant length scale). Thus, $\tau = aN/\langle v \rangle = aN\langle \Gamma \rangle/f$. With respect to the chain length, the complete relation is then

$$\tau \approx A(f,\eta)N^{1+\nu} + B(f,\eta)\tilde{\eta}_p N, \qquad (1)$$

where A and B are independent of N, and $\tilde{\eta}_p \equiv \eta_p/\eta$ is the dimensionless pore friction. This expansion of τ for finite N is one of the main results in this paper. It shows that the influence of the pore friction appears as a *correction-to-scaling* to the asymptotic value of the translocation exponent α, defined via $\tau \sim N^{\alpha}$, which approaches $\alpha_{\infty} = 1+\nu$ from below as

$$\alpha(N) = 1 + \frac{\nu}{1 + \frac{B}{A}\tilde{\eta}_p N^{-\nu}}. \qquad (2)$$

Here, the effective scaling exponent $\alpha(N)$ is defined as $\alpha(N) = \frac{\mathrm{d}\ln\tau}{\mathrm{d}\ln N}$. In addition, eqs. (1) and (2) suggest that if the dimensionless pore friction increases (*e.g.*, by either decreasing the solvent friction η or by reducing the pore radius), the exponent α becomes smaller, especially for

relatively short chains, in agreement with the theory [43] and MD simulations [20,22,28,31].

Our scaling analysis leaves the exact values of A and B in eqs. (1) and (2) undefined. However, we can expect the ratio B/A to be of the order of unity. In fact, one may use the tension propagation formalism [34–37,42,43] in the strong-stretching approximation to derive the value $B/A = 1+\nu \approx 1.588$. While we do not expect this value to match our simulations exactly (since, because of numerical reasons, they will be in the stem-flower scaling regime, instead of the strong-stretching regime), it should give us an indication of the expected range of B/A. The tension propagation formalism can also be used to derive a second correction-to-scaling term, proportional to $N^{2\nu}$. However, this term will be overshadowed by the other two terms, as the pore friction term already competes with the $N^{1+\nu}$ term. The argument holds even for significantly larger pore diameters, because the pore friction term has a non-vanishing contribution from the monomers in the vicinity of the pore [43].

Results and discussion. – To clarify the influence of the pore friction on the translocation time, we have solved τ time as a function of the chain length for different pore frictions using the BDTP model [42,43]. Using $\tau(N) \sim N^{\alpha}$, one can extract the effective scaling exponent $\alpha(N)$ as $\alpha(N) = \frac{\mathrm{d}\ln\tau}{\mathrm{d}\ln N}$, cf. eq. (2). Because of the linear subleading term in eq. (1), α has a weak dependence on the chain length, and approaches $1 + \nu$ extremely slowly with typical values of the parameters. Naturally, for larger $\tilde{\eta}_p$, the dependence on N is more pronounced, as shown in fig. 2. The other parameter values used in solving the BDTP model were $f = 5.0$ (driving force), $k_B T = 1.2$ (temperature), and $\nu = 0.588$.

To quantitatively show that the deviation from the asymptotic limit is caused by the pore friction, we subtract the correction-to-scaling term and define a rescaled translocation time $\tau^{\dagger}$ as $\tau^{\dagger} = \tau - B\tilde{\eta}_p N$ and the corresponding rescaled exponent as $\alpha^{\dagger}(N) \equiv \frac{\mathrm{d}\ln\tau^{\dagger}}{\mathrm{d}\ln N}$. According to eq. (1), the rescaled translocation time can be expressed as

$$\tau^{\dagger} = (\tau - B\tilde{\eta}_p N) \sim N^{\alpha^{\dagger}}, \qquad (3)$$

with the exponent $\alpha^{\dagger}$ independent of N at $\alpha^{\dagger} \approx 1 + \nu$. In practice, to obtain the rescaled $\tau^{\dagger}$, one has to find the numerical prefactor B by means of finite-size scaling. In the inset of fig. 2 this is done by plotting the translocation time data in the form $\tau/N^{1+\nu} = A + B\tilde{\eta}_p N^{-\nu}$. The coefficients A and B can then be obtained from a simple linear least squares fit.

The rescaled exponent $\alpha^{\dagger}$ as obtained from the BDTP model is shown in fig. 2 as solid symbols. All the curves corresponding to different values of $\tilde{\eta}_p$ *collapse onto a single master curve* within the numerical accuracy around $\alpha^{\dagger} = 1 + \nu$, also coinciding with the ideal $\tilde{\eta}_p = 0$ solution. For very short chains, the collapse is not perfect because of secondary finite chain length effects that come
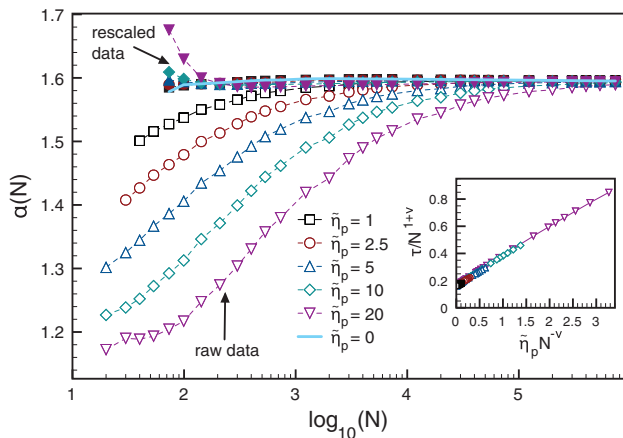
Fig. 2: (Color online) Open symbols, main plot: the effective exponent $\alpha(N)$ as a function of the chain length N for the BDTP model solved for different ratios $\tilde{\eta}_p$ of pore and solvent friction. Solid symbols: the same data rescaled to exclude the effect of pore friction, showing the collapse of the data to the asymptotic exponent $1+\nu$. Inset: the data collapse for different $\tilde{\eta}_p$ on a $(\tau/N^{1+\nu}, \tilde{\eta}_p N^{-\nu})$ plot used to extract the finite-size effect of the pore friction (see text for details). Numerical errors are of the order of the symbol sizes, or smaller.
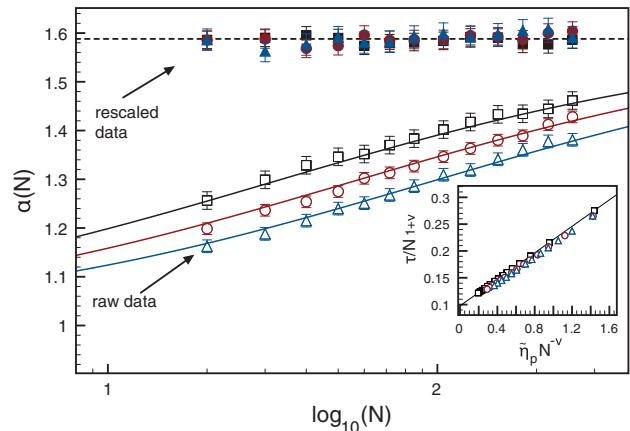
Fig. 3: (Color online) Open symbols, main plot: the effective exponent $\alpha(N)$ as a function of the chain length N from MD simulations with three different pore diameters (black squares: $d_p = 2.0$; red circles: $d_p = 1.6$; blue triangles: $d_p = 1.4$). The solid lines correspond to the theoretical value calculated from eq. (2), with the fitting parameter $B/A = 1.38$. Solid symbols: the same data rescaled as in fig. 2, showing the collapse to the value $\alpha^{\dagger} = 1 + \nu$ (dashed line). Inset: finite-size scaling plot used to extract the contribution of the pore friction.

into play, and also because as a continuum level description the BDTP model may not accurately describe very short chains.

We have confirmed that the rescaling scheme works for raw data obtained from MD simulations, too, by performing Langevin thermostatted MD simulations using the Kremer-Grest bead-spring model [46] with typical parameters found in the literature (for a more detailed description, see, *e.g.*, refs. [42,43]). We used the parameters $f = 5.0$, $k_B T = 1.2$, $\eta = 0.7$, and pore diameters d_p of 2.0, 1.6, and 1.4, and pore length $l_p = 1.0$ (both in units of the segment length a), which correspond to the dimensionless pore friction of about $\tilde{\eta}_p \approx 5.6$, 7.3 and 10.5, respectively [43]. The chain lengths in the simulations were $10 \leq N \leq 300$, with τ averaged over 5000–10000 successful events for each N.

Plotting the effective exponent $\alpha(N)$ reveals the same dependence on N as predicted by the theory. As shown in fig. 3, the measured values show excellent agreement with the theoretical values calculated from eq. (2) with $B/A = 1.38$. As expected, this value is fairly close to the predicted $1 + \nu$. Furthermore, by performing finite-size scaling similar to the BDTP case, we see that the rescaled exponent $\alpha^{\dagger}$ reaches the asymptotic value almost immediately; within the statistical error, the value is $\alpha^{\dagger} = 1 + \nu$ already for $N = 20$. *This shows that eq. (1) is valid for remarkably short chains and that the dominant finite-size effect in the driven translocation process is the frictional interaction between the pore and the polymer.*

Finally, we would like to point out another important feature of the scaling solution. Used in reverse, the finite-size scaling procedure can be used to estimate the term

$\frac{B}{A}\tilde{\eta}_p$ by varying $\tilde{\eta}_p$ so that the rescaled exponent becomes independent of N at $\alpha^{\dagger} \approx 1 + \nu$. This can be done for any geometry that satisfies $l_p \ll aN$. For instance, one could perform the measurement for pores of different diameters and use a relation between the diameter and pore friction (see, *e.g.*, refs. [8,43]) to determine both the ratio B/A and the pore friction $\tilde{\eta}_p$ separately from the data. This should be quite feasible, since the ratio B/A is expected to have only a weak dependence on the pore geometry, and thus slight changes in pore geometry will be reflected mostly in $\tilde{\eta}_p$. While measuring the pore friction directly from the monomer waiting time distribution as outlined in refs. [42,43] is more accurate, the reverse scaling procedure may be used even if the waiting time distribution is not available, as is typically the case in experiments.

Because the driven polymer translocation problem is inherently a dynamical, non-equilibrium process, it is expected that hydrodynamic interactions (HIs) from solvent should play a role. In the simplest approximation, the HIs can be included by considering the Zimm type of friction instead of the Rouse friction as in Langevin dynamics simulations. This means writing down the force balance condition such that the drag force (and the friction η_{cis}) is proportional to the linear length of the mobile subchain on the *cis* side, instead of being proportional to the number of mobile monomers. The rationale is that for intermediate forces, when the *cis* side subchain adopts a shape reminiscent of a trumpet (or a stem-flower), the solvent inside the trumpet is also set in motion and therefore the monomers inside the trumpet do not fully contribute to the drag force. Therefore, the overall drag force from the *cis* side subchain should be slightly smaller for the Zimm
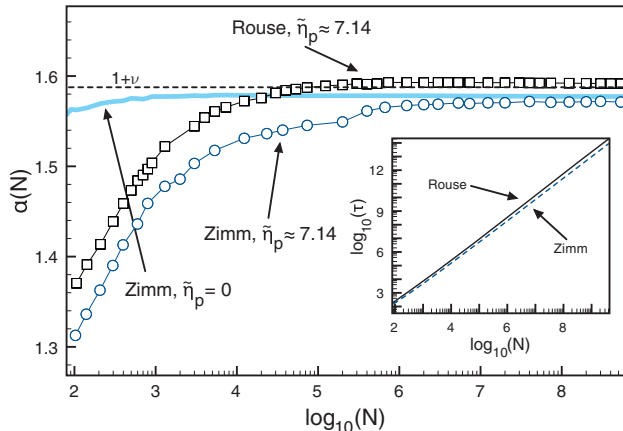
Fig. 4: (Color online) Main plot: the effective exponent $\alpha(N)$ as a function of the chain length N for the BDTP model with Rouse friction (black squares) and Zimm friction (blue circles) for $\tilde{\eta}_p \approx 7.14$, and for Zimm friction and $\tilde{\eta}_p = 0$ (light blue solid line). Inset: the mean translocation time τ as a function of the chain length N for the Rouse (solid black line) and Zimm friction (blue dashed line) for $\tilde{\eta}_p \approx 7.14$. Numerical errors are of the order of the symbol sizes, or smaller.

case. However, since the maximum linear length of the mobile part of the *cis* side subchain is still given by the end-to-end distance $R \sim aN^\nu$, we expect eq. (1) to hold even in this case, although with a smaller prefactor A in the leading term.

To test this simple argument, we have implemented the Zimm friction of the *cis* side subchain into the BDTP model. To this end, one merely modifies the force balance equation (*e.g.*, eq. (A1) in ref. [42]) so that the drag force is given by the size of the tension blob (ξ) instead of the number of monomers within the blob ($\xi^{1/\nu}$). This amounts to replacing the force balance equation of Rouse type as $f_{\text{drag}}^{\text{Rouse}}(x) = \frac{1}{a} \int_{-X}^{x} \eta v(x')[\xi(x')/a]^{1/\nu} dx' \rightarrow f_{\text{drag}}^{\text{Zimm}}(x) = \frac{1}{a} \int_{-X}^{x} \eta v(x') dx'$, where $v(x)$ is the instantaneous velocity of the monomers at position x, and $x = -X$ is the location of the last mobile monomer. One then carries out the same numerical implementation as described in refs. [42,43] using the modified force balance equation. The difference between the Zimm and Rouse frictions in the context of the tension propagation formalism is also further discussed in refs. [34,36,37,40,41].

The comparison between the Rouse and Zimm dynamics is shown in fig. 4. In both cases the BDTP model was solved with $f = 5.0$, $k_B T = 1.2$, $\eta = 0.7$, and $\tilde{\eta}_p \approx 7.14$ for up to $N = 5 \cdot 10^9$. For the Rouse friction, the effective exponent $\alpha(N)$ is consistently larger than for the Zimm friction, and eventually approaches $1 + \nu$ for large N. For the Zimm friction, the approach to the symptomatic limit is considerably slower. In fact, even for $N \approx 10^9$, the numerical value ($\alpha \approx 1.57$) still increases with N. To illustrate the importance of the pore friction term to the slow convergence, we have solved the model with zero pore friction ($\tilde{\eta}_p = 0$), showing considerably faster convergence.

Altogether, the numerical results in the large-N limit seem to be in agreement with $1 + \nu$, which has also been predicted to be the asymptotic value using analytical approximations to the tension propagation theory [40,41].

In the short-chain regime, we obtain $\alpha(N = 100) \approx 1.37 \pm 0.01$ and $\alpha(N = 100) \approx 1.31 \pm 0.01$ for the Rouse and Zimm cases, respectively. Although a detailed comparison with experiments or hydrodynamical simulations is difficult due to the lack of knowledge on the pore friction ($\tilde{\eta}_p$), the numerical value of 1.31 seems to be in good agreement with the experimental ($\alpha \approx 1.27 \pm 0.03$, ref. [8]) and lattice Boltzmann simulation results ($\alpha \approx 1.28 \pm 0.01$, ref. [33]). In particular, the difference in the exponents measured with and without HIs (0.06 ± 0.02) matches the difference reported in ref. [33] (0.08 ± 0.04). In addition, in agreement with computer simulations [18,33], the overall translocation time is reduced by the addition of the HIs, as shown in the inset of fig. 4.

Conclusions. – In this work, we have proposed, using theoretical scaling arguments, that the mean translocation time $\langle \tau \rangle$ of a polymer chain of length N driven through a nanopore by an external bias f can be written as a sum of two terms in the form $\tau \approx A(f, \eta)N^{1+\nu} + B(f, \eta)\tilde{\eta}_p N$, where the solvent friction is characterized by η. The first term is derived from the out-of-equilibrium dynamics of the *cis* side subchain and dominates for large N, while the second term stems from the interactions between the polymer and the pore and remains significant for the typical chain lengths in both experiments and computer simulations. This unified scaling form is an important physical result and powerful tool for the analysis of driven translocation. By eliminating the correction-to-scaling term one can isolate and quantify the effect of pore friction by means of finite-size scaling. We have demonstrated by using both a theoretical model of translocation dynamics and molecular-dynamics simulations that the rescaled exponent reaches the asymptotic limit already for extremely short chains ($N < 100$), whereas the conventionally defined exponent does not. In addition, we argue that in the presence of hydrodynamic interactions, the translocation time becomes shorter but can still be expressed as a sum of the two terms. We present results from the theoretical model proposed in refs. [42,43] with hydrodynamic interactions, obtaining quantitative agreement in the scaling exponent α with both theoretical and experimental results reported in the literature. The correction to the scaling ansatz can in principle be generalized to incorporate other effects, *e.g.*, chain stiffness, *cis-trans* solvent asymmetry etc. to study translocation dynamics of stiff biopolymers [44], a problem which has attracted considerable attention to understand translocation of protein and nucleic acids.

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