

Exploration of Neutral Versus Polyelectrolyte Behavior of Poly(ethylene glycol)s in Alkali Ion Solutions using Single-Nanopore Recording

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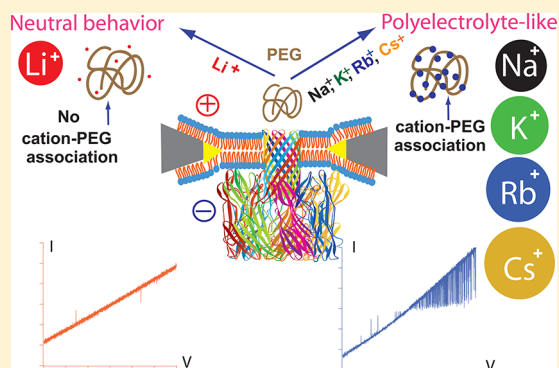
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S Supporting Information

ABSTRACT: We examine the effect of alkali ions (Li^+ , Na^+ , K^+ , Rb^+ , Cs^+) on the partitioning of neutral and flexible poly(ethylene glycol) into the alpha-hemolysin (α -HL) nanopore for a large range of applied voltages at high salt concentration. The neutral polymer behaves as if charged, that is, the event frequency increases with applied voltage, and the residence times decrease with the electric force for all cations except Li^+ . In contrast, in the presence of LiCl , we find the classical partitioning behavior of neutral polymers, that is, the event frequency and the residence times are independent of the applied voltage. Assuming that lithium does not associate with PEG enabled us to quantify the relative magnitude of the entropic and enthalpic contribution to the free-energy barrier and the number of complexed cations using two different arguments; the first estimate is based on the balance of forces, and the second is found comparing the blockade ratio in the presence of LiCl (no complexed ions) to the blockade ratio of chains in the presence of the other salts (with complexed ions). This estimate is in agreement with recent simulations. These findings demonstrate that the nanopore could prove useful for the rapid probing of the capabilities of different neutral molecules to form complexes with different ions.

SECTION: Glasses, Colloids, Polymers, and Soft Matter



The ability to drive charged macromolecules into a nanopore by an external electrical field was demonstrated in 1996 by Kasianowicz et al.¹ However, the nature of the driving force that leads to the partitioning into a conducting pore in the presence of an electric potential is a debated subject. The driving force for neutral molecules partitioning into conducting pores may be due to thermal fluctuation,^{2–7} osmotic pressure,^{8,9} or electro-osmosis resulting from the charge distribution within the pore.^{10,11} However, recently, neutral flexible poly(ethylene glycol) (PEGs) are seen to enter into an alpha-hemolysin (α -HL) pore preferentially in the direction of the applied electric field.^{12–14} It is believed that the electro-osmosis acts in the opposite direction because the pore is globally positively charged or slightly anionic-selective.¹⁴ This observation can be (and has been) interpreted as the PEG coordinating with the cations to form a charged complex (polyelectrolyte-like), which is then transported from the bulk into the pore by the applied electric field.^{13,14} This effect is enhanced in the case of PEG crowns.¹⁵

There are potential divergences with both of these interpretations; while it is known that neutral PEG does associate with, for example, the K^+ ions when in KCl solution in the correct solvent, the situation in water is unclear. Tasaki has

performed molecular dynamics simulations indicating the formation of charged complexes,^{16,17} while neutron scattering experiments and theoretical RPA calculations indicate that there is no formation of complexes with KCl in water.¹⁸ On the other hand, it has been argued that electro-osmosis would act in the opposite direction because the pore is globally positively charged.¹⁴ This is not necessarily the case because the distribution of the charges in the pore affects the electro-osmosis, and the pore has a ring of negative charges,¹⁹ which could induce a potentially significant electro-osmotic flow in the correct direction. There is another method of inducing a net flow in a small enough pore, related to the solvation of the cations and anions.¹⁰

The difficulty is that both of these effects will show up in a similar manner in the experimental data, at least for any given solution. One might hope to gain some insights into the nature of the translocation mechanism by varying a parameter that would affect more of one than the other, such as changing the ions in the solution.

Received: May 3, 2013

Accepted: June 20, 2013

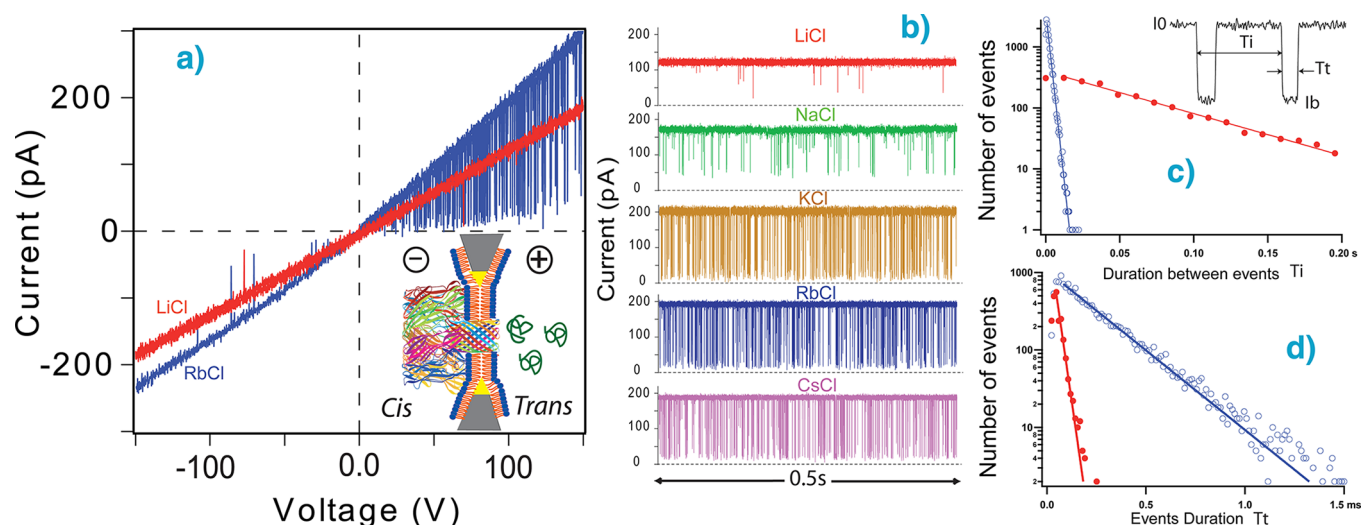


Figure 1. (a) Recorded I - V curve in the presence of 5 mM PEG 2000 added to the trans side, in 2 M RbCl (blue curve) and in 2 M LiCl (red curve). (b) Current traces at 100 mV for 5 mM PEG in different salts. The intervening time (c) and residence time distributions (d) are shown on a log-linear plot for RbCl (blue empty circles) and LiCl (red solid circles). The mean intervening times (inverse of the event frequency) and residence times are estimated from a single-exponential fit of the corresponding distributions (solid lines).

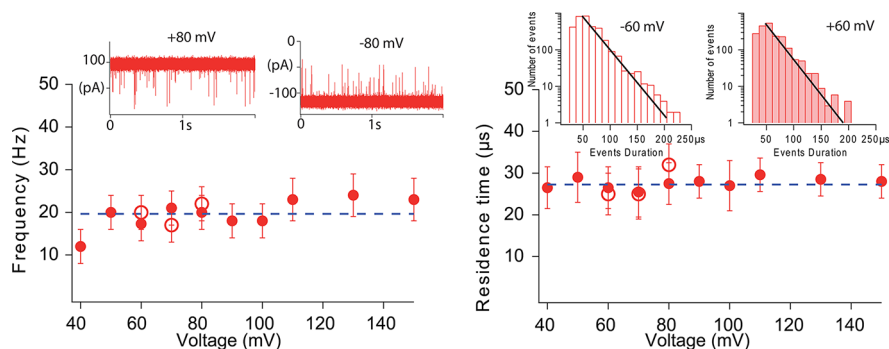


Figure 2. Dynamic properties of PEG 2000 in 2 M LiCl. (left) Current blockade frequency; the inset shows current traces at positive and negative voltages. (right) Residence time as a function of applied voltage; the inset shows residence time distributions for positive and negative voltages. The empty symbols correspond to data obtained at negative voltages. Error bars represent the mean ($\pm\sigma$) of three single nanopore experiments.

In this Letter, we present results for partitioning experiments where different alkali metals are used as the cation in solution. We find that the different cations produce similar results, and PEG chains behave like a polyelectrolyte.²⁰ The frequency of current blockades, the blockade times, and the current blockade ratio depend on the voltage, the energy barriers, the effect of salt concentration, and the polymer size, consistent with our interpretations. However, in the case of Li^+ , we show that the behavior of PEG is more like that expected from a neutral polymer, namely, the event frequency and the residence times are independent of the applied voltage. These results are discussed according to previous papers,^{3,13,14,21} recent simulations,^{16,17} and Daoud and de Gennes theory.²² Otherwise, in the case of an electro-osmotic flow, we might have expected a dependence on the ion type, but we would not expect its absence with any given ion, unless there is a fortuitous compensation by the difference in solvation and ion mobility, and therefore, we interpret these results as confirming the fact that PEG complexes with the cations in solution.

The partitioning of neutral, flexible PEG 2000 molecules into the α -HL nanopore is detected by using electrophysiology experiments.²³ The PEG chains are added on the trans side of the membrane (Figure 1a). We explore a large range of applied voltages (10–200 mV) using a 2 M M^+Cl^- (with $\text{M}^+ = \text{Li}^+$,

Na^+ , K^+ , Rb^+ , or Cs^+) salt concentration. The ionic current was detected using an Axopatch 200B amplifier (Molecular Devices). The signal was filtered with an 8th-order Bessel low-pass filter at 10 kHz before a digitization at 250 kHz. We detect at least 20000 events, using a two-threshold method.^{1,14,24} The first threshold is defined from the average current I_0 of the open pore as $I_0 - 4\sigma$, and the second threshold is defined as $I_0 - 5\sigma$, where σ is the standard deviation. The residence time of the chains, the frequency, and the amplitude of the blockade were estimated statistically (Figure 1c,d). Each value was averaged over at least three different single nanopore experiments.

Figure 1b shows the pulses created by the drop in the ionic current due to the presence of the polymer (PEG 2000) in the single α -HL pore. The frequency of these pulses is high when the voltage is positive, that is, when the cations flow from trans to cis, and very low when the voltage is negative (Figure 1a blue curve) for all of the cations except for LiCl, where the frequency of these spikes is low and almost the same whether a positive or negative voltage is applied (see Figure 1a, red curve). In Li^+Cl^- salt, the PEG has a residence time and entry frequency that are independent of the applied voltage (Figure 2), indicating that the partitioning is purely due to Brownian motion, as expected for a neutral polymer. In order to validate

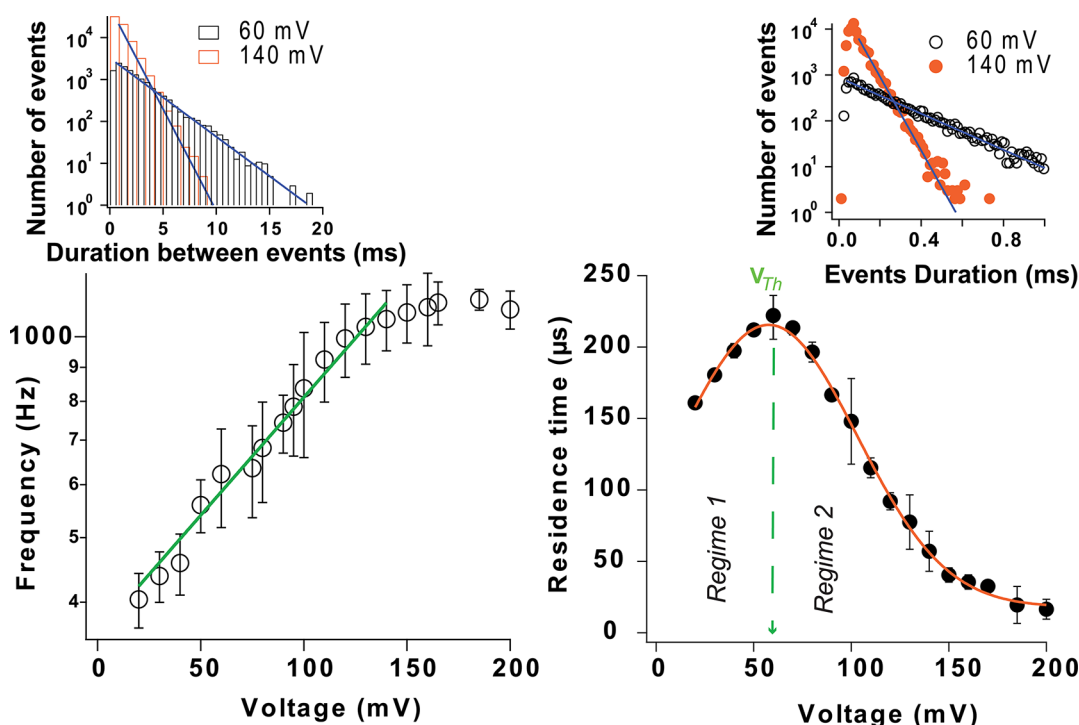


Figure 3. Dynamic properties: Current blockade frequency (left) and residence time (right) of PEG 2000 in 2 M RbCl as a function of applied voltage; V_{Th} is the voltage threshold, the necessary voltage to confine the whole random coiled chain inside of the pore. The intervening time and residence time distributions are shown on a log–linear plot for two voltages (inset). The mean intervening times and residence times were estimated from a single-exponential fit (solid lines). Error bars represent the mean ($\pm\sigma$) of at least three single nanopore experiments.

this hypothesis, we have performed experiments at very high LiCl salt concentration (4 M), which is a favorable condition for the cation–PEG complexation, and also, the time resolution is well-defined. Despite this, we observe the same behavior as that observed at 2 M LiCl shown in Figure 2, that is, the frequency and the residence time are independent of the applied voltage (Supporting Information SI 1), confirming our conclusion.

Assuming that the polymers in solution behave like spherical particles, we can estimate the number of chains expected to reach the pore mouth by Smoluchowski theory for absorption by a hemisphere^{25,26} of radius r

$$f = \frac{dn}{dt} = 2\pi D_{\text{diff}} c_{\text{bulk}} r_p$$

$$= \frac{k_B T c_{\text{bulk}}}{3\eta} \frac{r_p}{R_g} \approx 1 \text{ chain}/\mu\text{s}$$

where D_{diff} is the diffusion coefficient, $c_{\text{bulk}} = 3 \times 10^{24}$ chains/ m^3 is the bulk concentration, $r_p = 1$ nm is the pore radius, $\eta = 10^{-3}$ Pa·s is the bulk viscosity, and $R_g \approx 1$ nm is the PEG radius of gyration.

The diffusion time expected through the pore length $L_{\text{pore}} = 10$ nm is

$$\tau_{\text{diff}} = \frac{6\pi\eta R_g L_{\text{pore}}^2}{k_B T} \approx 0.5 \mu\text{s}$$

These values are far from those measured. A residence time of $0.5 \mu\text{s}$ is out of range of the resolution of the electrical detection method ($<20 \mu\text{s}$). While this could explain our very low measured frequency (only 0.2% of expected events), the fact that the estimated radius of gyration is of the same order as the

pore size would lead one to expect a significant entropic barrier, which would decrease the frequency of events corresponding to polymer insertions and would also increase the residence time of the polymer in the pore. In order to examine this possibility, we measured the event frequency for shorter (PEG 1000) and longer (PEG 3400) chains, where this effect should be smaller and larger, respectively. Indeed, the frequency of PEG 1000 was higher (on the order of 80 Hz) and that of PEG 3400 lower (less than 1 Hz) (Supporting Information SI 2). All frequencies were found to be independent of the applied voltage. The increased frequency for the PEG in other salts is consistent with the polymers being charged, which will have the dual effect of increasing the arrival rate to the pore mouth and lowering the free-energy barrier for the polymer to enter the pore by increasing the applied potential.

For the other cations, however, the pore–chain interaction is stronger^{3,7} and is dependent on the external field; the frequency of PEG partitioning into the pore increases with the applied voltage (Figure 3), in agreement with refs 13 and 14, suggesting that the origin of the behavior of PEG as a charged polymer arises from the ability of K^+ to form a complex with the neutral PEG. The frequency in LiCl of PEG partitioning in the α -HL nanopore is almost 200 times smaller when compared to the frequency for CsCl at the lower applied voltage of 10 mV (data not shown). The residence time in LiCl was also found to be 7 times smaller compared to those obtained for the other salts.

These results suggest that in the case of LiCl, the PEG molecule is uncharged and truly neutral; the Li^+ cation does not form a complex with the PEG chain.

Indeed, it has also been demonstrated that PEG will effectively form complexes with cations only if the lattice energy of a univalent metal salt MX is below a certain threshold value of $\sim 850 \text{ kJ mol}^{-1}$,²⁷ where M is an alkali metal, here Li^+ ,

Table 1. Values of the Energy Barrier (U^*) and the Effective Charge (z) for Different Alkali Metal Ions, Derived from van't Hoff Arrhenius Law $R = R_0 \exp(V/V_0)^a$

	R_0	err R_0	V_0	err V_0	$U^*(k_B T)$	err U^*	z	err z
NaCl	130	3	180	9	7.63	0.02	0.14	0.01
KCl	443	18	120	9	6.41	0.04	0.21	0.01
RbCl	337	3	112	2	6.68	0.01	0.23	0.01
CsCl	304	26	120	24	6.78	0.08	0.21	0.04

^a $R_0 = \nu \exp(-U^*/k_B T)$ is the zero-voltage capture rate and $\nu \simeq D_{\text{diff}} c_{\text{bulk}} A / L_{\text{pore}}$ is a frequency factor,^{21,31} where D_{diff} is the diffusion coefficient, c_{bulk} the bulk concentration, and A the pore sectional area; $V_0 = k_B T / ze$ is the necessary applied potential to allow a polymer to overcome the Brownian motion, and e is the elementary charge.

Na^+ , K^+ , Rb^+ , or Cs^+ , and X is an anion, here Cl^- . In fact, the lattice energy value (kJ mol^{-1}) of LiCl is higher compared to that of other alkali metals, $\text{LiCl}(853) > \text{NaCl}(787) > \text{KCl}(715) > \text{RbCl}(689) > \text{CsCl}(659)$, and slightly above the threshold value of 850 kJ mol^{-1} to form complexes with PEG.²⁷ This is in agreement with our observations at the single-molecule level, confirming that the origin of the behavior of PEG as a charged polymer arises from the ability of certain cations to form complexes with neutral polymers. Single-molecule detection could be a faster and cheaper method to probe if the complexation reaction takes place or not between ions and nonelectrolyte polymers before performing heavy experiments such as XPS, X-ray, and XAFS techniques.

In Figure 3, left, we show the frequency of partitioning of PEG 2000 in 2 M RbCl as a function of the positive applied voltage. The frequency of current blockades exhibits a nonmonotonic behavior; it increases exponentially with increasing applied voltage from 20 to 140 mV and reaches a plateau (saturation of the rate).

These results are in agreement with those obtained by Rodrigues et al. for KCl .¹³ They explained this behavior at very high voltage by a depletion of the PEG at the entry region of the pore, in agreement with the phenomenon of diffusion-limited transport well-known for charged analytes. However, this phenomenon could also be explained simply by the limitations of the detection apparatus,^{24,28} especially because the amplitude of the blockade will be reduced by a significant amount,²⁴ which could explain why we lose events at high voltage. This kind of observation and interpretation was also suggested by Mahendran et al.²⁹ This is correct if the current threshold used to search the events is at 70% of the blockade depth. However, times are still measurable if the threshold is taken at a lower current value, as is the case here (see the experimental discussion); the measured time is limited by the sampling (250 kHz or 4 μs) rather the inverse of the cutoff frequency (10 kHz or 100 μs), which explains why we still measure times less than 20 μs .^{24,30} In addition, note that our analysis is statistical. Although we lose the shorter events (distribution of time T_v , $T_t < 50 \mu\text{s}$ (Figure 3)), the rest of the distribution is not disturbed ($50 < T_t < 500 \mu\text{s}$) and can be well-fitted with an exponential fit. The times measured for LiCl range from 50 to 200 μs (histograms in Figure 2), and thus, the data are only slightly modified by the filter.²⁴ It should be noted that the T_t obtained here is a characteristic time, found from the exponential fit, and not a direct experimental measurement. This explains how it is possible to find a time this short.

Below 140 mV, the time between events decreases exponentially with the applied force, as expected for charged polymers. We exploit this regime to estimate the energy barrier and evaluate the effective charge in the pore for different electrolytes (Table 1).

These values are comparable to that measured for charged polymers initially for DNA by Henrickson³¹, those for synthetic polyelectrolyte in refs 32, 33, 35, and 36, and those for proteins recently in ref 34.

Crossing from the bulk to the nanopore involves hopping over a free-energy barrier that includes both enthalpic (polymer–pore interaction) and entropic terms including depletion of water and ions from the nanopore by the polymer.^{37,38} All of these factors should be taken into account when describing polymer dynamics.^{39,40} The energy barrier measured here is the activation energy of polymer entry inside of the pore; it takes into account both enthalpic and entropic contributions. To the best of our knowledge, the relative magnitudes of the entropic and enthalpic contributions to the free-energy barrier have not been established for neutral polymers, with the exception of ref 41 for polyelectrolytes, because of the difficulty of experiments (the channel's surface charges should be manipulated, and the temperature also should be varied). Here, we attempt to quantify the magnitude of the enthalpic and entropic contributions to the free-energy barrier. Our approach is based on the following: (i) In the case of LiCl , the polymer behaves as a neutral and is assumed not to have any associated charges; the energy barrier of entry is expected to be governed only by the entropy. However, in the case of other salts, entropic and enthalpic contributions would coexist. (ii) The estimate of the free-energy change of a single polymer partitioning caused by associated charges from the reduction in the partition coefficient gives the contribution of the enthalpic barrier. The free-energy change of a single polymer partitioning caused by associated charges from the reduction in the partition coefficient derived from⁴² reads

$$\Delta E_{\text{PEG}_{\text{Rb}} \rightarrow \text{PEG}_{\text{Li}}} = k_B T \ln \left(\frac{\Pi_{\text{PEG}_{\text{Rb}}}}{\Pi_{\text{PEG}_{\text{Li}}}} \right)$$

where $\Pi_{\text{PEG}_{\text{Li}}}$ and $\Pi_{\text{PEG}_{\text{Rb}}}$ are, respectively, the PEG's partition coefficient in the presence of LiCl (without cation association) and RbCl (with cation association). The partition coefficient Π reads⁶ $\Pi = (1/N_A V_{\text{barrel}})(\tau_{\text{occup}}/\tau_{\text{tot}}c)$, where, N_A is the Avogadro number, V_{barrel} is the β barrel volume, τ_{occup} is the time occupied per polymer inside of the pore, τ_{tot} is the total acquisition time, and c is the polymer concentration. Note that we used the same PEG 2000 molecular weight, the same concentration, and the same pore; thus, ΔE reads $\Delta E_{\text{PEG}_{\text{Rb}} \rightarrow \text{PEG}_{\text{Li}}} = k_B T \ln(P_{\text{PEG}_{\text{Rb}}}/P_{\text{PEG}_{\text{Li}}})$. Now, $P = (\tau_{\text{occup}}/\tau_{\text{tot}})$ is the residence time probability. In order to probe the enthalpic contribution, it is usual to choose the residence time probability at the voltage threshold (the necessary voltage to confine the whole random coiled chain inside of the pore), $\Delta E_{\text{PEG}_{\text{Rb}} \rightarrow \text{PEG}_{\text{Li}}} = k_B T \ln(P_{\text{PEG}_{\text{Rb}}}/P_{\text{PEG}_{\text{Li}}}) = U_{\text{enthalpic}} = 5.5 k_B T$, which is the enthalpic contribution;

thus, the entropic barrier reads $U_{\text{entropic}} = U^* - U_{\text{enthalpic}}$. We summarize in Table 2 the magnitude of the entropic and enthalpic contributions to the free-energy barrier.

Table 2. Magnitude of the Entropic and Enthalpic Contributions to the Free-Energy Barrier

	$U^*(k_B T)$	$U_{\text{enthalpic}}(k_B T)$	$U_{\text{entropic}}(k_B T)$	dominant barrier
NaCl	7.6	3.1	4.5	entropic
KCl	6.4	6.4	0	enthalpic
RbCl	6.6	5.5	1.1	enthalpic
CsCl	6.7	5.2	1.5	enthalpic

In the situation where cations are associated to the PEG, both enthalpic and entropic barriers coexist, and in most of the cases, the enthalpic barrier dominates. This is consistent with our experimental observation (Figure 3, right); below the voltage threshold, the applied voltage is not enough to detach the PEG from the pore mouth and to overcome the change of the entropy required to explore the interior of the pore.

Interestingly, in the case of KCl, the energy barrier is fully of enthalpic origin; one can exploit this situation to estimate the force required to detach the chain from the entrance of the pore. The electric force acting on one blob at the entrance of the pore reads $F \approx (Q_{\text{blob}} V_{\text{Th}} / D_{\text{blob}})$, where Q_{blob} is the total charge of the blob, V_{Th} is the potential threshold to overcome the enthalpic barrier, and D_{blob} is the blob size. By taking $Q_{\text{blob}} = 5e$ (see below), $V_{\text{Th}} \approx 50 \text{ mV} \approx (2k_B T / e)$, where e is the elementary charge; F reads $F \approx 10(k_B T / D_{\text{blob}})$. By taking $D_{\text{blob}} = 2 \text{ nm}$, we obtain $F \approx 20 \text{ pN}$ as the force required to detach the chain from the entrance of the pore, leading the chain to then explore the interior of the pore (20 pN is typically the force required to break the hydrogen bond). This value is slightly lower than those estimated for DNA ($\approx 44 \text{ pN}$)⁴³ and comparable to that measured at 2 °C for single-stranded polydA ($\approx 17 \text{ pN}$).⁴⁴

Otherwise, Ambjornsson et al.²¹ proposed a model to explain the presence of a barrier for ssDNA insertion into a nanopore. Using this model here predicts a minimum voltage for PEG insertion into the pore of about 7 V, which is clearly not the case here. The behavior of the PEG is however very different from that of the ssDNA; the ssDNA enters the pore in a stretched conformation (rigid), while the PEG is expected to still be coiled and flexible (the persistence length is $l_p(\text{DNA}) \gg l_p(\text{PEG})$). Not only is the DNA more charged than one would

expect of the PEG–ion complex, but the complexed ions are more mobile than the fixed charges on the DNA chain. The PEG 2000 used here is expected to just fill the pore, while the ssDNA is much longer than the pore length. All of these factors probably explain the failure of the latter model to capture what happens here.

The residence time of PEG in 2 M RbCl as a function of applied voltages $20 < V < 200 \text{ mV}$ exhibits two regimes (Figure 3, right); at low applied voltage ($20 < V < 60 \text{ mV}$), the residence time increases with the applied voltage, and at high voltages ($60 < V < 200 \text{ mV}$), the residence time decreases from 210 ± 4 to $20 \pm 7 \mu\text{s}$.

Below the voltage threshold V_{Th} (Figure 3, right), the electric driving force is not able to overcome the attractive interaction between the polymer and the mouth's charges of the pore (enthalpic barrier) and change in entropy required to confine the whole random coiled chain inside of the pore. If we assume that the work done by the electric force balances the enthalpy and the change in entropy due to confinement at the crossover between the first and the second regimes (typically between ~ 50 and 60 mV), one can estimate the effective charge of the polymer within the pore.

We consider the blob picture proposed by Daoud and de Gennes²² and represented in the inset of Figure 4, where each blob is considered as a piece of real chain containing g monomers. The portion of chain in the pore forms a necklace of spherical blobs, each of size D , where D is the diameter of the pore. The confinement energy corresponding to the formation of a blob is, in the scaling regime, $Ak_B T$, where A is a constant of order unity. In order for the polymer to enter the pore, the work performed by the electrical force acting on the PEG must at least compensate for this confinement energy. The electric force acting on the partially inserted polymer is given by $F_{\text{el}} = qE = neV/L$, where L is the distance over which the voltage drops and $q = ne$ is the effective electrical charge of the portion of the polymer within the pore. Once the polymer has managed to enter the pore a certain critical distance, the rest of the chain follows.⁴⁵ Sakaue et al.⁴⁶ estimated the balance between the confinement force and the pulling force by considering that the insertion of one blob was sufficient for the rest of the polymer to follow. This leads to $neV/L = Ak_B T/D$, where A is the constant of order one giving the confinement energy of one blob for a partially inserted chain and n is now the number of charges per blob. For long polymers and

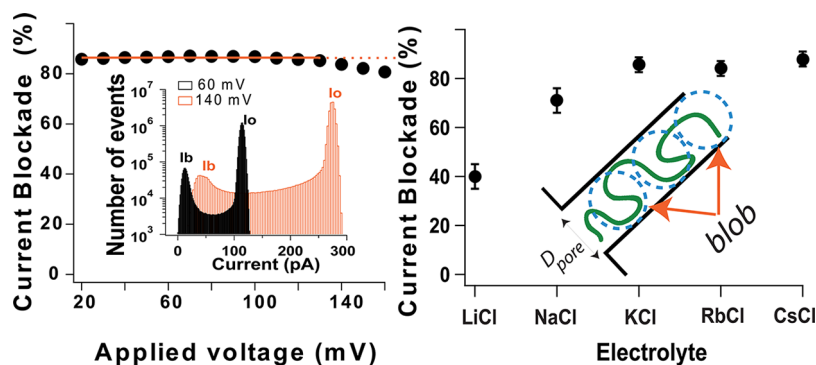


Figure 4. Static properties. (left) Current blockade ratio (%) of PEG 2000 in 2 M RbCl as a function of applied voltage; the inset shows histograms, for two voltages, to measure the current blockade ratio. (right) Current blockade ratio (%) of PEG 2000 at 2 M in different electrolytes at a fixed 100 mV voltage. The inset shows a coil PEG 2000 chain inserted in the stem of the α -HL pore as proposed by Daoud and de Gennes.²²

spherical pores, Klushin et al.⁴⁷ calculated numerically this constant to be $A \approx 4$.

The diameter of the pore is $D = 2$ nm, $V = 50$ mV, and $k_B T/e = 25$ mV. The voltage drops over the length of the pore, which is of length 10 nm, but the vestibule is wider than the stem, and therefore, the voltage drop across the stem will be greater than that across the vestibule. The effective length over which the voltage drops will then be larger than 5 nm (the length of the stem) but smaller than 10 nm (the length of the pore). This gives an estimate of the number of charges between roughly 5 and 10 per blob.

A recent analysis of the data of ref 14 on the residence times as a function of the PEG chain length reinterprets the data as showing a crossover behavior at a length of 38–40 monomers.⁴⁸ This would correspond to the chain length that just fills the stem; because the ratio of stem length to diameter is about 2.5, we conclude that PEG 2000 (corresponding to 45 monomers) should form about 2.5 blobs. This leads to the conclusion that about 13–25 ions complex with the PEG 2000 for all salts except LiCl. Recent simulations suggest that 3–7 PEG monomers are required to complex one ion (K^+ in the article) but that one monomer may participate in the complexing of more than one ion.¹⁶ The article shows a snapshot configuration where a chain of 16 monomers associates 5 K^+ ions, consistent with our estimates for 45 monomers. The estimate that PEG 2000 forms 2.5 blobs and just fits the stem of the α -HL pore is also compatible with the observation that PEG 2000 was found to fit better the α -HL pore.⁴²

The current blockade ratio is defined as $I_R = [1 - (I_b/I_o)]$, where I_o is the mean open pore current and I_b the mean current blockade (inset of Figure 1c and inset of Figure 4, left). The current blockade ratio is proportional to the volume occupied by coil chains inside of the pore. In Figure 4, we show the current blockade ratio in percentage $[1 - (I_b/I_o)] \times 100$ as a function of applied voltage. The blockade ratio $I_R = A_{occ}/(\pi r_{pore}^2)$, where A_{occ} is the sectional area of the pore that is occupied by the polymer and complexed charges. We can estimate the sectional area occupied by the polymer without complexed ions from the blockade ratio in the presence of LiCl; because the polymer behaves as a neutral and is assumed not to have any associated charges $A_{PEG} \approx 0.4\pi r_{pore}^2$. From the blockade ratio for RbCl, which is about 0.8, we find that $A_{PEG+Rb} \approx 0.8\pi r_{pore}^2$. Because the mean measured value of the covalence radius of Rb is $R_{cov} \approx 200$ pm,⁴⁹ taking the radius of the stem of the pore to be about 1 nm, the additional occupied volume corresponds to approximately $n = 0.4(r_{pore}/R_{cov})^2 \approx 10$ Rb ions, which we may take as an estimate of the number of charges per blob, leading to an estimate of about 25 charges for PEG 2000, which is consistent with the estimate calculated from the balance of forces calculated above.

In this Letter, we have shown that neutral polymer partitioning into a conducting ion channel depends on the type of alkali cation used in solution as a function of applied voltages. If the polymer chain coils have the capability to form a complex with alkali cations like Na^+ , K^+ , Rb^+ , and Cs^+ , they behave like charged polymers, the event frequency increases, and the residence time decreases with voltage. However, if the chain coils cannot trap the cations (Li^+) because of its smaller size and its higher lattice energy, we observe neutral polymer behavior; the dynamics is independent of the electric field. This difference in results indicates that the driving force is electrophoretic because an electro-osmotic force would not

be dependent on the coordination of the cations with the polymer and would be expected to act also in the presence of a LiCl solution. From the fact that lithium is assumed to not associate with PEG, we have succeeded to estimate the relative magnitude of the entropic and enthalpic contributions to the free-energy barrier and also to estimate the number of complexed cations to the PEG.

■ ASSOCIATED CONTENT

Supporting Information

(SI 1) Dynamic properties of PEG 2000 in 4 M LiCl; (SI 2) effect of chain size and applied voltage on the dynamics of chains in 2 M LiCl. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Agence Nationale de la Recherche. We are grateful to F. Piguet, S. Moriau, H. Cheradame, E. Braselmann, and B. Thiébot for useful discussions and a careful rereading of the manuscript. We would like to thank the two anonymous referees for their helpful work.

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