

pH-mediated regulation of polymer transport through SiN pores

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We characterize the pH controlled polymer capture and transport thorough silicon nitride (SiN) pores subject to protonation. A charge regulation model able to reproduce the experimental zeta potential of SiN pores is coupled with electrohydrodynamic polymer transport equations. The formalism can quantitatively explain the experimentally observed non-monotonic pH dependence of avidin conductivity in terms of the interplay between the electroosmotic and electrophoretic drag forces on the protein. We also scrutinize the DNA conductivity of SiN pores. We show that in the low pH regime where the amphoteric pore is cationic, DNA-pore attraction acts as an electrostatic trap. This provides a favorable condition for fast polymer capture and extended translocation required for accurate polymer sequencing.

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I. INTRODUCTION

The rapid progress in biotechnological applications requires an increasingly high degree of precision in bioanalytical approaches such as polymer translocation [1–5]. Accurate control over the mobility of confined polymers is vital for improving the sensitivity of this biosequencing technique [6]. Over the last two decades, this technological requirement has motivated intense research into the characterization of entropic [7, 8] and electrohydrodynamic effects [9–14] on polymer translocation.

In driven polymer transport through amphoteric silicon nitride (SiN) pores subject to protonation, the acidity of the buffer solution is a critical control factor enabling the radical alteration of the forces driving the polymer mobility. More precisely, the inversion of the pore surface charge upon pH tuning can reverse the direction of the electro-osmotic (EO) flow drag [15] and also switch the nature of polymer-membrane interactions between repulsive and attractive [16]. The quantitatively accurate characterization of this mechanism can thus provide an efficient control of the polymer translocation dynamics.

Previous charge regulation theories have ingeniously characterized the effect of surface protonation on macromolecular interactions [17–20]. However, a polymer translocation model able to account for the pH controlled alteration of the pore electrohydrodynamics and polymer-pore interactions is still missing. In this Letter, we develop such a polymer translocation model. Within our formalism, we first explain the experimentally measured non-monotonic pH dependence of avidin translocation rates in terms of the electrohydrodynamic forces

acting on the avidin protein of amphoteric nature [15]. Then, we investigate the dsDNA conductivity of SiN pores and shed light on an electrostatic polymer trapping mechanism allowing favorable conditions for fast polymer capture and slow translocation required for accurate biosequencing and related applications.

II. THEORY

A. Polymer transport model

We briefly review here the polymer translocation model initially developed in Ref. [13] for fixed surface charge conditions. The model is depicted in Fig. 1. The nanopore is a cylindrical hole embedded in an SiN membrane of surface charge density σ_m . In this work, the pore radius and length will be fixed to the experimental values of $d = 10$ nm and $L_m = 30$ nm of Ref. [15]. The pore is in contact with an ion reservoir confining the KCl solution of density ρ_b . The polymer translocates along the z axis is a rigid cylinder of radius $a = 1$ nm, length L_p , and surface charge density σ_p . The charge transport through the pore is driven by the externally applied hydrostatic pressure ΔP and voltage ΔV .

The coordinate of the polymer end z_p is chosen as the reaction coordinate of the translocation while l_p is the length of the polymer portion in the pore. The translocation dynamics is characterized by the diffusion equation

$$\partial_t c(z_p, t) = -\partial_{z_p} J(z_p, t); \quad (1)$$

$$J(z_p, t) = -D\partial_{z_p} c(z_p, t) + v_p(z_p) c(z_p, t), \quad (2)$$

where $c(z_p, t)$ is the density and $J(z_p, t)$ the flux of the translocating polymer, with the diffusion coefficient $D = \ln(L_p/2a)/(3\pi\eta L_p\beta)$ including the inverse thermal energy $\beta = 1/(k_B T)$ and solvent viscosity $\eta = 8.91 \times 10^{-4}$ Pa s [21]. In Eq. (2), the first term is Fick's law and the

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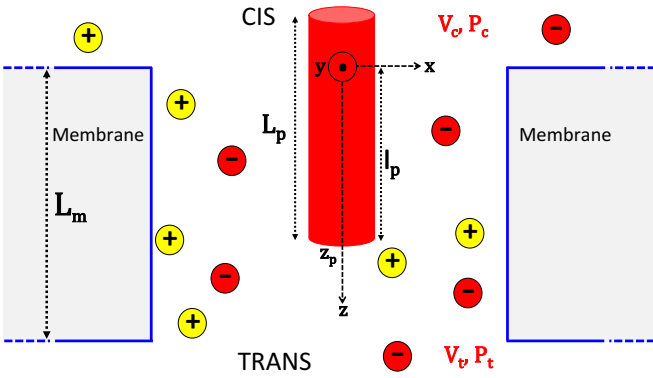


FIG. 1: (Color online) Schematic depiction of the polyelectrolyte translocating along the z axis of the pore confining the KCl solution of bulk concentration ρ_b . The polyelectrolyte is a cylinder of radius a , total length L_p , and its portion located in the pore is l_p . The pore is a cylinder of radius d and length L_m . Charge transport through the pore takes place under the effect of the voltage $\Delta V = V_t - V_c$ resulting in the field $\mathbf{E} = -\Delta V/L_m \hat{u}_z$ and pressure gradient $\Delta P = P_c - P_t$.

second term corresponds to the convective flux component characterized by the polymer velocity $v_p(z_p)$. In Ref. [13], from the coupled solution of the Stokes and Poisson-Boltzmann (PB) equations, the liquid velocity $u_c(r)$ and polymer velocity satisfying the no-slip conditions $u_c(d) = 0$ and $u_c(a) = v_p(z_p)$ were derived as

$$u_c(r) = \mu E [\phi(d) - \phi(r)] - \beta D_p(r) \frac{\partial V_p(z_p)}{\partial z_p} + \frac{\Delta P}{4\eta L_m} \left[d^2 - r^2 - 2a^2 \ln\left(\frac{d}{r}\right) \right]; \quad (3)$$

$$v_p(z_p) = v_{dr} - \beta D_p(a) \frac{\partial V_p(z_p)}{\partial z_p}. \quad (4)$$

The first term of Eq. (4) corresponds to the drift velocity induced by the the voltage and the pressure gradient,

$$v_{dr} = -\frac{\mu \Delta V}{L_m} [\phi(a) - \phi(d)] + \frac{\gamma a^2 \Delta P}{4\eta L_m}, \quad (5)$$

with the electrophoretic (EP) mobility coefficient $\mu = \varepsilon_w k_B T / (e\eta)$ including the electron charge e , the geometric coefficient $\gamma = d^2/a^2 - 1 - 2 \ln(d/a)$, and the electrostatic potential $\phi(r)$ induced by the polymer and membrane charges. The terms on the r.h.s. of Eq. (5) originate respectively from the EP and EO drag forces on the polymer. Then, the second term of Eq. (4) includes the pore diffusion coefficient $D_p(r) = \ln(d/r)/(2\pi\eta L_p\beta)$, and the electrostatic coupling potential between the polymer and membrane charges $\beta V_p(z_p) = \psi_p l_p(z_p)$. This potential includes the energy density

$$\psi_p = 2\pi a \sigma_p \phi_m(a), \quad (6)$$

with the polymer potential induced solely by the membrane charges $\phi_m(r) \equiv \lim_{\sigma_p \rightarrow 0} \phi(r)$, and the position-

dependent length of the polymer portion in the pore

$$l_p(z_p) = z_p \theta(L_- - z_p) + L_- \theta(z_p - L_-) \theta(L_+ - z_p) + (L_p + L_m - z_p) \theta(z_p - L_+), \quad (7)$$

with the auxiliary lengths $L_- = \min(L_m, L_p)$ and $L_+ = \max(L_m, L_p)$. The terms on the r.h.s. of Eq. (7) correspond respectively to the regimes of polymer capture, transport at drift velocity v_{dr} , and escape from the pore.

The polymer translocation rate follows from the steady-state solution of Eqs. (1)–(2) characterized by a uniform flux $J(z_p, t) = J_0$, with the fixed density condition at the pore entrance $c(z_p = 0) = c_{cis}$ and an absorbing boundary at the pore exit $c(z_p = L_p + L_m) = 0$. The translocation rate defined as $R_p \equiv J_0/c_{cis}$ reads [13]

$$R_p = \frac{D}{\int_0^{L_m+L_p} dz e^{\beta U_p(z_p)}}, \quad (8)$$

with the effective polymer potential

$$U_p(z_p) = \frac{D_p(a)}{D} V_p(z_p) - \frac{v_{dr}}{\beta D} z_p. \quad (9)$$

Defining the characteristic inverse lengths embodying the effect of the drift (5) and the barrier (6),

$$\lambda_d = \frac{v_{dr}}{D}; \quad \lambda_b = 2\pi a \sigma_p \phi_m(a) \frac{D_p(a)}{D}, \quad (10)$$

the effective polymer potential (9) can be expressed as

$$\beta U_p(z_p) = \lambda_b l_p(z_p) - \lambda_d z_p. \quad (11)$$

With the piecewise linear potential (11), the translocation rate in Eq. (8) can be analytically evaluated. The analytical expression for R_c can be found in Ref. [13]. We finally note that in the *drift regime* $\lambda_d \gg \lambda_b$ where polymer-pore interactions are negligible $V_p(z_p) \ll k_B T$, Eq. (8) yields the drift-driven polymer transport behavior $R_p \approx v_{dr}$.

The polymer translocation time defined as the mean first passage time between the cis and trans sides is

$$\tau_p = \tau_c + \tau_d + \tau_e, \quad (12)$$

with the time of polymer capture $\tau_c = I(0, L_-)$, diffusion $\tau_d = I(L_-, L_+)$, and escape $\tau_e = I(L_+, L_p + L_m)$, where we defined the auxiliary integral $I(z_i, z_f) = D^{-1} \int_{z_i}^{z_f} dz' e^{\beta U_p(z')} \int_0^{z'} dz'' e^{-\beta U_p(z'')} [6, 13]$. The analytical form of the translocation time can be also found in Ref. [13]. In the drift regime $\lambda_d \gg \lambda_b$, the translocation time reduces to its drift limit $\tau_p \approx \tau_{dr} = (L_p + L_m)/v_{dr}$.

B. Charge regulation model

Here, we derive the pH dependent surface charge density of the SiN pore. To this end, within the framework of the chemical reaction scheme proposed in Ref. [24], we

will extend the charge regulation model of Ref. [22] to include the positively charged amine groups. The surface of the SiN pore is composed of amphoteric silanol (SiOH) and primary amine (SiNH₂) groups. The hydrolysis reactions resulting in SiN



imply that on the pore surface, there are two silanol groups for every primary amine group [24]. Thus, the number of amphoteric groups N_a and primary amine sites N_p are related as $N_a = 2N_p$. In the following, we assume that the amphoteric and primary amine groups are characterized by the same surface number density $\sigma_{0m} = (N_a + N_p)/S = 3N_p/S$, with the area of the cylindrical pore $S = 2\pi dL_m$.

The reactions for the silanol groups on the pore are



with the corresponding mass action laws

$$K_m = 10^{-pK_m} = \frac{k_d}{k_r} = \frac{[\text{SiO}^-][\text{H}^+]}{[\text{SiOH}]}; \quad (16)$$

$$L_m = 10^{-pL_m} = \frac{l_d}{l_r} = \frac{[\text{SiOH}][\text{H}^+]}{[\text{SiOH}_2^+]}, \quad (17)$$

where K_m and L_m are the dissociation rates. Then, the H^+ binding reaction for primary amine groups is



with the reaction rate T_m defining the mass action law

$$T_m = 10^{-pT_m} = \frac{t_d}{t_r} = \frac{[\text{SiNH}_2][\text{H}^+]}{[\text{SiNH}_3^+]}. \quad (19)$$

In Eqs. (16)–(17) and (19), the H^+ density on the pore surface is given by $[\text{H}^+] = [\text{H}^+]_b e^{-\phi(d)}$ where the H^+ density in the bulk reservoir is related to the acidity of the solution as $\text{pH} = -\log_{10} \{[\text{H}^+]_b\}$.

In order to derive the pore surface charge density σ_m , we express first the density of the chemical species on the pore surface in terms of their rates α , β , and γ as

$$[\text{SiO}^-] = N_a\alpha; \quad [\text{SiOH}_2^+] = N_a\beta; \quad [\text{SiOH}] = (1-\alpha-\beta)N_a, \quad (20)$$

for the amphoteric surface groups and

$$[\text{SiNH}_3^+] = N_p\gamma; \quad [\text{SiNH}_2] = N_p(1-\gamma) \quad (21)$$

for the primitive amine groups. Noting that the net surface charge is $Q_{\text{net}} = S\sigma_m = (\beta - \alpha)N_a + \gamma N_p$, the pore surface charge density $\sigma_m = Q_{\text{net}}/S$ follows in the form $\sigma_m = \sigma_{0m} [2(\beta - \alpha) + \gamma]/3$. Calculating the rates α and

β from the solution of Eqs. (16)–(17) and (20), and the rate γ from Eqs. (19) and (21), one finally obtains

$$\sigma_m = \left\{ \frac{2 [10^{pL_m + pK_m - 2pH} e^{-2\phi(d)} - 1]}{1 + 10^{pK_m - pH} e^{-\phi(d)} [1 + 10^{pL_m - pH} e^{-\phi(d)}]} + \frac{1}{1 + 10^{pH - pT_m} e^{\phi(d)}} \right\} \frac{\sigma_{0m}}{3}. \quad (22)$$

In order to compute the electrostatic potential, we first note that in the acidity regime $2 \leq \text{pH} \leq 10$ considered in this work, H^+ ion density is considerably lower than the KCl concentration. Thus, H^+ ions will be considered as *spectator ions* that do not contribute to charge screening. Within this approximation, the PB equation reads

$$\frac{1}{r} \partial_r [r \partial_r \phi(r)] - \kappa_b^2 \sinh[\phi(r)] = -4\pi\ell_B \{ \sigma_p [\phi(a)] \delta(r-a) + \sigma_m [\phi(d)] \delta(r-d) \}, \quad (23)$$

with the screening parameter $\kappa_b = \sqrt{8\pi\ell_B\rho_b}$, and the polymer charge density $\sigma_p [\phi(a)]$ whose potential dependence will be specified below for the type of polymer under consideration. The integration of Eq. (23) around the pore and polymer surface yields the boundary conditions

$$\phi'(a^+) = -4\pi\ell_B\sigma_p; \quad \phi'(d^-) = -4\pi\ell_B\sigma_m. \quad (24)$$

To our knowledge Eq. (23) cannot be solved in closed form. Thus, we will solve this equation within an improved Donnan approximation that was introduced in Ref. [13] for fixed surface charges. At the first step, we inject into Eq. (23) a uniform Donnan potential ansatz $\phi(r) = \phi_d$. Integrating the result over the cross-section of the pore, one obtains

$$\sinh(\phi_d) = \frac{a\sigma_p [\phi_d] + d\sigma_m [\phi_d]}{\rho_b(d^2 - a^2)}. \quad (25)$$

Equation (25) quartic in the exponential of the potential ϕ_d should be solved numerically. Next we improve the pure Donnan approximation by taking into account the spatial variation of the potential. To this end, we express the potential as $\phi(r) = \phi_d + \delta\phi(r)$ and expand Eq. (23) at the linear order in the potential correction $\delta\phi(r)$ to get

$$\frac{1}{r} \partial_r [r \partial_r \phi(r)] - \kappa_d^2 [\sinh(\phi_d) + \cosh(\phi_d) \delta\phi(r)] = 0. \quad (26)$$

The solution of Eq. (26) reads

$$\phi(r) = \phi_d - \tanh(\phi_d) + c_1 I_0(\kappa_d r) + c_2 K_0(\kappa_d r), \quad (27)$$

with the pore screening parameter $\kappa_d = \kappa_b \sqrt{\cosh(\phi_d)}$ and

$$c_1 = \frac{4\pi\ell_B}{\kappa_d} \frac{K_1(\kappa_d a)\sigma_m(\phi_d) + K_1(\kappa_d d)\sigma_p(\phi_d)}{I_1(\kappa_d d)K_1(\kappa_d a) - I_1(\kappa_d a)K_1(\kappa_d d)}; \quad (28)$$

$$c_2 = \frac{4\pi\ell_B}{\kappa_d} \frac{I_1(\kappa_d a)\sigma_m(\phi_d) + I_1(\kappa_d d)\sigma_p(\phi_d)}{I_1(\kappa_d d)K_1(\kappa_d a) - I_1(\kappa_d a)K_1(\kappa_d d)}. \quad (29)$$

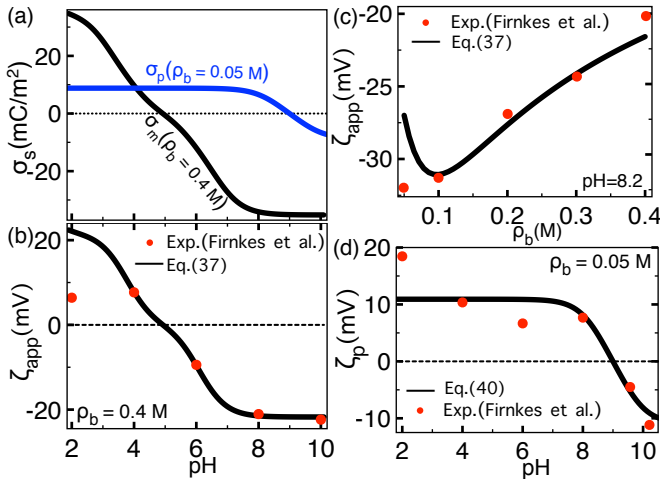


FIG. 2: (Color online) (a) pH dependence of the pore (black) and polymer surface charge density (blue). (b) Apparent pore zeta potential (37) versus the solution pH and (c) the salt concentration. (d) Polymer zeta potential (40) against pH. The experimental data in (b) are from Figure 2a of Ref. [15], the data in (c) from Figure 4 of the supporting information of Ref. [15], and the data in (d) from Figure 1b of Ref. [15]. The chemical reaction constants of the pore are $pK_m = 6.1$, $pL_m = 3.75$, and $pT_m = 1.0$, and the dissociable site density $\sigma_{0m} = 0.33$ e/nm². The reaction constants for the avidin protein are $pK_p = 9.5$ and $pL_p = 8.5$, and the surface density $\sigma_{0m} = 0.055$ e/nm².

III. RESULTS

A. Apparent zeta potential of the SiN pore

We compare here the experimentally determined apparent zeta potential of the pore obtained from the streaming potential measurements [15] with the theoretical prediction of the present formalism. In the derivation of the apparent zeta potential for the polymer-free pore (i.e. for $a = 0$ and $\sigma_p = 0$), we will use the notation of Ref. [25]. For a symmetric electrolyte with ionic charges $q_{\pm} = \pm 1$ and bulk density ρ_b , the net charge current through the pore is

$$I = 2\pi\epsilon\rho_b \sum_{i=\pm} q_i \int_0^d dr r e^{-q_i\phi(r)} [u_c(r) + u_{Ti}]. \quad (30)$$

In Eq. (30), the convective liquid velocity $u_c(r)$ is given by Eq. (3). Then, the conductive velocity component of the ionic species i reads $u_{Ti} = -\text{sign}(q_i)\mu_i\Delta V/L_m$, with the mobility of K^+ ions $\mu_+ = 7.616 \times 10^{-8}$ m²V⁻¹s⁻¹ and Cl^- ions $\mu_- = 7.909 \times 10^{-8}$ m²V⁻¹s⁻¹ [26]. Substituting into Eq. (30) the convective and conductive velocity components, and using the PB Eq. (23), one obtains

$$I = G_v\Delta V + G_p\Delta P, \quad (31)$$

with the conductance components

$$G_v = \frac{2\pi\epsilon\rho_b}{L_m} \sum_{i=\pm} \int_0^d dr r e^{-q_i\phi(r)} \{q_i\mu[\zeta - \phi(r)] - \mu_i|q_i|\}; \quad (32)$$

$$G_p = \frac{\pi d^2\mu\zeta}{L_m} \left\{ \frac{2}{d^2\zeta} \int_0^d dr r \phi(r) - 1 \right\}, \quad (33)$$

where we introduced the zeta potential $\zeta = \phi(d)$.

The streaming potential corresponds to the voltage that cancels the current (31), i.e. $\Delta V_{str} = -(G_p/G_v)\Delta P$. Introducing the reduced conductivities

$$K_v = \frac{2}{d^2} \left\{ \sum_{i=\pm} \frac{\sigma_i}{\sigma_T} \int_0^d dr r [e^{-q_i\phi(r)} - 1] + \frac{\mu e}{\sigma_T} \int_0^d dr r \sum_{i=\pm} q_i e^{-q_i\phi(r)} [\phi(r) - \zeta] \right\}; \quad (34)$$

$$K_p = \frac{2}{d^2\zeta} \int_0^d dr r \phi(r), \quad (35)$$

with the bulk conductivity of the species i $\sigma_i = e\mu_i|q_i|\rho_{bi}$ and the total conductivity $\sigma_T = \sigma_+ + \sigma_-$, one obtains

$$\Delta V_{str} = -\frac{\epsilon_w k_B T \zeta_{app}}{e\eta\sigma_T} \Delta P, \quad (36)$$

where the apparent zeta potential is given by

$$\zeta_{app} = \frac{1 - K_p}{1 + K_v} \zeta. \quad (37)$$

At the bulk KCl concentration $\rho_b = 0.4$ M, our computed bulk conductivity $\sigma_T = 6.0$ S/m compares well with the experimentally measured value of 4.7 – 5.1 S/m [15].

Figures 2(a) and (b) display the pH dependence of the surface charge and apparent zeta potential of the SiN pore [15]. The chemical parameters providing the best agreement with the experimentally measured zeta potential are given in the legend. Starting at pH = 10 and rising the acidity of the solution, H^+ binding to the silanol and primary amine groups increases the pore charge and zeta potential (pH \downarrow σ_m \uparrow ζ_{app} \uparrow), and turns them from negative to positive at pH ≈ 5 . Our model can accurately reproduce the pH dependence of the experimental data, except at pH = 2 where the data is overestimated.

Figure 2(c) displays the salt dependence of the apparent zeta potential ζ_{app} at pH = 8.2 where the pore is anionic. One sees that salt addition amplifies charge screening and lowers the magnitude of this potential, i.e. $\rho_b \uparrow |\zeta_{app}| \downarrow$. With the same model parameters as in Fig. 2(b), the theoretical prediction for ζ_{app} agrees well with the experimental data. As the apparent zeta potential (37) involves, in addition to the bare potential ζ , the pore conductance components (34) and (35), the agreement with experiments indicates that our model is also accurate in predicting the pressure and voltage-driven

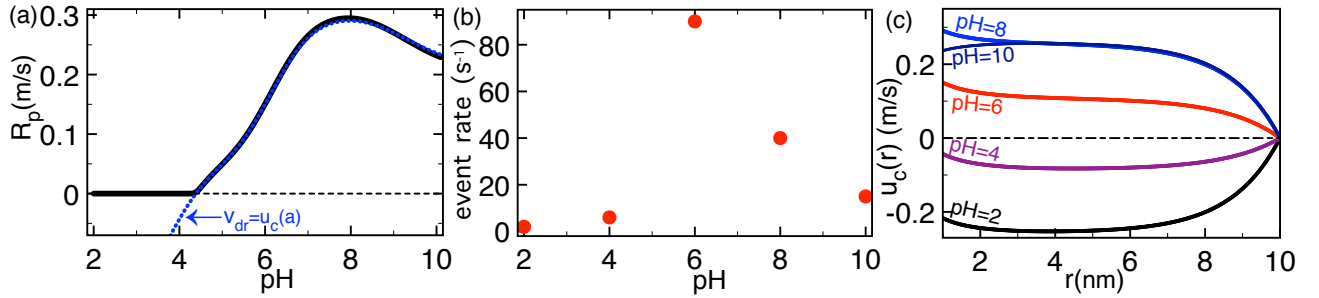
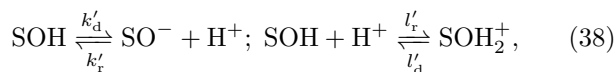


FIG. 3: (Color online) (a) pH dependence of the avidin translocation rate (black curve) and drift velocity (blue curve), and (b) experimental rate of translocation events from TABLE 1 of Ref. [15]. (c) Liquid velocity profile (3) at various pH. The salt concentration $\rho_b = 0.05$ M and external voltage $\Delta V = -150$ V are taken from of Ref. [15]. In the corresponding drift regime, the curves have no visible dependence on the precise value of the polymer length set to $L_p = 10$ nm.

charge conductivity of the pore. We finally note that the contribution from H^+ ions to salt screening is expected to increase at low pH or KCl concentration. Thus, in the corresponding regimes of Figs. 2(b) and (c), the deviation of the theoretical curves from the experimental data may originate from the spectator H^+ ion approximation introduced in Eq. (23).

B. Voltage-driven translocation of avidin proteins

We investigate here the pH controlled translocation of avidin proteins through SiN nanopores under an externally applied voltage [15]. According to the zeta potential measurements of Ref. [15], avidin is an amphoteric poly-electrolyte. Thus, we model the pH dependent inversion of the avidin charge by the chemical reaction scheme



with the characteristic dissociation rates $K_p = 10^{-pK_p} = k'_d/k'_r$ and $L_p = 10^{-pL_p} = l'_d/l'_r$. Following the derivation of Eq. (22), the protein charge density follows as

$$\sigma_p = \frac{10^{pL_p + pK_p - 2pH} e^{-2\phi(a)} - 1}{1 + 10^{pK_p - pH} e^{-\phi(a)} [1 + 10^{pL_p - pH} e^{-\phi(a)}]} \sigma_{0p}, \quad (39)$$

where σ_{0p} stands for the density of the dissociable groups.

Figure 2(d) compares the avidin zeta potential obtained from the charge regulation scheme of Eq. (38) with the experimental values of Ref. [15] extracted from the polymer mobility. The theoretical prediction for the zeta potential is obtained from the bulk limit of Eq. (27) where $\phi_d \rightarrow 0$ and $\kappa_d \rightarrow \kappa_b$, which yields

$$\zeta_p = \lim_{d \rightarrow \infty} \phi(a) = \frac{4\pi\ell_B\sigma_p(0)}{\kappa_b} \frac{K_0(\kappa_b a)}{K_1(\kappa_b a)}. \quad (40)$$

The chemical reaction parameters providing the best agreement with the experimental data are given in the legend of Fig. 2. One notes that the pH reduction increases the avidin charge (the blue curve in Fig. 2(a))

and the zeta potential ($\text{pH} \downarrow \sigma_p \uparrow \zeta_p \uparrow$), and switches their sign at the point of zero charge $\text{pH} \approx 9$. Within the experimental scattering, the charge regulation model (38) can account for the pH induced inversion of the avidin zeta potential with a reasonable accuracy.

Having established the pH dependence of the pore and protein surface charges, we characterize the avidin conductivity of the SiN pore. Figures 3(a) and (b) display respectively the translocation rate and the experimental rates of translocation events from Ref. [15]. One notes that for $\text{pH} \lesssim 4$, translocation events are rare. At $\text{pH} \gtrsim 4$, the translocation rate quickly rises ($\text{pH} \uparrow R_p \uparrow$), reaches a peak at $\text{pH} \sim 6 - 8$, and drops beyond this value ($\text{pH} \uparrow R_p \downarrow$). The comparison of Figs. 3(a) and (b) shows that our model can accurately reproduce the overall pH dependence of the experimental translocation data. The slower decay of the theoretical curve at large pH may be due to the contribution from the diffusion-limited capture regime not included in our model.

According to Eqs. (8) and (9), translocation is driven by electrostatic polymer-pore interactions embodied in the potential $V_p(z_p)$, and the EP and EO drags resulting in the velocity v_{dr} . In Fig. 3(a), the strong correlation between the v_{dr} and R_p curves implies that due to the weak avidin surface charge, avidin translocation is drift-driven and protein-pore interactions play a minor role.

To characterize the pH dependence of the avidin translocation rates in terms of the electrohydrodynamic drift, in Fig. 3(c) we report the liquid velocity profile (3) at various pH values. This plot should be interpreted together with the surface charge density plots in Fig. 2(a). We note that the electric field E induced by the negative voltage $\Delta V = -150$ mV is oriented towards the trans side corresponding to the positive velocity direction (see Fig. 1). From $\text{pH} = 2$ to 4, the Cl^- ions attracted by the cationic pore ($\sigma_m > 0$) result in a negative liquid velocity $u_c(r) < 0$. As $\sigma_m > \sigma_p$, the corresponding EO drag in the cis direction dominates the EP drift in the trans direction and results in a negative polymer velocity $v_{dr} = u_c(a) < 0$. Thus, the hinderance of polymer capture at $\text{pH} \leq 4$ stems from the drag force induced by the anionic EO flow.

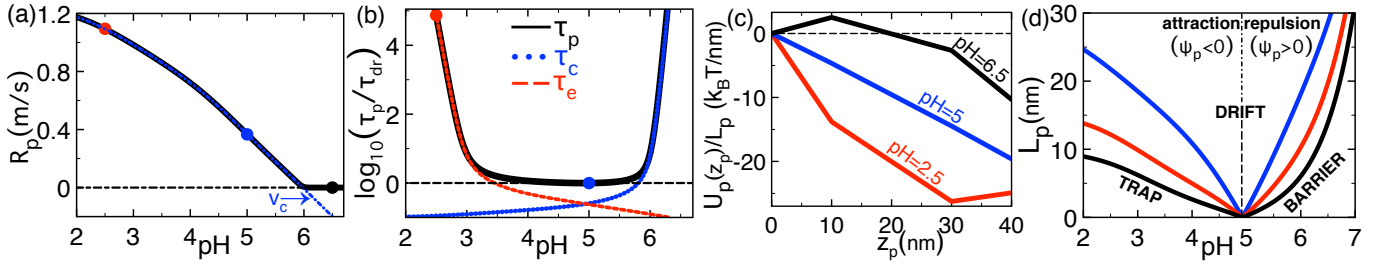


FIG. 4: (Color online) pH dependence of (a) the ds-DNA translocation rate (black curve) and capture velocity (41) (blue curve), and (b) translocation time, capture time, and escape time rescaled by the drift limit τ_{dr} . (c) Polymer potential (11) at various pH. In (a)–(c), the salt density is $\rho_b = 0.005$ M. (d) pH dependence of the critical polymer length (43) separating the polymer trapping, barrier, and drift transport regimes at the salt densities $\rho_b = 0.001$ (blue), 0.005 (red), and 0.01 M (black). The voltage is $\Delta V = 100$ mV in all plots. The remaining parameters are the same as in Fig. 3.

Rising the solution pH in the subsequent regime $4 \leq \text{pH} \leq 8$, the protein charge σ_p remains constant while the pore charge σ_m drops and turns from positive to negative. The resulting cation excess leads to a positive EO velocity $u_c(r) > 0$ and polymer drift velocity $v_{dr} = u_c(a) > 0$ (see Fig. 3(c)). Thus, the quick rise of the event rates at $\text{pH} > 4$ is induced by the cationic EO flow that drags the protein in the trans direction. Finally, increasing the pH beyond the value $\text{pH} \sim 8$, σ_m remains constant while σ_p turns from positive to negative. The protein charge inversion switches the sign of the avidin zeta potential $\phi(a)$ and turns the direction of the EP velocity component $v_{ep} = \mu E \phi(a)$ from trans to cis side, reducing the translocation rate in Figs. 3(a) and (b). Thus, beyond the charge inversion point $\text{pH} \approx 9$, protein capture is solely driven by the EO flow. These results confirm a similar mechanism that was proposed in Ref. [15] based on the comparison of the experimental pore and protein zeta potentials.

C. pH controlled DNA trapping

In nanopore-based biosensing approaches, serial polymer translocation necessitates fast polymer capture while accurate sequencing requires long signal duration, i.e. extended translocation time. We characterize the ds-DNA conductivity of SiN pores to show that mutual enhancement of the polymer capture speed and translocation time can be achieved by tuning the acidity of the solution. We have recently showed that ds-DNA transport can be accurately described by an inert polymer surface charge [14]. Thus, we fix the DNA surface charge density to the value $\sigma_p = -0.4$ e/nm² obtained from current blockade data [12].

Figures 4(a)–(c) display the pH dependence of the ds-DNA translocation rate R_p and rescaled translocation time τ_p/τ_{dr} (black curves), and the polymer potential profile $U_p(z_p)$. The behavior of these quantities can be described in terms of the inverse lengths $\lambda_{d,b}$ introduced in Eq. (10). At $\text{pH} = 6.5$ where the system is located in the barrier-dominated regime $\lambda_b > \lambda_d$, the pore en-

trance is characterized by an electrostatic barrier that reaches the value $U_p \approx 2.5 k_B T/\text{nm}$ at $z_p = L_p = 10$ nm. Figure 4(a) shows that this barrier leads to a negative capture velocity

$$v_c = v_p(z_p < L_p) = v_{dr} \left(1 - \frac{\lambda_b}{\lambda_d} \right), \quad (41)$$

resulting in a vanishingly small translocation rate R_p and large translocation time τ_p . Thus, at large pH values where the membrane is anionic, polymer capture is hindered by electrostatic DNA-pore repulsion. Then, the increase of the acidity to the point of zero charge $\text{pH} = 5$ suppresses the barrier and takes the system to the drift-driven regime $\lambda_d > \lambda_b > -\lambda_d$ where the polymer potential $U_p(z_p)$ turns to downhill. This enhances the capture velocity and translocation rate, and reduces the translocation time ($\text{pH} \downarrow v_c \uparrow R_p \uparrow \tau_p \downarrow$) by orders of magnitude.

Below the value $\text{pH} \approx 5$ where the pore becomes cationic, the translocation rate and time rise mutually with the acidity of the solution, i.e. $\text{pH} \downarrow R_p \uparrow \tau_p \uparrow$. This departure from the drift transport picture originates from the onset of opposite charge DNA-pore interactions. Indeed, Fig. 4(c) shows that the variation of the acidity from $\text{pH} = 5$ to 2.5 lowers the potential $U_p(z_p)$ and gives rise to an attractive potential minimum at the pore exit $z_p = L_m = 30$ nm. At the corresponding pH value, the system is located in the trapping regime $\lambda_b < -\lambda_d$ where the polymer-pore attraction enhances the DNA capture velocity (41) ($v_c > v_{dr}$) but also traps the molecule at the pore exit. Figure 4(b) shows that upon the variation of the acidity from $\text{pH} = 6.5$ to 2.5, this mechanism reduces the polymer capture time and increases the polymer escape time ($\text{pH} \downarrow \tau_c \downarrow \tau_e \uparrow$) from their drift limit by several orders of magnitude. This prediction is of high relevance for the optimization of nanopore-based biosensing techniques.

The effect of the polymer length on these features can be characterized by recasting the capture velocity (41) as

$$v_c = v_{dr} \left[1 - \text{sign}(\psi_p) \frac{L_p^*}{L_p} \right], \quad (42)$$

with the critical length

$$L_p^* = \frac{\ln(d/a) |\psi_p|}{2\pi\eta\beta v_{dr}} \quad (43)$$

separating the drift ($L_p > L_p^*$) and barrier/trapping regimes ($L_p < L_p^*$). Figure 4(d) displays the pH dependence of the length (43). The location of the barrier and trapping regimes below the critical line $L_p^* - \text{pH}$ stems from the fact that the external voltage acts on the whole polymer sequence while polymer-pore interactions originate solely from the polymer portion in the pore. Thus, polymer-pore interactions have a stronger effect on the translocation of shorter sequences. According to Eq. (42), this results in the faster capture of shorter polymers by cationic pores, i.e. $L_p \downarrow v_c \uparrow$ for $\psi_p < 0$. One also notes that in the same cationic pore regime of Fig. 4(d), due to the enhancement of the polymer-pore attraction, the upper length (43) for polymer trapping rises with increasing acidity ($\text{pH} \downarrow L_p^* \uparrow$) and decreasing salt ($\rho_b \downarrow L_p^* \uparrow$). This phase diagram may provide guiding information for probing the pH controlled polymer trapping in translocation experiments.

IV. SUMMARY AND CONCLUSIONS

In this Letter we have introduced an electrohydrodynamic model of pH controlled polymer translocation through SiN pores whose surface charge can be inverted upon protonation. Our model incorporates a charging procedure that can quantitatively reproduce the experimentally established pH and salt dependence of the pore surface charge. Within the framework of this model, we have investigated the electrohydrodynamic mechanism

behind the avidin conductance of SiN pores. Our model can accurately reproduce the experimentally measured non-monotonic dependence of the avidin translocation rates on the solution pH [15]. We showed that this peculiarity originates from the interplay between the EO drag and EP drift forces on the avidin protein.

We have also investigated the transport of ds-DNA molecules through SiN pores. Our analysis unraveled an electrostatic trapping mechanism that allows the mutual increase of the polymer capture speed and translocation time by pH tuning. As polymer trapping occurs in the escape regime $z_p > L_-$, the scanning of the entire polymer sequence at reduced velocity is possible only if the pore is longer than the polymer. Our finite-size analysis also shows that faster polymer capture followed by extended translocation occurs for sequences of length $L_p < L_p^*$. This inequality is consistent with the above-mentioned length hierarchy $L_p < L_m$ required for the slow sequencing of the entire polymer in the electrostatic trap. We have also shown that the upper sequence length L_p^* for polymer trapping can be tuned upon the variation of the acidity or the salt concentration. Future works can extend our model by including the diffusion-limited capture regime, the electrostatics of the finite membrane size, or entropic polymer fluctuations.

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