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# DNA capture into a nanopore: Interplay of diffusion and electrohydrodynamics

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(Received 29 June 2010; accepted 8 September 2010; published online 26 October 2010)

We present a detailed analysis of the process of voltage driven capture of DNA molecules by nanopores. We show that ionic current generates a nonuniform electric field that acts on both the DNA and on its counterions and that the response of DNA to the electric field is affected by its electroosmotic coupling to the mobile counterions. We calculate the voltage and molecular mass dependence of the radius of capture and of the capture rate in the diffusion limited regime. We argue that electroosmotic flow through the DNA coil is suppressed in the vicinity of the pore and present a tentative estimate of the capture rate in the barrier limited regime. © 2010 American Institute of Physics. [doi:10.1063/1.3495481]

## I. INTRODUCTION

DNA translocation through protein or synthetic solid state nanopores is a two stage process that involves capture of a DNA coil by the pore (including its delivery to the pore and insertion of one of its ends into it), followed by its motion through the nanochannel. The process may be driven by voltage  $\Delta V$  (typically a few hundred millivolts) applied between two macroscopic electrodes positioned on both sides of the partition separating the *cis* (where DNA is initially placed) and the *trans* (to where it translocates through the pore) chambers, as shown schematically in Fig. 1. Experiments are done at high added salt concentrations (typically about 1M KCl in water), such that ion current, usually of the order of nanoamps, flows between the electrodes through the nanopore, and translocation events are detected by monitoring the events of blockage of this current. The durations of current blockage events, their average, and distribution allow one to measure the corresponding translocation times, while the frequency at which such events occur determine the capture rate. See, e.g., Refs. 1–20 for further details.

In previous discussions of DNA translocation through nanopores it was usually assumed that the potential drop occurs exclusively across the pore. Most of the authors (with the important exception of Ref. 21) did not pay attention to the nature of the corresponding electric field. Recently, a combined experimental and theoretical study<sup>22</sup> has emphasized the importance of the electric field which exists in the *entire* system, not only in the pore. Importantly, this field, although time-independent, is not a regular electrostatic field created by immobile charges. Instead, this field exists because a salty solution is an ionic conductor, not a dielectric. In particular, this is why this field is not subject to Debye–

Hückel screening despite the very high ionic strength (at which the Debye screening length  $r_D$  is about 0.3 nm only). As the consequence, the electric field that acts on DNA is determined by Ohm's law as the product of the local ion current density and the resistance (and does not depend on the dielectric constants of either water or membrane). Fundamentally, this brings the entire problem from the realm of equilibrium or near equilibrium statistical mechanics to the field of electrohydrodynamics, because the coupling between charges is realized via viscous drag forces that give rise to solvent-mediated hydrodynamic interactions between the DNA backbone and its counterions. Current conservation leads to focusing of electric field lines at the entrance to the pore (the corresponding electric potential is identical to that of a point charge, with charge proportional to  $\Delta V$ ), resulting in electrophoretic funneling of DNA toward the pore. Combined with the observation that the electrophoretic mobility

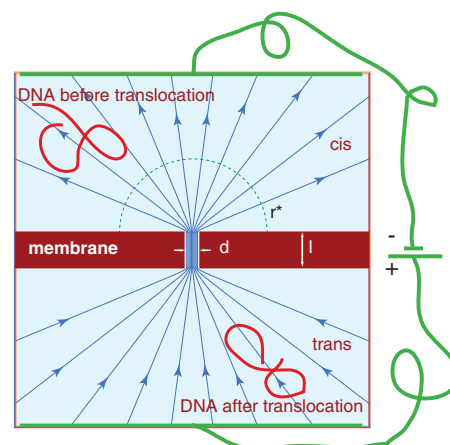


FIG. 1. Drawing of the *cis* (negative electrode) and *trans* (positive electrode) chambers. The arrows show the direction of electric field lines. The pore diameter  $d$  and length  $l$  and the capture radius  $r^*$  are also shown.

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of DNA is independent of its molecular weight,<sup>23</sup> this leads to the prediction that the capture rate in the, so called, diffusion limited, high molecular weight regime ( $>10^4$  basepairs) increases linearly with  $\Delta V$  and becomes independent of DNA length<sup>22</sup> (similar results were derived in Ref. 24). In the lower molecular weight range ( $<10^4$  basepairs) the capture rate is dominated by the barrier at the entrance to the pore; as the electric field increases, the height of the barrier decreases and, as the consequence, the rate increases exponentially with the voltage gradient (and with a power of molecular weight).

In this paper, we attempt to present a comprehensive yet simple theoretical description of DNA capture into nanopores. The paper is written in a somewhat informal style which we feel to be essential for the above goal. While formal derivations based on the generalized Smoluchowski equation<sup>25</sup> (in the presence of an electric field) and on the Kramers theory of chemical reaction rates<sup>26</sup> are presented where possible, the main emphasis is on intuitive arguments that capture the underlying physical mechanisms. Due to the complexity of the problem, some of these arguments are tentative and indicate qualitative trends rather than quantitative relationships (we will stress this repeatedly at appropriate places in the text). Throughout this work we focus on the nonequilibrium character of the problem: (1) ionic currents generate electric fields that act both on the charged DNA backbone and on its counterions, (2) moving charges apply frictional forces on the surrounding solvent, and (3) these hydrodynamic disturbances (electroosmotic flow) act back on DNA and modify its response to electric fields. In the following we assume that the pore walls (and all other walls) are uncharged and therefore do not create electroosmotic flow (see also the supplemental material for the article Ref. 22). Furthermore, since salt is overall electroneutral, the transfer of momentum from the positive ions to the solvent under the action of the external electric field is exactly canceled by the transfer of opposite momentum from the negative ions. In these circumstances no electroosmotic flow exists in the absence of DNA. Since excess concentration of small positive ions exists only within the DNA coils (as  $r_D$  is much smaller than the coil size), electroosmotic flow can exist only inside the coils (and in their immediate vicinity—since flow lines must be closed).

In Sec. II we present the general plan of the paper. In Sec. III we show that the nonequilibrium electric potential  $V(r)$  generated by the ionic current can be used to calculate the potential of stall force  $W(r)$  that defines the thermodynamic work needed to move DNA quasistatically between any two points in this electric field. We then use this potential to calculate the spatially nonuniform Boltzmann-like DNA density distribution and estimate the capture distance  $r^*$  defined as the distance from the pore at which the potential of the stall force becomes of order  $k_B T$ . Numerical estimates of the various physical quantities are presented, using the parameters of Ref. 22. In Sec. IV we present the generalized Smoluchowski equation which governs the diffusion of DNA and its response to electric fields. We present the solution of this equation subject to appropriate boundary conditions, calculate the DNA density distribution and the capture distance,

and compare them to the results obtained in the preceding section. The effects of spatially extended barriers at the pore are discussed and the possible contribution of polarization effects (dielectrophoresis) is considered. Our analysis of the barrier limited regime in Sec. V begins with considerations concerning the magnitude of the electric force on the stalled DNA at the entrance to the pore. We first review the analysis of the electroosmotic mobility of DNA *in bulk solution* (Ref. 27), according to which the force of the electric field on the DNA backbone is nearly completely balanced by the hydrodynamic drag against the electroosmotic flow of the solvent (which is carried along by oppositely moving counterions), resulting in molecular weight independent electrophoretic mobility of DNA. We argue that such electroosmotic flow inside the DNA coil sitting at the entrance to the pore is (at least partially) blocked by the presence of the surface and that therefore the coil experiences an electric force that increases with its molecular weight (the precise form of this dependence is necessarily tentative as the degree of screening of electroosmotic flow is unknown). We estimate the electric field enhanced probability to find a DNA coil at the entrance to the pore and calculate the rate at which DNA molecules traverse the free energy barrier, in the barrier limited regime. In Sec. VI we discuss our main results, emphasize their limitations, and outline directions for future study. Finally, in the three appendices to this paper, we present the derivation of the electric potential, estimate the value of the electrophoretic mobility of DNA, and review the phenomenological linear response theory of electrohydrodynamic flow through gels.<sup>28</sup>

## II. GENERAL CONSIDERATIONS AND PLAN OF WORK

In a recent paper<sup>22</sup> we argued that the process of DNA capture by a nanopore is significantly influenced by the relatively weak but nonuniform electric field extending out of the pore. We called the potential associated with that field  $V(r)$ , where  $r$  is the distance from the pore, and we showed that this potential is similar to that of a point charge located at the pore entrance:

$$V(r) = \frac{d^2}{8lr} \Delta V \equiv \frac{q_{\text{eff}}}{\epsilon r}, \quad q_{\text{eff}} = \epsilon \frac{d^2}{8l} \Delta V, \quad (1)$$

where  $l$  is pore length,  $d$  is pore diameter,  $\epsilon$  is dielectric constant of water, and  $\Delta V$  is the overall applied voltage (see Appendix A for details). As will be shown later on (see Sec. III B 4), in the parameter range relevant to the experiment,<sup>22</sup> the value of effective charge  $q_{\text{eff}}$  is of the order of 100 elementary charges,  $100e$ . Here, we emphasize from the outset that although  $V(r)$  is a static, time-independent potential, the problem is fundamentally a nonequilibrium one. In particular, the potential  $V(r)$  is created and supported by the fact that there is externally maintained current in the system. Among other things, this is the reason why the potential  $V(r)$  is not subject to Debye screening and extends much further than the Debye screening length (which is just a fraction of a nanometer under the typical experimental conditions).<sup>22</sup> Moreover, even though we included the dielectric constant of

water in the expressions for the potential and for the effective charge (in order to emphasize the similarity with the potential of point charge), this dependence cancels out and the potential does not depend on  $\epsilon$  [see Eq. (1)].

When the DNA coil is far away from the pore, it undergoes free diffusion; its diffusion coefficient, which we denote as  $D$ , decreases with DNA length  $N$ . When DNA approaches the pore, it starts drifting down the funnel-shaped potential  $V(r)$ . The electrophoretic mobility of DNA,  $\mu$ , is determined such that the speed of electrophoretic motion of DNA in the electric field  $\mathbf{E}(r) = -\nabla V(r)$  is equal to  $\mathbf{v}_E = -\mu \mathbf{E}$  (the minus sign reflects the fact that DNA charge is negative). It was predicted theoretically<sup>27</sup> and confirmed experimentally<sup>23</sup> that  $\mu$  does not depend on  $N$ . The reason is that while the charge of DNA,  $-Q$ , scales linearly with  $N$ , the corresponding electrostatic force  $-QE$  is almost entirely compensated by the force transmitted to DNA through hydrodynamic drag resulting from the motion of the positive counterions which are located inside the DNA coil (see Appendix B for further details and numerical estimate of  $\mu$ ).

When DNA is diffusing far away from the pore, it is sufficient to describe it as a pointlike object, phenomenologically characterized by the transport coefficients  $D$  and  $\mu$ . However, upon closer approach to the pore mouth, the spatial extent of the coil and its internal structure become increasingly important. In particular, once the DNA coil approaches the pore entrance, successful capture requires that the DNA end is properly aligned and introduced into the pore. This requires overcoming several kinds of barriers, associated with orienting and positioning the DNA terminal segment, as well as possibly placing the highly charged DNA in close proximity to the lower dielectric constant material of the channel walls.<sup>21</sup>

Therefore, as in Ref. 22, we will consider separately two limiting cases, the diffusion limited regime in Sec. III and the barrier dominated regime in Sec. V. In between, in Sec. IV, we will discuss the generalized diffusion equation, also called the Smoluchowski equation, which describes both limits, albeit in a very restrictive approximation of a pointlike particle. There, we will consider perturbatively the first correction to the pointlike particle approximation, which involves the effect of dielectrophoresis, i.e., additional pull on DNA in a nonuniform electric field due to coil polarizability.

We are considering only the case of sufficiently dilute DNA solution, in which interactions between DNA molecules can be safely ruled out. In this case the capture rate is proportional to DNA concentration ( $c$ ) in the *cis* volume,

$$J = R_c c. \quad (2)$$

In what follows we will only examine the quantity  $R_c$ , which we will refer to as the capture rate (subscript  $c$  stands for capture). Capture rates in the two limiting regimes will be denoted as  $R_c^{\text{diff}}$  and  $R_c^{\text{bar}}$ , respectively.

### III. DIFFUSION LIMITED REGIME

We first consider the limit in which DNA spends most of the time diffusing in the bulk, i.e., when its characteristics

time for reaching the pore exceeds the time to insert its end into the pore and begin the process of translocation.

#### A. Capture radius and the work of stall force

Our first argument begins by introducing a length scale  $r^*$  such that at the distances  $r > r^*$  DNA is freely diffusing in the bulk solution, with potential  $V(r)$  playing a marginal role, while at  $r < r^*$  DNA gets irreversibly captured and funneled down the potential  $V(r)$  directly to the pore mouth. If we manage to estimate  $r^*$ , then the diffusion controlled rate is given by the classical Smoluchowski result<sup>25</sup>

$$R_c^{\text{diff}} = 2\pi D r^*, \quad (3)$$

where  $D$  is the diffusion coefficient of DNA. In this formula, the coefficient is  $2\pi$  instead of familiar  $4\pi$ , because DNA gets absorbed by only a half of a sphere on the *cis* side.

How do we estimate  $r^*$ ? Naively, one could think that the radius  $r^*$  should be determined by the condition that energy at this distance should be about  $k_B T$ , i.e.,  $Q_{\text{eff}} V(r^*) \sim k_B T$ . The question is, however, what is the relevant charge  $Q_{\text{eff}}$  here? Definitely, it is not the bare charge of DNA backbone, because DNA is always accompanied by its counterions. But  $Q_{\text{eff}}$  is also not the charge of DNA together with all of its counterions—which is simply zero; this would be in direct contradiction to the fact that DNA does move in electrophoresis. Thus, we have to re-examine the question of effective charge and estimate the capture radius  $r^*$ .

Our argument below follows the work of Zhang and Shklovskii.<sup>21</sup> Although the field  $V(r)$  is of fundamentally nonequilibrium origin, it does not change with time. Therefore, to the extent that DNA motion does not appreciably affect the field itself [which is reasonable given that the field  $V(r)$  is created by the electric current and the contribution of DNA to the current is negligible], DNA fluctuations in the time-independent field  $V(r)$  should obey equilibrium statistical mechanics. Specifically, the probability of DNA moving from one place to another in the field  $V(r)$  should be proportional to  $\exp[-W/k_B T]$ , where  $W$  is the *minimal work* needed to move the DNA between the two points.<sup>29</sup> To be minimal, this work has to be performed infinitely slowly, which means that at every moment the force exerted on DNA must be equal the stall force, i.e., the force which is just sufficient to stop DNA from its electrophoretic motion in the gradient of  $V(r)$ . Once we found  $W(r)$ , we will determine  $r^*$  from the condition  $W(r^*) - W(\infty) \sim k_B T$ . Thus, we need to compute the work of the stall force.

To this end, let us recall how to compute the stall force itself, with the help of the ideas put forward by Long *et al.*<sup>27</sup> We will do it in a slightly more general form, not assuming any specific geometry of the potential  $V$  or its corresponding electric field  $\mathbf{E}$ . The stall force is found in the following four steps:

- (1) In the presence of electric field and in the absence of any other force, DNA moves with velocity  $\mathbf{v}_E = -\mu \mathbf{E}$  (minus because DNA charge is negative), where the mobility  $\mu$  is independent of molecular weight of DNA.

- (2) If there is no electric field, but some other force  $\mathbf{F}$  acts on DNA, then DNA moves with the speed  $\mathbf{v}_F = (D/k_B T)\mathbf{F}$ . Note that we wrote here the friction coefficient as  $k_B T/D$ , with  $D$  being the diffusion coefficient, because in this experiment the Einstein relation between the friction and the diffusion coefficient holds (counterions move together with DNA). However, since under the action of an electric field counterions move in opposite direction to DNA, there is no corresponding Einstein relation between the friction coefficient ( $k_B T/D$ ) and the electrophoretic mobility ( $\mu$ ).
- (3) The decisive observation of Long *et al.*<sup>27</sup> is that when both force  $\mathbf{F}$  and electric field  $\mathbf{E}$  are present, the velocities add up, because the equations of electrohydrodynamics are linear; thus

$$\mathbf{v} = -\mu\mathbf{E} + \frac{D}{k_B T}\mathbf{F}. \quad (4)$$

We will return to this result later on and discuss it further.

- (4) For now, we conclude from the Eq. (4) that the stall force is

$$\mathbf{F}_{\text{stall}}(\mathbf{r}) = \frac{\mu k_B T}{D}\mathbf{E}(\mathbf{r}). \quad (5)$$

Here, we indicated explicitly that the stall force depends on the spatial position, because the electric field does. The work of stall force as we move from  $\mathbf{r}_1$  to  $\mathbf{r}_2$  can be written as the integral over the trajectory  $\mathbf{r}_1 \rightarrow \mathbf{r}_2$ ,

$$\text{work}(\mathbf{r}_1 \rightarrow \mathbf{r}_2) = \int_{\mathbf{r}_1}^{\mathbf{r}_2} \mathbf{F}_{\text{stall}}(\mathbf{r}) \cdot d\mathbf{r}. \quad (6)$$

Since this work does not depend on the path of integration [ $\mathbf{E}$  is a potential field and, therefore,  $\mathbf{F}_{\text{stall}}(\mathbf{r})$  is also a potential field], we can define the potential of stall force  $W(\mathbf{r})$  such that  $\mathbf{F}_{\text{stall}}(\mathbf{r}) = -\nabla W$ , and thus

$$W(\mathbf{r}) = \frac{\mu k_B T}{D}V(\mathbf{r}). \quad (7)$$

The work of stall force (6) is then equal to the difference of potentials,  $\text{work}(\mathbf{r}_1 \rightarrow \mathbf{r}_2) = W(\mathbf{r}_1) - W(\mathbf{r}_2)$ .

Now we return to the determination of the relevant length scale  $r^*$  from the condition  $W(r^*) = k_B T$ . We find that this condition is equivalent to

$$V(r^*) = D/\mu, \quad (8)$$

in other words, the effective charge is  $Q_{\text{eff}} = k_B T \mu / D$ . With the help of Eq. (1), we find the capture distance

$$r^* = \frac{q_{\text{eff}} \mu}{\epsilon D} = \Delta V \frac{d^2 \mu}{8 l D}, \quad (9)$$

and then Eqs. (2) and (3) yield the capture rate in the diffusion controlled regime

$$R_c^{\text{diff}} = 2\pi D r^* = 2\pi \frac{q_{\text{eff}}}{\epsilon} \mu = \frac{\pi d^2 \mu}{4 l} \Delta V. \quad (10)$$

Let us first discuss the meaning and implications of the results (9) and (10) and then return to the subtleties of their derivation. The distance  $r^*$  depends on DNA length through  $D$  but since this dependence cancels out in the expression for  $R_c^{\text{diff}}$ , the capture rate is independent of DNA length  $N$  in this regime. We have to emphasize that this is a highly nontrivial result. Indeed, diffusion of DNA slows down considerably with increasing DNA length, but this is exactly compensated by the increase of  $r^*$ , i.e., by the fact that longer DNA gets captured by the funnel-shaped field at larger distances from the pore.  $N$ -independent capture rate was indeed observed for long DNA.<sup>22</sup> Another prediction of the above consideration is that the capture rate is linear in the applied voltage  $\Delta V$ ; this was also observed in Ref. 22.

## B. Further details on the diffusion limited regime

### 1. Alternative method to estimate capture radius $r^*$

The distance  $r^*$  can be thought of as the place where almost unbiased diffusion at  $r > r^*$  crosses over to almost pure down-hill sliding (or electrophoresis) at  $r < r^*$ . Specifically, if we are some distance  $r$  from the pore, then pure diffusion over this distance would require time  $r^2/D$ , which corresponds to the speed  $r/(r^2/D) \sim D/r$ , and since this has to be compared with electrophoretic velocity  $\mu E(r)$ , we conclude that directed electrophoresis dominates at  $\mu E(r) > D/r$ . Since  $rE(r) \approx V(r)$ , the transition from diffusion to electrophoresis dominated transport takes place at  $(\mu/D)V(r) \approx 1$ , which is equivalent to Eq. (8).

### 2. Comparison with capture by a nonelectric potential well

It is instructive to compare Eq. (8) with similar criteria for the case of motion in some nonelectric potential field  $U(r)$  that acts on DNA. In this case, the criterion would obviously look like  $U(r^*) = k_B T$ . Indeed, in a nonelectric potential field  $U(r)$ , the corresponding (nonelectrophoretic) mobility  $\mu_U$  would obey the Einstein relation  $D/\mu_U = k_B T$ . The difference between electric and nonelectric case in this context is that electric field acts not only on DNA, but also on the counterions. This is why, although the relation  $\mathbf{v}_E = -\mu\mathbf{E}$  can be rewritten as  $\mathbf{v}_E = -(\mu/Q)Q\mathbf{E}$ , where  $Q\mathbf{E}$  is electric force on DNA ( $Q \propto N$  is the charge of DNA) and  $Q/\mu$  is its friction coefficient, this friction coefficient and the diffusion coefficient of DNA are not connected by Einstein relation,  $QD/\mu \neq k_B T$ . This is of course consistent with the observation that  $D$  decreases with increasing DNA length  $N$  as  $1/N^\nu$  (where  $1/2 \leq \nu \leq 1$ ), while  $\mu$  is independent of  $N$ .<sup>23,27</sup>

### 3. Corollary: Quasi-Boltzmann distribution

It is perfectly conceivable that the electric potential  $V(\mathbf{r})$  can be created in a conducting electrolyte with a geometry completely different from that of the field of a point charge, Eq. (1). The above consideration of the work by the stall force allows us to conclude that the density distribution of DNA coils (or probability distribution for a single coil) is Boltzmann-like,

$$c(\mathbf{r}) = c \exp \left[ -\frac{\mu}{D} V(\mathbf{r}) \right], \quad (11)$$

the normalization factor here is written under the assumption that the potential vanishes at infinity. Although this distribution looks almost like a standard barometric formula, it is highly unusual in several respects. First, there is no  $k_B T$  in the traditional place under  $V$ . Second, transport coefficients  $D$  and  $\mu$  are present in what is supposed to be an equilibrium expression. Both of these features are closely related to one another and to the facts—already mentioned—that the problem is fundamentally a nonequilibrium one and that  $\mu$  and  $D$  are not connected by an Einstein relation. Of course, Eq. (11) is only valid as long as the potential is sufficiently smooth, i.e., does not change too much over distances of the order of DNA coil size.

#### 4. Numbers

The above theory treats the DNA coil as a point, which is reasonable as long as  $r^* > R_g$ , where, somewhat arbitrarily, we take the gyration radius of the coil  $R_g$  to characterize the coil size. We estimate this size as  $R_g \approx (L\ell_p/3)^{1/2}$ , where  $L$  and  $\ell_p$  are the contour length and persistence length of DNA, respectively; alternatively,  $R_g \approx a(NN_p/3)^{1/2}$ , where  $N$  is the number of base pairs,  $a \approx 0.34$  nm is chain length per one base pair, and  $N_p \approx 150$  is number of base pairs per one persistence length. In order to calculate the ratio

$$\frac{r^*}{R_g} = \Delta V \frac{d^2 \mu}{8lDR_g},$$

we use the Zimm theory expression for the DNA diffusion coefficient

$$D = \frac{k_B T}{6\pi\eta R_H}, \quad (12)$$

where  $R_H$  is the hydrodynamic radius of the coil. For  $\mu$ , we use the estimate (B1) provided in Appendix B which agrees reasonably well with experimental data.<sup>23</sup> This yields

$$\frac{r^*}{R_g} = \frac{3}{4} \underbrace{2\alpha}_{\approx 1} \times \underbrace{\frac{e\Delta V}{k_B T}}_{\approx 12} \times \underbrace{\frac{d^2}{la}}_{\approx 1.8} \times \underbrace{\frac{r_D}{b}}_{\approx 0.15} \times \underbrace{\frac{R_H}{R_g}}_{\approx 0.7} \approx 1.7, \quad (13)$$

where  $a = 0.34$  nm is the length of dsDNA per one base pair,  $b = 2$  nm is the dsDNA diameter, and  $\alpha < 1$  is the fraction of ionized phosphate groups, taking into account the Onsager–Manning condensation;<sup>30</sup> for the pore geometry, we used  $d = 3.5$  nm and  $l = 20$  nm. Thus,  $r^*$  is of the same order as  $R_g$ . This validates our estimate of the diffusion controlled rate, because as soon as DNA coil arrives to the distance of the order of its own size to the pore, it gets captured by the field  $V(r)$ , but it keeps diffusing unperturbed at  $r > r^*$ .

Let us now estimate the numbers in the expression (10) for the diffusion limited capture rate. Using  $1 \text{ nm}^3 = 6 \times 10^{-10} \text{ nM}^{-1}$  and using the estimate (B1) for electrophoretic mobility of DNA,  $\mu$ , derived in the Appendix B yields

$$R_c^{\text{diff}} \approx \left( 6.3 \frac{\text{nM}}{V_s} \right) \times \Delta V. \quad (14)$$

As we already mentioned, the experimentally observed<sup>22</sup> capture rate in the diffusion limited regime is indeed consistent with linear dependence on  $\Delta V$ . The coefficient in formula (14) is about a factor of 3 below the experimentally observed counterpart. Given the complexity of the phenomenon and the simplicity of the theory, we consider an agreement within a factor of 3 excellent. The discrepancy can be very plausibly attributed to an inaccurate estimate of electrophoretic mobility, as well as to the fact that DNA coil is not really a point given that  $r^*$  is of the same order as  $R_g$ . Later on, we will examine the consequences of the fact that DNA coil is not really a point and discuss the contribution of dielectrophoresis to DNA capture.

To conclude this section, we can use the same numerical values of parameters to estimate the effective charge of the pore introduced in Eq. (1). For instance, if  $\Delta V = 300$  mV, we have

$$\frac{q_{\text{eff}}}{e} = \frac{e\Delta V}{\underbrace{k_B T}_{\approx 12}} \times \frac{d^2}{\underbrace{8ll_B}_{\approx 0.1}} \times \epsilon \approx 100, \quad (15)$$

where the Bjorrum length is  $l_B = e^2 / \epsilon k_B T \approx 0.7$  nm.

#### 5. An alternative view on the diffusion limited rate

We are indebted to Shklovskii for the following remark. Our result (10) for the diffusion limited capture rate does not involve the size of the DNA coil. This is because our derivation was indeed based on considering DNA as a pointlike particle, with diffusion constant  $D$  and electrophoretic mobility  $\mu$ . It is then ought to be possible to continue the consideration of pointlike particles even as they travel to distances smaller than  $r^*$  and indeed into the pore itself. There, inside the pore, they are subject to electric field  $\Delta V/l$  and, therefore, they move with speed  $\mu\Delta V/l$ . With particle concentration  $c$  and pore cross-sectional area  $\pi d^2/4$ , this produces particle current (the number of particles per unit time)  $(\mu\Delta V/l) \times (\pi d^2/4) \times c$ , which is exactly the result (10).

Of course, the identity of these results is not surprising. Indeed, in a stationary process the current through any cross-sectional surface (properly drawn perpendicular to the local current lines) must be the same everywhere. While we calculated this current far away from the pore, the Shklovskii argument calculates it for pointlike particles inside the pore. Thus, the identity of the results confirms the correctness of our considerations, provided of course that DNA coil can be faithfully described as a pointlike object in the  $r > r^*$  zone, which is justified by the fact that  $r^* \approx R_g$ .

### IV. GENERALIZED SMOLUCHOWSKI EQUATION

#### A. Smoluchowski equation and its boundary conditions

We now present a more formal approach to the diffusion of DNA coils outside of the pore. As long as coils can be thought of as pointlike objects, their concentration satisfies the continuity equation

$$\frac{\partial c}{\partial t} + \nabla \cdot \mathbf{j} = 0, \quad (16)$$

thus, for stationary process  $\nabla \cdot \mathbf{j} = 0$ . The particle current  $\mathbf{j}$  is driven by the concentration gradient, by the gradient of electric potential  $V(\mathbf{r})$ , and, in general, also by the gradient of some nonelectric potential energy  $U(\mathbf{r})$ . We assume that potential  $V(\mathbf{r})$  as well as potential energy  $U(\mathbf{r})$  are smooth enough, such that we can consider DNA coil as pointlike to a first approximation. Then

$$\nabla \cdot \mathbf{j} = 0, \quad (17)$$

$$\mathbf{j} = -D \nabla c + \mu c \nabla V - \frac{D}{k_B T} c \nabla U.$$

We call this the Smoluchowski equation. Notice that  $\mathbf{E} = -\nabla V$  is the electric field, and that  $V$  and  $U$  enter with different signs because DNA is negatively charged, while electrophoretic mobility is defined to be positive,  $\mu > 0$ .

To avoid cumbersome expressions, we will suppress the  $U$  term in the calculations below; we will reintroduce it at the very end by the trivial replacement

$$V(\mathbf{r}) \rightarrow V(\mathbf{r}) - \frac{D}{\mu k_B T} U(\mathbf{r}). \quad (18)$$

Now we have to complement the Smoluchowski equation with proper boundary conditions. The first one is trivial,

$$c(\infty) = c, \quad (19)$$

where  $c$  is the bulk concentration of DNA which is supposedly known. The second boundary condition requires some discussion.

In the previous Sec. III, we artificially separated the problem into completely free diffusion at  $r > r^*$  and irreversible absorption by the pore at  $r < r^*$ . In fact, of course, the diffusion is somewhat biased even at  $r > r^*$  and does not become pure drift at  $r < r^*$ ; indeed,  $r^*$  is just a cross-over scale. In the spirit of classical reaction rate theory due to Kramers,<sup>26</sup> we should imagine that DNA keeps moving along its properly defined “reaction coordinate” into the very mouth of the pore, where it presumably overcomes the barrier [described by  $U(\mathbf{r})$ ] and where, accordingly, we have to impose the absorbing boundary condition,

$$c(r_0) = 0. \quad (20)$$

Notice that  $r_0$  is not the same as  $r^*$ ; the new distance  $r_0$  is the place where particles are supposed to be “instantly” captured and removed from the system.

In fact, the application of Smoluchowski Eq. (17) to the region within  $r^*$  is questionable, because  $r^*$  is of the same order as coil size  $R_g$ . In other words, the reaction coordinate in this region is probably not just the distance of the coil center from the pore and the relevant generalized diffusion coefficient is not just  $D$ . Nevertheless, it is an instructive warm-up to consider the Smoluchowski equation based capture theory with  $r_0 < r^*$ .

We should emphasize that the present approach (based on Smoluchowski equation) is both different and logically

simpler than the one pursued in Sec. III. There, talking about the work of stall force, we postulated a “quasiequilibrium” distribution of coils in the potential  $V(\mathbf{r})$ . Such a distribution would be obtained from the Smoluchowski equation by imposing the no-current, reflecting boundary condition instead of the absorbing one used here. This is justified because we determined  $r^*$  such that when DNA gets within a distance  $r^*$  from the pore, it is captured by the electric field and driven toward the pore, thus effectively imposing an absorbing boundary condition at  $r^*$ .

## B. Spherically symmetric case

We assume that both potential  $V$  and potential energy  $U$  are spherically symmetric which implies that the resultant concentration field  $c(r)$  is also spherically symmetric. Then, the current density  $\mathbf{j}$  and electric field  $\mathbf{E} = -\nabla V$  are both pointing in the radial direction. This means that the above second order ordinary differential equation has the physically obvious property that overall current  $J$  through any sphere of radius  $r$  must be the same, independent of  $r$ . Therefore,  $j(r) = J/2\pi r^2$  (it is  $2\pi$  and not  $4\pi$  because we are considering only a half-sphere at the mouth of the pore). Thus, the Smoluchowski equation is reduced to a first order equation,

$$-D \frac{\partial c(r)}{\partial r} + \mu c(r) \frac{\partial V(r)}{\partial r} = \frac{J}{2\pi r^2}. \quad (21)$$

Integrating this expression is a matter of standard technique. We first solve the corresponding homogeneous equation

$$-D \frac{\partial c(r)}{\partial r} + \mu c(r) \frac{\partial V(r)}{\partial r} = 0. \quad (22)$$

Not surprisingly, the solution of this equation is

$$c(r) = c_0 e^{\mu V(r)/D}. \quad (23)$$

Note that this *would be* the solution if the boundary condition was reflecting,  $J=0$ ; this is why this solution is identical to the quasi-Boltzmann distribution (11) obtained in Sec. III. Here, we want to impose the absorbing boundary condition. To do that, we formally consider  $c_0$  to be a function of  $r$  and substitute (23) back into Eq. (21), yielding an equation for  $c_0(r)$ ,

$$-D \frac{\partial c_0(r)}{\partial r} e^{\mu V(r)/D} = \frac{J}{2\pi r^2}. \quad (24)$$

This expression is trivially integrated and upon imposing the desired absorbing boundary condition  $c(r_0)=0$ , we obtain

$$c(r) = -\frac{J}{2\pi D} \int_{r_0}^r \frac{1}{r'^2} \exp\left[\frac{\mu}{D}(V(r) - V(r'))\right] dr'. \quad (25)$$

Finally, we determine the unknown constant  $J$  from the second boundary condition,  $c(\infty)=c$ , and arrive at the result

$$c(r) = c \frac{\int_{r_0}^r \frac{1}{r'^2} \exp \left[ \frac{\mu}{D} (V(r) - V(r')) \right] dr'}{\int_{r_0}^{\infty} \frac{1}{r'^2} \exp \left[ -\frac{\mu}{D} V(r') \right] dr'}. \quad (26)$$

The overall current is given by

$$J = - \frac{2\pi D c}{\int_{r_0}^{\infty} \frac{1}{r'^2} \exp \left[ -\frac{\mu}{D} V(r') \right] dr'}. \quad (27)$$

The sign is negative because the current points inward, toward the pore. Thus, the capture rate  $R_c = |J|/c$  is given by

$$R_c = \frac{2\pi D}{\int_{r_0}^{\infty} \frac{1}{r'^2} \exp \left[ -\frac{\mu}{D} V(r') \right] dr'}. \quad (28)$$

This reproduces the familiar result  $R_c^{\text{diff}} = 2\pi D r_0$ , Eq. (3), when there is no electric field imposed,  $V(r)=0$  (and  $U=0$ ). This is not surprising, because for  $V(r)=0$  our analysis reduces to the standard derivation of the Smoluchowski result (as it is well explained in the textbook by Berg).<sup>31</sup>

### C. Coulomb potential $V(r)$

The above integrals can be evaluated exactly when potential is of Coulomb type,  $V(r) = q_{\text{eff}}/\epsilon r$ . We obtain

$$R_c^{\text{diff}} = \frac{2\pi\mu q_{\text{eff}}/\epsilon}{1 - e^{-\mu q_{\text{eff}}/\epsilon D r_0}}. \quad (29)$$

As expected, when  $r_0$  is small compared to  $r^* = q_{\text{eff}}\mu/\epsilon D$ , Eq. (9), the rate  $R_c^{\text{diff}}$  becomes (exponentially fast) independent of  $r_0$ , and approaches the by now familiar result  $R_c^{\text{diff}} = 2\pi D r^*$ , Eq. (10).

The concentration field is also easy to determine for the Coulomb potential case,

$$c(r) = c \frac{1 - \exp \left[ \frac{q_{\text{eff}}\mu}{\epsilon D} \left( \frac{1}{r} - \frac{1}{r_0} \right) \right]}{1 - \exp \left[ -\frac{q_{\text{eff}}\mu}{\epsilon D r_0} \right]}. \quad (30)$$

Again assuming  $r_0 \ll r^*$ , we can simplify this expression, but cannot completely get rid of  $r_0$ . Nevertheless, if  $r_0 \ll r^*$ , then the overall shape of  $c(r)$  is such that with decreasing  $r$  from infinity,  $c(r)$  almost does not change as long as  $r > r^*$ , begins rapidly decreasing as soon as  $r$  becomes smaller than  $r^*$ , and finally vanishes at  $r=r_0$ . This is illustrated in the Fig. 2. Of course, this behavior is in perfect agreement with our qualitative expectations on which the discussion in the Sec. III was based.

### D. Barrier at entrance to pore

In reality, in addition to the Coulomb-like potential, there is also a potential energy barrier somewhere close to the entrance of the pore. Therefore, the Smoluchowski equation has to be generalized if one wants to move beyond the purely diffusion controlled regime. In particular, the absorb-

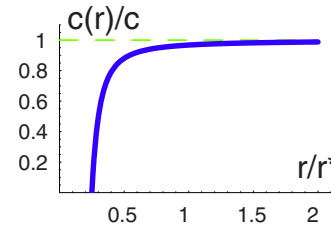


FIG. 2. Concentration profile of the stationary process in which DNA of concentration  $c$  at infinity is electrophoretically sucked by the Coulomb potential  $V(r)$  and then absorbed at  $r=r_0$ . For illustration purposes, the graph is plotted assuming  $r_0=0.25r^*$ . For smaller  $r_0$  it is even more flat at  $r>r^*$ .

ing point  $r_0$  will have to be chosen somewhere inside the barrier region. Even though the description based on considering DNA as a point will clearly break down in this region, it is useful to ignore this problem for the time being and address the Smoluchowski equation for the situation when DNA coil (considered as a point particle), after sliding down the potential  $V(r)$ , faces increasing potential energy due to the barrier.

Let us now assume that  $U$  is spherically symmetric. This is not very realistic at all, but we explore this case as an illustration (we do have a specific point to make out of it). In this case, upon replacement (18), the expression (28) for the capture rate reads

$$R_c = \frac{2\pi D}{\int_{r_0}^{\infty} \frac{1}{r'^2} \exp \left[ -\frac{\mu}{D} V(r') + \frac{1}{k_B T} U(r') \right] dr'}. \quad (31)$$

[Let us repeat that  $U(r)$  and  $V(r)$  come with different signs because the DNA is negatively charged.] Notice that the structure of this formula, particularly its characteristic denominator, is very similar to the corresponding expression in Kramers transition rate theory.<sup>26</sup>

Imagine now that  $U(r)$  is a high potential barrier located at very small  $r$ . Figure 3 shows both the potential energy and the concentration profile for such situation [for illustration purposes, we assumed a potential of the form  $U(r) = U_0 e^{-r/d}$ ]. The take home message from this figure is that there is a

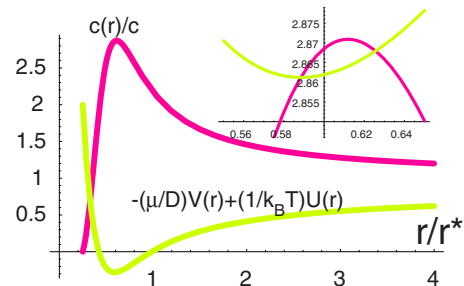


FIG. 3. Concentration profile of the stationary process in which DNA of concentration  $c$  at infinity is electrophoretically sucked by the Coulomb potential  $V(r)$ , absorbed at  $r=r_0$ , and also faces the potential barrier  $U(r)$ . For illustration purposes, the graph is plotted assuming  $r_0=0.25r^*$ , where  $r^*$  is defined such that  $(\mu/D)V(r)=r^*/r$ . Other parameters are chosen in the following way:  $U(r)/k_B T = 40e^{-8r/r^*}$  (barrier of  $40e^{-8 \cdot 0.25} k_B T \approx 5.4 k_B T$ ). The purple curve is the concentration profile in units of  $c$  and the green curve is the total potential in arbitrary units. Inset: same data blown up in the vicinity of maximal concentration (the curve for potential is appropriately moved up).

concentration maximum—a build-up—at the foothold of the barrier. The figure may create an impression that the concentration has a maximum at the minimum of potential, as one would expect in the case of an equilibrium system. This impression is illusory, as the inset of Fig. 3 indicates. It is clearly seen that the point of maximal concentration, where the diffusive flux vanishes, corresponds to the positive slope of the potential, i.e., at this point there remains a forced flux toward the center, in the direction of decreasing  $r$ . At the point of zero force, or minimum of potential energy, there is concentration gradient maintaining the same flux in the same direction.

To conclude this section, we emphasize that the nonequilibrium build-up of concentration at the foothold of the barrier, which we found here by solving the spherically symmetric Smoluchowski equation for pointlike particles, is in fact a rather general property of systems featuring in their potential landscapes a funnel-shaped attraction region in front of the barrier. Indeed, stationary flux through the barrier front region, where the force (barrier gradient) points against the flux, can be realized *only* by the formation of a concentration gradient sufficient to overcome the force. Conversely, if the barrier energy grows sharply enough, this inevitably results in build-up of concentration in front of the barrier.

## E. Dielectrophoresis

We emphasized several times that Smoluchowski equation approach relies on considering the DNA coil as a pointlike object. The first thing that happens to the extended coil is it can be polarized and thereby experience a force in a nonuniform electric field. The motion of a neutral object (DNA together with counterions) in a nonuniform electric field is called dielectrophoresis.<sup>32</sup> We want in this section to analyze the dielectrophoretic contribution to the DNA transport rate away from the pore. We begin by introducing the polarization energy,

$$U = -\frac{1}{2}\kappa\mathbf{E}^2, \quad (32)$$

where  $\kappa$  is the polarizability which at least in the scaling sense is proportional to the polymer volume,<sup>32</sup>

$$\kappa \approx \epsilon R_g^3. \quad (33)$$

In fact, it might be closer to the cube of hydrodynamic radius  $R_H$ , but such details play no role in scaling analysis.

To compute the rate, we substitute the new potential energy  $U$  into the Eq. (31). Replacing  $\mu q_{\text{eff}}/Dr' = \xi$  in the integral, we arrive at

$$R_c = \frac{2\pi\mu q_{\text{eff}}\epsilon}{\int_0^{\mu q_{\text{eff}}\epsilon Dr_0} \exp\left[-\xi - \frac{\kappa\epsilon^2 D^4}{2k_B T \mu^4 q_{\text{eff}}^2} \xi^4\right] d\xi}. \quad (34)$$

Note that the two terms in the exponential have the same sign since both Coulomb interaction and polarization act to attract DNA to the high field region at the pore.

Inspection of the above expression shows that dielectrophoresis contributes significantly to the capture rate if the  $\xi^4$

term becomes large compared to the  $\xi$  term in the integrand when  $\xi$  increases to the upper integration limit. This yields the condition

$$\frac{\kappa D q_{\text{eff}}}{2k_B T \mu \epsilon} \gg r_0^3. \quad (35)$$

Remembering the values of  $q_{\text{eff}}$  [Eq. (1)],  $D$  [Eq. (12)],  $\mu$  [Eq. (B1)],  $\kappa = \epsilon R_g^3$ , and the Björrum length  $l_B = e^2/\epsilon k_B T \approx 0.7$  nm, we arrive at the criterion (in which we keep the numerical coefficients, such as  $6\pi$ , because they accumulate to a large factor)

$$\frac{1}{100} \frac{e\Delta V d^2}{k_B T} \frac{b}{la} \frac{a}{r_D l_B} R_g^2 a \gg r_0^3. \quad (36)$$

Upon plugging in the numbers, this becomes  $R_g^2 a \gg r_0^3$ . However, since in our model  $r_0$  is an undetermined parameter with value anywhere between pore diameter  $d$  and coil size  $R_g$ , we cannot decide on purely theoretical grounds whether this condition is realistic or not. If  $r_0$  is close to the lower bound, the condition is satisfied and dielectrophoresis is important; if it is close to the upper bound, it is not.

Let us note, however, that if the condition is met, and the dielectrophoretic contribution is important, then formula (34) would predict a different voltage and  $N$ -dependence of the capture rate. In this sense, the experimental observations reported in the article<sup>22</sup> appear to be consistent with marginal role of dielectrophoresis. Nevertheless, the question deserves further theoretical and experimental attention.

## V. BARRIER LIMITED REGIME

### A. Transition state and barrier height

Delivery of the DNA coil to the pore mouth is necessary but not sufficient to start translocation; sooner or later, DNA must place its end into the pore, as shown in Fig. 4(a).<sup>33</sup> Placing the end into the pore requires climbing across the potential barrier that involves the entropy penalty for strictly orienting the chain end and, possibly, the electrostatic energy penalty for bringing the charged DNA end from the water environment to the proximity of the lower dielectric constant membrane material. Application of voltage reduces the barrier height through the mechanism discussed in detail in Ref. 21. The conclusion is that the barrier is reduced by a quantity linear in the applied voltage  $\Delta V$ , and, therefore, the barrier energy for the chain end can be written as

$$U - q\Delta V, \quad (37)$$

where  $q$  is of the order of one elementary charge, although does not quite coincide with it (the value of  $q$  calculated in Ref. 21 for the parameters of an  $\alpha$ -hemolysin pore, is only a rough estimate for the SiN pore of Ref. 22 which has a three to four times higher value of the dielectric constant and allows some leakage of the electric field into the surrounding membrane). The barrier also includes the entropic penalty of bringing the chain end close to the impermeable surface,<sup>34,35</sup> but we neglect this correction here for simplicity.

The most important point in the context of the present work is immediately visible in the Fig. 4(a): when the chain end is just introduced into the pore, most of the coil is by

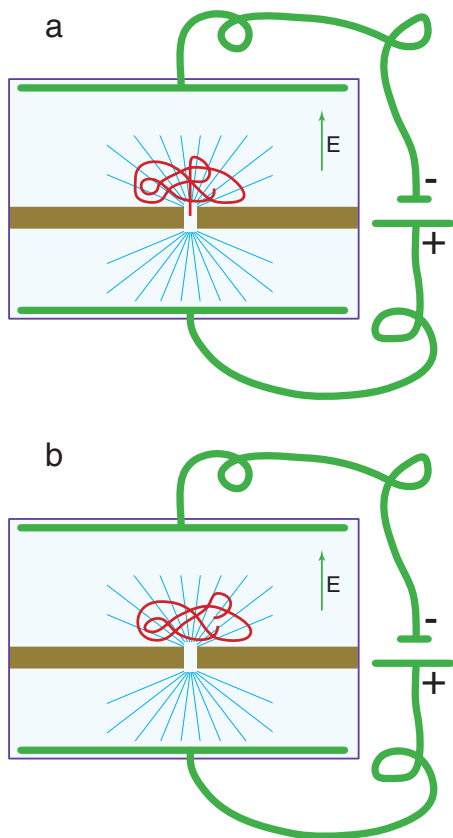


FIG. 4. (a) represents the transition state of the process: DNA terminal is just introduced into the pore, while the rest of the coil enjoys being in the potential well  $V(R_g)$ . (b) represents the state of kinetic intermediate on the pathway of DNA from the bulk solution infinity toward the transition state; it corresponds to the situation when coil is already in the potential well  $V(R_g)$ , but DNA end is not yet in the pore and just only searches for the entrance. In either case, hydrostatic pressure above DNA prevents electroosmotic flow through the coil.

necessity located in the vicinity of the pore and, therefore, is subject to the (attractive!) potential  $V(r)$ . We can state that the transition state (top of the barrier) of the whole process includes the DNA terminal at the top of the barrier (37) and the rest of DNA coil sitting in the potential well with energy, roughly,  $-Q_{\text{eff}}V(R_g)$ , where  $Q_{\text{eff}}$  is an effective charge of DNA in this situation. This transition state is depicted in Fig. 4(a). The potential well felt by the coil dramatically reduces the overall height of potential barrier for the process.

We estimated that the coil is located at the distance of the order of its gyration radius  $R_g$  from the pore mouth.<sup>36</sup> Its segments are, therefore, subject to electrostatic potential, on average,  $V(R_g)$ . The decisive point is that the effective charge of DNA sitting at the pore mouth is some fraction, denoted as  $\alpha' < 1$ , of its full charge  $2Ne$ ,  $Q_{\text{eff}} = 2\alpha'Ne$ . The latter estimate is highly nontrivial, it is in contrast with the situation discussed above [see formula (8)] when DNA is far from the pore mouth, and its effective charge  $Q_{\text{eff}} = k_B T \mu / D$  is a tiny fraction of  $Ne$  as it grows only as  $\sqrt{N}$ . We will discuss this important issue in great details below, in Secs. V B and V C.

Qualitatively, since  $V(R_g) \sim 1/R_g \sim 1/\sqrt{N}$ , we see that the barrier reduction goes as  $\alpha' \sqrt{N}$ . This mechanism produces quite dramatic speed up of the process with increasing

DNA length, all the way up until the chain length at which the system crosses over to the diffusion controlled regime. This qualitative prediction of the theory is definitely born out in the experiment.<sup>22</sup>

Returning to the more quantitative approach, since we have discussed the barrier, we can write down the most important exponential factor of the rate

$$R_c^{\text{bar}} \propto \exp \left[ -\frac{U}{k_B T} + \frac{q\Delta V}{k_B T} + \frac{2\alpha' Ne V(R_g)}{k_B T} \right]. \quad (38)$$

On the qualitative level, we see that the dependence on the applied voltage in this regime is exponential [because  $V(r)$  is linear in  $\Delta V$ , see formula (1)]. This prediction of the theory is also in agreement with the experiment<sup>22</sup> in the barrier limited regime.

What now remains to be done is two things. First, we have to discuss the issue of the effective charge of DNA at the pore mouth and why we think it is much higher than for DNA in the bulk. Second, we have to discuss the prefactor which must be present in the complete formula for the rate. To address these issues we found it useful to reinterpret formula (38) in the following way. Originally we obtained this formula by comparing the DNA free energy in infinity and in the transition state. Let us now consider a kinetic intermediate state which is sketched in Fig. 4(b): it is the state where DNA coil already arrived to the pore mouth and, therefore, already gained energy  $-Q_{\text{eff}}V(R_g)$ , while the DNA end was not yet introduced into the pore. We argue that in the barrier limited regime DNA goes many times between bulk solution and the pore vicinity, and, therefore, this kinetic intermediate state becomes effectively in equilibrium with the bulk. We will discuss this equilibrium in Sec. V D 1. This will require the use of effective charge, which we will address in Secs. V B and V C. There, our main idea is that when DNA is pressed against the membrane wall, the electroosmotic counterflow is stopped (or reduced), thus eliminating (or reducing) the upward hydrodynamic drag. Since it is precisely this hydrodynamic drag that nearly cancels the electric force on DNA in bulk solution, the total force on DNA approaches the electric force on it,  $\sim eNE$ , which is proportional to the full DNA length  $N$ . This strong force keeps DNA for a long time at the pore mouth, enhancing the attempt frequency of overcoming the potential barrier. To understand this, we should first recapitulate in quite some detail the main points of the work Ref. 27.

## B. Careful reconsideration of Long *et al.* theory

Consider once again, but more attentively the argument by Long *et al.*<sup>27</sup> leading to the expression (5) for the stall force. Note that the main predictions of the theory<sup>27</sup> are beautifully confirmed by experiment of Ref. 23. The idea of the present consideration is illustrated in Fig. 5(a).

When we act on DNA with a nonelectric force  $\mathbf{F}$  in the absence of electric field, DNA moves with the speed  $\gamma \mathbf{F}$  (we use here  $\gamma = D/k_B T$  for compactness of writing). Note that it entrains the water inside the coil which also moves with the same speed  $\gamma \mathbf{F}$ . Notice further that we must apply not only force  $\mathbf{F}$  to DNA, but also force  $-\mathbf{F}$  to the (infinitely) remote

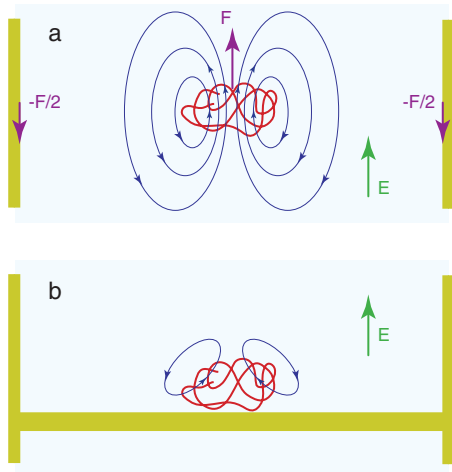


FIG. 5. Illustration of the flow structure in and around stalled DNA coil (a) in bulk solution and (b) at the surface of the membrane. The “fountain” electroosmotic flow is due to the (net) positive ions inside the coil which drive the liquid to enter the coil volume from below and leave it from above. Membrane disrupts a significant fraction of this circulation.

walls of the container—to obey the third Newton’s law; in other words (see also Ref. 21), when we apply force  $\mathbf{F}$  to DNA, we transfer momentum to DNA at the rate  $\mathbf{F}$ , this momentum gets transferred through viscous liquid to far away walls, and there it is transferred back to the source of force  $\mathbf{F}$ , so the momentum is happily conserved. The transfer of momentum over macroscopic distances is realized via long-range hydrodynamic field in which velocity of the fluid decays as  $1/r^2$  such that flow of momentum through the infinitely remote sphere is constant (like in Gauss theorem; see the last part of Sec. 20 on Stokes formula in the book,<sup>37</sup> where velocity field in the far zone is addressed and  $1/r^2$  asymptotics is obtained).

By contrast, when an electric field acts on the system, it provides momentum to DNA at the rate  $-QE$  and collects it back from the nearby counterions. No momentum is transferred to the faraway walls of the container. Water inside the coil does not travel with the coil. Hydrodynamic field decays much faster than  $1/r^2$ .

Consider now the case when both force  $\mathbf{F}$  and electric field  $\mathbf{E}$  are acting simultaneously. We know, Eq. (4), that DNA moves with the speed

$$\mathbf{v} = -\mu\mathbf{E} + \gamma\mathbf{F}. \quad (39)$$

But how is this superposition obtained? The velocity fields for the two separate problems, with force only and with electric field only, are difficult to combine, because they satisfy different boundary conditions. The trick, however, is this. Let us consider the situation from a reference frame which moves with the speed  $\gamma\mathbf{F}$ , i.e., from a frame in which DNA would have been immobile if there was no electric field. In this reference frame, the velocity field is caused by force  $-\mathbf{F}$  applied to the walls at infinity, it is a constant in infinity and zero in the vicinity of DNA. By contrast, the velocity field produced by the electric field force exerted on ions is non-zero in the vicinity of DNA, but it rapidly vanishes in infinity. It is these two fields that can be superimposed. Returning

to the laboratory reference frame yields the familiar formula (39).

The above careful consideration allows us to answer the following question: How does water move inside the coil? It moves with the speed  $\gamma\mathbf{F}$ . Thus, every segment inside the coil moves with the speed  $-\mu\mathbf{E}$  with respect to the nearby water, plus this nearby water moves with the speed  $\gamma\mathbf{F}$  with respect to far away water.

### C. Flow in and around stalled DNA

Let us now implement the above discussion for the special case when the applied force stalls the coil:  $\mathbf{F} = \mathbf{F}_{\text{stall}} = (\mu/\gamma)\mathbf{E}$ . All of the above considerations are applicable. As before, every segment moves with respect to the nearby water with the speed  $-\mu\mathbf{E}$ ; in other words, since DNA is immobile in laboratory frame, water inside the coil moves with the speed  $\mu\mathbf{E}$ . At the same time, water in the far away zone is driven by the force  $-\mathbf{F}$  exerted at infinity. These two flows connect to each other more or less the way sketched in Fig. 5(a).

How is this picture of flow in and around the DNA coil modified when DNA is pressed against the wall, as in Fig. 4? Obviously, the rolls of the solvent flow, as they are shown in Fig. 5(a), are blocked (or at least significantly suppressed) at the wall, roughly as sketched in Fig. 5(b). To suppress them, hydrostatic pressure must build up above the coil. As a result, the momentum transfer between DNA and positive counterions at distance  $r_D$  around the DNA backbone, which is normally realized through the viscous solvent, is now largely suppressed. The conclusion is that DNA is subjected to the full electric field force  $-2\alpha'Ne\mathbf{E}$ , corresponding to effective charge  $Q_{\text{eff}} = 2\alpha'Ne$ . Let us remind that  $\alpha' < 1$  expresses the surface-induced suppression of the electroosmotic flow of solvent through the DNA coil at the pore entrance (in the case of complete suppression,  $\alpha' \approx \alpha \approx 1/2$ , due to the fact that only a fraction  $\alpha$  of phosphate groups contribute to the DNA charge because of the Onsager–Manning condensation).<sup>30</sup> Although in the general case of partial screening of electroosmotic flow,  $\alpha'$  may be a decreasing function of  $N$  (i.e.,  $Q \propto N^\delta$  with  $\delta \leq 1$ ), here we will tentatively treat it as a numerical constant.

This important conclusion can be supported by considering a similar problem with simpler geometry, namely, a planar slab of charged sponge such as a polyelectrolyte gel, placed in conducting salty water, perpendicular to a uniform electric field. The coupling between electric current and hydrodynamic flow in such a system is subject to Onsager reciprocal relations. This was shown in the paper,<sup>28</sup> and the more detailed theory of the corresponding transport coefficients was developed in Ref. 38; to make the present work self-contained, we summarize the main findings of these works in Appendix C. In essence, when the hydrodynamic circuit is broken, hydrostatic pressure builds up and blocks the hydrodynamic momentum transfer from DNA to counterions. Let us now see how we can estimate the DNA capture rate based on these ideas.

## D. Capture rate in the barrier limited regime

According to Kramers theory,<sup>26</sup> the rate of penetration through the barrier equals the frequency of attempts to climb the barrier multiplied by the probability that the attempt is successful. We will apply this idea to the “nucleation” of the transition state, shown in Fig. 4(a), starting from the kinetic intermediate state, depicted in Fig. 4(b). The barrier height for this process is given by formula (37), but what about the attempt frequency? This frequency is given by the probability to find a DNA molecule at the entrance to the pore divided by the characteristic time it takes for a molecule located at this entrance to insert itself into the pore. We proceed to estimate the electric field driven enhancement of the probability to find a DNA molecule at the pore.

### 1. Attempt frequency: Enhancement effect

We assume that the barrier is so high that DNA is delivered many times to the pore mouth, moving back and forth between low potential energy at  $r < r^*$  and high potential energy at  $r > r^*$  regions, before it successfully overcomes the barrier and introduces its tail into the pore. Therefore, there is almost an equilibrium between free DNA coils in far away bulk solution of concentration  $c$  and DNA coils at the pore entrance. In the absence of any external forces, the probability to find the DNA coil in a volume  $R_g^3$  just above the pore entrance is given by  $P_{\text{entrance}}^{(0)} \approx R_g^3 c$ . Since DNA molecules slide down the funnel-shaped potential  $V(r)$  on their way to the pore, the probability of finding a DNA coil at the entrance to the pore must be enhanced compared to its unbiased value. We proceed to estimate this enhancement effect.

Just above the pore, DNA is subjected to the potential  $V(r)$ . As we explained above, the hydrostatic pressure will build-up above the DNA coil and stop the flow of the solvent through the coil. Once the latter is stopped, the motion of positive counterions along the electric field will no longer cause hydrodynamic drag to be exerted on DNA. The consequence is that now DNA starts feeling the full force of the electric field and its relevant energy becomes about  $Q_{\text{eff}}V(R_g)$ , where the effective charge of DNA is  $Q_{\text{eff}} = 2\alpha'Ne$ . As the consequence, we argue that the above mentioned probability enhancement effect must be determined by the Boltzmann exponent with relevant energy being  $2\alpha'NeV(R_g)$  and, therefore, the probability to find a DNA coil at the entrance to the core is given by

$$P_{\text{entrance}}^{(0)} \approx R_g^3 c \exp[2\alpha' eNV(R_g)/k_B T]. \quad (40)$$

### 2. Attempt frequency: End motion

What else is there in the attempt rate? The remaining factor can be thought of in the following way. Suppose DNA sits at the pore mouth, as in Fig. 4, and fluctuates, but we do not allow it to depart from this location. The question is: what is the time,  $\tau$ , before a chain end comes within distance about  $d$  from the pore? In fact, the quantity of interest is the mean first passage time of the chain end to the pore, and if this time is  $\tau$ , then  $\tau^{-1}$  is the relevant attempt rate. Collecting the contributions to the capture rate in the barrier limited regime together, this yields the expression (42) below.

Before we get there, let us speculate about  $\tau$ . The most naive estimate of  $\tau$  would be the Zimm time, the relaxation time of the whole coil, proportional to  $N^{3/2}$ .<sup>39</sup> While that would be the correct estimate in the absence of electric field  $V(r)$ , we may expect that the end is electrophoretically driven to the pore by the electric field faster than diffusion. Here we provide a simple estimate of it; somewhat to our own surprise, we find that this process still has the same Zimm time.

Suppose that the end segment of length  $x$  and charge  $ex/a$  is driven by the gradient of potential  $V$ . We assume that electroosmotic flow is suppressed even on these scales inside the coil, so the balance of forces acts between electric field force  $(ex/a)q_{\text{eff}}/\epsilon r^2$ , where  $q_{\text{eff}}/\epsilon r^2$  is the electric field at the distance  $r$  from the pore, and viscous drag  $\sim x\eta(r/\tau)$ , where  $r/\tau$  is the speed of motion covering distance  $r$  in time  $\tau$ . Here we neglect the elastic response of the rest of the coil to the driven motion of the end (such response can only slow down the process). Balancing the above forces, we find  $\tau \sim (\eta a \epsilon / e q_{\text{eff}}) r^3$ . We assume that initially  $r \sim R_g$  and arrive at

$$\tau \sim \frac{\eta a \epsilon}{e q_{\text{eff}}} R_g^3 \sim \tau_{\text{Zimm}} \frac{a k_B T \epsilon}{e q_{\text{eff}}} = \tau_{\text{Zimm}} \frac{k_B T}{e \Delta V} \frac{8 l a}{d^2}. \quad (41)$$

Clearly, the above expression is valid only for sufficiently large  $\Delta V$ , because it estimates the effect of the electric field that drives the DNA end into the pore. If the electric field is small, the introduction of chain end into the pore occurs via pure unbiased diffusion, yielding  $\tau \sim \tau_{\text{Zimm}}$ . Inserting typical experimental values of the parameters<sup>22</sup> we find that the electric field speeds up the rate at which the end is inserted into the pore,  $\tau < \tau_{\text{Zimm}}$ . Notice, however, that both  $\tau$  and  $\tau_{\text{Zimm}}$  scale similarly with molecular weight (as  $R_g^3 \propto N^{3/2}$ ).

### 3. Rate of capture

We can conclude from the previous two sections that the capture rate (per unit DNA concentration) is given by

$$R_c^{\text{bar}} = \frac{R_g^3}{\tau} \exp \left[ -\frac{U}{k_B T} + \frac{q \Delta V}{k_B T} + \frac{2\alpha' eNV(R_g)}{k_B T} \right], \quad (42)$$

where, as we mentioned above,  $q$  is an effective charge of order  $e$ . Comparing this with formula (38), we see that the prefactor [missing in formula (38)] is proportional to  $R_g^3/\tau$ . Let us emphasize that the above formula is valid provided that  $R_c^{\text{bar}} < R_c^{\text{diff}}$ . Knowing  $V(r)$ , we can rewrite it

$$R_c^{\text{bar}} = \frac{R_g^3}{\tau} \exp \left[ -\frac{U}{k_B T} + \frac{q \Delta V}{k_B T} + \frac{e \Delta V \sqrt{3} \alpha' d^2}{k_B T 2al} A \right], \quad (43)$$

where  $A$  arises from the expression for gyration radius of wormlike chain;<sup>40</sup> it is defined by formula

$$A = 1/\sqrt{\frac{4}{y} - \frac{12}{y^2} + \frac{24}{y^3} - \frac{24}{y^4}(1 - e^{-y})} \\ \approx \begin{cases} 1 & \text{when } N < 4N_p \\ \sqrt{N/4N_p} & \text{when } N > 4N_p, \end{cases} \quad (44)$$

where  $y = L/\ell_p = N/N_p$ , with  $N$  and  $N_p$  being the total number of base pairs and the number of base pairs per persistence length, respectively ( $N_p \approx 150$ ).

The above expression was fitted to the experimental data<sup>22</sup> confirming the predicted  $N^{1/2}$  dependence of the exponent [Eq. (43)] in the barrier limited regime. The predicted exponential dependence of the capture rate on  $\Delta V$  was also confirmed for molecular weights below  $10^4$  bp. The agreement with experiment should be taken with some care since only limited data are available at present (the molecular weight dependence was established only for  $\Delta V=0.3$  V and the voltage dependence in this regime was reported only for  $N=400$  and  $3500$  bp). Furthermore, the fit yields  $\alpha'=0.05$  which is an order of magnitude smaller than expected for complete blockage of electroosmotic flow through the DNA coil at the pore.

At present we do not have a definite explanation of this rather small value of parameter  $\alpha'$ . One contributing factor is that when DNA inputs its end into the channel to form a transition state, it reduces the electric current flowing through the pore and, therefore, suppresses the electric potential  $V(r)$ . Under the conditions of experiment,<sup>22</sup> the current is reduced by a factor about 2, which certainly reduces the discrepancy between the expected and fitted values of  $\alpha'$ , although does not eliminate it completely.

Nevertheless, despite the difficulty in understanding the numerical value of  $\alpha'$  as a fitting parameter, we would like to emphasize that our theory successfully predicts that there is a  $N$ -independent capture rate in the large  $N$  region, where rate is linear in  $\Delta V$ ; it also successfully predicts the sharp increase of the capture rate with  $N$  at smaller  $N$ , where this rate grows much faster than linear with  $\Delta V$ . All these highly non-trivial predictions are born out in the data.<sup>22</sup>

### E. Cross-over between diffusion limited and barrier limited regimes

Among the testable predictions of the present theory we concentrate here on the conditions at which diffusion and barrier limited regimes cross-over into one another. In general, the process is controlled by the slowest stage; for instance, it is limited by diffusion if  $R_c^{\text{bar}} > R_c^{\text{dif}}$ . Collecting together our results, Eq. (10) for  $R_c^{\text{dif}}$  and Eq. (43) for  $R_c^{\text{bar}}$ , and plugging in our estimates of  $R_g^3/\tau$  [Eq. (41)] and for  $\mu$  [Eq. (B1)], we arrive upon some algebra at the following condition of diffusion dominance:

$$\frac{e\Delta V}{k_B T} < \frac{\ln\left[4\alpha\frac{r_D}{b}\right] + \frac{U}{k_B T}}{\frac{q}{e} + \frac{\sqrt{3}\alpha'd^2}{2al}A}. \quad (45)$$

Obviously, the barrier dominates if the opposite inequality holds, while the equal sign in the above expression yields the cross-over condition, in this case presented as a line on the plane of two experimentally tunable parameters,  $N$  and  $\Delta V$ . Since  $A$  is a simple function of  $N$  [Eq. (44)], Eq. (45) gives the crossover condition in an explicit form. To emphasize its structure, it is useful to rewrite it as

$$\frac{e\Delta V}{k_B T} < \frac{B}{Z + \sqrt{N}}, \quad (46)$$

where  $Z$  and  $B$  are constants which can depend on temperature and ionic strength, but do not depend on  $\Delta V$  and on  $N$ .

The only point on the cross-over line known from experiment,<sup>22</sup> which is  $N=10^4$  at  $\Delta V=300$  mV, agrees quite reasonably with the prediction (45). Further experimentation will be necessary to test the entire curve.

## VI. CONCLUSION AND DISCUSSION

In this paper we discussed the process of capture of DNA (or other polyelectrolytes) by a nanopore. We showed that ionic currents generate a nonuniform electric field which funnels DNA into the pore and that the interaction of the macromolecule with this field is affected by counterion driven electroosmotic flow through the DNA coil. We demonstrated that this complex nonequilibrium process can be described in terms of the equilibriumlike concept of potential of stall force. Using this concept we calculated the nonuniform spatial concentration profile of DNA and the radius of capture at which diffusion turns into electrophoresis of DNA and showed the results are identical to those obtained by brute force solution of the generalized Smoluchowski equation. We then calculated the capture rate in the high molecular weight, diffusion limited regime; the predicted linear dependence on the applied voltage and the prediction that this rate does not depend on molecular weight of DNA are in complete agreement with both the results of other investigators<sup>24,41</sup> and with experimental data.<sup>22</sup>

While our understanding of the physical mechanism of DNA capture by a nanopore in the diffusion controlled regime appears to be quite satisfactory, our understanding of the physics of capture in the barrier controlled regime is much more tentative. It is based on the idea that when the DNA coil approaches the pore, the electroosmotic flow through the coil is blocked by the presence of the wall surrounding the nanopore. This blockage reduces the hydrodynamic drag on DNA, thus suppressing the hydrodynamic coupling between the DNA backbone and the surrounding counterions (the direct electrostatic coupling is suppressed by screening, due to high concentration of salt). As the result, DNA experiences the full force of the electric field, i.e., the force on the DNA is proportional to its total charge. While the qualitative predictions of the above mechanism, namely, that the capture rate in the barrier controlled regime increases exponentially with both applied voltage and with some power of molecular weight, concur with experiment,<sup>22</sup> the data are too limited to allow for quantitative comparison. More experiments and more elaborate theoretical modeling are clearly necessary in order to assess the degree of screening of electroosmotic flow and to complete the physical picture of the barrier limited regime.

## ACKNOWLEDGMENTS

The authors gratefully acknowledge collaboration with Amit Meller who introduced us to the problem of DNA capture by nanopores and provided invaluable experimental

feedback to our theoretical thinking. We are also grateful to Boris Shklovskii, Paul Chaikin, and Eric Siggia for useful constructive criticisms. We acknowledge useful exchange with Meni Wanunu. We thank M. Muthukumar for sharing with us his work<sup>41</sup> prior to its publication. A.Y.G. acknowledges the hospitality of the Aspen Center for Physics, where part of this work was performed. The work of Y.R. was supported by grants from the Israel Science Foundation and the Israel-France Research Networks Program in Biophysics and Physical Biology, and by the Materials Research Science and Engineering Center program of the National Science Foundation Grant No. DMR-0520513 at Northwestern University.

## APPENDIX A: ELECTRIC POTENTIAL $V(r)$ AWAY FROM THE PORE

Consider first an auxiliary problem. Suppose that steady electric current flows to infinity from a spherical electrode of diameter  $d$  sitting at the origin. Conductivity of the medium is  $\sigma$  and the applied voltage is  $\delta V$ . What is the potential  $V(r)$  at distance  $r$  from the origin? The problem is obviously spherically symmetric; therefore, if we consider a spherical layer between  $r$  and  $r+dr$ , the voltage drop across this layer, according to Ohm's law, is  $dV = -I dr / (4\pi r^2 \sigma)$ , where  $dr$  plays the role of the length of a conductor,  $4\pi r^2$  is its cross-sectional area, and, therefore,  $dr / (4\pi r^2 \sigma)$  is the resistance. Thus, we have

$$\frac{dV}{dr} = -\frac{I}{4\pi\sigma r^2}. \quad (\text{A1})$$

Since total current  $I$ , of course, does not depend on  $r$ , the solution of this equation reads

$$V(r) = \frac{I}{4\pi\sigma r} + V_\infty. \quad (\text{A2})$$

It varies as  $1/r$  in accord with the point charge analogy. Since we also know the voltage  $\delta V$  applied between infinity and the electrode at  $r=d/2$ , we have  $\delta V = I / (2\pi\sigma d)$ , from which we find current  $I$ . Finally, setting potential at infinity to be zero, the potential  $V(r)$  reads

$$V(r) = \frac{d}{2r} \delta V. \quad (\text{A3})$$

Our situation is slightly different, in the sense that the current from our "small electrode," the pore mouth, flows only into half-space, but Eq. (A3) remains valid without modifications. At the same time, the expression for the total current in terms of  $\delta V$  must be halved,

$$I = \pi\sigma d \delta V. \quad (\text{A4})$$

Now, we have to find  $\delta V$ , that is, the potential drop between the infinity on the *cis* side and the entrance of the channel. Given the overall symmetry of the situation, we expect also the same potential drop  $\delta V$  on the *trans* side between pore exit and the other infinity. Therefore, given the total applied voltage  $\Delta V$ , we expect voltage drop across the pore itself to be  $\Delta V - 2\delta V$ . The resistance of a pore of length  $l$  and diameter  $d$  is  $4l / (\pi d^2 \sigma)$ ; therefore, the current (A4) must be equal to

$$I = \frac{\Delta V - 2\delta V}{4l} \pi\sigma d^2. \quad (\text{A5})$$

Simple algebra then yields

$$\delta V = \Delta V \frac{d/4l}{1 + d/2l} \approx \frac{d}{4l} \Delta V. \quad (\text{A6})$$

As expected,  $\delta V$  is significantly smaller than the total applied voltage  $\Delta V$ , because the channel is long and narrow (in the experiment of Ref. 22,  $d \approx 3.5$  nm and  $l \approx 20$  nm, so  $d/4l \approx 0.04$ ). Thus, finally the electric potential outside the pore is given by formula (1) in the main text.

## APPENDIX B: NUMERICAL VALUE OF DNA ELECTROPHORETIC MOBILITY

Figure 9 in Ref. 23 presents the measurement data of electrophoretic mobility of DNA, and the answer is  $\mu \approx 4.2 \times 10^{-4}$  cm<sup>2</sup>/V s. The question is: can we reproduce this figure theoretically, at least in order of magnitude?

Here is the estimate. We consider DNA of length  $L$ . DNA has  $N = L/a$  base pairs ( $a \approx 0.34$  nm) and charge  $2aeL/a$ ; here,  $\alpha < 1$  is a numerical coefficient which reflects the fact that not all of the  $2N$  phosphate groups are ionized, since some of the counterions are Onsager–Manning condensed<sup>30</sup> and they do not contribute to the electrophoretic mobility. In electric field  $\mathbf{E}$  a rodlike object with the said amount of charge experiences the force  $(2aeL/a)\mathbf{E}$  which must be balanced by the drag. We estimate the drag as  $(\eta A/r_D)\mathbf{v}$  for a rod of surface area  $A$ , moving with velocity  $\mathbf{v}$  through the liquid of viscosity  $\eta$ , and assuming Debye screening length  $r_D$ . Here,  $r_D$  appears because when motion is caused by the electric field, the velocity gradient develops only on the length scale  $r_D$  from the surface of the double helix, and no viscous drag is exerted beyond  $r_D$ , since the system is neutral over the distance  $r_D$  or larger. These equations together mean  $(2aeL/a)\mathbf{E} = (\eta A/r_D)\mathbf{v}$ , or

$$\mu = \frac{2\alpha e}{\eta} \frac{r_D}{\pi ab}, \quad (\text{B1})$$

where  $A = \pi Lb$  for the cylinder of diameter  $b$ .

The same estimate can be derived in terms of the so-called  $\zeta$ -potential, using Smoluchowski theory<sup>42</sup> (another theory by the same Smoluchowski). It says that the electrophoretic mobility is given by

$$\mu = \frac{\epsilon \zeta}{4\pi \eta}, \quad (\text{B2})$$

where  $\zeta$  is the electric potential on a somewhat vaguely defined "slip" surface around the particle and  $\epsilon$  is the dielectric constant of the medium. We know only one way to justify this result, and this one works if and only if the ion surface is parallel to the electric field. This is possible for either planar or cylindrical ion parallel to the field. In this case velocity of the fluid has only the component parallel to the surface and parallel to the electric field. The Navier–Stokes equation for this component then reads

$$\eta \Delta v(z) = E \rho(z), \quad (\text{B3})$$

Where the right hand side is the volume force acting on the liquid with charge density  $\rho$  and  $z$  is the coordinate perpendicular to the plane. And of course the electrostatic potential satisfies

$$\Delta \phi(z) = -\frac{4\pi}{\epsilon} \rho(z). \quad (\text{B4})$$

Since “similar equations have similar solutions,”<sup>43</sup> we get

$$v(z) = \phi(z) \frac{\epsilon}{4\pi\eta} E, \quad (\text{B5})$$

which directly yields the Smoluchowski formula (B2). For reasons somewhat mysterious to us, this formula is believed to work for virtually any geometry of the ion. Moreover, if the charge density on the ion is not too strong, the  $\zeta$ -potential can be found as the potential of a charged planar surface submerged in a medium of Debye screening length  $r_D$ . This potential is equal to  $4\pi\sigma r_D/\epsilon$ , where  $\sigma$  is the surface charge density. Thus, in this approximation Smoluchowski formula yields  $\mu = \sigma r_D/\eta$ . Given that for cylindrical DNA  $\sigma = 2ae/\pi ab$ , we return exactly to the above estimate (B1).

Let us now estimate the numbers. One elementary charge is equal to

$$e = \frac{1 \text{ eV}}{V} = \frac{11 \ 600 \text{ K}}{V} = 1.6 \times 10^{-19} \frac{\text{J}}{V} = 0.16 \frac{\text{kg nm}^2}{V \text{ s}^2}. \quad (\text{B6})$$

We use  $\eta = 10^{-3} \text{ kg/m s} = 10^{-12} \text{ kg/nm s}$ . We also use  $\alpha = 0.5$ ,  $r_D = 0.3 \text{ nm}$ ,  $b = 2 \text{ nm}$ , and  $a = 0.34 \text{ nm}$ . The result is then

$$\mu \approx 2.2 \times 10^{10} \text{ nm}^2/\text{V s} = 2.2 \times 10^{-4} \text{ cm}^2/\text{V s}. \quad (\text{B7})$$

The unexpected agreement with the above mentioned measured data of Ref. 23 is probably coincidental. But it is quite reasonable that our estimate for  $\mu$  is smaller than the experimental result,<sup>23</sup> because the experiment was run at the ionic strength of 0.1 mM, corresponding to  $r_D \approx 1 \text{ nm}$ , about a factor of 3 greater than assumed in our estimate.

### APPENDIX C: CURRENT THROUGH GEL

Here we review the main points of the work.<sup>28</sup> Consider for simplicity a one-dimensional version of the problem. Suppose that the gel has the form of a planar slab sitting across the entire cross-section of a pipe filled with salty water. A cartoon of the experiment is shown in Fig. 6.

Let us start treating the problem phenomenologically, within linear response theory, considering the currents of electric charge  $J_Q$  and mass  $J_M$  driven by the voltage drop  $\Delta U$  and pressure drop  $\Delta p$  across the gel slab, respectively. According to Ref. 29, the prescription is as follows: we have to write down the dissipation (rate of entropy production) over the entire volume of the gel,

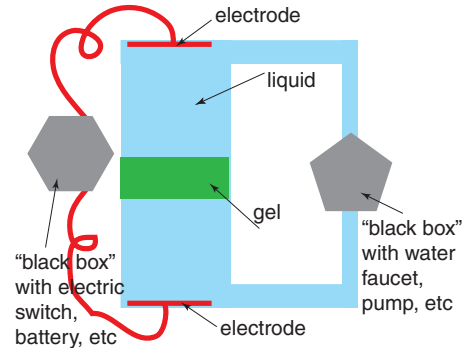


FIG. 6. A scheme of experiment in which electric current flows through a charged gel and simultaneously liquid can also flow through the gel. There might be driving source (e.g., a battery) in the electric circuit, and there might be also a pump of some sort in hydraulic circuit (both are shown as black boxes). Each of the circuits can also be either closed or broken, e.g., this can be achieved by the corresponding faucets and switches (or circuit breakers), also possible in the black boxes.

$$T\dot{S} = J_Q \Delta U + J_M \frac{\Delta p}{\rho}, \quad (\text{C1})$$

where  $\rho$  is the density of liquid, and, therefore,  $J_M/\rho$  is the “current of volume,” and from here we should “read out” the pairs of conjugate currents and thermodynamic forces. Thus, we see that  $\Delta p/\rho$  is the thermodynamic force conjugated to the current  $J_M$ , while of course  $\Delta U$  is conjugated to  $J_Q$ . Therefore, the phenomenological linear relations between currents and forces have to be written as follows:

$$J_Q = \frac{1}{R} \Delta U + \Gamma \frac{\Delta p}{\rho}, \quad (\text{C2})$$

$$J_M = \Gamma \Delta U + \frac{1}{\Xi} \Delta p, \quad (\text{C3})$$

where  $R$ ,  $\Xi$ , and  $\Gamma$  are transport coefficients;  $\Gamma$  is the same in both equations because of Onsager reciprocity relations.

Second law of thermodynamics dictates that dissipation (C1) be positive-definite for every choice of forces. This means that kinetic coefficients must satisfy

$$R > 0, \quad \Xi > 0, \quad \text{and} \quad \frac{\Gamma^2 R \Xi}{\rho} < 1. \quad (\text{C4})$$

The specific values of kinetic coefficients were computed, in some approximation, in Ref. 38. Note that in the absence of hydraulic driving, at  $\Delta p = 0$ , Eq. (C2) represents nothing more than Ohm’s law, while in the absence of electric driving, at  $\Delta U = 0$ , formula (C3) represents Darcy’s law.

Equations (C2) and (C3) must be complemented with some description of what happens outside the gel. For instance, suppose that electric circuit outside the gel is closed with resistance  $r$  and electromotive force  $W_Q$ . Then, Ohm’s law for the outside part of the electric circuit reads

$$W_Q - \Delta U = J_Q r. \quad (\text{C5})$$

Similarly, for the outside part of the hydraulic circuit we have

$$W_M - \Delta p = J_M \xi, \quad (\text{C6})$$

where  $W_M$  is the analog of electromotive force which represents a possible hydraulic pump in the system, while  $\xi$  is the hydraulic resistance of the outside contour.

In general, Eqs. (C2)–(C6) together determine self-consistently both  $\Delta U$  and  $\Delta p$  as well as the currents  $J_Q$  and  $J_M$  in terms of the driving forces  $W_Q$  and  $W_M$  and kinetic coefficients.

Let us consider an example. In our original system we assumed that the hydraulic circuit is not closed, which means  $W_M=0$  and  $\xi=\infty$ . As one should have expected, for this case formula (C6) gives  $J_M=0$ : mass does not flow anywhere, for the pipe is closed. Then, formula (C3) gives

$$\Delta p = -\Gamma \Xi \Delta U, \quad (\text{C7})$$

plugged in Eq. (C2), this yields

$$J_Q = \frac{\Delta U}{R_{\text{eff}}}, \quad (\text{C8})$$

or, using Eq. (C5),

$$J_Q = \frac{\Delta U}{R_{\text{eff}}} = \frac{W_Q}{R_{\text{eff}} + r} \quad (\text{C9})$$

and

$$\Delta U = \frac{R_{\text{eff}}}{R_{\text{eff}} + r} W_Q. \quad (\text{C10})$$

This of course looks like regular Ohm's law, with the effective resistance

$$R_{\text{eff}} = \frac{R}{1 - \frac{\Gamma^2 R \Xi}{\rho}} \geq R. \quad (\text{C11})$$

According to formula (C4), the effective resistance is certainly positive and larger than the resistance itself. That means, the effect of coupling between electric and hydraulic currents can, in principle, reduce the electric current, but cannot enhance and cannot reverse it. Let us remind that these results are valid for the system with hydraulics circuit broken, with no flow of liquid.

For the purposes of our main discussion, the most important result is Eq. (C7): if there is no possibility of the hydraulic current, then the hydrostatic pressure builds up proportional to the applied voltage. That means exactly that the system does not experience hydrodynamic drag and, therefore, is subjected to the full force of the electric field acting on the immobile gel only, without regard for the counterions.

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