PHYSICAL REVIEW E **74**, 041801 (2006)

Electrostatic effects in DNA stretching

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(Received 12 August 2004; revised manuscript received 27 May 2006; published 2 October 2006)

The response of a semiflexible polyelectrolyte chain to stretching in the regimes of moderate and weak screening is studied theoretically, with a special focus on DNA experiments. By using the nonlinear Poisson-Boltzmann description of electrostatic self-interactions of the chain, we explicitly demonstrate the applicability of the concept of effective charge to certain aspects of the problem. This charge can be extracted from the far-field asymptotic behavior of the electrostatic potential of the fully aligned chain. Surprisingly, in terms of the effective charge, the electrostatically renormalized persistence length can be formally described by the classical Odijk-Skolnick-Fixman formula, whose domain of applicability is normally limited to the linearized Debye-Hückel (DH) approximation. However, the short-scale behavior of the chain in the nonlinear regime deviates from the of DH-based result, even upon charge renormalization. This difference is revealed in the calculated stretching curves for strongly charged DNA. These results are in good agreement with recent experiments. In the limit of weak screening we predict the elastic response to have a distinctive two-stage character, with a peculiar intermediate "unstretchable" regime.

DOI: 10.1103/PhysRevE.74.041801 PACS number(s): 82.35.Rs, 82.37.Rs, 82.39.Pj

I. INTRODUCTION

Single-molecular micromechanical experiments are among the major tools of modern biophysics. Pioneered by studies of double-stranded DNA (dsDNA) [1], these techniques are now applied to a wide range of biologically relevant problems [2–4]. Theoretically, it has been demonstrated that the observed response of dsDNA to stretching (i.e., elongation vs pulling force) can be successfully described by the semiflexible wormlike chain (WLC) model [5,6], over a considerable range of applied forces. Within this model, the molecule is viewed as a rigid rod subjected to thermal fluctuations, and the only free parameter is its persistence length l_p which is proportional to the bending modulus of the rod.

Since DNA is strongly charged, the effects of the electrostatic interactions should in principle play a significant role in its elastic response. However, they are typically suppressed due to the strong screening under physiological conditions. In addition, it is implicitly assumed that the electrostatic effects can be incorporated by renormalization of the parameters of the effective models, e.g., the persistence length l_p in the WLC. This is indeed a valid assumption in certain regimes, as was shown in the work of Odijk and of Skolnick and Fixman (OSF) [7]. They have demonstrated that within the linearized Debye-Hückel (DH) approximation, there is an additive electrostatic correction to the persistence length of a semiflexible WLC, and this term scales quadratically with Debye screening length r_s. However, the classical result has to be significantly revised in the regime of highly flexible chains, which was in focus of numerous studies over the last two decades [8–11].

Another limitation of the OSF picture is that it is valid only on length scales larger than r_s. When the chain is strongly stretched, its properties on shorter scales are being probed. Within DH theory, this regime can be described in terms of *scale-dependent* electrostatic rigidity [12,6]. Finally, the OSF result is known to be inadequate outside the DH approximation, i.e., in the strongly nonlinear regime. Compared to other aspects of the problem, its nonlinear generalization has attracted only limited attention since the early work in the 1980s [13,14]. In this paper, we study electrostatic effects on the elastic response of a strongly charged WLC, in the regimes of moderate and weak screening. In these regimes, the DH approximation may no longer be applicable, and analysis of the nonlinear Poisson-Boltzmann equation is necessary. While stated as a generic problem, our study is especially important in the context of DNA stretching experiments.

The plan of the paper is as follows. In Sec. II, we formulate the problem and review the results obtained within DH theory. We reconsider the problem of scale-dependent rigidity, and demonstrate that, in the limit of weak screening, the chain exhibits a two-stage response. These two stages are characterized by the renormalized and bare persistence lengths, respectively, and they are separated by a peculiar "unstretchable" regime. In Sec. III, we study the problem beyond the linearized DH approximation. Our central result is that the effective rigidity in the nonlinear regime can be described by the classical OSF formula, in terms of the effective linear charge density determined by the far-field asymptotic of the chain's electrostatic potential. This is an explicit demonstration of the applicability of the concept of renormalized charge in the context of the nonlinear problem. While the notion of the effective charge is not new, in the past it was introduced in a purely heuristic manner. As follows from our results, the effective charge approach has significant limitations and it is not valid on a length scale comparable to r_s. As a result, the extension curve for strongly charged chains is different from the result of linearized DH theory, even upon the charge renormalization. Finally, in Sec. IV we discuss applications of the theory to both ds- and

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single stranded (ss)DNA, and compare our results to the existing experiments.

II. RESULTS OF LINEARIZED THEORY

In the presence of monovalent ions of concentration n, the electrostatic potential in water is well described by the Poisson-Boltzmann (PB) equation

$$\Delta\Psi(\mathbf{x}) - r_s^{-2}\sinh\Psi(\mathbf{x}) = -4\pi l_B \frac{\rho(\mathbf{x})}{e}. \tag{1}$$

Here, the reduced potential Ψ is expressed in units of kTD/e; D is the dielectric constant of water, $l_B = e^2/DkT \approx 7$ Å is the Bjerrum length, and $r_s = 1/\sqrt{4\pi l_B n}$ is the Debye screening length. For low values of Ψ, the above nonlinear equation can be linearized, which corresponds to the well-known DH approximation. In particular, one can obtain a Yukawa-type pair potential acting between two point charges e:

$$\frac{V(r)}{kT} = \frac{l_B}{r}\exp(-r/r_s). \tag{2}$$

The effective Hamiltonian of an electrostatically neutral WLC stretched by an external mechanical force is given by [6]

$$H_0 = \int_0^L \left[\frac{kTl_p}{2}\left(\frac{\partial^2\mathbf{x}}{\partial s^2}\right)^2 - \mathbf{f}\frac{\partial\mathbf{x}}{\partial s}\right]ds. \tag{3}$$

Here $\mathbf{f}$ is the stretching force applied at $s=L$. The function $\mathbf{x}(s)$ determines the chain conformation in space, and it is subjected to the constraint $|\partial\mathbf{x}/\partial s| = 1$ (i.e., the chain is not extendable). Within the DH approximation, the electrostatic self-interactions of a uniformly charged chain give rise to the following new term in the Hamiltonian:

$$H_{el} = \frac{e^2\alpha^2}{2Dl_B^2}\int_0^L\int_0^L \frac{\exp[-|\mathbf{x}(s)-\mathbf{x}(s')|/r_s]}{|\mathbf{x}(s)-\mathbf{x}(s')|}ds\,ds'. \tag{4}$$

Here $\alpha e/l_B$ is the linear charge density of the chain. The Manning parameter α has the physical meaning of the number of electron charges per Bjerrum length.

According to OSF theory [7] developed within the DH approximation, the electrostatic interactions lead to a higher effective bending modulus of a semirigid chain. This results in renormalization of its persistence length:

$$l_p^* = l_p + \alpha^2 r_s^2/4l_B. \tag{5}$$

For the case of flexible chains, OSF approach has been revised by Khokhlov and Khachaturian, who introduced the concept of electrostatic blobs [8]. On length scales smaller than the blob size, $\xi_e = (l_p^2 l_B/\alpha^2)^{1/3}$, the electrostatic effects may be neglected. On larger scales, a flexible polyelectrolyte can be viewed as a stretched chain of blobs, and the OSF picture can be recovered upon proper renormalization of its parameters. For a semiflexible chain, we can introduce a characteristic length which would play the same role as the size of the electrostatic blobs ξ_e in the flexible case: $l_e = DkT/(e\tau)^2 = l_B/\alpha^2$. This length defines the minimal scale at which electrostatic effects become relevant, and the semiflexible regime itself is determined by the condition $l_e \lesssim l_p$.

When the chain is strongly stretched, one may keep only terms quadratic in the transverse components of displacement, $\mathbf{u}_s = \mathbf{x}(s) - \mathbf{f}(\mathbf{f}\cdot\mathbf{x}(s))/\mathbf{f}^2$. After going to the Fourier representation, $\mathbf{u}_s = L^{-1/2}\Sigma_q \mathbf{u}_q \exp(iqs)$, the overall effective Hamiltonian $H \equiv H_0 + H_{el}$ can be written as

$$\frac{H[\mathbf{u}_q]}{kT} = \text{const} + \sum_q \frac{q^2\mathbf{u}_q\cdot\mathbf{u}_{-q}}{2}\left(l_p q^2 + \Lambda_{el}(q) + \frac{f}{kT}\right). \tag{6}$$

Here, all the electrostatic effects are collected within the term $\Lambda_{el}(q)$, which has the physical meaning of the scale-dependent electrostatic tension:

$$\Lambda_{el}(q) = \frac{\alpha^2}{2l_B}\left[\left(1 + \frac{1}{q^2 r_s^2}\right)\ln\left(1 + q^2 r_s^2\right) - 1\right]. \tag{7}$$

This electrostatic term was originally introduced by Barrat and Joanny [12], and later adapted to the case of dsDNA in the classical paper of Marko and Siggia [6]. By using the equipartition theorem, they calculated the difference between the end-to-end distance R and the length of the fully stretched chain, L:

$$\frac{L-R}{L} = -\frac{\langle\dot{\mathbf{u}}^2\rangle}{2} = \int_{-\infty}^{+\infty}\frac{1}{l_p q^2 + \Lambda_{el}(q) + f/kT}\frac{dq}{2\pi}. \tag{8}$$

The calculated stretching curves are shown in Fig. 1. Interesting observations can be made by further analysis of the above result in the limit of weak enough screening, $r_s \gg l_e \equiv \alpha^{-2}l_B$. In this case, the overall mechanical response has a striking *two-stage* character. For large forces, $f \gg kT/4l_e$ we recover the well-known result for a neutral WLC [6]

$$\frac{L-R}{L} \simeq \int_{-\infty}^{+\infty}\left(l_p q^2 + \frac{f}{kT}\right)^{-1}\frac{dq}{2\pi} = \frac{1}{2}\sqrt{\frac{kT}{fl_p}}. \tag{9}$$

In addition, one can identify a moderate-force regime $kTl_e/4r_s^2 \lesssim f \ll kT/4l_e$. In this case, Eq. (8) has two distinct contributions which correspond to the integration over wave numbers q much smaller and much larger than r_s^{-1}, respectively:

$$\frac{L-R}{L} \simeq \frac{1}{2}\sqrt{\frac{kT}{f(l_p + \alpha^2 r_s^2/4l_B)}} + \frac{1}{\alpha}\sqrt{\frac{l_B}{l_p}}\,g\left(\frac{\alpha r_s}{\sqrt{l_B l_p}}\right). \tag{10}$$

The first term here is similar to the interaction-free elastic response Eq. (9), with the renormalized persistence length $l_p^* = l_p + \alpha^2 r_s^2/4l_B$. This is consistent with the OSF result Eq. (5). The second term is independent of force, and it indicates that stretching virtually stops when $kTl_e/4r_s^2 \ll f \ll kT/4l_e$, while $(L-R)/L$ remains finite due to fluctuations on the scales smaller than r_s. We conclude that both the effective bending rigidity and the total chain length should be renormalized due to electrostatic interactions. In other words, the chain becomes nearly unstretchable when the end-to-end distance reaches a certain value $R^* < L$ (as shown in Fig. 1). Electrostatic effects are relevant only if $\alpha r_s \gtrsim \sqrt{l_B l_p}$. When this condition holds, the function g in Eq. (10) has only weak (inverse-logarithmic) dependence on the screening length:

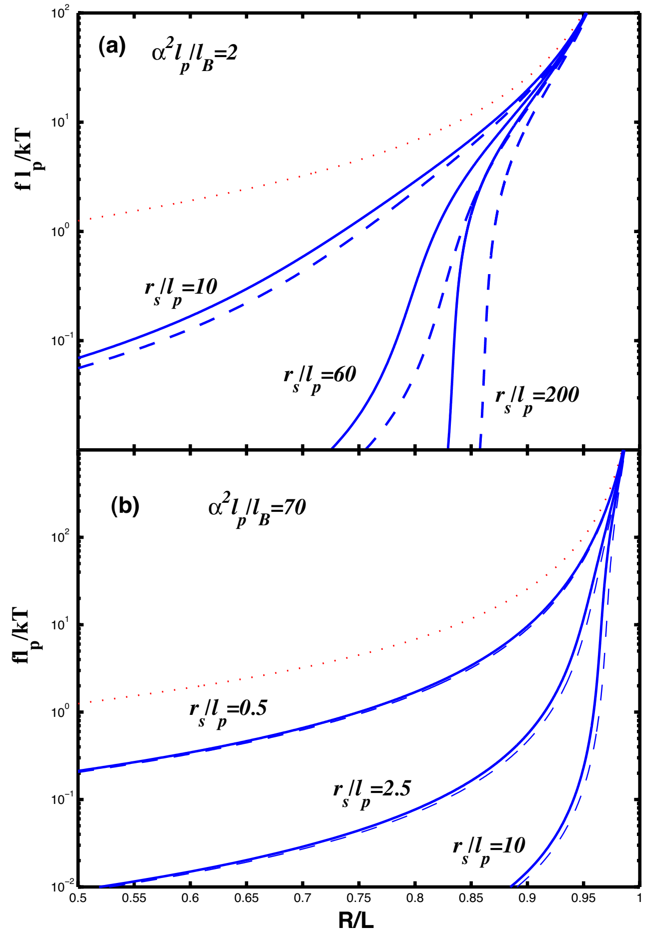

FIG. 1. (Color online) Stretching curves calculated for semiflexible polyelectrolytes at various conditions. The solid lines are obtained within the linearized DH approximation, while the dashed lines correspond to the complete nonlinear PB description of the electrostatics. The stretching curve of a neutral chain is shown with a dotted line.

$$\frac{L-R^*}{L} \simeq \frac{1}{2\alpha \ln(\alpha r_s/\sqrt{l_B l_p})}\sqrt{\frac{l_B}{l_p}}. \tag{11}$$

The chain remains unstretchable until the force becomes strong enough to suppress the small-scale fluctuations ($f \sim kTl_p/r_s^2$). After that, the crossover to the large-force regime (9), occurs.

III. NONLINEAR THEORY AND EFFECTIVE CHARGE

Strictly speaking, the linearization of Eq. (1) is possible only for weakly charged chains or very strong screening. In a more general case, one has to study the complete nonlinear equation. In order to apply our results for the case of strongly charged polymers like ds- or ssDNA, one has to go beyond the linearized DH approximation. Early attempts at such a generalization go back to the early 1980s [13,14]. At that time, it was shown by numerical studies that the effective rigidity clearly deviates from that of the linear OSF theory. However, no alternative model was proposed.

Various aspects of the PB equation in cylindrical geometry have been studied for several decades. Among other important advances was the discovery of counterion condensation by Manning [17]. It was shown that when the linear charge density on a thin rod exceeds a certain critical value, a finite fraction of the counterions gets localized within a near region of the rod, thus effectively reducing its overall charge. This phenomenon occurs at the critical Manning parameter $\alpha_c \simeq 1$. Upon condensation, the residual effective charge of the rod saturates at its critical value $\alpha_c/l_B \simeq 1/l_B$. For a strongly charged cylinder with a finite radius r_0, a similar phenomenon occurs with the effective charge becoming a function of aspect ratio r_0/r_s. Following Oosawa [18], the idea of separating condensed and free counterion components has been widely used in the literature. Nevertheless, it is hard to justify its applicability for our problem. First, there is an ambiguity in defining the "near" and "far" regions of the cylinder with a finite aspect ratio, and therefore the effective charge is not well defined. Furthermore, the electrostatic interactions are strongest on length scales shorter than r_s, exactly where the DH approximation is invalid (for $\alpha \gtrsim 1$).

The leading corrections to the free energy due to small fluctuation of the chain can be evaluated without any model assumptions; namely, one can linearize the PB equation near its solution for a static cylinder $[\Psi^{(0)}(\mathbf{x})]$, and couple the perturbations of the potential $\phi(\mathbf{x}) = \Psi(\mathbf{x}) - \Psi^{(0)}(\mathbf{x})$ to the conformational fluctuations $\mathbf{u}_s$. The displacements of the charged cylinder can be described by the local perturbations to the in-plane electrostatic moments. In particular, the monopole, dipole, and quadrupole moments have the following forms, respectively:

$$\tau_s = \frac{\tilde{\alpha} e}{2 l_B}\left(\frac{\partial \mathbf{u}_s}{\partial s}\right)^2, \tag{12}$$

$$\mathbf{d}_s = \frac{\tilde{\alpha} e}{l_B}\mathbf{u}_s, \tag{13}$$

$$Q_s^{ij} = \frac{\tilde{\alpha} e}{l_B}\left[\left(u_s^i u_s^j - \frac{\mathbf{u}_s^2 \delta^{ij}}{2}\right) + O\left(\left(r_0 \frac{\partial \mathbf{u}_s}{\partial s}\right)^2\right)\right]. \tag{14}$$

Here, $\tilde{\alpha} = \alpha_0 + (r_0/2r_s)^2 \sinh \Psi^{(0)}(r_0)$ takes into account the fact that a cylinder of radius r_0 with linear density density $e\alpha_0/l_B$ fluctuates in an oppositely charged environment with local charge density $ne \sinh \Psi^{(0)}(r_0)$. We have limited our consideration to the leading three electrostatic moments because they are the only ones containing the displacement $\mathbf{u}_s$ in orders no greater than 2. Thus, the general expression for the correction to the electrostatic Hamiltonian (second order in u) is

$$\delta H_{el} = \int_0^L \left[\frac{\delta H_{el}}{\delta \tau_s}\tau_s - \frac{H_{el}^{(0)}}{2L}\left(\frac{\partial \mathbf{u}_s}{\partial s}\right)^2\right] ds + \frac{1}{2}\int_0^L \int_0^L \left(\frac{\delta^2 H_{el}}{\delta \mathbf{d}_s \delta \mathbf{d}_{s'}}\right)\mathbf{d}_s \mathbf{d}_{s'} ds\, ds'. \tag{15}$$

Here, the first term accounts for the fluctuations of the local linear charge density, τ_s. For symmetry reasons, a similar term containing the quadrupole moment $\hat{\mathbf{Q}}_s$ is absent ($\delta H_{el}/\delta\hat{\mathbf{Q}}_s=0$). The second term in the above expression reflects the fact that the cylinder is no longer perfectly straight and its end-to-end distance is reduced by the amount $\int_0^L(\partial\mathbf{u}_s/\partial s)^2 ds/2$. The last term represents the dipole-dipole interactions, and this is the only nonlocal term in the effective Hamiltonian:

$$\frac{1}{2}\int_0^L\int_0^L\left(\frac{\delta^2 H_{el}}{\delta\mathbf{d}_s\delta\mathbf{d}_{s'}}\right)\mathbf{d}_{s'}\mathbf{d}_{s'}ds\,ds' = \frac{1}{D}\int_0^L\int_0^L\phi_q^{(1)}(r_0,s-s')(\mathbf{d}_s-\mathbf{d}_{s'})^2 ds\,ds' = \frac{2}{D}\sum_q[\phi_q^{(1)}(r_0)-\phi_0^{(1)}(r_0)]\mathbf{d}_q\mathbf{d}_{-q}. \qquad (16)$$

Here we have switched to the Fourier representation, and expressed the result in terms of the dipolar field $\phi_q^{(1)}(r)$. The latter satisfies the inhomogeneous linearized PB equation

$$\left[\partial_r^2+\frac{1}{r}\partial_r-\left(q^2+\frac{1}{r^2}+\frac{1}{r_s^2}\cosh\Psi^{(0)}(r)\right)\right]\phi_q^{(1)}=0, \qquad (17)$$

subject to the boundary condition

$$\left(\frac{1}{r}-\partial_r\right)\phi_q^{(1)}\bigg|_{r=r_0}=1. \qquad (18)$$

Thus,

$$\frac{\delta H_{el}[\mathbf{u}_q]}{k_BT}=\sum_q\left(\frac{2\tilde{\alpha}^2}{l_B}[\phi_q^{(1)}(r_0)-\phi_0^{(1)}(r_0)]\mathbf{u}_q\mathbf{u}_{-q}+Cq^2\mathbf{u}_q\mathbf{u}_{-q}\right). \qquad (19)$$

Here we have used the fact that the first two terms in Eq. (15) are local in $\partial\mathbf{u}_s/\partial s$:

$$\text{const}\times\int(\partial\mathbf{u}_s/\partial s)^2 ds=\sum_q Cq^2\mathbf{u}_q\mathbf{u}_{-q}.$$

We can determine the coefficient C by noting that the low-q behavior of the electrostatic correction to the Hamiltonian $H_{el}[\mathbf{u}_s]$ should still be dominated by bending modes, $q^4\mathbf{u}_q\mathbf{u}_{-q}$, and therefore all the terms containing $q^2\mathbf{u}_q\mathbf{u}_{-q}$ must cancel in that limit:

$$C=-\frac{\tilde{\alpha}^2}{l_B}\left(\frac{\partial^2\phi_q^{(1)}(r_0)}{\partial q^2}\bigg|_{q=0}\right). \qquad (20)$$

After substitution of this value of C into Eq. (19), we obtain a nonlinear generalization of the electrostatic tension term $\Lambda_{el}(q)$ that enters the earlier results Eqs. (6) and (8):

$$\Lambda_{el}^{(nonlin)}(q)=\frac{4\tilde{\alpha}^2}{l_B}\left(\frac{\phi_q^{(1)}(r_0)-\phi_0^{(1)}(r_0)}{q^2}-\frac{\partial^2\phi_q^{(1)}(r_0)}{2\partial q^2}\bigg|_{q=0}\right). \qquad (21)$$

By solving Eqs. (1) and (17) numerically, we found the function $\Lambda_{el}^{(nonlin)}(q)$ for various regimes. Its low-q asymptotic may significantly deviate from the classical OSF result, which is consistent with the earlier studies [13,14]. One could interpret this deviation in terms of renormalized effective charge, by defining the effective Manning parameter $\alpha^{(eff)}$ so that in the limit $qr_s \ll 1$,

$$\Lambda_{el}^{(nonlin)}(q)\simeq\frac{(\alpha^{(eff)}r_sq)^2}{4l_B}. \qquad (22)$$

Surprisingly, this effective charge appears to have a clear physical meaning. With excellent accuracy, $\alpha^{(eff)}$ has the same value as the effective Manning parameter α_∞ which can be extracted from the far-field behavior of the potential $\Psi^{(0)}(r)$, i.e.,

$$\Psi^{(0)}(r)\simeq 2\alpha_\infty K_0(r/r_s)$$

for $r \gtrsim r_s$ [16]. Here K_0 is the modified Bessel function, which is the solution to the DH equation in cylindrical geometry.

Figure 2(a) demonstrates a striking correlation between $\alpha^{(eff)}$ and α_∞, in a wide range of parameters. Each curve there corresponds to the fixed value of α_∞. The solid and dashed lines represent $\alpha^{(eff)}/\alpha_0$ and α_∞/α_0, respectively, as functions of the aspect ratio r_0/r_s. The close agreement between the two types of data shows that $\alpha^{(eff)}$ and α_∞ nearly coincide for an arbitrary value of the bare linear charge, as long as the aspect ratio r_0/r_s remains small. Figure 2(b) illustrates the dependence of $\alpha^{(eff)}$ on the aspect ratio for values of the bare charge close to those of dsDNA and ssDNA ($\alpha_0=4$ and 1, respectively). One can see that for practical purposes $\alpha^{(eff)}$ of ssDNA is close to 0.7, while its value for dsDNA follows the saturation curve (corresponding to an infinitely charged cylinder with the same radius). Note that the far-field definition of the effective charge is unambiguous, and it does deviate from the Oosawa-Manning result, even for zero aspect ratio [see Fig. 2(c)]. Furthermore, one can modify the Oosawa-Manning approach to evaluate the effective charge as a function of r_0/r_s, as demonstrated in Ref. [19]. The result of that calculation is also shown in Figs. 2(b) and 2(c), and it clearly deviates from our far-field-based definition of $\alpha^{(eff)}$.

We have explicitly demonstrated that the OSF result is formally applicable even outside the DH approximation, given that the effective charge is properly defined. While similar effective charge descriptions have been previously utilized in several works,[15,16] they were all introduced as purely empirical assumption. In fact, our result is rather nontrivial since the electrostatic interactions are strongest in the vicinity of the chain, where the effective description is not valid. The effective charge picture works only because the bending of the chain affects the far region more strongly than the near one. Indeed, the q^2 term in Eq. (17) is most relevant for $r \gtrsim r_s$.

Furthermore, for $q \gtrsim 1/r_s$ the effective charge description breaks down, and deviations from the DH approximation become considerable, as shown in Fig. 3. Qualitatively, this can be interpreted as an increase of the effective charge with q: as one goes to smaller length scales, $\alpha^{(eff)}$ should shift from its far-field value α_∞ toward the bare Manning parameter α_0.

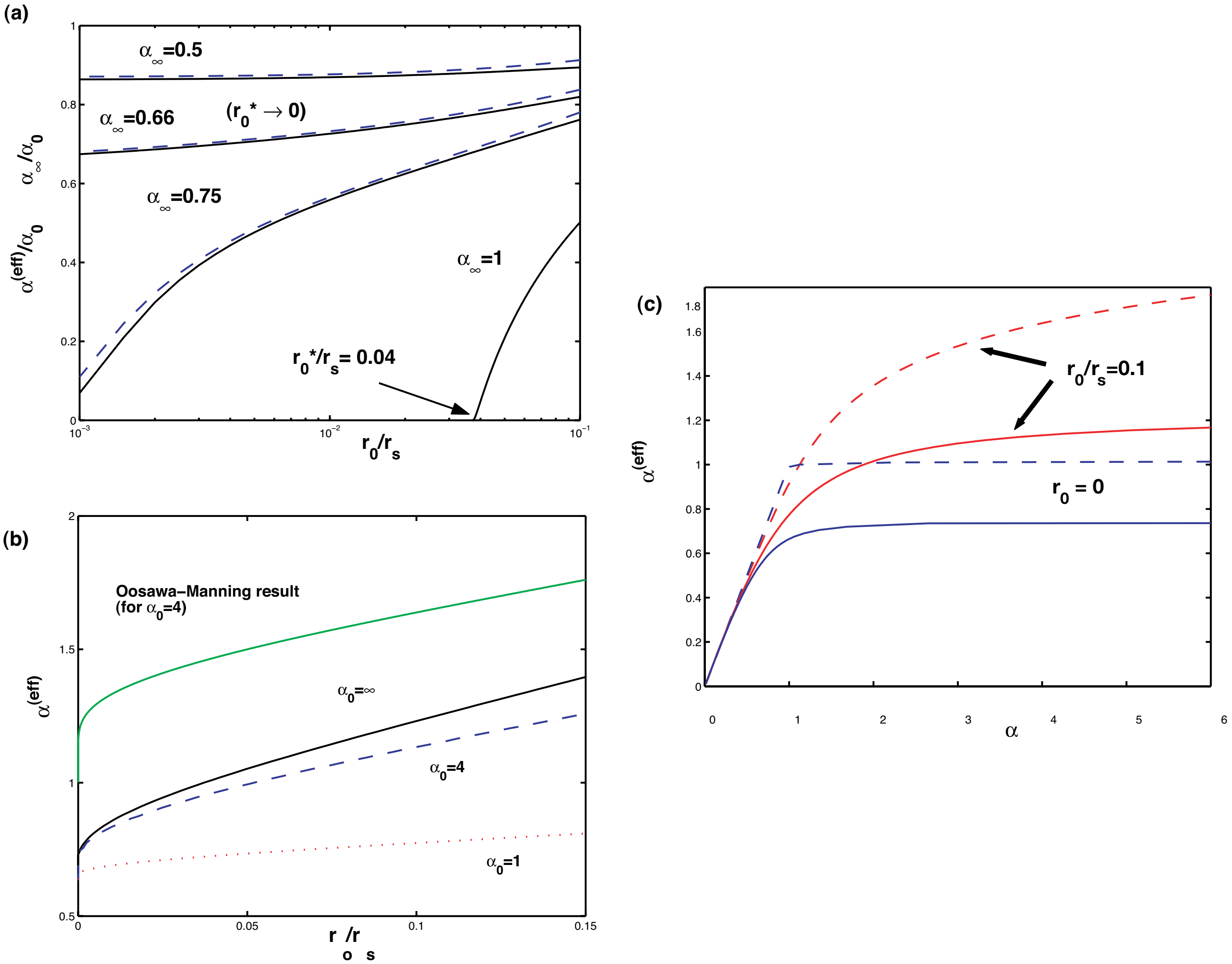

FIG. 2. (Color online) (a) Correlation between the effective Manning parameter $\alpha^{(eff)}$ obtained from the renormalized rigidity of the strongly charged chain, and the one extracted from the far-field behavior of the electrostatic potential, α_∞. Solid and dashed lines represent $\alpha^{(eff)}/\alpha_0$ and α_∞/α_0, respectively, for a fixed value of α_∞ and variable aspect ratio r_0/r_s. (b) $\alpha^{(eff)}$ as a function of aspect ratio for various values of the bare charge: $\alpha_0 \to \infty$ (the saturation curve, solid line), 4 (dsDNA, dashed line), and 1 (ssDNA, dotted line). Note that $\alpha^{(eff)}$ clearly deviates from the result obtained through an Oosawa-type calculation, Ref. [19]. (c) Effective vs bare charge dependence (solid lines), compared to similar result of Oosawa-Manning model (dashed lines). The two sets of plots correspond to the limit of an infinitely thin rod (r_0=0), and a finite aspect ratio (r_0/r_s=0.1), respectively.

The change of the overall shape of $\Lambda_{el}(q)$ gives rise to modification of the stretching curves, compared to the results of DH-based theory, as shown in Fig. 1. Naturally, these corrections are strongest for large ratios r_s/l_p, which correspond to a wider dynamic range of the relevant wave vectors.

IV. DISCUSSION

The above results can be applied to experiments on both ds- and ssDNA. The two cases are characterized by rather different values of the physical parameters. In particular, the persistence length of dsDNA, $l_p^{(ds)} \simeq 50$ nm $\simeq 70 l_B$, significantly exceeds that of the ssDNA chain, $l_p^{(ss)} \sim 1$ nm $\sim l_B$. In addition, their linear charge densities differ approximately by a factor of 4. Finally, while the WLC model is well established as a standard description of dsDNA, the situation with the elasticity of ssDNA is not as settled: the extensible version of the WLC is among several proposed models all of which are in reasonable agreement with the existing experimental data [20]. The plots in Figs. 1(a) and 1(b) roughly correspond to the parameters of ds- and ssDNA, respectively. As one can see from the figure, the two-stage behavior and the intermediate unstretchable regime become pronounced when r_s substantially exceeds the persistence length. Note, however, that this regime is unlikely to be accessible in the case of dsDNA, since the double helix would become unstable at such a weak screening due to the electrostatic repulsion between the strands. For ssDNA, the two-stage stretching must be observable at $r_s \gtrsim 100$ nm.

While Fig. 1 gives only a general idea about the mechanical response of a semiflexible chain with electrostatic inter-

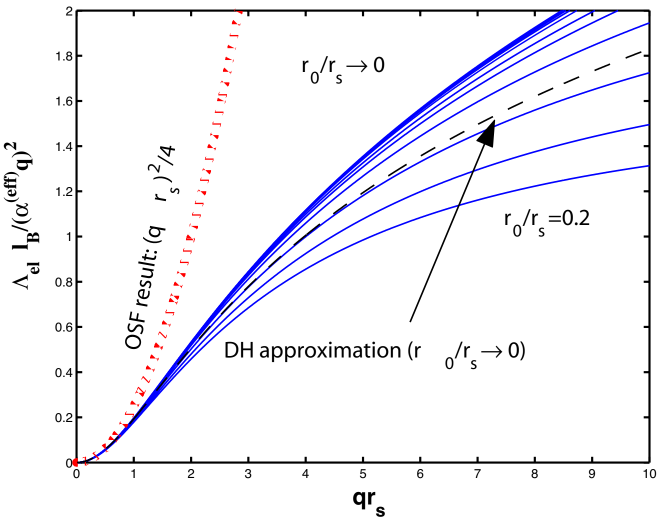

FIG. 3. (Color online) $\Lambda_{el}(q)$ obtained from the complete PB equation, for various aspect ratios (solid lines). Introduction of the effective Manning parameter results in matching of these curves with the DH (dashed) and OSF (dotted) results for low q. For $qr_s \gtrsim 1$, the DH approximation underestimates the effect of electrostatic interactions (compare the zero-aspect-ratio curves). Both PB and DH curves significantly deviate from the OSF parabola, indicating that the effective rigidity description is not valid on length scales smaller than r_s.

actions, a more detailed comparison of our results with experiments is presented in Fig. 4. The plot shows the stretching curves of ssDNA taken at various screening conditions, as reported in Refs. [2] and [4]. These experimental data are fitted by our theory with the Debye screening length calculated for each salt concentration. As a result, the only fitting parameter was the bare persistence length l_p, and the best fit is achieved at l_p=5.5 Å. This value is somewhat smaller that the earlier estimates of the effective persistence length $l_p^* \simeq 8$ Å; the difference is due to our explicit account for the electrostatic corrections to chain rigidity. Unlike the plots in Fig. 1 which for the sake of simplicity were calculated by assuming $r_0/r_s=0$, in Fig. 4 the nonzero diameter of the ssDNA chain is taken into account. Based on the known structure of the molecule, we have assumed $r_0=5$ Å, and this parameter was not used for fitting.

Even though the theoretical stretching curves were calculated with the WLC model, our approach can also be applied to alternative descriptions of ssDNA, such as the extensible freely jointed chain (EFJC) model. However, this modification is unlikely to produce any significant change since within the force range of interest, the competing models (WLC, EFJC, and discrete version of the WLC) are known to give nearly identical fitting to the electrostatic-free stretching behavior of ssDNA [20]. Indirectly, this model independence is supported by the fact that the above experimental data were also successfully fitted with numerical simulations based on the EFJC model [4]. In that work, in addition to electrostatic interactions described within the linear DH approximation with renormalized charges, the effects of excluded volume and hairpin formation were included [15]. Since these additional effects are important only for relatively small chain extension, they were neglected in the context of our work.

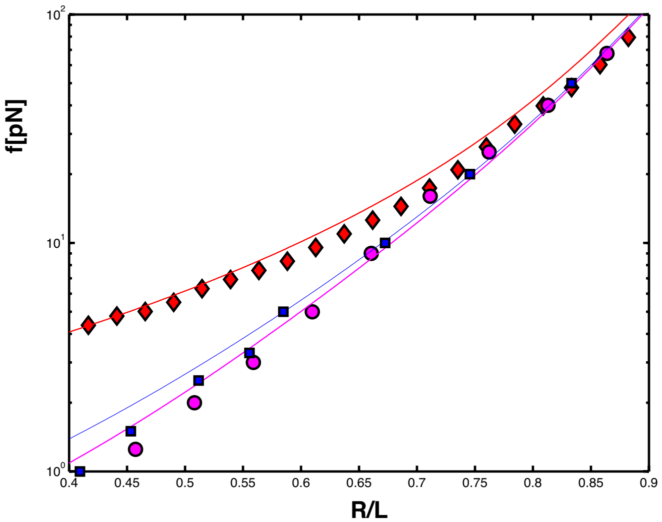

FIG. 4. (Color online) Comparison of the theoretical results to experimental data on the elastic response of ssDNA at various screening conditions. Data points are taken from Refs. [2] (2 mM NaCl, shown by circles), and [4] (1 and 10 mM PB data are represented by squares and diamonds, respectively). The theoretical curves were obtained by taking into account the calculated values of the Debye length for each case (6.9, 6, and 1.9 nm, respectively). ssDNA was approximated by a cylinder of radius r_0=0.5 nm. The only fitting parameter for all three curves is the bare persistence length l_p, whose optimal value is close to 5.5 nm.

V. CONCLUSIONS

In conclusion, we have studied the effects of electrostatic self-interactions on the elastic properties of a strongly stretched WLC, with application to ds- and ssDNA at moderate- and weak-screening conditions. By reconsidering the earlier studied problem of scale-dependent electrostatic rigidity we have demonstrated that, in the limit of weak screening, the mechanical response of the chain has a distinctive two-stage character. The two modes are characterized by the bare and the renormalized persistence length, respectively, and they are separated by intermediate unstretchable regime.

The central theme of our work is the effect of nonlinearity of the PB equation on the classical results obtained within the DH approximation. Consistently with previous studies of the problem [13,14], the OSF result for the electrostatic renormalization of the persistence length is not applicable in the nonlinear regime, and in particular the scaling $l_p^* - l_p \sim r_s^2$ is not valid. However, we have explicitly demonstrated that the OSF formula is formally correct if the actual line charge density is replaced with the effective one. The latter is determined from the far-field asymptotic of the electrostatic potential of the strongly stretched chain. In the light of this result, the deviation from OSF scaling is due to the nontrivial dependence of the effective charge on the aspect ratio r_0/r_s.

The renormalized OSF description is, however, only partially adequate since the electrostatic corrections to the chain rigidity do not follow the result of the DH theory on scales shorter that r_s, even upon the charge renormalization. This deviation is due to the fact that the effective charge itself is a scale-dependent concept. Our solution to the complete nonlinear problem is shown to give an adequate description of the experimentally observed stretching behavior of ssDNA at various salt conditions.

ACKNOWLEDGMENTS

The author thanks S. Safran, Y. Rabin, and H. Diamant for valuable discussions.

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