# Effect of Non-Pairwise-Additive Interactions on Bundles of Rodlike Polyelectrolytes

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Like-charged rigid polyelectrolytes can attract each other due to counterion-mediated interactions to form bundles. However, the resulting effective interactions between rods are not pairwise additive. Here we calculate the free energy of an $N$-rod bundle explicitly. We find that the breakdown of pairwise additivity dramatically affects the stability of bundles of $N$ rods and leads to a barrier in the free energy that grows with increasing salt concentration. [S0031-9007(98)06735-0]

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Experiments on a variety of stiff polyelectrolyte chains, such as DNA, $F$-actin, and tobacco mosaic virus, show that they can self-assemble in solution into bundles of a well-defined size of densely packed, approximately parallel chains [1,2]. For DNA, this phenomenon is known as condensation and has attracted attention because of its implications for packaging of viral DNA. Condensation is surprising because it implies an attractive interaction, but the chains carry the same sign of charge and Debye-Hückel theory and nonlinear Poisson-Boltzmann theory both predict that the interaction should be repulsive [3]. In order to understand the attraction, recent simulations and theories [4–7] focused on two-rod systems. In particular, we found that two charged rods can attract each other [7] due to the presence of condensed counterions (i.e., counterions near the rods) [8,9]. These counterions give rise to charge fluctuations on the rods that become correlated when the two rods are sufficiently close together. The resulting short-ranged attractive interaction is reminiscent of the van der Waals interaction and is in quantitative agreement with two-rod simulations [4] with no adjustable parameters [7]. As Podgornik and Parsegian [10] recently pointed out, however, these two-rod results cannot be applied to many-rod bundles, since the effective interactions among rods are not pairwise additive [7,10,11]. This is because the interactions are attractive only when the distance between rods is much smaller than the rod length; under these conditions, the multipole expansion diverges. The many-body, higher-order multipole interactions are not pairwise additive. As a result, it is not clear that the attractive interactions found between two rods persist for $N$-rod bundles. Moreover, given an attractive interaction, it is still not clear why the system chooses to form bundles of a well-defined size. This has been explained in terms of competition between the short-ranged attraction and long-ranged repulsion due to the net charge (not all counterions are condensed on the rods) [2]. However, this intuition is based on additivity of the two-rod interactions, and may fail for many-rod systems. To understand the formation of bundles and the electrostatics that control their stability, it is therefore imperative to study bundles explicitly, without assuming pairwise additivity.

In this paper, we present a closed-form expression for the electrostatic free energy of $N$-rod bundles, based on a highly nontrivial generalization of the approach we developed for two rods [7]. We find that the breakdown of pairwise additivity has dramatic effects. Contrary to previous expectation, the bundle size is *not* limited by long-ranged repulsion due to the net charge. At low temperatures, the rods prefer to aggregate into indefinitely large bundles. At high temperatures, where the interaction between rods is repulsive at all distances, the rods do not aggregate. These results hold even in the presence of salt, but they are *inconsistent* with the experimental observation of finite bundles. It is possible that nonelectrostatic mechanisms might limit the bundle size. However, our added-salt calculations suggest that kinetic effects might prevent the bundle from growing to its equilibrium size.

We study a system of $N$ negatively charged rods parallel to the $z$ direction. Since chains are highly concentrated within the bundle, we assume they are ordered on a square lattice with lattice constant $a$ [12]. Each rod consists of $M$ cylindrical monomers of length $b$ and radius $r_0$. Each monomer carries a negative charge of $-f_0$ (in units of the electronic charge $e$). The counterions have radius $r_c$ and charge $Z$ and are divided into two classes, condensed and free [8,9]. We define $f_c$ to be the average number of condensed counterions per monomer; we do not assume that $f_c$ is determined by the Manning criterion, but solve for it self-consistently as a function of the number of rods and the lattice constant $a$. A condensed counterion is approximated to lie on the nearest monomer, and to add a charge $Z$ to the net charge of that monomer. Because condensed counterions can move along the rods or exchange with free counterions, the charge of a monomer can fluctuate. The charge on monomer $s$ of rod $j$ can assume the values $q_j(s) = -f_0 + mZ$, where $m = 0, 1, 2, 3$, etc. is the number of condensed counterions occupying a given monomer. The average charge per monomer is $q = f_0 - Zf_c$ and the variance in the charge per monomer is $\delta q^2 \equiv \langle [q(s) - \langle q(s) \rangle]^2 \rangle_q = Z^2 f_c$. We allow for added salt by including free ions labeled by the index $\alpha$, carrying charge $\bar{q}_\alpha$. Finally, it is useful to introduce the Bjerrum length, $\ell_B = e^2/\epsilon k_B T$, namely, the length scale at which the electrostatic energy is comparable to the thermal energy. We will also use the dimensionless Bjerrum length in units of the monomer length, $\tilde{\ell}_B \equiv \ell_B/b$. The Manning-Oosawa parameter [8,9], a measure of the ratio of the electrostatic energy to the thermal energy, is given by $\xi = \tilde{\ell}_B f_0$ in our notation.

In terms of the charge variables $q_j(s)$ on the rods and the free ions $\bar{q}_\alpha$, along with their associated positions $\mathbf{r}_j(s)$ and $\mathbf{r}_\alpha$, the electrostatic interaction Hamiltonian is

$$\beta\mathcal{H} = \frac{1}{2}\,\ell_B\Bigg[\sum_{ij}^{N}\sum_{ss'}^{M}\frac{q_i(s)q_j(s')}{|\mathbf{r}_i(s) - \mathbf{r}_j(s')|} + 2\sum_{i}^{N}\sum_{s}^{M}\sum_{\alpha}\frac{q_i(s)\bar{q}_\alpha}{|\mathbf{r}_i(s) - \mathbf{r}_\alpha|} + \sum_{\alpha\alpha'}\frac{\bar{q}_\alpha q_{\alpha'}}{|\mathbf{r}_\alpha - \mathbf{r}_{\alpha'}|}\Bigg], \tag{1}$$

where $\beta = 1/k_BT$. The nonzero radii of the rods and counterions are incorporated by separating the radial and axial components of the separation $\mathbf{r}_i(s) - \mathbf{r}_i(s')$ for two charge variables on the *same* rod $i$, so that $|\mathbf{r}_i(s) - \mathbf{r}_i(s')|^2 = [z_i(s) - z_i(s')]^2 + d^2$. The cutoff length $d$ represents the minimum separation between two condensed counterions on the same rod; we take $d = 2(r_0 + r_c)$, where $r_c$ is the counterion radius [7].

The system can adjust the monomer charges $q_i(s)$ but not their positions $\mathbf{r}_i(s)$. It can also adjust the free ion positions $\mathbf{r}_\alpha$ but not their charges $\bar{q}_\alpha$. The partition function is therefore the sum over all realizations of the charge variables $q_i(s)$ and the integral over the free ion positions $\mathbf{r}_\alpha$:

$$\mathcal{Z} = \int \mathcal{D}\mathbf{r}_\alpha \langle e^{-\beta\mathcal{H}}\rangle_q = \int \mathcal{D}\mathbf{r}_\alpha \int \mathcal{D}q_i(s) e^{-\beta\mathcal{H}}. \tag{2}$$

We now make the Hubbard-Stratanovich transformation [13] and use the Gaussian approximation [7]. For simplicity, we assume that the counterions are identical to one of the ionic species of the added salt. We treat the free ions within the Gaussian approximation and trace over their positions first; this is equivalent to Debye-Hückel theory [6]. The effect of free ions is simply to replace the bare interaction, $\ell_B/r$, by a "screened" one, $\ell_B e^{-\kappa r}/r$ [6], where $\kappa$ is an inverse Debye screening length given by $\kappa^2 = 4\pi\ell_B Z^2 n$ (here we have assumed that both ions of the salt have valency $Z$).

To integrate out the remaining degrees of freedom associated with the monomeric charges $q_i(s)$, it proves useful to Fourier transform from $z$ to $k$. We define matrices $M(k)$ and ${}^0M$ to be

$$\begin{aligned} {}^0M_{ij} &= \delta q^{-2}\delta_{ij} + 2\tilde{\ell}_B K_0(\kappa R_{ij}), \\ M_{ij}(k) &= \delta q^{-2}\delta_{ij} + 2\tilde{\ell}_B K_0(R_{ij}\sqrt{\kappa^2 + k^2}), \end{aligned} \tag{3}$$

where $R_{ij}$ is the distance between rods $i$ and $j$, $R_{ii} \equiv d$, and $K_0(x)$ is the zeroth-order modified Bessel function of the second kind. The electrostatic free energy per monomer of the rods, for $a \ll L$, is

$$\beta\mathcal{F}_{\text{rods}}(a) = \frac{1}{2}\,q^2\sum_{ij}\left[\delta_{ij} - \frac{1}{\delta q^2}\,{}^0M_{ij}^{-1}\right]\frac{1}{\delta q^2} + \frac{b}{2}\int_{-\infty}^{\infty}\frac{dk}{2\pi}\,\ln[\det\delta q^2 M(k)] - bN\delta q^2\tilde{\ell}_B\int_{-\infty}^{\infty}\frac{dk}{2\pi}\,K_0(d\sqrt{\kappa^2 + k^2}). \tag{4}$$

The first term in Eq. (4) represents the repulsion due to the net charge on the rods. The second term represents the attraction due to fluctuations in the monomeric charge. When $N = 2$, then we obtain the two-rod result [see Eq. (6) in Ref. [7] ]. The last term is the self-energy that must be subtracted. The free energy in Eq. (4) cannot be written as the pairwise sum of the two-rod interaction unless we retain only the leading term in the expansion of Eq. (4) in powers of $\delta q^2$ (i.e., up to monopole-dipole interactions).

The electrostatic free energy in Eq. (4) depends on the average number of condensed counterions per monomer, $f_c$. To solve for $f_c$ self-consistently, we enclose the bundle in a large cylinder of radius $L_\perp$ and length $L$, and construct the total free energy in terms of the number of condensed and free counterions. We then equate the chemical potentials of condensed and free counterions. The total free energy valid for $\kappa^{-1} \ll L$ is then

$$\beta\mathcal{F}_{\text{total}} = Nf_c\left(\ln\frac{f_c M v_0}{Ld^2} - 1\right) + (Nf_f + \tfrac{1}{2}nbL_\perp^2)\left[\ln\left(\frac{Nf_f M}{LL_\perp^2} + \frac{n}{2}\right)v_0 - 1\right] + \tfrac{1}{2}nbL_\perp^2(\ln nv_0/2 - 1) + NZq\tilde{\ell}_B f_f K_0(\kappa d/2) + \beta\mathcal{F}_{\text{rods}} - \frac{LL_\perp^2}{12\pi}\kappa^3 + \tfrac{1}{2}q^2\frac{N}{nv_0}, \tag{5}$$

where $f_f = (f_0 - Zf_c)/Z$ is the number of free counterions per monomer and $v_0$ is the counterion volume. The first three terms in Eq. (5) correspond to the entropy of mixing of condensed counterions, free counterions (including the positively charged salt ions), and negatively charged salt ions, respectively. The fourth term is the interaction of free counterions with rods, and the fifth is given in Eq. (4). The sixth term is the standard Debye-Hückel result for the salt ions, and the last term corresponds to the repulsive interactions between free counterions. We solve for $f_c$ by minimizing $\beta\mathcal{F}_{\mathrm{total}}$ (see Ref. [7]). We have solved for the rod free energy numerically for small bundles ($N \leq 36$), and analytically in the asymptotic large $N$ limit.

To calculate the equilibrium bundle size, we have chosen $Z = 2$, $T = 300$ K, $\epsilon = 80$, $b = 1.7$ Å, and $f_0 = 1$. The rod radius is $r_0 = 4.2$ Å and the counterion radius is $r_c = 2.1$ Å. In addition, $M = 10^5$ and $L_\perp = L$; the results do not vary much for larger $M$ and $L_\perp$. We first discuss what one would expect if the interactions were pairwise additive. In Fig. 1, we have plotted the rod free energy $\mathcal{F}_{\mathrm{rods}}$ given in Eq. (4) as a function of the number of rods in the bundle, $N$, for two different salt concentrations. The lattice constant of the bundle is $a = 24$ Å. In all cases, the reference free energy corresponds to infinite separation of the rods ($a \rightarrow \infty$). In the lower salt case, $\kappa = 0.06$ Å$^{-1} \equiv 0.02$ M salt, the expectation based on pairwise additivity of the results in Ref. [7] is plotted as a bold solid curve in Fig. 1. Because the interaction consists of a short-ranged attraction and longer-ranged repulsion, the free energy has a minimum at $N \approx 16$. In the high salt case, $\kappa = 0.1$ Å$^{-1} \equiv 0.05$ M salt, on the other hand, the pairwise additive result is plotted as a bold dashed curve. In this case, the two-rod interaction at a spacing of $a = 24$ Å or larger is repulsive, so the minimum of the free energy lies at $N = 1$ (completely separated rods).

The results from the full $N$-rod calculation are quite different from the pairwise-additive results, as shown by the thin curves. At the higher salt concentration, $\kappa = 0.1$ Å$^{-1}$, we find qualitatively similar but quantitatively different behavior from the pairwise-additive case. In both cases, the minimum of the free energy lies at $N = 1$ because the interaction is repulsive. However, the magnitude of the free energy is significantly lower in the full analysis, implying that the repulsion is much weaker. Thus, the inclusion of additional charge fluctuations, neglected in the pairwise additive case, leads to more screening of the repulsive contribution to the free energy. At lower salt concentrations, there is a striking difference between the full analysis and the pairwise-additive one. At $\kappa = 0.06$ Å$^{-1}$, we obtain the thin solid curve. In contrast to the pairwise-additive result, the full numerical analysis yields a free energy that is monotonically decreasing up to the limit of our calculations, $N = 36$, implying an equilibrium bundle size of $N = \infty$. This extrapolation is borne out by our asymptotic analysis, where we find that the free energy per rod, $\mathcal{F}_{\mathrm{rods}}/N$, approaches a limiting value as $N \rightarrow \infty$, so that $\mathcal{F}_{\mathrm{rods}}$ scales linearly with $N$.

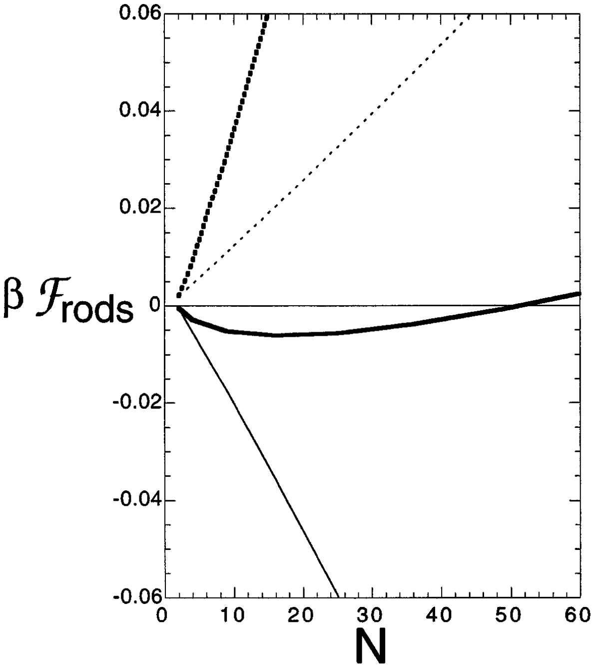

FIG. 1. Electrostatic rod free energy, $\mathcal{F}_{\mathrm{rods}}$, as a function of the number of rods in the bundle, $N$. The parameters used are $T = 300$ K, $\epsilon = 80$, $f_0 = 1$, and $Z = 2$ (divalent counterions). The lattice constant is $a = 24$ Å. The bold and thin solid curves correspond to $\kappa = 0.06$ Å$^{-1}$; the bold curve is the result assuming pairwise additivity, and the thin curve is the result of the full $N$-rod analysis. Similarly, the bold and thin dashed curves correspond to the pairwise-additive and full results for $\kappa = 0.1$ Å$^{-1}$.

As the salt concentration increases, the onset of attraction moves to smaller lattice spacings $a$. This is shown in Fig. 2, where we have plotted the rod free energy per monomer, $f_{\mathrm{rods}} \equiv \mathcal{F}_{\mathrm{rods}}/NM$, for 16 rods as a function of $a$. Since the system is free to adjust its lattice spacing, we must consider the global minimum of the free energy. As shown in Fig. 2, the free energy minimum is at small $a$, so the rods collapse to form a dense bundle, independent of salt concentration. This is true for all salt concentrations up to $\kappa_c = 0.25$ Å$^{-1} \equiv 0.3$ M of a 2:2 salt [14]. Above $\kappa_c$, the onset of attraction is smaller than the cutoff distance $d$, so there is no attractive regime. In other words, the equilibrium bundle size is $N = \infty$ for $\kappa \leq \kappa_c$, and $N = 1$ for $\kappa > \kappa_c$. Our calculations are consistent with Brownian dynamics [15] and molecular dynamics [16] simulations.

The physical reason why electrostatics prefer $N = \infty$ is that the condensed counterions along the rods can become correlated over the entire bundle, not just pair by pair. At very low temperatures, the system becomes an ionic crystal [4], and it is not surprising that the ionic crystal is not limited in size by electrostatic repulsion. However, our finding is in direct contradiction with the experiments [1,2], which find well-defined finite bundles. One possible explanation for the difference is that nonelectrostatic mechanisms are at play. Since we have treated rigid rods, we have not allowed repulsions due to conformational fluctuations [17] or topological defects that are introduced by the winding of chains into a torus [18]; these mechanisms might limit the bundle

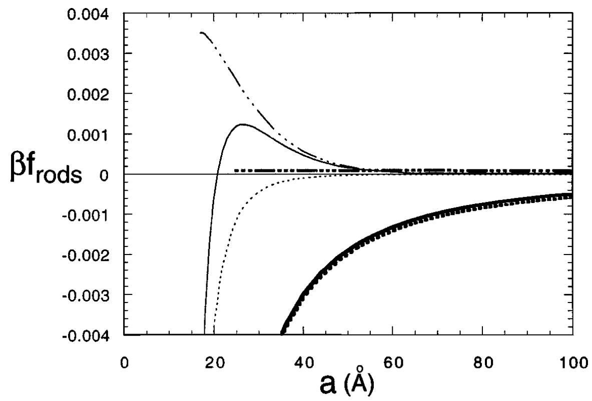

FIG. 2. The electrostatic rod free energy per monomer, $f_{\mathrm{rods}} = \mathcal{F}_{\mathrm{rods}}/NM$, as a function of the lattice constant $a$ for the same parameter values as in Fig. 1, for a 16-rod bundle. The bold solid curve corresponds to $f_{\mathrm{rods}}$, the bold dashed curve to the attractive contribution to $f_{\mathrm{rods}}$, and the bold dot-dashed curve to the repulsive contribution to $f_{\mathrm{rods}}$, for the case $\kappa = 0.001$ Å$^{-1}$. The thin solid, dashed, and dot-dashed curves correspond to $f_{\mathrm{rods}}$, and the attractive and repulsive contributions to $f_{\mathrm{rods}}$, respectively, for $\kappa = 0.1$ Å$^{-1}$. Note that the free energy develops a repulsive barrier as the amount of added salt increases.

size. Another possibility is that bundles cannot reach their equilibrium size for kinetic reasons. We find partial support for this hypothesis by looking at the free energy per monomer as a function of lattice constant, as in Fig. 2. The solid curves correspond to $f_{\mathrm{rods}}$. Note that there is a barrier in the high-salt case $\kappa = 0.1$ Å$^{-1}$. The free energy develops a repulsive barrier that increases with increasing salt. We find qualitatively similar behavior when we bring one rod up to a bundle of $N$ rods.

To understand the origin of the barrier, we have plotted the repulsive and attractive contributions separately [these correspond to the first and second terms in Eq. (4), respectively]. The attractive term is plotted as a dashed curve (heavy for $\kappa = 0.001$ Å$^{-1}$ and light for $\kappa = 0.1$ Å$^{-1}$). As the amount of salt increases, the attractive term decreases in magnitude because the attractive counterion-mediated interaction is screened [6]. The barrier, however, arises from the *repulsive* contribution to the free energy (dot-dashed curves). At low salt (heavy dot-dashed curve), the repulsive term is small and nearly independent of the separation between rods, while at high salt (thin dot-dashed curve), the repulsive contribution is large and depends strongly on the lattice constant $a$. This is because the amount of counterion condensation, $f_c$, decreases with salt. In addition, salt screens the one-dimensional charge fluctuations along the rods that screen the rod-rod repulsion.

Our results show that the breakdown of pairwise additivity leads to qualitatively new predictions. When is pairwise additivity valid? Podgornik and Parsegian [10] have shown that pairwise additivity is recovered at sufficiently high salt concentrations. Based on our asymptotic analysis for large $N$, we find the following criterion for pairwise additivity to hold: $\kappa^2 a^2 \gg \delta q^2 \ell_B / b$. For the case of $\kappa = 0.1$ Å$^{-1}$, the criterion requires $a \geq 30$ Å. In this regime, the interaction is repulsive. We always find that pairwise additivity is valid only far on the repulsive side of the barrier.

It has long been recognized that many-body, non-pairwise-additive interactions play an important role in electrostatic systems such as colloidal suspensions and polyelectrolyte solutions. The great difficulty has been to formulate a theoretical approach that includes these interactions. We have shown that it is possible to calculate the free energy explicitly for a many-rod system.

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