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Molecular Fluctuations in the Packing of Polymeric Liquid Crystals

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ABSTRACT: Recent measurements of forces between DNA polyelectrolytes have shown a direct and continuous coupling between intermolecular forces and molecular disorder in lattices of interacting particles. Over a wide range of conditions the work of assembly is dominated by the configurational entropy of molecules restricted by repulsive forces from their neighbors. This observed entropic force decays half as fast as what is predicted from the decay lengths for an electrostatic double layer or hydration forces between parallel molecules. It cannot be fit by the traditional model of flexible molecules with an effective hard wall radius. In this paper we develop a statistical mechanical model of a Gaussian randomly walking polymer surrounded by an effective "tube" of its neighbors, a model that can be solved in strict formal analogy to the problem of a bounded two-dimensional quantized oscillator. The doubling of the underlying exponential decay length emerges naturally. One may also extract the underlying direct intermolecular force through which molecular motion is restricted.

Introduction

Ever since the seminal work of Onsager[1] on the packing of stiff rods into ordered structures, it has been known that purely repulsive forces can act to create condensed assemblies of particles. The entropic consequences of steric repulsion have come to be a popular topic in statistical mechanics. The key simplifying feature of virtually all theories has been the assumption that the continuously variable repulsive force between rods can be replaced by that of a hard cylinder whose radius of sudden repulsion depends on the strength of the actual force (see, e.g., the discussion of Stigter[2]).

Recent simultaneous measurements of the molecular disorder of and the forces between polyelectrolytes in parallel arrays[3] suggest that this hard particle assumption is incorrect. For the specific system observed, parallel double helices of polyelectrolyte DNA, one sees two regimes of repulsion:

At separations less than 10 Å, molecules repel with an exponentially decaying force whose decay constant is about 3 Å and is negligibly dependent on salt concentration, as expected for hydration forces;[4] repulsion is so powerful that it suppresses energetically significant molecular disorder.

At greater separations, one observes the onset of molecular disorder and an exponentially decaying intermolecular force whose decay rate depends on salt concentration but is approximately one-half that expected from the standard double-layer theory.

Indeed, this extended decay is the key to the model that we develop here to explain molecular packing. Steric repulsion within an array of parallel flexible rods varies as a power of separation, R,[5–7] quite different from what is observed. The only effect of the underlying soft (e.g., electrostatic) potentials is to change the effective separation.[2] This assumption is again not substantiated by the observed forces.

To develop a better description of the observations, we have formulated a Gaussian model of a polymer enclosed in an effective "tube" of its neighbors confined to their main positions. Solution of this model, formally equivalent to a quantized two-dimensional harmonic oscillator held inside fixed circular boundaries, predicts the two experimentally observed regimes—one close in where forces are just those that act directly between molecules and a second one with appreciable molecular disorder, where forces decay exponentially at half the rate of the underlying direct force.

The length of the Gaussian polymer steps, a priori unknown for a free flight chain, is found to be ≅40 Å when the model is fit to measured values. This step length is essentially the same as the 45-Å length of the independently fluctuating unit length previously inferred thermodynamically from correlation of measured lateral fluctuations and osmotic compressibilities. It is also close to the "deflection" length introduced by Odijk[5–7] to describe

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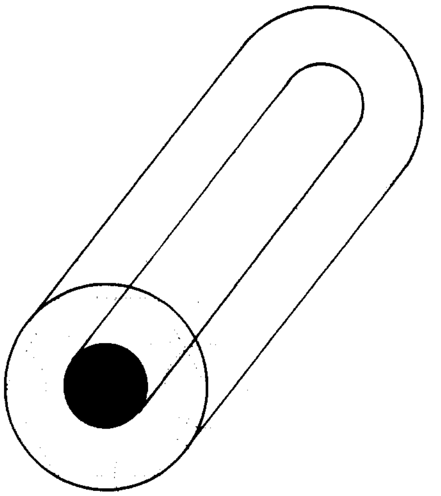

Figure 1. Scheme of a linear polymer in an effective tube of nearest neighbors in the hexagonal lattice. The radius R is based on the average location of neighbor axes. The variable $\rho(n)$ measures the deviation of the polymer axis from its mean position at the link n.

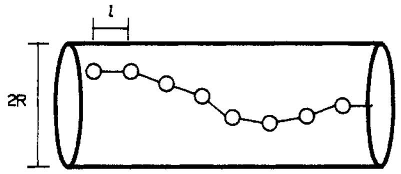

Figure 2. Nature of the Gaussian model of the confined polymer in an effective tube provided by its neighbors. Forward steps in length l to off-axis positions $\rho(n)$. Confinement is both by the potential $\phi(\rho)$ and the hard wall at $\rho = R$. In the regime of experimentally relevant R's the latter is negligible.

the behavior of an elastic polymer confined to a "hard wall" tube of radius R.

From this analysis we have concluded that the laws of polymer association by steric forces are rather different from those predicted by earlier statistical mechanical models of such systems. It explains deviations from expectation of observations made on other systems such as the muscle filaments[8,9] and tobacco mosaic virus particles,[9,20] which were the motivation for Onsager's early formulation. We are able also to estimate to good accuracy the linear charge density that is the source of the electrostatic double-layer potentials emanating from linear DNA polyelectrolytes.

Analysis

If we consider a single molecule in a hexagonal array (Figure 1), we can to lowest approximation replace its nearest neighbors by an effective tube wherein the forces exerted by these neighbors are written in the form of an axially symmetric restoring field. This construction is analogous to the Einstein model in solid-state physics.

More specifically, we will consider a free flight chain composed of N links each l long. The full polymer, of length Nl, is enclosed in a tube of radius R and with an imposed soft centrally symmetric potential depending only on the radial coordinate $\rho(n)$, a vector in the x,y direction, at a link n (Figure 2). Following Freed[10,11] we can write the partition function in the form of a functional integral

$$\Xi = \lim_{N\to\infty} \int_{(N)} \cdots \int e^{-S}\, \mathrm{d}\rho(1)\, \mathrm{d}\rho(2) \ldots \mathrm{d}\rho(N) \tag{1}$$

where the action of the functional integral can be obtained as

$$S = \frac{3}{2l^2}\int_0^N \left(\frac{\partial\rho(n)}{\partial n}\right)^2 \mathrm{d}n + \int_0^N \frac{\phi(\rho(n))}{kT}\,\mathrm{d}n \tag{2}$$

with $\phi(\rho)$ the external potential per step of length l. Introducing now the Green's function of the polymer starting at vector ρ' and ending at vector ρ we can obtain by standard methods[11]

$$\frac{\phi G}{\phi n} - \frac{l^2}{6}\nabla^2 G + \frac{\phi(\rho)}{kT}G = \frac{1}{\rho}\delta(\rho - \rho')\delta(n - n') \tag{3}$$

with the additional boundary condition at the walls of the tube in the form

$$G(|\rho| = R,\rho') = 0 \tag{4}$$

The free energy per unit length can be now obtained in the standard form[11]

$$W = -\frac{kT}{N}\ln\left(\int\int G(\rho,\rho')\,\mathrm{d}^2\rho\,\mathrm{d}^2\rho'\right) \tag{5}$$

Assuming now that the external potential $\phi(\rho)$ is a slowly varying function of ρ, we can develop it around its minimum up to second order, obtaining

$$\phi(\rho) = \phi(R) + (1/2)\phi''(R)\rho^2 \tag{6}$$

In this approximation the equation for the Green function becomes analogous to the Schrödinger equation of a bounded two-dimensional harmonic oscillator. Problems of this kind have been extensively studied by Chandrasekhar[12] and Auluck and Kothari[13] in a different physical context. Here we shall mainly follow their approach. We now use the standard ground-state-dominance ansatz[14]

$$G(\rho,\rho') = \exp(-WN)\psi(\rho)\psi(\rho') \tag{7}$$

and introduce the dimensionless variables

$$\zeta = \zeta(\rho) = \left(\frac{\phi(R)}{2kT}\frac{\kappa^2 l^2}{6}\right)^{1/4}\kappa\rho \tag{8}$$

with

$$\kappa^2 = \phi''(R)/\phi(R) \tag{9}$$

(In the special case where the variation in potential ϕ at $r = R$ is given by the linearized Poisson–Boltzmann equation, the quantity κ is the inverse Debye–Hückel length. In general, it is the quantity defined by eq 9 for whatever potential ϕ is appropriate.) We then get the following equation for $\psi(\zeta)$

$$\frac{1}{\zeta}\frac{\mathrm{d}}{\mathrm{d}\zeta}\left(\zeta\frac{\mathrm{d}\zeta}{\mathrm{d}\psi}\right) - (w - \zeta^2)\psi = 0 \tag{10}$$

where w is closely connected with the free energy of the polymer (cf. eq 11) and is determined from the boundary condition eq 4 at the walls (i.e., $\psi(\zeta_0) = 0$, where ζ_0 is the value of ζ at the wall). The free energy follows as

$$W = w\left(\frac{\phi(R)}{2kT}\frac{\kappa^2 l^2}{6}\right)^{1/2} \tag{11}$$

With these notations the solution of eq 10 can be obtained as

$$\psi(\zeta) = e^{-\zeta^2/2}\Phi\left(\frac{1}{2} - \frac{W}{4}; 1; \zeta^2\right) \tag{12}$$

where Φ(a; b; c) is the standard degenerate hypergeometric function.[15] We shall not follow the derivation of the energy in detail since it follows in almost every respect the analysis of Auluck and Kothari.[13]

We can derive two different regimes of behavior of W as a function of R, or better as a function of ζ_0. However, if we take the experimental values for the hydration/electrostatic double-layer soft potential we can convince ourselves that in the whole range of experimentally accessible values of R, only the $\zeta^0 \to \infty$ is physically relevant. We therefore investigate the asymptotic properties of the solution of eq 12 in this limit, which leads to the following approximation

$$\psi(\zeta) \cong \frac{1}{\zeta^{1/2}} M_{w/4;\pm 1/4}(\zeta^2) \tag{13}$$

where M is the standard parabolic cylinder function.[15] Since $\psi(\zeta)$ of eq 13 has its first zero at ζ_0, the free energy is obtained in the following approximate form

$$W \cong \phi(R) + kT\left(\frac{\phi(R)}{2kT}\frac{\kappa^2 l^2}{6}\right)^{1/2}\left[1 + 2(8/\pi)^{1/2}\exp\left(-\frac{1}{2}\zeta_0^{\,2}\right)\zeta_0\right] \tag{14}$$

Clearly, the total free energy per unit length decouples into a "mean field" term, $\phi(R)$, plus a contribution of fluctuations around the mean position ($\rho = 0$). The remarkable feature of this relation is that the energy of the confined polymer is a sum of a term with the direct interparticle potential $\phi(R)$ itself and a term in the square root of that same potential. If, as is the case for electrostatic double layer or hydration forces,[3,4] $\phi(R)$ decays exponentially, then one expects the energy to decay either with the fundamental decay constant or with an apparent constant exactly one-half the fundamental value. This is what has been reported experimentally.[3,9]

The origin of electrostatic interactions is of course the fixed negative charges of the phosphate groups on the DNA backbone. After the counterions condense, a residual negative charge creates an electrostatic double-layer potential around the helix. This potential can be calculated within the framework of the Poisson–Boltzmann theory. We shall not follow the details of the derivation, extensively treated elsewhere (e.g., refs 8 and 16–18) but will instead use a simple form convenient for the present case.[16,17] At distances between molecules greater than the Debye decay length $\lambda_D = \kappa^{-1}$, the double-layer potential about each molecule takes on a form

$$\varphi(r) = \frac{\nu}{2\pi\epsilon\epsilon_0} K_0(\kappa r) \tag{15}$$

where $K_0(x)$ is the zero-order Bessel function of the second kind, r is the distance from the cylinder axis, ϵ is the dielectric constant, and ν is proportional to the density of charge on the molecule. An analogous equation can also be obtained in the formalism of the Marčelja theory[19] of the hydration forces, where the inverse hydration decay length replaces κ, while the magnitude is dependent on the extent of perturbation of water molecules at the surface of DNA.

The mutual energy of interaction per unit length between parallel molecules of radius a at a separation R is obtained as

$$\frac{\phi(R)}{l} = 2\frac{kT}{L_b}\xi^2 \frac{K_0(\kappa R)}{(\kappa a K_1(\kappa a))^2} \tag{16}$$

where L_b is the Bjerrum length and ξ is the dimensionless linear charge density defined as L_b/b, where b is the distance between the charges along the DNA backbone. In the limit of large (κa), this result would result in the limiting form used by Parsegian and Brenner[17] in their analysis of forces acting in TMV arrays. Equation 16 is for charges set at a radius a but again stated as hypothetical charges that set up a potential following the linearized PB equation.[3]

Experimentally, the free energy W/l *per unit length* of polymer is taken from the integral of the force per unit length versus separation as determined by osmotic stress measurements.[3,4]

Numerical Results

Before proceeding to test and to apply the *constrained random walk formula,* eq 14, *one must convince* one's self of the inapplicability of any flexible hard rod model. By quite general arguments, Helfrich and Harbich[6,21] have shown that the free energy needed to confine a flexible hard rod will have the form of an inverse 2/3 power of the effective diameter d_{eff} of an encasing tube. Later, Odijk[5-7] showed that the confinement basically acts to divide the polymer into statistically independent segments, each one deflection length long. He derived the deflection length for a sterically confined polymer in the form

$$\mathcal{L}_d^{\,3} = d_{\text{eff}}^{\,2}\mathcal{L}_p \tag{17}$$

where $\mathcal{L}_p$ is the persistence length of the polymer. The confinement free energy then follows as

$$F \cong kT\frac{L}{\mathcal{L}_d} \tag{18}$$

with L the total length of the polymer. (Both expressions follow conventions in the polyelectrolyte field; their use does not imply that we believe that the linearized equation gives more than a convenient language for codifying data and comparing parameters with their equivalents derived by other methods.) This is basically the same result as derived by Helfrich and Harbich. The force per unit length acting to confine a single polymer can be now obtained as

$$f(R) = \frac{2}{3}\frac{kT}{\mathcal{L}_p^{\,1/3}} d_{\text{eff}}^{\,-5/3} \tag{19}$$

The effective diameter is given as the polymer intersurface separation minus a distance corresponding to an extra effective exclusionary region of thickness $\alpha\lambda$, where λ is the decay distance of the underlying exponential repulsive force and α an adjustable parameter for setting the hypothetical "effective" rod diameter.

Attempts to fit the above formula to forces measured between polymers (Figure 3) *clearly show that the experimental* data belong to a different class of interaction potentials. This discrepancy was the original motivation for the present work to reconsider the interaction of densely packed polymers.

We may now proceed to compare the derived result, eq 14, with experimental data. In the physically relevant limit of large R the interaction free energy per unit length, W/l (cf. eq 14), can be approximated to sufficient accuracy by a simpler expression that neglects the extra confinement of a hard wall

$$\frac{W}{l} \cong \frac{\phi(R)}{l} + kT\left[\left(\frac{\phi(R)}{l}\right)\frac{\kappa^2 l}{12kT}\right]^{1/2} \tag{20}$$

(This simplification will also be verified below after comparison of the theoretical expression with measured forces versus separation. For cases of very soft potentials with consequent large spatial fluctuations of the central chain, one must, of course, retain the second term in the square brackets in eq 14.)

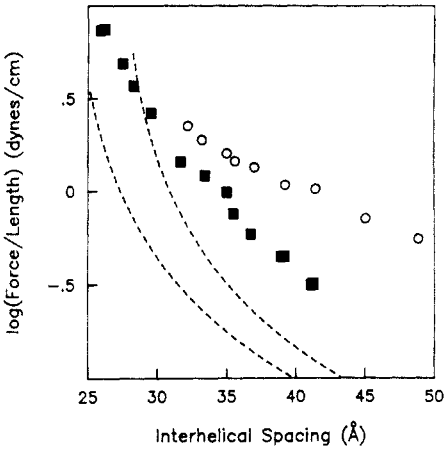

Figure 3. Failure of a flexible rod model to predict experimentally observed behavior. The data, for DNA in 1 and 0.2 M NaCl solutions, show two exponential decays and not the $(R - 2a - \alpha\lambda)^{-5/3}$ dependence that can be deduced from an equivalent hard elastic rod picture. λ was set equal to 3.14 or 6.7 Å and $\alpha = 1$, thereby mimicking the hydration or electrostatic forces,[3] respectively. Cylinder radius a was taken as 10 Å.

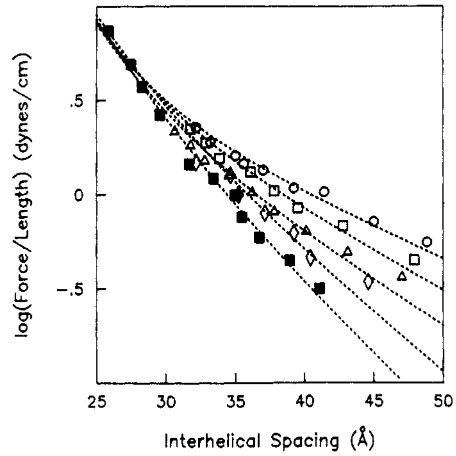

Figure 4. Repulsion between DNA double helices in NaCl solutions of concentrations 0.2, 0.3, 0.4, 0.8 and 2 M, fitted with the effective step length l = 40 Å by using eq 20 and the force curve in the high ionic strength case (I = 2 M), which clearly displays the mean-field and the fluctuation-enhanced region. This step length is very close to the 45-Å coherence length inferred directly from thermodynamic analysis of the experimental data on forces in DNA arrays.[3] The electrostatic parameters obtained from the fit via eq 16 to the low-salt region, where only the fluctuation-enhanced interaction potential is seen experimentally, are displayed in Table I.

Table I
Na-DNA Parameters[a]

I, M	λ_D, Å	b, Å
0.2	6.7	3.3
0.3	5.5	3.8
0.4	4.7	4.6
0.8	3.6	4.2

[a] Ionic strength I, Debye–Hückel decay length λ_D, and effective distance between the charges b for low-salt Na-DNA.

The experimental data are for the force per unit length, $f(R)$, acting between molecules in a hexagonal array.[3] In the effective tube model, this is equal to the derivative of interaction free energy per unit length, W/l, with respect to R. We recognize that only at large values of ionic strength ($I \geq 0.8$ M NaCl) can one measure a force curve that reflects the action of the same $\phi(R)$ throughout, both in the "mean-field" and fluctuation-enhanced regions. At these concentrations electrostatic double-layer forces are completely screened,[3] and $\phi(R)$ is an exponentially varying hydration force. At lower ionic strengths, the mean-field part of the measured force curves still corresponds to these powerful forces that dominate most interactions at ≤10 Å separation but the fluctuation-enhanced part of the force curve now reflects underlying electrostatic double-layer forces. The sensible thing to do is therefore to obtain the value of l from the set of high salt measurements and then use this value to extract the parameters describing the electrostatic interaction. This procedure is validated by a thermodynamic analysis showing that the independently fluctuating segment length does *not* depend crucially on the ionic strength.[3]

We begin then by examining data for forces between DNA double helices in NaCl solutions of greater than 0.8 M ionic strength. Above this concentration, where there is no sensitivity of forces to ionic strength; one is apparently observing forces of molecular hydration. One sees the two decay rates that would be predicted by eq 20. The points at shorter range give the direct potential $\phi(R)/l$; those at greater separation, with one-half the earlier decay rate, then provide a clean demonstration of the square-root term and a value, 40 Å, for the Gaussian step length. This value is effectively the same as the thermodynamic estimate of 45 Å for the fluctuating unit size[3] and is close to the corresponding values of Odijk's deflection length. From the magnitude of the soft potential in the range of relevant R, it is also clear that the ζ_0 term in eq 14 can be safely neglected.

At lower ionic strengths, the electrostatic double-layer force expected at shorter separations is overwhelmed by the more powerful hydration forces, but salt concentration dependent forces do appear at interaxial distances greater than 30 Å. In this long-range salt concentration dependent regime, the decay is close to half the expected Debye length, again showing the behavior expected from the square root term in eq 20. We use the second term in eq 19 with l = 40 Å to estimate the coefficient of the direct force potential $\phi(R)$. Then by eq 16 we turn the magnitude of the force potential into an effective linear charge density expressed through the effective distance b between the charges (cf. Table I). The actual fits to the data are presented in Figure 3 and clearly show the mean-field and the fluctuation-enhanced regions at larger values of R.

The forces measured have thus been described in terms of a linear charge density, b, for charges residing on the surface of a cylinder taken at 10-Å radius and computed from measured forces by the linearized Poisson–Boltzmann equation. Interested readers can convert the tabulated b so computed for other radii of charge location or other forms of the Poisson–Boltzmann equation.

Discussion

Though our model is deliberately simplified, it still retains all the essential features of the system revealed by the experiment.[3] These include the independently fluctuating unit of a size much smaller than the persistence length (≅600 Å for native DNA) and the reduction of the decay rate produced by the action of thermal fluctuations in the shape of the molecule.

Within the framework of our basically phenomenological random walk model, it is not possible to derive the step length from microscopic considerations. We expect, however, that a more detailed analysis taking into account the elastic bending energy as well as the actual full form of the interaction potential, and not only its small fluctuation expansion (cf. eq 6), can provide an independent estimate for the size of the Gaussian step. First, there is likely to be an association between our step length l and Odijk's[6] deflection length $\mathcal{L}_d$ (eq 17), which can be computed for d_{int} = 30–40 Å as $\mathcal{L}_d \cong$ 40–60 Å, close to the fitted step length or the thermodynamically obtained independently fluctuating unit size. Second, it has been observed experimentally[3] as well as in preliminary numerical simulations[22] that the effect of the bending stiffness on the properties of a confined polymer is small and probably indirect, as seen in the case of $\mathcal{L}_d$ that depends only weakly on $\mathcal{L}_p$.

In any event we circumvented the problem of choosing a step length a priori by connecting the predictions of our model with the results of experimental measurements on the forces between DNA molecules. The step length was deduced from the hydration force curve that clearly exhibits that bare and the fluctuation-enhanced regions. We used the step length so obtained also in the electrostatic regime, where only the fluctuation-enhanced region is observable and thus extracted the electrostatic parameters.

We are now aware of a new broad class of phenomena occurring in a polymer assembly. The qualitative truth of Onsager's early idea is still correct; packing is dominated by configurational entropic factors. But the operative changes in entropy are tightly coupled to slowly varying long-range forces between assembling particles. The continually varying interplay of these electrostatic double-layer or hydration forces and macromolecular disorder creates a variation between packing free energy and separation quite unlike predictions from earlier theories. In particular, it is now apparent that the unexpectedly slow variation of forces measured between muscle fibers[9] or TMV particles[20] might reflect changes in configurational disorder rather than anomalous decay of electrostatic double-layer potential fields. If one can obtain an independent estimate of the polymer configurational parameters (e.g., l in the case of our Gaussian model), it should be possible to derive far better estimates of the electrostatic double-layer potentials in these polymer assemblies.

We would therefore like to encourage further theoretical work that would take into account more microscopic features of the system, e.g., dealing appropriately with the elastic part in the hamiltonian, and may be leading to an estimation for the step size in terms of persistence length and soft potential parameters. Also it might be appropriate to put more effort into the numerical simulations of spacially constrained polymers in external confining fields.

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