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The effect of anisotropic bending elasticity on the structure of bent DNA

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Abstract

The response of a short DNA segment to bending is studied, taking into account the anisotropy in the bending rigidities. It is shown that due to the helical structure of DNA, the anisotropy in the bending rigidities can lead to the formation of kinks and modulations in the curvature, depending on the values of the elastic constants. The typical wavelength for the modulations, or the distance between the neighbouring kinks, is found to be set by half of the DNA pitch.

1. Introduction

The elastic description of the response of DNA to mechanical stresses has been developed over the past 20 years, taking on different approaches that include Lagrangian mechanics [1–3], statistical mechanics [4–6], and computer simulations [7, 8]. Motivated by the DNA structure in various DNA–protein complexes such as the one involving RNA polymerase [9] and nucleosomes [10, 11], we study the bending of short DNA segments using an elastic model. We assume that the length scale set by the helix pitch $P \simeq 3.4$ nm that involves ten base pairs is long enough that we can use a continuum elastic theory, and yet short enough that the spatial anisotropy of DNA matters. The elastic model of DNA is used with anisotropic bending rigidities [12], while neglecting the linear phenomenological twist–bend [13] and twist–stretch [14] couplings. Whereas an isotropic elastic model predicts uniform curvature for a bent rod, we find that due to the helical structure of DNA the anisotropy in the bending rigidity can lead to a variety of bending structures.

Depending on the relative strengths of the bending elastic constants, we observe three different regimes: (1) a regime in which curvature is localized in the form of kinks in a periodic arrangement, while the kinks are separated by virtually flat (rod-like) parts, (2) a regime with synchronized smooth modulations of the curvature, (3) a regime with a uniform curvature. These different 'forms' of bent DNA are presented in figure 1 below. We find that

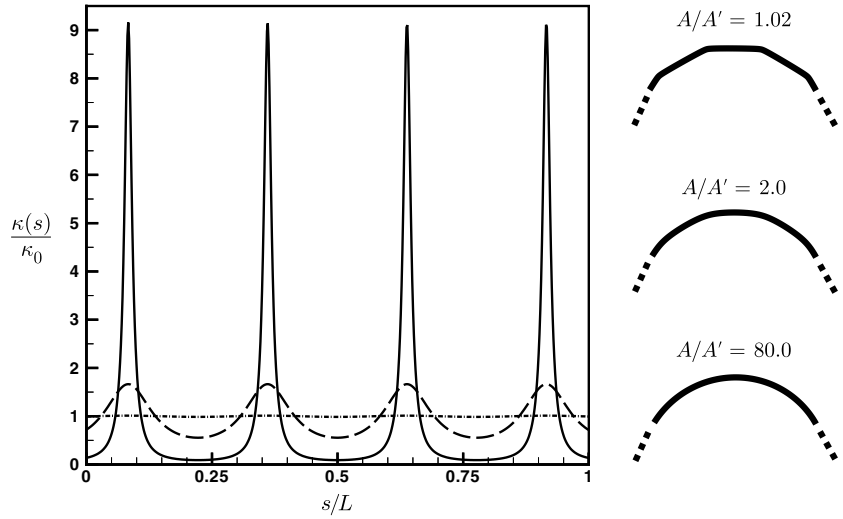

Figure 1. Different possible conformations of the DNA for various values of A/A'. The DNA length is 18 bp. The curvature is normalized by $\kappa_0 \equiv \theta_0/L$. The solid curve corresponds to $A/A' = 1.02$, the dashed curve corresponds to $A/A' = 2.0$, and the dash–dotted line corresponds to $A/A' = 80.0$. On the right, a schematic picture of bent DNA for various A/A' is shown.

the period of modulations as well as the distance between neighbouring kinks is always set by half of the DNA pitch, i.e. 5 bp, to a good approximation.

The rest of the paper is organized as follows. Section 2 describes the model that is used in studying the mechanical response of DNA. This is followed by the presentation of the results in section 3. Finally, section 4 concludes the paper.

2. The model

The elastic model of DNA represents the molecule as an elastic rod. The rod is parametrized by the arc length s, and at each point, an orthonormal basis is defined with $\hat{e}_1$, $\hat{e}_2$, and $\hat{e}_3$. In the undeformed state, the $\hat{e}_3$-axis becomes parallel to the rod, and $\hat{e}_1$ shows the direction from minor groove to major groove [15]. Therefore, due to the helical structure of the DNA, $\hat{e}_1(s)$ and $\hat{e}_2(s)$ rotate with the helix. The deformation of the elastic rod is then parametrized by a mapping that relates the local coordinate system to a reference one, specified by the Euler angles $\theta(s)$, $\phi(s)$, and $\psi(s)$. The elastic energy is written as [16]

$$\beta E = \tfrac{1}{2}\int_0^L \mathrm{d}s\,[A_1\Omega_1^2 + A_2\Omega_2^2 + C(\Omega_3 - \omega_0)^2], \tag{1}$$

in the dimensionless units, where A_1 and A_2 are the bending rigidities for the 'hard' and 'easy' axes of DNA cross section, C is the twist rigidity, and $\omega_0 = 2\pi/P = 1.85\ \mathrm{nm}^{-1}$ is the spontaneous twist of the helix. In terms of Euler angles, we have

$$\begin{aligned}
\Omega_1(s) &= \dot{\theta}\cos\psi + \dot{\phi}\sin\theta\sin\psi,\\
\Omega_2(s) &= -\dot{\theta}\sin\psi + \dot{\phi}\sin\theta\cos\psi,\\
\Omega_3(s) &= \dot{\psi} + \dot{\phi}\cos\theta,
\end{aligned} \tag{2}$$

where we have used $\dot{\theta} \equiv \frac{\mathrm{d}\theta}{\mathrm{d}s}$, $\dot{\phi} \equiv \frac{\mathrm{d}\phi}{\mathrm{d}s}$, and $\dot{\psi} \equiv \frac{\mathrm{d}\psi}{\mathrm{d}s}$.

We assume that the DNA is constrained to bend in a plane, and hence set $\phi = 0$. This assumption seems to be reasonable in the case of RNA polymerase, in view of its anticipated bending mechanism [9]. Similarly, the 1.9 Å resolution crystal structure of the nucleosome core particle containing 147 DNA bp reveals the conformation of the nucleosomal DNA [11]. There it is shown that the bending takes place in a confined geometry provided by the local structural binding of the core particles to DNA. The bending is characterized by an overall angle θ_0, and we assume that the bent segment of DNA is attached to undeformed tails, so it corresponds to bending of a piece of a long DNA. This gives us a constraint on the deformation of bent rod that can be written as

$$\int_0^L \mathrm{d}s\, \kappa(s) = \theta(L) - \theta(0) = \theta_0, \tag{3}$$

where $\kappa(s) \equiv \dot{\theta}(s)$ denotes the local curvature of the bent rod. Since the tails have a uniform twist characterized by ω_0, we assume that the twist at the two ends of the DNA segment is also ω_0, to preserve continuity. It has been shown that the twist of the bent DNA is not changed a lot and at the first order of approximation one can ignore the small changes in the twist [3]. Therefore, we assume $\frac{\mathrm{d}\psi}{\mathrm{d}s} \simeq \omega_0$, which gives $\psi(s) = \omega_0 s + \psi_0$, where ψ_0 is the initial twist angle that denotes the angle between the minor–major groove direction at the first point of the bent segment with respect to the plane of the bent rod.

After defining $A \equiv \frac{1}{2}(A_1 + A_2)$ and $A' \equiv \frac{1}{2}(A_1 - A_2)$ we have

$$\beta E = \tfrac{1}{2} \int_0^L \mathrm{d}s\, [A + A' \cos 2\psi] \kappa(s)^2. \tag{4}$$

We can find the extremum of βE by applying standard variational techniques to the above energy expression with respect to the constraint that is given by equation (3). The resulting Euler–Lagrange equation for $\theta(s)$ is found as

$$\kappa(s) = \frac{\lambda}{A + A' \cos(2\omega_0 s + 2\psi_0)}, \tag{5}$$

where λ is the Lagrange multiplier corresponding to the constraint on the curvature; the overall bent angle is θ_0.

3. The results

Using equations (5) and (3), one finds $\lambda = \frac{A'\omega_0}{I}\theta_0$, where I is defined as

$$I \equiv \int_{\psi_0}^{\omega_0 L + \psi_0} \mathrm{d}x\, \frac{1}{\frac{A}{A'} + \cos 2x}. \tag{6}$$

We should mention that I is a number depending on the various parameters, namely, the spontaneous twist, the overall length of the bent segment, the bending elastic modulus, and ψ_0. After some manipulation, the curvature and the total bending energy of the bent segment can be written as

$$\kappa(s) = \frac{\omega_0 \theta_0}{I} \frac{1}{\frac{A}{A'} + \cos(2\omega_0 s + 2\psi_0)}, \tag{7}$$

$$\beta E = \frac{1}{2} \frac{A'\omega_0}{I} \theta_0^2. \tag{8}$$

The mean bending rigidity A is known to be about 50 nm in the salt saturation limit [4]. While there are some estimates for the anisotropy in the bending rigidity [12, 17, 18] (see below), a direct experimental determination to this end is still lacking. Let us first study the

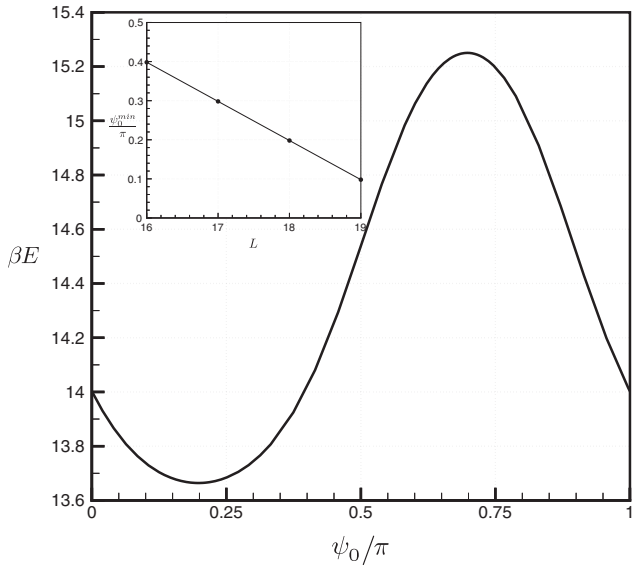

Figure 2. The bending energy as a function of ψ_0, which is determined by equation (8). This plot corresponds to $\omega_0 = 1.85\ \mathrm{nm}^{-1}$, $A' = 300$ Å, $\theta_0 = 120°$, and $L = 18$ bp. Inset: the dependence of $\psi_0^{\min}$ on the length of the bent segment L.

overall magnitude of the bending energy of the bent segment using equation (8) as a function of ψ_0 for various values of the anisotropic bending rigidity A' for several DNA lengths. In figure 2, the dependence of the bending energy βE on the initial twist angle ψ_0 is shown for the length $L = 18$ bp. The magnitude of the bending energy is calculated for $A' = 30$ nm, $\theta_0 = 120°$, and $\omega_0 = 1.85\ \mathrm{nm}^{-1}$. When the length is exactly equal to $nP/2$ bp, the value of I which is defined in equation (6) does not depend on ψ_0 and it is equal to $\frac{n\pi}{\sqrt{(A/A')^2-1}}$. Therefore the bending energy does not depend on ψ_0.

The bending energy of the bent DNA has a minimum at $\psi_0^{\min}$. In figure 2 (inset), the dependence of $\psi_0^{\min}$ on the bent segment length L is shown. It is worth mentioning that the behaviour does not depend on the other parameters of DNA such as the anisotropic bending rigidity A' and overall bending angle θ_0 and the spontaneous twist of the helix ω_0.

For each value of the DNA length, we find three distinct types of behaviour for various values of A/A', as presented in figure 1. All of these conformations correspond to $\psi_0^{\min}$ which give the lowest energy case. When the ratio of A/A' (which is by definition always greater than 1) is somewhat close to 1, the combination $A/A' + \cos(2\omega_0 s + 2\psi_0)$ could be close to zero, and then κ must be large. This corresponds to the kinks in the curvature. For intermediate values of A/A', the term $A/A' + \cos(2\omega_0 s + 2\psi_0)$ imposes periodicity and the curvature modulates along the length. When A/A' is very large, which corresponds to the isotropic rod, the curvature approaches a constant value. In figure (1), these different conformations are shown for length $L = 18$ bp for the lowest energy case which is determined by $\psi_0^{\min} \simeq \pi/5$.

One could ask how the conformation of bent DNA changes when the value of ψ_0 changes. For example, in the kink–rod structure regime, when the DNA length is between $5n$ bp and $5(n+1)$ bp with n being an integer number, the number and position of kinks are changed when ψ_0 is changed. For $\psi_0 = \psi_0^{\min}$, that is corresponding to the lowest energy in figure 2, the number of kinks is $n + 1$ and the kinks are located in the interior; however, the configuration of the rod has symmetry around the mid-point. When ψ_0 is getting larger, the number of kinks

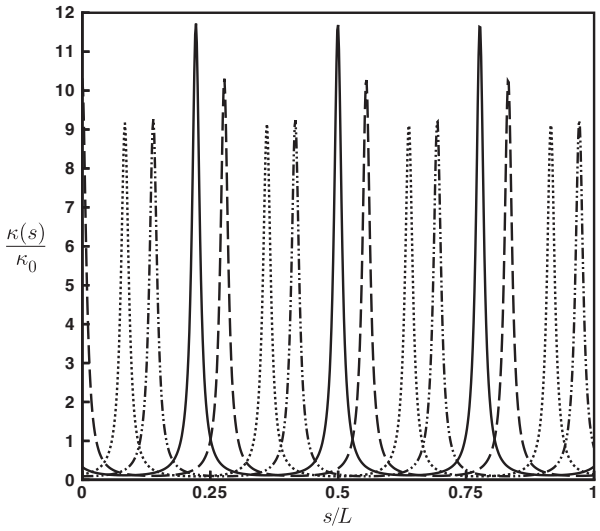

Figure 3. Different possible conformations of the DNA for various values of ψ_0 for $A/A' = 1.02$. The DNA length is 18 bp. The curvature is normalized by $\kappa_0 \equiv \theta_0/L$. The solid curve corresponds to $\psi_0 = \psi_0^{\min} + \pi/2 = 7\pi/10$, the dotted curve corresponds to $\psi_0 = \psi_0^{\min} = \pi/5$, the dashed curve corresponds to $\psi_0 = \pi/2$, and the dash–dotted curve corresponds to $\psi_0 = 0$.

does not change, but they move to the left. Therefore, the bent rod has no symmetry around its mid-point. For $\psi_0 = \psi_0^{\max}$, that is corresponding to the highest energy in figure 2, the number of kinks is n and the kinks are located in the interior and the rod has a symmetry around its mid-point. In figure 3, several conformations of bent DNA for various values of ψ_0 for $L = 18$ bp and $A/A' = 1.02$ are shown.

4. Discussion

In a recent high precision measurement, Richmond and Davey have determined the structure of the 147 bp DNA in the nucleosome core particle with 1.9 Å resolution [11]. They have observed that the structure of such highly bent DNA segments could be considerably different from the normal B-DNA form, and, in particular, that modulation patterns exist in the curvature profile of the bent DNA. Interestingly, they find that the period of this structure is set by half of the DNA pitch, 5 bp, to a good approximation, which is in agreement with the predictions of the present theoretical analysis. A detailed quantitative comparison to the findings of the experiment will be presented elsewhere [18].

In conclusion, we have studied the response of a finite DNA segment to bending, taking into account the anisotropy in the bending rigidity. We have shown that the anisotropy in bending rigidity can lead to formation of kink–rod patterns and modulations in the curvature. This effect may be related to the recent observation with high resolution x-rays, that DNA is not uniformly bent around the histone octamer and its curvature is larger at some places in the nucleosome [10, 11].

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