Can pulling cause right- to left-handed structural transitions in negatively supercoiled DNA double-helix?

Zhou Haijun
Institute of Theoretical Physics, Academia Sinica, P.O. Box 2735, Beijing 100080, China
State Key Lab. of Scientific and Engineering Computing, Beijing 100080, China

Ou-Yang Zhong-can
Institute of Theoretical Physics, Academia Sinica, P.O. Box 2735, Beijing 100080, China
(February 1, 2008)

The folding angle distribution of stretched and negatively supercoiled DNA double-helix is investigated based on a previously proposed model of double-stranded biopolymers (H. Zhou et al., Phys. Rev. Lett. 82, 4560 (1999)). It is shown that pulling can transit a negatively supercoiled DNA double-helix from the right-handed B-form to a left-handed configuration which resembles DNA Z-form in some important respects. The energetics of this possible transition is calculated and the comparison with recent experimental observations is qualitatively discussed.

Because of its vital biological significance, the elasticity of DNA has invoked considerable interest during recent years, and it is now known experimentally that radical transitions in DNA internal structure can be induced by the action of mechanical forces and/or torques. For example, pulling a DNA chain with a force of 70 piconewtons (pN) will convert DNA standard B-form conformation into a over-stretched S-form and at the joint action of a positive torque and a force about 3 pN a DNA will take on a novel P-form with exposed bases. Here we suggest a further possibility for this transition scenario and show that under-twisted (negatively supercoiled) DNA can take on a left-handed configuration under the action of a moderate stretching force. Such a left-handed conformation is found to resemble DNA Z-form in some important respects. The energetics of this possible transition is calculated and a qualitative comparison with very recent experiments is also performed.

The extension vs supercoiling relation for under-twisted DNA is studied based on a model proposed earlier (see Fig. 3a). For small pulling forces (\(\leq 0.3\) pN), a supercoiled DNA can shake off its twisting stress by writhing its central axis and forming plectonemic structures. However, this leads to shortening of DNA end-to-end distance and hence becomes very unfavorable as the force increases. At this stage, the torsional stress caused by supercoiling begins to unwind the B-form double-helix and triggers the transition of DNA internal structure, where a continuously increasing portion of DNA takes on some certain new configuration as supercoiling increases, while its total extension keeps almost invariant.

Information about the new configuration can be revealed by the folding angle \(\phi\) distributions \(P(\phi)\). This distribution is calculated by

\[
P(\phi) = \int \Phi^2(t, \phi)dt,
\]

where \(t\) is the tangent vector of DNA’s central axis and \(\Phi(t, \phi)\) is the (normalized) ground-state eigenfunction of the Green equation Eq. (9) in Ref. 8. The folding angle distribution (Fig. 4a) has the following aspects: When the torsional stress is small (with the supercoiling degree \(|\sigma| < 0.025\)), the distribution has only one narrow and steep peak at \(\phi \approx +57.0^\circ\), indicating that DNA is completely in B-form. With the increase of torsional stress, however, another peak appears at \(\phi \approx -48.6^\circ\) and the total probability for the folding angle to be negatively-valued increases gradually with supercoiling.

Since negative folding angles correspond to left-handed configurations, we can conclude that, with the increasing of supercoiling, left-handed DNA conformation is nucleated and it then elongates along the DNA chain as B-DNA disappears gradually. The whole chain becomes completely left-handed at \(\sigma \approx -1.85\).

It is worth noticing that, (i) as the supercoiling degree changes, the positions of the two peaks of the folding angle distribution remain almost fixed and, (ii) between these two peaks, there exists an extended region of folding angle from 0 to \(\pi/6\) which always has only extremely small probability of occurrence. Thus, a negatively supercoiled DNA can have two possible stable configurations, a right-handed B-form and a left-handed configuration with an average folding angle \(\approx -48.6^\circ\). A transition between these two structures for a DNA segment will generally lead to an abrupt and finite variation in the folding angle.

The sum of the average base-stacking energy and torsional energy caused by external torque (see caption of Fig. 3b) as a function of torque \(\Gamma\) is shown in Fig. 3a and the relation between \(\sigma\) and \(\Gamma\) in Fig. 3b. From these figures we can infer that, (i) for negative torque less than the critical value \(\Gamma_c \approx -3.8\) k_B T, DNA can only stay in B-form state; (ii) near \(\Gamma_c\) DNA can either be right- or be left-handed and, as negative supercoiling increases (see Fig. 3b) more and more DNA segments will stay in the left-handed form, which is much lower in energy (\(\approx -2.0\) k_B T per base pair (bp)) but stable only when torque
reaches $\Gamma_c$; (iii) for negative torque greater than $\Gamma_c$ DNA is completely left-handed. B-form DNA at $\Gamma_c$ has energy about 0.0 kBT per bp, indicating that the work done by external torque just cancels the base-stacking energy. Therefore, it might not be enough to further break the hydrogen bonds between DNA complementary bases and cause denaturation. Nevertheless, since the transition from right- to left-handed structure requires radical rearrangement of DNA base pairs, the possibility of transient denaturation in DNA double-helix can not be ruled out. This is a subtle question, and maybe transient denaturations can occur in the weaker AT-rich regions, or even be induced and then captured by the added homologous single-stranded DNA probes in the solution.

For the left-handed state revealed by Figs. 1b and 2 we have obtained that, at $\Gamma = -4.0$ kBT (where DNA is completely left-handed) the average rise per bp is about 3.83 Å, and the pitch per turn of helix is 46.76 Å, with the number of bps per turn of helix being 12.19. Notice these characteristic quantities are very similar with those of DNA left-handed Z-form, which are 3.8 Å, 45.6 Å, and 12 bps, respectively. We suspect that the identified left-handed configuration belongs to DNA Z-form. Recently, Léger et al. also pointed out that Z-form structure should be included to qualitatively interpret their experimental result.

---

**FIG. 1.** a, DNA extension vs supercoiling degree. The supercoiling degree $\sigma$ is defined as $\sigma = (lk - lk_0)/lk_0$, where $lk_0$ and $lk$ are, respectively, the linking number of a relaxed and a torsionally constrained DNA. Experimental data (symbols) are from Ref. 4. b, folding angle distributions for a DNA pulled with a force of 1.3 pN. Here, the folding angle $\varphi$ is defined in the range from $-\pi/2$ to $\pi/2$, with negative (positive) values corresponding to left (right)-handed configurations.
FIG. 2. a, The sum of average base-stacking and torsional energy per base pair at force 1.3 pN. For highly extended DNA only these two interactions are sensitive with torque. The torque-related torsional energy density is $\mathcal{E} = -\Gamma \sin \varphi / R$, where $R$ is DNA molecular radius. b, The relation between DNA supercoiling degree and external torque at force 1.3 pN.