

## Influence of Supercoiling on the Disruption of dsDNA

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**U**nzipping of double-stranded DNA (dsDNA) as a prelude to transcription is a basic process of life.

There are presently two mechanisms that are considered for modeling this phenomenon. One is the Peyrard-Bishop model, in which localization of energy via a Fermi-Pasta-Ulam scenario of coupled nonlinear oscillators causes thermal bubbles to form spontaneously at specific locations along a dsDNA chain. The other mechanism is modeled by representing proteins, which cause unzipping, as an external force. This latter class of models envisions dsDNA as composed of coupled flexible Gaussian chains. It may be a reasonable approximation to treat a long semiflexible chain as an effective Gaussian chain with the monomer length substituted by the persistence length in order to investigate global characteristics. But a realistic attempt to treat the unzipping process through the application of an external force to a small region of the dsDNA must necessarily take into account the semiflexible nature of the system.

There is an additional outstanding issue that complicates our understanding of the unzipping of dsDNA. It arises through the observation that one can estimate the base-pair force as  $\sim O(100 \text{ pN})$ , while the experimentally observed minimum (external) disruptive force is only of the order of  $\sim O(10 \text{ pN})$ . Thus there would appear to be an intrinsic source of energy that allows the dsDNA to overcome this mismatch. What subtle mechanism comes into play during base-pair separation to explain this mismatch?

Supercoiling is an ubiquitous feature of semiflexible rods. One might conjecture that supercoiling plays a role in the packing of dsDNA. We can make the case that supercoiling energy can have an appreciable effect on this phenomenon, by providing extra energy to overcome the free energy barrier to disruption.

Benham was the first to suggest a phenomenological model to describe the influence of supercoiling on base-pair disruption. Benham's seminal model is an effective single-strand helical representation of DNA. He obtained the parameters for his (nonlinear) Ising-like model by calibrating it to one set of DNA data, then verified that the same choice of parameters worked for another experiment.

The model developed in this paper provides a deeper and more detailed, analytical insight into the mechanism of base pair disruption in dsDNA. Marko and Siggia described the supercoiling of DNA by appealing to an evocative image of an over-twisted shoelace. The analogy that best describes the results of our model is that dsDNA is like a ladder made out of bamboo. If the ladder is twisted beyond its normal, equilibrium planar state, one can imagine that it would be easier to break the rungs.

We assert that this is precisely what happens in dsDNA. Supercoiling, or over-twisting, energizes the dsDNA, making it more likely that thermal fluctuations will cause a given base-pair to be disrupted. Our theory provides qualitative insight into the experimental observations that superhelicity can make pBR322 DNA and *E. coli* duplex unwinding elements susceptible to strand separation even if the over-twisting spans only a few base-pairs. This phenomenon is called stress induced duplex destabilization.

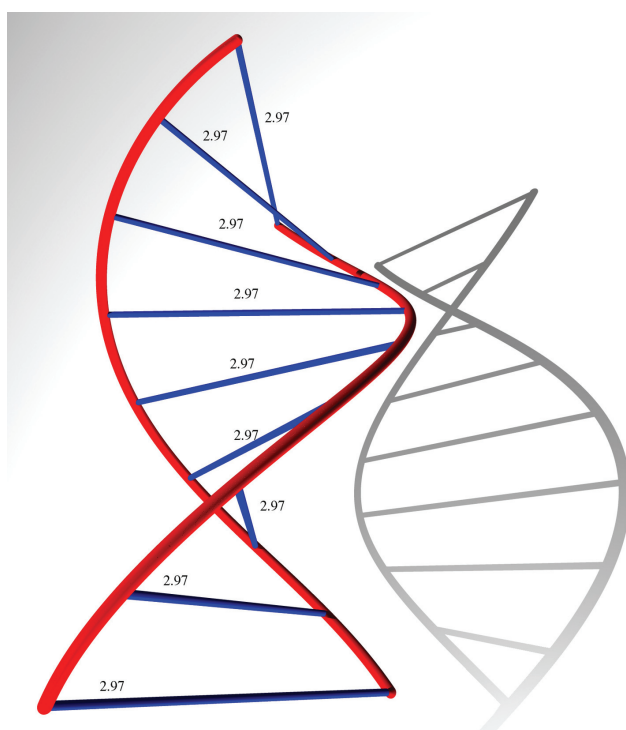
We have attached two figures that show how supercoiling can lead to localized distension of a modeled dsDNA. The first figure shows a putative segment of

dsDNA undistorted and in equilibrium. The second displays how supercoiling can lead to localized distension of bonds.

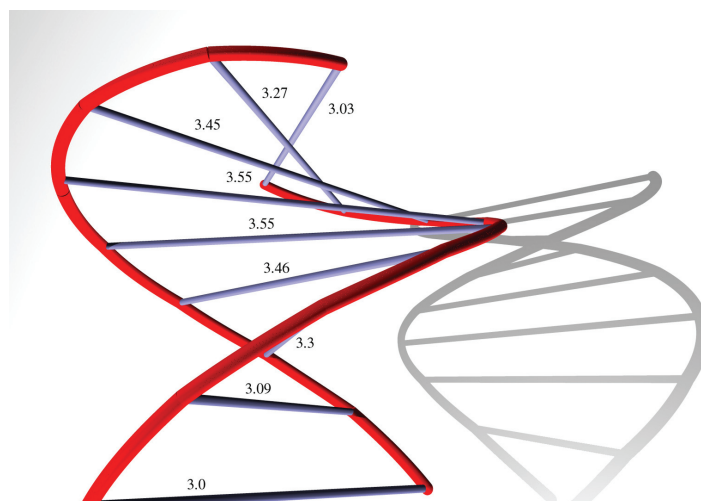
A paper on this subject was recently published [1]. It was also selected to appear in the *Virtual Journal of Biology* as reflective of papers at a research frontier.

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[1] S.M. Chitanvis and P.M. Welch, *J. Chem. Phys.* **123**, 124901 (2005).



**Fig. 1.**  
*A putative segment of dsDNA undistorted and in equilibrium.*



**Fig. 2.**  
*How supercoiling can lead to localized distension of bonds.*