HIGH FLEXIBILITY OF DNA ON SHORT LENGTH SCALES PROBED BY ATOMIC FORCE MICROSCOPY

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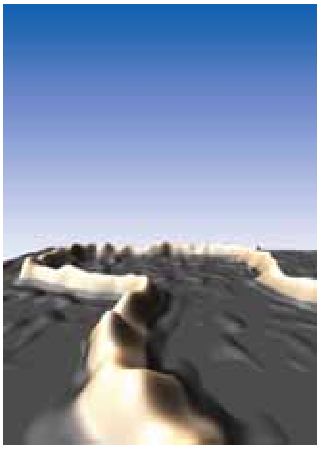
DNA bending on length scales of 5–100 nm plays a key role in many cellular processes [1]. The wormlike chain model (WLC) has come to dominate physical discussions of DNA mechanics [2]. We argue, however, that WLC's success depends on the long length scales probed by classic experiments such as force spectroscopy on single DNA molecules. Using high-resolution atomic force microscopy (AFM) on single DNA molecules of random sequence, we deduce the energy versus bending angle relationship appropriate for biologically relevant length scales (down to 5 nm). We formulate a very different, but equally simple, mathematical model of DNA mechanics that unlike WLC, simultaneously succeeds at describing all our AFM data across a wide range of length scales. Our measurements imply that the configurational free energy of highly bent DNA conformations, for example those observed in protein-DNA complexes, is significantly lower than predicted by harmonic elasticity models such as WLC [3].



Additional work, done on unusual but natural hyperperiodic DNA sequences, shows that sequence also plays a role in the mechanical properties of DNA. Hyperperiodic sequences from *C.elegans* adopt a more compact coil structure and, while their flexibility is retained, hyperperiodic DNA shows long-scale intrinsic bending[4]. It appears, therefore, that regions of the *C.elegans* genome display a significant correlation between DNA sequence and unusual mechanical properties.

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2. Bustamante, C., et al., *Single-molecule studies of DNA mechanics.* Curr Opin Struct Biol, 2000. **10**(3): p. 279-85.
3. Wiggins, P.A., et al., *High flexibility of DNA on short length scales probed by atomic force microscopy.* Nature Nanotechnology, 2006. **1**: p. 137-141.
4. Moreno-Herrero, F., et al., *Structural analysis of hyperperiodic DNA from Caenorhabditis elegans.* Nucleic Acids Res, 2006. **34**(10): p. 3057-66.