Dynamics of Double-Stranded DNA

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We introduce a Monte Carlo technique that allows accurate simulations of the dynamics involved in forced unzipping of double-stranded DNA as modeled by the Peyrard-Bishop-Dauxois model.

First, we show [1] that our results agree quantitatively with experimental results for homogeneous DNA, and for λ-phage DNA by reproducing the recently obtained experimental force-temperature phase diagram. Based on this agreement with experimental results and the insight the model gives us we argue that there may be fundamental and important differences between *in vivo* and *in vitro* DNA unzipping.

Second, using our method we systematically analyze fundamental limitations [2] on the viability of using mechanical unzipping of DNA as a fast and inexpensive sequencing method. Standard unzipping techniques, where double-stranded DNA is unzipped through the application of a force at one end of the molecule, are shown to be inadequate. Emerging techniques that unzip DNA by local force application are more promising, and we establish the necessary experimental requirements that must be met for these techniques to succeed as single molecule sequencing tools.

Finally, we consider DNA hairpin dynamics [3]. We present new measurements of the opening rate of single DNA hairpin loops for different applied mechanical forces, and compare with previous experiments. The force field brings the opening rate of otherwise very stable bonds into an experimentally accessible regime, allowing comparison of the dynamics for a range of hairpin structures with zero-force opening rates differing by many orders of magnitude. It then becomes apparent that the canonical approach of extrapolating finite force rates to zero force assuming a simple barrier hopping dynamics yields results which are completely inconsistent between the different experiments. Using our methodology to simulate the different experiments, we trace the inconsistencies in the measured lengthscale, representing the position of the transition state in the energy landscape, to the different data analysis methods of the different experiments.

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[1] *Probing the Mechanical Unzipping of DNA*, N.K. Voulgarakis, A. Redondo, A.R. Bishop, and K. Ø. Rasmussen, Phys. Rev. Lett. **96**, 248101 (2006).

[2] *Sequencing DNA by dynamic force spectroscopy: limitations and prospects*, N.K. Voulgarakis, A. Redondo, A.R. Bishop, and K. Ø. Rasmussen, Nano Letters **6**, 1483 (2006).

[3] *Opening rates of DNA hairpins under tension*, J. Hanne and G. Zocchi, N. Voulgarakis, A. R. Bishop, K. Ø. Rasmussen (submitted 2006).