Kinetics of Force-Induced DNA Melting.

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The nature of the cooperative phase transition induced by force applied to the opposite ends of torsionally relaxed double stranded (ds) DNA at ~65 pN remains controversial. One model suggests that this is the transition from B-DNA to 1.7-fold longer double stranded S-DNA. The alternative picture argues that this is simply the DNA strand-separation, i.e. DNA force-induced melting (FIM). Historically, the major argument in favor of B-to-S transition was kinetic. Thus, the apparently pulling rate-independent force plateau was associated with the fast B-to-S transition, while the last ~10-20% of DNA elongation prior to strand separation happening at strongly rate-dependent forces far exceeding the equilibrium transition force were attributed to DNA melting from its S-state.

This work theoretically considers kinetics of the DNA FIM. We interpret the rate-dependent high forces of final DNA strand separation as DNA "ripping", in contrast to equilibrium DNA melting, that happens at pulling rates < v^*~1000 nm/s. Such "ripping" happens when the terminal DNA base pair (bp) is forced to open with the rate higher then it's natural opening rate $k^*=v^*/\Delta x \sim 10^4$ s^{-1} (where Δx~0.2 nm is the bp elongation upon melting). k^* is significantly smaller then the bp opening rate for the thermal melting transition ~10^6 s^{-1}. This happens, because, in contract to the temperature, that destabilizes duplex DNA by increasing bp opening rate, the force destabilizes duplex DNA by slowing its closing. Quantitative analysis of the pulling rate dependence of strand separation force yields the characteristic bp elongation associates with its opening, x_{op}~0.05 nm « Δx. Thus, very high DNA strand separation forces at high pulling rates come from the poor ability of the force to facilitate bp opening beyond its natural rate k^*. In contrast to the equilibrium FIM of DNA, the non-equilibrium "ripping" is expected to be sensitive to the DNA strand attachment (i.e. 3'3' vs 5'5'), as indeed was observed in several recent experiments.

Furthermore, we predict that for the slow DNA pulling rates $\nu \ll \nu^*$, the majority of bp will open inside the ds DNA starting with long regions of relatively low stability. The melting force for such process is expected to be very weakly rate-dependent. Such inside DNA melting can happen despite of the free energy preference for melting from the ends, and due to the heterogeneity of the bp stability. The later is expected to make the end - melting of sufficiently long random heteropolymeric DNA at the equilibrium average melting force infinitely slow. We show, however, that this inside melting can dominate only in solutions of high ionic strength, when the mutual repulsion between the two melted strands within the bubbles is well screened. In lower salt, or at higher DNA puling rates approaching v^*, DNA melting is expected to switch to the free DNA ends or nicks, and to become more pulling rate dependent. Finally, once the pulling rate significantly exceeds the critical rate, i.e. for $v \gg v^*$, the transition force is expected to switch into the strongly rate-dependent "ripping" mode. This "ripping" mode for the transition midpoint force is similar to the "ripping" mode for the final strand separation, except that the later sets in at much lower pulling rates, since only a few helix/coli boundaries survive the end of strand separation transition.