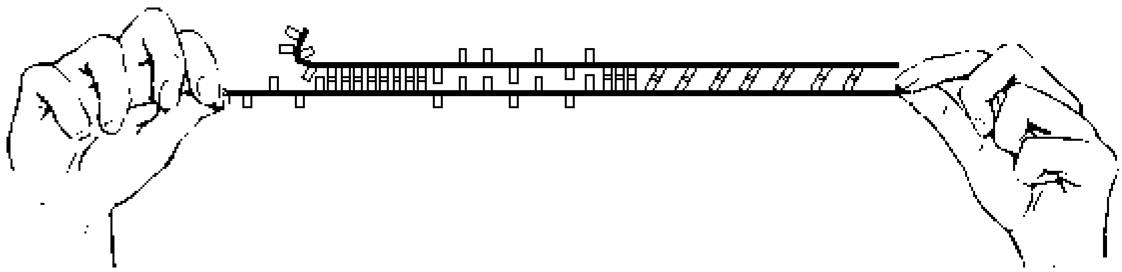
NUS and SMART Researchers revealed three distinct structural reorganizations of DNA by mechanical stretching

To perform its multiple functions, double-strand DNA (dsDNA) can undergo transitions to multiple structures. It was reported in 1996 that torsion-unconstrained dsDNA could undergo structural reorganizations when it was placed under sufficiently large tension (1,2). Since then, it has been debated on the possible structures that can be induced by applying large tension on torsion-constrained ds DNA. Three possible structures, 1) a single-stranded DNA (1ssDNA) under tension, 2) two parallel, separated ssDNA strands (2ssDNA) under tension, and 3) a new form of dsDNA termed "S-DNA", have been proposed. However, to demonstrate which of these structures actually formed in the experiments is challenging, as any external perturbations used to probe the overstretched structures will affect their respective stabilities and therefore the resulting interpretation of experiments.

In a series of recent studies led by Jie Yan (NUS investigator of Singapore-MIT Alliance for Research and Technology (SMART)), Fu et al. reported that multiple transitions existed, whose selections depended on exact experimental conditions (3-4). In a more recent collaborative research led by Jie Yan, NUS investigator of SMART, and Patrick Doyle, MIT investigator of SMART, Zhang et al. reported the first single-molecule calorimetric measurement for the structural transitions of torsion-unconstrained dsDNA induced by large tension (5). In that work, in addition to a transition to the 1ssDNA structure associated with large negative entropy change expected from DNA melting, another transition associated with a small positive entropy change was identified. The remained question is whether this latter transition indicates the formation of the 2ssDNA state, or the S-DNA state, or both.

In their most recent work (6), which is published in PNAS back-to-back with another study by King et al. (7), this question was answered. They demonstrated that all the three DNA structures, 1ssDNA, 2ssDNA, and S-DNA, could form through distinct transitions whose selections were dependent on the solution factors that affect DNA base pair stabilities. The transitions to the 1ssDNA and 2ssDNA structures are associated with DNA melting-like positive entropy changes, while the transition to the S-DNA structure is associated with the small positive entropy change. The small negative change in the transition to the S-DNA suggests that the S-DNA is a double-stranded, highly ordered structure. Further, the mechanical and thermo dynamical properties of the three overstretched DNA structures were fully characterized. In addition to bringing clarity to this 17-years of scientific debate, these results raise a new question regarding the possible physiological functions of the respective transitions, in particular, the B-to-S transition that leads to the formation of the mysterious S-DNA.



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