

NUS research published novel findings on DNA overstretching in the Proceedings of the National Academy of Sciences (PNAS)

Research led by Yan, associate professor at the department of physics and principal investigator at MBI, NUS, reveals the intricacies of DNA mechanics in highly sensitive single-DNA stretching experiments. A series of latest findings from the Yan lab, published in *Nucleic Acids Research* and PNAS, reveal how DNA undergoes perplexing structural transitions when subjected to large forces. This transition, termed overstretching, has been a topic for debate for many years due to the uncertainty over precisely what structural changes result from it. Work from the Yan lab finally sheds some light on the conflicting experimental findings in this field.

Yan Lab Research: Stretching DNA

A/P Yan studies how B-DNA, the predominant form of DNA found in living organisms, changes in structure in response to force. Overstretching of DNA, which leads to DNA elongation by ~ 1.7-fold, has in some experiments been suggested to transform B-DNA into single-stranded DNA, whilst in others has been suggested to likely produce a novel form of double-stranded DNA termed S-DNA. Results from the Yan lab show that overstretching does in fact bring about both of these conformations depending on minor changes in the physiological environment [1,2].

Latest Findings: New Insights from Thermodynamics

In collaboration with Patrick Doyle from the Singapore-MIT Alliance for Research and Technology, Yan and colleagues now report the first simultaneous determination of the entropy and enthalpy changes that occur during DNA overstretching [3]. High-resolution measurements of the thermodynamic changes that occur during these conformational changes highlighted key differences during the production of S-DNA versus single-stranded DNA. In addition to bringing clarity to this 16-year of scientific debate, these results provide important insights to the structure of the mysterious double-stranded S-DNA. They also lay the foundations for further research into the possible physiological roles and applications of S-DNA.

Publications

1. Fu, H., Chen, H., Marko, J.F. and Yan, J. Two distinct overstretched states. *Nucleic Acids Research*, 2010, 38(16), 5594-5600.
2. Fu, H., Chen, H., Zhang, X., Qu, Y., Marko, J.F. and Yan, J. Transition dynamics and selection of the distinct S-DNA and strand unpeeling modes of double helix overstretching, *Nucleic Acids Research*, 2011, 39, 3473-3481.
3. Zhang, X., Chen, H., Fu, H., Doyle, P. S., and Yan, J. Two distinct overstretched DNA structures revealed by single-molecule thermodynamics measurements, *PNAS*, 2012. In press (published online on April 24, 2012 [[doi:10.1073/pnas.1109824109](https://doi.org/10.1073/pnas.1109824109)]).