Structural basis of pathway-dependent force profiles in DNA

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It is widely recognized that for DNA to perform many of its important functions it must bend and/or stretch. Therefore, understanding the mechanical properties of DNA is necessary to more completely comprehend the dynamic behavior of DNA. Over the past decade and a half single molecule experiments have been developed which study the response of DNA to applied forces. One particularly interesting result is that at high loading rates a greater force is required to stretch DNA when pulling from the 3' ends as opposed to the 5' ends. While these experiments have provided valuable insights into the stability of DNA, it is often not possible to relate the experimental data to specific structural changes. We have used molecular dynamics (MD) simulation methods to study the structure and dynamics of DNA under a tensile load. A combination of MD simulations of end-to-end stretching using either constant force or constant velocity and umbrella sampling simulations were performed on a variety of DNA sequences up to 30 base-pairs in length. Different stretched DNA structures are observed depending on whether pulling occurs from the 5' ends or 3' ends. Detailed analysis of these structures provides a direct structural explanation of the observed difference between 3' and 5' pulling.