

Nanomechanics of single and double stranded DNA

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We use atomic force spectroscopy to examine the fundamental mechanical properties of single and double stranded DNA and we also attempt to apply this methodology for developing nanoscale DNA diagnostics. While measuring the elasticity of synthetic single-stranded DNA homopoly-deoxynucleotides, poly(dA) and poly(dT), we determined that as expected, poly(dT) exhibited the simple entropic elasticity behavior. However, poly(dA) unexpectedly displayed two overstretching transitions in the force-extension relationship. We suggest that these transitions, which occur at ~23 pN and ~113 pN directly captured the mechanical signature of base-stacking interactions among adenines in DNA, in the absence of base-pairing. Using a similar experimental approach we observed solvent driven structural transitions within polyadenylic acid, poly(A). Both AFM imaging and pulling measurements revealed complex strand arrangements within poly(A) induced by acidic pH conditions, with a clear fraction of double stranded molecules that increased as pH decreased. These molecules displayed the plateau transition forces similar to the BS transition previously observed for native double-stranded DNA (dsDNA). These results strongly suggests that in acidic pH conditions poly(A) can form duplexes that are mechanically stable. We hypothesize that under acidic conditions, similar structures may be formed by the cellular poly(A) tails on mRNA.

DNA mechanics critically affects the fundamental biological processes of transcription, replication, recombination and repair. We hypothesized that UV damage to DNA affects DNA mechanics and such alterations may have a detrimental effect on these fundamental DNA transactions. We used atomic force spectroscopy to investigate the effects of UV radiation on the mechanics of individual DNA duplexes. We find that the characteristic B-S plateau in the force spectrograms of irradiated DNA shortens in a UV dose dependent manner as compared to untreated DNA. The effect is stronger for homopolynucleotides such as polydA-polydT and polydG-polydC than for native DNA such as lambda-phage DNA. These mechanical effects likely represent the local unwinding of the double helix caused by a massive formation of pyrimidine dimers and (6-4) lesions. We propose that simple stretch-release measurements on individual DNA duplexes may have a diagnostic value.

Finally, we note that in atomic force spectroscopy, it is tacitly assumed that the pulling direction coincides with the end-to-end vector of the molecule fragment being stretched. By systematically varying the position of the attachment point on the substrate relative to the AFM tip, we investigated empirically and theoretically the effect of the pulling geometry on force-extension characteristics of double-stranded DNA. We found that increasing the pulling angle can significantly lower the force of the characteristic overstretching transition and increase the width of the plateau feature beyond the canonical 70%. We caution that these effects, when neglected, can adversely affect the interpretation of measured force-extension relationships of DNA and other molecules.