Simulating the interaction of sequence and writhing in nucleic acids

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Abstract

Under many biologically important circumstances, DNA and RNA are subject to topological constraints which exert superhelical stress on the molecule. As common response modes, known to exist in both bacterial and eukaryotic chromosomes [1], nucleic acids can writhe to form plectonemes, or undergo doube-strand denaturation. Both mechanical [2,3,4] and more recently also dynamical [5] properties of denaturation bubbles and plectonemes have been measured on a single-molecule level using optical and magnetic tweezer assays.

Here, we use recently developed coarse-grained models of DNA and RNA to complement experimental observations and study the influence of the base-sequence on plectoneme structures in silico. Good agreement with experimental data is observed. We find that for biologically relevant levels of supercoiling and linear tension, double-strand denaturations occur which are strongly co-localised with plectoneme end-loops [6].

We predict that plectoneme structures therefore preferentially localise in weak, AT or AU-rich regions of the base sequence. By this mechanism, local sequence properties can influence the conformational state of the double strand on a scale much larger than an individual base pair. Coupling of global writhe and local denaturation sheds new light on possible mechanisms for processes common in superhelically stressed DNA, such as genome organization, topoenzyme action or the regulation of DNA-protein interactions [7].

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