

THE SLENDER MECHANICS OF DNA AND ITS MANY ROLES IN BIOLOGY

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DNA is arguably one of the most slender “structures” in existence. At the molecular level, this long-chain biopolymer has a contour length that is seven orders of magnitude greater than its diameter and it must achieve an organized, ten thousand-fold compaction merely to ‘fit’ within the micron-sized dimensions of the cell nucleus. In nature, this amazing molecule is subject to considerable bending and twisting, often through the actions of numerous proteins. At these length scales, the energetic cost of bending and twisting (strain energy) is significant in that it may rival or even exceed the available thermal energy. Thus, understanding the functioning of DNA in the cell naturally requires a fundamental knowledge of how the molecule becomes bent and twisted.

We will open this talk by reviewing the basic chemistry, length scales, and functions of DNA in the cell. We will learn that major DNA functions (e.g., compaction in forming chromatin, gene transcription, replication and repair) are intricately linked to DNA ‘structure’. By structure, we refer to the topology and energetics of the molecule and on multiple length scales. Following this introduction, we shall explore the structure of the molecule by first introducing a mechanics-based ‘rod’ model for the nonlinear, two-axis bending and torsion of the DNA double helix. A computational form of this model will then be used to examine canonical deformations of the molecule including DNA supercoils and loops. One example will focus on the twisting of the molecule into interwound supercoils known as plectonems. A second example will include the looping of the molecule by regulatory proteins. In particular, we shall predict the DNA loops for wild-type and mutated forms of the so-called lactose-repressor protein from the bacterium *E. coli*. We will close by critically comparing these predictions to the experimental evidence now available in the literature.