Predictive Models for Atomic to Continuum Modeling of DNA Molecules

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ABSTRACT

Understanding the complex biophysical function and mechanical behavior of life's most important macromolecule at scales spanning from atomic to continuum is of critical importance to life science. Development of predictive computer simulation tools for biological processes which are difficult or impossible to observe experimentally is the key to the life science advancement. Engineers have recently exploited the properties of DNA to construct self-assembled nanomachines, such as artificial DNA-based devices driven by strand displacement, or chemically induced structural rearrangements. DNA micromanipulation techniques will help assess the utility of this new class of molecular machines for which force and torque generation have yet to be measured. The past decade has provided a new perspective of the mechanical nature of the double helix. The next decade promises deeper insight into its interactions with the cellular machinery and its potential for constructing sophisticated nanomachines. The deformation of DNA has very important biological implication. For example, the bending and twisting rigidities of DNA affect how it wraps around histones to form chromosomes, supercoils during replication, bends upon interactions with proteins and packs into the confined space within a virus. Up until now, these phenomena have not been well understood from biological investigation.

The objective of this work is to develop predictive computational models of DNA mechanics for biophysical studies, including sequence-dependent mechanical properties, the mechanics of nucleosome accessibility and packing, and DNA translocation through nanopores. We proposed multi-scale coarse graining method and multi-level homogenization formulation for effective numerical simulation of DNA subjected to complex forms of deformation. We developed wavelet-based multi-scale formulation for the first level homogenization of potential function for representation of superatoms. Based on superatom molecular structures, we introduced second level homogenization by constructing an equivalent continuum strain energy density function of the DNA to yield a continuum hyperelastic multi-scale beam formulation for continuum modeling of DNA molecules. The effectiveness of the proposed methods is validated by comparing the predicted DNA stretching load-displacement curves, DNA loop formation mechanisms and DNA-repressor interactions with experiment data. This work will be extended in the future for constructing generic mathematical tools for modeling proteins and other biological macromolecules.