Continuum Modeling of DNA

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***Short Abstract* —Structural deformations of DNA play a central role in many biological processes including gene expression. The elastic rod model, which uses a continuum approximation, has emerged as a viable tool to model the deformation dynamics of bio-filaments. Rod model predictions are however very sensitive to the constitutive law (springiness) of the filament. Estimation of the constitutive law from experimental data and molecular dynamics simulations remains a significant challenge. In this presentation, we will illustrate a two-step technique that can use a rod model in combination with high-fidelity molecular dynamics simulation data to estimate the constitutive law.**

***Keywords* — Rod Model, Constitutive Law, Estimation, MD Simulations, Biofilaments, DNA.**

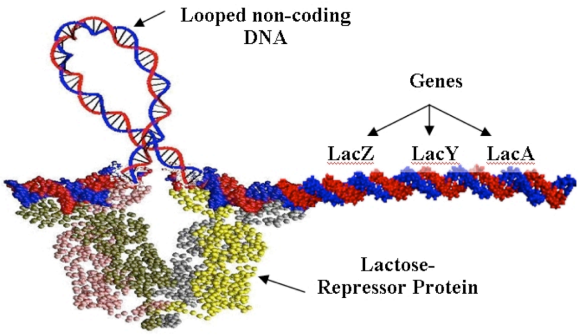

Fig. 1: Schematic diagram of Lac-Operon in bacterium E.coli. This example illustrates the role of looping of the non-coding DNA in regulating genes, namely, LacZ, LacY and LacA. The looping is mediated by binding with a V-shaped protein, the Lactose-Repressor. (This figure is adopted from [1].)

Designing and engineering DNA molecules to achieve desired biological activity has numerous applications that can lead to advances in disease prevention, diagnosis, and cure. The biological activities of DNA including gene expression are significantly influenced by its structural deformations such as looping, which in turn are tied to its chemical make-up, the base-pair sequence. For example, as shown in Figure 1, activity of the genes in lac-operon is governed by the sequence-dependent looping behavior of its "non-coding" DNA segment (portion of DNA that does not contain genes).

The success of designed DNA molecules for disease prevention or genetic engineering applications therefore depends on understanding not only the genetic information contained in the DNA but also the structural deformations of non-coding "junk DNA." Non-coding DNA is a significantly larger part of the genome (more than 98 % in the human genome) than the part that contains genes. The sequence-dependent structural deformation of non-coding DNA is thus a major design criterion for engineering synthetic DNA that has been mostly ignored so far. Both static and dynamic deformations of non-coding DNA play a significant role in its biological activity. Understanding and modeling these deformations and their relationship with base-pair sequences represents a significant challenge.

Among the several existing approaches to model structural deformation in DNA molecules, elastic rod models are based on a continuum approximation. Rod models are computationally efficient and are applicable to long length scales. In this approach, DNA molecules are viewed as continuous filaments. The elastic rod model predictions are, however, very sensitive to the constitutive law (material properties) of the molecule, which in turn, vary along the molecule's length according to its base-pair sequence. However, a key component of these elastic rod models is a constitutive law (material law), which follows from the bond stiffnesses and other atomistic-level interactions. A simplistic view of this constitutive law is that it represents the "springiness" of the DNA molecule and its relationship to its atomistic structure.

The general form of constitutive law remains largely unknown, and the capability to estimate the correct form that governs DNA structure and dynamics is severely limited by the absence of a systematic approach to best leverage the limited data available. In this presentation, we will discuss the associated challenges and illustrate a recently developed two-step technique [1] that can use a rod model in combination with high-fidelity molecular dynamics simulation data to estimate the constitutive law.

References

[1] Palanthandalam-Madapusi H J, Goyal S (submitted 2010) Estimation of Nonlinear Three-dimensional Constitutive Law for DNA Molecules. *Automatica.*

Acknowledgements: This abstract is summarized from [1].

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