MOLECULE-TO-BEAM HOMOGENIZATION, APPLIED TO DNA

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INTRODUCTION

Mechanical properties of deoxyribonucleic acid (DNA) are of great biological interest, as duplication and expression are processes involving force-driven deformations. In traditional approaches towards understanding the mechanical behavior of DNA sequences, the latter were considered as straight and isotropic beams of cylindrical shape [1], leading, however, to unrealistic ratios between torsional and bending rigidities. In fact, DNA sequences resemble deformation characteristics (such as bending, stretching, torsion, or shearing) which are well known from a key concept of continuum mechanics, that is beam theory. On the other hand, molecular dynamics (MD)-based modeling tools, which are standardly applied nowadays to macromolecules (such as DNA), provide detailed information as to the different energy states such molecules are in under specific (thermal and mechanical) boundary conditions, but are not directly interpretable in terms of mechanical constants allowing for quantifying the aforementioned deformation modes [2]. This contribution aims at filling this gap, by providing an upscaling procedure, relating the output of MD simulations, performed on a sequence of base pairs, to beam theory-related deformation modes.

METHODS

While the subsequently described method can be applied to any kind of polymer, we here study, for the sake of demonstration, a poly(A)-poly(T)-B-DNA molecule. This molecule is reconstructed in the MD software Amber, at a length of 20 base pairs, while the molecule is clamped at both ends, see Figure 1. Then, the molecule is initially deformed to a homogeneous strain state, such as uniaxial stretch or uniaxial torsion. Eventually, the molecule relaxes, and takes up an equilibrium state.

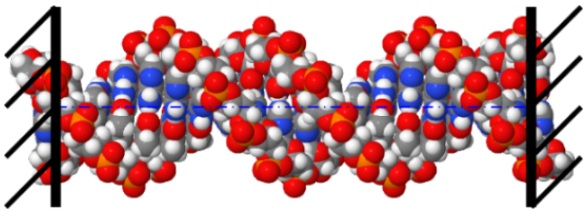

Figure 1: The DNA equilibrates, while fixing both ends at specific deformations states.

One of the key novelties of this contribution is the adaptation of the classical intersection principle ("free body diagram") to the molecular structure. In particular, the potential energies extracted from the MD simulation are translated into a corresponding system of equilibrated forces and moments [2,3], while formally representing the interaction lines between atoms as beams, see Figure 2. The forces and moments are then inserted into the principle of virtual power [4,5], which allows for "homogenizing" the molecular DNA assembly to a beam-like structural element, with corresponding bending, torsional, and axial rigidities.

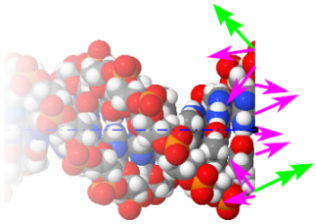

Figure 2: Potential-derived forces and moments in "beam cross sections", as input for the principle of virtual power.

RESULTS AND DISCUSSION

The molecule-to-beam homogenization method clearly evidences that the axial and torsional deformation modes of DNA are coupled; and increased stretch induced a greater rotational twist, see Figure 3. This computational result is fully consistent with experimental observations in rotor bead tracking experiments [1].

To our knowledge, the overwinding behavior of DNA, which is only known from rotor bead tracking experiments [1], could be predicted by means of computer simulations for the first time.

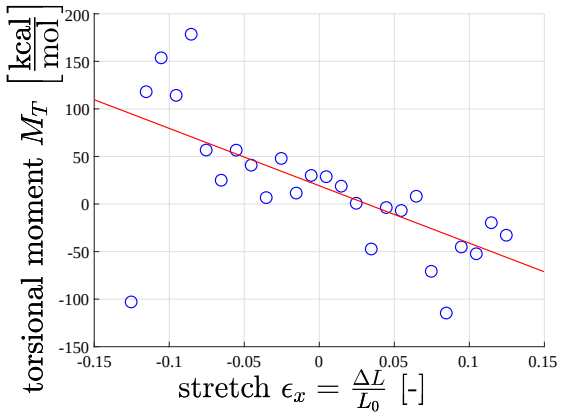

Figure 3: Overwinding behavior observed while stretching the studied DNA sequence; blue circles represent the torsional moment vs. the stretch imposed in the MD simulations, the red line represents the linear fit of the data.

CONCLUSION

This work represents an unprecedented approach a to the transition of molecular dynamics into beam theory-related mechanical properties: In the long run, the implication of this work can be potentially far-reaching. On the one hand, the replication behavior of DNA, which is believed to be influenced by its mechanical properties, potentially affects the initiations of genetic diseases such as cancer [6]. On the other hand, the proposed strategy can be straightforwardly adopted for any other chain polymer, opening a wide range of further applications.

ACKNOWLEDGMENT

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