COARSE-GRAINED DNA MODEL ABLE TO REPODUCE RIBOSE FLEXIBILITY

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Local DNA flexibility is crucial for its biological function. The deformation of the double helix is achieved through three types of mobility in the DNA backbone: concerted rotations around α and γ , ζ and ε torsions, and ribose flexibility. The last mentioned type makes the main contribution into providing the observed DNA flexibility, and it enables DNA to assume B-DNA and A-DNA forms. Geometry of the polymorphs of DNA is a result of a balance of many factors: angles in the backbone; sugar puckers; sequence dependent base pair stacking; electrostatic interactions of DNA with solvent molecules and with salt ions. From the physical point of view, the understanding of this balance is equivalent to the construction of a coarse-grained (CG) DNA model able to reproduce key features of the DNA behavior. The last ten years witnessed the extensive development of CG models for many substances, particularly for large biomolecules. For DNA, several CG models with different level of ”coarseness” have been developed, but none of them is able to reproduce ribose flexibility.

We propose [1] a ”sugar” CG DNA model capable of simulating both biologically significant B- and A-DNA. The model also demonstrates both the A to B and the B to A transitions. The number of degrees of freedom is reduced to six grains per nucleotide. We show that this is the minimal number sufficient for this purpose. The key features of the model are (1) simulation of sugar repuckering between C2’-endo and C3’-endo by the use of one nonharmonic potential and one three-particle potential, (2) explicit representation of ions in solution around the DNA, (3) implicit solvent approach and (4) sequence dependence. We obtain parameters of the model from the all atom AMBER force field.

The offered sugar CG model is adequate, physically clear, computationally cheap, allows to promptly check physical hypotheses, and so can be employed for the study of many interesting problems, including the cases in which all atom DNA models can not be used. For example, the CG model can be applied for investigation of large local mechanical deformations of long DNA molecules (when they package into chromosomes). The introduced sequence dependence allows to use the model for studying of DNA-protein interactions, including the interactions with CG proteins. A small change of the potentials enables base opening, and offers the possibility to simulate DNA melting, and investigate transcription and replication. Another large area of applications - modeling of electrostatic interactions of DNA with different types of ions in different kinds of solutions.

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References.

1. Natalya A. Kovaleva, Irina P. Kikot, Mikhail A. Mazo, Elena A. Zubova. Coarse-grained DNA model capable of simulating ribose flexibility // arXiv:1401.2770v2