C-A TEST OF DNA FORCE FIELDS

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The DNA duplex may be locally strongly bent in complexes with proteins, for example, with polymerases or in a nucleosome. At such bends, the DNA helix is locally in the non-canonical forms A (with a narrow major groove and a large amount of north sugars) or C (with a narrow minor groove and a large share of BII phosphates). To model the formation of such complexes by molecular dynamics methods, the force field is required to reproduce these conformational transitions for a naked DNA. We analyzed the available experimental data on the B-C and B-A transitions under the conditions easily implemented in modeling: in an aqueous NaCl solution. We selected six DNA duplexes which conformations at different salt concentrations are known reliably enough. At low salt concentrations, poly(GC) and poly(A) are in the B-form, classical and slightly shifted to the A-form, respectively. The duplexes ATAT and GGTATACC have a strong and salt concentration dependent bias toward the A-form. The polymers poly(AC) and poly(G) take the C- and A-forms, respectively, at high salt concentrations. The reproduction of the behavior of these oligomers can serve as a test for the balance of interactions between the base stacking and the conformational flexibility of the sugar-phosphate backbone in a DNA force field. We tested [1] the AMBER bsc1 and CHARMM36 force fields and their hybrids, and we failed to reproduce the experiment. In all the force fields, the salt concentration dependence is very weak. The known B-philicity of the AMBER force field proved to result from the B-philicity of its excessively strong base stacking. In the CHARMM force field, the B-form is a result of a fragile balance between the A-philic base stacking (especially for G:C pairs) and the C-philic backbone. Finally, we analyzed some recent simulations of the LacI-, SOX-4-, and Sac7d-DNA complex formation in the framework of the AMBER force field.

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References.

1. C-A test of DNA force fields, Ivan A. Strelnikov, Natalya A. Kovaleva, Artem P. Klinov, and Elena A. Zubova, https://doi.org/10.48550/arXiv.2211.10711