ABSTRACT

Extending the NARES-2P coarse-grained model of nucleic acids to interactions with metal cations and introducing global optimization algorithms

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The aim of my PhD thesis was to develop one of the theoretical methods for studying nucleic acids - the NARES-2P coarse-grained force field. I expanded the NARES-2P model in two directions: by explicitly accounting for nucleoside-cation specific interactions and by introducing the CSA (Conformational Space Annealing) method for global optimization.

I studied nucleoside-cation interactions for eight systems - pairs of all four deoxynucleosides found in DNA with sodium and potassium cations. For each system I prepared 100 000 structures by adding a cation in random-generated position to the canonical structure of nucleoside. For each structure I calculated energy at MP2/6-31G(d,p) level. Based on potential energy hypersurfaces produced this way, I calculated potentials of mean force, which served as a basis for fitting analytic expressions for energy. I implemented the model potentials derived in this fashion in the UNRES 4 package. I performed simulations using the new version of the force field for three DNA-cation complexes: G-quadruplex, G-triplex and a mini-dumbbell. Tests of the new energy component suggest excellent agreement with experiment.

The other part of my PhD thesis was application of the CSA method to studies of nucleic acids in NARES-2P coarse-grained representation. This method allows for fast and accurate energy minimization. Tests show, that using constraints for predicted secondary structure, or performing an additional simulation based on results of the first one, makes it possible for CSA to solve even very hard problems.

Both methods are effective tools for studying of nucleic acids and their introduction prepares the ground for further theoretical studies of biologically important systems.