

ABSTRACT

INVESTIGATION OF STRUCTURE AND DYNAMICS OF SELECTED PROTEINS BY COARSE-GRAINED SIMULATIONS

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The use of the theoretical methods to investigate the biological systems requires large time- and size- scale simulations, which are possible using coarse-grained force fields, for instance the UNRES force field. During my doctoral research I accomplished tasks based both on the application of this force field, and testing its new features.

Firstly, I investigated the conformational changes of arginine-binding protein from a hyperthermophilic bacteria *Thermotoga maritima* in the presence and absence of ligand. The results indicate that binding of the arginine ligand promotes a closed conformation, which conforms with the experimental data. However, the sensitivity of the protein conformation to the presence of arginine decreases and the protein becomes more flexible with increasing temperature.

Subsequently, I assessed the effect of modelling the contributions of the solvent in implicit representation to the energetics and dynamics of proteins in the UNRES force field on the simulated structures and folding kinetics of model proteins. Because of the role that the environment plays in the functioning of proteins, the proper representation of the protein interactions with solvent is a very important direction of the development of theoretical methods. I took into consideration two aspects: hydrodynamic interactions (solvent-mediated apparent drag of two objects moving through a liquid) and shielding effect (reducing hydration of peptide groups by side-chains). It has been found that introducing hydrodynamic interactions slows down the protein folding process. The reason was the faster collapsing of the polypeptide chain and formation of persistent intermediates that contain nonnative residue-residue contacts. The introduction of the shielding effect, that was tested in blind prediction experiment CASP12, improved the quality of the predicted structures.