Nearly 50 % of the protein structures deposited in the PDB (Protein Data Bank) contain ions. In some structures the ions were introduced artificially to enable structure determination by X-ray crystallography. Nevertheless, for many proteins, metal ions play significant biological roles, e.g. alkali and alkaline earth metal cations are important in cellular response. Moreover, ions can stabilize protein structure, or even be actively involved in the protein folding process. Therefore, accurate treatment of the ions is crucial to model biological phenomena properly.

The main goal of this project is to extend the coarse-grained UNRES (United RESidue) force field to investigate the interactions between proteins and four alkali and alkaline earth metal cations of biological significance, i.e. calcium, magnesium, sodium and potassium. To achieve electroneutrality of the systems studied, chloride anions will be introduced as counter-ions and, consequently, included in force-field parameterization. Subsequently, the UNRES force field will be modified in order to enable us to carry out the molecular dynamics simulations in the presence of the cations. Finally, the new force field will be tested with the set of the proteins with known three-dimensional structure that contain metal ions in the structure. The second aim of this project is to investigate, with the new UNRES force field, the influence of the ions on the folding and structure of selected proteins.

UNRES provides an about 1000-fold speed-up with respect to all-atom calculations. Therefore, the models developed in this project, will enable us to study the calcium, magnesium, potassium, sodium and chloride ion-binding sites (most ion-binding proteins are large multichain subunits). In future, this tool will enable us to study many important biological phenomena that involve ion-protein interactions (such as, e.g., signal transduction and ion transport) and, eventually, to simulate such a complicated systems as sodium-potassium pump in the lipid bilayer.