Getting divalent ion–biomolecule interactions right in Molecular Dynamics simulations

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Abstract

Ion-biomolecule interactions are ubiquitous and play a central role in a number of fundamental biological processes, from calcium signaling to the formation of DNA–protein complexes. Molecular level understanding of these key biological processes first requires to characterize the interaction between biomolecules (proteins and nucleic acids) and divalent cations, which is both an experimental and computational challenge. Indeed, standard biomolecular simulations using non-polarizable force fields suffer from severe overbinding artefacts-especially with divalent cations like Ca 2+ and Mg 2+ -that prevent them to properly capture ion-biomolecule interactions. We aim to improve the description of divalent cations in simulations and use it to tackle biologically relevant problems. Our strategy is to start with small model systems, where simulation results can be directly compared both to experimental data (e.g. neutron scattering, capillary electrophoresis, etc.) and to reference high-level ab initio simulations in order to systematically assess the validity of our descriptions. These results are used to develop a scaled charge description of the ions and charged biomolecular groups, which takes into account electronic polarization in a mean field way. Such a description has been shown to successfully improve ion-binding properties in different biosystems. This new original method opens the way to large-scale, accurate, and computationally
cheap simulations of divalent cation containing biosystems. Future plans are to use it to improve our molecular understanding of the impact of ions on nucleic acid structure and reactivity.

Keywords: molecular modeling, ions, proteins, nucleic acids

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