Exploiting electrostatic models in biomolecular and hybrid system simulation

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ABSTRACT

The importance of electrostatics for structure and dynamics of molecular and supramolecular systems is paramount. In the computational framework, this reflects in the relevance of having suitable models and efficient implementations able to deal with and exploit electrostatic-related problems.

In the first application of this work, the electrochemical investigation of redox-active proteins at electrodes from the computational standpoint is treated via coupling continuum electrostatics with integral equations theory. This kind of analysis is a particularly challenging task, especially if the considered fields are so strong to induce high concentrations where ion-ion correlations cannot be neglected. This makes mean field approaches such as Poisson-Boltzmann equation less predictive of experimental outcomes. In these cases, a better description of the short-range interactions, which means also incorporating the granularity of the solvent, including ions, becomes unavoidable. Integral equations theories (IET) of liquids can provide statistical-mechanics-based alternatives, or integrations, to mean field approaches. In particular, we focus on 3D-RISM. Taking as an input partial charges and Lennard-Jones parameters (or other short-range potentials) 3D-RISM equations output detailed description of the water and ionic density surrounding solutes, e.g. biomolecules, nanoparticles, walls, etc. These densities can be used per se or as an input for Poisson equation for further analysis of the electrostatic interactions. Such treatment is hampered, for instance, in areas where the electrostatic potential is externally controlled, such as in scanning tunneling microscopy, organic electronics, electrochemistry etc. Here, the coupling of 3D-RISM and Poisson equation in an iterative scheme is presented, aiming at including the electrostatic potential control in the integral equations based simulations. The object of the study is the Gold/Cytochrome-C field effect transistor, which is has been extensively investigated in recent times [1-2].

In the second application, a specific use of an electrostatics-inspired external field for the Molecular Dynamics (MD) simulation of drug-target recognition and binding is illustrated. In fact, the efficient and accurate protein-ligand complex determination using computational methods is still a challenging task. This is mainly due to the insufficient incorporation of protein flexibility inherent to ligand binding and the excessive approximation of current scoring schemes. Plain MD could in principle correctly describe the binding process but present algorithms and computational resources do not still allow a full description in reasonable times. In turn, so called enhanced sampling methods try to accelerate the collection of a statistically significant number of configurations spanning across free energy basins that are separated by a high energy barrier. The novel protocol presented here, based on the combination of an electrostatics-inspired collective variable and an adaptive behavior, is used to implement a flexible docking method in explicit solvent. This allowed to enhance the ligand-receptor recognition processes including full flexibility of the binding partners. Main results are illustrated.

REFERENCES

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