Biomolecular simulations on different time- and length-scales

Two key challenges of simulating biomolecular systems are i) the typically large system sizes required, and ii) the long time-scales involved. These two aspects are often closely intertwined, since larger systems usually have longer correlation and relaxation times, thus aggravating the computational challenges. In the talk, I will discuss two case examples from our recent work to illustrate how the above challenges can be overcome.

In the first example, coarse-grained (CG) and all-atom MD simulations are combined to study lipid nanodiscs [1]. The computationally efficient CG force field is used to directly simulate the slow (multi-microsecond) self-assembly process, whereas the subsequent all-atom simulations yield accurate structural and dynamic properties, such as lipid order parameters and entropies. In addition, the adopted sequential dual-scale approach enables a quantitative comparison of the all-atom and coarse-grained results.

The second part of the talk will focus on the tapasin-MHC I complex as a prime example for protein-protein association [2,3]. Conventional simulation approaches involve approximations such as treating the proteins as rigid bodies, describing the systems at a coarse-grained representation, or modeling the solvent as a dielectric continuum. Indeed, we found that for the tapasin-MHC I encounter, any of these approximations severely hampers the accuracy of the results. We thus used all-atom MD simulations in explicit solvent to study the protein association, which takes place on the multi-microsecond time scale. The obtained structure of the complex, which was hitherto unknown at the atomic level, enables us to address open questions concerning the biological function of the tapasin-MHC I complex, which is a key player in the mammalian adaptive immune system.

In the final part of the talk, if time permits, I will briefly discuss current methodological challenges involved with hybrid all-atom/coarse-grained approaches [4,5].

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[5] A. B. Kuhn, S. M. Gopal, L. V. Schäfer. On Using Atomistic Solvent Layers in Hybrid All-Atom / Coarse-Grained Molecular Dynamics Simulations, *J. Chem. Theory Comput.*, 2015, 11 (9), 4460-4472.