Influence of Protein-Solvent Interactions on the Molecular Dynamics of Reduced Point Charge Models of Proteins - COMP5

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Published in:
Abstracts of the 255th Annual Meeting and Exposition of the American Chemical Society

Publication date:
2018

Document Version
Publisher's PDF, also known as Version of record

5 - Influence of protein-solvent interactions on the molecular dynamics of reduced point charge models of proteins

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Abstract

We investigate the influence of various solvent models on the structural stability and the protein-water interface of three Ubiquitin complexes (PDB access codes: 1Q0W, 2MBB, 2G3Q) modelled using Amber99sb with two different point charge distributions. A previously developed reduced point charge model (RPCM), where each amino acid residue is described by a limited number of point charges, is tested and compared to its all-atom (AA) version. The complexes are solvated in TIP4P-Ew or TIP3P water molecules, involving either a correction of the Lennard-Jones protein-O_{water} interaction parameters or the coarse-grain SIRAH water description. Molecular Dynamics (MD) simulation conditions are first refined for complex 1Q0W, whose ligand is a single helix structure that has the ability to bend due to a low α-propensity region occurring in its amino acid sequence. Results are further confirmed by MD simulations carried out on complexes 2MBB and 2G3Q.

MD results show that the best agreements between the RPCM and AA models are obtained when using the TIP4P-Ew water force field (FF) with a correction factor $\gamma = 0.7$. At the RPCM level, a decrease in γ, or the consideration of SIRAH solvent particles, allow to weaken the protein-solvent interactions. It results in a slight collapse of the protein 3D structure and a less dense hydration shell, thus involving a decrease in the protein-water and water-water H-bonds. The dynamics of the surface protein atoms and of the water shell molecules is also slightly refrained, thus allowing to generate stable RPCM trajectories, at a reduced computational cost. Conversely, solvation conditions such as the uncorrected TIP4P-Ew FF favor the unfolding of protein RPCMs. Interestingly, deconstructed structures appear to be stable when simulated back at the AA level, as illustrated for system 1Q0W.

Time	**Sunday, March 18, 2018 10:45 AM**
Session	COMP: Molecular Mechanics: AM session (8:30 AM - 11:45 AM)
Location	**New Orleans Marriott Convention Center**
Room	**New Levee**