Refining the calibration of a coarse-grained force field for protein complexation

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Theoretical studies of the molecular mechanisms responsible for the formation and stability of protein complexes have gained importance due to their practical applications in the understanding of the molecular basis of several diseases, in protein engineering and biotechnology. The objective of this work is to refine a constant-pH coarse-grained force field for protein-protein interactions based on experimental thermodynamic parameter called second virial coefficient. Our ultimate goal is to generate knowledge for a better understanding of the physical mechanisms responsible for the protein associations in different environments. By means of computational tools and mesoscopic models solved by Monte Carlo simulations, the homo-association of lysozyme and chymotrypsinogen was used in the calibration process. Our model is composed of two contributions namely Coulombic (with charge fluctuation as a function of the pH) and Lennard-Jones. A better description for van der Waals contribution was necessary to improve the quantitative theoretical results in different salt regimes. Our main interest is focused on how to deal with hydrophobic molecules within the continuum dielectric framework. We found that there is an inherent difficulty in reproducing the experimental data when low salt concentrations and pH values far from pI are considered. However, considering moderate salt concentrations a reliable description of the experimental data is possible. There is an ongoing study to discuss how the exposition of hydrophobic amino acids at pH conditions far from pI can be still captured in this simplified model.

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