UCLA College | Physical Sciences Chemistry & Biochemistry

Chem 218: Student Exit Seminar

Chemical Change in Protein Molecular Dynamics: Developing Computational Tools for Metal Binding and pH Sensitivity

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Molecular dynamics (MD) is a powerful tool to study atomic scale changes in proteins underpinning biological pathways. However, simulations traditionally sample a fixed chemical state and struggle to achieve quantitatively accurate energies, making comparisons of different chemical ensembles challenging. Hybrid quantum mechanical-classical approaches (QM/MM) can provide accurate energies for small regions of interest, such as the active site, but cannot readily capture all chemical transformations relevant to protein function. This talk will focus on developments and applications of hybrid methods to study the metal binding preferences and pH sensitivity of proteins. We will first discuss how we used QM/DMD combined with a competitive metal affinity method, a semi-empirical thermodynamic cycle, to obtain relative binding affinities for a wide range of metals to human serum transferrin (hTF), an iron transport protein. Our results clarified a mechanism for promiscuous metal binding in hTF and the role the protein may play in transport of non-physiological and potentially cytotoxic metals. We will then discuss the development of a titration feature for constant pH simulations with DMD (titr-DMD). Our method features stochastic protonation and deprotonation of amino acids while treating solvent implicitly, which makes it computationally efficient compared to other techniques. We successfully benchmarked titr-DMD on experimentally verified pH-dependent conformational changes. Our work demonstrates the utility of molecular dynamics, and QM/DMD in particular, to study chemical changes in proteins with good accuracy and speed.

Thursday, March 11th, 2021
12:00 p.m.
Via Zoom

For questions, please contact: jzabala@chem.ucla.edu