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An Integrative Experimental-Computational Approach to Study Structure and Disorder

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Technological advances in single-molecule techniques, such as single molecule fluorescence resonance energy transfer (smFRET) spectroscopy, have paved the way for the study of protein structural dynamics under biologically relevant conditions. Unlike high-resolution structure determination techniques such as x-ray crystallography, however, single molecule techniques provide limited information spatially. Fortunately, such low-resolution data combined with computational techniques such as molecular dynamics (MD) simulations may provide enough information to model the structural dynamics of proteins. The starting point of these simulations is often based on crystal structures or other high-resolution structures of proteins. Unfortunately, such structures are not available for intrinsically disordered proteins (IDPs) or intrinsically disordered regions (IDRs) of partially structured proteins. We have recently employed enhanced sampling techniques in combination with all-atom MD and smFRET data to model the structural dynamics of IDPs and IDRs. This novel methodology uses enhanced sampling techniques to first generate an ensemble of protein conformations and then predict FRET efficiency distributions for candidate labeled proteins. An iterative procedure is then used to efficiently design smFRET experiments based on computational predictions and refine the conformational ensemble of protein, until a convergence is reached. We have successfully used this approach to study the structural dynamics of the C-terminal domain of membrane insertase Alb3, which is known to be intrinsically disordered.

Date: Mar. 4, 2020
Time: 4:30-5:30 pm
Location: 208 Clark Hall

Students, meet the speaker over coffee and cookies in the Bennett Conference room at 3:30 pm