

“Predicting and Controlling Stability and Protein-Protein Interactions for Therapeutic Antibodies”

**Wednesday
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Wu and Chen Auditorium
Levine Hall**



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Abstract

Protein-based biopharmaceuticals are among the fastest growing segment of the pharmaceutical market, including monoclonal antibodies that are focused on a range of oncology targets and auto-immune diseases. Candidate selection for biopharmaceuticals such as therapeutic antibodies has traditionally focused only on clinical attributes such as target selectivity, in vivo half-life, and other features that may implicitly and inadvertently lead to poor biophysical properties from the perspective of manufacturability and product development. Prediction of biophysical properties such as solubility, self-association, and aggregation-propensity remains an outstanding challenge. This is particularly difficult if one requires atomic- or near-atomic-scale resolution. For purposes of selecting therapeutic protein candidates and product formulations, this must be balanced with the need for rapid or high-throughput approaches to allow a large range of candidates to be tested in parallel, as well as to consider both dilute and concentrated protein solutions. Advancements in coarse-grained molecular modeling and algorithms for more rapid / efficient sampling have the potential to make these predictions more routine, while also providing “design rules” that can be implemented without the need for expensive simulations. This seminar focuses on a combination of different levels or scales of molecular modeling, combining these with “minimalist” experimental data, and development of design rules based on protein sequence and three-dimensional structures. This includes effects of the product formulation or manufacturing conditions, with an emphasis on antibodies and other anisotropic protein structures. Finally, additional challenges exist when one encounters competing routes for protein instability, and how these are exacerbated in different stages of the life cycle of biopharmaceutical products.

Bio

Christopher J. Roberts is a Professor in the Department of Chemical and Biomolecular Engineering at the University of Delaware. He is the Associate Institute Director for the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL), and the Director of the Biomolecular Interaction Technology Center (BITC). He received a Bachelor’s of Chemical Engineering degree from UD, and a Ph.D. in Chemical Engineering from Princeton University. Prior to joining UD in 2002, he worked in the pharmaceutical industry as a formulation scientist for protein and small-molecule based drugs. The Roberts laboratory focuses on experimental and theoretical fundamentals and applications of protein physical and chemical stability, (mis)folding, aggregation, statistical mechanics, and kinetics to address questions of biopharmaceutical product design, stability, and manufacturing.

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