Dr. Brenda Rubenstein

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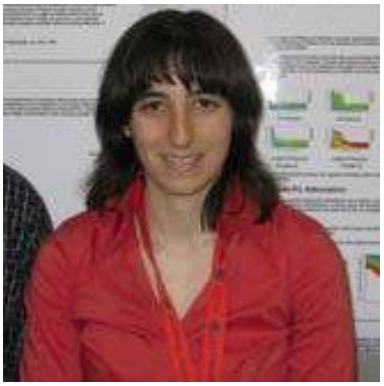

Predicting Viability: **How Protein Folding, Binding, and Dynamics Correlate with Fitness**

One of the long-standing holy grails of molecular evolution has been the ability to predict an organism's fitness directly from its genotype. With such predictive abilities in hand, researchers would be able to more accurately forecast how organisms will evolve (as during our current COVID-19 pandemic) and how proteins with novel functions could be engineered, leading to revolutionary advances in medicine and biotechnology. In this talk, I will describe my group's recent efforts to determine how - *and how well* - the thermodynamic and dynamic properties of key functional proteins can be used to predict fitness in different organisms. As a first case study, I will discuss our combined computational/experimental work on the antibiotic resistance-conferring enzyme, β-lactamase, that shows that, while computation does a commendable job predicting the thermodynamic properties of this enzyme, these properties can only explain a modest fraction of β-lactamase fitness data. I will then describe our more recent endeavors predicting the pathogenicity of missense variants that suggests that, although protein sequence and structure are most strongly predictive of fitness, protein thermodynamics and dynamics can still play determinative roles. Altogether, our work sheds a bright light on which characteristics of proteins are most useful for inferring fitness, as well as what types of fitness information are still lacking from our current computational models.

Biography:

Dr. Brenda Rubenstein is currently the Joukowsky Family Assistant Professor of Chemistry at Brown University. While the focus of her work is on developing new electronic structure methods, she is also deeply engaged in rethinking computing architectures. Prior to arriving at Brown, she was a Lawrence Distinguished Postdoctoral Fellow at Lawrence Livermore National Laboratory. She received her Sc.Bs. in Chemical Physics and Applied Mathematics at Brown University, her M.Phil. in Computational Chemistry while a Churchill Scholar at the University of Cambridge, and her Ph.D. in Chemical Physics at Columbia University. Ask her about basketball - you may be surprised!