Non-equilibrium coupling of protein structure and function to translation-elongation kinetics

Protein folding research has been dominated by the assumption that thermodynamics determines protein structure and function. And that when the folding process is compromised, the proteostasis machinery of cells - chaperones, deaggregases, the proteasome - work to restore proteins to their soluble, functional form or degrade them to maintain the cellular pool of proteins in a quasi-equilibrium state. During the past decade, however, more and more proteins have been identified for which altering only their speed of synthesis alters their structure and function, the efficiency of the down-stream processes they take part in, and cellular phenotype. Indeed, evidence has emerged that evolutionary selection pressures have encoded translation-rate information into mRNA molecules to coordinate diverse co-translational processes. Thus, non-equilibrium physics can play a fundamental role in influencing nascent protein behavior, mRNA sequence evolution, and disease. I will discuss my labs efforts to understand this non-equilibrium coupling through the development and application of theoretical and computational methods, including coarse-grained simulations, chemical kinetics and statistical mechanics, and physical bioinformatics.

Host: Prof. Marina Rodnina