

For many decades, after Anfinsen's seminal work, protein folding research has been dominated by the assumption that thermodynamics determines protein structure and function. However, recently accumulated evidence has supported the emerging paradigm of non-equilibrium control of protein behavior. Namely, speed of synthesis of proteins in the ribosome greatly influences their properties, mRNA sequence evolution, and diseases. Thus, identifying the factors that govern the kinetics of protein formation is vital for understanding the function of nascent (formed but not yet folded) proteins in living organisms.

We will focus on the effect of the electrostatic interaction of proteins with the exit tunnel in the ribosome on the rate of their synthesis using coarse-grained and all-atom steered molecular dynamics simulations. An analysis of ribosome profiling data from *E. coli* bacteria will be performed to determine whether the presence of slow ejecting sequences relates to ribosomes spending more time at stop codons, indicating the ejection process may delay ribosome recycling.

Two proteins often form complexes, called dimers, which are popular structures that are found in living organisms, especially in prokaryotes. They play an important role in catalysis of metabolic reactions or act as regulatory enzymes. Recent experimental evidences have suggested that the protein synthesis kinetics may affect the formation of protein complexes in cell. We will study how translation-elongation rates change the structure and building affinity of dimers. Our results would reinforce the new notion that the protein function depends on the kinetics of its synthesis in the ribosome.

Hydrophobicity seems to be required for sustainable life and plays an important role in a wide range of chemical phenomena, such as protein folding, the gating of ion channels etc. However, water-mediated hydrophobic interactions inside the ribosome exit tunnel have not been studied. Due to the interaction between charged rRNA and water molecules in the form of electric dipoles, the hydrophobicity in the tunnel should be very different from the one in solvent. This problem will be clarified by calculating the interaction between hydrophobic methane molecules and between the side chains of hydrophobic amino acids using molecular simulations.

Finally, understanding the role of charge in the release of proteins from the ribosome and the effect of synthesis rates on protein dimerization in the solvent will shed light on a new concept showing the relevance of non-equilibrium translation-elongation kinetics to protein structure and function. A knowledge of the hydrophobic interactions in the exit tunnel of the ribosome should be useful for computer-aided drug design, as this helps to understand antibiotics transport and their interaction with the ribosome. From this prospect, our research is not only of academic interest but can also help to improve the quality of human life.