Computer simulations of biological macromolecules allow detailed mechanistic studies of how structure and dynamics relate to biological function. We are interested both in the development of new simulation methods and their application to challenging biophysical problems. In particular we are focused on employing multi-scale simulation methodologies that combine fully atomistic descriptions with coarse-grained models and implicit mean-field descriptions of solvent environments. Such methods allow us to explore conformational dynamics over long time scales and across large spatial scales ranging from supramolecular assemblies all the way to cellular scales. The ultimate goal of our research is to bridge between our current understanding of single-molecule dynamics and biological function at the cellular level.

One area of specific interest involves protein-nucleic acid complexes that are involved in replication and transcription. We are studying the recognition of post-replication DNA mismatches by MutS and the human homolog MSH2-MSH6 and subsequent initiation of DNA repair. A detailed understanding of the DNA mismatch repair system is relevant for many types of cancer that often result from DNA mutations that are left unrepaird. We are also interested in mechanistic details of how transcription is carried out by RNA polymerase because of its fundamental importance in biology.

A second area of emphasis is the study of membrane-bound proteins and peptides. Specific systems of interest are the regulation of Ca\(^{2+}\) transport in heart muscle by SERCA through interactions with phospholamban and the structure and dynamics of viral fusion peptides. Especially in the case of fusion peptides we are also interested in aggregation in the context of the membrane since oligomers appear to be critical for fusion activity.

A third area of interest is the prediction of protein structures from its amino acid sequence at levels of accuracy similar to experimental data. While it has become relatively easy to generate native-like models if structural templates are available from related proteins, such models often lack detailed features of amino acid side chain packing in the native structure. We are applying enhanced sampling techniques in combination with accurate energy functions in order to refine approximate protein structures towards the actual native conformation.

**Selected Publications**


PRIMO/PRIMONA: A coarse-grained model for proteins and nucleic acids that preserves near-atomistic accuracy, Srinivasa M. Gopal, Shayantani Mukherjee, Yi-Ming Cheng, Michael Feig, Proteins 2010, 78, 1266-1281.

Sampling of near-native protein conformations during protein structure refinement using a coarse-grained model, normal modes, and molecular dynamics simulations, Andrew Stumpf-Kane, Katarzyna Maksimiak, Michael S. Lee, Michael Feig, Proteins 2008, 70, 1345-1356.