Probing the Multiscale Dynamics of Linear and Branched Polypeptides: Computational and Experimental Approaches.

Jay D. Shieber [1] and Jorge A Iñiguez-Lluhí[2]

[1]Department of chemical engineering, Illinois Institute of Techniology and [2]Department of Pharmacology, University of Michigan Medical School

Macromolecules are central constituents of living systems and their dynamic behavior is important for active processes over multiple scales ranging from enzymatic catalysis, through multiprotein complex assembly and cell contractility culminating in the macroscopic physiological and biomechanical behavior of tissues and organisms. Macromolecular dynamics are also important in many bioanalytical approaches such as separation in gel electrophoresis, or to understand the mechanical properties of biomaterials such as actin filament scaffoldings. The modeling of macromolecular dynamics is challenging since it must span a large range of length and timescales and not directly amenable to molecular dynamics approaches. We have therefore developed a multiscale, coarse-graining approach utilizing slip-links to model entanglements on the mesoscopic level. The system relies on only three free parameters that are either accessible through Monte Carlo (MC) and Molecular Dynamics (MD) or easily treated phenomenologically. The model has been well validated for synthetic polydisperse linear polymers.

We are now extending this approach to the analysis of biological macromolecules where recent advances in protein modification allows for the synthesis of linear and branched proteins of defined composition and topology. To explore the behavior of these proteins at various levels of entanglement with an immobile matrix, we are developing tools to characterize their diffusion in polyacrylamide gels and their mobility during electrophoresis.

Experimentally, we have generated fluorescently labeled proteins and are examining their diffusion in polyacrylamide gels using laser interferometry. In this technique, fluorescently labeled protein molecules embedded in the gel are spatially bleached at regular intervals by interfering high-intensity “writing” laser beams. The resulting grating can then be monitored by its ability to diffract a low intensity “reading” laser beam. By following the time course of decay of the diffraction, it is possible to monitor the diffusion of the proteins. Through the combination of theoretical and experimental components, the multiscale modeling approach we are pursuing is uniquely suited to provide both a theoretical framework as well as the modeling tools to capture the dynamics and macroscopic behavior of linear and branched polypeptides.