

Dynamical and Mechanical Behavior of Reversible Protein Hydrogels

by David R. Heine¹ and Gary S. Grest, Sandia National Laboratories
Darina Danova-Okpetu² and James L. Harden³, Johns Hopkins University

Motivation—Hydrogels are hydrated polymer networks that are highly swollen by water. Natural protein hydrogels, such as the collagen-based extracellular matrix, are found in many biological systems. Recently, biomimetic protein hydrogels have been created from engineered telechelic proteins. Reversible gelation has been demonstrated for these telechelic proteins. These protein hydrogels have a variety of applications, including scaffolds for cell culture, contact lenses, and delivery devices for drugs. However, the molecular origins of gel formation are still poorly understood for these systems.

These engineered telechelic proteins have a triblock architecture composed of a central flexible domain with associating helical groups on each end (Fig. 1a). The helical ends are amphiphilic leucine zippers designed to reversibly assemble into trimeric bundles. As a result, solutions of the triblock proteins reversibly self-assemble into hydrogels (Fig. 1b). Our goal is to develop a coarse grained model to capture the secondary structure and reversible aggregation of these artificial proteins. This would allow us to study systems containing thousands of proteins, which would not be computationally tractable with an explicit atom model.

Accomplishment—We developed a coarse-grained bead-spring model for associating helix-coil-helix protein polymers where each bead represents an amino acid. Each pair of amino acids interacts via a Lennard-Jones potential. The end blocks of the triblock proteins adopt helical conformations as a result of hydrogen bonding along the axis of the helix. This behavior was incorporated into the coarse-

grained model by replacing the standard harmonic dihedral potential with an asymmetrical potential that favors a 60° dihedral angle. The hydrophobic face of the amphiphilic helices was modeled by assigning every first and fourth bead of each heptad repeat attractive LJ parameters, which were adjusted to optimize the formation of trimer helix bundles. Subsequently, the self-assembly of three triblock proteins into hydrogels and their response to uniaxial and shear deformation were studied. Figure 2 shows a snapshot of such a hydrogel network. Figure 3 shows the temporal stress response of these hydrogels to a step uniaxial deformation.

The specific aims of this research are to relate the molecular conformation and association behavior of the protein elements to the amino acid sequences of the protein modules, to determine the dependence of hydrogel microstructure and viscoelasticity on the molecular characteristics of the protein constituents, and to study the thermodynamics of the reversible assembly process of the hydrogels.

Significance—Insights gained through this project on the sequence–structure–property relationships can have an immediate impact on the way biomimetic materials are designed. Although a model system, the insights gained from our system should be transferable to many biomaterials. Multi-scale modeling is an essential part of establishing connections between the material properties of the networks at the nanoscale and the molecular behavior of their constituents, as many important molecular and materials parameters span a wide range of time and length scales.

¹Corning Incorporated; ²Vrije Universiteit; ³University of Ottawa

Sponsor for various phases of this work include: DOE Office of Basic Energy Sciences/Center for Integrated Nanotechnologies (CINT)

Contact: Gary Grest, Surface & Interface Sciences, Dept. 1114
Phone: (505) 844-3261, Fax: (505) 844-5470, E-mail: ggrest@sandia.gov

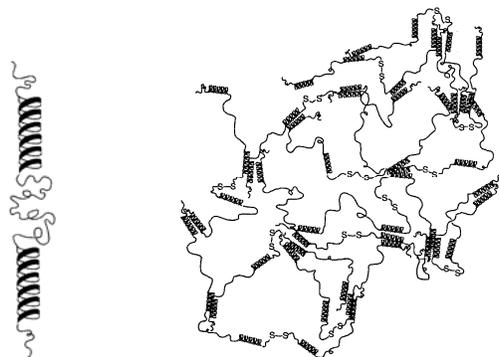


Figure 1. Triblock architecture of artificial protein (left) and proposed structure of associated proteins (right).

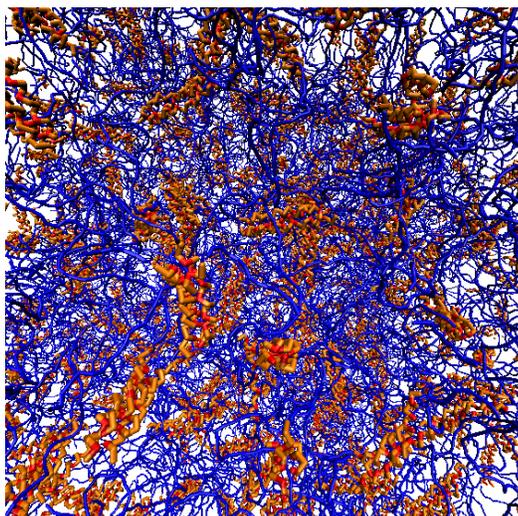


Figure 2. Snapshot from a molecular dynamics simulation showing the formation of doublet and triplet aggregates. The flexible middle segment of each protein is shown in blue and the outer helical segments are orange with the hydrophobic sites colored red.

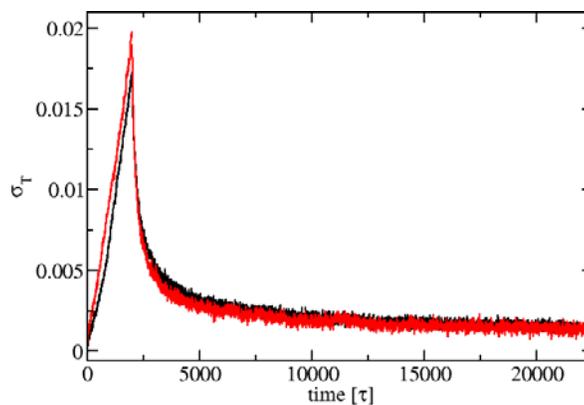


Figure 3. Tensile stress for hydrogels undergoing uniaxial strain for both flexible (black) and stiff (red) middle segments.