Driving Forces of Self-Assembly in Protein–Polymer Bioconjugates

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Abstract

Protein–polymer bioconjugates have shown great promise as high-performance biomaterials, with applications in fields as diverse as catalysis, drug delivery, and biosensing. Bioconjugation has proven to be an effective protein immobilization strategy that allows the protein to maintain or even enhance activity while imparting self-assembly capabilities to the overall material. The self-assembly behavior provides control over the orientation and nanostructure of the bioconjugates, enabling the design of functional materials with superior transport properties and high stability. The phase behavior of globular protein–polymer bioconjugates is analogous to that of traditional synthetic polymer block copolymers and leads to the formation of many of the same nanostructures. Despite these similarities, there are also several key differences between fully synthetic and protein–polymer block copolymers. The phase behavior of protein–polymer bioconjugates is affected by coarse-grained properties such as protein size, protein virial coefficient, protein overall charge, polymer chemistry, and polymer topology. However, a unifying theory describing the self-assembly of these materials does not yet exist.

The goal of this thesis was to understand interaction-based and structural driving forces of bioconjugate self-assembly. Partial structure factor analysis and subsequent inverse Fourier transformation showed that protein–polymer interactions could be quantified and understood in the context of physical phenomena such as depletion through a real-space correlation function. The nature of these interactions can affect the propensity of a bioconjugate system to order. In addition, polymer–water interactions were probed using contrast variation small-angle neutron scattering, which showed that polymer hydration is affected by both polymer chemistry and concentration. This dependence likely underpins the significant effect that polymer chemistry has on self-assembly.

On the structural side, the self-assembly of protein–rod block copolymers was investigated using homochiral polymer blocks that formed α-helices. Protein–rod bioconjugates self-assembled at all conditions tested, while the chemically identical protein–achiral coil bioconjugate remained disordered. The achiral coil polymer was found to be non-repulsive to the protein block. Thus, the rigidity of the rod block can drive self-assembly in weakly segregated systems.

Finally, a hard sphere–soft sphere dumbbell model for protein–polymer bioconjugates was built to understand the role of coarse-grained structural properties in phase behavior. Molecular dynamics simulations showed that this model was able to reproduce the most notable features of bioconjugate self-assembly, including an asymmetrical phase diagram and a lyotropic reentrant order-disorder transition at high concentrations. The success of this highly coarse-grained model revealed that colloidal interactions are sufficient to effect self-assembly in the globular protein–polymer block copolymer system.

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