Rheology of Concentrated Protein Solutions and Attractive Colloidal Dispersions

by

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Abstract

Therapeutic protein products with high solution concentration often possess extremely high viscosity and have difficulties in processing and delivery. It is desirable to predict and control the viscosity of protein solutions based on their interactions at the molecular level. Fundamental understanding on their rheology will greatly facilitate the development and engineering of biopharmaceuticals. In general, viscosity of attractive colloidal dispersions increases with their concentration and attraction strength, and diverges at the gel point. In this thesis, we investigate the mechanism of enhanced viscosity of concentrated protein solutions and colloidal dispersions due to inter-particle attractions.

Coarse-grained models of protein solutions and colloidal dispersions are developed. We improve a previously developed 12-bead model by considering the hydrodynamic interactions and using the correct forms of screened electrostatic potential and dispersion forces to simulate monoclonal antibody solutions. The model captures anisotropic effects and correctly recovers the solution micro-structures. A random patchy sphere model with controllable surface patchiness is also developed to describe more general colloidal particles with anisotropic interactions. We observe significant deviations in micro-structure and thermodynamics from isotropic particles at modest particle concentrations. Dynamics and rheology are sensitive to near-field non-central interactions and the resulting rigid constraints. Considering these constraints improves the viscosity prediction of concentrated antibody solutions and explains the diverging viscosity during gelation of attractive colloidal dispersions. It is also noticed that the rigid constraints in physical gels play a similar role in rheology as the cross-links in chemical gels. We have demonstrated that the rigid constraints, which are seldom accounted for in previous works, are indispensable when computing the stress of a sheared suspension.

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