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Contributions of equilibrium and non-equilibrium clusters to viscosity in concentrated protein solutions PRASAD SARANGAPANI, Drug Delivery and Devices, MedImmune, STEVEN HUDSON, Materials Science and Engineering Division, NIST, JAI PATHAK, Drug Delivery and Devices, MedImmune, KALMAN MIGLER, Materials Science and Engineering Division, NIST — Equilibrium and non-equilibrium clustering are ubiquitous phenomena in soft matter physics and are typically observed in systems ranging from colloidal suspensions to monoclonal antibodies (mAbs). Such phenomena are central to understanding and preventing irreversible aggregation in addition to controlling viscosity challenges related to formulation and drug delivery of protein therapeutics. Curiously, little work has been done in exploring the cluster size dependence of low-shear viscosity and intrinsic viscosity in protein solutions in a controlled manner. In this work, we carefully control cluster size of reversible and irreversible clusters formed by globular proteins or monoclonal antibodies over a concentration range of 2 mg/mL-500 mg/mL and pH from 3-9. We find a marked dependence of low-shear viscosity on cluster size using custom-designed silicon-based microfluidic viscometers. Measurements of cluster sizes using static light scattering reveal a correlation of low shear viscosity as well as intrinsic viscosity with the average cluster size. We model the composition dependence of viscosity for the case of equilibrium and non-equilibrium clusters using an adaptation of a model recently presented by Minton for protein mixtures.

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