Abstract Submitted
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Aggregation of concentrated monoclonal antibody solutions studied by rheology and neutron scattering[1] MARIA MONICA CASTELLANOS, Department of Materials Science and Engineering, Pennsylvania State University, University Park, PA, 16802, JAI PATHAK, Formulation Sciences Department, Drug Delivery Group, MedImmune, Gaithersburg, MD, 20878, RALPH COLBY, Department of Materials Science and Engineering, Pennsylvania State University, University Park, PA, 16802 — Protein solutions are studied using rheology and scattering techniques to investigate aggregation. Here we present a monoclonal antibody (mAb) that aggregates after incubation at 40 °C (below its unfolding temperature), with a decrease in monomer purity of 6% in 10 days. The mAb solution contains surfactant and behaves as a Newtonian fluid when reconstituted into solution from the lyophilized form (before incubation at 40 °C). In contrast, mAb solutions incubated at 40 °C for 1 month exhibit shear yielding in torsional bulk rheometers. Interfacial rheology reveals that interfacial properties are controlled by the surfactant, producing a negligible surface contribution to the bulk yield stress. These results provide evidence that protein aggregates formed in the bulk are responsible for the yield stress. Small-angle neutron scattering (SANS) measurements show an increase in intensity at low wavevectors ($q < 4*10^{-2}$ nm^{-1}) that we attribute to protein aggregation, and is not observed in solutions stored at 4 °C for 3 days before the measurement. This work suggests a correlation between the aggregated state of the protein (stability) and the yield stress from rheology.

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