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Small-Angle Neutron Scattering and Neutron Spin Echo Characterization of Monoclonal Antibody Self-Associations at High Concentrations ERIC YEARLEY, MacroGenics, Inc., ISIDRO (DAN) ZARRAGA, Genentech, Inc., PAUL (DOUG) GODFRIN, University of Delaware, TATIANA PEREVOZCHIKOVA, National Institute of Standards and Technology, NORMAN WAGNER, University of Delaware, YUN LIU, University of Delaware/National Institute of Standards and Technology — Concentrated therapeutic protein formulations offer numerous delivery and stability challenges. In particular, it has been found that several therapeutic proteins exhibit a large increase in viscosity as a function of concentration that may be dependent on the protein-protein interactions. Small-Angle Neutron Scattering (SANS) and Neutron Spin Echo (NSE) investigations have been performed to probe the protein-protein interactions and diffusive properties of highly concentrated MAbs. The SANS data demonstrate that the inter-particle interactions for a highly viscous MAb at high concentrations (MAb1) are highly attractive, anisotropic and change significantly with concentration while the viscosity and interactions do not differ considerably for MAb2. The NSE results furthermore indicate that MAb1 and MAb2 have strong concentration dependencies of dynamics at high Q that are correlated to the translational motion of the proteins. Finally, it has also been revealed that the individual MAb1 proteins form small clusters at high concentrations in contrast to the MAb2 proteins, which are well-dispersed. It is proposed that the formation of these clusters is the primary cause of the dramatic increase in viscosity of MAb1 in crowded or concentrated environments.

Eric Yearley
MacroGenics, Inc.

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