MAR10-2009-000313

Abstract for an Invited Paper
for the MAR10 Meeting of
the American Physical Society

**Composition-Gradient Static Light Scattering and the Quantification of Biomolecular Interactions in Therapeutic Proteins**

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Macromolecular interactions of interest to the pharmaceutical industry cover a variety of phenomena: binding of proteins to form well-defined complexes; reversible and irreversible oligomerization; and non-specific intermolecular interactions. The analysis and manipulation of these phenomena are crucial to the successful development, manufacture, storage and delivery of biological drugs such as antibodies. Light scattering (LS) has proven to be one of the most versatile free-solution and label-free methods for studying proteins and their interactions. Previously limited primarily to assessing molar mass, size and oligomerization state, the recent emergence of automated Composition-Gradient Static Light Scattering (Attri, A.; Minton, A.P. *Anal. Biochem.* **2005**; 346(1), 132–8), or CG-SLS, extends the range of biotech LS applications to equilibrium binding affinity and stoichiometry of bound complexes, kinetics of association and dissociation, and non-specific interactions (attractive and repulsive). In this talk I present progress in CG-SLS for biophysical characterization of pharmaceutical protein-protein interactions. In the drug development phase, CG-SLS studies of antibody-antigen complexes compliments other biomolecular interaction techniques commonly found in the biotech world such as surface plasmon resonance (SPR). In the formulation development stage, long-term stability of drug product is sought. Protein degradation modes include irreversible aggregation, which may lead to adverse physiological effects, and reversible self-association, which affects solution viscosity and hence injectable drug delivery. CG-SLS addresses both of these, the former via determination of virial coefficients, which describe the overall non-specific attraction or repulsion between molecules and may be used to optimize the formulation buffer to minimize aggregation, and the latter by binding affinity and stoichiometry of the associated complexes.