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Determination of reversible protein equilibrium association coefficients using light scattering

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The characterization in solution of reversible protein associations as well as associations between proteins and small molecules is essential in many areas of science. Understanding cellular function or developing and formulating pharmaceuticals or other biologically active materials often requires quantitation of such associations. Most pharmaceuticals have functionality due solely to association with molecules within the body, and the discovery and accurate characterization of these associations is a key element for pharmaceutical development. Unfortunately, most methods used to measure associations of proteins require either immobilizing the protein on a surface (e.g. surface plasmon resonance), which potentially alters the protein characteristics, or require considerable time and effort and large quantities of sample (e.g. analytical ultracentrifugation, isothermal titration calorimetry). Light scattering based measurements of reversible association coefficients require much less sample and may be performed much more rapidly than other free solution techniques. In this talk I describe how static and dynamic light scattering may each independently be used to measure equilibrium association coefficients between proteins in free solution, and may also be used to observe and quantitate the association of small molecules with them. I present background theory for both static and dynamic light scattering measurements of equilibrium associations, and examples of measurements made of both model systems and of systems with commercial relevance in the pharmaceutical industry.