User Profile

Allen P. Minton
National Institutes of Health

Protein-protein interactions (PPI), which give rise to much of the amazing complexity of biology, are in themselves deceptively diverse. The range of biologically relevant interactions spans at least 9 decades in affinity as well as a multitude of categories such as specific vs. non-specific, self vs. hetero, monovalent vs. multivalent, cooperative vs. independent, steric vs. allosteric and more. Few scientists have been as instrumental in the quantitative study of PPI across that entire span as Dr. Allen Minton, Senior Investigator in the National Institutes of Health. Dr. Minton carries out his research under the auspices of the National Institute for Diabetes and Digestive and Kidney Diseases (NIDDK), Laboratory of Biochemistry and Genetics, in the Physical Biochemistry Section. He is particularly interested in the impact on PPI of the diverse and crowded macromolecular environment found in the cellular medium (cytoplasm). Among the biophysical techniques that he employs are analytical ultracentrifugation (AUC), circular dichroism, fluorescence intensity and anisotropy, and of course light scattering.

Allen's work combines the relentless pursuit of solid science with a knack for inventing new twists on instrumentation. His expertise in applications of AUC to the characterization of PPI lead to several innovations in AUC technology and methodology, including micro-fractionation and tracer sedimentation. Recently his group developed a novel capillary viscometer aimed at deciphering colligative rheological phenomena.

The 'gold standard' for characterizing PPI in solution was, for many years, AUC/sedimentation equilibrium (SE). Attending a seminar by Dr. Philip Wyatt on modern multiangle light scattering (MALS) technology, Allen conceived of the light-scattering analog to SE:

"composition-gradient multi-angle light scattering', or CG-MALS.

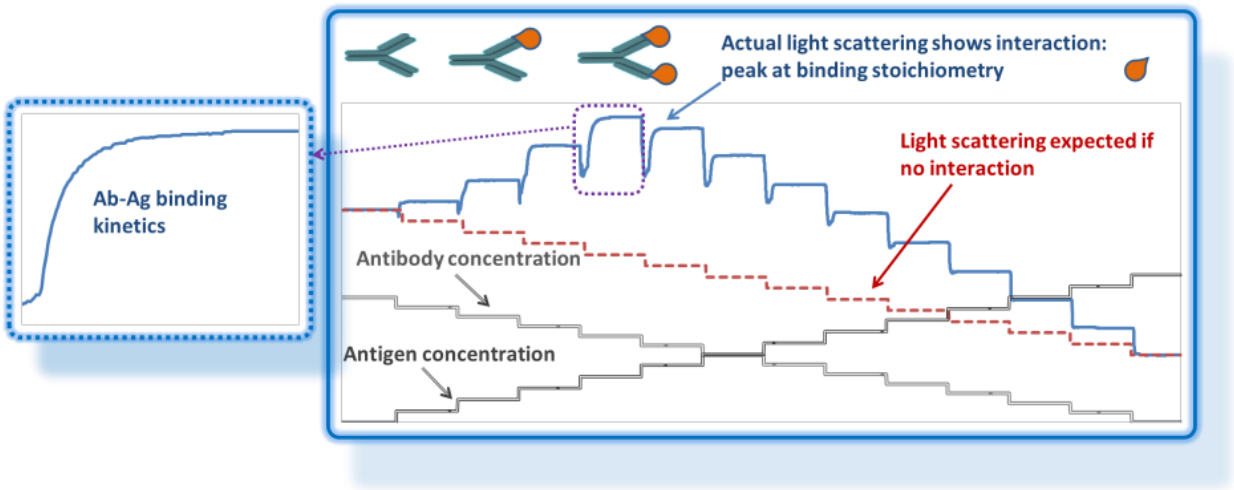
While the idea of using static light scattering to characterize PPI was not novel, Minton - along with his colleague A. Attri and additional co-workers – pioneered the combination of automated liquid handling with a sensitive Wyatt DAWN MALS detector and new analysis algorithms that, for the first time, made CG-MALS a practical and robust technique. CG-MALS addresses a remarkable range of PPI and other macromolecular interactions without labeling or immobilization, providing equilibrium binding constants, absolute molecular stoichiometry and reaction kinetics.

Collaboration between the NIH group and Wyatt R&D led to the Commercial implementation of CG-MALS, the Calypso system. Some of the theory and applications

of CG-MALS were reviewed in a special edition of *Biophysical Reviews*, produced in honor of Allen Minton's 70th birthday (this article is open-access and freely downloadable).

After demonstrating excellent agreement between SE and CG-MALS for ideal, specific protein binding, Allen went on to develop a practical theoretical framework for analyzing PPI in crowded (thermodynamically non-ideal) environments via CG-MALS. This theory was utilized in several experimental studies. Altogether, 15 articles in the Wyatt Bibliography have been co-authored by Dr. Minton, amongst his complete list of 164 (his purely theoretical publications are not listed in the Wyatt Bibliography).

More recently, Allen has turned his attention to the benefits of high-throughput dynamic light scattering (DLS) for PPI analysis by means of the DynaPro Plate Reader II. A guest speaker at no less than two International Light Scattering Colloquia (2004 and 2009), we were honored to have Allen, as well as his post-doc Di Wu, present some of their latest light scattering PPI results at the Greater D.C. Region Protein & Biotech User Meeting on April 30, 2014.



CG-MALS measurement of antibody-antigen binding. Each step consists of an injection of a new protein composition, indicated by the lower traces. The MALS signal reaches a maximum at the 1:2 stoichiometric ratio. The equilibrium data are analyzed to determine binding affinity and absolute molecular stoichiometry.

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