Forces in Biomolecular Systems SFB 863

Label-free visualisation of biomolecular complex formation using interferometric scattering mass photometry

Nikolas Hundt

University of Oxford

Abstract:

Every process in a living organism whether physiological or pathological is orchestrated by biomolecules that come together, interact and promote specific functions. However, a major difficulty in investigating these interactions is the number of molecular species involved which can range from individual molecules to large multicomponent complexes. Many ensemble-based techniques lack the required size resolution and dynamic range necessary to distinguish all components in a strongly polydisperse sample. Fluorescence can be used to visualise processes at the single-molecule level but is very limited in providing quantitative information about the size of the observed molecules. Interferometric scattering microscopy (iSCAT) enables direct, label-free and dynamic observation of biomolecular complexes at the single-molecule level. Furthermore, because the light scattering signal of the imaged molecules scales with their size, it can be used for quantification of the size distribution in a polydisperse sample similar to native mass spectrometry, while leaving the molecules in their native solution environment. As any molecule will scatter light, the technique is universally applicable to any kind of interaction study including but not limited to proteins, nucleic acids, lipids and small molecules. I will show previous examples studied in our lab such as the interaction of HIV-envelope protein with an HIV inhibitor, amyloid aggregation on a lipid bilayer, the motion of motor proteins and actin filament formation. I also want to point out future directions for iSCAT, e.g. how it can be applied to the investigation of amyloid fibril nucleation and as a drug screening approach.

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Contact: Claudia Veigel, claudia.veigel@med.uni-muenchen.de, phone: 089-2180-71561