Columbia | Special Symposium
Frontiers in Biology Through Mass Spectroscopy

Wednesday, April 25, 2018 at 1:00pm at The New York Structural Biology Center at 89 Convent Avenue

Towards a "Molecular Microscope" for the Cell

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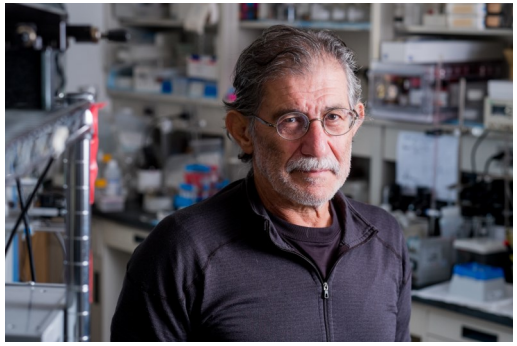
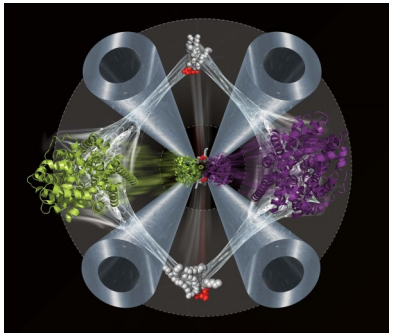


The myriad events that occur in living cells (replication, organellar assembly, transport, genome organization, transcription etc.) are to a large extent carried out through dynamic associations and assemblies of macromolecules. I will describe our efforts to develop and integrate sets of tools that are designed to throw light on the evolution, structure and function of these macromolecular machines.

To do this, we are developing approaches for elucidating proximal, distal, and transient protein-protein interactions in cellular milieus, as well as for determining distance restraints between amino acid residues within large protein assemblies by chemical cross-linking and mass spectrometry. The long-term goal of this research is to develop what I loosely term a "molecular microscope" for defining cellular systems with scales spanning all the way from dimensions of the cell to atomic resolution of molecules.

Membrane proteins
The lipid connection

Carol Robinson
University of Oxford



The realisation that the lipid environment is crucial for maintaining the structure and function of membrane proteins prompts new methods to understand lipid interactions. One such method, mass spectrometry, is emerging with the potential to monitor different modes of lipid binding to membrane protein complexes. Initial studies monitored the addition of lipids and deduced the kinetic and thermodynamic effects of lipid binding to proteins. Recently however, we have focused on identifying lipids already present, explicitly in plugs, annular rings or cavities. Lipids that bind within these orifices to membrane proteins will have higher residence times than those in the bulk lipid bilayer and consequently can be quantified and characterized by mass spectrometry. In special cases, lipids identified within cavities have been proposed as substrates following activity assays. Alternatively, a gas phase unfolding protocol can be used to distinguish lipids that are important for stability. In this lecture I will provide an overview of recent advances in mass spectrometry, with a particular focus on the distinction of the various modes of lipid binding, their implications for structure and function, as well as new directions that lie ahead.

Associated paper: - The role of interfacial lipids in stabilizing membrane protein oligomers. K. Gupta, J. A. Donlan, J. T. Hopper, P. Uzdavinys, M. Landreh, W. B.Struwe, D. Drew, A. J. Baldwin, P.J. Stansfeld, C.V. Robinson. Nature, 2017, 541: 421-424

https://www.nature.com/articles/nature20820?WT.feed_name=subjects_analytical-chemistry

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