UCMERCED | CHEMISTRY & BIOCHEMISTRY

DATE 04/26/2024 | TIME 10:30am | LOCATION COB1 110

CHEMISTRY & BIOCHEMISTRY SEMINAR SERIES:

Single-molecule and mesoscale biophysics of disordered proteins/biomatter

Ashok Deniz

Professor, Integrative Structural and Computational Biology
The Scripps Research Institute

Abstract:

Disordered proteins and larger biomatter assemblies are widely represented in biology, and their structural and dynamic features are critical to biological function. In this lecture, I will discuss aspects of our work on the biophysics of these complex systems over a range of spatiotemporal scales. In one line of work, I will discuss insights we have gained into complex binding-folding landscapes resulting from interactions of intrinsically disordered proteins (IDPs). In particular, I will focus on our use of single-molecule methods, which can provide nanoscale information about IDP interactions and folding, often "hidden" in other types of experiments. In addition, I will discuss aspects of our work on the physical chemistry of protein/RNA biomolecular condensates, including reentrant phase transitions and non-equilibrium substructure formation, features that could give rise to memory effects/feedback loops relevant to dynamic compartmentalization and function in cells. Overall, my presentation will highlight the strengths of our biophysical approaches to map dynamic nanoscale to mesoscale complexity related to disordered biomatter and corresponding function.

For more info, contact: Shahar Sukenik, ssukenik@ucmerced.edu

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About the Speaker:

Ashok Deniz received his PhD in Physical Organic Chemistry from the University of Chicago. His main work involved using sound to measure the thermodynamics of the short-lived, prototypical antiaromatic species Cyclobutadiene. He also used pump-probe spectroscopy to study the picosecond and femtosecond dynamics of transient intermediates involved in SN1 chemical reactions. He then began postdoctoral work at the University of California, Berkeley – here he was involved in early developments in single-molecule FRET methods, including the first demonstration of its distance-measurement capability. He then started his own single-molecule and soft matter biophysics lab at Scripps Research in La Jolla, where he is currently Professor.

Prof. Deniz's research interests have centered around gaining a fundamental mechanistic understanding of how biological systems function. To achieve this overall goal, his lab has sought to perform detailed mechanistic studies of proteins, RNA and other macromolecules from molecular- to macro-scales. Deniz has made several major contributions towards understanding the biophysics of IDPs and biomolecular condensates with deep implications for biology, regulation and disease. His lab discovered several important features of the IDP binding-folding process, including complex binding-folding landscapes, influence of disease mutations, temporal sequence of binding and folding events, and several principles underpinning IDP/RNA condensation. His work has tackled these problems for the neuronal/Parkinson's disease linked α-synuclein, transcription factors CREB/PPARγ, multifunctional protein nucleophosmin, yeast prion protein Sup35, viral oncoprotein E1A, ALS linked FUS, and others. In the area of larger scale biomatter including condensates, Deniz lab has made discoveries related to complex non-monotonic phase behavior, dynamic substructure formation and memory effects. For example, they predicted and tested the concept of reentrant phase transitions for protein/RNA/other condensates, demonstrating this broadly applicable concept with potential for resulting in feedback loops,

In parallel, Deniz has pushed the development of novel technologies (primarily single-molecule and related biophysical methods) that can be leveraged to uncover "hidden" information that is often obscured in traditional experiments. In this context, Deniz has been closely involved in making a number of innovative advances. These have included the first demonstration of the distance dependence of single-molecule smFRET and application to protein folding. Advances include the first and subsequent applications of smFRET to understand structural dynamics, interaction and related function of IDPs, their folding and misfolding, and early work on use of smFRET and other methods to probe IDP/protein structure during biomolecular condensation. Advances also include being one of first two labs to develop multicolor smFRET for global studies of protein conformation and binding, first uses of unnatural amino-acids for site-specific protein FRET labeling, and early development of microfluidics for studying rapid IDP processes.

His interests also include biophysics of coupling of IDP conformation and binding to surfaces, studies of non-equilibrium dynamics at the molecular and larger scales, uncovering complex behavior exhibited in multicomponent and charge-mediated phase separation, application of pump-probe methods for studies of rapid kinetics, and study of plausible lipid chemical evolution scenarios in the origin of life.

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