Yale Institute for Nanoscience and Quantum Engineering

Friday- October 2, 2015

12:00 to 1:00 p.m.

BECTON SEMINAR ROOM

Professor Ziad Ganim

Department of Chemistry, Yale University

"Force-Detected Single Molecule Absorption Spectroscopy"

Single molecule manipulation and optical detection have been revolutionary tools for biophysics, but find limited application at the chemical level due to a lack of structural resolution. We propose that the technical difficulties associated with observing the change in light transmission affected by a single molecule can be circumvented by encoding absorption spectroscopy into a force signal. The optical trap is used to isolate a single molecule and to position it near a metallic microsphere, which functions as nanoscale electrostatic force sensor and replaces the spectrometer. Model calculations and ongoing experiments are described.

Peter Koo

Department of Physics, Yale University

"Extracting Diffusive States of Proteins in Live Cells: Towards In Vivo Biochemistry"

We describe a novel, machine-learning based classification methodology, which we call perturbation expectation-maximization (pEM and pEMv2), that simultaneously analyzes a population of fluorescent protein trajectories obtained in living cells to uncover the system of diffusive behaviors realized by the protein. pEM will have a broad impact on studies of a wide range of biological systems where different biochemical interactions result in distinct diffusive behaviors, because uncovering the diffusive states of a protein, and eventually characterizing the transitions between different diffusive states within a protein's trajectory will permit the endogenous in vivo biochemistry of the diffusing protein to be probed and monitored within a live cell with single molecule resolution. Here, we validate the performance of pEM in silico and demonstrate that pEM is fully capable of uncovering the proper number of underlying diffusive states with an accurate characterization of their diffusion properties. We then apply pEM to experimental protein trajectories of the protein, Rho GTPases, which is a regulator of cytoskeletal dynamics and cellular homeostasis. Remarkably, pEM uncovers six distinct diffusive states conserved across several cell variants and two protein variants. These results demonstrate the power and potential of pEM by (1) uncovering the number of diffusive states, (2) determining the properties of each such diffusive state, and (3) classifying statistically each protein's trajectory to a respective diffusive state. In the future, it will be interesting, for example, to investigate how the propensities for each diffusive state change spatially and temporally under various kinds of exogenous stimulation in both healthy and cancerous cells.

Host: Professor Eric Altman