CPLC/Biophysics Graduate Student/Postdoc Symposium

Monday, November 17, 2014 - Room 1005 Beckman Institute

Student Hosts: John Cole and Thuy Ngo

Organization: Schulten group

8:30 am Continental Breakfast

9:00 am **Shahar Sukenik** (Gruebele group)
Faces in the Crowd: Disparate Mechanisms of Protein Stabilization by Crowding and Chemical Chaperones

9:15 am **Alex Krieg** (Myong group)
Profiling G-quadruplex Formation within Double-Stranded DNA

9:30 am **Mehdi Roein-Peikar** (Ha group)
The Princess and the Pea: A Story of Cell Mechanics

9:45 am Discussion / Coffee Break / Raffle #1

10:00 am **Kin Lam** (Schulten group)
Molecular Basis of Neuronal Signaling

10:15 am **Manish Shankla** (Aksimentiev group)
Conformational Transitions and Stop-and-Go Nanopore Transport of Single-Stranded DNA on Charged Graphene

10:30 am **Tyler Earnest** (Luthey-Schulten group)
Towards A Whole-Cell Model of Ribosome Biogenesis: Kinetic Modeling of SSU Assembly

10:45 am Discussion / Coffee Break / Raffle #2

11:00 am **Jason Merritt** (Kuehn group)
Environmental Fluctuations and Ecosystem Robustness

11:15 am **Sukrit Suksombat** (Chemla group)
Unwrapping of SSB from ssDNA Facilitates RecA Filament Formation

11:30 am **Sophia Yi** (Gennis group)
Probing the High-Affiinity Quinone Binding Site in Menaquinol Cytochrome aa_3-600 Oxidase from *Bacillus subtilis* by Pulsed EPR.

11:45 am Discussion / Coffee Break / Raffle #3

12:00 pm **Neil Kim** (Kuhlman group)
Watching Transposable Elements Jumping Inside Cells in Real Time.

12:15 pm **Sixue Zhang** (Hammes-Schiffer group)
Role of the Active Site Guanine in the glmS Ribozyme Self-Cleavage: Quantum Mechanical/Molecular Mechanical Free Energy Simulations

12:30 pm **Tommaso Biancalani** (Goldenfeld group)
Stochastic Recruitment Leads to Symmetry Breaking in Foraging Populations

12:45 pm Discussion / Lunch / Announcement of Best Speaker Prize

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Symposium Program

Student hosts: John Cole and Thuy Ngo
Organized by the Schulten group

8:30 am

Continental Breakfast

9:00 am

Faces in the Crowd: Disparate Mechanisms of Protein Stabilization by Crowding and Chemical Chaperones
Speaker: Shahar Sukenik (Gruebele group)

The cell is a complex environment occupied by myriad molecular species. Most of these do not specifically interact with a protein of interest. "Molecular crowding" theory explains how, by simply taking up space, such species can stabilize a protein in its native state. Here I present new findings that challenge molecular crowding theory. By examining the thermodynamics of protein stabilization in the presence of different crowder molecules, we find thermodynamically distinct stablization mechanisms that depend on crowder chemical nature.

9:15 am

Profiling G-quadruplex Formation within Double-Stranded DNA
Speaker: Alex Krieg (Myong group)

G-quadruplexes (GQs) are alternative DNA secondary structures that recently have been identified to stably form throughout the human genome. Computational studies have shown these structures are highly enriched in promoter sequences, and thus have been suggested to be functionally important in transcriptional regulation. Current methods of investigating GQs rely heavily on studying these structures in ssDNA. This single stranded context fails to provide a realistic platform for the study of the approximately 400,000 possible GQ-folding sequences found throughout the human genome. We developed an ensemble fluorescence method used in parallel with standard single molecule techniques to map the folding propensity of GQ structures within a double stranded DNA context.

9:30 am

The Princess and the Pea: A Story of Cell Mechanics
Speaker: Mehdi Roein-Peikar (Ha group)

We study cell adhesion using tethers with different rupture forces. Cells do spread on strong tethers but not on weak ones. Surprisingly, we found if a few strong tethers are added (at the level of 2-3 tethers per cell) to many weak tethers, cells spread. This shows cells are ultra-sensitive to the existence of strong tethers in their environment.

9:45 am

Discussion/Coffee Break/Raffle #1

10:00 am

Molecular Basis of Neuronal Signaling
Speaker: Kin Lam (Schulten group)

Voltage-gated sodium and potassium channels regulate membrane potential for the transmission of neuronal electrical signals in many animals. A single-channel kinetic model was constructed for both channels based on the kinetic rates of their voltage-sensor domains. The modeling results indicate that neural signaling cast successfully in the form of Hodgkin-Huxley equations can arise from a single (fast) sodium / (slow) potassium channel pair. A sodium channel homology model provides insights into how key residues contribute to the kinetic difference between sodium and potassium channels.

10:15 am

Conformational Transitions and Stop-and-Go Nanopore Transport of Single-Stranded DNA on Charged Graphene
Speaker: Manish Shankla (Aksimentiev group)

Control over interactions with biomolecules holds the key to applications of graphene in biotechnology. We investigate how interactions of single-stranded DNA and a graphene membrane can be controlled by electrically biasing the membrane. Our molecular dynamics simulations reveal that different DNA homopolymers, including methylated DNA, adopt unique conformations on electrically charged graphene. The graphene charge can also modulate the speed of DNA motion through the nanopore enabling the exciting possibility of on-demand transport, useful for DNA sequencing.

10:30 am

Towards A Whole-Cell Model of Ribosome Biogenesis: Kinetic Modeling of SSU Assembly
Speaker: Tyler Earnest (Luthey-Schulten group)

We report on our progress on the construction of a whole-cell model of ribosome biogenesis. Here we describe a detailed kinetic model accounting for the association of 18 of the 20 ribosomal proteins to the 16S rRNA to form the small subunit in vitro. Integration of this assembly model into an in vivo, spatially resolved whole-cell model will be discussed.

10:45 am

Discussion/Coffee Break/Raffle #2

11:00 am

Environmental Fluctuations and Ecosystem Robustness
Speaker: Jason Merritt (Kuehn group)

It is believed that fluctuations in environmental parameters drive the evolution of robustness in ecosystems, but this hypothesis has not been tested directly. We report progress on a chemostat-microscope apparatus capable of both precise, variable control of environmental parameters and real-time single-cell counting of bacterial populations. This experimental setup will allow us to quantitatively relate environmental fluctuations, population dynamics and evolution for the first time.

11:15 am

Unwrapping of SSB from ssDNA Facilitates RecA Filament Formation
Speaker: Sukrit Suksombat (Chemla group)

E. coli RecA is an essential protein for DNA repair. During the repair, RecA must bind and form nucleoprotein filaments on single-stranded DNA (ssDNA) in direct competition with single-stranded DNA binding protein (SSB). Despite extensive studies, the mechanism behind this competitive process remains unclear. Here, we use high-resolution optical tweezers with simultaneous fluorescence microscopy to observe directly the mechanical properties of ssDNA-SSB-RecA complexes. Our results show that tension-induced unwrapping of the SSB makes ssDNA available for RecA to bind and nucleate a filament.

11:30 am

Probing the High-Affinity Quinone Binding Site in Menaquinol Cytochrome aa_3-600 Oxidase from *Bacillus subtilis* by Pulsed EPR.
Speaker: Sophia Yi (Gennis group)

Cytochrome aa_3-600 is a terminal oxidase in the electron transport pathway that contributes to the electrochemical membrane potential by actively pumping protons. A remarkable feature of this enzyme complex is that it oxidizes menaquinol instead of cytochrome c. Pulsed EPR has been used to demonstrate that the enzyme stabilizes a semiquinone radical and, furthermore, defines the hydrogen bonding from the protein responsible for this stabilization. Although expected, histidine is clearly not a hydrogen bond partner stabilizing the semiquinone.

11:45 am

Discussion/Coffee Break/Raffle #3

12:00 pm

Watching Transposable Elements Jumping Inside Cells in Real Time.
Speaker: Neil Kim (Kuhlman group)

Transposable elements (TEs) are also known as jumping genes. We present a simple synthetic TE, which will permit real time, in vivo observation of TE-related events in *Escherichia coli* through time-lapse fluorescence microscopy in microfluidic devices. The system is capable of tracking large population of cells ($> 10{,}000$) for $\sim$15 generations, allowing analysis at both single cell level and population level.

12:15 pm

Role of the Active Site Guanine in the glmS Ribozyme Self-Cleavage: Quantum Mechanical/Molecular Mechanical Free Energy Simulations
Speaker: Sixue Zhang (Hammes-Schiffer group)

The glmS ribozyme catalyzes a self-cleavage reaction at the phosphodiester bond between residues A-1 and G1. This reaction is thought to occur by an acid-base mechanism involving the glucosamine-6-phosphate cofactor and G40 residue. Herein quantum mechanical/molecular mechanical (QM/MM) free energy simulations and pKa calculations, as well as experimental measurements of the rate constant for self-cleavage, are utilized to elucidate the mechanism.

12:30 pm

Stochastic Recruitment Leads to Symmetry Breaking in Foraging Populations
Speaker: Tommaso Biancalani (Goldenfeld group)

When an ant colony is faced with two identical equidistant food sources, the foraging ants are found to concentrate more on one source than the other. Analogous symmetry-breaking behaviours have been reported in various population systems, (such as queueing or stock market trading) suggesting the existence of a simple universal mechanism. Past studies have neglected the effect of demographic noise and required rather complicated models to qualitatively reproduce this behaviour. I will show how including the effects of demographic noise leads to a radically different conclusion. The symmetry-breaking arises solely due to the process of recruitment and ceases to occur for large population sizes. The latter fact provides a testable prediction for a real system.

12:45 pm

Discussion/Lunch/Best Talk Award

The winner of the best lecture contest will be announced, and a prize awarded!