Symposium Program

Student hosts: Kiran Girdhar and Boon Chong Goh
Organized by the Schulten group

8:30 am

Continental Breakfast

9:00 am

Single molecule FRET reveals the pore size and opening mechanism for MscL
Speaker: Yong Wang, Selvin group

The mechanosensitive channel of large conductance (MscL) serves as a model system for mechanosensitive ion channels gated by the bilayer mechanism. Here we report our measurements of the distance changes of multiple residues of MscL using smFRET. These measurements were then used to develop a molecular dynamics model for the open structure of the protein. We find that its open pore size is 2.8 nm in diameter and that the channel opens via the helix-tilt model.

9:15 am

Spatial organization of ribosome biogenesis of Escherichia coli
Speaker: Cac Nguyen, Kuhlman group

The ribosomal RNAs are synthesized through the transcription of seven ribosomal RNA (rRNA) operons, which contain 99% identical genes. The presence of seven closely identical copies of rRNA and their possibly distinguishable contributions to the total complement of ribosomes remains unrevealed knowledge. In this work, I will develop a system to label and distinguish the individual operons and will be able to distinguish and track the ribosomes generated by each operon from the other ribosomes. A short sequence is inserted into the 23S rRNA of the target rRNA enabling high resolution imaging of the ribosomes generated from each operon by single molecule FISH (smFISH). The outcome spatial distributions of ribosomes generated from each operon will further reveal the biogenesis of ribosomes.

9:30 am

New directions in biological imaging: discovery and engineering of LOV domain based fluorescent proteins
Speaker: Arnab Mukherjee, Schroeder group

We describe the application of genome mining and directed evolution to discover and engineer new fluorescent proteins based on the LOV domain. We demonstrate that LOV-proteins are thermostable and oxygen-independent reporters with a broad pH range and rapid fluorescence maturation, making them potentially powerful alternatives to the popular GFP-based reporters.

9:45 am

Discussion/Coffee Break

10:00 am

Catalysis in the Hepatitis Delta Virus ribozyme described by QM/MM free energy simulations
Speaker: Abir Ganguly, Hammes-Schiffer group

The Hepatitis Delta Virus ribozyme performs site-specific cleavage in RNA. This ribozyme uses a combination of metal ion and nucleobase catalysis in the self-cleavage reaction. We performed quantum mechanical/molecular mechanical (QM/MM) free energy simulations to investigate the mechanism of this reaction. Our results provide fundamental insights into ribozyme catalysis.

10:15 am

Emergence of rapid evolution from demographic stochasticity
Speaker: Hong-Yan Shih, Goldenfeld group

Rapid evolution can significantly change the eco-dynamics. We model the phenomena by considering population fluctuations in the ecosystem of a predator and two sub-populations of prey arising from rapid evolution. Through a generalized approach, demographic stochasticity yields the novel phase shift between sub-populations, which is in agreement with experimental observations.

10:30 am

AT nucleotides of the world, unite!
Speaker: Jejoong Yoo, Aksimentiev group

Eukaryotic chromatin organization is essential for gene regulations, however, its underlying physical principle is hardly known yet. In collaboration between Aksimentiev and Ha groups, we demonstrate that AT-rich and GC-rich domains can form their own clusters in the presence of polyamines and hypothesize that this sequence-dependent clustering mechanism is a key determinant of the chromatin organization.

10:45 am

Discussion/Coffee Break

11:00 am

Profiling double-stranded RNA binding proteins
Speaker: Shirley Wang, Myong group

We found that double-stranded RNA binding proteins with various functions exhibit diverse RNA-substrate specificity and that the interaction between protein and RNA could be dynamic. These results reveal the molecular mechanism underlying dsRNA recognition and underscore the diversity of essential biological tasks performed by dsRNA-related processes.

11:15 am

DNA sequence and DNA modifications direct nucleosome directional unwrapping
Speaker: Thuy Ngo, Ha group

We combined optical tweezers with smFRET to investigate the dynamics of nucleosomes - the packaging unit of eukaryotic genome. We discovered the nucleosome unwraps directionally under tension. Interestingly, the direction of unwrapping is governed by the local flexibility of DNA, which is, in turn, controlled by DNA sequence and modifications. Our work elucidates the fundamental principles of how DNA sequence and modifications regulate DNA metabolism.

11:30 am

Endothelial mechanotransduction: local tension sensing regulates global cell mechanics
Speaker: Adrienne Barry, Leckband group

Using mechanical perturbations of cell surface adhesion receptors, we investigated mechanisms of force transduction across cell membranes. Local mechanical stress on specific receptors triggered global changes in cell mechanics that propagated across cells through cell-cell junctions and the actin cytoskeleton. This work reveals a novel mechanism for force propagation through tissues and has direct relevance for human pathologies such as ventilator-induced lung injury.

11:45 am

Discussion/Coffee Break

12:00 pm

Physical mechanism of Rho hexameric helicase
Speaker: Wen Ma, Schulten group

The Rho hexameric helicase is an exemplary molecular motor protein that utilizes the energy from ATP hydrolysis to participate in transcription termination. How this hexameric ring-shaped motor generates mechanical force to translocate along RNA remained a mystery for a long time. Molecular dynamics simulations reveal now that the six identical subunits of the motor remain largely unaltered inside, but rotate relative to each other through surface-surface generated forces stemming from the ATP hydrolysis cycle. The six-subunit motions collaboratively translate the helicase along RNA.

12:15 pm

Stochastic simulations of cellular processes: from single cells to colonies
Speaker: John Cole, Luthey-Schulten group

Software advances have enabled simulations of chemical reaction networks in realistic spatially-resolved environments. These simulations rely on kinetic parameters that are often not available; the largest biochemical networks, like metabolism, tend to be simulated at steady-state using flux balance analysis (FBA). We have developed a modeling approach integrating both RDME sampling with an FBA metabolic model to study how different cells in dense bacterial colonies use the nutrients available to them.

12:30 pm

Visualizing large-scale motions of membrane transporters at atomic resolution using non-equilibrium simulations
Speaker: Mahmoud Moradi, Tajkhorshid group

For their function, membrane transporters rely on large-scale conformational changes whose computational study is hampered by the slow dynamics. Here we present a novel non-equilibrium approach to characterize the conformational transition of a membrane transporter, using system-specific reaction coordinates resulting in an unprecedented level of detail on the the mechanism of transport.

12:45 pm

Discussion/Lunch

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