Workshop on Computer Modeling and Simulation of Biomolecular Systems

Sep. 22 (Mon), 2014, RIKEN Wako Campus
Welfare and Conference Building 2F

13:10-13:20 **Opening remarks**
Yuji Sugita (Theoretical Molecular Science Laboratory, RIKEN)

13:20-14:10 **"A Polarizable Force Field for Biological Macromolecules based on the Classical Drude Oscillator Model"**
Alexander D. MacKerell, Jr. (University of Maryland, USA)

14:10-15:00 **"Biomolecular Modeling and Simulation using CHARMM-GUI"**
Wonpil Im (University of Kansas, USA)

15:00-15:10 Coffee Break

15:10-16:00 **"Chromosomal Dynamics and Correlations between Gene Location and Protein Function from Experimentally-Driven Models of Bacterial Nucleoids"**
Michael Feig (Michigan State University, USA)

16:00-16:50 **"Dynamics and Interactions of Macromolecules in the Cytoplasm of Mycoplasma Genitalium: All-atom Molecular Dynamics Study"**
Isseki Yu (Theoretical Molecular Science Laboratory, RIKEN)

16:50-17:00 **Closing remarks**
Yuji Sugita (Theoretical Molecular Science Laboratory, RIKEN)

A Polarizable Force Field for Biological Macromolecules based on the Classical Drude Oscillator Model

Alexander D. MacKerell, Jr.
University of Maryland, USA

ABSTRACT: Explicit treatment of electronic polarizability in empirical force fields offers the potential to significantly improve the accuracy of molecular simulations of macromolecules in condensed phases. Towards achieving this we have developed a polarizable force field based on the classical Drude oscillator model. An overview of the model and the parameter optimization approach will be presented. Results will then be presented on MD simulations of macromolecules including carbohydrates, proteins, lipids and nucleic acids with emphasis on the ability of the model to more accurately reproduce quantum mechanical and experimental data. Results include microsecond molecular dynamics (MD) simulations of multiple proteins in explicit solvent. In addition, the polarizable model more accurately treats cooperative helix formation of the (AAQAA)3 peptide and yields improved agreement with experiment for base flipping in DNA. Data obtained to date indicate that the inclusion of explicit electronic polarizability leads to significant differences in the physical forces affecting the structure and dynamics of macromolecules, which can be investigated in a computationally tractable fashion in the context of the Drude model.

Biomolecular Modeling and Simulation using CHARMM-GUI

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ABSTRACT: CHARMM-GUI, http://www.charmm-gui.org, is a web-based graphical user interface to prepare molecular simulation systems and (CHARMM and NAMD) input files to facilitate the usage of common and advanced simulation techniques. Since its original development in 2006, CHARMM-GUI has been widely adopted for various purposes and now contains a number of different modules designed to setup a broad range of simulations: Membrane Builder for protein-bilayer or membrane-only simulation system generation, Ligand Binder for free energy perturbation molecular dynamics (FEP/MD) simulations for protein-ligand binding affinity calculations, Micelle Builder for protein-micelle complex simulation system generation, GCMC/BD ion simulator for Brownian dynamics of ions across ion channels, Glycan Reader for preparation of simulation systems containing carbohydrates or proteoglycans, and, PACE CG Builder for coarse-grained simulation system preparation. Recently, new functionalities that have been integrated into CHARMM-GUI PDB Manipulator, such as ligand force field generation, incorporation of methanethiosulfonate (MTS) spin labels and chemical modifiers, and substitution of amino acids with unnatural amino acids. These new features together with existing modules are expected to be useful in advanced biomolecular modeling and simulation of proteins. In this talk, I will talk about the past, present, and future of CHARMM-GUI.

Chromosomal Dynamics and Correlations between Gene Location and Protein Function from Experimentally-Driven Models of Bacterial Nucleoids

Michael Feig

Michigan State University, USA

ABSTRACT: Recent experimental data from chromosome conformation capture (3C/5C/HiC) experiments provide constraints for the structure of chromosomal DNA. In a multi-scale modeling approach a plectonemic model of bacterial DNA was sampled with such experimental constraints to obtain high-resolution models of the genomic DNA of Caulobacter crescentus. Resulting models are highly consistent with the experimental data but show significant conformational diversity. The conformational ensemble for the chromosomal structure is interpreted in terms of dynamics through clustering followed by a Markov-state analysis. Chromosomal structures are furthermore used to map gene locations on the genome to three-dimensional distributions that allow an exploration of the correlations between gene locations and protein functions of the resulting gene products.

Dynamics and Interactions of Macromolecules in the Cytoplasm of Mycoplasma Genitalium: All-atom Molecular Dynamics Study

Isseki Yu

Theoretical Molecular Science Laboratory, RIKEN

ABSTRACT: Discovering the molecular-level dynamics and interactions of macromolecules in realistic cellular environment is one of the major challenges for biophysical scientists. For this purpose, we constructed all-atom model of cytoplasm in the Mycoplasma Genitalium, the smallest known bacteria. The size of the system is 100 nm x 100 nm x 100 nm, which is greatly exceeds that of typical molecular dynamics (MD) simulations, covering about 10% of the volume of an entire bacterium cell. Using the atomic trajectories generated by highly parallelized MD program GENESIS on K computer, characteristics of the diffusion of macromolecules and metabolites are analyzed. The influence of local cellular environment and protein-protein interactions on the dynamics of each individual macromolecules are discussed.