3rd Symposium on Biophysics Postgraduate Research in Hong Kong

Event Schedule

Date: 17/01/2017 (Tuesday)

Morning Session		
8:40 – 9:30	Breakfast & Tea	
9:00 – 9:15	Opening Speech: AP Head Prof. Xun-Li Wang	
9:15 – 10:00	Greg Voth, University of Chicago	Ultra-Coarse-Graining and Its Application to Multi-Protein Complexes
10:00 – 10:25	Jhih-Wei Chu, National Chiao Tung University	Multiscale Simulation via the Hybrid Hydrodynamics / Molecular Dynamics method
10:25 – 10:50	Feng Wang, University of Arkansas	Mapping MP2 potential energy surface to simple molecular mechanics force fields, accurate prediction of hydration free energy of simple salts from first principles
10:50 – 11:15	Takafumi Yamashita, University of Tokyo	On Quantitative Understanding on Antigen-Antibody Interaction through All-atom Molecular Dynamics Simulations
11:15 – 11:40	Xuhui Huang, Hong Kong University of Science and Technology	Investigating Conformational Changes of Biological Macromolecules Using Kinetic Network Models
11:40 – 12:05	Jian Zhou, South China University of Technology	Multiscale Modeling and Simulations of Protein Adsorption
12:05 – 12:30	Lanyun Lu, Singapore Nanyang Technology	Course-grained Modeling of Small-angle X-ray Scattering Intensity
12:30 – 2:00	Poster Session	

Afternoon Session		
2:00 – 2:25	Wei Zhuang, Fujian Institute of Research on Structure of Matters	Ion Effect on Hydrogen Bonding Network in Water
2:25 – 2:50	Kin-Yiu Wong, HKBU	Using Isotope Effects to Determine the Reaction Mechanisms behind RNA Transphosphorylation in Acidic and Alkaline Solution, and in Enzyme
2:50 – 3:15	Zhiyong Zhang, University of Science and Technology of China	Integrative Modeling of Large Biomolecules with Low-Resolution Structural Data
3:15 – 3:35	Discussion Topic: Future Directions in Computational Biophysics Moderator: Greg Voth, University of Chicago	
3:35 – 4:05	Tea Break & Poster Session	
Students' Presentations		
4:05 – 4:15	Ying-Chih Chiang	The role of intramolecular nonbonded interaction and angle sampling in single-step free energy perturbation
4:15 – 4:25	Chun Chan	Molecular Details of PH Domain of ACAP1 BAR-PH Protein Binding to PIP2-Containing Membrane
4:25 – 4:35	Yonghui Zhang	Lipid Absorption and Phase Transition Induced by Boron Nitride Nanosheet
4:35 – 4:45	Lizhe Zhu	Automated path searching for biomolecular systems
4:45 – 5:00	Awards for Best Student Poster & Best Student Talk Presenter: Greg Voth, University of Chicago	

* Please kindly scan the QR code to find more details about these talks and posters.

Ultra-Coarse-Graining and Its Application to Multi-Protein Complexes

Gregory A. Voth

Department of Chemistry, James Franck Institute, and Institute for Biophysical Dynamics, The University of Chicago, Chicago, IL, USA

Abstract:
Recent advances in theoretical and computational methodology will be presented that are designed to simulate biomolecular and other soft matter systems across multiple length and time scales. The approach provides a systematic connection between all-atom molecular dynamics, coarse-grained modeling, and mesoscopic phenomena. At the heart of the approach are methods for deriving coarse-grained models from molecular structures and their underlying atomic-scale interactions. This particular aspect of the work has strong connections to the theory of renormalization, but it is developed and implemented for heterogeneous biomolecular. An important component of the methodology has become the concept of the "ultra-" coarse-grained (UCG) model and its associated computational implementation. The latter aspect of this research concerns the unique numerical algorithms for these highly coarse-grained molecular dynamics simulations, leading to fast execution speeds that can be scaled over hundreds of thousands of computational cores. Illustrations of the UCG approach will first be provided for highly coarse-grained models of liquids, while more complex applications will be provided for large multi-protein complexes such as HIV-1 virus capsid assembly and actin filaments.

Multiscale Simulation via the Hybrid Hydrodynamics/Molecular Dynamics method

Jhih-Wei Chu

National Chiao Tung University, Taiwan

Abstract:
I will present the hybrid fluctuating hydrodynamics and molecular dynamics (hybrid FHD/MD) method for effective simulation of complex molecular systems at the mesoscopic scale. This method is combined with a multiscale computational framework to bridge molecular and field mechanics for allowing the mixed representation in the hybrid FHD/MD model to interface and communicate with simulations at a finer-scale, typical with all-atom force fields. The development of the hybrid FHD/MD simulation method and the conjugate framework of multiscale coarse gaining aims to accomplish two main objectives. The first is to make accessible the dynamics and statistics at the mesoscopic scale that are impractical to obtain with atomic models. The second is to enable the hybrid model to be used as a mesoscopic-scale theory to bridge the phenomenological and atomic scales of biology. This platform is specially designed to simulate the functional dynamics of protein machines and to trace the molecular origin of emergent properties, such as the free-energy landscapes and diffusion dynamics.

Mapping MP2 potential energy surface to simple molecular mechanics force fields, accurate prediction of hydration free energy of simple salts from first principles

Feng Wang

University of Arkansas, USA

Abstract:

The accuracy of a molecular dynamics simulation is determined by the underlying interaction model. Although electronic structure calculations can be very accurate, it is associated with a high computational cost, which severely limits its applicability for large systems. In order to address this challenge, the adaptive force matching (AFM) method has been developed that is capable of mapping an electronic structure potential energy surfaces to simple pair-wise energy expressions as used in standard molecular mechanics force fields. With only MP2 as reference, we have shown that force fields for various salts developed by AFM can reproduce the experimental hydration free energies with an error less than 2%. The ion potentials also gave good dynamical properties, such as the diffusion constants. We have also shown that cross terms from AFM can be used with traditional water potentials without seriously influencing the accuracy of the prediction. This opens up the possibility of combining AFM models with other existing models in large scale simulations.

On Quantitative Understanding on Antigen-Antibody Interaction through All-atom Molecular Dynamics Simulations

Takefumi Yamashita

University of Tokyo, Japan

Abstract:
We have studied the antigen-antibody interaction through all-atom molecular (MD) simulation and developed several analysis methods applicable to antibody design. From a technical aspect, we will discuss how the fragility of protein would make the free energy calculation difficult. In addition, we discuss complex mutation effects on affinity. We observed that even small modification of interface could change the binding affinity. In particular, a few interface water molecules affect the binding affinity significantly.

Investigating Conformational Changes of Biological Macromolecules Using Kinetic Network Models

Xuhui Huang

Hong Kong University of Science and Technology, Hong Kong

Abstract:
Simulating biologically relevant timescales at atomic resolution is a challenging task since typical atomistic simulations are at least two orders of magnitude shorter. Markov State Models (MSMs), a kinetic network model, built from molecular dynamics (MD) simulations provide one means of overcoming this gap without sacrificing atomic resolution by extracting long time dynamics from short MD simulations through the coarse graining on the phase space and time. In this talk, I will demonstrate the power of kinetic network models by applying it to simulate the complex conformational changes, that occurs at tens to hundreds of microsecond timescales for a large RNA Polymerase II complex containing nearly half million atoms. Furthermore, I will introduce a new efficient dynamic clustering algorithm for the automatic construction of MSMs for multi-body systems. We have successfully applied this new algorithm to model the protein-ligand recognition and self-assembly of co-polymers. Finally, I will introduce a new algorithm using the projection operator approach to identify optimal kinetic lumping and recover slowest conformational dynamics of complex systems.

Multiscale Modeling and Simulations of Protein Adsorption

Jian Zhou*

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Abstract:

Protein adsorption plays an important role in many applications such as protein chromatography, drug delivery on solid substrates, biosensors, biofuel cells and biomaterials. For these processes and applications, one key issue is the orientation of adsorbed proteins on surfaces. Controlled antibody adsorption orientation on surfaces is necessary to ensure that their active sites are away from the surface and accessible to bulk solution for immunoassay applications. For biofuel cell applications, to enable fast electron transfer, adsorbed cytochrome c should have an orientation with the heme ring close and perpendicular to surfaces. Another key issue that determines the activity of adsorbed proteins is their conformation (*i.e.*, how the conformation of the adsorbed protein resembles that of its native state). In this work, the protein orientation and conformation on charged surfaces are investigated by a hierarchical approach, *i.e.*, studied by colloidal, coarse-grained and all-atom models. Parallel tempering Monte Carlo and molecular dynamics simulations are used. Effects of surface charge density and sign, and solution ionic strength are examined in our simulations. Simulation results show that van der Waals and electrostatic interactions codetermine the orientation of adsorbed proteins. It is found that the electric dipole and hydrophobic dipole of adsorbed proteins play important roles in determining the protein orientation on charged and hydrophobic surfaces.

References

(1) J. Liu, C.Y. Liao, J. Zhou. *Langmuir*, **2013**, 29:11366-11374.
(2) G.B. Yu, J. Liu, J. Zhou. *J. Phys. Chem. B*, **2014**, 118:4451-4460.
(3) C.Y. Liao, J. Zhou. *J. Phys. Chem. B*, **2014**, 118:5843-5852.
(4) C.W. Peng, J. Liu, D.H. Zhao, J. Zhou. *Langmuir*, **2014**, 30:11401-11411.
(5) J. Liu, G.B. Yu, J. Zhou. *Chem. Eng. Sci.*, **2015**, 121:331-339.
(6) D.H. Zhao, C.W. Peng, J. Zhou. *Phys. Chem. Chem. Phys.*, **2015**, 17:840-850.
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(9) J. Liu, C.W. Peng, G.B. Yu, J. Zhou. *Langmuir*, **2015**, 31:10751-10763.
(10) C.W. Peng, J. Liu, Y.Xie, J. Zhou. *Phys. Chem. Chem. Phys.*, **2016**, 18:9979-9989.
(11) D.H. Zhao, D.H. He, L.B. Li, J. Zhou. *Appl. Surf. Sci.*, **2016**, 377:324-334.

Course-grained modeling of small-angle X-ray scattering intensity

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Abstract:

Coarse-grained (CG) modeling is widely used in molecular simulation to improve computational efficiency and achieve large temporal and spatial scales of the studied molecular system. The experimental small-angle X-ray scattering (SAXS) data contain the low-resolution structural information of proteins, which is an ideal case for the implementation of CG models. We recently systematically developed CG computational approaches for modeling the scattering amplitudes of proteins and their hydration layers. As a result, a CG computational framework was established for modeling experimental scattering profiles. Compared with the traditional atomistic approaches, our method is more efficient in SAXS-based protein structure optimization because of the significant reduction of degrees of freedom. For the purpose of method validation, our CG modeling approach was tested against theoretical and experimental SAXS profiles for selected proteins from the protein data bank (PDB). Additionally, the performance of our SAXS-based structure optimization approach was demonstrated by driving protein conformational changes for a number of proteins with known multiple conformations.

Ion Effect on Hydrogen Bonding Network in Water

Wei Zhuang1

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Abstract:
Ions effect on water structure and dynamics have significant specificity which is far from being fully comprehended. Various vibrational spectroscopies are among the most powerful experimental tools to explore this issue. The interpretation of these spectroscopy signals is, however, usually non-trivial and requires the help from theoretical studies. We've developed a series of theoretical approaches to simulate the analyze the vibrational spectroscopies of the ionic solution, which reproduce nicely the spectra including THZ, Raman, fsIR,2DIR, IRPD and Raman-THZ. Based on these simulations, we attempt to address several important issues about the ion effect on water hydrogen bonding network, including 1) ion specificity in their effects on water dynamics and 2) spatial range of ion effects. Novel techniques including complex network recognition and gaussian field model are employed to assist the analysis.

Using Isotope Effects to Determine the Reaction Mechanisms behind RNA Transphosphorylation in Acidic and Alkaline Solution, and in Enzyme

Kin-Yiu Wong

Department of Physics, Hong Kong Baptist University, Hong Kong

Abstract:
Enzymatic reactions are integral components in many biological processes. The iconic point of each reaction path is the structure of the rate limiting transition state (RLTS). But RLTS is difficult to get caught by experimentalists. Nevertheless, we still can trace out the RLTS unique "fingerprints" by measuring the isotope effects on the reaction rate. By contrast, for computer simulations, oftentimes molecular structures of a number of TSs can be precisely visualized on computer screen, however, theorists are not sure which TS is the actual rate-limiting one. As a result, this is an excellent stage setting for a perfect "marriage" between experiment and theory for determining the structure of RLTS, along with the reaction mechanism, i.e., experimentalists are responsible for "fingerprinting", whereas theorists are responsible for providing candidates that match the "fingerprints".

In this talk, we discuss the quantum origin of isotope effects from the Bigeleisen equation to Feynman's path integral. In addition, we also demonstrate a perfect "marriage" between experiment and theory on RNA transphosphorylation in three different environments. To our surprise, the RLTS of RNA transphosphorylation in the acidic environment is quite different from that in alkaline solution and in enzyme.

Integrative Modeling of Large Biomolecules with Low-Resolution Structural Data

Zhiyong Zhang*

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Abstract:

Biological function of a large biomolecule (protein, DNA, RNA, or complex) relies on its three dimensional structure, which involves conformational changes when performing the function. To better understand the structure-function relationship of the biomolecule, it would be beneficial to determine the structures of all its conformational states. Although X-ray crystallography or solution nuclear magnetic resonance (NMR) is widely used in solving high-resolution structures of biomolecules, it is sometimes difficult to capture all the conformational states or characterize the flexibility of a biomolecule with atomistic details. In this case, some alternative experimental techniques, such as small-angle X-ray scattering (SAXS), can be conducted to obtain structural information of the biomolecule at relatively low-resolution level. In order to unravel the structural information encoded in the low-resolution data precisely, computational tools are needed to construct an atomic model (or an ensemble) of the biomolecule that best fits the data. Molecular dynamics (MD) simulation is popularly used. However, for a highly dynamic biomolecule, one single unbiased MD simulation might be inadequate to cover the conformational space. In such a case, we have demonstrated that by combining iterative multiple independent MD simulations and appropriate screening algorithms, one can efficiently interpret structural information of large biomolecules from SAXS or other low resolution data like electron microscopy (EM). Moreover, enhanced sampling techniques or coarse-grained modeling can also be used in the integrative structural modeling, especially for very large biomolecules.

Student Presentation #1:

The role of intramolecular nonbonded interaction and angle sampling in single-step free energy perturbation

Ying-Chih Chiang, Yui Tik Pang, Yi Wang

Department of Physics, Chinese University of Hong Kong, Hong Kong

Abstract:

Single-step free energy perturbation has often been proposed as an efficient tool for a quick free energy scan due to its straightforward protocol and the ability to recycle an existing molecular dynamics trajectory for free energy calculations. Although the method is expected to fail when the sampling of a system is inefficient, it is often expected to hold for an alchemical transformation between ligands with moderate difference in their sizes, e.g. transforming a benzene into an ethylbenzene. Yet, exceptions were observed in calculations for anisole and methylaniline, which have similar physical sizes as ethylbenzene. We show that such exceptions arise from the sampling inefficiency on an unexpected rigid degree of freedom of a bond angle [1]. Our studies shed light on the interrelation between the ligand conformation and the intramolecular nonbonded interactions, and naturally suggest an alternative solution to the usual approach of an enhanced sampling on this rigid angle.

[1] Y.-C. Chiang, Y. T. Pang, Y. Wang, J. Chem. Phys. **145**, 234109 (2016).

Student Presentation #2:

Molecular Details of PH Domain of ACAP1 BAR-PH Protein Binding to PIP2-Containing Membrane

Chun Chan1, Lanyuan Lu2, Fei Sun3, Jun Fan1

1Department of Physics and Materials Science, City University of Hong Kong, Hong Kong; 2School of Biological Sciences, Nanyang Technological University, Singapore; 3National Laboratory of Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China.

Abstract:
ACAP1 protein dimers were previously reported to specifically bind to PIP2-containing cell membranes and form well-structured protein lattices in order to conduct membrane tubulation. We first carried out unrestrained molecular dynamics (MD) simulations to characterize orientation of the PH domains with respect to the BAR domains of the protein dimer. Owing to the atomic precision, we present a comprehensive orientation analysis of PH domain under different lipid-bound states. Furthermore, we sought to investigate nature of the two binding pockets on the PH domain revealed by our MD simulations. We performed additional restrained MD simulations and multiple PMF profiles of the two pockets were presented in order to account for their preference to PIP2 over other charged lipids, e.g. POPS lipids. Combining orientation analysis and studies of binding pockets, our simulations results reveal valuable molecular basis for protein-lipid interactions of ACAP1 proteins during membrane remodeling process.

Student Presentation #3 & Student Poster #5:

Lipid Absorption and Phase Transition Induced by Boron Nitride Nanosheet

Yonghui Zhang1, Zhen Li1, Chun Chan1, Xiaolin Cheng2, Chunyi Zhi1 & Jun Fan1

1Department of Physics and Materials Science, City University of Hong Kong, 83 Tat Chee Avenue, Hong Kong, China;
2Department of Biochemistry and Cellular and Molecular Biology, University of Tennessee, Knoxville, Tennessee, United States.

Correspondence and requests for materials should be addressed to J. F. (e-mail: junfan@cityu.edu.hk).

Abstract:
The integrity of cell membrane is critical to a living cell as it serve as a selectively permeable barrier involved in a variety of cellular processes. Boron nitride nanosheets are novel promising nanomaterials which have great potential in biomedical applications. However, there is very few reports about how they interact with the cell membrane. Here we employed all atom molecular dynamics simulation to study the interaction between the boron nitride nanosheet and lipid membranes. Six different single component lipid membranes are systematically examined. Our results reveal that the boron nitride nanosheet can extract phospholipids from the lipid bilayer and finally is enveloped by the membrane, which further affect the properties of the bilayers. The bending modulus of six bilayers all increase. The corresponding molecular mechanism is the local ordering of lipids is strengthened. After the insertion of nanosheet, the acyl chain become more order. Furthermore, phase transition is observed in the 1,2-dimyristoyl-sn-glycero-3-phosphocholine bilayer along with the insertion. Our study may yield novel insights to the understanding the biocompatibility of boron nitride nanosheets and offer new perspective for the design of safer nanocarrier, antibiotics as well as other biomedical applications.

Student Presentation #4:

Automated path searching for biomolecular systems

Lizhe Zhu

Department of Chemistry, Hong Kong University of Science and Technology

Abstract:
Path-searching or the "reaction coordinate problem" in high dimensional biomolecular processes has been a long-standing issue. The overall efficiency and degree of automation of existing path-searching methods are unsatisfactory because they are based on restrained_or unbiased sampling and in particular on a static coordinate space that is non-trivial to choose a priori. I present a novel path-searching method that avoids these requisites by using path-collective-variables (PCV) and an automated path node reorder scheme. Preliminary results on simple peptide systems show that this new method is more efficient than the established string method by an order of magnitude.

Student Poster #1:

Estimation of Nanodiamond Surface Charge Density from Zeta Potential and Molecular Dynamics Simulations

Zhenpeng Ge

Department of Physics, the Chinese University of Hong Kong, Hong Kong

Abstract:
Molecular dynamics simulations of nanoparticles (NPs) are increasingly used to study their interactions with various biological macromolecules. Such simulations generally require detailed knowledge of the surface composition of the NP under investigation. Even for some well-characterized nanoparticles, however, this knowledge is not always available. An example is nanodiamond, a nanoscale diamond particle with surface dominated by oxygen-containing functional groups. In this work, we explore using the harmonic restraint method developed by Venable et al., to estimate the surface charge density (σ) of nanodiamonds. Based on the Gouy–Chapman theory, we convert the experimentally determined zeta potential of a nanodiamond to an effective charge density (σeff), and then use the latter to estimate σ via molecular dynamics simulations. Through scanning a series of nanodiamond models, we show that the above method provides a straightforward protocol to determine the surface charge density of relatively large (> ~ 100 nm) NPs. Overall, our results suggest that despite certain limitation, the above protocol can be readily employed to guide the model construction for MD simulations, which is particularly useful when only limited experimental information on the NP surface composition is available to a modeler. Molecular dynamics simulations of nanoparticles (NPs) are increasingly used to study their interactions with various biological macromolecules. Such simulations generally require detailed knowledge of the surface composition of the NP under investigation. Even for some well-characterized nanoparticles, however, this knowledge is not always available. An example is nanodiamond, a nanoscale diamond particle with surface dominated by oxygen-containing functional groups. In this work, we explore using the harmonic restraint method developed by Venable et al., to estimate the surface charge density (σ) of nanodiamonds. Based on the Gouy–Chapman theory, we convert the experimentally determined zeta potential of a nanodiamond to an effective charge density (σeff), and then use the latter to estimate σ via molecular dynamics simulations. Through scanning a series of nanodiamond models, we show that the above method provides a straightforward protocol to determine the surface charge density of relatively large (> ~ 100 nm) NPs. Overall, our results suggest that despite certain limitation, the above protocol can be readily employed to guide the model construction for MD simulations, which is particularly useful when only limited experimental information on the NP surface composition is available to a modeler.

Student Poster #2:

Gaussian Accelerated Molecular Dynamics in NAMD

Yui Tik Pang†⊥, Yinglong Miao‡ § ⊥, Yi Wang†, and J. Andrew McCammon‡ § //

†Department of Physics, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong;
‡Howard Hughes Medical Institute, §Department of Pharmacology, and //Department of Chemistry and Biochemistry, University of California at San Diego, La Jolla, California 92093, United States;
⊥These authors contributed equally to this work.

Abstract:
Gaussian accelerated molecular dynamics (GaMD) is an enhanced sampling method developed recently. Like its ancestor accelerated molecular dynamics (aMD), GaMD allows unconstrainted sampling by applying a boost potential to the system, thereby, smoothening its energy landscape. GaMD significantly improves the free energy reweighting accuracy by using a boost potential which is designed to follow a Gaussian-like distribution. It allows an accurate reweighting by using the cumultant expansion to the second order. In this work, we implemented GaMD in NAMD 2.11 and tested the code against three biological systems: alanine dipeptide, the chignolin fast-folding protein, and the M3 muscarinic G protein-coupled receptor (GPCR). For alanine dipeptide, the 30 ns GaMD simulations recover all five main energy wells of the free energy profile generated from a 1000 ns conventional molecular dynamics (cMD) simulation. For chignolin, GaMD simulations successfully fold the protein in a much shorter time than in cMD simulations. GaMD simulation of ligand binding to the M3 muscarinic GPCR, as a model of membrane-protein system, also agrees well with the previous cMD and aMD simulations. All of the tested systems show a very low anharmonicity of the boost potential, suggesting that accurate free energy reweighting calculation was achieved.

Student Poster #3:

Optimal Simulation Configurations for Probing Structure and Dynamics of Lipid Microdomains with Tagged Proteins

Xinhong Liu, Jun Fan

Department of Physics and Materials Science, City University of Hong Kong, Hong Kong

Abstract:

It is believed that compositional lipid microdomains ("lipid rafts") in mammalian plasma membranes are responsible to facilitate many important cellular processes. Although several physically distinct scenarios which predicted the presence of finite-sized microdomains in vivo have been proposed in the past, direct experimental verification or falsification of model predictions has remained to be conducted. Fan et al[1] have demonstrated that the existing theoretical scenarios can be unambiguously differentiated using the combination of the spatial correlation and temporal fluctuation spectra of the lipid. Fan et al[2] further explored the feasibility of employing multi-particle tracking techniques to extract the requisite spatio-temporal correlation data in living cells and developed a hybrid continuum-discrete particle simulation method, which is then to demonstrate that spatial correlation and temporal fluctuation spectra can indeed be extracted from the multi-particle tracking data[2]. In this work, we explore the optimal simulation configuration for these two parameters: number of probing particles and repulsion coefficient as a reference for future experiments.

[1]Fan, J., Sammalkorpi, M. & Haataja, M. Lipid microdomains: Structural correlations, uctuations, and formation mechanisms. Phys. Rev. Lett. 104, 1–4 (2010).

[2]Fan, J. & Sammalkorpi, M. Probing structure and dynamics of lipid microdomains with tagged proteins and lipids : a hybrid particle-continuum simulation approach. Program 8544, 1–14 (2011).

Student Poster #4:

Temperature-dependent Lipids Extraction from Membrane by BN Nanosheet

Zhen Li, Yonghui Zhang, Jun Fan*

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Abstract:
2D materials like graphene and BN nanosheet have attracted great interest in nanomedicine ranging from nanoimaging to drug delivery. However, they may damage cells in human body, which is one of the most crucial challenges. To realize the extensive promising applications, understanding the cytotoxicity of 2D materials in depth is urgently important. In this project, we focused on the interaction between BN nanosheet and lipids membrane with molecular dynamics (MD) simulation and potential of mean force (PMF) calculation. We observed that the free energy difference ΔG of pulling a DMPC lipid out from membrane is smaller than the ΔG of pulling a DMPC lipid from BN surface, demonstrating that adsorbing onto BN surface is a lower free energy state. That explains why BN nanosheet can extract lipids out from DMPC membrane. Interestingly, PMF results predicted that the DMPC lipids extraction should be temperature-dependent at temperature ranging from 290 K to 310 K, which was further confirmed by MD models. We deemed that the temperature sensitivity is resulted from the phase transition of membrane, and POPC models provided evidence. This work is expected to give insights into the cytotoxicity of 2D materials, and to facilitate further development of biocompatible and non-toxic nanomaterials.

Student Poster #6:

Microscopic Insights into Melittin Induced Changes in Molecular Dynamics of Lipid Bilayer Membranes: Role of Physical State and Composition of the Bilayers

Zhiyao Xie1#, Huanbo Jiang2#, V. K. Sharma3, Jun Fan2*, and Xiaolin Cheng4*

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3Solid State Physics Division, Bhabha Atomic Research Centre, Mumbai 400085, India;
4Center for Molecular Biophysics, Oak Ridge National Laboratory

Abstract:
Melittin is an important antimicrobial peptide, and its membrane disruption mechanism has been attributed to its strong interaction with the cell membrane. Recently, Sharma et al (Soft Matter 2015, 11, 6755-6767) have investigated effects of melittin on the dynamics of dimyristoylphosphocholine (DMPC) membrane using neutron scattering techniques. Their measurements showed that effects of melittin on the dynamics of membranes strongly depend on the physical state of the bilayers and the presence of cholesterol. However, the details at the molecular level remain elusive. In this study, extensive molecular dynamics (MD) simulations are performed on DMPC membranes with and without cholesterol in a range of temperatures 280-310K to investigate the effects of melittin on the microscopic dynamics of the membrane. Through the decomposition of membrane dynamics into the translational (lateral diffusion), rotational and internal motions of individual lipid molecules, our MD simulations suggest that in the fluid phase, the nanoscale membrane dynamics observed in the neutron experiments arises primarily from the lateral diffusion, while in the gel phase, it is dominated by the local internal motion. Due to the different nature of the lateral diffusion and the local internal motions, the effects of melittin on the membrane dynamics thus highly depend on the phase state of the membrane. In the fluid phase DMPC, the addition of melittin disrupts the 'collective flow' like lateral diffusion motions, leading to the overall hindered dynamics observed in experiment. However, due to an increase in specific volume of the gel phase DMPC, the addition of melittin enhances the local internal motions slightly, giving rise to the apparent faster dynamics observed in experiment. In contrast, when 20% cholesterol is present, the bilayer abolishes the gel-to-fluid transition, the lateral diffusion is greatly suppressed across the entire experimental temperature range, exhibiting negligible differences in the membrane dynamics when melittin is added. Taken together, our simulations provide a unified mechanism for the effects of melittin on the DMPC bilayers both with and without cholesterol.

Student Poster #7:

Insertion of Human Islet Amyloid Polypeptide into the Lipid Membrane

Xiangze Zeng 1, Xiaoxu Li 2, Qin Qiao 1, Lianghui Gao 2 and Xuhui Huang1*

1 Department of Chemistry, The Hong Kong University of Science and Technology, Hong Kong
2 College of Chemistry, Beijing Normal University, China
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Abstract:
Amyloidosis is a class of diseases featured in the amyloid formation by the abnormal aggregation of proteins, including Alzheimer's, Parkinson's and type II diabetes. In type II diabetes, human islet amyloid polypeptides (hIAPP) form the amyloid deposit. This amyloid deposit is spatially correlated with the lose of pancreatic β cells. Increasing experimental evidences suggest that the growth of amyloid fibrils or the intermediate oligomeric form causes the death of pancreatic β cells by disrupting the cell membrane. However, the molecular mechanism of membrane damage induced by hIAPP is still not fully understood due to the limited spatial and temporal resolution of current experimental techniques. In this study, we used dissipative particle dynamics (DPD) simulations to study the membrane damage process and identified a key intermediate state, the insertion of monomeric hIAPP into the membrane, which could further induce the proceeding of the damage process.

Student Poster #8:

Dynamics of Opening and Closing Motions of the Clamp of Bacterial RNA Polymerase

Ilona Christy Unarta1, Lizhe Zhu2, Xuhui Huang 1,2

1 Department of Bioengineering, Hong Kong University of Science and Technology
2 Department of Chemistry, Hong Kong University of Science and Technology

Abstract:
RNA Polymerase (RNAP), the essential enzyme in transcription process, has conserved quaternary structure across different species. Its structure resembles a pair of pincer, which are composed of a part of beta domain and the clamp domain. The clamp domain can be open or closed depending on the transcription step. According to smFRET experiments, bacterial RNAP in solution without nucleotides can adopt 3 states, i.e.: open, closed, collapsed, with the open state being the predominant one [1]. It has been hypothesized that the opening motion contributes to the separation of dsDNA resulting in exposure of template DNA during the initiation step of transcription. Hence, it is important to find the contributing factors of opening and closing motion of RNAP and the reason for this oscillating of opening and closing motion of free RNAP. Numerous positive residues found on the inner cleft of the pincers of RNAP may cause repulsion leading to the opening motion. The relatively rigid part of RNAP under the clamp domain, however, may prevent the clamp to open too wide. MD simulation has proven successful to reveal the mechanisms underlying RNAP II function [2], thus it is chosen to address RNAP clamp motion. Using MD simulations of bacterial RNAP without nucleotides, we have seen the high flexibility of the beta domain compared to clamp domain within 160 ns unbiased all-atom MD (AA-MD) simulation time. The rigidness of clamp domain definitely sustains for longer than 160 ns. Therefore, we have resorted to multi-basin coarse-grained MD (CG-MD) simulation, which allows longer simulations and observation of transition with just a fraction of AA-MD computational cost. CG-MD simulations were done to obtain RNAP conformations during transitions. We will further refine the model by running sall-atom MD simulations starting from the chosen conformations of CG-MD simulation.

[1] Chakraborty, A., Wang, D., Ebright, Y.W., et al. (2012). Opening and Closing of the Bacterial RNA Polymerase Clamp. Science, 337, 591-595.
[2] Silva, D.A., Weiss, D.R., Avila F.P., Da, L.T., et al. (2014). Millisecond dynamics of RNA polymerase II translocation at atomic resolution. PNAS, 111(21), 7665-7670.

Student Poster #9:

Kinetics-controlled Amphiphiles Self-assembly Processes

Xiaoyan Zheng

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Abstract:
Amphiphiles self-assembly is an essential bottom-up approach of fabricating advanced functional materials. Self-assembled materials with desired structures are often obtained via thermodynamic control. Here, we demonstrate that selections of kinetic pathways can lead to drastically different self-assembled structures, underlining the significance of kinetic control in self-assembly. By constructing kinetic network models from large-scale molecular dynamics simulations, we show that two largely similar amphiphiles PYR and PYN prefer distinct kinetic assembly pathways: PYR prefers an incremental growth mechanism and forms a nanotube, while PYN favors a hopping growth pathway leading to a vesicle structure. Such preference was found to originate from the subtle difference in the distributions of hydrophobic and hydrophilic groups in their chemical structures, which subsequently leads to different rates of the adhesion process between the micellar aggregates when they grow. Consistent with known experimental results, our study accentuates the role of kinetics in the rational design of amphiphiles self-assembly.