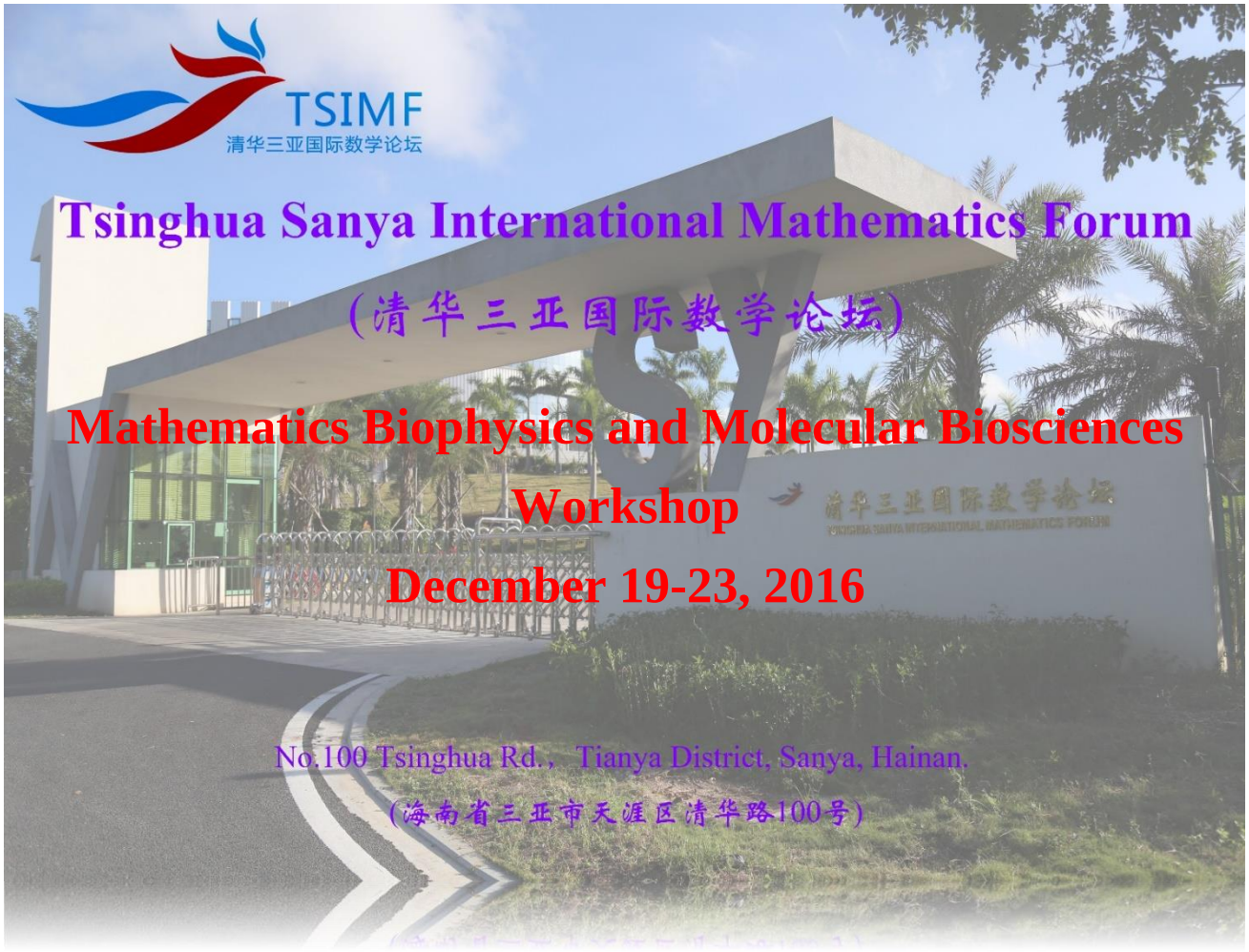
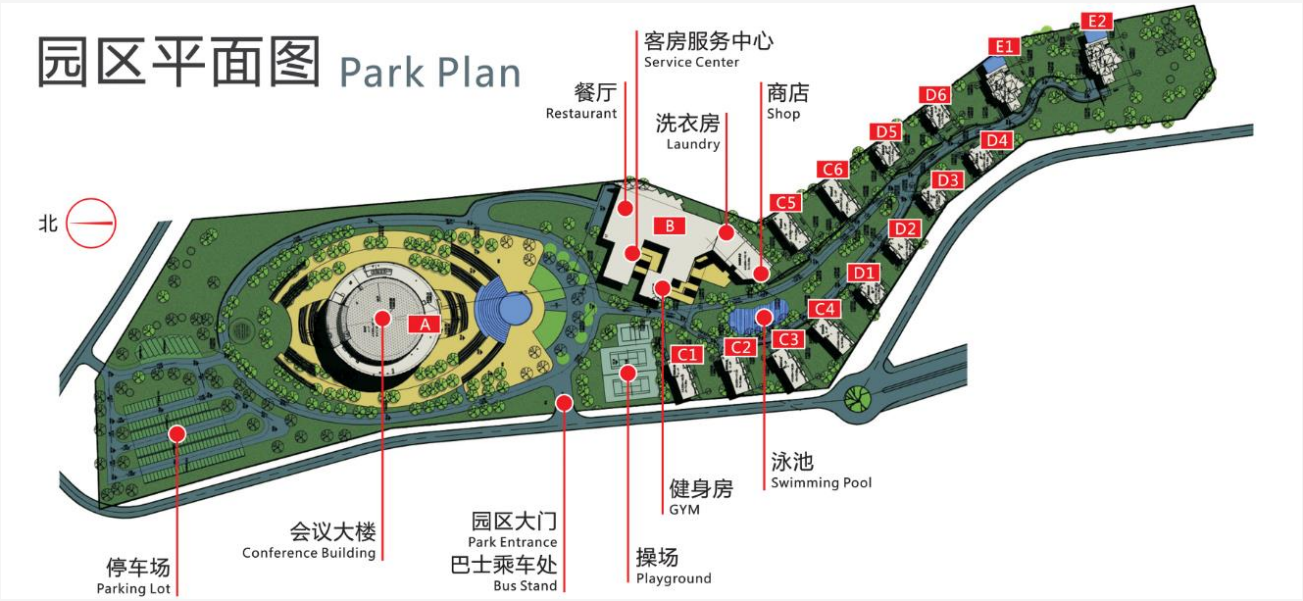


Welcome to TSIMF

The facilities of TSIMF are built on a 23-acre land surrounded by pristine environment at Phoenix Hill of Phoenix Township. The total square footage of all the facilities is over 29,000 square meter that includes state-of-the-art conference facilities (over 10,000 square meter) to hold many international workshops simultaneously, two libraries, a guest house (over 10,000 square meter) and the associated catering facilities, a large swimming pool, gym and sports court and other recreational facilities.

Mathematical Sciences Center (MSC) of Tsinghua University, assisted by TSIMF's International Advisory Committee and Scientific Committee, will take charge of the academic and administrative operation of TSIMF. The mission of TSIMF is to become a base for scientific innovations, and for nurturing of innovative human resource; through the interaction between leading mathematicians and core research groups in pure mathematics, applied mathematics, statistics, theoretical physics, applied physics, theoretical biology and other relating disciplines, TSIMF will provide a platform for exploring new directions, developing new methods, nurturing mathematical talents, and working to raise the level of mathematical research in China.

About Facilities



Registration

Conference booklets, room keys and name badges for all participants will be distributed at the Registry. Please take good care of your name badge. It is also your meal card and entrance ticket for all events.

Guest Room

Conference Center can receive about 378 people having both single and double rooms, and 42 family rooms.

All the rooms are equipped with: free Wi-Fi, TV, air conditioning and other utilities.

Family rooms are also equipped with kitchen and refrigerator.

Library

Opening Hours: 08:00am-22:00pm

TSIMF library is available during the conference and can be accessed by using your room card. There is no need to sign out books but we ask that you kindly return any borrowed books to the book cart in library before your departure.

Restaurant

All the meals are provided in the Chinese Restaurant (Building B1) according to the time schedule.

Breakfast	07:30-08:30
Lunch	12:00-13:30
Dinner	17:30-19:00

Laundry

Opening Hours: 24 hours

The self-service laundry room is located in the Building 1 (B1), next to the shop.

Convenience Store

The convenience store is located in Building 1 (B1), next to the laundry. The store sells snacks, beer, soft drinks, notepads, bathing suits and various etc.

Gym

The gym is located in the Building 1 (B1), opposite to the reception hall. The gym provides various fitness equipment, as well as pool tables, tennis tables and etc.

Playground

Playground is located on the east of the central gate. There you can play basketball, tennis and badminton. Meanwhile, you can borrow table tennis, basketball, tennis balls and badminton at the reception desk.

Swimming Pool

Please note that there are no lifeguards. We will not be responsible for any accidents or injuries. In case of any injury or any other emergency, please call the reception hall at +86-898-38882828.

Shuttle Service:

We have shuttle bus to take participants to the airport for your departure service. Also, we would provide transportation at the Haipo Square （海坡广场） of Howard Johnson for the participants who will stay outside TSIMF.If you have any questions about transportation arrangement. Please feel free to contact Ms. Li Ye (叶莉), her cell phone number is (0086)139-7679-8300.

Contact Information of Administration Staffs

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Schedule for the Mathematics Biophysics and Molecular Biosciences Workshop, December 19-23, 2016

Time&Date	Monday (Dec. 19)	Tuesday (Dec. 20)	Wednesday (Dec. 21)	Thursday (Dec. 22)	Friday (Dec. 23)
7:30-8:30	*Breakfast*				
Chair	*Guowei Wei*	*Julie Mitchell*	*Emil Alexov*	*Qi Wang*	Discussion
8:30-9:10	Weitao Yang	Keith Promislow	Bob Eisenberg	Tom Chou	
9:10-9:50	John Zeng Hui Zhang	Weihua Geng	Julie Mitchell	Derek Frydel	
9:50-10:30	Yi Xiao	Ching-Shan Chou	Xinqi Gong	Zhijie Tan	
10:30-11:00	*Tea Break*				
11:00-11:40	Emil Alexov	Shan Zhao	Guowei Wei	Hong Guo	Discussion
11:40-12:00	Discussion	Discussion	Discussion&&Group Photo	Discussion	
12:00-13:30	*Lunch*				
Chair	*Minxin Chen*	*Weitao Yang*	Free Discussion 13:30-17:00	*Huan-Xiang Zhou*	Departure
13:30-14:10	Huan-Xiang Zhou	Qi Wang		Xuhui Huang	
14:10-14:50	Haiyan Liu	Minxin Chen		Bin Tu	
14:50-15:30	Guohui Li	Lei Zhang		Guanghong Wei	
15:30-16:00	*Tea Break*			*Tea break*	
16:00-16:40	Ray Luo	Kelin Xia		Jianpeng Ma	
16:40-18:00	Discussion			Discussion	
18:00-19:30	*Dinner*	*Banquet 18:00-20:00*	*Dinner*		

Titles and Abstracts

1. Emil Alexov, Computational Biophysics and Bioinformatics, Department of Physics, Clemson University, USA

Title: Multi-scale Modeling of Kinesin and Dynein Binding to Microtubules

Abstract: Electrostatics plays major role in molecular biology because practically all atoms carry partial charge while being situated at Angstroms distances. Many biological phenomena involve the binding of proteins to a large object. Because the electrostatic forces that guide binding act over large distances, truncating the size of the system to facilitate computational modeling frequently yields inaccurate results. Here we report a multiscale approach that implements a computational focusing method that permits computation of large systems without truncating the electrostatic potential and achieves the high resolution required for modeling macromolecular interactions, all while keeping the computational time reasonable. We tested our approach on the motility of various kinesin and dynein motor domains. We found that electrostatics help guide kinesins as they walk: N-kinesins towards the plus-end, and C-kinesins towards the minus-end of microtubules. In case of dynein, we show that electrostatic binding energy forms a guiding funnel that navigates the stepping of the long legs of dynein at the right biding pocket on the microtubule. Furthermore, we demonstrate that the running length and velocities of dynein and dynein mutants are correlated with the magnitude of the binding energy. Our methodology enables computation in similar, large systems including protein binding to DNA, viruses, and membranes.

2. Minxin Chen, Department of Mathematics, Soochow University, China

Title: Efficient and Qualified Mesh Generation for Gaussian Molecular Surface Using Piecewise Trilinear Polynomial Approximation

Abstract: Recent developments for mathematical modeling and numerical simulation of biomolecular systems raise new demands for qualified, stable, and efficient surface meshing, especially in implicit-solvent modeling. In our former work, we have developed an algorithm for manifold triangular meshing for large Gaussian molecular surfaces, TMSmesh. In this talk, I will introduce our recent work on a new algorithms to greatly improve the meshing efficiency and qualities, and implement into a new program version, TMSmesh 2.0. In the first step of TMSmesh 2.0, a new adaptive partition and estimation algorithm is proposed to locate the cubes in which the surface are approximated by piecewise trilinear surface with controllable precision. Then, the piecewise trilinear surface is divided into single valued pieces by tracing along the fold curves, which ensures that the generated surface meshes are manifolds. Numerical test results show that TMSmesh 2.0 is capable of handling arbitrary sizes of molecules and achieves ten to hundreds of times speedup over the previous algorithm. The result surface meshes are manifolds and can be directly used in boundary element method (BEM) and finite element method (FEM) simulation.

3. Ching-Shan Chou, Ohio State University, USA

Title: Modelling of Yeast Mating Reveals Robustness Strategies for Cell-Cell Interactions

Abstract: Cell-to-cell communication is fundamental to biological processes which require cells to coordinate their functions. In this talk, we will present the first computer simulations of the yeast mating process, which is a model system for investigating proper cell-to-cell communication. Computer simulations revealed important robustness strategies for mating in the presence of noise. These strategies included the polarized secretion of pheromone, the presence of the alpha-factor protease Bar1, and the regulation of sensing sensitivity.

4. Tom Chou, University of California, Los Angeles, USA

Title: Path Integration and Regularization in Uncertainty Quantification: Reconstruction of Bond Energies and Mobility in Dynamic Force Spectroscopy

Abstract: A Bayesian interpretation is given for regularization terms for parameter functions in inverse problems. Fluctuations about the extremal solution depend on the regularization terms - which encode prior knowledge - provide quantification of uncertainty. After reviewing a general path-integral framework, we set up a number of applications that arise in biophysics. The inference of bond energies and bond coordinate mobilities from dynamic force spectroscopy experiments are worked out in detail.

5. Bob Eisenberg, Rush University(Chicago), USA

Title: Electricity is Different

Abstract: Electricity is different from other force fields because it is universal. Electricity follows Maxwells equations of electrodynamics exactly, in the nuclei of atoms and the nuclei of galaxies, from times much shorter than those of atomic motion (0.1 femtoseconds) to thousands of years. Electricity is different because it is so strong. One per cent charge imbalance (in an 80 kg object) produces a force enough to lift the earth. Electrodynamics enforce the conservation of current when current includes Maxwells vacuum displacement term . Analysis shows that the time rate of change of the electric field can take on whatever value is needed to ensure conservation of this current no matter what are the properties of matter or its polarization. Properties of matter rearrange themselves to satisfy conservation of this current. Theories of matter often treat electrodynamics cavalierly. Vacuum displacement current is usually ignored and so conservation of current is not enforced. Kinetic models of chemistry and Markov treatments of atomic motion are ordinary differential equations in time and do not satisfy conservation of current unless amended significantly. Enforcing the laws of electrodynamics is necessary to understand the properties of oceans, animals, and the molecules of life, because all depend on electrically charged ions. All are complex fluids in which everything interacts with everything else by the universal laws of electrodynamics. Amending theories of matter to include electrodynamics is likely to produce significant improvement in applications to the real worlds of technology,

biology, and medicine. Proofs and discussion are at https://arxiv.org/abs/1609.09175 and references cited there.

6. Derek Frydel, Institute for Advanced Study, Shenzhen University, China

Title: The Random-phase Approximation as a General Beyond-Mean-Field Approximation

Abstract: The mean-field theory is the simplest theory taking into account particle interactions. Its simplicity comes at the price of the neglect of correlations. Despite this neglect, the mean-field proves to be a useful and accurate tool for many situations. Among the classical systems, electrolytes are the most representative example, where the mean-field formulation yields the Poisson-Boltzmann equation. In recent years there has been a growing effort to go beyond the mean-field description since the neglect of correlations may not always be justified. An extreme example is the strong-coupling limit and the counter-intuitive attraction between the same-charged objects. However, even within the weak-coupling limit the correlational contributions can be important. By way of a simple example let's take neutral surfaces. The mean-field theory yields a flat density profile, but the inclusion of correlations imparts a structure to that profile. In narrow channels this structure my be significant.

Most of the attempts to include correlations are formulated within the field-theoretical framework and focus on Gaussian fluctuations around the mean-field solution. The self-consistent version of this approach is known as the variational Gaussian approximation. In my talk I will show that the variational Gaussian approximation can be derived within the more intuitive and well established liquid-state framework based on the Ornstein-Zernike equation and the intuitive procedure of adiabatic connection, wherein particle interactions are slowly switched on. Within the liquid-state framework the variational Gaussian approximation is revealed to be the same as the well known random phase approximation extended to inhomogeneous fluids. The advantage of this new formulation is that the resulting equations do not presuppose any special form of pair interactions and in principle can be applied to any system of particles. Consequently we apply the resulting "generalized" random phase approximation to the Gaussian core model, Coulomb particles, and the penetrable spheres. Finally, I will briefly discuss some ramifications of the adiabatic connection framework to other types of integral equation theories, such as the Percus-Yevick or hypernetted chain approximation.

7. Weihua Geng, Department of Mathematics, Southern Methodist University, USA

Title: Multipole Methods and their Application to Mesoscale Chromatin Model in Monte Carlo Sampling and Brownian Dynamics

Abstract: Fast Multipole Method (FMM) and Treecode are popular tree-based multipole algorithms with rigorous error estimates and wide applications in computing N-body particle interactions. FMM takes both near-field and far-field expansions, resulting in the revolutionary $O(N)$ computations. Treecode takes only the far field expansion, receiving relatively less efficient $O(N(\log N))$ computations while gaining

saved memory and improved parallelization efficiency for high performance computing. This project first compares both methods under the Cartesian expansion in terms of efficiency, memory use, and parallel performance. Following that, the idea of the multipole expansion is used on a mesoscale chromatin model, in which the charge interactions cannot be uniformly accelerated using FMM or Treecode due to long-range cutoff, exclusion of local contacts, inhomogeneous particle distributions, specified interaction mechanisms, etc. The multipole expansion scheme on nucleosomes, the building blocks of the chromatin, circumvents the nonuniform difficulty to achieve significant speedup while maintains the flexibility of interactions. The scheme is used on both Monte Carlo sampling and Brownian Dynamics for the mesoscale chromatin model.

8. Xinqi Gong, Renmin University of China, China

Title: New Algorithms for Protein-protein Interaction Predictions

Abstract: Proteins perform biological functions usually using specific 3D structures and interacting with other partners. Here I will present how our computational methods help to predict the protein-protein interactions of some biologically interesting cases based on 3D structures. Especially I will illustrate our recently developed deep learning architecture and multi-dimensional space algorithms for this aim.

9. Hong Guo, Department of Biochemistry, Cellular and Molecular Biology, M407 Walters Life Sciences, University of Tennessee, UT/ORNL Center for Molecular Biophysics, Oak Ridge National Laboratory, USA

Title: Computer Simulation and Analysis of Proteins: from Study of One Protein at a Time to Analysis of One Million Proteins Together

Abstract: Applications of different computational approaches to study proteins in biological systems will be discussed in this talk. We will first show how molecular dynamic (MD) simulations with QM/MM potentials can be applied to understand the catalytic mechanisms of individual enzymes or enzyme complexes as well as their specificity. It is demonstrated that such computational approaches can serve as powerful tools for understanding details of enzyme catalysis. As we know, determination of complete genome sequences from a number of organisms have offered an unprecedented opportunity for biological research and transformed biology into a discipline that depends significantly on how to interpret large-scale data sets. By selecting representative proteomes from three domains of life, two giant DNA viruses, and collective gene sets from viruses and organelles including mitochondria, chloroplast and plasmids, we will demonstrate that systematical analyses of the interplay between protein length (L, i.e., the amino acid sequence length) and protein disorder (D, i.e., percentage of residues in a so-called intrinsically disordered state) may allow us to construct a two-dimensional LD-space for describing the proteomes or gene sets. It is found that the gene distributions in this LD-space may serve as an architectural fingerprint shaped by the evolutionary processes.

10. Xuhui Huang, The Hong Kong University of Science and Technology

Title: Investigating Conformational Changes of Biological Macromolecules Using Kinetic Network Models

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 multibody systems. We have successfully applied this new algorithm to model the proteinligand 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.

11. Guohui Li, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, China

Title: Polarizable Force Field Development of Lipid Molecules and their Applications

Abstract: Polarizable force field development of lipid molecules and their applications Abstract: Structure, dynamics and functions of membrane proteins are regulated precisely by their environments including lipids and membrane components. Point charge model of traditional force field cannot reproduce correct experimental measurements of ion conductance of membrane channels, for example, gramicidin A. This is a challenging problem for molecular modeling.

AMOEBA force field is multipole expansion-based polarizable force field and has been approved to be accurate. The combination of AMOEBA with GPU and enhanced sampling algorithm has showed that the computational efficiency can be improved and used for large membrane proteins. We have developed and validated ANOEBA polarizable force field for lipids and cholesterol. The ppplication for ion conductance of gramicidin A showed that it can reproduce experimental results accurately and better than all other traditional point charge models. It has been used to study the functional mechanism of GLUT1 and other complicated membrane proteins.

12. Haiyan liu, University Science and Technology of China, China

Title: Statistical Energies for Protein Design: Amino Acid Sequences and Backbone Structures

Abstract: A fundamental goal of protein design is to create artificial proteins that stably fold into well-defined three-dimensional structures, like many natural proteins does. To address this problem, we may divide it into two sub-problems. One is to define protein backbone structures that are actually designable, which means there

do exist amino acid sequences that fold into them. The other is to design amino acid sequence for a given backbone structure. To address the second sub-problem, we have developed a backbone-dependent statistical model, ABACUS. It has been experimentally shown that for several natural backbone structures of different fold types, de novo sequences designed with ABACUS fold into desired structures with high structural stability. In the meanwhile, we are applying statistical approaches to address the first sub-problem. A statistical energy model for the 3-dimensional arrangements of secondary structural elements, TetraBASE, has been developed and computationally tested. For backbone loops connecting secondary structural elements, statistical analysis of properties associated with designability will be discussed.

13. Ray Luo, University of California, Irvine, USA

Title: ar Simulation: Methodology Advancements and Applications to Drug Discovery

Abstract: Molecular simulation has become an important tool in modern computational chemistry and biochemistry. Nevertheless accuracy and efficiency of the approach still need further improvement to achieve the goal of robust and predictive simulation, particularly for large and complex biomolecular systems. The accuracy issue arises from the intrinsic limitations of classical models that have to be used to approximate the quantum molecular processes. The efficiency issue is a direct consequence of the high dimensionality of biomolecular systems: sophisticated molecular machines are complexes of thousands to millions of atoms. What further complicates the picture is the need to realistically model the interactions between biomolecules and their surrounding water molecules. In this talk, I will review our developments of biomolecular simulation models and methods and their applications to interesting biomedical systems. For developments, I will go over our recent works for more accurate biomolecular force fields for explicit or implicit consideration of electronic polarization. I will also highlight our developments for efficient modeling solvation-mediated energetics and dynamics, covering both polar and nonpolar interactions, membrane environments, crucial in structure-based drug design.

14. Jianpeng Ma, Department of Biochemistry and Molecular Biology, Baylor College Medicine; Department of Bioengineering, Rice University, USA

Title: Enhanced Sampling and Applications in Protein Folding in Explicit Solvent

Abstract: We report a single-copy tempering method for simulating large complex systems. In a generalized ensemble, the method uses runtime estimate of the thermal average energy computed from a novel integral identity to guide a continuous temperature-space random walk. We first validated the method in a two-dimensional Ising model and a Lennard-Jones liquid system. It was then applied to folding of three small proteins, trpzip2, trp-cage, and villin headpiece in explicit solvent. Within 0.5 1 microsecond, all three systems were folded into atomic accuracy: the alpha carbon root mean square deviations of the best folded conformations from the native states were 0.2, 0.4, and 0.4 ?, for trpzip2, trp-cage, and villin headpiece, respectively. Discussion of folding much larger helical proteins in explicit solvent will also be given.

15. Julie Mitchell, University of Wisconsin-Madison, USA

Title: Predicting Nucleic Acid Binding Sites

Abstract: The DNA Binding Site Identifier is a machine learning model for predicting binding sites for nucleic acids on the surface of proteins. DBSI combines biophysical features related to electrostatics and hydrogen bonding with evolutionary information to make predictions. The electrostatic features represent a new class of calculations on protein surfaces, and information from these calculations may have important structural consequences.

16. Keith Promislow, Michigan State University, USA

Title: Free Energy Models of Multicomponent Lipid Bilayers

Abstract: Lipid bilayers are composed of a multitude of lipid constituents, and their distribution over the inner and outer leaflets of the plasma membrane are known to have predetermining influence on membrane curvature and endocytotic events. We present a 'minimal' continuum model of lipid membranes that supports families of bilayer morphologies, allows for bifurcation to higher co-dimensional morphologies, such as filaments and micelles, and provides for a rich mathematical competition between intrinsic curvature and morphological evolution.

17. Zhijie Tan, Department of Physics, Wuhan University, China

Title: Coarse-grained Modeling for 3D Structure and Stability of RNAs in Salt Solutions

Abstract: Three-dimensional structures and their stability are essential for the biological functions of RNAs, and due to the polyanionic nature, salt condition is critical for RNA 3D structure and stability. However, there is still lack of a physical model for predicting 3D structure and stability of RNAs in salt solutions. In the work, we have proposed a coarse-grained model for predicting 3D structure and stability of RNAs, including RNA hairpins, duplexes and RNA pseudoknots, and the model can account for the effect of monovalent and divalent ions on their structures and stability. The predicted structures, and melting temperatures for RNA hairpins, duplexes and pseudoknots in various monovalent/divalent ion solutions are in excellent agreement with the extensive experimental measurements.

18. Bin Tu, National Center for Nanoscience and Technology of China, China

Title: PNP Simulations of Ion and Electron Coupling Transport through Nanostructured Materials

Abstract: A class of nanomaterials made from metal nanoparticles functionalized with charged organic ligands shows great potential, in which the electrical conductance through charged metal nanoparticles is modulated by the dynamic gradients both of mobile counterions surrounding the nanoparticles and conduction electrons on the nanoparticle cores. The gradients are unique in that they persist throughout the entire material and are long lived. These derive from the coupling between ion and

electron distributions and are essential for controlling the transient electronic properties of the nanomaterial. The Nernst-Planck equation has been used previously to describe electron transport through nanoparticle materials. Here, we used the PNP model to simulate ion and electron coupling transport through metal nanoparticle materials. In this process, the counterions and the conduction electrons can (1) diffuse in response to concentration gradients and (2) migrate due to local electric fields. In the case of electrons, these continuum transport mechanisms ultimately derive from the microscopic processes by which electrons tunnel and/or hop from one nanoparticle core to another. In the absence of conduction electrons, mobile ions can migrate only small distances (of the order of the Debye length) before completely screening any applied electric field. The simulation results agree well with experimental results.

19. Qi Wang, Beijing Computational Science Research Center and Univ of South Carolina

Title: Modeling and simulation of cell dynamics using complex fluid models

Abstract: In this talk, we will discuss a framework based on multiphase complex fluid models to study cell dynamics including cytokinesis and cell motility. The guiding principle in the theoretical development is the generalized Onsager principle which defines the constitutive relation. A energy stable numerical strategy is developed to devised efficient and accurate numerical methods. 2 and 3D numerical simulations will be presented to show the modeling and numerical results.

20. Guanghong Wei, State Key Laboratory of Surface Physics, Key Laboratory for Computational Physical Sciences (MOE), and Department of Physics, Fudan University, China

Title: Self-assembly and Co-assembly of Polypeptides Studied by All-atom and Coarse-grained Molecular Dynamics Simulations

Abstract: The self-assembly and co-assembly of polypeptides have attracted great attention due to their important roles in the design of novel bio-nanomaterials and in biological processes such as amyloid fibrillation associated with numerous neurodegenerative diseases. For example, the nanotubes formed by the self-assembly of diphenylalanine (FF)-based peptides can be used as nanoscale molds for the casting of metallic nanowires, and the amyloid deposits formed by the pathological self-assembly (aggregation) of amyloid-β (Aβ) peptide are hallmarks of Alzheimers disease. However, the assembly mechanisms and the structures of the nano-assemblies are not well understood. We have investigated the self-assembly and co-assembly of polypeptides using both atomistic and coarse-grained molecular dynamics (MD) simulations. In this talk, I will present our simulation results of the self-assembly and co-assembly of a few of short peptides including FF, FFF, AAAAAAK (A_6K) and VVVVVVK (V_6K). We find that FF peptides spontaneously assemble into hollow nanovesicles and nanotubes, whereas FFF peptides self-organize into solid nanospheres and nanorods, consistent with experimental results. The co-assembly of FF and FFF leads to varied nanostructures in a FFF:FF ratio-dependent manner. The toroid nanostructure, whose geometry and topology are distinct from the nanostructures formed solely

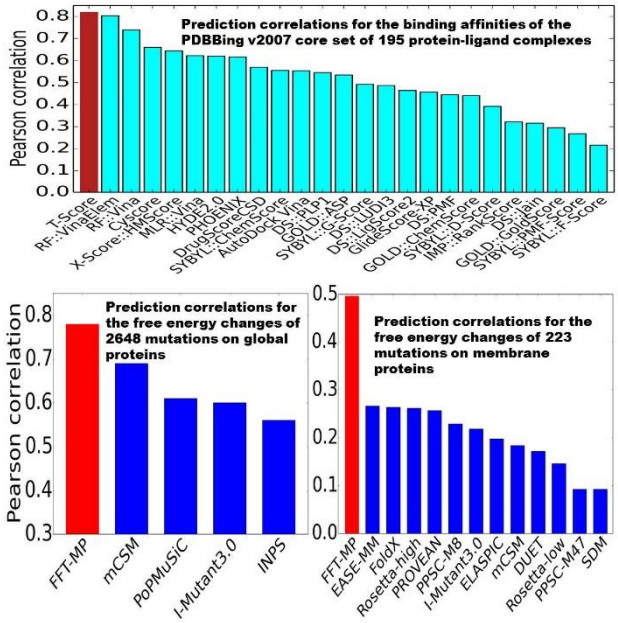
by FF or FFF, is often observed in the co-assembly simulations and confirmed by SEM experiments. A_6K and V_6K peptides display different assembly capabilities and nanostructures, and the former form monolayer lamellas while the latter assemble into plate-like assemblies. The driving forces underlying the self-assembly and co-assembly of these peptides are also discussed. Our findings provide mechanistic insights into the mechanism of peptide self-assembly and co-assembly at molecular level, which might be helpful for the design of bio-nanomaterials.

References:
(1) C Guo, Y Luo, R Zhou, and G Wei. ACS Nano. 2012, 6, 3907.
(2) C Guo, Y Luo, R Zhou, and G Wei. Nanoscale. 2014, 6, 2800.
(3) Y Sun, Z Qian, C Guo, and G Wei. Biomacromolecules. 2015, 16, 2940.
(4) C Guo, ZA Arnon, R Qi, Q Zhang, L Adler-Abramovich, E Gazit, and G Wei. ACS Nano. 2016, 10, 8316.

21. Guowei Wei, Department of Mathematics, Michigan State University, USA

Title: Mathematics is the Champion of Biomolecular Data Challenges

Abstract: Biology is believed to be the last forefront of natural sciences.



Recent advances in biotechnologies have led to the exponential growth of biological data, which paves the way for biological sciences to transform from qualitative, phenomenological and descriptive to quantitative, analytical and predictive.Mathematics is becoming a driven force behind this historic transformation as it did to quantum physics a century ago. I will discuss how to combine differential geometry, algebraic topology, graph theory and partial differential equation with machine learning to

arrive at the cutting edge predictions of a vast variety of experimental data, including solvation free energies, partition coefficients, protein-drug binding affinities, and protein mutation impacts.

22. Kelin Xia, Nanyang Technological University, Singapore

Title: Topological Modeling and Analysis of Complex Data in Biomolecules

Abstract: The understanding of biomolecular structure, flexibility, function, and dynamics is one of the most challenging tasks in biological science. We have introduced flexibility and rigidity index (FRI) for biomolecular flexibility analysis, particularly the B-factor prediction. Our FRI is highly accurate and computationally-efficient. We also introduce persistent homology for extracting molecular topological fingerprints (MTFs) based on the persistence of molecular topological invariants. MTFs are utilized for protein characterization, identification, and classification. The multidimensional persistent homology is proposed and further used to quantitatively predict the stability of protein folding configurations generated by steered molecular dynamics. An excellent consistence between my persistent homology prediction and molecular dynamics simulation is found. Further, we introduce multiresolution persistent homology to handle complex biomolecular data. The essential idea is to match the resolution with the scale of interest so as to represent large scale datasets with appropriate resolution. By appropriately tuning the resolution of a density function, we are able to focus the topological lens on the scale of interest. The proposed multiresolution topological method has potential applications in arbitrary data sets, such as social networks, biological networks and graphs. Finally, we offer persistent homology based new strategies for topological denoising and for resolving ill-posed inverse problems in Cryo-EM data.

23. Yi Xiao, Institute of Biophysics, School of Physics, Huazhong University of Science and Technology, China

Title: Dimensionality Reduction and Efficiency of in Vivo Protein Folding: A Molecular Dynamics Study

Abstract: In vivo proteins can efficiently fold into their native states to perform their functions. However, the physical mechanism of this efficient folding is still not well understood. A lot of solutions have been proposed to solve this problem. The key point of all these proposals is how to reduce the dimensionality of conformational space that a protein needs to search. Levinthal suggested a nucleation mechanism1. Similar point of view was also proposed by Dill et al2. From the point of view of computational complexity3, 4, the paradox could be solved if only near-neighbor interactions of each amino acid were involved. Here we show that cell has developed a special way to solve the problem of protein folding efficiency. The confined-space folding in the ribosomal exit tunnel and co-releasing folding from the tunnel restricted the conformational space searching by proteins and guaranteed the formation of stable local interactions. This greatly reduced the dimensions of the conformational space searched by proteins and makes them fold along a well-defined pathway. Our results indicate that the folding environment and manners are important for efficient

protein folding. We should focus not only on proteins themselves but also their folding manners and environments in order to solve the protein folding problem.

Reference:
(1). C. Levinthal, Journal de chimie physique 65, 44-45 (1968).
(2). V. A. Voelz and K. A. Dill, Proteins 66 (4), 877-888 (2007).
(3). J. T. Ngo and J. Marks, Protein engineering 5 (4), 313-321 (1992).
(4). M. Karplus, Folding design 2 (4), S69-75 (1997).

24. Weitao Yang, Department of Chemistry and Physics, Duke University, USA; and Key Laboratory of Theoretical Chemistry of Environment, School of Chemistry and Environment, South China Normal University, China

Title: Bimolecular Simulations with Quantum Mechanical Linear Response Theory and Machine Learning

Abstract: Department of Chemistry and Physics, Duke University and Key Laboratory of Theoretical Chemistry of Environment, School of Chemistry and Environment, South China Normal University We focus on our recent development of computational methodology for accurate and efficient biomolecular simulations.

We developed a new method to calculate the atomic polarizabilities by fitting to the electrostatic potentials (ESP) obtained from quantum mechanical (QM) calculations within the linear response theory. This parallels the conventional approach of fitting atomic charges based on electrostatic potentials from the electron density. Our ESP fitting is combined with the induced dipole model under the perturbation of uniform external electric fields of all orientations. QM calculations for the linear response to the external electric fields are used as input, fully consistent with the induced dipole model. The molecular polarizabilities obtained from our method show comparable accuracy with those from fitting directly to the experimental or theoretical molecular polarizabilities. Since ESP is directly fitted, atomic polarizabilities obtained from our method are expected to reproduce the electrostatic interactions better.

To model reactions in solution, we have developed a neural network method for QM/MM calculation. Using neural network, the potential energy of any configuration along the reaction path can be predicted at the ab initio QM/MM level based on the previous semi-empirical QM/MM simulations. We further applied this method into three reactions in water to calculate the free energy changes. The free-energy profile obtained from the semi-empirical QM/MM simulation is corrected to the ab intio QM/MM level by using the potential energies predicted by the constructed neural network. The results are in excellent accordance with the reference data that are obtained from direct ab initio QM/MM molecular dynamics simulations. Our method shows a speed-up of one or two order of magnitude, suggesting that the neural network method combined with the semi-empirical QM/MM calculation is an efficient and reliable strategy for biochemical simulations.

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25. Lei Zhang, Beijing International Center for Mathematical Research, Center for Quantitative Biology, Peking University, China

Title: A Mechanochemical Model for Cell Polarity

Abstract: Cell polarization toward the attractant is related to both physical and chemical factors. Most existing mathematical models are based on reaction diffusion systems and only focus on the chemical process during cell polarization. However, experiments reveal that membrane tension may act as a long-range inhibitor for cell polarization. Here we present a mathematical model that incorporates the interplays between Rac, filamentous actin (F-actin), and cell membrane tension for the formation of cell polarity. We also test the predictions of this model with singe cell measurements on the spontaneous cell polarization of cancer stem cells (CSC) and non-cancer stem cells (NCSS) as the former have smaller cell membrane tension. Both our model and experimental results show that the cell polarization is more sensitive to stimuli under low membrane tension, and high membrane tension improves the robustness and stability of cell polarization so that polarization is persistent under random perturbations. Furthermore, our simulations for the first time reproduce the results from the aspiration-release experiment and the pseudopod-neck-cell body morphology severing experiment, demonstrating that aspiration (elevation of tension) and release (reduction of tension) result in decrease and recover of the activity of Rac-GTP, respectively, and relaxation of tension leads to the formation of new polarity of the cell body when the cell with morphology of pseudopod-neck-body is severed

26. John Z.H. Zhang, School of Chemistry and Molecular Engineering, East China Normal University, China

Title: Ab Initio Molecular Dynamics Approach to Studying Protein Structure and Dynamics

Abstract: Due to the complex nature of biomolecules, computational studies of interaction in proteins are primarily based on classical force fields. However, the inherent limitations of the classical force fields significantly reduced the accuracy and reliability of computational predictions of protein structure and dynamics, protein-ligand binding, protein-protein interaction, etc. In order to significantly improve the accuracy of computational predictions of biomolecular interactions in a fundamental way, it is important to develop practical computational approaches that describe biomolecular interactions based on fundamental theory of quantum mechanics. In this talk, we will discuss our recent effort to develop quantum fragment based computational methods to study protein structure and interaction dynamics, with an emphasis on ab initio molecular dynamics (AIMD) approach to studying protein structure and interaction dynamics.

27. Shan Zhao, Department of Mathematics, University of Alabama, Tuscaloosa, USA

Title: On Developing Stable Finite Element Methods for Pseudo-time Simulation of Biomolecular Electrostatics

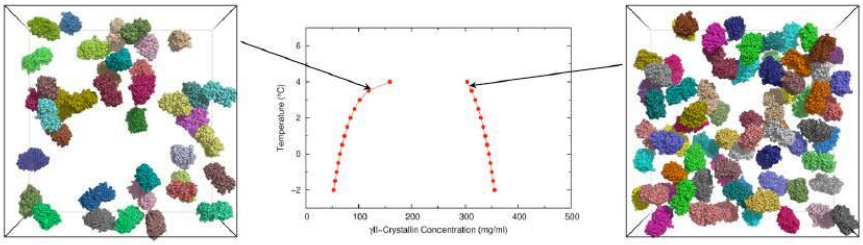
Abstract: The Poisson-Boltzmann Equation (PBE) is a widely used implicit solvent model for the electrostatic analysis of solvated biomolecules. To address the exponential nonlinearity of the PBE, a pseudo-time approach has been developed in the literature, which completely suppresses the nonlinear instability through an analytic integration in a time splitting framework. This work aims to develop novel Finite Element Methods (FEMs) in this pseudo-time framework for solving the PBE. Two treatments to the singular charge sources are investigated, one directly applies the definition of the delta function in the variational formulation and the other avoids numerical approximation of the delta function by using a regularization formulation. To apply the proposed FEMs for both PBE and regularized PBE in real protein systems, a new tetrahedral mesh generator based on the minimal molecular surface definition is developed. Numerical experiments of several benchmark examples and free energy calculations of protein systems are conducted to demonstrate the stability, accuracy, and robustness of the proposed PBE solvers.

This is a joint work with Weishan Deng and Jin Xu (Institute of Software, CAS, China).

28. Huan-Xiang Zhou, Florida State University, Tallahassee, USA

Title: Liquid-Liquid Phase Separation of Proteins and Regulation of Cellular Functions

Abstract: Chemical potential is a fundamental property for determining thermodynamic equilibria involving exchanges of molecules such as between two phases of molecular systems. Previously we developed the FMAP method for calculating excess chemical potentials according to Widom insertion [1-2]. Intermolecular interaction energies were expressed as correlation functions and evaluated via fast Fourier transform. Here we extend this method to calculate liquid-liquid phase equilibria of macromolecular solutions [3]. Chemical potentials are calculated by FMAP over a wide range of molecular densities and the coexistence line between low- and high-density phases is identified by the Maxwell equal-area rule. When benchmarked on Lennard-Jones fluids, our method produces an accurate phase diagram at a fraction ofthe computational cost of the current best method. Importantly, the gain in computational speed increases dramatically as the molecules become more complex, potentially reaching many orders of magnitude in speedup for atomistically represented proteins. We demonstrate the power of FMAP by reporting the first results for the liquid?liquid coexistence curve of γII-crystallin represented at the all-atom level. Our method may thus open the door to accurate determination of phase equilibria for protein mixtures, which underlie the regulation of a variety of cellular functions [4].



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