**Mathematics in Action (MiA2018): Modeling and analysis in molecular biology and electrophysiology**

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| **June 15, Friday** |
| Registration at Nanlin Hotel  Dinner at Nanlin Hotel from **18:00** to **20:30** |

**Suzhou, June 16-18, 2018**

**Meeting Room:　苏州大学本部精正楼二楼**

**（Second Floor, Integrity Building）**

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| **June 16, Saturday, Morning** | |
| **8:45-8:55** | **Open speech, Chun Liu** |
| **Chairman: Jingfang Huang** | |
| **9:00-9:30** | Bob Eisenberg, Rush University Medical Center |
| **9:30-10:00** | Fred Cohen, Rush University Medical Center |
| **10:00-10:30** | Wei Cai, Southern Methodist University |
| **10:30-11:00** | Tea break: Group Photo |
| **Chairman: Wei Cai** | |
| **11:00-11:30** | Bo Li, University of California, San Diego |
| **11:30-12:00** | Huaxiong Huang, York University |
| **12:00-13:30** | Lunch at Dongwu Hotel |
| **June 16, Saturday, Afternoon** | |
| **Chairman: Huaxiong Huang** | |
| **13:30-14:00** | Guowei Wei, Michigan State University |
| **14:00-14:30** | Weishi Liu, University of Kansas |
| **14:30-15:00** | Dexuan Xie, University of Wisconsin, Milwaukee |
| **15:00-15:30** | Tea break |
| **Chairman: Guowei Wei** | |
| **15:30-16:00** | Jie Liang, University of Illinois at Chicago |
| **16:00-16:30** | Lei Zhang, Peking University |
| **16:30-17:00** | Xiaofan Li, Illinois Institute of Technology |
| **18:00-20:30** | Dinner at Nanlin Hotel |

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| **June 17, Sunday, Morning** | |
| **Chairman: Bo Li** | |
| **9:00-9:30** | Yan Levin, UFRGS, Brasil |
| **9:30-10:00** | Zhonghan Hu, Jilin University |
| **10:00-10:30** | Duan Chen, University of North Carolina, Charlotte |
| **10:30-11:00** | Tea break |
| **Chairman: Shenggao Zhou** | |
| **11:00-11:30** | Nir Gavish, Technion-Israel Institute of Technology |
| **11:30-12:00** | Douglas Zhou, Shanghai Jiaotong University |
| **12:00-13:30** | Lunch at Dongwu Hotel |
| **June 17, Sunday, Afternoon** | |
| **Chairman: Weishi Liu** | |
| **13:30-14:00** | Tai-Chia Lin, National Taiwan University |
| **14:00-14:30** | Zhiliang Xu, Notre Dame University |
| **14:30-15:00** | Rio Yokota, Tokyo Institute of Technology |
| **15:00-15:30** | Tea break |
| **Chairman: Jie Liang** | |
| **15:30-16:00** | Shan Zhao, University of Alabama |
| **16:00-16:30** | Ren-Shiang Chen, Tunghai University |
| **16:30-17:00** | Tzyy-Leng Horng, Feng Chia University |
| **18:00-20:30** | Dinner at Nanlin Hotel |

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| **June 18, Monday, Morning** | |
| **Chairman: Zhenli Xu** | |
| **9:00-9:30** | Qi Wang, University of South Carolina |
| **9:30-10:00** | Dan Hu, Shanghai Jiaotong University |
| **10:00-10:30** | Xiaolin Cheng, The Ohio State University |
| **10:30-11:00** | Tea break |
| **Chairman: Benzhuo Lu** | |
| **11:00-11:30** | Shuangliang Zhao, East China University of Science and Technology |
| **11:30-12:00** | Zhenli Xu, Shanghai Jiaotong University |
| **12:00-13:30** | Lunch at Dongwu Hotel |
| **June 18, Monday, Afternoon** | |
| **Chairman: Qi Wang** | |
| **13:30-14:00** | Benzhuo Lu, Chinese Academy of Sciences |
| **14:00-14:30** | Weihua Geng, Southern Methodist University |
| **14:30-15:00** | Jinn-Liang Liu, National Tsinghua University |
| **15:00-15:30** | Tea break |
| **Chairman: Chun Liu** | |
| **15:30-16:00** | Cheng Wang, University of Massachusetts, Dartmouth |
| **16:00-16:30** | Chunmei Wang, Texas State University |
| **16:30-17:00** | Shenggao Zhou, Soochow University |
| **18:00-20:30** | Dinner at Nanlin Hotel |

**Title and Abstract**

**Stochastic computational methods for electromagnetic problems in layered media**  
Wei Cai

Southern Methodist University

**Abstract**

We will present several numerical methods for modeling and optimizing random meta-materials (MM), including stochastic model for MM with geometric constraints, desingularized accurate volume integral equations, heterogeneous fast multipole methods and hierarchical random compression methods for fast integral operator evaluations for layered Green's functions. These methods can also be applied for electrostatic interactions in ion channel and membrane simulations.

**Fractional Poisson–Nernst–Planck Model for Ion Channels**

Duan Chen

University of North Carolina, Charlotte

**Abstract**

In this work, we propose a fractional Poisson-Nernst-Planck model to describe ion permeation in gated ion channels. Due to the intrinsic conformational changes, crowdedness in narrow channel pores, binding and trapping introduced by functioning units of channel proteins, ionic transport in the channel exhibits a power-law-like anomalous diffusion dynamics. We start from continuous time random walk model for a single ion, and use a long-tailed density distribution function for the particle jump waiting time, to derive the fractional Fokker-Planck equation. Then it is generalized to the macroscopic fractional Poisson-Nernst-Planck model for ionic concentrations. Necessary computational algorithms are designed to implement numerical simulations for the proposed model and the dynamics of gating current is investigated. Numerical simulations show that the fractional PNP model provides a more qualitatively reasonable match to the profile of gating currents from experimental observations. Meanwhile, the proposed model motivates new challenges in terms of mathematical modeling and computations.

**Identification of pore-facing side-chains at the internal entrance of KcsA channels – working towards a physics-based model of ion conductance in potassium channels**

Ren-Shiang Chen

Tunghai University

**Abstract**

The efflux of K+ ions critically shapes the kinetics of membrane potential in virtually all cells. Although the selective filter structure is almost identical in all crystallized potassium channels (such as MthK, KvAP, Kv1.2, and KcsA), the conductance of these channels vary widely. Clearly the potassium channel conductance is not determined by the selective filter alone. Recent researches showed that the two negatively charged amino acids (E321 and E324) at the internal pore entrance of BK channels attract potassium, leading to increased potassium concentration at the pore entrance and elevated channel conductance. Similarly, when the A108 at the internal entrance of KcsA channel is mutated to aspartate (D), the conductance of KcsA channel was significantly increased. Moreover, Furini and colleagues (2007) suggested that A108E and T112E mutations in the KcsA channel can increase conductance in their simulation with the Poisson-Nernst-Planck (PNP) model. However, the above hypothesis has not been fully confirmed by experiments. In this study, we created several mutant KcsA channels by introducing negative charges at the A108, A111 and T112 positions. Single-channel currents at different membrane potential were recorded with the planar lipid bilayer technique. The A108E mutation caused increased channel conductance over the control channel, consistent with the results in the literature. Furthermore, channels with A111E, but not T112E, mutation displayed increased channel conductance in both intracellular pH 4 and 5, indicating that the carboxyl group of the A111E side-chain is pointing to the channel pore and help attracting K+ ions. Our results indicated that the A108/A111 positions in the KcsA channel correspond to the E321/E324 positions in the BK channels and play a similar function. Our future work will include changing the side-chain volume at A108/A111 positions and quantifying the corresponding decrease in KcsA channel conductance. Because the KcsA channel has several well-defined crystal structures, our work will allow us and collaborators to build a model of ion conduction through potassium channels that is based on both physics and detailed 3-dimensional biological channel structures.

**Exploring Emergent Properties in Biomembranes**

Xiaolin Cheng

The Ohio State University

**Abstract**

The lipid raft hypothesis presents insights into how the cell membrane organizes proteins and lipids to accomplish its many vital functions. Yet basic questions remain about the physical mechanisms that lead to the formation, stability, and size of lipid rafts. In the talk, I will discuss our efforts towards addressing these fundamental questions by combining high-performance computer simulations and neutron scattering experiments. Taking advantage of neutron’s unique sensitivity to the isotopes of hydrogen, we were able to measure the bending moduli of nanoscopic lipid domains embedded in the continuous phase surrounding them. Specifically, we isolated the bending modulus of ∼13 nm diameter domains residing in 60 nm unilamellar vesicles, whose lipid composition mimics the mammalian plasma membrane outer leaflet. Corresponding all-atom molecular dynamics simulations provided critical insights into the domain interfaces and further confirmed that nanoscopic domains are in-register across the bilayer leaflets. Taken together, these results inform a number of theoretical models of domain/raft formation and highlight the fact that mismatches in bending modulus must be accounted for when explaining the emergence of lateral heterogeneities in lipid systems and biological membranes.

**Implications of Measuring Chemical Potentials of Cholesterol in Membranes and Its Theoretical Challenges**

Fred Cohen

Rush University Medical Center

**Abstract**

The majority of cholesterol in the human body resides within the plasma membranes of cells. It is common to measure cholesterol concentrations, see no changes under varied cellular conditions, and conclude that changes in cholesterol are not relevant to the phenomenon under investigation. But concentration cannot yield the number of cholesterol molecules that are free to react. Our laboratory has developed the first way to measure the chemical potential of membrane cholesterol, allowing interactions of cholesterol in cell membranes to be quantified. We have found that even when cholesterol concentration remains the same, changes in chemical potential can be large, demonstrating the importance of measuring this chemical potential. I will describe the method for measuring chemical potential, and illustrate its applications to plasma membranes and intracellular membranes. The implications of results of these measurements will be discussed.

**Electricity is Different: it is universal**

Bob Eisenberg

Rush University Medical Center

**Abstract**

Mathematicians and physicists usually work with approximate laws. Scientists have developed exquisite skills to use their approximate knowledge to precise effect. I argue that our electronic technology is so powerful because it depends on a physical law that is universal and exact, no matter what the material context, even though material properties are not exact or universal, even approximately. I argue that our successful electronic technology is implemented in branched one dimensional circuits because they implement a universal law, exact from protons to stars. Maxwell wrote and showed that light was an electromagnetic phenomenon. Physicists now know that is ***nothing like*** the positive real constant that Maxwell assumed: current needs to be redefined to include ***all*** movement of charge (with mass) including classical dielectric polarization, but also currents driven by fields (like convection and diffusion) not mentioned in electrodynamics at all. Then is as universal as electrodynamics. Then shows that ***current is conserved perfectly everywhere and at every time*** that Maxwell’s equations are valid. In a series circuit, current is equal in every element no matter what the microphysics of conduction because is different in each element, taking on the value needed to make total current equal everywhere at every time. Conservation of current has immediate consequences on the atomic and molecular scale: in biological systems it forces the currents through the membrane of a typical cell to sum to zero. At steady state this means that currents are coupled by conservation laws, ***even if there is no mechanistic or chemical coupling in the channels or transporters that control them***.

**Bi-stable steric Poisson-Nernst-Planck models and ion channel gating**

Nir Gavish

Technion - Israel Institute of Technology

**Abstract**

Experiments measuring currents through single protein channels show unstable currents, a phenomena called the gating of a single channel. Channels switch between an `open' state with a well defined single amplitude of current and ?closed? states with nearly zero current. The existing mean-field theory of ion channels focuses almost solely on the open state. The theoretical modeling of the dynamical features of ion channels is still in its infancy, and does not describe the transitions between open and closed states, nor the distribution of the duration times of open states.

One hypothesis is that gating corresponds to noise-induced fast transitions between multiple steady (equilibrium) states of the underlying system. Particularly, the literature focuses on the steric Poisson-Nernst-Planck model since it has been successful in predicting permeability and selectivity of ionic channels in their open state, and since it gives rise to multiple steady states.

In this work, we show that the PNP-steric equation is ill-posed in the parameter regime where multiple solutions arise. Following these findings, we introduce a novel PNP-Cahn-Hilliard model that is well-posed and admits multiple stationary solutions that are smooth and stable. We show that this model gives rise to a gating-like behavior, but that important features of this switching behavior are different from the defining features of gating in biological systems. Furthermore, we show that noise prohibits switching in the system of study. The above phenomena are expected to occur in other PNP-type models, strongly suggesting that one has to go beyond over-damped (gradient flow) Nernst-Planck type dynamics to describe spontaneous gating of single channels.

Joint work with Chun Liu and Bob Eisenberg.

**A fast boundary integral Poisson-Boltzmann solver and its biological applications**

Weihua Geng

Southern Methodist University

**Abstract**

We recently developed a treecode-accelerated boundary integral (TABI) Poisson-Boltzmann solver for computing electrostatics of solvated biomolecules. In this talk, we report recent progresses in improving the solver such as cyclic parallelization and block-diagonal preconditioning. In addition, we report biological applications using TABI solver such as computing binding energy and pKa values.

**3D Poisson-Boltzmann computation of KcsA potassium channel**

Tzyy-Leng Horng

Feng Chia University

**Abstract**

Ion channels are pore-forming trans-membrane proteins that allow ions to enter/leave cell. There are many important cell functions involving ion channel, e.g., establishing and regulating action potential in neurons and myocytes. The average time for an ion passing through ion channel is in the order of ms, which is infeasible for molecular dynamics simulation so far. Continuum model like Poisson-Boltzmann equation (PB) and Poisson-Nernst-Planck (PNP) equations are popular to describe ion channel in equilibrium and non-equilibrium situations. KcsA potassium channel is chosen to be studied here, since it is one of few ion channels having X-ray crystallographic structure. 3D PB and PNP simulations of KcsA channel have been a challenging task, since (1) geometry is complicated especially the narrow filter part requiring high resolution when generating meshes; (2) mathematical models are complicated since there are various versions of modified PB/PNP to choose; (3) physics is complicated such as distributions of dielectric constant and diffusion coefficient, necessity to employ steric effect or not and solvation energy should be included or not. Here, a PDB 3F7Y KcsA structure with filter part replaced by that of PDB 1K4C is used as the structure for simulation. Unlike all other KcsA PDB structures, this synthetic structure guarantees that the channel is open. PB and modified PB equations are first extended to be pseudo-time-dependent with the steady-state solution being our only interest. The numerical framework adopted here to solve these time-dependent equations for electric potential is method of lines (MOL). Governing equation is first semi-discretized in space by 2nd order finite volume method under Cartesian grids with the edge value to cope with interface condition. This semi-discretized system forms a system of ordinary differential algebraic equations (ODAE) that can be further integrated by popular ODAE solvers. Mathematical models simulated here are (I) Classical PB, (II) modified PB with steric effect described by Bikerman model, and (III) modified PB as (II) with solvation energy included in addition. From simulation results, we found potassium ion is unrealistically crowded in the filter for model (I). For model (II), though potassium ion is no more unrealistically crowded in filter due to the inclusion of steric effect, there is no room for water to be in the filter. Finally, model (III) delivers the most reasonable physical result among all three models by obtaining reasonable potassium concentration under steric effect and allowing water residence in the filter at the same time.

**Weighted least square analysis method for free energy calculation**

Dan Hu

Shanghai Jiaotong University

**Abstract**

Free energy calculation is an efficient way for studying rare event dynamics. For a complex rare event dynamics, multiple reaction coordinates may be required to describe the transition path between equilibrium states. Theoretically, a one dimensional sampling along the transition path can provide sufficient information to calculate the potential of mean force (PMF) along the transition path. In the widely used free energy analysis method Wham, the sample data are divided into a series of bins to calculate PMF. However, bin segmentation in Wham is coupled with the umbrella potentials applied in each window, because each umbrella potential is assumed to have a close value for all sample points in each bin. This coupling makes it difficult to perform one-dimensional bin segmentation along the transition path when multi-variable umbrella potentials are used in sampling. Here we develop a \underline{we}ighted \underline{l}east \underline{s}quare \underline{a}nalysis \underline{m}ethod (Welsam) to take the place of Wham for free energy analysis. In the new method Welsam, bin segmentation is decoupled from application of umbrella potentials. As a result, it becomes very convenient to perform one-dimensional bin segmentation and calculate one-dimensional potential of mean force along the transition path. Our simulation results suggest that Welsam has a comparable statistical error with Wham. Furthermore, Welsam can be used to reduce waste of sample data obtained during exploration of reaction coordinates.

**A symmetry-preserving mean-field view of the Ewald sum and its related boundary conditions in molecular simulations**

Zhonghan Hu

Jilin University

**Abstract**

The relation between the net amount of the surface charges and the applied electric voltage for systems of vacuum (a) or water (b) insulator using different setup of insulator lengths (20, 40, or 60 angstroms). Simulation data (symbols) are taken from Figure 6 and Figure 8 of ref. [5]. The straight line indicates the invariant zero net charge point (8.9V, 0e) for any insulator, which is predicted by our theory.

Four years ago, we suggested a pairwise formulation of the Ewald sum associated with any infinite boundary term [1] and an accurate symmetry-preserving mean-field treatment for electrostatics in non-uniform systems [2]. It turns out that the ideas developed in refs. [1,2] are useful for analyzing the simulation data and understanding or even predicting the electrostatic boundary effect in most, if not all, molecular simulations of explicit molecules in their condensed phase [3-4]. In this talk, I will use an example of charged insulator/electrolyte interfaces studied by Chao Zhang and Michiel Sprik [5] to demonstrate that the symmetry-preserving mean-field theory combined with the pairwise form of the Ewald sum takes fully account of the effect arising from the alternating electric field in supercell modeling of the interfaces and therefore are able to predict both the linear relation for the vacuum insulator and the nonlinear relation for any dielectric insulator, which are in excellent agreement with the simulation data in the literature [5].

References:

1. Hu, Zhonghan; “Infinite Boundary Terms of Ewald Sums and Pairwise Interactions for Electrostatics in Bulk and at Interfaces”, Journal of Chemical Theory and Computation, (2014), 10, 5254-5264.

2. Hu, Zhonghan; “Symmetry-preserving mean field theory for electrostatics at interfaces”, Chemical Communications, (2014), 50, 14397-14400.

3. Pan, Cong; Yi, Shasha; Hu, Zhonghan; “The Effect of electrostatic boundaries in molecular simulations: symmetry matters”, Physical Chemistry Chemical Physics, (2017), 19, 4861-4876.

4. Yi, Shasha; Pan, Cong; Hu, Zhonghan; “Note: A pairwise form of the Ewald sum for non-neutral systems”, Journal of Chemical Physics, (2017), 147, 126101.

5. Chao Zhang and Michiel Sprik, “Finite field methods for the supercell modeling of charged insulator/electrolyte interfaces”, Physical Review B, (2016), 94, 245309.

**TBA**

Huaxiong Huang

York University

**Abstract**

**Simulations of Coulomb systems confined by polarizable surfaces**

**using periodic Green functions**

Yan Levin

UFRGS, Brasil

**Abstract**

We present an efficient approach for simulating Coulomb systems confined by planar polarizable surfaces. The method is based on the solution of Poisson equation using periodic Green functions. It is shown that the electrostatic energy arising from the surface polarization can be decoupled from the energy due to direct Coulomb interaction between the ions. This allows us to combine an efficient Ewald summation method, or any other fast method for summing over the replicas, with the polarization contribution calculated using Green function techniques. We apply the method to calculate density profiles of ions confined between charged dielectric and metal surfaces.

**Multi-Scale Modeling and Simulation of the Growth of Bacterial Colony with Mechanical Interactions**

Bo Li

University of California, San Diego

**Abstract**

The growth of bacterial colony exhibits striking patterns that result from the interactions among individual cells and between cells and the surrounding environment. Understanding the principles that underlie such growth has far-reaching consequences in biological and health sciences. In this work, we construct a hybrid three-dimensional model of the growth of E. coli cells on agar surface. Our model consists of microscopic descriptions of the cell growth, division, and movement, and macroscopic diffusion equations for the nutrient and waste. The cell movement is driven by the cell-cell and cell-environment mechanical interactions for which we detail the interaction forces. We use the velocity Verlet algorithm to simulate the motion of individual cells and an iterative algorithm to update the nutrient. Our large-scale simulations reproduce experimentally observed growth scaling laws and complex patterns of an E. coli colony. This work is the first step toward detailed computational modeling of bacterial growth with mechanical and chemical interactions. This is joint work with Mya Warren, Hui Sun, Yue Yan, and Terence Hwa.

**Motion of particles in unsteady Stokes and linear viscoelastic fluids**

Xiaofan Li

Illinois Institute of Technology

**Abstract**

Studying effects of moving particles on fluids is of fundamental importance for understanding particle dynamics and binding kinetics. Conventional asymptotic solutions may lead to poor accuracy for neighboring particles. We present an accurate boundary integral method to calculate forces exerted on particles for a given velocity field. The idea is to exploit a correspondence principle between the unsteady Stokes and linear viscoelasticity in the Fourier domain such that a unifying boundary integral formulation can be established for the resulting Brinkman equation.

**Modeling of Conformatonal Ensembles of Loops for Understanding Gating**

**Mechanism of Omp Channel and Chromatin Folding**

Jie Liang

University of Illinois at Chicago

**Abstract**

Outer memberane protein (Omp) channel as bionanopore has emerged as an important class of molecular sensor that has the promise of detecting a wide variety of molecules through measurment of gating signals. Chromosome folding in three-dimensional space provides important control mechanism for selective activation and repression of gene expression. In both cases, characterizing conformational ensembles of chain polymers in the form of protein loops and chromatin loops are of central important. We discuss recent progresses in deep sampling for studying channel loop ensembles and chromatin ensembles, and present results on OmpG gating mechanism and on discovery of specific interactions of chromatin folding. These results can be useful for developing mathematical theories and models to gain additional conceptual understanding on these important biological problems. (Joint work with Alan Perez-Rathke, Gamze Gursoy, Monifa A. Fahle and Min Chen).

**A new class of approximate Lennard-Jones potentials**

Tai-Chia Lin

National Taiwan University

**Abstract**

The Lennard-Jones (LJ) potential, a well-known mathematical model for the interaction between a pair of ions, has important applications in many fields of biology, chemistry and physics. Using band-limited functions, we obtained a class of approximate LJ (LJ\_a) potentials which can be used to derive PNP-steric equations as a model to describe the ion transport through (biological) channels (with B. Eisenberg, 2014). However, due to the strong singularities of LJ potentials, it is difficult to calculate the Fourier transform of LJ\_a potentials. In this lecture, a new class of approximate LJ (LJ\_na) potentials with precise formulas of Fourier transform will be introduced. We may prove that the energy of ions interacting by the LJ\_na potential can approach to the energy of ions interacting by the LJ\_a potential. This may provide a new PNP type model for the ion transport through channels.

**Biological Ion Channels: Theory and Simulation**

Jinn-Liang Liu

National Tsinghua University

**Abstract**

Ion channels are porous membrane proteins that control the flow of ions across cell membranes and play vital roles in various physiological processes in human body. Ion channel dysfunction can cause many diseases such as cardiac, neurological, renal, endocrine, and bone disorders. Single channel recordings are performed in thousands of laboratories worldwide on a daily basis using the patch clamp technique invented by the Nobel laureates Sakmann and Neher in the 1970s. However, there are relatively very few simulation tools for calculating single ion currents under physiological or experimental conditions, which can assist experimentalists in the study of normal or mutated ion channels based on the crystal structures provided by the Protein Data Bank before experimentation. The Poisson-Nernst-Planck-Fermi theory we proposed in recent years is a Continuum-Molecular theory that can be used to simulate ion currents in biological ion channels under physiological or experimental conditions. PNPF treats ions and water as non-uniform hard spheres, and accounts for interstitial voids between spheres, as well as important physical properties such as water polarization and ion correlation.

**Permanent charge effects: Analysis and numerics of flux ratios and bifurcations**

Weishi Liu

University of Kansas

**Abstract**

In this talk, we will report our analytical and numerical studies of permanent charge effects on ionic fluxes via Poisson-Nernst-Planck type models. A flux ratio $\lambda$ associated to each ion species was identified through analysis that quantifies a key effect of permanent charges in the sense that $\lambda>1$ (resp. $\lambda<1$) corresponds to an enhancing (resp. a reducing) effect of the permanent charge on the flux. For two ion species case, a universal property of the flux ratio is established; furthermore, for small and for large permanent charges of a special class, the analysis is able to provide a rather complete understanding of the behavior of $\lambda$. The numerical case study is able to

(i) reproduces the analytical predications for the two extrema of permanent charges;

(ii) fills the gap for permanent charges between the two extrema;

(iii) reveals new phenomena -- bifurcations of critical effect relation $\lambda=1$.

**Continuum modeling of selective ion permeation in potassium channel**

Benzhuo Lu

Chinese Academy of Sciences

**Abstract**

The Poisson-Nernst-Planck (PNP) model describing electrodiffusion processes can qualitatively capture some macroscopic properties of certain ion channel systems such as current-voltage characteristics, conductance rectification, and inverse membrane potential. In this talk, (1) we will present a proper free energy form for self-consistent variational analysis for inhomogeneous charged system with general nonhomogeneoous boundary conditions. (2) As the continuum mean-field PNP model has no or underestimates the discrete ion effects, in particular the ion solvation effect, it is not applicable to selective permeation simulations. Potassium channels are much more permeable to potassium than sodium ions, although potassium ions are larger and both carry the same positive charge. This puzzle cannot be solved based on the traditional PNP model because it treats all ions as point charges and has no any ion size information, therefore cannot discriminate potassium from sodium ions. It is known that the dehydration effect (closely related to ion size) is crucial to selective permeation in potassium channels. We incorporated Born solvation energy into the PNP model to account for ion hydration/dehydration effects when passing through the inhomogeneous dielectric channel environments. A variational approach was adopted to derive a Born-energy-modified PNP (BPNP) model. The model was applied to study a cylindrical nanopore and a realistic KcsA channel, and three-dimensional finite element simulations were performed. The BPNP model can distinguish different ion species by ion radius and predict selectivity for K+ over Na+ in KcsA channels. Furthermore, ion current rectification in the KcsA channel was observed by both the PNP and BPNP models. The I -V curve of the BPNP model for the KcsA channel indicated an inward rectifier effect for K+ (rectification ratio of ∼3/2) but indicated an outward rectifier effect for Na+ (rectification ratio of ∼1/6). These phenomena can be properly explained by the electrostatic energy landscape of the permeative ion along the channel resulted from the BPNP model. (3) We will also demonstrate that these simulations can be performed online on the website xyzgate.com.

**A uniquely solvable, energy stable and convergent numerical scheme for the**

**Poisson-Nernst-Planck equation**

Cheng Wang

University of Massachusetts, Dartmouth

**Abstract**

A numerical scheme for three-dimensional (3-D) Poisson-Nernst-Planck (PNP) equation, which models the ion transport process, is proposed and analyzed in detail. To keep the variational structure, a nonlinear diffusion form has to be utilized, and the singular nature of the logarithmic energy potential makes the corresponding analysis very challenging. A careful energy minimization analysis ensures the unique solvability and positivity-preserving property of the numerical solution, based on a subtle fact that the singular nature of the logarithmic term prevents the numerical solution approach the singular limit values. In turn, the energy stability could be derived by the variational inequality. To obtain the optimal rate convergence analysis of the numerical scheme, two levels of estimates have to be undertaken:

a preliminary error estimate is expected to yield a desired bound estimate between the numerical solution and the limit values, while a refined error estimate would give an optimal rate analysis.

**A Primal-Dual Weak Galerkin Finite Element Method for Fokker-Planck Type Equations**

Chunmei Wang

Texas State University

**Abstract**

The speaker will present a primal-dual weak Galerkin (PD-WG) finite element method for a class of second order elliptic equations of Fokker-Planck type. The method is based on a variational form where all the derivatives are applied to the test functions so that no regularity is necessary for the exact solution of the model equation. The numerical scheme is designed by using locally constructed weak second order partial derivatives and the weak gradient commonly used in the weak Galerkin context. Optimal order of convergence is derived for the resulting numerical solutions. Numerical results are reported to demonstrate the performance of the numerical scheme.

**Thermodynamically Consistent Models for Electrolytic Fluids**

Qi Wang

University of South Carolina

**Abstract**

I will discuss various ways to derive thermodynamically consistent models for electrolytic fluids, discuss their reduction to MHD models and address their applications to ionic fluids in small scales where size effect and compressibility of the fluid matters. Numerical treatment of the models to obey thermodynamical consistence at the discrete level will also be discussed as well.

**Integrating algebraic topology and machine learning for drug design and discovery**

Guowei Wei

Michigan State University

**Abstract**

Designing efficient drugs for curing diseases is of essential importance for the 21st century's life science. Computer-aided drug design and discovery has obtained a significant recognition recently. However, the geometric complexity of protein-drug interactions remains a grand challenge to conventional methods. We integrate algebraic topology and deep learning algorithms for the predictions of protein-ligand binding affinity, drug toxicity, drug solubility, and drug partition coefficient. We demonstrate that element specific persistent topology is able to retain crucial biological information during the topological abstraction and offers some of the best result in high throughput drug screening, protein flexibility analysis and protein stability change upon mutation. I will discuss how deep learning and algebraic topology, has led my team to be a top performer in recent two D3R Grand Challenges, a worldwide competition series in computer-aided drug design and discovery

(<http://users.math.msu.edu/users/wei/D3RFreeEnergy.pdf>,http://users.math.msu.edu/users/wei/D3R\_GC3.pdf ).

This work is supported in part by NIH, NSF, Bristol-Myers Squibb, Pfizer and Michigan State University.

**Nonuniform Ionic Size Modified Dielectric Models and Fast Finite Element Solvers**

Dexuan Xie

University of Wisconsin, Milwaukee

**Abstract**

In this talk, I will report the recent progresses that we made in the development of nonuniform ionic size modified dielectric continuum models and fast finite element solvers for a mixture with multiple ionic species. In particular, I will introduce a new nonuniform size modified Poisson-Boltzmann equation (nuSMPBE) for protein and a new nonuniform size modified nonlocal Poisson-Fermi double-layer model (nuNPF) for an electrolyte mixture of ionic species. A new electrostatic free energy functional will also be introduced to show the derivation of nuSMPBE and nuNPF. Furthermore, the fast solvers for nuSMPBE and nuNPF will be reported. Finally, numerical results will be given to demonstrate the high performance of the new solvers, and to show the importance of considering nonuniform ionic size effects in the calculation of ionic concentrations.

**Harmonic surface mapping algorithm for fast electrostatic sums**

Zhenli Xu

Shanghai Jiaotong University

**Abstract**

We present a harmonic surface mapping algorithm (HSMA) for fast electrostatic sums of finite sources and infinite image sources. Compared to the popular PME method, this algorithm can be useful for more general boundary conditions rather than periodic boundary, and it is much easier for parallelization. The HSMA uses the property the induced potential due to infinite images is harmonic and can be expanded into a Harmonic series. The analytical harmonic series is mapped into a boundary integral over a surface containing the simulation box. After the discretization of the boundary integral, we obtain an equivalent system composed of the point sources finite number of point image charges, which is calculated by FMM or the GPU calculations. The performance of the algorithm is shown by numerical examples.

**Models of Blood Clot Formation**

Zhiliang Xu

Notre Dame University

**Abstract**

Blood clotting is a multiscale process involving blood cells, fibrinogen polymerization, coagulation reactions, ligand-receptor interactions and blood plasma flow. Detailed multiscale models of blood clotting to cover all aspects of clotting are, if not possible, extremely difficult to develop. Models focusing on specific events across one or two spatial-temporal scales seem to be plausible. In this talk, ligand-receptor binding kinetics model, computational model of fluid-structure interaction (FSI) for simulating flow-elastic membrane with mass and the continuum model for studying the structural stability of clots will be presented. The binding kinetics model revealed that platelet αIIbβ3 integrin and fibrin interacts through a two-step mechanism. The new FSI model is derived by using the energy law and distributed-Lagrange-multiplier/fictitious-domain (DLM/FD) formulation. The continuum model for studying the structural stability of clots utilized the phase field and energetic variational approaches. Simulation results show that rheological response of the blood clot to the flow is determined by mechanical and structural properties of its components. Two main mechanisms are shown to significantly affect volume of the already formed clot: dynamic balance between platelet adhesion and platelet removal by the flow on the blood clot surface and removal of parts of the clot through rupture.

**Energy conserving fast multipole methods for the calculation of long-range interactions**

Rio Yokota

Tokyo Institute of Technology

**Abstract**

Particle mesh Ewald (PME) is the preferred method for calculating long-range interactions in molecular dynamics simulations. However, PME becomes heavily bottlenecked by the scalability of FFT as the number of nodes increases. Fast multiple methods (FMM) on the other hand have been shown to scale much better, and can be considered an interesting alternative for the calculation of long-range interactions on massively parallel architectures. One problem with FMM was its poor energy conservation compared to PME, which is caused by the discontinuity between the near field and far field in FMM. By smoothing this discontinuity with a regularization function we have improved the energy conservation of FMM.

**Phase field modeling of Cellular Systems**

Lei Zhang

Beijing International Center for Mathematical Research, Center for Quantitative Biology,

Peking University

**Abstract**

Control of cellular behaviors plays a critical role in pattern formation, growth regulation and regeneration. Numerous developmental processes have been extensively studied from a mechanistic perspective, but only recently have serious efforts been directed toward systems biology approach. In this talk, I will present a phase field framework to model various cell systems. First, we present a mathematical model that incorporates the interplays between Rac, filamentous actin (F-actin), and membrane tension for the formation of cell polarity. Then, I extend a phase field approach to study the neuroblast delamination in Drosophila. Dynamics of cell ingression and role of actin-myosin network in apical constriction reveal that the myosin signaling drives neuroblast delaminiation in such rare event. The joint work with Feng Liu (PKU), Yan Yan (HKUST), Anchang Shi (McMaster).

**Effects of Kinetic Dielectric Decrement on Ion Diffusion and Capacitance in Electrochemical Systems**

Shuangliang Zhao

East China University of Science and Technology

**Abstract**

Diffusion of ionic components in electrolytes not only changes the gradients of ion concentrations but also alters the local dielectric environment. Despite the significant progress of non-equilibrium molecular theories on diffusion process driven by the gradients of ion concentrations, the effect of kinetic dielectric decrement on ion diffusion dynamics is still poorly understood. Herein, taking the charging process in electric double layer systems as a case study, we conduct a multiscale investigation of ion diffusions in aqueous electrolytes by combining the dynamic density functional theory and an ion-concentration dependent dielectric constant model. Using this multiscale method, we demonstrate that the time evolutions of local dielectric constant and ion concentration can be simultaneously predicted, and the coupling effects in-between on the charging speed and differential capacitance are significant especially when the hydration ability of the ion is strong, in accordance with the experimental measurements.

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**A two-component regularization for charge singularity in implicit solvation**

Shan Zhao

University of Alabama

**Abstract**

The Poisson-Boltzmann Equation (PB) equation is a widely used implicit solvent model for the electrostatic analysis of solvated biomolecules. Singular source is known as one of major numerical difficulties for solving the PB equation. In this talk, we will present a new regularization method for treating charge singularities. In a regularization method, by decomposing the potential function into two or three components, the singular component can be analytically represented by the Green's function, while other components possess a higher regularity. Our new regularization combines the efficiency of two-component schemes with the accuracy of the three-component schemes. Based on this regularization, a new matched interface and boundary (MIB) finite difference algorithm is developed for solving both linear and nonlinear PB equations. Compared with the existing MIB PB solver based on a three-component regularization, the present algorithm is simpler, easier to implement, and faster, while maintains the same second order accuracy. This is numerically verified by calculating the electrostatic potential and solvation energy on the Kirkwood sphere and a series of proteins.

This is a joint work with Weihua Geng (Southern Methodist).

**A probability polling state of neuronal systems underlying maximum entropy coding principle**

Douglas Zhou

Shanghai Jiaotong University

**Abstract**

How to extract information from exponentially growing recorded neuronal data is a great scientific challenge. In recent experiments, it has been found that the second order maximum entropy model, by using only firing rates and second order correlations of neurons as constraints, can well capture the observed distribution of neuronal firing patterns in many neuronal networks, thus, conferring its great advantage in that the degree of complexity in the analysis of neuronal activity data reduces drastically from O(2^n) to O(n^2), where n is the number of neurons under consideration. In this talk, we address the question of what kind of dynamical states of neuronal networks allows the network to possess a coding scheme dictated by the Maximum Entropy Principle (MEP). For asynchronous neuronal networks, when considering the probability increment of a neuron spiking induced by other neurons, we found a probability polling (p-polling) state that underlies the success of the second order maximum entropy model. We show that this p-polling state can arise in vitro and in vivo. Our theoretical analysis of the p-polling state and its relationship to MEP provides a new perspective to the information coding of neuronal network dynamics in the brain.

**Positivity preserving, conservative, and free energy dissipating finite difference methods for multi-dimensional PNP-type equations**

Shenggao Zhou

Soochow University

**Abstract**

In this talk, we will present simple but effective finite difference methods for solving the multi-dimensional Poisson--Nernst--Planck (PNP) equations with multiple ionic species. A novel central-differencing discretization based on harmonic-mean approximations is proposed for the Nernst--Planck (NP) equations. Numerical analysis proves that the numerical schemes respect three desired properties that are possessed by analytical solutions: I) ionic mass conservation, II) positivity of ionic concentrations, and III) free-energy dissipation. The semi-implicit scheme is further shown to preserve positivity unconditionally, whereas a constraint on a mesh ratio is required for the explicit scheme to ensure positivity. The positivity preservation is established based on advantages brought by the harmonic-mean approximations. In addition, theoretical and computational investigations are performed to study condition numbers of the semi-implicit discretization of the NP equations, further revealing advantages of the scheme in computational efficiency and stability. Our estimates on the upper bound of condition numbers indicate that the developed discretization based on harmonic-mean approximations can effectively solve a known issue---a large condition number is often accompanied by the use of Slotboom variables. Numerical tests verify that the numerical solution respects desired properties, and is second-order accurate in space and first-order accurate in time. An application of the numerical scheme to an electrochemical charging system demonstrates its effectiveness in solving realistic problems.

This is a joint work with Jie Ding, Yiran Qian, and Zhongming Wang.