WORKSHOP ON MATHEMATICAL MODELS OF ELECTROLYTES WITH APPLICATION TO MOLECULAR BIOLOGY

WORKSHOPS

CASTS

理論科學研究中心

Center for Advanced Study in Theoretical Sciences

2013. 12. 25-27

Multiscale multiphysics and multidomain models for biomolecules

Prof. Guowei Wei

For material related to this talk, click here.

New Solutions are Needed for Old Problems

Prof. Bob Eisenberg

For the abstract of this talk, please click here.

For material related to this talk, click here.

A Poisson-Fermi Theory for Biological Ion Channels: Models and Methods

Prof. Jinn-Liang Liu

A Poisson-Fermi theory that includes both steric and correlation effects is presented for electrolytic systems. The steric effect is described by a Fermi like distribution, which is derived from the configuration entropy of spherical ions and water molecules with different sizes and valences. The correlation effect is described by a dielectric coefficient function from a decomposition of the Coulomb interaction into short and long components. The maximum allowable close packing (saturation) condition at high fields and the variation of dielectric coefficient from low to high concentration area are two of the most important features of the theory. The classical Poisson-Boltzmann theory generally fails to provide these features. Geometric singularities of molecular surfaces, strong nonlinearity of model systems, and the wide range of bath concentrations (up to 108 order variation in magnitude) in channel experiments pose severe challenges for theoretical investigations. We shall also present several numerical methods to tackle these problems. Numerical results in 3D for electric double layers, Born ion model, gramicidin A channel, and L-type calcium channel will be given to demonstrate the novelty of the theory and the effectiveness of numerical methods. All results are verified with either those of exact solutions, Monte Carlo, or molecular dynamics. For material related to this talk, click here.

Traveling wave solutions of the FitzHugh-Nagumo equations

Prof. Chiun-Chuan Chen

The FitzHugh-Nagumo system describes the electrochemical behaviors in nerve fiber and cardiac myocytes. It captures the mathematical properties of excitation and propagation in these tissues and has become a favorite model in excitable media. We will discuss some aspects of recent studies of this system.

Ligand-Perturbed Protein Dynamics Enlightened with Hierarchical Markov State Model Analysis

Prof. Jung-Hsin Lin

Dynamics is a crucial part for understanding the function of a biomolecule. Although information about intramoelcular dynamics is difficult to obtain with experiments, it is rather accessible via molecular dynamics simulations. Recently, microsecond time scale for simulations of membrane proteins, namely, receptors, transporters, pumps, have become widely affordable, and it is therefore timely to ask whether molecular dynamics simulations at this time scale can already provide sufficient dynamical information ready for functional interpretation and to distinguished different functional types of ligands. Standard analyses for dynamics of biomolecules include atomic fluctuations, dynamic cross-correlation matrix (DCCM), principal component analysis, mutual information analysis, etc. However, with the substantial lengthening of time scale, these analyses should be performed with care, especially when molecule conformations are represented in cartesian coordinates. In this talk, I will present how to use a systematic coarse-graining appraoch, namely, Markov State Model Analysis, to analyze the dynamics of a G-protein coupled receptor and its kinetic states to determine the functional types of ligands. With the Markov State Model Analysis, we could reach a very comprehensive dynamic picture of how ligands of different functional types affect the conformational waves of a protein.

Modification of PNP-steric model with additional bi-Laplacian diffusion

Prof. Tzyy-Leng Horng

PNP-steric model was developed from MPNP model [1] by Eisenberg and Lin [2]. PNP-steric model simplifies the Lennard-Jones (LJ) potential of MPNP model by a band-limited function, which turns the non-local LJ integral into a local derivative. This makes the computation more efficient by avoiding the time-consuming convolution when dealing with non-local LJ potential. One may think of the localization of LJ potential in PNP-steric model as a low-frequency-mode approximation of it. PNP-steric model has been successfully applied to study the selectivity in Ca channel [3]. However, a pitfall was observed that it causes high-frequency instability as the inter-species LJ parameters gets somewhat larger than their intra-species counterparts. This would set a constraint on those important parametric values, that might further fail to describe significant physics related to electrolyte. One example is the over-screening phenomenon of charged-wall problem with 1:2 electrolyte, which has been depicted by many molecular dynamics studies. Motivated by by the single-file diffusion observed in a narrow single-walled carbon nanotube (SWCNT) [4], a bi-Laplacian diffusion is added to PNP-steric model to account for over-crowdedness of particles. This bi-Laplacian diffusion can suppress the high-frequency instability mentioned above that Fickian

diffusion fails to. The new model was tested on the over-screening phenomenon of charged-wall problem happening at 1:2 electrolyte, and the result agrees well with [5] by choosing a larger inter-species LJ coupling parameter. Multiple over-screening loops in ionic concentration distributions were also observed when further increasing inter-species LJ coupling parameter, which was also observed by some MD studies. The new model was also tested on the single-file diffusion case of [4]. Discarding Fickian diffusion and choosing appropriate LJ parameters, simulation showed out-of-phase traveling concentration waves of particles that mimics the single-file transportation of particles in a narrow SWCNT as shown in [4]. All these imply that a better application to ion channel is expected by using this newly modified model.

[1] Eisenberg, B., Y. Hyon, and C. Liu, Energy Variational Analysis EnVarA of Ions in Water and Channels: Field Theory for Primitive Models of Complex Ionic Fluids. Journal of Chemical Physics, 2010. 133: p. 104104.

[2] Eisenberg, B. and T. C. Lin, A New Approach to the Lennard-Jones Potential and a New Model: PNP-Steric Equations, to appear in Communications in Mathematical Sciences.

[3] T.-L. Horng, T.-C. Lin, C. Liu and B. Eisenberg, PNP Equations with Steric Effects: a Model of Ion Flow through Channels, Journal of Physical Chemistry B, 2012. 116: 11422-11441.

[4] Q. Chen, J. D. Moore, Y.-C. Liu, T. J. Roussel, Q. Wang, T. Wu, and K. E. Gubbins, Transition from Single-File to Fickian Diffusion for Binary Mixture in Single-Walled Carbon Nanotubes, J. Chem. Phys., 2010. 113, 094501. [5] D. Boda, W. R. Fawcett, D. Henderson and H. Sokolowski, Monte Carlo, Density Functional Theory, and Poisson-Boltzmann Theory Study of the Structure of an Electrolyte near an Electrode, J. Chem. Phys., 2002. 116: 7170-7176.

For material related to this talk, click here.

What Can Charge Conserving Poisson-Boltzmann Equations Describe?

Prof. Chiun-Chang Lee

The Charge Conserving Poisson-Boltzmann Equations (CCPB Equations, Named by Prof. Ping Sheng & Chun Liu) is a nonlocal nonlinear elliptic equation for describing the ion transport with electroneutrality and non-electroneutrality. In this talk, the limiting behavior for radial solutions of CCPB equations will be introduced. In particular, when the total charges of negative ions (positive ions, respectively) is less than that of positive ions (negative ions, respectively) in the electrolyte, we prove rigorously that the electrolyte tends to (pointwise) electroneutrality in the bulk, while it occurs strong non-electroneutrality near the boundary.

Numerical study on the population genetic drift problems

Prof. Xingye Yue

We focus on numerical methods to solve the diffusion equation for the random genetic drift that occurs at a single unlinked locus with two alleles. It is a degenerated convection-dominated parabolic equation. Two finite volume methods, upwind (UFVM) and central (CFVM) schemes are used to solve the equation numerically. We observed that the long time behaviors of the numerical solutions of these methods are totally different. Based on the conservations of total probability and the mean gene frequency (expectation), the conclusion is drawn that the results of UFVM are not correct since it destroys the conservation of the mean gene frequency. However, in general, the upwind scheme is a better choice for the convection-dominated problem to achieve stability due to its intrinsic numerical viscosity. To see what's wrong here, we appeal to the method of vanishing viscosity, i.e., a small viscosity term is first added in, then the limit behavior of the solution is investigated when the added viscosity tends to zero. We see that the limitation of the steady state solution is uniquely determined and has nothing to do with the initial conditions. This means that the long time behavior of the original problem will be changed by any added infinitesimal viscosity. That is the reason why the upwind scheme does not work for the genetic drift problem.

Furthermore, we have to answer another question, why central scheme works well for a convection-dominated problem? To this purpose, we find that convection should be classified into 2 types: one is related to the stability of the numerical scheme and the other has nothing to do with the stability of the numerical scheme, no matter whether it is dominated. This is totally a new observation for convection-diffusion community.

This is a joint work with Minxin Chen, Chun Liu, David Waxman and Shixin Xu.

For material related to this talk, click here.

Modeling and Simulating Asymmetrical Conductance Changes in Gramicidin Pores.

Dr. Shixin Xu

Gramicidin A is a small well characterized peptide that forms an ion channel (transmembrane protein) in lipid membranes. An important feature of gramicidin A (gA) pore is that its conductance is affected by the electric charges near the entrance of the gramicidin A pore. This properly has led to the application of gramicidin A as a biochemical sensor for monitoring and quantifying a number of chemical and enzymatic reactions. Here, a mathematical model of conductance changes of gramicidin A pores in response to the presence of electrical charges near its entrance, either on membrane surface or attached to gramicidin A itself, is presented. In this numerical simulation, a two dimensional computational domain is set to mimic the structure of a gramicidin A channel in the bilayer surrounded by electrolyte. The transportation of ions through the channel is modelled by the Poisson-Nernst-Planck (PNP) equations that are solved by Finite Element Method (FEM). Preliminary numerical simulations of this mathematical model are in qualitatively agreement with the experimental results in the literatures.

For material related to this talk, click here.

Keller-Segel model in acupuncture

Prof. Tony Wen-Hann Sheu

For the abstract of this talk, please click here.

Modeling and simulation of moving contact lines in multi-phase flows

Prof. Weiqing Ren

I will first discuss a contact line model derived from principles of non-equilibrium thermodynamics and molecular dynamics simulations. Macroscopic thermodynamic principles are used to place constraints on the form of the boundary conditions, and the detailed constitutive relations are computed from molecular dynamics. This meso-scale contact line model consists of the Navier-Stokes equation, a boundary condition for the slip velocity, and a relation between the dynamic contact angle and the contact line velocity. In the second part of my talk, I will discuss numerical methods for the contact line model, its extension to fluids with surfactants, and modeling of moving contact lines at the macroscale.

For material related to this talk, click here.

An Energetic Variational Approach to Ion Channel Dynamics

Prof. YunKyong Hyon

Abstract. We introduce a mathematical model to study the transport of ions through ion channels. The system is derived in the frame of the energetic variational approaches, taking into account the coupling between electrostatics, diffusion, and protein (ion channel) structure. The geometric constraints of the ion channel are introduced through a potential energy controlling the localmaximum volume inside the ion channel. A diffusive interface (labeling)description is also employed to describe the geometric configuration of the channels. The surrounding bath and channel are smoothly connected with the antechamber region by this label function. A corresponding modified Poisson-NernstPlanck channel system for ion channels is derived using the variational derivatives of the total energy functional. The functional consists of the entropic free energy for diffusion of the ions, the electrostatic potential energy, the repulsive potential energy for the excluded volume effect of the ion particles, and the potential energy for the geometric constraints of the ion channel. For the biological application of such a system,we consider channel recordings of voltage clamp tomeasure the current flowing through the ion channel. The results of one-dimensional numerical simulations are presented to demonstrate some signature effects of the channel, such as the current output produced by single-step and double-step voltage inputs.