Department of Molecular Biology and Biochemistry *and* Center for Mathematical and Computational Biology
University of California, Irvine

Distinguished Seminar in Computational and Mathematical Biology

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Variational Implicit Solvation: Empowering Mathematics and Computation to Understand Biological Building Blocks

Thursday, Oct 25, 2012 - 11:00am
200 Howard Schneiderman Lecture Hall (Bldg. 501)
http://today.uci.edu/pdf/UCI_12_map_campus_core.pdf

Abstract: Biomolecules, such as proteins, DNA, and lipid membranes, are biological building blocks. Their structures and dynamics determine how cells, organs, and other biological systems function or dysfunction. For instance, it is evident that misfolded proteins can lead to impaired cellular functions and ultimately to diseases. Efficient and accurate modeling of biomolecules is, however, extremely challenging due to their enormous complexity.

In this talk, I will present a variational implicit-solvent model (VISM) together with a robust level-set computational method for the structure of biomolecules. Central in VISM is an effective free-energy functional of all possible solute-solvent (e.g., protein-water) interfaces, coupling together the solute surface energy, solute-solvent van der Waals interactions, and electrostatic contributions. The level-set relaxation of such a functional determines numerically biomolecular equilibrium conformations and minimum free energies. Comparisons with experiments and molecular dynamics simulations demonstrate that the level-set VISM can capture the hydrophobic hydration, dry-wet fluctuation, and many other important structure properties of biomolecules. After reviewing the initial success of the level-set VISM, I will continue to present some new developments around the VISM. These include: (1) the coupling of solute molecular mechanical interactions in the VISM; (2) the effective dielectric boundary forces; (3) continuum electrostatics with nonuniform ionic sizes; and (4) the solvent fluid fluctuations. I will emphasize how concepts and methods of the classical differential geometry, partial differential equations and their numerical solutions, shape derivatives, and stochastic differential equations can all be used to the fundamental studies of biological building blocks.

Much of the work presented here results from close collaborations between our MBB (Mathematics and Biochemistry-Biophysics) group and biological scientists.

References:

[1] Li-Tien Cheng, Joachim Dzubiella, J. Andrew McCammon, and Bo Li, Application of the level-set method to the implicit solvation of nonpolar molecules, J. Chem. Phys., 127, 084503, 2007.

[2] Li-Tien Cheng, Yang Xie, Joachim Dzubiella, J. Andrew McCammon, Jianwei Che, and Bo Li, Coupling the level-set method with molecular mechanics for variational implicit solvation of nonpolar molecules, J. Chem. Theory Comput., 5(2), 257-266, 2009.

[3] Piotr Setny, Zhongming Wang, Li-Tien Cheng, Bo Li, J. Andrew McCammon, and Joachim Dzubliella, Dewetting-controlled binding of ligands to hydrophobic pockets, Phys. Rev. Lett., 103, 187801, 2009.

[4] Bo Li, Continuum electrostatics for ionic solutions with nonuniform ionic sizes, Nonlinearity, 22, 811-833, 2009.

[5] Shenggao Zhou, Zhongming Wang, and Bo Li, Mean-field description of ionic size effects with non-uniform ionic sizes: A numerical approach, Phys. Rev. E, 84, 021901, 2011.

[6] Bo Li, Xiaoliang Cheng, and Zhengfang Zhang, Dielectric boundary force in molecular solvation with the Poisson-Boltzmann free energy: A shape derivative approach, SIAM J. Applied Math., 71, 2093-2111, 2011.

[7] Zhongming Wang, Jianwei Che, Li-Tien Cheng, Joachim Dzubiella, Bo Li, and J. Andrew McCammon, Level-set variational implicit-solvent modeling of biomolecules with the Coulomb-field approximation, J. Chem. Theory Comput., 8, 386-397, 2012.

About the Speaker: Dr. Bo Li obtained his Ph.D. degree in mathematics and M.S. degree in mechanics from the University of Minnesota in 1996. Subsequently, he did a three-year postdoctoral training at UCLA and then became an assistant professor at the University of Maryland, College Park. Since 2004, he has been on the faculty of the Department of Mathematics, UC San Diego, initially as an associate professor and then full professor starting from 2010. Since 2007, he has also been a senior scientist of the NSF Center for Theoretical Biological Physics (CTBP).

In his early research, Dr. Li developed numerical methods for partial differential equations. He later worked much on the physical modeling, mathematical analysis, and numerical computation of materials, including mechanics of materials, solid-solid phase transitions, crystalline defects, and molecular beam epitaxy. In recent years, he has been focusing on the interdisciplinary research at the interface of mathematics and biochemistry-biophysics (MBB). In close collaborations with biological scientists, he and his MBB group have developed mathematical concepts and computer techniques for solving some fundamental biological problems at the molecular and cellular levels. These include biomolecular interactions, molecular recognition, RNA diffusion and gene expressions, and cell motility and dynamics. Dr. Li's research has been supported by the NSF, DOE, and more recently the NIH.

Anyone wishing to meet with Dr. Li is encouraged to contact: Ray Luo ray.luo@uci.edu

Thursday, Oct 25

10:30 – 11:00am: Arrival and prep for presentation (200 Howard Schneiderman Lecture Hall)

11:00 – 12:00pm: Variational Implicit Solvation: Empowering Mathematics and Computation to Understand Biological Building Blocks (200 Howard Schneiderman Lecture Hall)

12:00 – 1:30pm: Lunch with students at the Faculty Club

1:30 – 2:10pm:

2:15 – 2:55pm:

3:00 – 3:40pm:

3:45 – 4:25pm: Ray Luo, MBB/BME, x4-9528 (Natural Sciences I 3206)

5:00pm: Dinner hosted by Ray Luo