

Curriculum Vitae

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EDUCATION

Ph.D.: University of Illinois at Urbana-Champaign, Physics, May 2005
Thesis topic: *Quantum Mechanical/Molecular Mechanical
Studies of F_1 -ATPase and a Plant Photoreceptor*
Thesis advisor: Professor Klaus Schulten

Diploma: University of Regensburg, Physics, September 2000

PROFESSIONAL EMPLOYMENT

May 2006 – present: Postdoctoral research associate at the Center for Quantitative Biological Simulation, Pittsburgh Supercomputing Center, Carnegie Mellon University.

October 2005 – present: Developer for Gentoo Foundation, Inc., Scientific Applications.

May 2005 – May 2006: Postdoctoral research associate in the Theoretical and Computational Biophysics Group, Beckman Institute, University of Illinois at Urbana-Champaign.

January 2001 – May 2005: Graduate research assistant in the Theoretical and Computational Biophysics Group, Beckman Institute, University of Illinois at Urbana-Champaign. Supervisor: Professor Klaus Schulten.

Spring 2000: Teaching assistant, Biophysics Department, University of Regensburg, Germany.

Fall 1996/Spring 1999: Teaching assistant, Math Department, University of Regensburg, Germany.

ACADEMIC HONORS

University of Illinois at Urbana-Champaign (2001-2006)
Renato Bobone Award, Physics Department (2003)

University of Regensburg, Germany (1994-2000)
DAAD Scholarship (1997)

RESEARCH ACCOMPLISHMENTS

Chemo-Mechanical Coupling in F₁-ATPase with Shigehiko Hayashi and Klaus Schulten. QM/MM and MD simulations were used to study the ATP hydrolysis reaction in the catalytic binding pockets of F₁-ATPase and its coupling to mechanical rotation of the central stalk. Our simulations revealed a novel proton relay mechanism as the energetically most favorable pathway for efficient hydrolysis. Furthermore, we were able to identify a specific arginine residue as essential for synchronizing the catalytic sites in F₁ to achieve the cooperativity observed during its operation. Finally, we were able to show that the ATP hydrolysis reaction itself has an equilibrium constant of $K \sim 1$ and, therefore, does not constitute the force generating step during F₁ operation.

Photoexcitation in LOV Domains with Peter Freddolino and Klaus Schulten. In this project, the photocycle of a light, oxygen, and voltage (LOV) sensitive domain in a blue-light photoreceptor found in the algae *C. Reinhardtii* was investigated using QM/MM and MD simulations. For the first time, the ground and the flavin-cysteinylyl adduct state as well as several triplet intermediate states of a complete LOV domain could be characterized at electronic level detail. In addition, our simulations allowed the unambiguous classification of the adduct formation pathway as being of the radical pair type.

Development of QM/MM code with Shigehiko Hayashi and Klaus Schulten. This project was concerned with the design and the implementation of a QM/MM computer code that was used to conduct all QM/MM simulation studies in my doctoral dissertation. The QM/MM method is based on the quantum chemistry package GAMESS and uses the AMBER force field for the classically modeled region of the biomolecular system. Our code runs efficiently on up to 32 processors and is capable of performing Hartree-Fock as well as density functional based calculations.

Coarse-Graining Methods for Biomolecules with Rob Phillips and Klaus Schulten. The focus of this project was the development and investigation of a coarse-graining scheme for proteins that builds upon methods used in materials science. Our approach employed a residue-centric description via a local basis system to reduce the number of the system's degrees of freedom.

Protein Dynamics of LOV Domains with Peter Freddolino and Klaus Schulten. This project investigated how photon induced flavin-cysteinylyl adduct formation in LOV domains is able to induce signaling events to a neighboring kinase domain in light of only minor structural differences observed in available crystal structures. This project involved the parameter-

ization of the chromophore flavin mono-nucleotide using quantum chemistry calculations. Extensive MD simulations were then carried out for both the dark and photo-reacted species and revealed distinct differences in the system's dynamical properties which were suggested to be responsible for the observed signaling mechanism.

DNA Translocation in PcrA helicase with Klaus Schulten. Complementing my previous studies of F₁-ATPase, the chemo-mechanical coupling of ATP hydrolysis to DNA translocation in PcrA helicase was investigated. Lacking the catalytic site cooperativity of F₁-ATPase, PcrA helicase provided an ideal test system to study the coupling of a chemical reaction to mechanical force generation. The calculations revealed two distinct pathways for ATP hydrolysis in the PcrA catalytic site which both proceeded via the proton relay mechanism proposed in our earlier work on F₁-ATPase. The simulations shed light on the coupling mechanism between ATP hydrolysis and DNA translocation through PcrA helicase.

CURRENT RESEARCH

Spatially Realistic Monte Carlo Simulations of Neurotransmitter Release with Joel Stiles. This project focuses on the development of a comprehensive and spatially realistic computational model of action potential triggered, Ca²⁺ dependent neurotransmitter release from neuromuscular synapses.

PROFESSIONAL REGISTRATIONS

Member: American Physical Society.

Member: Biophysical Society.

Member: German Physical Society.

Member: Honors Society of Phi Kappa Phi.

PUBLICATIONS

F. Luo, M. Dittrich, J.R. Stiles, and S.D. Meriney, "Calcium channel density and opening probability in subregions of motor nerve terminal active zones," (submitted).

R. Kerr, T.M. Bartol, B. Kaminsky, M. Dittrich, J.C.J. Chang, S. Baden, T.J. Sejnowski, and J.R. Stiles, "Fast Monte Carlo Simulation Methods for Biological Reaction-Diffusion Systems in Solution and on Surfaces," (submitted).

P. Freddolino, M. Dittrich, and K. Schulten, "Dynamic switching mechanisms in LOV1 and LOV2 domains of plant phototropins," *Biophysical Journal*, **91**, 3630 (2006).

M. Dittrich and K. Schulten, "PcrA helicase, a prototype ATP-driven molecular motor," *Structure*, **14**, 1345 (2006).

M. Dittrich, J. Yu, and K. Schulten, "PcrA helicase, a molecular motor studied from the electronic to the functional level," *Topics in current chemistry*, **268**, 319 (2006).

M. Dittrich and K. Schulten, "Zooming in on ATP hydrolysis in F_1 ," *Journal of Bioenergetics and Biomembranes* **37**, 441 (2005).

M. Dittrich, P. Freddolino, and K. Schulten, "When Light falls in LOV: A QM/MM Study of Photoexcitation in Phot-LOV1 of *C. Reinhardtii*," *J. Phys. Chem. B* **109**, 13006 (2005)

M. Dittrich, S. Hayashi, and K. Schulten, "ATP hydrolysis in the β_{TP} and β_{DP} catalytic sites of F_1 -ATPase," *Biophysical Journal* **87**, 2954 (2004)

M. Dittrich, S. Hayashi, and K. Schulten, "On the mechanism of ATP hydrolysis in F_1 -ATPase," *Biophysical Journal* **85**, 2253 (2003)

R. Phillips, M. Dittrich, and K. Schulten, "Quasicontinuum representations of atomic-scale mechanics: From proteins to dislocations," *Ann. Rev. Mat. Res.* **32**, 219 (2002)

TALKS

"Insights into the mechanism of molecular motors," Seminar, Stiles Laboratory, Pittsburgh Supercomputing Center, Pittsburgh, PA, March 30, 2006.

"Quantum mechanical/molecular mechanical simulations of biomolecular systems," Seminar, Sandia National Laboratory, Albuquerque, NM, March 2, 2006.

"Quantum mechanical/molecular mechanical simulations of biomolecular systems," Seminar, A. Sali Laboratory, UCSF, San Francisco, CA, December 14, 2005.

"Quantum mechanical/molecular mechanical simulations of biomolecular systems," Seminar, D. Baker Laboratory, Univ. of Washington, Seattle, WA, October 25, 2005.

"When light falls in LOV: A computational study of a plant photoreceptor," Biophysics and Computational Biology Summer Symposium, Illinois Biophysics Society, Urbana, IL, July 26, 2005.

"Quantum mechanical/molecular mechanical simulations of biomolecular systems," International Workshop on Classical and Quantum Dynamical Simulations in Chemical and Biological Physics, Max Planck Institut für die Physik Komplexer Systeme, Dresden, Germany, June 9, 2005.

“Computational Study of the Chemomechanical Coupling and ATP Hydrolysis in F_1 -ATPase,” Biophysical Society Annual Meeting, Long Beach, CA, February 16, 2005.

“Insights into the molecular mechanism of ATP synthase,” Gordon Conference on Molecular and Cellular Bioenergetics, Andover, NH, June 24, 2004.

POSTER PRESENTATIONS

“A Computational Study of ATP Hydrolysis and Force Generation in PcrA Helicase,” Biophysical Society Annual Meeting, Salt Lake City, UT, February 2006.

“QM/MM study of ATP hydrolysis in F_1 -ATPase,” Biophysical Society Annual Meeting, Baltimore, MD, February 2004.

“ATP hydrolysis in F_1 -ATPase: A combined ab initio QM/MM study,” Biophysical Society Annual Meeting, San Antonio, TX, February 2003.