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Supercomputing Institute
for Advanced Computational Research

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Fall 2011 Research Bulletin

Biochemistry, Molecular Biology, and Biophysics

Simulations of Fluorescent Probes Attached to the Sarcoplasmic Reticulum Ca^{2+}-ATPase (SERCA)

Research performed in the laboratory of Professor David D. Thomas (Biochemistry, Molecular Biology, and Biophysics; MSI Fellow) is focused on the study of muscle proteins. The goals are to understand the fundamental molecular motions and interactions that are responsible for muscle contraction or cellular movement, to determine the molecular bases of muscle disorders, and to apply the insights gained into therapeutic design. The muscle research is conducted with a multidisciplinary approach using a wide range of techniques—physiology, enzyme kinetics, molecular genetics, peptide synthesis, and computer simulation—but the main technique of the Thomas lab is site-directed labeling in combination with spectroscopy. Other Thomas lab researchers involved in this work include research associate Dr. Bengt Svensson and graduate student Elizabeth L. Lockamy.

After attaching spectroscopic probes (spin labels, fluorescent dyes, phosphorescent dyes, or isotopes) at specific sites within selected muscle proteins, in solution or in living cells, magnetic resonance or optical spectroscopy is performed to directly detect molecular motion. Specifically, the focus is on the force-generating proteins actin and myosin, or the calcium pump in the sarcoplasmic reticulum membrane (SERCA) and phospholamban (PLB, its regulatory partner in the heart). The research involves several types of muscle, but the laboratory is increasingly focused on the heart, with the aim to use the principles of structural biophysics to design new molecular therapies for heart failure. The SERCA-PLB complex has been identified as a key thera-

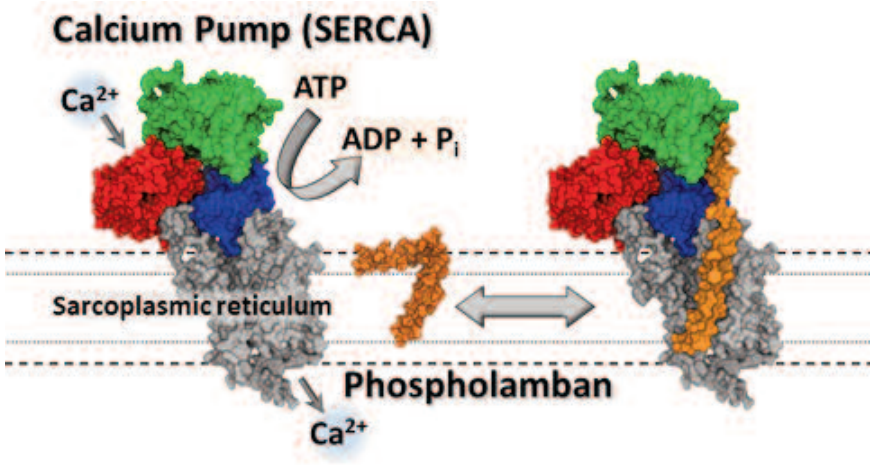

Figure 1: The calcium pump SERCA and its regulatory partner phospholamban.

Also in This Issue

peutic target for treating heart failure.

SERCA is an integral membrane protein that uses energy from ATP hydrolysis to pump calcium into the sarcoplasmic reticulum, thus relaxing the muscle and providing the calcium gradient needed for the next contraction. In the heart SERCA is regulated by phospholamban (PLB), a small integral membrane protein that inhibits SERCA (Figure 1). Physiologically, SERCA inhibition is relieved by PLB phosphorylation as part of the fight-or-flight response.

X-ray crystal structures suggest that SERCA undergoes large conformation changes during its catalytic cycle. In the transmembrane segments of SERCA, movements of α-helices are proposed to be involved in the Ca^{2+} transport (Møller et al. 2005 *Curr. Op. Struct. Biol.* 15, 387–393). Large-scale movements within the cytoplasmic domains have been observed in the Thomas lab by attaching probes to SERCA and performing electron paramagnetic resonance (EPR) and phosphorescence spectroscopy (Mueller at al. 2004 *Biochemistry* 43, 12846–12854). By expressing fluorescent fusion derivatives of SERCA and measuring distance changes by FRET (Fluorescence Resonance Energy Transfer) from CFP (Cyan Fluorescent Protein) to the fluorescent probe FITC (Fluorescein isothiocyanate), the researchers have observed structural changes within the SERCA cytoplasmic domains depending on the presence or absence of Ca^{2+} (Winters et al. 2008 *Biochemistry* 47, 4246–4256). However, these structural changes observed in the functional protein, in its native membrane environment and by molecular simulations, were much smaller than predicted from the crystal structures. Therefore, the researchers concluded that either (a) the headpiece retains a compact structure throughout its catalytic cycle or (b) the structure is dynamically disordered and samples both open and closed conformations.

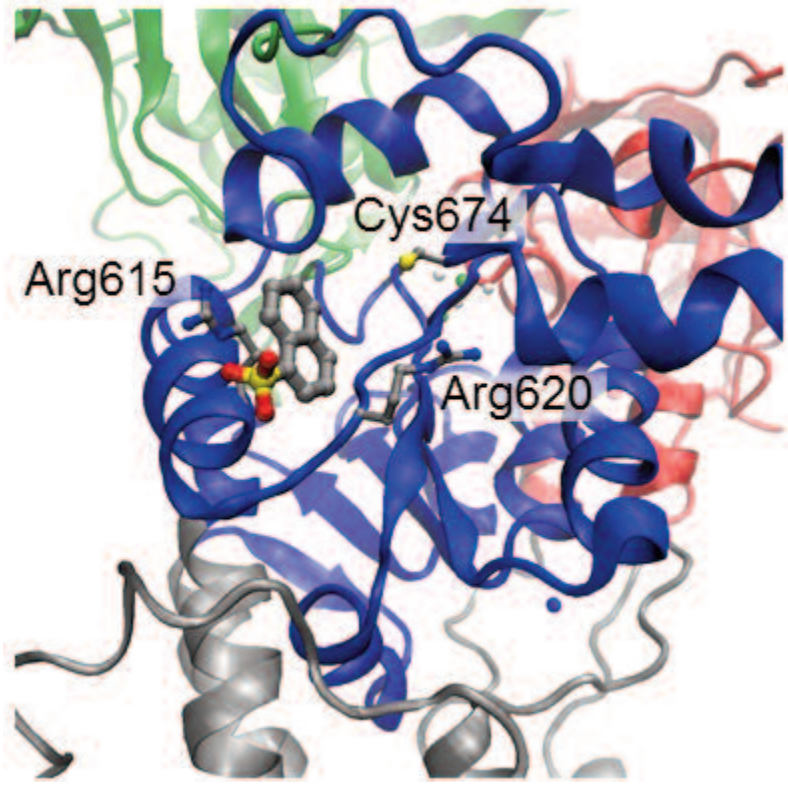

Figure 2. The new X-ray crystal structure of IAEDANS-labeled SERCA showing the region surrounding the probe.

This project is part of a larger effort that attempts to address another question that has risen from structural biology. X-ray crystal structures suggest that there may be two modes of nucleotide-binding (e.g., of ATP) in SERCA. In the canonical binding mode of ATP, the adenine ring is coordinated by Phe487, Lys515, and Arg560 of the P domain. In the presence of CPA (cyclopiazonic acid), an inhibitor of SERCA, a different nucleotide binding mode is observed, in which the adenine ring is between Arg489 and Arg678 of the N and P domains of SERCA (Moncoq et al. 2007 *J. Biol. Chem.* 282, 9748–9757).

To study this question, the researchers have designed experiments using fluorescent probes. Cys674 in the P-domain of SERCA was labeled with the fluorescent probe IAEDANS with the aim to measure distances using FRET to TNP-ADP, a fluorescent nucleotide analog. The FRET efficiency is dependent on the distance between the donor and the acceptor probes, R_{DA}. However, FRET is also dependent on the orientational and dynamical distribution of the probes (described by the orientation factor, κ^2). If the researchers can simulate the motion of the fluorescent probe when

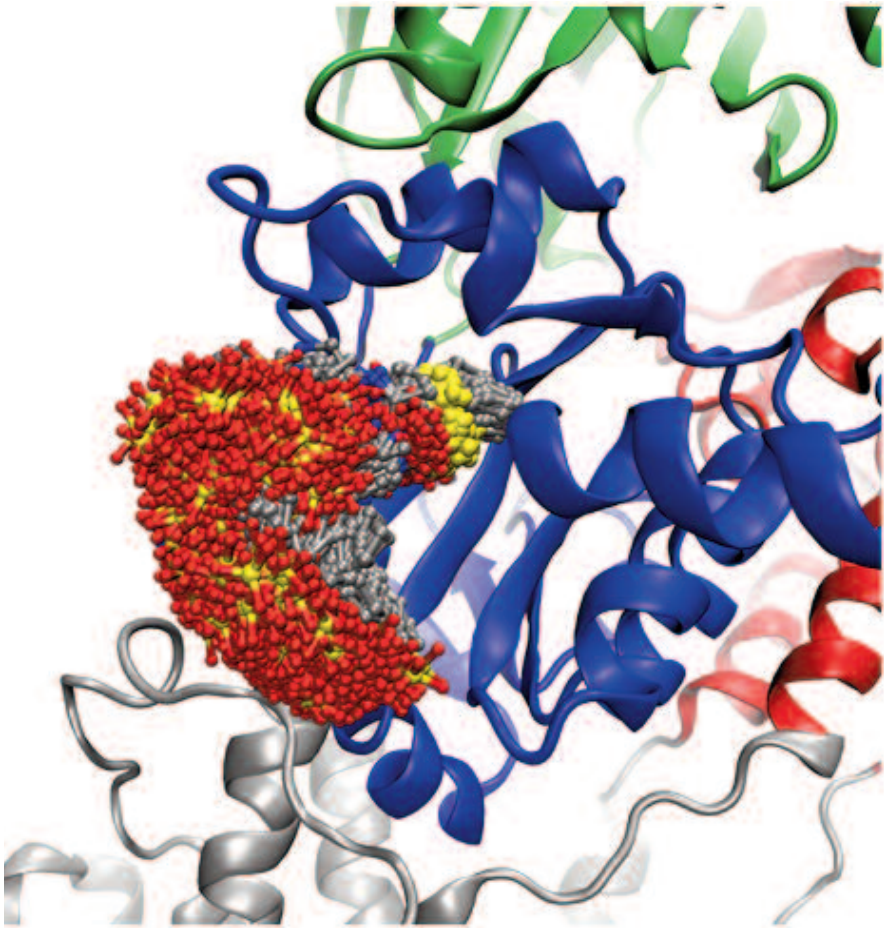

Figure 3. Conformations of AEDANS from a 96ns simulation.

it is attached to the protein accurately and thus calculate a realistic κ^2, they can then determine distances and distance changes from FRET more accurately.

The first step is the need to verify that one can accurately simulate the dynamics of probes attached to the protein. The experimental verification of these simulation results can be obtained most directly by comparing the simulations with time-resolved fluorescence anisotropy results. Fluorescence anisotropy detects the rate of motion of a chromophore by measuring the time-dependence of the polarized components of fluorescence emission. The time dependent anisotropy can also be computed from a trajectory by the auto correlation of a unit vector along the transmission dipole.

Molecular dynamics (MD) simulations are used to study the dynamics of the fluorescent probe IAEDANS when it is attached to SERCA. The starting point for the MD simulations was based on a new crystal structure of AEDANS-labeled SERCA, determined in collaboration with Dr. Howard Young (University of Alberta, Canada). In the crystal structure, which has a 3.4 Å resolution, the AEDANS label is observed in close proximity to residues Arg615 and Arg620 (Figure 2).

To carry out MD simulations, CHARMM force-field parameters for AEDANS were developed. CHARMM 27 force-field topology and parameters were developed according to standard procedures (*http://mackerell.umaryland.edu/Empirical_FF_Dev.html*). As required, *ab initio* quantum chemistry calculations were done with the software package Gaussian03. Langevin dynamics simulations were performed with CHARMM using implicit solvation. The SCPISM solvation model was used with a friction coefficient (FBETA=50) to set a viscosity similar to that of water. Residues farther than 22.5 Å from the labels were fixed, and Cα atoms of residues farther than 20 Å were harmonically restrained (0.3 kcal/mol force constant). The temperature was stepwise increased to 300 K over 100 ps. The system was then allowed to equilibrate for 300 ps by gradually decreasing the force constant on the Cα atom constraints. A total of nine individual simulations were run, each for 96 ns. Figure 3 shows the region in space that is sampled by the AEDANS probe during the simulation. Most of the time, the naphthalene moiety is in van der Waals contact with protein residues.

The rotational correlation function r(t) was computed from the trajectories for comparison with time resolved fluorescence anisotropy. This analysis of the trajectories requires that the absorption and emission transition dipoles of AEDANS are known. The vector describing the orientation of the transition dipole moment was determined from quantum chemistry calculations using the CI-Singles method at HF/6-31+g* level with Gaussian03. The dipole moment for the $\pi \rightarrow \pi^*$

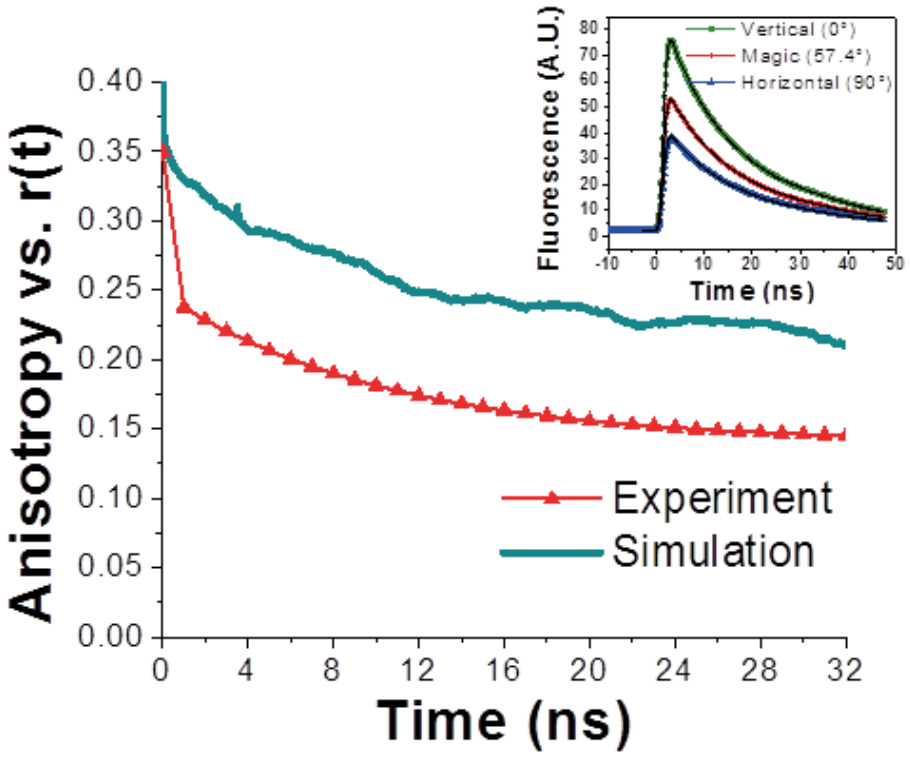

Figure 4. Fluorescence anisotropy of AEDANS-SERCA and rotational correlation function from AEDANS-SERCA simulations. The time-resolved fluorescence waveforms at 0°, 57.4° and 90° are shown in the inset.

transition was found to be similar to published experimental results.

The time-resolved fluorescence anisotropy was measured at 25°C on a SERCA sample purified from rabbit skeletal muscle and labeled with IAEDANS. The sample concentration was 10 μM AEDANS-SERCA. Fluorescence measurements were taken with an instrument constructed by the Thomas laboratory in collaboration with Dakota Technologies, Inc. (Muretta et al. 2010 *Rev. Sci. Instrum.*, 81, 103101). A pulsed laser (frequency-tripled NdYAG, 355 nm) was used to excite AEDANS-SERCA.

Both the experimental anisotropy and the simulated anisotropy, r(t), curves were fitted using a two-component exponential decay function to determine anisotropy parameters (Figure 4). The order parameter, S, was calculated by $S= (r_\infty/r_0)^{1/2}$. The shape of the experimental anisotropy curve, with its non-zero r_∞ (anisotropy at long times), and relatively high order-parameter (S = 0.63), indicate that AEDANS is quite restricted in its motion. The simulations show a similarly shaped curve but both r_0 and r_∞ are a bit higher. The order parameter calculated from the simulation data is also high (S = 0.72). This suggests that the conformation sampled by AEDANS is slightly more restricted in the simulations than in the experiments. A likely explanation for this is that the X-ray crystal structure (on which the simulation is based) shows a more compact domain conformation than what actually occurs in the real sample. Other possible reasons for the experimental and simulation data being different could be due to experimental uncertainties such as sample heterogeneity, etc. However, the rotational reorientation times are very similar between the experimental data and the simulations: τ_R = 10.5 ns for experimental and τ_R = 11.2 ns for simulations. This means that the rate of the probe motion is simulated accurately.

The results here show that the Thomas lab has established a reliable framework for both fluorescence experiments and simulations in this system. The results show that molecular dynamics simulations of the AEDANS probe can be used to determine the orientation factor, κ^2, needed for analysis of FRET results. As a next step, the researchers aim to combine simulations and data from fluorescence experiments to generate new structural and dynamical models that better represent the protein conformations in their native environments.

This work was supported by NIH (GM27906, AR007612). Dr. Svensson presented a poster about this research, *Molecular Dynamics Simulations of the IAEDANS Fluorescent Probe Attached to the Sarcoplasmic Reticulum Ca^{2+}-ATPase (SERCA),* at the MSI Research Exhibition on April 25, 2011 (see *www.msi.umn.edu/events/researchexhibition2011.html*). This poster was selected as one of the six finalists in the poster competition.

Save the Date!

Third Annual MSI Research Exhibition

Friday, April 13, 2012

Fourth Floor, Walter Library

All MSI users are invited to submit posters for this annual poster competition. Prizes will be awarded to the finalists and the Grand Prize winner.

Call for Posters will be sent in January 2012. Watch the MSI website, *www.msi.umn.edu*, for more information.

Undergraduate Internship Program 2011

The Supercomputing Institute's Undergraduate Internship Program, now in its 21st year, gives undergraduates the opportunity to experience working in a research environment. The interns get to participate in a challenging and enriching educational experience that helps them decide whether they want to pursue graduate or professional education and research. The program encompasses all aspects of high-performance computing and scientific modeling and simulation, including graphics, visualization, informatics, and high-performance network communications. Interns work with Principal Investigators at the Supercomputing Institute and their research groups on their projects. At the end of the program, each intern gives a presentation about their research. These presenations are attended by the intern group, the faculty and members of the research groups, and members of the MSI staff. The interns also prepare a written report.

The Summer 2011 program included nine interns who worked on projects in a wide variety of fields. They were selected from over 100 applicants at colleges and universities in the United States and Puerto Rico.

Robin L. Alonge, who attends the University of Maryland in College Park, Maryland, worked with Assistant Professor Elizabeth A. Amin, (Medicinal Chemistry; MSI Associate Fellow). Ms. Alonge is a chemistry major with a math minor. Her project was "*In Silico* Protein Engineering Approaches to Neutralize Organophosphorus Nerve Agents."

Nathaniel M. Beaver worked in the group of Ryan S. Elliott (Aerospace Engineering and Mechanics; MSI Associate Fellow) on a project called "Half a Car: Silicon Potentials in the OpenKIM Project." Mr. Beaver attends Gustavus Adolphus College in St. Peter, Minnesota, where he is a physics major.

Jay W. Cole attends Augustana College in Sioux Falls, South Dakota, where he is an engineering and physics major. He worked in the research group of Professor Thomas W. Jones (Astronomy; MSI Fellow). His project was "Synthesizing Astrophysical Observations and Theory."

Two interns worked in the research group of Professor Victor Barocas, (Biomedical Engineering;

Interns and other program participants at the Welcome Lunch. At the table in the foreground are Nathaniel Beaver (left front), Thomas Iadecola (left rear), Jay Cole (right front), and John Wentworth (right rear). At the rear table are (left to right) Professor Victor Barocas, Colleen Witzenburg, MSI consultant Pratik Jagtap (standing), Jeffrey Hyypio (right rear), and Benjamin Halbach.

Left to right, 2011 interns: Jay Cole, Ben Halbach, Cory Ruegg, Tom Iadecola, Jeff Hyypio, Robin Alonge, John Wentworth, Deanna Thorson, Nathaniel Beaver

MSI Fellow). **Benjamin A. Halbach**, who attends the University of Alabama in Tuscaloosa, Alabama, worked on a project called "Optimization of Partitioning Schemes for the Extraction of Materials Properties From Anisotropic Tissue." University of Minnesota biomedical engineering major/chemistry minor Jeffrey D. **Hyypio** worked on "A Microscale Model for Collagen and Fibrin Fiber Networks Using Delaunay and Voronoi Fiber Geometries."

Thomas P. Iadecola was in the research group of Professor J. Woods Halley (Physics; MSI Fellow). Mr. Iadecola is a mathematical physics major at Brown University in Providence, Rhode Island. His project was entitled "Mesoscale Molecular Dynamics of Liquid Argon From a Microscopic Simulation."

Cory S. Ruegg, who attends Gustavus Adolphus College in St. Peter, Minnesota, worked with Professor David A. Yuen (Geology and Geophysics; MSI Fellow). Mr. Ruegg is a computer science major with a music minor. His project was "Web Services and Visualization."

Deanna L. Thorson, who is a chemistry and physics major at St. Olaf College in Northfield, Minnesota, worked with Professor David D. Thomas (Biochemistry, Molecular Biology, and Biophysics; MSI Fellow). Her project was "Molecular Dynamics Simulation of Site-Directed Methionine Oxidation in Calmodulin."

Physics major **John S. Wentworth** worked with Professor Jorge Viñals (Physics; MSI Director and Fellow) on a project called "Stochastic Models of Gene Regulation." Mr. Wentworth attends Harvey Mudd College in Claremont, California.

MSI is planning a program funded by an NSF Research Experiences for Undergraduates (REU) grant in Summer 2012. The theme of the REU is "Computational Molecular Biophysics." Ten MSI Principal Investigators in a variety of fields under this broad theme are participating. See the announcement on page 8 for more information. Complete information, including application instructions, can also be found on the MSI website:

www.msi.umn.edu/programs/undergraduateresearch.html

Summer 2012
Research Experiences for Undergraduates

The Supercomputing Institute is pleased to announce its Research Experiences for Undergraduates program for Summer 2012. The theme of this program is Computational Molecular Biophysics.

This program is an excellent opportunity for students interested in applying high-performance scientific computing methods to research topics in biology, biochemistry, biophysics, and related topics. Many different projects are available.

Appointments are for full-time, 10-week research internships, and will run from June 4 through August 10, 2012. A student interested in becoming an intern must still be an undergraduate in August 2012 and must be a citizen or permanent resident of the United States or its possessions. Interns will be paid a stipend of $5,000. Room and board at the University residence hall are free to the interns. If interns wish to live elsewhere, they will receive a per-diem food allowance and can request reimbursement for housing costs.

All applications are evaluated competitively based on the qualifications of the applicant and the availability of a suitable project. Prospective applicants should review the research projects list and indicate projects in which they are interested, although they may be offered other projects due to availability.

Complete application information, application forms, and project lists are available on the Supercomputing Institute website at:

www.msi.umn.edu/programs/undergraduateresearch.html

Applications, transcripts, and letters of recommendation can be emailed, faxed, or mailed as shown below.

Email: uip@msi.umn.edu

Fax: 612-624-8861

Undergraduate Internship Coordinator
University of Minnesota
Supercomputing Institute
599 Walter
117 Pleasant Street SE
Minneapolis, MN 55455
Phone: (612) 624-2330

All applications and letters of recommendation must be received by February 29, 2012.

Visitors to MSI

The LCSE-MSI Visualization Laboratory hosted some VIPs during the fall of 2011. On September 21, incoming University President Eric Kaler and his wife, Karen Kaler, visited the lab as part of their tour of the College of Science and Engineering (CSE). Three MSI PIs, Professor Art Erdman (Mechanical Engineering), Professor Fotis Sotiropoulos (Director, St. Anthony Falls Laboratory; MSI Fellow), and Professor Dan Keefe (Computer Science and Engineering), are working together as part of a project for the Medical Devices Center (MDC). MSI Director Jorge Vinals gave a brief introduction to MSI and President and Mrs. Kaler got to experience a 3D virtual-reality visualization of blood flow through an artificial heart valve. This visualization was created using MSI's supercomputers and visualization equipment. This kind of visualization may eventually be approved by the FDA as a way to design medical devices.

U.S. Congressman Erik Paulsen, who represents Minnesota's Third District, also saw the MDC's virtual-reality visualization at the lab on September 26. Rep. Paulsen was on campus to meet with officials from the Office of Technology Commercialization and a start-up company spun out of the University to talk about the U's process for moving research innovations from the lab to the marketplace. He also met with President Kaler.

The LMVL has been a popular destination for visitors to the University of Minnesota this year. By October, the number of visitors to the lab in 2011 had topped 1,000. These visitors included government officials and business representatives who are interested in research being done at the U; elementary-, middle-, and high-school students participating in various camps and programs; prospective University students; and undergraduate and graduate students from the University and other local colleges and universities. MSI faculty members also use the LMVL the show visitors to their departments the visualizations they create using MSI resources.

Top: MSI Director Jorge Viñals introduces MSI to President and Mrs. Kaler. Bottom: Bill Hellriegel, MSI Assistant to the Director, describes MSI's mission to Representative Erik Paulsen.

Agronomy and Plant Genetics

2011/110
Phenotypic and Genomic Analyses of a Fast Neutron Mutant Population Resource in Soybean
Y.-T. Bolon, W.J. Haun, W.W. Xu, D. Grant, M.G. Stacey, R.T. Nelson, D.J. Gerhardt, J.A. Jeddeloh, G. Stacey, **G.J. Muehlbauer**, J.H. Orf, S.L. Naeve, **R.M. Stupar**, and **C.P. Vance**

2011/111
The Composition and Origins of Genomic Variation Among Individuals of the Soybean Reference Cultivar Williams 82
W.J. Haun, D.L. Hyten, W.W. Xu, D.J. Gerhardt, T.J. Albert, T. Richmond, J.A. Jeddeloh, G. Jia, **N.M. Springer**, **C.P. Vance**, and **R.M. Stupar**

Animal Science

2011/144
Genome-Wide Association Analysis of Thirty-One Production, Health, Reproduction and Body Conformation Traits in Contemporary U.S. Holstein Cows
J.B. Cole, G.R. Wiggans, L. Ma, T.S. Sonstegard, T.J. Lawlor, B.A. Crooker, C.P. Van Tassell, J. Yang, S. Wang, L.K. Matukumalli, and **Y. Da**

2011/145
Genome-Wide Association Study of Body Weight in Chicken F2 Resource Population
X. Gu, C. Feng, L. Ma, C. Song, Y. Wang, **Y. Da**, H. Li, K. Chen, S. Ye, C. Ge, X. Hu, and N. Li

Astronomy

2011/97
MHD Turbulence Simulation in a Cosmic Structure Context
T.W. Jones, D.H. Porter, D. Ryu, and J. Cho

Biomedical Informatics and Computational Biology (BICB)

2011/125
Multilevel Parallelization of AutoDock 4.2
A.P. Norgan, P.K. Coffman, **J.-P.A. Kocher**, D.J. Katzmann, and **C.P. Sosa**

2011/128
Scalable Computation and Analysis of Elementary Modes in Metabolic Networks
D. Jevremovic, **D. Boley**, and **C.P. Sosa**

Chemistry

2011/117
Validation of Electronic Structure Methods for Isomerization Reactions of Large Organic Molecules
S. Luo, Y. Zhao, and **D.G. Truhlar**

2011/121
pH-Dependent Equilibrium Isotope Fractionation Associated with the Compound Specific Nitrogen and Carbon Isotope Analysis of Substituted Anilines by SPME-GC/IRMS
M. Skarpeli-Liati, A. Turgeon, A.N. Garr, **W.A. Arnold**, **C.J. Cramer**, and T.B. Hofstetter

2011/122
Using Nitrogen Isotope Fractionation to Assess the Oxidation of Substituted Anilines by Manganese Oxide
M. Skarpeli-Liati, M. Jiskra, A. Turgeon, A.N. Garr, **W.A. Arnold**, **C.J. Cramer**, R.P. Schwarzenbach, and T.B. Hofstetter

Chemical Engineering and Materials Science

2011/101
Segregation and Interface Shape Control During EDG Growth of CZT Crystals
J.J. Derby, N. Zhang, and A. Yeckel

2011/102
Effects of a Traveling Magnetic Field on Vertical Gradient Freeze Growth of Cadmium Zinc Telluride
A. Yeckel and **J.J. Derby**

2011/108
Simulation of DNA Extension in Nanochannels
Y. Wang, D.R. Tree, and **K.D. Dorfman**

2011/109
Continuous-Time Random Walk Models of DNA Electrophoresis in a Post Array:Part II. Mobility and Sources of Band Broadening
D.W. Olson, S. Dutta, N. Laachi, M. Tian, and **K.D. Dorfman**

2011/114
First Principles Study of Electronic and Structural Properties of CuO
B. Himmetoglu, **R.M. Wentzcovitch**, and **M. Cococcioni**

2011/139
Dispersible Exfoliated Zeolite Nanosheets and Their Application as a Selective Membrane
K. Varoon, X. Zhang, B. Elyassi, D.D. Brewer, M. Gettel, S. Kumar, J.A. Lee, S. Maheshwari, A. Mittal, C.-Y. Sung, **M. Cococcioni**, L.F. Francis, **A.V. McCormick**, **K.A. Mkhoyan**, and **M. Tsapatsis**

2011/140
Routes to Identification of Intrinsic Twist in Helical MoS_2 Nanotubes by Electron Diffraction and Annular Dark-Field Scanning Transmission Electron Microscopy Imaging
A. Mittal, D.-B. Zhang, C. Teresi, **T. Dumitrica**, and **K.A. Mkhoyan**

Names of Supercomputing Institute principal investigators appear in bold type. This list contains reports entered into the reports database during August–November 2011.

2011/141
Limits in Detecting an Individual Dopant Atom Embedded in a Crystal
A. Mittal and **K.A. Mkhoyan**

Civil Engineering

2011/121
pH-Dependent Equilibrium Isotope Fractionation Associated with the Compound Specific Nitrogen and Carbon Isotope Analysis of Substituted Anilines by SPME-GC/IRMS
M. Skarpeli-Liati, A. Turgeon, A.N. Garr, **W.A. Arnold**, **C.J. Cramer**, and T.B. Hofstetter

2011/122
Using Nitrogen Isotope Fractionation to Assess the Oxidation of Substituted Anilines by Manganese Oxide
M. Skarpeli-Liati, M. Jiskra, A. Turgeon, A.N. Garr, **W.A. Arnold**, **C.J. Cramer**, R.P. Schwarzenbach, and T.B. Hofstetter

Civil Engineering–St. Anthony Falls Laboratory

2011/90
Large-Eddy Simulation of Stably-Stratified Flow Over a Steep Hill
F. Wan and **F. Porté-Agel**

2011/91
Large-Eddy Simulation of Wind-Turbine Wakes: Evaluation of Turbine Parametrisations
Y.-T. Wu and **F. Porté-Agel**

2011/92
Large-Eddy Simulation of Atmospheric Boundary Layer Flow Through Wind Turbines and Wind Farms
F. Porté-Agel, Y.-T. Wu, H. Lu, and R.J. Conzemius

2011/93
Large-Eddy Simulation of a Very Large Wind Farm in a Stable Atmospheric Boundary Layer
H. Lu and **F. Porté-Agel**

Computer Science and Engineering

2011/103
A Filtered Lanczos Procedure for Extreme and Interior Eigenvalue Problems
H.-R. Fang and **Y. Saad**

2011/104
Modification and Compensation Strategies for Threshold-Based Incomplete Factorizations
S. MacLachlan, D. Osei-Kuffuor, and **Y. Saad**

2011/128
Scalable Computation and Analysis of Elementary Modes in Metabolic Networks
D. Jevremovic, **D. Boley**, and **C.P. Sosa**

2011/142
A Spectrum Slicing Method for the Kohn-Sham Problem
G. Schofield, J.R. Chelikowsky, and **Y. Saad**

2011/143
Graph Partitioning With Matrix Coefficients for Symmetric Positive Definite Linear Systems
E. Vecharynski, **Y. Saad**, and M. Sosonkina

Earth Sciences

2011/94
Bent-Shaped Plumes and Horizontal Channel Flow Beneath the 660 km Discontinuity
N. Tosi and **D.A. Yuen**

2011/95
Collaborative Web-Based Visualization of Tsunami Waves Using Web-Viz
Y. Zhou, D.A. Sanchez, R.M. Weiss, E.O.D. Sevre, **D.A. Yuen**, M.R. Knox, E. McArthur, and X. Yao

2011/106
Numerical Analysis of Wave Hazards in a Harbor
H. Jing, H. Zhang, **D.A. Yuen**, and Y. Shi

2011/130
Asymmetric Instability Induced by Shear Modulus Contrast in Lithosphere: Implications for Efficient Nucleation of Weak Zone
B.-D. So, **D.A. Yuen**, K. Regenauer-Lieb, and S.-M. Lee

Electrical and Computer Engineering

2011/119
A GPU-Based Simulation for Stochastic Computing
P. Li, W. Xiao, and **D.J. Lilja**

Geological Sciences, Duluth

2011/135
Large Shift in Source of Fine Sediment in the Upper Mississippi River
P. Belmont, **K.B. Gran**, S.P. Schottler, P.R. Wilcock, S.S. Day, C. Jennings, J.W. Lauer, E. Viparelli, J.K. Willenbring, D.R. Engstrom, and G. Parker

Horticultural Science

2011/100
Examination of Expansin Genes as Related to Apple Fruit Crispness
D.I. Trujillo, H.S. Mann, and **C.B.S. Tong**

Names of Supercomputing Institute principal investigators appear in bold type. This list contains reports entered into the reports database during August–November 2011.

Institute for Therapeutics Discovery and Development

2011/127
Na,K-ATPase α4 as a Target for Male Contraception
K.H. Hong, N. Labello, G. Blanco, and **G.I. Georg**

Laboratory Medicine and Pathology

2011/137
Molecular Subtypes of Osteosarcoma Identified by Reducing Tumor Heterogeneity Through an Interspecies Comparative Approach
M.C. Scott, A.L. Sarver, K.J. Gavin, V. Thayanithy, D.M. Getzy, R.A. Newman, G.R. Cutter, K. Lindblad-Toh, W.C. Kisseberth, L.E. Hunter, **S. Subramanian**, Matthew Breen, and **J.F. Modiano**

2011/146
Ebf1 or Pax5 Haploinsufficiency Synergizes With STAT5 Activation to Initiate Acute Lymphoblastic Leukemia
L.M. Heltemes-Harris, M.J.L. Willette, L.B. Ramsey, Y.H. Qiu, E.S. Neeley, N. Zhang, D.A. Thomas, T. Koeuth, E.C. Baechler, S.M. Kornblau, and **M.A. Farrar**

Mathematics

2011/120
A Theoretical Analysis of Filament Length Fluctuations in Actin and Other Polymers
J. Hu and **H.G. Othmer**

Mechanical Engineering

2011/98
Determination of the Transition Regime Collision Kernel From Mean First Passage Times
R. Gopalakrishnan and **C.J. Hogan**

2011/99
Collision Limited Reaction Rates for Arbitrarily Shaped Particles Across the Entire Diffusive Knudsen Number Range
R. Gopalakrishnan, T. Thajudeen, and **C.J. Hogan**

2011/116
The Minnesota Pelvic Trainer: A Hybrid VR/Physical Pelvis for Providing Virtual Mentorship
V. Konchada, **Y. Shen**, D. Burke, O.B. Argun, A. Weinhaus, **A.G. Erdman**, and R.M. Sweet

2011/131
Determination of the Transition Regime Collision Kernel from Mean First Passage Times
R. Gopalakrishnan and **C.J. Hogan**

2011/132
Collision Limited Reaction Rates for Arbitrarily Shaped Particles Across the Entire Diffusive Knudsen Number Range
R. Gopalakrishnan, T. Thajudeen, and **C.J. Hogan**

2011/133
First-Passage Prediction of the Conductivity of Unpercolated Quasifractal Networks
T. Thaseem and **C.J. Hogan**

2011/134
Forced and Natural Convection in Aggregate-Laden Nanofluids
T. Thajudeen and **C.J. Hogan**

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