2005 Annual Research Report of the
Supercomputing Institute
for Digital Simulation
and Advanced Computation

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This report was prepared by Supercomputing Institute researchers and staff.
Editor: Tracey A. Bartlett

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Introduction
Introduction

Overview

Founded in 1984, the Supercomputing Institute is an interdisciplinary research program spanning all colleges of the University of Minnesota. The Supercomputing Institute provides supercomputing resources and user support to faculty and students and is a linchpin program in the University’s broad-based digital technology effort. The mission of the Supercomputing Institute is supercomputing research. This includes all aspects of high-performance computing and scientific modeling and simulation, as well as graphics, visualization, high-performance network communications, informatics, and data mining.

Supercomputing research is defined broadly to include a variety of research activities from many disciplines. This research involves the use of high-performance computing environments to address problems in science and engineering that could not otherwise be attempted. Such efforts often result in domain-specific algorithms and codes that exploit the available computing environments as well as visualization techniques to enhance insight, make displays more informative, and add multimedia value to communications and work environments. In many cases, these activities may involve research aimed at the design or evaluation of high-performance computing hardware, operating systems, networking, and general-purpose algorithms and software.

The Supercomputing Institute’s resources are available to researchers at the University of Minnesota and other post-secondary educational institutions in the State of Minnesota. In addition, the Supercomputing Institute organizes and hosts symposia, workshops, and seminars, and coordinates other educational and collaborative activities to promote supercomputing research, increase university–industry collaboration, and promote technology transfer.

Hardware resources include both core resources and laboratories. In addition to hardware and software, the Institute provides an extensive program of user support and training.

Digital Technology Center

The Supercomputing Institute plays a central role in the University of Minnesota’s digital technology initiative. This initiative includes technologies based on computers, electronics, telecommunications, digital design, computational biology, systems recognition and verification, graphics and visualization, databases and data mining, networks, storage, artificial intelligence, robotics and vision, signal processing and wireless technology, and electronic commerce. Key to this initiative was the renovation, completed in 2002, of Walter Library on the University’s East Bank Campus into a Digital Technology Center. This $63.4 million renovation brought state-of-the-art hardware and user support to the center of the campus. The Supercomputing Institute joined the Digital Technology Center in 2001 and moved to the home of the Digital Technology Center in Walter Library in March 2002, where it is located on the fifth floor and part of the fourth floor and basement.
Core Resources

In 1981, the University of Minnesota was the first American university to acquire a supercomputer (a Cray-1B). The Supercomputing Institute was created in 1984 to provide leading-edge, high-performance computing resources to the University of Minnesota's research community. The supercomputing resources offered to the University of Minnesota research community have included a Cray-2, an ETA 10, a Cray X-MP, an IBM 3090, a Cray M90, a Cray T3D, a Cray C90, a Cray T3E-900, an IBM SP based on Silvernodes, two SGI Altix 3800s, an ES7000 Orion 230, an IBM SP based on WinterHawk and NightHawk nodes, an IBM Power4 with p690+ (Regatta) and p655+ nodes, a LINUX Cluster, an SGI Altix 3000, a QuantumCube cluster, and an ES7000 Orion 430.

The Supercomputing Institute has continued the strong tradition of providing University of Minnesota researchers with leading-edge, high-performance computing technologies and diversified programs that complement these technologies. In addition, the Institute has developed a strong program of user support, including tutorials and applications support across the physical, biological, mathematical, and computer sciences, engineering, and other disciplines that use high-performance computing, informatics, and data mining.

The Institute’s IBM SP supercomputer consists of 96 shared-memory nodes with a total of 376 processors and 616 GB of memory. The characteristics of the nodes are:

- Seventy-seven 4-processor WinterHawk+ nodes with 375 MHz Power3 processors; 15 nodes have 8 GB of memory each; the remaining nodes each have 4 GB of memory.
- Fifteen 4-processor NightHawk nodes, each with 222 MHz Power3 processors and 16 GB of memory.

The nodes available for computation are:

- Four NightHawk nodes for interactive use.
- Seventy-four WinterHawk+ nodes available through the queuing system.
- Eleven NightHawk nodes available through the queuing system.

Four additional WinterHawk+ nodes act as file servers, serving a total of 4 TB of disk space. (Three of the 77 WinterHawk+ nodes server the scratch filesystems and are not available for computation.)

The IBM Power4 system is a constellation of several shared-memory nodes. The operating system is AIX, IBM’s brand of the UNIX operating system. The nodes are either pSeries 690+ nodes (called Regatta nodes) or p655+ nodes. All nodes are connected with IBM’s HPS switch for faster interprocess communication and file access. The detailed characteristics of the nodes are as follows:

- One 32-processor Regatta node with 128 GB of memory and 1.7 GHz Power4 processors.
- One 32-processor Regatta node with 64 GB of memory and 1.7 GHz Power4 processors.
- One 32-processor Regatta node with 64 GB of memory and 1.3 GHz Power4 processors.
- One 24-processor Regatta node with 24 GB of memory and 1.3 GHz Power4 processors.
- Thirteen 8-processor p655+ nodes with 16 GB of memory each and 1.5 GHz Power4 processors.
- Eleven 8-processor p655+ nodes with 16 GB of memory each and 1.7 GHz Power4 processors.

The interactive node is one of the 8-processor p655+ 1.7 GHz nodes, and there are four 4-processor P655+ nodes used as file servers. There is 6 TB of disk space shared across all 32 nodes.

The Institute’s LINUX Cluster consists of 80 2-processor Netfinity nodes from IBM. Characteristics of the nodes are:

- Ten 2-processor nodes with 1.5 GB of memory and 2.6 GHz Intel Pentium 4 processors (Gigabit Ethernet).
- Sixty 2-processor nodes with 3.25 GB of memory and 1.26 GHz Intel Pentium III processors (Fast Ethernet and Myrinet).
- Ten 2-processor nodes with 1 GB of memory and 733 MHz Intel Pentium III processors (Fast Ethernet and Myrinet).

Seventy-four nodes are available for computation through a queuing system, one node is for interactive use, and the remaining three nodes are file servers. The
nodes are connected using Fast Ethernet and Myrinet. A cluster file system provides 2.5 TB of disk that is shared by all nodes.

The SGI Altix consists of 11 shared-memory machines:

- One 256-processor compute server with 512 GB of memory and 1.6 GHz Intel Itanium 2 processors.
- One 48-processor compute server with 96 GB of memory and 1.3 GHz Intel Itanium 2 processors.
- One 4-processor interactive machine with 4 GB of memory and 900 MHz Intel Itanium 2 processors.
- Eight 16-processor Altix 350 compute nodes with 32 GB of memory and 1.5 GHz Intel Madison processors.

All machines run the Linux operation system and share 5 TB of disk space. The disk space is made available using CXFS filesystems running on a storage area network.

The QuantumCube from Parallel Quantum Solutions consists of four 2-processor nodes with 4 GB of memory and 1.8 GHz AMD Opteron processors. One of the nodes serves 37 GB of disk space over NFS to the other nodes. Each node has local scratch disk space (116 GB on one node and 200 GB on the other three nodes).

The major supercomputing resource program and long-term planning at the Institute are guided by the Institute’s Planning Committee.

**Planning Committee**

Donald G. Truhlar, Supercomputing Institute Director, Chemistry, Chemical Physics, Nanoparticle Science and Engineering, and Scientific Computation, chair

Graham V. Candler, Aerospace Engineering and Mechanics and Scientific Computation

James R. Chelikowsky, Chemical Engineering and Materials Science and Scientific Computation

Jiali Gao, Chemistry and Scientific Computation

Yiannis Kaznessis, Chemical Engineering and Materials Science

Vipin Kumar, Computer Science and Engineering and Scientific Computation

David J. Lilja, Electrical and Computer Engineering and Scientific Computation

Alon V. McCormick, Chemical Engineering and Materials Science

Douglas H. Ohlendorf, Biochemistry, Molecular Biology, and Biophysics

Yousef Saad, Computer Science and Engineering and Scientific Computation

George L. Wilcox, Neuroscience and Scientific Computation
Research Laboratories

Basic Sciences Computing Laboratory

Since 1996, the Supercomputing Institute has provided high-performance graphics and visualization workstations to the University of Minnesota research community through the Basic Sciences Computing Laboratory (BSCL). The BSCL is located in Nils Hasselmo Hall (formerly the Basic Sciences and Biomedical Engineering Building) on the East Bank of the Twin Cities campus. The unique mixture of computational servers, workstations, visualization tools, software, and technical consulting resources offered through the BSCL are made available to all University researchers. With its location in Hasselmo Hall, the research at the BSCL is heavily focused on such areas as biomedical engineering and structural biology (x-ray crystallography and nuclear magnetic resonance).

Linux, Unix, and Windows computing and visualization systems from Dell, IBM, SGI, and Sun are housed at the BSCL. These resources include multiple graphics workstations and a visualization/computation system purchased through a National Institutes of Health Shared Instrumentation Grant. The visualization/computation system consists of a 48-processor SGI Altix, a 16-processor SGI Onyx4, and a large (4 ft. by 6 ft.), high-resolution screen for stereo viewing.

This laboratory was overseen and guided during 2004–05 by the following people:

**Laboratory Manager**

Patton Fast

**Executive Committee**

Douglas H. Ohlendorf, Biochemistry, Molecular Biology, and Biophysics
Donald G. Truhlar, Supercomputing Institute Director, Chemistry, Chemical Physics, Nanoparticle Science and Engineering, and Scientific Computation

**Steering Committee**

Kevin H. Mayo, Biochemistry, Molecular Biology, and Biophysics, chair
Eric D. Ganz, Physics and Astronomy
Timothy J. Griffin, Biochemistry, Molecular Biology, and Biophysics
David H. Live, Biochemistry, Molecular Biology, and Biophysics
Hiroshi Matsuo, Biochemistry, Molecular Biology, and Biophysics
Kylie J. Walters, Biochemistry, Molecular Biology, and Biophysics
Carrie M. Wilmot, Biochemistry, Molecular Biology and Biophysics
Research Laboratories (continued)

Computational Genetics Laboratory

The Computational Genetics Laboratory (CGL) of the Supercomputing Institute is managed jointly with the Center for Microbial and Plant Genomics and the Biomedical Genomics Center. The laboratory is located in the Cargill Microbial and Plant Genomics Building on the St. Paul campus. In addition, the laboratory has a secondary home in Nils Hasselmo Hall (formerly the Basic Sciences and Biomedical Engineering Building). The laboratory is designed to meet the emerging computational needs of the computational biology community, especially in the areas of bioinformatics, proteomics, computational genomics, and computational genetics.

The CGL is equipped with many state-of-the-art computers, including one 16-CPU and two 4-CPU Sun servers, two Sun workstations, two SGI workstations, one IBM LINUX workstation, four Dell WINDOWS computers, and a Macintosh G5. In addition, users can access the supercomputers at the Institute.

The CGL has more than 70 popular software packages for bioinformatics (BLAST, GCG, EMBOSS, PHRED/PHRAP, DNASTAR, PATHWAY MODULE, MASSARRAY, and others), evolution (PHYLIP, PAUP, PAML, and others), microarray data analysis (EXPRESSIONIST, GENEtraFFIC, GENEspring, SPOTFIRE, and others), and proteomics (MASCOT, ProTS DATA, CLINproTOOLS). The laboratory also has numerous local biological databases available, including Genbank and many genome databases. Statistic packages such as SAS and R are available and can be used for biological data analysis. Furthermore, there are numerous bioinformatics database projects hosted at the CGL.

This laboratory was overseen and guided during 2004–05 by the following people:

**Laboratory Manager**
Zheng Jin Tu

**Executive Committee**
Ronald L. Phillips, Agronomy and Plant Genetics
Ashley T. Haase, Microbiology
Donald G. Truhlar, Supercomputing Institute
Director, Chemistry, Chemical Physics, Nanoparticle Science and Engineering, and Scientific Computation

**Steering Committee**
Vivek Kapur, Microbiology, chair
John V. Carls, Computer Science and Engineering
Scott C. Fahrenkrug, Animal Science
Yiannis Kaznessis, Chemical Engineering and Materials Science
Arkady Khodursky, Biochemistry, Molecular Biology, and Biophysics
David A. Largaespada, Genetics, Cell Biology, and Development
Kenneth D. Vernick, Microbiology
Lawrence P. Wackett, Biochemistry, Molecular Biology, and Biophysics
Research Laboratories (continued)

Digital Technology Computational Biology Laboratory

The basic objective of the Digital Technology Computational Biology Laboratory is to provide computing resources to faculty members and students involved in computational biology.

While computational biology faculties have full access to all Institute resources, this laboratory is dedicated to computational biology in a way that allows special and focused stimulation of interdisciplinary and interdepartmental digital technology collaboration among University of Minnesota faculties and their research groups. The goal of the laboratory is to encourage collaboration and high-performance computing research within the computational biology community at the University of Minnesota as well as with other academic and industrial organizations in the state of Minnesota. The laboratory also provides user support, training, and knowledge sharing services.

The laboratory is equipped with an 8-processor Compaq ES40 with a processor speed of 500 MHz and 8 GB of memory.

This laboratory was overseen and guided during 2004–05 by the following people:

**Laboratory Manager**

Yuk Sham

**Executive Committee**

Hans G. Othmer, Mathematics and Scientific Computation, chair

Donald G. Truhlar, Supercomputing Institute Director, Chemistry, Chemical Physics, Nanoparticle Science and Engineering, and Scientific Computation

**Steering Committee**

Hans G. Othmer, Mathematics and Scientific Computation, chair

Jiali Gao, Chemistry and Scientific Computation

Alexander Y. Grosberg, Physics and Astronomy and Scientific Computation
Research Laboratories (continued)

Laboratory for Large-Scale Data Analysis

The Laboratory for Large-Scale Data Analysis provides a computational environment that encourages experimental use of the Unisys Orion supercomputer for large problems that demand high capabilities of the equipment and software. The goal of the Supercomputing Institute–Unisys partnership is to foster the growth of research that takes advantage of the unique capabilities of the hardware and operating system of the Unisys supercomputing platform. The key hardware in this laboratory is a 32-processor Intel Itanium 1.5 GHz ES7000 Orion 430 supercomputer with 64 GB of memory. The machines is configured into two partitions running the 64-bit Windows DataCenter 2003 operating system on one partition and Red Hat Enterprise’s Linux AS operating system on the other. Microsoft SQL Server and Oracle are installed on the machines, which enables researchers to carry out database-oriented or data-mining-intensive types of research projects. An example of such projects is the recent collaboration with the Jane Goodall Foundation, which created a database for all of Dr. Goodall’s various forms of data associated with her extensive research on primates. The laboratory staff provides interactive user support and is working directly with the researchers. The staff members are able to understand the researchers’ problems better and are therefore able to help them more effectively. Their combined efforts have made these types of research possible and productive.

For 2004–05, the Laboratory for Large-Scale Data Analysis was overseen and guided by the following people:

**Laboratory Manager**

Yuk Sham

**Steering Committee**

Yiannis Kaznessis, Chemical Engineering and Materials Science, *chair*

Wei-Shou Hu, Chemical Engineering and Materials Science

Fumiaki Katagiri, Plant Biology

Vipin Kumar, Computer Science and Engineering and Scientific Computation

Michael J. Olesen, Digital Technology Centre, *ex officio* member

Friedrich Srenc, Bioprocess Technology Institute and Chemical Engineering and Materials Science
Research Laboratories (continued)

Medicinal Chemistry/Supercomputing Institute Visualization–Workstation Laboratory

The Medicinal Chemistry/Supercomputing Institute Visualization–Workstation Laboratory (VWL) is co-sponsored by the Department of Medicinal Chemistry and the Supercomputing Institute. The laboratory is located in Weaver-Densford Hall, home of the College of Pharmacy and the Center for Drug Design. Being within the University’s Academic Health Center campus, the laboratory is heavily used by biomedical researchers. While the scope of studies carried out within the laboratory is very broad, some of the main focuses of the laboratory include structure determination of pharmaceutical compounds and the design of potent drugs for treatment of cancer and HIV (human immunodeficiency virus). The laboratory contains a wide variety of Sun, SGI and LINUX workstations, WINDOWS PCs, and state-of-the-art commercial software applications. The laboratory is available to all University of Minnesota researchers and their collaborators.

This laboratory was overseen and guided during 2004–05 by the following people:

**Laboratory Manager**

Yuk Sham

**Executive Committee**

Yusuf J. Abul-Hajj, Medicinal Chemistry
Donald G. Truhlar, Supercomputing Institute Director, Chemistry, Chemical Physics, Nanoparticle Science and Engineering, and Scientific Computation

**Steering Committee**

Carston R. Wagner, Medicinal Chemistry, *chair*
Elizabeth A. Amin, Chemistry
David J. W. Grant, Pharmaceutics
Research Laboratories (continued)

Scientific Development and Visualization Laboratory

The Supercomputing Institute’s Scientific Development and Visualization Laboratory (SDVL), which is located in the Supercomputing Institute’s facilities on the fifth floor of Walter, provides Institute researchers with access to SGI, Sun, and Linux workstations, Macintosh workstations, PCs, hardware and software for the production of short videos, and associated software and technical support.

The SDVL recently added a SunFire V440 Visualization/Computation Server. This is a 4-processor shared-memory system with 16 GB of memory and a Sun XVR-1200 graphics accelerator for high-quality visualization. The system helps users to run compute-intensive and large-memory visualization applications interactively. The resource will especially benefit researchers working in areas of computational fluid dynamics and other engineering disciplines.

The SDVL also added a three-dimensional liquid crystal display called True View MkIII from Ampronix Inc. This 20” display allows glasses-free real-time viewing of three-dimensional images. The display is attached to a dual 3.2 GHz processor workstation with NVIDIA Quadro FX 3400 graphics and runs Windows XP. The technology assists researchers in visualizing volumetric data from various fields in medicine, engineering, seismology, geochemistry, atmospheric research, fluid dynamics, and molecular structures.

Researchers use workstations for code development, submission and monitoring of jobs on the Institute’s supercomputers, and workstation queues. SDVL machines support various computer engineering applications, scientific computing, and visualization software.

The SDVL also serves as a permanent facility to hold tutorials and hands-on workshops offered regularly by the Institute. The Institute’s summer undergraduate internship program activities are organized in the laboratory premises, turning it into a vibrant hub for participants.

For 2004–05, the Scientific Development and Visualization Laboratory was overseen and guided by the following people:

**Laboratory Manager**

Seema Jaisinghani

**Steering Committee**

Alon V. McCormick, Chemical Engineering and Materials Science, *chair*

Thomas W. Jones, Astronomy and Scientific Computation

Krishnan Mahesh, Aerospace Engineering and Mechanics

Gary W. Meyer, Computer Science and Engineering
Graduate Programs

Scientific Computation Graduate Program

The graduate degree program in scientific computation encompasses coursework and research on the fundamental principles necessary to use intensive computation to support research in the physical, biological, and social sciences and engineering. There is a special emphasis on research issues, state-of-the-art methods, and the application of these methods to outstanding problems in science, engineering, and other fields that use numerical analysis, symbolic and logic analysis, high-performance computing tools, parallel algorithms, supercomputing and heterogeneous networks, and visualization.

Scientific Computation is gradually emerging as an important field of its own in academia and industry. In the last decade, it has become clear that solving a given scientific problem often requires knowledge that straddles several disciplines. This interdisciplinary program provides a new combination of studies for solving today’s scientific computational problems. It is a degree program that builds on the strength of existing programs at the University of Minnesota in formulating real problems based on the physical system or the traditional discipline, and it augments field-specific work relating to the mathematical and numerical modeling with state-of-the-art techniques for scientific computation in an integrated manner.

The Scientific Computation Program offers Ph.D. and M.S. degrees. The current Director of Graduate Studies is Jiali Gao of the Department of Chemistry.

Computational Neuroscience Program

The Computational Neuroscience Program is an interdisciplinary pre-doctoral fellowship program that integrates training in neuroscience with physical-computational studies. Fellows pursue the Ph.D. degree with a major in graduate programs in Biomedical Engineering, Chemistry, Computer Science, Mathematics, Neuroscience, Physics, or Scientific Computation. Those fellows majoring in Neuroscience pursue a minor of supporting program in computation or physical science, and those majoring in any of the other disciplines minor in Neuroscience. Participating faculty include representatives from Biomedical Engineering, Chemistry, Computer Science and Engineering, Mathematics, Neuroscience, Scientific Computation, and Physics. The Program Director is Timothy J. Ebner, Neuroscience, and the Program Co-Director is Donald G. Truhlar, Supercomputing Institute Director, Chemistry, Chemical Physics, Nanoparticle Science and Engineering, and Scientific Computation. The program is funded by a National Institutes of Health Neuro-Physical-Computational Science Training Grant, awarded in September 2004.
Partnerships

Computational Life Sciences Program

The Computational Life Sciences Program is an initiative of the University of Minnesota Supercomputing Institute that is intended to foster the growth of research in computational biology. To do this, the Supercomputing Institute has entered into a special partnership with IBM, which provides the following mutual benefits:

- IBM receives feedback through personal communications of user support and systems staff and through the Supercomputing Institute's research report series.
- University of Minnesota/IBM partnership activities with researchers, including joint efforts with affiliates, are fostered.
- The Supercomputing Institute provides a specially focused program for meeting needs of the entire University of Minnesota high-performance computing research community and the emerging computational needs of the biology community.
- Both IBM and the University benefit from the development of the software expertise needed to take advantage of IBM's DB2 and DISCOVERYLINK software.

- IBM staff members have offices at the Supercomputing Institute, which increases the opportunities for partnership interactions.

IBM has awarded the Supercomputing Institute several Shared University Research (SUR) grants, which promote this initiative.

This initiative also includes an affiliates program that provides an opportunity for Minnesota industry and other Minnesota research institutions with interests in the area of computational biology to have access to these computational resources, software, and technical support. The current affiliates are Cargill, the Hormel Institute, and the Mayo Clinic College of Medicine.

Further information about this program is available at:

www.msi.umn.edu/general/Programs/uofmibm/index.html
Partnerships (continued)

Grid and BlueGene Computing

The following committee explored new opportunities in the areas of grid and BlueGene computing:

**Grid and BlueGene Computing Committee for 2004–05**

Thomas W. Jones, Astronomy and Scientific Computation, chair
Graham V. Candler, Aerospace Engineering and Mechanics and Scientific Computation
James R. Chelikowsky, Chemical Engineering and Materials Science and Scientific Computation
Jiali Gao, Chemistry and Scientific Computation
Sean C. Garrick, Mechanical Engineering
William B. Gleason, Laboratory Medicine and Pathology
J. Woods Halley, Physics
Yiannis Kaznessis, Chemical Engineering and Materials Science
Vipin Kumar, Computer Science and Engineering and Scientific Computation
David J. Lilja, Electrical and Computer Engineering
Krishnan Mahesh, Aerospace Engineering and Mechanics
Robert Numrich, Supercomputing Institute
Yousef Saad, Computer Sciences and Engineering and Scientific Computation
Jon Weissman, Computer Science and Engineering
Renata M. Wentzcovitch, Chemical Engineering and Materials Science
David A. Yuen, Geology and Geophysics and Scientific Computation

Laboratory for Computational Science and Engineering

The Supercomputing Institute partners with the Laboratory for Computational Science and Engineering (LCSE). Through this partnership, Supercomputing Institute researchers are able to participate in the LCSE program.

The LCSE encourages the participation of Supercomputing Institute researchers with applications that demonstrate or test new technologies under active development, applications requiring very large online data sets, particularly if they must be accessed at very high bandwidth, and applications requiring very high-resolution visualizations, particularly if image animations are needed. Distributed computing applications with tight coupling of computing resources on a fast network are also encouraged.

**Program Committee for the Cooperative Program in 2004–05**

Paul R. Woodward, Astronomy and Scientific Computation, chair
Baoquan Chen, Computer Science and Engineering
David H. Du, Computer Science and Engineering
Thomas W. Jones, Astronomy and Scientific Computation
Ernest F. Retzel, Center for Computational Genetics and Bioinformatics
David A. Yuen, Geology and Geophysics and Scientific Computation
Research Scholarship Program

The Supercomputing Institute offers a Research Scholarship Program that provides grants to enhance the supercomputing research programs of University of Minnesota faculty. These grants, which are peer reviewed and competitively awarded, are for the partial support of research associates who work closely with Supercomputing Institute principal investigators on their research projects. Over the past 13 years, the Supercomputing Institute has awarded 198 Research Scholarships. These Research Scholarships have provided an important opportunity for the creation and pursuit of research projects that might not have otherwise been attempted.

Research Scholars, 2003–2004

Manuel Alemany, Department of Chemical Engineering and Materials Science
Boyko Dodov, St. Anthony Falls Laboratory
Taras Gerya, University of Bochun, Bochun, Germany
Alexandar Lazarevic, Army High Performance Computing Research Center
Hai Lin, Max Planck Institut fuer Kohlenforschung, Muelheim, Germany
Jouni Pyynonen, VTT Technical Research Centre of Finland, Finland
Jun Mimaki Tsuchiya, University of Tokyo, Tokyo, Japan
Martin Wosnik, University at Buffalo–State University of New York, Buffalo, New York

Research Scholars, 2004–2005

Divesh Bhatt, Department of Chemical Engineering, University of California, Berkeley, California
Yuhua Duan, Department of Chemical Engineering and Materials Science
Daniel Goldstein, Department of Mechanical Engineering, University of Colorado, Boulder, Colorado
Ahren Jasper, Department of Chemistry
Benjamin Lynch, Department of Chemistry
Shuhua Ma, Department of Chemistry
Murilo Tiago, Department of Physics, University of California, Berkeley, California
Taku Tsuchiya, Department of Chemical Engineering and Materials Science
Koichiro Umemoto, Department of Chemical Engineering and Materials Science
Jean-Francois Vinuesa, Saint Anthony Falls Laboratory

Research Scholarship Peer Review Panel for 2004–05

David J. Lilja, Electrical and Computer Engineering and Scientific Computation, chair
Jiali Gao, Chemistry and Scientific Computation
Vipin Kumar, Computer Science and Engineering and Scientific Computation
Alexander Y. Grosberg, Physics and Astronomy and Scientific Computation
Douglas H. Ohlendorf, Biochemistry, Molecular Biology, and Biophysics
Renata M. Wentzovitch, Chemical Engineering and Materials Science
Supercomputing Institute Resources and Programs

Undergraduate Internship Program

The Supercomputing Institute provides an Undergraduate Internship Program for undergraduate students throughout the country. The focus of the program is the application of computational approaches and visualization methods to supercomputing research. Faculty from various disciplines have contributed projects and supervise the undergraduate students in their daily work. This program provides an opportunity for a challenging and enriching educational experience for undergraduate students interested in pursuing graduate or professional education. The program has sponsored 450 interns in its 15 years of existence.

Undergraduate Internship Committee for 2004–05

Victor H. Barocas, Biomedical Engineering and Scientific Computation, chair
Donald G. Truhlar, Supercomputing Institute Director, Chemistry, Chemical Physics, Nanoparticle Science and Engineering, and Scientific Computation
Dong Wang, Soil, Water, and Climate

Undergraduate Interns, Summer 2004

Nicha Chitphakditai, Johns Hopkins University, Baltimore, Maryland
Nicole Flohr, University of Minnesota, Morris, Minnesota
Loren Greenman, University of Minnesota
J. Mark Hubenthal, Whitman College, Walla Walla, Washington
Jacob Kilian, University of Minnesota
Daniel Lebewitz, University of Colorado, Boulder, Colorado
Eric Lindgren, Carleton College, Northfield, Minnesota
Arnaldo Marrero, Universidad Metropolitana, San Juan, Puerto Rico
Richard O’Konski, Kansas State University, Manhattan, Kansas
Brenda Saxton, University of Minnesota
Paul Shearer, University of Minnesota

2005 Annual Research Report of the Supercomputing Institute
Fellows of the Institute, 2004–2005

Fellows

Douglas N. Arnold
Daniel L. Boley
Graham V. Candler
James R. Chelikowsky
Bernardo Cockburn
Christopher J. Cramer
H. Ted Davis
Philippe de Forcrand (adjunct)
Jeffrey J. Derby
David H. Du
David M. Ferguson
Efi Foufoula-Georgiou
Jiali Gao
William B. Gleason
Alexander Y. Grosberg

J. Woods Halley
Dennis A. Hejhal
John R. Hiller
Thomas W. Jones
Daniel D. Joseph
Thomas H. Kuehn
Vipin Kumar
David J. Lilja
John S. Lowengrub
Mitchell B. Luskin
Kevin H. Mayo
Alon V. McCormick
Douglas H. Ohlendorf
Hans G. Othmer
Suhas V. Patankar

Yousef Saad
L. E. Scriven
J. Ilja Siepmann
Charles C. S. Song
Kumar K. Tamma
David D. Thomas
Donald G. Truhlar
Oriol T. Valls
Randall H. Victoria
Renata M. Wentzcovitch
George L. Wilcox
Paul R. Woodward
David A. Yuen

Associate Fellows

Leonard J. Banaszak
Victor H. Barocas
Charles E. Campbell
Robert W. Carr
Cynthia A. Cattell
Jane H. Davidson
Robert J. Dexter (deceased, Nov. 2004)
Roger L. Fosdick
Sean C. Garrick
Steven L. Girshick
Richard J. Goldstein
Anand Gopinath
Satish C. Gupta
Bojan Guzina
Jerome F. Hajjar

Franz Halberg
Shaul Hanany
Joachim V. Heberlein
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Steven R. Kass
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Katherine Klink
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Kenneth R. Leopold
David G. Levitt
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Yuan-Ping Pang
Fernando Porté-Argel
David Y. H. Pui
Shri Ramaswamy
P. Paul Ruden
Lanny D. Schmidt
Terrence W. Simon
Friedrich Srienc
Heinz G. Stefan
Henryk K. Stolarski
Vaughan R. Voller
Dong Wang
Darrin M. York
National Advisory Board

The National Advisory Board is made up of national experts in several areas of high-performance computing. The Board is shown in the picture below:

*Left to right:* Daniel Reed, University of North Carolina at Chapel Hill and President’s Information Technology Advisory Committee; Albert Wagner, Argonne National Laboratory, chair; David E. Keyes, Columbia University, Brookhaven National Laboratory, and Lawrence Livermore National Laboratory; Robert Jernigan, Iowa State University

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Administrative Staff

Director
Assistant to the Director
Research Programs Administrator
Executive Administrative Specialist
Executive Administrative Specialist
Executive Administrative Specialist
Web Developer
DTC Assistant Director for Human Resources
DTC/MSI Senior Accountant
DTC/MSI Accountant
DTC/MSI Senior Accounts Assistant
DTC/MSI Principal Administrative Specialist and Receptionist

Donald G. Truhlar
William Hellriegel
Jane Zirbes
Tracey Bartlett
Annice Larkin
Deborah Schutta
Abdul Azeem Khan
Ann Johns
Brian Carlton
Shaun Kershner
Pam Allen
Marni Anderson-Brown
## Technical Support Staff

**Chief of Technology**
Barry Schaudt

### User Support
- **User Support Manager; Scientific Computation Consultant**
  H. Birali Runesha
- **Web Interface Programmer**
  Wen Dong
- **Basic Sciences Laboratory Manager; Computational Biology and Biochemistry Consultant**
  Patton Fast
- **Scientific Development and Visualization Laboratory Manager; Scientific Visualization Consultant**
  Seema Jaisinghani
- **Computational Chemistry Consultant**
  Benjamin Lynch
- **Medicinal Chemistry Visualization-Workstation Laboratory Manager; Digital Technology Computational Biology Laboratory Manager; Laboratory for Large-Scale Data Analysis Manager; Computational Biology/Biochemistry Consultant**
  Yuk Sham
- **Computational Genetics Laboratory Manager; Computational Biology Consultant**
  Zheng Jin Tu
- **Data Mining Consultant**
  Haoyu Yu
- **Computational Genomics Consultant**
  Wayne Xu
- **Scientific Computation Consultant**
  Shuxia Zhang
Researchers and Administration

Technical Support Staff (continued)

Large Systems Group
Large Systems Group Manager and Coordinator of Systems; IBM SP/Power4 System Administrator  
Kirk Deen
LINUX Cluster/UNIX Systems Administrator  
Ben Kochie
UNIX Systems Administrator  
Gabe Turner

UNIX Group
UNIX Group Manager; UNIX Systems Administrator  
Bridget Kromhout
UNIX Systems Administrator  
Dack Anderson
UNIX Systems Administrator  
John Griffin-Wiesner
UNIX Systems Administrator  
Yectli Huerta
Tape Backup/UNIX Systems Administrator  
Thomas Kniffen
UNIX Systems Administrator  
John Vestrum
Accounts Creation  
Evan Fletcher

WINDOWS/Mac Group
WINDOWS/Macintosh Group Manager;  
WINDOWS/Mac Administrator  
Richard Flesvig

Networking Group
Networking Group Manager; Network Administrator  
Samantha Thomas
Network Assistant  
Jose Rivera
Researchers and Administration

Committee and Panel Members, 2004–2005
Yusuf J. Abul-Hajj, Medicinal Chemistry
Elizabeth A. Amin, Chemistry
Leonard J. Banaszak, Biochemistry, Molecular Biology, and Biophysics
Victor H. Barocas, Biomedical Engineering and Scientific Computation
Graham V. Candler, Aerospace Engineering and Mechanics and Scientific Computation
John V. Carlis, Computer Science and Engineering
James R. Chelikowsky, Chemical Engineering and Materials Science and Scientific Computation
Baoquan Chen, Computer Science and Engineering
Christopher J. Cramer, Chemistry and Scientific Computation
David H. Du, Computer Science and Engineering
Scott C. Fahrenkrug, Animal Science
Eric D. Ganz, Physics and Astronomy
Jiali Gao, Chemistry and Scientific Computation
Sean C. Garrick, Mechanical Engineering
William B. Gleason, Laboratory Medicine and Pathology
Jon Gottesman, Neuroscience
David J. W. Grant, Pharmaceutics
Timothy J. Griffin, Biochemistry, Molecular Biology, and Biophysics
Alexander Y. Grosberg, Physics and Astronomy and Scientific Computation
Satish C. Gupta, Soil, Water, and Climate
Ashley T. Haase, Microbiology
J. Woods Halley, Physics
Wei-Shou Hu, Chemical Engineering and Materials Science
Ashley James, Aerospace Engineering and Mechanics
Thomas W. Jones, Astronomy and Scientific Computation
Vivek Kapur, Microbiology
Fumiaki Katagiri, Plant Biology
Yiannis Kaznessis, Chemical Engineering and Materials Science
Arkady Khodursky, Biochemistry, Molecular Biology, and Biophysics
Vipin Kumar, Computer Science and Engineering and Scientific Computation
David A. Largaespada, Genetics, Cell Biology, and Development
David J. Lilja, Electrical and Computer Engineering and Scientific Computation
David H. Live, Biochemistry, Molecular Biology, and Biophysics
Krishnan Mahesh, Aerospace Engineering and Mechanics
Committee and Panel Members, 2004–2005 (continued)

Hiroshi Matsu, Biochemistry, Molecular Biology, and Biophysics
Kevin H. Mayo, Biochemistry, Molecular Biology, and Biophysics
Alon V. McCormick, Chemical Engineering and Materials Science
Gary W. Meyer, Computer Science and Engineering
John Nieber, Biosystems and Agricultural Engineering
Robert Numrich, Supercomputing Institute
Douglas H. Ohlendorf, Biochemistry, Molecular Biology, and Biophysics
Michael J. Olesen, Digital Technology Center
Hans G. Othmer, Mathematics and Scientific Computation
Ronald L. Phillips, Agronomy and Plant Genetics
Ernest F. Retzel, Center for Computational Genetics and Bioinformatics
Yousef Saad, Computer Science and Engineering and Scientific Computation
J. Ilia Siepmann, Chemistry and Scientific Computation
Terrence W. Simon, Mechanical Engineering
Friedrich Srien, Biotechnology Institute and Chemical Engineering and Materials Science
Donald G. Truhlar, Supercomputing Institute Director, Chemistry, Chemical Physics, Nanoparticle Science and Engineering, and Scientific Computation
Oriol T. Valls, Physics and Astronomy
Kenneth D. Vernick, Microbiology
Lawrence P. Wackett, Biochemistry, Molecular Biology, and Biophysics
Carston R. Wagner, Medicinal Chemistry
Kylie J. Walters, Biochemistry, Molecular Biology, and Biophysics
Dong Wang, Soil, Water, and Climate
Jon B. Weissman, Computer Science and Engineering
Renata M. Wentzovitch, Chemical Engineering and Materials Science
George L. Wilcox, Neuroscience and Scientific Computation
Carrie M. Wilmot, Biochemistry, Molecular Biology and Biophysics
Paul R. Woodward, Astronomy and Scientific Computation
David A. Yuen, Geology and Geophysics and Scientific Computation
## External Support

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<th>Source of Funding</th>
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<td>Roger E. A. Arndt</td>
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<td>Jon Gottesman</td>
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<td>Fumiaki Katagiri</td>
<td>Panasonic Mobile Communications</td>
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2005 Annual Research Report of the Supercomputing Institute
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Outreach Program

Internet2 Presentation: Supercomputing and the Brain
January 22, 2004

On January 22, 2004, the Supercomputing Institute joined with Technology and Information Services (TIES) of St. Paul, Minnesota to present a program about supercomputing over Internet2 connections. Two schools participated in this event: South Saint Paul High School in Minnesota and HollandWoods Middle School in Michigan.

Dr. H. Birali Runesha and Dr. Yuk Sham, both of the Supercomputing Institute’s User Support staff, gave a presentation to the students. Dr. Runesha presented an overview of supercomputers and how they are used. Dr. Sham talked about how supercomputing helps scientists study the human brain; he showed a computer-generated movie created from a magnetic resonance imaging scan performed while the subject was tapping his fingers. The students also asked questions about supercomputing research.

The Supercomputing Institute has developed a partnership with TIES to help extend its outreach program to students in grades K–12. The Institute has formal and informal means of interacting with these students. Other events have included tours of the Supercomputing Institute and Digital Technology Center by participants in the Management Information Camp for girls in grades 7–8 and presentations on developments in supercomputing to educators attending a class in emerging technologies.
Sponsored Symposia

Particle-Based Mesoscale Simulation Techniques Symposium
March 31–April 2, 2004

The goal of the Particle-Based Mesoscale Simulation Techniques Symposium, hosted by the Supercomputing Institute at the University of Minnesota, was to assemble several of the world’s leading experts who have made the most significant recent contributions to the development of mesoscale simulation techniques in order to increase communication and enable collaboration between the various groups. Particle-based simulation techniques have recently emerged as an attractive alternative to more traditional methods for studying such diverse behavior as rarefied gas dynamics, flow and transport in complex geometries and nanometer devices, and the dynamics and rheology of complex liquids such as amphiphilic mixtures, polymer solutions, and colloidal suspensions.

The focus of the symposium was on recent developments of mesoscale particle-based simulation techniques. Topics discussed included:

- General aspects of modeling, computer simulation, and visualization of soft matter systems.
- Coarse-graining and how to ensure thermodynamic consistency in coarse-grained models.
- Coarse-grained algorithms such as dissipative and smoothed particle dynamics, direct simulation Monte Carlo, and stochastic rotation dynamics.
- Hybrid models and practical approaches for multiscale modeling.
- Applications of these techniques to study rarefied gas dynamics, nanofluids, and complex fluids.

The conference organizer was Daniel M. Kroll, Department of Medicinal Chemistry.

Speakers

Victor H. Barocas, University of Minnesota
Iain D. Boyd, University of Michigan
Rafael Delgado-Buscalioni, University College London, United Kingdom
Andrea Ferrante, Unilever R&D, Port Sunlight Laboratories, United Kingdom
J. Woods Halley, University of Minnesota
Thomas Ihle, Universität Stuttgart, Germany
Yasuhiro Inoue, University of Tokyo, Japan
Ashley James, University of Minnesota
Raymond Kapral, University of Toronto, Canada
Satish Kumar, University of Minnesota
Ellen Longmire, University of Minnesota
Christopher P. Lowe, University of Amsterdam, Netherlands
Charles W. Manke, Wayne State University
Ignacio Pagonabarraga, Universitat de Barcelona, Spain
Marisol Ripoll, Forschungszentrum Jülich, Germany
Ilpo Vattulainen, Helsinki University of Technology, Finland
Julia M. Yeomans, Oxford University, United Kingdom
Sponsored Symposia (continued)

Bioinformatics: Building Bridges
April 15, 2004

On April 16, 2004, the Third Annual Bioinformatics: Building Bridges Symposium was held at the Digital Technology Center. This symposium includes participants from academics, industry, and non-profit institutions who are experts in: computer science; physics; math; statistics; molecular, cellular and developmental biology; biochemistry and biophysics; animal science; ecology, evolution, and behavior; and the health sciences.

Speakers presented research in a number of areas of importance to the bioinformatics field, including analysis of a large human red cell microarray dataset, modeling the yeast cell cycle, evolution of genes and genomes, computer-based visualization of cell signatures, substructure approaches to drug design, exploring and mapping global gene expression, and proteins as information processing devices.

There was also a poster session with 22 participants from the University of Minnesota, the Mayo Clinic, the University of St. Thomas, and St. Olaf College. Research topics included computational work involving custom genome searching, protein interactions, genome sequencing, molecular dynamics of an antimicrobial peptide, morpholino design, segmental and tandem gene duplications, three different methods for analyzing microarray data, deoxyribonucleic acid base calling, gene expression profiling, spatial patterns of transcriptional activity, genome analysis of bacterial motility variants, cancer suppression genes in plants, the vertebrate secretome, the mouse cochlea database, and predicting biodegradation.

The symposium was Webcast live to the world via UNITE; the Webcast archive was available for two weeks after the event.

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University of Minnesota:
Division of Health Informatics
Graduate Faculty in Bioinformatics
Digital Technology Center
Graduate School
Supercomputing Institute
College of Biological Sciences
Academic Health Center
Institute of Technology

Speakers

Jonathan Arnold, University of Georgia
Timothy Behrens, University of Minnesota
Nikolaos G. Boubakis, Wright State University
Patrick O. Brown, Stanford University
Alexander Grosberg, University of Minnesota
George Karypis, University of Minnesota
Georgiana May, University of Minnesota
**Sponsored Symposia (continued)**

Computational Chemical Dynamics From Gas-Phase to Condensed-Phase Systems

**October 7–9, 2004**

On October 7–9, 2004, the Supercomputing Institute hosted a symposium on Computational Chemical Dynamics From Gas-Phase to Condensed-Phase Systems at the University of Minnesota Twin Cities Campus. The focus of the symposium was advancements made by theoretical and computational chemistry to our understanding of the structure, energetics, and dynamics of molecules in gas and condensed phases. The symposium was also an opportunity to celebrate the 60th birthday year of Professor Donald G. Truhlar, Department of Chemistry and Director of the Supercomputing Institute. Many of Professor Truhlar’s colleagues and students from throughout his career presented talks at the symposium.

**Sponsors**

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Pacific Northwest National Laboratory  
SGI  
Unisys  
University of Minnesota  
Supercomputing Institute for Digital Simulation and Advanced Computation  
Digital Technology Center  
Department of Chemistry

**Organizing Committee**

Christopher Cramer, University of Minnesota  
Bruce Garrett, Pacific Northwest National Laboratory  
Davarajan Thirumalai, University of Maryland  
Thanh N. Truong, University of Utah

**Speakers**

Wesley D. Allen, University of Georgia  
Xavier Assfeld, Université Henri Poincaré  
Kim K. Baldrige, University of Zürich and San Diego Supercomputer Center  
Juan Bertrán, Universitat Autònoma de Barcelona  
Piergiorgio Casavecchia, Universita degli Studi di Perugia  
David C. Clary, University of Oxford  
J. N. L. Connor, University of Manchester  
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Angels González-Lafont, Universitat Autònoma de Barcelona  
Mark S. Gordon, Iowa State University and Ames Laboratory  
Odd Gropen, University of Tromsø  
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William L. Jorgenson, Yale University  
Hyung J. Kim, Carnegie Mellon University  
Ammnon Kohen, University of Iowa  
Aron Kuppermann, California Institute of Technology  
Yuzuru Kurosaki, Japan Atomic Energy Research Institute  
Jiabo Li, SciNet Technologies


Sponsored Symposia (continued)

Computational Chemical Dynamics From Gas-Phase to Condensed-Phase Systems (continued)

Gillian Lynch, University of Houston
Laura Masgrau, University of Leicester
C. Alden Mead, University of Minnesota
Vincent Moliner, Universitat Jaume I
Keiji Morokuma, Emory University
Kunizo Onda, Tokyo University of Science
Modesto Orozco, Parc Científic de Barcelona
Yuan-Ping Pang, Mayo Clinic College of Medicine
John C. Polyan, University of Toronto
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Mark A. Ratner, Northwestern University
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Gregory K. Schenter, Pacific Northwest National Laboratory
J. Ilja Siepmann, University of Minnesota and
Lawrence Livermore National Laboratory

Rex T. Skodje, Academia Sinica and University of Colorado
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William C. S. Stwalley, University of Connecticut
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Ongoing and Recently Completed Research Projects

January 1, 2004–March 15, 2005
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Leng Chee Chang, Principal Investigator
Evaluation of Natural Products as Protein Kinase C Inhibitors

Nature has produced many effective anticancer agents. Examples are microbial-derived drugs such as bleomycin and mitomycin C. The initial focus of this research is to identify noncytotoxic potent protein kinase inhibitors of eukaryotic with novel structures that may be useful in the treatment of human disease. The researchers are screening a variety of natural product extracts for inhibition of protein kinase using the *Streptomyces* 85E. There is evidence that a compound that inhibits aerial hyphae formation in *S. 85E* will also inhibit eukaryotic protein kinases.

The specific aims of this research are: to evaluate the extracts as protein kinase inhibitors; to isolate and characterize the novel structures of bioactive compounds; and to perform several two-dimensional nuclear magnetic resonance experiments for structure elucidation of biological active compounds. The researchers are using the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory for this work.

Paul Kiprof, Associate Fellow
High-Valent Transition Metal Arene Complexes and Carboxonium Ions

This research project studies high-valent transition metal arene complexes and the stability of rearrangement of carbocations. High-valent transition metal arene complexes are rare and generally unstable compared with their low-valent counterparts. A detailed study of the factors governing the stability of these complexes is necessary and is performed at high levels of theory accounting for the effect of substituents.

The second focus area concerns carbocations, which are stabilized by oxygen atoms. This leads to unusual reactions that have not been studied systematically. The researchers are exploring the effect of the heteroatoms at high levels of theory and are studying the reactions that these species undergo.
Viktor N. Nemykin, Principal Investigator
Theoretical Modeling of the Group and Excited-State Properties in Polynuclear and Mixed-Valence Porphyrins, Tetraazaporphyrins, and Phtalocyanines

This project involves using the software program GAUSSIAN 03 to calculate the geometries, electronic ground states, and spectroscopic properties of different poly(ferrocenyl)-containing and other polynuclear macrocycles. In addition, the researcher is predicting the electronic absorption and circular dichroism spectra of these metallo-complexes. Finally, he is using density functional theory methods to investigate multi-electron oxidation processes, formation of the mixed-valence states, and electron-migration properties of these compounds.

Paul D. Siders, Principal Investigator
Monte Carlo Simulation of the Driven Lattice Gas on a Penrose Tiling

The critical temperature of a two-dimensional lattice gas depends on the strength of the driving field and on its orientation relative to lattice vectors. On the square lattice, and with the field directed along a lattice vector, interfaces are parallel to the field and the critical temperature is increased by the field. Recent simulations of other field orientations and on non-square lattices show interfaces perpendicular to bond directions on the lattice, even when such directions are not along the field. Separating the effects of lattice orientation and field orientation is difficult. Simulation on Penrose lattices having no long-range translational order avoids the lattice-orientation effects. These researchers are performing Monte Carlo simulations of the driven lattice gas on rational approximates to Penrose tilings.
Ted Pedersen, Principal Investigator
Word Sense Disambiguation in High-Dimensional Feature Spaces

Most words in natural language have multiple possible meanings. This simple fact causes no end of difficulties for computer systems that seek to understand human language. The goal of this project is to develop computational methods that automatically determine which meaning of a word is intended in a particular context, and easily adapt to the variations in word meaning that accompany changes in the subject matter and intended audience of a text. Word meanings are central to language understanding, and success in this research will improve the ability of computer systems to perform translation, retrieve information from the Web, and summarize documents.

Masha Sosonkina, Principal Investigator
Optimization of a Parallel Algebraic Recursive Multilevel Solver

Parallel communication overhead may substantially affect the overall performance of a scientific distributed application. For a given parallel algorithm, one may attempt to analytically model and predict communication overhead. Fine-tuning and detailed experimental study is also needed, however, to account for such issues as communication library implementation and parallel architecture performance.

These researchers are using a sample distributed application, parallel Algebraic Recursive Multilevel Solver (pARMS), and are studying its most communication-intensive tasks. In particular, they are considering several message-passing implementations of the distributed sparse matrix dense vector multiplication used in pARMS for distributed preconditioning operations and iterative acceleration. They are also investigating how pARMS performance changes depending on the choice of mapping to the nodes in a cluster.

Research Group
Anagha Kulkarni, Graduate Student Researcher
Mahesh Joshi, Graduate Student Researcher
Amruta Purandare, Graduate Student Researcher

Research Group
Sam Storie, Graduate Student Researcher
Meng-Shiou Wu, Graduate Student Researcher
John R. Hiller, Fellow

Nonperturbative Analysis of Field Theories Quantized on the Light Cone

The interactions between fundamental particles can be described with quantum field theories, and the use of light-cone coordinates can be advantageous in determining the properties of the bound states that these particles can form. The resulting coupled system of integral equations for the bound-state wave functions must be solved numerically. These equations, however, contain infinities that must be removed in order to properly define the given theory. This project considers two methods for the removal of such infinities: Pauli-Villars regularization, which requires the introduction of unphysical massive particles, and supersymmetry. This researcher has applied these methods to various field theories, in particular Yukawa theory, quantum electrodynamics (QED), and super Yang-Mills (SYM) theory, and is continuing to explore their use with the ultimate goal of applying them to quantum chromodynamics (QCD), the theory of the strong interactions that determine the properties of mesons and baryons. Recent work has been in the dressed-fermion sectors of Yukawa theory and QED, where the problem has been solved for two and one-boson truncations, respectively, and in the calculation of thermodynamic functions and a stress-energy correlator in SYM theory.

Arun Goyal, Principal Investigator

Development of High-Value Protein Production in Hybrid Poplar

Safeners are used to protect crops against herbicide damage by enhancing herbicide metabolism in the plant. The identification and analysis of gene expression patterns by safener treatment may lead to a better understanding of molecular events involved in safener action. These researchers used a carrier deoxyribonucleic acid (cDNA) microarray composed of fluxogenim-treated subtractive cDNA clones to identify expression patterns of genes using different safeners and three abiotic stresses. They used three different safeners—flufenacet, oxabetrinil, and benoxacor, all of which detoxify chloroacetanilide herbicides—and water, chilling, and wind stresses to evaluate differences in the gene expression pattern. The comparison of expression patterns between different safener chemicals revealed that structurally similar molecules show almost identical gene expression. Many of the genes that were upregulated by safeners were not induced by the three abiotic stresses. The researchers are now using cDNA microarray chips to identify genes that may be used for identifying genes and unique chemical-inducible promoters.

Research Group and Collaborators
Vivek Kapur, Faculty Collaborator
Neil D. Nelson, North Central Research Station, USDA Forest Service, Rhinelander, Wisconsin
A. S. Rishi, Research Associate
The objective of this research is to determine if young and adult animals differ in their sensitivity to allergens, both in the induction phase of asthma as well as in elicitation of the asthma symptoms. Besides examining pulmonary function and inflammation in the lung, this project examines gene expression in the lungs of both young and adult mammals to determine if differences can be identified in the mechanism of asthma depending on age and gender. Molecular differences discovered in different asthma phenotypes may provide information regarding appropriate therapy for the disease depending on the age and gender of the individual. The researchers are using the resources of the Computational Genetics Laboratory to assist in the analysis of the gene expression data.
Hormel Institute
Zigang Dong .................................................................45

University of Minnesota
Rochester Campus

Department of Electrical and Computer Engineering
Hal H. Ottesen ..............................................................45
These researchers are using Supercomputing Institute laboratories to work with models of adenosine receptors and phosphodiesterases with xanthines. They choose the models of these compounds from the Protein Data Bank and create models of xanthine molecules. They then study the interaction of different types of adenosine receptors and phosphodiesterases with xanthines, and they perform correlation analysis between the docking scores (virtual data) and in vitro experiments (from literature data). Using the software application CACHe, the researchers are able to estimate the efficiency of the virtual data.

Research Group
Sergey Fedorov, Research Associate
Evgeny A. Rogozin, Research Associate

These researchers use the Scientific Development and Visualization Laboratory to run phase-retrieval functions of the digital image storage and transmission algorithm on varying sizes of images. They are analyzing the precision and computing speed of the retrieval process.

Research Group
Thomas Kjosmoen, Graduate Student Researcher
University of Minnesota Twin Cities Campus

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Stephen S. Hecht, Principal Investigator

Biochemistry, Biology, and Carcinogenicity of Tobacco-Specific N-Nitrosamines

These researchers are studying the cytochrome P450-mediated bioactivation of the tobacco carcinogen, 4-(methylamino)-1-((3-pyridyl)-1-butane (NNK). This nitrosamine causes lung tumors in all animal models in which it has been tested and is a putative human lung carcinogen in tobacco products. In vitro metabolism assays have revealed that closely related cytochrome P450 enzymes (P450s), both within and between species, exhibit markedly variable regioselectivity for the metabolism of NNK. Recent work by this group has attempted to elucidate the structural basis for these biochemical data. They have also constructed homology models of P450 2A enzymes, for which crystal structures are not currently available. The researchers are now broadening their studies with the homology models to other carcinogenic nitrosamines. The ultimate goal of this research is to use these models as tools to construct potent and specific inhibitors of nitrosamine bioactivation. Such inhibitors would ideally reduce its carcinogenicity.

Research Group
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Hansen Wong, Graduate Student Researcher

John H. Kersey, Principal Investigator

Gene Expression Profiles of Leukemia Cells

Translocations involving the Mixed Lineage Leukemia (MLL, ALL-1, HRX) gene are encountered in both myeloid and lymphoid leukemias. These MLL-leukemias are often found in infants and in adults previously treated with chemotherapy for other cancers. There are more than 30 different partner genes identified that participate in these translocations, and the mechanisms by which the translocations cause leukemia remain unknown.

These researchers have shown that expression of certain genes is increased in the bone marrow of mice carrying the MLL-AF9 translocation as a knock-in mutation. These mice develop myeloid leukemia. The group has also developed a knock-in mouse model carrying the MLL-AF4 translocation; these mice display an increase in the proliferative capacity of their lymphoid progenitors, but it is yet unknown what type of leukemia they develop, if any.

The group is now studying the gene expression profiles of the MLL-AF4 mice to identify the deregulated genes that are common to and different from those of the MLL-AF9 mice. This will help identify relevant downstream targets of the MLL-fusion gene and assist in developing novel therapies for these resistant leukemias.

Research Group
Ashish Kumar, Research Associate
Jennifer J. Westendorf, Principal Investigator

LEF1 Regulation of Gene Expression

LEF1 is a transcription factor that regulates gene expression during development and carcinogenesis. These researchers are studying LEF1’s role in bone formation. They have created stable osteoblast cell lines that express less LEF1 than normal. These cell lines form bone at a faster rate than normal cells. The researchers are using microarray analysis to identify the molecular events that accelerate bone formation in LEF1-suppressed cells. These results may increase understanding of bone formation and may lead to new therapeutic targets for osteoporosis.

UM TC–Center for Computational Genomics and Bioinformatics

Ernest F. Retzel, Principal Investigator

Genome Sequence Analysis

This project involves the analysis of plant genomes, both those that have been completed and those that are in progress. One of the group’s primary tools is the Ensembl pipeline, a genome-analysis environment that requires considerable computational power for processing. The researchers have adapted these tools for the Supercomputing Institute’s LINUX Cluster.

Research Group
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Research Group
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Jay Vadsedani, Staff
Nobuaki Kikyo, Principal Investigator

Reversible Disassembly of Nucleoli by Germ Cell Proteins

In *Xenopus* somatic cell nuclear cloning, the nucleoli of the donor nuclei rapidly and almost completely disappear in egg cytoplasm. These researchers previously showed that the germ cell-specific proteins FRG2a and FRG2b were responsible for this unusually drastic nucleolar disassembly. Since the nucleolar disassembly occurs independently of ongoing pre-rRNA transcription, whose inhibition is known to trigger nucleolar segregation, the disassembly mechanism remains largely unknown. This group is currently isolating FRG2a-interacting proteins that are mechanistically involved in the nucleolar disassembly. This study will contribute to the understanding of structural and functional organization of the nucleolus.

Research Group
Hiroshi Tamada, Research Associate

Catherine M. Verfaillie, Principal Investigator

Stem Cell Research

The objective of this project is to study stem cell behavior, including proliferation, differentiation, and possibly “de-differentiation” to further our understanding of the potential of stem cells to improve human and animal health. This involves basic research into genetics and genomics, developmental biology, cell biology, and the physiology of stem cells and their differentiated progeny. The researchers have initiated studies to identify the expression gene profile of umbilical cord blood stem and progenitor cells. They hypothesize that specific transcription factors, signaling molecules, cell membrane receptors, and secreted factors will play important roles in regulating proliferation versus differentiation decisions. The researchers are using the Computational Genetics Laboratory for their microarray experiments.

Research Group
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Stephanie Salese, Research Associate
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Fernando Ulloa, Graduate Student Researcher
Michael Weinreich, Graduate Student Researcher
James A. Anderson, Principal Investigator
Haplotype Polymorphism in Polyploid Wheats and Their Diploid Ancestors

These researchers are interested in breeding improved varieties of wheat. They are using the Basic Sciences Computing Laboratory and the Scientific Development and Visualization Laboratory to investigate single nucleotide polymorphism (SNP). They select 6,000 expressed sequence tag (EST) unigenes detecting single or at most two genes per wheat genome from the database of mapped ESTs and other EST databases, and are designing conserved polymerase chain reaction primers for the development of sequence tagged sites (STSs) spanning one or more introns. They use STS polymorphism among the three wheat diploid ancestors to develop A-, B-, and D-genome-specific primers, and then amplify STSs from the wheat A, B, and D genomes in a sample of wild emmer and bread wheat lines, sequence the amplicons, and assess haplotype polymorphism in wild and cultivated wheats. The final step will be to integrate these new SNPs into wheat genetic maps.

Rex N. Bernardo, Principal Investigator
In Silico Gene Mapping From Phenotypic Pedigree and Genomic Data in Plant Breeding

Plant breeding programs in major crop species have accumulated massive amounts of performance data for different traits of economic importance. To date, however, the data routinely generated in plant-breeding programs have been underutilized in gene mapping. The goal of this project is to develop methods for mapping genes from phenotypic data that are routinely generated in a plant-breeding program, from pedigree records that are kept in the course of a breeding program, and from genomic sequence data that are, or will be, generated from genomic screens of breeding germplasm. The researchers are using computer modeling to evaluate the usefulness of in silico mapping via mixed-model analysis in the context of a breeding program for soybean, a self-pollinated crop, and maize, a cross-pollinated crop. This project aims to develop computational methods for finding genes from existing data, thereby allowing a greater leverage of current investments in cultivar development and in plant genome research.
Gary J. Muehlbauer, Principal Investigator

Gene Expression Analysis in Barley

This group uses resources at the Computational Genetics Laboratory to study aspects of the barley genome. One area of interest is the gene expression profiles of barley plants challenged with the fungal pathogen *Fusarium graminearum*. *F. graminearum* infection of barley flowers causes Fusarium head blight, a major disease in barley. These researchers are comparing gene expression profiles in uninfected and *F. graminearum*-challenged plants.

The Muehlbauer group is also interested in gene expression profiles during vegetative branching. They are examining and comparing the gene expression profiles in a barley mutant that does not branch, unicultm2, and wild-type branching plants.

A final research area involves using gene expression data to physically map genes to barley chromosomes. Using a combination of microarray technology and specialized cytogenetic stocks, they have developed an approach to map thousands of genes to chromosomes.

Research Group
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Warren Kruger, Research Associate
Soong Joong Yun, Research Associate

Ronald L. Phillips, Principal Investigator
Howard W. Rines, Co-Principal Investigator

Evaluating the Repetitive Fraction of the Maize Genome

The maize genome is composed of 60–80% repetitive sequences and is theorized to have evolved from an ancient allotetraploid. These characteristics of a high repetitive portion and a diploidized polyploidy give maize a complex genome structure. This project is evaluating the repetitive fraction of maize to better understand how the genome is arranged. The main focus of the work comes from a microarray trial that measures the relative chromosomal abundance of the major repetitive sequences in maize. The trial was set up as an unbalanced reference design utilizing genomic deoxyribonucleic acid from oat-maize addition lines. The researchers are using resources at the Computational Genetics Laboratory and the Digital Technology Computational Biology Laboratory for this project.

Research Group
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Evan Ribnick, Undergraduate Student Researcher
Kevin P. Smith, Principal Investigator

Genetic Mapping of Valuable Traits in Barley

These researchers are investigating the genetics of numerous traits in barley. Much of this work involves construction of genetic linkage maps with molecular markers using experimental mapping populations. The group is also developing new genetic markers for mapping. Polymerase chain reaction primers for simple sequence repeat markers are designed from deoxyribonucleic acid sequence information from barley expressed sequence tag libraries. These new markers are designed to fill in gaps and improve overall coverage of the barley genetic map. Current quantitative trait locus mapping studies focus on disease resistance genes, genes that contribute to yield and agronomic performance, and genes that are involved in malting quality. Another area of interest for these researchers is the use of mixed models to detect marker-trait associations using breeding germplasm.

Research Group
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Lexintons Nduulu, Research Associate
Ahmad Sallam, Graduate Student Researcher
Song Joong Yun, Research Associate

David A. Somers, Principal Investigator

Investigating Transgene Locus Structure

This project uses a bioinformatics approach to investigate the role of topoisomerase II in creating doubled stranded breaks (DSBs) in deoxyribonucleic acid (DNA) during integration of delivered DNA into the genome of the plant Arabidopsis thaliana. The researchers have characterized topoisomerase II from A. thaliana to determine its DNA binding and cleavage properties, and have determined cleavage consensus sequences. They are now in the process of mining and mapping the Arabidopsis genome for these sites and determining the association of the sites with transferred DNA (T-DNA) integration sites reported in genome-wide databases. Determining this association will allow investigation of mechanism(s) of T-DNA integration in plant genomes and transgene locus formation.

Research Group
Irina Makarevitch, Graduate Student Researcher
Scott C. Fahrenkrug, Principal Investigator
Vertebrate Comparative and Functional Genomics for Medical and Agricultural Research

The Fahrenkrug group is developing a database to facilitate the integration of physical and genetic data from human, mouse, zebrafish, and livestock genomes. This database will allow for collection, storage, and analysis of genetic and sequence data from these species and will allow for the identification of regions of conserved synteny. This conserved synteny, as well as phenotypic and gene-expression data, has been used to functionally annotate vertebrate genes. The group uses microarrays to analyze gene expression in porcine and bovine tissues. Due to their potential use in treating diabetes, the group is examining gene expression in isolated and cultured porcine islets for indicators of islet function, immunogenicity, and quality. Identification and monitoring of such indicators has implications for the quality control of islets before xenotransplantation. Transcriptional profiling of bovine liver and mammary tissues is being used to identify genes responsible for differences in dairy cattle metabolism and milk performance. The database has proven indispensable for analyzing and integrating heterogeneous data types and will be crucial for connecting differences in gene expression to variation in animal phenotype and genotype. This knowledge can be used to identify and select for superior animals.

Research Group and Collaborators
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Lynda B. M. Ellis, Faculty Collaborator
Min Wang, Staff
Hehuang Xie, Research Associate

Ann M. Fallon, Principal Investigator
Computational Analysis of Mosquito Genes

This researcher is cloning and sequencing genes that may be used to interfere with disease transmission by mosquito vectors. She uses the Computational Genetics Laboratory to analyze genes and their homologs in other species, including Drosophila and the malaria mosquito, Anopheles gambiae.
Susan J. Weller, Principal Investigator  
Molecular and Morphological Studies of Insects and Other Arthropods in a Phylogenetic Context

This research focuses on reconstructing the phylogenetic relationships of Lepidoptera (moths and butterflies) and other arthropods with the goal of producing useful, predictive frameworks for both basic and applied research. The approach is to use both molecular and morphological data to reconstruct relationships using computer-assisted analyses. Morphological data is critical to this study for identification purposes and because it is a rich source of information.

This work has three parts. The first project studies relationships between tiger moths and their placement in the Noctuoidea. This is a biologically relevant species of interest to researchers. The second project focuses on the phylogeny of the “quadrifid noctuids” and their relationship to the remaining quadrifine families. The third project focus is to respond to emerging questions that require systematic expertise (identification of cryptic species, exotics, etc.) in a timely fashion. These phylogenetic investigations target questions of medical, plant disease, or conservation importance. This project also involves research questions at the interface of species and population-level structure.

Research Group  
Michelle Da Costa, Graduate Student Researcher

Christian A. Thill, Principal Investigator  
Potato Breeding and Genetics

This group’s research includes breeding, genetics, cytogenetics, and the utilization of wild germplasm in potato cultivar development and enhancement. The group’s emphasis includes both basic and applied research and includes developing efficient breeding techniques to incorporate traits from wild germplasm to cultivated potato and developing breeding materials and cultivars with high yield, yield stability, pest resistance, and quality. The researchers are using several of the Supercomputing Institute laboratories for this project.

Research Group  
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Angel Lara-Chavez, Graduate Student Researcher  
Dimitre Mollov, Graduate Student Researcher
Robert A. Blanchette, Principal Investigator
Identification and Characterization of Fungi Associated With *Salix arctica* and Non-Indigenous Wood in the Canadian High Arctic

An understanding and appreciation for biodiversity in arctic ecosystems is imperative for future efforts to monitor and protect these fragile natural resources. Although a major contributor to biodiversity, fungal phytopathogens and saprophages have been given very little attention in biological surveys in the arctic even though these microbes have a great influence on many processes such as plant growth and development, succession, phytogeography, biodegradation, and nutrient cycling.

Wood-destroying fungi that occur in the arctic are different from the types of decay fungi found in temperate and tropics biomes. A unique group of wood-degrading fungi occurs on native arctic willow species. These researchers are using arctic willow and introduced historic wood as model substrates for their investigations into rust diseases. They are determining the impact of rusts on willows, evolutionary relationships on different hosts and geographical locations, life cycles of the pathogen, and effects on the arctic ecosystem.

Research Group
Brett Arenz, Graduate Student Researcher
Jason A. Smith, Graduate Student Researcher

James M. Bradeen, Principal Investigator
Expanded Genomics Resources for Disease-Resistant Potato Species

Genetic control of potato diseases can reduce grower and environmental costs. Wild potato species are promising resistance-gene sources. Complementing their phenotype and molecular analyses, these researchers are constructing linkage and physical maps for the late-blight-resistant *Solanum bulbocastanum*. They are evaluating an *in vitro* analog of meiosis and amplified fragment length polymorphism markers previously mapped in cultivated potato for the construction of a medium-density linkage map. They are also developing genome-wide physical maps for putative disease-resistance genes. The linkage and physical maps will allow rapid isolation of important disease-resistance genes and make emerging potato and tomato genomics tools accessible for important *Solanum* species. This project provides preliminary data for expanded future efforts to develop comparative linkage maps and genome-wide physical maps for disease-resistance genes for species throughout the genus.

Research Group
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Dimitre Mollov, Staff
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Maria Sanchez, Graduate Student Researcher
Ryan Syverson, Research Associate
H. Corby Kistler, Principal Investigator

Functional Genomics of *Fusarium graminearum*

*F*usarium head blight or scab caused by *Fusarium graminearum* is a destructive disease on wheat and barley that has resulted in billions of dollars of economic loss to U.S. agriculture. Better understanding of *F. graminearum* pathogenesis and differentiation is critical because effective fungicides and highly resistant plant varieties are not available for controlling the disease. The goals of this project are to identify and characterize genes important for plant infection and colonization, secondary metabolism, and sexual development of *F. graminearum* using microarray analyses and targeted mutation of selected genes. One objective is to use the available sequence information to develop a whole genome microarray of *F. graminearum*. Another objective is to analyze gene expression profiles of *F. graminearum* in different infection and colonization stages, in mutants defective in plant infection or toxin production, and in different developmental stages. A third objective is to experimentally determine the biological functions of selected candidate genes identified in microarray experiments.

**Research Group**
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Rubella Goswami, Graduate Student Researcher
Karen Hilburn, Staff

Deborah A. Samac, Principal Investigator

Transcriptome Analysis of Microbial Interactions With the Model Legume *Medicago truncatula*

The annual medic, *Medicago truncatula* (barrel medic), is the focus of functional and comparative genomic studies in a number of laboratories worldwide. Functional genomic studies are currently focusing on plant-microbe interactions, particularly nodulation by *Sinorhizobium meliloti*, mycorrhizal interactions, and host-pathogen interactions. Over 182,460 expressed sequence tags (ESTs) have been sequenced, resulting in the identification of 17,720 contigs and 18,992 singleton sequences. The Samac group has successfully developed EST microarrays consisting of 6,144 clones and long oligonucleotide arrays of 10,000 genes. The arrays are used to investigate plant responses to pathogenic microorganisms. The researchers are using *GENEEXPRESSIONIST* software and other software packages available at the Computational Genetics Laboratory to identify expression patterns and develop hypotheses for further experimentation. The group has analyzed expression patterns in resistant and susceptible plants infected with foliar diseases and the response of plants to toxic amounts of aluminum.

**Research Group**
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Silvia Penuela, Research Associate
Judy Schnurr, Research Associate
Mesfin Tesfaye, Research Associate
Brian J. Steffenson, Principal Investigator

Investigations Into Cereal Crop Pathogens

These researchers are using resources at the Supercomputing Institute laboratories for their investigations in pathogens of cereal crops. In one project, they constructed molecular lineage maps of cereal crop populations and their pathogens. Another project concerns sequencing the Rpg1 stem rust resistance gene locus in wild barley. They are using software available at the laboratories to analyze deoxyribonucleic acid sequence trace files and to manipulate the sequences for further analysis. Finally, the group is investigating the spot blotch pathogen (*Cochliobolus sativus*).

Nevin D. Young, Principal Investigator

Sequencing the Gene Space of the Model Legume *Medicago truncatula*

These researchers are part of a consortium of laboratories in the United States and Europe that will fully sequence the gene-space of *Medicago truncatula* by 2007. A combination of cytogenetic and bacterial artificial chromosome (BAC) sequence data demonstrates that the *M. truncatula* genome is organized into distinct gene-rich euchromatin separate from repeat-rich pericentromeric heterochromatin. Thus, the *M. truncatula* gene-space can be sequenced in a highly efficient manner using a BAC-by-BAC strategy. This map-based approach to sequencing *M. truncatula* can be leveraged through structural genomic comparison with both *Arabidopsis* and crop legumes.
These researchers are conducting land-atmosphere flux studies as part of AmeriFlux and the North American Carbon Plan (NACP). These studies involve high-frequency atmospheric measurements of turbulence and other atmospheric variables, including temperature, humidity, and level of greenhouse gases. These measurements are made continuously on an annual basis and result in very large datasets, and the researchers are using the Basic Sciences Computing Laboratory and the Laboratory for Large-Scale Data Analysis for their analyses. The goals of this research are improved understanding of the processes and feedback controlling carbon exchange in agrosystems that are currently under-represented in the AmeriFlux network and improved ability to develop and test biophysical models that include fast (i.e., photosynthetic), slow (i.e., soil carbon turnover), and coupled (i.e., nitrogen, carbon, water) processes that will be of significant value to the AmeriFlux and NACP modeling community.

Research Group
Iyabo Lawal, Research Associate
Jianmin Zhang, Graduate Student Researcher

These researchers are sequencing and annotating the genome of the bacterium Arthrobacter aurescens. They are using the resources at Supercomputing Institute laboratories for annotation analysis and genome assembly.

Research Group
Kevin Drees, Research Associate
Nir Shapir, Research Associate
Dong Wang, Associate Fellow
Modeling Two-Dimensional Fumigant Gas Transport in Subsurface Soils and Volatilization Into the Atmosphere

The dynamics of pesticide volatilization are strongly controlled by the subsurface transport and ambient environmental conditions, which may be described with process-based transport models. Application of simulation models can provide accurate characterizations of fate and transport of volatile organic chemicals such as 1,3-dichloropropene and chloropirrin and their concentration dynamics that may be used as an index for pest control efficacy. Many parameters are often required for these types of mathematical models that translate to the initial and boundary conditions. Selection of a combination of sets of parameters optimized for better distribution uniformity and the least volatilization loss has a practical value for field application by pesticide specialists and farm managers.

These researchers have developed a simulation model and have recently incorporated into it a stochastic parameter generator using Monte Carlo simulations. The next step is to expedite the run times by adopting more computationally efficient numerical schemes.

Research Group
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Jindong Wu, Graduate Student Researcher

Daniel J. O’Sullivan, Principal Investigator
Comparative Genome Analysis of Two Strains of Bifidobacterium longum

These researchers have undertaken a genomics approach to better understand the characteristics of a Bifidobacterium longum strain that is important for probiotics. The complete genome sequence of B. longum DJO10A was recently elucidated in a collaborative effort involving the O’Sullivan laboratory, the Joint Genome Institute, and the Lactic Acid Bacteria Genome Consortium. The finished sequence is undergoing quality-assurance testing to ensure its accuracy. All the predicted open reading frames have been preliminarily annotated and will be rechecked following the verification of the finished sequence. The researchers plan to compare this genome to a published genome sequence for another B. longum strain, NCC2705. This genome comparison will involve both deoxyribonucleic acid and protein comparisons to shed light on how strains within a species diverge from each other. The group is using the Computational Genetics Laboratory for this project.

Research Group
Ju-Hoon Lee, Graduate Student Researcher
Haiping Li, Graduate Student Researcher
Antony M. Dean, Principal Investigator
Evolution of an Enzyme Through an Adaptive Landscape

These researchers worked on the redesign of modern enzymes and construction of ancient enzymes to determine how function has evolved through time. They used the Computational Genetics Laboratory and the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory to model site-directed mutants to determine the likelihood that they will be functional, to construct phylogenies, and to visualize which sites in protein structures evolve rapidly and which sites are conserved.

Friedrich Srienc, Associate Fellow
Elementary Mode Analysis for Biochemical Networks

Evolution has supplied biological organisms with a highly coupled network of hundreds of enzyme-catalyzed reactions. Scientific advances in recent decades, like polymerase chain reaction, have provided means of altering the topography of these reaction networks. Analysis of native and recombinant networks has been simplified by a number of theoretical tools. One such method is elementary mode analysis. An elementary mode is the simplest balanced combination of substrates, products, and reactions that enforces a no-accumulation restriction on internal metabolites.

These researchers are using elementary mode analysis to identify all genetically independent flux distributions for the production of biomass and other metabolites in the yeast Saccharomyces cerevisiae. They are also developing a database to bridge the gap between fluxomics and genomics of Escherichia coli to investigate how the gene regulation of genetic mutants is phenotypically expressed.
Marc G. von Keitz, Principal Investigator

Data Management for High-Throughput Screening Facility

The University of Minnesota's High-Throughput Screening (HTS) Facility is a campus-wide resource managed by the Biotechnology Institute. One of the primary services of the facility is to screen small molecule libraries against a wide array of protein- and cell-based assays. The HTS facility is running their data-management software program on the ORACLE database servers managed by the Supercomputing Institute. Researchers from several departments at the University are using the HTS Facility's small molecule screening capability.

Sarah E. Hobbie, Principal Investigator

Nitrogen Dynamics in Biodiversity, CO₂, and Nitrogen

Biodiversity, CO₂, and Nitrogen (BioCON) is a long-term field experiment being conducted at the University of Minnesota's Cedar Creek Natural History Area. The central objective of BioCON is to determine how the composition and diversity of plant species influence community and ecosystem responses to CO₂ and N, and how these interactions are mediated by microbial mutualists, herbivores, pathogens, decomposers, and higher trophic levels in the soil, including the consequences of these interactions for ecosystem C and N dynamics and for autotroph and heterotroph communities.

These researchers used resources in the Computational Genetics Laboratory to analyze a complex dataset from this experiment that encompasses 371 field plots with 5 years of data. These data are most accurately analyzed with a repeated measures analysis, which first requires a maximum likelihood comparison of approximately 11 covariance structures to find the best model.
Sharon A. Jansa, Principal Investigator

Molecular Phylogenetic Studies of Mammals

This research focuses on reconstructing the evolutionary history for two groups of mammals: didelphid marsupials and muroid rodents. Didelphid marsupials are a small radiation of approximately 20 genera endemic to South America. The project investigates the phylogenetic relationships among these genera using deoxyribonucleic acid sequences from five nuclear-encoded genes. The resulting data will not only illuminate the evolutionary history of this small radiation, but will provide the basis for investigating patterns of molecular evolution among mammals.

Muroid rodents are the most speciose group of mammals, but their evolutionary history remains poorly understood. This research focuses on using slowly evolving nuclear gene sequences to reconstruct phylogenetic relationship among rodent genera, concentrating on Madagascar and the Philippines. Each of these regions has an endemic rodent fauna, but it is not understood how rodents got to the islands or how they speciated once they arrived.

This researcher is using the Computational Genetics Laboratory for these phylogenetic studies.

Scott M. Lanyon, Principal Investigator

Phylogeny and Evolution of the Passerine Birds

The avian order Passeriformes is one of the largest terrestrial vertebrate radiations. Testing alternative explanations for this remarkable radiation depends critically on analysis of morphological, molecular, behavioral, and ecological variation in conjunction with a thorough understanding of evolutionary relationships within the group. This project focuses on interpreting phenotypic variation among species of passerines in the context of phylogenies derived from molecular data. The researchers are collecting deoxyribonucleic acid sequence data from approximately 750 species of birds. They use the Computational Genetics Laboratory to employ a variety of optimality criteria in exploring the evolutionary relationship among these species. They also may explore a variety of graphical projections of the resultant evolutionary trees, including hyperbolic techniques.

Research Group
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Muir D. Eaton, Graduate Student Researcher
Georgiana May, Principal Investigator

Evolutionary Genetic Analyses of Host/Microbe Interactions

These researchers use a number of evolutionary, genetic, and genomic computer analyses and tools to investigate the evolution of host/microbe interactions. Some analyses test statistical significance by permutation of an empirically derived dataset, and thus require computational resources beyond that of a desktop computer. The researchers are using resources at the Computational Genetics Laboratory for their projects, which include large datasets for resistance gene families in plants and deoxyribonucleic acid sequence-based population genetic data for fungal pathogens.

Joseph P. McFadden, Principal Investigator

Modeling Effects of Land Cover Heterogeneity on Regional Climate and Hydrology in the Arctic

This project uses a version of the regional atmospheric models RAMS that was developed for seasonal to interannual simulations (ClimRAMS) to study the effects of land cover heterogeneity on the climate and hydrology of arctic Alaska. The model represents the effects of vegetation, seasonal permafrost evolution, snow accumulation, snowmelt, and the resulting changes in surface moisture and energy exchange. This researcher is developing a coupled modeling system that will incorporate a snow-transport model (Snow-Tran-3D) and a new, community land surface model (CLM).

Simulations can now be performed for 12- to 13-month periods using three two-way-interactive, nested model grids. The model grids have horizontal resolutions of 60, 20, and 5 kilometers. The next phase of the research is to increase the horizontal resolution by a factor of four or five, increase the time period being simulated, and implement ensemble or factorial model experiments.

Research Group and Collaborator

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David Schladt, Graduate Student Researcher
Russel Spangler, Research Associate
Peter Voth, Graduate Student Researcher
Anne E. Pusey, Principal Investigator

Creation of a Visual Database of Chimpanzee Behavior

The study of the chimpanzees of Gombe National Park, Tanzania, has been continuous since 1960. Over this period, 35mm photographs have been taken of the chimpanzees, both in black and white and in color. Since 1993, over 600 hours of video have been shot during daily follows of the chimpanzees through the forest. The purpose of this project is to enter all this visual material into a database. The material will be stored at several different resolutions so that it can be used both for high-quality illustrations and as Web images. The database will be constructed so that the material can be indexed in progressively more detail. The long-term aim is to make the database searchable on the Web to qualified users for research and education. The project uses the Scientific Development and Visualization Laboratory.

Ruth G. Shaw, Principal Investigator

Spontaneous Mutation Affecting Quantitative Traits in Arabidopsis thaliana

These researchers are conducting maximum likelihood analysis of two large-scale experiments on Arabidopsis thaliana to assess the magnitude of the variance introduced by mutation in each generation. They are analyzing eight traits, including phenological, morphological, and fitness traits. The group is using the Basic Sciences Computing Laboratory and the Computational Genetics Laboratory for this project.
J. Stephen Gantt, Principal Investigator

Gene Function in Legumes

Legumes comprise the third largest family of flowering plants and are an important food source for humans and animals. They also form symbiotic associations with rhizobial bacteria that can lead to fixation of atmospheric nitrogen, providing the major source of biologically available nitrogen. Little is known, however, about the legume genes that are involved in bacterial and fungal symbioses, nitrogen fixation, pathogen defense, or environmental interactions. These researchers are using ribonucleic acid interference to silence specific genes in transgenic roots that are then examined for altered symbiotic relationships, nitrogen fixation, and development. They have already targeted about 100 genes and plan to target 1,500 more. Work to date indicates that the system works well and can be used to infer gene function.

The group is creating a database that will allow them to track, organize, and publicize their data. The goal is to easily input multiple forms of data that can be used by bench scientists and analyzed by researchers around the world.

Research Group
Sajeet Haridas, Graduate Student Researcher
Sergey Ivashuta, Research Associate
Chev Kellogg, Staff
Colby Starker, Research Associate

Susan I. Gibson, Principal Investigator
Identification of Sugar-Regulated Genes From the Model Plant Arabidopsis thaliana

The levels of soluble sugars, such as glucose and sucrose, are known or postulated to help regulate diverse aspects of plant development, metabolism, and physiology. Although the role of sugar levels in some plant processes has been well documented, whether sugar levels help regulate many other processes remains unknown. In addition, very little is known about the molecular mechanisms by which plants sense and respond to sugar levels. To help address these questions, these researchers are using Affymetrix GeneChips containing information from ~24,000 Arabidopsis genes to identify those plant genes that are regulated by sucrose, glucose, mannose, and/or sorbitol at the steady-state messenger ribonucleic acid level. The group is using the Computational Genetics Laboratory to analyze this data to determine which genes are expressed at significantly different levels in response to feeding different sugars.

Research Group and Collaborator
Tim Heisel, Graduate Student Researcher
Yadong Huang, Graduate Student Researcher
Kat Larson, Staff
Chun-Yao Li, Research Associate
Donna Pattison, Department of Biochemistry and Cell Biology, Rice University, Houston, Texas
Shu Wei, Research Associate
Jane Glazebrook, Principal Investigator

Genetic Analysis of Disease Resistance in *Arabidopsis thaliana*

These researchers are using the Computational Genetics Laboratory to design polymerase chain reaction-based polymorphic markers for genetic mapping of disease-resistance loci. In addition, they have begun to obtain microarray data from plants infected with a bacterial pathogen and are analyzing this data using software available through the laboratory.

### Research Group
- Raka Mitra, Research Associate
- Lin Wang, Graduate Student Researcher

Fumiaki Katagiri, Principal Investigator

Elucidation of Plant Disease Resistance Mechanisms

This group is studying how plants defend themselves from pathogens. One important form of defense is inducible defense, i.e., the defense mechanisms are turned on upon recognition of pathogen attack. The researchers are focusing on resistance gene-mediated disease resistance, which is usually strong and highly specific. Using *Arabidopsis* as a plant host and *Pseudomonas syringae* as its pathogen, the researchers investigate how plants recognize molecular signals of pathogen attack and how they coordinate defense responses upon recognition. The project uses molecular biology, biochemistry, genetics, reverse genetics, genomics, expression profiling, proteomics, structural biology, and computational biology to gain insights into these topics. Understanding plants’ natural defense mechanisms will lead to plant disease control methods that are safer to humans and to the environment.

### Research Group
- Charles Hernick, Staff
- Anand Janakiraman, Graduate Student Researcher
- Yiping Qi, Graduate Student Researcher
- Masano Sato, Research Associate
- Remco van Poecke, Research Associate
David J. McLaughlin, Principal Investigator

Assembling the Fungal Tree of Life

This group is engaged in a collaborative project, Assembling the Fungal Tree of Life (AFTOL), to contribute toward a comprehensive phylogenetic hypothesis of the fungi. AFTOL is developing broad datasets of molecular and subcellular characters, which will be accessible via the World Wide Web in continuously updated databases. The project will sample seven molecular regions in approximately 1,500 species in all major groups of fungi. The researchers will perform diverse phylogenetic analyses of these data, including analyses that incorporate evidence from subcellular characters. This project is based in five laboratories at four universities. The McLaughlin group is studying subcellular characters as well as phylogeny of selected species in two genera. They use resources at the Basic Sciences Computing Laboratory and the Computational Genetics Laboratory for phylogenetic analyses and for three-dimensional reconstruction of subcellular features.

Research Group
Peter Avis, Graduate Student Researcher
Gail Cello, Research Associate
Bryn Dentigner, Graduate Student Researcher
Mahajabeem Padamsee, Graduate Student Researcher

Nathan M. Springer, Principal Investigator

Polymorphism Detection in Maize Genomic DNA

This project uses oligonucleotide microarrays to detect polymorphisms in maize genome deoxyribonucleic acid (DNA). One part of the project involves bioinformatics work to choose the appropriate sequences to use for array design. The group also uses microarray data analysis software to analyze the results of the microarray hybridizations. The researchers are using the Computational Genetics Laboratory for this project.

Research Group
William Haun, Graduate Student Researcher
Soma Narasimhulu, Research Associate
Kathryn A. VandenBosch, Principal Investigator

Analysis of Gene Expression in *Medicago truncatula*

This project investigates the genome function of a model legume, *Medicago truncatula*, with an emphasis on interactions with microbes and utilization of nutrients. The researchers are using deoxyribonucleic acid (DNA) microarrays as one of the approaches to study reproductive and vegetative development in this plant and its response to pathogenic and symbiotic microbes and different nutrient conditions. For their microarray experiments, the researchers have constructed two types of carrier DNA chips, representing about 1,000 or 6,000 unique genes. They have also begun to use oligonucleotide (70mer) arrays constructed to represent 16,000 unique genes from *Medicago*. Existing microarray technologies require implementation of statistical methods in experimental designs as well as in interpretation of results. The researchers perform normalization and analysis of significance, which produces lists of genes with statistically reproducible behavior in the experiment. The last step in data analysis includes gene clustering, principal component analysis, and other approaches.

**Research Group**
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Dasharath Lohar, Research Associate
Vladimir Portyanko, Research Associate
Natasha Sharopova, Research Associate

George D. Weiblen, Principal Investigator

Developing a Phylogenetic Framework for the Moraceae Family Based on Plastid and Nuclear Sequence Data

The Moraceae family comprises 37 genera and approximately 1,100 primarily tropical and subtropical species. In addition to containing several important food and fiber sources, the Moraceae display an amazing array of inflorescence structures, pollination syndromes, breeding systems, floral characters, and growth forms. This diversity makes it an excellent group for addressing many intriguing evolutionary questions. A phylogenetic framework, however, is lacking, and evolutionary relationships within the family are problematic and have not been tested with a large number of genera. These researchers have sequenced the plastid gene *ndhF* and 26S nuclear ribosomal deoxyribonucleic acid for 80 taxa representing 10 outgroup and 28 ingroup genera. Combining the datasets provides greater resolution than either dataset alone. Parsimony analysis strongly supports the monophyly of the Moraceae family and two of the five tribes. The results provide the basis for revised Moraceae classification as well as for future detailed evolutionary studies within the family.

**Research Group**
Wendy Clement, Graduate Student Researcher
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Summer Silvieux, Graduate Student Researcher
Nyree Zerega, Research Associate
Ian M. Armitage, Principal Investigator
Structure/Function of Biomolecules Involved in Alzheimer’s Disease, Immune Suppression, and Cellular Metal Homeostasis

These researchers are using multi-nuclear/dimensional magnetic resonance (NMR) methods to forge new inroads into the following areas: the structure and metal exchange properties of proteins involved in the maintenance of metal homeostasis in vivo; structural-functional studies of select molecules involved in the immune response and Alzheimer’s disease; and the structure, dynamics, and mechanism of activation of specific zinc finger deoxyribonucleic acid transcription factors upon zinc binding.

The researchers use the Basic Sciences Computing Laboratory to process the multidimensional NMR datasets, to calculate the three-dimensional structures of the biomolecules, and to visualize those calculated structures.

Research Group and Collaborators
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David Lahti, Research Associate
Bruce L. Martin, Faculty Collaborator
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Abigail M. Tokheim, Staff
Klaus Zangger, Institute of Chemistry, University of Graz, Graz, Austria

Leonard J. Banaszak, Associate Fellow
Structure/Function Studies of Biological Macromolecules

These researchers are performing studies to uncover the nature of the interactions between lipid and proteins and to use structural studies to aid in the understanding of lipoprotein assembly. To do this, they are producing recombinant proteins including a liver microsomal protein called “microsomal transfer protein” and fragments of the protein labeled “apoB.” Both are involved in the production of low-density lipoprotein. The researchers then carry out crystallization trials and collect x-ray diffraction data. They use the facilities at the Basic Sciences Computing Laboratory to perform the computationally intensive analyses of the x-ray data and to construct the molecular model.

Another goal of the project is to gather x-ray diffraction data and eventually determine the molecular structure of translocatable proteins. These are nuclear coded proteins that eventually reside in a cellular organelle. Because these are also biological macromolecules with thousands of atoms, the analyses of the x-ray data and refinement of the molecular coordinates involve computationally intense methods.

Research Group and Collaborators
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Ed Hoefner, Staff
Wasantha Ranatunga, Staff
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James R. Thompson, Proteomic Center and Department of Physiology and Biophysics, Mayo Medical Foundation, Rochester, Minnesota
Todd Weaver, Department of Chemistry, University of Wisconsin–La Crosse, La Crosse, Wisconsin
David A. Bernlohr, Principal Investigator
Role of Adipocytes in Mammalian Lipid Metabolism

These researchers are primarily concerned with lipid metabolism, specifically the mechanism(s) that cells use to move water-insoluble lipids across membranes and within cells, a process called lipid trafficking. To do this, the researchers study both plasma membrane fatty acid transporters and cytoplasmic fatty acid binding proteins (FABPs).

One project examines the mechanism of fatty acid transport across the plasma membrane and the molecular regulation of transport gene expression by insulin and lipids. The major goals are determining the biochemical components of the transport system and the mechanism of fatty acid transfer across membranes and its regulation at the protein and gene levels.

A second project examines the structure/function relationships of FABPs and their genes, focusing on the adipocyte (FABP4) and keratinocyte (FABP5) members of this large, multigene family. The group is studying the physiological roles of FABPs in health and disease.

Research Group
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Sandra Lobo, Research Associate
Anne Smith, Staff
Lisa Ann Smith, Staff
Brian Thompson, Graduate Student Researcher
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Josh T. Wilson-Grady, Undergraduate Student Researcher
Bruce Wittyhuhn, Research Associate

Anja-Katrin Bielinsky, Principal Investigator
Monitoring Replication Origin Activation During S Phase in Yeast Checkpoint Mutants

In eukaryotic cells, at the onset of S phase, deoxyribonucleic acid (DNA) replication initiates at specific sites, called replication origins, across the entire genome. Once the cell has initiated DNA replication, it is committed to undergoing cell division. Thus, activation of replication origins is a highly regulated process that plays an important role in providing genomic stability to the cell.

Replication origins are activated continuously during S phase according to a temporal program. Activating different subsets of origins allows for cell cycle control of replication in the event of DNA damage or blocks to replication. In the presence of hydroxyurea, an inhibitor of ribonucleotide reductase, replication forks stall due to depletion of deoxyribonucleotide triphosphate pools. S phase checkpoint proteins Mec1 and Rad53, which function to delay entry into mitosis until the entire genome is duplicated, are activated. These checkpoint proteins inhibit activation of late-firing origins. In Mec1 and Rad53 mutants, late-firing origins are activated early. It is currently unknown if deregulation of origin activation occurs genome-wide.

These researchers are studying the ~430 potential origins in the yeast genome to determine their activation during S phase in wild-type cells and S phase checkpoint mutants.

Research Group
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Sharbani Chattopadhyay, Graduate Student Researcher
Miruthubashini Raveendranathan, Graduate Student Researcher
Victor A. Bloomfield, Principal Investigator
Ioulia Rouzina, Co-Principal Investigator

Molecular Modeling and Visualization of Protein/DNA Interactions

These researchers are using molecular modeling and visualization tools to illustrate and interpret the results of protein/deoxyribonucleic acid (DNA) interactions obtained from the studies of single DNA molecule stretching by optical tweezers in the presence of these proteins. They are using resources at the Basic Sciences Computing Laboratory and the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory for this work.

Research Group
Sidhartha Jena, Research Associate
Beskik Kankia, Research Associate

Bianca M. Conti-Fine, Principal Investigator

Modeling the Folding of Human T Cell Receptors

The ability to recognize unrelated sequences is not uncommon among T cell receptors (TCRs). The TCR’s ability to cross-react with different targets may be important for increasing the T cell repertoire. Also, it is possible that autoimmune phenomena are triggered by T cells activated by exogenous antigens and are able to cross-react with epitopes from self-antigens.

These researchers have propagated monoclonal CD4+ T cell lines that are able to recognize the same unrelated sequences. Each T cell clone expresses a different TCR, as judged by the sequence of its Vα and Vβ regions of several such cross-reactive TCRs. The goal of this project is to take advantage of the coordinates of the many solved TCR structures to model the sequences the researchers have obtained. This will allow identification of characteristics that would explain their cross-reactivity with unrelated sequences.

Research Group and Collaborator
Brenda M. Diethelm-Okita, Staff
Mark Reding, Faculty Collaborator
Yexun Wang, Graduate Student Researcher
Timothy J. Griffin, Principal Investigator

Proteomic Analysis Using Mass Spectrometry

In the evolving era of genome biology, mass spectrometry has emerged as a leading tool by which to measure the various properties of the protein products expressed by the genome. The complexity of biological systems, however, continually proves challenging to these existing methodologies, necessitating the development of novel tools to obtain the information required to gain a comprehensive understanding of these systems. The Griffin laboratory is interested in developing proteomics methods using mass spectrometry to investigate mechanisms of cellular regulation and protein function. Among the ongoing projects in this laboratory is the development of free-flow electrophoresis as a high-resolution separation tool, which they are applying to characterize diagnostic protein biomarkers in whole human saliva for the detection of oral cancer. Another project is the development of a new approach for studying the dynamics of chromatin-associated proteins and protein complexes, providing new insights into a fundamental mechanism of cellular regulation. A third research objective is the development of a novel approach to study oxidative-stress induced carbonyl modification of proteins, which is an important aspect of cellular damage implicated in cellular malfunction and disease.

Research Group

Suzanne Grindle, Research Associate
Mikel Roe, Graduate Student Researcher
Hongwei Xie, Research Associate

Eric A. Hendrickson, Principal Investigator

DNA Repair, Telomeres, and Genetic Stability

This research is aimed towards a somatic cell genetic analysis of the Ku86:KARP-1 locus in human cells. Ku86:KARP-1 plays an essential role in human somatic cells that is probably related to its ability to regulate telomere length and genomic stability. This project includes experiments that elucidate the genetic and molecular role(s) of Ku86 and KARP-1 in deoxyribonucleic acid (DNA) double-strand break (DSB) repair, telomere length regulation, and genomic stability in human cells. The importance of identifying and understanding the genes that control human DNA repair is underscored by the existence of a large number of cancer predisposition syndromes where it appears that the underlying molecular defects reside in DNA repair genes. The ultimate goal of this research is to use Ku86 and KARP-1 mutant cell lines as tools to understand the molecular mechanisms of DNA DSB repair in humans.
Christine B. Karim, Principal Investigator
Modeling of Phospholamban Including Spin Labels

Phospholamban (PLB) is a small membrane peptide that inhibits the Ca-ATPase in the heart muscle. These researchers have used chemical synthesis and electronic paramagnetic resonance to probe the structural dynamics of PLB in lipid bilayers. They then synthesized derivatives of monomeric PLB, each of which contained a single spin-labeled TOAC amino acid providing direct insight into the conformational dynamics of the peptide backbone. The group is now using modeling resources at the Basic Sciences Computing Laboratory to clarify the experimental data on PLB.

Romas Kazlauskas, Principal Investigator
Catalytic Plasticity in Enzymes

Enzymes evolve into new enzymes by acquiring new catalytic abilities. These researchers are mimicking this process in the laboratory to create new enzymes for organic synthesis. They are using the Basic Sciences Computing Laboratory and the Computational Genetics Laboratory to perform molecular modeling and visualizations.

Recent activity by this group includes modeling the enantioselectivity of subtilisin and attempting to identify the origin of the catalytic plasticity of subtilisin for chiral sulfur compounds.
Arkady Khodursky, Principal Investigator

Analysis of Transcription in Escherichia coli Genome

Growing cells cycle through overlapping stages of responses to internal and external cues. Some responses required concerted switching from the cycling routine. These researchers have shown that microarray analysis of messenger ribonucleic acid (mRNA) levels can be very useful in delineating such responses by determining transient changes in mRNA abundances, as well as transcripts’ composition and levels corresponding to new steady states. Even for well-established processes, however, the exact sequence of transcriptional events accompanying the process is not known. Temporal sequencing of such events is needed to understand the basis of regulation, pathway connectivity, intracellular flow of information, and the “logic” behind it. These researchers are using the Computational Genetics Laboratory to store and retrieve results of microarray experiments as well as to carry out multivariate analysis of transcriptional data.

Research Group
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Betsy Martinez-Vaz, Research Associate
Matt Rasmussen, Undergraduate Student Researcher
Dipen Sangurdekar, Graduate Student Researcher
Zhigang Zhang, Graduate Student Researcher

John D. Lipscomb, Principal Investigator

Structure and Mechanism of Oxygenase Enzymes

Oxygenase enzymes use molecular oxygen to oxidize a wide range of biological and man-made compounds with the incorporation of one or both atoms of oxygen from molecular oxygen in the products. These researchers are using the Basic Sciences Computing Laboratory to study the crystal structure of some of these enzymes and to plan mutagenesis studies.

The first project studies a series of dioxygenase enzymes. These enzymes interact with aromatic compounds, which causes enormous amounts of carbon to reenter the carbon cycle and also allows manmade aromatics, some of which are carcinogens, to be degraded. In the second project, the researchers are investigating another type of oxygenase that is typified by methane monooxygenase. This enzyme catalyzes the oxidation of methane to methanol with the incorporation of one atom of oxygen. Methane is generated in large quantities in the environment and is a potent greenhouse gas.

Research Group
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Matthew Nebiegall, Graduate Student Researcher
Codrina Popescu, Research Associate
Michael Valley, Graduate Student Researcher
Matt Wolfe, Graduate Student Researcher
Jingyan Zhang, Research Associate
Hui Zheng, Research Associate
David H. Live, Principal Investigator
Structure and Dynamics of Mucin Glycoproteins

These researchers are working to determine the structural and dynamic properties of mucin motifs. These motifs, characterized by regions of highly O-glycosylated protein, can be found in secreted mucin glycoproteins, in mucin domains of integral membrane cell-surface glycoproteins, and as components of the glycoprotein complexes in connective tissue. They can function both as purely structural elements and in molecular recognition by virtue of their ability to display a variety of carbohydrate epitopes on the same protein core. These researchers have reported on the structure of a mucin glycopeptide that has offered new insights into the intramolecular interactions between sugar and peptide components that aid in understanding the conformational features displayed by mucins. A noteworthy aspect of the nuclear magnetic resonance experiments was strong evidence for a well-defined organization even for a short mucin segment based on a glycosylated pentapeptide STTAV from the cell surface protein CD43. The importance of the comparatively rigid conformation in the physical properties related to mucin solutions, and in their ability to display locally high concentrations of carbohydrate epitopes in enhancing interactions with receptors, has prompted a more extensive investigation of the dynamic properties of such structures.

Research Group
Andrew Borger, Graduate Student Researcher

Hiroshi Matsuo, Principal Investigator
Structural Studies of Human DEK Protein

The mammalian protein DEK was first identified in patients with a subtype of acute myelogenous leukemia. This 43-kDa nuclear protein has since been implicated in several cellular pathways and associated with a number of human neoplastic, neurodegenerative, and autoimmune diseases. Biochemical data suggest the presence of a C-terminal functional domain, as this region can partially reverse abnormal genetic instabilities of cells from ataxia telangiectasia patients and appears to confer antigenicity to anti-DEK antibodies in juvenile rheumatoid arthritis. These researchers use nuclear magnetic resonance (NMR) spectroscopy to reveal the molecular mechanism by which this C-terminal domain functions in the development of diseases. They are using Supercomputing Institute resources to analyze the NMR data and to calculate three-dimensional structures of proteins.

Research Group
Kuan-ming Chen, Graduate Student Researcher
Matthew H. Devany, Graduate Student Researcher
Prasad Kotharu, Graduate Student Researcher
Kevin H. Mayo, Fellow

Protein-Protein Interactions

This project focuses on the investigation of three proteins from the CXC-chemokine family: platelet factor 4 (PF4), known for its anticoagulant heparin-binding activity; interleukin 8 (IL8), a known chemoattractant of neutrophils; and a chimeric mutant of PF4 called PF4-M2, which substitutes the first 11 N-terminal residues for the first 8 residues from homologous IL8. The group has shown that these three CXC-chemokines interact with each other, forming heterodimers. Their studies of the interactions allowed them to build a model of a heterodimer, and they checked its stability by using molecular dynamics simulations of IL8/PF4 and IL8/PF4-M2 heterodimers. They have confirmed that the heterodimer is a stable complex and that formation of heterodimers is energetically stable.

The researchers are now expanding their study to introduce several homologous representatives of the CXC-chemokine family. Specifically, they are testing NAP-2 and Groa-a for possible heterodimer formation with PF4.

Research Group
Monica M. Arroyo, Graduate Student Researcher

Gary L. Nelsestuen, Principal Investigator

Proteomics Biomarker Discovery

These researchers are using software available at the Computational Genetics Laboratory and the Scientific Development and Visualization Laboratory for mass spectrometry data analysis. Their goal is to find biomarkers related to transplantation rejection.

Research Group
Yan Zhang, Graduate Student Researcher
Douglas H. Ohlendorf, Fellow

Structural Analysis of Macromolecules

The goal of these studies is to understand the structural basis of how macromolecules function. The current focus is on two groups of proteins: dioxygenases that use metal ions to cleave aromatic rings and proteins from gram-positive pathogens. Examples of dioxygenases are protocatechuate 3,4-dioxygenase (PCD), homoprotocatechuate 2,3-dioxygenase (HPCD), and 1,2-catechol dioxygenase (CTD). Examples of proteins from gram-positive pathogens are pyrogenic toxin superantigens, exfoliative toxins, streptococcal C5a protease, and aggregation substance and the pheromone response protein prgX from Enterococcus faecalis.

The researchers are refining structures of substrate and inhibitor complexes of mutants of PCD, HPCD, and CTD, and are solving and refining the structures of several proteins from pathogens.

Research Group
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C. Kent Brown, Graduate Student Researcher
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Rebecca Hoef, Graduate Student Researcher
Medora Huseby, Undergraduate Student Researcher
Oana Lungu, Undergraduate Student Researcher
Noelle Moncada, Undergraduate Student Researcher
Gosu Ramachandraith, Research Associate
Ke Shi, Research Associate
Greg Vath, Graduate Student Researcher
David D. Thomas, Fellow
Molecular Dynamics of Muscle Proteins

The goal of this research is to understand the molecular motions that occur during muscle contraction, correlating these to muscle biochemical and mechanical states. The researchers use electron paramagnetic resonance (EPR) and time-resolved optical spectroscopy to report probe motions that yield useful data from dynamic and disordered systems. These probes, either spin labels or luminescent dyes, are chemically attached to specific sites on proteins of interest. The reports from the probes are either fitted by spectral simulations or compared to predictions derived from molecular dynamics simulations. The group has used supercomputing resources to determine which labeling sites will yield the most information with the least structural perturbation, to more accurately interpret spectroscopic data through simulation, and to improve current molecular models by integrating spectroscopic results.

A related project investigated the structure, function, and dynamics of phospholamban using in silico and EPR methods. The researchers used molecular dynamics simulations in combination with results from EPR spectroscopy to determine the dynamic behavior of phospholamban.

Research Group and Collaborators
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Michael J. Enz, Undergraduate Student Researcher
Yao Fan, Graduate Student Researcher
Nicole Flohr, Supercomputing Institute Undergraduate Intern
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Mohac Tekmen, Graduate Student Researcher
Nicolas Ward, Undergraduate Student Researcher
Deb Winters, Research Associate
Jamillah Zamoon, Graduate Student Researcher
Lawrence P. Wackett, Principal Investigator

Identification of Novel Metabolism and Biocatalysis

This project is focused on identifying novel metabolism and biocatalytic reactions through a combination of computational and experimental techniques. The Wackett laboratory has developed two approaches to identifying novel biocatalysis. The first involves experimentally identifying genes involved in novel metabolism, then analyzing the sequence of these genes computationally, using such resources as genome analysis, phylogenetic analysis, and protein scheduling. These techniques allow for determining how widespread the gene is and what ancestral links the gene may share, and may give insights into the potential catalytic mechanisms or mechanism of action of the gene product.

The second method is based upon mining information from the available genomes. Experimental identification of an organism with a novel metabolism can be used as a starting point for comparative genome analysis with the sequenced genomes of a similar organism. Using this methodology, gene targets for the novel metabolism can be identified and cloned, and the clones tested for functionality and whether they are responsible for the novel metabolism.

Research Group
Jeff Osborne, Research Associate
Jennifer Seffernick, Research Associate

Kylie J. Walters, Principal Investigator

Studying DNA Repair by Nuclear Magnetic Resonance Spectroscopy

These researchers are studying the mechanisms that have evolved in mammals for deoxyribonucleic acid (DNA) repair. Nucleotide excision repair (NER) and base excision repair (BER) remove damaged DNA, which could otherwise cause cell death, tissue degeneration, aging, and cancer. The hHR23 proteins are required for recognition of damaged DNA and stimulation of NER and perform a similar function in BER. The hHR23 proteins also play a role in proteasome-mediated degradation, suggesting that they serve as a link between regulated protein degradation and DNA repair. These researchers are solving the solution structure of the 40 kDa hHR23a protein. Furthermore, by using nuclear magnetic resonance spectroscopy, they are elucidating the proteasome-binding surface of hHR23a. From this knowledge, they will design mutant versions of hHR23a that no longer bind the proteasome and use these to ascertain the relevance of the hHR23-proteasome interaction in NER.

Research Group and Collaborator
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Jeannette Zinggeler, Graduate Student Researcher
Carrie M. Wilmot, Principal Investigator
X-ray Crystallographic Studies of Reaction Intermediates in Proteins Containing Organic or Metal Co-Factors

This research focuses on the dynamics of molecular catalysis, particularly involving novel co-factors and metal ions, as well as the role played by metalloproteins in disease states. The principal tool of the research is macromolecular x-ray crystallography. The project involves freeze-trapping catalytic intermediates in the crystal, both anaerobically and aerobically, leading to “snapshots” along the reaction pathways. These can be assembled into “movies of catalysis” at the molecular level. By understanding these reactions in such detail, better drugs can be designed, proteins can be rationally engineered for biotechnological purposes, and chemists can design simpler industrial catalysts to control analogous reactions. Specific topics of interest to this group include structural enzymology involving the co-factor tryptophylquinone of methylamine dehydrogenase, dioxygen activation by the copper-containing amine oxidase from yeast, and structural enzymology of the dinuclear copper-containing enzyme tyrosinase.

Research Group
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Ed Hoeffner, Staff
Bryan Johnson, Graduate Student Researcher
Binbin Liu, Research Associate
Arwen Pearson, Research Associate
Kevin Watts, Graduate Student Researcher

Vivian J. Bardwell, Principal Investigator
Molecular Control of Testis Development by Dmrt1

DM domain proteins are a class of minor groove binding transcription factors related to the Doublesex and MAB-3 sexual regulatory proteins. A vertebrate DM domain protein, Dmrt1, has been implicated in testis differentiation in all vertebrates examined, and may control male sex determination in some species.

These researchers have used deoxyribonucleic acid microarrays to identify messenger ribonucleic acids that are differentially expressed in wild-type versus Dmrt1-null mutant testes. Real-time quantitative reverse transcriptase-polymerase chain reaction has confirmed the array results. The researchers are now performing immunohistochemistry and in situ experiments to study the role of Msrl target genes in the testis.

Research Group
Umut Fahrioglu, Graduate Student Researcher
Judith G. Berman, Principal Investigator

Microarray Analysis of *Candida albicans*

This group studies the human pathogenic fungus *Candida albicans*. Together with a consortium of seven different research groups, they have built and now use whole-genome microarrays. The Berman laboratory was responsible for deciding which primers to design for amplification of fragments representing virtually all the open reading frames (ORFs) in the organism. They have used these primers to generate over 6,000 different amplified ORFs, which have been printed to glass slide arrays. The arrays have been used to generate transcription profiles as well as to analyze the deoxyribonucleic acid content of clinical and laboratory strains that have undergone genome changes. The group is now performing analysis of these datasets, along with performing analysis of all microarray experiments performed to date by the many laboratories working with *C. albicans*.

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Robert J. Brooker, Principal Investigator

Structure/Function of the Lactose Permease of *Escherichia coli*

These researchers are investigating how the structure of the lactose permease defines its function. This involves characterizing protein function after creating site-directed mutants, isolating cation and/or sugar specificity mutants, and isolating second-site suppressor mutants. In addition, the group is attempting to crystallize the lactose carrier, and will then analyze the crystal structure. They are using the computers and software at several Supercomputing Institute laboratories for this project.

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**Research Group and Collaborator**

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Anna Selmeci, Graduate Student Researcher

**Research Group**

Samantha Durand, Undergraduate Student Researcher
Peter Franco, Research Associate
Heather Hrodey, Graduate Student Researcher
Jerry Johnson, Research Associate
Liz Matzke, Research Associate
Jinyan Zhang, Research Associate
Lihsia Chen, Principal Investigator

Cell Adhesion Receptors in *Caenorhabditis elegans*

Cell adhesion is essential to the organization of multicellular organisms. Cells' adhesion must be stable and strong enough to maintain tissue integrity against forces exerted by the environment and the organism itself, but must also be dynamic enough to allow cells to migrate during gastrulation and tissue morphogenesis. The same adhesion molecules, however, typically mediate the entire spectrum of cell adhesion events. To carry out such diverse activities, these cell adhesion molecules have to integrate extracellular cues with various intracellular signaling pathways.

The Chen laboratory is studying the function and regulation of the L1 family of cytoskeletonally linked cell adhesion receptors in *Caenorhabditis elegans*, using genetic, molecular, and biochemical approaches. Mutations in human L1 result in a neurological disorder whose symptoms are characterized by the acronym CRASH (Corpus callosum hypoplasia, mental Retardation, Adducted thumbs, Spastic paraplegia, and Hydrocephalus).

Duncan J. Clarke, Principal Investigator

Analysis of Yeast Cell Cycle Control

The goal of this group’s research is to understand mechanisms that cause genome instability. In humans, genome instability contributes to the incidence of birth defects and spontaneous abortion, and is a key factor in the etiology of cancer. More specifically, the group works on cell cycle checkpoint controls, sister chromatid cohesion, chromosome dynamics, and ubiquitin-dependent proteolysis. Each of these related areas are critical for the maintenance of a stable genome. The researchers use yeast as a model system to rapidly discover new concepts that can then be translated to the human system. They use genetic approaches traditionally used to study yeast combined with more modern approaches that rely on access to databases such as genome sequence and proteome databases.
Kathleen F. Conklin, Principal Investigator

Characterization of a Novel, Nucleolar eIF4A Binding Protein

These researchers are working on a novel gene identified in humans called NOM1. There are homologs to this gene in yeast, worms, and flies, and the group is using the genome databases available through the Supercomputing Institute laboratories to research what is known about NOM1 homologs in other species.

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Stephen C. Ekker, Principal Investigator

Microarray Analysis of Zebrafish Models

These researchers are using the zebrafish as a model vertebrate system. They are using a technology developed at Thomas Jefferson University that creates microarrays with enhanced signal:noise hybridization signals. This promises to significantly enhance the value of the microarray comparisons. The current bottleneck with these arrays is the downstream annotation, and the researchers are establishing an annotation pipeline. This project uses resources at the Computational Genetics Laboratory.
David P. Fan, Principal Investigator

Effects of Persuasive Information on Public Knowledge, Attitudes, and Behaviors

This researcher takes text from traditional news sources and Internet sources and scores them. The results are used in mathematical models to predict time trends of public knowledge, attitudes, and behaviors. The researcher is using resources at the Computational Genetics Laboratory.

David A. Largaespada, Principal Investigator

Microarray Analysis of Myeloid Leukemia

These researchers are performing microarray analyses on acute myeloid leukemia (AML) samples from mice. AML samples with specific gene mutations are compared to controls without these mutations. In addition, the researchers are comparing parental AML samples with subclones derived by selection for resistance to chemotherapeutic drugs. The group is using the Computational Genetics Laboratory for this project.

Research Group
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Diane Hasz, Research Associate
Kelly Morgan, Research Associate
Kevin Roberg-Perez, Research Associate
Michaela Tsai, Graduate Student Researcher
Bin Yin, Research Associate
Michael B. O’Connor, Principal Investigator

Homology Modeling of *Drosophila* BMP-1-like Metalloproteases

*Drosophila* BMP-1-like metalloproteases are enzymes of the astacin family with important developmental roles. The structure for the crayfish astacin, the founder of the family, was solved and revealed a wide catalytic site. The O’Connor laboratory characterized two such enzymes from *Drosophila melanogaster*, identified several biologically relevant substrates, and defined the corresponding processing sites. Biochemical data indicated that selective substrates have co-substrate requirements. These researchers are using the Basic Sciences Computing Laboratory to perform homology modeling of the catalytic site of these enzymes. They are fitting various substrates in them in search for the molecular basis for their experimental observations.

Laura P. W. Ranum, Principal Investigator

Genetic Mapping of a Novel Familial ALS Gene

In a simple autosomal dominant family, the goal of lineage analysis and a genome screen is to identify regions of the genome that are shared among affected individuals in the family. To enhance the power of the amyotrophic lateral sclerosis (ALS)-A family for informative linkage analysis, these researchers have generated a panel of haploid cell lines for all available affected family members and other key individuals in the pedigree. This genome-wide panel of haploid cell lines generated over the past two and one-half years now allows the researchers to directly establish and compare haplotypes for entire chromosomes among affected individuals. The results of this method allow the researchers to directly identify regions that are shared by all affected family members and are thus candidates regions for the ALS-A gene, as well as regions that are clearly excluded. In addition to understanding ALS, an equally important goal of this project is to develop and validate the proposed haplotype genome screening strategy as a novel method to enhance the power of genetic mapping studies for other diseases.
Ann E. Rougvie, Principal Investigator

Understanding Cellular Timekeeping

Work in the Rougvie laboratory seeks to understand how cells execute specific events at precise times during development. To understand how a cellular timekeeper works, the researchers studied a developmentally simple organism, the nematode *Caenorhabditis elegans*. Specifically, they dissected the timing mechanism that restricts the differentiation of hypodermal cells to a time late in the life of the worm, the transition from the larval to adult form. The approach is to identify mutations that cause this event to occur at the wrong time during development, and then to study the genes defined by these mutations. These genes are referred to as “heterochronic” genes because their mutation alters the relative timing and sequence of many developmental events in the animal.

The long-term goal of this research is to determine how developmental timing mechanisms are integrated with the spatial and sexual cues required for proper development of a multi-cellular organism.

Research Group
Aric Daul, Research Associate
Masamitsu Fukuyama, Research Associate
Ming Li, Graduate Student Researcher
Jason Tenneson, Graduate Student Researcher

Jocelyn E. Shaw, Principal Investigator

Processes of Embryogenesis and Nervous System Development

The overall goal of the Shaw laboratory’s research is to gain insight into processes involved in embryogenesis and in nervous system development. The research focus is on *Caenorhabditis elegans*, a simple and developmentally well-described animal for which the wiring diagram of the nervous system is known. The group is studying the role that gap junctions play in animal embryogenesis using *C. elegans* as a model organism. Gap junctions allow direct intercellular communication through channels that permit small molecules, such as second messenger signals, ions, and metabolites, to pass between cells. Although gap junctions are present in all types of embryonic cells in animals, their function in embryonic development is not understood. The group is investigating several gap junction genes, which are essential for normal development, to understand the processes for which they are required.

Research Group
Leslie Bell, Research Associate
Angela Spartz, Graduate Student Researcher
Todd Starich, Research Associate
John Yochem, Research Associate
Margaret A. Titus, Principal Investigator

Cellular Function of Uncommon Myosins

This project studies the cellular function of several classes of unconventional myosins in both the simple eukaryote *Dictyostelium discoideum* and the nematode *Caenorhabditis elegans* through a combined approach that includes genetics, molecular genetic, cell biological, and biochemical techniques. In one area, the researcher is trying to determine if class I myosins play a role in the manipulation of the actin-rich cortex underlying the plasma membranes. In another area, the researcher has identified a *Dictyostelium* class VII myosin and analyzed its function by gene targeting. Interestingly, myosin VII mutants have a specific, and severe, defect in phagocytosis. Future experiments will be directed at identifying the step in phagocytosis that requires myosin VII through videomicroscopic analysis and immunolocalization. A final goal of these studies is to understand the role of unconventional myosins in development and in neurosensory function.

Brian G. Van Ness, Principal Investigator

Expression Profiling of Mouse Plasma Cell Tumors

This project involves the genetic characterization of plasma cell tumors in a transgenic mouse model of multiple myeloma by microarray analysis. The profiles will be used to examine the genes involved in tumor progression and localization, and for comparison of the mouse tumor model to human myeloma.

Research Group
Kristin Boylan, Research Associate
Paula Croonquist, Graduate Student Researcher
Byron R. Egeland, Principal Investigator
Minnesota Logitudinal Study of Parents and Children

These researchers are conducting a longitudinal study, which began in 1975, of high-risk children and their families. The assessments, which were detailed and comprehensive, began before the birth of the first child and continued at regular intervals until the children reached age 26. Originally, the researchers were interested in predicting good and poor parenting and parent-child relationship outcomes in the high-risk sample with a particular interest in understanding the causes and consequences of child maltreatment. The current aims include determining the antecedents and developmental pathways leading to competence and maladaptation in childhood, adolescence, and young adulthood. This includes studying school drop-outs, drug and alcohol abuse, adolescent depression, conduct disorder, and other forms of psychopathology as well as resilience.

The group is using the software application S-PLUS at the Scientific Development and Visualization Laboratory, which allows them to analyze the data by methods that are not available in ordinary statistical software packages.

Research Group
Michael F. Lorber, Research Associate

Thomas Stoffregen, Principal Investigator
Recurrence Quantification Analysis of Postural Sway Data

These researchers are conducting experimental research on body sway in standing humans. This includes collecting around 60,000 points per trial; the researchers do recurrence quantification analysis on these postural data points. Using ordinary desktop computers would be excessively time-consuming, so the researchers are using supercomputing resources to process the data, provide some of the results, and to visualize and graph some of the more complex results.

Research Group
Cedrick Bonnet, Graduate Student Researcher
Zvi Eckstein, Principal Investigator
Estimation of Discrete Stochastic Dynamic Programming Models of Economic Behavior

The goal of this project is to develop new methods to solve and estimate discrete stochastic dynamic programming (DS-DP) models, and to use these to study decision-making in areas such as human capital investment, occupational choice, and investment in health. In recent years, it has become common in economics to model individuals who are making choices as if they were solving a DS-DP problem to determine their optimal decisions. Empirical implementation of such models has been hampered because their solution and estimation requires that very high order numerical integrations be performed. These researchers are investigating the use of simulation methods to circumvent these integration problems. They are applying these methods to three problems: a model of life cycle decisions of young women, a model of the childcare use and return-to-work decisions of working women after childbirth, and a model of the impact of education on marriage market opportunities for women.

Research Group and Collaborator
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Suqin Ge, Graduate Student Researcher
Michael P. Keane, Department of Economics, Yale University, New Haven, Connecticut
Ahmed Khwaja, Graduate Student Researcher
Eric Olson, Graduate Student Researcher

Andrea Moro, Principal Investigator
Structural Estimation of Political Economy Models

This project investigates two political economy questions that have a crucial impact on electoral design. In the first project, the researcher is empirically estimating what affects voter turnout. This question has received considerable theoretical attention, but there have been difficulties in testing the implications of different theories using a reduced-form framework. This approach estimates structurally the parameters of different theoretical models of voter turnout in order to test which theory performs best against the data.

The second project applies structural methods to empirically discover the reasons why incumbents in the United States Congress are re-elected disproportionately often. This research can provide insight about the effects of changes in electoral design, such as the length of congressional terms or the introduction of term limits.
Julia K. Thomas, Principal Investigator
Models and Measurement: (S,s) Inventories and Investment Under Adjustment Costs

This research uses quantitative dynamic general equilibrium analysis to study the aggregate effects of nonconvexities at the individual level. Dynamic equilibrium models typically assume technologies and preferences that deliver smooth individual decisions. Abstractions from such nonconvexities as fixed costs, irreversibilities, and indivisibilities are expedient for the computation of general equilibrium, but microeconomic evidence indicates lumpy adjustments more consistent with models that include them. Unfortunately, the substantial heterogeneity that characterizes such models makes general equilibrium difficult, so economics researchers have often relied on partial equilibrium analysis to examine these more realistic environments. This work develops theoretical models and numerical methods to study nonconvex adjustments in general equilibrium.

One aspect of this research includes introducing additional heterogeneity and irreversibilities to examine whether nonconvexities may help to explain features of micro-level investment other than its lumpiness. One example would be the persistence of establishment-level investment rates. Another area examines a general equilibrium (S,s) model that reproduces the procyclicality of inventory investment and its positive correlation with final sales. This model delivers a nontrivial distribution of inventories across firms and includes capital, allowing quantitative business cycle analysis.

Shri Ramaswamy, Associate Fellow
Visualization and Characterization of Three-Dimensional Bulk Structure of Porous Materials

This research attempts to visualize and characterize the three-dimensional bulk structure of paper and board using non-intrusive techniques. Recent work has explored the use of x-ray micro-computed tomography to visualize the structure of porous materials. These images are binarized (black and white) and are then analyzed for pore structure characterization. Structural parameters of interest include pore size distribution, average pore diameter, porosity distribution and average porosity, tortuosity, available transfer surface area, and fiber-fiber bonded area. The researchers are also conducting numerical deconvolution of the three-dimensional images to sharpen the image as well as to obtain better characterizations of the structure.

In addition, this group has developed a model to simulate the physics of simultaneous permeation and absorption of liquid in porous media. The results indicate that, in additional to inherent absorption characteristics of cellulose fibers, the rate of permeation through the pore space has a strong influence on the overall absorption by porous media.

Research Group
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Matt Ryan, Graduate Student Researcher
Lei Wang, Graduate Student Researcher
Huigang Zuo, Graduate Student Researcher
Simo Sarkanen, Principal Investigator

Macromolecular Lignin Replication

Lignin, the second most abundant biopolymer after cellulose, contributes prominently to cell-wall architecture in all vascular plants and trees. The configuration of macromolecular lignin chains is determined by the sequences of inter-unit linkages between the monomer residues. This project investigates the possibility that lignin primary structure is controlled by a direct template polymerization mechanism governed by noncovalent interactions between corresponding aromatic residues in the putative daughter and parent chains.

Andrew M. Simons, Principal Investigator

Systematics and Phylogeography of North American Freshwater Fishes

The phylogenetics and phylogeography of North American freshwater fishes continue to pose interesting and difficult questions for systematists. This research group gathers mitochondrial and nuclear sequence datasets in order to infer evolutionary relationships and demographic patterns of these fishes. These datasets are very large and computationally challenging, so the researchers are using resources from the Computational Genetics Laboratory. They are using parsimony, maximum likelihood, and Bayesian methods for their analyses.
Peter B. Reich, Principal Investigator
Modeling of Forest Community Dynamics

Recent data from this group’s research suggests that the assumption of additive positive feedback in some models of forest dynamics is incorrect. Preliminary models suggest that non-additive feedback may result in vastly different ecological outcomes from additive feedback, which has not been previously recognized. This project uses resources at the Computational Genetics Laboratory and the Scientific Development and Visualization Laboratory to simulate ecological data incorporating null models, additive feedback, and non-additive feedback on realistic temporal and spatial cases in a spatially explicit environment.

John St. Peter, Principal Investigator
Obesity and Insulin Resistance After Exposure to Nuclear Receptor Agonists and Antagonists

Insulin resistance is a major factor in the development of type 2 diabetes and is commonly noted in those with obesity. Recent pharmacologic therapy has been developed that directly improves the insulin resistant state via stimulation of the peroxisome proliferator-activated receptor (PPAR) system. Currently, there are two PPAR agonists, pioglitazone and rosiglitazone, that are marketed for human use based upon their blood glucose lowering effect. These drugs have additional significant effects on lipid profile, fibrinolysis, and markers of the inflammatory state. These researchers have noted significant differences between these agents with respect to their lipid-lowering effects, but mechanisms related to these clinical observations as well as changes in other surrogate markers are lacking.

This project, which uses the Computational Genetics Laboratory, uses gene expression profiling to investigate potential mechanisms underlying this group’s clinical observations. This may provide insight into mechanisms related to emerging therapies for insulin resistance. Additionally, findings will provide comparative data for comparison with future pharmacologic agents and may guide design of future studies.

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Research Group
Ian Dickie, Research Associate

Research Group and Collaborator
Suzanne Grindle, Research Associate
Sidney Jones, Faculty Collaborator
Robert J. Straka, Principal Investigator
Discordance of Slow Acetylator Phenotype and Genotype for N-acetyltransferases in a Hmong Population

Polymorphisms of N-acetyltransferase (NAT-2) acetylation have relevance to isoniazid serum levels and are associated with a differential susceptibility to select cancers. The Hmong have a high prevalence of tuberculosis and certain cancers. This study seeks to confirm or refute an unexpected phenotypic predominance of slow acetylators (SAs) in the Hmong and to examine the relationship of NAT-2 genotype to phenotype.

The researchers used the Computational Genetics Laboratory and the Scientific Visualization and Development Laboratory to analyze samples from 60 Hmong subjects. They have confirmed the predominance of the SA phenotype, but there appears to be a lack of correlation between genotype and phenotype for NAT-2. The predominance of SA by phenotype would not be predicted by knowledge of the genotype alone, which underscores the importance of having both genotype and functional assays for metabolic pathways to evaluate associations with drug metabolism and disease prevalence.

Research Group
R. Todd Burkhart, Research Associate

Tim Tracy, Principal Investigator
Substrate/Inhibitor Binding Modes of Cytochromes P450

The hepatic human cytochromes P450 are involved in the oxidative metabolism of xenobiotics such as drugs. For these enzymes, substrate specificity is broad and often difficult to predict. Yet understanding specificity is important in designing better drugs because P450s affect the rate of drug clearance. Therefore, P450 metabolism helps determine drug dosage. Also possible is the competition or non-mutually exclusive binding of more than one drug for the same P450 isoform, resulting in lower or higher than usual clearance, respectively.

These researchers are employing computational models that will quickly screen drugs for their ability to activate the metabolism of another drug. They have previously developed comparative molecular field analysis (CoMFA) models to describe drug affinity and activator drug pharmacophores, but it is not clear which distinct sites in the enzyme these models describe. In order to understand the differences in P450 substrate binding modes, the researchers are: further developing CoMFA models by adding heme iron-substrate distance restraints to improve substrate alignments; obtaining high-resolution structural data for P450s though multi-dimensional protein nuclear magnetic resonance data processing; and performing molecular dynamics simulations of structurally characterized of homology modeled P450s with multiple combinations of substrates and activators.

Research Group and Collaborator
Vikas Kumar, Graduate Student Researcher
Charles Locuson, Research Associate
Hiroshi Matsuo, Faculty Collaborator
Lian Wei, Graduate Student Researcher
S. Mbua Ngale Efang, Principal Investigator
Development of Pharmacological Agents for Studying Central Cholinergic Function

Acetylcholine released from central, sympathetic, and peripheral neurons is involved in a wide range of biological functions. Cholinergic dysfunction has been implicated in a number of pathologic states, including Alzheimer’s disease, olivopontocerebellar atrophy, and Parkinson’s disease, among others. Conversely, modulation of cholinergic function has been found to have beneficial effects in a number of pathologies. Such modulation may be effected through one or more of the following molecular targets: sodium-dependent high affinity choline transporter, choline acetyltransferase, muscarinic acetylcholine receptors, nicotinic acetylcholine receptors (nAChR), the vesicular acetylcholine transporter (VaChT), and acetylcholinesterase. Using the prototypical nAChR and VaChT ligand nicotine and besamicol, respectively, this project’s primary focus is to develop pharmacological agents and radioligands that are directed at the nAChR and VaChT. In addition, the researcher is interested in the development of new medications for the treatment of cocaine and other psychostimulant dependence. These investigations involve the design, synthesis, radiolabeling, and biological evaluation of new molecular entities, thus providing exposure to a broad spectrum of drug development activities.

David M. Ferguson, Principal Investigator
Opiate Bivalent Ligands: Structure/Function Studies

This project investigates the function of opioid receptor dimerization in ligand binding, selectivity, and signal transduction using structure-based modeling techniques. A key step in understanding the function of dimerization in ligand binding and function involves the design and development of three-dimensional models of the homo- and heterodimeric receptor structures. These researchers constructed initial models of μ-δ receptor heterodimers using concepts borrowed from chimeric studies of adrenergic and muscarinic receptors. They evaluate the complexes using sequence analysis techniques, including evolutionary trace and correlated mutation methods, and can further refine them using a combination of molecular dynamics simulations and ligand docking studies.
Patrick E. Hanna, Principal Investigator

Studies of Arylamine N-acetyltransferases

Arylamine N-acetyltransferases (NATs) catalyze the acetyl-coenzyme-A-dependent detoxification of a variety of xenobiotics. The NATs also catalyze the bioactivation of carcinogenic aryldihydroxylamines and arylhydroxamic acids. The overall objective of this project is to develop a comprehensive understanding of the molecular basis of the catalytic mechanism, the active site topologies, and the substrate specificities of mammalian NAT isozymes. The researchers have conducted three-dimensional homology modeling studies of hamster NATs based on the crystal structure of Salmonella typhimurium NAT. These investigations are being extended to include evaluation of the interactions of substrates and inactivators with NAT active sites. The results derived from these studies are expected to contribute to the design of isozyme-selective inhibitors of NATs. The researchers are using the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory for this project.

Research Group
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Li Liu, Graduate Student Researcher
Haiqing Wang, Graduate Student Researcher

Rodney L. Johnson, Principal Investigator

Design of Peptidomimetics of the Dopamine Receptor Modulator Pro-Leu-Gly-NH₂

These researchers are designing and synthesizing conformationally constrained peptidomimetics of the dopamine receptor Pro-Leu-Gly-NH₂. The peptidomimetics are used to construct a pharmacophore model of the modulatory site. Peptidomimetic photoaffinity labeling agents are made in order to label the modulatory binding site and to use the G protein-coupled receptor model of the dopamine receptor to identify the modulatory site on the receptor. The researchers are using the Basic Sciences Computing Laboratory and the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory for this project.

Research Group
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Bhooma Raghavan, Graduate Student Researcher
Ravindranadh Somu, Research Associate
Ashish Vartak, Graduate Student Researcher
Daniel M. Kroll, Associate Fellow

Mesoscale Simulations of the Statics and Dynamics of Complex Fluids

Particle-based simulation techniques have recently emerged as an attractive alternative to more traditional methods for studying phenomena as diverse as rarefied gas dynamics and the dynamics and rheology of soft materials such as polymer solutions and melts, biological macromolecules, colloids, and amphiphilic mixtures and membranes. The unique problems associated with the modeling and analysis of these systems has led to the development of new coarse-grained simulation techniques that mimic the behavior of atomistic systems on the length scales of interest.

This group's research involves the development and implementation of advanced simulation techniques for studying this class of problems. Specifically, the group is developing and applying a new particle-based simulation technique for studying rarefied gas dynamics, flow and transport in complex geometries, and the dynamics and rheology of complex liquids, including polymer solutions, binary and tertiary mixtures, and biological macromolecules in solution.

Ramaiah Muthyala, Principal Investigator

Design of Antiviral, Antimicrobial, and Anticancer Drugs

These researchers use Supercomputing Institute laboratories to computationally examine interactions between proteins and candidate drug molecules. These computations help the researchers to decide which molecules to synthesize. Previous work has concentrated on drugs targeting the human immunodeficiency virus, protease, and integrase; the group is now expanding its research into antimicrobial and anticancer analogs of the enzyme co-factor NADH.
Philip S. Portoghese, Principal Investigator

Molecular Dynamics Simulation of Opioid Receptors in a Phospholipid Bilayer

This research involves the construction and optimization of three-dimensional models of opioid receptors and simulation of ligand binding in the environment of a phospholipid bilayer and water interface. The researchers are building homology models of the opioid receptors \( \mu, \delta, \) and \( \kappa \), based on the x-ray structure of bovine rhodopsin.

The purposes of this study are: to further optimize the structures of the opioid receptors, especially the amino acid side chains; to study the local conformational changes of the receptors when ligands are docked onto the recognition site; to evaluate the possible interaction of extracellular loop II with the ligand as well as with other residues in the binding sites; and to study to agonist states of opioid receptors using the information from reporter affinity labels.

Research Group
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Shijun Zhang, Research Associate

Shana J. Sturla, Principal Investigator

Molecular Recognition of Alkylated Bases in Double-Stranded DNA

Cancer incidence is linked to environmental factors that can give rise to genomic alterations. These mutations are initiated by carcinogen-induced structural changes that reflect the critical and fundamentally chemical first step in the complex process of cancer development. A paradox of enzymatic metabolism is that, in the body’s efforts to detoxify xenobiotic compounds, chemically reactive entities with the potential to modify deoxyribonucleic acid (DNA) may be generated.

The goal of this research is to characterize precise molecular interactions that influence these initial reactions. With the ability to control regiochemical and stereochemical properties of chemically altered DNA, the researchers synthesize and structurally characterize specifically modified nucleotides and DNA sequences. They use molecular modeling methods to visualize the structural impact of these modifications in double-stranded DNA. Their goal is to establish a relationship between adduct structure, repair efficiency, and biological endpoints. Understanding how certain chemicals initiate cancer will help researchers establish diagnostic tools for carcinogen exposure.

Research Group
Thu Nguyen, Research Associate
Natalia Tretyakova, Principal Investigator
Structural Studies of DNA Cross-Links by Anti-Tumor Drugs and Bifunctional Carcinogens

Deoxyribonucleic acid (DNA)–DNA cross-linking appears to be essential for the cytotoxic and anticancer activity of many anti-tumor drugs, including nitrogen mustards, nitrosoureas, and psoralens. The presence of a single interstrand cross-link can prevent DNA replication and transcription, eventually resulting in cell death and the inhibition of tumor growth. Paradoxically, DNA cross-linking is also a common mode of action of some potent carcinogens.

These researchers use molecular dynamics simulations to investigate the cause of the observed difference in the biological outcomes of DNA cross-linking by bifunctional carcinogens and anti-tumor drugs. The results will help in understanding the mechanisms of action of these agents and in developing anti-tumor agents with minimal side effects.

Research Group
Shawn Balcome, Research Associate
Danae Dorr, Research Associate
Colleen Murray, Undergraduate Student Researcher
Rachel Loeber Rowan, Graduate Student Researcher

Carston R. Wagner, Principal Investigator
Computational Analysis of Chemically Induced Protein Dimerization

The control of protein-protein interactions is a necessary requirement for cellular biological processes. Synthetic systems that emulate this control, such as chemical inducers of protein dimerization (CIDis), have diverse potential as model systems, as bioprobes, and as therapeutic tools. These researchers have developed a CID system based upon bivalent methotrexate ligands (bis-MTX) that dimerize dihydrofolate reductase (DHFR), and are investigating the role of ligand conformation in governing dimerization, the effects of protein surface cooperativity, and the contribution of individual residues to the dimer interface. The group has conducted extensive dynamics simulations of the chemically induced dimer, with periodic-boundary condition solvation and particle mesh Ewald treatment of electrostatic interactions. The dynamics data have been used to calculate protein interaction energies and 11 point-mutants of DHFR have been constructed in the laboratory and used to validate the results of the simulations.

Additionally, the researchers have extended their studies of DHFR assembly to the construction of reversibly oligomerized nanostructures from engineering dimeric DHFR proteins and bix-MTX.

Research Group
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Phalguni Ghosh, Research Associate
Swati More, Graduate Student Researcher
Chunkyung Park, Research Associate
Matt Swenson, Research Associate
Brian White, Graduate Student Researcher
**Chengguo Xing, Principal Investigator**

**Apoptosis Regulation**

The primary focus of this research is related to Bcl-2 proteins, a family of proteins that regulate apoptosis, which is a programmed cell death response. The researchers concentrate on three main areas of research.

In the first area, the researchers are developing small molecules that target specific Bcl-2 proteins as potential anticancer agents and biological tools. The second area concentrates on elucidating the chemical and biological processes in apoptotic regulation by Bcl-2 proteins. The third research area studies apoptotic processes in different tumors induced by different stimuli.

This group is using the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory for their research.

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**David J. W. Grant, Principal Investigator**

**Molecular Modeling of Drug Crystals**

The focus of this research is to develop and evaluate means of engineering the properties of drugs and excipients in solid state to improve the performance and quality of pharmaceutical dosage forms. The researchers are studying the relationship between the chemical properties of solid drugs and their solid-state structures, both crystalline and amorphous.

The Grant group uses molecular modeling to supplement and improve experimental results and inferences and to enhance the understanding of the physico-chemical interactions occurring in pharmaceutically important systems. The group is working on the following specific projects: prediction of crystal structures from powder patterns; calculations of lattice energy of crystals from their unit cells; calculations of interaction energy between various solutes and solvents; calculations of solvation energy of solutes by solvents; poly-

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**Research Group**

- Jignesh Doshi, Graduate Student Researcher
- Garg, Graduate Student Researcher
- Yusheng, Graduate Student Researcher
- Yuchuan Gong, Research Associate
- Sachin Lohani, Graduate Student Researcher
- Enxian Lu, Graduate Student Researcher
- Agam Sheth, Graduate Student Researcher
- Yuegang Zhang, Research Associate
- Deliang Zhou, Graduate Student Researcher
Ronald J. Sawchuk, Principal Investigator

Graphical Representation of Pharmacokinetic Functions of Time and Distance

This project involves the analysis of concentration-time data at three to five discrete sites in a biological matrix, such as cerebrospinal fluid, during drug dosing. The researcher is studying antibiotics and antiviral agents in a rabbit model; the drugs are infused intrathecally to steady state. Samples are taken from the subarachoid space adjacent to the spinal cord at lumbar, thoracic, and cervical locations, and possibly from the cisterna magna. The samples are assayed for drug levels and the data are analyzed using a pharmacokinetic model. This model provides the parameters to generate functions representing the profiles as \( f(\text{time}, x) \). The researcher is using resources at the Basic Sciences Computing Laboratory and the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory to create the graphical representation of the observed data and the fitted functions.

Ronald A. Siegel, Principal Investigator

Use of Hydrogels in Biomedical Devices

This group is working on two related projects investigating the use of hydrogels in biomedical devices. The purpose of the first project, research into a drug delivery oscillator, is to further understanding of the spatiotemporal behavior of a pH-sensitive polyelectrolyte hydrogel as it functions as a nonlinear transducer in a chemomechanical drug delivery oscillator. It has been shown that pulsatile delivery improves the efficacy of certain drugs, particularly hormones. These researchers are working with a device to deliver drugs in a pulsatile rhythm. The group is studying the spatiotemporal response of the gel by applying a reaction-diffusion mathematical model to the system.

The goal of the second project is to develop a hydrogel-based implantable micromachined transponder for wireless glucose measurement. This transponder will be of invaluable use for metabolic monitoring of military personnel and for the management and control of insulin-dependent diabetes.

Research Group

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Sidhartha S. Jena, Research Associate
Siddharthya Mujumdar, Research Associate
Jon Urban, Graduate Student Researcher
Raj Suryanarayanan, Principal Investigator

Material Science of Pharmaceutical Solids

A large fraction of pharmaceutical products are administered as solids. These researchers are interested in the material science of pharmaceutical solids with a specific emphasis on their physical characterization. They are investigating the polymorphic forms, degree of crystallinity, and the nature and extent of interaction with water for drugs and excipients. The methods used include x-ray powder diffraction, thermophysical characterization, spectroscopic, and microscopic techniques. The researchers are specifically interested in monitoring and quantifying phase transitions at various stages of pharmaceutical processing. While the active ingredient is of predominant concern, there are cases where phase transitions of excipients may be of relevance and importance. The goal is to ensure reproducible and predictable performance of solid dosage forms with minimum batch-to-batch variations.

Research Group
Xiangmin Liao, Research Associate
Cletus Nunes, Graduate Student Researcher
Jaidev Tantry, Research Associate

Timothy S. Wiedmann, Principal Investigator

Characterization of Solids by Nanoindentation

The most commonly used dosage is the tablet. Tablets are typically produced by the application of force to a loose bed of powder to form a cohesive compact. Successful tablet compression is critically dependent on the material properties of the drug. These researchers have investigated the relationship between the material properties measured by nanoindentation for four different polymorphic forms of sulfathiazole. These polymorphic forms have unique crystalline structures with variable numbers of slip plane systems as assessed by their crystalline structures, which were used to interpret data from an instrumented tablet press. These results suggest that nanoindentation may be useful in identifying polymorphic forms of drugs amenable to tableting.

This project uses resources at the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory and Scientific Development and Visualization Laboratory to analyze the four different polymorphic forms of sulfathiazole and interpret elasticity and hardness measures by nanoindentation.

Research Group
Cory Hitzman, Graduate Student Researcher
Xiangmin Liao, Research Associate
Guifang Zhang, Research Associate
Mitchell S. Abrahamsen, Principal Investigator
Host Response to Cryptosporidium parvum Infection

Cryptosporidium parvum is an obligate intracellular protozoan parasite that is a major cause of gastrointestinal disease. C. parvum primarily infects epithelial cells of the gastrointestinal tract, resulting in acute watery and profuse diarrhea that, while self-limiting in healthy patients, can be persistent and ultimately life-threatening in immunocompromised patients.

This project uses microarray technology to elucidate the host epithelial response to C. parvum infection. The researchers characterize host gene expression in mock- and C. parvum-infected human and bovine epithelial cell lines as well as primary bovine intestinal epithelial cells by using both Affymetrix high-density oligonucleotide array and custom-designed cDNA (carrier deoxyribonucleic acid) microarrays. By comparing expression levels between mock- and C. parvum-infected epithelial cells, the researchers can identify the genes that are differentially expressed in response to cryptosporidial infection. This study will provide a comprehensive foundation for further analyses of the role of specific biochemical pathways during C. parvum infection and in the progression of cryptosporidiosis, which will be valuable in developing treatments for this disease.

Research Group
Juan Abrahante, Research Associate
Mingqi Deng, Research Associate
Jin Liu, Graduate Student Researcher
Shidong Ma, Graduate Student Researcher

Alvin J. Beitz, Principal Investigator
Gene Expression in Mouse Spinal Cord

These researchers are using Affymetrix microarray technology to identify changes in gene expression in the spinal cord of three different mouse models: one for cancer pain, one of inflammatory pain, and one for multiple sclerosis. They have previously found significant changes in different sets of genes in each of the three mouse models. While some genes that are up- or down-regulated in tumor pain are also changed in inflammatory pain, many genes are uniquely changed in one of these conditions and not in the other. These data reinforce the hypothesis that the pain experienced by cancer patients is different from that experienced by patients suffering from inflammatory conditions. The alterations in spinal cord gene expression found in a mouse model of multiple sclerosis is quite different from that observed in either of the mouse pain models and reflect the role of autoimmunity in this disease state. The researchers are performing more replications of their current data.

Research Group
Mary Braddock, Graduate Student Researcher
Jessica Lynch, Graduate Student Researcher
Kay S. Faaberg, Principal Investigator
Analysis of Porcine Reproductive and Respiratory Syndrome Virus and Swine Influenza Virus

The Faaberg laboratory studies the molecular pathogenesis of porcine reproductive and respiratory disease syndrome virus (PRRSV). They have produced an infectious clone of this agent, and routinely induce changes in the nucleotide sequence in order to further characterize implicated nucleotide or amino acid sequences associated with disease. They are also involved in producing new vaccine strategies for this pathogen, the number one infectious agent of swine in the United States. In much of this work, they need confirmation of desired mutations and use genetic analysis software to assemble and compare nucleotide and amino acid sequences.

PRRSV and swine influenza virus are both agents of pig respiratory disease and vary considerably between isolates. Therefore, the researchers routinely sequence the ORF5 gene of PRRSV and the hemagglutination and neuraminidase genes of swine influenza virus to follow the evolution of these two viruses over time. The group’s database now consists of over 2,200 PRRSV isolates and approximately 100 swine influenza virus isolates. The researchers also perform full-length genome sequence analysis on select isolates of PRRSV.

Research Group
Marie Gramer, Graduate Student Researcher
Jun Han, Graduate Student Researcher
Sarah Herrin, Staff
Gongping Liu, Research Associate
Carrie Wees, Staff
Shannon Whittet, Staff

Yinduo Ji, Principal Investigator
Functional Genomics and Molecular Pathogenesis of Staphylococcus aureus

Staphylococcus aureus is an important human and animal pathogen, causing both superficial skin and life-threatening infections worldwide. The rapid emergence of multi-drug resistance among S. aureus is generating an enormous public health concern.

This project’s goals are to understand the molecular mechanisms of the pathogenesis and to identity the novel targets for delivering efficacious preventative and/or therapeutic agents against S. aureus infections. The researcher employs a systematic and comprehensive evaluation of the requirement for each gene for both cell growth and infection and has developed a regulated antisense ribonucleic acid interference system in S. aureus to selectively control gene expression during culture and infection. The objectives are to create a library for high-throughput screening of gene products that are required for S. aureus pathogenesis and to define gene products that contribute to different S. aureus infections.
James R. Mickelson, Principal Investigator
Genetic Linkage Analysis of Heritable Neuromuscular Disorders in Domestic Animals

Simple and complex heritable diseases are relatively common in companion animal species due to selected breeding schemes that use common founders and family lines to propagate highly desirable traits. These researchers are using genetic linkage analyses to begin to identify the genetic loci responsible for a number of heritable disorders in dogs and horses. The researchers obtain genotypes for microsatellite deoxyribonucleic acid (DNA) markers located at evenly spaced intervals across the genome and analyze them for statistically significant linkages to the trait in large, often-complex pedigrees. By identifying DNA markers that co-segregate with the trait, the researchers can essentially map the gene for the trait to that region of a specific chromosome represented by that marker where the gene can ultimately be identified. The researchers are using the Computational Genetics Laboratory and the Digital Technology Computational Biology Laboratory.

Research Group
Patricia Dranchak, Graduate Student Researcher
Ned Patterson, Graduate Student Researcher
Monica C. Roberts, Graduate Student Researcher
Michelle Wagner, Research Associate

Michael P. Murtaugh, Principal Investigator
Porcine Peyer’s Patch Expressed Sequences Associated With Disease

The Murtaugh laboratory is creating tools to understand the balance between acceptance and uptake of nutrients in the gut of animals, versus detection and resistance to toxins and pathogens. They isolated genes that are expressed in gut immune tissue, constructed deoxyribonucleic acid (DNA) oligonucleotide microarray chips, and analyzed the patterns of gene expression in different gut immune tissues. A total of 6,000 genes were identified of which nearly half appear to be new or have unknown functions. Since genes give the proteins that are responsible for biological functions of a tissue, this high frequency of genes with unknown functions means that new biological processes or regulatory functions are involved in nutrient uptake and disease resistance in the gut.

The researchers have used the microarray chips for hybridization experiments of tissues collected under different conditions and from various regions of the gut. They are using Supercomputing Institute laboratory resources to analyze the data from these experiments.

Research Group
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Colleen Finnegan, Research Associate
Linda Foster, Research Associate
Martha Fuentes, Staff
Geoff G. Hirsch, Graduate Student Researcher
Kendra Hyland, Graduate Student Researcher
Craig Johnson, Research Associate
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Ratna Prasad Mulupuri, Graduate Student Researcher
Chad Ramler, Graduate Student Researcher
Brenda Saxton, Supercomputing Institute Undergraduate Intern
M. Kariuki Njenga, Principal Investigator

Full Genome Sequencing of Avian Pneumovirus

These researchers are analyzing avian metapneumovirus subtype C (AMPV/C). They have determined the nucleotide sequence of the ribonucleic acid polymerase L gene of this virus, completing the full genome sequence of the virus. The researchers have confirmed earlier classification of the United States viruses into their own subtype C. Phylogenetic analysis also corroborated earlier findings that AMPV/C clusters with human metapneumovirus away from other pneumoviruses.

Mark S. Rutherford, Principal Investigator

Intrinsic Responses of Macrophages to Porcine Reproductive and Respiratory Syndrome Virus

Macrophages are ubiquitously distributed, bone marrow-derived mononuclear phagocytes responsible for numerous homeostatic, antimicrobial, inflammatory, and tissue repair processes. Their wide tissue distribution makes macrophages well positioned to provide an immediate defense against infectious elements.

Respiratory disease in pig production systems extracts a high economic toll and includes pathogens that usurp macrophage antimicrobial processes. Nonetheless, most knowledge of pig immunity is centered around adaptive immune responses. To understand antimicrobial macrophage function in pigs, it is necessary to delineate molecular changes that occur in stimulated macrophages, particularly under relevant product system conditions. These researchers are trying to determine whether profiles of macrophage gene expression change over the course of an infection, especially for chronic and persistent infections. They are using the Computational Genetics Laboratory and the Scientific Development and Visualization Laboratory for this project.
Pamela J. Skinner, Principal Investigator

Genomic Studies of Transmissible Spongiform Encephalopathies

Transmissible spongiform encephalopathies (TSE) or prion diseases are fatal neurodegenerative diseases with no known cure. One focus of this laboratory is to gain insights into prion disease pathogenesis in order to understand the molecular events that lead to the neurodegeneration, and to develop early diagnostic tools and new drug therapies. Current efforts by this group involve the use of carrier deoxyribonucleic acid microarrays to identify alterations in gene expression that occur in mouse brain infected with different strains of scrapie.

Bruce K. Walcheck, Principal Investigator

Mutational Analysis of Cell Adhesion Proteins

The Walcheck laboratory is investigating the function and regulation of various leukocyte cell surface determinants, such as adhesion molecules involved in leukocyte extravasation from the blood into the tissue. Numerous copy deoxyribonucleic acid constructs are being generated in order to examine the structure-function relationship of particular leukocyte membrane proteins. The researchers are using software available through the Laboratory for Large-Scale Data Analysis as support software (designing polymeric chain reaction primers, performing restriction mapping, and for protein analysis) for engineering mutations.
Douglas J. Weiss, Principal Investigator
Role of Interleukin-10 and Mitogen-Activated Protein Kinases in the Interaction of Bovine Macrophages With Mycobacterium avian Subspecies Paratuberculosis Organisms

John's disease (also called paratuberculosis) is a chronic granulomatous enteritis of ruminants that is caused by Mycobacterium avian subspecies paratuberculosis (M. a. ptb). The disease has only recently been fully recognized as a worldwide epidemic of domestic livestock and wildlife. M. a. ptb has also been incriminated as a causative agent in Crohn's disease, a chronic granulomatous enteritis of human beings. This group's preliminary studies have identified interleukin-10 (IL-10) as a critical factor in attenuating inflammatory and immune responses in John's disease. The long-range goal of this research is to define the unique aspects of the interaction of M. a. ptb organisms with mucosal immune cells that can be exploited to enhance resistance to infection. As an outcome of this project, the group expects to identify unique aspects of the mucosal immune response that lead to over-production of IL-10 and resultant development of tolerance to M. a. ptb. These studies are expected to provide avenues that can be exploited to develop effective vaccination strategies.

Research Group
Cleverson de Sousa, Graduate Student Researcher
Oral Evanson, Research Associate

Ioulia D. Ioffe, Principal Investigator
Arbitrage Violations and Implied Volatility Option Markets

Implicit in the values of options is the volatility of the underlying asset. Economic intuition suggests that the values of these implied volatilities should be the same for options written on the same underlying asset and having the same maturities. There is vast empirical finance literature, however, that indicates otherwise and tries to justify, rather than invalidate, this fact. The results in this literature are model-dependent and still do not resolve the disagreement.

The key issue of this project is to determine if the reason one sees such an occurrence must be due to the fact that certain significant market features are not taken into account. In particular, market frictions and the seeming arbitrage in the data are ignored. This project considers takes market frictions into account when considering arbitrage in option markets, and tests whether this invalidates or diminishes apparent anomalies of the implied volatilities.

Research Group and Collaborator
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Eliezer Z. Prisman, Finance Specialization
Department, Schulich School of Business, York University, Toronto, Ontario, Canada
Brian P. McCall, Principal Investigator

Determinants of Educational Attainment in Florida

This project uses unique administrative data from the Florida Department of Education to study student transitions from high school into college, and then to examine a host of college outcomes. Florida collects detailed information on student educational and life histories and they are providing access to this data so that the researcher can construct a file that contains a longitudinal history for all students from the time they are in high school until they (potentially) graduate from college. This “event history file” will contain demographic, academic, social, economic, financial, and institutional data that will be used to study many important education issues.

Paul E. Johnson, Principal Investigator

Patient Adaptation Analysis Using Bootstrapped Estimates of DEA Efficiency Scores

This study models patient adaptation to the conditions of a specific chronic disease, type 2 diabetes. The researchers employ data envelopment analysis (DEA) methodology to describe each patient’s adaptation relative to the adaptation of the most successful patients. DEA has been applied in health service research, but its estimates of efficiency scores have been shown to be biased upwards. By “bootstrapping” DEA, these researchers can correct the biases and also make statistical inferences from DEA estimates.

The study is conducted at two levels, patient level and physician level. At patient level, self-care behaviors of selected type 2 diabetes patients are used as inputs to the DEA method; patient satisfaction and percent change in patient glycosylated hemoglobin are outputs. Fitness is estimated by bootstrapping DEA to measure how well patients are adapted to their environment of chronic disease care.

At physician level, DEA is used to model physician efficiency using patients included in the first-level analysis. The medical cost for each patient is used as the input variable and patient satisfaction, patient self-efficacy, and percent change in patient glycosylated hemoglobin are used as output variables.
William Li, Principal Investigator  
Christopher J. Nachtsheim, Co-Principal Investigator  
Model-Robust Designs, Construction of Mixed-Level Designs, and Model-Discriminating Designs

The first object of this research is to construct model-robust designs that include supersaturated designs and response-surface design. Model-robust designs usually consider many different possible models that can increase exponentially with the run size. The second objective is to construct complete catalogs of mixed-level designs. Orthogonal designs are the most commonly used experimental designs in practice. The choice of optimal designs depends on criterions and complete catalog catalogs of the candidate orthogonal designs. These researchers are using a newly developed efficient algorithm and a theory based on the indicator function to construct complete sets of orthogonal designs with economic run sizes.

In a third research area, completed this year, the researchers constructed a class of model-discriminating designs. Sometimes two models may generate the same responses and thus cannot be distinguished from each other. The researchers developed a criterion that maximizes the capability of a design to discriminate among competing models.

Collaborator  
Kenny Ye, Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York

UM TC–Department of Aerospace Engineering and Mechanics

Graham V. Candler, Fellow  
Simulation of Reacting Flows

These researchers are continuing their numerical simulations of high-temperature reacting flows. This work has several applications: supersonic flow control using laser energy deposition, generation of atmospheric-pressure air plasmas for materials processing and flow control, the study of how the Navier-Stokes equations fail in high-speed, low-density flows, the study of micro-scale aerodynamics, and the analysis of turbulent reacting flows. The researchers use a suite of computational fluid dynamics (CFD) codes developed for parallel supercomputers. These codes use implicit time integration to reduce the computational cost, and have been optimized for the IBM and SGI supercomputers. The group also uses an efficient parallelized direct simulation Monte Carlo code for low-density flow simulations for comparison with the continuum CFD simulations. This work is leading to an improved understanding of how chemical reactions and fluid motion interact in a variety of technologically relevant applications.

Research Group and Collaborators  
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Travis Drayna, Graduate Student Researcher  
Marie-Claude Druguet, Research Associate  
Mark Emerick, Graduate Student Researcher  
Ryan Gosse, Graduate Student Researcher  
Heath Johnson, Research Associate  
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Ivan Marusic, Faculty Collaborator  
Ioannis Nompelis, Research Associate  
David Peterson, Graduate Student Researcher  
Krish Sinha, Research Associate  
Joseph Stecher, Graduate Student Researcher  
Kelly Stephanie, Undergraduate Student Researcher  
Pramod Subbareddy, Graduate Student Researcher  
Kerry Trumble, Graduate Student Researcher
Roger L. Fosdick, Associate Fellow
Large Deformations in Nonlinear Elasticity and the Thermomechanics of Propagating Phase Boundaries

The goal of this program is to carry out a theoretical and computational investigation of coexistent phase structures in solids when subject to external load or environmental temperature, or to electrical or magnetic stimulation. The existence and growth of zones of evolving microstructure is not only responsible for the failure of materials but also plays an important part in the design of devices and in many emerging applications that depend on sophisticated nonlinear material behavior. As technology advances, it is clear that materials that support internal phase structures are becoming increasingly important, and a better understanding of the difficult mechanics and materials issues will surely enhance their applicability.

The framework for this research is a thermomechanical model including capillarity, viscosity, and thermal conductivity. Because the free energy is nonconvex, the governing equations are of mixed type: hyperbolic in regions of pure single phase and elliptic in the intervening spinodal region. The researchers are implementing and testing several finite difference and finite element methods for solving these equations and are also developing their own approach.

Collaborators
Adair Roberto Aguiar, Department of Mechanical Engineering, Federal University of Paraná, Curitiba, Paraná, Brazil
Eric Petersen, United Defense, Minneapolis, Minnesota

Ashley James, Principal Investigator
Numerical Simulations of Liquid-Fluid Interface Flows With Topological Transitions and Surfactant Effects

This research project simulates interfacial fluid flow to gain an improved understanding of how topological transitions of liquid-fluid interfaces occur and of the effect of surfactant on the evolution of physical systems. The researchers have developed an interfacial flow solver incorporating the dynamics of interfacial surfactant.

The group is working on simulations to understand the dynamics of several problems. One is an investigation of the coalescence of two drops, including van der Waals forces, with the goal of developing a physically based model of the topological transition. A second project involves simulations of the break-up of a drop in an extensional flow, aimed at understanding the role of surfactant in pinch-off processes. Finally, the group is investigating the effect of surfactant on the pinch-off of a periodic liquid thread.

The researchers are continuing to modify their code to improve its accuracy and extend its capabilities. One improvement is a higher-order method to reconstruct the interface. The method is being implemented on an unstructured, adaptive mesh and will include surfactant solubility. The researchers will also model contact line dynamics.

Research Group
Xueli Jiang, Graduate Student Researcher
Richard Martin, Undergraduate Student Researcher
Scott Williams, Graduate Student Researcher
Xiaofeng Yang, Graduate Student Researcher
This research group is continuing their investigation of the fundamental dynamics of three-dimensional motions of solid particles in Newtonian and viscoelastic fluids. The researchers have developed two separate scalable and highly efficient parallel finite-element codes, the arbitrary Lagrangian-Eulerian (ALE) particle mover and the disordered local movement (DLM) particle mover. The ALE particle mover is based on a generalization of the standard Galerkin finite-element method that uses an unstructured mesh and an ALE scheme to handle the time-dependent domain. The DLM particle mover is based on a fictitious-domain method, in which the fluid flow equations are enforced inside, as well as outside, the particle boundaries. Both methods use a combined fluid-particle weak formulation in which the hydrodynamic forces and torques are eliminated. The researchers are studying the migration of particles in three-dimensional pressure-driven flows and are seeking explicit formulas of the life forces on the particles by correlating data from direct numerical simulation.
Perry H. Leo, Associate Fellow

Studies of Crystal Morphologies

The goal of this project is to investigate three-dimensional, diffusively evolving crystals in “ mushy” zones where there is freezing and melting, and where there are multi-crystal interactions. An important aspect of the research concerns the three-dimensional morphology of growing solid crystals in a liquid melt as well as the growth of precipitates in solid-solid phase transformations. This involves solving a diffusional evolving free boundary problem.

These researchers have found that, under certain conditions, the morphology of growing crystals may be controlled; this is confirmed by numerical experiments. They have developed a fully adaptive, three-dimensional boundary integral method to solve the diffusional evolution of interfaces. The work has begun with isotropic surface tension and anisotropic interface kinetics.

Research Group and Collaborators

- Anthony M. Anderson, Undergraduate Student Researcher
- Joel Bell, Graduate Student Researcher
- Vittorio Cristini, Department of Biomedical Engineering, University of California, Irvine, California
- Herng-Jeng Jou, Questek, Evanston, Illinois
- Jun-Seok Kim, Graduate Student Researcher
- Shuwang Li, Graduate Student Researcher
- Xiangrong Li, Department of Mathematics, University of California, Irvine, California
- Xiaofan Li, Department of Applied Mathematics, Illinois Institute of Technology, Chicago, Illinois
- Ellen Longmire, Faculty Collaborator
- John S. Lowengrub, Department of Mathematics, University of California, Irvine, California
- Saswata Majumder, Graduate Student Researcher
- Qing Nie, Department of Mathematics, University of California, Irvine, California
- Michael Renardy, Department of Mathematics, Virginia Polytechnic Institute and State University, Blacksburg, Virginia
- Antheunis Versluis, Faculty Collaborator
- Steve Wise, Department of Mathematics, University of California, Irvine, California
- Yubao Zhen, Graduate Student Researcher
- Xiaoming Zheng, Research Associate
- Hua Zhou, Research Associate
These researchers are working with large-eddy simulation (LES) of turbulent flows in realistic engineering geometries. They have developed a non-dissipative, numerical algorithm for turbulent flow on unstructured grids. The use of unstructured grids allows arbitrarily complex geometries to be efficiently gridded. A novelty of the algorithm is that it discretely conserves not only momentum, but also kinetic energy. This allows robustness without numerical dissipation. Such robustness is imperative to perform accurate simulations in complex geometries at high Reynolds numbers.

Recent work by this group includes a project that showed that the trajectory of jets in cross-flow depends not only on the momentum ratio, as is commonly assumed, but also on the distribution of momentum. In another project, the researchers performed direct simulations of scalar mixing in a spatially evolving turbulent round jet, and demonstrated the importance of accounting for near-field entrainment. For the first time, the group also performed simulations of propeller crashback, which showed significant unsteadiness in the out-of-plane loads as observed in experiment. Another project developed a novel algorithm that is non-dissipative yet robust for shock-free compressible turbulent flows over a range of Mach numbers. This group has also initiated work on the interaction of turbulent flows with plasmas and combustion in high-speed flows.

Research Group
Pradeep C. Babu, Graduate Student Researcher
Jeffrey Doom, Graduate Student Researcher
Shankar Ghosh, Graduate Student Researcher
Yucheng Hou, Graduate Student Researcher
Suman Muppidi, Graduate Student Researcher
Martin Vysohlid, Graduate Student Researcher
This group continued its pioneering work in computational astrophysics, centered on improving the fundamental understanding of the behaviors of high-energy charged particles, also known as cosmic rays (CRs), and magnetic fields in cosmic plasmas. The researchers also apply this knowledge to the understanding of some recognized “key” astrophysical problems, particularly the origins of the cosmic rays themselves and the nature of the most energetic phenomena in the universe—giant radio galaxies, enormous “cosmic structures” that form by gravitational collapse against the expansion of the universe, and supernova remnants. This work is based on state-of-the-art codes for cosmic structure evolution and compressible magnetohydrodynamics (MHD) plus novel schemes for following the acceleration and propagation of cosmic rays. Some specific areas of research include three-dimensional MHD simulations of “radio plasma bubbles” in galaxy clusters, two-dimensional simulations of MHD “superbubbles” in the Milky Way, and the dynamics of supernova remnants and the origin of cosmic rays.

Research Group and Collaborators
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Sean O’Neill, Graduate Student Researcher
Dongsu Ryu, Department of Astronomy and Space Sciences, Chungnam National University, Daejeon, Korea
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Paul Shearer, Supercomputing Institute Undergraduate Intern
Ian L. Tregillis, Los Alamos National Laboratory, Los Alamos, New Mexico
Dan Weisz, Graduate Student Researcher
Victor H. Barocas, Associate Fellow

Computations of Biomechanics and Biotransport

The Barocas group is continuing its work on projects in computational biomechanics and transport. In one project, the researchers study the coupled mechanics of the aqueous humor (a passive Newtonian fluid) and the iris (an active elastic solid) in the anterior portion of the eye. The emphasis is on the issue of dynamic behavior, improving upon previous studies that treated the eye as a steady-state system. Another continuing project involves the groups’ novel macroscopic-microscopic finite element approach to the modeling of fibrillar tissues. This approach, although computationally intensive, offers the potential to provide much more insight into the mechanical behavior of tissues and tissue equivalents (formed by cells entrapped in a reconstituted biogel). The group has demonstrated the effectiveness of their approach on a test problem using workstations, but to study real systems, they must use much greater mesh refinement and three dimensions, and must include transient behavior.

The group has also begun a third project on the design of a tissue-engineering cardiovascular valve. In this project, the researchers are embedding a shell model of the valve leaflet within a three-dimensional transient solution of the Navier-Stokes equations for the blood.

Research Group and Collaborator
Devesh Amatya, Graduate Student Researcher
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Nicha Chitphakdithai, Supercomputing Institute Undergraduate Intern
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Shramik Sengupta, Graduate Student Researcher
Neda Shahghasemi, Undergraduate Student Researcher
David Shreiber, Department of Biomedical Engineering, Rutgers University, Piscataway, New Jersey
Matthew Stay, Research Associate
Triantafyllos Stylianopoulos, Graduate Student Researcher

Bin He, Principal Investigator

Computational Study of EEG-Based Source Estimation

The aim of this project is to develop and evaluate novel computational algorithms for estimating sources from noninvasive electroencephalograms (EEGs). There are two parts to this project: the estimation of source number and the estimation of source parameters such as location, orientation, and amplitude. The researchers are using the supercomputers to create a model developed with parallel matrix operation software and their own computational routines developed for EEG-based three-dimensional source estimation.

Research Group
Xiaoxiao Bai, Research Associate
Lei Ding, Graduate Student Researcher
Yingchun Zhang, Research Associate
**Peter N. Steinmetz, Principal Investigator**  
Modeling the Electric Field Imposed by Deep Brain Stimulations of the Subthalamic Nucleus

Deep Brain Stimulation (DBS) has been widely used for the treatment of various disorders. DBS of the subthalamic nucleus is particularly used in Parkinson’s disease patients. Even though this technique has been used for more than five years, it is not clear where the beneficial effects come from and what type of responses the stimulation elicits in different brain structures. Previous research treats the area of interest as a homogeneous and isotropic region. These researchers are implementing a realistic-geometry, anisotropic, and inhomogeneous model that includes basal ganglia structures like the subthalamic nucleus, the substantia nigra, the zona incerta, the fields of forel H2 (lenticular fasciculus), the internal capsule, and the stimulating electrode. The ultimate goal is to study the way the electric field (imposed by the electrode) spreads throughout this area and which structures are influenced more. The role of the position of the electrode can also be studied and excitation patterns may be extracted. A three-dimensional finite-element model, implemented using Ansoft’s Maxwell 3D, is used to create the model and to solve for the potentials at each node of the finite-element mesh resulting from the external electrode stimulation.

**Research Group**  
Gabriela C. Miyazawa, Graduate Student Researcher  
Stamatiou Sotiropoulos, Graduate Student Researcher

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**J. Thomas Vaughan, Principal Investigator**  
Frequency Limits and Radiation Losses of Radio Frequency Volume Coils in Magnetic Resonance Imaging

High field magnetic resonance imaging (MRI) scanners have many advantages over their lower-field counterparts, including a much higher signal-to-noise ratio and higher spectral resolution. While high-field MRI systems provide stronger support for clinical applications and medical research, they also demand more complicated and elaborate radio frequency (RF) coil design. Two significant field-dependent constraints to successful RF coil design are imposed by coil efficiency and coil resonant frequency limitations. Without solutions to the limitations of loss and self-resonance for high-frequency coils, the benefits of high-field MRI will be lost. The overall goal of this project is to investigate and solve these problems.

**Research Group**  
Can E. Akgun, Graduate Student Researcher  
Jinfeng Tian, Graduate Student Researcher
Robert W. Carr, Associate Fellow

Atmospheric Chemistry of Halogen-Containing Organic Compounds

These researchers are using Supercomputing Institute resources for their computational chemistry research on the atmospheric chemistry of organic oxy radicals. They perform \textit{ab initio} molecular orbital and/or density functional calculations on alkoxy radicals and halogenated alkoxy radicals that are formed in the atmosphere, and investigate chemical pathways for their removal. The researchers perform calculations to predict optimized geometries, vibrational frequencies, and total energies of reactants, products, and transition states. The computations yield detailed information on the mechanisms for removal that is difficult and laborious to obtain experimentally. In conjunction with molecular theories of chemical kinetics, the calculations provide estimates of rate coefficients that can then be used to evaluate removal rates. Comparison of the simulated rate coefficients with experiment for cases where data exist gives information on the accuracy of the calculations and will facilitate development of rate coefficient models that are accurate over the entire range of atmospheric conditions. This is much wider than the range of conditions accessible by most experimental methods. The calculations will also provide valuable information on the effects of halogen substitution on the reaction of alkoxy radicals.

\begin{center}
\textbf{Research Group}
Fuxiang Wu, Research Associate
\end{center}
James R. Chelikowsky, Fellow
Yousef Saad, Fellow
High-Performance Algorithms for Electronic Materials

These researchers are continuing their investigations on electronic materials. These materials include ceramics such as silica and semiconductors such as silicon, germanium, gallium arsenide, and zinc telluride. A major part of this research program is to develop and implement new and novel algorithms for examining the electronic and structural properties of complex systems. The researchers’ applications focus on systems with numerous atoms and many degrees of freedom, such as surfaces, liquids, glasses, large clusters and quantum dots (including magnetically doped dots), and complex solids. The researchers have also initiated a program on nanowires and on molecular transport.

Research Group and Collaborators (cont.)
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Shen Li, Graduate Student Researcher
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Undergraduate Intern
Marie Lopez del Puerto, Graduate Student Researcher
Dmitriy Melnikov, Research Associate
Serdar OgUT, Department of Physics, University of Illinois, Chicago, Illinois
Murilo Tiago, Supercomputing Institute Research Scholar
M. Claudia Troparevsky, Department of Chemistry and Henry Euring Center for Theoretical Chemistry, University of Utah, Salt Lake City, Utah
Igor Vasiliev, Department of Physics, New Mexico State University, Las Cruces, New Mexico
Yunkai Zhou, Research Associate

H. Ted Davis, Fellow
Simulation Studies of Processing and Properties of Surfactants in Nanostructure-Tailoring Solvents and Ions

Salts of fatty acids, called “soaps,” comprise a class of chemicals that is of tremendous commercial importance. There is emerging industrial interest in the crystallization behavior and nanostructure of soaps to make advanced materials of various types. Many aspects of crystallization in soaps, however, are not fully understood. These researchers performed simulation computations to augment their experimental results on the crystallization processes in various solutions subjected to different heating and cooling cycles. They used Monte Carlo techniques, combined with theoretical techniques that had already been developed, to calculate the free energy and phase behavior of mixed amphiphiles and of amphiphile-additive mixtures, to understand the mechanism of the micellar shape transformation, and to predict the effect of the inclusion of organic additives into the micellar structures.

Research Group and Collaborators
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Jeffrey J. Derby, Fellow
Materials Processing Fundamentals

The Derby group develops, implements, and employs large-scale numerical modeling to understand processes that are used for the production of advanced crystalline and ceramic materials. Of special emphasis is the representation of three-dimensional and transient continuum transport (flows and heat and mass transport), phase-change phenomena, and system design (such as furnace heat transfer during melt growth). The researchers are developing and employing phase change and transport in the processes under study. These processes include Bridgman crystal growth, model-based control of crystal growth processes, the sintering of crystalline ceramics, the dynamics of solution crystal growth, and microgravity crystal growth.

Research Group and Collaborator
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Andrew Yeckel, Research Associate

C. Daniel Frisbie, Principal Investigator
Theoretical Characterization of the Transport Properties of Organic Semiconductors

Molecular organic semiconductors in general and oligoacenes in particular are currently the object of much interest because of their potential application in (opto)electronic devices, especially field-effect transistors. Understanding the charge transport mechanisms in these materials is a key point for device design and performance improvement.

The main goal of this project is to calculate the electronic band structure and some molecular properties, such as ionization potentials, electron affinities, and isomerization barriers, of novel organic semiconductors. The result of these calculations, in combination with experimental data, will allow the development of an integrated picture of the important factors affecting the electronic and the charge transport properties of organic semiconductors.

Collaborator
Demetrio da Silva Filho, School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, Georgia
William W. Gerberich, Principal Investigator
Combinatorial Approach to Properties Determination of Ultra-Thin ALD-Based Films

Atomic layer deposition (ALD) is a recently developed technique for producing thin, hard conformal coatings that improve the mechanical performance of microelectronic devices and micro-electromechanical systems. These coatings are usually grown to thicknesses ranging from 1–50 nm. To optimize the performance of these devices, the properties of the ALD coatings must be determined; however, current techniques cannot accurately separate the mechanical properties of such thin coatings from those of the substrate. To address this difficulty, these researchers combined nanoindentation-based mechanical tests and same-scale finite-element-based simulations to determine the elastic modulus, yield stress, and indentation hardness of the coatings. Using the finite-element simulation software package ABAQUS, the researchers simulated indentations to separate the mechanical properties of the thin film from the composite response of the film/substrate system. The results of these experiments contributed to the understanding of the indentation size effect and small volume mechanical deformation.

Research Group
John Jungk, Graduate Student Researcher
Wei-Shou Hu, Associate Fellow
Genomic Exploration on Chinese Hamster Ovary Cells; Secondary Metabolite Biosynthesis in *Streptomyces*

These researchers are involved in two projects using the Supercomputing Institute laboratories. In the first, they are continuing their long-term project investigating Chinese hamster ovary cells and the genetic traits that confer these cells’ many desirable phenotypic traits. The researchers have taken a comprehensive approach by combining genomic and proteomic tools and physiological studies to identify and isolate relevant genes. They use microarray and proteomic analysis to identify important genes and expression patterns and to use these to genetically modify cells. The results and tools obtained from these efforts represent a significant step toward large-scale gene expression profiling for these cells.

In a new project, the Hu group is studying *Streptomyces*, the largest producers of industrially important, naturally occurring secondary metabolites. Secondary metabolite biosynthesis in *Streptomyces* is controlled by a complex regulatory network consisting of a large number of pathway-specific and global regulators organized in a hierarchical tree. The goal of this project is to identify the possible positions of important genes on the regulatory hierarchy of secondary metabolism. This would serve as a model for studying synthesis and regulation of a variety of industrially important natural products produced by other related species.

**Research Group and Collaborators**

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**Yiannis Kaznessis, Principal Investigator**

**Computer Simulations of Antimicrobial Peptides and of Protein-Protein Interactions**

These researchers are involved in three projects using Supercomputing Institute resources. In the first, they implement large-scale molecular dynamics simulations of a large number of antimicrobial peptides with model lipid micelles. The data arising from these simulations is analyzed to develop structural bioinformatics tools in order to derive a cognitive quantitative structure activity relationship with predictive ability that will facilitate the rational design of peptide antimicrobials.

A second project investigates protein-protein interactions, which are involved at the root of all biological processes. This group has developed an efficient ranking algorithm to predict the structure of protein-protein complexes. This method focuses on the refinement stage to improve the ranking structure, so that the near-native structures are ranked on top. The researchers are extending and improving the scope of current docking methods and are using their improved ranking procedure to refine these methods.

The third project involves stochastic simulations of gene regulatory networks. The group has developed a hybrid stochastic-discrete and stochastic-continuous algorithm for simulating the dynamic behavior of cascades of biomolecular interactions involved in gene regulation, which guide the rational design of gene networks such as oscillators and bistable switches.

**Research Group**

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**Satish Kumar, Principal Investigator**

**Continuum and Nanoscale Simulations of Polymer Dynamics**

These researchers were involved in several projects aimed at simulating various aspects of polymer dynamics at the nanometer and continuum scales. A completed project, motivated by the growing importance of microfluidic devices, involved Brownian dynamics simulations of the electric field-driven motion of a deoxyribonucleic acid molecule through a narrow slit. The group investigated transport with the goal of understanding how trap geometry influences migration speed.

A second project involves the simulation of hydrodynamic instabilities that arise in fluid flow past polymer gels. The researchers are developing a finite-element code to simulate this instability and are in the process of code validation.

The third project concerns finite-element simulations of fluid flow between a flexible wall and a cavity. The work aims at clarifying the highly nonlinear elastohydrodynamic interaction between the elastic stresses in the wall and the viscous stresses in the fluid.

**Research Group and Collaborator**

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Chris W. Macosko, Associate Fellow
Analysis and Properties of Co-Continuous Blends

Co-continuous polymer blends consist of distinct phases. The microstructure is sponge-like where one of the phases plays the role of the sponge and other(s) its complement. While there have been previous studies of such blends, most have been experimental and the physical processes leading to the development of co-continuous morphologies and their properties are still poorly understood. These researchers are working on theoretical, numerical, and experimental studies that they hope will provide a unique insight into characterizing these processes.

Large-scale computation and computational mathematics are now primary tools in studying physical processes characterized by randomness and nonlinearity. Co-continuous polymer blends are ideal examples of such processes in which complex, randomly oriented patterns form by nonlinear interaction among interfaces, flow, and phase transitions. A study of these processes is inherently multidisciplinary and involves fluid dynamics, thermodynamics, material science, computational mathematics, and interactions with experiments.

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Richard B. McClurg, Principal Investigator
Molecular Crystal Global Phase Diagrams

These researchers are developing methods for construction of molecular crystal global phase diagrams. The phase diagrams present the crystalline phase as a function of the coefficients of a general intermolecular potential based on molecular symmetry-adapted basis functions. Using the mean-field approximation, the researchers begin in a high-temperature, disordered reference state, then seek spontaneous symmetry-breaking phase transitions and phase structure information at lower temperature. They can then deduce potential parameters consistent with a molecular point group and crystal space group symmetry by using the organic molecular crystal structures contained in the Cambridge Structural Database available at the Basic Sciences Computing Laboratory. The group has developed a working code for constructing the phase diagrams and is in the process of testing the method for tetrahedral molecules. The phase diagrams offer a knowledge-based means to improve intermolecular potential formulation and provide a means of rational guidance for crystal engineering of homologous molecular species.

Research Group
J. Brandon Keith, Graduate Student Researcher
Jonathan Mettes, Graduate Student Researcher
Alon V. McCormick, Fellow

Molecular-Scale Chemical Reaction Engineering of Materials Synthesis

These researchers use molecular-scale models to characterize chemical engineering systems that pose special process modeling difficulties. To model the polymerization of silicon alkoxide and (meth)acrylates, they use Monte Carlo simulations to extract information about polymer size distribution, structure, and gelation. They use rigidity percolation modeling to predict the mechanical properties of these systems.

Another project concerns the volume relaxation and changing mechanical properties in curing systems. The goals of this project are: to trace the extent of reaction with time and location in the coating; to account for the development of viscoelastic properties; and to predict the course of stress development and relaxation.

The McCormick group is also using Monte Carlo simulations to calculate the free energy and phase behavior of mixed amphiphiles and of amphiphile-additive mixtures, to understand the mechanism of the micellar shape transformation, and to predict the effect of the inclusion of organic additives into the micellar structures.

David C. Morse, Principal Investigator

Computational Polymer Physics

This group’s work in computational polymer physics focuses on elucidating molecular origins of both equilibrium and dynamic behavior of polymer fluids. The project includes three focus areas. The first investigates dynamical and viscoelastic behavior of semi-flexible polymers. The researchers are conducting Brownian dynamics simulations of tightly entangled solutions of these semi-flexible polymers. The second research area concerns statistical thermodynamics of self-assembling structures of block copolymers. This project involves self-consistent field theory, a classical statistical mechanical mean-field theory for spatially inhomogeneous equilibrium structures formed by block copolymers or immiscible homopolymers. The third area concerns shear-induced slip along interfaces between immiscible polymer liquids. The researchers have developed a parallel molecular dynamics code, which they will use to conduct non-equilibrium molecular dynamics simulations of slip along an interface between immiscible polymer melts induced by shear flow with flow parallel to the interface.
Lanny D. Schmidt, Associate Fellow
Two-Dimensional Short-Contact-Time Reactor and Catalytic Radiant Burner Modeling

Short-contact-time reactors used for the partial oxidation of alkanes to make synthesis gas (syngas), olefins, and oxygenates have been extensively studied for chemical manufacture for carbon monoxide (CO)-free hydrogen streams for fuel cells. This research group is studying the partial oxidation of alkanes to syngas and subsequent shift of CO to CO₂ to obtain pure hydrogen streams on noble metal catalysts in millisecond tubular reactors. A major focus is the partial oxidation of ethane to ethylene, as well as catalytic wall reactors that couple exothermic reactions with endothermic reactions in order to eliminate thermal boundary layers. All of these projects involve coupling reaction kinetics with complex fluid dynamics to obtain models that describe these processes.

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L. E. Scriven, Fellow
Slitting of Magnetic Tapes

Many coated products are formed by first coating a wide (but thin) web or film and then slitting, cutting, or punching the web to yield a narrow tape or other shape much smaller than the original. A general problem of the slitting process associated with these coated products is maintaining or achieving a defect-free cut edge. Such edges are crucial for yielding products that maximize the useful surface areas of the slit component.

This project’s goal is to investigate and understand the slitting process so as to generate materials and process guidelines that optimize the edge quality of tapes formed by slitting. The researchers are using several ABAQUS finite element models, including two-dimensional and three-dimensional models with different cutting mechanisms, a mode III fracture model to simulate the crack in the magnetic supported layer, and a plane-strain mode II “sliding” fracture model to study delamination. The project also includes testing of the different mechanical, fracture, and adhesive properties of the films to be studied, with ABAQUS finite element models used to complement the experimental work.

Collaborator
Paul Andruet, Imation, Oakdale, Minnesota
These researchers continued their investigations into computational aspects of continuum and network theories of fluid physics and transport in thin layers, in films, and in porous media structures. The research is part of coordinated research programs on the fundamentals of liquid structure, flow, and transport in commercially important process technologies, such as precision coating, drying and curing of liquid films, injection molding, and multiphase contacting in packed beds. The problems are typically multidimensional and often time-dependent, resulting in systems of coupled partial differential equations that are solved by Galerkin-type methods with finite element techniques, Newton iteration, parametric continuation for mapping of the solution space, and integration in time with differential-algebraic equations’ solvers. The stability of the steady-state solutions, which leads to eigenanalysis, as well as their response to small sinusoidally forced disturbances, is also important. To obtain comprehensive results, the basic problem must be solved many times; this demands the speeds offered by the high-end workstations and massive parallelization capabilities of the Supercomputing Institute.

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- Jianping Zeng, Graduate Student Researcher
Michael Tsapatsis, Principal Investigator
Simulations of Diffusion and Gas Transport

These researchers are using the Supercomputing Institute for two projects. Both of the projects use Monte Carlo (MC) simulations to gain insight into the mechanisms that occur during the aging and coalescence of zeolite nanoparticles. In order to produce zeolite nanoparticles with a controlled size distribution, the nucleation and growth of zeolite nanoparticles must be better understood in order to optimize synthesis conditions. In the first project, Kinetic Monte Carlo (KMC) simulations of the aging and coalescence process are performed and the simulations provide predictions of the particle size distribution as a function of time. One advantage of using the KMC technique to study this system is that it is simple to change the aging mechanism and the coalescence kernel, which implicitly contains mechanistic information, in order to test different mechanistic hypotheses. The aging part of the KMC model has been validated with a kinetic model and the coalescence part of the KMC model has been validated with several known solutions of the Smoluchowski equation.

In the second project, MC simulations are used to analyze Small-Angle X-ray Scattering (SAXS) experimental data. The MC simulations produce pair distance distribution functions (PDDF) and scattering curves that can be compared to SAXS experiments. Comparing the simulations and experiments provides insight into the size, shape, and particle size distribution of zeolite nanoparticles.

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Renata M. Wentzcovitch, Fellow

Theory of Materials at High Pressure and Temperatures

Research by the Wentzcovitch group has shown that high pressure and temperature elasticity is no longer a theoretical challenge. They have calculated the full elastic constant tensor of MgSiO₃-perovskite, the most important lower mantle phase. This has allowed them to calculate seismic wave velocities of this mineral and address fundamental questions regarding the temperature and composition of the lower mantle. The group is now expanding its investigations to other mantle minerals, ices, and materials used as high-pressure standards (e.g., gold, platinum, NaCl, MgO, etc.).

This group also investigates the elasticity and vibrational/thermodynamic properties of ordered structures of ice. This information is critical to establishing a basis for understanding pressure-induced amorphization in H₂O-ice.

The researchers are also concerned with the magnetic state of materials. Their main interest is the investigation of conductive materials where there exists a strong relationship between magnetism and transport. They are particularly interested in potentially novel half metal systems, such as CoS₂.

Research Group and Collaborators
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Yonggang Yu, Graduate Student Researcher
Elizabeth A. Amin, Principal Investigator
Novel Descriptor-Based Bioinformatics Modeling of Zinc-Binding Metalloproteins

Zinc metalloproteins play critical roles in many different pharmacological processes and have been identified as important drug targets. Examples include the matrix metalloproteinases (MMPs), insulin, metallothionein, *Escherichia coli* deoxyribonucleic acid topoisomerase, zinc-finger proteins and anthrax toxin lethal factor (LF). Inaccurate force-field representation of active-site metal environments has long hampered metalloprotein modeling, however, and has greatly complicated the computational drug-design process. This project focuses on the design of new parameters for zinc-binding proteins and, by extension, other metal-binding macromolecules. These parameters are being implemented as part of a new force field for metalloprotein simulations; the researcher is also creating data-mining algorithms that add computational characterization of metalloenzyme active sites to a federated database structure to facilitate data correlation and analysis.

This researcher uses Supercomputing Institute resources to analyze zinc model compounds with various levels of density-functional theory, as well as to design three new sets of natural-product-based MMP-3, MMP-8, and MMP-13 inhibitors for use as potential antirheumatic therapeutics. She is also investigating protein-protein interactions involved in tissue remodeling and extracellular matrix protein degradation.

George Barany, Principal Investigator
Design and Characterization of Biomolecules From Protein Core Modules to Cyclic Peptidic Nucleic Acid

The engineering of stable folded and functional biomolecules has recently attracted much research attention. Within this field, the Barany group is particularly interested in the design, synthesis, and characterization of protein core modules and cyclic peptidic nucleic acid (PNA). In globular proteins, core motifs can be identified and their elements can be combined in suitable peptides to construct native-like molecules. The designed peptides consist of core elements from bovine pancreatic trypsin inhibitor and/or B1 immuno-globulin binding domain linked by natural or designed sequences, and they contain a strategically placed cross-link to limit conformational space to more collapsed conformations. The studies carried out by these researchers exemplify new approaches and are leading to significant and general-ized insights that contribute to the protein-folding problem.

Cyclic PNAs are promising candidates for generating nanotubular structures, which can be useful as new catalysts, wire conductors, or drug transport systems. The Barany group is designing cyclic PNAs by means of molecular modeling studies.

Research Group
Sharon Gazal, Research Associate
Mian Liu, Research Associate
Dan Mullen, Research Associate
David A. Blank, Principal Investigator
Calculations of Molecular Structures, Energetics, and Dynamics for Comparison With Ultrafast Spectroscopy

The Blank group continued their investigations into the dynamics of various molecular species in response to electronic excitation. They are working with coumarin dyes, 1,5-disubstitute anthraquinones, and Ru(II) transition metal complexes. They are primarily interested in computing the dipole moment, polarizability, and ionization energy of these compounds in both their ground and excite electronic states. These calculations aid in understanding the energetic solute-solvent coupling that the researchers investigate experimentally.

The researchers plan to continue calculations on water-coumarin complexes and begin calculations on Ru(II) transition metal complexes to start modeling both types of complexes at surfaces such as TiO₂. In addition, the researchers are beginning experiments on protein-solute systems and are pursuing the use of molecular dynamics simulations to model the dynamics of protein-solute complexes.

Research Group
Sarah Schmidtke, Graduate Student Researcher
David Underwood, Research Associate
Nathan Wells, Graduate Student Researcher
The Cramer group uses supercomputing resources to stress the limit of present-day computational chemistry tools in order to examine large systems of relevance to one or more areas in chemistry. In general, they focus on systems containing unpaired electrons (because the solution of their electronic structure is more complicated) or on systems containing multiple metal atoms or of a very large organic nature (because they are difficult to deal with without supercomputing resources). Furthermore, the group tries to include any condensed-phase effects, such as solvation, into the calculations in order to make them more relevant to experimental observations.

These researchers are working on several specific projects. They include: including condensed-phase effects in quantum chemical calculations; calculation of accurate multiplet splitting in open-shell systems; characterization of organometallic systems with respect to structure and reactivity; and modeling the reactive conversion of crystalline gallazanes to gallium nitride.

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Nathaniel Woodrum, Graduate Student Researcher
Mark D. Distefano, Principal Investigator

Design of Intestinal Fatty Acid Binding Protein Analogs

The Distefano group has extensively used Supercomputing Institute resources in modeling mutant intestinal fatty acid binding proteins with several different analogs attached (pyridoxamine, flavin, fluorescein, etc.). They are continuing to model these proteins with many more diverse analogs. They are also modeling a 16-mer peptide with many of the same analogs.

Craig J. Forsyth, Principal Investigator

Conformation and Configuration of Complex Natural Products

These researchers are using the Basic Sciences Computing Laboratory for their project to determine the conformation and configuration of complex natural products. They are particularly studying the marine toxin azaspiracid (AZA). The researchers use GAUSSIAN 03 to calculate free energies (gas phase) for the C1–C20 domain of AZA and its epimers. Comparing the difference in energies to account for the anomeric effect and the conformational effects will guide the selection of synthetic targets.

The group is also using solvation modeling to investigate the structures of solvents, especially MeOH and CHCl₃.
Jiali Gao, Fellow

Computer Simulation of Chemical and Biochemical Interactions

The Gao group continued their multi-faceted research concerning the dynamics and mechanism of enzyme reactions, the structure and interactions of proteins, the simulation of trajectories on protein dynamics, and solvent effects on chemical reactions and interactions in condensed phases. Their approach is based on statistical Monte Carlo and molecular dynamics (MD) simulations, making use of combined quantum mechanical and molecular mechanical (QM/MM) potentials.

The group is involved in several project areas. These include: MD simulations of enzymatic reactions; developing a simulation system to understand protein diffusion processes in a cellular environment; studying the importance of dynamic effects of enzyme catalysis; and the development of novel computational techniques in combined QM/MM calculations and applications to modeling solvent effects on SN1 and SN2 reactions and the contributions from equilibrium and non-equilibrium solvation.

Research Group and Collaborators

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Jiali Gao, Fellow  
Jeffrey T. Roberts, Co-Principal Investigator  
Computational Chemistry at the Research Site for Educators in Chemistry at the University of Minnesota

The Department of Chemistry at the University of Minnesota has received a National Science Foundation grant to establish a Research Site for Educators in Chemistry (RSEC). The focus of this RSEC is interdisciplinary research in chemical biology, computational chemistry, environmental chemistry, and materials chemistry. Specific areas of research include: alkyl effect on reaction rates of hydrogen atoms with alcohols in gas and solution phases; alkoxy and alkylperoxy radicals formed in the atmosphere; complexes of substituted 1,8-naphthyrides; condensed phase effects on the structure and bonding of nitrile donor-acceptor complexes; mixed aggregates of lithium compounds; and electrochemiluminescence reactions of organic molecules in the solution phase. This work is being performed in collaboration with researchers from Drake University, the University of St. Thomas, the University of Wisconsin–Eau Claire, Macalester College, Fisk University, and Illinois College.

Collaborators
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Wayne L. Gladfelter, Principal Investigator
Mixed Fluid Dynamics and Chemical Reaction Modeling of a Combinatorial Low-Pressure Chemical Vapor Deposition Reactor

This project models the behavior of a low-pressure chemical vapor deposition (LPCVD) reactor that is used for combinatorial LPCVD experiments. The researchers used CFD-ACE+ to create a computational model of the physical reactor and to create a three-step surface chemical reaction mechanism using parameters from literature and experimentation. The model includes: transport and chemical properties for the molecular species used in the model; gas-phase reaction chemistry, to increase the correlation of predicted to experimentally measured deposition rates; and kinetic parameters for the gas-phase reactions, which are taken directly from experimental work done in the Gladfelter laboratory. The group is exploring the difference between gas-phase and surface reaction chemical models. Computational modeling of the LPCVD process will help elucidate the chemistry involved in the formation of thin films from organometallic precursors under moderate vacuum. The accuracy of the model is being confirmed by direct comparison of theoretical deposition rate profiles to the physical deposition rate profiles in the LPCVD reactor.

Research Group
Tyler Moersch, Graduate Student Researcher
Amber Runge, Undergraduate Student Researcher

Marc A. Hillmyer, Principal Investigator
Monte Carlo Simulations of Polydisperse Diblock Copolymers

Diblock copolymers consist of two chemically distinct polymer chains tethered together at one end by a covalent bond. Current understanding of block copolymer melts has been based on the results of mean field theory (MFT). MFT is, however, least accurate in the region of the block copolymer phase diagram near the order-disorder transition (ODT). Predictions based on MFT about the effects of a broad chain length distribution in this region of the phase diagram do not agree with experimental results for asymmetrical diblock copolymers. Monte Carlo simulations offer another method by which the effects of polydispersity index on block copolymer melts may be examined. This project uses Monte Carlo simulations of diblock copolymer systems with a broad distribution of chain lengths to examine the change in the location of the ODT as the distribution in chain lengths is independently broadened [(N)ᵢ constant]. The researchers are also examining the effects of this on the morphology and periodicity of the microphase separated structures.

Research Group
Nathaniel Lynd, Graduate Student Researcher
Nuclear magnetic resonance (NMR) spectroscopy is the single most powerful spectroscopic tool for determining the three-dimensional structure (i.e., stereostructure consisting of the relative and absolute configurations of the molecule) of organic compounds, including the important subset of natural (and unnatural) products having useful biological activities. The precise stereostructure imparts the biological function to such compounds. Thus, methods for determining their unambiguous stereostructure are of considerable value. The Hoye group has begun to develop new methodologies that involve the comparison of computed with experimental spectroscopic parameters. The two principal features at the very core of nearly all NMR spectroscopic analyses are chemical shifts and coupling constants ($J$). The researchers have had experience and success applying $J$s to interesting structural problems, and are now beginning to exploit chemical shifts. The new hypothesis is that comparison of computed chemical shifts for each member of a family of possible stereoisomers with the experimental chemical shifts for a single stereoisomer for which the relative configuration is not yet known, will allow the configuration of that compound to be deduced with confidence.

Research Group
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Jizhou Wang, Graduate Student Researcher
Jennifer Werness, Undergraduate Student Researcher
name withheld, Graduate Student Researcher
Peng Zhao, Graduate Student Researcher
Richard P. Hsung, Principal Investigator

Synthetic Methodologies

These researchers have developed a formal [3+3] cycloaddition reaction that can construct complex dihydropropyran and dihydropyridinyl heterocycles from simple α,β-unsaturated iminiums and 1,3-dicarbonyl equivalents such as vinylogous amides or others. This reaction proceeds through a tandem process consisting of a Knoevenagel condensation followed by a 6π-electron electrocyclic ring-closure of the 1-oxa- or 1-aza dienes. The net result of this step-wise or formal reaction is the formation of two σ-bonds along with a new stereocenter adjacent to the heteroatom. The new stereocenter can be controlled using chiral vinylogous amide, and an intramolecular variant of this reaction has also been recently developed. The researchers are applying this strategy towards the synthesis of a variety of natural products.

The researchers are also examining two unique classes of organic building blocks or organic synthons: chiral allenamides and ynamides. These electron-deficient chiral variants of allenamines and ynamines are thermally more stable and experimentally easier to handle than traditional allenamines and ynamines, and can be synthetically more useful.

Research Group
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Kevin Tung, Undergraduate Student Researcher
Xuejun Zhang, Graduate Student Researcher
Yanshi Zhang, Graduate Student Researcher

Steven R. Kass, Associate Fellow

Understanding Organic Systems via Molecular Orbital Calculations

The Kass group is continuing to carry out *ab initio* molecular orbital and density functional calculations on a variety of chemical systems. The researchers pay particular attention to zwitterions (critical species in biological processes), reactive intermediates (key intermediates in numerous chemical and industrial processes), and antiaromatic compounds (potential substrates for the design of novel materials). These results aid in the design and interpretation of experimental data.

Research Group and Collaborators
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ZhiXin Tian, Research Associate
Doreen G. Leopold, Principal Investigator
Studies of Neutral and Anionic Coordinatively Unsaturated Metal-Ligand Complexes

These researchers are performing density functional theory (DFT) studies of coordinatively unsaturated metal-ligand complexes, with a current emphasis on neutral and anionic \( M(C_nH_{2n}) \) species, where \( M = \text{vanadium (V)} \) or niobium (Nb) and \( n = 2, 4, \) or 6. They have studied these complexes by anion photoelectron spectroscopy, and supplementing these data with calculations enables the extraction of more detailed information. Recent work has focused on DFT studies of neutral and anionic \( \text{VC}_6H_6 \) and \( \text{NbC}_6H_6 \) and their perdeuterated isotopomers, with the goal of identifying the observed isomers and electronic states of these Group 5 transition metal complexes. The researchers compare calculated electron affinities, electronic state energies, vibrational frequencies, and deuterium shifts for the ground and low-lying excited electronic states with the spectroscopic data to help identify the geometric and electronic structures of the observed states.

Research Group
Stephen Richard Miller, Graduate Student Researcher

Kenneth R. Leopold, Associate Fellow
Computational Studies of Molecular Complexes

This group is carrying out quantum chemical calculations on acid-base complexes and microsolvated acid-base complexes. These studies are part of a continuing effort to elucidate the effects of near-neighbor interactions on chemical reactions and, as such, constitute fundamental investigations related to solvation. Supercomputing Institute resources enhance ongoing microwave spectroscopic experiments by providing information about bond energies and electronic structure that is not otherwise available from experiments. Thus, the combination of theory and experimental spectroscopy provides a particularly complete picture of this group’s systems of interest, one that could not be obtained from either theory or experiment alone. Ongoing and future work involves calculating barriers to internal motion in molecular complexes and studying systems containing an open-shell moiety.

Research Group
Carolyn Brauer, Graduate Student Researcher
Matthew Craddock, Graduate Student Researcher
Galen Sedo, Graduate Student Researcher
Kent R. Mann, Principal Investigator

Conformational Isomerization in Quinoid Oligothiophene Molecules

These researchers have prepared thiophene oligomers for use as semiconducting materials in both n-type and ambipolar thin-film transistors. To better understand structure-property relationships, they have focused on one group of oligothiophene molecules with a quinoid structure. X-ray crystallographic studies of this family of molecules have shown that they adopt a trans conformation (with respect to the thiophene rings) in the solid state. Interestingly, variable-temperature $^1$H nuclear magnetic resonance (NMR) results have shown that these molecules undergo conformational isomerization at relatively low temperatures.

This project has three parts: using NMR software to predict the chemical shifts of various quinoidal isomers; using the software package MATHEMATICA to set up and solve the secular equations for the time-dependent NMR Hamiltonian; and also using MATHEMATICA to extract the imaginary part of the NMR lineshape function so that non-linear curve fitting of the experimental spectra can be accomplished.

Research Group
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Daron Janzen, Graduate Student Researcher
Kari Mitchell, Graduate Student Researcher

Kristopher McNeill, Principal Investigator

Computational Studies in Environmental Chemistry

These researchers have begun taking a computational chemistry approach to their research into chemical problems of environmental interest. They have used nuclear magnetic resonance software available through the Supercomputing Institute and plan to undertake electronic structure calculations using semi-empirical and $ab$ initio methods. The group is currently working on two project areas, chlorocarbon pollution and pharmaceutical pollutants in surface waters.

Research Group
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Ann McNally, Graduate Student Researcher
Alicia Peterson, Graduate Student Researcher
Kris Wammar, Research Associate
Jeff Werner, Graduate Student Researcher
Karin M. Musier-Forsyth, Principal Investigator
Homology Modeling of the Escherichia coli Proline tRNA Synthetase; Nucleocapsid Protein Interaction

These researchers are working to develop a three-dimensional homology model of the Escherichia coli proline transfer ribonucleic acid synthetase (ProRS). Using this new model, they plan to study interactions of insertion domain with the catalytic site residues in the presence of substrate, and to dock modified proline analogs onto the active site of the enzyme and perform molecular dynamics (MD) simulations to identify different side-chains of ProRS that are critical for substrate binding. They are also performing computational studies using molecular docking and MD simulations to study the editing active site of E. coli ProRS.

Another project studies human immunodeficiency virus (HIV)-1 nucleocapsid protein (NC), a 55 amino acid protein involved in the various stages of the viral life cycle, like virus packaging and replication. The focus of this project is to study the interactions of NC with trans-activation response (TAR) ribonucleic acid at the molecular level. The group has model the NC-TAR complex and is carrying out MD simulations with this model.

R. Lee Penn, Principal Investigator
Elucidating the Link Between Reactivity and Nanoparticle Size, Shape, and Microstructure

The main objectives of the Penn group are to develop a set of guiding principles for the controlled growth of crystalline nanoparticles and to elucidate the link between microstructure and chemical reactivity. They are using the Scientific Development and Visualization Laboratory to simulate high-resolution transmission electronic microscopy images, simulate powder x-ray and electron diffraction patterns, perform Rietveld refinements, model nanoparticle aggregation as a function of orientation, and use computational chemistry software. This research is at the intersection of materials chemistry and environmental chemistry. Much of the work focuses on solid state materials commonly found in the environment, such as iron oxide nanoparticles, and electron transfer reactions between those materials and naturally occurring and anthropogenic chemicals.
J. Ilja Siepmann, Fellow
Molecular Simulations of Phase Equilibria and Development of Transferable Force Fields and Efficient Monte Carlo Algorithms

The Siepmann group's research can be divided into two main areas: particle-based simulations of phase equilibria and development of force fields and algorithms.

In the study of phase equilibria, recent work has focused on retention processes in chromatography, solvation in supercritical fluids, structure and solvation in micellar surfactant systems, liquid and solid nucleation from vapor phases, polymorphism and solvate formation for drug molecules, and prediction of phase equilibria from first principles. Accurate predictions of phase equilibria and other thermophysical properties of complex chemical systems are of great fundamental and practical importance.

The second broad area of research concerns transferable force fields and efficient Monte Carlo algorithms. Some recent projects in this area include parallel tempering Gibbs ensemble simulations, density-of-states methods applied to fast calculations of nucleation free energy barriers, and development of efficient Monte Carlo algorithms for the computation of phase equilibria from first principles.

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Investigations Into Acyl-CoA Dehydrogenases

The acyl-CoA dehydrogenases are homotrameric flavoenzymes and catalyze the first step of the β-oxidation cycle—the α,β-dehydrogenation of fatty acid acyl-CoAs to their corresponding enoyl-CoA forms. The binding of substrates to acyl-CoA dehydrogenases enzymes causes large changes in the redox potentials of both, resulting in thermodynamically favorable electron transfer. The causes of such large thermodynamic change are not understood. Crystallographic studies have shown that, upon substrate binding, water molecules are ejected from the active site and two hydrogen bonds form to the carbonyl of the substrate, resulting in polarization; finally, two glutamic acid groups move. The extent of polarization plays a significant role in the catalytic electron transfer. These researchers are extending combined quantum mechanical and molecular mechanical simulations to free energy perturbation analysis of these enzymes (medium- and short-chain) in their free and substrate/product bound states as well as their mutants. Analysis of the system will further improve understanding of the role of these residues in the electron transfer process. The researchers are also performing detailed, bioinformatics statistical correlation analysis of the sequences as a separate method of investigating the question of mutations of residues.

Research Group
Sudeep Bhattacharyay, Research Associate

T. Andrew Taton, Principal Investigator

Complementary Assembly of Hard and Soft Nanomaterials

These researchers use mesoscale, molecular dynamics simulations to investigate how nanostructured soft materials such as block copolymers and liquid crystalline polymers respond to the presence of inorganic nanostructures such as nanoparticles and nanorods. The group is using the Medicinal Chemistry/Supercomputing Institute Visualization-Workstation Laboratory and the Scientific Development and Visualization Laboratory for this research.

Research Group
Castro Laicer, Graduate Student Researcher
The Truhlar group conducts research in the following areas: the structure, dynamics, and thermodynamics of few-body systems; the thermal and photochemical reaction dynamics of organic, metal-organic, and enzymatic systems; the simulation of the reactivity of nanoparticles; catalysis; new methods for electronic structure calculations; and the influence of solvation in ordinary liquids and supercritical liquids on structure and dynamics. This research utilizes quantum mechanical, quantum statistical, semiclassical, and classical mechanical methods. The researchers use both serial and parallel computer codes designed to run on the supercomputers; most of these have been developed by this group, but they also use electronic structure and molecular modeling packages that they have specially modified for their work.

**Research Group and Collaborators**

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**Research Group and Collaborators (cont.)**

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Structure Determination of Protein Structures Using Residual Dipolar Couplings

The goal of this project is to develop computational methods for rapid determination of the high-resolution structure of proteins using residual dipolar couplings (RDCs). Nuclear magnetic resonance (NMR) is the only spectroscopic method able to obtain atomic resolution information about biomacromolecules in solution near physiological conditions. Nonetheless, the classical methods used for structural determination by NMR pose many challenges. In particular, spectral assignments and structure calculations make the whole process very time-consuming. The recent introduction of RDCs has opened new avenues to structure determination by NMR. The incorporation of these new data into structural refinement software has made it possible to obtain global protein folding faster and more accurately.

The immediate goal of this project is to use only RDCs to calculate protein folds. The long-term goal is to devise a robust computational protocol for determining the structure of both soluble and membrane-bound proteins based only on backbone RDCs. This will have a major impact on proteomics, where high-throughput protein structure determination is a prime target.

Research Group
Becky Eggimann, Graduate Student Researcher
Alessandro Mascioni, Research Associate
Jamillah Zamoon, Graduate Student Researcher

Darrin M. York, Associate Fellow

Multiscale Quantum Models for RNA Catalysis

This project involves concurrent development and application of theoretical methods to model the molecular mechanisms of ribonucleic acid (RNA) catalysis. The particular focus of the project is on five main areas that integrate method development and application. These include: development of many-body force field methods for molecular simulation; construction of a database of quantum calculations for RNA catalysis; design of new semiempirical Hamiltonian models for phosphoryl transfer reactions; application of hybrid quantum mechanical/molecular mechanical methods to phosphate hydrolysis reactions in enzymes and ribosomes; and development and application of linear-scaling methods for deoxyribonucleic acid and RNA systems.

The application focus of this project is currently on the study of non-enzymatic transphosphorylation reactions in solution, and on three prototype ribozyme and enzyme systems, namely, the hammerhead and hairpin ribosomes and the β-glucosidase enzyme. The researchers hope to provide new insight into nucleic acid structure and stability and shed light into the molecular mechanisms of RNA catalysis.

Research Group and Collaborators
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Adam Moser, Graduate Student Researcher
Kwamgho Nam, Graduate Student Researcher
William A. Arnold, Principal Investigator

A Computational Chemistry Study of the Reduction of Disinfection Byproducts

When drinking water is disinfected by chlorination, a large number of small halogenated organics, including trihalomethanes, haloacetic acids, halonitromethanes, haloketones, and haloacetonitriles, are produced. Many of these compounds are known or suspected carcinogens. This researcher is studying the chemical reduction reactions that may be important in the fate of these compounds. There is little available information about potential reaction products, and no parameters exist that could be used to develop predictive linear free energy relationships. The goal of this project is to conduct a computational chemistry study to investigate potential mechanisms and pathways of disinfectant byproduct transformation in aqueous solution.

Steven L. Crouch, Principal Investigator

Viscoelastic Analysis

In order to deal with the problem of an infinite isotropic viscoelastic plane containing an arbitrary number of circular holes and elastic inclusions, these researchers have developed a direct boundary integral approach with time stepping. They have verified their approach for the simple case that only includes one circular elastic inclusion, by comparing it to the available analytical solution. In order to test the approach for the large-scale problem with multiple circular holes and inclusions, the researchers are using other numerical methods to carry out the comparison computation. This requires the use of Supercomputing Institute resources. The researchers also plan to extend their approach to consider varying loading and a finite exterior boundary for the viscoelastic plane–holes–elastic inclusions coupling system.

Research Group and Collaborator
Yun Huang, Graduate Student Researcher
Sonia Mogilevskaia, Faculty Collaborator
Hamid Sadrzade, Graduate Student Researcher
Robert J. Dexter, Associate Fellow

Finite-Element Modeling of Structures

The Dexter group was involved in a number of projects investigating metal fatigue in a variety of structures. These projects included: investigating the effectiveness of adhesively bonded retrofits on out-of-plane distortion-induced fatigue cracks; modeling ductile tearing in high-performance steel; and studying fatigue strength of cantilevered traffic signs, signals, and lights used in the state of Minnesota. The researchers used the supercomputers to perform finite-element modeling, which supplemented their experimental work in these areas.

Robert J. Dexter passed away on November 16, 2004. He had been a principal investigator of the Supercomputing Institute since 1997 and was selected to be an Associate Fellow in 2003. The staff and researchers of the Supercomputing Institute extend their deepest condolences to the Dexter family.

Catherine W. French, Principal Investigator
Carol K. Shield, Co-Principal Investigator

Behavior of an Integral Abutment Bridge

The objective of this project is to investigate the behavior of integral abutment bridges. For the past five years, field data has been collected from an integral abutment bridge to investigate the effects of environmental and vehicle loading on the bridge response. This project consists of an analytical study to develop appropriate models to characterize the bridge behavior. A key component of this study is the soil-structure interaction caused by seasonal temperature changes and the integral effect of the whole bridge. This requires the use of the finite-element program ANSYS. The results of the analytical studies are compared to those of the experimental study.

Research Group and Collaborator
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Dan Krzmarzick, Graduate Student Researcher
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Carol K. Shields, Faculty Collaborator
David S. Peter, Graduate Student Researcher
Clifford Youngberg, Graduate Student Researcher

Research Group
Jimin Huang, Graduate Student Researcher
Bojan Guzina, Associate Fellow
Fast Solutions for Elastic-Wave Imaging of Solid Bodies

The aim of this research project is the development of an advanced analytical and computational framework for the rapid, three-dimensional imaging of subterranean obstacles using elastic (i.e., seismic) waves. It is an inverse scattering problem focused on resolving the location and shape of underground inclusions from non-invasive measurements performed on the group surface. The researchers are using the supercomputers to develop an efficient numerical technique for the inverse scattering problem that would account for the full three-dimensional nature of the induced wave propagation. In addition, they are systematically and rigorously tackling the associated forward scattering problem. An imaging approach for the rapid identification of subsurface obstacles using be especially useful in defense applications, oil prospecting, construction in urban areas, and medical diagnosis. Specific techniques used include the linear sampling method and the concept of topological sensitivity.

Raymond M. Hozalski, Principal Investigator
Modeling Perchloroethylene Degradation in Anaerobic Aquifers

These researchers have developed a finite-differences computer model to simulate tetra-chloroethylene (PCE) dechlorination in an anaerobic aquifer using a membrane-curtain permeable-barrier approach. One implementation of this approach might be to install woven gas-permeable hollow-fiber membrane fabric within a trench and supply H_2 gas to the membranes, from which it would be transferred directly to the groundwater without causing bubbles. This would stimulate growth of H_2-utilizing dechlorinating bacteria.

One potential obstacle is that H_2-utilizing dechlorinators must compete with other H_2-utilizing microbial populations. Initial modeling work assumed that H_2-utilizing methanogens would be the primary competing population. Soil column studies, however, have indicated that the competing population may actually be H_2-utilizing homoacetogens. The researchers have modified their model to incorporate H_2 utilization by homoacetogens and are running simulations to test whether H_2-derived acetate can serve as a significant electron donor source for downgradient dechlorinator populations.

Research Group
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Sylvain Nintcheu, Research Associate

Research Group
Lee Clapp, Research Associate
Balagopal Dharanidharan, Graduate Student Researcher
Joseph F. Labuz, Associate Fellow

Displacement Measurement With Electronic Speckle Pattern Interferometry

Electronic speckle pattern interferometry (ESPI) is an optical method that can measure surface displacements of a specimen. Illumination of an optically rough surface causes interference of scattered light, which produces visible speckles. As a material is stressed, its surface displaces and changes the observed speckle pattern. By comparing two slightly different speckle images, it is possible to obtain fringes, which represent contours of equal surface displacement. The method is advantageous due to the sensitivity with which the displacements can be measured and the ability to capture the full displacement field over an illuminated region.

These researchers are using the Scientific Development and Visualization Laboratory for their work with ESPI. They are observing and measuring displacements in brittle materials such as rock. Ultimately the ESPI measurements could be combined with microcrack locations obtained from acoustic emissions to gain valuable insight into failure of a brittle material.

Mihai Marasteanu, Principal Investigator

Low-Temperature Cracking of Asphalt Concrete Pavements

Good fracture properties are an essential requirement for asphalt pavements built in the northern part of the United States and in Canada, for which the prevailing failure mode is cracking due to low-temperature shrinkage stresses. This research group is investigating the use of the semicircular bend test to determine the low temperature fracture properties of asphalt mixtures. The complex geometry of the semi-circular bending specimen makes it hard to find the solution analytically. The researchers are using the finite element method to analyze the stress and strain status numerically. Current results show that a specimen with a thickness of 25 mm can be considered in a plane stress state. The arch effect in both notched and un-notched specimens generates a complex stress condition that makes the explanation of the failure strength measured with this geometry ambiguous. The laboratory results show a different trend of fracture toughness and fracture energy when the material changes. These results have been compared with the results from other software or computed by other researchers. Further study focuses on the simulation of crack propagation with a cohesive crack model.
Arturo Schultz, Principal Investigator  
Catherine W. French, Co-Principal Investigator  
Stability of Prestressed Concrete Through-Girder Pedestrian Bridges Under Lateral Impact

Prestressed concrete through-girder pedestrian bridges, in which two prestressed bridge girders support a deck on the bottom flanges, are easy to construct, economical, and durable. These researchers are investigating two safety issues regarding these bridges. The first is the ductility of the prestressed concrete girders. These girders are long-span members and require a large amount of prestressing steel to prevent sagging of the bridge under its own weight. As a result, the girders do not meet current ductility requirements in the design specifications promoted by the American Association of State Highway and Transportation Officials. The researchers are investigating the ductility and strength characteristics of prestressed concrete bridge girders analytically and have proposed modifications to correct for errors.

Research Group  
Eray Baran, Graduate Student Researcher

Michael J. Semmens, Principal Investigator  
Behavior of Aerated Membrane-Supported Biofilms in Crossflow

This project extends an existing MATLAB model that examines the growth of biofilm on parallel hollow fiber membranes. The membranes are aerated and supply the biofilm with oxygen. Wastewater flows between the membranes and a biofilm grows on them. This biofilm grows together since the membranes are closely spaced to each other. The result is a continuous bacterial biofilm that can provide a high level of treatment in a very short detention time. This system has great practical application in wastewater treatment. This study will allow the researchers to explore the effects of multiple bacteria and more realistic conditions. The researchers are using the Basic Sciences Computing Laboratory for this project.

Research Group  
Ali Reza Ahmadi Motlagh, Graduate Student Researcher
Charles C. S. Song, Fellow
Large-Scale Computation of “Large Re–Small M” Industrial and Environmental Flows

This group continues to develop large-scale flow computation methods and computer codes for scientific and engineering applications. They deal with complex industrial and environmental subsonic turbulent flows. The weakly compressible flow equations are solved with the finite volume method.

Recent work has focused on developing computer codes for unsteady cavitating flows with and without ventilation. The group has developed a virtual single-phase approach for natural cavities with no ventilation and a two-phase approach for ventilated cavities. The group is now developing a two-phase approach for natural cavities occurring in water containing dissolved incondensable gas. In this model, water and water vapor are treated as virtual single-phase fluids following a reversible process while the dissolved gas follows an irreversible process. The researchers are also continuing their simulations of ventilated and non-ventilated cavitating flows, and are simulating interaction between micro-bubbles and small-scale turbulence for the purpose of drag reduction.

The code is also being used to simulate flow in a low noise cavitation tunnel to be built in South Korea. This includes the design of contraction, test section, diffuser, and turning vanes for good quality flow.

Research Group
Xiang Ying Chen, Research Associate
Jianming He, Research Associate
Qiao Qin, Graduate Student Researcher

UM TC–St. Anthony Falls Laboratory

Roger E. A. Arndt, Principal Investigator
Partially and Fully Cavitating Flows

Cavitation is an important consideration in a variety of important engineering applications. As the performance of pumps and turbines is increased and hydrofoil ships are designed for higher speeds, it becomes necessary to design lifting surfaces that can operate effectively in the cavitating mode. The Arndt group’s research indicates that sheet/cloud cavitation is a highly complex and very important subset of the overall problem. Their earlier work investigated the highly periodic formation of cloud cavitation that leads to a highly structured wake consisting of vortical clouds of bubbles. This phenomenon leads to unsteady lift that cannot be accurately predicted at this stage.

The group has now extended their research to include fully cavitating and ventilated flows. Their aim is to develop the computational tools to study a variety of cavitation problems. They are supplementing their computational efforts with detailed experimental work.

In a related project concerning microbubble drag reduction, the researchers are developing direct numerical simulation tools to simulate the interactions between small-scale turbulence and microbubbles.

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Efi Foufoula-Georgiou, Fellow
Stably Stratified Atmospheric Boundary-Layer Turbulence

Prediction of turbulent fluxes of heat, momentum, water vapor, and pollutants by weather and air-quality models is hindered by our limited ability to parameterize the subgrid-scale physics in strongly stratified stable boundary layers (SBLs). This is a consequence of the intrinsic complexities in the dynamics (e.g., occurrences of intermittency, Kelvin-Helmholtz instability, gravity waves, low-level jets, meandering motions, etc.) and the peculiar nature of the turbulent transport and mixing in these flows. The overall goal of this project is to better understand and characterize the dynamics and subgrid-scale physics of the stably stratified atmospheric boundary layer turbulence. Such an understanding will improve the ability to parameterize these processes in low-resolution weather and air-quality models. The specific goals of the project are to: improve large-eddy simulation (LES) as a tool to study land-atmosphere exchange physics; evaluate the capabilities of new-generation LES schemes in simulating strongly stratified atmospheric boundary layers; reconcile the outstanding issues related to the SBL turbulence research; characterize the SBL turbulence via a suite of mathematical approaches and LES; and develop and improve turbulence and surface flux parameterizations for regional and large-scale numerical weather prediction models.

Research Group
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Rohit Gupta, Graduate Student Researcher
Daniel Harris, Research Associate
Deborah Nykanen, Graduate Student Researcher
Jamie Smedsmo, Graduate Student Researcher
Venugopal Vuruputur, Research Associate

Miki Hondzo, Principal Investigator
John S. Gulliver, Co-Principal Investigator

Computer Modeling of Bubbly Two-Phase Flows in Aerated Reservoirs

These researchers have developed a six-equation, two-fluid (Eulerian) model for bubble plumes. The models simulate the flow in aerated tanks that include an overlying air layer to model the deforming free surface. The top of the air layer is defined as a constant pressure outlet boundary. This treatment of the free surface overcomes ambiguity found in previous models. The model results compare satisfactorily with four independent sets of experiments that include detailed measurements in small tanks, a bubble column that exhibited oscillatory behavior, and a 9.14-meter-deep aerated tank. The comparison between predictions and experimental data include water and air phase velocities, water turbulent kinetic energy, and air volume fraction.

Future work involves development of the model water quality component through user-defined functions. The U.S. Army Corps of Engineers is planning the construction of the McCook Reservoir to store combined sewer overflows in Chicago, and the scale of that reservoir is beyond the existing technology of aeration systems. The design will be supported by a combination of laboratory experiments and computational modeling.

Collaborator
Hector Bravo, Department of Civil Engineering and Mechanics, University of Wisconsin, Milwaukee, Wisconsin
Fernando Porté-Agel, Associate Fellow

Large-Eddy Simulation of the Atmospheric Boundary Layer

Researchers use large-eddy simulation (LES) to study the turbulent transport of heat, momentum, water vapor, and pollutants in the atmospheric boundary layer. LES is the state-of-the-art numerical technique to calculate the unsteady three-dimensional transport in turbulent flows. Until now, LES has not been sufficiently faithful to the physics of the atmospheric boundary layer, the main weakness being associated with the limited ability to account for the dynamics that are not explicitly resolved in the simulations. The main goal of this research is to address those limitations in order to make LES a more reliable tool to study land-atmosphere exchange processes. In particular, the objectives are: to develop and implement better subgrid-scale models to accurately account for the effect of the non-resolved scales (smaller than grid size) on the dynamics of the resolved turbulent fields; to develop improved boundary conditions for the simulations, based on results from wind tunnel experiments as well as numerical experiments; and to increase the resolution and speed of the simulations through the use of parallel computing resources.

Research Group and Collaborators
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Jean-Francois Vinuesa, Supercomputing Institute Research Scholar
Feng Wán, Graduate Student Researcher
Kyung Mi Won, Research Associate

Heinz G. Stefan, Associate Fellow

Simulations of Seasonal Water Quality in Freshwater Systems

This research group has developed deterministic, unsteady, year-round lake water quality and fish habitat simulation models, and they are expanding, validating, and applying them. These models simulate water temperature and dissolved oxygen distributions in various classes of lakes, rivers, and streams, including both open-water conditions and the ice-cover period. The simulations can be made for continuous long-term periods in all regions of the contiguous United States. Current projects include simulations of the distribution of wind stress over a lake surface, statistical analysis of stream temperatures, analysis of lakes with submersed plants, and diffusive boundary layers at the sediment/water interface.

Research Group and Collaborator
Travis Bogan, Graduate Student Researcher
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James Thill, Graduate Student Researcher
Qin Qian, Graduate Student Researcher
Jesus Zepeda-Arce, Graduate Student Researcher
David H. Du, Fellow

Address Caching in Peer-to-Peer Overlay Networks

Dynamic address caching in peer-to-peer defines shortcuts through the overlay that shortens the object lookup path to the requested destination and increases overlay network connectivity. These researchers are investigating how to optimize the caching based on limited cache space at each node.

Research Group and Collaborator
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Dingshan He, Graduate Student Researcher
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Keqiang Wu, Graduate Student Researcher
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George Karypis, Principal Investigator

Scalable Algorithms for Graph Partitioning and Data Mining

This project focuses on developing scalable algorithms for multi-constraint and multi-objective graph partitioning and for mining large scientific datasets. This work builds on the researchers’ earlier research on developing highly effective and scalable graph partitioning algorithms and on developing clustering algorithms for high-dimensional datasets and scalable pattern discovery algorithms.

Research Group
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Huzefa Rangwala, Graduate Student Researcher
Nikil Wale, Graduate Student Researcher
Ying Zhao, Graduate Student Researcher
Vipin Kumar, Fellow

High-Performance Data Mining

The objective of this research is to develop novel, high-performance data mining algorithms and tools for mining large-scale datasets that arise in a variety of applications. Some examples are: gigabyte datasets collected by Earth-observing satellites that need to be processed to find potentially useful patterns and to better understand global-scale changes in biosphere processes; data generated by scientific simulations that can be used to gain insight into the underlying physical processes; data obtained through monitoring traffic networks to detect illegal network activities; collections of text and hypertext analyzed to extract relevant information; and large biological databases to analyze and discover models in order to better understand various biological processes underlying these databases. The key technical challenges in mining these datasets include: high volume, dimensionality, and heterogeneity; spatio-temporal aspects of the data; possible skewed class distribution; distributed nature of the data; and the complexity in converting raw collected data into high-level functions. High-performance data mining is essential to analyzing the growing amount of data and to provide analysts and domain scientists with automated tools that facilitate some of the steps needed for hypothesis generation and evaluation.

Research Group and Collaborators

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Michael S. Steinbach, Graduate Student Researcher
Hui Xiong, Graduate Student Researcher
Jieping Ye, Graduate Student Researcher
Pusheng Zhang, Graduate Student Researcher

Gopalan Nadathur, Principal Investigator

Higher-Order Metalanguages

This project involved the development of methods, formalisms, and languages to support the specification and realization of systems that manipulate complex syntactic objects such as formulas, proofs, programs, and types. Systems that have this character include compilers, program verification systems, theorem provers, logical frameworks, systems for symbolically manipulating mathematical expressions, and natural language recognizers. This researcher advocated a new higher-order approach for the representation of the various objects that need to be manipulated in these contexts; this approach has proved to be extremely useful. The researcher has developed a language called Lambda Prolog to support this approach to the programming of such systems. He used the Scientific Development and Visualization Laboratory to continue implementing the various new features embedded in the language and to develop improved compilation methods.
Haesun Park, Principal Investigator

Protein Secondary Structure Prediction

Gene expression data often contains missing expression values. Missing value estimation methods are needed, since many algorithms for gene expression data analysis require a complete matrix of gene array values. These researchers are developing imputation methods based on a least squares formulation to estimate missing values in gene expression data. These methods exploit local similarity structures in the data as well as the least squares optimization process. The group’s least-squares imputation method, LSimpute, represents a target gene that has missing values as a linear combination of similar genes. In comparisons with other methods, LSimpute is proving to be competitive in missing value estimation for deoxyribonucleic acid microarray gene expression data.

Research Group
Hyunsoo Kim, Graduate Student Researcher
Cheong Hee Park, Graduate Student Researcher

Yousef Saad, Fellow

Parallel Algebraic Recursive Multilevel Solvers and Applications

The goal of this research is to investigate robust preconditioning techniques for solving general large sparse linear systems with an emphasis on parallel techniques. The group’s first version of the package pARMS (Parallel Algebraic Recursive Multilevel Solvers), is available at www.cs.umn.edu/~saad. The researchers are continuing their investigations into the use of these techniques for solving linear systems that arise from realistic applications such as computational fluid dynamics and other application areas.

Recent activity by this group includes improving the performance of parallel iterative methods from the pARMS library and continuing to work on the Schur complement preconditioning. They have also proposed a theoretical analysis of automated multilevel substructuring that is based on a purely algebraic framework; the algebraic setting has allowed a number of promising improvements over the original method. Finally, the group has investigated the use of polynomial filtering techniques in information retrieval.

Research Group and Collaborators
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Yunkai Zhou, Research Associate
Richard M. Voyles, Principal Investigator

Three-Dimensional Radio Frequency Devices

These researchers are developing an automated process for assembling radio frequency devices. This would involve stacking multiple devices vertically on top of one another and using columns of solder for both mechanical stability and electrical conductivity. The researchers are using software available at the Basic Sciences Computing Laboratory for this project.

Research Group
Seth Hulst, Graduate Student Researcher

Jon B. Weissman, Principal Investigator

Community Services

The Community Services project is constructing next-generation middleware and systems software for dynamic grid services. A focus of this project is the definition of an adaptive grid service and a system architecture to support a fully dynamic grid service lifecycle. Dynamic grid services are an important substrate to support collaboration.

These researchers have deployed dynamic grid services onto workstations in the Scientific Development and Visualization Laboratory. In their grid testbed, the laboratory acts as a compute provider. The researchers have demonstrated this grid testbed to various visiting speakers and researchers.

Research Group
Darin England, Graduate Student Researcher
Tariq Islam, Graduate Student Researcher
Seonho Kim, Graduate Student Researcher
Nathan Mukesh, Graduate Student Researcher
Rahul Trivedi, Graduate Student Researcher
Pen-Chung Yew, Principal Investigator
Performance Analysis and Optimization of Molecular Dynamics Simulation Tools

These researchers are analyzing the performance bottlenecks of molecular dynamics modeling tools on a uniprocessor machine and on multi-processor cluster. The researchers compile tools using an open research compiler for an Itanium machine and monitor the performance issues. They then identify the potential bottlenecks and apply compiler optimization schemes.

Zhi-Li Zhang, Principal Investigator
Traffic Engineering With Interface-Specific Forwarding in an Internet Protocol Network

Traffic engineering in Internet Protocol (IP) networks aims at distributing data traffic to optimize some performance matrices (e.g., balance of load). Several factors contribute to the difficulty of traffic engineering. First, current routing protocol is restrained to the “shortest-path”-based mechanism. Secondly, current implementations of protocols support only equal-splitting among equally short paths.

This project explored the implications of an “interface specific forwarding” mechanism to improve traffic engineering. Initial results showed good potential for the group’s methods. The first simulations, however, were on relatively small-scale synthetic network topologies. The group used the supercomputers to perform more realistic, larger-scale simulations and large numbers of simulation runs.
This project investigates a new classification algorithm called Multiple Model Classification. This method is based on extending the support vector machine (SVM) approach to data mining applications concerned with both high generalization and good interpretability. The researchers are using Supercomputing Institute laboratories to perform empirical comparisons between the proposed approach and standard SVM classifiers for several real-life datasets.

**Research Group**
Tao Xiong, Graduate Student Researcher

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**Rhonda Franklin Drayton, Principal Investigator**

Analysis of an Aperture-Fed Patch Antenna and a Honeycomb Lattice Photonic Crystal

This group is using the Basic Sciences Computing Laboratory for two projects. The first uses Ansoft’s High Frequency Structure Simulator (HFSS) software package to analyze the performance of an aperture-fed patch antenna with a feed network on a porous silicon film. This architecture would allow a majority of a wireless communication system’s components to be fabricated on a single substrate, thus significantly reducing its overall size and cost. In addition, the aperture-fed design for the antenna would allow the most efficient radiation of the communication signal in such an architecture.

The second project uses HFSS to analyze a waveguide formed by a defect channel in a honeycomb lattice photonic crystal sandwiched between two metallic planes. The honeycomb lattice has a considerably wider bandgap than square and triangular lattices. Moreover, the size of the honeycomb lattice is smaller than that of other lattices. The honeycomb lattice can be used to fabricate highly integrated broadband devices.

**Research Group**
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Isaac Itotia, Graduate Student Researcher
Hosaeng Kim, Graduate Student Researcher
Ethan Miller, Graduate Student Researcher
Anand Gopinath, Associate Fellow
Modeling of Optical and Microwave Structures

These researchers are involved in several computer-modeling projects whose computational requirements necessitate use of the supercomputers. One involves modeling photonic band gap structures using finite difference time domain codes. For this project, the researchers designed colloidal opal and inverse opal structures with band gaps at a 1,550 nm wavelength, to coat optical waveguides. Another project examines electromagnetic scattering from thin films with identical particles forming a multilayer photonic band gap structure, and also from surface relief structures in the form of gratings. The group is writing codes based on integral equation methods.

The Gopinath group has also begun two new projects during the past year. One involves designing an integrated optical modulator for linear response. In the other, the researchers are modeling coils for magnetic resonance imaging using integral equation methods.

Heiko O. Jacobs, Principal Investigator
Computer Modeling of Electrostatically Directed Self-Assembly of Silicon Nanoparticles in Argon Media

The theory behind the derivation of Brownian motion can be traced to its earliest form at the beginning of the 19th century. Critical aspects of this widely used fundamental theory were developed through the work of Einstein, Brown, Schultz, Ornstein, and others in their dealings with gas kinetics. Their findings consolidate into a concrete statistical analysis from which computational modeling was built. This research is based on the constructs made by these scientists. These researchers simulate a self-directed deposition process of silicon nanoparticles suspended in argon media as part of the process called nano-xerography. The model takes into account several different parameters, including: gas rarefication of the silicon nanoparticles; electrostatic attraction and repulsion; and substrate charge pattern geometry. Results are presented with a time-step analysis showing the dependency of the deposition pattern to both the physical parameters and the geometrical consideration of the simulation. The researchers compare these results to experimental work to demonstrate the reliability and accuracy of the model.

Research Group
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Jae Sang Oh, Graduate Student Researcher
Ross Schermer, Graduate Student Researcher

Research Group
Thomas J. Hatch, Graduate Student Researcher
Mostafa Kaveh, Principal Investigator
Ray Tracing for Modeling Wave Propagation in Wireless Terminal Localization

These researchers have developed a method for localizing a transmitter in microcellular environments based on multipath characteristics of the received signal transmitted from a particular location. The cosine of the angle between subspaces of the received signal and signals that are already available in a database is used for localizing the transmitter using one antenna array receiver. This approach appears to accommodate non-line-of-sight propagation, which is commonly encountered in urban settings. The technique requires the construction of a database of the signal characteristics received from different locations.

Rather than performing actual measurements, this group is computing these characteristics through the use of site-specific ray tracing. They plan to construct a database of characteristics of received signals from different locations in the city of Yokosuka, Japan. Because three-dimensional ray tracing is computationally very demanding, the researchers are using the supercomputers to create this database.

David J. Lilja, Fellow
The Impact of Emerging Technologies on the Design of Computer Architecture

The primary focus of this research is to develop processor architectures that satisfy a desired set of constraints. The constraints typically require non-obvious trade-offs in performance, power consumption, and cost. These researchers are particularly interested in how changes in the underlying technology, such as the trend towards smaller feature sizes in very-large-scale integration circuits, affect how circuits should be designed. The Lilja group is working on several projects in this broad area, including a study of the impact of soft errors on processors constructed with deep sub-micron and nanoscale devices, the development of techniques to control transistor leakage currents in processors using sleep transistors, the development of a program profiling tool to improve simulation efficiency and dynamic performance optimization, and the development of an algorithm to automatically perform design space exploration for new processor architectures. They are also developing parallel algorithms for mining spatial data, such as that obtained from geographic information systems.
**Ned Mohan, Principal Investigator**

Investigation of Non-Linear Mutual Coupling in Switched Reluctance Motors

Dynamic modeling of a switched reluctance machine (SRM) usually assumes independent operation of each phase. Since SRMs are mostly used with simultaneous excitation of two or more phases, it is necessary to account for mutual couplings between different phases in the presence of magnetic saturation. These researchers have formulated a dynamic model for simultaneous excitation of two phases and have designed three machines to study non-linear mutual effects. They used finite element analysis (FEA) to obtain static characteristics and flux linkage and torque for the designs, which have very small differences in geometry. Even small differences in the geometry of the stator pole of SRMs lead to significant changes in the static characteristics, emphasizing the need for accurate modeling and FEA. The SRM design has been finalized, and the motor has been fabricated. The researchers are performing FEA on the final design. Once this is complete, they will experimentally verify the dynamic model of the SRM; the dynamic model will be used to obtain the optimum control parameters for the machine.

**Research Group**
- Nitin B. Bhiwapurkar, Graduate Student Researcher
- Amit Kumar Jain, Graduate Student Researcher
- Rinkle Surend, Graduate Student Researcher

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**Jaijeet Roychowdhury, Principal Investigator**

**Analog Verification**

These researchers used the Scientific Development and Visualization Laboratory for a variety of projects related to analog verification. Specific project areas included automatic macromodeling, phase noise algorithms, modeling and simulation of digital switching noise, fast optical fiber simulation, multi-time methods, Monte Carlo methods for noise in analog systems, and phase-locked loop verification.

**Research Group**
- Kapil Dev Boianapally, Graduate Student Researcher
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- Abhishek Garg, Graduate Student Researcher
- Amit Kumar Jain, Research Associate
- Xiaolue Lai, Graduate Student Researcher
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- Nakul Tandon, Graduate Student Researcher
- Yayun Wan, Graduate Student Researcher
- Zhe Wang, Graduate Student Researcher
- Mankit Wong, Graduate Student Researcher
P. Paul Ruden, Associate Fellow

Properties of Semiconductor Materials and Devices

These researchers are working on the electronic structure and related properties of semiconductor materials and novel devices. Recent research by this group has centered on electron transport simulations for large band-gap III-nitride materials using the Monte Carlo technique. The current focus is the creation of device models for large gap semiconductor devices, in particular III-nitride sensors, and devices fabricated from organic materials. This task requires significantly higher levels of precision than conventional semiconductor modeling, primarily due to the much wider range of values assumed by variables such as the electron and hole concentrations. For this reason, the researchers must use resources of the Supercomputing Institute.

This group has also recently begun work on electron spin transport in large gap semiconductors.

Research Group and Collaborator
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Dominic Schroepfer, Graduate Student Researcher

Sachin S. Sapatnekar, Principal Investigator

Fast Computation of the Temperature Distribution in Very-Large-Scale Integration Chips

Thermal effects have become increasingly important in the design of high-performance integrated circuits. The objective of this project is to develop a thermal simulation program that can accurately and efficiently obtain the on-chip temperature field from a given power distribution. The proposed algorithm is a combination of the Green function method and the table look-up approach. The discrete cosine transform is used to establish the look-up table.

So far, these researchers have used the algorithm to compute the temperature distribution for the single-layered rectangular-shaped chip geometry, and have compared the results to those obtained from commercial computational fluid dynamics software. The relative error of this algorithm can be controlled to well below 1% and the runtime can be hundreds of times shorter than that of the pure Green function method as described in the literature.

The next steps are to extend the single-layered substrate model to the multi-layered substrate model, reducing the time complexity by group the heat sources in a hierarchical way, and improving the algorithm such that true three-dimensional power distributions can be taken into consideration in simulations.

Research Group
Yong Zhan, Graduate Student Researcher
Guillermo R. Sapiro, Principal Investigator

Three-Dimensional Electron Microscopy Image Segmentation

Infected macrophage volumes contain membrane surfaces as well as virus particles in different stages of assembly. These researchers are working with input data taken from electron microscopy three-dimensional sets. They believe that most of the “hexagonal” shapes are empty viruses, while spherical shapes are full viruses. The first goal of this project is to segment out the different types of viral particles in each tomogram, and to classify and quantify them using histograms. The ultimate application is to apply this in the context of screening for the effects of drugs that may affect assembly of the virus in infected cells. The group is using the Basic Sciences Computing Laboratory for this research.

Randall H. Victora, Fellow

Micromagnetic Simulations of Head and Media for High-Density Magnetic Recording

Current magnetic recording technology is approaching several new technical barriers that may limit the further increase of hard disk recording density. Examples of these barriers include fundamental limitations in the thermal stability and switching speed of the magnetic domains. Instead of the current longitudinal recording method, one of the alternatives is to record the media perpendicularly, which may require significant technological changes. These researchers have developed micromagnetic models that simulate the characteristics of perpendicular recording media and recording heads. In recent work, the group tested two experimental techniques for determining anisotropy dispersion of recording media, predicted transition shift owing to neighboring bits in the presence of a side shield, and predicted the switching behavior of an exchange biased system. Future work includes continuing the investigations of exchange bias and transition shift, as well as applying these simulations to a new type of “composite” recording media that they have recently developed.

Research Group

Alberto Bartesaghi, Graduate Student Researcher

Research Group

Mohammed Khan, Graduate Student Researcher
Mohammed Patwari, Graduate Student Researcher
Jyotirmoy Saha, Graduate Student Researcher
Xiao Shen, Graduate Student Researcher
Sissay Yoseph, Graduate Student Researcher
 Enhong Yuan, Graduate Student Researcher
**Babak Ziaie, Principal Investigator**

Integrated Inductor Quality Factor Degradation in Tissue

Many implantable wireless Microsystems (passive and active) use integrated inductors for power transmission and signaling. A high-quality factor coil improves the power transmission efficiency and signal-to-noise ratio. The effect of tissue proximity on the quality factor of these coils, however, is not adequately investigated. These researchers are using experimental and computational methods to measure and model the effect of various tissues (e.g., muscle, fat, and skin) in quality factor degradation of integrated inductors. Initial measurements in muscle tissue have indicated a 50% decrease in the quality factor. The researchers are now performing electromagnetic simulations on multi-turn integrated inductors embedded in various tissues. This will increase their understanding of different sources of loss and its dependence on tissue properties such as resistivity, anisotropy, and dielectric constant. This will also allow the researchers to optimize the inductor design and implantation technique in order to prevent significant quality degradation.

**Research Group**

Richard S. Bennett, Graduate Student Researcher
Ra Cha, Graduate Student Researcher
Joe Guimont, Graduate Student Researcher
David A. Yuen, Fellow
Large-Scale Numerical Modeling, Data Analysis and Mining, and Visualization in Geophysical and Biomedical Sciences

The Yuen group's research is focused toward a quantitative understanding of the Earth's interior with numerical and fluid-dynamical processes. Recently, the group has also applied these models to biomedical applications. They have engaged in scientific visualization, also called "visual computing," and feature extraction. Many of the complicated phenomena with fine features must be visualized at high resolution in order to fully understand the nonlinear processes inherent in flow problems. For this reason, the research requires the use of Supercomputing Institute resources.

The specific research areas include: three-dimensional mantle convection with variable thermal conductivity and variable viscosity and phase change; discrete-particle modeling, including molecular dynamics, dissipative-particle dynamics, and fluid-particle models as applied to multiphase flow in blood arteries and veins with ten million particles; visualization and analysis of very large datasets in both geophysics and biomedical sciences; and numerical simulations of the Earth's lithosphere-mantle thermal-chemical system with complex nonlinear physics and multi-component nonlinear rheologies and thermodynamics.

Research Group and Collaborators (cont.)
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Shuo Mark Wang, Undergraduate Student Researcher
Chris Wijns, Commonwealth Scientific and Industrial Research Organisation, Australia
Tomo Yanagawa, Graduate Student Researcher
Lilli Yang, Undergraduate Student Researcher
Jane H. Davidson, Associate Fellow
Thermal and Chemical Processes in Environmental Systems

These researchers are involved in three projects using supercomputing resources. The first addresses convective heat transfer in novel heat exchangers made of polymeric materials. The objective of this study is to determine the flow field and heat transfer in tube bundles of non-circular tubes.

The second project concerns the development of a numerical model for ozone production in clean and humid air by direct current (DC) corona discharges from a thin wire. The model is based on prior models of ozone production by DC coronas in dry air, with modifications to incorporate the effect of water vapor on the electrical characteristics and the chemistry of the discharge.

The objective of the third project, a new one for this group, is to simulate the transient flow structure and temperature field in a thin rectangular enclosure cooled by a cylindrical tube at the top. The enclosure geometry is a new solar collector design made of polymeric materials to reduce cost. Numerical results will provide information on flow field within the collector and will allow the researchers to determine optimum geometries to enhance overall heat transfer rate.

Research Group and Collaborators
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Mark Emery, Undergraduate Student Researcher
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Wei Liu, Graduate Student Researcher
Yan Su, Graduate Student Researcher
Pengxiang Wang, Department of Mechanical Engineering, University of Wisconsin, Milwaukee, Wisconsin
Yana Wang, Graduate Student Researcher

Arthur G. Erdman, Principal Investigator
Optimum Design and Development of Male Urinary Anti-Incontinence Device Using Finite Element Analysis

In the United States alone, there are approximately four million males who struggle with urinary incontinence. One of the three options of treatment is to use an external urethra clamping device. Current devices available on the market, however, often fail to perform satisfactorily and patients complain of leaking and discomfort.

The objective of this project is to characterize the penile structure, build an analytical model, and eventually develop an improved device. This will certainly be of great help to the people who are suffering from incontinence and will be a step forward in the field of biomedical engineering research.

Research Group
Seogwan Kim, Research Associate
Sean C. Garrick, Associate Fellow

Large-Scale Simulation of Turbulent Reacting Flows

This research uses computational fluid dynamics, aerosol dynamics, chemistry, and physics to develop computational tools to simulate particle formation and growth in turbulent reacting flows. The methodology unites the latest mathematical and phenomenological models with robust simulation techniques to create a new regime of computational flow/chemistry. This new approach will facilitate the prediction and control of nanoscale particles production for materials processing.

Specific projects for this group include: investigating the effects of turbulence on homogeneous nucleation rates; simulating nanoparticle growth in a turbulent opposed-jets flow field; simulating formation and growth of titania nanoparticles in three-dimensional turbulent reacting flows; numerically simulating a three-dimensional chemically reacting round jet; developing subgrid-scale models for turbulent flows that encompass nanoparticle coagulation; and using molecular-based computation to understand the growth of nanoparticles formed from the vapor and the high-temperature oxidation of hydrocarbons in microcombustors.

Research Group and Collaborator
Brandon Crook, Graduate Student Researcher
Takumi Hawa, Research Associate
Mehrzad Khakpour, Graduate Student Researcher
Soo H Jung Kim, Research Associate
Juha Kurkela, Research Associate
Saurav Mitra, Graduate Student Researcher
Dibyendu Mukherjee, Graduate Student Researcher
Nathan Murfield, Undergraduate Student Researcher
Pralhalad Parthangal, Graduate Student Researcher
Jouni Pyykonen, Supercomputing Institute Research Scholar
Nelson Settumba, Graduate Student Researcher
Shekar Sonwane, Research Associate
Guanghai Wang, Graduate Student Researcher
Patrick Wells, Research Associate
Michael R. Zachariah, Department of Mechanical Engineering, University of Maryland, College Park, Maryland
Steven L. Girshick, Associate Fellow
Modeling Plasma Synthesis of Materials

These researchers are investigating plasma processing and plasma chemistry in three contexts of practical importance: particle formation and transport in semiconductor processing systems; synthesis of nanostructured materials in a thermal plasma expansion process; and fundamental studies of thermal plasma chemical vapor deposition. These projects involve the development of computer models in concert with ongoing experiments. Key issues include the detailed chemistry that governs film growth, and the nucleation, growth, and transport of particles in plasmas.

Richard J. Goldstein, Associate Fellow
Heat Transfer in Gas Turbine Passages and Rayleigh-Bernard Convection

These researchers are using supercomputing resources for two projects. In the first, they are computing the flow and heat transfer on the blade and bottom endwall surfaces of a linear gas turbine cascade. The geometry and flow conditions match those of the linear cascade located in the Heat Transfer Laboratory of the Mechanical Engineering Department, from which detailed experimental results are available to validate the numerical simulation. Once they have assessed the predictive capabilities of the code, the researchers will perform simulations to design new leading-edge modifications with the objective of reducing fluid dynamic losses and heat transfer.

The second project uses the method of Chebyshev collocation, which has been shown to be ideal for simulating problems involving hydrodynamic stability and transition to turbulence, to study turbulent Rayleigh-Bénard convection. The researchers are interested in the global heat transfer behavior, represented in terms of the Nusselt number as a power-law function of the Rayleigh number. The simulations will try to resolve the controversy regarding the value of the exponent in the power-law relationship.

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Research Group
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Vinod Srinivasan, Graduate Student Researcher
Justin E. Waldron, Graduate Student Researcher
Plasma Computation

Plasma processing is increasingly being used to develop new materials processing technologies and improve existing ones. Process models may be used as design tools to simulate complex phenomena, such as magneto-fluid-dynamic interactions, turbulence, and particle breakup and transport, that take place in processes such as wire-arc spraying, plasma deposition, and plasma spraying.

These researchers have developed a computer code that accurately calculates thermodynamic and transport properties of different plasma mixtures and are currently modifying it. These transport properties are used to simulate the various processes listed above. This research involves the iterative or transient solution of a large set of strongly coupled non-linear equations, often with a very fine grid resolution in a two- or three-dimensional geometry, and thus requires the computing resources available at the Supercomputing Institute.

Research Group
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Giovanni Zelioli, Graduate Student Researcher

Uwe R. Kortshagen, Associate Fellow

Highly Realistic Modeling of Low-Pressure Processing Plasmas

These researchers investigate new approaches for fast realistic modeling of processing plasmas both at low temperatures and atmospheric pressures. One focus of this research is the accurate prediction of the electronic energy distribution function. In this area, the researchers use a highly realistic Monte Carlo approach, based on first principles, to accurately determine the electron energy distribution function in a low-pressure plasma. These results will provide new insights into the physics of electron transport processes both in configuration and in energy space.

A second focus is the study of the chemical nucleation of nanometer-sized particles in plasmas, namely the chemical nucleation of clusters. Here, the researchers are developing plasma-chemical reaction mechanisms that include neutral as well as ion-neutral chemistry. The group is beginning to couple plasma-chemical models to detailed plasma models.

Finally, the researchers have begun to model atmospheric pressure glow discharges with two-dimensional time-dependent fluid codes.

Research Group
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Perry Y. Li, Principal Investigator

Using Flow-Induced Instability for High-Performance Electrohydraulic Valves

Hydraulics are heavily used in agricultural, construction, manufacturing, material and structural testing, and entertainment industries. The control of hydraulic systems involves the operation of an electrohydraulic valve in which a spool is stroked within the valve sleeve using a solenoid stroking actuator, in order to mechanically meter the fluid flow into and out of the hydraulic piston. A determinant of the dynamic performance of such systems is the speed and rate at which the spool can be stroked. For high flowrate, high bandwidth applications, the flow forces that the solenoid needs to overcome in order to move the spool become significant, thus limiting the performance of the valves. This research aims to overcome this difficulty by designing the geometry of the spool so that, as the fluid flows through the valve, the fluid flow induced forces on the spools are open-loop unstable. The researchers use computational fluid dynamics analysis to predict flow forces in the valves.

Research Group
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Susan C. Mantell, Principal Investigator

Finite Element Analysis Modeling of Composite Perforated Plates

Most heat exchangers are made of metal, but making them out of polymers is desirable because of polymers’ reduced cost and weight and increased resistance to chemicals. One of the issues inhibiting the design of the polymer heat exchanger is that the mechanical behavior of composite, perforated plates has not been properly modeled. The perforated plate joins the heat exchanger tubes together and acts like part of the manifold. This modeling is important in order that the plate dimensions can be designed to endure the liquid pressure inside the heat exchanger. Specifically, the effective elastic modulus ($E^*$) of this composition, perforated plate should be modeled using finite element analysis (FEA) so that the plate can be properly designed.

These researchers have found a way to predict a modulus loss in a composite by knowing the change in the aspect ratio of the glass fibers in the composite. The aspect ratio changes when holes are drilled in the composite plate, which causes a loss in elastic modulus. The researchers are modeling this loss of modulus using the FEA program ABAQUS.

Research Group
Michael Eggen, Research Associate
Virgil A. Marple, Principal Investigator

Electrodynamic Focusing of Aerosols

Concentration of aerosols from a large volume of air into a small sample volume is essential in increasing the sensitivity of their detection. The use of electrodynamics forces to achieve particle focusing and thereby concentrating them is the prime objective of this project. The researchers are currently studying the resulting electrostatic fields from different electrode shapes and configurations for their suitability for focusing aerosols. They are using software available at the Scientific Development and Visualization Laboratory.

Previous work investigated the static fields for different electrodes and the use of non-uniform electrostatic fields for dielectrophoretic focusing of aerosols. After selecting suitable electrode configurations and shapes from the electrostatic studies, the researchers plan to study forces on charged particles in electrodynamic fields.

Peter H. McMurry, Principal Investigator

Numerical Analysis of Nanoparticle Transport

These researchers are using the software package FLUENT and its supporting software to simulate transport phenomena inside critical components of nanoparticle characterization devices. The steps in this research include: deposition of charged nanoparticles by Brownian diffusion and electrostatic deposition on the surface of a particle classification device; simulation of the degree of perturbation to laminar flow at the critical region of the instrument; and implementation of the User-Defined Scalar Transport Modeling feature within FLUENT to simulate growth of (sub-)nanometer particles as heterogeneous nucleation of vapor takes place inside the condenser tube of a condensation nucleus counter.
David Y. H. Pui, Associate Fellow
Dynamic Filtration Simulation of Pleated Filter Cartridges Under Pulse-Jet Cleaning in a Baghouse

To complement their experimental studies of a pulse-jet cleaned baghouse, these researchers use computational fluid dynamics (CFD) to analyze the filtration and cleaning processes necessary to understand and design a baghouse system. CFD can obtain information that cannot be found from experiment investigation. This includes pressure drop distribution along the filter surface and the particle trajectory during air filtration and pulse-jet cleaning. The former is important to dislodge dust cakes on the filter surface, while the latter can be used to predict the particle redeposition rate during cleaning.

This group has established a two-dimensional numerical model incorporating Porous Media Model and has calculated the pressure drop distribution along the filter surface during filtration and cleaning processes. The numerical results show a non-uniform distribution of pressure drop during pulse-jet cleaning—the dust cake located at the top of filter cartridges is the most difficult part to remove, because of lower over-pressure. The numerical results from the model demonstrate that a cone under the jet nozzle can improve the uniformity of pressure drop distribution along the filter surface, but the overpressure is attenuated. The Porous Media Model in the two-dimensional model can be simplified to the Porous Jump Model, which helps the researchers reduce computation complexity for modeling pleated filters. In addition to calculating clean air flow, the two-dimensional model uses the Discrete Phase Model to consider dust collection and cleaning. The researchers are building a three-dimensional model, based on the results from the two-dimensional model, to model the pleated filters.

Research Group
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Rajesh Rajamani, Principal Investigator
Development of a Gyroscope for Absolute Angle Measurement

These researchers have developed an innovative design for a vibrating gyroscope that can directly measure angle. The design is based on the principle of measuring the angle of free vibration of a suspended mass with respect to the casing of the gyroscope. Several critical challenges must be solved before the theoretical sensing concept can be converted into a reliable practical sensor, including compensating for the presence of dissipative forces, mismatched springs, cross-axis angle stiffness, and transmission of rotary torque. The researchers are developing a composite linear feedback control system to compensate for these effects and to ensure that the mass continues to behave as a freely vibrating structure.

Research Group
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Simulations of Turbulent Flow and Heat Transfer in Propulsion Studies

These researchers use Reynolds Averaged Navier-Stokes (RANS), detached-eddy simulation (DES), and large-eddy simulation (LES) to study turbulent and transitional flows in aerodynamics and power and propulsion systems. Recent activities have included: large-eddy simulation of flow in a square duct with heat transfer and rotation; the simulation of pipe, rod bundle, and annular passage flows with large property variations (including supercritical fluids), rotation, and buoyancy; the simulations of film cooling flows; LES of dilute particle-laden flow; and LES of chemical reaction flow. Another small portion of the work is the simulation of porous media in support of the group’s measurements of thermal dispersion.

The long-term objective of this research is twofold. The first part is to evaluate the accuracy of RANS, DES, LES, and subgrid turbulence models by comparing predicted results with experimentally measured ones. The second is to contribute to the physical understanding of flows and transition in aerodynamics and propulsion systems.

Research Group and Collaborators

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Patrick J. Starr, Principal Investigator

This project consists of using industry-standard one-dimensional and three-dimensional modeling software to improve engine performance by increasing volumetric efficiency. The computer model and its calibration are based on a four-cylinder, four-stroke motorcycle engine. The engine differs from a stock configuration in that it utilizes a 20 mm intake air orifice and a multi-port fuel injection.

Recent focus areas for this project include cylinder-to-cylinder air distribution, taper/curvature of intake manifold runners, and pulsed choked flow through an orifice/venturi restrictor. The results of the computer simulations are compared with dynamometer experiments. The researchers are expanding their investigations into diffuser design, suppression of vortex shedding within the intake manifold, application of passive flow-control techniques to limit adverse shock-wave/boundary layer interactions, and experimentation with using wavelet analysis to identify coherent internal flow structures.

Research Group
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Paul J. Strykowski, Principal Investigator
Terrence W. Simon, Associate Fellow

Computational Modeling of Flow and Heat Transfer in a Heat Exchanger

These researchers are conducting a numerical study of fluid flow and heat transfer in a heat exchanger configuration using a model based on volume-averaging theory, where the shell-side flow passage is treated as a porous medium with anisotropic effective properties. They have constructed a database of effective properties such as permeabilities, Forchheimer coefficients, thermal conductivities, and heat transfer coefficients using a micro-model analysis. In the micro-model, a unit cell is analyzed by imposing a varying mean flow direction relative to the unit cell and a varying Reynolds number. The velocity and temperature fields within the unit cell are then calculated using the micro-model to characterize the porous media. In the macro-model analysis, the velocity and temperature distributions in the heat exchanger configuration are obtained by solving the volume-averaged equations supplemented with effective properties. The researchers validate the combined micro/macro model by direct numerical simulation.

Research Group and Collaborators
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Kumar K. Tamma, Fellow
Computational Mechanics and Multi-Disciplinary Applications to High-Performance Supercomputing

This project is concerned with the development of unified computational methodologies, solution algorithms and finite elements, and discontinuous Galerkin and meshless modeling/analysis strategies for rigid-flexible multi-body dynamics, contact-impact-penetration, electromagnetics, multi-disciplinary flow-thermal-structural problems, and micro/nano-scale effects in heat conduction. The philosophy and rationale of this work is based on employing a common numerical methodology for each of the individual disciplines in conjunction with common computational algorithms for applicability to supercomputing systems in solving large-scale engineering problems. Various research activities include: development of new time integration computational algorithms for transient/dynamic problems; development of effective finite element-based methodologies that can be used in multi-disciplinary problems; new physically correct contact models for penetration and impact problems; and application of finite element methods in manufacturing simulations to provide a paradigm for virtual manufacturing. The application areas include a wide range of engineering problems involving multiphysics and space/time domain decomposition with interface to graph partitioning techniques. The overall efforts focus attention on providing new, effective, and robust approaches for not only improving the existing capabilities for applicability to supercomputing environments, but also towards providing an accurate understanding of the physics and mechanics relevant to multi-disciplinary engineering problems.

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Xiangmin Zhou, Graduate Student Researcher
Charles E. Campbell, Associate Fellow

Micromagnetic Simulations

This research program on micromagnetic materials made extensive use of supercomputing resources for large micromagnetic simulations. The group focused primarily on two areas of research: simulation of the structure and dynamics of submicron patterned media, and the simulation of possible nanomagnetic digital devices. These are simulations of magnetic material on length scales of between several nanometers and several microns. The objective of these simulations is an understanding of the dynamics, the domain structure, and the structure of domain walls of useful magnetic materials such as permalloy, Ni, Fe, Co, and FeCo.

Cynthia A. Cattell, Associate Fellow

Storm-Time Acceleration of Ions in the Earth’s Magnetosphere

When the sun is active, it often ejects very large, fast-moving clouds of plasma, known as coronal mass ejections (CMEs). When these dense, fast-moving clouds impact on the Earth’s magnetic field, they strongly compress it, exciting large-amplitude waves than can result in energization of ions in the radiation belts and ring current. Recent observations have raised many questions about the energization mechanism; satellite observations at two different altitudes were not consistent with any of the currently proposed mechanisms. These researchers tested possible acceleration mechanisms and the resulting signatures at the two altitudes using a particle-tracing code that the researchers previously developed to examine non-adiabatic ion motion in field-reversed geometry. The group modified the code to model the inner magnetosphere and to include the models of the types of waves excited by CMEs.
Paul A. Crowell, Principal Investigator

Micromagnetic Studies of Spin Dynamics in Magnetic Nanoparticles

Small ferromagnetic grains are the building blocks of storage media, and these researchers are studying arrays of thin film magnetic nanostructures as prototypical patterned media. The dynamics of these systems are influenced by the interplay of short-ranged exchange interactions and longer-range magneto-static interactions. The characteristic frequencies are in the gigahertz range and damping times for excitations are typically a few nanoseconds.

This research project focuses on two problems. First, the group is addressing the real-time dynamics of particles with an inhomogeneous magnetic microstructure. Typical examples include magnetic vortices and other structures showing topological defects such as domain walls. Second, the group is examining the stability of small magnetic particles under pulsed excitation as well as high amplitude continuous-wave excitation. This aspect of the work addresses applications such as ultrafast switching and the stability of storage media. The researchers use the supercomputers to perform real-time micromagnetic simulations to address spin-wave dynamics in inhomogeneous media. The results are used to interpret time-resolved Kerr microscopy measurements.

Research Group
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David Toyli, Undergraduate Student Researcher

Eric D. Ganz, Principal Investigator

Quantum Chemistry Studies of Hydrogen Storage in Metal Organic Frameworks

Recently, a new concept for hydrogen storage has been demonstrated that involves storing hydrogen gas in a porous solid material. In particular, metal organic frameworks have been developed that are inexpensive to manufacture, lightweight, and stable.

These researchers are using quantum chemistry methods to study the hydrogen-storage properties of these materials. The gravimetric and volumetric storage efficiency can be increased by increasing the surface area of by increasing the binding energy of the crystal. The researchers use Moeller-Plesset many-body perturbation theory to calculate the binding energy for hydrogen on the metal organic framework materials, and use grand canonical Monte Carlo simulations to calculate the sorption as a function of temperature and pressure. A wide range of structures is possible with metal organic frameworks, and the group is also studying the fundamental design principles for creating the storage devices. This research should contribute to the realization of a portable, efficient, and safe storage method for hydrogen gas.

Research Group
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Andrew Thompson, Graduate Student Researcher
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Alexander Y. Grosberg, Fellow

Knots in Polymer Physics; DNA in a Channel

The Grosberg group is working on a project to investigate the swelling seen in looped polymer chains based on the sort of knot the chain formed. Their computational work strongly confirmed that the swelling a simply knotted loop undergoes is very similar to that experienced by a polymer with physical, non-overlapping volume, known as “excluded volume.” The researchers also looked at the probability distributions of size for various knot types and saw a rescaling that is very interesting theoretically. This study of knot swelling carries computational work to the largest size loops ever addressed.

The researchers are now expanding their work. Excluded volume is commonly idealized in terms of a bead-stick model, where beads join persistent-length sticks of the polymer. In such a model, larger beads correspond to stronger swelling forces within the polymer. The researchers are investigating whether certain bead diameters corresponds to the asymptotic swelling a trivial knot experiences.

In another project, this group is working on a coarse-grained molecular dynamics simulation of deoxyribonucleic acid (DNA) through a narrow channel. This problem involves difficulties due to strong electrostatic interactions, which are made even more difficult to address by the strong dielectric contrast between water and lipids.

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J. Woods Halley, Fellow

Numerical Studies of Fluids and Disordered Solids

These researchers are continuing their computational research in the fields of electrochemical interfaces, disordered polymers, and Bose-Einstein condensed systems. The computational methods used include direct dynamics, classical molecular dynamics, hydrodynamics, continuum mechanics, and Monte Carlo simulation. The group is developing several new methods, including self-consistent tight binding molecular dynamics and temporally renormalized molecular dynamics.

Research Group and Collaborators

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Shaul Hanany, Associate Fellow

Cosmic Microwave Background Data Analysis and Mission Design

The Hanany group has continued to analyze data from MAXIPOI, a balloon-borne cryogenic experiment launched in 2003 that is attempting to detect polarization in the cosmic microwave background (CMB). The group has also begun preparatory work on two future missions to further study the polarized CMB. These efforts promise to yield strong constraints on models of the origin and evolution of the universe. Conversion of MAXIPOI data into polarization maps and statistical results involves manipulations of dense matrices of $10^8$ to $10^{12}$ elements, which are only feasible using massive parallel computing resources. Optical design efforts for the NASA-funded EBEX experiment and for the EPIC satellite mission study also require significant computing power because of the need to calculate detailed diffusion properties of the proposed telescopes. The researchers are also performing finite element analysis to identify the mechanical requirements of the telescope reflectors.

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Norton M. Hintz, Principal Investigator

Nuclear Reaction and Structure Calculations

During the late 1980s and early 1990s, experiments on proton elastic and inelastic scattering and two-neutron pickup reactions were performed at the Los Alamos Meson Physics Facility and the Indiana University Cyclotron. Their purpose was to investigate the basic nucleon-nucleon (NN) interaction as modified in the nuclear medium. There are several controversial and somewhat conflicting theories as to how the free NN interaction is modified by the presence of other nucleons. Fundamentally, the underlying quark structure of the nucleons is involved.

The purpose of this project is to analyze these data. The analysis of the two-neutron transfer experiments has been completed and published, and the analysis of the proton inelastic scattering data is ongoing. The results of this work have important applications in astrophysics, particle physics, and condensed matter physics.

Research Group
Michael A. Franey, Research Associate
Robert L. Lysak, Associate Fellow
Numerical Investigations of Solar Wind-Magnetosphere-Ionosphere Coupling

This project is centered on several problems involving the coupling of mass, momentum, and energy between the solar wind, magnetosphere, and ionosphere. This work involves both the development of new codes and the modification and use of existing codes to address the problem of solar wind-magnetosphere-ionosphere coupling. Specific areas of research include: investigation of the dynamics of the magnetospheric tail using a three-dimensional version of the total variance diminishing magnetohydrodynamic code developed by the Jones group in the Department of Astronomy; the development of a nonlinear-two-fluid code in a low-β plasma to model the auroral acceleration region more completely; applying the group’s three-dimensional model for the propagation of compressional and shear Alfvén waves through the auroral ionosphere and atmosphere by looking at the excitation and propagation of waves propagating in the so-called ionospheric waveguide, and by looking at the detailed structure of the ionosphere including collisional effects; and considering the effects of a kinetic description of electrons in the auroral zone.

Research Group and Collaborators
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Oriol T. Valls, Fellow
Numerical Studies on Superconducting/Magnetic Structures and on the Superconducting Vortex Lattice Phase Diagram

These researchers continued their investigations into two areas: proximity effects in heterostructures involving superconductors and ferromagnets, and phase diagram and density structure of superconducting vortex systems in the presence of pinning centers. In the first area, the group studies the behavior of high-quality multilayers and superlattices composed of superconducting and ferromagnetic materials, using a numerical method they have developed to solve the exact microscopic equations for such systems. In the second area, the researchers study the phase diagram of type II superconductors in the vortex state, in the presence of both a magnetic field and pinning centers. They use numerical minimization of the appropriate free energy function (in terms of the time-averaged density variables) to find the free energy from which the phase diagram is obtained. The density structure at each minimum yields the correlation functions and the nature (crystal, glass, or liquid) of the phase.

Research Group and Collaborators
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Quantum Chromodynamics at Finite Density

One prediction of quantum chromodynamics (QCD) is that quarks are confined at low temperature, but that a quark-gluon plasma forms above some temperature $T_c$. Current experiments on heavy-ion collisions may provide evidence for this plasma, so it is important to predict $T_c$. The critical temperature $T_c(\mu)$ depends on the relative excess of matter over antimatter in the heavy-ion collision, or equivalently on the quark chemical potential $\mu$. Unfortunately, lattice QCD simulations can only directly probe the case $\mu = 0$, because otherwise the notorious “sign problem” prevents Monte Carlo sampling over a positive measure. These researchers are pursuing an approach that is free of the sign problem and that gives the most accurate results to date: they consider an imaginary chemical potential $\mu_i$ for which traditional Monte Carlo methods apply, and determine the critical temperature $T_c(\mu_i)$. The result is fit to a truncated Taylor series followed by analytic continuation to real $\mu$.

Collaborator
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Bernardo Cockburn, Fellow
Adaptive Methods for Hamilton-Jacobi Equations; High-Order Runge-Kutta Discontinuous Galerkin Methods of Computational Electromagnetics

These researchers are involved in two projects using the supercomputers. The objective of the first project is to develop adaptive methods for efficiently approximating viscosity solutions of Hamilton-Jacobi equations. They are devising methods that provide approximations with a given arbitrary precision in the uniform norm. To achieve this, they use an a posteriori error estimate specially devised for these equations and a new algorithm that is able to automatically tell where to refine and where to unrefine the mesh in order to achieve the error control with maximum efficiency.

The objective of the second project is to develop a new Runge-Kutta Discontinuous Galerkin method for problems of wave propagation that achieves high-order convergence both in time and space. The algorithm is based on a method of lines and relies on modal expansions to resolve spatial variations in the fields. For the time integration, the researchers derive an extension to non-autonomous linear systems of a recently designed $m^{th}$-order $m$-stage low-storage Runge-Kutta method. This extension allows for a high-order treatment of the inhomogeneous (time-dependent) terms that enter the semi-discrete problem and thus it results in an overall high-order scheme.

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Luis Yunes, Graduate Student Researcher
Dennis A. Hejhal, Fellow

Computational Aspects of Analytic Number Theory

This research group continued its computational analyses of high frequency eigenfunctions of the Laplacian on fuchsian groups. During this year, they have optimized their code so that it is suitable for applications wherein the underlying multiplier systems have nonzero weight. They have been working on getting this code running on the IBM SP supercomputer. Also, using the Fourier coefficients obtained from this program, they have conducted statistical analyses of these coefficients of a more refined nature than previously carried out.

Collaborators
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John S. Lowengrub, Fellow

Topological Transitions and Singularities in Fluid, Crystal, and Biological Interfaces

These researchers studied topological transitions and singularities of interfaces in fluid flows and biological systems, using their dual approach of sharp and diffuse interface methods. In fluid systems, the group investigated interfacial flows with and without surfactants and determined critical conditions for coalescence and break-up. The focus of this project was on the development of multiphase flows with interpenetrating (co-continuous) components and on performing high-resolution simulations of droplet coalescence and breakup. In crystals, the researchers studied the evolution of three-dimensional crystals during melting, freezing, and in “mushy” zones. The research into crystals also included investigation of dense systems of crystals to determine the effect of volume fraction on the coarsening kinetics. In biological systems, the research focus was on the morphology of growing tumors.

Research Group and Collaborators
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Antheunis Versluis, Faculty Collaborator
Xiaoming Zheng, Research Associate
Hua Zhou, Research Associate
Mitchell B. Luskin, Fellow  
Richard D. James, Co-Principal Investigator  

Numerical Tools for Active Martensitic Thin Films

The purpose of this project is to develop computational methods for nonlinear partial differential equations that model the dynamics of the austenitic-martensitic transformation in active thin films. The computation of active thin films is essential to the development of micromachines for wide-ranging applications from medicine to aerospace. The goal is to develop the ability to simulate the behavior of shape memory materials that undergo a martensitic transformation. The researchers are developing a computational model that can simulate experimental work performed on a Cu-Al-Ni shape memory alloy.

Andrew M. Odlyzko, Principal Investigator

Statistical Analyses of Zeros of the Riemann Zeta Function

This project involves a database of over 20 billion zeros of the Riemann zeta functions, most near zero number 1023, that the researcher previously computed. These zeros verify numerically the correctness of the famous Riemann Hypothesis, and also support further far-reaching conjectures that tie together number theory and physics. Some preliminary studies have already been computed. Further studies include looking for extremal behavior of gaps between zeros, examples of violations of Rosser’s rule, asymptotics of moments of the zeta function, and related questions.
Hans G. Othmer, Fellow
Mathematical Modeling of Cell Motility and Tissue Development

These researchers are continuing work on their model for vertebrate limb development and are beginning to work on a model for the motility of single amoeboid cells. They have obtained numerical solutions to the two components of the limb-development model, the reaction-diffusion system governing morphogen kinetics (on a fixed domain) and the system governing the mechanics of the limb. It is clear that growth will affect the spatio-temporal distributions of the limb morphogens, so the researchers’ next goal is to combine the two sub-systems and solve the full model numerically.

Despite apparent differences between limb bud differentiation and outgrowth and amoeboid cell motility, the equations governing the kinetics and mechanics of the two systems are mathematically and numerically similar. Using experimental evidence, these researchers are developing a three-dimensional model for the early stages of polarization, actin kinetics, and the mechanics of “crawling” of *Dictyostelium discoideum*, a widely studied single-cell organism. The general goal for this research is to provide a large-scale computational tool that can be used to explore the effects of various mutations, varying stress distribution, and experimental interventions on the outgrowth and patterning of tissues and on the motility of amoeboid cells.

Research Group and Collaborators
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Magdalena Stolarska, Research Associate
Vasfiye Hande Tuzel, Graduate Student Researcher
David Umulis, Graduate Student Researcher

Fernando L. Reitich, Principal Investigator
High-Order Methods for Computational Electromagnetics and Acoustics

These researchers have developed a variety of efficient numerical techniques for the simulation of electromagnetic- and acoustic-wave scattering processes in the time and frequency domains. Their novel procedures are based on effective, high-order treatments of integral and differential formulations of the scattering problem. Their initial work on a wide array of test cases demonstrated the viability of the newly developed schemes for scattering simulations, and it also proved that they offer the potential for substantial improvement in simulation capabilities over currently available methods. The confirmation of these advantages for practical, realistic geometric arrangements at frequencies of interest, however, demands the use of supercomputing resources. The researchers are using the supercomputers to improve and expand their current codes to efficiently run simulations of practical interest.

Research Group and Collaborators
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Catalin Turc, Graduate Student Researcher
Fadil Santosa, Principal Investigator
Energy Methods in Three-Dimensional Spline Approximations

In this project, the researchers use splines of arbitrary degree and arbitrary smoothness to find approximations of the three-dimensional Navier-Stokes equations in velocity-pressure formulations. Using functional arguments, they derive the discrete Navier-Stokes equation in terms of B-coefficients of trivariate splines over a tetrahedral partition of any given polygonal domain. Smoothness conditions, boundary conditions, and the divergence-free condition are enforced through Lagrange multipliers. The pressure is computed by solving a Poisson equation with Neuman boundary conditions. The researchers have implemented this approach in MATLAB and have found numerical evidence of the convergence rate as well as experiments on the lid-driven cavity flow problem.

Research Group and Collaborator
Gerard Awanou, Research Associate
Dacian Daescu, Research Associate
J. Mark Hubenthal, Supercomputing Institute Undergraduate Intern
Anton Leykin, Graduate Student Researcher
Mihalis Sigalas, Agilent Laboratories, Palo Alto, California

Arnd Scheel, Principal Investigator
Mathematics of Materials and Macromolecules

The Institute for Mathematics and Its Applications is hosting a program aimed at the synthesis of the problems at the interface between mathematics, materials science, condensed matter physics, and biology. Scientific computation plays a major role in the development of materials theory and its validation by experiment. Mathematicians and materials scientists are beginning to confront the computational challenges of multiscale modeling, singularities, and disorder. Contemporary computational algorithms for the study of matter such as “hyperdynamics,” however, are often developed in the context and language of physical theories that are not part of the traditional education of computational mathematicians. This program strives to enable interactions and research between mathematicians and materials scientists on computational problems that are important in the study of matter, but have been given little attention by the mathematics community.

Research Group and Collaborators
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Richard Kollár, Research Associate
Matthias Kurzke, Research Associate
Frederic Legoll, Research Associate
Xiantao Li, Research Associate
Peter Philip, Research Associate
Yitzhak Rabin, Department of Physics, Bar-Ilan University, Ramat-Gan, Israel
Motohiko Tanaka, National Institute for Fusion Science, Toki, Japan
Lynda B. M. Ellis, Principal Investigator

Seeking the Vertebrate Secretome

Secreted proteins (the secretome) make up approximately 10–20% of the vertebrate proteome, control cell-cell interactions, and are major targets for drug discovery. Secreted protein prediction has traditionally relied on N-terminal signal sequences identification. These techniques assume predictions are based on full-length protein sequences and performance significantly decreases when analyzing N-terminally incomplete sequences, such as protein sequences encoded by expressed sequence tags. Truncated signal peptides may reduce the sensitivity, and N-terminal truncations near transmembrane domains may reduce the specificity, of these techniques.

These researchers have developed csP, a technique that uses protein domain classification instead of signal sequence identification to predict secreted proteins. Protein domains reported to be more prevalent in the mouse secretome than in other mouse proteins by Grimmond and co-workers are used as reference.

Protein domains in csP query sequences are identified using INTERPro, an integrated documentation resource for protein families, domains, and sites. INTERPro combines a number of databases (referred to as member databases) that use different methodologies and a varying degree of biological information on well-characterized proteins to derive protein signatures. High-throughput use of INTERPro, available at the Supercomputing Institute, requires high performance computing and large amounts of disk space. csP can be used in conjunction with other packages to help identify secreted proteins.

Research Group and Collaborator
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Kyong-Jin Shim, Graduate Student Researcher
Carlos Sosa, IBM, Minneapolis, Minnesota

Michael A. Farrar, Principal Investigator

Regulation of Lymphocyte Development and Activation by STAT5

The transcription factor STAT5 plays a key role in the development of both B and T lymphocytes. These researchers have demonstrated that activation of this transcription factor is sufficient to restore lymphocyte development in the absence of the cytokine IL7. They are using STAT5 chromatin immunoprecipitation assays and gene microarrays to identify STAT5 target genes required for this process. These studies should shed light on the molecular mechanisms that entrain lymphocyte development.

STAT5 also plays an important role in regulating numbers of mature T cells. The cytokine IL7 is important in ensuring that T cell numbers remain relatively constant (referred to as T cell homeostasis). The researchers have identified two genes, bcl-xl and pim-1, as key target genes in this process and are characterizing the mechanism by which STAT5 drives T cell homeostasis.

Finally, STAT5 plays a key role in promoting the development of a subset of T cells, called suppressor T cells, which play an important role in preventing autoimmunity. The group is identifying STAT5 target genes that regulate suppressor T cell development and functional activity.

Research Group
Matt Burchill, Graduate Student Researcher
Chris Goetz, Graduate Student Researcher
Wynette Will, Research Associate
Jianying Yang, Graduate Student Researcher
William B. Gleason, Fellow
Applications of Advanced Computation and Digital Simulation to Problems of Biological Relevance

These researchers continued their investigations of problems of clinical relevance, particularly those that can benefit from the parallel processing or molecular visualization capabilities of the Supercomputing Institute. This work includes both applications of immediate practical importance, such as the interpretation of mass spectral data for proteomics, or longer-term basic research projects, such as understanding the biomolecular recognition involved in heparin-binding proteins. More than a hundred heparin-binding proteins have been identified and the number is rapidly increasing. They are involved in a variety of clinically relevant activities ranging from anticoagulation to normal and pathological growth and development.

Recent activities by this group include using the genetic algorithm method as implemented in AUTODOCK 3.05 to investigate the specificity of interaction of proteins with heparin analogs. They have obtained results that are in good agreement with experimentally determined x-ray structures of protein/heparin complexes. The group is also working on using the results of docking calculations as a "front end" for molecular dynamics simulations.

Research Group
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Eric Eccleston, Research Associate
Elliot McSherry, Undergraduate Researcher
Lee G. Stanek, Graduate Student Researcher

Myron D. Gross, Principal Investigator
DNA Repair Genes and Breast Cancer

These researchers are using supercomputing resources to identify potentially important single nucleotide polymorphisms in the deoxyribonucleic acid (DNA) nucleotide excision repair (NER) pathway. They are studying the interactions between different genes in the NER pathway and their relationship to breast cancer risk.

Research Group
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Waseem Khakiq, Graduate Student Researcher
Chris Lessard, Research Associate
Bharat Thyagarajan, Graduate Student Researcher
Franz Halberg, Associate Fellow
Germaine G. Cornélissen, Co-Principal Investigator

Assessment of Physiologic Chronomes From Womb to Tomb

Strokes and other adverse vascular events are major cripplers at an estimated yearly cost of over $30 billion. These researchers are developing a system for the chronobiologic analysis of cardiovascular records with focus on disease prevention, but also addressing the question of the optimal kind and scheduling of treatment. Ambulatory devices are used in different geographic locations to monitor blood pressure for seven days at the outset. Chronobiologic analyses of such records serve first and foremost to improve screening, diagnosis, and treatment, but also to assess how environmental factors affect human physiology, notable heart rate and blood pressure.

The researchers use supercomputing resources to: analyze beat-to-beat records for resolving chronobiologic and chaotic endpoints; automatically update reference standards as added data accumulate; detect the earliest risk by means of chronome alterations; and follow up at-risk individuals longitudinally by means of control charts.

Collaborator
Miguel A. Revilla, Department of Applied and Computational Mathematics, Faculty of Sciences, University of Valladolid, Valladolid, Spain

Kristin A. Hogquist, Principal Investigator

Protein Expression and Signalling in T Cell Development

The vast majority of hematopoietic progenitor cells entering the thymus will die by apoptosis, while only a small percentage successfully develop into mature T cells. The Hogquist laboratory is interested in identifying key signaling pathways required for successful development of CD8+ T cells within the thymus. Using microarray analysis, flow cytometry, genetic manipulation, and quantitative polymerase chain reaction, these researchers and others have identified hundreds of proteins/genes that play important roles in the signaling pathways required for successful T cell development. The group is using resources at the Basic Sciences Computing Laboratory and the Scientific Development and Visualization Laboratory to link the expression data generated to meaningful signaling pathways.

Research Group
Tom McCaughtry, Graduate Student Researcher
Verity Mick, Graduate Student Researcher
Timothy Starr, Graduate Student Researcher
Matthew F. Mescher, Principal Investigator

Gene Array Analysis of CD8 T Lymphocyte Activation

CD8 T lymphocytes are the “killer cells” of the immune system, and can recognize and eliminate virus-infected cells and tumor cells. In order to carry out this function, the naive cells must first be stimulated in an antigen-specific manner to proliferate and undergo a differentiation process to develop effector function. Naive CD8 T lymphocytes require three signals to become fully activated: antigen, costimulation, and a third signal that can be provided by IL-12 or Type I interferon. Using artificial antigen-presenting cells to provide antigen and costimulation, the researchers perform gene array analysis to determine the genes that are regulated by the third signal cytokines. Studies so far have revealed several families of regulated genes and have identified candidate transcription factors that may play key regulatory roles in proliferation, survival, and differentiation of the cells. The group is performing additional gene array analyses to determine changes in expression patterns when these candidate molecules are absent, using T cells from mice with selective gene knockouts.

Harry T. Orr, Principal Investigator

Microarray Analysis of Spinocerebellar Ataxia Type 1

Spinocerebellar ataxia type 1 (SCA1) is a progressive neurodegenerative disease caused by the expansion of a polyglutamine repeat in the disease protein, ataxin-1. To understand the basic mechanism involved in SCA1 pathology, these researchers are using microarray technology to analyze the pattern of gene expression in a conditional mouse model in which the expression of mutant ataxin-1 in cerebellar Purkinje cells can be controlled by a tetracycline-regulated system. They are screening two groups of these mice (treated and untreated) at 12 weeks of age as well as two groups (treated and untreated) of 12-week-old wild-type animals. Genes capable of reversing the pathology will be useful in understanding SCA1 and in developing therapeutic treatment for the disease. The researchers are using software available through the Supercomputing Institute laboratories for their analyses.

Research Group
Pujya Agarwal, Graduate Student Researcher

Research Group
Heliane Serra, Research Associate
Christopher A. Pennell, Principal Investigator

Human RNase-Based Immunotoxins for Leukemia Therapy

This project uses Supercomputing Institute laboratories for analyses of mutant human RNase proteins. These RNases will be incorporated into immunotoxins (ITs). ITs are a class of cancer therapeutics designed to eradicate specific subpopulations of cells. They have several advantages over other therapies. They work catalytically, so they are more potent than stoichiometric chemotherapeutic drugs. ITs do not have toxicities similar to other anti-leukemic agents and have not been observed to generate cross-resistance to other cytotoxic drugs. They also have the advantage of killing both dividing and non-dividing cells.

These researchers are incorporating human RNase mutants in IT constructs. Because of their human origin, they will not elicit neutralizing immune responses in patients. They also have fewer side effects than plant and bacterial toxins, yet they potentially degrade ribonucleic acid, leading to cell death. The disadvantage of native RNase is that it is inhibited by a naturally occurring cytosolic protein in mammalian cells. The researchers have therefore constructed a series of mutant RNases designed to evade inhibition yet maintain catalytic function. Additional mutations may be made based on molecular modeling trials.

Research Group
Heidi Erikson, Research Associate

Amy P. N. Skubitz, Principal Investigator

Gene Expression in Ovarian Cancer

In ovarian carcinoma, cancer cells are shed from the surface of the ovary into the peritoneal or ascitic fluid and then throughout the body, eventually killing the patient. These researchers are exploring the role of integrins and CD44 in the interaction between ovarian carcinoma and mesothelial cells, and are also investigating how ovarian cells shed into the ascitic fluid are kept in a nonadherent and/or noninvasive state.

The researchers used gene expression data to identify genes that code for proteoglycans and proteolytic enzymes that are upregulated in ovarian cancer cells and may play a role in ovarian cancer cell adhesion, migration, and invasion. They have also confirmed the gene expression results for seven of the genes by immunohistochemistry experiments using ovarian carcinoma tissues and normal ovary tissues.

These studies represent an approach towards understanding the molecular mechanisms modulating the phenotypic behavior of carcinoma cells and may potentially aid in designing biomarkers or biopharmaceuticals for therapeutic use in ovarian cancer.

Research Group and Collaborator
Suzanne Grindle, Research Associate
Keith Skubitz, Faculty Collaborator
Sherif Tawfic, Principal Investigator

Study of CD10 in Prostatic Adenocarcinoma

Prostate cancer is the most common non-skin malignancy and the second leading cause of cancer death in men in the United States. Molecules that are differentially expressed in prostate cancer and/or normal glands have the potential to be used as diagnostic/prognostic markers, to enhance the understanding of the pathogenesis and to help in developing specific therapies. Preliminary data have shown that CD10, a cell-surface enzyme that inactivates several biologically active peptides, is downregulated in low-grade prostatic adenocarcinoma and in its precursor lesion. The decline of CD10 in the precursor lesion indicates that CD10 downregulation temporally precedes the development of prostatic adenocarcinoma and may be involved in the process of oncogenesis.

This project studies a larger number of cases to examine the potential use of CD10 expression as a diagnostic/prognostic marker, and to examine the level of regulation of CD10 expression in prostatic adenocarcinoma. The project uses resources at the Basic Sciences Computing Laboratory to show the three-dimensional distribution of the tumor within the gland.

Timothy W. Behrens, Principal Investigator

Discovery of Biomarkers for Rheumatic Diseases

The goal of this research project is to integrate a variety of cutting-edge discovery technologies in order to discover novel biomarkers that will be clinically useful in one of the two major rheumatic diseases, rheumatoid arthritis and systemic lupus erythematosus. These technologies include broad gene expression profiling using deoxyribonucleic acid microarrays, combined with novel approaches to multi-parameter analysis of cell surface and soluble proteins relevant to inflammatory disease states. The group is using the Computational Genetics Laboratory and the Basic Science Computing Laboratory for their research.

Research Group and Collaborator (cont.)
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Scott Selby, Staff
Brian Schram, Research Associate
Mark Stenglein, Graduate Student Researcher
Neil Wenberg, Staff
Beth Ziemba, Graduate Student Researcher
Peter B. Bitterman, Principal Investigator

Elucidating the Rules of Translation Control

In the past ten years, a growing body of literature has documented that messenger ribonucleic acid translation is an important control point, especially in embryonic development, regulation of cell growth, and differentiation and tumorigenesis. The goal of this study is to identify the elements and the rules of translational control. The Bitterman laboratory uses polyribosome assay, gene expression profiling, and data-mining methods to further the understanding of translation control, which will enable them to study in detail various aspects of health and disease.

Yingjie Chen, Principal Investigator

Genetic Alteration in the Hypertrophied and Failing Heart

Development of congestive heart failure is associated with mitochondrial misfunction. These researchers focus on the alteration of nitric oxide synthases and the proteins related to adenosine triphosphate-sensitive potassium channels in the failing heart.

Research Group and Collaborators
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Shunan Li, Research Associate
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Research Group
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Ping Zhang, Research Associate
William C. Duane, Principal Investigator

Serum Factors Activating Ileal Bile Acid Transport Gene

Hypertriglyceridemia is associated with decreased expression of the apical sodium dependent bile acid transporter (ASBT) in human ileum. These researchers have found that human serum transactivates the promoter of the human ASBT gene and that this transaction is independent of the peroxisome-proliferation activity alpha receptor. High density lipoprotein (HDL) appears to be responsible for most of the stimulatory activity, but cortisol may be responsible for about 20%.

These researchers are performing a number of experiments to determine if transactivation attributable to cortisol correlates with free cortisol levels and to determine if transactivation not attributable to cortisol correlates with serum levels of HDL cholesterol and/or apolipoprotein AI as well as other variables associated with hypertriglyceridemia, including body mass index, age, diabetes, and atherosclerosis. These experiments may help explain the association of decreased bile acid absorption with hypertriglyceridemia. They will also provide a novel approach to determining how genetic regulation by transcription factors governs functioning of the human organism, both in health and disease.

Patrick M. Gaffney, Principal Investigator

Gene Expression Profiling in Head and Neck Cancers

Molecular studies of squamous cell carcinoma of the head and neck (HNSCC) have demonstrated multiple genetic abnormalities. In order to identify gene expression signatures that may serve as biomarkers, these researchers have studied 41 squamous cell carcinoma tumors and 13 healthy oral mucosal biopsy samples with microarray analysis. Several gene expression signatures were readily identifiable in the HNSC tumors, including signatures associated with proliferation, extracellular matrix production, cytokine/chemokine expression, and immune response. Of particular interest was the association of a gene expression signature enriched for genes involved in tumor invasion and metastasis with patients experiencing locally recurrent disease. Notably, these tumors also demonstrated a marked absence of an immune response signature, suggesting that modulation of tumor-specific immune responses provide evidence for a new gene expression-based biomarker of local treatment failure in HNSCC.
Kalpna Gupta, Principal Investigator

Opioids in Cancer, Nephropathy, and Wound Healing

These researchers are creating three-dimensional renditions of confocal multicolor images of blood vessels, lymphatics, and nerves. They are using resources at the Basic Sciences Computing Laboratory for this work.

Jennifer L. Hall, Principal Investigator

Genomics Analysis of Cardiovascular Disease

A goal of the Hall laboratory is to use genomics-based strategies to define novel genes and signaling networks in multiple cardiovascular diseases. A primary focus has been to build a compendium of genomics data from paired human heart failure samples taken at the time of implant and explant of an assist device. The researchers are using data generated from these studies to put forth new hypotheses into networks governing the reversal and recovery of heart failure.
These researchers are testing the idea that clinical phenotype of human vascular disease is, in part, determined by genetic determinants of endothelial cell biology. To test this hypothesis, they are applying microarray technology to analysis of blood outgrowth endothelial cells, as reporter cells of constitutive endothelial genetic phenotype. The researchers are using resources at several of the Supercomputing Institute’s laboratories for this project.

Robert P. Hebbel, Principal Investigator
Genetic Heterogeneity of Endothelial Cell Gene Expression

This group’s research is focused on elucidating basic mechanisms of cancer pathogenesis and progression using molecular and comparative genomic approaches. The project can be categorized into three thematic areas: identification of molecular markers and gene-expression profiles in tumor development and progression; characterization of the cancer genome through analyses of human and feline tumor carrier deoxyribonucleic acid (cDNA) libraries and bacterial artificial chromosome libraries; and elucidation of molecular response to chemotherapeutic agents and discovery of novel drug targets.

The group is using resources at the Computational Genetics Laboratory to store and analyze batches of sequence files and microarray datasets, both from Affymetrix GeneChip and custom cDNA array experiments. Further work will involve visualizing, accessing, and querying the information using existing or custom software tools.

Sagarika Kanjilal, Principal Investigator
Vivek Kapur, Co-Principal Investigator
Comparative Cancer Genomics

UM TC–Department of Medicine

Research Group and Collaborators
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Kalpna Gupta, Faculty Collaborator
Taryn Hall, Undergraduate Student Researcher
Aixiang Jiang, Research Associate

Research Group
Nilanjana Banerji, Research Associate
David T. Kiang, Principal Investigator
Gene Profile on the Protective Effect of HCG Against Breast Cancer Development in Rats

Early pregnancy and lactation have protective effects against mammary carcinogenesis in humans. The underlying mechanism of this prevention is still elusive. Using a rat model, this researcher is investigating the mechanism of the protective effect of human chorionic gonadotropin (HCG) against N-nitrosomethylurea-induced mammary tumor and studying the changes in genetic profiles using the microarray technique.

Richard A. King, Principal Investigator
Marshall I. Hertz, Co-Principal Investigator
Gene Expression Microarrays in Lung Rejection

Obliterative bronchiolitis (OB) is a fibroproliferative process that represents the most significant limiting factor for long-term survival in lung transplant recipients. OB occurs unpredictably and is undetectable in a preclinical state. In addition, the major risk factor for OB is acute rejection, which can only be diagnosed by invasive lung biopsies. Therefore, these researchers are using microarrays to identify patterns of gene expression associated with acute rejection and also patterns that can serve as biomarkers of risk for OB. The researchers are using resources at the Supercomputing Institute laboratories to load, normalize, and analyze their data.

Research Group
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Lisa Bolin, Research Associate
Vincent Gimo, Research Associate
Jeffrey Lande, Graduate Student Researcher
Jagadish Patil, Research Associate
Anna M. Masellis, Principal Investigator
Gene Array Analysis of Bone Marrow Stromal Cells in Multiple Myeloma

In multiple myeloma, the bone marrow microenvironment is abnormal and plays a role in disease status and response to chemotherapeutic treatment. Effective disease management will ultimately depend not only on the elimination of tumor cells but also on the reestablishment of a bone marrow environment that supports normal cell growth. These researchers have used their established in vitro cell culture systems to identify genes differentially expressed in bone marrow stromal cells derived from myeloma patients compared to healthy donor bone marrow stromal cells. They found approximately 34 genes differentially expressed in myeloma bone marrow stromal cells, comprising cytokines/growth factors, transcription factors, cell signal transduction proteins, and components of the extracellular matrix. The preliminary data indicate that myeloma bone marrow stromal cells uniquely express genes compared to their normal age-matched donor controls that may impact the growth and function of the bone marrow microenvironment. These researchers’ ultimate goal is to broaden their understanding of the involvement of the bone marrow microenvironment in myeloma pathogenesis and to determine whether clinical response in myeloma can be attributed, in part, to the impact of therapy on bone marrow mesenchymal cell function.

Research Group
Nandita Bose, Research Associate
Suzanne Grindle, Research Associate

Jeffrey S. Miller, Principal Investigator
Use of Gene Arrays to Understand the Biology of Human Natural Killer Cells

Despite progress made in the understanding of natural killer (NK) cell development, the molecular mechanisms directing differentiation of NK cells and killer-immunoglobulin receptor acquisition during development are poorly understood. These researchers are using the Computational Genetics Laboratory and the Laboratory for Large-Scale Data Analysis to investigate the differentiation of human NK cells using microarray analysis.

Research Group
Feng Xiao, Research Associate
Kathy L. Moser, Principal Investigator

Gene Expression Profiling of Rheumatic Autoimmune Disorders

These researchers are using the Computational Genetics Laboratory for two closely related projects. The first uses gene expression profiling to investigate Sjögren’s Syndrome (SS), a chronic autoimmune disease that preferentially affects the lachrymal and salivary glands. These researchers have hypothesized that SS patients have characteristic gene expression profiles that may reflect underlying pathophysioligic processes. They are using microarray technologies to examine the expression of thousands of genes simultaneously in cells from SS patients.

The second project investigates Antiphospholipid Syndrome (APS), a condition where the immune system mistakenly produces autoantibodies that bind to various phospholipids, resulting in clinical manifestations such as recurrent clotting, strokes, and spontaneous miscarriages. These researchers are working to assess the activity of thousands of genes simultaneously. They hope to identify gene expression signatures that are specifically associated with APS. This could provide important new opportunities for designing more effective diagnostic tools and therapies for APS.

Research Group and Collaborators
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Martha Grandits, Research Associate
Amber Leiran, Research Associate
Joanise Leon, Graduate Student Researcher
Carolyn Meyer, Research Associate
Nelson Rhodus, Faculty Collaborator
Barbara Segal, Faculty Collaborator

Daniel L. Mueller, Principal Investigator

Role of CH1-b in Anergy Induction

These researchers studied the function and mechanism of ch1-b in regulating the immunitiy of Th1 cells. In their in vitro anergy model, the researchers found that ch1-b is up-regulated in anergic T cells. This project focused on the molecular mechanism of ch1-b.

Research Group
Ruan Zhang, Graduate Student Researcher
Eric J. Peterson, Principal Investigator

Gene Expression in Profiling Autoimmune Diseases

These researchers are studying gene expression profiling differences in patients with psoriatic arthritis. They analyze ribonucleic acid from patient blood cells and compare the data with data from age- and sex-matched control subjects. The researchers are using software available at the Basic Sciences Computing Laboratory and the Computational Genetics Laboratory for this project.

Keith M. Skubitz, Principal Investigator

Gene Expression in Sarcoma and Other Malignancies

This project examines differences in gene expression in various malignant conditions. The major focus is directed toward better understanding of mesenchymal tumors, including sarcomas and fibromatoses. Other tumors are also under study, including renal cell cancer. Identification of potential targets of new drug development in these and other tumors is a major goal. The researchers are performing microarray experiments and are analyzing them using software available at the Computational Genetics Laboratory.

Research Group
Joanna Dluzniewska, Research Associate
Lindsey Fostel, Research Associate
Felipe Mendez, Research Associate
Angela Stoeckman, Research Associate
Liangxing Zou, Research Associate

Collaborator
Amy P. N. Skubitz, Faculty Collaborator
Clifford J. Steer, Principal Investigator
Betsy J. Kren, Co-Principal Investigator

β or γ Globin Sleeping Beauty Transposon System for Gene Therapy of Sickle Cell Disease

This project aims to develop a gene therapy method for treating sickle cell disease. They are using the Sleeping Beauty transposon system to work with β or γ globin, which they will then test in a mouse model of the disease. The researchers are using the Computational Genetics Laboratory for this project.

Research Group
Jianhui Zhu, Research Associate

Patricia E. Tam, Principal Investigator

Enterovirus Infection as an Environmental Trigger of Chronic Disease

The Tam laboratory studies the role of myopathic coxsackievirus infection in the development of chronic inflammatory muscle disease. They have developed a panel of amyopathic viruses that infect muscle but do not cause chronic disease. Although the acute infections caused by myopathic and amyopathic viruses appear similar, there may be differences in the way they interact with the muscle itself and/or the immune system that ultimately leads to the development of chronic muscle disease. Using a reverse genetics approach, the laboratory has identified four viral genetic determinants that cause chronic weakness and inflammation in infected mice. One of these is a point mutation in the non-coding regulatory region of the viral ribonucleic acid (RNA). Current studies are focused on how this mutation alters the predicted RNA secondary structure. The other three pathogenic determinants are located in capsid proteins, and homology modeling will be used to predict whether these mutations change the predicted three-dimensional structure of the viral capsid.

A second aspect of this model explores the effect of persistent viral double-stranded ribonucleic acid (dsRNA) on muscle cell metabolism. Gene microarrays are being used to identify genes and pathways that are differentially regulated by persistent viral dsRNA. The researchers have begun to analyze a small pilot set of arrays. These studies should advance the field of coxsackievirus biology by providing a global picture of the molecular events that occur during acute and persistent infection.

Research Group
Maribeth Sandager, Research Associate
Jaime Nugent, Staff
Wade Schultz, Undergraduate Student Researcher
Anthony Varghese, Principal Investigator

Structural Basis of Redox Sensitivity of Voltage-Gate Potassium Channels

Ion channels are a class of proteins responsible for permitting flow of ions through cell membranes. Voltage-gated potassium channels are ion channels that are selectively permeable to potassium and activated by changes in the cell transmembrane potential difference. In addition to cell electrical potentials, potassium channels are regulated by other ions and cellular second messages.

This research project focuses on uncovering the role of cellular redox (reduction-oxidation) status in regulating potassium channels. Redox regulation of ion channels is an important signaling mechanism in the modulation of cell function by oxygen levels in the lung, heart, and neuroendocrine cells of the adrenal glands, carotid body, and neuroepithelial bodies. The mechanistic basis of regulation of potassium channels by redox state is not known. This project’s aim is to use molecular-biology techniques to isolate specific areas of potassium channels that may be responsible for redox control.

UM TC–Department of Microbiology

Paul R. Bohjanen, Principal Investigator

Global Analysis of mRNA Decay in T-Lymphocytes

The activation and proliferation of T-lymphocytes upon antigen stimulation is a critical step in the response of the human immune system to pathogens. Regulation of T-lymphocyte gene expression at the level of messenger ribonucleic acid (mRNA) stability facilitates rapid, selective, and temporally precise responses to activation stimuli. These researchers use Affymetrix microarrays to investigate the stimulation-dependent changes in T-lymphocyte mRNA stability and gene expression. The results suggest that the coordinate regulation of many important genes, at both transcriptional and post-transcriptional levels, is essential for normal cellular function. Using this genome-wide approach, the researchers have investigated mRNA stability and gene expression changes in reovirus and human immunodeficiency virus (HIV)-infected cells. They are extending their studies on the role of mRNA stability in gene expression, by measuring genome-wide changes in expression intensities and mRNA decay rates at different time points following T-lymphocyte stimulation.

Research Group and Collaborator

Sharon Chen, Graduate Student Researcher
George Karypis, Faculty Collaborator
Rachel Ogilvie, Graduate Student Researcher
Arvind Raghaven, Research Associate
Nuzha Tahoe, Research Associate
Jayprakash N. Vaswani, Graduate Student Researcher
Irina Vlasova, Research Associate
Richard Walsh, Research Associate
Darlisha Williams, Staff
Gary M. Dunny, Principal Investigator

Analysis of Enterococcus faecalis in Biofilm Growth

The enterococci are frequent causes of opportunistic infections, particularly among hospital patients. It is highly likely that biofilm formation contributes significantly to the medical problems caused by enterococci, since biofilms on catheters, feeding tubes, and other implanted devices may serve as inocula for systemic infections, and as a niche for efficient horizontal transfer of antibiotic resistance and virulence genes. Endocarditis, the most serious enterococcal infection, also involves surface colonization and growth on heart valves in a biofilm-like state. These researchers are working to define the molecular and genetic basis of biofilm formation by Enterococcus faecalis and are determining the effects of disruption of selected genetic determinants for biofilm formation on the virulence of the organism. They are using the Computational Genetics Laboratory and the Scientific Development and Visualization Laboratory to analyze data from microarray experiments designed to identify highly expressed genes in Enterococcal bacteria from biofilms or from other physiological states.

Research Group
Christopher Kristich, Research Associate
Jesper Marklund, Research Associate

Ashley T. Haase, Principal Investigator

Response to Anti-Retroviral Therapy in Lymphatic Tissues

While it is known that highly active anti-retroviral therapy (HAART) curtails HIV-1 (human immunodeficiency virus) replication in lymphatic tissues, and partially reverses the pathological damage associated with infection, the genes that mediate these pathological and reparative processes remain largely unknown. This group used microarrays to profile gene expression in serial lymph node biopsies before and after treatment. The reduced expression after treatment of numerous type I and II interferon system, natural killer cell, and other innate immunity system genes points to a surprisingly prominent role for innate immunity in limiting HIV-1 replication before treatment. Because these genes were expressed in patients in later as well as acute stages of infection, innate immunity may significantly contribute to host defenses at all stages of infection. Based on the decreased expression after treatment of mediators and moderators of immune activation and defenses, this group is working on a model in which the treatment of mediators and moderators account for HIV-1 infection's slow dynamics before treatment. Anti-inflammatory agents alone or in combination with HAART could have a role in treating HIV-1 infection, by tipping this balance to mitigate pathology and promote lymphatic tissue healing.

Research Group and Collaborators
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Lijie Duan, Staff
Jacob Estes, Research Associate
Michelle Irvin, Graduate Student Researcher
Qingsheng Li, Research Associate
Cavan Reilly, Faculty Collaborator
Timothy W. Schacker, Faculty Collaborator
Stephen Wietgrefe, Staff
Marc K. Jenkins, Principal Investigator

CD4 T Cell Biology

CD4 T cells produce lymphokines when their antigen receptors bind to foreign peptides displayed on the surface of other cells, so-called antigen-presenting cells. The lymphokines produced by CD4 T cells regulate many aspects of the immune response, including antibody production and the microbicidal activities of other cells. The Jenkins laboratory has developed a system in which the activation status of CD4 T cells of known specificity can be monitored by flow cytometry, immunohistology, or confocal microscopy in vivo. They have used this system to define the roles of several lymphokines and surface receptors in the in vivo activation of CD4 T cells and antigen-presenting cells as they occur in the lymphoid tissues. By studying the activation of CD4 T cells in the body, the researchers hope to gain information that can be used to improve vaccines and inhibit deleterious T cell responses such as autoimmunity and graft rejection.

Research Group
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Stephen Huddleston, Research Associate
Andrea Itano, Research Associate
James McLachlan, Research Associate
James Moon, Research Associate
Kathryn Pape, Research Associate
Lori Schneider, Research Associate
Jennifer Walter, Staff
Traci Zell, Research Associate
The focus of this research program is to understand the basic processes by which bacteria and viruses cause disease and how their hosts respond to infection. To address this problem, the researchers apply genomics tools, including whole-genome sequencing, expression profiling using microarrays, and proteomics, to characterize microbial pathogens and the host response to infection. Many pathogens that affect humans also affect other animals, or have close relatives that cause animal infection. Comparative genomics using such pathogens can be beneficial in elucidating the specific pathogenic mechanisms driving human and animal disease. The ultimate goal of this research is to understand pathogenesis and identify novel drug targets and diagnostic tools for the identification and control of multiple infections, such as Johne's Disease (Mycobacterium paratuberculosis), avian pneumonia (avian pneumovirus, Newcastle Disease virus), porcine enteropathies (Lawsonia intracellularis), fowl cholera (Pasteurella multocida), bovine mastitis and toxic shock syndrome (Staphylococcus aureus), and tuberculosis (Mycobacterium tuberculosis).
These researchers are evaluating the response of human vaginal epithelial cells to superantigens, such as toxic shock syndrome toxin-1 and enterotoxins, viable bacteria, and other virulence factors. They incubate these agents with human vaginal epithelial cells for up to six hours, isolate the eukaryotic ribonucleic acid from the treated and control cells, and perform microarray analysis. The responses of treated cells are compared with the control untreated cells. The researchers are using the Computational Genetics Laboratory, the Basic Sciences Computing Laboratory, and the Laboratory for Large-Scale Data Analysis for this project.

Peter Southern, Principal Investigator

Human Organ Cultures and Microbial Infections at Mucosal Surfaces

These researchers have developed human organ culture systems to analyze the cellular and molecular mechanisms that underlie microbial infections at mucosal surfaces. Intact epithelial surfaces from tonsil, ectocervix, and endocervix have been infected by exposure to the human immunodeficiency virus (HIV) to validate the feasibility of this novel experimental approach. The group is developing protocols to assess synergy between different microbes to determine whether HIV susceptibility can be increased by pre-existing or simultaneous infections with unrelated microbes. They have developed a multi-microscope approach to reconstruct the infectious process and create a valid model to study natural routes of infection with human pathogenic microbes.

The researchers are using resources at the Basic Sciences Computing Laboratory to analyze the confocal microscopy data and to create three-dimensional reconstructions of mucosal surfaces that have been exposed to cell and HIV virions.

Research Group
Diane Maher, Graduate Student Researcher
Kenneth D. Vernick, Principal Investigator

Pathogenomics of Malaria-Host Interactions

These researchers are using the Computational Genetics Laboratory for analysis of functional genomic, genetic, and proteomic data relating to host response to malaria infection.

Research Group
Fred Oduol, Research Associate
Jun Li, Research Associate
Jiannong Xu, Research Associate
Yan Zhang, Graduate Student Researcher

Christopher M. Gomez, Principal Investigator

Genetics of Dominantly Inherited Spinocerebellar Ataxias

The dominantly inherited spinocerebellar ataxias are a clinically and genetically heterogeneous group of neurodegenerative disorders characterized by progressive imbalance, dysarthria, and uncoordination. Genetically distinct subtypes differ clinically, due in part to involvement of extracerebellar neuronal populations. These researchers have identified a five-generation family with progressive ataxia in which all affected males are infertile. Identification of the gene responsible for this unique phenotype may shed additional light onto the pathogenesis of ataxia, mental retardation, and male infertility. In addition to this family, the researchers are also studying several pure ataxia families. They are using the Computational Genetics Laboratory to perform linkage-wide genome analyses in all the families.

Research Group
Guo-Yun Yu, Research Associate
**Bagrat Amirikian, Principal Investigator**

Neuronal Structure With Coherent Properties

The long-term goal of this research project is to elucidate a relationship between the structure and function of fundamental distinct areas in the neocortex, in general, and the motor cortex, in particular, by a combination of theoretical methods with experimental approaches. The researchers are working to advance the understanding of whether and how the spatio-structural constraints on intrinsic connectivity affect the segregation of neurons into functional modules. They are working on a three-dimensional lattice model that allows for a fundamentally novel approach to studying directional operations performed in the motor cortex by providing means for explicit exploration of the link between the underlying local cortical structure and global collective properties of interacting cells that are substrates of this structure. The model will allow the researchers to bridge theoretical frameworks and experimental data in the domain of very large-scale simulations of networks of simplified neurons.

**Research Group**
Pavlos Gourtzelidis, Research Associate
Thomas Naselaris, Graduate Student Researcher

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**Jon Gottesman, Principal Investigator**
**Robert F. Miller, Co-Principal Investigator**

Monte Carlo Modeling of a Retinal Ribbon Synapse

These researchers are simulating neurotransmitter diffusion, ligand-reception interactions, and ligand-transporter interactions in three-dimensional space. This project extends previous work performed on desktop computers, and will implement a complex spatial geometry to more accurately represent the relationships between transmitter release sites, post-synaptic receptors, transmitter transporters, and a more complex extracellular space.

Prior simulations of single vesicular release events, including a tonic concentration of transmitter in the simulation space, have demonstrated that this tonic level plays a substantial role in the amplitude and threshold of postsynaptic processes. Furthermore, the researchers have discovered that N-methyl-D-aspartate receptors can be located as close as 250 nm from the site of vesicle release without responding to a single exocytotic event, but will contribute to stimulus-evoked release of multiple vesicles. This conforms to physiological observations.

The researchers will quantify the sources of variability in neural responses after they have completed the simulation runs and subsequent analysis. They have also developed a new model of both the pre- and postsynaptic cell that allows them to begin to study the release of multiple vesicles from a single ribbon site in an effort to characterize the response of the synapse to light-evoked activity.

**Research Group and Collaborator**
Tom Bartol, Computational Neurobiology Laboratory, Salk Institute for Biological Studies, La Jolla, California
Josh Mrazek, Undergraduate Student Researcher
Alexander E. Kalyuzhny, Principal Investigator
Immunohistochemical Study of Interactions of Opioid Receptors With GABA-ergic Systems

This research is focused on investigating interactions of opioid- and gamma-aminobutyric acid (GABA)-ergic neurotransmitter systems within the descending antinociceptive brainstem circuits, including the periaqueductal gray, the rostroventral medulla, and the dorsal horn spinal cord. To study these interactions, the researcher employs multi-color fluorescence immunohistochemistry on cryostat sections of rat brain in combination with retrograde tracing techniques to label spinally projecting neurons. Stained brain tissues are analyzed using both conventional fluorescence and confocal microscopy. In some cases, the researcher performs quantification of profiles, which co-express several target proteins. This work helps to understand cellular mechanisms underlying antinociception so more efficient therapies can be developed to treat pain.

Naoko Koyano, Principal Investigator
Steven C. McLoon, Co-Principal Investigator

Analysis of Gene Cascade Regulating Vertebrate Neurogenesis

A fundamental question in developmental neurobiology is how multipotential progenitor cells differentiate appropriately as specified by temporal and topographic coordinates to construct the intricate composition of neurons and glia. This project investigates the functions of transcription factors regulating this process.

In order to dissect the gene cascade used in neuronal differentiation, these researchers examined the genetic cascade initiated by neurogenin, a basic helix-loop-helix transcription factor. They overexpressed neurogenin under various conditions in *Xenopus* embryos, prepared carrier deoxyribonucleic acid (cDNA) probes from them, and analyzed gene expression profiles on *Xenopus* cDNA microarrays. They identified numbers of neurogenin targets and are further examining individual downstream pathways using the microarray. The group plans to use data-mining techniques to analyze the data in detail.

Other projects include differentiation of retinal cells and stem cell manipulation using various molecular biology techniques. The researchers are using the Basic Sciences Computing Laboratory and the Computational Genetics Laboratory for this work.

Research Group
Hyun-Jin Yan, Graduate Student Researcher
Tongbin Li, Principal Investigator
Support Vector Regression Approach to Capturing Peptide Sequence Characteristics

The primary structure (sequence) determines crucial properties of short peptides, such as their binding affinities with histocompatibility complex molecules and some categories of enzymes, such as protein kinases, phosphatases, and proteases. How to quantitatively represent features of a peptide pattern required for these reactions is a challenging problem. These researchers are using the support vector regression method to attack this problem, because of its demonstrated superiority in generalization/prediction performance among available machine learning tools. Preliminary exploration using a set of peptide array data suggests that good performance can be achieved with reasonably small sizes of peptide binding data.

Research Group
Wuming Gong, Research Associate
Jian Guo, Research Associate
Wen Liu, Research Associate
Yongliang Research Associate
Feng Xiao, Research Associate

A. David Redish, Principal Investigator
Electrode Localization Through Reconstruction of Three-Dimensional Patch/Matrix Anatomy

These researchers are studying the behavior of striatal cells in awake, behaving rats—they record the firing of striatal neurons and ask what information is carried by those firing patterns. The group has technology, consisting of 12 individual electrodes, that allows them to record from large ensembles of 50 striatal cells simultaneously, yet separately. The stratum consists of a complex, interdigitated structure called patch and matrix. Although these two “components” consist of similar cell types, they have different input and output pathways and should process different information. The researchers can detect the compartments and detect the positions of the electrodes that record the firing, but cannot tell which electrode corresponds to which marker. They are using visualization resources at Supercomputing Institute laboratories to create a three-dimensional structure that will allow them to determine the exact paths of the electrodes and to see the three-dimensional structure of patch/matrix.

Research Group
Deborah Bang, Graduate Student Researcher
Martin W. Wessendorf, Principal Investigator

Heterodimerization of Opioid Receptors

Pairs of different g-protein coupled receptors have been reported to heterodimerize. By doing so, they should exist within a few nanometers of each other. If these receptors do in fact heterodimerize, it should be possible to use light microscopy to detect single structures in the central nervous system that are labeled for both receptors.

These researchers have been able to detect single structures at the limit of resolution by confocal microscopy (i.e., smaller than 0.3 mm) that are labeled for two different types of receptors. Resolution could in principle be improved by deconvolving the confocal images, however. The researchers are using the resources of the Basic Sciences Computing Laboratory to deconvolve such images. Obtaining higher-resolution images will improve their ability to test which receptors, if any, may exist as heterodimers and to determine their distributions.

Research Group
Ming Gu, Graduate Student Researcher

George L. Wilcox, Fellow
Development of a Scalable, Parallelizable Surrogate Partitioning Algorithm for Large-Scale Multivariate Data Analysis

The Wilcox group is interested in developing scalable, parallelizable partitioning algorithms for large-scale multivariate data analysis. They are currently developing a surrogate-based algorithm for multivariate partitioning multichannel data acquisitions from whole-head magnetoencephalographic recordings from human brain. Component mixtures discovered by partitioning are compared with linear cross-correlogram analyses of the whole-head sensor map display to reveal commonalities between a subset of the distribution components and the observed linear interaction structure.

The group’s current effort is geared towards porting the datasets to the IBM SP and the Netfinity Cluster to compare performance metrics across architectures, while also incorporating instruction-level and loop-level parallelism into the code. They are adapting single-processor code that will facilitate batch data analysis on these two parallel architectures.

Research Group and Collaborators
Carolyn Fairbanks, Faculty Collaborator
Douglas W. (Chip) Hart, Graduate Student Researcher
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Marius Poliac, Poliac Research Corporation, Burnsville, Minnesota
Laura Stone, Research Associate
Pradyumna Upadrashta, Graduate Student Researcher
Antony Varghese, Faculty Collaborator
Stephen J. Haines, Principal Investigator

Three-Dimensional Surface Reconstruction of Brain Stem Neurovascular Relations

Certain anatomic relationships between the nerves and vessels of the brain stem are known to have an etiologic relationship to clinical conditions, such as trigeminal neuralgia and hemifacial spasm. It has not been possible to reliably predict the presence of the clinical syndrome from interpretation of two-dimensional scans of these anatomic relationships. It is possible that a three-dimension surface reconstruction of the neurovascular relationship will allow reliable identification of patients with these clinical conditions from the imaging data alone.

To this end, this project takes existing magnetic resonance scanning data and processes it using image-processing programs available through the Basic Sciences Computing Laboratory and the Scientific Development and Visualization Laboratory. Scans from normal patients and from patients with trigeminal neuralgia will be processed and evaluated against clinical information.

UM TC—Department of Neurosurgery

Stephen K. Juhn, Principal Investigator

Structure of Stereocilia Extracellular Links and Morphology and Hair Bundles

Stereocilia are connected together by extracellular links, which are involved in mechanoelectrical transduction, force transmission across the bundle, and maintenance of the hair bundle structure. Despite various studies, there is much that is poorly understood about the organization of the links and their properties. The objective of this project is to obtain more detailed information about the structure, properties, and function of the stereocilia links and their relationship to abnormalities of the stereocilia bundle caused by acoustic trauma.

The specific aims of this research are to study the structure of stereocilia links and the structure of the side link and its relationship to abnormalities of the stereocilia bundle caused by acoustic trauma, and underlying hearing dysfunction. The structural study of the stereocilia links is performed using transmission electron microscopy methods of protein crystallography and computer image analysis. The researchers are using resources at Supercomputing Institute laboratories for this project.

Research Group
Vladimir Tsiprun, Research Associate
Jizhen Lin, Principal Investigator
Mucous Cell Metaplasia in Otitis Media

Otitis media is one of the most common causes for visits to the emergency room and the second ranking for visits to a physician’s office in the United States. Approximately 5–10% of children with acute otitis media develop chronic otitis media with effusion.

One of the histological hallmarks of chronic otitis media is mucous cell metaplasia/hyperplasia in the middle ear that is progressive, irreversible, and destructive, and which frequently leads to hearing loss. The pathogenesis of this condition is poorly understood, so there is no effective treatment. These researchers studied the molecular mechanisms of mucous cell metaplasia induced by middle ear pathogens, especially pneumococcus, using cellular and molecular biology techniques. The three-step process was designed to: identify pneumococcal virulent components that trigger mucous cell metaplasia; determine the cellular events that mediate mucous cell metaplasia; and determine transcription factors that drive the basal cells in the middle ear into proliferation and differentiation to mucous or goblet cells.

Research Group and Collaborators
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Vivek Kapur, Faculty Collaborator
Wei Pan, Research Associate
Vladimir Tsuprun, Research Associate
Jennifer Zhao, Graduate Student Researcher

UM TC–Department of Pediatrics

Bruce R. Blazar, Principal Investigator
Angela Panoskaltsis-Mortari, Co-Principal Investigator
Identification of Gene Expression in Type II Pneumocytes

Keratinocyte growth factor (KGF) is a potent mediator of epithelial cell proliferation, as well as a growth factor for type II pneumocytes. It has also demonstrated cytoprotective properties against chemotherapy and radiation-induced injury. Investigations into the role of KGF in the lung have observed increased lung surfactant levels, increased alveolar fluid clearance, and decreased hyperoxic injury of type II pneumocytes. In order to further evaluate the mechanism of KGF-induced protection of the lung, these researchers are performing microarray analysis on KGF receptor-positive cells in the lung.

The researchers hypothesize that they will find increases in expression of genes involved in deoxyribo nucleic acid repair, surfactant production, alveolar fluid clearance, and other protective processes. They think they may also see a decrease in expression of apoptotic genes. After characterization of genes important for protection by KGF, the researchers may be able to investigate possible avenues for increasing the therapeutic benefit of KGF treatment.

Research Group
Andrew Price, Staff
Kevin Tram, Staff
Rolf R. Engel, Principal Investigator
Richard A. Oriani, Co-Principal Investigator

Mapping CR-39 Chips for the Distribution and Size Profile of Nuclear Tracks

CR-39 plastic chips acquire nuclear tracks when they are in proximity to the anode or cathode during the electrolysis of either D2O or H2O. Through digital imaging of these tracks, these researchers are trying to determine the identity of the responsible energetic particles and the conditions that promote their formation. Each image entails etching the CR-39 chip followed by digital photography of 1 mm² areas and subsequent stitching of 100 images with precise matching of the boundaries to permit automated subtracting of the pre-exposure tracks from the post-exposure image for the entire 1 cm² chip. The researchers have demonstrated the feasibility of this project by obtaining digital images of CR-39 chips before and after exposure to a known neutron source. This confirmed that it is possible to generate a digital image that represents the difference between the pre- and post-neutron exposure tracks for the entire chip. Further objectives are to streamline the process, to improve the quality of the image, to quantitate the number of tracks, to analyze the distribution of the tracks, and to characterize the different types of tracks formed during electrolysis experiments.

Wayne R. Godfrey, Principal Investigator

Gene Expression Analysis of Suppressor T Cells

This group is studying a particular type of immune cell called a suppressor T cell. It has recently been shown that these cells have broad relevance to almost all immune reactions, and in particular can prevent transplant rejection immune responses and interfere with immune responses to cancer cells. They have been shown in mouse models to prevent a serious complication of bone marrow transplantation, graft versus host disease (GVHD), and to regulate organ transplant immune rejection responses. Thus, study of these cells will aid in the development of tools to overcome their suppressive effects for inducing anti-cancer immune responses, as well as more directly to be utilized to suppress GVHD and facilitate bone marrow transplantation for leukemia patients. These researchers are studying the basic biology of these cells as well as developing the technical means by which to use these cells directly to prevent GVHD. They are conducting large-scale analysis of gene expression these suppressor T cells and comparing it to that of conventional T cells.

Research Group
Seth Baker, Graduate Student Researcher
Ying Ge, Staff
Stephen Porter, Staff
Elizabeth G. Ingulli, Principal Investigator
Simulation With Self-Peptide MHC Class-II Ligands

Self-peptide MHC class-II ligands (self-ligands) are required for thymic selection of a functional and self-tolerant T cell repertoire. Recent evidence suggests that self-ligands are also crucial for T cell activation in the periphery. These researchers have observed a progressive defect in CD4 T cell activation, proliferation, and interaction with antigen-presenting dendritic cells in the secondary lymphoid tissue after prolonged periods of self-ligand deprivation. Although antigen-specific CD4 T cells and antigen-presenting dendritic cells are present in the secondary lymphoid tissue, CD4 T cells seem to ignore their specific antigen. The researchers believe that self-ligand deprivation leads to a defect in CD4 T cell motility. They are using in vivo video microscopy and software available at the Basic Sciences Computing Laboratory for this research.

Michael Mauer, Principal Investigator
Youngki Kim, Co-Principal Investigator
Microarray Studies of Skin Fibroblasts in Type 1 Diabetes

Diabetic nephropathy (DN) is the leading cause of kidney failure and was responsible for 44% of all the new cases of kidney failure in the United States in 2001. These researchers are studying cultured skin fibroblast (SF) and renal proximal epithelial cells (PTEC) from type I diabetic patients in order to better understand the differences in behavior of these in patients with and without DN. They are testing the hypothesis that there are inherent cellular differences between type I diabetic patients with or without DN and that these differences are genetically determined and are associated with altered SF and/or PTEC gene expression. The goal is to use microarray techniques to test for gene expression differences in total ribonucleic acid isolated from SF and PTEC from type I diabetes patients that have been structurally and functionally polarized into two groups: one a “fast-track” group (high risk of DN) and one a “slow-track” group (low risk of DN).

The researchers are using the Basic Sciences Computing Laboratory and the Computational Genetics Laboratory for this project.
Duanqing Pei, Principal Investigator

Regulation of MT-MMPs by Trafficking in Cancer Cells

The goal of this project is to integrate the studies of membrane type 1 matrix metalloproteinase (MT1-MMP) and membrane type 3 matrix metalloproteinase (MT3-MMP) to test whether tumor cells modulate their invasiveness by controlling the trafficking of membrane-type matrix metalloproteinases (MT-MMPs) through their cytoplasmic domains. The project has three specific aims. The first is to define the trafficking of MT1-MMP and MT3-MMP from cell surface to the clathrin coated vesicles, early endosomes, late endosomes, trans-Golgi networks, and lysosome, and to characterize the impact of growth factors and extracellular matrix on their trafficking. The second is to define the role of cytoplasmic domains of MT1-MMP and MT3-MMP in mediating their trafficking and characterize their interactions with cellular components including adaptor protein-2 adaptins. The third aim of the project is to define the regulatory role of trafficking on MT1-MMP and MT3-MMP mediated cell growth and invasion within or through three-dimensional type 1 collagen matrix.

The results from this research may yield insights into how tumor cells gain a growth and invasive advantage by regulating MT-MMP trafficking. Such insights may lead to the development of novel drugs for therapy and chemoprevention of cancer.

Research Group
Ping Cui, Research Associate
Kris England, Research Associate
Ping Wang, Research Associate
Xing Wang, Research Associate

Li-Na Wei, Principal Investigator

Studies of Orphan Receptors and the κ Opioid Receptor Gene

This project aims to identify regulatory factors for the κ opioid receptor gene and those affected by the orphan receptors TR2 and TR4. The project involves characterization of the regulatory regions, identification of protein factors binding to these regions, examination of protein interactions among these factors, and the study of how chromatin structure of the regulatory region is affected by these protein factors. The researchers are using various molecular biological approaches, and they are collecting sequences and structure information and align them to the databank for future characterization. They are also performing computational studies.

Research Group
Jing Bi, Graduate Student Researcher
**W. Gibson Wood, Principal Investigator**

**Cholesterol-Lowering Drugs and Gene Expression in the Brain**

This project investigates statins and the mechanism by which they lower the risk of Alzheimer’s Disease. Statins have pleiotropic effects in addition to lowering cholesterol and they may act on several different pathways involving distinct gene expression patterns that would be difficult to determine by focusing on a few genes or their products in a single study. In addition, gene expression patterns may be specific to a particular statin. Using deoxyribonucleic acid (DNA) microarrays to identify gene expression patterns in the cerebral cortex of mice chronically treated with lovastatin, pravastatin, and simvastatin, and determining brain statin levels using liquid chromatography-tandem mass spectrometry, the researchers revealed 15 genes involved in cell growth, signaling, and trafficking that were similarly changed by all three statins. Overall, simvastatin had the greatest influence on expression as demonstrated by its ability to modify the expression of 23 genes, in addition to those changed by all three drugs. Of particular interest was expression of genes associated with apoptotic pathways that were altered by simvastatin. RT-PCR experiments confirmed the microarray findings. All three drugs were detected in the cerebral cortex and acute experiments revealed that statins are relatively rapidly removed from brain. These results provide new insight into possible mechanisms for the potential efficacy of statins in reducing the risk of Alzheimer’s disease and lay the foundation for future studies.

**Research Group**
- Tammy Butterick, Graduate Student Researcher
- Urole Igbaibo, Research Associate
- Leslie N. Johnson-Anuna, Graduate Student Researcher
- Ximena Rossello, Graduate Student Researcher

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**Robert P. Patterson, Principal Investigator**

**Modeling of Electric Potentials in Human Thorax**

This project investigates various electrical measurements in the body. Three-dimensional models of the human thorax are generated from magnetic resonance images. These images are segmented and all tissues are assigned a corresponding electrical resistivity. Current paths through the body may then be studied by placing electrodes in the thorax model and solving the resulting forward problem. This group’s finite difference models consist of 3.8 million elements. Applications include design of implantable pacemakers and defibrillator electrode systems, impedance cardiology, body fluid and fat measurement, and electrical impedance tomography.

Recent work has focused on ways to quantify the amount of fluid in the lungs. This has required generating curves of the impedance of the thorax with various simulated hydration levels and various thoracic electrode configurations. The researchers are using the IBM Regatta supercomputer to run their models.

**Research Group**
- Andres Belalcazar, Graduate Student Researcher
- Hua Wang, Graduate Student Researcher
- Fei Yang, Research Assistant
- Jie Zhang, Graduate Student Researcher
Jürgen F. Fohlmeister, Principal Investigator
Neural Excitation Across Species of Vertebrate Retinal Ganglion Cells: Temperature Effects and the Function of Membrane Capacitance

This project analyzes nerve impulse trains elicited from retinal ganglion cells (RCGs) of the cat and rabbit and compares them with similar data from the tiger salamander and with the Hodgkin-Huxley model to determine the complement and magnitudes of active ion currents and to study effects of changing temperature. Among the numerous functions of membrane capacitance in shaping impulse waveforms and determining their amplitudes, its presence determines the minimum conductances necessary for excitation. It may also be the basis for extending the dynamic range of impulse-frequency responses, that is, the basis relative to which these central neurons optimize their ion channel densities for their information integration-function. The excessively large (by about a factor of four) ion conductances of the Hodgkin-Huxley model, while suitable for the spike-propagation function of axons, appear to suppress this potential function of membrane capacitance. Phase-plot analyses, which yield the precise magnitudes of current flowing during impulses, show a high degree of similarity in the complement of ion channels that underlie the impulse waveforms among RCGs of the amphibian and mammalian preparations. Among the quantitative differences is a substantially smaller Ca-current in rabbit RCGs relative to both tiger salamander and cat. These results and this analysis will be extended to the full morphology of RCGs, which involved non-uniform channel densities and a great enlargement in excitation phenomena.

David G. Levitt, Associate Fellow
Development of Software for Automated Fitting of X-ray Crystallographic Electron Density Maps

There have been huge technical advances in recent years in the solution of protein structures. The combination of synchrotron x-ray sources and selenomethione multi-wavelength anomalous dispersion phasing techniques made the generation of high-resolution electron density maps a routine procedure. The most time-consuming step is now the building of the initial protein structure into the electron density map. This procedure takes several weeks to months by a skilled investigator working at a high-performance graphics station.

This researcher has developed a new software routine that automates this function. The software is freely available (www.msi.umn.edu/~levitt) and is being used at a large number of research and industrial laboratories. The researcher is now working on fixing minor bugs and answering queries. The batch version of the program is written in standard C++ and can run on either the SGI or LINUX operating systems.
Doris A. Taylor, Principal Investigator

Cell Transplantation for Cardiovascular Repair

The objective of research in the Taylor laboratory is to develop alternative therapeutic strategies for the treatment of cardiovascular injury and disease states. The goal of this project is to evaluate how cell type, specific cell delivery conditions, and injury type interrelate to affect the safety and efficacy of autologous skeletal myoblasts or bone marrow mononuclear cell transplantation in damaged myocardium. The researchers believe that optimizing the relationship between these three factors will lead to maximizing functional benefit and minimizing risk for cell-based myocardial regeneration. They are attempting to discover the best cell types, doses, and locations for cell delivery and/or routes of administration to obtain the greatest improvements in function with minimal increase in toxicity, depending on whether the injury is acute or chronic.

Research Group
Harald Ort, Research Associate
Xiangrong Xin, Graduate Student Researcher

Bruce E. Hammer, Principal Investigator

Design of Electrode to Facilitate Fluid Transfer

These researchers are designing radio frequency electrodes that facilitate rapid vapor expansion and create directional fluid flow. The electrodes should be miniature in design but maximize the given area. The researchers are using finite element modeling tools to optimize the design for electrode area and electrolyte fluid and concentration, and also to understand heat convection and electromagnetic properties.

Research Group
Swagata Riki Banerjee, Graduate Student Researcher
Noam Harel, Principal Investigator
Visualization of Cortical Microvascular System Using High-Resolution Magnetic Resonance Imaging

Functional magnetic resonance imaging (fMRI) is the chief method for studying human brain function in vivo. The technique relies on the fact that, during increase in neuronal activity, there is a localized increase in blood flow. Oxygenated blood that rushes to the active region alters the MRI signal and consequently allows visualization of the localized brain regions “at work.” Thus, the detection of changes in neuronal activity is closely tied to the underlying vascular organization.

To improve the spatial specificity of fMRI, better understanding of cortical vascular and microvascular architecture is needed. These researchers are creating three-dimensional visualizations of microvascular systems. Three-dimensional reconstruction and visualization of the vascular volume will provide much-needed information about the spatial organization of the cortical microvascular system, including vessel sizes, orientations, and densities. This will enhance the ability to design image acquisition techniques and improve the interpretation of fMRI signals.

UM TC–Department of Surgery

Peter S. Dahlberg, Principal Investigator
Gene Expression in Esophageal Adenocarcinoma

The incidence of esophageal adenocarcinoma (EAC) has risen dramatically in the last two decades. As with other malignancies, changes in gene expression play a key role in the development and progression of other tumors.

These researchers have recently looked at the gene expression patterns from a small subset of EAC. They are now working to identify specific gene expression patterns from ERBB2 amplified tumors and ERBB2 amplified tumors with or without Herceptin® (generic name, trastuzumab) treatment.
Lester F. Harris, Principal Investigator
Leonard S. Schultz, Co-Principal Investigator

Dynamic Simulations of Solvated Protein/DNA Complexes

These researchers are conducting experiments investigating the mechanism(s) of a genetic switch controlled by deoxyribonucleic acid (DNA) regulatory proteins. They are interested in steroid hormone receptor protein interactions with DNA in the pathogenesis of breast cancer. The researchers have previously reported on a mechanism describing how these DNA regulatory proteins recognize and bind to their specific sites on DNA. They are conducting Particle Mesh Ewald periodic boundary molecular dynamics simulations investigating atomic interactions between amino acids of the DNA regulatory proteins and nucleotides of their cognate DNA binding sites. They are studying models of the 434 bacteriophage proteins in complex with DNA sites involved in regulation of a classical genetic switch.

They are also studying a nucleosome DNA model containing specific DNA binding sites for steroid hormone receptor proteins that regulate genes associated with breast cancer development in mice. Finally, this group intends to use gene expression and phylogenetic alignment software in the Computational Genetics Laboratory to help characterize how the mouse mammary tumor virus under the regulation of steroid hormones contributes to development of breast cancer.

Research Group
Pamela D. Popken-Harris, Research Associate
Michael R. Sullivan, Research Associate

Bernard J. Hering, Principal Investigator

Mixed Chimerisms in Non-Human Primate

Mixed chimerism is a platform strategy to: permit transplantation without the need for chronic immunosuppression; control autoreactivity in autoimmune disorders; alleviate clinical symptoms in hemoglobinopathies, genetically based immunodeficiencies, and enzymatic deficiencies; and reduce risk of graft-versus-host disease through subsequent same-donor lymphocyte infusions for the treatment of hematological and selective non-hematological malignancies. To be clinically useful in these treatments, stable mixed chimerism must have minimal toxicity; to make it more widely applicable in transplantation, major histocompatibility complex barriers must be transgressed. These researchers have made several steps towards achieving these goals. Because of the complexity of the research protocol and the desirability of sharing the information with other researchers, this group is using resources at Supercomputing Institute laboratories to build a robust computerized electronic information system for this project.

Research Group
Tor Aasheim, Research Associate
Sue Clemmings, Research Associate
Melanie Graham, Research Associate
Maria Hardstedt, Research Associate
Tun Jie, Research Associate
Kevin Larson, Staff
Michael A. Maddaus, Principal Investigator

NSCLC Malignant Potential Defined by Microarray Analysis

Recurrence of disease in non-small cell lung cancer (NSCLC) is likely related to the presence of undetected micrometastases at the time of original surgical resection. Relapse and development of metastases commonly result in death. Since micrometastases represent the earliest manifestation of tumor dissemination, this project aims to identify the molecular mechanisms permitting micrometastatic cell growth and migration. The researchers hypothesize that identification of the set of genes critical to the early metastatic process will characterize the invasive phenotype and genotype of micrometastatic cells. The project includes acquiring molecular data using quantitative real-time polymerase chain reaction and carrier deoxyribonucleic acid microarrays and establishing a biological assay to study oncologic aggressiveness. The researchers will correlate molecular analyses from cell lines to biological assay characteristics. Thus, three significant relations can possibly be discerned: differences between a micrometastatic cell and its primary tumor; differences between lymph node micrometastases and circulating tumor cells in blood; and differences between primary tumors with and without accompanying micrometastases. The potential impact of this study may lie in the ability to translate microarray genetic information from individual patients through an easily obtained blood sample for novel therapeutic strategies.

Research Group and Collaborator
Chuong Hoang, Graduate Student Researcher
Robert Kratzke, Faculty Collaborator

Carl S. Smith, Principal Investigator

Dynamics of Urethral Sphincter Activity

Dynamical analysis is a mathematical tool that provides a powerful alternative to traditional biologic signal processing. Traditional approaches quantitate and characterize signals by parameters such as frequency, amplitude, and waveform in an effort to discover the underlying relationships within the system under study. A dynamical approach utilizes the same time-dependent information but constructs a visual picture, an attractor, of the nature of interaction found with the system that generated the signal. This is an extraordinary unexpected result in dynamical analysis; for the first time, there is a technique that allows a glimpse at the richness of structures that create the biologic signal. Furthermore, despite the apparent system complexity, a dynamical analysis can reveal a series of simple rules that govern the system’s behavior. This study examines the electromyographic signal present in the urethral striated muscle during bladder filling.
James R. Fricton, Principal Investigator
Sandra L. Myers, Co-Principal Investigator

Implants for Temporomandibular Joint Disorders

Temporal mandibular joint disorders (TMJs) are common disorders causing facial pain, headaches, clicking, locking, and diminished functioning in the jaw. In some cases, there is degeneration of the temporomandibular joint structure (bone and articulated cartilage) leading to pain, dysfunction, and destructive changes in the joint. TMJ implants have been used with surgery to treat these conditions. Further research is needed to explain the diverse outcomes associated with TMJ patients and to discover what characteristics of TMJ implants are best tolerated and most successful in these patients.

This project will develop a nationally recognized research registry and repository that is designed to collect clinical information and biological specimens on patients with TMJ disorders throughout the United States. This will simulate more research in TMJ disorders and advance the understanding and success of treatment of patients with this painful condition.

Research Group and Collaborators
Mike Davin, Staff
Patricia Carlson, Research Associate
Nancy Hardie, Faculty Collaborator
Wenjun Kang, Graduate Student Researcher
Lois Kehl, Faculty Collaborator
John Look, Research Associate
Wei Ouyang, Graduate Student Researcher

Joel D. Rudney, Principal Investigator

Extracrevicular Invasion by Periodontal Pathogens

A major goal of this project is to determine whether mucosal cells taken directly from the mouth contain intracellular oral bacteria. Fluorescent probes to conserved and species-specific regions of bacterial 16S ribosomal ribonucleic acid are used to label bacteria associated with human buccal epithelial cells. The researchers then use confocal microscopy to collect z-stacks of cells that appear to contain intracellular bacteria. Using software available at the Basic Sciences Computing Laboratory, the researchers can create three-dimensional reconstructions to confirm that the labeled bacteria are actually present within the bounds of the cell membrane.

Research Group
Ruoqiong Chen, Staff
Massimo Costalonga, Principal Investigator

Study of the Pathogenesis of Periodontitis in Vivo in a Mouse Model

These researchers are using Supercomputing Institute laboratory resources to stably transform Porphyromonas gingivalis with a series of genes. Their objective is to study the pathogenesis of periodontitis in vivo in a mouse model. They are testing the immunological response to a series of antigens, namely hen egg lysosome, E Alpha, and ovalubimin.

Patrick W. Mantyh, Principal Investigator

Molecular Mechanisms of Bone Cancer Pain

The overall goal of this project is to gain a better understanding of the factors that generate and maintain bone cancer pain due to a mixed tumor, i.e., one that induces both bone destruction and formation. The researchers are examining how peripheral factors such as tumor growth, bone destruction, and sympathetic neurons excite or modulate sensory neurons and thus contribute to bone cancer pain. Also, they are examining how inputs from sensory fibers that innervate the tumor-bearing bone alter the cellular and neurochemical characteristics of the spinal cord and dorsal column nuclei and thus contribute to central sensitization. While the present project focuses on bone cancer pain, these experiments may also provide insight into non-osseous types of cancer pain and aid in the development of novel strategies for controlling cancer pain in humans.
Lynn E. Eberly, Principal Investigator
Model Comparison in Gamma Frailty Models

Clinical trials conducted at more than one clinical center often result in correlated survival data: observations taken on patients within a clinic may be correlated or recurrent observations from the same patient may be correlated. Ignoring such correlation can lead to biased estimates of and underestimated variances for the effect being tested, such as the comparison of two medical treatments or procedures. To accommodate both kinds of correlation, several types of frailty models could be used. This leads to a need for appropriate statistical tests to choose among these types (model selection). These researchers worked on a project to explore and characterize the theoretical properties of likelihood ratio tests for comparing frailty models. To accomplish this goal, they carried out a simulation study using at least 1,000 datasets for each simulation scenario for good precision.

Research Group
Xin Zhi, Graduate Student Researcher

Patricia M. Grambsch, Principal Investigator
James D. Neaton, Co-Principal Investigator
Interim Monitoring of Randomized Clinical Trials With Multiple Endpoints

Many clinical trials have multiple outcomes and formal interim monitoring guidelines that can be useful to Data and Safety Monitoring Committees. These researchers have developed an approach for stopping trials that takes into account cases where there is not a clear difference between a safety and efficacy endpoint, or where there is interest in more than one disease outcome. They consider trials with two treatments and develop sets of two boundaries, a higher and a lower one, permitting one endpoint to be primary and other supportive or secondary, with or without pre-specifying which one is primary. The boundaries control the overall type 1 error with consideration of the endpoint correlations through multivariate integration. The results show that the boundaries from the new decision rules depend on the correlation between the two outcomes. For low to moderate correlation, critical values based on the O’Brien Fleming error spending function that consider the correlation are lower than those that do not. The researchers also carried out extensions of current bivariate sequential tests to allow more interim looks and to consider the correlation between endpoints.

Collaborator
Yanli Zhao, Lilly Company, Indianapolis, Indiana
Peter C. Raynor, Principal Investigator
Supercomputer Modeling of Airborne Particle Filtration

Fibrous filters are important tools for controlling exposure to potentially hazardous particles. New synthetic fibers with irregular cross-sectional shapes may improve filter performance beyond the capabilities of filters made with conventional fibers. The objective of this project is to determine how much filter performance is improved by using fibers with irregular cross-sections. The specific aims are to: develop flow fields for air moving past two-dimensional arrays of irregularly shaped filter fibers; model the movement of particles through the flow fields; and calculate the efficiency of particle collection by the fibers. The researchers use the computational fluid dynamics software program FIDAP on the supercomputers for this work.

This research will provide the first analysis of the possible advantages of using irregularly shaped fibers in filters. With this new information, filter manufacturers may be able to produce filters that can protect people better than is possible now.

Research Group
Seung Won Kim, Graduate Student Researcher

James S. Pankow, Principal Investigator
Michael B. Miller, Co-Principal Investigator

Genetic Epidemiology of Cardiovascular Disease and Associated Risk Factors

This research project seeks to detect, localize, and characterize genes involved in the development of cardiovascular disease (CVD) and its associated risk factors (e.g., diabetes, high blood pressure, elevated cholesterol, etc.). Recent technological advances in molecular biology and genetics have provided new opportunities to explore the genetic architecture of complex diseases and traits such as CVD. Genetic epidemiological research on such traits, however, requires data on thousands of individuals, hundreds of genetic markers, and complex statistical models that are computationally demanding. Supercomputing resources are used to construct models with high order gene-gene or gene-environment interactions that cannot be practically evaluated otherwise, and to conduct simulation experiments.

Research Group and Collaborators
Donna Arnett, Faculty Collaborator
Suzette Bielinski, Graduate Student Researcher
David R. Fermin, Graduate Student Researcher
Projwal Ghosh, Graduate Student Researcher
Adele Jiang, Graduate Student Researcher
Joanlise Leon, Graduate Student Researcher
Na Michael Li, Faculty Collaborator
Greg Lind, Research Associate
Yuhong Liu, Research Associate
Amy Lynch, Graduate Student Researcher
James Peacock, Research Associate
Laura Rasmussen, Graduate Student Researcher
Richard Sherva, Graduate Student Researcher
Weihong Tang, Research Associate
Kim Weis, Graduate Student Researcher
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   Sreekumar Raghavakaimal .............................................242
K. Sreekumaran Nair, Principal Investigator

Regulation of Gene Transcription in Diabetes

These researchers compared gene expression profiles using skeletal muscle biopsy samples from type 2 diabetic patients and healthy control subjects. They used Affymetrix GeneChip arrays available at the Computational Genetics Laboratory for this project.

Iftikhar J. Kullo, Principal Investigator

Evolution of Regulatory Regions of Candidate Genes for Atherosclerotic Vascular Disease

In order to provide formal population genetics-based evidence of molecular selection on candidate genes for atherosclerotic vascular disease, these researchers are performing a systematic analysis on candidate genes. They are using the LINUX cluster to calculate the measures of population differentiation, to perform several neutrality tests, and to perform permutation tests for the significance of neutrality tests based on coalescent simulation.
Mayo Clinic–Department of Molecular Pharmacology and Experimental Therapeutics

Yuan-Ping Pang, Associate Fellow

In Silico Drug Design

This project’s goal is to develop and apply computational (in silico) methods for determining three-dimensional structures of drug targets from genomes and identifying drug candidates from chemical databases. This group has developed the Cationic Dummy Atom Approach for molecular dynamics simulations of metalloproteins. The group has recently developed small-molecule inhibitor leads of Severe Acute Respiratory Syndrome (SARS) virus protease using the information from the SARS genome and multiple molecular dynamics simulations. The researchers are further testing the practicality of their in silico methods in identifying small-molecule inhibitor leads of West Nile Virus protease, botulinum neurotoxin serotype A light chain, Bacillus anthracis lethal factor, XIAP, and BlyS. Successful completion of these projects will lead to in silico approaches that complete experimental approaches in drug discovery, and ultimately result in therapeutics for treating cancers and infectious diseases.

Research Group
Paramita Dasgupta, Research Associate
Alfonso Garcia-Sosa, Research Associate
Candace Kash, Staff
Kevin J. Langenwalter, Research Associate
Isidro Merino, Research Associate
John Streiff, Research Associate
Jason Thompson, Research Associate
Qi Wang, Graduate Student Researcher
James D. Xidos, Research Associate

Mayo Clinic–Department of Neuroscience and Neurology

Charles L. Howe, Principal Investigator

Modeling the Signaling Endosome Hypothesis

The signaling endosome hypothesis in its broadest interpretation states that all cells, regardless of size or architecture, compartmentalize signals generated by transmembrane receptor tyrosine kinases into membrane-bounded organelles of endocytic origin. These signal transduction platforms are long-lived, self-renewing transport vehicles that utilize cytoplasmic motor proteins such as dynamin to move a signal from the plasma membrane to the nucleus along microtubules. The traditional model for signal transduction from the plasma membrane depends upon simple diffusion of signaling molecules through the cytoplasm, with signals reaching the nucleus essentially as the result of a random walk from the plasma membrane. Because, however, the equations for diffusion are not vectorial, they only provide a measure of average root mean square particle movement without specifying direction. In contrast, facilitated transport of signaling endosomes is inherently vectorial and nucleus-directed because of the intrinsic properties of the microtubule network within cells. In order to quantify the efficiency of transport versus diffusion, this researcher is modeling the diffusion of several known signal transduction molecules as a random walk from the plasma membrane to the nucleus.
**Endothelial Marker Sequences**

This group used Supercomputing Institute laboratories for various projects during this year. One project dealt with osteosarcoma, a highly malignant bone tumor. For this project, the researchers analyzed microarray data of nearly 100 tumor samples and 10 normal osteoblast samples to identify differentially expressed genes between the two categories. Another project attempted to answer several questions about polyadenylation signal sequences. In their most recent project, the group is employing sequence alignment (paired and/or multiple) strategies to discover any nucleotide sequences among various tumor endothelial marker genes.

**Research Group**

Dinakar Desai, Research Associate
Alok Srivastava, Research Associate

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**Structure/Function Studies of Biological Macromolecules Related to Cardiovascular Functions**

The goal of this research project, which used the resources of the Basic Sciences Computing Laboratory, was to define the conformations and interactions of proteins of medical interest with cardiovascular functions. The studies specifically focused on corin and paraoxanase. Corin may cleave pro-B atrial natriuretic hormone in the heart. Paraoxanase appears to metabolize oxides lipids of oxidized low-density lipoprotein, activate the hormone gherlin, and catalyze organophosphates such as the warfare agents VX, soman, and sarin. Other goals were to pursue structural knowledge of frizzled proteins and vitamin D receptors involved in bone morphology and protein-protein interactions involving the co-regulatory protein RIP140. The project included x-ray crystallography, molecular biology, and biochemistry as well as computational and biophysical studies.
Sreekumar Raghavakaimal, Principal Investigator

Microarray Data Analysis

These researchers are involved with data analysis of four main types of microarray projects. These projects include: determining gene expression profiles in samples subjected to different treatments; analyzing gene expression profiles over a time course (for example, embryo development or cell cycle); studying changes in gene expression profiles in samples with different genotypes; and analyzing gene expression profiles in different tissue or cell types. The researchers use software available at Supercomputing Institute laboratories to aid in their analyses.

Research Group and Collaborators
Kathleen Barentes, Research Associate
Unnikrishnan Gopinathan, Faculty Collaborator
Michelle Hoeltzle, Faculty Collaborator
William Johnson, Faculty Collaborator
Christopher Kolbert, Research Associate
Alexey Leontovich, Staff
Michael W. Lin, Research Associate
The goal of this project is to create an experimental environment for analyzing and evaluating the performance of parallel computational geometry algorithms. The environment has three major components: a data-acquiring system, a communication system, and a computation system. The data-acquiring system will be established using graphic user interface technology so that the user can freely define the scenarios for testing and evaluation purposes. The communication system is based on the Unix PC mechanism using TCP/IP protocols and works as a connection component between the data-acquiring and computation systems. The computation system is dedicated to the implementation of the existing and newly developed parallel computation geometry algorithms on the IBM SP supercomputer and the Linux cluster.

The hop-constrained min-sum arborescence with outage costs problem consists of selecting links in a network so as to connect a set of terminal nodes $N = \{2,3,...,n\}$ to a central node with minimal total link cost. The maximum number of links between the central node and each terminal node $j$ is limited to a predefined number $h_j$ (the hop constraint). Each terminal node in the network has an associated outage cost, which is the economic cost borne by the network user whenever that node is disconnected from the central node due to failure of a link. This has been formulated as an integer programming problem and uses a Lagrangian relaxation-based heuristic. Lower bounds found as a byproduct of the solution procedure will be used to assess the quality of the heuristic solutions. Computational results over a wide range of problem structures can be used to show the effectiveness of the approach.
Diabetes mellitus is one of the most widespread diseases in the world. It is a metabolic as well as hormonal disorder characterized by relative or absolute lack of insulin. Several vanadium-containing compounds can serve as insulin mimics in the treatment of diabetes, but it is unknown what electronic or structural features are important for biological activity.

These researchers are investigating the chemical structure of several vanadium complexes using density functional theory. The main goal is to develop the three-dimensional structure around the vanadium atom as a function of ligand structure and the oxidation state of the metal. The researchers will use results from the computational work in conjunction with solid and solution phase data to help develop a more comprehensive relationship of the structure of vanadium complexes and their biological activity. This may help achieve the ultimate goal of developing new vanadium-containing compounds that could be used to treat diabetes.

**Research Group**
Jake Rafferty, Undergraduate Student Researcher
Luke Roskop, Undergraduate Student Researcher

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The self-organizing map (SOM) algorithm was developed in the 1980s. SOMs are useful in a variety of engineering and scientific applications, including speech and pattern recognition, image recognition, and signal processing. In addition, SOMs are widely used in visualization as a dimensional (feature) reduction tool. Because of the massive advance in the amount of data available, however, the high execution times required to train the SOM puts a limit to its use in many application domains, where either very large datasets are encountered and/or interactive response times are required. One approach is to improve the execution time of the SOM through parallelizing it on parallel computers. This project investigates a parallel implementation of one of the variants of SOM, Asynchronous Self-Organizing Map, which has proven to be efficient in theory.

**Research Group**
Jing Cheng, Graduate Student Researcher
Biao Xu, Graduate Student Researcher
Liqiang Zhang, Graduate Student Researcher
The effectiveness of impinging jets for augmenting convective heat transfer processes is well known and gas- and liquid-jet cooling finds many applications in industrial fabrication and manufacturing. In a recently completed project, these researchers used computational fluid dynamics to simulate the heat transfer processes that occur between a submerged laminar jet and a solid surface when the jet is oriented orthogonally to that surface. In particular, they characterized the effect of jet-velocity development on the local heat transfer coefficients. They used two simulation-minimization techniques: the first involved a complete nondimensionalization of the flow boundary conditions, the thermal boundary conditions, and the physical geometry; the second incorporated the design of simulations method to minimize the number of simulations required to characterize the solution domain.

In a new project, these researchers have begun developing numerical simulations of fluid flow in biological systems. These simulations are complicated by the fact that the walls that bound the flow passages are not stationary, but move as the fluid passes through the channels. This interaction between fluid and the boundary is one of the most difficult of all simulation problems to solve, and therefore requires Supercomputing Institute resources.

**Research Group**
Ryan Barrows, Graduate Student Researcher
Paul Chevalier, Graduate Student Researcher
Dean Hacker, Undergraduate Student Researcher
Sandra Sparr, Graduate Student Researcher
Jimmy Tong, Graduate Student Researcher
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