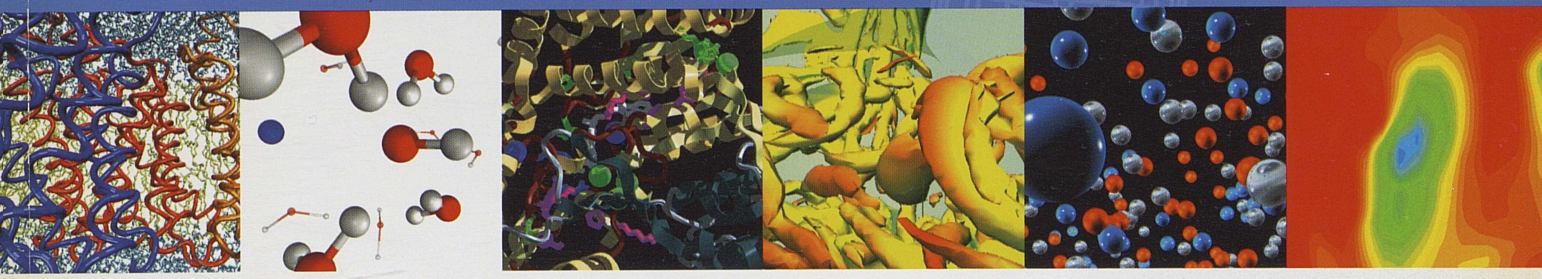
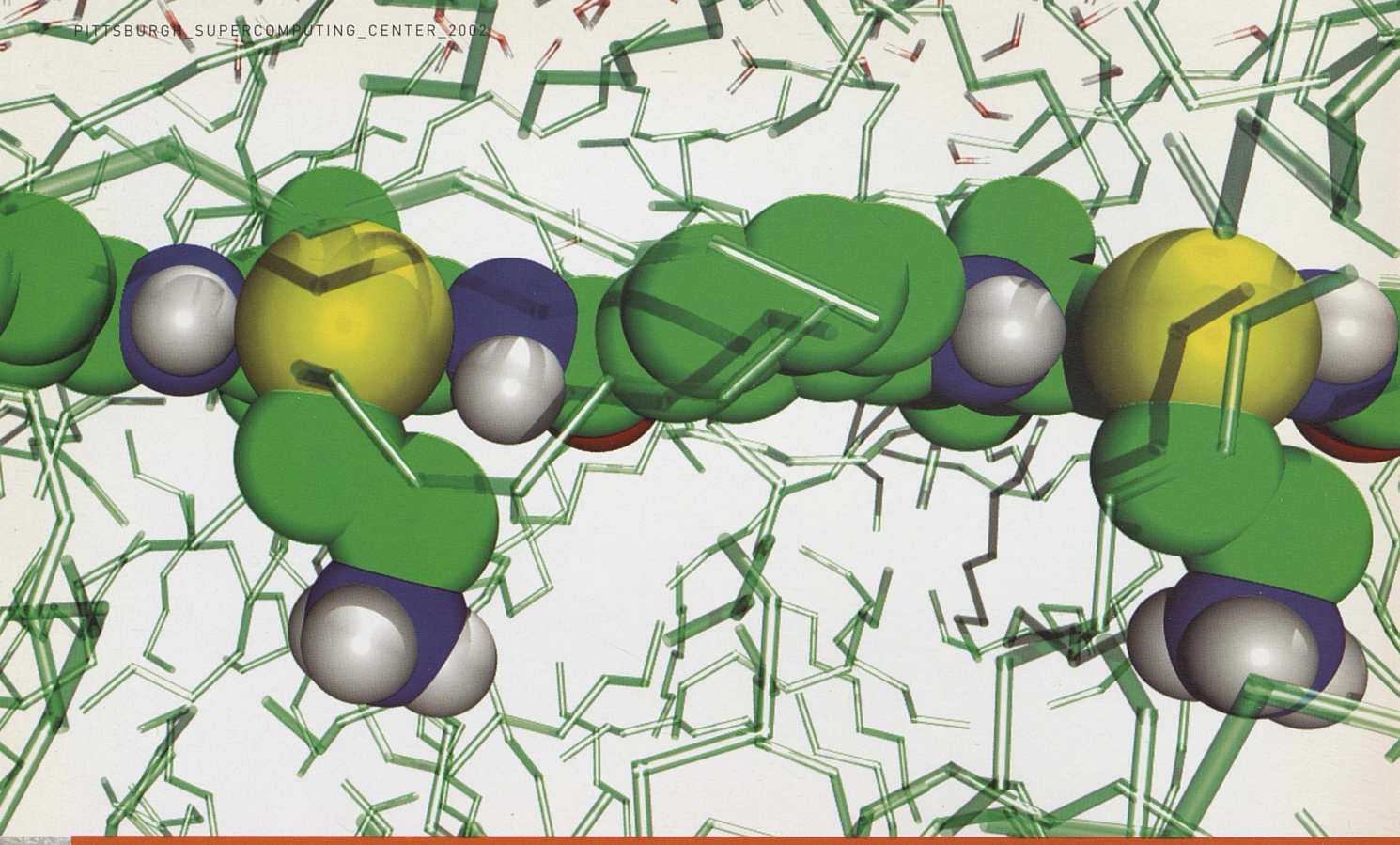
# PITTSBURGH SUPERCOMPUTING CENTER 2002



→ PROJECTS IN SCIENTIFIC COMPUTING



# PSC.EDU/02

PITTSBURGH_SUPERCOMPUTING_CENTER/2002→

The Pittsburgh Supercomputing Center provides academic, government, and industrial researchers with access to the most powerful public resource in the United States for high-performance computing, communications and data-handling. PSC advances the state-of-the-art in high-performance computing, communications and informatics and offers a flexible environment for solving the largest and most challenging problems in computational science. **WWW.PSC.EDU TEL:412-268-4960**

# FOREWORD_FROM_THE_DIRECTORS

A year ago we gathered with friends to celebrate installation of our 3,000-processor Terascale Computing System. This unprecedented system, based on the Alpha processor, was implemented with tremendous efforts from Compaq and, especially, the PSC staff, and at that ribbon-cutting event we anticipated that it would unleash the creative potential of the nation's scientists and engineers.

Only 12 months later, we are able to report that this investment in research technology, which culminated a National Science Foundation planning process, is paying major dividends. LeMieux, French for "the best," our name for the TCS, quickly caught on among the academic research community.

"This machine has been absolutely fantastic, enabling us to do calculations that were previously impossible." This comment from one researcher sums up the experience of many. The reports included here represent a selected sample of what LeMieux has accomplished.

In protein research, LeMieux quickly flexed its muscles. An April issue of *Science* reported new findings from Schulten and colleagues in Illinois solving a long-standing puzzle in the mechanism of aquaporin, an important protein family (p. 18). A team of PSC and University of Pittsburgh scientists used LeMieux to demonstrate a powerful approach to enzyme studies and in the process appear to have uncovered a mechanism for proton transfer that no one previously suspected (p. 26).

Michael Klein's group at the University of Pennsylvania exploited LeMieux for a range of large-scale simulations. Among them is their fascinating and important work (p. 22) on anti-microbial polymers, which has vast potential to improve our ability to protect ourselves from disease.

A multi-disciplinary Chicago team used LeMieux to push their research on blood flow to a new level (p. 30), capturing for the first time the transition from laminar to turbulent flow in a stenosed carotid artery. Their results will make it possible to study correlations between carotid artery flow patterns and risk for stroke.

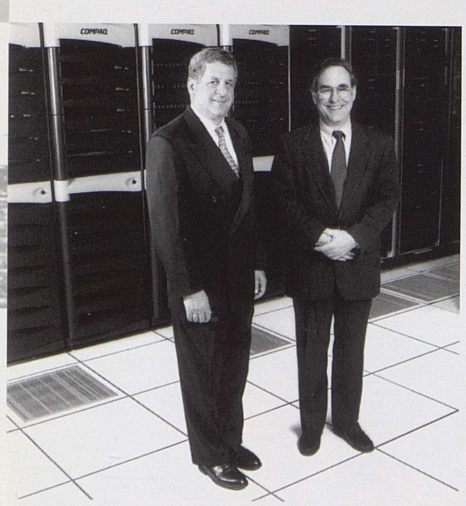
With a new simulation capability developed on the CRAY T3E — supported by the National Energy Technology Laboratory through the auspices of the regional Super Computing Science Consortium — Paul Cizmas is analyzing a new design for power-generating turbines (p. 34). With future work on LeMieux, he'll move to an advanced level of realism that may improve turbine efficiency, saving the country billions of fuel dollars.

The MILC team, among the earliest LeMieux users, used substantial computing resources to generate the most realistic lattices for QCD physics that are now available (p. 38). In combination with high-energy experiments, their results are closing in on fundamental parameters that define what we know about nature's smallest particles and most energetic interactions.

As we go to press, NSF has announced its award for the Extensible Terascale Facility (p. 4), which connects PSC with the TeraGrid, establishing a new level of cyber-infrastructure in this country. We are eagerly looking forward to the new science, and new modes of doing science, that this infrastructure will foster.

A 30 gigabit per second network will link the major NSF resources, including PSC, at unprecedented bandwidths, providing the physical basis for a much tighter coupling among these resources, which will become the nucleus for an evolving, national cyber-infrastructure. Through this award, we will also deploy new large shared-memory machines — from Hewlett-Packard — with superb memory bandwidth and data-handling capability that will enable new scientific breakthroughs.

We gratefully acknowledge our support from the National Science Foundation, the U.S. Department of Energy, the National Center for Research Resources of the National Institutes of Health, the Commonwealth of Pennsylvania and many others.




Ralph Roskies (left) and Michael Levine, Pittsburgh Supercomputing Center.

MICHAEL J. LEVINE, SCIENTIFIC DIRECTOR

RALPH Z. ROSKIES, SCIENTIFIC DIRECTOR

# CONTENTS

# Big Iron On a Fast Grid

## THE NATION'S MOST POWERFUL SYSTEMS ON THE WORLD'S FASTEST NETWORK

On October 10, 2002, the National Science Foundation awarded $35 million to PSC and its two sister supercomputing centers to create new technological infrastructure that will harness the nation's most powerful computing systems for open research into a seamless grid.

The grant will tie LeMieux, PSC's terascale computing system — the most powerful system in the country committed to unclassified research — into the world's fastest network.

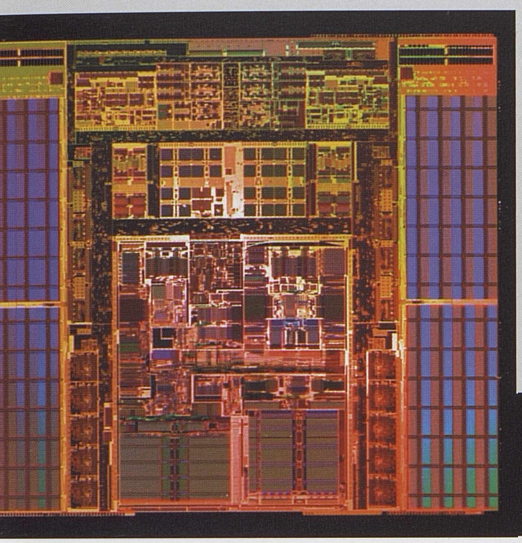
This optical-fiber, dedicated research network will transmit data at 30 gigabits per second, 500,000 times faster than typical Internet dial-up — fast enough, for instance, to download 750 copies of the complete works of Shakespeare every second. For scientists, this means it would be possible to download the entire Protein Data Bank in less than a second or all the x-ray data at a large technological hospital in about half a minute.

The TeraGrid will link PSC with two other NSF-supported supercomputing centers: the National Center for Supercomputing Applications (NCSA) at the University of Illinois, Urbana-Champaign, and the San Diego Supercomputer Center (SDSC) at the University of California, San Diego. The TeraGrid will also include a specialized facility at the Argonne National Laboratory (ANL) for data visualization and a data collection and analysis environment at the California Institute of Technology (Caltech).


With central hubs in Chicago and Los Angeles, the network will connect PSC and four other research centers in a unified national resource called the TeraGrid. Analogous to an electrical power grid, the TeraGrid will make computational power available to scientists and engineers nationwide, who will be able to submit their work without regard to geographical location of the systems.

PSC and other TeraGrid participants will develop software and policies to integrate resources so that a researcher needs to know only one protocol to log on, submit data, schedule jobs, etc. for computing systems, storage or other facilities at a TeraGrid site.

"This award will create the first wide-area computational grid encompassing terascale systems of differing architectures," said PSC scientific directors Mike Levine and Ralph Roskies. "This heterogeneity, which results from linking Pittsburgh and the TeraGrid, will enable new forms of science by coordinating resources at the five sites."



For PSC, the award boosts disk storage to 150 terabytes and it also augments LeMieux with a new system based on "Marvel" servers from Hewlett-Packard. This system, which employs the newest generation of Alpha processors, the EV7, will provide an unprecedented amount of memory and high-bandwidth interconnection among processors.

"The Marvel memory structure," said Levine and Roskies, "will provide an entirely new capability to the national research community. It will significantly boost certain kinds of research, including large-scale protein simulations and genome sequencing."

**ALPHA CHIP FOR THE HP MARVEL SERVER**

Micro-circuitry of Hewlett-Packard EV7, newest generation in the line of processors, the Alpha, that has served for three-generations of PSC massively-parallel systems. The EV7 is the heart of the new HP Marvel server.

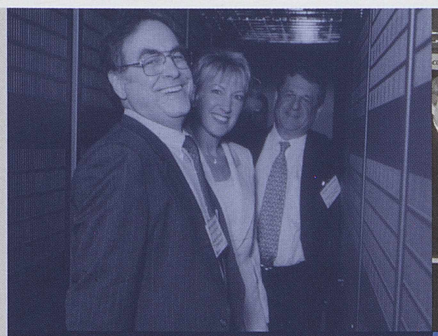
## CYBERINFRASTRUCTURE: IMPACT ON THE PITTSBURGH REGION

"This investment in technological infrastructure builds on our recent successes," said Jared L. Cohon, president of Carnegie Mellon University. "PSC, home of the most powerful computing resource for public research in the country, will now be linked with other powerful systems on the fastest public research network. It's one more statement that the high-technology assets of this region are second to none."

"Basic research is the foundation of our national economic strength," said Mark Nordenberg, chancellor of the University of Pittsburgh. "Our region and our two great universities — Pitt and Carnegie Mellon — are leaders in scientific innovation, and this award to the Pittsburgh Supercomputing Center both acknowledges and extends this leadership."

"The Pittsburgh Supercomputing Center is well known for pushing the boundaries of computational science and advanced networks," said Congressman Mike Doyle (D, 18th Dist). "This expansion of technological infrastructure is good news for the country and for the Pittsburgh region because once again PSC is recognized as a leader in high-performance computing."



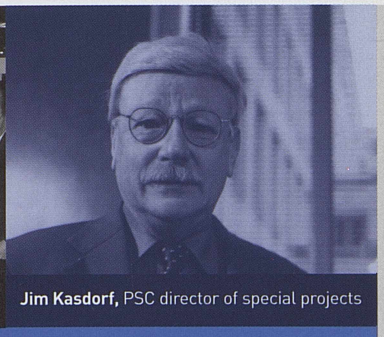


**HEWLETT-PACKARD CEO CARLY FIORINA VISITS PSC**

On August 22, 2002, Carly Fiorina, chief executive officer and chair of the Hewlett-Packard Company, visited PSC and toured the machine room at Westinghouse Energy Center, site of LeMieux, PSC's HP AlphaServer Terascale Computing System. PSC scientific directors Mike Levine and Ralph Roskies briefed Fiorina on research produced with LeMieux.

**RIBBON-CUTTING FOR LEMIEUX**

On Oct. 29, 2001, PSC scientific directors Mike Levine and Ralph Roskies showed the fine points of ribbon-cutting to PSC friends from Pitt, Carnegie Mellon, Westinghouse, Compaq, the National Science Foundation and the U.S. Congress. About 200 people in attendance at Westinghouse Energy Center watched via webcam broadcast and cheered as the ribbon fall signaled the public debut of this newest PSC system, the most powerful in the United States committed to unclassified research. The latest in a line of PSC systems in Pittsburgh black and gold, the Terascale was christened LeMieux, alluding to the Pittsburgh Penguins hockey great whose name in French means "the best."



**Jim Kasdorf,** PSC director of special projects

# Supercomputing in Pennsylvania

## WITH COMMONWEALTH OF PENNSYLVANIA SUPPORT, PSC PROVIDES EDUCATION, CONSULTING, ADVANCED NETWORK ACCESS AND COMPUTATIONAL RESOURCES TO SCIENTISTS AND ENGINEERS IN PENNSYLVANIA.

### WORKFORCE DEVELOPMENT

PSC workshops provide training for industry researchers as well as for university faculty and students. They include extensive hands-on sessions, either in PSC's Computer Training Center or at corporate and academic sites around the state. During the past year, along with many workshops in Pittsburgh, PSC presented a workshop in Parallel Programming Techniques at Penn State.

At the Bechtel Bettis Atomic Power Laboratory in Pittsburgh, PSC prepared and presented the second of two customized technology briefing days. PSC consultants provided Bechtel Bettis staff with information on how to develop, manage and use a parallel distributed-computing environment. The training included grid computing, hierarchical storage and scientific visualization.

PSC outreach includes presence at numerous conferences and science fairs. This June, Governor Mark Schweiker visited the PSC booth at BIO 2002 in Toronto. At this years BIO, an international life sciences conference, PSC joined over 200 representatives of Pennsylvania government and industrial academic organizations to launch the Pennsylvania Life Sciences Greenhouse Initiative.

Beverly Clayton, PSC executive director, coordinates PSC's program for Pennsylvania researchers. On Oct. 29, 2001, she em-ceed the ribbon-cutting celebration for PSC's terascale computing system, named LeMieux, for the Pittsburgh Penguins hockey great, whose name in French means the best. "The Terascale is the latest in a line of PSC systems," said Clayton, "that honor the Pittsburgh tradition of hard work by connecting its legacy of championship sports with PSC's computational achievements."

Governor Schweiker and PSC industrial coordinator Cheryl Begandy at BIO 2002

PSC trains Pennsylvania students through undergraduate internships. Since 1986, over 400 students have been interns at PSC, and many have gone on to find jobs in Pennsylvania. During the past year, PSC employed 37 undergraduate students from Carnegie Mellon, the University of Pittsburgh, Indiana University of Pennsylvania, Penn State and St. Vincent College.

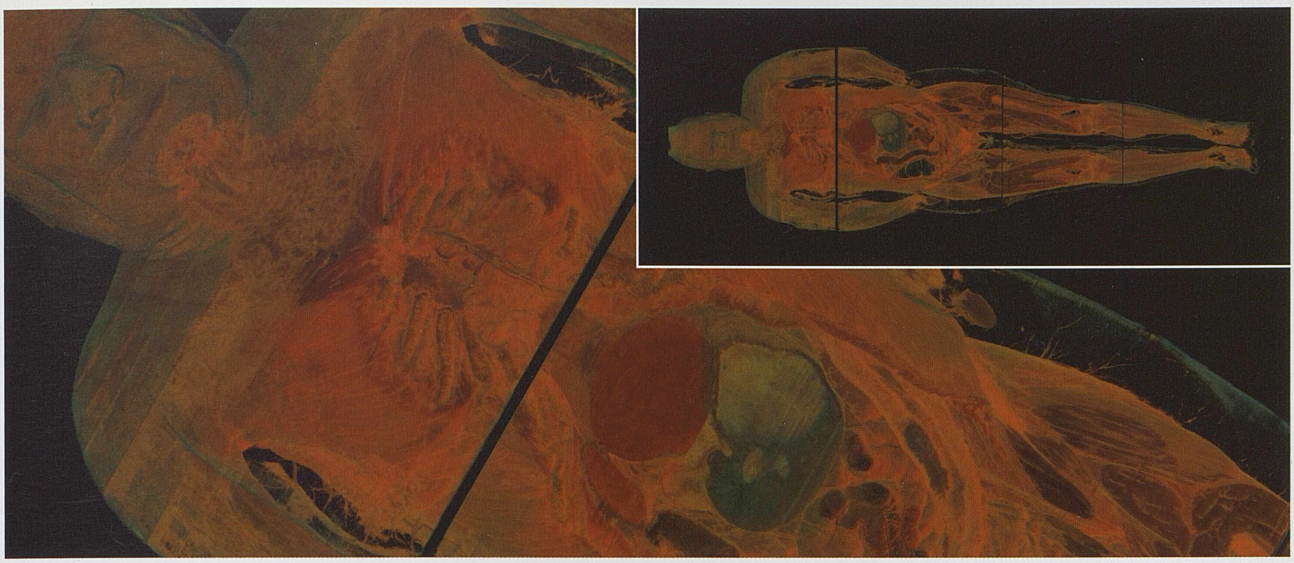
### ECONOMIC DEVELOPMENT

PSC's high-performance computing and networking resources help to boost the competitiveness of Pennsylvania business and industry. During the past year, PSC consultants have worked with a major Pittsburgh corporation to identify ways in which they can exploit the resources of PSC's CRAY T3E and Terascale Computing System to support their work in computational chemistry and quantum mechanics.

Other outreach includes briefings and tours, which this year included several public-school groups as well the members of the Pennsylvania Senate Communications and High Technology Committee.

### RESEARCH IN PENNSYLVANIA

By supporting Pennsylvania university researchers, PSC resources help to attract research funds to the state. During the past year, more than 700 Pennsylvania researchers from 14 institutions used more than a million CRAY T3E processor hours through PSC's Pennsylvania program. In addition, Pennsylvania campus researchers used nearly two million processor hours on the Terascale Computing System through the National Science Foundation allocation process. The projects represented here, along with other Pennsylvania projects featured in this booklet (pp. 26-29, 43, 44, 46), exemplify how supercomputing plays a role in scientific and engineering research in Pennsylvania.



## THE VISIBLE HUMAN

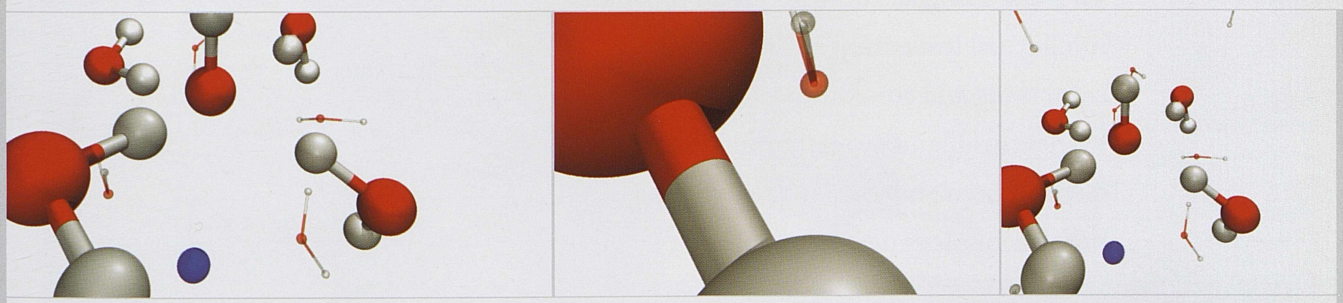
With funding from the National Library of Medicine, PSC scientists for the past three years have worked to develop software and networking to make better use of some unique data, the NLM's Visible Human Data Set. Compiled from painstaking preparation of two cadavers, a man and woman, with cross-sectional slices converted into digital form for computer access, the Visible Human is a powerful resource for education and training in human anatomy and for planning of surgery and radiation therapy.

Its effectiveness has been limited, however, because viewing technologies have allowed access only by 2D cross-sections from top, front or side views. The spinal column, for instance, isn't a straight line, so a single horizontal cross-section can't display more than a section of the spinal cord in one view. Similarly, looking at the heart from only a frontal or side view doesn't show how close it is to the spinal cord.

In collaboration with University of Michigan researchers, PSC has developed innovative software tools for interactive viewing that overcome these limitations. The Visible Human Browser, released in October, allows users to zoom in or out on the data and to select views from any angle or surface they choose. The software then reconstructs the corresponding image in real time.

Other browser capabilities to be incorporated in the future include advanced visualization features, as exemplified in this image. With a technique called "ray casting," the skin and fatty tissue become translucent. At the same time, muscular tissue is more opaque. As a result, veins in the legs, normally hard to see, stand out, a view that faciliates segmenting arterial tissue from surrounding tissue.





## FUNDAMENTAL STUDIES IN CHEMISTRY

Using PSC's Terascale System, University of Pennsylvania scientist Michael Klein and colleagues are carrying out fundamental studies of an important chemical system, the hydroxide ion (OH-) in water. This system has drawn the attention of chemists for years, even centuries, because of high electrical conductivity. In spite of many experimental studies in recent years — including neutron diffraction analyses and spectroscopic studies — there's not settled understanding about what molecular forms of hydroxide occur.

Klein's research team employed a powerful, quantum-theory based simulation technology called Car-Parinello molecular dynamics. They used up to 128 Terascale processors in parallel to simulate varying concentrations of sodium hydroxide and potassium hydroxide solutions. Prior computational studies of the hydroxides excluded the counterions, sodium and hydroxide, due to the added computational difficulty.

Their results, reported in the *Journal of American Chemistry*, include several important findings. Among them is that the clustered molecular structures of water change dramatically with the presence of hydroxide ions at high concentrations. Another important finding is that the solvation structure of hydroxide varies with concentration. At low concentration, $H_9O_5^-$ is preferred. At high concentrations $H_9O_5^-$ remains, but other structures are also present — $H_7O_4^-$ and $H_{11}O_6^-$.

This study, say the researchers, could not have been carried out except for LeMieux. Another paper in progress from these simulations will put forth a detailed atomic-level explanation of the proton-transfer mechanism in this system.

# The Super Computing Science Consortium

## PENNSYLVANIA-WEST VIRGINIA PARTNERS IN DEVELOPMENT OF CLEAN POWER TECHNOLOGIES.

Formed in 1999, the Super Computing Science Consortium $(SC)^2$ is a regional partnership of research and education institutions in Pennsylvania and West Virginia. New partners during the past year are Duquesne University, Pennsylvania State University and The Institute for Scientific Research in Fairmont, West Virginia. The goals of $(SC)^2$ are to provide intellectual leadership and advanced computing and communications resources to solve problems in energy and the environment and to stimulate regional high-technology development.

In the spring of 2000, a high-speed fiber optic network linked the National Energy Technology Laboratory (NETL) campuses in Pittsburgh and Morgantown, West Virginia and PSC. With this high-speed data channel, researchers at NETL and West Virginia University have used PSC resources to simulate fluidized-bed combustion of silane and the effects of lean-fuel mixes in next-generation power-generating turbines. In recent work (pp. 34-37), $(SC)^2$ provided the computational resources for simulations of a new turbine design, called a turbine-combustor, that can provide a power reserve for periods of high electricity demand.

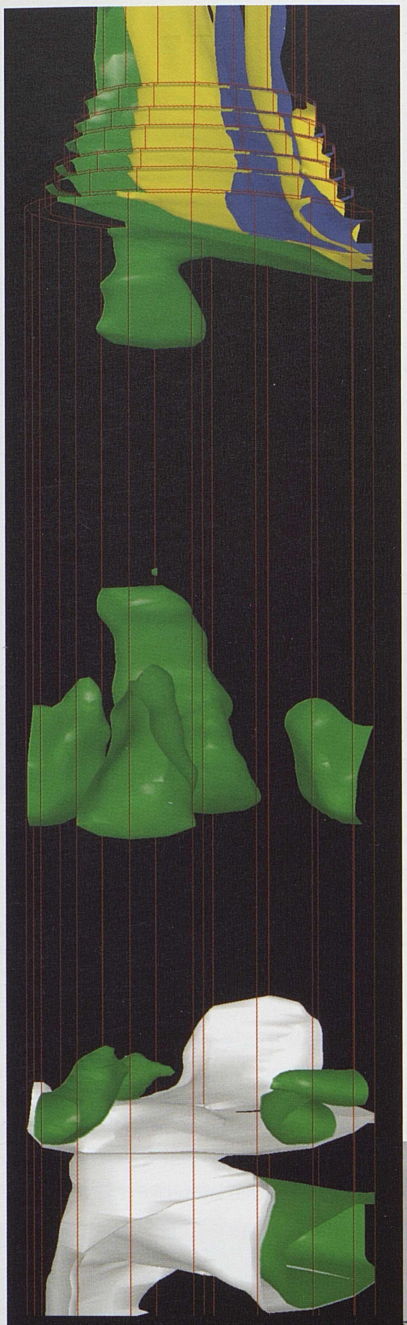
"PSC has been an active partner with NETL in supporting regional initiatives," said Rita A. Bajura, director of NETL. "$(SC)^2$ makes PSC's computing capabilities available not only to the region but also to the nation to further research in the efficient production and use of coal, oil, and natural gas — the resources that provide 85 percent of the nation's energy supply."

**MORE INFORMATION:** http://www.sc-2.psc.edu

Lynn Layman (left), Westinghouse Electric Company and Randy Harris, National Energy Technology Laboratory, co-directors of the Super Computing Science Consortium. "SC squared," says Harris, "began as a partnership between NETL and PSC to advance energy research and has grown to be a significant force for regional development and cooperation."

**$(SC)^2$ PARTNERS**

Carnegie Mellon University
Duquesne University
The Institute for Scientific Research
The National Energy Technology Laboratory
The Pennsylvania State University
The Pittsburgh Supercomputing Center
The University of Pittsburgh
West Virginia University
The West Virginia Governor's Office of Technology



This image from an MFIX simulation on PSC's LeMieux shows concentrations of methane (blue), carbon monoxide (green) and carbon dioxide (yellow) in the transport reactor mixing zone where it necks down into the riser. The simulation also tracks void fraction, the degree of unburnt solid material. The isosurface (white) represents a void fraction of 0.8 (20 percent solid) and shows how the flow becomes more dilute as it rises.

## COAL GASIFICATION

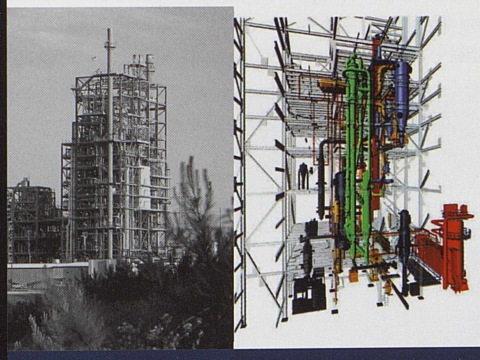
Environmentally clean, affordable power is the goal of research at NETL, and coal gasification is one of the technologies that will make a difference. "There are two issues with coal," says Jack Halow, director of NETL's simulation and multi-phase flow analysis division. "As a solid, it's difficult to transport compared to liquids and gas, and fundamentally it's difficult to remove contaminants from a solid. Once it's gasified, you can pipe it wherever you want, and in the gas phase, it's much easier to separate and remove the environmental contaminants."

In recent studies using LeMieux, PSC's terascale system, NETL researchers under the direction of project managers James Longanbach and Daniel Cicero carried out 3D simulations of the transport reactor from the Power System Development Facility in Wilsonville, Alabama. PSDF is a U.S. Department of Energy demonstration plant for advanced electric-power technologies, and the PSDF transport reactor is a "circulating fluidized-bed" that can operate as a coal gasifier.

In this plant-sized technology — the reactor unit is 80 feet tall — coal and recycled material feed into the lower part of the gasifier, called the mixing zone, where the coal combusts at high temperature and pressure. Hot gas and unburnt solids rise from the mixing zone into the riser. At the top of the riser, unburnt solids are collected and fed back into the bottom of the mixing zone. Eventually coal converts with nearly 100 percent efficiency into gas.

Among the research tools NETL has developed is simulation software called MFIX (Multiphase Flow with Interphase Exchanges), which realistically models the gas and particle dynamics, chemical reactions and heat transfer involved in coal gasification and other power-generating combustion processes. "Capturing the correct hydrodynamics in a circulating fluidized bed," says NETL consulting engineer Chris Guenther, who coordinated the MFIX computations, "is critical."

In this study, the NETL researchers simulate the flow as it moves from the mixing zone into the riser. They track the hydrodynamics of both the gas and solid phases along with heat transfer between the two phases and production of gas species, such as methane, carbon monoxide and carbon dioxide. "Design engineers," says Guenther, "want to see how design changes affect the hydrodynamics and the chemistry, which isn't readily available from experiments. With simulations, design changes can be tested at a fraction of the cost of building and doing experiments with a scale model."



The transport reactor (green) at The Power Systems Development Facility, a DOE supported experimental plant in Wilsonville, Alabama. NETL simulations complement testing and development at this plant-sized research facility.

## WORKFORCE DEVELOPMENT & EDUCATION

In spring 2001, with local government agencies, $(SC)^2$ helped to establish the EverGreene Technology Park in Waynesburg, Pa. To encourage research-oriented companies to locate in this primarily rural area, EverGreene offers a high-speed fiber-optic pipeline to the Internet and to PSC resources. During the past year, a materials analysis firm — expected to provide 60 high-technology jobs — committed to EverGreene and began architectural design for the site.

At Waynesburg College, $(SC)^2$ sponsored an outreach program for researchers at small colleges, with participants from a dozen colleges in three states. The program provided information on supercomputing, cluster technology and scientific visualization. The program also presented information on how to participate in $(SC)^2$. "The objective," says $(SC)^2$ co-director Lynn Layman, "is to provide exposure to high-performance computing resources and to encourage participation in the grant process."

An $(SC)^2$ summer program for middle schools included participants from three schools in West Virginia and Pittsburgh. The program presented teaching materials for high-performance computing. See http://www.netl.doe.gov/coolscience. "These are lesson plans," says Layman, "that teachers can use to supplement work in physics, chemistry or mathematics."

# Notes & Highlites

# BIOMEDICAL SUPERCOMPUTING

## NATIONAL LEADERSHIP IN COMPUTATIONAL RESOURCES FOR BIOMEDICAL RESEARCH.

In 1987, the PSC biomedical program became the first extramural biomedical supercomputing program in the country funded by NIH. Since then, with support from NIH's National Center for Research Resources, PSC has fostered exchange between PSC expertise in computational science and experts in biology and medicine to solve important problems in the life sciences.

PSC workshops and courses on computational biology have trained more than 2,000 researchers in the use of high-performance computing for biomedical research, in such areas as sequence analysis in genome research, the structure of proteins and DNA, and biological fluid dynamics. The National Human Genome Research Initiative this year renewed its decade-long support for PSC's workshop in Nucleic Acid and Protein Sequence Analysis. "Our training reaches hundreds of biomedical scientists each year," says biochemist David Deerfield, who directs the PSC program. "Techniques we've developed are helping scientists nationwide cope with the explosion of genome data."

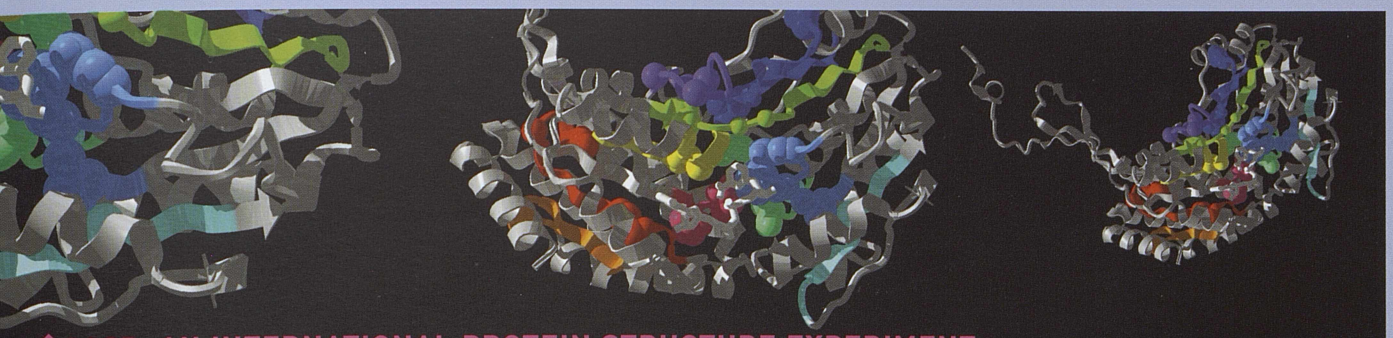
Since its inception, PSC's biomedical program has provided computing resources for more than 800 biomedical research projects involving nearly 1,800 researchers in 43 states and the District of Columbia. Among these are several projects featured in this booklet (pp. 18-29, 43), including research by PSC scientists on an important enzyme mechanism.

In addition to training and access to computational resources, the biomedical group carries out research in structural biology, protein and nucleic-acid sequence analysis, computational neuroscience and microphysiology. Its researchers collaborate with scientists at many other institutions, including the University of Pittsburgh Medical School, Carnegie Mellon University, the University of Michigan, Duke and the University of Edinburgh.

**MORE INFORMATION:** http://www.psc.edu/biomed

**DEVELOPING BIOINFORMATICS PROGRAMS →**

From July 8 to 19, PSC hosted 23 participants for a two-week course in the concepts and methods of "bioinformatics" — the field that marries information technology and the life sciences. Taught by PSC scientists, the course introduced the participants, from five colleges and universities, to the computational, mathematical and biological issues of this still-emerging field and prepared them to teach bioinformatics courses at their campuses. This course was supported by a grant from the Minority Access to Research Careers Branch of the Division of Minority Opportunity in Research of the National Institute of General Medical Sciences.



## ↑CASP: AN INTERNATIONAL PROTEIN STRUCTURE EXPERIMENT

**Deriving protein structures from genomic sequence data is the major challenge of contemporary computational biology. Genes are the blueprints for proteins, and the next step in harnessing the flood of data from genome research is using it to deduce the 3-D structure of proteins. For practical purposes, these problems are insoluble without advanced software and powerful computers.**

Among research groups worldwide, many methods have arisen. CASP (Critical Assessment of Techniques for Protein Structure Prediction) is a community-wide experiment held every two years to assess these various computational approaches. "Through CASP," says PSC biochemist David Deerfield, "the field moves toward consensus on such questions as which methods are most accurate, which most cost-effective, where can future effort most effectively be directed?"

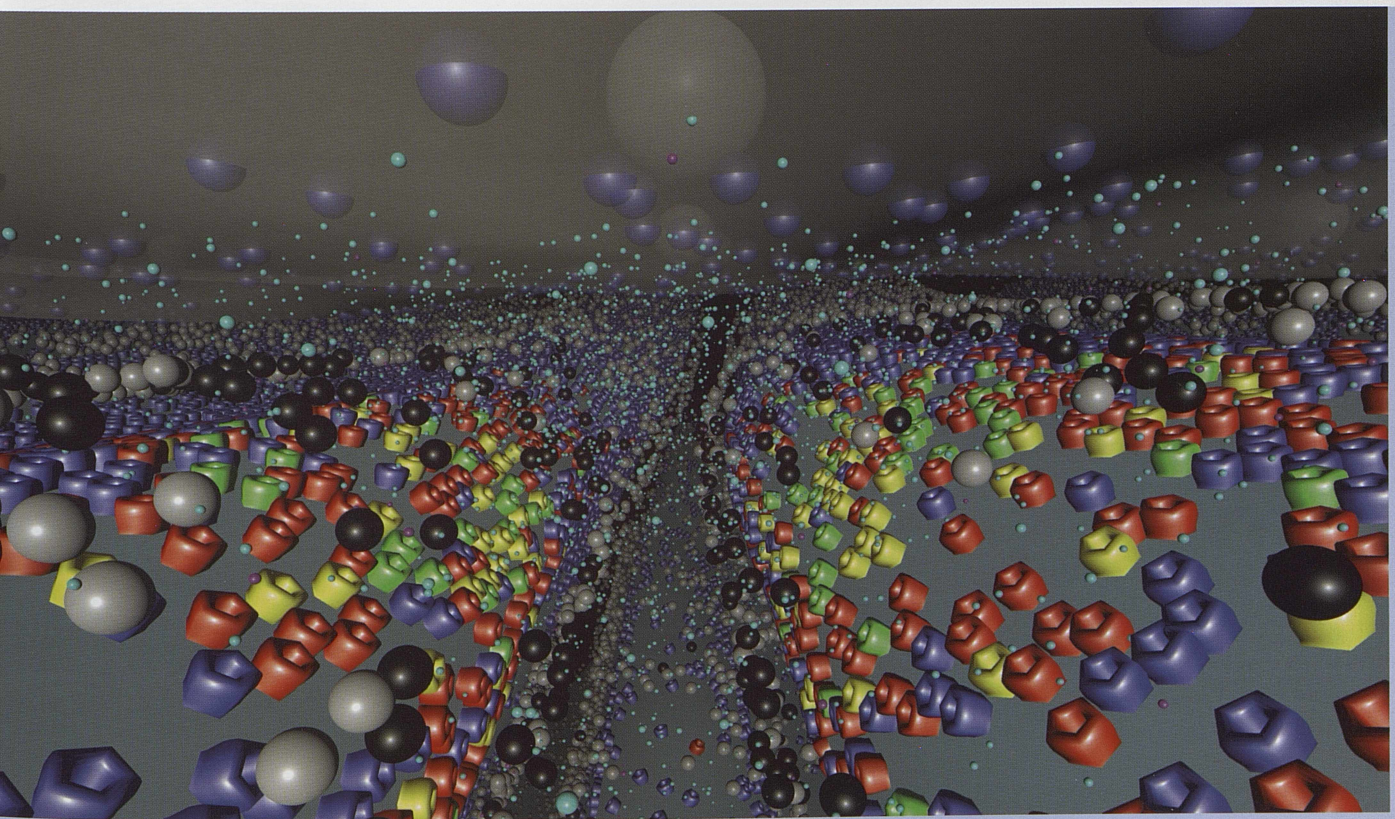
This year PSC and the Hewlett-Packard Company teamed to provide large-scale computational resources for CASP5, the fifth convening of this every-other-year event, for which participation has steadily grown to nearly 200 research groups worldwide. HP provided computing time on a 100-processor cluster of AlphaServer systems, and PSC made time available on LeMieux, PSC's terascale AlphaServer-based system.

## ↓WHERE NERVES END

With support from PSC's biomedical group and the Salk Institute, many research labs around the world use MCell and DReAMM, powerful software for simulating and visualizing chemical reactions that occur as molecules diffuse within, around and between cells. In recent work, PSC scientist and MCell/DReAMM co-developer Joel Stiles used MCell to simulate the mechanism of a degenerative neuromuscular disease. His studies predicted a never-before-seen defect in a protein involved in nerve-muscle communication, leading to experiments that verified his computational finding.

This image — from an MCell simulation — represents a closeup of a nerve-muscle junction and shows neurotransmitter molecules (small blue spheres) releasing from a synaptic vesicle (large white sphere, upper center). The valley represents a cleft in the geometry of the muscle cell. The colored markers indicate receptor proteins embedded in the muscle-cell wall. They're shown in four different states of interaction with the neurotransmitters, ranging from unbound (purple), to intermediately bound (red), fully bound (green) and activated (yellow). Other markers (white and black) represent two states of an enzyme that breaks down the transmitter to a non-transmitter molecule (small red spheres). In a normal muscle membrane, yellow becomes predominant at later times as receptors open and make current to stimulate the muscle cell.





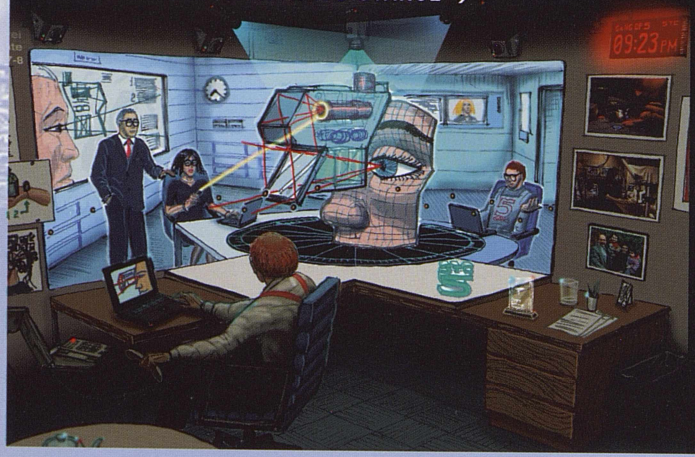
# NETWORKING THE FUTURE

## ONE OF THE LEADING RESOURCES IN THE WORLD FOR NETWORK KNOW-HOW.

PSC's team of network engineers, the National Center for Network Engineering (NCNE), is one of the leading resources in the world for network know-how. They provide engineering consulting for advanced networking nationally, and they conduct seminars that disseminate knowledge to engineers around the country. Since 1998, when an NSF grant established NCNE, their training activities have reached more than 2,600 people. In projects such as Web100 and Net100, they're actively involved in developing technologies that will define networks of the future.

**MORE INFORMATION:** http://www.ncne.org

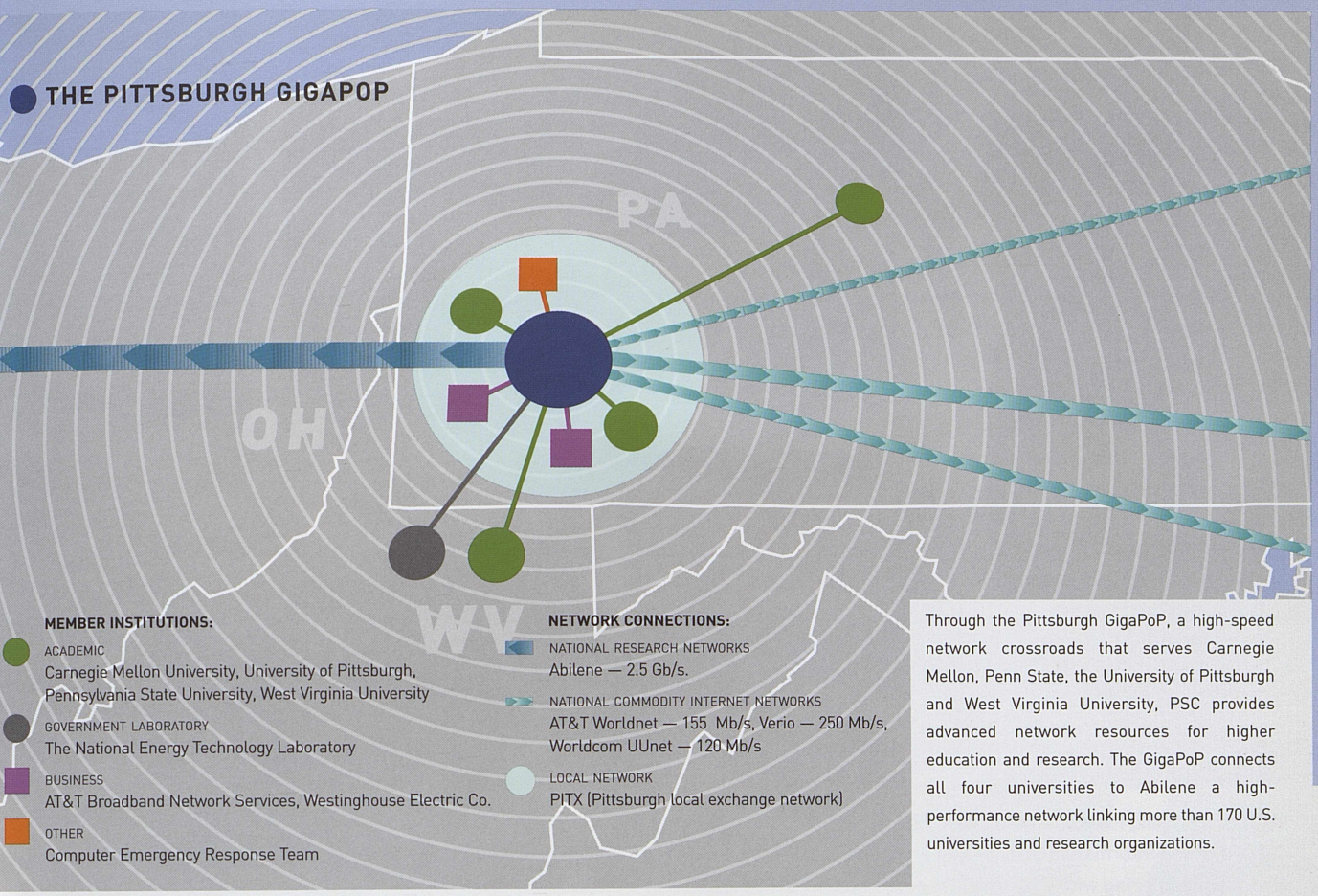
**TELE-IMMERSION:**
**HUMAN INTERACTION AT A DISTANCE →**




Offices equipped with computer vision and graphics systems that present the illusion you're in the same physical space as others who may be thousands of miles away — the idea is called tele-immersion. It will foster realistic human interaction across geographical distance.

In October 2001, PSC received an award — through the National Science Foundation Information Technology Research program — to collaborate with computer scientists at the University of North Carolina, Chapel Hill, and the University of Pennsylvania to develop and test a prototype tele-immersion system. The real-time focus of tele-immersion presents a novel use of large-scale computing systems, such as LeMieux, PSC's terascale system. The PSC networking group is developing mechanisms to minimize delays in data transmission to and from other sites.

Graphic created by Andrei State of the Department of Computer Science at the University of North Carolina at Chapel Hill.




Through the Pittsburgh GigaPoP, a high-speed network crossroads that serves Carnegie Mellon, Penn State, the University of Pittsburgh and West Virginia University, PSC provides advanced network resources for higher education and research. The GigaPoP connects all four universities to Abilene a high-performance network linking more than 170 U.S. universities and research organizations.



## GETTING IN TUNE WITH THE WEB100 & NET100

They call it the Information Superhighway, so why drive if you're going to putter along in second gear? This question, in various forms, inspired Web100, a research program funded by Cisco Systems and the National Science Foundation to help researchers realize the network's data-transfer potential.

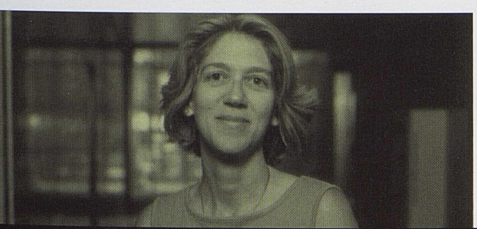
Most high-performance networks have bandwidth that can transfer data at 100 million bits per second (Mbps) or faster, but until recently researchers have seldom realized rates above a few Mbps. Network engineers at PSC, the National Center for Atmospheric Research (NCAR) and the National Center for Supercomputing Applications, have collaborated to improve this situation by developing software to "tune" computer operating systems to better exploit available network bandwidth.

The problem is that most computer operating systems come configured to transfer data at only one speed — usually slow — regardless of the underlying network. The network throttle of computer operating systems is controlled through the Transmission Control Protocol (TCP). By making adjustments to TCP settings, networking experts can tweak the operating system to move data faster.

The goal of Web100, which released its software publicly in February, is to eliminate the need for a human expert by automatically tuning the TCP settings to optimize performance. "We want to make it easier for everyone to move data across networks at 100 Mbps or higher," says Matt Mathis, PSC network research coordinator. Many research projects nationwide, including the NASA Earth Observer and the Visible Human (see p. 7), are now using Web100.

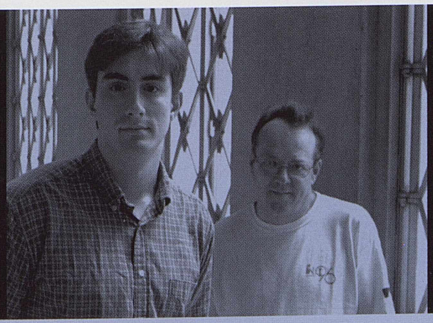
In September 2001, the U.S. Department of Energy awarded $2.5 million for a related project called Net100. In this project, which expands on Web 100, PSC's network group is collaborating with NCAR, Lawrence Berkeley National Laboratory and Oak Ridge National Laboratory. The goal is to make the operating system tune itself in response to changing conditions on the network. Net100 will develop tools to probe the state of the network and feed this information to an auto-tuning capability based on Web100.

net100 Web100



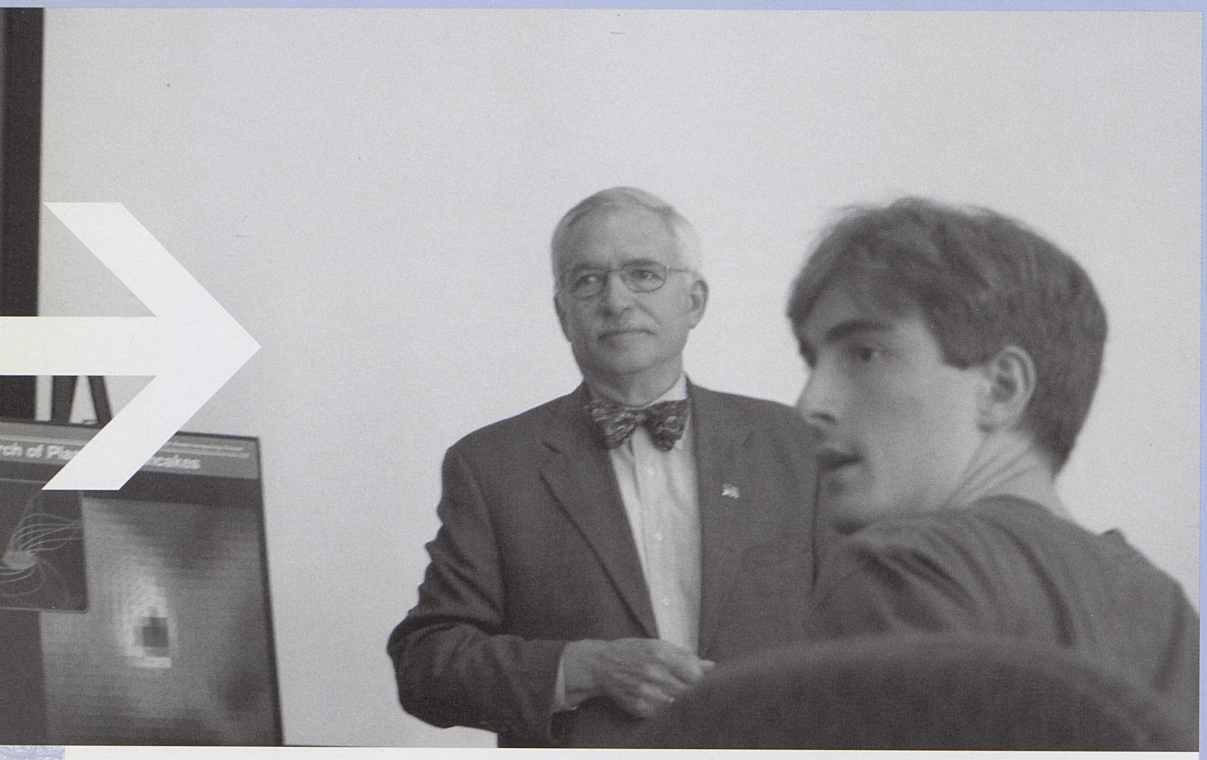
**↑ DIRECTOR OF THE QUILT**

In September 2001, Gwendolyn Huntoon, PSC assistant director for networking, agreed to serve as the first executive director of The Quilt, an effort of many U.S. regional networking organizations to promote and extend research network services. She has continued in her leadership role at PSC while taking responsibility, through The Quilt, to coordinate many groups nationwide in development of next-generation network technologies.



**←UNDERGRAD EXCELLENCE**

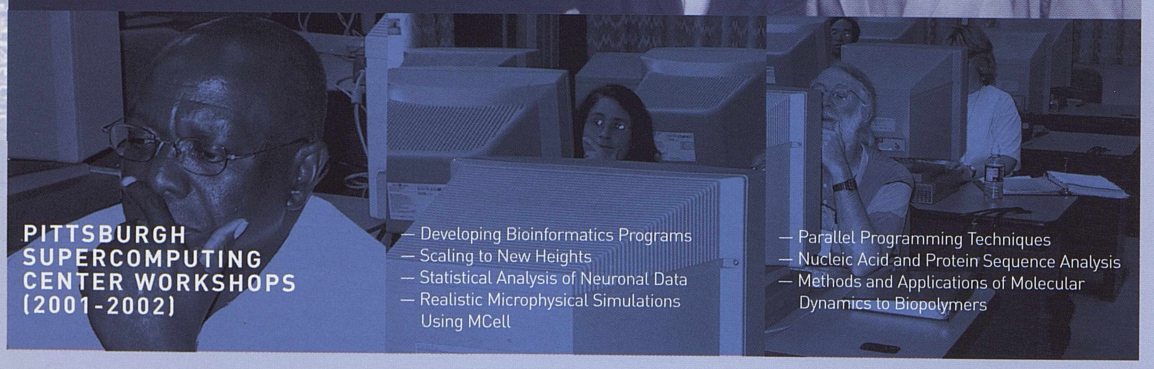
In May, John Heffner (left), who worked for two years as a student intern at PSC on the Web100 project, under the direction of PSC network engineer Matt Mathis (right), received the Alan Newell Award for Excellence in Undergraduate Research from Carnegie Mellon University. Heffner received the honor for his senior thesis, "High Bandwidth TCP queueing." In September, he joined the PSC staff full-time.



**On June 19, 2002, Peter Freeman, new director of the National Science Foundation's Computer and Information Science and Engineering directorate, visited PSC. At an afternoon gathering with PSC staff, Freeman noted the importance of the NSF cyber-infrastructure program. "In case after case," he said, "the capabilities of modern high-end cyberinfrastructure provide opportunities to revolutionize the conduct of science."**

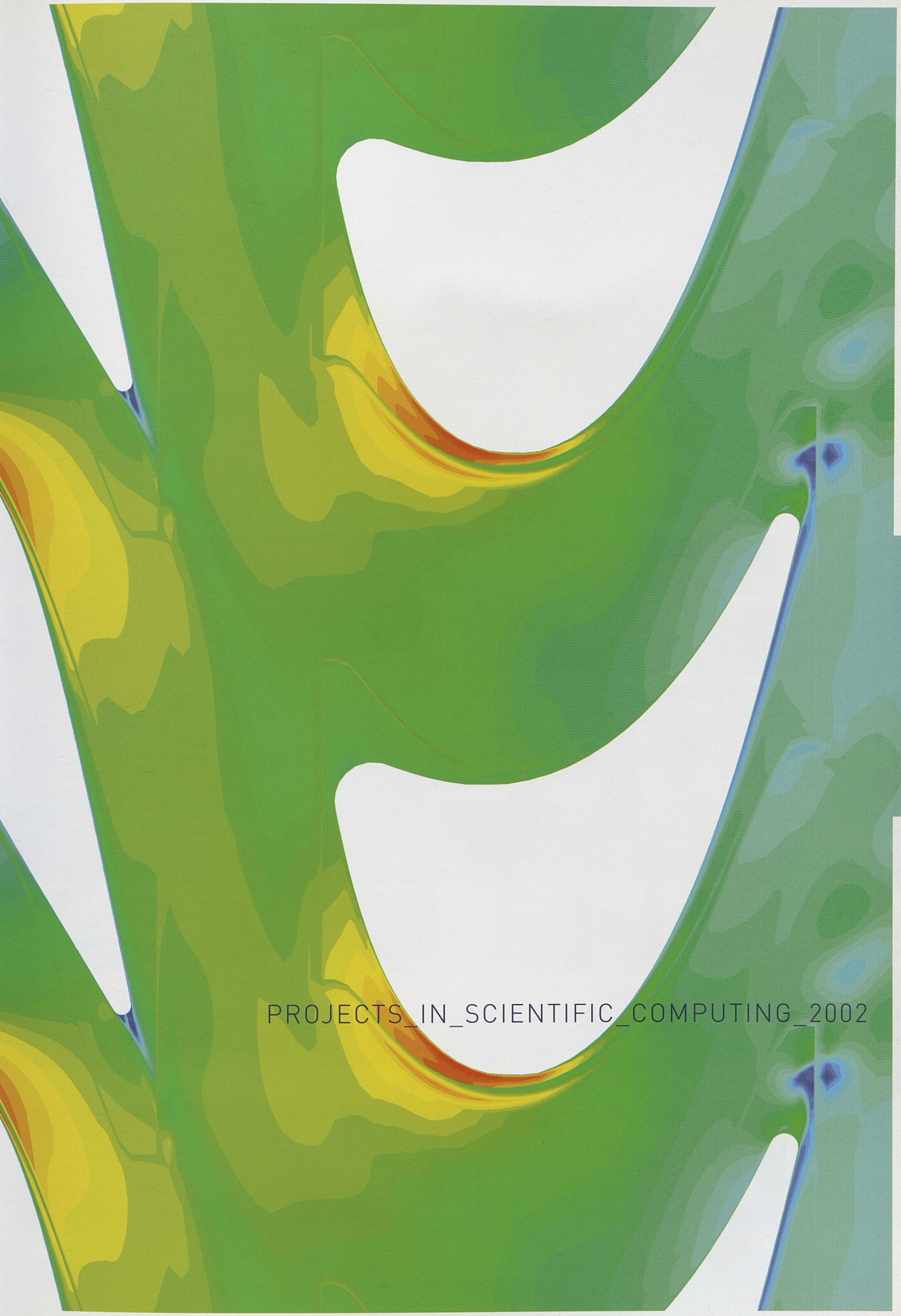
Still, the challenges of solving hardware and software problems, said Freeman, pale in comparison to the difficulties of building a team of people to serve the science and engineering community and work together with them to effectively exploit the powerful technologies of cyberinfrastructure. "Machines come and go," said Freeman. "I know how important the people are to a center like this."

**THE PSC OPERATIONAL MANAGEMENT TEAM (L TO R):**
J. Ray Scott, assistant director, systems and operations; David Kapcin, manager, financial affairs; Bob Stock, associate director; David Deerfield, assistant director, biomedical initiative; Sergiu Sanielevici, assistant director, scientific applications and user support; Rich Raymond, manager, user support; Elvira Prologo, manager, administrative staff. Not in photo: Janet Brown, manager, networking.



**PITTSBURGH SUPERCOMPUTING CENTER WORKSHOPS (2001-2002)**

- Developing Bioinformatics Programs
- Scaling to New Heights
- Statistical Analysis of Neuronal Data
- Realistic Microphysical Simulations Using MCell
- Parallel Programming Techniques
- Nucleic Acid and Protein Sequence Analysis
- Methods and Applications of Molecular Dynamics to Biopolymers



# PROJECTS_IN_SCIENTIFIC_COMPUTING_2002

# PROJECTS 2002 CONTENTS

STRUCTURE_OF_PROTEINS_AND_DNA



1

# precious *bodily* *fluids*

*With crucial help from LeMieux, researchers answered a long-standing question about the permeability of biological cells.*

If you could travel through the body, a swamp boat might be a good vehicle. Each of us is a walking, talking Everglades, about 75 percent water, and we can't survive for more than a few days without fresh intake of the life-giving juice. With water as the main ingredient, our internal machinery brews a variety of fluids — including blood, sweat, saliva and tears, and our ability to do this, to absorb water and move it place to place as needed, depends critically on a protein called aquaporin.

Completely unknown until 10 years ago, when it was discovered accidentally by researchers at Johns Hopkins, aquaporin is a family of related proteins that reside in cell walls. As their name suggests, aquaporins are pore-like channels for water to flow into and out of cells, and their discovery solved a physiological mystery.

Why does water pass through some cells — such as in the kidneys and the glands that produce saliva and tears — much faster than others? The answer is aquaporins. Lab studies show they have the remarkable ability to conduct water at rates of up to a billion molecules per second. In the human kidneys, this means as much as 400 pints a day.

"They're very common proteins," says Klaus Schulten, director of Theoretical Biophysics at the University of Illinois Beckman Institute, "in plants, bacteria and mammals. More than 10 different aquaporins have been found in the human body, and several diseases have been traced to their malfunction." Defects in aquaporin underlie diabetes insipidus, a kidney malfunction that leads to thirst and frequent urination. Aquaporin is also a culprit in dry-mouth syndrome and in cataracts in the eyes.

When aquaporin was identified, several teams of molecular biologists began work to find its structure, an effort that culminated two years ago when Robert M. Stroud and colleagues at the University of California San Francisco succeeded. That success, however, still left important questions unanswered.

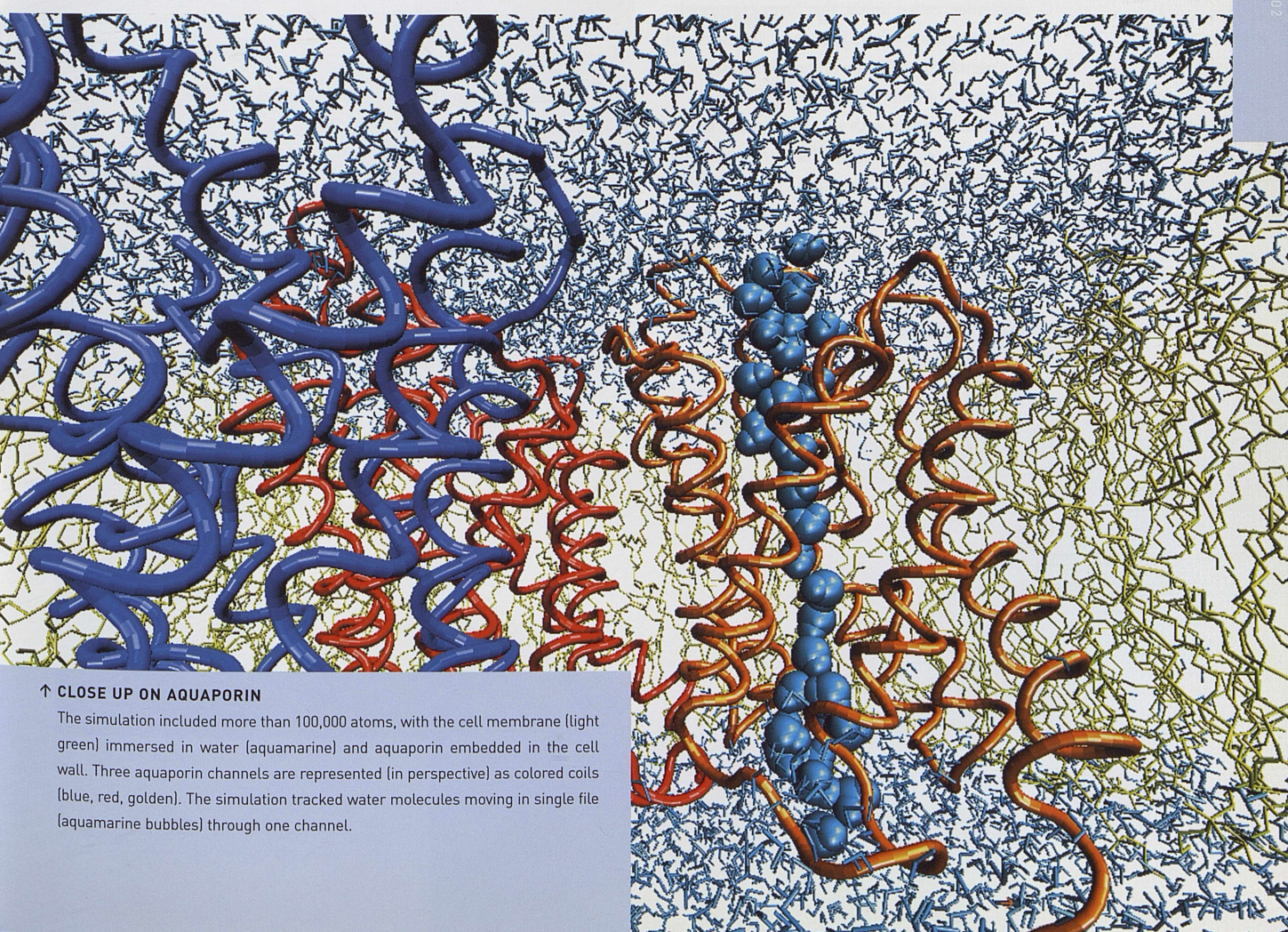
How is it that aquaporin lets water molecules flow unimpeded while, at the same time, remarkably, it acts like a molecular doorman, refusing passage to the uninvited? The uninvited in this case is protons — positively charged hydrogen ions, what you get when a hydrogen atom separates from water and leaves its single electron behind. Healthy metabolism depends on not allowing protons to travel at will through the cell wall.

"Every living cell is its own battery," explains Schulten. "If you let protons escape with the water, as they're naturally inclined to do, the battery would run down. Too many of these run-down batteries, and you're in big trouble."

Several other channel proteins allow protons to pass, and it's been perplexing that aquaporins don't. Experiments show what happens but can't say how. Working in collaboration with Stroud's group and using PSC's Terascale Computing System, Schulten and University of Illinois colleagues Emad Tajkorshid and Morten Jensen launched a series of aquaporin simulations. Their results, reported in SCIENCE (April 19, 2002), appear to answer this long-standing question.

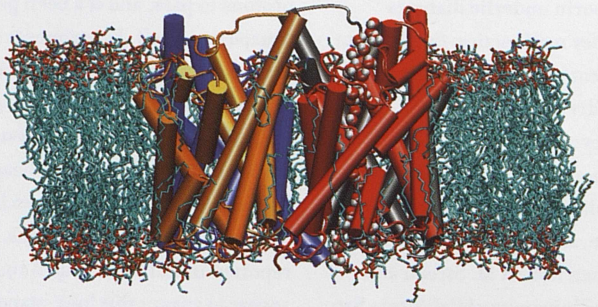
CONT'D →

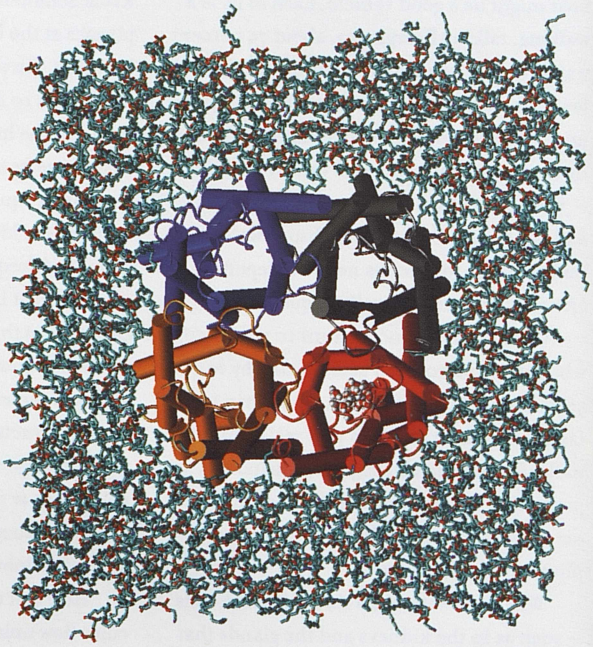




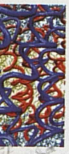
↑ **CLOSE UP ON AQUAPORIN**

The simulation included more than 100,000 atoms, with the cell membrane (light green) immersed in water (aquamarine) and aquaporin embedded in the cell wall. Three aquaporin channels are represented (in perspective) as colored coils (blue, red, golden). The simulation tracked water molecules moving in single file (aquamarine bubbles) through one channel.









1

## SINGLE FILE WATER

When the structural data of aquaporin — spatial coordinates of each atom in relation to the others — became available, Schulten's team used it to build a computer model of the protein within its cellular environment. They inserted aquaporin into a patch of cell membrane, represented by long-chain fatty molecules, called lipids, that form a sandwich-like seal against water. They then, in effect, put this membrane with the embedded aquaporin into a pool of water, surrounding the membrane and protein with water molecules to realistically emulate the cell's watery environs.

With this kind of model, a computational approach called molecular dynamics can track atom-by-atom movements, like recording a movie one frame at a time. Schulten and his team used molecular dynamics software called NAMD, developed in their laboratory to exploit large-scale parallel systems, such as PSC's Terascale, comprising thousands of processors. NAMD includes several features designed to capture the atomic-level details of protein movement with the highest possible realism. "With this machine, the Terascale, and this program that can use it effectively," says Schulten, "we have quite an achievement in technology development for our science."

**↑ BUILDING A MODEL**

A single aquaporin has four separate channels, each represented as a rod-like coil (red, yellow, blue, gray). The protein (15,000 atoms) sits within a patch of cellular membrane, long-chain molecules (40,000 atoms) that align with their "head-groups" (red) facing outward as a seal against water. For the simulations, this model of protein and membrane swims in a bath of water, not shown (51,000 atoms). The simulation tracks a single file of water molecules (oxygen-red, hydrogen-white) in one channel (red).

The amount of computing depends, in large part, on the model's size, and since the aquaporin model included over 106,000 atoms, a huge number, availability of the Terascale system was crucial. "These are formidable simulations," says Schulten, "particularly since they have to be done at a high level of exactness, with the best simulation conditions that can be achieved today. Only the Terascale system at Pittsburgh permitted us to do this in a timely manner."

Earlier work, before the detailed aquaporin structure was available, indicated that water molecules line up single file in the aquaporin channel. "It's a narrow channel," says Schulten, "not much more than one molecule wide." A first round of simulations with the new model confirmed a single-file alignment of seven to nine water molecules, and it went further, identifying the position and orientation of each molecule in line as it moves through the channel.

This gave Stroud's group in California something to work with, and they found good agreement with the simulation for the position of the water molecules. The experimentalists, however, had no way to verify how each water molecule was oriented. "We saw something they couldn't recognize," says Schulten, "because the resolution of their observations isn't fine enough."

## SLAMMING THE DOOR ON PROTONS

With another round of work, the researchers assessed the accuracy of their simulations. Using a version of aquaporin altered by changing two amino acids, results with the computer model closely matched the laboratory structure, giving a high degree of confidence. "We found very close agreement," says Schulten, "and we realized we could trust our findings about the orientation."

Those findings, it turns out, reveal the secret behind aquaporin's ability to let water flood through the cell membrane while, at the same time, locking out protons. As Schulten watches a movie from the simulation, he sees a molecular ballet. One after another, each water molecule enters the channel with its oxygen atom leading the way. At mid-stream, the molecule does a half-pirouette and exits facing the direction it came from.

"They orient with the oxygen atom into the channel," says Schulten, "and then they reverse, so that the hydrogens lead the way out. It's a very relevant finding because for water to conduct protons, orientation matters."

The ability of protons to pass along a single file of water molecules, as they do in other channel proteins, depends on a particular arrangement of water molecules and surrounding protein atoms. Called a "proton wire," this arrangement is like a stepping-stone pathway for protons, and the pathway is blocked by the mid-channel flip-flop that occurs in aquaporin.

"WITH THIS MACHINE, THE TERASCALE, AND THIS PROGRAM THAT CAN USE IT EFFECTIVELY, WE HAVE QUITE AN ACHIEVEMENT IN TECHNOLOGY DEVELOPMENT FOR OUR SCIENCE."

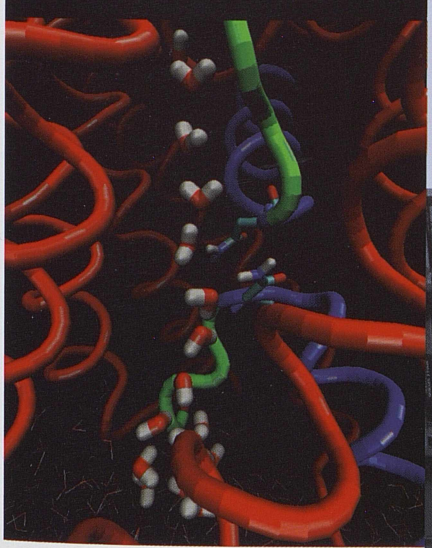
The simulations show that aquaporin's mid-channel architecture is a stable feature of the protein's structure. "We tested with simulations to see how strongly the channel preferred this orientation," says Schulten, "and we found it's very strongly preferred. As a result, it filters against the conduction of protons."

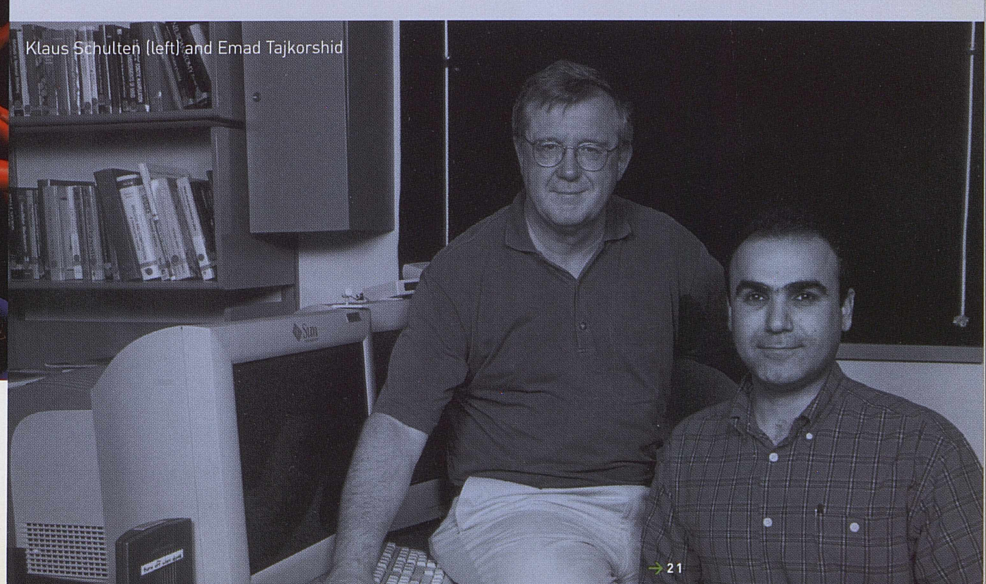
These results culminate more than ten years of effort, first, to find the three-dimensional structure of aquaporin and then to use structural data to understand how the protein works. By providing a picture of the atom-by-atom details that experiment can't provide, computational simulations appear to have solved the second part of this problem. "We could see this orientation of the water molecules in simulation," says Schulten, "but you can't recognize this experimentally."

Knowing these atomic details could eventually help with treatment of aquaporin-related disease. Perhaps also, says Schulten, it can lead to improved approaches for water treatment. "The kidneys are a filtering system that relies on aquaporin, and it suggests what kind of technologies might give us better water purifying filters." Since aquaporin filters ions it also suggests an approach to removing salt, an ion, from sea water. "It's possible that we can learn from these proteins and make filters designed according to the principles mother nature uses."

**MORE INFORMATION:**
http://www.psc.edu/science/schulten2002.html

**↓ MID-STREAM FLIP-FLOP**
This closeup snapshot shows the single-file line of water molecules as they progress through the aquaporin channel. Because the water flips at the mid-point of the channel, protons can't pass through.





Klaus Schulten (left) and Emad Tajkorshid

STRUCTURE_OF_PROTEINS_AND_DNA

# NEW WEAPONS FOR THE GERM WARS

**INEXPENSIVE POLYMERS CAN EXTEND THE RANGE OF NATURE'S GERM-FIGHTER ARSENAL.**



2

This story begins with frogs. A lily pad is a fine place to perch in the moonlight and broadcast mating calls if you're a frog, but the picturesque lily pond of a Monet painting is a cesspool of microorganisms. If you or I swam in similar water, we'd risk our lives.

How do frogs manage to live happily in filthy water? It's a simple question that no one asked until the 1980s when it intrigued a scientist named Michael Zasloff. In 1986 he found the answer — the skin of a frog harbors armies of protein-like germ fighters. Zasloff isolated a molecule he named magainin — Hebrew for "shield." Structurally like a protein only smaller — just a few amino acids on a peptide chain — magainin has the instincts of a secret service agent. Squads of these agents patrol a frog's skin, where they attack and destroy the cells of bacteria that threaten infection.

The discovery of magainin launched a worldwide wave of research that's still going. Since 1986 scientists have identified nearly 500 other anti-microbial peptides. They've learned that plants and animals, including some that lack the immune system of mammals, harbor a diverse collection of defensive peptides, and they've learned that each species has its own unique peptide arsenal, targeted to the bacteria, viruses and other pathogens of that species' environment.

The prospects to create new germ fighters from the model of mother nature's peptides are potentially boundless. Topping the list is the need for new antibiotics that can defeat the protean ability of bacteria to resist conventional penicillin-like antibiotics. That promise is especially tantalizing in that a range of studies show that bacteria have little or no ability to resist antimicrobial peptides.

But the practical obstacles are huge. "The big catch," says Michael Klein, Hepburn Professor of Physical Science at the University of Pennsylvania, "is you need 20 or 30 steps of organic synthesis to make these molecules, and you end up with such high cost that it's equivalent to grinding up diamonds."

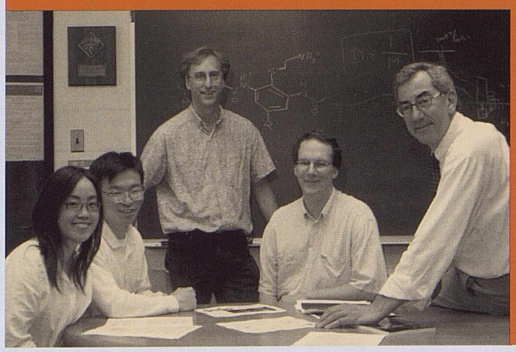
Still other possibilities involve using molecules modeled on magainin and its cousins to create germ-resistant materials such as bandages that kill bacteria or toilet seats that sanitize themselves. With recent studies citing hospital-acquired infection as the fourth-leading cause of death in the United States, such possibilities and others — antiseptic operating tables, surgical gowns, pillows and sheets — provide a strong impetus for research.

## PLAYING COPYCAT WITH MOTHER NATURE

Initial efforts to mimic nature's molecular germ fighters led to several laboratory-synthesized peptides, one of which came from Klein's University of Pennsylvania colleague William DeGrado. While these synthetic peptides represent a step forward, they also come with built-in obstacles to practical use. "These natural peptides as well as their synthetic analogues are expensive to prepare and difficult to produce on a large scale," says DeGrado, George W. Raiziss Professor of Biochemistry and Biophysics, "which limits their potential use."

Klein, who directs Penn's Center for Molecular Modeling, collaborated with DeGrado, providing theory-based molecular simulations to help guide his laboratory work. In 2001 these two scientists joined forces again to explore in a different, potentially more practical direction. "We posed a question," says Klein. "Can we mimic the peptide with something that's cheap to make?" Based on initial results, the answer appears to be yes.

Klein and his co-workers Bin Chen and Robert Doerksen used LeMieux, PSC's terascale system, to test the possibilities of creating a polymer — an organic molecule easier to make than peptides — structurally similar to magainin and with similar germ-fighting ability.



University of Pennsylvania research team (left to right): Dahui Liu, Bin Chen, William DeGrado, Robert Doerksen and Michael Klein. Not in photograph: Gregory Tew, now at University of Massachusetts, Amherst.

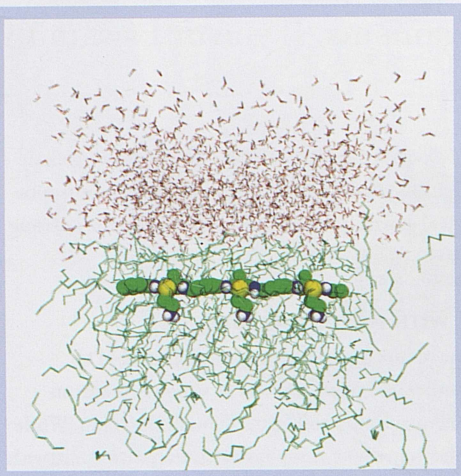
With a series of computations, they developed an accurate computational model to forecast how the polymer would behave in the cellular environment.

With design guided by these computations, DeGrado's team — Greg Tew, Dahui Lihui and Justin Kaplan — synthesized this relatively simple polymer, called an arylamide. Lab tests show the arylamide has antibacterial action similar to magainin and other peptides. The good news of this work — reported in the *Proceedings of the National Academy of Sciences* (April 2002) — is that a feasible new pathway is now open to extend the range of mother nature's anti-microbial arsenal.

CONT'D →

## MOLECULAR DYNAMICS OF ARYLAMIDE

These snapshots show the arylamide polymer in two sets of simulations, both in an oil-water solution. In one set (right), the polymer starts out in the water (red & white); in the other (left), it's inside the oil (green). In both simulations, the polymer moves to the oil-water interface and stays there. Time is in picoseconds (trillionths of a second). The arylamide polymer is composed of carbon (green), oxygen (red), nitrogen (blue), hydrogen (white) and sulfur (yellow).



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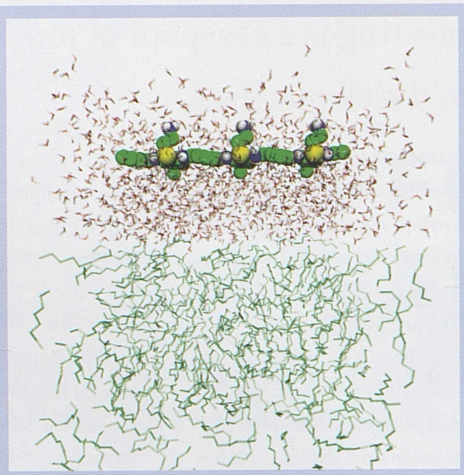

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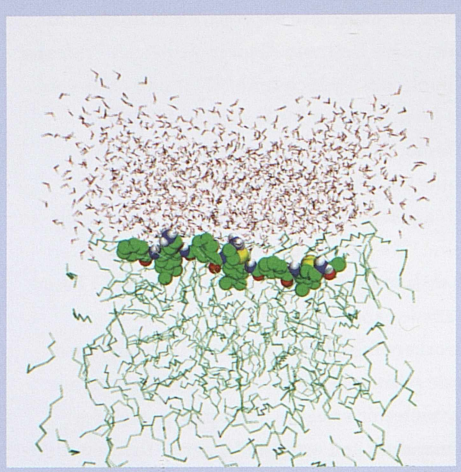

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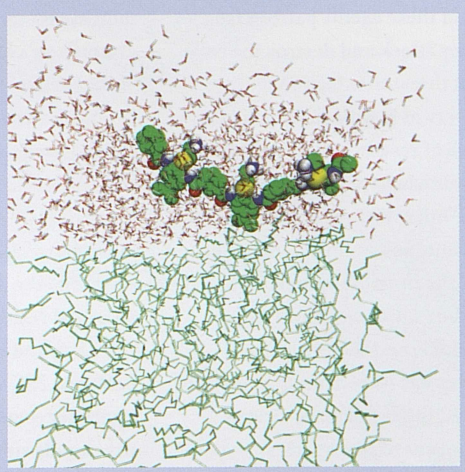

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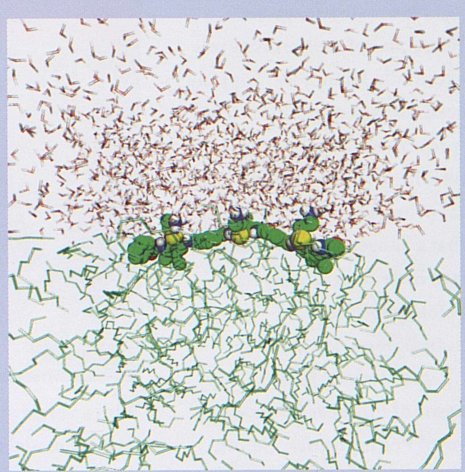


t = 500

**WITH HOSPITAL-ACQUIRED INFECTION AS THE FOURTH-LEADING CAUSE OF DEATH IN THE UNITED STATES, APPLICATIONS SUCH AS ANTISEPTIC OPERATING TABLES AND SURGICAL GOWNS PROVIDE A STRONG IMPETUS FOR RESEARCH.**

## TWO-FACED MOLECULES

What do nearly 500 different natural germ-killer peptides have in common? Like Janus, the Roman god of gates and doors, they face in and out at the same time. All these small anti-microbes can, when circumstances dictate, assume a shape in which, in chemical terminology, they're amphiphilic — one side of the molecule avoids water (hydrophobic) while the other side likes it (hydrophilic).

This two-faced structure — scientists believe — is an essential part of how nature equips peptides to destroy bacterial cells. While the hydrophilic face turns out to the watery environs of the cell exterior, the hydrophobic face can attach to lipids, the oil-like molecules that form cell membranes, to pierce the membrane and create holes that eventually kill the cell.

To create a polymer with similar properties, DeGrado and Tew approached Klein and asked him to model a class of polymers with a fairly simple structure, called arylamides. "We were taking a further step away from the protein backbone as the structural model," says DeGrado, "which should give us good stability at reduced expense. We had a shape that we thought should be compatible with the biological activity we want. But this molecule could adopt many shapes, and the question was whether it's really happy in this shape, whether it's energetically favorable."

To answer this question, Klein, Chen and Doerksen set out to simulate the arylamide polymers in solutions that represent the cellular membrane and its surrounding water, to see if they maintain structure and behave similarly to magainin. The modeling tool for this job is molecular dynamics, a method that tracks the shape and movement of a molecule and its interaction with surrounding atoms. Most often used to model proteins, molecular dynamics relies on "force fields" to represent the forces acting between the atoms of the molecules. Initial attempts to model the arylamide polymer showed that standard force fields gave inaccurate results.

The problem had to do with the uniqueness of the arylamide backbone structure, chosen so that it wouldn't freely rotate, keeping hydrophobic side chains on one side and hydrophilic on the other. To solve this problem, Klein's team carried out a series of demanding quantum computations, an approach called density functional theory, to systematically derive accurate readings of the rotational resistance of the arylamide backbone. With about 60,000 hours of computing using 128 LeMieux processors at a time, they derived the force fields they needed.

The researchers confirmed the accuracy of their revised molecular dynamics model by simulating an arylamide structure and comparing it to the actual structure from experiment. They then ran molecular dynamics with several different versions of the arylamide polymer in an oil-water solution. These simulations (facing page) show the polymer moving toward the oil-water interface and lodging there, mimicking the behavior of the natural anti-microbial peptides.

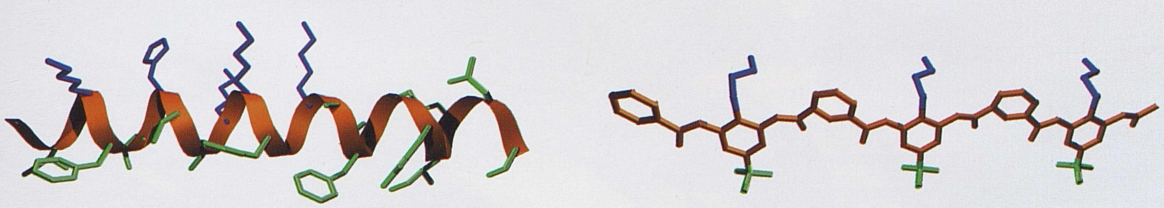
Taking their cue from these results, DeGrado's team synthesized the polymer and tested its antibacterial properties. Based on the success of this work, the University of Pennsylvania filed for several patents and created a company, POLYMEDIX, to exploit the possibilities for useful applications.

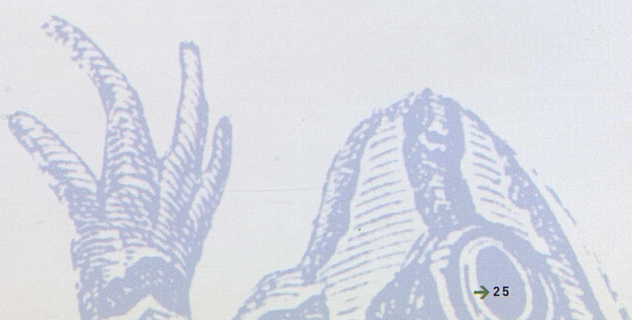
"We've identified a class of compounds," says Klein, "that the drug industry would refer to as a possible lead compound. Some of these short polymers are effective, but it will require systematic studies to develop this further." While it's only a first step, it's a big one, demonstrating not only the possibilities of using polymers to mimic nature's peptide germ fighters, but also how computational simulations and laboratory experiment can work together to custom design molecules for particular purposes.

**MORE INFORMATION:** http://www.psc.edu/science/klein2002.html



The structure of magainin (left) compared to the arylamide polymer mimic (right). Amphiphilic structure is apparent, with hydrophobic side chains (green) on one side and hydrophilic (blue) on the other.





STRUCTURE_OF_PROTEINS_AND_DNA





# WHAT HAPPENS AT THE ACTIVE SITE

**BETTER UNDERSTANDING OF AN ENZYME THAT METABOLIZES CHEMOTHERAPY DRUGS MAY PERMIT BETTER CANCER-FIGHTING WITH SMALLER DOSES.**

Biochemically speaking, enzymes make things happen. Action is their motto. If metabolism were a party, it would be inert, as good as dead, until the enzymes arrive. When they show up, suddenly the whole place starts jumping.

Enzymes — nearly all of which are proteins — are such amazing catalysts that it's hard to appreciate how much difference they make. What they do seems simple enough. A molecule undergoing reaction — called the substrate — swims into contact with the enzyme for that reaction and finds a place where it fits, usually a pocket or crease in the enzyme's 3D shape — called the active site. Seemingly, the next thing you know the substrate has changed to the product of the reaction.

The enzyme itself is unchanged and from outward appearance has done nothing beyond provide a port in a storm for a wandering molecule. Yet incredibly, the reaction happens a million times faster than it would without the enzyme. And with some reactions, the speedup is much more than that, a billion-trillion times faster with enzymes.

What biomolecular magic is happening here? "Over the past 50 years of so," says biochemist David Deerfield, "we've made enormous progress in filling in the big picture of what enzymes do and how they do it at an ever increasing level of detail. But we're a long way from precisely understanding what happens in the transition from substrate to product, the atom-by-atom details of these changes and exactly how enzymes play their role."

For the past few years, in research supported through the NIH National Center for Research Resources, PSC scientist Troy Wymore has worked with Deerfield, who directs the PSC biomedical program, and with others — PSC scientist Hugh Nicholas, University of Pittsburgh biologist John Hempel and computational chemist Martin Field — to elucidate the mechanism of an enzyme called aldehyde dehydrogenase.

"ALDH is a big family of enzymes that show up in one form or another in just about every living thing," says Nicholas. "They help to metabolize and detoxify chemicals called aldehydes." Among the aldehydes is ethanal, a byproduct of alcohol, and ALDH's ability to break down ethanal is what pulls us through a hangover. About half of all Asians lack a liver ALDH needed to metabolize ethanal and as a result become sick and potentially risk their lives if they drink alcoholic beverages.

ALDHs also affect cancer treatment, where one of the most used chemotherapy drugs breaks down to an aldehyde. "With cancer therapy," says Hempel, "ALDH just does what it's supposed to do, detoxify an aldehyde. The aldehyde in this case, though, is a therapeutic agent. By doing its job, ALDH reduces effectiveness of the drug, which means you have to use a larger dose than would otherwise be necessary, which increases side effects. If we understood this enzyme better, we could presumably design drugs to block the ALDH that eats up the cancer drug and use smaller doses to attack the cancer."

With LeMieux, PSC's terascale system, Wymore has at hand a powerful tool to attack his problem. In 2001, with a fellowship from the Human Frontier Science Program, he spent a month in Grenoble, France working with Field, a leader in the development of computational methods to understand how enzymes work. Over the past year, with a creative approach that combines less costly, non-quantum methods with detailed quantum techniques, Wymore employed LeMieux in simulations that pin down previously unknown details about how ALDH does its job. In the process, he and his colleagues appear to have discovered an interesting chemical event no one has seen before — a proton transfer from the enzyme backbone. CONT'D →

## CLOSING IN ON THE ACTIVE SITE

This ribbon model (top left) depicts the symmetrical two-part (dimer) structure of ALDH3, with the helices and sheet structure of one subunit (tan) differentiated from the other (deep green) and loops (rust & gray) also differentiated.

The closeup (above) identifies ALDH active-site amino acids according to Hempel and Nicholas' sequence-analysis studies. Some amino acids (pink, bonded representation) distinguish ALDH3 from other classes of ALDH. A few (dark blue) occur in all classes of ALDH. Others (green) show some variability but are nevertheless essential to structure and function of the enzyme.

## BREAKING UP IS HARD TO DO

Wymore's ALDH simulations arise from work started by Hempel, who in 1997 collaborated with others to determine the 3D structure of an ALDH enzyme for the first time. Not long after that, Hempel and Nicholas, a specialist in DNA and protein sequence analysis, teamed up on a sequencing study of the ALDHs. Their work grouped this "superfamily" of nearly 200 enzymes into 13 distinct sub-families or classes, structurally related by their amino-acid sequences and differing in the aldehydes they catalyze.

As an entry point into this huge enzyme family, Wymore focused on ALDH class 3, one of the smallest ALDHs and therefore a good choice, by the economics of computing time, to work out computational strategies. ALDH3 is the ALDH most involved in metabolizing cancer-therapy drugs, and it's also the subject of Hempel's lab work. "It's a big plus," says Deerfield, "that we have this strong connection with a wet biology group. Experiment and computation can feed each other. When the calculations identify certain amino-acid groups as being important, the lab team can do the experiments that test these findings."

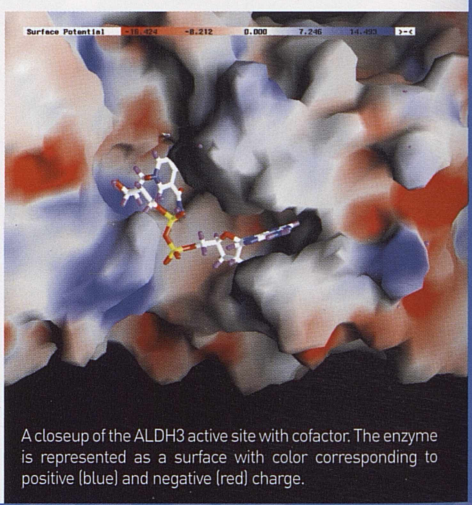
What's going on at the ALDH3 active site? In other words, what happens chemically, atom-by-atom, between the substrate, an aldehyde called benzaldehyde, and the amino-acid groups that surround it like a big easy chair? Experiments help to determine which amino acids are involved in changing the substrate to the reaction product, but chemical reactions happen with many fleetingly transient intermediate states. Understanding these transient states can be the key to intervening with drugs to regulate an enzyme reaction. Wymore's challenge was to precisely identify each step in the ALDH3 mechanism.

It's a challenge that calls for quantum methods. The most widely used approach to simulating proteins — called molecular dynamics — shows structure and movement, but doesn't show reactions, the making and breaking of bonds. To get at these pesky, crucial details, Field pioneered hybrid methods that zoom in on the active site with quantum theory while, at the same time, maintaining the less costly approach for the rest of the enzyme. It's a complex approach — called QM/MM (quantum mechanics/molecular mechanics) — that Wymore added to his toolbox before going to work on ALDH3.

## KEEPING TRACK OF PROTONS

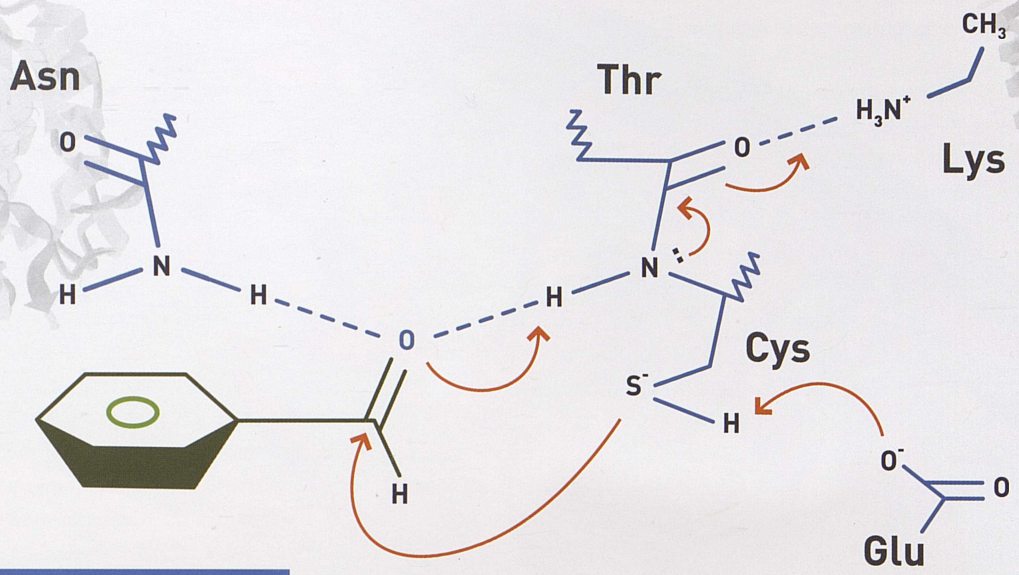
A big question had to do with the chemistry involved in the first intermediate state of the reaction — in particular, what's going on with the hydrogen atoms? Experiments show the first intermediate forms when an active-site cysteine, an amino acid with a sulfur atom bonded to hydrogen, binds with benzaldehyde. Cysteine's sulfur binds with a benzaldehyde carbon, and the untested thinking was that the cysteine was "deprotonated" — gave up its hydrogen — before forming the bond with benzaldehyde.

The researchers had their doubts, and Wymore undertook a series of calculations, using various methods, to address this question, which was a prerequisite to using QM/MM to simulate the reaction. One strong result came from molecular dynamics computations that included benzaldehyde in the active site. With the cysteine deprotonated, benzaldehyde was unwilling to orient itself as needed to form the intermediate state.




A closeup of the ALDH3 active site with cofactor. The enzyme is represented as a surface with color corresponding to positive (blue) and negative (red) charge.

**"WE SEEM TO HAVE DISCOVERED A NOVEL ENZYME MECHANISM."**




**↗ WHAT HAPPENS AT THE ACTIVE SITE**

Among the amino acids that surround benzaldehyde (six-sided figure) as it sits in the active site, are (from the top, clockwise) asparagine, threonine, lyseine, cysteine and glutamate. (squiggly lines indicate where the enzyme structure continues before looping back to the active site.)

The first intermediate forms when the sulfur (S) from cysteine binds (arrow) with the carbon of the aldehyde (-CHO, C not shown). Contrary to thinking prior to Wymore's simulations, this sulfur keeps its hydrogen (H) when it binds to form the intermediate and only then donates it to glutamate.

Prior to the simulations, researchers believed that hydrogen bonds (dotted lines) from asparagine and the backbone nitrogen stabilized the intermediate in the active site. The simulations show, however, that the backbone proton actually transfers (arrow) to the oxygen, a stronger chemical bond. Preliminary results indicate that this transfer occurs through a complex "proton relay mechanism" (arrows show the direction electrons move) that involves a hydrogen in the active-site lysine. With further calculations, the researchers are analyzing this mechanism.

Guided by this clue and others, Wymore did several different computations with the cysteine protonated. With a series of simulations of the enzyme with cofactors — molecules also involved in the enzyme mechanism — surrounded by water, a total of 56,000 atoms, he systematically studied the active-site interactions. The results show a two-stage process. The cysteine is protonated when it first interacts with the substrate and only then becomes deprotonated — through interaction with a nearby amino-acid group.

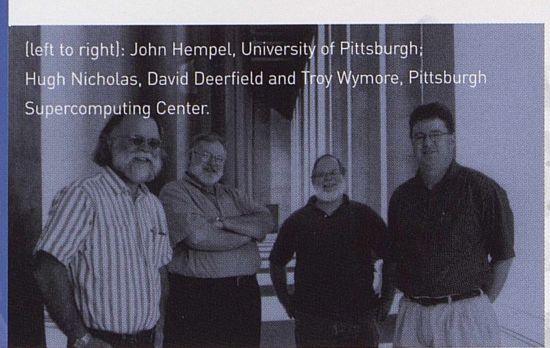
It was also the prevalent view that another hydrogen atom at the active site formed a hydrogen bond with benzaldehyde to help stabilize this first intermediate. Wymore's simulations showed, however, that rather than forming a hydrogen bond, the enzyme actually donates a proton to the intermediate state. This proton transfer happens as a concerted reaction at the same time as cysteine's sulfur binds with benzaldehyde.

Perhaps the biggest surprise is that this donated proton comes from a nitrogen atom on ALDH3's backbone, next door to the cysteine. "It's quite interesting," says Wymore. "We seem to have discovered a novel enzyme mechanism. We wouldn't have looked for this because the backbone is structural. You expect the side chains to do all the chemistry."

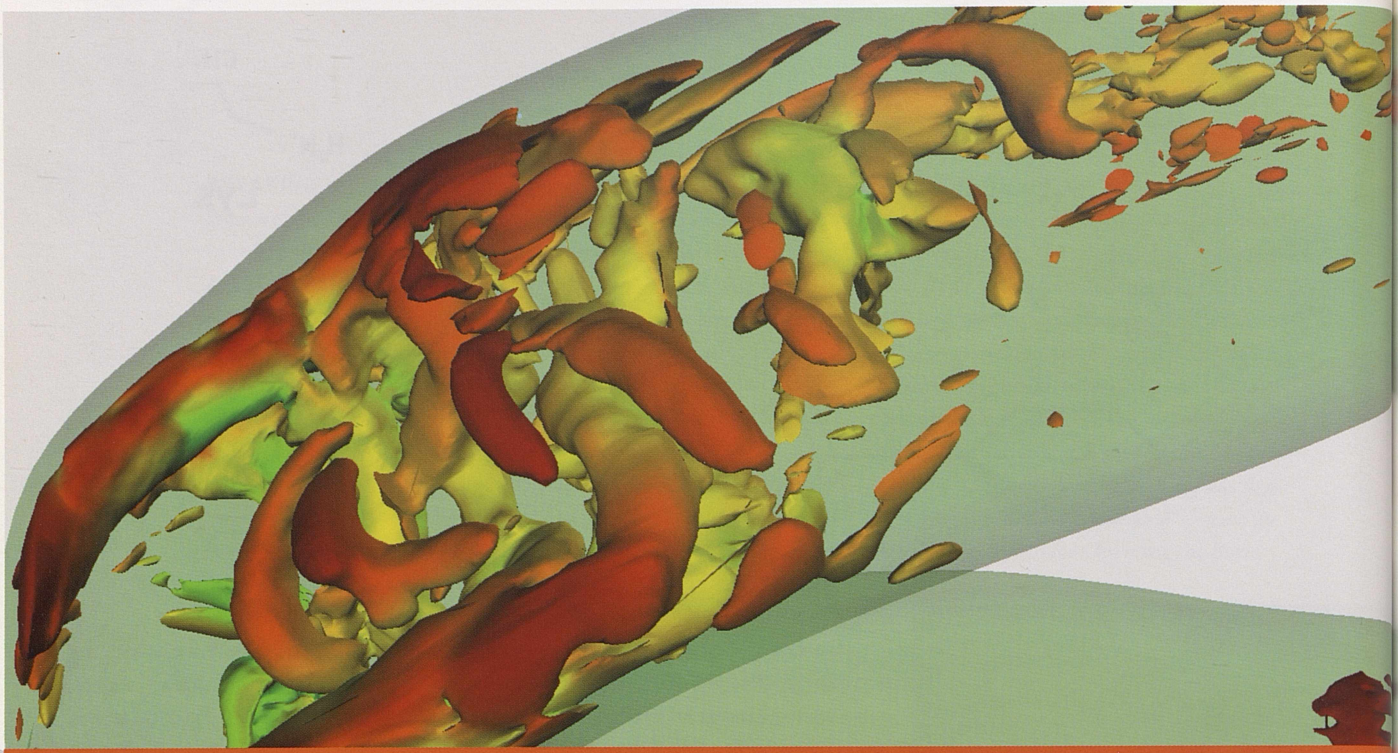
The key, says Deerfield, is the QM/MM approach. "We did a series of calculations of just the active site and substrate, without all the protein interactions around it. Then we backed up again, using the quantum framework but now tied to the protein with molecular mechanics. This gives you a more realistic model."

Wymore has more work ahead with ALDH3 and then expects to move on to simulations of ALDH2, the ALDH involved in metabolizing ethanal. He has support from the National Institute on Alcohol Abuse and Alcoholism and from this standpoint ALDH3 is a first step to understanding the bigger enzyme's mechanism. "This has given us the clue to look for a proton donor," says Wymore, "where we wouldn't have thought to look."

**MORE INFORMATION:** http://www.psc.edu/science/wymore.html



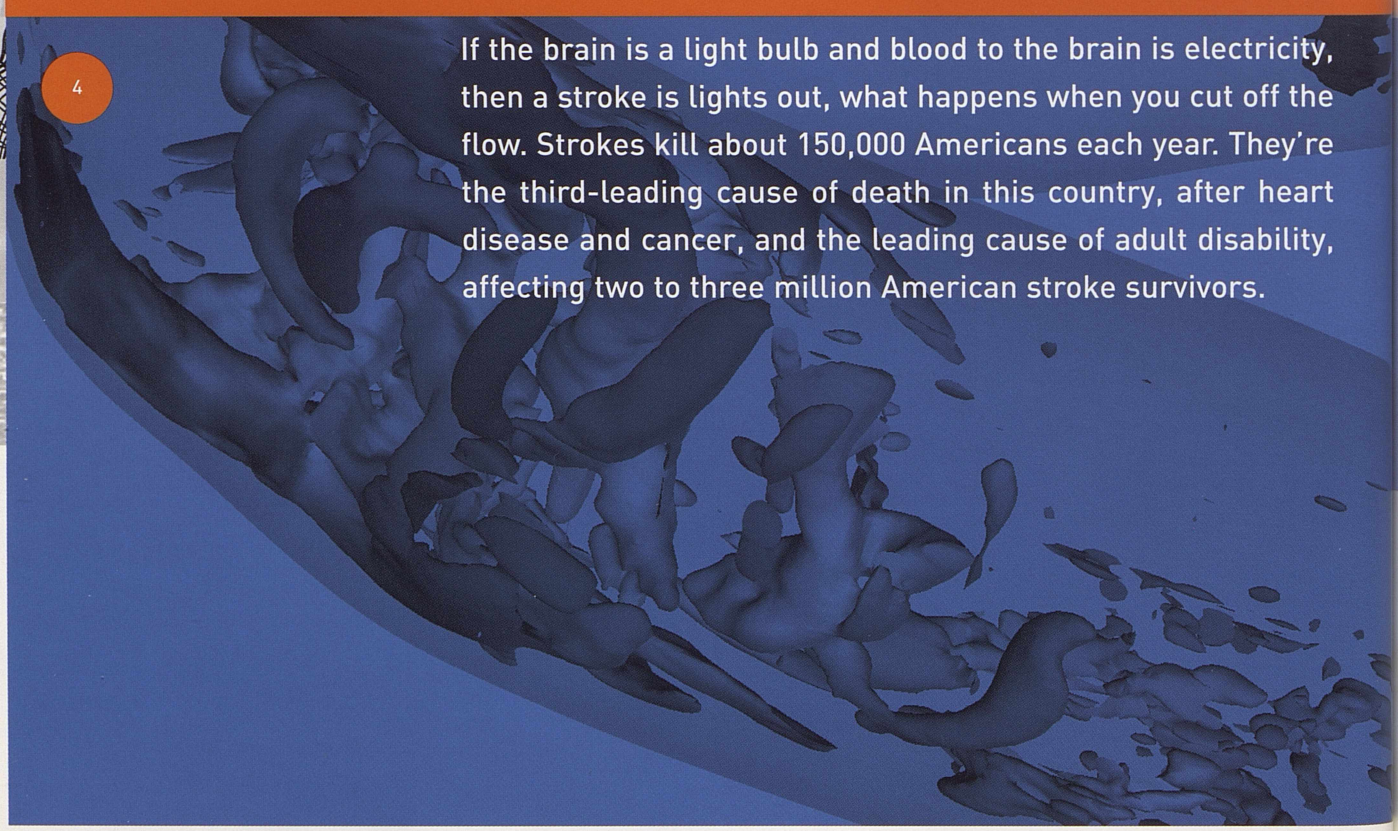
(left to right): John Hempel, University of Pittsburgh; Hugh Nicholas, David Deerfield and Troy Wymore, Pittsburgh Supercomputing Center.





# STROKE BUSTERS *in* TURBULENT BLOOD

**THE TOOLS ARE IN PLACE TO ZERO-IN ON THE CORRELATIONS BETWEEN TURBULENT FLOW AND STROKE.**



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If the brain is a light bulb and blood to the brain is electricity, then a stroke is lights out, what happens when you cut off the flow. Strokes kill about 150,000 Americans each year. They're the third-leading cause of death in this country, after heart disease and cancer, and the leading cause of adult disability, affecting two to three million American stroke survivors.

Most strokes — about 80 percent of 700,000 a year in the U.S. — happen because an artery that carries blood uphill from the heart to the head gets clogged. Most of the time, as with heart attacks, the problem is atherosclerosis, hardening of the arteries, calcified buildup of fatty deposits on the vessel wall. The primary troublemaker is the carotid artery, one on each side of the neck, the main thoroughfare for blood to the brain.

Awareness of a relation between strokes and the carotid artery is at least as old as the name — from the Greek verb *karoun*, to plunge into deep sleep or stupor. Only within the last 25 years, though, have researchers been able to put their finger on why the carotid is especially susceptible to atherosclerosis.

"Blood has the same level of cholesterol in our toes as in our coronary arteries," says Frank Loth, a biomechanics professor at the University of Illinois, Chicago, "so you might expect that atherosclerosis would be a diffuse disease, that we'd get it anywhere. But we don't. There are particular sites — coronary arteries, abdominal aorta, carotid arteries and others."

Loth's specialty is hemodynamics, fluid dynamics of the blood — a relatively recent and growing field of work that has produced some answers about atherosclerosis. For the past 15 years, Loth has teamed with University of Chicago vascular surgeon Hisham Bassiouny to study vascular hemodynamics. Among other things, they've worked on understanding flow in the carotid artery, both healthy and with arterial narrowing — called stenosis — due to the plaque buildup of atherosclerosis.

"We're trying to define the hemodynamics for different degrees of carotid stenosis," says Bassiouny, who specializes in carotid artery disease and in endarterectomy, a life-saving surgical procedure to remove plaque from the carotid artery.

"Our hypothesis is that there are specific flow patterns, turbulent and non-turbulent, that may predispose to plaque progression or plaque breakdown."

Four years ago, Loth and Bassiouny joined forces with two computer scientists, Paul Fischer of Argonne National Laboratory and his associate Henry Tufo, experts in the numerical methods of flow modeling. The objective: Develop the ability, with computational modeling, to provide a detailed readout of the flow patterns and forces in the carotid arteries of patients, information that doctors can then use to help identify who's at high risk for stroke.

With a mix of disciplines to fit the job — vascular surgery, fluid mechanics, advanced numerical methods — the Chicago-based team has made rapid strides. This year, with availability of LeMieux, PSC's terascale system, they've done what hasn't been done before. Starting with a CT scan from a patient's severely clogged carotid artery, they've simulated the transition from smooth to turbulent flow that occurs in that artery over the course of one heartbeat. Just as importantly, they've demonstrated that it's feasible to produce this kind of information quickly, within 24 hours, so it can be used in treatment planning.

## SHEAR STRESS

Over the last 20 years, hemodynamics has established a relation between flow patterns and the likelihood of atherosclerosis. The vessel sites most susceptible to disease are like the outside bank of a stream where there's a sharp turn. "You might have a region where water is slow," says Loth, "and you'll see leaves and branches in a recirculation area with a little sandy beach. The same thing happens in arteries."

When there's low flow velocity and recirculation, the vessel wall feels "low shear stress." Like the force you exert on a desktop as you slide your hand across it, shear stress is force in the direction of flow. Low shear stress, research has shown, is one of the key factors in predicting whether someone with healthy arteries will develop atherosclerosis.

In the carotid artery, low shear stress tends to happen near a particular site — the carotid bifurcation — where the artery splits in two. In one branch, just past the fork, a healthy artery is spacious and then narrows as it turns inward toward the brain. In the spacious region, flow along the outer wall is often slow with recirculation, prime territory for trouble.

Over time, as plaque builds up, the flow patterns at this site change. In a healthy, spacious artery, the flow is smooth. In a stenosed, narrow artery, flow into the bend is faster and, with enough narrowing,

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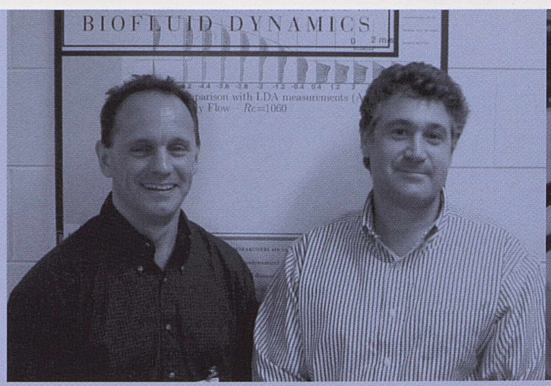



Paul Fischer (left) and Henry Tufo, Argonne National Laboratory.

Frank Loth (middle) and graduate student Seung Lee, University of Illinois, Chicago, and Hisham Bassiouny, University of Chicago Hospital.

becomes turbulent. The increased force of this flow can disrupt plaque, a potentially fatal problem. "The mechanism of a stroke in half the cases," says Bassiouny, "is plaque in the carotid artery that breaks apart. As fragments travel upstream, they can block a vital artery."

The choice of treatment for carotid atherosclerosis — blood-thinning medication, surgery, or no treatment — depends not only on the degree of narrowing, but also on whether the plaque is likely to fragment. Knowing the flow patterns and forces, says Bassiouny, would lead to better decisions. "Not every patient who has plaque has a stroke. For someone with 60 percent stenosis, we could decide the case is non-conducive to progression and instability. Another patient with 60 percent stenosis but with different plaque configuration and flow dynamics might need an endarterectomy."

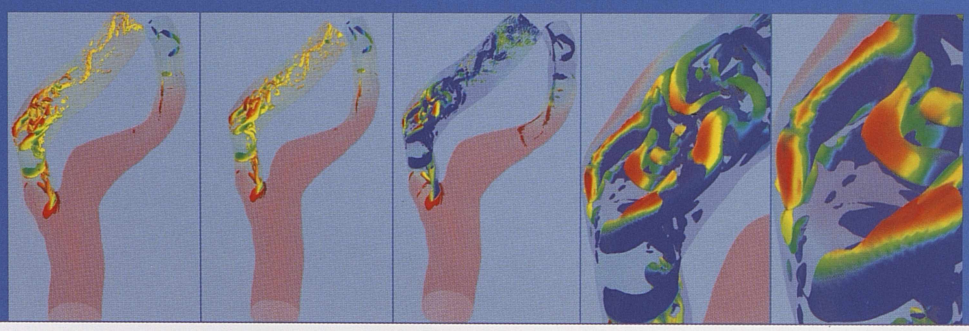
Bassiouny provided CT scans from a 55-year-old man with a 70 percent stenosed carotid artery. With the scan data as input, Seung Lee, a University of Illinois, Chicago graduate student who works with Loth, used a series of programs to construct a mesh-like computational grid. Doppler ultrasound measurements from the patient provided the initial flow velocity.

Using 256 processors for this first real-case simulation, the researchers were able to simulate a full cardiac cycle — one heartbeat — in 11 hours of wall-clock time. An animation depicts the results at a cross-sectional slice through the artery, as if looking down at a river in which the flow alternately rushes forward and then slows as the heart relaxes. Just around the bend from where the carotid turns inward toward the brain, as the flow feels the force of the heart's contraction, a slow, lazy river transforms to a torrent with violent swirls of turbulence.

**TRANSITION TO TURBULENCE IN A STENOSED CAROTID ARTERY**

These snapshots from the simulation show increasing turbulence (left to right) as the flow approaches the systolic peak, when it feels the force of the heart's contraction. The complex twisted structures (seen in closeup of the last snapshot) are vortex surfaces, a way to visualize the structure of turbulent flow, with color (red to blue) indicating decrease in pressure. The pressure drops markedly, corresponding to increased flow rate, in the stenosed region (before the turn), and the high flow rate and low pressure continue around the bend.

"This is somewhat surprising," says Fischer, "since people generally expect turbulence to result from separation past the stenosis, rather than due to transition inside the stenosis. The strong three-dimensionality of the structures shows the importance of full three-dimensional modeling of these flows."



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## TURBULENCE AND SPECTRAL ELEMENTS

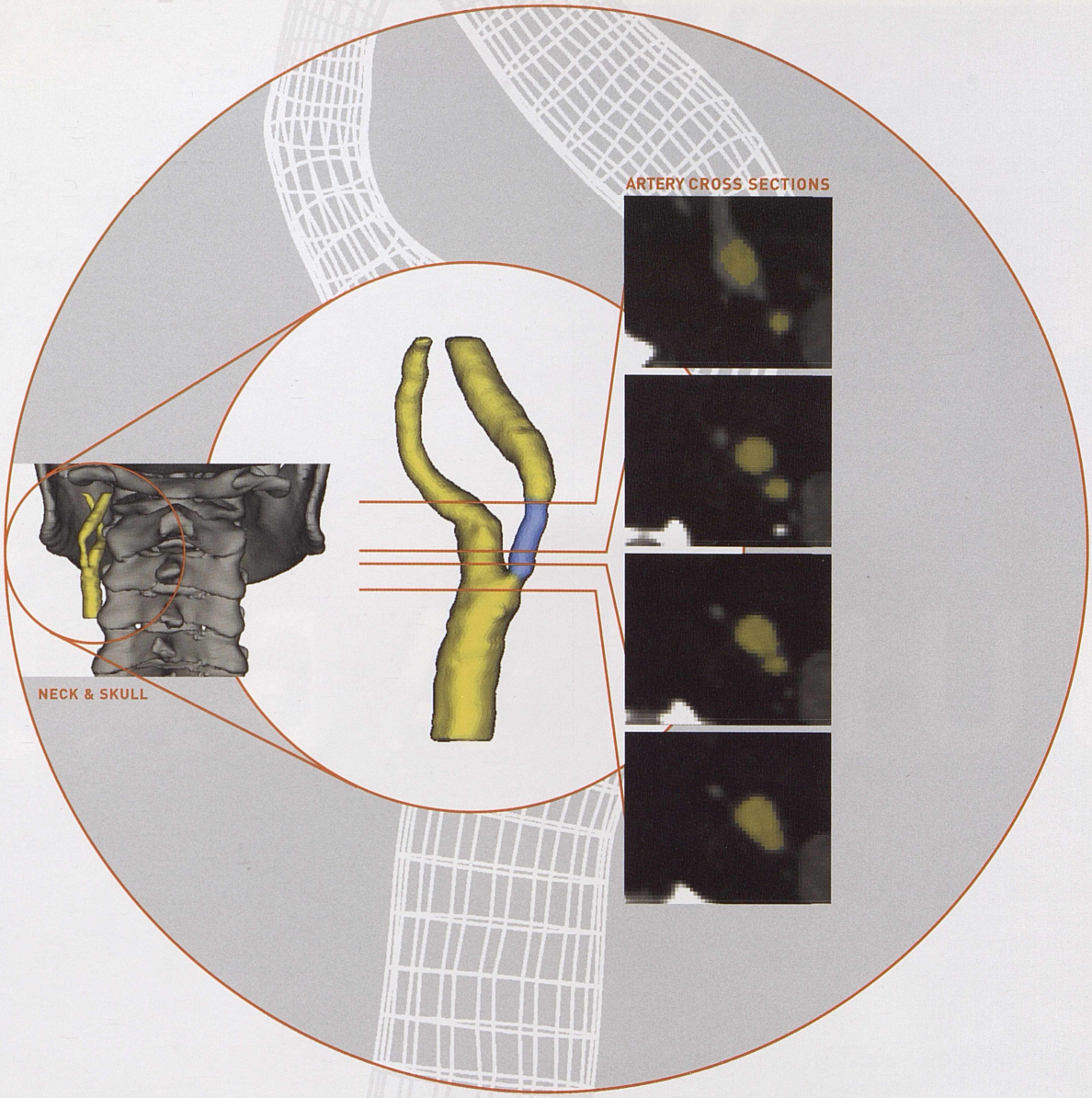
The flow in healthy carotid arteries has been simulated before, but there's good reason why it hasn't been done until now in a stenosed artery. Turbulent flow is much more complex and greatly complicates the numerical problem, multiplying the demand on computing at least 100 times, well beyond the ability of most hemodynamics software and workstation computers.

Fischer is a pioneer in an advanced numerical approach called "the spectral element method," having worked on his dissertation at MIT with its originator, Tony Patera. The advantage is high accuracy with efficient use of computing resources. In 1999, a major computing award, the Gordon Bell Prize, recognized Fischer and Tufo for the quality algorithm and fast performance of Nek5000, their spectral element program.

Loth and Fischer spent the first two years of their collaboration adapting Nek5000 to simulate vascular hemodynamics. Tufo is a specialist in "scaling," software techniques to maximize the teamwork among hundreds or thousands of processors in massively parallel systems, and he took charge of getting Nek5000 up and running efficiently on LeMieux. With his fine tuning and using 2,048 processors in test runs, Nek5000 steps through its paces at 1.25 trillion calculations per second.

It's the first time this transition has been captured by simulation of an actual patient's carotid artery. Fischer is pleased not only with the flow results but also with the computing turnaround. "I didn't think we'd be in this 24-hour range on our first shot. We're ahead of the curve for two reasons: the numerical methods we use and having access to a machine like Pittsburgh's."

Part of the objective for this first round of simulation was to measure how rapidly flow velocity fluctuates with time, from which the researchers can judge how thinly to slice the calculations in the next round of




**A CAROTID ARTERY SNAPSHOT: FROM SCANS TO COMPUTATIONAL MESH**

From CT scans at cross-sectional slices along a patient's carotid artery, the researchers construct a computational mesh, which becomes the framework for highly detailed simulations. The narrow region of the internal branch of this artery (see blue shaded area), just past the carotid bifurcation, is the stenosed region, where 70 percent of the healthy flow cross-section is blocked. In a healthy artery, this region is larger than the downstream region after the artery turns.



## A DETAILED READOUT OF THE FLOW PATTERNS IN CAROTID ARTERIES WILL HELP DOCTORS IDENTIFY WHO'S AT HIGH RISK FOR STROKE.

10 cardiac cycles. At the turbulence peak, the midstream flow velocity fluctuates at about 350 cycles per second, which means they'll need to take a computational snapshot every thousandth of a second to capture details of the flow.

It's the first good look at the transition to turbulence in a carotid artery, and along with new information, it demonstrates that tools are in place to zero in on the correlations between turbulent flow and stroke. "Within five years," says Fischer, "it should be possible to routinely simulate weakly turbulent hemodynamic flows." For medical researchers, this means it's feasible to gather flow data on a range of patients with diseased carotid arteries and carry out long-term studies. What degree of turbulence and high shear stress under what conditions means serious risk of stroke? Getting the answers is now within sight.

**MORE INFORMATION:** http://www.psc.edu/science/tufo.html

MANUFACTURING_PROCESS_DESIGN

# BURN AGAIN



5

## A NEW TURBINE DESIGN COULD REDUCE THE COST OF ELECTRICITY.

Light, heat, kitchen appliances, television and stereo, air conditioners, computing — life as we know it runs on electricity, and electricity comes from turbines. Think of them as jet engines bolted to the floor. Rather than thrust to lift an aircraft off the ground, these turbines produce powerful rotation that drives generators to produce megawatts of electricity, which flows through wires into your home.

# TURBINE

The process starts with fossil fuel, still the raw energy source for nearly 90 percent of electrical power worldwide. Two kinds of turbines, steam and gas, share the load. For steam turbines, coal and fuel oil heat boilers from which pressurized steam turns the windmill-like turbine blades. In gas turbines, combustors ignite the fuel and blast hot, pressurized exhaust gas to do the turning work.

As a cleaner-burning fuel, natural gas is favored for low-emission, nearly pollutant-free turbines of the present and foreseeable future. High efficiency — as complete as possible conversion of raw energy into turbine rotation — is the key not only to low $CO_2$ emission, but also to the cost of electricity. Small gains in efficiency that slightly reduce cost per megawatt translate to huge savings overall, and turbine engineers measure efficiency in tenths of a percent.

One new way of thinking about gas turbines is to let combustion carry over from the combustor into the turbine and even to inject additional fuel into the turbine for an extra kick of power, roughly analogous to a jet engine afterburner. This potentially would allow more complete burning and more overall work from the fuel as well as a healthy power boost. The idea is called a "turbine-combustor" and actually, says Paul Cizmas of Texas A&M, it's an old idea revived for new times.

"The idea started in the 1960s, but we didn't have the technology to test it," says Cizmas, a former senior scientist at Westinghouse in Pittsburgh, "and until two or three years ago, it was considered bad to have flame in the turbine, mainly because of the problem of cooling the blades. Then we realized we already design the first row of blades, the vanes, as if the flame is there. The problems come in the rows after that, and recent studies have shown we need to worry about how to cool these rows anyway, even if we don't have turbine combustion."

In September 2000, the U.S. Department of Energy (DOE) Strategic Center for Natural Gas selected Siemens-Westinghouse Power Corp. to study the turbine-combustor idea, with Texas A&M on board to focus on computational simulation. "There's an opportunity to significantly reduce the cost of an engine," says Tom Lippert, manager of science and technology center combustion programs at Siemens-Westinghouse, "and to reduce the cost of electricity."

A necessary step out of the starting blocks is to develop a reliable way to simulate the physical processes. "This could be a different combustion process altogether from what we're used to," says Lippert. "You have to have analytical tools that allow you to combine combustion kinetics with aerodynamics. This hasn't been done before, at least in this fashion."

In work a few years ago at PSC, Cizmas developed software that simulates the complex flows involved in turbine blade design. By relying on the computing power of massively parallel systems, Cizmas's approach proved to be both faster and more accurate than prior approaches. In 2001, through the Super Computing Science Consortium (p. 6), a southwest Pennsylvania-West Virginia regional partnership that links DOE's National Energy Technology Laboratory with PSC, Cizmas used the 512-processor CRAY T3E at Pittsburgh to develop and test a computational method for the much more complex flow problems involved in a turbine-combustor.

CONT'D →

## UNEXPLORED TERRITORY

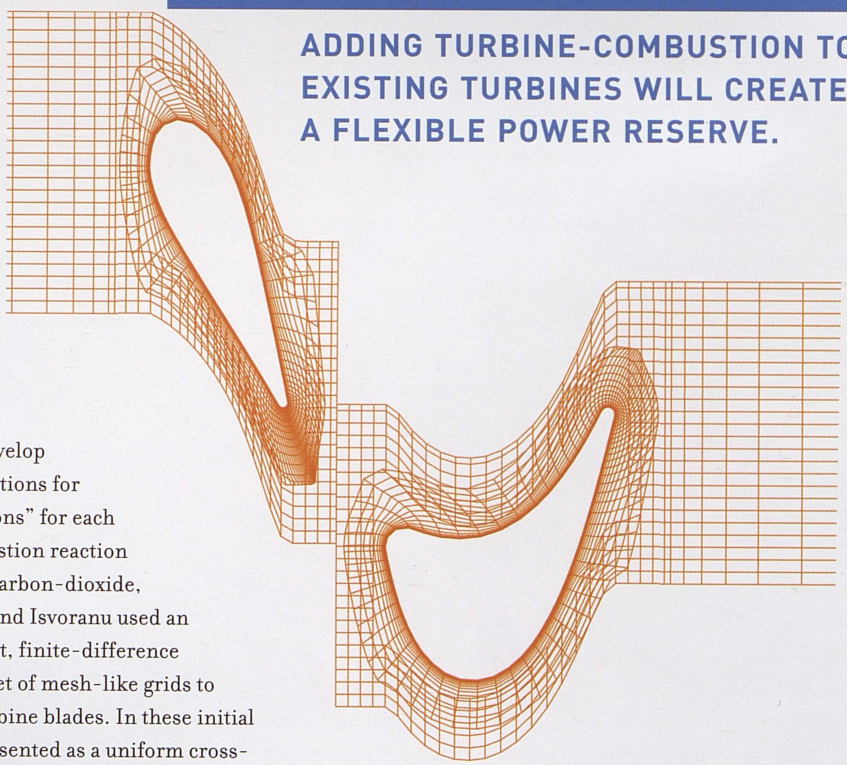
As they began this project, Cizmas and his colleague, Dragos Isvoranu of Politehnica University Bucharest, soon realized they had an interesting opportunity. A literature search revealed no prior data on combustion within a turbine.

The first challenge was not a new one — simulating flow in the alternating rows of stationary and rotating blades, vanes and rotors, that characterize modern power turbines. The passageway between vanes is like a nozzle that speeds up the hot gas and shoots it toward the spinning rotors. Each vane-rotor series is called a stage, with many stages, hundreds of blades, in operational turbines. Although these flows are complicated, Cizmas had already tackled this problem with success.

The added complication is combustion, which changes everything. By itself, combustion has been modeled, but not when the flow is this complicated. "Flow in the turbine," says Cizmas, "is like a nightmare because of the rotor-stator interaction. Now on top of this, we want to have a stable flame. Flow in the combustor is almost steady, if not steady, but in this case, it's very unsteady. So you have the problem not only of correctly simulating the combustion, but also unsteadiness in the combustion — a very challenging problem."

Added heat not only increases temperature, it also can radically change the flow patterns. Flow from the combustor alone induces "hot streaks" downstream in the turbine, which affect blade life and blade design. With the added stress of combustion within the turbine, these problems are exacerbated.

As a practical matter, computer simulation is the only hope for gaining enough understanding to arrive at a design concept. "The question is how should we inject fuel," says Cizmas, "at what location, what pressure, what quantity? Should it be continuous or pulsed? The possible variations are infinite. Experimental investigation with scale models would take years."



Two overlapping grids are employed to divide the computational geometry. Close to the blades, a fine grid captures the complex "boundary layer" effects of fluid interaction with a surface. A coarser grid, which involves less computing time, is used for the space more distant from the blades.

**ADDING TURBINE-COMBUSTION TO EXISTING TURBINES WILL CREATE A FLEXIBLE POWER RESERVE.**

## WHEN THE FUEL HITS THE ROTOR

The numerical challenge was to develop an algorithm that coupled the equations for fluid flow with the "species equations" for each chemical constituent of the combustion reaction — natural gas (methane), oxygen, carbon-dioxide, carbon-monoxide, water. Cizmas and Isvoranu used an efficient approach — a fully implicit, finite-difference method — that employs a moving set of mesh-like grids to subdivide the space around the turbine blades. In these initial computations, the blades are represented as a uniform cross-section extended from the turbine hub.

Using the CRAY T3E to put their software through its paces, the researchers modeled a one-stage turbine-combustor with 32 vanes and 49 blades — a relatively simple configuration that corresponds to an existing turbine. The work is shared among processors, one for each blade. For this initial test, they modeled fuel injection with basic parameters — through a single small hole at the trailing edge of the vanes, at low velocity, and relatively high temperature and pressure.

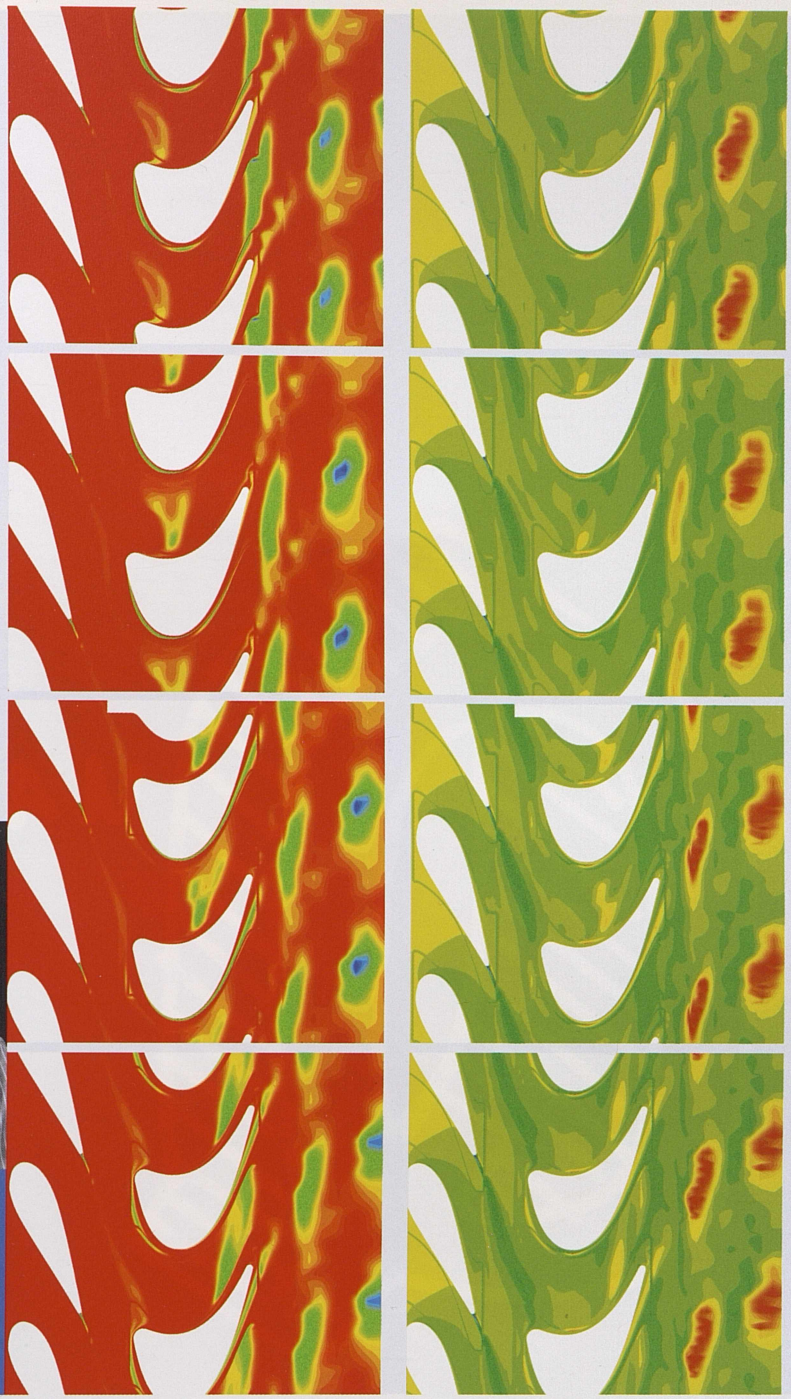
As Cizmas expected, the simulations show delayed ignition. In the space between blades, the fuel rapidly gains heat and mixes with oxygen and then ignites as it hits the rotating blades. Ignition, however, occurs with unexpected intensity, almost like an explosion, says Cizmas. "At the moment when the wake of fuel from the stator hits the rotor, you see rapid acceleration of the reaction. We were expecting strong coupling between the flow and combustion, but we didn't know we'd see this quite important increase in reaction speed."

To assess accuracy, Cizmas ran the simulations with three different grid resolutions — coarse, medium and fine — with nearly 50,000 processor hours on the T3E. Analysis showed good agreement between the high and medium resolution grids, a strong indication that the modeling is accurately representing the physical process. An innovative correction algorithm for the species computation, says Cizmas, appears to work well. Coupling between the equations for flow and combustion raised a theoretical question about reaction thermodynamics, a specialty of Isvoranu, which the researchers are looking at and which may necessitate a revised approach.

Cizmas expects that the Siemens-Westinghouse research program will lead to operational turbine-combustors within five years with implementation in power plants in ten years. One possibility envisioned by this research is a turbine-combustor unit

**OXYGEN AND TEMPERATURE IN TURBINE-COMBUSTION**

These snapshots from simulation of turbine-combustion show how oxygen decreases (left) and temperature increases (right) as markers of combustion in the flow. Each sequence shows a turbine rotation, with each frame representing a quarter turn. A traveling burst of flame begins as the injected fuel hits the rotors and expands as it crosses the rotor path. A coherent flame forms downstream of the rotor's trailing edge.



Paul Cizmas, Texas A&M

that eliminates the combustor as a separate component. "This is an opportunity," says Lippert, "to significantly reduce the cost of an engine. If you integrate the combustion system into the blade path, you eliminate a big piece of hardware."

A more immediate use, though, is likely to come from adding turbine-combustion to existing turbines, creating a flexible power reserve. "If there's a point in the day that the plant needs to produce more power," says Cizmas, "it can be done by turning on combustion in the turbine." The only current option for a sudden power crunch is to bring an additional turbine on-line, potentially producing more power than required, which gluts the bidding market for power and lowers profitability.

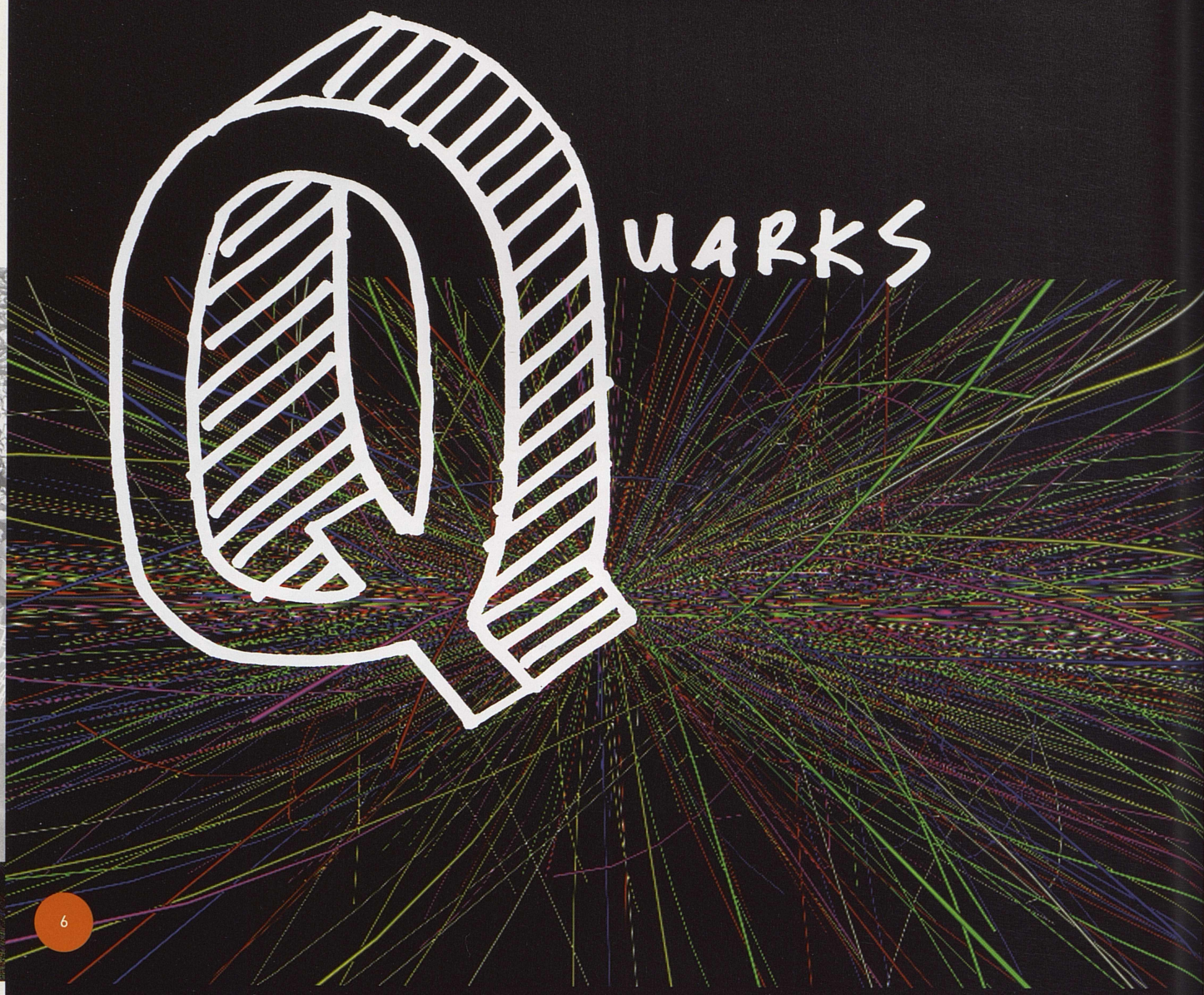
Cizmas is preparing his turbine-combustor software for a more comprehensive series of simulations on PSC's 3,000-processor Terascale system. These studies will incorporate a fully 3D representation of the blades, with one processor assigned to each of 50 cross-sectional slices per blade to capture the finely detailed aerodynamics of blade curvature with Terascale massive parallelism.

Though results are preliminary, the first round of simulations offers new understanding to help point the way ahead. The accelerated ignition at the rotors suggests the fuel may need to be pulsed in time with rotor frequency. "Other issues," says Cizmas, "include what angle to inject. We're looking at a variation of angles to increase turbulence, which helps mixing. And at what velocity should we inject? What temperature and pressure? How many injection points per blade? How should they be spaced? We're also looking at fuel composition. Should we use pure methane, or methane mixed with air? And what about using hydrogen? We're going to be busy for awhile."

MORE INFORMATION:
http://www.psc.edu/science/cizmas2002.html

AT_THE_FRONTIER_OF_PHYSICS

# The Strange Flavor *of*



**AMONG THE PAYOFFS OF QCD CALCULATIONS ARE FUNDAMENTAL PARAMETERS CALLED CKM MATRIX ELEMENTS.**

"Three Quarks For Muster Mark!
Sure He HASN'T GOT much of a Bark
AND SURE ANY He HAS IT'S ALL BESIDE THE MARK."
— JAMES Joyce, FINNEGAN'S WAKE

Who says physicists aren't fun? When we want to talk about the fundamental particles of matter, the rock-bottom, indivisibly smallest of the small things deep within the nucleus of an atom, we can be grateful that the person who thought them up read James Joyce and had a sense of humor.

In 1963, theoretical physicist Murray Gell-Mann needed a name for his idea for the building blocks of protons, neutrons and related subatomic particles, till then thought to be indivisible. He settled on quark, a word that combines a dog's bark with a sea gull's squawk and that in German means curd, the fundamental constituent of cheese. Gell-Mann's quarks, which originated as a mathematical glimmer in his mind, have since been substantiated in many experiments, though no one — for reasons inherent in the nature of quarks — has yet tasted, touched, seen or in any way directly observed one.

Gell-Mann won a 1969 Nobel Prize, and by the early 1970s, quarks were key ingredients in a powerful theory, called quantum chromodynamics or QCD, that describes the strongest force in nature — the interactions that hold together the nucleus of an atom. QCD is a major component of modern physics' integrated theory of the fundamental particles and their interactions, called The Standard Model.

"The Standard Model," says Indiana University physicist Steven Gottlieb, "has been enormously successful, having passed all the experimental tests to which it's been put. But what we know about it is incomplete, because it's been difficult to extract many of the most interesting predictions of QCD."

Enter supercomputing. Though frightfully challenging and demanding the most powerful systems that can be built, computational simulations of QCD are crucial to expanding what's known in high energy and nuclear physics.

Gottlieb began doing QCD computations in the early 1980s, and since the 1990s he's been part of a nationwide team of theoretical physicists who collaborate to gain maximum advantage from the available computing time. They call themselves the MILC collaboration, an acronym, MImd Lattice Computation, that points both to scientific computing (multiple instruction, multiple data — mimd — the technology of massively parallel processing) and to the computational approach — the "lattice" — that makes it feasible to solve QCD equations.

LeMieux, PSC's terascale system, has been a major boost to their work. Beginning in early 2001 with the TCSini prototype and since October, when grownup LeMieux came online, the MILC team has milked every drop of computing available to it from this system. The result is their most realistic QCD calculations yet. "We've made exceptional progress," says Gottlieb, "that wouldn't have been possible without this system."

### MAY THE FORCES BE WITH YOU: THE STANDARD MODEL & CKM MATRIX ELEMENTS

The Standard Model is a pedestrian name for one of the more glorious achievements of science. It's a tidy summing up of much of the knowledge that has blossomed, if not exploded, from the 20th century revolutions of quantum theory and relativity. It links the tiniest particles inside an atom with the big bang and what we know about evolution of the cosmos.

Four forces — that's all you need to know. From the standpoint of modern physics, everything that happens is at

CONT'D →

root level a result of gravity, electromagnetism, the strong force and the weak force. For The Standard Model, gravity is the stepchild that doesn't quite fit. The weakest of the four — weaker even than the weak force — gravity affects us only when matter aggregates into huge masses, such as planets and stars.

The Standard Model's fame lies in bringing the other three forces under one umbrella. It includes a unified theory of electromagnetism and the weak force (electroweak theory) and QCD, the theory of the strong force. In other words, if a dream of modern physics is (and it is) a theory of everything (TOE), The Standard Model is close to three-fourths of a TOE.

The Standard Model sums up what we've learned about fundamental particles and how they interact at the extremes, such as when atoms are smashed in a collider and "decay" into other particles. Most fundamental particles exist only for fleeting instants as traces from these high-energy events, in which scientists force them out from hiding.

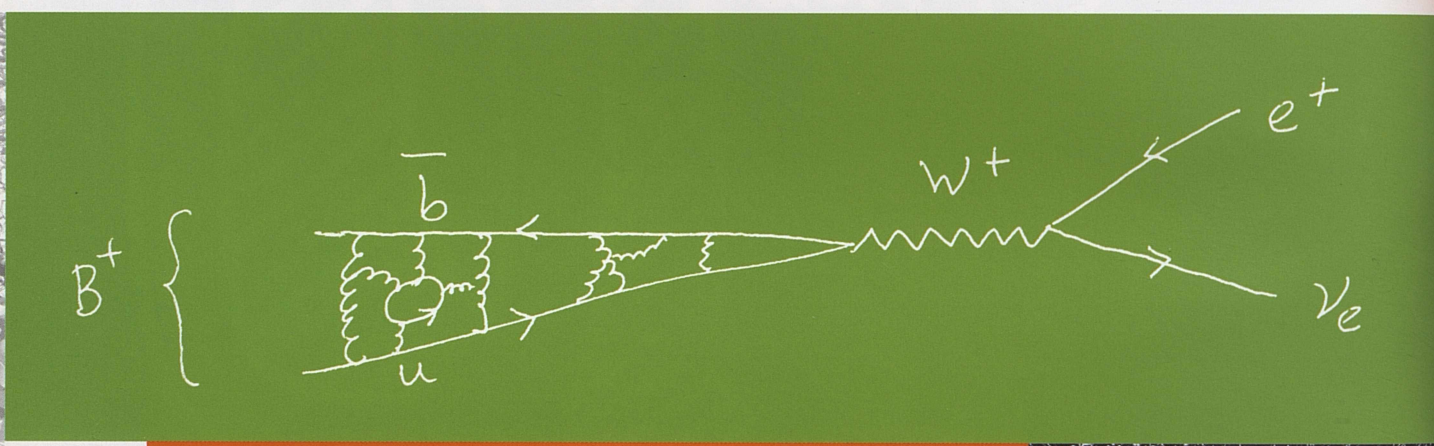
elements. Named for three physicists, Cabibbo, Kobayashi and Maskawa, CKM matrix elements are of great interest to contemporary physics. They are fundamental parameters of The Standard Model, similar to Planck's constant at the core of quantum theory. They define the intersection between the strong and weak force in events that involve both. Some of the CKM elements are known. Others are more intractable. Pinning them down could lead the way to deeper levels of understanding in particle physics.

### QUARKS, MESONS & WEAK DECAY

According to QCD, quarks come in six "flavors" — up, down, strange, charm, bottom and top (in ascending order by mass) — that mix in

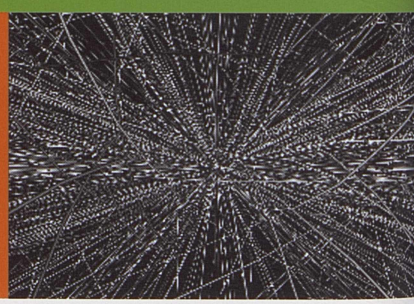


## FOR THE FIRST TIME IN QCD, LATTICES INCLUDE DYNAMICAL STRANGE QUARKS.




**WEAK DECAY**

Called a Feynman diagram, after Nobel physicist Richard Feynman who originated them, this drawing by Steve Gottlieb starts on the left with a B meson (B+). The strong force confines an up quark (u) and bottom anti-quark ($\bar{b}$) inside the B meson, where they interact until they annihilate. "For a moment," says Gottlieb, "there's a W boson (W+), carrier of the weak force. Then that W boson, because it's a virtual particle, decays to an anti-electron, also called a positron (e+), and an electron neutrino ($\nu_e$)."





As successful as The Standard Model has been, physicists know it's a plateau in the progress of science — a grand edifice that with every piece of knowledge added reveals another question to be resolved. QCD calculations are the only way "to confront experiment with theory," says PSC physicist and co-scientific director Ralph Roskies — to compute quantities needed to answer some of the questions. While we spend hundreds of millions annually on powerful accelerator experiments, QCD calculations — which aren't backed with this level of resources — are an equal partner in the intellectual effort.

"We need simulations to determine a number of the basic parameters of The Standard Model," says Gottlieb, "for quantitative understanding of physical phenomena controlled by the strong interactions, and to do precision tests of the Standard Model."

Among the payoffs ahead — awaiting accurate QCD calculations to interact with experimental data — are quantities called CKM matrix

different combinations to form many varied species of the subatomic particle zoo. The big particles of the nucleus, protons and neutrons, are bundles of three quarks. Two ups and a down make a proton, an up and two downs a neutron.

From the mid-1960s forward, accelerator experiments have set out to break quarks free from the larger nuclear particles they inhabit. No luck. The problem, as it's been theorized within QCD, is that when you add great amounts of energy to a proton — trying to smash it in an accelerator — rather than freeing a quark, the added energy becomes new matter. Out of thin air, another particle

appears. The particle that forms is a meson — a quark paired with an anti-quark.

There are many mesons, and one of them in particular, the B meson — B for the bottom anti-quark (paired with an up or down flavored quark) — is the subject of a tantalizing question, one the MILC group is aiming at with LeMieux. The question — "weak decay" — is one of the places where QCD calculations are crucial to determining CKM matrix elements.

The weak force — in some ways the most mysterious of the four forces — is responsible for nuclear decay, of which the best known example is radioactivity. Because of the weak interaction, the vast majority of fundamental particles when left to themselves disintegrate to one of only a few apparently stable particles — prominently including protons, electrons and neutrinos.

With a B meson, a "leptonic" weak decay happens when the heavy anti-quark and light quark annihilate each other due to the weak interaction. (Bottom, the next to heaviest quark, is 1,000 times heavier than up, the lightest.) What comes out of this decay, roughly analogous to sex change, is no longer a nuclear particle but a pair of non-nuclear particles. Called leptons (Greek for light and swift), the most prevalent are electrons and neutrinos.

Gottlieb and his colleagues and many others want to accurately describe how the weak interaction contributes to this leptonic decay. But the strong interaction gets in the way. The quark and anti-quark stay inside the meson, interacting through the strong force before they annihilate. "If we don't understand how they interact strongly," says Gottlieb, "we can't get the detailed probability of how they'll decay."

Major accelerator experiments now underway, one at Stanford and another in Japan, are focused on producing B mesons and analyzing their decay. At the same time, with big help from LeMieux, the MILC group is zeroing in on a quantity — called the B meson decay constant — that's needed, along with data from the experiments, to arrive at the CKM matrix elements that define this decay.

Members of the MILC group, colleagues and canine friends at a recent Lattice QCD conference in Salt Lake City (left to right): Carleton DeTar, Eric Gregory, Tom Burch, James Osborn, Roberta Toussaint, Doug Toussaint, Steve Gottlieb, Phillip Toussaint.

**THE MILC QCD COLLABORATION**

Claude Bernard
WASHINGTON UNIVERSITY

Tom DeGrand
UNIVERSITY OF COLORADO

Carleton DeTar, James Osborn
UNIVERSITY OF UTAH

Steven Gottlieb
INDIANA UNIVERSITY

Urs M. Heller
FLORIDA STATE UNIVERSITY

James Hetrick
UNIVERSITY OF THE PACIFIC

Robert Sugar
UNIVERSITY OF CALIFORNIA, SANTA BARBARA

Tom Burch, Eric Gregory, Doug Toussaint
UNIVERSITY OF ARIZONA

## BUILDING A BETTER LATTICE

The prerequisite to calculating the B meson decay constant is realistic QCD lattices, a scaffold-like framework that divides the continuum of space-time into discrete regions in which to compute physical quantities. "We're generating the most realistic set of lattices we've ever produced," says Gottlieb of the past year's work with LeMieux. The major part of the MILC effort has been to generate the best lattices possible with available resources. With over a million single-processor hours of LeMieux (nearly 3,000 hours on 512 processors), their new lattices are more finely resolved than ever (grid spacing is .09 femtometers, a million-billionth of a meter).

Significantly, the LeMieux lattices also reflect a more realistic representation of dynamical quarks — the sea-like background of quark, anti-quark pairs that affect QCD physics. Prior QCD lattices have included only up and down dynamical quarks. The new lattices, for the first time in QCD, include dynamical strange quarks. Preliminary analysis indicates that these quarks influence the value of the decay constant.

With the new lattices and more computations, the MILC group is progressively closing in on the elusive pieces of knowledge it seeks. As powerful an explanatory work as it is, The Standard Model is replete with mystery. "Why are the quark masses what they are?," asks Gottlieb. "The top quark is 175 times the mass of the proton. It's amazing. Quarks and leptons come in pairs of three generations. Why?"

The CKM matrix elements represent a key that may unlock the next layer of mystery. "A more basic, deeper theory," says Gottlieb, "would have to make an accurate prediction of the CKM matrix elements. Until we can accurately extract these parameters, there will be uncertainty when people propose more fundamental theories. We all think there may be something beyond The Standard Model, something we don't yet understand."

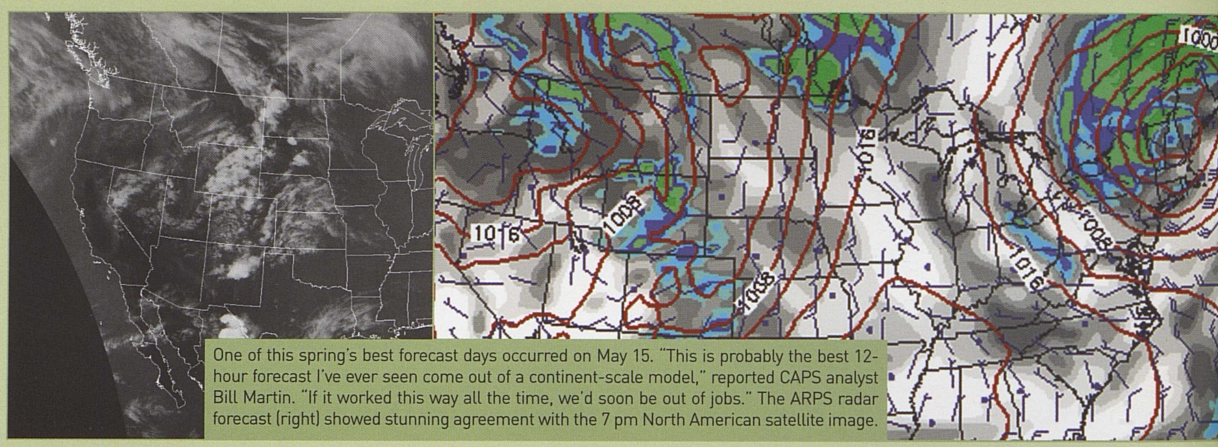
**MORE INFORMATION:** http://www.psc.edu/science/milc.html

# In Process

## BETTER STORM FORECASTING

Severe thunderstorms inflict death and property loss adding up to billions of dollars a year. New weather-forecast technologies on the horizon will reduce this loss by giving improved warning — a few hours compared to current forecasting, which if we're lucky lets us know a half-hour before a severe storm hits.

This year, from May 13 to June 25, CAPS used LeMieux, PSC's terascale system, to produce daily forecasts at three different scales — continental U.S., the south-central Great Plains states, and a storm-scale forecast for Oklahoma and southern Kansas. This experiment, carried out as part of a program called The International $H_2O$ Project, focused on implementing ARPS in the LeMieux environment. By the end of the experiment, the team had fully ported the ARPS software to LeMieux, achieving impressive daily turnarounds of little over an hour to generate a storm-scale forecast for 12 hours ahead.




One of this spring's best forecast days occurred on May 15. "This is probably the best 12-hour forecast I've ever seen come out of a continent-scale model," reported CAPS analyst Bill Martin. "If it worked this way all the time, we'd soon be out of jobs." The ARPS radar forecast (right) showed stunning agreement with the 7 pm North American satellite image.

**THE PITTSBURGH ENVIRONMENT HAS BEEN PHENOMENAL.**

The Center for Analysis and Prediction of Storms (CAPS) at the University of Oklahoma, Norman has over the last decade developed a number of technologies — including innovative use of Doppler radar — that are the foundation of the new forecast technologies. Their award-winning numerical forecast system, the Advanced Regional Prediction System (ARPS), has already been deployed by some airlines and insurance companies.

PSC staff worked closely with the CAPS team to debug, optimize, benchmark and prepare software, to tune file-handling procedures, and to provide dedicated time and reservation-based scheduling. "As far as the ability of what we can do," says CAPS director Kelvin Droegemeier, "the Pittsburgh environment has been phenomenal."

**MORE INFORMATION:** http://www.caps.ou.edu

## A FREE ENERGY LANDSCAPE ON THE GRID

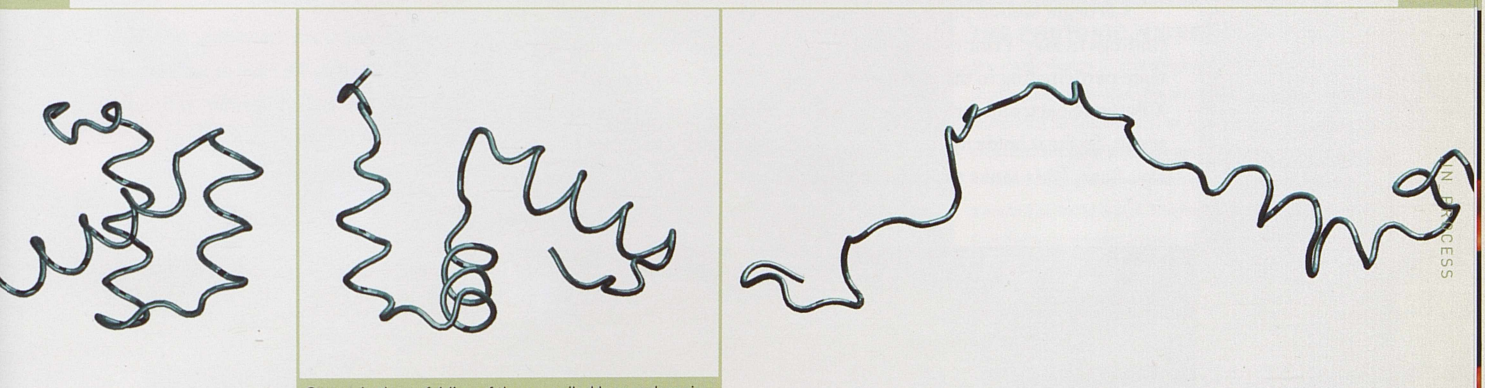
For about 36 hours on May 29 and 30, researchers in California attacked a problem in protein biology with four different computer systems in three parts of the country. Special software called Legion, developed at the University of Virginia, harnessed the four diverse systems like a trained team of horses pulling one wagon. This "grid" approach to large-scale computing is the wave of the future, and this large-scale experiment — which produced important research results — helped to test some of the tools and demonstrate feasibility.

Scientists Charlie Brooks and Mike Crowley at Scripps Research Institute near San Diego used the experiment to study protein folding for a protein fragment called "the engrailed homeodomain." From the fruitfly, this fragment contains much of the genetic information of much larger proteins in which it resides. Because of this, the engrailed homeodomain is of great interest to the theory of protein folding, one of the grand problems of contemporary biology.

On May 29 and 30, Brooks and Crowley carried out long sampling simulations of specific parts of the homeodomain's folding pathway to generate its "free-energy landscape," a map of how a protein changes energy in relation to changes in its 3D shape. They employed the IBM-SP "Blue Horizon" system at San Diego Supercomputer Center, a workstation cluster at the University of Virginia and two PSC systems — Jaromir, the CRAY T3E, and LeMieux, PSC's terascale system. The Legion software provided an interface that allowed them to submit simulations to the system most available and to gather output from all the systems.

PSC's Collaboratory Research Project participated in the experiment. Supported through NIH's National Center for Research Resources, this project studies technologies to improve the ability of biomedical scientists at separate locations to collaborate effectively. Brooks and Crowley in California coordinated with computer scientists in Virginia, who developed the Legion software, and with consultants at PSC using collaboratory tools tested through PSC's program, including an AOL Instant Messenger chatroom.

**USING A "GRID" OF FOUR DIVERSE SYSTEMS IN THREE PARTS OF THE COUNTRY, RESEARCHERS CARRIED OUT A MAJOR STUDY OF PROTEIN FOLDING.**



Stages in the unfolding of the engrailed homeodomain, as simulated by Charles Brooks and Mike Crowley.

## BLOOD FLOW AND ARTIFICIAL ORGANS

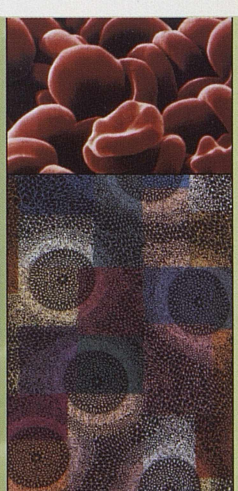
By recent estimates, 80,000 Americans are waiting for organ transplants, and 8 percent of them — about 6,500 people — will die waiting. "Artificial organs represent the only real hope for most of these people," says Omar Ghattas, professor of biomedical engineering and civil and environmental engineering at Carnegie Mellon. Ghattas leads the Sangria Project, a team of researchers from several universities working to overcome some of the obstacles that hinder the design of artificial heart devices.

One of the main obstacles is that current computational models of blood flow see only the forest and not the trees of this vital fluid, which up close is a mix of hemoglobin-filled cell membranes and fluid plasma. Experiments show that these up-close details make all the difference in design of artificial organs. As blood flows through artificial devices, red blood cells are often damaged, and clotting occurs that can drastically change flows.

Models of blood flow that account for these factors could avoid many false trails and potentially save years of design time, but current models, which treat blood as a homogeneous fluid, won't do the job. With an NSF Information Technology Research grant, Ghattas and co-principal investigators Guy Blelloch, Gary Miller and Noel Walkington of Carnegie Mellon and James Antaki of the University of Pittsburgh Medical Center are using LeMieux, PSC's terascale system, to do what no one has done before — realistically simulate blood flow at the microstructural level.

"We're making steady progress," says Ghattas, "on this very challenging problem." Initially, the group's calculations were limited to 2D approximations of a cell. They've since incorporated an elastic model of the cell membrane, and they've simulated the mechanism that's responsible for the bi-concave disk-like shape of a red blood cell in its low-energy or "resting" state. They're now directing their work toward modeling the dynamics of many thousands of cells within a fluid flow in 3D.

"We've solved the main conceptual problems," says Ghattas. With access to LeMieux, he expects such simulations will be routine within two years. **"Teraflop supercomputing is essential and critical to the viability of this enterprise."**



A microscope view of red blood cells and a 2D dynamic computational mesh developed by the Sangria Project for simulating blood flow at the microstructural level.

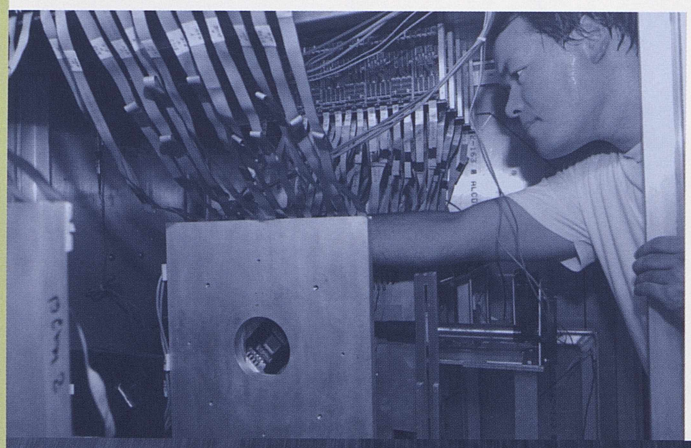
MORE INFORMATION:
http://www.cs.cmu.edu/~sangria

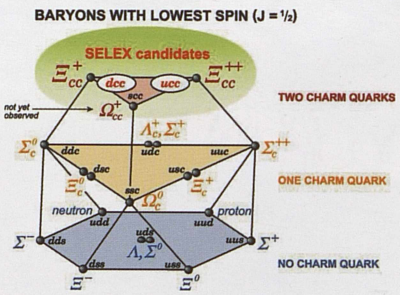
## FINDING THE DOUBLY CHARMED BARYON

Two charm quarks plus one up or down — that's the flavoring for Mother Nature's recipe to create the "doubly charmed baryon." Predicted by modern physics' theory of fundamental particles, The Standard Model (see pp. 38-41), this elusive particle remained a theoretical possibility, not an observed reality, until Carnegie Mellon doctoral student Mark Mattson (now a post-doc at Wayne State) noticed something in the massive data from an experiment at Fermilab in Illinois.

Carnegie Mellon physicist Jim Russ announced the new particle findings in May. Prior to that, he and colleagues from the international team participating in the experiment — called SELEX (Segmented Large X Baryon Spectrometer) — spent months analyzing data to verify the result. So far it holds up to scrutiny. "By the standards of the field," says Russ, "this ranks as a discovery."

Nevertheless, Russ is collaborating with PSC to provide massive data archiving for further analysis. Steadily over six months, at an average rate of a megabyte per second, PSC transferred 15 terabytes of data into tape storage, indexed by unique file names for retrieval. "There are ways these particles decay," says Russ, "that we have to come back to with more sophisticated analysis. We have an international team, including people in Russia and Mexico. We have to package the information and get it to people at remote sites. PSC provides us with a unique capability to accomplish this."

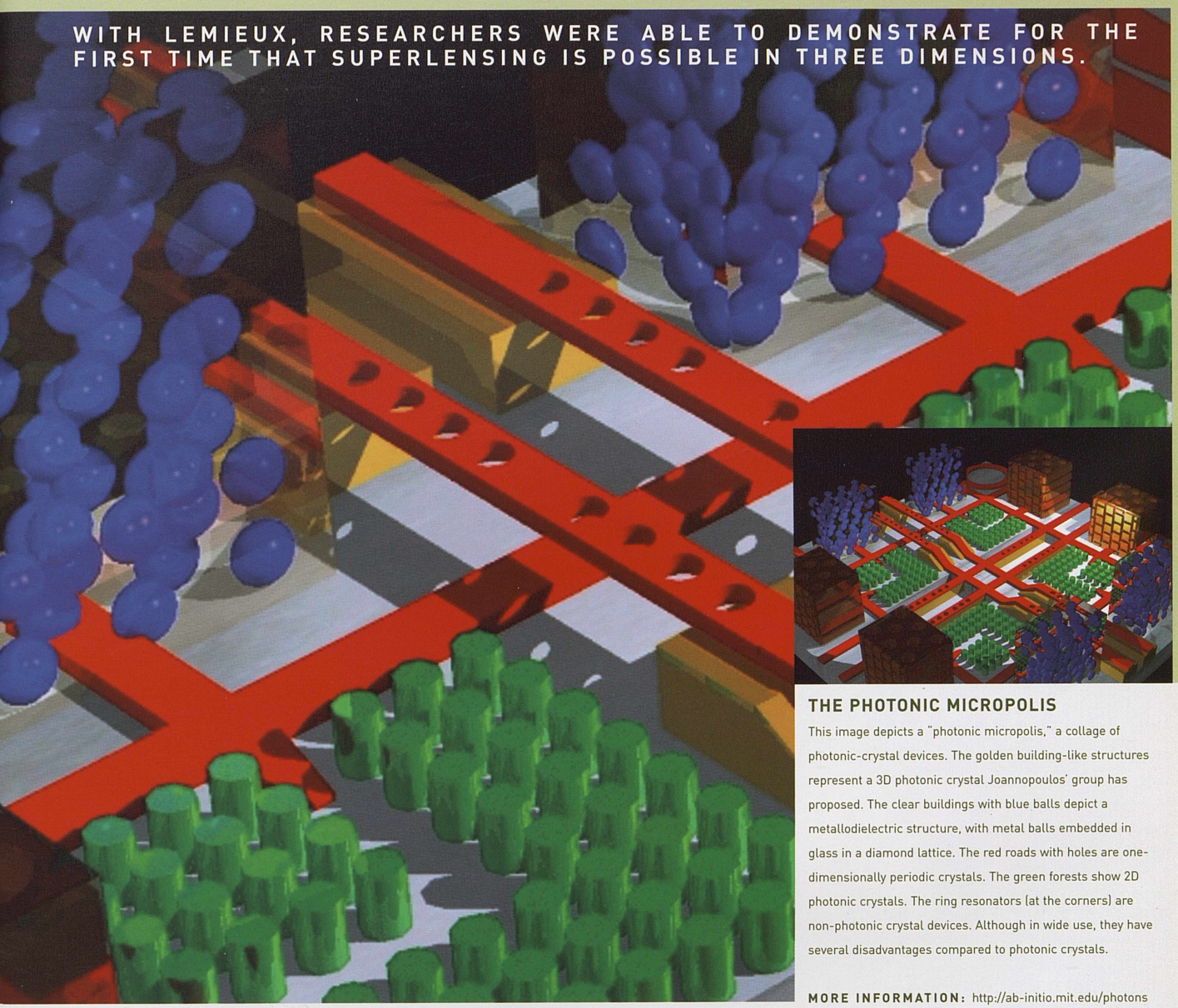





**Mark Mattson** checks silicon vertex detectors, which allow for precise measurement of particle tracks, in the SELEX experiment. (Fermilab Photo)

**RESEARCHERS RELY ON PSC'S MASS DATA STORAGE CAPABILITY TO CONFIRM THE DISCOVERY OF NEW PARTICLES.**

WITH LEMIEUX, RESEARCHERS WERE ABLE TO DEMONSTRATE FOR THE FIRST TIME THAT SUPERLENSING IS POSSIBLE IN THREE DIMENSIONS.



**THE PHOTONIC MICROPOLIS**

This image depicts a "photonic micropolis," a collage of photonic-crystal devices. The golden building-like structures represent a 3D photonic crystal Joannopoulos' group has proposed. The clear buildings with blue balls depict a metallodielectric structure, with metal balls embedded in glass in a diamond lattice. The red roads with holes are one-dimensionally periodic crystals. The green forests show 2D photonic crystals. The ring resonators (at the corners) are non-photonic crystal devices. Although in wide use, they have several disadvantages compared to photonic crystals.

**MORE INFORMATION:** http://ab-initio.mit.edu/photons



## SETTING A TRAP FOR LIGHT

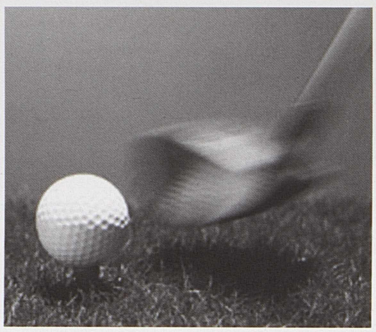
**The technology of semiconductors brought us home entertainment, computers and the information age. An emerging technology called "photonic crystals" is to light what semiconductors are to electricity, and these fascinating devices promise to make an impact on 21st century communications.**

"Photonic crystals," says MIT physicist John Joannopoulos, "provide what is essentially a new mechanism for controlling, confining and manipulating the properties of light." Computer chips work by exploiting energy "gaps" in layered crystals of silicon to regulate the flow of electrons, and photonic crystals do much the same for photons, the quantum constituents of light. Layers of material with differing indexes of refraction create conditions in which light can't exist at certain wavelengths and therefore is in effect trapped within the crystal. These properties can overcome some current limitations in the speed and capacity of optical fibers, and they could play an important role in creating hyperfast computing that uses light rather than electrons.

Joannopoulos and his colleagues at MIT carry out a program of laboratory research in these materials, and they have developed software designed especially to simulate their properties. Since April 2002, they've used LeMieux, PSC's terascale system, to advance their research on several photonic-crystal projects. Among this work is simulations of a phenomenon called "superlensing." Taking advantage of LeMieux, Joannopoulos' team for the first time carried out a numerical experiment demonstrating that superlensing is possible in three dimensions.

With a similar simulation in 2001, Joannopoulos and colleagues also demonstrated superlensing for the first time in two dimensions. They had been unable to do the more complex 3D simulation until LeMieux became available. "We simply couldn't do this without LeMieux," says Joannopoulos. "We tried and couldn't make it work. This machine has been absolutely fantastic, enabling us to do calculations that were previously impossible."

## RECIPES FOR AMORPHOUS METAL



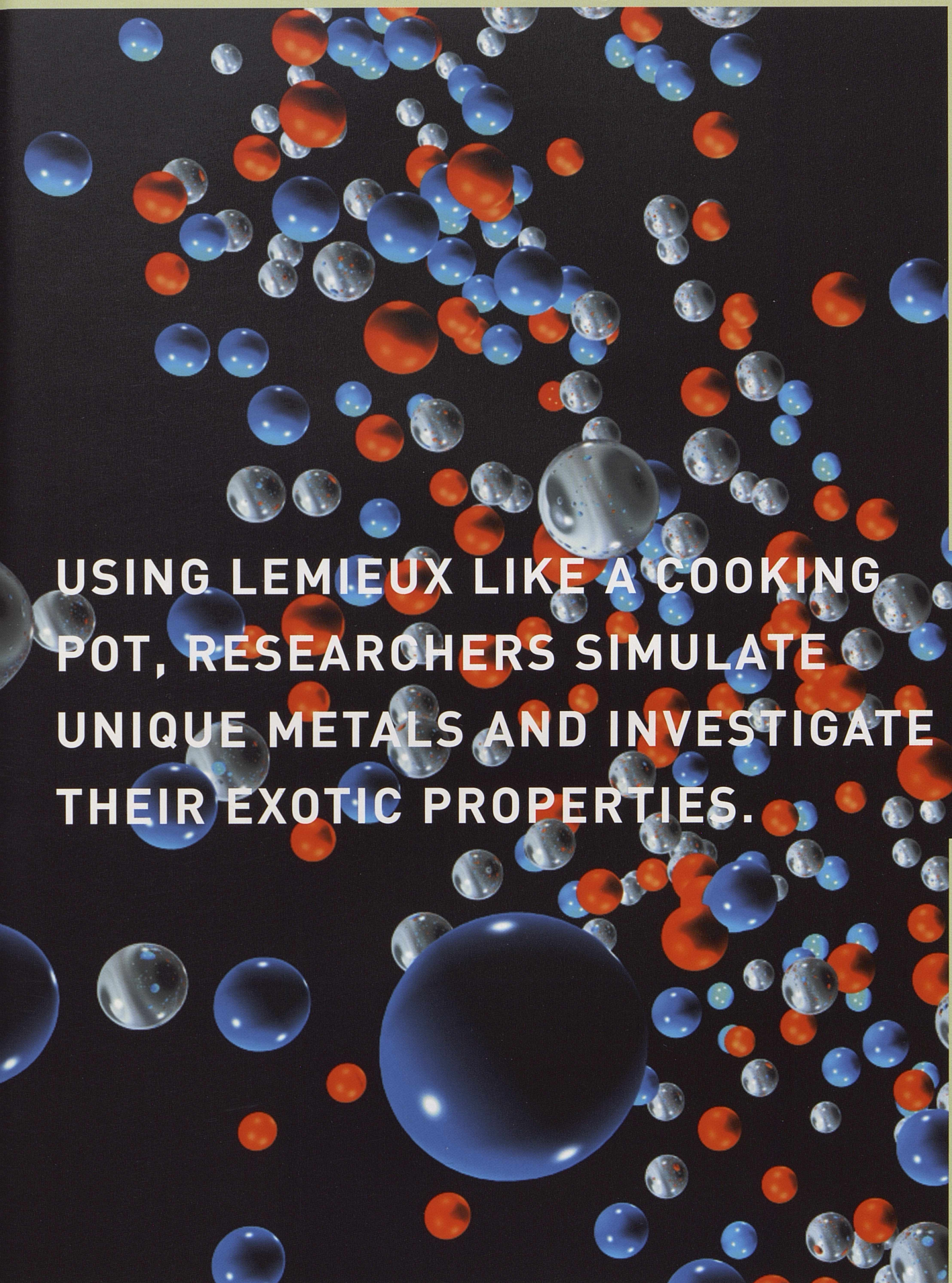
Amorphous metal — isn't that an oxymoron? Metals in bulk, meaning usable forms like tin cans and steel hammers, are close-packed, regular arrangements of atoms. Like members of a three-dimensional marching band, the atoms line up at precise spacing and angles from each other, repeated over and over in a pattern called a lattice.

Modern science finds ways to do many things Mother Nature hasn't done yet and among them is creating bulk metals without a lattice structure. Called amorphous metals — also known as "metallic glasses" — these materials have a random atomic structure that, for reasons not well understood, gives them unique properties — notably including a quality called "soft" magnetism and rust resistance. Many of them also combine strength and hardness with flexibility. Their trampoline-like springiness, for instance, makes amorphous metals the choice for the heads of high-performance golf clubs.

PSC solid-state physicist Yang Wang collaborates with Carnegie Mellon physicist Mike Widom and Oak Ridge National Lab material scientist Don Nicholson on computational simulations of these materials. Their approach uses LeMieux, PSC's terascale system, like a cooking pot to stir in a little of this, a little of that — some iron, zirconium, boron, a dash of manganese and maybe some carbon. Cook it up and see what happens.

Wang employs software he helped to develop, called LSMS (Locally Self-Consistent Multiple Scattering Method), a quantum-theory based approach to calculating the electronic, magnetic and other properties of metal systems. LSMS is designed to exploit massively parallel systems like LeMieux, and in 1998 it was the first research software to achieve sustained performance exceeding a teraflop (a trillion calculations a second). On LeMieux, it runs well above four teraflops.

In collaboration with Widom and Nicholson, Wang uses LSMS to simulate various amorphous metal "recipes" and to compare the results from simulation with experiments on the same materials. Results to date show good agreement, indicating that the simulations accurately reflect reality. With further work, Wang and Widom expect to make progress toward answering deeper questions that experiments can't resolve, such as why do amorphous metals form and why do they have such interesting properties?



# USING LEMIEUX LIKE A COOKING POT, RESEARCHERS SIMULATE UNIQUE METALS AND INVESTIGATE THEIR EXOTIC PROPERTIES.



This representation of a metallic glass of iron (orange), zirconium (blue) and boron (silver) was rendered by PSC visualization specialist Greg Foss using data from LSMS simulations by Yang Wang.

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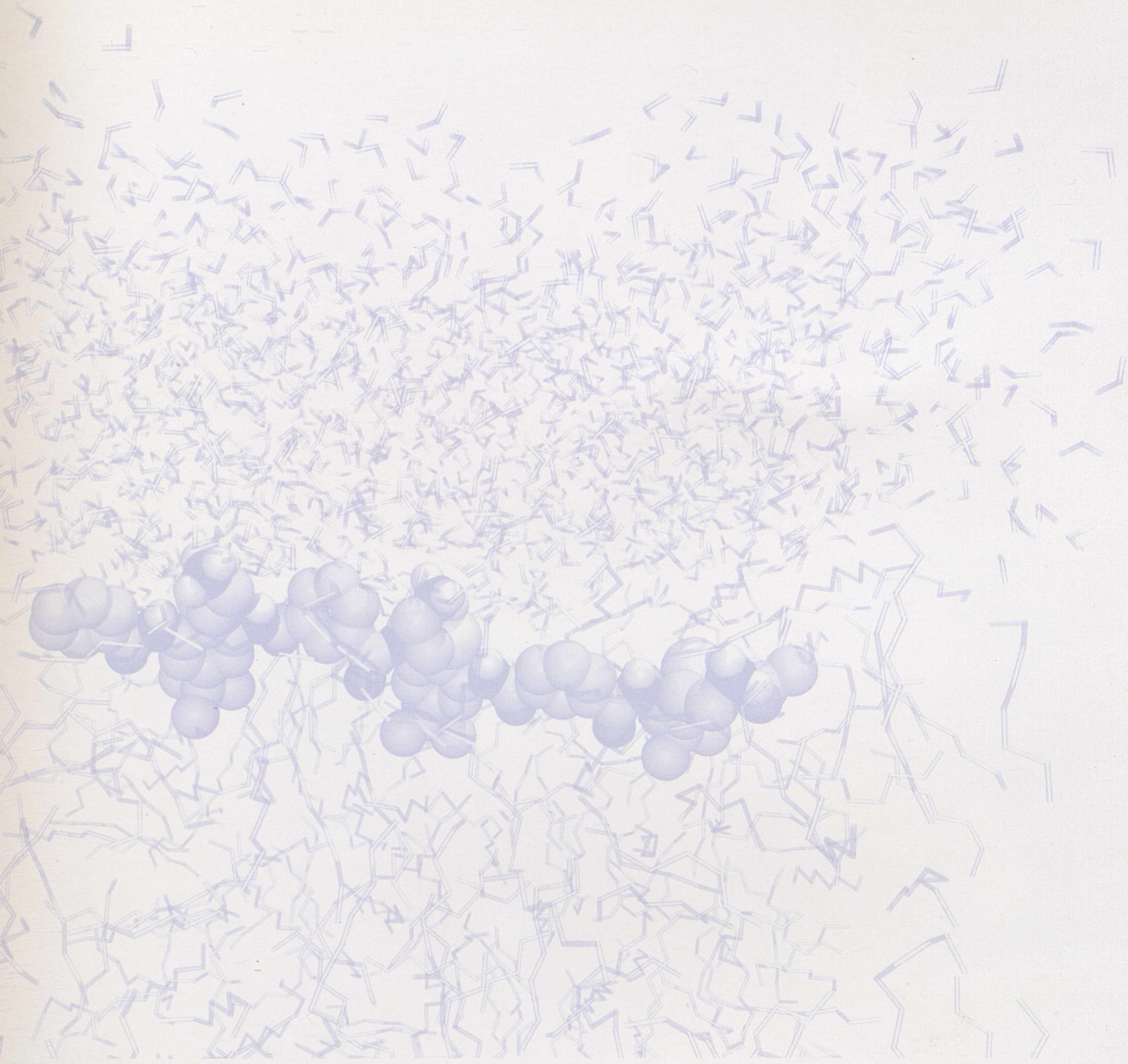

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**PITTSBURGH SUPERCOMPUTING CENTER**
MELLON INSTITUTE BUILDING
4400 FIFTH AVENUE
PITTSBURGH, PENNSYLVANIA 15213