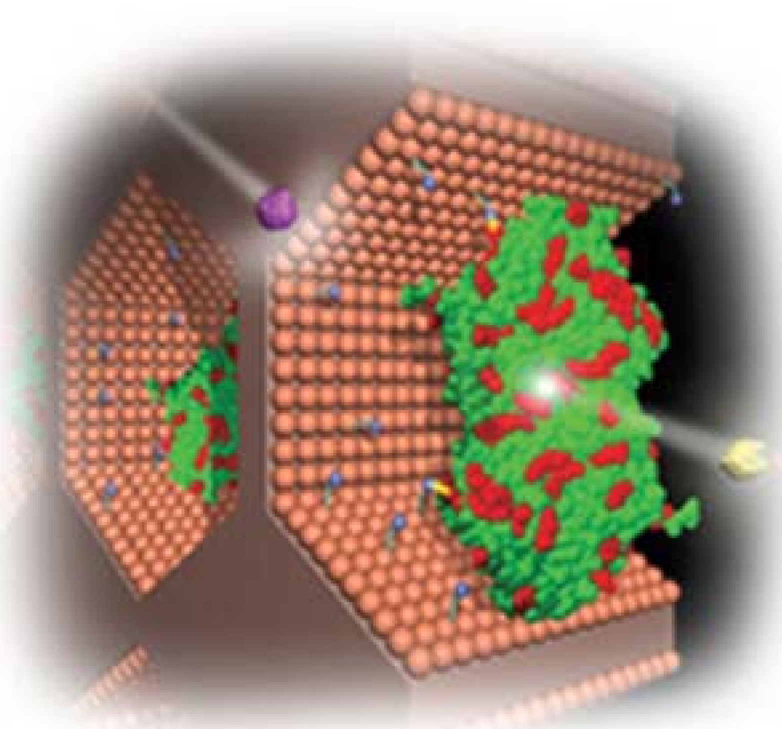
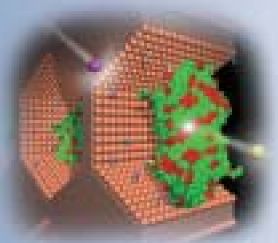
2—Science



2.0 Fundamental Science Research

PNNL's fundamental science research is making significant contributions to some of the most difficult and important science issues of our time by integrating our science disciplines, expanding our signature capabilities, and collaborating with the best scientists in the world.



Science

Our intent is to create new science, new understanding, and enduring national assets around our facilities and scientific staff. The William R. Wiley Environmental Molecular Sciences Laboratory (EMSL) is one such asset; we will strengthen EMSL by focusing its user program on the scientific Grand Challenges of biogeochemistry and biology with broad extramural collaboration. In the future, we plan to develop Grand Challenges in other areas, including complex interfacial catalysis. The outcomes of this research will advance fundamental understanding in each of these fields and speed application into the programs supporting the applied missions of DOE.

Our science strategy requires an approach dependent on integration across classic disciplinary boundaries. The technical goals associated with our vision are ambitious and aligned with the principal initiatives and programs of the DOE's Office of Science (SC). As described below, they are also aligned with our strengths.

Systems Biology

The DOE Genomics:GTL Program is the top priority in life sciences of the DOE Office of Biological and Environmental Research (BER). Our science focus in systems biology will enable the Laboratory to make important contributions in this area.

As the most conspicuous element of our science strategy, we are developing a rapidly growing signature at the intersection of biology, physics, chemistry, and computing. We will place particular emphasis on environmental microbiology and the application and integration of high-throughput analytical and computational technologies at a large scale. This is the key to advancing the understanding of biology at the systems level.

In developing our leadership position for systems biology, we will focus on developing high-resolution, high-throughput technologies for whole proteome and metabolome analysis, and enhancing strengths in microbiology, molecular biology, cell biology, and biochemistry. We will develop capabilities within EMSL around international user collaborations focused on scientific challenges in biology, physical chemistry, and biogeochemistry. Our objective is to play a key role in developing a comprehensive, quantitative, and predictive understanding of cellular and organismal functions. Under the DOE Genomics:GTL Program, we will scale our proteome and protein characterization capabilities into a new high-throughput user facility. We will manage this facility with our partner laboratories and universities as part of the set of four facilities planned for the DOE Genomics:GTL Program. To the scientific community, these newly available capabilities will enable studies of a wide variety of system-level biological problems that previously were impossible to solve.

Chemical Transformation at Complex Interfaces

Building on exceptional facilities and signatures in physical and theoretical chemistry and the geosciences, we will be recognized for our world-class research in the chemical sciences. We will emphasize research on molecular-scale behavior—the key to controlling chemistry, chemical transport, and materials properties in the condensed phase, leading to more effective separations methods for chemical analysis; more specific, efficient, and environmentally friendly catalysts; enhanced capabilities for detecting chemical species in complex environments; and improved understanding of the migration of chemicals in natural environments.

Tools and techniques in nanoscience, chemical physics, and high-performance computing will be developed and used to understand chemical processes important to the energy and environmental sciences and the applied missions of DOE. Our investments will establish new state-of-the-art facilities in critical areas such as catalysis science and attract scientific leaders to the Laboratory. In partnership with other national laboratories and universities, we will increase our focus on fundamental research in catalysis to understand the physiochemical nature in control of catalytic activity and selectivity, and also will establish a collaborative research facility for catalysis science at PNNL.

PNNL has widely recognized capabilities in computational chemistry, climate modeling, and subsurface reactive transport, each with a long history of close collaboration with experimentalists. We will strengthen our capabilities and programs in each of these areas by building staff expertise and program depth in computer science and mathematics with the Office of Advanced Scientific and Computational Research.

Atmospheric Science and Global Change Research

We intend to expand our national and international leadership in atmospheric science and global change research. Our research will focus on atmospheric chemistry, continued development of the ARM Program and facilities, and on next-generation, physics-based climate models.

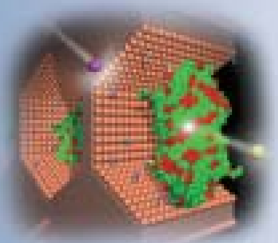
With our partners we will develop and implement a new program in climate physics simulation for development and testing of next-generation climate physics packages for high-resolution climate models. These new parameterizations will improve the performance of climate models and enable more accurate projections of the effects of climate change on the regional scale by explicitly describing cloud formation, precipitation, and energetics associated with cloud dynamics. We will also build upon our established expertise in integrated assessment modeling, and will develop the next generation of models for informing effective climate policy decisions.

Computational Science, Modeling, and Simulation

Critical to our success will be the development of highly impactful computational science research. We will place particular emphasis on providing a stable ultrascale computing environment as an integral component of the EMSL; advancing computer science research to ensure efficient use of ultrascale systems; and developing new methods in computational molecular science, biology, subsurface science, and climate simulation. Our long-term goals focus on developing computational methods for specific science and engineering domains or applications, along with the high-performance computing systems and infrastructure tuned for optimum performance for specific classes of computational problems.

The following modules detail specific programmatic activities and strategies we will pursue to implement our fundamental science research agenda.

PNNL has developed a pilot production facility for high-throughput proteomic analysis in its Life Sciences Laboratory-2 as a model environment to the planned Whole Proteome Analysis Facility.


Science

2.0.1 Science Mission Funding and Staff

PNNL estimates growth of up to 50 percent in its fundamental sciences research activities between FY 2004 and FY 2008, as well as the addition of a new user facility for Whole Proteome Analysis.

Key Growth Areas

The Laboratory has a high potential for growth in SC research programs for the next five years. The most important opportunity is for growth in the DOE Genomics:GTL Program and facilities construction. We will compete for a new user facility for whole proteome analysis. Construction of this new user facility could begin in FY 2006, and it could begin operations in late FY 2008. Research within the DOE Genomics:GTL Program is also on a steep increase, and we will compete well for new multi-investigator projects within this program. Other areas of growth during this period will include opportunities in catalysis science funded by the Office of Basic Energy Sciences (BES), which could include the establishment of a facility or center of excellence, and opportunities in ultrascale computation funded by the Office of Advanced Scientific Computing Research (ASCR).

Office of Biological and Environmental Research

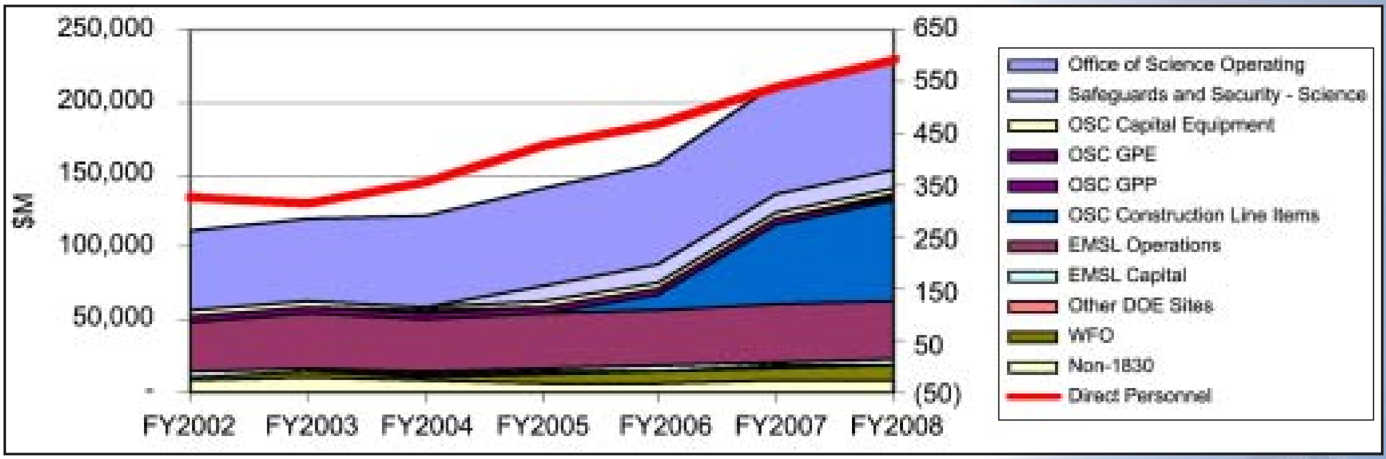
Our increasing program presence in the biosciences is a reflection of the investments in staff, facilities, and customer relationships made over the last decade. With the completion of the Human Genome Project, biology has been expanding and the research horizons moving toward gene function, proteomics, and systems biology. We are well positioned to be a significant participant in the DOE Genomics:GTL Program. Our particular strengths are in biology of prokaryotic and microbial communities and proteomics, areas that are critical to the success of the DOE Genomics:GTL Program.

Basic Energy Sciences, Chemical Sciences Division

Growth potential for the Chemical Sciences programs (including Geoscience and Energy Biosciences) can be significant. The largest opportunities depend on whether or not PNNL is chosen as the site for a Catalysis Sciences User Facility/Center. In 2003, PNNL presented a proposal to the Facilities Subcommittee of the Basic Energy Sciences Advisory Committee (BESAC) outlining the research capabilities need for a user facility to enable advanced research in complex interfacial chemistry. The concepts presented have broad support among the national laboratories and universities and are focused principally on fundamental issues in catalysis. The proposal was well received by the committee with a recommendation that if such an investment were made, such a facility be competed openly among the national laboratories.

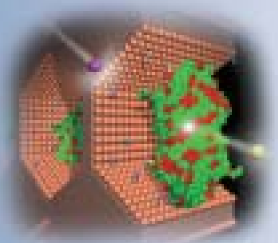
Advanced Scientific Computing Research

Significant changes in priority have occurred in ASCR with an increased emphasis in ultrascale computing, new computer architectures, and Grand Challenge research. Grand Challenge research focuses on multiple topics and, most recently, an emphasis in computational nanoscience and computational biology. While DOE has committed great effort to the development of an ultrascale program, the timing and calls for proposals and awards remain uncertain at the time of this report. We expect that this initiative will continue to focus on the high-performance computing in specific science domains; in particular, the highest priorities will be in the development of algorithms, methods, and tools that enable optimum computational performance within domain applications.



PNNL is estimating growth of approximately 50 percent in fundamental sciences research activities through FY 2008. Staff growth is projected to increase most strongly in biology, computational science, and more modestly in the physical sciences.

2.1 William R. Wiley Environmental Molecular Sciences Laboratory: Maximizing the Scientific Impact of the User Program



Science

The EMSL, a major national user facility stewarded by the Office of Biological and Environmental Research, provides advanced and one-of-a-kind experimental and computational resources to scientists engaged in fundamental research at the interface of the physical, chemical, and biological processes that underpin environmental and other critical scientific issues facing DOE and our nation. It represents one of the most impactful research assets at PNNL.

Within the Office of Science (SC) user facilities, EMSL has set the standard for organizing and executing collaborative research in chemistry, biochemistry, and computation. Enhancements to the EMSL user program will increase the pace and impact of scientific discovery in areas critical to DOE missions.

The science performed using EMSL facilities has helped to establish PNNL as a DOE asset for excellence in chemical, biological, and environmental sciences research. EMSL now is a very important element of our S&T agenda. To maximize the scientific productivity of the EMSL user program, we have developed three signature characteristics:

1. The integration of theory, modeling, and simulation with experiments in each of the fields where research is performed.
2. The use of multidisciplinary teams and collaborative modes of operation to solve major scientific challenges.
3. Deployment of teams of scientists/engineers to develop extraordinary tools and methodologies.

These characteristics distinguish EMSL from academic research centers and other DOE user facilities. Research using EMSL is internationally recognized for excellence in the areas of advanced computational methods, chemical physics, nanoscience and technology, oxide chemistry, high-throughput proteome analysis, structural biology, and biogeochemistry.

The long-term objectives of the EMSL user program are to:

- Operate the user facility with distinction as a best-in-class facility for fundamental research in chemistry, materials science, biology, and computation.
- Increase the impact of the user program by organizing the study of some of the most difficult and important scientific questions facing the broad research community in biology and biogeochemistry.
- Continually upgrade the capabilities/facilities to maintain a state-of-the-art research environment for the scientific community.
- Develop EMSL as the standard for collaborative research environments.

Increasing Scientific Impact Through Grand Challenges in Biogeochemistry and Biology

With program leaders at BER, we have conceived of several mechanisms to increase the impact of EMSL's resources on the broader research community, the highest priority of which is the establishment of scientific Grand Challenge research within the EMSL user program. Beginning in 2003, we will implement scientific Grand Challenges in biogeochemistry and biology in the EMSL user program.

These Grand Challenges are consistent with DOE missions, focused on critical milestones in the advancement or utilization of science. They are user-driven and take full advantage of the set of unique capabilities, resources, and technical expertise available in EMSL. The scopes of these scientific problems require multidisciplinary teaming, and are so broad that they cannot be addressed at any other existing single facility. This approach will increase the scientific impact of the EMSL as a user facility.

The 11.8-teraflop supercomputer housed in the EMSL Molecular Science Computing Facility is one of the fastest operational open systems in the United States.

Biogeochemistry Grand Challenge

Biogeochemistry processes are fundamental to DOE mission areas of clean energy, carbon management, and waste remediation. The theme for this biogeochemistry Grand Challenge is microbe-mineral electron transfer mechanisms. The microbe-mineral interface is a complex and relatively unexplored subject. The molecular-scale mechanistics and linkages across this complex region are poorly characterized and the science involved spans broad fields in biology and the physical sciences.

Important scientific questions include:

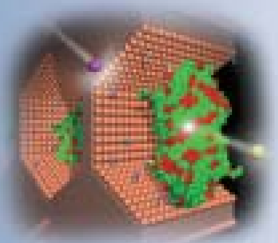
- What is the structure and molecular architecture of the bacterial cell envelope-mineral surface region?
- What molecular interactions/reactions occur within this region to regulate electron flux to and from microorganisms?
- How do microorganisms sense and respond to physical and chemical shifts that occur at mineral surfaces?

During its first five years of operation as a national user facility, EMSL has made a lasting scientific impact. EMSL has hosted over 2000 user projects with more than 5500 users from all continents and each of the 50 states. This use has resulted in approximately 1300 publications in archival journals.

The significance of this Grand Challenge topic is great and the potential impacts far-reaching. For example, it will provide BER's Natural and Accelerated Bioremediation Research (NABIR) program the basic knowledge and concepts necessary to harness microbiological electron transfer reactions to reduce and immobilize migrating radionuclides and metals at DOE weapons sites for remedial purposes.

Maintaining EMSL's capabilities at a world-class level and increasing the impact of its research on Grand Challenges of biogeochemistry and biology will lead to major breakthroughs in areas of S&T critical to DOE missions. Further, it will ensure that EMSL continues as the cornerstone of our S&T agenda and will help ensure that we continue building new programs and impacting new scientific areas such as systems biology.

This superconducting magnet is a part of the 900-MHz wide-bore nuclear magnetic resonance (NMR) spectrometer at EMSL. This spectrometer is now operational and is one of the world's most powerful and sensitive instruments for chemical, biological, and materials research.



Science

2.2 The BER

BER is one of PNNL's most important strategic partners in defining our science future.

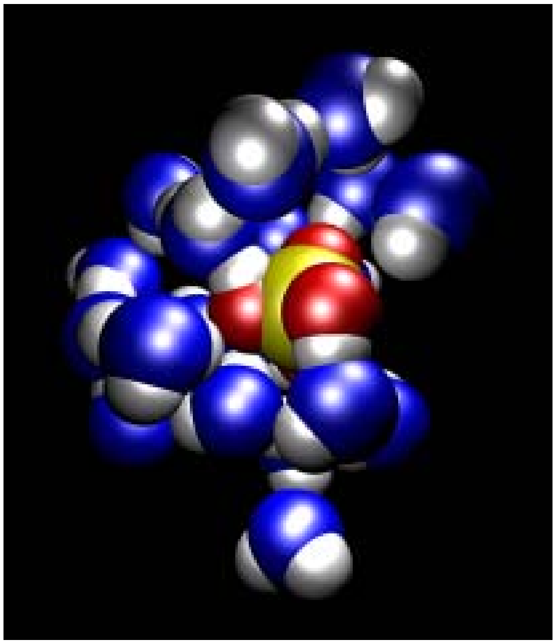
Our research for BER in biology, subsurface science, and atmospheric science and global change addresses the following scientific issues:

- biotechnology solutions for clean energy, carbon sequestration, and environmental cleanup.
- low-dose radiation effects as biological systems at the molecular level
- high-throughput proteomics and analysis to enable systems biology
- response of the earth system to different levels of greenhouse gases in the atmosphere
- novel solutions to DOE's most challenging environmental problems.

Our research contributes to each of the four divisions of BER: Life Science Research, Environmental Remediation Sciences, Climate Change Research, and Medical Sciences. Our contribution over the next five years will be focused to achieve major successes in:

- Environmental microbiology, biogeochemistry, and the development of world-class capabilities in proteomics, mass spectrometry, computation, and NMR spectroscopy and imaging. Advances in these areas will provide the foundation for new systems-level understanding of biological processes relevant to DOE missions.
- Greater accuracy in climate modeling by developing the next generation of simulation codes that explicitly describe cloud physics, and the implementation of these codes for high-performance computer systems.
- Development of the intellectual basis and technical foundations to solve currently intractable problems of contaminant fate and transport. This critical knowledge will lead to development of improved remediation strategies, and allow federal leaders to make scientifically credible risk-based decisions for environment stewardship.

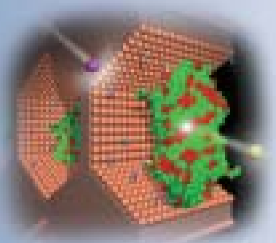
The following modules detail our plans for accomplishing research for BER programs and using EMSL during the next five years. We believe that this research will contribute directly to applied programs from other offices of DOE, and for the DHS.



With support from BER, PNNLis focusing research to achieve more accurate, high-resolution climate models. By understanding the fundamental processes involved in aerosol nucleation, our researchers are fine-tuning the microphysics used in climate models, enabling more accurate predictions of not only global warming, but also climate changes and the weather.

2.2.1 Systems Biology Research in Progress

PNNL will become an international leader in systems biology.



Science

Our systems biology research focuses on the DOE Genomics:GTL Program, low-dose radiation, structural biology of bioremediation and DNA repair proteins, and innovative diagnostic and treatment technologies for biological and biomedical research. This research will increase understanding of the incredibly complex functions of whole cells and cell assemblies (e.g., microbial communities, tissues), their structures, and the networks that regulate gene expression and biological function. Our current research is focused on applying high-throughput technologies, such as proteomics and microarrays, to determine how cells and collections of cells sense and respond to their environment.

Our goal is to develop and apply advances in chemistry, physics, and computing to provide a seamless integration of experimentation, analysis, and modeling. This research will provide fundamental new molecular-level information on biological systems and provide the foundation for developing new biological technologies and processes to expedite environmental cleanup, create energy for feedstock products, and enhance human health.

Microbial Systems

Our researchers are key participants in the "Shewanella Federation," a consortium of the DOE Genomics:GTL projects focused on a systems biology approach to the study of the biology of versatile dissimilatory metal-reducing bacterium *Shewanella oneidensis*. Metal reduction by microorganisms is a viable bioremediation strategy for immobilizing mobile uranium, technetium, and chromate in groundwater at DOE sites. Using a combination of 1) mutagenesis to delete key regulatory and functional genes, 2) controlled continuous culture (chemostats) methods, and 3) high-throughput array and proteome approaches, our biologists are defining the pathways and regulatory mechanisms by which *S. oneidensis* senses and responds to changes in electron acceptor.

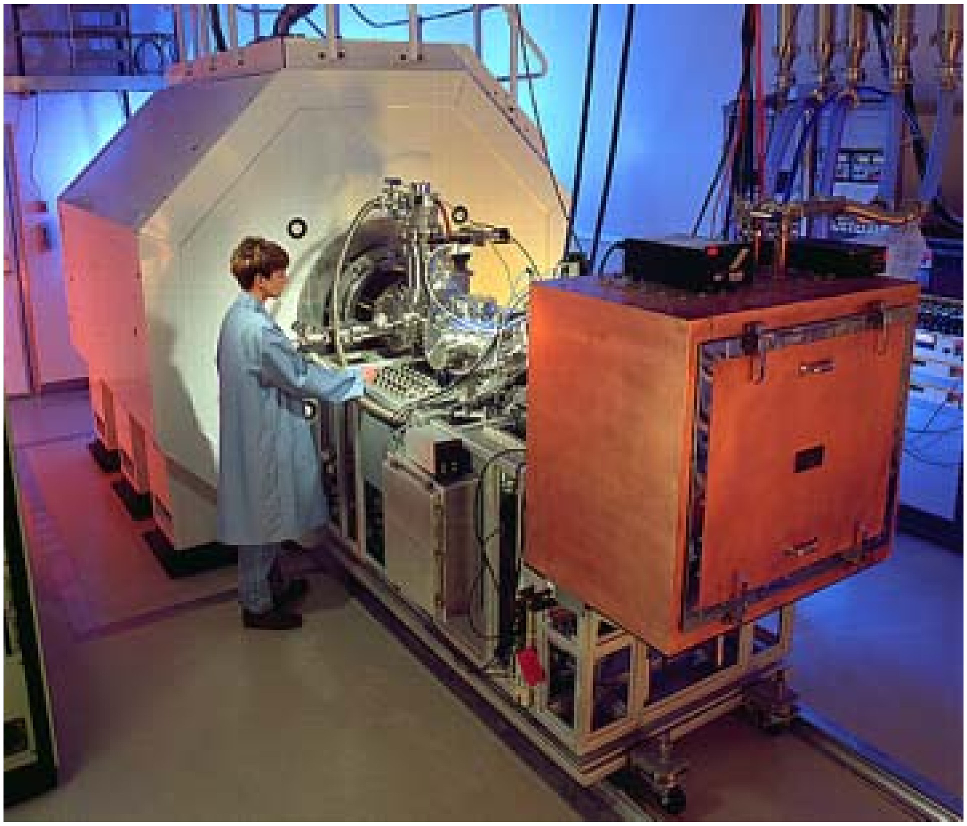
Under fully aerobic conditions, transcriptional and proteome profiling revealed that *Shewanella* exhibits an oxidative stress-like response and initiates biofilm development. As oxygen concentration decreases, cells rapidly induce anaerobic respiratory genes and become motile.

With researchers from Oak Ridge National Laboratory (ORNL), we are also co-leading the DOE Genomics:GTL project focused on protein complex production and identification. We are focusing on the protein complexes from *S. oneidensis*.

We are also leaders in high-throughput whole proteome analysis using Fourier transform ion cyclotron resonance mass spectrometry to identify and quantify the levels of all proteins present in a cell. The technology uses "accurate mass and time" tags to identify peptides or parts of the protein as a signature of the protein's presence and provides a level of throughput that greatly exceeds that previously possible. We can identify thousands of proteins in a single analysis, resulting in an extent of proteome coverage that is much more comprehensive than previously possible. Future advances in this technology will revolutionize biological research by enabling researchers to inventory nearly all of the proteins present in a cell at a given time and under a set of physiological conditions, and to use this information to map regulatory pathways responsible for the fundamental function of the cell.

We are also applying this technology to determine the whole proteome of various microbes including *Deinococcus radiodurans* and *S. oneidensis*. Such whole proteome analysis is critical to understanding biological systems and to revolutionizing large-scale systems biology in the 21st century. Identified by DOE as one of it's four Genomics:GTL planned facilities, capabilities in Facility II (WholeProteome Analysis Facility) will focus on the high-throughput analysis of all the proteins and metabolites present in a cell under a variety of environmental conditions. Insights gained from this research are critical to developing a better understanding of biochemical networks, cell function, and gene expression for a wide variety of biological systems.

Our whole proteome analysis of *D. radiodurans* identified 83 percent of the predicted proteome, the most complete proteome coverage of any organism to date.



PNNL is the leader in high-throughput whole proteome analysis using Fourier transform ion cyclotron resonance mass spectrometry for identifying and quantifying the levels of all proteins present in biological systems.

2.2.1.1 Biomolecular Systems Initiative

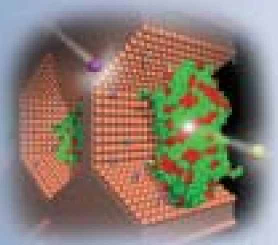
PNNL is building expertise and infrastructure in systems biology; our research will have a profound impact on how biologists perform experiments on cellular systems, how they analyze and interpret their data, and how biological systems are described and understood.

The Biomolecular Systems Initiative (BSI) is positioning PNNL to become a leader in systems biology. While BSI is aligned with the DOE Genomics:GTL Program, the scientific capabilities under development support research projects in a variety of important areas that are beyond the scope of the program.

The four scientific thrust areas of the BSI are 1) mechanisms of microbial sensing, 2) regulation of microbial communities, 3) cellular response to oxidative stress, and 4) active cell signaling. Teams of biologists are assembled to create nationally renowned efforts in these research areas. A computational infrastructure is being built to support the research teams, including software for bioinformatics, modeling, and information management. We are also investing in new technologies for cell imaging, proteomics, and metabolite analysis. Most importantly, we are creating a cadre of interdisciplinary scientists that can productively work across scientific disciplines. These efforts, in conjunction with an aggressive collaborative outreach program, will provide outstanding new opportunities for scientific growth at PNNL.

The BSI is designed to achieve the following goals:

- Align PNNL with major new growth areas in interdisciplinary biological research and to help build strong national constituency in this area. On a national level, we will be one of the leaders in the design and creation of both an intellectual and resource infrastructure for the new field of systems biology.
- Ensure that our researchers help define the science to drive the DOE Genomis: GTL Program.
- Build the scientific expertise necessary for a strong biological sciences program in areas including molecular biology, cell biology, biochemistry, microbiology, and bioinformatics. The BSI is building specific capabilities in gene expression, gene knockout, protein expression, antibody generation, protein interactions, visualization of cell signaling, protein quantification, cell modeling, and data integration. The development of these capabilities is coordinated with the BSI's scientific research areas to create capability "modules" that can be combined in different ways to solve a variety of problems.
- Create sophisticated, high-resolution, high-throughput technologies to help drive the development of systems biology and to exploit our strength in instrument development and automation. Pilot facilities are being constructed for high-throughput sample preparation and global proteome analyses. We are also developing the bioinformatics infrastructure to capture the enormous amount of generated data and the visualization tools to interpret it.



Science

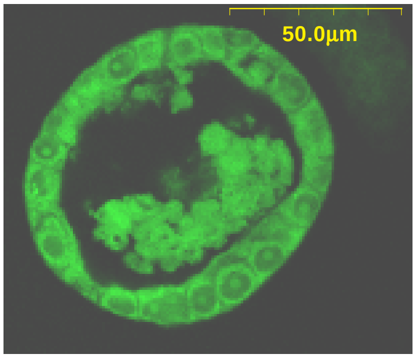
Examples of recent BSI accomplishments:

- A breakthrough in single-chain anitibody generation, creating a "library" with more than 109 distinct types of antibodies and demonstrating a high-throughput capability to select antibodies. Now, affinity-probes may be created that are suitable for more rapidly detecting pathogens and cancer-associated pathogens.
- Successfully performing the most complete analysis of human plasma proteome, almost doubling the amount of biomarkers available for drug testing and studying health effects.

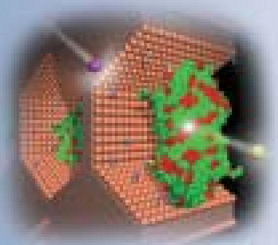
- Lead the effort to design and acquire a new facility at PNNL for global proteome and metabolite analysis of cells. This user facility is one of four proposed by DOE to support its Genomics:GTL Program and will vastly increase the current national capacity for proteomics studies in microbes. It will incorporate large-scale deployment of highly automated new technologies for whole-proteome and metabolome measurement and for imaging the distribution of proteins within living cells, and the computational tools needed to manage, analyze, and archive information on microbial proteomes under varying environmental conditions.
- Transform how scientists are able to study cells as complete biological systems, and fundamentally change the level at which biological systems can be used and manipulated for practical applications to address DOE mission needs. DHS interests include sensor applications in microfluidics and rapid detection systems of multiple pathogens. Department of Health and Human Services (DHHS) interests include improved understanding of human diseases and novel approaches to their diagnosis and treatment.

Progress

The BSI enhances S&T across the Laboratory in key areas of information technology, microscopy, and sensor development for national security, human health, and other areas. Its series of web-based resources is already improving the dissemination of information on system biology and providing access to the tools being developed at PNNL, such as antibody libraries and software (www.sysbio.org). The BSI also holds the annual Northwest Symposium on Systems Biology, and supports other workshops on systems biology and topics related to our facility efforts.



PNNL's transgenic cells and fluorescent proteins can quantify gene expression in living cells. The ability to rapidly insert genes into normal cells and simultaneously track their distribution and activities presents many opportunities to understand the molecular basis of complex cellular networks.



Science

We participate in the ARM Program by conducting basic research as members of the ARM Science Team and by providing leadership in both the scientific and operational components of the program.

2.2.2 Understanding the Effects of Energy-Related Emissions on the Atmosphere

In support of the U.S. Climate Change Program Strategic Plan and DOE's energy and environmental missions, we conduct research to identify, understand, and anticipate the long-term health and environmental consequences of energy use and development.

Our recent climate research has led to physics-based models. This research is currently focused on the problem of climate change, and in conducting it we have made significant contributions to scientific understanding of as well as the ability to model:

- The effects of clouds on the radiative energy balance of the atmosphere.
- The effects of regional climate change on climate-sensitve natural resources and human activities. PNNL will continue this work under the climate change prediction plan and SciDAC, and may expand it into effects of aerosols or described in the next item.
- The effects of energy-related emissions on tropospheric aerosols and gas-phase chemistry on local to global scales.
- The turbulent transport of energy and mass in the atmosphere and how this transport affects atmospheric chemistry and climate.
- The roles of energy technology and energy policy in reducing carbon emissions to the atmosphere.

The ARM Program

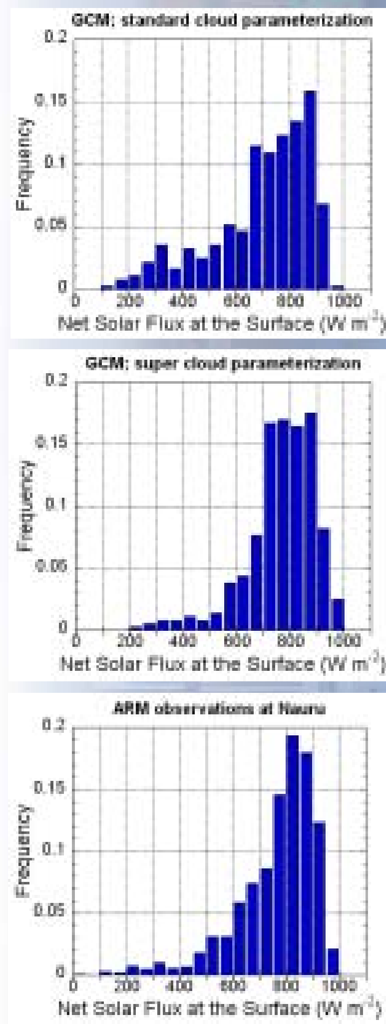
We are a major participant in the ARM Program. The ARM Program is a DOE multilaboratory, multi-institutional effort with involvement of universities and other federal agencies. The principal goal of the program is to improve understanding of the effect of clouds on the radiative energy budget of the earth and to improve the representation of cloud processes in climate models.

The ARM Program is at a critical juncture. Through the accumulation of insights from past ARM research and through recent improvements in computational capacity, we now have the ability to implement and test new mechanisms for representing cloud processes, and their effects, in climate models. These new mechanisms enable more realistic representations of cloud processes. We intend to collaborate with university and other federal laboratory scientists who are developing new mechanisms for simulating cloud processes in climate models. We will work with these scientists in using ARM data and other climate observations to evaluate the performance of these new parameterizations in simulating observed cloud properties and effects and in improving the ability of climate models to simulate the climate system, and we will continue to do the kinds of basic research on cloud processes and aerosols that will lead to even better process parameterizations in the future. We also believe that cloud and regional-scale models can be effective tools for testing parameterization schemes and for diagnosing scale-dependent performance problems in global models. Thus, we will be working with scientists at the National Center for Atmospheric Research to use coupled regional-scale ocean/atmosphere models to examine how the simulation of deep tropical convection and topography can affect the behavior of climate models in various difficult-to-simulate regions of the planet.

An Emphasis on Aerosols

In FY 2005, DOE will redirect its Atmospheric Science Program to an exclusive focus on the effects of atmospheric aerosols on the earth's radiation budget. A new science plan will be developed in FY 2004; however, we expect the focus of the program will be on the microphysical, meteorological, and chemical processes that govern the optical properties of atmospheric aerosols and their effects on the optical properties of clouds. We will be directing a substantial fraction of our atmospheric science capabilities toward the support of this new program.

Through a new EMSL Collaborative Access Team (CAT), we will be partnering with leading atmospheric chemists and other atmospheric scientists in academia and industry to apply the capabilities of EMSL to the study of the complex processes of atmospheric chemistry. A major emphasis will be on processes that govern the formation and transformation of atmospheric aerosols. However, the CAT will also make these resources available to the study of other atmospheric chemistry problems of interest to DOE and other federal agencies. Detailed plans for the CAT will be developed in FY 2004, and these plans will incorporate input from non-DOE members of the research community. We expect there will be an emphasis on the development of new instruments for characterizing the chemical composition of aerosols, on improving the understanding of heterogeneous chemical reactions in the atmosphere, and on exploring the application of computational chemistry to atmospheric chemistry problems.



ARM observations were used to evaluate new methods for simulating cloud radiative feedback in climate models. Net solar radiative flux at the earth's surface, as simulated by a standard cloud parameterization scheme (top figure) and by a new technique (superparameterization) that models cloud formation and dissipation explicitly (middle), is compared to actual observations (bottom). The new method does a better job of representing the observed radiative flux.

Measurement Tools, Techniques, and Teaming

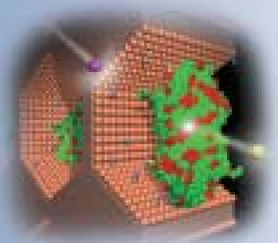
In addition to the CAT, we will operate our Gulfstream 159 research aircraft in support of DOE research missions, and we will continue to develop state-of-the-art measurement systems, such as our Atmospheric Remote Sensing Laboratory, to support DOE's atmospheric and climate research agenda.

We will continue to operate the Joint Global Change Research Institute in cooperation with the University of Maryland. Scientists at the institute have been leaders in the development and application of integrated assessment models for understanding the relationships among global environmental change, human welfare, and economic development. In particular, the institute will continue its research into the role of technology in reducing carbon emissions to the atmosphere. Through the institute's Global Technology Strategy Project, we will partner with industry to identify the technologies that have the greatest promise for reducing these emissions and the strategies that can most effectively bring these technologies into widespread use.

BER has been funding PNNL since 1999 through a research consortium to conduct fundamental research on methods to enhance carbon sequestration in terrestrial ecosystems (CSiTE). These methods will be key components of a carbon management strategy to mitigate climate change. Three national laboratories (PNNL, ORNL, and Argonne National Laboratory [ANL]) and several universities participate in CSiTE. The goal of CSiTE is to discover efficient and environmentally acceptable ways to create large, long-lived carbon pools in terrestrial ecosystems.

2.2.3 The Science of Environmental Remediation

PNNL is providing the technical foundations to solve currently intractable problems of contaminant fate and transport at DOE sites, to develop improved remediation strategies, and to make scientifically credible, risk-based decisions for environmental stewardship.



Science

Multidisciplinary, multiorganizational teams couple expertise in biology, chemistry, physics, geohydrology, applied mathematics, and computational science to address critical problems involving the molecular mechanisms of key processes, reaction and transport at the microscopic and macroscopic scales, and field-scale behavior. DOE user facilities, including EMSL and various synchrotron light sources, are used to interrogate the chemistry and structure of geologic waste materials and engineered materials, minerals, microbes, and their associations as a basis for understanding the chemical and biological processes involved.

Metal Reduction Through Microbial Processes

PNNL's bioremediation research couples microbial processes with geochemistry and modeling to understand how the behavior of metal and radionuclide contaminants is controlled by coupled microbial and biogeochemical processes in subsurface soils and sediments.

The principal goal of the NABIR program is to provide the scientific basis for the development of cost-effective bioremediation of radionuclides and metals in the subsurface at DOE sites. The focus of the program is on strategies leading to long-term immobilization of contaminants in place to reduce the risk to humans and the environment.

Our scientists are currently conducting research to identify the microbial and geochemical factors controlling the microbial reduction of iron and manganese, the natural substrates of dissimilatory metal-reducing bacteria, and the long-lived radionuclide contaminants technetium and uranium. Results from this research will provide important insights needed to make critical decisions regarding the cleanup of DOE sites.

For example, our researchers are examining how metal-reducing species of *Shewanella* can indirectly reduce soluble technetium through the enzymatic reduction of Fe(III) in mineral phases to Fe(II). Surface-associated Fe(II) in turn is able to reduce soluble technetium to an insoluble form. The role of potential competing reactions with manganese oxides and nitrate as well as the specific forms and concentrations of biogenic Fe(II) necessary to facilitate Tc(VII) reduction is being investigated in detail.

The stability of reduced technetium and uranium phases in the subsurface, specifically in regards to their susceptibility to oxidation by dissolved oxygen and subsequent remobilization, is under preliminary investigation. Issues related to re-oxidation and remobilization of metal and radionuclide contaminants is anticipated to be a major focus area in the future.

Science for Site Cleanup

DOE's Environmental Management Science Program (EMSP) fosters the development of fundamental science and technologies for DOE site cleanup and closure. Our EMSP research portfolio is the largest of all the national laboratories, and our management approach of linking science solutions to cleanup problems has proven highly effective in our application of fundamental research for solving the complex legacy waste problems at DOE sites. Our research portfolio in support of the EMSP focuses on:

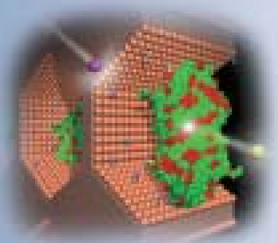
- Subsurface contaminant fate and transport.
- Remediation science.
- Nuclear waste chemistry, separations, and waste forms.
- Actinide chemistry.
- Development of novel characterization and sensor tools.

EMSP research is highly valued at the Hanford Site through our proactive efforts to engage scientific researchers directly with problems. Results from EMSP-funded efforts have provided the primary scientific bases for major corrective action decisions in Hanford's tank farms, and will soon be used for similar purposes with river corridor plumes of uranium and ^{90}Sr. EMSP research has also resolved high-visibility Hanford problems of gas generation in tank wastes and spent fuel, expedited ^{137}Cs migration in the tank farms, the subsurface mineral residence and speciation of U(VI), and chemical sensors for accurate and rapid detection of technetium.

The EMSP transitioned this past year from DOE's Office of Environmental Management (EM) to SC. A strong contingent of nationally recognized scientists in the Biological and Chemical Sciences Divisions at PNNL will provide for the continuation of its leadership role in this important program.

An EMSP workshop held at PNNL on May 6–7, 2003, brought together regulators, Hanford experts on vadose zone and groundwater contamination and tank waste, DOE Program Managers, and EMSP Principal Investigators for a scientific forum on groundwater remediation and tank waste research. The objective of this fourth-in-a-series workshop was to enhance the impact of fundamental EMSP research at Hanford by establishing strong collaborative linkages between researchers and Hanford Site problem holders.

DOE's EMSP supports development of technologies for DOE site cleanup and closure. PNNL's management approach to EMSP-funded research has been cited as "the model to emulate" for solving complex legacy waste problems at DOE sites.



Science

We will continue to be a leader in condensed phase and interfacial chemical physics, the chemistry and physics of oxides and wide band-gap materials, defects and corrosion in materials, mass spectrometry and ionic processes, catalysis, and low-temperature geochemical processes.

2.3 Basic Energy Sciences

By integrating experiment with theory, modeling, and simulation, PNNL researchers have developed an internationally recognized fundamental research program focused on developing a molecular-level understanding of complex chemical and material systems and phenomena important to the nation's energy, environmental, and security needs.

With scientific expertise in molecular and nanoscale science, engineering, and technology and high-performance computing, our scientists are enabling an atomic and molecular-level understanding of complex multiphase chemical, material, and nanoscale systems. As part of multidisciplinary, multi-institutional teams, we will provide the conceptual framework and the experimental and computational tools required to understand chemical transformation at interfaces and photonic and molecularly assembled nanostructural materials.

DOE user facilities, especially the EMSL and the various synchrotron light sources at other national laboratories, are critical to this program. We anticipate increased application of neutron scattering. Application of our unique high-throughput proteomics and metabolomics capabilities to problems in energy biosciences is also anticipated.

Chemical Sciences

The Chemical Sciences research program focuses on condensed phase and interfacial chemical physics (especially in aqueous systems), advanced methods of separations and analysis (particularly mass spectrometry, ionic processes, and the chemistry and physics of nanoparticles), and catalysis and chemical transformation (especially at nanostructured interfaces and in confined local environments).

Based on our strengths in these and other areas, we anticipate making significant contributions to DOE's Grand Challenge of developing the increased understanding required to design catalyst structures to control catalytic activity and selectivity.[a] Key to successful realization of this Grand Challenge goal will be the development and application of an integrated suite of advanced experimental and computational resources to model, design, synthesize, and characterize kinetically and dynamically in situ catalysts from the nanoscale to the macroscale. Such advanced resources are not available to the community of catalysis scientists today, nor are they part of any planned user facility (including the Nanoscale Science Research Centers currently under development). The Complex Interfacial Catalysis Facility proposed by PNNL in 2003 would fill this need.

(a) This Grand Challenge is articulated in the 2003 BESAC report entitled *Opportunities for Catalysis in the 21st Century*.

Geosciences

The Geosciences research program focuses on unraveling the fundamental bio-geochemical interactions between minerals, solutions, and microorganisms that occur in geologic environments and control the transport and fate of contaminants in the environment. The program emphasizes developing a molecular-level understanding of these interactions through the use of advanced surface spectroscopies and molecular and thermodynamic modeling simulations. Current areas of study include:

- developing molecular models for describing iron oxide surfaces and adsorption reactions
- unraveling the molecular-to-micron-scale reactions at carbonate surfaces
- developing molecular models for lipopolysacchardides present on the outer surface of environmentally important bacteria
- understanding the role of microorganisms in iron reduction and their attachment to mineral surfaces.

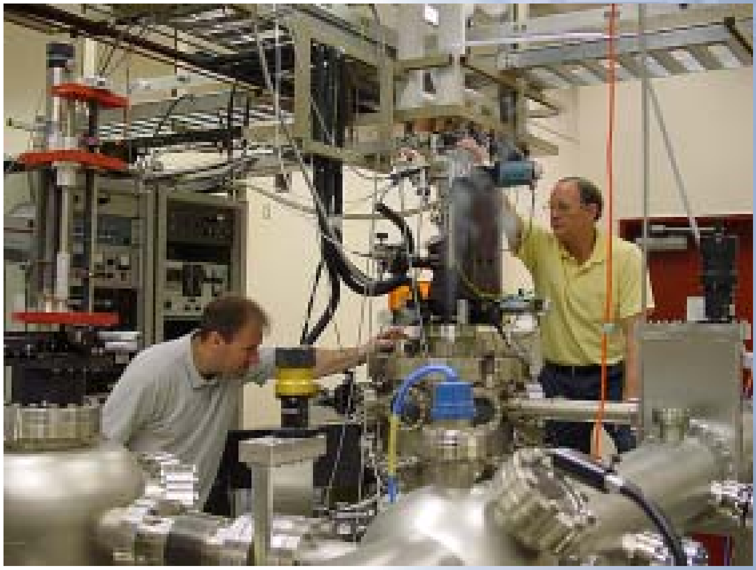
Future research plans are in the areas of nanogeoscience, neutron research, and in investigating the influence of transport on reactivity at the nano to micron scale.

In support of our material sciences work, our research staff regularly coordinate DOE workshops and lead multinational laboratory activities that promote the development of advanced industrial materials.

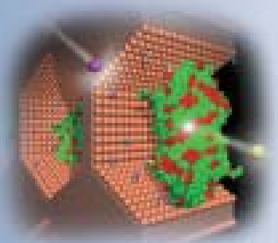
Materials Sciences

Core projects within the Materials Sciences program suite focus on developing innovative synthesis and processing methods, modeling and affirming structure property relationships particularly in materials containing intentionally introduced defects, investigating materials-environment interactions at the atomistic level, and using molecular probes such as NMR in consort with beam techniques available at the DOE user facilities to characterize structural nuances at different length scales. Building on previous program successes, PNNL's evolving materials science research activities focus on molecular assembly routes to nano-architectured materials, the design of photonic materials that exhibit a predicted and reversible response to light, and a new class of spin transport oxide films to enable next-generation computers.

PNNL's dynamic research team integrates theory with experiment, pursues leading-edge research centered on the formation of defects in materials, and the role of defects in molecular adsorption on, chemical reactivity at, and charge transport through oxide surfaces. Results of this research will influence science directions that significantly impact DOE mission areas ranging from waste sequestration; to energy storage, generation, and transformation; to infrastructure reliability.



Support from BES allows researchers at PNNL to make significant contributions to nanoscale and molecular research in the areas of chemical sciences, geosciences, and materials sciences. Here, PNNL researchers use the state-of-the-art molecular beam epitaxy system housed in the EMSL to create a continuous thin film of metal layer on metal oxide.



Science

Examples of recent Nanoscience and Technology Initiative accomplishments:

- Developed a new class of thin film epitaxial magnetic semiconductors based on doped conductive oxides which retain magnetization significantly above room temperature, enabling future spintronic devices.
- Demonstrated composite nanobiological materials with potential applications in catalysis and detection. Single enzyme nanoparticles are modified natural enzymes armored with a synthetic silicate shell that extends by orders of magnitude the lifetime of the enzyme without destroying its activity.

2.3.1 Nanoscience and Technology Initiative

The Nanoscience and Technology Initiative (NSTI) creates the capability to manipulate structures at an atomic scale, enabling fundamental changes to the properties of materials and making possible new materials, chemistry, and functions.

Nanoscience is the investigation of phenomena that occur on the nanoscale (0.1 to 100 nanometer); nanotechnology is the application of these phenomena. Our researchers seek to create functional materials, devices, and systems by controlling matter on the nanometer scale to exploit novel phenomena and properties (physical, chemical, biological) at this scale. For instance, the manipulation of electronic structure to produce chemically tailored surfaces promises substantial advances in several application areas critical to DOE missions.

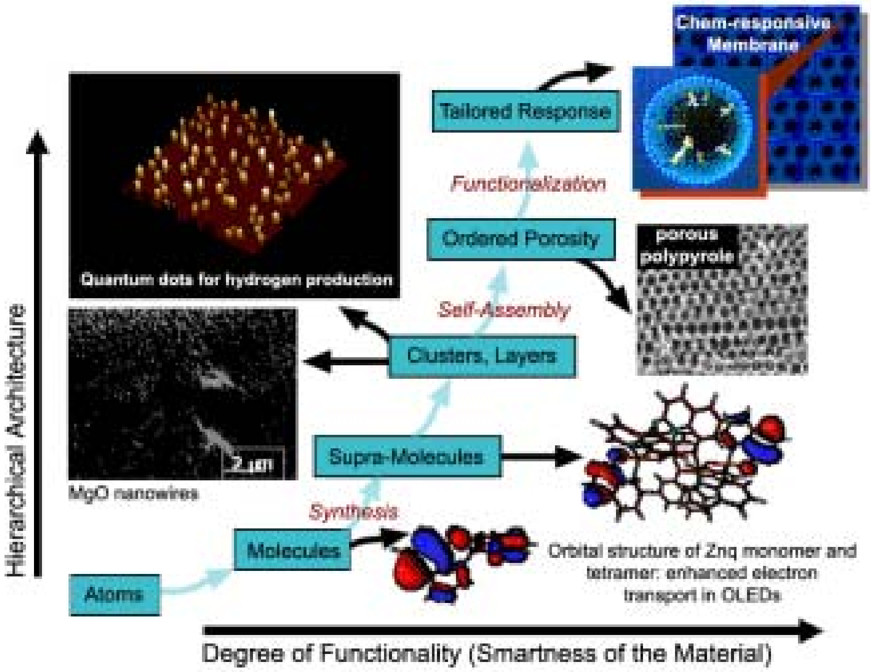
The first and broadest of these areas is catalysis, where chemically active nanostructures facilitate environmental remediation, enable the clean production of hydrogen (and may play a key role in new hydrogen storage media), and control the direct reaction of chemical feedstocks with oxygen to produce electricity in high-efficiency fuel cells. The second key area is high-specificity detection of chemical, biological, and nuclear agents. Here, the tunable chemistry of nanoparticles, particularly nanobiological structures such as enzymes, promise simultaneous high sensitivity and a high-rejection ratio of chemically similar but benign species. The high-surface-area-to-volume ratio intrinsic to nanostructures enables further development in active preconcentrators for analyte treatment prior to detection.

The NSTI is crosscutting, and interdisciplinary priorities for the initiative are as follows:

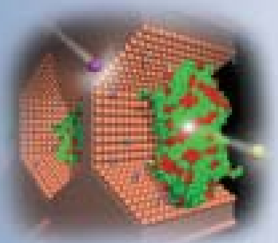
- Understand chemical interactions at the nanoscale, enabling the tailoring of chemically functional surfaces using “bottom-up” assembly techniques.
- Develop a core scientific strength in nano-catalysis including controlled synthesis, characterization, and modeling techniques to understand single-site reactivity.
- Develop the field of nanobiology, focusing on biocatalysis and the use of enzyme-based nanoparticles for detection and remediation of contaminants.
- Increase the visibility of nanoscale research at PNNL both regionally and nationally via leadership of symposia and workshops, hosting visiting scientists, and promoting the use of EMSL for collaborative research in nanoscience.
- Operate the Joint Institute for Nanoscience with the University of Washington and form a broader umbrella organization for nanoscience in the Pacific Northwest.

Nanoscience is an interdisciplinary research field at the interfaces of physics, chemistry, and biology. The NSTI is similarly interdisciplinary and crosscutting and, as such, targets growth in several PNNL programs, specifically:

- SC: Early work funded by NSTI has transitioned to programmatic support from both divisions of BES and EMSP. Current and future projects will develop capability to support a significant new catalysis facility.
- DOE Office of Energy Efficiency and Renewable Energy (EERE): Nanocatalysis projects with a particular emphasis on improved fuel cell efficiency and hydrogen production and storage are part of NSTI.
- DHS: In collaboration with the Homeland Security Initiative, NSTI is building the capability to use the tunable chemistry and high surface area of nanostructures to selectively adsorb and detect analytes at low concentration.



This figure illustrates the concept of hierarchical assembly for tailored functionality. Nanoscience revolutionizes the way we think about making materials. Until recently, we were limited to starting with naturally occurring (bulk) materials and using tools to shape them into useful products. This is called "top-down" fabrication. Using nanoscale engineering, we create molecules with desired functionality and invoke molecular-level forces to cause them to assemble themselves into clusters or layers ("bottom-up" fabrication), yielding new tailored materials that could not be produced by top-down techniques.



Science

2.4 Computational Science and Applied Mathematics: Scaling Computation to Meet Science Challenges

PNNL researchers will achieve better accuracy, resolution, and simulation fidelity in modeling physical systems by developing new mathematical and computational methods that integrate physical phenomena across wide scales of distance and time.

Computational science applications and systems must scale with problem size, accuracy requirements, computer capability, number of collaborators, data volume, and number of datasets. Efficiently and effectively employing both the current and next-generation massively parallel computers, massive databases, and high-speed communications requires advances in programming models, system software, collaboratory and grid middleware, computational mesh tools, data transport, numerical algorithms, statistical approaches, and data visualization techniques. Therefore, our successful computational science efforts require a robust set of crosscutting fundamental research capabilities in computer science, applied mathematics, and statistics.

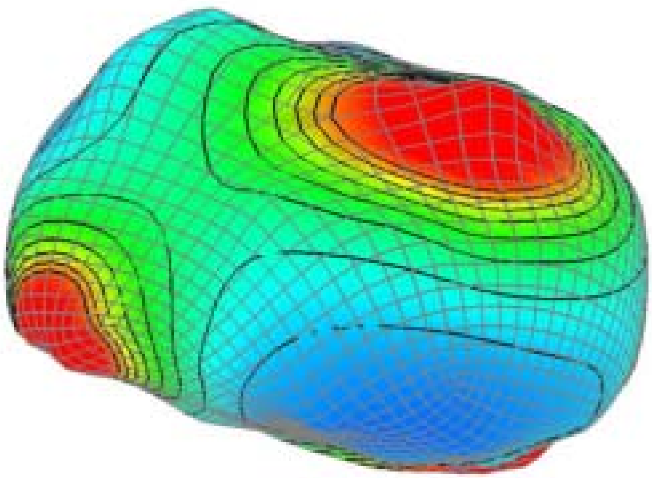
Advanced Scientific and Computational Research

With an established nucleus of programs and senior investigators, we will strengthen our capabilities and programs in the areas described above by building staff and program depth with the ASCR. During the next several years, our major thrusts are keyed to research aligned with the research program thrusts of ASCR.

- We will continue to carry out and diversify research programs that are creating efficient and productive programming environments and systems software for scientific applications on the very largest computer systems, including first-of-a-kind computational infrastructure. These tools are integral to research in EMSL's Molecular Science Computing Facility and to research programs in nanoscience, bioinformatics, climate physics, and subsurface transport, to name a few.
- We will continue to develop scalable, adaptive mesh refinement techniques to enable computational models of new classes of systems. These capabilities are core components of computational applications in cellular biology, organ modeling, and nanoscience, with future application to materials science and computational engineering. They are also integral to comprehensive modeling tool suites being developed with our collaborators for SC applications.
- We will develop new basic research projects in mathematical and statistical methods to deal with the scale and complexity of large science problems, with emphases in bioinformatics analysis, informatics for homeland security, environmental risk assessment, and model uncertainty in contaminant transport.

- To improve the ability of researchers to interact with very large datasets, we will develop new research programs directed at creating interactive visual analysis techniques that accelerate discovery with new approaches to scientist-information interaction. Our initial science application targets include the systems biology of microbes, and the analysis of regional and global climate models.
- To enable scientists to productively use widely distributed computing resources and databases, and to collaborate with experts regardless of their location, we will continue our research thrusts and pilot projects in architectures and middleware for collaborative problem-solving environments. These tools will enable new approaches to distributed science efforts in a wide range of mission areas, with current emphases in protein structure, systems biology, and chemistry.
- PNNL will be a full partner in the DOE Science Grid. We will provide and support grid services on our major computer facilities for science research (e.g., the 11.8-teraflop computer in the EMSL). PNNL will continue to participate in the development of grid systems, tools, and policies to further the reach and accessibility of computational science applications and data.

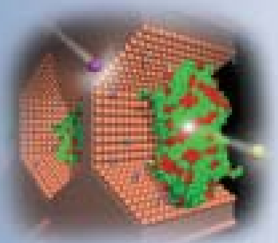
Although this work is primarily directed toward ASCR capabilities, it also leverages investments in new computer science, applied mathematics, and statistics capabilities being developed in our Computational Sciences and Engineering Initiative, as described in Module 2.4.1.



Efficient, scalable mesh-based computational techniques are essential for modeling a wide range of biological systems from signal propagation in microbes (above), to aerosol particle movement in lungs, to salmon interactions with dam structures. PNNL is developing adaptive mesh refinement capabilities as part of a multi-institution collaboration in Terascale Simulation Tools and Technology, an ASCR applied mathematics Integrated Software Infrastructure Center in the Scientific Discovery Through Advanced Computing Program.

2.4.1 Computational Sciences and Engineering Initiative

The Computational Sciences and Engineering Initiative (CS&EI) will develop advanced modeling and simulation capabilities that will be broadly used by PNNL's R&D programs.



Science

Computational science is an integral capability required throughout the Laboratory and is key to our future success. Through CS&EI, we will develop special capabilities for computational science in specific core areas to achieving the vision for the Laboratory, including chemistry, biology, climate, remediation, and national security. Our long-term goals focus on developing a series of major modeling and simulation suites for specific science and engineering domains, along with high-performance computing systems and infrastructure that are optimized for these suites, and the underlying support for these capabilities and their users.

An overarching scientific theme of CS&EI is developing computational capabilities across PNNL mission areas that deal with complex behavior on different temporal and spatial scales, and that enable us to carry out the demanding and sophisticated simulation, modeling, and analysis necessary to distinguish our research programs in chemistry, biology, atmospheric sciences, national security, materials engineering, and subsurface science.

Computational science draws upon and blends the advanced skills of many domains. Success requires strong capabilities in core areas of computer science, applied mathematics, and statistics. In addition, a core infrastructure of networks and computers is required to meet the computational demands of the scientific domains.

This initiative is characterized by:

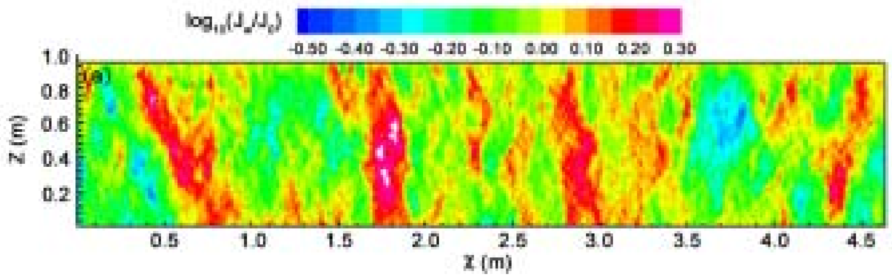
- Creating new modeling, simulation, and analysis techniques that expand the boundaries of the study of complex systems essential to our missions in chemistry, bioinformatics, subsurface transport, nanoscience, materials engineering, and information analytics.
- Developing innovative computer science, mathematics, and statistics approaches for highly effective and efficient use of tera- to peta-scale computing, sophisticated problem-solving environments, and massive data analyses that minimize time to solution and accelerate scientific discovery.
- Providing advocacy and leadership for forefront computational facilities, state-of-the-art networks, and other technical computing infrastructure needed to serve PNNL and the external user communities in support of our science and engineering programs.
- Increasing the visibility of our computational science and engineering activities and capabilities throughout the science community through peer-reviewed publications, seminars, visiting scientists, technology exhibitions, and scientific symposia/workshops.

Example of recent CS&EI accomplishments:

- Demonstrated self-consistent-charge density functional tight-binding models to include atomic forces, and coupled them to drivers for energy minimization, transition-state determination, force-constant calculation, and molecular dynamics simulations. This permits quantum modeling and simulation of systems that are at the heart of biochemical reactivity and nanoscale science.
- Completed the development and implementation of a damage model for short-fiber composites using a multiscale mechanistic approach.
- Developed a novel visual data mining method to provide exploration and navigation capabilities to our ongoing whole-genome alignments work.

Because the focus of this initiative spans missions in each of the Laboratory's directorates, a wide range of our programs are targeted for substantial growth, with major emphasis on the following research programs.

- Key roles in the new ASCR science computing initiative planned for FY 2005; defining new programs in subsurface science simulation, climate physics, computational biology and bioinformatics in BER and ASCR; and extending the impact of computational chemistry and computational nanoscience in BES.
- EERE programs in lightweight materials and hydrogen fuel systems.
- DOE and DHS programs in homeland security, with an emphasis on dynamic information analysis in collaboration with Homeland Security Initiative (see Module 4.5.1).



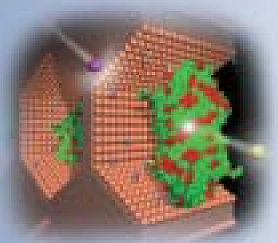
High-resolution clastic dike simulation yields new insights on vadose zone transport. At the Hanford Site, the presence of vertical clastic intrusions has raised concerns over potential expedited contaminant transport pathways through the vadose zone. In conjunction with millimeter-scale geophysical measurements, high-resolution simulations of flow, and reactive transport using parallel processing subsurface simulators have identified distinct and complementary pathways under natural and leaking conditions. Contaminants present in the leaking events may be considerably less mobile when natural conditions return.

Example of recent CS&EI accomplishments (contd):

- Completed a one-dimensional test problem involving the migration of carbon tetrachloride through Hanford soils using the parallel implementation of the Water-Air-Oil operational mode of the Subsurface Transport Over Multiple Phases (STOMP) simulator on the Molecular Science Computing Facility supercomputer. A three-dimensional test problem developed under the Hanford Science and Technology project was used for the final verification of the parallel implementation of the Water-Air-Oil operational mode of the STOMP simulator. The successful execution of these three-dimensional simulations on multiprocessor computers completed the development and demonstration requirements for the parallel implementation of the Water-Air-Oil operational mode.

2.5 Research for the Department of Health and Human Services

Growing research supported by the National Institutes of Health (NIH) is aligned with the Laboratory vision to build an internationally recognized program in systems biology.



Science

Our systems biology approach that integrates experimental biology with the physical and computational sciences is attracting support from NIH programs and is an example of beneficial leveraging of the strengths among DOE and other federal agencies. Our ability to translate fundamental research to application forms the base for establishing relationships with the Centers for Disease Control and other DHHS programs beyond the NIH. DHHS is becoming a critical partner in carrying out successful cross-disciplinary and multi-institutional research in systems biology centered on our capabilities in structural biology, molecular and cellular imaging, high-throughput global proteomics, and bioinformatics and computational biology.

The continued development of NIH programs relies on our state-of-the-art capabilities. Growth in the scientific impact of our NIH research depends on the unique capabilities of the proposed facility for high-throughput proteomics and metabolomics, and also builds on existing research strengths in cell signaling, structural genomics, molecular toxicology, and microbiology. The awarding in 2003 of a large, multiyear National Center for Research Resources project in mass spectrometry to PNNL to support research in proteomics across the NIH is evidence that the leading-edge technology being developed in EMSL is recognized by the biomedical community.

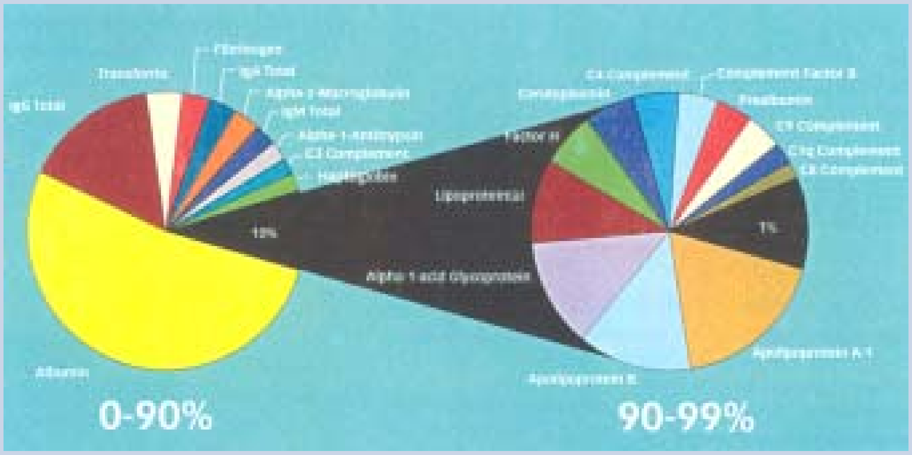
Under the BSI, PNNL has leveraged the investments in developing capabilities supporting DOE programs to build an NIH portfolio of investigator-initiated projects focused on fundamental cell biology. The Laboratory now plans to use this base to develop larger, multi-institutional program projects with NIH support, such as the ongoing Superfund Basic Research Center project funded by the National Insitute of Environmental Health Sciences (NIEHS) in collaboration with the Oregon Health and Science University and Oregon State University.

Human Health Research

The Laboratory also conducts applied research and technology development in support of the DHHS human health mission. Monitoring workers for chemical exposures during environmental cleanup is an important DOE issue and a critical scientific challenge. We are developing real-time, noninvasive biomonitors that can be used to measure chemical exposures to workers by integrating systems biology with our strengths in personnel dosimetry, chemical toxicology, microtechnology, and sensors. The National Institute for Occupational Safety and Health is funding research projects that further develop this technology and study exposure to dose to health effects in selected populations.

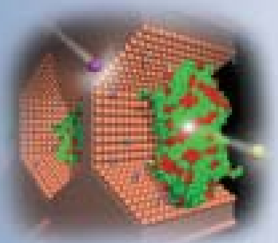
With support from NIEHS, our scientists identified or confirmed 490 proteins in human blood serum, nearly doubling the number of known serum proteins. Blood serum holds clues to all the major processes in our bodies; by knowing what proteins exist in that serum, it may be possible to predict disease susceptibility, monitor disease progression, or diagnose disease.

"After a long period of slow progress, research on the plasma proteome has begun a period of explosive growth attributable to new multidimensional fractionation methods," said N. Leigh Anderson, founder and chief executive officer of The Plasma Proteome Institute. "PNNL's work is an important early demonstration of the power of these methods, and suggests that hundreds, if not thousands, of new candidate markers will be found."



Adkins JN, SM Varnum, KJ Auberry, RJ Moore, NH Angell, DS Wunschel, RD Smith, DL Springer, and JG Pounds. 2002. Global Proteomics for Human Blood Serum I: Multidimensional Separation of Peptides Coupled with Mass Spectrometry. *Molecular Cellular Proteomics 1*: 947-955.

Relative abundance of the proteins that make up 99 percent of the protein mass in blood plasma. The final 1 percent represents thousands of proteins (Image courtesy of Plasma Proteome Institute).



Science

Currently, PNNL is exploring biological systems through proteomics research. Proteomics, the study of protein expression patterns in organisms, extends beyond genomics. Whereas the genome is the potential of a cell, the proteome is the realization of that potential.

In the future, the Microbial Cell Dynamics Facility will be housed in a new Multiprogram Science Laboratory devoted to systems biology, biogeochemistry, and other capabilities of particular interest to SC.

2.6 New Whole Proteome Analysis Facility for Systems Biology

A critical aspect of the DOE Genomics:GTL Program is the establishment of four major scientific facilities. PNNL is developing a proposal to build and operate one of these, the Whole Proteome Analysis Facility.

The DOE Genomics:GTL Program is an ambitious program to achieve a fundamental, comprehensive, and systematic understanding of microbial life. As noted in DOE's *Genomes to Life: Realizing the Potential of the Genome Revolution* document, "GTL is designed to help launch biology onto a new trajectory to comprehensively understand cellular processes in a realistic context. This new level of exploration, known as **systems biology**, will empower scientists to pursue completely new approaches to discovery, transforming biology to a more quantitative and predictive science." Major research projects were initiated in FY 2002 and proposals in response to a second call were submitted in April 2003. Along with this substantial programmatic research commitment, DOE determined the need for four major new scientific facilities.

These facilities will use advanced high-throughput technologies, will be highly automated, and will include tools necessary for building an integrated environment of software for data management, analysis, and simulation. DOE intends to provide open access to these facilities as well as the data they generate— "a plan to democratize access to systems biology resources." The four planned facilities are: I. Production and Characterization of Proteins Facility; II. Whole Proteome Analysis Facility; III. Characterization and Imaging of Molecular Machines Facility, and IV. Analysis and Modeling of Cellular Systems Facility.

We are in a very competitive position for facility II because of our key expertise in microbiology, proteomics, and advanced analytical technologies and tools, such as high-field mass spectrometery and NMR imaging, advanced data visualization environments, and high-performance computing.

Additional Biology Prototype Facilities Needed

The DOE Genomics:GTL facility development effort is an integral element of our BSI. As discussed in Module 2.2.1.1, BSI is investing in critical scientific programs and capabilities in proteomics and is providing support for the development, delivery, and operations of this facility. An important part of this support is the creation of two biology prototype facilities. One is the Proteomics Sample Processing Facility in PNNL's LSL-2 Building, and the other is the Microbial Cell Dynamics Facility currently in the 331 Building. Plans are under development to expand these prototypes to further support the DOE Genomics:GTL Program facility development efforts.

Preparing to Win

We are establishing the significant partnerships, constituents, and advocacy required to be successful throughout the DOE Genomics:GTL Program facility-development process. Building and operating the Whole Proteome Analysis Facility is a critical long-term goal for the Laboratory. Near-term efforts to achieve this goal consist of the following:

- holding workshops/technical exchanges on various scientific, technical, and operations aspects of the facility to refine the facility concept and establish appropriate third-party relationships
- establishing a pilot high-throughput production facility for protein and metabolite analysis inclusive of critical research and development efforts
- expanding the two PNNL biology prototype facilities as a part of establishing the pilot production facility
- continuing with the appropriate BSI programs and investments
- hiring/identifying key persons to lead various aspects of the facility development
- continuing work with DOE and national laboratories, universities, private organizations, and others, to be positioned to successfully compete for the Whole Proteome Analysis Facility.

To support the DOE Genomics:GTL Program, PNNL is proposing to build and operate Facility II — the Whole Proteome Analysis Facility. The facility concept is a production-oriented laboratory that merges with nonlaboratory space to facilitate collaboration, communication, and access with the scientific community.