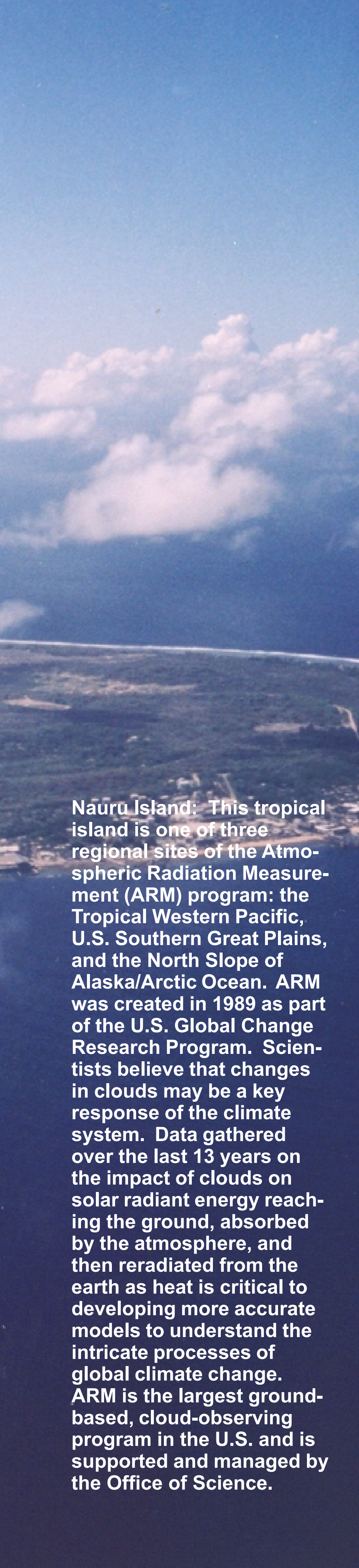
Biological and Environmental Research



Nauru Island: This tropical island is one of three regional sites of the Atmospheric Radiation Measurement (ARM) program: the Tropical Western Pacific, U.S. Southern Great Plains, and the North Slope of Alaska/Arctic Ocean. ARM was created in 1989 as part of the U.S. Global Change Research Program. Scientists believe that changes in clouds may be a key response of the climate system. Data gathered over the last 13 years on the impact of clouds on solar radiant energy reaching the ground, absorbed by the atmosphere, and then reradiated from the earth as heat is critical to developing more accurate models to understand the intricate processes of global climate change. ARM is the largest ground-based, cloud-observing program in the U.S. and is supported and managed by the Office of Science.

PNNL-ARM

2 Harness the Power of Our Living World

Provide the biological and environmental discoveries necessary to clean and protect our environment, offer new energy alternatives, and fundamentally alter the future of medical care and human health.

Over billions of years of evolution, Nature has created life's machinery—from molecules, microbes, and complex organisms to the biosphere—all displaying remarkable capacities for efficiently capturing energy and controlling precise chemical reactions. The natural, adaptive processes of these systems offer important clues to designing solutions to some of our greatest challenges. In the next decade, science will reveal the mechanisms and genetic secrets by which microorganisms develop, survive, and function in different environments. We will be able to manipulate matter at the micro, nano, and molecular scales; and we will be able to model and predict biological and environmental interactions on a regional and global basis. Such capabilities will provide us unprecedented opportunities to forge new pathways to energy production, environmental management, and medical diagnosis and treatment.

To realize this vision, many challenging scientific questions will have to be answered:

- What are the fundamental genetic processes, structures, and mechanisms that living systems use to control their responses to their environment, and how can we predict and repeat those processes to put Nature to work for us?
- How do we design new and revolutionary technologies and processes, using and combining principles of biological and physical systems that offer new solutions for challenges from medicine to environmental cleanup?
- How do clouds influence climate change, and how does human activity affect the behavior of clouds? How sensitive is climate to different levels of greenhouse gases and aerosols in the environment?

Answers to these and other questions will come only through effective convergence of the physical, life, and computational sciences. We have the track record and infrastructure to conduct the large-scale, complex, and interdisciplinary research to meet the challenge. Already, the Office of Science has delivered genome sequencing, protein crystallography, advanced tools for understanding the environment at the molecular level, integrated climate modeling, and advanced imaging tools. With anticipated new facilities, such as those for Genomics: GTL, as well as high-performance computational platforms and cutting-edge measurement tools, we are prepared to harness the power of our living world for a secure, environmentally sound, and energy-rich future.

As an integral part of this Strategic Plan, and in *Facilities for the Future of Science: A Twenty-Year Outlook*, we have identified the need for four future facilities to realize our Biological and Environmental Research vision and to meet the science challenges described in the following pages. Two of the facilities are near-term priorities: the **Protein Production and Tags** facility and the **Characterization and Imaging of Molecular Machines** facility. The Protein Production and Tags facility will use highly automated processes to mass produce and characterize tens of thousands of proteins per year, create "tags" to identify these proteins, and make these products available to researchers nationwide. The facility for Characterization and Imaging of Molecular Machines will build on capabilities provided by the Protein Production and Tags facility to provide researchers with the ability to isolate, characterize, and create images of the thousands of molecular machines that perform the essential functions inside a cell. All four facilities are included in our Biological and Environmental Research Strategic Timeline at the end of the chapter and in the facilities chart in Chapter 7 (page 93), and they are discussed in detail in the *Twenty-Year Outlook*.

Our Strategies

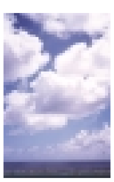
2.1 Tap the power of genomics and microbial systems for solutions to our Nation's energy and environmental challenges.

After launching the Human Genome Project in the 1980s, the Office of Science was part of an international collaboration that recently finished sequencing the entire human genome. Yet, we have only begun to understand how complex biological systems work—going from single genes to genetic networks to complex biological functions and characteristics, whether in humans or single-celled microbes. We continue to push the frontiers of biology, including the complex systems interactions, by studying microbes that can be used to help us solve DOE mission needs.

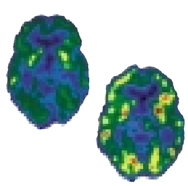
Microbes have been found in every conceivable environment on Earth, from boiling deep-ocean thermal vents to Arctic ice flows to toxic environments. The remarkable ability of microbes to flourish in extreme conditions demonstrates that they long ago developed systems for novel energy conversion and environmental cleanup.

Our challenge is to put those microbes—and their systems of molecular machines that allow them

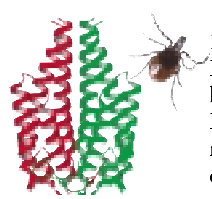
Our History of Discovery…Select Examples



1970
Discovered the complex processes and interactions behind acid rain.



1990
Imaged the biochemistry of human addiction using Positron Emission Tomography. (PET technology was enabled by DOE science breakthroughs.)

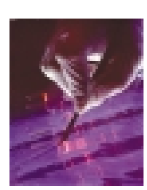


1995
Determined the structure of key surface proteins in Lyme Disease bacteria, offering new opportunities for detection and treatment.

1970 *1980* *1990*

1986
Pioneered the quest to sequence the Human Genome.

1995
Sequenced the tiny pathogen, *Mycoplasma genitalium*, the smallest genome that sustains life.



1996
Provided fundamental research in capillary-based DNA sequencing that led to development of DNA sequencing machines that revolutionized genome sequencing . . . and modern biotechnology.

LBNL

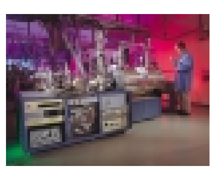
Frontiers in genomic science: Why would the Department of Energy's Office of Science be interested in this beautiful but peculiar fish? It turns out that the Fugu, or puffer fish, contains essentially the same genes as the human genome but in about one-eighth the total amount of DNA. Human gene hunters can sort through the Fugu genome much faster and easier than the human genome because it has far less non-coding DNA. DOE's Joint Genome Institute (JGI), the world's major public genome sequencing center, conducted this research as part of the Human Genome Project, an initiative pioneered by DOE, to give scientists a powerful new tool to help them better understand the human genome—from insights into diseases to the impacts of energy and energy byproducts on human physiology and health. Under the Office of Science Genomics: GTL program, JGI is now shifting attention to a new and equally promising frontier. By studying the genomes of a variety of micro-organisms, scientists are exploring the capabilities of the natural world to produce energy, clean up waste, and possibly slow or halt climate change.

to survive—to work for us. Nature has designed remarkable arrays of multiprotein molecular machines with exquisitely precise and efficient functions and controls. With the help of the DOE Joint Genome Institute, and the future Genomics: GTL facilities, we will uncover the mysteries of biological systems that will enable our Nation's scientists to harness the power of genomics and microbial systems. Our strategy includes the following emphases:

- Decode and compare the genetic instructions of diverse microorganisms by unraveling their DNA sequences to reveal their capabilities for energy production, carbon sequestration, and environmental cleanup.
- Discover the molecular machines encoded in each microbe's genetic instructions, determining what molecular machines are present, what proteins they are made of, where they are found in cells, and how they do their work.
- Produce computational models of molecular machines in action to understand the fundamental principles controlling the function of molecular machines and thus biological systems, providing us with knowledge to use or even redesign these machines.
- Examine genetic regulatory networks to understand the genetic circuitry in a cell that controls the molecular machines.
- Explore the biochemical capabilities of complex microbial communities to fully utilize the potential found in natural microbial communities.

1996
Verified the existence of the third branch of life (Archaea)—*Methanococcus jannaschi.*

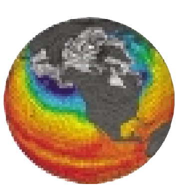
1998
Developed computational tools for discovering genes.



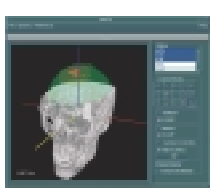
2000
Developed mass spectrometry for rapid determination of bacterial proteome that reduces analysis time from years to days.

2001
Published a complete draft of the DNA sequence of the human genome as part of an international consortium.

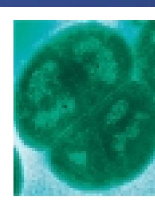
2000



1996
Delivered high-resolution ocean model for climate simulation.

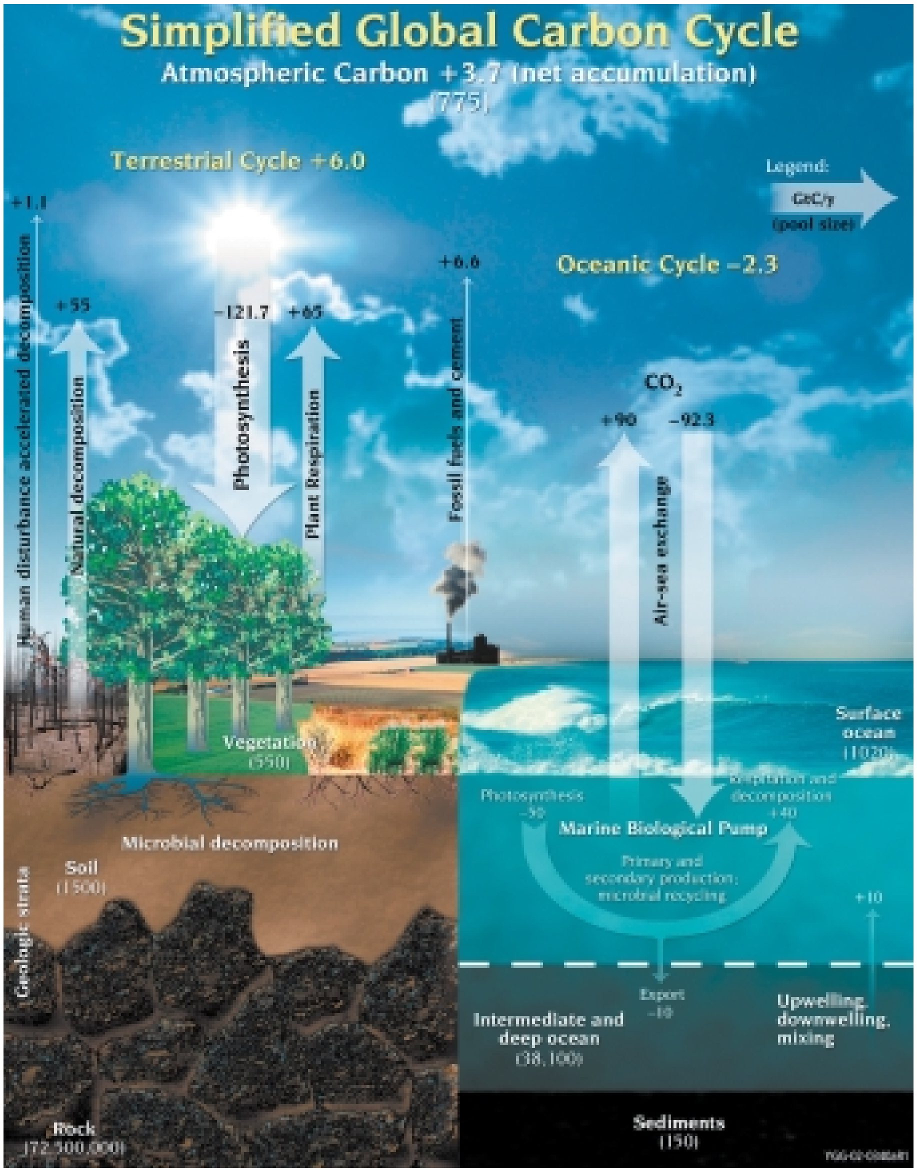


1999
Improved neutron beams for cancer treatment.



2000
Engineered radiation-resistant bacteria for bioremediation.

- Develop predictive models of complete microbial communities to anticipate how they will behave and change in response to various signals from their environment.



ORNL

Carbon cycle: In the past 60 years, the amount of anthropogenic carbon dioxide emitted to the atmosphere, primarily from use of fossil fuels, has risen from preindustrial levels of 280 parts per million to present levels of over 365. The relationship between climate change and increasing levels of carbon dioxide is a matter of intense study. Predictions of global energy use in the next century suggest a continued increase in carbon emissions and rising concentrations of atmospheric carbon dioxide unless major changes are made in the way we produce and use energy. Carbon sequestration is receiving attention as a promising solution, and the Office of Science is performing much of the basic research. In carbon sequestration, the gas is trapped or "fixed" in solid form in the terrestrial biosphere, underground, or in oceans, thus slowing or halting the buildup of greenhouse gasses. Research emphases range from the possible use of engineered geologic repositories, to enhancing Nature's own tool kit and sequencing the genomes of promising micro-organisms, putting them to work on this global problem.

2.2 Unravel the mysteries of Earth's changing climate and protect our living planet.

We are making progress in measuring and modeling changes in climate. This is no simple matter given the complex interactions of air, land, and ocean processes that affect climate. Despite our progress, we still cannot definitively distinguish between natural and human-caused climate changes, we do not fully understand the effects and roles of clouds and aerosols on climate, and we have limited ability to predict regional effects. More importantly, we have only begun to explore ways to mitigate and/or adapt to these effects. Ultimately, we need to be able to understand the factors that determine Earth's climate well enough to predict climate and climate impacts decades, or even centuries, in the future. We are developing the novel research tools, models, and integrated experiments and computational science to find the answers. Our strategy includes the following emphases:

- Determine the effects of clouds and aerosols on climate, in particular their interactions with long-wave radiation, how and where clouds form and dissipate in the atmosphere, and how changes in clouds and aerosol distributions alter the Earth's radiation balance.
- Predict future climate at regional scales, advancing mathematics and computation to simulate the

dynamics, chemistry, and biology of the Earth system on decade to century time scales.

- Distinguish natural and human-caused climate change based on improved climate models that more accurately reflect changes in radiative forcing due to increases in greenhouse gases and aerosols in the atmosphere.
- Understand and enhance Nature's processes for sequestering atmospheric carbon from fossil fuel use, including the capacity of terrestrial and oceanic ecosystems and opportunities to capitalize on the biophysical and biochemical mechanisms that control uptake in plants, soils, and ocean plankton.
- Determine how ecosystems respond to environmental change, developing a theoretical and empirical basis spanning molecular interactions to whole ecosystems.
- Predict and assess the effects of climate change based on models of human actions and costs and benefits of alternatives for mitigation and adaptation.

2.3 Understand the complex physical, chemical, and biological properties of contaminated sites for new solutions to environmental remediation.

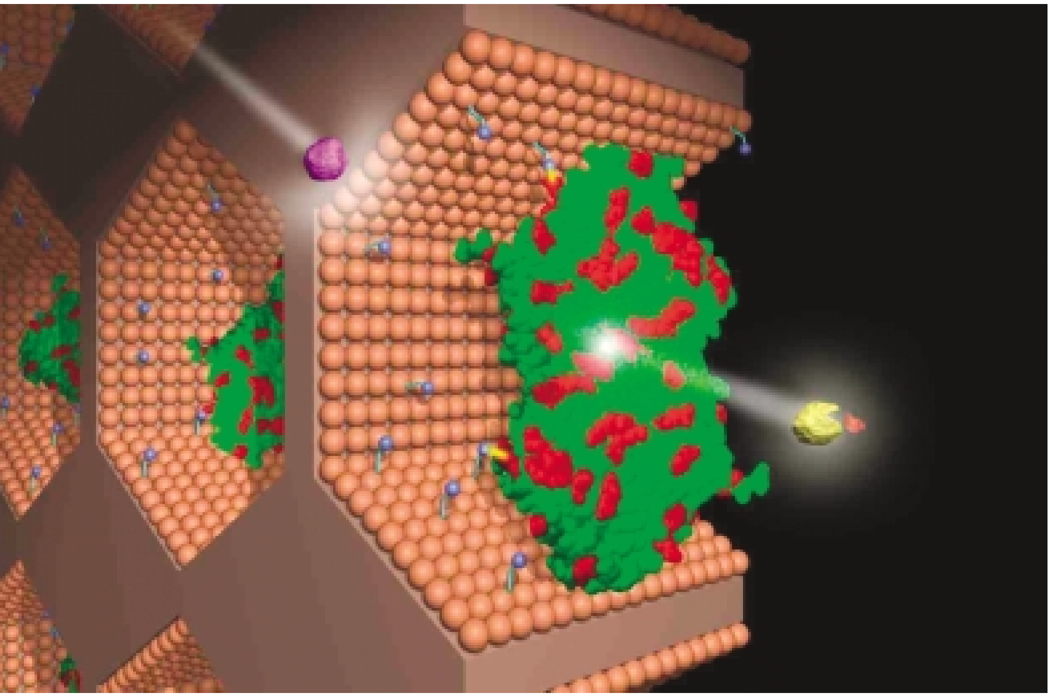
As a legacy of DOE's nuclear security mission over the last half-century and extending through the Cold War, large tracts of land surrounding DOE weapons production and other sites became contaminated. The magnitude of some of these problems is enormous, and many cannot be addressed using current technology. Despite progress on many fronts, efficient, effective, and affordable solutions to environmental contamination continue to elude us, whether the contaminants are radionuclides, toxic metals, or organic compounds. There is much we need to learn. How do contaminants interact with minerals, plant materials, and microbes in soils? How do they move to the groundwater or other locations where they can adversely affect human health?

PNNL

Microbes for environmental cleanup: Many of the aging waste tanks built on the Hanford Site in Richland, Washington, contain radioactive and chemical waste, a legacy from plutonium production. Some of the tanks are leaking into the soil and groundwater around the sites. Research to remediate these waste sites requires a clear understanding of both the environment and the contaminants. Microbes are being studied for their natural or engineered abilities to assist in environmental cleanup. Individual microbes and communities of microbes have already "found" solutions for many of our current challenges in environmental cleanup and energy production. *Shewanella oneidensis* (offset left) can convert soluble metals into insoluble forms, which could keep some contaminants from migrating into groundwater. Other microbes use toxic or radioactive substances as energy sources, rendering them into harmless byproducts.

This poor understanding of how contaminants behave in Nature restricts the development of cost-effective cleanup strategies and, in some cases, our ability even to recognize problems. Our challenge is to understand natural cleanup methods, put them to work, and improve cleanup decisions in the future. Our strategy includes the following emphases:

- Predict the fate and transport of contaminants with improved tools and understanding of interdependent biological, chemical, and physical processes.
- Take laboratory experiments and theory to the field, testing our theoretical predictions and models of the complex natural environment over considerable distances and time scales.
- Provide the next generation of computational and experimental capabilities for detailed understanding of contaminant behavior, including synchrotron light sources and the William R. Wiley Environmental Molecular Sciences Laboratory at the Pacific Northwest National Laboratory.
- Use Nature's own tool kit and rely on new understanding of the biology of microbes and microbial communities, geochemistry, plants and ecosystems, biomimetic agents, and nanomachines to explore innovative options for cleaning up the environment.
- Develop a basic understanding of complex chemical behavior of stored radioactive wastes to enable the discovery of novel separations and other treatment methods that can dramatically reduce the costs and risks of radioactive waste treatment and disposal.



PNNL

Biotechnology teams with nanotechnology for deactivation of toxic substances: Specially developed enzymes (green) embedded in a synthetic material, which was created to immobilize the enzymes and enhance their activity and stability, can transform toxic substances (purple molecule at left) to harmless byproducts (yellow and red molecules at right). Such nanostructures could eventually be used for a broad range of enzyme-based methods to produce energy, remove or deactivate contaminants, and store carbon to mitigate global climate change.

2.4 Master the convergence of the physical and the life sciences to deliver revolutionary technologies for health and medical applications.

The Office of Science has been at the center of medical technology innovations, with a focus on energy's impact on human health and the powerful imaging and radioisotope tools that have been the foundation of nuclear medicine. The future of technology development appears even brighter with the availability of micro- and nano-structured materials and the emerging capability to actually “see” genes and networks of genes in action in living tissues. This makes possible the ability to track the progression of disease as it unfolds at the genetic level. Also, new radiotracers and imaging concepts will explore both normal and abnormal health, from the development of cancer to brain function. On a larger physical scale, medical imaging may be possible for patients in motion, such as infants. Our strategy includes the following emphases:

- Restore sight to the blind using the microelectronics, material science technologies, and specialized expertise of the national laboratories to design and fabricate an implantable artificial retina.
- Enable medical imaging of moving patients with modified PET and MRI technology, capitalizing on advances in mathematics, computation, and detectors from high-energy physics to compensate for motion.
- Develop highly selective, ultra-sensitive biosensors based on the national laboratories’ expertise in miniaturized optical systems and single-molecule detection, for medical, environmental, and national security applications.

SNL

Artificial retina: This project, funded by a $9 million, three-year grant from the Office of Science, will build a prototype that creates 1000 points of light through 1000 tiny microelectromechanical systems (MEMS) electrodes. The tiny electrodes may eventually be positioned on the retinas of those blinded by diseases such as age-related macular degeneration and retinitis pigmentosa to help them see again.

- Image genes as they are turned on and off in any organ of the body by forming fluorescent or radioisotopic images, giving us new capabilities for the diagnosis of disease.
- Develop new radiotracers and molecular tags to image the chemistry of life and disease, built around our capabilities in structural genomics, proteomics, radiochemistry, and more generally, the physical sciences.
- Determine the health risks of exposure to low doses of ionizing radiation to adequately and appropriately protect DOE nuclear workers and the general public while making effective use of our national resources.

"Medical advances may seem like wizardry. But pull back the curtain, and sitting at the lever is a high-energy physicist, a combinatorial chemist, or an engineer."

—Harold Varmus, president of Memorial Sloan-Kettering Cancer Center, former Director of the National Institutes of Health, and 1989 Nobel laureate, in an October 2000 *Washington Post* article where he noted that the physical sciences sponsored by the Office of Science are of critical value to the Nation.

Our Timeline and Indicators of Success

Our commitment to the future, and to the realization of **Goal 2: Harness the Power of Our Living World,** is not only reflected in our strategies, but also in our Key Indicators of Success, below, and our Strategic Timeline for Biological and Environmental Research (BER), at the end of this chapter.

Our BER Strategic Timeline charts a collection of important, illustrative milestones, representing planned progress within each strategy. These milestones, while subject to the rapid pace of change and uncertainties that belie all science programs, reflect our latest perspectives on the future—what we hope to accomplish and when we hope to accomplish it—over the next 20 years and beyond. Following the science milestones, toward the bottom of the timeline, we have identified the required major new facilities. These facilities, described in greater detail in the DOE Office of Science companion report, *Facilities for the Future of Science: A Twenty-Year Outlook,* reflect time-sequencing that is based on the general priority of the facility, as well as critical-path relationships to research and corresponding science milestones.

Additionally, the Office of Science has identified Key Indicators of Success, designed to gauge our overall progress toward achieving Goal 2. These select indicators, identified below, are representative long-term measures against which progress can be evaluated over time. The specific features and parameters of these indicators, as well as definitions of success, can be found on the web at **www.science.doe.gov/measures**.

Key Indicators of Success:

- Progress in characterizing the multi-protein complexes (or the lack thereof) that involve a scientifically significant fraction of a microbe's proteins. Develop computational models to direct the use and design of microbial communities to clean up waste, sequester carbon, or produce hydrogen.
- Progress in delivering improved climate data and models for policymakers to determine safe levels of greenhouse gases. By 2013, reduce differences between observed temperature and model simulations at subcontinental scales using several decades of recent data.
- Progress in developing science-based solutions for cleanup and long-term monitoring of DOE contaminated sites. By 2013, a significant fraction of DOE's long-term stewardship sites will employ advanced biology-based cleanup solutions and science-based monitors.

Strategic Timeline for Biological and Environmental Research

Strategic Timeline—Biological

2003 2005 2007 2009 2011 2013

The Science

Life Sciences

- Initiate Genomics: GTL research program (2003)
- Develop artificial chromosome (2006)
- Complete mathematical model for microbial community that detoxifies uranium (2007)
- Complete photosynthetic microbe able to continuously make hydrogen (2008)
- Develop new knowledge base for cost-effective cleanup of environmental contamination (2012)
- Design new strategies for enhanced capture of atmospheric carbon dioxide (2012)
- Increase biobased sources of fuel and electricity (2012)

Climate Change Research

- New measurements of clouds where observations are missing (2006)
- Include realistic clouds in a climate model (2007)
- Measure ecosystem responses to climate change, measurements never made before (2008)
- Provide a climate model that links the Earth's climate system with the Earth's biological systems (2010)

Environmental Remediation

- Create Environmental Remediation Sciences Division (2003)
- Develop alternative cesium separations process for HLW to be deployed at SRS, ensuring vitrification will remain on schedule (2006)
- Complete work on the technical basis for leaving in place cesium, technetium, uranium, strontium, or other radionuclides from soils beneath tank farm at the Hanford Site (2007)
- Provide new technologies for in situ characterization of contaminants that cannot be identified today (2008)
- Validate bioremediation of metals and rads in the field (2008)
- Provide a suite of field characterization techniques for long-term monitoring of closed sites (2012)

Medical Sciences

- Test new biocompatible materials for chip, electrodes, and hermetic seal for the artificial retina (2002)
- Design and microfabricate 60-electrode artificial retina device (2003)
- Radiotracer chemistry/probes to detect defective gene expression (2003)
- Complete in vitro testing of 60-electrode artificial retina device and implant prototype into dogs (2004)
- Implant and test 60-electrode devices in humans (2005)
- Begin design and fabrication of 1000-electrode artificial retina device (2005)
- Complete microfabrication of 1000-electrode prototype artificial retina (2006)
- Preclinical testing of radiolabeled probes for imaging defective genes (2006)
- Complete in vitro testing and implant 1000-electrode artificial retina devices into dogs (2007)
- Complete in vitro testing and implant 1000-electrode artificial retina devices into dogs (2009)

Future Facilities**

Protein Production and Tags: This facility will use highly automated processes to mass-produce and characterize tens of thousands of proteins per year, create "tags" to identify these proteins, and make these products available to researchers nationwide.

Characterization and Imaging of Molecular Machines: This facility will build on capabilities provided by the Protein Production and Tags facility to provide researchers with the ability to isolate, characterize, and create images of the thousands of molecular machines that perform the essential functions inside a cell.

***These strategic milestones are illustrative and depend on funds made available through the Federal budget process.**

****For more detail on these facilities and the overall prioritization process, see the companion document, *Facilities for the Future of Science: A Twenty-Year Outlook.***

l and Environmental Research*

2015	2017	2019	2021	2023	2052

- Save billions of dollars in toxic waste cleanup (2032)
- Stabilize atmospheric carbon dioxide to counter global warming (2042)
- Mature bioenergy industry established (2052)

- Unambiguous detection of human-induced climate change (2015)

- Deliver an Earth system model capable of robustly predicting natural and human-induced climate change and its environmental consequences (2020)

- Enable determination of a safe level of greenhouse gases in the atmosphere (2030)

- Deliver accurate predictive models that eliminate unneeded remediation strategies (2018)

- Use genomic and nanoscience capabilities to develop remediation strategies for individual waste sites (2027)
- Completion of high-level waste treatment, saving tens of billions in cost (2029)

Analysis and Modeling of Cellular Systems: This facility will combine advanced computational, analytical, and experimental capabilities to study how multi-cellular systems, including microbial communities, function at the molecular level.

Whole Proteome Analysis: This facility will provide researchers with the ability to investigate how microbes adapt to changes in their environment by turning certain portions of their genome “on” and “off.”