DOE Genomic Science Program Overview

Systems Biology for Energy and Environment

science.doe.gov/ober/BSSD/genomicsgtl.html

Advancing Scientific Discovery through Genomics and Systems Biology

Natural systems, from simple microbes to complex, highly diverse ecosystems, hold secrets of life that fascinate curious minds, drive scientific inquiry, and offer biological solutions to many energy and environmental challenges facing us today. Even the simplest of these systems, the single microbe, is so complex that we do not yet possess a full understanding of how a living system works, how life processes are regulated at the molecular level, and how organisms interact with and modify their environments.

The Department of Energy (DOE) Genomic Science program* is driven by a grand challenge in biology: understanding biological systems so well that we can develop predictive, computational models of these systems (see figure below, Genomic Science Program Goal and Objectives). By revealing the genetic blueprint and fundamental principles that control plant and microbial systems relevant to DOE missions, the Genomic Science program is providing the foundational knowledge underlying biological approaches to producing biofuels, sequestering carbon in terrestrial ecosystems, and cleaning up contaminated environments. The fundamental scientific advances emanating from this program are transferable to a broad range of application areas and lay a foundation for new generations of industrial biotechnologies.

*Formerly Genomics:GTL

Addressing extremely complex science questions that span all scales of biology, research supported by DOE's Genomic Science program requires the collective expertise of scientists from many disciplines and the coordinated application of a wide range of technologies and experimental approaches—genome sequencing, gene expression profiling, proteomics, metabolomics, imaging, research technology development, and computational biology. Research is conducted at national laboratories, national user facilities, and universities and includes single-investigator projects, multi-institutional collaborations, and fundamental research centers (see sidebar, DOE Bioenergy Research Centers, p. 2). The Genomic Science program is run by the Office of Biological and Environmental Research (BER) within DOE's Office of Science.

In addition to supporting the Genomic Science program, BER is collaborating with other governmental agencies to advance genomics. A research program jointly sponsored by BER and the U.S. Department of Agriculture (USDA) Cooperative State Research, Education, and Extension Service supports genome-based approaches to accelerate plant-breeding programs and improve potential bioenergy crops.

Genomic Science Program Goal and Objectives

Genome Sequence → **System-Wide Biological Investigations** → **Predictive Understanding**

Goal: Achieve a predictive, system-level understanding of plants, microbes, and biological communities, via integration of fundamental science and technology development, to enable biological solutions to DOE mission challenges in energy, environment, and climate.

- **Objective 1:** Determine the genomic properties, molecular and regulatory mechanisms, and resulting functional potential of microbes, plants, and biological communities central to DOE missions.
- **Objective 2:** Develop the experimental capabilities and enabling technologies needed to achieve a genome-based, dynamic system-level understanding of organism and community function.
- **Objective 3:** Develop the knowledgebase, computational infrastructure, and modeling capabilities to advance the understanding, prediction, and manipulation of complex biological systems.

From Genome Sequences to Understanding

The DNA code—the genome—is the starting point to understanding any biological system. The genomes of individual organisms and systems of organisms (e.g., plants, microbes, and their communities and ecosystems) contain the information and operating capabilities that determine structure and function across multiple scales of biological organization. Exploring biological systems across all scales in a comprehensive and integrated way is essential to understanding how these systems operate in nature or in more applied contexts related to new technology endpoints for DOE missions (see figure, DOE Genomic Science Program, A Mission-Inspired Fundamental Research Approach). The biological systems investigated by researchers in the Genomic Science program include protein and molecular interactions, pathways, and vast interconnected networks within whole cells, communities, and ecosystems.

Systems biology is the holistic, multidisciplinary study of complex interactions that specify the function of an entire biological system—whether single cells or multicellular organisms—rather than the reductionist study of individual components in isolation. As a leader in systems biology research, the Genomic Science program builds on a foundation of sequenced genomes to identify the common fundamental principles that drive living systems. These principles guide the translation of genomic code into functional molecules underlying biological system behavior. For example, understanding these principles could determine the biological mechanisms controlling changes in the production of cellulose-degrading enzymes in an industrial bioreactor or the amount of carbon stored in a plant's roots under different environmental conditions. Knowledge of these common principles revealed by studying organisms for one DOE mission inevitably will lead to breakthroughs in basic biology important to other DOE and national needs.

DOE Bioenergy Research Centers

Bringing together top scientists from multiple disciplines, DOE BER established three Bioenergy Research Centers in 2007 to deliver high-risk, high-return breakthroughs in cellulosic biofuel production. DOE's Oak Ridge National Laboratory leads the BioEnergy Science Center in Tennessee. The University of Wisconsin–Madison leads the Great Lakes Bioenergy Research Center. DOE's Lawrence Berkeley National Laboratory leads the Joint BioEnergy Institute in California. Each center is using genomics and advanced analytical technologies to understand (1) how to make grasses, wood, and other cellulosic materials easier to break down into sugars for biofuel synthesis; (2) which enzyme systems degrade plant cell walls most efficiently; and (3) how to develop microbes that streamline the cellulosic biofuel production process and produce next-generation, petroleum-like biofuels. More information about the centers is available at genomicscience.energy.gov/centers/.

Genomic Science Program Investigations

In addition to funding a broad portfolio of single-investigator and team projects that target microbial and plant systems relevant to DOE missions, the Genomic Science program supports three fundamental research centers focused on bioenergy production (see sidebar, below left). The genome sequences of organisms studied in these projects are provided largely by the DOE Joint Genome Institute, an important user facility and a world leader in generating sequences of microbes, microbial communities, plants, and other organisms.

By leveraging the increasing availability of sequences from whole organism genomes and environmental samples (metagenomes), Genomic Science researchers are using and developing advanced methods to facilitate the translation of genome sequence into predictive understanding of function. These methods cut across DOE missions in energy production, carbon cycle science, climate change, and environmental remediation. For example, technologies used to image and characterize microbes interacting with contaminants in subsurface environments could also provide insights into plant-microbe interactions that increase carbon fixation and biomass yield in plants or carbon accumulation in soils.

Global Molecular Analyses. Transcriptomics, proteomics, and metabolomics—collectively described as "omics" analyses—identify and measure the abundance and fluxes of key molecular species indicative of organism or community activity under defined environmental conditions at specific points in time. Global analyses of RNA transcripts, proteins, and metabolites inform scientists about organisms' physiological status, provide insights into gene function, and indicate which genes are activated and translated into functional proteins as organisms and communities develop or respond

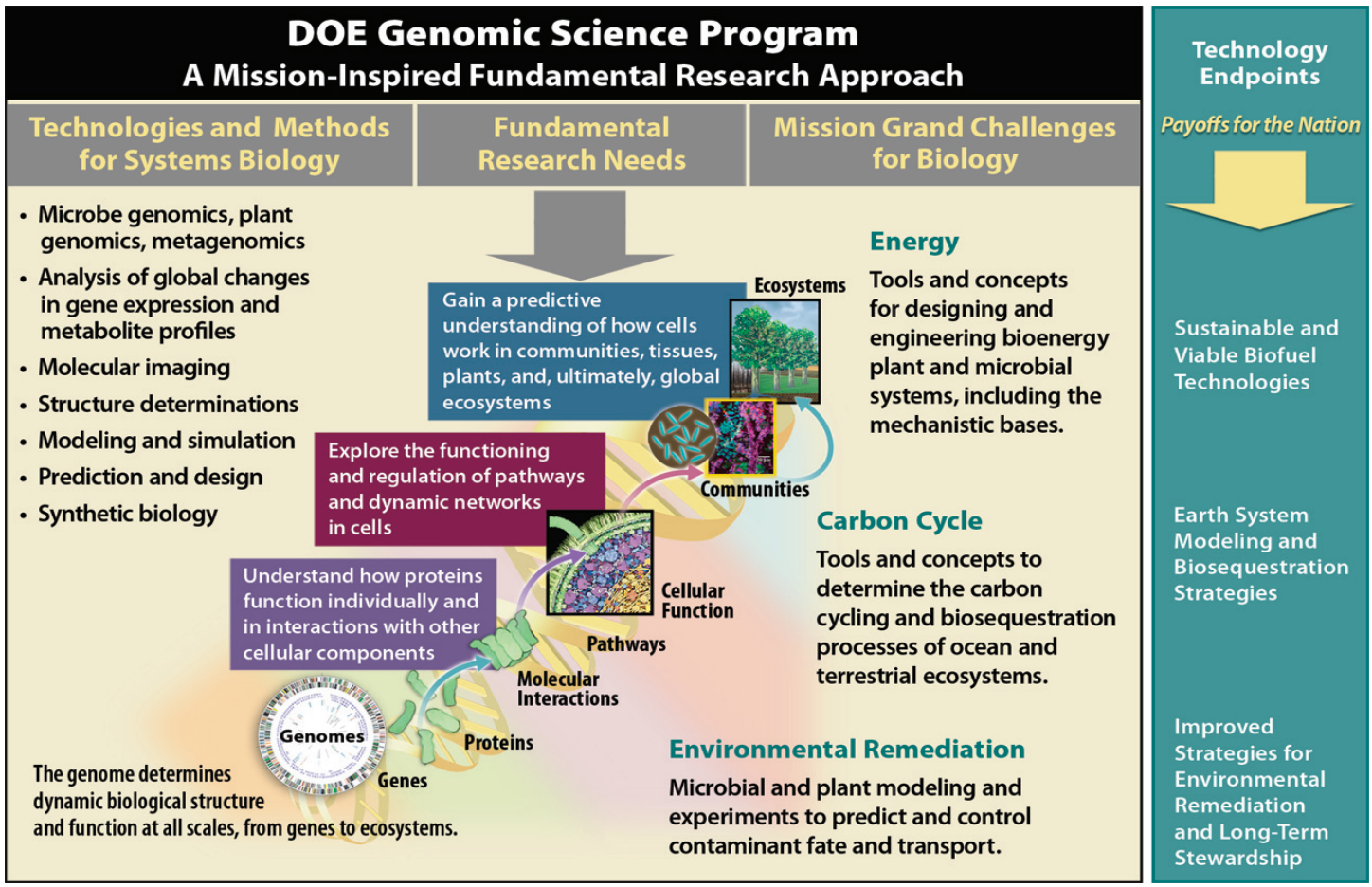
to environmental cues. Metamethods that analyze DNA, RNA, and proteins extracted from complex microbial communities in terrestrial and marine environments are enabling discovery of new biological processes and providing novel insights into natural microbial diversity and interdependencies among microbial community members.

Imaging and Structural Characterization. Genomic Science investigators are developing and using new methods for characterizing the chemical reaction surfaces, organization, and structural components in molecular complexes and tracking molecules to view cellular processes as they are occurring. Depending on the spatial scale, a variety of imaging technologies can be used to visualize the complex molecular choreography within biological systems. Some of these structural and imaging tools (e.g., synchrotrons, neutron sources, and electron microscopes) are available or are being developed at DOE Office of Science user facilities that provide photon, neutron, electron, magnetic, and mechanical instrumentation with state-of-the-art spatial, temporal, and chemical sensitivity.

Synthetic Biology. Synthetic biology is the design and construction of biological systems that do not exist in the natural world. This research approach may involve building entirely new microorganisms from a set of standard parts—genes, proteins, and metabolic pathways—or radically redesigning existing biological systems to enable capabilities that the systems would not possess naturally.

Systems Biology Knowledgebase

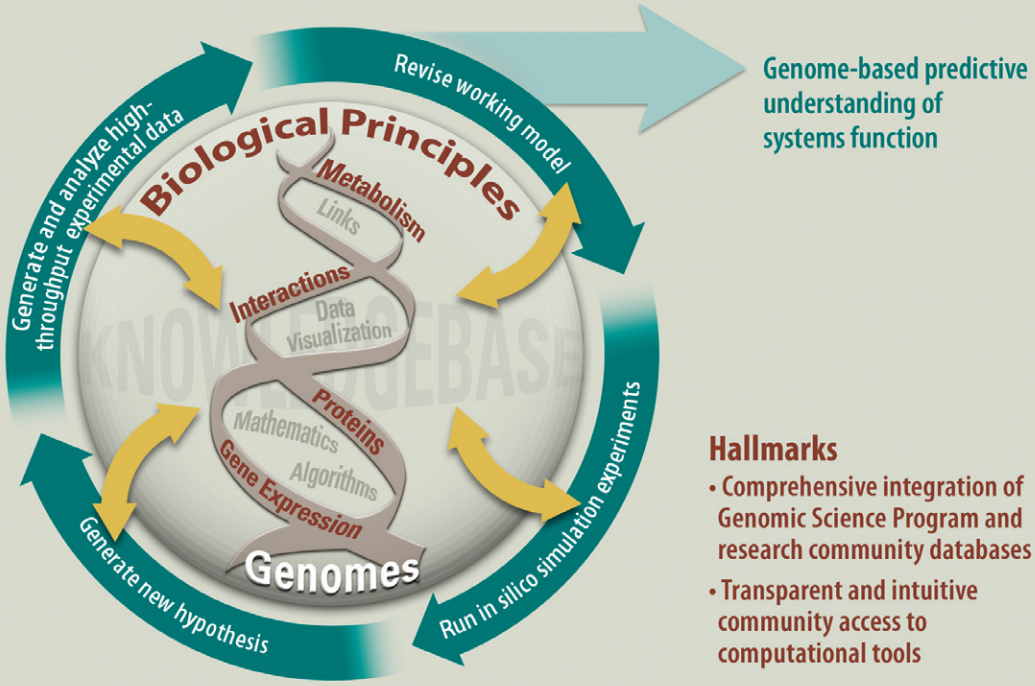
Achieving a predictive understanding of biological systems is a daunting challenge and will require the integration of immense amounts of diverse information—functional descriptions assigned to DNA sequence, molecular interactions, images of molecules or physical structures within an organism, and details about the environment in which an organism lives. These types of information typically have not been integrated and compared, and the heterogeneous mix of data emanating from the Genomic Science program will span diverse environmental conditions, spatial scales (nanometers to kilometers), and temporal scales (nanoseconds to decades).



To address this grand challenge, DOE will develop a Systems Biology Knowledgebase to facilitate a new level of scientific inquiry (see figure, Building the Systems Biology Knowledgebase). The Genomic Science program defines the Knowledgebase as an integrated experimental framework for accessing, analyzing, modeling, and testing diverse data on complex biological systems. In addition to empowering scientists with free and broad access to diverse data types, the Systems Biology Knowledgebase will also provide sophisticated tools for data analysis, visualization, and integration. The Knowledgebase will enable a more comprehensive understanding of how biological systems work and more accurate predictions of system behaviors—knowledge needed to develop biologically inspired solutions to some of the most pressing energy and environmental challenges.

Building the Systems Biology Knowledgebase

Revealing biological principles will lead to an increasingly accurate understanding of function



Hallmarks

- Comprehensive integration of Genomic Science Program and research community databases
- Transparent and intuitive community access to computational tools

DOE Office of Science

DOE's Office of Science, which operates 10 world-class national laboratories, is the nation's single-largest supporter of basic physical science research and helps ensure U.S. world leadership across a broad range of scientific disciplines. Within the Office of Science, BER manages facilities and the Genomic Science program and supports research in life sciences, climate change, environmental remediation, and medical applications and measurement science.

Contact and Websites for More Information

U.S. Department of Energy Office of Science
Office of Biological and Environmental Research
Email: genomic.science@science.doe.gov

DOE Genomic Science Program (formerly Genomics:GTL)
science.doe.gov/ober/BSSD/genomicsgtl.html
genomicscience.energy.gov

Genomics:GTL Strategic Plan genomicscience.energy.gov/strategicplan/

Genomics:GTL Roadmap genomicscience.energy.gov/roadmap/

DOE Mission Focus: Biofuels genomicscience.energy.gov/biofuels/

DOE Bioenergy Research Centers genomicscience.energy.gov/centers/

DOE BER Structural Biology
science.doe.gov/ober/BSSD/struct_bio.html

DOE Joint Genome Institute jgi.doe.gov

DOE Environmental Molecular Sciences Laboratory
www.emsl.pnl.gov/emslweb/

Genomic Science Information and Data Sharing Policy
genomicscience.energy.gov/datasharing/

Genomic Science Image Gallery genomics.energy.gov/gallery/

Breaking the Biological Barriers to Cellulosic Ethanol: A Joint Research Agenda
genomicscience.energy.gov/biofuels/b2bworkshop.shtml

DOE Carbon Cycling and Biosequestration Workshop
genomicscience.energy.gov/carboncycle/

DOE Characterizing Biological Systems Workshop
genomicscience.energy.gov/characterization/

DOE Systems Biology Knowledgebase Workshop
genomicscience.energy.gov/compbio/

DOE–USDA Sustainability of Biofuels Workshop
genomicscience.energy.gov/biofuels/sustainability/

DOE–USDA Plant Feedstock Genomics for Bioenergy
genomicscience.energy.gov/research/DOEUSDA/

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DOE Office of Science Grants and Contracts
science.doe.gov/grants/grants.html

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