DOE Genomic Science Program

Systems Biology for Energy and the Environment

genomicscience.energy.gov science.energy.gov/ber/research/bssd/genomic-science/

Advancing Scientific Discovery Through Genomics and Systems Biology

Understanding the instructions for life encoded in the DNA sequence, or genome, of natural systems offers a wealth of potential for advancing biological solutions to many of today's energy and environmental challenges. To harness this potential, the U.S. Department of Energy (DOE) Genomic Science program supports fundamental research to understand the systems biology of plants and microbes as they respond to and modify their local environments. 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—synthesizing decades of reductionist studies that identified and characterized individual components.

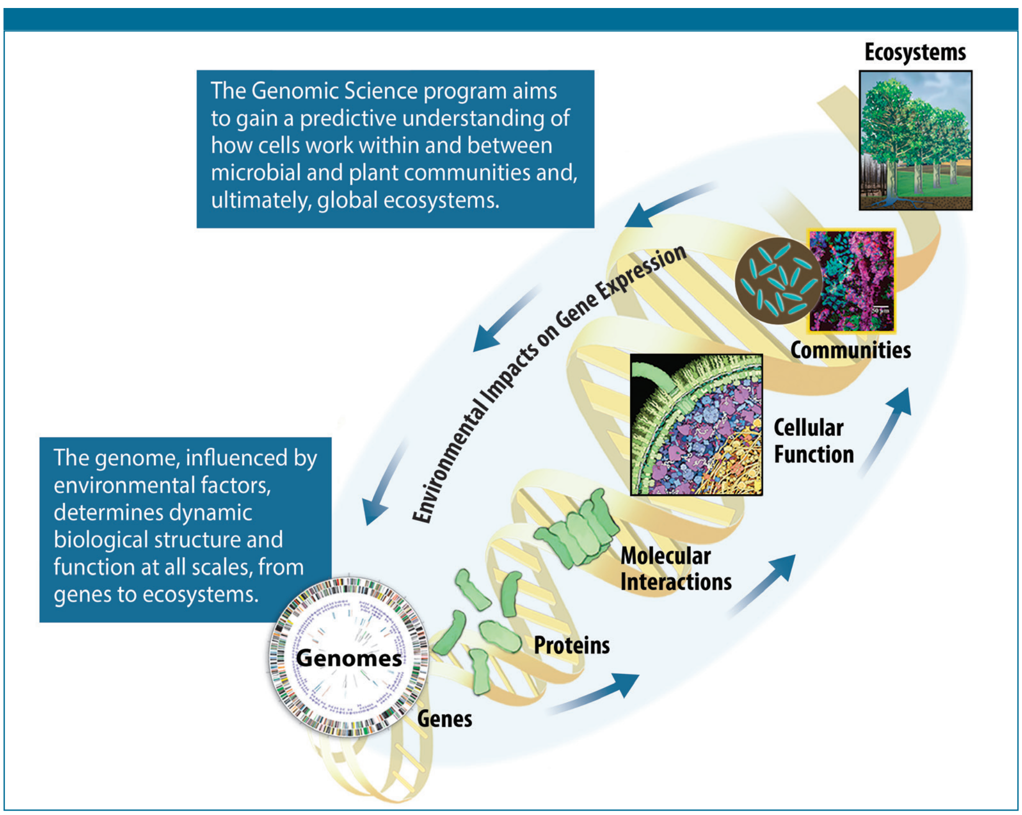
As a leader in systems biology research, the Genomic Science program uses genome sequences as the blueprint for understanding the common principles that govern living systems. Knowledge of these common principles revealed by studying organisms relevant to one DOE mission facilitates breakthroughs in the basic biology important to other DOE and national needs.

By examining the translation of genetic codes into functional proteins, biomolecular complexes, metabolic pathways, and regulatory networks, Genomic Science research focuses on the grand challenge of developing a mechanistic, predictive understanding of plant and microbial system behavior across a range of scales, from genes to small ecosystems (see figure, Multiscale Explorations for Systems Understanding). Scientific insights achieved in pursuit of this challenge will enable, for example, the design and re-engineering of plants and microbes for DOE missions in sustainable advanced biofuels and bioproducts, improved carbon storage capabilities, and controlled biological transformation of materials such as nutrients and contaminants in the environment.

The Genomic Science program is part of the Office of Biological and Environmental Research within DOE's Office of Science.

Genomic Science Approaches

Addressing extremely complex science questions that span all scales of biology, research supported by the 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, including



Multiscale Explorations for Systems Understanding. *Achieving a predictive understanding of fundamental life processes requires investigations that span multiple levels, from the information encoded in individual plant and microbial genomes to the functioning of cells as communities in an ecosystem. Important to this challenge is understanding the complex interactions between each level of biological organization and the environment.*

GENOMIC SCIENCE PROGRAM

Systems Biology for Energy and the Environment

Fundamental Genomic Science research includes single-investigator projects, multi-institutional collaborations, and research centers at universities and national laboratories across the country.

RESEARCH PORTFOLIO

BIOENERGY RESEARCH CENTERS

Provides technologies and scientific insights across four multi-partnership centers laying the groundwork for sustainable, cost-effective advanced biofuels and bioproducts from lignocellulosic plant biomass.

SYSTEMS BIOLOGY FOR BIOENERGY

Improves fundamental understanding of microbes with bioenergy-relevant traits for deconstructing biomass and synthesizing biofuels and bioproducts.

PLANT SCIENCE FOR BIOENERGY

Elucidates and validates the functional role of genes, gene families, and associated pathways to enhance understanding of critical processes in DOE-relevant plant systems.

SUSTAINABILITY RESEARCH FOR BIOENERGY

Investigates plant-soil-microbe interactions in laboratory and field settings to enhance biomass productivity under changing biotic and abiotic conditions.

BIOSYSTEMS DESIGN

Develops knowledge for engineering useful traits into plants and microbes to produce biofuels and bioproducts and to advance biotechnology.

ENVIRONMENTAL MICROBIOME SCIENCE

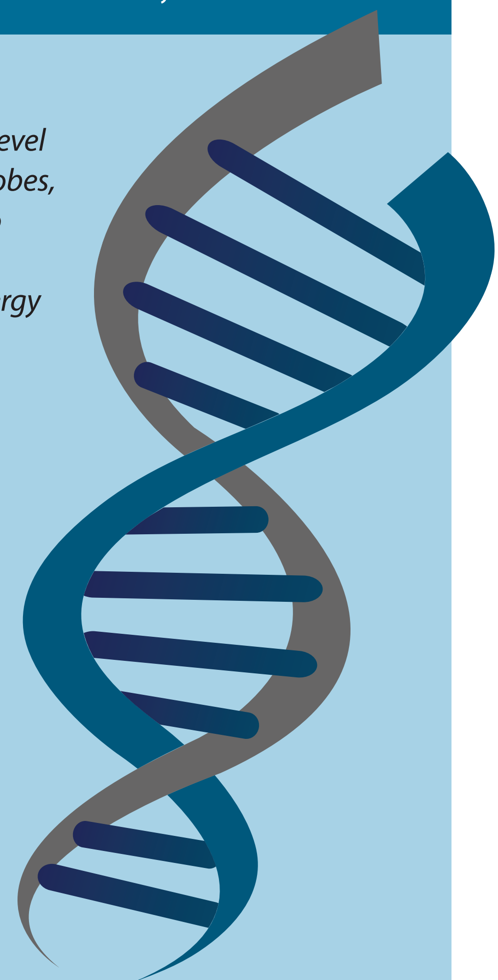
Links structure and function of microbial communities in the field with key environmental or ecosystem processes.

COMPUTATIONAL BIOLOGY

Provides new computational approaches and hypothesis-generating analysis techniques, data, and simulation capabilities such as the DOE Systems Biology Knowledgebase (KBase) to accelerate collaborative, reproducible systems science.

GOAL

Achieve a predictive, systems-level understanding of plants, microbes, and biological communities to enable biobased solutions to DOE mission challenges in energy and the environment.



OBJECTIVES

1. **Determine the molecular mechanisms, regulatory elements, and integrated networks needed to understand genome-scale functional properties of biological systems.**
2. **Develop omics experimental capabilities and enabling technologies needed to achieve dynamic, systems-level understanding of organism and community function.**
3. **Flexibly scale understanding of biological processes from defined subsystems to individual organisms, consortial assemblies of multiple organisms, or complex communities operating at ecosystem scales.**
4. **Understand the principles governing living systems and develop tools for more sophisticated biosystems design, enabling the targeted modification of functional properties at the genome scale.**
5. **Develop the knowledgebase, computational infrastructure, and modeling capabilities to advance predictive understanding and manipulation of biological systems.**

genomicscience.energy.gov

SYNERGIES WITH ENABLING BER PROGRAMS AND USER FACILITIES

DOE JOINT GENOME INSTITUTE

jgi.doe.gov

Provides high-quality sequence data and analysis techniques for plants, microbes, and their communities in support of bioenergy and environmental research.

BIOIMAGING TECHNOLOGY

science.energy.gov/ber/bioimaging-research/

Develops imaging, measurement, and characterization platforms to visualize the spatial and temporal relationships of key plant and microbial metabolic processes.

STRUCTURAL BIOLOGY INFRASTRUCTURE

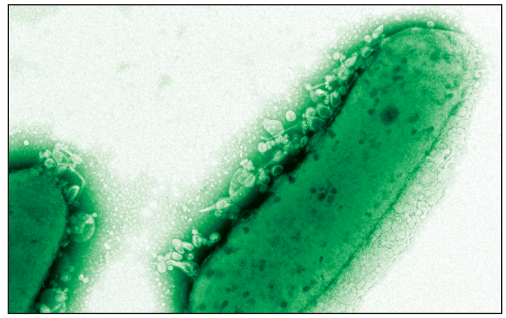
www.berstructuralbioportal.org

Provides specialized instruments at light and neutron facilities to understand the properties and structures of biological molecules and link this information to function.

ENVIRONMENTAL MOLECULAR SCIENCES LABORATORY

www.emsl.pnl.gov

Provides tools for characterizing molecules to organisms, including the chemical constituents and dynamics of complex natural systems (e.g., soil microbiome).



Research in Sustainable Bioenergy. *(Left)* Miscanthus*, shown here, and energy cane will be engineered for high oil production in the cells of plant stems to create a sustainable supply of biodiesel. (Right) Lipid droplets escape from a bacterium cell through the cell envelope, which researchers modified to increase lipid production. [Left image courtesy Brian Stauffer, University of Illinois. Right image courtesy Donohue Lab, University of Wisconsin–Madison, and Great Lakes Bioenergy Research Center]*

genomics and metagenomics, analytical "omics," molecular imaging and structural analysis, predictive modeling, and genome-scale engineering.

Genomics and Metagenomics. Sequencing and analyzing DNA from individual organisms (genomics) or microbial communities in environmental samples (metagenomics) form the foundation for systems biology research. The DOE Joint Genome Institute is an important scientific user facility that generates high-quality sequences and analysis techniques for diverse microbes, plants, and other organisms relevant to DOE energy and environmental missions.

Analytical Omics. Transcriptomics, proteomics, metabolomics, and other analyses—collectively described as "omics"—identify and measure the abundance and fluxes of key molecular species indicative of organism or community activity. Global analyses of important cellular components such as RNA transcripts, proteins, and metabolites inform scientists about organisms' physiological status. This research, along with chemical and structural analytical technologies including stable isotope tracking and nano secondary ion mass spectrometry (NanoSIMS), also provides insights into gene function and indicates which genes are activated and translated into functional proteins as organisms and communities develop or respond to environmental cues. Methods that analyze DNA, RNA, proteins, and other molecules extracted directly from environmental communities enable discovery of new biological processes and provide novel insights into relationships between the composition of communities and the functional processes that they perform.

Molecular Imaging and Structural Analysis. Genomic Science program 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 tools (e.g., synchrotrons, neutron sources, and electron microscopes) are available at DOE Office of Science user facilities that provide state-of-the-art spatial, temporal, and chemical measurement sensitivity.

Predictive Modeling. Computational models are used to capture, integrate, and represent current knowledge of biology at various scales. Researchers are using genome sequences and molecular, spatial, and temporal data to build models of signaling networks, gene regulatory circuits, and metabolic pathways that can be iteratively tested and validated to refine system understanding.

Genome-Scale Engineering. Genomes and systems-level understanding are uncovering the principles that govern system behavior, enabling genome-scale redesign of organisms. This research approach may involve building entirely new microbes 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.

Investigations and Research Areas of Interest

Bioenergy. Development of innovative approaches for sustainable bioenergy production will be accelerated by systems biology–based understanding of both nonfood plants that can serve as dedicated bioenergy feedstocks and microbes that can break down plant cellulosic biomass (e.g., stems and leaves) and synthesize biofuels and bioproducts from the component cell wall monomers (see image, Research in Sustainable Bioenergy). In addition to funding single-investigator and team projects in this research area, the Genomic Science program supports four DOE Bioenergy Research Centers (see sidebar, on back).

Biosystems Design. Research in this area continues to help advance the rapidly developing field of bioengineering, often referred to as synthetic biology. Cutting-edge genome-scale engineering tools are opening new avenues for systems biology research, enabling the design of tailored plants and microbes while advancing fundamental understanding of biological function and inspiring novel approaches for its manipulation on a large scale.

DOE Bioenergy Research Centers

Bringing together top scientists from multiple disciplines, the Genomic Science program launched the next phase of the DOE Bioenergy Research Centers (BRCs) to provide the fundamental insights, technologies, and knowledgebase underpinning sustainable, cost-effective production of advanced biofuels and bioproducts from lignocellulosic plant biomass.

Over the past decade, the BRCs have led the world in fundamental biofuels research. Progress and breakthroughs include a deepened understanding of sustainable biomass production practices, targeted re-engineering of biomass feedstocks, development of new methods for their deconstruction, and engineering of microbes for more effective production of diverse biofuels. Building on these successes, the centers are conducting new research to tackle remaining basic science challenges in sustainability, feedstock development, lignocellulosic deconstruction and separation, and conversion to advanced biofuels (beyond ethanol) and bioproducts. A new focus for BRC research, bioproducts include nonpharmaceutical chemicals that can directly replace chemicals currently derived from petroleum or natural gas as well as novel chemicals that cannot be efficiently produced from petroleum.

The BRCs are structured to facilitate knowledge sharing among multiple disciplines so that breakthroughs in one area can be leveraged in other areas. Moreover, the centers approach the science challenges from varied perspectives to accelerate progress and speed translation of fundamental insights and results to industry.

Selected through a scientific peer review process, the four BRCs are based in geographically diverse locations—the Midwest, Southeast, and West Coast. BRC partners include universities, private companies, nonprofit organizations, and DOE national laboratories.

- **Center for Advanced Bioenergy and Bioproducts Innovation** (CABBI; University of Illinois at Urbana-Champaign) seeks to enable the production of fuels and chemicals directly in plants as sustainable biofactories for a range of bioproducts.
- **Center for Bioenergy Innovation** (CBI; Oak Ridge National Laboratory) is accelerating the domestication of bioenergy crops and targeted consolidated bioprocessing innovations to improve cost efficiencies within the bioenergy supply chain.
- **Great Lakes Bioenergy Research Center** (GLBRC; University of Wisconsin-Madison) aims to develop the science and technological advances to ensure sustainability at each step in the process of creating biofuels and bioproducts from lignocellulose.
- **Joint BioEnergy Institute** (JBEI; Lawrence Berkeley National Laboratory) is broadening and maximizing production of economically viable biofuels and bioproducts from plant biomass to enable biorefinery development.

More information on the BRCs is available at genomicscience.energy.gov/centers/.

Environmental Microbiome Science. Omics-driven tools of modern systems biology are used to analyze interactions among microbial communities, plants, and their surrounding environments. Understanding the relationships between molecular-scale functional biology and ecosystem-scale environmental processes illuminates the basic mechanisms that drive key processes such as biogeochemical cycling of metals and nutrients, carbon biosequestration, and greenhouse gas emissions in terrestrial ecosystems. As part of this research, new techniques are being developed to analyze key bioprocesses in field settings.

Computational Biology. The ever-increasing complexity and diversity of data emanating from research within the Genomic Science program requires computational approaches to integrate these datasets and simplify their analysis and interpretation. The DOE Systems Biology Knowledgebase (KBase; kbase.us) is developing hypothesis-generating analysis techniques and simulation capabilities on high-performance computing platforms to accelerate collaborative, reproducible systems biology science, paving the way for new knowledge generation. Current KBase capabilities include apps for genome assembly, annotation, comparative genomics, metabolic modeling, expression analysis, and more. Also supported are capabilities for tool development and integration by third parties.

DOE Office of Science

The DOE Office of Science manages fundamental research programs in basic energy sciences, high-energy physics, fusion, biological and environmental sciences, and computational science. It also manages 10 world-class national laboratories with unmatched capabilities for solving complex interdisciplinary scientific problems and oversees the construction and operation of some of the nation's most advanced scientific user facilities, located at national laboratories and universities. These include particle and nuclear physics accelerators, synchrotron light sources, neutron scattering facilities, supercomputers and high-speed computer networks, nanoscale science centers, genome sequencing and analysis facilities, and advanced resources in imaging and analysis for biological and environmental systems.

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