Office of Biological and Environmental Research Biological Systems Science Division Strategic Plan

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U.S. DEPARTMENT OF ENERGY | Office of Science

Office of Biological and Environmental Research

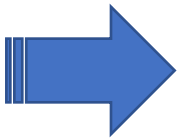
Fundamental Guiding Questions for BER Genomic Science

1. What information is encoded in a genome sequence, and how does this information direct the functional characteristics of cells, organisms, and whole biological systems?

2. How do interactions among cells regulate the functional behavior of living systems, and how can these interactions be understood dynamically and predictively?

3. How do plants, microbes, and communities of organisms adapt and respond to changing environmental conditions (e.g., temperature, water and nutrient availability, and ecological interactions), and how can their behavior be manipulated toward desired outcomes?

4. What organizing biological principles need to be understood to facilitate the design and engineering of new biological systems for beneficial purposes?



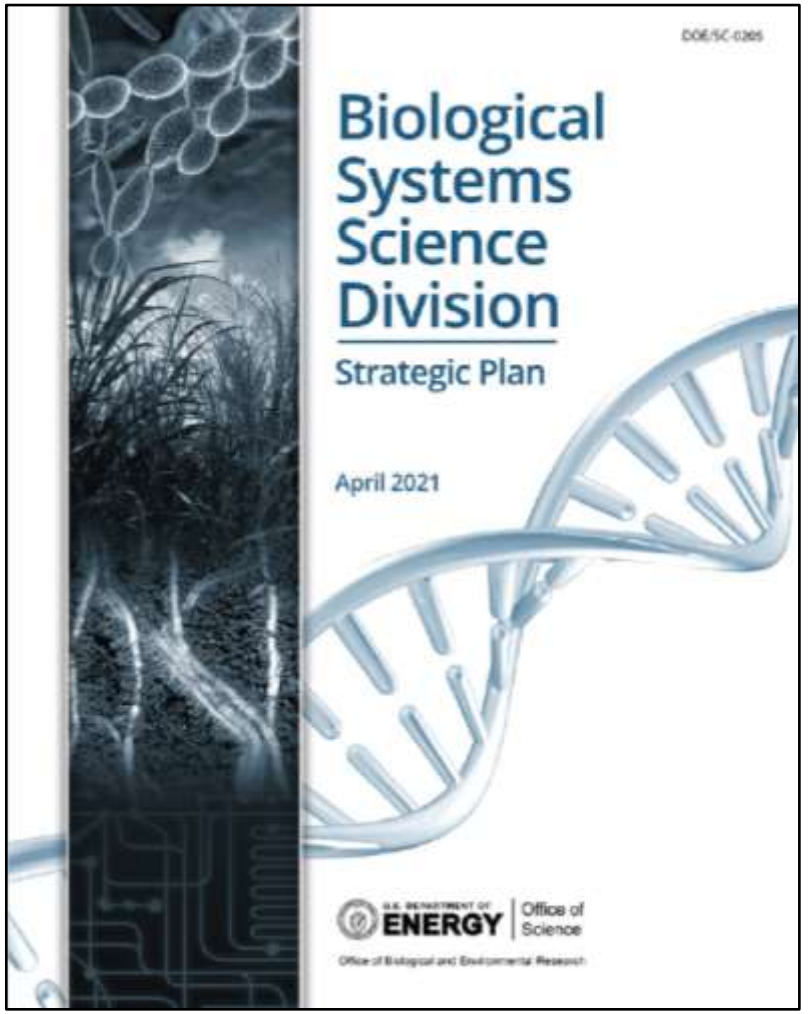
DOE Mission Areas in Bioenergy and Environmental Research

Update and Revision to the 2015 Biological Systems Science Division Strategic Plan

- Communicate a more integrative structure to the BSSD portfolio
- Provide more detail on science directions
- Identify areas for future efforts

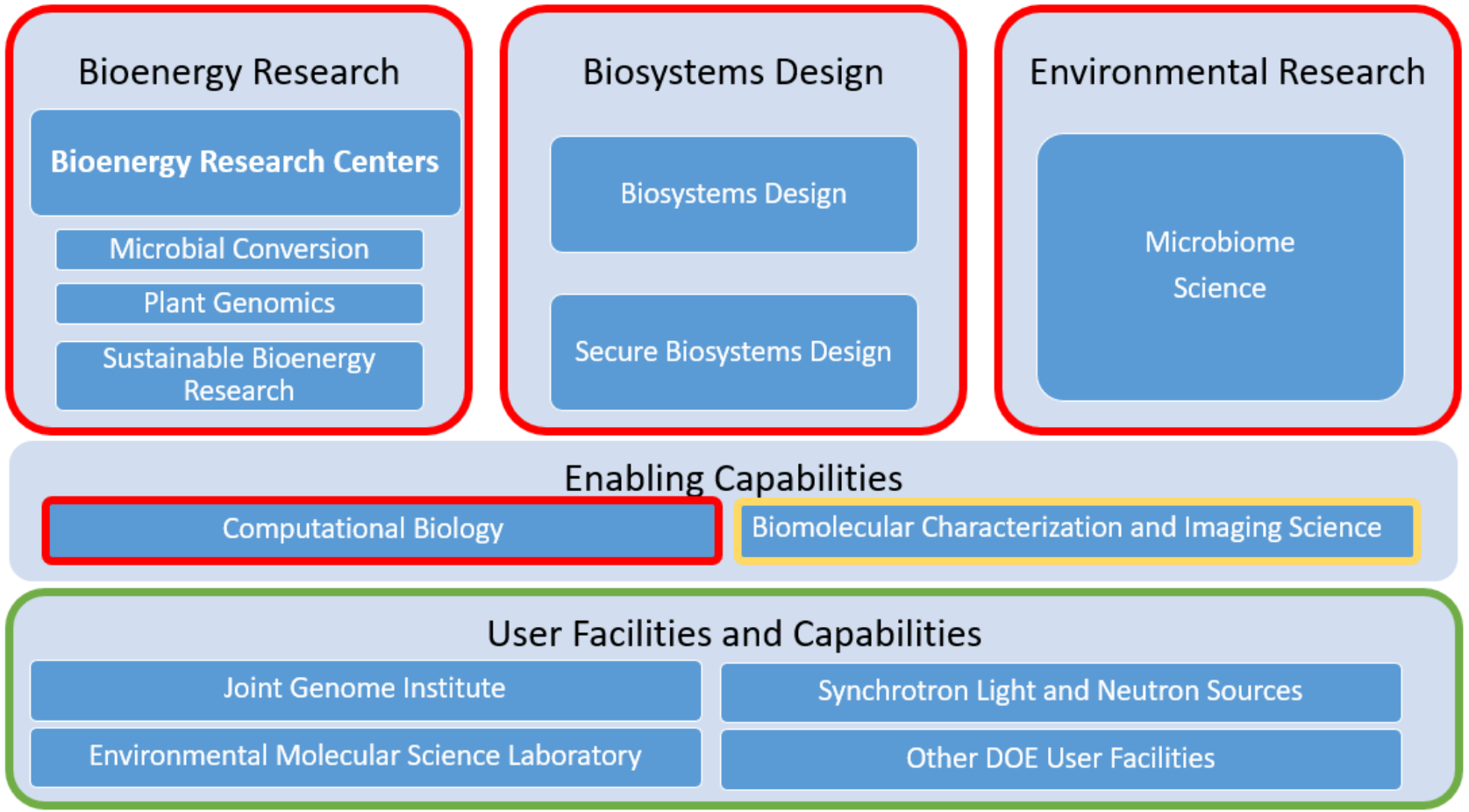
Overall Goal

Provide the necessary fundamental science to understand, predict, manipulate, and design biological systems that underpin innovations for bioenergy and bioproduct production and enhance our understanding of natural, DOE-relevant environmental processes.



[BSSD Strategic Plan - April 2021]

BSSD Research Portfolio



- Three main Research efforts:
  - Bioenergy
  - Biosystems Design
  - Environmental Research
- Range of large and small team projects and individual PI efforts.
- Supported by Enabling capabilities
- Access to JGI, EMSL and the DOE Light sources

Complemented by:

- Small Business Innovative Research (SBIR/STTR) awards
- Early Career awards
- SC Graduate Student Research
- EPSCoR (intermittent)

Genomic Science Program

Biomolecular Characterization and Imaging Science

User Facilities and Capabilities

Bioenergy Research

Goal: Provide the basic science needed to convert renewable biomass to a range of fuels chemicals, and other bioproducts in support of a burgeoning bioeconomy.

- *Plant Genomics*

Subgoal: *Gain a genome-level understanding of plant metabolism, physiology, and growth to develop new bioenergy feedstocks with traits tailored for bioenergy and bioproduct production.*

- *Microbial Conversion*

Subgoal: *Develop an understanding of microbial and fungal metabolism necessary to design new strains, communities, or enzymes capable of converting plant biomass components into fuels, chemicals, and bioproducts.*

- *Sustainable Bioenergy*

Subgoal: *Understand the genomic properties of plants, microbes, and their interactions to enable the development of new approaches that improve the efficacy of bioenergy crop production on marginal lands with few or no agricultural inputs, while minimizing ecological impacts.*

Bioenergy Research Mechanisms

Bioenergy Research Centers (BRCs)

- **Great Lakes Bioenergy Research Center (GLBRC)**
  University of Wisconsin, Michigan State University (https://www.glbrc.org/)
- **Joint BioEnergy Institute (JBEI)**
  Lawrence Berkeley National Laboratory (https://www.jbei.org/)
- **Center for Bioenergy Innovation (CBI)**
  Oak Ridge National Laboratory (https://cbi.ornl.gov/)
- **Center for Advanced Bioenergy and Bioproducts Innovation (CABBI)** University of Illinois (UIUC) (https://cabbi.bio/)

Complementary FOA-led and Lab-Led Efforts in:

- *Plant Genomics*
- *Microbial Conversion*
- *Sustainability Bioenergy*

Large Team-oriented science addressing a continuum of bioenergy challenges

Small teams and/or single PIs. Broaden research on:

- ***bioenergy plant species***
- ***microbial species with bioenergy traits and,***
- ***interactions between microbes and plants in the field***

Plant Genomics

Subgoal: *Gain a genome-level understanding of plant metabolism, physiology, and growth to develop new bioenergy feedstocks with traits tailored for bioenergy and bioproduct production.*

- Discover and functionally characterize key plant genes that influence yield and/or confer adaptability or resilience to a range of environmental conditions.
- Understand the distinct functions of genes, proteins, and metabolites of the multiple cell types.
- Investigate genetic and epigenetic regulatory mechanisms and methods to discern regulatory differences among gene family members. Develop comparative approaches to enhance knowledge of the organization of plant genomes and to identify reduced sets of candidate genes for detailed functional characterization across related species.
- Determine high-resolution molecular structures of proteins/enzymes and assemblies to identify and prioritize structural features affecting their function and specificity.
- Dissect complex phenotypes (e.g., yield as well as water and nutrient use) into genetic components and use natural variants, mutants, gene editing, and transgenes to validate gene function and impact on phenotype.
- Develop and validate methods to map quantitative associations within clades using synteny, homology, cross-species co-expression networks, and other such analyses.
- Examine the complex interactions between bioenergy feedstock plants and their environment and the influence of these interactions on plant growth and adaptation to changing environments.
- Develop new knowledge of biomass deconstruction processes to convert a broader range of biomass types into a range of precursors that are readily convertible into biofuels and bioproducts.
- Increase degradability and expand usability of biomass components (e.g., hemicellulose and lignin monomers).

Microbial Conversion

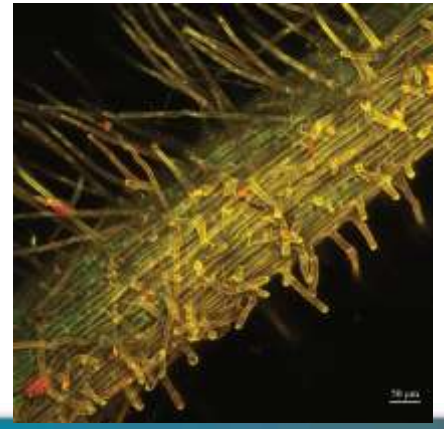
Subgoal: *Develop an understanding of microbial and fungal metabolism necessary to design new strains, communities, or enzymes capable of converting plant biomass components into fuels, chemicals, and bioproducts.*

- Discover and develop new microorganisms with unusual or enhanced capabilities for converting plant biomass to next-generation biofuels, bioproducts, or biomaterials.
- Identify and characterize novel molecular structures, functional capabilities, and biosynthetic pathways that may help to increase the yield and/or synthesis of advanced biofuels, bioproducts, and biomaterials.
- Uncover the functional relationships within microbiomes and defined consortia that harbor the potential to produce biofuels, bioproducts, or biomaterials.
- Identify mechanisms for enhanced strain tolerance to physicochemical stresses associated with industrial-scale production (e.g., elevated temperature, altered pH levels, product toxicity, and toxin release).
- Develop the necessary high-throughput omics-based tools to design, build, and test microbial solutions and enhance their biofuel, bioproduct, and biomaterial production properties.

Sustainable Bioenergy

Subgoal: *Understand the genomic properties of plants, microbes, and their interactions to enable the development of new approaches that improve the efficacy of bioenergy crop production on marginal lands with few or no agricultural inputs, while minimizing ecological impacts*

- Develop high-throughput, nondestructive, and analytical techniques to measure plant and microbial phenotypes or functional processes in the environment.
- Expand understanding of genetic diversity and validate the functions of genes, genomic regulatory networks, and metabolites in plants and microbes, particularly those that enable crop adaptation to extreme conditions, changing environments, and episodic environmental events.
- Use biological data to model resource allocations and bottlenecks within bioenergy crop production systems to identify plant functional properties that can be modified to increase biomass degradability, increase yield, and enhance other desirable traits.
- Advance understanding of plant-microbe interactions and their influence on plant growth and stress responses and improve insights on how microbiome and plant diversity help deliver sustained ecological services in the environment.
- Understand microbially mediated soil biogeochemical processes (e.g., nitrogen cycling, greenhouse gas emissions, or carbon stabilization) and their impact on the sustainability of bioenergy cropping systems.
- Develop computational tools to process and use complex and large data architectures that include physiological, molecular, and spatial information such as above- and belowground plant architecture, soil chemistry, nutrient and water use efficiency, and multiomics data.
- Develop process-based, multiscale models to predict cropping and ecosystem behavior under changing environmental conditions.



Biosystems Design Research

Goal: *Advance fundamental understanding of genome biology and develop the genome-scale engineering technologies needed to design, build, and control plants and microbes for desired beneficial purposes.*

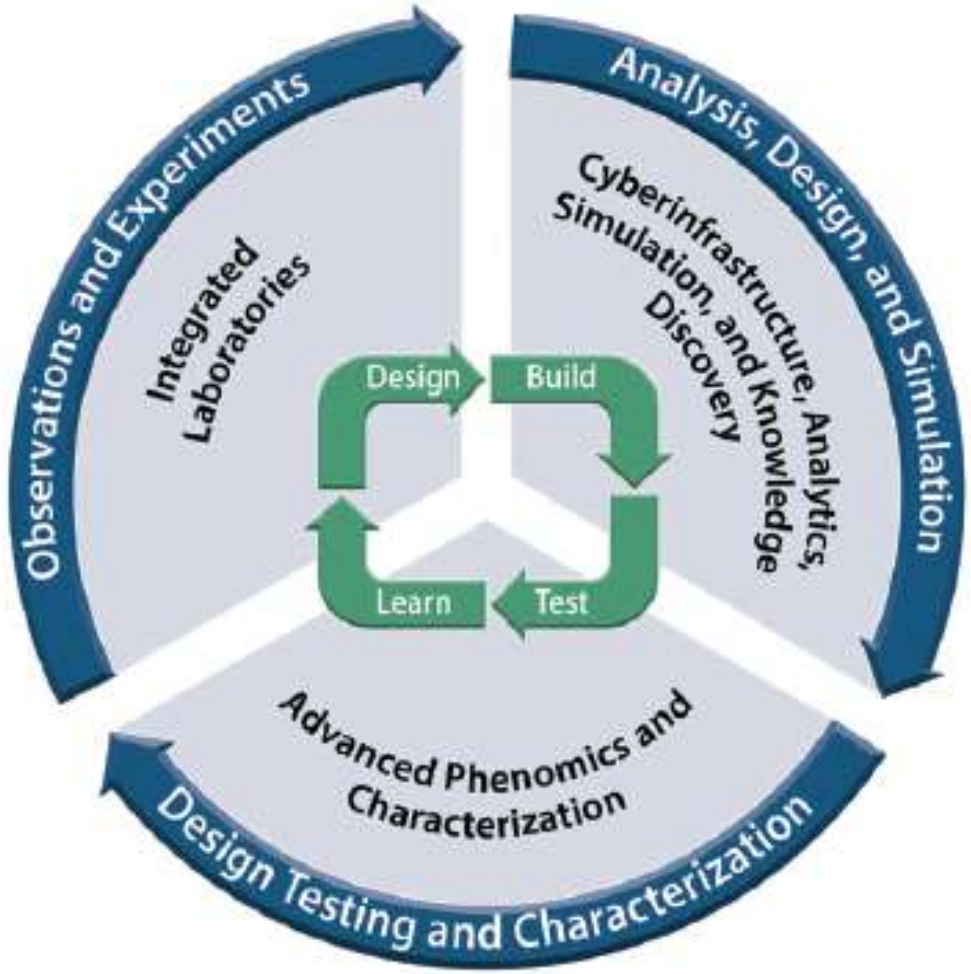
- Develop platform organisms across a range of physiologies as chassis for synthetic biology.
- Develop genome-engineering tools, including large-scale DNA synthesis and intracellular delivery, recoded and minimal genomes, orthogonal pathways, and cell-free systems.
- Develop high-throughput genome editing, screening, characterization and phenotyping of engineered organisms.
- Elucidate gene function at the genome scale to develop generalized approaches for biological engineering.
- Provide computer-aided design tools, including AI/ML techniques, in an integrated, open-access platform for plants and microbes as part of an *in silico* or virtual laboratory capability.
- Develop characterization tools to understand processes of organic and inorganic synthesis and degradation in engineered organisms.
- Elucidate mechanisms for the acquisition, storage, transport and transformation of substrates in engineered organisms.
- Build new genetic, regulatory, and biosynthetic networks to biologically produce useful molecules and materials.
- Develop new approaches for novel macromolecular design, characterization, and testing.
- Expand the “design-build-test-learn” cycle to organismal consortia.

Accelerating Biotechnology

DOE-Supported Research at National Laboratories and Universities

DOE Scientific User Facilities

- Environmental Molecular Sciences Laboratory
- Joint Genome Institute
- Light and Neutron Sources
- Nanoscale Science Research Centers



DOE and Community Resources for Data and Computational Analysis

- DOE National Microbiome Data Collaborative
- DOE Systems Biology Knowledgebase
- DOE Materials Project
- DOE Supercomputing Capabilities
- Protein Data Bank

Secure Biosystems Design

Subgoal: *Build on advances in genome science and synthetic biology to design and engineer DOE-relevant biological systems with built-in biocontainment measures and develop strategies to address risks of unintended consequences, while enabling a sustainable bioeconomy.*

- Develop approaches to understand and enhance stability, resilience, and controlled performance of DOE-relevant plant and microbial systems in their natural environments.
- Research novel biocontainment strategies such as gene drives, non-natural metabolite dependency, and genetic isolation, as well as prevention of evolution and horizontal gene transfer.
- Develop computational and experimental strategies to detect, predict, and ameliorate the effects of engineered organisms in different environments.
- Explore the potential for engineering plants, microbes, and microbiomes to detect or control other engineered organisms released into the environment.

Environmental Microbiome Research

Goal: *Develop a process-level understanding of microbiome function and be able to predict ecosystem impacts on the cycling of materials (carbon, nutrients, and contaminants) in the environment.*

- Develop environmental omics approaches and tools to investigate microbial community function.
- Facilitate realistic recapitulations of microbial ecosystems that move beyond the simple characterization of microbial diversity in the environment.
- Consider complex interkingdom biological dependencies among soil microbial community.
- Provide a framework for predictive modeling to understand community function and dynamics by using omics data.
- Leverage omics and modeling approaches to understand the rate and magnitude of microbially mediated biogeochemical cycles to understand feedbacks with and responses to global change.
- Develop techniques to manipulate microbiomes for beneficial purposes.
- Facilitate novel approaches to functional gene characterization, including the use of data science tools (e.g., AI/ML) and infrastructure elements of BSSD's portfolio (e.g., KBase, JGI, and NMDC).
- Develop techniques to image microbial community structure and function in terrestrial environments, with an emphasis on technically challenging settings such as soils, sediments, and key interfacial environments.
- Combine omics with *in situ* technologies that enable nondestructive, high-throughput sampling or measurements of microbial communities to understand process-level interactions.
- Seek a mechanistic understanding of cell-to-cell interactions, signaling, resource sharing, and communication at molecular, cellular, and community scales.

Enabling Capabilities

Goal: *Support the development of computational and instrumental platforms to enable broader integration and analysis of large-scale complex data within BER's multidisciplinary research efforts.*

Computational Biology: Integrated Computational Platforms

Subgoal: *Create open-access and integrated computational capabilities tailored to large-scale data science investigations for molecular, structural, genomic, and omics-enabled research on plants and microorganisms for a range of DOE mission goals.*

Biomolecular Characterization and Imaging Science

Subgoal: *Improve or develop new multifunctional, multiscale imaging and measurement technologies that enable visualization of the spatiotemporal and functional relationships among biomolecules, cellular compartments, and higher-order organization of biological systems*

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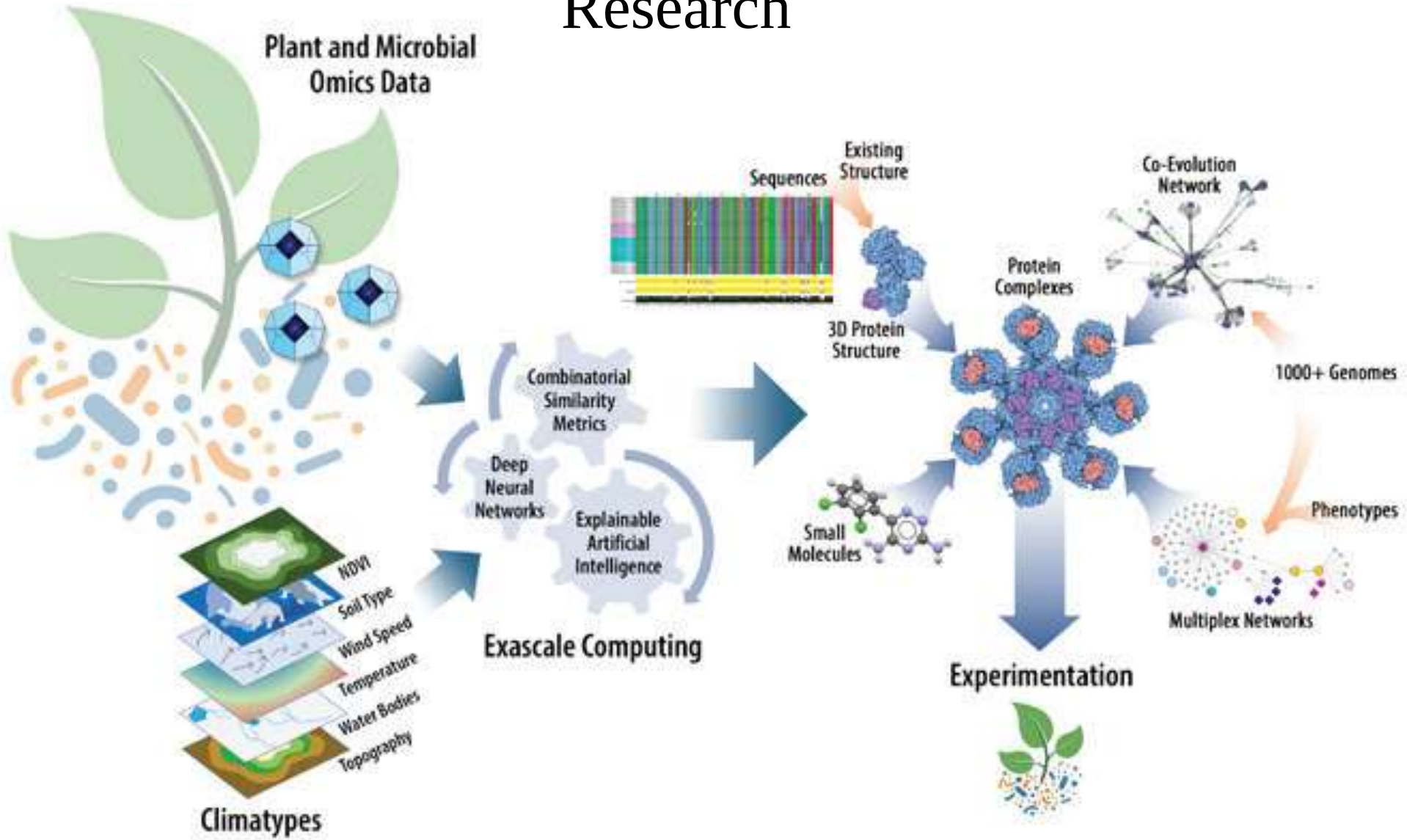
*Spans both the Genomic Science Research and Enabling Capabilities

- Assemble capabilities for processing large, complex systems biology data into open-access analysis platforms addressing DOE missions.
- Create the next-generation data systems needed for large-scale systems biology data science that connects observations across scales and integrates molecular, structural, genomic, and other omics data with cellular and multicellular processes.
- Develop explainable AI algorithms to identify relationships among different parts of genomes and build integrated biological models that capture higher-order complexity of the interactions among cellular components that lead to phenotypic differences.
- Generate advanced algorithms and data-handling techniques to integrate imaging and structural biology data with simulations and other biological measurements.
- Develop advanced simulation capabilities to model key processes at varying scales occurring within or among cells building toward whole-cell simulation.
- Assemble an integrated systems biology virtual laboratory to accelerate *in silico* ideation and collaboration within the research community.

KBase

NMDC

Integrated Systems Biology and High-Performance Computing Research



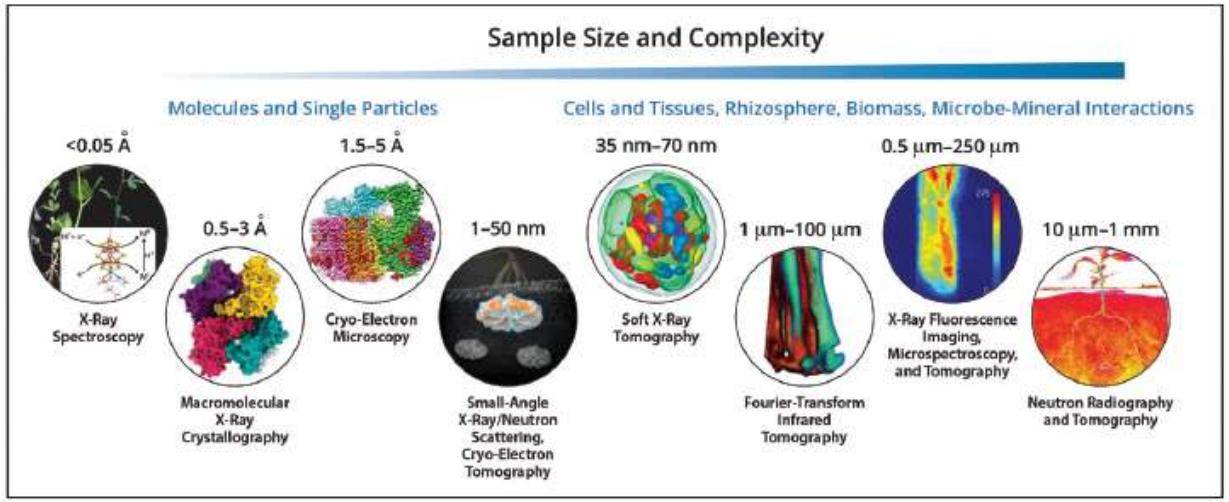
Biomolecular Characterization and Imaging Science

Structural Biology Portal and Cryo-EM

BER supports structural biology and imaging research via unique crystallography, scattering, spectroscopy, imaging, and cryogenic electron microscopy (cryo-EM) and tomography capabilities available at national neutron and light source user facilities operated by DOE's Office of Basic Energy Sciences. Cryo-EM is a novel technique that enables characterization of cellular structures and proteins without the need for crystallization.
(berstructuralbioportal.org)

Bio- and Quantum Imaging

BSSD supports research on multifunctional technologies to image, measure, and model key metabolic processes within and among microbial cells and multicellular plant tissues. This research includes new efforts to leverage quantum-based phenomena to develop novel imaging modalities.
(science.osti.gov/ber/bioimaging-research)



Biomolecular Characterization and Imaging Science

Subgoal: *Improve or develop new multifunctional, multiscale imaging and measurement technologies that enable visualization of the spatiotemporal and functional relationships among biomolecules, cellular compartments, and higher-order organization of biological systems*

- Enhance the accessibility of bioimaging and structural biology infrastructure within the research community and at DOE user facilities.
- Develop and enhance tools for sample handling and transfer, optimizing the samples for multiple imaging modalities and approaches.
- Develop fast and sensitive detectors with extremely high rates of data collection and the necessary computational tools to handle large, real-time, noisy, multimodal, and multiscale data.
- Develop multifunctional, *in situ*, and nondestructive observation technologies for repetitive sample analyses for systems biology research.
- Visualize the spatial and temporal dynamics of expressed biomolecules within or between living plant or microbial cells and their communities.
- Explore quantum science concepts for optical imaging and sensing of cellular processes.
- Incorporate newly developed technologies into DOE user facilities or provide opportunities for commercial development through DOE programs for Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR).

User Facility Integration

Goal: *Build unique, best-in-class capabilities within Office of Science user facilities (including JGI, EMSL, and DOE's light and neutron sources) to enhance the multidisciplinary Bioenergy Research, Biosystems Design, and Environmental Microbiome Research supported by the Division.*

- Establish scientific connections among multiple DOE user facilities to enable multidisciplinary users engaged in BSSD research.
- Align and create joint collaborative efforts among user facilities whose capabilities complement current research efforts within the Division.
- Create new capabilities at existing BER user facilities and among existing collaborative BSSD
- research efforts.
- Develop capabilities for integrating data within and among user facilities and capabilities for BER science.
- Provide platforms to enable integrated analysis of data generated across BER user facilities and capabilities.

Other Opportunities and Impact Multipliers

Office of Science Graduate Student Research Program

BSSD will seek to make a sustained commitment supporting the Office of Science Graduate Student Research (SCGSR) Program, which enables U.S. graduate students to conduct a portion of their research at a DOE national laboratory or facility. These graduate research awards are a key conduit for professional development and recruitment into the community of DOE-supported researchers.

Early Career Research Program

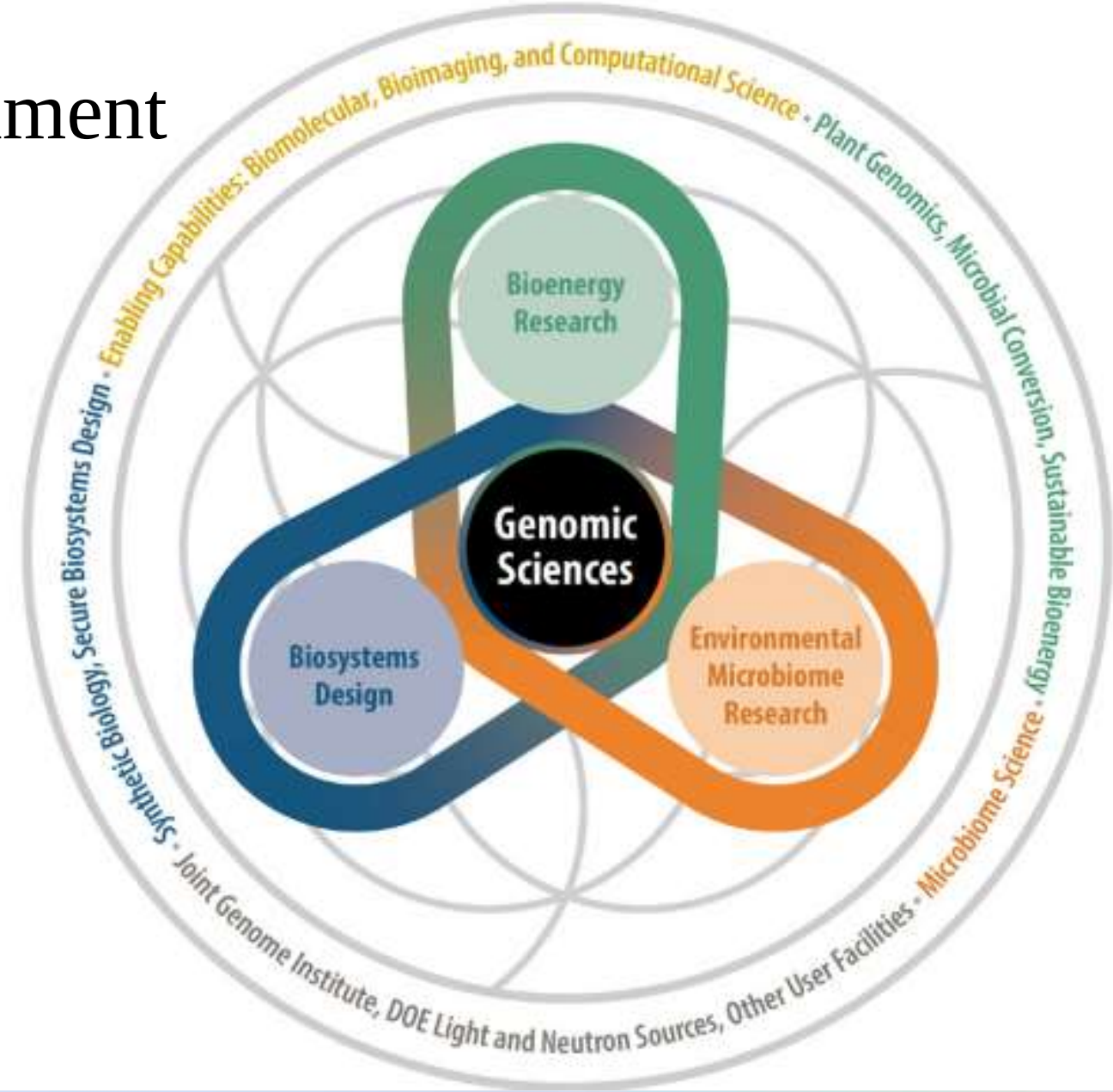
BSSD will continue to participate in DOE's Office of Science Early Career Research Program that supports exceptional young scientists and emerging thought leaders. BSSD topics within funding opportunity announcements (FOAs) for the Early Career Research Program will be tailored to reinforce existing portfolio elements
and will aim to support researchers with crosscutting, mission-relevant, and budding research programs.

Small Business Innovation Research and Small Business Technology Transfer

Complementary to its main basic science efforts, BSSD will provide opportunities for the small business commercial sector to pursue parallel research objectives through the SBIR/STTR Program

Building Towards a more Integrative Research Environment

Combining research with computational systems, enabling capabilities and User Facilities to meet DOE's basic science needs for bioenergy and environmental research



Thank you

https://science.osti.gov/ber

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