Physical Biosciences

Portfolio Description

This program supports basic research that combines physical science techniques with biochemical, chemical, and molecular biological approaches to discover the underlying physical and chemical principles that govern how plants and non-medical microbes capture, convert, and store energy. Fundamental research supported by the program includes studies that will provide a better understanding of the structure/function, mechanistic and electrochemical properties of enzymes that catalyze complex multielectron redox reactions (especially those involved in the interconversion of CO_2/CH_4, N_2/NH_3, and H^+/H_2), determine how the complex metallocofactors at the active sites of these enzymes are synthesized, and understand how the potential of these cofactors can be "tuned" using ligand coordination to reduce overpotential and better enable catalysis using earth-abundant metals. The program also funds mechanistic studies on electron bifurcation and catalytic bias in enzyme systems, and identifies the factors that direct and regulate the flow of electrons through energy-relevant metabolic pathways on larger spatial and temporal scales. Limited support is provided for basic research on the biosynthesis and structure of important electron stores in biological systems (such as plant cell walls, lipids, and terpenes), as well as for studies that will provide insight into the self-assembly and maintenance of biological energy transduction systems.

Scientific Challenges

The application of physical science and, increasingly, computational tools to understand at a fundamental level biological energy capture, conversion, and storage systems will provide important new insights that help address BES Grand Challenges (https://science.energy.gov/bes/community-resources/reports/). Analysis and control of electron flow in biological systems across a wide range of spatial and temporal scales is a significant scientific challenge, and can only be addressed with state-of-the-art techniques contributed from a wide variety of scientific disciplines. In this regard, the use of advanced molecular imaging, light sources, or neutron scattering methods will likely provide new and essential insights into enzyme catalysis and metabolic electron flux, as well as other ways that biological systems manage to efficiently meet their energy needs via mastery of several of the BES grand challenges. These scientific challenges require researchers to be trained in diverse disciplines; substantial progress has been made in developing the next generation of scientists with multidisciplinary expertise precisely because this activity is not defined by scientific discipline but rather by the nature of the problem to be solved. As such, this activity provides the unique opportunity for investigators with diverse backgrounds in chemistry, physics, microbiology, plant biology, and other fields to effectively and synergistically collaborate to solve these challenges for societal benefit.

Projected Evolution

Future impact is, in general, envisioned through increased integration of physical science and computational tools (e.g. ultrafast laser spectroscopy, current and future x-ray light sources, and theory and modeling techniques) to probe structural, functional, and mechanistic properties of enzymes, enzyme systems, and energy-relevant biological reactions and pathways related to energy capture, conversion, and storage. These studies will identify principles that will provide a basis for the design and synthesis of highly selective and efficient bioinspired catalysts, allow us to carefully control the flow of electrons in biological systems to achieve desired metabolic outcomes (e.g. enhance lipid or terpene production), and give us an unprecedented architectural and mechanistic understanding of such systems. Investment in research on the plant cell wall biosynthesis and structure research is being deemphasized and the program is not considering new projects in this area at this time.

Physical Biosciences does not fund research in: 1) animal systems; 2) prokaryotic systems related to human/animal health or disease; 3) development and/or optimization of devices and/or processes; 4) development and/or optimization of microbial strains or plant varieties for biofuel/biomass production; 5) cell wall breakdown or deconstruction; 6) transcriptional or translational regulatory mechanisms and/or processes mediated by plant hormones; 7) environmental remediation and/or identification of environmental hazards. Projects should ideally be hypothesis-driven; projects that develop or rely primarily on high-throughput screening approaches will not be supported nor will theory/modeling projects that lack experimental verification.

Significant Accomplishments

The Physical Biosciences program has a strong record of scientific impact as exemplified by its support of research that was instrumental in defining *Archaea* as the third kingdom of life. Recent significant accomplishments of the program include:

- The determination that the final step of anoxygenic methane biosynthesis occurs via a methyl radical intermediate, which could provide the information needed to design energy-efficient catalysts and enable the cost-effective capture and use of stranded methane.
- Studies of hydrogenase and nitrogenase structure, function, and biosynthesis have provided a wealth of information on the assembly and mode of action of complex metal-organic cofactors and gated electron flow that are critical for the production of hydrogen and reduction of nitrogen in biological systems. Such foundational knowledge can help enable the design of more selective and efficient catalysts and processes aligned with achieving BES objectives.
- Studies of plant lipid biosynthesis and degradation have revealed new details of the biochemical pathways involved in conversion of carbon dioxide into fatty acids, storage of fatty acids as oil, and breakdown of oil in leaves. As a result of this research, plants were generated that had approximately a 150-fold increase in leaf oil content, providing a possible new approach for sustainable fuel production.
- The determination of the detailed structures of many of the complex polysaccharide components of the plant cell wall, as well as many important aspects of its supramolecular structure, have guided strategies aimed at improving the conversion efficiencies of plant biomass to fuel molecules.

Unique Aspects

Physical Biosciences is a unique federal program that lies at the interface of the biological, chemical, and physical sciences. A significant fraction of the supported research directly addresses BES Grand Challenges, especially the challenges of "controlling processes at the level of electrons", "designing and perfecting atom- and energy-efficient syntheses of revolutionary new forms of matter with tailored properties", and "creating new technologies with capabilities rivaling those of living things." The program is not strictly defined by scientific discipline and is unique in promoting multi- and cross-disciplinary approaches that provide the foundational scientific knowledge required for the development of bioinspired energy-relevant technologies and processes.

Mission Relevance
The research provides basic structure/function and mechanistic information necessary to accomplish bioinspired rational design of catalysts and more efficient biological energy transduction and storage. This impacts numerous DOE interests, including improved biochemical pathways for biofuel production, next-generation energy conversion/storage devices, and efficient, environmentally-benign catalysts.

Relationship to Other Programs
This research activity interfaces with several complementary activities within BES as well as within DOE and other federal agencies.

- Within BES, research efforts are closely coordinated with the Photosynthetic Systems program in the areas of natural photosynthesis, carbon fixation, and the organizational and structural principles of the cellular machinery; with the Solar Photochemistry and Catalysis Science programs in the areas of gating and control of electron flow, proton-coupled electron transport, and enzyme and biomimetic catalysis; and with the Separations and Analysis program in the area of analytical tool and technology development. To a more limited extent, Physical Biosciences coordinates with the Condensed Phase and Interfacial Molecular Science (CPIMS) and Computational and Theoretical Chemistry (CTC) programs.
- This research activity sponsors—jointly with other core research activities and the Energy Frontier Research Centers program as appropriate—program reviews, principal investigators' meetings, roundtables, and programmatically-relevant workshops.
- The more chemistry- and physics-oriented projects supported by this activity are synergistic with, and complementary to, the more genomics- and systems biology-oriented activities supported by the DOE Office of Biological and Environmental Research (BER). Communication and coordination with BER, as well as the DOE Office of Energy Efficiency and Renewable Energy and the Advanced Research Projects Agency-Energy, is achieved through quarterly meetings to ensure the effective and efficient use of DOE resources.
- The program collaborates and coordinates its activities with the National Science Foundation, U. S. Department of Agriculture, and National Institutes of Health in areas of mutual interest where there are multiple benefits.