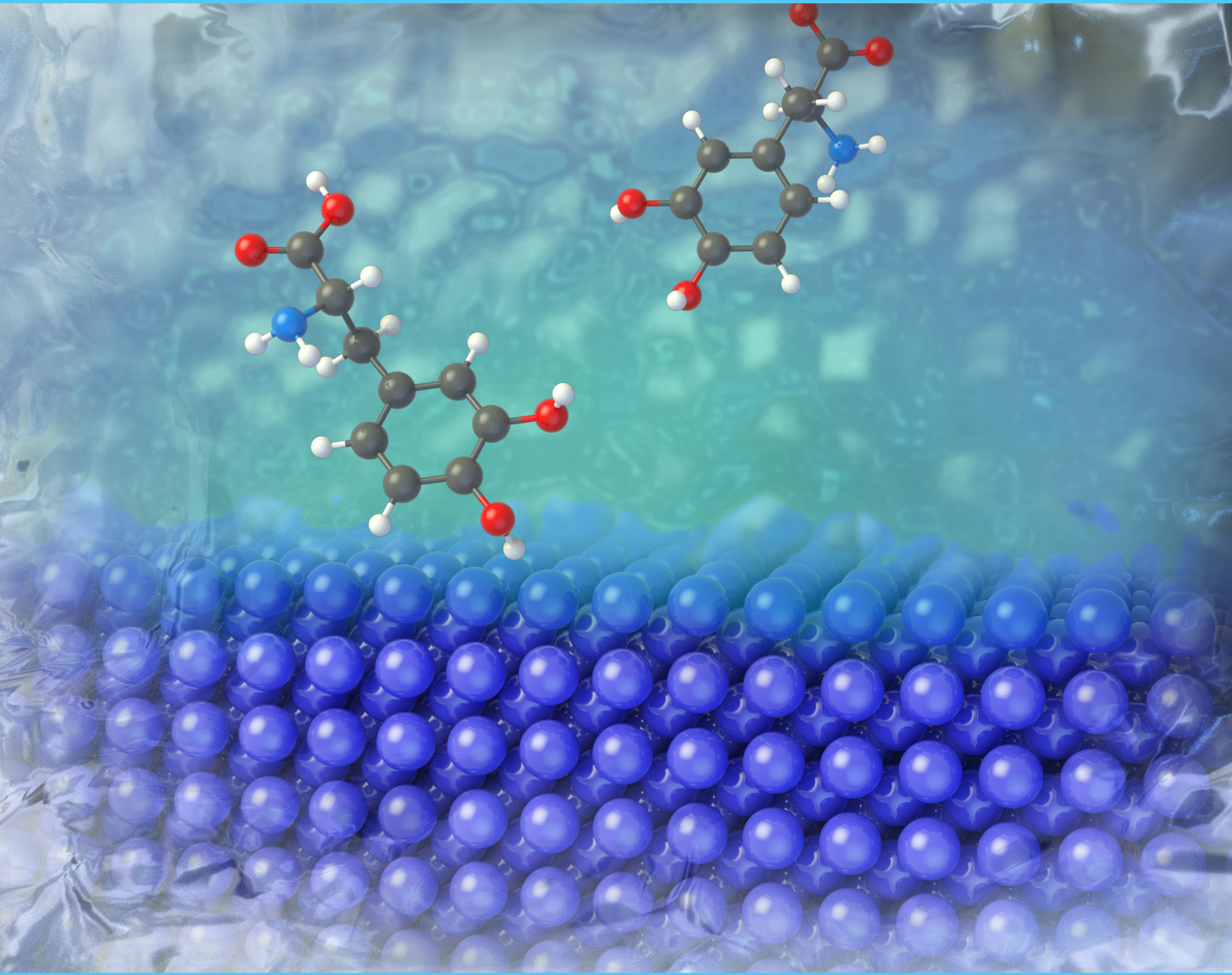
Basic Energy Sciences Roundtable

Research Opportunities in the Physical Sciences Enabled by Cryogenic Electron Microscopy



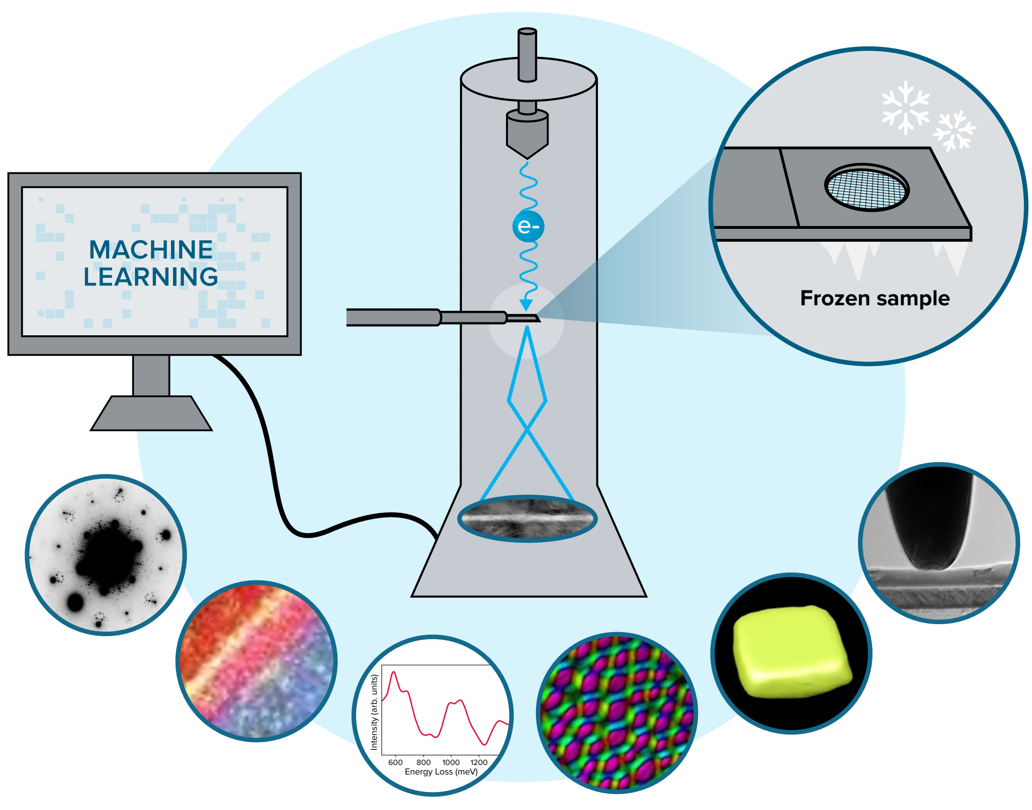
Discovery Science Enabled by Low-Temperature Electron Microscopy

Identifying the key science drivers, research priorities, and research strategies in the area of cryogenic electron microscopy (cryoEM) for the physical sciences.

The properties of materials as well as the pathways and outcomes of chemical and biological processes are controlled by microstructure, composition, and chemical and physical processes at the atomic- to nano-scale. Electron microscopy (EM) has long been used to understand the fundamental properties of materials and chemical systems because of the *local* information — as distinct from global or ensemble information — that it can provide. For numerous systems of interest, however, the powerful methods of room-temperature EM are insufficient. Challenges arise when the materials or molecules are sensitive to the incident electron beam, when fluids or solids are mobile at room temperature, or when phases or phenomena exist only at low temperatures. An emerging approach to meet these challenges is to study the samples cold, at temperatures that are below, typically far below, the freezing point of water.

Cryogenic electron microscopy (cryoEM) has proven to be a powerful method for visualizing beam-sensitive biological macromolecules and has had significant successes in material, chemical, and geochemical sciences. However, its full impact for advancing the scientific understanding of matter and chemistry has not yet been fully realized. In particular, the potential for going beyond the analysis of structure and composition to reveal the mechanisms of complex pathways and the interactions that underpin dynamic behavior has remained relatively unexplored.

To identify the most pressing research opportunities for the use of cryoEM as a decisive tool for physical sciences research, the U.S. Department of Energy, Office of Basic Energy Sciences (BES) convened a roundtable of scientists with expertise in chemistry, materials science, geoscience, bioscience and cryoEM. This group of experimentalists and theorists met remotely May 4 – 6, 2021, to explore research opportunities that would leverage existing cryoEM capabilities, develop forward-looking opportunities for new data acquisition and analysis approaches, and advance the broader science mission of BES. The findings of this cryoEM roundtable are summarized in the four Priority Research Opportunities (PROs) outlined below. The full roundtable report is posted at http://science.osti.gov/bes/Community-Resources/Reports.



Schematic illustrating the accessible information on structure, composition, chemical bonding and properties that can be obtained from cryoEM experiments on frozen samples.

Priority Research Opportunities

- ## Discover emergent behavior and coupled processes at interfaces

Key question: *How do complex and dynamic processes give rise to chemical functionality and physical properties at interfaces?*

Chemical reactions and physical phenomena at interfaces play a vital role for energy production, conversion, and storage, as well as for information storage and communications. Meeting the increasing demands on these technologies will require the design of new types of compositionally diverse and dynamically evolving interfaces that enable new processes as well as control of those processes. CryoEM can play an essential role by elucidating the molecular-to-nanoscale, three-dimensional structure and composition of complex internal interfaces. In addition, it could capture the chemical processes and reveal the low-temperature quantum states that underpin emergent interfacial behavior and function.

- ## Elucidate the role of heterogeneity in hierarchical systems

Key question: *What are the dominant interactions across length and time-scales that control behavior in hierarchical systems?*

Hierarchical systems are ones in which structure and composition at different length and time scales can interact to influence mesoscale and macroscale behavior. Hierarchical systems include liquids, soft and hard materials, and biosystems and have applications including batteries, bio-inspired catalysis, water-purification membranes and some magnets. These systems are intrinsically heterogeneous, providing opportunities for cryoEM to elucidate how different components interact to generate hierarchical behavior and to learn to control that behavior. CryoEM can lead to a clearer understanding of important processes such as charge transport in soft materials, the formation of quantum states, and chemical separations.

- ## Understand the evolution of matter in variable environments across length and time scales

Key question: *How is matter assembled from its constituent units? How can we map the energy landscape that controls dynamic behavior and processes?*

The dynamic behavior of matter in response to changes to its environment influences many of the properties that are harnessed for energy-related applications. Much needs to be learned about how matter is assembled from its constituents and how the dynamic behavior and processes of matter can be controlled. CryoEM has the potential for breakthroughs in understanding the assembly of matter, the emergence of quantum states, the subtleties of chemical transformations, and the dynamics of materials systems that are excited by an external stimulus. Integrating theory, experiment, and simulation, each enhanced by data science methods, will open new approaches to understanding dynamic behavior and harnessing it for new applications.

- ## Harness data analytics and automation to expand the role of cryoEM in enabling scientific discoveries

Key question: *What advances in artificial intelligence and machine learning can be harnessed to enable cryoEM to advance beyond what is currently possible?*

Data science and data analytics will dramatically expand the capabilities and impact of cryoEM by capturing phenomena that were previously inaccessible. There are opportunities to develop machine learning (ML) and artificial intelligence (AI) approaches, to discriminate signals from noise or artifacts, and facilitate data interpretation. The ultimate goal will be autonomous discovery in which automated cryoEM experiments are guided by data science. Automated microscope tuning, high-throughput data acquisition, and "on the fly" control of cryoEM experiments can revolutionize microscope operation, data collection and mining of large-scale data sets. Data science and analytics applied to cryoEM are crucial to research efforts across the other three PROs and promise an acceleration in the rate of scientific discovery.

Outlook

CryoEM has had an important impact on a large and diverse number of materials and systems of direct relevance to fundamental energy sciences, yet there are still entire fields of study to be explored. *In situ* control of sample temperature and the ability to drive transport or transformations can lead to the ability to correlate local (atomic or electronic) structure to behavior and properties at the meso- and macro-scale. This will provide new insights into the behavior of matter and the pathways of chemical processes critical for addressing the needs of fundamental energy science research.

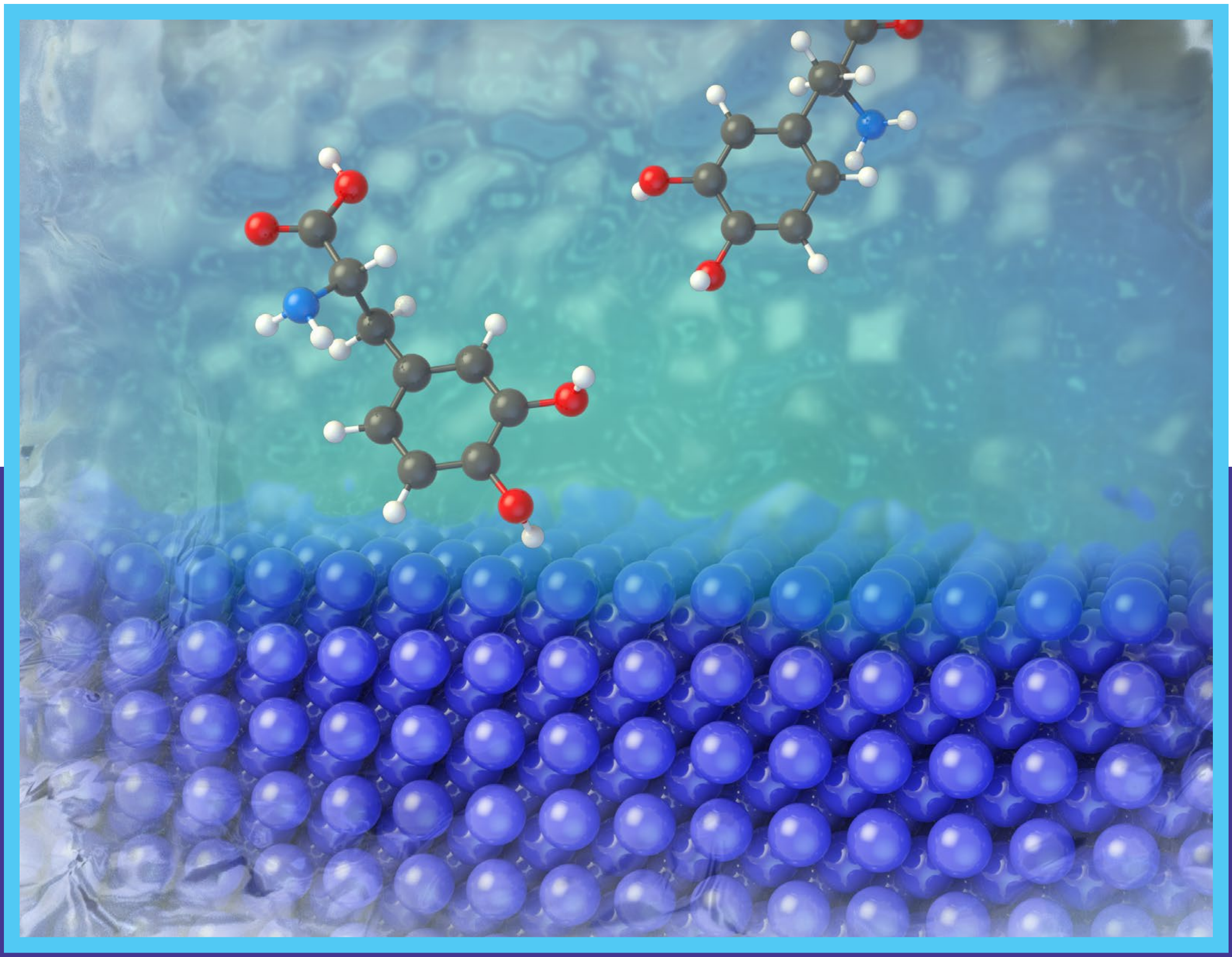


Image courtesy of Argonne National Laboratory

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