Statement of Mission Need for

High Resolution and Mass Accuracy Capability for Systems Biology and Proteomics Research

as a

Major Item of Equipment

Non-Major System Acquisition

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Mission Need Statement for
High Resolution and Mass Accuracy Capability for Systems Biology and Proteomics Research
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Climate and Environmental Sciences Division
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A. Statement of Mission Need

The mission of the Department's Biological and Environmental Research (BER) program is to advance world-class biological and environmental research programs and scientific user facilities to support DOE's energy, environment, and basic research missions. As part of its strategic mission, and in accordance with the Energy Policy Act of 2005, the BER program supports fundamental research and technology development to achieve a predictive, systems-level understanding of complex biological systems to advance DOE missions. In addition, the BER program plans, constructs and operates several major scientific user facilities that contain specialized instrumentation that enable researchers to conduct leading-edge systems biology and proteomics research.

To enable BER-supported scientists to continue to make new discoveries in systems biology and proteomics that could lead to advances in biomass conversion for biofuels, contaminant bioremediation and terrestrial carbon sequestration high resolution and accuracy instruments, equipment and systems are needed to resolve the lowest abundance components of complex mixtures. This information will enable innovation in systems biology for application to biomass conversion for biofuels, contaminant bioremediation and carbon sequestration.

B. Alignment

Strategic Fit of Mission Need

The legislative bases of the BER program are the Atomic Energy Act of 1954 (42 U.S.C. 2011 et seq.), the Energy Reorganization Act of 1974 (42 U.S.C. 5801 et seq.), the Department of Energy Organization Act of 1977 (DOE Act; 42 U.S.C. 7101 et seq.), the Energy Policy Act of 1992 (Public Law 102-486, October 24, 1992), and the Energy Policy Act of 2005 (Public Law 109-58, August 8, 2005).

1 http://www.law.cornell.edu/uscode/42/ch23.html
2 http://www.law.cornell.edu/uscode/42/ch23.html
3 http://www.law.cornell.edu/uscode/42/ch84.html
4 http://thomas.loc.gov/cgi-bin/query/z?c102:H.R.776.ENR:

Specifically, the BER program research and user facilities missions are provided in the Energy Policy Act of 2005 (Public Law 109-58). Section 971 of the Energy Policy Act of 2005 is summarized below:

> *Research Program Mission*
>
> The Secretary shall conduct, through the Office of Science, programs of research, development, demonstration, and commercial application in high-energy physics, nuclear physics, **biological and environmental research,** basic energy sciences, advanced scientific computing research, and fusion energy sciences, including activities described in this subtitle.
>
> *User Facility Mission*
>
> The programs **shall include support for facilities** and infrastructure, education, outreach, information, analysis, and coordination activities.

The BER program addresses the research mission by focusing on four priorities:

1. Developing biofuels as a major secure national energy resource.
2. Understanding relationships between climate change and Earth's ecosystems and assessing options for carbon sequestration.
3. Predicting the fate and transport of subsurface contaminants.
4. Developing new tools to explore the interface of biological and physical sciences.

The BER program directly supports the 2006 DOE Strategic Plan Theme 3, Scientific Discovery and Innovation, which seeks to "strengthen U.S. scientific discovery, economic competitiveness, and improving quality of life through innovations in science and technology," as well as all three strategic goals for this theme:

> Goal 3.1, Scientific Breakthroughs—achieve the major scientific discoveries that will drive U.S. competitiveness to address the Nation's energy, national security and environmental quality challenges.
>
> Goal 3.2, Foundations of Science—deliver the scientific facilities…and provide the laboratory capabilities and infrastructure required for U.S. scientific primacy.
>
> Goal 3.3, Research Integration—integrate basic and applied research to accelerate innovation and to create transformation solutions for energy and other U.S. needs.

These goals stress the importance of new technologies and tools, the role of powerful new scientific instruments, and the complexities of the energy and environmental issues facing DOE and the Nation. In addition, BER funding to operate several DOE Scientific User Facility supports the 2006 DOE Strategic Plan Strategic Theme 3, to "increase investments in the U.S. scientific infrastructure, particularly at the Department's scientific user facilities, to ensure the U.S. an order of magnitude dominance in key scientific fields that will transform the 21st century global economy, e.g., biotechnology, nanotechnology, materials science, high-speed computing, and climate change research."

In addition, BER's user facilities contribute to the crosscutting science integration activities that are required to accomplish DOE Strategic Theme 1, Energy Security; Strategic Theme 2, Nuclear Security; and Strategic Theme 4, Environmental Responsibility. Specifically, instrument capabilities at the user facilities provide crosscutting science integration activities for Energy Security, including the need for breakthroughs in biofuels (including cellulosic ethanol), remote sensing and analysis of radioactive/fissile materials, and investigating biological processes to better understand the capabilities of microorganisms to affect contaminant transport in the subsurface.

In the area of biological processes, the Energy Policy Act of 2005 provides specific direction to the BER program and to the use of user facilities to support systems biology research:

> *Systems Biology Program*
>
> The Secretary shall establish a research, development, and demonstration program in **microbial and plant systems biology**, **protein science**, and computational biology to support the energy, national security, and environmental missions of the Department.
>
> The program shall have the goal of **developing technologies** and methods based on the biological functions of genomes, microbes, and plants that
>
> (1) can facilitate the production of fuels, including hydrogen;
> (2) convert carbon dioxide to organic carbon;
> (3) detoxify soils and water, including at facilities of the Department, contaminated with heavy metals and radiological materials; and
> (4) address other Department missions as identified by the Secretary.
>
> *User Facilities and Ancillary Equipment*
>
> Within the funds authorized to be appropriated pursuant to this subtitle, amounts shall be available for projects to develop, **plan, construct, acquire**, or operate **special** equipment, **instrumentation**, or facilities, **including user facilities** at National Laboratories, **for** researchers conducting research, development, demonstration, and commercial application in **systems biology and proteomics and associated biological disciplines**.

The BER program provides funding for researchers to conduct research, development, demonstration and commercial application in systems biology and proteomics and associated biological disciplines. The systems biology focus of the BER program is primarily supported by the research programs within BER's Biological Systems Science Division (BSSD), which "supports fundamental research and technology development to achieve a predictive, systems-level understanding of complex biological systems to advance DOE missions in energy, climate, and environment." The environmental focus of BER's missions and goals is supported by its Climate & Environmental Sciences Division (CESD), which "supports fundamental research to achieve a predictive, systems-level understanding of climate change, as well as subsurface contaminant fate and transport, to advance DOE missions in energy, climate, and environment." Both focus areas require the development and application of novel approaches and capabilities to realize world-class science and discovery.

The proposed project will enable users to contribute substantially to research funded by programs within each of BER's divisions by allowing the scientific community to gain a molecular-level understanding of biochemical pathways, cellular communication, microbial communities, and other interactions between molecules and their environments. Advances in these areas of research will enable innovation in systems biology, environmental remediation, carbon sequestration and climate change, biomass conversion to biofuels, energy efficiency, national security, health improvements, and drug discovery.

Priority of Mission Need

Priorities for the current Administration and the Secretary of Energy are focused on policies to advance energy and climate security by developing a clean energy industry; investing in the next generation of energy technologies; developing domestic energy supplies, including biofuels; promoting energy efficiencies; stemming carbon emissions; and promoting U.S. competitiveness. The specific DOE missions include an overarching mission to advance the national economic and energy security of the United States, a supporting mission to promote scientific and technological innovation, and ensuring the environmental cleanup of the national nuclear weapons complex.

The BER program advances world-class biological and environmental research programs and scientific user facilities to support DOE's energy, environment, and basic research missions. One way the BER program does this is by supporting fundamental research and technology development to achieve a predictive, systems-level understanding of complex biological systems to enable new discoveries that could lead to advances in biomass conversion for biofuels, contaminant bioremediation and terrestrial carbon sequestration.

The proposed project is a high priority for the BER program because it will directly address the need to understand complex biological systems by enabling scientists to resolve the lowest abundance components of complex mixtures. Such mixtures are expected to include microbial communities found in contaminated subsurface environments, proteins found in microorganisms and plants involved in the biomass conversion of biofuels, and the cellular components and regulatory molecules in microorganisms involved in terrestrial carbon sequestration. Without a fundamental understanding of the lowest abundance proteins and cellular components, the scientific community will be unable to optimize natural and synthetic processes for biomass conversion, microbial contaminant remediation and carbon sequestration.

In addition, the project will provide a capability that should be able to resolve the specific aerosols and other particulates found in atmospheric samples from multiple locations as well as the reactions of specific components of catalytic processes that occur at various types of interfaces. Without a fundamental understanding of the components of atmospheric samples and processes involved in catalytic reactions, scientists will be restricted in their ability to understand the factors contributing to climate change or to design more efficient catalysts for conversion of multiple types of energy supplies.

Internal/External Drivers

In accordance with the Energy Policy Act of 2005, the BER program is required to "establish a research, development and demonstration program in microbial and plant systems biology, protein science…to support the energy, national security and environmental missions of the Department." In addition, within the funds authorized, the BER program is to develop, plan, construct, acquire or operate special equipment, instrumentation or facilities…for researchers…in systems biology and proteomics and associated biological disciplines." The proposed project will directly address these requirements.

In accordance with the 2006 DOE Strategic Plan, the BER program directly supports the three goals within Theme 3, Scientific Discovery and Innovation, by delivering the laboratory capabilities and infrastructure to enable the achievement of major scientific discoveries to drive U.S. competitiveness. Again, the proposed project will fulfill the need for appropriate laboratory capabilities to achieve major scientific discoveries.

C. Capability Gap

The Gap

Among the most useful instruments for systems biology and proteomics research are mass spectrometry capabilities for resolving the lowest abundance components of complex mixtures. The highest field mass spectrometer currently available to BER supported researchers within the DOE complex is located at a DOE Scientific User Facility, is more than 10 years old, and has reached the end of its operational life.

BER needs to provide the scientific community with the most advanced instruments, equipment, and systems that incorporate recent advances in high field magnet technology, ionization methods, chemical imaging and data analysis so that researchers can resolve the lowest abundance proteins and cellular components in complex mixtures. An instrument, equipment, and/or system that incorporate these technology advances will close the capability gap and will facilitate unequivocal identification of complex biochemical compounds and their molecular structures, including proteins.

While the BER program could obtain commercially available systems for proteomics and systems biology research, these systems would only be able to detect proteins and other cellular components that occur at high levels; the lowest abundance proteins and cellular components would be missed. Commercially available mass spectrometers are therefore useful for "production-type" proteomics. However, for extremely low levels of detection, other options with the highest possible resolution and mass accuracy are needed. This type of capability would enable BER-funded scientists to identify proteins and other cellular components of the lowest possible abundance. No other instrumentation is currently available that would provide such high resolution and mass accuracy. Developing this capability could provide a transformational advance for conducting

research applicable to DOE's strategic goals and to the BER programs, and specifically for systems biology and proteomics research.

Other Potential Capabilities

High magnetic-field mass spectrometry is generally recognized as the technique of choice for reaching the highest mass-resolving power and mass measurement accuracy.

The National High Magnet Field Laboratory (NHMFL), a National Science Foundation (NSF) "multi-user research facility" at Florida State University (FSU), currently operates a 14.5 Tesla, Fourier Transform Ion Cyclotron Resonance Mass Spectrometer (FT-ICR Mass Spec). While this system is made available to (NSF defined) "users," FSU currently focuses the use of this capability on "biomolecular analysis, hydrogen-deuterium exchange and environmental and petrochemical analysis" (http://www.magnet.fsu.edu/usershub/scientificdivisions/icr/index.html). Use of this capability by BER funded investigators might be possible, but the scope of FSU's current focus does not appear to be well aligned with the Energy Policy Act requirement for BER to establish research efforts in "microbial and plant systems biology" or "proteomics."

Another facility that might have a HFMS system that could be used by BER-funded researchers is the Atomic and Molecular Physics Institute (AMOLF) in Amsterdam, The Netherlands. AMOLF (http://www.amolf.nl/) is one of the research laboratories of the Foundation for Fundamental Research on Matter (FOM), which is the physics division of the Dutch National Science Foundation (DNSF). If AMOLF has a HFMS system, it is not entirely clear whether it would be available to BER-funded scientists.

Benefits from Closing the Gap

Comprehensive identification of various types of biomolecules (e.g., DNA/RNA, proteins, lipids, glycans, and metabolites) is required to characterize multi-protein complexes (the interactome) and define cell biology at a molecular level. The ability to determine all the proteins (e.g., lipids, glycans, and metabolites) in a cell and their variation over time and in response to stimuli is a major analytical challenge. From an analytical perspective, significant advances in sensitivity and dynamic range of detection are needed for these extremely complex samples (e.g., microbial and plant communities), extremely small samples (e.g., single cells), and high dynamic range samples (e.g., a microbial community) with sufficient speed to obtain a statistically meaningful number of analyses (e.g., to account for biological variability). Achieving these proposed advances will dramatically impact biological, chemical, and physical sciences and the ability to address the most important questions in the energy, environmental and health sciences.

More advanced investigation tools can deliver low parts-per-billion mass measurement accuracy, which will be a milestone achievement in MS-based proteomics (and metabolomics). This level of performance will facilitate highly confident identification of various cell components and even specification of the elemental composition for a

significant fraction of peptide metabolites, which are at present notoriously difficult to characterize. It will minimize errors that can lead to years of misdirected research, and will greatly advance biological sciences. When combined with the entire genomic, transcriptomic, and proteomic profile of an organism, the resulting biological understanding provides a basis for manipulating protein expression for a broad spectrum of applications, such as for producing biofuels, cleaning up waste, and sequestering carbon.

Consequences of Not Filling the Gap

The impact of not obtaining a next generation capability would be to limit the ability of the BER program to meet DOE's energy, science and environmental missions as well as BER program goals. Specific consequences would be to:

- negatively impact the ability of the BER program to meet the requirements set forth in the Energy Policy Act of 2005 to develop technologies applicable to systems biology, and to acquire instrumentation for systems biology and proteomics;
- negatively impact the ability of the BER program to meet the three goals within DOE Strategic Theme 3;
- constrain the ability of the BER program to contribute "crosscutting science integration activities" to accomplish DOE Strategic Theme 1, Energy Security; Strategic Theme 2, Nuclear Security; and Strategic Theme 3, Environmental Responsibility; and
- limit the ability of the entire scientific community to have access to a world-leading resource that would be configured to meet the systems biology and proteomics research requirements of the Energy Policy Act of 2005 and the three goals within DOE Strategic Theme 3.

D. Planned Approach

High magnetic-field mass spectrometry is generally recognized as the technique of choice for reaching the highest mass-resolving power and mass measurement accuracy.

The project will evaluate commercially available technology; the potential to use other facilities such as NHMFL and AMOLF; the option of designing, developing, and building a high field mass spectrometry capability for the improved molecular characterization of intact proteins and other complex mixtures; and the option of doing nothing.

Because the planned project is expected to have a funding range of greater than $16M but less than $18M, BER intends to manage the project in accordance with the principles of DOE Order 413.3A, Program and Project Management for the Acquisition of Capital Assets. In accordance with those principles, BER has prepared this Mission Need Statement for approval by the Acquisition Executive. If approved, the next step would be

to undertake conceptual planning, including the development of an Acquisition Strategy, Risk Analysis, preliminary Project Execution Plan and Alternatives Analysis.

Assumptions

The following high-level assumptions were considered for this mission need:

- Congressional direction for the BER program will remain as outlined in the Energy Policy Act of 2005 – to undertake a research program in plant and microbial systems biology and proteomics to address DOE's energy, national security and environmental missions.
- Funding for this project will be provided through multi-year Congressional appropriations.

Constraints

Functional and Technical

No significant technical or functional constraints are expected other than those associated with this type of technology to users.

Operational

No unusual operational constraints are expected with this project.

Staffing

Skilled technical staff with expertise in research relating to systems biology and proteomics as well as general instrumentation design and engineering would be needed.

Environment, Safety, and Health

The appropriate DOE Site Office will undertake the analysis of potential environmental impacts associated with this project. If placed at a DOE laboratory, that laboratory will assist the Site Office in complying with all National Environmental Policy Act requirements and implementing regulations. No unusual design criteria or use of any materials is anticipated.

Safeguards and Security

BER will ensure that an effective safeguards and security program is in place to provide appropriate confidentiality, integrity, and availability, as well as protect information commensurate with the level of risk and magnitude of harm resulting from loss, misuse, unauthorized access, or modification.

Legal and Regulatory Constraints or Requirements

This mission need will fully comply with all applicable federal, state, and local requirements. Permits associated with power supply wiring and HVAC hookup will be obtained, as appropriate. National Environmental Policy Act requirements will be evaluated, as appropriate.

E. Resource and Schedule Forecast

Estimated Project Cost

The preliminary Total Project Cost for the project is expected to range between $16M to $18M. To meet the proposed schedule and achieve a Total Project Cost within this estimate, funding is required in FY10 to start the project pending approval of this Mission Need Statement. Procurement of the capability will be accommodated within the BER target budget subject to annual Congressional appropriations.

Estimated Funding Profile

The table below outlines the capital funding profile needed to fund the necessary resources to meet this mission need.

Three-Year Funding Profile				
Fiscal Year	**10**	**11**	**12**	**Total**
Funding Profile	$3M	$7. 5M	$7. 5M	$18M

Conceptual Schedule

A conceptual schedule of major activities and milestones is shown in Table 1. The schedule to develop this capability is approximately four and one half years. Appropriate project documentation will be prepared after CD-0 is approved.

Table 1 – Project Conceptual Schedule

Schedule Item	Description	Estimated Complete Date
CD-0	Approve Mission Need Statement	Oct 2009
CD-1	Approve AA & Preliminary PEP	Dec 2009
CD-2	Approve RFP for high resolution and mass accuracy system	Aug 2010
CD-3	Approve contract award for system	Nov 2010
CD-4	Accept high resolution and mass accuracy system	Mar 2014