Free Executive Summary

Research at the Intersection of the Physical and Life Sciences

Committee on Forefronts of Science at the Interface of Physical and Life Sciences; National Research Council


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Traditionally, the natural sciences have been divided into two branches: the biological sciences and the physical sciences. Today, an increasing number of scientists are addressing problems lying at the intersection of the two. These problems are most often biological in nature, but examining them through the lens of the physical sciences can yield exciting results and opportunities. For example, one area producing effective cross-discipline research opportunities centers on the dynamics of systems. Equilibrium, multistability, and stochastic behavior—concepts familiar to physicists and chemists—are now being used to tackle issues associated with living systems such as adaptation, feedback, and emergent behavior. Research at the Intersection of the Physical and Life Sciences discusses how some of the most important scientific and societal challenges can be addressed, at least in part, by collaborative research that lies at the intersection of traditional disciplines, including biology, chemistry, and physics. This book describes how some of the mysteries of the biological world are being addressed using tools and techniques developed in the physical sciences, and identifies five areas of potentially transformative research. Work in these areas would have significant impact in both research and society at large by expanding our understanding of the physical world and by revealing new opportunities for advancing public health, technology, and stewardship of the environment. This book recommends several ways to accelerate such cross-discipline research. Many of these recommendations are directed toward those administering the faculties and resources of our great research institutions—and the stewards of our research funders, making this book an excellent resource for academic and government officials committed to promoting scientific discovery in the disciplines.

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Summary

“... the action most worth watching is not at the center of things but where edges meet... shorelines, weather fronts, international borders...”

Anne Fadiman, The Spirit Catches You and You Fall Down

Almost since their inception, the natural sciences, those fields that use the scientific method to study nature, have been divided into two branches: the biological sciences and the physical sciences. In part, this division can be viewed as a convenient social contrivance. However, over time it has also served more functional purposes. Physical scientists, when seeking the fundamental laws, have found it necessary to focus on the simplest of systems—elementary particles, atoms, and molecules—items clearly not alive. It also has been convenient for biological scientists to investigate the immense diversity of living things and their elaborate inner workings without simultaneously accepting the burden of trying to follow these complexities down to their atomic level roots.

Today, while it still is convenient to classify most research in the natural sciences as either biological or physical, more and more scientists are quite deliberately and consciously addressing problems lying at the intersection of these traditional areas. This report focuses on their efforts. As directed by the charges in the statement of task (see Appendix A), the goals of the committee in preparing this report are several fold. The first goal is to provide a conceptual framework for assessing work in this area—that is, a sense of coherence for those not engaged in this research
about the big objectives of the field and why it is worthy of attention from fellow scientists and programmatic focus by funding agencies. The second goal is to assess current work using that framework and to point out some of the more promising opportunities for future efforts, such as research that could significantly benefit society. The third and final goal of the report is to set out strategies for realizing those benefits—ways to enable and enhance collaboration so that the United States can take full advantage of the opportunities at this intersection.

CONCEPTUAL FRAMEWORK FOR ASSESSING THIS INTERSECTION

Any attempt to provide an all-inclusive framework for this work will inevitably leave out research that belongs within it. With that caveat, a good way to think of research at this intersection is that it turns ways of looking at things—both figuratively and literally—from their original purpose and uses them to tackle new problems, often in ways far removed from when they were first conceived.

Most—but not all—of the new problems being addressed at this intersection are biological ones, largely because of the incredible richness of this field. The realm of biology is immense, involving complicated structures as small as molecules and as large as the biosphere and timescales that range from submicroseconds to eons. Answers to these problems seek not only to describe how the individual structures, in their immense complexity and diversity, work but also how they interplay. A very rich source of potential questions indeed.

The ways of looking often come from the physical sciences. Those ways might be conceptual—approaches for looking at and solving problems—or analytical—methods for extracting understanding from data—or technical—tools for collecting information needed to address the problem at hand. But it is this intermingling of problems from one arena and ways of looking at them from another arena that makes this intersectional area between the biological and physical sciences so rich and offers many of the opportunities that reside there. The committee expects that ideas will emerge from such studies that will go well beyond the intersection and transform both the biological and physical sciences.

CURRENT WORK AT THE INTERSECTION

What, then, are some of the areas being explored at this intersection? Interestingly, many share common conceptual themes, several of which are discussed in this report. Interactions appear in both branches, albeit with much different content and contexts. Describing how individual particles interact—what forces and energy exchanges cause crystalline materials to form, and matter in all phases to display characteristic behavior and to undergo phase changes—are mainstays of the world of physics. However, these ways of thinking about and discussing how inanimate
objects interact have been found useful to scientists attempting to answer questions about the interplay of biological matter at many different levels.

Another area finding fertile ground and producing fruitful cross-research opportunities centers on the dynamics of systems. Equilibrium, multistability, and stochastic behavior—concepts familiar to physicists and chemists—are now being used to tackle issues involved in living systems such as adaptation, feedback, and emergent behavior. Ideas of pattern formation that are at the heart of condensed matter physics now help us to understand biological self-assembly and the development of biological systems.

This report also discusses how some of the mysteries of the biological world have been unraveled using tools and techniques developed in the physical sciences. These tools include not only imaging devices, both photon- and matter-based, but also computational models and algorithms. While many of them are used interchangeably by the two fields, others must be modified. However, to reach the heart of biological systems, even more sophisticated investigatory technologies and tools will be needed, many of which have not even been imagined much less developed.

In preparing this report, the committee was mindful of the vastness of the number of topics that arguably comes within the ambit of this report’s subject matter. Work taking place at the intersections of engineering and the life sciences and of materials development and the life sciences covers but two of such topics. Both are fascinating examples of where the meshing of different cultures and sets of ideas can produce much fruitful discussion and advancement. However, the statement of task for this committee focuses on research, limiting this report to more basic activities than those typically involved in engineering and materials development. Further, the committee acknowledges that the research that is the subject matter of this report both arises from and depends upon the rich, ongoing efforts taking place within the core disciplines of the physical and life sciences. Such intersectional research serves to supplement rather than to supplant the scientific advances being made in the more traditional fields.

PROMISING OPPORTUNITIES FOR FUTURE EFFORTS

Some of the most fundamental challenges in this area and near-term prospects for successfully meeting them are discussed in the form of five Grand Challenges:

• **Grand Challenge 1.** Natural substances display remarkable architecture, demonstrating the immense breadth of what can be achieved in developing structures and systems. Can the skills and knowledge-sets of biological and physical scientists be combined to provide greater insight into identifying those structures, capabilities, and processes that form the basis for living systems, and then to use that insight to construct systems with some of the characteristics of life that are capable, for example, of synthesizing materials or carrying out functions as yet unseen in natural biology?

• **Grand Challenge 2.** The human brain may be nature’s most complex system. Can we understand how it works and build on that understanding to predict brain function? Addressing this challenge will require drawing on the resources of the physical sciences, both existing and to be developed, from imaging techniques to modeling capabilities.

• **Grand Challenge 3.** Genes and the environment interact to produce living organisms. Can we deepen our understanding of those interactions to begin to comprehend how organisms change over time—how they age and heal, for example—and from that understanding realize the promise of personalized medicine and access to better health care?

• **Grand Challenge 4.** Earth interacts with its climate and the biosphere through strikingly different yet intertwined mechanisms that operate over vast ranges of time and space. Can life and physical scientists develop an effective approach for understanding how these mechanisms interplay and use that understanding to develop strategies that will preserve this heritage?

• **Grand Challenge 5.** Living systems display remarkable diversity, serving to protect communities from harm. This diversity is declining, however, as the result of human activities, yet efforts to understand its role in the health of a species or an ecosystem have only recently been undertaken. Can knowledge gained at the intersection of the life and physical sciences teach us how to prosper while sustaining the diversity that allows life to flourish?

Further research at this intersection not only will advance our understanding of the fundamental questions of science, but will also significantly impact public health, technology, and stewardship of the environment for the benefit of society. In the world of technology, our economy clearly is based on materials, but no synthetic material in use today is as complex as a dead piece of wood, let alone a living organism. Prospects for a material world as adaptive and robust as living things have been the stuff of science fiction for decades. To achieve these dreams requires a greater understanding of the organizing principles of life. For public
health, the complexity of molecular recognition and the emergent regulation of 
physiology must be better understood if drug design is to progress from the art 
it is to engineering science. Without understanding the diversity encompassed in 
human biology, personalized medicine will remain more a hope than a reality.

We often think of environmental challenges as being biological (“Save the 
whales!”) or physical (“Limit greenhouse gases!”) but, again, this distinction 
between the disciplines is a distortion. The constant interplay between the bio-
logical sciences and the physical sciences is profound when Earth is viewed as an 
entire system.

STRATEGIES FOR ENABLING AND ENHANCING WORK 
AT THE INTERSECTION

Throughout the report, the committee recommends ways to accelerate progress 
in this field. Some of these recommendations are implicit. By describing the vast 
array of outstanding questions at this intersection, it hopes to intrigue some of its 
fellow scientists to venture into this area and perhaps find interesting questions 
to address. Of the report’s explicit recommendations, several are directed to those 
administering the faculties and resources of our great research institutions. In both 
the academic and business world, the cultures of the biological and physical sci-
ences have evolved separately. Indeed both of these broad areas maintain numerous 
subcultures within themselves. It might seem that the daily life of a physician and 
that of a professor of theoretical physics would have nothing in common, but they 
must appreciate each other’s insights if the scientific challenges at this interface are 
to be met and the societal benefits realized. Just as important, educational institu-
tions need to develop multidisciplinary research and education opportunities that 
transcend the traditional departmental structure. They need to establish curricula 
and training opportunities to prepare the next generation of scientists to grapple 
with the questions posed at this intersection.

The committee recognizes that the needed changes will not come about just 
because of this report. Federal and private funding agencies will have to estab-
lish policies and programs that provide the appropriate incentives. Professional 
societies will need to break down disciplinary barriers and promote scholarships 
at the intersection of disciplines. And academic leaders will need to take what 
steps they can to facilitate the changes. This report describes the many profound 
and societally important scientific issues yet to be explored in this area. In it, the 
committee hopes to make the case that inertia and the understandable resistance 
to change must be overcome and that necessary structural changes in academic 
departments and curricula need to be undertaken.
RECOMMENDATIONS

- Universities should establish science curriculum committees that include both life scientists and physical scientists to coordinate curricula between science departments and to plan introductory courses that prepare both those who would major in the life sciences and those who would enter the physical sciences.
- Professional scientific societies should partner with peer societies across the life and physical sciences to organize workshops and provide resources that will facilitate multidisciplinary education for undergraduates.
- Federal and private funding agencies should offer seed grants to academic institutions to develop new introductory courses that incorporate both the physical and life sciences and to professional societies for organizing workshops and developing resources for multidisciplinary education. They should also support research to identify best practices in such education.
- Federal and private funding agencies should offer expanded training grants that explicitly include graduate students and postdoctoral researchers from fields across the life and physical sciences and that require the involvement of academic departments from both the physical and life sciences. Funding agencies should also offer administrative supplements to existing research grants that would enable a principal investigator in the life sciences to support a postdoctoral researcher with a background in the physical sciences, or vice versa.

The report also makes recommendations to help provide better support and guidance for research in these areas. The committee hopes that this report makes the case that much of the best science at this intersection has difficulty finding a financial home and resources. All too often, the most interesting questions that researchers seek to address here do not readily fall within the purview of a particular agency program or review structure. Accordingly, the committee calls for changes in funding mechanisms that will produce effective collaboration and cooperation among federal agencies that support research in the physical and life sciences.\(^2\) Established investigators trained in one discipline should have the opportunity to receive training in another, so they may apply their experience to multidisciplinary problems. Mechanisms need to be put in place to support investigator-initiated multidisciplinary research where review of the proposal assesses the candidate’s previous work rather than just the research being proposed.

RECOMMENDATION
The Office of Science and Technology Policy (OSTP) and the Office of Management and Budget (OMB) should develop mechanisms to ensure effective collaboration and cooperation among federal agencies that support research at the nexus of the physical and life sciences. In particular, OSTP and OMB should work with federal science agencies to establish standing mechanisms that facilitate the funding of interagency programs and coordinate the application and review procedures for such joint programs. Moreover, the National Science and Technology Council should establish a standing interagency working group on multidisciplinary research within its Committee on Science, with focus on the intersection of the physical and life sciences.

RECOMMENDATION
Federal and private funding agencies should offer opportunities for both early-career and established investigators trained in one discipline to receive training in another and apply their experience and training to interdisciplinary problems. In particular, postdoctoral career awards should be established that facilitate the transition of a candidate prepared in a physical science field to apply that training to important questions in the life sciences and vice versa. Funding agencies should also provide expanded support for experienced investigators to receive training in a new field, perhaps in the form of sabbatical fellowships.

RECOMMENDATION
Federal and private funding agencies should enhance the ability of more than one researcher to serve as principal investigator (PI) on research projects. Each PI should receive full credit for participation on the grant, with the lead PI serving as the administrative contact.

RECOMMENDATION
Federal and private funding agencies should devote a portion of their resources to support potentially transformative research, including opportunities at the intersection of the physical and life sciences. These sponsors should have peer review procedures that incorporate the viewpoints of scientists from a variety of disciplines. Moreover, they should continually assess the effectiveness of these grant programs and the review procedures to ensure that they are meeting the desired aims.
RECOMMENDATION

Federal and private funding agencies should expand support for interdisciplinary and multidisciplinary research and education centers. In particular, extramural funding should be provided to establish and maintain center infrastructure and research expenses. Initial (e.g., 5-year) salary support for investigators performing research that spans disciplines should also be included, with continuing salary support for faculty associated with the center provided by the host institution(s) or department(s). To support these centers, universities will need to implement multidepartment hiring practices and tenure policies that support faculty working collaboratively within and across multiple disciplines, establish shared resources, and provide incentives for departments to promote multidepartmental research and cross-disciplinary teaching opportunities.

Many of these recommendations are not new, but instead resemble those rendered by previous committees about the need to break away from "stove piping"—narrowly focused and isolated funding programs—and to implement new ways for evaluating funding opportunities and prioritizing funding for the most promising research. These resemblances should be seen as a renewed acknowledgement by this committee that such changes remain important and continue to be necessary to take full advantage of the research opportunities at this interface.

As noted by President Obama in his remarks to the National Academy of Sciences in April 2009, change and convergence are key to fully meeting the challenges and opportunities at this intersection:

In biomedicine . . . we can harness the historic convergence between life sciences and physical sciences that’s underway today [by] undertaking public projects—in the spirit of the Human Genome Project—to create data and capabilities that fuel discoveries in tens of thousands of laboratories and identifying and overcoming scientific and bureaucratic barriers to rapidly translate scientific breakthroughs into diagnostics and therapeutics that serve patients.3

New cultures must be forged and scientists must grow as comfortable in them as they are in their existing subcultures. There must be funding for work in those new cultures that extends beyond existing-culture “stove pipes.” Most important, they must prepare the rising generation to mine new-culture opportunities without losing touch with scientists in the traditional disciplines or the principles of such disciplines. The future will be driven by progress at this intersection.

Research at the Intersection of the Physical and Life Sciences

Committee on Research at the Intersection of the Physical and Life Sciences

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Cover: Work at the intersection of the life sciences and the physical sciences has often been depicted in new ways of imaging or modeling biological specimens, some of which are illustrated on the cover: (1) three-dimensional distribution of membrane proteins within a cell revealed through iPALM imaging (courtesy of Harald F. Hess, Howard Hughes Medical Institute); (2) xylose isomerase crystal (courtesy of Department of Energy Office of Basic Energy Research (BER)-funded neutron Protein Crystallography Station at Los Alamos National Laboratory (LANL)); (3) simulation of confinement of DNA in viral capsid (courtesy of Molecular Dynamics and Statistical Mechanics Research Group, University of Wisconsin at Madison); (4) diffusion tension imaging of the human brain (courtesy of Thomas Schultz, University of Chicago); (5) chromosome pairs; (6) modeled structure for the enzyme D-xylose isomerase (courtesy of Department of Energy BER-funded neutron Protein Crystallography Station at LANL; (7) anglerfish ovary obtained using autofluorescence (courtesy of James E. Hayden, Wistar Institute, Philadelphia); and (8) rat cerebellum obtained using two-photon excitation fluorescence microscopy (courtesy of the National Center for Microscopy and Imaging Research at the University of California at San Diego and the National Institutes of Health.

IMAGE SOURCES: (1) Harald F. Hess, Howard Hughes Medical Institute; (2) Department of Energy Office of Basic Energy Research (BER)-funded neutron Protein Crystallography Station at Los Alamos National Laboratory (LANL); (3) Molecular Dynamics and Statistical Mechanics Research Group, University of Wisconsin at Madison; (4) Thomas Schultz, University of Chicago; (6) Department of Energy BER-funded neutron Protein Crystallography Station at LANL; (7) James E. Hayden, Wistar Institute, Philadelphia; and (8) National Center for Microscopy and Imaging Research at the University of California at San Diego and the National Institutes of Health.

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This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Research Council’s Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their review of this report:

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## Contents

**SUMMARY**  
1

**1 INTRODUCTION**  
9

**2 GRAND CHALLENGES**  
12  
Grand Challenge 1. Synthesizing Lifelike Systems, 12  
Grand Challenge 2. Understanding the Brain, 14  
Grand Challenge 3. Predicting Individual Organisms’ Characteristics from Their DNA Sequence, 15  
Grand Challenge 4. Interactions of the Earth, Its Climate, and the Biosphere, 16  
Grand Challenge 5. Understanding Biological Diversity, 18

**3 SOCIETAL CHALLENGES**  
20  
Identifying and Combating Biological Threats, 21  
Early Detection and Intervention, 21  
Prediction of Susceptibility to Disease and Its Prevention, 22  
Climate and Its Interface with Biology, 23  
Complex Feedback Loops in Climate Science, 23  
Implications of Renewable Energy, 23  
Medicine, 24  
Imaging, 24  
Treatment and Devices, 25
Agriculture as a Resource for Food and Energy, 25
Building Better Plants and Getting More Out of Them, 26
Hydrogenases and Synthetic Photosynthesis, 27
Beyond Combustion, 27
Materials Science, 28
Opportunities, 28
References, 29

4 COMMON THEMES AT THE INTERSECTION OF BIOLOGICAL AND PHYSICAL SCIENCES
Interaction and Information: From Molecules to Organisms and Beyond, 30
Dynamics, Multistability, and Stochasticity, 36
Self-organization and Self-assembly, 42
Conclusion, 48
References, 49

5 ENABLING TECHNOLOGIES AND TOOLS FOR RESEARCH
Introduction, 51
Physical Basis of Molecular Recognition, 52
Structures and Dynamics Within Cells, 53
   Cellular Environment, 53
   Interactions Within Cells, 55
   Examining Structures Within Cells, 56
Theory and Simulations, 60
Collective Dynamics, 64
Complex Community Signals and Shared Resources at Large Length Scales, 65
References, 68

6 ENABLING RESEARCH AT THE INTERSECTION: PROMOTING TRAINING, SUPPORT, AND COMMUNICATION ACROSS DISCIPLINES
Connections Between Disciplines, 70
   Culture of Separation Between the Life and Physical Sciences, 70
   Culture and Organization of Academia, 72
Organization of Support for Research, 73
Supporting Transformative Research, 78
Educating Scientists at the Intersection of the Physical and Life Sciences, 82
C O N T E N T S

Enabling Interdisciplinary Research Starting at the Undergraduate Level, 82
Integrating Life and Physical Sciences for Graduate Students and Postdoctoral Researchers, 85
References, 89

APPENDIXES

A  Statement of Task  93
B  Meeting Agendas  94
C  Biographies of Committee Members  99