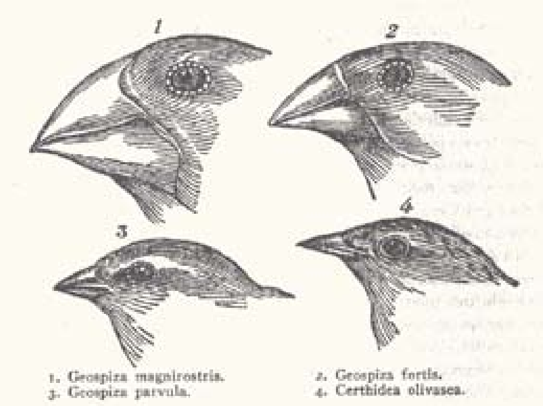
THE NATIONAL ACADEMIES
REPORT IN BRIEF

The Role of Theory in Advancing 21st Century Biology:
Catalyzing Transformative Research

Though rarely explicitly recognized, theory is an integral part of all biological research. Biologists' theoretical and conceptual frameworks inform every step of their research, affecting what experiments they do, what techniques and technologies they develop and use, and how they interpret their data. An increased focus on the theoretical and conceptual component of biological research has the potential to catalyze transformative research that will lead to creative, dynamic, and innovative advances in our understanding of life.

Biologists use observation, exploration, and experiments to gather information and test hypotheses about the living world. Although biologists tend not to think of themselves as "theoretical scientists," theoretical and conceptual frameworks profoundly influence research throughout the many subdisciplines of biology. Theory is critical to understanding what is observed in the natural world; it also enables biologists to make predictions, develop new approaches, and translate biological research into practical applications. A greater recognition of the theoretical frameworks involved in biological research would likely facilitate the development of new questions and experiments and expand existing theoretical frameworks to advance the future of the field.

How might we maximize the potential for future advances in biological research? At the request of the National Science Foundation, the National Research Council assembled a committee to examine whether a greater emphasis on theory might be useful in advancing biology. This report concludes that theory is already an inextricable thread running throughout the practice of biology; but that by explicitly giving theory equal status with other components of biological research (experimentation, observation, analysis), biology can become even more productive in the 21st century.



Darwin's finches. Darwin's exposition of the theory of evolution represents a "tranformative moment" in the history of biology. Greater recognition of the role of theory in biology could help catalyze such transformative research and lead to advances in biology.

The Role of Theory in Biology

Theory is one of many components of the practice of biology, including research tools, experimentation, and descriptions of the natural world. While some "transformative moments" in biology, such as Darwin's exposition of the theory of evolution, resulted directly from efforts to develop a new conceptual framework to explain a large collection of facts, others, such as Watson and Crick's discovery of the structure of DNA, could not have happened without new tools (in this case, the X-ray machine). On the

What is a theory?

The word “theory” serves so many purposes in the English language that confusion is almost inevitable. Theory has been used to describe concepts ranging from a speculative idea (“it’s just a theory”) to a law of nature (the “theory” of gravity).

This report suggests that a useful way to define theory in biology is as a collection of models. Biologists use models—which can be verbal, mathematical, visual, or physical—to represent various aspects of nature for particular purposes. Most biological systems are too complex to be described by a single model; often, biologists use several models to approach a research question.

The models a biologist uses—or the theoretical and conceptual frameworks they apply—inform the entire scientific process, from the tools used, to the experiments done, to the interpretation of the results, and more. For example, the techniques a biologist might use to analyze a sequence of DNA would vary depending on the researcher’s conceptual framework. If one’s model of the genome assumes that only those DNA sequences that code for proteins are important, one may use a technique that only analyzes these sequences. An alternative model that assumes that non-coding DNA sequences have an important role would require a different extraction technique. Only the second technique could have discovered that non-coding sequences are responsible for preventing a cell from turning cancerous or allowing a plant to resist a predatory insect.

other hand, technological advances were also important in enabling Darwin to conduct the research that led to his theoretical insights, and Watson and Crick also used a theoretical model for what the X-ray of a helical molecule should look like to help them interpret X-rays of DNA. In retrospect, it is clear that all transformative moments result from complex interactions among the many components that make up the practice of biology.

For a variety of reasons—the fragmentation of biology into many subdisciplines, the rapid expansion of data and approaches that are available, and the difficulty of making connections among research results from apparently disconnected areas—it may be challenging for biologists to recognize the theoretical framework within which they conduct their work. Giving more recognition to theoretical and conceptual frameworks would likely enable biologists to make connections between their work and work in other subdisciplines and, indeed, other fields of science, inspiring them to rethink their assumptions to ask innovative new research questions. Answering these new questions could in turn lead to new experimental approaches and the birth of new theoretical frameworks. Increasing the focus on the theoretical and conceptual frameworks of biology could, therefore, help pave the way to new transformative moments that would enable major advances in biological research.

To illustrate how recognizing and rethinking theoretical frameworks can help biologists to answer broad questions in biology and address grand challenges for society, the report explores a set of seven questions with relevance to many of biology’s subdisciplines:

1. **Are there still new life forms to be discovered?**
2. **What role does life play in the metabolism of planet Earth?**
3. **How do cells really work?**
4. **What are the engineering principles of life?**
5. **What is the information that defines and sustains life?**
6. **What determines how organisms behave in their worlds?**
7. **How much can we tell about the past—and predict about the future—by studying life on earth today?**

Examining how biologists might use different models or conceptual frameworks to approach these broad questions highlights the ways a greater recognition of these frameworks may help advance the work of biologists.

Increasing the Focus on Theory throughout Biology

The report recommends that theory should be given a measure of attention commensurate with that given other components of biological research (such as observation and experiment). Theoretical approaches to biological problems should therefore be recognized as an important and integral component of funding agencies’ research portfolios. The report emphasizes that all subdisciplines of biology would benefit from explicitly examining the theoretical and conceptual framework that characterizes their discipline. Exploring the underlying connections and conceptual frameworks among seemingly unrelated research areas could lead to unexpected insights that make the connection between basic research and practical solutions. Explicitly recognizing the crucial role of theory in biological research can be an effective way to help make such connections and enable major scientific breakthroughs.

Supporting 'High-Risk, High-Impact' Research Proposals

It can be difficult for researchers to find adequate support for exploring entirely new ways of looking at the natural world. Research proposals that aim to challenge long-held theories and concepts are likely to be held to a higher standard of evidence than more conventional research proposals. Proposals aiming to break new ground by, for example, crossing traditional subdisciplinary boundaries, taking a purely theoretical approach, or potentially destabilizing a field by challenging conventional wisdom are likely to be perceived as 'high-risk' in that they are likely to fail. However, such proposals also have a great potential for high impact should they succeed.

The report recommends that some portion of the basic research budget should be devoted to supporting more of these 'high-risk, high-impact' proposals. Evaluation processes for these proposals should be carefully designed to ensure that reviewers with the requisite technical, disciplinary, and theoretical expertise are involved and that they are aware of the goal of supporting potentially paradigm-shifting research.

Maximizing the Benefits of Technological Advances through Interdisciplinary Collaboration

Major technological advances, such as high-throughput gene sequencing, remote sensing, miniaturization, wireless communication, high-resolution imaging, and others, combined with increasingly powerful computing resources and data analysis techniques, are dramatically expanding the reach of biological research. Questions can now be asked, and answered, that were well beyond our grasp only a few years ago.

All too frequently, scientific horizons are unintentionally limited by the technology that is available. Theoretical frameworks profoundly affect which tools and techniques are available to biologists for use in their work; increasing the focus on the theoretical and conceptual basis of biology would encourage biologists to ask even more complex questions and conceive of experiments that cannot yet be conducted.

Illustrating How Theoretical Frameworks Catalyze Transformative Research: Case Study on Life's Diversity

In exploring the question "Are there still new life forms to be discovered?" the report points out that, although Earth is home to an astounding diversity of life, the study of life's diversity involves more than just going into the field or the laboratory to look for new organisms. The places scientists look, the tools they use, and the experiments they do are influenced by a theoretical and conceptual understanding of the limits of life, the mechanisms of evolution, and the role and significance of diversity.

In the 18th century, for example, the prevailing theory was that there was a fixed number of species and that the job of naturalists was to name and catalog each of them. While this is now known to be false (the number of species is not fixed and species do change over time), research carried out based on that theoretical framework nevertheless provided the body of data that Darwin used to develop the new theory of evolution. What enabled the development of Darwin's theoretical breakthrough? First, an accumulation of facts (in the form of fossil remains) emerged that were difficult to reconcile with the prevailing theory of a fixed and unchanging collection of species. Second, the thousands of biological specimens in the museums of 19th century Europe, as well as Darwin's own observations and collections during his famous voyage—in other words, the curiosity-driven collection of data about the living world—provided the raw material that enabled Darwin's theoretical insight. Darwin's work, therefore, resulted from a combination of tools, experimentation, description, and theory.

Since the identification of DNA as the molecule of heredity and the development of technology to determine the order of biochemical building blocks in DNA, biologists have been able to use genetic data to study the relationships among organisms by comparing their genetic sequences. These technological advances and expanding conceptual frameworks now allow the study of biological diversity at many levels, from DNA sequences, to protein functions, to genome organization, to differences between and among species, communities, and entire ecosystems. At all of these scales, biologists seek to understand the limits and significance of biological diversity. Theoretical and conceptual advances across the different scales could help scientists develop solutions to pressing problems such as the extinction of species and loss of biodiversity. Having multiple conceptual frameworks available and being able to work across different scales thus greatly enriches our ability to study the "bigger picture" of the diversity of life on Earth.

Once biologists envision questions and experiments that reach beyond current technologies, interaction and collaboration between biologists and physicists, engineers, computer scientists, mathematicians, and software designers can help steer research in these areas to help develop new tools and technologies specifically to answer far-reaching new questions to advance biology.

> ***He who loves practice without theory is like the sailor who boards ship without a rudder and compass and never knows where he may cast.***
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> ***—Leonardo da Vinci***

Getting the Most out of Large Data Sets

While technology is making it increasingly cost-effective to collect huge volumes of data, the process of extracting meaningful conclusions from those data remains difficult, time-consuming and expensive. Theoretical approaches show great promise for identifying patterns and testing hypotheses in large data sets. It is increasingly likely that data collected for one purpose will have relevance for other researchers. Therefore, the value of the data collected will be multiplied if it is accessible, organized and annotated in a standardized way. The report recommends that attention should be devoted to ensuring that biological data sets are stored and curated to be accessible to the widest possible population of researchers.

Conclusion

Human beings are intimately connected with and dependent on the living world. The ways in which biological research contributes to medical advances are obvious; less appreciated is the critical contribution that understanding biological systems can make to addressing such pressing problems as global warming, pollution, inadequate food supplies, unsafe drinking water, and dependence on fossil fuels. Biology can provide solutions to problems not only in sectors that directly depend on living organisms–like agriculture, fisheries, and forestry management–but also to sectors like transportation, information processing, materials science, and engineering that could benefit from incorporating the flexibility, robustness and ingenuity of living organisms into human-designed systems. A greater recognition of the theoretical and conceptual frameworks of biological research could help stimulate new transformative moments that lead to major advances in 21st century biology.

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This report brief was prepared by the National Research Council based on the committee's report. For more information or copies, contact the Board on Life Sciences at (202) 334-1289 or visit http://nationalacademies.org/bls. Copies of *The Role of Theory in Advancing 21st Century Biology: Catalyzing Transformative Research* are available from the National Academies Press, 500 Fifth Street, NW, Washington, D.C. 20001; (800) 624-6242; www.nap.edu.

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