

# 21ST CENTURY BIOLOGY

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HEARING  
BEFORE THE  
SUBCOMMITTEE ON RESEARCH AND SCIENCE  
EDUCATION  
COMMITTEE ON SCIENCE AND  
TECHNOLOGY  
HOUSE OF REPRESENTATIVES  
ONE HUNDRED ELEVENTH CONGRESS

SECOND SESSION

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JUNE 29, 2010  
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## **21ST CENTURY BIOLOGY**

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**TUESDAY, JUNE 29, 2010**

HOUSE OF REPRESENTATIVES,  
SUBCOMMITTEE ON RESEARCH AND SCIENCE EDUCATION  
COMMITTEE ON SCIENCE AND TECHNOLOGY  
*Washington, DC.*

The Subcommittee met, pursuant to call, at 2:07 p.m., in Room 2318 of the Rayburn House Office Building, Hon. Daniel Lipinski [Chairman of the Subcommittee] presiding.

BART GORDON, TENNESSEE  
CHAIRMAN

RALPH M. HALL, TEXAS  
RANKING MEMBER

U.S. HOUSE OF REPRESENTATIVES  
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(202) 225-6375  
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Hearing on

*21<sup>st</sup> Century Biology*

**June 29, 2010**  
**2:00 p.m. – 4:00 p.m.**  
**2318 Rayburn House Office Building**

**Witness List**

***Dr. Keith Yamamoto***

*Chair, National Academy of Sciences' Board on Life Sciences*  
*Professor, Cellular and Molecular Pharmacology*  
*University of California, San Francisco*

***Dr. James Collins***

*Virginia M. Ullman Professor of Natural History and the Environment*  
*Department of Ecology, Evolution, & Environmental Science*  
*Arizona State University*

***Dr. Reinhard Laubenbacher***

*Professor*  
*Virginia Bioinformatics Institute and Department of Mathematics*  
*Virginia Tech*

***Dr. Joshua N. Leonard***

*Assistant Professor*  
*Department of Chemical and Biological Engineering*  
*Northwestern University*

***Dr. Karl Sanford***

*Vice President, Technology Development*  
*Genencor*

HEARING CHARTER

**COMMITTEE ON SCIENCE AND TECHNOLOGY  
SUBCOMMITTEE ON RESEARCH AND SCIENCE  
EDUCATION  
U.S. HOUSE OF REPRESENTATIVES**

JUNE 29, 2010  
2:00 P.M.—4:00 P.M.  
2318 RAYBURN HOUSE OFFICE BUILDING

**1. Purpose:**

The purpose of the hearing is to examine the future of the biological sciences, including research occurring at the intersection of the physical sciences, engineering, and biological sciences, and to examine the potential these emerging fields of interdisciplinary research hold for addressing grand challenges in energy, the environment, agriculture, materials, and manufacturing.

**2. Witnesses:**

- Dr. Keith Yamamoto, Chair, National Academy of Sciences, Board on Life Sciences and Professor, Cellular and Molecular Pharmacology, University of California, San Francisco
- Dr. James Collins, Virginia M. Ullman Professor of Natural History and the Environment, Department of Ecology, Evolution, & Environmental Science, Arizona State University
- Dr. Reinhard Laubenbacher, Professor, Virginia Bioinformatics Institute and Department of Mathematics, Virginia Tech
- Dr. Joshua N. Leonard, Assistant Professor, Department of Chemical and Biological Engineering, Northwestern University
- Dr. Karl Sanford, Vice President, Technology Development, Genencor

**3. Overarching Questions:**

- What is the future of research in the biological sciences? What potential does research at the intersection of the biological sciences, physical sciences, and engineering hold for addressing grand research challenges in energy, the environment, agriculture, materials, and manufacturing? What new technologies and methodologies, including computational tools, are enabling advances in biological research? Are there promising research opportunities that are not being adequately addressed?
- What is the nature of the interactions and collaborations between physical scientists, engineers, and biological scientists? How might these disparate research communities be better integrated? Is the National Science Foundation playing an effective role in fostering research at the intersection of the physical sciences, engineering, and the biological sciences? Is research in the biological sciences, including research at the intersection of the biological sciences, the physical sciences, and engineering being effectively coordinated across the Federal agencies? If not, what changes are needed?
- What changes, if any, are needed in the education and training of undergraduate and graduate students to enable them to work effectively across the boundaries of the physical sciences, engineering, and the biological sciences without compromising core disciplinary depth and understanding? How do you achieve that balance?
- How are advances in the biological sciences affecting the biotechnology industry? What are the research needs of the biotechnology sector and are they being adequately addressed? Are science and engineering students being adequately trained by colleges and universities to be successful in the biotechnology industry? Is the National Science Foundation playing an effective role in fostering university-industry collaborations?

#### 4. Background:

Research in the biological sciences is the largest area of research supported by the Federal Government, representing 27 percent of Federal research obligations in 2007. Currently over 20 Federal agencies support biological sciences research ranging from bioterrorism-related research at the Department of Homeland Security to stream ecology at the National Science Foundation. Over the last 30 years there have been rapid advances in DNA sequencing technologies, the real-time imaging of cells and organisms, and computational power. These technical advances, among others, have enabled significant accomplishments in biological research, including the sequencing of the human genome in 2003 and more recently, the creation of a synthesized genome by the J. Craig Venter Institute<sup>1</sup>. Many believe biological research is on the verge of a revolution, moving from a field that has focused primarily on “identifying parts” (i.e. plant species, cells, genes, and proteins) and defining complex systems to one that can design, manipulate, and predict the function of biological systems at all levels of organization from the individual cell to an entire ecosystem. Many experts predict that just as the 20th century was the golden era for physics the 21st century will be the “age of biology”, and advances and discoveries in the biological sciences will transform society.

A deeper understanding of biological systems and the ability to address biology-based societal problems such as the production of a sufficient amount food to sustain the growing human population or the generation of clean energy are increasingly being tackled through interdisciplinary research. The trend toward interdisciplinary research, specifically, research at the intersection of the biological sciences, engineering, mathematics, and the physical sciences has been termed the “new biology”<sup>2</sup>. Within the “new biology” three areas are emerging as foundational fields: computational biology, systems biology, and synthetic biology. Computational biology is the use of mathematical tools and techniques in the examination of biological processes and systems; for example the use of math to describe and understand heart physiology. Systems biology is the study and predictive modeling of biological processes through a holistic examination of the dynamic interaction of the individual components of a system; for example the study of an organism, viewed as an integrated and interacting network of genes, proteins and biochemical reactions. Synthetic biology is an emerging field that applies the principles of engineering to the basic components of biology. The aim of synthetic biology is to make predictable and easy to use genetically-engineered cells, organisms, or biologically-inspired systems for industrial applications like the production of biofuels or therapeutic applications to treat disease.

A number of issues need to be considered as these new trends in biological sciences research develop. Specifically, the type of education and training necessary for undergraduate and graduate students to work effectively across traditional disciplines, the effectiveness of Federal support for interdisciplinary research and education, and the increasing need for interagency coordination of biological sciences research.

#### *The Role of NSF in Biological Sciences Research*

The Directorate for Biological Sciences (BIO) at the National Science Foundation supports 68 percent of the non-medical, basic biological sciences research performed at academic institutions, including plant biology, environmental biology and biodiversity research. The fiscal year 2011 budget request for BIO is \$767.8 million, an increase of 7.5 percent over fiscal year 2010 (see table below). BIO is separated into 5 divisions and supports research to advance understanding of the underlying principles and mechanisms governing life. Research supported by BIO ranges from the examination of the structure and dynamics of biological molecules to more complex systems and scales, including organisms, communities, ecosystems, and the global biosphere.

<sup>1</sup><http://www.sciencemag.org/cgi/rapidpdf/science.1190719v1.pdf>

<sup>2</sup>[http://www.nap.edu/catalog.php?record\\_id=12764](http://www.nap.edu/catalog.php?record_id=12764)

<b>BIO Funding</b>						
(Dollars in Millions)						
	FY 2009	FY 2009	FY 2010 Estimate	FY 2011 Request	Change Over	
	Omnibus Actual	ARRA Actual			FY 2010 Estimate	FY 2011 Request
Molecular & Cellular Biosciences (MCB)	\$121.28	\$61.53	\$125.59	\$133.69	\$8.10	6.4%
Integrative Organismal Systems (IOS)	212.34	61.71	216.25	226.70	10.45	4.8%
Environmental Biology (DEB)	120.37	63.23	142.55	155.59	13.04	9.1%
Biological Infrastructure (DBI)	117.95	38.74	126.86	145.63	18.77	14.8%
Emerging Frontiers (EF)	84.68	34.80	103.29	106.20	2.91	2.8%
<b>Total, BIO</b>	<b>\$656.62</b>	<b>\$260.00</b>	<b>\$714.54</b>	<b>\$767.81</b>	<b>\$53.27</b>	<b>7.5%</b>

Source: National Science Foundation FY 2011 Budget Request to Congress

<http://www.nsf.gov/about/budget/fy2011/toc.jsp>

The Division of Molecular and Cellular Biosciences (MCB) supports research to understand the dynamics and complexity of living systems at the molecular, biochemical and cellular levels. Projects funded through MCB often focus on the regulation of genes and genomes, properties of biomolecules, and the structure of subcellular systems. Activities supported by MCB are increasingly interdisciplinary with the use of tools and technologies developed in the physical sciences, mathematics, and engineering becoming routine.

The Division of Integrative Organismal Systems (IOS) supports a systems-level approach to the understanding of plants, animals, and microorganism; this holistic approach includes the study of an organism's development, function, behavior, and evolution. The Plant Genome Research Program (PGRP), which is part of the National Plant Genome Initiative, is supported through IOS. The PGRP, with a budget request of \$105.4 million in fiscal year 2011, supports basic research to improve crop production, and to identify and develop new sources for bio-based fuels and materials.

The Division of Environmental Biology (DEB) supports fundamental research on the origins, functions, relationships, interactions, and evolutionary history of populations, species, communities, and ecosystems. Research on the complexity and dynamics of ecosystems and evolution are essential to improving our ability to understand and mitigate environmental change.

The Division of Biological Infrastructure (DBI) supports a variety of activities from the development of instruments, software, and databases to the improvement and maintenance of biological research collections and field stations to the transformation of undergraduate biology education. DBI provides the infrastructure, including the human capital, necessary for contemporary research in biology. DBI oversees BIO's participation in cross-cutting programs at NSF including, the Graduate Research Fellowships program, the Integrative Graduate Education and Research Traineeship (IGERT) program (described in detail later) and the Major Research Instrumentation program.

Developing programs and priority areas often start in the Emerging Frontiers (EF) Division and then are integrated into BIO's core programs. EF supports novel partnerships across disciplines and enables the development of new conceptual frameworks. Additionally, EF develops and implements new forms of merit review and mechanisms to support high-risk, high-reward research.

In addition to the research and education activities supported by BIO, the National Ecological Observatory Network (NEON) was included in NSF's fiscal year 2011 budget request for the Major Research Equipment and Facilities Construction (MREFC) account. NEON, a continental-scale research platform for discovering and understanding the impacts of climate change, land-use change, and invasive species on ecosystems, is the first biological sciences related project funded through the MREFC process.

#### *The Role of NSF in Interdisciplinary Education and Training*

NSF supports interdisciplinary education primarily through the IGERT program. Since 1998 the IGERT program has made 215 awards to over 100 universities and has provided funding for nearly 5,000 doctoral-level graduate students. IGERT awards average \$3.0 million over five years with the major portion of the funds being used for graduate student stipends and training expenses. While each IGERT award is unique, the overall goal of the program is to develop scientists and engineers who will pursue careers in research and education from a strong interdisciplinary background and catalyze a cultural change in graduate education, for students, faculty, and institutions, by establishing innovative models that transcend tradi-

tional disciplinary boundaries. For example, there are currently 15 IGERT awards in the area of bioinformatics all seeking to create professionals who can translate scientific problems in biology into mathematics and computations.

NSF also supports a number of research centers that are interdisciplinary in nature and undergraduate and graduate students working in the context of those research centers are exposed to interdisciplinary research, education, and training. For example, through the Centers for Analysis and Synthesis Program, the iPlant Center led by the University of Arizona integrates biologists, computer scientists, and engineers to address grand challenges in the plant sciences, and through the Engineering Research Centers program, the Center for Biorenewable Chemicals led by Iowa State University seeks to transform the chemical industry by integrating biologists and chemists to produce sustainable biochemicals. However, centers are not required to be interdisciplinary and the degree of formal graduate and undergraduate education programs associated with the centers varies.

#### *Interagency Biological Sciences Research Programs*

The National Plant Genome Initiative (NGPI) was established in 1998 and includes the U.S. Department of Agriculture (USDA), the Department of Energy (DOE), the National Institutes of Health (NIH), and NSF. According to the initiative's strategic plan<sup>3</sup>, the goal of the initiative is translate basic research and understanding of economically important plants and plant processes, including a deeper understanding of the structures and functions of plant genomes into the enhanced management of agriculture, natural resources, and the environment to meet societal needs.

The U.S. Global Change Research Program (USGCRP), which began as a presidential initiative in 1989 and includes 13 Federal agencies, was formally established by Congress through the Global Change Research Act of 1990 (P.L. 101–606). The USGCRP coordinates and integrates Federal research on global climate change. While the USGCRP extends beyond biological sciences research one of the program's strategic goals is to “understand the sensitivity and adaptability of different natural and managed ecosystems and human systems to climate and related global changes.”<sup>4</sup>

On a smaller scale, NSF and NIH are jointly funding grants in mathematical biology and the ecology of infectious diseases. Specifically, NSF and NIH sponsor a collaborative research program in computational neuroscience that could lead to significant advances in the understanding of nervous system function and the underlying mechanisms of nervous system disorders such as Alzheimer's disease.

### **5. Questions for Witnesses:**

*Dr. Keith Yamamoto*

- Please summarize the findings and recommendations of the National Research Council's report, *A New Biology for the 21st Century*.
- Are there promising research opportunities at the intersection of the biological sciences, the physical sciences, and engineering that are not being adequately addressed? Are Federal agencies, in particularly NSF, playing an effective role in fostering research at this intersection? If not, what recommendations would you offer?
- Is research in the biological sciences, including research at the intersection of the biological sciences, the physical sciences, and engineering being effectively coordinated across the Federal agencies? If not, what changes are needed?
- What changes, if any, are needed in the education and training of undergraduate and graduate students to enable them to work effectively across the boundaries of the physical sciences, engineering, and the biological sciences without compromising core disciplinary depth and understanding? Specifically, what recommendations or changes, if any, would you offer regarding the portfolio of education and training programs supported by NSF?

<sup>3</sup> [http://www.csrees.usda.gov/business/reporting/stakeholder/pdfs/pl\\_iwg\\_plant\\_genome\\_yearPlan.pdf](http://www.csrees.usda.gov/business/reporting/stakeholder/pdfs/pl_iwg_plant_genome_yearPlan.pdf)

<sup>4</sup> <http://www.climate-science.gov/Library/stratplan2008/CCSP-RRP-FINAL.pdf>

*Dr. James Collins*

- In your opinion, what is the future of research in the biological sciences and what potential does research at the intersection of the biological sciences, the physical sciences, and engineering hold for addressing grand challenges in the environment? What tools and methodologies need to be developed and what are the most promising research opportunities?
- As the most recent Assistant Director for Biological Sciences at the National Science Foundation,
  - How is NSF fostering research at the intersection of the biological sciences, the physical sciences, and engineering? What recommendations, if any, would you offer regarding NSF's current portfolio of programs supporting research at this intersection?
  - What education and training programs at NSF provide undergraduate students, graduate students, and postdocs with the skills necessary to work at the intersection of the biological sciences, the physical sciences, and engineering? What recommendations, if any, would you offer regarding NSF's education and training programs?
  - How is NSF fostering university-industry research collaborations in the biological sciences? What recommendations, if any, would you offer regarding NSF's university-industry programs?
- Is research in the biological sciences, including research at the intersection of the biological sciences, the physical sciences, and engineering being effectively coordinated across the Federal agencies? If not, what changes are needed?

*Dr. Reinhard Laubenbacher*

- In your opinion, what is the future of research in the biological sciences and what role does research at the intersection of biology and mathematics hold for addressing grand challenges in energy, the environment, agriculture, materials, and manufacturing? What computational tools still need to be developed? Are there promising research opportunities that are not being adequately addressed? Is the National Science Foundation playing an effective role in fostering research at the intersection of the physical sciences, engineering, and the biological sciences? If not, what recommendations would you offer?
- What is the nature of the interactions and collaborations between mathematicians and biological scientists at the Virginia Bioinformatics Institute (VBI)? How is VBI facilitating these interdisciplinary collaborations and what lessons can we learn from VBI? Is research at the intersection of the biological sciences, the physical sciences, and engineering being effectively coordinated across the Federal agencies? If not, what changes are needed?
- What changes, if any, are needed in the education and training of undergraduate and graduate students to enable them to work effectively across the boundaries of the physical sciences, engineering, and the biological sciences without compromising core disciplinary depth and understanding? Specifically, what recommendations or changes, if any, would you offer regarding the portfolio of education and training programs supported by NSF?

*Dr. Joshua N. Leonard*

- In your opinion, what role does research at the intersection of biology and engineering hold for addressing grand challenges in energy, the environment, agriculture, materials, and manufacturing? Specifically, describe the emerging field of synthetic biology, including the work of your research group and your involvement in the recent NSF sponsored "sandpit" and National Academies Keck Futures Initiative on synthetic biology. Is the National Science Foundation playing an effective role in fostering research in synthetic biology? If not, what recommendations would you offer?
- Is research in the biological sciences, including research at the intersection of the biological sciences, the physical sciences, and engineering being effectively coordinated across the Federal agencies? If not, what changes are needed?
- What changes, if any, are needed in the education and training of undergraduate and graduate students to enable them to work effectively across the

boundaries of the physical sciences, engineering, and the biological sciences without compromising core disciplinary depth and understanding? Specifically, describe the ongoing efforts of Northwestern University and the Department of Chemical and Biological Engineering to improve interdisciplinary graduate education. What recommendations or changes, if any, would you offer regarding the portfolio of education and training programs supported by NSF?

*Dr. Karl Sanford*

- Please provide a brief overview of Genencor, including a description of the development of new products and processes in the areas of bioenergy and biomaterials.
- In your opinion, what is the future of research in the biological sciences? How are research advances in the biological sciences driving industrial biotechnology? Does the current range of federally supported research adequately address the needs of the biotechnology industry? If not, what are the research gaps?
- Are science and engineering students being adequately trained by colleges and universities to be successful in the biotechnology industry? If not, what kind of education and training is needed and at what levels of education?
- What is the nature of Genencor's partnerships with U.S. universities, including Genencor's involvement in the Synthetic Biology Engineering Research Center at the University of California-Berkeley? Are the Federal agencies, including the National Science Foundation playing, an effective role in fostering university-industry collaboration? Are these research partnerships effective in the transfer of knowledge and technology from U.S. universities to industry? If not, are there best practices, training, or policies that should be put in place to facilitate the commercialization of federally funded research in the biological sciences?

Chairman LIPINSKI. The hearing will now come to order.

Good afternoon, and welcome to today's Research and Science Education Subcommittee hearing on 21st century biology.

There are an increasing number of reports showing how cheap DNA sequencing and computing power, together with our growing ability to control molecules at the smallest scales, are driving us toward a revolution in biology. Some believe that if we can combine vastly increased amounts of data with increased collaborations between biologists, computer scientists, mathematicians and engineers, we might be able to understand, manipulate, predict or even design the most complex system there is: a living organism.

Although biology was not my favorite subject in high school—although that may be because it was first semester freshman year and we had to dissect the fetal pig, and I can still remember the smell of the formaldehyde—the new, 21st century biology has me much more interested. I was trained as a mechanical engineer, and when I hear people talking about cells as a systems design problem, I understand the important role of engineers and physicists working in biology, and how “new biology” may be able to deliver on promises to solve critical problems in fields like energy, the environment, manufacturing and agriculture.

This afternoon we are going to take a closer look at the promise of 21st century biology by exploring research happening at the intersection of the biological sciences, the physical sciences, engineering and mathematics, and its potential to address real-world problems. We will also look at how these potential advances can be translated into technologies that benefit society, and what we need to do to train researchers who can thrive in an area that doesn't fit into any one department.

For example, research at the intersection of biology and engineering, known as synthetic biology, which we will learn more about today from Dr. Leonard, could lead to the development of bacteria that could help clean up the oil spill in the Gulf of Mexico, produce cellulosic biofuels, or even lead to an organism that can detect and destroy cancer cells. The current market for synthetic biology-based products is estimated at \$600 million and it is expected to grow to over \$3.5 billion within the next decade. This trend highlights the importance of today's hearing: the need to link research outcomes to American companies and American jobs.

As a former university professor, I have seen firsthand the difficulty of overcoming cultural and institutional barriers between academic departments and schools. Even within a single discipline like political science, researchers often stay safely within their subspecialties. But the potential successes that can be realized by having interdisciplinary teams working on biological problems mean that we need to ensure these collaborations continue to grow.

I am interested in hearing recommendations from today's witnesses about how the National Science Foundation can foster interdisciplinary research and how it can improve education and training for students who want to work at the intersection of the biological sciences, engineering, and the physical sciences. Finally, I would like to hear the panel's thoughts on the need to increase research coordination and collaboration in the biological sciences across the Federal agencies.

I thank the witnesses for being here this afternoon and look forward to their testimony.

[The prepared statement of Chairman Lipinski follows:]

PREPARED STATEMENT OF CHAIRMAN DANIEL LIPINSKI

Good afternoon and welcome to today's Research and Science Education Subcommittee hearing on 21st century biology. There are an increasing number of reports showing how cheap DNA sequencing and computing power, together with our growing ability to control molecules at the smallest scales are driving us toward a revolution in biology. Some believe that if we can combine vastly increased amounts of data with increased collaborations between biologists, computer scientists, mathematicians, and engineers, we might be able to understand, manipulate, predict, or even design the most complex system there is—a living organism.

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As a former university professor, I've seen firsthand the difficulty of overcoming cultural and institutional barriers between academic departments and schools. Even within a single discipline like political science researchers often stay safely within their specialties. But the potential successes that can be realized by having interdisciplinary teams working on biological problems mean that we need to ensure these collaborations continue to grow. I'm interested in hearing recommendations from today's witnesses about how the National Science Foundation can foster interdisciplinary research and how it can improve education and training for students who want to work at the intersection of the biological sciences, engineering, and the physical sciences. Finally, I'd like to hear the panel's thoughts on the need to increase research coordination and collaboration in the biological sciences across the Federal agencies.

I thank the witnesses for being here this afternoon and look forward to their testimony.

Chairman LIPINSKI. The Chair now recognizes Dr. Ehlers for his opening statement.

Mr. EHLERS. Thank you, Mr. Chairman. I thank you for having this hearing. This is a very important topic, and frankly a very difficult topic, and I will get into some details of that in just a moment. Let me also mention that I have, as often happens here, something else going on simultaneously, so I may be dashing in and out, but I will always be in earshot of what is going on here so I will keep track.

The collaborations between the biological sciences, physical sciences and engineering are becoming much more common at our major research institutions. Young investigators have discovered that to remain on the cutting edge of their research, they need to be partnering with various departments to solve challenges that

are much larger than a single discipline. This type of research arrangement will inevitably benefit students by preparing them for today's workforce much more than an education bound by a single discipline. At the same time, we need to ensure that our graduate students do not become overly broad instead of gaining a great level of expertise in a disciplinary area.

I can emphasize from some personal observations the difficulty of doing first-class, high-quality research in two different fields. I have a friend who has a Nobel Prize, not in biology, but decided some years ago that the future was in biology and related fields and so transferred over, and even though he earned a Nobel Prize in one area of science, he has never, to the best of my knowledge, contributed significantly to the area that he entered into involving biological sciences. So I think it is very important for us to respect that fact, particularly as we discuss funding for the future, and it is not at all clear that funding decisions up to this point at the various funding institutions in fact show recognition of that and how difficult it is, particularly for the older researchers, to switch from one field to another or try to combine two fields. I think this is clearly a case where we have to make certain that the young scientists coming along are, early on, recognized and given grants so that they can grow equally in both fields at the same time instead of first mastering one and then attempting to master another. So I think that is probably the most important thing we can learn here in this committee, and that relates to the funding and how to fund appropriately to ensure that the good scientists do have the money they need to accomplish success in two, maybe even three fields simultaneously.

As this committee determines how to foster new models for science and engineering research, today's witnesses will provide valuable insights on both conducting research in the new biology and integrating with other disciplines. I certainly look forward to hearing about this topic from our witnesses. I thank you for putting together a good panel, Mr. Chairman, and I am sure we can learn a lot about the issues that I raised a moment ago from this distinguished panel we have before us today.

With that, I yield back.

[The prepared statement of Mr. Ehlers follows:]

PREPARED STATEMENT OF REPRESENTATIVE VERNON J. EHLERS

Thank you, Chairman Lipinski. I am pleased that the Committee is holding this important hearing today.

Collaborations between the biological sciences, physical sciences and engineering are becoming much more common at our major research institutions. Young investigators have discovered that to remain on the cutting edge of their research they need to be partnering with various departments to solve challenges that are much larger than a single discipline. This type of research arrangement will inevitably benefit students by preparing them for today's workforce much more than an education bound by a single discipline. At the same time, we need to ensure that our graduate students do not become overly broad instead of gaining some level of expertise in a disciplinary area.

As this Committee determines how to foster new models for science and engineering research, today's witnesses will provide valuable insights on both conducting research in the "new biology" and integrating it with other disciplines.

I look forward to hearing about this topic from our witnesses.

Chairman LIPINSKI. Thank you, Dr. Ehlers, and I know this is a very busy time. I actually have two other hearings going on with

subcommittees I am on, so hopefully if you do have to go, we will——

Mr. EHLERS. I will be in and out, so——

Chairman LIPINSKI. We will carry on without you.

I wanted to point out an article in the New York Times yesterday that calls attention to why we are holding this hearing today. The issue of new biology, or 21st century biology—obviously our witnesses all understand it very well. The general public certainly does not have that great of an understanding of what all this means. I can't say that I have—certainly I don't come close to what our witnesses know, the knowledge that they have. But this article in the New York Times provides an example of some of the exciting research that is happening at the intersection of biology and material sciences. An interdisciplinary team is converting methane to ethylene using genetically engineered viruses. Now, ethylene is used widely in industrial products and processes such as manufacturing of solvents, but the process of producing ethylene hasn't changed since the 19th century. The work of this group is a significant step toward a more sustainable and less expensive process, so clearly there are many things going on right now in the new biology that will allow us to make great advances, and it is one of the reasons why we are holding this hearing here today.

So at this point, if there are Members who wish to submit additional opening statements, your statements will be added to the record at this point of the record.

So right now I want to start by introducing our witnesses. First we have Dr. Keith Yamamoto, who is Chair of the National Academy of Sciences' Board on Life Sciences as well as Professor of Cellular and Molecular Pharmacology at the University of California, San Francisco. Dr. James Collins is the Virginia M. Ullman Professor of Natural History and the Environment in the Department of Ecology, Evolution and Environmental Science at Arizona State University. Dr. Reinhard Laubenbacher is Professor in both the Virginia Bioinformatics Institute and the Department of Mathematics at Virginia Tech. Dr. Joshua N. Leonard is an Assistant Professor in the Department of Chemical and Biological Engineering at Northwestern University. And Dr. Karl Sanford is the Vice President for Technology Development at Genencor.

As our witnesses should know, you will each have five minutes for your spoken testimony. Your written testimony will be included in the record for the hearing. When you have all completed your spoken testimony, we will begin with questions. Each Member will have five minutes to question the panel.

So we will start here with Dr. Yamamoto.

**STATEMENT OF KEITH YAMAMOTO, CHAIR, NATIONAL ACADEMY OF SCIENCES' BOARD ON LIFE SCIENCES, AND PROFESSOR, CELLULAR AND MOLECULAR PHARMACOLOGY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO**

Dr. YAMAMOTO. Thank you. Good afternoon, Chairman Lipinski and Members of the Subcommittee. I am Keith Yamamoto, a Researcher, Professor, Executive Vice Dean of the School of Medicine at the University of California, San Francisco, and Chairman of the Board on Life Sciences of the National Research Council. Thank

you for the invitation to discuss with you today this report, the report from that board on the National Research Council called “*A New Biology for the 21st Century*.” The report was sponsored by the NSF [National Science Foundation], the NIH [National Institutes of Health], the Department of Energy, and was co-chaired by MIT professor and Nobel laureate Phillip Sharp and Dupont Senior Vice President Thomas Connelly. I also served as a member on that study committee.

To begin to describe the New Biology report, allow me to weave an imaginary scenario of research and science education for you in the biology 101 classroom of a college or university in your district. So here is the professor. I am good at this part. “In this course, we are going to dig into the fundamental principles of biology, and you will see that there are exciting mysteries waiting to be solved and within your reach. You will also learn that more than ever before, deepening our basic knowledge could help solve major societal problems. For example, discoveries in biology could allow us to breed new food crops that thrive under terrible growth conditions and give each region of the United States a thriving biofuel industry with transportation fuels produced from locally and sustainably grown biomass. To achieve this, you will need to team up with your classmates in physics, chemistry, engineering, math, and computer science to crack the deepest secrets of how living organisms obtain energy, grow, resist stress, combat disease and dispose of waste. Getting there will require a focused effort to apply that understanding to invent new technologies, and of course, getting there will require your curiosity and excitement about biological discovery and its potential for profound social impact.”

The New Biology committee proposed that this scenario become reality, that our current biological research enterprise, that remarkable discovery engine spread across more than 20 Federal agencies, be augmented with a small number of ten-year challenges that are urgent and inspiring but unreachable without a coordinated approach that aligns the separate strengths of multiple agencies.

Why this approach and why now? Because many of the pieces are in place to make it work. The unity of biology means that knowledge gained about one genome, one cell, organism, ecosystem is useful in understanding many others. Physical scientists, mathematicians and engineers are already entering this field and contributing unique approaches to biological puzzles. Scientists are exploiting the benefits of the Human Genome Project, new information and imaging technologies and whole new fields such as synthetic biology. Nevertheless, the committee found that we are missing critical synergies and leveraging opportunities because the new biology is currently poorly recognized, inadequately supported and delivering only a fraction of its potential.

The committee recommended that the United States can better capitalize on emerging knowledge in the life sciences by coordinating efforts toward urgent societal challenges in four broad areas: food, energy, the environment and health.

Why go after these huge sweeping issues? First, because we are in crisis mode with each. We must find ways to provide food and energy to a growing population without destroying our ecosystems.

We must reduce the burden of chronic disease in our society and of malnutrition and infectious disease in the developing world. Second, because big goals like putting a man on the moon or sequencing the human genome can inspire both scientists and the public. Big goals can focus the imagination, creating the technological breakthroughs essential for achieving those goals. Finally, big goals provide accountability, a commitment to concrete measurable results in return for sustained investments. The committee called for visionary scientists and engineers from the various focus areas to meet to identify some big goals, some great challenges.

In March, New Biology committee members briefed Department of Energy Secretary Steven Chu, Department of Agriculture Secretary Tom Vilsack and Howard Hughes Medical Institute President Robert Tjian, who then agreed to sponsor an early June workshop to generate challenge ideas that could provoke quantum leaps toward sustainable production of food and biofuels. The workshop brought together 30 extraordinary scientists and engineers who converged on a common overall goal: to sharply increase productivity in agriculture and biofuel production while simultaneously making both of those sectors carbon neutral.

Clearly, neither USDA [United States Department of Agriculture] nor DOE [Department of Energy] alone can achieve this goal. Rather, a coordinated effort will be required, a National New Biology Initiative that harnesses the capabilities of these and other agencies: NSF to stimulate necessary advances in fundamental knowledge of plants and ecosystems, NASA [National Aeronautics and Space Administration], NOAA [National Oceanic and Atmospheric Administration], USGS [U.S. Geological Survey] and NIST [National Institute of Standards and Technology] to work with DOE's AmeriFlux program and NSF's NEON [National Ecological Observatory Network] program to develop the ability to monitor carbon flows, NIH to contribute its expertise in genomics, basic cellular, molecular and microbial biology and bioengineering.

Finally, to return to the college classroom scenario that opened my testimony, a new biology initiative would demand reassessment of biology education. The committee strongly endorsed three major recommendations from the 2003 NRC report, "*Bio 2010*." First, ensure that biology students are well grounded in math, physical sciences and engineering; second, offer interdisciplinary independent lab research experience as early as possible; and third, provide faculty development time to embrace the integration of biology with the physical sciences, math and engineering, and to revise courses accordingly.

The New Biology Initiative adds a new layer to the traditional strategies, marshalling basic science purposefully toward solving urgent societal dilemmas, focusing teams of researchers, technologies and foundational sciences across agency boundaries. The initiative is a daring maneuver with great potential benefits: a more productive life sciences community, a better educated citizenry, a broad range of new bio-based industries, and most importantly, a science-based strategy to produce food and biofuels sustainably, monitor and restore ecosystems and improve human health.

[The prepared statement of Dr. Yamamoto follows:]

## PREPARED STATEMENT OF KEITH R. YAMAMOTO

Good afternoon, Chairman Lipinski and Members of the Subcommittee. Thank you for the invitation to present a statement before you today. I am Keith R. Yamamoto, Professor of Cellular and Molecular Pharmacology and Executive Vice Dean of the School of Medicine at the University of California, San Francisco, and Chairman of the Board on Life Sciences of the National Research Council. The National Research Council is the operating arm of the National Academy of Sciences, National Academy of Engineering, and the Institute of Medicine, chartered by Congress in 1863 to advise the government on matters of science and technology. In 2008, the Board on Life Sciences established the Committee on A New Biology for the 21st Century: Ensuring the United States Leads the Coming Biology Revolution, whose report I am very pleased to discuss with you today. The report "A New Biology for the 21st Century," which was released in August 2009, was sponsored by the National Science Foundation, the National Institutes of Health, and the Department of Energy. The study committee was co-chaired by MIT Professor and Nobel Laureate Philip Sharp and Dupont Senior Vice President and Chief Innovation Officer Thomas Connelly. I also served as a member of the study committee.

To begin to describe the New Biology report, allow me to weave for you an imaginary scenario, a scenario of research and science education, in the classroom or lecture hall of the introductory biology course this September in a college or university in your district. Listen in with me to the professor:

*"Thirty years from now, farmers in the United States and around the world could be producing sufficient food locally to nourish people in their regions, with no net increase in arable land and fresh water use, and a decrease in use of fertilizer, pesticides and fossil fuels. Furthermore, each region of the United States could have a thriving and sustainable biofuel industry, with liquid transportation fuels produced from locally grown biomass. Importantly, these advances in food and biofuel production could be carbon neutral, in other words, releasing no more greenhouse gases than they consume. And carbon flows into and out of the environment could be monitored by sensors that also assess ecosystem health, and provide immediate warning and simple restitution of environmental stress.*

*How will we achieve this? We must find ways to quickly and safely breed new and different food crops to achieve maximum production under any growing condition. We must find ways to adapt biomass crops to capture solar energy efficiently and convert it into easily processed biomolecules. We must find ways to detect early signs of stress to our ecosystems, and ways to restore them when they've been damaged. These are all challenges that demand aggressive and substantial advances in our knowledge and understanding of biology. Getting there will demand your best efforts should you become a biologist. But getting there will also require that some of your classmates who become physicists, chemists, engineers, mathematicians and computer scientists apply their skills to biological problems. It will take all of you, working together, to crack the deepest secrets of how living organisms obtain energy, grow, interact, resist stress, combat disease, reproduce, and dispose of waste. And it will take all of you to apply that understanding, and invent the technologies to advance our knowledge and achieve these goals.*

*The United States has determined that it must and will lead the world in achieving carbon neutral and sustainable agriculture and biofuel production. A national New Biology effort has been undertaken jointly by the National Science Foundation, the Departments of Agriculture, Energy, Interior and Education, the National Institutes of Health, and many other partners both public and private. The scope and scale of this challenge are such that no individual, no university, no company, no Federal agency could possibly solve it alone. Today you begin the process of learning how biology—the New Biology—can enable the United States to meet these challenges."*

The Committee on a New Biology for the 21st Century recommended that just such an imaginary scenario become reality—perhaps not by this September, but very soon. The scientists and engineers on the committee agreed that biology is at an inflection point – poised on the brink of major advances that could address urgent societal problems. Importantly, these problems demand bold action—they cannot be solved by a 'business as usual' approach. The United States has invested wisely to make us the world leader in life science discovery by promoting and supporting the curiosity and creativity of individual scientists. It is crucial that this investment continues and expands. But in addition, the committee recommended that now is the time to recognize some profound challenges, and to address those challenges by undertaking a bold experiment—to augment current life sciences research,

which is spread across more than 20 Federal agencies, with a small number of ten-year challenges that are urgent and inspiring, but unreachable without a coordinated approach that draws from and aligns the separate strengths of multiple agencies.

Why did the committee decide that a new approach is needed? For two reasons: first, the science is ready. And second, it is clear that we are missing important synergies and opportunities to leverage advances being made across the life sciences.

The report details five reasons why biology is ready to take on major challenges:

- First, the fundamental unity of biology has never been clearer or more applicable. Knowledge gained about one genome, cell, organism, or ecosystem is useful in understanding many others. The same technologies that allow us to survey human genomes for disease-associated genes also power high-throughput approaches to screening millions of plant seeds for desired genetic characteristics. It no longer makes sense to talk about biomedical research as if it is unrelated to biofuel or agricultural research; advances made in any of these areas are directly applicable in the others and all rely on the same foundational technologies and sciences.
- Second, new players are entering the field, bringing new skills and ideas. Physicists, chemists, mathematicians and engineers are increasingly attracted to the field of biology because of the fascinating questions it poses—questions that they can uniquely contribute to answering.
- Third, a strong foundation has already been built. Life science research has been amazingly productive for the last fifty years. The effort to construct the “parts list” for living systems has been a tremendously exciting intellectual adventure in its own right, and has had revolutionary outcomes in agriculture, health and industry.
- Fourth, past investments are paying big dividends. The Human Genome Project and subsequent advances in other high-throughput approaches and computational analysis have dramatically increased the productivity of life sciences researchers no matter what organism they study. Being able to collect and analyze comprehensive data sets allows researchers to study biological phenomena at the level of systems. The explosion of unanticipated benefits of the Human Genome Project demonstrates how biology can benefit from large-scale interdisciplinary efforts.
- Finally, new tools and emerging sciences are expanding what is possible. In addition to high-throughput approaches, information and imaging technologies have dramatically expanded the kinds of questions biologists can ask and answer. Systems, computational and synthetic biology are contributing to advances across the field of biology, from biomedicine to bioremediation.

The report gives many examples of advances that have been made possible by interdisciplinary teams integrating past discoveries and new technologies to produce major advances. The committee called this new approach the ‘New Biology’ and examples of the new approach are already emerging in many universities. But the committee’s discussions with scientists and supporting agencies made it clear that the New Biology is as yet poorly recognized, inadequately supported, and—critically—delivering only a fraction of its potential.

The committee concluded that the United States has an unprecedented opportunity to capitalize on the new capabilities emerging in the life sciences by mounting a multi-agency initiative to marshal resources and provide coordination to empower and enable the academic, public, and private sectors to address major societal challenges.

### **Why major challenges?**

First, because the problems are urgent. We must find ways to provide food and energy to a growing population without destruction of our ecosystems; we must find solutions to the increasing burden of chronic disease in our society, and to malnutrition and infectious disease in the developing world.

Secondly, because big goals—like putting a man on the moon, or sequencing the human genome—can inspire both scientists and the public. Big goals can attract the efforts of scientists and engineers who currently may not see how they could contribute their expertise to solving these urgent problems. Big goals can focus the imagination, creating the technological breakthroughs essential for achieving the goals. Finally, big goals provide explicit accountability: in enunciating a major challenge, the New Biologists and the public sector make a compact—a commitment to a sustained investment that will produce concrete, measurable results.

In the report, the committee described four broad areas of urgent need—food, energy, the environment, and health—and gave examples of the kinds of challenges that the New Biology could take on. In the area of food, for example, the committee suggested that the New Biology might develop ways to quickly, inexpensively, and safely adapt any crop plant to any growing condition. Success could enable local production of sufficient food, even on land that is considered non-arable today.

But the committee avoided prescribing specific projects or action plans. Instead, they called for visionary scientists and engineers from each area to identify great challenges for the New Biology that seem impossible now, but within reach if attacked in a coordinated way. A recent workshop demonstrated that the scientific community is more than up to the task.

The starting point was a March 16th meeting, where Department of Energy Secretary Stephen Chu, Department of Agriculture Secretary Tom Vilsack and HHMI President Robert Tjian agreed after a briefing from members of the New Biology committee to sponsor a workshop to generate challenge ideas at the scope and scale envisioned in the report. Secretaries Chu and Vilsack, and President Tjian all recognized the interconnections among their missions—human health depends on achieving sustainable production of food and energy in the face of multiple environmental stressors, including climate change. Clearly, none of these challenges can be addressed in isolation, but equally clearly, all four challenges are critically dependent on rapid advances in biological understanding and application.

The resulting June 3–4 workshop sought to develop broad ideas and project areas that could provoke quantum leaps of progress toward sustainable production of both food and biofuels. (Subsequent workshops will focus on other combinations of the four areas of need identified by the committee.) The workshop brought together an extraordinary group of scientists and engineers that spanned the scales, from molecules to ecosystems, and spectrum, from viruses to microbes to plants to animals, of modern biology. Each participant arrived at the workshop armed with a transformative idea to be presented in a three-minute talk during the first session. After hearing these short talks, the group broke into small subgroups to separately mold this collection of thirty bold ideas into a few decadal challenges, map out strategies for reaching them, and identify knowledge and technology gaps.

Upon reconvening, the subgroups swiftly converged on a common overall goal: to sharply increase productivity in agriculture and biofuel production while simultaneously making both of these sectors carbon neutral. All agreed that reaching this goal would require major advances in our fundamental understanding of plants and microbial communities, substantial investment in computational theory and infrastructure, and development of a quantitative and biologically-informed system for measuring the flow of carbon and other greenhouse gas constituents. It became very clear that not only could neither USDA nor DOE achieve this goal alone, but that a coordinated effort would be required—a National New Biology Initiative that harnesses the capabilities of these and other agencies: NSF to stimulate necessary advances in fundamental knowledge of plants and ecosystems; NASA, NOAA, USGS and NIST to work with DOE's Ameriflux program and NSF's NEON program to develop the ability to monitor carbon flows; NIH to contribute its expertise in genomics, basic cellular, molecular and microbial biology, and bioengineering.

I would be remiss if I failed to return to the vision that opened my testimony—college students being challenged from the first day of class to consider how life science research is relevant, indeed essential, to the solution of serious societal problems. A New Biology Initiative would give students interested in real-world problems an incentive to learn fundamental principles of science, mathematics and engineering, and to acquire an integrated view of those disciplines.

At the same time, the Initiative would provide the opportunity to establish and evaluate new educational and training opportunities. Many reports have appeared that recommend ways to improve science education in the United States; few of the recommendations have been implemented. To promote and enable the New Biology Initiative, the committee strongly endorsed three major recommendations from the 2003 NRC report, *Bio2010*: First, design curricula to ensure that biology students are well grounded in mathematics, physical and chemical sciences, and engineering; conversely, biological concepts and examples should be included in all science courses. Second, laboratory courses should be interdisciplinary, and independent research experience should be offered as early as possible. Finally, development time should be provided to enable faculty to appreciate fully the integration of biology with the physical sciences, math and engineering, and to revise their courses accordingly.

The New Biology committee issued a call to devote a modest portion of the life sciences research enterprise to empowering this new approach—to adding a new layer to the traditional strategies, a New Biology Initiative that marshals basic science purposefully toward solving urgent societal dilemmas, that focuses teams of

researchers, technologies and foundational sciences required for the task and coordinates efforts across agency boundaries to ensure that gaps are filled, problems addressed, and resources brought to bear at the right time. Close interaction between these problem-oriented efforts and the more decentralized basic research enterprise will be critical—and mutually beneficial—as the traditional approaches will make relevant unanticipated discoveries, and advances that benefit all researchers will spin out from problem-based projects. A New Biology Initiative to address major challenges would represent a daring addition to the nation’s research portfolio, with remarkable and far-reaching potential benefits: a more productive life sciences research community; a citizenry better informed about the logic and potential impact of biological research; a broad range of new bio-based industries; and, most importantly, a science-based strategy to produce food and biofuels sustainably, monitor and restore ecosystems, and improve human health.

This concludes my testimony. I would be pleased to answer your questions or address your comments. Thank you again for the opportunity to discuss this important matter with you.

#### BIOGRAPHY FOR KEITH R. YAMAMOTO

Dr. Keith Yamamoto, Ph.D., is Professor of Cellular and Molecular Pharmacology and Executive Vice Dean of the School of Medicine at the University of California, San Francisco. He has been a member of the UCSF faculty since 1976, serving as Director of the PIBS Graduate Program in Biochemistry and Molecular Biology (1988–2003), Vice Chair of the Department of Biochemistry and Biophysics (1985–1994), Chair of the Department of Cellular and Molecular Pharmacology (1994–2003), and Vice Dean for Research, School of Medicine (2002–2003). Dr. Yamamoto’s research is focused on signaling and transcriptional regulation by intracellular receptors, which mediate the actions of several classes of essential hormones and cellular signals; he uses both mechanistic and systems approaches to pursue these problems in pure molecules, cells and whole organisms. Dr. Yamamoto was a founding editor of *Molecular Biology of the Cell*, and serves on numerous editorial boards and scientific advisory boards, and national committees focused on public and scientific policy, public understanding and support of biological research, and science education; he chairs the Coalition for the Life Sciences (formerly the Joint Steering Committee for Public Policy) and for the National Academy of Sciences, he chairs the Board on Life Sciences. Dr. Yamamoto has long been involved in the process of peer review and the policies that govern it at the National Institutes of Health, serving as Chair of the Molecular Biology Study Section, member of the NIH Director’s Working Group on the Division of Research Grants, Chair of the Advisory Committee to the NIH Center for Scientific Review (CSR), member of the NIH Director’s Peer Review Oversight Group, member of the CSR Panel on Scientific Boundaries for Review, member of the Advisory Committee to the NIH Director, Co-Chair of the Working Group to Enhance NIH Peer Review, and Co-Chair of the Review Committee for the Transformational R01 Award. Dr. Yamamoto was elected as a member of the American Academy of Arts and Sciences in 1988, the National Academy of Sciences in 1989, the Institute of Medicine in 2003, and as a fellow of the American Association for the Advancement of Sciences in 2002.

Chairman LIPINSKI. Thank you, Dr. Yamamoto.  
Dr. Collins.

#### **STATEMENT OF JAMES COLLINS, VIRGINIA M. ULLMAN PROFESSOR OF NATURAL HISTORY AND THE ENVIRONMENT, DEPARTMENT OF ECOLOGY, EVOLUTION AND ENVIRONMENTAL SCIENCE, ARIZONA STATE UNIVERSITY**

Dr. COLLINS. Thank you very much, Chairman Lipinski, Ranking Member Ehlers and Committee members. I appreciate the opportunity to testify before you today on 21st century biology. It is a topic of vital importance to sustaining America’s leadership in science and technology.

The biological sciences will flourish in the 21st century by sustaining strength in its core disciplines while simultaneously supporting research at the intersection of the natural, physical and social sciences as well as engineering. Interdisciplinary methods cut

across disciplines to combine, in powerful ways, basic research with solving real-world problems.

Biology itself emerged as an interdisciplinary science late in the 19th century when researchers studying physiology, natural history, anatomy and other sciences argued for uniting them as the new discipline of biology focused on the study of life. Some late 19th and early 20th century life scientists also conceived of their research more within the realm of engineering. They thought that their studies should be focused on controlling life. They envisioned manipulating, transforming and even replicating living systems in order to understand nature and also to help solve human problems. It is a 19th century perspective reminiscent of modern synthetic biology. Throughout the 20th century, the two great themes of understanding and controlling life wove together even as biology divided itself into the basic subdisciplines of genetics, cell biology, ecology and evolution.

Two things stand out as we look to biology's 21st century future. First, more and more research questions require reintegrating biology subdisciplines, and the fields are making progress in carrying out that integration. The second thing we see is the biological sciences as a growing source of inspiration for and collaboration with engineering and the physical and social sciences. Computational biology, systems biology and sustainability science are products of this merger. However, even as we imagine biology's role in addressing today's challenges, we cannot forget that these will change over time. This means that U.S. institutions that fund and conduct research must be innovative and adaptable. Reinforcing this need is the fact that many of the challenges ahead will not be solved by business as usual. Innovation must be the hallmark of research and education if "*A New Biology*," envisioned in the recent NRC report, is to be realized.

Creating and sustaining an innovation ecosystem in the life sciences means that all of the pieces must function as a system, which generally means lowering the barriers that block the ready flow of knowledge and ideas between, for example, academic departments, funding agencies, or the public and private sector.

As we look at the history of science, it is also clear that the process of discovery changes. In an obvious sense, new tools and methods are developed and that remains true today. But modern research also joins individuals into larger and larger teams. New methods like crowdsourcing and prediction markets are linking experts across the globe, effectively lowering those barriers I mentioned earlier. Funding agencies can also use these innovative methods to help fund the very best research, and NSF, for example, is already using some of these methods.

In a rapidly changing world, the process of discovery itself is also changing, and our students must learn how to keep up. Modern biology curricula should expose students to this sort of thinking and more. Because today's students are tomorrow's problem solvers, we must integrate research and education to prepare the next generation to address 21st century challenges.

I urge this subcommittee and Congress to support innovative agency efforts to catalyze transformative research and education at levels that sustain reasonable success rates; disciplinary and inter-

disciplinary programs that drive the ready exchange of knowledge and ideas; efforts to advance curriculum reform in biology; and establishing appropriate metrics to judge programs.

The Subcommittee asked me to comment on university and industry collaborations and coordination across U.S. Federal agencies. These topics are related. Knowledge creation and use along with the best ideas to identify and fund research and education should not start or stop at the borders of one organization. In the best cases, the relationship between a university and an industry partner, or either of these with a Federal funding agency, should be a two-way process of learning best practices from each other. Coordination across Federal agencies builds coalitions and lowers barriers while leveraging the innovative ideas of several institutions. At its best, this really creates an open-source environment for innovation.

One last thought. In the NRC's "A New Biology" report, we see the central themes of biology's origins—understanding life, controlling life, and a call for broad engagement with other disciplines—recast in new forms around contemporary problems. Modern science, engineering and technology are full of breathtaking discoveries. It would be wrong, however, to conclude that scientists and engineers can solve all the problems of food, health, energy and the environment. Social scientists call questions in these areas 'wicked problems' for a reason. They are full of complex interdependent parts, and solving one aspect of a problem often reveals or even creates other problems. Simply put, so-called 'wicked problems' will not yield to only scientific or technological fixes. America's best researchers and their students must engage in a process of discovery that transforms the way in which research is conducted and students are educated. If the changes needed are to occur at a sufficiently fundamental level, it will also mean transforming our research institutions.

I have envisioned a future for biology that has three elements: first, sustaining disciplines while blurring their boundaries; second, innovation as a central feature of life science research and education; and third, building coalitions among institutions. In combination, these three elements are a vision for how the life sciences will play a key role in addressing the great intellectual and social challenges of the 21st century. At the same time, we will sustain America's leadership in science, engineering and technology innovation during the years ahead.

Once again, thank you, Mr. Chairman, for giving me the opportunity to testify on this very important subject. I will be pleased to answer any questions that you have.

[The prepared statement of Dr. Collins follows:]

PREPARED STATEMENT OF JAMES P. COLLINS

Chairman Lipinski, Ranking Member Ehlers, and committee members: I am James P. Collins, Virginia M. Ullman Professor in the School of Life Sciences at Arizona State University (ASU). I am also an Affiliated Scholar in the Consortium for Science and Policy Outcomes at ASU. Prior to returning to Arizona State University, I served in the Federal Government during the George W. Bush and Barack H. Obama Administrations as Assistant Director for Biological Sciences at the National Science Foundation (NSF) from October 2005 to October 2009. I am currently a consultant at NSF.

The biological sciences will flourish in the 21st century by sustaining strength in its core disciplines while simultaneously supporting research at the intersection of the natural, physical, and social sciences as well as engineering. Research at these disciplinary edges holds great promise for addressing problems in energy, the environment, agriculture, materials, and manufacturing. Interdisciplinary methods cut across disciplines to combine in powerful ways basic research with solving real world problems. Because today's students are tomorrow's problem solvers we must also integrate research and education to prepare the next generation to address 21st century challenges. But the problems confronting us are complex and will not be solved by business as usual: innovation must be a hallmark of both research and education in 21st Century Biology.

### **Sustaining disciplines while blurring their boundaries**

Biology itself emerged as an interdisciplinary science late in the 19th century. At that time researchers from diverse areas such as physiology, natural history, and anatomy realized their research had a common theme and argued for uniting these largely separate areas of scholarship into the new discipline of biology focused on the study of life: How did life originate? Why are there so many species? How does heredity influence development of individuals? What organizes living systems from the complexity of a cell to the complexity of a forest?

Some late 19th and early 20th century life scientists also conceived of their research more within the realm of engineering. As the historian of science Dr. Philip Pauly argued, they thought that their research should be focused on controlling life. They envisioned manipulating, transforming, and even replicating living systems, in order to understand nature and also to help solve human problems. "Nature was raw material to be transformed by the power of the biologist" wrote Dr. Pauly (Pauly, P.J. 1987. *Controlling Life. Jacques Loeb and the engineering ideal in biology*. Oxford University Press, Oxford). Straight from the first decade of the 20th century this is a perspective that we can easily imagine finding in a 21st century discussion of synthetic biology or nanotechnology.

Throughout the 20th century the two great themes of understanding and controlling life wove together even as biology itself divided into sub-disciplines such as genetics, cell biology, ecology, and evolution. Discoveries such as the molecular structure of DNA advanced our basic understanding of genetics, and this knowledge was then applied through biotechnology to control living organisms such as genetically modified crops. Discoveries in embryology led to fertility treatments, while discoveries in ecology led to improved environmental quality. Yet until recently, the sub-disciplines have not worked together as effectively as they might.

Two things stand out as we look to biology's 21st century future:

- First, more and more research questions require reintegrating biology's sub-disciplines, and the fields are making progress in carrying out that integration.

For example, systems biology seeks a deep quantitative understanding of the emergent properties of complex biological systems—properties such as resilience, adaptability and sustainability—through the dynamic interaction of components that may include multiple molecular, cellular, organismal, population, community, and ecosystem functions (after *A New Biology*. 2009. National Academies Press, Washington, DC: p. 61).

- The second thing we see is the biological sciences as a growing source of inspiration for and collaboration with engineering and the physical and social sciences.

A recent National Research Council report, *Inspired by Biology: from molecules to materials to machines* (2008. National Academies Press, Washington, DC), calls for three research strategies: biomimicry or learning how a living system's mechanistic principles achieve a function and then replicating that function in a synthetic material; bioinspiration where a task achieved by a living system inspires making a synthetic system; and bioderivation which involves hybridizing a biological and artificial material. Developing these biologically inspired materials advances basic science, improves U.S. competitiveness, and addresses national challenges in materials and manufacturing. This sort of visionary research at disciplinary edges is transforming and selectively dissolving the boundaries of the life and physical sciences as well as engineering.

Biology in the 21st century is rapidly changing before our eyes as life scientists engage in innovative ways with many other areas of scholarship. Today's biologists conduct research in areas that did not exist as recently as ten or even five years ago: computational biology, systems biology, and sustainability science are exam-

ples. These interdisciplinary fields are emerging as a result of new questions, new tools such as sensors, new methods such as computational thinking, and new ways of conducting research especially in large group collaborations supported by new cyberinfrastructure.

At the Subcommittee's request I'll comment on the environmental sciences, which offer many promising research opportunities. Interdisciplinary research is advancing our basic understanding of challenges such as global change and global loss of biodiversity and suggesting ways in which we might mitigate these changes. NSF-supported sensing systems in the Long Term Ecological Research Network (LTER) and in the proposed National Ecological Observatory Network (NEON) are designed to gather enormous quantities of data continuously. These networks of sensors, computers, and people promise to transform how we test basic ecological theory and apply the results to environmental problem solving. Molecular methods are accelerating the description of new species, including the discovery of novel microbes that add to our basic understanding of the biosphere while serving as "bio-inspiring" sources of novel energy technologies. At NSF the new Dimensions of Biodiversity initiative is supporting just this sort of grand challenge research in which new knowledge is developed.

As this research matures, researchers will need new tools such as sensors that run on small, very long life power sources. New methods must include fast, highly accurate molecular techniques for identifying species and efficient computer algorithms for analyzing, visualizing, and storing large quantities of data. Students entering these fields must be skilled in quantitative and computational methods, understand how to draw on multiple disciplines to address problems, and learn to do science in nationally and globally connected communities.

We must remember, however, that even as we envision biology as a way to address today's problems we cannot forget that today's "grand challenges" eventually will change. Our research institutions must remain agile and capable of responding to new and evolving problems that we cannot yet imagine. Part of the agility and capability needed must come from supporting researchers conducting basic research that generates new knowledge. In addition, the agility and capability needed must come from educating students and ourselves in innovative ways. Failing to do both of these things would cause the U.S. to lose out in two ways: first, we would not have the basic knowledge needed to respond to a future challenge and second, in the near term we fail to sustain ourselves as science and technology leaders. Research agencies and universities must be innovative and adaptable if "a new biology" envisioned in the recent NRC report by the same name is to be realized.

#### **Innovation as a central feature of life science research and education**

When I testified before this Subcommittee in October 2009, I observed that NSF was first and foremost an innovation agency with a long history of success in supporting research with far-reaching impacts on the U.S. economy and the well-being of all Americans (*Investing in high-risk, high-reward research*; available at: [http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111\\_house\\_hearings&docid=f:52484.pdf](http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_house_hearings&docid=f:52484.pdf)).

In particular I argued that, "The challenge for agencies like NSF that fund research done by other organizations is to create and sustain a culture of innovation in which the flow of information among its members creates an institutional culture and framework that stimulates, reinforces, and rewards creativity, and pervades the agency and guides its decision-making process." That remains true today for NSF, and in general creating and sustaining an innovation ecosystem is a wider challenge for our funding agencies, America's universities, and industry.

At the heart of this ecosystem is what we can call the process of discovery, which begins with an idea that is tested and developed by one or a few individuals. Increasingly, however, the testing is done by large groups that may or may not be in one place. Networks of computers unite investigators in problem solving efforts using what is called "the wisdom of the crowd." It is an approach that can be very effective in bringing together widely separated experts for solving problems rapidly. Crowd sourcing models, prediction markets, and prizes are modern components of the process of discovery (Collins, J.P., *Investing in high-risk, high-reward research*).

Innovation is not just an idea, but it is a process that links a few to many individuals. In a rapidly changing world the process of discovery itself is also changing rapidly, and our students must learn how to keep up. Modern biology curricula should expose students to this sort of thinking and more. Learning is the creative process by which new knowledge is discovered; learning is not memorization of facts as an end in itself. Too often students imagine biology as the latter, perhaps because it is commonly taught that way, but no characterization of the biological sciences could be further from the truth.

One innovative reform effort in biology curricula is called Vision and Change in Undergraduate Biology which is a joint effort of NSF and the American Association for the Advancement of Science or AAAS (<http://visionandchange.org/>). A second international effort focused on undergraduate curricula in general is emerging from an international consortium at the Wissenschaftskolleg zu Berlin/Institute for Advanced Study (Appendix I). Both are opportunities for the U.S. to assume a leadership role in shaping student learning and problem solving in the 21st century.

But as the saying goes, a vision (or idea) without resources is a mirage. Funding is needed for developing innovative ideas and here is where researchers/entrepreneurs turn to public and private sources for help.

NSF is one choice for U.S. researchers and educators. The Directorate for Biological Sciences advances transformative science by building on fundamental disciplinary strengths and also by encouraging high risk/high reward research. The directorate is experimenting with new methods of review such as crowd sourcing and prediction markets to support transformative science and learning at the interface of biology and many other disciplines. Experimenting with innovative methods for finding the best ideas to fund in research and education must be a central feature of NSF and other Federal agencies.

Especially as budgets tighten it is easy for any institution to be satisfied with sustaining what it does well. But the magnitude of some of the challenges and the need to respond quickly means that business as usual is not good enough. Agencies like NSF should be bold and adopt policies that foster innovation as they seek to fund high risk, high reward research—and education.

A central value at NSF is the integration of research and education. In response to a question from the Subcommittee I'll note that the NSF supports a wide range of programs from undergraduate REUs (Research Experiences for Undergraduates), to graduate IGERTs (Integrated Graduate Research and Training), and postdoctoral fellowships.

As contributors to the U.S. scientific enterprise students also need an understanding of the historical, philosophical, and ethical context within which research questions are asked and answered. Students must understand that knowledge is not a static set of facts but is always evolving within a historical and cultural context. We must instill in students an interest in and a healthy respect for the societal implications of their research because the best of them will make discoveries that will have huge implications for society.

The radical transformations enabled by modern technologies for generating and disseminating knowledge quickly and widely can be a great help in enabling the basic discoveries needed for understanding life and addressing real world problems. Much of the future will be about networks of investigators and networks of institutions.

### **Building coalitions among institutions**

The Subcommittee asked me to comment on university-industry collaborations and coordination across U.S. Federal agencies. These topics are related: knowledge creation and use along with the best ideas to identify and fund research and education should not start or stop at the borders of one organization.

University-industry partnerships are increasingly a feature of the modern educational landscape. NSF funds major Science and Technology Centers that connect universities and colleges to private sector technology development. At the Subcommittee's request I have appended to this testimony examples of NSF activities at the intersection of federally funded basic research, the private sector, and universities (Appendix II).

In the best cases the relationship between a university and industry partner, or either of these with a Federal funding agency, should be a two-way process of learning. For example, the process of discovering marketable ideas within industry can be very innovative. In my last discussion with the Subcommittee I described how "The recent Netflix million-dollar prize competition is a compelling example of the successful use of crowd sourcing for technological discovery while also contributing to a culture of innovation." A recent *New York Times* (June 27, 2010: B1–B8) report described "proof-of-concept centers" to bridge university researchers studying basic problems to the business world. The report noted that "Rather than offering seed money to businesses that already have a product and a staff, as incubators usually do, the universities are harvesting great ideas and then trying to find investors and businesspeople interested in developing them further and exploring their commercial viability." Universities are acting as very early risk takers to help bridge the so-called "valley of death" separating people with ideas from people willing to invest in them.

As NSF fosters university-industry collaborations in biology the Foundation can learn best practices from this process. Institutions should be open to using great ideas wherever they are found.

Coordination across Federal agencies is another way to build coalitions while also serving as a way to leverage the innovative ideas of several institutions. For example, the National Institute for Mathematical and Biological Synthesis is jointly supported by NSF's Directorate for Biological Sciences, Directorate for Mathematics and Physical Sciences, U.S. Department of Agriculture (USDA), and Department of Homeland Security. Two Nanotechnology Centers are supported by NSF's Directorate for Biological Sciences and the Environmental Protection Agency. The Plant Genome Research Program (PGRP) is an excellent example of coordination across Federal agencies. NSF, USDA, Department of Energy, National Institutes of Health, and the U.S. Agency for International Development collaborate to support PGRP, which is an exceptionally effective National Science and Technology Council collaboration for fostering basic plant research and its translation to agriculture.

Institutional coalitions are not the answer to every challenge, but in selected cases they can be very effective ways to leverage resources and facilitate innovation.

#### **Modern problem solving requires more than science and technology**

In the U.S. National Research Council's *New Biology* report we see the central themes of biology's origins—understanding life, controlling life and a call for broad engagement with other disciplines—recast in new forms around contemporary problems. Modern science, engineering, and technology are full of breathtaking discoveries. It would be wrong, however, to conclude that scientists and engineers can solve all of the problems of food, health, energy, and the environment. Social scientists call questions in these areas “wicked problems” for a reason: they are full of complex, interdependent parts and solving one aspect of a problem often reveals or even creates other problems. Simply put, so-called wicked problems will not yield to only scientific or technological fixes.

America's best researchers and their students must engage in a process of discovery that transforms the way in which research is conducted and students are educated. If the changes needed are to occur at a sufficiently fundamental level it will also mean transforming our research institutions. Solving problems must not be limited by disciplinary or institutional borders. Global change and the global loss of biodiversity are part of a litany of important and pressing problems. Challenges such as these have the quality that the longer we delay addressing them the worse they become. The process of discovering solutions must include students as partners with our senior researchers. Because they are young, students have great energy to invest in realizing a future in which they have the greatest stake as planetary stewards. Agility and adaptability, which are available in great quantities in young people, will be indispensable qualities for problem solvers in a rapidly changing world.

I have envisioned a future for biology that has three elements: sustaining disciplines while blurring their boundaries; innovation as a central feature of life science research and education; and building coalitions among institutions. In combination these three elements are a vision for understanding how the life sciences will play a key role in addressing the great intellectual and social challenges of the 21st century. At the same time, we will sustain America's leadership in science, engineering, and technology innovation during the years ahead.

Once again Mr. Chairman, thank you very much for giving me the opportunity to testify on this very important subject. I would be pleased to answer any questions that you have.

**Appendix I. Principles for Rethinking Undergraduate Curricula for the 21st Century: A Manifesto** (From: Principles of curricular reform developed by a Wissenschaftskolleg zu Berlin/Institute for Advanced Study 2009–2010 working group and revised at the Workshop on “The University of the 21st Century,” Wissenschaftskolleg zu Berlin/Institute for Advanced Study, June 5–6, 2010.)

The current crisis of the university is intellectual. It is a crisis of purpose, focus and content, rooted in fundamental confusion about all three. As a consequence, curricula are largely separate from research, subjects are taught in disciplinary isolation, knowledge is conflated with information and is more often than not presented as static rather than dynamic. Furthermore, universities are largely reactive rather than providing clear forward-looking visions and critical perspectives. The crisis is all the more visible today, as the pace of social, intellectual and technological change inside and outside the universities is increasingly out of step. While universities worldwide are undergoing many, often radical, structural transformations, ranging from the Bologna Process in Europe and the Exzellenzinitiative in Germany to the rapid expansion of universities in India and China, the accelerating decline of public investments in universities in the United States and elsewhere and an ever growing demand for university access everywhere, much less attention has been paid to university curricula. But for the university as a community of scholars and students, that is its central function and the key to its internal renewal. Universities are embedded in multiple institutional, economic, financial, political, and research networks. All of these generate pressures and constraints as well as opportunities. The curriculum, however, is the core domain of the university itself.

Here we present a set of eleven overlapping principles designed to inform an international dialogue and to guide an experimental process of redesigning university undergraduate curricula worldwide. There can be no standard formula for implementation of these principles given the huge diversity of institutional structures and cultural differences amongst universities but these principles, we believe, provide the foundational concepts for what needs to be done.

1. As a central guideline teach disciplines rigorously in introductory courses together with a set of parallel seminars devoted to complex real life problems that transcend disciplinary boundaries.
2. Teach knowledge in its social, cultural and political contexts. Teach not just the factual subject matter, but highlight the challenges, open questions and uncertainties of each discipline.
3. Create awareness of the great problems humanity is facing (hunger, poverty, public health, sustainability, climate change, water resources, security, etc.) and show that no single discipline can adequately address any of them.
4. Use these challenges to demonstrate and rigorously practice interdisciplinarity avoiding the dangers of interdisciplinary dilettantism.
5. Treat knowledge historically and examine critically how it is generated, acquired, and used. Emphasize that different cultures have their own traditions and different ways of knowing. Do not treat knowledge as static and embedded in a fixed canon.
6. Provide all students with a fundamental understanding of the basics of the natural and the social sciences, and the humanities. Emphasize and illustrate the connections between these traditions of knowledge.
7. Engage with the world’s complexity and messiness. This applies to the sciences as much as to the social political and cultural dimensions of the world. This will contribute to the education of concerned citizens.
8. Emphasize a broad and inclusive evolutionary mode of thinking in all areas of the curriculum.
9. Familiarize students with non-linear phenomena in all areas of knowledge.
10. Fuse theory and analytic rigor with practice and the application of knowledge to real-world problems.
11. Rethink the implications of modern communication and information technologies for education and the architecture of the university.

Curricular changes of this magnitude and significance both require and produce changes in the structural arrangements and institutional profiles of universities. This is true for matters of governance, leadership, and finance as well as for systems of institutional rewards, assessment, and incentives; it is bound to have implications for the recruitment and evaluation of both professors and students as well as for the allocation of resources and the institutional practice of accountability. The experimental process of curriculum reform we hope to stimulate by offering these

guiding principles will thus require the collaboration of scholars and educators willing to transform their scholarly and educational practices and of administrators willing to support experimentation and to provide the necessary structural conditions for it to succeed.

These principles are the conclusion of deliberations by a working group of scholars that met at the Wissenschaftskolleg zu Berlin during the academic year 2009/10. Participants represented diverse disciplines (from the natural and social sciences and the humanities), geographical origins (Europe, North America, and India) as well as career stages (from former university presidents to students). They invite their colleagues around the world to join in this effort of re-thinking and re-shaping teaching and learning for the university of the future.

**Appendix II: Examples of NSF activities at the intersection of federally funded basic research and the private sector and universities.** (from Collins, J.P. 2009. *Investing in high-risk, high-reward research*. available at: [http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111\\_house\\_hearings&docid=f:52484.pdf](http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_house_hearings&docid=f:52484.pdf)).

NSF-funded Centers are designed from the outset with built-in flexibility so that investigators can pursue innovative ideas within the context of a defined program of research. Examples are legion, and include the Mosaic web browser developed at NSF's National Center for Supercomputing Applications at the University of Illinois. NSF's creation of two Centers for the Environmental Implications of Nanotechnology (CEIN) in 2008 exemplify innovative networks that are connected to other research organizations, industry, and government agencies to strengthen our nation's commitment to understanding the potential environmental hazards of nanomaterials and to provide basic information leading to the safe environmentally responsible design of future nanomaterials.

The **Industry/University Cooperative Research Centers (I/UCRC)** program develops long-term partnerships among industry, academe, and government. Each I/UCRC contributes to the Nation's research infrastructure, enhances the intellectual capacity of the STEM workforce by integrating research with education, and encourages and fosters international cooperation and collaborative projects. For example, the NSF Industry/University Collaborative Research Center (I/UCRC) known as the Berkeley Sensor and Actuator Center conducts industry-relevant, interdisciplinary research on micro- and nano-scale sensors, moving mechanical elements, microfluidics, materials, and processes that take advantage of progress made in integrated-circuit, bio, and polymer technologies. This I/UCRC has developed and demonstrated a handheld device that allows verified diagnostic assays for several infectious diseases currently presenting significant threats to public health, including dengue, malaria, and HIV. The device uses a dramatically simplified testing protocol that makes it suitable for use by moderately-trained personnel in a point-of-care or home setting. The center has also created many spin-off ventures including companies in the areas of wireless sensor networks for intelligent buildings; MEMS mirror arrays for adaptive optics; and optical flow sensors for industrial, commercial, and medical applications.

The objective of the NSF **Small Business Innovation Research (SBIR)** program is to increase the incentive and opportunity for small firms to undertake cutting-edge research that would have a high potential economic payoff if successful. For example, in 1985, Andrew Viterbi and six colleagues formed "QUALity COMMUNICATIONS." In 1987–1988 NSF SBIR provided \$265,000 (Phase I 8660104 and Phase II 8801254) for single chip implementation of the Viterbi decoder algorithm. Qualcomm introduced CDMA (code division multiple access) which replaced TDMA (time division multiple access) as a cellular communications standard in 1989. This advance led to high-speed data transmission via wireless and satellite. Now the \$78B company holds more than 10,100 U.S. patents, licensed to more than 165 companies. Another example—Machine Intelligence Corp. was supported by SBIR Phase I and Phase II awards to develop desktop computer software that could alphabetize words, a feat that previously had been accomplished only on supercomputers. When Machine Intelligence went bankrupt, principal investigator Gary Hendrix founded Symantec and continued the project. The line of research resulted in the first personal computer software that understood English, marketed as "Q&A Software." Q&A quickly became an extremely successful commercial product and remains a widespread commercial application of natural language processing. Symantec research supported by NSF SBIR eventually led to six other commercial products and contributed to 20 others. Now, Symantec is a leading anti-virus and PC-utilities Software Company valued at \$12B with more than 17500 employees worldwide.

NSF launched the **Integrative Graduate Education and Traineeship Program (IGERT)** in 1997 to encourage innovative models for graduate education at colleges and universities across the Nation that would catalyze a cultural change in graduate education—for students, faculty and institutions. IGERT was designed to challenge narrow disciplinary structures, to facilitate greater diversity in student participation and preparation, and to contribute to the development of a diverse, globally-engaged science and engineering workforce. The result has been a cadre of imaginative and creative young researchers. For example, an NSF-funded IGERT award to the Scripps Institute of Oceanography (NSF #0333444) supported a doctoral student who successfully modeled the extinction of the Caribbean monk seal and demonstrated the magnitude of the impact of over-fishing on Caribbean coral reefs. This research developed improved ecological models, which may influence en-

vironmental policy and ultimately lead to the preservation of species and ecosystems for future generations.

#### BIOGRAPHY FOR JAMES P. COLLINS

Dr. James Collins received his B.S. from Manhattan College in 1969 and his Ph.D. from The University of Michigan in 1975. He then moved to Arizona State University where he is currently Virginia M. Ullman Professor of Natural History and the Environment in the School of Life Sciences. From 1989 to 2002 he was Chairman of the Zoology, then Biology Department. At the National Science Foundation (NSF) Dr. Collins was Director of the Population Biology and Physiological Ecology program from 1985 to 1986. He joined NSF's senior management in 2005 serving as Assistant Director for Biological Sciences from 2005 to 2009. NSF is the U.S. government's only agency dedicated to supporting basic research and education in all fields of science and engineering at all levels. Collins oversaw a research and education portfolio that spanned molecular and cellular biosciences to global change as well as biological infrastructure. He coordinated collaborations between NSF and other Federal agencies through the President's National Science and Technology Council where he chaired the Biotechnology Subcommittee and co-chaired the Inter-agency Working Group on Plant Genomics. He was also NSF's liaison to NIH.

Dr. Collins's research has centered on the causes of intraspecific variation. Amphibians are model organisms for field and laboratory studies of the ecological and evolutionary forces shaping this variation and its affect on population dynamics. A recent research focus is host-pathogen biology as a driver of population dynamics and even species extinctions. The role of pathogens in the global decline of amphibians is the model system for this research.

The intellectual and institutional factors that have shaped Ecology's development as a science are also a focus of Dr. Collins's research, as is the emerging research area of ecological ethics. Federal, state, and private institutions have supported his research.

Dr. Collins teaches graduate and undergraduate courses in ecology, evolutionary biology, statistics, introductory biology, evolutionary ecology, and professional values in science; he has directed 33 graduate students to completion of doctoral or Masters degrees. Collins was founding director of ASU's Undergraduate Biology Enrichment Program, and served as co-director of ASU's Undergraduate Mentoring in Environmental Biology and Minority Access to Research Careers programs.

Honors include the Pettingill Lecture in Natural History at The University of Michigan Biological Station; the Thomas Hall Lecture at Washington University, St. Louis; Distinguished Lecturer in Life Science, Penn State University, and serving as Kaeser Visiting Scholar at the University of Wisconsin-Madison. ASU's College of Liberal Arts and Sciences awarded him its Distinguished Faculty Award. He is a Fellow of the American Association for the Advancement of Science, a Fellow of the Association for Women in Science, and President Elect of the American Institute of Biological Sciences (AIBS).

Dr. Collins has served on the editorial board of *Ecology* and *Ecological Monographs* as well as *Evolution*. He is the author of over 100 peer reviewed papers and book chapters, co-editor of three special journal issues, and co-author with Dr. Martha Crump of *Extinction in Our Times. Global Amphibian Decline* (Oxford University Press, 2009).

Chairman LIPINSKI. Thank you, Dr. Collins.  
Dr. Laubenbacher.

#### **STATEMENT OF REINHARD LAUBENBACHER, PROFESSOR, VIRGINIA BIOINFORMATICS INSTITUTE, DEPARTMENT OF MATHEMATICS, VIRGINIA TECH**

Dr. LAUBENBACHER. Good afternoon, Chairman Lipinski, Ranking Member Ehlers and Members of the Committee. Thank you for the invitation to testify today on 21st century biology. My name is Reinhard Laubenbacher and I am a Professor at the Virginia Bioinformatics Institute at Virginia Tech. I am also the Vice President for Science Policy for the Society for Industrial and Applied Mathematics, an organization with approximately 13,000 members who work in academia, government and industry. While our mem-

bers come from many different disciplines, we have a common interest in applying mathematics and computational science toward solving real-world problems. I will speak to three areas in my testimony today: first, research to address grand challenges; second, fostering interdisciplinary collaborations and cross-agency coordination; and third, workforce development, education and training.

The first area I want to discuss is research to address the grand challenges. A central finding of the National Research Council report is that new information, technologies and sciences will be essential to achieving the new biology for the 21st century and meeting challenges in health, food, energy and environment. Two examples of how mathematics can contribute to the new biology are, first, through modeling. The ability to describe the essence of complex biological systems with mathematical equations will allow researchers to test their understanding of a system and make predictions about how whole organisms and ecosystems behave. And secondly, through ways to deal with data. Mathematics provides techniques to access, analyze, visualize and understand the ever-growing amounts of data generated in the life sciences, be it DNA sequence data or satellite surveillance data. My written testimony goes into more detail on specific research areas in mathematics that should be supported as part of the new biology. To support this research, an array of complementary Federal programs will be needed from those that focus on building expertise, or enabling research networks in a single topic area, often at a single agency, to application-driven programs that cross agencies.

The second area I want to address is fostering interdisciplinary collaborations and cross-agency coordination. The Virginia Bioinformatics Institute where I work is part of Virginia Tech's response to the challenge of fostering interdisciplinary research on its campus. I am a mathematician by training, and at the Institute, my office neighbors are a statistical geneticist on one side and a biochemist on the other side. From our experience, it is clear to me that locating researchers with different areas of expertise under one roof can serve as an important accelerator of interdisciplinary research. Co-location allows researchers to develop a common culture and allows multiple disciplines to merge and organically develop together. The Federal Government should support this type of collaboration with programs that allow for co-location of disciplines by enabling new biological and new mathematical and computational research to be carried out within the same project. This way, the computational scientists developing algorithms, the engineers developing new technologies, and the biologists asking questions about the fundamental principles of life can advance the science in tandem. So this sort of interdisciplinary activity, the Federal programs that pool agency resources to allow the funding of larger-scale projects, are needed.

The third and final area that I want to discuss is workforce training at several levels. In graduate education, both departmental and interdisciplinary Ph.D. programs can be very effective in preparing students to conduct new biology research, with the key issues being an integration of curricula, the need for a balance between diversity and depth and training, as you mentioned, Mr. Chairman, and the opportunity to develop a common culture across

disciplines. Federal support for efforts to align graduate education with these goals is needed, as creating and maintaining such programs requires a major investment of time and resources.

At the undergraduate level, the two most important elements for preparing students to work in the areas of new biology are, again, an integrated curriculum and research experiences. Close partnerships between teaching and research institutions can help in both areas. In addition, improved opportunities for faculty professional development, such as workshops that bring together faculty from diverse disciplines, will be critical.

Finally, realizing the potential of the new biology will depend on future generations of scientists still to be nurtured. At Virginia Bioinformatics Institute, we conduct outreach programs that involve hundreds of children every year. I have seen the excitement on the face of a nine-year-old who in a lecture hall with 400 other children stands up and asks an insightful question after listening to a scientist talk about nanotechnology—a nine-year-old. Experiences such as this convince me that science in this country has a bright future. However, to get there, we all must engage in a joint effort to inspire and mentor the children who are the future of science.

Again, thank you for giving me the opportunity to testify today. I have provided additional detail and recommendations in my written testimony and I am happy to answer any questions. Thank you. [The prepared statement of Dr. Laubenbacher follows:]

PREPARED STATEMENT OF REINHARD LAUBENBACHER

My name is Reinhard Laubenbacher and I am a professor at the Virginia Bioinformatics Institute, where I lead the Applied Discrete Mathematics Group and am the Director for Education and Outreach. I am also a professor of mathematics at the Virginia Polytechnic Institute and State University and an adjunct professor in the Cancer Biology Department at the Wake Forest University School of Medicine.

Since 2009 I have served as Vice President for Science Policy for the Society for Industrial and Applied Mathematics (SIAM). SIAM is a community of approximately 13,000 applied and computational mathematicians, computer scientists, numerical analysts, engineers, statisticians, and mathematics educators who work in academia, government, and industry. While SIAM members come from many different disciplines, we have a common interest in applying mathematics in partnership with computational science towards solving real-world problems.

In my invitation to testify on the New Biology, the Subcommittee raised questions in three areas, and I have organized my testimony accordingly into three sections:

- Research to Address Grand Challenges and Areas of Scientific Opportunity
- Interdisciplinary Collaborations—Culture and Cross-Agency Coordination
- Workforce—Education and Training

In each of these sections, I offer observations from my experiences at the interface of mathematics and biology and specific comments and recommendations about National Science Foundation (NSF) programs. Specifically, the testimony highlights

- ways in which mathematical and computational research will contribute to New Biology research to tackle societal challenges in food, energy, the environment, and health;
- mechanisms for support of research at the interface between mathematical and life sciences, and examples of successful programs in this area;
- lessons learned on the integration of cultures to enable interdisciplinary research; and
- recommendations for ways to enhance graduate and undergraduate education to prepare students to conduct research in the New Biology.

I note that many of the descriptions of research opportunities and the recommendations in this testimony reflect discussion within SIAM on the opportunities interface between the mathematical and computational sciences and the life sciences, as reflected in a white paper SIAM has produced in this area.<sup>1</sup>

#### RESEARCH TO ADDRESS GRAND CHALLENGES, AREAS OF SCIENTIFIC OPPORTUNITY

*First Set of Questions from the Committee.* In your opinion, what is the future of research in the biological sciences and what role does research at the intersection of biology and mathematics hold for addressing grand challenges in energy, the environment, agriculture, materials, and manufacturing? What computational tools still need to be developed? Are there promising research opportunities that are not being adequately addressed? Is the National Science Foundation playing an effective role in fostering research at the intersection of the physical sciences, engineering, and the biological sciences? If not, what recommendations would you offer?

The 2009 National Research Council report “A New Biology for the 21st Century: Ensuring the United States Leads the Coming Biology Revolution”<sup>2</sup> proposes a national initiative to promote the New Biology that focuses on problem-centric, interdisciplinary research in the life sciences to solve societal challenges in Health, Food, Energy, and Environment. A central finding of the report is that new information technologies and sciences will be essential to achieving the New Biology and meeting these challenges. Biology has become a highly technology driven, fast moving science. New technologies typically produce new data types and larger volumes of data, and allow that data to be generated more cheaply. At the same time, the expertise, tools, and time needed to analyze that data, to turn it from numbers into knowledge and understanding, is becoming more complex and more expensive. For example, while the cost of sequencing a person’s genome is moving toward the \$100 level, the cost of extracting information from the sequence that is meaningful for that person’s health is likely in the \$1 million range. **So the real bottleneck in biology is already shifting toward data analysis. Breakthroughs in mathematics, statistics, and the computational sciences will be necessary to assure that data analysis can keep up with data generation.**

For each challenge area, the report outlines how biology can contribute directly and which research and technological needs must be met in order to do so. **In each area, new approaches to information analysis, data, and modeling will be needed to advance our understanding of the natural world**, as biology develops as a predictive science.

*Food:* In order to help ensure a sustainable and responsibly grown food supply, particularly in light of the changing global climate, one of the challenges is to understand and quantify how plants grow and interact with their environment. This involves characterizing the relationship between the genotype and phenotype of organisms, a fundamental problem in biology. At the genome level biology is essentially digital, and genetic sequence information is translated into dazzlingly complex interacting networks of genes, proteins, and metabolites, making up cellular function. Cells organize into tissues, which, in turn form the whole plant.

Functioning of the cellular networks is directly influenced by features of the environment the plant finds itself in, such as climate, resource availability, and microbial communities.

*Environment:* In order to sustain ecosystem functions in the face of rapid change, we need to be able to monitor multiple heterogeneous variables spanning a range of temporal and spatial scales. **The vast amount of data so collected needs to be integrated and used to construct unifying mathematical models that help guide environmental policy, and have the predictive capability to assess consequences of informed intervention.** Here too, the models need to integrate interconnected networks and systems of complex systems at vastly different scales, all affected by a common environment.

*Energy:* In order to expand sustainable alternatives to fossil fuels, new approaches beyond ethanol derived from corn must be developed. Microbial biocatalysis, for example, is a promising direction. In order to make it a reality, solving the genotype-phenotype problem will lead to the capability to engineer microbes from standard DNA modules that perform a specified metabolic function. Another promising approach is to engineer plants with molecular networks that produce more leaves and fruit without using additional fertilizer, thereby increasing energy production

<sup>1</sup>The SIAM white paper on “Mathematics: An Enabling Technology for the New Biology” is available online at [http://www.siam.org/about/science/pdf/math\\_bioloev.pdf](http://www.siam.org/about/science/pdf/math_bioloev.pdf).

<sup>2</sup>National Research Council, *A New Biology for the 21st Century: Ensuring the United States Leads the Coming Biology Revolution* (2009), <http://dels.nas.edu/Report/Biology-21st/12764>.

through photosynthesis. **With predictive models of the intertwined gene, protein, and metabolic networks, it becomes feasible to engineer and optimize the organism for efficient biofuel production.**

*Health:* To make a transformational contribution to human health, solution of the genotype-phenotype problem will contribute to **integrating genomics information with complex genetic, protein, and metabolic networks, on up to the tissue and organism levels, all of which react to the external environment.** In fact, environmental influences are known to play a very important role in several important diseases, such as cancer and neurological disorders.

The importance of developing better modeling, computational, statistical, and analytical tools to enable a better understanding of biological systems and detailed discussion of the potential impact and key problems are also described in the 2005 National Research Council report "Mathematics and 21st Century Biology."<sup>3</sup> We are approaching a time when gathering the data necessary to truly begin to comprehend complex life as a whole system will be possible. This will be done through consolidating the ever-increasing amounts and types of available information at an ever-increasing level of completeness and granularity. The development of mathematical and computational tools to use this information in sophisticated models should be a priority. To date, exploiting modeling in biology has led to progress on understanding small pieces of large complex systems. But for the biological sciences to bring their full potential to bear on solving the most challenging problems humankind faces in the 21st century, we must now turn our attention to the comprehension of whole systems, and the mathematical and computational sciences are a key enabling technology in this quest.

#### Common Themes from Challenges in New Biology Report

Three common themes emerge from the challenges described in the report.

1. **All four challenges require the construction and analysis of predictive mathematical models of large, nonlinear dynamic networks that span several spatial and temporal scales.** Understanding and manipulating these systems will require large, multi-scale, nonlinear, and hybrid models. Existing simulation and analysis tools for such models are in their infancy, or nonexistent in some cases. For instance, an increasingly popular modeling paradigm for complex networks in fields ranging from molecular biology to ecology is agent-based modeling, which captures the important feature of many complex systems that global behavior emerges from local interactions. Very few analysis tools exist for such models. For many applications it is desirable to use models to predict how interventions on one level will impact biological systems on other levels, such as in the development of therapeutics. This process requires control approaches, but for the systems at the heart of the New Biology challenge areas, it is sometimes difficult or impossible to apply existing control theoretic approaches.
2. In all problem areas **high performance computation will play a crucial role, from simulating complex multi-scale models to analyzing sequence data, e.g., multiple sequence alignment. This will require new breakthroughs in algorithm development,** since we cannot expect significant increases in clock speed due to silicon technology. Performance improvements in computation will come from more cores on a chip. This means significant changes in algorithms to take advantage of parallelism on the chip as well as parallelism between computational nodes comprised of multiple chips. In order to achieve high rates of performance, algorithms that minimize data movement, possibly at the expense of doing additional computations, will be the most efficient. Algorithm developers will need to take these facts into account as they develop multi-scale, multi-physics algorithms.

It is also important to mention that **the speedup in scientific computation achieved over the last four or five decades owes more to the development of new numerical algorithms than to hardware improvements.** Several reports have documented the ways in which the contribution of algorithms has surpassed the improvements due to better technology (Moore's Law),<sup>4</sup> but the impact from both has been critical. Together, hard-

<sup>3</sup>*Mathematics and 21st Century Biology* (2005) is available at [http://www.nap.edu/catalog.php?record\\_id=11315](http://www.nap.edu/catalog.php?record_id=11315).

<sup>4</sup>See, for example, Figure 5, page 53 of *Computational Science: Ensuring America's Competitiveness*, a 2005 report to the President of the United States from the President's Information

ware and mathematical improvements account for an increase in the speed at which we are able to perform the calculations to model important systems, such as in numerical weather prediction, by a factor of roughly 10,000,000 in the period between the 1960s and the 1990s.

3. In all four challenge areas we face **ever-growing data volumes**, from DNA sequence data to satellite surveillance data. As an example, the amount of DNA sequence data stored in GenBank, a data repository maintained by the NIH, has grown by a factor of 100,000 over the past 25 years. Currently, there are over 150 million genetic sequences stored in this publicly-available database. **Genetic data like this, and the many other types of data generated by the application of new imaging tools and other technologies to biological systems, need to be stored in databases that are easily accessible, organized, and searchable, requiring increasingly sophisticated and scalable data mining algorithms.** In addition, the data from heterogeneous sources need to be integrated, within databases as well as within models. Once accessible in databases, the typically high dimensional data sets need to be analyzed using statistical methods. In order to meet these challenges, new tools from multivariate statistics and discrete mathematics are needed, in particular graph theory and combinatorics.

### **Biology to Inform Mathematical Research**

As happened with physics in the last century, we can expect that an increasingly strong feedback loop will develop between biology and the computational disciplines that now serve as tools, such as mathematics, statistics, computer science, and engineering. For instance, the National Science Foundation is already capitalizing on this feedback with its program “Quantum and Biologically Inspired Computing.” We mention here two more examples.

It is well appreciated that the human immune system has important lessons to teach us about computer security. But the immune system is also a vast distributed information-processing network that adapts to ever-changing tasks. Once we understand its design principles well enough to build mathematical models capturing its key capabilities we will be able to transfer these principles to engineered networks. The immune system’s complexity and the multiple spatial and temporal scales involved offer several mathematical and computational challenges that can only be overcome by fundamental breakthroughs in these fields.

As another example, it is observed frequently by experimentalists that after engineering an organism with a gene deletion, even an apparently essential one, its phenotype remains unchanged. That is, the organism is robust to many such changes and can remodel its molecular networks after a change in its genome to maintain function. The underlying fundamental problem of understanding the genotype-phenotype relationship is mirrored by the analogous mathematical problem, namely understanding the relationship between the structure of a dynamical system and its resulting dynamics. This problem is still largely unsolved and poorly understood. Biological insights about the sources of this robustness in organisms can help generate hypotheses about solutions to the corresponding mathematical problem in dynamical systems. In turn, these solutions can be applied to better understand and control other complex systems such as the power grid and computer networks.

### **Recommendations—Research Areas**

This analysis makes clear that mathematics is indeed an important enabling technology for the New Biology. **We recommend that any funding programs related to the New Biology initiative provide support for mathematical research related to the problems identified above in the following areas:**

1. Complex networks, both in the graph-theoretic sense and in the dynamical systems sense.
2. Multi-scale modeling and simulation, including computational science research to enable new approaches.
3. Systems of partial differential equations.
4. Algorithms for high performance computation.
5. Algorithms for new multi-core computer architectures.
6. Multivariate statistics.
7. Dynamical systems.

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Technology Advisory Committee (PITAC). See also Figure 13, page 32 of the DOE Office of Science report *A science-based case for large-scale simulation*, 2003.

8. Hybrid models.
9. Control theory.
10. Combinatorics and graph theory.
11. Data mining algorithms.
12. New methodologies for modeling complex stochastic biological systems.
13. Quantification of model uncertainty.

In addition to research in these areas, it is becoming increasingly clear that there is much untapped potential in mathematical fields that are not traditionally considered as applied. Good examples are recent applications of algebraic geometry to biological problems and the use of methods from algebraic topology for high dimensional data analysis. (Within SIAM, recognition of these emerging opportunities has led to the establishment of a new SIAM Activity Group in Algebraic Geometry.)

### **Recommendations—Research Support Mechanisms, Examples of Successful Programs**

To support the research areas outlined above, programs at individual agencies and interagency initiatives will be needed. Specifically, an **array of complementary approaches will be needed—from those that focus on building expertise in a single topic area, often at a single agency, to application-driven programs that combine mission agency’s user communities and discipline-organized research programs.** Agencies likely to have relevant expertise, communities, programs, and missions include: the National Science Foundation (NSF), the National Institutes of Health (NIH), the Department of Energy (DOE), the U.S. Department of Agriculture (USDA), the Department of Defense (DOD), the Environmental Protection Agency (EPA), the Department of Homeland Security (DHS), and others.

**The National Science Foundation has been a leader in the development of models for stimulating and funding interdisciplinary research in general and as it relates to biology in particular.** There are several existing programs that effectively support research at the interface of the life sciences on the one hand and mathematics, the computational sciences, and statistics on the other. **These programs could be expanded or used as models for the establishment of new programs at NSF or other agencies.**

One particular inter-agency program has been very successful and enormously valuable to research at the interface of mathematics and biology. **The Joint DMS/NIGMS Initiative to Support Research in the Area of Mathematical Biology is a collaborative program between NSF and NIH,** originally established in 2001 and is now in its second five-year cycle. (A recent meeting of investigators supported by the program over the course of its existence, organized jointly by NSF and NIH, showcased some of the projects that have been funded and demonstrated the truly innovative nature of the program.) **The key characteristic of this program is that it is one of the very few existing programs at any of the Federal funding agencies that allows for new biological AND new mathematical research to be conducted at the same time within the same project proposal.** (While the program has been very successful, an ongoing concern is that award sizes are too small to tackle larger-scale ambitious projects.)

This dual approach is critically important because, for many of the new technologies being developed to generate biological data (such as next-generation sequencing or in vivo imaging), we still lack the mathematical and statistical tools needed to analyze and interpret these data so that they can be used to increase our understanding of biological systems and provide input for the construction of predictive models. To fully and efficiently tap the expertise of all the different kinds of researchers in this equation—e.g. the mathematicians developing data analysis algorithms, the engineers developing imaging technologies, and the life scientists defining the questions about biological system functioning—**the Federal Government should be looking for ways to support the development of all elements of a research problem (the tools, models, and experiments) in tandem.** (I will discuss this point more in the section below on the Virginia Bioinformatics Institute and effective environments for interdisciplinary research).

In a related, but broader area, NIH and NSF announced a new program this spring, *New Biomedical Frontiers at the Interface of the Life and Physical Sciences*. While no projects have been selected and funded yet by this new program, the emphasis in the solicitation on supporting efforts that involve multiple investigators who represent the physical, computational or engineering and life or behavioral sciences is to be lauded.

Other examples of exemplary NSF programs include:

- *Cyber-enabled Discovery and Innovation (CDI)* is an NSF-wide initiative established in 2007 and designed to fund projects that use innovation in computational thinking to make advances in any discipline supported by the agency. (At NSF, computational thinking is defined as encompassing computational concepts, methods, models, algorithms, and tools.) This program encourages researchers to think boldly about challenges in data, complexity, and collaboration across multiple disciplines without being constrained by disciplinary cultures and programs.
- *Frontiers in Integrative Biological Research*, a program, phased out in 2008, was designed to support integrated teams of researchers from different scientific fields, focused on biological problems that transcend traditional disciplinary boundaries.
- *Algorithms for Threat Detection*, a joint program between the NSF Division of Mathematical Sciences and the Defense Threat Reduction Agency in DOD, is intended to support the development of the next generation of mathematical and statistical algorithms and methodologies in sensor systems for the detection of chemical and biological materials.

**Mechanisms should be available to support a variety of sizes of research projects, from individual investigators to center-scale collaborations.** Examples of multi-agency and single-agency center-scale initiatives in this area include:

- The National Institute for Mathematical and Biological Synthesis (NIMBioS), jointly supported by the NSF Biological Sciences Directorate and DMS, together with USDA and DHS.
- NSF DMS supports the Mathematical Biosciences Institute (MBI) at the Ohio State University.

Both institutes focus on research at the interface between the mathematical and computational sciences and biology and foster interactions between mathematical scientists and bioscientists.

Thus, NSF has developed and tested successful models to foster interdisciplinary research at the interface of biology and computation, both within the agency and in collaboration with other Federal funding agencies. These can serve as models for the broader cross agency funding structure advocated by the New Biology report.

In addition to programs that support research activities, Federal agencies should focus on raising awareness in the biological and mathematical communities about science at the interface and facilitating cross-disciplinary collaborations, as creating research teams and partnerships across disciplines takes more time and conversation than building teams of people who are within a discipline and share a common culture (this point is discussed in more depth later in my testimony). In addition, outreach within each community about interesting results in one discipline that may potentially be relevant to problems in the other discipline could have a significant impact (i.e. the discovery of applications of algebraic geometry to biological problems mentioned above). Such unexpected linkages can bring very high returns, and their development should be systematically fostered and supported.

**To accomplish the above goals, programs that support network creation, workshops, travel, and summer programs, would be useful. “Sabbatical” cross-disciplinary opportunities for researchers, post-doctoral students, and graduate students also might be effective in creating a new community of researchers more alert to and equipped to conduct interdisciplinary research.**

An example of a Federal effort focused on enabling the creation and sustaining of connections between researchers with common interests is the NSF Research Coordination Networks program, which in 2010 is expanding to include a special track supporting networks of researchers focused on problems at the interface of the biological and mathematical or physical sciences.

#### **INTERDISCIPLINARY COLLABORATIONS—CULTURE AND CROSS-AGENCY COORDINATION**

*Second Set of Questions from the Committee: What is the nature of the interactions and collaborations between mathematicians and biological scientists at the Virginia Bioinformatics Institute (VBI)? How is VBI facilitating these interdisciplinary collaborations and what lessons can we learn from VBI? Is research at the intersection of the biological sciences, the physical sciences, and engineering being effectively coordinated across the Federal agencies? If not, what changes are needed?*

Much of the scientific research in biology and related disciplines happens at universities. By and large, the **nature of the interactions among scientists from**

**different disciplines is constrained by existing academic administrative structures**, which generally do not encourage interdisciplinary research. This has been well documented in the 2004 National Research Council report “Facilitating Interdisciplinary Research,”<sup>5</sup> which also puts forward solutions to this part of the problem. Many universities are addressing the issue of interdisciplinary research by creating research centers that are more flexible administratively and are sometimes organized in a problem-centric rather than discipline-centric way. Some of these centers are “virtual,” in the sense that the researchers all have primary appointments in academic departments, with some shared research infrastructure. Other centers have dedicated buildings that provide primary laboratory space. **The institute I work in is part of Virginia Tech’s response to the challenge of fostering interdisciplinary research on its campus.**

The Virginia Bioinformatics Institute (VBI) was established on the campus of Virginia Tech in 2000 and is focused on research at the interface of the experimental and computational sciences. The institute currently has a staff of approximately 230, including approximately 150 scientific personnel and a dedicated 130,000 square foot building, completed in 2004, with in-house computational and data generation cores. Researchers at VBI are engaged in a wide range of interdisciplinary research projects that bring together diverse disciplines such as mathematics, computer science, biology, plant pathology, biochemistry, systems biology, statistics, economics, medicine, and synthetic biology.

My own research is focused on systems biology, in particular the development of mathematical algorithms related to the modeling of molecular networks. My research group has worked on applications to understanding gene regulatory networks, infectious diseases, and, more recently, cancer. During my eight years at VBI I have collaborated with experimental biologists, biochemists, and computer scientists, both at VBI and elsewhere. Based on my experience, **the single most important factor for making VBI an excellent environment for interdisciplinary research is the fact that a wide range of disciplines are brought together under one physical roof.** I am trained as a mathematician and most of my research group consists of mathematicians. But a statistical geneticist occupies the office on one side of me, and my neighbor on the other side is a biochemist. Similarly, my Ph.D. students might share office space with experimental biologists or computer scientists. The two most important benefits of such an arrangement are that, firstly, it becomes very easy to share information. Even in this age of instant electronic access to information and video chats with colleagues around the world nothing can replace a face-to-face conversation or chance encounter at the proverbial water cooler. Secondly, sharing physical space on a daily basis allows for the merging of different scientific cultures. In my opinion, **the most important and difficult challenge in fostering interdisciplinary research is the creation of a common culture and a common language**, even at the most basic level. In a mathematician or a physicist, the word “vector” might elicit the image of an arrow depicting the direction and velocity of a moving object, whereas in a biologist the same word might bring to mind the image of a disease-carrying mosquito or a rat.

A common obstacle in applying quantitative data analysis methods effectively in life sciences research is that biological experiments are often designed without the involvement of a modeler or bioinformatician or statistician. Once the data from these experiments are generated, often at considerable cost, they sometimes turn out to be unsuitable for the desired data analysis or modeling method. It is important, therefore, to assemble the entire team for a project ahead of time, so that everybody can contribute to all phases of the project. The laboratory of one of my collaborators, for instance, is just across the hall from me and I can easily provide input, suggestions, and answers to questions, as I visit frequently. In fact, computational modeling and analysis will become an increasingly important component of the experiments themselves and their design. An integrated environment such as VBI makes the transition to “computer aided design” of experiments easier. It also facilitates biologists’ input into the subsequent generation of biological hypotheses through computational methods.

**A thorny problem in creating an interdisciplinary environment, one that we have struggled with for a long time, is performance evaluation.** In a scientifically more homogeneous academic department it is easier to evaluate the quality of someone’s research, since colleagues are more familiar with the different scientific journals in the field and their quality. A common and problematic practice is to replace this domain knowledge with metrics such as the impact factor of a journal. It is well known that it is possible for a journal to influence its impact factor

<sup>5</sup>Facilitating Interdisciplinary Research (2004) is available at [http://www.nap.edu/catalog.php?record\\_id=11153](http://www.nap.edu/catalog.php?record_id=11153).

in ways that do not reflect its actual scientific importance. Also, cultural factors in different scientific communities affect this metric. For instance, while *Science* and *Nature*, two of the very best journals in the physical and life sciences, have very high impact factors, the top rated mathematics journals, such as *Annals of Mathematics*, have impact factors that are an order of magnitude smaller. So the impact factor of journals can be only one of several measures to be used. Extramural funding through grants and contracts is another factor that is commonly taken into consideration in academic institutions. **Preparing grant applications for interdisciplinary research tends to take considerably more time and effort than single investigator grants**, and budgets typically need to be larger. Since there are fewer funding programs available for interdisciplinary research than for research within a single discipline, success rates tend to be lower. It is important to provide incentives for scientists to nonetheless embrace interdisciplinary research.

At VBI we are continually working to refine our evaluation process that takes these and other factors into account. For instance, the institute also wants to encourage its scientists to engage in entrepreneurial activities to ensure that their scientific discoveries translate into tangible products that benefit society. So entrepreneurial activity is another criterion in our evaluation process.

The most important lesson I can draw from VBI's experience is that **integration** of different areas of expertise into one physical and administrative structure that is problem centric rather than discipline centric **can serve as an important accelerator of interdisciplinary research**. While this is common practice in industry, it is less so in academe. But it resonates well with the central theme of integration in the New Biology report.

I frequently serve on grant review panels for several agencies, including the NSF, NIH, the postdoctoral program for Federal research laboratories run by the National Academy of Sciences, and a variety of foreign funding agencies. Panels I have served on have focused on a wide range of disciplines, including mathematics, biology, engineering, computer science, oncology, and several interdisciplinary panels. In addition to these agencies, the Office of Science within the Department of Energy, and the U.S. Department of Agriculture also support research at the interface of biology and the computational sciences. In my experience as a reviewer, I have come to realize, that such research takes place in a large variety of settings, including academic departments such as biology, computational biology, biochemistry, physics, bio- and biomedical engineering, electrical engineering, systems engineering, computer science, mathematics, to name the most common ones, as well as a variety of academic and nonacademic research centers, medical schools, government laboratories, and companies. My experience shows me that the scientific community is already mobilizing on a broad scale to meet the challenges outlined in the New Biology report.

While this diversity of computational biology research is a very encouraging sign, it also represents a challenge to funding agencies that need to tailor programs to the different communities. I have described earlier some examples of funding programs that cross disciplines within agencies or span across agencies. The agencies are tapping into a broad and partly overlapping pool of reviewers. It happens to me frequently, that I meet somebody at an NSF review panel, who I had met a few months before at an NIH study section, for instance. And program officers from different funding agencies communicate with each other regularly, in my experience. However, **there are still many opportunities for the agencies to coordinate programs, and a particular need is to pool resources for funding larger-scale projects**. We now have some good case studies we can draw on of programs that create synergy between agencies' expertise, such as the DMS/NIGMS program I mentioned earlier, and can, as discussed in the previous section, be a model for larger-scale cross-agency activities.

#### **Lessons Learned about Interdisciplinary Collaboration and Cross-Agency Coordination**

- From our experience at VBI, it is clear to me that integration of different areas of expertise into one physical and administrative structure that is problem centric rather than discipline centric can serve as an important accelerator of interdisciplinary research. The value of colocation is at least two-fold: (1) It allows researchers to develop a common culture and learn each other's language; and (2) It allows multiple disciplines to contribute to the development of hypotheses, the methods for making predictions, and the design of experiments from the beginning of a project.
- One of the major challenges facing interdisciplinary research is that of performance evaluation. One growing problem is how those in a discipline can

assess the quality of research of someone publishing outside that field. Another problem is the greater time for preparing proposals to support large interdisciplinary teams and the lower success rate for such large grants.

- Finally, from my experience with multiple Federal agencies as a grantee and a reviewer, I am pleased to report that I see good individual collaborations among these agencies—the program officers communicate regularly with each other, the expertise of reviewers are tapped and shared across agencies, and a number of joint programs have been established (as highlighted in the previous section). However, there are still many opportunities for the agencies to coordinate programs, and a particular need is ways to pool agency resources to allow the funding of larger-scale projects.

#### WORKFORCE—EDUCATION AND TRAINING

*Third Set of Questions from the Committee: What changes, if any, are needed in the education and training of undergraduate and graduate students to enable them to work effectively across the boundaries of the physical sciences, engineering, and the biological sciences without compromising core disciplinary depth and understanding? Specifically, what recommendations or changes, if any, would you offer regarding the portfolio of education and training programs supported by NSF?*

As Director of the VBI Education and Outreach Program I devote part of my time to education and training in computational biology from the K–12 to postgraduate levels, in formal and informal settings. The program has four full-time staff members, in addition to myself, including one at the Ph.D. level.

#### Graduate Education

I will first address education at the graduate level. As the New Biology report states: “Certain institutions have recognized these limitations of traditional departments for establishing the New Biology, and have responded not by eliminating departmental structures, but rather by supplementing or overlaying them with interdisciplinary programs or institutes that have both research and educational objectives. **Virginia Tech** is one of those institutions. In 2003, we **created a Ph.D. program with the name “Genetics, Bioinformatics, and Computational Biology (GBCB)” that was designed to train students at the interface of experiment and computation in the life sciences.** The program is administered by the Graduate School and draws on faculty from several departments and institutes, including VBI. While the program was one of a handful at the time, there are now a number of such Ph.D. programs at other institutions in the U.S. and worldwide. The structure of the program is fairly typical, with each student choosing a major area of expertise, such as computer science or one of the life sciences, together with topics from other minor areas of expertise, and a dissertation research project that involves more than one area. In designing the program, we tried to strike a balance between the need for diversity and depth of training. Other programs may strike this balance in more or less different ways, with varying administrative structures. **Our graduates are sought after in both academic institutions and industry and have no difficulties finding attractive employment opportunities.**

Most of the research in my group is such that it typically requires fairly deep training in mathematics, so that most of my Ph.D. students are enrolled in the mathematics Ph.D. program. (In fact, I have had excellent experiences also with postdoctoral mathematicians with no prior background in biology, who have acquired significant biology skills in a short period of time and have made important research contributions.) In order to learn the requisite biology they take courses designed for the GBCB program and, in effect, their course of study could qualify for the GBCB program as well. Most departmental Ph.D. programs are flexible enough to allow students such a diverse plan of study. So both departmental and interdisciplinary Ph.D. programs can be very effective in training students for New Biology research. **An important prerequisite for the success of departmental programs in this endeavor is, again, integration.** In addition to integration of **curricula**, students need to have an opportunity to **develop a common culture** with other disciplines.

While Virginia Tech has had great success with the GBCB program and other interdisciplinary graduate programs, creating and maintaining such programs is a major investment of time and resources on the part of the institution and its faculty. To date, the NSF Integrative Graduate Education and Research Traineeship Program (IGERT) program has played an important role in creating integrated graduate programs across the scientific spectrum at universities across the U.S. For example, Virginia Tech currently has four IGERT awards, and their cumulative effect is beginning to transform the institution.

To educate the future scientists who will be critical in realizing the New Biology, universities will have to transform graduate education in many areas, some interdisciplinary, some not. While the IGERT program is excellent at supporting the creation of programs at *newly* established interdisciplinary boundaries, **academic institutions and departments will also have to revisit existing disciplinary programs and established interdisciplinary areas (e.g. the intersection of biology and mathematics). Support from NSF for these efforts**—such as for the design of the structure and curricula associated with such programs, faculty development and training, and the development, coordination, and execution of related activities such as internships, laboratory rotations, fieldwork, and seminars—**would enable universities to create integrated, flexible programs**, as described above, that will prepare the next generation of researchers for the New Biology and other emerging opportunities. The graduate experiences developed by this sort of Federal program will benefit multiple disciplines and application areas, and hence such a program may be appropriate for cross-agency partnerships and collaborations.

### **Undergraduate Education**

**At the undergraduate level the two most important factors**, in my experience, for New Biology training, **are an integrated curriculum and research experiences. In order to create an integrated curriculum there is a tremendous need for faculty professional development, especially at the many undergraduate institutions.** For instance, a few weeks ago I lectured at a week-long workshop for college faculty, entitled “Mathematical Biology: Beyond Calculus,” which was supported by the Mathematical Association of America and was held at Sweet Briar College in Virginia. The participants came from undergraduate teaching institutions around the country, and some came in teams of two: a biologist and a mathematician. The goal was to develop integrated teaching modules that faculty could use in both mathematics and biology classes, and to plan curricula for integrated courses. In my opinion, many more workshops of this type across all the disciplines contributing to the New Biology are needed to allow faculty to develop and teach courses that will interest students in this area and prepare them for interdisciplinary graduate study and research.

Beyond such professional development workshops, **teaching institutions could benefit additionally from close partnerships with research institutions that incorporate professional development, expertise in curriculum development, and research opportunities for faculty and students.** This will enable faculty at these institutions to keep their curriculum up to date, both within and across disciplines, and will allow them to train their students in ways that make them competitive for cutting edge graduate programs. For instance, we are working with three minority-serving undergraduate institutions to set up such partnerships. For the second summer now we are hosting their faculty at VBI where they engage in research and professional development, and we are hosting their students for research experiences. I have found this to be an effective way to help undergraduate institutions keep pace with scientific developments and training needs. It is not clear to me whether there are any funding programs that are particularly targeted at or well-suited to support such partnerships.

**The NSF has established the program *Interdisciplinary Training for Undergraduates in Biological and Mathematical Sciences*, that addresses curriculum integration and research experiences. The program is very successful, in my opinion, and should be expanded.** It can also serve as a model for similar programs involving other New Biology disciplines. And its scope could be modified to include partnerships of the kind mentioned above.

**Genuine research experiences play a tremendously important role in getting undergraduate students interested in the sciences and in preparing them for graduate programs.** The NSF’s Research Experiences for Undergraduates (REU) program has played an important role in attracting students to science and engineering careers and in preparing them to begin research earlier in their training. For admission to many of the best Ph.D. programs an REU or similar experience has become an important criterion. As I am talking to you here, we have over 30 undergraduates from all over the country at VBI who are doing research with our scientists during the summer, including students from half a dozen states with Representatives on this committee. The students are supported by grants from NSF and NIH. In addition, we have a dozen undergraduates from foreign countries at the institute for the summer. I can see every day what a powerful effect this experience has on the students, and e-mails and letters from past participants make clear that such programs have a lasting impact on them and their career choices.

### Recommendations—Graduate and Undergraduate Education

In graduate education, both departmental and interdisciplinary Ph.D. programs can be very effective in preparing students to conduct research in the New Biology, with the key issues being an integration of curricula, the flexibility to strike a balance between the need for diversity and depth of training, and the opportunity to develop a common culture across disciplines. Creating and maintaining graduate programs with these characteristics is a major investment of time and resources on the part of institutions and faculty. Federal support for university efforts to transform graduate education would greatly help prepare the next generation of researchers for the New Biology and other emerging opportunities.

At the undergraduate level the two most important elements for preparing students to work in the areas of the New Biology are an integrated curriculum and research experiences. In order to create an integrated curriculum there is a tremendous need for faculty professional development, especially at the many predominantly undergraduate institutions in the U.S. This could be enabled by programs that support professional development workshops that, for example, bring together faculty from mathematics and biology. In addition, teaching institutions could benefit from close partnerships with research institutions, in which the partnerships provide professional development, expertise in curriculum development, and research opportunities for faculty and students. The NSF programs *Interdisciplinary Training for Undergraduates in Biological and Mathematical Sciences* and *Research Experiences for Undergraduates* have been successful in supporting enhancements in undergraduate education and improving access to critical research experiences, and these programs should be expanded.

### Researchers of the Future—K–12 Education and the Perception of Mathematics and Science

Realizing the potential of the New Biology is a long-term effort. It will depend strongly on the generations that are now in the K–12 educational system, their parents who influence their career choices, and their teachers who prepare them for those careers. **There is a tremendous need for teacher training and for providing children with opportunities to experience practitioners of science, engineering, technology, and mathematics (STEM) as what they are: explorers of fascinating mysteries on the most important frontiers of knowledge.** Without changing the image of the STEM disciplines in the minds of the public and our children, we will not succeed in reversing the trend of ever smaller numbers of students choosing STEM careers.

During the last year we hosted over 5000 K–12 students at VBI and we are carrying out programs that involve hundreds of children, their parents, and teachers, in partnership with other organizations, such as Virginia 4H. In my experience, engagement with science and technology at this level can have a huge payoff in the future. Seeing the excitement and genuine interest on the face of a 9-year-old who, in a lecture hall with 400 other children, stands up and asks an insightful question after listening to a scientist talk about nanotechnology convinces me that the number of students electing to study STEM in higher education can be increased, if all stakeholders work together to affect the needed cultural change. There are wonderful examples of such efforts. The U.S. Science Festival later this year will be a signature event for shining the public spotlight on science, and VBI will do its share in our booth to showcase New Biology research. And there are many other smaller events and programs of this type taking place across the country. But given the size of the challenge and the large potential benefit to the U.S. economy and well being, a national effort may be required to affect the needed cultural change. An example of such a larger-scale program is the 2007–2008 “Year of Mathematics,” a massive effort by the German mathematical community to help the public experience mathematics. (The program was funded through a public-private partnership with approximately 11 million Euros.)

### CONCLUSION

Enabling and exploiting the intersection between the life sciences and the mathematical and information sciences will have great benefits for society, in health, food, energy, and the environment, as noted in the New Biology report. This alone is a reason for the U.S. to explore and invest in this area. However, like in many other fields, such as information technology, medicine, and security, the work in New Biology also has the potential for significant economic benefit to the Nation that makes the discoveries and is first to turn them into products and services. The U.S. is not

the only nation to see the potential of this area,<sup>6</sup> and the investments of other countries in their research and education infrastructures to produce 21st century innovations lend urgency to our efforts to improve our own research and training capabilities.

#### BIOGRAPHY FOR REINHARD LAUBENBACHER

Dr. Reinhard Laubenbacher is a professor at the Virginia Bioinformatics Institute, where he leads the Applied Discrete Mathematics Group and is the Director for Education and Outreach. He is also a professor of mathematics at the Virginia Polytechnic Institute and State University and an adjunct professor in the Cancer Biology Department at the Wake Forest University School of Medicine. He holds a Ph.D. in mathematics from Northwestern University.

Since 2009 he has served as Vice President for Science Policy for the Society for Industrial and Applied Mathematics (SIAM). SIAM is a community of approximately 13,000 applied and computational mathematicians, computer scientists, numerical analysts, engineers, statisticians, and mathematics educators who work in academia, government, and industry.

Dr. Laubenbacher's research focuses on the development of cutting edge mathematical tools to allow for a comprehensive understanding of biological systems. Specifically, his group develops mathematical algorithms related to the modeling of molecular networks with applications to yeast, infectious diseases, and cancer. Dr. Laubenbacher's research has been supported by grants from the National Science Foundation, the National Institutes of Health, and the Department of Defense. He has authored or coauthored over 80 publications and co-authored or edited 5 books. His work as an educator has also been supported by grants from the National Science Foundation.

Chairman LIPINSKI. Thank you, Dr. Laubenbacher.  
Dr. Leonard.

#### **STATEMENT OF JOSHUA N. LEONARD, ASSISTANT PROFESSOR, DEPARTMENT OF CHEMICAL AND BIOLOGICAL ENGINEERING, NORTHWESTERN UNIVERSITY**

Dr. LEONARD. Mr. Chairman, thank you for this opportunity to discuss these important issues related to the transformative shifts now occurring in research and education at the interface of biology, engineering and the physical sciences.

I am an Assistant Professor of Chemical and Biological Engineering at Northwestern University and my expertise and research interests center on engineering biological systems for applications in biotechnology and medicine using synthetic biology, a field that I will describe today. I am honored to be here today and speak with you and this subcommittee about these topics.

Over the last three decades, molecular biology has revolutionized our ability to explore the living world, and we now stand at another transformative moment in the biological sciences. Through technological advances, it is possible to collect a wealth of biological data, and we now need new conceptual, computational and experimental tools to transform this information into useful understanding and practical applications. Already, it is clear that by developing these capabilities, we may use the richness of biology to meet pressing needs in areas including energy, through the sustained production of advanced biofuels; in the environment, including cleanup, remediation and ecosystem management; in agriculture, including crops that withstand harsh conditions or chang-

<sup>6</sup>For a discussion of international efforts, see the WTEC *International Assessment of Research and Development in Simulation-Based Engineering and Science*, which includes a chapter on Life Sciences and Medicine, available at [http://www.wtec.org/sbes/SBES-GlobalFinalReport\\_BW.pdf](http://www.wtec.org/sbes/SBES-GlobalFinalReport_BW.pdf).

ing environmental conditions; materials, including the production of industrially useful materials, like polymers from renewable biomass instead of from petroleum; in manufacturing, by carrying out chemical synthesis inside microorganisms to transform cheap biological feedstocks into high-value products like pharmaceuticals; and in health, by harnessing our own biology to treat cancer, to generate vaccines on demand and to extend the quality of life.

At the leading edge of these efforts is synthetic biology, a nascent technical discipline whose central goal is to transform biology into a system that can be engineered as we engineer mechanical and electrical systems today. Synthetic biology seeks a new paradigm of biology by design in which one can conceive a desired biological function, design a biological system to perform this function, build the system and have it work as predicted. We are still some distance from realizing this goal, but synthetic biology provides a framework for proceeding. In this model, basic biological parts such as genes are constructed and characterized such that they can be interconnected and assembled into novel configurations to generate new functions, which are designed with the assistance of computational tools and rigorous quantitative methods.

As in all areas of applied science, construction and understanding are connected. First, we build to learn how to design. Understanding the principles of aeronautics did not directly provide the Wright Brothers with the ability to achieve controlled flight. This was achieved only through an ongoing cycle of design, construction, testing and refinement, and the same is true for engineering biological systems. We also build to understand. Sometimes understanding comes through failure. For example, through unsuccessful attempts to engineer bacterium to perform a simple task—for example, turning a gene on and off in a regular fashion—we learned that cells do not function as well-oiled machines, but rather, their inner workings proceed through bursts of activity. In these ways, synthetic biology is intrinsically part of the new biology of the 21st century as described by the National Research Council. Synthetic biology is not a change within biology, engineering or the physical sciences, but rather it is an effort that must span traditional disciplinary boundaries and integrate these strengths. Work in synthetic biology also spans the funding and oversight priorities of our Federal agencies.

At this stage, the basic challenges, technologies and frontiers are largely independent of whether the eventual application is in energy, health or the environment. For example, my research group works to engineer cell-based devices and networks, approaches that have applications in both biotechnology and medicine. Interagency cooperation is therefore required to make the best use of our collective capabilities and resources.

The NSF has supported early synthetic biology efforts through the multi-institutional center SynBERC [Synthetic Biology Engineering Research Center]. Now, we must also develop interdisciplinary centers throughout our research infrastructure to build a national synthetic biology community that is integrated with other facets of 21st century biology. Given the early state of synthetic biology and its vast potential for benefiting society, investing in high-risk, high-reward projects should form a major part of our national

strategy. In 2008, the NSF conducted such an experiment, along with partners in the United Kingdom, by running a sandpit event that brought together a multinational group of researchers to foster innovation in synthetic biology and develop competitive projects targeted at grand challenges. For example, our team is building a technology inspired by the evolution of bacterial ecosystems that could transform our ability to construct complex functions in bacteria, such as the challenging biochemical synthesis of the anticancer drug Taxol.

The National Academy's Keck Futures Initiative also held a synthetic biology conference in 2009, using interdisciplinary teams to develop field-wide perspectives on major scientific and ethical issues. These findings also generated several innovative projects. For example, our team is developing a technology to enable engineered symbiotic bacteria which might patrol the colon for signs of cancer, for example, to communicate this information to their hosts.

Finally, addressing challenges in 21st biology requires training a new generation of students prepared to integrate diverse areas of expertise. At the graduate level in particular, we need to engage a broad pool of students and move towards models in which training is an interdepartmental effort, a strategy that we are developing and implementing at Northwestern. Nationwide, our students are already eager to apply their capabilities to meet today's pressing challenges. With the United States' adaptable and entrepreneurial cultures in both research institutions and the private sector, we are positioned to continue to lead this revolution in biology and biotechnology. By fostering a national synthetic biology community and investing in high-risk, high-reward research, we can capitalize upon our capabilities to realize the benefits of biology by design.

Mr. Chairman, thank you again for this opportunity to share my perspective on this important topic, and I would be happy to address any questions you may have.

[The prepared statement of Dr. Leonard follows:]

PREPARED STATEMENT OF JOSHUA N. LEONARD

Mr. Chairman, thank you for this opportunity to discuss these important issues related to the transformative shifts now occurring in research and education at the interface of biology, engineering, and the physical sciences. I am an Assistant Professor of Chemical and Biological Engineering in the McCormick School of Engineering and Applied Science and member of the Robert H. Lurie Comprehensive Cancer Center at Northwestern University, in Evanston, Illinois. My expertise and research interests center on engineering biological systems for applications in biotechnology and health through "synthetic biology", a nascent technical discipline that holds immense promise for helping to meet our most pressing societal needs. I am honored to be here today and to speak with you and the members of this subcommittee about these topics.

**Why are new approaches for engineering and understanding biological systems needed?**

Over the last three decades, molecular biology has revolutionized our ability to investigate and utilize the diversity of the living world in unprecedented ways. We now stand at another transformative moment in the biological sciences. Technological advances such as high-throughput DNA sequencing have made it possible to collect massive amounts of biological data, and what is needed now are new conceptual, computational, and experimental tools to transform this wealth of information into useful understanding and practical applications. Already, it is clear that by devel-

oping these capabilities, the versatility of biology may be harnessed to meet our most pressing societal needs, including:

- **Energy**—through the sustainable and affordable production of advanced biofuels
- **The Environment**—including cleanup and remediation as well as ecosystem management
- **Agriculture**—including the production of food crops that grow in water and resource-poor areas and can tolerate changing climactic conditions
- **Materials**—both by taking inspiration from natural innovations, like spider’s silk whose strength exceeds that of steel, and by producing substances that are outside the existing realm of biology, such as industrially-useful polymers, from renewable feedstocks like sugar or biomass
- **Manufacturing**—for example, by carrying out customized and complex chemical synthesis reactions inside microscopic yeast or bacteria to transform cheap biological feedstocks to high value specialty products
- **Health**—for example, to harness our own biology to treat cancer, to generate vaccines on demand, to resolve chronic infections and autoimmune disease, and to extend quality of life to meet the needs of our changing population demographics

Our research infrastructure is already making headway towards these goals, with notable and early successes in biotechnology (e.g., the production of specialty products in microorganisms) and energy (especially in the realm of biofuels). This is a transformative moment in both the basic and applied biological sciences, and the steps we take to act on this opportunity will guide our ability to lead the development of this central technological and scientific capacity through the 21st century.

#### How will “synthetic biology” help to achieve these goals?

At the leading edge of these efforts is a nascent technical and scientific discipline called synthetic biology. The central goal of this field is to transform biology into a system that can be engineered just as we design and engineer mechanical and electronic systems today. In this way, **synthetic biology seeks to enable a new paradigm of biology by design**, which can be summarized as follows:

- **Conceive** a given desired biological function
- **Design** an engineered biological system to perform this function
- **Build** the system
- The system **works** as predicted

We are still some way from realizing this ambitious goal, but synthetic biology provides a framework for addressing each of these steps. A central part of this concept is constructing and characterizing basic biological parts (such as a genes that encode enzymes or other proteins), which can be interconnected and assembled into novel configurations. Also important is the use of computational tools and rigorous quantitative methods to help design a configuration that will perform a given function. New technological advances are also required to provide reliable, affordable, and accessible assembly of large biological components (especially large pieces of DNA that may compose many genes, or other DNA-based “parts”). Together, this is more than a technological advance; it is a conceptual shift. **Synthetic biology will enable us to move from what does exist, to what *can* exist.**

Synthetic biology is also intrinsically linked to fundamental biological sciences, including systems and computational biology, and as such, it is a central component of the New Biology described in the recent report on this topic from the National Research Council. As in all areas of applied science, construction and understanding are connected through these general approaches:

- **Build to learn how to design.** We know that understanding the principles of aeronautics did not directly provide the Wright Brothers with the ability to achieve controlled flight. This was achieved only through the ongoing cycle of designing, constructing, testing, and refining the design. The same is proving true for engineering biological systems to performed in desirable and predictable ways.
- **Build to understand.** Since its inception, synthetic biology has provided new biological understanding through failure. For example, through unsuccessful attempts to genetically engineer a bacterium to perform a simple task (for example, turning a gene on, off, and then back on in a regular fashion), we learned that cells do not function as stable and well-oiled machines, but rath-

er their inner workings proceed through bursts of activity mixed with stretches of inactivity. Thus, attempting to engineer biology reveals new fundamental biological insights, perhaps especially when it fails.

### **What types of research infrastructure and support are required?**

Synthetic biology, like other areas of 21st century biology, requires an inherently interdisciplinary approach. It is not just a change within biology, engineering, or the physical sciences, but rather it is an effort that must continue to span traditional disciplinary boundaries. Consequently, this field is not a replacement for existing core competencies—it is a new meeting place.

The fundamental work required to develop synthetic biology capabilities spans the funding and oversight priorities of our Federal agencies. At this stage, the basic challenges, technologies, and frontiers are largely independent of whether the eventual application is in energy, health, or the environment. For example, my group works to engineer multicellular networks and build cellular devices, approaches that have applications in both biotechnology and medicine. Various component disciplines (including biology, engineering, physics, chemistry, computer science, and medicine) are already involved in these efforts, but **what are needed are mechanisms for supporting the integration of these diverse strengths**. Thus, inter-agency cooperation is required to maximize the progress that can be achieved.

The NSF is taking early action to support the development of synthetic biology. SynBERC (the Synthetic Biology Engineering Research Center) is an NSF Engineering Research Center, which serves as a multi-institutional home for foundational research in this field. The NSF is also supporting the new International Open Facility Advancing Biotechnology (Biofab) project, which will work to scale up the manufacturing and dissemination of technologies developed through SynBERC. These models established a foundation for synthetic biology research and have helped to coordinate activities between member institutions. **To continue the development of this field and capitalize upon diverse types of core competencies, we must also develop interdisciplinary centers throughout our research infrastructure to build a national synthetic biology community, which must be closely integrated with other facets of 21st century biology.**

Building this community may be achieved through establishing regional centers, or in other cases an institution-level organization may be successful. In any implementation, it is essential that the program be sufficiently flexible to allow for innovative models that can integrate different institutional cultures and organizational structures. Furthermore, a key goal of this program should be to foster the growth of this nascent field, rather than to merely reinforce existing efforts, so a substantial component of any support should go towards activities that build new interactions. Particularly effective approaches may include pilot projects, multi-year graduate student and postdoctoral training fellowships tied to interdisciplinary advising, and activities that promote communication and dissemination such as seminars, local scientific meetings, and internet-based media.

**Given the rapidly expanding scope of synthetic biology as a discipline, as well as its potential for transformative contributions to society, it is essential that we invest in high-risk, high-reward projects.** In November 2008, The NSF conducted an experiment in this area by running a so-called “Sandpit” event dedicated to fostering innovation and identifying new directions in the field of synthetic biology.<sup>1</sup> This event was run in conjunction with the U.K.’s counterpart organization—the Engineering and Physical Sciences Research Council (EPSRC). I had the opportunity to attend this competitive event that brought together 15 researchers from the U.S. and 15 from the U.K. The EPSRC has run a number of such events since 2004, but this was the first event to be held in the U.S. or by the NSF. The aim was to address basic questions, identify challenges and opportunities, and create novel research directions that wouldn’t be supported through existing mechanisms, and moreover, wouldn’t be proposed without this unique opportunity for collaborative interactions. By design, the resulting projects were targeted at grand challenges that both drive basic scientific capabilities and could enable transformative applications.

To provide an example of the projects that were generated through this event, my group, along with Jay Keasling at the University of California, Berkeley and four other collaborators across the U.K., is developing a technology that could transform the way we engineer microorganisms for biotechnology. Existing approaches to engineering a microbe to carry out a useful function, for example to synthesize a valu-

<sup>1</sup>Profiled in “Digging for fresh ideas in the sandpit” (2009) *Science*. Vol. 324. no. 5931, pp. 1128–9.

able small molecule through modifying the organism's metabolism, require substantial investments of resources, time, and labor. Much of the difficulty arises from the extensive work required to tweak and optimize the system. In this project, we are building a new engineering technology inspired by a set of natural mechanisms by which communities of bacteria modify and optimize their own biology. This capability should eventually enable researchers to carry out the optimization of engineered biological functions with great savings in time, resources, and labor. Other projects addressed similarly ambitious and potentially transformative challenges.

This Sandpit was an experiment and perhaps a model for driving innovation in other nascent areas of research. Importantly, the NSF has also followed this event with calls to develop networks for coordinating research efforts in this area. This emphasis on driving high-impact, high-reward research while developing our collective capacity to carry out work in synthetic biology reflect two effective strategies for leveraging and enhancing our existing research infrastructure.

The NSF/EPSCRC sandpit also dovetails with other national-level efforts including the National Academies Keck Futures Initiative's conference on "Synthetic Biology: Building on Nature's Inspiration", which was held in November 2009.<sup>2</sup> This conference invited some 150 researchers to work in interdisciplinary teams to address some of the major questions facing the field. This process was structured to assess and develop field-wide perspectives on major scientific and ethical topics related to synthetic biology. The resulting findings were disseminated to the public in several forms, including a series of summaries written by graduate students in science journalism, one of whom was part of each interdisciplinary team.

In comparison to the Sandpit event, the emphasis of the NAKFI conference was more on community and field development than on directly driving innovation at the meeting. However, NAKFI also recognizes the need to foster high-risk, high-impact research in synthetic biology and, accordingly, supported 13 pilot projects developed by attendees after the completion of the meeting. Most of these projects targeted problems identified as major challenges and opportunities at the event.

For example, my group and our collaborators are working on a project to address the need for new systems for engineering communication between cells. Specifically, we are seeking to develop a synthetic molecular communication system that can send information between bacteria and human cells. This is a fundamental technical challenge, and it could also eventually result in applications. As a hypothetical example, one could engineer a symbiotic bacteria "probiotic" to patrol within the colon for pathogenic microbes or signs of emerging colon cancer and respond by directing the immune system to respond appropriately.

Continued investment to **foster the growth of a national synthetic biology community** and provide **mechanisms to drive high-risk, high-reward research** as an essential part of our national research strategy will enable the development of this new scientific enterprise and catalyze the development of transformative technologies and applications in areas including energy, agriculture, the environment, materials, and health.

#### **What educational strategies will prepare students and trainees to pursue these challenges?**

Addressing challenges in synthetic biology, and 21st century biology more generally, requires training a new generation of undergraduates, graduate students, and postdoctoral fellows who will be uniquely prepared to integrate diverse areas of expertise. Working effectively on interdisciplinary teams requires the development of a common language. Combining rigorous quantitative methods with open-ended biological design challenges requires balanced development of both analytical and creative capacities—we need to train whole-brain thinkers.

At the graduate level, we must move beyond current models in which training in synthetic biology often occurs as an outgrowth of training within a single existing department. To engage a broad pool of students and develop the interdisciplinary capacities they require, we must move towards models in which training occurs as part of a broader interdepartmental effort. An especially important mechanism for promoting these changes would be to provide faculty with support to develop and teach new courses designed for this new training model. This might be particularly important to implement in institutions where there currently exist barriers to interdisciplinary training and co-advising across departmental boundaries. For such reasons, it is imperative that efforts to promote interdisciplinary training be flexible enough to allow for innovative models that can thrive within different institutional cultures and organizational structures.

<sup>2</sup><http://www.keckfutures.org/conferences/synthetic-biology.html> (accessed June 25, 2010).

As an example of what such a model might entail, I can describe how we are approaching these challenges at Northwestern University. Our highly interdisciplinary biological sciences Ph.D. program is an excellent model for how graduate education may support 21st century biology. It is a life sciences training program that includes a high concentration of training faculty drawn from engineering, chemistry, and the physical and quantitative sciences. Students benefit from broad interdisciplinary training that challenges them to become fluent in the languages of multiple disciplines, and to bridge those disciplines in order to carry out cutting-edge innovative research projects that move life sciences research in exciting new directions.

We are currently implementing a new innovation in which graduate biology education is structured around thematic clusters designed to balance depth in certain competencies with flexibility to cross disciplinary boundaries. Over the past year, I have led an effort, along with Prof. Michael Jewett and other colleagues, to create an interdepartmental organization for integrating systems and synthetic biology efforts across the university. This organization will include training activities including boot camps, to build basic competencies and facilitate the development of a common language, ongoing research interactions, and new course offerings. Our goal is that such training activities will eventually be integrated into the graduate education of students with primary homes in biology, engineering, and physical and quantitative science departments. Training a new generation of scientists and engineers that can fluidly cross traditional disciplinary boundaries is critical to achieving the goals of a new biology for the 21st century.

Interdisciplinary training in synthetic biology at the undergraduate level is already an active area, driven in large part through the International Genetically Engineered Machines (iGEM) experience originally developed at MIT.<sup>3</sup> Each year over the summer, teams of undergraduates work on synthetic biology projects of their own design, which culminate in gathering to share their results and experiences at a “Jamboree” held at MIT in Cambridge, MA. By 2009, only the fifth year of this event, participation had swelled to include 112 teams from 26 countries, comprising over 1000 participants.

An examination of student-selected project topics suggests that the enthusiasm for iGEM is partly explained by the fact that it builds upon the existing desire of our students to apply their capabilities to solving real problems and meeting pressing societal needs. Recurrent themes include global health, environmental stewardship, and community-based technology development. Importantly, iGEM also requires that teams consider and discuss possible secondary uses of any technologies they may develop. By facing these security and ethical issues head-on in a tangible context, this experience should help these students to carry these considerations forward, to their careers in industry and academia, and as informed members of society. Perhaps most importantly, this competition promotes innovation, creativity, and self-reliance, all of which translate to fostering an entrepreneurial spirit.

Ongoing challenges in undergraduate education are to incorporate interdisciplinary training, and perhaps some elements of an iGEM-like experience, into existing discipline-based undergraduate curricula. One option is to create interdisciplinary courses that supplement, or serve as electives, within multiple existing undergraduate programs. For example, an undergraduate synthetic biology elective may bring together engineers, biologists, and computer scientists to work in teams to tackle problems that involve both computational modeling and wet laboratory experiments and insights. I have personally implemented such a model of team-based “cooperative learning” using synthetic biology in my teaching of a core chemical engineering course. Although this course focuses on strategies for predicting and controlling the dynamics of chemical processes, I regularly use examples drawn from the context of biology to build an appreciation for the general applicability of these methods. The course culminates in a team-based project in which students apply process dynamics and control principles to understand and ultimately redesign engineered synthetic biological systems. This shift in context helps students to develop their abilities to apply their core competencies to new challenges and unfamiliar disciplines. Similar strategies may be incorporated throughout the various core disciplines that contribute to 21st century biology, since developing student capacities to work on interdisciplinary challenges will benefit them in any career they eventually pursue.

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<sup>3</sup>Smolke, Christina D. “Building outside of the box: iGEM and the BioBricks Foundation” (2009) *Nature Biotechnology*. Vol. 27. no. 12, pp. 1099–1102.

**How will synthetic biology serve the United States' national interests?**

Synthetic biology taps into a vast potential to grow the industries that will lead 21st century economies and meet societal needs in energy, biotechnology, high-value manufacturing, environmental technologies and services, and health. Our international partners and competitors in Europe and elsewhere are also investing heavily in this sector. However, the U.S. already possesses the essential ingredients required to build a competitive advantage and lead the growth of this sector. Our adaptable and entrepreneurial culture, in both the private sector and in our academic research institutions, positions the U.S. to continue to lead this next revolution in biological technology. Through capitalizing upon our intellectual resources and rededicating ourselves to training the next generation of biologists, engineers, and scientists to take on these challenges, we can realize the benefits of achieving biology by design.

### Summary

We stand at a transformative moment in the biological sciences, where we can collect massive amounts of biological data, and what is needed now are new conceptual, computational, and experimental tools to transform this information into useful understanding and practical applications.

**Developing these capabilities will allow us harness this knowledge to meet pressing societal needs** in energy (e.g., renewable fuels), the environment (e.g., cleanup and ecosystem management), agriculture (e.g., climactically robust food crops), materials (e.g., to achieve special properties and utilize renewable feedstocks), manufacturing (e.g., microbial factories), and health (e.g., advanced vaccines and biological therapies).

At the leading edge of these efforts is a nascent technical and scientific discipline called synthetic biology, the central goal of which is to transform biology into a system that can be engineered. **Synthetic biology seeks to enable a new paradigm of biology by design:**

- **Conceive** a given desired biological function
- **Design** an engineered biological system to perform this function
- **Build** the system
- The system **works** as predicted

Synthetic biology is intrinsically linked to the fundamental biological sciences as part of the New Biology of the 21st century. It is not a change within biology, engineering, or the physical sciences, but rather it is an effort that must span traditional disciplinary boundaries. Mechanisms for supporting the integration of these diverse strengths are needed.

The fundamental work required to develop synthetic biology capabilities spans the funding and oversight priorities of our Federal agencies. Thus, interagency cooperation is also required to maximize the progress that can be achieved.

NSF has supported early synthetic biology efforts through projects such as SynBERC. **Now, we must also develop interdisciplinary centers throughout our research infrastructure and build a national synthetic biology community that is integrated with other facets of New Biology.**

**Given the early but rapidly expanding scope of synthetic biology as a discipline, as well as its potential for transformative contributions to society, it is essential that we invest in high-risk, high reward projects as a major portion of our national research investment strategy.**

Addressing challenges in synthetic biology, and 21st century biology more generally, requires training a new generation of undergraduates, graduate students, and postdoctoral trainees who will be uniquely prepared to integrate diverse areas of expertise.

**The U.S. is positioned to continue to lead this next revolution in biological technology and fundamental science, and through capitalizing upon our public and private sector capabilities, we can realize the benefits of achieving biology by design.**

Mr. Chairman, thank you again for this opportunity to share my perspective on this important topic, and I will be happy to address any questions you may have.

#### BIOGRAPHY FOR JOSHUA N. LEONARD

Joshua N. Leonard, Ph.D. is an Assistant Professor of Chemical and Biological Engineering in the McCormick School of Engineering and Applied Science and is a member of the Robert H. Lurie Comprehensive Cancer Center at Northwestern University in Evanston, IL. Leonard's research interests center on using engineering principles to build synthetic multicellular networks for applications in biotechnology and medicine. Ongoing projects in his research group include developing programmable cellular devices, with applications in cancer immunotherapy and regenerative medicine, and developing foundational synthetic biology technologies for engineering complex functions in microbial systems.

Leonard received a B.S. in chemical engineering from Stanford University in 2000, and a Ph.D. in chemical engineering from the University of California, Berkeley in 2006. For his doctoral thesis, Leonard employed computational and experimental approaches to develop novel gene therapies for treating HIV infections in such a way that the therapy suppresses the emergence of treatment-resistant viruses. Leonard and collaborators also patented a technology for enhancing the production of certain gene therapy vehicles. While at Berkeley, Leonard also studied entrepreneurship in biotechnology at the Haas School of Business and received a certificate in the Management of Technology in 2005. From 2006–2008, Leonard

trained in immunology as a postdoctoral fellow at the National Cancer Institute, Experimental Immunology Branch, at the National Institutes of Health intramural campus in Bethesda, MD. While at the NIH, Leonard led a project that elucidated a central mechanism by which the immune system recognizes viral infections and initiates an appropriate antiviral response. This knowledge led to the development of a family of novel and targeted vaccine adjuvants that should be useful in vaccines against viruses and cancer. In 2008, he was recruited to his current position as an Assistant Professor of Chemical and Biological Engineering at Northwestern University. In addition to leading his research group and teaching, Leonard serves as faculty mentor for Northwestern's international Genetically Engineered Machines (iGEM) team, which will participate in this undergraduate synthetic biology experience for the first time this year.

Chairman LIPINSKI. Thank you, Dr. Leonard.  
Dr. Sanford.

**STATEMENT OF KARL SANFORD, VICE PRESIDENT,  
TECHNOLOGY DEVELOPMENT, GENENCOR**

Dr. SANFORD. Good afternoon. My name is Karl Sanford. I am Vice President of Technology Development for Genencor, and I am honored to present this testimony to your Committee.

Genencor, a division of Danisco, is a leader in industrial biotechnology innovation and manufacturing on a global scale. We have multiple manufacturing, R&D and sales locations throughout the world with a central location in Palo Alto, California, and offices and manufacturing plants in Cedar Rapids, Iowa, Beloit, Wisconsin, and Rochester, New York. Our goal is to push the boundaries of what is achievable in the realm of biotechnology and accelerate development of the bio-based economy.

This opportunity for my testimony comes at an exciting time for Genencor. Recently, we have made some exciting new advances in making isoprene from renewable feedstocks that promises to help our Nation increase its technological competitiveness and decrease its dependency on imported foreign oil, while also protecting the environment.

Genencor started in 1982 as a spin-out company from pharmaceutical biotechnology pioneer Genentech, with an aspiration of bringing to industrial and everyday customers the benefits of recombinant DNA technology to new product features and manufacturing efficiencies. Over the past 28 years, we have roughly doubled our revenues every five years such that our business now approaches \$1 billion annually. Our manufacturing processes are based on the conversion of biorenewable feedstocks, like corn and soy, into bioproducts like enzymes, using efficient, large-scale fermentation processes. Every day, you eat, use or wear something made with Genencor enzymes.

Collaboration is a key for success. The rate of improvement in the seminal technologies of DNA synthesis, DNA sequencing and synthetic biology is continuing to provide accelerating innovation opportunities. No single enterprise can go it alone, and hence the need for developing effective networks that connect the players. As an example, we are an industrial member of SynBERC, the Synthetic Biology Engineering Research Center, which is an NSF-funded multi-institution research effort establishing a foundation for the emerging field of synthetic biology. SynBERC's vision is to catalyze biology as an engineering discipline by developing foundational understanding and technologies, to allow researchers

to design and build standardized, integrated biological systems to accomplish many particular tasks. In essence, SynBERC is making biology easier to engineer. It is also engaged in training students who can leverage the investments and training as they go forward into industry. Powerful new technologies such as synthetic biology must also include governance and oversight to fully understand any potential unintended consequences. Hence, centers such as SynBERC also provide initiatives in which ethics and biosafety approaches are purposely incorporated into synthetic biology research and development. The collaborative human practices model within the NSF-funded SynBERC project was the first initiative in which social scientists were explicitly integrated into a synthetic biology research program.

Increasing the science and technology acumen of our society and engaging young minds in science and engineering are key success factors for improving our innovation potential and social receptivity for technology-based solutions. Science Bound, Iowa State University's premier pre-college program, prepares and empowers Iowan ethnic minority students to earn college degrees and pursue careers in science. In its 20th year, SCIENCE BOUND has worked with more than 800 middle and high school students and offered college scholarships to 200 program graduates. The program asks 12- and 13-year-olds to make a five-year commitment. Working in tandem with expert teachers, students can emerge academically equipped as well as socially and culturally empowered to earn a college degree in science or engineering. We need to further support and expand this concept of making science fun and exciting and the learning process friendly enough to encourage commitment to a career in technology.

Biotechnology and technology in general are played on an international stage. U.S. centricity is insufficient in providing the education and training necessary to be among the best, brightest and most successful. Language skills, cultural perceptivity and global perspective are requirements for biotechnology players of the future. International awareness is an area for improvement in U.S. education and training.

The President's Innovation and Technology Advisory Committee, PITAC, has identified a technological congruence that is called the "Golden Triangle". Each side of the Golden Triangle represents one of the three areas of research that together are transforming the technology landscape today: information technology, biotechnology and nanotechnology. Each of these research fields has the potential to enable a wealth of innovative advances in medicine, energy production, national security, agriculture, manufacturing, and sustainable environments—advances that in turn help to create jobs and increase the Nation's gross domestic product.

In combination, these fields have an even greater potential to transform society. It is this interplay of technologies, along with the ever more demanding societal needs, which creates grand challenges. Industrial biotechnology is one of the tributary themes to this Golden Triangle. Continued investment in research, education, business and legal developments is necessary to achieve our collective aspiration of meeting the needs of the present without compromising the ability of future generations to meet their needs. Inter-

disciplinary collaborations that work the Golden Triangle in different patterns of innovation may offer routes to success, provided the membership, results and ownership outcomes are based on transparency, trust and data-based decision making.

Mr. BAIRD. [Presiding] Dr. Sanford, I am going to ask you to conclude as quickly as you can.

Dr. SANFORD. I thank the Committee for the opportunity to present these views and welcome any questions and comments.

[The prepared statement of Dr. Sanford follows:]

PREPARED STATEMENT OF KARL J. SANFORD

**Introduction**

Good afternoon—My name is Karl Sanford. I am Vice President of Technology Development for Genencor, and I am honored to present this testimony to your Committee.

This opportunity for my testimony comes at an exciting time for Genencor. Recently, we have made some exciting new advances in making isoprene from renewable feedstocks that promises to help our Nation increase its technological competitiveness and decrease its dependency on imported foreign oil while also protecting the environment.

**Genencor Background: A Pioneer in Industrial Biotechnology**

Genencor, a division of Danisco A/S, is a leader in industrial biotechnology innovation and manufacturing on a global scale. We have multiple manufacturing, R&D and sales locations throughout the world with a central location in Palo Alto, California and offices and manufacturing plants in Cedar Rapids, Iowa, Beloit, Wisconsin and Rochester, New York. Our goal is to push the boundaries of what is achievable in the realm of biotechnology and accelerate development of the bio-based economy.

Genencor started in 1982 as a spin-out company from pharmaceutical biotechnology pioneer, Genentech, with an aspiration of bringing to industrial and everyday customers the benefits of recombinant DNA technology through new product features and manufacturing efficiencies. Over the past 28 years we have roughly doubled our revenues every five years such that our business now approaches about one billion dollars annually. Our manufacturing processes are based on the conversion of bio-renewable feedstocks like corn and soy into enzymes using efficient large scale fermentation processes. Every day you eat, use or wear something made with Genencor enzymes. We discover, produce and market enzymes to large industrial manufacturers. Our products touch people's lives in many ways—getting dirty clothes cleaner while using less energy and water doing it; getting clothes to feel better, softer, nicer to wear with dramatic reductions to water, energy usage and backed by the first textile industry LCA; improving the nutritional efficiency of livestock while reducing environmental impact by using less chemicals; improving quality, nutrition and safety of human foods; converting biomass into sugars, a critical step in the production of cellulosic ethanol, other advanced biofuels and biochemicals; creating a suite of enzymes for biorefiners who convert grain into higher value products such as sweeteners and bioethanol; developing microbial cell factories that convert sugars to biochemicals, such as the Biolsoprene™ product we are developing with The Goodyear Rubber and Tire Company. Our manufacturing processes include innovative processes to convert bio-renewable feedstocks like corn into enzymes using efficient large-scale fermentation processes.

**Networks and Partnerships make a Difference**

Partnerships play an important role in getting the right products to the right customer segments in a timely manner. We have teamed with the Departments of Energy, Commerce and Defense, and some of the largest consumer, food product and chemical companies in the world. For example, we partnered with DuPont in the mid 1990s to design and develop the bioprocess for making BioPDO™ monomer from corn. That project took almost ten years before the first commercial sale was realized in 2006. We teamed with DuPont again in 2008 to form the joint venture company, Dupont Danisco Cellulosic Ethanol LLC (DDCE), to commercialize the technology for conversion of biomass to ethanol. DC. aims to be the world's leading cellulosic ethanol company and a key player in facilitating global energy independence and sustainable fuel supply. At present, we are working with The Goodyear

Rubber and Tire Company to commercialize a bioprocess for making isoprene, a key ingredient for synthetic rubber, from renewable feedstocks. Our technology allows for the bio-based production of isoprene and represents a significant move away from the use of and reliance on petroleum-derived isoprene. A concept tire made with our BioIsoprene™ product was on display at the United Nations Climate Change Conference in Copenhagen (the COP 15 meeting) in December, 2009.

#### **Sustainability is Good Business**

Genencor has made sustainability a centerpiece of its business strategy. The goal of sustainable development is to meet the needs of the present without compromising the ability of future generations to meet their needs. This means that we pursue the long-term viability and progress of our business while taking responsibility for improving the environmental, economic, and social conditions resulting from our work. Examples of our commitment and leadership in business practice include winning the 2003 Presidential Green Chemistry Award for the microbial production of 1,3-propanediol along with DuPont and in 2009 winning the national Sustainable Energy Award from the American Institute of Chemical Engineers (AIChE) for our Accellerase© family of enzymes for cellulosic ethanol. The AIChE Sustainable Energy Award recognizes the critical impact of chemistry and biochemistry innovations in developing sustainable energy solutions. In addition, we recently introduced our PrimaGreen® EcoWhite product, which is a unique and first-to-market enzyme. This enzyme powers the system that will be sold by Huntsman Textile under the name Gentle Power Bleach™. This novel bio-bleaching technology significantly reduces energy and water consumption in wet textile processing, while improving fabric quality. Our commitment to sustainable and environmentally responsive innovative solutions is also demonstrated by our work on biologically based methods for producing isoprene. Our BioIsoprene™ research and development collaborator, The Goodyear Rubber and Tire Company, won the Environmental Achievement of the Year Award in 2010 for the concept tire made with our BioIsoprene™ product—a breakthrough alternative to petrochemically produced tires.

#### **Collaboration boosts Innovation**

Genencor is a leader in industrial biotechnology and a participant along with university, business and government laboratories in further developing the underlying technologies that propel this platform of innovation forward. Collaboration is a key theme for success. The rate of improvement in the seminal technologies of DNA synthesis, DNA sequencing and synthetic biology is continuing to provide accelerating innovation opportunities. No single enterprise can do it alone and hence the need for developing effective networks that connect the players. As an example, we are industrial members of SynBERC, The Synthetic Biology Engineering Research Center, which is an NSF funded multi-institution research effort establishing a foundation for the emerging field of synthetic biology. SynBERC's vision is to catalyze biology as an engineering discipline by developing the foundational understanding and technologies to allow researchers to design and build standardized, integrated biological systems to accomplish many particular tasks. In essence, SynBERC is making biology easier to engineer. It is also engaged in training students who can leverage the investments and training as they go forward into industry. Powerful new technologies such as synthetic biology must also include governance and oversight to fully understand any potential unintended consequences. Hence, centers such as SynBERC also provide initiatives in which ethics and biosafety approaches are purposely incorporated into synthetic biology research and development. The collaborative Human Practices model within the NSF-funded SynBERC project was the first initiative in which social scientists were explicitly integrated into a synthetic biology research program. The Woodrow Wilson International Center for Scholars also provides new opportunities for collaboration emerging between scientists and social scientists working on synthetic biology.

#### **Making Biotechnology Interesting Enough to Learn About**

Increasing the science and technology acumen of our society and engaging young minds in science and engineering are key success factors for improving our innovation potential and social receptivity for technology based solutions. Science Bound, Iowa State University's premier pre-college program, prepares and empowers Iowan ethnic minority students to earn college degrees and pursue careers in science. In its 20th year, Science Bound has worked with more than 800 middle and high school student and offered college scholarships to 200 program graduates. The program asks 12 and 13 year olds to make a five-year commitment. Working in tandem with expert teachers, students can emerge academically equipped as well as socially

and culturally empowered to earn a college degree in science or engineering. We need to further support and expand this concept of making science fun and exciting and a learning process friendly enough to encourage commitment to a career in technology. To this end, we have a very active summer intern program that brings undergraduate and graduate level college students to Genencor to work on a variety of biotechnology projects over the summer months. In addition, we have representatives engaged with various community and local industry boards to help educate and foster public awareness and policy. We are also active members in industry groups such as the Biotechnology Industry Organization (BIO), Europabio and BayBio, an association serving the life science industry in Northern California.

#### **International Awareness**

Biotechnology and technology in general are played on an international stage. U.S. centricity is insufficient in providing the education and training necessary to be among the best, brightest and most successful. Language skills, cultural perceptivity and a global perspective are requirements for biotechnology players of the future. International awareness is an area for improvement in U.S. education and training.

#### **The Golden Triangle**

The President's Innovation and Technology Advisory Committee (PITAC), has identified a technological congruence that is called the "Golden Triangle." Each side of the Golden Triangle represents one of three areas of research that together are transforming the technology landscape today: "information technology, biotechnology, and nanotechnology. Information technology (IT) encompasses all technologies used to create, exchange, store, mine, analyze, and evaluate data in multiple forms. Biotechnology uses the basic components of life (such as cells and DNA) to create new products and new manufacturing methods. Nanotechnology is the science of manipulating and characterizing matter at the atomic and molecular levels. Each of these research fields has the potential to enable a wealth of innovative advances in medicine, energy production, national security, agriculture, manufacturing, and sustainable environments—advances that can in turn help to create jobs, increase the nation's gross domestic product (GDP), and enhance quality of life." In combination, these fields have an even greater potential to transform society. It is this interplay of technologies along with ever more demanding societal needs, which creates grand challenges. Industrial biotechnology is one of the tributary themes to this Golden Triangle. Continued investment in research, education, business and legal developments is necessary to achieve our collective aspiration of meeting the needs of the present without compromising the ability of future generations to meet their needs. Interdisciplinary collaborations that work the Golden Triangle in different patterns of innovation may offer routes to success provided the membership, results and ownership to outcomes are based on transparency, trust and data-based decision making.

A recent study by the National Research Council, "A New Biology for the 21st Century", recommends the integration of the many sub-disciplines of biology, and the integration into biology of physicists, chemists, computer scientists, engineers, and mathematicians. The most effective leveraging of investments would come from a coordinated, interagency effort to encourage an integrated approach to biological research focused on key problem solving areas. This study provides a roadmap to "21st Century Biology".

#### **Fostering University—Industry Collaboration**

The Bayh-Dole Act provides the process through which technology transfer from university laboratories to industry happens. University patents and start-up companies based on these intellectual assets have provided a significant boost to U.S. economic growth over several decades. There is opportunity to do more and a process to assess current barriers and potential new incentives should be undertaken. Examples are the following: current procedures do not allow companies that fund work in universities to own the IP; legal processes are cumbersome and the opportunity exists to slim-line these processes so that investments are largely for the technology development not the legal negotiation.

I thank the Committee for the opportunity to present these views and welcome any questions or comments.

## BIOGRAPHY FOR KARL J. SANFORD

In reference to the invitation from Chairman Lipinski to testify before the Subcommittee on Research and Science Education on June 29, 2010 with respect to 21st Century Biology, I (Karl J. Sanford) provide the following biographical information. I am currently Vice President of Technology Development at Genencor, a Division of Danisco and have a substantial track record of success as an industry leader in establishing the industrial biotechnology industry as we know it today.

Specific examples of my track record pertinent today's testimony are the following: 1) member of founding management team for Genencor International which has grown from nothing to over \$800 M in industrial product sales 2) 25 years of continuous technology and research activities in bringing many industrial enzymes to the market place addressing customer needs in detergent, grain processing, textile manufacturing, animal feed and human nutrition, biomass hydrolysis, bio-bleaching, silicon biotechnology and metabolic pathway engineering/synthetic biology. 3) leader in developing productive collaborations which include ADM/amino acid processes, Eastman Chemical/ascorbic acid continuous bio-catalysis, DuPont/BioPDO pathway engineering, Dow Corning/Silicon Biotechnology development and The Goodyear Rubber and Tire Co/BioIsoprene synthetic biology development. The commercial contribution in terms of annual product sales that derive from these and other related activities in the biotechnology sector exceed \$3 billion USD. 4) Advisor to various government led initiatives that were seminal in laying the foundation for the current industrial biotechnology and biofuels sectors. Highlights include: a) Compact signing for the Plant/Crop-Based Renewables at the Commodity Classic, Long Beach, CA., February, 1998 b) Plant/Crop-Based Renewables 2020 Vision and Road Map. c) Congressional testimony to House Committee on Science Subcommittee on Technology on Industrial Biotechnology National Competitiveness, February 1998 d) Testimony to Senate Committee on Agriculture, Nutrition and Forestry Hearing on The New Petroleum: S. 935, the National Sustainable Fuels and Chemicals Act of 1999 May 27, 1999 on importance of industrial biotechnology and bioenergy e) Thought leader and participant for Global Energy Technology Strategy Program (GTSP) in generating Applications of Biotechnology to the Mitigation of Greenhouse Warming, 2003.

I believe that my record demonstrates a substantial contribution to the industrial biotechnology sector. Genencor has established itself as a world leader in this sector which includes enzymes for corn bioethanol processing, enzymes for biomass hydrolysis, total solution for cellulosic ethanol production through our joint venture with DuPont, the DC. Company, and production of hydrocarbon biofuels from our BioIsoprene™ platform. I believe this combination of pioneer and thought leadership in anticipating what the technology and customer needs could be and the persistence and tenacity to design and build the products and processes to meet them distinguishes my record.

Mr. BAIRD. Great. Thank you, Dr. Sanford. I apologize for the interruption. Those beeps or noises you heard are a call to a vote. We have about 15 minutes. We are Pavlovian here. We begin to salivate when we hear those.

Thank you to all the witnesses for the testimony. Dr. Lipinski departed so that he can vote and then come back, and our goal will be to try to keep the hearing going rather than have a prolonged interruption while we go and congratulate sports teams and name post offices.

I want to thank the witnesses, believe it or not, for their expertise and their input. I will recognize myself for five minutes, followed by Dr. Ehlers.

I am intrigued by this concept and excited by it. As I get it, basically the idea is that we are going to—the new biology refers to the integration, sort of cross-disciplinary integration of lots of other fields—physics, chemistry, computational technologies, engineering—and the report suggests that one of the ways we develop this cross-disciplinary new biology is to apply it to kind of ‘grand challenges,’ and that all makes good sense to me. So my question is, NRC makes this report. Distinguished folks like you folks seem to be behind it. The biological section of NSF already receives a lot

of money, a \$767 million request for the next year. What is going to happen? Do you think—and maybe Dr. Collins, this is appropriate to ask you. Dr. Laubenbacher, you seem to be working in an area where, actually, you are applying this, as many of you do. But what happens to NSF now? Do they look at this NRC report and say, by golly, these folks are right, let us start focusing our research funding on this, or do they keep in the same kind of channels they may have been in?

Dr. COLLINS. Congressman, NSF played a role, actually, in calling for the report. We were one of the agencies that were involved in it, and in fact, we have already started to marshal resources. I shouldn't say "we" since I am no longer with NSF. But the Foundation has already started to marshal resources along these lines—some of the things I referred to, actually, in terms of these new ways to look at interdisciplinarity. NSF has hired program officers jointly between directorates, for example. The sandpit process that Dr. Leonard referred to was one that we called for.

Mr. BAIRD. Give us a 15-second summary of a sandpit other than children playing in sand. With five-year-olds, my mind goes there.

Dr. COLLINS. So the sandpit is in fact the sandbox but it is out of the United Kingdom. That is where we got it. So your image is exactly the right image. We posted a question in synthetic biology: give us your best ideas. A hundred and seventy two-page applications came in, front page, what is your idea, back page, a series of questions prepared by an industrial psychologist—how well do you play in groups, for example, interest in interdisciplinarity. A committee chose 30 of those individuals and they were all brought here, just outside Washington, D.C., for a week, put together with program offices for real-time review of their questions, and groups were put together and matched within that week-long period. And at the end of it, we got five to eight exciting proposals, some funded by the United Kingdom, some funded by the NSF.

Mr. BAIRD. So get some really bright people who work well together, get them together and set them loose?

Dr. COLLINS. Set them loose.

Mr. BAIRD. Neat.

Dr. COLLINS. And it was a really creative way, the sandpit, sandbox, however you want to think about it. And we picked this edgy, innovative area with emerging stuff that is rough, that is right at the edges, and synthetic biology was the first place that we went to, for all the reasons that are in the report.

Mr. BAIRD. Got you. So NSF is already working on this. As they are selecting their new person to replace your position, that person presumably will be savvy to this integrated issue. The other directors of other NSF programs are also on board?

Dr. COLLINS. They are, so when we decided to do this area of synthetic biology in the sandpit, engineering came on board very quickly, and then as the other directorates heard about it, all of a sudden we had the social sciences in, we had education and human resources, math and physical sciences. At the end of the day, all the groups had a piece of it.

Mr. BAIRD. Great. How will this affect grant applications and then how does it affect your training? You know, when I used to chair at a psychology department, I had this fun idea that we

would just put all these disciplines and faculty members in a hat and we would draw another discipline out, so I might draw nursing faculty or chemistry faculty or PE and all kinds of neat things would come. All the other faculty freaked out. They said oh, we can't do that. It seemed to me pretty exciting. But how is it affecting your educational enterprise in preparing the students who will feed this new biology effort?

Dr. COLLINS. So look, I think the real challenge is to get students to be comfortable going into that sort of arena. Faculty members, as I suggested in here, have to get much more comfortable with lowering the barriers, much the way they are often lowered in industry where folks can move around much more easily.

Mr. BAIRD. Any others wish to comment on that? I have only got about 40 seconds left, so Dr. Laubenbacher?

Dr. LAUBENBACHER. Yes. I think in terms of training, it reminds me a little bit of the 1990s when we introduced calculators into teaching calculus. It is difficult to teach an old dog new tricks, as they say, and the students were far ahead of the professors at that time, and I think similar things will happen here, that students, as they grow up, if they are provided with the right environment, they will be way ahead in terms of interdisciplinary thinking.

Mr. BAIRD. Thank you.

I am going to recognize—thanks to all your answers. I have to be brief, so I recognize Dr. Ehlers for five minutes.

Mr. EHLERS. Your questions were so brilliant, Dr. Baird, that they leave me wordless, so if you wish to pursue yours any further, go ahead. I just want to say I found this very enlightening, and I have got to wrap my mind around it a bit more. But I really—what you are doing is wonderful and it is what I would love to do if I could return to science today. It is just so exciting to hear this again. It brings back the memories of how exciting science was when I first encountered it, and I would love to join you.

Mr. BAIRD. I do have a follow-up, and both Dr. Ehlers and I are going to retire. Maybe, Vern, we should go back in and both of us sign up and take this coursework if our aging brains could—but, see, they will come up with a device that will allow our aging brains to comprehend what they are doing.

Mr. EHLERS. Speak for yourself.

Mr. BAIRD. Oh, okay. Sorry.

On a more serious note, though, so I am very intrigued by this issue of how we train people for this, because it is already a pretty challenging thing to get a Ph.D. in biology. Now you have got to somehow be able to interface with physics, chemistry. I mean, there is already a certain base level of awareness, et cetera, but are we going to need a longer amount of time in the training process, or is there just a new way of sort of wrapping one's head around the multidisciplinary approach? And I open that to everybody but Dr. Yamamoto and maybe Dr. Sanford, you can talk about how you are doing this in your applied realm.

Dr. YAMAMOTO. Well, let me begin and say that I am hopeful that not only will we not require more time for the training, but we will require less. The training periods in biology have gotten to be very extended to the point that investigators don't really begin their independent work until in their 40s and may have passed or

at least lost some of the kind of age in which they are doing their boldest thinking and their boldest research. So hopefully the amount of time can come down. So the question then, of course, is a very good one, and that is, how can this happen? And I would say that there are two ways to think about this. One is that we need increasingly to be thinking about working in teams, that increasingly we will have scientific endeavors that are carried out by groups of people who don't share the same expertise but have enough familiarity that they know the kinds of tools that are needed, the kinds of experiments that need to be done, even though they themselves may not know how to do them.

Mr. BAIRD. So it seems to me that needs to—not to pat myself on the back, but that model I had of working at a very early undergraduate age where you are just really used to saying, okay, so I am a social science major, but this semester I am taking a course with physics students—that needs to happen very, very early on, so it is integrated into who you are.

Dr. YAMAMOTO. Your model is exactly right, and so that in the teaching of biology we need to be integrating some of these physical principles that weren't really needed before. We have passed through an era in which biology was mostly descriptive. We were trying to identify all the characters, see what they look like in the microscope, for example, and we have now advanced to a point where we really need to understand in a quantitative way how these things interact. And we are moving on to being able to require the physical principles, mathematical manipulations to be able to understand what these things are. And students can comprehend that and understand it early on and be able to integrate that learning. So it will be teams, and a broader education from the outset, exactly as you said.

Mr. BAIRD. I have got to run and vote, as probably does Dr. Ehlers. Dr. Lipinski will resume the Chair. I apologize, I won't be here to hear the answer. Any quick comment before I go?

Dr. SANFORD. Yes, I would emphasize the word "teams," building interdisciplinary teams where the team has a composition of the expertise required to solve the problem and the problem is very important to help focus the attention of the team members on working together.

Mr. BAIRD. Thank you.

Chairman LIPINSKI. The Chair will now recognize himself. I will have the opportunity now to ask my questions and conclude the hearing. I ran out there to vote to make sure that we could have this time to conclude the hearing rather than have you sit here probably waiting 45 minutes at least for us to finish with our votes and give the opportunity for those members to ask questions.

A couple things that I wanted to ask, and I will keep watching. As soon as this vote ends, I am going to have to run out of here quickly, finish up here, dismiss you and run out. But a couple questions. First, a broad question, mainly for Dr. Sanford and Dr. Leonard but for anyone else who has any—wants to offer any views on this. How does the U.S. position in synthetic biology compare to other nations? If we have an edge, what are our primary obstacles to keeping that edge? Dr. Sanford, why don't you start?

Dr. SANFORD. Yes. My view is that the United States is number one in the world in terms of leading this thrust around synthetic biology, even defining the term and integrating the disciplines that are required to make synthetic biology work. Having said that, I think there is broad participation around the world, and frankly there is much more eagerness that I see on the part of students and numbers of students in other parts of the world, that I think the United States needs to really make the science and engineering, math and technology a number one agenda for bringing students into this field versus transaction specialists.

Chairman LIPINSKI. Dr. Leonard?

Dr. LEONARD. I guess I can comment on an aspect that is related to sort of the previous question as well, which has to do with the undergraduate synthetic biology competition called iGEM [international Genetically Engineered Machine], so this is an international competition, and over the five years that it has been around it has seen increasing international participation. And the teams that participate from outside of the United States are strong in taking the top prize several years now going so there is a groundswell outside the United States as well in interest in this area. So I would just second Dr. Sanford's comment—that in my experience, it is still a hotbed of activity and probably the majority of the driving laboratories are currently in the United States, although there is potential for competition and growth all over the world.

Chairman LIPINSKI. Do any other witnesses have any comments on this?

Dr. COLLINS. Well, I think in terms of sustaining our edge, it really does go to the comments that were made by all of us, and that is, whatever can be done to facilitate the open sharing of knowledge between different groups, whether it is within departments in terms of universities or across our Federal funding agencies, this openness is really going to be important as far as powering something like synthetic biology where you do need the basic biological information reinforced by physicists, by engineers, mathematicians. And it is that culture, that environment of innovation that—however we can continue fostering that is going to be central to keeping the edge in terms of synthetic biology.

Chairman LIPINSKI. Dr. Yamamoto.

Dr. YAMAMOTO. The New Biology report would suggest that by enunciating these major challenge areas, that it will generate the technologies that we need to be able to answer the questions, and this was really the case when the decision was made to put a man on the moon, the decision was made to sequence the human genome. In neither of those cases, at the time that the challenges were enunciated, were the technologies available to actually achieve the goals, and it was by enunciating the challenge and capturing the imagination of scientists about the ways that they could contribute to these challenges that those technologies became generated. And the impact of being able to achieve those challenges has been immeasurable.

There is an article in Nature magazine today about the impact of sequencing the human genome that goes well beyond being able to simply know the order of the nucleotides and the genome, and

so that is a long way of saying that I think that the capacity for the United States to maintain a lead in synthetic biology and these other areas could actually hinge on the decision by our government, or by ourselves, to enunciate these kinds of challenges, capture the imagination of scientists as well as the public at large, in ways that they can contribute. And that will certainly include this new, exciting field of synthetic biology that really has a place, as we heard, in each of these areas.

Chairman LIPINSKI. Following up a little bit on that, if a new biology research initiative were created by the Federal Government, what should be done to ensure that the private sector is actively engaged and that the resulting research discoveries are translated to the marketplace? Whoever wants to start. Dr. Sanford?

Dr. SANFORD. One of the very important elements of working with universities, from a Genencor standpoint, is access and a window into new technologies. And I would use SynBERC as an example of such a consortium of not only universities, but companies that can participate and exchange ideas and learn together, also offer students training in the companies where we use internships, for instance, in the summer to host some of the SynBERC students, and this is a great way to get dialog and the exchange of information of developers of the technology and the users of the technology. Second, I think we have an opportunity to make the legal system a little bit more responsive and easier to negotiate in terms of licensing technologies from the universities into companies.

Chairman LIPINSKI. Dr. Yamamoto, do you want to add something?

Dr. YAMAMOTO. I think that one of the other key elements of the *New Biology* report was the whole notion of cooperation between agencies that are supporting life sciences research, and we have entered an exciting—one of the ways to think about the exciting area of biology that we have now entered is that we have in place kind of—we have all the cards on the table. You can play a different card game when you know that all the cards are on the table, and that is really where we are now, and having reached that, we can enunciate challenges that go from the most fundamental sort of question to the capacity to apply them. And I think the role that the government could play in being able to contribute to this is to be able to make funds available that will bring together these sectors. So one of the things that the *New Biology* report talks about in particular is different agencies within the Federal Government, over 20 of them, as you know, that are supporting life sciences research, being motivated by funding to be able to be working together—funds available, for example, only for projects that require the expertise of two or more Federal agencies. Exactly the same sort of scheme could be used for bringing together the public and private sector, and putting together exciting new decadal-level challenge ideas that can be accomplished only through application of fundamental research that takes place within academia, and its development and application in the private sector.

Chairman LIPINSKI. Dr. Collins.

Dr. COLLINS. In my written testimony, I alluded to an article in Sunday's New York Times on these proof-of-concept centers that are being tried at a variety of universities now that have to do with

funding ideas very early in the stream, as far as getting them transferred into technology. Our funding agencies could play a role there. That is a policy decision as far as the government is concerned—where Federal money should be used in crossing this so-called ‘valley of death’ between an idea and getting it into technology. But there is also a place, as far as basic research organizations like the NSF is concerned, for funding individuals who want to study this entire process of moving from idea into technology. Upstream, how do you get it started, and downstream, what are the conditions under which it is successful or not successful, and what can we learn from both of those sorts of things? So it seems to me there are a variety of places where this could be thought through, both in terms of injecting funds, but also studying the process itself and how it works.

Chairman LIPINSKI. Dr. Laubenbacher.

Dr. LAUBENBACHER. I think synthetic biology is a real poster child for the kind of research that the National Academies’ report advocates, and I think everything that the members of this witness panel have talked about apply to it, and in particular as Dr. Leonard mentioned, the iGEM competition is an incredibly good tool to get students excited. We have one of those. We field a team at our institute, and it has been terrific to watch.

In terms of making sure that the fruits of basic research get turned into products that actually help society, I think that, again, synthetic biology in other areas—for example, I am a bit familiar with research done by pharmaceutical companies. As basic research becomes very important, I think there will be more opportunities for research collaborations between companies and academics that do not involve IP issues, and intellectual property is, in many cases, the stumbling block between successful—for successful collaborations.

Chairman LIPINSKI. Thank you.

One very quick, and if I can get an answer quickly from Dr. Sanford and maybe you want to follow up in a written form, how well do you think the current regulatory guidelines apply to synthetic genomics? Do we need a different set of guidelines for synthetic genomics relative to natural genomics?

Dr. SANFORD. Yes, I do. I think that is true. We do need additional guidelines with regard to synthetic biology. One example is that in the regulatory terminology there is no such thing as a chassis. What is used as a host strain would be another terminology. So when a synthetic biology company brings forward to their regulatory experts terminologies that they are not familiar with and that really don’t have a track record, probably at the very least, the regulatory trail is now complicated and lengthened. So I think there is an opportunity here to get ahead of the wave, so to speak, and do some definitions and some exchange of information with regulatory experts to get advice on how to do this without undue problems.

Chairman LIPINSKI. Thank you for being quick there. Anything else you want to add, I would appreciate a follow-up in writing if there is anything else you want to add to that answer. But I want to thank all the witnesses today for their testimony. The record will remain open for two weeks for additional statements from the

Members and for answers to any follow-up questions the Committee may ask of the witnesses. It was a very good hearing and we had—despite all the competition, we had a good turnout of Members and I expect there will be some follow-up questions to this, and with that, the witnesses are excused and the hearing is now adjourned.

[Whereupon, at 3:12 p.m., the Subcommittee was adjourned.]

## Appendix 1:

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ANSWERS TO POST-HEARING QUESTIONS

## ANSWERS TO POST-HEARING QUESTIONS

*Responses by Dr. Keith Yamamoto, Chair, National Academy of Sciences' Board on Life Sciences, and Professor, Cellular and Molecular Pharmacology, University of California, San Francisco*

**Questions submitted by Representative Brian P. Bilbray**

*Q1. Assuming a national Electronic Medical Records (EMR) infrastructure is eventually developed, what are the existing impediments to the future utilization of EMR data for research?*

A1. We are very far from a national EMR, but it is an important and worthy goal that could have enormous impact for both health and research. A range of potential impediments to utilization of EMR data for research would need to be recognized and addressed:

- a. Privacy/Security. Robust, broad-based but stratified consenting for collection, archiving, accessing different categories of information, tissues, etc. coupled with assurance of appropriate protection of information.
- b. Access. Standardization of identifiers for medical care purposes; mechanisms for removal of identifiers for many research purposes; firewall separation of different categories of information for access by different stakeholders and interested parties: the individual subject of record, emergency medical personnel, clinical caretakers (primary and subspecialists), insurers, researchers.
- c. Standardization. Information fields; nomenclature; preservation, fixation, storage, recovery and distribution protocols for tissues/fluids/images/molecules
- d. Scope. Range of information and materials to be included; ongoing updating of information and materials for longitudinal analysis.
- e. Integration. Systems and network computational methodologies for organization and analysis of multiple classes of information—pathophysiological, epidemiological, behavioral, histological/imaging, molecular.

*Q2. Unfortunately, the capacity to quickly generate enormous amounts of data has grown far more rapidly than our investments in mid-level cyber-infrastructure—e.g. high-performance computers, mass storage, and database development and support. Are there opportunities to promote increased efficiency regarding our investments in cyber-infrastructure, especially as the capacity to generate data continues to soar?*

A2. The two largest barriers to efficient utilization of research data, databases and material repositories are lack of standards and enforced access/sharing of information/materials at appropriate times/levels. The Federal Government, via the power of funding, could potentially address both problems, but setting of missions, standards and funding are currently fragmented (e.g., life sciences research is supported by >20 Federal agencies with separate budgets, overlapping but commonly competing missions) across agencies that often themselves host multiple noninteractive information systems. If project funding was made conditional, dependent upon agreements to share information and materials, and to provide information access through a common data platform, these barriers could be significantly ameliorated.

*Q3. How do you envision the “new biology” approach achieving a reasonable balance between funding fundamental basic science and applied research?*

A3. President Obama has established clearly the rationale for sustained commitment of public support of basic science: “An investigation . . . might not pay off for a year, or a decade, or at all. And when it does, the rewards are . . . enjoyed by those who bore its costs, but also by those who did not. That’s why the private sector under-invests in basic science—and why the public sector must invest in this kind of research.” Hence, while the opportunities for translation and application of fundamental discoveries clearly deserve attention and require focus, Federal funding must also maintain a central focus on basic research; the NIH, for example, has long maintained a ratio of approximately 60:25:15 for basic:translational:clinical research. The New Biology report describes three strategies to help ensure that the funding balance effectively promotes and achieves applications of fundamental discoveries:

- a. Enunciate and adopt decadal challenges to inspire and focus efforts extending from discovery to application on urgent societal needs in the areas of health, energy, food and the environment.
- b. Better recognize the unity of biology, and thus the potential for basic science advances or applications in one area to contribute to others, by developing programs that facilitate and drive cooperative research programs across two or more agencies that address questions not otherwise accessible by a single agency.
- c. Establish new models for public-private research ventures that reduce barriers in the continuum from basic discovery in academia to development and application in industry.

## ANSWERS TO POST-HEARING QUESTIONS

Responses by Dr. Karl Sanford, Vice President, Technology Development, Genencor

**Questions submitted by Chairman Daniel Lipinski**

*Q1. How well do you think the current regulatory guidelines apply to synthetic genomics? Do we need a different set of guidelines for synthetic genomics relative to natural genomics?*

*A1.* At the conclusion of the oral testimonies of the invited witnesses at the U.S. House of Representatives Committee on Science and Technology Subcommittee on Research and Science Education on 21st Century Biology, on June 29, 2010, Subcommittee Chairman Daniel Lipinski (D-IL) invited additional input regarding regulatory implications on this subject matter. Specifically, Mr. Lipinski asked how the current regulatory guidelines apply to synthetic genomics, and whether we need a different set of guidelines for synthetic genomics relative to natural genomics. We respectfully submit this additional perspective.

The new biology for the 21st century builds upon the existing regulatory framework that has provided for the safe and effective development, manufacture and use of many bio-products that are in commerce today across the health, food, agricultural and industrial sectors. We anticipate continued rapid advancement in this field due to many factors; the ongoing development of DNA synthesis and sequencing technologies, more efficient molecular and microbiology methods and continued integration of nano- and information technologies. In addition, synthetic biology will catalyze the transformation of biology to an engineering discipline through design and construction of standardized, integrated biological parts, components and systems broadening the potential for private sector applications. All of these advances will shorten product development times and accelerate the pace of innovation, improving economic outcomes for the private sector thereby improving our nation's ability to compete in the global economy based on a 'faster, better and cheaper' model.

As Synthetic Biology is an emerging field, it is still too early to know precisely what will be required to ensure that the science is conducted in a safe and ethical manner and that any products resulting from it are also safe. However, past models offer insight into how we should move forward in a collaborative, productive manner to ensure our dual goals of safety and continued innovation. To guide the regulatory process of 21st Century Biology, we submit three major points for consideration:

- The Golden Triangle of information technology, biotechnology and nanotechnology, described by the President's Innovation and Technology Advisory Committee (PITAC) can be used as a guide to identify agencies and individuals who understand the science behind innovations as well as its ramifications with regard to safety and ethics.
- Government can also utilize the model of study and policy formation that was carried out for biotechnology in the early 1980s by the FDA, USDA, OSHA and EPA. The proposed policies published by the Office of Science and Technology Policy, Coordinated Framework for Regulation of Biotechnology, FR 51 (123): 23302-23393, June 26, 1986, allowed industry and interested persons to comment and resulted in the final biotechnology regulatory policies and rules which proved vital in helping guide the science and industry forward.
- In addition, the NIH Guidelines for Research Involving Recombinant DNA molecules, instituted to assure safe use of rDNA technology in research, may need to be modified to include the new concepts of synthetic biology. (Please see: [http://oba.od.nih.gov/oba/rac/guidelines\\_02/NIH\\_Guidelines\\_Apr\\_02.htm](http://oba.od.nih.gov/oba/rac/guidelines_02/NIH_Guidelines_Apr_02.htm)) Also, EPA's TSCA biotechnology regulation is based on the concept that intergeneric microorganisms are new. It is therefore a specific regulation which will also need revision to include the concepts of synthetic biology. (Please see: [http://www.epa.gov/biotech\\_rule/index.htm](http://www.epa.gov/biotech_rule/index.htm))

Due to the above described existing framework, we do not recommend the formation of a new agency or regulation at this time, but strongly suggest that key individuals from the existing agencies are involved in the process of identifying risks and safeguards in order to arrive at well-informed decisions on modifications of existing guidelines.

In summary, given the number of unknowns and the many facets of New Biology, close collaboration between industry, academia and regulators is required to ensure all decisions made are from a well-informed position, are based on sound science, and with international coordination (e.g., the EU has ongoing discussions on syn-

thetic biology: link [http://ec.europa.eu/research/biotechnology/ec-us/workshop-on-standards-in-synthetic-biology-2009\\_en.cfm](http://ec.europa.eu/research/biotechnology/ec-us/workshop-on-standards-in-synthetic-biology-2009_en.cfm)) as this new field of science is emerging quickly in many regions of the world. This close collaboration will ensure that together we can explore the science involved, anticipate new technologies or combinations of technologies, discuss potential outcomes, identify any new ethical and safety issues that require guidance and begin to craft any new regulatory modifications that are identified. As the committee heard during the testimony on June 29th, this new frontier offers many promising developments for a more sustainable future. We look forward to working with regulators and our colleagues in academia to ensure that the appropriate safeguards are in place so synthetic biology can flourish in the 21st century and bring forth the many promising advancements it holds to the people of the United States and the world.



## Appendix 2:

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ADDITIONAL MATERIAL FOR THE RECORD

STATEMENT OF DR. JAMES SULLIVAN, VICE PRESIDENT FOR PHARMACEUTICAL  
DISCOVERY, ABBOTT LABORATORIES

I am pleased to submit this statement for the record for the hearing entitled, "21st Century Biology." The purpose of this statement is to highlight the importance of a new trend of interdisciplinary research—what we call "new biology"—and state my support for the National Research Council's call for a multi agency, multidisciplinary new biology initiative, so we can more fully explore the potential of this field.

"New biology" lies at the intersection of the fields of biological sciences, engineering, mathematics, and the physical sciences—and its utility is apparent in the novel tools that are now available to the biotechnology industry. These "new biology" tools are driving medical innovation in not only the discovery of the pathways that underlie complex diseases, but also in the creation of new and better therapies.

As a pharmaceutical scientist at Abbott, I have firsthand knowledge of the importance of "new biology." I work to create treatments that address significant medical problems. It is a goal that is easy to articulate, and vastly more difficult to achieve. Additionally, the way we meet this goal has evolved over time as our understanding of biological processes grows.

Over the past century, the pharmaceutical industry has been able to create breakthrough treatments for some of the world's most devastating diseases. In the past 40 years alone, for example, new drugs that help control blood pressure and normalize lipid levels have helped cut in half the number of deaths from heart disease, and reduce by 70 percent the incidence of stroke. Scientific discoveries from Abbott's own laboratories have been key elements in the transformation of HIV infection from a death sentence to a more manageable chronic disease.

Over the years, as scientists have gained a more comprehensive understanding of the molecular interactions that underlie biologic processes, we in the pharmaceutical industry have been focused on discovering medicines that treat disease by interacting with a single protein, or target, involved in the disease process. We've developed complex technologies to help us identify appropriate targets, built chemical compounds designed to interact with those targets, and then rapidly screened hundreds of thousands of potential compounds in an effort to identify likely candidates for further study. We've developed incredibly detailed computer models to help us better predict the way these compounds will behave in the body. We have more ways than ever before to generate data and more *experts* than ever before to analyze that data to drive the creation of new drug molecules. The process of creating new medicines is now the ultimate team sport. It requires coordinated efforts from experts in multiple disciplines, from biochemists and pharmacologists, to MDs and engineers.

A current ongoing program at Abbott provides a useful example. We are one of many companies working to develop more effective treatments for Hepatitis C infection, a condition that impacts more than 70 million people worldwide. Abbott is developing a compound that blocks the activity of a key enzyme involved in the replication of the hepatitis C virus (HCV). The challenge here is that some molecules that are most effective at blocking this enzyme, (HCV polymerase) can exhibit a high degree of adverse events. Our task was to design a molecule that was effective against HCV *without* causing those adverse events. We started with thousands of possibilities that needed to be evaluated. This required the use of high-throughput screening technologies; nuclear magnetic resonance and x-ray crystallography to better understand the protein structures we were dealing with; and sophisticated molecular modeling techniques to design a series of molecules that blocked the polymerase. But we weren't finished. That series was then screened using another multidisciplinary approach that draws on cellular biology and systems engineering to rapidly eliminate compounds that may cause cardiac adverse events. This process represents a multi-year effort that brought us to the point where we could advance a compound into the clinic (treating patients)—where we have an industry average 1-in-10 chance of creating a viable medicine for patients.

And the process is only getting more complex. Diseases like cancer, schizophrenia and Alzheimer's disease have proven difficult to treat because they involve the interactions of multiple, interdependent proteins designed to interact with multiple targets, increasing the complexity of the discovery process exponentially. Without putting the necessary resources into fields like "new biology," we will not have the tools or the scientists capable of generating treatments for these complex, devastating diseases.

At Abbott, our research program has established a strong paradigm for multidisciplinary research, one that relies on the coordination and integration of expertise from a variety of fields. But finding solutions to the increasingly complex problems

we face today is beyond the scope of any single institution's efforts. We need to ensure that we have an integrated systems approach to biologic science that spans academia, biotechnology and the pharmaceutical industry. This is why, as a scientist deeply interested in the next generation of medical research, I believe we need to support the National Research Council's proposal for a multi agency, multi-disciplinary new biology initiative.

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