Written Statement of

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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, is clear that by developing 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.

<u>How will "synthetic biology" help to achieve these goals?</u>

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 rather 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.

<u>What types of research infrastructure and support are required?</u>

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, interagency 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.[1] 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 valuable 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/EPSRC sandpit also dovetails with other national-level efforts including the National Academies Keck Futures Intiative's conference on "Synthetic Biology: Building on Nature's

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[1] Profiled in "Digging for fresh ideas in the sandpit" (2009) *Science*. Vol. 324. no. 5931, pp. 1128-9.

Inspiration", which was held in November 2009.[2] 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.

<u>What educational strategies will prepare students and trainees to pursue these challenges?</u>

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

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

innovative models that can thrive within different institutional cultures and organizational structures.

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 PhD 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.[3] 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.

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[3] Smolke, Christina D. “Building outside of the box: iGEM and the BioBricks Foundation” (2009) *Nature Biotechnology*. Vol. 27. no. 12, pp. 1099-1102.

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 21^{st} century biology, since developing student capacities to work on interdisciplinary challenges will benefit them in any career they eventually pursue.

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

Synthetic biology taps into a vast potential to grow the industries that will lead 21^{st} 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.