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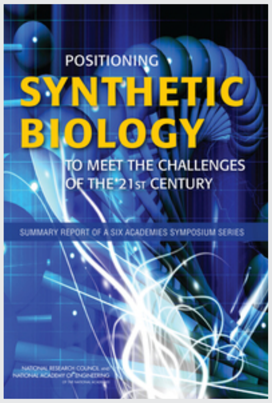

Positioning Synthetic Biology to Meet the Challenges of the 21st Century: Summary Report of a Six Academies Symposium Series

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POSITIONING SYNTHETIC BIOLOGY TO MEET THE CHALLENGES OF THE 21ST CENTURY

SUMMARY REPORT OF A SIX ACADEMIES SYMPOSIUM SERIES

Stephanie Joyce, Anne-Marie Mazza, and Steven Kendall, Rapporteurs

Committee on Science, Technology, and Law
Policy and Global Affairs

Board on Life Sciences
Division on Earth and Life Studies

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1

Introduction

> *Laws and institutions must go hand in hand with the progress of the human mind. As that becomes more developed, more enlightened, as new discoveries are made, new truths discovered and manners and opinions change, with the change of circumstances, institutions must advance also to keep pace with the times.*
>
> *Thomas Jefferson*

The turn of the millennium brought into view a new research landscape in which the biological sciences loom large and where technical possibilities barely dreamt of decades ago seem legitimately attainable. The biological sciences of this century are the product of decades of advances in, for example, genetics and genomics, molecular and systems biology, and bioengineering technologies. Modern biology also draws upon and incorporates discoveries from beyond the life sciences. Disciplines as diverse as engineering, chemistry, computing, and social science have all played important roles in shaping the biology of the 21st century.

Interconnectedness defines today's biology and offers, in places, an unprecedented and exponentially increasing linkage of many streams of discoveries and innovations.[1] Biology also has become a global endeavor, with networking technologies enabling new modes of collaboration amongst multidisciplinary teams from around the world. In this networked world, researchers have the ability to develop partnerships that foster novel approaches to scientific inquiry, ask new questions about the mechanisms of life, and address global needs in innovative ways.

But the new century brings new challenges. An ever-increasing world population means a host of new problems—climate change, increasing food and

[1]Thomas Lee, Director, Microsystems Technology Office, Defense Advanced Research Projects Agency.

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energy needs, the dispersion of existing and emerging diseases—and a host of unanswered questions about how human and natural systems might offer solutions. Many scientists and engineers believe that some of the challenges of the new century might be met through a young and potentially transformative field—synthetic biology—that seeks to accelerate improvements in how we partner with nature to meet our needs.

In the simplest terms, synthetic biology is an emerging discipline that combines both scientific and engineering approaches to the study and manipulation of biology. For example, one branch of synthetic biology seeks to apply engineering principles to realize standardized biological parts that can be reliably reused "off the shelf" to perform specific functions. Rather than asking "How does an existing natural biological system work?," such synthetic biologists ask, "What components are necessary to encode a specific behavior within an engineered living system?" By asking different questions, synthetic biologists hope to improve our collective capacity to engineer customized biological systems designed to meet specific human needs. Scientists using synthetic biology-based approaches also hope that constructive approaches to studying biology will yield a deeper understanding of natural living systems.

Various approaches are being pursued so as to best practically realize "learning by building" and "scaleable engineering" in synthetic biology. For example, full genome synthesis, when combined with evolutionary screening or selection, can yield improved cellular strains for biomanufacturing while directly supporting "reverse genetics" approaches to scientific discovery.

It is important to note that some aspects of synthetic biology research have been technically controversial. Some ask, for example, whether genetic parts can ever be reliably standardized for reuse across changing genetic and environmental contexts.

Within the research community, synthetic biology fosters relationships across a unique and global assemblage of practitioners that extends beyond established academics and students working in traditional institutions and includes members of the do-it-yourself (DIY) community of amateur researchers. Further, the connectivity offered by the World Wide Web gives researchers an unprecedented opportunity to network, collaborate, and share research results across communities and nations.

Although synthetic biology is still in its infancy—core research has largely been confined to efforts to identify and refine biological units that perform specific genetic or biochemical functions and to improve DNA synthesis and construction methods—the collective vision for the field is ambitious. Progress in synthetic biology, proponents believe, will enhance human potential through an interlocked cycle in which incremental advances expand our understanding of life. Deepening our understanding of natural biological processes will, in turn, improve the biological "toolbox" that gives scientists and engineers the means to engineer organisms that offer new forms of pollution control, novel medications, and sources of energy. Ultimately, synthetic biologists hope to design and build engineered biological systems with capabilities that do not exist in natural sys-

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tems—capabilities that may ultimately be used for applications in manufacturing, food production, and global health. Even though research has largely been limited to work at the molecular or cellular level, governments and industries worldwide are investing significant resources in synthetic biology research and product development.

Synthetic biology—unlike any research discipline that preceeds it—has the potential to bypass the less predictable process of evolution to usher in a new and dynamic way of working with living systems. Thus, while synthetic biology is still a nascent area of research, it has attracted significant attention. Many questions, however, remain:

- What solutions can synthetic biology realistically offer for today's global challenges?
- How may we best prepare researchers for work in synthetic biology?
- What are the commercial, industrial, and medical possibilities for synthetic biology?
- What ethical and social concerns does synthetic biology raise, and how can they be addressed locally or collectively?
- How should we best engage the public to enable understanding of the promise and risks of this emerging field?
- What intellectual property, patent, sharing and ownership arrangements will best allow synthetic biology to advance?
- How should synthetic biology be regulated, and what form should any oversight or governance frameworks take?
- Does synthetic biology pose new biosafety and biosecurity concerns, and if so, how may they be addressed effectively?

Stakeholders around the world are grappling with such questions. In the United States, for instance, the President's Commission for the Study of Bioethical Issues has identified essential principles and recommendations for the purpose of guiding ongoing research in synthetic biology.[2] And, in response to advances in synthetic biology, the National Institutes of Health has revised its guidelines on recombinant DNA[3] based upon the National Science Advisory Board for Biosecurity's consideration of synthetic biology in the context of dual use research.[4]

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[2]Anita L. Allen, Henry R. Silverman Professor of Law and Professor of Philosophy, University of Pennsylvania Law School and a member of the Presidents' Commission, discussed the commission's recommendations at the Shanghai symposium. See page 22 of this report.

[3]Department of Health and Human Services, National Institutes of Health March, 2013. *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines).* Online at http://oba.od.nih.gov/rdna/nih_guidelines_oba.html (accessed March 27, 2013).

[4]National Science Advisory Board for Biosecurity (NSABB), April 2010. *Addressing Biosecurity Concerns Related to Synthetic Biology: Report of the National Science Advisory*

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Nevertheless, as serious discussions about synthetic biology are only beginning, many questions remain about how to best manage, stimulate, and govern the continued development of the field. The resolution of these questions requires input from the public and private communities of stakeholders.

Importantly, synthetic biology is an area of science and engineering that raises technical, ethical, regulatory, security, biosafety, intellectual property, and other issues that will be resolved differently in different parts of the world. Inevitably, this will affect how the field develops within nations and internationally.

As science and engineering research becomes more global, international engagement on emerging technologies is critical. It has becoming increasingly difficult to place limitations on scientific advances or to expect that norms and protocols developed in one country will be followed in another. Only with an international exchange of ideas on scientific and technical challenges—as well as policy, regulatory, and legal challenges that arise around emerging scientific fields—will it be possible for the global network of scientists, engineers, and policymakers to develop mechanisms that encourage continued advances in emerging fields while increasing awareness of—and proactively addressing—challenges that may arise.

As a better understanding of the global synthetic biology landscape could lead to tremendous benefits, six academies—the United Kingdom's Royal Society (RS) and Royal Academy of Engineering (RAE), the United States' National Academy of Sciences (NAS) and National Academy of Engineering (NAE), and the Chinese Academy of Science (CAS) and Chinese Academy of Engineering (CAE) organized a series of international symposia on the scientific, technical, and policy issues associated with synthetic biology. The symposia, which were primarily funded by the Alfred P. Sloan Foundation,[5] built upon previous collaboration between the RS and U.S. agencies and included China because of the country's growing investment in engineering, scientific research, and biotechnology. The Organisation for Economic Co-operation and Development (OECD) also contributed participants and perspectives.

Board for Biosecurity (NSABB). Online at http://oba.od.nih.gov/biosecurity/pdf/NSABB%20SynBio%20DRAFT%20Report-FINAL%20(2)_6-7-10.pdf (accessed March 27, 2013).

[5]The Sloan Foundation, which supports research on science, technology, and economic institutions, has supported research in synthetic biology since 2005. The foundation's grants support responsible development of synthetic biology and focus on ethical, regulatory, and public policy implications and on risks inherent in the field. Sloan grants have included projects to articulate ethical issues, inform the policy and journalism communities, assess the regulatory aspect of synthetic biology, and educate policy makers and the public. The foundation-sponsored Synthetic Biology Project provides a web-based information clearing-house that includes important events in the field; provides information and analysis on regulatory, ethical, and business developments related to synthetic biology; and a regularly updated global map of ongoing projects. The Synthetic Biology Project is hosted by the Woodrow Wilson International Center for Scholars (see http://www.synbioproject.org, accessed May 15, 2013).

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The three symposia, attended by approximately 500 participants in total, brought together researchers from numerous disciplines—experts in law, property rights, and ethics; representatives from industry; policymakers; and members of the public—in the first collaboration among the United States, the U.K., and China on synthetic biology. Participants were asked to discuss synthetic biology in terms of its present and future value and to examine the scientific, engineering, societal, and policy implications of this emerging field.

The individual symposia, which were held in London, Shanghai, and Washington, DC, were each organized around a specific aspect of synthetic biology.[6] The first symposium, in London in April 2011, provided an overview of synthetic biology and developments in the past five years. Participants discussed estimates of what might be achieved in the next 5, 10, and 25 year periods, requirements and resources necessary for realizing value creation from synthetic biology, and conditions needed for an enabling environment. The focus of the second symposium, in Shanghai in October 2011, was the scientific and technical challenges that must be met to enable further development of the field. The final symposium, in Washington, DC in June 2012, focused on next-generation tools, platforms, and infrastructure necessary for continued progress in synthetic biology and the associated policy implications. Over the course of the three symposia, the collaborating institutions and participants gained a deeper perspective on each country's national and insitutional aspirations and accomplishments in synthetic biology. Further, presenters and attendees had the opportunity to witness and share in a progression of knowledge and perspective amongst the participating countries from the initial to the final symposia.

This report summarizes the major topics addressed during the symposia by symposium participants. These included the development and potential of synthetic biology, national and regional plans for the advancement of synthetic biology, and potential benefits and concerns associated with the field. The summary has been prepared by the symposia rapporteurs as a factual summary of what occurred at the symposia. The statements made are those of the rapporteurs or individual symposia participants and do not necessarily represent the views of all symposia participants, the planners of the symposia, or the U.S. National Academies.

[6] For details on the specific agendas, see Appendixes A-C.

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2

Synthetic Biology: Science and Technology for the New Millennium

The definition of synthetic biology remains fluid because its full potential is not yet clear and because researchers are exploring many problem solving approaches. In general, however, the discipline is seen as involving the application of engineering principles to "design and construct…new biological parts, devices and systems" and re-design "existing natural biological systems for useful purposes."[1] Work is often motivated by the underlying goal of making biology easy to engineer. Synthetic biology research is conducted and facilitated by individuals trained in a variety of disciplines including biology, engineering, chemistry, genetics, and computational sciences. Synthetic biology also includes work to manufacture biological elements (for example, molecules, genetic sequences, systems, and simple organisms) different from those existing in nature for the purpose of achieving predictable and reliable performance of specific functions. Over time, proponents hope to develop a large portfolio of simplified biological modules—parts, devices, and systems[2]—that can be used to perform predictable, pre-determined functions with various applications.

Biological parts in scientists' current inventory are capable of performing basic functions at the cellular level. Examples include engineered biological circuits[3] and oscillators.[4] However, researchers hope to achieve goals ranging from

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[1]Definition from syntheticbiology.org, a community of individuals, groups, and labs committed to "engineering biology in an open and ethical manner." The site provides community news, discussions, and various resources (see http://syntheticbiology.org, accessed March 27, 2013).

[2]"Part" modules contain the instructions for basic biological functions. "Devices" contain multiple parts arranged to carry out more complicated designer-determined functions. "Systems" carry out advanced tasks.

[3]Engineered biological circuits are cellular subsystems wherein cellular DNA has been altered in order to produce specific new functions—such as signaling the presence of a given chemical or producing a certain protein. A major goal of synthetic biology is to

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tissue engineering and bio-computer interfaces to the creation of organisms that are capable of efficient, large-scale biofuel production.

At the symposium in Shanghai, Drew Endy, Assistant Professor of Bioengineering, Stanford University, noted that while the current definition will likely always be incomplete, the ultimate definitions of synthetic biology will take into account the dynamism and potential of synthetic biology which, if it achieves its potential, may change many aspects of how we live our lives.

At a fundamental level, synthetic biology seeks to take the creative force of nature and harness it technologically in order to solve problems of varying scale. In London, Huanming Yang, Director, Beijing Genomics Institute, optimistically described synthetic biology as "a science changing the world and the future of man," and proposed a motto for the field: "Life is what we make it."

Building on a Heritage of Biological Discovery

Though the practice of synthetic biology is new, the concept was coined a century ago in two publications by the biologist Stéphane Leduc.[5]

Modern synthetic biology has its roots in the 1953 discovery of the double helix structure of deoxyribonucleic acid (DNA) by scientists James Watson and Francis Crick (See Box 2-1).

The discovery of DNA was the key to understanding development and specialization in cells and organisms and ushered in a new era of genetic manipulation. Copying, editing, sequencing,[6] engineering, and synthesizing DNA and RNA (ribonucleic acid) all emerged from that discovery.

In Shanghai, Farren Isaacs, Assistant Professor of Molecular, Cellular, and Developmental Biology, Yale University School of Medicine, reflected on the developments that followed the early research on DNA. "Not so long ago," he observed, "we had questions on how to decode DNA. That [is what] led to understanding of gene functions and interactions at the molecular level. Now we get to change DNA at new scales, to both learn and make new systems."

By the 1970s, scientists had successfully created recombinant DNA (rDNA)—genetic material formed by combining DNA from more than one organism. This facilitated the development of genetic engineering and manipulation.

In the early 1980s, technical innovation led to the ability to rapidly sequence DNA.

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develop a large portfolio of engineered biological circuits for use in various applications or systems.

[4]Oscillators are genetically controlled, rhythmically repeated cycles of response and chemical production that govern the development, growth, and death of cells and organisms.

[5]*Théorie physic-chimique de la vie et generations spontanées* (1910) and *La biologie synthétique, etude de biophysique,* ed. A. Poinat (1912).

[6]Determining the nucleotide sequence of a particular fragment of DNA.

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BOX 2-1
DNA and Biological Parts

Deoxyribonucleic acid (DNA) is a molecule that contains the hereditary material of a living organism. It is found in every cell of known living organisms. The DNA molecule has a double-stranded, ladder-like structure. Genetic information is encoded as a sequence of nucleotides (adenine, cytosine, guanine, and thymine) that are arranged in pairs which form the "rungs" of the ladder. DNA is replicated during cell division.

A strand of DNA may contain thousands of genes, a unit of heredity which influences a particular characteristic in an organism. Genes contain anywhere from 1,000 to 1 million nucleotide base pairs. Genes are stored on chromosomes—a single, very long DNA double helix. The complete set of genes in a given organism is called the genome.

Genes contain chemical "instructions" for manufacturing proteins and other chemicals. Proteins are large molecules composed of amino acids. They are an essential component of a living organism. Body structures, functions, and the regulation of the body's cells, tissues and organs cannot exist without proteins. The manufacture of proteins entails transcribing genetic information into ribonucleic acid (RNA). RNA molecules then direct the assembly of proteins on ribosomes.

Synthetic biology seeks to design new types of cellular machinery that perform a desired function or produce a desired substance. Synthetic biologists achieve this by creating simple cellular parts which, when assembled, simplify gene expression and the cellular synthesis of proteins and other chemicals. Synthetic biologists also seek to elicit predictable cellular functions in, for example, regulatory and metabolic systems.

In 1974, geneticist Waclaw Szybalski heralded the next stage of biological innovation: "Up to now we are working on the descriptive phase of molecular biology." "But the real challenge will start when we enter the synthetic biology phase of research in our field. We will then devise new control elements and add these new modules to the existing genomes or build up wholly new genomes. This would be a field with unlimited expansion potential." "I am not concerned that we will run out of exciting and novel ideas."[7]

Synthetic Biology and Converging Scientific Disciplines

While synthetic biology arises from a century's worth of work in biology and related fields, its practice would not be possible without breakthroughs in such diverse fields as engineering, computer science, and information technology.

Stated differently, interconnectedness has been central to the development of synthetic biology. Advances in microscopy and electronics multiplied the capacity for data-gathering and analysis in biology. Simultaneously, progress in computer

[7]Waclaw Szybalski, 1974. "In Vivo and in Vitro Initiation of Transcription," in A. Kohn and A. Shatkay (Eds.), *Control of Gene Expression*, pp. 23-24, and Discussion pp. 404-405. New York: Plenum Press.

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and internet technology revolutionized the ability to process and transfer data and provided ideas and methods for how to manage complexity when engineering multi-component integrated systems. Calculations that only a decade ago would have taken weeks on a mainframe computer now take minutes: a gene sequence may be processed on a laptop. Increasingly sophisticated software allows for continuing improvements in three-dimensional imaging and modeling. Advanced technology has enabled real-time imaging of processes ranging from bacterial reproduction to the behavior of nanoparticles. The development of optical fibers has increased the capacity of data transfer—and global networking—by orders of magnitude.[8]

By the turn of the 21st century, progress in synthetic biology had accelerated as researchers began to exploit the concept of "forward engineering," which amalgamates custom-made or commercially available biological parts in order to test functionality.[9,10] Commercial gene synthesis became a global enterprise.[11]

Next generation gene sequencing machines now provide faster and less expensive methods for indexing genetic code.

Currently, synthetic biologists have the ability to design genetic code to elicit a specific function, pre-test the code for functionality using computer modeling, order the relevant genetic material from a commercial or open-source gene synthesis facility, and insert the material into a cell body in order to test real world functionality. Some DNA designs are now working the first time they are tested, replacing what has historically been a tedious trial-and-error based approach to engineering novel phenotypes.

What Makes Synthetic Biology Special?

Synthetic biology builds on discoveries in, and is the result of collaborations across, many fields (See Box 2-2). The field has several important characteristics. It:

- Represents a novel approach to studying biology
- Applies engineering methods to living systems

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[8]National Research Council, 2009. *A New Biology for the 21st Century*. Washington, DC: The National Academies Press.

[9]Akst, Jef, 2011a. "Tinkering with Life: A Decade's Worth of Engineering-infused Biology," *The Scientist,* October 11. Online at http://www.thescientist.com/?articles.view/articleNo/31193/title/Tinkering%20With%20Life (accessed March 27, 2013).

[10]Pennisi, Elizabeth. 2013. "Synthetic Genome Brings New Life to Bacterium," *Science* 328, p. 958. Online at http://www.sciencemag.org/content/328/5981/958.full.pdf (accessed March 27, 2013).

[11]As of 2009 there were approximately 50 gene synthesis companies around the world. See Maurer, Stephen, et al., 2009. "Making Commercial Biology Safer: What the Gene Synthesis Industry Has Learned About Screening Customers and Orders," Working Paper. Online at http://gspp.berkeley.edu/assets/uploads/page/Maurer_IASB_Screening.pdf (accessed May 15, 2013).

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BOX 2-2
Synthetic Biology Tools and Technology Timeline

Synthetic biology is a tool and technology-based science. Institutional, industrial, scientific, and technical developments have all contributed to the discipline's evolution as a global, networked discipline.

1941: First functional program-controlled computer (Konrad Zuse)
1953: Crick and Watson describe the double helix structure of DNA
1960: First computer-aided drafting (CAD) program (Sketchpad)
1961: Discovery of mathematical principles in gene regulation
1971: First genetically modified organism (*Escherichia coli*)
1972: First synthetic gene (yeast)
1973: Cohen, Boyer, and Berg create first genetically engineered organism (*Escherichia coli*)
1974: First U.S. patent on rDNA (Stanley Cohen and Herbert Boyer)
1975: Asilomar Conference on Recombinant DNA
Early genome sequencing techniques established
1976: First biotechnology firm founded (Genentech)
NIH guidelines for Recombinant DNA
1978: Term "bioinformatics" coined
Synthetic insulin gene inserted into *E. Coli*
1980: In Diamond v. Chakrabarty, the U.S. Supreme Court rules that "a live, human-made micro-organism is patentable subject matter."
1982: U.S. Food and Drug Administration (FDA) approves use of synthetic insulin
1983: Development of the polymerase chain reaction (PCR) DNA amplification technology
1984: First commercialized genetically modified food (Flavr Savr tomato)
1990: Human Genome Project (HGP) launched
1991: First public availability of the World Wide Web
1996: First cloned mammal (Dolly the sheep)
2000: International Human Genome Sequencing Consortium announces "working draft" of human genome
Genetic oscillators and toggle switches published
2002: Rice genome decoded
Chemical synthesis of polio virus genome
2003: First BioBrick DNA assembly standard published
Human Genome Project completed
Defense Advanced Research Projects Agency (DARPA) synthetic biology study[a]
2004: Synthetic Biology 1.0 (first international meeting on synthetic biology)
2005: First International Genetically Engineered Machines (iGEM) competition
2008: Virus attenuation achieved via synthetic genome-scale changes in codon usage
2010: First fully synthesized self-replicating genome (*Mycoplasma mycoides*)
2013: Successful engineering of digital amplifying genetic logic gates and memory systems

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[a]See Endy, Drew, 2007. "2003 Synthetic Biology Study." Online at http://dspace.mit.edu/handle/1721.1/38455, accessed June 18, 2013.

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- Relies on non-hierarchical research and commercialization networks
- Views addressing social concerns as integral to the field's progress

A Novel Approach to Studying Biology. Synthetic biology, with its focus on engineering customized living units and systems, represents a novel approach to the study of life.

Synthetic biology reverses traditional approaches to understanding the mechanisms of life. In his keynote address at the Washington, DC symposium, Michael Elowitz, Professor of Biology, Bioengineering, and Applied Physics; Bren Scholar; and Investigator, Howard Hughes Medical Institute, California Institute of Technology, described the new thinking this way: "Under routine biological approaches, one perturbs an existing system [and asks:] How does the system respond to perturbation? What components are necessary for it to work? When conducting research in synthetic biology, one can ask different questions, such as: 'What genetic circuits are sufficient to generate a particular behavior?' and, 'How can existing systems be re-wired to provide new functionality?'"

An expressed impulse in synthetic biology is to abstract or simplify—seeking, within the complexities of cells and bacteria, the minimum number of components required to achieve a desired function. This conceptual model may be a defining characteristic of the field,[12] but an ultimate goal of synthetic biology also includes the building of customized cells, organisms, and living systems.

Engineering Living Systems. Synthetic biology often uses engineering principles to design simplified biological components that perform specified functions. These approaches include:

- Abstraction (or abstraction hierarchy): a system for managing biological complexity by eliminating unnecessary details; abstraction allows researchers at various levels (and in various fields) to work with and share details about biological data without specialized knowledge
- Modularization: developing interconnecting parts that can be combined in various ways
- Standardization: devising a broad consensus on the composition of parts, devices, and systems so that they may be used reliably in any setting
- Decoupling: de-linking the requirements for design from requirements for manufacture to allow non-biologists to use biological components in various applications
- Modeling: testing the projected design and its function

The principles of abstraction, modularization, standardization, decoupling, and modeling are not new per se: they transformed the textile industry in the 18th

[12]Sheila Jasanoff, Pforzheimer Professor of Science and Technology Studies, John F. Kennedy School of Government, Harvard University.

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century with the development of the Jacquard loom,[13] shaped the Industrial Revolution,[14] and led to the transformation of the integrated circuit industry in the 20th century.

The application of engineering principles to biology offers, however, a different perspective on how to work with and use biological resources. "When we turn to biology, it tends to be [to address] a very pressing problem," Endy said. "I think that over-selects for applications and under-selects for improvements in the engineering process." By building simplified biological circuits, systems, or protocells (known as the "bottom-up" approach) while developing organisms with enhanced or novel functions (the "top-down approach"),[15] researchers are seeking to improve our capacity to both understand and engineer living systems. "Incremental improvements in our capacity to navigate the 'design, build, test' cycle at the core of engineering biology, over time, can lead to geometric improvements in our capacity to engineer living systems. We have to invest in the engineering fundamentals too, not just the immediate applications," added Endy.

One hope of synthetic biologists, said Rob Carlson, Principal, Biodesic, is that by providing renewable materials through engineered cells, synthetic biology "may radically change the way we produce many materials in the future."

Non-hierarchical Networks. In Washington, DC, Robert Wells, former Head, Biotechnology Unit, Directorate for Science, Technology, Organisation for Economic Co-operation and Development (OECD), differentiated synthetic biology from other fields, citing its tendency to develop in a horizontal, global way that takes advantage of social networking and draws an international cadre of young scientists. As Sheila Jasanoff, Pforzheimer Professor of Science and Technology Studies at Harvard's John F. Kennedy School of Government, observed in Shanghai, because of its inherent heterogeneity, synthetic biology gains coherence not from a single set goal, but rather from a conceptual focus on simplification.

Synthetic biology has also created a unique opportunity for input from outside traditional academic venues—from amateur scientists at community labs to undergraduate institutions to high schools. At the Washington, DC symposium, Meagan Lizarazo, Vice President of Operations at iGEM, and fellow panelists discussed a prominent example where such collaboration is the norm: the International Genetically Engineered Machine competition (iGEM). iGEM is a competition in which undergraduates develop biological "machines" to address real-world problems (See Box 2-3). The iGEM competition represents a new type of educational pipeline for students interested in hands-on science and en-

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[13] Lee.

[14] Richard Kitney, Professor of Biomedical Systems Engineering, Department of Bioengineering, Senior Dean and Director of the Graduate School of Engineering and Physical Science, Imperial College London.

[15] Bedau, Mark A., Emily C. Parke, Uwe Tangen, and Brigitte Hantsche-Tangen, 2009. "Social and Ethical checkpoints for bottom-up synthetic biology, or protocells," *Syst Synth Biol* 3(1-4): 65-75, December. Online at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2759431 (accessed May 16, 2013).

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gineering, Lizarazo said. Launched in 2005 by the Massachusetts Institute of Technology, iGEM became, in early 2012, an independent nonprofit endeavor. In 2012, Lizarazo reported, the iGEM competition attracted participants from 190 colleges, 40 high schools, and 210 labs in five regions—Asia, Europe and Africa, Latin America, Americas East, and Americas West.

The organizational structure of the iGEM competition—the competition and collaboration, the interactions among team members of widely differing disciplines with various levels of experience—gives students non-threatening entry into the complexities of science and engineering, said Karmella Haynes, Assistant Professor, School of Biological and Health Systems Engineering, Arizona State University. Participants in the iGEM competition applaud the mind-expanding potential of the iGEM experience for developing scientists and engineers. "We learned the importance of collaboration and integrating human practices into our research—those can be useful in our future careers," said Nikki Kapp, a graduate student at Penn State University who represented Imperial College London at iGEM as an undergraduate. "As undergraduates, we don't know clearly what isn't possible. That's conducive to innovation."

Inclusion of Social Concerns. Early on, synthetic biology researchers recognized the need to engage with government and the public about social concerns arising in conjunction with the practice of synthetic biology. This engagement is, in part, a reflection of a desire to ensure that the public understands this new technology. Researchers believe that a failure to engage with the public—as exemplified by opposition to genetically modified food in Europe—may adversely affect ongoing and future innovation.

In Shanghai, Professor Jasanoff located U.S. scientific advancements of the 20th century in the context of scale. In the United States, she observed, major technical achievements such as the moon landing or the launch of the Hubble Space Telescope were the result of large-scale national investments designed to achieve specific goals and end points. By contrast, most synthetic biologists work independently to achieve transformation at a microscopic level.

The decentralized nature of synthetic biology, in union with the revolutionary nature of the field, may demand the development of a new approach to the broad societal issues and aspects raised by advances in the field, she observed. These include the ethical, legal, and social implications (ELSI) of the technology (referred to as ELSA, or ethical, legal, and social aspects, in Europe) as well as biosecurity, biosafety, regulatory, and intellectual property concerns.[16]

[16]The synthetic biology community is beginning to address these concerns. For example, in 2009, in collaboration with a panel of stakeholders, the International Association Synthetic Biology developed a Code of Conduct for Best Practices in Gene Synthesis, focused on DNA sequence screening, customer screening, and safety in gene synthesis (see http://www.ia-sb.eu/go/synthetic-biology/synthetic-biology/code-of-conduct-for-best-practices-in-gene-synthesis, accessed May 15, 2013). That same year, the International Gene Synthesis Consortium developed a "Harmonized Screening Protocol" for gene sequencing and customer screening to protect biosecurity (see http://www.ia-sb.eu/tasks/sites/synthetic-biology/assets/File/pdf/iasb_code_of_conduct_final.pdf, accessed May 15, 2013).

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Jasanoff noted that a multi-country comparison of ELSI concerns revealed wide variations and suggest an urgent need to include the public in discussions of ELSI issues. She suggested that, given the public's increasing interest in science and technology and its willingness (and, through the Internet, its ability) to engage in or collaborate in research and interface with technology, synthetic biology might, in fact, be considered a "post-ELSI science."

Realizing the potential of synthetic biology depends on overcoming significant challenges. These include not only technological challenges but also mitigating potential biosafety and biosecurity dangers, attending to social, legal, and political imperatives, and addressing intellectual property issues. These challenges are discussed in detail in Chapter 4.

BOX 2-3
The International Genetically Engineered Machine (iGEM) Competition

iGEM has captivated a generation of young scientists and engineers from around the world. Many of those involved believe that synthetic biology offers a unique opportunity to address world needs related to food, disease, energy, and material.

Each year, iGEM participants undertake a summer-long project wherein a multidisciplinary team designs biological solutions to real-world problems. By using parts from the Registry of Standard Biological Parts (or by creating new parts), teams engineer living systems designed to carry out specific functions. Participants assemble their own teams, raise funds for their projects, and solicit advice from experts across disciplines. In 2012, projects included:

- Generating a bacterial "detect and alert" system to help defend crop plantations against pathogens (Universidad de los Andes, Bogotá, Colombia—Latin America Grand Prize Winner)
- Engineering a bacillus bacterium to produce blue or yellow pigments in meat that has spoiled (University of Groningen, Holland—Europe Grand Prize and World Championship Winner)
- Developing a low-cost biosensor to indicate the presence of pathogenic bacteria in water (Arizona State University—Best Human Practices Advance, Americas West)
- Building a protein-based light sensor (Chinese University of Hong Kong—Championship Competition)

Teams post the stories of their research on individual "wikis" on the iGEM website.

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3

Strategies for Advancing Synthetic Biology

Despite the challenges that lie ahead, both governments and non-governmental organizations take the promise of synthetic biology seriously. During the two-year period when the three symposia were taking place, the governments of the United Kingdom and China made investments in synthetic biology a priority. Both nations advanced formal strategies and benchmarks for this purpose. Additionally, in Europe, the European Commission (EC)[1] and the Organisation for Economic Co-operation and Development (OECD) have taken an active interest in the field. During the course of the symposia series, representatives from China, the United Kingdom, the United States, and the OECD discussed national plans, as well as planned and ongoing international collaborations, for stimulating progress in synthetic biology.

China

In Washington, DC, Xian-en Zhang, Director General, Basic Research Department, China Ministry of Science and Technology, stated that the People's Republic of China is seeking to position itself as a global leader in synthetic biology. This effort, he said, is motivated by the country's urgent need to address public health, nutrition, and resource needs, as well as a national strategy to promote progress in science and technology. Beginning in 1978, with reforms launched by Deng Xiaoping, China has pursued an aggressive strategy of industrialization and technological development. Investments in bioscience and bio-

[1] As of early 2012, the EC's Sixth Framework Programme for Research, Technologic Development and Demonstration had funded 18 synthetic biology projects totaling over €24 million (Pei, Lei, Sibylle Gaisser, and Markus Schmidt, 2012. "Synthetic biology in the view of European public funding organisations," *Public Understa Sci.* February; 21(2): 149-162. Online at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3311122, accessed May 15, 2013).

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technology are part of this strategy. Zhang noted that since the 1990s, Chinese leaders have prioritized economic development through science and education.

China's aggressive S&T policies have led to significant advances on many scientific fronts, including synthetic biology. China now contributes about 10 percent (some 400 papers) of the annual papers published on synthetic biology.[2] These publications are ranked seventh globally in terms of citations. China has several databanks related to synthetic biology. These include a database of genes that have been identified as essential for an organism's survival and a separate database on prokaryotic and eukaryotic genes.

In China, several organizations support research in synthetic biology, Zhang said. These include the Chinese Academy of Science (CAS) (the major science policy advisor to the central government), the Chinese Academy of Engineering, the national and local offices of the China Academy of Machinery Science and Technology (CAM), and medical universities. Funding for synthetic biology research comes from many sources, including the National Natural Science Foundation of China, state-level labs, and the CAS Knowledge Innovation Program.[3] Expenditure on research now totals 800 billion Yuan per year (about $U.S. 100 billion), with 260 million Yuan allocated for synthetic biology.[4] This total research budget accounts for 1.8 percent of China's gross domestic product or GDP (though this is still less than research funding in the OECD, which accounts for 2 percent of GDP, and in the United States, which accounts for 2.7 percent of GDP).[5]

Despite the many technical challenges facing the field, China sees synthetic biology as ushering in a new era of economic growth powered by technology. According to Dr. Zhang, China has drafted a strategic roadmap that specifies desired achievements in technology, industrial applications, medicine, and agriculture in five, 10, and 20 year periods (See Box 3-1). In the case of synthetic biology, the roadmap includes goals related to the availability of comprehensive databases for synthetic parts, a timeframe for the commercial application of engineered parts, and a timeframe for clinical application of devices and systems.

Guo-ping Zhao, Director, Laboratory of Synthetic Biology, Institute of Plant Physiology and Ecology, Shanghai Institutes for Biological Sciences, noted that, besides seeking technological advances, future tasks for China include addressing legal, ethical and security questions such as ensuring that the benefits of synthetic biology will be distributed equitably. Dr. Zhao noted that intellectual property, ownership, and sharing arrangements are another concern. Dr. Qiu,

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[2] Xian-en Zhang, Director General, Basic Research Department, China Ministry of Science and Technology.

[3] China is also conducting multi-country research, such as a bilateral project on risk assessment and biosafety needs for synthetic biology in Austria and China (see http://www.markusschmidt.eu/fwf/Home.html, accessed May 15, 2013).

[4] Zhang.

[5] Zhang.

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BOX 3-1
Strategic Targets for Synthetic Biology in China

5 years:

- Database of standardized parts and computational competency for designing parts and devices
- Module design and production of chemicals and biomaterials
- Validated design of devices to increase plant tolerance of drought and salinity

10 years:

- Expanded database of standardized parts and devices and computational competency for design of bio-systems
- Commercial production of selected chemicals and biomaterials
- Validated design of synthetic devices for nitrogen fixation

20 years:

- Integrated platforms for design, modeling, and validation of bio-systems
- Commercial production of a range of natural compounds, drugs, chemicals, and biofuels
- Clinical application of devices and bio-systems for detecting, controlling, or treating major diseases
- Creation of artificial microbial life

Emeritus Professor of the Institute of Philosophy and Honorary Director, Center for Applied Ethics, Chinese Academy of Social Sciences, added that protecting the health and safety of those who work in the discipline is also a priority, and Dr. Zhao stated that China seeks to work with international collaborators to develop approaches to all these issues.

United Kingdom

In Washington, DC, John Perkins, Chief Scientific Adviser, Business & Skills Group, Department for Business, Innovation & Skills, U.K. Government, stated that the U.K. government is keen to assume a leadership role in synthetic biology. According to Perkins, the U.K. government views synthetic biology as a potentially revolutionary platform with very promising commercial possibilities. The U.K. government is actively seeking to build a thriving synthetic biology community with strong links to industry. Further, Perkins stated that the government has made a commitment to establish a Synthetic Biology Leadership Council[6] co-chaired by a Minister and a senior industry figure. This council

[6]The Synthetic Biology Leadership Council (SBLC) was established in December 2012 under the joint chairmanship of the Right Honorable David Willets, MP and Lionel

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will serve as the major vehicle of "vertical policies" designed to stimulate discussion and partnership among various sectors.

The Cabinet of the United Kingdom sets strategic direction. The Research Councils and the Technological Strategy Board (TSB) provide independent evaluations of scientific issues. The U.K.'s TSB, a public entity focused on increasing innovation in technological fields with commercial potential, has included synthetic biology on its short list of the top four emerging technologies and has estimated that the field will generate a market worth up to $20 billion by 2020. This projection, Perkins said, caused an independent, industry-led group to develop a roadmap for making the U.K. a leader in synthetic biology. The roadmap, which presents five recommendations, emphasizes as a necessary first step building a strong and multifaceted community of stakeholders.[7]

The United Kingdom intends to make investments in synthetic biology in the following areas:

- Public funding of £50 million, including up to £6.5 million to encourage investment by industry
- Funding of £6 million from the Engineering and Physical Science Research Council to encourage universities to investigate the commercialization of new products
- Integration of funding for studies in both research and development and related ethical, legal, and social implications (ESLI)[8]
- Support from the Biotechnology and Biological Science Research Council for 16 agencies for five transnational research projects
- Earmarking £100 million to sequence 100,000 whole genomes of patients of the National Health Service over the next three to five years.

According to Perkins, the U.K. government's next step will be to form a minister-led leadership council that will manage the direction of ongoing research.

Perkins noted that, from the U.K. perspective, major challenges are the management of the complexity and expectations of synthetic biology, the translation of innovations in synthetic biology from "lab to life," and the need for continued public engagement. A failure to engage the public in discussion of synthetic biology, he said will hamper the field's future development.

In Shanghai, Paul Gemmill, Director of Communications and Information Management, U.K. Biology and Biotechnology Research Council, emphasized

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Clarke. The Council's purpose is to coordinate interventions taken to implement the U.K.'s synthetic biology roadmap (see https://connect.innovateuk.org/web/synthetic-biology-special-interest-group/synbio-leadership-council, accessed May 14, 2013).

[7]UK Synthetic Biology Strategy Group, 2012. *A Synthetic Biology Roadmap for the UK*. Swindon, UK: Technology Strategy Board (TSB). Online at http://www.rcuk.ac.uk/documents/publications/SyntheticBiologyRoadmap.pdf, accessed March 27, 2013.

[8]Pei, Lei, Sybille Gaisser, and Markus Schmidt, 2012. "Synthetic biology in the view of European public funding organisations," *Public Underst Sci* 21(2): 149-162, February.

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the seriousness of the U.K.'s effort to engage the public by stating that doing so is an integral part of the country's plan for synthetic biology. "We have had problems in the past explaining novel technologies," he said. "The public thought that their questions were not properly answered."

In 2009, the U.K. government initiated a series of public dialogues on synthetic biology. During these dialogues, a diverse group of citizens met with scientists to explore questions regarding synthetic biology and to discuss mechanisms for oversight and governance of the field. Gemmill said that these public dialogues revealed that there is a high level of support for synthetic biology by the British public. Communities see opportunities to use synthetic biology to address numerous global problems, he said, but they also express concerns about where the technology will lead, how quickly it will proceed, and what the long-term consequences might be.

The report on the dialogues addresses three broad areas:

- Questions for scientists on the purpose and benefits of synthetic biology
- Recommendations for regulation—including a recommendation against self-regulation, a requirement that laws stay current with changes in science, and an emphasis on alignment with international regulations
- Recommended applications including medicine (approved by 80 percent of those polled), energy (78 percent), environment and bioremediation (58 percent), and food (55 percent).

The last recommendation clearly indicates the public's priorities, Gemmill said. These align, he observed, with the priorities of scientists. Gemmill stated that the next step will be to integrate the findings from the public dialogues into discussions on future topics. Gemmill concluded his remarks by observing that, "These are the people who one day might, or might not, be buying your product."

United States

The United States has been an early leader in synthetic biology. The American synthetic biology community plays a vital role in research and in the development of multi-country partnerships. The U.S. government has invested about $140 million annually in synthetic biology research (See Box 3-2). At the federal level, however, the U.S. government has not developed an overarching funding or governance plan for the field. Though synthetic biology is mentioned in the current administration's National BioEconomy Blueprint, specific initiatives for the field are not defined.[9]

[9]The White House, 2012. *National Bioeconomy Blueprint.* April. Online at http://www.whitehouse.gov/sites/default/files/microsites/ostp/national_bioeconomy_blueprint_april_2012.pdf.

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BOX 3-2
Publicly Funded Synthetic Biology Research in the United States

The U.S. government supports research in synthetic biology through a variety of national organizations and institutions. For example, the National Science Foundation (NSF) has invested about $72 million in research associated with synthetic biology. A 2008 event, the Ideas Factory Sandpit, brought researchers and mentors together to investigate major questions in the field and develop solutions. NSF also supports the Synthetic Biology Engineering Research Center (SynBERC), a multi-institution effort to develop foundational principles and technologies to help synthetic biology advance.

Support from the Department of Defense is aimed at speeding production capacity in synthetic biology. The Department's Defense Advanced Research Project Agency's (DARPA) Microsystems Technology Office's Living Foundries program, launched in 2011, seeks to advance synthetic biology as a manufacturing platform.

The Department of Energy has launched several initiatives around synthetic biology, including several focused on the mechanisms underlying biofuel production.[a]

[a]Woodrow Wilson International Center for Scholars, Synthetic Biology Project, 2012. "Recommendation 2: Support for Promising Research." Online at http://www.synbioproject.org/scorecard/recommendations/research/support-for-promising-research, accessed March 27, 2013.

In 2010, after the J. Craig Venter Institute publicized the creation of the first cell containing a complete, self-replicating synthetic genome, President Obama directed the Presidential Commission for the Study of Bioethical Issues to review the field of synthetic biology and develop ethical guidelines aimed at providing maximum public benefits while minimizing risks. In Shanghai, Anita L. Allen, Henry R. Silverman Professor of Law and Professor of Philosophy, University of Pennsylvania Law School and a member of the Presidents' Commission, reviewed the Commission's findings and noted that the report did not find a need for new regulation or regulatory mechanisms at this time. The Commission did, however, offer 18 recommendations based on five ethical principles: 1) public beneficence, 2) responsible stewardship, 3) intellectual freedom and responsibility, 4) democratic deliberation, and 5) justice and fairness.[10]

At the Washington, DC symposium, Jetta Wong, a staff member of the United States House of Representatives' Committee on Science, Space, and Technology, noted that Congress has established a bipartisan caucus on synthetic biology but has not developed a strategic plan for the field. "Right now, Congress is focused on jobs, the economy, and the budget deficit. Synthetic biology is not getting much attention," she said.

[10]A follow-up report that was to provide recommendations for agency-specific actions has not been released as of June 2013.

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Wong observed that limitations in the public's understanding of or reaction to scientific developments are an obstacle that may affect the advance of technology-based projects in developing areas such as biofuel production and genetically modified food. She observed that government infrastructure, including the organization of Congressional committees and the mandates and focus areas of government institutions, can also create a "stovepipe" effect. Advancing synthetic biology will require mechanisms that enable collaboration among these different entities, Wong said. An additional challenge is that, in the American political system, action is focused on immediate concerns and expressed public interests. Without strong input from the public or interested groups, issues tend not to advance. Wong noted, however, that timely input by citizens and interest groups can influence legislation. This was the case with the National Research Council publication, *A New Biology for the 21st Century*. According to Wong, as a result of the report, the House of Representatives included provisions on synthetic biology in the recently passed Manufacturing Competitiveness Act.

According to Wong, funding for science—considered a vital element of economic development by the present administration and the Congress—is relatively strong in the United States. In the case of synthetic biology, the U.S. National Science Foundation contributed $16 million to the Synthetic Biology Engineering Research Center (SynBERC) based at University of California, Berkeley. A joint effort by the U.S. Department of Energy and British Petroleum (BP) created the $500 million Energy Biosciences Institute, where synthetic biology will play a significant role. Private philanthropy is also contributing to synthetic biology: the Bill & Melinda Gates Foundation have invested $43 million into medical applications of synthetic biology, for example.

Organisation for Economic Co-operation and Development

In Washington, DC, Gerardo Jiménez-Sanchez, Chairman, Working Party on Biotechnology, OECD and Chair, HUGO Committee on Genomics and the Bioeconomy, National Academy of Medicine, Mexico, reported that the OECD views genomics, biotechnology, and sustainable production of biomass as priority development areas for the next 30 years.[11,12] Jiménez-Sanchez noted that interest in the potential of emerging technologies (and in their potential effect on social and economic well-being) has risen among member countries. He stated that half of the OECD's 34 countries are conducting initiatives on synthetic biology. Responding to this interest, the OECD has participated or collaborated in

[11]OECD, 2009. *The Bioeconomy to 2030: Designing a Policy Agenda.* CITY? OECD International Futures Project. Online at http://www.oecd.org/futures/long-termtechnologicalsocietalchallenges/42837897.pdf, accessed March 27, 2013.

[12]European Scientific Advisory Council (EASAC), 2010. "Realising European Potential in Synthetic Biology: Scientific Opportunities and Good Governance," EASAC *Policy Report* 13. Halle, Germany: German Academy of Sciences Leopoldina.

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a series of events designed to explore synthetic biology's potential as a driver of economic growth.

Jiménez-Sanchez stated that the OECD has strategic alliances with other international agencies conducting activities related to synthetic biology. Events and publications resulting from these collaborations include:

- *Opportunities and Challenges in the Emerging Field of Synthetic Biology: A Symposium* (in collaboration with the U.S. National Academies and The Royal Society), 2009 and the summary report, *Symposium on Opportunities and Challenges in the Emerging Field of Synthetic Biology: Synthesis Report*, 2010 (Royal Society and OECD).
- Workshop on genomics and the bioeconomy, May 2010, Montpelier, France. Participants reached consensus on the need for guidelines on international cooperation, innovative intellectual property management, and ways of measuring the impact of genomics.
- *Delivering Economic Value from Synthetic Biology,* a summit in Sydney, Australia, in March 2012.

Jiménez-Sanchez also reported that the OECD has also engaged in discussions with the international collaborative project SynBio[13] and the U.S.-based BioBricks Foundation.[14] As a result of these discussions, the OECD has identified three areas where it might focus future attention: 1) needed infrastructure; 2) approaches for IP access and sharing; and 3) standards and interoperability.[15]

[13]SynBio is a collaborative project to create new biologically based pharmaceutical products. It was launched in 2011 with participation from companies in Russia, the U.K., and Germany.

[14]The BioBricks Foundation is a nonprofit organization that seeks to provide open-source biological parts—DNA sequences with specific structures and functions that can be introduced into living cells to create new functions.

[15]OECD and Royal Society, 2010. *Opportunities and Challenges in the Emerging Field of Synthetic Biology: Synthesis Report.* Paris: OECD and Royal Society.

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4

Opportunities and Challenges Emerging via a Networked World

Research in synthetic biology has the capacity to revolutionize our understanding of biological processes and genetics, suggesting a human potential that builds on and beyond evolutionary processes. The environment in which synthetic biologists hope to operate—a decentralized, networked ecosystem unconstrained by the boundaries of traditional research institutions—may be the leading edge of this transformation. Synthetic biology, in the words of Richard Johnson, CEO of GlobalHelix LLC, represents the "new normal" of global research—networked, decentralized, collaborative, and multidisciplinary. The novelty and promise of this environment are cause for both excitement and caution.

Next industry wave. Industry has made significant investments in synthetic biology, with the view that the field, coupled with continuing advances in genetics and systems biology, has the potential to revolutionize the development of products and substances through the application of biologically-based manufacturing. Synthetic biology's emergence parallels trends in advanced manufacturing in which operations are becoming increasingly global and networked-based.[1] With this movement, companies are beginning to commercialize products developed through synthetic biology (See Box 4-1).

By the mid-2000s there were already some 3,000 biotechnology companies globally[2] and gene synthesis companies operating in five continents[3] and produc-

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[1]Shipp, Stephanie S. et al., 2012. *Emerging Global Trends in Advanced Manufacturing*. Report by the Institute for Defense Analyses, Alexandria VA. March.

[2]Finnegan, Stephanie and Karl Pinto, 2006. *"Globalisation of biotech offshoring*," Pharmabiz.com. May 16. Online at http://www.goodwinbio.com/web/PharmabizDec06.pdf, accessed December 5, 2012

[3]Garfinkel, Michele S., Drew Endy, Gerald L. Epstein, and Robert M. Friedman, 2007. *Synthetic Genomics: Options for Governance.* Rockville, MD: J. Craig Venter Institute, Center for Strategic and International Studies, and Massachusetts Institute of Technology.

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ing some 50,000 genes annually.[4] Biological products have become economically important. In 2010, it is estimated that the bio- economy in the United States (genetically modified crops, biological products, and industrial biotechnology) generated more than $300 billion in revenue (the equivalent of over 2 percent of

BOX 4-1
The Commercialization of Synthetic Biology: Amryis, Inc.

The commercialization of synthetic biology products is in its very early stages, but both investors and entrepreneurs are exploring opportunities. Amyris, Inc. is using synthetic biology to produce products on a commercial scale. In Shanghai, Lishan Zhao, Head of Enzymology and Protein Engineering, Amyris, Inc., described his company's work with yeast cells engineered for novel functions. One application is to produce a semi-synthetic version of artemisinin, a chemical traditionally derived from the Chinese wormwood plant. Artemisinin is used in anti-malarial drugs, but the chemical is difficult and expensive to extract. By engineering yeast to produce artemisinin—a process developed by Amyris' co-founder, Jay Keasling—Amyris worked to provide a steady, non-seasonal, and affordable supply of artemisinin for use in developing countries. In partnership with the nonprofit organization OneWorldHealth and with a $42.6 million grant from the Bill and Melinda Gates Foundation, Amyris developed the ability to produce artemisinin at a scale suitable for global distribution. Production was managed by the French pharmaceutical Sanofi. Sanofi announced in April 2013 that it has begun large-scale commercialization of artemisinin using a process that is based on the process developed at Amyris. The drug will be sold at cost.[a]

Amyris has also explored yeast-based production of farnesene, an aromatic oil used in fuels, cosmetics, pharmaceuticals, and fragrances. Production, however, has been inadequate to justify a planned venture into biofuels.[b] Nevertheless, Amyris views synthetic biology as viable technology that offers solutions to global challenges. Recently, for example, the company announced a multi-year agreement with the global company International Flavors & Frangrances, Inc. to develop renewable fragrance ingredients using a synthetic biology platform.[c] "I strongly believe that if we all work together, we can pave the road for synthetic biology to play an important role in replacing petroleum one day," Zhao said.

[a]UC Berkeley News Center, 2013. "Launch of Antimalarial Drug a Triumph for UC Berkeley, Synthetic Biology," April 11. Online at http://newscenter.berkeley.edu/2013/04/11/launch-of-antimalarial-drug-a-triumph-for-uc-berkeley-synthetic-biology, accessed May 17, 2013.

[b]Bullis, Kevin, 2012. "Amyris Gives Up Making Biofuels: Update," *MIT Technology Review.* February 10. Online at http://www.technologyreview.com/view/426866/amyris-gives-up-making-biofuels-update, accessed March 27, 2013.

[c]CNBC, 2013. "BRIEF-IFF, Amyris to jointly develop ingredients for flavors, fragrances market," Business news, April 29. Online at http://www.cnbc.com/id/1006861 85, accessed May 17, 2012.

[4]Maurer, Stephen M. et al., 2009, "*Making Commercial Biology Safer: What the Gene Synthesis Industry Has Learned About Screening Customers and Orders," Working Paper*, online at http://gspp.berkeley.edu/iths/Maurer_IASB_Screening.pdf.

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gross domestic product).[5] Recently, BBC Research LLC, a market research company, estimated that the global value of the synthetic biology marketplace (including supporting technologies, biological parts, and the products developed using these parts) was $1.6 billion in 2011 and projected that the value would rise to $10.8 billion in 2016.[6]

Successes with engineered biological systems promise a wide range of applications. For example, a trial of engineered male mosquitoes—described at the London symposium by Luke Alphey, Chief Scientist, Oxitec—resulted in a 90 percent reduction in the population of dengue-carrying mosquitoes in the 16-hectare test area.[7] Alphey's team has suggested using this approach—known as the sterile insect technique—for control of agricultural pests such as moths.[8]

Industry is continuing to make investments in promising engineered bio-products. Monsanto, for example, recently announced the acquisition of certain microbes developed by Agradis—a synthetic biology company launched by Synthetic Genomics Inc. (SGI) and the Mexican company Plenus, SA. Monsanto also is collaborating with SGI in research on plant-microbe relationships. Other industrial ventures include investments in plant-based production of rubber, bio-based acrylics, "green" chemicals made from biological waste, vitamin production, and biologically based diesel production using renewable carbohydrates.[9]

In Washington, DC, Darlene Solomon, Senior Vice President and Chief Technology Officer, Agilent Technologies, a global firm specializing in measurement, described Agilent's analysis of market trends since 1940—including the growth of measurement technology, electronics, chemical analysis, communication and the Internet, and personalized medicine. Solomon projected that the growth of the market for the products of synthetic biology will outstrip growth in all of the other categories. She described synthetic biology as "the next wave," and noted that biologically-based manufacturing will likely transform the production of all types of products by replacing products made with traditional materials with products made of sustainable materials. This will lead, she concluded, to a more sustainable global economy.

[5]Carlson, Rob, 2011. "Biodesic Bioeconomy Update. Document 20110811_01. Biodesic. Online at http://www.biodesic.com/library/Biodesic_2011_Bioeconomy_Update.pdf, accessed December 5, 2012.

[6]BCC Research, 2011. *Synthetic Biology: Emerging Global Markets*. Market report number BIO066B. Online at http://www.bccresearch.com/pressroom/report/code/BIO066B, accessed May 15, 2013.

[7]Harris, Angela F. et al., 2011. "Field Performance of Engineered Male Mosquitoes," *Nature Biotechnology* 29: 1034-1037.

[8]Jin, Li et al., 2013. "Engineered Female-Specific Lethality for Control of Pest Lepidoptera," ACS Synth. Biol, January 8. Online at http://pubs.acs.org/doi/abs/10.1021/sb300123m, accessed March 27, 2013.

[9]Biotechnology Industry Organization (no date), "Current Uses of Synthetic Biology for Chemicals and Pharmaceuticals." Online at http://www.bio.org/articles/current-uses-synthetic-biology, accessed March 27, 2013.

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Engagement by Law Enforcement. The Federal Bureau of Investigation (FBI) has been proactive in its engagement with the synthetic biology policy and research communities. Edward You, Supervisory Special Agent in the FBI's Weapons of Mass Destruction, Biological Countermeasures Unit, described the Bureau's involvement with synthetic biology in the context of the FBI's overall effort to prevent terrorism and ensure the safety of those working in the field. The FBI, he said, maintains a dialogue with scientists, students, and members of the DIY community for the purposes of keeping abreast of current developments and educating the synthetic biologists on the broader security picture. "Many people in the life sciences," he observed, "have never heard of the Biological Weapons Convention. As sponsors of iGEM," You said, "we've had discussions about this—we need to educate people on these issues" (See Box 4-2).

Challenges for Synthetic Biology

Unlocking the potential of synthetic biology depends on the development of new interfaces for worldwide collaboration and, most likely, new types of creative commons that allow for flexibility in the regulation and ownership of scientific and technological innovations.

Technical Challenges

At present, only the leading edge of synthetic biology is visible, and the technical challenges are enormous. Synthetic biologists have yet to develop a broad understanding of the scientific foundations and engineering processes needed to sustain rapid increases in the capacity to engineer biology.[10] A chief challenge is that, compared to other engineered systems, e.g., automobiles and computers, biological systems are infinitely more complex and do not behave in a linearly predictable way.[11] Working at the molecular and cellular level is very difficult. Moving from the cellular to the systems level—producing engineered tissues, for example—increases complexity by orders of magnitude.

The problem, Dr. Elowitz observed, is that even if reliable biological parts were available, scientists lack the knowledge to use them effectively. "Biological functions," he noted, "are implemented by genetic circuits of interacting genes and proteins. But the circuits in question are often embedded in other complex circuits. We can't see the core design. We only understand a portion of what mammal cells are designed to do."

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[10]Drew Endy, Assistant Professor, Bioengineering, Stanford University and President, The BioBricks Foundation.

[11]Marc Salit, Research Chemist, National Institute of Standards and Technology.

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BOX 4-2
Cooperative Arrangements for Discussions about Benefits and Risks

A continuous discussion about biosafety, biosecurity, and risk mitigation is critical to the development of synthetic biology. In the United States, the FBI recently began discussions with amateur synthetic biologists on topics ranging from mitigation of biological risks to the broader topic of ensuring responsible scientific innovation. The Bureau holds workshops with the DIY community and has routinely been a sponsor of iGEM. The FBI presence at iGEM has a dual purpose; to discuss security issues with iGEM participants and to allow security agencies to keep pace with rapid advances in the field.

> It starts with a fundamental biological question—how many genes do you need to have a functioning living cell? It's a simple question about an important biological problem, and people will continue to work on it without worrying about whether you can use it to make biofuels.
>
> Peter Leadlay,
> Cambridge University

Elowitz hopes that by asking new questions and using the cell-building process as a means of understanding cell processes, the engineering approach to biology will provide new insights into the fundamentals of genetic design.

Dr. Solomon reminded symposia participants that many apparently ubiquitous technologies took years to reach maturity. In the particular case of synthetic biology, she said, both the development of large-scale applications and the market penetration of these applications will take decades (See Box 4-3). She noted, however, that advances in synthetic biology will likely be accelerated by the parallel growth of related technologies, such as DNA sequencing and computing. In the interim, she said, synthetic biology (as is the case with other emerging technologies) must necessarily move forward incrementally.

Parts and Applications. An immediate challenge for synthetic biology is the development of a large portfolio of standardized, modular biological parts and tools that behave predictably and may be used in a wide range of applications. Though thousands of biological parts have been cataloged—over 10,000 in the Registry of Standard Biological Parts,[12] for example—reproducible, reliable parts are still not widely available.

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[12]This searchable registry is the best-known of a growing registry of biological parts. It contains some 2,000 "BioBrick," parts, devices, and systems. The availability of these biological parts eliminates the need to develop each biological part separately, resulting in significant time savings. In standard biology, for example, it might take a month to assemble a given biological part. Using parts from a registry, a synthetic biologist can assemble 20 parts over the same period. See http://partsregistry.org. The parts in partsregistry.org were moved to parts.igem.org in May 2013.

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BOX 4-3
What Can We Expect from Synthetic Biology?

Participants in the symposia—while acknowledging the difficulty of prediction in synthetic biology—suggested possible short- and long-term developments in the field.

In 5 years?

- Multiple global intercommunicating synthetic biology research platforms, including public-benefit facilitities

In 10 years?

- $20 billion in synthetic biology products
- Cells routinely engineered to produce desired bulk and fine chemicals

In 20 or 30 years?

- Rationally engineered multi-cellular tissues or organs
- Widely deployed cellular computing systems
- Novel biological manufacturing processes for non-biological products

The first tools and applications of synthetic biology are being developed at the molecular and cellular level. The "wish list" for synthetic biology is long, including not just interchangeable biological parts and systems, but also customized cellular functions and designed bacteria and other organisms that can be used to speed chemical production—in, for example, for industrial processes.

Multi-cellular development, tissue engineering, and industrial applications lie in the future, but will inevitably depend upon investments made now.[13] While the ultimate products of synthetic biology are still unknowable, the immediate utility of synthetic biology—designing and constructing biological parts to increase our understanding of fundamental biological processes—is already becoming manifest. At this moment, Dr. Endy observed, the immediate benefits of synthetic biology research include a greater understanding of how living organisms work.

Inter-operability. Richard Kitney, Professor of Biomedical Systems Engineering and Senior Dean and Director of the Graduate School of Engineering and Physical Science, Imperial College London, stated that a key to the success of synthetic biology will be the development of standardized biological parts that can be reliably combined as modules and adapted as necessary. To become universally accepted and used, every element of designed parts and systems, databases, measurement units, and scalable systems must be compatible, and compatibility must extend across scales and levels—from molecular- to tissue-level, from lab to lab, from one operating system to another, and across regions

[13]Darlene Solomon, Senior Vice President and Chief Technology Officer, Agilent Technologies.

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and countries. At present, Kitney noted, the modularity of biological parts is considerably limited, in part because of the complex interactions that occur among biological parts.

Kitney stressed the need to increase understanding of how biosynthetic pathways function and to find new ways to test and control the interactions of synthesized biological material. Karmella Haynes suggested that a first step to achieving this goal could be a requirement that a rigorous, standardized characterization accompany any biological part entered in a registry. In addition to a common language, Haynes continued, the success of the field will depend on standardized descriptive protocols. She suggested, for example, that each description for a biological part listed in a registry or database should include a common set of information.

Solomon commented that historically, timing the development of standards has been a balancing act for developing technologies—whether to stay open in terms of standards, because the knowledge base is still developing, or to develop convergent standards that improve efficiency. Marc Salit, Research Chemist, National Institute of Standards and Technology, reminded participants that existing standards institutes can serve as a resource and provide methodologies for the development of interoperable modular parts. A possible place to begin, he added, would be in areas with the potential for commercialization.

Measurement. The accurate measure of systems performance is an immediate and pressing challenge in synthetic biology. In Washington, DC, Peter Carr, Senior Researcher, Massachusetts Institute of Technology Lincoln Laboratory, noted that reliable measurement standards are a critical factor in a biologist's ability to replicate biological parts. The biology community, he said, is still learning to think like engineers, for whom measurement of systems performance is standard. Measurements of the performance of the synthetic part or system and of the individual parts that contribute to the system's performance are required. It would be useful, Carr noted, to create cells and sensors that perform logical operations as well as those that can report back on the performance of the operation. The ability to receive feedback from a system is crucial, Carr observed, especially in the context of living cells, given their range of complexity.

Carr's co-panelists agreed that it is essential to have an infrastructure capable of supporting multiple types of metrics including:

- The number of parts, their designs, their construction, and the extent of their utilization
- The actions and results of tools used for computing, scanning, and communication
- The interconnective capacity of biological parts across scales and across national borders

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Reshma Shetty, Co-founder, Ginkgo BioWorks, encouraged participants to take advantage of measurement improvements currently in use in gene sequencing and mass spectrometry. She also suggested several measurement priorities: acquiring measurements of all engineered cell strains; focusing on 100 important cell proteins; designing a "stress test" chassis explicitly for measurement; and redesigning cells for measurement.

In the future, global acceptance of the units of measure will be as vital as the measurements themselves. François Képès, Research Director, Centre Nacionale de Recherche Scientifique (National Center for Scientific Research), noted the importance of developing standardization, akin to the universality of the chemical formula for water, to ensure that global collaboration flourishes.

Cost Control for Scale-up. Since the early days of genome sequencing, DNA sequencing costs have fallen dramatically. The sequencing of a genome can now be completed within two weeks at a cost of less than $10,000. The project to sequence the human genome, by contrast, took 13 years and cost $27 billion.[14] These decreases in time and cost coupled with early successes in the production of commercially important chemicals (such as biofuels, agricultural products, and medicines) fueled industry investment in synthetic biology.

However, cost-effective production of industrial chemicals requires engineering of highly efficient microbial strains.[15] The development of a viable product containing synthetic parts, however, remains a "herculean" effort, said Endy, who observed that it cost $25 million to genetically engineer *E. coli* and yeast to produce the chemical precursor to the antimalarial drug artemisinin.

At this early stage of its development, synthetic biology generally has a modestly scaled production capability and a decentralized structure with developments taking place in multiple locations, Solomon said. For fields such as specialty chemicals, pharmaceuticals, and agriculture, or for fuel production in developing economies, the current scale is adequate, she said. In the case of renewable energy in more mature economies, however, large-scale production may require government subsidies. Professor Kitney suggested that the cost problem may be solved as biological parts proliferate and become more refined.

Tools and Software. Improved data-gathering tools, software, and hardware are as important to the development of synthetic biology as improvement in the modularity of biological parts—especially if the ultimate object is industrialization.[16] A number of labs and researchers have developed online tools for use in developing and working with synthetic biology products. These include DNA

[14]The Human Genome Project, completed in 2003, was a 13-year collaborative project coordinated by the U.S. Department of Energy and the National Institutes of Health, with contributions from the U.K.'s Wellcome Trust as well as China, France, Germany, Japan, and others. The project's goals included identifying and storing information on all the genes in human DNA. Analysis of the data is continuing. See http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml, accessed March 13, 2013.

[15]Lishan Zhao, Head of Enzymology and Protein Engineering, Amyris, Inc.

[16]Kitney.

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assembly programs, applications for modeling protein structures, and biological parts registries.[17] However, the growth of synthetic biology is inhibited by a lack of field specific computational tools, e.g., computer-assisted design and modeling tools[18] as well as automated processes that can reduce the cost of synthesizing biological parts.[19] There is also a need for software that allows communication among multiple complex datasets,[20] and for linked software/hardware systems that can feed information back into biological models.[21] Other enabling technologies include faster, cheaper DNA sequencing technologies, improved software for designing and simulating biological systems and circuits, and improved measurement technologies.[22]

Regulatory Challenges

> It isn't just that the future of synthetic biology is uncertain—there's no way we can know the future. So regulatory regimes must be open, adaptive, and dynamic.
>
> Nikolas Rose, Professor of Sociology and Head of the Department of Social Science, Health and Medicine, King's College, London

Because the boundaries of synthetic biology are so fluid, the field may not fit neatly within existing regulatory frameworks. In the United States, under the current regulatory framework for biotechnology, the Department of Agriculture, Food and Drug Administration, and Environmental Protection Agency are responsible for oversight of genetically modified animals, plants, and microbes. Recently, policymakers have begun to focus on the regulation of synthetic biology and are considering whether and how current regulations apply to the products of synthetic biology. In the U.K. and China, legislators have developed strategic plans designed to advance synthetic biology.

Recognizing that science tends to move forward much faster than policy formation, early attention to issues associated with the governance and regulation of synthetic biology seem to be particularly appropriate. Patrick Boyle, Postdoctoral Fellow, Wyss Institute for Biologically Inspired Engineering, suggested that it would be best for synthetic biologists to continue their efforts to engage with regulatory bodies now, before the number of products becomes overwhelming.[23]

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[17]OpenWetWare, a project to promote information-sharing among researchers in biology and biological engineering. Online at http://openwetware.org/wiki/Synthetic_Biology:Tools, accessed Marcy 27, 2013.

[18]Cesar Rodriguez, Senior Research Scientist, Autodesk.

[19]Todd Peterson, Vice President, Synthetic Biology R&D, Life Technologies Corporation.

[20]Peterson.

[21]Reshma Shetty, Co-founder, Ginkgo Bioworks.

[22]Syntheticbiology.org. Online at http://syntheticbiology.org/FAQ.html, accessed March 27, 2013.

[23]There are numerous examples of engagement between those representing the interests of the synthetic biology community and regulatory bodies. The U.S. Department of

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Boyle suggested that one approach might be to build legislation around prototypes, such as synthesized molecules shown to be safe.

Intellectual Property Issues

Questions about Property. The concept of constructing new biological parts raises questions about whether rights to parts should be privately owned, how the parts should be registered, whether they should be patented, and how different intellectual property and sharing arrangements will affect advances and innovation in synthetic biology.

Patent law is not uniform globally. At the Shanghai symposium, Gordon Zong, Managing Director of The Office of Technology Transfer at Shanghai Institutes for Biological Sciences and Adjunct Professor at Shanghai Intellectual Property Research Center, noted that in China, intellectual property law is not well developed and that patent considerations have not played a large role in the early stages of developments in synthetic biology. Rochelle Cooper Dreyfuss, Pauline Newman Professor of Law, New York University School of Law, noted that, in the case of biological materials, U.S. intellectual property laws present a kind of double-edged sword. On one hand, she said, knowledge about the structure and function of biological elements such as proteins and genes is valuable. Conferring patent or copyright protection can encourage both investment and innovation. On the other hand, she observed, securing a patent may be a lengthy and costly process wherein the benefits of securing a patent do not justify the associated investment of time and capital.

In the United States, the pace of biological discoveries has tested intellectual property statutes. A watershed event was the 1980 Supreme Court case Diamond v. Chakrabarty. In this case, the Court ruled that "a live, human-made micro-organism is patentable subject matter." This opened the door to the patenting of modified plants and animals (although, under the 13th Amendment to the U.S. Constitution, human beings cannot be patented). Individual genes are eligible for certain patent protections. Today, about 20 percent of human genes (some 4,000 genes) are mentioned in patent claims.[24] Speaking in Washington, DC, Arti Rai, Elvin R. Latty Professor of Law, Duke University School of Law,

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Health and Human Services, for instance, developed its 2010 *Screening Framework Guidance for Synthetic Double-Stranded DNA Providers* with input from, among others, the International Gene Synthesis Consortium, the International Association for Synthetic Biology, and the International Council for the Life Sciences.

[24]The patent claim describes the scope of protection granted in a patent. The holder of a gene patent does not own the gene, as is widely believed—that is prohibited—but can claim man-made or isolated DNA molecules as well as novel ways to use them. Patent infringement is not a risk in whole gene sequencing in general, but may be a risk where a sequence being used corresponds to a portion of a human gene. See Holman, Christopher, 2012. "Debunking the myth that whole-genome sequencing infringes thousands of gene patents," *Nature Biotechnology* 30(3): 240-244. March.

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stated that around 60,000 patents have been issued for DNA-related innovations. Co-panelist Daniel Kevles, Stanley Woodward Professor of History, Yale University, observed that the problem for synthetic biology is that the patent system, in granting broad rights to a patent holder, may, as a result, limit and prohibit researchers' and the public's full access to the potential benefits of the field.

Linda Kahl, Legal Scholar, Department of Bioengineering, Stanford University, observed that the U.S. patent system was not designed to handle the complex intellectual property issues that arise in the practice of synthetic biology. The practice of synthetic biology, she continued, entails three major processes: abstraction (developing low-complexity biological parts, devices, and systems); decoupling (obtaining specific DNA sequences that are distinct from the natural DNA design); and standardization (uniform composition and function of biological parts). She noted that these processes can enable non-biologists to generate organisms, such as a bacterium that destroys tumors, without needing special knowledge about DNA and genetics. She observed, however, that within the patent system, each process can be hindered by high costs and the threat of patent infringement:

- *Abstraction:* The availability of simple biological components allows non-biologists to generate organisms, such as tumor-destroying bacteria, without needing special knowledge about DNA or its functions. Registries provide information or materials, but conducting freedom-to-operate searches (searches to determine whether a product infringes claims on patents already issued) can run into thousands or tens of thousands of dollars. Royalty stacking (when a single product may potentially infringe on multiple patents) may add costs that make it cost-prohibitive to market a product.
- *Decoupling:* Specialists can now develop software to design specific genetic sequences that can then be ordered from DNA synthesis companies—exponentially increasing the speed of DNA production and testing. However, in producing the genetic material, synthesis companies may inadvertently infringe on patented sequences.
- *Standardization* geometrically increases the quantity of parts being produced, distributed, and re-used. Synthetic biologists are developing standards for the physical composition of parts, but there are many types of standards—functional standards, for instance—that may be subject to patent hold-ups if an uncooperative third-party patent holder were to refuse to issue a non-exclusive license to use, for example, a standard bacterial promoter that measures and reports on the relative activity of a sample promoter.

Thus, a major question for researchers is whether synthetic biology can thrive within existing intellectual property systems or whether a new national or international intellectual property framework is needed. In synthetic biology, the

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resolution of intellectual property issues is especially important given the number of synthetic parts already developed (over 10,000 in the iGEM Registry alone) and the strong interest in eventually commercializing these products.

Over the course of the three symposia, Professor Dreyfuss, Nita Farahany, Associate Professor of Law and Associate Professor of Philosophy, Vanderbilt University, and Mark Lemley, William H. Neukom Professor of Law, Stanford University, suggested several ownership alternatives:

- Registering new parts in a searchable clearinghouse that provides partial or conditional exemptions for information providers, intermediaries, users, and contributors
- Depositing standard parts in an information commons available to members who share costs and profits
- Research and educational patent exemptions
- Copyrights and utility model (shorter-term) patents
- Petty patents, which are regulated but do not require patent examination
- Obligations for funders and investors to make resources available through non-exclusive licensing
- Development of software tools for the patent environment.

> Keep in mind a vision we'd like to strive towards: imagine creating a collection of genetic functions that we're free to use and compose—free of fear of liability, limitation of uses, and transaction costs.
>
> Linda Kahl, Legal Scholar, Department of Bioengineering, Stanford University

Inclusiveness

Synthetic biology is a hybrid field that grew out of and feeds back into a range of disciplines. Continued inclusiveness is essential for the field's continued growth.

Engagement with the Business, Regulatory, and Policy-Making Communities. Many symposia participants emphasized that continued investment and buy-in by industry and policymakers is essential for the development of synthetic biology. At the three symposia, presenters representing petroleum, microchip, and genetic synthesis organizations, business collectives, and national and regional trade organizations described potential alliances and strategies that might strengthen synthetic biology.

In Washington, DC, Lionel Clarke, Biodomain Global Strategic Programme Manager, Shell Global Solutions, observed that industry views synthetic biology as a promising field with the potential to offer solutions to many problems. Unfortunately, Clarke observed, at present large companies only have the infrastructure

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for existing technologies. Readying synthetic biology for the market, he said, would require simultaneous progress along many fronts—development of benchmarks, partnerships with industries, capital investment, and proof of effectiveness—to achieve a technological "push" met by a market "pull."

Ian Fotheringham, President, Ingenza, observed that, while many large companies are interested in using biological tools, they have shared concerns about high costs, feasibility, and reliability. Fotheringham suggested addressing these concerns by furnishing evidence of the reliability of a given product, defining approaches that increase the speed of production while reducing costs and risks, and ensuring a clear agreement about the allocation of intellectual property. Furthermore, he suggested that managers need to build interdisciplinary teams and network actively to find new users and remain current on developing trends.

Engaging the Public. At the symposia, considerable attention was paid to involving a larger community of stakeholders in discussions about synthetic biology. One reason for paying attention, said Jaydee Hanson, Policy Director, International Center for Policy Assessment, is that the public has a right to know about publicly funded research. Hanson called for a moratorium on the use of synthetic biology to change human genetic makeup and cited several possible dangers inherent synthetic biology, e.g. the unintended effects of exposure to synthetic organisms that have not been proven to be safe; potential misuse, inequitable distribution of beneficial products from the technology; and a lack of clarity about how to maintain public health and worker safety.

An important part of any discussion with the public includes addressing concerns about biosafety and biosecurity. There is an excellent opportunity, Solomon observed, for a global collaboration to improve communication about synthetic biology. She noted that a bad outcome for an engineered biological product can quickly go viral but observed that the Internet is equally effective as a tool for spreading news about the benefits of synthetic biology.

> Something we don't always appreciate is the power of convening—working cooperatively and leaving institutional baggage at the door.
>
> Robert Wells, former Head, Biotechnology Unit, Directorate for Science, Technology and Industry, Organisation for Economic Cooperation and Development

Laurie Zoloth, Professor of Medical Humanities & Bioethics and Religion and Director, Center for Bioethics, Science and Society, Northwestern University, suggested six points to consider on the ethics of science and synthetic biology:

- What methodologies and paradigms should the field adopt?
- Is there a moral problem with creating life?
- What ideas of justice would work for the field?
- When are the risks that will arise morally justifiable?

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P o s i t i o n i n g   S y n t h e t i c   B i o l o g y   t o   M e

- How can we interpret and address moral and religious concepts on what constitutes life, safety, and social values?
- How will the field be regulated?

Synthetic biologists recognized early the importance of public acceptance in preparing to commercialize synthetic biology products. Experiences with the European rejection of genetically modified food, for example, illustrate the perils of not involving the public often and early in discussions about emerging technologies. Since the public pays for a large proportion of research funding and is, ultimately, the beneficiary of the research or the consumer of products that result (and sometimes the bearer of the burdens of technologies gone wrong) many symposia speakers agreed that the public must be included in dialogues about synthetic biology, its limitations, and its future.

Professor Qiu noted the urgency of having stakeholder input and true partnerships with the public, nongovernmental organizations, and the media—with mutual learning on all sides. Besides discussing the balance of risks and benefits, Qiu said, partners should discuss ethical issues—such as how to ensure that synthetic biology benefits a whole society (rather than benefitting a select few). Joy Zhang, BIOS Centre, London School of Economics and Françoise Roure, Chair, Committee on Technologies and Society, French High Council for Industry, Energy and Technologies, discussed to the effects of including sociologists and ethicists in discussions on synthetic biology. These are fields, she observed, that can help in discussions about the intersections between science and justice, the morality of creating life, and the moral obligations of science and society in the metamorphosis of technology.

Preparing for a Networked World

Advancement in synthetic biology requires more than collaboration: it requires practitioners who are prepared to maximize the benefits of working across disciplines. While this implies changes in education, it may not necessarily suggest the need for a new degree curriculum in synthetic biology. Gautum Mukunda, Assistant Professor in the Organizational Behavior Unit, Harvard Business School, suggested that one model might be a kind of networked curriculum in which students of various disciplines work together and learn to understand both the fundamental principles of several fields and the strengths that each discipline can bring to new research. A skill set would likely extend beyond the natural sciences—for example to include the social and behavioral sciences—and students might have the opportunity to work with experienced mentors and researchers from various countries. Foundational skills for young researchers might also include an understanding of the regulatory environment and the ability to assemble an effective team.

C o p y r i g h t   N a t i o n a l   A c a d e

The iGEM model, with its emphasis on projects that may yield "real-world" applications, has worked well. The current generation of students may have a more ready understanding of how science can affect the world around them. However, symposia participants suggested that other models—perhaps along the lines of the competitions run by engineering schools[25]—might enrich the field. These included:

- A program that features a course combining engineering design with communication and is taught by faculty in both specialties, a model used at Northwestern University, that might be appropriate for graduate and postdoctoral students.[26]
- The Engineering Research Center at the National Science Foundation (NSF), which provides on-campus centers for cross-disciplinary experimental research. The centers expose students to the nature and problems of cross-disciplinary research and provide opportunities to learn from experts in industry and academia.[27]
- The NSF's Ideas Factory Sandpit, which fosters high-risk, high-reward research that would otherwise not receive support. This model facilitates interdisciplinary research on global problems and has led to collaborative multi-country projects.[28]

Several symposia participants endorsed the importance of agreeing on milestones to help guide the development of synthetic biology. Dr. Clarke said that as part of a move toward a market, roadmaps can support development of an emerging field by simultaneously addressing goals and synergies. A roadmap can identify short- and long-term goals and help create communities that are focused on those goals. However, too close a focus could undermine innovation, he added. The ideal roadmap is not a straitjacket but a marker showing targets to address but also allows shifts to other areas as the knowledge base grows, or as breakthroughs occur, said Guo-ping Zhao. Richard Johnson suggested that the best way to advance synthetic biology would be to produce a consensus-based global roadmap. While doing so will be complicated, there are numerous examples of roadmaps that address aspects of this complexity—such as those of the U.S. National Weather Service, the National Aeronautics and Space Administration, and the Cloud Computing industry.[29] The urgency of engaging multiple

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[25]Karmella Haynes, Assistant Professor, School of Biological and Health Systems Engineering, Arizona State University.

[26]Michael Jewett, Assistant Professor of Chemical and Biological Engineering, Northwestern University.

[27]Sohi Rastegar, Acting Division Director, Office of Emerging Frontiers in Research and Innovation, Directorate for Engineering, National Science Foundation.

[28]Rastegar.

[29]Johnson, Richard A., 2012. "Enabling the Synthetic Biology Commons: The Role of a Strategic Global Roadmap" (draft).

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stakeholders, noted Johnson, comprises in itself a way to enrich and enhance the field and its potential as more and more partners share their expertise.

> [Synthetic Biology] is a very exciting enabling technology. It […has] the potential to drive a new industrial revolution for the 21st century […,but] we,…both in Britain and across the world, have a responsibility for the right regulatory environment which enables rapid scientific progress whilst ensuring public safety and confidence around… ethical issues.
>
> David Willetts, Minister for Universities and Science, U.K. Government

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Appendixes

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Appendix A

London Symposium Agenda

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THE ROYAL SOCIETY

The Royal Academy of Engineering

The economic and social life of synthetic biology

The first symposium in an international collaboration between the UK's Royal Society and Royal Academy of Engineering, the USA National Academy of Sciences and National Academy of Engineering, and the Chinese Academy of Sciences and Chinese Academy of Engineering.
To be held at the Royal Society and The Royal Academy of Engineering, 13-14 April 2011.

Wednesday, 13 April

(all events at the Royal Society, 6-9 Carlton House Terrace, London SW1Y 5AG)

Opening Session

8:30 **Registration**

9:00 **Introduction**

- Sir William Wakeham FREng, *Honorary International Secretary, The Royal Academy of Engineering*

9:10 **Keynote**

- Dr George Poste FRS CBE, *Chief Scientist, Complex Adaptive Systems Initiative, and Del E. Webb Chair in Health Innovation, Arizona State University*
  Synthetic Biology: Mapping the Design Principles of Biological Systems and the Rise of Biomimetic Engineering

  Introduced by Professor Richard Kitney OBE FREng, *Co-Director EPSRC Imperial College Centre for Synthetic Biology and Innovation*

Plenary Session 1: Progress to date and prospects for the future

9:45 **Research environment**

- Professor Guoping Zhao, *Director, Laboratory of Synthetic Biology, Institute of Plant Physiology and Ecology, Shanghai Institutes for Biological Sciences*
  From molecular microbiology towards synthetic biology – A long march via new vehicles with sophisticated steering
- Professor Paul Freemont, *Co-director, Centre for Synthetic Biology and Innovation, Imperial College London*
  Establishing foundational technologies to deliver the vision of synthetic biology: from biosensors to biofuels

10:40 **Coffee break**

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CSynBI Imperial College London EPSRC Centre for Synthetic Biology and Innovation · MRC Medical Research Council · BBSRC · TATE & LYLE

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THE ROYAL SOCIETY

The Royal Academy of Engineering

11:10 **Global infrastructure and innovation**

- Dr Drew Endy, *Assistant Professor, Bioengineering, Stanford University and President, The Biobricks Foundation*
  BIOFAB International Open Facilities Advancing Biotechnology

- Professor Richard Kitney OBE FREng, *Co-Director EPSRC Imperial College Centre for Synthetic Biology and Innovation*
  Towards an Infrastructure for Synthetic Biology Design, Innovation and Education

12:00 **Lunch**

Plenary Session 2: Realising the vision

13:30 **Visions of the future**

- Dr Luke Alphey, *Chief Scientific Officer, Oxitec Ltd, and Visiting Professor, Department of Zoology, University of Oxford*
  Translational synthetic biology in insects

- Professor Huanming Yang, *Director, Beijing Genomics Institute*
  Genomics and its relevance to synthetic biology

14:30 **From rhetoric to reality**

- Professor Peter Leadlay FRS, *Co-founder, Biotica*
  Developing natural product-based drugs through biosynthetic engineering

- Dr Kirstin Eley, *External Programme Manager, TMO Renewables Ltd*
  Synthetic Biology: the adventure begins

15:15 **Tea break**

15:45 **From rhetoric to reality (continued)**

- Roel Bovenberg, C*orporate Scientist, DSM, Netherlands, and Honorary Professor of Synthetic Biology and Cell Engineering, University of Groningen*
  Synthetic Biology from an industrial perspective

- Lionel Clarke, *Global Strategic Programme Manager, Shell Global Solutions*
  Biotech to Biofuels

16:45 **Closing remarks**

- Professor Peter Leadlay FRS, *Herchel Smith Professor of Biochemistry, University of Cambridge*

17:00 **Reception**

19:30 **Close**

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THE ROYAL SOCIETY

The Royal Academy of Engineering

Thursday 14 April
(all events at The Royal Academy of Engineering, 3 Carlton House Terrace, London SW1Y 5DG)

9:00 **Introduction**

- Professor Richard Kitney OBE FREng, *Co-Director EPSRC Imperial College Centre for Synthetic Biology and Innovation*

9:10 **Ministerial address**

- Rt Hon David Willetts MP, *UK Minister for Universities and Science*

Plenary Session 3: Creating an enabling environment

9:40 **An enabling environment for research**

- Dr François Képès, *Director, Epigenomics Project*
  Synthetic Biology: what is needed from a strategic and research point of view?
- Professor Ben Davis, *Organic Chemistry, University of Oxford*
  Synthetic Biology: a molecular perspective
- Hai-Yan Liu, *University of Science and Technology of China*
  Developing reusable designs of new regulatory components for synthetic biology based on the modularity of native elements

10:40 **Coffee break**

11:00 **An enabling environment for innovation**

- Nigel Jones, *Intellectual Property Partner and Co-Head Healthcare Sector, Linklaters LLP*
  Encouraging Innovation: The Role of Intellectual Property
- Dr Ioannis Economidis, *Advisor, the EC-US Task Force on Biotechnology Research, Working Group on Synthetic Biology*
  The Emerging/Enabling role of Synthetic biology in the development of biotechnological applications
- Professor Rifat Atun, *Director of Strategy, Performance and Evaluation Cluster, The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva*
- Professor Robert Edwards, *Chief Scientist, The Food and Environment Research Agency (Fera)*
  SPPI-Net: a UK Network in Applied Synthetic Biology

12:30 **Lunch**

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THE ROYAL SOCIETY

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13:30 **An enabling environment for users**

- Dr Joy Zhang, *BIOS Centre, London School of Economics*
  The international governance of synthetic biology

- Dr Françoise Roure, *Chair, Committee on Technologies and Society, French High Council for Industry, Energy and Technologies*
  A Global Governance for Synthetic Biology? Lessons learned from Nanotechnology

Break-out session: hindsight and foresight

14:15 **A roadmap for syn bio**

Four mixed break-out groups

15:15 **Tea break**

Plenary Session 4: hindsight and foresight

15:45 **Panel discussion**

- Professor John McCarthy, *Head of Life Sciences, University of Warwick*
- Professor Richard Jones FRS, *Pro-Vice Chancellor for Research and Innovation, University of Sheffield*
- Heather Lowrie, *ESRC Centre for Social and Economic Research on Innovation in Genomics (Innogen), University of Edinburgh*

Chaired by

- Professor Richard Kitney OBE FREng, *Co-Director EPSRC Imperial College Centre for Synthetic Biology and Innovation*
- Professor Peter Leadlay FRS, *Herchel Smith Professor of Biochemistry, University of Cambridge*

16:45 **Closing remarks from panel chairs**

17:00 **Close & Coffee**

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Appendix B

Shanghai Symposium Agenda

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Enabling Technology for Synthetic Biology

Six-Academy Synthetic Biology Symposium Ⅱ

Oct. 12-14, 2011, Shanghai, China

Oct. 12 (Wednesday), Grand Lecture Hall, SIBS, 320 Yueyang Road	
Morning	**09:00 am – 11:45 am**
09:00 am	**Opening Ceremony** Chair: Sheng-li Yang
09:00 am	Introduction to the Symposium Guo-ping Zhao (Shanghai Institutes for Biological Sciences, CAS, China)
09:15 am	Opening Address
	1.Xian-en Zhang (Director, Department of Basic Research, Ministry of Science and Technology of China) 2. Dai-ming Fan (Vice President, Chinese Academy of Engineering)
09:35 am to 11:45 am	Two Keynote Presentations (40 min plus 10 min Q&A for per keynote presentation) Chair: Guo-ping Zhao
09:35 am	***The Synthetic Biology of Antibiotic Natural Products***
	Peter Leadlay (University of Cambridge, UK)
10:25 am	Tea and Coffee Break
10:55 am	***Tools for Engineering Biology***
	Drew Endy (Stanford University, USA)
11:45 am	**Group Photo of Speakers & Lunch Break**
Afternoon	**01:30 pm – 05:30 pm**
01:30 pm	**Opening Address** Chair: Guo-ping Zhao
01:30 pm	***The Grand Synthesis***
	Thomas Lee (Director, Microsystems Technology Office, Defense Advanced Research Projects Agency, USA)
	Session A*: Designing Modules and Pathways Session Chairs: Richard Kitney & Zi-xin Deng
01:50 pm	***The Application of Systematic Design to Synthetic Biology***
	Richard Kitney (Imperial College, UK)
02:15 pm	***Construction of the Simplified Genomes of Escherichia Coli and Streptomyces Coelicolor***

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	Zhong-jun Qin (Shanghai Institutes for Biological Sciences, CAS, China)
02:40 pm	***Biological Network Engineering in Synthetic Biology***
	Qi Ou-yang (Peking University, China)
03:05 pm	Tea and Coffee Break
03:35 pm	***Design and Evolution of Biological Pathways and Networks***
	Hui-min Zhao (University of Illinois at Urbana-Champaign, USA)
04:00 pm	***Synthetic Production of 3-hydroxybutyrate (3HB) Monomers and Biobutanol Directly from CO_2 in Cyanobacteria***
	Wei-wen Zhang (Tianjing University)
04:25 pm	Panel discussion
05:05 pm	***From Single Cell Biotechnology towards Synthetic Biology***
	Wei Huang (University of Sheffield, UK)
05:30 pm	End of Session A
Oct. 13 (Thursday), National Engineering Center for Biochip at Shanghai, 151 Libing Road, Pudong	
Morning	**09:00 am –12:00 noon**
09:00 am	Opening Address Chair: Guo-ping Zhao
09:00 am	Jing-hai Li (Vice President, Chinese Academy of Sciences)
	Session B*: Synthetic Genome and Cell Session chairs: Peter Leadlay & Drew Endy
09:10 am	***The Emergence of Synthetic Life with De Novo Chemical Alphabets***
	Jeffrey Tze Fei Wong (Hong Kong University of Science & Technology, China)
09:35 am	***Genome Engineering Technologies for Rapid Programming & Evolution of Organisms***
	Farren Isaacs (Yale University, USA)
10:00 am	***Size Dependent Genome Synthesis/Cloning***
	Mitsuhiro Itaya (Keio University, Japan)
10:25 am	***Towards Development of a Robust Simplified Cell***
	Barry L. Wanner (Purdue University, USA)
10:50 am	Tea and Coffee Break
11:20 am	Panel discussion
12:00 noon	**Lunch Break**
Afternoon	**01:30 pm – 04:55 pm**

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	Session C*: Synthetic Biology from an Industrial Perspective
	Session Chair: Roel Bovenberg
01:30 pm	***Rational Design - Applications in Industrial Biotechnology***
	Liang Wu (DSM Biotechnology Center, Netherlands)
01:55 pm	***Building an Efficient Yeast Cell Factory for the Production of Isoprenoids***
	Lishan Zhao (Amyris Inc., USA)
02:20 pm	Panel discussion
03:00 pm	Tea and Coffee Break
	Session D: *i*GEM: Scientific, Technological, and Educational Impact upon Synthetic Biology
	Session Chairs: Ying-jin Yuan & Qi Ou-yang
03:30 pm	***Building a Re-Coded Yeast Genome Powered by an Army Of Undergraduates***
	*Yizhi Patrick Cai (Johns Hopkins University School of Medicine, USA)
03:55 pm	***A Novel Approach for Synthetic Biology: Exploiting Wisdom in Natural Systems***
	**Haoqian Zhang (Peking University, China)
04:15 pm	***Rule-based Modeling Approach for Synthetic Biology***
	**Chen Liao (University of Science and Technology of China, China)
04:35 pm	***Modular Design and Synthesis of Energy Products***
	**Duo Liu (Tianjin University, China)
04:55 pm	End of Session D
Oct. 14 (Friday) , Grand Lecture Hall, SIBS, 320 Yueyang Road	
Morning	**9:00 am –12:10 noon**
	Session E:Ethical, Legal and Social Implications (ELSI) for Synthetic Biology**
	Session Chair: Huan-ming Yang
09:00 am	***Life in the Gray Zone: From ELSI to Responsible Innovation***
	Sheila Jasanoff (Harvard University, USA)
09:20 am	***Legal Implications for Synthetic Biology: Intellectual Property Rights in Biologicals***
	Rochelle Dreyfuss (New York University School of Law, USA)
09:40 am	***Intellectual Property and Technology Transfer Issues Associated with Synthetic Biology***
	Gordon Zong (Shanghai Institutes for Biological Sciences, CAS, China)
10:00 am	***The Ethics of Synthetic Biology: The Perspectives of the US Presidential Commission***

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	Anita L. Allen (University of Pennsylvania Law School, USA)
10:20 am	***The UK Research Councils' Synthetic Biology Dialogue***
	Paul Gemmill (Biotechnology and Biological Sciences Research Council, UK)
10:40 am	Tea and Coffee Break
11:00 am	**Discussion – Synthetic Biology Futures**
12:00 noon	Close Speech
12:10 noon	End of Symposium

* For per speaker we allocate 20 min talk plus 5 min Q&A.

** For per speaker we allocate 15 min talk plus 5 min Q&A.

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Appendix C

Washington, DC Symposium Agenda

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Synthetic Biology for the Next Generation: A Symposium

The National Academy of Sciences Building Auditorium
2101 Constitution Avenue, NW
Washington, DC 20418
June 12-13, 2012

AGENDA

Tuesday, June 12, 2012

7:30 Continental Breakfast

8:00 Welcome

Charles Vest, President, The National Academy of Engineering

8:10 Meeting Global Challenges

Moderator: Pamela Silver, Harvard Medical School

Speakers: Daniel P. Schrag, Harvard University
Saul Griffith, Engineer and Entrepreneur

9:00 Overview of Research in Key Application Areas

Moderator: Guo-ping Zhao, Shanghai Institutes for Biological Sciences

Speakers: Jindong Zhao, Institute of Hydrobiology, Chinese Academy of Sciences (Agriculture and Environment)
Gregory Stephanopoulos, Massachusetts Institute of Technology (Industrial Applications)
Alexandra Daisy Ginsberg, Designer, Artist, and Writer (Arts/Humanities)
Christina Smolke, Stanford University (Health and Medicine)

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10:00 Discussion with Participants

10:15 Break

10:30 Organizational Strategies in Support of Synthetic Biology

Moderator: Rob Carlson, Biodesic

Speakers:
Lionel Clarke, Shell
Ian Fotheringham, Ingenza
Jason Kelly, Ginkgo BioWorks
Meagan Lizarazo, iGEM
Darlene Solomon, Agilent Technologies
Guo-ping Zhao, Shanghai Institutes for Biological Sciences

11:30 Discussion with Participants

11:45 Lunch

1:00 National Strategies for Advancing Synthetic Biology

Moderator: Jonathan Margolis, U.S. Department of State

Speakers:
Gerardo Jiménez-Sanchez, Organisation for Economic Co-operation and Development
John Perkins, Department for Business, Innovation & Skills, U.K. Government
Xian-en Zhang, Ministry of Science and Technology of China

2:00 Discussion with Participants

2:15 Perspectives on Synthetic Biology from within the Political System

Moderator: Aristides Patrinos, Synthetic Genomics

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Speakers: David Uffindell, Department for Business, Innovation & Skills, U.K. Government

Jetta Wong, U.S. House of Representatives

Guo-ping Zhao, Shanghai Institutes for Biological Sciences

3:15 Discussion with Participants

3:30 Break

3:45 Roundtable Discussion – Rebuilding the Social Contract

Moderator: Jonathan Moreno, University of Pennsylvania

Speakers: Jaydee Hanson, International Center for Technology Assessment

Thane Kreiner, Santa Clara University

Renzong Qiu, Chinese Academy of Social Sciences Institute of Philosophy

Nikolas Rose, Kings College London

Edward You, Federal Bureau of Investigation

Laurie Zoloth, Northwestern University

4:45 Discussion with Participants

5:00 Adjourn

5:15 Reception in Great Hall

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Wednesday, June 13, 2012

7:30 Continental Breakfast

8:00 Welcome

Drew Endy, Stanford University

8:10 Roundtable Discussion – Exploring Fundamental Questions in Biology

Moderator: Peter Leadlay, University of Cambridge

Keynote Address:

Michael Elowitz, California Institute of Technology

Respondents / Discussants:

Maitreya Dunham, University of Washington
Paul Freemont, Imperial College London
Jason Micklefield, University of Manchester
Weiwen Zhang, Tianjin University

9:30 Discussion with Participants

9:45 Roundtable Discussion – Advancing Fundamental Needs in Engineering

Moderator: Richard I. Kitney, Imperial College London

Discussants:

Peter Carr, Massachusetts Institute of Technology (Measures and System Performance)

Todd Peterson, Life Technologies Corporation (DNA Synthesis, Assembly, and Strain Engineering)

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Cesar Rodriguez, Genome Compiler Corporation (Computer-Aided Design/ Data Exchange)

Reshma Shetty, Ginkgo BioWorks (Metrology)

Zhihua Zhou, Shanghai Institutes for Biological Sciences (Genetically Encoded Sensors)

10:45 Discussion with Participants

11:00 Break

11:15 Enabling the Next Generation of Leadership and Community

Moderator: Megan Palmer, Synthetic Biology Engineering Research Center (SynBERC) and Stanford University

Discussants:

James Field, Imperial College London

Karmella Haynes, Arizona State University

Michael Jewett, Northwestern University

Chenli Liu, Guangzhou Institute of Advanced Technology

12:00 Discussion with Participants

12:15 Lunch

Roundtable Discussions – Governance: Needs Beyond the Bench

1:30 Session A: Prudent Practice - Lessons from Real World Case Studies

Moderator: David Rejeski, Woodrow Wilson International Center for Scholars

Discussants:

Patrick Boyle, Harvard University

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Nikki Kapp, Imperial College London

Christopher Schoene, Imperial College London

Gautam Mukunda, Harvard University

Zhong-jun Qin, Shanghai Institutes for Biological Sciences

2:30 Discussion with Participants

2:45 Session B: Ownership, Sharing, and Innovation

Moderator: Drew Endy, Stanford University

Opening Remarks:

Linda Kahl, Synthetic Biology Engineering Research Center (SynBERC) and Stanford University

Discussants:

Arti Rai, Duke University

Daniel Kevles, Yale University

Nita Farahany, Vanderbilt University Law School

Mark Lemley, Stanford University

3:45 Discussion with Participants

4:00 Break

4:15 Roundtable Discussion – Critical Issues for Success

Moderator: Richard Johnson, Global Helix LLC

Discussants:

François Képès, Le Centre national de la recherche scientifique

Carlos Olguin, Autodesk

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Sohi Rastegar, National Science Foundation

Marc Salit, National Institute of Standards and Technology

Robert Wells, Organisation for Economic Co-operation and Development

Youli Xiao, Shanghai Institutes for Biological Sciences

5:15 Discussion with Participants

5:30 Adjourn

This symposium was organized by the National Academy of Sciences' Committee on Science, Technology, and Law, the National Academy of Sciences' Board on Life Sciences, and the National Academy of Engineering with support from the Alfred P. Sloan Foundation.

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