Report from

Department of Energy (DOE) – Alfred P. Sloan Foundation Workshop on

"Societal Issues Arising from Synthetic Biology: What Lies Ahead"

Hosted by the Woodrow Wilson International Center

November 7-8, 2010

Executive Summary

Prominent individuals in the fields of synthetic biology research, law, and social science/ethics from more than a dozen research institutions, DOE laboratories, and federal agencies gathered at the Woodrow Wilson International Center (Wilson Center) on November 8-9, 2010 for a workshop on "Societal Issues Arising from Synthetic Biology: What Lies Ahead." The workshop was organized by the Department of Energy (DOE) Office of Biological and Environmental Research and the Alfred P. Sloan Foundation, and plenary presentations the first day included talks on: 1) what synthetic biology is and what it can do; 2) the evolution of research on the ethical issues arising from technologies emerging from the Human Genome Project; and 3) overviews of ongoing synthetic biology ELSI projects funded by the Sloan Foundation and by DOE. The participants then broke into groups to discuss potential uses and applications of synthetic biology, as well as legal and economic, societal and public policy, and public acceptance and understanding issues that will need to be addressed as the field of synthetic biology advances. The participants identified a number of societal challenges and pressing research needs, which were summarized as closing remarks by 2 presenters and are included in this report. Participants understood the tremendous potential for synthetic biology to contribute to human and societal challenges, to explore the scientific unknown, to contribute to the economic wellbeing of the US. But participants also acknowledged the challenges of ensuring that these exciting technologies are managed with caution, that benefits are justly distributed, that wise regulations are instituted to maximize benefits and minimize risks, and that a mindset of responsibility be encouraged among everyone involved.

DOE-Sloan Foundation-Wilson Center Joint Workshop on Synthetic Biology

DOE and the Alfred P. Sloan Foundation organized a two day invitation-only workshop titled "Societal Issues Arising from Synthetic Biology: What Lies Ahead," which was hosted by the Wilson Center in Washington, DC on November 8–9, 2010. There were 33 attendees (participants and observers), nine from academia, three from DOE National Labs, nine from non-profit research centers, one from industry, three from DOE, one from the Sloan Foundation, two from the President's Bioethics Commission, and 7 from other US government agencies (including NIH, EPA, and OSTP). The participants included scientists engaged in synthetic biology research and social scientists/ethicists with a diversity of backgrounds and affiliations. Co-organizers Libby White (DOE) and Paula Olsiewski (Sloan Foundation) worked with Dan Drell (DOE) and Dave Rejeski of the Wilson Center, in selecting the invitees and formulating the agenda. The feedback from the attendees was very positive, with the consensus that this was a unique, stimulating, and productive event. Prior to arriving at the workshop, participants were tasked to submit one-pagers addressing three questions about synthetic biology: lessons learned from past comparable technologies, relevant experiences they may have had that could inform the discussions, and thoughts on urgent research needs. (The agenda, participant list, and one-pagers are appended at the end of this report.)

On the morning of the first day of the workshop, 3 individuals made plenary presentations of about 30 minutes each. These presentations covered ongoing synthetic biology research and the historical landscape of ethical analyses of new technologies emerging from the Human Genome Project. Brief presentations then followed from current DOE and Sloan Foundation grantees working on societal implications arising from synthetic biology research. In the afternoon, breakout groups focused on questions of what the likely first uses of synthetic biology, and attendant societal issues, might be. On the morning of the second day, separate breakout groups were convened to discuss legal, societal, and communication issues that may be expected to arise from synthetic biology research. In the afternoon, participants were asked to list gaps in knowledge that could contribute to a research agenda going forward.

The workshop began with opening remarks by *John Glass* of the J. Craig Venter Institute, who discussed the recent work synthesizing the genome of *Mycoplasma mycoides* and its successful transplantation into the "shell" of a different mycoplasma followed by the "booting up" of this synthesized genome to give rise to a line of reproducing cells entirely determined by the synthesized genetic information. Dr. Glass explained that the aim of such work is to build a minimal cell that would allow exploration (and, it is hoped, the elucidation) of first principles of biological organization and functioning. Glass noted the difficulties associated with this research, some of the barriers that had to be overcome to achieve it, and its potential benefits. From a biological perspective, these potential benefits include generating new vaccines and other high-value products, and advancing the understanding of fundamental biological processes that these new tools will enable. In pursuing these benefits, he asked that we strive to anticipate potential deleterious consequences of synthetic biology research so that appropriate protections can be put in place at the outset.

The next presentation was from *Nathan Hillson* of the Lawrence Berkeley National Lab. Dr. Hillson is both a practicing synthetic biologist as well as a DOE grantee exploring ethical, legal, and societal issues (ELSI) associated with ongoing research on the stability of engineered organisms. He pointed out that there is a critical definitional issue to synthetic biology, specifically what qualifies as "synthetic" biological research? Referring to the Venter Institute work, he asked if that was synthetic biology or just biology using synthetic DNA? Is synthetic biology the entire synthesis of a living organism or something less ambitious than that, such as the large scale reengineering of multiple enzymatic pathways inside a cell? Where does one draw the line and what implications follow? He asked "what can you DO with synthetic biology that would otherwise be impossible?"

Tom Murray, the President of the Hastings Center in New York, Sloan grantee and an original member of the ELSI Working Group formed at the outset of the Human Genome Project, focused his remarks on historical lessons learned about ELSI. He analyzed the types of previous ELSI activities that were and weren't effective as a basis for suggesting what to focus on as synthetic biology and related ELSI researches evolve. He started with a fundamental principle of bioethics, that "good ethical policy begins with good facts about the relevant science" and observed that context is everything, e.g., that if the first outcomes are beneficial, greater likelihood of acceptance will follow. He then observed that, with respect to synthetic biology, what was needed was practical ethics and not abstract moral theory. Also, he suggested that important questions need to be spelled out in terms accessible to everyone. He noted that, while it would be hard to identify ELSI issues that were new or particular to synthetic biology, the relevant issues deserved serious examination in the new contexts created by developments in synthetic biology. In addition, it would be critical that benefits (when realized) be disseminated with a sense of justice for all.

After the plenary talks, the grantees of the Sloan and DOE programs gave brief descriptions of their activities.

Dave Rejeski (Wilson Center) is studying public perceptions of synthetic biology along with associated concerns about risks. He noted that the public (so far) is largely unfamiliar with the science, that public perceptions of the science are being shaped by the media (with different emphases in the U.S. versus Europe), and that messages about synthetic biology propagated by the science community have thus far been largely uncoordinated and ad hoc. There is also a perception on the part of the public that "no one is in charge" of synthetic biology in the government. The focus of the Presidential Bioethics Commission on synthetic biology will likely result in greater scrutiny on the science and more expressed concerns about accidents or misuses. (*Sloan grantee*)

Jason Bobe (Harvard) talked about his efforts to ensure safety in the "do-it-yourself" (DIY) biology movement. He addressed the fact that regional groups are establishing "community labs" where members of the general public can participate in hands-on workshops and educational events. While some professional scientists are involved, many of the participants in the DIYbio community have no formal laboratory training or professional experience. Bobe stated that we cannot expect these individuals to be up-to-speed on best practices in laboratory safety and proper disposal of biological waste, etc., and that survey results demonstrate a significant need to establish norms in the DIYbio community and provide practical biosafety resources. (*Sloan grantee*)

Greg Kaebnick (Hastings Center) is exploring the spectrum of ethical issues raised by synthetic biology. He stated that the Hastings Center's charge from Sloan was to kick-start a thoughtful, nuanced discussion of the "intrinsic" concerns about synthetic biology—those that do not have to do with whether the technology will have good or bad *consequences* for human well-being, but about the implications of the technology itself. The Hastings Center is carrying out the charge by assembling an interdisciplinary group of experts to develop and critique analyses of these issues. Anticipated products include a volume of essays setting out these analyses, along with other writings and lectures. The Hastings Center's goal in the public discussion, he indicated, has been to establish salient terms for the discussion and to share a preliminary assessment of the technology. He stated that, while the technology may raise deep and important moral questions about the human relationship to nature, but that these questions should not make a difference in public policy at this stage of the development of synthetic biology, as they do not yet generate distinctive policy positions beyond those that concerns about consequences generate independently. *(Sloan Foundation)*

Andrea Loettgers (Cal Tech) is studying engineering metaphors applied to synthetic biology. She informed the group that the use of engineering concepts and metaphors in synthetic biology has become common practice in synthetic biology. Concepts such as robustness, modularity, redundancy, and noise as well as metaphors such as LEGO bricks in depicting genes and DNA have important impacts on our understanding and conceptualization of biological systems. She said that biological systems become 'engineerable' in the same way as electrical and mechanical engineered systems do. The Caltech study, which is part of a study in the laboratory of the synthetic biologist Michael Elowitz, showed that the concept of noise in biology functions as an umbrella concept that comprises a large number of as yet not well understood biology specific fluctuations. This insight triggers important questions for the basic science-oriented branches of synthetic biology as well as for the application-oriented branch. What are the sources of these fluctuations? How do they affect the functioning of biological systems? For the purposeful engineering of biological systems it will be of great importance, she indicated, to clarify whether and how the different forms and sources of noise may affect the engineered synthetic system. Results and methods of the basic science branches of synthetic biology need to get more attention in synthetic biology and one should aim for an exchange between the two different branches. (*Sloan Foundation)*

Anne-Marie Mazza (National Research Council) is looking at international opportunities and reactions to synthetic biology. Specifically, on July 9-10, 2009, the National Academies, together with the Royal Society, and the Organisation for Economic Co-operation and Development (OECD), held an international symposium on the *Opportunities and Challenges in the Emerging Field of Synthetic Biology.*

The meeting, which received support from Sloan, the National Science Foundation, and the Biotechnology Industry Organization (BIO), drew speakers and attendees from around the world including Europe, Australia, Asia, Africa, South America, and the United States. The two-day meeting covered a wide range of topics including: 1) an overview of synthetic biology; 2) government perspectives and approaches; 3) innovation in tools and techniques, eco-products, and health and medicine; 4) needs of academia and industry in order to develop the field; 5) investment models for synthetic biology; 6) governance issues regarding health, safety, the environment, and security; and 7) public engagement and participation. Dr. Mazza indicated that the National Academies, in collaboration with The Royal Society, Royal Academy of Engineering, Chinese Academy of Sciences, and Chinese Academy of Engineering, with support from Sloan, is planning to organize symposia in 2011 in each of the three countries on synthetic biology: The enabling science and technology of synthetic biology (China); Innovation and realizing the commercial promise of synthetic biology (the UK); and Next generation tools, platforms, and infrastructure for synthetic biology (US). *(Sloan grantee)*

Holly Million (BioBricks Foundation) is working on engaging the synthetic biology science community in discussing societal implications. The BioBricks Foundation is developing social networking and other Web 2.0 tools to help unite the scientific/engineering community. To date, she reported, BioBricks has: 1) completed a master redesign of its collection of existing, related websites; 2) developed a prototype website for a BioBricks Public Agreement which will allow scientists to contribute and use standard biological parts in the public domain; 3) launched its SB5.0 site and created written content and structural design for the www.biobricks.org site including key Web 2.0 features; 4) designed a new home page for the portal site at www.syntheticbiology.org; and 5) created a draft communications plan that will be used to finalize messaging across the related sites. *(Sloan grantee)*

Paul Thompson (Michigan State University, MSU) presented on the Sloan-funded collaboration with Lori Knowles (University of Alberta, Health Law Institute, HLI) and Michele Garfinkel and Bob Friedman of the Venter Institute to examine both ethical issues and communication issues that would be associated with possible applications of synthetic genomics. He indicated that the results suggest that in many respects, ethical and communication issues in this area will track closely with those of genetically engineered organisms: applications in human health will be much less problematic than those that have the potential for widespread environmental impact or that are incorporated into foods; applications in animals will be most sensitive; and failure to attend to questions of distributive justice or the totality of environmental impacts will lead activists to mount campaigns that many scientists will regard as obfuscatory. He reported that they did note that the standardization and technological power of synthetic genomics has the potential to create a sector of innovators who move rapidly and who escape both public scrutiny and regulatory oversight. He indicated that while the freedom and beneficence of innovators who operate outside large institutions has been viewed positively in information technology, it may not be true in synthetic genomics. It seems just as likely that the presence of rapid, unchecked and unregulated innovators will be used to create a (possibly justified) climate of fear surrounding synthetic genomics. He said that MSU and Venter have concluded that scientists working in this field have an unprecedented ethical responsibility to engage in constructive communication and deliberation efforts with the full range of stakeholders and potentially affected parties. *(Sloan grantee)*

Nathan Hillson (LBNL) is working on creating the foundations for studying risks associated with the introduction of genetically engineered organisms into various environments so that the implications of different technical designs to add a function or functions can be accurately assessed. He indicated that arguments about the risk and return of synthetic biology rest on our technological understanding of the fitness of the modified organism in the environment and the stability of the organism in the surrounding environment once the engineered cells are deployed. LBNL is working to understand how the modifications we make to organisms promote their persistence and containment within the target environment and prevent their drift and failure due to endogenous mutational processes and exogenous interaction and transfer of genetic material. *(DOE grantee)*

Bob Friedman and *Michele Garfinkel* (J. Craig Venter Institute) are looking at the applicability of the regulatory framework (first established for recombinant DNA methods) for synthetic biology and to explore if adaptations may be required. Friedman explained that although many of the technologies used in synthetic biology are likely to fall under regulations originally designed for the oversight of biotechnology generally, there may be gaps in these regulatory frameworks. He indicated that, during this study, the Venter Institute will evaluate current regulatory authorities, particularly those described in the *Coordinated Framework for Regulation of Biotechnology,* proposed in 1986 in response to the then emerging field of genetic engineering. The Venter Institute will employ a variety of approaches (expert papers; meetings and interviews with regulators; workshops), and then distribute findings both in printed reports and in presentations to agencies and other audiences. *(DOE grantee)*

In the afternoon, three parallel breakout groups were charged with considering what the potential uses of synthetic biology might include, and what potential "game changers" might result. Across the three breakout groups, the main conclusions were these:

Potential applications of synthetic biology: a principal outcome will be biological discovery, greater understandings of biological processes, organizations, regulation, and activities. This was viewed as important for anything to which biology contributes, which is, in short, nearly every process on Earth. Additional expectations include bioproduction of many things, among them industrial products, fuels, drugs and other therapeutics, detergents, and vaccines. Uses will be seen in health, industry, environmental areas, agriculture, water, perhaps architecture, space, and various forms of waste cleanup. Synthetic biology might serve as a "molecular printer" in the sense that a product is ordered after being designed on a computer. This list, no doubt, is highly conservative and more speculative uses were mentioned as well. There may be "hybrid" uses in the microelectronics and nanotechnology areas. Personal medicine might entail the development of specially mutated self-products, radically modified (or even entirely redesigned) organisms, cells with different operating systems capable of biology or even properties (skin color alteration) that can be externally regulated.

Potential "game changers" for synthetic biology could come in a variety of ways, not all of them benign. A game-changer that would promote synthetic biology strongly, as analogous to the impact of the introduction of recombinant human insulin on recombinant DNA technologies, could allay many public concerns about synthetic biology as an innovative technology. Recombinant insulin was introduced in 1980, after several years of public concern (the Asilomar conference was held in 1975, introducing a moratorium on recombinant DNA research while safety issues were considered and the NIH Recombinant DNA Advisory Committee instituted as a regulatory mechanism); very rapidly, the FDA approved rDNA human insulin for clinical use and sale, it was immediately accepted by the public, also the affected industry, and succeeded in proving itself both therapeutically and economically. A series of rDNA-produced products soon followed, with little if any public reaction. If, by contrast, the first uses of synthetic biology were military, affected human behaviors, or an accident occurred, or venture capital failed to materialize (for any of several reasons), or the first uses were seen as trivial (cosmetic or stigmatizing) and the benefits were viewed as unfairly distributed, imposed by an arrogant or elitist community, or a particular community was (intended or not) the victims of an application that had unforeseen negative consequences, then the acceptance of the technology might at best be much slower and at worst retarded to a significant degree.

On the morning of the second day, three reconfigured breakouts were convened. One looked at legal issues, another at societal issues, and a third at public acceptance issues.

Legal issues: Many issues could potentially raise legal challenges (for a legal system ill-prepared to consider them). As examples, biodiversity issues might arise from copying the biological heritage of a country that is protective and asserts that synthesizing (copying) its biological material is a wrong. Can information be controlled in the same way that materials can be? Competitiveness will be an issue as the US is not the only country engaged in synthetic biology. Thus, intellectual property will be disputed. How will synthetic biology research be regulated and by whom? Synthetic biology is less a "thing" than a toolkit and as such it is the uses to which it is put that matter; who will judge those uses? USDA for agriculture, FDA for therapeutics, EPA for everything else? Can a regulatory framework be built, or can the existing regulatory framework adapt, to evolve with a technology?

Public Policy and Societal: The provision of objective information about the science underlying synthetic biology was emphasized. The perspectives of additional communities, including religious perspectives, need to be invited in, and respect given to all. Fellowships to bridge the gap between communities of scientists and those more engaged in policy, journalism, ethics, etc. may be worth exploring.

Public Engagement: Without a common understanding of what synthetic biology is, as well as what influences public awareness and reaction to controversial issues, it may be hard to get the public engaged. An open discussion is needed both about its promise and its potential risks. It is not clear who should be responsible for introducing or engaging in such discussions, although many have begun to participate (iGEM, computer games, museums, etc.) Engagement needs to be undertaken in a way that is not paternalistic of the public, to avoid the "if you knew what we know, you'd agree with us" mindset that can quickly become toxic.

Joyce Tait (Innogen Center, University of Edinburgh) contributed an overview rooted in the "strategic triad" of scientific research mutually interacting with governance and regulation, interacting with public and stakeholder concerns. In the past, regulation affected principally the application of knowledge, now it is also seems to affect the generation of knowledge. She noted that a shift seems to be occurring from "interest-based" conflicts (leading to a "Not in My Backyard [NIMBY] response that can often be resolved) to a more ideologically based reaction (leading to a "Not in Anyone's Backyard [NIABY] response that can be highly refractory to resolution) which was harder to deal with, but could be influenced by engagement with interested parties earlier in the process. She suggested that it could be helpful to work to understand motivations as well as ethical perspectives, be equitably skeptical, to develop standards for engagement, and maintain freedom of choice for those affected by new technologies as long as possible. A consequence of this is that efforts to involve policy makers, and efforts to raise their awareness and knowledge of the relevant issues are worthwhile.

Conclusions

Lori Knowles (University of Alberta) summed up the workshop, noting the many remaining questions, among them definitional issues: What is synthetic biology, who belongs in the community of synthetic biology practitioners? What is not synthetic biology? Can you self-identify as a "synthetic biologist"? These questions have implications for the "synthetic biology" community, also for communications about synthetic biology and who is doing it. How do you bring in the DIY (Do-it-Yourself) folks, iGEM, high school students, and other potential synthetic biology practitioners? Are these sub-communities part of the “synthetic biology” culture and, if not, should they be? Knowles noted that in preparing for a world in which synthetic biology is more common, public engagement is required, including recognition that there are multiple relevant publics, including religious groups. These publics must be respected and the presumption that if “they” only “knew” what the experts knew, then they’d be more accepting of synthetic biology is naïve. Consequently, those with subject matter expertise, the insiders, those familiar with the challenges of this new technology, need to be at the forefront of raising the issues.

The potential promise is huge, not only for high-value chemicals and drugs, but also societal “game-changers” such as new energy sources. At some point in the future, the Human Microbiome may be a potential target for synthetic genomics, assuming appropriate targets that are both relevant to human health/performance/diet/phenotype (read: obesity) and engineer-able can be identified and a whole spectrum of potential human safety and human subjects ethical issues can be satisfactorily addressed. In addition, environmental release issues need to be meaningfully addressed. What unifies all these potential applications of synthetic biology is a stark reality: The first big success will be a game changer but the first failure, no matter of what scale, will also be a game changer in the other direction.

Additional issues include approaches to regulation and IP laws that will need to be studied and addressed and which will clearly affect economic impacts. Collaborative and adaptive models for regulation, the roles of government bodies, all need to be analyzed. How does one incorporate welfare concerns (and whose welfare)? If there is to be a formal regulatory structure, how would it be structured, how would it work, how would it retain (or evolve) currency, and how could or would practitioners of synthetic biology fit in?

Finally, how can ELSI be used meaningfully? Should it be embedded or integrated? How can its relevance (accepting that it HAS relevance) be increased? How can its contributions be measured? How can communications be fostered both of the science and the societal implications?
The meeting was closed following a brief exercise in which all participants were asked to consider, given all the discussions at the workshop:

“What important issues or questions do you think still need to be addressed in the field of synthetic biology as they relate to societal issues?”

Legal and Economic Questions:

1) Anticipatory/adaptive governance and/or regulation - how to govern a fast-moving technology whose future directions, risks and impacts cannot be predicted in advance
2) How to incorporate social, ethical, religious concerns into governance or regulatory structures?
3) What should government involvement look like? Who should make decisions about what research directions to pursue? How should the DIY bio community be monitored/regulated?
4) How do we assess and frame progress (with metrics) in overcoming issues?

Intellectual Property-related Questions**:**

1) Are there IP-related issues peculiar to synthetic biology and can (or should) the current patent system be altered to address them?

2) What IP regimes for new “disruptive” technologies have worked “best” (in terms of technology dissemination, economic return, fairness) in the past and can we learn from them for synthetic biology?
3) Is “open source” biology a better business model than alternatives involving more restriction?
4) Does the current IP regime affect synthetic biology research in a way that promotes innovation or constrains it?
5) How can the apparent historical conflicts between life scientists’ approach to IP and ownership and engineers’ approach to IP and ownership be resolved to the benefit of society?

Public Policy-related Questions:

1) Should the products/outcomes of synthetic biology be tagged or labeled so as to clearly identify their method of manufacture? How important is this for public acceptance?
2) For potential synthetic biology applications that are intended to have an enduring effect (e.g., changing human microbiome, an environmental application, production of synbiofuel) instead of a short-term applications (flu vaccine, etc.) - how might one ensure the intended effects are achieved and unintended consequences are benign (or limited) in changing systems (aging humans, ecosystems etc.)?
3) How best can we educate decision-makers (policy-makers, Congress, judges) about synthetic biology and more generally the culture of science? What do they need to know and who should influence the development of this “curriculum”?
4) Can we come up with a clearer definition (of synthetic biology?)

Public Engagement and Communication-related Questions**:**

1) How can the case for synthetic biology ELSI be forcefully, convincingly, persuasively stated - why it matters, why it is important?
2) What are creative mechanisms for engaging both the “public” and the social and ethical synthetic biology communities in dialogue about opportunities/needs/values?
3) How can the risk assessment process better engage the publics’ differing view/values concerning risk? Can we foster an interdisciplinary “deep dive” on ethical and conceptual assumptions/foundations of risk estimation and evaluations?
4) With regard to synthetic biology communications what should be communicated to whom (and why) and who decides?

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The Woodrow Wilson International Center for Scholars

November 8-9, 2010

List of Participants

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AGENDA

Societal Issues Arising from Synthetic Biology: What Lies Ahead

Hosted by the Alfred P. Sloan Foundation, the U.S. Department of Energy, and the Woodrow Wilson International Center for Scholars

November 8 – 9, 2010

Meeting Location: Woodrow Wilson International Center (Wilson Center)
One Woodrow Wilson Plaza, 1300 Pennsylvania Ave., NW, Washington, DC 20004-3027)

Meeting Co-Chairs: Lori Knowles, University of Alberta and David Rejeski, Wilson Center

Monday, November 8, 2010

9:00 – 9:30 AM: Welcome and Introductions (*Morning Plenary Sessions in 5th Floor Conference Room)*

9:30 – 10:30 AM: Plenary 1: What synthetic biology is and what it can (currently) do. What are the potential game-changers?

John Glass, the J. Craig Venter Institute (Venter Institute)

Nathan Hillson, Lawrence Berkeley National Laboratory (LBNL)

10:30 – 10:45 AM: BREAK

10:45 – 11:15 AM: Plenary 2: The Evolution of ELSI, where it is today, and how it could respond to Synthetic Biology. What are the potential game-changers?

Tom Murray, the Hastings Center

11:15 AM – 12: 45 PM: Plenary 3: Overviews of ongoing Sloan and DOE Projects (10 minutes for each)

Sloan Foundation Projects:

Wilson Center: Risks Perceptions Associated with Synthetic Biology: David Rejeski

Wilson Center: To ensure safety in the DIYBIO movement: Jason Bobe

Hastings Center: Ethical Issues in Synthetic Biology: Tom Murray or Greg Kaebnick

Caltech: Application of Engineering Metaphors and Concepts in Synthetic Biology: Andrea Loettgers

NAS: International Opportunities and Challenges in Synthetic Biology: Anne-Marie Mazza

Biobricks: Engaging the Synthetic Biology Research Community on Societal issues: Holly Million

Venter Institute: Societal Concerns in Synthetic Genomics: Paul Thompson

DOE Projects:

LBNL: Engineering and Assessment of Fitness and Failure in Genetically Engineered Microorganisms in Simple and Complex Environments: Nathan Hillson

Venter Institute: Managing Risks of Synthetic Biology: Assessing the U.S. Regulatory Systems: Bob Friedman

12:45 – 1:45 PM: Lunch *(Provided by Wilson Center)*

1:45 – 2:00 PM: Instructions to Breakout Groups *(5th Floor Conference Room)*

Questions for all Breakout Groups to Address:

What are the potential uses and applications of synthetic biology?

What is going to be done with this technology?

What are the potential game changers (both inside/directly related to the science and technology, and outside)?

2:00 - 3:30 PM: Breakout Groups

Group 1: 4th Floor Conference Room
Group 2: 5th Floor Conference Room
Group 3: 6th Floor Anteroom

3:30 – 3:45 PM: Break

3:45 - 4:30PM: Report outs from Breakout Groups *(5th Floor Conference Room)*

4:30 – 5:00 PM: Open Discussion

5:00 PM: Adjourn

6:30 PM: Dinner at M&S Grill *(600 13th Street NW; Washington, DC 20005)*

Tuesday, November 9, 2010

8:45 – 9:00 AM: Summary of Previous Day and Instructions to New Breakout Groups *(6th Floor Board Room)*

9:00 – 10:45 AM: Breakout Groups:

1) Legal and economic issues *(6th Floor Board Room)*
2) Societal and public policy issues *(6th Floor Board Room)*
3) Public Acceptance and Understanding issues *(4th Floor Conference Room)*

10:45 – 11:30 AM: Report from Breakout Groups - 15 minutes each *(6th Floor Board Room)*

11:30 AM -12:30 PM: Lunch in Wilson Center Café (*6th Floor*)

12:30 – 1:30 PM: General Discussion *(Meet in 5th Floor Conference Room for entire afternoon session)*

1:30 – 2:30 PM: Summary comments: Perspectives on Societal Challenges from Synthetic Biology and Research Needs

Joyce Tait, the Innogen Center, University of Edinburgh
Lori Knowles, University of Alberta

2:30 – 3:00 PM: Next Steps and Meeting Wrap-up
Meeting Co-Chairs (Lori Knowles and David Rejeski)
Representatives from Sponsoring Organizations (Paula Olsiewski, Sloan Foundation and Libby White, DOE)

Introductory Material from the Chairs:

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We hope to spend November 8th and 9th exploring the unexpected events, innovations, convergences and results that often falls off the table at many workshops -- game changers within and outside the field of synthetic biology that may give rise to new societal issues. Here is some initial food for thought.

Lori Knowles & Dave Rejeski, Co-Chairs

Some thoughts on systemic risks, early warnings, surprises, and disruptions

Systemic Risks

Systemic risks have characteristics that differentiate them from ordinary risks. One of the most important is that actions taken by individual actors or single institutions to address frequent, low-impact events can actually predispose a system to fail when a low-probability and high impact event occurs.[1] For example, the overuse of antibiotics to combat common infections has created a system prone to larger-scale bacterial outbreaks. Parsing, rationalizing, and addressing the risks from synthetic biology in 'safety' and 'security' components or addressing the risks piecemeal though uncoordinated regulations or policy could create and/or exacerbate systemic risks. Disaggregated solutions to individual risks won't add up to effective or lasting solutions, because the risks stem from the interactions within the system and its structural characteristics, i.e., the way we do science or create institutional regimes for regulation.[2]

Predictable Surprises and Early Warnings

Systemic risks often result in a predictable surprise or event "that takes an individual or group by surprise, despite prior awareness of all the information necessary to anticipate the events and their consequences."[3] Many times, people in the field are aware of the problem; it is getting worse over time; and existing policies and behaviors perpetuate the status quo. Not only do we ignore early

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[1] Another example is the construction of levees in New Orleans designed to deal with intermediate storms that failed catastrophically during Katrina, a low-probability, extreme event. From: NRC 2007. New Directions in Understanding Systemic Risks, Washington, DC: National Research Council.

[2] Despite attempts to reform the financial markets, hidden structural flaws at a systems level left us susceptible to the "flash crash" that occurred on March 6, 2010, when the Dow fell 600 points within a few minutes.

[3] Bazerman, M.H. & Watkins, M.D. 2008. Predictable Surprises, Cambridge, MA: Harvard Business School Press.

warnings, but we ignore what have been termed “late and loud warnings.”[4] As former CIA director George Tenet so famously noted prior to the 9/11 attacks, “the system is blinking red." So, are there any warnings in the synthetic biology community that we are ignoring – the red blinking lights (or even yellow)?

Surprises

Then, or course, there are the things we are not even paying attention to, that are outside of our peripheral vision (intellectually or geographically), obscured by cognitive biases, or hidden by institutional restrictions to our thinking. They could have these characteristics:

1. The event shocks us (Wow! How did that happen? Why now?).
2. The event has a major impact on the development of synthetic biology (negative or positive unintended consequences – accelerating the development of the field or putting the brakes on).
3. After the fact, the event would be rationalized by hindsight, as if it had been expected. Probabilities could be run ex post facto, but not ex ante.[5]

In this situation, prediction is not the answer or even possible. We need to figure out how to build robust systems and strategies that mitigate bad things and exploit positive occurrences. What would these systems and strategies look like? Who is responsible for creating them?

Disruptions

When disruptive technologies appear, they often perform at a level that is actually below what is already on the market. This is exactly what makes it difficult to perceive their potential. Think about digital photography versus film; e-commerce versus bricks-and-mortar retailing; classroom educations versus internet-based, distance learning – all greeted with yawns and skepticism. But these disruptive technologies created new market opportunities, especially for people focused on higher performance options, and that is what drove their adoption.

The strategic inflection point occurs sometime after the introduction of the new technology but before its advantages are obvious or market-tested. The new technology does not replace the old, it provides new capabilities. Schematically, this is represented in Figure 1 (based on the work of Clayton Christensen at Harvard).[6] Figure 2 appeared in a recent DOE-supported study on synthetic biology and

[4] EEA 2001. Late lessons from early warnings: the precautionary principle 1896–2000, Brussels, European Environmental Agency, Report No. 22.

[5] Taleb, N.N. 2007. The Black Swan, Penguin.

[6] Christensen, Clayton 1997. The Innovator’s Dilemma, NY: Harper Business.

shows the anticipated performance increase of the enabling tools of synthetic biology compared to traditional recombinant DNA techniques.[7]

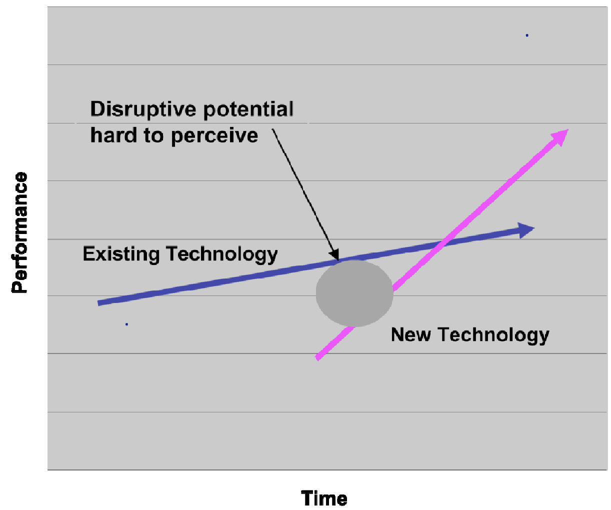


Figure 1

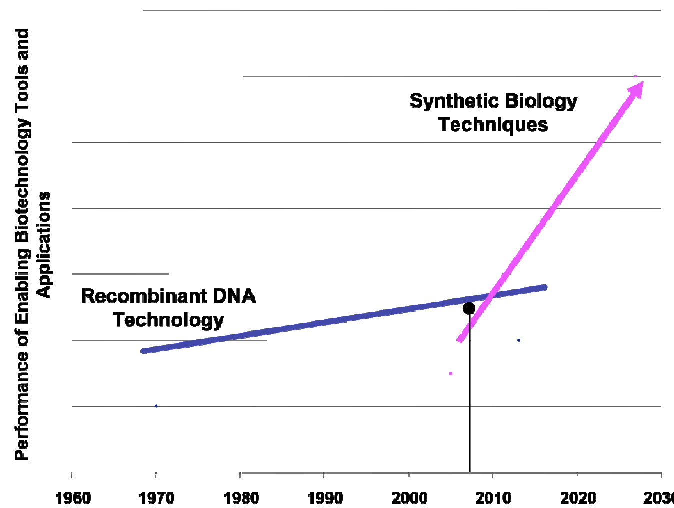


Figure 2

This may look like interesting management theory, but disruptive shifts in technologies can have large implications for governance. Rapid technological change often leaves the science of risk assessment catching up with the risks, outstrips the ability of governments to provide adequate oversight, and leaves little time for democratic deliberation and public dialogue. As Charles Fine at MIT's Sloan School has pointed out, when the "clock speed" of government falls far behind industry, public policies can either become irrelevant or badly designed as policymakers rush to close the governance gap.[8] It makes better sense to assume possible disruptive effects and plan for them rather than react after the fact.

[7] Bio-Era 2007. "Genome Synthesis and Design Futures: Implications for the U.S. Economy, Cambridge, MA: Bio Economic Research Associates, p. 38,

[8] Fine, Charles 1998. Clockspeed: Winning Industry Control in the Age of Temporary Advantage, NY: Perseus Books.

One-Pagers Submitted by Participants Prior to the Workshop

Response to Pre-workshop Questions from Participant 1

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

In a review of previous efforts to regulate emerging technologies, Marchant et al identify five lessons that need to be considered: 1. the central importance of public confidence and trust; 2. regulators should avoid the temptation to impose discriminatory regulatory burdens on new technologies – even if public sentiment weighs in favor of it; 3. oversight frameworks need to be adaptive and flexible to keep pace with rapidly evolving technologies; 4. public concerns tend to have a strong social or ethical element and must be considered by regulators in order for the public to feel its voice was heard; and 5. international harmonization needs to be considered

2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.**

Increasing attention has been paid to concerns regarding biodiversity and the potential synbio has to disrupt the ecosystem. What warnings signs do we need to pay attention to in order for us to understand whether disruptions are occurring?

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**

What is the right balance between public and private sector investment in the construction of genetic material (basic research, tools, etc.) Should the US government be encouraged to have a more significant role?

What is the right IP regime for synthetic biology? Should a commons be created to ensure the availability of standard biological parts?

Response to Pre-workshop Questions from Participant 2

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

I would propose a *non-technical* precedent: During the 1980s university biologists experienced a dramatic shift in the place of intellectual property in relation to their work. In the early part of the decade the role of IP in defining the worth and purpose of biological research was, relatively speaking, minimal for many researchers. By the end of the decade it was common practice for university departments to have IP lawyers on standing contract. These developments underscore the role of cultural, institutional, and political factors in the formation of biotechnical research programs as well as biotechnical researchers. To use an older sociological vocabulary, in the case of biology and IP external constraints became a vector for the constitution of internal conditions. This presses the question and possibility of how institutional demands for the consideration of the ethical ramifications of research might similarly be made an integral part of scientific practice.

2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.**

On several occasions I have encountered what might be cast as a kind of vocational uncertainty among young researchers in synthetic biology. In its simplest form this uncertainty concerns the framing of biological practice in terms of the norms and goals of engineering. A more poignant uncertainty is connected to the defense of research in on instrumental grounds. Although the young researchers I am working with are committed to the goods of health and prosperity, they are unsure how to relate these long-term goods to the curiosity and passion that often animate daily scientific practice.

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**

A) Given the fact that an overwhelming majority of the population in the US identifies with one or another religious tradition, the relation of these traditions to synthetic biology needs to e taken up in a more practical and sustained manner. Such a need should be considered all the more pressing in light of the significant religious lobbies and religiously aligned voting blocs who take the question of religion and biology so utterly seriously.

B) Synthetic biologists, in a fashion similar to other biotechnical and biomedical researchers today, are being asked to simultaneously embody the demands of scientific excellence as well as moral responsibility. In a parallel mode, ethicists and other adjacent researchers are expected to help formulate the terms of responsibility with a deeply informed understanding of current scientific practice. Given that the norms, objects and objectives of research are currently unsettled, the question has arisen: what understandings of responsibility and which pedagogical practices connected to such understandings might be adequate to this double demand?

Response to Pre-workshop Questions from Participant 3

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

Focusing on intellectual property rights (IP), there are many lessons regarding issues that may arise, but fewer lessons over the outcomes that may ultimately obtain and the guidelines that could address adverse outcomes. To draw upon biomedical patents, for example, the nature of the sequencing technology that led to the identification of gene fragments also led to speculation over the promotion of an anticommons, a situation in which large numbers of property rights (patents) might lead to an underutilization of the resource (gene sequence information). This set off a flurry of activity over the precise nature of an anticommons, the potential extension of the anticommons to a patent "thicket," and the general conclusion of a National Academy Committee investigating biomedical patenting that to date patenting issues had not yet significantly blocked access to genomic information for researchers or practitioners. The committee also suggested that they still might serve as roadblocks in the future. Controversy continues, as is illustrated by the recent SACGHS report.

Related, but different, inquiries examined other sectors of the economy, including information technology, nanotechnology, and increasingly synthetic biology. Many such studies have proposed solutions to potential patent roadblocks, ranging from patent pools and related common property instruments to Federal management of key intellectual assets, using Bayh-Dole powers. At present, there is a court case questioning whether information directly derivative from the fundamental human physical makeup should be an appropriate subject matter for patenting. The case is now going to the Circuit Court and perhaps the Supreme Court. More generally, some researchers suggest that patents are appropriate and perhaps necessary for some subject matter/industry structures and not for others. Others suggest that patents, in general, have outlived their usefulness, if usefulness is measured by the need for incentives to motivate creative enquiry, apart from other expected profits. There is no common ground for comparing IP issues among sectors.

At present, the markets anticipated to accompany biomedical innovations have begun to develop but have failed to approach their revenue potentials. As these potentials begin to be realized, incentives will change and the ownership and exercise of IP may yet confound access to key bodies of protected knowledge.

2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.** None apart from those described.

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**

As the field of synthetic biology continues to develop, it presents a body of scientific and technology information with attributes that resembles a mixture of information technology and biomedical science and technology. The topical matter derives from human structure but S&T findings may be more clearly a product of human creation. While some research tools and practices used in synthetic biology research are closely similar to those of biomedicine, others appear more like the computer codes that drive IT applications, and which are subject to copyright rather than patenting. Furthermore, the industry itself has created an information commons intended to block efforts to patent key enabling and other technologies.

At present there is no clear statement of guidelines that could potentially govern intellectual property practices for advanced technologies of different characters. There is likewise no accepted body of validated theory that can be used to predict the consequences for different choices over such guidelines. While it is true that potential profits provide incentives for industry players to accommodate each other's needs, they also provide incentives to enforce IP aggressively.

In my view, research that helps to integrate the various components of the system – the behavior, technology, laws (including case law and USPTO practices) and markets for final products – and to describe how the components interact would be valuable. It is desirable to base policy deliberations on the best possible understanding of the consequences of alternative decisions. This understanding would benefit from a foundation combining social goals, economic and behavioral theory, and relevant data, coupled with key elements of the law and the technologies.

Response to Pre-workshop Questions from Participant 4

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

Cell Phones -- These days nearly everyone in the world has a super computer in their pocket. In the 1960s, decades before the "personal computer" emerged, Douglas Engelbart wrote a letter to Stanford University proposing that their department of engineering hire him to figure out how to develop new interfaces for super computers so individuals might use and benefit from them. He got an indignant response. As Engelbart recollects: "Dear Dr. Engelbart. Thank you for your interest in Stanford. Unfortunately, our School of Engineering is a small department, and we have chosen to focus only on those areas which we feel offer real potential. Since computers are only useful to service entities, we have no interest in developing a focus in them. Best of luck, etc."[9] He got a similar response from Hewlett-Packard. It was hard for people to imagine that one day children and grandparents all over the world would own and operate devices far more powerful than the specialized "super-computers" of their era.

Web 2.0 -- "Web 2.0" catalyzed incredibly productive forms of community-building and collaboration. Practically overnight, loose-knit communities of contributors challenged established media institutions. Newspapers, encyclopedia publishers, and many other forms of life have not yet fully recovered – and they may not. Do lessons exist here for synthetic biology and "institutional science" related to the potential impacts of democratization? Maybe. A more potent lesson, in my opinion, is how Web 2.0 technologies became a new platform for "being seen" in the world. Not only did they enable individuals to spread their identities around cyberspace, some viewed the absence of an online presence as an existential crisis: "If you aren't posting [on the web], you don't exist. People say, 'I post, therefore I am.'"[10]

Synthetic biology has the potential to be a platform for enabling individuals to spread their identities around cellular space. Venter's recent synthetic organism was encoded with the names of the scientists who created it, quotes, and even a web address. How long before Calvin Klein inserts their brand name

[9] http://www.superkids.com/aweb/pages/features/mouse/mouse.html

[10] Wired, December 2006, available online: http://www.wired.com/wired/archive/14.12/youtube.html

into the cotton genome, so each thread in an article of clothing carries their distinctive message? Will a new breed of gardeners emerge that add molecular labels to their varieties of heirloom tomatoes and ornamental flowers? Will bakers and brewers who dabble in molecular gastronomy also develop signature yeast strains and add their own memes to meals?

2) Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.

Yes, the biggest challenge I face on an almost daily basis is how to deal with questions from amateur biological engineers who plan to perform some set of research experiments, but they are not sure how to evaluate the safety of their proposed protocols. There is currently no good place for these individuals to seek guidance and no tools for individuals to evaluate the risks of their research.

3) What urgent ELSI research needs, arising from synthetic biology, can you suggest?

a. We need to refactor existing safety guidelines and best practices so they are understandable to non-institutional scientists, starting with the NIH's Biosafety Level 1 guidelines and other biosafety training materials.

b. We need to incentivize transparency among DIYbio practitioners, so that we can monitor the types of activities being practiced. Furthermore, we need to create interfaces between biosafety professionals and the DIYbio community in ways that individuals are not afraid to ask for help (this helps with both monitoring and mitigating risks).

c. We need to further catalyze and support a "green biology" movement within the DIYbio community. We need to create standards for low environmental impact practices and celebrate those.

Response to Pre-workshop Questions from Participant 5

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

To begin with most of what is called 'synthetic biology' is more recombinant DNA technology but with more advanced *de novo* design and DNA synthesis. Even the most advanced reported examples are not pushing the limits and to my mind, 'synthetic biology'. The challenges of GMO and biotechnology are the best and most aligned with synthetic biology. As an exemplar then the failure to fully disclose and inform the general public on GMOs is most appropriate. There have been many published reports on the mishandling and best practices for GMO should the similar technology emerge again. The major issue is the current state of scientific literacy in the general public. The lack of knowledge in the basics especially those of size and scale confounds a rational discussion on matters that include synthetic biology. The debate is then stripped of facts and any opportunity for most of the general public to assess reality on the basis of mostly accepted biology, chemistry and physics rules. The challenge then is to inform and then advise with the former being accepted as the factual basis for formulating the latter. The contrary position, *synthetic biology is inherently bad* can then be put forth as a premise without regard or adherence to any fact-based foundation. Nanotechnology is most ripe for that kind of opposition movement, the *gray goo* that is posited despite the lack of a factual construct upon which the fabrication of things like nanobots was even possible.

2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.**

No. this is a funny question. I have never experienced discrimination because I have knowledge of synthetic biology.

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**

The trajectories in the ELSI for nano have been toward surveying the public perception/understanding (little) and trying to develop ways to improve science literacy. Among the latter those efforts have predictably fallen into formal and informal education. Formal education is a challenge given the lack of state-wide standards that include area appropriate for nano. Informal education is challenged by the attention span of the general public and competing interests.

Research in this area needs to be pursued to understand what are the best means of informing the general public. The baseline should be (1) the general public has a basic understanding of DNA, (2) they know little about size, scale and the potential for realistic advances in synthetic biology and (3) they will obtain most of their information from public media sources that are not fact-checked in a uniform rigorous fashion. Moving forward then the urgent need is to formulate an approach to provide the general public with a base of information from which they can formulate informed opinions. Then research as well as an executable plan needs to be put into place to reach to a wide general audience regardless of their motivation to be informed. The latter is important because to reach out to only the cognoscenti means losing a wide swath of the general public that has little active interest in science, let alone synthetic biology. In the end what concerns the general public is the benefits to their lives and the risks that might come along with synthetic biology. *Should synthetic biology be used to make a better chocolate cake?* Will elicit a much different response than *should synthetic biology be used to cure cancer?*

Response to Pre-Workshop Questions from Participant 6

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

I agree that there are many lessons to be learned from the introduction of past technologies. At the now defunct Congressional Office of Technology Assessment (where I worked for many years), it was commonplace to solicit insights from colleagues examining different technologies and problems. Some of these lessons were quite technology specific, some much broader in scope. I think the latter (learned painfully from many missteps and mistakes) are the more significant.

Key ones that I try to incorporate in my work: "Inform/fix/address" near-term, hot-button issues first. Further out, perhaps the best one can do is to help put in place a system that can quickly adapt to whatever the future might bring. One cannot forecast the future, but exploring a series of alternative future scenarios (based on plausible, but unknowable, assumptions) often provides the information one might need. Analog technologies and problems are most helpful for stretching the mind, but the particular societal/policy reaction to a new technology depends as much on what is happening in the larger society, as the characteristics of the particular technology or problem. (For example, Sept 11, 2001 completely changed the then nascent societal consideration of synthetic biology.)

2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.**

One of the biggest challenges that this new field faces is how easy it is to let one's imagination run wild and focus on exciting but implausible scenarios, rather than more mundane, but ultimately, likely more important ones for society A recent request from a reporter typifies this. (And I should add that this is not only reporters. Scientists who should know better do this, too.)

> I'm a freelance reporter for (name withheld) magazine, and am on assignment for a piece about DARPA's BioDesign program.
>
> My topic, specifically, is 'what could go wrong?', and the article is exploring/hypothesizing about potential downsides or undesirable consequences of engineering biological creatures designed to live forever. I'm not looking for an in-depth analysis: I'm aiming for a short, interesting think piece. Would you be able to lend me an opinion?

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**

I am grateful to DOE for funding JCVI and coworkers to undertake what I believe is the most urgent remaining research need: a review of the 1986 Coordinated Framework for regulating the products of biotechnology, to examine in detail how well it applies to anticipated technologies and products of synthetic biology.

In general, I think the greatest ELSI research needs are either "client focused" (e.g., for the Congress and Administration, regulation and technology policy) or focused on the societal and policy implications of representative applications of the new technology.

Response to Pre-workshop Questions from Participant 7

1) **Lessons learned from the past introductions of technologies**

This is an issue we are dealing with in our current Alfred P. Sloan Foundation project. There may be some specific lessons that can be gleaned from the introduction of any given technology. At the same time, the specific concerns about new technologies tend to be idiosyncratic to time and place of introduction, and even with the best technology assessments, possible applications (and thus societal implications) may be overlooked initially. So the lesson may be more about the need for flexibility in governance and re-assessing technologies as new issues emerge.

2) **Situations/conversations presenting challenges arising from synthetic biology and society**

The few personal conversations I have had with individuals were generally oriented more toward people trying to figure out where business opportunities might arise (including for the legal community), or more generally, what the applications of synthetic biology will be.
More generally, the potential issue of concern is the jump that many people or institutions (in their roles as journalists, policymakers, a subset of environmental NGOs) make from the science and engineering underlying the emerging technologies to science fiction scenarios. There are serious societal issues that could be at least partially mitigated by synthetic biology, and at the same time a few serious (and obvious) societal concerns that arise from synthetic biology. But these are not the challenges that are pointed out.

3) **Urgent ELSI research needs**

More so than research, the urgent ELSI needs appear to be with respect to practitioners needs. Right now, decision makers (including groups as diverse as research administrators, federal agencies, and international bodies) are confronting specific and general issues surrounding synthetic biology. While not especially large compared with other social science literatures, current work in synthetic biology/ELSI is robust and of high quality. The question is how to get that information to decisionmakers in such a way that they can rigorously apply it in their work.

Response to Pre-workshop Questions from Participant 8

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology?**

   We live in a scientifically illiterate society that is easily scared by hyperbolic propaganda. Consider the failure to adopt genetically modified crops to address many of the world's nutritional needs. Oddly, after 20 years of fighting against adoption of genetically modified plants many in the environmental movement have come to realize that plants designed to thrive in difficult environments have the potential to be the salvation of agriculture in much of the developing world.

2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society?**

   There is a man with an Egyptian email address who has been emailing me for the last couple of years. At first he wanted copies of our papers on genome assembly and genome transplantation. His comments and questions seemed thoughtful and scientifically informed. After our publication about the cell with the chemically synthesized genome in May 2010, his tone changed and he wrote that god would punish me for this work.

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**
   The patent system seems ill equipped to deal with many of the issues that will be raised by inventions of the synthetic biology community. It is not clear that patent laws designed for the electronics industry will be conducive to progress by synthetic biologists.

Response to Pre-workshop Questions from Participant 9

1) Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.

The intention of this question isn't entirely clear to me. What, precisely, is meant by "introduction"?
If the intention were along the lines of "the introduction of the term *synthetic biology*, and what it means, to the public", I would imagine that there are several examples that might be especially relevant. These would certainly include genetic engineering and genetic modification, which in the absence of sufficient public understanding, have developed pejorative connotations, driven by the (often sensible and rational) inherent distrust of the associated corporate interests and motivations behind the underlying technologies, the lack of confidence in safety data resulting from industry-sponsored field trials, and the minimal perceived benefit that these technologies deliver to the public good. I suppose genetic modification would be a lesson in what to avoid doing, and how to frame synthetic biology in such a light so as to mitigate or preempt adverse connotations. Another poignant example would include the field of nanotechnology, which has contemporaneously emerged (or shortly before) synthetic biology. Some of the recent lessons from nanotechnology (here specifically in terms of introducing a new concept to the public) are especially relevant, although since nanotech devices are not alive and do not (yet) self-replicate as living organisms do, synthetic biology faces a different set of challenges and societal concerns. I believe that the Woodrow Wilson Center has already been conducting excellent research along these lines.

If the intention were along the lines of "the introduction of synthetic biological technologies, e.g. organisms, *into the environment*", decades of genetic engineering environmental impact studies, and more recently, nanotechnology environmental impact studies, can serve as very good guides. Perhaps synthetic biology is a slightly different than its predecessors, in that the metrics for "impact" and the new tools required (and now possible) to measure them, have changed with the times and are now quite distinct.

2) Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.

When discussing the engineering of micro-organisms that could be used for consolidated bioprocessing (namely bacteria, archea or fungi that can simultaneously digest cellulosic biomass and produce biofuels or other chemical products of interest), it is often the case that members of the public are (rationally) concerned that if these organisms were unintentionally released into the environment, we could lose control over them and they would decompose all of the plants and trees on the planet. The "dual use" dilemma for synthetic biology, namely utilizing its tools to engineer super-pathogens or biological weapons, is also frequently a concern. To a certain extent, these societal concerns are no different than the worry that the Large Hadron Collider would create a black hole that would destroy our world, the best responses to these concerns are likely very analogous as well.

3) What urgent ELSI research needs, arising from synthetic biology, can you suggest?

I think that that there clearly need to be better metrics and tools available to access the environmental impact of synthetic biological applications, to provide better quantitative data for risk assessment that can be utilized to guide public policy. It would also be extremely beneficial to have an effective public relations campaign around how synthetic biology is contributing to the public good in very tangible and very extensive ways, such as lower fuel costs and cheaper and higher quality medicines and vaccines.

Response to Pre-workshop Questions from Participant 10

1) Pertinent lessons from the introduction of past technologies:

- HGP, "common variants hypothesis," and "personalized medicine": beware emphasizing simplistic solutions and near-term benefits.
- GMOS: beware top-down introduction of a technology. The public needs to be given a voice in assessing the potential outcomes and in thinking about the intrinsic values at stake. "Public discussion" has to mean more than merely "public education."

2) Experiences that raised ELSI issues about synthetic biology:

A recent discussion with a group of environmentalists brought home to me the depth of latent skepticism many people may have about synthetic biology. They had not heard of synthetic biology, and my presentation aimed to describe the field agnostically, but they gravitated very quickly to a critical stance. They thought the potential for harm seemed limitless and the odds of significant social benefit (as opposed to personal benefit) very poor. They viewed the field as private industrial enterprise posing as easy technological fix to problems they viewed as intricate systemic phenomena. They suspected that neither the technology nor the problem was adequately understood by those in the field. They thought it was these gaps in understanding that created the potential for harm, along with the biohazard threat (which they viewed as a near-certainty if the technology became widespread). They were also concerned that creating and altering microbes was an intrinsically unacceptable human activity.

3) Two urgent ELSI research needs arising from synthetic biology:

a) What if we could synthesize people? If technical progress in synthetic biology continues, both the possible consequences and the intrinsic values may require deeper analysis. The synthesis of microbes for contained use in laboratories and factories poses one set of challenges, but as the field develops, other kinds of applications may pose even more complex challenges. These further applications include the synthesis of complex organisms (even humans or humanoid organisms) and the field use of synthetic microbes (such as in environmental remediation and for so-called "geo-engineering," such as the release of synthesized microbes into the ocean to rebuild ocean food chains).

b) Can we steer an industrial revolution? Several speakers at the second meeting of the PCSBI underlined the need for fresh scholarly work on the debate over the precautionary principle and the proactionary stance typified by CBA and risk assessment. This debate is fundamentally about the philosophy of evaluating outcomes: how should a society weigh a new technology? Progress requires better understanding of further questions: What is the right way of bringing together technical knowledge and social values in the process of evaluation? How should that process integrate deliberation by expert bodies with public participation? What may a liberal government legitimately do with those findings? In the context of synthetic biology, these questions are exacerbated by the nature of the risks, which are thought to include low probability but high impact events and broad evolutionary changes in global social and economic relationships. In principle, a society might decide to stop a technology. In practice, it is likelier to want to steer it, to ensure that the outcomes are optimal.

Response to Pre-workshop Questions from Participant 11

1) Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.

I recently co-authored an article identifying five lessons from the history of technology that apply to the regulation of emerging technologies such as nanotechnology and synthetic biology (Marchant et al., *What Does the History of Technology Regulation Teach Us About Nano Oversight*, 37 J. Law, Medicine & Ethics 724-731 (2009)). These five lessons are:

i. Public confidence/trust is the most important criteria for a successful oversight system.
ii. Emerging technologies should be subject to a level regulatory playing field – not subject to more lenient or stringent requirements than comparable products made without the emerging technology.
iii. Regulatory responses must be designed to be adaptive to the rapidly changing technology.
iv. The oversight system must be designed to expressly consider and respond to the public's ethical and social concerns.
v. In a globalized world, oversight frameworks must be designed with an eye toward international coordination or harmonization.

2) Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.

When teaching a course at Vanderbilt law school a couple years ago, a student came up to me in the break and said that he and his buddy (a masters bio student) had bought a bunch of used equipment and were trying to create s design some "new critters" in their garage. He was asking me about regulatory issues – I was bothered by how cavalier and haphazard they seemed to be, but ended up saying nothing.

3) What urgent ELSI research needs, arising from synthetic biology, can you suggest?

i. How to design an oversight site system that will be capable of evolving dynamically in synch with the rapidly changing technology
ii. How should the public's ethical and social concerns about synethtic biology be incorporated into regulatory decision-making?

Response to Pre-workshop Questions from Participant 12

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

Scientists believe in the value of science. They believe that the work they do will create a better world. They don't set out to create suffering through their work. However, when science becomes technology, and it is turned into products, it becomes very hard for scientists to control the outcomes of their work. Agent Orange is an excellent example of this process. The atomic bomb is another excellent example. This same issue is going to stay with us. It is with us now in relation to synthetic biology. In fact, because synbio involves the engineering of living organisms, it is even more imperative that we recognize the gap between science and technology and the gap between intention and reality. We need to involve players from all fields that touch on synbio – scientists, legal experts, policymakers, capitalists, and the general public – early, and we need to shape systems and safeguards to ensure the best outcomes possible.

2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.**

As a non-scientist just starting to work with a nonprofit synbio organization, I am constantly challenged by people's reaction to my describing my job. My friends want to know if I am engaged in genetic engineering! Genetic engineering has gotten a bad name. "Synthetic biology" is also a loaded term and a terrible label for our field. Whose idea was that? Worse, science as a whole has been under attack by reactionary groups who fear its power. If we can't converse with the public about what we do, we face grave obstacles to working toward positive solutions.

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**

We need to work out the foundational technology of synbio. If we make biology easier to engineer, and we create quality, standardized, functionally sound parts, and if we encourage the contribution of these parts to the public domain, we will empower scientists. They will not have to invent the wheel each time they set to work. They can use the basic science to perform higher-level work. By creating common conventions governing synbio and by building a strong community with shared values around the use of the technology, we will minimize the potential negative outcomes from synbio.

Response to Pre-workshop Questions from Participant 13

1) Lessons learned from past technologies

A central theme in Bioethics throughout its history has been ethical, legal and social issues arising with new technologies. Many have been clinical—from respirators and organ transplantation to genetic testing and screening. But not all, certainly not in their early days. The Human Genome Project is the major modern scientific initiative I am most familiar with, having proposed an ELSI program as part of the HGP to Congress in 1988. How effective the HGP ELSI program has been is a matter of contention. From my inside position in its early years I saw a serious effort to (1) identify issues important to the public, to policy makers, and in the views of scholars; (2) analyze and evaluate the significance of candidate issues through a combination of conceptual and normative analyses along with data gathering; (3) shape possible policy responses (as in the Task Force on Genetics and Insurance, EEOC rulings, and GINA). Well-done normative and conceptual work proved, in my view, to be illuminating for the public, policy makers and scientists. A lingering problem is forging fruitful communications and collaborations between social scientists and bioethicists. (Curiously, it has proven much easier to create collaborations between bioethics scholars, basic scientists and clinicians.)

2) Challenges arising from synthetic biology and society

I've found a wide range of responses from great enthusiasm for such a "cool" technology to fear and suspicion. From these reactions, I take important challenges to include: (1) providing the public with an honest, realistic, unhyped picture of synbio that inspires neither unrealistic hopes nor unwarranted fears; (2) clarifying the concerns that people have, which are largely distinguishable into concerns about consequences (including highly unlikely but potentially catastrophic events along with far more realistic and mundane scenarios) and concerns that are not simply reducible to consequences. In relation to issues that become public controversies, I've introduced a distinction between those that implicate mainly *interests* and those that involve *identities.* This distinction has found remarkable resonance among the audiences I've spoken to over the past year. The future of synthetic biology may depend, in some measure, on whether the ethical issues arising with it are seen as more a matter of interests or identities, conflicts around identities being far more resistant to resolution.

3) Urgent ELSI research needs arising from synthetic biology

a) The tools we use to assess and weigh risks and benefits are shot through with assumptions about ethics and values, yet those assumptions often go unexamined. Public discourse and public policy could benefit immensely from a thorough interdisciplinary inquiry into the ethics and values assumptions in the context of synthetic biology that drew on experts in risk analysis, synthetic biology, ethics, philosophy, law and social science.

b) The WWIC survey data show 25% of respondents agreeing that their top concern about synthetic biology is "It is morally wrong to create artificial life." It would be very interesting to learn more about the roots of such beliefs, to identify the underlying assumptions and arguments, and to examine them as interests vs identities concerns.

Response to Pre-workshop Questions from Participant 14

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

Here I would like to draw your attention to an article written by my colleague Helge Torgersen titled "Synthetic biology in society: learning from past experience?" http://www.springerlink.com/content/h81458455710n37n/fulltext.pdf

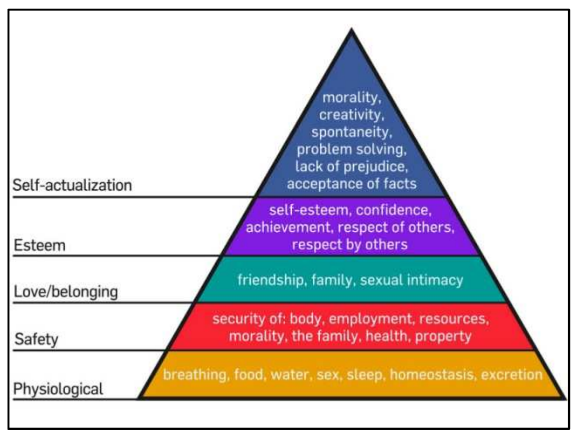
2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.**

Yes, many. We summed them up in "A priority paper for the societal and ethical aspects of synthetic biology". See: http://www.springerlink.com/content/4322114h310x3xu9/fulltext.pdf

Another aspect that seems very important is the way we deal with the uncertainties that appear when thinking about possible future ramifications of synthetic biology for society.

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**

The questions for urgency is in contradiction to the quest for more distant, "over the horizon" issues. I will try to answer both. I think urgent ELSI needs are apparent in the energy sector. Energy related applications of synbio receive by far the highest financial support by public and private investors. Impact of large scale synbiofuel production will be a highly contested area, and relatively little has been done so far to assess upcoming implications (I could elaborate about that during the workshop). For the over the horizon issues, a look at Maslow's Hierarchy of Needs might inspire our thinking. Environmental effects, safety, health issues, biothreat, and bioterrorism can be assigned to the basis of Maslow's pyramid, the very things that we were asked to exclude from our elaborations. In fact, most ELSI work focuses on the lower layers of the pyramid. But over the long term synbio might as well help to express our creativity, enable our spontaneity, and definitely support problem-solving skills. Synbio could easily help/affect our self esteem and self-actualization needs. Doing ELSI while focusing on the top of the pyramid is indeed very different than focusing on the bottom. In addition to avoiding unsafe technologies and unethical behaviour (negative driving forces), synbio can be embraced as a tool to empower people (positive driving forces). With the Science, Art and Filmfestival Bio-Fiction (www.bio-fiction.com) we are actually trying to steer the debate towards that end.



Response to Pre-workshop Questions from Participant 15

1) Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.

Synthetic biology is being portrayed by environmental groups as next generation GM (see the recent report from FoE which echoes the previous report from the Canadian ETC group. European advocacy groups are still as adamantly opposed to GM technology as they were ten years ago. This background is inhibiting research in Europe and the advocacy groups will be looking to extend their influence internationally. Some thought needs to be given to the role of the precautionary principle in enabling pressure groups with ideological motivations to frame new technologies negatively in the public mind. How can we ensure a 'fair hearing' for new technologies? Is this just a European issue or might it become problematic for the US?

2) Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.

Synthetic biologists often refer to the possibility of using 'suicide genes' to provide biological containment to ensure that modified organisms cannot reproduce in a natural environment. These ideas have been around for some time, elsewhere referred to as 'terminator' or genetic use restriction technologies (GURTs). The ideas are politically contentious (for example they are part of the suite of arguments used by NGOs against GM crops). The technology is also banned in international treaties (e.g. Convention on Biodiversity). I have yet to meet a scientist who will argue for it (I think the reasons for this need researching – it seems to be related partly to being seen as an admission that there is a risk that needs to be avoided). If synthetic biology is going to require this technology, we should start preparing the ground now, in terms of scientific, public and regulatory acceptance.

3) What urgent ELSI research needs, arising from synthetic biology, can you suggest?

In my opinion, although ELSI has been useful, it has become stale and routine, and we need a new model to cope with the challenges of new technologies like synthetic biology. Its deficiencies lie in its strong focus on ethics and public engagement to the exclusion of other relevant factors and constituencies. Ethics should be seen as an important part of the picture, alongside other important governance issues, for example the ability of regulatory or technology restraints or incentives to improve the ethical performance of a technology. And ELSI has tended to treat 'the public' as an insufficiently complex voice and to ignore other stakeholder constituencies. For example it has failed to ask the question "Under what circumstances should we allow the strong opinions of one societal group to restrict the options open to others?"

Response to Pre-workshop Questions from Participant 16

1) **Are there lessons learned from the introduction of past technologies that may be pertinent to synthetic biology? Please elaborate.**

I think that there certainly are lessons learned from the introduction of past technologies that may be pertinent to synthetic biology, but that we may be lacking the evidence necessary to discern with accuracy or precision *which* lessons might be applicable in particular contexts. So, for instance, one broad lesson is that societal acceptability of new technologies is context-dependent, rather than technology-dependent. Thus, for example, nuclear technologies are (or, were) largely unacceptable for the generation of power in the U.S., while they generally are/were acceptable in the realm of medical diagnosis and treatment. On the other hand, it may be the case that the "synthetic" attribute of synthetic biology may raise ethical and societal concerns regardless of its application—at least for some lengthy period of time. This statement links to another lesson, that some attributes of technologies may make them controversial regardless of their application. Both of the above examples lead to lesson 3, that the issues and conditions of acceptability associated with technologies and their applications may shift over time, as knowledge, conditions, and experiences change. Lesson 4: the issues/concerns associated with new technologies tend to be variable, conditional, and *not* uniform within or across populations or geographic locales (said otherwise, the same technology sometimes has been accepted and sometimes has been rejected in seemingly similar circumstances). Lesson 5: experiences—particularly negative experiences—associated with a technology may "spill over" to affect issues/concerns attached to (a) later applications of the same technology used for the same purpose; (b) applications of the same technology in other contexts; and (c) applications of similar technologies in a variety of contexts.

2) **Have you experienced or encountered any situations or conversations that presented you with any challenges arising from synthetic biology and society? Please elaborate.** No.

3) **What urgent ELSI research needs, arising from synthetic biology, can you suggest?**

Given that synthetic biology research is being conducted by government, academia, and private sector organizations simultaneously, (a) who is responsible for moving research to use; (b) what rules apply to whom; and (c) what are the implications of alternative answers to the preceding questions for different subsets of the population, society at large, and the environment?