Engineering Biology for Science & Industry: Accelerating Progress

Executive Summary

Nancy J Kelley & Associates, The Woodrow Wilson International Center for Scholars, and The Alfred P Sloan Foundation

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Prepared by Feinstein Kean Healthcare

Overview

The U.S. has been a world leader in the emerging field of engineering biology, producing more high-impact foundational and translational research – and commercial products – than any other nation. Technical advances in the field continue to open up new possibilities in healthcare, agriculture, chemicals, energy, and bioremediation, promising potential solutions to pressing global problems. With an expected market value of $10.8 billion by 2016, engineering biology will play an important role in the bioeconomy and holds increasing implications for future global employment and competitiveness.

The Synthetic Biology Engineering Research Center (Synberc), established in 2006, was an early U.S. endeavor designed to lay the foundation for the field and nurture the development of the industry. Despite its early success in coordinating the scientific community and building industrial relationships, Synberc will sunset in 2016 when the organization's National Science Foundation grant expires. At that time, new leadership will be required in order to bring the community together and continue to drive the field forward.

On April 17,2015, emerging and established leaders of engineering biology came together at the Alfred P Sloan Foundation in New York City to lay the groundwork for accelerating progress in this highly important field. The success of such an endeavor lies in the ability of the public, private, philanthropic and academic sectors to work together on foundational and applied research, industry collaboration, infrastructure, policy development, education, and public engagement, amongst other topics, with a special emphasis on how to mobilize the resources the community needs to realize its potential. The Agenda setting forth the topics discussed is attached as Appendix A to this executive summary of the meeting.

Attendees included nearly 60 scientific, business, governmental and philanthropic leaders with a strategic interest in the development of the field. Industry representatives included instrument and tools providers, as well as start-up and mature companies engaged in the development of products for a variety of industry segments, including specialty chemicals, energy, agriculture and bioremediation. Although not every perspective on every topic discussed throughout the day could be captured, the most common themes discussed are represented in this executive summary.

This conference was an outgrowth of a one-year sustainability initiative led by Nancy J Kelley & Associates (co-funded by Synberc and the Alfred P. Sloan Foundation). The purpose of the initiative was to develop a strategic action plan to advance the field of engineering biology in the U.S. More information about this effort can be found here: http://nancyjkelley.com/engineering-biology/. Information about additional topics on engineering biology can be found here: http://www.synbioproject.org.

Engineering Biology for Science & Industry: Accelerating Progress was a one-day conference co-sponsored by the Alfred P Sloan Foundation, the Woodrow Wilson International Center for Scholars, and Nancy J Kelley & Associates. This meeting report is available to the public at http://nancyjkelley.com/engineering-biology/ and http://www.synbioproject.org. Check back regularly for videotaped interviews with meeting participants.

State of the Field of Engineering Biology

Four panels were held during the morning session in which both seasoned and emerging leaders from various communities, including academia, the public sector, industry, and Do-It-Yourself biology (DIYbio), provided their insights on the state of the field of engineering biology. The common themes that emerged from these discussions are summarized after significant, specific comments for each panel are noted.

State of the Field: Industry Trends, Future Challenges and Potential Solutions

This panel focused on the accomplishments of the last ten years in synthetic biology and what remains to be done.

- A history of the science, which ultimately gave birth to synthetic biology, described the evolution of the Human Genome Project from its birth in the Department of Energy as a moonshot program for biology to its adoption by the National Institutes of Health (NIH). The resulting public/private race between the NIH and Craig Venter to complete the sequencing of the human genome sparked the notion of discovering a minimal genome, triggering the birth of synthetic genomics. It also marked a transition in scientific approaches, from the single principal investigator managing a small RO1 grant to large, multi-disciplinary teams using instrumentation and high performance computing to create breakthroughs.

- The National Science Foundation (NSF) is an independent U.S. government agency responsible for promoting science and engineering through research programs and education projects. NSF's two major priorities focus on improving the fundamental understanding of biology and developing biological processes and products in order to impact global problems of sustainability and stimulate economic growth. Engineering biology fits with these priorities perfectly by fostering the creation of new knowledge, materials and processes at the intersection of biology and engineering. NSF programs focus on four broad categories of activities: (i) increase the fundamental understanding of materials and systems at the intersection of physics, biology, engineering and computer

science; (ii) enable the design and production of biological toolkits; (iii) generate reliable scientific knowledge that can advance the policy debate; and (iv) educate the next generation of scientists and engineers. NSF wants to enable the scientific community and participate in global activities around engineering biology. It has made one of the largest investments in the field to date – through the Engineering Research Center program.

- DIYbio is synthetic biology's biggest fan. The DIYbio community began with a small meeting of 30 people at Asgarth's Pub in Cambridge, MA. Two years later that small meeting had turned into a global movement dedicated to creating unconventional innovators through public engagement in science and technology. From this movement grew the concept of the community lab where people pay a monthly fee to get access to scientific infrastructure. There have been numerous achievements and accomplishments in DIYbio, which has attracted not just amateurs and citizen scientists but also independent scientists in nontraditional career paths who are looking for new ideas and training. This community has tremendous potential as a forum to educate and as a source of innovation. Unfortunately, the community caught the attention of the FBI in a post 9/11 world, which heightened awareness in biosecurity and caused much confusion about what DIYbio is and could be.

Visions of the Future: Insights from the Next Generation of Scientific Leaders

In this panel discussion, younger investigators commented on their hopes for future developments in engineering biology, what they hope to accomplish with their work, what excites them… and what worries them the most. All of them were extremely excited and hopeful about their work and the potential of engineering biology to contribute to global sustainability. Concerns focused on how to define a moonshot program that would attract funding, build infrastructure and tools, organize a strong community, and educate people about the value and importance of what they are doing. Several panelists discussed the need for public engagement and finding the language to accurately and positively communicate engineering biology.

Innovation Starts Here: Startup Companies that are Changing the World

The fledging field of synthetic biology has begun to spawn a number of start-up companies (featured on this panel), with revolutionary ideas aimed at solving some of the planet's most fundamental problems. The founders of these companies talked about the challenges of creating products that are 'transformationally' better (meaning an exponential improvement) to what exists today and the public perceptions they must manage in order to innovate.

The Promise Delivered: Disruptive Innovation from Concept to Market

Many mature companies are also working in this area and are bringing products to market in spite of the challenges and difficulties. Nevertheless, the challenges are daunting. When an established company is presented with and considers adopting a new technology, a number of factors are taken into consideration. These factors include the scale up potential, the size of investment needed, the regulatory environment, and the ability to operate freely without intellectual property challenges.

The ability to gain public trust is also critical for the success of the field, and the need for transparency cannot be over-emphasized. The research community needs to talk about what they are doing and why, highlight the promise and benefits of engineering biology, and stress the field's successes. Small groups can have powerful voices. The following rule of thumb was provided as a guide: one-third of time should be spent listening; one-third of time spent articulating what you do; and one-third of time spent thinking about what you heard in response.

Common Themes

In addition to the specific comments described above, some common themes emerged from these four sessions.

Industry Trends

Engineering biology is at the early stages of a technological revolution that will transform several markets, including energy, agriculture, healthcare, chemicals and bioremediation. A number of industry attributes and trends that are proving unique to the field were discussed, with the democratization of science as one of the most noteworthy. Included in this trend are the DIYbio and open source movements, as well as crowdsourced problem solving. Unlike previous waves in the biotechnology industry, the DIYbio movement is producing 'citizen scientists' and unconventional innovators; the open source movement is making foundational tools and technologies accessible to all; and crowdsourced problem solving is allowing *anyone* to participate in engineering biology problems virtually *anywhere* in the world.

A palpable shift in the funding environment is also driving new trends within engineering biology. With a reduction in NIH funding, scientists are increasingly relying upon the private sector, including philanthropic donations from wealthy individuals and organizations such as the Alfred P. Sloan Foundation, as well as crowdfunding to fill the gap.

Current Challenges

One of the biggest challenges facing engineering biology is that of maintaining U.S. leadership in the field this country has pioneered. With the sunset of Synberc scheduled to take place in 2016, the entire ecosystem will face a leadership gap and will need to organize itself in new structures to ensure continued responsible advancement of the field. These efforts will need to encompass educating and funding the next generation of scientists and their 'moonshot' projects, building and funding common infrastructure, and making the infrastructure more accessible to a broader research community, beyond just the top-tier academic centers where it has been advanced to date.

Additional challenges for the field will center on managing public perception, overcoming technological hurdles, and navigating regulatory oversight. The field is currently grappling with negative publicity (e.g., Africa's agricultural industry is "under threat") and long-standing public anxiety over GMOs. Clearly, it is advisable to avoid the strategies and negative results that occurred in the GMO arena. Moreover, it is very important to address the current technological hurdles, including the ability to

turn sequencing data into knowledge, and reducing the lengthy design, build, test, learn cycle for engineering metabolic pathways and networks. Finally, the looming regulatory challenge is to ensure that regulators have a strong foundation by which to understand the science and technology, so that that they can approach their regulatory role in an informed and methodical way. The latter will also intersect with the public perception issues, since government regulation is one component of public trust.

Potential Solutions to Advance the Field

A national organization could be created to fill the looming leadership gap within engineering biology prior to the sunset of Synberc in 2016 to avoid any disruption or gap that would prolong splintering or diffusion of effort. Such an organization could convene the entire community – including industry, academia, DIYbio, philanthropy, the general public and government – to create research infrastructure, advance policy, prioritize the development of tools, technologies and research, educate the next generation of scientists, and engage the public. With industry engagement, this organization could also nurture a community of entrepreneurs that straddles science and business to help accelerate translational research towards safe and productive commercialization of societally valuable products.

Moreover, such a national organization could invest in planning and implementation. Such an effort could be inclusive of all the constituencies in the ecosystem, intended as a long-term effort modeled on the biotechnology field to ensure an informed national dialogue and gradual acceptance of the science, technology, and emerging products in the field.

H.R.591: The Engineering Biology Research and Development Act of 2015

The "*Engineering Biology Research and Development Act of 2015*", a bipartisan bill sponsored by Rep. Eddie Johnson (D-Tx) will provide for a coordinated Federal research program to ensure continued U.S. leadership in engineering biology. The bill codifies a number of elements in the national bioeconomy blueprint and lays the foundation for a national strategy that will maintain U.S. leadership, retain engineering biology jobs, and avoid duplication of efforts. This is an authorization, not an appropriations bill, so there is no funding behind it at present.

If passed, the legislation will create a national program that could provide research grants for individuals, teams and centers; education and training for undergraduate and graduate students; mechanisms for tracking and quantifying the outputs and economic benefits of the field, and activities to accelerate the translation and commercialization of new products, processes and technologies. Program activities will take into account ethical, legal, environmental, and social issues, including the need for safeguards and monitoring systems. The bill will also establish an inter-agency committee on engineering biology.

Many within the community hope that passage of the bill will offer larger companies greater confidence – and spur investment – in engineering biology. Even if the bill does not pass, it will serve to elevate the conversation about this important field across Federal agencies and serve as a call to action towards the acceleration of engineering biology.

A Center of Excellence for Engineering Biology

In 1997, Craig Venter wrote that if the 20th century was the Century of Physics, the 21st Century will be the Century of Biology. Just fifteen years in, engineering biology has become a part of this nation's innovation narrative. The field is still in an early stage of development, presenting a unique opportunity to direct its growth in a coordinated manner. There is a real need to resolve open questions about intellectual property, funding, education, safety and regulation in order to maximize the field's potential.

Nancy J Kelley & Associates conducted a comprehensive strategic planning process with the engineering biology community in 2013/14 (co-funded by Synberc and the Alfred P. Sloan Foundation). This process identified a number of community needs in the near future, including the following:

- A research community that continues to lead the development of both foundational tools and applications
- A growing portfolio of commercial successes and industrial collaborations
- Funding for projects that maximally advance the field and mechanisms that connect these projects
- Another generation of researchers and advocates

- A research community trained in responsible innovation
- Public engagements that inform and build support for the goals of the synthetic biology community, both nationally and globally
- A shared vision, roadmaps, and execution strategies to achieve all of the attributes listed above
- Transparent regulatory environment that clarifies framework of regulation
- International collaboration

In addition, there is the need to establish and strengthen a common infrastructure that would be open to and support the efforts of the national and international engineering biology communities.

One common theme that emerged throughout the strategic planning process is that the public sector could, but has not yet, taken the lead in this sector. Other countries like the United Kingdom, have a more engaged public sector. Since we are currently in the midst of an election cycle, it is important to organize in a manner that will attract stronger public sector support in order to accelerate the field.

A national nonprofit Center of Excellence for Engineering Biology, dedicated to the above activities, would represent a visible, stable, accountable and long-term commitment to advancing synthetic biology in the public interest, sustaining U.S. leadership in this area and fostering global cooperation. This meeting will be followed with a proposal for a new national Center of Excellence. The proposal focuses on three key areas during an initial 6-month planning process:

- Content and Community
- Infrastructure Technology and Industry Engagement
- Roadmaps and Planning, which will be driven by all organizations represented at the meeting, and by those individuals and organizations that have already started working on the challenges that need to be addressed

There are a number of trends that will support these efforts.

- Changing ways science is done – the democratization of science
- Increasing strains on the way science has traditionally been done
- An evolving landscape of stakeholders

- Shifting funding environment, and
- State of the industry itself

Roadmap Planning

A number of panels were held during the afternoon session that focused on roadmap planning for the field. A number of common themes emerged from these discussions.

Responsible Innovation: Foundational and Applied Research

Responsible innovation is a design challenge. The research infrastructure must be designed to responsibly support and advance these emerging technologies. Yet, the decentralized means of production in this field is fundamentally challenging the structure of our institutions, which cannot work effectively in this field in the traditional command and control / hierarchical way. New decision-making processes should be established that allow communities to make important decisions.

One illustrative example of the challenge is when researchers realized that the flu could be engineered: they immediately had to determine how this information should be released, or whether it should be released at all. This event prompted the realization within the community that adequate mechanisms have not been put in place to control certain levels and types of scientific information. As a result, new policies were implemented by the NIH – dual use research of concern – that holds individual researchers accountable for investing in the safety and security of their work and for determining whether their technology can result in a security threat. However, such issues are hugely complex and potentially daunting for self-governance by individual researchers, and will most likely require a community-based approach. Clearly, the field needs to have a decision-making process that encompasses foresight, expertise, and a setting for community discussion.

Infrastructure of the Commons

An Infrastructure of the Commons (IOC; instruments, tools, integrated processes, intellectual property, integrated federal funding, oversight, standards, etc.) should be

created and shared with the engineering biology community to accelerate progress. One approach to consider is the creation of a non-profit organization to build the public research infrastructure that is required for the broader scientific community. Successful non-profit models have been developed in the U.S. and Europe. For example, The Jackson Laboratory began as a distributor for mouse models (JAX® mice) and has since become the leading mammalian genetics research center as well as supporting global biomedical research. In an era of limited federal resources, innovative approaches to finance the IOC will need to be identified.

With respect to intellectual property (IP) versus open source, a tipping point may have been reached already, where IP is less important than alleviating a key bottleneck step for important endeavors, such as healthcare. However, the community as a whole will have to decide on the best model for the field. Open source as a development model may be the best approach at the early stages of development so that everyone can freely innovate, but the community is also responsible for translating these discoveries into commercial products with the freedom to operate. Key questions such as "*When do the rules change*?" and "*How do they change*?" will need to be answered by the community in the near future.

Policy Solutions

The field of engineering biology is moving very rapidly, with significant uncertainty in how the technology will unfold and what effects the technology will have on the environment and health. Thus, there is an acute need for the community to focus on risk assessment and risk management in order to establish appropriate policy frameworks. These frameworks will require the potential for adaptation and learning to allow for updates in policies as our understanding of the risks and benefits evolve. The forces against learning and adaption can be quite strong, however, for a number of reasons. For example, industry may be reluctant to embrace change in the regulations within which they have been working, and regulators may be reluctant to embrace change that may impugn the correctness of prior policies. In addition, the general public can become skeptical when changes are made due to a 'new' view of the science (e.g., changes in dietary standards or disease screening guidelines), which can in turn negatively affect public perceptions and acceptance of the entire field. Regardless, it is essential that provisions be built into policies for the systematic collection and integration of new information as it emerges, so that it can be used to update and revise regulations.

Funds are flowing in for applications of engineering biology from a variety of funding sources, but the areas that tend to be underfunded are the development of tools, policies and ethics, all of which are needed for the field to advance. In addition to funding, there is a critical need for education of budding entrepreneurs and policymakers. Entrepreneurs, especially those from academia, require education on the regulatory and legal infrastructure in order to get these innovative products to market quickly. A formal structure also needs to be in place to educate policymakers on the science and technology of engineering biology to ensure that they understand the field well enough to develop appropriate policies. One recommendation for funding such activities is to initiate a model based on the concept of user-funded government regulation, such as the Prescription Drug User Fee Act (PDUFA) for FDA.

Finally, regulations and access to data, intellectual property, privacy and informed consent are key factors that determine where innovative developments take place. If the U.S. is to maintain leadership in this field, it must have a place at the international table. For example, the U.S. has signed but not ratified the treaty for the Convention on Biological Diversity (CBD) and is therefore precluded from ratifying the Nagoya Protocol. As a result, the country is prevented from assuming its natural leadership role in these important international standard-setting activities.

Industry Engagement

There is a phenomenon in biomedicine, known as the 'valley of death', in which many scientific discoveries languish for lack of support from either government or industry – in essence, when the discovery is too far advanced for government/academic support and infrastructure, but not developed enough for traditional industrial investment and involvement. Sometimes, such discoveries are delayed for many years, and in some cases are *never* translated into a commercial product. This sobering situation is partially due to the fact that commercialization requires a different set of skills and expertise that are not readily available in the academic laboratory setting. New types of institutions that offer industry involvement can offer an evolving career path for young scientists – and hence ensure the translational success of more scientific discoveries. For example, Synberc's research program includes synthetic biology's leading academic and industrial scientists and researchers. As a result, a very high percentage of Synberc scientists – approximately 50 percent – go into industry. The New York Genome Center (NYGC), a consortium of academic, medical and industry

leaders from across the globe, also serves as a model for industry involvement. Before launch of the NYGC, New York City was not a bioinformatics hub; today, there are hundreds of bioinformaticians working with the biomedical community there to translate genomic research into clinical solutions for serious disease.

Within engineering biology, the promise of industry engagement is to accelerate solutions to the most challenging problems. Industry players such as Autodesk are focused on turning the design of biological systems, which has mainly been a hands-on craftsman approach, into one that is digital and automated. Companies such as Gen9 are trying to incentivize innovative thinking and the development of new applications among academics and startups by giving away at least one million bases each year. Others, such as New England Biolabs that develop enabling reagents and technologies for the field, are engaging directly with the engineering biology community to identify their needs and then pointing their development engine towards meeting those needs. Ultimately, the field needs industry support to help develop the tools that will enable large-scale biology.

Building the Trust Infrastructure

The community can only build trust only by earning it in a long-term process of transparency, engagement, and addressing concerns. The scientific community needs to talk about what they are doing and why, and for what potential clear-cut benefits to the public. While there are numerous examples of scientific endeavors that have gained public trust, there is an unfortunate legacy of mistrust around GMOs, and in some cases an "us/them" attitude between scientists and the public that needs to be mitigated. Organizations such as Genspace can be extremely valuable in these efforts.

The history of the biotechnology industry in healthcare can be illustrative. Initially, there were concerns among both the scientific community and the public about the potential risks of the new recombinant DNA approaches. The Asilomar Conference on recombinant DNA (1975) was held by concerned scientists, followed by years of discussion, debate (much of it convened by an industry organization), and finally consensus on what regulatory framework and standard protocols would be needed to ensure biosafety and public trust. In addition, an ecosystem of professionals, comprised of scientists, attorneys, communications professionals, journal editors, top-tier journalists, and business executives, all worked together for decades in the biotechnology field to ensure that scientific advances were reported in the scientific

literature, and then disseminated to the public in a methodical and accurate way that would build credibility. As a result, biopharmaceutical products have become accepted as an integral part of healthcare.

Today's environment, however, is quite different from what existed during the emergence of the biotech industry, including such factors as:

- The existence of an active, engaged citizen science community that is able to embrace and practice these technologies outside regulated laboratories;
- The existence of a citizen journalist community that is actively engaged in public and online in conversations on engineering biology;
- Communication vehicles that are more varied and complex than they were in the early decades of the biotech revolution, making it far more complex to stimulate and inform the national dialogue around engineering biology; and
- Traditional credibility-building techniques, such as the presence of articles in top-tier newspapers, have weakened, giving way to a plethora of news sources and opinion drivers that are completely de-centralized.

To address these challenges, a communications strategy for the entire field, with coordinated effort, is greatly needed to help inform the public; stimulate a national dialogue; and overcome the misperceptions that will inevitably arise. Moreover, such a strategy will have to be consistent, long-term, and woven into the entire community, since the engineering biology field will develop over many years.

In the meantime, it is very important for the community to engage in the social conversation aggressively, describing with credibility and authority what they are doing, why they are doing it and why is important.

MEETING AGENDA

ENGINEERING BIOLOGY FOR SCIENCE & INDUSTRY: ACCELERATING PROGRESS

April 17th, 2015

MORNING SESSION

8:00 – 8:15	Welcome to the Sloan Foundation
8:15 – 9:15	State of the Field: Industry Trends, Future Challenges and Potential Solutions
9:15 – 10:00	Visions of the Future: Insights from the Next Generation of Scientific Leaders
10:00 – 10:15	BREAK
10:15 – 11:00	Innovation Starts Here: Startup Companies that are Changing the World
11:00 – 12:00	The Promise Delivered: Disruptive Innovation from Concept to Market

LUNCH

12:15 – 1:00	H.R. 591: The Engineering Biology Research and Development Act of 2015

AFTERNOON SESSION

1:00 – 1:30	Accelerating Progress: A Center of Excellence for Engineering Biology

ROADMAPPING

1:30 – 2:30	Responsible Innovation: Foundational and Applied

	Research
2:30 – 3:15	Infrastructure of the Commons: Defining and Building the Foundational Elements
3:15 – 3:30	BREAK
3:30 – 4:15	The Path Forward: Policy Solutions to Responsibly Advance the Field
4:15 – 5:00	Industry Engagement: Technology Development, Applied Research and Commercialization
5:00 – 5:45	A Foundation of Trust: Content, Community and Public Engagement

WRAP-UP AND NEXT STEPS

5:45 – 6:00	Nancy J Kelley
6:00	Wine Reception (Alfred P Sloan Foundation)