

Commentary

The Promise and Challenge of Engineering Biology in the United States

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Introduction

Synthetic biology—the design and construction of new biological parts, devices, and systems, and the redesign of natural biological systems for useful purposes—is contributing sustainable and innovative solutions to numerous, pressing human needs and global challenges.¹ First established as a scientific discipline around 2000, technical advances in the field continue to open up new possibilities in healthcare, agriculture, chemicals, materials, energy, and bioremediation. With an expected global market of \$10.8 billion by 2016, synthetic biology will play an important role in the bioeconomy and has increasing implications for future US competitiveness and employment.²

How far the US, as a nation, can go with this technology depends on our ability to bring together diverse researchers and stakeholders with a big vision, carefully considered strategy, and the support to carry it through. The frontier is still just beginning to be explored, and there is much to be done to fulfill the promise of engineering biology safely and responsibly.

Synberc: An Early US Initiative

The Synthetic Biology Engineering Research Center (Synberc, Emeryville, CA; www.synberc.org) was launched in 2006 as an early US endeavor to develop the foundational understanding and technologies needed to build biological solutions as an engineering practice. Its primary financial support has come from the US National Science Foundation's (NSF's) competitively awarded Engineering Research Center (ERC) Program, which unites academia, industry, and government in the pursuit of technological advances that have the potential to create or reinvent industries. The ERC program represents a 10-year funding commitment, with Synberc's NSF funding due to end in 2016.

Synberc was created with two audacious and related goals:

- To create a new field of synthetic biology
- To build an industry around it

Within a very short period of time, it has accomplished both. Upon the foundation laid by Synberc and others, synthetic biology is establishing itself as an important new discipline, with the US leading the world in intellectual conception, research, and commercial development.^{2,3} Many new research centers and programs have been launched in the US, resulting in fundamental advances, including highly multiplexed genome engi-

neering, rational design tools, standardized parts and registries, and engineered cell traits. Such advances have led to the tripling of companies in this emerging industry in the last 4 years, with products on the market and in development pipelines including specialty chemicals, enzymes, synthetic genes and other DNA parts, pharmaceuticals, biofuels, and chassis microorganisms (organisms that host the engineered biological machinery).⁴ Early commercial successes will likely include microbially produced malaria drugs, biofuels from non-food biomass, and rapid vaccine production.

From its early beginnings in 2006 advancing an unproven concept, with 12 principal investigators at University of California Berkeley, Harvard University, MIT, University of California San Francisco, and, later, Stanford University, Synberc has gone on to help shape the research agenda of the field. It has advanced numerous foundational technologies, served as an important venue for convening researchers throughout the synthetic biology community, and developed programs to ensure that science in this area is conducted safely and securely. Synberc has also led the effort to attract industry support and participation, help train many of today's synthetic biology leaders and investigators, support the development of global training initiatives (e.g., iGEM, www.igem.org), and highlight the viability of commercial applications for synbio technology. Synberc has built an infrastructure (through registries, repositories, "fabs" [biological design-build facilities], software tools, new scientific centers, and numerous affiliated organizations) that supports constructive competition and the production of tools and knowledge needed to advance synthetic biology responsibly and productively.

Through these numerous achievements, Synberc now stands at the center of the synthetic biology field and community. Its collaborative and educational work is accomplishing what would simply be impossible through a narrow or individual approach. It has directed a community-wide effort to create a transformative new discipline applying engineering design to the practice of biology and has brought together and trained researchers from across multiple disciplines to work collaboratively in this effort.

The Next 10 Years: What Is Needed?

As NSF support for Synberc ramps down, ceasing entirely in 2016, new funding sources and a new approach will be needed to organize, fund, and propel this growing synbio community over the next decade. Continued leadership will be required to pull together all the elements of the synthetic biology community—people, ideas, and material—and cooperatively shape them into a coherent strategy. Absent that, the momentum that Synberc has created may be lost, allowing the community to splinter. At

the same time, other countries (the UK and China, in particular) have demonstrated their understanding of the field's potential, with clear national strategies and large coordinated investments. The US thus must act quickly or risk falling behind in an industry and research sector that it has pioneered. Now is the time to bring together the public and private actors to create a new national organization to lead synthetic biology in strategic directions consistent with US national priorities and values.

Foreseeing this challenge and opportunity, in July 2013, Synberc, with support from the Alfred P. Sloan Foundation, initiated a 1-year independent sustainability initiative led by Nancy J. Kelley & Associates (NJK&A) to develop a strategic action plan to extend the efforts begun by Synberc and advance the field of synthetic biology in the US. Initial findings and recommendations were summarized in a report published in February 2014 (<http://bit.ly/NJKAsynbio>; see the Industry Report "Engineering Biology to Address Global Problems: Synthetic Biology Markets, Needs, and Applications" in this issue of *IB*, pgs 140–149). It is intended to explore the emerging synthetic biology market and the global synbio landscape, including regulatory frameworks, funding initiatives, and social and ethical aspects. That report places Synberc within these contexts and examines its relationship to the past, present, and future of synthetic biology, highlights the potential of synthetic biology and its explosive growth over the last 15 years, and illustrates many of the social and ethical implications, regulatory and funding challenges, and issues of public perception and acceptance.

The findings contained in that initial report and in related project documents are the product of a broad range of primary and secondary research. NJK&A conducted over 110 interviews with members of the Synberc community (including Synberc Principal Investigators, members of the Strategic Advisory Board, and representatives of the Industrial Advisory Board), and members of the broader synbio community, along with numerous follow-up conversations. The team augmented these interviews with extensive secondary research and review of a library of nearly 500 reports, journal articles, presentations, and government and public documents, as well as attendance at major synbio events and targeted regional visits to relevant institutions. Finally, NJK&A engaged Synberc on a community-wide basis, beginning with the presentation of a preliminary set of findings presented to nearly 300 members of the Synberc community and invited guests at a Synberc retreat in September 2013, followed by a moderated discussion among 60 members on the final day of the retreat. These efforts culminated in the creation of nine working groups comprising 100 participants that met once monthly for three months, from October through December 2013. These discussions helped to frame the recommendations in the report, which the Synberc community met in January 2014 to consider, followed by a more detailed discussion at the Synberc retreat in March 2014.

If the growth in synthetic biology over the past 15 years is any indication, the growth over the coming years stands to be even more significant. During the next decade, for the US to continue to make progress toward Synberc's original audacious goals and serve as a catalyst of synbio progress, the synthetic biology community will need a strong central organizing force going

forward that can support this community, grow its leaders, and serve as a mobilizer of researchers, industry, government, and philanthropy. This will require:

- 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, nationally and globally
- A shared vision with roadmaps and execution strategies to achieve these

Synberc must evolve into an entirely new organization—one that will flourish through a strong set of relationships with industry partners, governmental agencies, academic institutions, philanthropists, community organizations, and the general public, both in the US and globally. Its mission would be to create "biologically engineered solutions for a sustainable future." A new organization would engage in pioneering research, in which scientists from many disciplines gather to collaborate on some of science's most challenging problems. It would provide a national and global resource to support diverse stakeholders for the benefit of many programs.

Such an organization must be designed to build on the strengths that Synberc has demonstrated, while recognizing and serving the changing scientific, regulatory, and public landscape in both national and global environments. This organization would need:

- The right structure to manage and solve issues of the "commons" such as intellectual property policies and guidelines
- Incentives to provide solutions or capacity that will benefit the larger community
- An extension of best practices from Synberc and other organizations, in a way that will maximize value
- A shared infrastructure to catalyze innovation for academic institutions and commercial entities
- A national roadmap to provide strategic direction that can be defined, implemented, and reported on
- Support for better-coordinated funding among agencies such as NSF, National Institutes of Health (NIH), US Department of Energy (DOE), Defense Advanced Research Projects Agency (DARPA), and National Institute of Standards and Technology (NIST)

The new organization envisioned would establish and strengthen a common infrastructure that would be open to and support the efforts of the national and international synthetic biology communities, which would include a fully integrated, rapid design and prototyping infrastructure that spans design tools and includes scalable, automated, and parallelized design fabrication, high-throughput evaluation, and validation that would close the gap between the laboratory and commercial applications. It would strengthen early efforts to foster industry

collaboration and technology transfer, build on educational programs and accomplishments, engage public discussion about the risks and benefits of synthetic biology, and work with regulators to implement clear and transparent regulatory regimes. Finally, it would serve as an important participant in international and policy efforts to solve global challenges.

Conclusions

Synthetic biology in the US is an undervalued asset in a field that has not yet approached, let alone reached, its potential. Without continued strategic, financial, and intellectual investment, that value will never be realized. Now is the time to engineer the future for the US in this important field and for the entire global synbio community.

A new national center for synthetic biology would represent a visible, stable, accountable long-term commitment to advancing synthetic biology in the public interest and maintaining US leadership in this area. Work in the next 6 months should focus on broad-based roadmapping activities that will develop a clear path forward for synthetic biology research, development, and commercialization in the US built on a shared language and understanding that represents a broad cross-section of constit-

uents including academic, commercial, governmental, philanthropic, and public interests. Such a roadmap would provide strategic direction that could be implemented by the new center, other institutions, and programs across the US.

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