synberc

Building the Future with Biology

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Ten years at the genesis of synthetic biology

Synberc, the Synthetic Biology Engineering Research Center, has been a major U.S. research program to make biology easier to engineer. With support from the National Science Foundation from 2006 to 2016, it has built the foundational tools, technologies, and communities needed to create innovative solutions to some of the most challenging problems of our time, including healthcare, energy, and the environment. This book highlights many of Synberc's achievements over those ten years and points to the directions of the synthetic biology community in the coming decade.

Acknowledgements

We would like to acknowledge Synberc Managing Director Kevin Costa and Synberc Education, Outreach, and Diversity Manager Shaila Kotadia for oversight and production, Rachel Bernstein for authoring the content, Karen Ingram for graphic design, Frazier Phillips for stills and video production, and Sergio Bello for printing production. We are grateful for in-depth review by Synberc Director of Research and Industrial Affairs Leonard Katz, and Synberc Director Jay Keasling. In addition, we thank our final content reviewers Christopher Voigt and Pamela Silver, and Jemma Hostetler for design review. This book was supported by NSF grant #0540879. Finally, we offer a special thank you to everyone in Synberc for the past ten years for building a strong community and advancing the field of synthetic biology.

The field of synthetic biology has blossomed since Synberc's 2006 founding.

Synberc members exit a scientific talk at the semi-annual retreat

Table of Contents

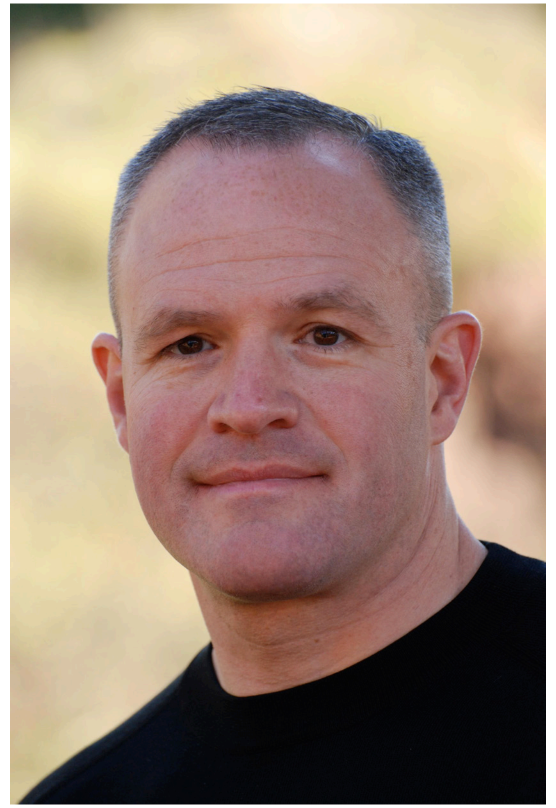
Letter from Jay Keasling

Synberc was established in 2006 with a grant from the National Science Foundation. Its mission was to make biology easier to engineer. In the ten years of its existence, Synberc built the foundations for synthetic biology: we established many new tools to engineer biology, set standards for construction and measurement to advance the field, initiated dialogues among practitioners and the public, and trained a new cadre of scientists and engineers. In turn, those students established their own academic labs, started careers in industry, and established new start-ups that further push the envelope of biological engineering. Synberc universities have initiated their own new synthetic biology centers and institutions, and companies have grown up around this new kind of engineering biology.

I'm very proud of what the Synberc community has accomplished. I believe that we'll look at the Synberc years as the formative years of synthetic biology, the years that we brought the community together and established the foundations for making biology easier to engineer. We will look at this as the turning point for products developed using engineered biology, a period where the field matured. Biologists, engineers, computer scientists, and bioinformaticists, all of these disciplines and more coming together to build a field, and Synberc helped make it happen.

Just as important, the tools and technologies we built have begun to mature and are having a direct impact on the world. Synthetic biology is beginning to reduce illness, poverty, and hunger. Although the pursuit of knowledge and discovery is what drives us as scientists and engineers, the desire to solve real problems and make the planet a better place is what drives us as human beings. And developments made possible by Synberc that have not yet impacted society could have a significant impact far into the future.

Biology will be a tremendous growth engine of the future. As we launch the Engineering Biology Research Consortium as our new organizational home, I am very excited to sustain the traditions and work of Synberc and the synthetic biology community.



The Synberc community gathers for a group photo at the semi-annual retreat

Why Synthetic Biology is Important

What is Synthetic Biology?

What if we could engineer our immune cells to recognize and attack cancer cells that are impervious to current cancer drugs? Or what if we could engineer a strain of yeast to produce jets fuels, and in doing so reduce carbon emissions and the need for foreign fossil fuels? How about if we could engineer a friendly gut microbe that detects when we're sick and produces medicine directly in our stomach?

These are some of the futuristic capabilities that synthetic biology aims to achieve. Synthetic biology is the convergence of advances in chemistry, biology, computer science, and engineering that enables us to go from idea to product faster, cheaper, and with greater precision than ever before. It can be thought of as a biology-based "toolkit" that uses abstraction, standardization, and automated construction to change how we build biological systems and expand the range of possible products. With the same ease that technicians assemble computers from standardized parts, biologists are increasingly able to design and build biological solutions to real-world problems in a safe, responsible, reliable, and precise manner. We will soon replace many conventional manufacturing practices with more sustainable and efficient bio-based approaches, as with biofuels and industrial chemicals. At the same time, advances in areas like biosensors and biomaterials will offer us completely new capabilities and enable us to solve problems currently beyond our reach.

The Synthetic Biology Engineering Research Center (Synberc) is a research community that has brought together leaders in academia and industry to create a vision for synthetic biology. Through a coordinated and multidisciplinary effort, Synberc has served as a leading voice of the synthetic biology community to more effectively bring the benefits of synthetic biology to the public. Together, we articulate and pursue compelling research visions aligned with pressing national and global challenges.

We want to make biology easier to engineer. Synberc researchers have developed the foundational understanding and technologies that are required to build biological components and assemble them into integrated biological solutions for the world. Synberc universities are training a new generation of biological engineers to design and build such systems. We have also engaged with policymakers and the general public about the benefits and challenges of modern biological engineering to make sure we are moving forward responsibly and with broad support.

Advances in biological engineering are transforming how we interact with the biological world and enabling solutions to many important challenges. Just as the invention of semiconductors led to the Information Age in the late 20th century, many see the 21st century as the Age of Biology. Synberc's efforts to establish the foundations of synthetic biology will be key to making that future possible.

Synberc by the Numbers

PUBLICATIONS RESULTING FROM SYNBERC FUNDING

IN PEER-REVIEWED JOURNALS
269

210 CO-AUTHORED WITH SYNBERC STUDENTS

105 AUTHORS FROM MULTIPLE INSTITUTIONS

24 AUTHORS FROM ENGINEERING AND NON-ENGINEERING FIELDS

19 CO-AUTHORED WITH INDUSTRY

TECHNOLOGY TRANSFER

INDUSTRY PARTNER COMPANIES
47

PATENT APPLICATIONS FILED
97

SYNBERC START-UP COMPANIES
8

START-UP EMPLOYEES
136

SPIN-OFF NON-PROFIT ORGANIZATIONS
4

OTHER FUNDING AWARDED TO SYNBERC INVESTIGATORS
$100M+

EDUCATION AND TRAINING

DEGREES AWARDED

DOCTORAL **89**

BACHELORS **25**

SYNBERC POSTDOCS
50

COURSES DEVELOPED
95

OUTREACH

CONFERENCES, WORKSHOPS, AND SHORT COURSES
130

SEMINARS AND INVITED TALKS
1300+

TOTAL NUMBER OF PARTICIPANTS
83,000+

K-12 STUDENTS

EVENTS — ATTENDEES

63 STUDENTS **9,000+** TEACHERS **700+**

NON-SYNBERC UNDERGRADUATE STUDENTS

EVENTS — ATTENDEES

40 STUDENTS **15,000+** UNDERGRADUATE FACULTY **400+**

10 Years of Synberc

2006
- **7.2006** SYNBERC FOUNDED BY NATIONAL SCIENCE FOUNDATION — PAGE 06
- **7.2006** TUMOR-DESTROYING BACTERIUM TESTBED INITIATED — PAGE 31
- **7.2006** GLUCARIC ACID TESTBED INITIATED — PAGE 30

2007
- **1.2007** FIRST SYNBERC INDUSTRY PARTNER — PAGE 38
- **7.2007** FIVE NEW COURSES BASED ON SYNBERC RESEARCH — PAGE 44

2008
- **1.2008** CHURCH LAB BEGINS DEVELOPING MAGE — PAGE 24
- **7.2008** FIRST SYNBERC START UP GINGKO BIOWORKS, FOUNDED — PAGE 42
- **12.2008** DUEBER LAB INITIATES SCAFFOLD PROJECT — PAGE 25

2009
- **1.2009** CLOTHO BIOCAD FRAMEWORK INITIATED BY DENSMORE, ANDERSON LABS — PAGE 26
- **5.2009** VOIGT LAB PRODUCES METHYL HALIDES FROM BIOMASS WITH ENGINEERED MICROBES — PAGE 22
- **5.2009** IGEM SURPASSES 100 TEAMS — PAGE 48
- **7.2009** SEED ACADEMY'S FIRST SYNTHETIC BIOLOGY CLASS — PAGE 50
- **12.2009** SYNBERC REGISTRY IS ESTABLISHED — PAGE 22

2010
- **1.2010** SYNBERC LAUNCHES WORLD'S FIRST PUBLIC BENEFIT BIOFAB — PAGE 27
- **7.2010** ADVANCED FERMENTATION ORGANISM TESTBED ESTABLISHED — PAGE 22
- **8.2010** SYNBERC-ASSOCIATED PROJECT SUPPORT EXCEEDS $10M — PAGE 10
- **9.2010** UNDERGRADUATE SYNTHETIC BIOLOGY CONCENTRATION CREATED AT UC BERKELEY — PAGE 48
- **9.2010** PRINCIPLES OF SYNTHETIC BIOLOGY BI-COASTAL COURSE STABLISHED BY WEISS, ARKIN — PAGE 48
- **11.2010** FIRST "WHAT YOU CAN BE WITH A PHD" WORKSHOP HELD AT PVAMU — PAGE 44
- **11.2010** SYNBERC TESTIMONY TO PRESIDENTIAL BIOETHICS COMMISSION ON SYNTHETIC BIOLOGY — PAGE 62

2011
- **1.2011** BIOBUILDER ESTABLISHED BY KULDELL — PAGE 51
- **2.2011** TUMOR-DESTROYING BACTERIUM TESTBED GRADUATES — PAGE 31

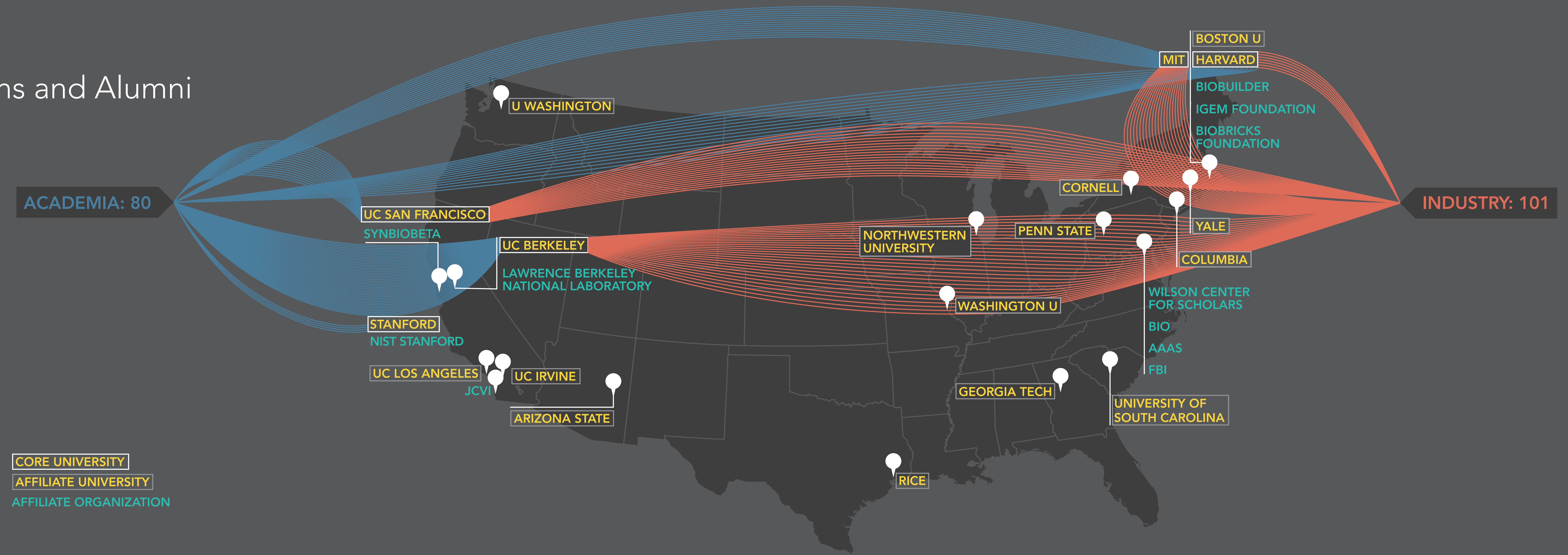
2012
- **1.2012** LEADERSHIP EXCELLENCE ACCELERATOR PROGRAM (LEAP) LAUNCHES — PAGE 34
- **2.2012** PROGRAMMABLE ORGANOIDS TESTBED ESTABLISHED — PAGE 28
- **2.2012** NITROGEN FIXATION TESTBED ESTABLISHED — PAGE 29

2013
- **1.2013** INAUGURAL SYNBERC DIVERSITY FELLOW APPOINTED — PAGE 55
- **7.2013** SYNBERC GRADUATES 50TH DOCTORAL STUDENT — PAGE 47
- **9.2013** IGEM BECOMES INDEPENDENT NON-PROFIT ORGANIZATION — PAGE 48

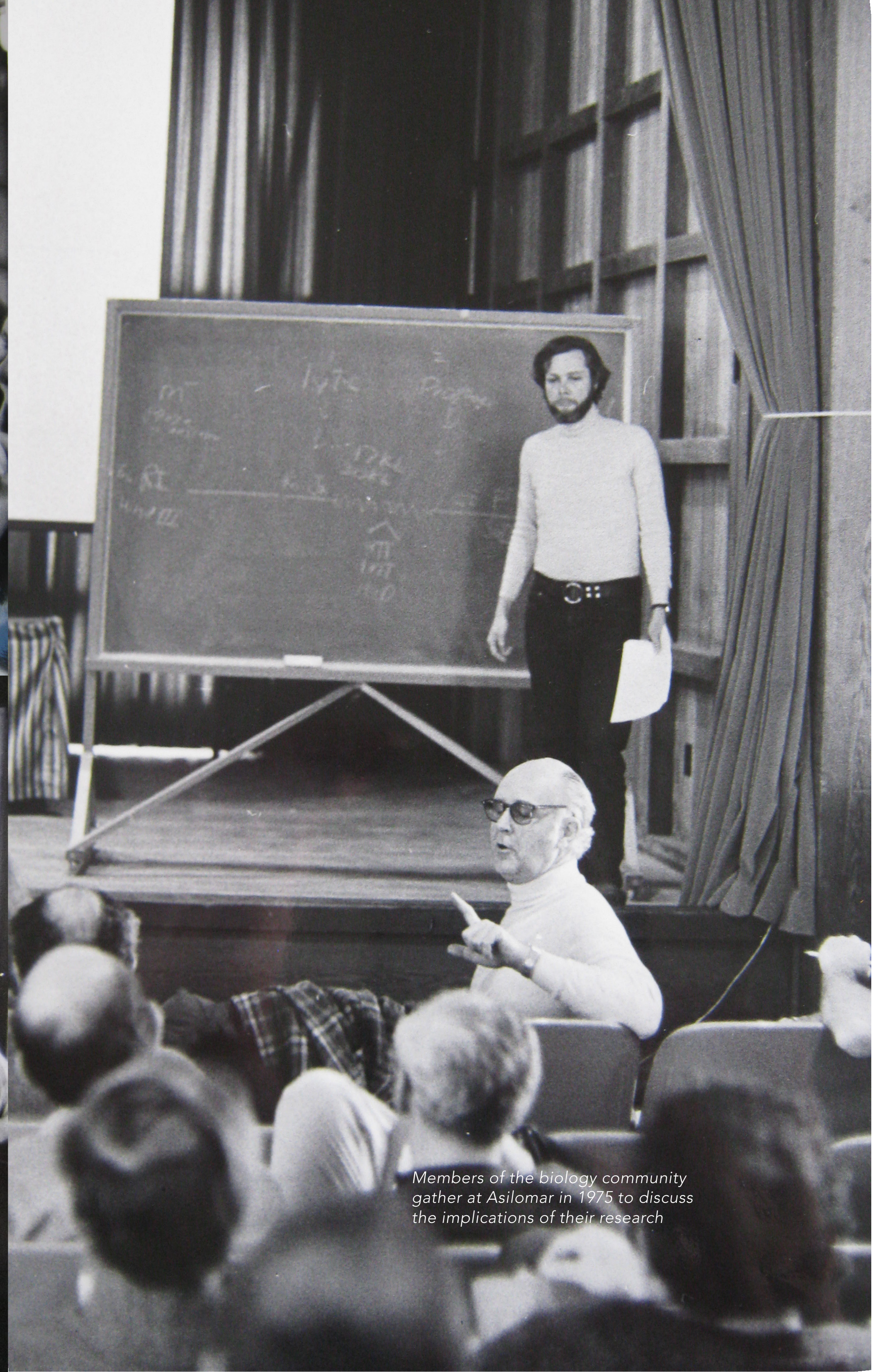
2014
- **1.2014** 40th SYNBERC INDUSTRY PARTNER JOINS — PAGE 39
- **1.2014** SYNBERC PUBLISHES 200TH NSF-FUNDED PAPER — PAGE 10
- **2.2014** SYNBERC OUTREACH PROGRAMS EXCEED 35,000 STUDENTS, TEACHERS, COLLEAGUES — PAGE 58
- **7.2014** SYNBERC CONGRESSIONAL TESTIMONY ON SYNTHETIC BIOLOGY — PAGE 62
- **11.2014** INAUGURAL EXPANDING POTENTIAL DIVERSITY WORKSHOP TAKES PLACE — PAGE 57

2015
- **5.2015** SYNBERC AWARDED ITS 10th PATENT — PAGE 39
- **7.2015** BIOBUILDER TEXTBOOK IS PUBLISHED — PAGE 51
- **11.2015** ENGINEERING BIOLOGY RESEARCH CONSORTIUM (EBRC) IS ANNOUNCED — PAGE 65

Institutions and Alumni



A window to a new world of genetic engineering began to appear.



Members of the biology community gather at Asilomar in 1975 to discuss the implications of their research

Looking Back: Synthetic Biology in Context

Humans have a long tradition of engineering biology to address societal problems and to improve lives. Perhaps the earliest example is the domestication of crops and livestock to provide stable sources of nutritionally rich food for growing civilizations. Farmers guided the evolution of these species by controlling which animals were allowed to breed and experimenting with plant crossings. They did not know the basis of inheritance, but that did not stop them from guiding the evolution of the organisms around them to help serve societal needs.

These types of indirect genetic modification played a crucial role in shaping and advancing agriculture and breeding of domesticated species for thousands of years, and still continues today. But as Charles Darwin, Gregor Mendel, Rosalind Franklin, James Watson, Francis Crick, and others began to understand evolution and its molecular underpinnings, a window to a new world of genetic engineering began to appear.

This possibility became a reality in the 1970's when scientists harnessed molecular tools to manipulate DNA directly. New techniques were developed that allowed scientists to engineer DNA in days instead of the decades that would have been required to generate comparable changes through traditional breeding methods—if such modifications would have even been possible.

Amid the excitement about these new tools, and the possibilities they offered for engineering biology, researchers in the field were also aware that they were entering a potentially contentious area. Breeding animals and plants for certain outcomes was one thing, but the newly emerging ability to precisely manipulate specific genetic sequences required some additional thought to ensure that the research proceeded responsibly and ethically.

In 1975, barely twenty years after the discovery of the double helix, leaders in the field called for a voluntary moratorium on DNA modification. They convened an historic meeting at Asilomar, CA among 150 scientific leaders, lawyers, and media members to discuss the implications of engineering biology and the types of regulations and oversight that might be appropriate. They sought to balance enabling groundbreaking research with respecting principles of human dignity, paying special attention to safety concerns of the public. The set of guidelines that emerged from the meeting is the foundation for many of the regulations that exist today.

Looking Back: Synthetic Biology in Context

In the 30 years that followed the Asilomar meeting, the field grew and developed by leaps and bounds. In that time, a boom in technologies has allowed researchers to build even more complex genetic systems. The technologies now available allow researchers to generate new sequences more and more quickly and easily, again accelerating the process of engineering biology.

An example includes the production of the anti-malarial drug artemisinin, which is used to treat over 100 million people annually. Artemisinin was previously produced by extracting the compound from the sweet wormwood plant. Researchers engineered a strain of yeast with wormwood genes to produce artemisinin reliably and efficiently. This is one example of how synthetic biology can be used to produce important compounds in more environmentally friendly and cost-effective ways than previously possible.

Today's success stories are just the beginning of the revolutionary products that researchers will be able to create by engineering biology. And, just as was the case in the 1970's, today's synthetic biologists are keenly aware of the social and ethical considerations their field raises. Together with lawmakers, ethicists, and other stakeholders, scientists are careful and thoughtful as they work to push the field to meet its full potential so it can address the crucial medical, environmental, and technological challenges our world currently faces.

The advances that biological engineering has made so far are just the beginning of what work in this field promises for the future. Much of the groundwork has been laid, and researchers are now poised to use biological engineering to create solutions for many of the complex issues we face today.

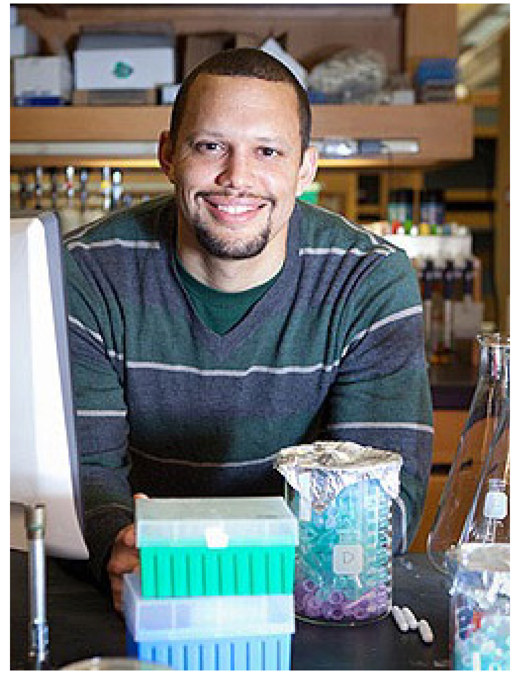
Lawrence Hall of Science,
University of California, Berkeley

Emily Leprout

Synberc Industry Member

CEO, Twist Bioscience

Synthetic biology has tremendous potential to improve many aspects of life today. Already, synthetic biology is reducing the number of toxic gasses released into the atmosphere by reducing our dependence on petrochemicals for everyday products like carpet, plastic, tires, and other specialty chemicals. The impact on agricultural production to feed the world will be significant with the ability to make self-fertilizing and disease-resistant plants. And the opportunity to save lives from disease - like those with malaria treated with microbially-produced artemisinin - is just the beginning of the effect I believe synbio will have on the future of medicine in the 21st century.

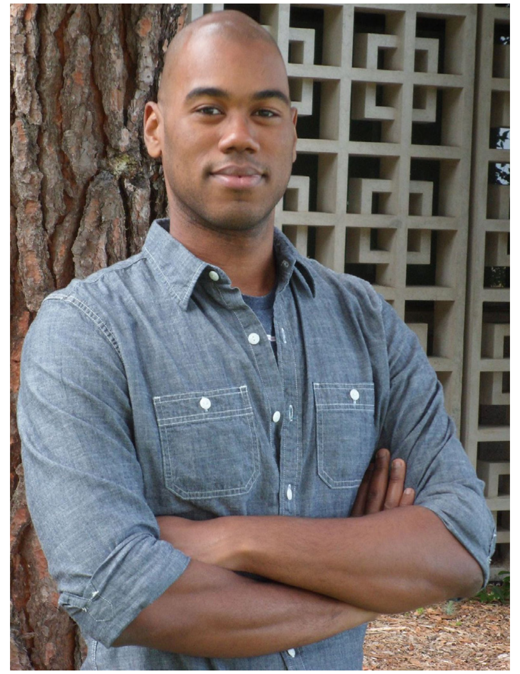


Douglas Densmore

Synberc Affiliated Investigator

Associate Professor,
Boston University

Making a better cell phone was not interesting to me. I chose to pursue synthetic biology because I could help define the foundational problems and work on things that were going to change the world in my lifetime. I want biology to be as easy to program in my lifetime as it is to write these words on my laptop. It is rare that you get to be part of the "ground floor" in a field.



Kevin Solomon

Former Synberc Student Postdoc Association Member

Assistant Professor,
Purdue University

Synberc has led me down richer lines of thought leading to new innovation. Our regular meetings spawn many fruitful conversations and interdisciplinary collaborations that literally define a field and push the boundaries of what's possible when engineering biology. I am able to see the far-reaching impact of my research and think more broadly about the scientific, technological, ethical, and political ramifications of my work.

Adam Paul Arkin

Synberc Principal Investigator

Professor, UC Berkeley

You cannot over-value the power of bringing together diverse people with aligned ambitions to do big things - and Synberc did just that. It has been a privilege to be able to collaborate with Synberc investigators and I have learned a heck of a lot from them. Synberc really has been an intellectual home for a long time.

Kenneth Oye

Synberc Director of Policy
and Practices

Synberc Principal Investigator

Associate Professor, MIT

Working as part of Synberc has kept my work focused on the real rather than the imaginary. Problems facing technologists have led to studies on how to evaluate benefits of synthetic biology projects while limiting risks. My hope is that technologists, policy communities, and civil society will work to assess and address these issues.

Roel Bovenberg

Synberc Industry Member

Corporate Science Fellow, DSM

Not exactly knowing what to expect, I joined the Berkeley retreat of 2007, which left me with a slightly puzzling mixture of impressions of interesting, thought-provoking concepts and research, education, and language of a field I thought I understood. Since then Synberc has been part of our strategic research agenda at DSM, including collaborations with different PIs, student exchanges, and the development of in-house translational projects. The retreats are real highlights and in fact one-stop opportunities for covering many aspects of responsible research and open innovation (science, technology platforms, education, outreach, and regulation). I hope we can address the concerns around synthetic biology and develop compelling examples of its responsible use in society.

Ginni Ursin

Synberc Industry Advisory Board
Vice Chair

Technology Prospecting Lead,
Monsanto

One is always changed by the communities they are engaged with. The Synberc community that grows and changes over time is one of the most vibrant, thought-provoking, and engaging groups that I have had the privilege to be associated with in my professional life. Synberc's values of inclusion, openness, and responsiveness show that scientific achievement is not only compatible with this value system, but reaches higher and achieves more because of it.

Kristala L. J. Prather

Synberc Principal Investigator

Associate Professor, MIT

Synberc as a community is big and brilliant! It is unique in the interactions between faculty, students (graduate and undergraduate), postdoctoral researchers, industry representatives, lawyers, ethicists, policymakers and thinkers, and so on and so on. It's the only experience I've ever had – in either academia or industry – that enables such a broad view of both the execution of scientific objectives as well as the implications of those objectives to society at large. It is vibrant, engaging, and intriguing in many ways, and it provides an opportunity for personal and professional development for my students and postdocs that would be hard to independently replicate.

Synberc Successes: Tools and Technologies

Synthetic biology researchers at the Joint BioEnergy Institute

Tools and Technologies

Synthetic biologists aim to engineer biological systems to address important, real-world problems. In the early history of bioengineering, much of the work was artisanal, and reliable, standardized tools and technologies were not yet in place for researchers to build upon. Early pioneers in the field found some success developing novel biological systems, but their work also highlighted the importance of developing foundational technologies that can enable future projects and accelerate our ability to go from idea to system faster, cheaper, and more reliably. In other words, we need to make biology easier to build with so that we can better tackle real-world problems.

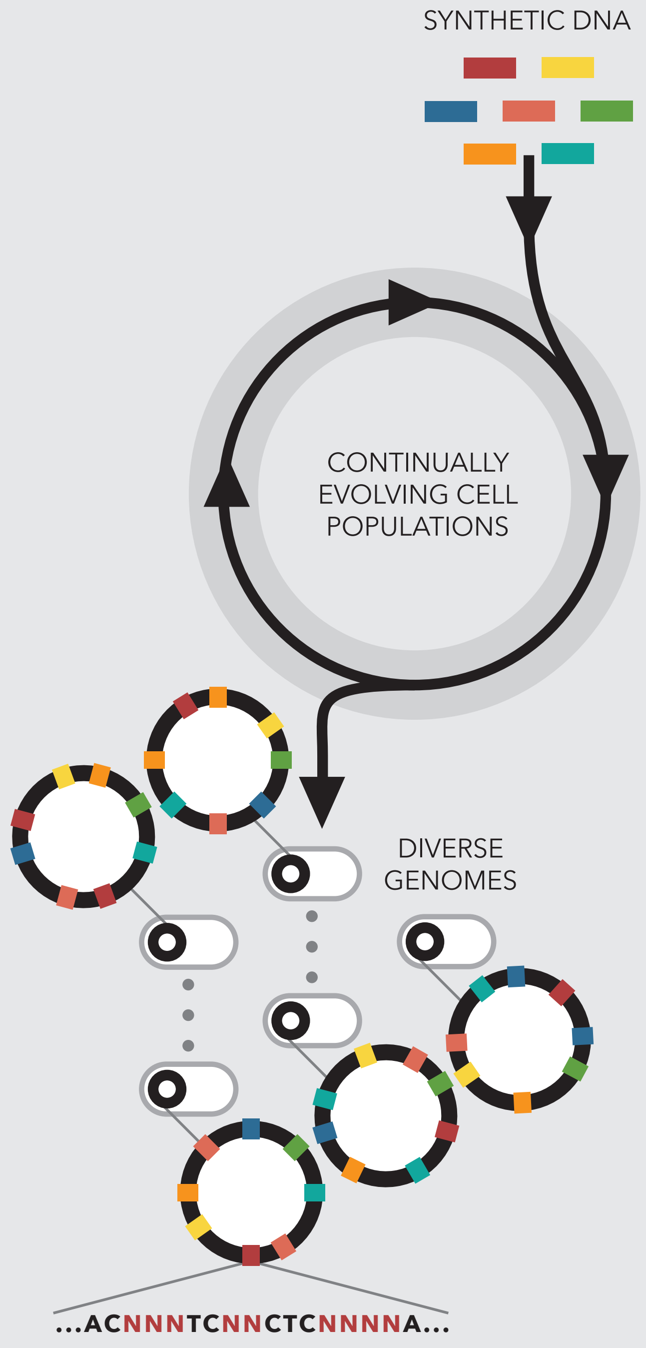
To this end, synthetic biology is transforming the field of biology into an engineering discipline by introducing concepts developed in other fields of engineering, including access to reliable off-the-shelf parts and standards for the basic building blocks of biology that enable their easy integration into larger systems. These developments, and more to come in the future, will make the engineering of biology easier, more efficient, and more predictable.

Today's synthetic biology landscape includes researchers tackling problems all along this spectrum, from developing the foundational tools that will allow biological engineers to edit genomes with extremely high precision to building sophisticated systems to treat specific diseases, for example. These areas of work, while distinct, propel each other forward, and together are pushing synthetic biology to meet its full potential.

MAGE (MicroArray and Gene Expression)

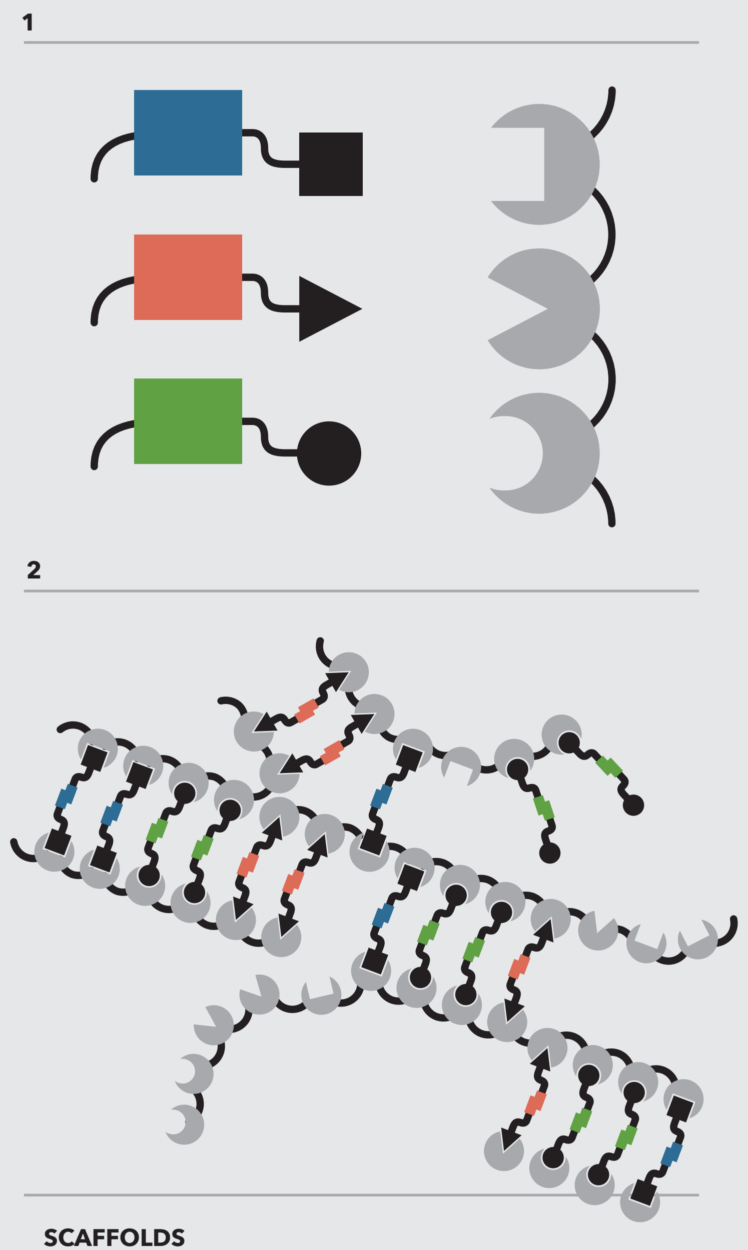
As biological engineers endeavor to design and build ever more complicated genetic systems, the technologies available for the genetic construction of these engineered systems can be a bottleneck. Starting in 2007, George Church and his lab have been developing a system called Multiplex Automated Genome Engineering, or MAGE, that facilitates the building of these complex genetic systems. MAGE allows researchers to simultaneously and specifically edit multiple target sites in bacterial genomes using short DNA fragments called oligonucleotides, or oligos for short. In a single application, the automated MAGE device creates a large bacterial library that the researchers can then screen and subsequently optimize for various purposes.

The Church lab has used MAGE to rapidly and dramatically change the genome of the commonly used lab bacterium *Escherichia coli*. In one case, the team needed just three days to develop a strain of the bacterium that produced high levels of the antioxidant lycopene commonly found in tomatoes. In another project, the researchers used 13,000 oligos to modify much of the regions of the genome by inserting new, reliable regulatory sequences that control more than 2,500 *E. coli* genes, which are responsible for regulating the production of proteins and small molecules. This altered version of the bacterium offers a valuable platform for much further experimentation and development.



MAGE

Multiplex Automated Genome Engineering (MAGE) allows researchers to specifically and rapidly edit multiple sites in a bacterial genome using synthetic DNA fragments called oligonucleotides (multi-colored rectangles).



SCAFFOLDS

Scaffolds recruit biosynthetic enzymes and orient them relative to each other to optimize the pathway.

1. Desired enzymes (colored rectangles) are fused to peptides (black square, triangle, and circle) that interact specifically with the protein-protein interaction domains (grey) that make up the synthetic scaffold (right).
2. The system can be designed so that enzymes can bind multiple scaffolds, creating large complexes.

Scaffolds

One of the promises of biological engineering is the potential to use living cells as self-replicating factories to inexpensively and sustainably produce various desirable compounds. The desired production lines, however, are often made up of enzymatic parts that originate from a variety of different host organisms and are not optimized to work together. These engineered metabolic pathways may be limited or restricted by the availability or activity of enzymes at certain points, compromising the efficiency of the process.

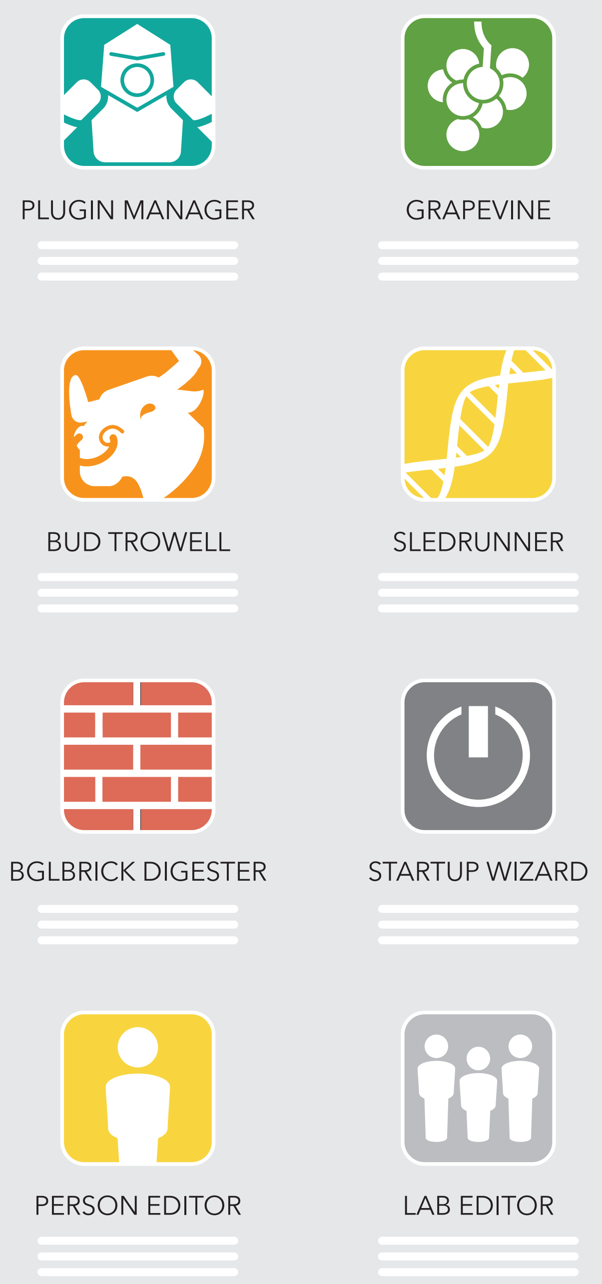
Scaffolds provide one potential solution for this problem. These scaffolds physically hold the enzymes in place in a configuration that facilitates the optimal functioning of the engineered metabolic pathway. The scaffold itself is an engineered protein consisting of multiple domains that co-target enzymes that have been tagged to be recognized by these domains. The end result is that, when both the scaffold and enzyme are present, the pathway enzymes are co-assembled on the scaffold. The scaffold therefore creates a physical assembly line that facilitates the efficient creation of the desired compound.

In one example, John Dueber, Jay Keasling, and colleagues assembled three enzymes on a variety of different scaffolds in the bacterium *Escherichia coli* to produce mevalonate, an important intermediate in the production of the anti-malarial compound artemisinin and of some biofuels. One of the scaffolds resulted in a 77-fold increase in mevalonate production, as compared to the amount produced by the pathway without the scaffold, illustrating the potential value of this design approach. A similar scaffolding strategy was used in a Synberc collaboration with Kristala Prather to increase efficiency of glucaric acid production.

Computer-Aided Design for Biology

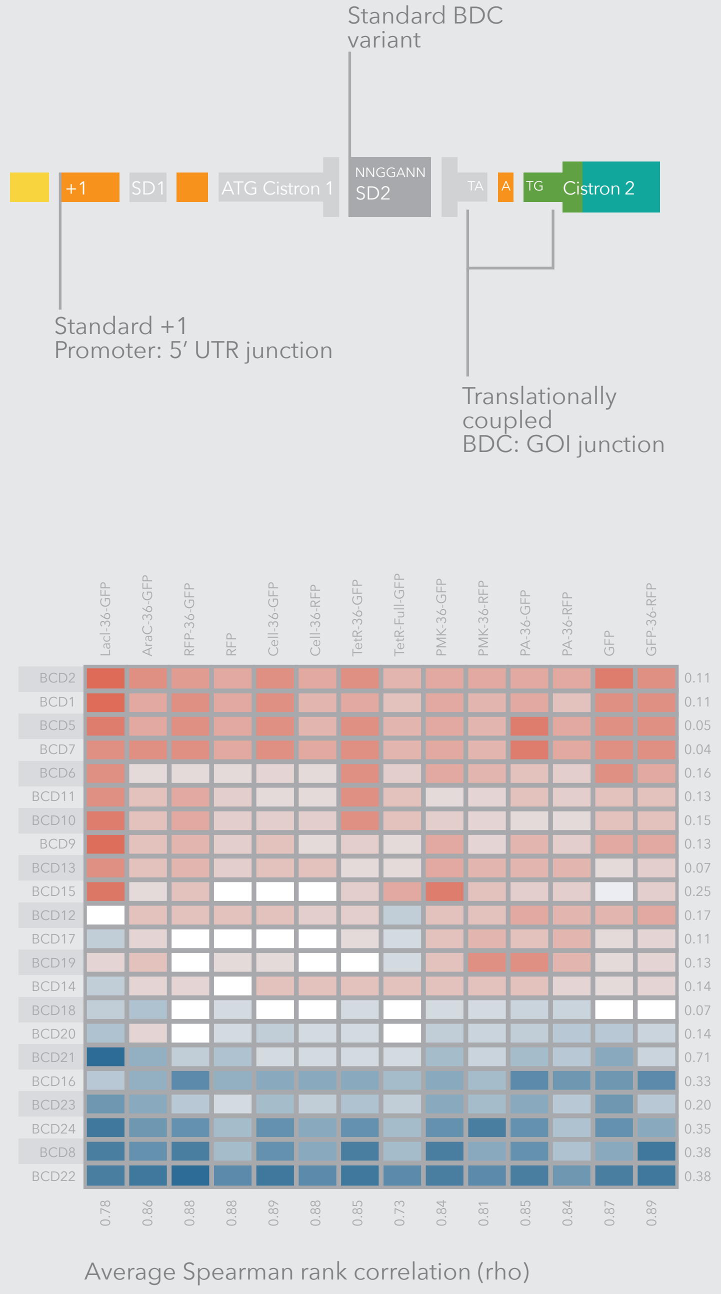
A single researcher at the laboratory bench can only carry out a limited number of experiments, record a certain amount of data, and remember a finite set of experimental parameters. Introducing computational tools greatly increases the number and type of experiments, metabolic pathways, genetic circuits, and environmental conditions that a researcher can explore and share. Exploiting modern computing power and data storage is the essence of computer-aided design, in which researchers use various computational tools and workflows to help guide their specification, design, assembly, and testing of new biological systems.

Currently, there is a vast and growing library of computer-aided design (CAD) tools, each with their own advantages and applications. Some tools focus on modeling metabolic pathways, so, for example, researchers can swap components of the pathway in and out with just the push of a button to determine the design that is likely to be most efficient. This approach saves valuable time and resources and finds designs that would not be possible manually. Another tool is Clotho, the result of a collaboration between J. Christopher Anderson and Douglas Densmore. Clotho allows users to create modular “apps” which share common data to ease standardizing and managing biological designs among labs. Together, these tools, and the experiments they facilitate, accelerate the progress of biological engineering in a way that could not be accomplished without harnessing the power of computation.



COMPUTER-AIDED DESIGN FOR BIOLOGY

A growing list of computer-aided design (CAD) tools can be offered in an app-like menu to help synthetic biologists design and model their systems before building them.



BIOFAB

BIOFABs facilitate the work of engineering biologists by generating standardized parts (top) that are reliable and well-characterized (bottom).

BIOFAB

Just as electrical engineers can buy standardized components (e.g., transistors and capacitors) and mechanical engineers can easily obtain standardized screws, biological engineers require easy access to standardized biological materials to facilitate their work. The BIOFAB, founded in December 2009 and led by Drew Endy, Adam Arkin, and Jay Keasling, aimed to meet this need. The first facility of its kind, it has made freely available standardized, quantitatively characterized parts, with the aim of improving the efficiency of many biological engineering projects. At the end of the two-year funded project, the BIOFAB team, managed by Vivek Mutalik, collectively deposited more than 2500 standardized genetic parts in the public domain. These parts were mainly involved in regulating the rates of expression of genes.

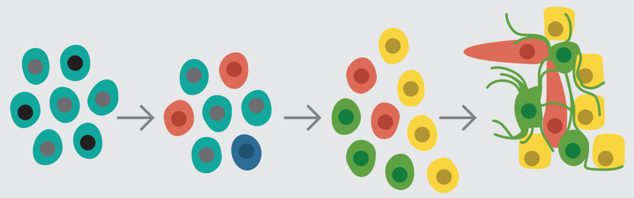
This first facility serves as a proof of concept that such a fabrication lab can have great value to the biological engineering community. Exhaustively isolating, characterizing, and optimizing thousands of genetic elements, and then providing these reliable parts to researchers in an accessible form, is no small task. BIOFABs that undertake this challenge offer an important support system for biological engineers as they work to make it easier to build biological solutions to many problems.

Programmable Organoids

Developing drugs to treat human diseases is a long and arduous path that involves identifying possible treatments, followed by painstaking testing and optimization in non-human systems, including tissue cells, mice, pigs, and other animals, before finally reaching the patient. Unfortunately, even after all this effort, when people take these drugs, the compounds frequently fail to work as the developers intended.

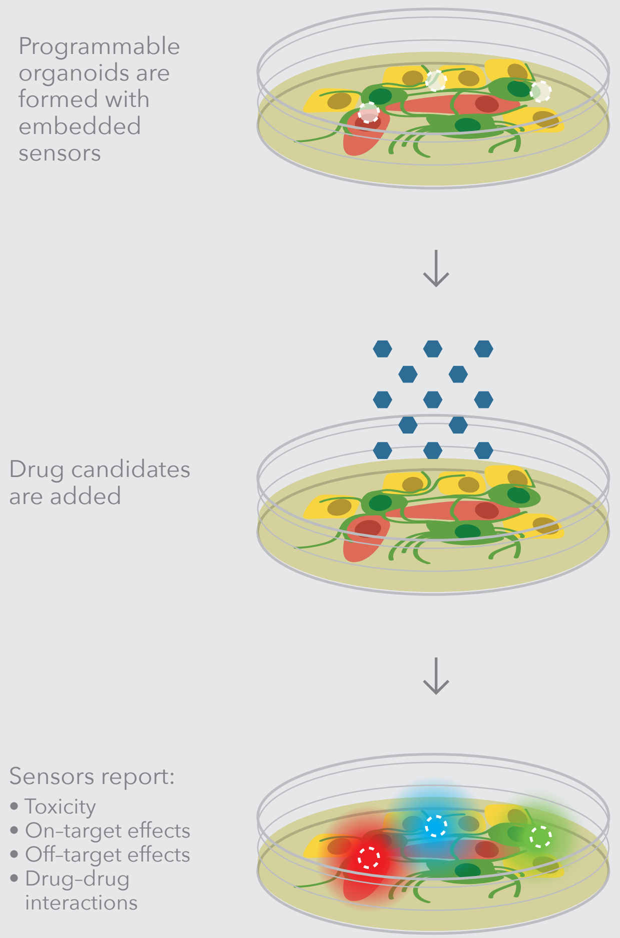
To help address this limitation of the drug development process, Ron Weiss and his lab are working to develop a system called programmable organoids. These organoids are created from mammalian stem cells grown in a sophisticated environment so that the resulting tissue mimics the form of an actual human organ. These organoids can then be used to test candidate drugs, and the results more accurately predict how the drugs will function when treating human patients. Organoids are also a potentially valuable tool for personalized medicine. For each patient, an organoid can be grown, and various drugs can be tested, to determine which will best treat the patient's specific disease. Such an approach could result in significant savings, in terms of time, money, and, most importantly, lives.

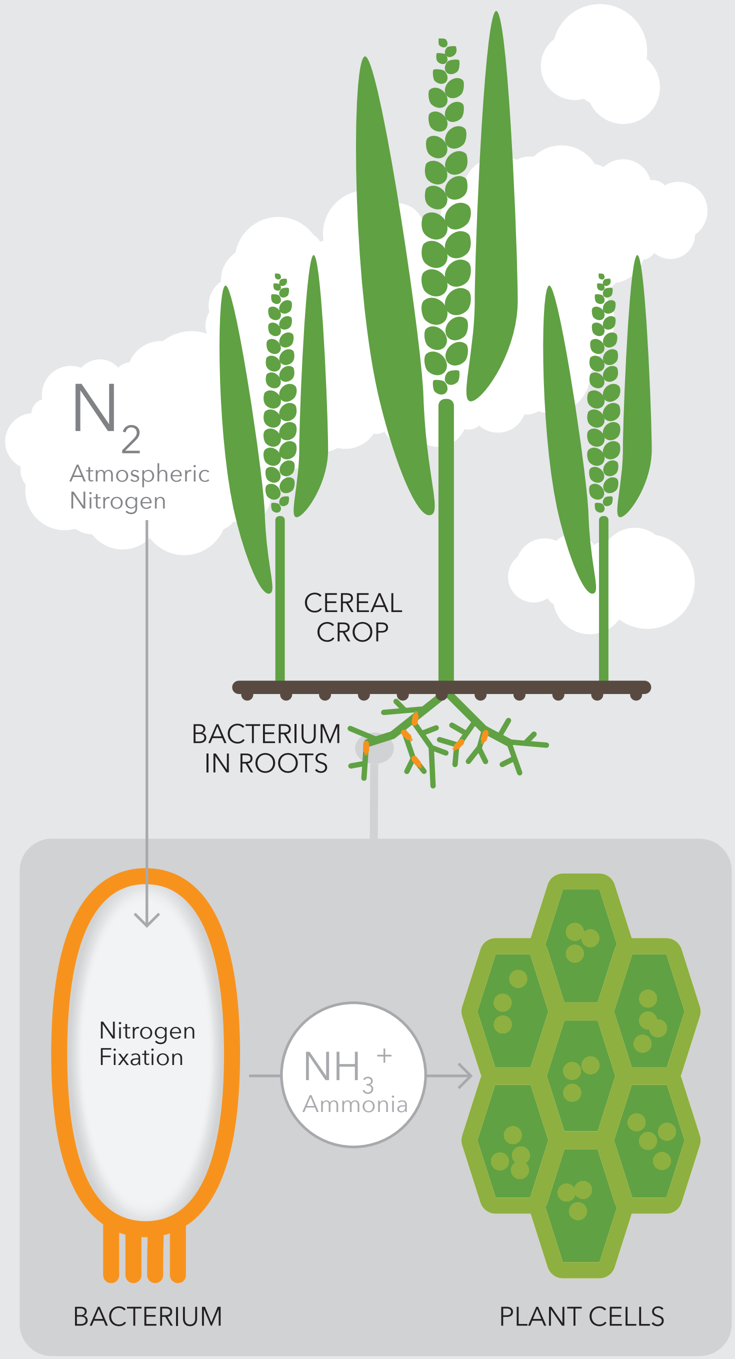
In addition, to fully take advantage of the research opportunities these organoids present, the researchers have made them programmable, so they can provide direct, unambiguous results about whether a treatment is effective. Specifically, they can be genetically programmed to contain sensors for various biological molecules that provide a detailed view of what is happening in the organoid system. If, for example, a researcher applies a potential drug to the organoid, the sensors will tell the researcher exactly what effect the compound is having. Overall, these tools have the potential to significantly aid the drug development process and greatly improve patient treatment.



PROGRAMMABLE ORGANOIDS

Programmed cells (*left, top*) can be developed and manipulated to produce organ-like tissues (*right, top*) with various applications, such as testing whether a drug is effective or has side effects (*below*).





NITROGEN FIXATION

In natural systems, the symbiotic bacteria in soil around plant roots take in nitrogen (N_2) and convert it to a form that plants can use, ammonia (NH_3^+). Synthetic biologists are working to develop plants that can complete this transformation themselves.

Nitrogen Fixation

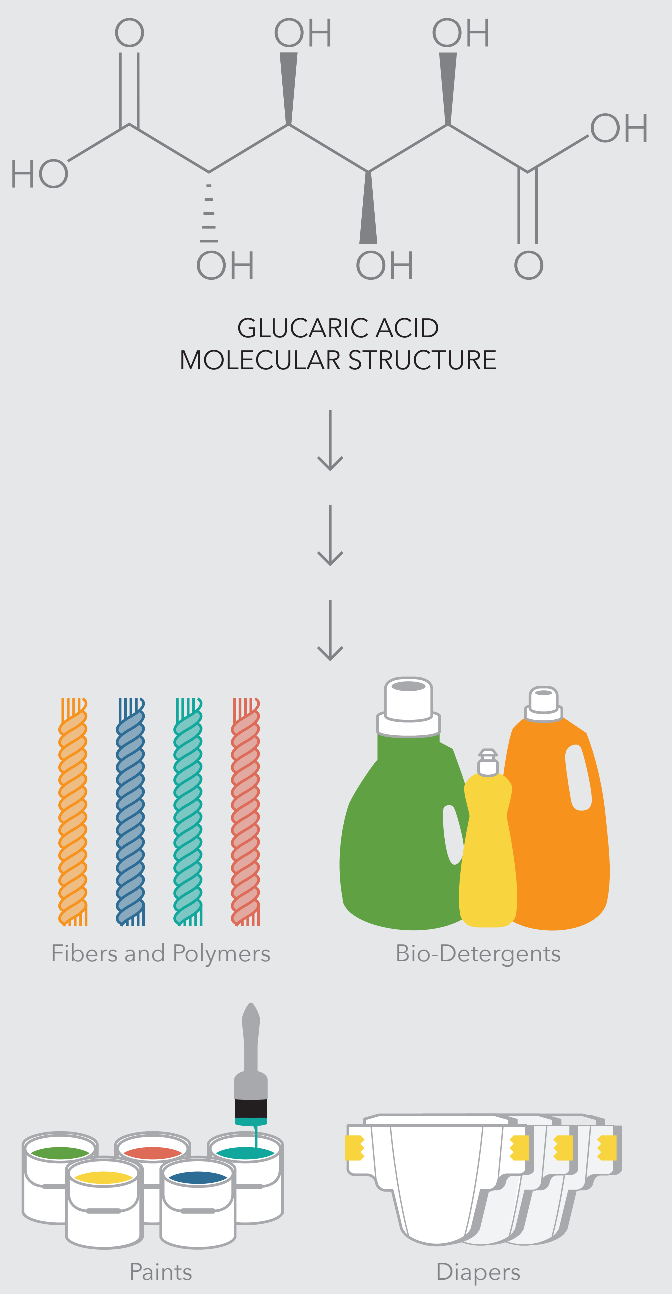
Plants need nitrogen to survive and grow, but many of them can't access it from abundant atmospheric nitrogen gas. This includes agriculturally important food crops, such as the cereals rice, corn, and wheat. These crops rely on nitrogen from soil, so farmers use chemically produced fertilizer for ammonia as their nitrogen source. Production of these fertilizers is expensive and energy-intensive, and their use can be environmentally harmful when the run-off makes its way into natural waterways, where it fertilizes blooms of algae that deplete oxygen and create vast "dead zones" where no fish or natural species can survive. Given the costs and disadvantages of many fertilizers, it would be of great commercial use and environmental benefit if cereal crops could obtain nitrogen by making it themselves or deriving it from a microorganism that can deliver it to the plant. Synthetic biologists are working toward that goal.

The first hurdle is the fact that the ample and sophisticated tools available for engineering bacteria and yeast are largely lacking for plants and soil bacteria. Therefore, synthetic biologists must first build up the required parts and high-throughput screening techniques to lay the foundation for further agricultural engineering projects. Towards this end, Christopher Voigt and his lab have developed a synthetic nitrogen fixation pathway that can be transferred to microbes that associate with cereals. They are also working on engineering the chloroplast so it can host the nitrogen fixation process. This highlights the important role that biological engineering can have in tackling some of the world's most challenging environmental issues.

Glucaric Acid

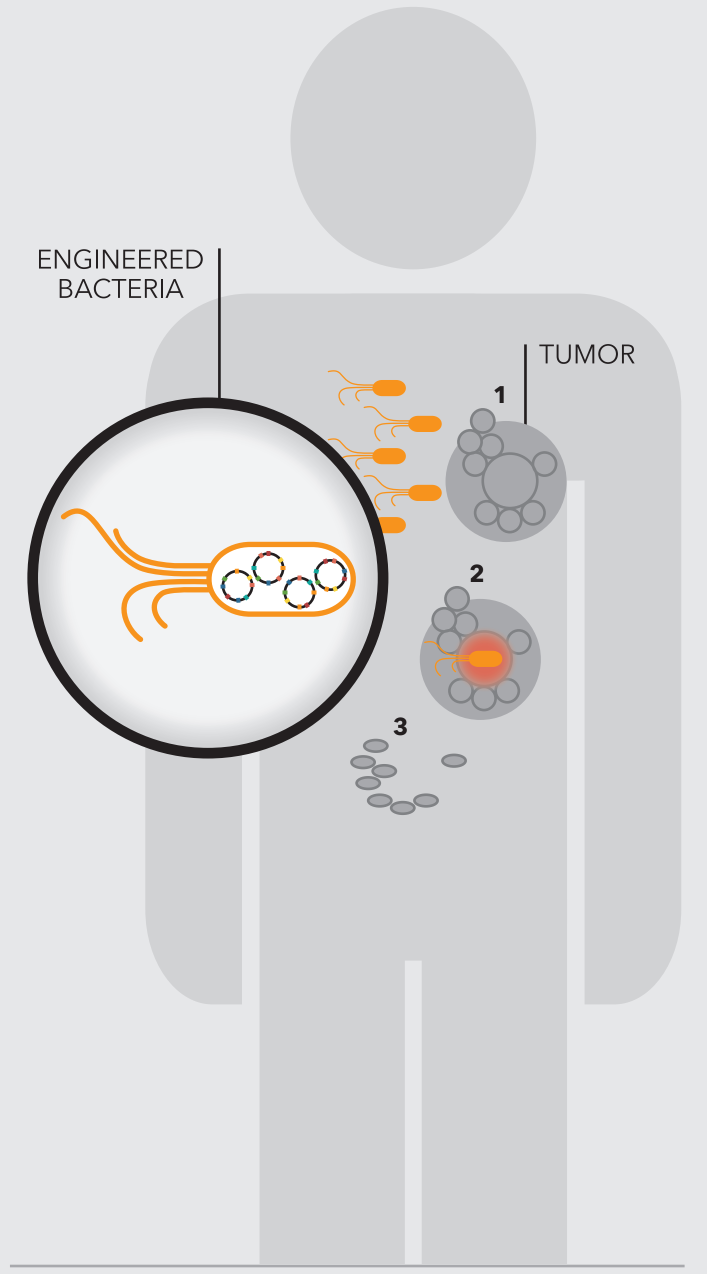
Glucaric acid, a derivative of the sugar glucose, has many important uses, including in detergents, fertilizers, health supplements, and building materials. It can even be converted to the commodity chemical adipic acid. Given its importance, developing a method to efficiently produce this valuable compound is of great interest. It is naturally found in various plants and animals, but extraction is impractical, so for commercial use, it is currently produced industrially by processing sugar. This process, however, is nonselective and expensive, and requires use of corrosive nitric acid. Therefore, efficient production via biological engineering would be highly beneficial, resulting in a more economical and environmentally friendly process.

To achieve this goal, Kristala Prather and her colleagues set out to assemble a synthetic pathway in *Escherichia coli* for producing glucaric acid from glucose. The pathway, originally consisting of enzymes from the yeast *Saccharomyces cerevisiae*, the bacterium *Pseudomonas syringae*, and mouse, successfully produced the acid, but Prather and her colleagues thought they could improve the efficiency by using the scaffold approach pioneered by John Dueber. Using the scaffold approximately doubled the amount of acid produced. New iterations of the pathway include replacement of the mouse enzyme with a homolog from a fungus. In addition, work to move the pathway into an industrial yeast host has been undertaken. Synberc start-up Kalion is now working to bring this production process to industrial levels. Overall, this project demonstrates that enzymes from different species can be assembled into functional pathways to produce valuable compounds that are otherwise difficult to generate.



GLUCARIC ACID

Glucaric acid is an important industrial compound used to manufacture detergents, fertilizers, health supplements, and even building materials. Using engineered bacteria to produce glucaric acid offers a green, renewable alternative source relative to the current chemical process.



TUMOR-DESTROYING BACTERIA

1. Engineered bacteria are injected into the patient's bloodstream.
2. When the bacteria detect a tumor's environment, they produce invasin, a protein that allows them to infiltrate the tumor cells. This prompts the cell to engulf the bacteria.
3. Once the bacteria are inside the tumor cell, the bacteria burst, releasing a toxic compound that kills the cell.

Tumor-Destroying Bacteria

Cancer is one of the leading health challenges of the modern world, and the team that developed the tumor-destroying bacterium believed that biological engineering has a place in addressing it. The team, led by J. Christopher Anderson, developed a proof-of-concept bacterial strain that delivers an anti-tumor drug directly and specifically to tumor cells. The concept is that this bacterium would be injected into a patient's bloodstream. From there, it would identify and invade cancer cells within solid tumors, and only at this point would it release its lethal load of tumor-killing agents. Such an approach would be a great improvement over traditional cancer treatment approaches like chemotherapy and radiation, which kill many non-cancerous cells in addition to their targets.

Developing these tumor-destroying organisms addressed a number of areas of biological engineering, including developing bacteria that are not otherwise harmful to the mammalian patient and building devices that can evade the host defense system, accurately identify a tumor, and release the tumor-killing compound at the correct point. Together, the final products that emerged from this project are of great potential value for medical applications, and the pieces all have individual value as well. For example, some of the devices can integrate multiple input signals from different sources and generate a variety of appropriate outputs in response. The successful development of devices that can accomplish this type of complex logic demonstrates the power of biological engineering to address many complicated biological problems. Moreover, other engineers can now take advantage of this foundation to develop their own sophisticated logic systems. In fact, many of the devices that were developed as part of this project have been taken up by other researchers for other products and purposes, highlighting the cross-pollination and reuse of tools in novel and unexpected ways that biological engineering allows for and encourages.

Synberc Successes: Policy and Practices

Policy and Practices Deputy Director Megan Palmer (center) engages with researchers at a poster session

Policy and Practices

Synberc's foundational advances have accelerated the introduction of a broad range of biologically engineered products to the market. These products can have new uses, costs, benefits, and risks for society. From its inception, Synberc has developed new collaborative approaches to explore and address the economic, legal, ethical, safety, and security aspects of synthetic biology research and development.

Synberc's Policy and Practices researchers explore the drivers and implications of synthetic biology as well as the products it creates. During the first half of Synberc's span, Policy and Practices had a dual focus on the broad structures that guide engagement between social scientists and their natural science and engineering colleagues, and on developing long-term strategies for such engagements. This work provided an exploration of the ways that synthetic biology development might be guided by, and contribute to, human flourishing. More recently, Policy and Practices researchers focused on direct collaboration with other Synberc investigators to foster responsible research in areas as diverse as biosynthesis of chemicals, modification of crops for nitrogen fixation, development of organoids for diagnostics, and the creation of gene drives to contain vector-born disease. They examine both application-specific and cross-cutting foundational issues on topics such as safety, containment, and intellectual property. This work is important as biological engineers grow and develop more sophisticated and scalable technologies that enable a wider variety of products and uses.

The Policy and Practices investigators represent a diversity of disciplines including political science, science and technology studies, law, engineering, and public policy. Their approach is based on experience in areas with shared challenges such as nanotechnology, air toxins, and pharmaceuticals. Their strategy goes beyond simply pointing to the risks and benefits of emerging engineering biology technologies after they are developed. Instead, it focuses on promoting responsible innovation as the research is being done, creating credible methods for measuring benefits and risks, and developing transparent guidelines for allowing research to proceed safely.

LEAP fellows visit the Woodrow Wilson International Center for Scholars in Washington, D.C.


A joint Wilson Center-Synberc workshop on biocontainment

Fostering Leadership and Responsible Innovation

To foster leadership in the responsible conduct of synthetic biology, Synberc established the Synthetic Biology Leadership Excellence Accelerator Program (LEAP). LEAP is a year-long international fellowship program for emerging leaders across disciplines and organizations working in synthetic biology. Each class of LEAP Fellows is competitively selected and participates in a series of workshops with a world-class network of mentors. The program aims to help build Fellows' practical skills, tools, and networks to help responsibly shape the field as they assume positions of leadership within the engineering biology community. Through the program, LEAP Fellows develop collaborative strategies to address their top challenges in synthetic biology. Their efforts have catalyzed many broadly participatory and sustaining initiatives in areas such as safety education, standards, and community organization and governance.

Synberc also encourages biotechnologists to incorporate best practices into their research and education. The Policy and Practices team partners with iGEM to engage the next generation of synthetic biologists in considering the risks of their work. iGEM's size and international diversity make it ideal for developing and evaluating biosafety and biosecurity practices. It is also an important venue for training the next generation of scientists and engineers how to design engineering biology projects with broader impacts as a central consideration. In the area of intellectual property, the team has provided information and educational materials for policymakers and legal practitioners to support innovation in synthetic biology. The Policy and Practices effort has extended broadly as Synberc researchers have engaged with policymakers, U.S. and Canadian regulatory and law enforcement agencies, and the United Nations to improve global safety and security.

Safeguarding Human Health and the Environment

One concern Synberc addresses is the impact of releasing biologically engineered organisms into the wild, either intentionally or unintentionally. Partnering with regulators, policy experts, and researchers, the Policy and Practices team has examined several near-future projects to address biosafety risks before rather than after problems arise. Analysis includes potential environmental effects, areas of uncertainty, and regulatory deficiencies. This helped define specific ecological research needs for the field of synthetic biology. The team also has examined how security issues are framed within the community of synthetic biologists.

Just as important, the Policy and Practices team has worked with Synberc technologists to develop organisms that incorporate safety features to reduce potential harm to humans and the environment. Such features include engineering cells to die outside of their intended host, and methods to prevent cells from exchanging DNA with natural organisms. These features not only increase safety but also help test technical safeguards to develop ever more reliable safety standards and techniques.

Natalie Kuldell

Synberc Associate Director of Education

Synberc Principal Investigator

President, BioBuilder Educational Foundation

Through BioBuilder, I have met hundreds of science teachers across the nation, who have in turn reached thousands of classroom students. All of this is a direct result of Synberc's support and community. Being so closely connected to the synthetic biology community has enabled us to develop the idea that authentic research questions can inspire meaningful learning.

John Dueber

Synberc Affiliated Investigator

Assistant Professor, UC Berkeley

Synberc was extremely supportive during my postdoc. I gained immensely from being able to see how the PIs successfully approached a new field. It also presented research collaborations due to continued interaction at retreats. Later, as an affiliated investigator, Synberc's infrastructure helped me build a more impactful broader impacts program than I could have made on my own. Additionally, the retreats have been an excellent opportunity for my students to learn about the cutting-edge research being done in the community as well as a chance to showcase their work.

Eli Groban

Synberc Industry Member

Senior Manager, Autodesk

Recently I reflected on the original group of students in Synberc around 2006. As I think about where these students are now, it defies the odds. Most of them started companies or are very successful professors at major institutions. I knew I was surrounded by an amazing group of students, postdocs, and professors during my time in Synberc as a student. Only reflecting now do I realize how truly special that moment was and that something like that may never come again in my lifetime. Synberc was an amazing community of which to be a part and I really cannot imagine my life and my career without it.

Sabriya N. Rosemond

Former Synberc Diversity Fellow

Postdoctoral Fellow, UC Berkeley

Prior to serving as the Synberc Diversity Fellow, I knew that my long-term goals included working to increase diversity in STEM but was unsure what that looked like as a career. Working to help develop a diversity program gave me a glimpse of what was needed and more importantly what is possible. The skills and insights gained have served me well in my current roles.

Jenn A.N. Brophy

Former Synberc Student Postdoc Association President

Graduate Student, MIT

Synberc has helped me build a great network of friends and colleagues in synthetic biology. I served as co-president of the SPA for two years, which was an amazing opportunity to meet awesome graduate students, postdocs, staff, and industry partners. The connections I've made in the center have enriched my understanding of the field and its future, preparing me for a career in synthetic biology.

Bernardo Cervantes

Synberc Diversity Fellow

Graduate Student, MIT

Synberc brings together a group of scientists, entrepreneurs, and other non-academics that share synthetic biology's core goal – to solve big problems using biotechnology. The problems that we try to solve are as diverse as our own personal backgrounds. The result is a community of highly motivated individuals looking to collaborate in the pursuit of answers. Surprisingly, we are finding that the technologies being developed for one problem can be applied to many of the others.

Harris Wang

Synberc Affiliated Investigator

Assistant Professor, Columbia University

Synberc has been the best group of scientists, mentors, colleagues, and friends that I have had the pleasure of knowing. It is creative, collaborative, visionary, inspiring. I am excited to see the second generation of Synberc participants starting their own research groups and continuing to advance the field of synthetic biology.

Susan Marqusee

Synberc Education Director

Synberc Principal Investigator

Professor, UC Berkeley

Being a part of Synberc was transformational for me and my students. In addition to the exciting science, Synberc opened my eyes to the impact and importance of a directed effort on education and outreach. Because of my experience as the Education Director for Synberc, I am now actively involved in building career development programs at my home institution, UC Berkeley.

Everyone in my lab, regardless of what they were studying or whether they were working on a Synberc-related project, benefited from being part of the Synberc community. Because of this, many of my students have gone on to careers in synthetic biology. For several, participation in a Synberc education program inspired them to pursue careers in education and outreach.

Community Vignettes

Industrial Achievements: Synberc Inside

Inside Ginkgo Bioworks[1]

From Bench to Market

The power of biological engineering to improve the world depends on academic collaboration with established and emerging industrial firms so that foundational discoveries can be advanced to create market-ready products at a commercial scale.

Many Synberc researchers, from graduate students to senior researchers, are at the forefront of transferring engineering biology projects from the academic benchtop to the commercial market. Since 2008, Synberc technology has launched eight start-up companies. These companies are tackling challenges as diverse as engineering spider silk production for high-performance materials, building software to better engineer biology, and engineering microbes to produce high-value chemicals. Whether creating more sustainable methods of industrial production or developing foundational tools and technologies, all of these companies help to advance the possibilities of engineering biology.

The Synberc industry partners are a part of Synberc's Industrial Advisory Board (IAB). The IAB recommends specific projects or areas of research that can meet industrial needs at the pre-competitive level. The IAB advises Synberc about industrial approaches to scaling engineered biological solutions to the commercial level, which also helps guide laboratory research. Industry partners benefit from direct access to the cutting-edge research and results emerging from Synberc labs and the opportunity to develop collaborations and recruit potential future employees. The mutually beneficial nature of these relationships highlights the high value of collaboration between academia and industry for biological engineering's success.

Bolt Threads

Bolt Threads is, as they put it, "planning to change your clothes." A Synberc start-up company, Bolt Threads, founded by Synberc alumni Dan Widmaier and Ethan Mirsky along with David Breslauer, is using engineering biology approaches to create spider silk and other high-performance fibers.

Spider silk has remarkable properties, including its strength, elasticity, durability, and softness, but current manufacturing processes are limited by reliance on the spider itself to create the fiber. The researchers at Bolt Threads have developed methods for large-scale, sustainable, yeast-based silk production to cut out this bottleneck and create quality fabrics.

In addition to the efficiency benefits of their approach, using engineering biology opens the door to a potentially vast array of previously unknown and unexplored varieties of silks with novel and useful properties. Spiders can naturally produce only the relatively small set of silk proteins they have the genes for, but the ease of genetically modifying yeast allows for the creation of a practically unlimited set of fibers for investigation and manufacturing.

Silk fibers woven out of synthetically produced proteins at Bolt Threads

Genomatica Innovation Center

Genomatica

Synberc industrial partner Genomatica had a goal: develop a commercially-advantaged, biologically-based manufacturing process to produce 1,4-butanediol (BDO), a compound used as an industrial solvent and for manufacturing plastics and elastic fibers, including Spandex. As part of their overall project, they evaluated and licensed software developed in a Synberc laboratory and took inspiration from a number of Synberc products, including biosensors, scaffolding pathways, MAGE, and Clotho.

In February 2014, Genomatica announced that it had successfully produced over 5 million pounds of the compound in just five weeks. Just three months later, Genomatica licensed the technology to BASF, a multinational chemical manufacturing company, allowing them to build a world-scale production facility that would use the Genomatica process to manufacture BDO at commercial levels using renewable raw materials.

This success offers an excellent illustration of the synergy that can exist between basic researchers and industrial players in the engineering biology community.

Ginkgo Bioworks

Ginkgo Bioworks has a simple mission on the surface: to make biology easier to engineer. But the advances they could power with their products are far from small. The company, founded in 2008 by Synberc investigator Tom Knight and Synberc alumni Austin Che, Reshma Shetty, Jason Kelly, and Barry Canton, has designed an organism foundry called Bioworks1 that can efficiently develop engineered microbial strains to serve many different industrial purposes. Building on this foundational technology, the company is tackling a variety of commercial targets, including designer fragrances like rose essence, capturing natural gas and converting it into more valuable compounds, and advanced probiotics.

Ginkgo was one of the first Synberc start-ups, and it came full circle in 2014 by becoming a Synberc industry partner. Its success highlights the strength of the early training and preparation that Synberc provided the four students-turned-founders as they transitioned from conducting academic research to developing commercial applications.

Gingko Bioworks's organism foundry, Bioworks1

Beyond the Bench: Education

Synberc researchers interact at the semi-annual retreat

Education: Training the Next Generation of Researchers

Synthetic biology is an emerging discipline with tremendous potential impact. Therefore, developing educational resources and supporting trainees is vital. Synberc has engaged in various endeavors to support education and training at all levels, from high school students to postdoctoral scholars.

The mission of Synberc's education and outreach program is to prepare a new cadre of biological engineers for success. Synberc aims to develop a pipeline of highly effective, motivated young researchers who will push the field forward. Synberc's education programs reinforce our diversity goals by offering programs that support trainees from underrepresented backgrounds.

Discussions at a poster session at a Synberc retreat

Participants listen to a presentation at a Synberc retreat

Graduate Students and Postdoctoral Researchers

Graduate students and postdoctoral researchers are the core of the research workforce at Synberc. They lead cutting edge projects in Synberc labs, which helps advance their education and training and prepare them for careers in academia, industry, government, and other sectors. Synberc also supports graduate students and postdocs with the mentoring they need to further their training. For example, in the Industry Mentoring Program, launched in fall 2013, students learn how research is conducted in industry and how they can effectively pursue industrial careers. The understanding gained through the program enables students and postdocs to build strong relationships with industry leaders and helps them make informed career choices.

In addition, about 40 Synberc students and postdocs participate each year as mentors and teachers in the programs discussed below. This gives them valuable career development and mentoring experience. Many Synberc trainees also have been involved in the Student Postdoc Association (SPA), both as leaders and participants in SPA-organized activities, such as hosting social events and industry visits at Synberc's semi-annual retreats and supporting various working groups.

Participants in the International Genetically Engineered Machine (iGEM) competition gather for the annual Jamboree

Undergraduates

Undergraduate education is a crucial training ground for young researchers who will bring their fresh ideas and enthusiasm to push biological engineering forward. Synberc offers a number of programs and opportunities to introduce these students to synthetic biology.

Because the discipline is relatively new, curriculum and academic program development is continuously evolving, and Synberc is at the forefront of these efforts. Our investigators have developed nearly 100 course offerings to cover foundational topics in synthetic biology and have worked to incorporate synthetic biology concepts into existing courses. Some of the most popular courses are offered as online modules and also made freely available through Synberc's website.

Synberc has also been the largest sponsor of the International Genetically Engineered Machines (iGEM) Competition, the premiere undergraduate synthetic biology research competition. iGEM participants, which in recent years have included nearly 300 teams and over 5,000 students, faculty, and instructors, spend a summer conceiving of, designing, and building a system using engineering biology principles and parts and then come together to share their work with other teams at an annual Jamboree.

The Synberc Research Experiences for Undergraduates (REU) program also invites a diverse group of students to engage in engineering biology research by spending a summer working in a research lab. Preference is given to students who are underrepresented in STEM: those who are economically or educationally disadvantaged, the first in their families to attend college, or enrolled in community college or other primarily undergraduate institutions. Synberc also offers a week-long Lab Fundamentals Bootcamp program at UC Berkeley, taught by Synberc graduate students and postdocs, to provide intensive hands-on training for REU students before they begin their research internship.

The 2015 iCLEM class at the Joint BioEnergy Institute

High School Students

High school is a time when many students have the opportunity to fall in love with science. Therefore, it's a crucial time to introduce students to the excitement and potential of biological engineering to stoke their interest in science, especially for students whose schools are under-resourced and cannot offer laboratory experiences.

One Synberc program that addresses this need is the Introductory College Level Experience in Microbiology (iCLEM), an eight-week paid internship program for eight high school students each year, targeting low-income students that are often underrepresented minorities, the children of immigrants, and/or first generation to go to college. The students spend the summer doing hands-on work in a cutting-edge laboratory environment at the Joint BioEnergy Institute, where they can be inspired by the potential of biological engineering to create novel solutions for some of the world's greatest problems.

Synberc also partners with MIT's Saturday Engineering Enrichment and Discovery (SEED) Academy to develop and teach an engineering biology course to high school seniors. SEED aims to provide academic enrichment and technical training to promising but traditionally underserved high school students by offering engaging, hands-on courses in synthetic biology.

Natalie Kuldell, President, Founder, and Executive Director of the BioBuilder Educational Foundation, leads a workshop

Teachers

To truly have an impact on educational practices around engineering biology, science teachers must be taught about this new field and be provided opportunities to learn about it themselves so they can share it with their students. Synberc supports these efforts with a number of programs.

The nonprofit BioBuilder Educational Foundation, started within Synberc and directed by Synberc's Associate Director of Education Natalie Kuldell, develops and provides physical and supporting written materials for engineering biology activities for secondary and post-secondary school classrooms and laboratories. Because the material covered in the lessons is new for many high school science teachers, BioBuilder also offers teacher workshops to support them as they incorporate these activities into their classrooms.

Synberc also offers Research Experiences for Teachers (RET) through the BERET program (Berkeley Engineering RET), which pairs undergraduate students training to be science and math teachers with practicing high school teachers in these subjects, most of whom teach at socioeconomically disadvantaged schools. The practicing teachers design curriculum, and the teachers-in-training have the opportunity to teach a lesson in their partner's classroom. In addition to providing teachers with state-of-the-art training, this program has a broad impact on the thousands of students these teachers reach.

George Church

Synberc Principal Investigator

Professor, Harvard Medical School

Synberc has been quite helpful in communicating occasionally counter-intuitive visions. We need to communicate with a broad variety of citizens – ideally, far in advance of the first experiment – about transformative technologies that can be economically disruptive, or accidentally or intentionally misused.

Dan Widmaier

Synberc Industry Member

CEO and Co-founder, Bolt Threads

Biology is one of the most powerful technologies on the planet. The ability to harness the best of what nature has to offer could solve many of our most challenging problems. Synberc has been a great resource for passionate people to share ideas, failures, and progress in the field. There is still an enormous potential for further development and application of biological engineering and Synberc will play a role in providing access to the framework, tools, and community for groups and individuals to work together to advance technology.

Steve Evans

Former Synberc Industry Advisory Board Chair

Science Fellow, Dow AgroSciences

Synberc has been the most productive blend of academic, industrial, and government interests that I have ever experienced. The community has experimented with constructs, both the ones built with A, C, T, G and the ones built with people. Some worked. Some didn't. But that is okay. Synthetic biology reinvigorates the "classical" biotechnology universe and broadens the footprint to make biotechnology products really globally accessible. My hope is that my children's children live in a world so enriched by synthetic biology products that how they are made is unimportant, so that a current Synberc postdoc will one day start a story with, "Well back when I first started it was a really big deal to … ," and the kids listening will react with incredulity.

Theresa Good

Former Synberc Program Manager

Deputy Division Director, NSF

As the Program Director for Synberc in 2006, when it was the largest federal investment in the field of synthetic biology, I had the opportunity to observe and participate in a number of scientific and policy activities to advance the field of synthetic biology nationally and internationally. Synberc's creativity, thoughtfulness, graciousness, and generosity have served synthetic biology well for the last ten years.

Ron Weiss

Synberc Principal Investigator

Professor, MIT

I'm really excited to see the field moving into translational work for real health-related applications. We want to see genetic circuits used in real therapies, for example with the use of programmable organoids for drug discovery and organ transplant. I am concerned but optimistic that we are building solid foundations for standards, safety, performance evaluation, and products.

Megan Palmer

Synberc Deputy Director of Policy and Practices

Synberc Affiliated Investigator

Senior Research Scholar, Stanford University

It was forward thinking to establish a policy and practice-focused research thrust within a center dedicated to advancing the forefront of genetic engineering. The acknowledgment that synthetic biology involved more than usual levels of uncertainty and complexity created space for a diversity of practitioners to engage meaningfully in issues "beyond the bench." Future endeavors should learn from and evolve organizational experiments of this type to mature our governance systems to keep pace with the globalization of emerging technologies.

Caroline Peres

Synberc Industry Member

Staff Scientist, DuPont Industrial Biosciences

Synberc has helped me and my company make sure we were not missing any useful techniques or results. It has forced us to be even more innovative than we already were. Some tools, like the ribosome calculator, are so easy to use and make such a big difference that we integrated them into our pipeline. Synberc is a large pool of fantastic scientists – we hired a Synberc postdoc. Synberc also allows me to meet industrial and academic researchers with similar interests.

Pamela Silver

Synberc Diversity Director

Synberc Principal Investigator

Professor, Harvard Medical School

I believe that engineering biology is the technology of this century and that we have a responsibility to make sure this happens in a productive and ethical way.

Beyond the Bench: Diversity and Inclusion

Fostering Inclusivity in Synthetic Biology

Fostering diverse, inclusive communities is a crucial goal across science and engineering, and Synberc is actively engaged in addressing this issue, both within the center and in the broader community. We believe that we can better serve our entire community by making sure that the voices of all of its members are heard. We have implemented various programs and efforts to make sure this is the case.

Synberc works to develop a diverse community of researchers at all levels. At one end of the spectrum we create an inclusive environment for a diverse group of leaders in the synthetic biology community. At the other end of the spectrum we encourage students from historically underrepresented groups to participate in synthetic biology research. The importance of this effort is a crucial focus of many of our educational programs, including the Research Experiences for Undergraduates, the Introductory College Level Experience in Microbiology (iCLEM) program, and Saturday Engineering Enrichment and Discovery (SEED) Academy, as discussed in the previous section. In addition, in 2013 Synberc enacted a diversity fellows program, through which a selected member of a Synberc lab participates in the Synberc diversity team. This individual provides a first-hand perspective on the true nature of inclusivity in the classroom and workplace.

Fostering Inclusivity in Synthetic Biology

Synberc tackles various elements of diversity and the importance of inclusion at our semi-annual retreats by bringing in expert speakers on various related topics. For example, one speaker focused on the underrepresentation of women among science and engineering faculty, recalling her own battles with changing the environment at the university to welcome more female faculty. Another speaker introduced attendees to the concept of implicit bias, or the unconscious beliefs people have about certain groups, including their aptitudes and preferences. These biases can reinforce the existing lack of diversity in science. Thus, increasing awareness of them is a crucial first step toward addressing their effects to ultimately support a diverse and inclusive biological engineering workforce.

Synberc is working to promote diversity in the researchers who speak at conferences and meetings. In particular, women are poorly represented among speakers. To help address this problem and to make it easier for organizers to find female speakers to invite to their events, Synberc has developed the "Suggested Women Speakers in Synthetic Biology" list. In addition, Synberc has created a list of resources about the issue of designing inclusive meetings. For meeting attendees who want to bring the topic to the attention of meeting planners, Synberc provides a form letter that points to both lists.

Expanding Potential

Since Synberc researchers come from varying backgrounds, we have a unique opportunity to influence the diversity of STEM via a larger community. Synberc has thus created the Expanding Potential program, which focuses on the systemic issues that affect underrepresented groups. The program aims to broaden participation in synthetic biology by helping students and professionals recognize and understand social problems that may hinder progress of underrepresented groups and by encouraging and supporting programs that change STEM cultures and increase inclusivity. To this end, Expanding Potential offers a variety of activities and resources, including an annual workshop, seed funding for projects that enact positive change for diversity in STEM, and meet-ups. This programming builds community, helps people better understand the challenges to underrepresented groups in STEM, and shares strategies for overcoming them.

The annual Expanding Potential Workshop offers participants a safe, productive space to dig into important phenomena that can affect diversity. Topics include implicit biases, or the unconscious beliefs people have about certain groups, including their aptitudes and preferences; stereotype threat, or the phenomenon by which people's anxiety about confirming negative stereotypes about their social group hinders their ability to reach their full potential; impostor syndrome, which causes highly capable individuals, frequently from historically underrepresented groups, to doubt their abilities and fear being exposed as frauds; and microaggressions, or the daily, seemingly minor slights and insults that together create hostile work environments for many people from historically underrepresented groups. Workshop participants discuss how to address these problems individually and through programs. By bringing together students, established academic researchers, and industry scientists, the workshops offer an opportunity for individuals from across the biological engineering community to come together and tackle these difficult problems.

Expanding Potential also provides seed funding to help bootstrap innovative new programs that increase diversity and can be easily implemented across many institutions to broaden their impact. Recipients of the seed grants receive $1,000-$5,000 to develop their initiatives. So far, funded projects cover topics including unconscious bias, the relationship between art and STEM, and diversity data visualization.

Together, the multiple facets of the Expanding Potential program offer a variety of approaches to help address the lack of diversity and inclusion that currently exists in biological engineering, and across STEM.

Beyond the Bench: Engagement and Outreach

Visitors explore the "Building with Biology" exhibit at the Science Museum of Minnesota in 2015

Terry Johnson, Shaila Kotadia, Danielle Tullman-Ercek, and Nathan Hillson at Chabot Space & Science Center in Oakland, CA

Engagement and Outreach

Recent advances in chemistry, computing, biology, and engineering are converging to enable biological engineers to go from idea to biological product faster, more inexpensively, and with greater precision than ever before. These products present both new benefits and new risks for society. With this in mind, Synberc has sought to create a culture of responsible innovation in biological engineering. It also seeks to engage policymakers and the broader public about important questions that can arise from these advances, such as: What are the risks and how do we ensure safety? Who benefits from the technology?

Biological engineers and social scientists are working together to wrestle with these questions, but that is only part of the picture. If the public is not also brought into the discussion, misunderstandings and misinformation could hinder the field's progress and slow biological engineers' ability to develop meaningful tools that can address some of the world's most difficult problems. Synberc also believes that the public should have a voice in deciding what science and technologies should be pursued for the greatest benefit of society. Synberc is committed to facilitating interactions between biological engineers and the broader public to both help the public to better understand the research and to gain valuable input from non-experts about their hopes and concerns about this fast-growing discipline.

Building with Biology

Synberc partners with the Museum of Science in Boston and the American Association for the Advancement of Science to promote public engagement with biological engineering through the Building with Biology program. Building with Biology offers activities and forums developed in collaboration between museum professionals and researchers to introduce the public to the promise of biological engineering and to solicit their ideas and recommendations about how the technology should be used. These activities and forums aim to foster discussion between scientists and the public about this exciting but at times controversial emerging discipline so that both sides of the conversation learn and benefit from each other. The activities spark discussions around various topics, including genetically modified foods, environmental issues, and synthetic biology products on the horizon. In 2016, the activities will be distributed to 200 sites across the country as part of a series of events being called "the summer of synbio."

Visitors explore the "Building with Biology" exhibit at the Science Museum of Minnesota in 2015

#meetsynbio and Engaging the Public

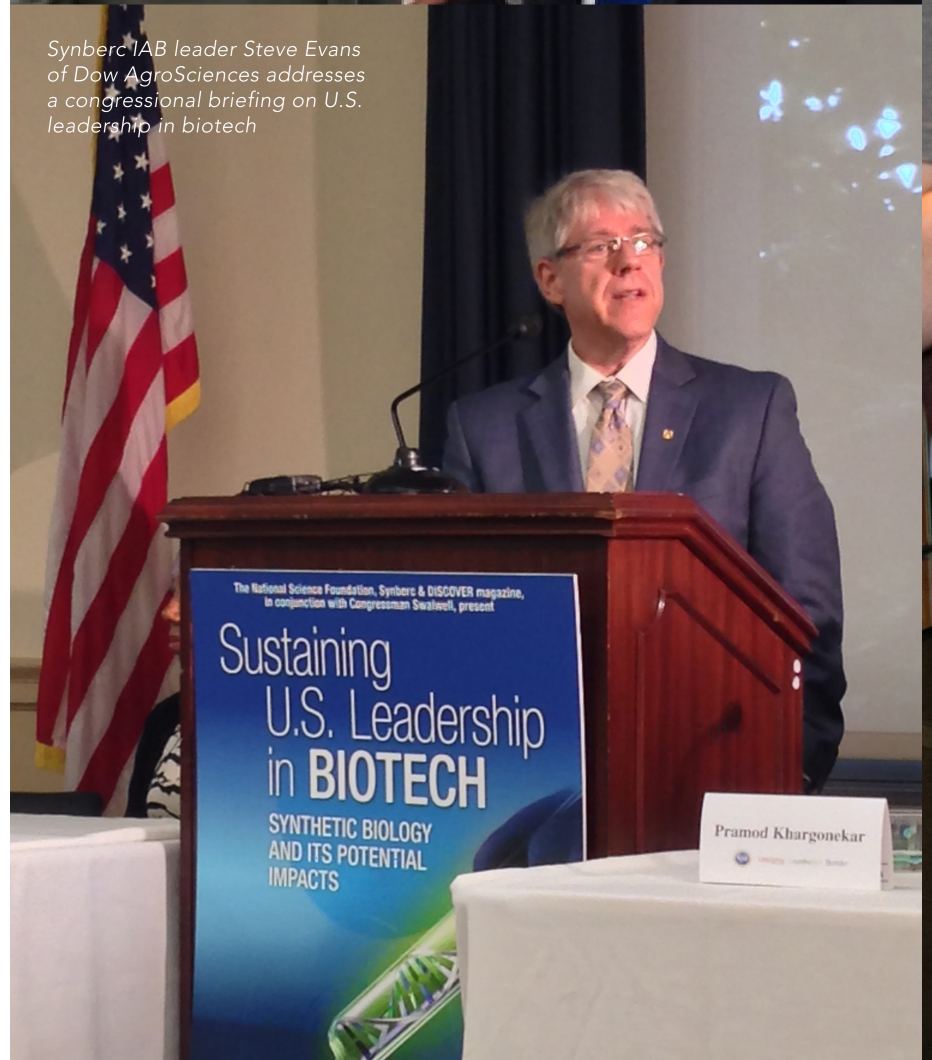
The #meetsynbio social media campaign promotes public engagement by introducing the general public to the people behind biological engineering research. Synberc encourages biological engineers to use the #meetsynbio hashtag to discuss their work on Twitter, which connects many millions of people from all walks of life and across the world, as well as other social media platforms. The intention is to open up a two-way conversation so that both researchers and the public learn and benefit from each other.

Synberc also offers opportunity for in-person engagement via various events that bring together scientists and members of the public to discuss biological engineering research, such as the "Conversations about Synthetic Biology" series. Together, these activities aim to give scientists and the broader public an opportunity to share their motivations and concerns about how we can together shape the responsible advancement of biological engineering to solve important problems in the world.

Policy Engagement

In addition to engaging with the public, Synberc has played a leading role within the broader biological engineering community to ensure that policymakers and federal agencies understand the complexities and nuances of the field in order to make well-informed decisions. For example, Synberc academic and industrial members frequently appear before Congress to testify about biological engineering and national policies for sustaining a robust bioeconomy. Synberc coordinated a congressional briefing in Washington, D.C. to emphasize the importance of sustaining U.S. leadership in biotech and synthetic biology. In addition, Synberc investigators have served on key groups to develop U.S. science policy, including the National Science Advisory Board for Biosecurity and various National Academy of Science committees. Finally, Synberc has produced various white papers and other publications about important aspects of biological engineering in areas including mammalian synthetic biology, plant synthetic biology, and developing globally coordinated policies in biological engineering. Together, these policy activities put Synberc at the forefront of political engagement.

Jay Keasling talks with San Diego Rep. Scott Peters following a subcommittee hearing of the House Committee on Science, Space and Technology



Synberc IAB leader Steve Evans of Dow AgroSciences addresses a congressional briefing on U.S. leadership in biotech

Synberc videographer Frazier Phillips (left) films interviews of researchers discussing the importance and impact of synthetic biology

Introducing the EBRC

Visions of Future Biotech

Just as transistors ushered in the Information Age at the end of the 20th century, advances in biological engineering promise to catalyze the Age of Biology in this century. We stand at the threshold of almost unimaginable, seemingly endless possibilities of what we can accomplish by harnessing the capabilities of the natural world. Each researcher has their own moonshot dream. While these visions may seem farfetched now, synthetic biology has made tremendous strides in a relatively short time, and we can only begin to guess as to what we may be able to accomplish with this technology moving forward. The true promise of synthetic biology is to empower biological engineers to go from vision to reality, and to unleash scientists' and engineers' boundless creativity on the incredible beauty and possibilities of biology.

Addressing the Challenges of the Future

Today, humans find themselves facing many serious threats: an increasing population and the need for food; increasing energy use and the concomitant production of greenhouse gases; the need for more and improved pharmaceuticals. We have the opportunity to change the way we approach these problems, and moreover, we can take advantage of powerful new tools and technologies. Synthetic biology will play a crucial role in developing necessary solutions.

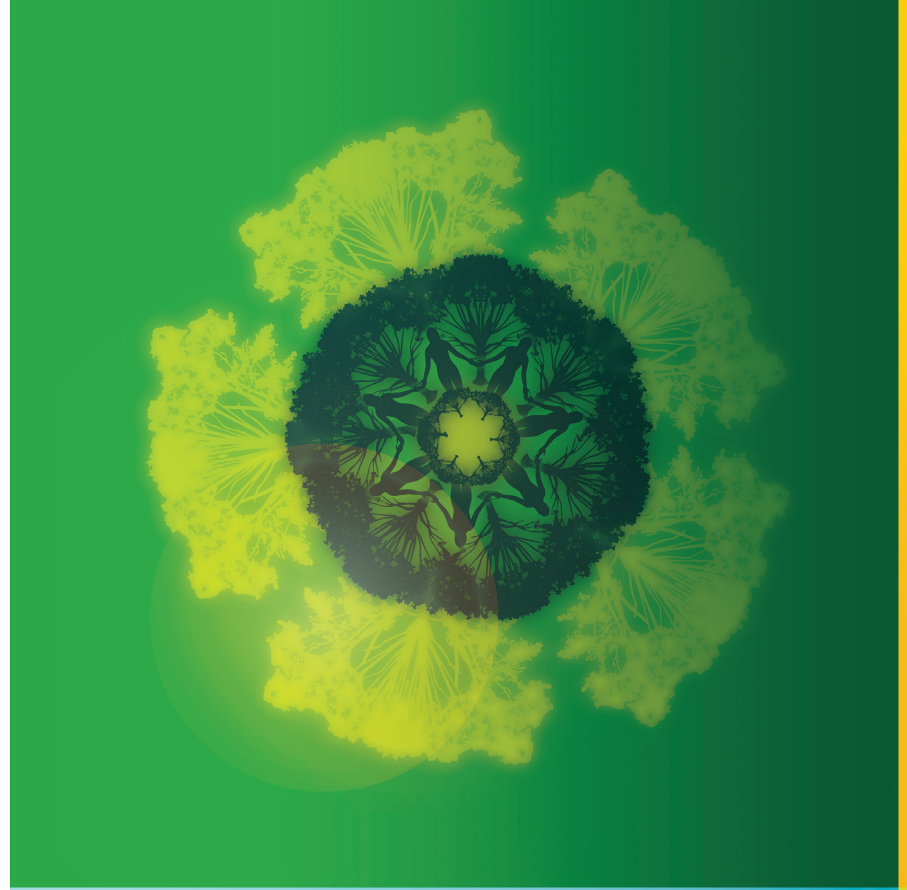
To help push synthetic biology forward to meet these needs, Synberc has made powerful steps to advance the field in the United States. Among its accomplishments since it was established in 2006, Synberc has developed numerous foundational technologies and sophisticated synthetic biology systems; trained a cadre of synthetic biology practitioners that populate universities, government laboratories and agencies, and industry; and established a unique industrial-academic partnership.

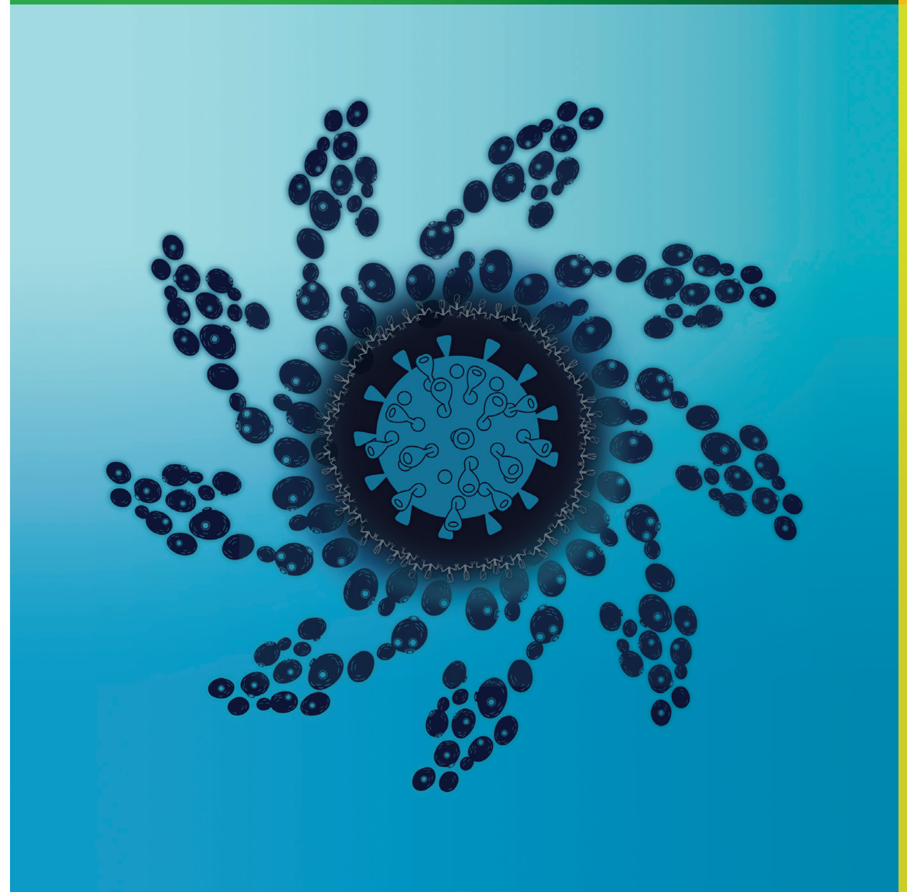
With Synberc's funding ending in 2016, a new organizational model and new funding sources are needed to propel this growing field and its community over the next ten years and keep the U.S. competitive with international efforts. The Engineering Biology Research Consortium, or EBRC, intends to fill that role. EBRC will provide the infrastructure and organizing principles to bring scientists, engineers, social scientists, and policymakers together from across the field. Moreover, it will support these stakeholders as they work together to develop a comprehensive national roadmap and vision to lead the field into its next chapter.

A Continuing Vision

EBRC will sustain Synberc's effort to bring together the synthetic biology community to provide the future vision for the field. Among other activities, EBRC will spur leading-edge research and education programs and promote dialogue with policymakers and members of the public. EBRC will provide the catalyst and infrastructure to bring together various stakeholders from both the public and private sectors and continue pushing biological engineering forward in the U.S. and internationally.

A key function of EBRC will be to create roadmaps for the future vision of biological engineering that can be used to align research aims with pressing national and global challenges. It will articulate compelling research visions and help catalyze research teams to pursue them. EBRC will also identify the education and training needs of academia and industry, and similarly catalyze the teams needed to build a workforce for the future. Continuing Synberc's tradition, EBRC will hold regular scientific retreats that bring together leaders from academia and industry. It will also expand its offering of topical workshops in areas such as mammalian synthetic biology and plant synthetic biology to push the boundaries in new areas and grow the community. EBRC will create resources and venues for biological engineers to engage with the public in order to share their work and motivations while exploring broader issues of importance with community members. Finally, EBRC will create new forums for connecting policymakers with the engineering biology community. This will help create new opportunities for pursuing the most promising research while addressing the challenges of engineering biology from a coordinated, national, and global approach.





Become a Part of our Community

Becoming a part of the EBRC community offers many benefits to researchers from across the synthetic biology spectrum, including both industry and academia.

First and foremost, being an EBRC member means playing a key role in the future of synthetic biology. EBRC members will have access to the most current, cutting-edge research and become part of a network of world-class academic and industrial researchers. In addition to being inspired by colleagues' work, being part of the EBRC community will facilitate opportunities to collaborate, extending research in new unexpected and exciting directions that would not otherwise be possible. Finally, EBRC membership means connecting with extremely talented future employees and employers. Scientists trained in EBRC labs will have a broad view of their continuing opportunities, and those running academic and industrial labs will have the foundation to build relationships with these exceptional individuals.

Beyond the research, involvement in EBRC will also place its members at the forefront of guiding synthetic biology as a field. Members will have the opportunity to participate in road-mapping and vision-setting meetings to identify vital future research directions and garner funding support. Members can also play a role in EBRC's advocacy for synthetic biology. EBRC will speak as an independent, credible scientific voice in matters of public policy, research funding, and presenting engineering biology to the public. In addition, EBRC can help represent consortium members' needs to funding agencies, regulators, and public stakeholders. Finally, EBRC is committed to responsible innovation. To that end, EBRC members will work together to responsibly advance engineering biology and ensure the highest possible standards of ethics, safety, and security.

Synberc Principal Investigators

J. Christopher Anderson

University of California, Berkeley
Associate Professor, Department of Biological Engineering

Chassis Thrust Leader • Tumor-Destroying Bacteria Testbed Leader

The Anderson Lab addresses foundational bottlenecks in synthetic biology. It uses microarray gene synthesis to construct 1000-member libraries of parts, then translates the sequence of these parts into function information through simple biochemical assays with deep sequencing readouts. The Act Ontology is used to encapsulate that information to enable automated design of genetic devices.

Adam Paul Arkin

University of California, Berkeley
Professor, Department of Bioengineering

The Arkin Lab seeks to uncover the evolutionary design principles of cellular networks and populations and to exploit them for applications. It uses a framework to effectively combine comparative functional genomics, quantitative measurement of cellular dynamics, biophysical modeling of cellular networks, and cellular circuit design to ultimately facilitate applications in health, the environment, and bioenergy.

George Church

Harvard Medical School
Professor, Department of Genetics

Chassis Testbed Leader

The Church Lab pursues a wide range of biotechnology research areas. Synthetic biology projects include MAGE, a machine that harnesses the natural principles of evolution to advance genome design and automate steps to dramatically shorten engineering times. The Church Lab also advances genome engineering tools like CRISPR, and was the first to demonstrate its use in mammalian cells.

Jay Keasling

University of California, Berkeley
Professor, Departments of Chemical Engineering & Bioengineering

Synberc Director • EBRC Chair of the Board of Directors

The Keasling Lab research themes include synthetic biology, metabolic engineering, and systems biology. It engineers biological components for use in controlling the expression of genes in metabolic pathways designed to solve specific problems. It has engineered microorganisms to synthesize the anti-malarial drug artemisinin, various flavor and fragrance molecules, biodegradable plastics, and biofuels.

Tanja Kortemme

University of California, San Francisco
Professor, Department of Bioengineering & Therapeutic Sciences

Parts Thrust Leader • EBRC Board Member

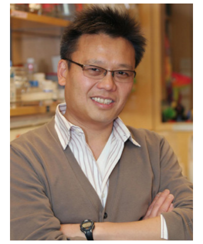
The Kortemme Lab is interested in designing and building new biological structures and functions to advance both studies of fundamental biological mechanisms and practical applications. Computationally, the lab has developed components of the design program Rosetta, including parts of its simple physical energy function and solutions to the long-standing problem of modeling structural changes during computer-aided design of proteins with atomic accuracy. In engineering applications, we have generated new pairs of interacting proteins to control behaviors in living cells, reprogrammed a protein machine to be fueled by light instead of ATP, created proteins that sense and respond to new molecular signals, and reengineered bacteria to reveal insights into microbial physiology.

Natalie Kuldell

President, BioBuilder Educational Foundation

Synberc Associate Director of Education

Dr. Kuldell established the BioBuilder Foundation in 2011 to convert cutting-edge science and engineering into engaging teachable modules. BioBuilder's curricula and teacher training capitalize on students' need to know, to explore and to be part of solving real world problems. From 2003 to 2015 Dr. Kuldell also taught in the Department of Biological Engineering at MIT.



Wendell Lim

University of California, San Francisco
Professor, Departments of Cellular and Molecular Pharmacology & Biochemistry and Biophysics

Synberc Deputy Director

The Lim Lab uses synthetic biology approaches to construct or rewire cellular networks to understand their design principles. The lab studies diverse cell types (yeast, T cells, neurons) to elucidate the general logic that cells use to solve common regulatory problems. It seeks to apply this knowledge to engineer designer cells that carry out therapeutic functions, such as sensing and destroying cancer.

Susan Marqusee

University of California, Berkeley
Professor, Department of Molecular and Cell Biology

Synberc Education Director

The Marqusee Lab seeks to understand the structural and dynamic information encoded in the linear sequence of amino acids. It is developing the biophysical knowledge to translate sequence information into functional insights. The laboratory uses a combination of biophysical, structural, and computational techniques to understand these features.

Ken Oye

Massachusetts Institute of Technology
Associate Professor, Departments of Political Science & Engineering Systems

Synberc Policy and Practices Director • EBRC Board Member

The Oye Group applies theories and methods from political economy to problems of science and technology policy, with emphasis on evaluating institutions and processes in the face of uncertainty over risks, benefits, and interests. It collaborates with many stakeholders to improve assessment and management of risks in synthetic biology, as well as to design adaptive approaches to pharmaceuticals licensing.

Kristala L. J. Prather

Massachusetts Institute of Technology
Associate Professor, Department of Chemical Engineering

Glucaric Acid Testbed Leader • EBRC Board Member

The Prather Lab works on the design and assembly of recombinant microorganisms for the production of small molecules. Current efforts include the development of methodologies for novel biosynthetic pathway design, as well tools for control of cellular metabolism. The research combines the traditions of metabolic engineering with the practices of biocatalysis to expand and optimize the biosynthetic capacity of microbial systems.

Pamela Silver

Harvard Medical School
Professor, Department of Systems Biology

Synberc Diversity Director • EBRC Board Member

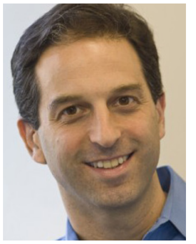
The Silver Lab works at the interface between systems and synthetic biology to design and build biological systems in both mammalian and prokaryotic cells. Current projects include novel therapeutic design strategies, building a programmable human artificial chromosome, engineering the gut microbiota, and developing a "bionic lead" to harness sunlight and capture carbon.

Christopher Voigt

Massachusetts Institute of Technology
Professor, Department of Biological Engineering

Nitrogen Fixation Testbed Leader • Devices Thrust Leader • EBRC Board Member

The Voigt Lab develops platforms to facilitate large genetic engineering projects. Cellular functions are divided into systems (sensory, control, actuators, regulators, etc.) that can be developed independently and then combined. This enables a wide range of applications, such as cells that communicate to build a material, navigate the human body to treat a disease, or protect plants by responding to the environment.



Ron Weiss

Massachusetts Institute of Technology
Professor, Department of Biological Engineering

Programmable Organoids Testbed Leader

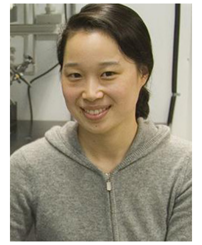
The Weiss Lab seeks to create integrated biological systems that perform useful tasks, and to elucidate the design principles underlying complex phenotypes. It uses engineering principles of abstraction, composition, and interface specifications to program cells with that are precisely controlled by analog and digital logic circuitry for foundational and applied projects spanning prokaryotes to mice.

Synberc Affiliated Investigators

James Carothers

University of Washington, Seattle
Assistant Professor, Department of Chemical Engineering

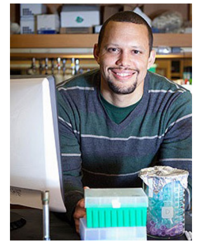
The Carothers Lab focuses on developing designable genetic control systems to enable larger, more complex synthetic biological systems. Work combines biochemical and biophysical modeling, computational design and analysis, in vitro selection, and genetic engineering to construct RNA-based control systems in microbes and mammalian cells to address unmet needs for renewable chemicals, therapeutic tissues, and low-cost global health materials.



Michelle Chang

University of California, Berkeley
Associate Professor, Department of Chemistry

The Chang Lab utilizes the approaches of mechanistic biochemistry, molecular and cell biology, metabolic engineering, and synthetic biology to address problems in energy and human health. Current projects include designing new metabolic pathways in microbial hosts for the production of biofuels and pharmaceuticals, the latter employing the biological generation of covalent C-F bonds.



Douglas Densmore

Boston University
Associate Professor, Department of Electrical and Computer Engineering

The Densmore (CIDAR) Lab focuses on the development of software tools for the specification, design, and assembly of synthetic biological systems. A research goal is to raise the level of abstraction in synthetic biology by employing standardized biological part-based designs which leverage domain-specific languages, constraint-based device composition, visual editing environments, and automated microfluidic and liquid handling robotic assembly.

John Dueber

University of California, Berkeley
Associate Professor, Department of Bioengineering

The Dueber Lab develops strategies for introducing designable, modular control over living cells. It creates technologies for improving engineered metabolic pathway efficiency and directing flux, useful for biofuels, specialty chemicals, and environmentally friendly processes. Recent achievements include the creation of a highly characterized yeast toolkit for modular, multi-part DNA assembly.

Paula T. Hammond

Massachussetts Institute of Technology
Professor, Department of Biological and Health Systems Engineering

The Hammond Lab focuses on the self-assembly of polymeric nanomaterials, with a major emphasis on the use of electrostatics and other complementary interactions to generate functional materials with highly controlled architecture. Applications include macromolecular design and synthesis, targeted drug delivery for cancer, and nanoscale assembly of synthetic biomaterials.

Karmella Haynes

Arizona State University
Assistant Professor, School of Biological and Health Systems Engineering

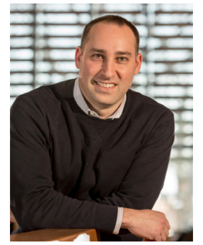
EBRC Board Member

The Haynes Lab explores the use of protein engineering to create new epigenetic machinery that regulates genes at will. The group assembles interchangeable protein modules to build unique synthetic transcription factors that regulate gene activity in human cells by reading chromatin modifications. The use of strong gene activators of this type may potentially enhance cancer treatment.

Nathan Hillson

Joint BioEnergy Institute
Director of Synthetic Biology

Dr. Hillson's research group develops experimental wetware, software, and laboratory automation devices that facilitate, accelerate, and standardize the engineering of microbes. Examples of web-based software tools developed in the Hillson Lab include the ICE "Web-of-Registries" platform used by Synberc, JBEI, JGI, and ACS Synthetic Biology repositories of microbial strains/DNA sequences/seeds.



Farren Isaacs

Yale University
Assistant Professor, Department of Molecular, Cellular, and Developmental Biology

The Isaacs Lab develops foundational genomic and cellular engineering technologies to better understand natural systems and to program systems with new biological function. The lab seeks to apply these advances to address global challenges in medicine, energy supply and the environment. Current projects are focused on integrating engineering and evolution through the construction of genes, gene networks and whole genomes alongside quantitative models to gain a better understanding of whole biological systems.

Terry Johnson

University of California, Berkeley
Associate Teaching Professor, Department of Bioengineering

Terry Johnson teaches a broad range of courses relating to bioengineering and chemical engineering. He is interested in writing, public speaking, biotechnology, and public engagement. He has been involved with iGEM as a mentor, a judge, and an emcee. Johnson has received numerous teaching awards, including the 2010 Golden Apple Teaching Award from students at UC Berkeley.

Sriram Kosuri

University of California, Los Angeles
Assistant Professor, Department of Chemistry and Biochemistry

The Kosuri Lab develops technologies in DNA synthesis, DNA sequencing, and genome engineering to understand and build biological systems faster and simpler, across a wide range of cell types. Current projects include expanding the length of synthetic libraries, writing digital information in DNA, and engineering sensors in animal olfaction.

Chang Liu

University of California, Irvine
Assistant Professor, Department of Biomedical Engineering

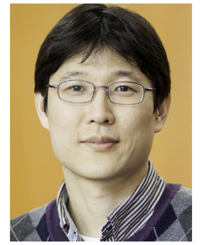
The Liu Lab focuses on synthesizing genetic systems that can accelerate the speed of evolution, reinterpret the genetic code, and record non-genetic information. These systems can be used to discover useful biomolecules, biopolymers, and therapeutics, and to study molecular evolution.

Julius Lucks

Cornell University
Assistant Professor, Department of Chemical Engineering

EBRC Board Member

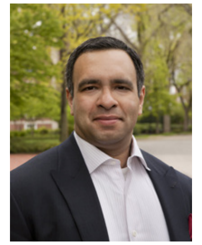
The Lucks group uses synthetic biology to ask fundamental questions at two levels. The first question we ask is, how can we design RNA sequences to fold into specific RNA structures that regulate gene expression inside cells? Using our designed RNA regulators as tools, the second question we ask is, what are the design principles of constructing gene regulatory networks out of well-characterized building blocks that have predictable function? Through innovative technological developments we have been answering these questions with implications for understanding and engineering cellular systems.



Tae Seok Moon

Washington University in St. Louis
Assistant Professor, Department of Energy, Environmental, and Chemical Engineering

The Moon Lab creates programmable cells that process multiple input signals and produce desirable outputs for real-world applications. Current projects include programmed killing of parasite eggs by probiotic bacteria, nitrogen fixation by photosynthetic bacteria, and conversion of lignin to triacylglycerols (biodiesel precursors) using a hybrid biological and thermochemical process.



Gautam Mukunda

Harvard Business School
Assistant Professor, Organizational Behavior Unit

Dr. Mukunda's research focuses on leadership, international relations, and the social and political implications of technological change. He is a member of the Council on Foreign Relations and MIT's Security Studies Program and Program on Emerging Technologies. He has published on leadership, network-centric warfare, and the security and economic implications of synthetic biology.

Megan Palmer

Stanford University
Senior Research Scholar, Center for International Security and Cooperation

Synberc Policy and Practices Deputy Director

Dr. Palmer's work seeks to develop and advise on best practices and policies for responsibly advancing biotechnology. Her research focuses on risk governance and dual use issues in biotechnology and other emerging technologies. She has contributed to and directed projects in biological safety and security, property rights, and governance. She has also launched many programs on the societal aspects of biotechnology, including the Synthetic Biology Leadership Excellence Accelerator Program (LEAP).

Pamela Peralta-Yahya

Georgia Institute of Technology
Assistant Professor, Department of Chemical Engineering

The Peralta-Yahya Lab develops foundational technologies to more effectively engineer biological systems for chemical synthesis. Current work focuses on biosensors to screen chemical-producing microbes, which could identify strains that produce chemicals at industrially relevant yield. This could be useful for microbial production of pharmaceuticals and high energy density fuels.

Howard Salis

Pennsylvania State University
Assistant Professor, Departments of Chemical Engineering & Biological Engineering

The Salis Lab develops predictive biophysical models and optimization algorithms to automatically design synthetic genetic system sequences for optimal performance, including biosensors, genetic circuits, metabolic pathways, and synthetic genomes. Our design algorithms provide tunable control of gene expression levels and efficient parameterization of system-wide models to convert high-level design specifications into optimized DNA sequences (a "DNA compiler"). Our web portal has over 6000 registered users who have designed over 100,000 synthetic DNA sequences.

David Savage

University of California, Berkeley
Assistant Professor, Department of Molecular and Cell Biology

The Savage Lab is interested in the molecular strategies used by microbes to facilitate and regulate their metabolism, with a particular emphasis on carbon dioxide assimilation. The lab also develops protein engineering-based tools for measuring and perturbing physiology.

Jeff Tabor

Rice University
Assistant Professor, Department of Bioengineering

The Tabor Lab programs living cells to sense, compute, and respond to information in the environment. The lab has developed technologies enabling bacterial two-component systems (TCSs), the primary means by which bacteria sense the outside world, to be computationally identified, transported between species, screened against possible inputs in high throughput, and engineered to function as high performance sensors. We have engineered light switchable TCSs as optogenetic tools and used them for precise dynamical characterization of synthetic gene circuits. Finally, we are mining TCSs from the microbiome to engineer synthetic probiotic bacteria that can diagnose and treat disease.

Danielle Tullman-Ercek

Northwestern University
Associate Professor, Department of Chemical and Biological Engineering

The Tullman-Ercek Lab aims to control the transport of all kinds of molecules across cellular membranes. Projects include engineering naturally occurring biological parts, systems, and organisms to improve product yields for industrial and pharmaceutical applications. The lab also explores structural proteins as a building block for useful biomaterials, and is engineering them for applications such as fabrics, drug delivery devices, and templates for nanowires.

Harris Wang

Columbia University
Assistant Professor, Department of Systems Biology

The Wang Lab works on understanding the key principles that drive the formation, maintenance, and evolution of genomes within and across microbial populations. It also develops synthetic approaches in ecological engineering to manipulate disease-relevant microbial ecosystems, such as those found on the human body and in the human gut, with the goal of improving human health.

Fuzhong Zhang

Washington University in St. Louis
Assistant Professor, Department of Energy, Environmental, and Chemical Engineering

The Zhang Lab works to turn microbial cells into microfactories for the efficient production of biofuels, pharmaceuticals, and other value-added chemicals. It develops systems to solve environmental problems and to understand complex biology systems. A current project involves engineering microbes for the production of advanced biofuels from sustainable resources.

Synberc Affiliated Investigators

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26 & 27	CAD for Biology and BIOFAB, Karen Ingram & Associates
28 & 29	Programmable Organoids and Nitrogen Fixation, Karen Ingram & Associates
30 & 31	Glucaric Acid and Tumor-Destroying Bacteria, Karen Ingram & Associates
32	Synberc poster session, Frazier Phillips
34	2015 LEAP fellows, David Kong
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46	Synberc poster session, Bruce Cook
47	Stanley Hall at UC Berkely, Bruce Cook
48 & 49	iGEM competition participants, David Kong
50	iCLEM students in the Lawrence Berkeley National Lab, Roy Kaltschmidt
51	Natalie Kuldell leading a workshop, Karen Ingram
52 & 53	Headshots courtesy of Synberc community members
54 & 55	Candid photos courtesy of Synberc community members
56	Expanding Potential hand composition, Kristina McLinden and Karen Ingram
58	Science Museum of Minneapolis photo courtesy of the "Building with Biology" program
59	"Building with Biology"at Chabot Space & Science Center in Oakland, Kevin Costa
60	Science Museum of Minneapolis photo courtesy of the "Building with Biology" program
61	#meetsynbio images, SnapFiesta
62a	62a - Congressional hearing, Michelle Moskowitz
62b	62b - Congressional briefing, Kevin Costa
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64	Leaves design, Karen Ingram
66 & 67	Bio Mandalas, Karen Ingram
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