EBRC Engineering Biology Research Consortium

# Engineering Biology

## A Research Roadmap for the Next-Generation Bioeconomy

Doug Friedman and Emily Aurand

October 16, 2019 | NSTC Interagency Workshop on Synthetic Biology

EBRC is the leading **U.S.-based non-profit, public-private partnership** dedicated to bringing together an inclusive community committed to advancing engineering biology to address national and global needs. We showcase **cutting-edge research** in engineering biology, identify pressing challenges and opportunities in research and application,  articulate compelling **research roadmaps and programs** to address these challenges and opportunities, and **provide timely access** to other key developments in engineering biology.


Agilent Technologies













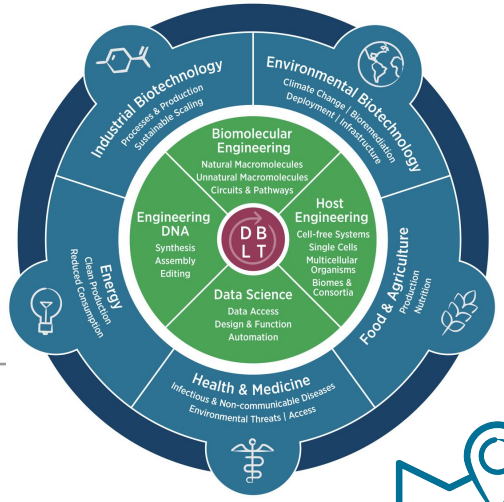


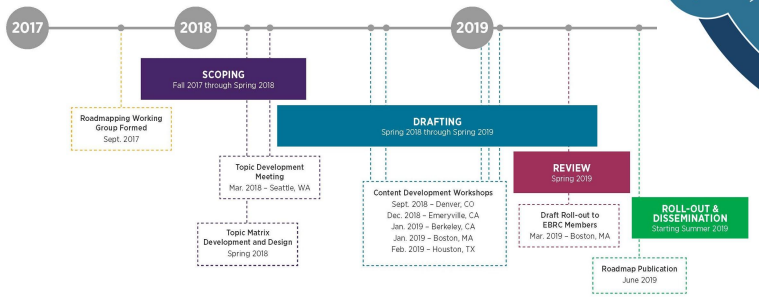


www.ebrc.org


Berkeley Lab
Columbia University in the City of New York
MIT
NC State
University of Michigan
Pacific Northwest National Laboratory
Georgia Tech
Rice
The University of Chicago
Boston University
UIC
NUS National University of Singapore
Yale
University of Washington
Johns Hopkins University
Northwestern University
UCSF
Wisconsin University of Wisconsin–Madison
Caltech
KIST
Northwestern University
UC Davis University of California
Colorado State University
Emory
Korea Institute of Science and Technology
Washington University in St. Louis
UConn University of Connecticut
Rensselaer
Purdue University
J. Craig Venter Institute
Illinois
Sandia National Laboratories
UC Santa Cruz
UC Santa Barbara
Stanford University
Berkeley University of California
Arizona State University
Imperial College London
UCI
University of Minnesota
UCLA
Penn State
The University of Utah
Harvard University
John Innes Centre
Texas The University of Texas at Austin
EBRC
www.ebrc.org

# Technical Research Roadmapping




EBRC Engineering Biology Research Consortium

# Security & Synthetic Biology

**Malice Analysis**

**Considering Security Implications in Engineering Biology Research**

Clem Fortman

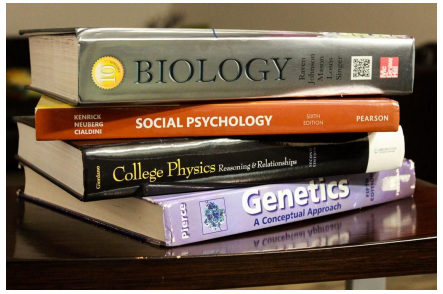
September 2019

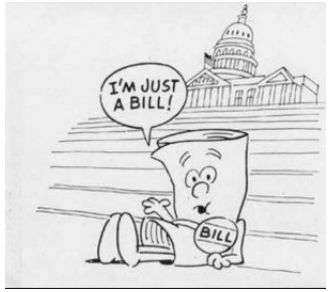
www.ebrc.org

EBRC Engineering Biology Research Consortium

YouTube

ebrc.org/YouTube




*Global Forum on Engineering Biology*

# Synthetic Biology Education

# Policy & International Engagement

EBRC Engineering Biology Research Consortium

# Roadmap Development

Doug Friedman

# Leadership Team

**Emily Aurand**
EBRC
Director of Roadmapping

**Jay Keasling**
UC Berkeley
Working Group Chair
*Energy* Sector Lead

**Douglas Friedman**
EBRC
Executive Director

## *Technical Theme Leads*

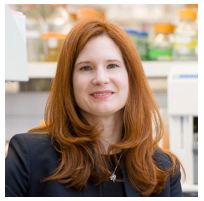
**Howard Salis**
Penn State
*Gene editing, synthesis, and assembly*

**Chang Liu**
UC Irvine
*Biomolecule, pathway, and circuit engineering*

**Pamela Peralta-Yahya**
Georgia Tech
*Host and consortia engineering*

**James Carothers**
Washington
*Host and consortia engineering*

**Adam Arkin**
UC Berkeley
*Data analytics, design, and modeling*



**Cynthia Collins**
RPI
*Data analytics, design, and modeling*

## *Working Group Members*

**Visu Annaluru**
Corteva Agriscience

**Roel Bovenberg**
DSM

**Paul Carlson**
Cornell

**Lydia Contreras**
UT Austin

**Paul Freemont**
Imperial College

**Fumiaki Hamazato**
Hitachi High-Tech

**Michael Jewett**
Northwestern

**Ahmad Khalil**
BU

**Jens Plassmeier**
BASF

**Hans Roubos**
DSM

**Jeffrey Sampson**
Agilent

**Matthew Chang**
Nat. U of Singapore

## *Application and Impact Sector Leads*

**Ute Galm**
Zymergen, Inc.
*Industrial Biotechnology*

**Carrie Cizauskas**
Zymergen, Inc.
*Industrial Biotechnology*

**Karmella Haynes**
Emory U
*Health & Medicine*

**Albert Lu**
Corteva Agriscience
*Food & Agriculture*

**David Savage**
UC Berkeley
*Environmental Biotechnology*

EBRC

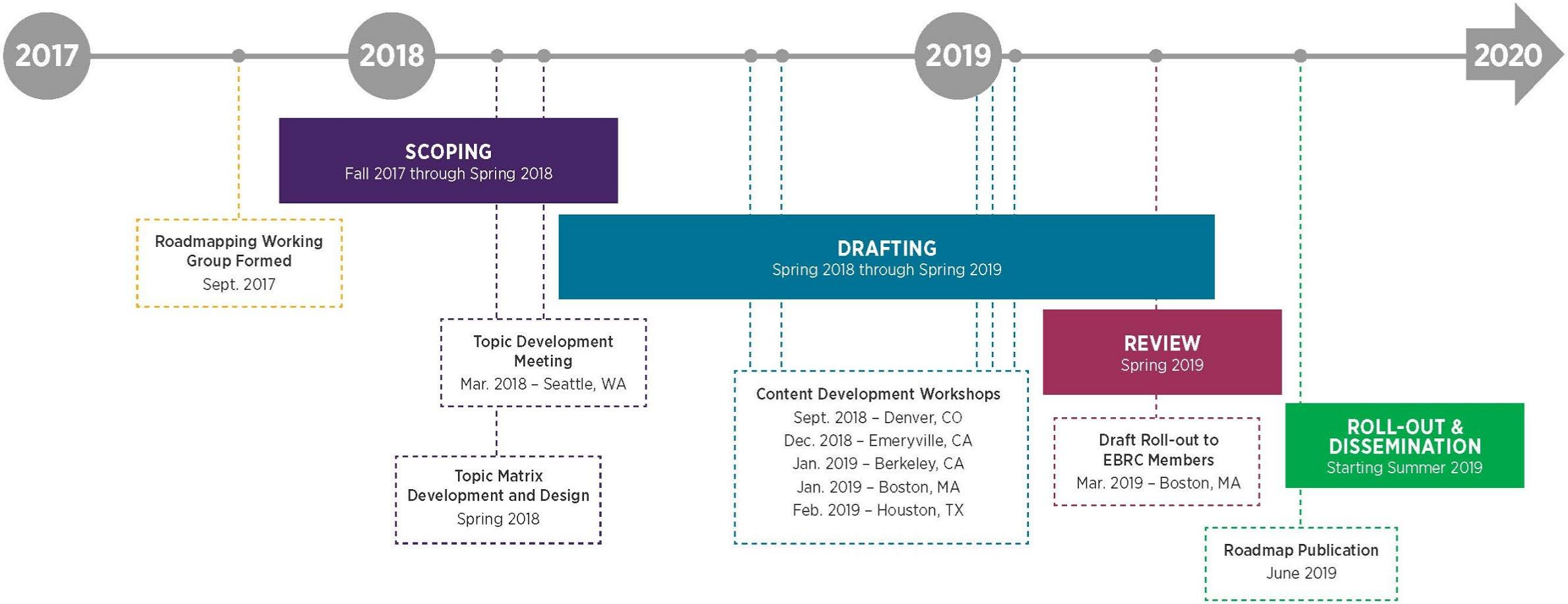
www.ebrc.org

# Contributors

Jason Aulds, Scientist, US Department of Defense
Ania Baetica, Postdoctoral Researcher (El-Samad Lab), University of California, San Francisco
Cassandra Barrett, Graduate Student (Haynes Lab), Arizona State University
Allison Berke, Scientist, The Good Food Institute
Daniel Brauer, Graduate Student (Francis Lab), University of California, Berkeley
Kathryn Brink, Graduate Student (Tabor Lab), Rice University
Yvonne Chen, Assistant Professor, University of California, Los Angeles *
George Church, Professor, Harvard University
Austin Cole, Graduate Student (Ellington Lab), University of Texas
Rhiju Das, Associate Professor, Stanford University
Jason Delborne, Associate Professor, North Carolina State University *
Doug Densmore, Associate Professor, Boston University *
James Diggans, Director, Bioinformatics and Biosecurity, Twist Bioscience Corporation *
John Dueber, Associate Professor, University of California, Berkeley *
Mary Dunlop, Assistant Professor, Boston University *
Chris Earnhart, Acting Joint Product Lead, US Department of Defense
Robert Egbert, Staff Scientist, Pacific Northwest National Laboratory
Andrew Ellington, Professor, University of Texas at Austin *
Steven Evans, Retired, Dow AgroSciences *
Mike Fero, Chief Executive Officer, TeselaGen Biotechnology, Inc. *
Clem Fortman, Director of Security Engagements, Engineering Biology Research Consortium
Larry Gilbertson, Scientist & Genomics Strategy Lead, Monsanto
Jimmy D. Gollihar, Synthetic Biologist, US Army Research Laboratory
Tahlia Haeuser, Scientist, Zymergen *
Emily Hartman, Graduate Student (Francis Lab), University of California, Berkeley
Nathan Hillson, Staff Scientist, Lawrence Berkeley National Laboratory *
Cyan James, Medical and Life Science Analyst, Peraton, support to US Dept. of Defense
Richard Johnson, Chief Executive Officer, Global Helix LLC *
Terry Johnson, Associate Teaching Professor, University of California, Berkeley *
Kristala Jones Prather, Professor, Massachusetts Institute of Technology *
Richard Kitney, Professor, Imperial College of London *
Cody Krivacic, Graduate Student (Kortemme Lab), University of California, San Francisco
Natalie Kuldell, Executive Director, BioBuilder Educational Foundation *
Joshua Leonard, Associate Professor, Northwestern University *
Julius Lucks, Associate Professor, Northwestern University *
June Medford, Professor, Colorado State University *
Jeremy Mills, Assistant Professor, Arizona State University
Richard Murray, Professor, California Institute of Technology *
Vincent Noireaux, Professor, University of Minnesota *
Michael P. O'Keefe, Principal, Science & Technology, LMI, support to US Dept. of Defense
Kenneth Oye, Associate Professor, Massachusetts Institute of Technology *
Megan Palmer, Senior Research Scholar, Stanford University *
C. Nicole Rosenzweig, Division Chief, US Department of Defense
Heike Sederoff, Professor, North Carolina State University
Patrick Shih, Assistant Professor, University of California, Davis
Pamela Silver, Professor, Harvard University *
Michael Smanski, Assistant Professor, University of Minnesota *
Liz Specht, Associate Director of Science & Technology, The Good Food Institute
Ranjan Srivastava, Professor, University of Connecticut
Mark Styczynski, Associate Professor, Georgia Institute of Technology *
Kersh Thevasundaram, Graduate Student (Chang Lab), University of California, Berkeley
Kurt Thorn, Director of Data Science, Zymergen *
Danielle Tullman-Ercek, Associate Professor, Northwestern University *
Alon Wellner, Postdoctoral Researcher (Liu Lab), University of California, Irvine
Wilson Wong, Associate Professor, Boston University
Peng Yin, Professor, Harvard University
Jesse Zalatan, Assistant Professor, University of Washington
Alexandre Zanghellini, Co-Founder and CEO, Arzeda
Jeremy Zucker, Computational Scientist, Pacific Northwest National Laboratory

* Denotes EBRC Member at time of publication

# Roadmap Development Timeline



# Stakeholders

Who is the roadmap for?

**Research Community**

- By the community, for the community.
- *Coalesce around societal challenges for which synbio can be impactful.*
- Ideas for collaborations, proposals, projects.
- *Useful for postdocs interested in academia.*

**Funders and Government**

- Statement on opportunities in the field.
- *Milestones and targets to consider in program development.*
- Examples for senior leaders in government.
- *Regular updates to track the field.*

EBRC Engineering Biology Research Consortium

# Engineering Biology

## A Research Roadmap for the Next-Generation Bioeconomy

Emily Aurand

*This presentation is based upon work supported by the National Science Foundation under Grant No. 1818248.*

www.ebrc.org

# A Matrixed Approach

***Technical Themes***

| ***Sectors*** | Engineering DNA | Biomolecular Engineering | Host Engineering | Data Science |
|---|---|---|---|---|
| Industrial Biotechnology | | | | |
| Health & Medicine | | | | |
| Food & Agriculture | | | | |
| Environmental Biotechnology | | | | |
| Energy | | | | |

EBRC

www.ebrc.org

# Scope & Content

## Four Technical Themes:

1. **Engineering DNA** - Gene editing, synthesis, and assembly
2. **Biomolecular Engineering** - Biomolecule, pathway, and circuit engineering
3. **Host Engineering** - Host and consortia engineering
4. **Data Science** - Data integration, modeling, and automation

# Technical Theme Organization

**Definition and Introduction**

**Transformative Tools & Technologies**

**Roadmap Elements:**

- **Goals**
  - **Breakthrough Capabilities**
    - **Milestones (2, 5, 10, and 20 years)**
      - **Bottlenecks and Potential Solutions**

**Bottom Up**

# Milestones

**2 Years:** Active and ongoing research. Currently supported.

**5 Years:** May build on current work, but also will require specific coordination and targeted investment (not just financial).

**10 Years:** Ambitious goals that will require considerable attention to achieve.

**20 Years:** Represents a substantial change in capacity or understanding.

# Connecting to the Case Studies

## Examples from the EBRC Roadmap

**Case:** Transforming Bioenergy & Agriculture with Synthetic Biology

**EBRC Roadmap Example:** Food & Agriculture Sector

**Case:** Transforming Cellular Factories with Synthetic Biology

**EBRC Roadmap Example:** Host Engineering Theme

**Case:** Transforming Medicine with Synthetic Biology

**EBRC Roadmap Example:** Biomolecular Engineering Theme

**Case:** Transforming Biomanufacturing with Synthetic Biology

**EBRC Roadmap Example:** Industrial Biotechnology Sector

# HOST AND CONSORTIA ENGINEERING

## Case: Transforming Cellular Factories with Synthetic Biology

| Goal | Breakthough Capability | Milestone |
|---|---|---|

## Cell-free systems capable of natural and/or non-natural reactions.

| 2 Years | 5 Years | 10 Years | 20 Years |
|---|---|---|---|
| **Ability to build reproducible and comparable cell-free systems for practical applications in bioengineering and biomanufacturing from multiple organisms, including non-model hosts.** | | | |
| Complete characterization of the general effects of cell-growth harvest conditions and extract preparation parameters on bacterial cell-free extract behavior. | Complete standardization of common-use bacterial cell-free system. | Complete library of user-defined reaction components that could be used in a customizable cell-free system. | Consistent ability to generate cell-free systems from any organism or a subset of organisms that make all types of desired products. |
| **Long-lasting, robust, and low-cost cell-free system for protein synthesis and biomanufacturing.** | | | |
| Identify reagent instabilities in cell-free systems across multiple organisms and all biological kingdoms. | Alleviate reagent instabilities and prolong the half-life of cell-free reagents from a few hours to several days using inexpensive substrates.<br>Avoid inhibition (poisoning) of cell-free reactions by byproducts or the desired products. | Stabilize catalysts to facilitate cell-free reactions on the order of weeks. | Robust and scalable production of cell-free systems that last for weeks. |

# BIOMOLECULE, PATHWAY, AND CIRCUIT ENGINEERING

## Case: Transforming Medicine with Synthetic Biology

| Goal | Breakthough Capability | Milestone |
|---|---|---|

## Holistic, integrated design of multi-part genetic systems (i.e., circuits and pathways).

**Ability to rationally engineer sensor suites, genetic circuits, metabolic pathways, signaling cascades, and cell differentiation pathways.**

| 2 Years | 5 Years | 10 Years | 20 Years |
|---|---|---|---|
| Reliable engineering of genetic circuits with more than 10 regulators for sophisticated computations. | Reliable engineering of novel, many-enzyme pathways utilizing combinations of bioprospected enzymes with well-characterized kinetics. | Reliable expression of redesigned synthases to produce secondary metabolites. | Simultaneous, tunable, timed expression of many transcription factors controlling mammalian cell state. |
| | Five-time improvement and expansion of inducers/promoters for model organisms that respond to environmental inputs and any intracellular metabolite. | Computational design of protein-ligand and RNA-ligand interfaces suitable for engineering protein-based or RNA-based sensors. | |
| | Utilize machine-learning approaches to use the vast amount of uncurated literature results within pathway design. | | |

# A Matrixed Approach

***Technical Themes***

| ***Sectors*** | Engineering DNA | Biomolecular Engineering | Host Engineering | Data Science |
|---|---|---|---|---|
| Industrial Biotechnology | | | | |
| Health & Medicine | | | | |
| Food & Agriculture | | | | |
| Environmental Biotechnology | | | | |
| Energy | | | | |

EBRC

www.ebrc.org

# Scope & Content

## Five ‘Application & Impact’ Sectors:

1. Industrial Biotechnology
2. Health & Medicine
3. Food & Agriculture
4. Environmental Biotechnology
5. Energy


1 NO POVERTY
2 ZERO HUNGER
3 GOOD HEALTH AND WELL-BEING
4 QUALITY EDUCATION
5 GENDER EQUALITY
6 CLEAN WATER AND SANITATION
7 AFFORDABLE AND CLEAN ENERGY
8 DECENT WORK AND ECONOMIC GROWTH
9 INDUSTRY, INNOVATION AND INFRASTRUCTURE
10 REDUCED INEQUALITIES
11 SUSTAINABLE CITIES AND COMMUNITIES
12 RESPONSIBLE CONSUMPTION AND PRODUCTION
13 CLIMATE ACTION
14 LIFE BELOW WATER
15 LIFE ON LAND
16 PEACE, JUSTICE AND STRONG INSTITUTIONS
17 PARTNERSHIPS FOR THE GOALS
SUSTAINABLE DEVELOPMENT GOALS

EBRC

# Sector Organization

**Definition/Sector Description**

**Societal Challenges**

**Science/Engineering Aims**

**Engineering Biology Objectives**

**Technical Achievements**

for each technical theme

Top Down

# Connecting to the Case Studies

## Examples from the EBRC Roadmap

**Case:** Transforming Bioenergy & Agriculture with Synthetic Biology

**EBRC Roadmap Example:** Food & Agriculture Sector

**Case:** Transforming Cellular Factories with Synthetic Biology

**EBRC Roadmap Example:** Host and Consortia Engineering Theme

**Case:** Transforming Medicine with Synthetic Biology

**EBRC Roadmap Example:** Biomolecular Engineering Theme

**Case:** Transforming Biomanufacturing with Synthetic Biology

**EBRC Roadmap Example:** Industrial Biotechnology Sector

# Food & Agriculture

Case: Transforming Bioenergy & Agriculture with Synthetic Biology

**Societal Challenge:** Produce more food for a growing global population.

- Science/Engineering Aim: Improve agricultural yields by increasing crop efficiency and production.
  - Engineering Biology Objective: Improve photosynthesis in crops and other food plants.
    - **Engineering DNA**: Edit genes in the photosynthetic pathway for improved properties, including stability, catalytic activity, and substrate specificity.
    - **Biomolecular Engineering**: Improved efficiencies of key enzymes in the photosynthetic pathway.
    - **Host Engineering**: Introduce synthetic (heterologous or modified) enzymes/ complexes/pathways to improve photosynthetic efficiency.
    - **Data Analytics**: Enable and improve models for engineered photosynthetic pathways.

Select Engineering Biology Achievements

# Industrial Biotechnology

Case: Transforming Biomanufacturing with Synthetic Biology

**Societal Challenge:** Enable next-generation production through sustainable, cost-competitive, flexible, and efficient manufacturing processes.

- Science/Engineering Aim: Modular manufacturing to enable flexible, on-demand production of a range of target chemicals.
  - Engineering Biology Objective: Development of commercial systems for on-demand manufacturing of commodity and high-value chemicals.

Select Engineering Biology Achievements

- **Engineering DNA**: Ability to edit genomes of diverse hosts, including microbes, fungi, and protists.
- **Biomolecular Engineering**: Assembled sets of proteins that can completely degrade sustainable feedstocks.
- **Host Engineering**: Engineered microbial consortia with predictable composition, dynamics and function, to feed off of sequential byproducts in an (almost) closed-loop system.
- **Data Analytics**: Novel analytics tools to enable prediction and manipulation of holistic microbial ecosystem function by incorporating both biological and environmental data.

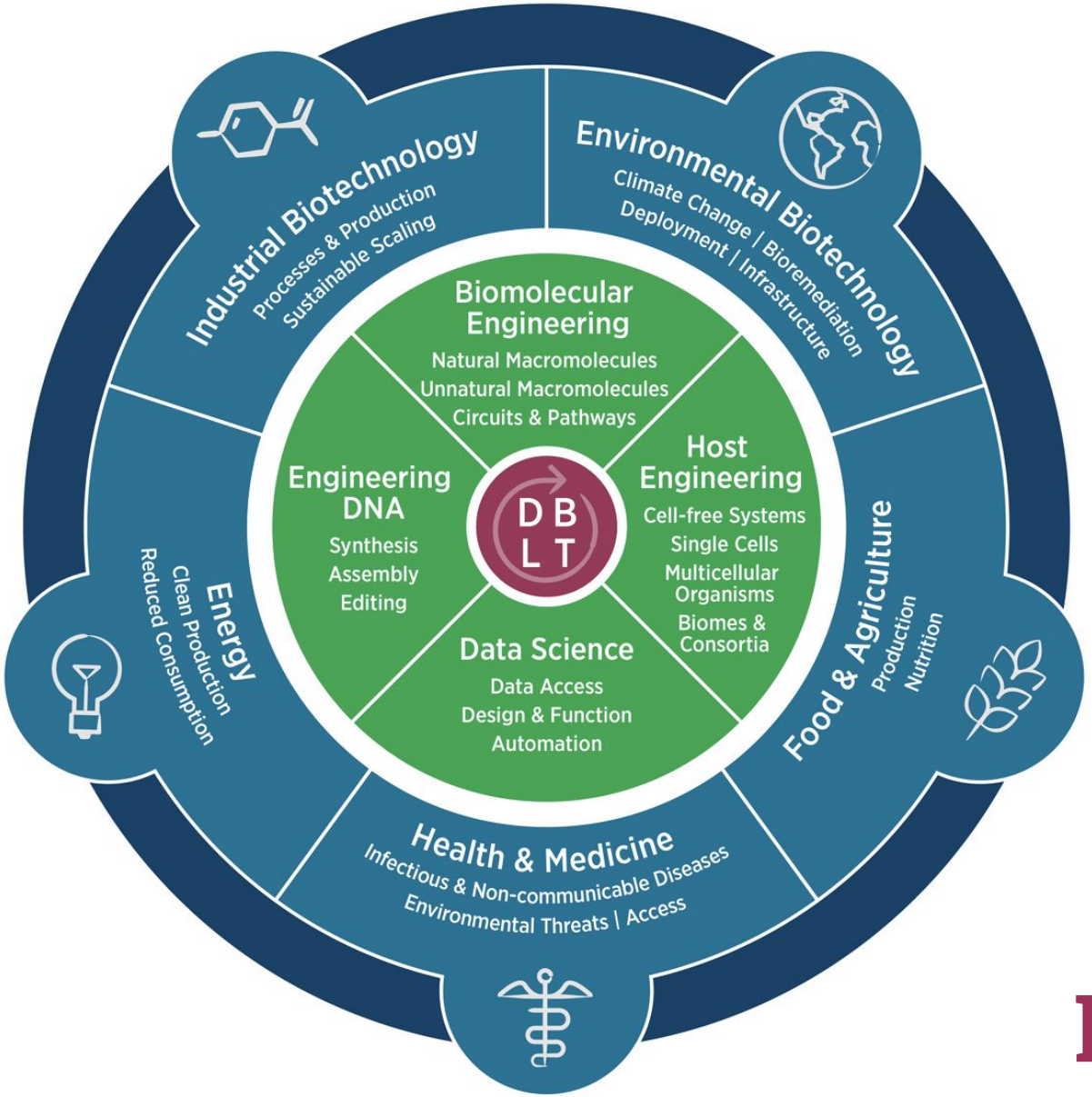
# Expanding Scope & Content

## Additional Considerations:

- Ethical Challenges
- Education and Workforce Development
- Policy and Regulation
- Security and Safety Implications

**Future Roadmapping:** updates, new topics, deep-dives

- 2019-2020: Materials | Microbiomes




# Engineering Biology

## A Research Roadmap for the Next-Generation Bioeconomy

| Technical Themes | Application Sectors |
|---|---|
| Engineering DNA | Industrial Biotechnology |
| Biomolecular Engineering | Health & Medicine |
| Host Engineering | Food & Agriculture |
| Data Science | Environmental Biotechnology |
| | Energy |

**https://roadmap.ebrc.org**

EBRC

*This material is based upon work supported by the National Science Foundation under Grant No. 1818248.*