EBRC Engineering Biology Research Consortium

Intro to Engineering Biology

Goals of this lecture

You will be able to answer:

- What is synthetic/engineering biology?
- How can I Design, Build, Test, and Learn from biological systems?
- What are the Core Tools of engineering biology?
- How and where can engineering biology be applied to positively impact society?

You will have:

- Planned a design cycle to approach a current problem
- Learned about engineering biology tools that can help you develop your idea
- Discovered the many sectors that engineering biology can positively impact

Recommended knowledge: “biology 101” level, generally how DNA & cells work

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Concept 1-1

What is Synthetic, or Engineering, Biology?

What is Engineering Biology?

Engineering Biology (a broader term for Synthetic Biology) is the **design and construction of new biological entities** such as enzymes, genetic circuits, and cells or the redesign of existing biological systems.

Engineering biology **builds on the advances** in molecular, cell, and systems biology and **seeks to transform** biology in the same way that synthesis transformed chemistry and integrated circuit design transformed computing.

The element that distinguishes engineering biology from traditional molecular and cellular biology is the **focus on the design and construction of core components** (e.g., parts of enzymes, genetic circuits, metabolic pathways) that can be modeled, understood, and tuned to meet specific performance criteria, and the assembly of these smaller parts and devices into larger integrated systems to solve specific problems.

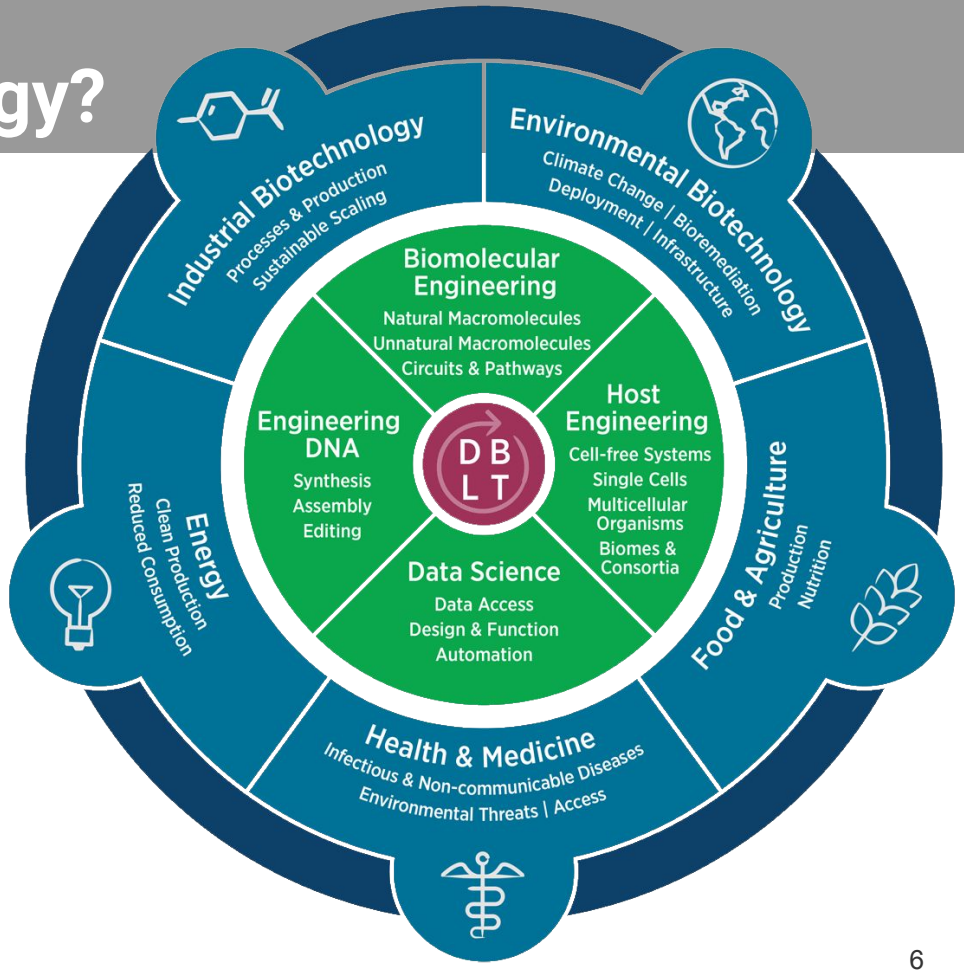
Unlike many other areas of engineering, biology is incredibly non-linear and less predictable, and there is less knowledge of the parts and how they interact.

Hence, the overwhelming physical details of natural biology (gene sequences, protein properties, biological systems) must be organized and recast via a set of design rules that hide information and manage complexity, thereby enabling the engineering of many-component integrated biological systems.

It is only when this is accomplished that designs of significant scale will be possible.

What is Engineering Biology?

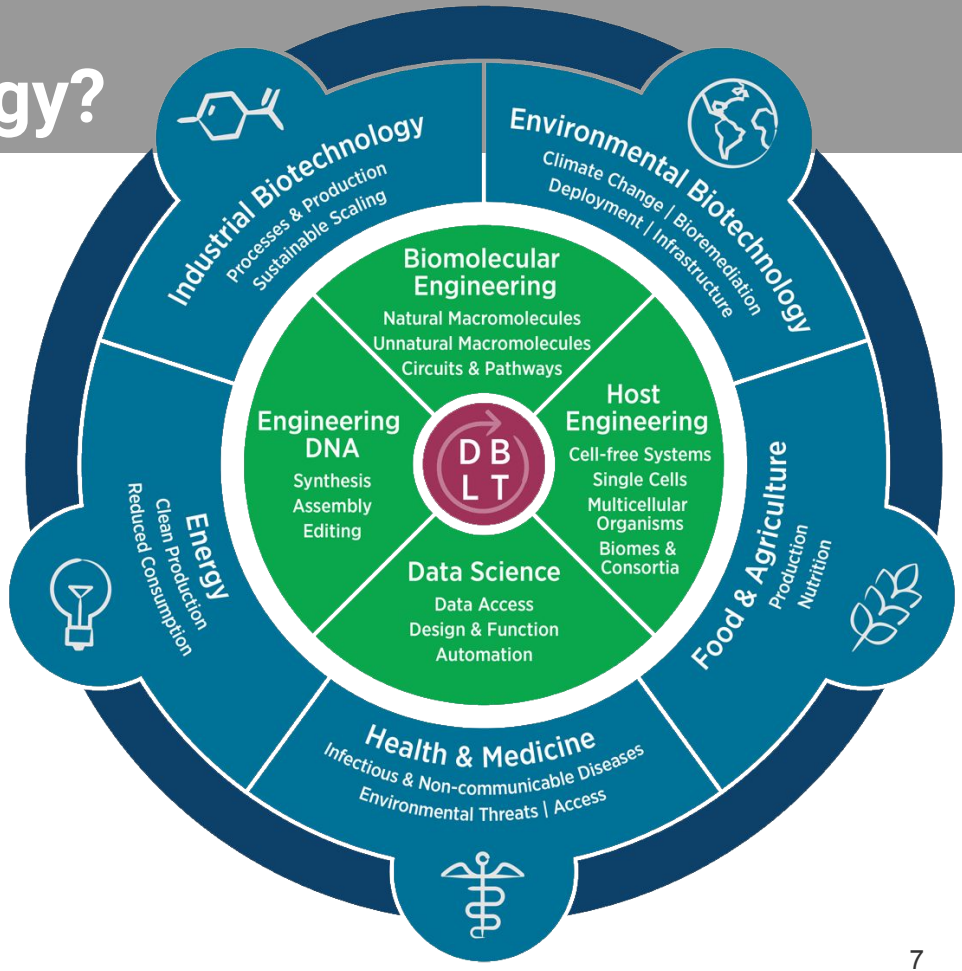
The goal: “engineer living cells to do something useful; for example, treat a disease, sense a toxic compound in the environment, or produce a valuable drug.” *(BioBuilder)*



Engineering Biology Research Consortium (2019). *Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy*. Retrieved from http://roadmap.ebrc.org. doi: 10.25498/E4159B.

What is Engineering Biology?

Example: using industrial biotechnology to treat a disease



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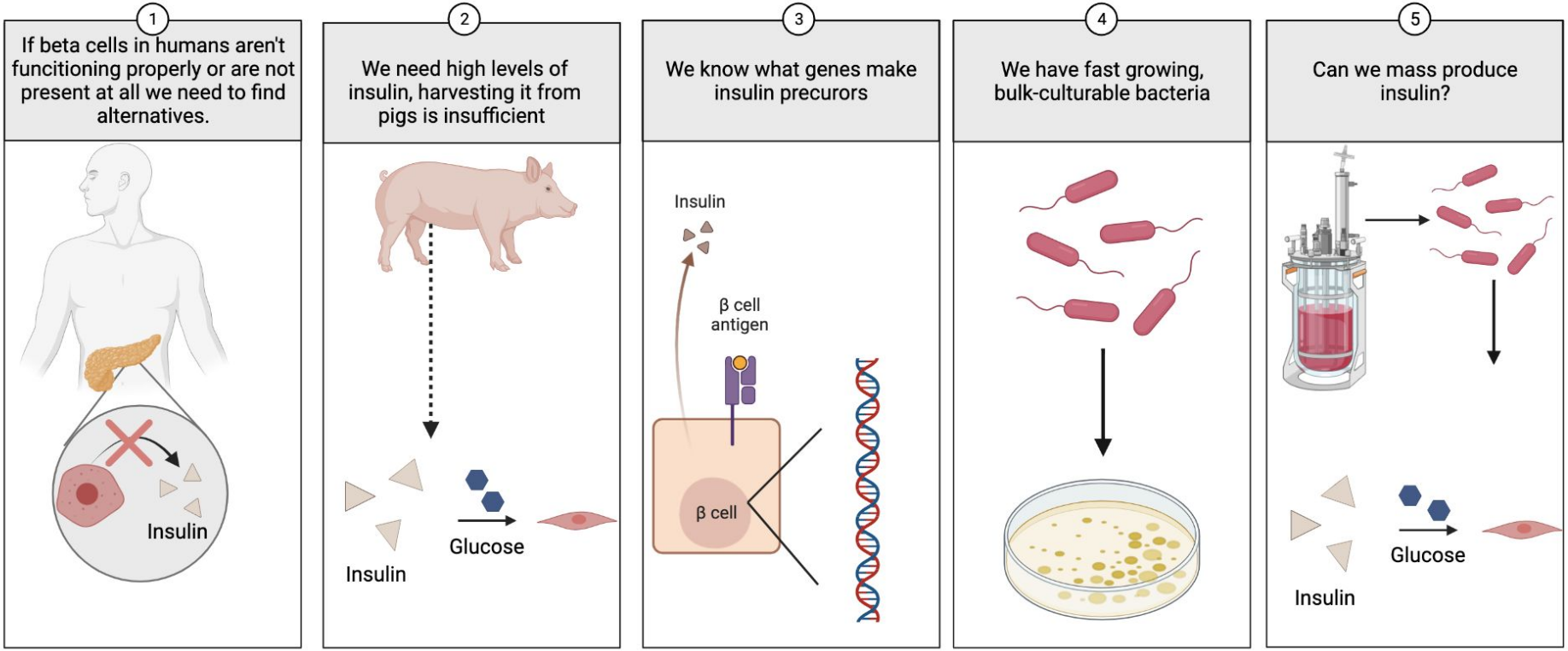
Industrial: Bacterial production of insulin



Mona Dabbas & Javin Oza, California Polytechnic State University. Created with Biorender.com.

Industrial: Bacterial production of insulin

What tools do we need?

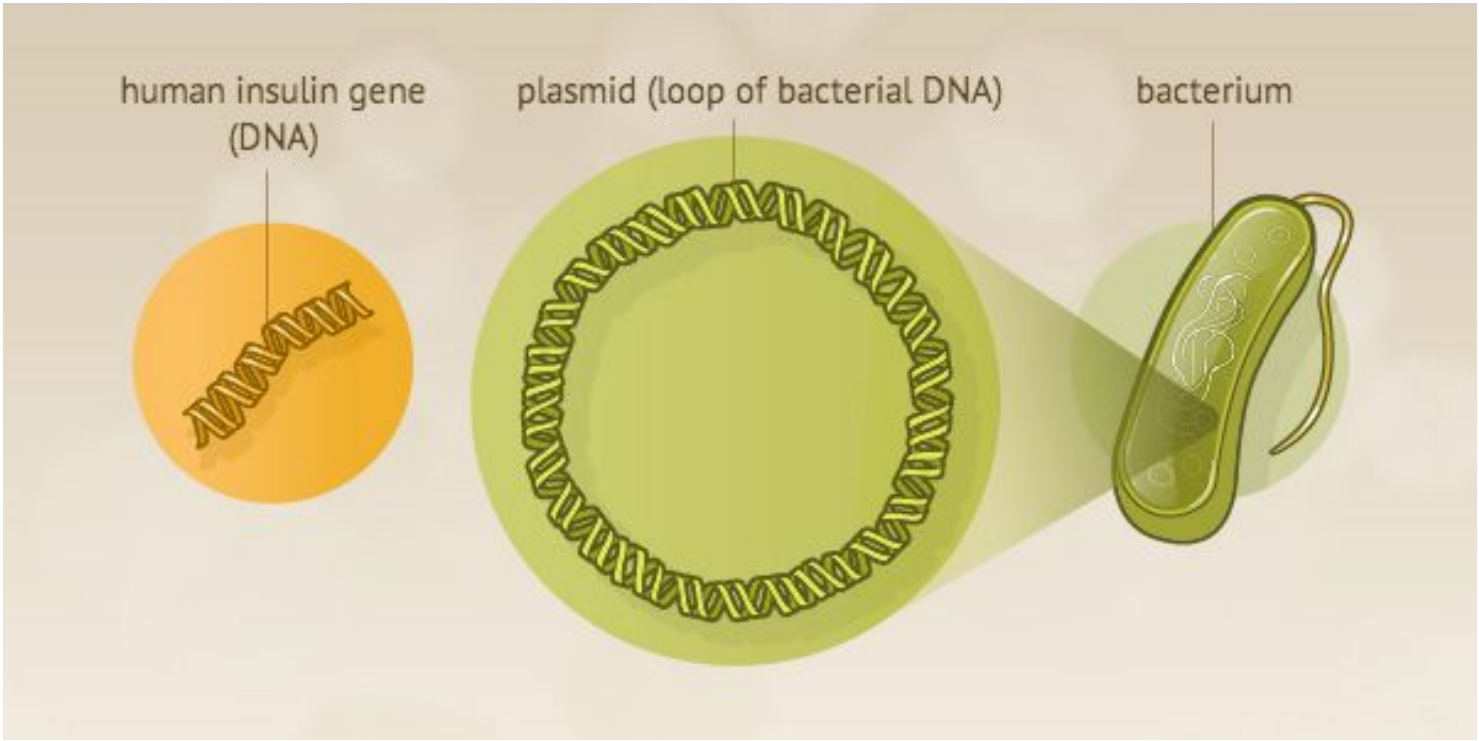
- Insulin precursor genes
- Genetic parts for gene expression in *E. coli*
- Way to assemble these genetic parts
- The *E. coli* cells themselves
- Way to get the DNA into the cells
- Way to harvest insulin from bacteria
- Way to measure insulin production

Industrial: Bacterial production of insulin

What steps do we need to take?

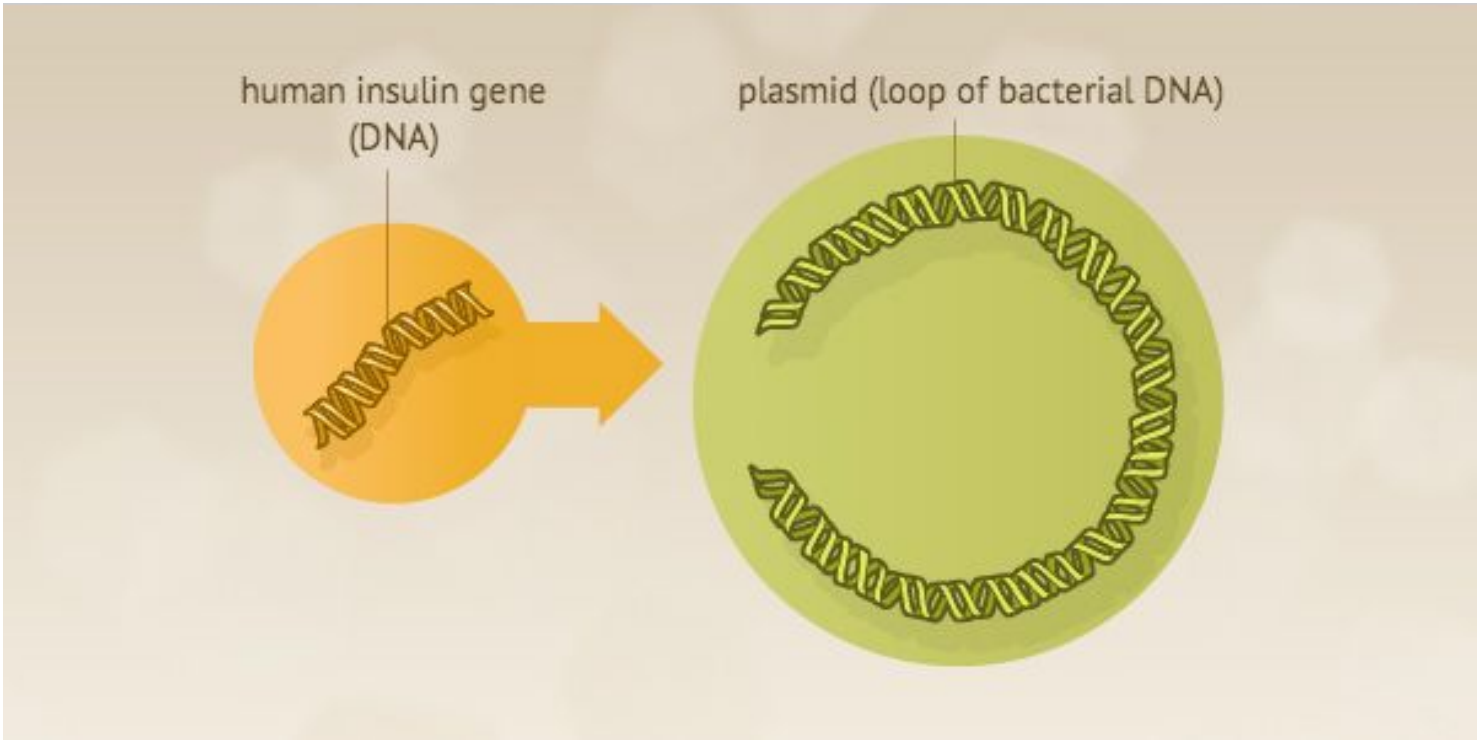
- Design a genetic circuit that will produce insulin in *E. coli*
- Build the genetic circuit, and put it into bacteria
- Test how much insulin is made
- Learn what did/didn’t work, change design accordingly

Industrial: Bacterial production of insulin



NIH. From DNA to Beer: Harnessing Nature in Medicine & Industry. 2013.

Industrial: Bacterial production of insulin



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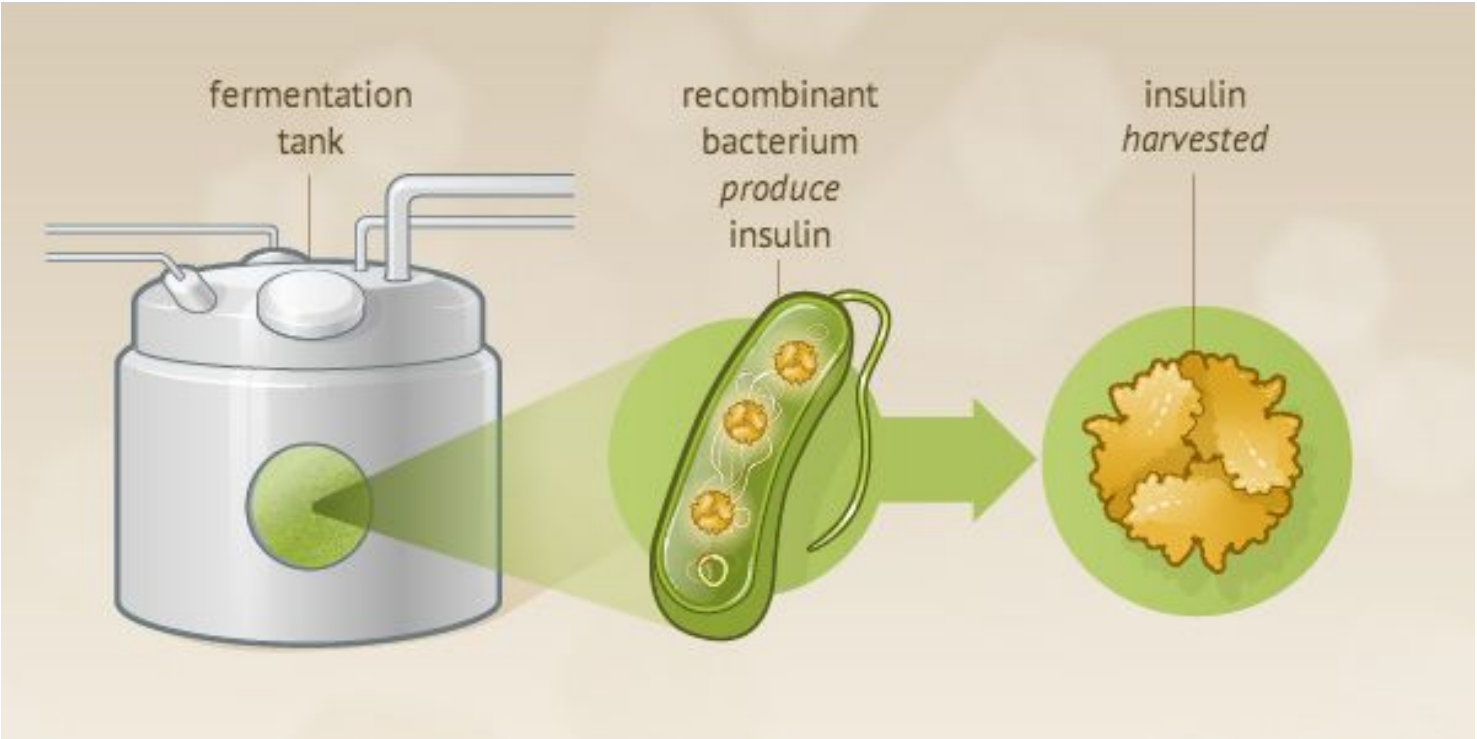

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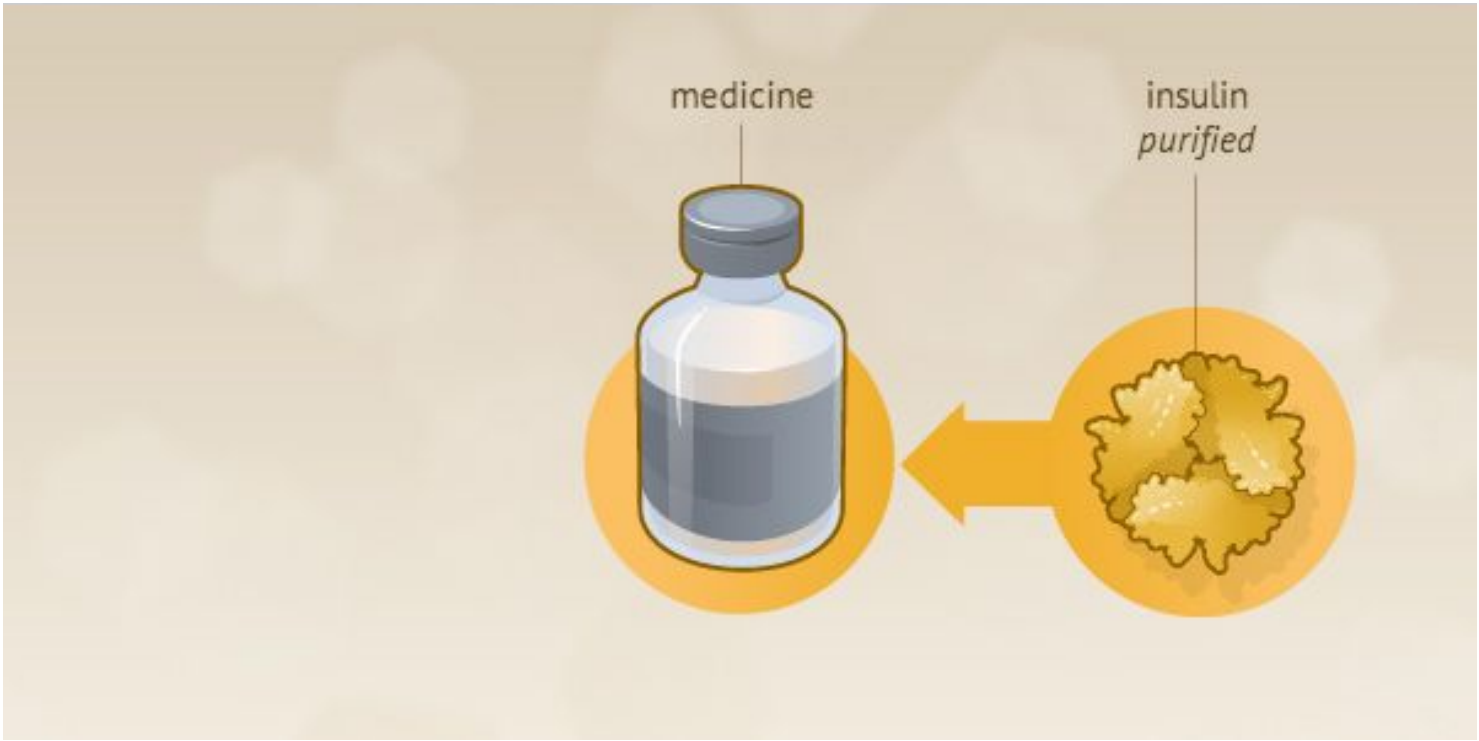
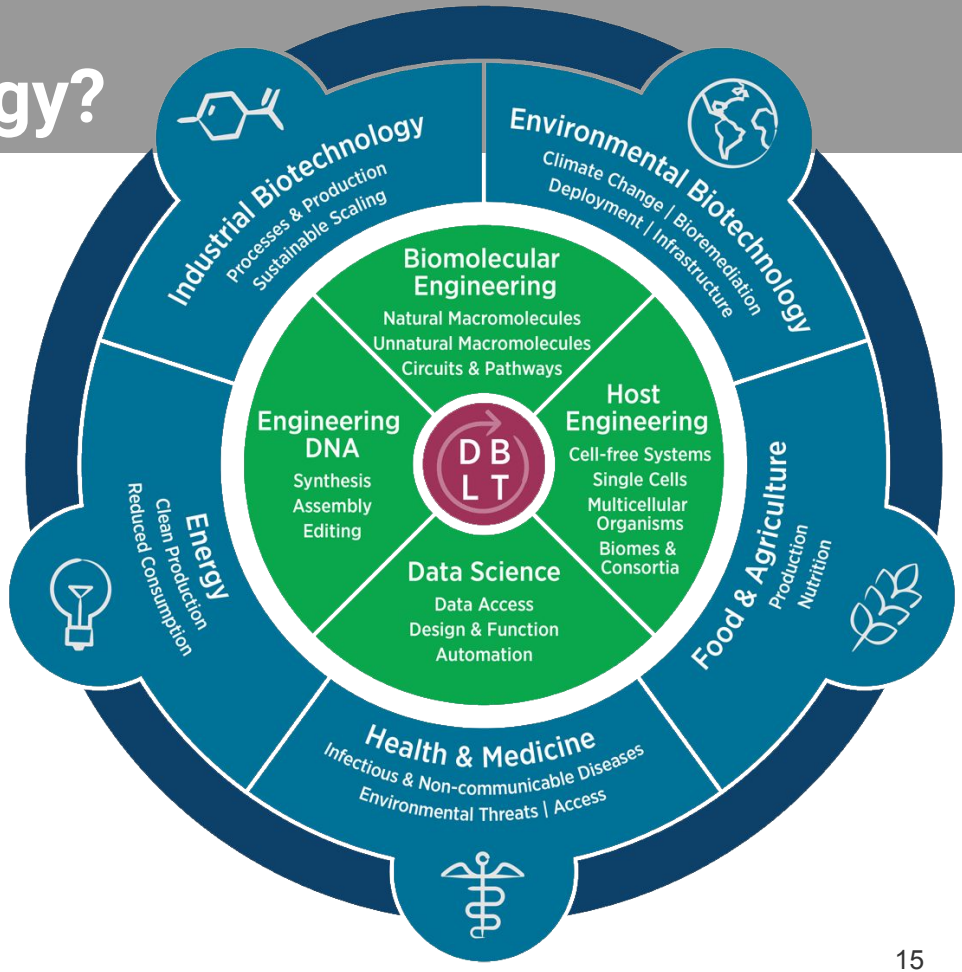


NIH. From DNA to Beer: Harnessing Nature in Medicine & Industry. 2013.

What is Engineering Biology?

- Example: use genetic circuits to mitigate an environmental pest



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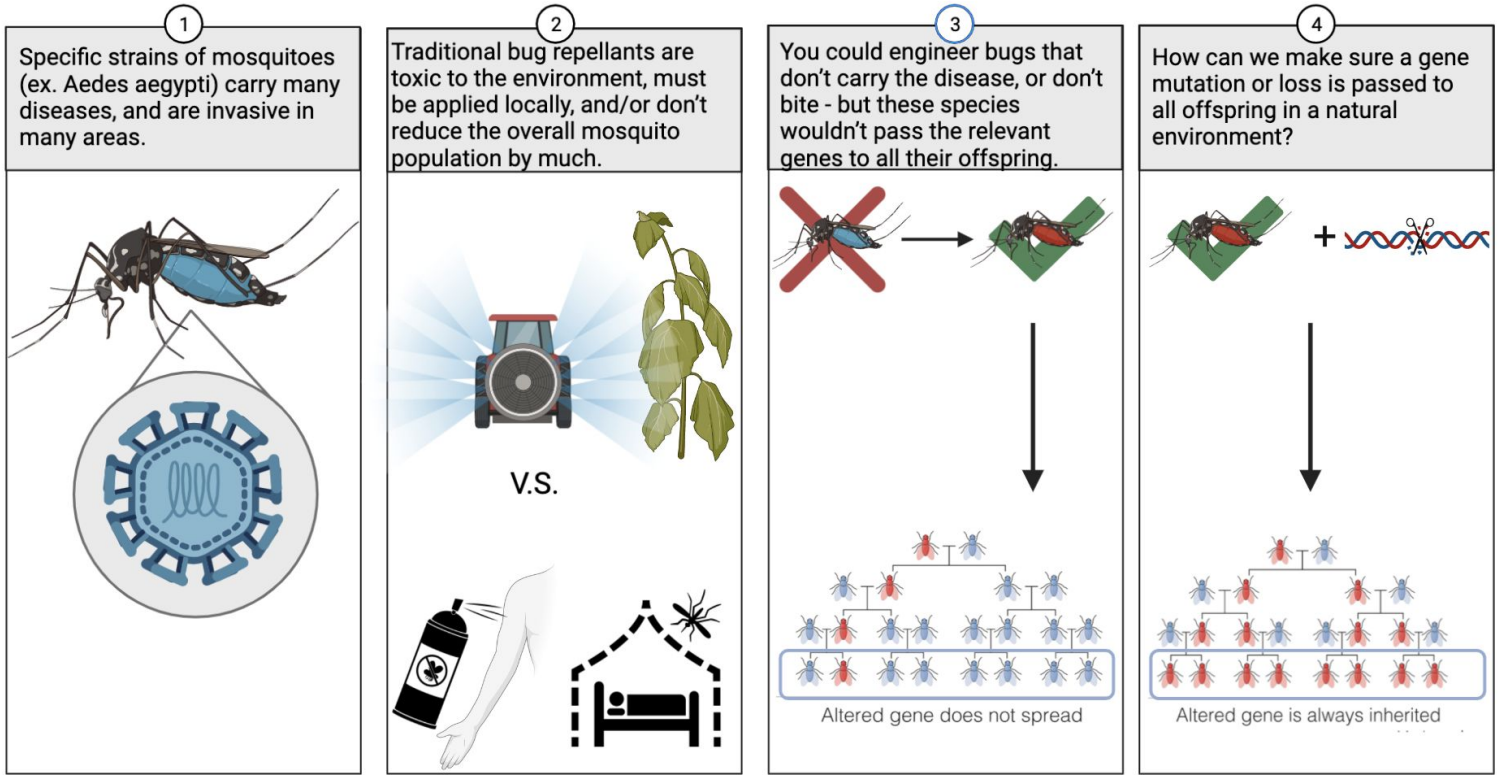
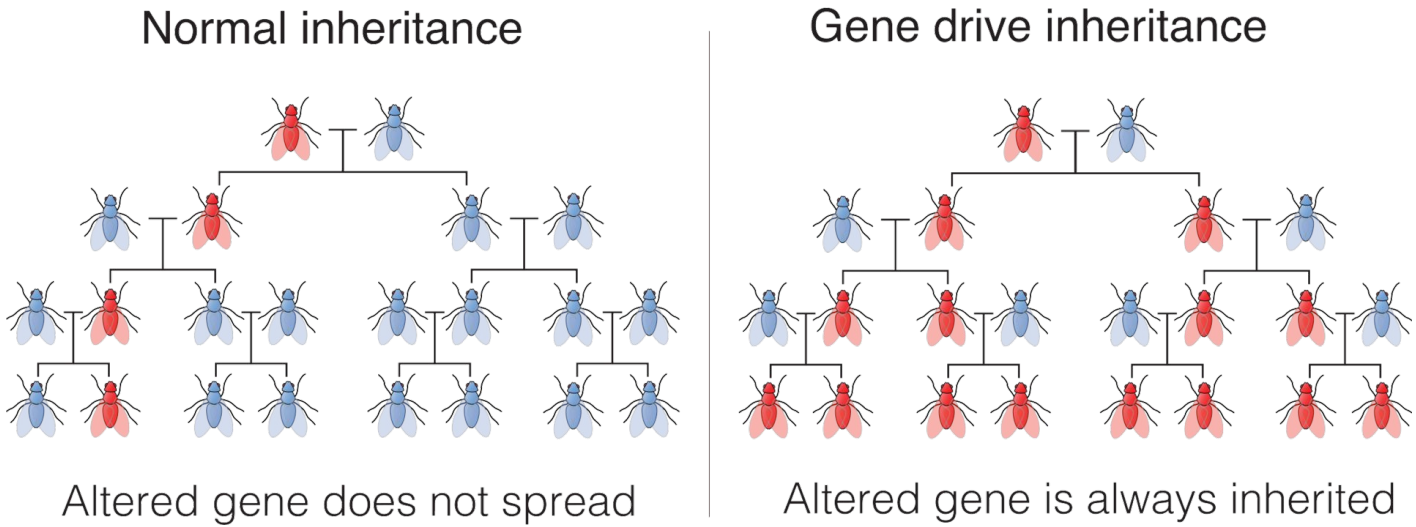
Environment: Gene drives limit mosquito populations



Marius Walter, "Gene Drive." Mona Dabbas & Javin Oza, California Polytechnic State University. Created with Biorender.com.

Environment: Gene drives limit mosquito populations



Marius Walter, “Gene Drive.”

Environment: Gene drives limit mosquito populations

What tools do we need?

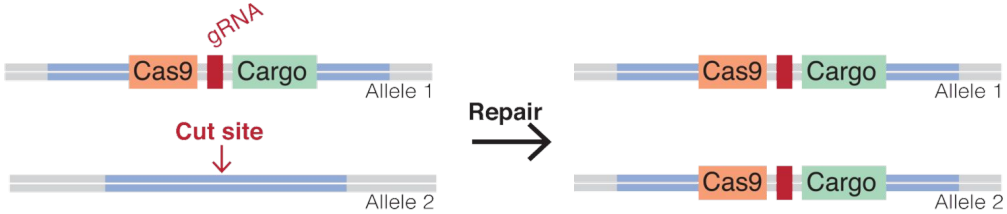
- Gene target to “knock out” or edit
- Genetic tool that will ensure these edits in all offspring
- Way to edit genes in mosquitoes
- Way to measure phenotypic changes from gene edits
- LOTS of safety testing strategies

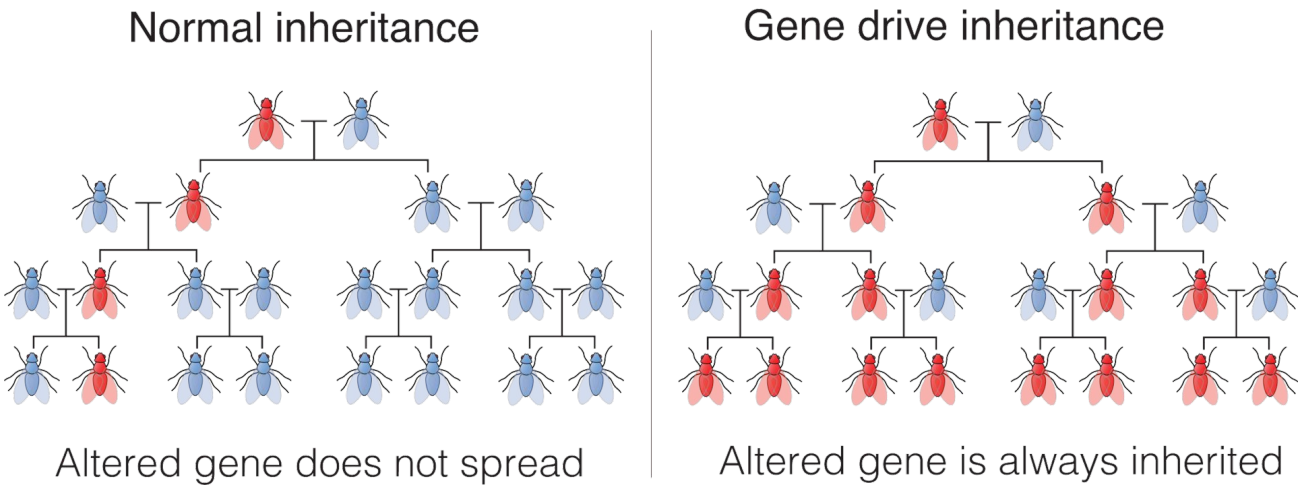
Environment: Gene drives limit mosquito populations

What steps do we take?

- Design a system that will knock out the selected gene in all offspring
- Build mosquitoes that carry this system
- Test the safety, efficacy, and spread of this gene system
- Learn by assessing how this impacts the mosquito population, overall environment, and disease spread

Environment: Gene drives limit mosquito populations





Marius Walter, "Gene Drive."

Environment: Bioethics of gene drives

Gene Drives:

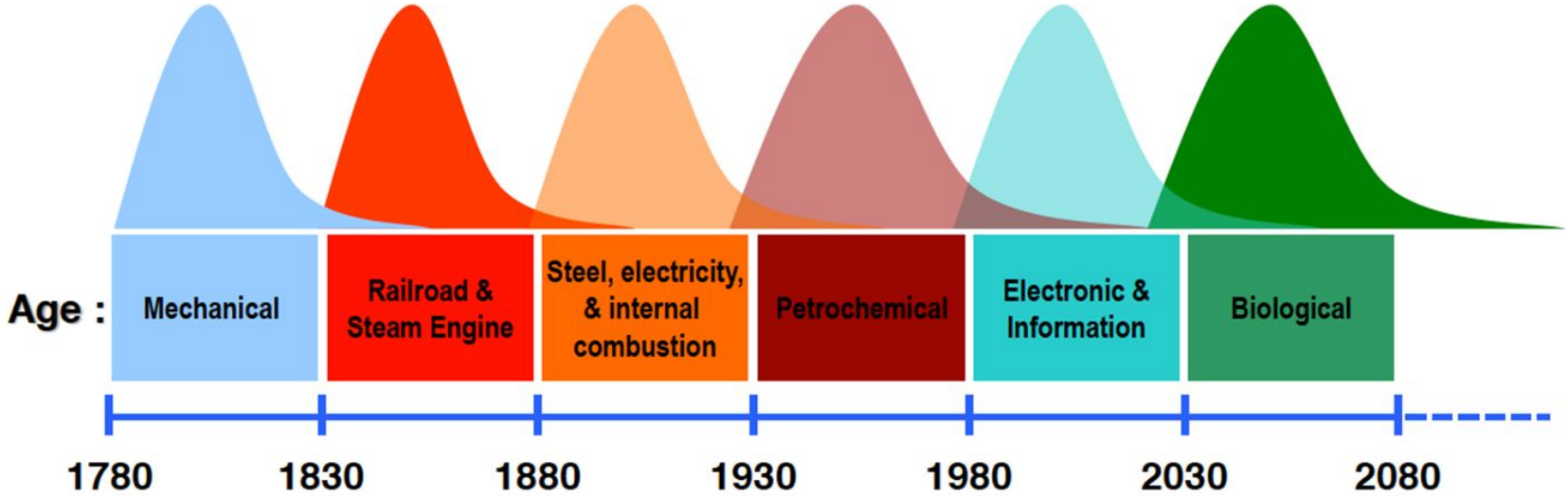
- What are potential safety concerns of gene drives?
- Who should decide when and where gene drives are used?
- How can gene drives be contained, or “undone” after use?

Core Principles:

1. Use engineering biology to benefit the world
2. Weigh benefits of research against potential harms
3. Incorporate justice into all aspects of engineering biology
4. Share research
5. Protect the freedoms of individuals and researchers
6. Support open communication between researchers and other stakeholders

Mackelprang, R., *et al*. (2021). “Guiding ethical principles in engineering biology research.”

Engineering biology as the next Kondratiev Wave



Michael Jewett, Northwestern University.

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Concept 1-2

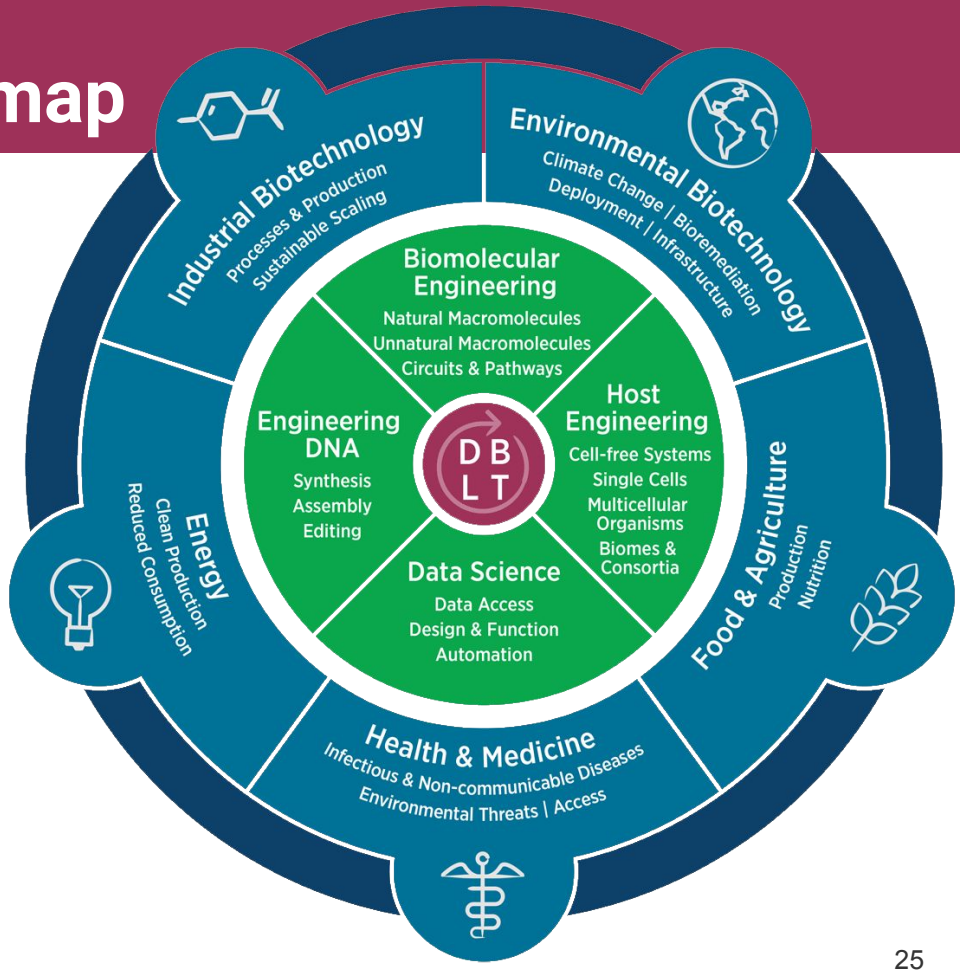
Engineering Biology Roadmap & the DBTL Cycle

Engineering Biology Roadmap

From a Design, Build, Test, Learn centered approach

Uses biological, engineering, and computational tools

To positively impact multiple sectors



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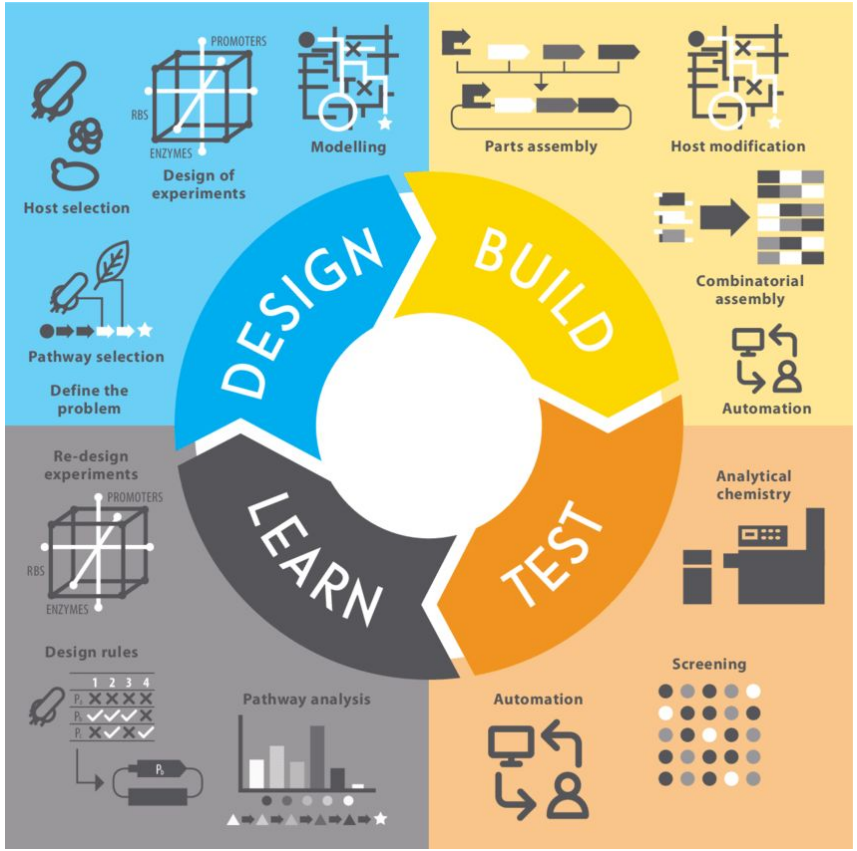
The DBTL Cycle



Design a biological circuit or system for a specific function using literature & computational tools.

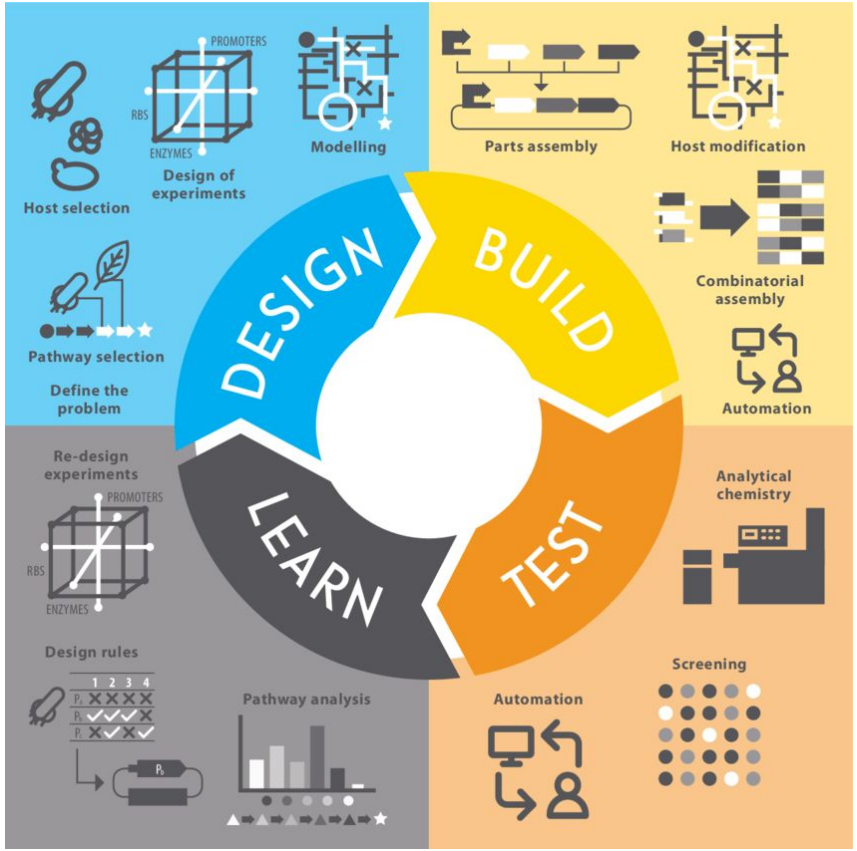
Build your system by assembling, editing, and installing genetic parts.

Test system functionality using robust metrics & controls.

Learn from how the system (doesn't) work to create new design rules, and share your knowledge.

Gray, P. et al. *Synthetic Biology in Australia: An Outlook to 2030* (Australian Council of Learned Academies, 2018).

DBTL: In Practice



Design by finding genes for human insulin precursors, and optimize/model *E. coli* expression.

Build gene sequence including insulin precursor genes though synthesis & assembly.

Test your circuit in cells by measuring for insulin precursor proteins chemically via an assay.

Learn how well your system works, and what optimization is necessary.

Gray, P. et al. *Synthetic Biology in Australia: An Outlook to 2030* (Australian Council of Learned Academies, 2018).

DBTL: Exercise

1. Choose a technology or problem that is impactful to you.
2. Think about what an engineering biology solution would look like:
    a. What would an initial **design** of the system look like?
    b. What tools and knowledge would you need to **build** this?
    c. How would you **test** whether your system worked?
    d. What might you **learn** about the problem through testing your solution? What might be issues when developing your system?
    e. And don’t get too bogged down in the details! We’ll go over more tools for each phase later.

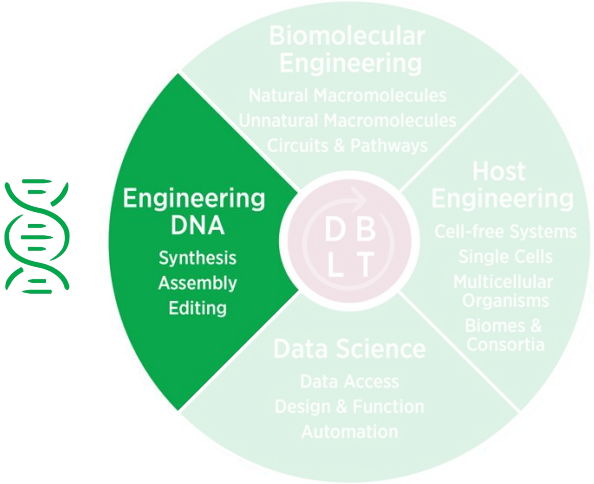
Example ideas: trees with fireproof wood, drought-resistant cabbage, sustainable bioplastics, engineered probiotics for gut health, cell-free water quality sensors

Concept 1-3

Core Tools Part 1:
Engineering DNA,
Biomolecular Engineering

Core Tools for Engineering DNA

- What are the current tools for engineering DNA?
- Tools enabling a engineering DNA DBTL
  - Synthesis
  - Sequencing
  - Standardization
  - Assembly
  - Editing



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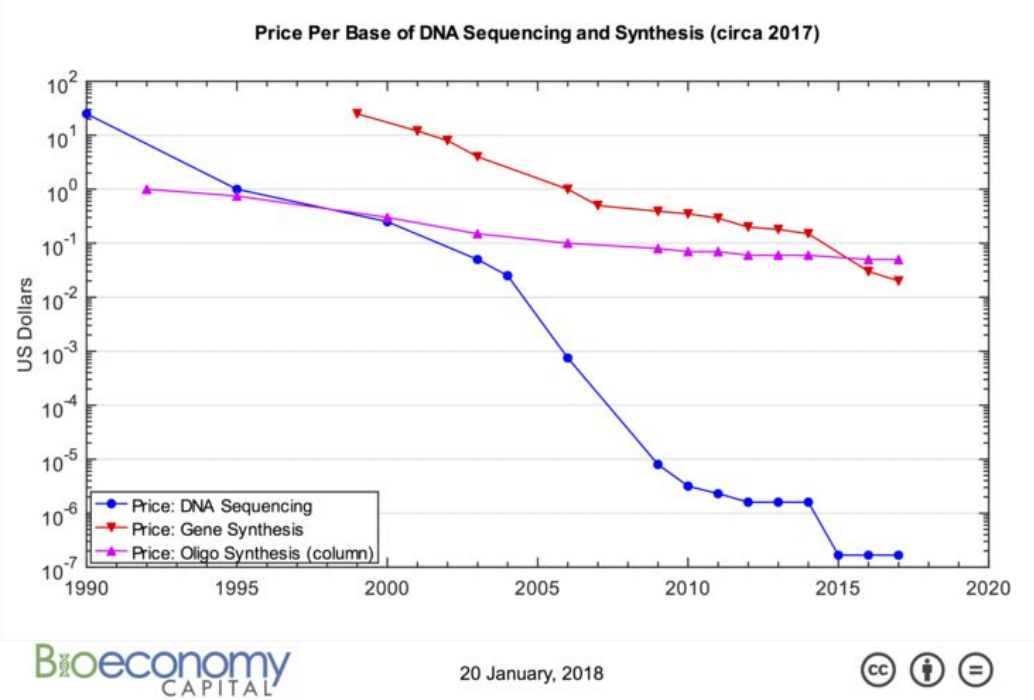
Engineering DNA: Synthesis and Sequencing

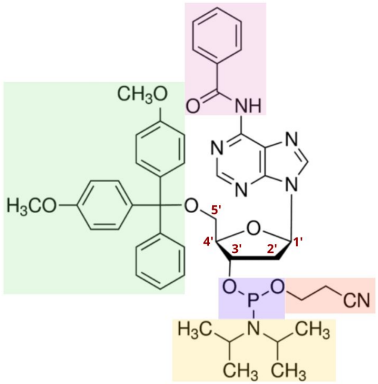
- Gene synthesis and sequencing are becoming exponentially cheaper
- Entire genes can be synthesized in a matter of hours-days at relatively low cost
- This rapid reduction in cost and time for sequencing and synthesis allows large-scale testing of new genetic constructs



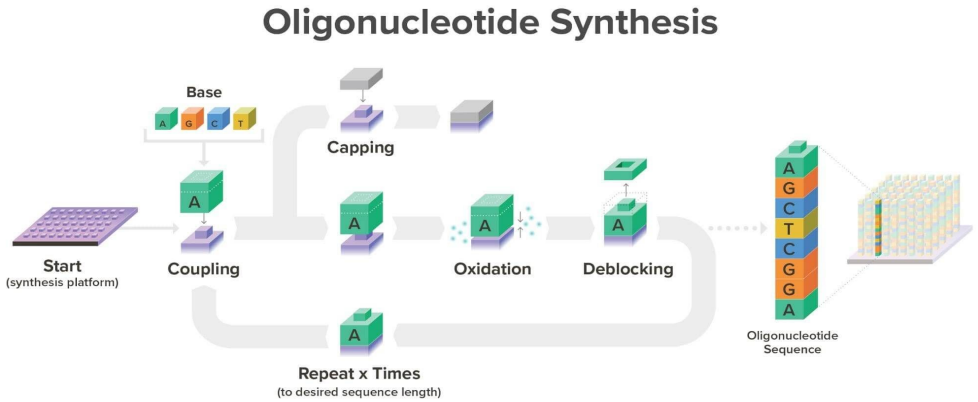
Carlson, R. *Synthesis*. "On DNA and transistors."

Engineering DNA:
How single-stranded DNA is synthesized

- Phosphoramidite chemical synthesis
  - Pioneered by Marvin Caruthers in 1983 at CU-Boulder
- Single-stranded DNA oligos are synthesized using solid-phase chemistry performed on solid supports
  - Controlled pore glass beads (IDT, GenScript)
  - Silicon chip (Twist, Agilent)



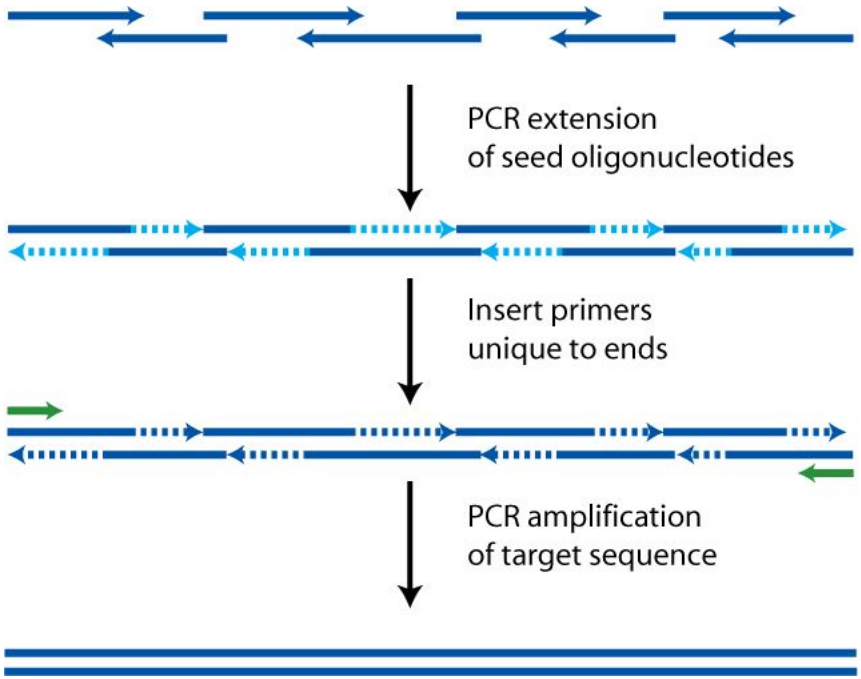
Twist Bioscience.



Twist Bioscience.

Engineering DNA: How double-stranded genes are synthesized

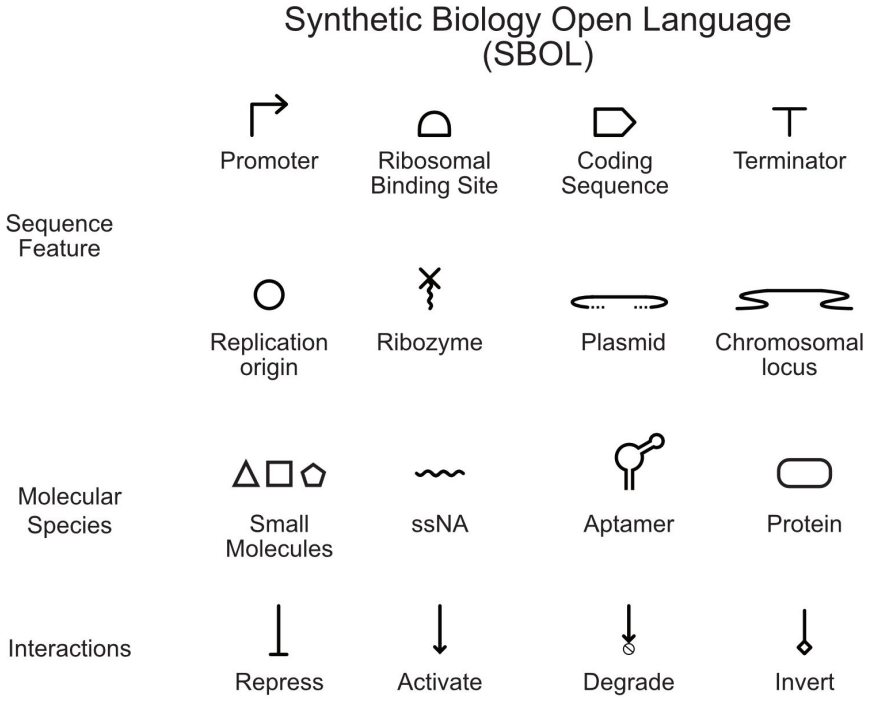
- Larger genes can be constructed using polymerase chain assembly of shorter synthetic fragments
- Short single-stranded oligos are stitched together and filled in using DNA polymerase and PCR to produce double-stranded genes



Dhorspool, "PCA polymerase cycling assembly."

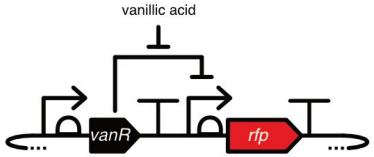
Engineering DNA: Standardized depiction of gene circuits

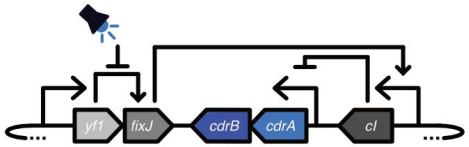
- Engineering Biology often requires descriptions of the DNA sequences used and how they function
- With the wealth of easy to synthesize DNA parts how do we communicate what pieces of synthetic DNA do?
- The Synthetic Biology Open Language (SBOL) is a framework for describing synthetic DNA sequences and their functional relationships



Engineering DNA:
Examples of SBOL based diagrams

- On the left is a plasmid for chemically-inducible expression red fluorescent protein
- On the right is a plasmid for the light-inducible expression of the adhesins CdrAB
- Both of these plasmids express components that control the expression of other components
- The logical interpretations of the diagrams are listed below the image.






```
if(vanillic acid) :
      express(rfp)
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```
if(blue light):
      inhibit(yf1)
if(yf1):
      activate(fixJ)
if(fixJ-active):
      express(cI)
if(no-cI):
      express(cdrAB)
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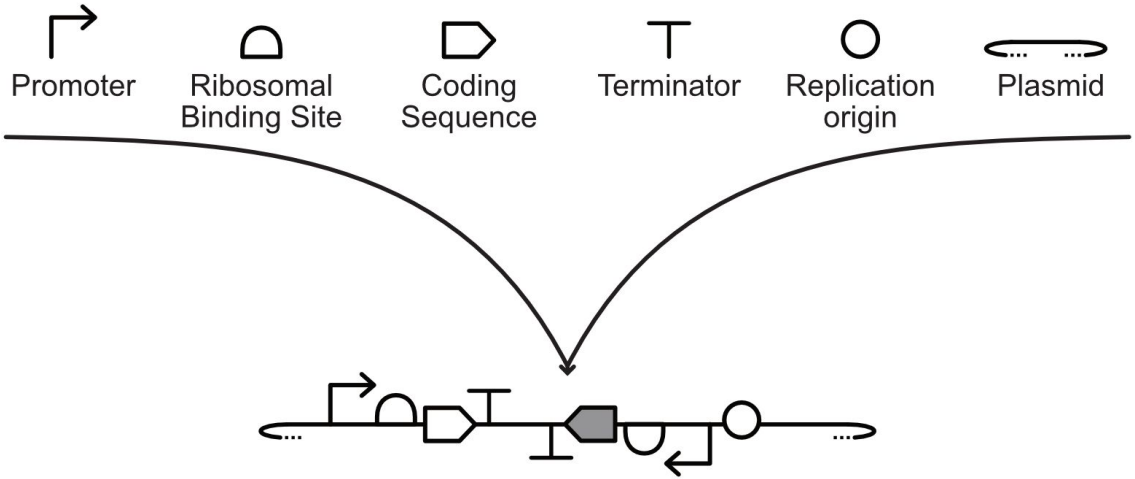
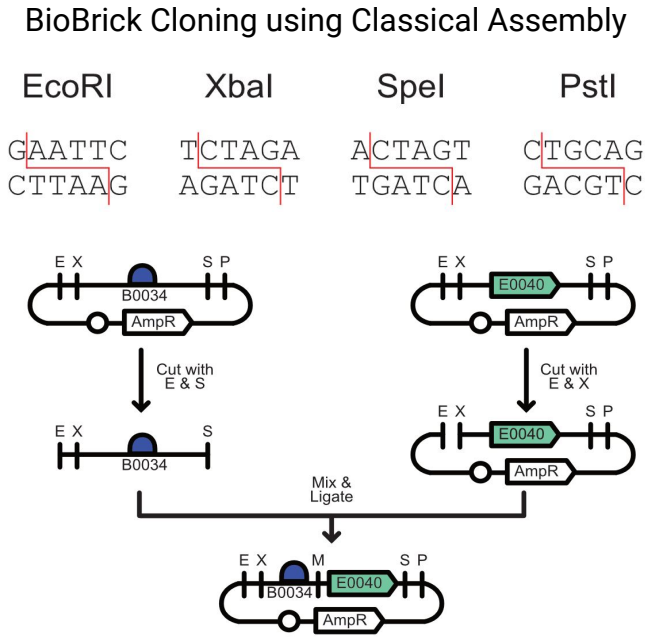
Engineering DNA:
DNA assembly methods



- There are a range of techniques for assembling genetic parts into genetic constructs and plasmids *in vitro*
  - Classical assembly (restriction enzyme + ligation)
  - Golden gate assembly
  - Gibson assembly

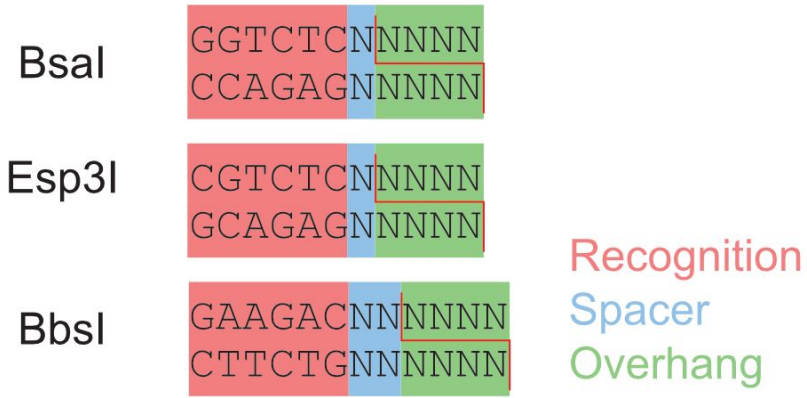
Engineering DNA:
DNA assembly using Classical Assembly

- This approach has been used for vector cloning in molecular biology since the 1970s (Cohen SN, *et al.* *PNAS* (1973)70(11):3240-4)
- **Type II restriction enzymes (RE)** cut dsDNA typically within 6 bp palindromic sequences leaving 4 bp ssDNA overhangs
- Complementary overhangs can be ligated together using a **DNA ligase**
- This is also used in BioBrick cloning (EcoRI/XbaI, SpeI/PstI)
- Leaves behind RE site scars between DNA parts



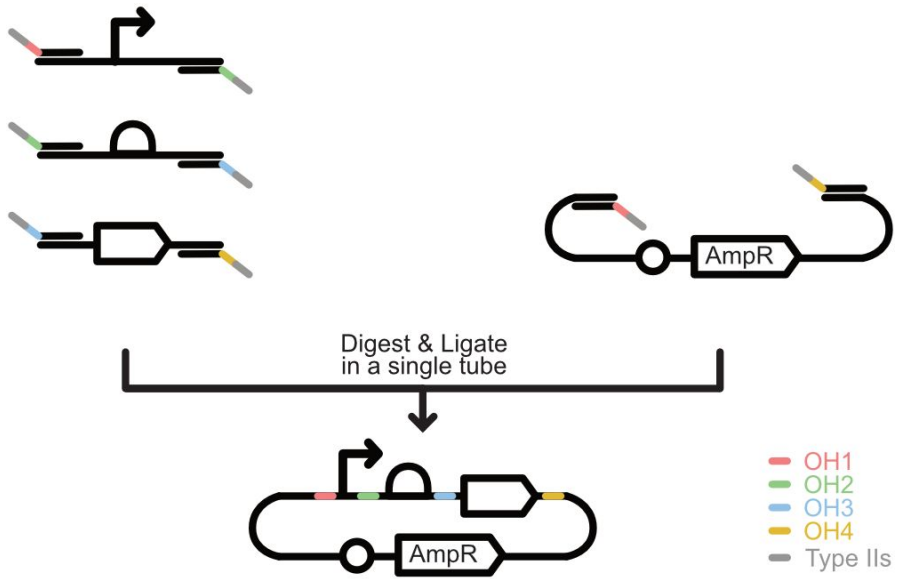
Engineering DNA:
Multipart assembly using Golden Gate

- To overcome the limitation of scar sites and to improve ligation efficiency Golden Gate cloning was developed in 2008 (Engler C, *et al.*, *PLoS One* (2008) 3(11):e3647)
- **Type IIs restriction enzymes** bind recognition sites, but cut outside of them
- This allows for the generation of programmable overhangs that eliminate scare sites between DNA parts and do not reform the original cut site improving efficiency



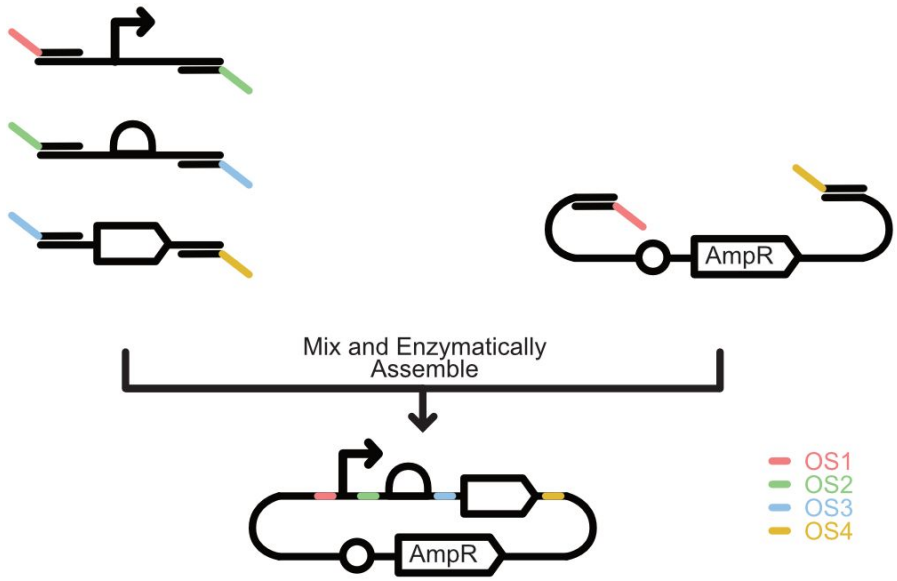
Engineering DNA:
Multipart assembly using Golden Gate

- Golden Gate assembly can be easily achieved using PCR with primers that introduce Type IIs restriction sites (*e.g.*, BsaI, BbsI, Esp3I) that flank parts
- Parts have unique complementary overhangs (OH1-4) that guide their assembly in the correct order
- This can be scaled to >50 fragments allowing for high-throughput multipart assembly



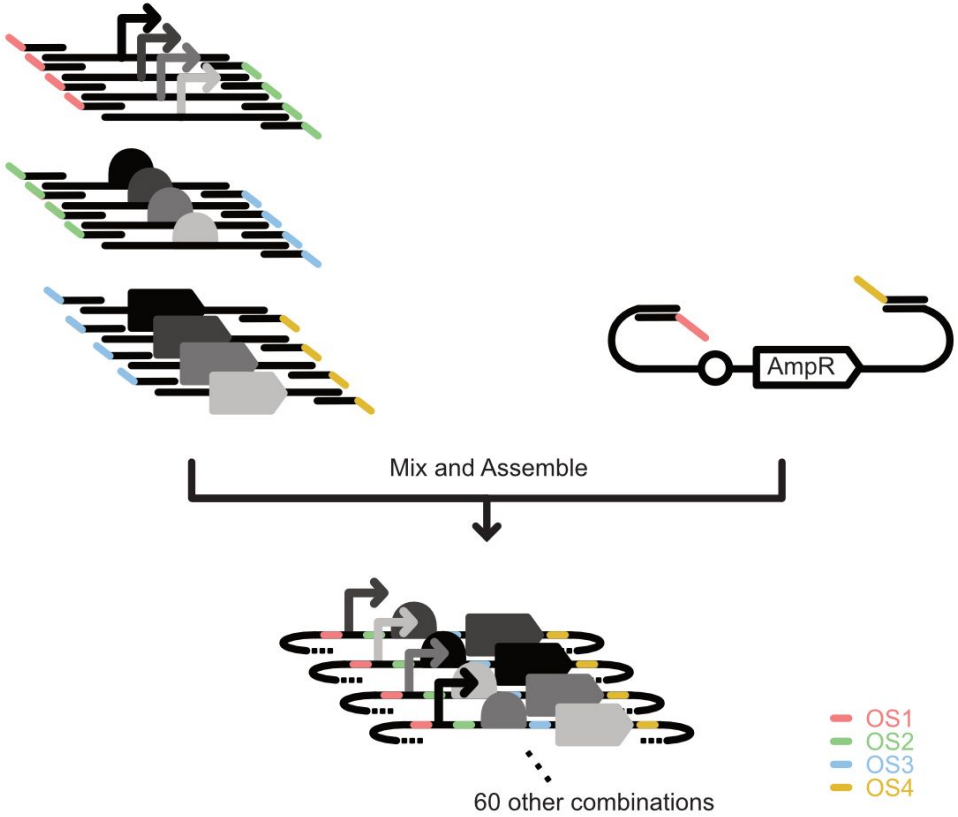
Engineering DNA:
Multipart assembly using Gibson Assembly

- To facilitate large-scale DNA assembly in 2009 Gibson DNA assembly was developed (Gibson D.G., et al., Nat. Methods (2009) 6(5)343-345)
- This method utilizes *in vitro* **homologous recombination** facilitated by T5 exonuclease, Phusion polymerase, and Taq ligase
- This requires the introduction of ~40-60 bp of overlapping sequences (OS) on the ends of the sequences to guide DNA parts to assemble
- Has been scaled to assembly of entire genomes



Engineering DNA:
High-throughput combinatorial DNA assembly

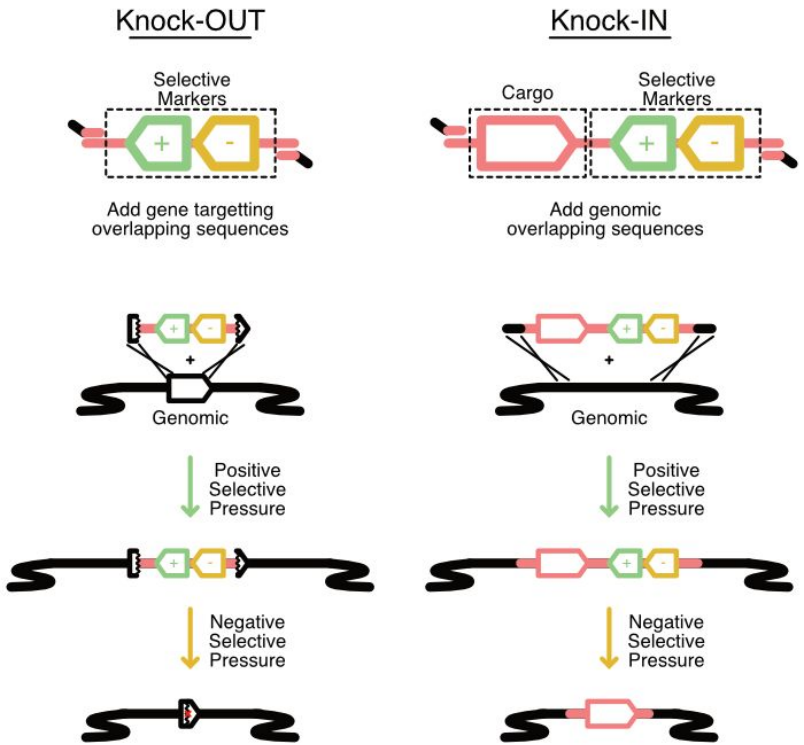
- The use of multi-part DNA assembly techniques enables the construction of large scale combinatorial libraries of DNA sequences
- This is useful when optimizing expression of multiple genes at once allowing for rapid exploration of parameter spaces
- This approach is often used for enhancing yield of metabolic pathways and engineering proteins



Joshua Atkinson, University of Southern California

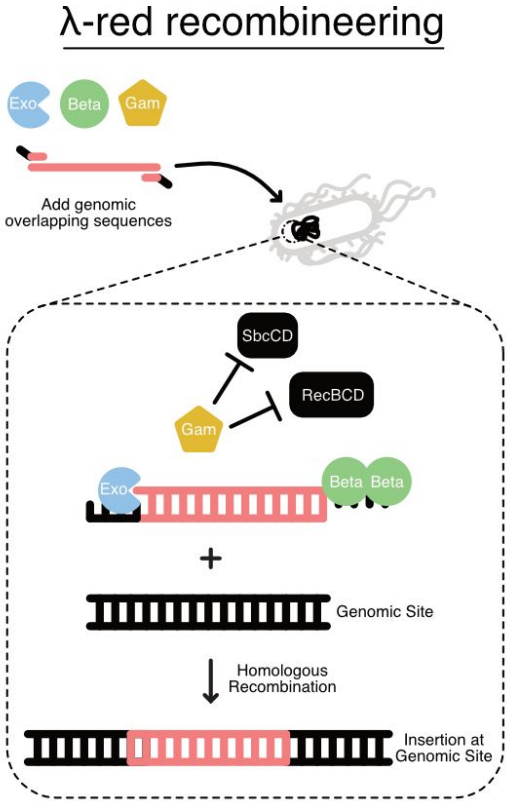
Engineering DNA:
Editing Genomes by Knocking-IN or Knocking-OUT

- Genomes can also be engineered
- One strategy for genome editing is to leverage homologous recombination to delete genes (Knock-OUT) or to introduce entirely new sequences (Knock-IN)
- This can be achieved by introducing selective markers to select for cells within populations that have either gained (positive selection) or lost the engineered DNA (negative selection)



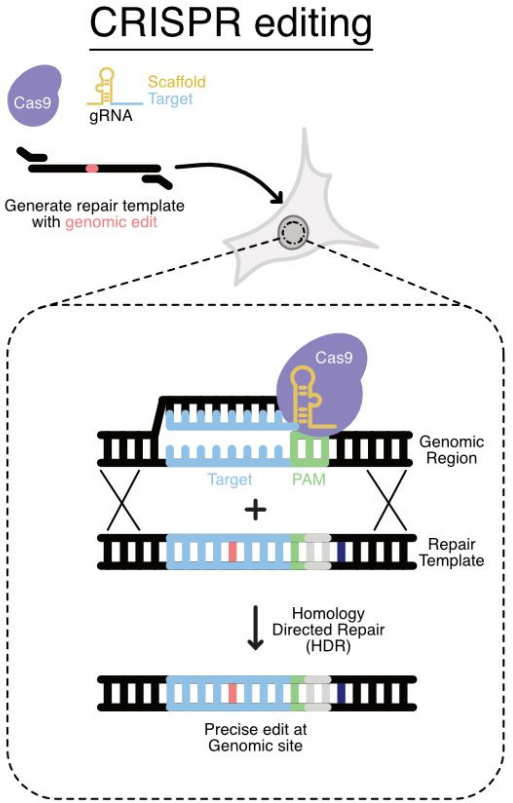
Engineering DNA:
Using Recombineering to edit genomes

- Viral mechanisms for DNA integration have been co-opted to increase genomic engineering efficiency
- One approach, called ‘recombineering’, leverages the *E. coli* lambda prophage (Yu D, et al., *PNAS* (2000), 97(11):5978-5983)
- Prophage proteins Exo, Beta, and Gam improve integration of DNA harboring genomic overlapping sequences by chewing back dsDNA to generate ssDNA, protecting ssDNA from degradation, and blocking host exonucleases, respectively



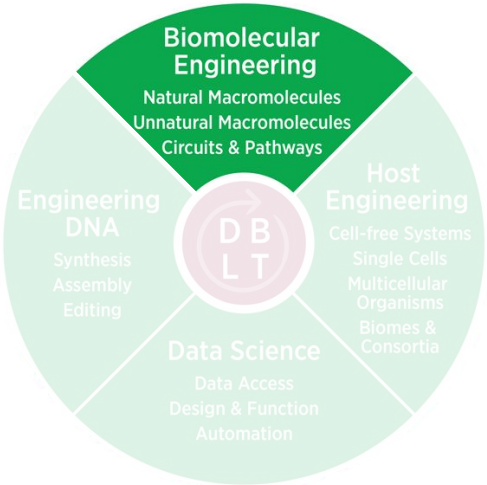
Engineering DNA:
Using CRISPR-Cas9 to make precise genome edits

- Adaptive-immunity mechanisms from bacteria have been co-opted to enable precise genomic edits
- Clustered Regularly Interspaced Short Palindromic (CRISPR) systems from diverse bacteria have enabled a revolution in genomic editing
- Cas9 is one of the most widely used CRISPR systems used for genome engineering (Jinek M., et al., *Science* (2012) 337(6096):816-821)
- Cas9 is an RNA-guided endonuclease that makes double-stranded breaks at specific sites.
- Guide RNAs (gRNA) can be engineered target Cas9 to specific DNA sequences that precede PAM sites (NGG).
- One way to make genomic edits leverages homology directed repair to integrate an engineered repair template that eliminates the PAM site and subsequent retargeting.



Core Tools for Biomolecular Engineering

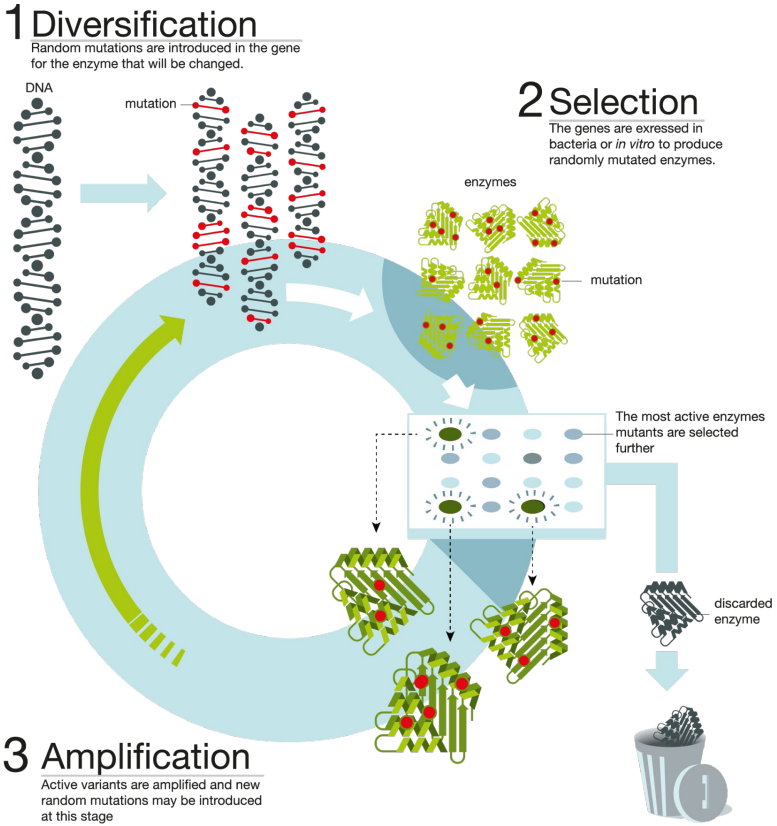
- What are our current tools for Biomolecular Engineering?
- Tools enable a Biomolecular Engineering DBTL
  - Comprehensive Mutagenesis libraries
  - Functional Screens
  - Functional Selections
  - Directed Evolution



Engineering Biology Research Consortium (2019). *Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy*. Retrieved from http://roadmap.ebrc.org. doi: 10.25498/E4159B.

Biomolecular Engineering: Natural Macromolecules

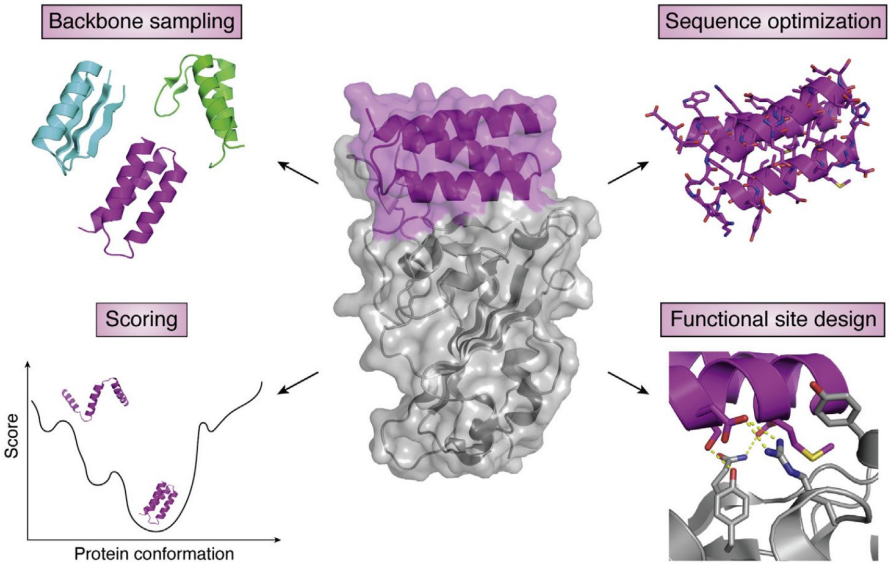
- Natural macromolecules including proteins and RNAs can be engineered to have new properties (*e.g.*, thermostability) or perform new functions (*e.g.*, binding, catalysis)
- Directed evolution can be used to tailor the function of proteins through rounds of sequence diversification, selection for function, and amplification of



[The Nobel Prize.]

Biomolecular Engineering: Unnatural Macromolecules

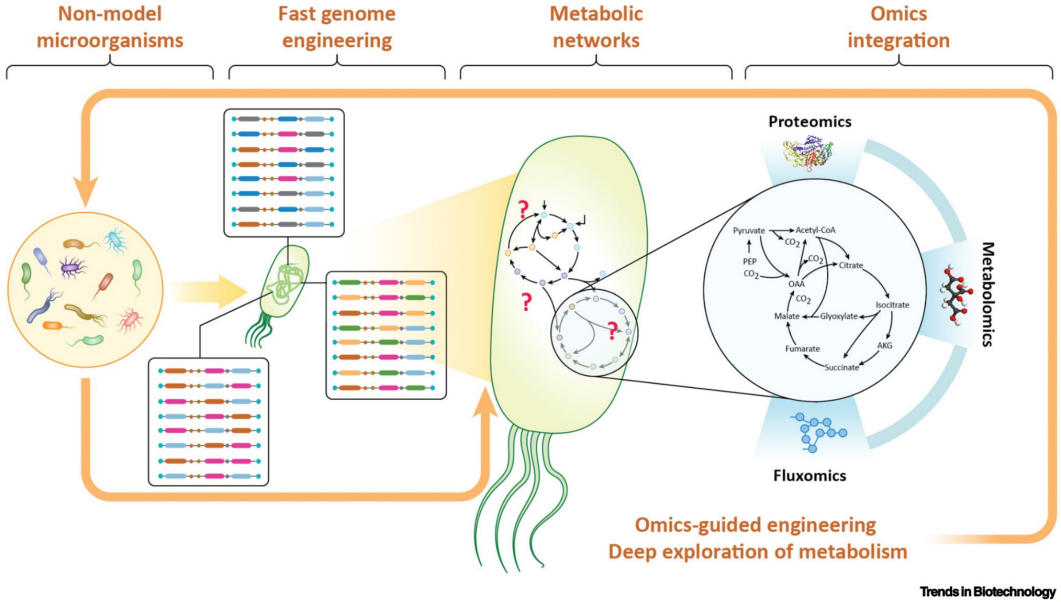
- Entirely new protein sequences not seen in nature can be generated through *de novo* protein design
- *De novo* design enables exploration of protein sequence space beyond what nature has itself explored



Pan X. and Kortemme T. *JBC Reviews* (2021) 296 100558

Biomolecular Engineering: Circuits and Pathways

- In addition to individual biomolecules large scale networks of biomolecules
- Novel metabolic pathways can be constructed using retrosynthesis approaches
- Combinatorial libraries can be used to optimize expression of pathways proteins
- Adaptive laboratory evolution can be used to optimize the host genome for improved yield of a target molecule



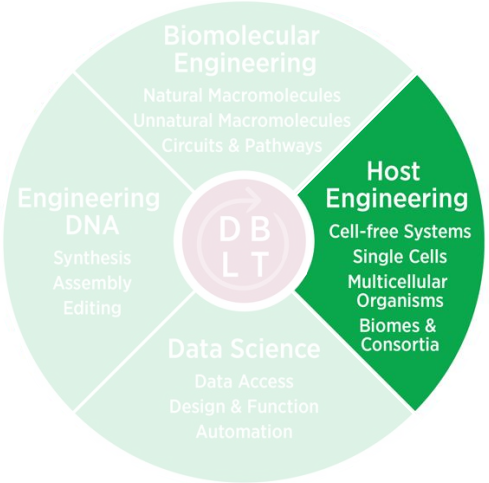
Gurdo N., Volke D.C., Nikel P.I. (2022) *Trends in Biotechnology*

Concept 1-4

Core Tools Part 2:
Host Engineering,
Data Science

Core Tools for Host Engineering

- What types of hosts are there?
- Model & non-model systems
- Thinking across scales

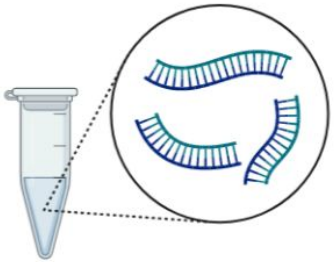


Engineering Biology Research Consortium (2019). *Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy*. Retrieved from http://roadmap.ebrc.org. doi: 10.25498/E4159B.

Host Engineering

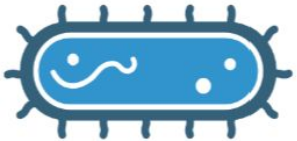
Host choice - what can systems do?

Cell-free



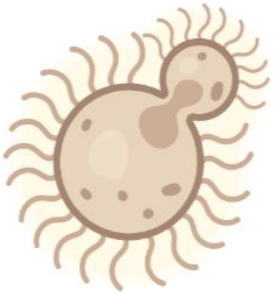
- Can quickly test gene expression
- Grow compounds too taxing for cells
- Needs to be extracted, purified

Bacteria



- Grows well in bulk
- Model for many diseases
- Prokaryotic
- Can't fold many human proteins

Yeast



- Grows well in bulk
- Can produce a variety of proteins
- Often used in foods (i.e. bread)

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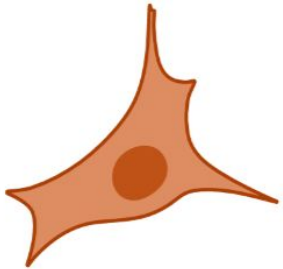
Host Engineering

Host choice - what can systems do?

Mammal



- Human protein folding
- Test drug therapies
- Difficult to grow in bulk

Plant

- Photosynthetic
- Produce a variety of compounds
- Fewer tools available

Whole organism

- Increased complexity
- Can study phenotypes *in vivo*
- More difficult to engineer at the cell level

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Host Engineering

“Model organism”: well-studied, often engineering tools available, widely used

<u>When to use a model organism</u>

- Maximizing production a compound that can be made in a model system
- Looking to use a specific, established tool or platform
- A known model organism is a good fit for the project you want to do

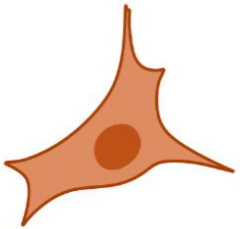
<u>When to use a non-model organism</u>

- Studying a specific process in its native context
- Making complex or unusual proteins
- Looking for specific, niche host characteristics

Host Engineering

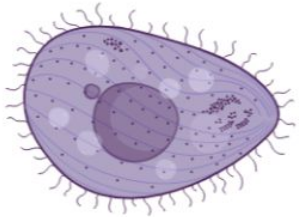
Example: producing human ion channels in bulk (for crystallography or drug discovery)

If you use a model human cell strain…



- Easy to get in correct genes inserted
- Difficult to produce in non-neural cells, or large quantities
- Cannot grow easily in bulk

If you use non-model *Tetrahymena*…



- More difficult to insert genes
- Can produce in large quantities
- Can grow in bulk (if you have the specific expertise to work with it)

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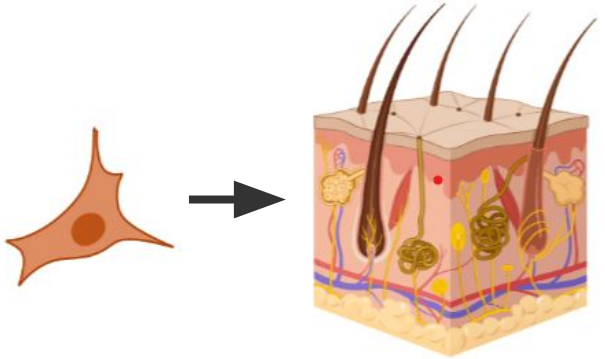
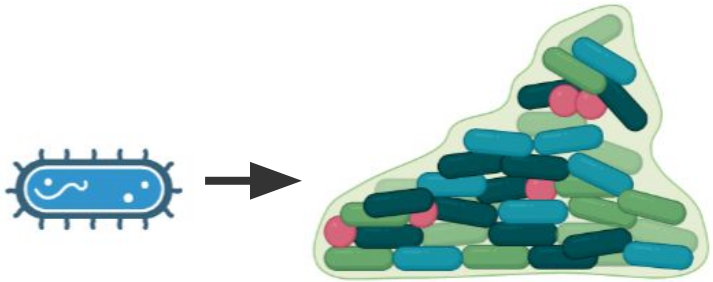
TetraGenetics

Host Engineering: Engineering across scale

- Very few cells are naturally isolated
- Cell tissues and microbial consortia are complex
  - Often more difficult to engineer
  - Can carry out complex tasks
- Can give better understanding of natural systems

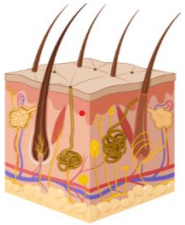




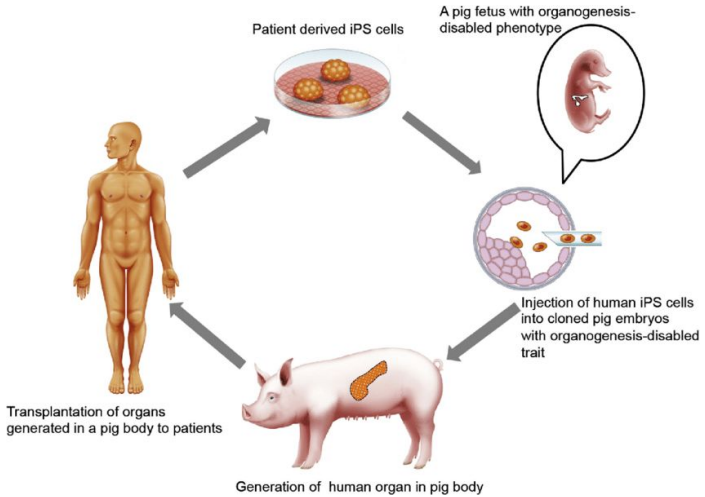
Created with Biorender.com.

Host Engineering: Tissue scale

- Example: humanized organs in pigs for xenotransplantation
- Can edit genes in pigs to prevent human immune rejection
- Requires initial transplant of human cells to start
- Often use existing systems with some *de novo* engineered parts



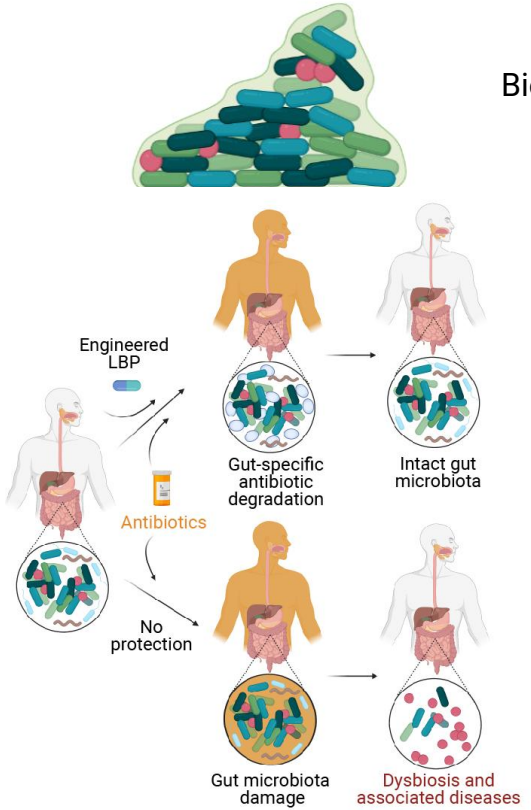
Created with Biorender.com.



Nagashima & Matsunari. (2016). *Theriogenology.*

Host Engineering: Consortia scale

- Example: engineered live biotherapeutic products to protect the microbiome from antibiotics
- Allows antibiotic to clear pathogen from bloodstream, without harm to native gut microbiota
- Specific changes that lead to known broader outcomes

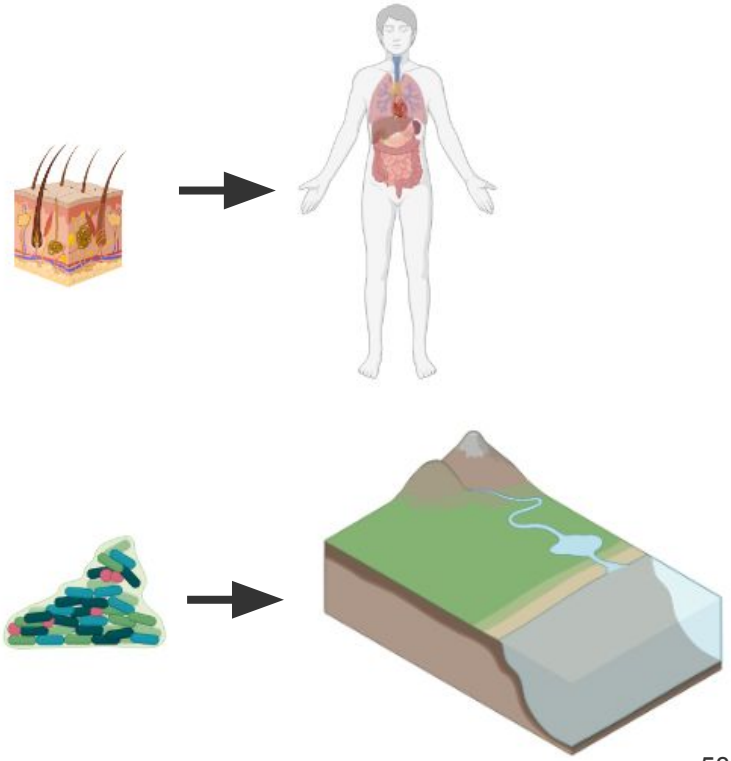


Created with Biorender.com.

Wyss Institute at Harvard University.

Host Engineering: Engineering across scale

- Beyond tissues are organisms
  - High-level, complex interactions and functions
  - Often limited to making singular, distinct edits
- Beyond consortia are ecosystems
  - Many consortia and organisms interacting
  - Potential for “terraforming”
  - Difficult to recapitulate in lab



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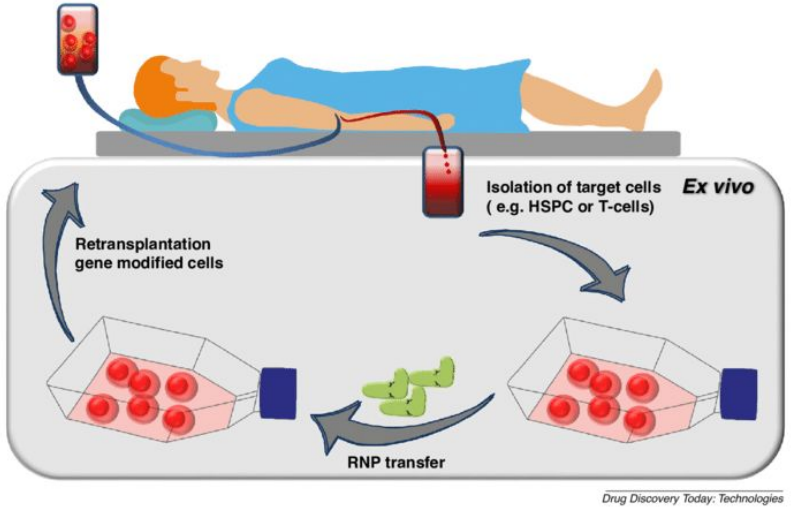
Host Engineering: Organism scale

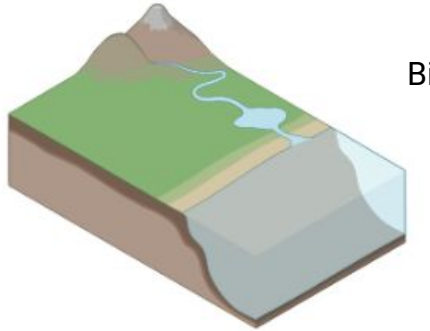
- Example: use of CRISPR to treat sickle cell anemia
- Modification of one codon can revert to non-sickle phenotype
- Specific, targeted changes



Sürün, *et al.* (2018). Drug Discovery Today: Technologies.

Host Engineering: Ecosystem scale

- Example: Using of gene drives to suppress pest populations
- Recall introduction!
- Also for specific, targeted changes



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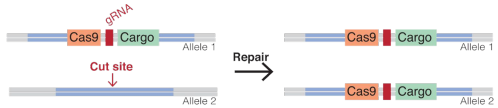
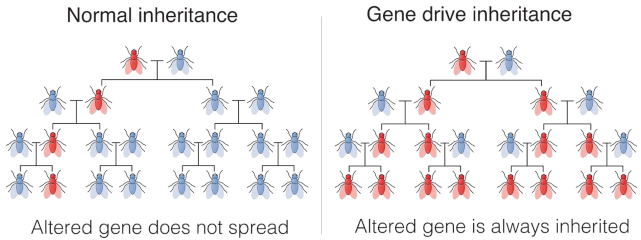
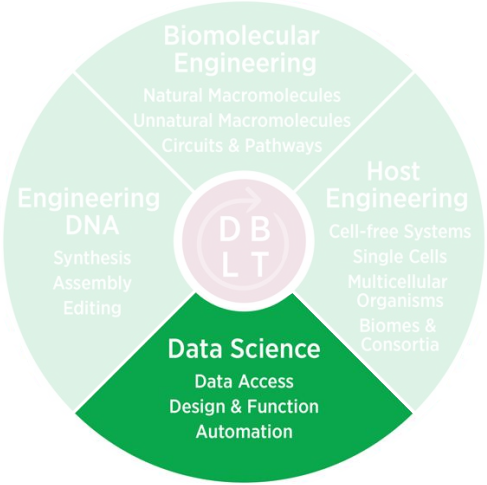




Mariuswalter, "Gene Drive."

Core Tools for Data Science

- What data is out there?
- Modeling & Machine Learning
- Automation



Engineering Biology Research Consortium (2019). *Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy*. Retrieved from http://roadmap.ebrc.org. doi: 10.25498/E4159B.

Data Science: “Omics data”

Genome
Who is there?
What can they make?

- Species identification
- Mutation rate in a population

Transcriptome
What are they saying to making?

- Gene regulation
- Population heterogeneity

Proteome
What are they making?

- RNA regulation
- Protein stability & degradation

Metabolome
What are they doing?

- Metabolic pathway efficiency
- Cellular inputs & outputs

Then integrate!

Created with Biorender.com.

Data Science: Genomics

- Why:
  - Discover members of a large population
  - Understand the variation between/within populations
  - Epigenomics: how DNA modifications impact expression
- How:
  - Large-scale sequencing
  - Reassembly (what pieces are from whom)
  - Comparing regions of interest (species identifiers, important coding regions)

Created with Biorender.com.

Data Science: Transcriptomics

- Why:
  - mRNA - what genes are cells expressing under specific conditions
  - ncRNA - regulation and more
- How:
  - RNA sequencing (similar to DNA-seq)
  - Microarrays (quantify a set of specific sequences)

Created with Biorender.com.

Data Science: Proteomics

- Why:
  - Know what proteins make up a cell/tissue
  - Know if cells are making a product of interest
- How:
  - Immunoassays (antibodies)
  - Protein purification (pull out and quantify a protein of interest, often through a tag)
  - Mass spectrometry (look for proteins with known chemical profiles)

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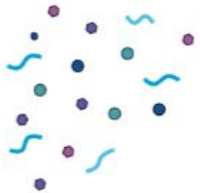
Data Science: Metabolomics

- Why:
  - Know what chemical products a cell is making
  - Quantify signalling molecules or chemical product production
- How:
  - Spectrometry methods (gas/liquid chromatography)
  - Assays for specific molecules of interest



Created with Biorender.com.

Data Science: Databases

- National Center for Biotechnology Information (NCBI)
  - GenBank - NIH genetic seq. collection
  - Nucleotide BLAST - search gene seqs.
- UniProt
  - Protein seq. and functional information
- RCSB Protein Database (PDB)
  - Characterized protein structure and models
- Other, more specific DBs:
  - FPBase - fluorescent protein characterization and lineages

Data Science:
Modeling genetic parts

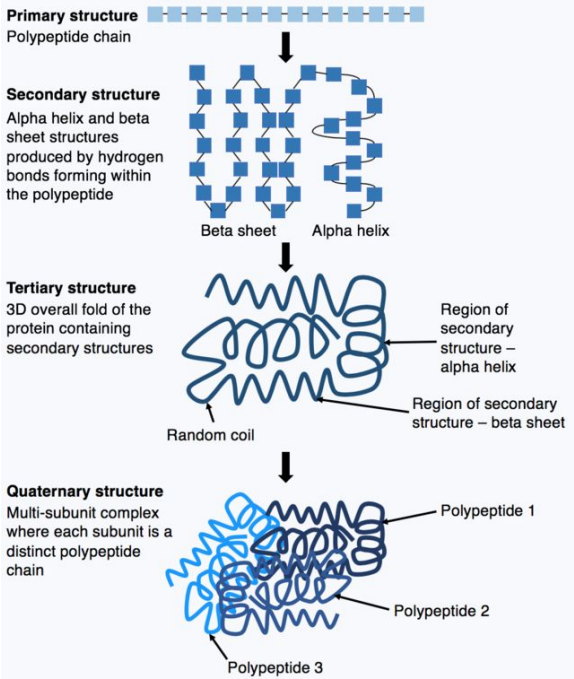
- Can use first principles thermodynamics to predict function of parts in some cases
- Can integrate larger datasets with machine learning models to make more sophisticated predictions

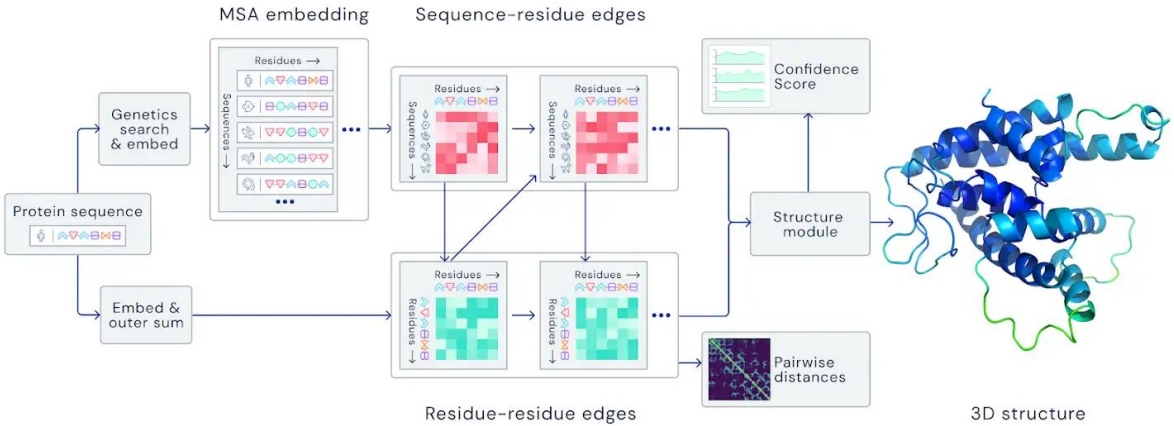
De Novo DNA

Predict RBS output based on both RBS and protein sequence

Benchling

Data Science:
Modeling proteins (AlphaFold)



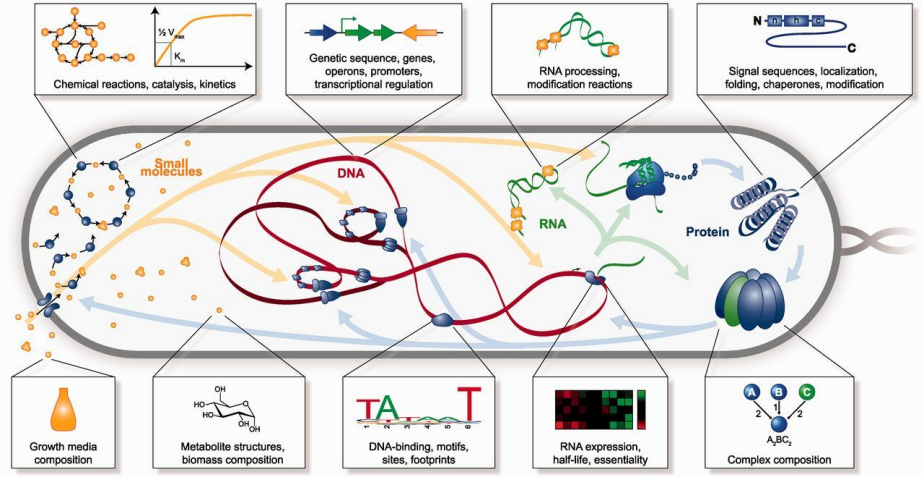


Kep17, “Amino acid chains.”

DeepMind.

Data Science:
Modeling whole systems

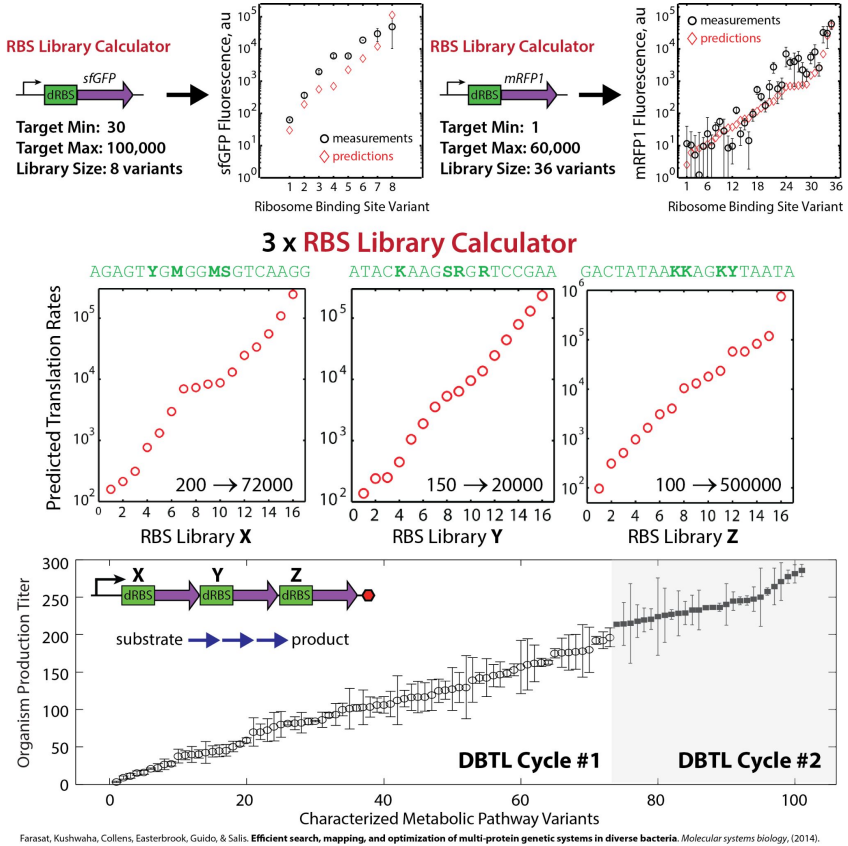
- Quantify what is there (-omics)
- Determine inputs and outputs
- Apply equations to determine system functions - metabolic efficiency, protein activity, etc.
- NIH: ‘Systems biology is an approach to understand the larger picture—be it at the level of the organism, tissue, or cell—by putting its pieces together. ‘



Karr, *et al.* (2012). *Nucleic acids research.*

Data Science: Automation of design

- CAD (Computer-Aided Design) of gene constructs
- Automation of gene synthesis

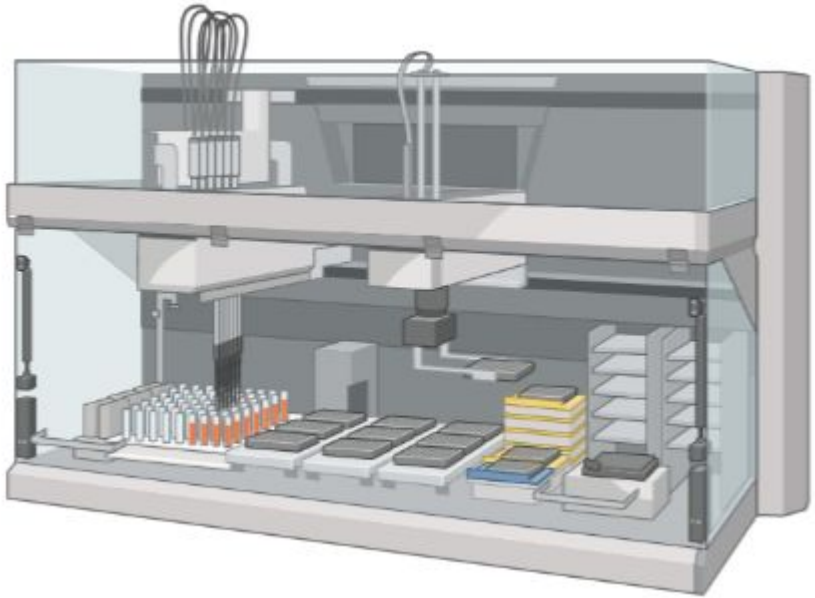


[De Novo DNA, "RBS Library Calculator."]

Farasat, Kushwaha, Collens, Easterbrook, Guido, & Salis. **Efficient search, mapping, and optimization of multi-protein genetic systems in diverse bacteria**. *Molecular systems biology*, (2014).

Data Science:
Automation of laboratory processes

- Liquid handlers to automate Building & Testing genetic constructs
- Increase throughput to test multiple constructs simultaneously
- Integrated analysis for -omics



Created with Biorender.com.

Data Science:
Automation of laboratory processes

OpenTrons.

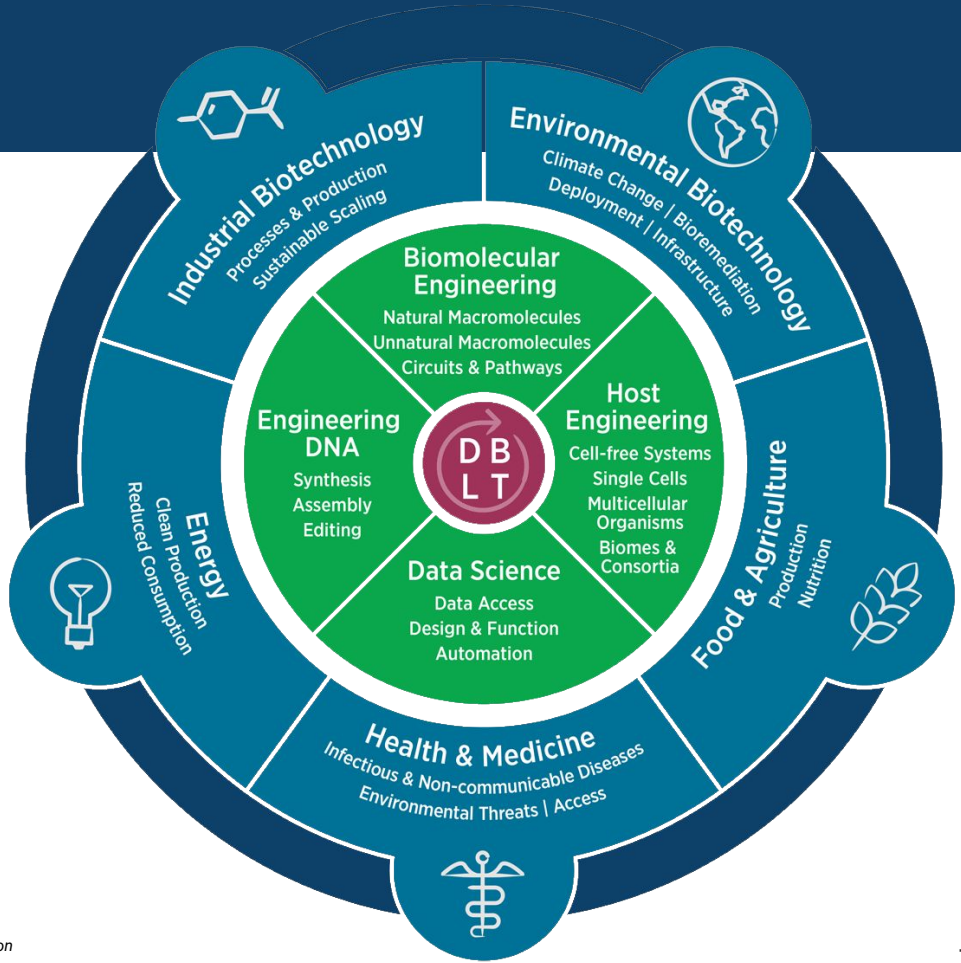
Concept 1-5

Impacts & Applications

Engineering Biology

We group the impacts of Engineering Biology into five major sectors:

- Industrial Biotechnology
- Environmental Biotechnology
- Food & Agriculture
- Health & Medicine
- Energy



Engineering Biology Research Consortium (2019). *Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy*. Retrieved from http://roadmap.ebrc.org. doi: 10.25498/E4159B.

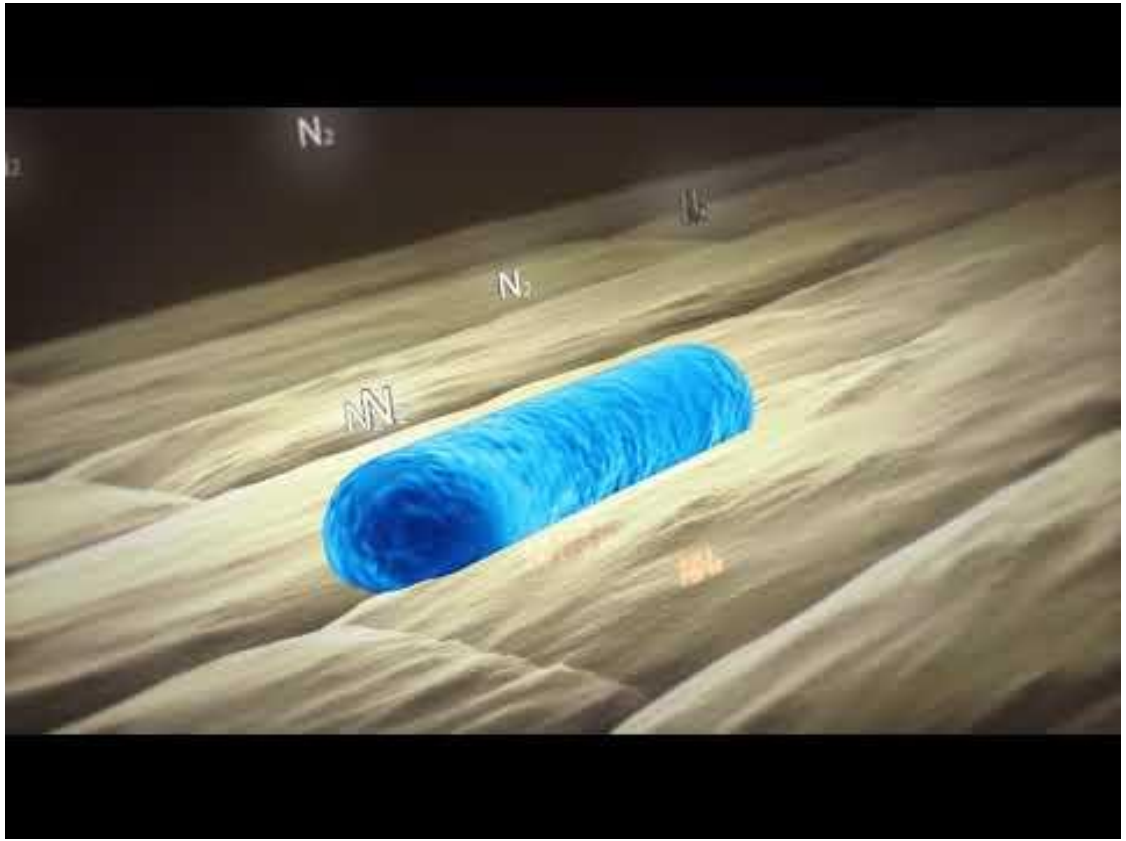
Food & Agriculture

Microbial symbiont fertilizers

- Plants need nitrogen in the soil to grow - often from fertilizer
- Current methods to make nitrogen-rich fertilizers use large amounts of energy and have many negative environmental impacts
- Some microbes are great at fixing nitrogen - can we engineer microbes to grow on plant roots and fix nitrogen for us?

PIVOT BIO PROVEN®40

Food & Agriculture

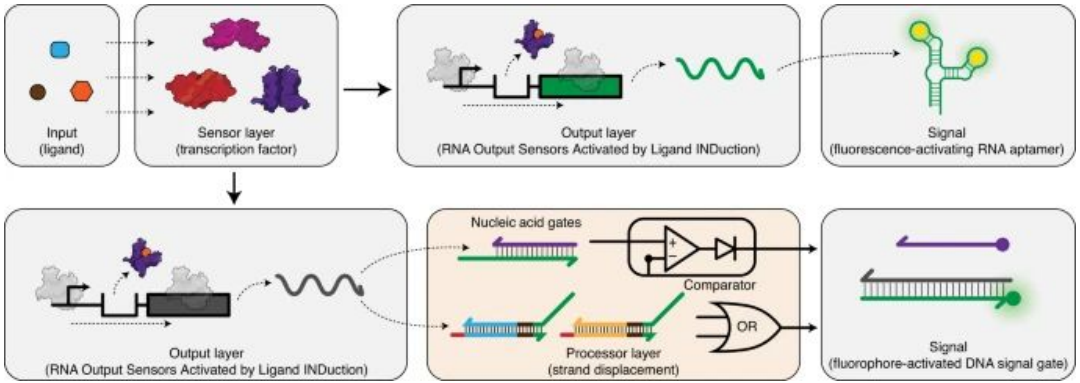


Pivot Bio.

Health & Medicine

At-home water quality testing

- Clean water is vital for health - need fast, accurate, affordable assessment
- Many possible contaminants (pathogens, heavy metals, pharmaceuticals)
- ROSALIND - cell-free diagnostic that combines natural sensor machinery with human-readable fluorescent or colorimetric output of water quality



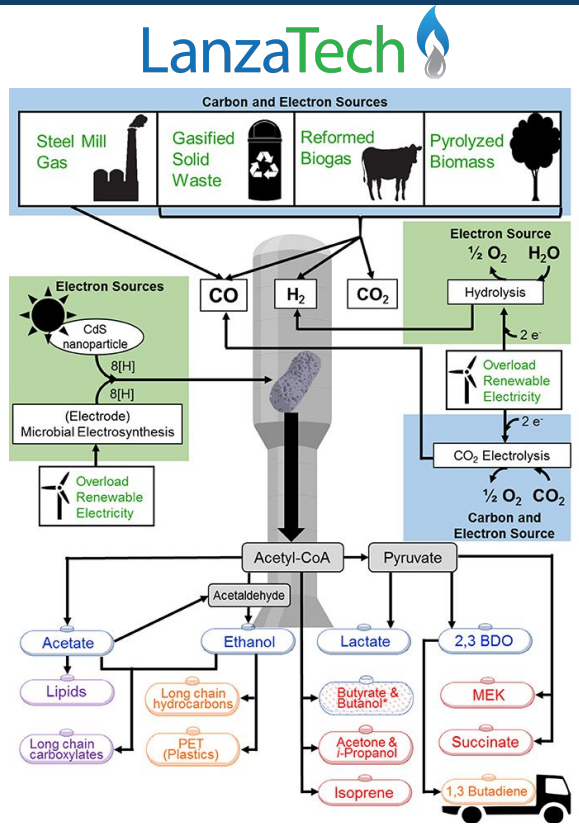
Jung, J.K., Archuleta, C.M., Alam, K.K. *et al. Nat Chem Biol* 18, 385–393 (2022).

Health & Medicine

Northwestern U.

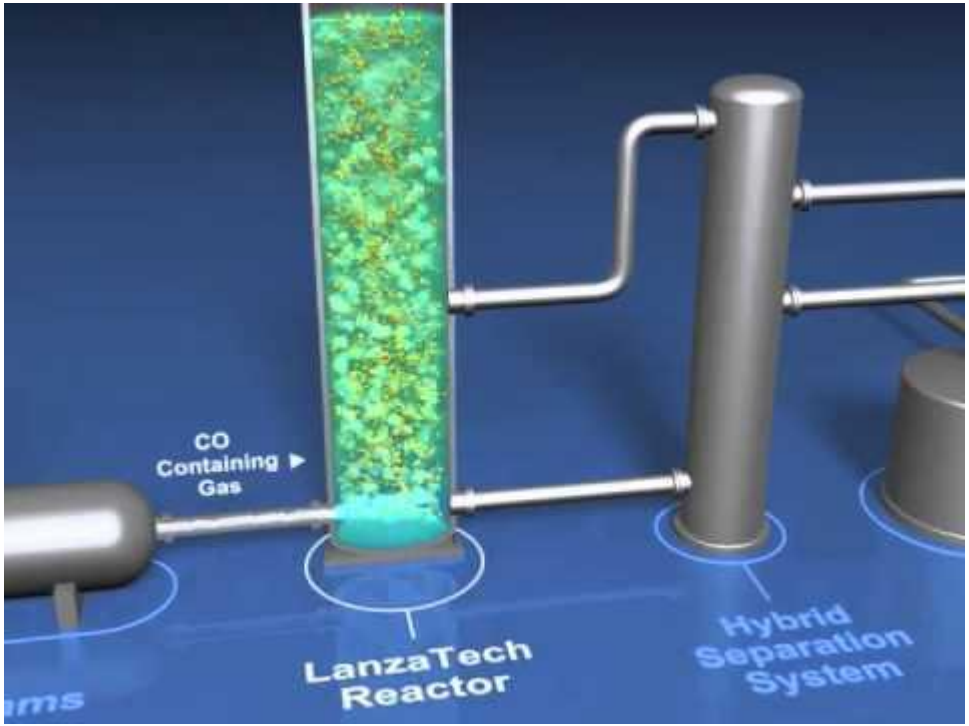
Energy

- Microbial metabolism can be engineered to turn cells into chemical factories to meet the needs of human resources
- Using the core-tools of engineering biology, cells can be engineered to use simple feedstocks like CO2, CO, H2 and turn these into useful products with lower carbon impacts than conventional fossil fuel derived alternatives.



Liew F., et al. (2016) *Front. Microbiol.* 7:694.

Energy



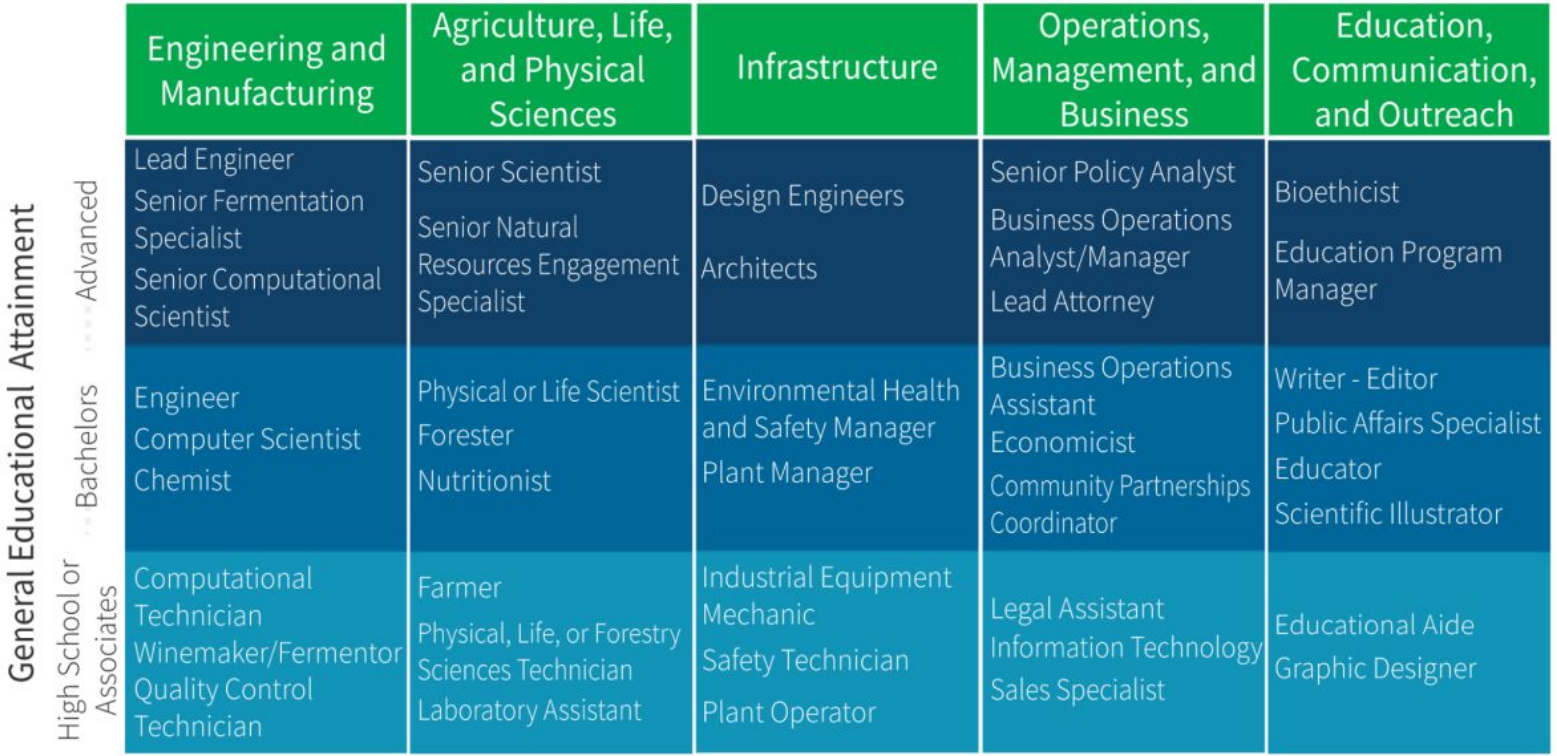
LanzaTech

LanzaTech.

Career Sectors in Engineering Biology

- Each sector has its own culture, pacing, and roles
- **Academia:** tenure-track PI, lecturer, core facility manager
- **Government:** national lab scientist, funding agency program manager, admin
- **Industry:** research scientist, customer support, consultant
- Between & beyond:
  - Science communication, journalism
  - Patent lawyer, tech transfer specialist
  - Policy, regulations, governance
- Explore digital resources:
  - EBRC *In Translation* podcast
  - BioBuilder *Life-Changing Science* podcast
  - AAAS *myIDP* website

Diverse Careers in Engineering Biology



General Educational Attainment

	Engineering and Manufacturing	Agriculture, Life, and Physical Sciences	Infrastructure	Operations, Management, and Business	Education, Communication, and Outreach
Advanced	Lead Engineer Senior Fermentation Specialist Senior Computational Scientist	Senior Scientist Senior Natural Resources Engagement Specialist	Design Engineers Architects	Senior Policy Analyst Business Operations Analyst/Manager Lead Attorney	Bioethicist Education Program Manager
Bachelors	Engineer Computer Scientist Chemist	Physical or Life Scientist Forester Nutritionist	Environmental Health and Safety Manager Plant Manager	Business Operations Assistant Economicist Community Partnerships Coordinator	Writer - Editor Public Affairs Specialist Educator Scientific Illustrator
High School or Associates	Computational Technician Winemaker/Fermentor Quality Control Technician	Farmer Physical, Life, or Forestry Sciences Technician Laboratory Assistant	Industrial Equipment Mechanic Safety Technician Plant Operator	Legal Assistant Information Technology Sales Specialist	Educational Aide Graphic Designer

Hinman, A.W., Friedman, D.C. *EBRC.* (2022).

Engineering Biology is driven by a collaborative network of dedicated professionals

Many possible roles:

Bioinformatician in an academic lab who applies data analysis, modeling, and statistics to large datasets to delineate complex biological processes.

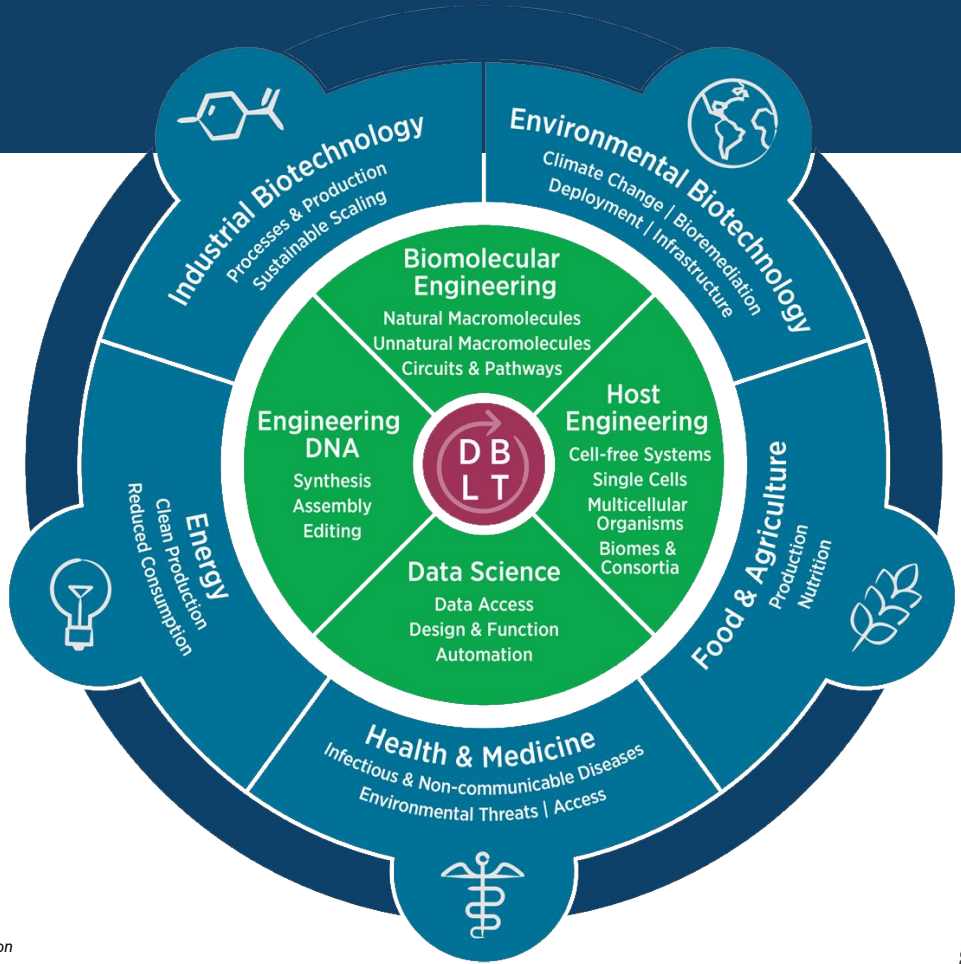
Program manager in a government agency who develops and writes research & training initiatives, and discusses research priorities with academic labs.

Biosecurity specialist in a biotech company who coordinates the development and operation of security screening processes.

Summary

Engineering biology:

- Uses a DBTL framework
- To apply key biology & engineering technologies
- For impact in sectors across aspects of life and the planet



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Credits

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Extended Resources

EBRC video playlist: https://youtube.com/playlist?list=PLf4eUKhxEIurvaNwNSpyXlKf_LoFRlZZm

iBiology Synthetic Biology course: https://www.ibiology.org/playlists/synthetic-biology/

Raj Lab Synbio Transcript course: https://youtu.be/3xJI8j7YIrI

EBRC Synthetic Biology & Machine Learning series: https://ebrc.org/synbio-ml-education/

CalTech Biomolecular Feedback Systems resource**:** http://www.cds.caltech.edu/~murray/BFSwiki/index.php

Ben Thuronyi Designing and Building Synthetic Biology Constructs resource: http://bit.ly/synbioguide or https://docs.google.com/document/d/1k3H1xBC_gu_F0B6lPPZeSilcfYtxn4o7bkbBUT_McTc/edit

BioBuilder courses and content: https://biobuilder.org/

Paper: Dymond JS, *et al*. (2009). Teaching synthetic biology, bioinformatics and engineering to undergraduates: the interdisciplinary Build-a-Genome course. *Genetics*, 181(1), 13-21. https://doi.org/10.1534/genetics.108.096784

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