

Intro to Synthetic Biology





Goals of this lecture

You will be able to answer:

- What is synthetic biology?
- How can I Design, Build, Test, and Learn from biological systems?
- What are the Core Tools of synthetic biology?
- How and where can synthetic 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 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.

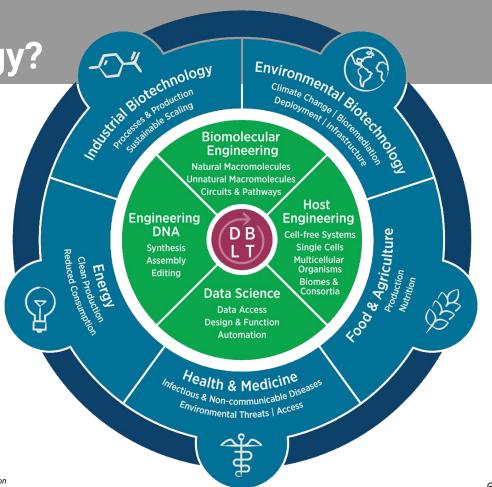
The element that distinguishes engineering biology from traditional molecular and cellular biology is the **focus on the design and construction of core components** (e.g., parts of enzymes, genetic circuits, metabolic pathways) that can be modeled, understood, and tuned to meet specific performance 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.

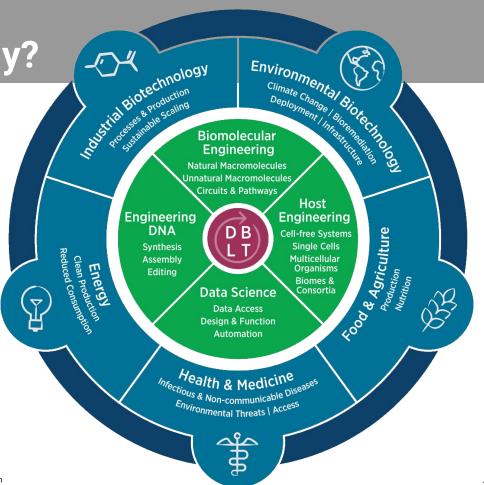
Hence, the overwhelming physical details of natural biology (gene sequences, protein properties, biological systems) must be organized and recast via a set of design rules that hide information and manage complexity, thereby enabling the engineering of many-component integrated biological systems.

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

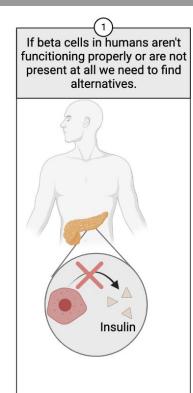
The goal: "engineer living cells to do something useful; for example, treat a disease, sense a toxic compound in the environment, or produce a valuable drug." (BioBuilder)

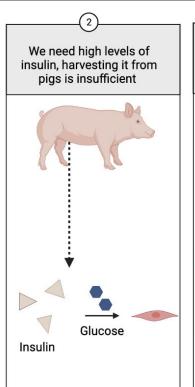


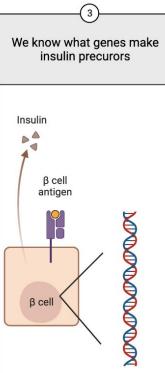
Example: using industrial biotechnology to treat a disease

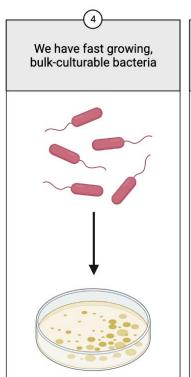


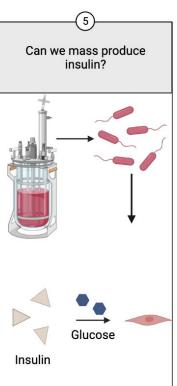
Engineering Biology Research Consortium (2019). Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy. Retrieved from http://roadmap.ebrc.org. doi: 10.25498/E4159B.









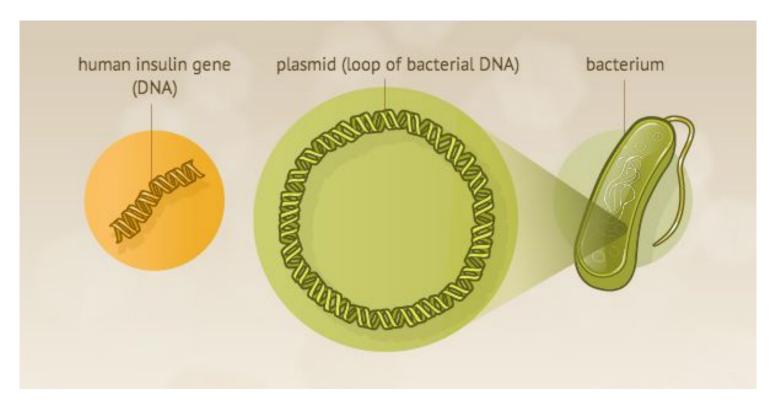


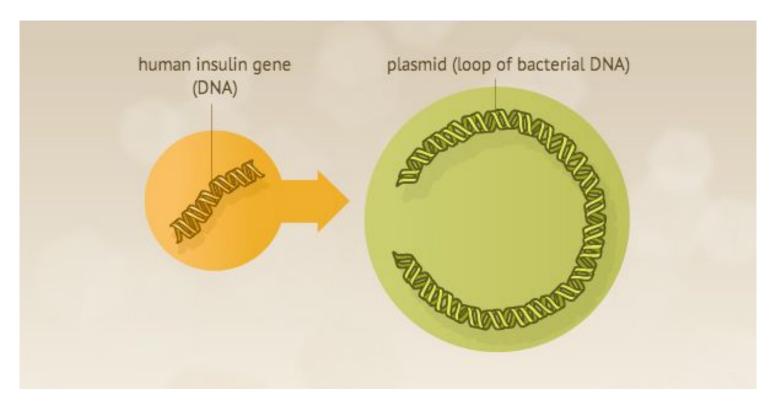
What tools do we need?

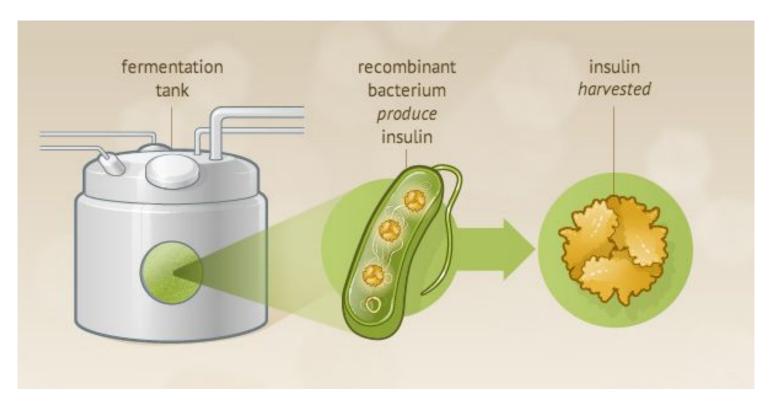
- Insulin precursor genes
- Genetic parts for gene expression in E. coli
- Way to assemble these genetic parts
- The E. coli cells themselves.
- Way to get the DNA into the cells
- Way to harvest insulin from bacteria
- Way to measure insulin production

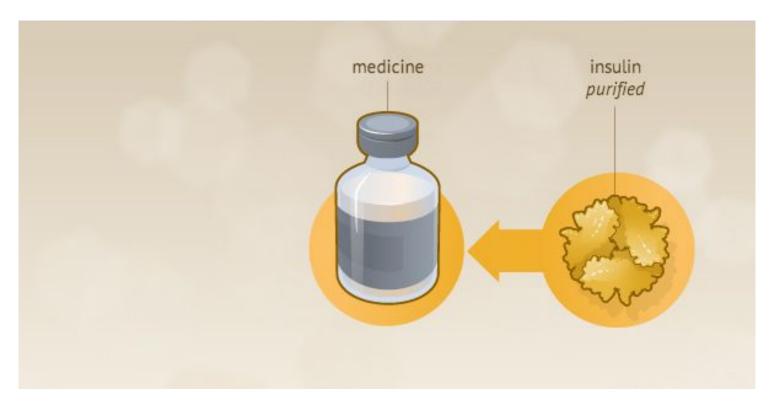
What steps do we need to take?

- 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

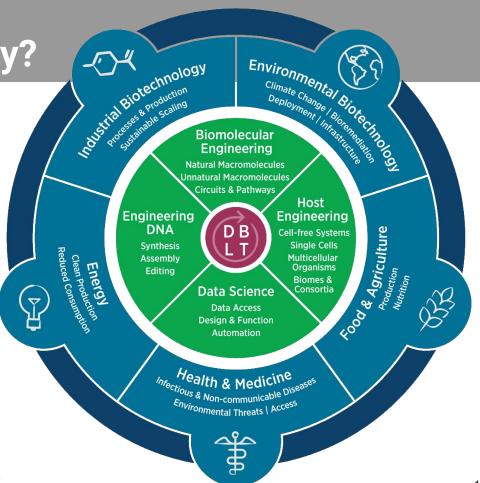






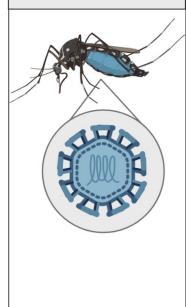


Example: use genetic circuits to mitigate an environmental pest

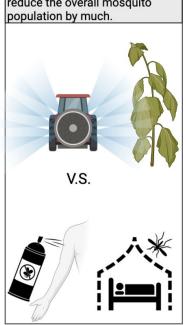


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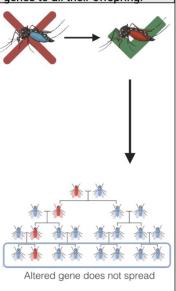
Specific strains of mosquitoes (ex. Aedes aegypti) carry many diseases, and are invasive in many areas.



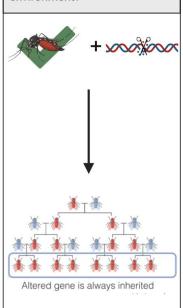
Traditional bug repellants are toxic to the environment, must be applied locally, and/or don't reduce the overall mosquito population by much.



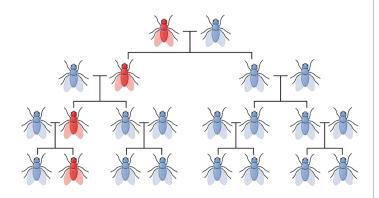
You could engineer bugs that don't carry the disease, or don't bite - but these species wouldn't pass the relevant genes to all their offspring.



How can we make sure a gene mutation or loss is passed to all offspring in a natural environment?

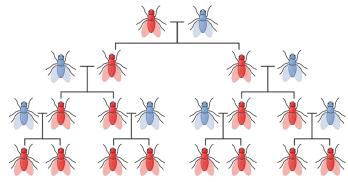


Normal inheritance



Altered gene does not spread

Gene drive inheritance



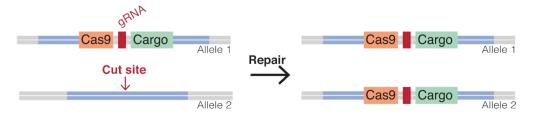
Altered gene is always inherited

What tools do we need?

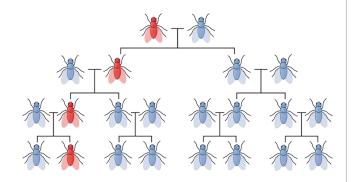
- Gene target to "knock out" or edit
- Genetic tool that will ensure these edits in all offspring
- Way to edit genes in mosquitoes
- Way to measure phenotypic changes from gene edits
- LOTS of safety testing strategies

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

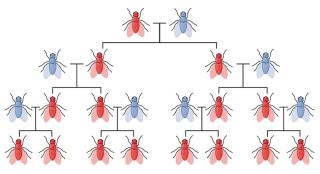


Normal inheritance



Altered gene does not spread

Gene drive inheritance



Altered gene is always inherited

Environment: Bioethics of gene drives

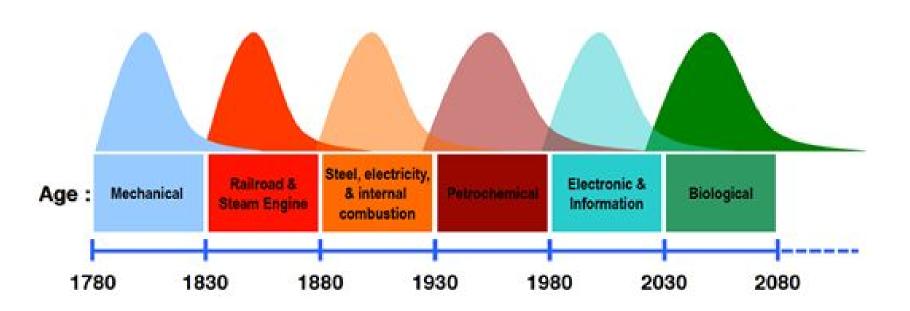
Gene Drives:

- 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:

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

Engineering biology as the next Kondratiev Wave



Engineering Biology (aka 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.

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Concept 1-2

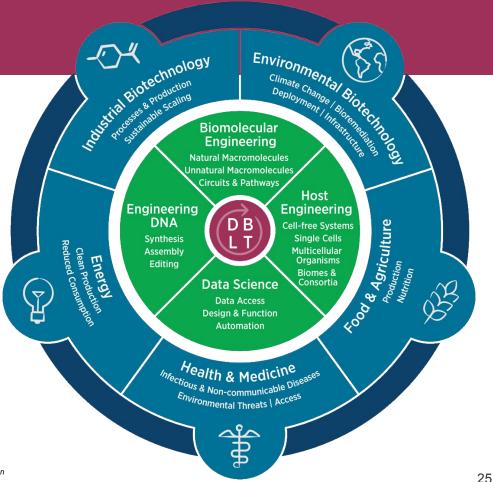
Engineering Biology Roadmap& the DBTL Cycle

SynBio Roadmap

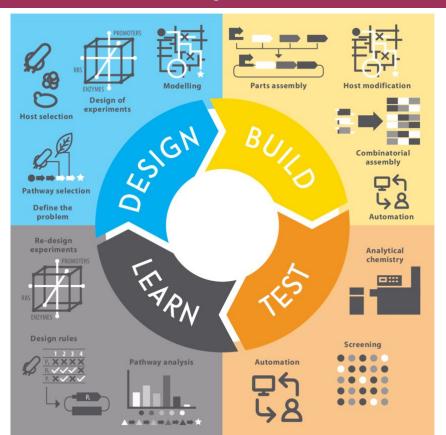
From a Design, Build, Test, Learn centered approach

Uses biological, engineering, and computational tools

To positively impact multiple sectors



The DBTL Cycle



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

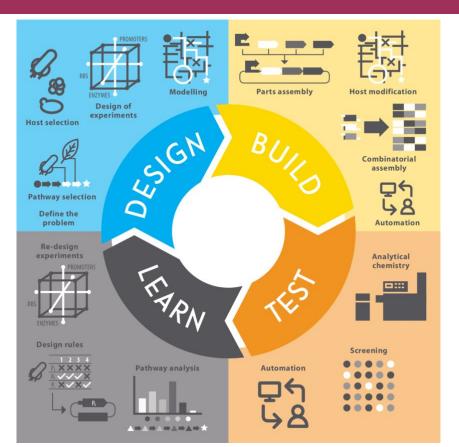
Build your system by assembling, editing, and installing genetic parts.

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

- 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.

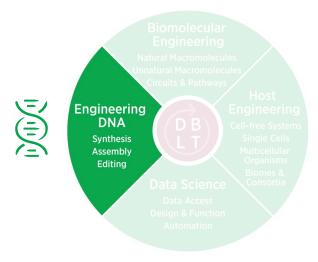
Example ideas: trees with fireproof wood, drought-resistant cabbage, sustainable bioplastics, engineered probiotics for gut health, cell-free water quality sensors

Concept 1-3

Core Tools Part 1:
Engineering DNA,
Biomolecular Engineering

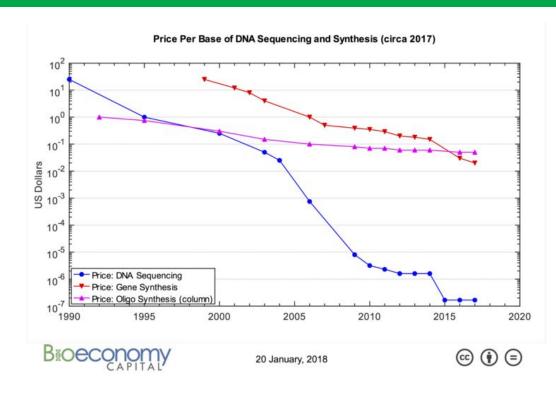
Core Tools for Engineering DNA

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



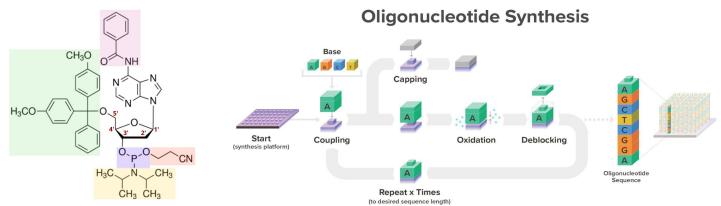
Engineering DNA: Synthesis and Sequencing

- 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



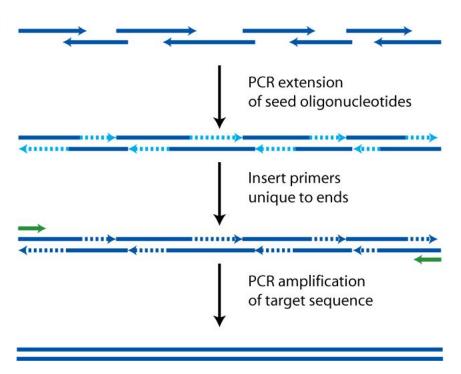
Engineering DNA: How single-stranded DNA is synthesized

- 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)



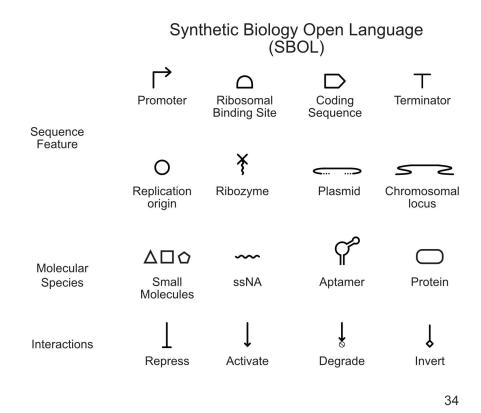
Engineering DNA: How double-stranded genes are synthesized

- 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



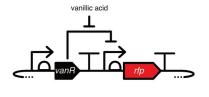
Engineering DNA: Standardized depiction of gene circuits

- 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 <u>Synthetic Biology Open</u>
 <u>Language</u> (SBOL) is a framework
 for describing synthetic DNA
 sequences and their functional
 relationships

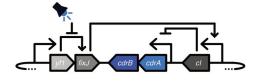


Engineering DNA: Examples of SBOL based diagrams

- 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.

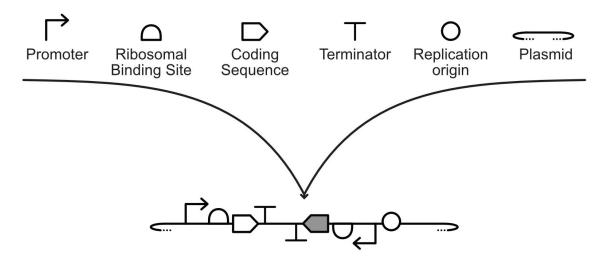


if(vanillic acid): express(rfp)



```
if(blue light):
    inhibit(yf1)
if(yf1):
    activate(fixJ)
if(fixJ-active):
    express(cl)
if(no-cl):
    express(cdrAB)
```

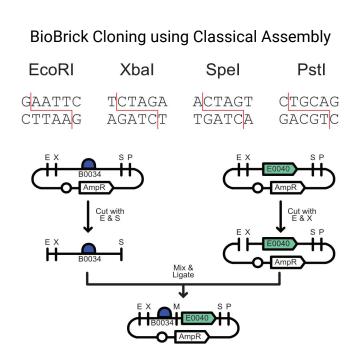
Engineering DNA: DNA assembly methods



- 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 (<u>Cohen SN, et al.</u> <u>PNAS (1973)70(11):3240-4</u>)
- 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 <u>BioBrick</u> cloning (EcoRI/Xbal, Spel/Pstl)
- 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

Bsal

GGTCTCNNNNN

CCAGAGNNNNN

Esp3l

GGTCTCNNNNN

GCAGAGNNNNN

GCAGAGNNNNN

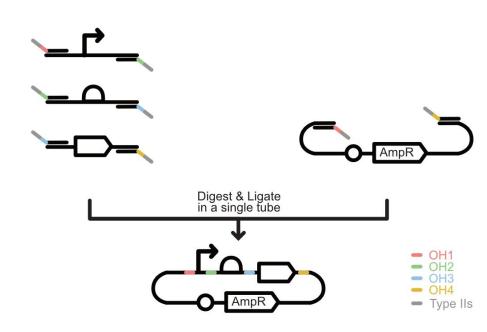
GAAGACNNNNNN

CTTCTGNNNNNN

Recognition
Spacer
Overhang

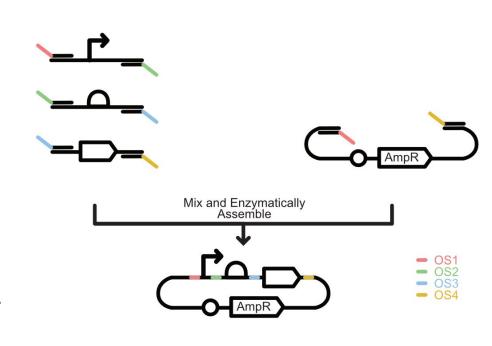
Engineering DNA: Multipart assembly using Golden Gate

- Golden Gate assembly can be easily achieved using PCR with primers that introduce Type IIs restriction sites (e.g., Bsal, Bbsl, 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



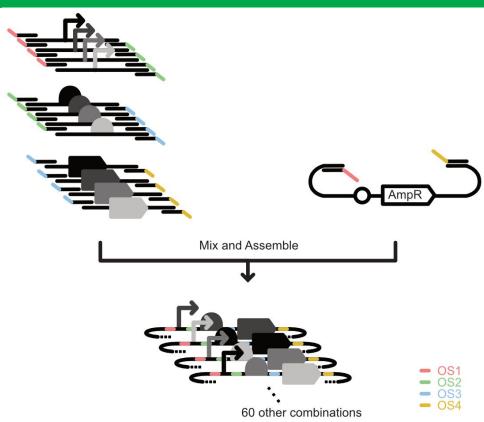
Engineering DNA: Multipart assembly using Gibson Assembly

- 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



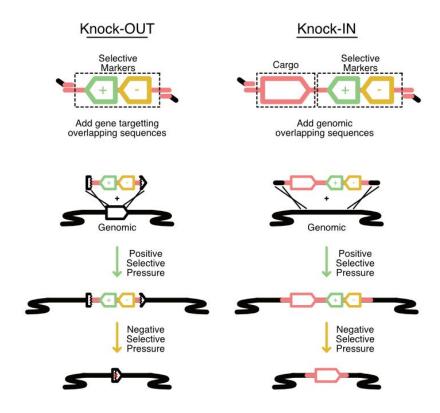
Engineering DNA: High-throughput combinatorial DNA assembly

- 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



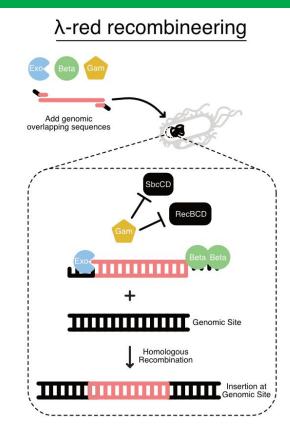
Engineering DNA: Editing Genomes by Knocking-IN or Knocking-OUT

- 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)



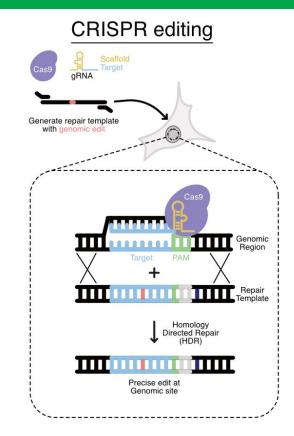
Engineering DNA: Using Recombineering to edit genomes

- 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



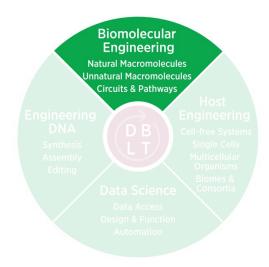
Engineering DNA: Using CRISPR-Cas9 to make precise genome edits

- 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 (<u>Jinek M., et al., Science</u> (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.



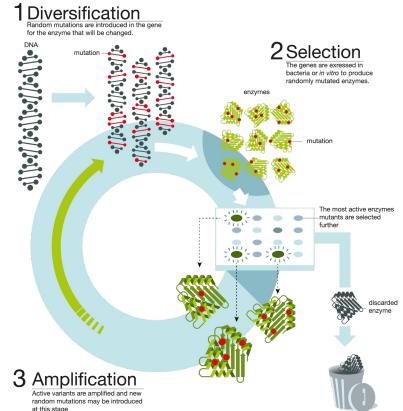
Core Tools for Biomolecular Engineering

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



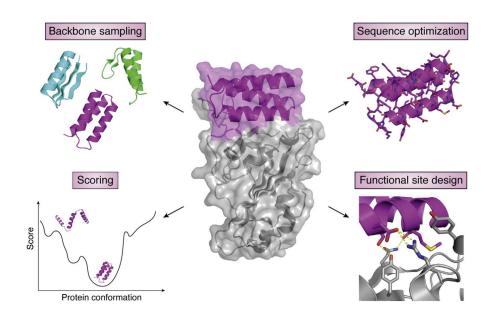
Biomolecular Engineering: Natural Macromolecules

- 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



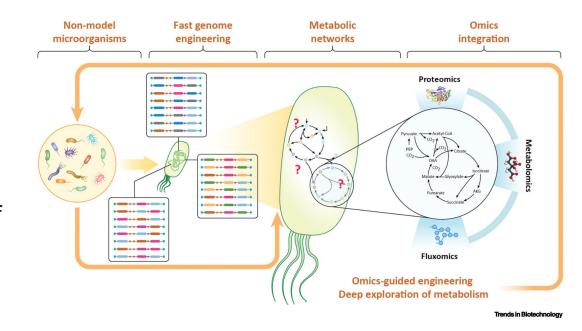
Biomolecular Engineering: Unnatural Macromolecules

- 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



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

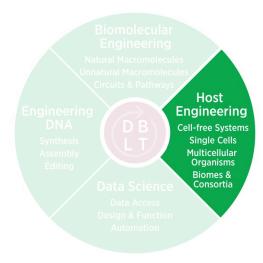


Concept 1-4

Core Tools Part 2: Host Engineering, Data Science

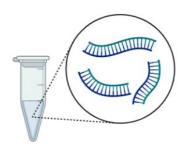
Core Tools for Engineering Biology

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



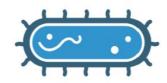
Host choice - what can systems do?

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

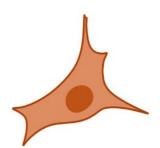
Yeast



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

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

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

When to use a model organism

- 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

When to use a non-model organism

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

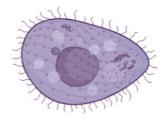
Example: producing human ion channels in bulk (for crystallography or drug discovery)

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...

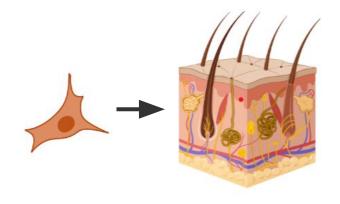


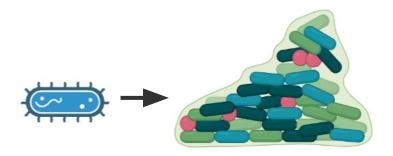
- More difficult to insert genes
- Can produce in large quantities
- Can grow in bulk (if you have the specific expertise to work with it)



Host Engineering: Engineering across scale

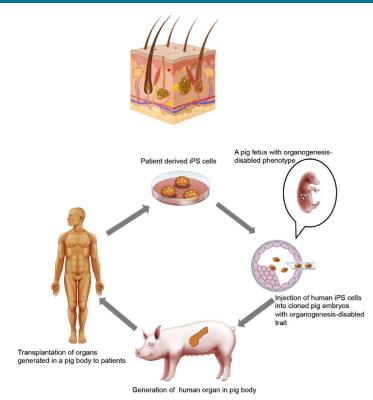
- Very few cells are naturally isolated
- Cell tissues and microbial consortia are complex
 - Often more difficult to engineer
 - Can carry out complex tasks
- Can give better understanding of natural systems





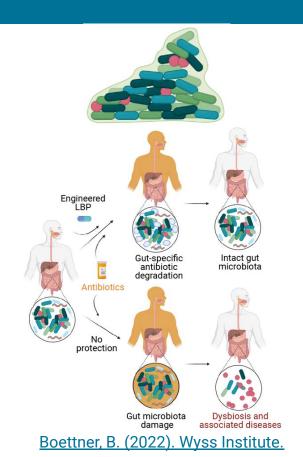
Host Engineering: Tissue scale

- 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



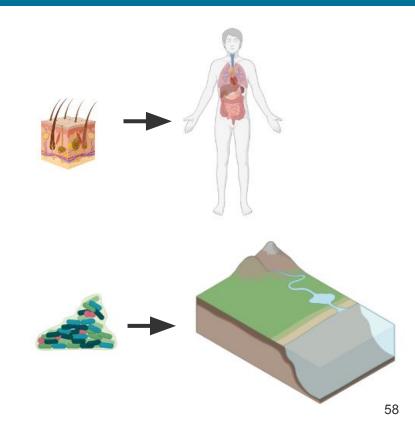
Host Engineering: Consortia scale

- Example: engineered life 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



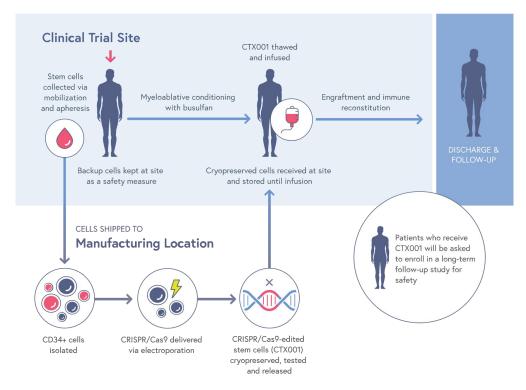
Host Engineering: Engineering across scale

- 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



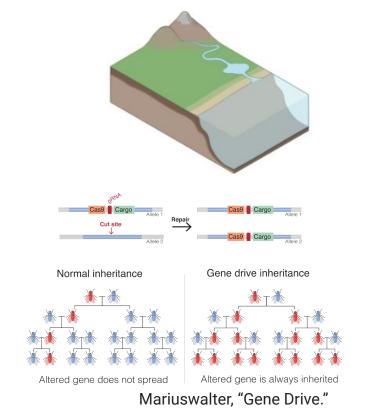
Host Engineering: Organism scale

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



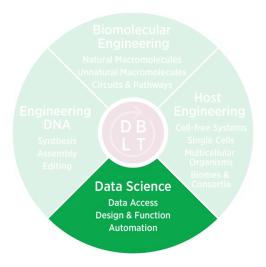
Host Engineering: Ecosystem scale

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



Core Tools for Engineering Biology

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



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!

Data Science: Genomics

Why:

- Discover members of a large population
- Understand the variation between/within populations
- Epigenomics: how DNA modifications impact expression

- Large-scale sequencing
- Reassembly (what pieces are from whom)
- Comparing regions of interest (species identifiers, important coding regions)



Data Science: Transcriptomics

Why:

- mRNA what genes are cells expressing under specific conditions
- ncRNA regulation and more

- RNA sequencing (similar to DNA-seq)
- Microarrays (quantify a set of specific sequences)



Data Science: Proteomics

- Why:
 - Know what proteins make up a cell/tissue
 - Know if cells are making a product of interest

- 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)



Data Science: Metabolomics

- Why:
 - Know what chemical products a cell is making
 - Quantify signalling molecules or chemical product production

- Spectrometry methods (gas/liquid chromatography)
- Assays for specific molecules of interest



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

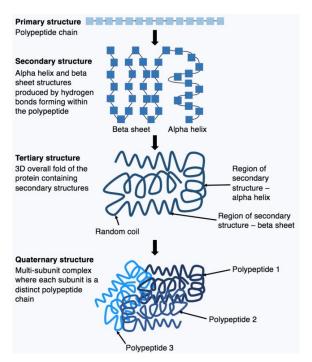


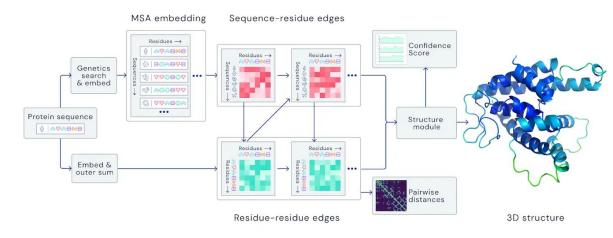
De Novo DNA

Predict RBS output based on both RBS and protein sequence



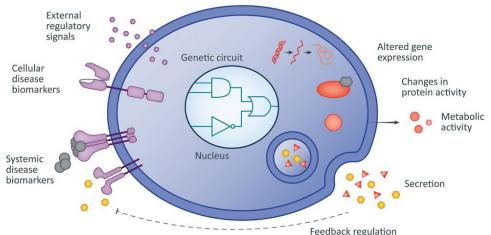
Data Science: Modeling proteins (AlphaFold)





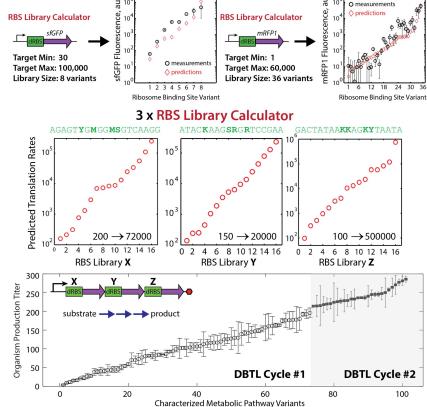
Data Science: Modeling whole systems

- 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.'



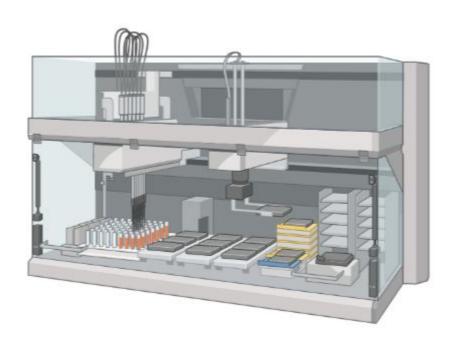
Data Science: Automation of design

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



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



Data Science: Automation of laboratory processes



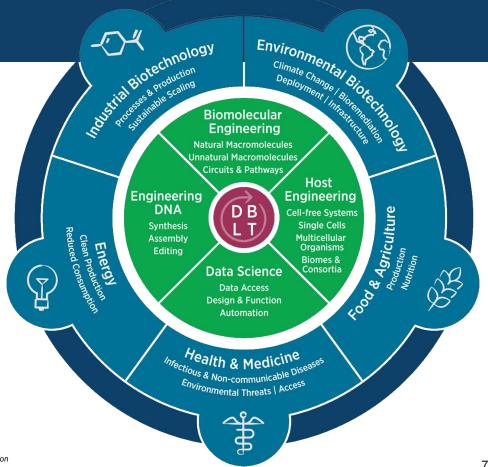
Concept 1-5

Impacts & Applications

Engineering Biology

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

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





Food & Agriculture

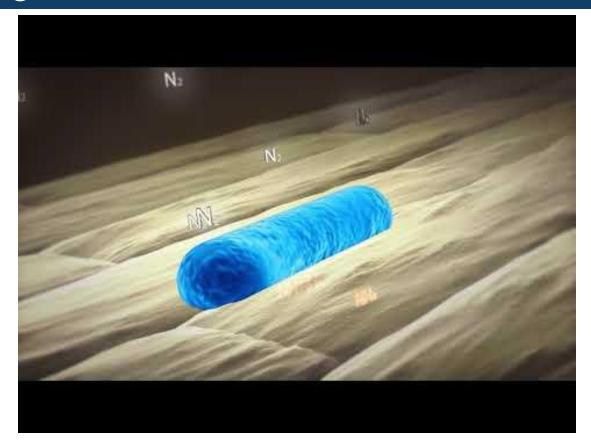
Microbial symbiont fertilizers

- 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?





Food & Agriculture

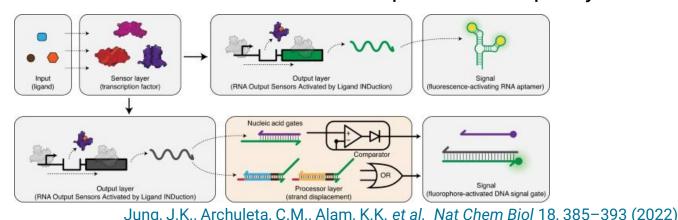




Health & Medicine

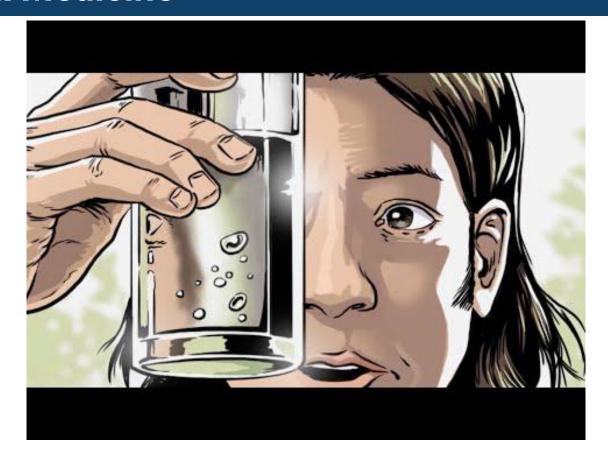
At-home water quality testing

- 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





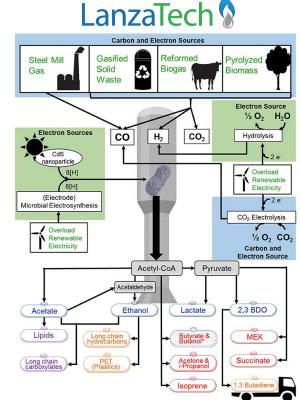
Health & Medicine





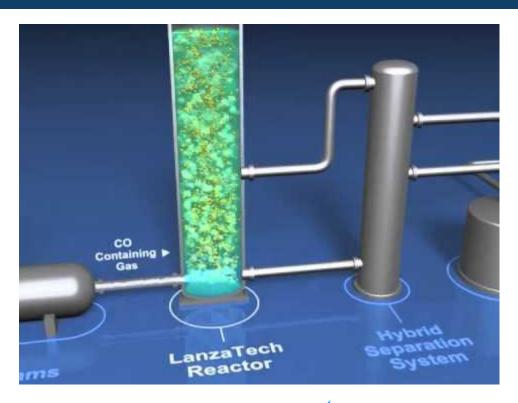
Energy

- 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.





Energy





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
- Explore digital resources:
 - EBRC In Translation podcast
 - BioBuilder Life-Changing Science podcast
 - AAAS myIDP website





Diverse Careers in Engineering Biology

Agriculture, Life,

and Physical

Infrastructure

Engineering and

	Manufacturing	Sciences		Business
Educational Attainment Bachelors 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
	Engineer Computer Scientist Chemist	Physical or Life Scientist Forester Nutritionist	Environmental Health and Safety Manager Plant Manager	Business Operations Assistant Economicist Community Partnerships Coordinator
General E 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

Operations,

Management, and

Education,

Communication, and Outreach

Education Program

Public Affairs Specialist

Scientific Illustrator

Bioethicist

Manager

Educator

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.

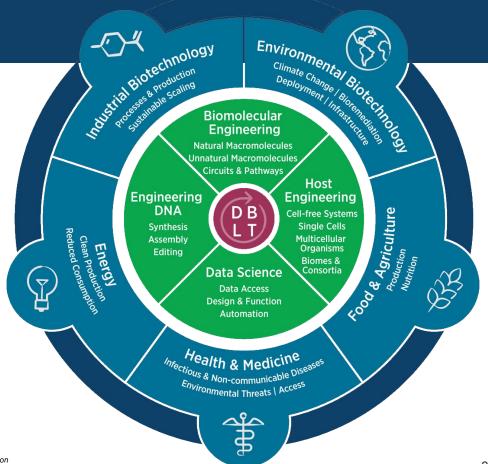
Program manager in a government agency who develops and writes research & training initiatives, and discusses research priorities with academic labs.

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

Summary

Synthetic biology:

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



Credits

Slides developed by Joshua Atkinson & Michael Sheets.

Graphics from BioRender, courtesy of BioBuilder Educational Foundation.

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Figure Credits

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Extended Resources

EBRC video playlist: https://youtube.com/playlist?list=PLf4eUKhxElurvaNwNSpyXlKf LoFRIZZm

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

Raj Lab Synbio Transcript course: https://youtu.be/3xJl8j7Ylrl

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_F0B6IPPZeSilcfYtxn4o7bkbBUT_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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