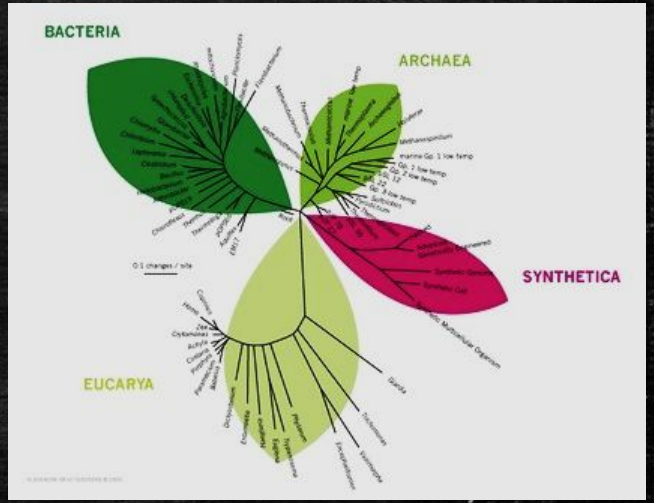
Synthetic Biology 101

Synthetic Biology

- Applying rational and systematic principles of engineering to biological systems
- Reconstructing life from the bottom-up and top-down
- Synthesizing biologically-based constructs not found in nature
- Standard, interchangeable parts



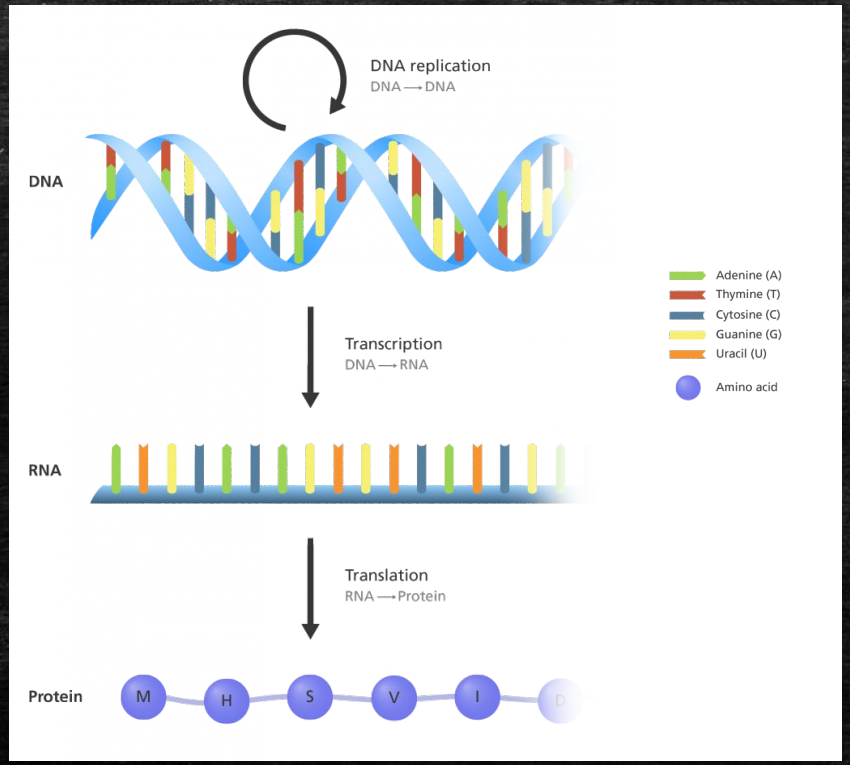
Uses of Synthetic Biology







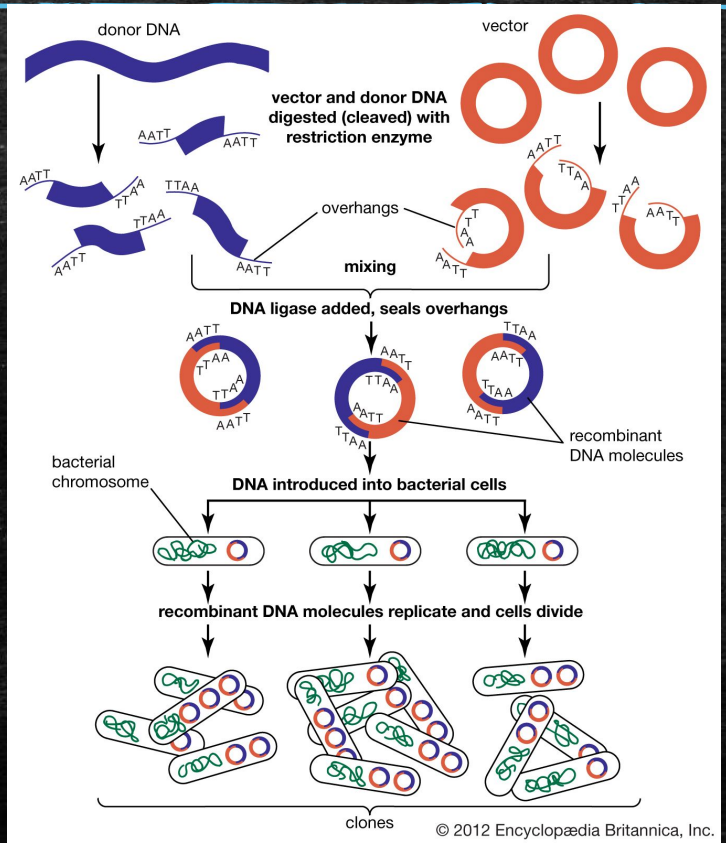

Central Dogma of Biology



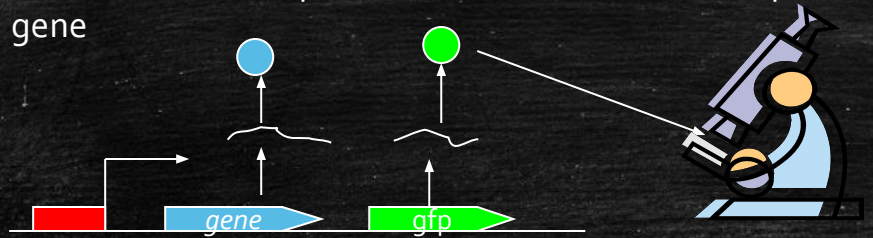
Key Enabling Technology

Recombinant DNA technology: allows to cut and paste pieces of DNA at desired locations cleaved by restriction enzymes

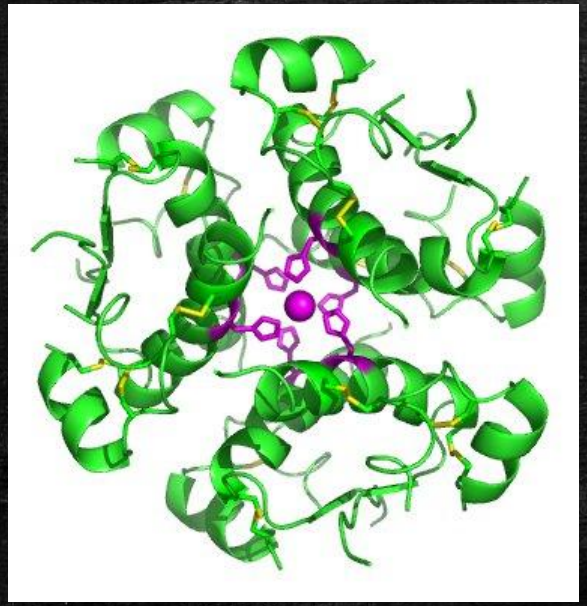
Key Enabling Technology

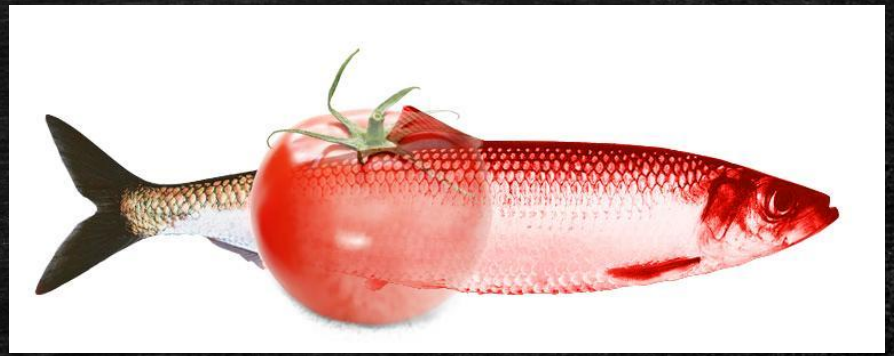


Fluorescent Proteins: allow through fluorescence microscopy to measure the concentration of a protein and thus the level of expression of the corresponding gene

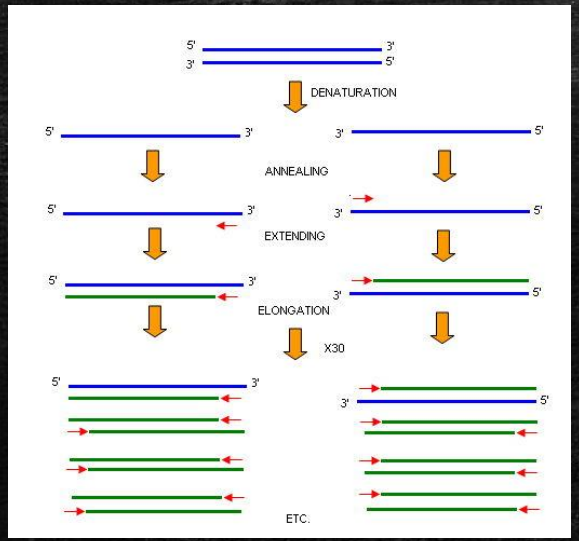


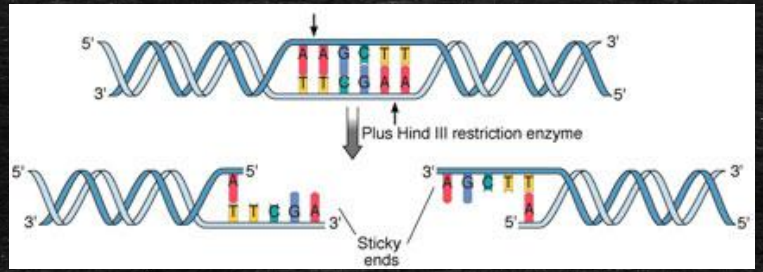
Recombinant DNA Technology

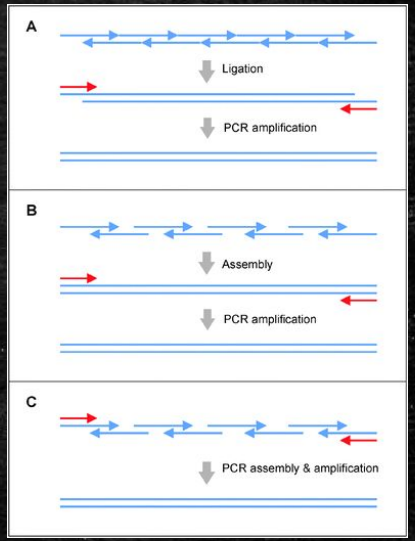




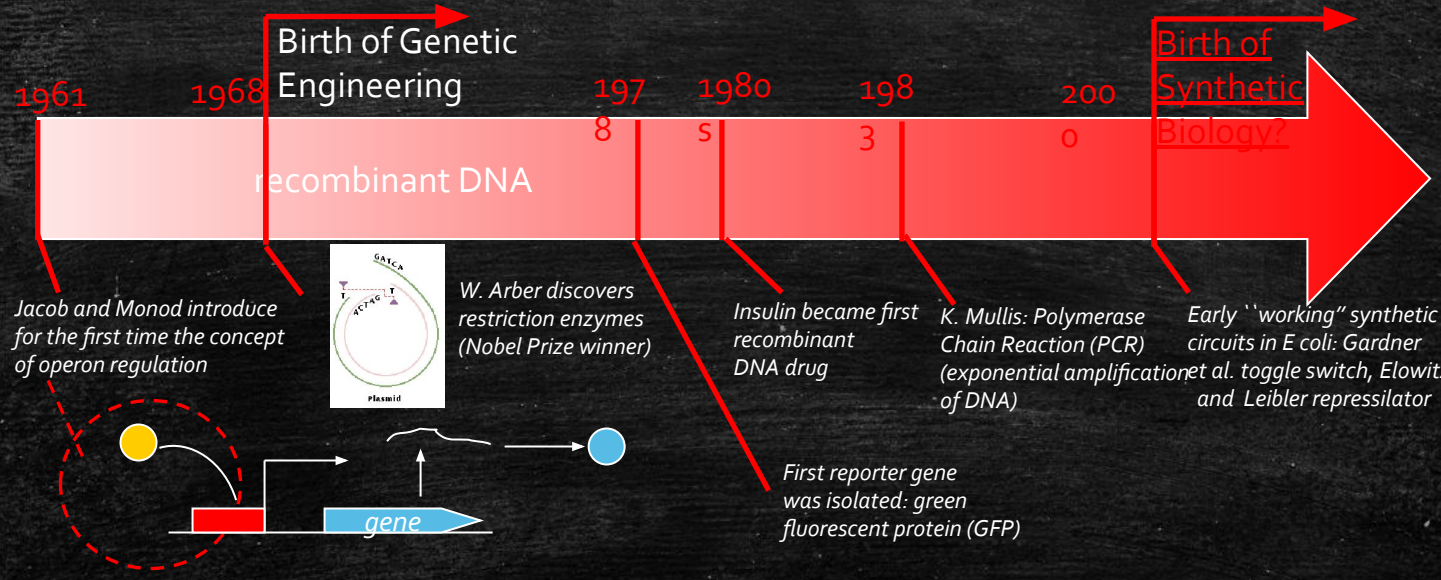
Advances in Synthetic Biology – The Early Years



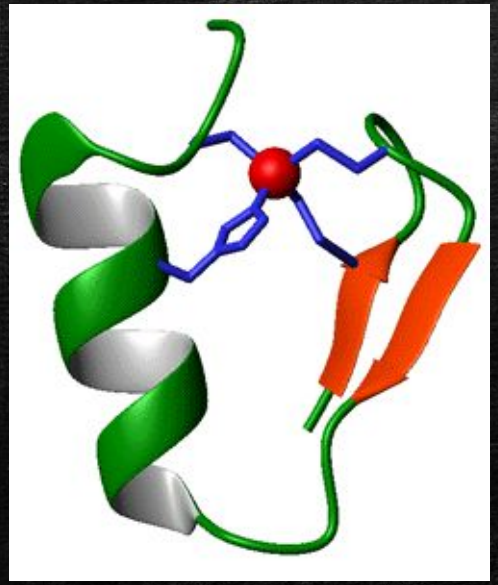


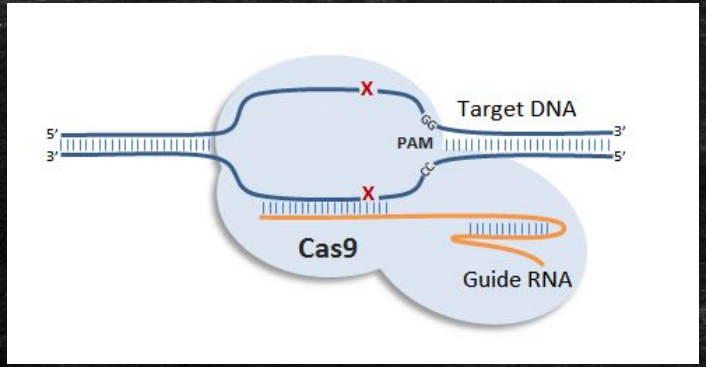


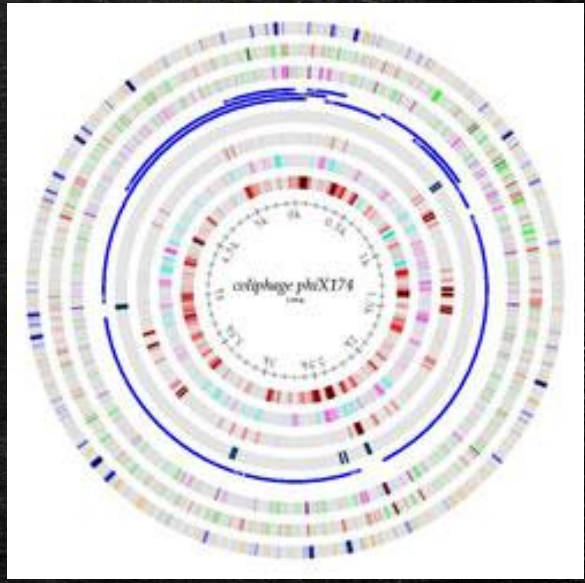
Synthetic Biology: A Historical Perspective



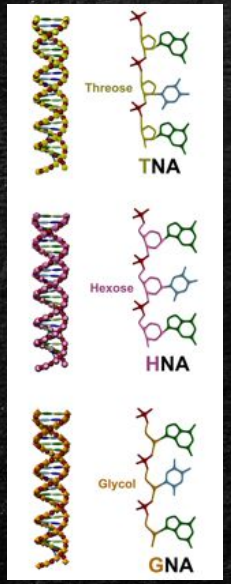
Advances in Synthetic Biology – Precise Editing

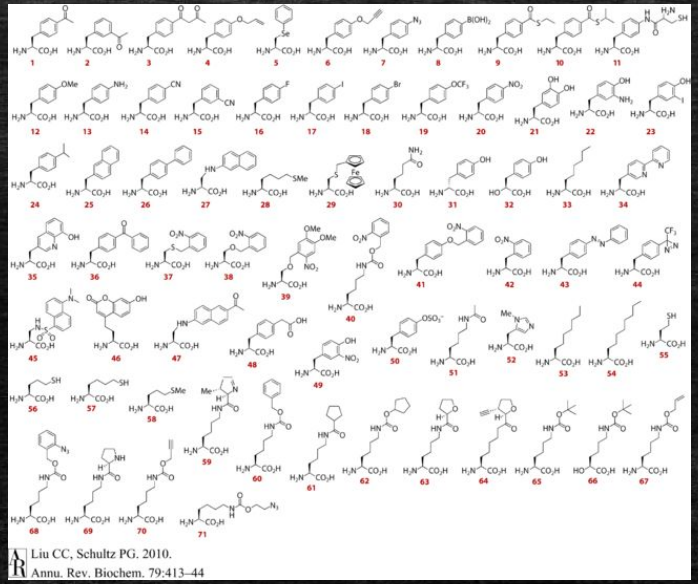


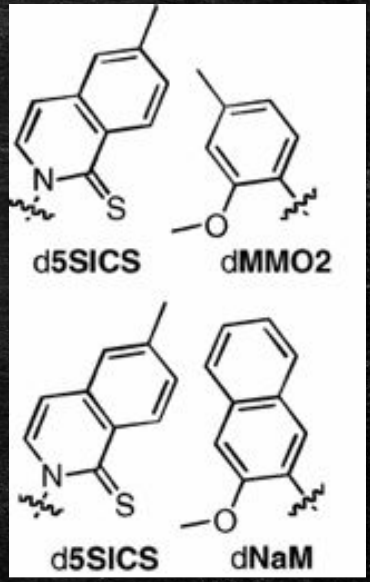




Advances in Synthetic Biology – Artificial Life





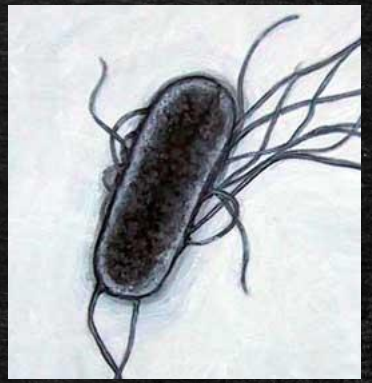


CASE STUDY

Thinking Like a Synthetic Biologist

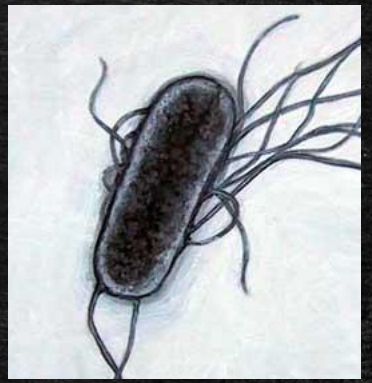
1. Coming Up with a Plan

- Identify the problem : Safe and efficient way of getting rid of microbial pathogens in the body



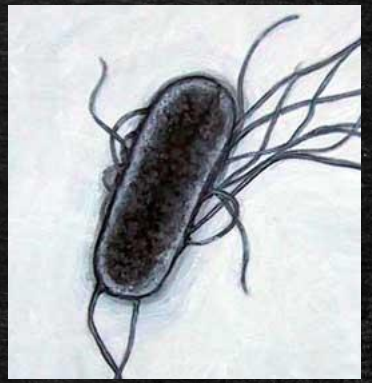
Thinking Like a Synthetic Biologist

Applying concepts of Synbio:
Genetically engineer bacteria to defeat infections



Thinking Like a Synthetic Biologist

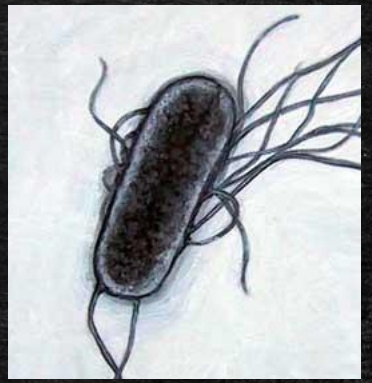
Insert gene that, when activated, can produce an antimicrobial compound



1. Coming Up with a Plan

Thinking Like a Synthetic Biologist

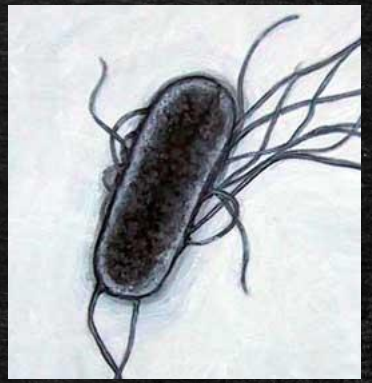
Place gene under regulation so that only expressed in conjunction with nearby pathogen



1. Coming Up with a Plan

Thinking Like a Synthetic Biologist

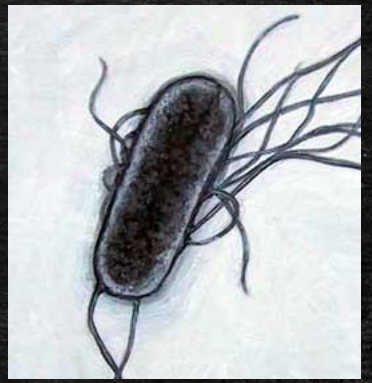
Introduce stand-in for pathogen that can be easily quantified



1. Coming Up with a Plan

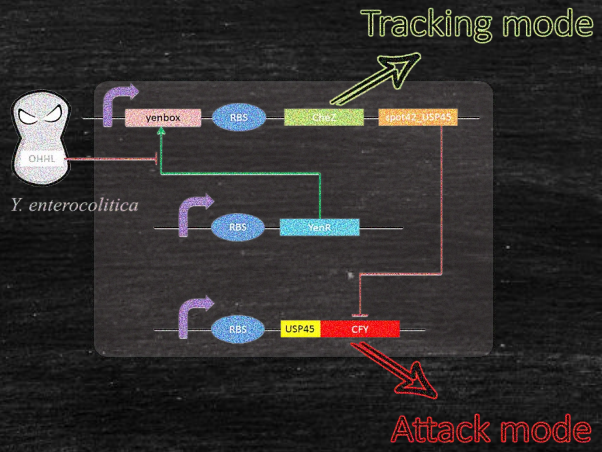
Thinking Like a Synthetic Biologist

Incorporate additional mechanisms to increase efficiency and safety



2. Designing a System

Thinking Like a Synthetic Biologist



2. Designing a System

- Sensing:
  - Distinct signal produced by target pathogen that can detected by system
  - Specificity of signal. Unique to pathogen
  - Tie reception of signal to activator of gene regulatory element controlling both the targeting and attacking modes

2. Designing a System

Thinking Like a Synthetic Biologist

- Targeting:
  - Introduce proteins that enhance general cell mobility or guide targeting mobility (chemotaxis)
  - Selectively turn off motility to remain in sufficient contact with pathogen once detected

2. Designing a System

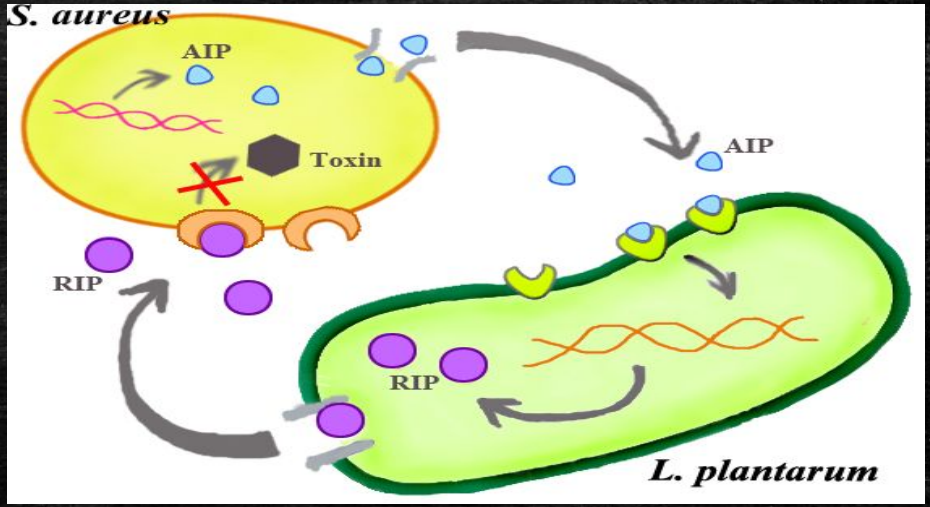
Thinking Like a Synthetic Biologist

- Attacking:
  - Express antimicrobial protein once sensing and targeting systems activated
  - Secrete antimicrobial to reach pathogen
  - Finely tune gene activation for quick shut down to prevent autotoxicity and quick activation to maximize lethality

3. Creating a Strategy

Thinking Like a Synthetic Biologist

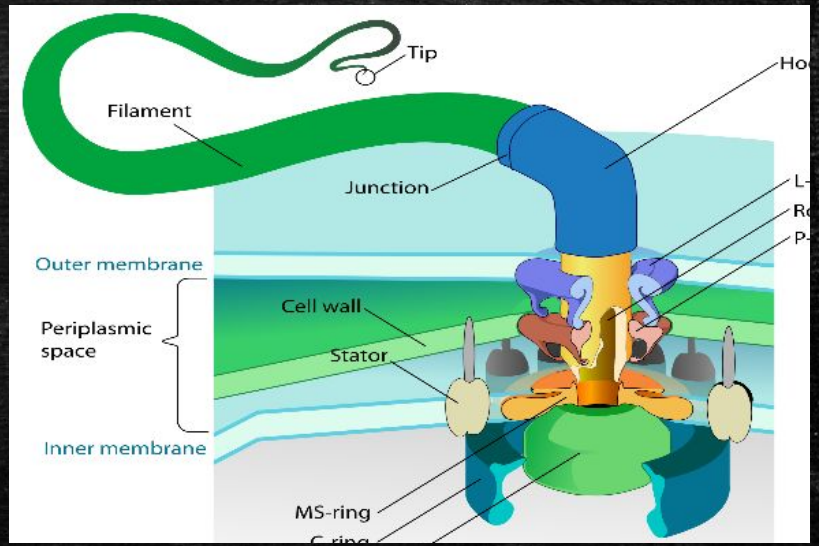
- Sensing:
  - "Quorum Sensing" signals secreted by pathogen species
  - Bound quorum receptor inhibits genes with certain promoter (in this example)



3. Creating a Strategy

Thinking Like a Synthetic Biologist

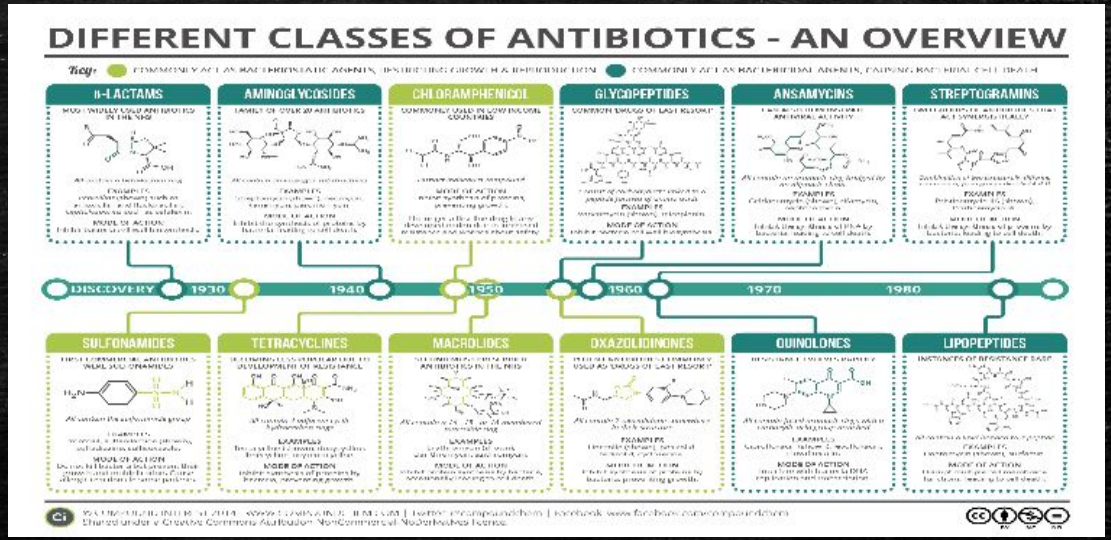
- Targeting:
  - Knock out endogenous protein responsible for inhibiting flagella movement for "search" mode
  - Re-insert chemotaxis protein under control of quorum receptor promoter



3. Creating a Strategy

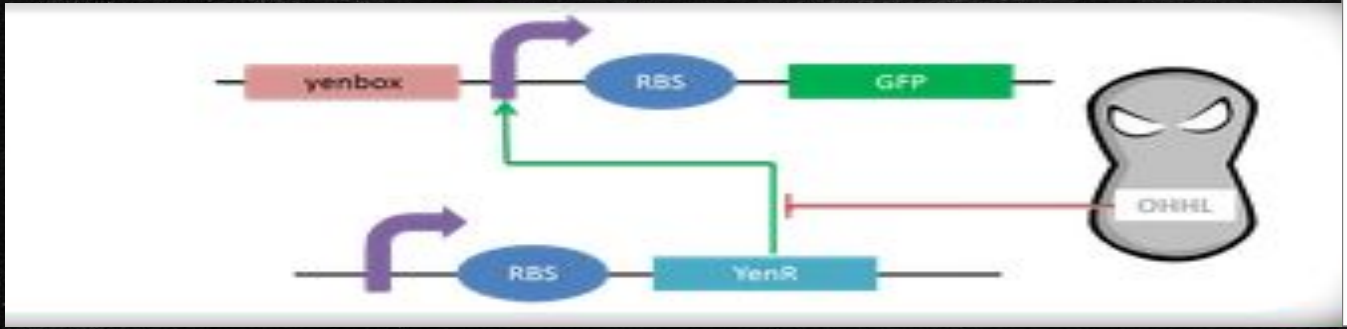
Thinking Like a Synthetic Biologist

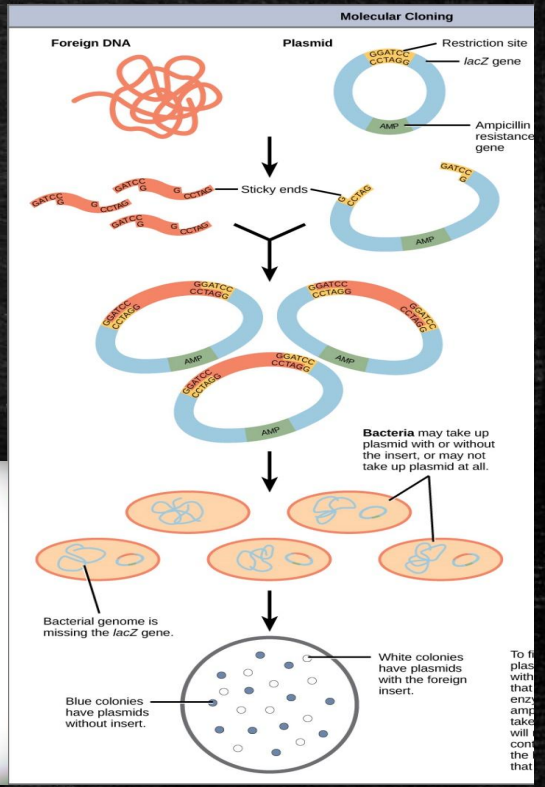
- Attacking:
  - Insert genes for biosynthesis of antimicrobials, specialized for lethality against type of cell of interest
  - Add second gene to help rapidly halt the system after activation



4. Building a System

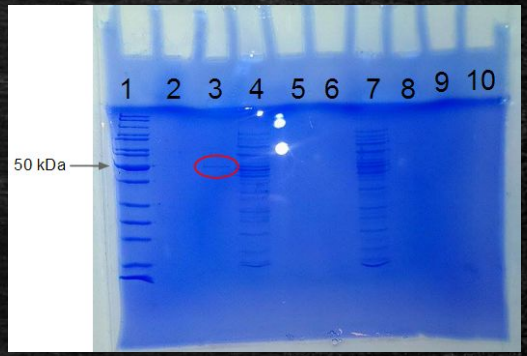
1. Put together each gene with its corresponding regulatory elements on a vector
2. Repeat for all genes and regulatory proteins that make up gene circuit
3. Introduce and test vectors one at a time. After confirmation, consolidate into single system

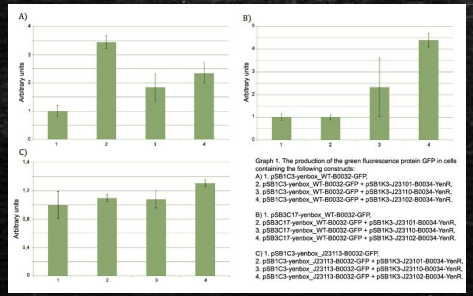


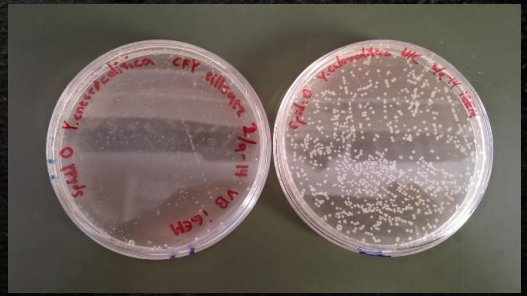


5. Testing

- Measure each component of circuit individually
  - Check for levels of expression, if expressed at right time, and if being toxic to system
  - Check that gene products are all functional
- See if parts of circuit interact properly when combined
  - Check that expression of quorum receptor is inhibiting the parts of the circuit it is supposed to
  - Check nothing in the circuit is breaking the sequence of events



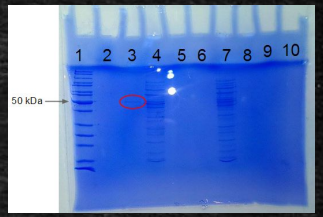


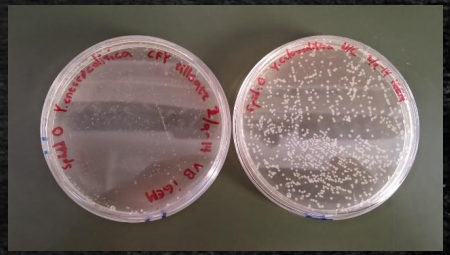


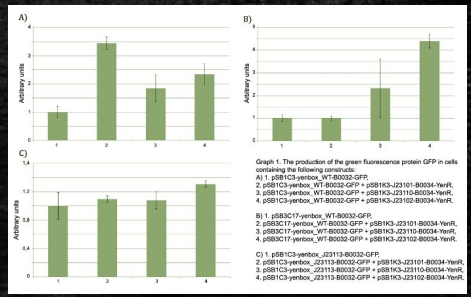
Thinking Like a Synthetic Biologist

5. Testing that it Works

- Make sure parts are functioning under controlled conditions
  - Check that able to detect quorum signal
  - Check chemotaxis mechanism is working for targeting
  - Check that toxin being produced and is lethal on short time scale
- Simulate experimental conditions
  - Check that system able to effectively and selectively kill pathogen







THANK YOU!