Building with Biology

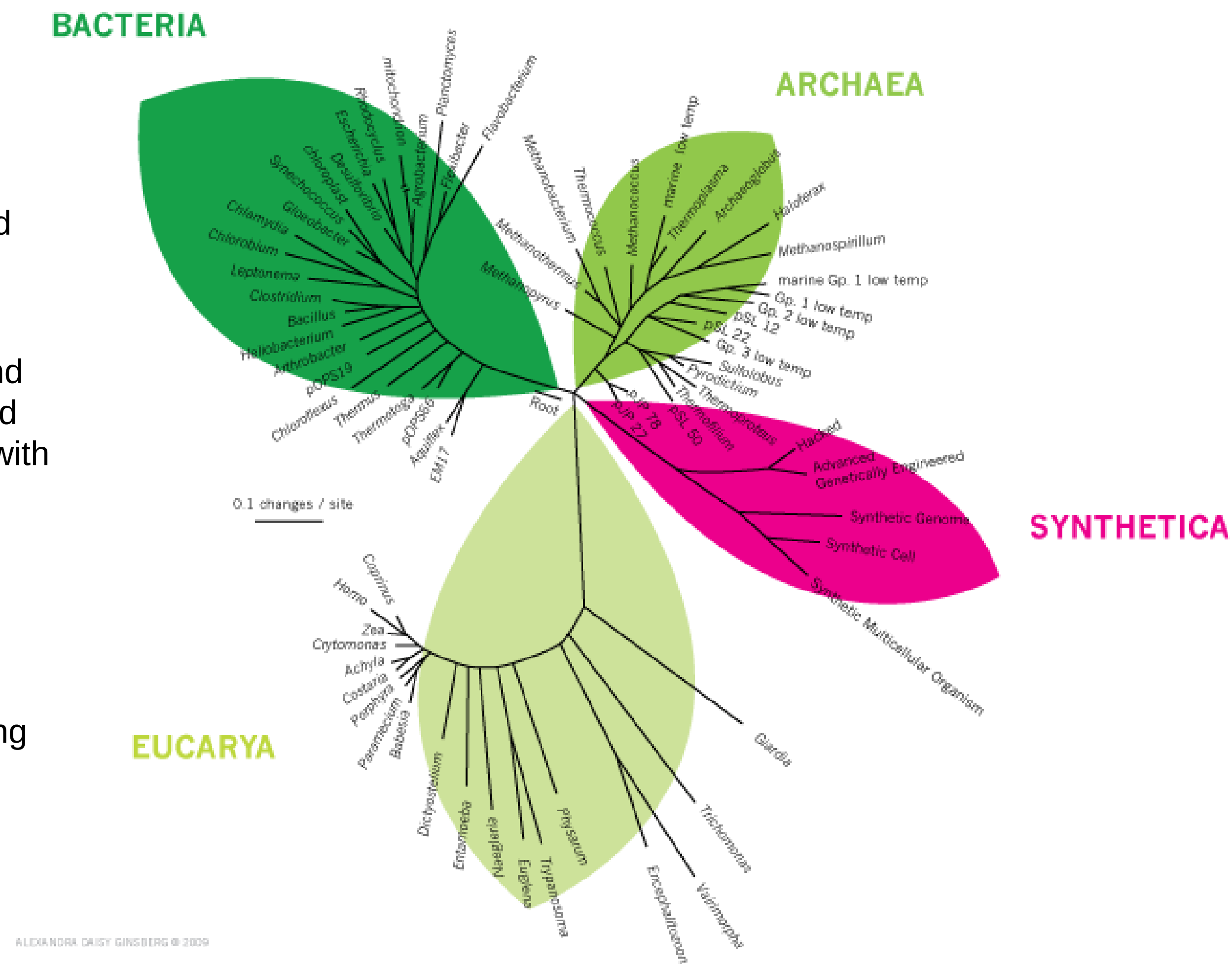
Activities and Conversations about Synthetic Biology

Synthetic Biology

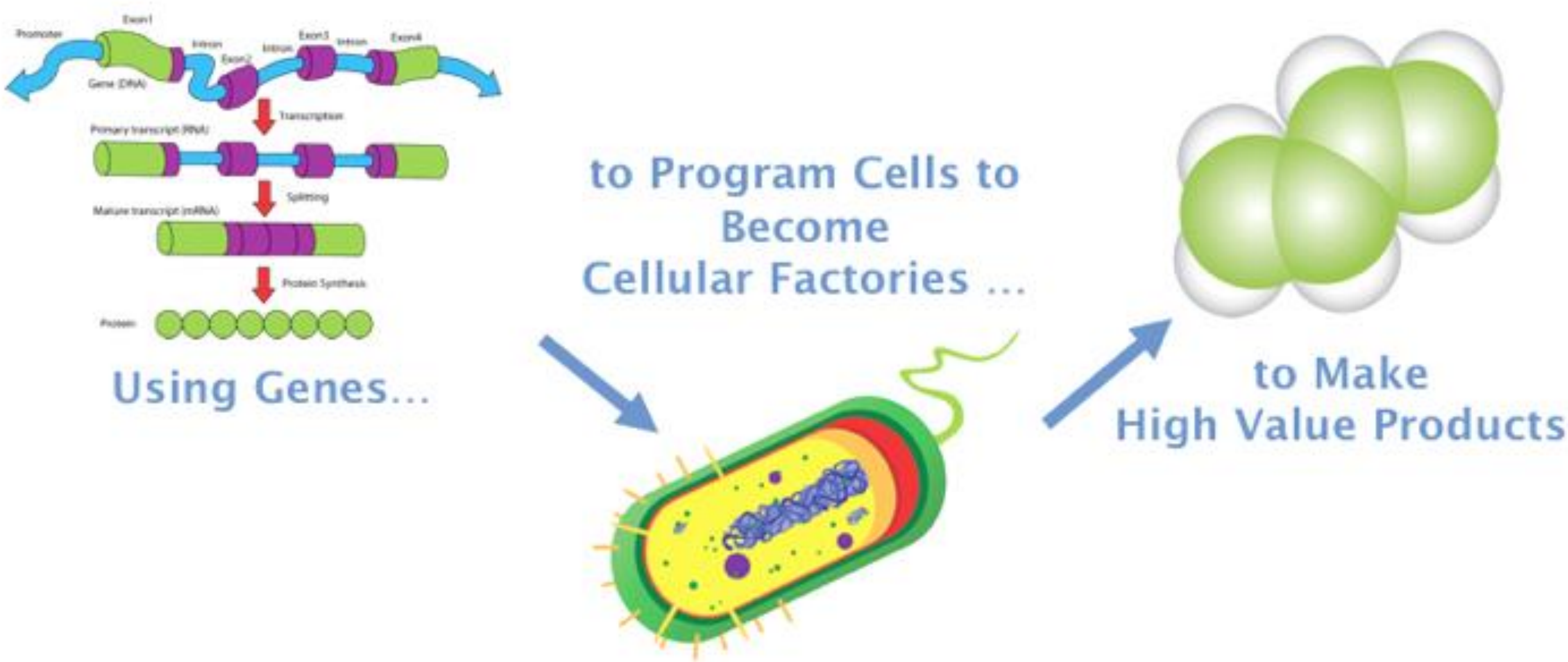
Synthetic biology is the design and construction of biological devices and systems for useful purposes.

It is an area of biological research and technology that combines biology and engineering, thus often overlapping with bioengineering and biomedical engineering.

It encompasses a variety of different approaches, methodologies, and disciplines with a focus on engineering biology and biotechnology.



Synthetic Biology



“Synthetic Biologists want to engineer living cells to do something useful; for example, treat a disease, sense a toxic compound in the environment, or produce a valuable drug.”

Synthetic Biology: Engineering Life

ISBN 978-1-62703-625-2 (eBook) DOI 10.1007/978-1-62703-625-2

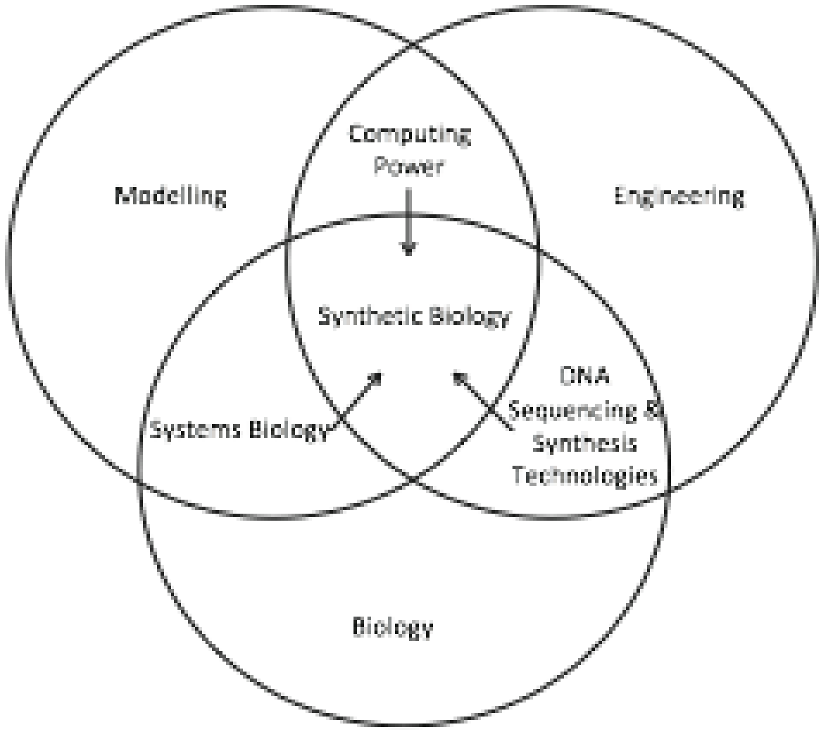


Fig. 1 Synthetic biology is a set of research activities at the intersection of engineering, computational modelling, and biological sciences. It builds on a variety of technologies and tools including improvements in DNA sequencing, cheaper gene synthesis technologies, increased computational power, and a better understanding of biological systems gained through systems biology

What is Synthetic Biology?

- Putting the ‘engineering’back into genetic engineering…

- https://www.youtube.com/watch?v=rD5uNAMbDaQ

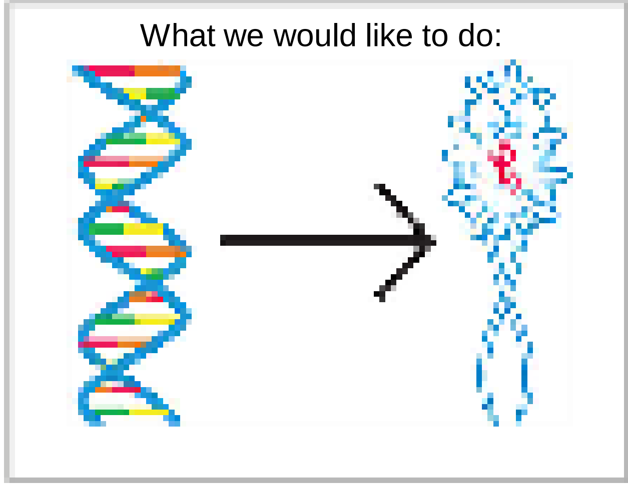
- https://youtu.be/EtADBcxWpVg

- **Synth.Bio takes advantage of:**
  - reasonably well-characterized model systems (bacteria, yeast, algae)
  - Tons of sequence data
  - A growing ‘molecular toolbox’

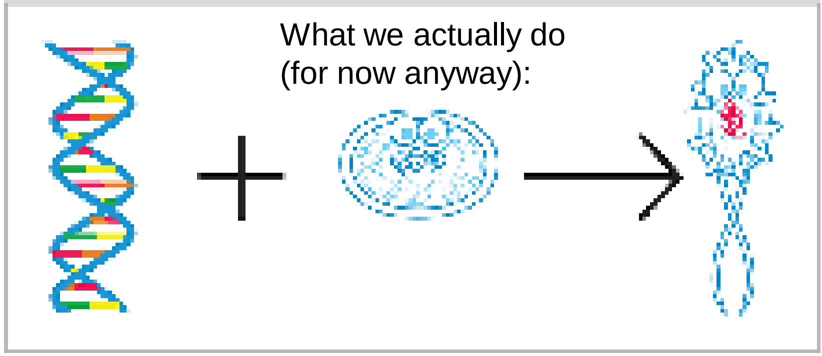
http://www.archinode.com/fab-tree-hab-3.html

Why Synthetic Biology?

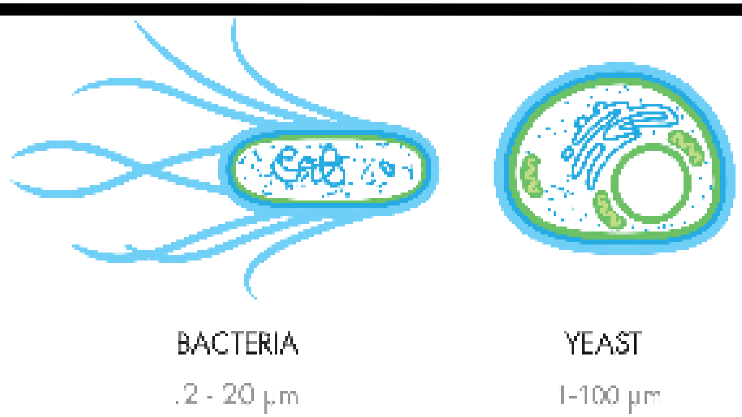
- **Advantages:**
  - Cells can make copies of themselves (unlike electronics)
  - Some cells replicate as fast as 30 minutes!
  - Cells contain the biological machinery to carry out many complex tasks— specific chemical reactions, for example—that would be difficult, if not impossible, to accomplish otherwise.
  - Synthetic biology has the potential to produce eco-friendly solutions to many difficult problems.



  - Synthetic biology is also a fantastic approach to learn more about the workings of natural systems.



The Framework



The organism used is called the "chassis"

- We are still in the early days of this developing discipline.
- Synthetic biology raises philosophical questions as we begin to think about cells as tiny living machines built to do our bidding.
- Do we know enough about cells to reliably engineer them?
- Research so far has been conducted primarily on relatively simple unicellular organisms such as bacteria (especially *E. coli*) and yeast (*S. cerevisiae*)

Introduction to Engineering and Design

- Engineers cycle through **design**, **building**, and **testing** phases, often doing rapid prototyping of different designs to find the most promising direction.
  - engineering approach will not focus on why a design works as long as the prototype tests successfully
- Scientific method: cycles through **hypotheses**, **experiments**, and **analysis**
  - aims to understand the precise details of how something works

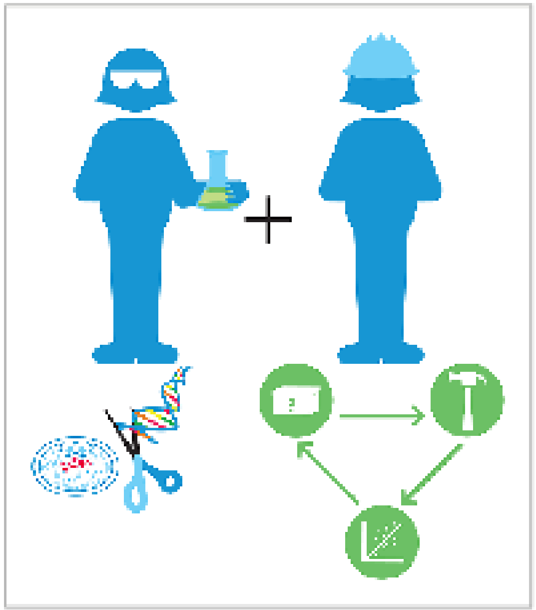


FIGURE 1-3 *The interdisciplinary nature of synthetic biology. Synthetic biologists combine the wealth of knowledge and techniques from molecular biology (left) with engineering principles (right), including the design-build-test cycle that's a hallmark of engineering disciplines.*

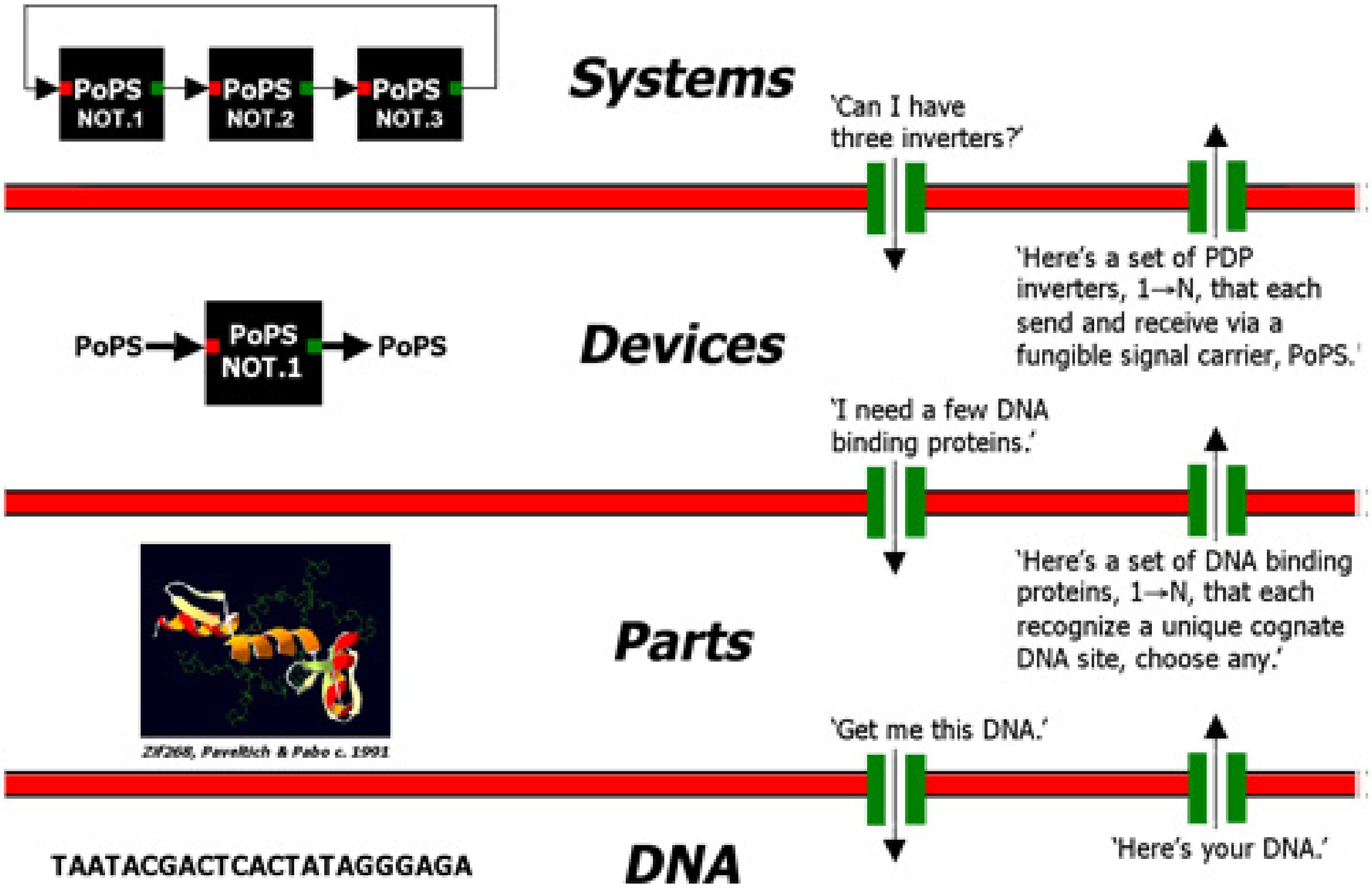
“BIO-Building”

- Learn the fundamentals of biodesign and DNA engineering
- Explore important ethical issues raised by examples of synthetic biology
- Investigate the BioBuilder labs that probe the “de[illegible] build-test” cycle
- Test synthetic living systems designed and built by engineers
- Measure several variants of an enzyme-generating genetic circuit
- Model “bacterial photography” that changes a strain’s light sensitivity
- Build living systems to produce purple or green pigment
- Optimize baker’s yeast to produce ß-carotene

Building with Biology
Southern Connecticut State University SCSU
NSF
crisp
BioPath Bioscience Academic and Career Pathway
iGEM
SCSU Office for STEM Innovation & Leadership

Candidate abstraction hierarchies

http://syntheticbiology.org/Abstraction_hierarchy.html



Types of Synthetic Biology Research

Table 1
Types of synthetic biology research

Type of research	Examples
Nonnatural systems	Expanded genetic code, orthogonal ribosomes, proteins containing noncanonical amino acids, biology of reversed chirality
Self-replicating chemical systems	Photochemical systems, self-replicating RNA systems, protocells
Minimal cells	Genome reduction, natural minimal cells, synthetic cells, vesicles harboring minimal genetic circuits
Advanced metabolic/genetic/protein engineering	Rational strategies for metabolic engineering, metabolic flux analysis, pathway design, computation modelling of whole cell metabolism, protein design
Engineering-based approaches	Forward engineering based on computational modelling, computer-aided design of pathways/organisms, parts/devices/systems, modular construction of pathways

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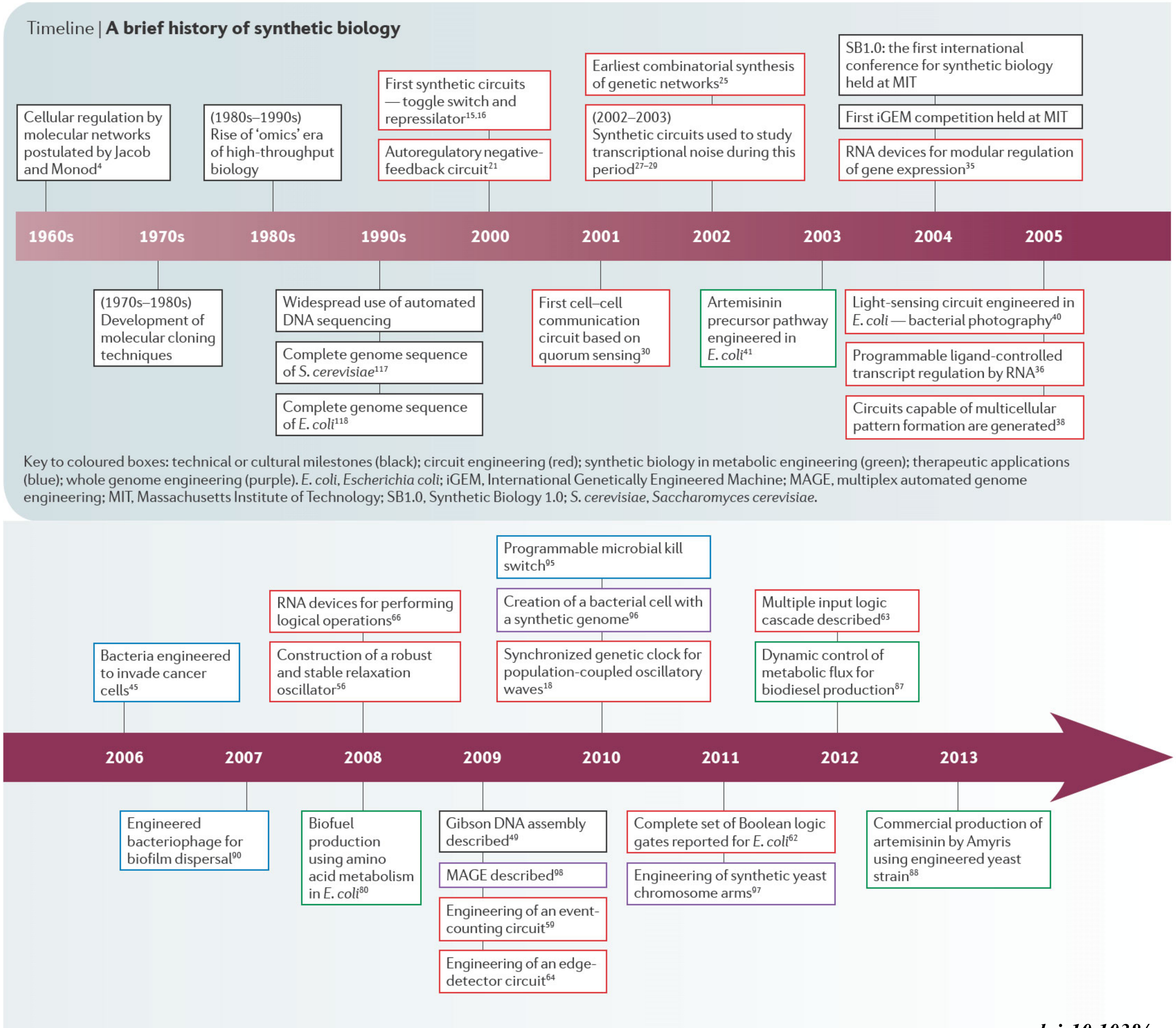
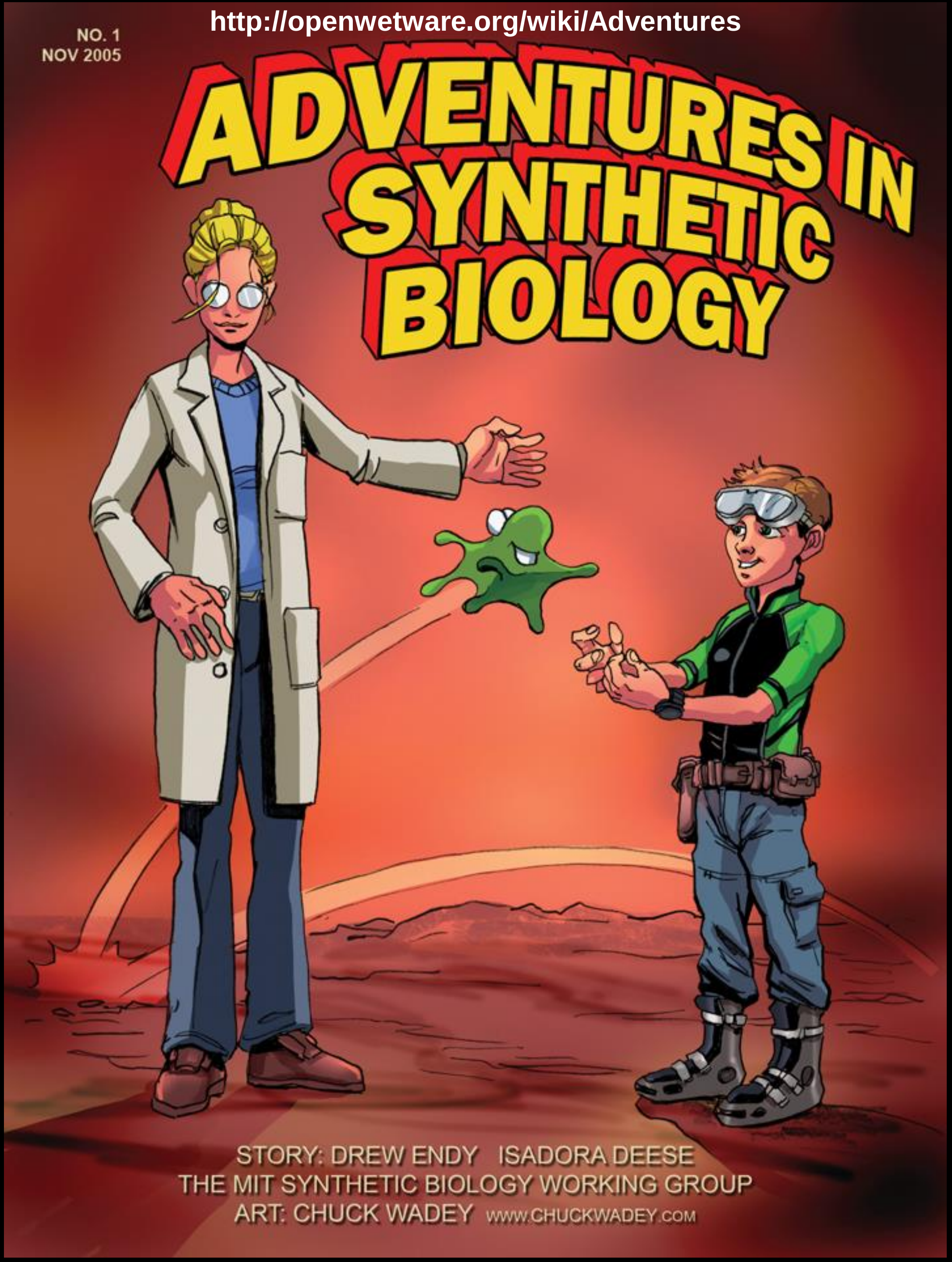


Timeline | **A brief history of synthetic biology**

Key to coloured boxes: technical or cultural milestones (black); circuit engineering (red); synthetic biology in metabolic engineering (green); therapeutic applications (blue); whole genome engineering (purple). *E. coli*, *Escherichia coli*; iGEM, International Genetically Engineered Machine; MAGE, multiplex automated genome engineering; MIT, Massachusetts Institute of Technology; SB1.0, Synthetic Biology 1.0; *S. cerevisiae*, *Saccharomyces cerevisiae*.

doi:10.1038/nrmicro3239

http://openwetware.org/wiki/Adventures



The SCSU Phage Hunter's Program

- SEA-PHAGES = Science Education Alliance's Phage Hunters Advancing Genomics & Evolutionary Science
- It is a two-course research-based program for Biology Freshman & Sophomore Undergraduates.
- SCSU was accepted into the 4th cohort of Universities and Colleges for the Howard Hughes Medical Institute's SEA-PHAGES program, and is now in it's 5th year.

What do the Students Learn?

- Course Objectives
  - Instill in each student a sense of ownership of a scientific problem
  - Discover new scientific information
  - Encourage close student-faculty interactions and effective mentoring
  - Enable faculty development via training and inter-institutional collaboration
  - Critical Thinking
  - Data analysis and interpretation
  - Experimental design
  - Reading and analysis of primary literature
  - Understanding applications of mathematical modeling in problem solving

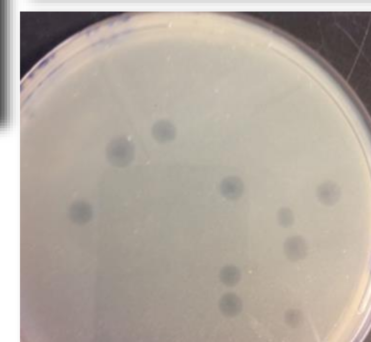

EM of "McGuire"

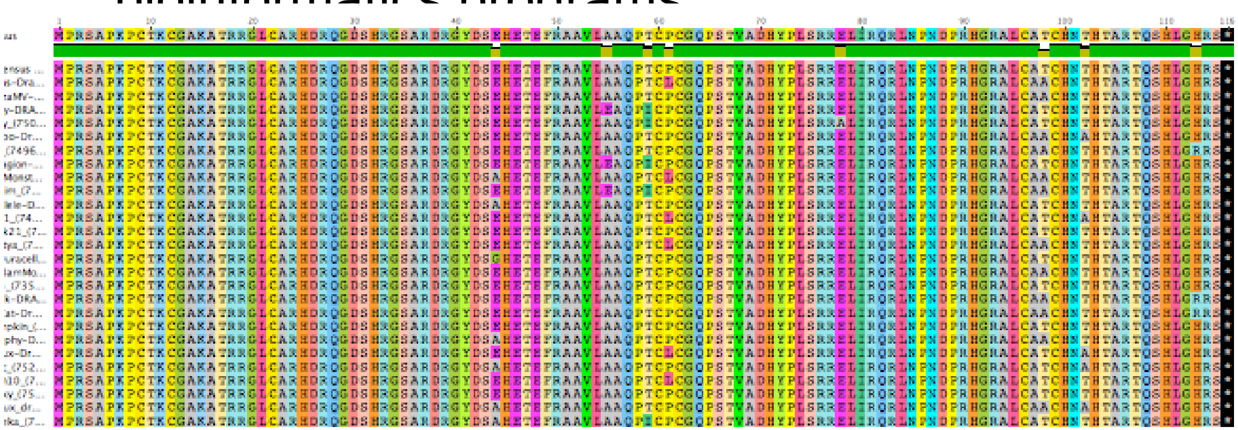
- Laboratory Experiences
  - Aseptic technique
  - Microbiology
  - Molecular biology
  - Electron microscopy
  - DNA sequencing
  - Comparative genomic analysis
  - Functional genomic analysis
  - Genome annotation

- Professional Development
  - Effective presentation of research
  - Networking with other SEA participants
  - Dissemination of research findings & submissions to genomic databases

Students learn how the scientific method works by doing Science

- *First term:* Students isolate bacteriophages from soil samples they collect. They see their phage with electron microscopy, isolate phage DNA, and submit phage genomes for sequencing.
- *Second term:* Students analyze the phages genomes using bioinformatics programs

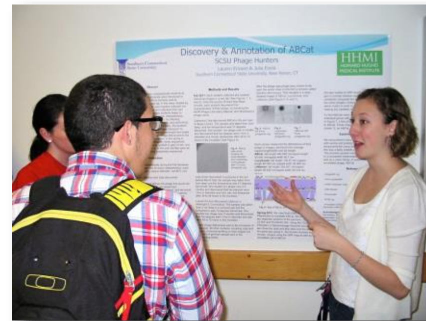




science education alliance
HOWARD HUGHES MEDICAL INSTITUTE

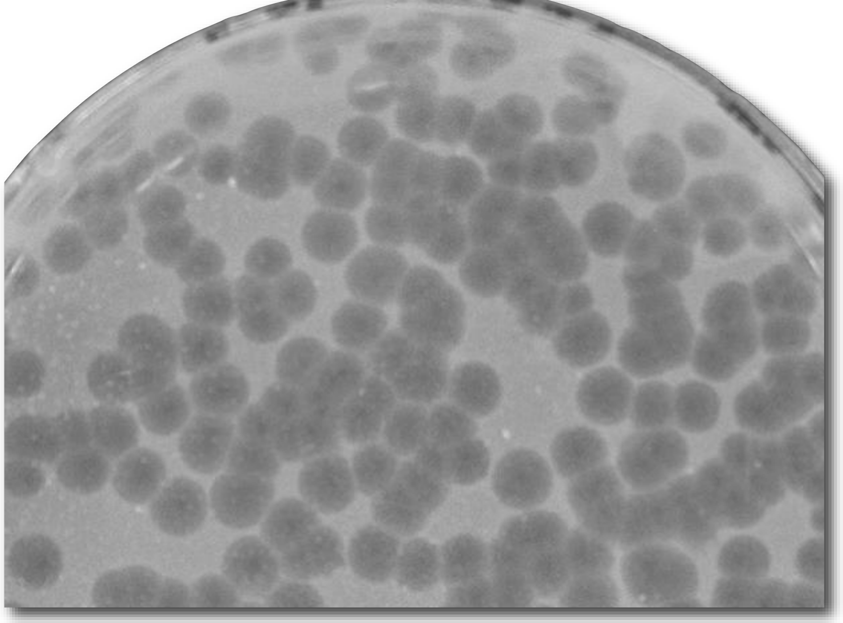
After the bioinformatics

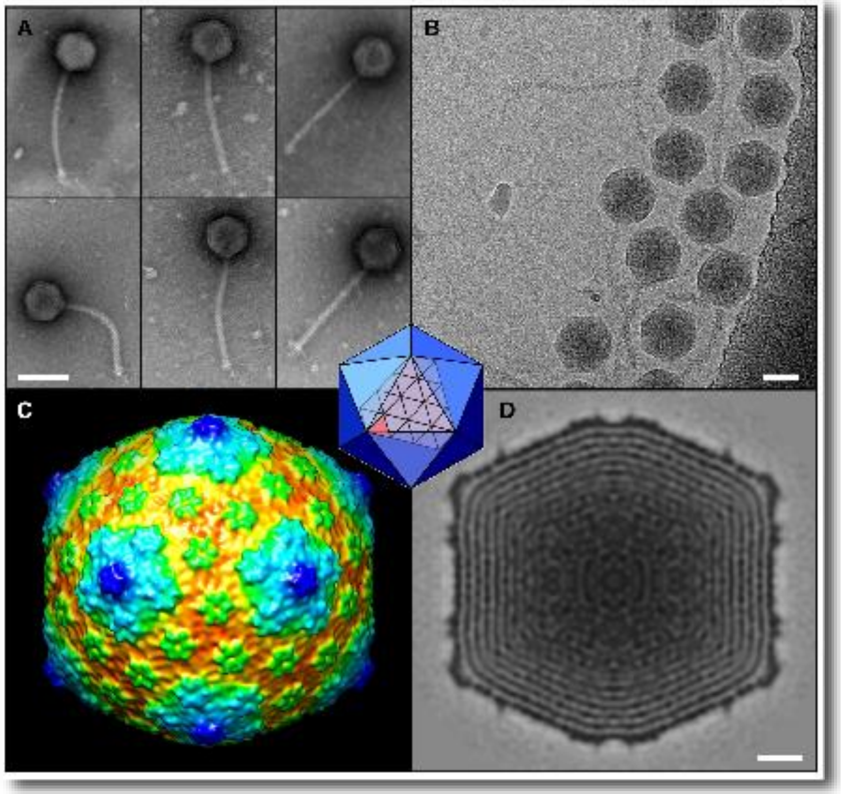
- Students maintain lab research notebooks, write reports, discuss primary literature, and in pairs, present their data in a poster format at the end of the year.
- HHMI invites 1-2 students to attend a national SEA-PHAGES Symposium at the Janelia Farm Research Campus in Ashburn VA in June. (& covers the cost!)
- The annotated genomes get published to the NCBI databases
- Often the discoveries are published in peer-reviewed publications with student authors.

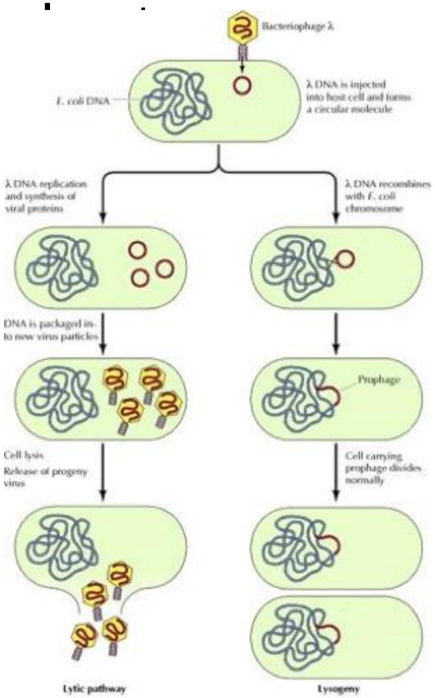


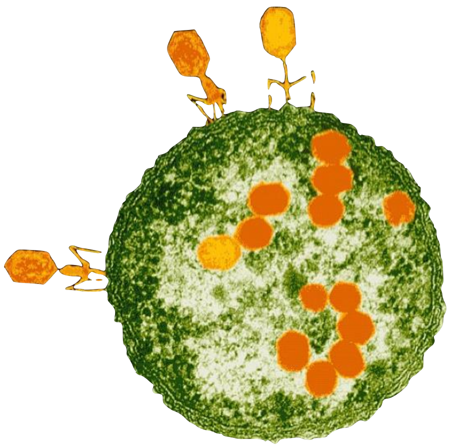
What are bacteriophages?

- Bacteriophages are viruses that infect bacteria
- Some can ‘hide’(integrate) their DNA into the host’s genome,
- & others can quickly make more infectious copies of themselves & destroy (lyse) the host



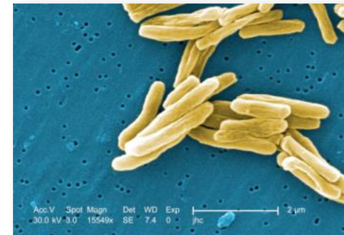


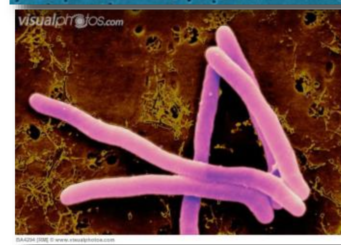




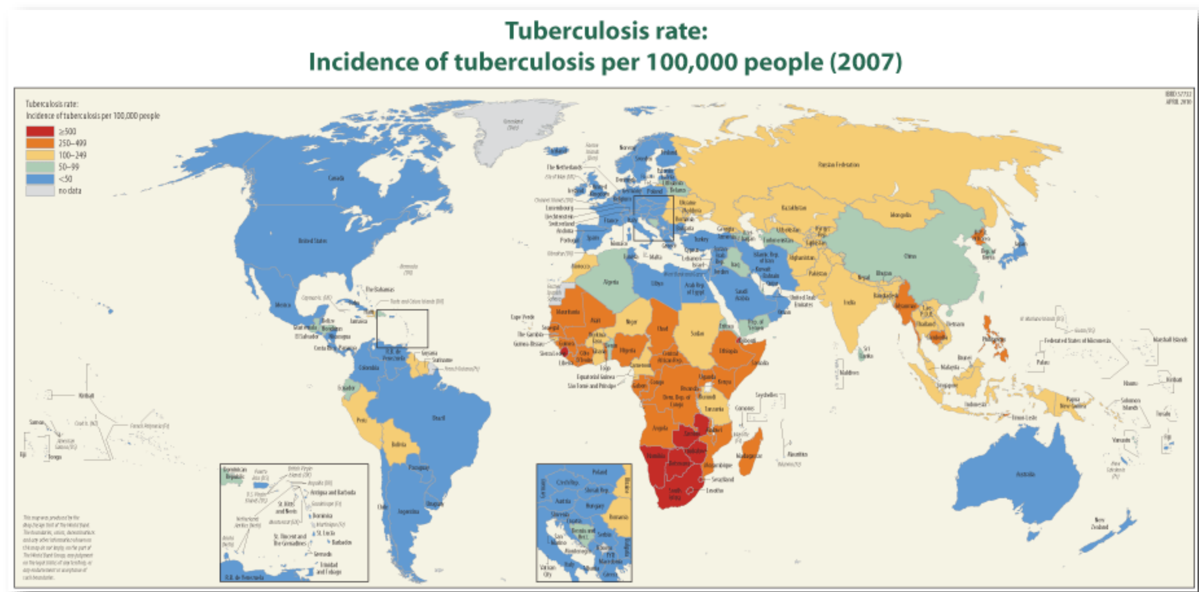
Why study phages that infect *Mycobacterium smegmatis?*

- *Mycobacteriophages* specifically attack mycobacteria, which includes the important human pathogens that cause:
  - leprosy (*Mycobacterium leprae*) and
  - tuberculosis (*Mycobacterium tuberculosis*), as well as
  - the harmless soil bacteria *Mycobacterium smegmatis (M. smeg).*



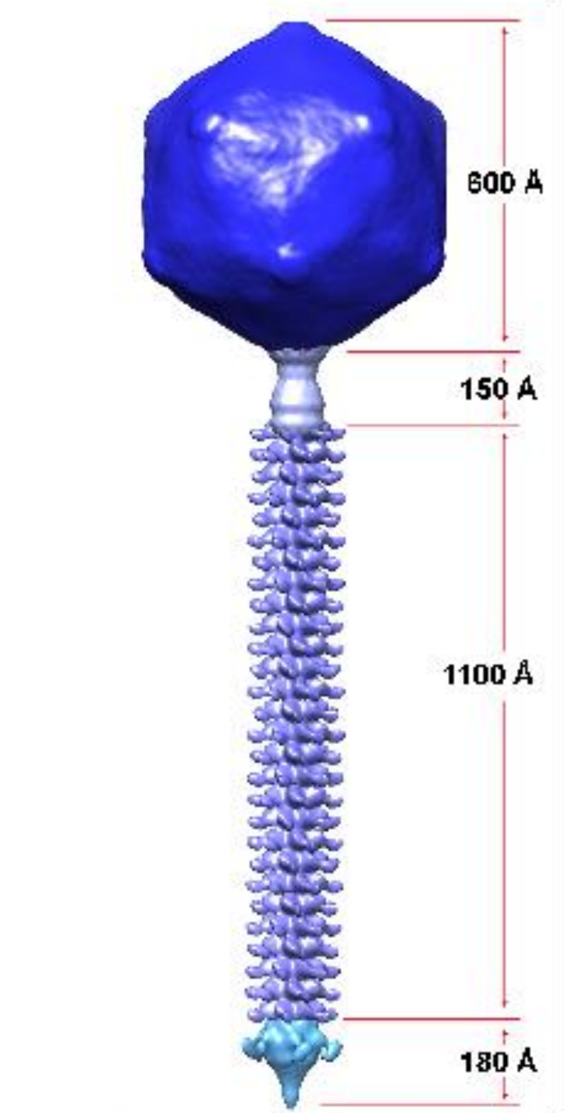


- According to the WHO:
  - Tuberculosis is <u>*second largest killer*</u> (after HIV) by infection of a single infectious agent, &
  - 1/3 of the entire Earth's human population is infected with latent tuberculosis.



What is the benefit of understanding mycobacteriophages?

- Biosensors/ Diagnostic tool tool for *M. tuberculosis* infection diagnosis
- ~80% of mycobacteriophage genes have no known function, yet are highly conserved
- An untapped molecular toolbox for Scientists
- Phage therapy to cure infections
- How do viruses evolve to attack new host species?
- Why are there different cluster families if they all infect a common host?
- How much genomic diversity exists out in



The first structure of a mycobacteriophage, Araucaria, Mohamed Sassi1, May 2013 J. Virol. doi:10.1128/JVI.01209-13

A Broadly Implementable Research Course in Phage Discovery and Genomics for First-Year Undergraduate Students

Tuajuanda C. Jordan, Sandra H. Burnett, Susan Carson, et al.

2014. mBio 5(1): doi:10.1128/mBio.01051-13.

- "The educational model of the SEA- PHAGES program integrates course-based learning within a framework of scientific activity, including:
  - a real-world scientific research agenda,
  - professional networking, &
  - scientific dissemination of results."

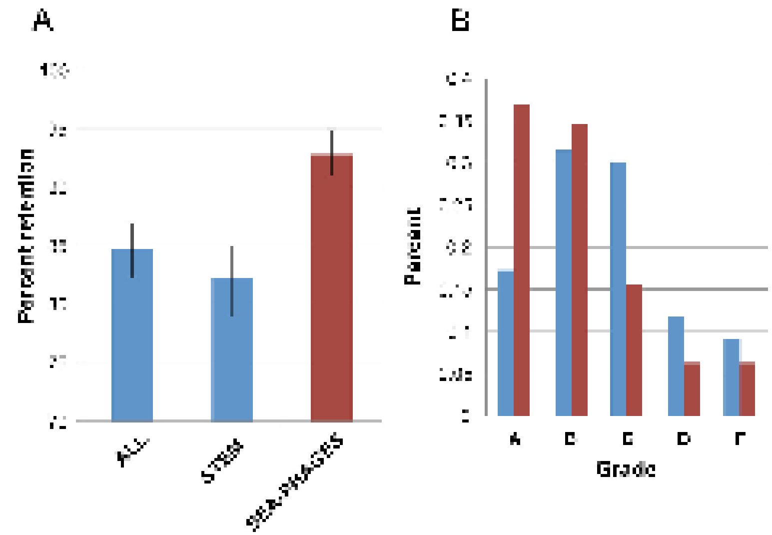


FIG 3 (A) Retention of SEA-PHAGES participants (red) compared to other students at the same institution (blue), year 1 to year 2 of their college experience. Retention data were gathered from 20 institutions, with some institutions contributing data from multiple years, resulting in 27 sets of comparison data. Retention data were analyzed with a between-group analysis of variance with 3 levels of the independent variable (all majors, STEM majors, and SEA-PHAGES students) for 171 reports. The result was interpreted as significant at the 0.05 level. (B) SEA-PHAGES students (red) perform better than peers (blue) in traditional laboratory sections in the introductory lecture course. Results are for 127 SEA-PHAGES students and 1,120 students in the traditional laboratory course from six institutions. In the lecture course, SEA-PHAGES students averaged 2.95 on a 4.0 scale, compared to the 2.58 average of students in traditional lab sections. This difference was significant ($t = 2.64$; $P < 0.05$).

- "We show here that this alliance-sourced model not only:
  - substantially advances the field of phage genomics but also
  - stimulates students' interest in science,
  - positively influences academic achievement, &
  - enhances retention in (STEM) disciplines."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SEQUENCING
Discovery & Annotation of ABCat
SCSU Phage Hunters
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