From Synthetic Biology to Natural Learning

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Biology Department and **GCAT**

DAVIDSON

Wofford College
September 12, 2011

Outline of Presentation

1. Introduce synthetic biology

2. Applications of synthetic biology

3. Synthetic biology research at Davidson College

4. Why make biological computers?

5. How do we prepare undergraduates for SynBio?

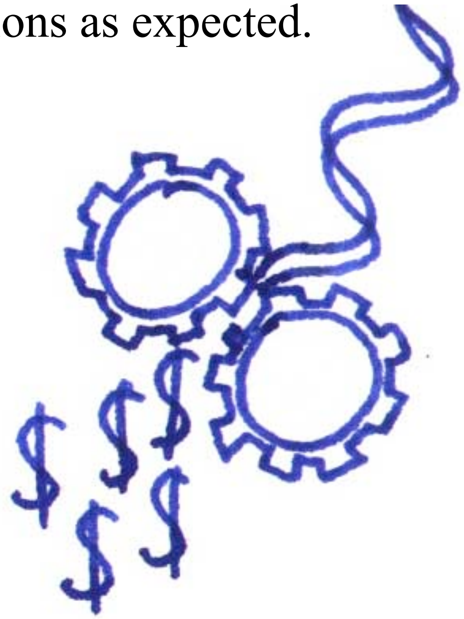
What is Synthetic Biology?

Implementation of engineering principles and mathematical modeling to the design and construction of biological parts, devices, and systems with applications in energy, medicine, and technology.

www.bio.davidson.edu/projects/gcat/Synthetic/What_Is_SynBio.html

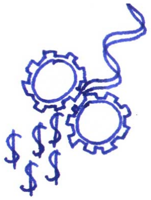
Synthetic Biology: Win-Win

Win #1: your design functions as expected.

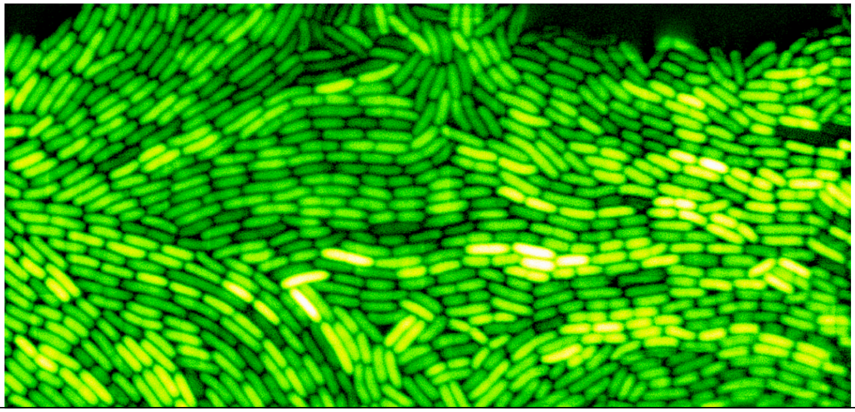


Synthetic Biology: Win-Win Research

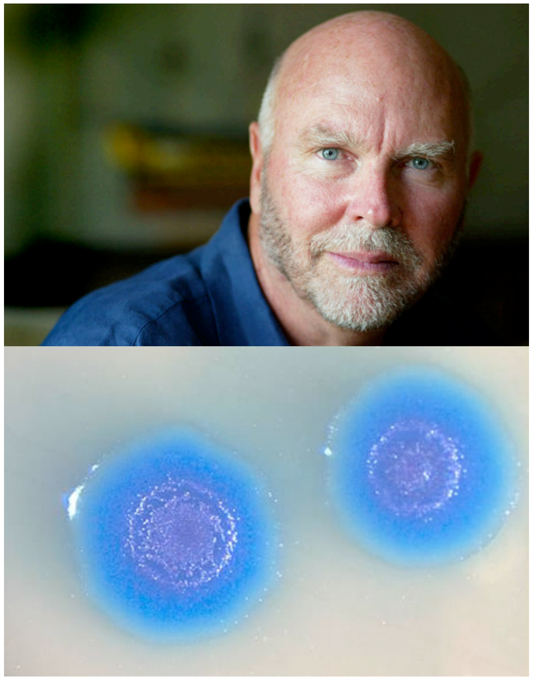
Win #1: your design functions as expected.



Win #2: your design fails but you uncover basic biology



How is Synthetic Biology Different?



Abstraction

Modularity

Standards

Designing and modeling

Abstraction

Abstraction

Modularity

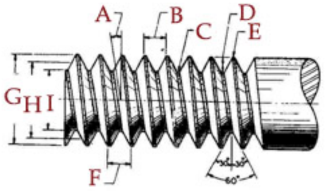
USB ports on computers

Modularity

Standardization

On a Uniform System of Screw Thread

“In this country, no organized attempt has as of yet been made to establish any system, each manufacturer having adopted whatever his judgment may have dictated as best, or as most convenient for himself.”



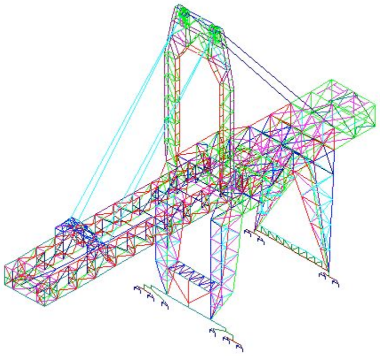
William Sellers April 21, 1864

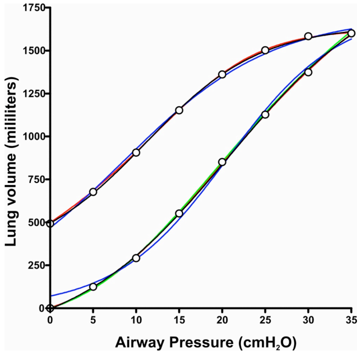
http://openwetware.org/images/b/bd/BBFRFC9.pdf

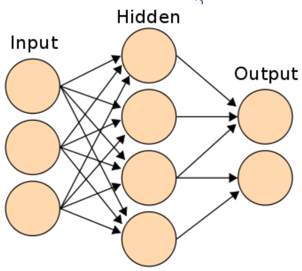
Standardization

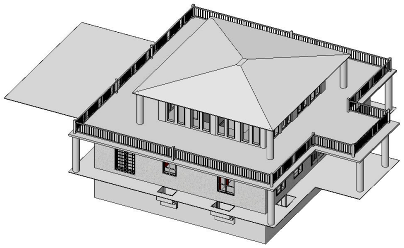
On a Uniform System of Screw Thread

Modeling of Designs







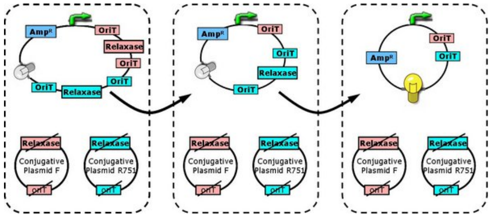


What is iGEM?

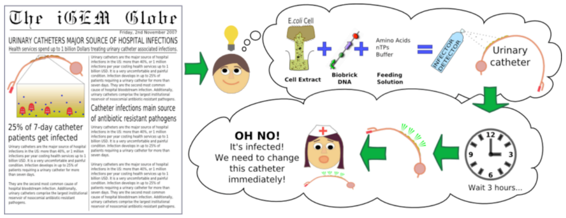
at a glance:

1925 minutes of talks
1200 participants
825 jamboree attendees
84 teams
77 presentations
24 awards
22 weeks of work
21 countries

http://2009.igem.org/Main_Page

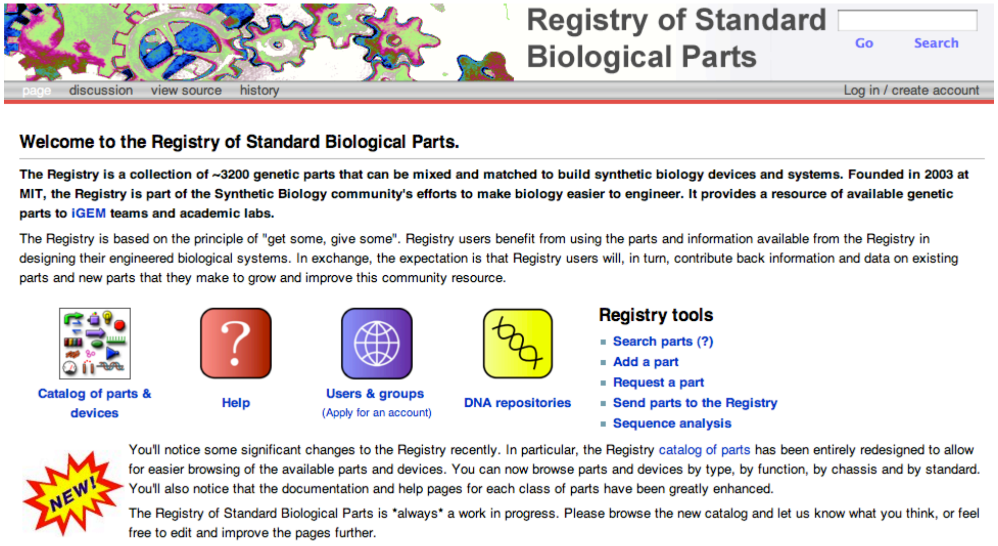


Peking University



Imperial College

Standardized and Modular DNA



Welcome to the Registry of Standard Biological Parts.

The Registry is a collection of ~3200 genetic parts that can be mixed and matched to build synthetic biology devices and systems. Founded in 2003 at MIT, the Registry is part of the Synthetic Biology community's efforts to make biology easier to engineer. It provides a resource of available genetic parts to iGEM teams and academic labs.

The Registry is based on the principle of "get some, give some". Registry users benefit from using the parts and information available from the Registry in designing their engineered biological systems. In exchange, the expectation is that Registry users will, in turn, contribute back information and data on existing parts and new parts that they make to grow and improve this community resource.

Registry tools

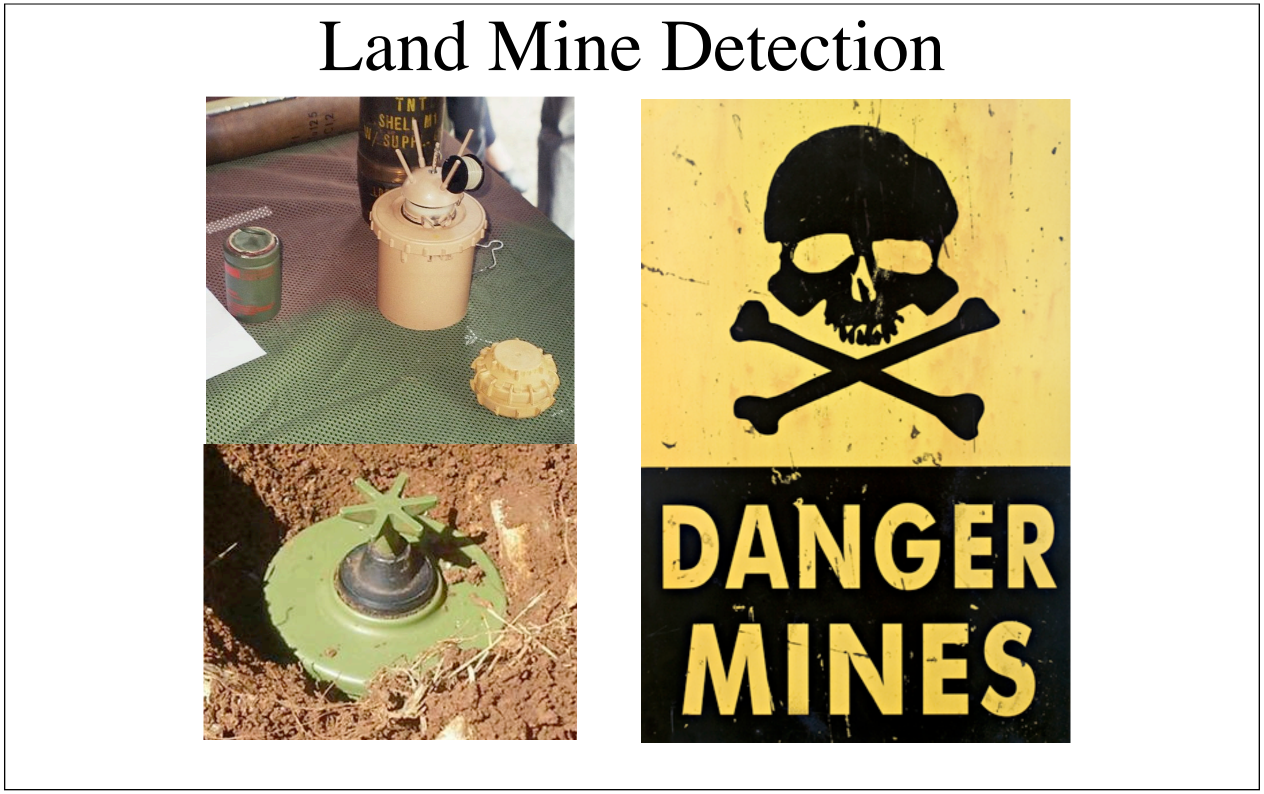
- Search parts (?)
- Add a part
- Request a part
- Send parts to the Registry
- Sequence analysis

You'll notice some significant changes to the Registry recently. In particular, the Registry catalog of parts has been entirely redesigned to allow for easier browsing of the available parts and devices. You can now browse parts and devices by type, by function, by chassis and by standard. You'll also notice that the documentation and help pages for each class of parts have been greatly enhanced.

The Registry of Standard Biological Parts is *always* a work in progress. Please browse the new catalog and let us know what you think, or feel free to edit and improve the pages further.

Think of Radio Shack for DNA parts.

Real World Applications
of
Synthetic Biology



Land Mine Detection

About 20,000 people injured or killed each year.

Land Mine Detection

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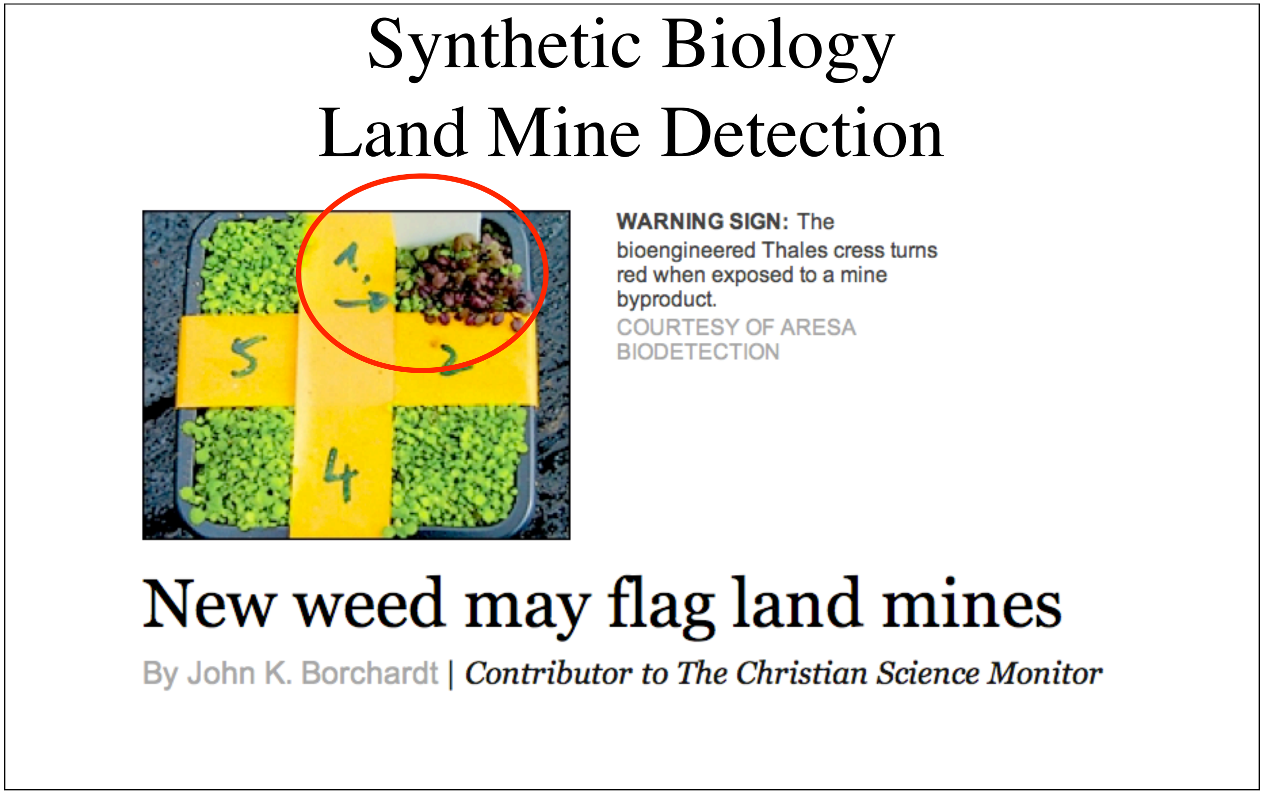


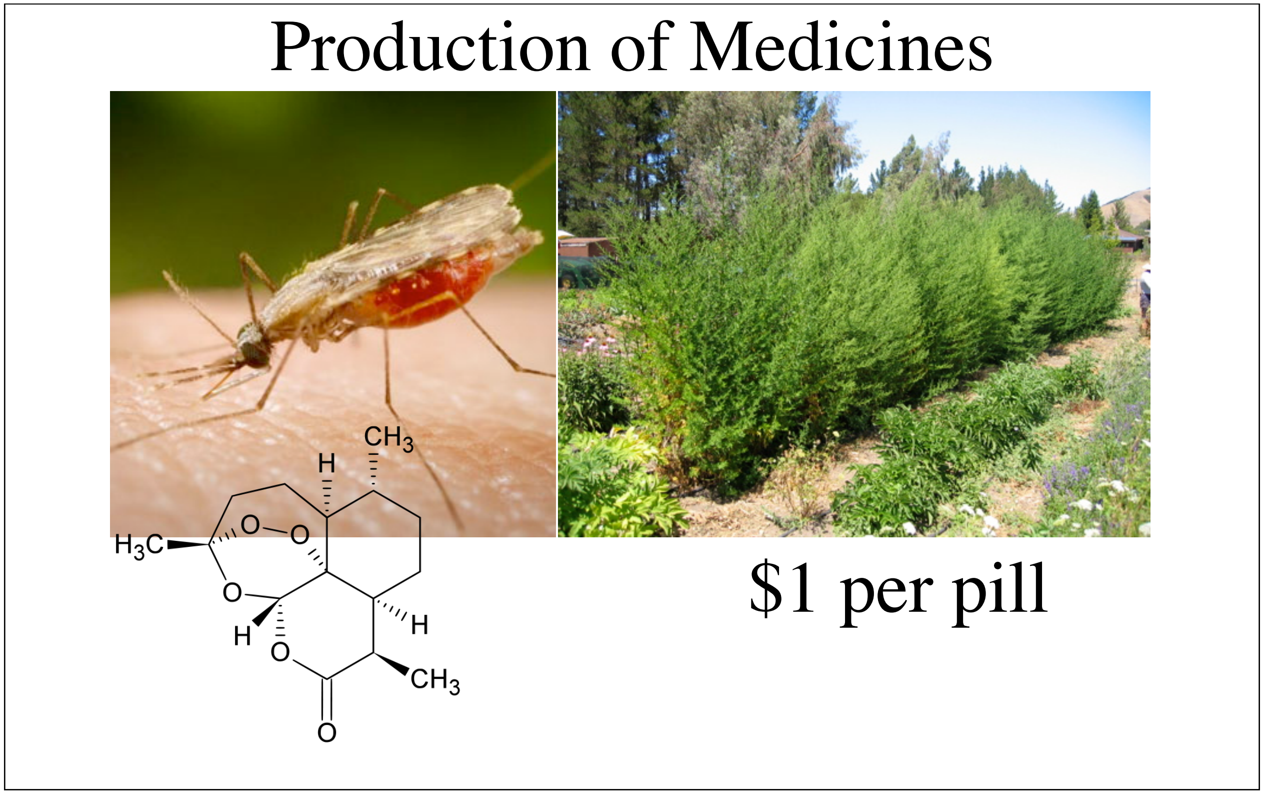
Synthetic Biology
Land Mine Detection

WARNING SIGN: The bioengineered Thales cress turns red when exposed to a mine byproduct.
COURTESY OF ARESA BIODETECTION

New weed may flag land mines

By John K. Borchardt | *Contributor to The Christian Science Monitor*

About 20,000 people injured or killed each year.

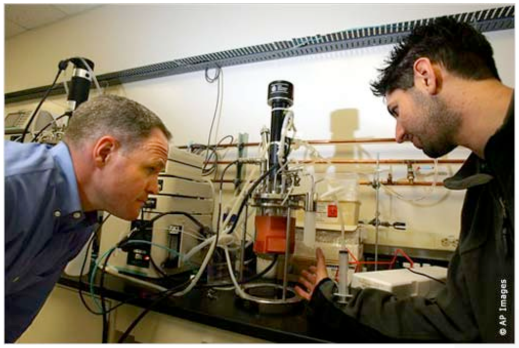


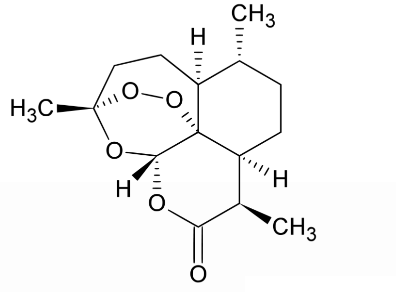
Production of Medicines

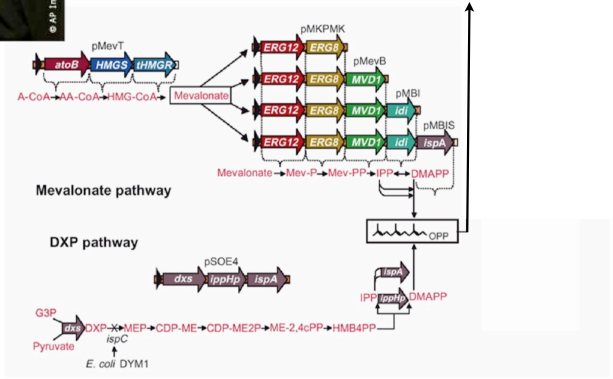
$1 per pill

1 million people die each year from malaria, most of them children under the age of 5.

Production of Medicines



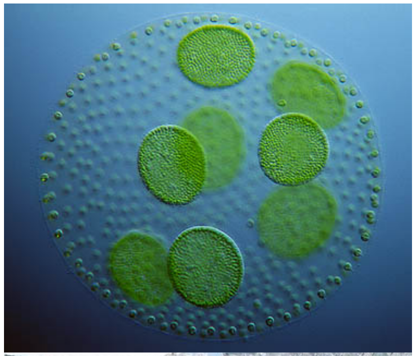




10¢ per pill

1 million people die each year from malaria, most of them children under the age of 5.
Jay Keasling at UC Berkeley

Biofuels from Algae



CO_2-neutral

1,000,000 gallons in 2008

Synthetic Biology
at
Davidson College

DAVIDSON

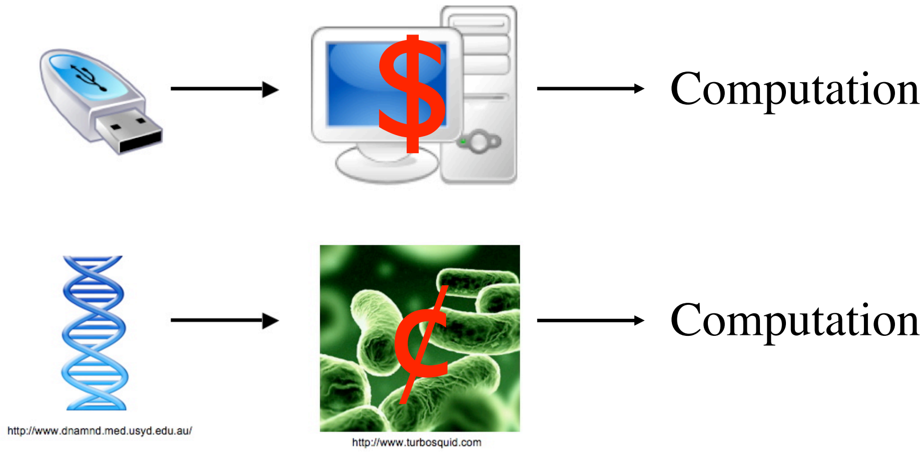
Discover gold WESTERN

Laurie Heyer, Todd Eckdahl & Jeff Poet

Building Bacterial Computers

Advantages of Bacterial Computation

Software → Hardware → Computation



→ → Computation

→ → Computation

http://www.dnamnd.med.usyd.edu.au/

http://www.turbosquid.com

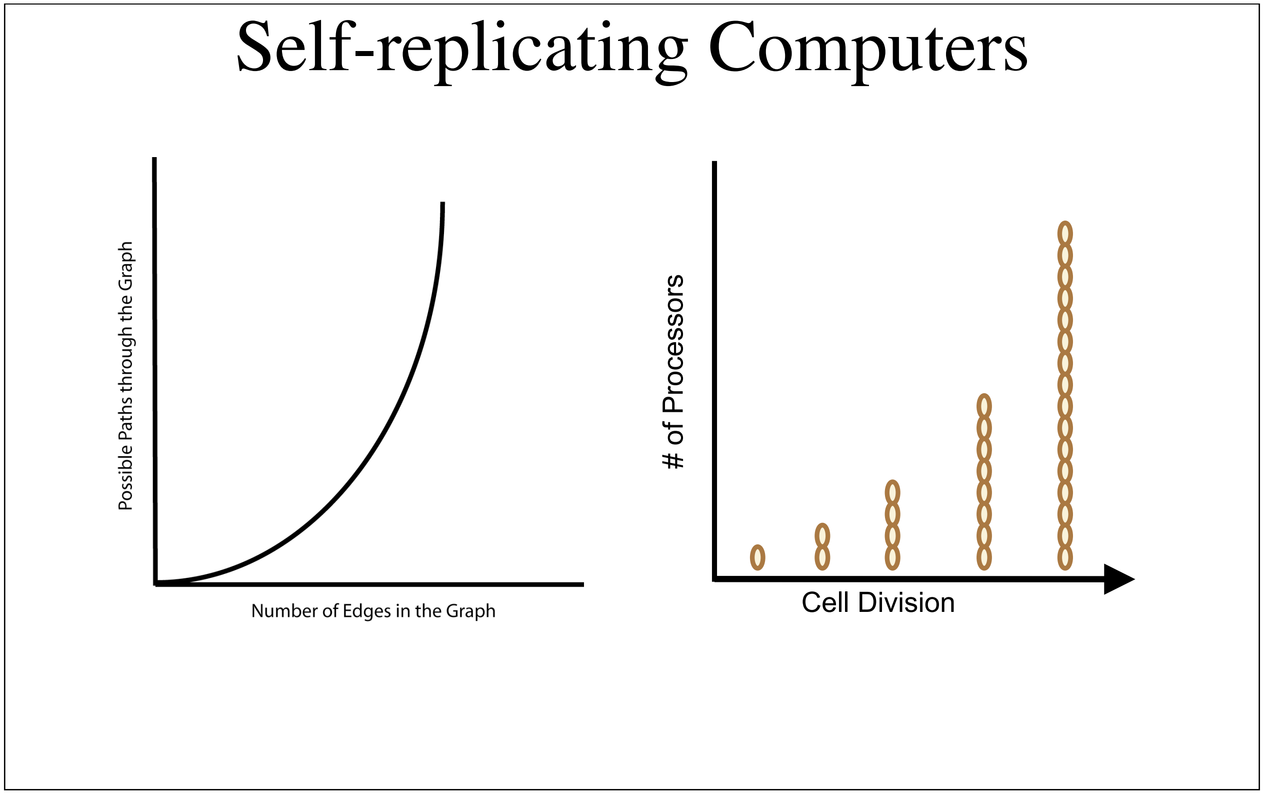
Advantages of Biological Computers

go anywhere - arctic, thermal vents, inside organisms

no electricity

self-replicating

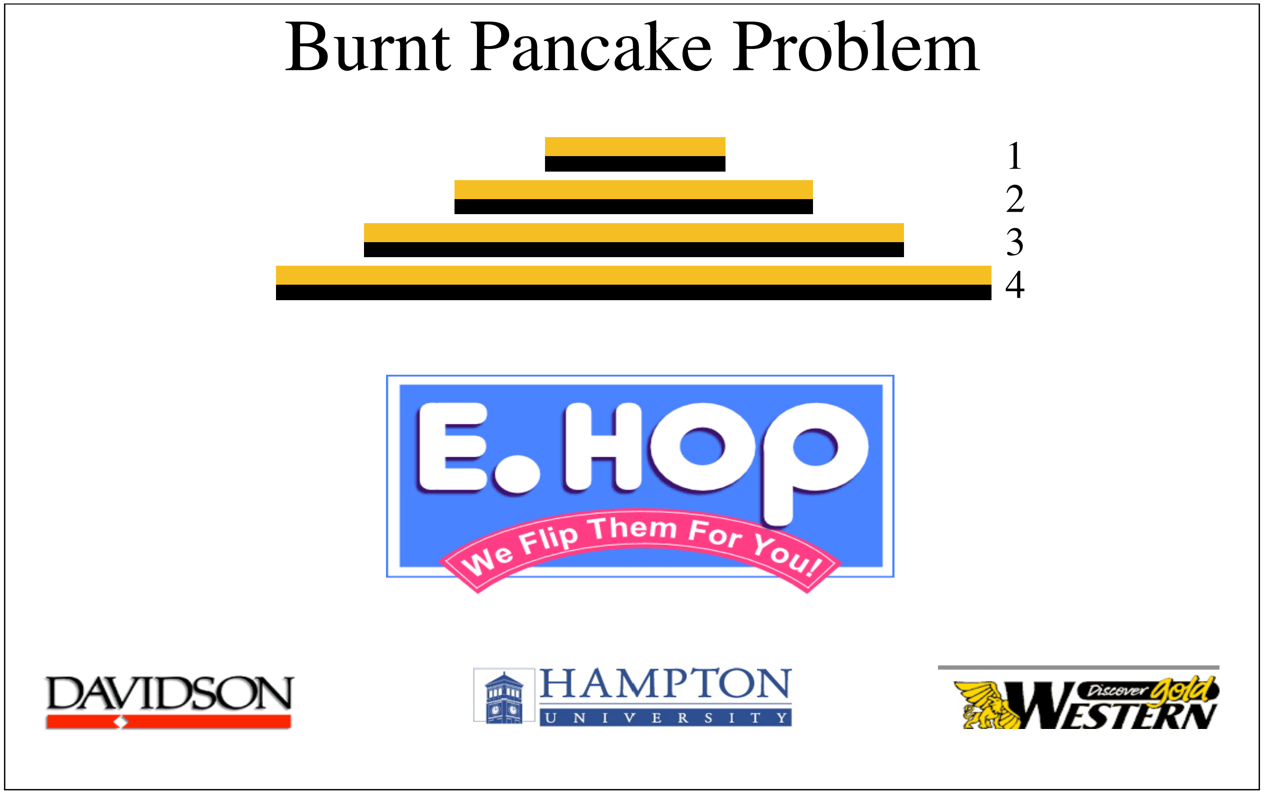
no immune rejection



Self-replicating Computers

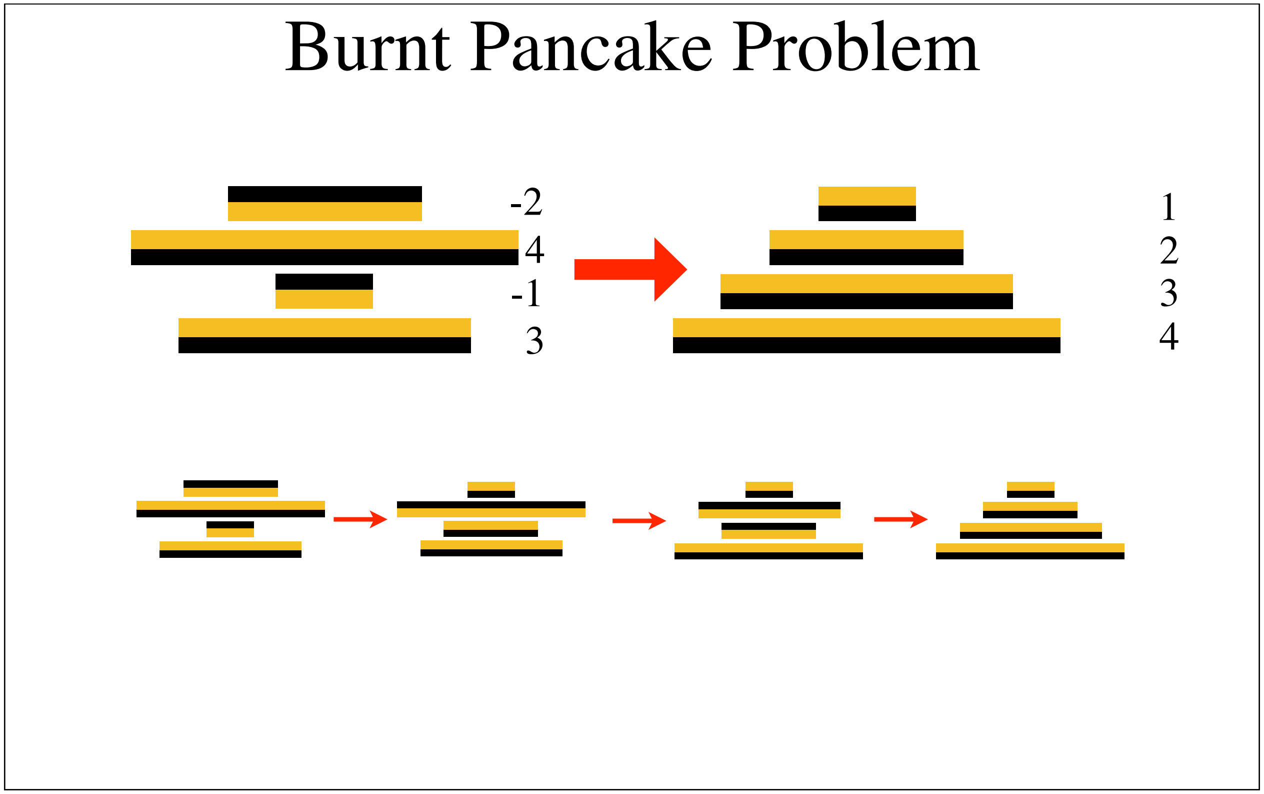
Some problems get more complex in a linear fashion but it takes traditional computers exponentially longer to solve.

Two Undergraduate Research Projects



Burnt Pancake Problem

Only academic publication by Bill Gates.

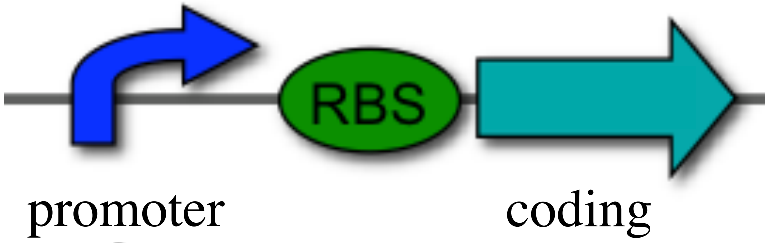


Burnt Pancake Problem

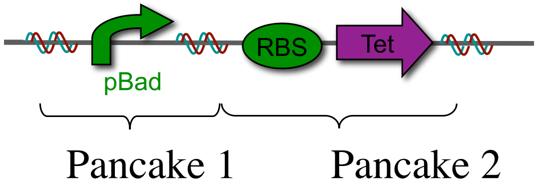
Using two spatulas, one to lift and the other to flip.

DNA = Burnt Pancakes

one gene

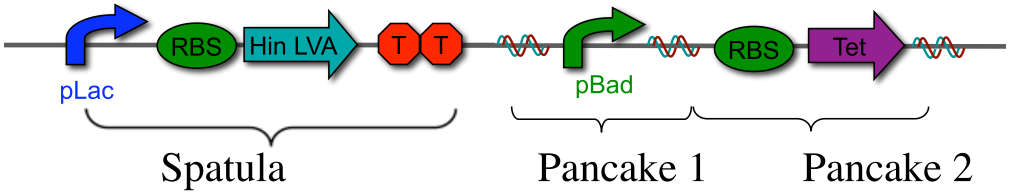


DNA Burnt Pancakes



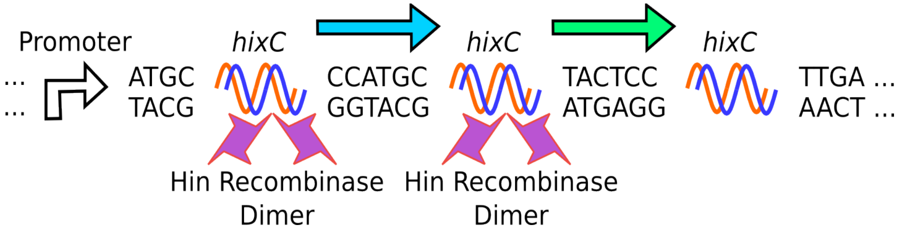
abstractions of DNA parts

DNA Burnt Pancakes



abstractions of DNA parts

Flipping DNA with Hin/*hixC*



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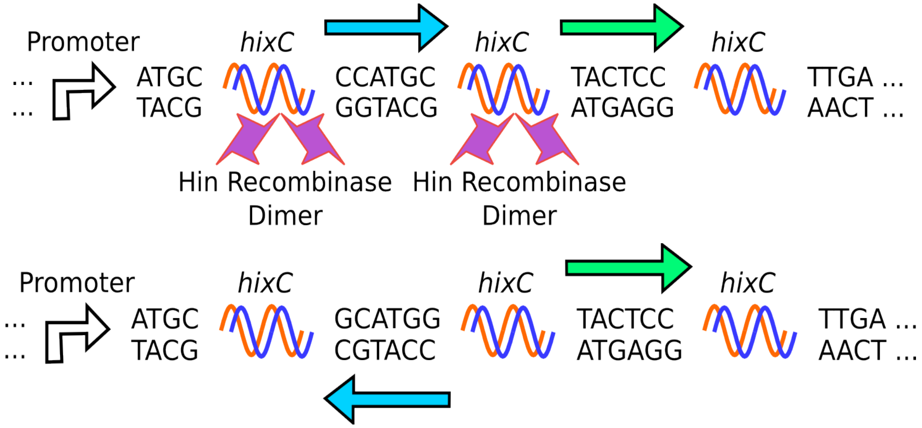


Promoter *hixC* *hixC* *hixC*

... ATGC CCATGC TACTCC TTGA ...

... TACG GGTACG ATGAGG AACT ...

Hin Recombinase Dimer

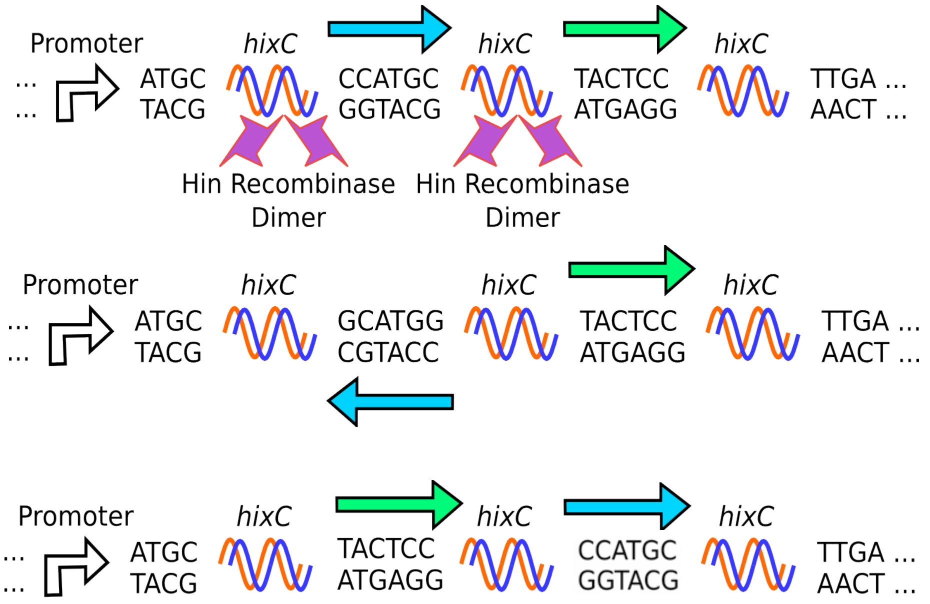
Hin Recombinase Dimer

Promoter *hixC* *hixC* *hixC*

... ATGC GCATGG TACTCC TTGA ...

... TACG CGTACC ATGAGG AACT ...

Flipping DNA with Hin/*hixC*



Promoter *hixC* *hixC* *hixC*

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Hin Recombinase Dimer Hin Recombinase Dimer

Promoter *hixC* *hixC* *hixC*

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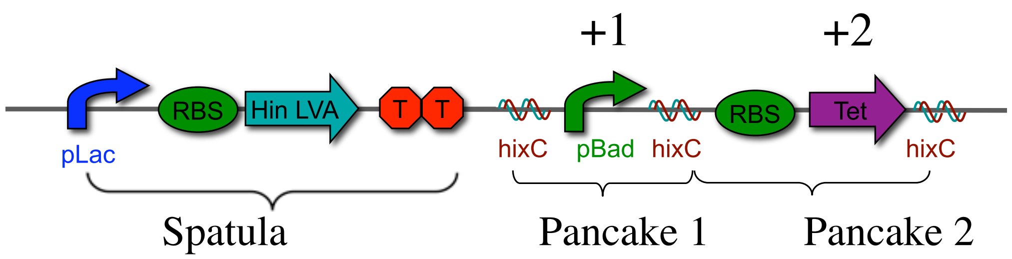
Promoter *hixC* *hixC* *hixC*

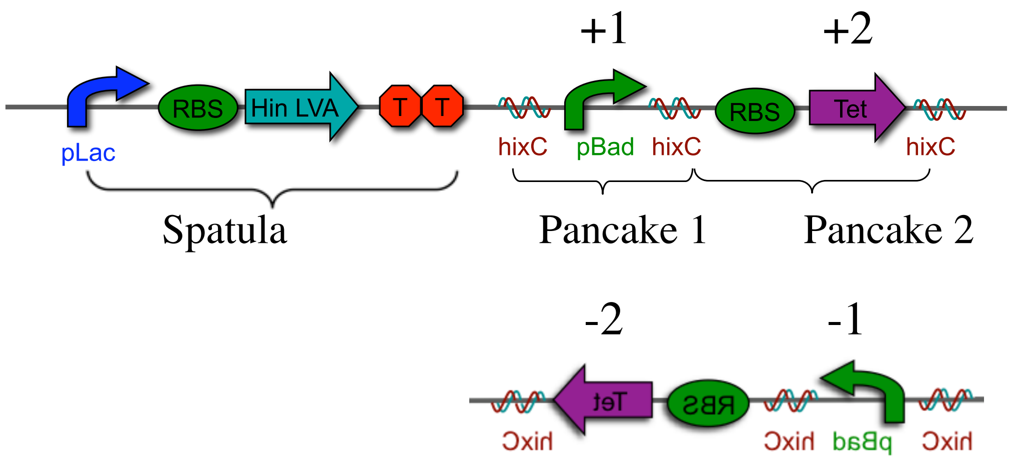
... ATGC TACTCC CCATGC TTGA ...
... TACG ATGAGG GGTACG AACT ...

DNA Burnt Pancakes



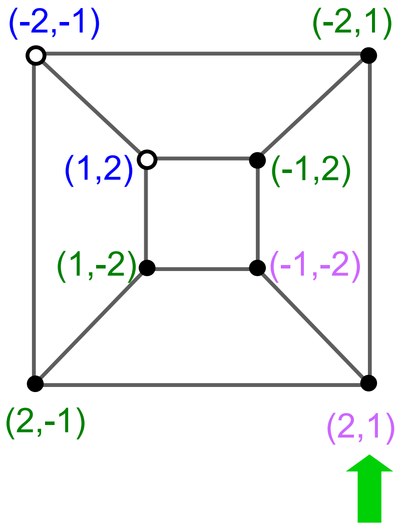
convert to signed numbers

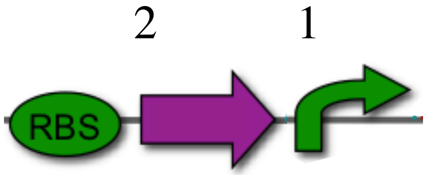
DNA Burnt Pancakes



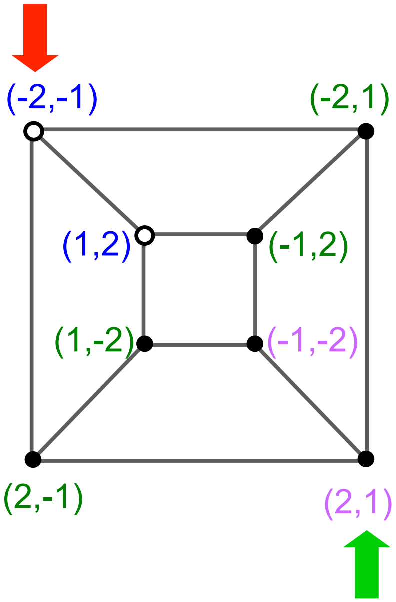
biologically equivalent,
mathematically distinct

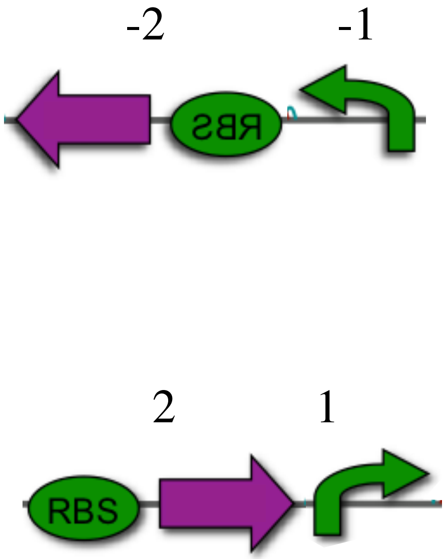
Modeling Burnt Pancakes





Modeling Burnt Pancakes





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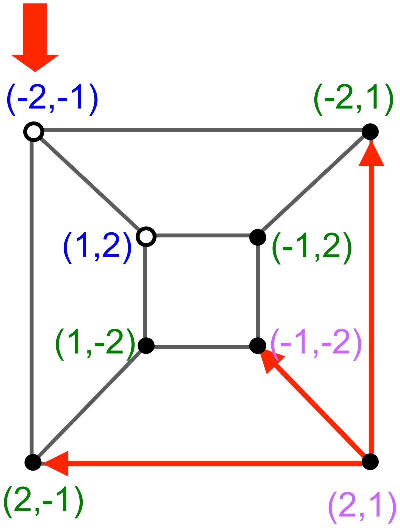

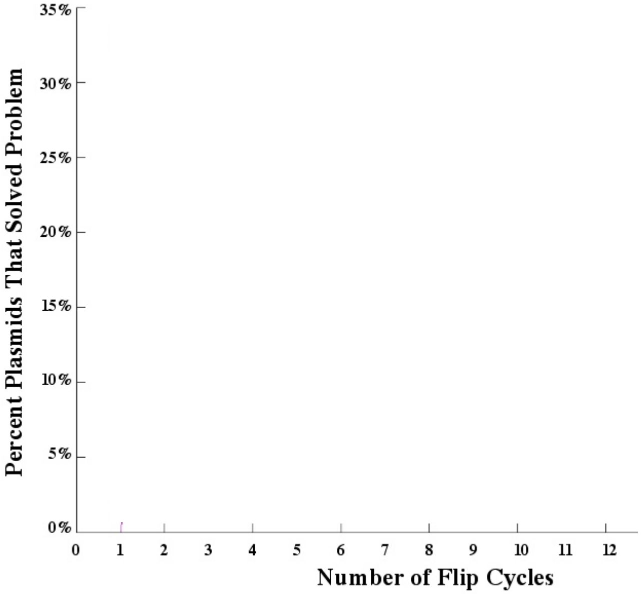

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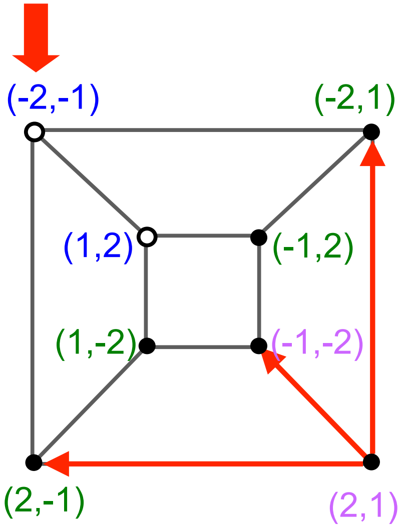
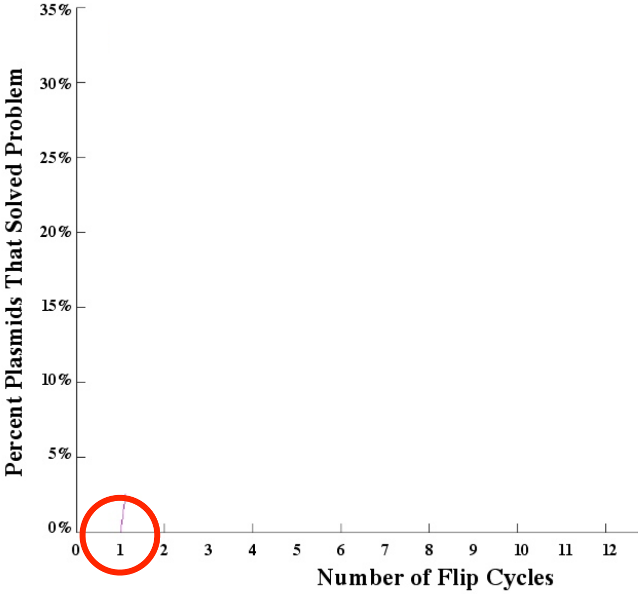
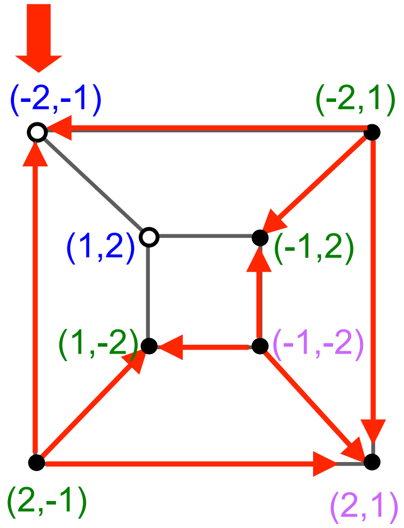
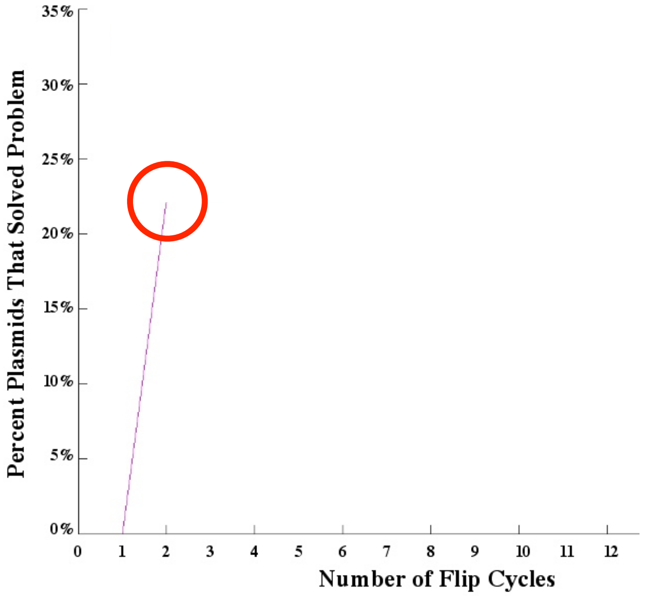


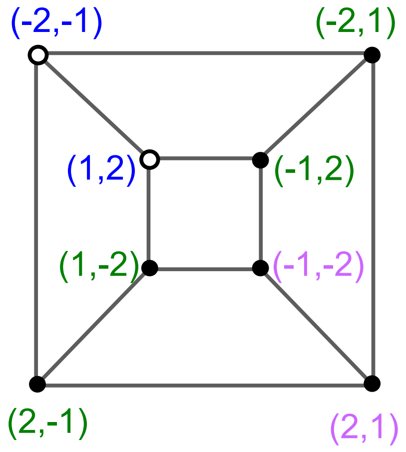


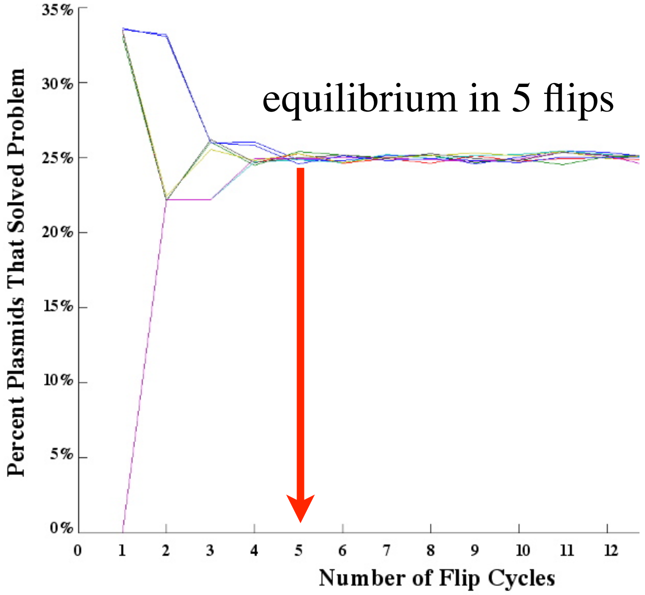
Modeling Burnt Pancakes





Modeling Burnt Pancakes




equilibrium in 5 flips

International Success

iGEM 2006

International Genetically Engineered Machine Competition

Runner Up, Best Poster

Sabriya Rosemond
Davidson College

November 4 & 5, 2006
Cambridge, Massachusetts

iGEM 2006

International Genetically Engineered Machine Competition

Runner Up, Best Conquest of Adversity

Lance Harden
Davidson College

November 4 & 5, 2006
Cambridge, Massachusetts

iGEM 2006

International Genetically Engineered Machine Competition

Runner Up, Best Part

Samantha Simpson
Davidson College

November 4 & 5, 2006
Cambridge, Massachusetts

iGEM 2006

International Genetically Engineered Machine Competition

Runner Up, Best Cooperation and Collaboration

Erin Zwack
Davidson College

November 4 & 5, 2006
Cambridge, Massachusetts

DAVIDSON

HAMPTON UNIVERSITY

Discover gold WESTERN

I hate to mention any names, but Duke and Harvard did not get any prizes.

Outstanding Publication of 2008
in the
Journal of Biological Engineering

On behalf of the editors of *Journal of Biological*
Engineering, we recognize the contribution of the follow
authors for the most outstanding publication of the year.

"Engineering bacteria to solve the Burnt Pancake Problem"
Karmella A Haynes, Marian L Broderick, Adam D Brown, Trevor L Butner,
James O Dickson, W Lance Harden, Lane H Heard, Eric L Jessen, Kelly J
Malloy, Brad J Ogden, Sabriya Rosemond, Samantha Simpson, Erin Zwack,
A Malcolm Campbell, Todd T Eckdahl, Laurie J Heyer, Jeffrey L Poet
Journal of Biological Engineering 2008, 2:8 (20 May 2008)

JOURNAL OF BIOLOGICAL
ENGINEERING

Mark R. Riley, 2006-2008 Editor-in-chief

Institute of Biological Engineering

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Accesses
21801

Research Open Access Highly accessed
Engineering bacteria to solve the Burnt Pancake Problem
Karmella A Haynes, Marian L Broderick, Adam D Brown, Trevor L Butner, James O Dickson, W Lance Harden, Lane H Heard, Eric L Jessen, Kelly J Malloy, Brad J Ogden, Sabriya Rosemond, Samantha Simpson, Erin Zwack, A Malcolm Campbell, Todd T Eckdahl, Laurie J Heyer, Jeffrey L Poet
Journal of Biological Engineering 2008, **2**:8 (20 May 2008)
[Abstract] [Full Text] [PDF] [PubMed] [Related articles]

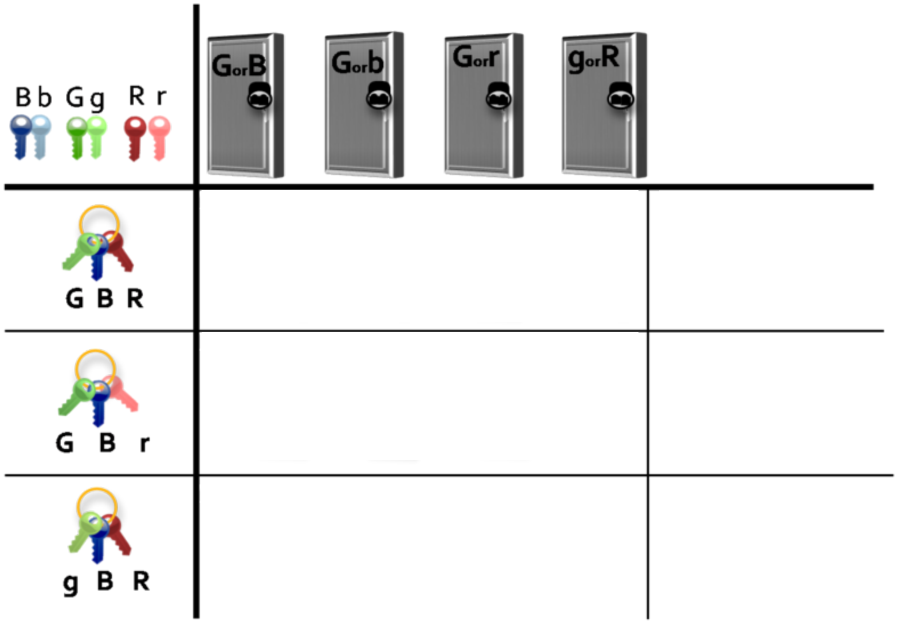
12 undergraduate coauthors

Having the number 2 paper of all time for the journal is really nice.

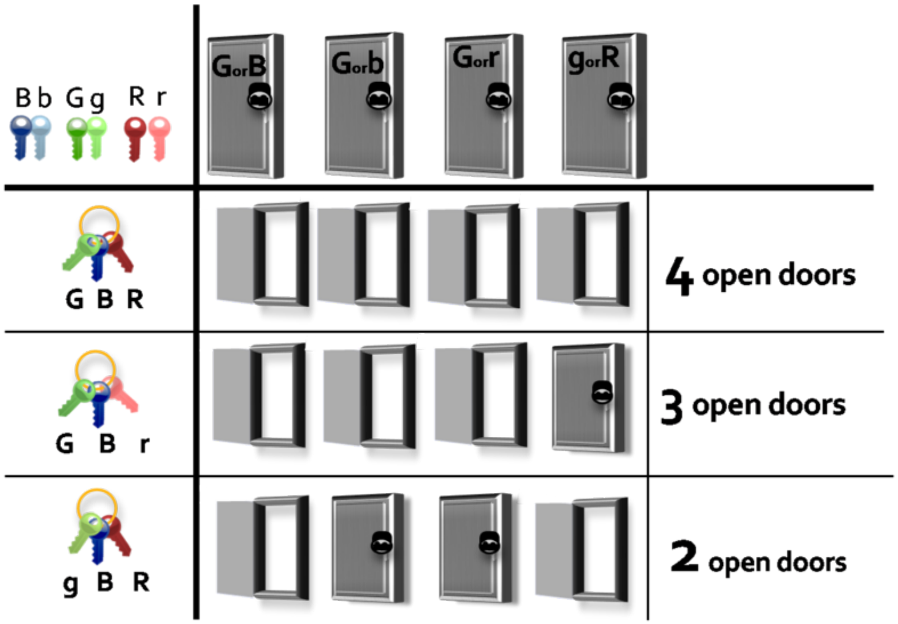
Can we solve the SATisfiability problem?

Define the SATisfiability Problem

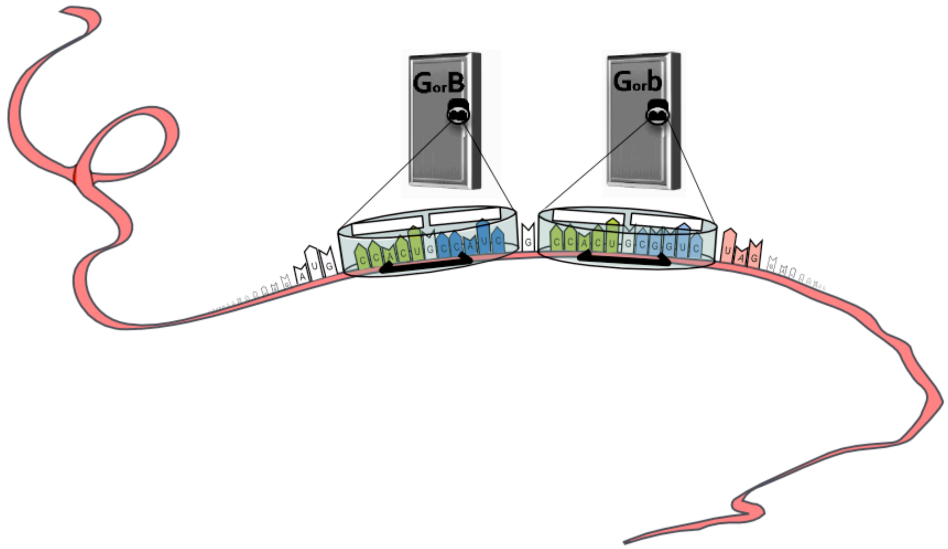
Define the SATisfiability Problem



Define the SATisfiability Problem



Converting Math to Biology



Central Dogma

DNA
atgccctactcactacctatagcgcat

↓ transcription

mRNA
aug ccc uac uca cua ccu aua ccg cau

↓ translation

Protein

M P Y S H P I P H

Frameshift Mutation

DNA atgccctactcactacctatagcgcat		DNA atgccc**TC**tactcactacctatagcgcat
↓	transcription	↓
mRNA **aug ccc uac uca cua ccu aua ccg cau**		mRNA **aug ccc UCu acu cac uac cua uac cgc au**
↓	translation	↓
Protein		Protein
M P Y S H P I P H		**M P S T H Y H Y R**

Frameshift Suppression

DNA

atgccctactcactacctatagcgcat

mRNA

aug **ccc uac uca cua ccu aua ccg cau**

Protein

M P Y S H P I P H

DNA

atgccc**TC**tactcactacctatagcgcat

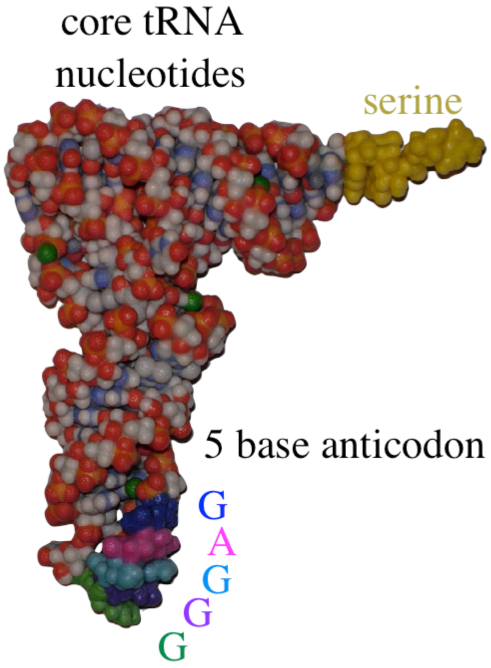
5 base suppressor tRNA

aug cccUC uac uca cua ccu aua ccg cau

Protein

M S Y S H P I P H

Suppressor tRNA



Coding 2-SAT Clause

G ATG NNNNNN gNN NNN → satisfied

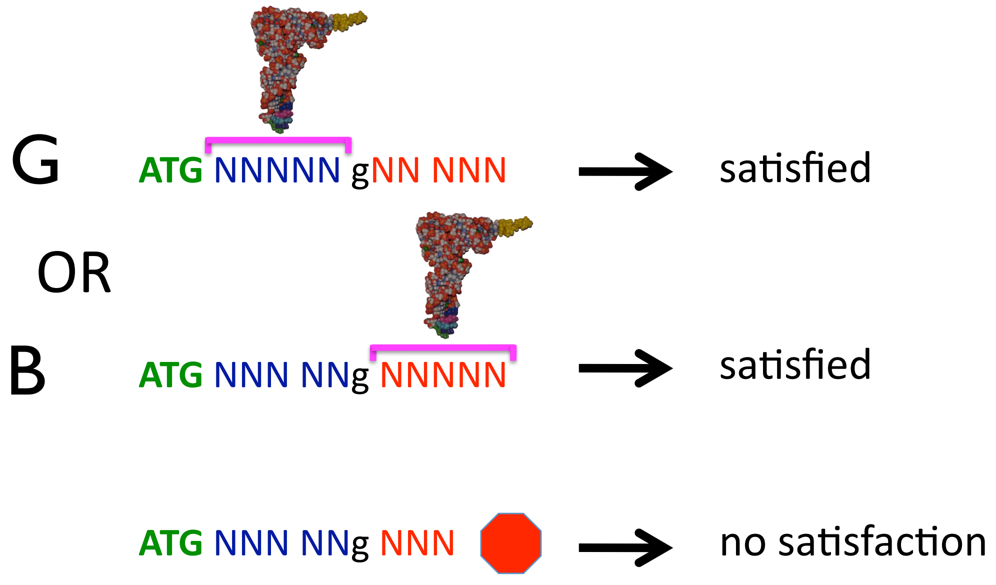
Coding 2-SAT Clause

G ATG NNNNNN gNN NNN → satisfied

OR

B ATG NNN NNg NNNNN → satisfied

Coding 2-SAT Clause



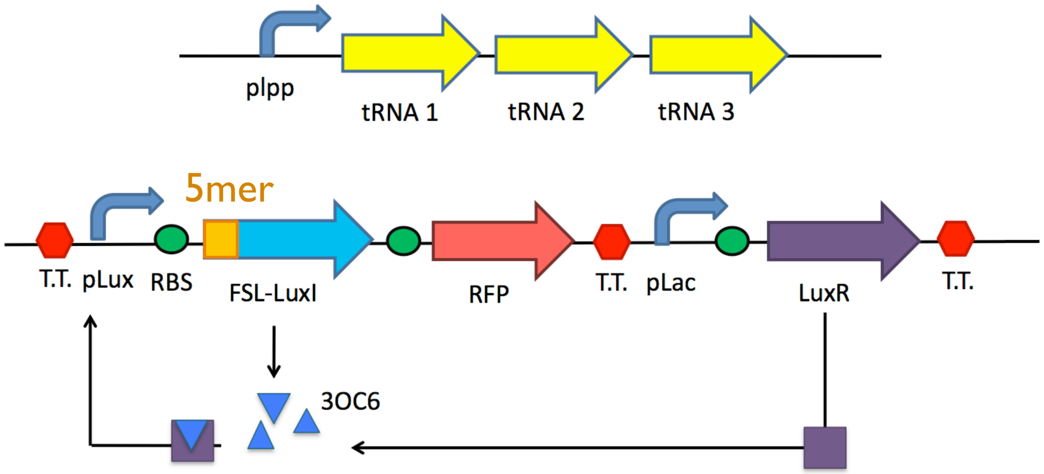
G ATG NNNNNN gNN NNN → satisfied

OR

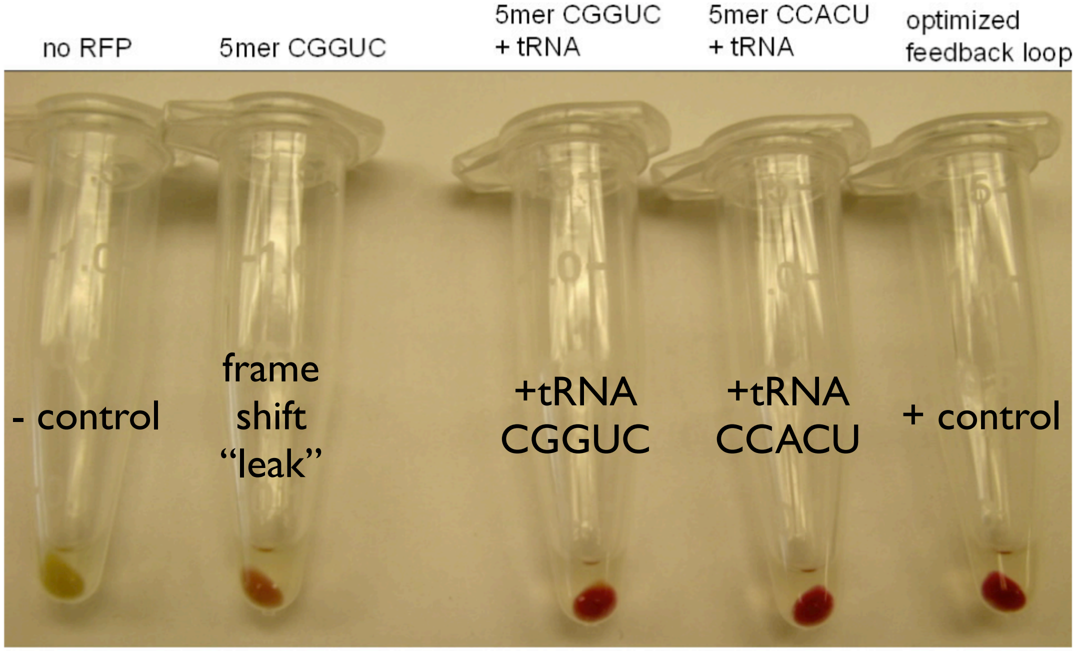
B ATG NNN NNg NNNNN → satisfied

ATG NNN NNg NNN 🛑 → no satisfaction

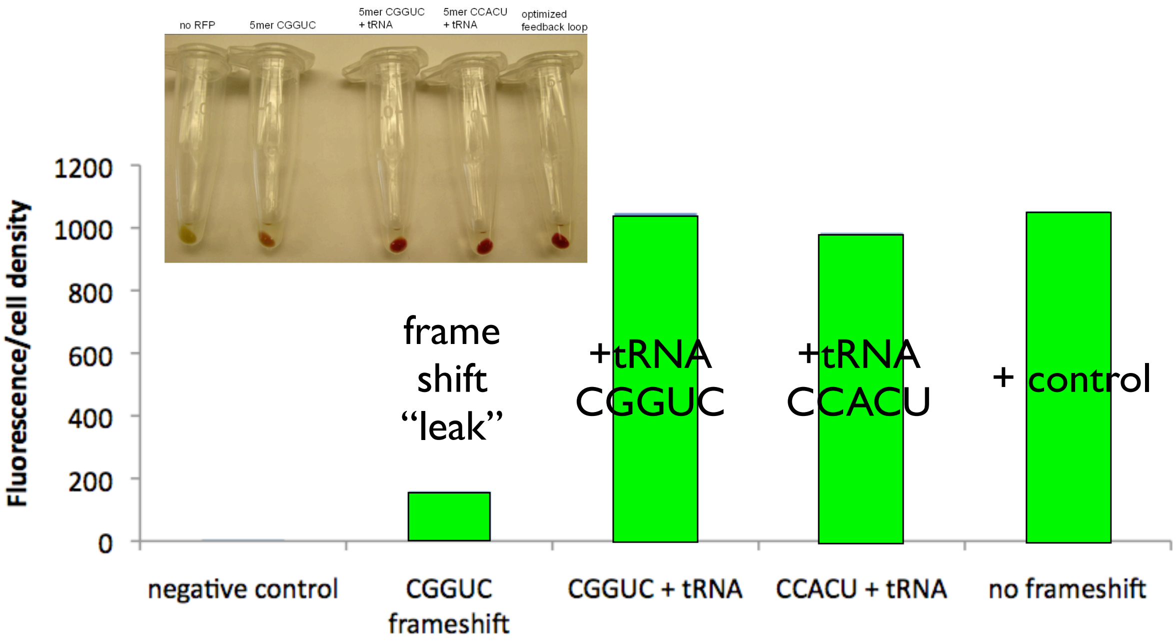
Redesign System v2.0



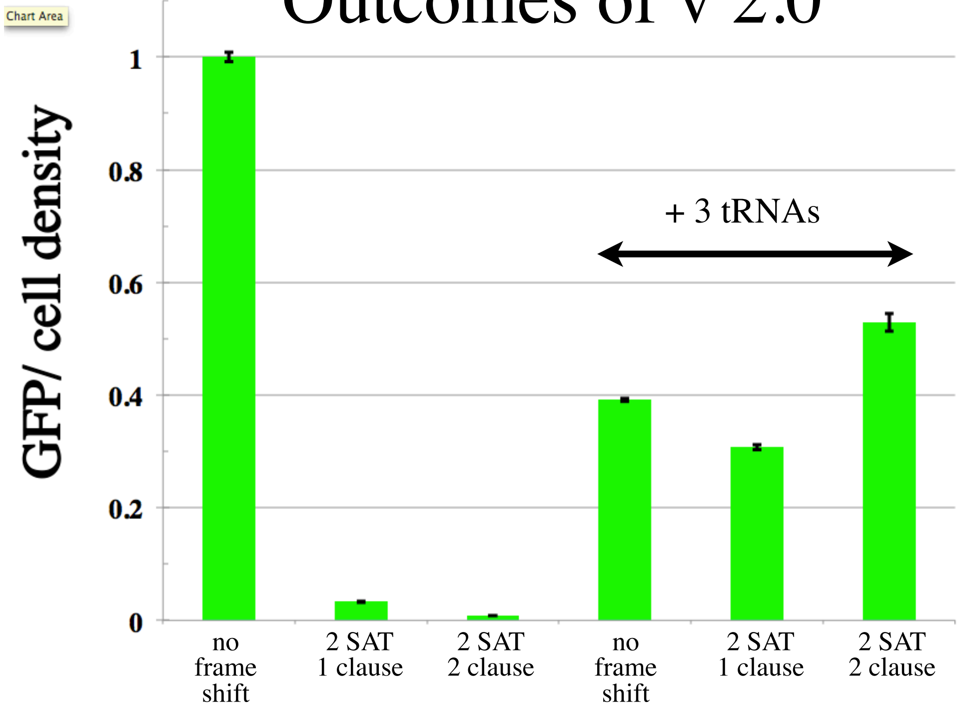
Outcomes of v 2.0



Outcomes of v 2.0

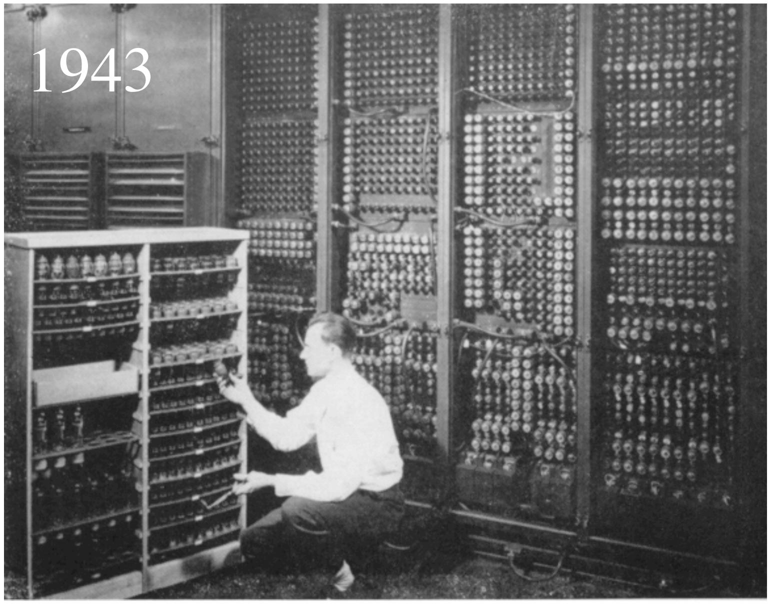


Outcomes of v 2.0



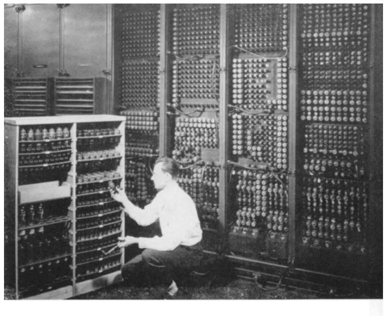
Why build bacterial computers?

Evolution of Computers

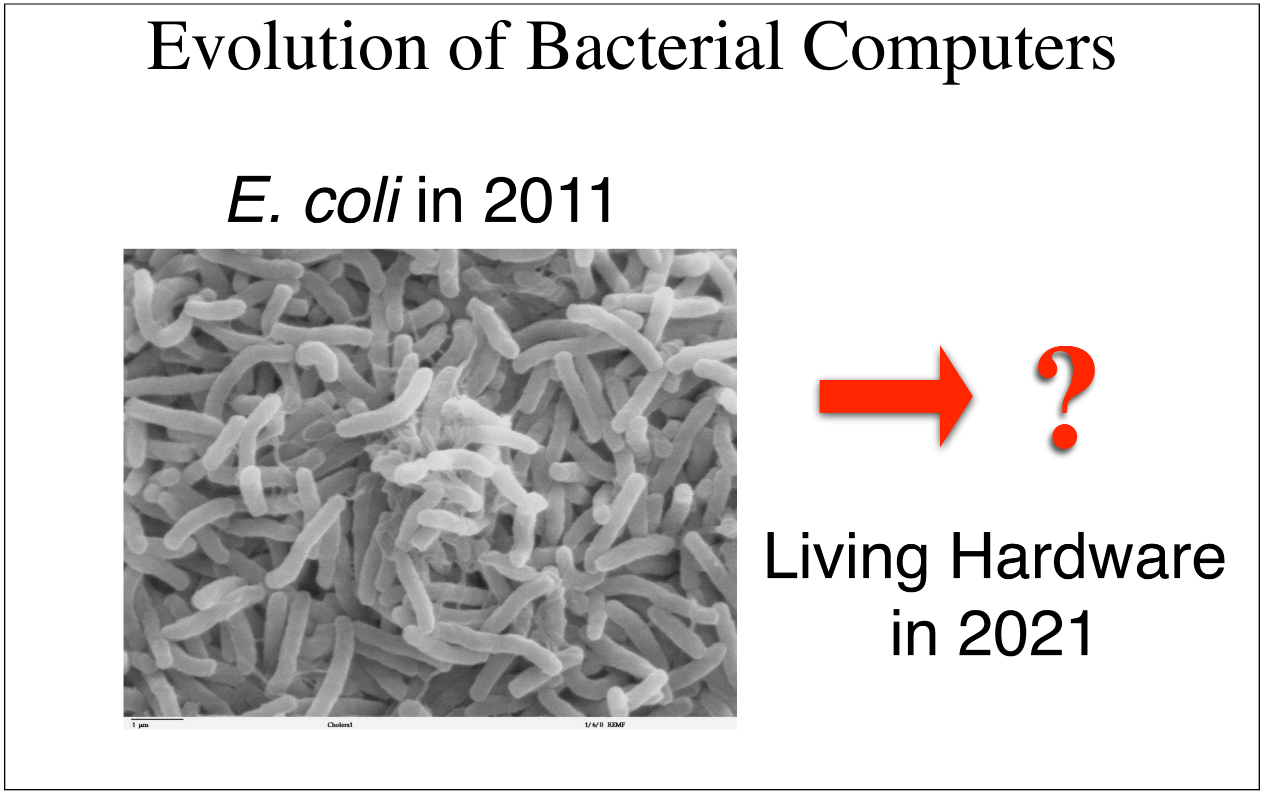

1943

Evolution of Computers

iPhone in 2011



67 years difference



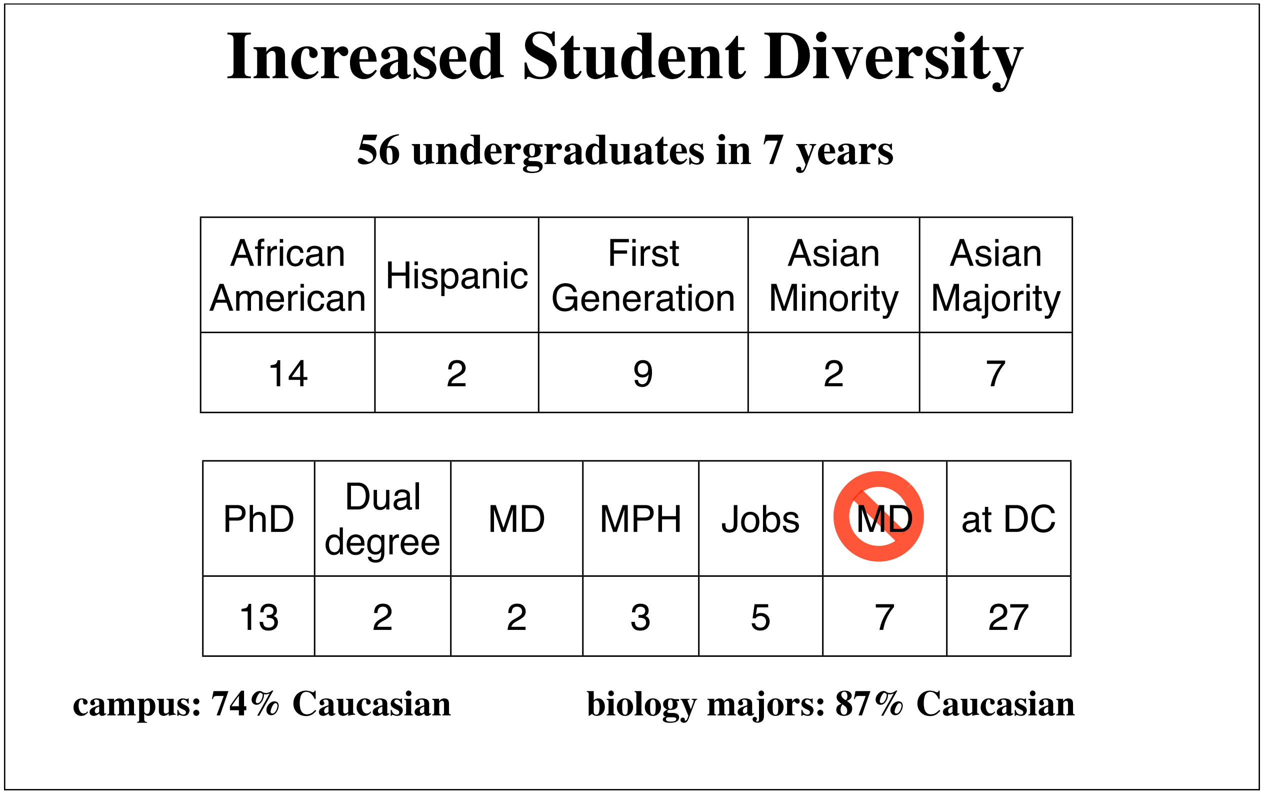
Evolution of Bacterial Computers

E. coli in 2011

→ ?

Living Hardware
in 2021

10 years difference



Increased Student Diversity

56 undergraduates in 7 years

African American	Hispanic	First Generation	Asian Minority	Asian Majority
14	2	9	2	7

PhD	Dual degree	MD	MPH	Jobs	🚫MD	at DC
13	2	2	3	5	7	27

campus: 74% Caucasian **biology majors: 87% Caucasian**

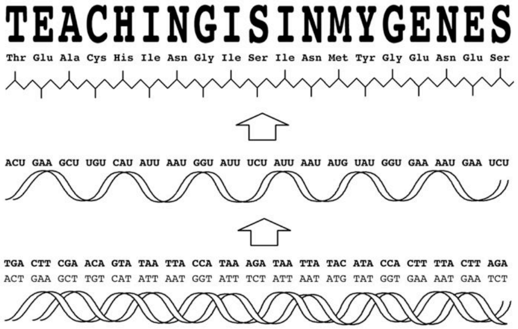
27 students are seniors or have graduated
20 are still in school and undecided

GCAT Faculty Workshop
Synthetic Biology

15 pairs of faculty

1 Bio + 1 Other

NSF & HHMI funding for 3 summers

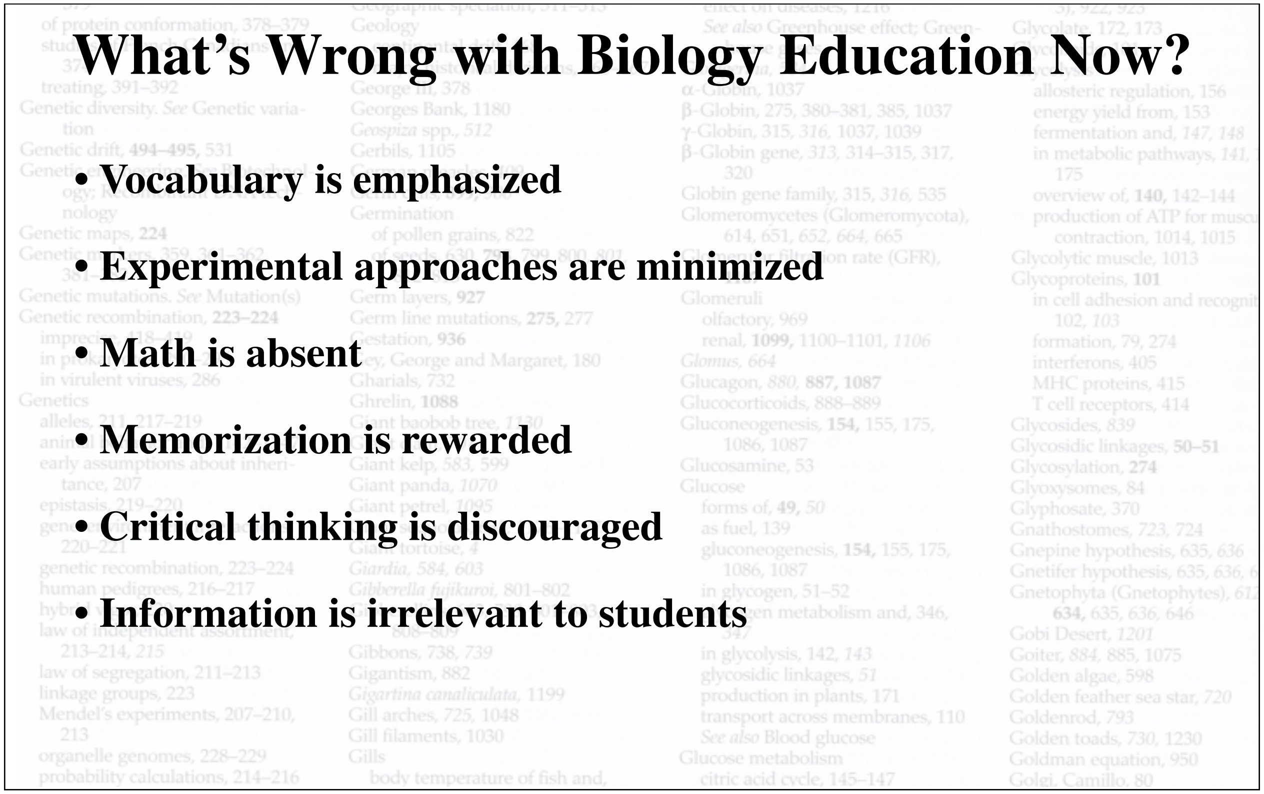


HHMI
HOWARD HUGHES
MEDICAL INSTITUTE

Our Current Challenge: Introductory Biology

Integrating Concepts in Biology

by
A. Malcolm Campbell, Laurie J. Heyer
and Christopher J. Paradise



What’s Wrong with Biology Education Now?

- Vocabulary is emphasized
- Experimental approaches are minimized
- Math is absent
- Memorization is rewarded
- Critical thinking is discouraged
- Information is irrelevant to students

If we currently cover all the important stuff….

…how can we add more content?

Too much content for the containers

When you cram too much information into students, the outcome is unnatural and unpleasant to look at.

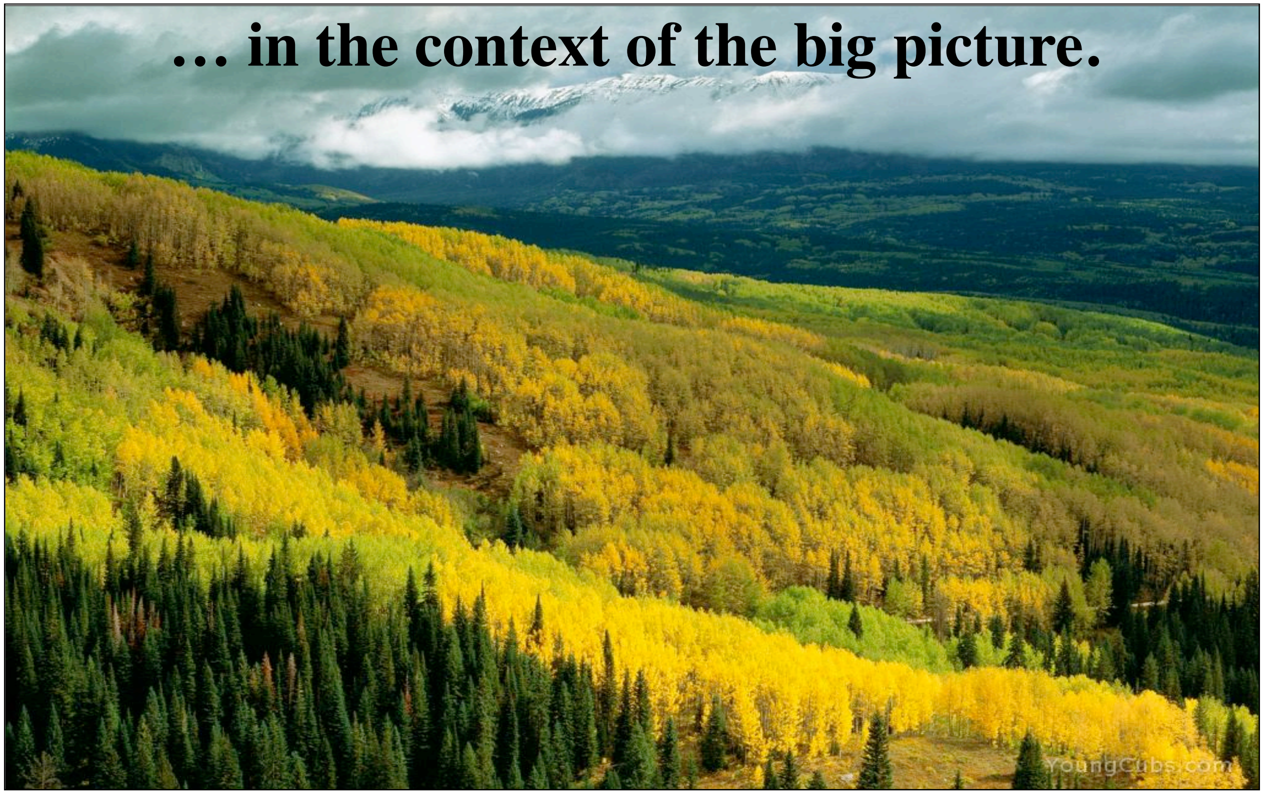
Too much content for the containers

When you cram too much information into students, the outcome is unnatural and unpleasant to look at.

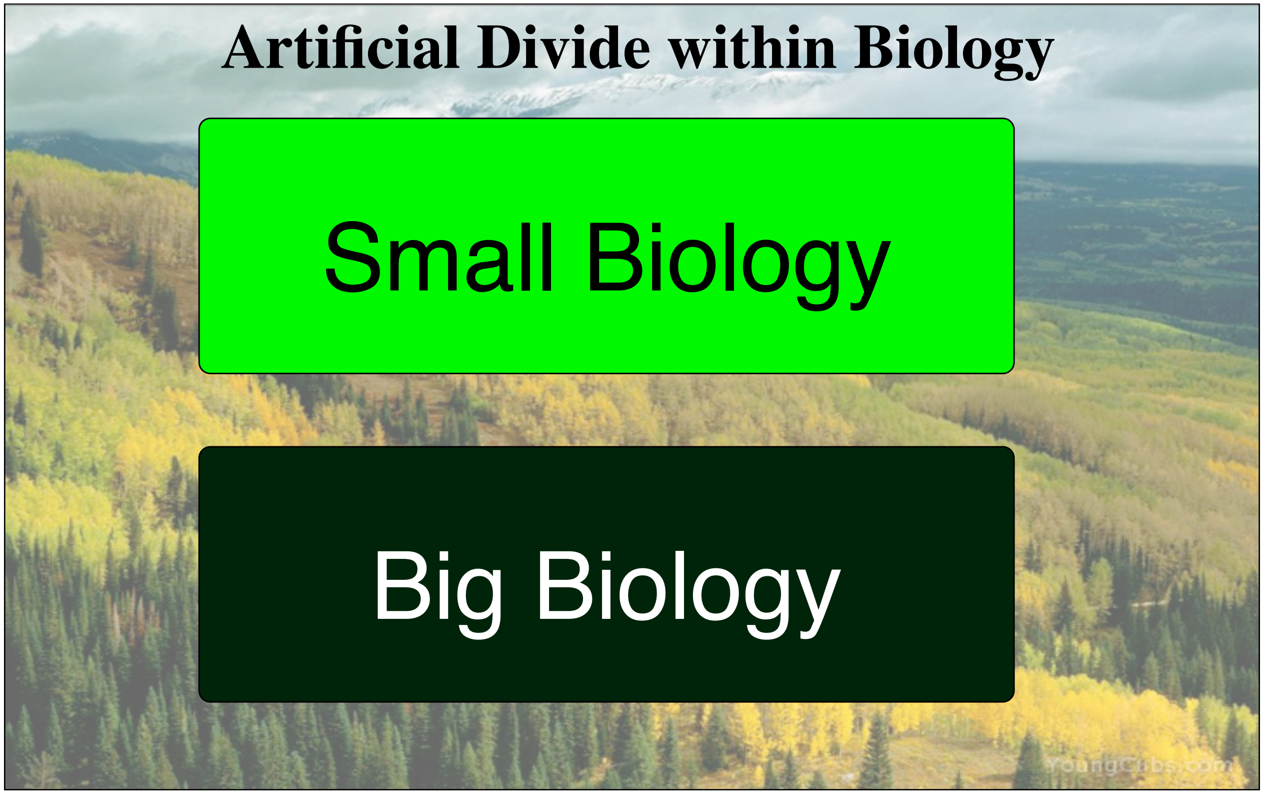
Start with the literature…

Present information and data…

… in the context of the big picture.



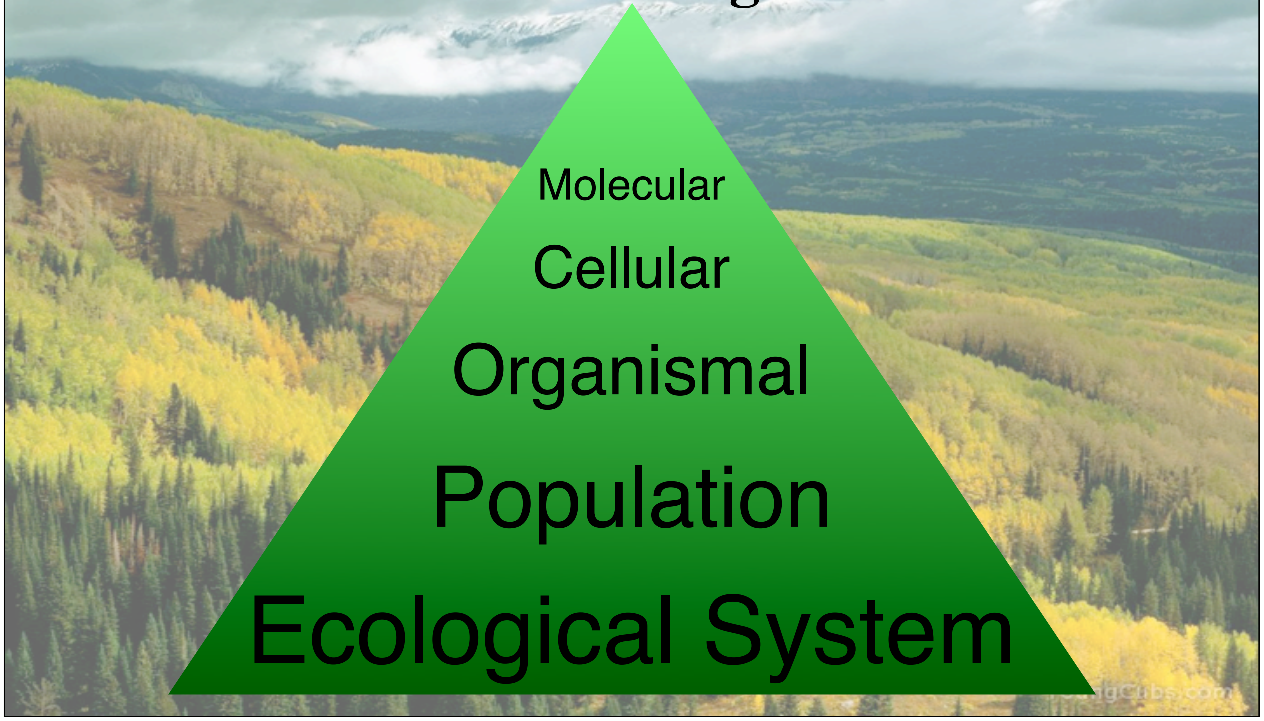
Artificial Divide within Biology



Small Biology

Big Biology

Five Levels of Organization



Molecular

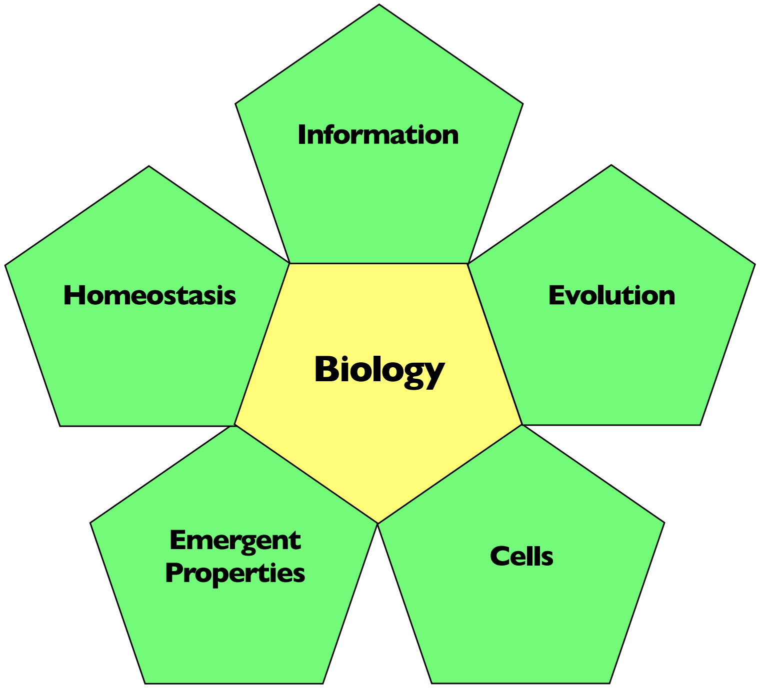
Cellular

Organismal

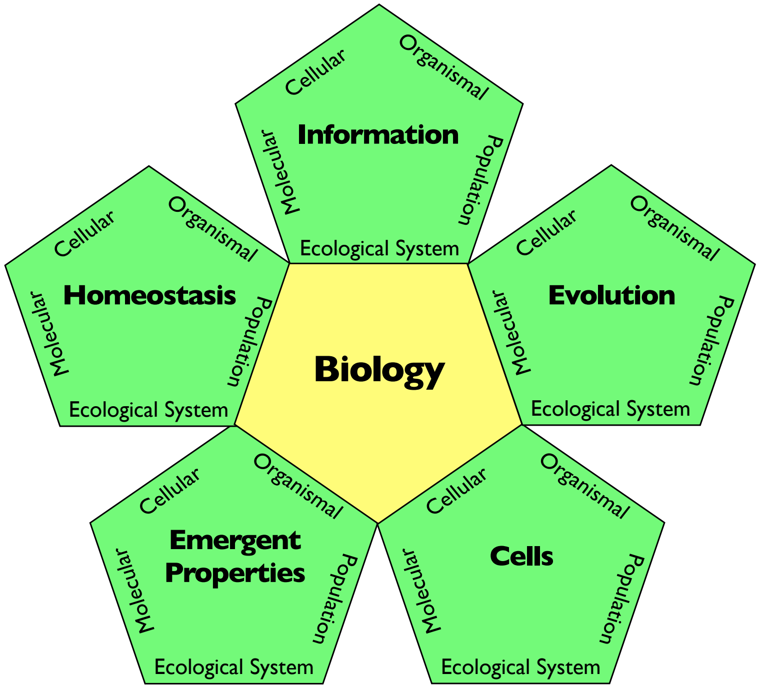
Population

Ecological System

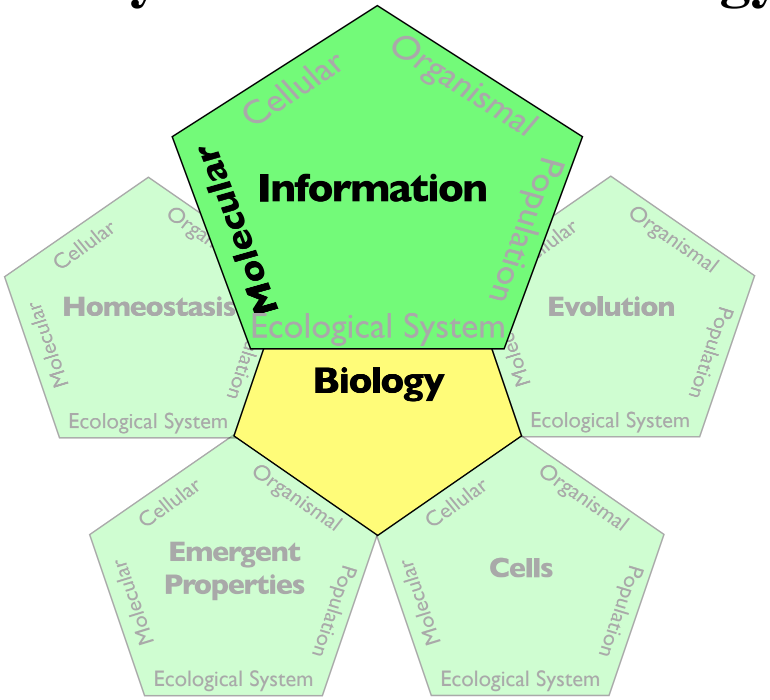
Five Big Ideas of Biology



Five by Five Matrix of Biology



Five by Five Matrix of Biology



Cellular
Organismal
Molecular
Information
Population
Ecological System

Cellular
Organ
Molecular
Homeostasis
lation
Ecological System

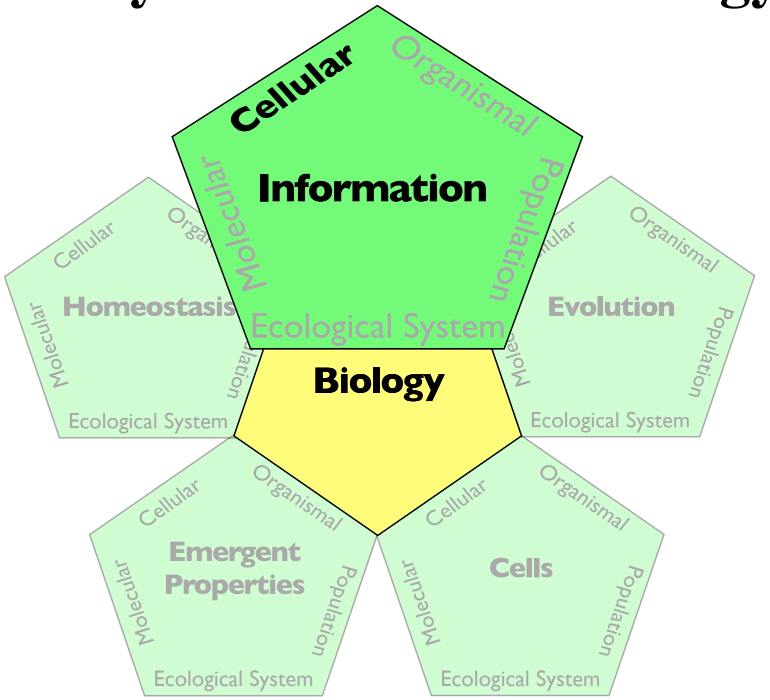
Biology

lular
Organismal
Molecular
Evolution
Population
Ecological System

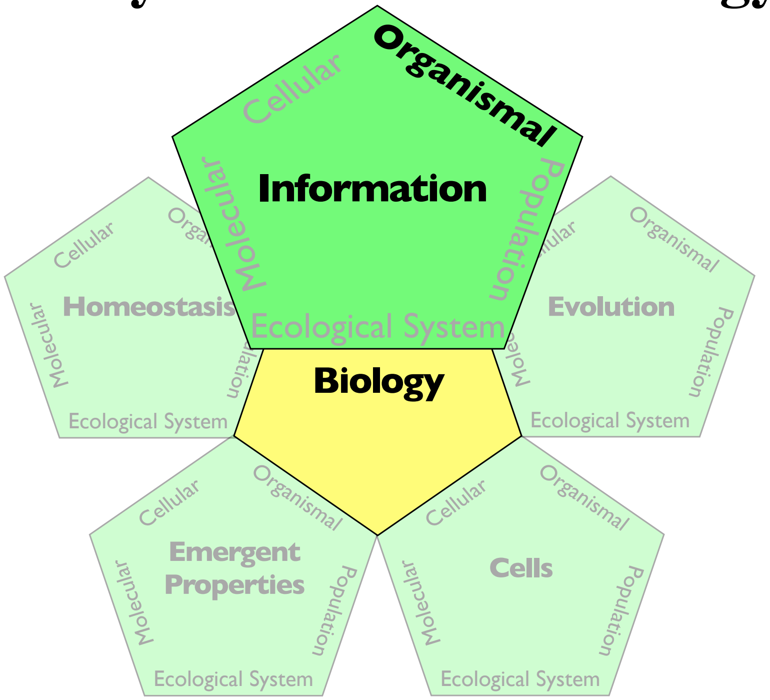
Cellular
Organismal
Molecular
Emergent Properties
Population
Ecological System

Cellular
Organismal
Molecular
Cells
Population
Ecological System

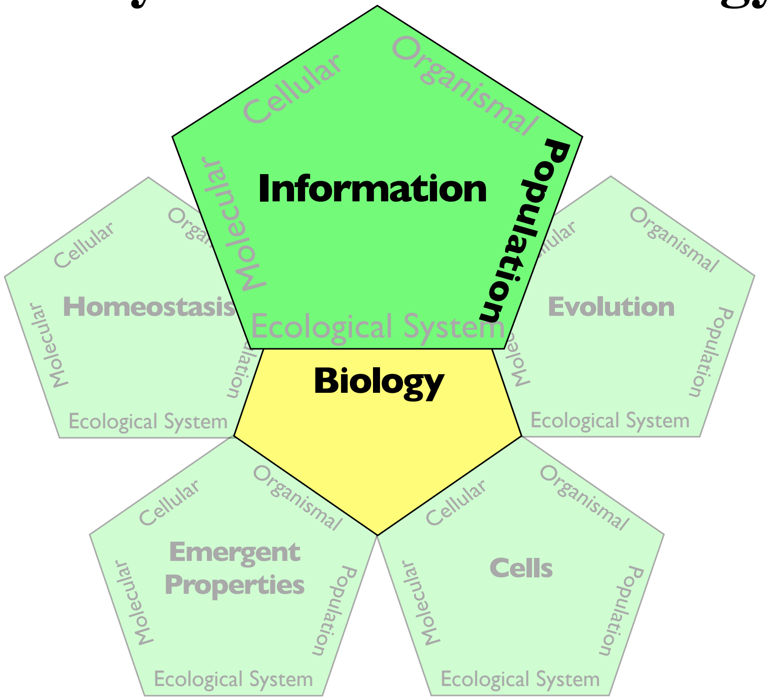
Five by Five Matrix of Biology



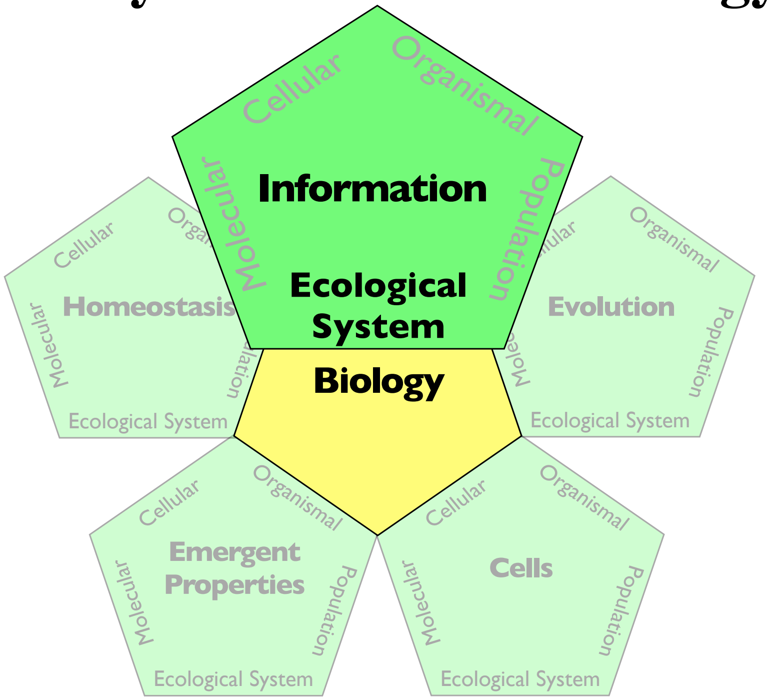
Five by Five Matrix of Biology



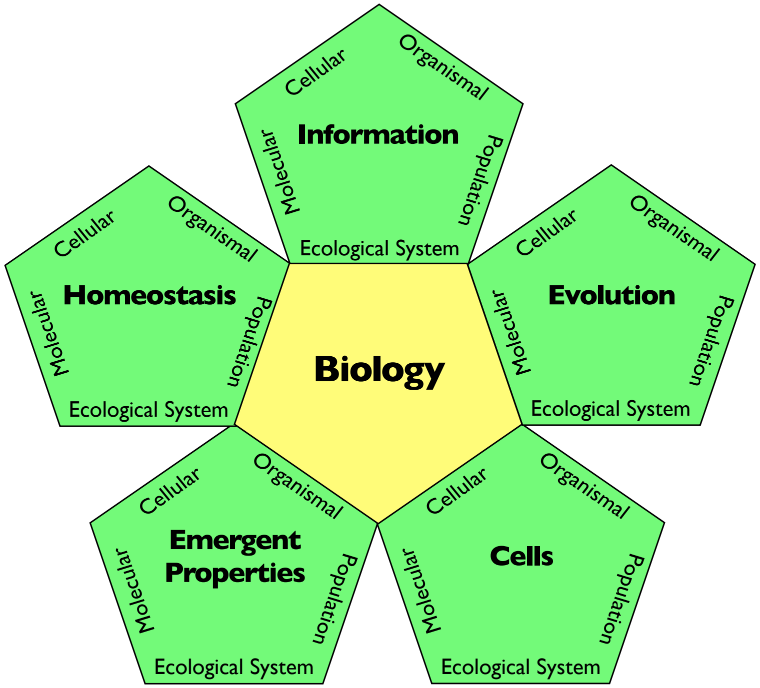
Five by Five Matrix of Biology



Five by Five Matrix of Biology



Five by Five Matrix of Biology



Biology

Information
Molecular
Cellular
Organismal
Population
Ecological System

Homeostasis
Molecular
Cellular
Organismal
Population
Ecological System

Evolution
Molecular
Cellular
Organismal
Population
Ecological System

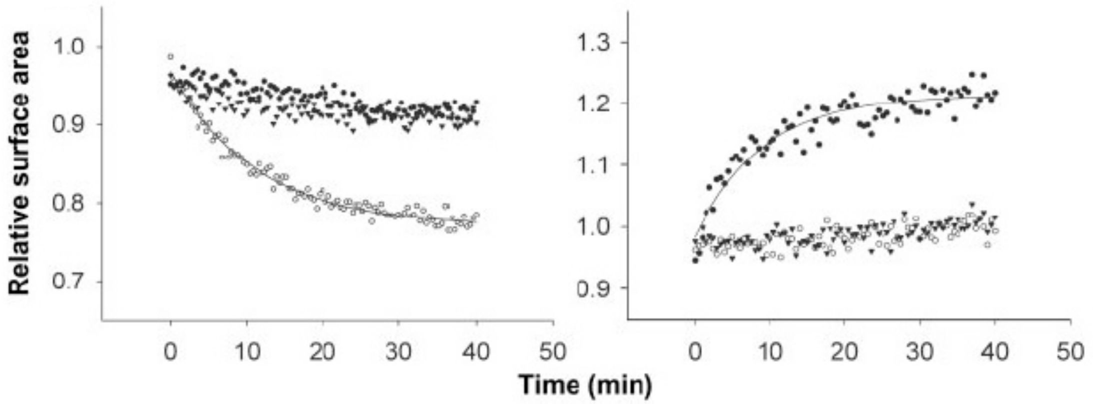
Emergent Properties
Molecular
Cellular
Organismal
Population
Ecological System

Cells
Molecular
Cellular
Organismal
Population
Ecological System

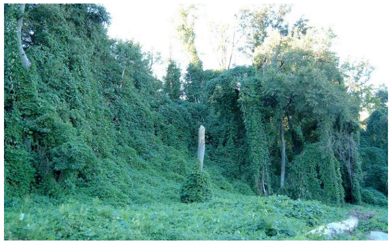
BioMath Explorations

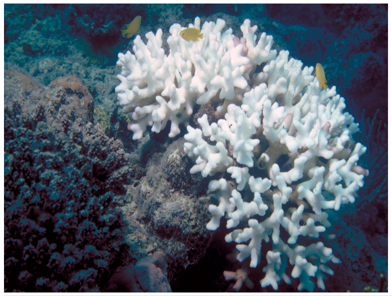
BioMath Exploration 6.3

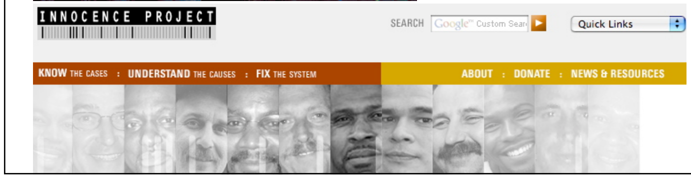
How can you fit exponential curves to data?



Ethical, Legal and Social Implications







Are religion and evolution compatible?

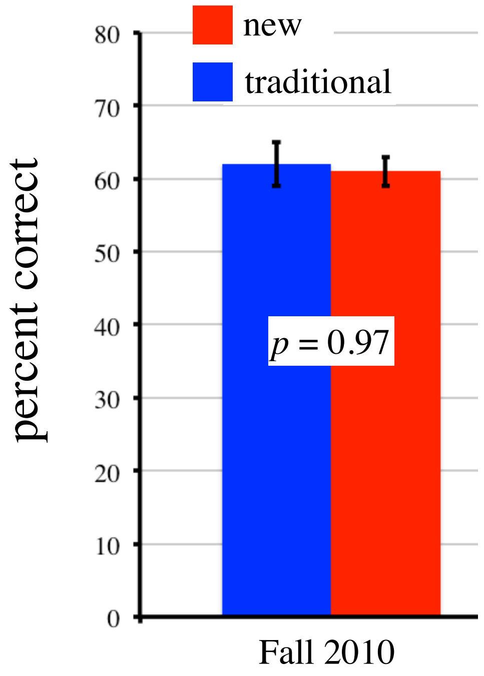
Is science possible if you are uncertain about what is true?

Does basic biology have any impact on the real world?

Who owns your DNA?

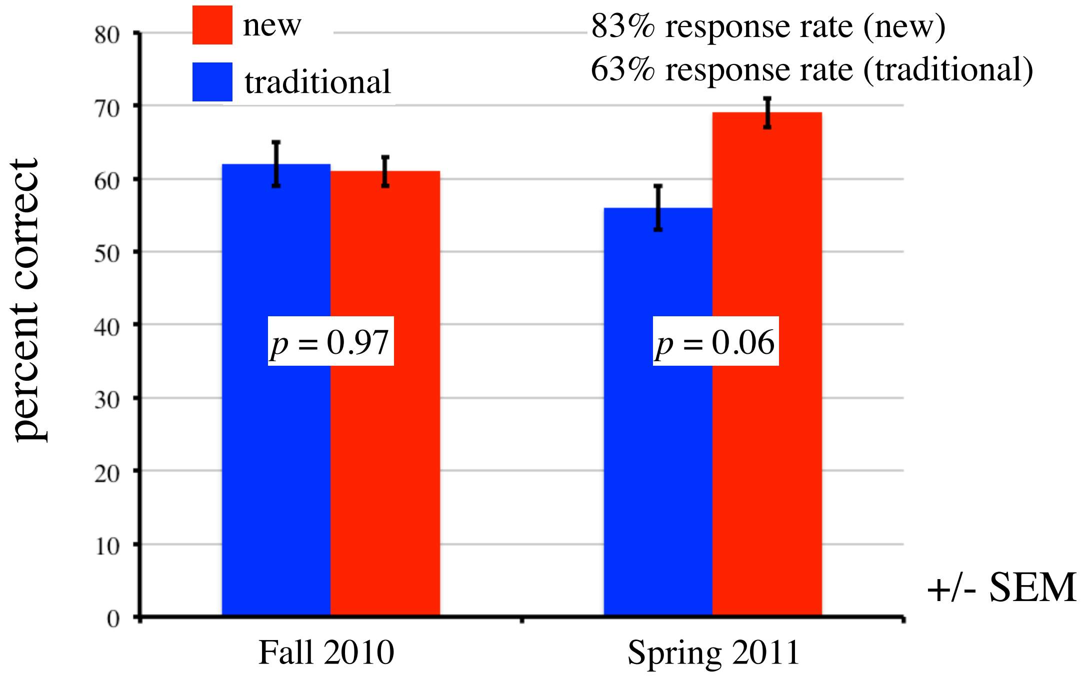
Did my students learn less content?

Student Content Assessment



+/- SEM

Student Content Assessment

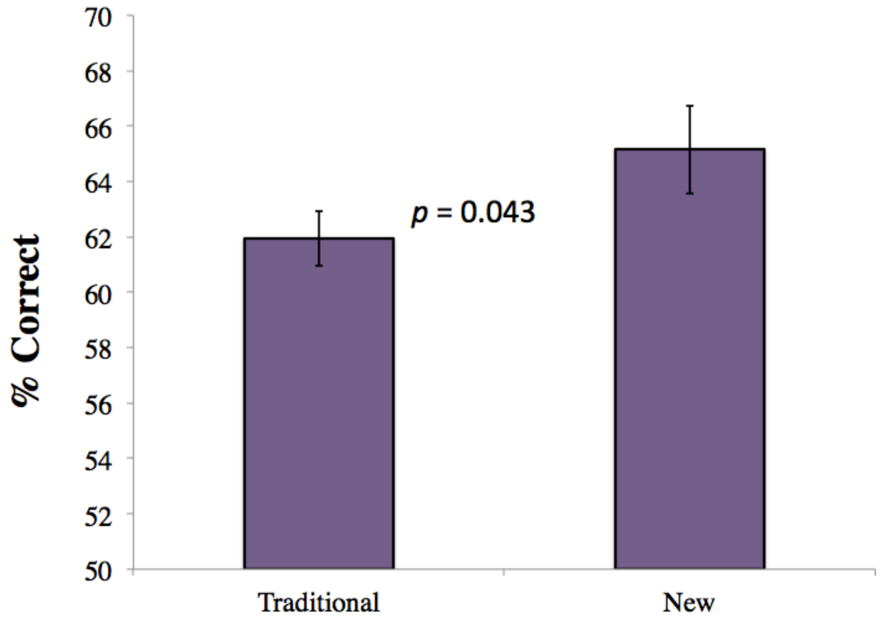


83% response rate (new)
63% response rate (traditional)

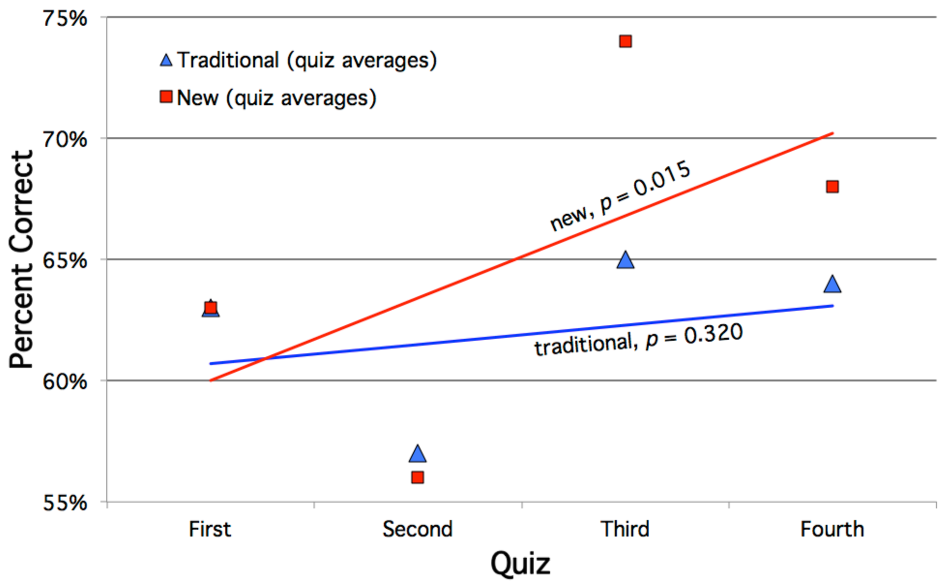
+/- SEM

Can my students analyze data better?

Student Skills Assessment



Student Skills Assessment



What did my students think about this approach to intro bio?

> “The method of learning, placing emphasis on the interpretation of data, has helped me not only in this class, but also in others.”

anonymous student course evaluation, Dec. 2010

“I found it much more beneficial using this approach compared to straight memorization. It allowed me to gain interpretation skills I was lacking before.”

anonymous student course evaluation, Dec. 2010

“The data-driven approach is brilliant. It alleviates the issues that I’ve always had of asking, ‘How do we know that? What’s the supporting data?’ ”

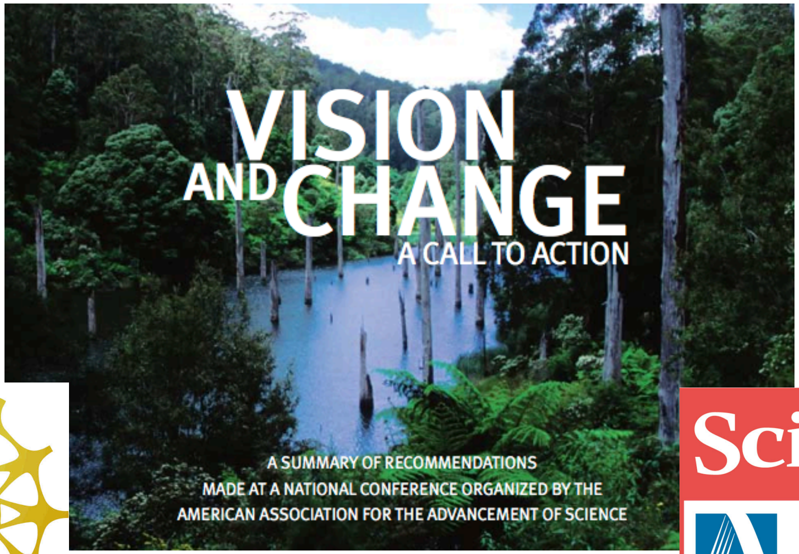
anonymous student course evaluation, Dec. 2010

“Emphasis on big picture and understanding how to pull information from real data was an easier and more beneficial format than memorization of facts (which used to be a struggle for me).”

anonymous student course evaluation, Dec. 2010

Why bother changing?

National Recognition of Need to Change



VISION AND CHANGE

A CALL TO ACTION

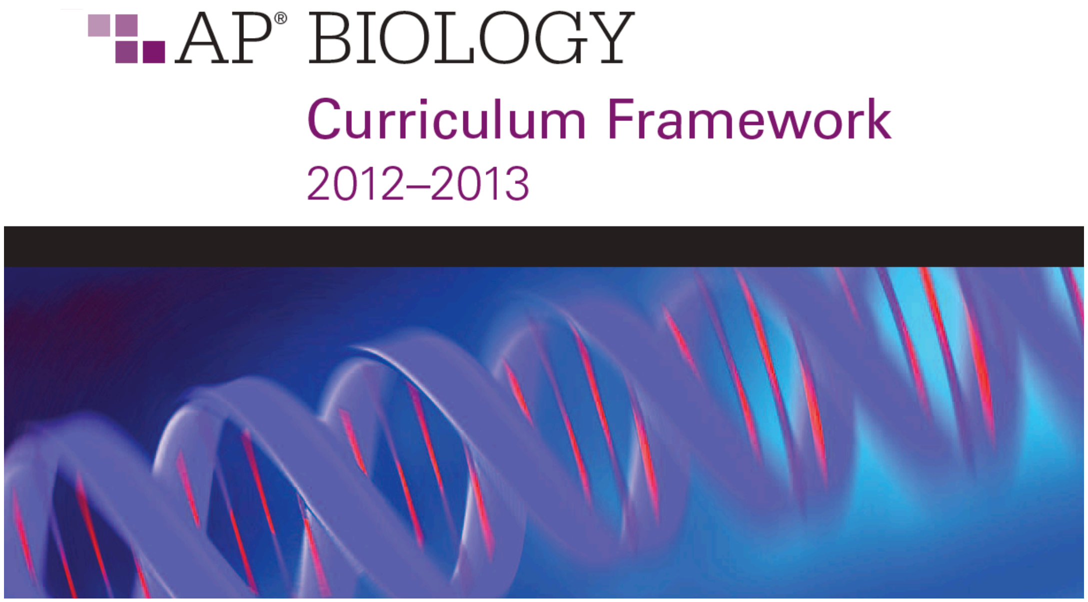
A SUMMARY OF RECOMMENDATIONS
MADE AT A NATIONAL CONFERENCE ORGANIZED BY THE
AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

NSF

Science

AAAS

AP Biology is Changing to Match Our Design



AP® BIOLOGY

Curriculum Framework

2012–2013

Acknowledgements

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The Duke Endowment, NSF, HHMI
Genome Consortium for Active Teaching (**GCAT**)
Davidson College James G. Martin Genomics Program
MWSU SGA, Foundation & Summer Research Institute

[redacted]

How did I test student learning?

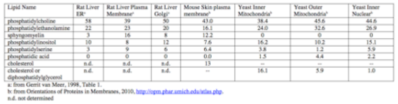
Four Exams Per Semester

8 pts.

9) Limit your answers to a maximum of **2 sentences for each part**.

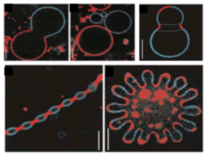
a) Explain why it is adaptive for each eukaryotic organelle to be composed of a different lipid composition. Use data to support your answer.

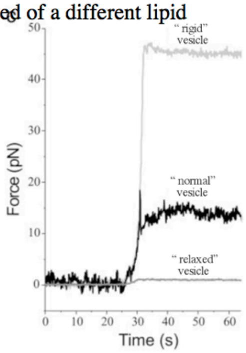
Each one has a particular surface area to volume ratio and different lipids have different bending capacity. Rigid lipids produce larger volumes while relaxed lipids produce bends and small volumes inside membranes.



Lipid Name	Rat Liver ER[a]	Rat Liver Plasma Membrane[a]	Rat Liver Golgi[a]	Mouse Skin plasma membrane[b]	Yeast Inner Mitochondria[b]	Yeast Outer Mitochondria[b]	Yeast Inner Nuclear[b]
phosphatidylcholine	58	39	50	43.0	38.4	45.6	44.6
phosphatidylethanolamine	22	23	20	16.1	24.0	32.6	26.9
sphyngomyelin	3	16	8	12.2	0	0	0
phosphatidylinositol	10	8	12	7.6	16.2	10.2	15.1
phosphatidylserine	3	9	6	6.4	3.8	1.2	5.9
phosphatidic acid	0	0	0	0.0	1.5	4.4	2.2
cholesterol	n.d.	n.d.	n.d.	13	--	--	--
cholesterol or diphosphatidylglycerol	n.d.	n.d.	n.d.	--	16.1	5.9	1.0

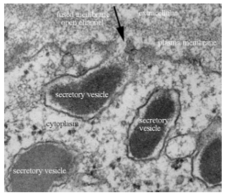
a: from Gerrit van Meer, 1998, Table 1.
b: from Orientations of Proteins in Membranes, 2010, http://opm.phar.umich.edu/atlas.php.
n.d. not determined



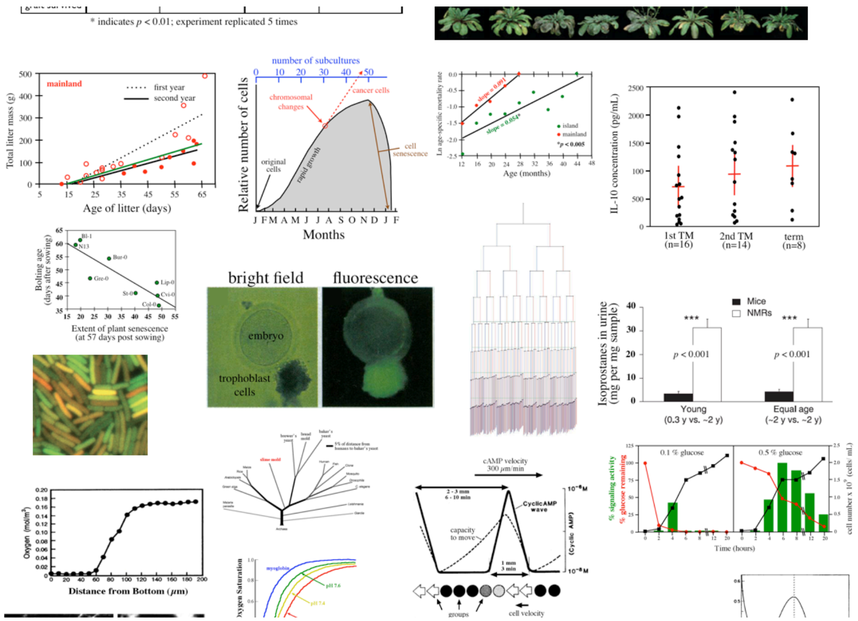


b) Would you predict that the secretory vesicles containing epinephrine would contain more rigid lipids, or flexible lipids? Use data to support your answer.

relaxed due to large surface area to volume ratio



Data Gallery for Answers



When did the students feel they were learning something different than in high school?

Table of Contents

Chapter 7 Evolution at the Cellular Level

- 7.1: How are new species formed? Discover how genomes can change dramatically to produce new species.
  - *BME 7.1: What information is in a dot plot? Discover how to construct and interpret a dot plot for comparing whole genomes.*
  - *ELSI 7.1: Are GMOs safe?*
- 7.2 Why doesn’t your stomach digest itself? Analyze experimental results showing that eukaryotes evolved a shared mechanism to retain proteins inside the endoplasmic reticulum.
  - *BME 7.2: Cause or effect? Explore the meaning of correlation, and how it is quantified.*
- 7.3 Why do my allergies get worse each year? Determine that B cells evolve in days to produce stronger immune responses.
  - *ELSI 7.2: Banning PB&J: How far should a society go to protect the rights of an individual?*
- 7.4 Why are corals dying around the world? Realize that species can coevolve as symbionts and become interdependent.
  - *BME 7.3: Can you predict coral bleaching? Evaluate the fit and predictive ability of a trendline.*

Table of Contents

Chapter 17 Emergent Properties at the Cellular Level

17.1 Do unicellular species have to work solo? Realize that microbes use quorum-sensing, biofilms and communal behavior to enhance their functions.

17.2 How can changes in two cells affect an entire plant? Appreciate how guard cells change their shape to regulate plant gas exchange through stomata.

BME 17.1: Can local decisions have global effects? Model the opening of stomata using a simulation of local rules.

17.3 How do brain cells store memories? Discover how long-term memories are formed by analyzing classic experiments on *Aplysia* learning.

ELSI 17.1: If pills could make you remember or forget, would you take them?

17.4 Does the genome allow random actions by cells? Learn how random movements of molecules determine cell phenotypes which can be transmitted across generations.

BME 17.2: What is chaos?

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Chapter 22 Homeostasis at the Cellular Level

Student Skills Assessment