Synthetic Biology Leads to Organic Learning

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Biology Department and **GCAT**

DAVIDSON

UNCC
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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?

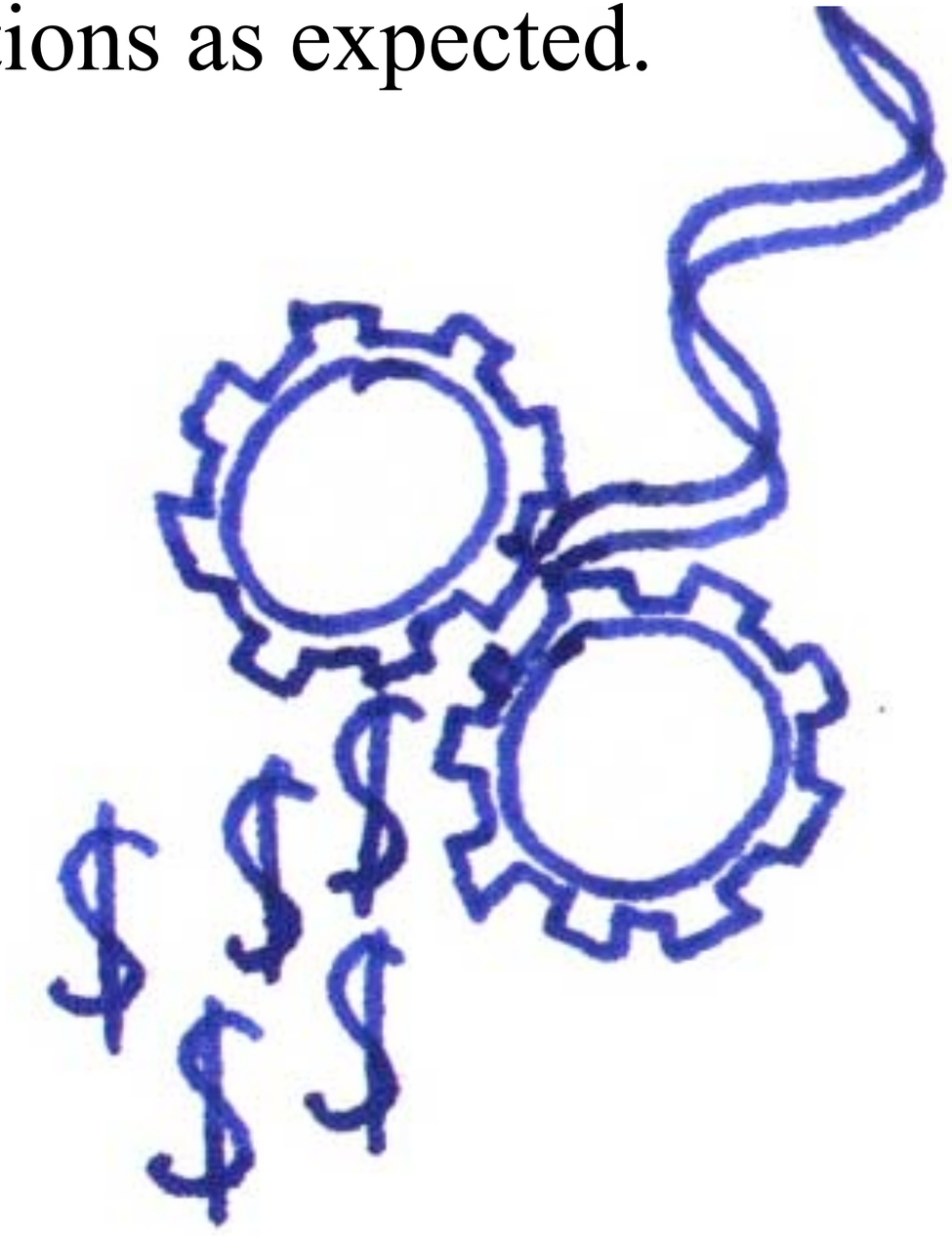
What is Synthetic Biology?

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

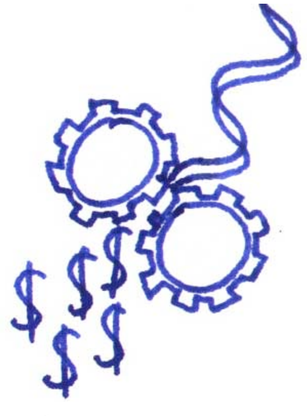
Synthetic Biology: Win-Win

Win #1: your design functions as expected.

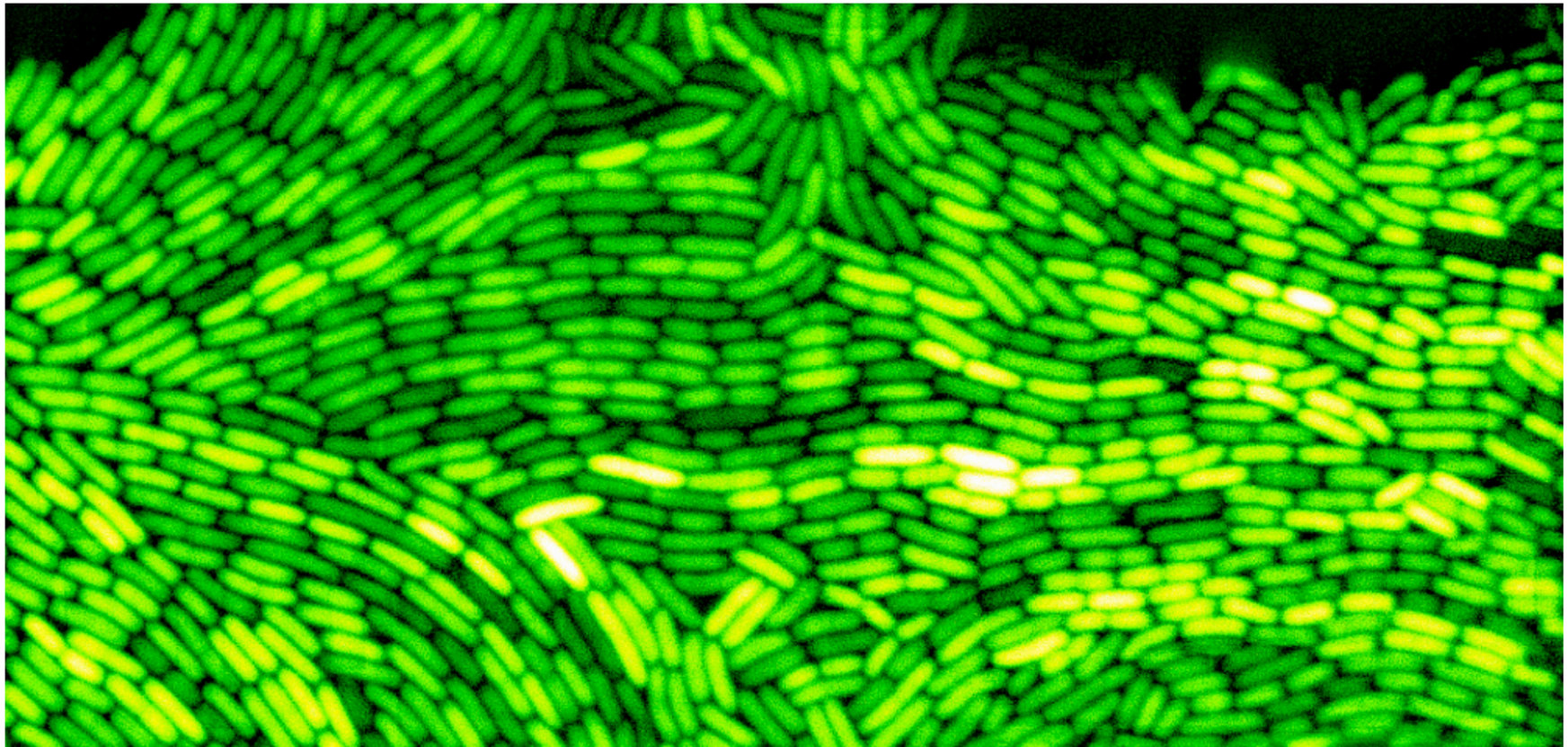


Synthetic Biology: Win-Win Research

Win #1: your design functions as expected.



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



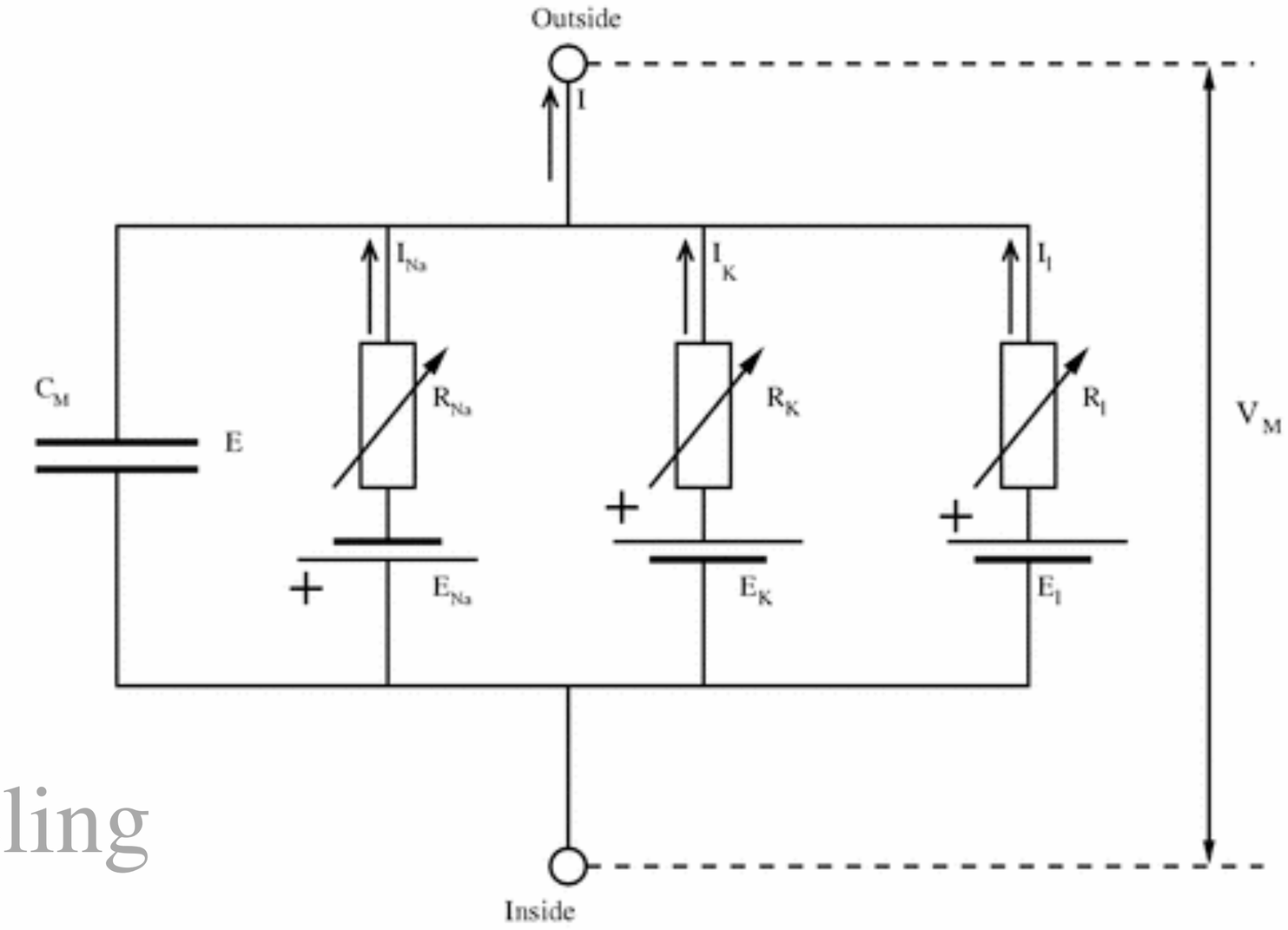
How is Synthetic Biology Different?

Abstraction

Modularity

Standards

Designing and modeling



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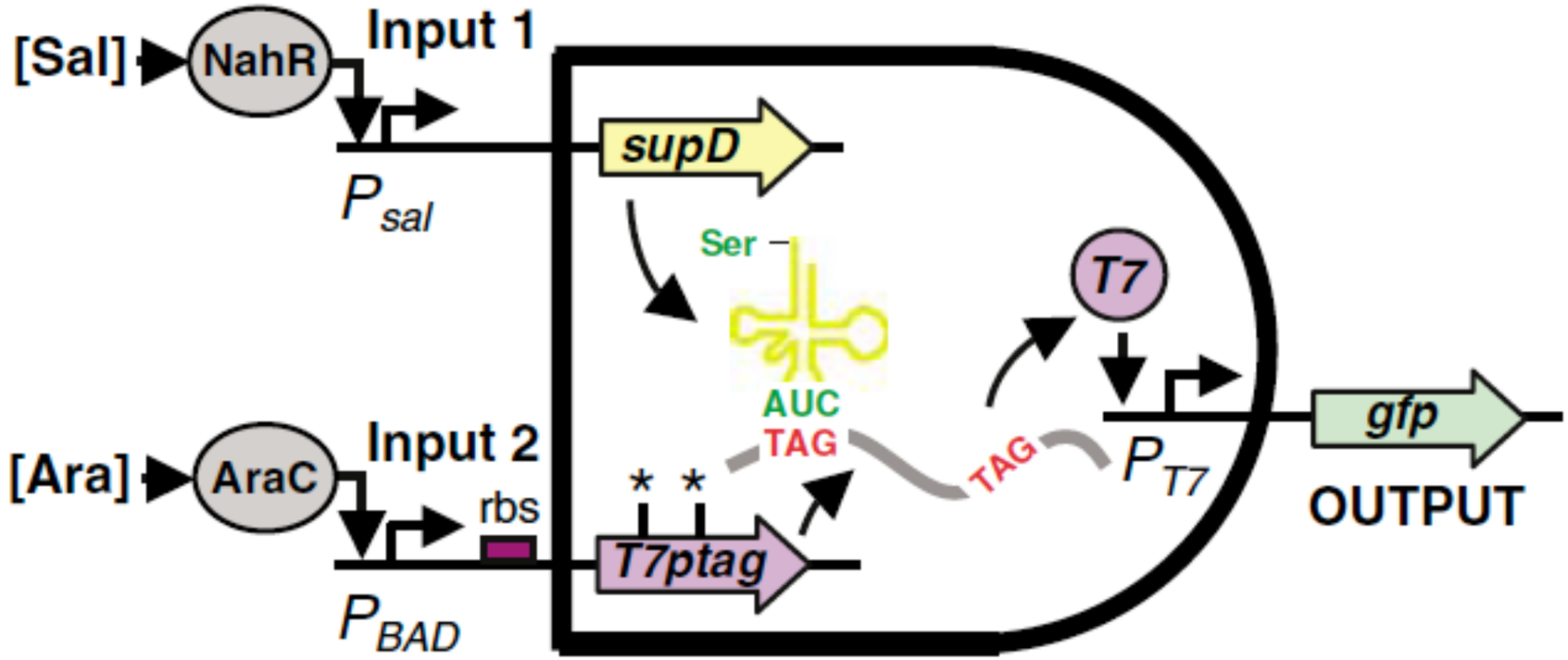

AND Logic Gate

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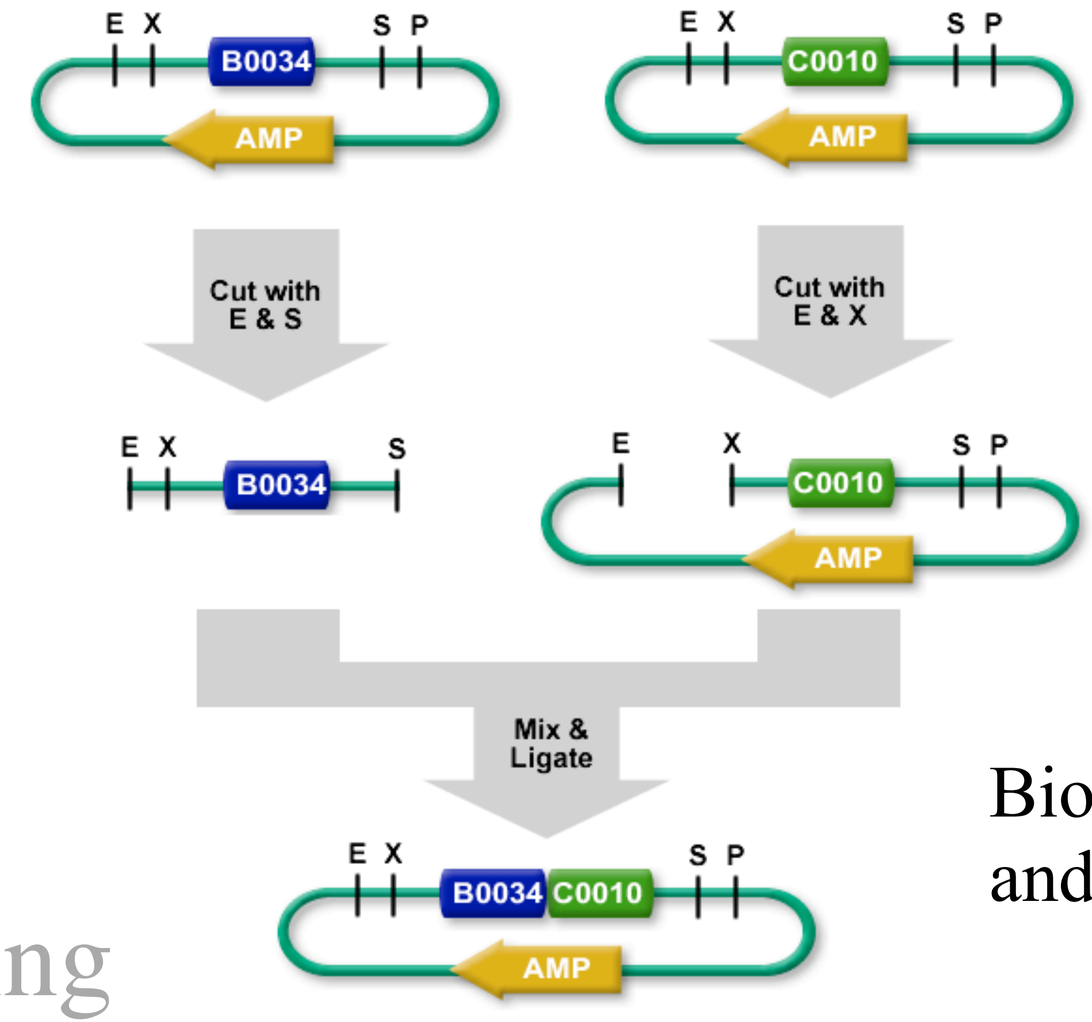

BioBrick Ends and Ligation

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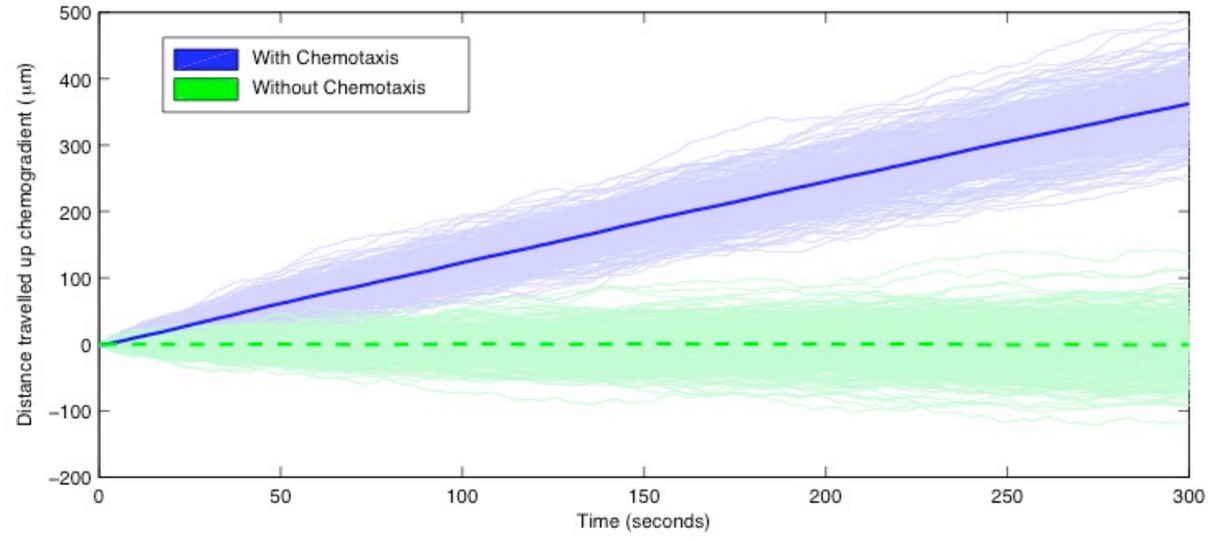
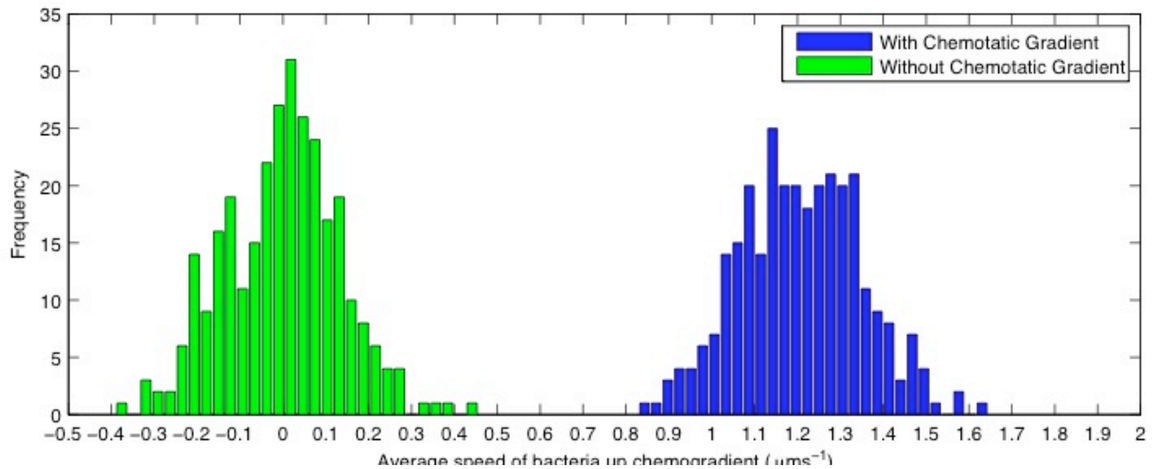


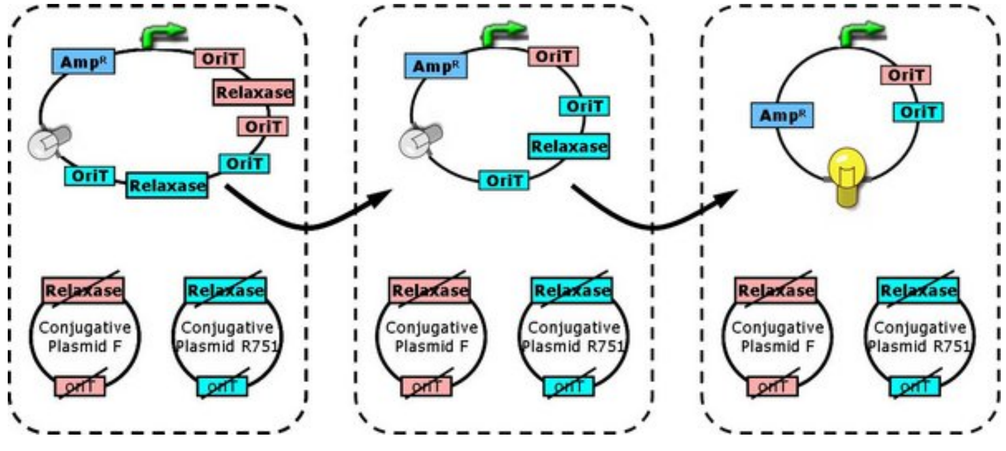


What is iGEM?

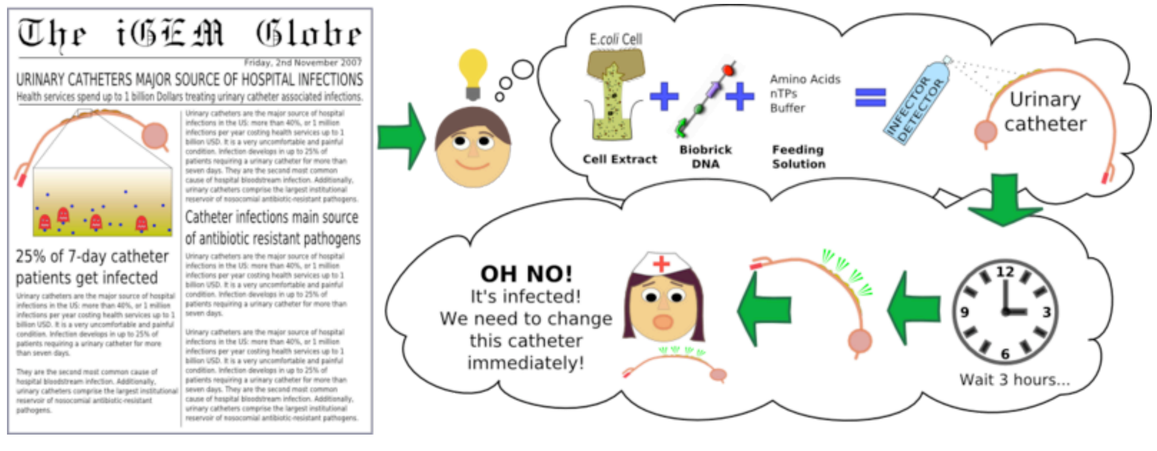
at a glance:

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

http://2009.igem.org/Main_Page

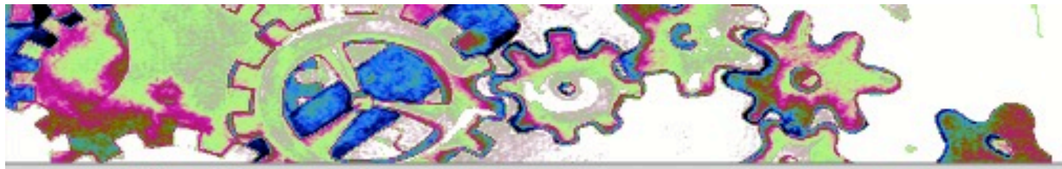


Peking University



Imperial College

Standardized and Modular DNA



Registry of Standard Biological Parts

Go Search

page discussion view source history Log in / create account

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.

Catalog of parts & devices

Help

Users & groups
(Apply for an account)

DNA repositories

Registry tools

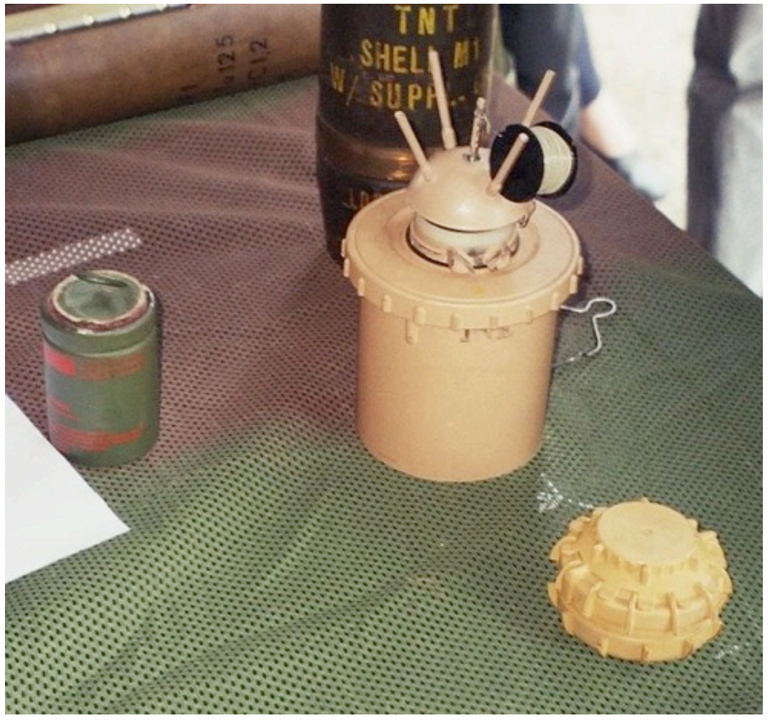
- **Search parts (?)**
- **Add a part**
- **Request a part**
- **Send parts to the Registry**
- **Sequence analysis**

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.

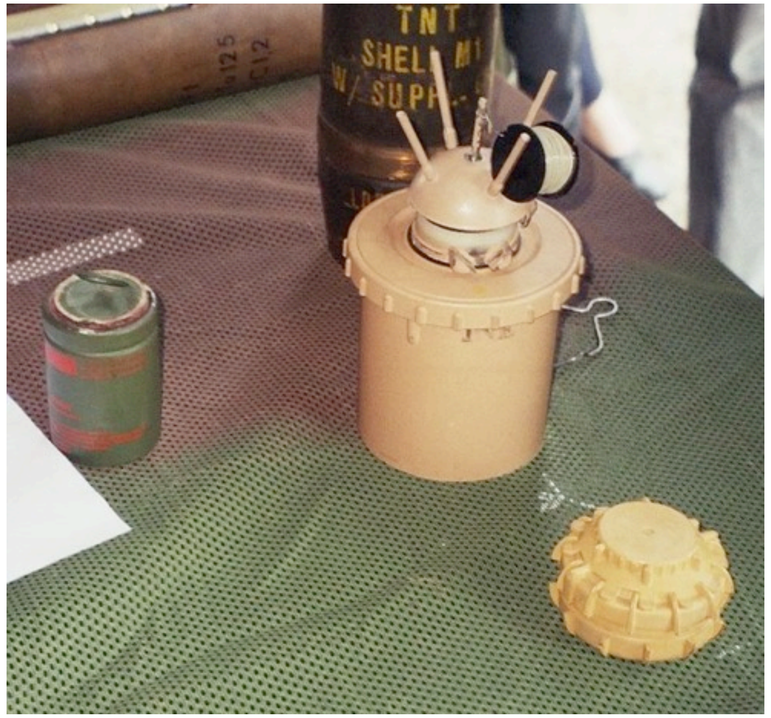
The Registry of Standard Biological Parts is *always* a work in progress. Please browse the new catalog and let us know what you think, or feel free to edit and improve the pages further.

Real World Applications of Synthetic Biology

Land Mine Detection



Land Mine Detection



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*

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Land Mine Detection

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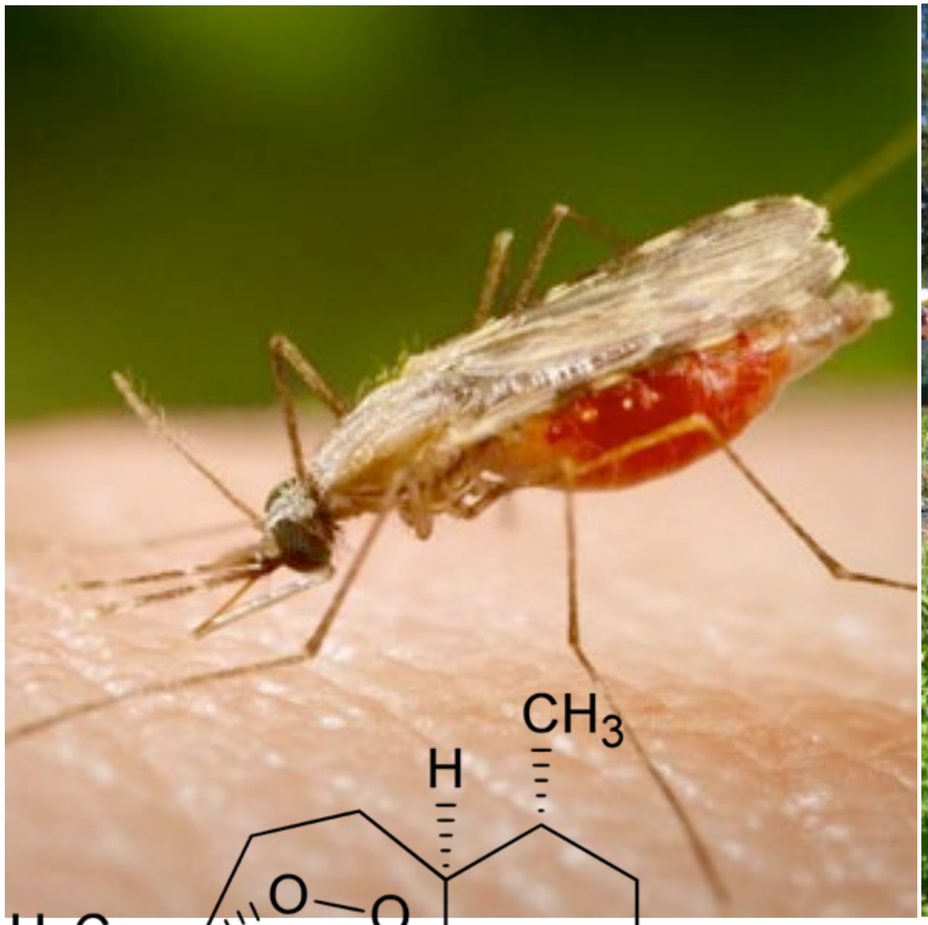
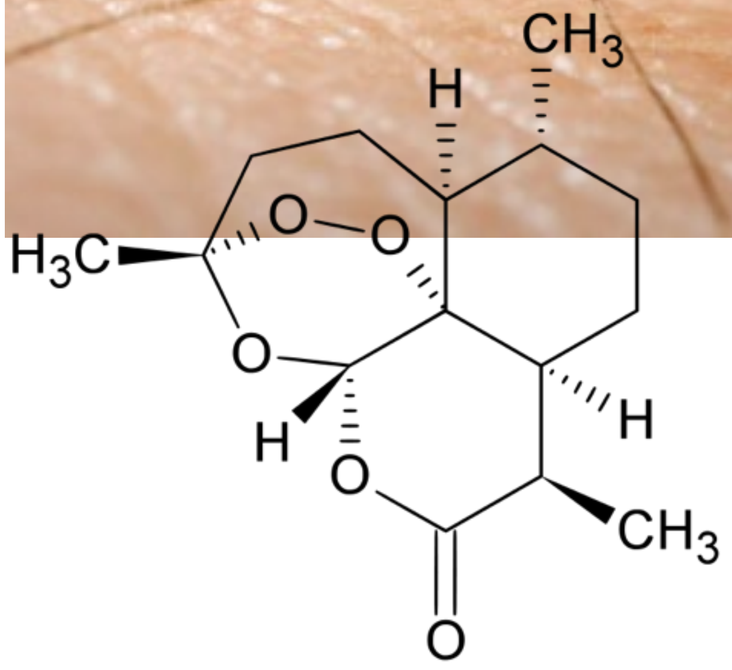
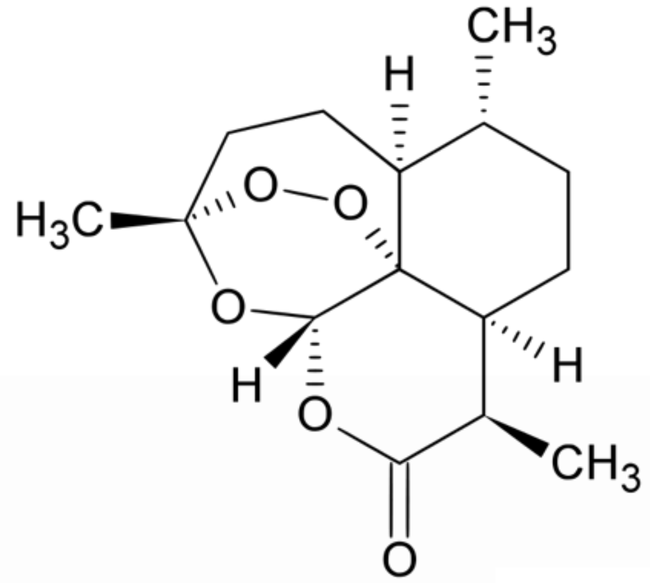
Production of Medicines



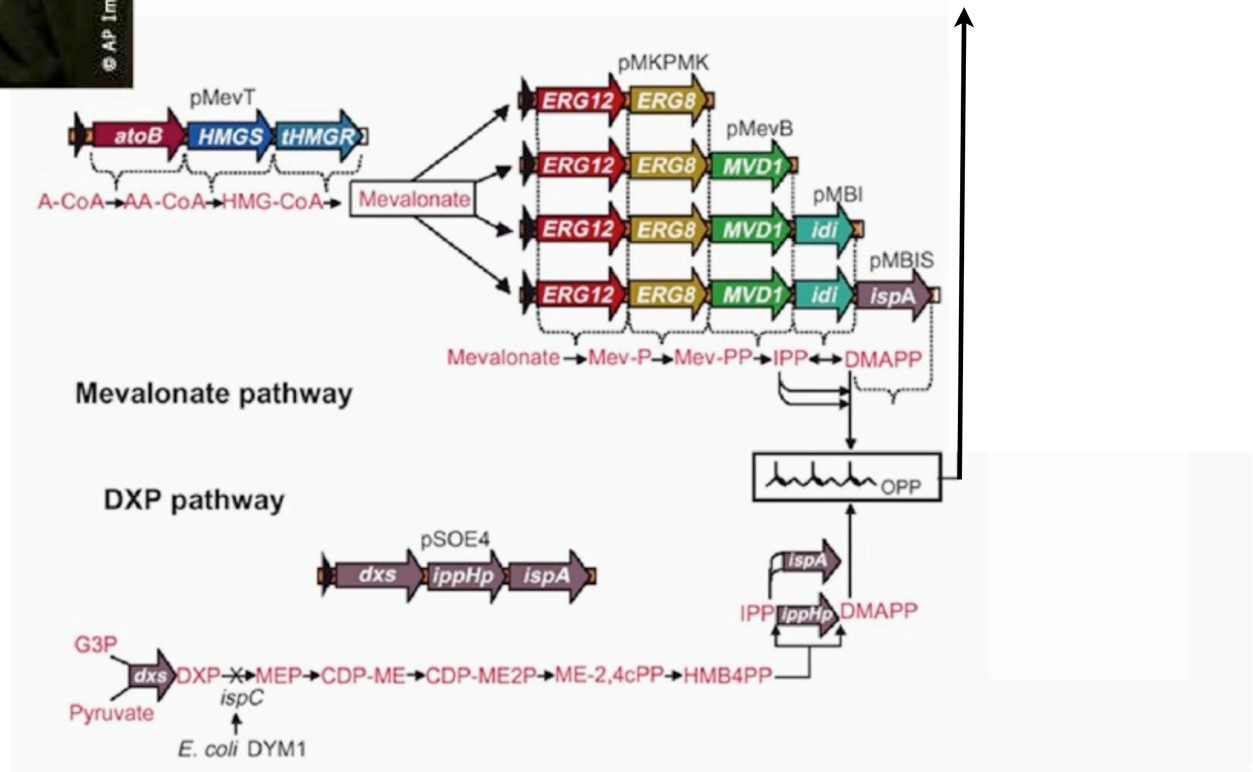


$1 per pill

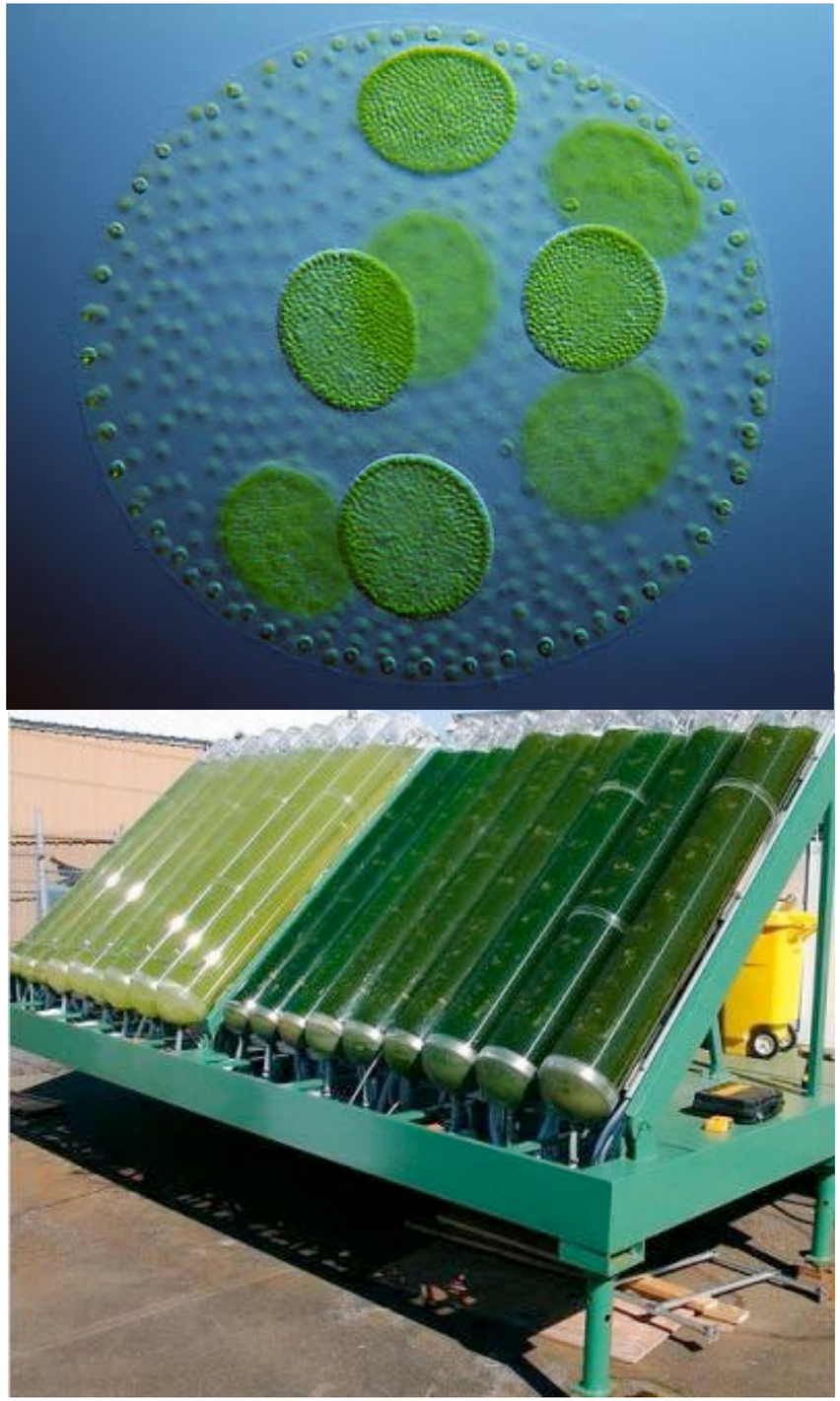
Production of Medicines



10¢ per pill



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

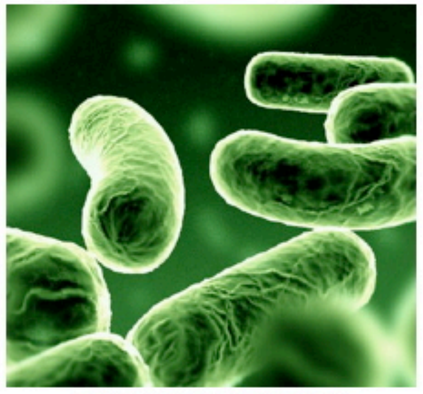
Building Bacterial Computers

Advantages of Bacterial Computation

Software ⟶ Hardware ⟶ Computation

Computation

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

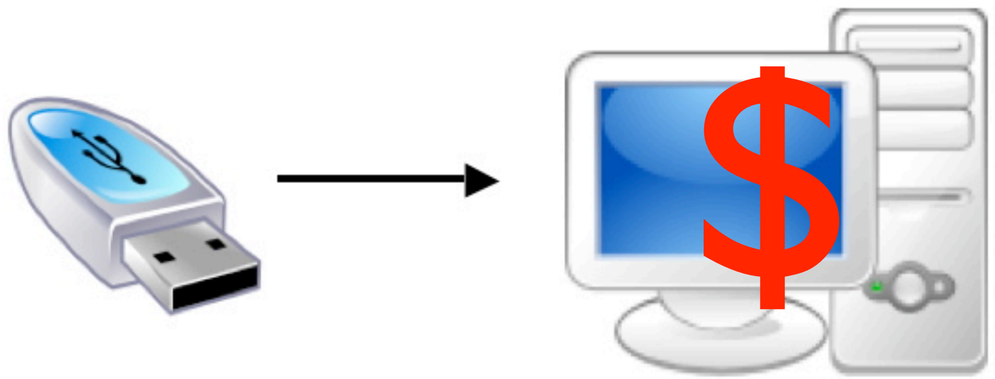


http://www.turbosquid.com

Computation

Advantages of Bacterial Computation

Software ⟶ Hardware ⟶ Computation



Computation

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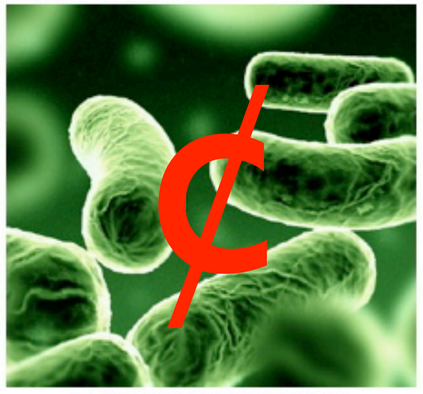


http://www.turbosquid.com

Computation

Advantages of Biological Computers

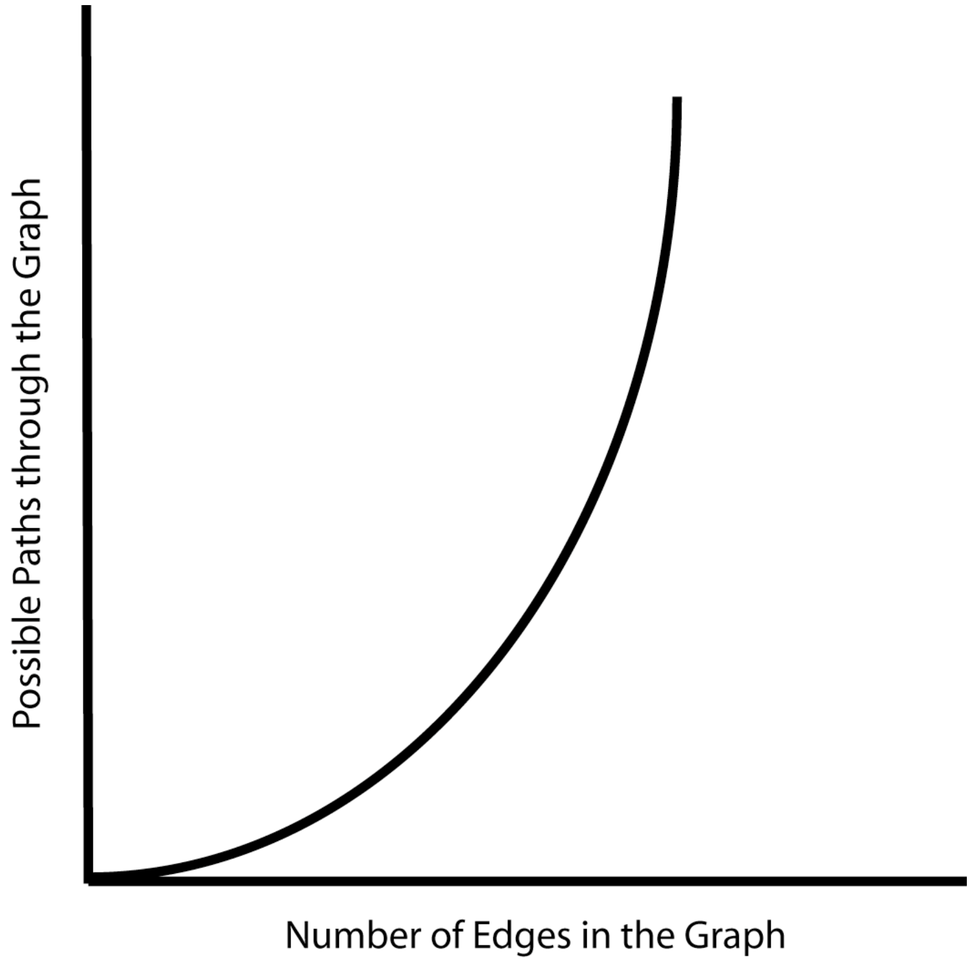
go anywhere - arctic, thermal vents, inside organisms

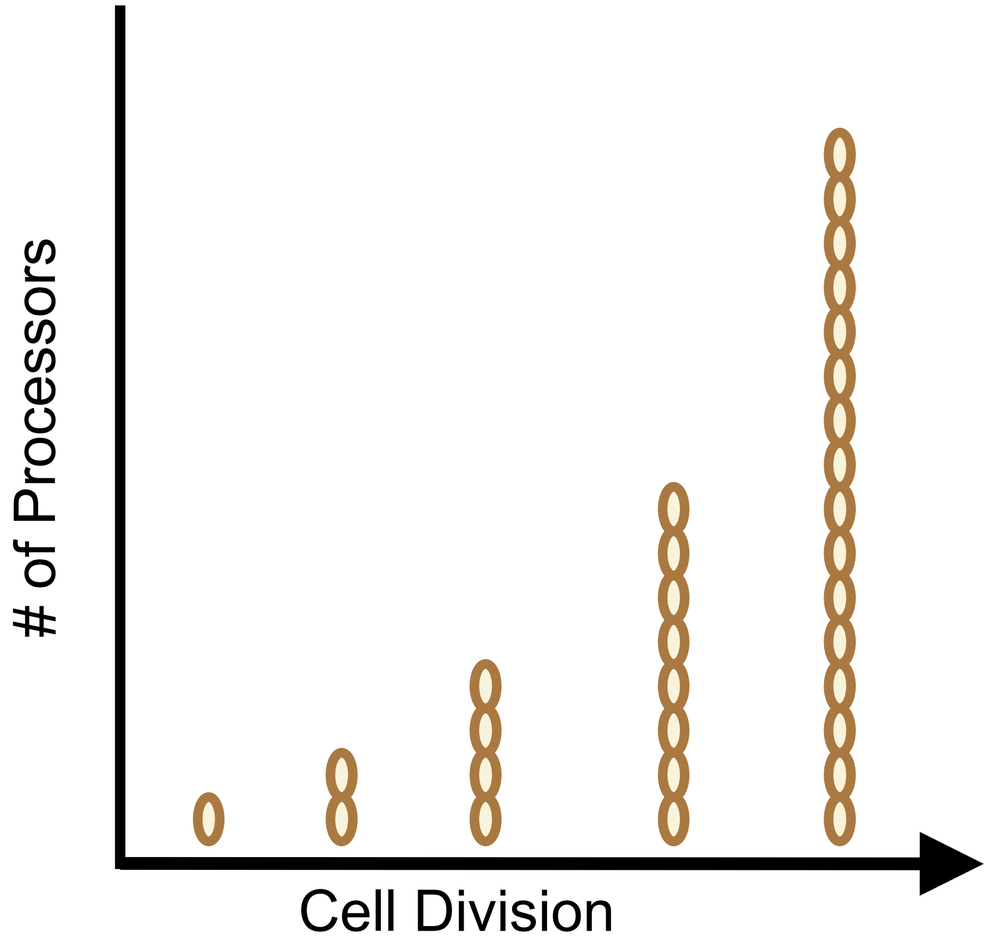
no electricity

self-replicating

no immune rejection

Self-replicating Computers



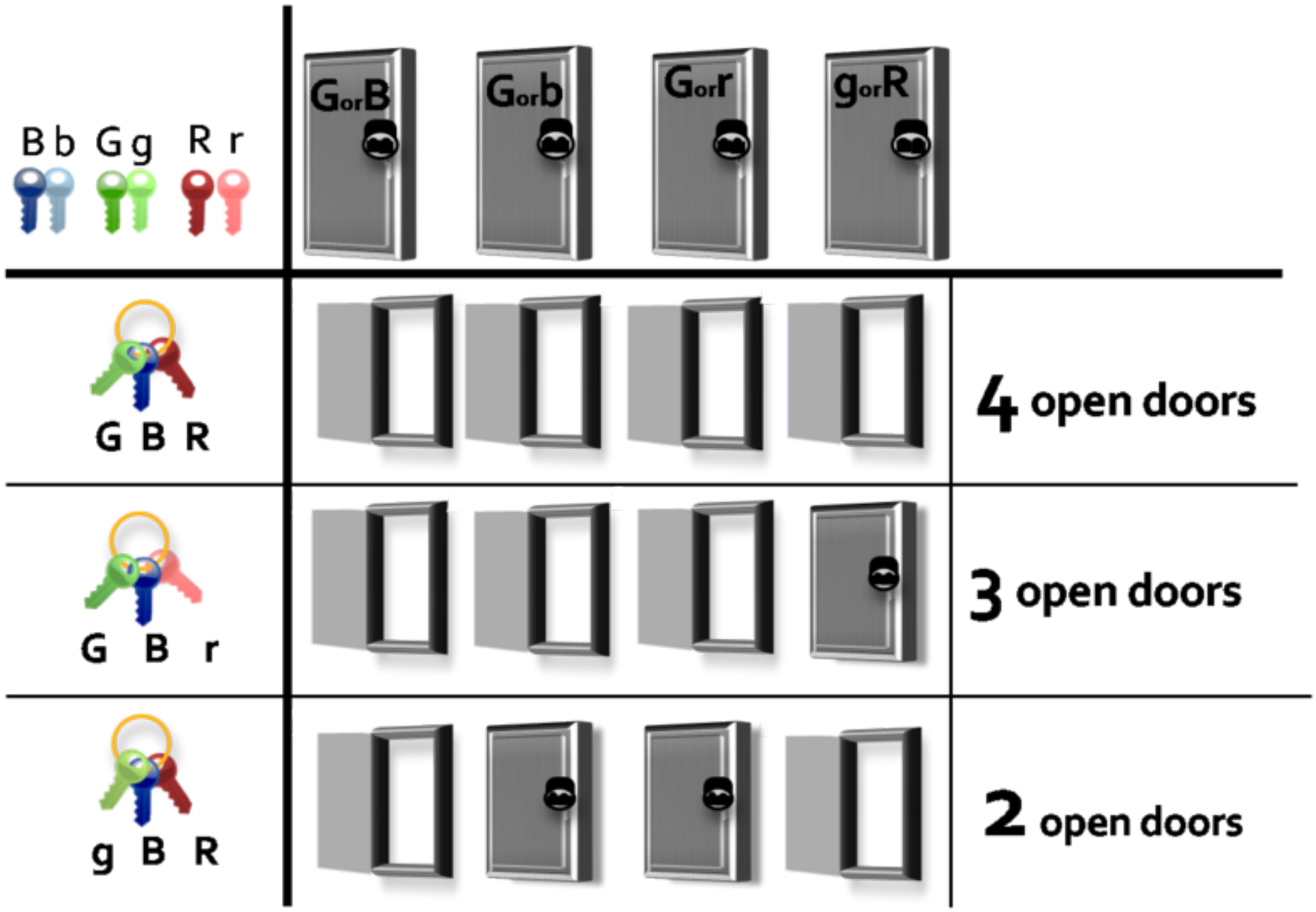


Two Undergraduate Research Projects

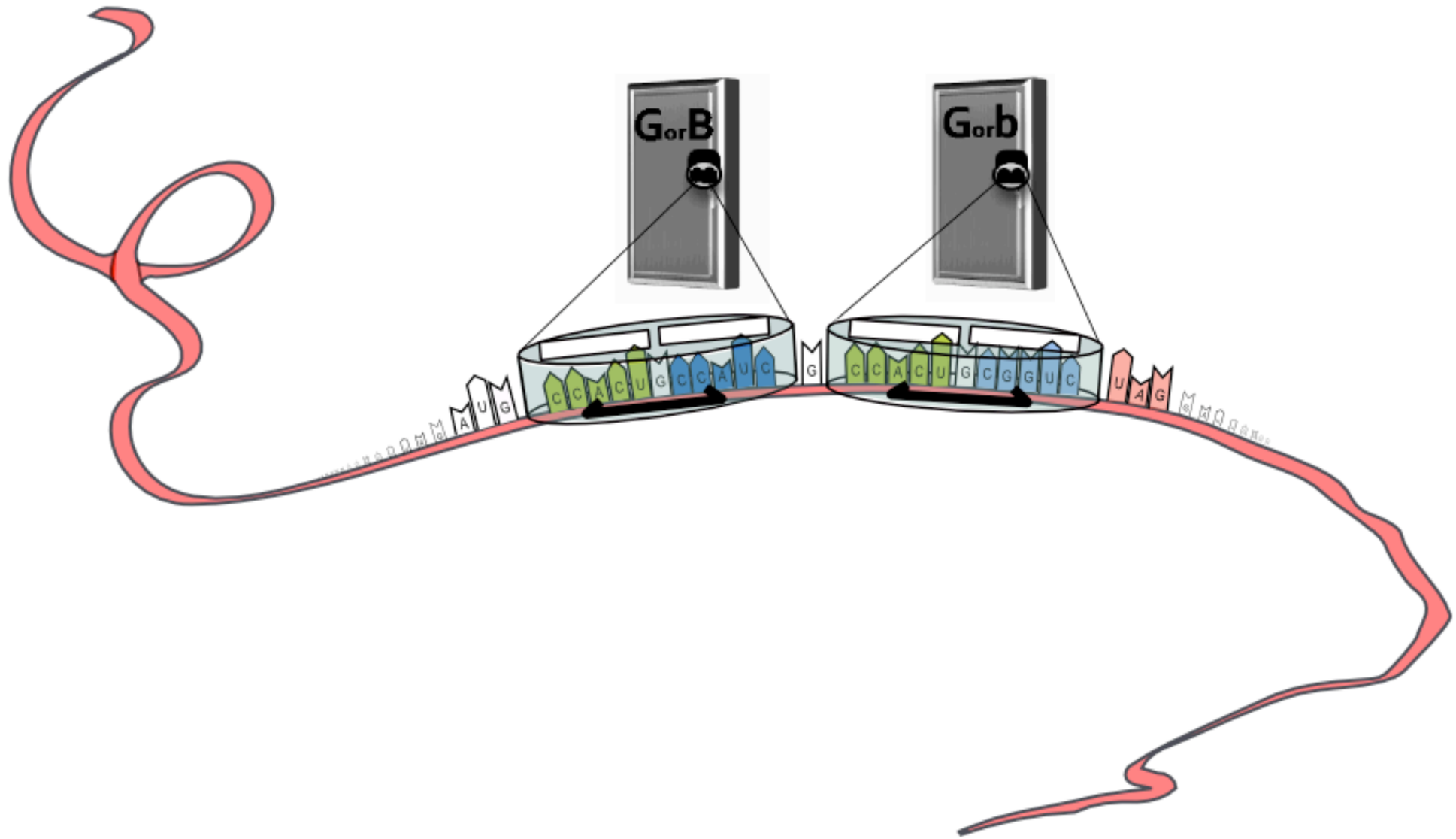
Define the SATisfiability Problem

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

↓ transcription

mRNA
aug ccc uac uca cua ccu aua ccg cau

↓ translation

Protein

M P Y S H P I P H

DNA
atgccc**TC**tactcactacctatagcgcat

↓ transcription

mRNA
aug ccc UCu acu cac uac cua uac cgc au

↓ translation

Protein

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

↓

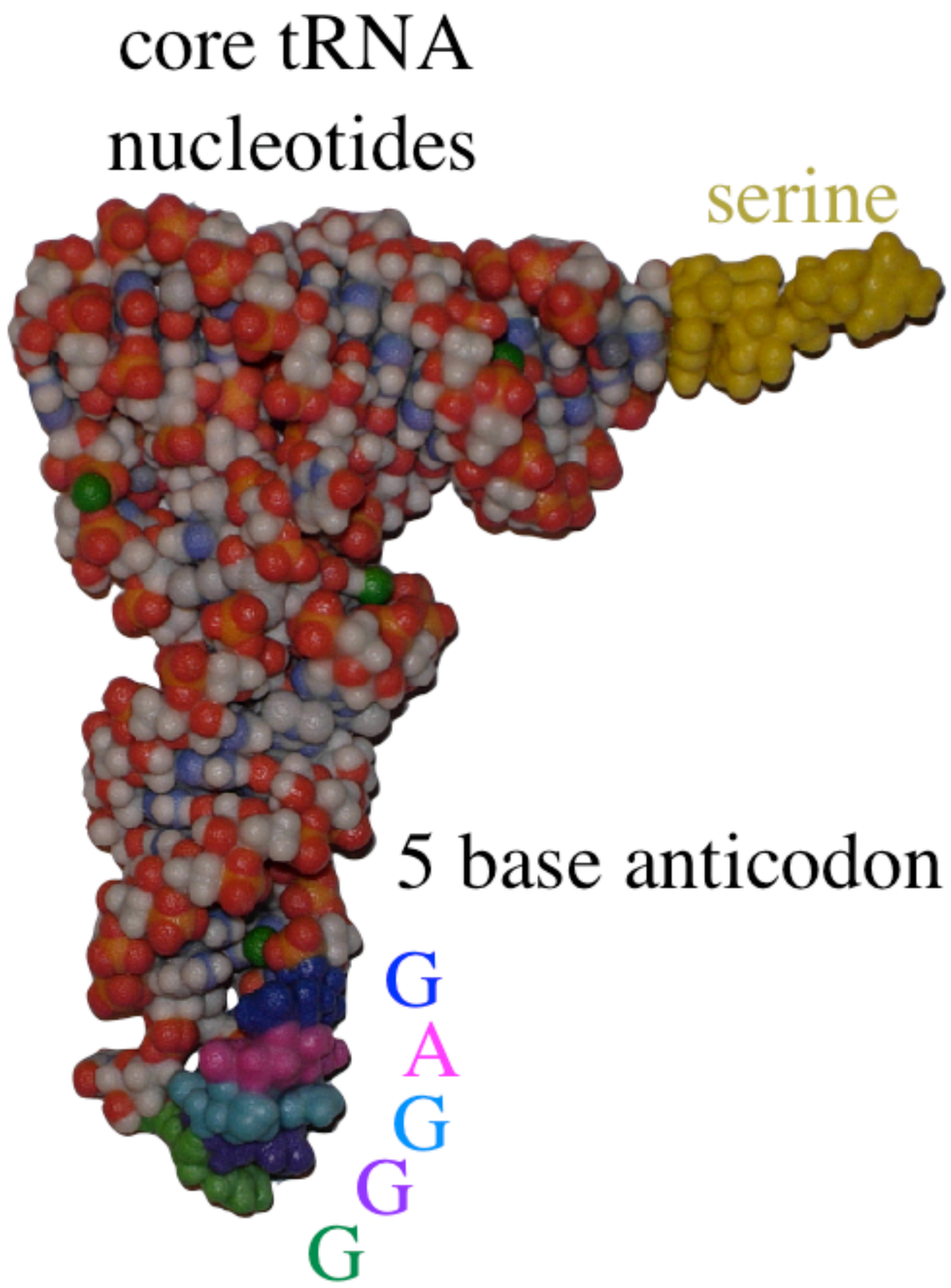
aug cccUC uac uca cua ccu aua ccg cau

↓

Protein

M S Y S H P I P H

Suppressor tRNA



Coding 2-SAT Clause

G ATG NNNNN gNN NNN → satisfied

Coding 2-SAT Clause

G 

ATG NNNNN gNN NNN → satisfied

OR

B 

ATG NNN NNg NNNNN → satisfied

Coding 2-SAT Clause

G 

ATG NNNNN gNN NNN → satisfied

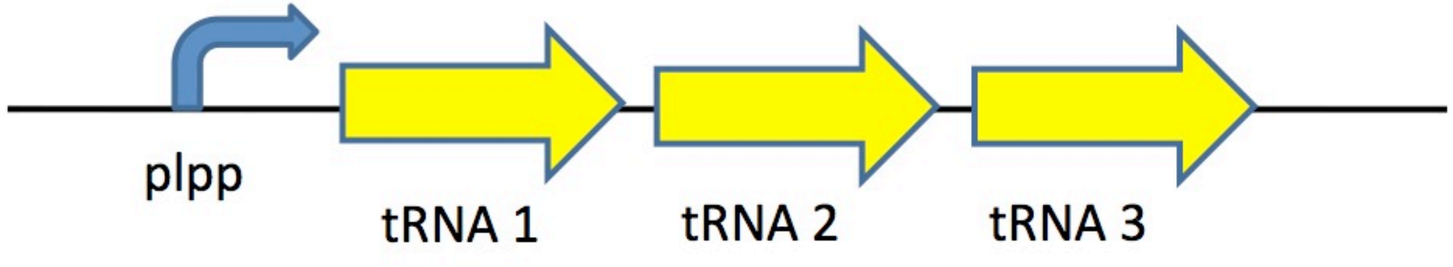
OR

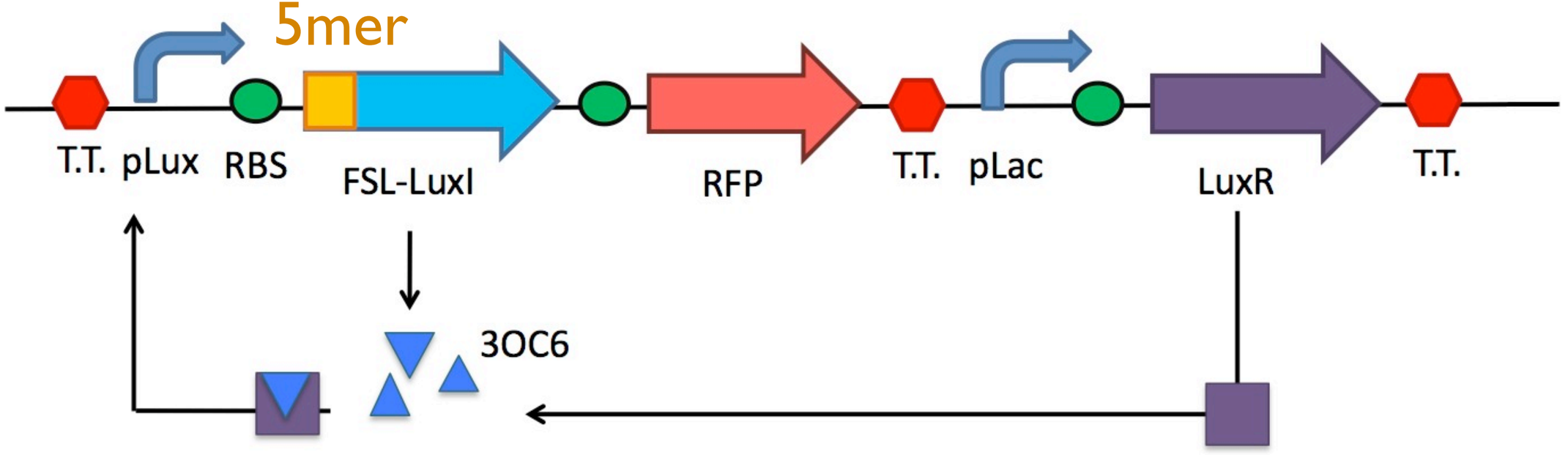
B 

ATG NNN NNg NNNNN → satisfied

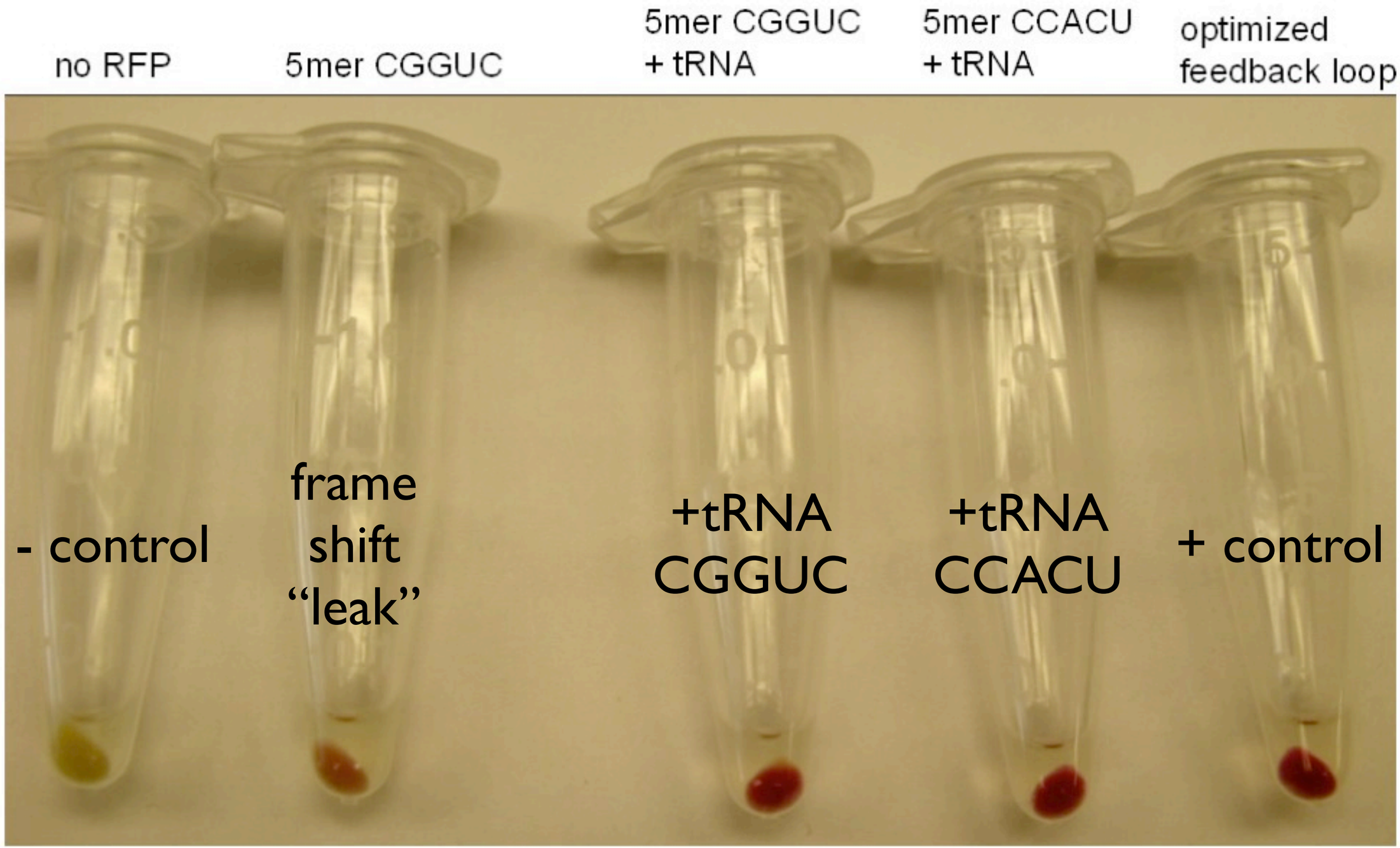
ATG NNN NNg NNN → no satisfaction

Redesign System v2.0

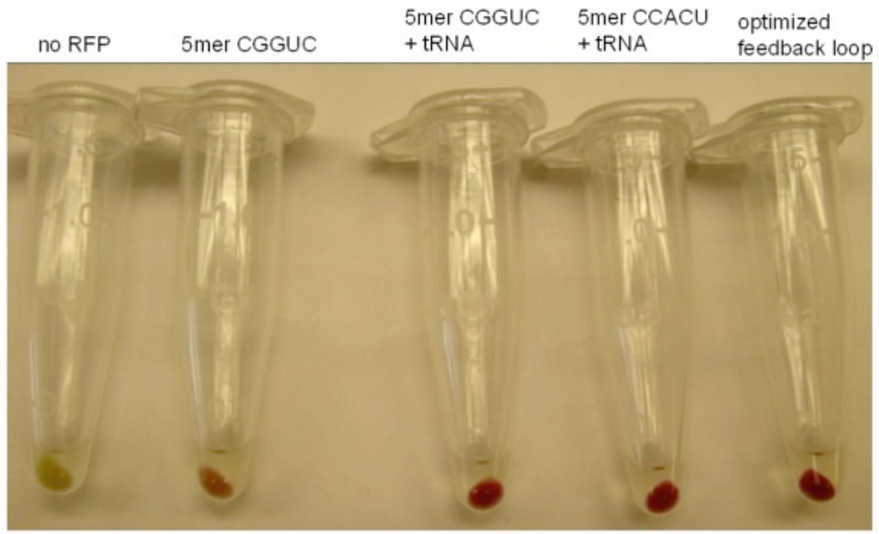


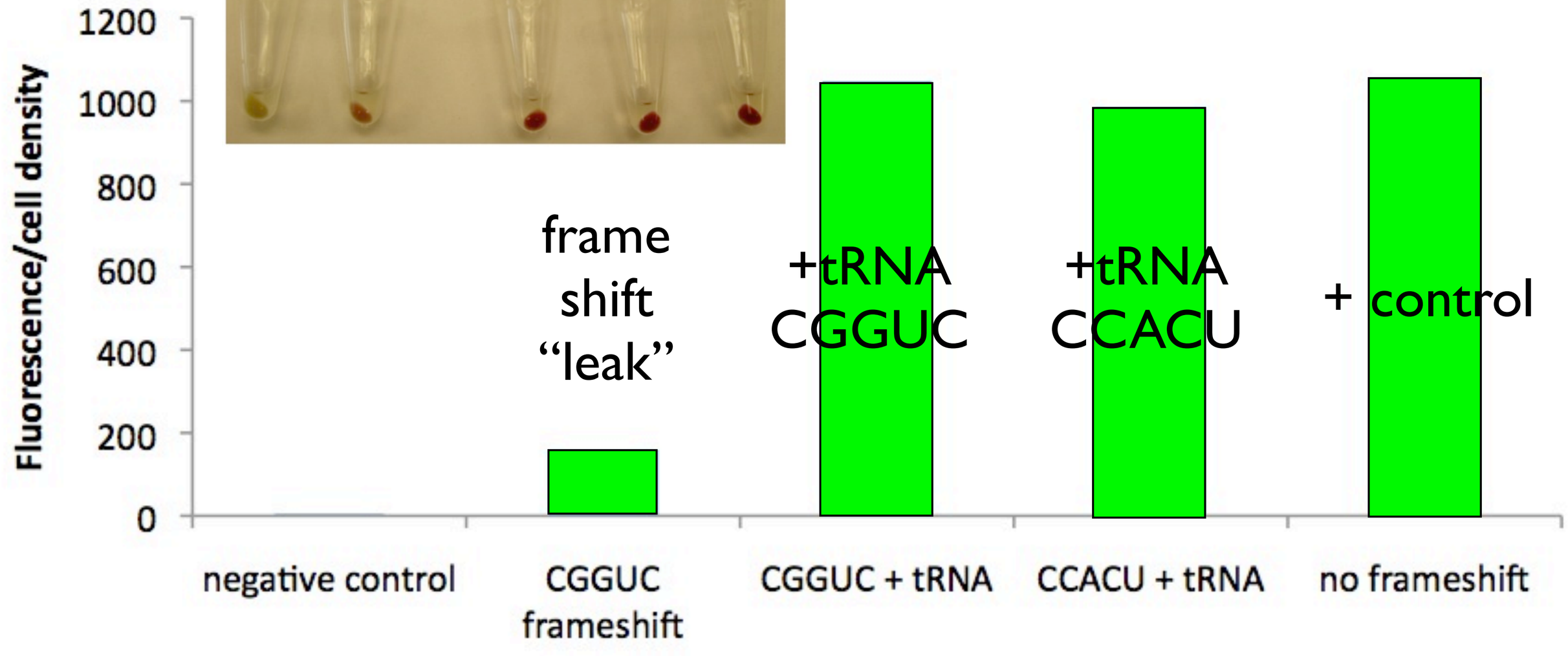


Outcomes of v 2.0

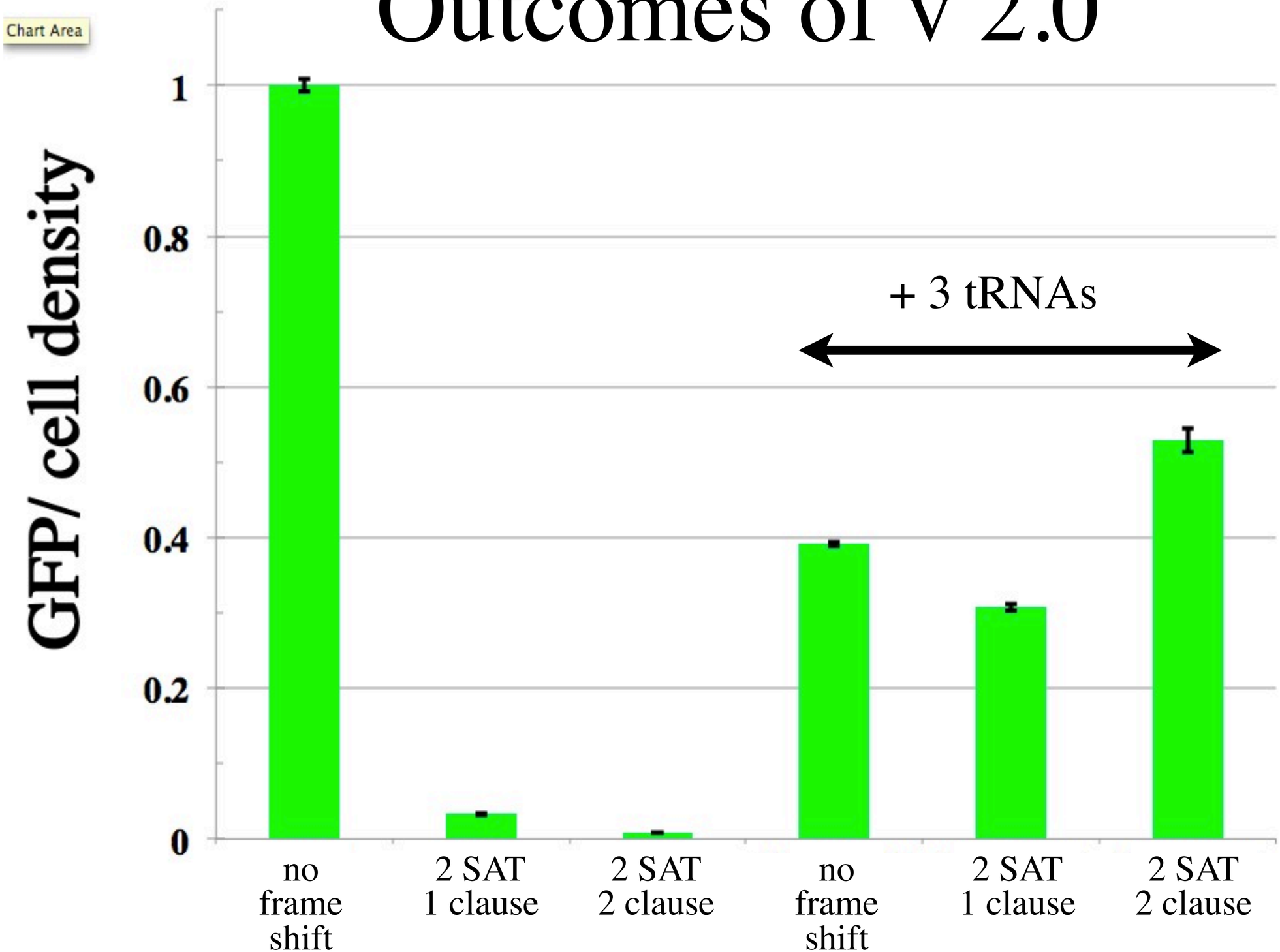


Outcomes of v 2.0





Outcomes of v 2.0

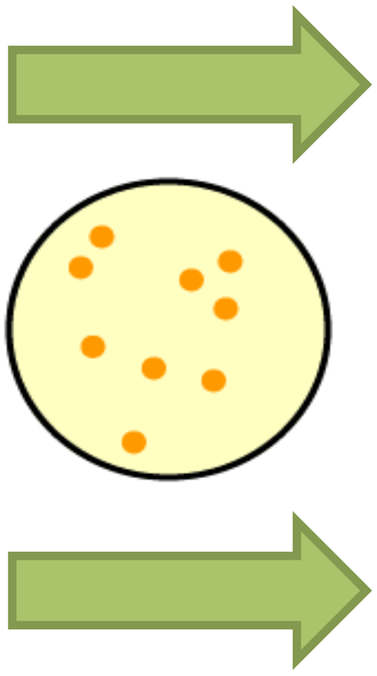


Can we build a bacterial cryptographic hash function?

What is a hash function?

HGTf34$2

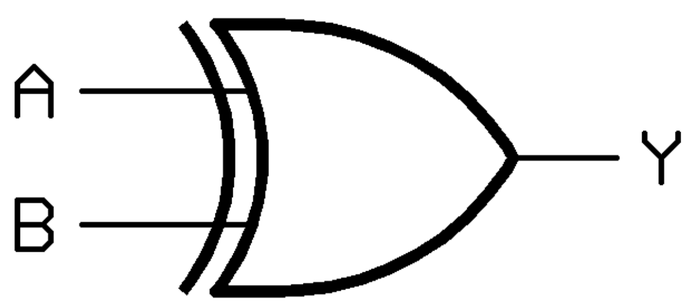
Can Bacteria Perform a Hash Function?



HGTf34$2

Use XOR Logic Gate for Hash Function

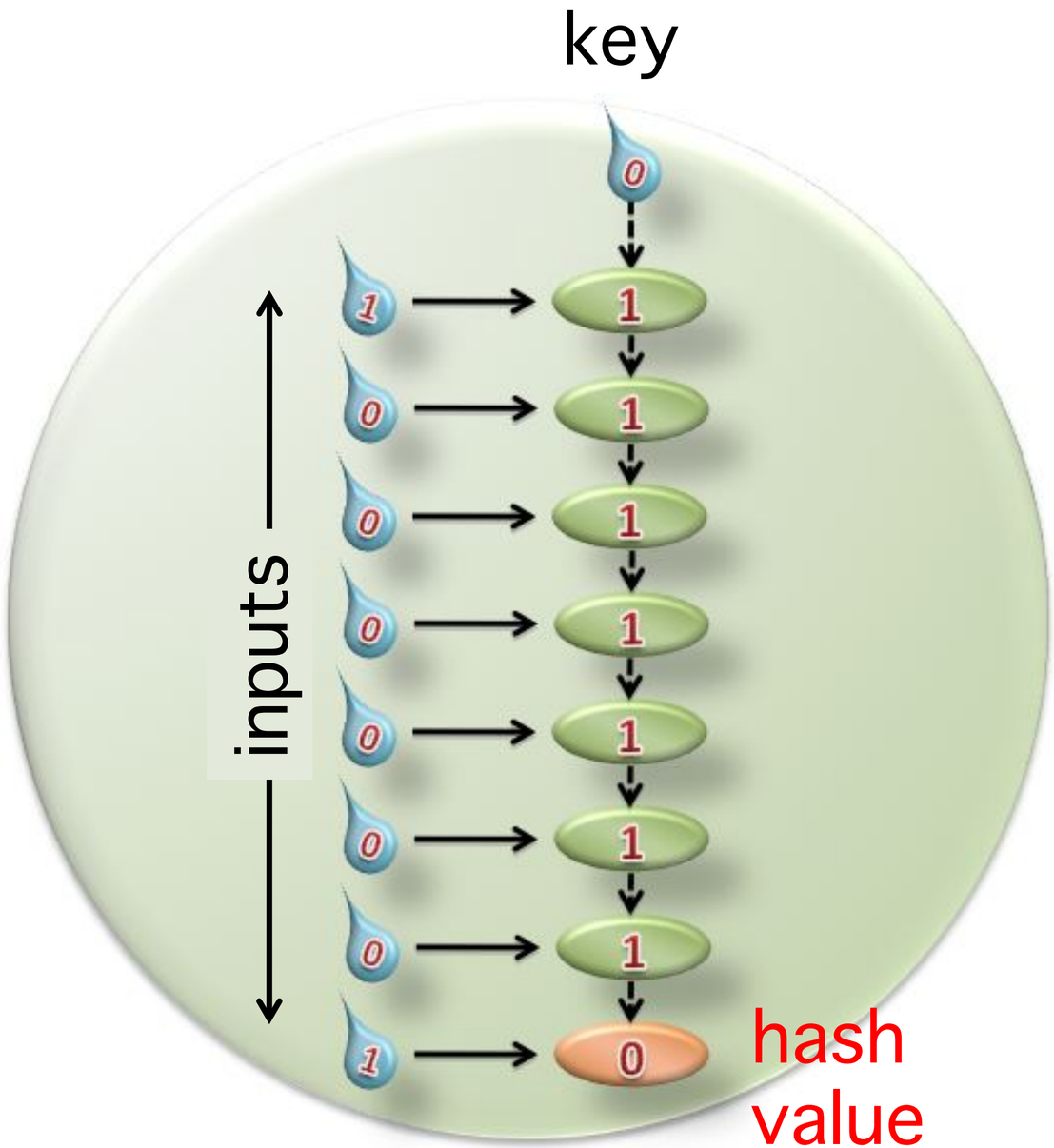
Input 1	Input 2	Output
0	0	0
0	1	1
1	0	1
1	1	0



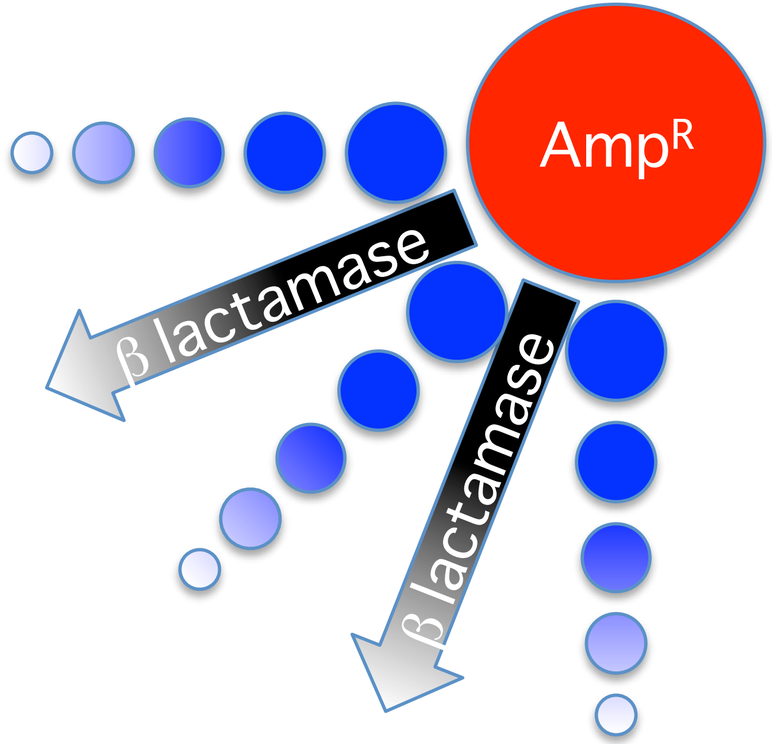
Design Linear Bacterial Hash Function

CAB = 010000001

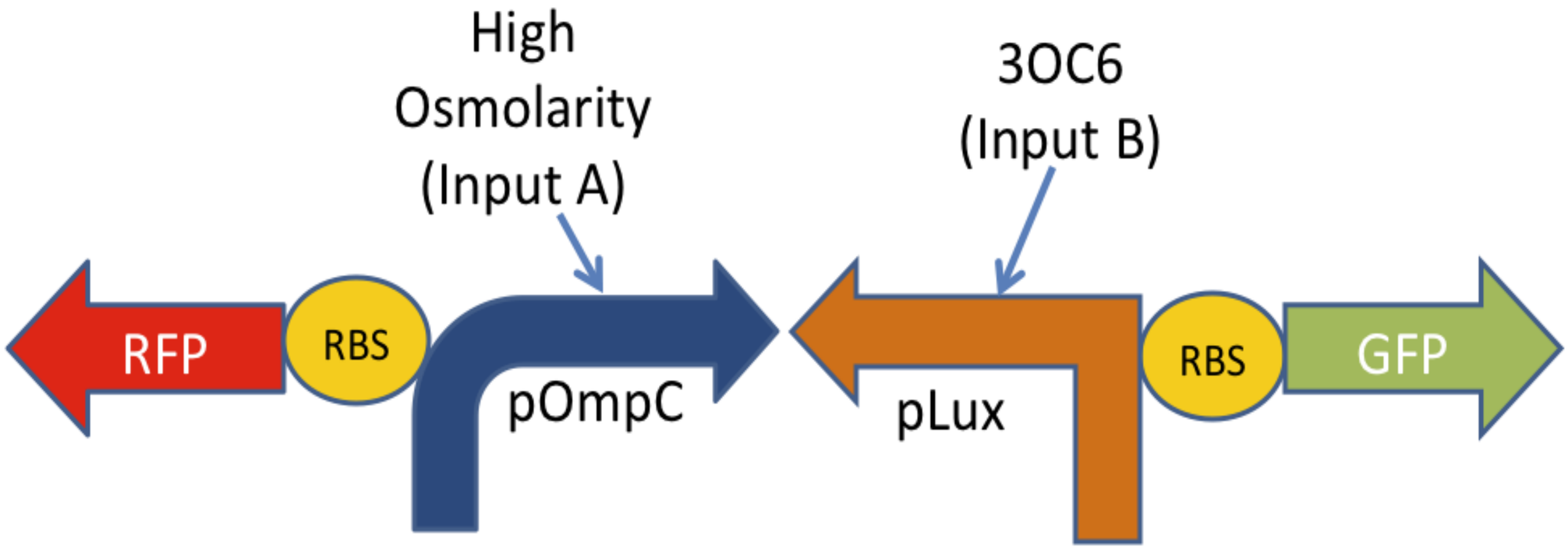
HASH VALUE = 0



Time-Delayed Bacterial Growth

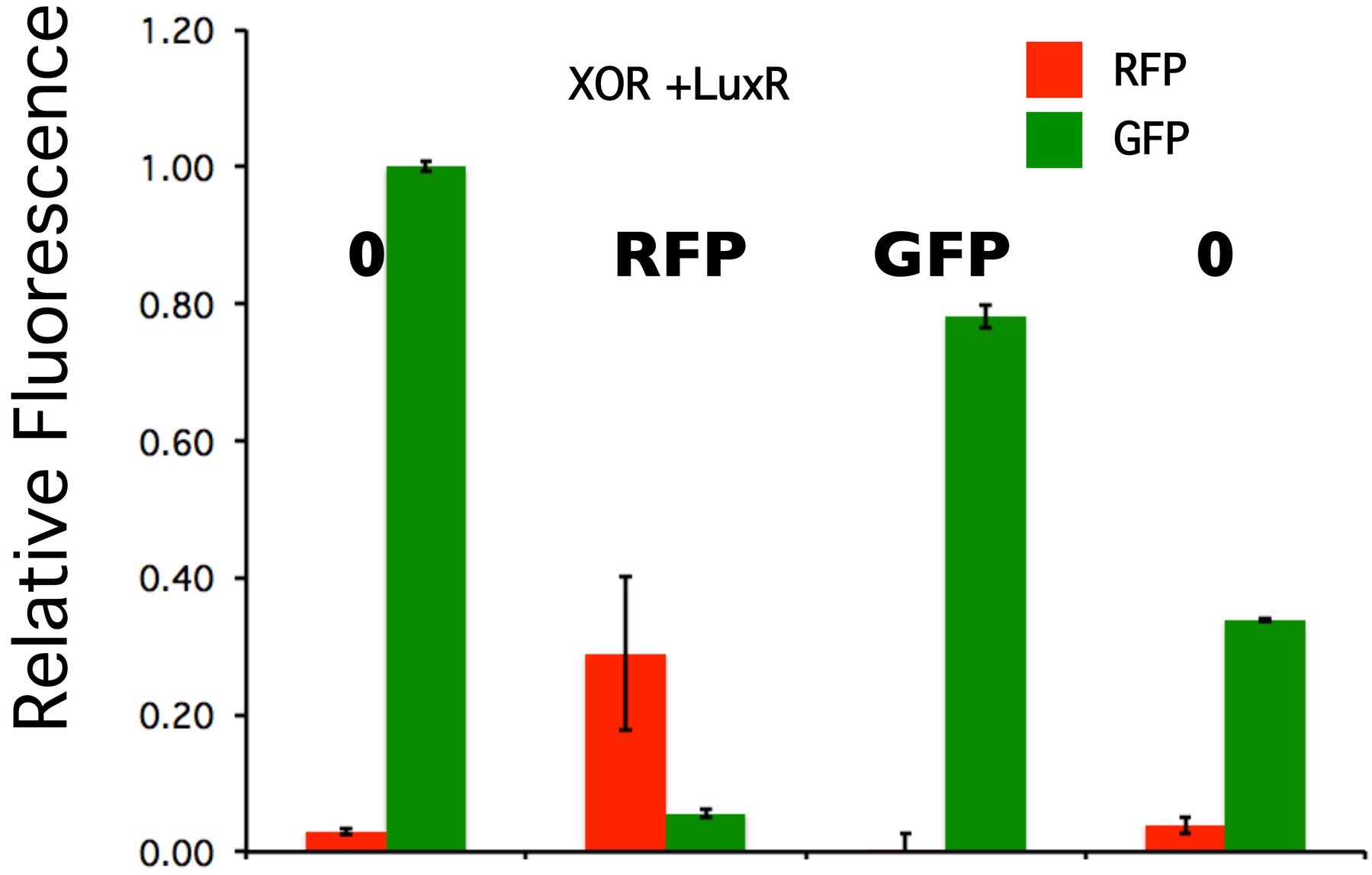


DNA-based XOR Logic Gate



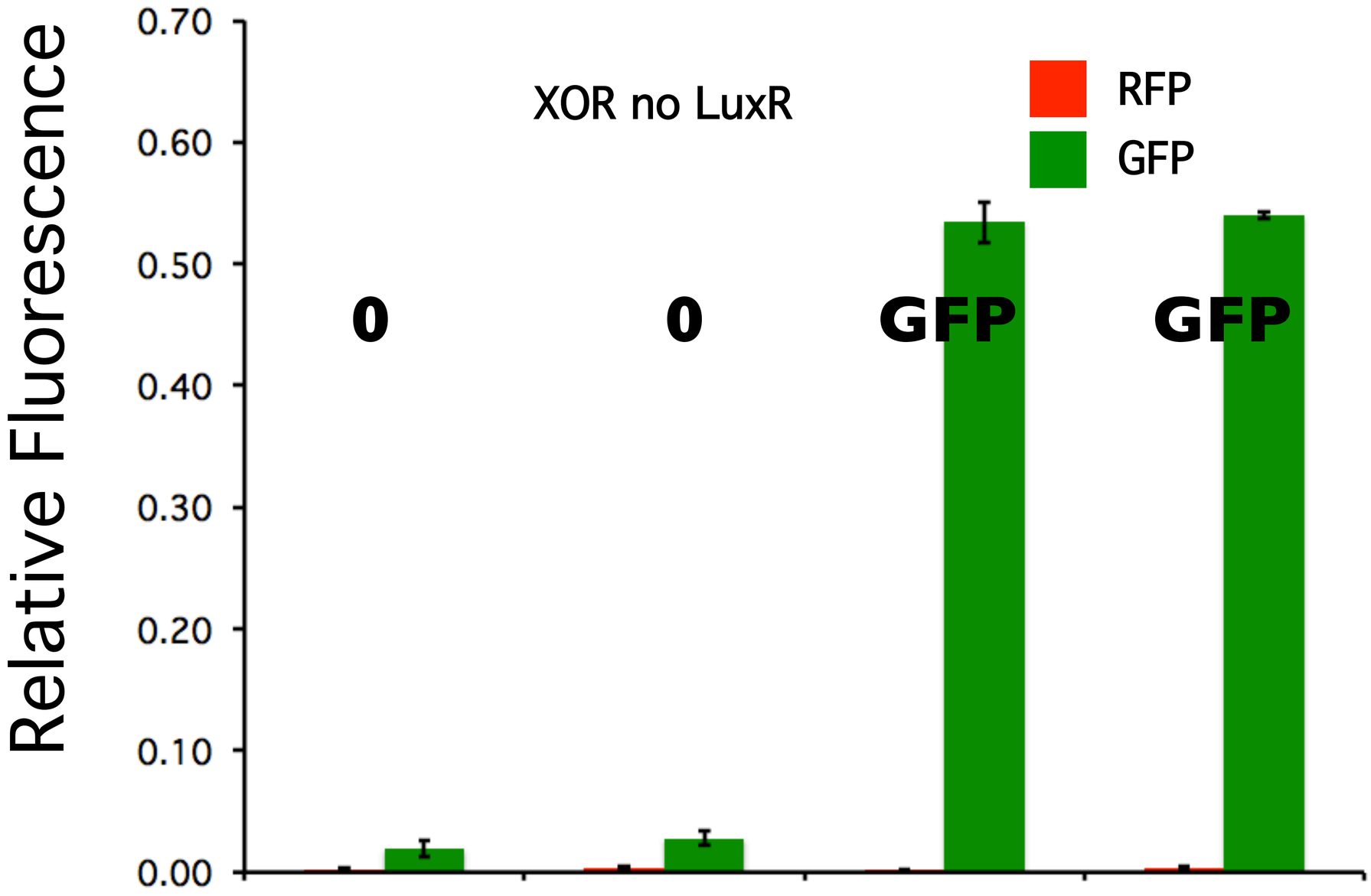
High Osmolarity (Input A)	3OC6 (Input B)	Fluorescence (Output)
0	0	0
1	0	1 (GFP)
0	1	1 (RFP)
1	1	0

Testing Bacterial XOR Logic Gate



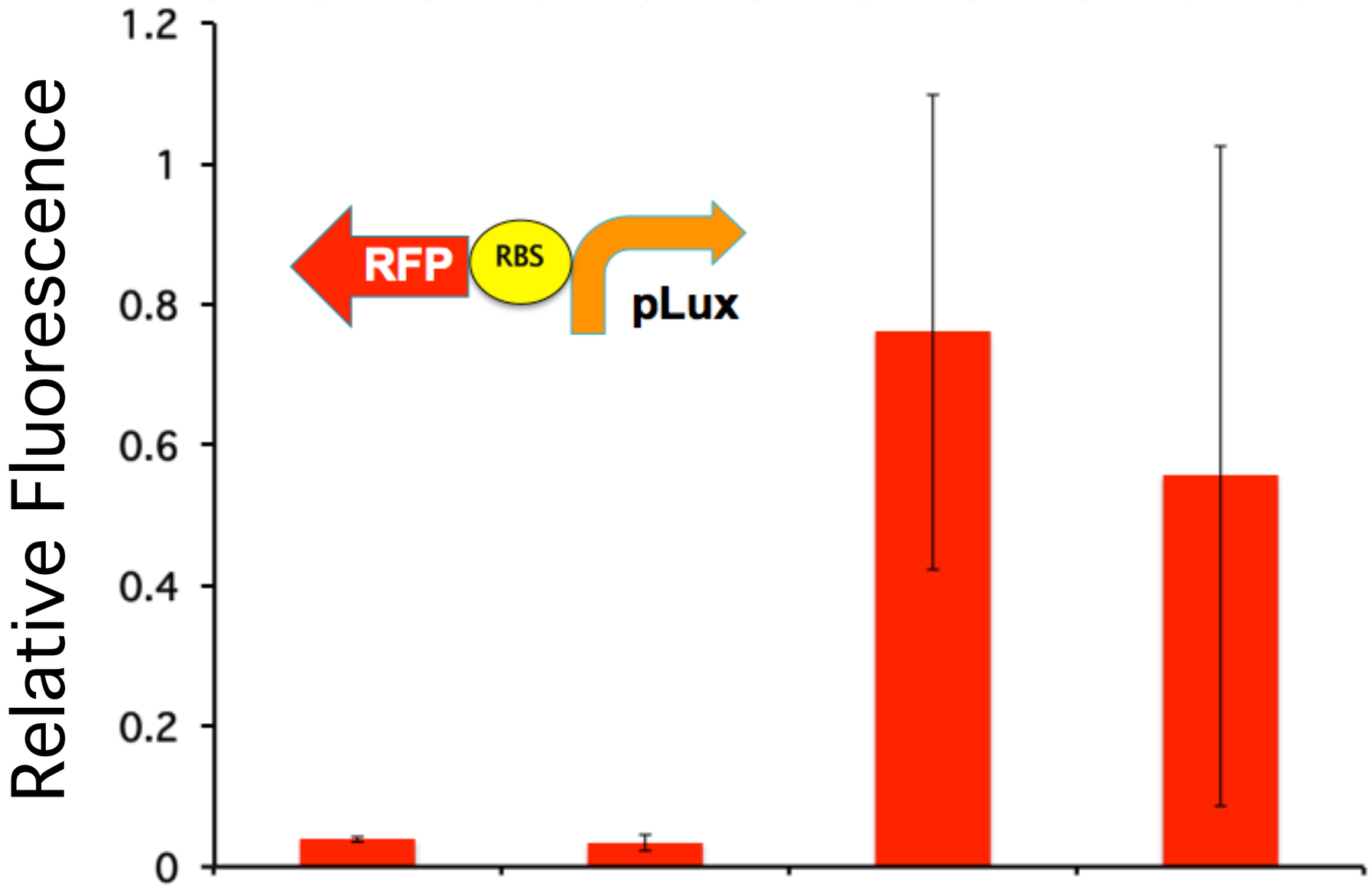
LB	-	-	+	+
3OC6	-	+	-	+

Why did XOR Gate Fail?



LB	-	-	+	+
3OC6	-	+	-	+

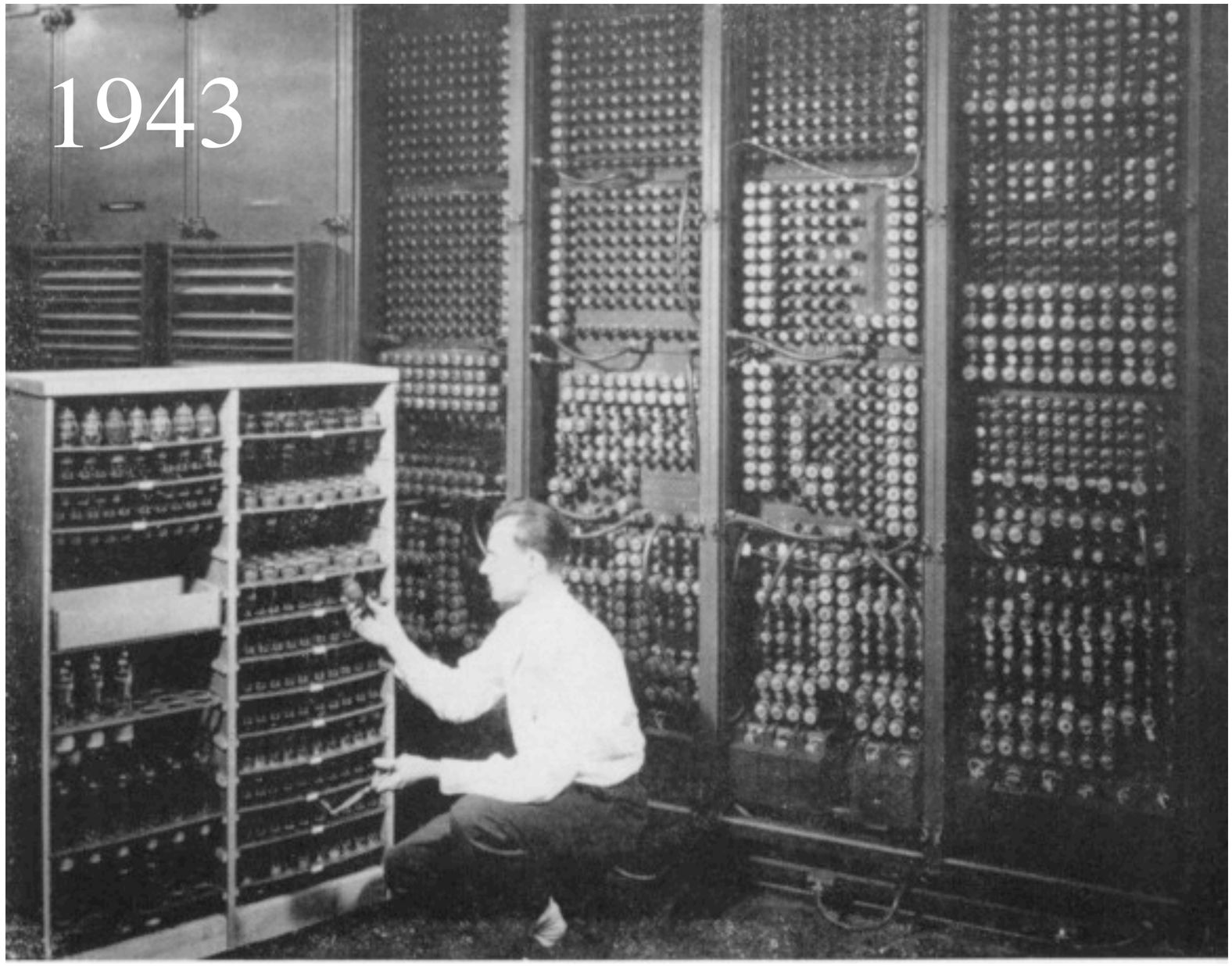
pLux + LuxR Promotes Backwards



LuxR	-	-	+	+
3OC6	-	+	-	+

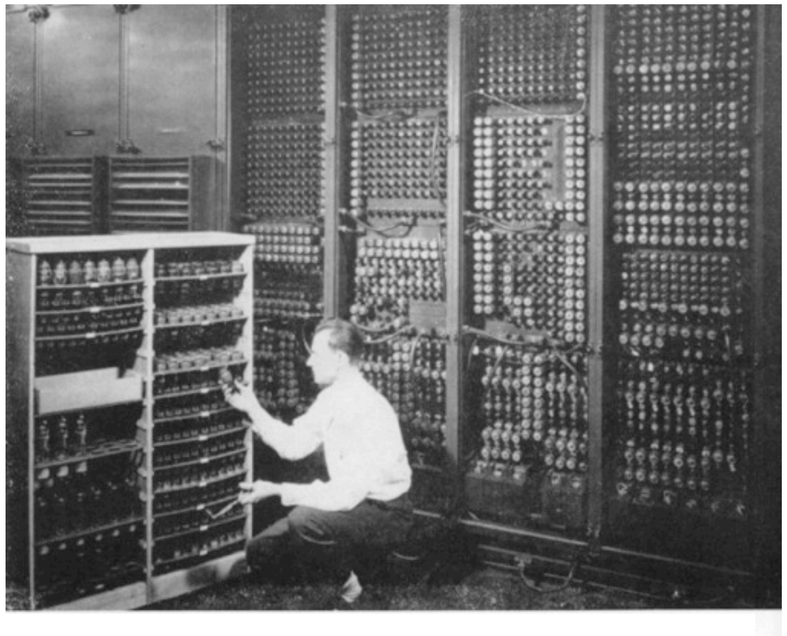
Why build bacterial computers?

Evolution of Computers



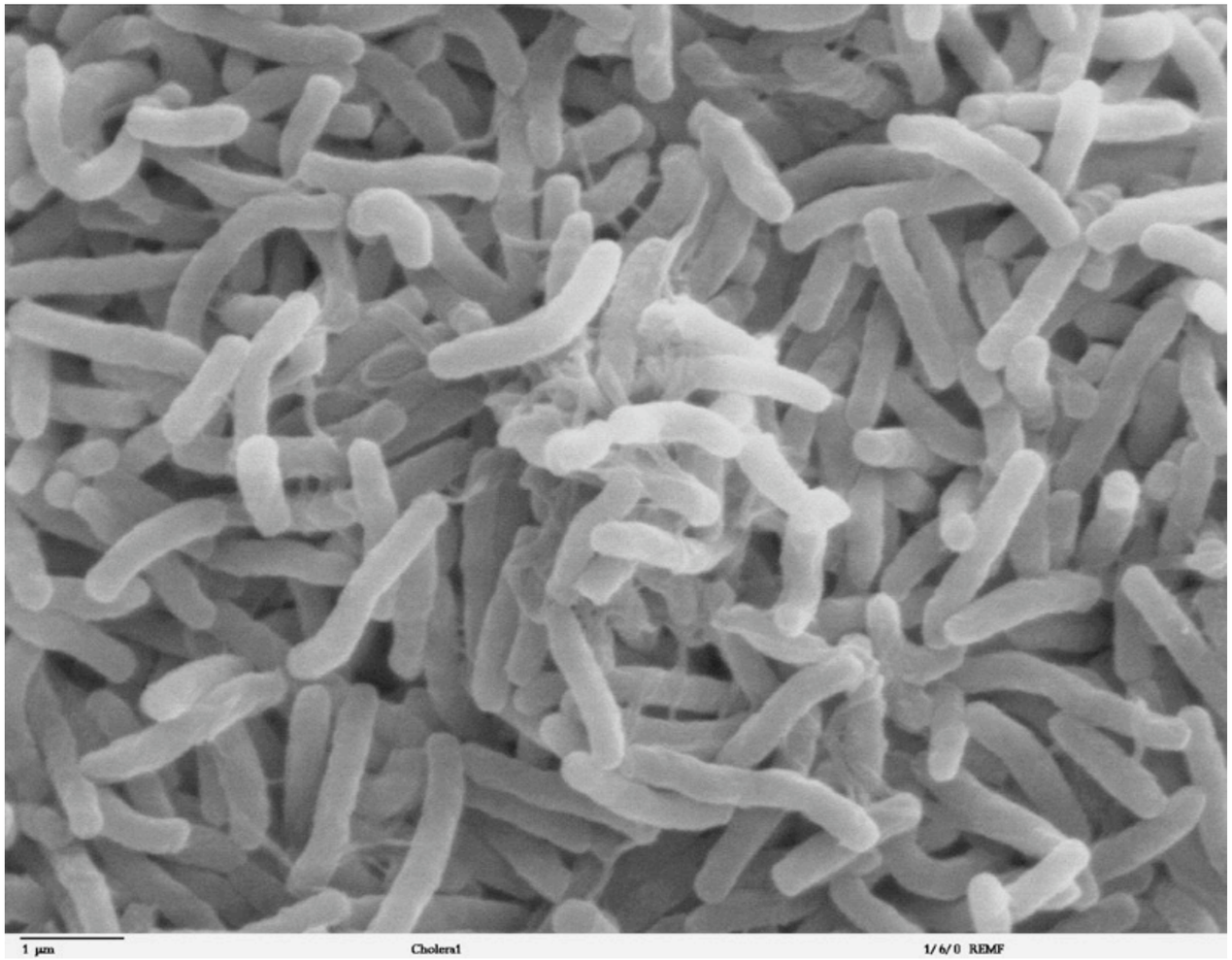
Evolution of Computers

iPhone in 2011



Evolution of Bacterial Computers

E. coli in 2011



?

Living Hardware in 2021

Increased Student Diversity

56 undergraduates in 7 years

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

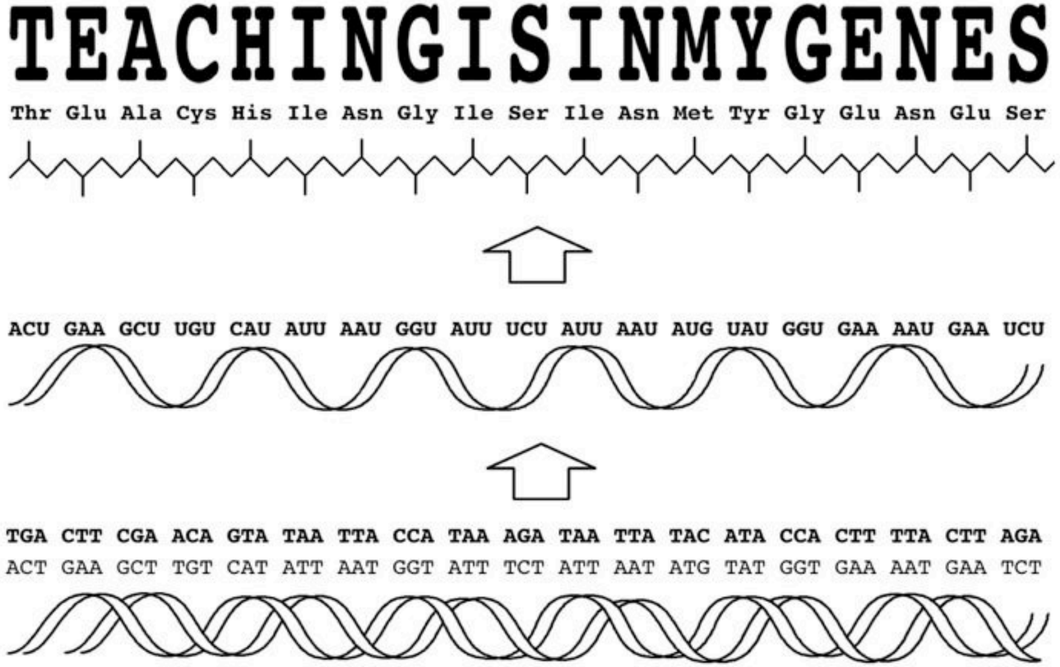
PhD	Dual degree	MD	MPH	Jobs		at DC
13	2	2	3	5	7	27

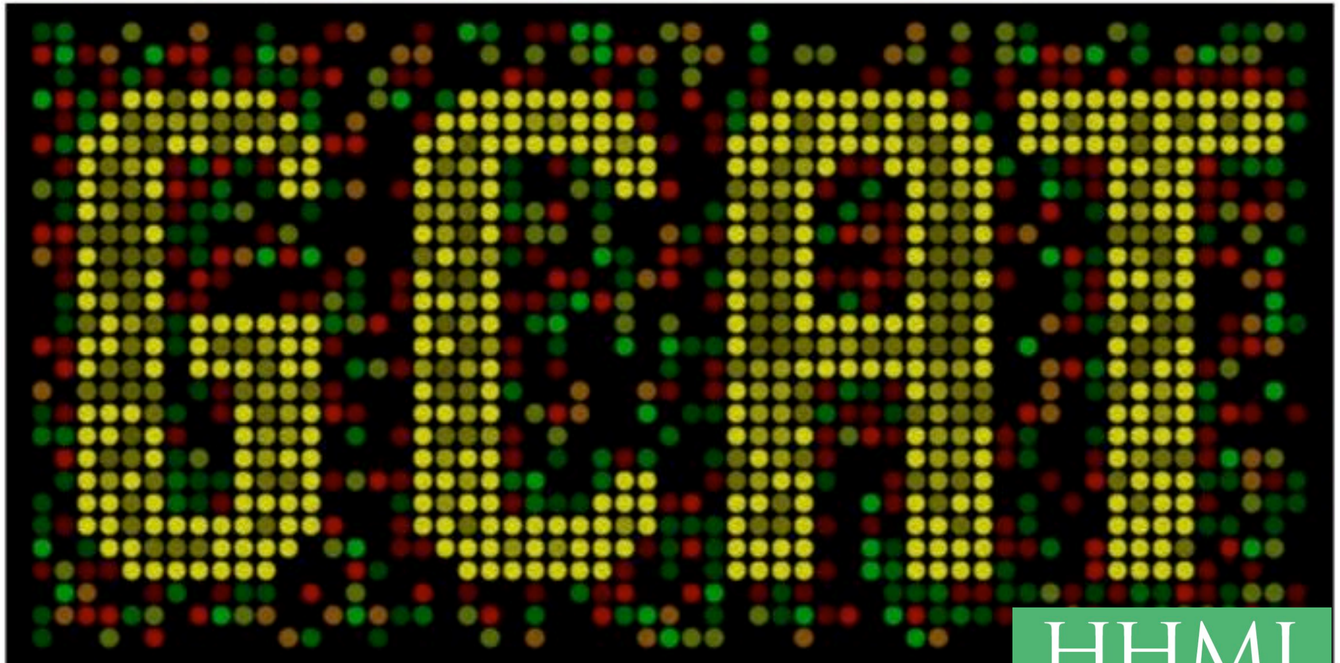
campus: 74% Caucasian

biology majors: 87% Caucasian

GCAT Faculty Workshop
Synthetic Biology

20 pairs of faculty
1 Bio + 1 Other
pending at NSF





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**

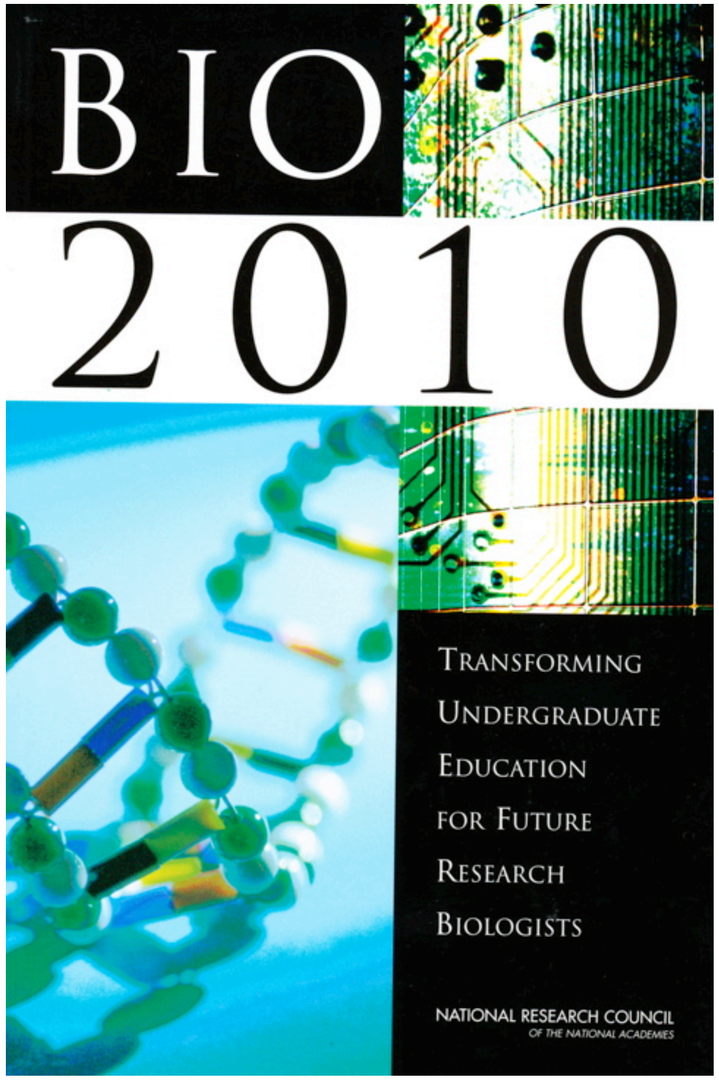
If we currently cover all the important stuff….

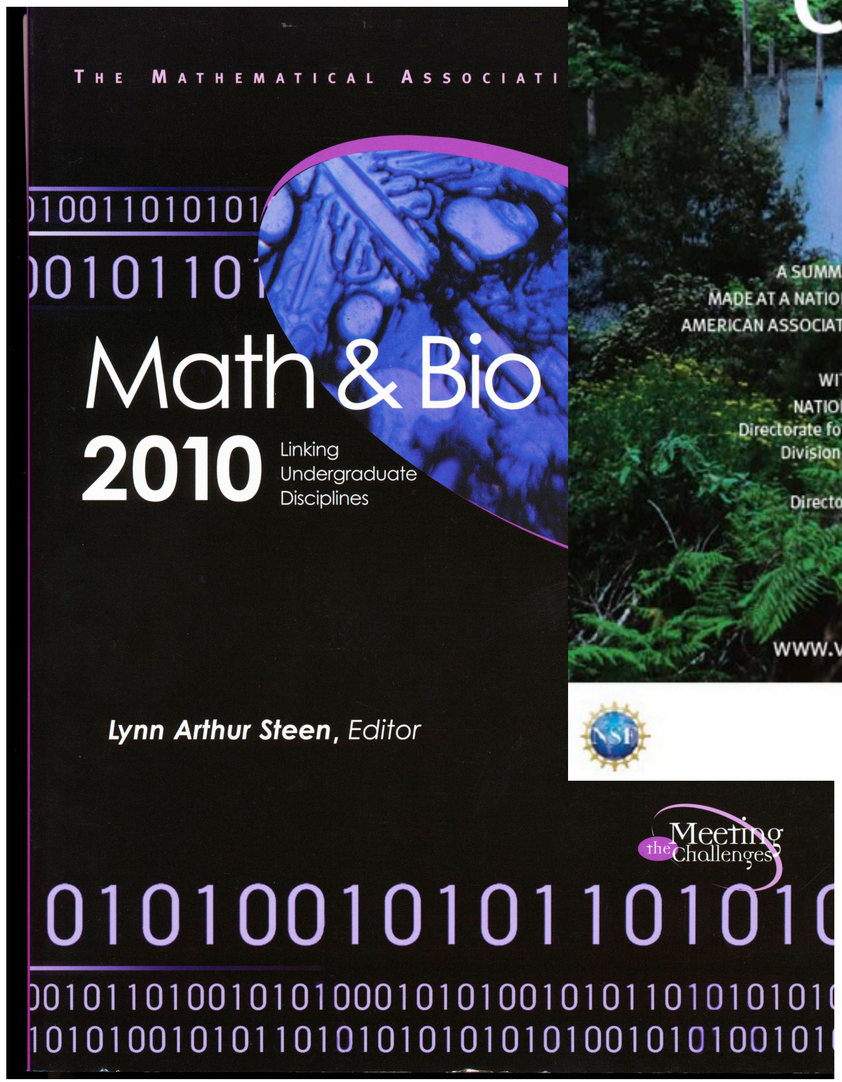
…how can we add more content?

Too much content for the containers

Too much content for the containers

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

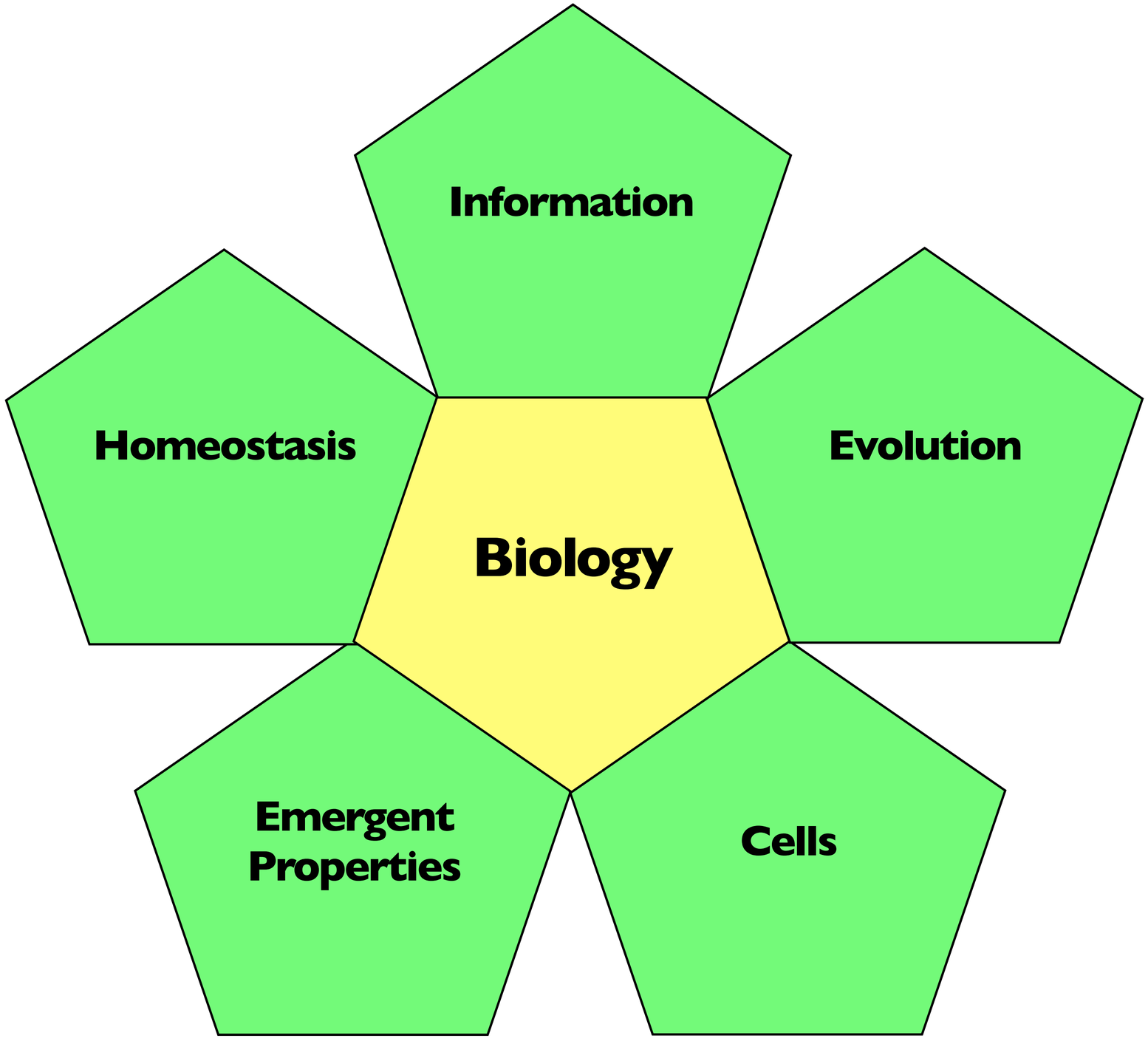
Cellular

Organismal

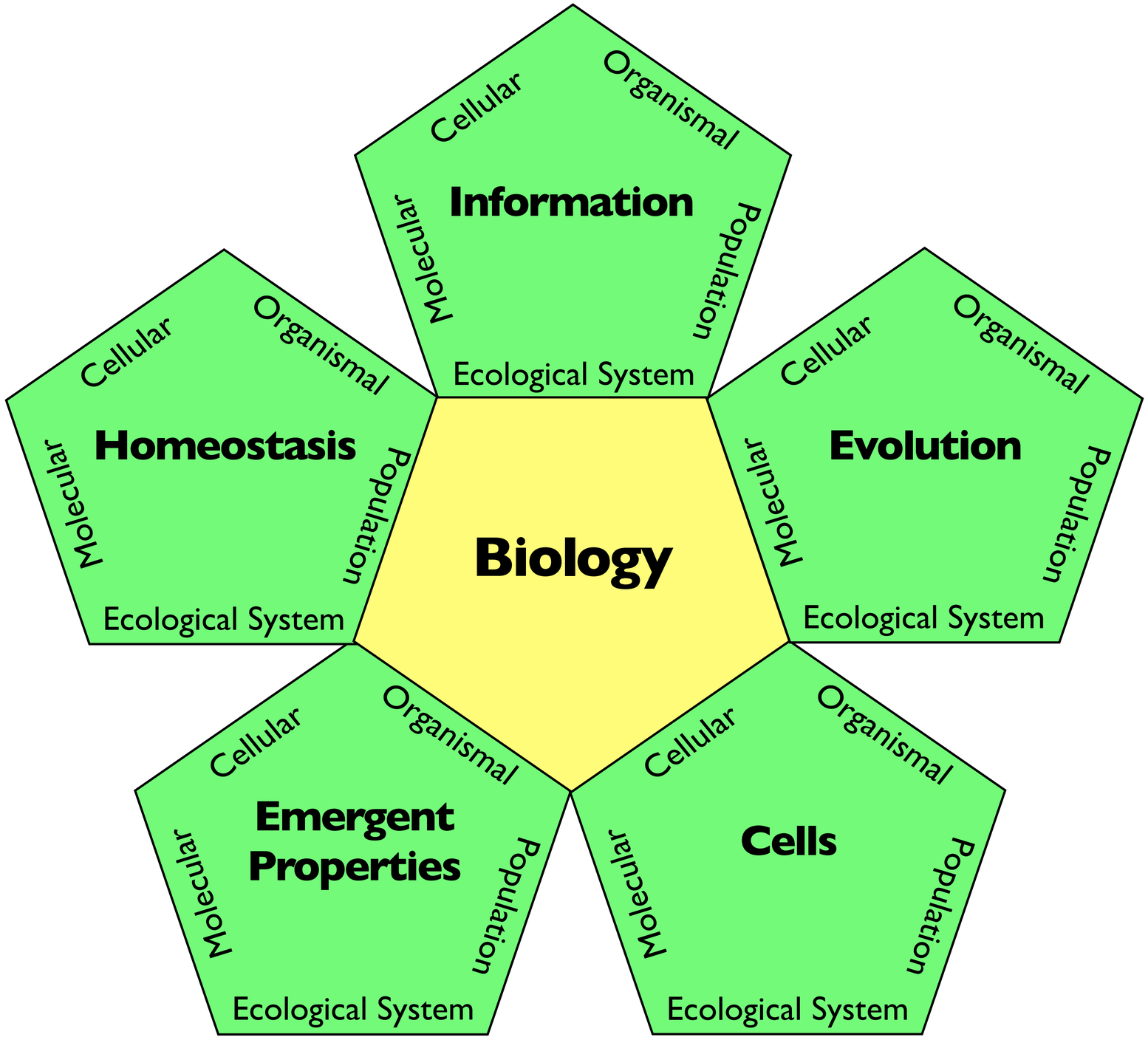
Population

Ecological System

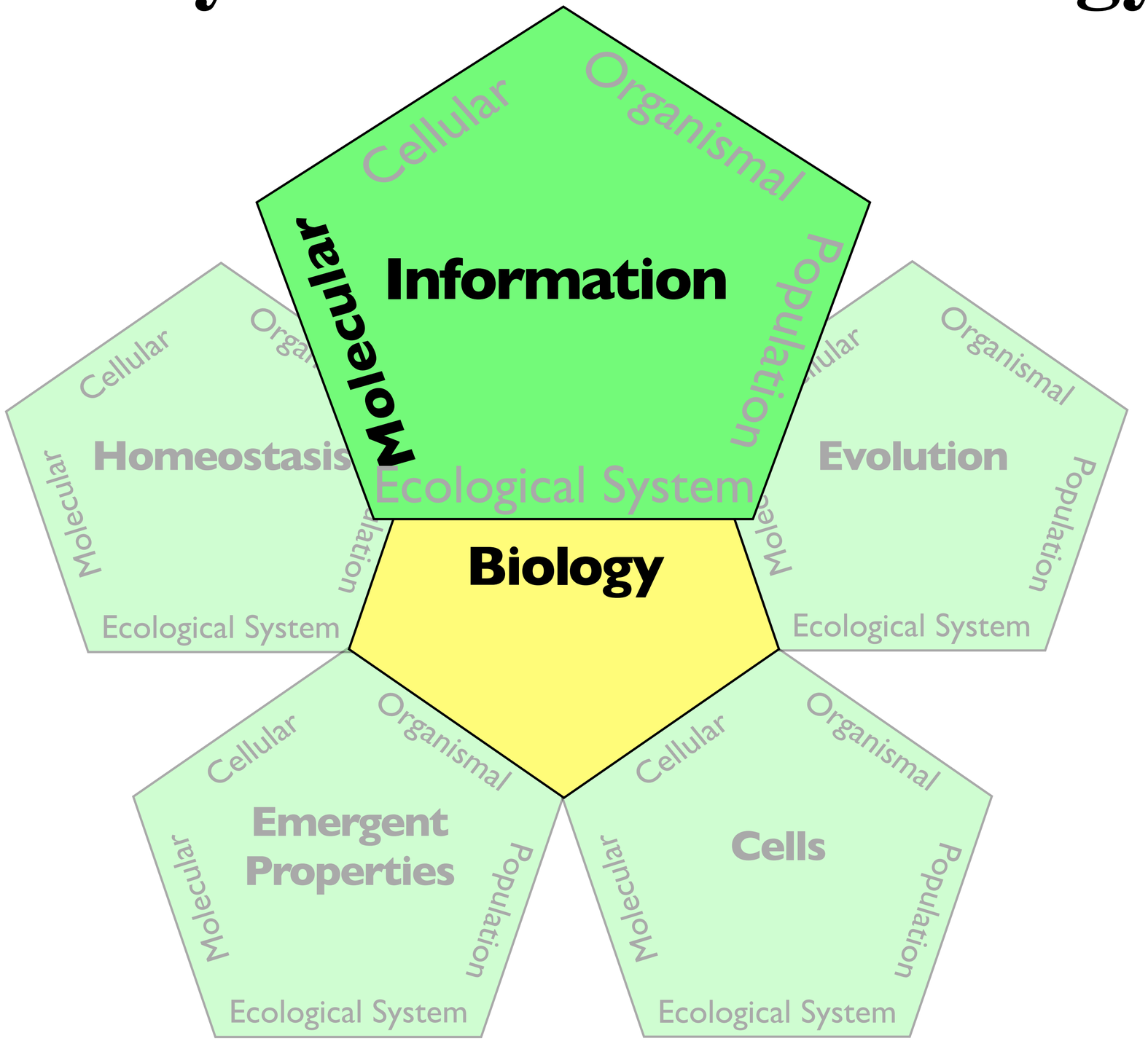
Five Big Ideas of Biology



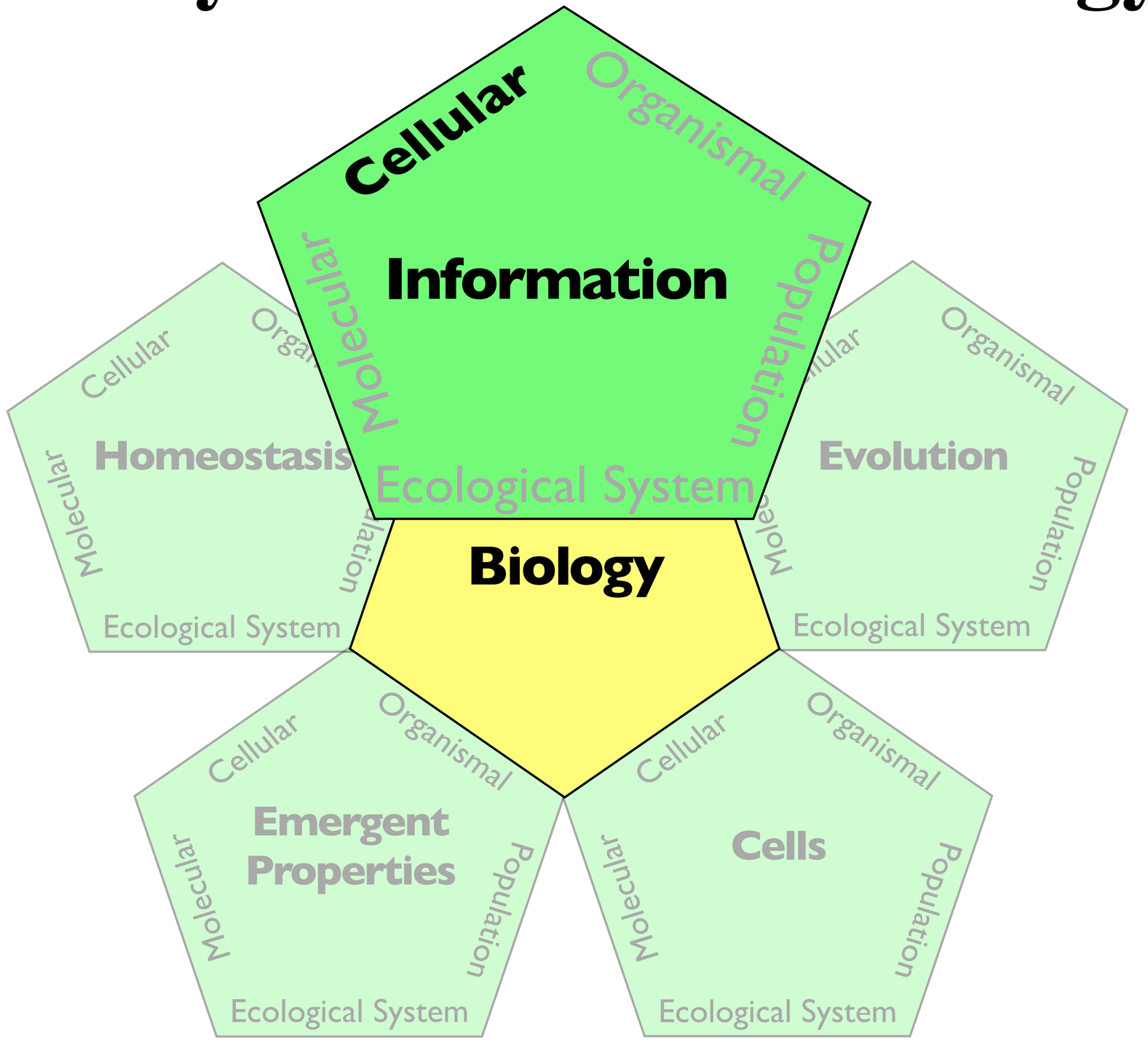
Five by Five Matrix of Biology



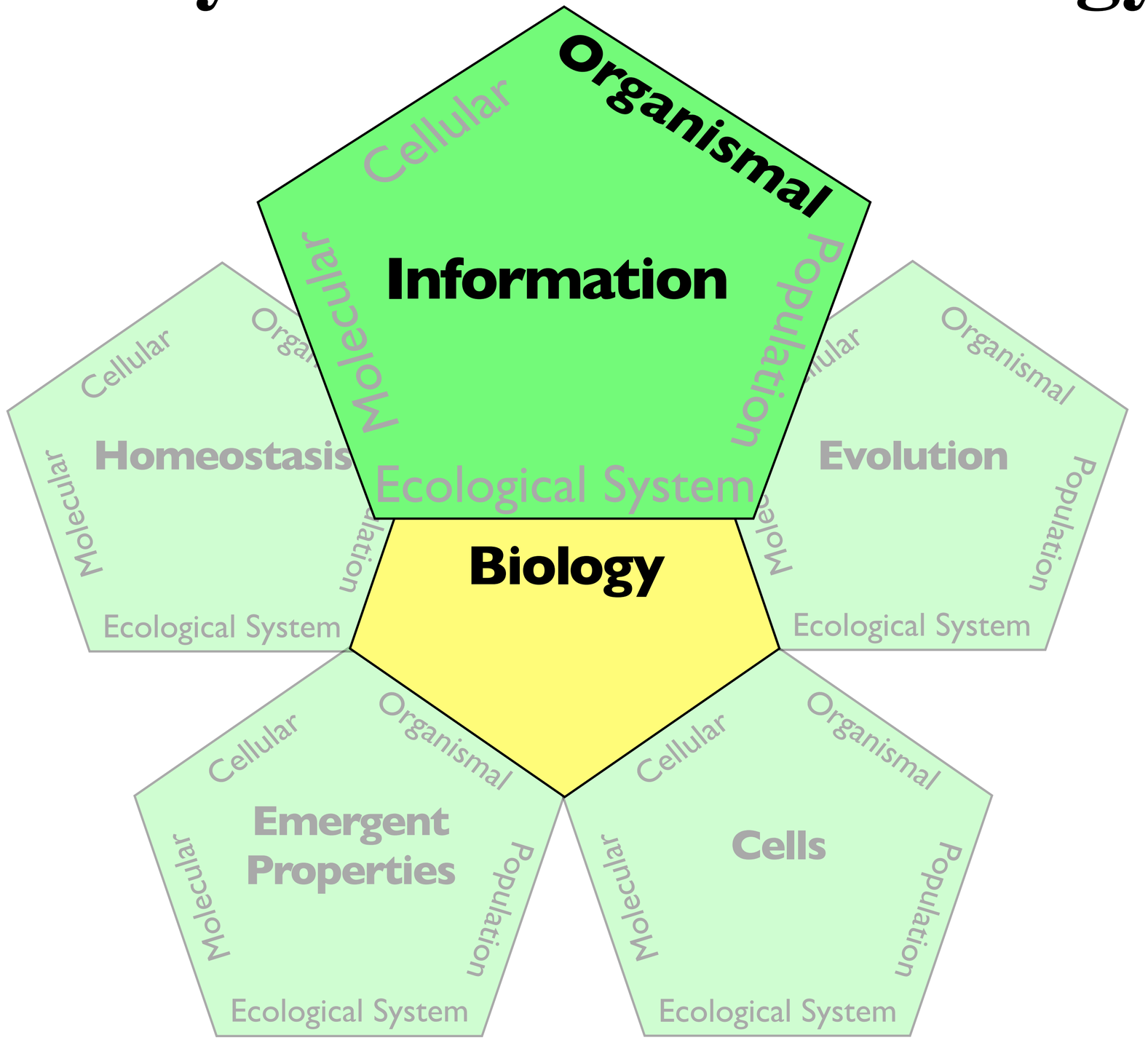
Five by Five Matrix of Biology



Five by Five Matrix of Biology



Five by Five Matrix of Biology



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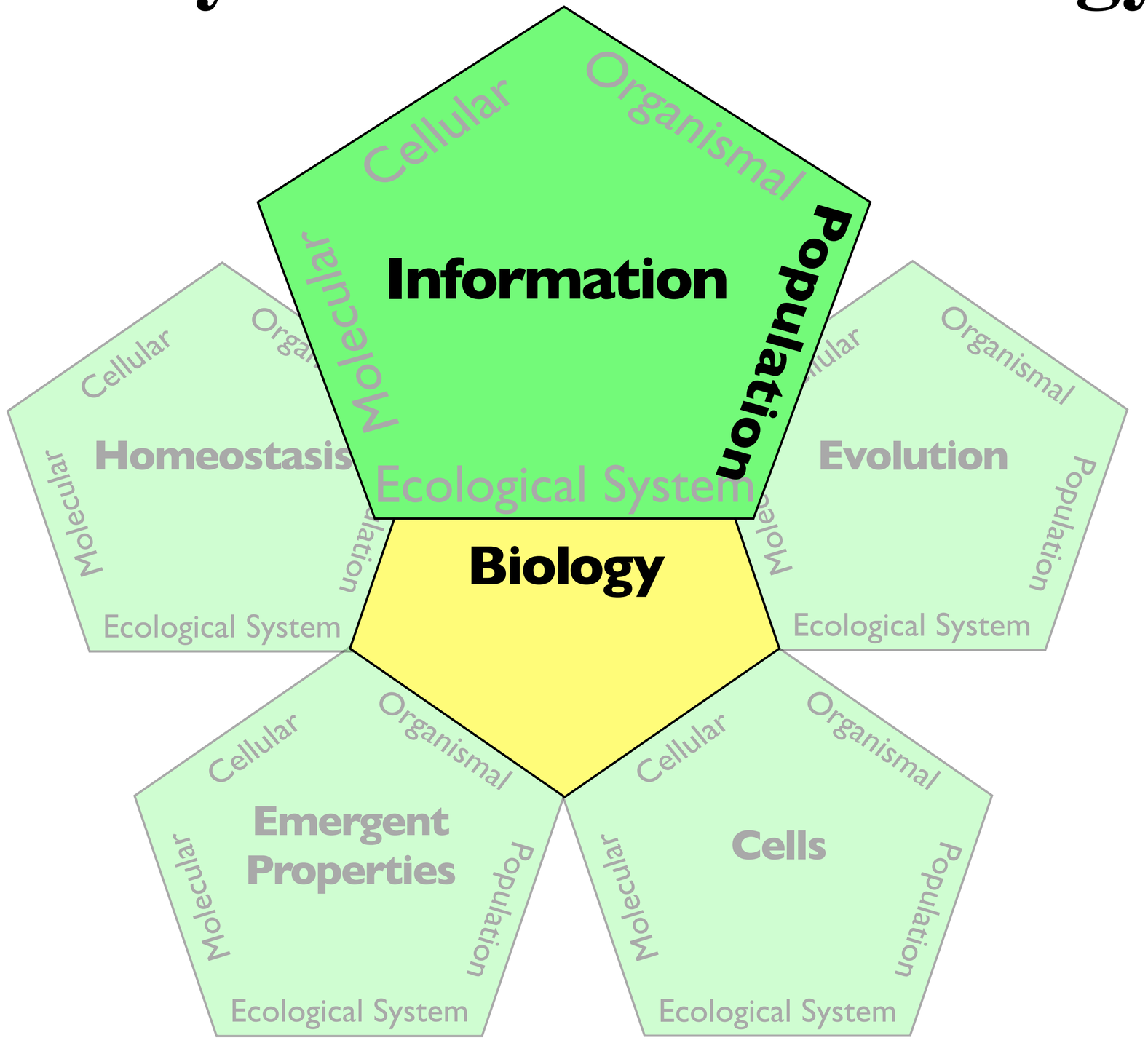
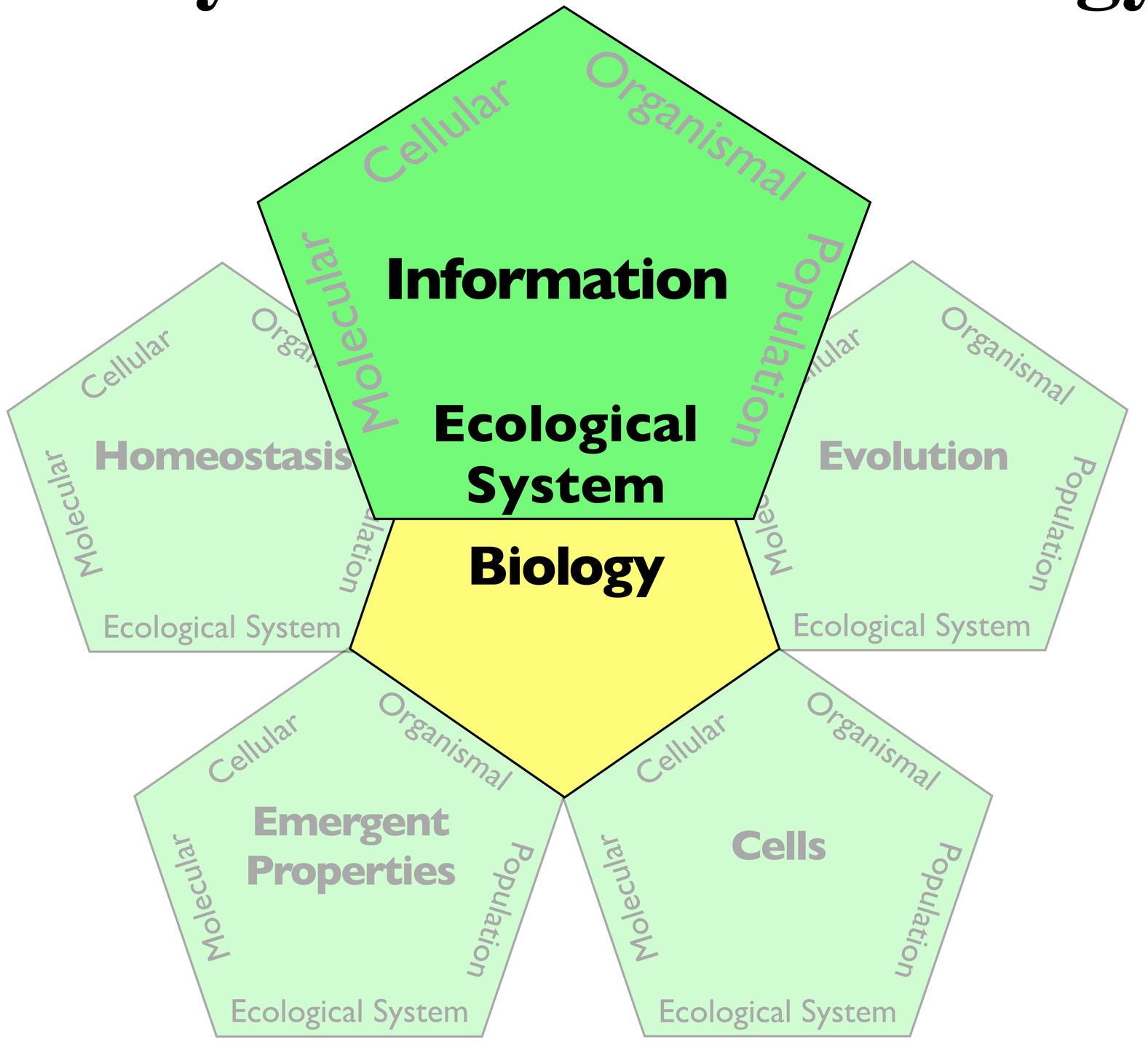
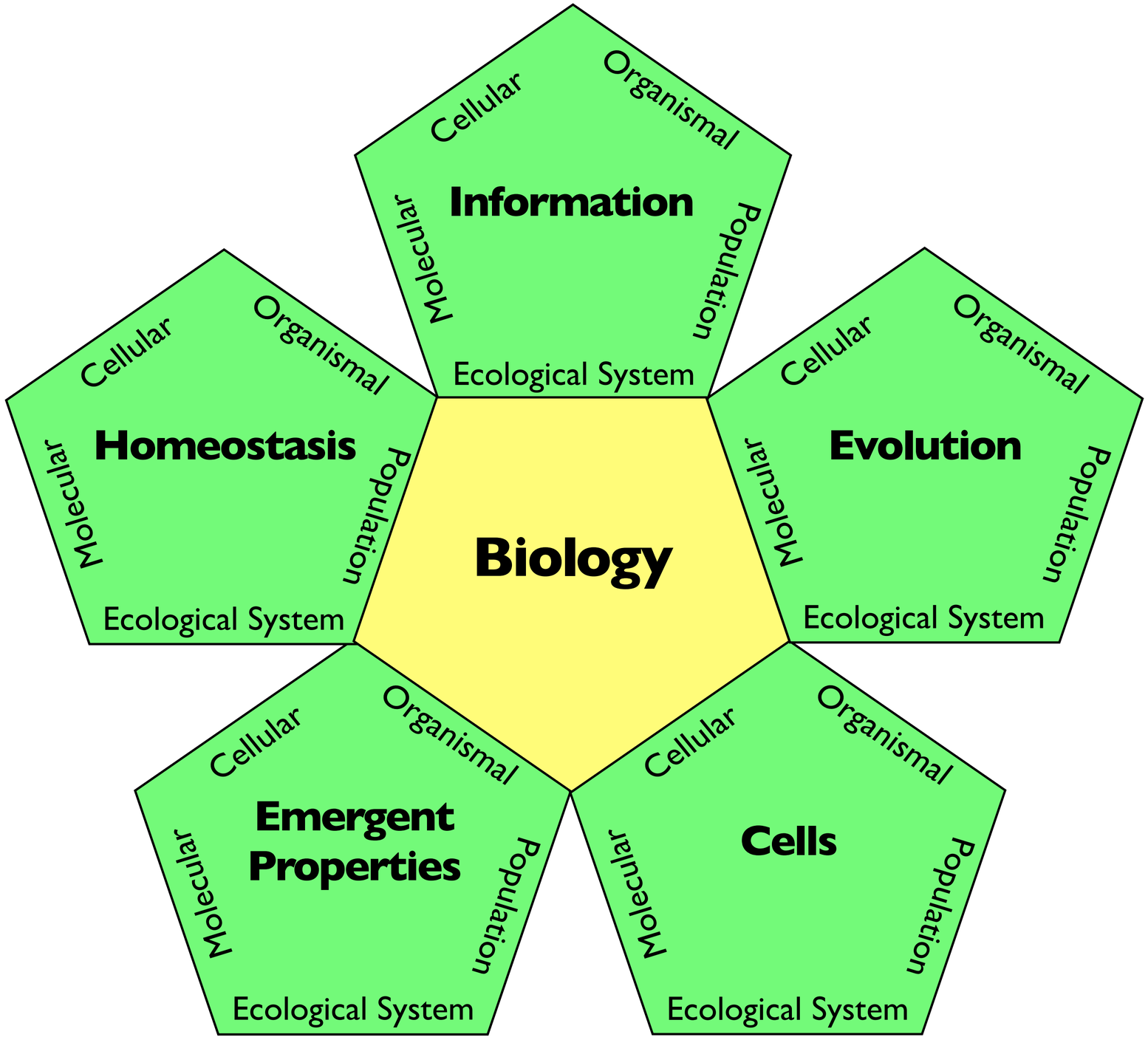


Five by Five Matrix of Biology



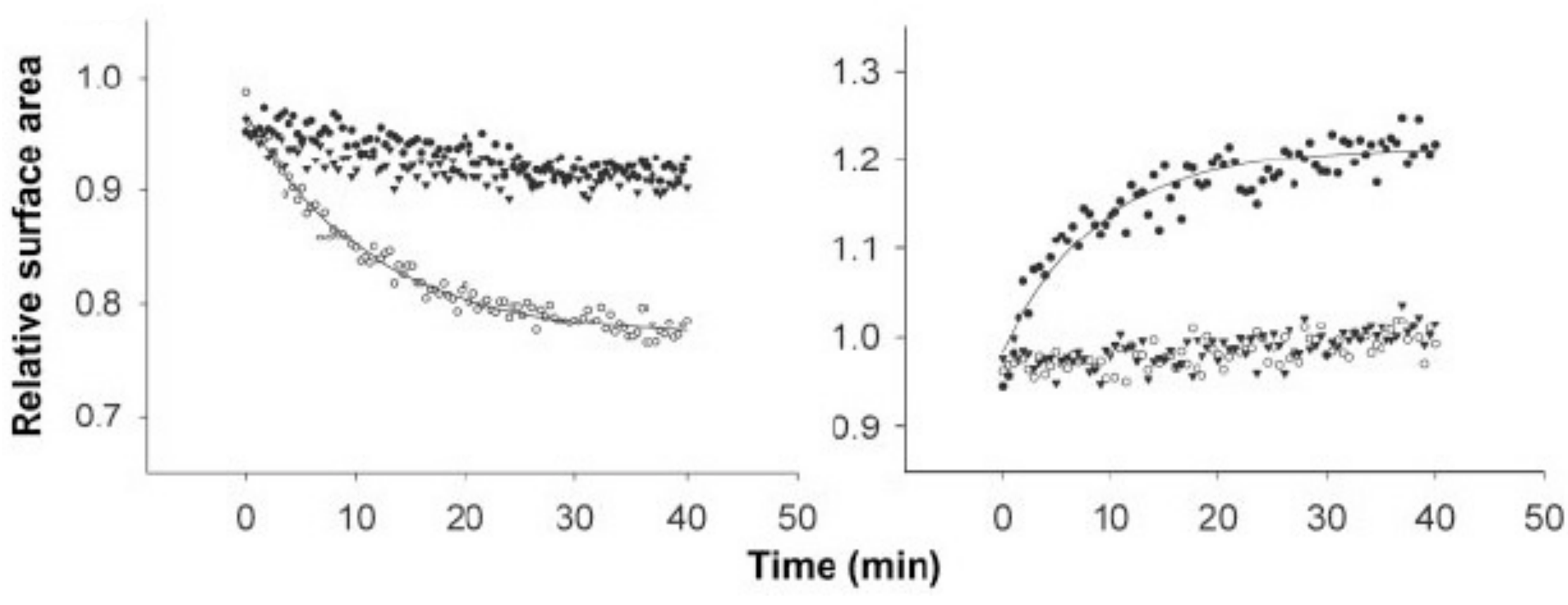
Five by Five Matrix of Biology



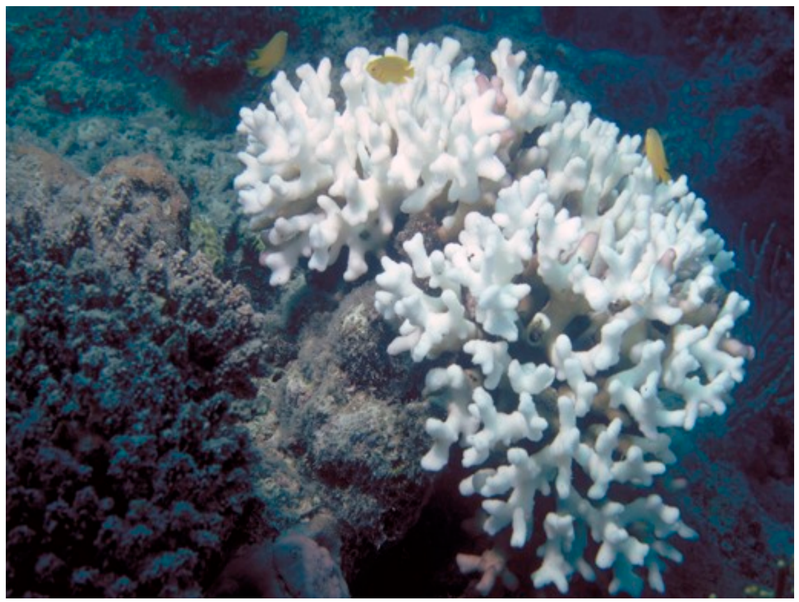
BioMath Explorations

BioMath Exploration 6.3

How can you fit exponential curves to data?



Ethical, Legal and Social Implications

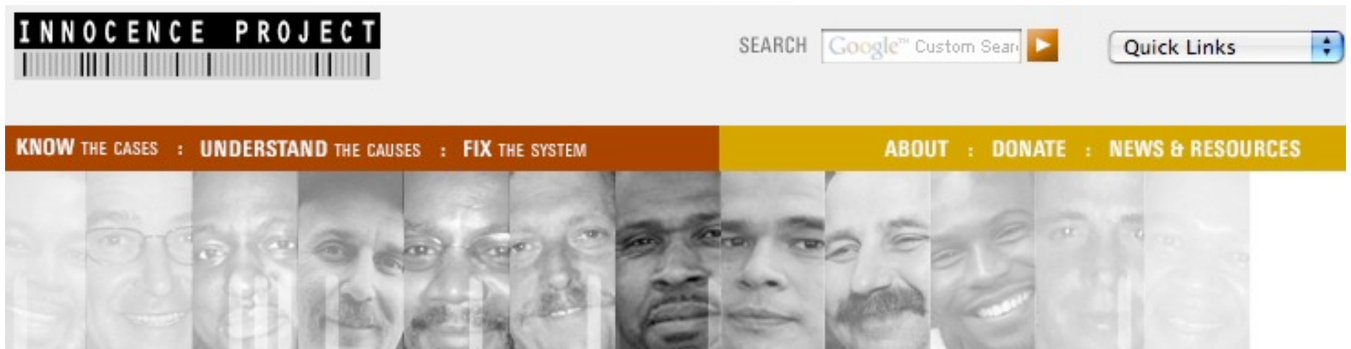


Are religion and evolution compatible?

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

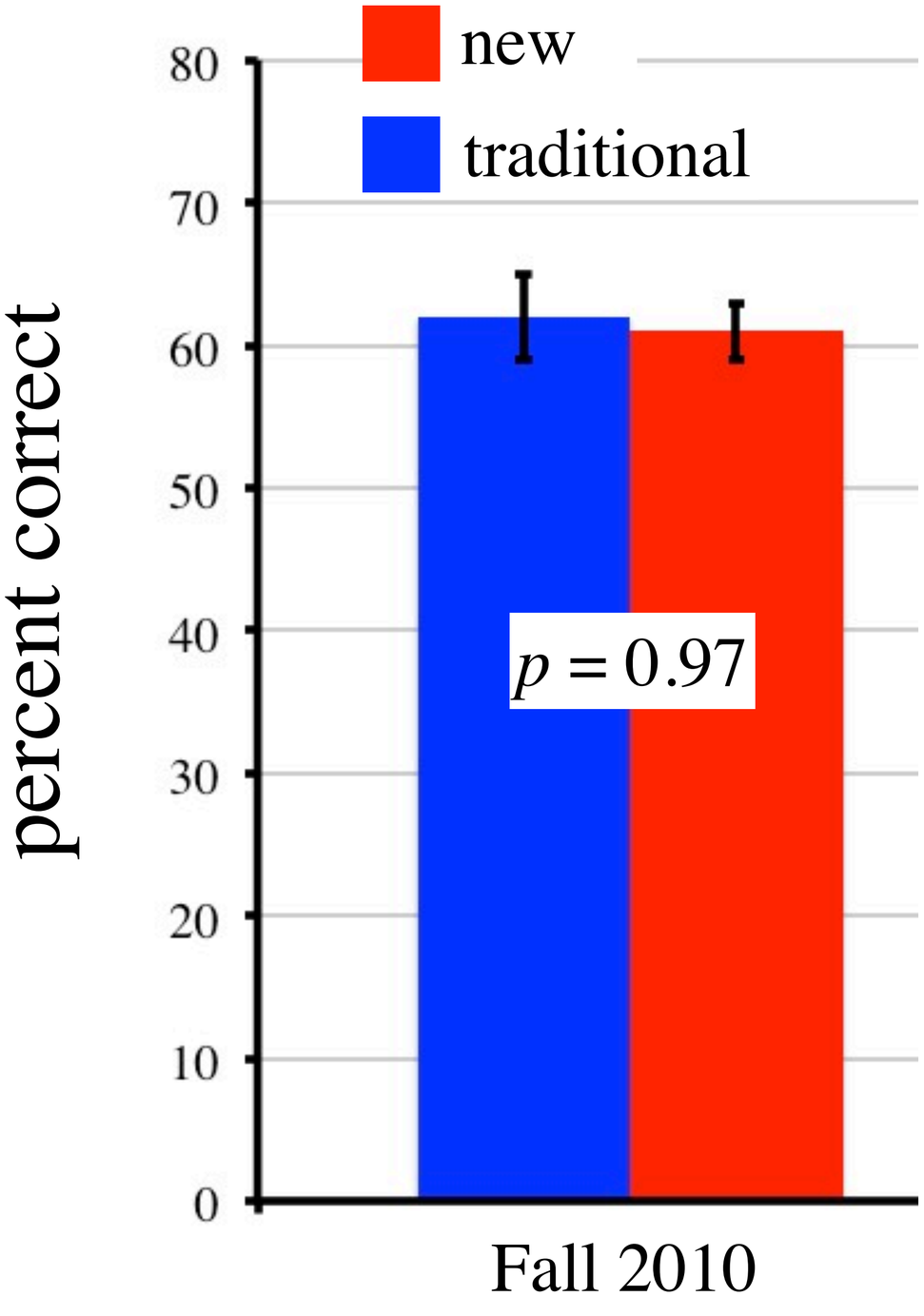
Does basic biology have any impact on the real world?

Who owns your DNA?



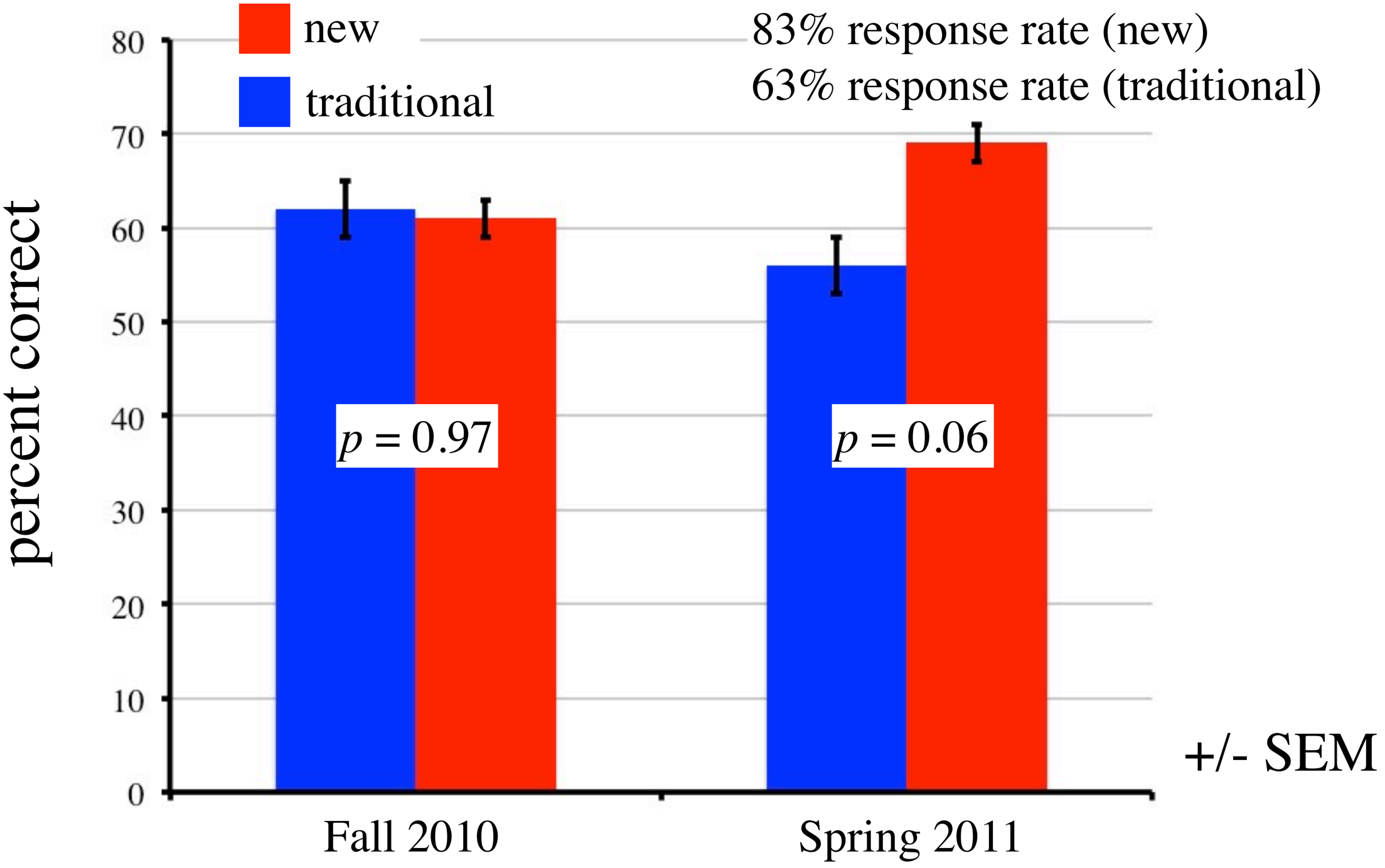
Did my students learn less content?

Student Content Assessment



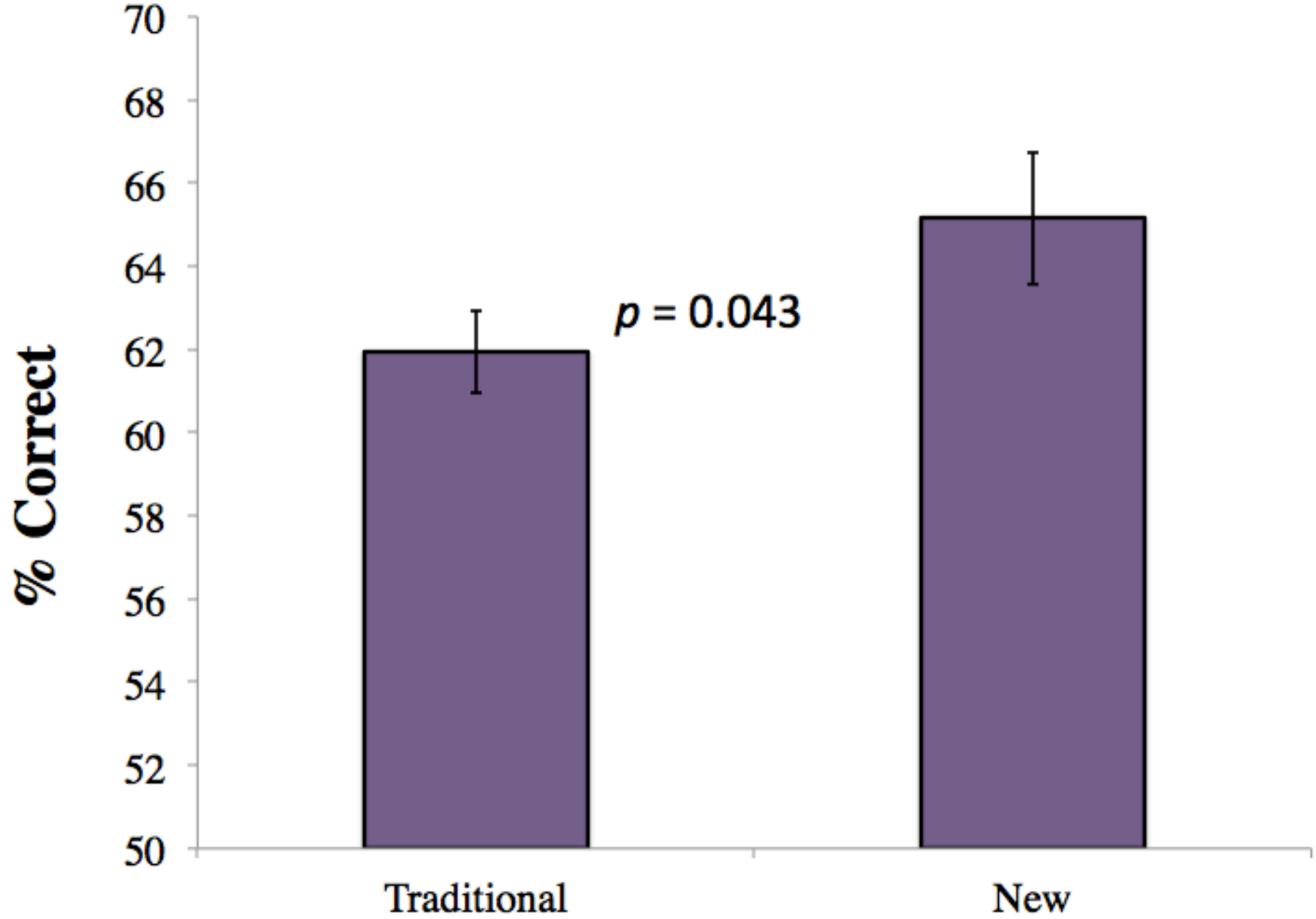
+/- SEM

Student Content Assessment

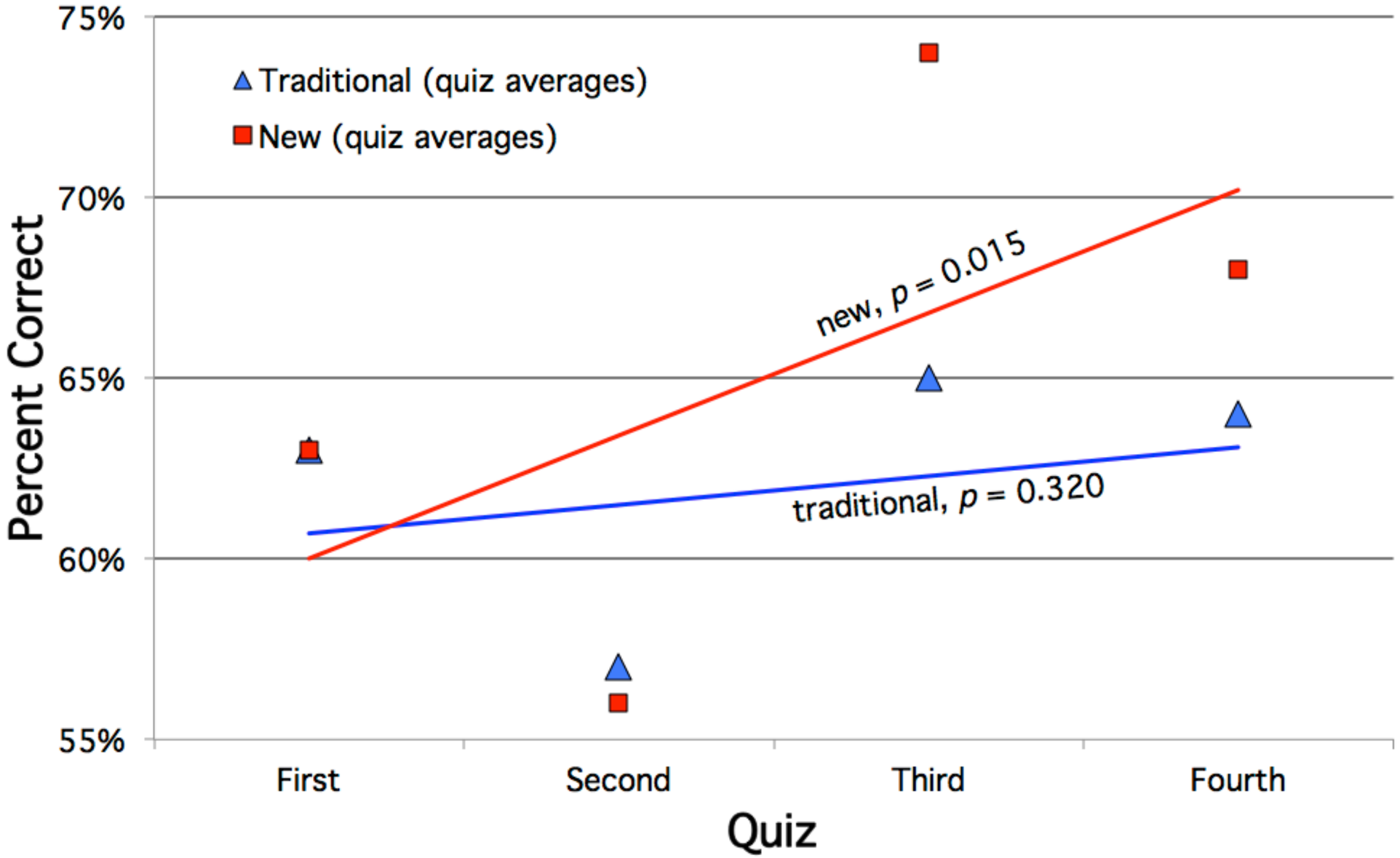


Can my students analyze data better?

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?’ ”

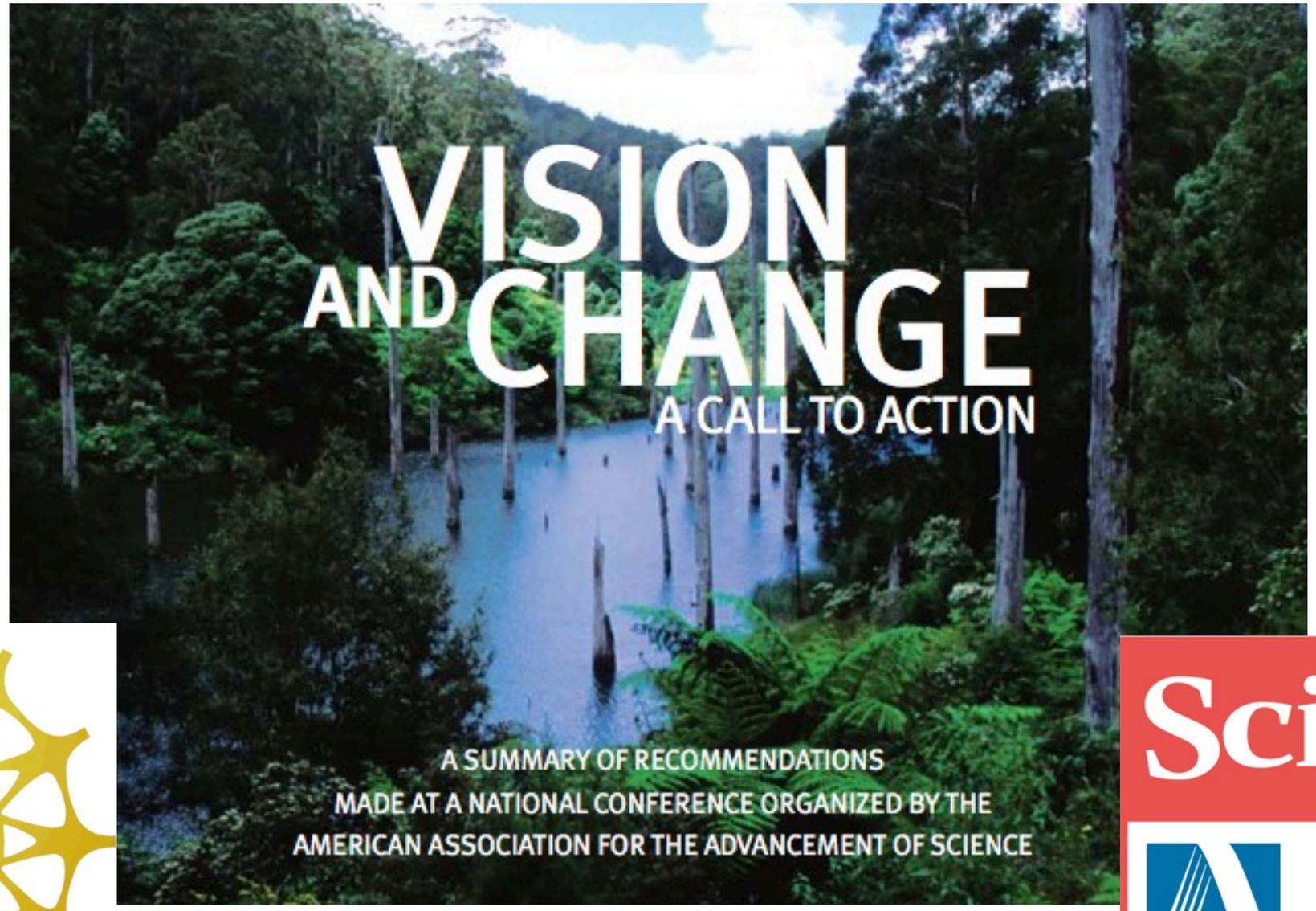
anonymous student course evaluation, Dec. 2010

“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



NSF

Science

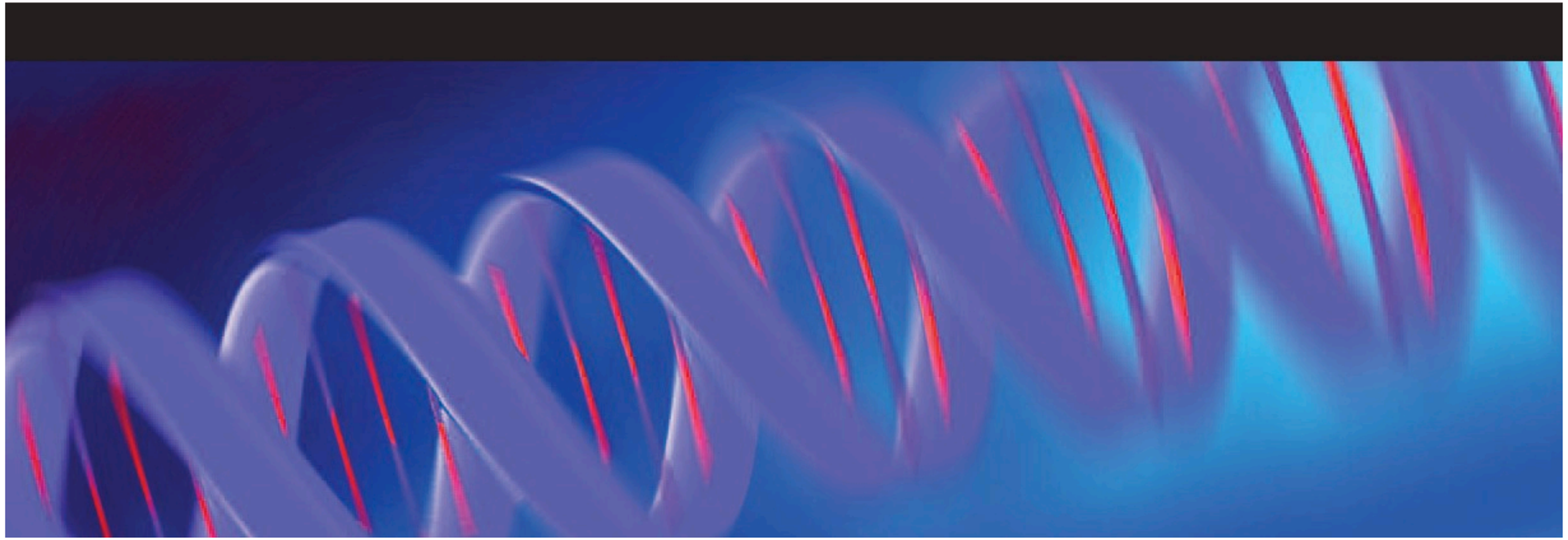
AAAS

AP Biology is Changing to Match Our Design

AP® BIOLOGY

Curriculum Framework

2012–2013



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Davidson College James G. Martin Genomics Program
MWSU SGA, Foundation & Summer Research Institute

How did I test student learning?

Four Exams Per Semester

8 pts.

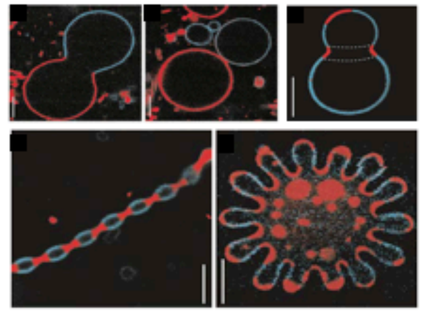
9) Limit your answers to a maximum of **2 sentences for each part**.

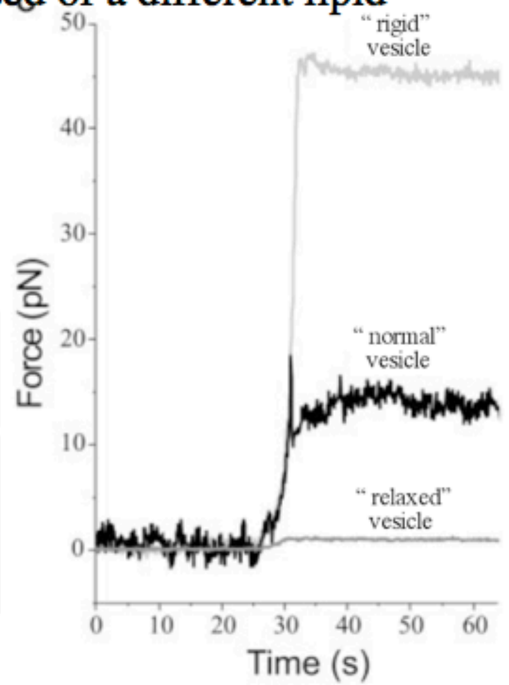
a) Explain why it is adaptive for each eukaryotic organelle to be composed of a different lipid composition. Use data to support your answer.

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

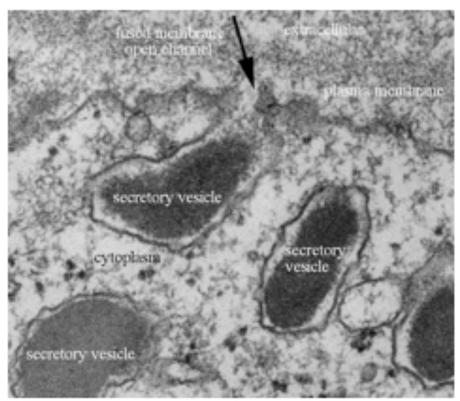
a: from Gerrit van Meer, 1998, Table 1.
b: from Orientations of Proteins in Membranes, 2010, http://opm.phar.umich.edu/atlas.php.
n.d. not determined



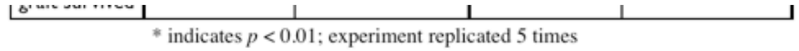


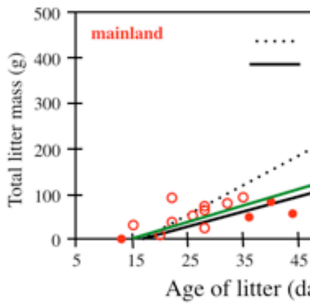
b) Would you predict that the secretory vesicles containing epinephrine would contain more rigid lipids, or flexible lipids? Use data to support your answer.

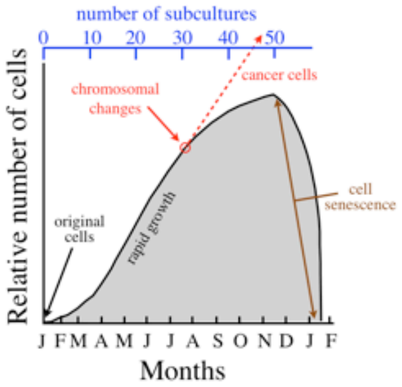
relaxed due to large surface area to volume ratio

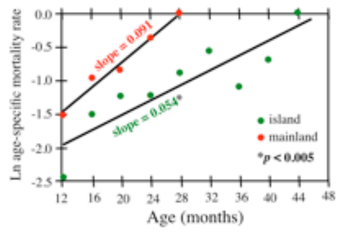


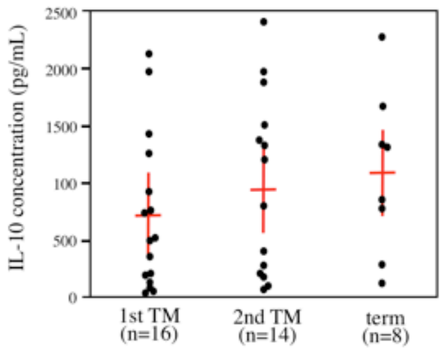
Data Gallery for Answers

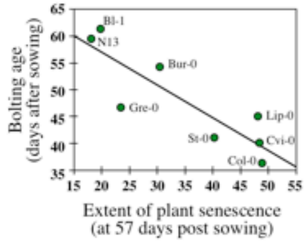


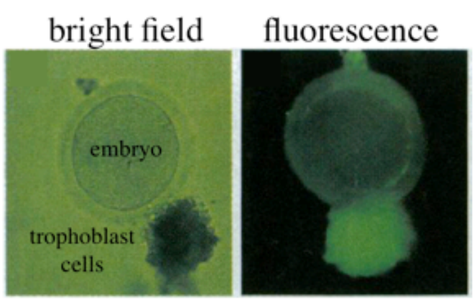


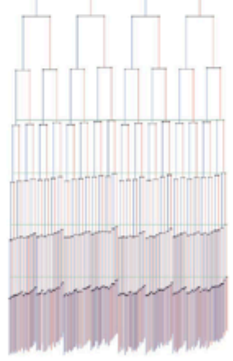


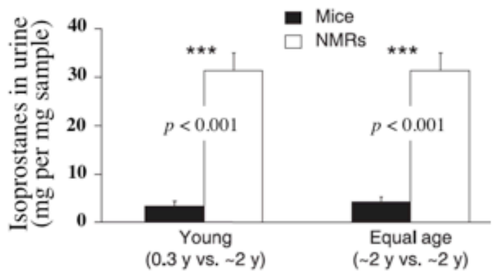


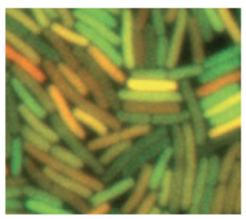


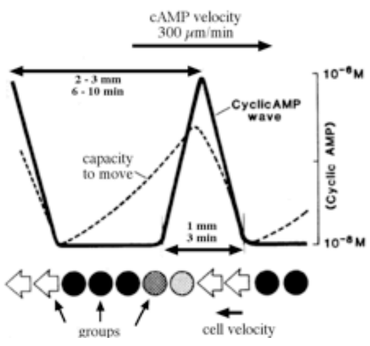


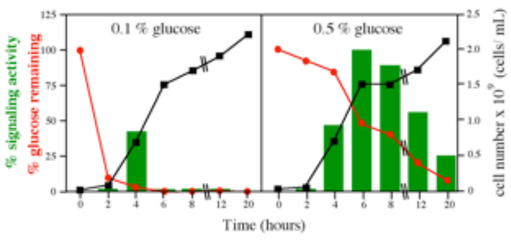


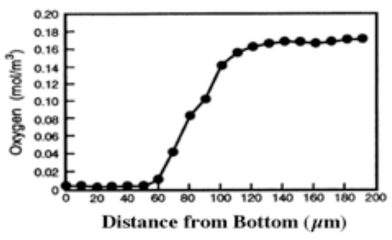


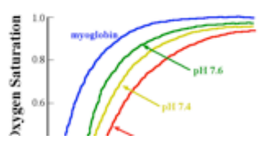












When did the students feel they were learning something different than in high school?

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