GCAT, Synthetic Biology, and a Summer Faculty Workshop Opportunity

A. Malcolm Campbell

Free Synthetic Biology Workshop

June 24-27, 2014

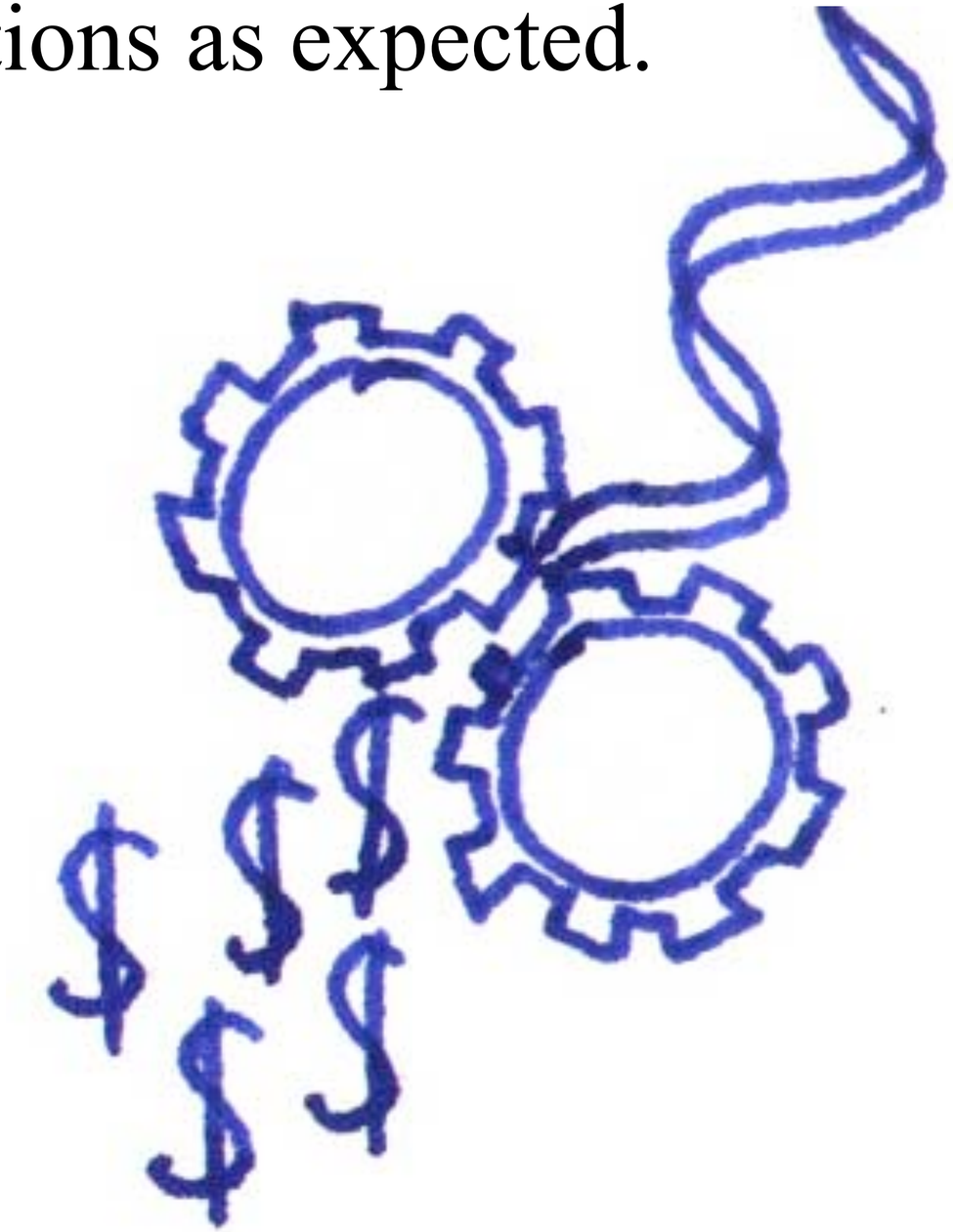
What is Synthetic Biology?

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

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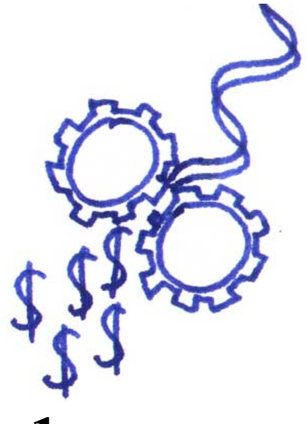
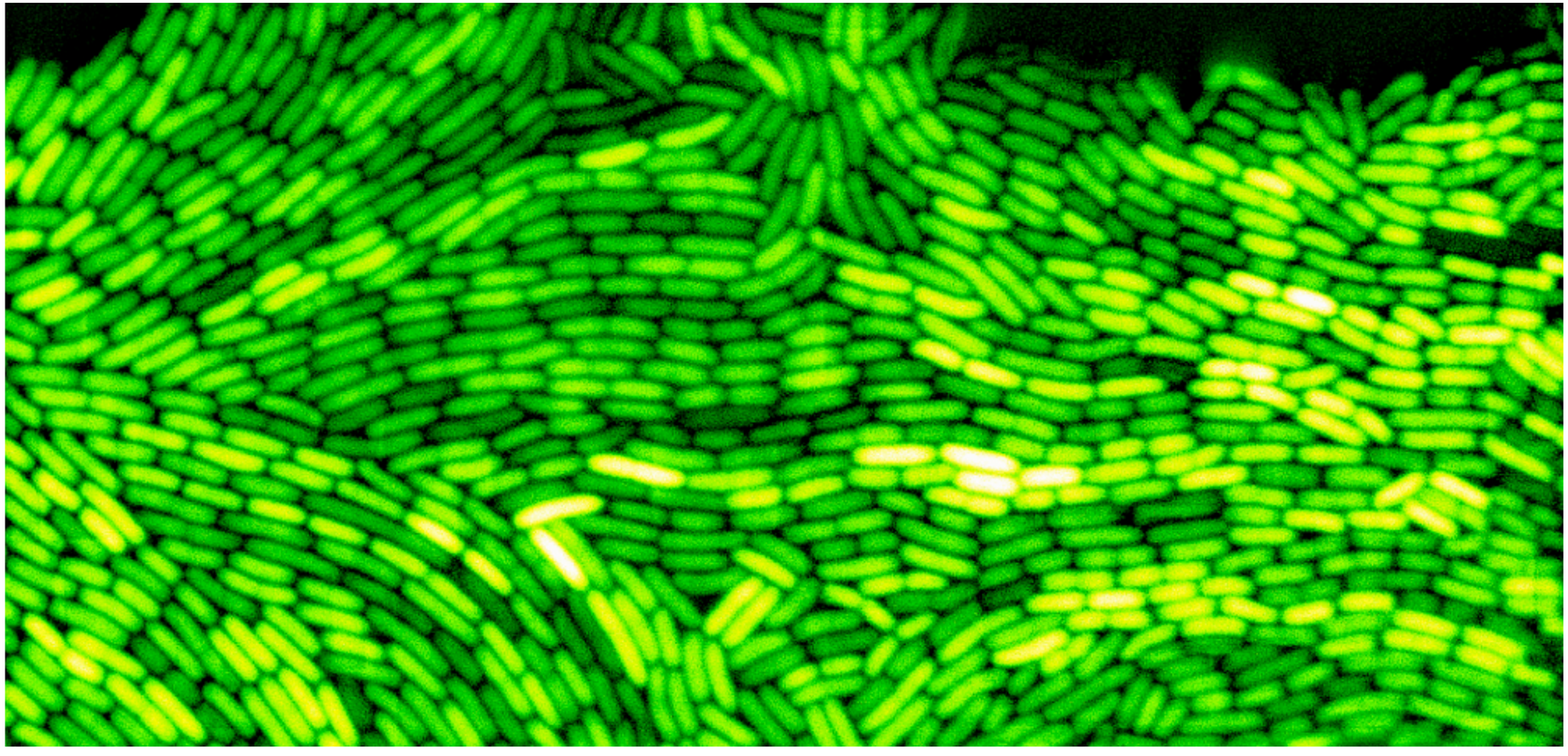
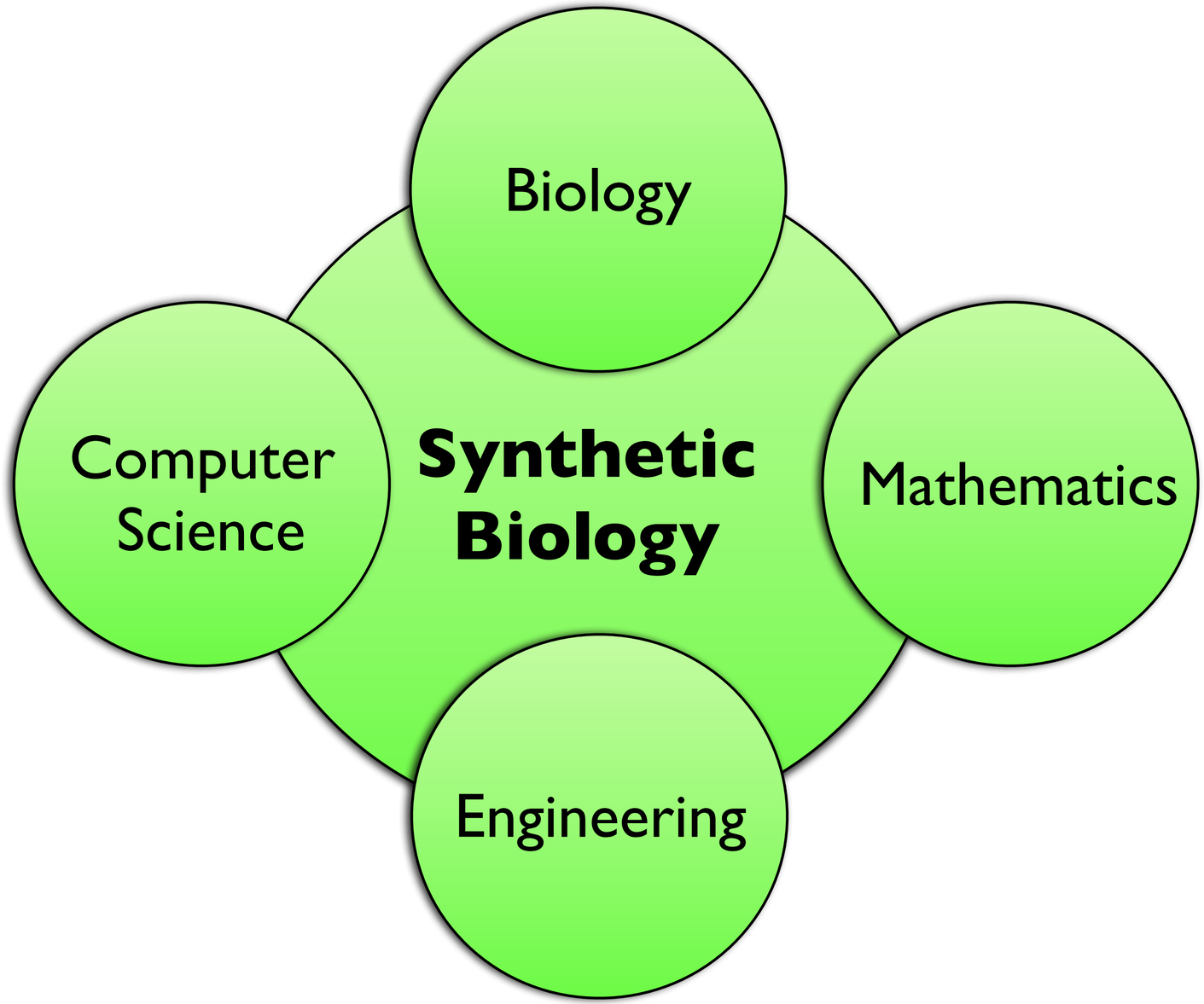


Win #2: your design fails but you uncover basic biology



Synthetic Biology



Synthetic Biology

Genetic engineering on a new scale.

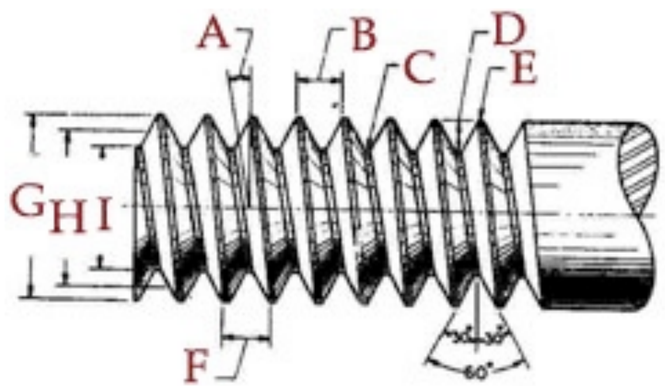
Four Characteristics:

- Standardization
- Modularity
- Abstraction
- Modeling of Designs

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

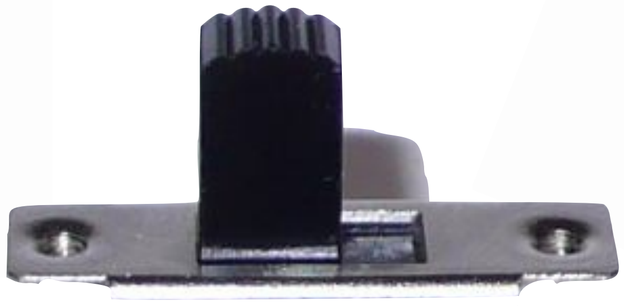
On a Uniform System of Screw Thread

Modularity

USB ports on computers

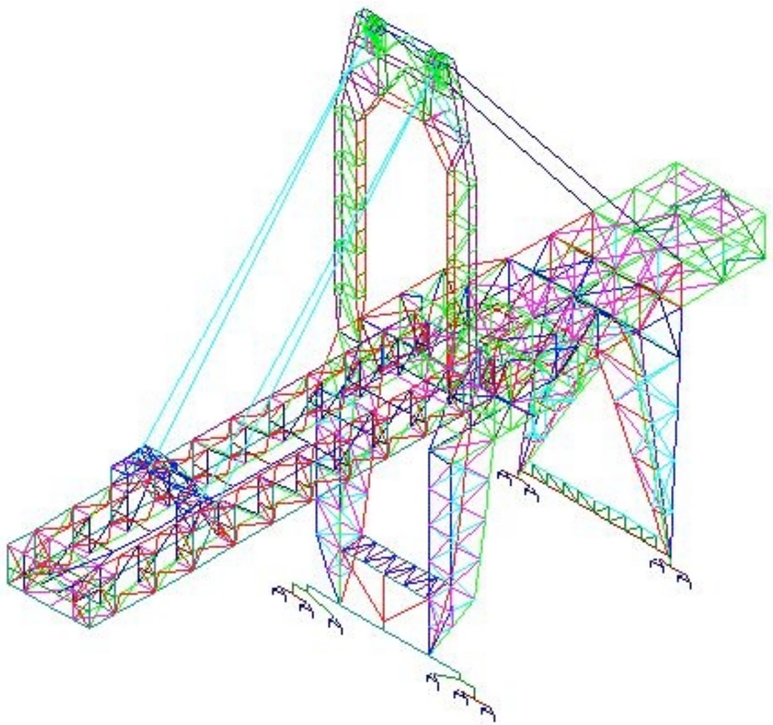
Modularity

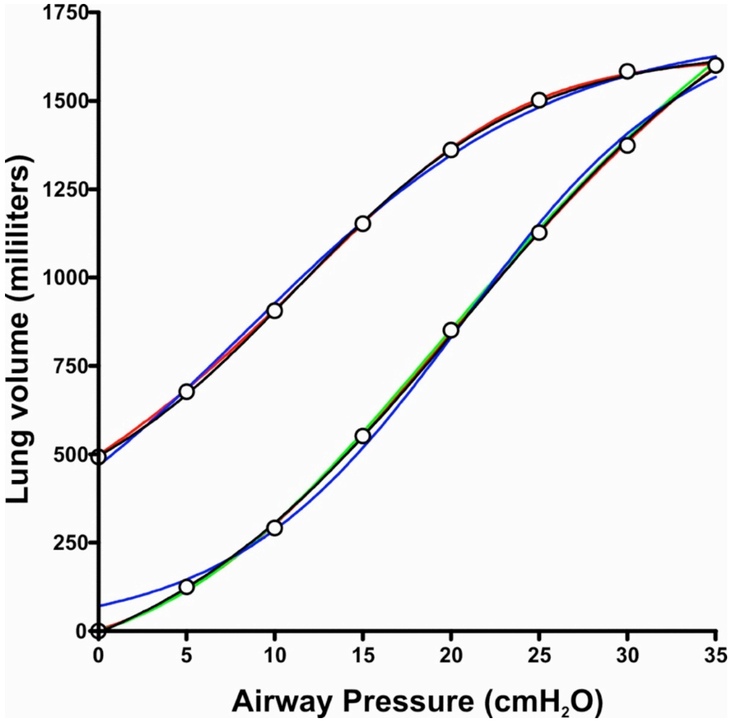
Abstraction

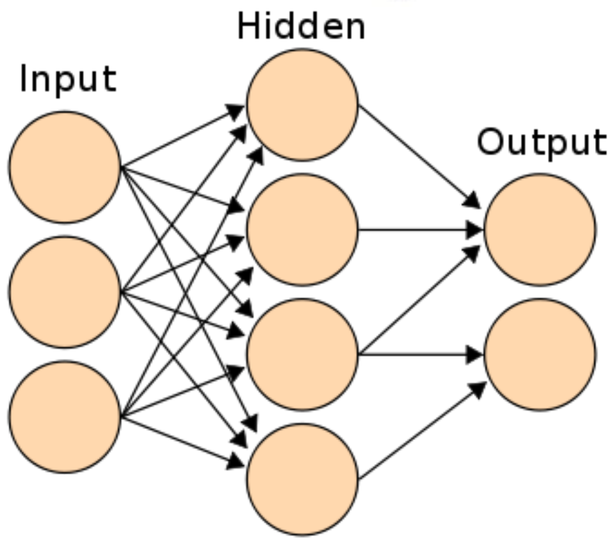


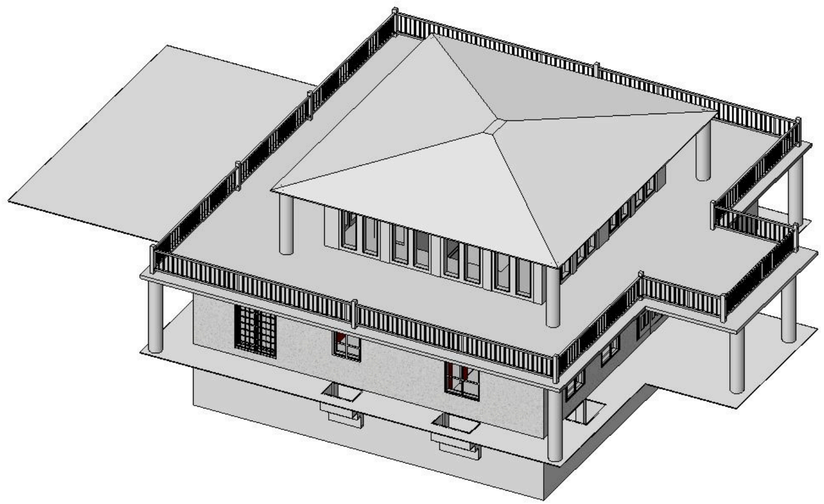
Abstraction

Modeling of Designs

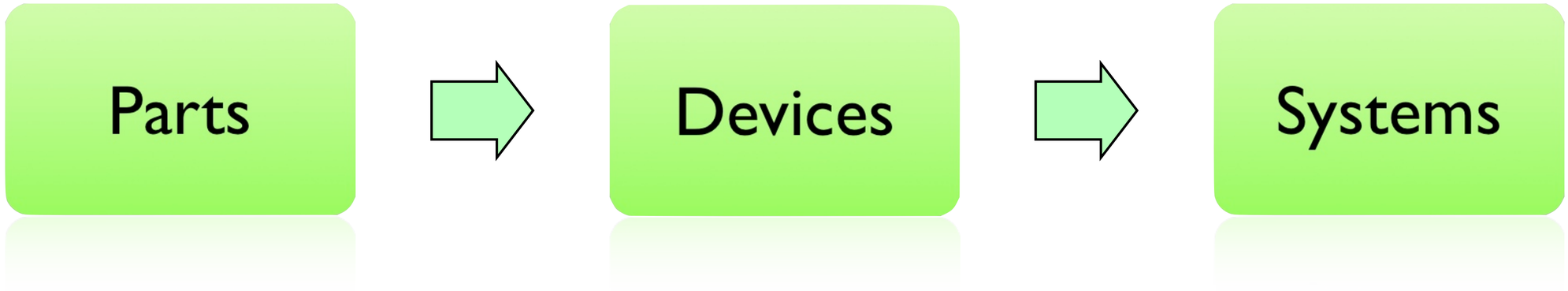






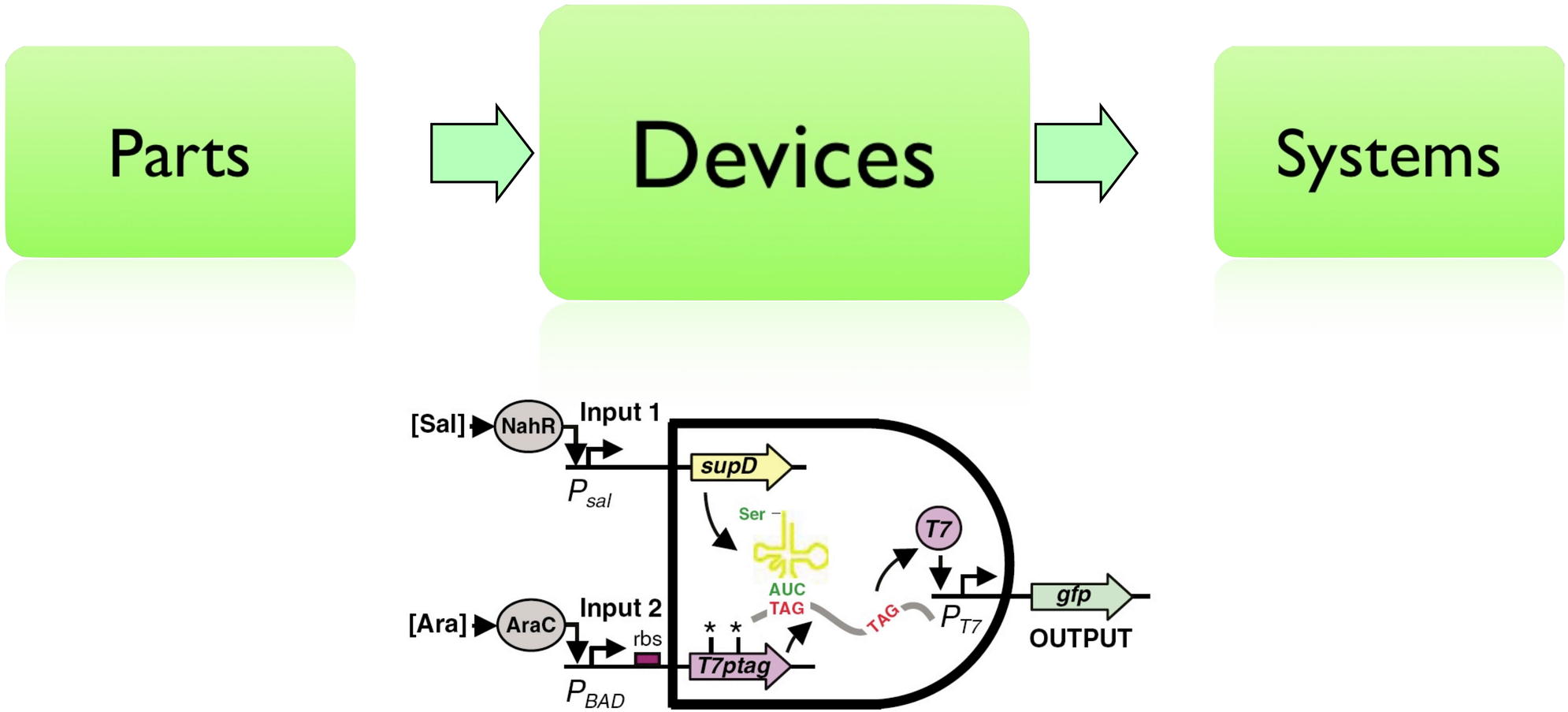


Synthetic Biology



Synthetic Biology

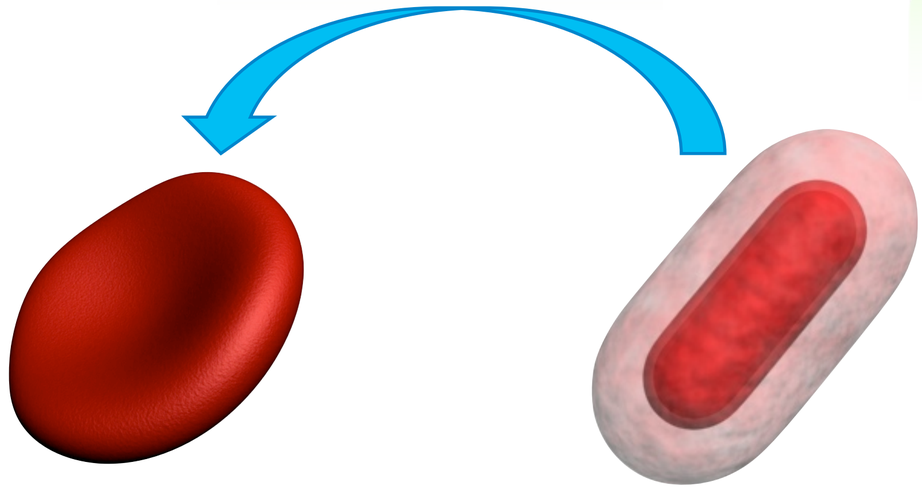
Synthetic Biology



Anderson *et al. Mol Sys Bio*. 2007.

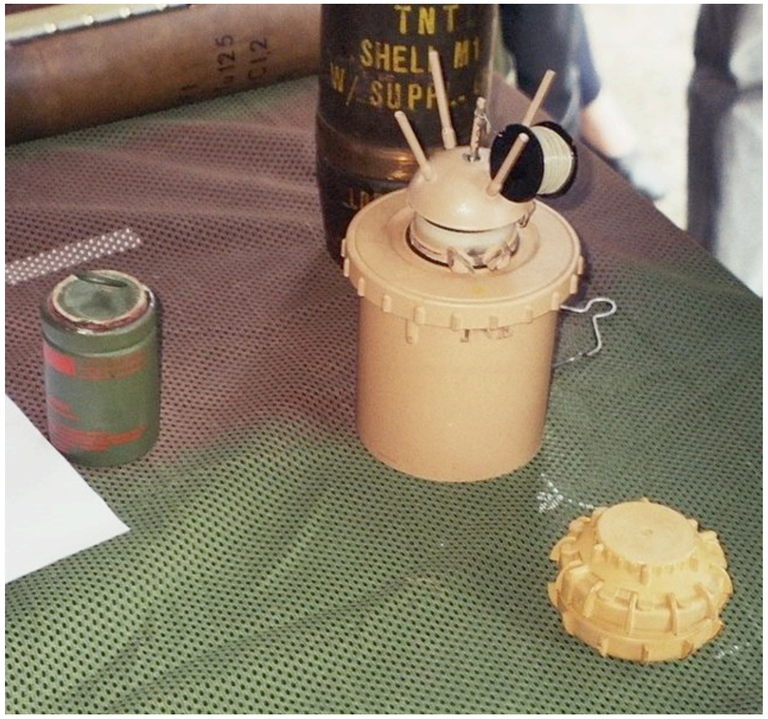
Synthetic Biology

Parts → Devices → Systems

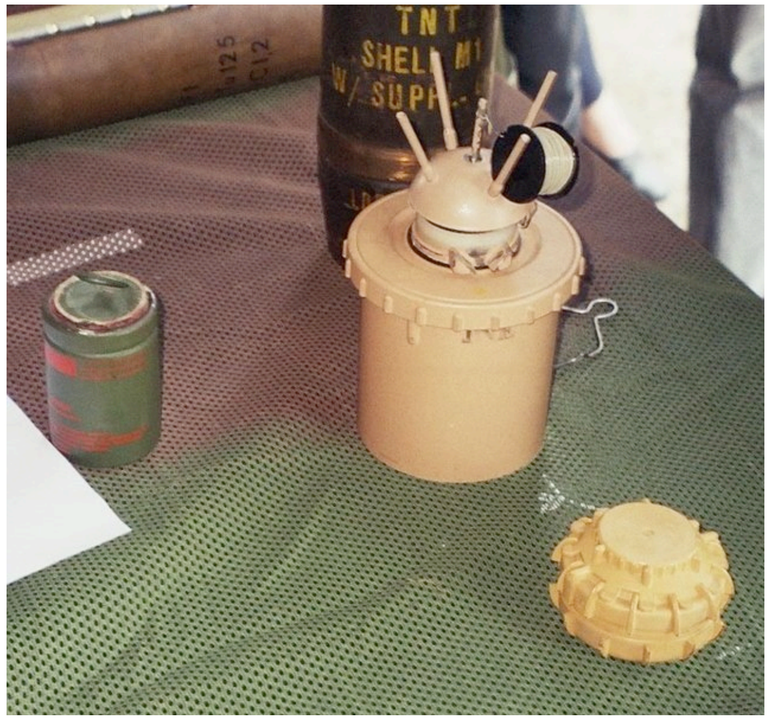


Real World Applications of Synthetic Biology

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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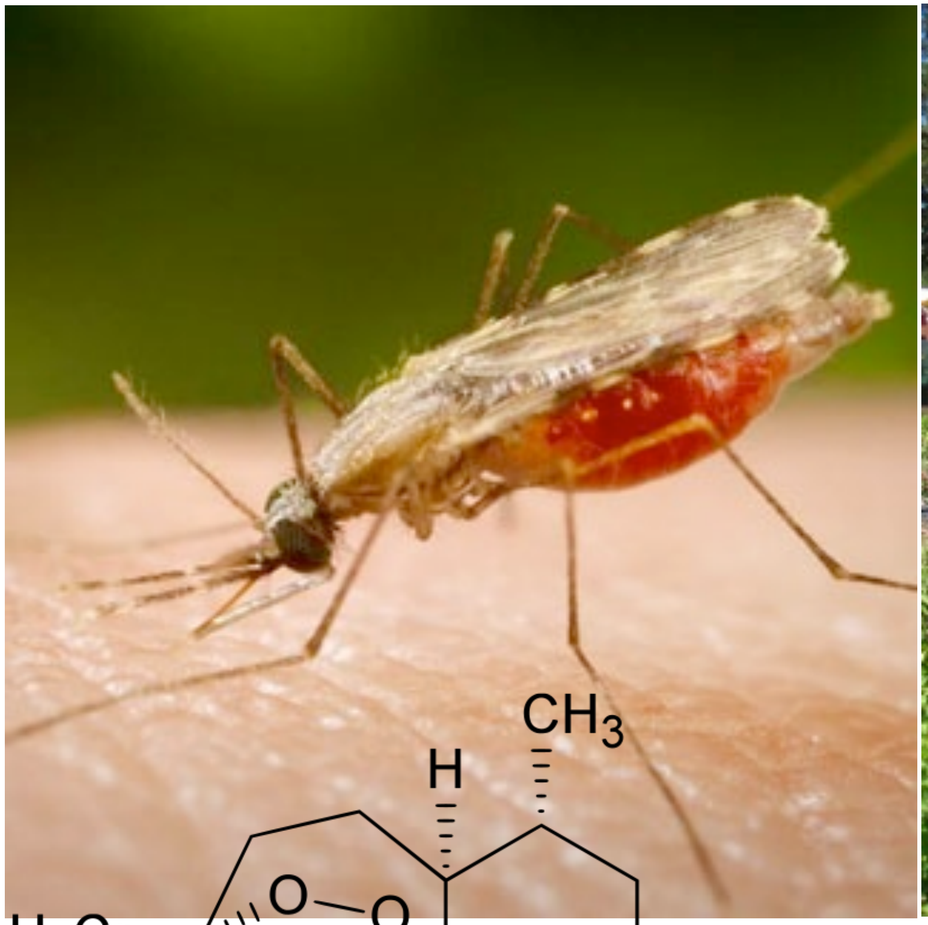
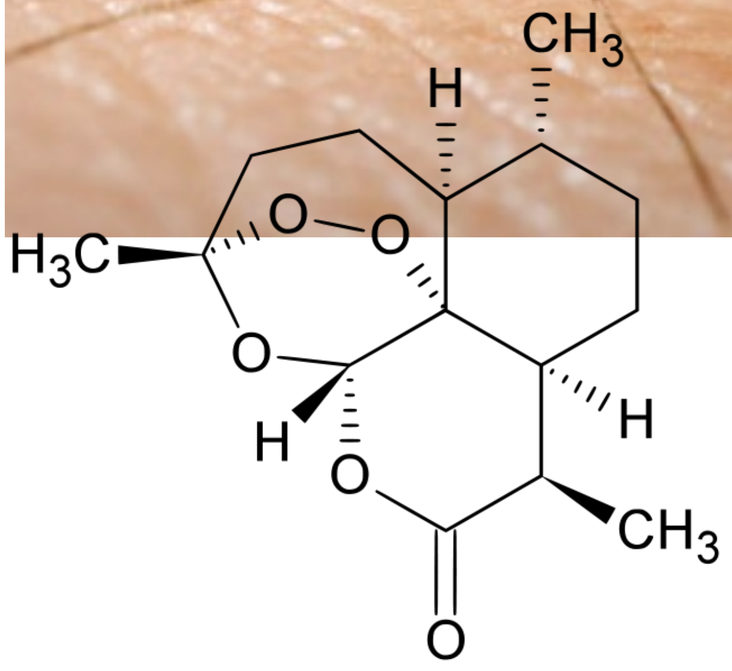
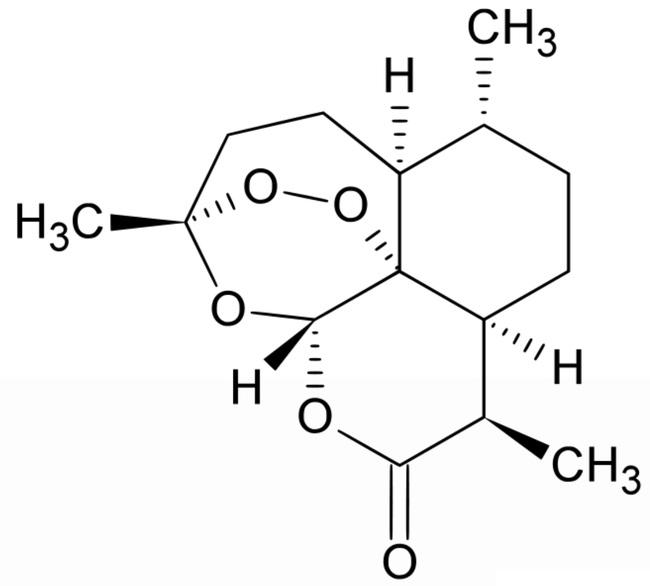
Production of Medicines



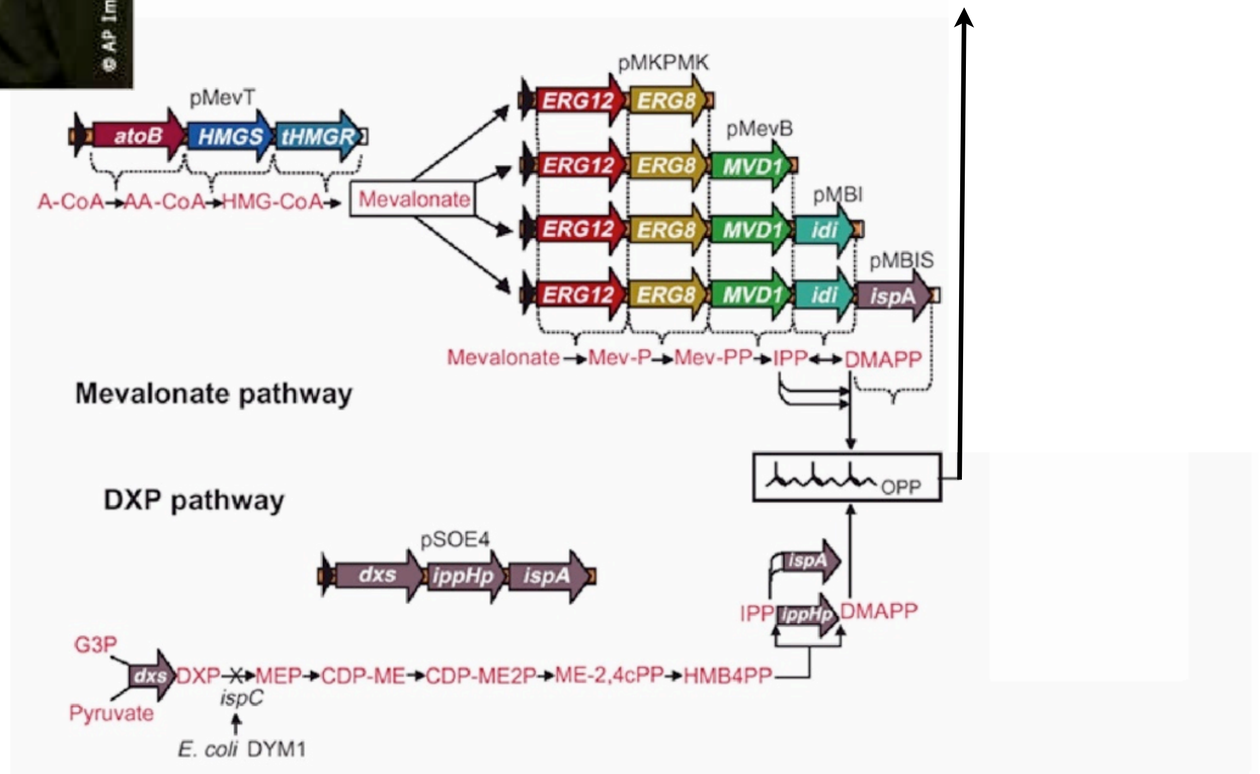


$1 per pill

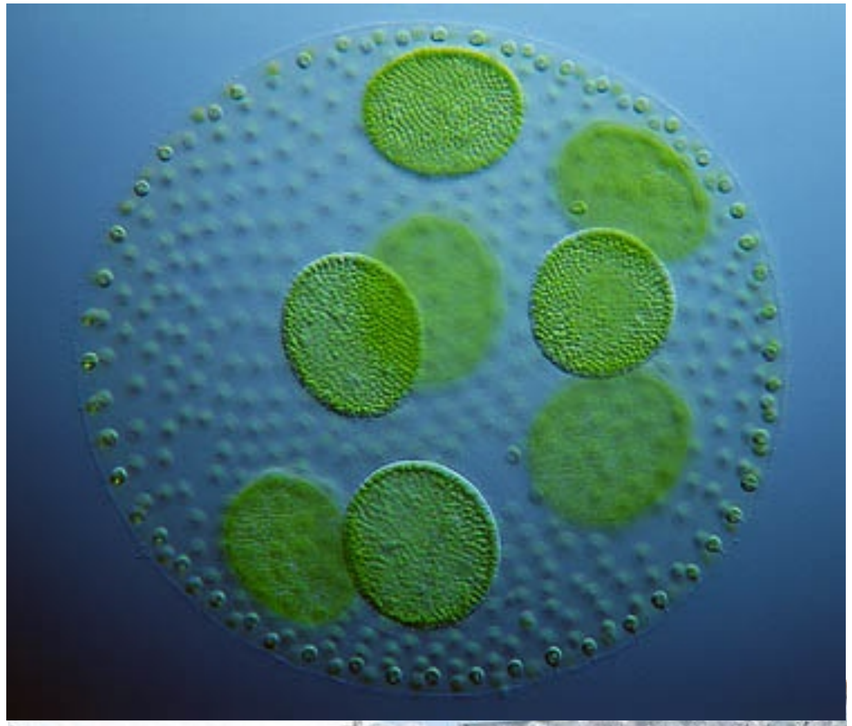
Production of Medicines



10¢ per pill



Biofuels from Algae

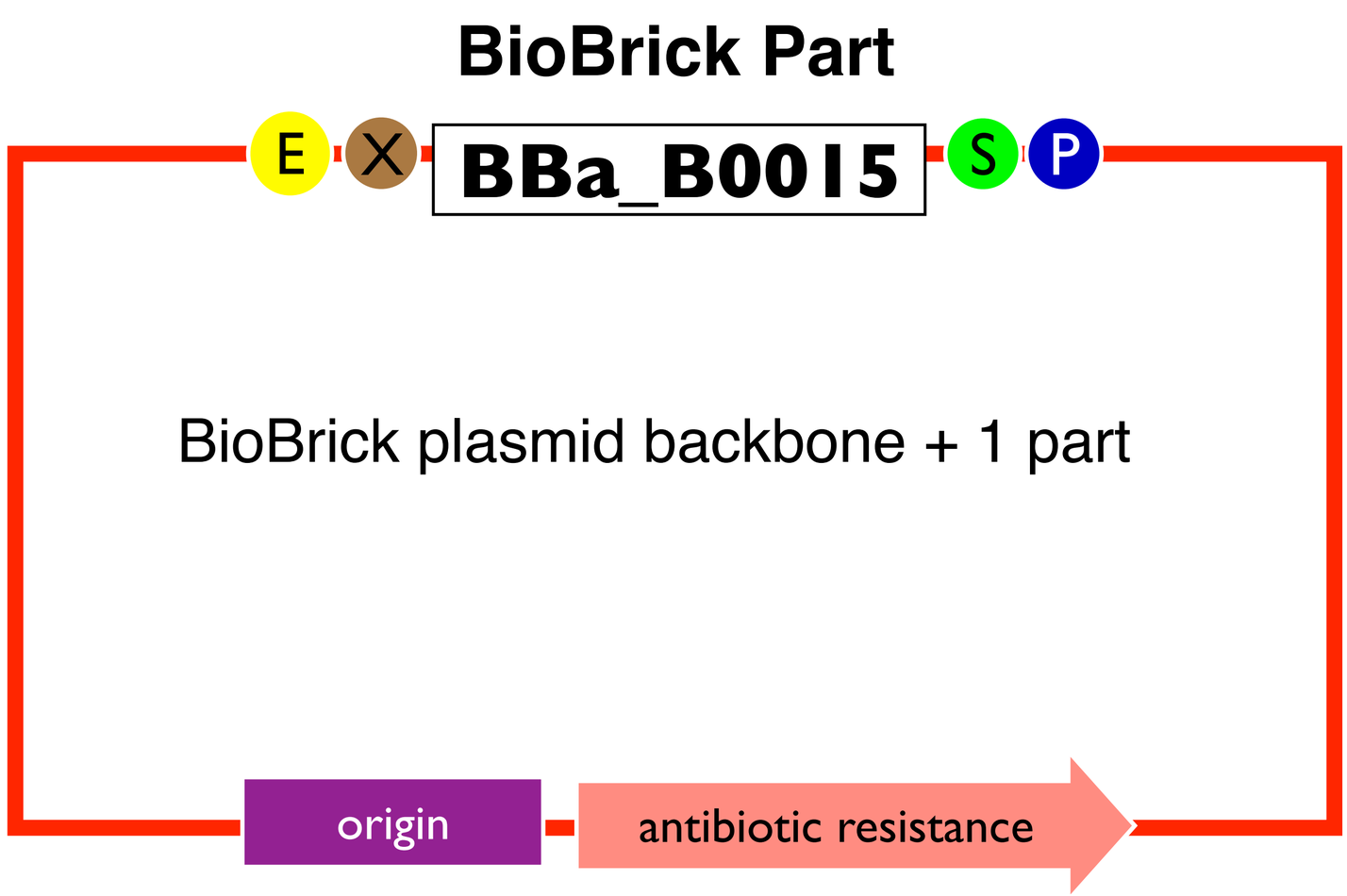


CO_2-neutral

1,000,000 gallons in 2008

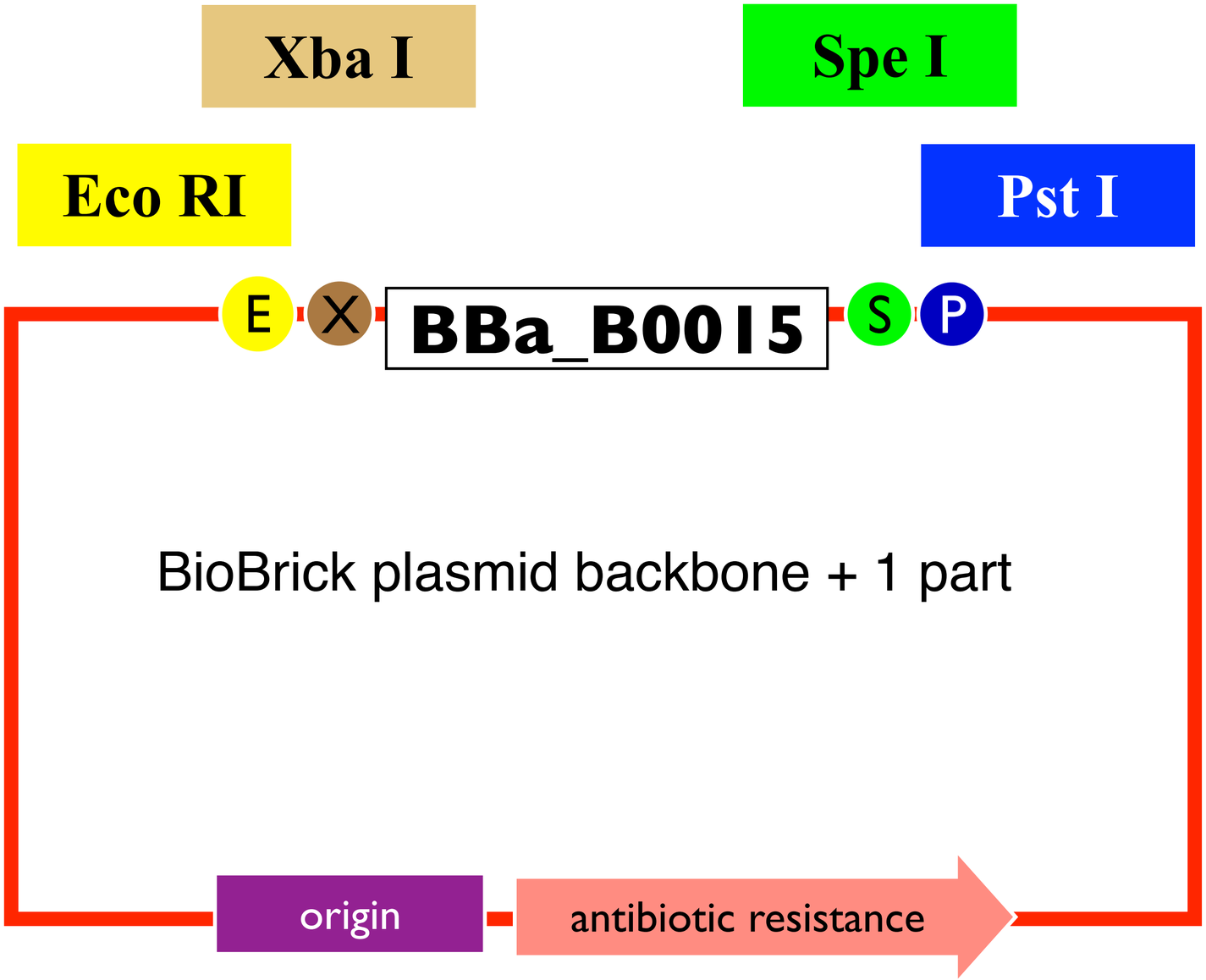
Intro Bio Students Conduct Promoter Research Using Synthetic Biology

BioBricks



(http://partsregistry.org/Plasmids)

BioBricks



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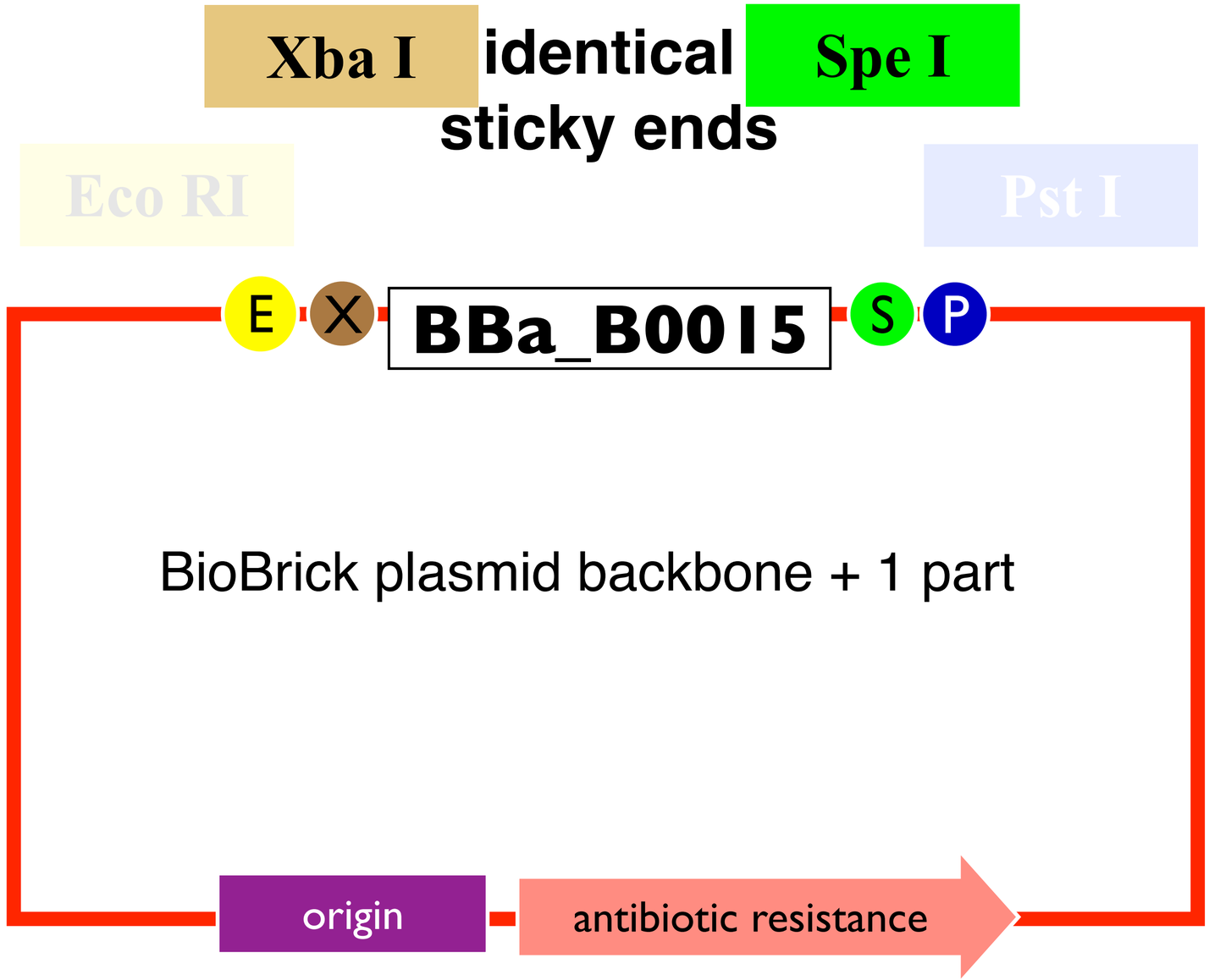

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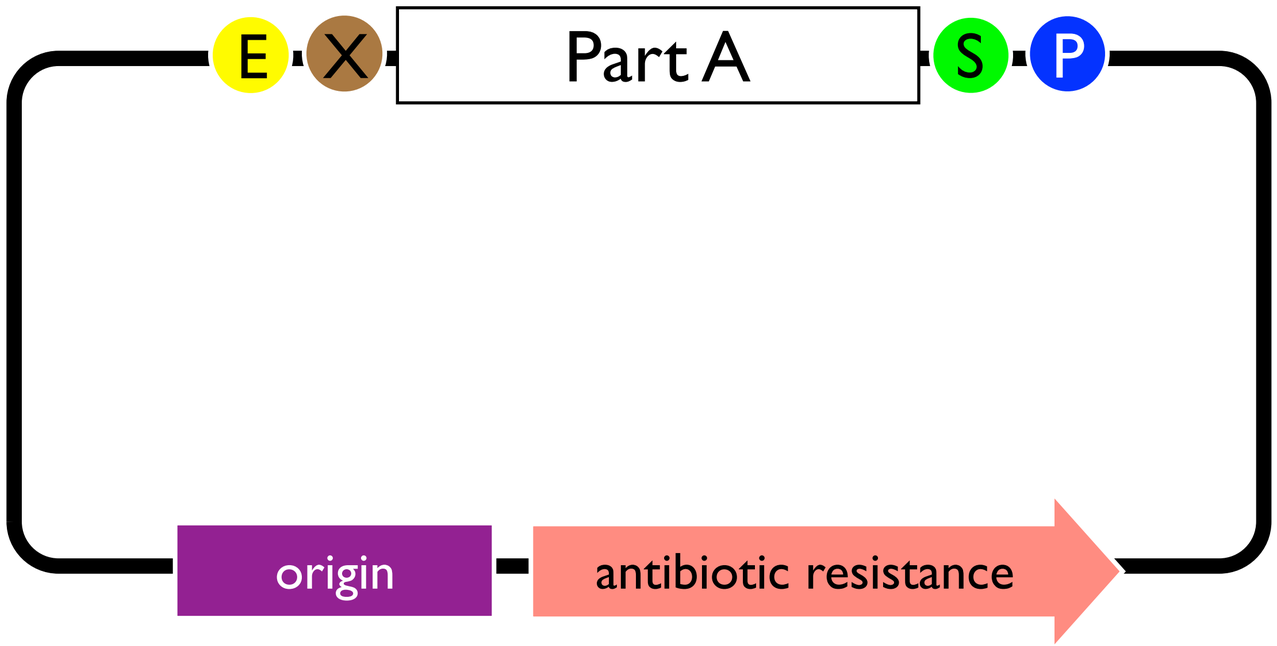
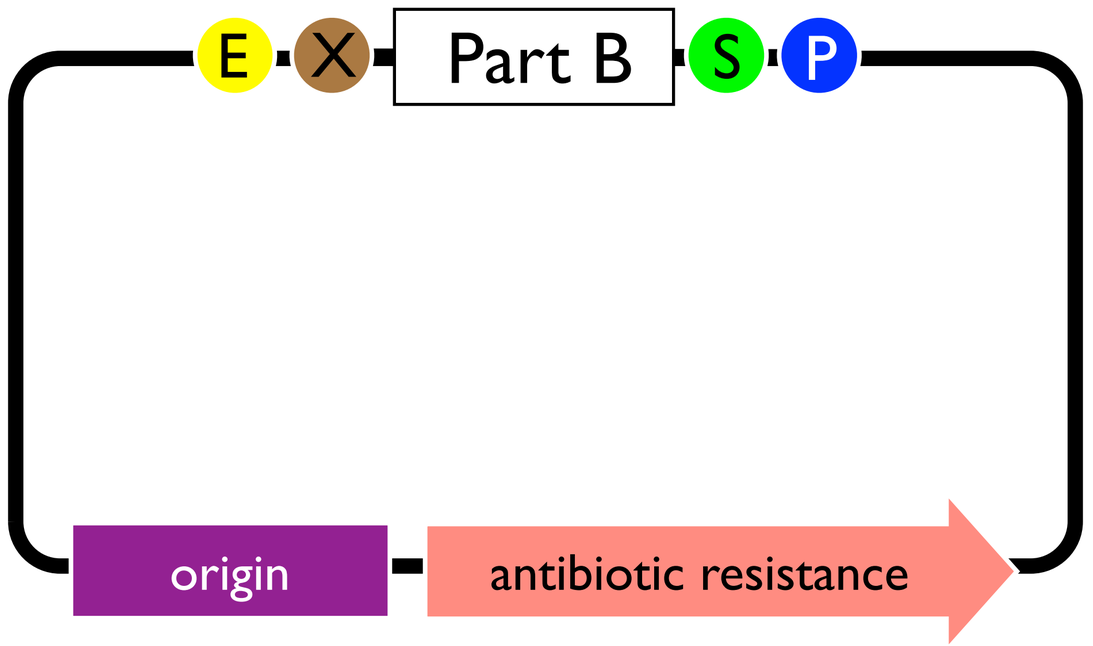
BioBricks

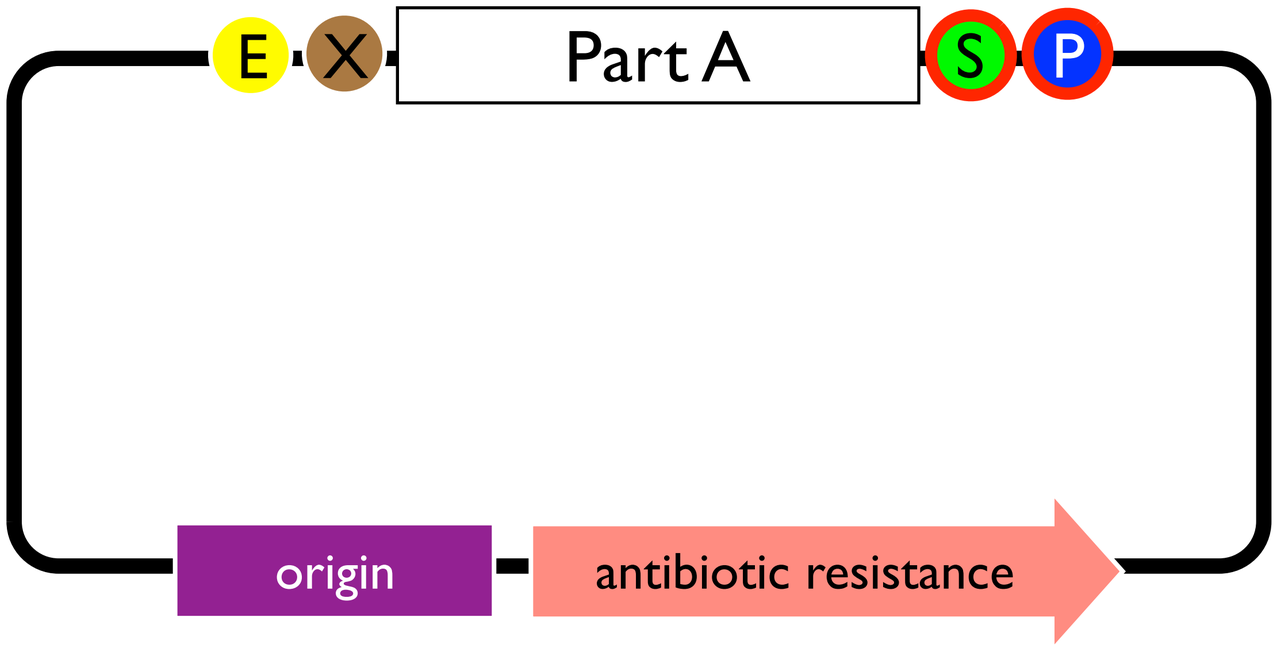
put B downstream of A



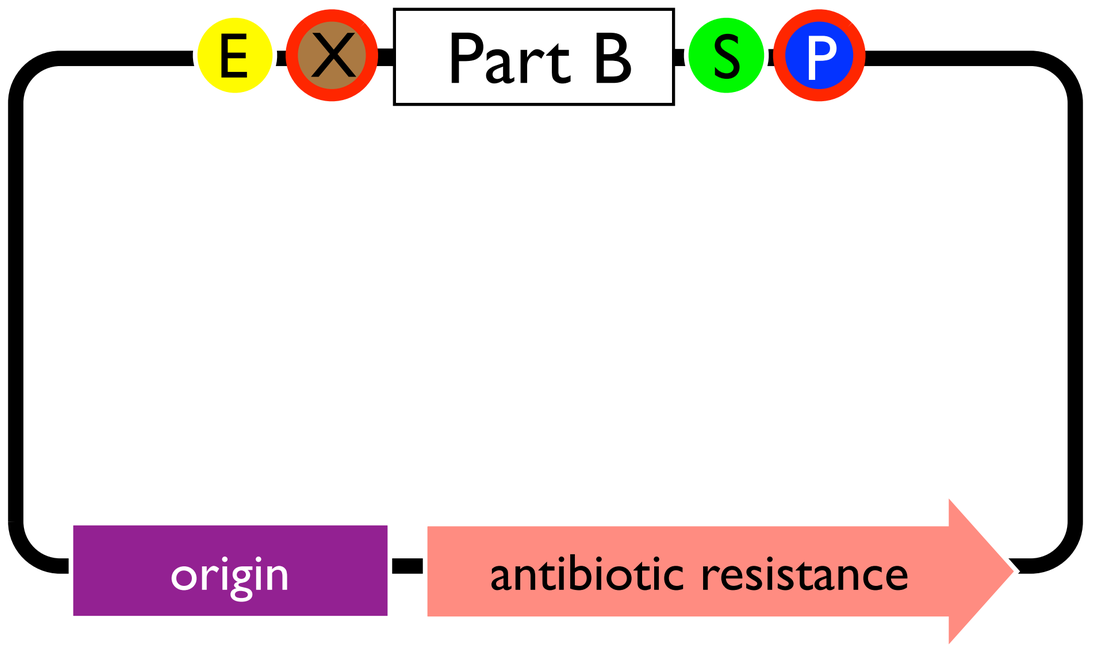


BioBricks

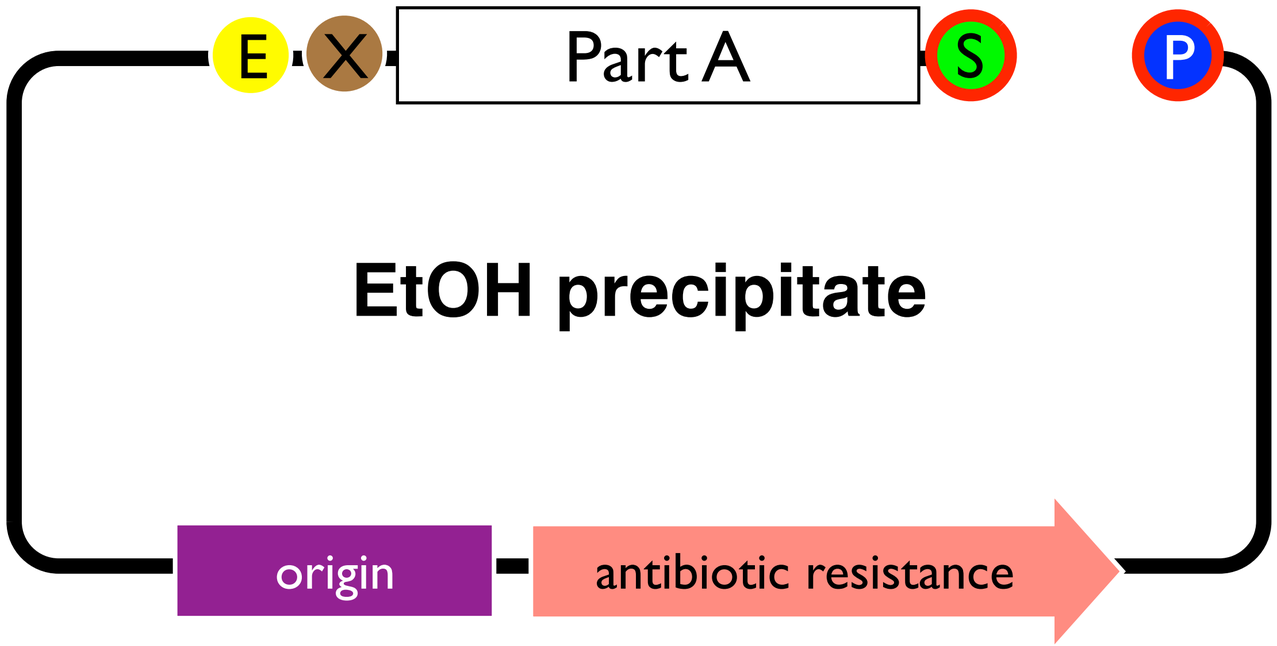
cut with Spe and Pst



cut with Xba and Pst

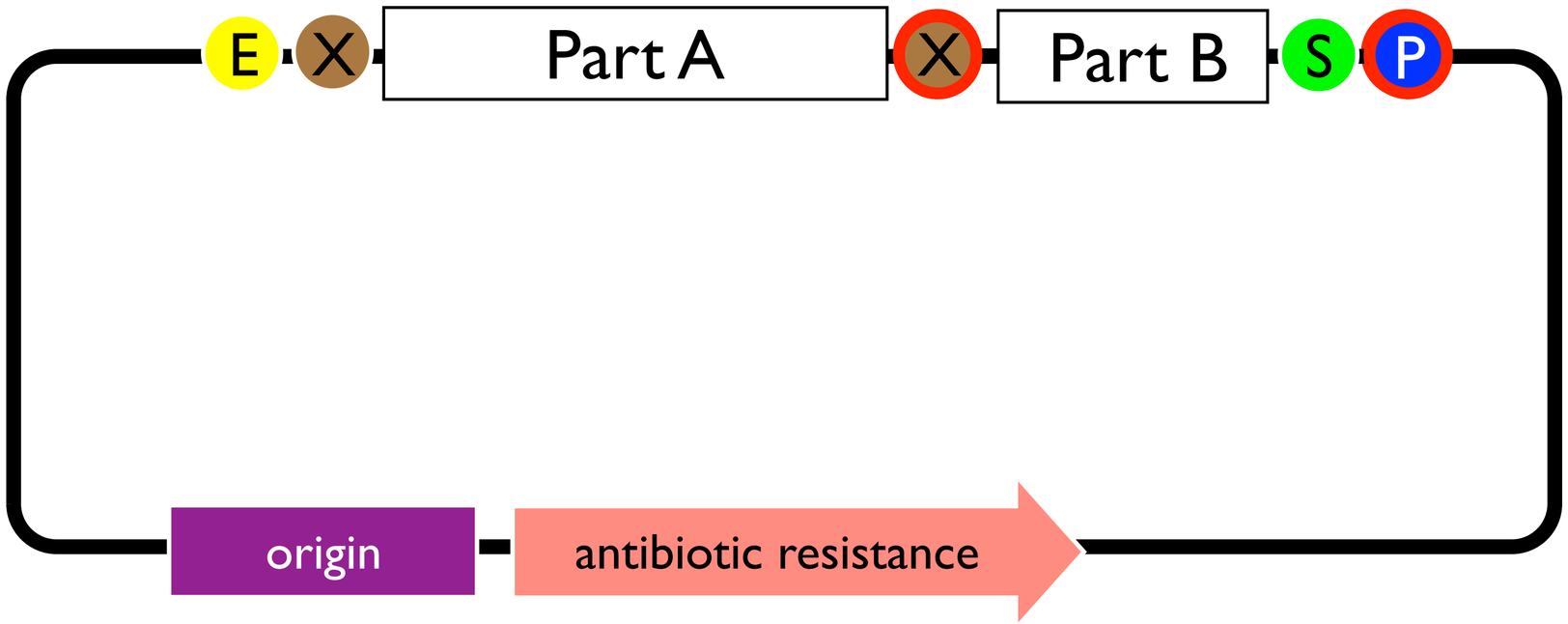


BioBricks



gel purify

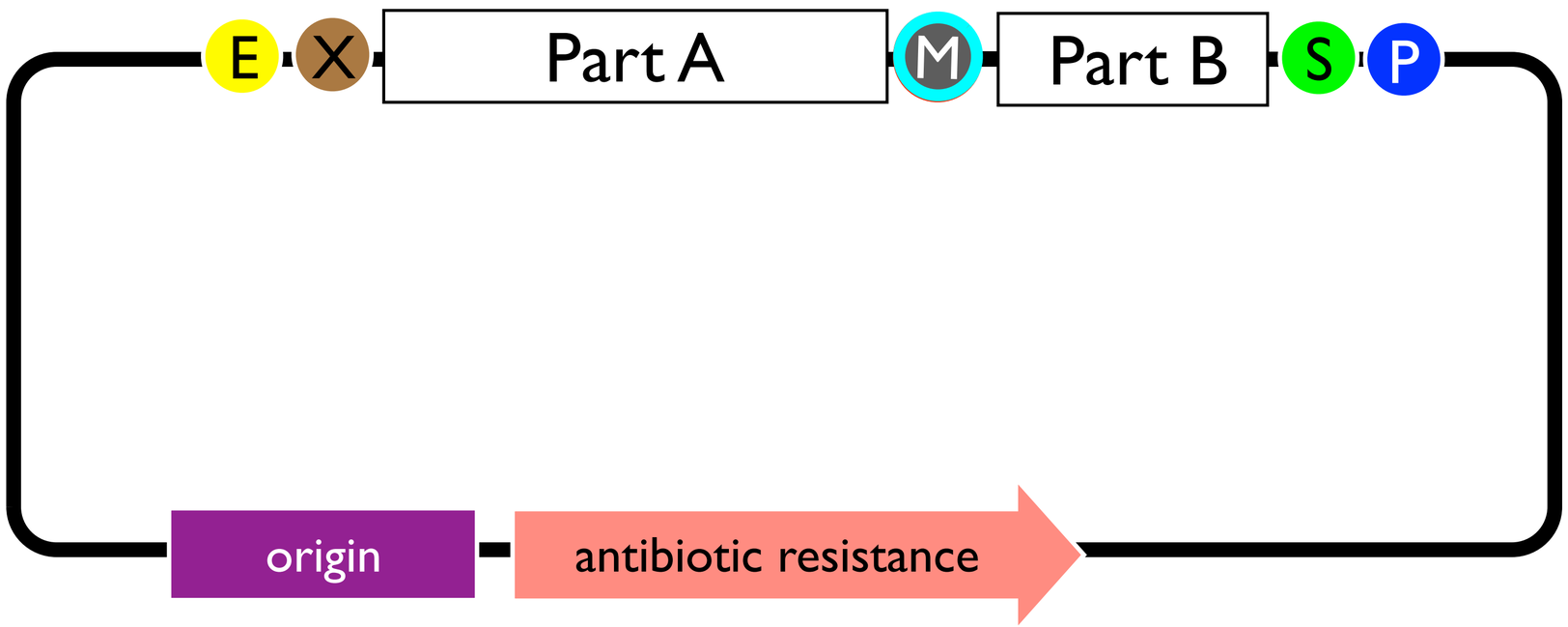
BioBricks



ligate

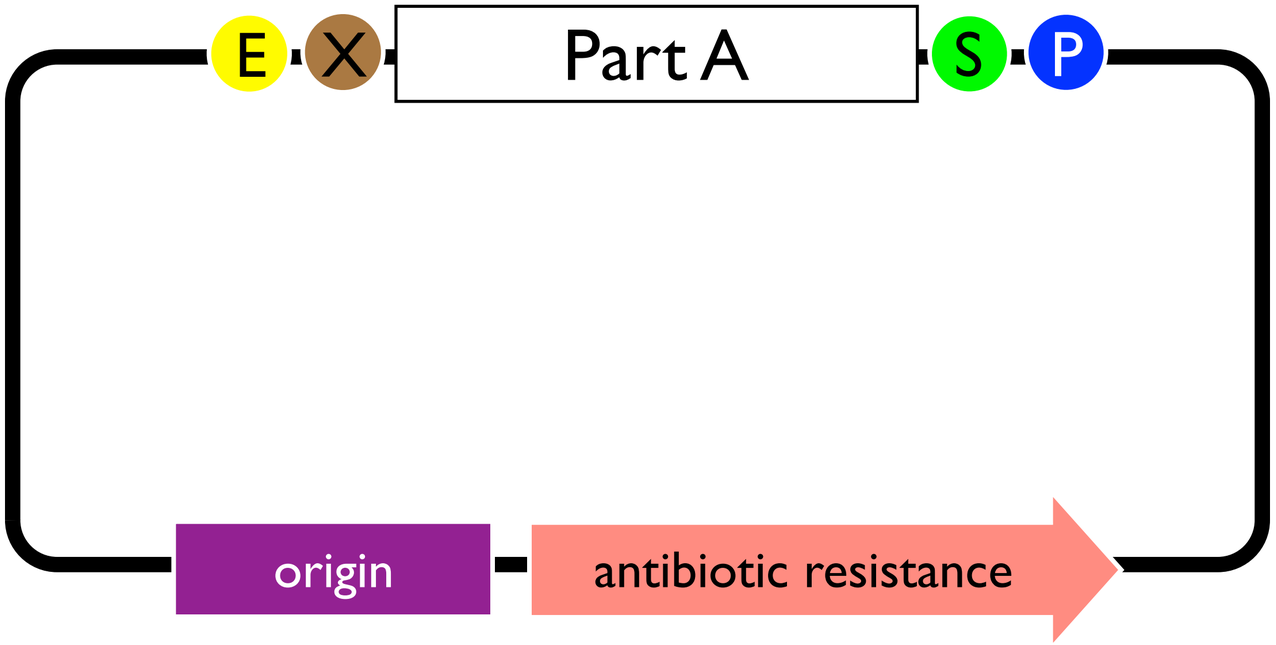
BioBricks

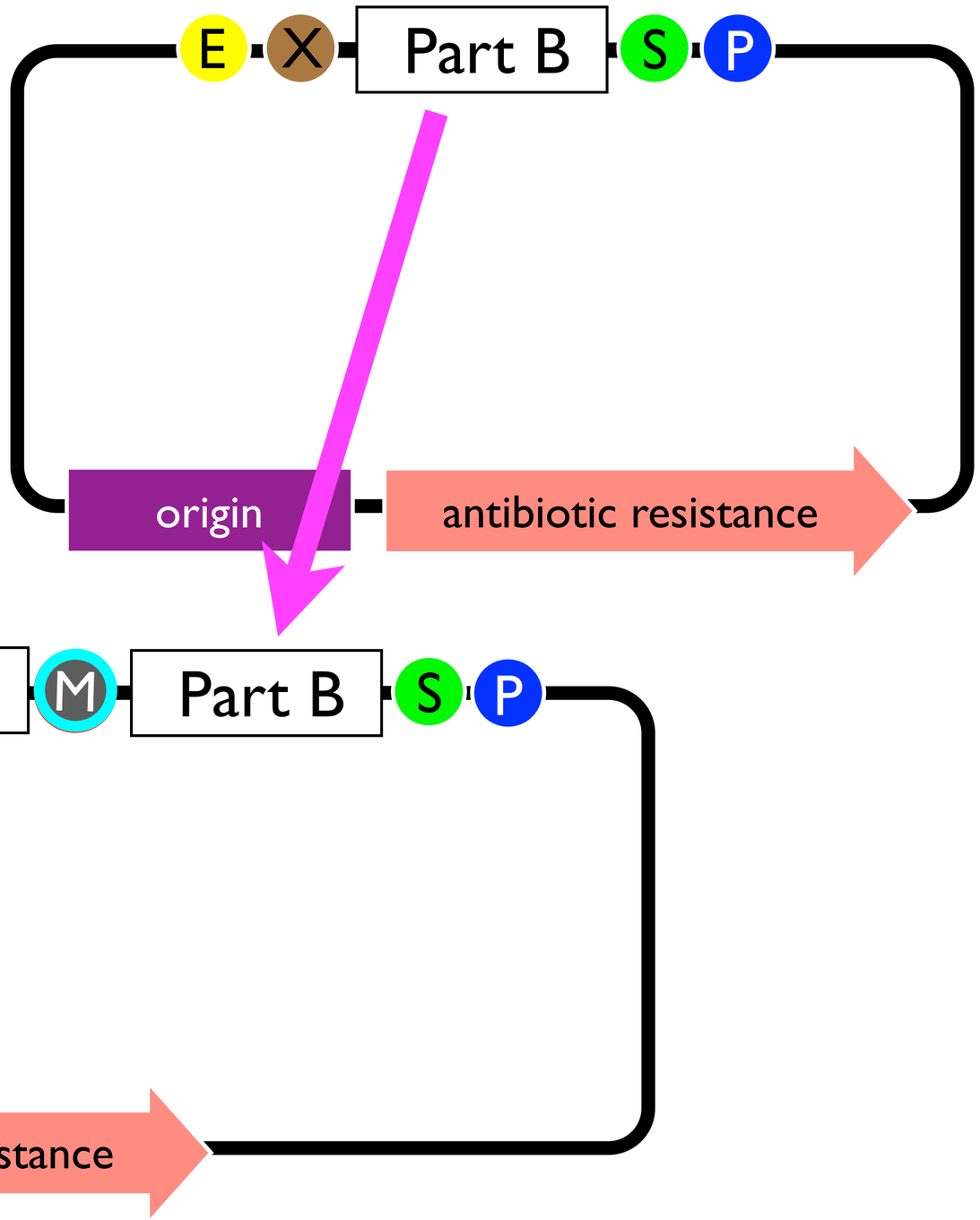
mixed site = scar



transform

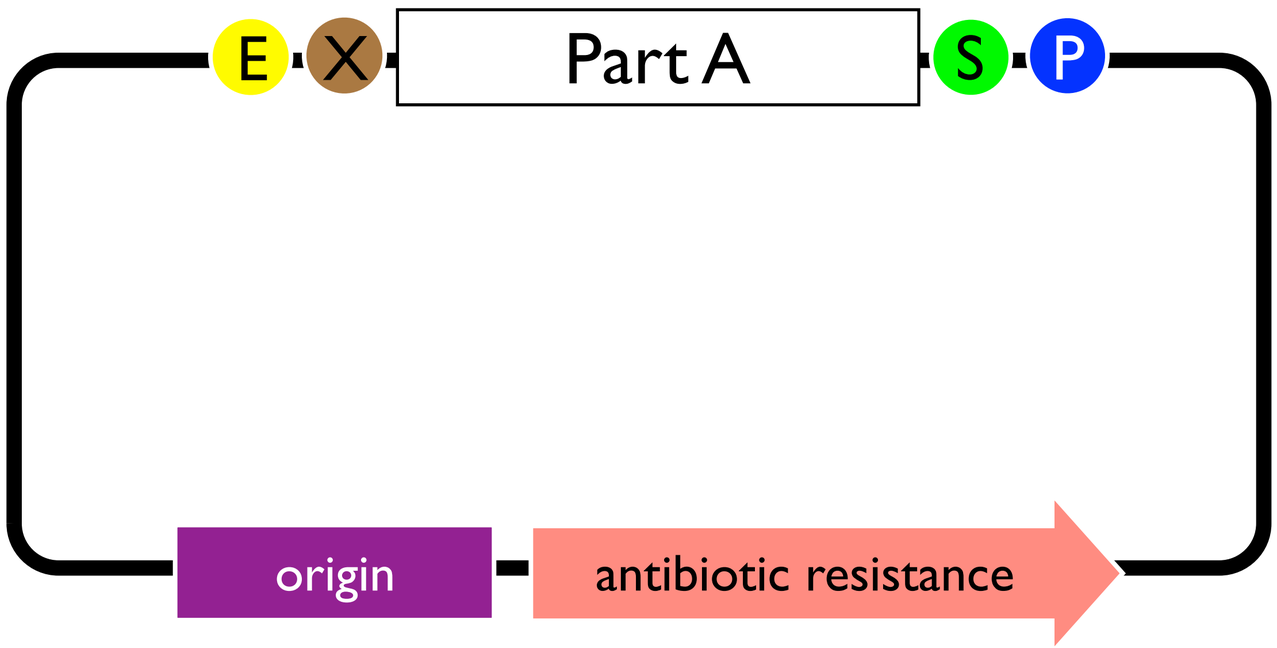
BioBricks

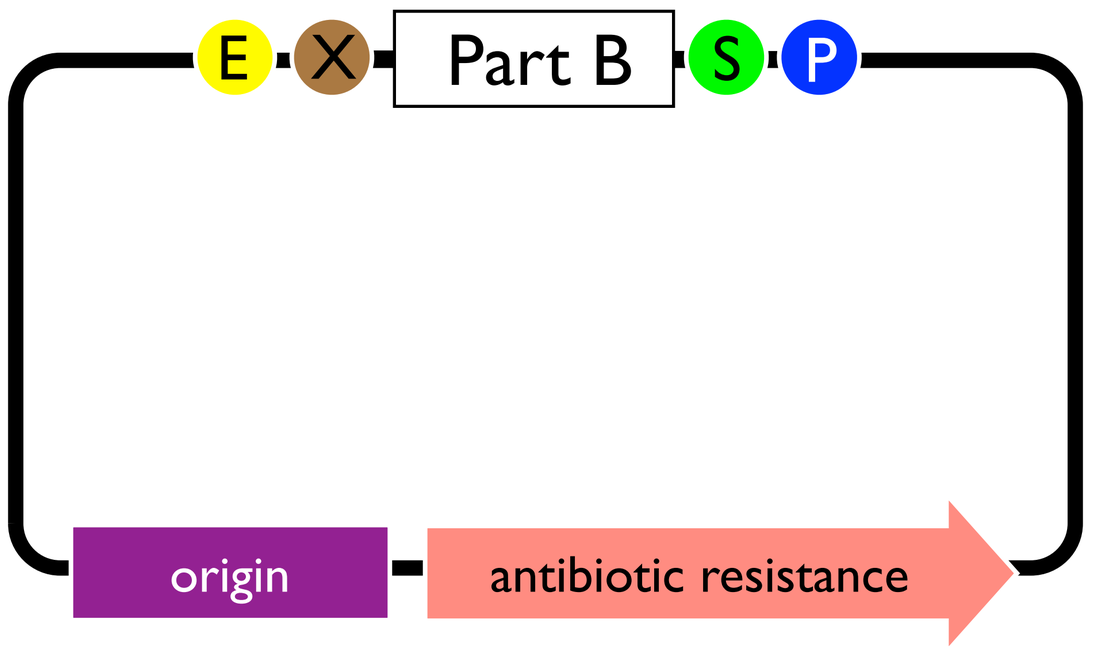

E
X
Part A
S
P
origin
antibiotic resistance


E
X
Part B
S
P
origin
antibiotic resistance
E
X
Part A
M
Part B
S
P
origin
antibiotic resistance

Challenge:

put A upstream of B



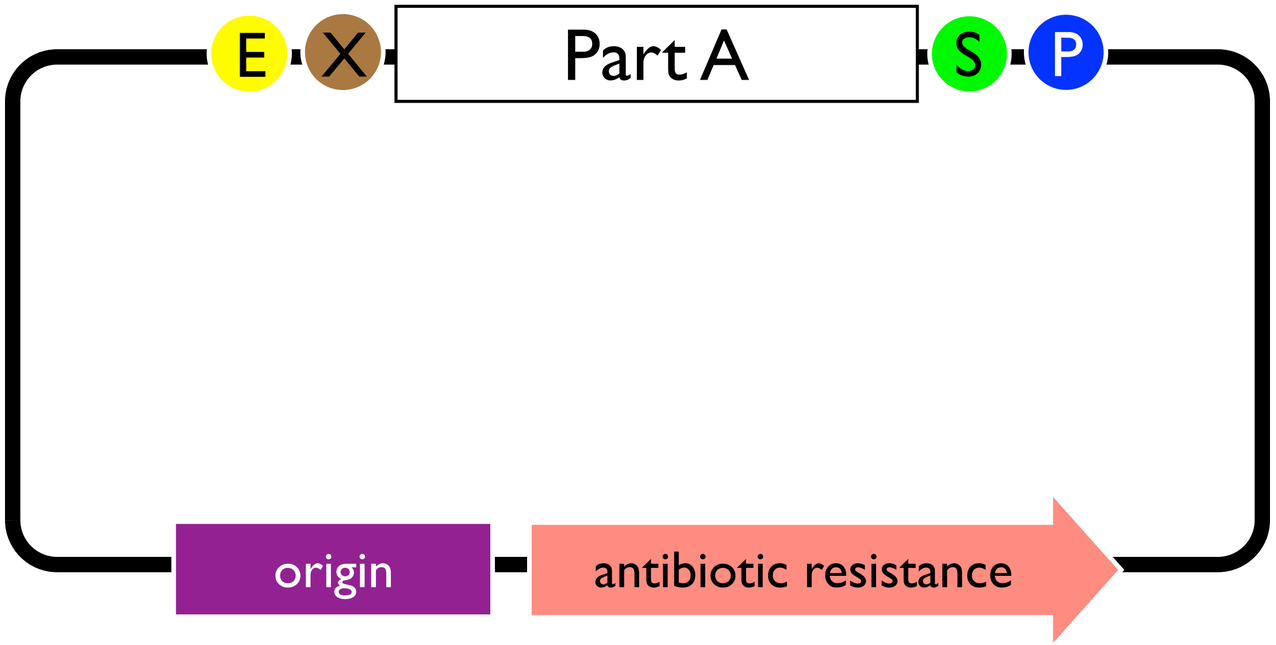


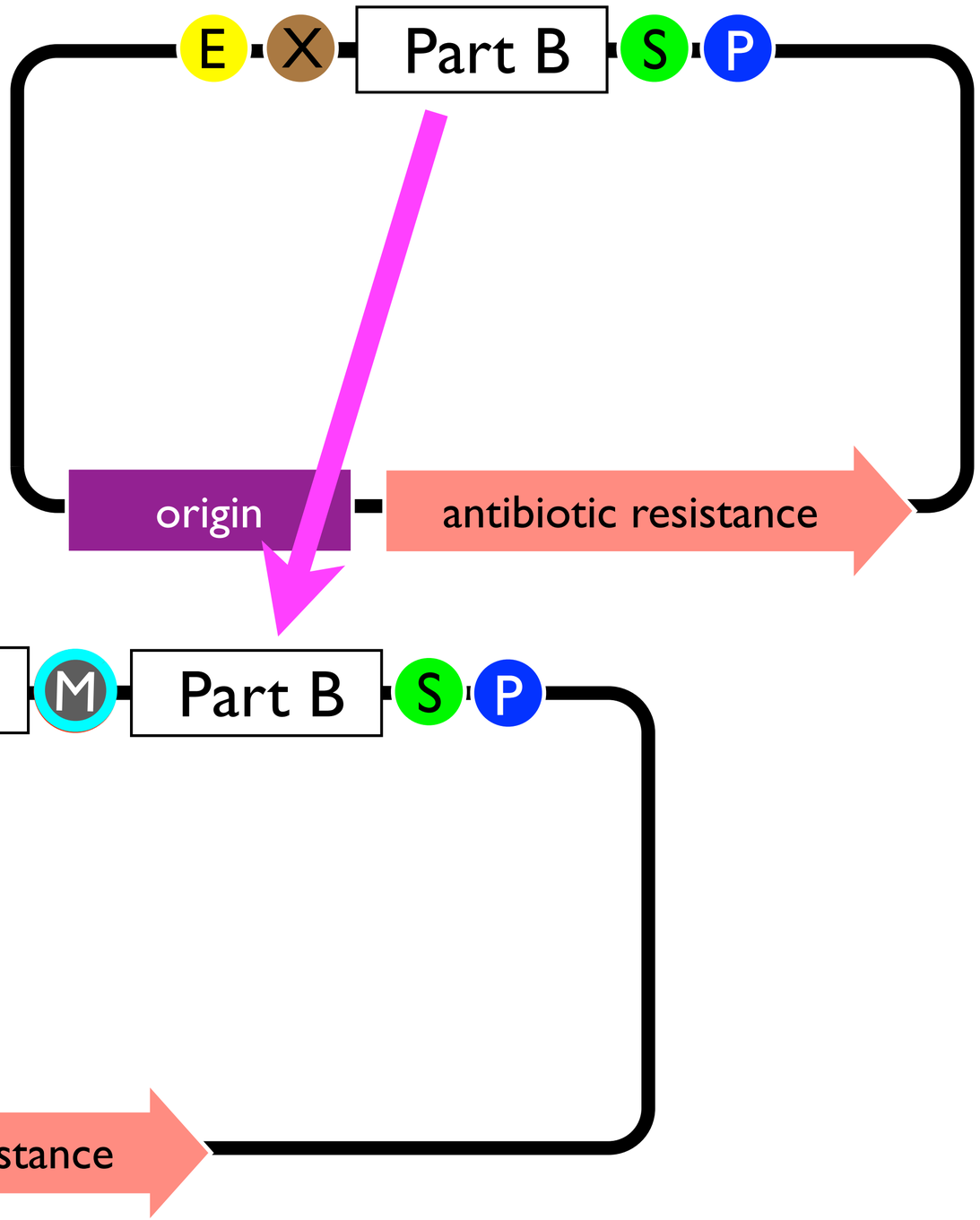
Golden Gate Assembly Method

Todd Eckdahl and A. Malcolm Campbell

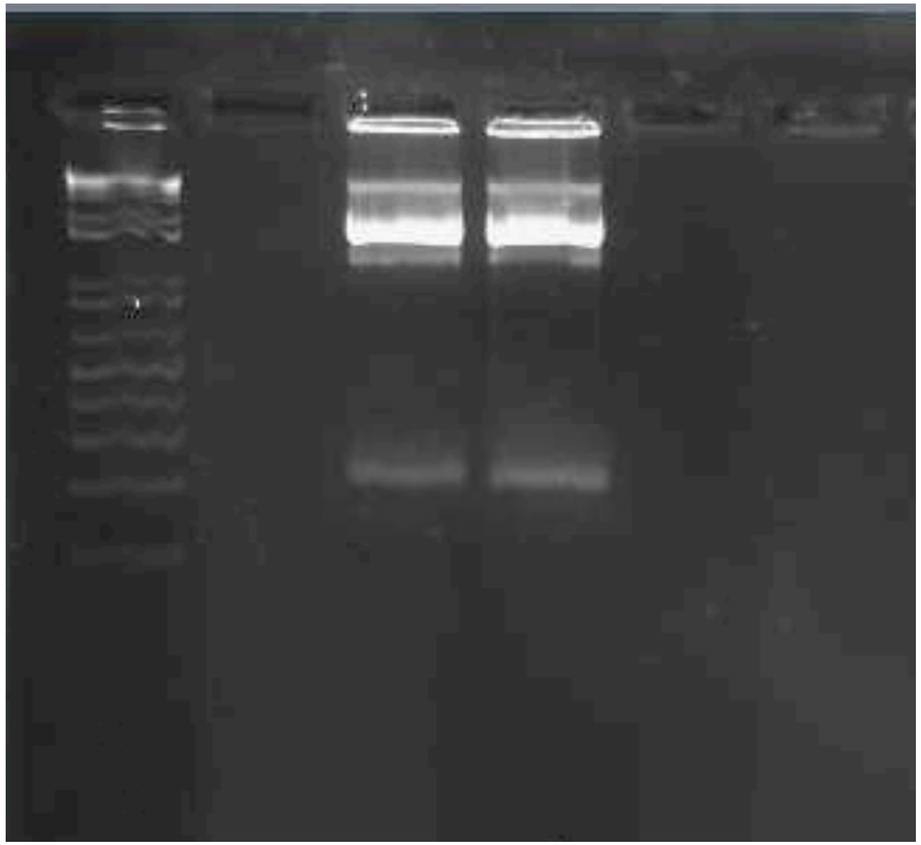
current status as of
November, 2013

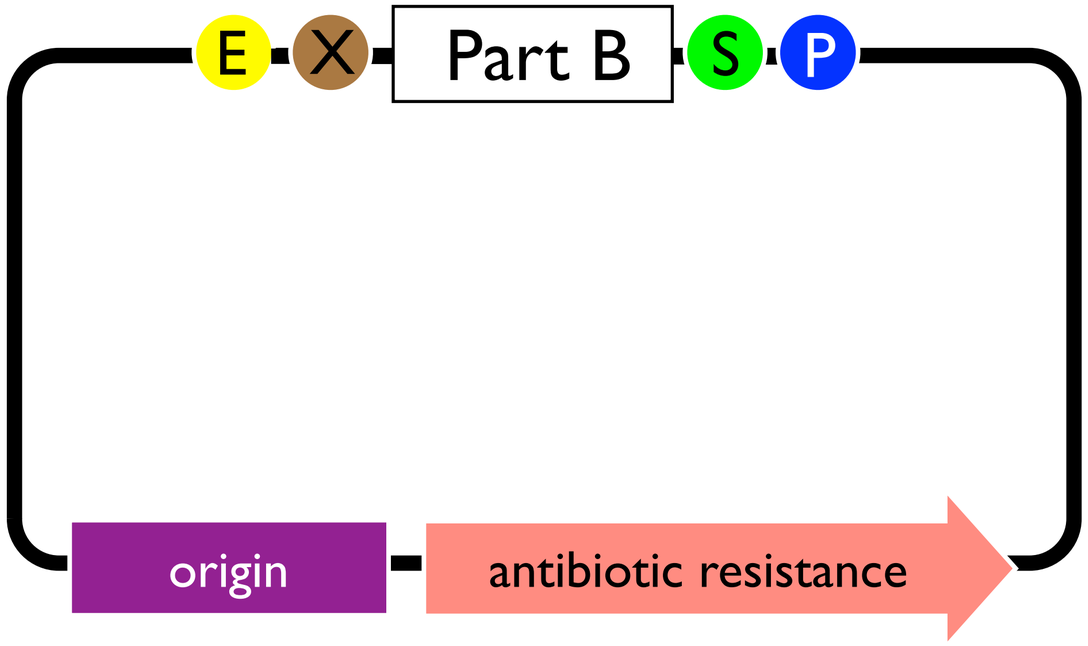
BioBricks


E
X
Part A
S
P
origin
antibiotic resistance

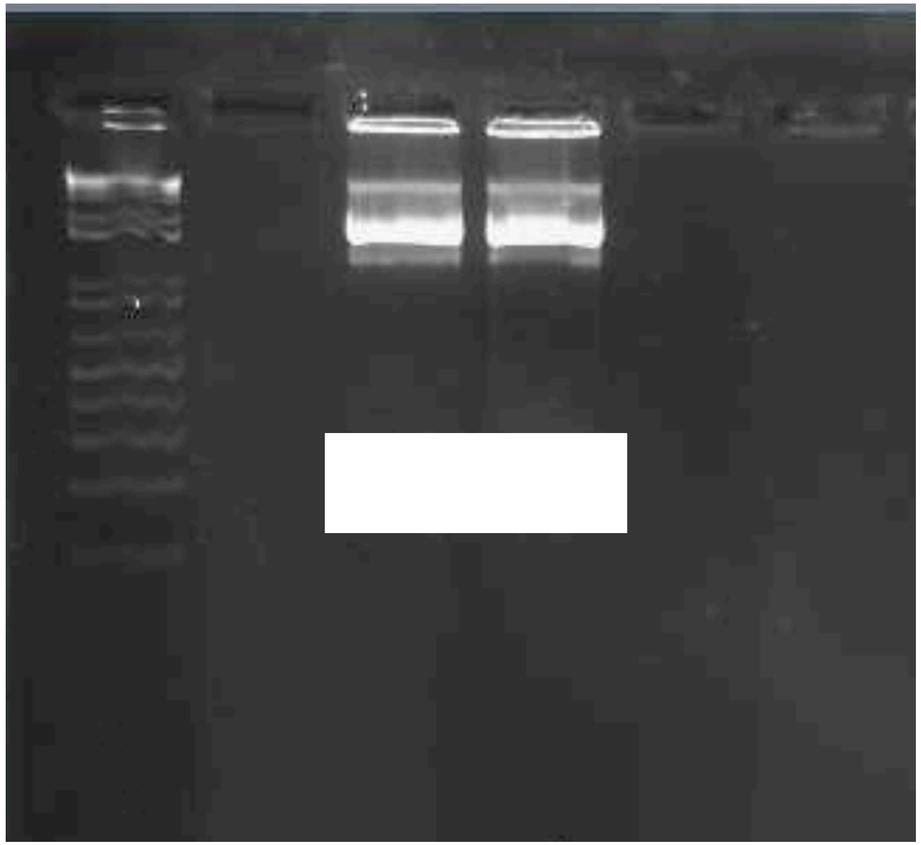

E
X
Part B
S
P
origin
antibiotic resistance
E
X
Part A
M
Part B
S
P
origin
antibiotic resistance

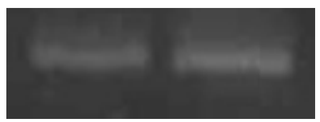
Gel Purification

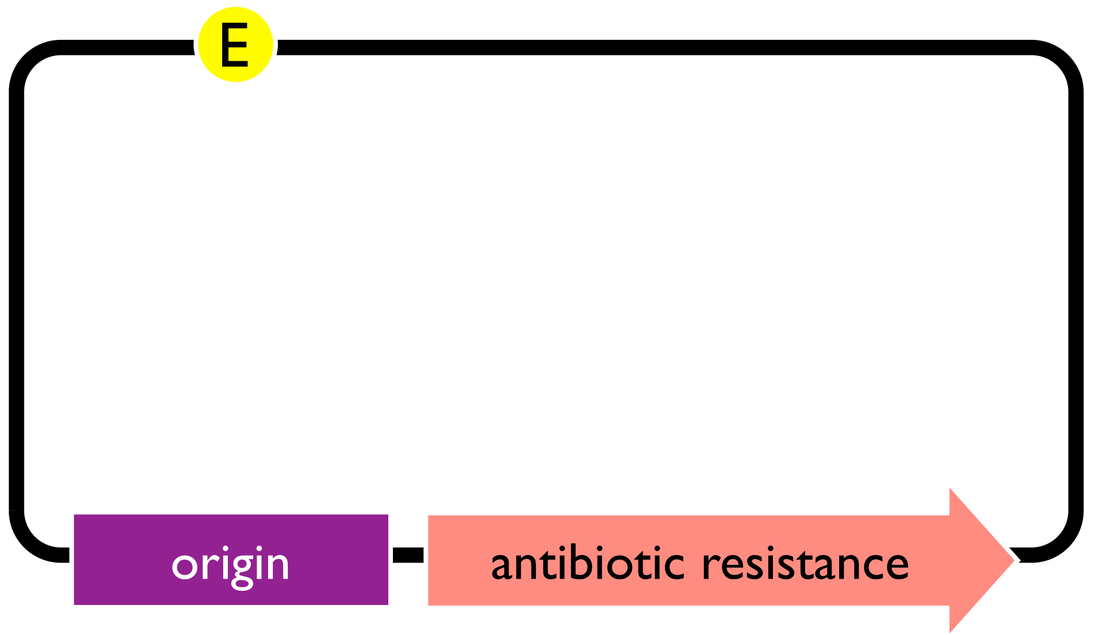


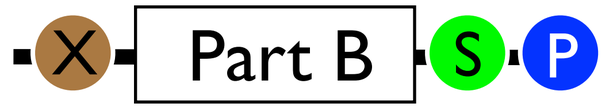


Gel Purification









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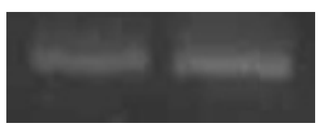

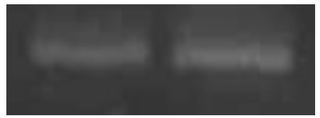

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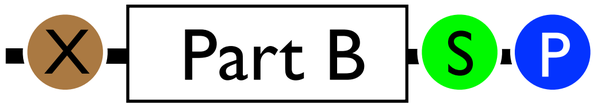

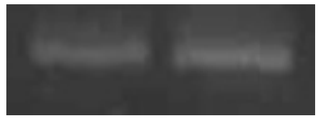

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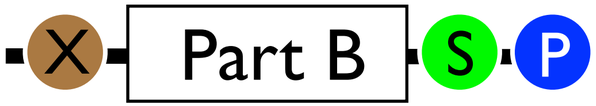
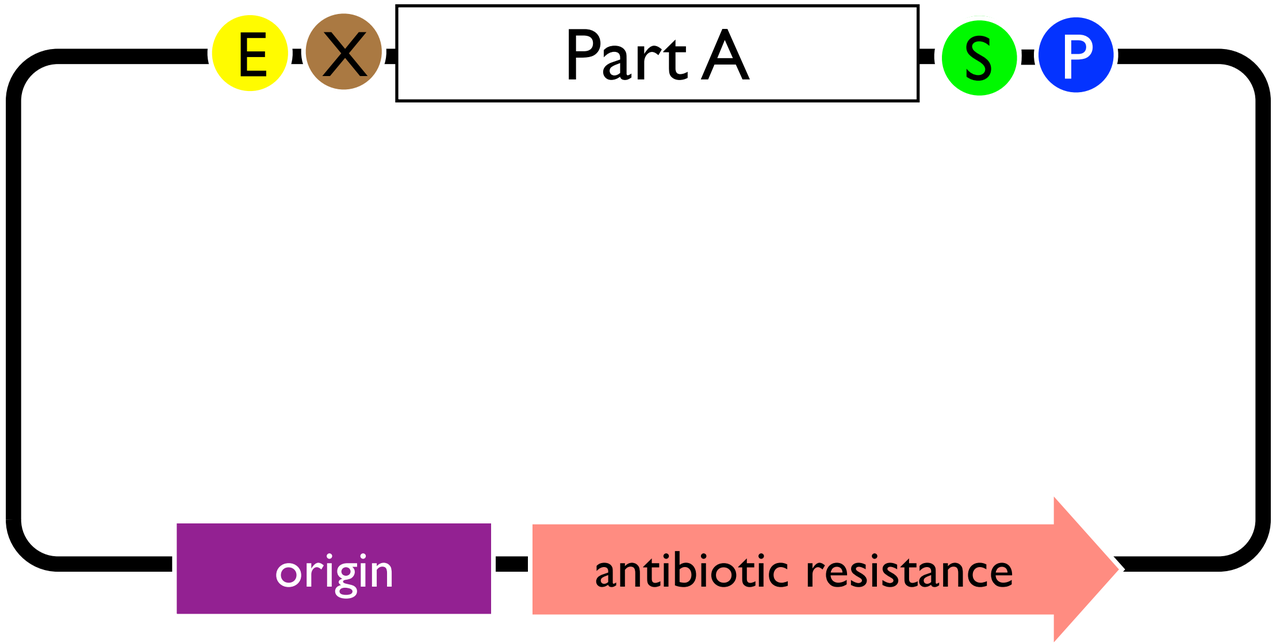
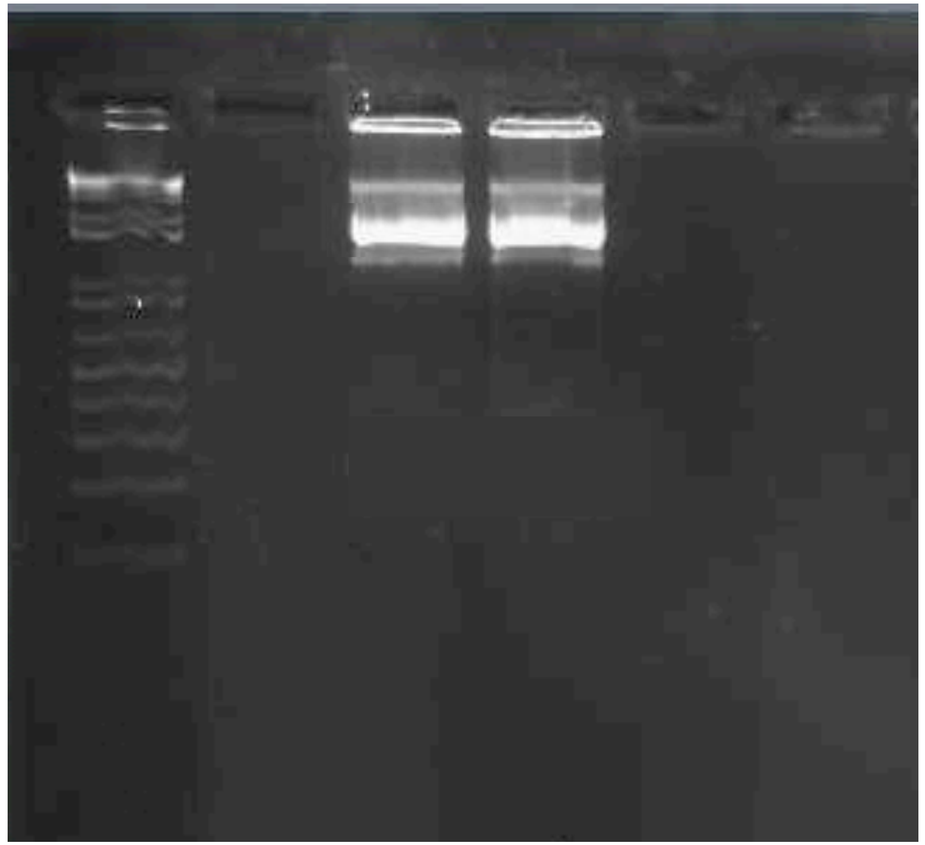
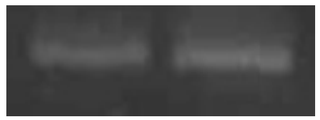




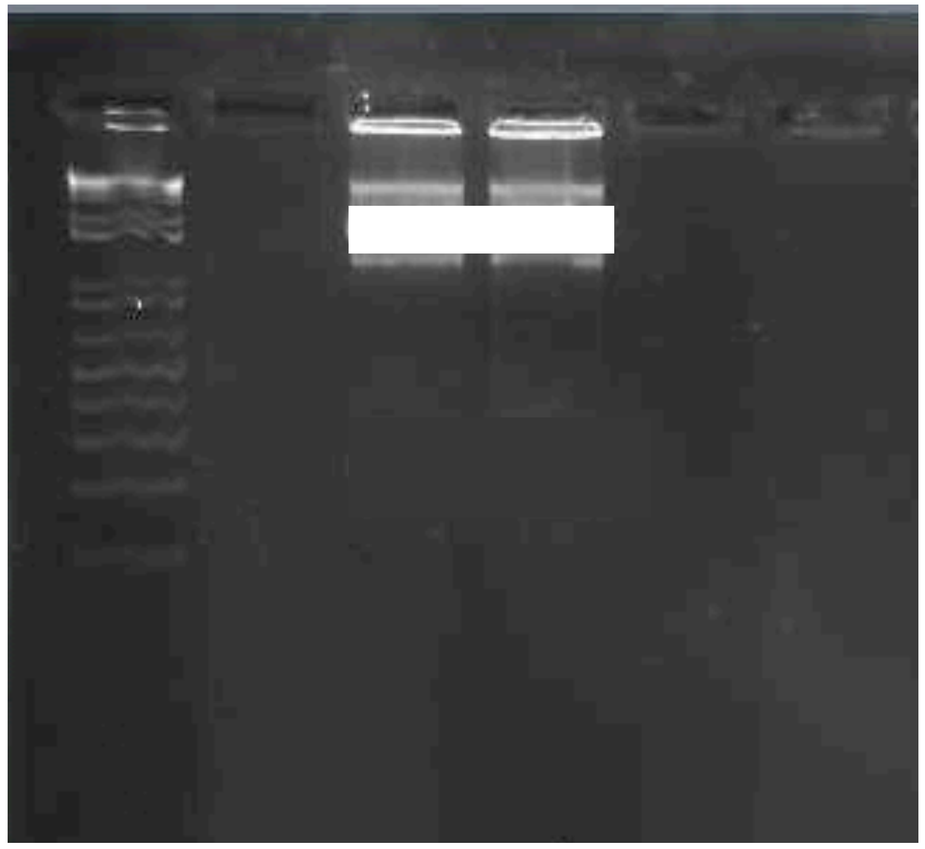




Gel Purification

X Part B S P

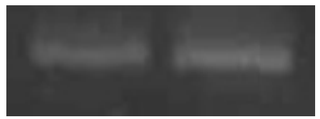
S P



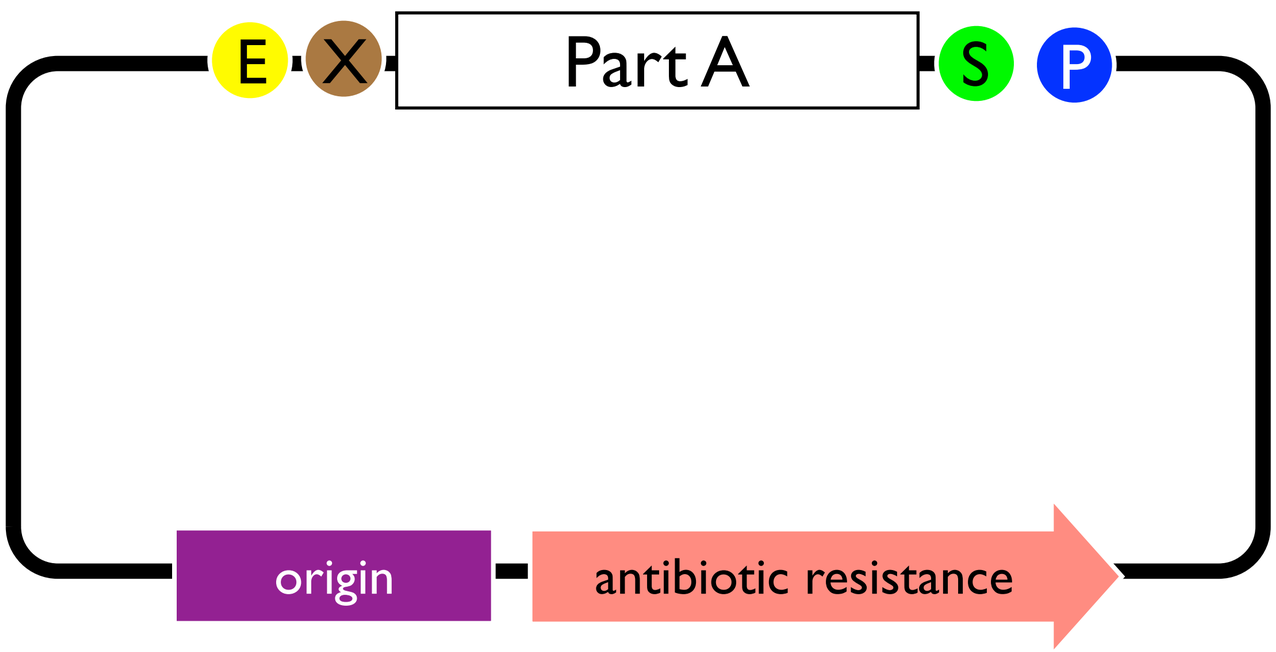
E X Part A S P

origin

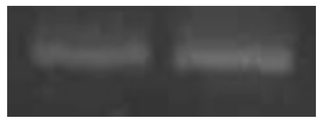
antibiotic resistance

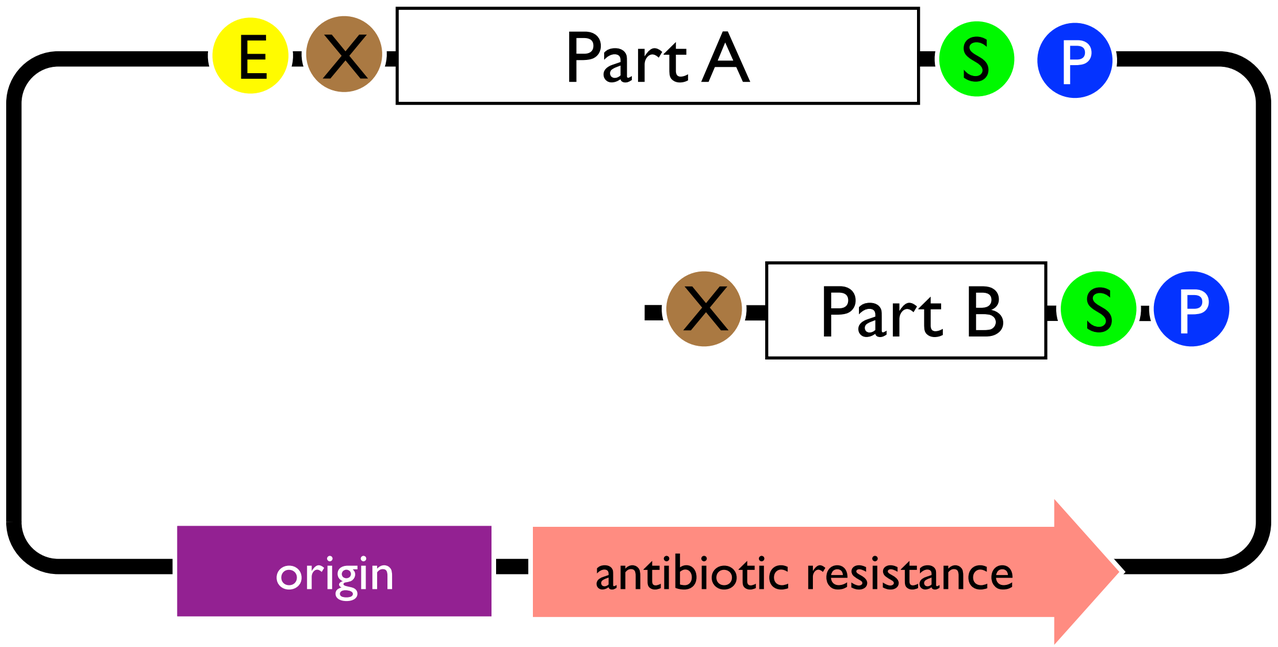


Gel Purification

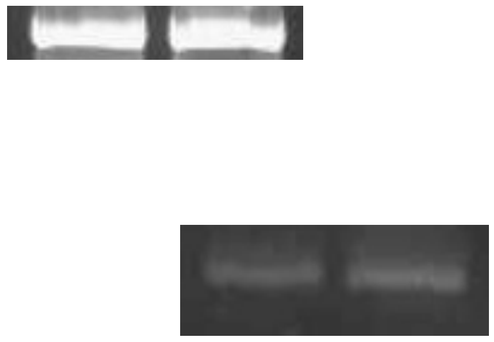


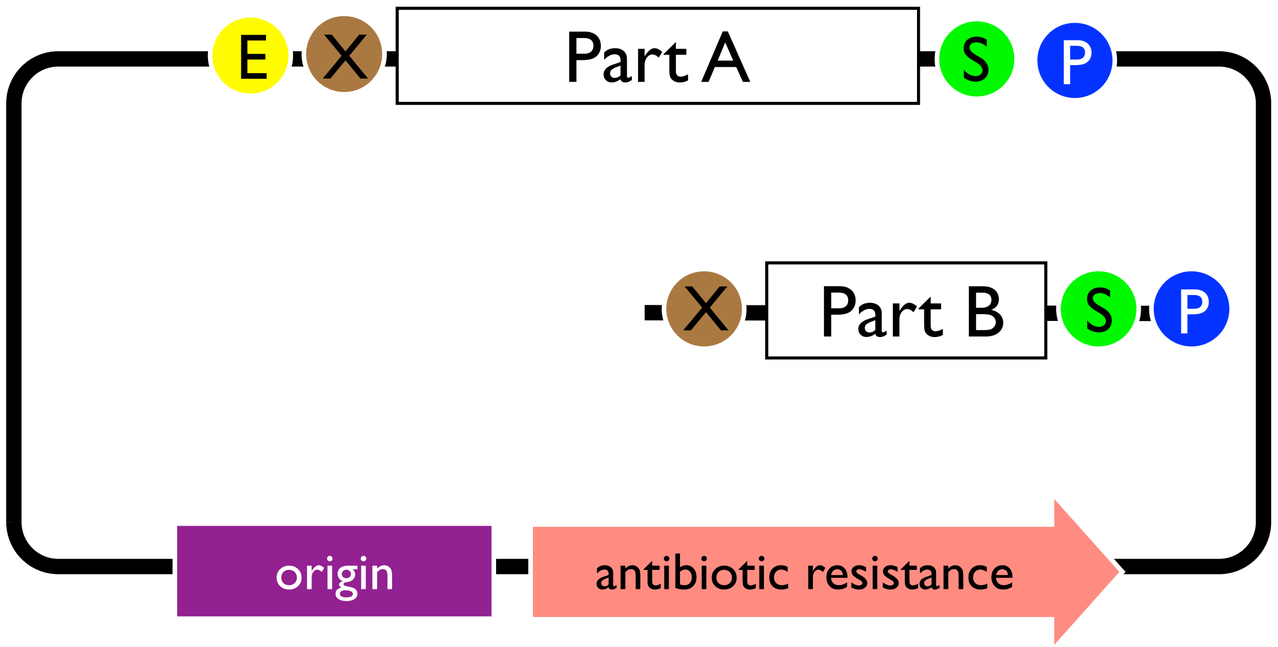
Gel Purification





Ligation





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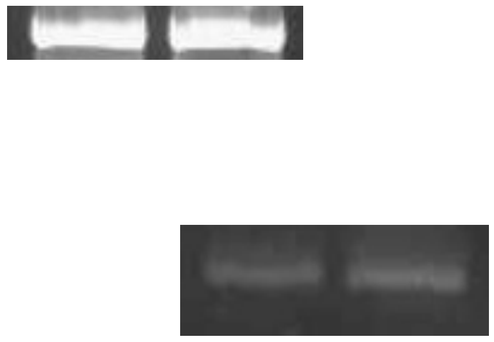
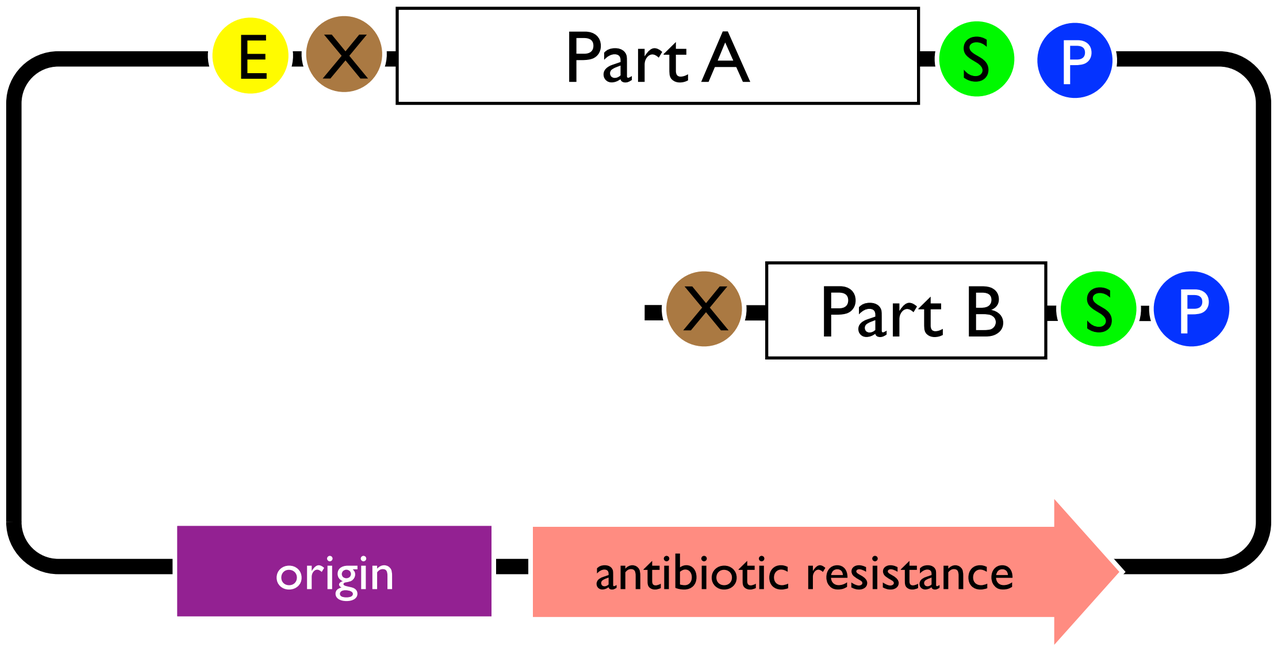
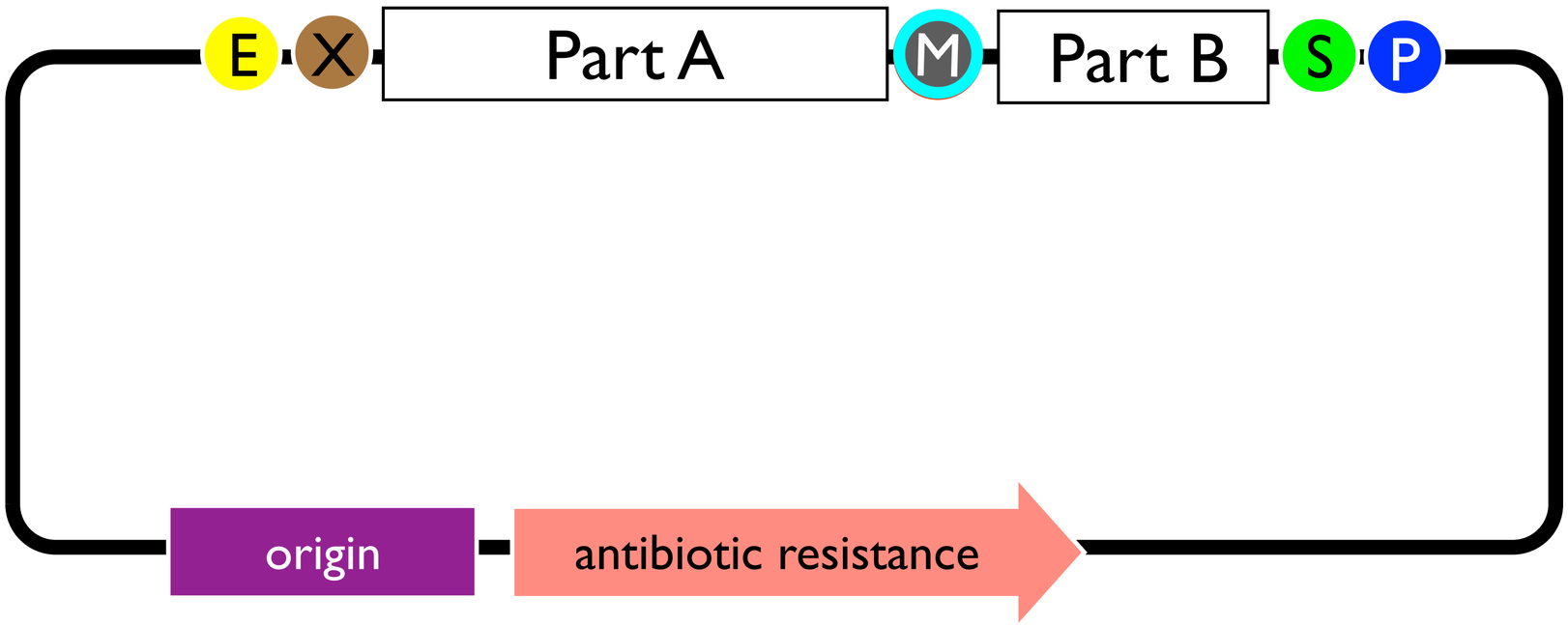


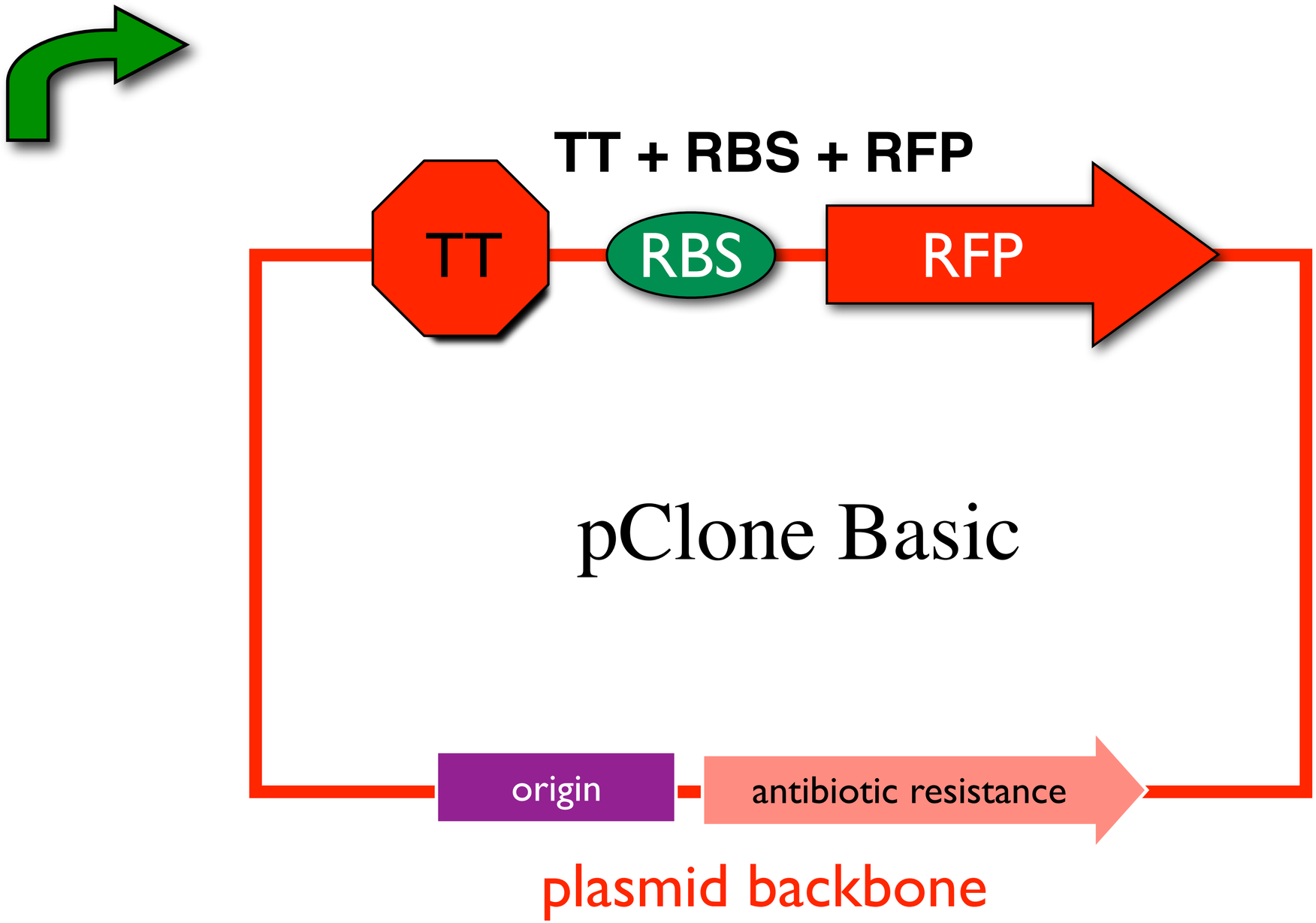


Ligation

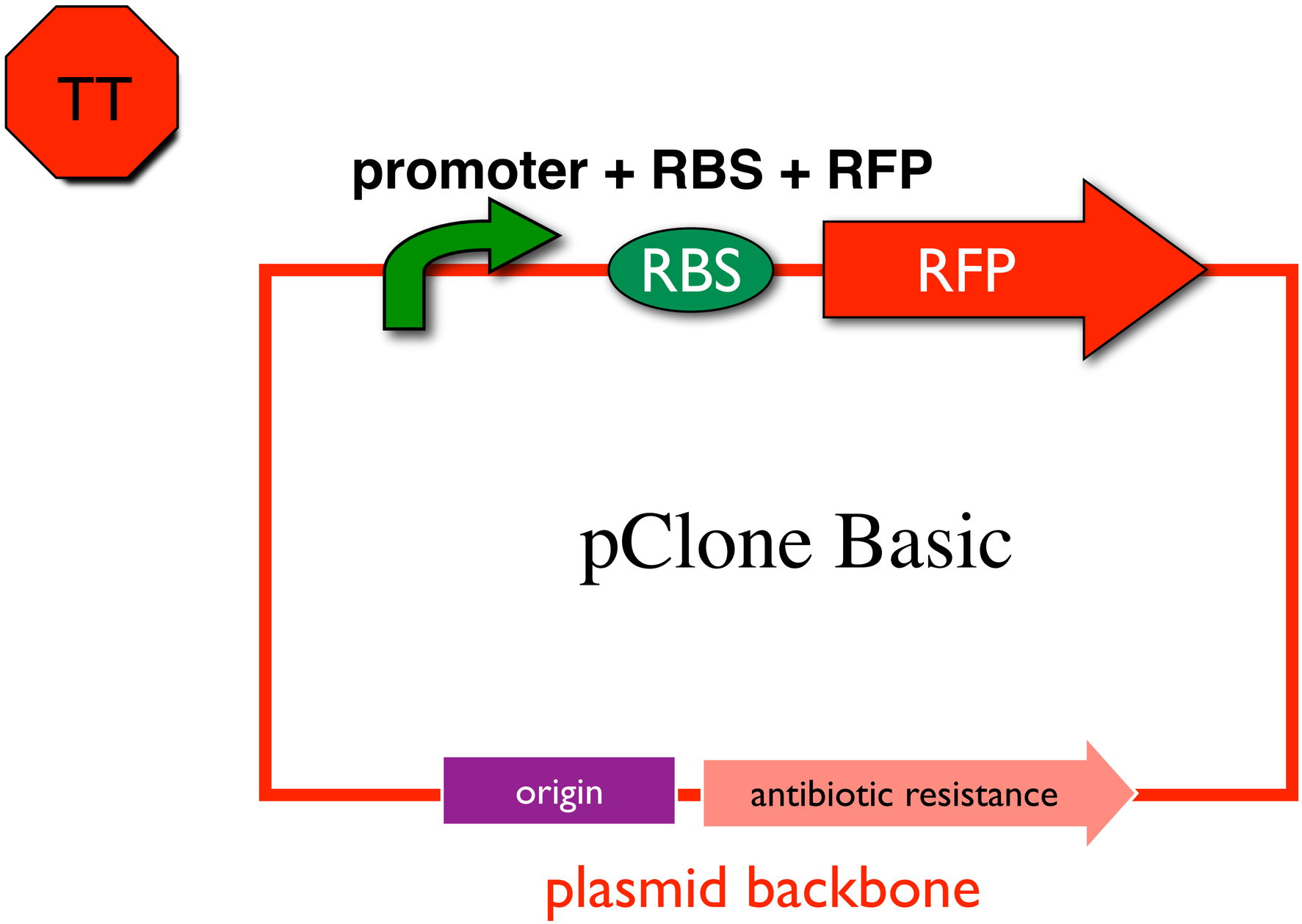


How can we clone DNA without all the hassle?

Golden Gate Assembly Method



Golden Gate Assembly Method



Eco RI

GAATTC

CTTAAG

palindrome

type II

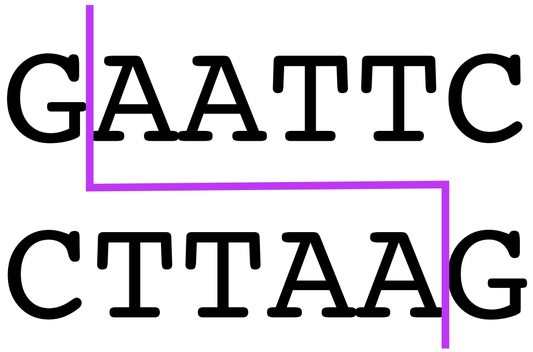
Eco RI

GAATTC
CTTAAG

palindrome

type II

Eco RI



type II

Eco RI

G AATTC

CTTAA G

type II

Bsa I

GAGACC

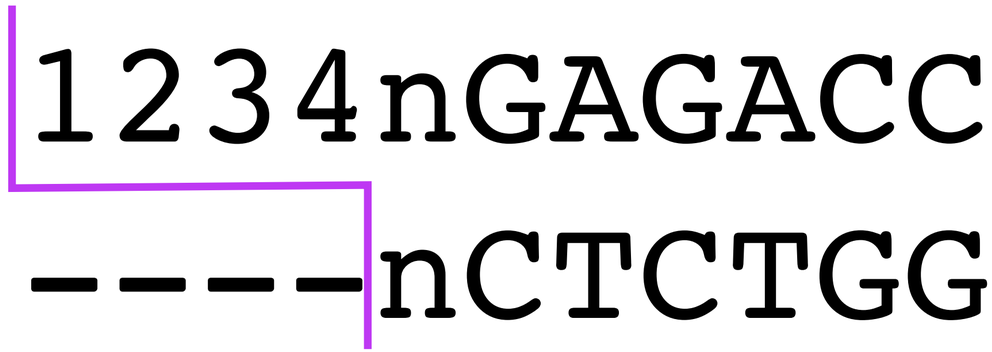
CTCTGG

G

not a palindrome

type IIs

Bsa I



type IIs

Bsa I

1234nGAGACC

----

nCTCTGG

type IIs

Bsa I

```
GGTCTCn----
CCAGAGn1234
```

type IIs

Bsa I

```
GGTCTCn                ----
CCAGAGn1234
```

type IIs

Bsa I

cuts left

1234nGAGACC

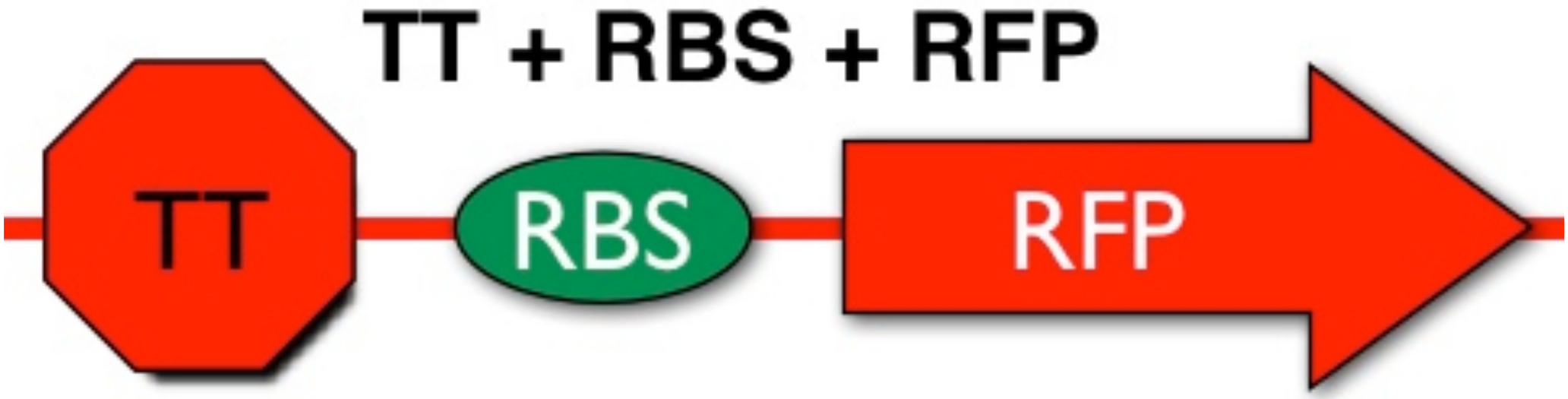
----nCTCTGG

GGTCTCn----

CCAGAGn1234

cuts right

pClone Basic



pClone Basic

Bsa I

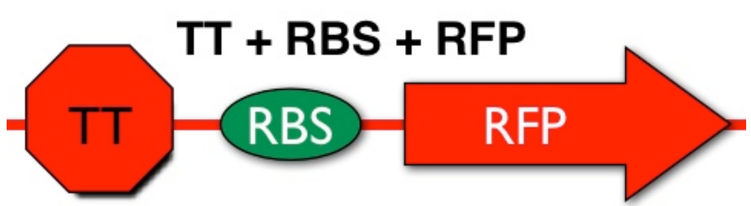
CGACtGAGACC(TT)GGTCTCaGCGG

GCTGaCTCTGG(TT)CCAGAGtCGCC

ligase

Bsa I

ligase



CGACtGAGACC(TT)GGTCTCa

aCTCTGG(TT)CCAGAGtCGCC

Bsa I

[redacted] **GCTG**

GCGG [redacted]

ligase

ligase

Bsa I

pClone Basic

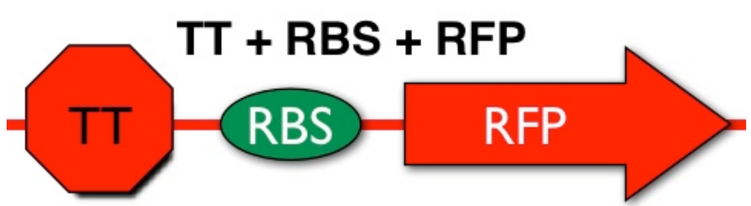
Bsa I

CGACtGAGACC(TT)GGTCTCaGCGG

GCTGaCTCTGG(TT)CCAGAGtCGCC

ligase

Bsa I ligase



CGACtGAGACC(TT)GGTCTCa

aCTCTGG(TT)CCAGAGtCGCC

Bsa I

Bsa I

GCGG

GCTG

ligase

ligase

CGAC(promoter)

(promoter)CGCC

Bsa I

CGACtGAGACC(TT)GGTCTCa

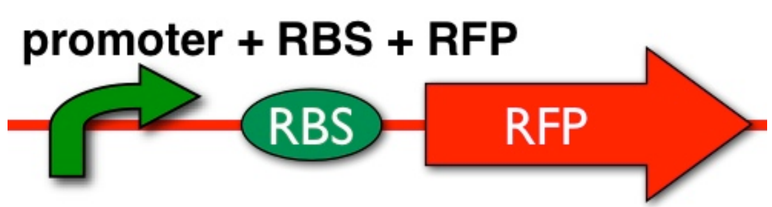
aCTCTGG(TT)CCAGAGtCGCC

Bsa I

[redacted] CGAC(promoter)GCGG [redacted]

[redacted] GCTG(promoter)CGCC [redacted]

ligase ligase



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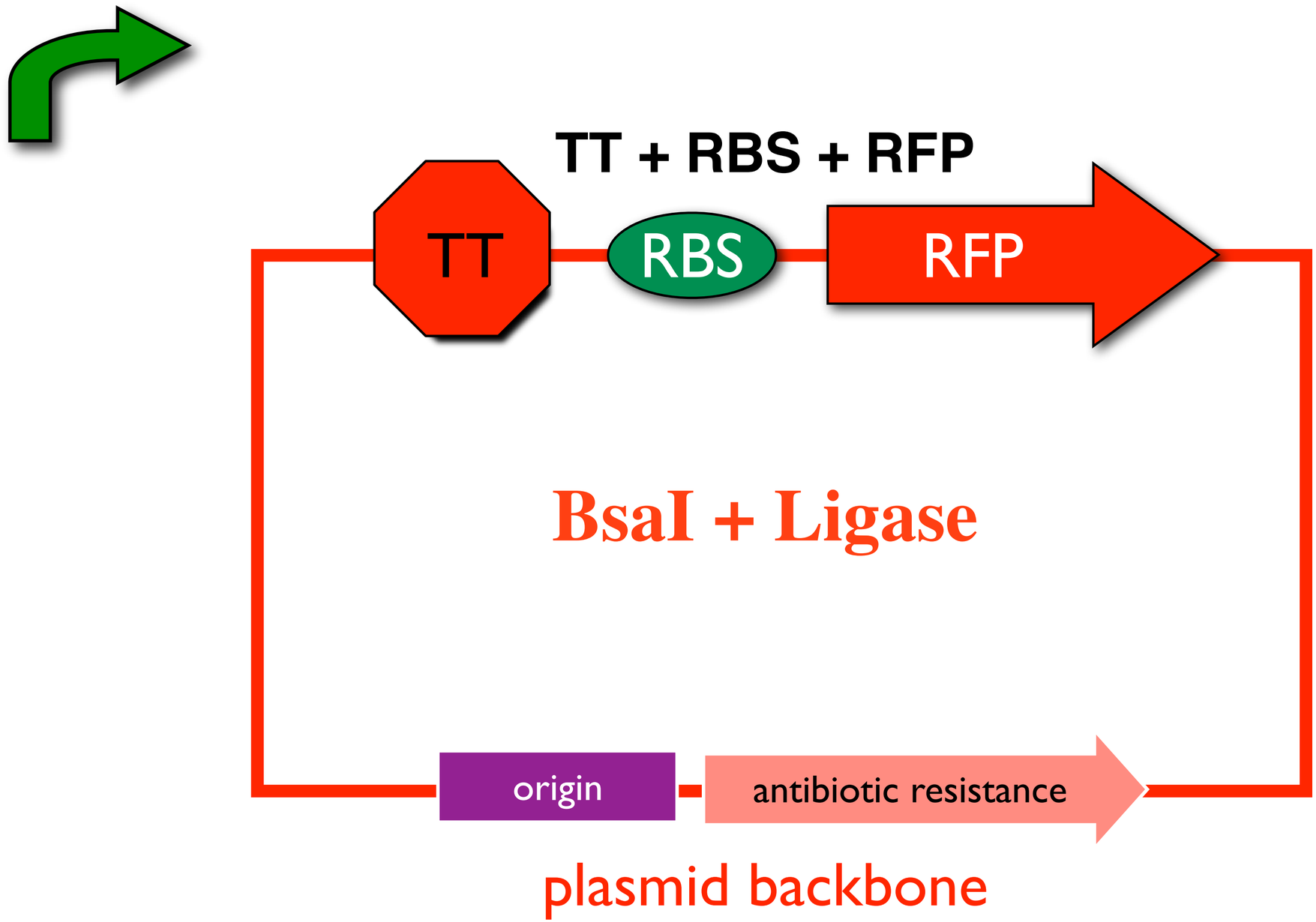
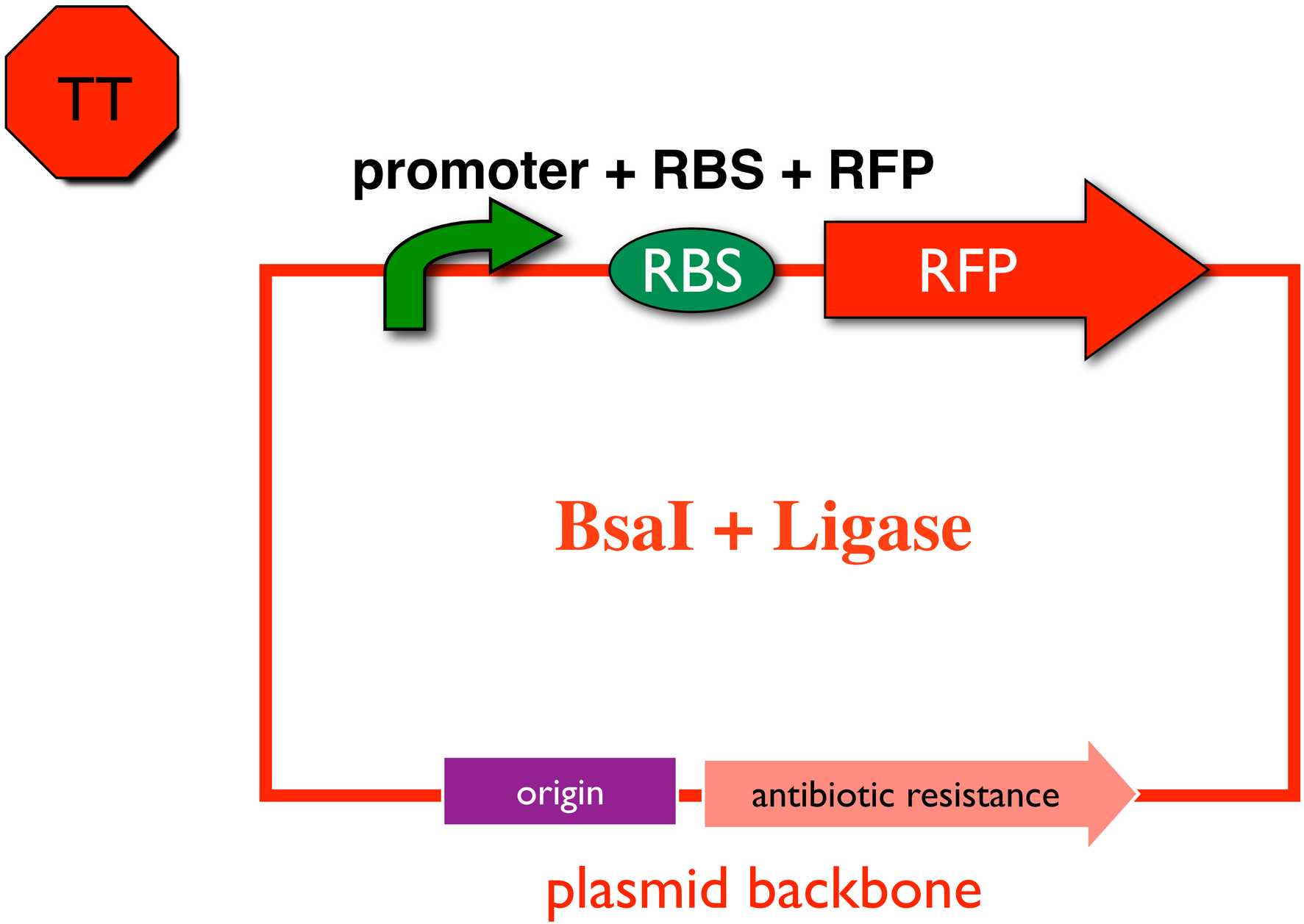


pClone Basic



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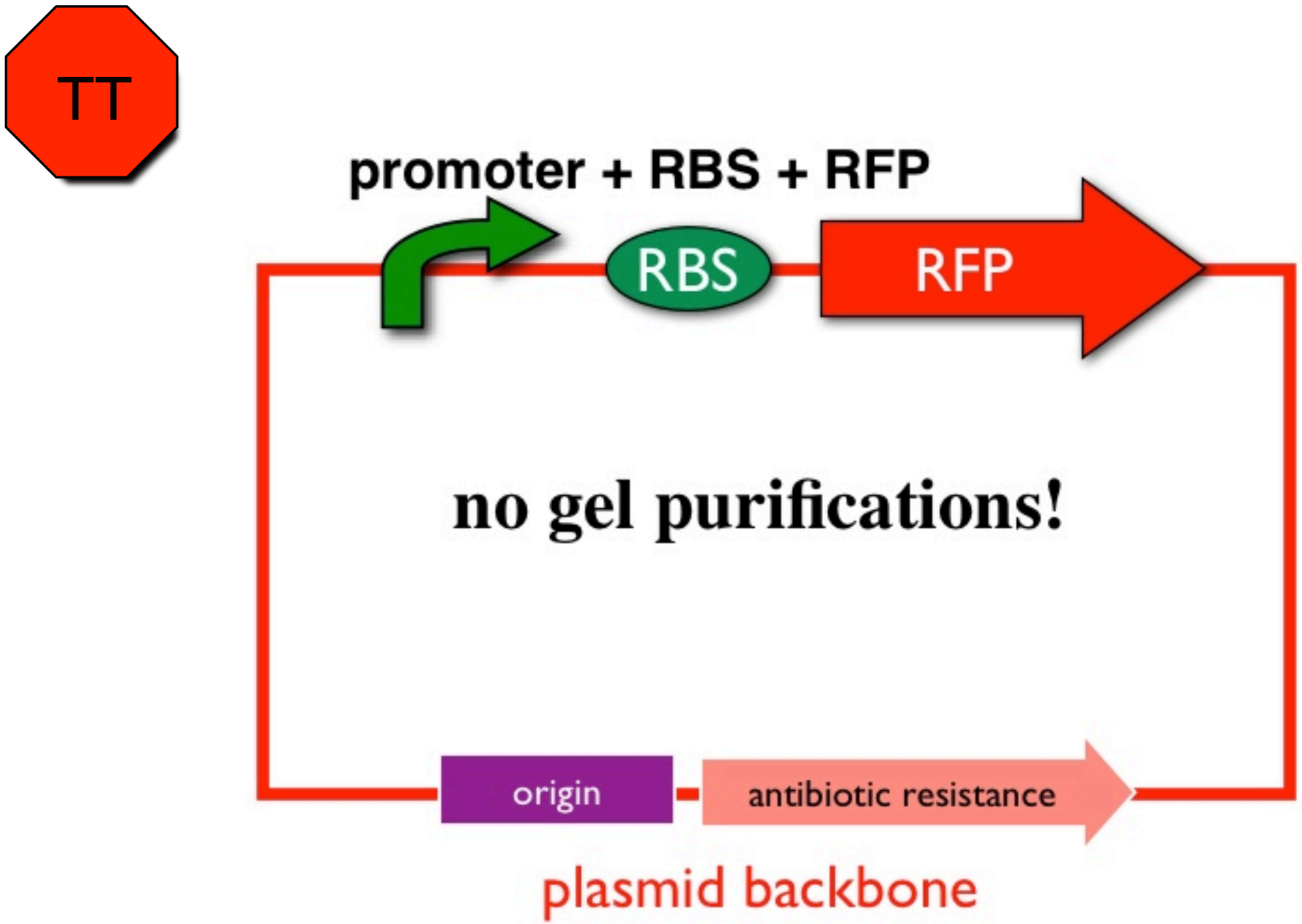
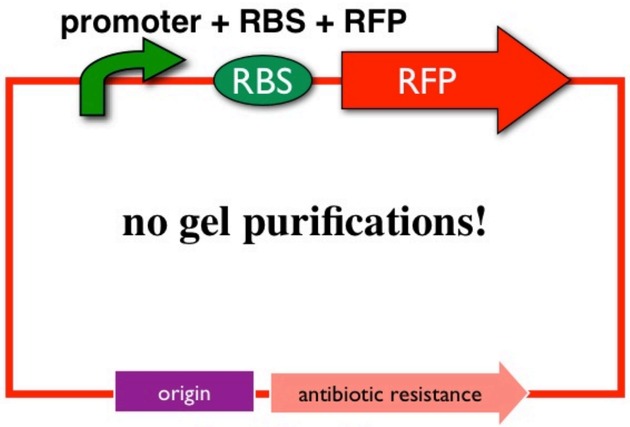
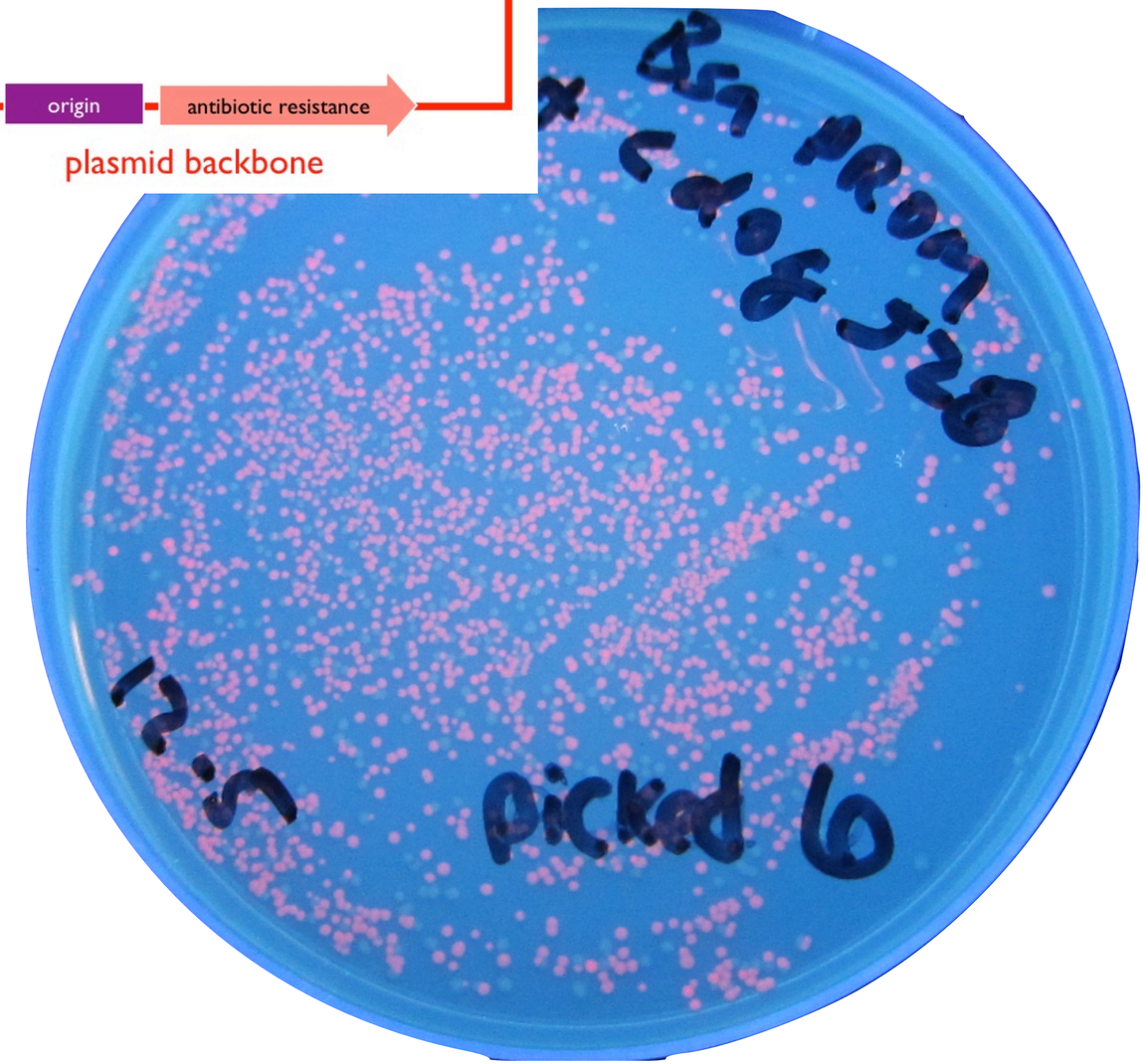
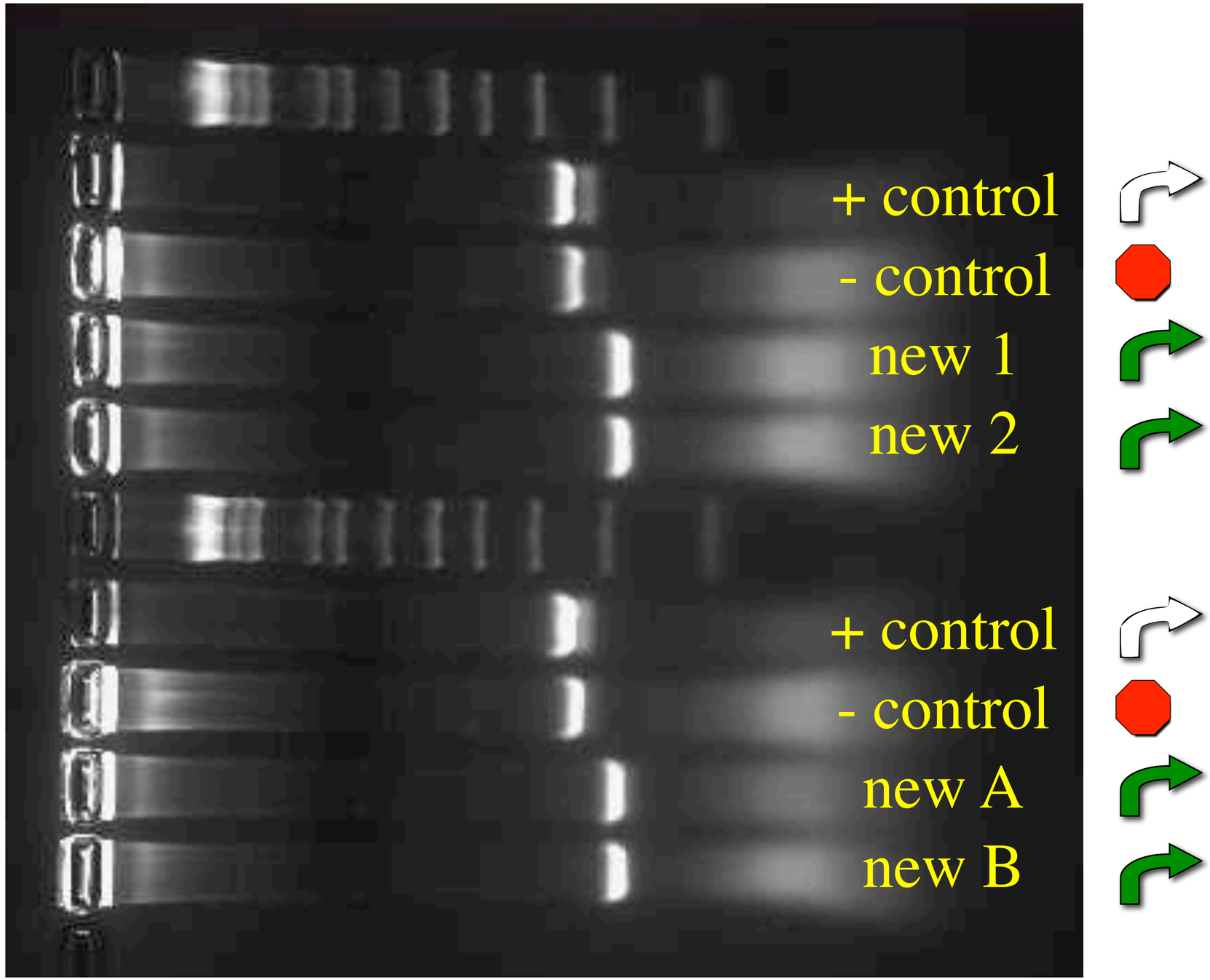


pClone Basic

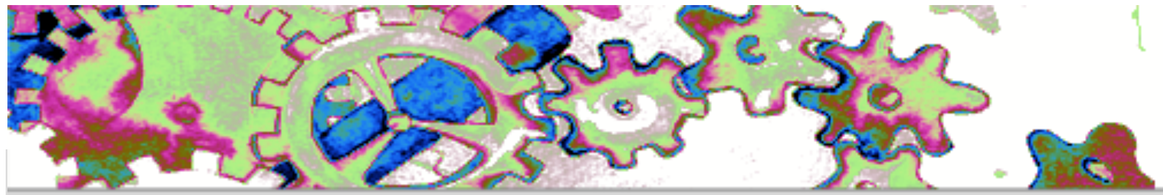




Student Sample, September 2012



Student Sample, September 2012



Registry of Standard Biological Parts

		BBa_J100067	Regulatory	fadB promoter (long sequence)	Meredith Nakano	85
		BBa_J100068	Regulatory	fadB promoter (short sequence)	Meredith Nakano	61
		BBa_J100069	Reporter	Superfolder GFP	Rebecca Evans	770
		BBa_J100070	Coding	Superfolder GFP	Rebecca Evans	720
		BBa_J100071	Regulatory	cadA promoter	Ben Clarkson	334
		BBa_J100072	Regulatory	LcpxP promoter--Long cpxP promoter	Ben Clarkson	392
		BBa_J100073	Regulatory	ScpxP--Short cpxP promoter	Ben Clarkson	94
		BBa_J100074	Regulatory	Long pLux Promoter	Betsy Gammon	197
		BBa_J100075	Regulatory	CydAP1 Long Promoter	Betsy Gammon	158
		BBa_J100076	Regulatory	CydAP1 Short Promoter	Betsy Gammon	151
		BBa_J100077	Composite	J10068:K0903005	Meredith Nakano	793
		BBa_J100078	Composite	J100067:K0903005	Meredith Nakano	817
		BBa_J100079	Device	Riboswitch and GFP	Rebecca Evans	879
		BBa_J100080	Device	Riboswitch and GFP	Rebecca Evans	882
		BBa_J100081	Reporter	J100071+E0240	Ben Clarkson	334
		BBa_J100082	Reporter	J100072+E0240	Ben Clarkson	1276
		BBa_J100083	Composite	LuxI Long + RBS + GFP	Betsy Gammon	1081
		BBa_J100084	Composite	CydAP Long + RBS + GFP	Betsy Gammon	1042
		BBa_J100085	RNA	short CRISPR sequence with GFP target spacer	Caroline Vrana	240
		BBa_J100086	Composite	CydAP Short Promoter + RBS + GFP	Betsy Gammon	1035
		BBa_J100087	Reporter	J100073+E0240	Ben Clarkson	978
		BBa_J100088	Generator	J100071+J10063	Ben Clarkson	2965
		BBa_J100089	Generator	J100072+J10063 (LcpxP+LRE, Luciferase)	Ben Clarkson	3023
		BBa_J100090	Regulatory	CRISPR sequence with GFP and AmpR targets	Caroline Vrana	412
	W	BBa_J100092	Regulatory	Constitutive promoter for M1-162	Natalie Spach	50
	?	BBa_J100093	Regulatory	rrnB P1 promoter	Kayla McAvoy	60
	?	BBa_J100094	Regulatory	Lac promoter E. Coli	Cameron Bard	44
	?	BBa_J100095	Regulatory	malE1 Maltose induced promoter.	Pooja Potharaju	65
		BBa_J100096	Regulatory	PBAD Promoter from araE Gene	Elizabeth Brunner	27
	W	BBa_J100097	Regulatory	Anhydrotetracycline inducible promoter with BsaI sticky ends	Sarah Kim	55
		BBa_J100098	DNA	Promoter for the argF gene	Erin Nieusma	44
	W	BBa_J100099	Regulatory	A promoter (CydAB) activated by the FNR enzyme	Phoebe Parrish	64

Student Sample, September 2012

Registry of Standard Biological Parts

Go Search

page discussion view source history Log in / create account

BBa J100099 Main Page Part Design Physical DNA Hard Information Experience Tools

Part:BBa_J100099

Designed by Phoebe Parrish Group: Campbell_M_Lab (2012-09-13)

Regulatory

DNA Planning
Experience: Works
Get This Part

A promoter (CydAB) activated by the FNR enzyme

The promoter, CydAB, was found to be activated by the FNR enzyme, which is induced by the presence of (NH4)2Fe(SO4)2 and ascorbate. The oligo includes both CydAB, the FNR binding site, and the sticky ends needed for the Golden Gate Assembly method.

Sequence and Features

Format: Subparts | Ruler | **SS** | DS **Search:** **Length: 64 bp** **Context: Part only** Get selected sequence

```
     1          11         21         31         41         51         61         71         81         91
1    ggaattgata tttatcaatg tataagtctt ggaaatgggc atcaaaaaga gataaattgt tctc
```

FNR binding -35 -10

Assembly Compatibility: 10 12 21 23 25

Jeffrey Green. 1993. "Activation of FNR-dependent transcription by iron: An in vitro switch for FNR." FEMS Microbiology Letters 113 (1993) 219-222

[edit]

Student Sample, September 2012

Part:BBa_J100099:Experience

Designed by Phoebe Parrish Group: Campbell_M_Lab (2012-09-13)

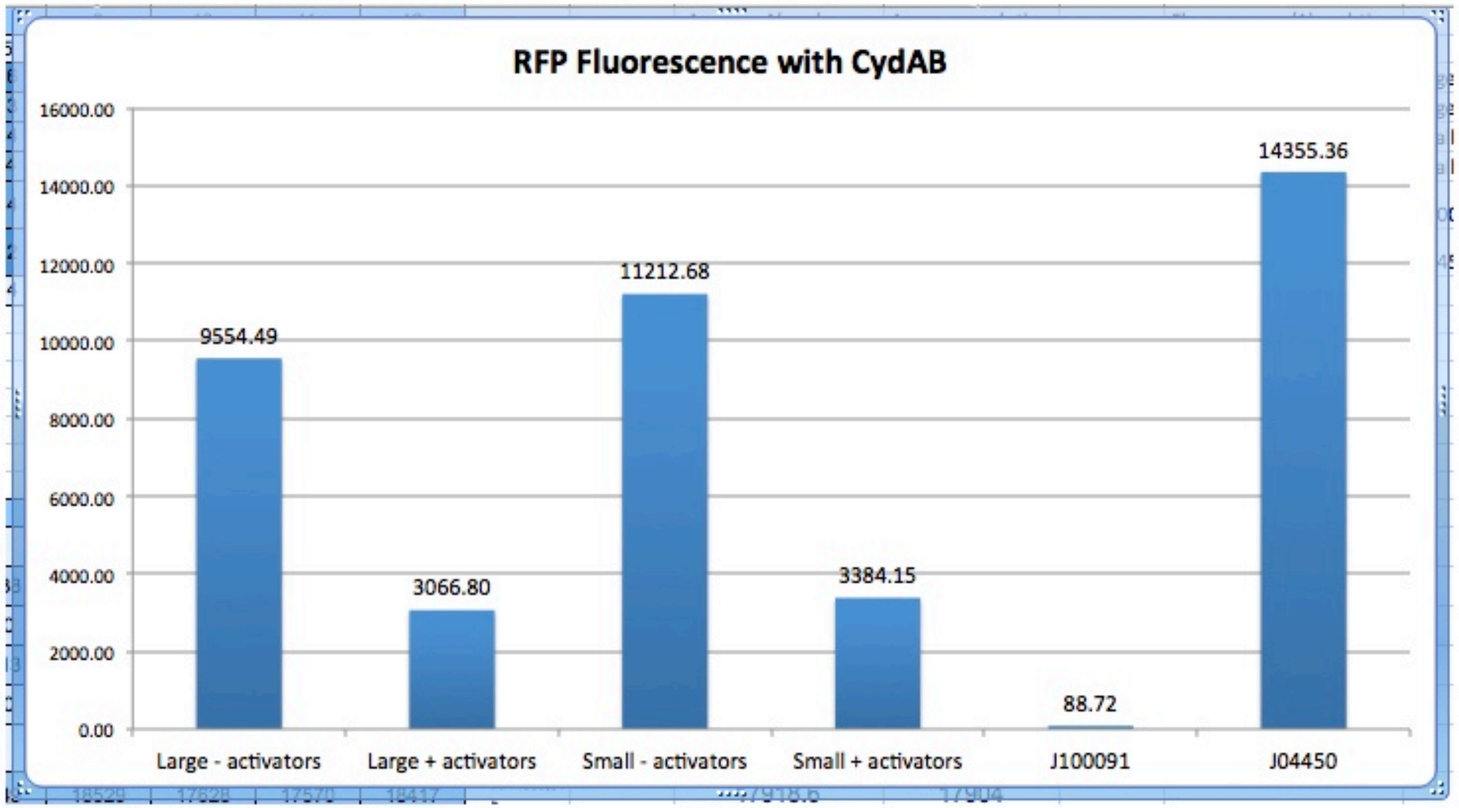
Regulatory

DNA Planning
Experience: Works
Get This Part

This experience page is provided so that any user may enter their experience using this part.
Please enter how you used this part and how it worked out.

Applications of BBa_J100099

We pipetted 200 microliters of one solution containing E coli cells from a small colony and the activators, one with cells from a small colony and no activators, one containing cells from a large colony and the activators, and one containing cells from a large colony and no activators. We also did a positive control with E coli cells containing a known promoter that causes red florescence (J04450) and a negative control with cells containing a the transcriptional terminator that does not cause red fluorescence (J100091). We tested both fluorescence of our samples using a fluorometer and the light absorbance using a spectrophotometer. We measured the fluorescence and absorbance of five samples of each solution, including a control solution that just contained the growth medium. We averaged the values for each solution and subtracted the average fluorescence/absorbance of the control. We then divided the average fluorescence by the average absorbance for each solution. These values are displayed on the accompanying graph.



Registry of Functional Promoters (RFP)

Registry of Functional Promoters (V1.0)

Welcome to the Registry of Functional Promoters

This Registry of Functional Promoters was developed by Bill Hatfield, Laurie J. Heyer, A. Malcolm Campbell at Davidson College and Todd Eckdahl of Missouri Western State University, through the support of HHMI grant 52006292 (GCA T main page) and is freely available for others to use though no support other than the user manual is available.

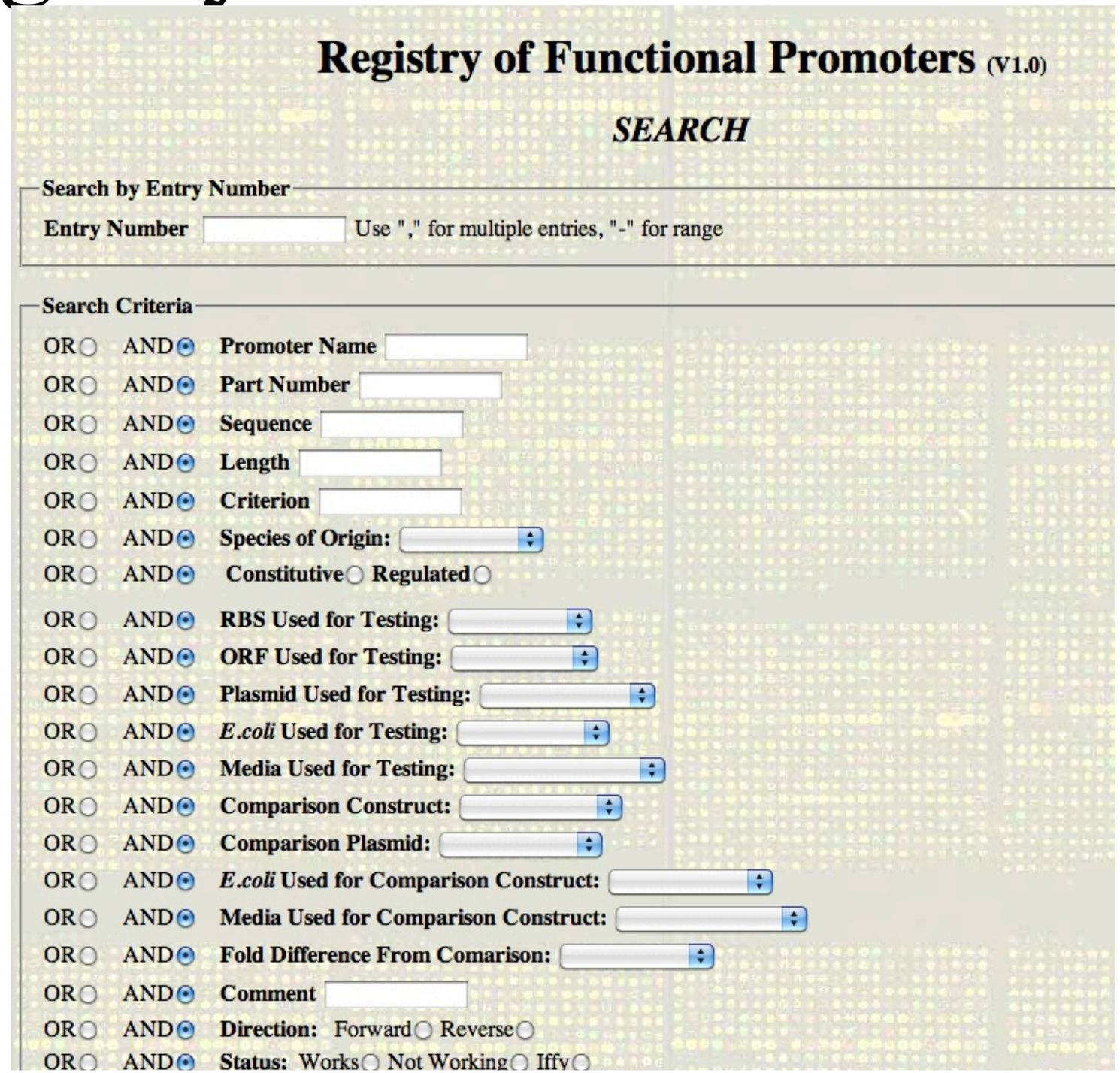
If your are already a Registered User of GCAT-alog , you do not need to Reregister

LOGIN REGISTER AS NEW USER

- For comments or questions about this website contact, Malcolm Campbell

gcat.davidson.edu/RFP/

Registry of Functional Promoters (RFP)



Registry of Functional Promoters (V1.0)

SEARCH

Search by Entry Number

Entry Number Use "," for multiple entries, "-" for range

Search Criteria

OR AND **Promoter Name**
OR AND **Part Number**
OR AND **Sequence**
OR AND **Length**
OR AND **Criterion**
OR AND **Species of Origin:**
OR AND **Constitutive** **Regulated**
OR AND **RBS Used for Testing:**
OR AND **ORF Used for Testing:**
OR AND **Plasmid Used for Testing:**
OR AND ***E.coli* Used for Testing:**
OR AND **Media Used for Testing:**
OR AND **Comparison Construct:**
OR AND **Comparison Plasmid:**
OR AND ***E.coli* Used for Comparison Construct:**
OR AND **Media Used for Comparison Construct:**
OR AND **Fold Difference From Comarison:**
OR AND **Comment**
OR AND **Direction:** Forward Reverse
OR AND **Status:** Works Not Working Iffy

gcat.davidson.edu/RFP/

Registry of Functional Promoters (RFP)

DC1	MekA mutated	J100126	caccggattcttcaaaccattcaccatttccttcaagcgtgaaacttgccctcattgttaccgttt	66	Nadja Graf & Josef Altenbuchner, 2013	*E. coli*	
DC1	GLNAP2	J100124	atggtgcgcatgataacgccttttaggggcaatttaaaagttggcacagatttcgctttatctttt	66	SCHNEIDER et al., 1991	*E. coli*	
DC1	light inducible promoter	J100123	gctgaggagatgcccggtggacgctttcacaaaggccgggacctcccgctccggcaatcacaacccg	67	Whitworth et al., 2004	*E. coli*	
DC1				0		*E. coli*	
DC1	DNA Q	J100125	ctgtttaagcatctctggtagacttcctgtaattgaatcgaactgtaaaacgacaagtctg	61	http://ecocyc.org/ECOLI/NEW-IMAGE?type=OPERON&object=TU0-6648	*E. coli*	
DC1	yqiHIK	J100127	CGACAAATTTTTTAAAATGAATAAAAAGTTGCTTCTTTCCGCTAATTTTTTCTAATT	57		Bacillus subtilis	
DC1	P1	J100128	TTTTGTTGACATTTAATGATAATGTATTTTACACATTAGA	40		*E. coli*	
DC1	Zur Box	J100130	GGCGAGTTGTTATACAGTAACATTTCTAG	29		Bacillus subtilis	
DC1	prpR	J100129	ttttttgttttaaacgtgtttcataaatgttgcaatgaaacagggtgattcgtttc	56		Salmonella typhimurium	

gcat.davidson.edu/RFP/

Research for Intro Courses!

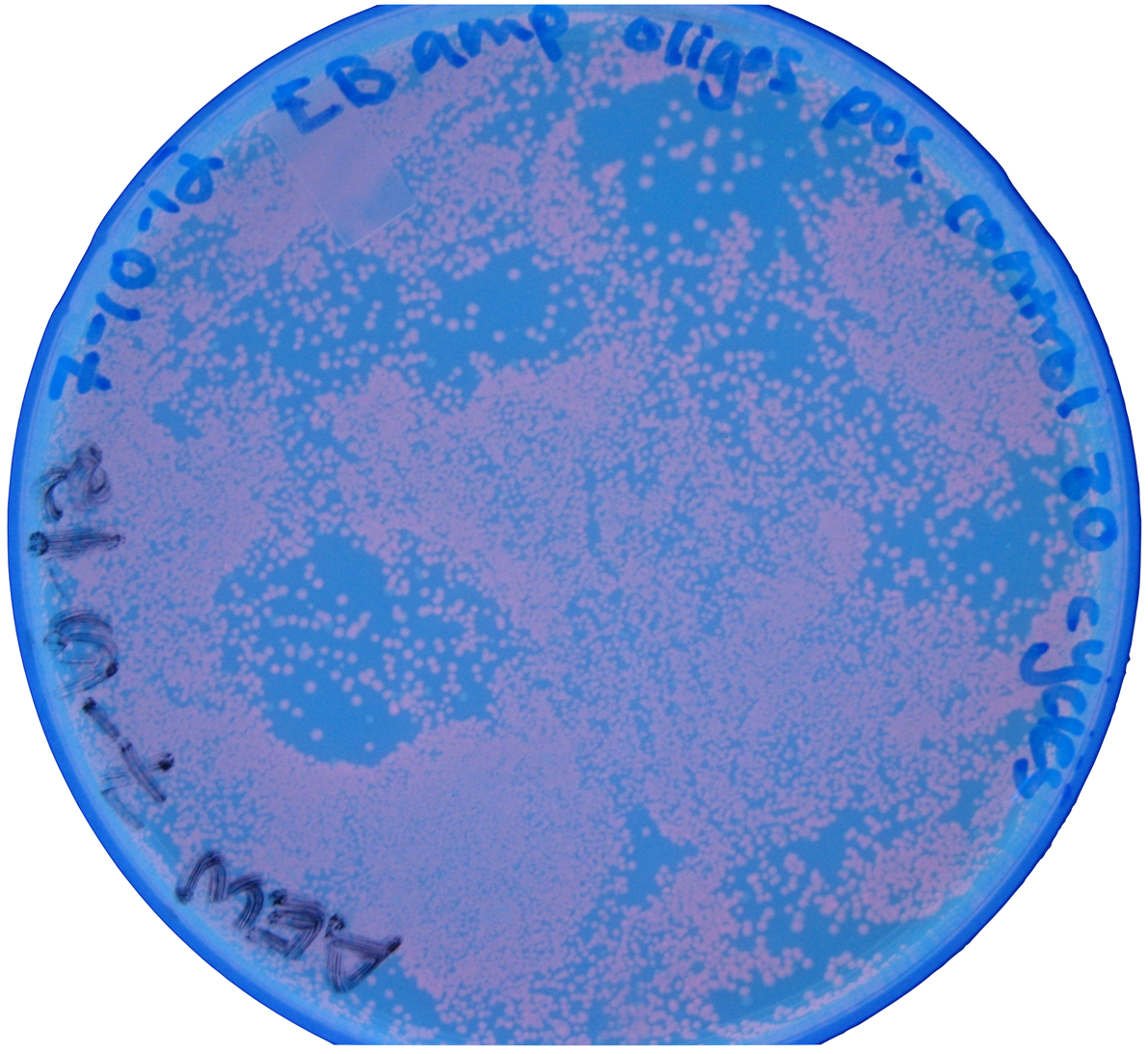
Without basic research, there can be no applications....

After all, electricity and the lightbulb were not invented by incremental improvements to the candle.

former French President Nicholas Sarkozy

Testing Known Promoters: Ptac

```
                -35                          -10
5′ CGACGAGCTGTTGACAATTAATCATCGGCTCGTATAATGTGTGGA      3′
3′     CTCGACAACTGTTAATTAGTAGCCGAGCATATTACACACCTCGCC 5′
```

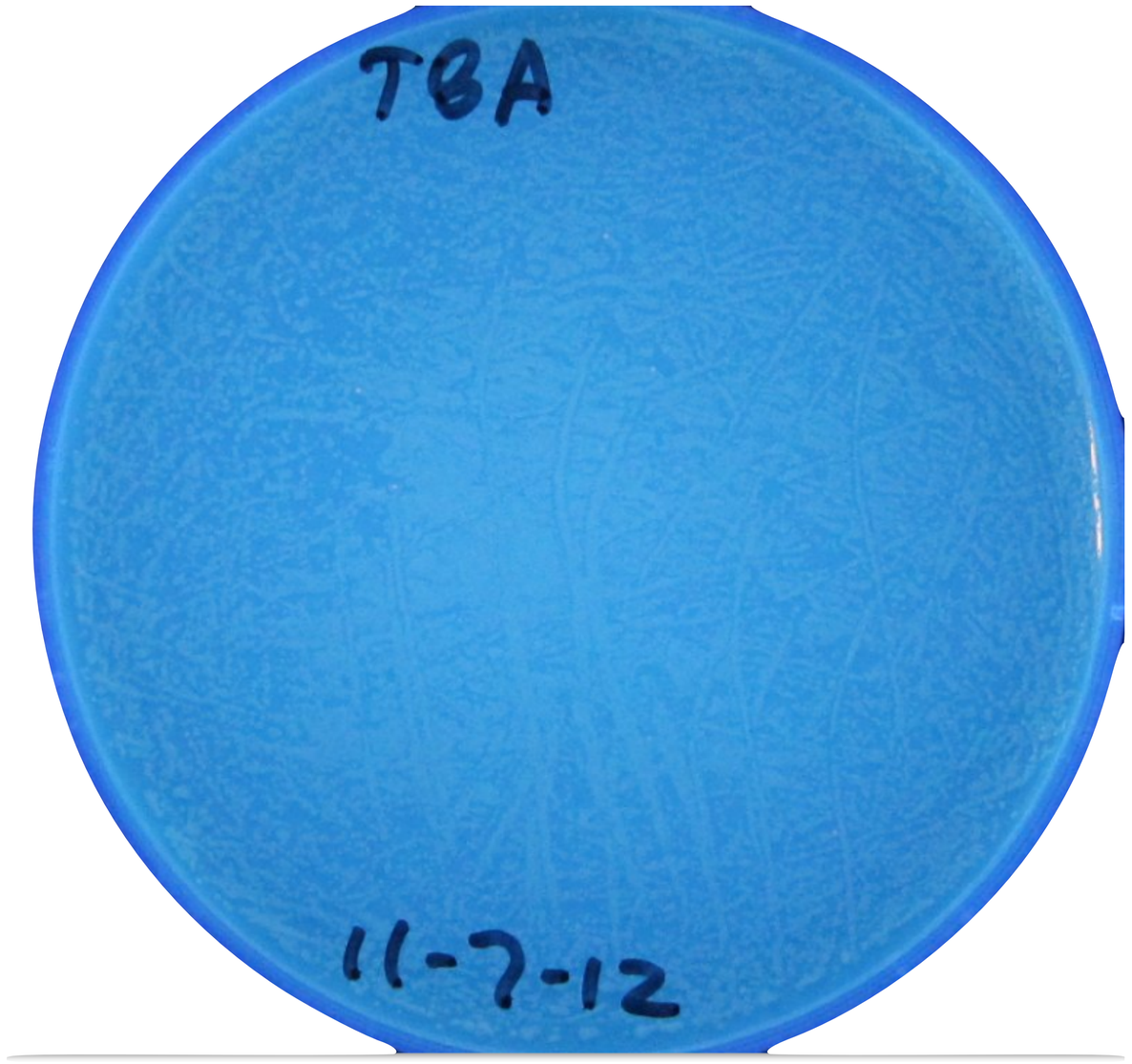


Student Sample, November 2012

-35 ATAA (deleted) -10

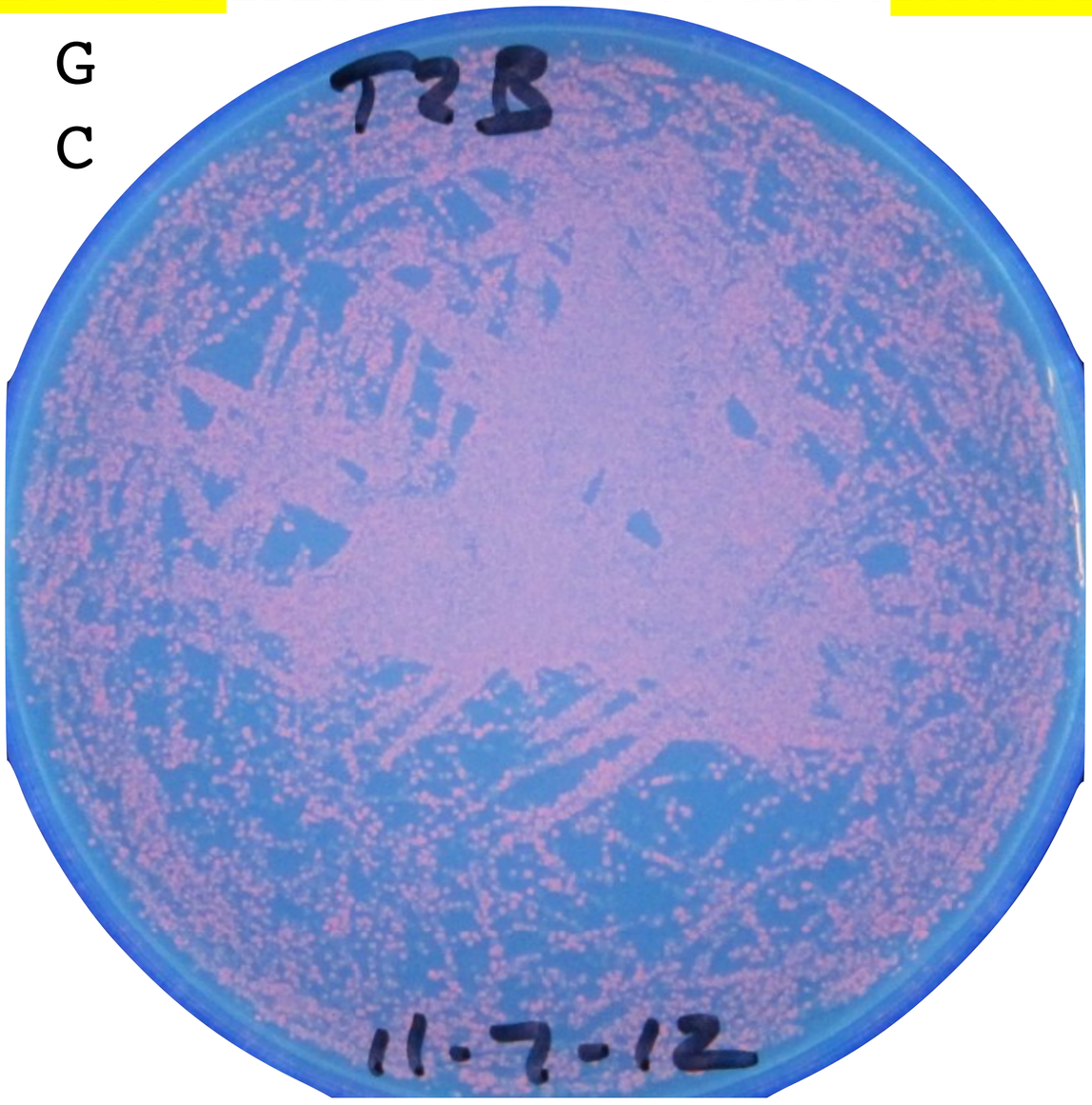
5′ CGACGAGCTGTTGACA----ATCATCGGCTCGTATAATGTGTGGA 3′

3′ CTCGACAACTGT----TAGTAGCCGAGCATATTACACACCTCGCC 5′



Student Sample, November 2012

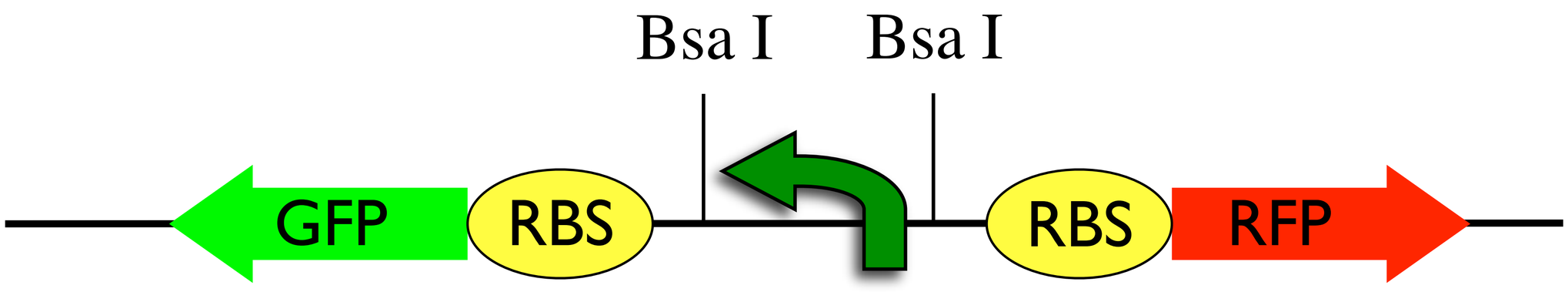
```
                -35                          -10
5′ CGACGAGCTGTTtACAATTAATCATCGGCTCGTATAATGTGTGGA      3′
3′     CTCGACAAaTGTTAATTAGTAGCCGAGCATATTACACACCTCGCC 5′
                G
                C
```

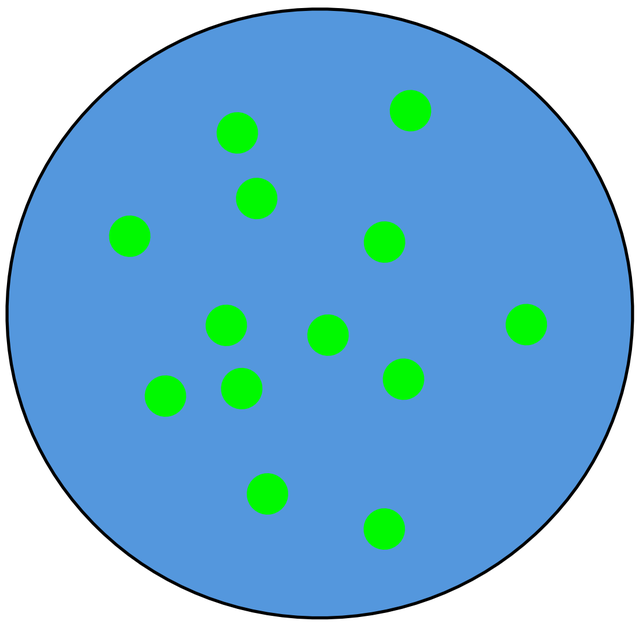


Synthetic Biology Plasmids to Facilitate Research with Your Students

pClone Green

J119137

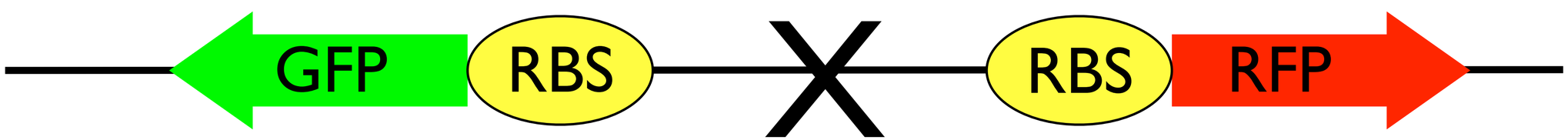


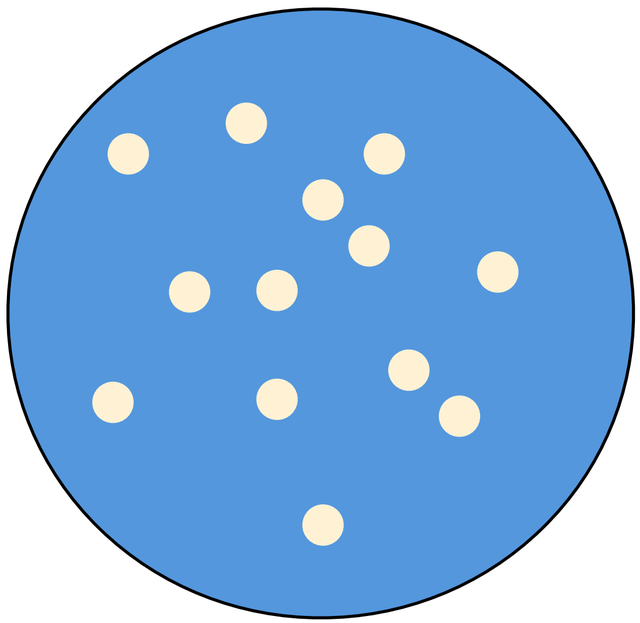


Monday, November 18, 2013

Remove Initial Promoter

J119137





Insert Non-functional Promoter

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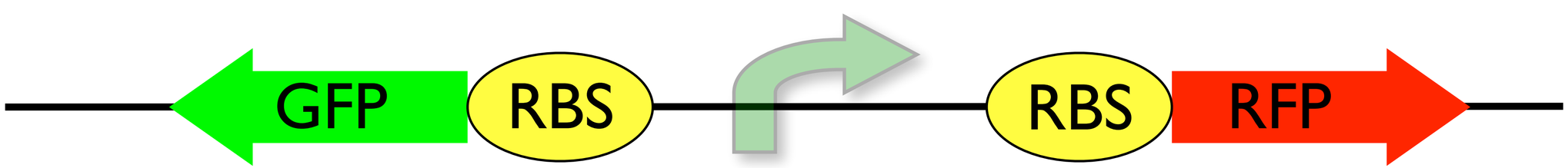

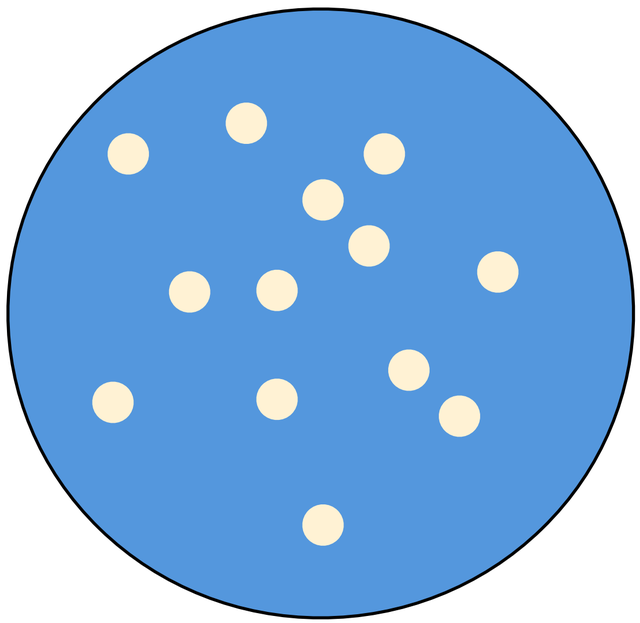

Insert Forward Promoter

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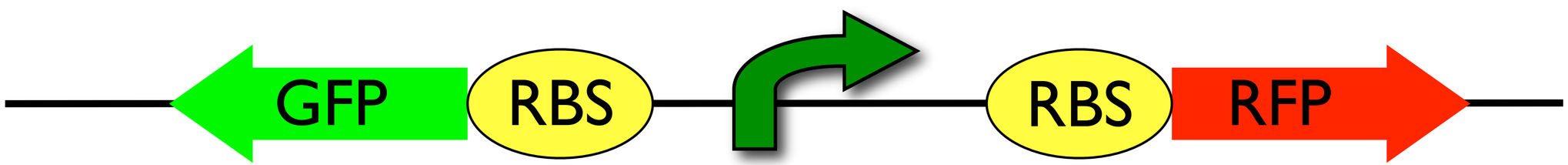

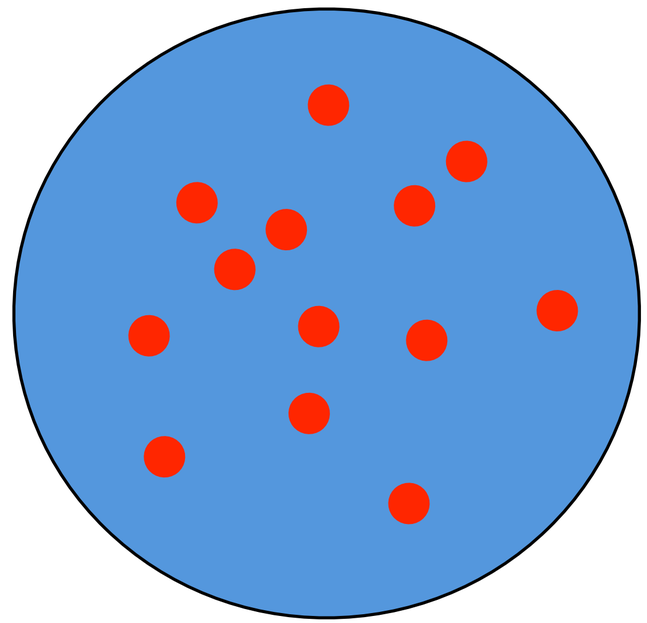

Insert Bi-directional Promoter

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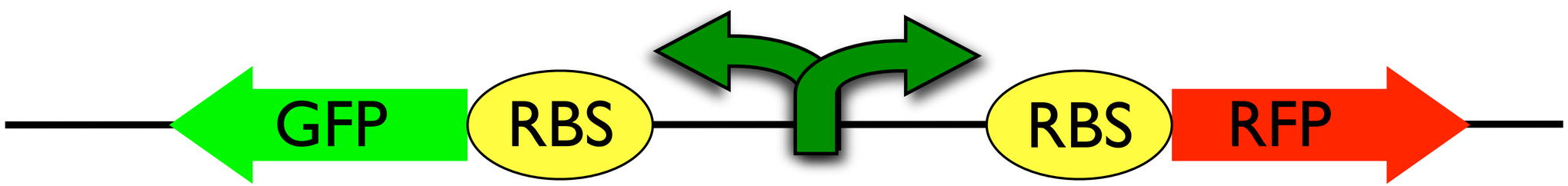
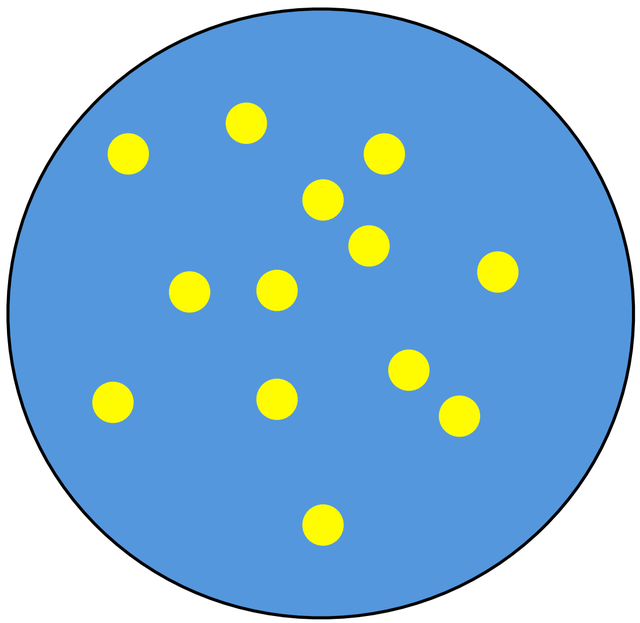
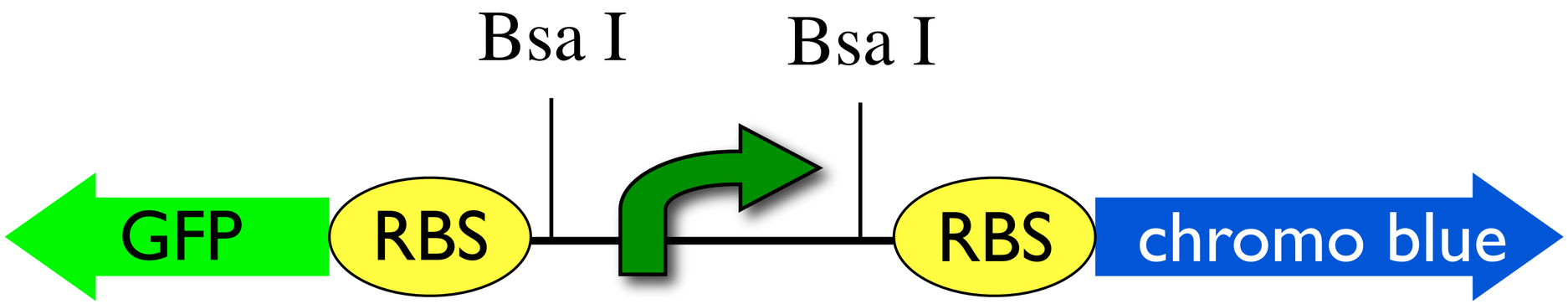
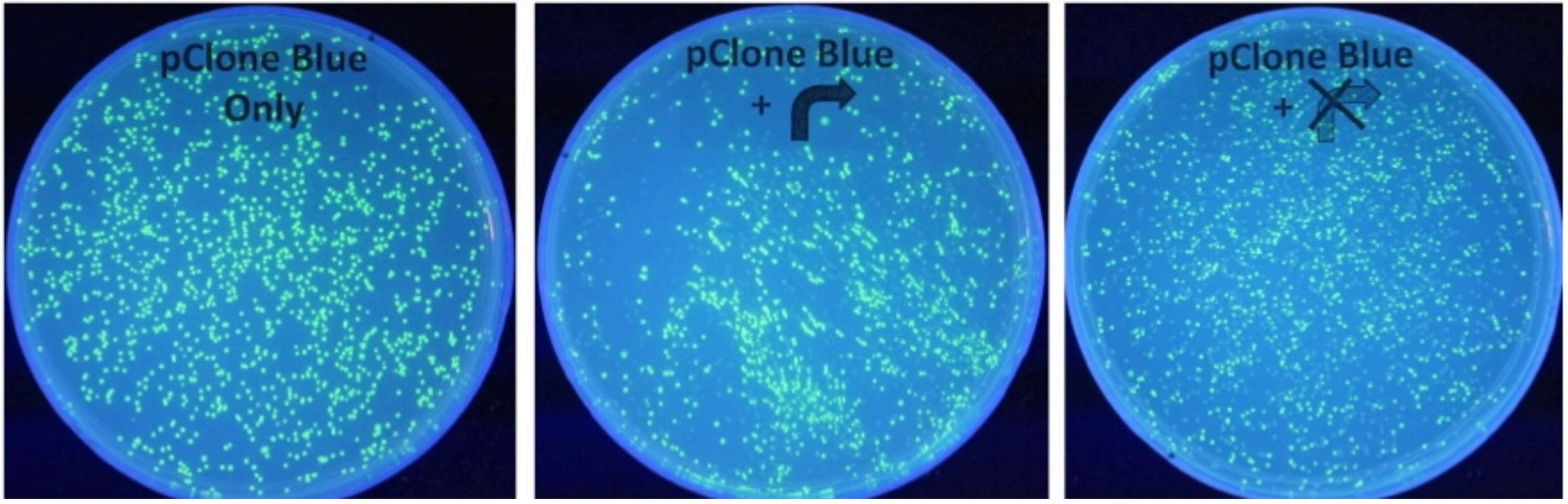




pClone Blue

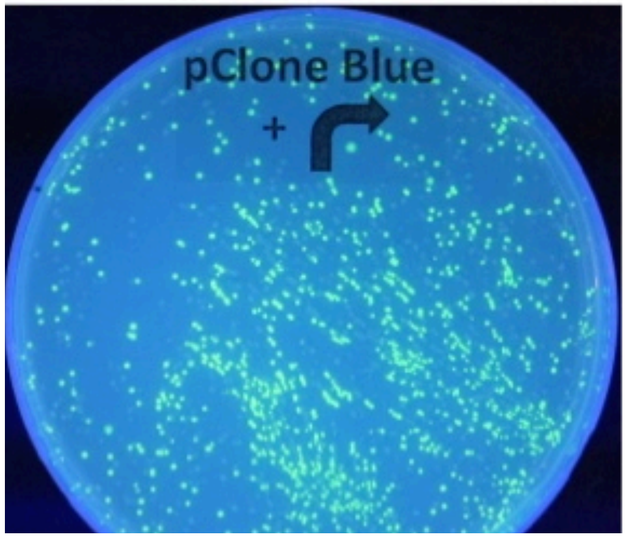
J119313

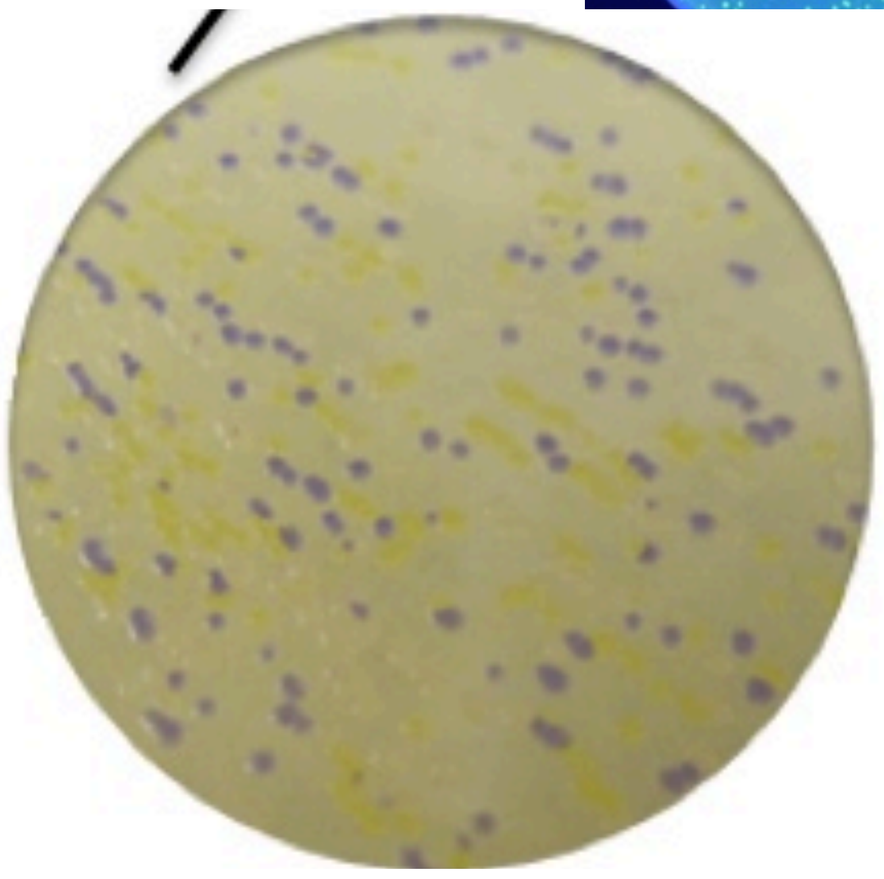


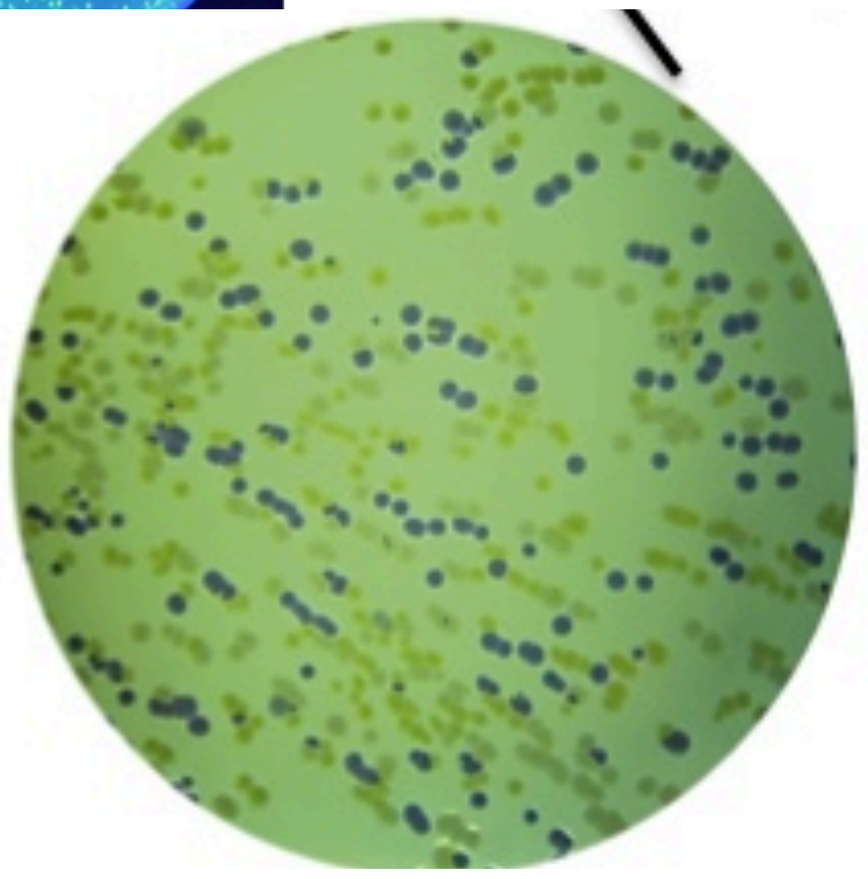


Monday, November 18, 2013

pClone Blue

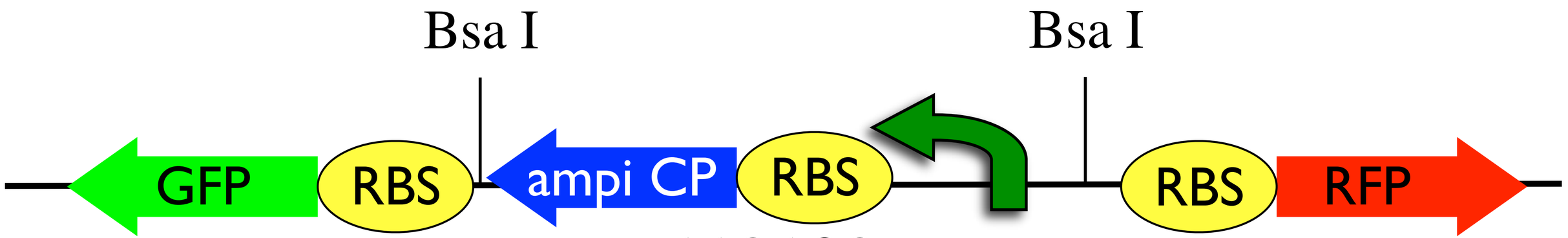






Design Cloning Steps

Explain Each Color



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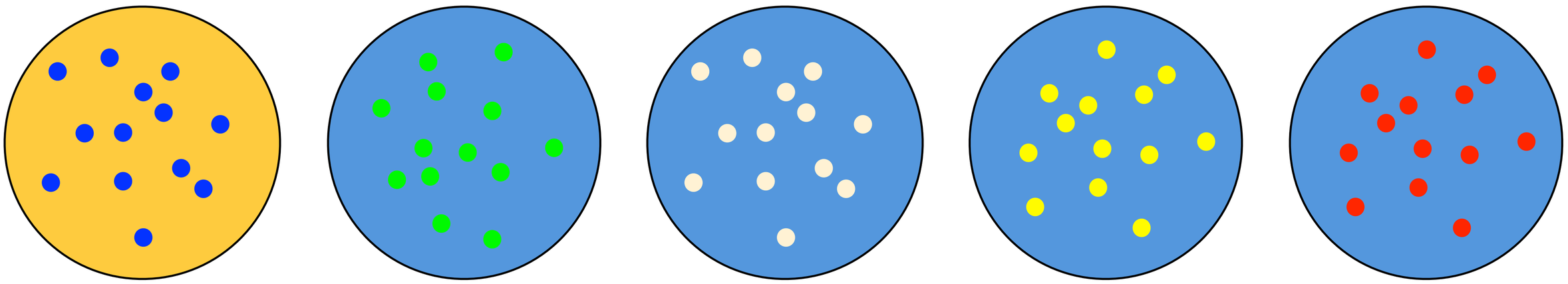


Our Prioritized Goals

1. Everyone learns
2. Have fun
3. Contribute to field of biology

Our 2008 iGEM Team

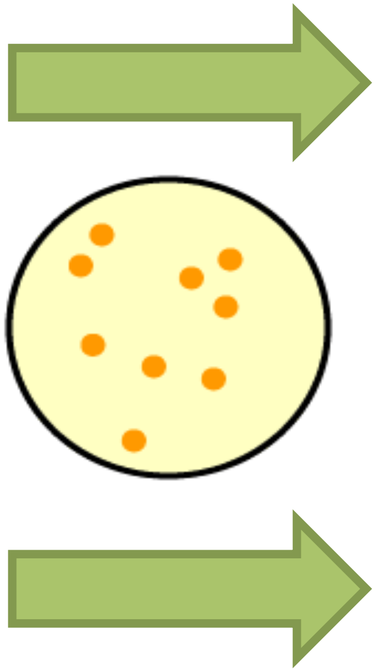
Our 2008 iGEM Project

Use *E. coli* to compute values of a cryptographic hash function

What is a hash function?

HGTf34$2

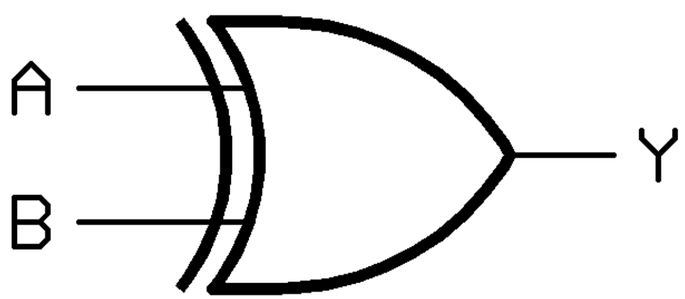
Can Bacteria Perform a Hash Function?



HGTf34$2

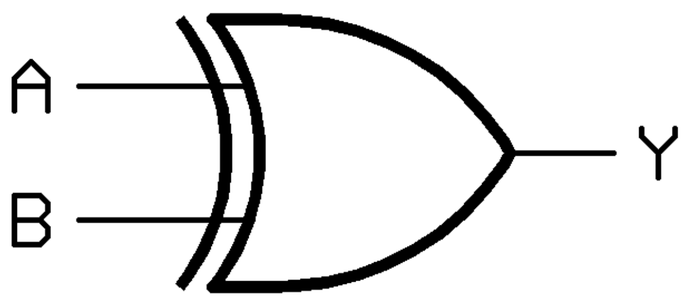
Use XOR Logic Gate for Hash Function

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



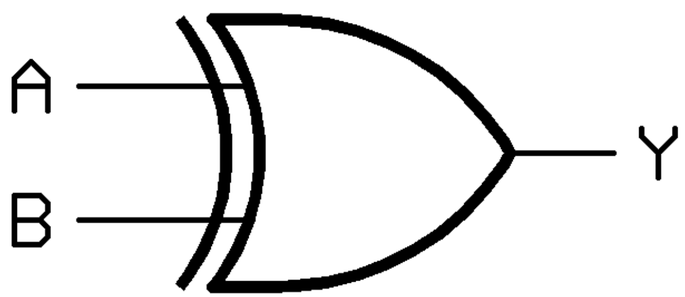
Use XOR Logic Gate for Hash Function

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



Use XOR Logic Gate for Hash Function

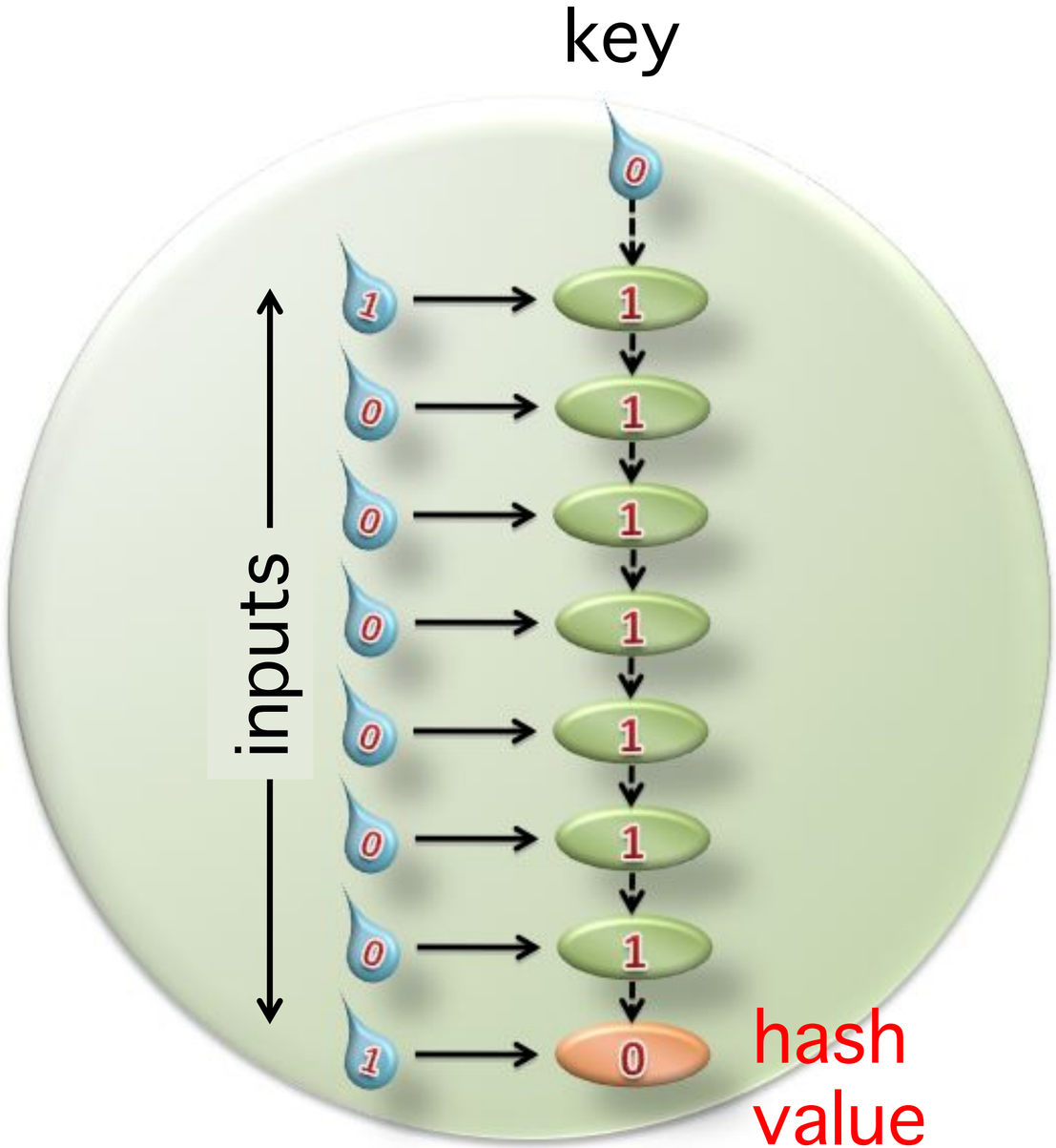
Input 1	Input 2	Output
0	0	0
0	1	1
1	0	1
1	1	0



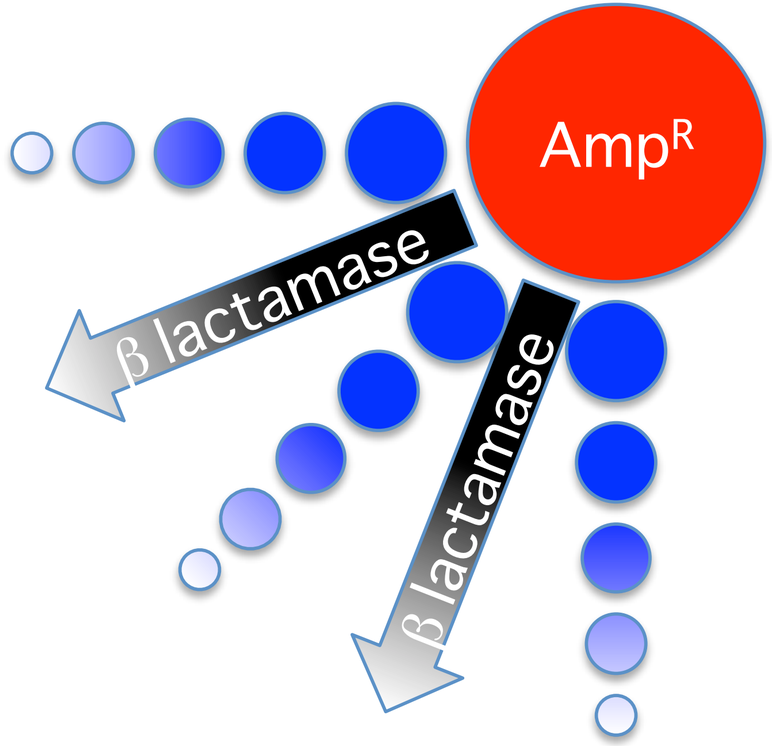
Design Linear Bacterial Hash Function

CAB = 010000001

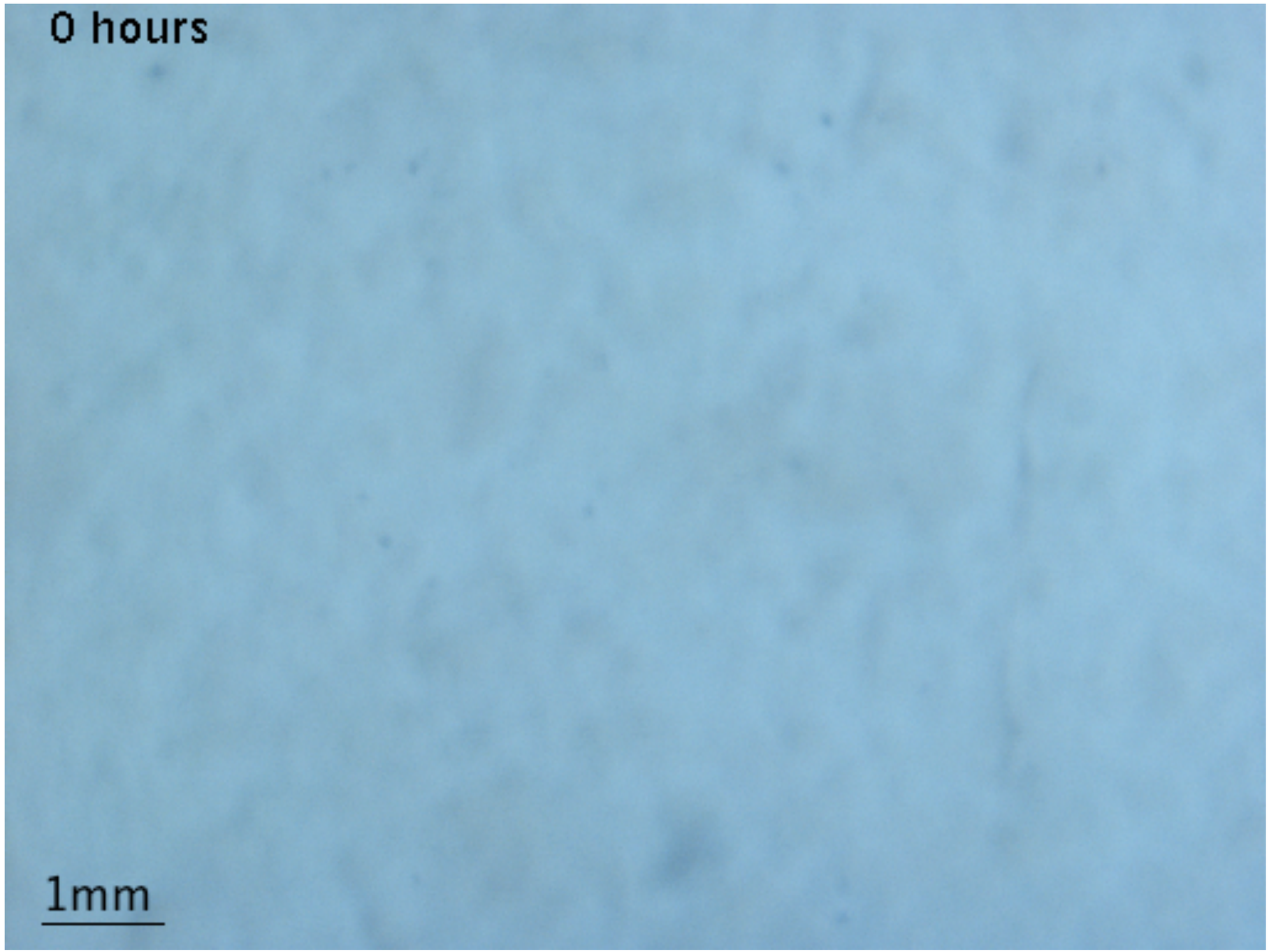
HASH VALUE = 0



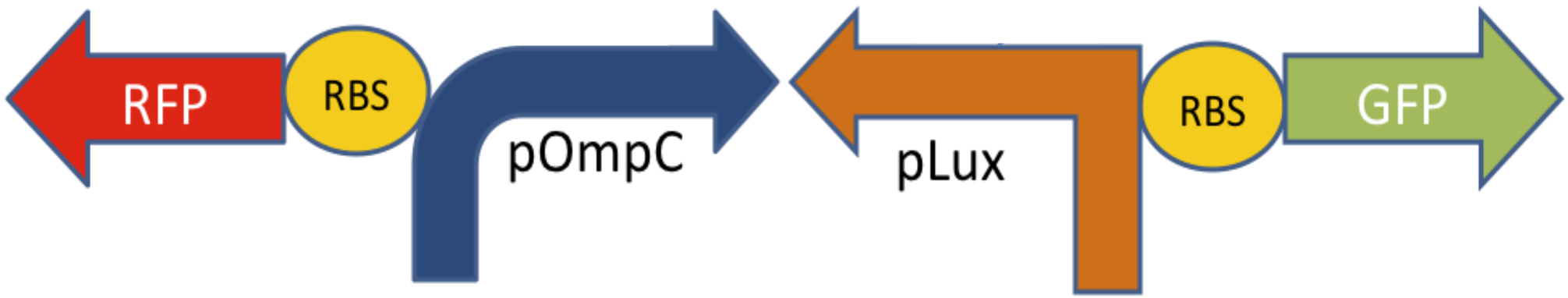
Time-Delayed Bacterial Growth



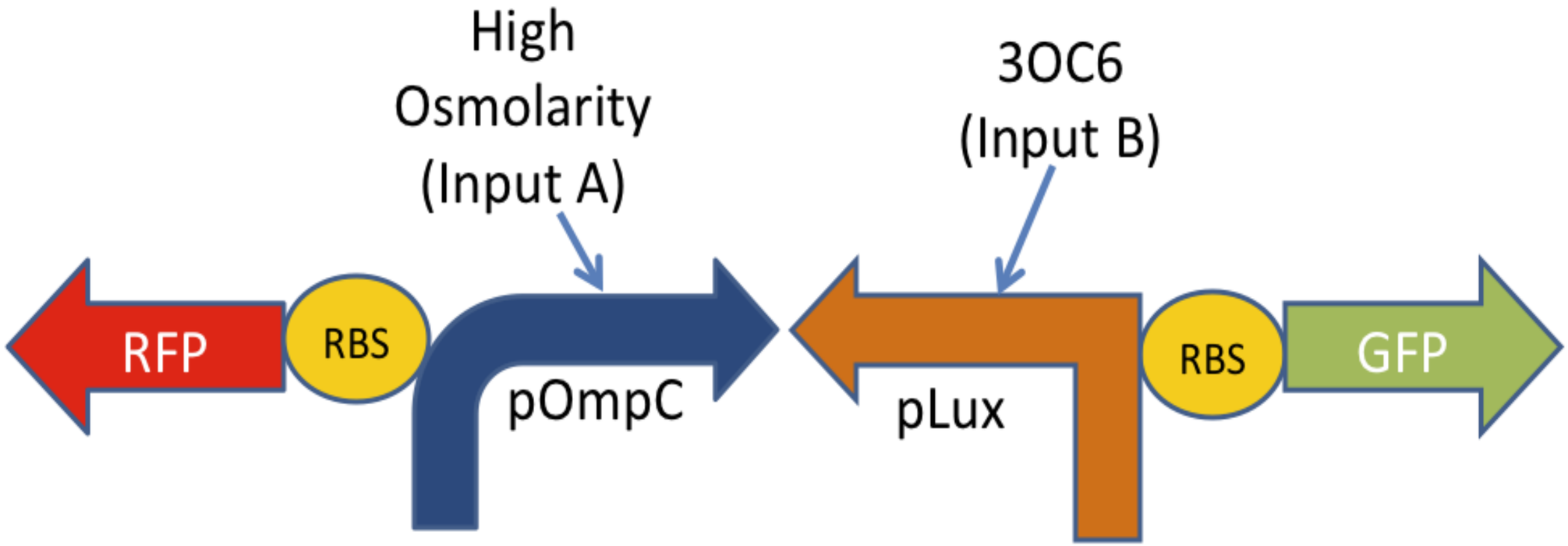
Time-Delayed Bacterial Growth



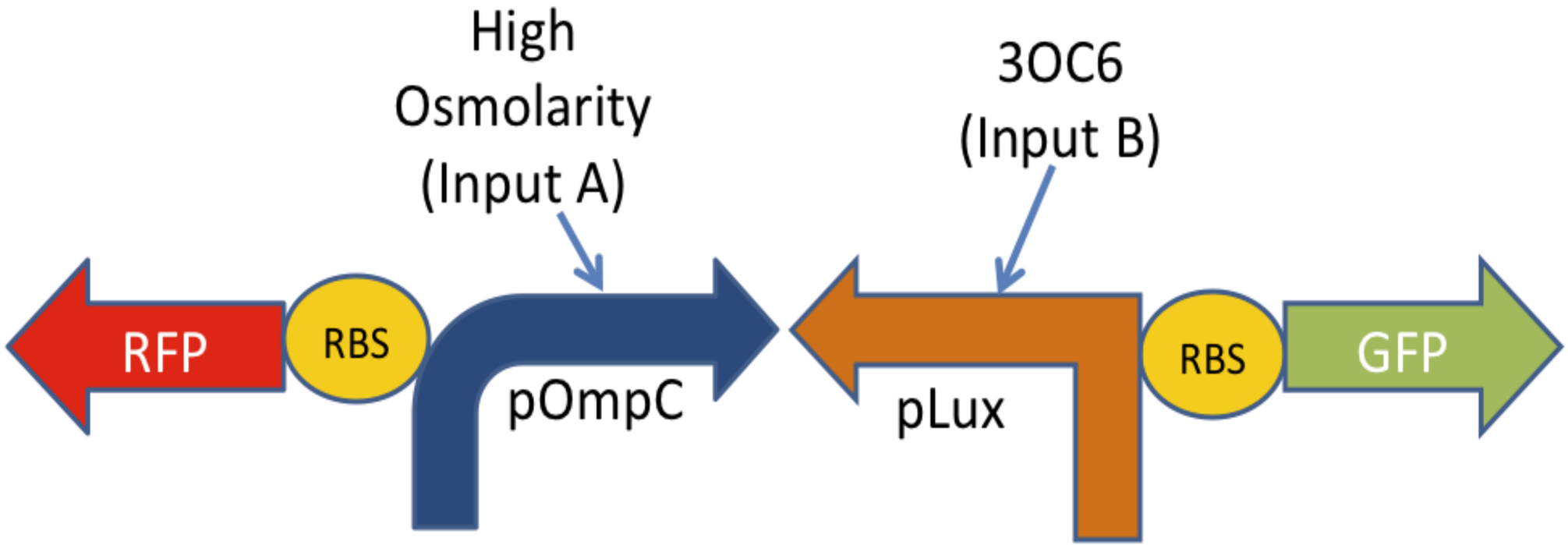
DNA-based XOR Logic Gate



DNA-based XOR Logic Gate

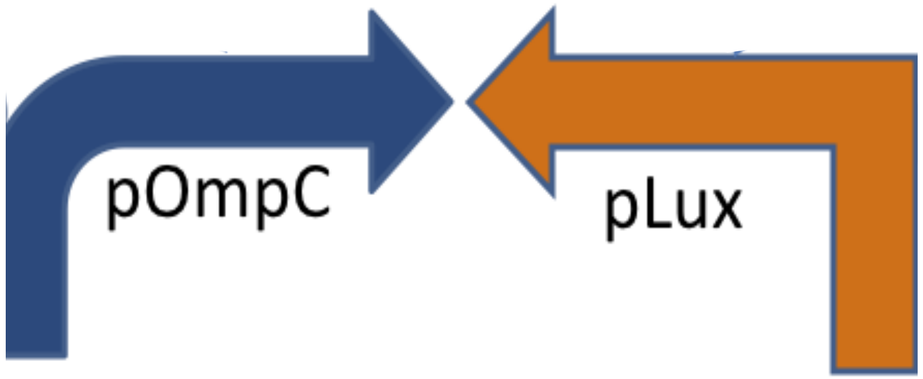


DNA-based XOR Logic Gate



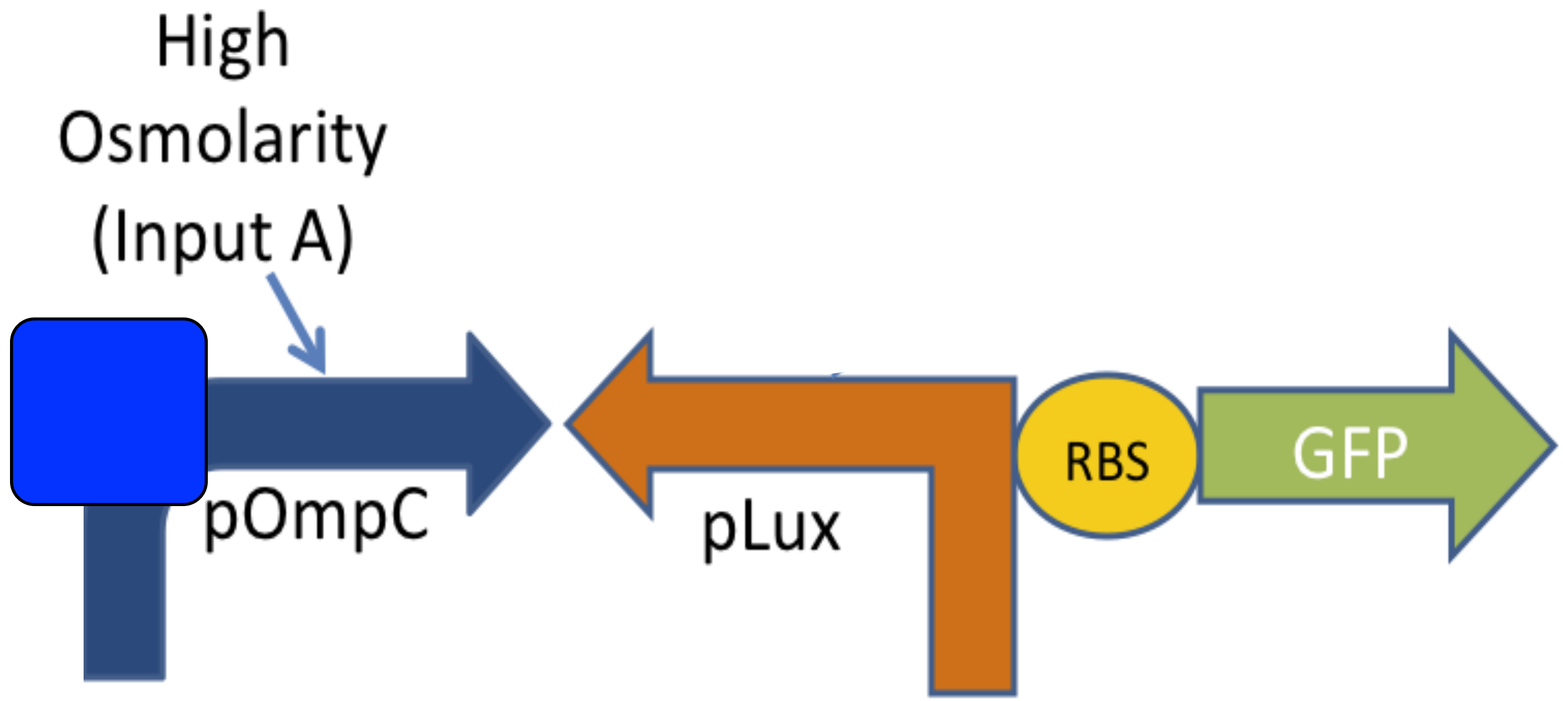
High Osmolarity (Input A)	3OC6 (Input B)	Fluorescence (Output)
0	0	0
1	0	1 (GFP)
0	1	1 (RFP)
1	1	0

DNA-based XOR Logic Gate



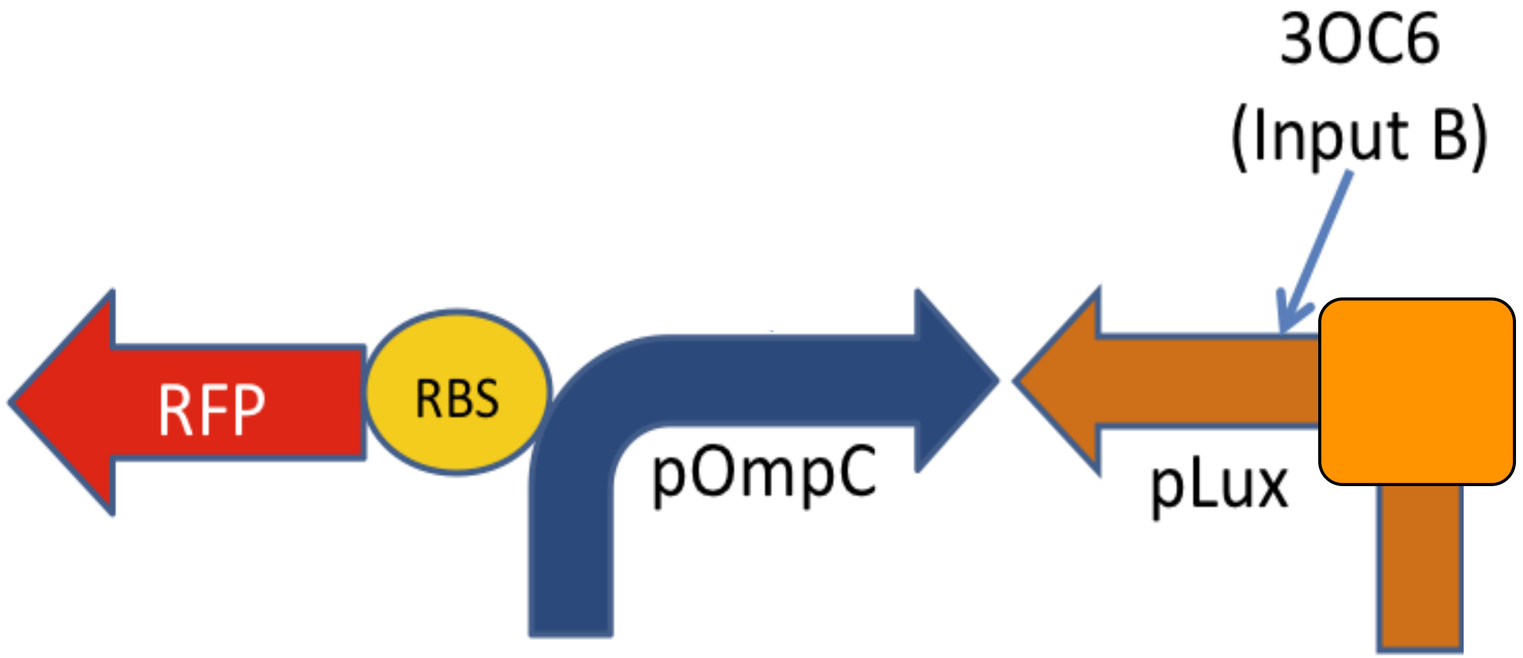
High Osmolarity (Input A)	3OC6 (Input B)	Fluorescence (Output)
0	0	0
1	0	1 (GFP)
0	1	1 (RFP)
1	1	0

DNA-based XOR Logic Gate



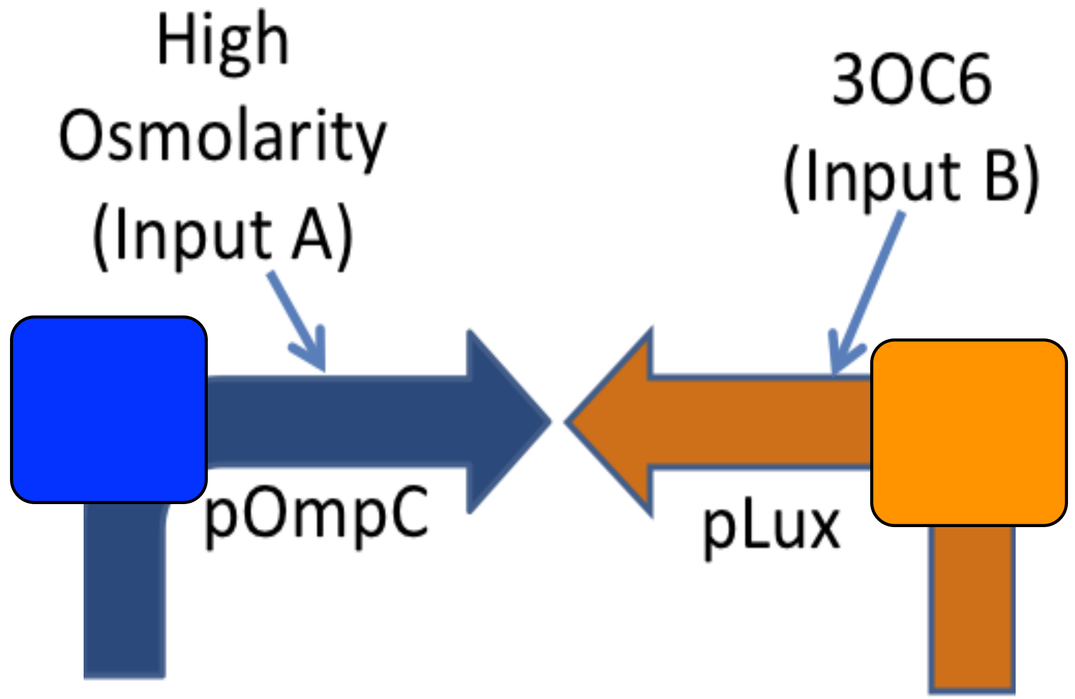
High Osmolarity (Input A)	3OC6 (Input B)	Fluorescence (Output)
0	0	0
1	0	1 (GFP)
0	1	1 (RFP)
1	1	0

DNA-based XOR Logic Gate



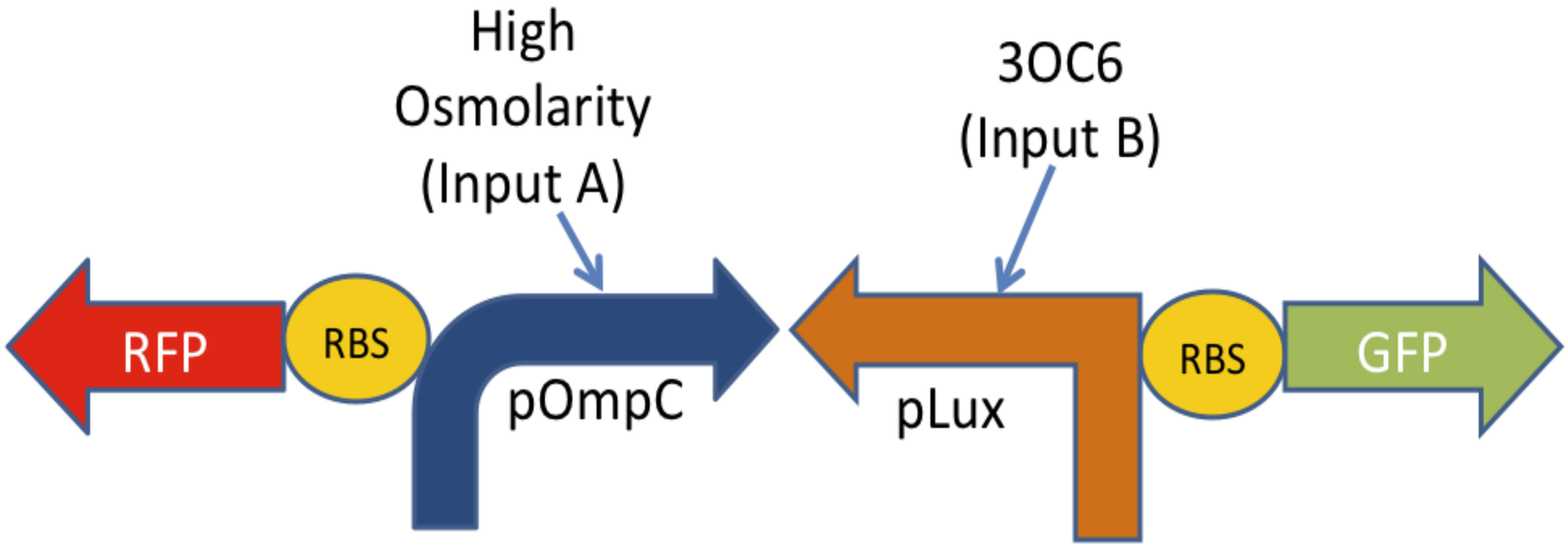
High Osmolarity (Input A)	3OC6 (Input B)	Fluorescence (Output)
0	0	0
1	0	1 (GFP)
0	1	1 (RFP)
1	1	0

DNA-based XOR Logic Gate



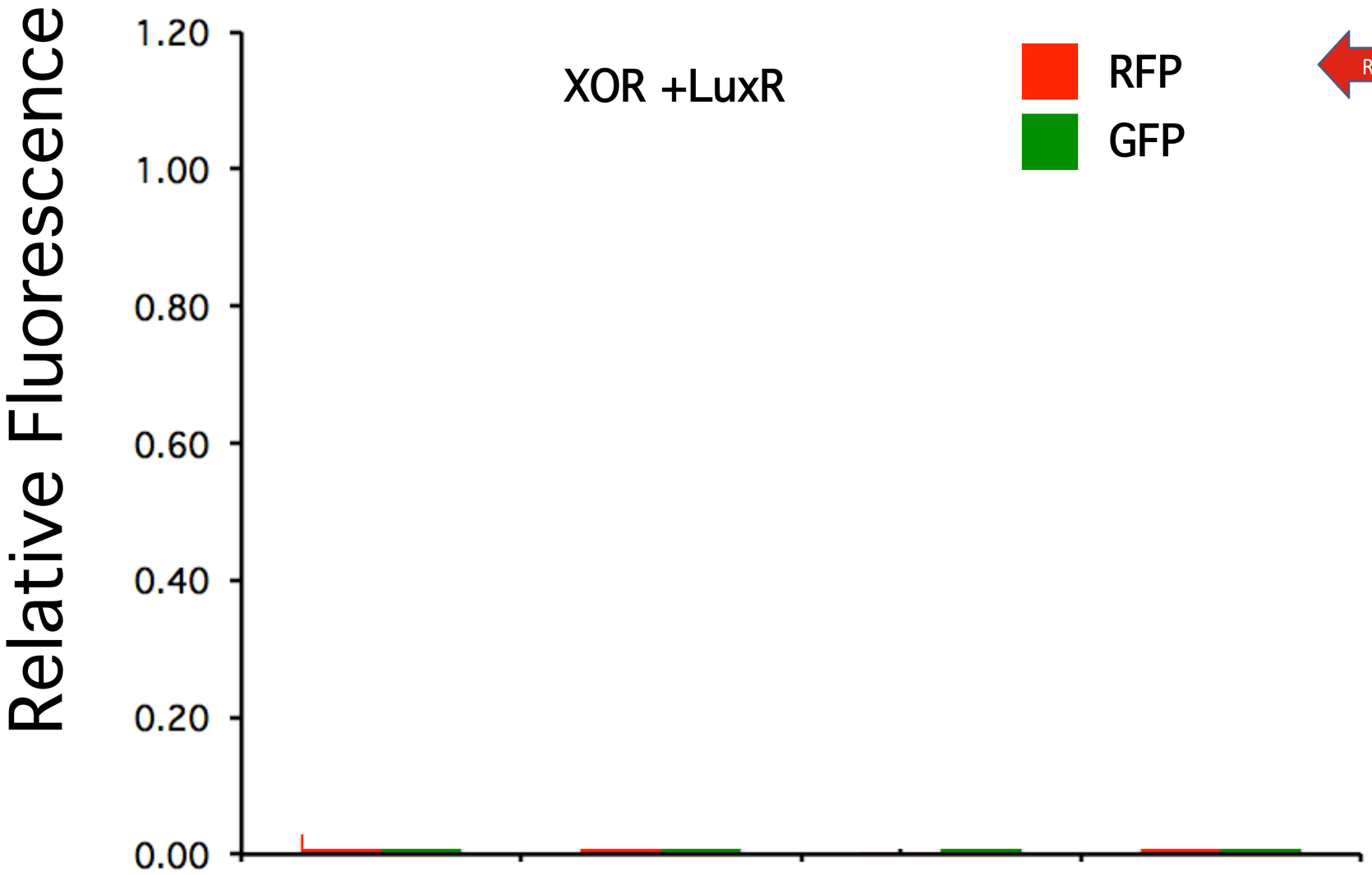
High Osmolarity (Input A)	3OC6 (Input B)	Fluorescence (Output)
0	0	0
1	0	1 (GFP)
0	1	1 (RFP)
1	1	0

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

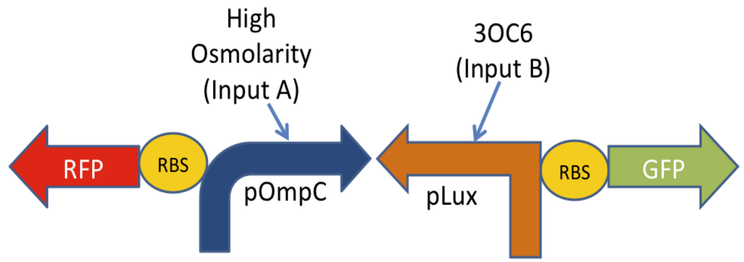
Testing Bacterial XOR Logic Gate



XOR +LuxR

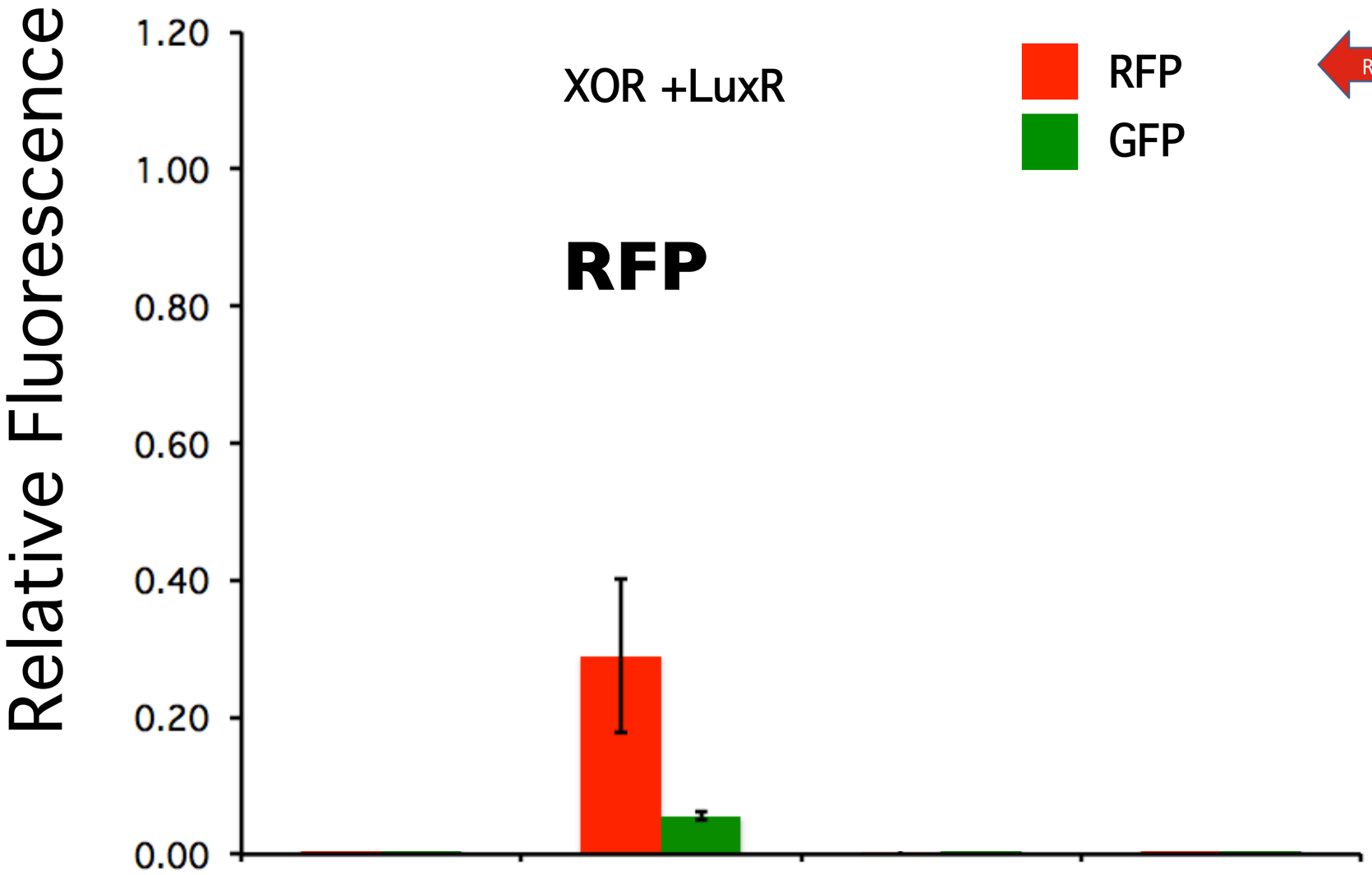
RFP

GFP



LB	-	-	+	+
3OC6	-	+	-	+

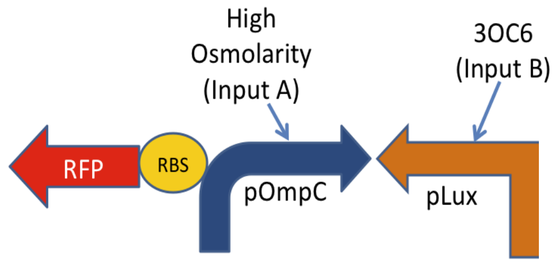
Testing Bacterial XOR Logic Gate



XOR +LuxR

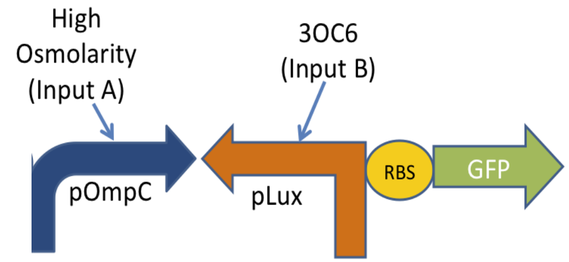
RFP

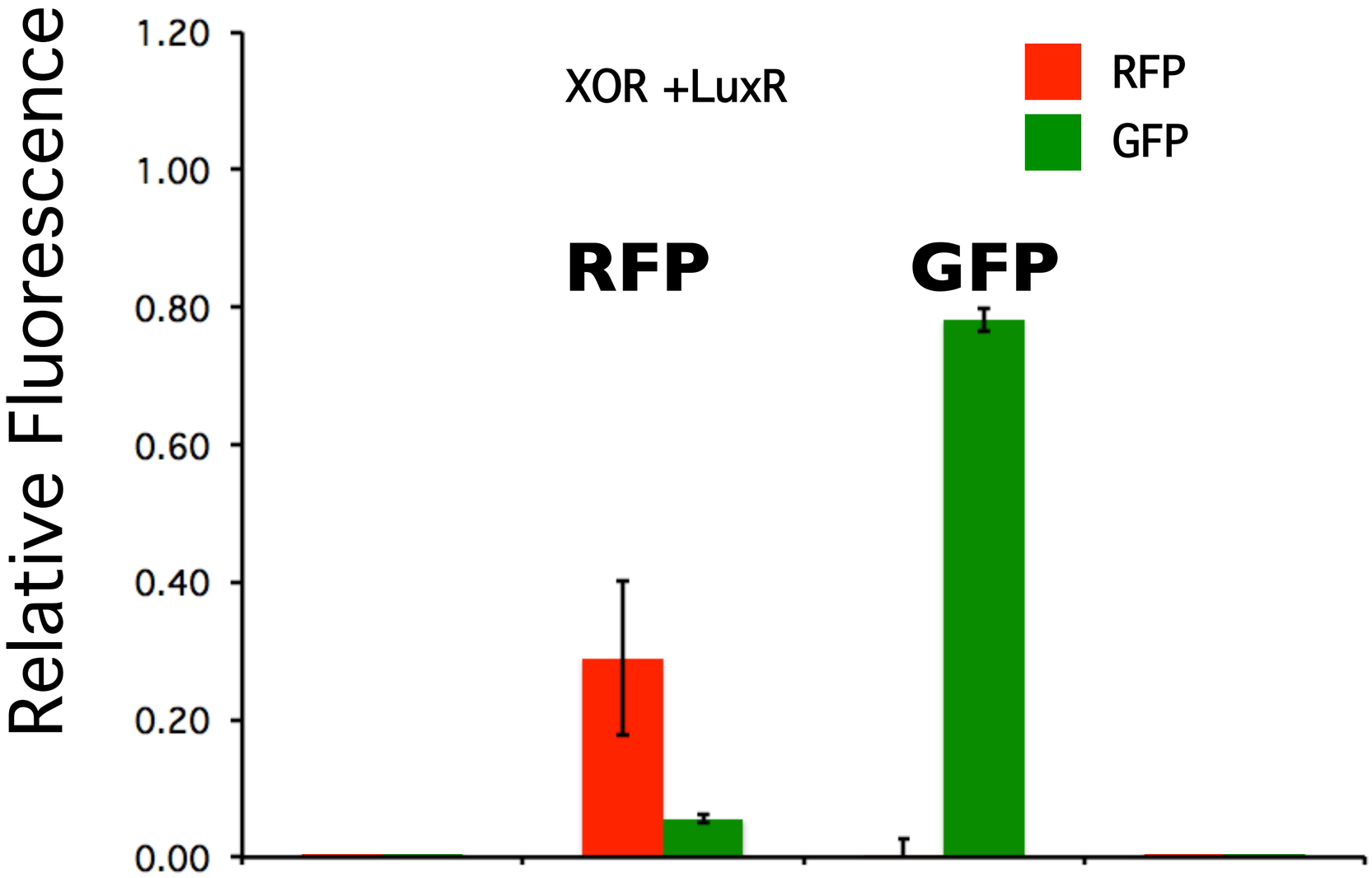
RFP
GFP



LB	-	-	+	+
3OC6	-	+	-	+

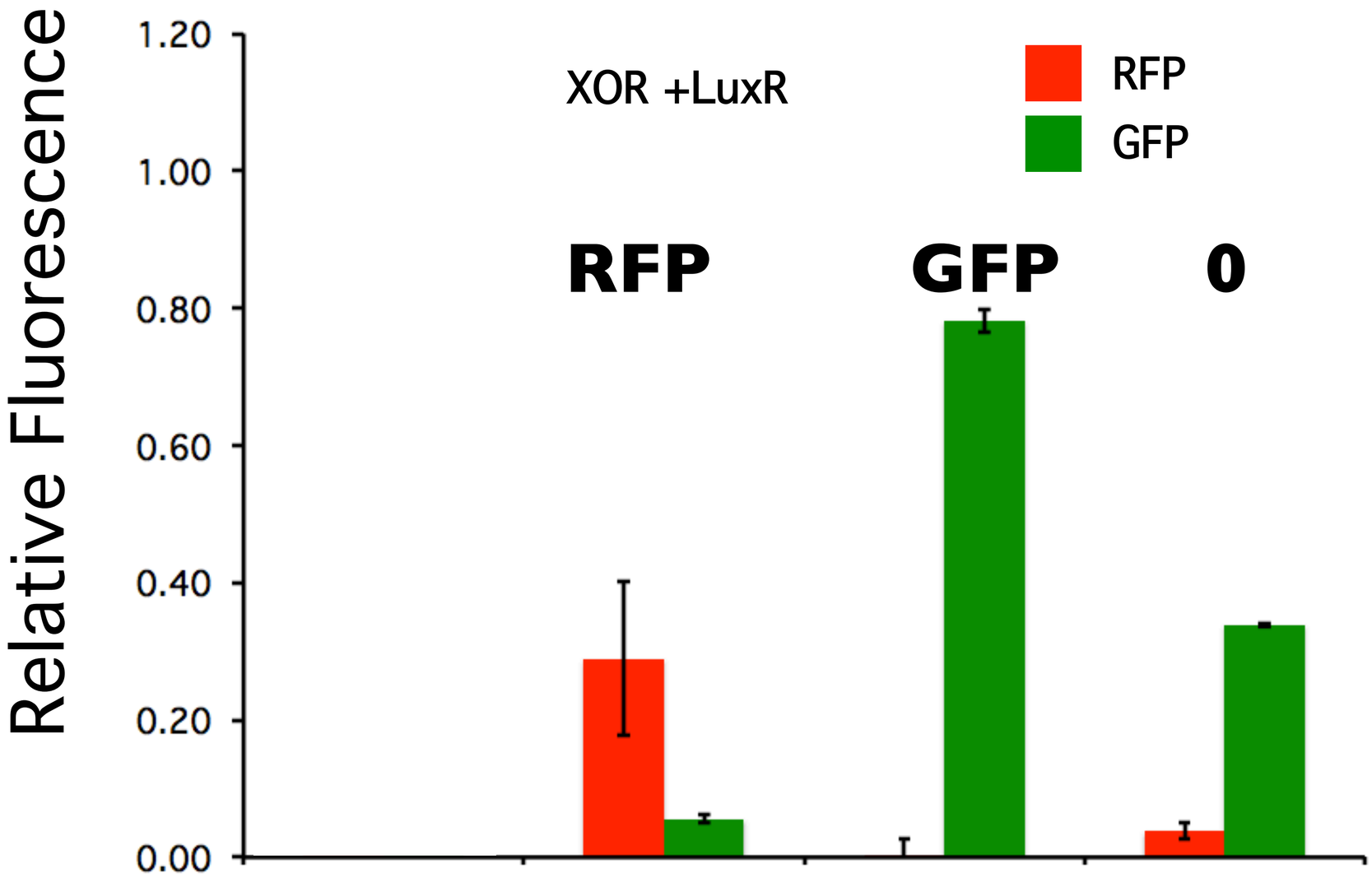
Testing Bacterial XOR Logic Gate

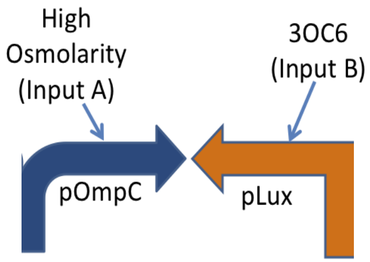




LB	-	-	+	+
3OC6	-	+	-	+

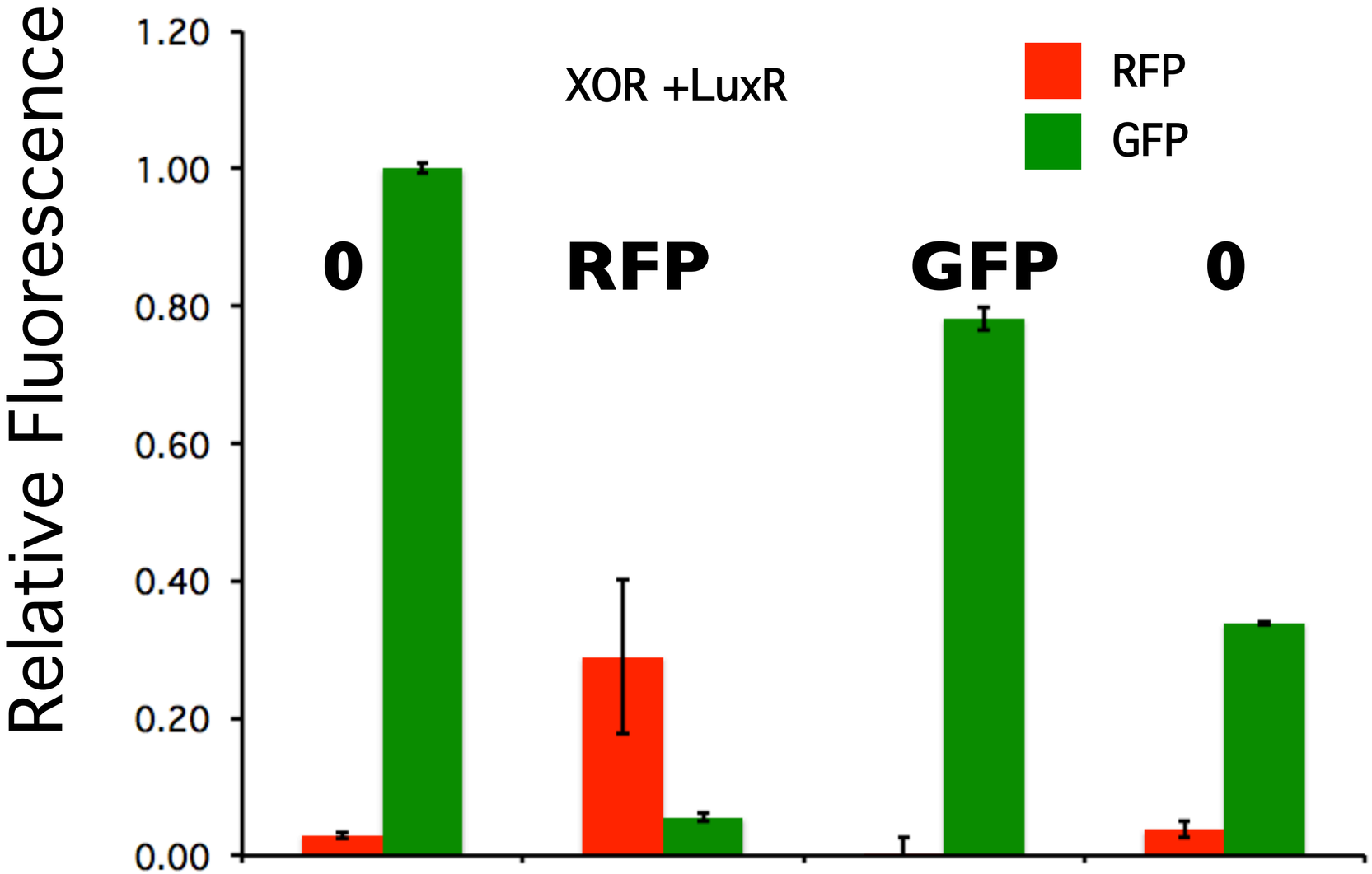
Testing Bacterial XOR Logic Gate

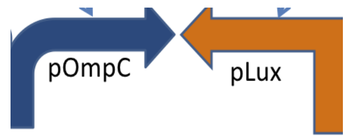




LB	-	-	+	+
3OC6	-	+	-	+

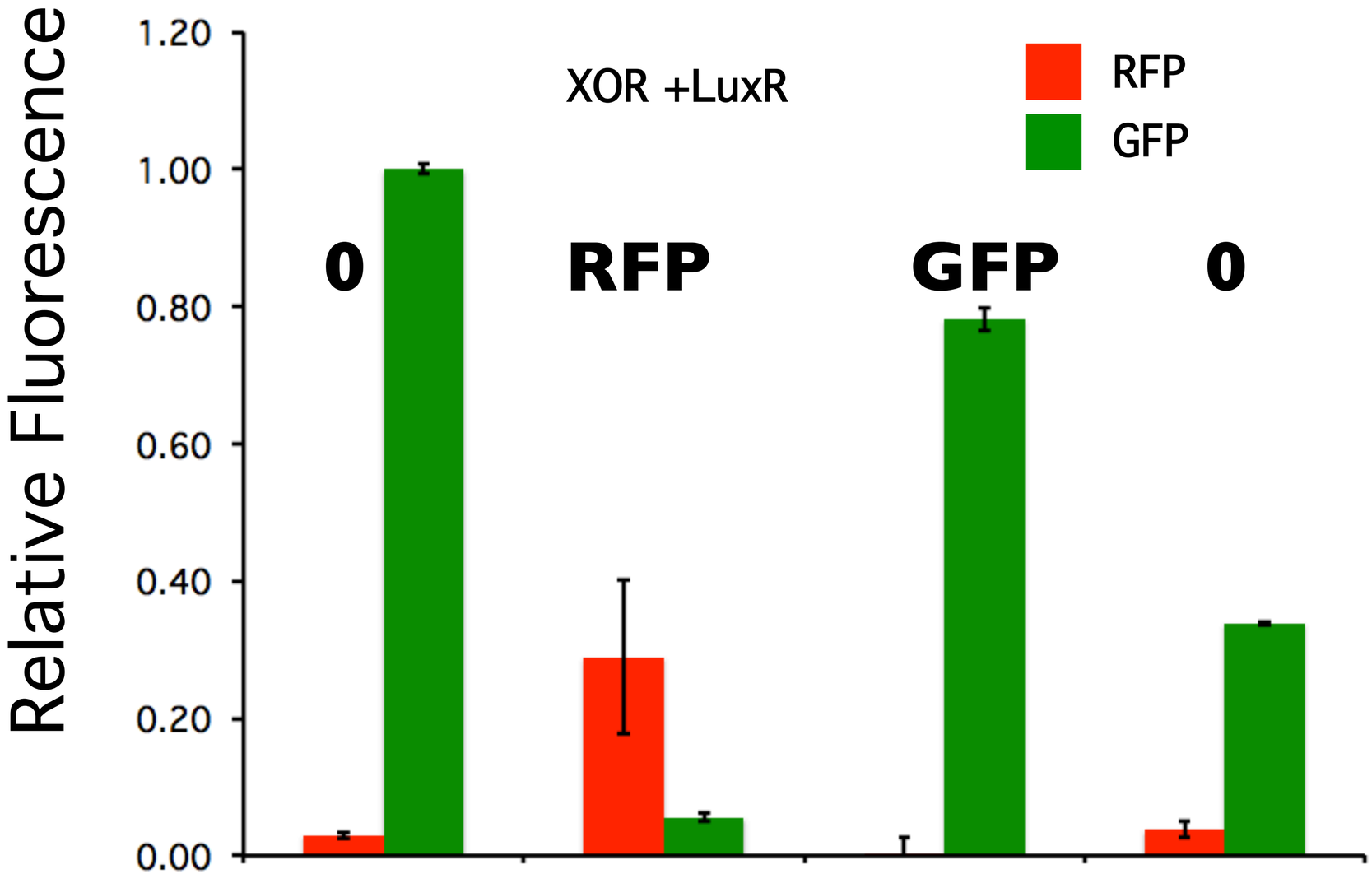
Testing Bacterial XOR Logic Gate

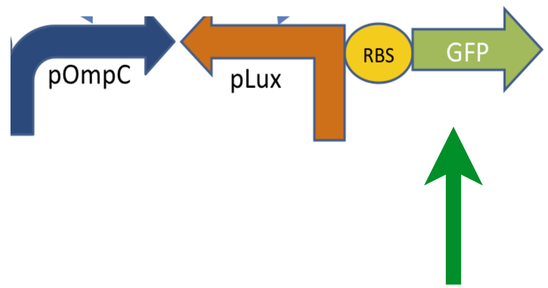




LB	-	-	+	+
3OC6	-	+	-	+

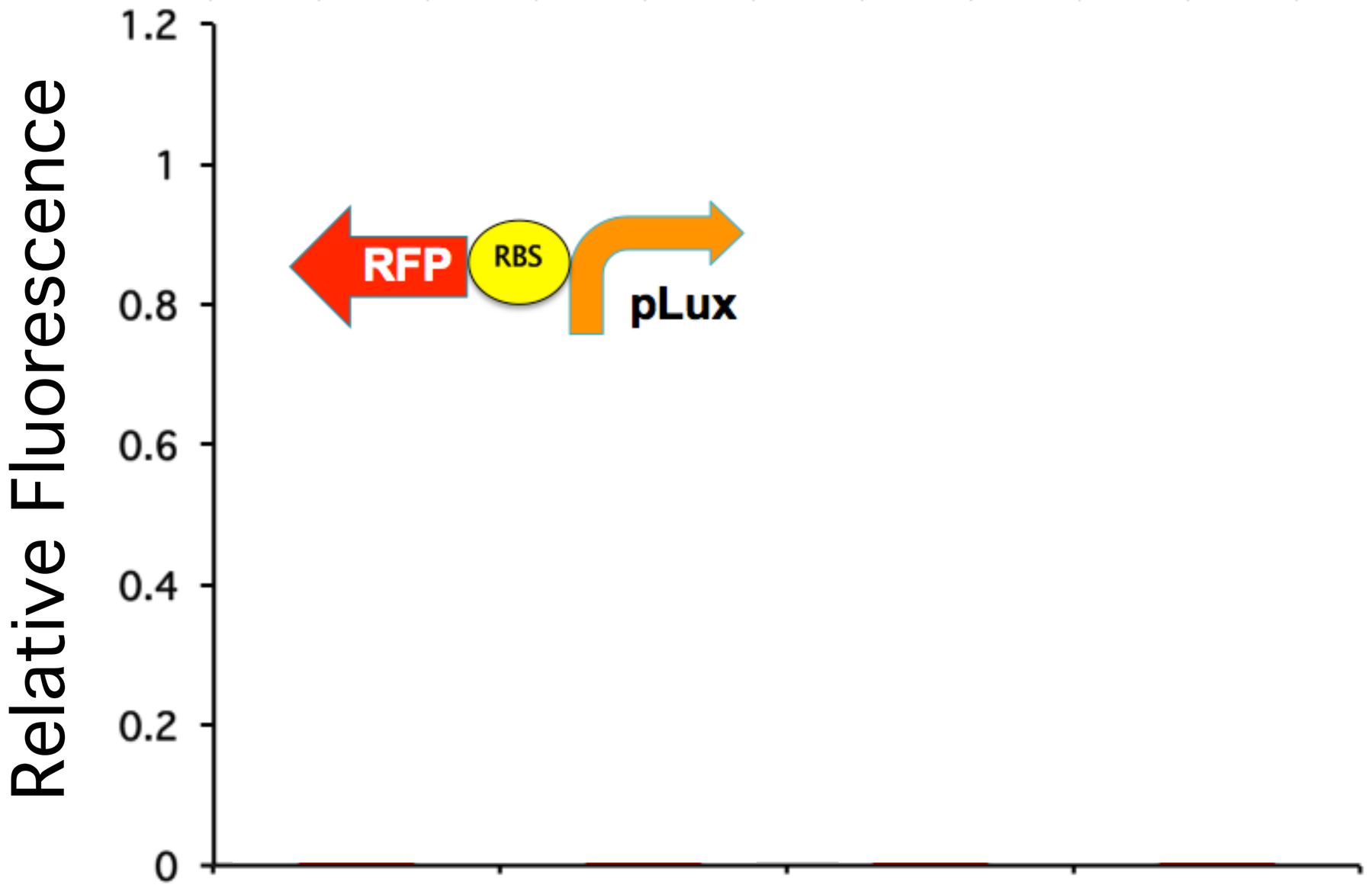
Testing Bacterial XOR Logic Gate





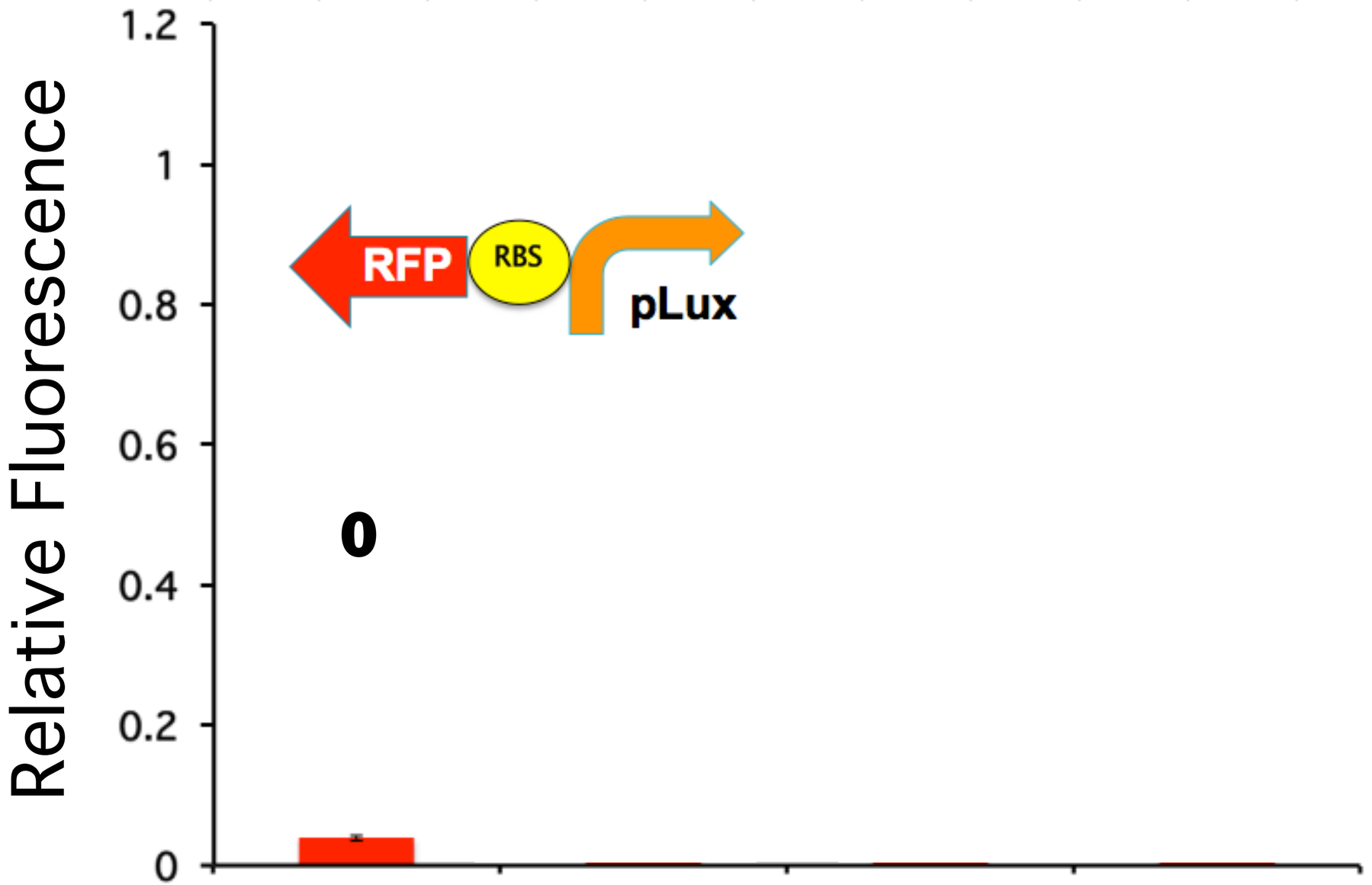
LB	-	-	+	+
3OC6	-	+	-	+

pLux + LuxR Promotes Backwards



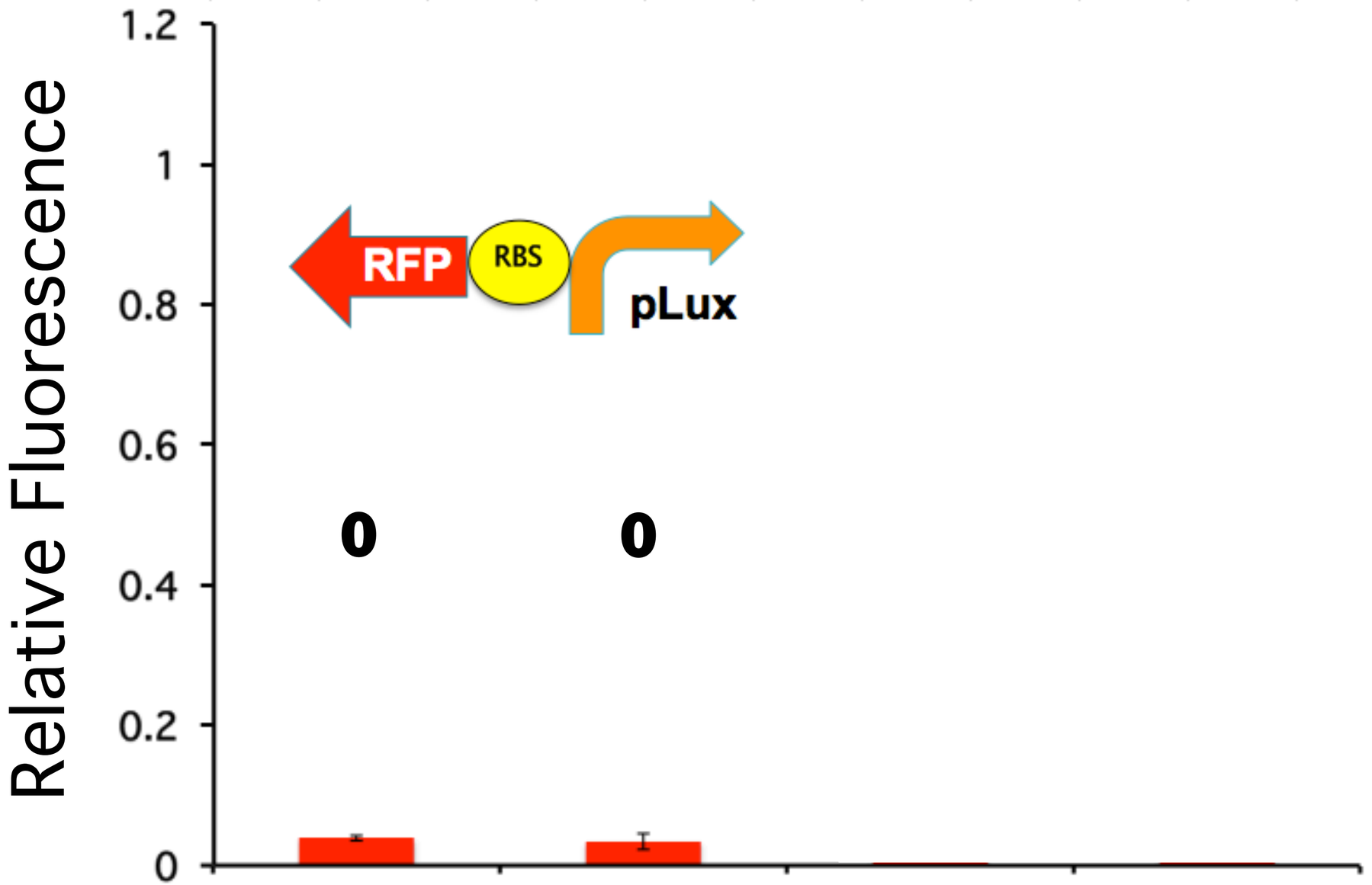
LuxR	-	-	+	+
3OC6	-	+	-	+

pLux + LuxR Promotes Backwards



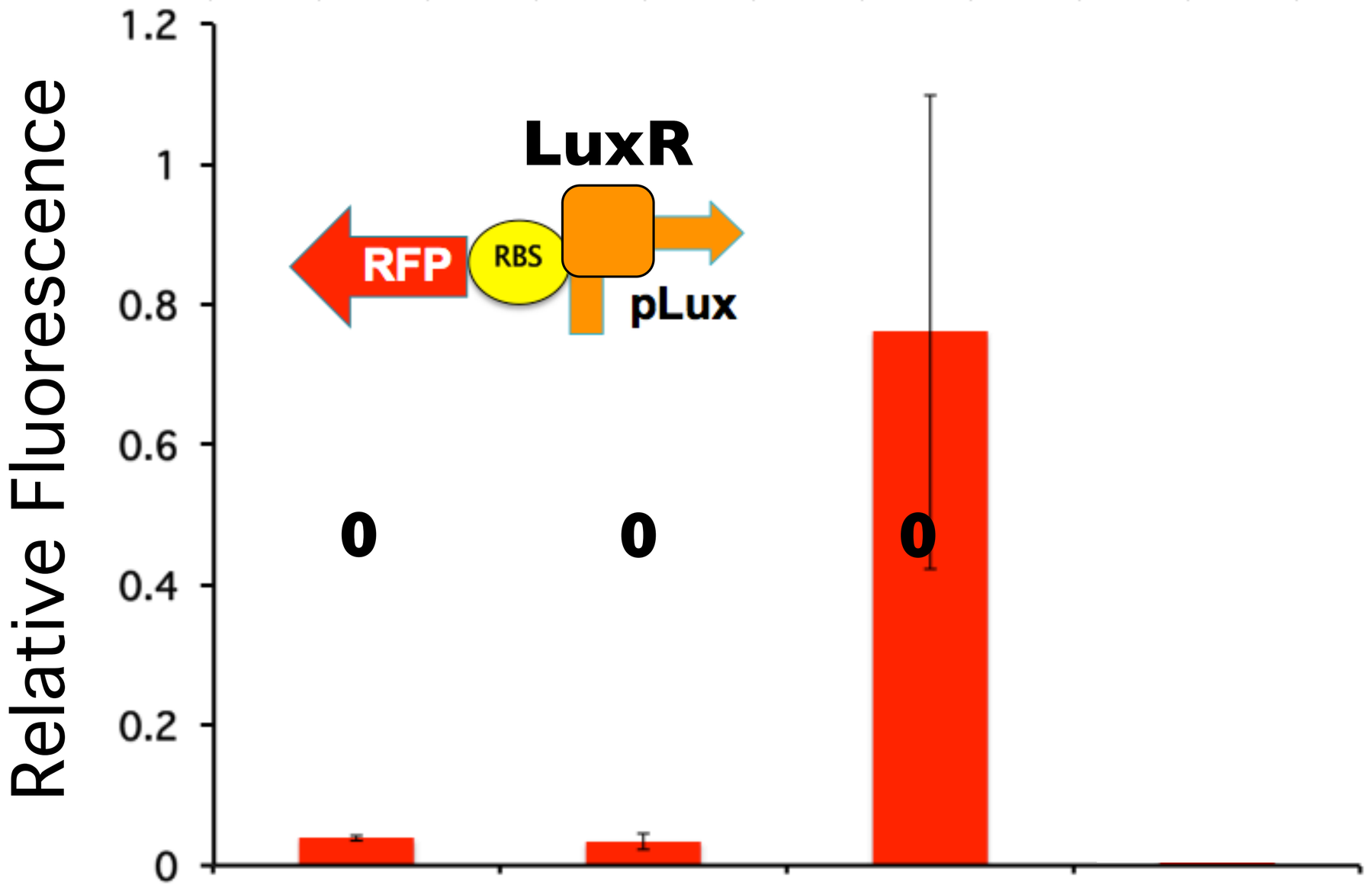
LuxR	-	-	+	+
3OC6	-	+	-	+

pLux + LuxR Promotes Backwards



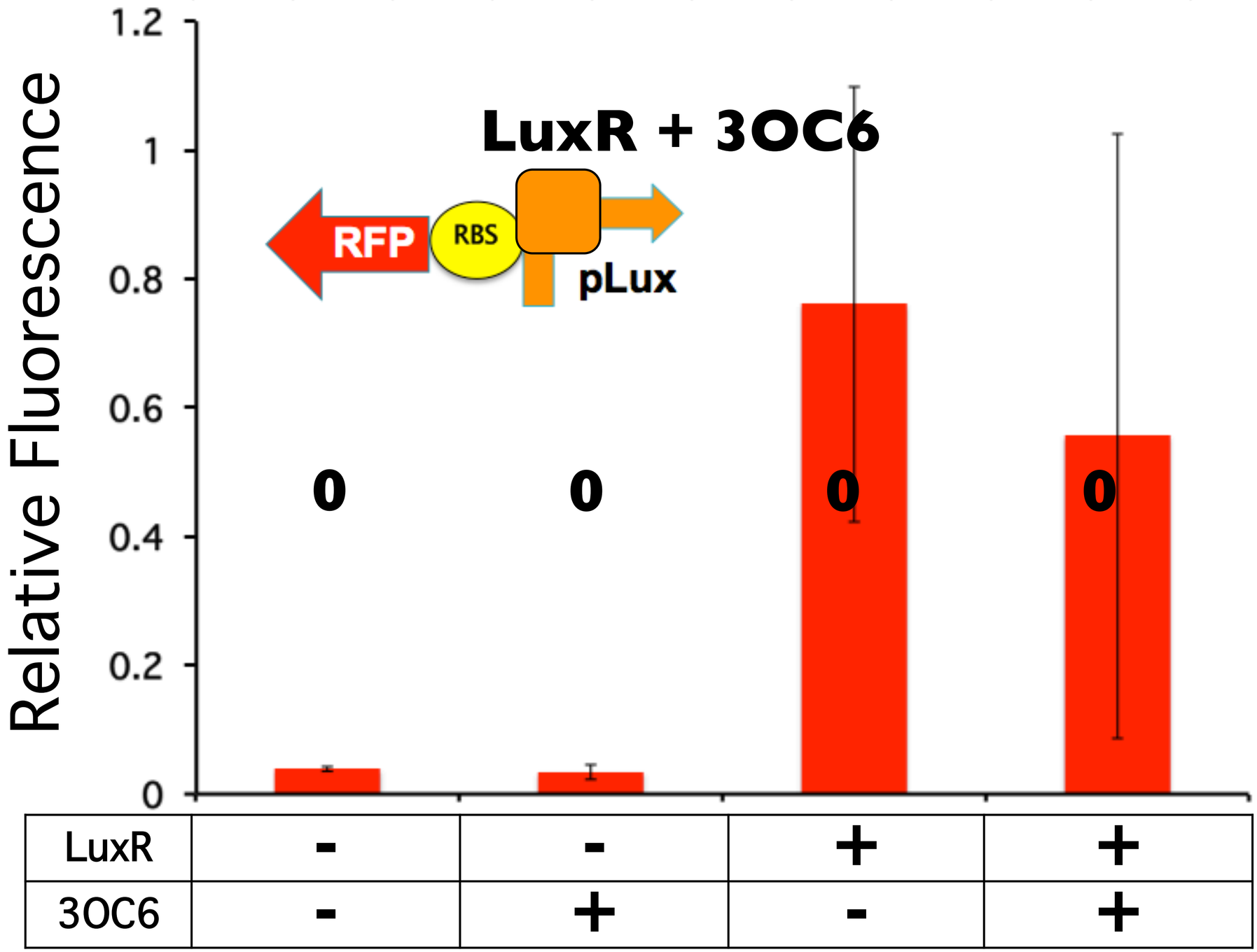
LuxR	-	-	+	+
3OC6	-	+	-	+

pLux + LuxR Promotes Backwards



LuxR	-	-	+	+
3OC6	-	+	-	+

pLux + LuxR Promotes Backwards



Paper Published in 2011

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IBC 2011;3:10, 1-10 • DOI: 10.4051/ibc.2011.3.3.0010

REPORT ON NEGATIVE RESULT

Bacterial Hash Function Using DNA-Based XOR Logic Reveals Unexpected Behavior of the LuxR Promoter

Brianna Pearson[1,†], Kin H. Lau[1,†], Alicia Allen[2], James Barron[1,3], Robert Cool[2], Kelly Davis[4], Will DeLoache[1], Erin Feeney[1], Andrew Gordon[2], John Igo[5], Aaron Lewis[5], Kristi Muscalino[4], Madeline Parra[4], Pallavi Penumetcha[1], Victoria G. Rinker[1,6], Karlesha Roland[1,7], Xiao Zhu[2], Jeffrey L. Poet[5,8], Todd T. Eckdahl[2,8], Laurie J. Heyer[4,8] and A. Malcolm Campbell[1,8,*]

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17 undergraduate co-authors

Programmed Evolution of *E.coli* for Optimization of Metabolic Pathways

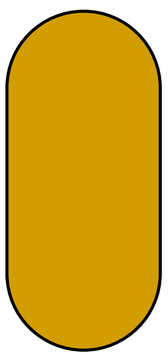
2012 - 2014

DAVIDSON

MISSOURI WESTERN STATE UNIVERSITY

Monday, November 18, 2013

Make *E. coli* Optimize Drug Production



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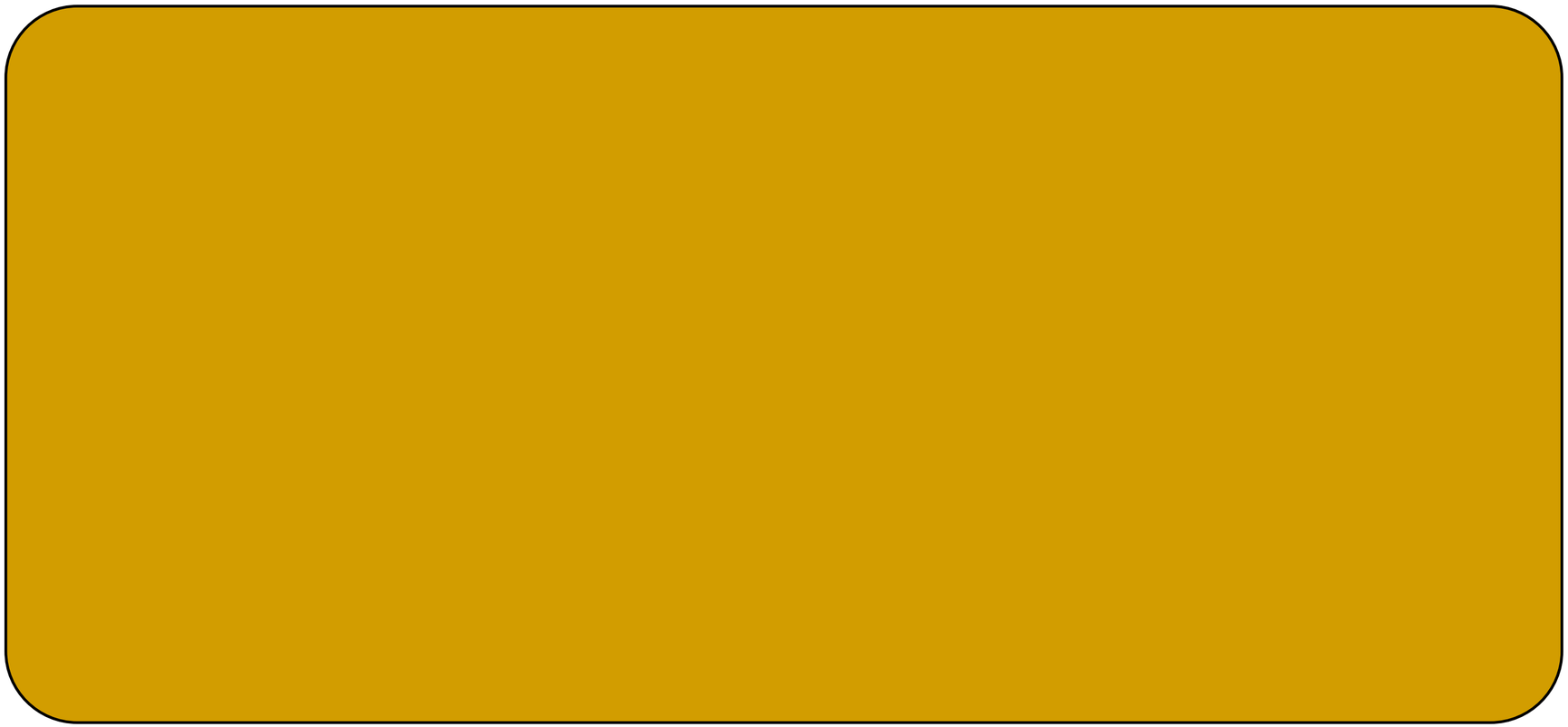

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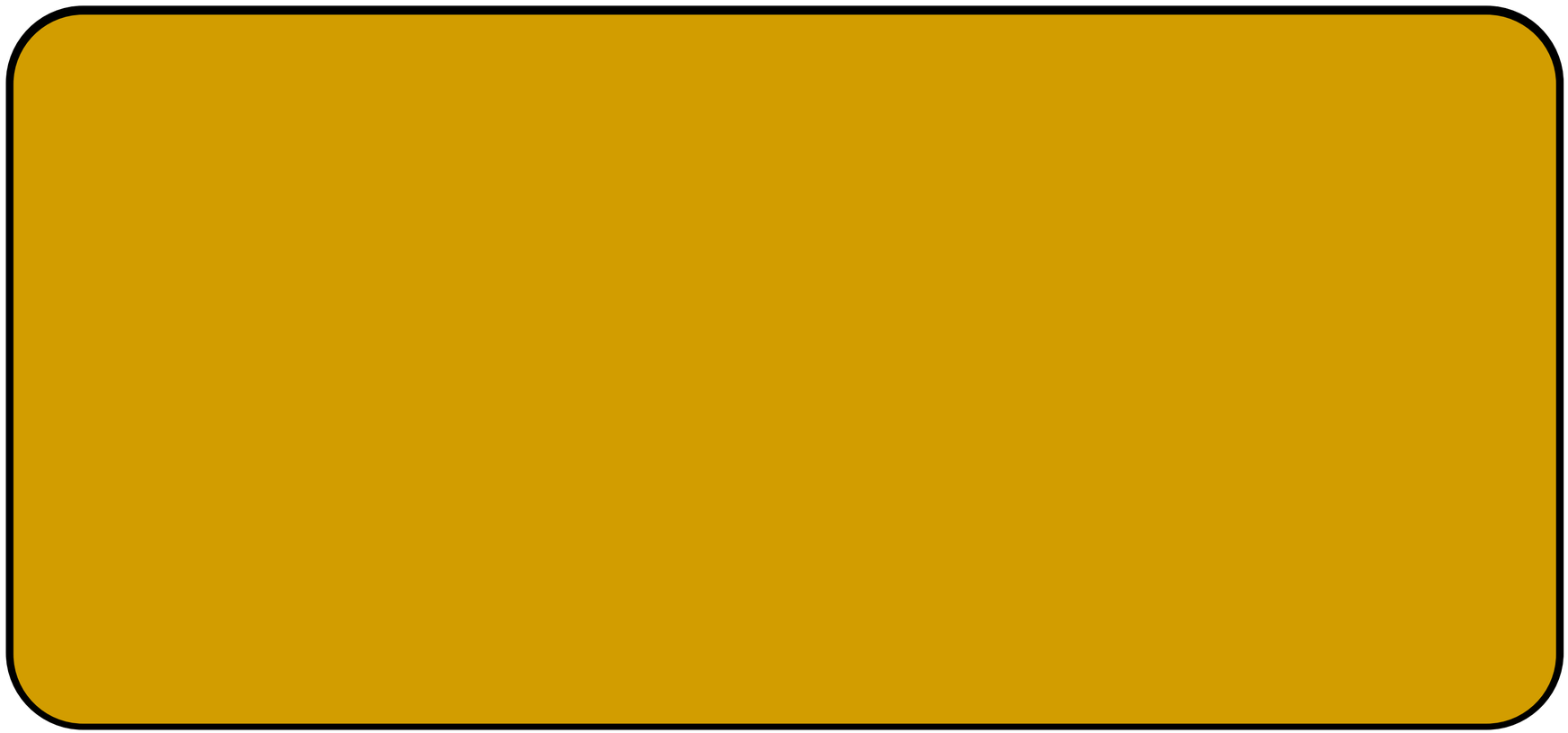

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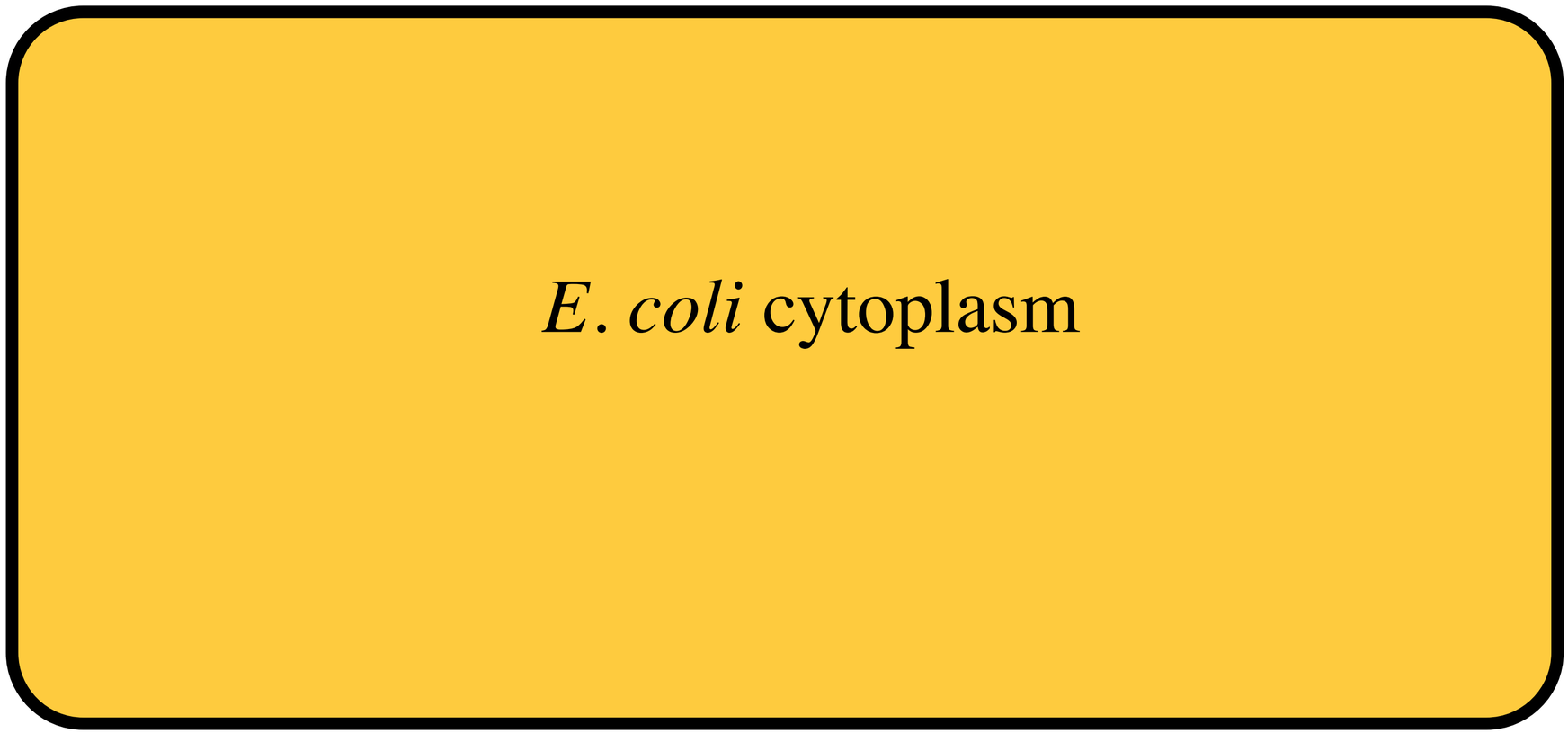

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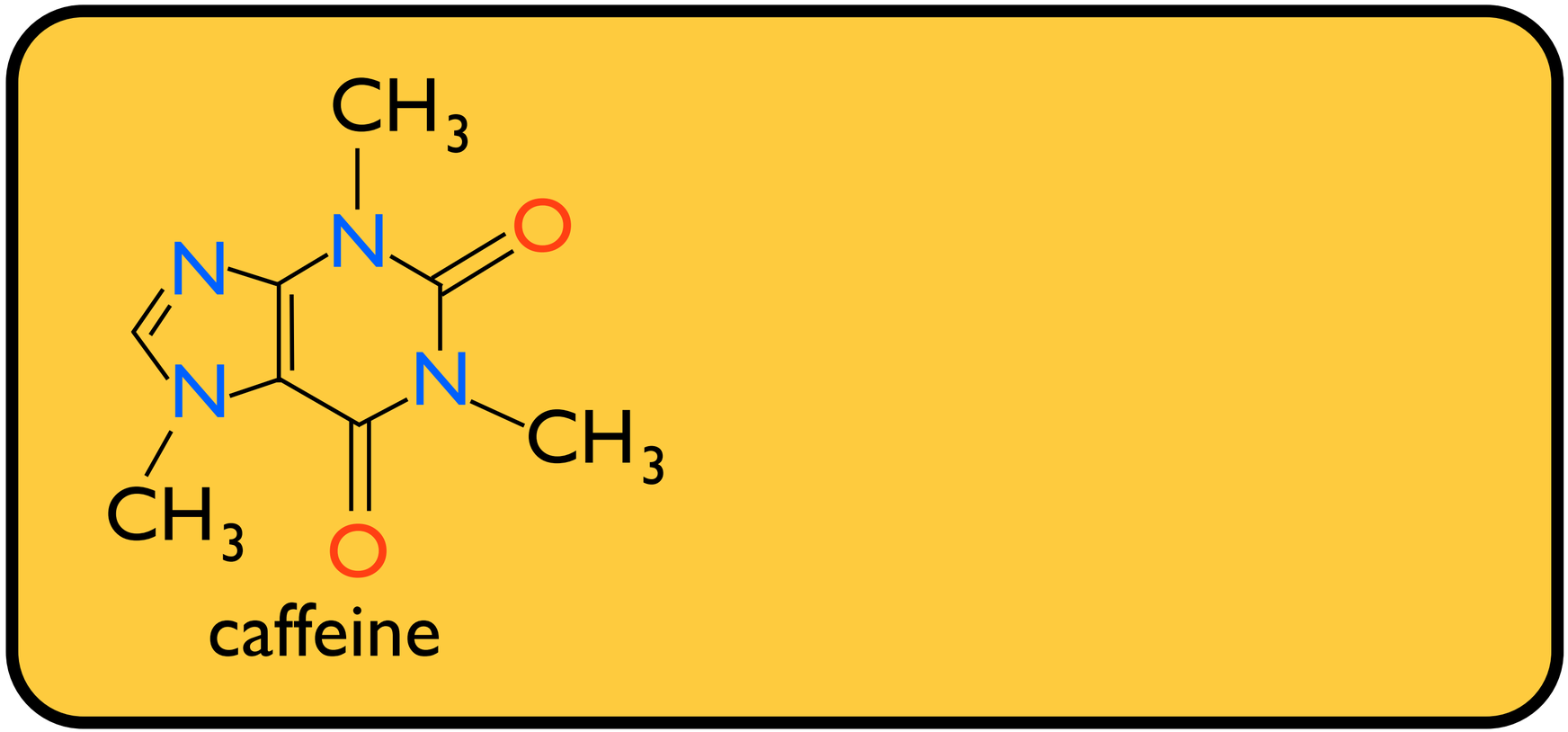
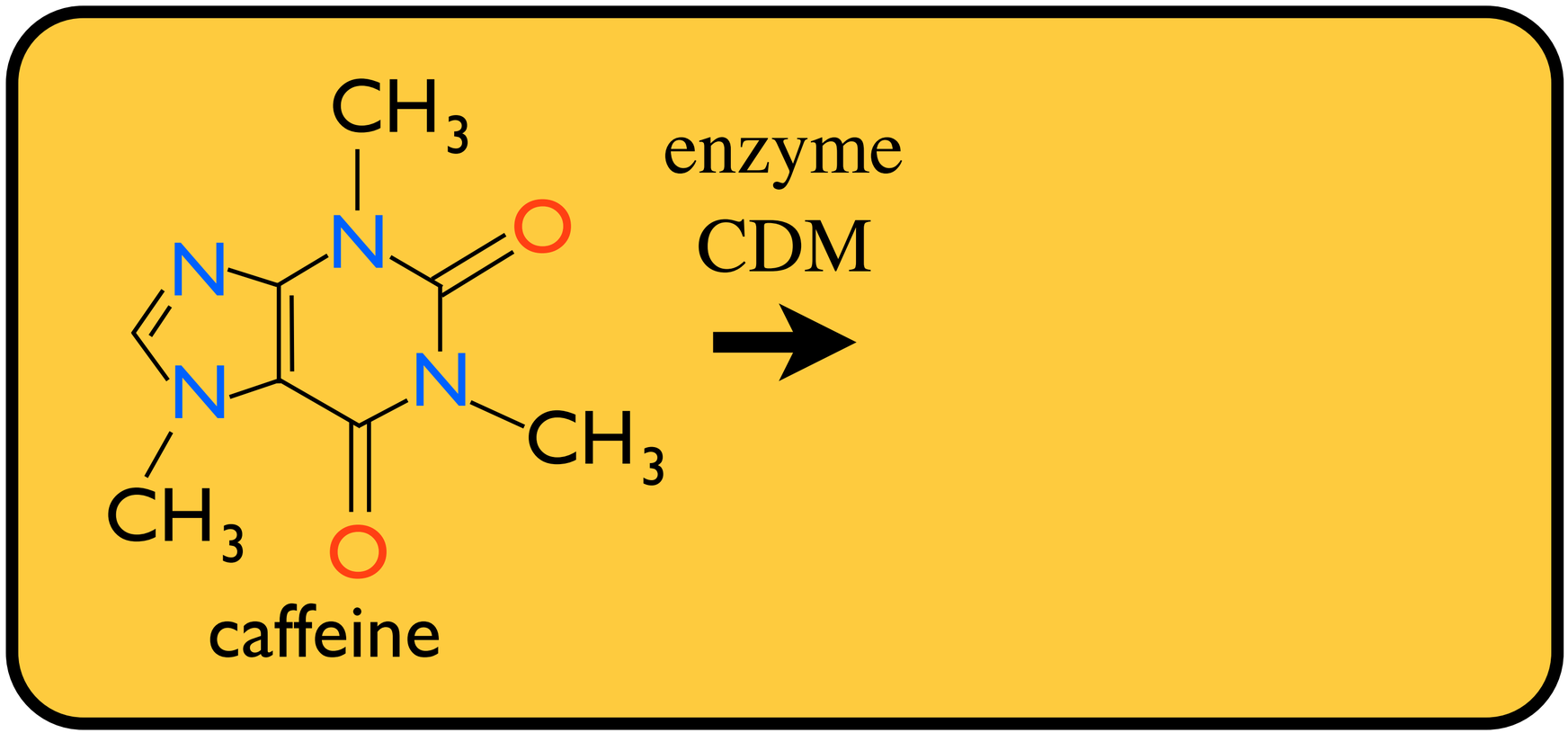
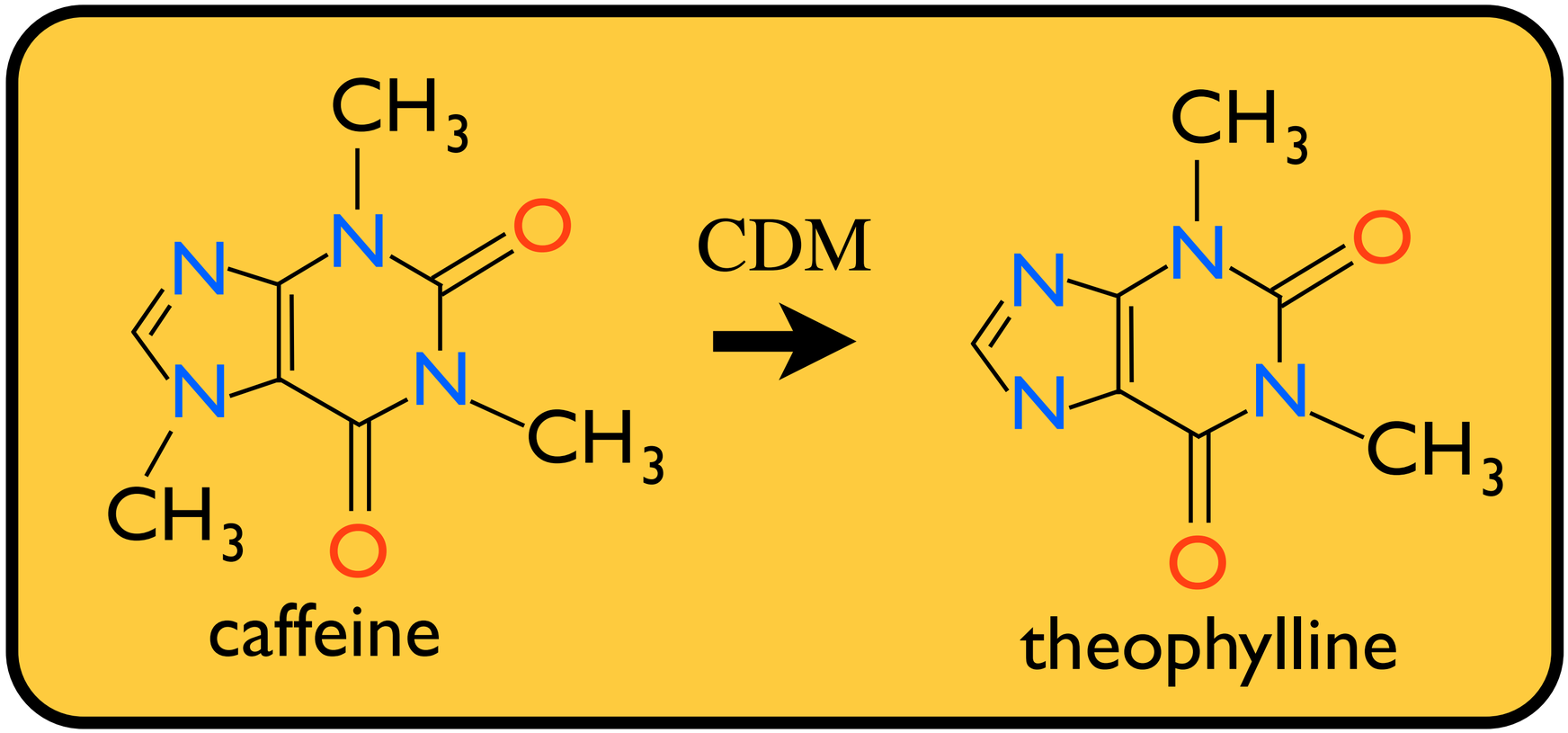


caffeine

Make *E. coli* Optimize Drug Production

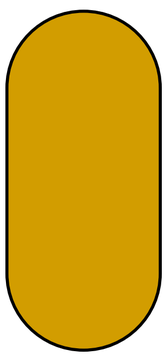


Make *E. coli* Optimize Drug Production



asthma medication

What Makes Optimization Difficult?



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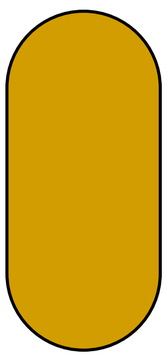

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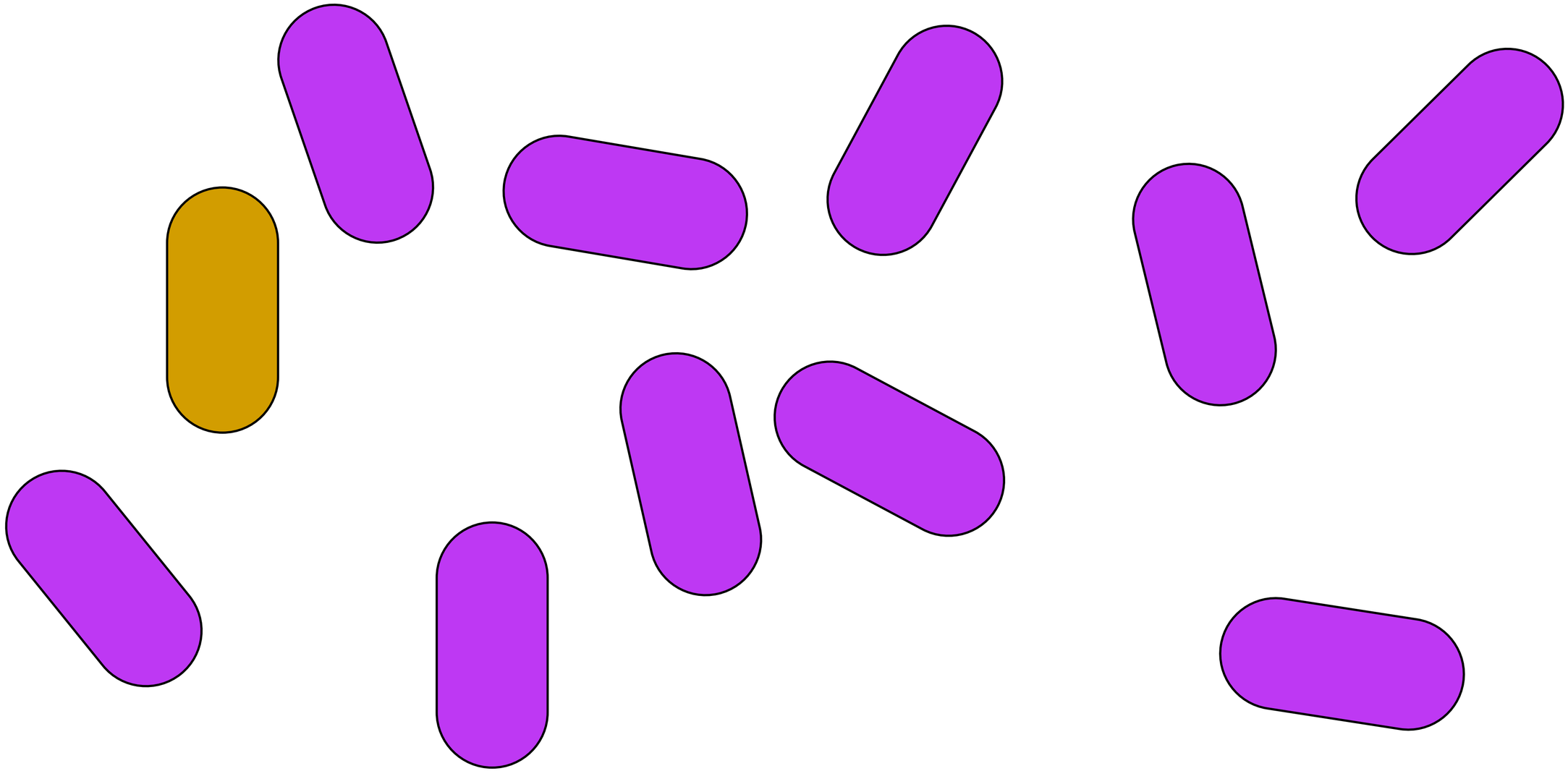

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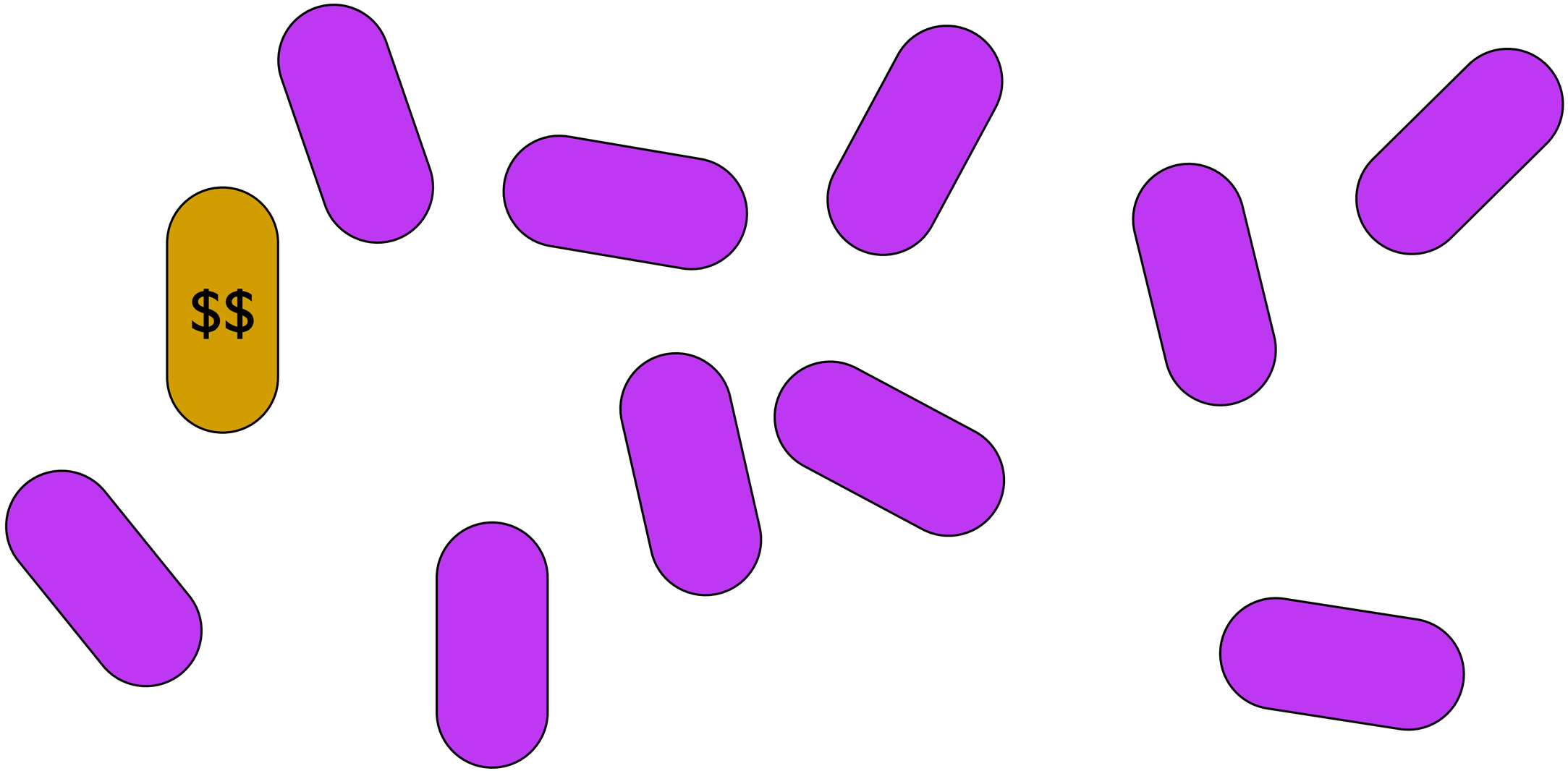
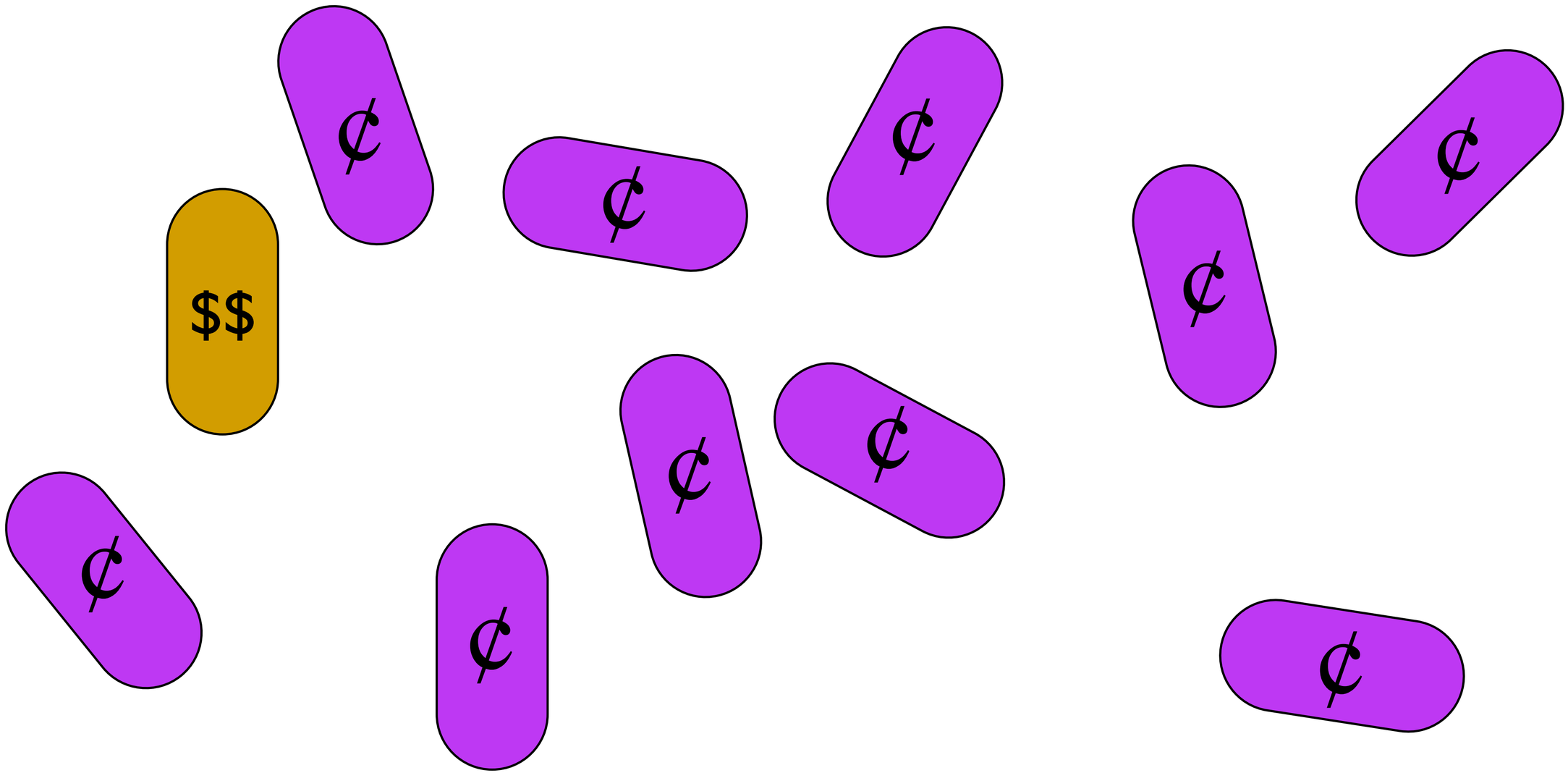


Natural Selection



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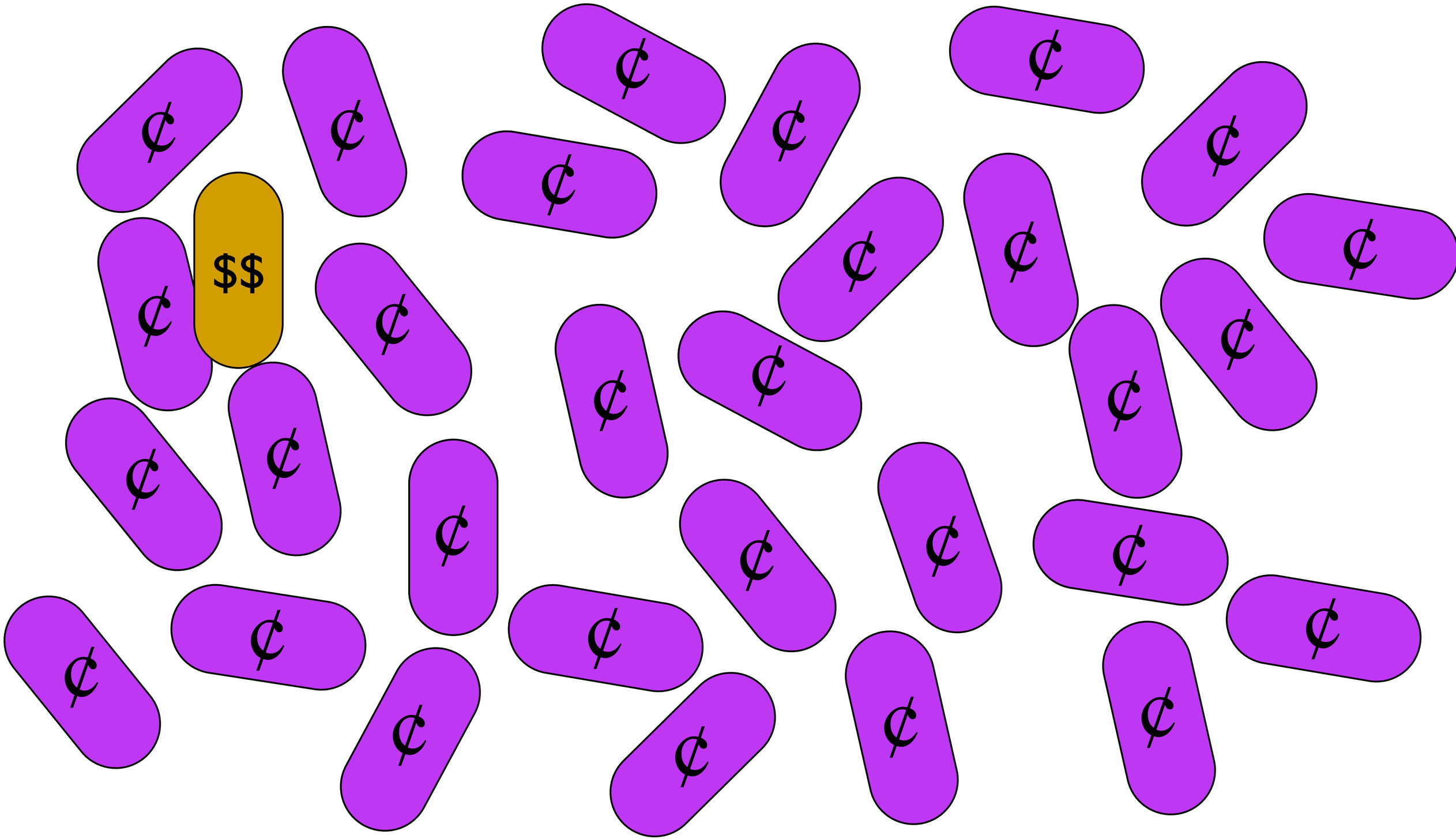
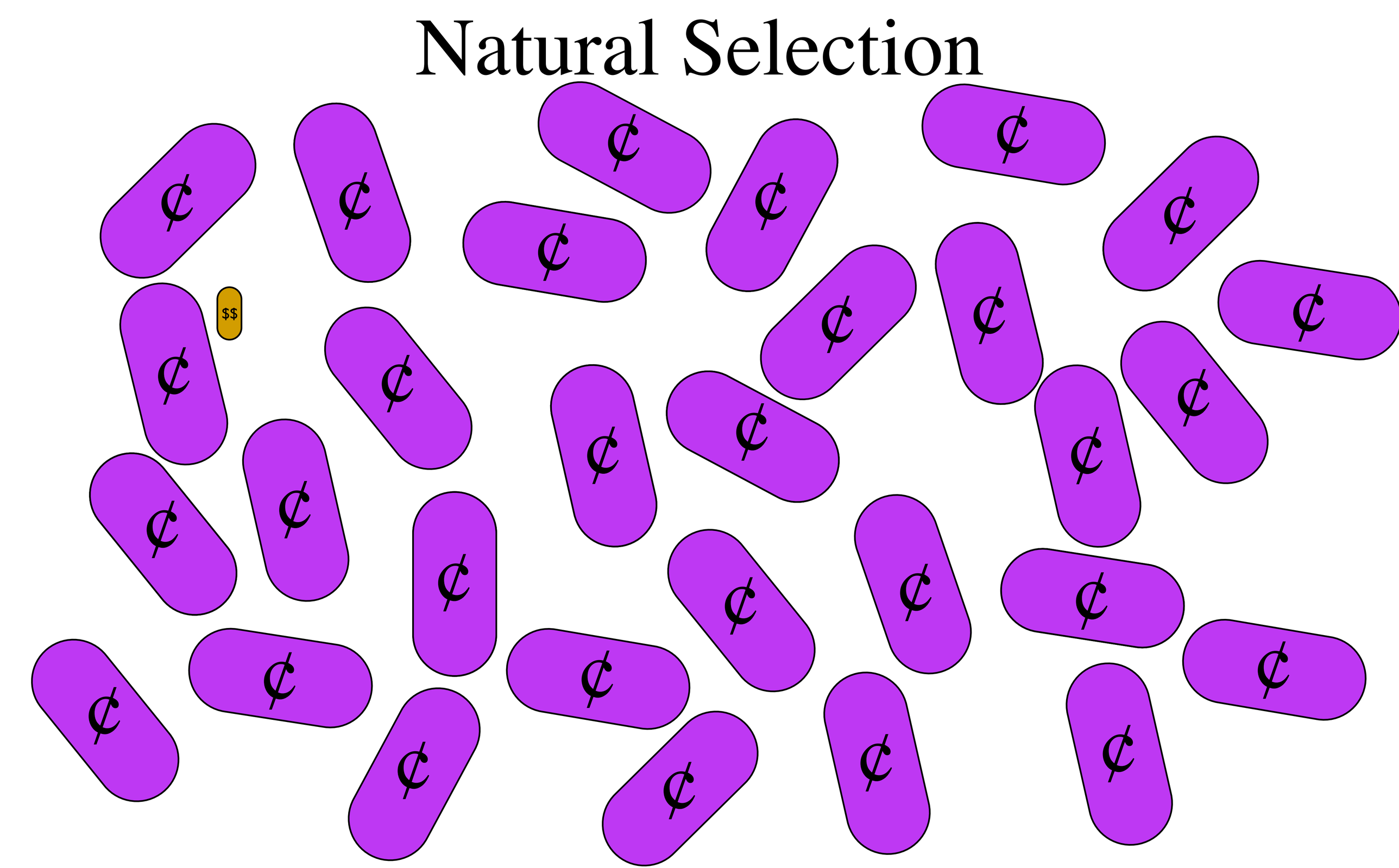
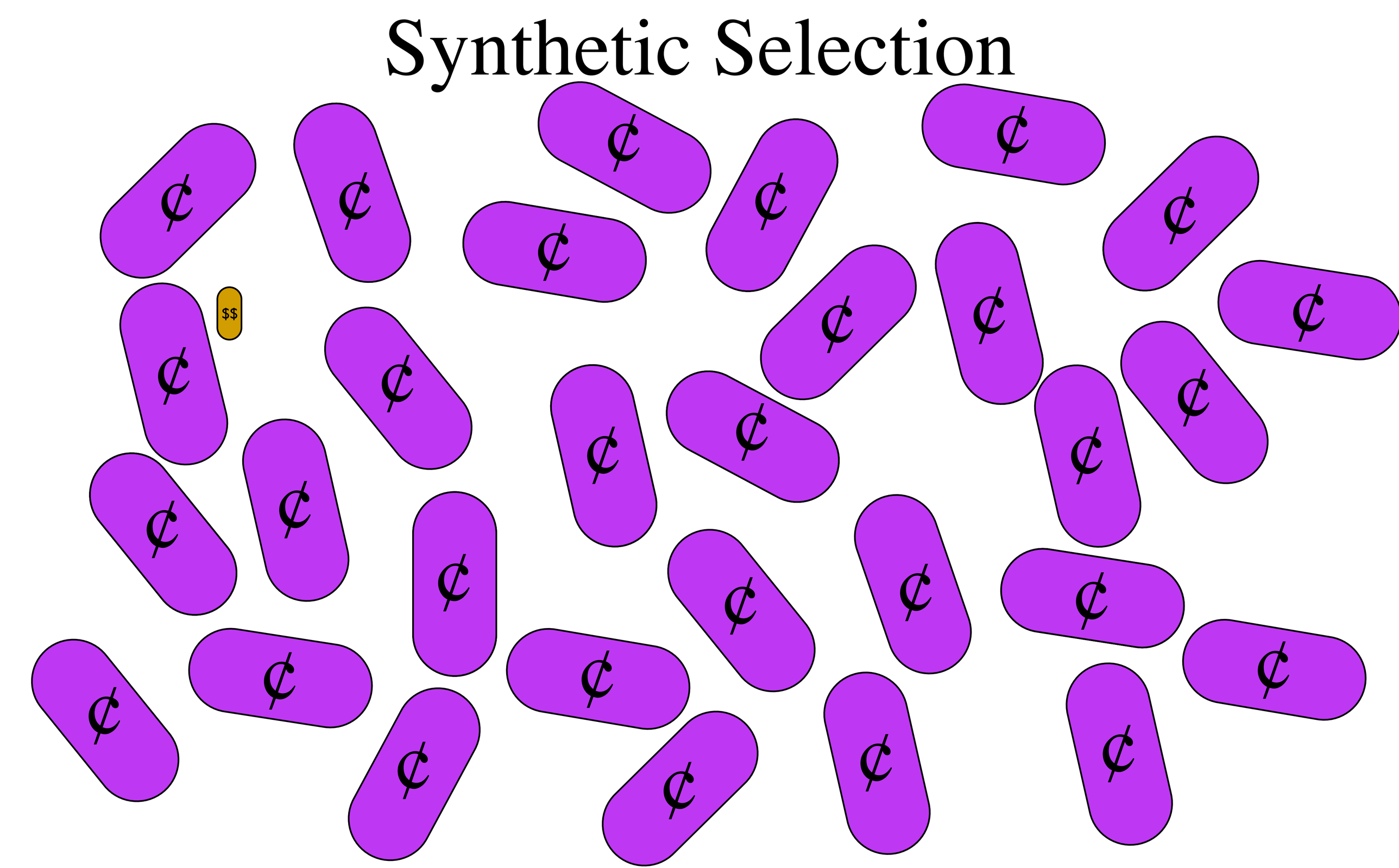


Natural Selection



Synthetic Selection



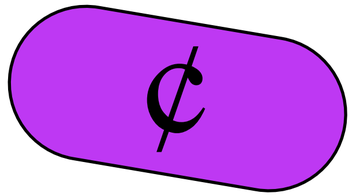
Synthetic Selection

Synthetic Selection

Synthetic Fitness

Synthetic Fitness

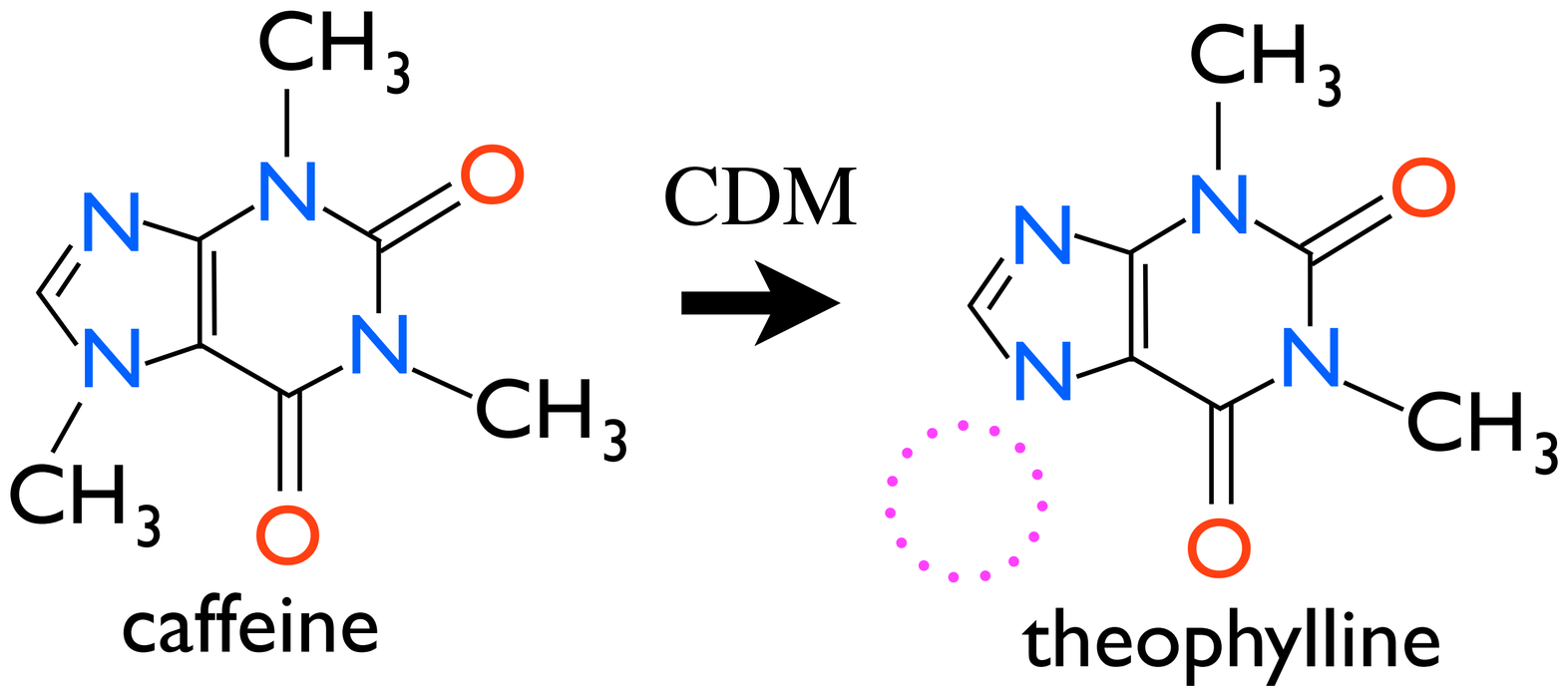
Synthetic Fitness



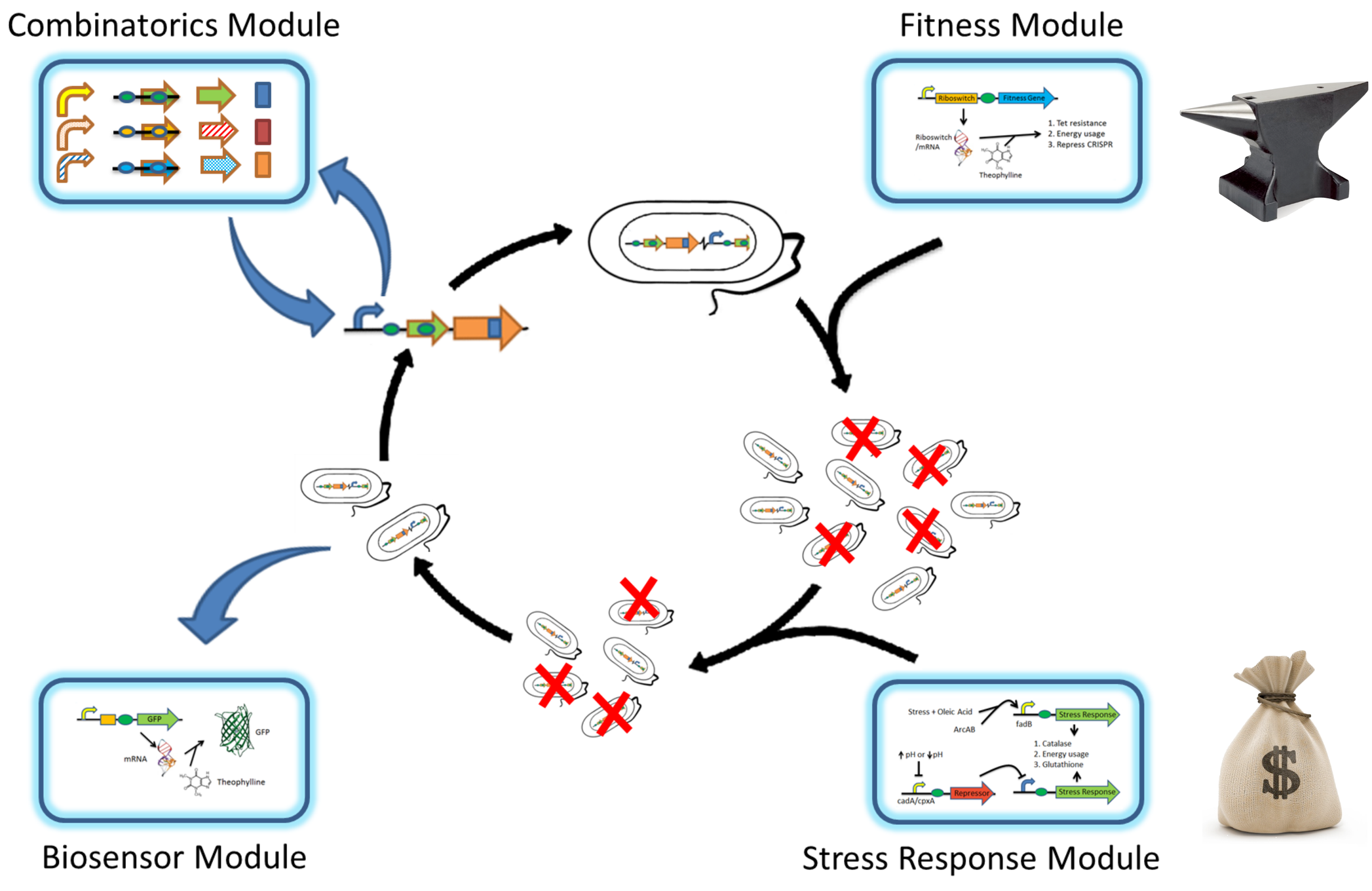
Synthetic Fitness

Engineering Programmed Evolution

Make *E. coli* Produce Optimal Theophylline



Programmed Evolution

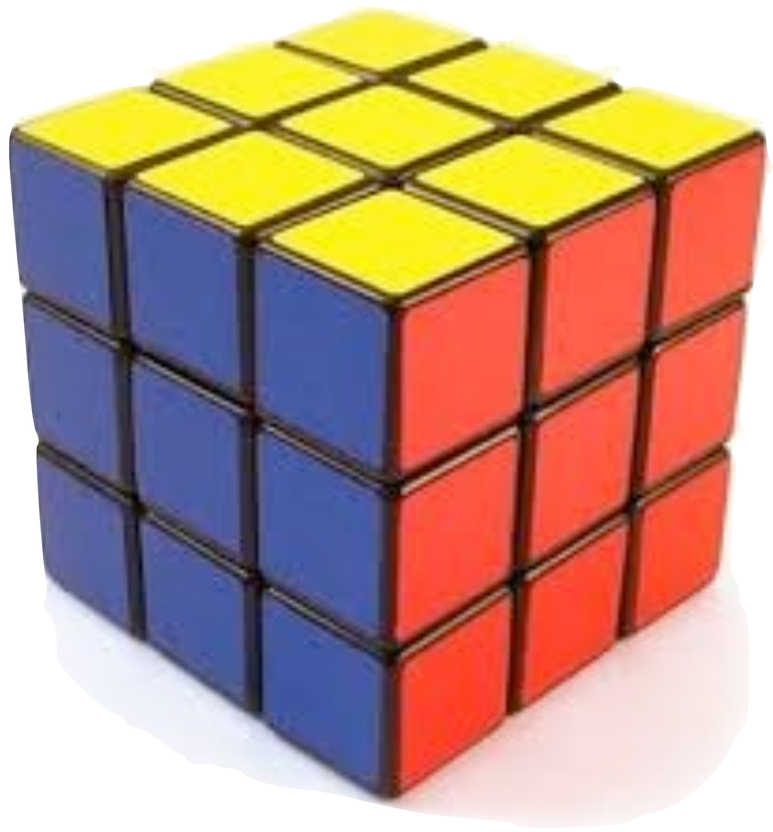


Math Modeling of Programmed Evolution

metabolic flux = f(promoter, RBSs, alleles, # plasmids)

humans

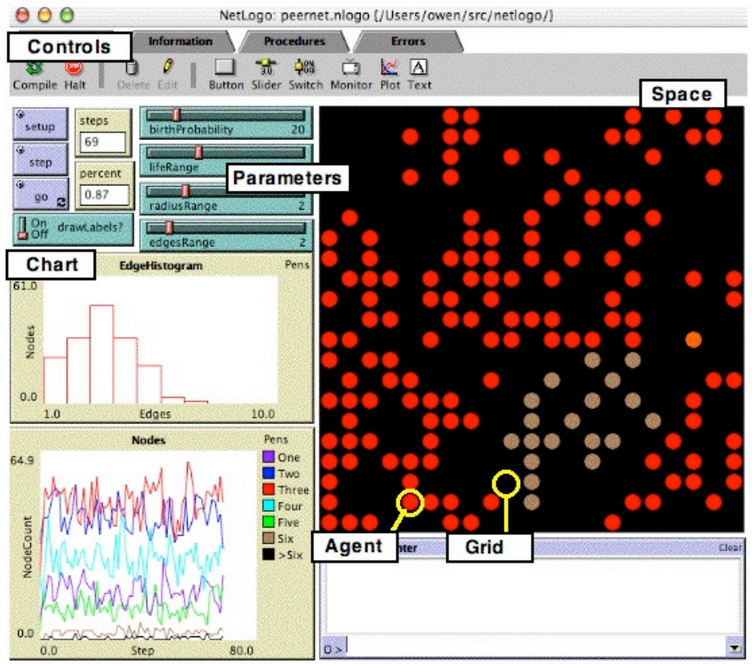
bacteria

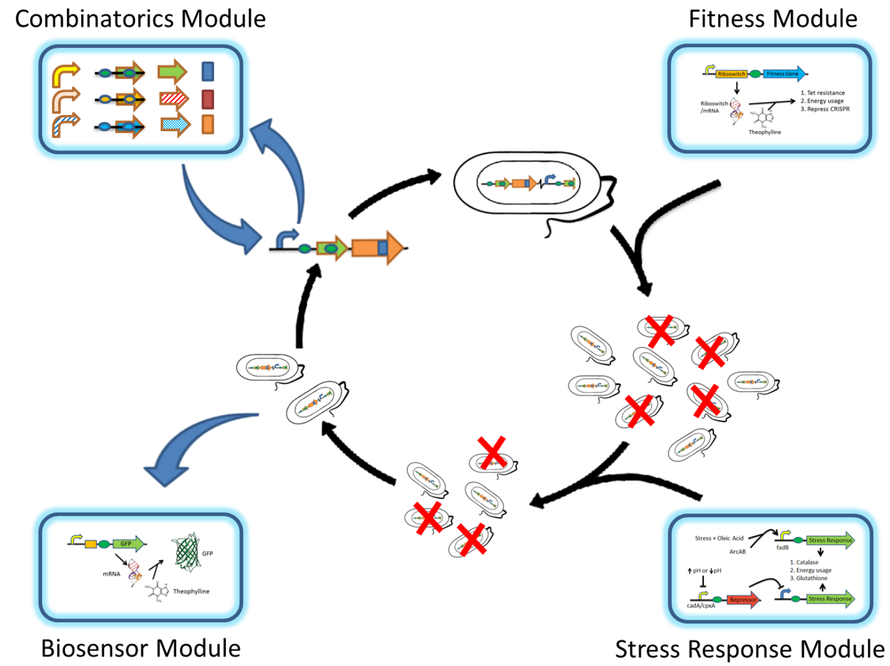


searching multi-dimensional space

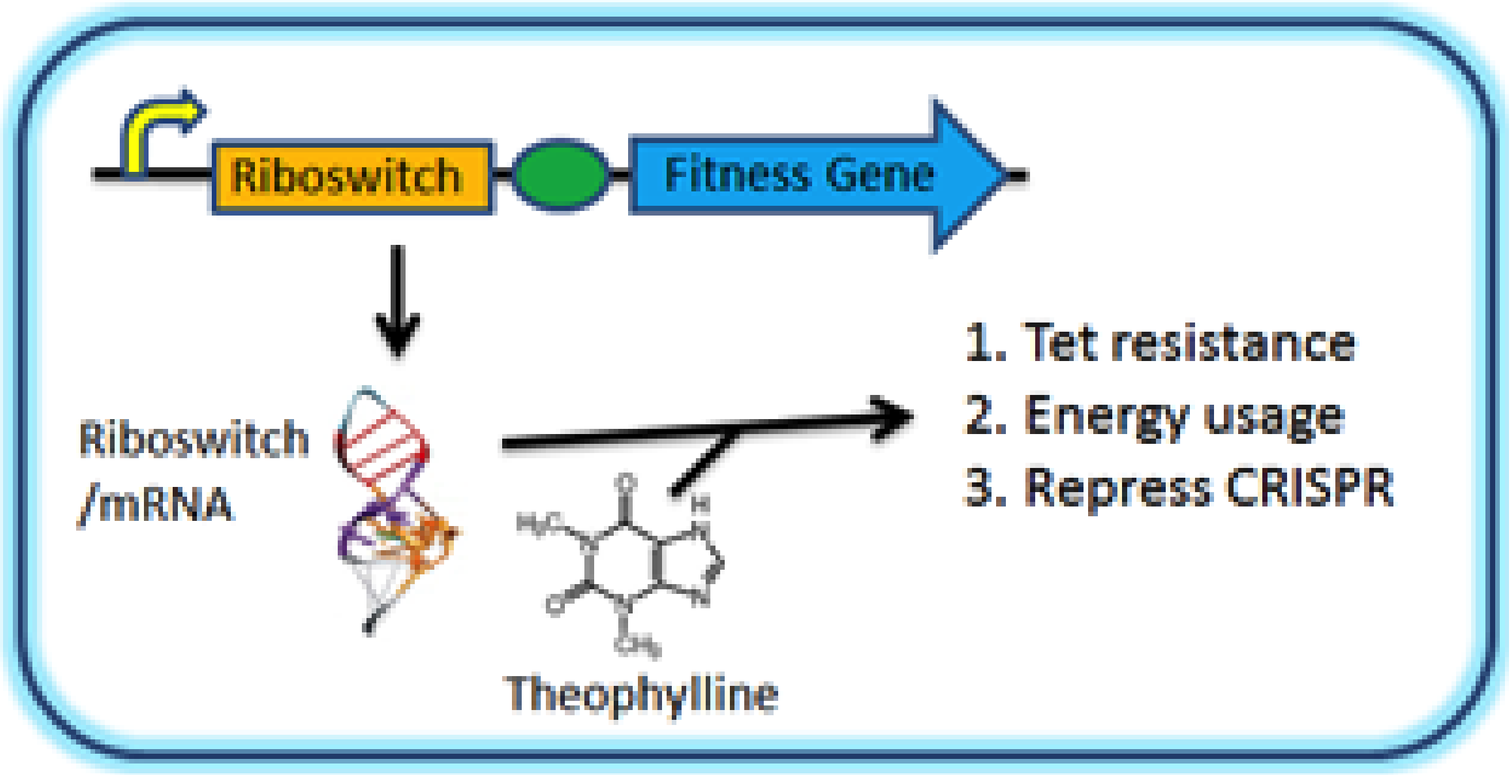
Agent-Based Models of Programmed Evolution

NetLogo

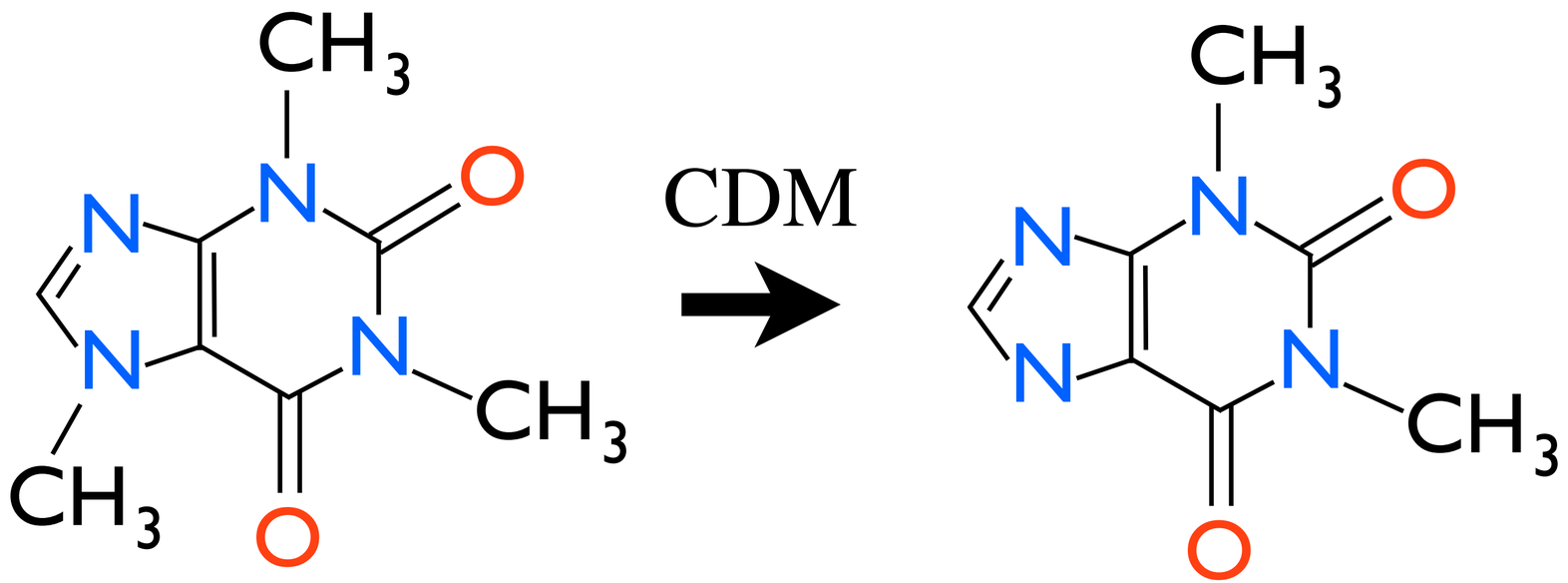




Fitness Module



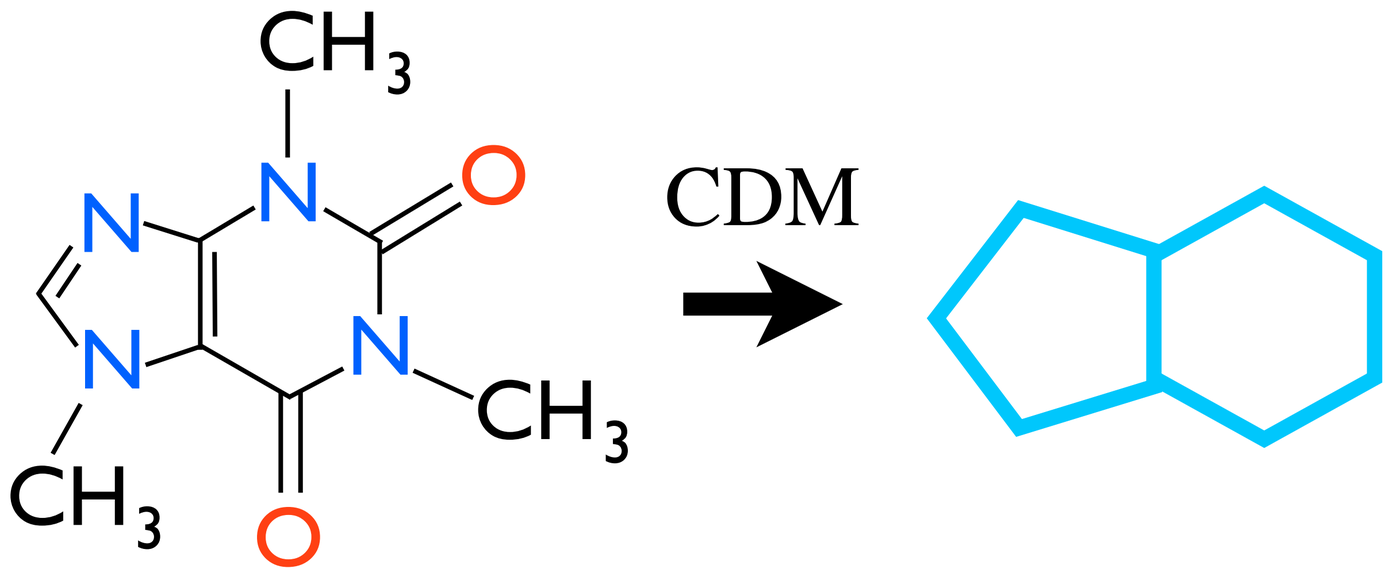
How to Build a Fitness Module?



caffeine

theophylline

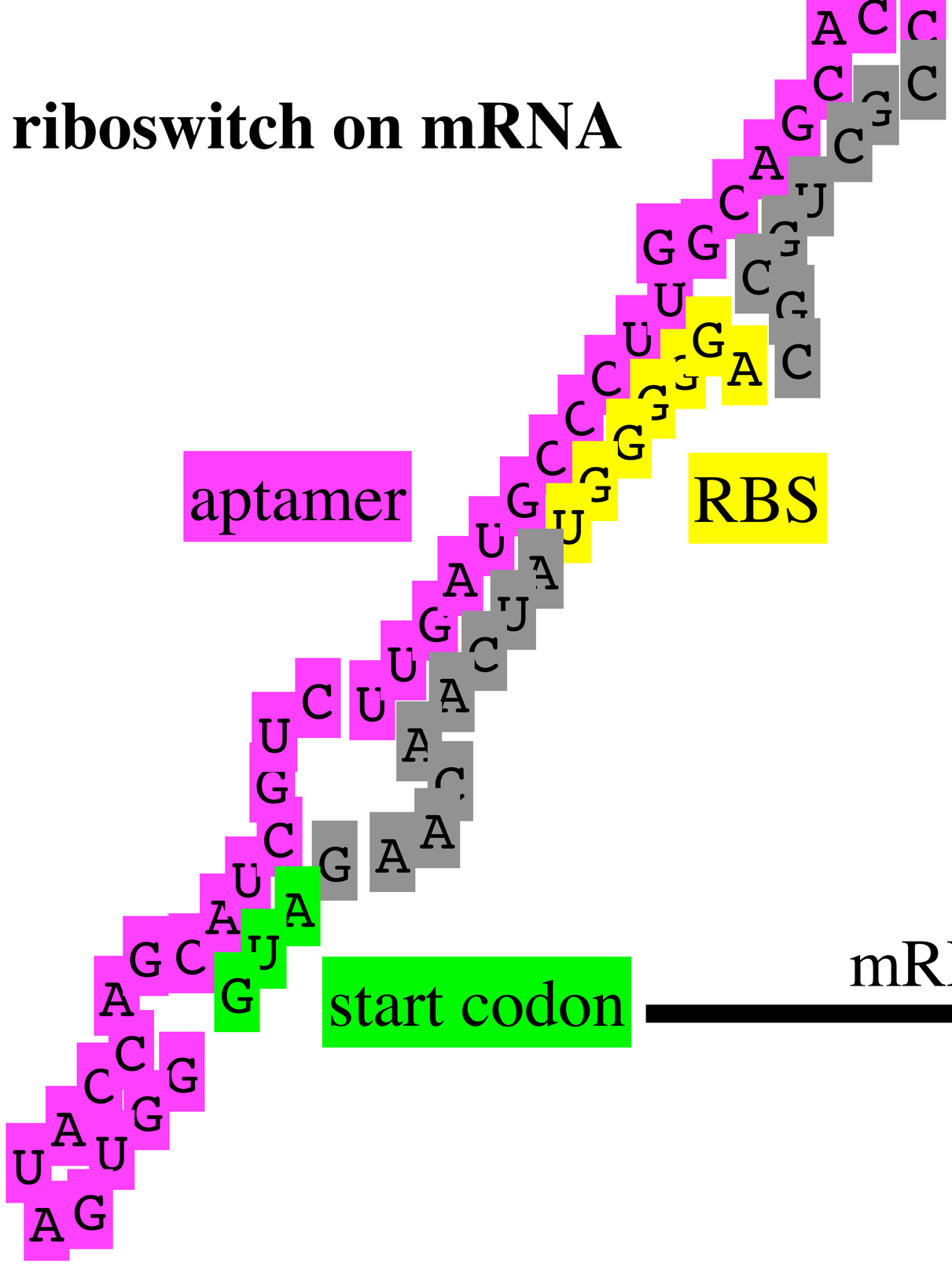
How to Build a Fitness Module?



caffeine

CDM

riboswitch on mRNA



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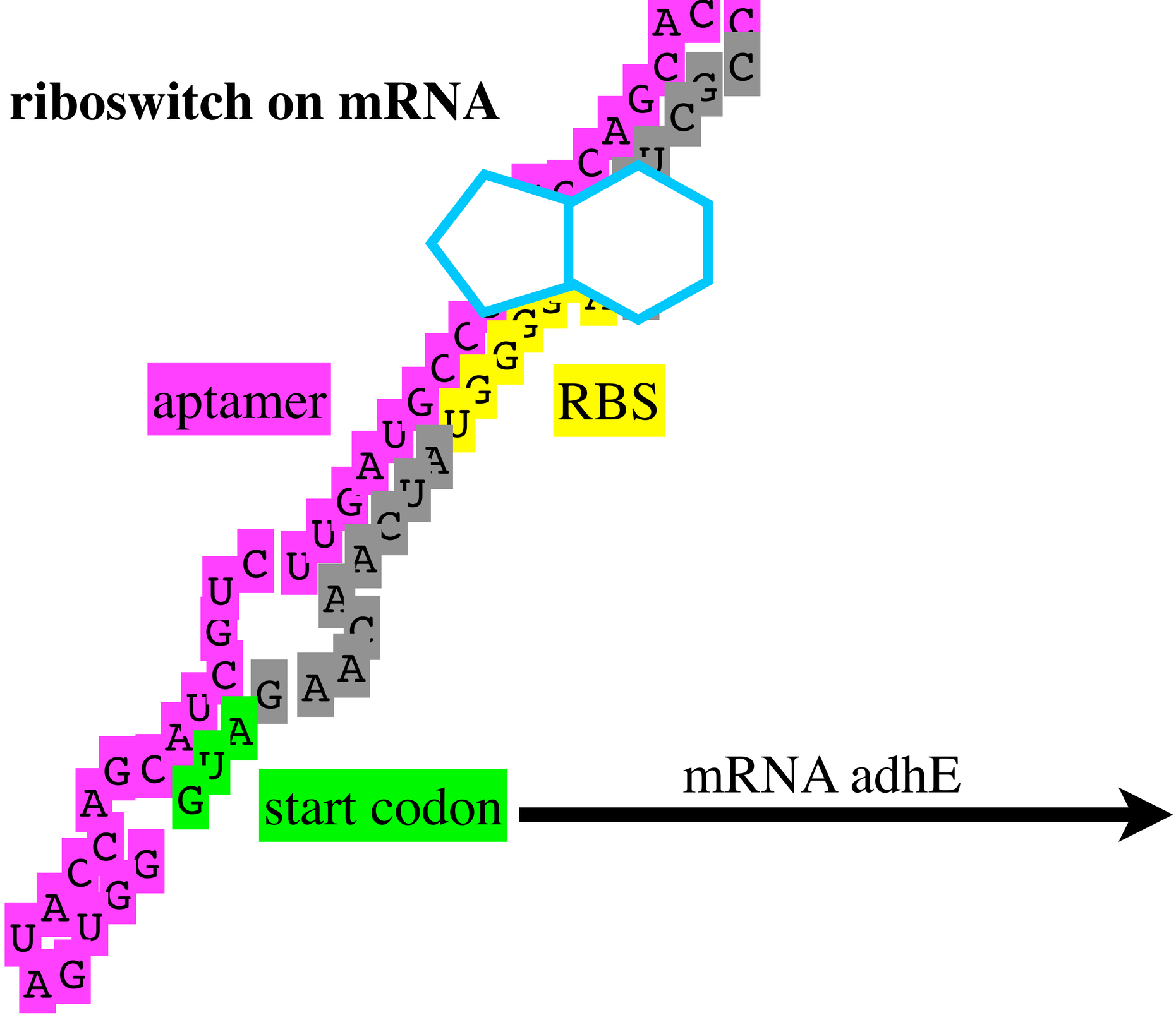
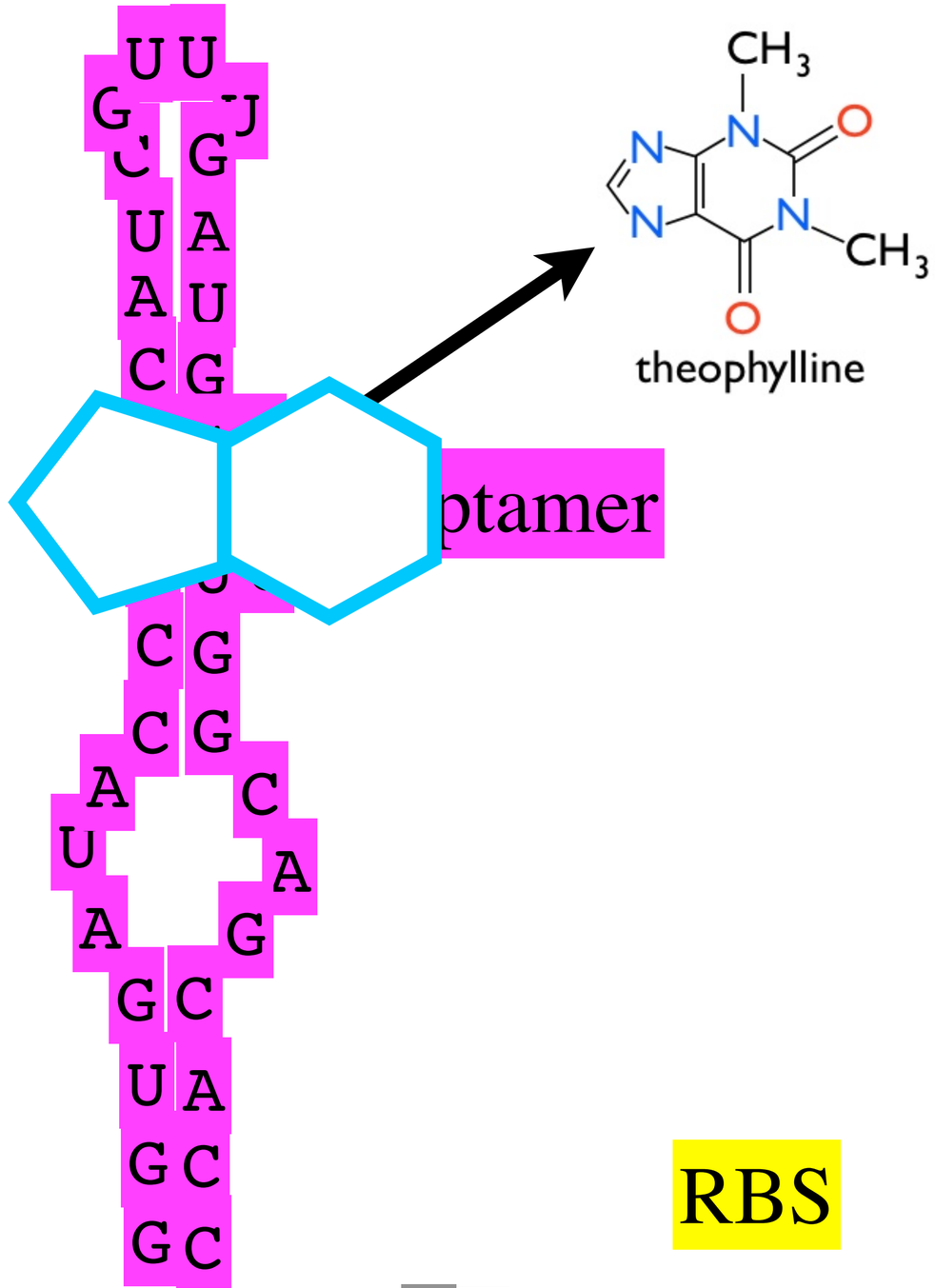
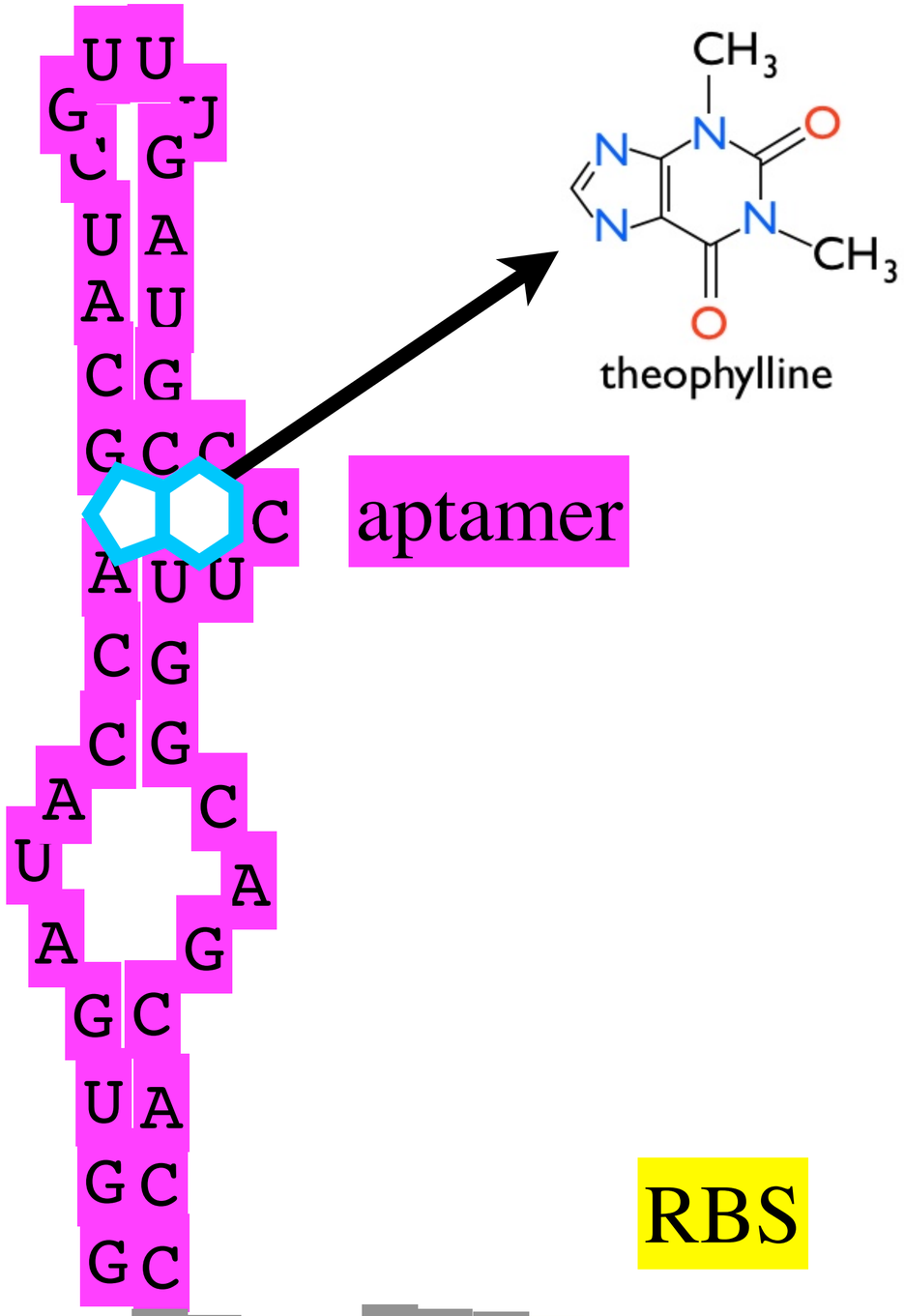


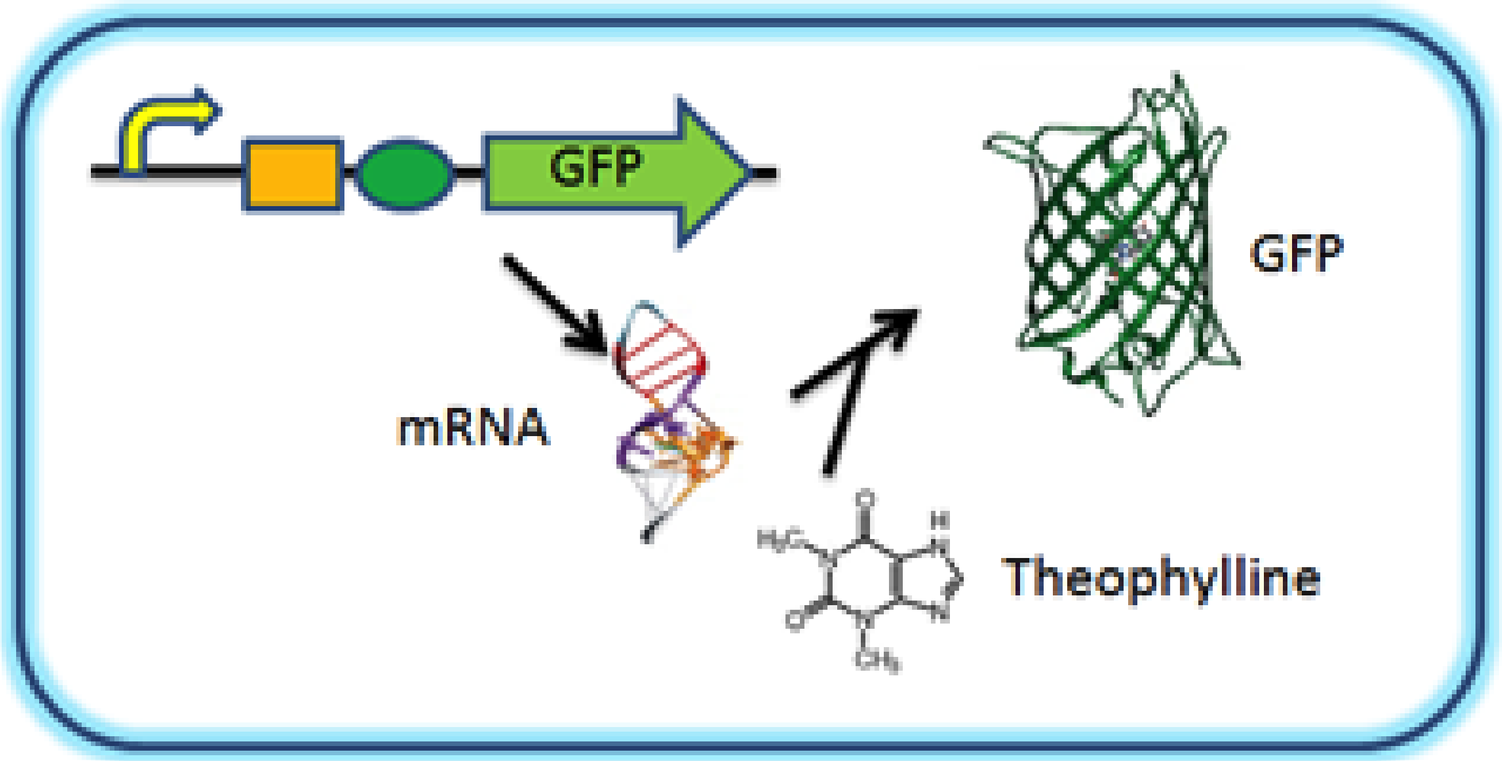


adhE protein

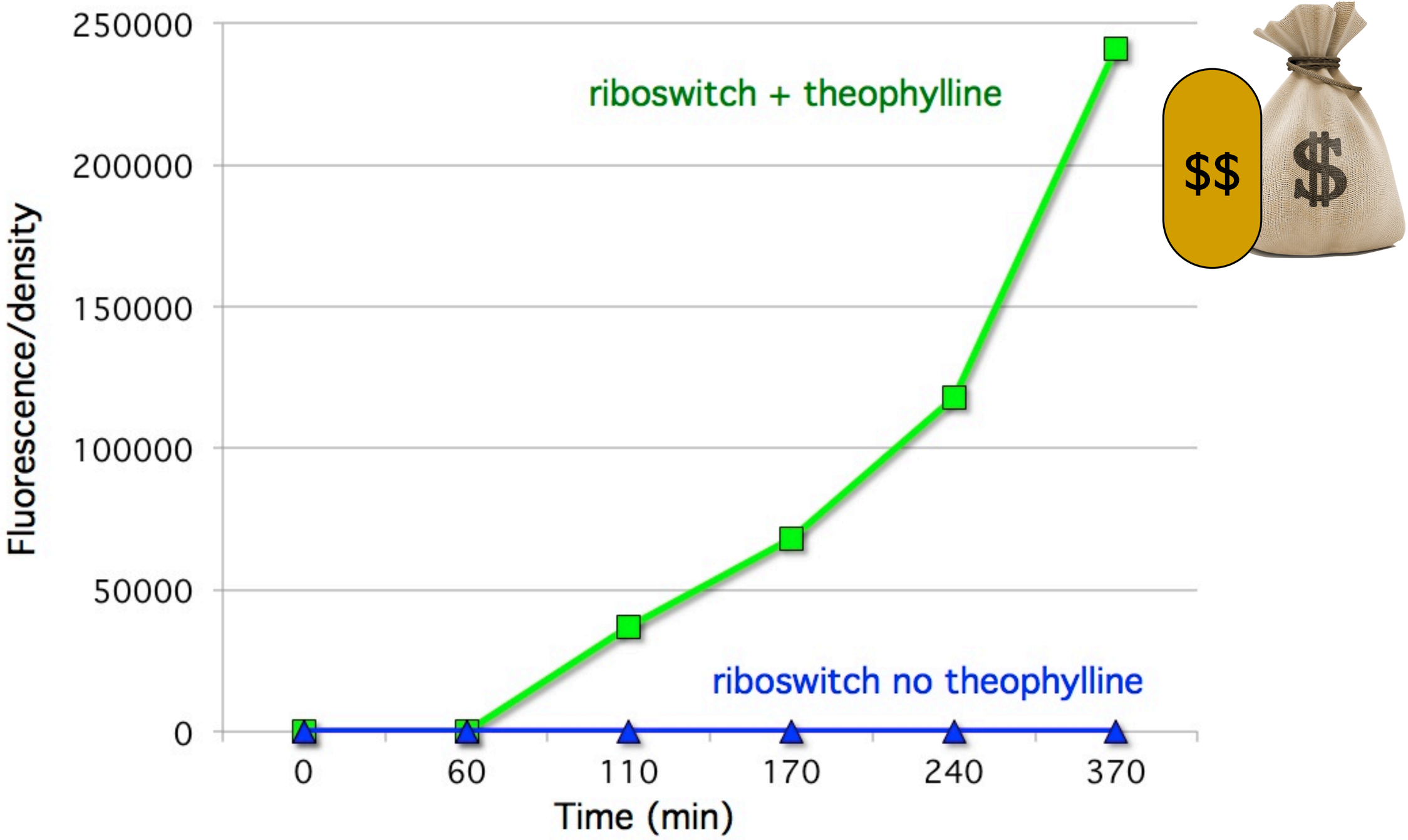


adhE protein

Biosensor Module



BioSensor Detects Theophylline



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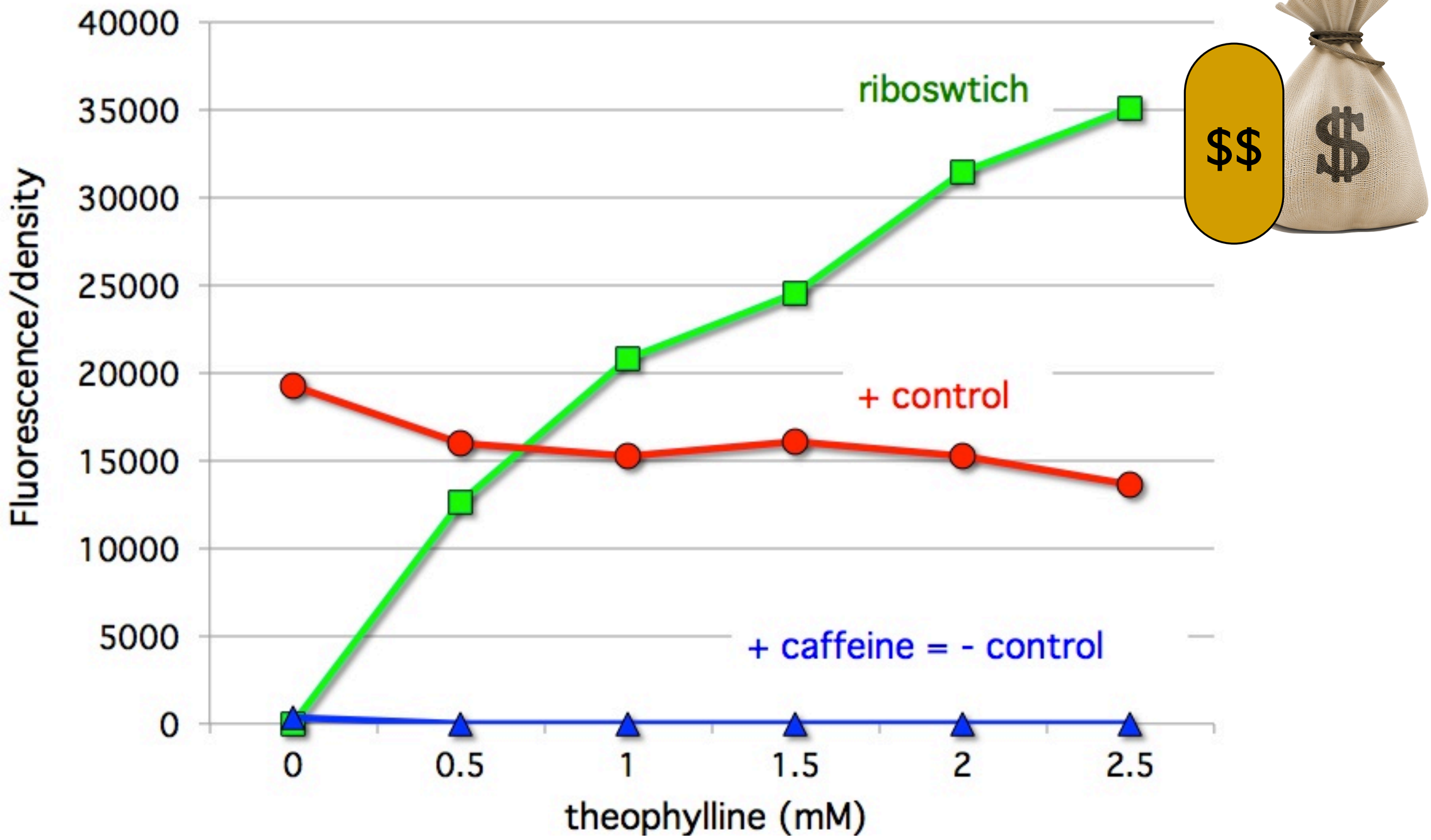
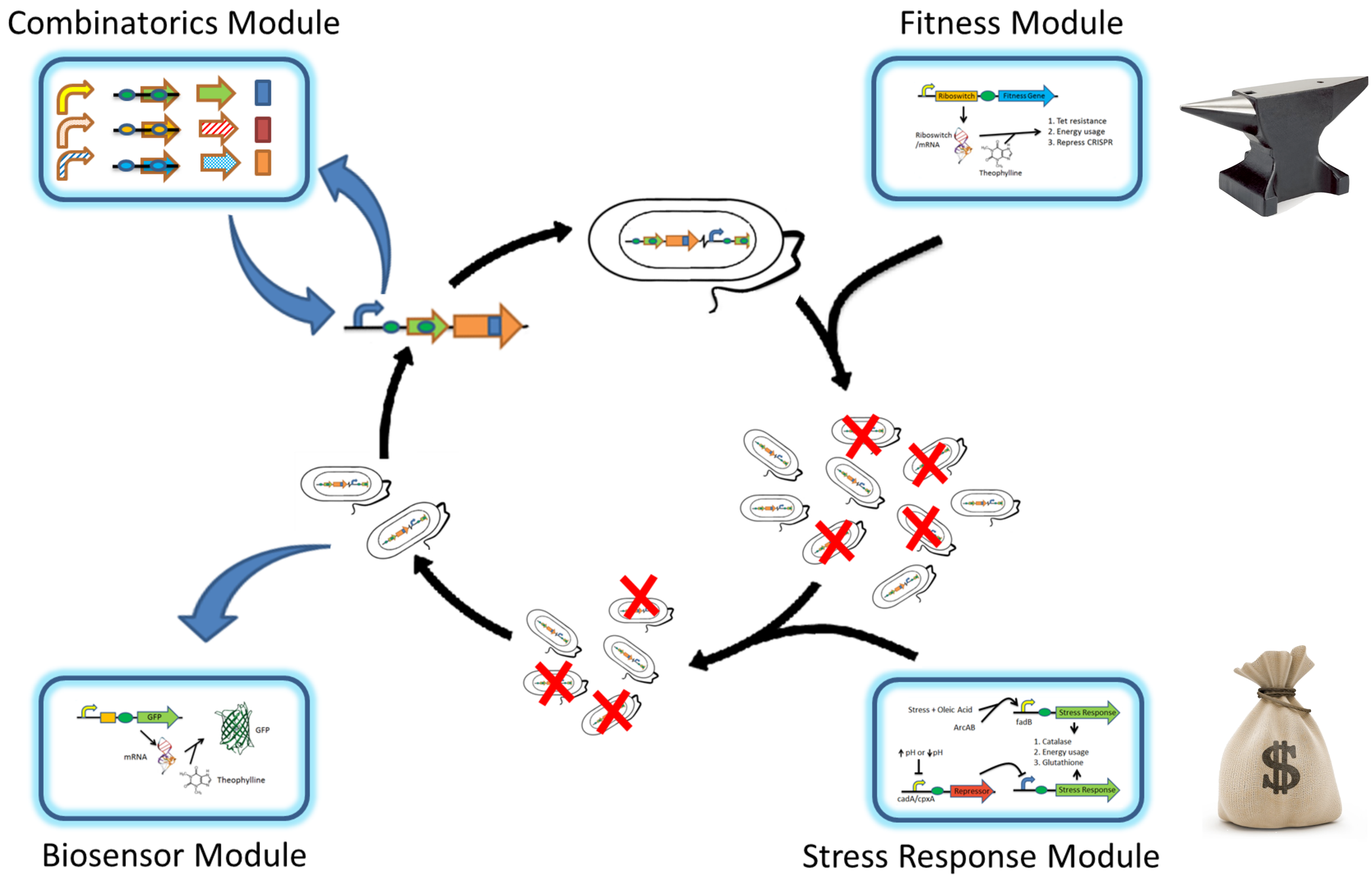
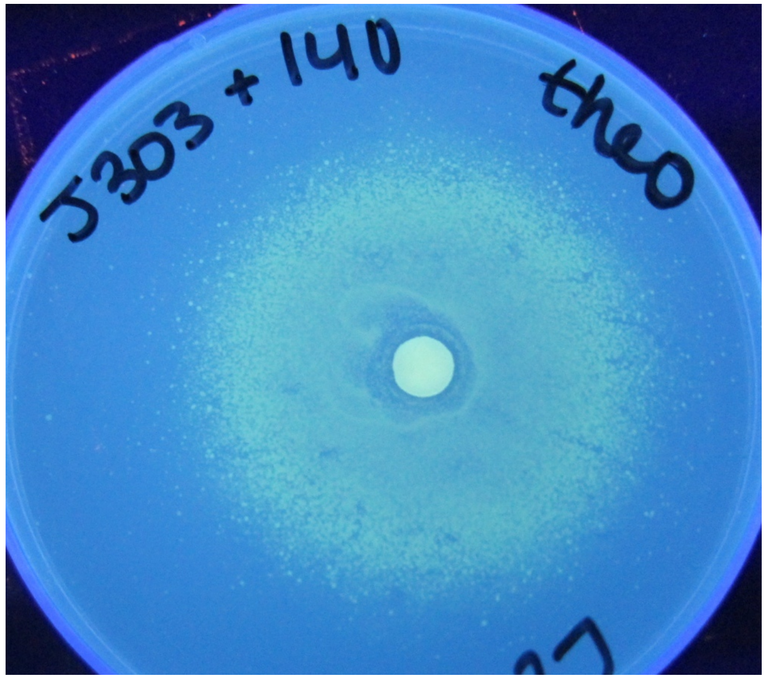


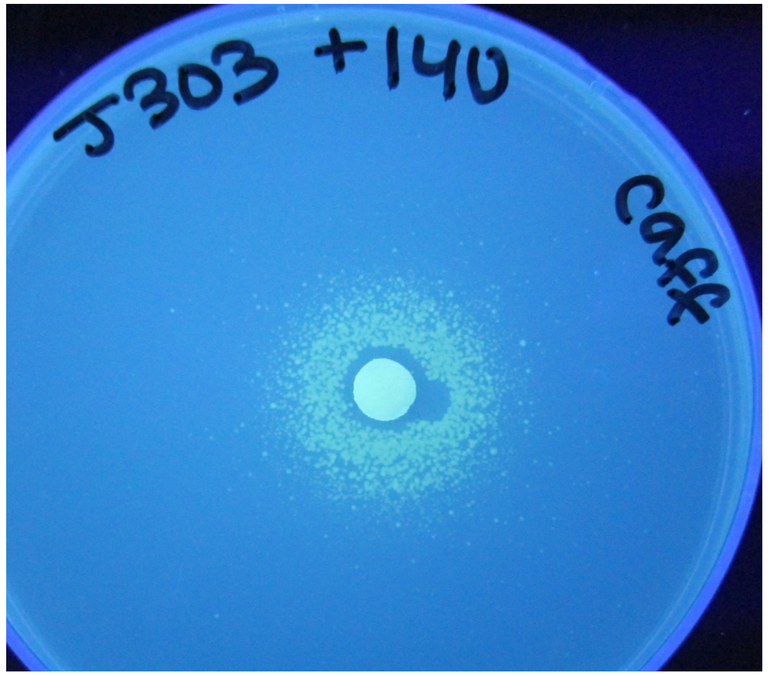
Programmed Evolution



First Fitness Module Results



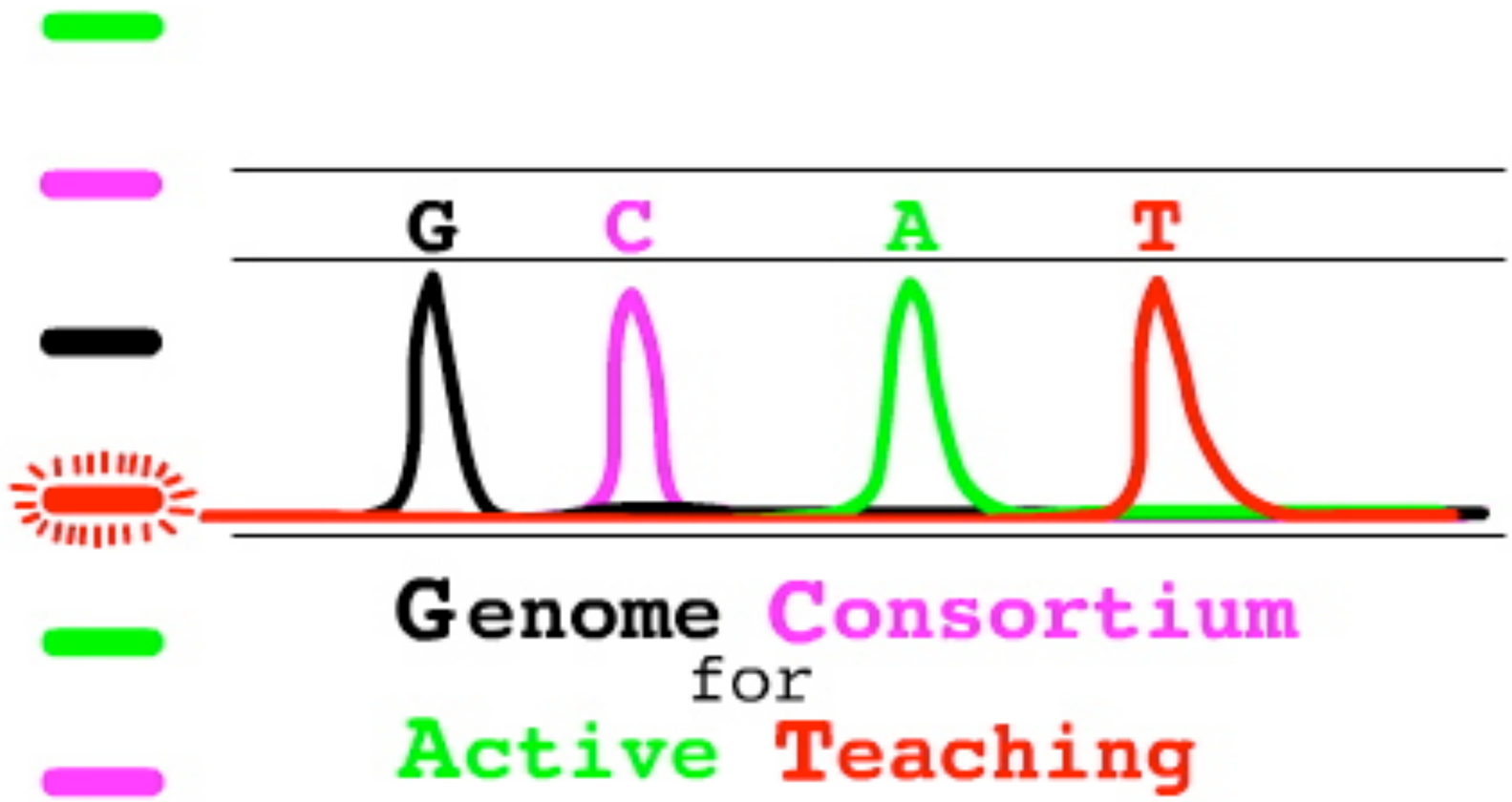
+ control



caffeine

- control

13 Year Collaboration
Three Countries

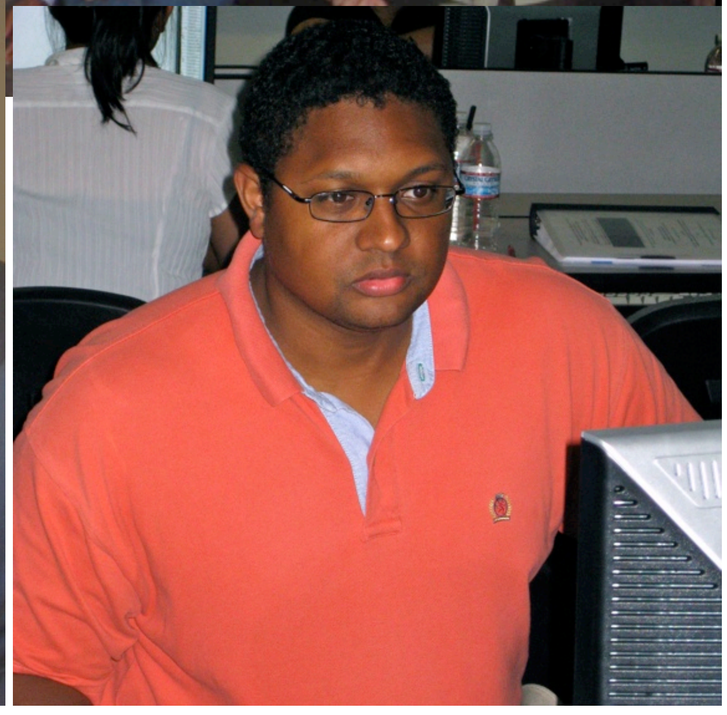


www.bio.davidson.edu/GCAT

GCAT

Faculty Development

NSF funded



GCAT

Faculty Development

12 workshops, 500 faculty

GCAT

Faculty Development

500 faculty

X 100 students each

50,000 students/year

Faculty Appreciate **GCAT** Resources

	Mean	SD
Use microarray technology without **GCAT**	1.5	0.75
Online **GCAT** protocols useful	4.4	0.69
The **GCAT** -Listserv helpful	4.2	1.0
GCAT network significant factor	4.2	0.79
Positive experience using **GCAT**	4.6	0.60
I would use **GCAT** again in the future	4.7	0.63

1 = strongly disagree
5 = strongly agree

GCAT

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SCIENCE ON A SHOESTRING

Teachers' group brings genomics revolution to minority colleges

When the human genome sequence was released in 1999, it meant two things to Edison Fowlks, a biology professor at Hampton University in Virginia.

First, genomics technologies were about to revolutionize science. And second, students and faculty of so-called minority-serving institutions such as Hampton, a historically black college, needed to be part of the revolution.

But where were such institutions going to come up with the funds to train faculty in the new technologies—much less buy microarrays and the scanners needed to read them?

In 2004, Fowlks found an answer when he met fellow biologist A. Malcolm Campbell, who since 2000 had been organizing a program called Genome Consortium for Active Teaching (GCAT) for faculty at small undergraduate institutions. Campbell is himself a researcher at

and genomics without all the powerful equipment that major universities have."

Fowlks joined forces with Campbell to expand GCAT's reach. The pair wrote a grant, awarded by the US National Science Foundation, to support a GCAT workshop at Morehouse College in Atlanta in 2005. The agency has committed to funding yearly workshops through 2009; the most recent of these, held

Bring on the revolution: Using donated microarrays and a single scan-

http://www.nature.com/naturemedicine

Genome Consortium for Active Teaching

EDUCATIONFORUM

COLLABORATIVE PROGRAMS

Genome Consortium for Active Teaching (GCAT)

A. Malcolm Campbell,[1,3]* Todd T. Eckdahl,[2,4] Edison Fowlks,[2,5] Laurie J. Heyer,[2,3] Laura L. Mays Hoopes,[2,6] Mary Lee Ledbetter,[2,7] Anne G. Rosenwald[2,8]

A supportive network of scientists and faculty brings sophisticated microarray experiments to the undergraduate lab and classroom.

Biological research has been transformed in recent years by substantial advances in efficient data accumulation. The transcription output for every gene in a genome now can be measured in an afternoon; before it might have taken years. However, the recent advances in technology have yet to be incorporated into many biology classrooms (*1*). Most undergraduates are taught the same way their instructors were taught, which seldom reflects leading-edge research practices. Training faculty in the latest research methods is not well supported on most campuses (*2*). Worse yet, when students with outdated undergraduate science experiences become primary and secondary school teachers, they condemn future generations to inadequate preparation for college. Today's teachers may also neglect the more quantitative aspects and increased interdisciplinary involvement of modern biology (*3–5*). Educational options that reflect quantitative, interdisciplinary, and technological trends would provide students with experiences that mirror today's scholarship.

We have developed the Genome Consortium for Active Teaching (GCAT) (*6*) to engage undergraduates in genomics experimental design and data analysis. GCAT faculty use DNA microarrays to bring the excitement of interdisciplinary research to students. Students discover the importance of quantitative data analysis, and the faculty are reinvigorated by the opportunity to learn new technology.

GCAT in the lab. Undergraduates prepare samples and scan microarrays as part of their research at Davidson College.

[1]Department of Biology, [2]Genome Consortium for Active Teaching, [3]Department of Mathematics, Davidson

Origins of GCAT

GCAT was formed in 1999 with the intent of bringing genomics into undergraduate curricula, primarily through student research (*7, 8*). Leading scientists donated materials and equipment. Undergraduates designed and performed experiments (see photograph above), mailed their microarrays for scanning, and then downloaded and analyzed their data (*9*).

Two limiting factors, long-term scanner access and a growing appetite for microarrays, were addressed by grant support and further donations from scientists (*10–12*). GCAT thus grew in size and expertise. GCAT supports free access to information and results through its Web site (*6*) and a listserv of more than 200 subscribers.

GCAT projects replaced student laboratory methods less prevalent in today's research, such as cloning and sequencing a gene and Northern blotting.

Rapid Growth

GCAT is committed to enabling any institution to adopt the use of microarrays in its undergraduate curriculum at affordable prices. To date, about 5000 undergraduates from 120 schools have used about 3400 microarrays. For the 2005–2006 academic year, GCAT provided more than 750 microarrays of nine plant, animal, and microbial species to students on 64 different campuses (*6, 9*). Tested protocols and teaching aids are available from GCAT. Continued grant support (*11*) covers the cost of microarrays.

Schools pay a nominal fee to GCAT for microarrays and scanning. Students produce and hybridize their own probes. Other than the scanners, only standard molecular biology equipment is required; the software is free. The summer workshop costs, which are currently covered by grant support, are about $2300 per participant.

The number of interested faculty continues to grow. Although this enthusiasm is more a measure of the importance of the microarray method in molecular biology today than of GCAT itself, it also serves as a testament to GCAT's user-friendly format.

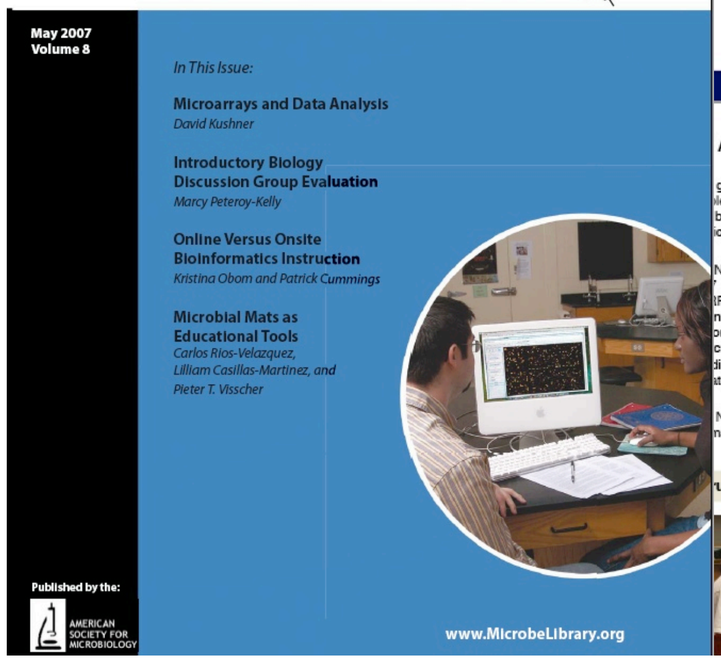
GCAT faculty use the microarrays in various ways. Some analyze existing data sets, such as the yeast diauxic shift data (*13*) that shows how yeast switch from one metabolic route to another. Other faculty members offer courses in which students collect their own microarray data. Students have studied the effects of environmental conditions on growth, aging in yeast, chromatin structure, and the cellular side effects of chemotherapy (*6*). Microarrays offer a view of the connections between different pathways in a cell in ways that are hidden by many other methods. For example, one student project looked for expression changes in DNA replication mutants and found cell wall assembly changes, thus linking cytokinesis to mitosis.

Dissemination Through Faculty Development

GCAT has sponsored data generation (wet lab) and data analysis (dry lab) workshops in various settings (*14*). Wet and dry lab sessions work best when they run 2 and 3 days, respectively. Participants learn data analysis using MAGIC Tool freeware (*15*). MAGIC Tool works on any computer platform and is designed to enhance student understanding of

GCAT: Genome Conso
for Active Tea

JMBE
Journal of Microbiology & Biology Education



NSF Current
Monthly Highlights of Research and Education Sponsored by the National Science Foundation

In This Issue: Latest Plant Genome Awards • Teachers Jockey Genes
RNA Plays Novel Role • New Nanotechnology Centers • NSF's 2005 Facility Plan

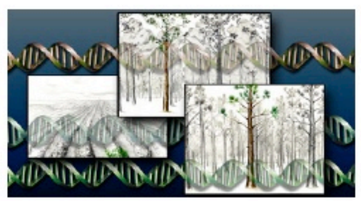
October 2005

Awards 19 New Plant Genome Research Projects

genomes of economically important plants are often large and lex, but through in-depth studies scientists uncover information that be translated into new and improved agricultural products and ices.

National Science Foundation (NSF) made 19 new awards totaling million in the eighth year of its Plant Genome Research Program P). The two- to five- year awards, ranging from $622,000 to $7.7 n, fund research and tools to reveal information in the genomes of omically important crop plants, such as wheat and soybean, as well as crease understanding of the genetics underlying plant processes ding disease resistance, flavor development, seed growth and wood ation.

NSF's press release and the list of 2005 PGRP awards for more nation.



NSF made 19 new awards in the eighth year of its Plant Genome Research Program. The awards will support genomics research in major crop plants such as soybean and also in trees including the loblolly pine and poplar. Credit: N. Rager Fuller, NSF.

ructors from Minority-Serving Institutions Learn to Teach Microarray Technology

Microarray technology, one of the hottest techniques in biological research, simultaneously measures the expression levels of tens of thousands of genes. Performing DNA microarray experiments and analyzing the mounds of resulting data are generally thought to be beyond the reach of all but a small number of undergraduates working in top research labs. However, the Genome Consortium for Active Teaching (GCAT), composed of faculty from over 120 primarily undergraduate institutions, has allowed over 4,000 undergraduates to conduct research using DNA microarrays.

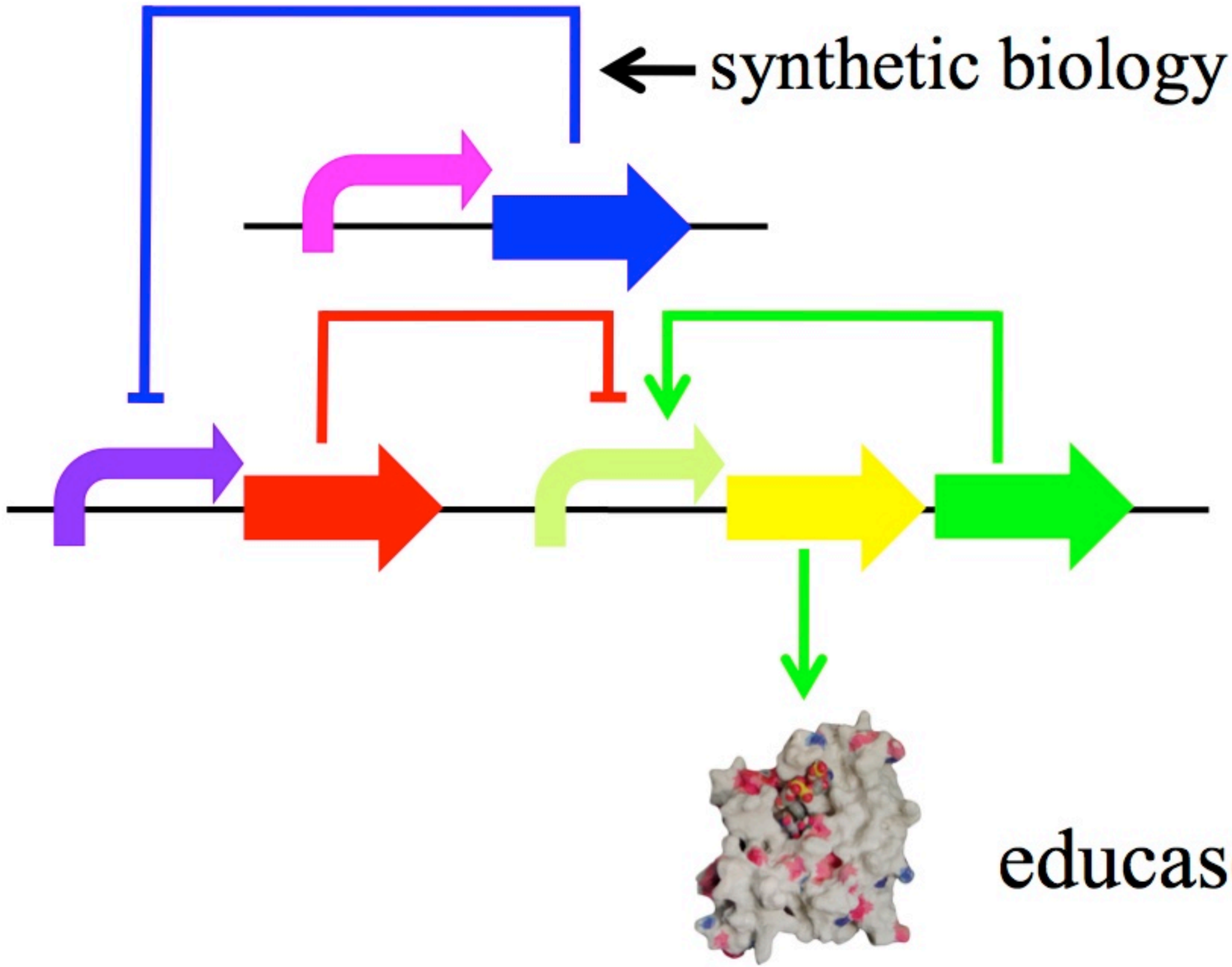
Research grants funded

Published basic research

Published pedagogy

Teaching awards

GCAT SynBio

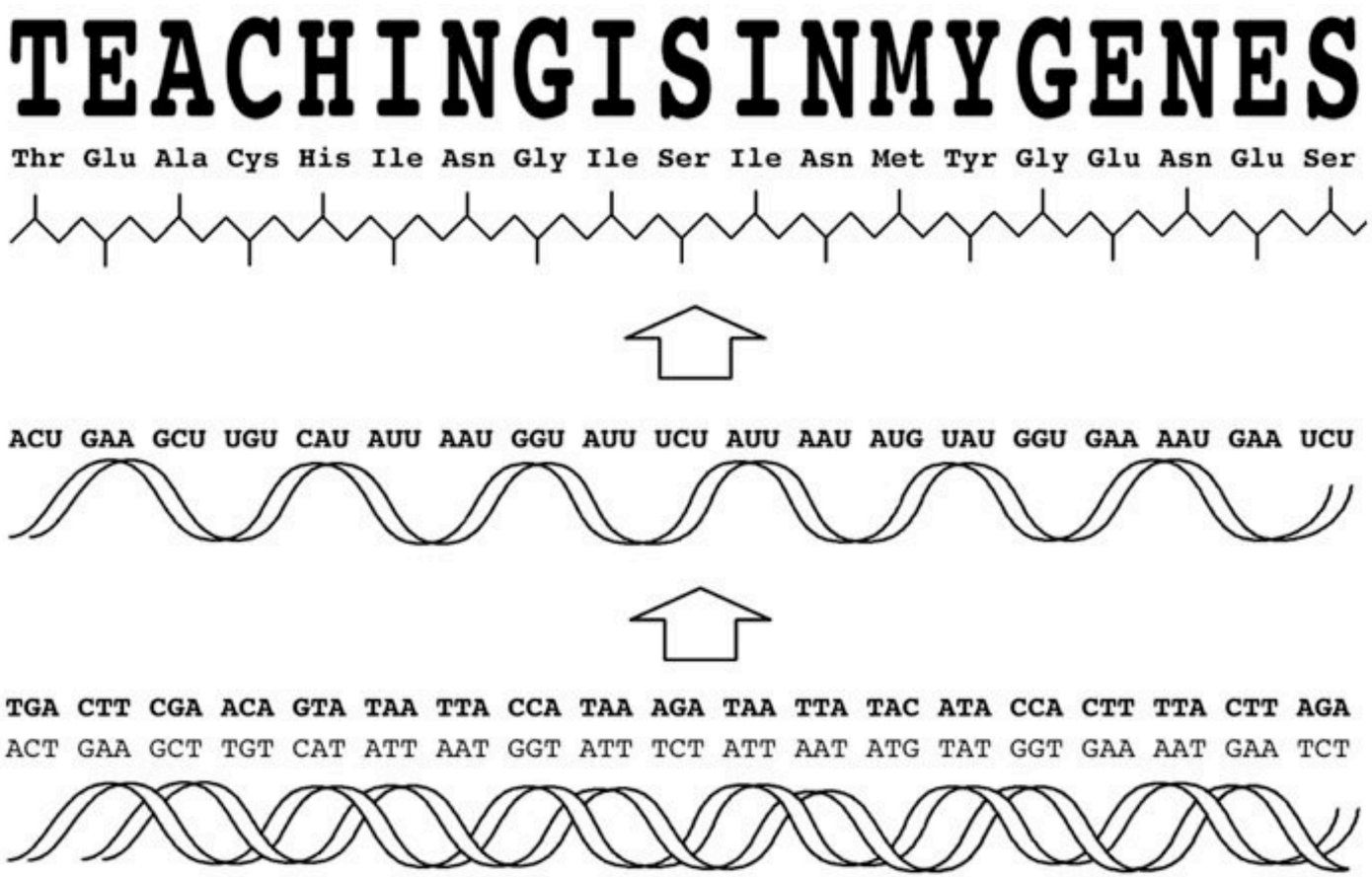


GCAT SynBio Faculty Workshops

15 pairs of faculty

1 Bio + 1 Other

June 24 - 27, 2014



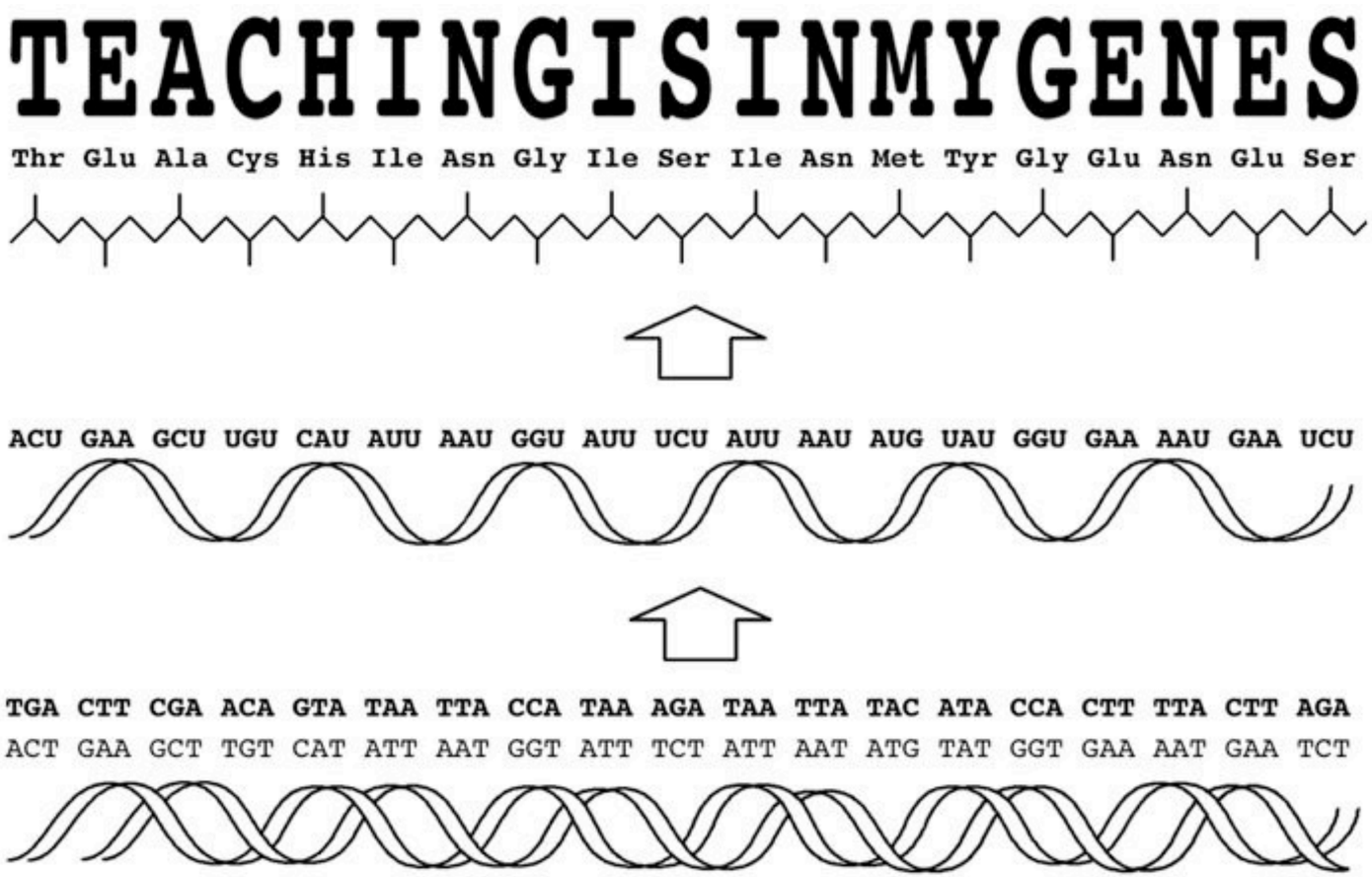
NATIONAL SCIENCE FOUNDATION

HHMI HOWARD HUGHES MEDICAL INSTITUTE

GCAT SynBio Faculty Workshops

30 faculty X 5 years X 100 students each

45,000 undergraduates over 5 years



The scenery only changes for the lead dog.

The scenery only changes for the lead dog.

What will you do for *your* Majors?

Acknowledgements

Faculty: Laurie Heyer, Jeff Poet, Todd Eckdahl, Karmella Haynes, Pat Sellers, Mark Barsoum

Students: Romina Clemente, Clif Davis, A.J. Grant, Mary Gearing, Kin Lau, Olivia Ho-Shing, Shamita Punjabi, Eric Sawyer, Ashley Schooner, Siya Sun, Shashank Suresh, Bryce Szczepanik, Leland Taylor, Annie Temmink, Alyndria Thompson, Will Vernon, Oyinade Adefuye, Will DeLoache, Jim Dickson, Andrew Martens, Amber Shoecraft, Mike Waters, Jordan Baumgardner, Tom Crowley, Lane Heard, Nick Morton, Michelle Ritter, Karen Acker, Bruce Henschen, Jessica Treece, Matt Unzicker, Amanda Valencia, Lance Harden, Sabriya Rosemond, Samantha Simpson, Erin Zwack, Marian Broderick, Adam Brown, Trevor Butner, Lane Heard, Eric Jessen, Kelley Malloy, Brad Ogden, Kelly Davis, Alicia Allen, James Barron, Robert Cool, Kelly Davis, Will DeLoache, Erin Feeney, Andrew Gordon, John Igo, Aaron Lewis, Kristi Muscalino, Madeline Parra, Pallavi Penumetcha, Karlesha Roland, Max Win, Xiao Zhu, Kristen DeCelle, Matt Gemberling, Oscar Hernandez, Andrew Drysdale, Nick Cain, Tamar Odel, and Jackie Ryan.

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