Improving Biology Learning Outcomes in Courses and Research

A. Malcolm Campbell
Davidson College

April 21, 2016
Outline for Talk

Synthetic Biology Research Topics

Introductory Biology SynBio Lab Research

Introductory Biology Overhaul

Learning Outcomes
Basic Research with Undergraduates: making bacterial computers
Burnt Pancake Problem
How to Make Flippable DNA Pancakes

DNA Burnt Pancakes

abstractions of DNA parts
Outstanding Publication of 2008
in the
Journal of Biological Engineering

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

"Engineering bacteria to solve the Burnt Pancake Problem"


12 undergraduate coauthors
Hamiltonian Path Problem
Hamiltonian Path Solution

Graph:
- Node 1
- Node 2
- Node 3
- Node 4
- Node 5

Edge Directions:
- From Node 1 to Node 3
- From Node 3 to Node 2
- From Node 2 to Node 3
- From Node 3 to Node 1
- From Node 4 to Node 5
- From Node 5 to Node 4
- From Node 1 to Node 2
- From Node 2 to Node 1
- From Node 1 to Node 4
- From Node 4 to Node 1
Split Genes to Encode Problem

[Diagram showing a gene with an RBS, promoter, and reporter]

[Diagram showing a gene with an RBS, promoter, reporter, and hixC]

gcat.davidson.edu/GcatWiki/index.php/Davidson_Missouri_W/Davidson_Protocols
Engineering Biological HPP

Hin-mediated recombination
Bacteria Report Solutions

Unflipped

Flipped

Yellow colonies indicate solution found
Paper Published 7/09

Paper of the year, 2009

1. 32729 Accesses

Solving a Hamiltonian Path Problem with a bacterial computer
Abstract | Full text | PDF | PubMed | F1000 Biology | Editor’s summary

15 undergraduate coauthors
Improving the Lac system for synthetic biology

Pallavi Penumetcha¹, Kin Lau¹, Xiao Zhu², Kelly Davis¹, Todd T. Eckdahl²,³, A. Malcolm Campbell¹,³

[Bar chart showing normalized fluorescence levels with and without IPTG for various conditions.]
Improving the Lac system for synthetic biology

Pallavi Penumetcha¹, Kin Lau¹, Xiao Zhu², Kelly Davis¹, Todd T. Eckdahl²,³, A. Malcolm Campbell¹,³
Can Bacteria Perform Hash Function?
Use XOR Logic Gate for Hash Function

<table>
<thead>
<tr>
<th>Input 1</th>
<th>Input 2</th>
<th>Output</th>
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<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>0</td>
<td>1</td>
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<td>1</td>
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<tr>
<td>1</td>
<td>1</td>
<td>0</td>
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</table>

![XOR Gate Diagram](image-url)
DNA XOR Logic Gate

![Diagram of DNA XOR Logic Gate](image)

<table>
<thead>
<tr>
<th>High Osmolarity (Input A)</th>
<th>3OC6 (Input B)</th>
<th>Fluorescence (Output)</th>
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<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>1 (GFP)</td>
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<tr>
<td>0</td>
<td>1</td>
<td>1 (RFP)</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>0</td>
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</table>
pLux + LuxR Promotes Backwards

Relative Fluorescence

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<tr>
<th></th>
<th>LuxR</th>
<th>3OC6</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
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\(^1,8\),*
Word selection affects perceptions of synthetic biology

Brianna Pearson, Sam Snell, Kyri Bye-Nagel, Scott Tonidandel, Laurie J Heyer and A Malcolm Campbell

Received: 4 July 2011 | Accepted: 21 July 2011 | Published: 21 July 2011

3 students, 3 majors
Bacterial Logic Devices Reveal Unexpected Behavior of Frameshift Suppressor tRNAs

Eric M. Sawyer¹,², Cody Barta², Romina Clemente¹, Michel Conn², Clif Davis², Catherine Doyle¹, Mary Gearing¹, Olivia Ho-Shing¹, Alyndia Mooney¹,³, Jerrad Morton², Shamita Punjabi¹, Ashley Schnoor⁴, Siya Sun⁴, Shashank Suresh⁵, Bryce Szczepaniak², D. Leland Taylor¹, Annie Temmink⁵, William Vernon², A. Malcolm Campbell¹, Laurie J. Heyer⁵, Jeffrey L. Poet⁴ and Todd Eckdahl²,*
Programmed Evolution for Optimization of Orthogonal Metabolic Output in Bacteria

Todd T. Eckdahl¹*, A. Malcolm Campbell², Laurie J. Heyer³, Jeffrey L. Poet⁴, David N. Blauch⁵, Nicole L. Snyder⁵, Dustin T. Atchley², Erich J. Baker², Micah Brown³, Elizabeth C. Brunner², Sean A. Callen⁴, Jesse S. Campbell¹, Caleb J. Carr¹, David R. Carr¹, Spencer A. Chadinha², Grace I. Chester⁴, Josh Chester⁴, Ben R. Clarkson², Kelly E. Cochran¹, Shannon E. Doherty², Catherine Doyle², Sarah Dwyer², Linnea M. Edlin⁴, Rebecca A. Evans², Taylor Fluharty⁴, Janna Frederick⁴, Jonah Galeota-Sprung³, Betsy L. Gammon², Brandon Grieshaber¹, Jessica Gronniger², Katelyn Gutteridge⁴, Joel Henningsen⁴, Bradley Isom⁴, Hannah L. Itell², Erica C. Keffeler¹, Andrew J. Lantz³, Jonathan N. Lim², Erin P. McGuire², Alexander K. Moore⁴, Jerrad Morton¹, Meredith Nakano², Sara A. Pearson¹, Virginia Perkins⁴, Phoebe Parrish², Claire E. Pierson¹, Sachith Polpityaarachchige¹, Michael J. Quaney¹, Abagael Slattery², Kathryn E. Smith², Jackson Spell³, Morgan Spencer³, Telavive Taye², Kamay Trueblood¹, Caroline J. Vrana², E. Tucker Whitesides³
### Bacteria as Analog Computers

<table>
<thead>
<tr>
<th>Promoter-RBS</th>
<th>Origin</th>
<th>Chaperone</th>
<th>Theophylline Production</th>
<th>Relative Fitness</th>
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<tr>
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<td>Low Copy</td>
<td>No Chaperone</td>
<td>0.44</td>
<td>1.00</td>
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<tr>
<td>High-High</td>
<td>Low Copy</td>
<td>pTf16</td>
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<td>0.49</td>
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<td>Low-Low</td>
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<tr>
<td>Low-Low</td>
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<td>pG-Tf2</td>
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<td>0.00</td>
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</table>
riboswitch on mRNA

aptamer

start codon

mRNA adhE

RBS
riboswitch on mRNA

aptamer

RBS

mRNA adhE

start codon
Can we bring real research into Introductory Biology?

Todd Eckdahl, MWSU
pClone: Synthetic Biology Tool Makes Promoter Research Accessible to Beginning Biology Students

A. Malcolm Campbell,* Todd Eckdahl,† Brian Cronk,‡ Corinne Andresen,† Paul Frederick,† Samantha Huckuntod,† Claire Shinneman,† Annie Wacker,* and Jason Yuan†

4 undergrads
2 HS students

pClone Red

J119137

pClone Red

all colonies green
Golden Gate Assembly Method

**Bsa I + ligase**

- GFP
- RBS
- RBS
- RFP

**Enzyme Digestion Sites:**
- Bsa I

**Diagram:**
- Linear DNA structure with arrow indicating direction of transcription.
- Enzyme digestion sites marked with Bsa I.
- Ligase indicated at the junction of GFP and RFP segments.
GGA Cloning Always Works

![Diagram showing gene expression with RBS (Ribosome Binding Site), GFP (Green Fluorescent Protein), and RFP (Red Fluorescent Protein).]
Remove Initial Promoter

J119137
Insert Bi-directional Promoter

J119137
Insert Non-functional Promoter

J119137
First Years in 3 Hour Lab: GGA

no gel purifications!

Diagram showing gene expression with GFP, RBS, and RFP.
pClone Red

![Diagram of pClone Red with gene expression elements such as GFP, RBS, and RFP, along with BsAl restriction sites. The diagram includes images of petri dishes showing green and red fluorescence.]
Student Sample, November 2012

-35 ATAA (deleted) -10

5’ CGACGAGCTGTGTTGACA----ATCATCGGCTCGTATAATGTGTGGA 3’
3’ CTCGACAACTGT----TAGTAGCCGAGCATATTACACCTCGCC 5’

11-7-12
Quantify with Phone and ImageJ

<table>
<thead>
<tr>
<th>Mutant</th>
<th>J119319</th>
<th>J119320</th>
<th>J119321</th>
<th>J119322</th>
<th>J119323</th>
<th>J119324</th>
<th>J119325</th>
<th>J119326</th>
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<tr>
<td>pClone Green plate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Isolated clones</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Expression Ratio</td>
<td>4.09</td>
<td>3.94</td>
<td>3.84</td>
<td>2.04</td>
<td>1.54</td>
<td>1.34</td>
<td>3.52</td>
<td>1.00</td>
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</tbody>
</table>
pClone: Exploring Promoters with Synthetic Biology

Give your students the opportunity to learn and explore transcription regulation right in your classroom. This unique approach to synthetic biology was developed by college professors focused on creating a unique activity to demonstrate gene regulation. This multi-part lab will expose students to cloning, restriction enzymes, transformation, microbiology, and so much more in an effective classroom protocol.

Selected items Compare Add to Cart Add to List

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
<th>Price</th>
<th>Quantity</th>
<th>Available</th>
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<tr>
<td>Item #211150</td>
<td>pClone: Exploring Promoters with Synthetic Biology Kit (with prepaid coupon)</td>
<td>$215.00</td>
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<td>Available 5/4/16</td>
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<td>Available 5/4/16</td>
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</table>
pClone Blue

Diagram A:
- GFP
- RBS
- CGAC
- Bsal
- GCGG
- RBS
- Blue

Diagram B:
- pClone Blue
  - Only
- pClone Blue
  - +
- pClone Blue
  - +

Images show different conditions and results for pClone Blue.
Measure Promoter Qualitatively

A

0% Blue  40% Blue  70% Blue  90% Blue  100% Blue
rClone Red (ribosome research)

J119384
rClone Red (ribosome research)

J119384

12 - 60 bp

RBS

Bsa I

RFP
rClone Red (student-designed RBS)
rClone Red (RBS library)
tClone Red (terminator research)

J119361
tClone Red (terminator research)

J119361

60 - 230 bp

Bsa I

RBS

RFP

tClone Red (terminator research)
tClone Red (terminator research)

J119361

60 - 230 bp (optional ligand)

Bsa I

RBS RFP

OR (+ ♦)
tClone Red (student-designed terminators)
tClone Red (student-designed terminators)
repClone Red

J100205
repClone Red

J100205

Ptet

54 bp

Bsa I

TetR

RBS

RFP
repClone Red
J100205
repClone Red

J100205
actClone Red

J100204

GFP → RBS → TT → RBS → RFP

Bsa I

3’ PompR
actClone Red

J100204

5' PompR

C1  C2  C3

60 bp

Bsa I

GFP  RBS

3' PompR

OmpC

RFP
actClone Red

J100204

all of *PompR*
How can we better prepare our undergrads for research?
National Recognition of Need to Change

VISION AND CHANGE
A CALL TO ACTION

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

NSF

Science

AAAS
GRE General Test

**Verbal Reasoning:** measures your ability to understand what you read and how you apply your reasoning skills.

**Quantitative Reasoning:** measures your ability to
- understand quantitative information
- interpret and analyze quantitative information
- solve problems using mathematical models
- apply basic mathematical skills and elementary mathematical concepts of arithmetic, algebra, geometry and data interpretation
- includes real-life scenarios

**Analytical Writing:** provide focused responses to prompts so you can demonstrate your ability to directly respond.
Critical Analysis and Reasoning Skills: analyze, evaluate, and apply information provided in passages

Natural Sciences: combine knowledge of natural science concepts with their scientific inquiry and reasoning skills to solve problems that demonstrate their readiness for medical school.

Psychological, Social, and Biological Foundations of Behavior
full disclosure

*ICB* is a commercial product

www.bio.davidson.edu/icb
Core Concepts = Big Ideas

Vision & Change
Evolution

Structure and Function
Information

Energy and Matter
Systems Biology

ICB
Evolution
Cells
Information
Homeostasis
Emergent Properties

AP Biology
Evolution
Information
Homeostasis
Emergent Properties
V&C Core Competencies

- Apply the process of science
- Use quantitative reasoning
- Use modeling and simulations
- Integrate different disciplines
- Communicate & collaborate
- Connect science & society
V&C Core Competencies (ICB)

- Apply the process of science (experimental design)
- Use quantitative reasoning (interpret raw data)
- Use modeling and simulations (work with models)
- Integrate different disciplines (chemistry, math, some physics)
- Communicate & collaborate (small group discussions, lab)
- Connect science & society (ELSI boxes)
What’s Wrong with Biology Education Now?

- Vocabulary is over-emphasized (800-1000 vs 1400)
- Experimental approaches are minimized
- Math is rarely used
- Memorization is rewarded
- Critical thinking is discouraged
- Information is irrelevant to students
Present information and data...
... in the context of the big picture.
Start with the literature...
Artificial Divide within Biology

Small Biology

Big Biology
Five Levels of Organization:

- Molecular
- Cellular
- Organismal
- Population
- Ecological System
Five by Five Matrix of Biology

- Information
- Emergent properties
- Homeostasis
- Evolution
- Cells

Cellular
Organismal
Population
Ecological System
Molecular
BioMath Exploration 4.2 (BME)

How fast is the vesicle size changing?
Ethical, Legal and Social Implications (ELSI)

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 *ICB* students “learn less” content?
Core Concepts Assessment

- **ICB**
- **traditional**

**percent correct**

- **Fall 2010**
  - 63% response rate (traditional)
  - 83% response rate (ICB)
  - \( p = 0.06 \)
  - \( p = 0.97 \)

\(+/-\) SEM
Core Concepts Assessment

- ICB: 83% response rate (new)
- Traditional: 63% response rate (traditional)

$p = 0.97$ (Fall 2010)
$p = 0.06$ (Spring 2011)

+/- SEM
Do *ICB* students analyze data better?
Core Competency Assessment

% Correct

<table>
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<tr>
<th>Method</th>
<th>% Correct</th>
</tr>
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<tbody>
<tr>
<td>Traditional</td>
<td>62</td>
</tr>
<tr>
<td>ICB</td>
<td>66</td>
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</table>

$p = 0.043$
Core Competency Assessment

- Traditional (quiz averages)
- New (quiz averages)

Percent Correct

Quiz

- First
- Second
- Third
- Fourth

new, $p = 0.015$

traditional, $p = 0.320$
Do *ICB* students see biology differently?

<table>
<thead>
<tr>
<th>1-5 scale</th>
<th>Average at Start Fall</th>
</tr>
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<tbody>
<tr>
<td>5 = extremely accurate</td>
<td>ICB</td>
</tr>
<tr>
<td>biology is definitions &amp; processes</td>
<td>2.86</td>
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<td>big questions of biology already answered</td>
<td>1.71</td>
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<tr>
<td>big/small division of biology describes nature</td>
<td>3.15</td>
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</tbody>
</table>

| 1-5 scale | Average at Start Fall |
| 5 = extremely important | ICB | Traditional |
| memorization | 3.96 | 3.64 |

* p<0.05, ** p<0.01, *** p<0.001, ^ p = 0.06

no
Do *ICB* students see biology differently?

<table>
<thead>
<tr>
<th>1-5 scale 5 = extremely accurate</th>
<th>Average at Start Fall</th>
<th>Δ in Average End of Fall</th>
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<tr>
<td></td>
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<tr>
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<td>memorization</td>
<td>3.96</td>
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</table>

* p<0.05, ** p<0.01, *** p<0.001, ^ p= 0.06
## Do ICB students see biology differently?

<table>
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<th>1-5 scale</th>
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<th>Δ in Average</th>
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<td>biology is definitions &amp; processes</td>
<td>2.86</td>
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<td>big questions of biology already answered</td>
<td>1.71</td>
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<td>3.15</td>
<td>3.02</td>
<td>-1.08***</td>
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</table>

* p<0.05, ** p<0.01, *** p<0.001, ^ p= 0.06

**yes!**
Do *ICB* students do poorly in upper level?
Intro Grades Correlated to Upper Grades

111 (other instructors) vs. 113 (AMC)
Intro Grades Correlated to Upper Grades

112 (other instructors) vs. 114 (CP)

mean upper level grade

introductory course grade
Does *ICB* chase away majors?
Compare *ICB* Yield for Majors

![Graph comparing ICB Yield for Majors](graph.png)

- **Campbell**
- **Paradise**
- **non-DIBS average**

% retention (conversion to biology majors)

ICB yield
Do students like *ICB* approach?
Self-assessed Engagement Each class

- $p < 0.001$
- $t_{26} = 4.17$

Proportion of responses vs. self-assessed engagement (1 = low, 9 = high)
Evaluate eBook Pre- and Post-semester

- Pre-term
- Post-term

$p = 0.000$

T-test
Our students accomplish Vision & Change Goals
Acknowledgements

**Synthetic Biology Research**
Laurie Heyer, Jeff Poet, Todd Eckdahl + undergrads!

**xClone Plasmids**
Todd Eckdahl + HS and undergrads!

**ICB textbook and Research**
Laurie Heyer, Chris Paradise, Kevin Smith, Pat Sellars, Mark Barsoum, Caylyn Harvey, Kyosung Koo, Kristen Eshelman,
What affect does Echo360 have?
Students Liked Echo360

Rating (0 = very unhelpful, 10 = very helpful)

Frequency (both courses F2015)
Lower Test Grade, Use Echo360 More

\[ y = -0.437x + 52.041 \]
\[ R^2 = 0.20826 \]
\[ F_{1,20} = 5.26, p = 0.03 \]
Great Impact on Student Grades

Exam Average (n = 4)

F2012
F2013
F2014

Students (sorted by grade)
pClone Red

GFP  RBS  RBS  RFP

Bsa I  Bsa I
The image contains a diagram with genetic sequences and labels. The sequences are represented in a specific pattern, and there are annotations indicating "ligase" at the bottom of the diagram.