10-14-2015

Research-driven facilitation of systems thinking with computational models in life sciences education

Heather E. Bergan-Roller  
University of Nebraska-Lincoln, heather.bergan@unl.edu

Nicholas Galt  
University of Nebraska-Lincoln, ngalt2@unl.edu

Tomáš Helikar  
University of Nebraska-Lincoln, thelikar2@unl.edu

Joseph T. Dauer  
University of Nebraska-Lincoln, joseph.dauer@unl.edu

Follow this and additional works at: http://digitalcommons.unl.edu/dberspeakers  
Part of the Science and Mathematics Education Commons

Bergan-Roller, Heather E.; Galt, Nicholas; Helikar, Tomáš; and Dauer, Joseph T., "Research-driven facilitation of systems thinking with computational models in life sciences education" (2015). DBER Speaker Series. 79.  
http://digitalcommons.unl.edu/dberspeakers/79

This Article is brought to you for free and open access by the Discipline-Based Education Research Group at DigitalCommons@University of Nebraska - Lincoln. It has been accepted for inclusion in DBER Speaker Series by an authorized administrator of DigitalCommons@University of Nebraska - Lincoln.
Abstract for DBER Group Discussion on 2015-10-15

Authors and Affiliations:
Heather E. Bergan-Roller¹, Nicholas Galt², Tomáš Helíkar², Joseph T. Dauer¹
¹School of Natural Resources, University of Nebraska-Lincoln
²Department of Biochemistry, University of Nebraska-Lincoln

Title
Research-driven facilitation of systems thinking with computational models in life sciences education

Abstract
Systems thinking, computational modeling, and simulating systems are examples of important skills stressed in life sciences education by Vision and Change. In response to these calls, we have designed a computational modeling and simulation-driven intervention to supplement current instruction in the life sciences curriculum. As part of our pre-intervention assessment we evaluated students on their systems thinking in the context of cellular respiration. For this assessment, we had students create conceptual models. We found that students with lecture instruction are able to recall more components associated with the cellular respiration process but are not better able to integrate these components into the system compared to students without lecture instruction. As a result, we have designed computational interventions to facilitate learning about complex biological processes. In these activities, we have students make and test predictions and apply simulation results to cellular mechanisms. We then assess student thinking to examine if the computational intervention improves systems thinking and modeling skills. Our preliminary data suggest that this intervention increases students’ mechanistic reasoning abilities. Currently, we are deploying computational activities and assessing students thinking on the topics of cellular respiration and gene regulation in all LIFE 120 laboratories. Finally, we are in the process of developing new computational activities to be used as learning tools for additional topics on complex biological systems.
Research-driven facilitation of systems thinking with computational models in life sciences education

Heather E. Bergan-Roller¹, Nicholas J. Galt²,

¹School of Natural Resources, University of Nebraska-Lincoln
²Department of Biochemistry, University of Nebraska-Lincoln
delete slide
Heather Bergan,

whatever terminology we use, we need to be consistent and are jargon-less as possible so the audience can easily follow
Heather Bergan,

Do you want me to talk here?
Heather Bergan,

are we cutting this slide? if so, can you move it to the end section?
Heather Bergan,

what does this mean? I don’t think we need to spend a lot of time talking about the new versus old user interface
Heather Bergan,

I vote we skip this and jump right into our CMI. I think I have set it up well for this.
Heather Bergan,

maybe move this to the beginning of your section (around slide 13) because my "baseline" results are in the context of cellular respiration, and then we switch to Gene regulation abruptly.
Heather Bergan,
Thank you!

STEM education seminar organizers
LIFE instructors, lab coordinators, TAs
Steve Harris

Helikar Group
Tomáš Helikar
David Tichy
Bryan Kowal
Bhargav Gorthi
Audrey Crowther

Dauer Group
Joe Dauer
Sinan Akkoseoglu
Jai Kumar Mediratta
McKenzie Kjose
Jacob Winters

National Science Foundation IUSE #1432001
Our world is complex
Core Concepts

- Systems
- Structure and function
- Information flow, exchange, storage
- Evolution
- Pathways and transformation of energy and matter

Core Competencies

- Modeling, simulations, computational, and systems-level approaches to discovery and analysis
- Process of science
- Quantitative reasoning
- Interdisciplinary communication and collaboration
- Science and Society

AAAS, 2011
Modeling and Learning

1. Externalize mental models
2. Decrease cognitive load
3. Address explicit interactions/mechanisms
4. Facilitate metacognition
5. Facilitate instructor feedback
6. Facilitate assessment of thinking
Computational model learning activities for improved systems thinking

Outline

1. Systems thinking in our students (baseline)
2. Computational model learning activities
3. Feedback from you!
What is the state of systems thinking in our introductory biology students?
Systems thinking hierarchy framework

Assaraf and Orion, 2010
Conceptual models to assess thinking

(Jordan et al., 2013; Dauer et al., 2013; Vattam et al., 2011; Ifenthaler, 2010; Hmelo, Holton, Kolodner, 2000)
Baseline Timeline

Days of lecture instruction groups: 0, 1, 2

- Wet Laboratory
- Conceptual Modeling

Week 1: Lecture (L)
Week 2: Lecture (L)
Week 3: Lecture (L)
Week 4: Lecture (E)
Week 5: Lecture (E)

n = 83
0: n = 30
1: n = 32
2: n = 21
Baseline Results

**Structures**

![Chart showing the increase in structures over days of lecture instruction]

- Days of Lecture Instruction: 0, 1, 2
- Values: a, b, ab

**Relationships**

![Chart showing the relationship values over days of lecture instruction]

- Days of Lecture Instruction: 0, 1, 2
- Values: n = 30, n = 32, n = 21
Baseline Results

Connectivity —

Days of Lecture Instruction

Correctness —

Days of Lecture Instruction

n = 30
n = 32
n = 21

n = 29
n = 20
n = 14
Baseline Conclusions

Instruction increases the number of structures

Instruction does not affect relationships, connectivity, or correctness

Assaraf and Orion, 2010
Computational Model Learning Activities

**Goals**
- Assess spectrum of systems thinking skills
- Provide systems thinking practice
- Improve systems thinking
- Address student misconceptions
Why computational modeling?

- Manage content knowledge
- Create, simulate and perturb complex biological systems
- Observe the dynamic behavior of systems
Why computational modeling?

- Manage content knowledge
- Create, simulate and perturb complex biological systems
- Observe the dynamic behavior of systems
- Promote systems thinking

Assaraf and Orion, 2010
Why computational modeling?

- Manage content knowledge
- Create, simulate and perturb complex biological systems
- Observe the dynamic behavior of systems
- Promote systems thinking
- Less memorizing = more fun

Assaraf and Orion, 2010
Computational Modeling Platform: Cell Collective

- Web-based (thecellcollective.org)
- Accessible and easy to use
- No entering/modifying mathematical expressions or computer code
Computational Model Learning Activities
Computational Model Learning Activities

Topic Selection
• What is needed?
Computational Model Learning Activities

**Topic Selection**
- What is needed?

**Literature**
- What does the literature recommend?
- What do experts value?
Computational Model Learning Activities

**Topic Selection**
- What is needed?

**Literature**
- What does the literature recommend?
- What do experts value?

**Learning Objectives**
Computational Model Learning Activities

Design
a. Background Information
b. Introduction to Computational Model
c. Simulation Setup
d. Investigations
Computational Model Learning Activities

Design
a. Background Information
b. Introduction to Computational Model
c. Simulation Setup
d. Investigations

Example using the tryptophan Operon
Computational Model Learning Activities Design

Part 1: Background Information

Gene Expression and Regulation in Prokaryotes
Nicholas Gaul, Heather Berges-Rochi, Joseph Daugh, and Tamal Hafker
University of Nebraska-Omaha

The Trp Operon
The trp operon is a cluster of genes that function together to produce the amino acid tryptophan. It is one of the most well-studied examples of gene regulation in response to changes in both the external and internal environments. When bacteria obtain tryptophan by synthesizing a tryptophanase that converts the amino acid into an amino acid, the enzymes for the tryptophanase are produced. However, when the bacteria are grown in a nutrient-enriched environment, the tryptophanase is not produced. To do this, the genes of the operon must be repressed.

The regulatory region of the operon consists of the promoter and the operator. The promoter is a region of DNA that is transcribed into messenger RNA (mRNA). The operator is a region of DNA that is not transcribed into mRNA. The mRNA is then translated into individual amino acids.

When the operon is turned on, the genes within the operon are transcribed by RNA polymerase into messenger RNA. When the operon is turned off, the genes within the operon are not transcribed. The mRNA is then translated into individual amino acids.

The Trp Operon
The trp operon is a cluster of genes that function together to produce the amino acid tryptophan. It is one of the most well-studied examples of gene regulation in response to changes in both the external and internal environments. When bacteria obtain tryptophan by synthesizing a tryptophanase that converts the amino acid into an amino acid, the enzymes for the tryptophanase are produced. However, when the bacteria are grown in a nutrient-enriched environment, the tryptophanase is not produced. To do this, the genes of the operon must be repressed.

The regulatory region of the operon consists of the promoter and the operator. The promoter is a region of DNA that is transcribed into messenger RNA (mRNA). The operator is a region of DNA that is not transcribed into mRNA. The mRNA is then translated into individual amino acids.

When the operon is turned on, the genes within the operon are transcribed by RNA polymerase into messenger RNA. When the operon is turned off, the genes within the operon are not transcribed. The mRNA is then translated into individual amino acids.

The Trp Operon
The trp operon is a cluster of genes that function together to produce the amino acid tryptophan. It is one of the most well-studied examples of gene regulation in response to changes in both the external and internal environments. When bacteria obtain tryptophan by synthesizing a tryptophanase that converts the amino acid into an amino acid, the enzymes for the tryptophanase are produced. However, when the bacteria are grown in a nutrient-enriched environment, the tryptophanase is not produced. To do this, the genes of the operon must be repressed.

The regulatory region of the operon consists of the promoter and the operator. The promoter is a region of DNA that is transcribed into messenger RNA (mRNA). The operator is a region of DNA that is not transcribed into mRNA. The mRNA is then translated into individual amino acids.

When the operon is turned on, the genes within the operon are transcribed by RNA polymerase into messenger RNA. When the operon is turned off, the genes within the operon are not transcribed. The mRNA is then translated into individual amino acids.

The Trp Operon
The trp operon is a cluster of genes that function together to produce the amino acid tryptophan. It is one of the most well-studied examples of gene regulation in response to changes in both the external and internal environments. When bacteria obtain tryptophan by synthesizing a tryptophanase that converts the amino acid into an amino acid, the enzymes for the tryptophanase are produced. However, when the bacteria are grown in a nutrient-enriched environment, the tryptophanase is not produced. To do this, the genes of the operon must be repressed.

The regulatory region of the operon consists of the promoter and the operator. The promoter is a region of DNA that is transcribed into messenger RNA (mRNA). The operator is a region of DNA that is not transcribed into mRNA. The mRNA is then translated into individual amino acids.

When the operon is turned on, the genes within the operon are transcribed by RNA polymerase into messenger RNA. When the operon is turned off, the genes within the operon are not transcribed. The mRNA is then translated into individual amino acids.

The Trp Operon
The trp operon is a cluster of genes that function together to produce the amino acid tryptophan. It is one of the most well-studied examples of gene regulation in response to changes in both the external and internal environments. When bacteria obtain tryptophan by synthesizing a tryptophanase that converts the amino acid into an amino acid, the enzymes for the tryptophanase are produced. However, when the bacteria are grown in a nutrient-enriched environment, the tryptophanase is not produced. To do this, the genes of the operon must be repressed.

The regulatory region of the operon consists of the promoter and the operator. The promoter is a region of DNA that is transcribed into messenger RNA (mRNA). The operator is a region of DNA that is not transcribed into mRNA. The mRNA is then translated into individual amino acids.

When the operon is turned on, the genes within the operon are transcribed by RNA polymerase into messenger RNA. When the operon is turned off, the genes within the operon are not transcribed. The mRNA is then translated into individual amino acids.
Computational Model Learning Activities Design

Part 2: Introduction to Computational Model

**Activity 1: Trp Operon**

Dynamic Simulation

In the activity, you will be using a computational model and simulation software called the Cell Collaboration to explore the regulation and expression of the trp operon. The trp operon, which is responsible for tryptophan biosynthesis, is regulated by a complex network of interactions including the trp repressor. By manipulating the values of gene expression and regulatory components, you can observe how the trp operon is activated or repressed.

---

**Table 1**

Describe/define what each interaction represents in Figure 3.

<table>
<thead>
<tr>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. RNA polymerase binds to the DNA at the trp promoter and begins to transcribe the trp operon genes into mRNA.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. The trp operon transcribes into a single mRNA.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| c. mRNA translates into 5 individual proteins which form 3 enzymes: 
  - trpE (trpD enzyme) hpr (enzyme 2) 
  - tryptophan from precursor molecules within the cell. |
| d. The three enzymes produce tryptophan from precursor molecules within the cell. |
| e. When levels are high, the tryptophan binds and activates the trp repressor |
| f. The trp repressor can change shape and bind to the trp operator when activated. The binding shuts off the trp operon when RNA polymerase is blocked. |
Computational Model Learning Activities Design

Part 3: Simulation Setup
The purpose of this section is to learn how the trp operon functions. You will be conducting simulations to verify your own predictions about the dynamic interactions between the components of the trp operon. Complete each statement thoroughly.

Consider the following scenarios:

Investigation 1:

a. Predict how the presence of tryptophan in the environment influences the expression of the genes in the trp operon. Support your prediction by describing the components involved and how they interact (mechanism).

b. Test your prediction by adjusting the “environmental tryptophan” slider to 100 (See blue box, Figure 8) (Hint: compare the activity of the trp_repressor, trp_operon, etc.). Record and describe the simulation results in the space below.

c. Do your simulation results match your prediction? (circle one) Yes No

d. Describe what your results indicate is occurring in the cell (use your results to support a mechanistic explanation).
Computational Model Learning Activities Design

Part 4: Investigations

a. Prediction
   • Support prediction by describing the components involved and how they interact (mechanism)
   • Encouraged to use diagram of the computational model
Computational Model Learning Activities Design

Part 4: Investigations

a. Prediction

a. Test Prediction and Record Results
Computational Model Learning Activities Design

Part 4: Investigations

a. Prediction

a. Test Prediction and Record Results

a. Describe what the results indicate is occurring in the cell.
   - Integrate results into a mechanistic description of the biological process
Computational Model Learning Activities
Computational Model (CM) Learning Activities

Implementation Timeline

- **Feedback Session**
  - 4 undergraduates
  - 4 teaching assistants
  - 12-3-14

- **Honor Student Session**
  - 14 undergraduates
  - 4-24-15

- **LIFE120L**
  - ~50 undergraduates
  - 2 CM learning activities
  - summer 2015

- **Honor Student Session**
  - 18 undergraduates
  - 3-6-15

- **BIOC437/837**
  - 7 undergraduates
  - 3 graduate students
  - 4-29-15

- **LIFE120L**
  - ~1000 undergraduates
  - 2 CM learning activities
  - fall 2015
Computational Model Learning Activities

Assessment and Refinement

**Systems Thinking**
- Conceptual models
- Interviews

**Mechanistic Reasoning**
- Student responses to module questions

**Quality Control**
- Student interviews
- TA interviews
- Usability testing
- Classroom observations
the formatting is really inconsistent among fonts, colors, bullets, etc.

Heather Bergan,
Evidence-based Refinement of Learning Activities

Refinement Timeline with Preliminary Data

Feedback Session
- clarify directions
- less recording of results

Honor Student Session
- include “hints”
- ask “How” not “Why” questions

Table 1. Prevalence of Mechanistic Reasoning (MR)

<table>
<thead>
<tr>
<th></th>
<th>MR</th>
<th>non-MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implicit Opportunities (94 Total)</td>
<td>1</td>
<td>93</td>
</tr>
<tr>
<td>Explicit Opportunities* (34 Total)</td>
<td>12</td>
<td>22</td>
</tr>
</tbody>
</table>
Evidence-based Refinement of Learning Activities

Refinement Timeline with Preliminary Data

Feedback Session
- clarify directions
- less recording of results

Honor Student Session
- include “hints”
- ask “How” not “Why” questions
- question clarity

| Table 1. Prevalence of Mechanistic Reasoning (MR) |
|---------------------------------|--------|--------|
| Implicit Opportunities (94 Total) | MR     | non-MR |
|                                 | 1      | 93     |
| Explicit Opportunities* (34 Total) | 12     | 22     |
Evidence-based Refinement of Learning Activities

Refinement Timeline with Preliminary Data

Feedback Session
- clarify directions
- less recording of results

12-3-14

3-6-15

6-9-15

Fall 2015

Honor Student Session
- include “hints”
- ask “How” not “Why” questions
- question clarity

12-3-14

3-6-15

6-9-15

Fall 2015

| Table 1. Prevalence of Mechanistic Reasoning (MR) |
|-----------------|-----------------|
| Implicit Opportunities (94 Total) | MR | non-MR |
| 1 | 93 |
| Explicit Opportunities* (34 Total) | 12 | 22 |

LIFE120L
- improved systems thinking?
- improved mechanistic reasoning?
- improved content knowledge?
Computational Models and Activities

**Currently Available**
- Fundamentals of Biology
- Cellular Respiration
- Positive/Negative Feedback
- Gene Regulation
- Lac/Tryptophan Operon
- Cell Communication During Cancer
- Breast Cancer Signaling Pathway
- T Cell Differentiation
- Cell Cycle
- Warburg Effect

**In Development**
- Operon Construction
- Food Web
- Population Dynamics
- Endocrine Systems
Audience Feedback

1. Questions?

1. What topics and/or concepts would you be interested in see as a computational learning module?

1. What other elements would you want to see in the activities?

1. How would you want these learning activities to be implemented in your class (e.g., in-class, homework, online courses, labs)
**Data Trp Operon**

**Figure 6: Prediction Correctness**
Comparing the frequency of correct predictions when MR was identified in student responses. (Q=question; n=13 per question; mean±SEM, *p<0.05)

**Figure 9: Mechanistic Reasoning Before and After Simulation**
Identifying the effect of the dynamic simulation on MR score. (TQ=trp operon question, LQ= lac operon question; n=20; mean±SEM, *p<0.05)
Enable learning about complex biological systems through computational modeling and simulations.
- E.g., by building, simulating, breaking, and re-simulating computer models of biological systems.

Increase systems and dynamical level thinking when learning about biological systems.

Our goals:
- address misconceptions (evidence based)
- improve systems thinking
- **stand alone! Easy to use**
- in-class, lab, take-home and demonstrations
Computational Learning Modules

1. Topic Selection

1. Identify Learning Objectives
   a. What does the literature recommend?
   b. What do instructors value?

1. Module Design
   a. Background Information
   b. Introduction to Computational Model
   c. Simulation Setup
   d. Inquiry-based Questions

2. Implementation
3. Assessment
4. Refinement

Goals
- designed to stand alone- start here, self-contained;
  no work for instructors
Fall 2015 Experimental Design
LIFE 120

Prior to class
- Background reading
- Worksheet
- Pre-conceptual model & questions
- Group conceptual model
- Simulation & questions
- Post-Conceptual model & Questions

During class

n = 543 students
Baseline Findings

Without any lecture instruction

With 1 lecture

more structures

With 2 lectures
Baseline Findings

Without any lecture instruction

With 1 lecture

With 2 lectures
Baseline Findings: replace with infograph
Baseline Findings

Without lecture instruction

With lecture instruction

produces

produces

goes to

goes to
Baseline Findings

Without any lecture instruction: 12.9 ± 0.9

With 1 lecture: 17.3 ± 1.2

With 2 lectures: 16.8 ± 2.1
Learning Activities Design

Tryptophan Operon

Static Diagrams

Interactive Dynamic Model
Refinement of Modeling Platform

Coming soon...
Background on Cell Collective

CC network screenshots
ease of use
Background on Cell Collective

CC network screenshots
ease of use
Computational Modeling Learning Activities

Implementation

- Feedback Sessions
  - ~10 undergraduates
  - ~5 Teaching Assistants
- Honor Student Sessions
  - ~15 undergraduates
- LIFE120 Lab Summer Pilot
  - 2 lab sections
  - ~20 undergraduates per section
- LIFE120 Lab Fall 2015 Full Implementation
  - Upper level
Evidence-based Refinement of Learning Activities

Refinement Timeline with Preliminary Data

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pilot 1</td>
</tr>
<tr>
<td></td>
<td>Major findings</td>
</tr>
<tr>
<td></td>
<td>Date</td>
</tr>
<tr>
<td></td>
<td>Honors Student Session 1</td>
</tr>
<tr>
<td></td>
<td>Major findings</td>
</tr>
</tbody>
</table>

Table 1. Prevalence of Mechanistic Reasoning (MR)

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>MR</th>
<th>non-MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implicit</td>
<td>1</td>
<td>93</td>
</tr>
<tr>
<td>(94 Total)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Explicit</td>
<td>12</td>
<td>22</td>
</tr>
<tr>
<td>Opportunities*</td>
<td>(34 Total)</td>
<td></td>
</tr>
</tbody>
</table>

![Graphs showing data before and after intervention](image)
Background on Cell Collective

observe dynamics
Computational Modeling Platform
Cell Collective

Features:
- Web-based (thecellcollective.org)
- Easy to use
  - No mathematical expression
  - No programming