Discovering Signal Transduction by Building and Simulating a Bacterial Chemotaxis Model

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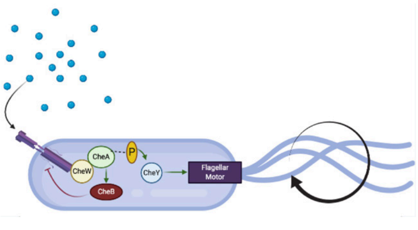

Abstract

The building and simulation of biological models is a valuable skill that can deepen student knowledge and promote systems thinking. Signal transduction networks are complex biological communication systems that regulate many interactions between an organism and its surrounding environment, creating dynamic behaviors. Bacterial chemotaxis exemplifies the basic principles of signal transduction and demonstrates core biology concepts like feedback inhibition, systems, and transfer and utilization of information. This system is ideal for learning about modeling. It contains a small number of components while still demonstrating key aspects of signal transduction: how an environmental signal is received and translated into a mechanical behavior and how feedback loops give rise to nonlinear dynamics. Using Cell Collective, we developed a model- and simulation-based lesson to help students grow their computational modeling skills while developing knowledge of these core concepts. Cell Collective and the lesson design allow students to build and simulate a model without extensive background knowledge of the technology or computer programming. It also targets common student misconceptions about the features of complex systems like emergent behaviors and randomness. The lesson contains all resources, assessment questions, and instructions needed for teaching signal transduction and having students practice modeling and system thinking.

Primary Image: The bacterial chemotaxis signal transduction network.

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Learning Goals

Students will:

◊ build a computational model to understand the basics of signal transduction networks.

◊ explore the usefulness of a model and its distinction with mechanistic accuracy.

◊ use a model to predict behavior under various environmental conditions.

◊ explore the dynamics of a signal transduction network by performing simulation experiments.

◊ relate simulated results to real cellular events.

◊ From the Cell Biology Learning Framework:

» How do cells send, receive, and respond to signals from their environment, including other cells?

Learning Objectives

Students will be able to:

◊ identify the stimuli and responses of bacterial chemotaxis. (Cell Structure & Function⋆, Structure and Function○)

◊ build a model to represent the transfer of the phosphoryl group from kinase CheA to CheY and the activation of the flagellar motors to run or tumble. (Cell Structure & Function⋆, Metabolic Pathways⋆, Structure and Function○, Information Flow, Exchange, and Storage○)

◊ describe the role of CheB in negative regulation by investigating cases of permanent binding or inability to bind receptors. (Cell Structure & Function⋆, Metabolic Pathways⋆, Structure and Function○, Information Flow, Exchange, and Storage○)

◊ use models to predict bacteria's behavior (running or tumbling) under varied conditions. (Microbial Ecology⋆, Information Flow, Exchange, and Storage○)

◊ simulate the behavior of a bacterial chemotaxis model under varied conditions and interpret the results. (Microbial Ecology⋆, Information Flow, Exchange, and Storage○)

◊ logically connect dynamic behaviors (*e.g.,* oscillation, stable activity) to the environmental conditions and survival needs of bacteria. (Microbial Ecology⋆, Information Flow, Exchange, and Storage○)

Learning Objectives

Students will be able to:

◊ identify and describe the limitations and potential for the expansion of a bacterial chemotaxis model. (Impact of Microbes*, Pathways and Transformations of Energy and Matter°)

◊ explore the concept of a model's value as a function of its usefulness and distinguish between this usefulness and mechanistic accuracy. (Impact of Microbes*, Pathways and Transformations of Energy and Matter°)

*Aligned with the American Society for Microbiology Learning Outcomes (1)

°Aligned with the American Association for the Advancement in Science Core Concepts (2)

INTRODUCTION

It is crucial for undergraduate students to study biology as a complex system. One reason is that studying biology from a systems perspective can engage students in system thinking through various practices such as computational modeling and simulation (2–11). This perspective also allows the integration of both core concepts and competencies in teaching biology—signal transduction in particular—to students and involves them in building semi-quantitative computational models (3).

Signal transduction is a hallmark example of an interconnected biological network that transforms an external signal into a mechanical response. Signaling networks rely on the transfer and utilization of information and can be studied by observing changes in cellular dynamics in response to changes in their surrounding conditions. While signal transduction encompasses a diverse range of prokaryotic and eukaryotic systems and regulates a wide range of behaviors, it has several key structures that are highly conserved through evolution and are crucial for studying its basic processes. Several of these structures are receptors, kinase protein cascades, and scaffold proteins (12).

Students often struggle with learning about the dynamics of signal transduction. Part of the problem is that students generally do not have a solid understanding of processes like causal mechanisms and randomness. For instance, it was observed that students across K-12 grades could not provide mechanistic explanations for a biological phenomenon; instead, they often described how the phenomenon occurred (13). In a study assessing students' system thinking skills by concept maps, upper-level students struggled to show the interconnection of biological components (14). They also had difficulties understanding how random events led to emergent behaviors and thus often avoided explaining the behaviors that involve randomness as a means to evolutionary behavior (15). To address these issues, researchers have found computational models promising in better teaching complex biological concepts and improving students' learning (3–11).

To study a system as a model, we need to decide which components and interactions to include and exclude to ensure the model represents the system but does not become unnecessarily complex. To this end, small, well-studied signaling networks are ideal candidates for computational modeling and simulation, as they allow for focused exploration and reduce the "learning fatigue" that may occur when studying large amounts of information at the surface level (12, 16).

Bacterial chemotaxis is a classic example of signal transduction and is an ideal system for exploring this basic biological concept. Like other higher-order organisms, bacteria sense stimuli from the environment using receptors, process the information through a communication network, and produce an appropriate response (17). Because the system represents a basic outline of how signal transduction works, it can provide insights about the processes for all students, including those with little enthusiasm for studying bacteria. Plus, practicing with a bacterial chemotaxis system, students will perform signal transduction modeling and simulations similar to other organisms which subsequently will allow them to apply the knowledge they have gained to other systems with similar network communication processes.

Bacterial chemotaxis has been used as a model to study network dynamics, but the majority of those models have been physical, requiring students to move around a classroom while following instructions on when to move forward or randomly reorient (18). While this approach is useful for understanding the behavior of bacteria in general, computational modeling provides students the opportunity to explore the processes in-depth and examine the interactions within the signaling network. For example, using bacterial chemotaxis as a model, students can describe how attractant or repellent environmental stimuli can lead to stable or oscillatory dynamic movement behaviors.

Building on our knowledge gained from previously published lessons on the platform Cell Collective Learn, we developed the *Bacterial Chemotaxis* lesson to teach signal transduction and bacterial chemotaxis while also addressing the issues students commonly encounter with respect to complexity in biological systems (8–11). Here, we describe a computational modeling and simulation lesson called *Bacterial Chemotaxis*. This lesson aims to help students build basic modeling and simulation skills by understanding how each component (node) of a model connects to the other ones using direct activating or inhibiting arrows. The model employs Boolean mathematics. However, no prior knowledge of this framework is required by students or instructors. This makes the lesson more accessible by eliminating the need for programming while still allowing students to engage in modeling and simulation (8, 19, 20).

The lesson also provides any details necessary to understand the dynamics of the model and eliminates the need for prior mathematical modeling experience. This allows students to actively develop a systems biology perspective on the bacterial chemotaxis network. It also allows them to do authentic scientific practices by carrying out a series of predictions and experiments on the network as a whole (2, 21). Throughout the lesson, background information is integrated into the model-building practices, and assessment questions are provided to encourage students to connect the biological information to the modeling process. This lesson was designed using evidence-based practices specific to modeling and simulation to support science learning (4, 5, 19, 22). This approach employs action items recommended by the American Association for the Advancement of Science to implement science education change by integrating core concepts and competencies and promoting student-centered learning (2).

Intended Audience

This lesson is designed for mid to upper-level undergraduate students with prior experience in introductory biology, microbiology, biochemistry, systems biology, or similar fields. It can also be implemented at the graduate level to build basic modeling skills and content knowledge of signal transduction networks.

Required Learning Time

This lesson is expected to take students approximately 1 hour to complete. The time it takes to build the network, run simulation experiments, and answer accompanying questions may vary depending on the student's previous experience with modeling and simulation technology and their background knowledge about bacterial chemotaxis. An additional 15 minutes is required if the instructor plans to complete the training module before starting the lesson.

Prerequisite Student Knowledge

Students should have basic knowledge about signaling networks, the function of proteins, and how bacteria respond to environmental changes. These topics are often discussed in introductory biology courses in a unit that includes content on prokaryotic mobility mechanisms or upper-level microbiology or biochemistry courses during units that include signal transduction. Familiarity with the following terms will help complete the *Bacterial Chemotaxis* lesson: receptor, protein, kinase, flagella, positive/negative regulation.

Students should also have the basic skills in reading graphs and interpreting scientific data. They are often familiar with graphs and data analysis basics from their K-12 education. However, it would be beneficial if students were reminded about such practices and noted that they would be exercising them throughout the lesson.

Students should be able to use a web browser to access the lesson, type in basic text responses, click the buttons to play/pause simulations, add components, and respond to assessment questions. Students should access the Cell Collective website at https://cellcollective.org/ and enter the software by clicking the Student Access button. This will direct them to the Student Learning side of the software, where they should select the *Bacterial Chemotaxis* card from the dashboard. Based on our extensive experience, we strongly recommend that students using Cell Collective for the first time complete the training lesson called *Cell Collective Training Module: Factors Influencing Exam Scores* (also accessible from the home dashboard page). This acontextual lesson is designed to help students become familiar with Cell Collective and the general concepts of network systems, modeling, and simulations.

Prerequisite Teacher Knowledge

You should complete the *Bacterial Chemotaxis* lesson before implementing it with students to provide guidance on technology and content-related questions. You should also have a thorough understanding of signal transduction and bacterial chemotaxis. It is also helpful if you understand the regulation of bacterial mobility using flagella, the function of kinase proteins, and the implications of particular patterns in simulation output behavior. This includes identifying the biological significance of oscillating or stable behavior and connecting these behaviors to the conditions that influence them. Much of the necessary information can be gained by simply completing the lesson before implementation. You can enhance your understanding and access additional instructor materials by requesting instructor access in Cell Collective by clicking the Instructor access button on the Cell Collective home page and selecting *Bacterial Chemotaxis*. It may also be helpful for you to complete the tutorial lesson.

SCIENTIFIC TEACHING THEMES

Active Learning

Students are active participants throughout the entire lesson. They will: (i) read background information about bacterial chemotaxis and the function of each component, (ii) build a model of the biological process by adding the necessary component(s) and connection(s), (iii) make predictions about the behavior of the model under various conditions, (iv) perform in silico experiments and evaluate the results, and (v) evaluate the modeling process as a whole. These activities align with the concept of active learning in the literature that refers to "short course-related individual and small-group activities that all students in a class are called upon to do, alternating with instructor-led intervals in which student responses are processed and new information is presented" (23). During each step, students will answer the in-lesson questions that will help them assess their understanding and think more deeply about their models and simulation experiments. Each student should be responsible for completing their work; however, students are encouraged to discuss their work in small groups as they complete each phase of the *Bacterial Chemotaxis* lesson. This type of group work may be useful as students may have varying technical skill levels and content knowledge of bacterial chemotaxis.

Assessment

You can assess student understanding using the (approximately 30) assessment questions provided throughout the lesson. For an outline of how each question lines up with a learning objective, see Table 1. Additionally, you may have students submit screenshots of their simulation results and complete computational models to ensure the system has been constructed correctly.

Inclusive Teaching

Students can work in small groups of two to four while completing the *Bacterial Chemotaxis* lesson. While each student should construct and simulate their model, the opportunity for discussion allows students with diverse strengths to contribute to the success of others in the group. This type of group work also helps students inexperienced in modeling to learn about modeling technology in a comfortable environment while also gaining a deeper understanding of a relevant biological topic. Furthermore, the lesson is scaffolded so that students are given more instruction at the beginning of their model-building process. They gradually receive less instruction to complete their models and simulations as they progress through the steps. This ensures the lesson can meet each student at a level appropriate for their skill while building independence (24, 25).

LESSON PLAN

An overview and timeline for the lesson plan are provided in Table 2. The learning objectives for this lesson are informed mainly by the core concepts and competencies for undergraduate biology (2). The lesson is modular, providing flexibility to adapt to different classroom needs. The module includes model-building practices based on background information about bacterial chemotaxis, simulation experiments, and a reflection on the strengths and weaknesses of the model. All modules are grouped in the *Bacterial Chemotaxis* lesson and are separated with labeled headers.

Below is a list of necessary and/or useful materials for teaching the lesson. All of them are available through supporting materials, links to websites, or via request to the authors.

- A computer with access to the internet. Tablets and mobile devices will not work for this activity.
- *Bacterial Chemotaxis* lesson (available under the "Student" side of Cell Collective, accessible from the Cell Collective website.
- *Bacterial Chemotaxis* assessment question answer key (available under the Instructor side of Cell Collective; Instructor access request can be made directly from the Cell Collective website).
- Instructor slides provided with this manuscript (Supporting File S1).
- *Cell Collective Training Module: Factors Influencing Exam Scores* (available under the "Student" side of Cell Collective, accessible from the Cell Collective website).

Before Class

Inform Students of the Upcoming Model-Based Activity

Inform students that they should bring a computer to class on the day of the activity. While Cell Collective supports multiple internet browsers, the Chrome/Chromium browser is highly recommended. Tablet and mobile devices are currently not supported. While we highly encourage students to have their own computers to gain the maximum benefit from the building and simulation activities, they can also work in groups with one computer. A computer lab could also be scheduled if feasible for your method of instruction and class size.

In preparation for the day of the lesson, you may have students create a Cell Collective account on the Cell Collective and complete the training module before class. The training module should take around 15 minutes to complete. We also recommend that you go through the entire *Bacterial Chemotaxis* lesson as if you were a student. This experience will provide you with a deeper understanding of the lesson content, develop your skills for navigating the Cell Collective platform, and help you prepare for potential issues and questions from your students.

In-Class

Facilitate the Bacterial Chemotaxis *In-Class Activities*

Exercise 1. Access Cell Collective Learn and Learn the Goals of Modeling

Instruct students to access Cell Collective under the Students option at the Cell Collective, create or log in to their account, and open the *Bacterial Chemotaxis* lesson from the dashboard page. If you choose to use the training module in class, allow students an additional 15 minutes to complete this exercise before starting the *Bacterial Chemotaxis* lesson.

Provide students with an overview of Cell Collective goals and practices. For example, tell them they will use Cell Collective to construct a computational model of bacterial chemotaxis in this module. Also, they will be responsible for adding components (*e.g.,* a repellent) and finding the relationship among them (*e.g.,* repellents activate the repellent receptor) to model the dynamics of bacterial chemotaxis. They will then simulate the system, perform in silico experiments, and reflect on the model's strengths and weaknesses.

The Cell Collective lesson provides students with all the background information, directions, and question prompts to complete the activities.

Exercise 2. Build a Model of the Components and Interactions of Bacterial Chemotaxis

In the first two sections of the activity, students are given background information about each component of the bacterial chemotaxis signal transduction system. In this regard, they are first directed to examine the overarching goals of the model: to simulate the real-life locomotive behavior of bacteria documented in biological literature (*e.g.,* how the concentration of attractants and repellents influence the frequency of a bacteria to run or tumble as it moves within its environment). Understanding the purpose of the model from the beginning will limit confusion as students begin to connect the individual components and gradually build up a more complex model.

Also, throughout the model-building phases, students are prompted with various questions that are designed to help them develop their ideas on what constitutes favorable or unfavorable environments for bacteria; for example: "Is an antibiotic a repellent or an attractant to a bacterium?" Such questions also address the common misconception that antibiotics are always helpful substances; for bacteria, they inhibit essential functions and are repellents.

Using Cell Collective, students build the model by adding each component of the system and then connecting them based on their understanding of the biological mechanisms (*e.g.,* whether the activation of the flagellar motor will cause running or tumbling). This model-building process engages students in translating information about the system into a system-wide model; they add and connect components using activating (green) or inhibiting (red) arrows. At first, this practice allows students to understand each part of the process separately. It then helps them gradually advance their knowledge of the system as a whole, complete their model, and have it ready for simulation.

Students' learning is scaffolded; they receive more instructions and information early in the process and receive less help as their knowledge of the system and modeling increases (25). The instructions begin by directing students on exactly which connections to place and why. As the lesson progresses, students must think about the biological information provided and build the model using their understanding of the previous steps with less direct instructions. This allows students to take an active role in building a model while slowly developing the skill to interpret the information and translate it into model components and connections. Aligned with scaffolding practices, the format of the module's questions becomes more open-ended as each section progresses. For example, the model building portion begins with True/False questions and builds up to more complex free-response ones that require students to analyze the "how" and "why" of the system more deeply (13, 25).

Exercise 3. Simulation: Predictions About the Behavior of the Model

After constructing their bacterial chemotaxis model, students will work on several scenarios that require them to make predictions about the behavior of bacteria. The scenarios will involve several combinations of the two modeled inputs: attractants and repellents. In scenario 1, bacteria encounter insecticide poison in an otherwise clean pond (+repellent). Students predict whether the bacteria's behavior will be stable (running only) or oscillatory (alternating between running and tumbling). They will also predict whether the tumbling frequency will increase or decrease as a bacterium approaches a repellent, which in turn increases the repellent concentration.

Similar predictions (hypothesis generation) are practiced in scenarios 2, 3, and 4. In scenario 2, bacteria are placed in a glass of purified water (no attractant or repellent). Scenario 3 involves bacteria placed into a petri dish with a mix of water and nutrient media, as they might be in a microbiology lab (+attractant). In scenario 4, a healthy gut microbiome with plenty of incoming nutrients has recently been exposed to a toxin (+attractant, +repellent).

Through these simulation experiments, students will test their predictions, observe the results, and analyze their predictions and observations (21). Indeed, in this exercise, they will examine the behavior of their models as they simulate the scenarios by them. During this practice, students will answer questions about their simulations (see Table 1 for alignment of these questions with learning objectives) and validate their models to ensure they behave according to published literature on the behavior of the lac operon for each condition.

For each scenario, students will set the levels of the external components "attractant" or "repellent" to mimic the environmental conditions of the scenario. Then, students begin the simulation and observe the modification of internal components on the y-axis of the simulation graph while the x-axis displays the relative time steps (9–11). While the activity level does not directly correspond to a specific measurement, such as concentration, students still can interpret the values semi-quantitatively by setting "high," "low," or "equal" activity levels for the external components as instructed in the lesson (8–11). They will then view the activity level of their possible outputs, "run" and "tumble," to determine whether one behavior dominates or the behaviors oscillate. Because the model is based on probabilistic logical modeling, the activity level displayed on the graph represents the proportion of time that each behavioral output may occur (7, 8). If the results do not match students' expectations, they are encouraged to revisit the model building portion and see how revisions would impact the model. This is similar to how researchers use computational models to replicate real-life situations and refine their simulations to predict novel behaviors in untested scenarios (26, 27). Accordingly, for each scenario in this module, students will carry out a full cycle of scientific practices.

We designed our scenarios in line with Steps A–F which are recommended as best practices for applying simulations to facilitate science learning (6, 21, 24):

- Make predictions (Step A) (21, 24),
- Provide reasons for predictions (Step B) (24),
- Test predictions by setting up computer simulations (Step C),
- Consider alternative predictions with simulation results (Step D) (6),
- Evaluate the consistency of predictions with results (Step E) (24), and
- Use evidence (from simulation results) to support findings (Step F) (21).

This approach has shown to be helpful for students using Cell Collective (9–11).

Exercise 4. Reflect on Model Strengths and Weaknesses

Reflection has been shown to be a valuable strategy to promote student learning (28). Accordingly, borrowing from the principles of the metacognitive teaching approaches (29), the final section of this lesson requires students to reflect on their model-building experience. In this practice, students will think about the purpose of their model and whether or not it effectively answered its laid-out questions. They will also examine the questions their model could not address (*e.g.,* how population density would affect the dynamics of a group of bacteria undergoing chemotaxis). They will subsequently ponder how they might expand their model to better represent the system.

Eventually, through a comparative teaching approach, this module will further prompt students' reflection by comparing and contrasting their model with a living cell performing the same process. Comparison is one of the most integral components of human thought (30). It is found to be a powerful approach for improving students' learning in various domains of knowledge (31).

Approaches to Facilitate the *Bacterial Chemotaxis* Lesson

While we recommend completing the lesson in small groups to promote inclusivity in learning, students may also complete the lesson individually. Instructor guidance is not required; however, it is helpful for you to answer questions on the biological concepts and technological challenges that may occasionally arise. All background information, model building instructions, simulation experiments, and assessment questions are included in the *Bacterial Chemotaxis* lesson (accessible at the Cell Collective website under the Students side of Cell Collective) and can be completed without additional guidance or instructional materials. This all-in-one lesson format makes *Bacterial Chemotaxis* an ideal computer modeling experience for both traditional and remote learning environments.

It may be helpful to guide less experienced students through a short introduction to the lesson using Supporting File S1. These are available on the "Instructor" side of Cell Collective, which can be requested directly from the Cell Collective website. These slides can also be used to provide background to both students and instructors.

Common Areas of Difficulty and Solutions

Some students may skip reading through the background information on each component and follow the model-building instructions to move through the lesson more quickly. This can lead to difficulty explaining the biological mechanisms behind interactions, even if the model itself is built with the correct components and connections. This will be most evident when students try to explain their reasoning behind how and why the model's dynamics are either stable or oscillatory. If students skip over the reading sections, they will have more difficulty connecting their simulation results to the scenarios presented and may believe their simulation results are incorrect. The activity is most successful when students take their time during the model building portion and answer the assessment questions based on the biological mechanism presented. These questions are designed to encourage students to explore the concepts presented in the background information and relate that information to their models.

Some students may skip model building or simulation instructions and haphazardly change the settings, resulting in unexpected or confusing results. Following the provided instructions will ensure the results of simulation experiments will be displayed on the graph and correspond to the correct environmental condition. If a student becomes frustrated, encourage them to go back and read the instructions carefully. If possible, encourage students to engage with peers to solve issues when building and simulating their models before consulting an instructor (9–11). This is particularly helpful since student peers involved in the same process may offer quick and productive feedback that is useful to both those asking and answering the questions.

TEACHING DISCUSSION

Lesson Implementation

We implemented this lesson in a small biochemistry and systems biology course ($N = 4$) during the Fall 2020 semester. The lesson was provided to upper-level students during a discussion period of up to one and a half hours. These discussion periods reinforced student knowledge of relevant material interactively before and during the computer-based modeling activity. They involved a 15-minute introduction to the modeling platform and the lesson's objectives. All students completed the lesson in the time allotted for the class period without additional outside work. Students completed the lesson individually but were still encouraged to discuss their work due to institutional restrictions at the time of this implementation. All data collected were from students consenting to participate in the study, which was classified as exempt from IRB review.

Student Reaction to the Lesson

To examine students' experience using the *Bacterial Chemotaxis* module, a pilot study was conducted in the Fall of 2020. We distributed a 1–5 Likert scale survey to students, entailing three statements about their activities in the module. Overall, the respondent upper-level undergraduate and graduate-level students ($N = 4$) reported that the model-based activities helped them learn about the biology topic (*i.e.,* bacterial chemotaxis) (Figure 1A), held their attention (Figure 1B), and that the Cell Collective software was easy to use (Figure 1C).

Possible Adaptations

Because Cell Collective provides editable access to this lesson for instructors, and the lesson has been designed in a modular fashion, you can adapt it to your needs and preferences. For example, as this lesson focuses more on the network dynamics of bacterial chemotaxis, specific attractant or repellant receptors were not named. If an instructor wishes to adapt the lesson to their specific needs, such as adding specific (chemo)receptors,

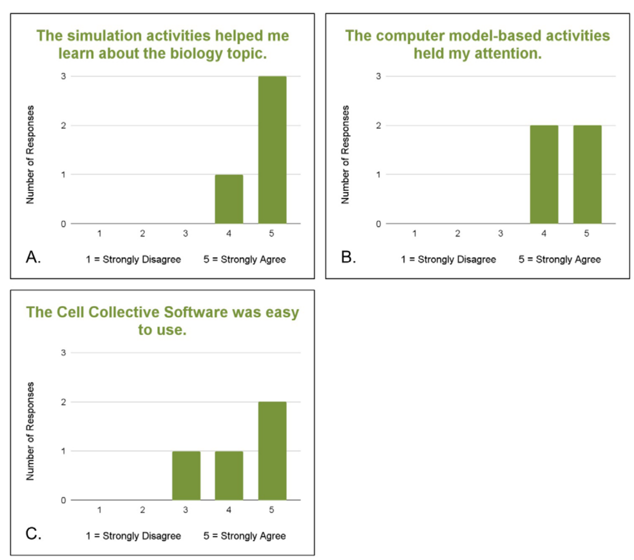

Figure 1. Student reactions to the lesson. Students felt that the *Bacterial Chemotaxis* module was a positive educational experience

they can do so by creating a copy of this lesson in their Cell Collective account. After creating a copy, the instructor can customize the lesson completely. Small changes can be made by adding nodes or reactions to the model or changing the text in existing activities. Instructors also have the option to expand the lesson to include new activities where students learn about other chemosensory pathways such as biofilm formation.

If, for example, time is limited in your class, you may have students complete some sections during one session and those remaining in the next. While we recommend that students complete the approximately 30 assessment questions, you may omit or instruct them to skip any or all of these questions if it better suits your course's needs. You may also assign portions or the entirety of the lesson as independently completed homework.

If bacterial chemotaxis is a particularly relevant content area in your course, like in microbiology, you may have students complete prior reading on the underlying mechanisms that regulate the system, like the structure and function of chemotactic receptors or the flagellar motor. If the general principles of signal transduction or computational modeling technology are more relevant to your course, you may target background reading in these areas based on the unit you are completing in conjunction with the *Bacterial Chemotaxis* lesson. An additional discussion on signal transduction or a lecture-style approach in which the instructor guides students more closely could also be implemented when completing the lesson with students who benefit from additional assistance. Finally, a comparative teaching approach in which students could discuss their bacterial chemotaxis model with bacterial chemotaxis behavior in the real world could further expand students' perspectives on the applications and limitations of modeling.

SUPPORTING MATERIALS

- S1. Bacterial Chemotaxis – Instructor Slides

ACKNOWLEDGMENTS

We would like to thank the National Science Foundation for supporting the creation and dissemination of this lesson.

Table 1. *Bacterial Chemotaxis* learning objective alignment. The assessment questions used throughout the lesson are aligned with the learning objectives.

Learning Objective	Assessment Questions	Notes
1. Identify the stimuli and responses of bacterial chemotaxis.	1. Q1. Consider the many harsh environments in which bacteria can successfully thrive. Think of 2 potential toxic chemical substances they may encounter. 2. Q10. Consider the many rich environments in which bacteria exist. Think of two chemical substances that could be considered attractants.	
2. Build a model to represent the transfer of a phosphoryl group from kinase CheA to CheY, and the activation of the flagellar motors to run or tumble.	1. Q2. T/F: The green arrow connecting CheA to CheY represents the transfer of a phosphoryl group from the CheA to CheY protein. 2. Q3. T/F: All green arrows in the model do not represent the same thing but are all usefully interpreted by the modeling program as activating. 3. Q4. T/F: A phosphorylated CheY is needed to interact with the motor switch. 4. Q5. If a bacterium had a genetic mutation that made its CheY protein nonfunctional, could the bacteria successfully perform chemotaxis? What consequences might be triggered in the bacterium's movement ability?	
3. Describe the role of CheB in negative regulation by investigating cases of permanent binding or inability to bind receptors.	1. Q6. If a bacterium had a mutation that caused CheB to permanently bind the repellent receptor, what would be some of the downstream consequences on the system?	
4. Use your models to predict the behavior (running or tumbling) of bacteria under varied conditions.	1. Q7. Scenario 1: Bacteria encounter an insecticide poison in an otherwise clean pond. (+Repellent) 2. Q8. As the bacterium approaches the repellent, and therefore the repellent concentration is increasing, tumbling frequency will: 3. Q9. Scenario 2: Bacteria are placed into a glass containing only purified water. (neutral) 4. Q11. Scenario 3: The bacteria are added to a petri dish with a mix of water and liquid nutrient media. (+attractant, 0 repellent) 5. Q12. When a bacterium approaches the attractant and therefore attractant concentration is increasing, tumbling frequency will: 6. Q13. Scenario 4: A healthy gut microbiome with incoming nutrient sources but has recently consumed a mild toxin. (+attractant, +repellent)	Q7, Q9, Q11, and Q13 ask students to predict the movement of the bacteria, in each set of environmental conditions, based on what they have learned while building their model. They will simulate these conditions later in the lesson.
5. Simulate the behavior of a bacterial chemotaxis model under varied conditions and interpret the results.	1. Q14. The result is: 2. Q16. The result is: 3. Q17. If the results are the same as the last scenario, why do you think this is when the inputs HAVE changed? If not, then why not? 4. Q18. The result is: 5. Q20. The result is:	Q14, Q16, Q18, and Q20, ask students to describe the movement of the bacteria after simulating each set of environmental conditions.
6. Logically connect dynamic behaviors (ex. Oscillation, stable activity) to the environmental conditions and survival needs of bacteria.	1. Q15. In the context of the repellent, why does the bacterium tumble and run in this scenario? Select all correct answers. 2. Q19. How does the graph change based on the amount of attractant added? How do you explain this biologically? 3. Q21. Experiment with various levels of attractant and repellent. What happens when they are equal? How do run/tumble change if they are adjusted to be unequal? 4. Q27. Different types of bacteria have varying needs. For example, acidophiles thrive in low-pH environments that are too acidic for most other life. How do you imagine their behavior would respond in a highly neutral environment compared to common bacteria who tend to thrive in this more neutral environment? Would you expect running and tumbling behavior to change?	

Learning Objective	Assessment Questions	Notes
7. Identify and describe the limitations and potential for the expansion of a bacterial chemotaxis model.	1. Q22. T/F Our model does not account for all population-level factors, such as density, regulatory dysfunction, and competition for attractants by surrounding organisms. 2. Q23. T/F Our model cannot account for changing levels of attractants and toxins in the environment. 3. Q24. How do you imagine your simulation results are different from real cellular events? What are the model's limitations? 4. Q25. How do you imagine your simulation results are similar to real cellular events? What are the model's strengths?	
8. Explore the concept of a model's value as a function of its usefulness and distinguish between this usefulness and mechanistic accuracy.	1. Q26. Do you agree with the following statement? Why or why not? The biochemical mechanisms of taxis regulation are complex but can be usefully interpreted through the building and simulating of simple models.	

Table 2. *Bacterial Chemotaxis* teaching timeline. An overview and timeline for the lesson plan.

Activity	Description	Estimated Time	Notes
Preparation for Class			
Review in-class materials	1. Familiarize yourself with the *Bacterial Chemotaxis* content. 2. Familiarize yourself with the Cell Collective. 3. Prepare for questions students may have during class, such as questions about bacterial chemotaxis, signal transduction, and how to use the modeling platform. 4. Instruct the students to bring computers to the in-class portion of the lesson. Tablets and cell phones are not yet supported by Cell Collective Learn.	1–2 hours depending on expertise on the chemotaxis content and modeling/ simulation skills	Go through the *Bacterial Chemotaxis* lesson in Cell Collective Learn as if you were a student.
In-Class Activities			
Exercise 1: Access Cell Collective Learn	1. Instruct students to use their computers to go to the Cell Collective. 2. If they have not yet registered for an account, students will need to create one to complete the lesson. 3. Instruct students to log in and open the *Bacterial Chemotaxis* lesson and click "start lesson."	5–20 minutes, depending on whether or not you choose to use the training lesson	Training lesson: "Cell Collective Training Module: Factors Influencing Exam Scores"
Exercise 2: Build a model of the components and interactions of bacterial chemotaxis	1. Instruct students to begin the activity. 2. Be available to answer questions about the model building portion of the lesson and to address technology issues. 3. Instruct students to read the background information on each page, follow the model building instructions, and answer the assessment questions before proceeding to the next step of the model building phase.	25 minutes	
Exercise 3: Make predictions about the behavior of the model	1. Have students make their own predictions about how 4 scenarios will affect the dynamics of the system in the next phase of the computer-based lesson. 2. Encourage students to think about what each output means in the context of the bacteria's environment and survival needs. 3. Promote the use of "how" in addition to "why" answers when discussing predictions with students.	5 minutes	Students begin the process of prediction in Exercise 3, then observe the behavior of the simulation and explain their results in Exercise 4.
Exercise 4: Perform simulation experiments to validate the model	1. After students have made predictions have them progress to the simulation portion of the lesson. 2. For each scenario, ensure students are performing the simulation experiments and understand the results. 3. Be available to help with common technology questions, such as how to adjust simulation settings.	15 minutes	
Exercise 5: Reflect on model strengths and weaknesses	1. Have students complete the final section to think more deeply about the modeling experience. 2. Encourage students to discuss the advantages and disadvantages of computational modeling.	10 minutes	

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