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Use of a Role-Playing Activity To Increase Student Understanding of Bacterial Gene Regulation

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Undergraduate students often struggle to understand the basics of bacterial gene regulation, a key concept in microbiology. They find it hard to visualize the architecture of a bacterial operon or how the gene, RNA, and protein components interact with each other to regulate the operon. To better visualize the molecular interactions, students engaged in a role-playing exercise on bacterial gene regulation in the classroom. Before beginning the activity, they received a shortened, traditional lecture on the architecture and function of the *lac* operon under "on" and "off" conditions. Students chose one or more placards detailing a molecular role (such as promoter, repressor, RNA polymerase, gene X, gene Y, etc.). Upon receiving instructor prompts, they assembled in linear order to mimic correct genomic locations of genes and regulatory elements on the operon. When given a prompt for "operon on" or "operon off" condition, students identified all the necessary components (roles) for that condition, assembled in the correct order, and then moved through the assembled operon to mimic what happens inside the cell under that condition. Students were tested before and after the activity using a set of eight multiple-choice questions. Students showed significant gains in their ability to answer these questions correctly immediately after the activity. More importantly, the improved understanding was also reflected in a high median score on summative assessments given a few weeks after the completion of the activity. This activity can also be readily adapted to online or a hybrid mode of teaching to benefit larger student populations.

KEYWORDS bacterial gene regulation, active learning, role-playing, molecular process, visualization

INTRODUCTION

Pedagogical research over the last 2 decades has completely reimagined the biology classroom. Now more than ever, the instructor-led, traditional lecture format is considered outmoded, as it exacerbates learning achievement gaps specifically in underrepresented minorities in science and first-generation college students (1). Active learning exercises have been shown to reduce achievement gaps and promote a more equitable learning environment (1, 2). While there are many ways in which active learning can be implemented in the biology classroom, the ones that are most successful at promoting higher-order cognitive skills are the ones that promote increased course structure by providing frequent and high-intensity feedback to students and faculty (2–4).

Bacterial gene regulation is a central concept in the field of microbiology that needs to be well-understood by all individuals who study or encounter microbes in their professional lives. The ability of bacteria to regulate expression of their genes is crucial to their ability to adapt to new environments where they might encounter new nutritional sources or presence of inhibitors (5). Antibiotic-resistant bacteria that can quickly adapt to the presence of antibiotics in their environment by changing their gene expression patterns are a big concern to health care systems worldwide (6). Ability to change gene expression patterns is also crucial to biofilm formation, a predominant mode of life for mixed prokaryotic and eukaryotic communities in natural environments (7). Thus, it is crucial that students of microbiology, genetics, and allied health fields have a good understanding of the topic of bacterial gene regulation. As such, the American Society for Microbiology (ASM), in their curriculum guidelines for undergraduate courses, has identified 27 fundamental statements, of which 5 statements indicate the central role of genetics and gene regulation in understanding metabolic capabilities of a microbe (statements 12 and 13); lifestyle choices such as biofilm formation and antibiotic resistance (statement 15); response to internal and external cues (statement 17); and understanding life processes (statement 25) (https://asm.org/Guideline/ASM-Curriculum-Guidelines-for-Undergraduate-Microb).

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Given the wide variety of microorganisms that exist around us and the diverse ecological niches occupied by them, it is not surprising that bacterial gene regulation can take many different forms. Apart from the common regulation of closely clustered genes in operons, gene regulation in bacteria can involve elegant cross talk mechanisms, such as quorum sensing, stringent response, and phase antigenic variation (5, 8–10). Alternatively, some bacteria use two-component systems to trigger virulence mechanisms based on signaling and subsequent gene expression changes (11). Recently, the role for small RNAs in initiating and modulating gene expression changes has become clearer (12). However, introductory courses in bacterial genetics or microbiology rarely have the curricular space to delve into details of the different systems described above. Bacterial gene regulation in biology classrooms is often restricted to discussions on inducible and repressible operons, such as the *lac* and *arg* operons.

Genetics and gene regulation are among the more complex biological phenomena that students are exposed to for the first time in introductory or intermediate biology classes. Undergraduate students' understanding of genetics is often lacking due to lack of proper foundation on the basics of genes, flow of genetic information, and central cellular processes such as transcription and translation in their high school biology curricula (13–15). Common misconceptions brought by the student into the classroom, such as assigning human-centered thinking to other animals and microbes or using the end or goal to explain the cause of a phenomenon, hinder their ability to learn new concepts (16). Further, students find it very hard to visualize submicroscopic processes happening inside the cell and therefore do not fully grasp the complex mechanistic details of gene regulatory processes.

Several different active learning strategies have been developed to improve the understanding of concepts of genetics and molecular biology. Detailed concept inventories have been generated, and new assessments were implemented that led to modest gains in student achievement in genetics courses (17–19). Peer-led workshops or peer discussions before instructor explanation have been shown to have a more positive effect on increasing student learning (20–22). Instructors specifically interested in the field of bacterial gene regulation have used clickers, case studies, and group discussions on operon models to stimulate higher-order thinking and analysis (23–25). Additionally, use of three-dimensional models to reconstruct operon structure, lab exercises such as Western blotting to measure leakiness of the *lac* or *ara* operon, and study of temperature-stimulated changes in fatty acid composition allow students to get a hands-on learning experience that augments their understanding of gene regulation (26–28).

Role playing is commonly used in medical school instruction so students can understand the interdisciplinary nature of modern medicine and the various "roles" that are important to get to better patient outcomes (29–31). In a simplistic format, role playing requires students to adopt one or more roles corresponding to a gene, protein, RNA, or small molecule in a process. On receiving guidance or cues from instructors, these role players assemble and interact with each other in a way that mimics the molecular processes taking place inside the cell. Role playing is easy to set up, has minimal costs, and allows students to be truly engaged in the classroom and visualize hard-to-understand biological processes in detail. Role playing has been adapted to promote understanding of multiple biological processes, such as the electron transport chain, endocrine regulation, protein synthesis, mitosis, etc. (32–35). Most of the activities were associated with positive feedback from students and some showed learning gains associated with specific learning objectives.

The activity I report here was developed based on my struggles with teaching bacterial gene regulation to allied health students who did not have a significant background in cellular structure and biological processes. They were unable to visualize how genes function and how they can be turned on and off in response to signals. Given that role playing has been shown to be effective in promoting student learning of complex biological processes, I hypothesized that a role-playing activity on gene regulation would be equally effective and well received.

Intended audience

This activity is intended for use by instructors teaching undergraduate courses in microbiology, genetics, or molecular biology. This activity was designed to improve understanding of gene regulation for allied health students who do not have prior exposure to details of molecular processes of the cell. The "roles" and "instructor prompts" chosen for this activity focus only on the major, granular details of the process of gene regulation of one catabolic (*lac*) and one anabolic (*arg*) operon. As such, this activity can be readily used in introductory courses for microbiology or molecular biology majors or nonmajors. For students with prior molecular biology experience, this activity can be expanded to emphasize detailed analysis of *lac* operon regulation or more complex operon regulation.

Learning time

This activity can be completed in one class session of 80 min. The first 20 min of the classroom time is a traditional lecture providing an overview of operon structure and function. In this lecture, students are provided standard pictorial representations of the arrangement of the *lac* and *arg* operons and how the operons' "on" and "off" states look and function. Students take a short, nongraded quiz before and after the activity, so that the instructor can assess the effectiveness of the activity and make changes as appropriate. The role-playing activity has 28 roles and 5 instructor prompts. Each instructor prompt, subsequent role-playing activity, and discussion takes about 5 to 8 min, for a total activity time of 30 to 40 min. The class session concludes with students taking a postactivity quiz that assesses their immediate learning gains. For courses with shorter class meeting times, it is recommended that instructors provide the lecture and prequiz during one session before the planned activity and use the entire class session for the activity and subsequent discussion.

Prerequisite knowledge

This activity and learning objectives are part of a unit on genes, genetics, and metabolism. Before this activity, students should have learned about molecular dogma and the role of transcription and translation in production of RNA and protein. A quick review at the start of the class is generally enough to help them remember the salient points. Students are also provided lecture slides on gene regulation and appropriate textbook readings to improve their preparedness for the class discussion and activity (see Appendix S1 in the supplemental material).

Learning objectives

Gene regulation is essential for microbes to adapt to changing internal and environmental signals. Students of microbiology need to understand how microbes turn genes on and off to change metabolic pathways, to adapt to new environments, cause disease, and resist the effects of antibiotics. In addition, understanding bacterial gene regulation allows us to better understand fundamental life processes. The subtopics discussed here include bacterial chromosome organization, molecular dogma, arrangement of *lac* and *arg* operons, and differential responses of repressor proteins to inducive and repressive signals. As such, the concepts covered by this activity fall under multiple fundamental concepts (statements 12, 13, 15, 17, and 25) of ASM's curriculum guidelines for undergraduate courses.

Upon completion of this activity, students will be able to:

1. Describe the arrangement of genes in bacterial chromosomes and broad steps of the central dogma of molecular biology.
2. Identify the proper arrangement of regulatory and coding elements in the *lac* operon.
3. Differentiate between function of the *lac* operator and *lac* repressor protein when inducer is present versus when inducer is absent.
4. Compare and contrast the process of turning on and turning off the *arg* operon and *lac* operon.
5. Analyze the consequences of turning on and turning off the *lac* and *arg* operons.

PROCEDURE

Materials

(i) Lecture slide deck (Appendix S1). The lecture slide deck will be used in the first 20 min to introduce the concepts of operons and the organization and function of operon on and off states. It includes some questions that can be used to stimulate discussion and thought in the classroom.

(ii) Pre- and postactivity quizzes (Appendix S2). A 9-question multiple-choice quiz covers the concept of operons and operon on and off states. Instructors will need two copies of this quiz per student. Correct answers are underlined for instructor reference.

(iii) Set of 28 role cards (Appendix S3). The set includes the major genes and mRNA and protein components of the *lac* and *arg* operons. They are set to be printed on standard 8.5 × 11 paper at a font size that is visible to all 30 to 40 students in the classroom. For larger class sizes, it might better to print on a larger paper size to increase visibility. Instructors with class sizes larger than 28 can choose to run multiple groups of the same activity or assign additional roles. Alternatively, they can run this activity in small group discussion sessions outside of class time. For class sizes smaller than 28, students can choose one role in the *lac* operon and one role in the *arg* operon sections.

(iv) Twenty-eight foam board pieces cut to 10″ × 13″ size. Each role card from step (iii), above, should be pasted to the foam board to generate sturdy "role cards" that can be held up by the students. If printing on paper larger than standard letter size, the size of the foam board needs to be increased as necessary.

(v) Slide deck of 5 instructor prompts for the activity (Appendix S4). Faculty can use these slides to direct the activity in the classroom.

Student instructions

A detailed student handout is included in Appendix S5. In the week prior to the activity, students are provided with the lecture slide deck (Appendix S1) and any other assigned reading from appropriate texts. On the day of the activity, students are given a traditional lecture using the lecture slide deck. Questions on the slide deck can be used to promote higher-order thinking and class participation. Students are given 10 min to complete the preactivity quiz. They choose one or more roles (depending on class size). They follow instructor prompts to assemble as bacterial chromosomes and *lac* and *arg* operons in the on and off states. At the end of the activity, students complete the same 9-question quiz as before the activity.

Faculty instructions

Faculty should assign textbook reading and make the slide deck for the lecture (Appendix S1) available to students 1 week before the planned activity date. Before the day of the activity, instructors will print and prepare the 28 role cards (Appendix S3) and print two copies of the quiz (Appendix S2) per student. The font or paper size of the role cards might need to be increased depending on size of classroom, so they are visible to students in the back of the classroom. Depending on the number of students in the classroom, instructors can choose to give each student a role, have students take one or more roles, or have some students observe the activity without taking part. Alternatively, for large class sizes, students can be split into groups where each group gets a complete set of 28 role cards and the activity runs on multiple tracks at the same time. It is also helpful to make space in the classroom for students to assemble and move about and be visible to other students at the same time. Faculty can also project the instructor prompts that drive this activity onto the screen during the activity (Appendix S4).

Instructor prompts used in this activity are the following:

1. Build a linear chromosome with at least five genes; how will the chromosome shape change if it were from bacteria?
2. Assemble the genomic structure of the *lac* operon; introduce RNA and protein components and show how they will function in the default state of the *lac* operon.
3. There is lactose in the environment; using the assembled genomic structure of the *lac* operon, show how the position and function of the RNA and protein components will change due to the presence of lactose.
4. Assemble the genomic structure of *arg* operon; introduce RNA and protein components and show how they will function in the default state of *arg* operon.
5. Cells have accumulated a large excess of arginine; using the assembled genomic structure of *arg* operon, show how the position and function of the RNA and protein components will change due to the presence of arginine.

Instructors will provide students with one prompt at a time so that only the roles players required for that prompt meet in the middle of cleared space. The role players are given 2 to 3 min to discuss the order in which they will assemble and move as necessary. As the role players assemble and move, other students in the classroom can provide suggestions to get to the correct answer. At the end of the prompt, instructors can provide clarifications and corrections as needed so students understand the correct order of assembly and movement that will mimic the operon structure and function. It is also helpful to have the role players repeat the process so that all students can visualize and understand the structure and function of the operon in that condition. Detailed faculty instructions are provided in Appendix S6.

Determining student learning

Students' understanding of the topic can be assessed before and after the completion of the activity using the same 9-question multiple-choice quiz (Appendix S2). This quiz can be administered on paper in the classroom or can be easily modified to clicker or online testing formats. As this activity was conducted as part of a research project, the pre- and postactivity quizzes were not graded for correctness. All students who participated in this activity were given a bonus of ∼2 points that was applied to their next exam grade. Additionally, the classroom discussions throughout the lecture and activity portion allowed students to self-evaluate their understanding of the topic and bring out any common misconceptions on the topic that could be addressed.

Sample data

Representative photographs of students participating in this activity are shown in Appendix S7. Instructors with larger classroom spaces will be able to spread out the role players more to allow for better visualization.

Safety issues

There are no biological or chemical safety issues associated with this activity, as students or faculty are not handling any biological or hazardous material. Students might experience some psychological discomfort over having to move to the center of the classroom if they are not expected to do so for other activities in this course. There is no need for physical contact in this activity, but there might be some loss of personal space, especially when assembly and movement occur during the activity. Faculty instructors might want to allot the inducer repressor and arginine repressor roles to two sets of students who are comfortable with each other, as they will have to work in concert at certain stages of the activity.

DISCUSSION

Field testing

This activity was tested in two sections of a Microbiology in the Health Sciences course with students who were majoring in Health Sciences, Nursing, Veterinary Technology, or other allied health-related fields. A total of 37 students took part in this activity as role players in groups of 20 and 17 in two sections of the course.

All students provided informed consent to be included in the activity, and subsequent data gathering was approved by Long Island University-Post campus Institutional Review Board under the exempt category of human subject research (20/02-045).

The students were asked to rate their understanding of the topic before and after the role-playing activity on a scale of "very poor" to "very good." As can be seen in Fig. 1A, 32/37 students (86.5%) rated their understanding of the topic as poor or very poor before the activity. However, after the activity, only 2/37 students (5.4%) rated their understanding as poor or very poor. After the activity, 18/37 students (48.6%) rated their understanding as good or very good, showing that students self-reported an increased understanding of the topic because of attending and taking part in this activity. Further, 27/37 students (73%) provided feedback that they found the activity was

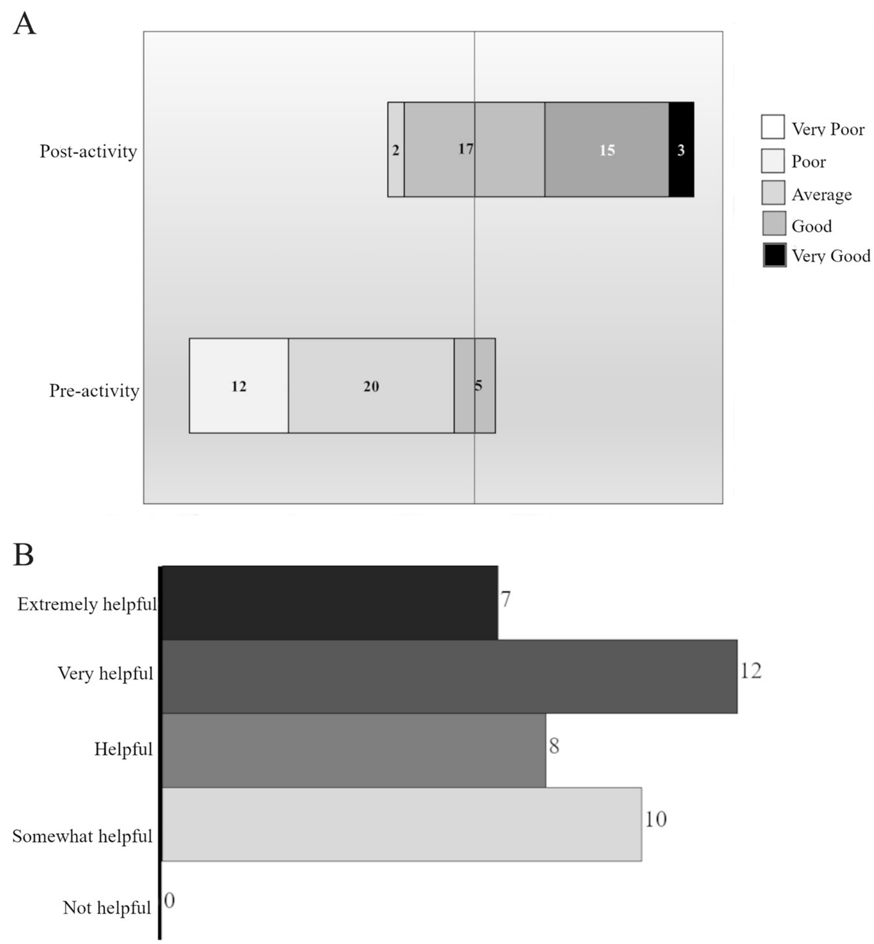

FIG 1. (A) The divergent bar graph shows student perceptions of their own understanding of the topic pre– and post–role-playing activity. Students rated their understanding of the topic as very poor, poor, average, good, or very good on a nongraded assessment performed before and after the role-playing activity. Boxes are shaded as per the figure legend on the right. The numbers in the shaded areas represent the number of students who rated their understanding in that category. (B) The bar graph shows student feedback on the usefulness of the role-playing activity. Students rated the usefulness of the activity as not helpful, somewhat helpful, helpful, very helpful, or extremely helpful. The number on the right of the bars represents the number of students who chose that response.

helpful, very helpful, or extremely helpful in increasing their understanding of the topic (Fig. 1B). This showed that the activity was well-received by the students and allowed them to self-evaluate their understanding of the topic.

Evidence of student learning

The objective of this activity is to increase student learning of bacterial gene regulation. The data gathered from testing of this activity supported the hypothesis that visualizing the assembly and movement of the molecular role players increases student understanding of operon structure and function. On both the pre- and postactivity questionnaires, students answered the same 8 questions that were directly related to the topic (Appendix S8). Questionnaires were anonymous, but students were assigned random numbers so that their individual performance pre- and postactivity could be compared. As can be seen in Fig. 2A, overall performance of the students increased from an average of 26.35% correct answers across the 8 questions to 68.58% correct answers after the activity. This increase was statistically significant, with a t score of -5.19 and a P value of 0.0013. The statistical tools used were housed at http://vassarstats.net/. A detailed analysis of student performance on individual questions in the quiz showed that for 6/8 questions on the quiz, students showed a statistically significant improvement in understanding after the activity than before the activity, with a P value of <0.001 by McNemar test (Fig. 2B). These questions correlated to subtopics, such as the proper structural arrangement of the operons, conditions that result in activation or repression of the operons, and consequences of the activation or repression. It is important to emphasize that the four learning objectives directly related to operon structure and function were clearly met by this activity and that student understanding of the material was significantly improved by taking part in the activity (student learning objectives [SLO] B to

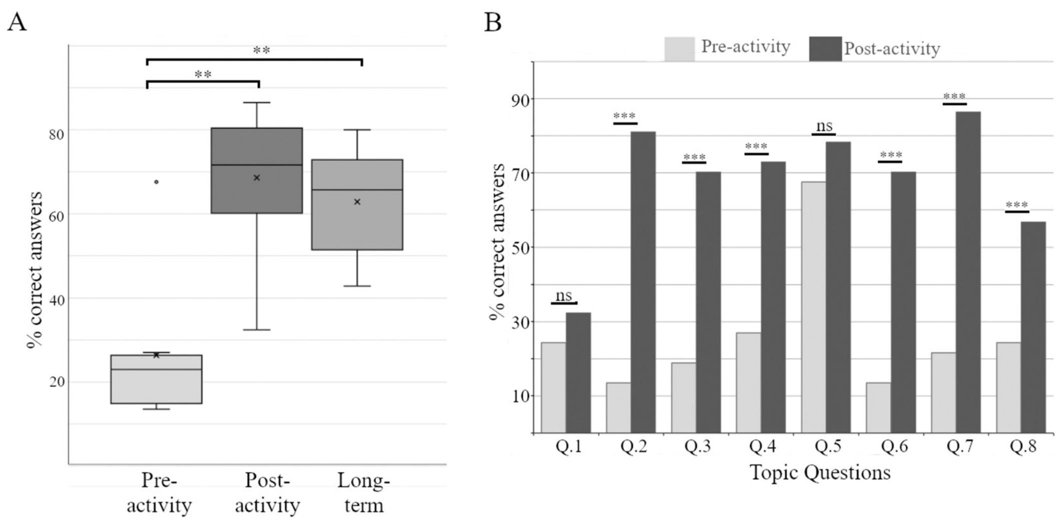

FIG 2. (A) The box and whiskers plot shows the overall performance of students on all 8 questions of the pre- and postactivity questionnaires and on 5 questions on the topic 3 weeks after the activity (long-term). The average and median percent correct answers is indicated by an "x" and horizontal line, respectively. The pairwise comparisons between the average percentage of correct answers were statistically significant (**, $P < 0.01$, Student's *t* test). (B) The graph shows the percent correct answers for each of the 8 questions on the pre-and postactivity questionnaires. The pairwise comparisons of the nominal correlated data were statistically significant for student performance on 6/8 questions (***, $P < 0.001$, McNemar test).

E). This improvement in understanding was also sustained when students were tested in a summative assessment on these topics 3 weeks after the activity. As can be seen in Fig. 2A, an average of 62.82% of students had correct answers on the 5 questions related to operon structure and function on the exam (*t* score of −3.99 and a *P* value of 0.0021). The statistical tools used were housed at http://vassarstats.net/. Students showed a high preactivity understanding of the consequences of presence of lactose in the environment, suggesting that the topic was covered in adequate detail during the lecture portion (Fig. 2B) and therefore students didn't make significant gains in understanding after the activity on this question.

The learning objective that was not met in this test of the activity was on bacterial chromosome structure and molecular dogma (SLO A). As seen in the sample images from the classroom in Appendix S7 and the instructor prompts in Appendix S4, this topic was covered during the activity, but it might need to be emphasized more. Additionally, it is possible that the quiz question needs to be reworded to avoid confusion, as further discussion with students suggested that they knew the correct arrangement of bacterial chromosomes and formation of RNA. To improve readability and avoid confusion, the first quiz question has now been split into two questions, one on proper chromosomal arrangement in bacteria and another on flow of genetic information. Modified versions of the quiz questions are now included in Appendix S2.

Possible modifications

This activity can be readily modified by instructors to fit their needs. Instructors teaching advanced classes can incorporate more detailed steps, including the action of cyclic AMP and cyclic AMP receptor protein in the *lac* operon or discuss more complex operon structural features, such as use of divergent promoters in the *arg* operon or the use of temporal regulation by the lambda phage. Alternatively, students can be provided mutant versions of "gene" roles here and be asked to predict changes that would occur under different environmental stimuli. Additionally, faculty teaching large classes, or online students, can modify this exercise to a Jamboard or other whiteboard collaborative session. In an online session, faculty can provide a list of names and have students draw the corresponding shapes and arrange or move them. Alternatively, faculty can have predrawn shapes corresponding to the different genes, proteins, and RNA components and have students arrange and move them to mimic operon structure and function. Assessment methods can also be modified to incorporate clickers, short-answer questions, or online quizzes. This activity can also be modified by instructors teaching other complex biological processes, such as carbohydrate metabolism, the viral replication cycle, etc.

In conclusion, the role-playing activity described here is easy to use, inexpensive, and can be readily implemented with minimal resources. The activity allows students to visualize operon structure and function by taking a hands-on approach to their learning. It allows students and faculty to evaluate the progress toward meeting the learning goals for this topic.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, PDF file, 1 MB.

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