INQUIRY & INVESTIGATION

An Evolving Outbreak Simulation Using Active Learning

NABT BioClub RECOMMENDATION

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Abstract

Despite the inclusion of a lab component in many STEM courses, college students often struggle to apply these skills in different situations. This outbreak simulation gives students a taste of some of the challenges associated with being in charge of an essential research project. Students will hone their grant writing, presentation skills, experimental design, data analysis, ability to prepare for failed experiments, and ability to understand the big picture of their research. Senior undergraduate biology students are split into small groups that represent distinct laboratories. Each laboratory receives the same starting information about an emerging pandemic. The laboratories must use their knowledge and innovation to design a series of experiments to identify the pathogen, and progress toward a treatment and/or a vaccine to limit the global spread of infection. My students unanimously felt that the outbreak simulation helped solidify their understanding of research and improved their engagement. One student reflected that "[the simulation] was very effective in furthering my limited knowledge on pandemics, the characteristics of disease spread, experimental design, writing grants, types of assays, and vaccine development. Despite studying science for so many years, experimental research is not something that had been well addressed."

Key Words: *outbreak; active learning; pathology; evolving simulation; experimental design; data analysis; biology; pandemics.*

○ Introduction

Students often expect instructors to provide a list of facts they will need to memorize for an exam. It can be difficult for students to accept that there are not always clearly defined right and wrong answers, and that scientific knowledge is constantly evolving (Alters et al., 2002). As instructors, it is our job to foster critical-thinking and problem-solving skills in our students so that they are able to become more active in the learning process (Walker et al. 2015). While the use of simulations to enhance student engagement with material is a common element of many nursing and medical curricula, the development and use of this teaching method has been surprisingly limited for other STEM fields in higher education (Okatch et al., 2016). It is possible that for curricula in which lab courses are a pillar of learning, educators feel the push to engage in hands-on activities rather than simulation-based learning. Laboratory-based learning is an invaluable element of a thorough education in biology; however, it should not preclude the use of other types of inquiry-based learning to reinforce and enhance topics already covered, as well as introduce ideas that would be difficult to address during a laboratory period (Hofstein & Lunetta, 1982; Crawford, 2000; Amolins et al., 2015). It can often be difficult for students to understand how the techniques they are learning in lab fit into the larger picture of advancement of scientific progress (Segers, 2001). Furthermore, many laboratory activities are costly and may be limited by departmental resources. The addition of a simulation allows students to practice the cognitive aspects of laboratory-based skills and place these skills in a broader context, free of cost.

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At Villanova University, "capstone courses" are non-lab classes designed to ensure that senior biology majors are graduating with the skills necessary to succeed as biologists. I was consistently surprised to see that, while students could easily generate a list of experimental techniques they had performed, the same students understood very little about how and why those experiments were performed, or how to analyze data produced outside of the clear direction provided in the laboratory setting. STEM fields are rapidly evolving and expanding with advances in technology. With even basic tenets of fields constantly being updated, it is the job of instructors to give students the tools necessary to teach themselves once they leave the classroom. Simulations provide a safe space in which students can discover how to fail, reassess, and learn. Here, I present an

The American Biology Teacher, Vol. 82, No. 8, pp. 545–552, ISSN 0002-7685, electronic ISSN 1938-4211. DOI: https://doi.org/10.1525/abt.2020.82.8.545.

outbreak simulation designed to polish students' ability to design experiments, analyze data, synthesize information, write grants, and understand the flow of the scientific process.

○ Goals of the Simulation

I created this outbreak simulation with four main goals in mind. (1) Students will leave this class with a clear understanding of how to design experiments to answer a broad scientific question. The students will have to analyze data from previous experiments they designed, and set up their subsequent experiments accordingly. (2) Students will gain a general understanding of the requirements for running a research laboratory. Experimental design and analysis are often considered the job of a scientist; however, the importance of grant writing, collaboration, and publishing for a researcher is often not clear to students. Many biology majors continue to a master's or PhD program and it is important for them to understand what being a research scientist entails, enabling them to make an educated decision regarding their career path. (3) This simulation will highlight the necessity of flexibility in scientific exploration. Many laboratory courses are specifically designed to allow students to succeed and clearly answer a research question. Carefully curated success helps improve student engagement but is not an accurate representation of the multitude of struggles that must often be overcome during scientific exploration. This simulation establishes a balance between the reality of failure and the motivation of success, representing a more realistic view of research progression that students appreciate (Figure 1). (4) Students will enjoy this simulation. Research has consistently shown that emotional investment greatly improves learning outcomes (Immordino-Yang & Damasio, 2007). This simulation cultivates a thrill of discovery that helps improve student engagement and subsequent retention of material.

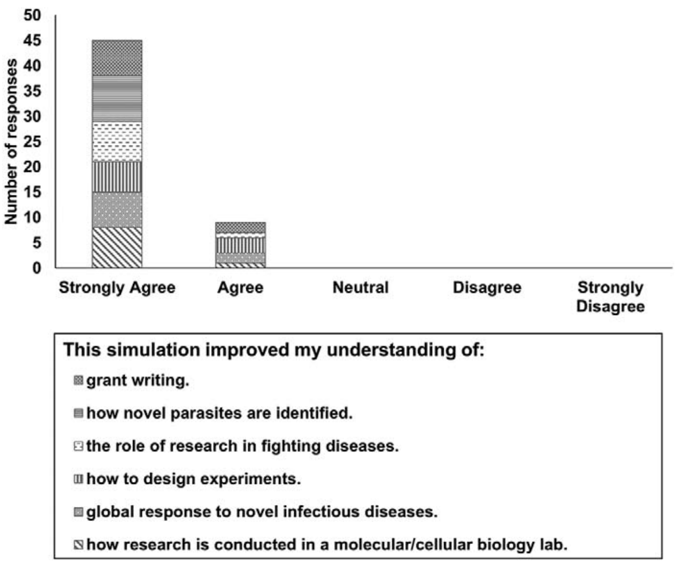

Figure 1. Students felt that the outbreak simulation was successful in achieving a variety of learning goals. Following completion of the outbreak simulation in spring 2020, the students were asked to anonymously assess their level or agreement with prompts addressing the learning goals of the simulation ($n = 9$).

Given the extensive nature of the goals detailed above, I split the simulation into multiple classroom sessions ("episodes") that were inserted into class periods throughout the semester (Figure 2). This episodic approach increased the complexity of student engagement with the material over the course of the semester. Furthermore, this approach utilizes the benefits of punctuated learning and allows students to receive large amounts of feedback, which helps them improve their subsequent plans (Lang, 2016).

While the activity described below is targeted to seniors in a traditional class setting, it could easily be adapted for courses earlier in a biology curriculum or to function as an online activity. In this simulation, students work in laboratory groups as researchers racing to identify a novel infectious agent that is rapidly approaching pandemic levels of infection. The simulation includes a variety of realistic challenges that researchers face when dealing with outbreak situations.

○ Materials for the Simulation

- *A list of "actions" that students can take in order to identify and fight the pathogenic agent.* This list of actions and their associated costs gives students a basic starting point to offset the

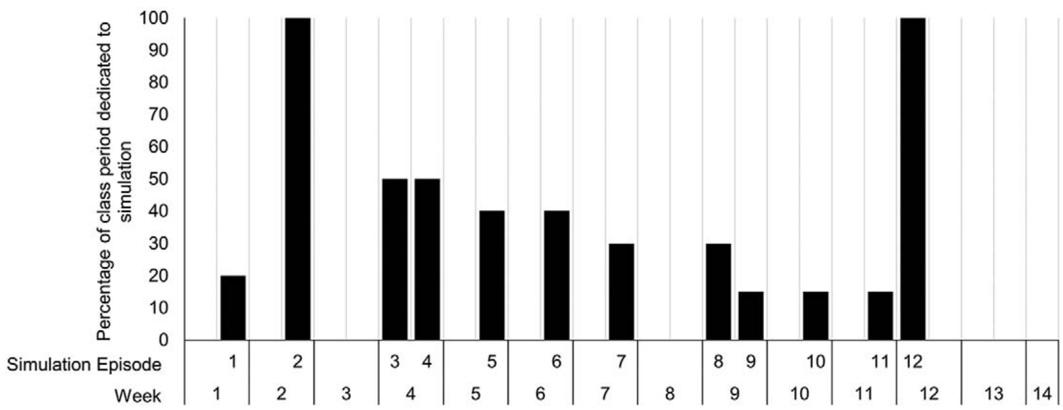

Figure 2. Examples of how the simulation episodes can be distributed throughout a semester. One or two episodes occur each week, with variable amounts of dedicated class time based on students' comfort with the material and the requirements of each episode.

enormous undertaking involved in pathogen identification, characterization, and treatment (Table 1). This action list is not exhaustive. This simulation is designed to encourage students to think outside the box. When a student wants to perform an action that does not fall under the rubric of the currently specified actions, the instructor can add a new action and assign an "action point" (AP) cost. The instructor should keep notes on any variations made so that they can be held constant for any other lab that would like to perform that action. In my experience, students feel the most excited and learn the most when they come up with an experiment that is not on the list.

- *A spreadsheet to track the spread of the infection during the simulation.* I created a very basic model of a disease whose mortality and capacity for transmission can be altered between iterations of the simulation. This spreadsheet calculates the spread of the disease each week, assuming that the government is taking some reasonable precautions to prevent disease spread and limit death. As the students discover more information about the pathogen, the instructor can alter the efficacy of the treatments performed by the health care industry accordingly, thereby decreasing the death rate. These numbers can also be determined manually by the instructor.

Table 1. Potential actions and their action point (AP) cost.

Action	AP Cost	Required Submissions	Usage Restrictions	What This Action Does
Animal Studies	2	A description of how you are conducting your study, plus one cultured sample	Must have successfully performed the Establish Maintenance/ Growth Conditions to use	Can test the mechanism of transmission of the disease in an animal model Chance of uninterpretable results = 50%)
Collaboration	1		Can only be used once/ Episode	Allows all groups who use this action to share information with other groups using this action and allows groups to look at *all* previous information shared via the collaboration action
Establish Maintenance/ Growth Conditions	1	One infected sample	Must have performed at least three separate, successful sample analyses	Allows the researchers to learn to cultivate the pathogen in the lab Taking this action does not guarantee success For every time this action is taken the group has a 10% chance of success This chance of success is improved (by 5%) by use of any sample analysis action
Grant Writing	2	Short paragraph or presentation about why your lab should be funded	Can only be used once per episode	Labs apply for funding If funded, the lab will receive 5 AP for each of the next two episodes
Grow/Culture Samples	1			For each use of this action, the lab will receive two infected samples of a requested type or the pathogen cultured in isolation
Loan	0		Can only be used once per episode	This loan will provide the 5 AP for use in *this* episode This loan must be paid back before the end of the simulation, with an interest rate of 1 AP per episode
Make Antibody	2	One cultured sample	Must have successfully performed the Establish Maintenance/Growth Conditions to use	Make an antibody specific to the isolated pathogen For each use, the lab will receive enough antibody for use in two experiments
Potential Vaccine Identification	1	Submit the vaccine that you have identified		The researchers use the VIOLIN database (http://www.violinet.org/) to determine if there is already a vaccine in development that could be modified to treat this outbreak

(continued)

Table 1. Continued

Action	AP Cost	Required Submissions	Usage Restrictions	What This Action Does
Request Samples	1	A description of what types of samples you are requesting		For 1 AP, researchers can receive two infected samples of one sample type, four uninfected samples of the same type, or one infected and two uninfected samples of the same type These specimens will be available for use during the following episode and can be used twice unless they are degraded during an analysis
Microscope Imaging	1	A description of the experiment you are performing), plus samples for analysis		Obtain pictures of samples at specified magnification using a type of microscope specified by the researcher All samples used in this assay have a 5% chance of degradation Chance of uninterpretable results = 30%
Directed Protein Analysis	1	A description of the experiment you are performing), plus samples for analysis		The researchers to look for a specific protein or group of proteins All samples used in this assay have a 5% chance of degradation Chance of uninterpretable results = 30%
Undirected Protein Analysis	2	A description of the experiment you are performing), plus samples for analysis		General changes in protein expression between specified samples All samples used in this assay have a 5% chance of degradation Chance of uninterpretable results = 50%
Directed Nucleotide Analysis	1	A description of the experiment you are performing), plus samples for analysis		A specific gene sequence or class of sequences present in analyzed samples All samples used in this assay have a 5% chance of degradation Chance of uninterpretable results = 30%)
Undirected Nucleotide Analysis	2	A description of the experiment you are performing), plus samples for analysis		General changes in gene expression between specified samples All samples used in this assay have a 5% chance of degradation Chance of uninterpretable results = 50%)
Interaction Analysis	1	A description of the experiment you are performing), plus samples for analysis		Examine the interactions between two groups of proteins or nucleotides This action must be used in concert with an assay that can properly visualize the results of the interaction assay All samples used in this assay have a 5% chance of degradation (chance of uninterpretable results = 40%)
Vaccine Development	6	A short paragraph explaining your general plan for vaccine development, plus infected or cultured samples	Can only be used once per episode	If there is not a vaccine that is already in development, then the researchers must develop their own This is a process that normally takes months at best In this simulation a vaccine can be developed following four uses of this action in a highly accelerated fashion

(continued)

Table 1. Continued

Action	AP Cost	Required Submissions	Usage Restrictions	What This Action Does
Vaccine Testing	8	A short paragraph explaining your general plan for vaccine testing	Must have successfully performed the Establish Maintenance/Growth Conditions *and* Potential Vaccine Identification or Vaccine Development actions to use Can only be used once per episode	In order to move a vaccine from the research lab to the clinic the vaccine must go through three phases of clinical trials, each of which takes months In this simulation this process will be accelerated A vaccine can be tested for safety following three uses of this action Every time that this action is performed there is a 20% chance of failure If failure occurs, then the vaccine will not be considered safe for use in humans
Write a Paper	1	A brief summary of the information you wish to include in your paper	Can only be used once per episode	This action allows the laboratories to convey salient information about the disease-causing agent to the instructor and the community at large For improvements in treatment to occur papers must be published

- *A list of random events that can alter students' ability to perform the actions during each episode.* To help the simulation remain fresh and interesting throughout the semester, I included an opportunity for "random events" that create problems that the students must adapt to. These random events represent real-world issues that a research laboratory might have to deal with in addition to an outbreak (Table 2). Random events emphasize the idea that things do not always go as planned, and that human and technical errors are often unavoidable. At the start of each episode, one student from each lab rolls a large, 20-sided die whose result determines the random event that affects their lab. The students enjoy this element of pageantry, and it makes them feel involved in the fate of their lab. Furthermore, this strategy avoids students feeling that some labs are being treated unfairly.
- *Clearly defined parameters for the pathogen causing the outbreak.* A clearly established pathogen will ensure continuity of data throughout the simulation. For my simulation, I drew inspiration from malaria, ebola, and cholera. I strongly suggest altering the pathogen and mechanism of transmission based on your course and the students' familiarity with different types of infections. The pathogen can and should be modified with current events to further stimulate student engagement.
- *Data for students following their proposed experimental analyses.* The data provided will be highly variable, based on the types of experiments the students perform and the controls they include. Figure 3 provides some examples of the data I provided to my students.
- *Optional additional materials include* a 20-sided die, AP cards to help students keep track of their resources, patient sample cards to help students track the samples they can use in experiments, and markers to write on the cards. While not required, the students appreciate having physical game pieces to interact with. This helps increase the engagement of all the students in the group as multiple people can set up different experiments simultaneously. However, physical game pieces can easily be replaced by having the students submit their action plans online and by using random number generators if you have trouble getting the physical materials together.

○ Running the Simulation

As mentioned above, this simulation is composed of a series of episodes that build on one another to ensure that the students have a standardized platform for progression into the experimental-design aspects of the simulation.

Episode 1: The Introduction

The instructor explains the general purpose, logistics, and grading of the outbreak simulation within the course, and facilitates the students' selection of laboratory groups (three or four students each). This episode is the instructor's first opportunity to get the students interested in the disease they will be combating, by providing the students with some of the initial symptoms being observed in the general population.

During Episode 1, the goals of the simulation should be clearly defined for the students from a learning perspective (see above) as well as within the simulation (e.g., "To discover the pathogenic agent, the mechanism of transmission, and the best mechanism of treatment and prevention as quickly as possible to minimize death and spread").

Laboratories cannot function effectively without funding to pay for their experiments. Students will be required to compose short funding requests throughout the simulation, but early on it is helpful to have them write a very general, short-format grant application (like those for graduate NSF funding) as a laboratory group (see Supplemental Material available with the online version of this

Table 2. Random events as determined by rolls of a 20-sided die (D20).

Random Event	Roll on a D20	Description	Additional Rolls	Outcome
None	1–6	Nothing happens		
Broken Machine	7–14	One of the machines available to students for use is broken and cannot be used during this episode Re-roll the D20 to determine which machine	1–2	Bioanalyzer
			3–4	Confocal microscope
			5–6	Electron microscope
			7–8	Fluorescence analysis
			9–10	Light microscope
			11–12	Mass spectrometer
			13–14	Gel power source
			15–16	PCR machine
			17–18	Sequencer
			19–20	Hood
Lab Accident	15	A serious accident occurs in the laboratory Re-roll the D20 to determine the outcome	1–8	Chemical spill occurs Cannot use the sample analysis actions in this episode.
			9–10	Biohazard containment breach One randomly selected lab member is exposed to the infectious agent You must spend 3 AP to treat this group member during this episode You must spend 1 AP during each of the next three episodes to continue treatment
			11–20	Laboratory injury One randomly selected lab member contracts a small injury You must use 1 AP to treat this person during this episode
Lab Flooding	16	Your laboratory floods due to a hurricane		You are not allowed to use the Grow/Culture Samples or the Establish Maintenance/Growth Conditions actions until you have spent 2 AP to repair the damage
Mislabeling	17–19	Samples get mixed up		Two random samples are lost and cannot be used for the remainder of the simulation
Power Outage	20	Some samples degrade during a power outage		Four random samples are lost and cannot be used for the remainder of the simulation

article). In addition to giving the students valuable grant-writing experience, this exercise will give the instructor a clearer picture of the levels of conceptual mastery with which the students are entering this simulation.

Episode 2: Familiarization with Lab Techniques

In this episode, students will briefly present an assigned common experimental assay to the rest of the class. Their presentation should include a discussion of how the assay is performed, the types of samples the assay can be used with, an example of output data, and how to interpret the data. In addition to ensuring that the students are familiar with some techniques they can use, these presentations give students practice conveying scientific information to a lay audience, a skill that is vitally important for young scientists.

Following this episode, each lab should submit their grant proposal (see above) and the instructor should assign a starting number of action points to each laboratory based on the quality of their grant proposals (average = 10 AP).

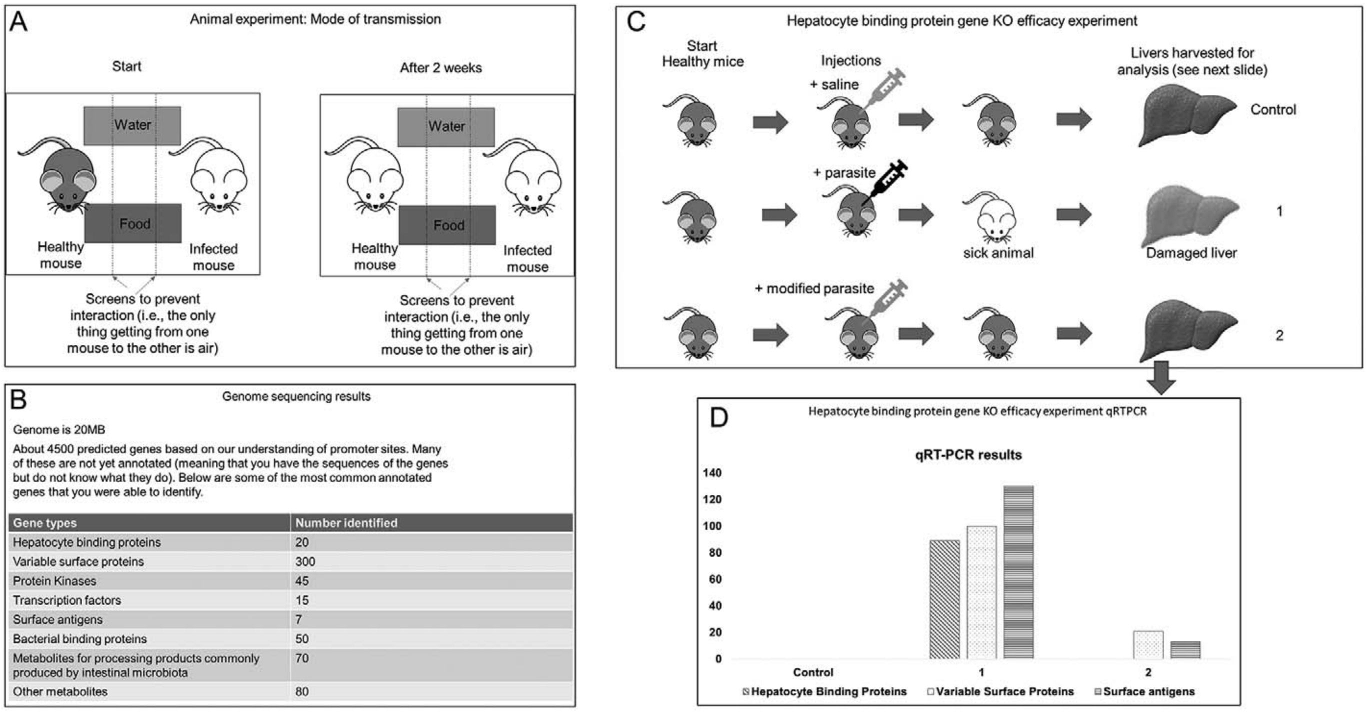

Figure 3. Sample data provided to students based on the experiments they designed. (**A**) Mode-of-transmission experimental results. (**B**) Data following a genome shotgun sequencing. (**C**) Animal experiment based on the results received in B. (**D**) Analysis of liver samples obtained in C. Note that data samples B–D were all taken from the same laboratory group.

Episodes 3–11: Research

The *instructor* should begin each research episode by updating the students on the progress of the disease as determined using the progression spreadsheet (e.g., the number of known infections and the number of dead patients). Episode 3 is the first iteration of the research that students will be doing for the remainder of the simulation, so it is important to make sure that they understand how the research will work. The instructor should clearly explain each of the possible actions a lab might use (Table 1) as well as the random events that will hinder the students during each episode (Table 2). During Episode 3, the majority of APs will be spent obtaining samples and writing grants. The instructor should circulate and help the students carefully consider the types of samples they want to request based on the symptoms, their hypotheses, and the future experiments they would like to perform (which should have been mentioned in their grant proposal).

Following Episode 3 (and every subsequent episode), the instructor should apportion samples and data. Each assay the students perform has a chance of having uninterpretable data, in which case the lab will not receive data for that experiment but will still lose the action points spent (Table 1). Once the instructor has created the data output for the successful student-designed experiments, this information should be returned to each lab quickly. Maximizing the students' time to consider the results before they are asked to design experiments again will help them more thoroughly process the data and devise innovative next steps. When the instructor sends the students their data, it is also advisable to provide some initial feedback on the experiments they performed, indicating how certain controls might help clarify their results in the future, and so on. Furthermore, during every research episode, the instructor should circulate and discuss plans and ideas with the students, ensuring that they are progressing as expected and providing support where required.

All papers published by the laboratories using the "Write a Paper" action should be shared with the other labs (regardless of whether the "Collaboration" action was used) to promote flow of ideas among groups (Table 1). Based on the accuracy of the claims in the paper, the instructor should improve the worldwide efficacy of pathogen treatment, which will be reflected in subsequent decreased death rates. In other words, as the students gain a clearer understanding of the pathogen, the death rate among infected individuals will drop.

Seven to nine research episodes is usually a good number to allow students to get the hang of the simulation without losing interest; however, this can be adapted on the basis of course constraints.

Final Episode: Simulation Debrief

Students should be given an opportunity in class to reflect on what they gained from the outbreak simulation. I have students write a paper about the outbreak from the point of view of a journalist who was reporting on the disease. Writing this short paper prompts the students to think about outbreaks from other perspectives than that of a researcher and provides a foundation for our in-class discussion. The simulation debrief is also a good time to show the students what they achieved. In many cases, the students will not completely eradicate the disease in the time provided, so it is important to demonstrate how much worse the death toll would have been without their interventions. This time can also be used to discuss how the outbreak simulation might be related to current events and how students' previous experiences with pandemics influenced their choices during the simulation.

○ Assessment of Learning Outcomes

The assessments that an instructor includes as part of the outbreak simulation should address the desired learning goals. I incorporate some low-stakes graded assessments (the group grant and protocol presentation) early in the simulation, but the majority of the simulation grade is based on participation and effort. This simulation is meant to provide a *safe space* for students to experience some of the challenges and successes they might encounter during careers as researchers. I employ surveys throughout the simulation to determine students' self-reported progress toward the learning goals I had established (Figure 1). Additionally, these surveys are helpful in determining student receptivity to the simulation, allowing the instructor to adjust aspects of the simulation to better suit the needs of each specific class. I also frame my course exams as based on experimental design and data analysis, which helps in monitoring student proficiency with these skills throughout the course.

○ Concluding Remarks

While literacy in experimental design and data analysis is a cornerstone of a thorough STEM education, it can be difficult to cultivate student engagement with these concepts, especially in courses that lack a laboratory component. In my experience, the use of game-like simulations greatly enhances student engagement in and retention of the knowledge relevant to the topics addressed. I have shared this outbreak simulation – designed to polish students' ability to perform essential scientific skills – in the hope that others might be able to utilize this or similar activities in their own courses. This simulation is intended to act as a scaffold on which others can be built to conform to the needs of each individual class. A continuous cycle of student feedback and revision is an important aspect of creating a simulation that will best serve the needs of each instructor.

○ Acknowledgments

I would like to thank Christine Brewer and Gabriele Bauer for their help in solidifying these ideas and the Villanova VITAL for providing summer funding to develop this simulation.

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