Challenges in Mentoring Mathematical Biology Model Construction: Mechanisms and Listening

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The researcher observed the project proposal week of an undergraduate research program in applied mathematics, where students took the lead in choosing a topic and developing their own research question. Results from the stories of two of the groups suggest that students struggled with identifying mechanisms that would inform the development of their research question and model, while mentors struggled with allowing students to direct the project and presentations.

Keywords: Mathematical biology, mathematical modeling, mechanism, research question, student-led project

Mathematics as it is taught in secondary and post-secondary classes differs greatly from mathematics as it is practiced by professionals (Lewis & Powell, 2017). Mathematics as it is taught in undergraduate classes is also divorced from the immediate needs of partner disciplines in the sciences, humanities, and social sciences (Ganter & Barker, 2004; Ganter & Haver, 2011). Reports from industry and professional societies repeatedly emphasize the importance of professional skills in communication, collaboration, problem solving, mathematical modeling, and creativity on top of a solid foundation of procedural skills and coherent mathematical understandings (Bliss et. al., 2016; Casner-Lotto & Barrington, 2006; Ganter & Barker, 2004; Ganter & Haver, 2011).

The skill of interest to this report is a skill for STEM and non-STEM described undergraduate mathematics classes described by Bliss et. al. (2016) as "Distilling a large ill-defined problem into a tractable question," which I will simply call "developing a research question." Smith, Haarer, and Confrey (1997) found that graduate students in applied mathematics struggle with developing research questions and mathematical models that are too applied and mathematically intractable, or are too mathematical with little application.

Camacho, Kribs-Zaleta, and Wirkus (2003) found that choosing one's own project and research question creates situations in which students' take the lead in researching topics far outside a mentors' area of expertise, essentially reducing the mentor to a role of consultant rather than leader. And these unique situations create opportunities to identify key components of soft-skills such as developing a research question. Encouraging students to follow their interests and positioning students as experts is also an equity directed practice that engages students with high level questions where students can participate and succeed in more ways than just performance, and students are engaged in contexts that connect with and respect their own experiences (Aguirre, 2013; Castillo-Garsow & Castillo-Chavez 2020; Goffney et al, 2018; Rubel, 2017).

This study follows two groups of undergraduate students who developed a topic of their own interest into a research question and accompanying mathematical model. Because the students in this project work in close collaboration with both graduate and undergraduate mentors, we have an opportunity to see how mathematicians at different stages of their career view the task of developing a research question and accompanying model. The purpose of this paper is to identify challenges than mentors and students may encounter while collaborating on a student led applied mathematics project, both to inform mentors and to inspire future research.

These two groups were selected for discussion due to a common theme in the results. A recurring idea that students encountered in constructing their projects was mechanisms. Although the meaning of “mechanism” remains debated in the scientific community (Craver & Taber, 2015; Hunt et al., 2018), the term mechanism comes from the idea of describing the function of a machine that would replicate a hypothesized scientific process (Craver & Taber, 2015). For our purposes, a mechanism is an interaction between biological parts that could explain an observed behavior, and is precise enough to suggest a mathematical relationship.

Methods

This study occurred in the fifth week of an eight-week summer research experience for undergraduates (REU) in mathematical biology. Prior to this study, the students had taken a three-and-a-half-week course consisting of lecture, computer lab work, and textbook exercises in dynamical systems. Following this course work, students self-recruited into groups of three to five, and chose a topic of interest. During the fifth week, students made daily presentations on their topic to a panel of faculty and graduate mentors who provided feedback. In the final three weeks of the program, students completed the analysis of their model and wrote a technical report on their project. Four groups of students chose to participate in the study, and this a case study from two of those groups. Analysis of the other groups can be found elsewhere (Castillo-Garsow, 2021, 2022).

The two groups in this study were formed of four undergraduate students each. One group wanted to study the relationship between eating disorders and the menstrual cycle (menstrual group). The other group was interested in developing a spatial simulation of tumor growth (tumor group). Both groups completed a technical report that was reviewed by the mentors. Neither group has published their research in a peer-reviewed journal by the time this paper was written. Both groups presented over six days to a panel of faculty and graduate mentors who provided feedback to the students. The menstrual group presented once per day. The tumor group gave seven presentations over the six days, with two presentations on day five. Each presentation was video and audio recorded, and the recordings were transcribed. Transcripts were open coded (Corbin & Strauss, 2014), and themes emerged that identified and explained the primary areas of conflict in goals between mentors and students. The results here are a case study of those transcripts, focusing on creating a narrative of those conflicts (Flyvbjerg, 2006).

Results

Menstrual Cycle Model

The menstrual group was interested in studying the interactions between eating disorders and disruptions to the menstrual cycle. They identified a mediating hormone: leptin, that affected both appetite and the secretion of hormones related to the menstrual cycle (Figure 1). However, the group’s final model did not include any leptin or eating disorders, focusing only on modeling the menstrual cycle.

Mentoring Challenge: Following the students’ lead. Students in this group were extremely consistent about their interests and research question. Their research question changed very little over the six day period, from “Tracking eating disorders through hormonal irregularities in the menstrual cycle” (day 1) to “what is leptin's effect on the induction of the menstrual cycle?” (day 6). However, mentors expressed concern that this research question would lead to a model complex enough to have interesting dynamics: “You cut from [leptin] because that only can impact to the forward. You do not have anything feedback.” (day 2). Eventually, mentors simply forbade students to work on leptin and appetite. “This is your model, only focus on this one, no leptin yet… then, if there is time, you go adding the leptin.” (day 6).

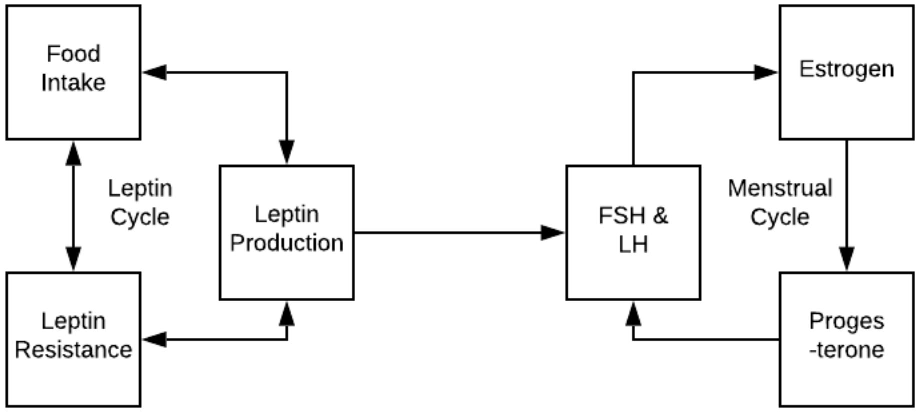

Figure 1. Leptin influences both eating habits and the release of hormones involved in the menstrual cycle.

This problem occurred because the students struggled to explain the mechanisms and relationships that they were interested in when describing their research question. Fundamentally their biological context had two feedback cycles: a cycle in which eating habits and leptin influence each other, and the cycle of hormones that regulate menstruation (Figure 1). What students were interested in studying was really the dynamics of eating disorders (Figure 2).

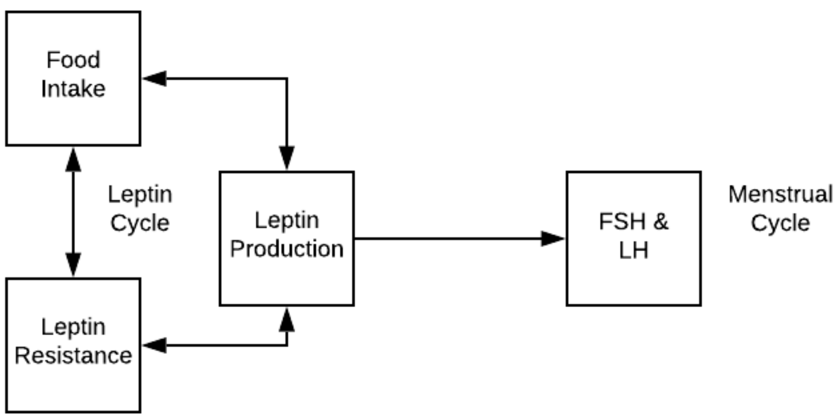

Figure 2. Representations of the part of the problem that held the students' interest.

The mentors had three objections. First was that there were other regulatory processes that influenced the hormones FSH and LH (Figure 1), and that made isolating these hormones from the entire menstrual cycle difficult. Second is that students focused early on leptin early on, and simplified their message to "We're studying the effect of leptin on the induction of the menstrual cycle." This created in the mentors an understanding that students were interested in studying a problem more like Figure 3. This led to the last objection: In both Figures 1 and 3, the effect of Leptin is only feed-forward. There was no obvious impact of the menstrual cycle on leptin production, meaning that leptin could be reduced to a simple input function in a menstrual cycle model, and didn't need to be studied dynamically.

Additionally, with the students found and presented prior modeling research on the menstrual cycle, and mentors, encouraged the students to dive deeper into these models, giving the project a greater and greater appearance of being about the menstrual cycle over time. The mentors did also make recommendations for prior modeling research on leptin, but as the mentors focused more and more on menstruation, opportunities to present leptin research didn't occur.

The students could likely have completed a successful project studying only the leptin cycle that would have been more in line with their interests. However, due to the problems in communication, the mentors steered the group towards a successful project studying only the menstrual cycle.

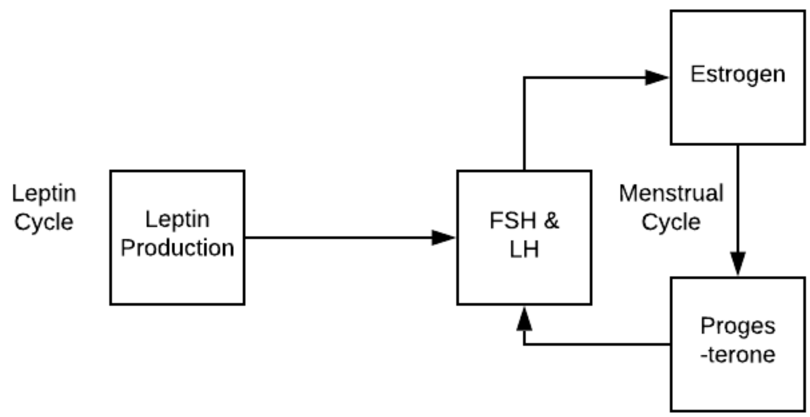

Figure 3. A depiction of a mentor's understanding of the menstrual cycle group's problem.

Student Challenge: Behavior vs. Mechanism. The menstrual group's communication difficulties were exacerbated by their confusion over biological behavior and mechanism. Students would answer questions about mechanisms with answers about biological behaviors. See this excerpt from day 2:

Mentor The levels of FHS and LH, how do they change?
Student: Here's a phase here called the follicular phase and that's where there's follicles that the FSH-- when the secretion of FSH happens, they create follicles that create granules that create the LH. Once the LH is there, these two hormones are able to mature the whole egg for release into the fallopian tube.

In this excerpt, the mentor is asking about mechanisms: asking the students to explain interactions that cause concentrations of FSH and LH to go up and down, or impact the rates at which these concentrations go up and down. The student responds not with an explanation of how FSH and LH change (a mechanism), but instead with an explanation of what FSH and LH do, how they impact the body (a behavior).

The idea of a mechanisms as a biological interaction that defines mathematical expressions is a relatively nuanced idea, and at least one mentor found it unsurprising that students struggled with this idea:

*Student***:** Can I ask a question? You're saying we're not understanding what is the mechanism. Honestly, I don't know what exactly that means in terms of mathematics I'm not sure what that means. Can you explain that to me?

Mentor: This is a very beautiful question that you're asking actually many of us are understanding in a different way also. That's why it will help you when you will draw that flowchart. We will precisely say, "Oh this is what we mean by saying mechanics." [The mentors] are using words like feedback which is almost the same thing as mechanism. Some people use different words for the same concept.

With feedback, students improved at describing mechanisms, "Estrogen at low concentrations has a decreasing effect on LH. The higher concentrations of estrogen, LH seems to have this peak at higher concentrations of estrogen" (day 3); however, they continued to struggle with this distinction and described biological behaviors when mechanisms were asked for: "FSH is entered through the ovaries through the capillaries." (day 3).

The Tumor Model

Student Challenge: Finding a research question. The tumor group was interested in simulating the growth of a tumor in the lungs using a spatial model. However, with this focus on methodology, the students in the group struggled to find a research question. Over seven presentations and five days, the group proposed several different research questions, including studying the effect of a treatment strategy, studying attacks between cells, studying competition between cells for nutrients or space, or studying the internal processes of a cancerous cell in the lung. Finally with the encouragement of mentors who provide prior modeling research, the students settled on studying a tumor's chemical defense against the immune system. What remained largely consistent for the group was the choice of topic: tumor growth in the lungs, and the choice of methodology: a two dimensional spatial simulation. The students were a group with a chosen topic and methodology in search of a problem.

Student Challenge: Mechanism vs. model. Part of the reason for the students' difficulty in identifying a research question was that they struggled to understand the biology in terms of mechanisms of interaction. In contrast with the menstrual cycle group, which described biological behaviors instead of mechanisms, the tumor model frequently described abstract modeling concepts instead of mechanisms.

The core of the tumor model's struggle was defining the concept of "fitness" in terms of mechanisms. The group wanted to explore a hypothesis that cells could sense the fitness of neighboring cells and induce apoptosis in neighboring cells that were less fit. However, the group struggled with explaining mechanisms that would determine which cells would win in an interaction cells. The could not identify what process a cell was sensing in a neighboring cell, how that process was being sensed, or what determined whether an attempt to induce apoptosis would be successful.

Definitions of fitness given by the students included "an ability of the cell to thrive in a given environment" (day 1), the growth rate of a cell (day 2), a change in the equilibrium of the tissue (day 2), "how normal the cell is" (day 2), "the length of a cell's cycle" (day 2), "the rate of protein synthesis" (day 2), and the number of cells that a cell divided into (day 2). Several of these ideas, such as "ability of a cell to thrive" or "how normal a cell" is were based on abstract concepts that a modeler might define a measure for, but that a cell would not be able to sense. Others, such as the number of cells a cell divided into, required access to information that the cell could not react to for the fitness sensing hypothesis, because the replication would have already completed. Some of these ideas, such as the rate of protein synthesis, provided potential explanations for what a neighboring cell might be sensing, but students did not follow up on these ideas. Students also answered questions about this fitness sensing process with modeling rules and assumptions, such as: “We wanted to do a spatial model using a grid… If the neighbor cells will have more fitness, it would be able to occupy their space.” (day 2).

One complete mechanistic explanation that the students provided was that a cell would sense a nearby cell’s preparation to divide and release a toxin, and that tumor cells were more fit because they were resistant to the toxin. However, this explanation was not consistent with the hypothesis that neighboring cells sensed “fitness,” as the fitness mechanism occurred after the cell released its toxin, instead of the toxin being released in response to what the cell sensed.

Ultimately students abandoned the fitness sensing hypothesis, and instead built their research question on a previously published model for the interaction between the immune system an tumor growth, focusing on the ability of tumor cells to inhibit the maturation of immune cells by releasing a chemical. The students retained the interest in spatial models and cancer modeling by focusing on the local effects of the chemical release on interactions between tumor cell and immune cell pairs.

Mentor Challenge: Letting students explain at their own pace. Once the students settled on a research question, they developed a spatial continuous time Markov-chain model to simulate the tumor growth. However, the students were not familiar with this terminology, and instead explained the model as a cellular automaton. “We're going to model this with a stochastic cellular automata where our events are going to be discreet and the time of the transmission between the pair of events is going to be continuous.” (day 5 presentation 1). The students had an outline in mind, where they would introduce the idea of a stochastic cellular automata, then random time between events, the list of possible events, examples of these events, and then finally introduce equations for how the probabilities of events were calculated. However, the students were quickly thrown off script.

One mentor focused on the idea of cellular automaton and imagined a simulation driven by simple rules, similar to Conway’s Game of Life. This mentor expected a slide of rules that would be explained all at once. The students felt their simulation was much more complex, and wanted to explain rules and interactions one at a time. This created in mentors the impression that students did not understand the rules that governed their simulation: “Please go learn about Conway's Game of Life and then this will make it much clearer” (day 5 presentation 1), “If T encounters this condition it does this. If T encounters this condition, you do this. You have to work all this out otherwise you're not going to be able to do it.” (day 5 presentation 1). The students were called back for a second presentation on the same day.

In the second presentation, the students maintained a similar structure. Introducing the random time between events before moving to a list of events. “We consider continuous-time Poisson process, the events on the wheel and the waiting time between events are continuous, distributed as exponential” (day 5, presentation 2). The main difference in the presentation was that as one student discussed each event on their slides, another student wrote the equation for the probability of the event on the whiteboard. Mentors were much more receptive in this second presentation, offering direct feedback on the equations and identifying the methodology as a “standard continuous time Markov chain” (day 5, presentation 2). In total, the first presentation lasted almost 42 minutes, while the second presentation was completed in under 10 minutes.

One factor that may have contributed to the mentors’ responses to the first presentation is concern about time. Mentors had previously expressed concern about the short time frame left to complete the project “Remember you have three weeks” (day 4), and this presentation on day 5 was supposed to be the second to last presentation, meaning the mentors had only one more opportunity to review the students’ model as a whole group. The time pressure may have contributed to the mentors’ anxiety about students not having a model or not presenting the model efficiently, leading mentors to take more control of the presentation than was helpful.

Discussion

Both groups of students struggled to understand the modeling concept of a mechanism. The menstrual cycle group identified biological behaviors – such as the maturation of a follicle, or the release of a hormone – rather than identifying causes of those behaviors. They also struggled with identifying mathematical quantities such as the concentration of a hormone, describing instead qualitative behaviors. The tumor group also struggled with identifying mechanisms, although rather than focus on biological behaviors, the tumor group identified abstract constructs such as fitness, and struggled with connecting those modeling concepts to biological behaviors such as sensing the concentration of a particular protein.

While the students struggled with identifying mechanisms, the mentors struggled with letting students take charge. In the case of the menstrual group, concerns about the potential for the project to generate interesting dynamics caused mentors to encourage students to move away from their interest in eating disorders to focus more on the menstrual cycle. In the case of the tumor group, taking charge of the research question was necessary. The students’ focus was primarily on methodology (a spatial simulation of cancer), and they struggled with identifying a problem that would match that methodology while providing innovative insights. Where mentors struggled with the tumor group was letting students take control of the presentation and present the tumor model in a way that made sense to the students. This may have been due to anxiety about the remaining time, or difficulty trusting in the students’ ability to construct a model.

These anxieties are not unique to faculty. For example, Smith et. al. (2021) found that pre-service teachers of mathematics also struggled with anxiety related to trusting students with open ended projects: concerns that students would be capable of completing the project, and anxiety about letting go of control of the classroom. Similarly, the mentors felt anxiety about the tumor group’s ability to construct a model in the one day remaining and took control of the presentation on day 5. In the menstrual group, anxiety about student’s ability to construct an interesting model also led mentors to take some control away from the group, but in a more subtle way.

Although neither group completed the project that the students initially envisioned, both groups successfully completed a project related to their initial idea. And the students in both groups expressed satisfaction and pride in their projects when they were complete.

Conclusion

The students in this study had stated interests in topics, and the mentors were concerned with ensuring that students could complete a scientifically significant project within the time limit. In both cases, students struggled to explain the mechanisms of their projects to mentors, and this led mentors to take more control over the direction of the projects. Understanding and identifying mechanisms is a key challenge in mathematical biology (Reed, 2004), and scientists continue to debate the precise meaning of the term (Craver & Taber, 2015; Hunt et al., 2018). More research is needed in the area of how scientists, mathematicians, engineers, and students understand mechanisms differently.

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