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Education Article

Math Bio or Biomath? Flipping the mathematical biology classroom

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Abstract

Mathematical and computational methods are vital to many areas of contemporary biological research, such as genomics, molecular modeling, structural biology, ecology, evolutionary biology, neurobiology, and systems biology. As such, the contemporary life science student needs to be exposed to, if not well-versed in, many areas of mathematics to keep pace. However, traditional ways of teaching mathematics may not be able to provide life science majors the skills and experiences necessary to effectively use mathematics in their careers as practitioners and/or researchers, as these skills and experiences (for example, mathematical modeling and interdisciplinary collaboration) are difficult to teach using lecture-style approaches. In this paper the authors describe the implementation and assessment of a flipped-classroom approach to teaching a sophomore-level mathematical biology course for life science majors.

Keywords: flipped classroom, course description

1 Introduction and Motivation

Modern discoveries in biology, and the life sciences in general, have opened up a plethora of interesting and important questions, many of which will unlikely be answered without significant mathematical modeling and analysis [42]. Despite this, the quantitative training of undergraduate life science students is generally considerably less rigorous than that of students in the physical or mathematical sciences, prompting the reports BIO 2010: Transforming Undergraduate Education for Future Research Biologists and Vision and Change in Undergraduate Biology Education: A Call to Action to argue for a significant increase in the mathematics training for future biology researchers [7, 27]. In response, some mathematics and biology departments have begun providing courses and, in rare cases, programs aimed at preparing students to become tomorrow's mathematical biologists (see contributions in [22, 35, 41] as well as [36]). For example, according to the Society for Mathematical Biology, at least 18 universities in the United States have undergraduate degree programs and at least 25 have graduate programs in mathematical and/or quantitative biology [40]. However, many universities without a program in mathematical biology offer only a few (often one) mathematical biology courses for life science students interested in mathematics, due to the large volume of courses required to complete a life science major [9, 21]. Additionally, these courses attempt to pitch the course content simultaneously towards many different life science student subpopulations. These realities come together to form a very difficult pedagogical task, one that has only recently gained the attention it deserves [22, 41].

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Much of the pedagogical difficulty associated with constructing and delivering a mathematical biology course stems from students' academic diversity and the role mathematical modeling plays in the interface between biology and mathematics. In any given mathematical biology course there may be students with majors in biology, biochemistry, cellular and molecular biology, chemistry, mathematics, microbiology, pre-medicine, pre-pharmacy, and physical therapy, among others, despite the relatively small (about 20 students) class size. These students both have a wide range of career goals [6] and mathematical preparation and maturity, possibly more so (at least per-capita) than many other courses in the traditional mathematics curriculum. This means that a traditional mathematical biology course is challenged to either start at such a low level so as to bore students aptly prepared for the course (freshmen straight from first-semester calculus, for example) or at a level too high for many of the students (seniors who haven't taken mathematics since freshman year, for example) to successfully assimilate. Thus, it is possible that no student ends up being the ideal audience.

A great deal of the process of solving real problems in mathematical biology involves continuously cycling through the mathematical modeling process. Mathematical modeling, a subdiscipline of mathematics that is, at best, scantly present in the background of today's students, is often described as more of an art than a science [5, 20, 22, 39]. Thus, developing the students' knack for mathematical modeling should be a main focus of a mathematical biology course for students in the biological sciences, as the students taking this course will likely eventually fall into a category of students that appreciate mathematics not for its own sake, but for what it can do for them in their careers.

Identifying these pedagogical issues prompted the first author's decision to deliver mathematical biology at the University of Wisconsin-La Crosse via an inverted, or "flipped" classroom environment in the spring of 2013 and 2014. The flipped classroom, described by Lage et al. [19], and popularized by Khan [18], is an environment in which "events that have traditionally taken place inside the classroom now take place outside the classroom and vice versa". This inversion can take many forms, from simply requiring students to read the book outside of class before spending class time working on well-crafted problem sets to the creation of large libraries of video lectures replacing all of the traditional lectures for the course so that class time can be used to explore deep, multifaceted problems with the help of the instructor.

There is growing evidence from rigorous assessments and anecdotal observations supporting the notion that inverted classroom environment improves student performance and long-term knowledge retention relative to the traditional lecture paradigm, and this evidence spans many disciplines and levels of instruction [2, 4, 12, 16, 18, 25, 26, 31, 43, 46]. Additionally, a number of reports over the last two decades have prompted those in the undergraduate biology education community to call for a more "student-centered classroom" (see Chapter 3 in [7]). In practice, student-centered classrooms tend to be interactive, inquiry-driven, cooperative, collaborative, and relevant. Classes authentically mirror the scientific process, convey the wonder of the natural world and the passion and curiosity of scientists, and encourage thinking [7]. Finally, the process of collaborating and interacting with individuals across the mathematical biology spectrum is essential to doing good interdisciplinary research, and is a skill that emerges especially well into a flipped classroom where students, coming in with a large variety of abilities, academic backgrounds and career goals [6], work in groups for much of the time in the classroom. These characteristics make the flipped classroom approach particularly well-suited for a course in mathematical biology aimed at life science students.

To implement the new inverted classroom in a sophomore-level mathematical biology course, the authors used a total of 35 biological case studies, which ranged from 15-minute modeling exercises to two-lecture-long problems involving multiple analysis techniques and computer programming. These case studies, many of which were gleaned and amended from existing mathematical biology, ecology, genomics and evolution textbooks [13, 14, 17, 22, 29, 23, 32], are intended to simulate various aspects of a real-world biological problem one would encounter as a researcher or professional in the life sciences. Many were broad enough to require the students to explore all of their accumulated mathematical modeling expertise in order to solve the problem. The students were also required to complete two individual writing projects, one of which consisted of reading a research paper and reproducing the mathematical results in this paper. In order to develop the mathematical maturity and computer programing skills necessary to tackle these case studies and the mathematics in these research papers, the authors produced 75 video lectures, ranging from 5 minutes to 25 minutes in length. These lectures replaced the aforementioned traditional model of teaching mathematics through a series of definitions, theorems and examples over the course of an in-class lecture. The students were required to view these video lectures prior to attending class, as the activities during class were often extremely difficult or impossible to participate in without the background presented outside of class. This aspect of the flipped classroom is initially the most frustrating for the students, as many are used to simply attending class without having invested time prior to class to prepare without any explicit consequences.

In the remainder of this paper we summarize the development, implementation and results of teaching mathematical biology via the flipped classroom at the University of Wisconsin-La Crosse (UW-L). We also discuss plans for moving forward with further development and refinement of the course, the struggles inherent in flipping a course, as well the development of additional courses in mathematical and computational biology at UW-L.

2 Goals for a Flipped Mathematical Biology Course

Inspired by the budding interdisciplinary research collaborations within their Mathematics Department and the Department of Biology, which resulted in the NSF-UBM-funded Collaborations on Riverine Ecology program (NSF Award Number 1029041), the Mathematics Department at the University of Wisconsin-La Crosse began offering MTH 265[1], Mathematical Models in Biology, as a substitute for the traditional Calculus II course in the spring of 2009. Thus, unlike many mathematical modeling courses focused on biological applications the level of mathematical aptitude necessary for this course is the completion of MTH 175, Applied Calculus or MTH 207, Calculus I (although see [21]). Most of the focus in this course is on the mathematical modeling process, with the main audience being roughly 25 students with majors in biochemistry, but the course has also attracted students from mathematics, microbiology, cellular and molecular biology, pre-pharmacy, physical therapy and chemistry. Additionally, students at all stages in their academic careers, from seniors in their final undergraduate semester to second-semester freshman who just finished Calculus I, enroll in the course.

When creating a mathematical biology course, it is important to ask the following question: What do faculty members in the life sciences want their students to bring to their courses from the mathematical courses they require as a part of their major? Or, possibly more importantly, what mathematical/quantitative skills and experiences do students need once they graduate and embark on careers in the life sciences? While the answers to these two questions may not be identical, there is evidence that they are starting to converge to one another. An answer to the first question can be found in the Mathematical Association of America (MAA)'s committee on Curriculum Renewal Across the First Two Years (CRAFTY, see [15]). Although this report focuses on precalculus courses, the results of this study can provide us with valuable insight into what quantitative skills are valued within the life sciences. Faculty members in the biological sciences, along with those from virtually every other discipline, stressed conceptual understanding, mathematical modeling and problem solving, as well as the interpretation of real-world data as being important skills for their students to acquire in mathematical courses. Some answers to the second question can be found in [7], and are similar to those for the first, which state that tomorrow's

[1] In this paper, we will refer to the mathematical biology course at UW-L as MTH 265.

life scientists will need to be able to work outside their disciplinary boundaries, integrating concepts across levels of organization and complexity and to synthesize and analyze information that connects conceptual domains. Mathematics, mathematical modeling and computer programming provide a wonderful set of tools for such organization.

In order to develop the aforementioned skillset in our life sciences students, we needed to create a setting in which students can

- identify when a biological problem could benefit from mathematical or theoretical treatment,
- create a rough conceptual model for a given biological problem,
- identify possible mathematical structures embedded within a given conceptual model,
- analyze a mathematical model to make predictions about the biological system of interest, and understand the uncertainty associated with these predictions,
- critically analyze the results of a mathematical model, and propose changes to the model when necessary.

For example, if students are asked to estimate the spread of H1N1 throughout North America, they should be able to create a rough conceptual model of how different stages of infection are connected through transmission. Many mathematical structures can be inferred from this conceptual model (e.g. differential or difference equations, individual-based models, directed graphs), with the students hopefully able to pick the most appropriate model for the question they are trying to answer with the maximum tractability. For example, if the goal is simply to estimate the basic reproduction number R_0, a differential equation model may suffice, while an individual-based model may be needed if the disease's spatial profile is needed. Once the students have a solution, it is our hope they can continue the modeling process by comparing this solution to reality (e.g. data or previously-established biological consensus) and go back and make adjustments to their conceptual and/or mathematical model if necessary (e.g. adding a vaccination term [49]), thus continuing the modeling feedback loop.

Many of the above skills are difficult to learn by simply watching the instructor solve a problem on the board, no matter how compelling the problem, and thus the authors' commitment to delivering the course via the flipped classroom setting. In this setting, the students take their class time and solve carefully chosen case studies: scientific problems that will often be posed as an amalgamation of facts and assumptions gleaned from various sources with the necessary mathematical approach possibly unclear at the onset. These case studies increase in their breadth and complexity as the semester progresses, leaving the students able to understand many of the mathematical models in the biological literature. This process can be accomplished by posing problems in a number of different biological settings. In MTH 265 we expose our students to problems in the following areas: population ecology, epidemiology, parasitology, genetics, genomics and natural selection, enzyme kinetics, stoichiometry, biological networks, empirical modeling, and parameter estimation.

In order for the students to make any headway on case studies in these areas of biology, the development of their "mathematical maturity" is necessary. However, the authors' interpretation of developing mathematical maturity as it pertains to the students in MTH 265 does not necessarily involve increasing the students' ability to manipulate mathematical expressions or prove theorems as in a traditional mathematics course. Instead, mathematical maturity in this setting is viewed as the ability to do the following:

- distinguish parameters from variables and independent variables from dependent variables,
- see the connections between models originating from seemingly different biological applications through dimensional analysis and scaling,

- distill a mathematical model down to an algorithm and study this model numerically,
- interpret a model's solution and perform sensitivity analysis on this solution,
- assign a measurement of uncertainty to a model's solution and identify the source of this uncertainty.

As a means to these ends, we introduce students to a collection of biological problems that require a plethora of different mathematical approaches and techniques. Each of these mathematical areas sharpen the students' mathematical maturity in different ways and include

- dimensional analysis and scaling,
- dynamical systems, difference and differential equations,
- stability and bifurcation analysis,
- probability theory and Markov chains,
- inferential statistics and parameter estimation,
- Boolean networks.

Dimensional analysis and scaling is visited throughout the course in order to show students that many of the models used in one area of biology are very similar to models seen in other areas. For example, differential equation models in epidemiology, once nondimensionalized, are very similar to differential equation models in enzyme kinetics. Additionally, it is more straightforward to perform stability and bifurcation analysis on a scaled model with fewer parameters than an unscaled model; the students can demonstrate key stability criterion that parameters need to satisfy without the cumbersome algebra that can often obscure the interesting biology predicted by these models. Through probability theory the students explore what uncertainty means and how it can be applied to biological systems through applications in genomics, genetics, natural selection, and agent-based population models. Inferential statistics and parameter estimation allow the students to see how models are created from data, and how the predictions of these models can be affected by noisiness in data. Finally, Boolean network models provide a non-standard example of the trade-off between model realism and tractability, as well as further highlight the power of mathematics as an organizational tool for understanding complex biological systems.

The goal of exposing students to all of the above areas of mathematical biology is certainly a lofty one. However, mathematical biology is a research discipline where even a trained mathematician is not afforded the luxury of being an expert in only one mathematical subdiscipline or technique. To solve biological problems is to allow the biology to dictate the mathematics used, and thus the goal should be to expose future life science researchers to as many modeling environments as possible. The obvious trade-off is depth. However, it is unreasonable to ask many life science researchers to be experts in any mathematical area, and thus is it preferable for these researchers to know of many different mathematical approaches, even if they are not comfortable executing the mathematics themselves, so that they can seek out the most appropriate resources or people to collaborate with when presented with a problem needing mathematics to solve. This survey approach is the one taken by almost all early courses in the natural sciences but is in contrast to the mathematical sciences' brick-by-brick approach, which is possibly why many life science students are driven away from mathematics (see "Mathematics as a 'Fraternity Initiation'" in [41]).

3 Methods: The flipped classroom

To reach our broad goal of preparing students to be able to use mathematical modeling in their future biological careers we needed to use our precious class time in the most productive way. As it pertains to MTH 265, we use the flipped classroom to devote in-class time entirely to case studies, selected computer programming exercises and assessment of student learning via examinations and mathematical modeling "competitions".[2]

3.1 Video Lectures, Case Studies, and Homework

The students' day-to-day classroom activities are designed to be the main event in a flipped classroom. There is evidence that passive classroom exercises that are not perceived to enhance student learning through collaboration with fellow students and the instructor can lead to students "checking out" of flipped classroom environments [47]. Thus, it is extremely important to structure class time in a way so that students are constantly expected to engage in higher-order learning activities. In MTH 265 we do this through carefully chosen case studies that challenge the students to use a multifaceted approach to gain insight about a particular biological system. These case studies are designed to both gauge the student's ability to use the material being introduced during that time period, as well assess how well he or she has retained the information learned throughout the course up until that point.

Each case study is accompanied by roughly 1–4 video lectures, ranging from 5 to 25 minutes long each. The video lectures, which are produced using either the ScreenChomp [37] or Explain Everything [11] application on the authors' iPad, provide the students with the necessary technical definitions, theorems and worked-out examples that will be necessary to approach the given case study each day, while leaving enough space for these case studies to illuminate some of the intricacies of the broad modeling topic to be explored. For example, when studying the dynamics of interacting populations through systems of differential equations, the video lectures provide the definitions of a system of differential equations, equilibria for a system of differential equations and stability of equilibria. Furthermore, the video lectures provide one example of a model used to study enzyme kinetics; the development of the model, nondimensionalization, computation of equilibria, construction of the Jacobian and phase portrait and interpretation of the mathematical conclusions. The general procedures learned through these lectures can then be applied to in-class case studies exploring the dynamics of consumer-resource interactions, compartmental models and models exploring the principle of competitive exclusion.

Once in this classroom, students work in well-defined groups of 2–3 students on the case studies, with the ancillary goal of fostering the skill of collaboration. This greatly helps the learning process, as some students have a natural knack for mathematical modeling, while some are more skilled at mathematical manipulation or computer programming, while other students need significant help in both of these areas. Often times the members of a group can address each other's concerns (for example, the question of which model to use in a given situation) without the consultation of the instructor. This is a very valuable experience for the students, as peer instruction [24] has been shown to accelerate the learning process in many settings [12, 33, 38]. This emphasis on group work can have consequences, however, and we will describe some of the challenges these consequences bring in the Results section.

As the class period progresses, the professor gauges the class' progress on the case study, as often times the problems require the assistance of the instructor. This assistance can take on many forms: the gentle nudge of one student in the right direction; allowing a student down a "wrong", or previously unanticipated, path to show them the limitations of their chosen model in a given situation; a full-out breakout session when many students are lost, which often resembles a mini-lecture given to the entire class. Great effort is taken to make sure that students are not simply "given" the answer when they ask for help, which is often frustrating for the students, especially considering that many different models can have validity in a given situation—meaning there may not be just one "right" answer for a given problem. Comparing the outcomes of multiple modeling approaches to the same problem is an extremely valuable exercise for learning the mathematical modeling process.

[2] See Supplementary Materials for example course material. All additional course content will be made available immediately upon request.

Many times the students are able to aptly solve all of the questions posed in a case study during the 55-minute class period, while other times the case study needs to be completed outside of class. In any event, a sufficient effort is necessary for each case study, as each week a randomly chosen case study will be turned in as a "group quiz" to be graded to make sure every group (although possibly not every student) is consistently engaged.

In addition to the in-class case studies, each week the students are also responsible for 6–8 homework questions out of the book *Mathematics for the Life Sciences* by Ledder [22]. The goal of these homework assignments is to introduce the students to other applications of the mathematical modeling settings and techniques in a given section. Most of the problems in each homework set are of the same level of sophistication as the case studies and, as a part of the flipped classroom environment, are fair game for assessment during the regular 55-minute class period.

3.2 Computer Programming

Often times the assistance of a computer is necessary to solve problems in mathematical biology. As such, computer programing and simulation is an important part of MTH 265. However, it is sometimes the case that, given the opportunity, students resort to the computer at every turn, often failing to appreciate the underlying structures that elicit different biological dynamics and processes. Thus, our goal is to have the students approach as much of the problem as they can without a computer, resorting to the computer when the limits of pencil and paper calculations have been met. This leaves the students with an appreciation for both for the power of their own faculties to understand a problem and for the ability of a computer to finish off the process of solving the problem.

For example, when studying single-species population models using differential equations, we ask the students to set up and nondimensionalize the model using the assumptions they derive from the case study's problem statement. Then, we ask them to find the equilibria and their stability by hand (if they can), so that they can study how sensitive these answers are to changes in parameter values. Only after this do we have them explore the phase line diagram for this model using the 'Manipulate" function in *Mathematica* [48]. These two processes complement each other well: the student learns the underlying structure of the model, which allows them to qualitatively predict the results of the phase line diagram beforehand. For more difficult models—ones where obtaining an analytical expression of the equilibria may be too difficult—the students are able to identify the need for the computer fairly quickly, and are able to make intellectual strides this way.

Because no one computer program does a completely adequate job of assisting with every problem in the course, we decided to use both R [34] and *Mathematica* [48] as programing languages for the course. UW-L has a site license for *Mathematica*, and R is free, meaning that the students all have unlimited access to both of these resources. We used R when teaching the students how to write scripts (e.g. for-loops, if-then and while statements), as well as for parameter estimation problems (e.g. linear and non-linear regression). We used *Mathematica* when graphically exploring how parameters affect the predictions of models. For example, the students used the "StreamPlot" function to explore the phase portrait for two-dimensional systems of differential equations.

3.3 Projects

Most of the mathematics courses at UW-L have a writing project, often completed in groups, as part of the assessment process, and MTH 265 is no different. This writing project is done in conjunction with the traditional second semester calculus course, which is MTH 208 at UW-L. The project involves the students working through a step-by-step procedure for determining the long-term behavior and stability of a single-species fish population in a fishery using a first-order nonlinear difference equation model. This is done through pencil-and-paper analysis and computer simulation, with an open-ended request to critique the model used throughout the project. Groups were asked to journal their progress using Google Docs, and used predetermined class time to work through the project with the observation of their instructor. The students' finished product for this project looked much like that of their weekly homework assignments, only typed out neatly at the request of the professor. The responses to the request to critique the model were well-thought-out, with many students suggesting what amounts to an Allee effect [1], which would be the natural response of a learned population modeler! Research comparing the approaches of second-semester calculus students to those of MTH 265 students is ongoing, and will be presented in a future manuscript.

Because part of the process of becoming a biologist involves learning how to read and interpret the primary literature in the field, and introducing research into lower-level courses can help students understand the processes of science [7], MTH 265 also includes a second, individual, class project that involves reading a research paper in mathematical biology. The research paper for this project was *Boolean Models Can Explain Bistability in the lac Operon*, by Alan Veliz-Cuba and Brandilyn Stigler [45]. This paper was chosen because a) most of the students have prior experience with the lac Operon and b) the paper provides a nice introduction into Boolean network models as an alternative to continuous models for systems with a large number of nodes. As with all of the course material, the background on Boolean networks was introduced via video lecture and smoothed out through classtime specifically allocated to the class project. The students, as a part of the project, provided definitions of terms they were not familiar with (often finding these definitions through a simple Google search), constructing the models used in the paper, reproducing some of the mathematical results presented in the paper, and adding to their interpretation. The students greatly enjoyed this exercise, as it shows them how close they are to their goal of being a research biologist, and how mathematical maturity accelerates this process.

3.4 Exams and Mathematical Modeling "Competitions"

One of the difficulties in teaching a class via the flipped classroom is how to properly assess and examine student learning [3]. Because the class is very modeling focused, and modeling is a time-consuming process, traditional exams are very difficult to administer in a course like MTH 265. The authors' solution to this problem is to do away with traditional exams in favor of both individual quizzes and group mathematical modeling competitions. The individual quizzes involve the students choosing two small modeling questions from a group of three questions and solving them with help from their class notes, homeworks, past computer programs and video lectures. These quizzes are given over a 55-minute time period. The questions in these quizzes are structured in such a way so that, after the student chooses which two problems to work on, he or she can solve both questions in a combined 40 minutes—meaning that some (but not all) of the modeling process is given to them. These exams provide the students with an incentive to learn the material on their own (which is nontrivial in a flipped course with a large group component), as well as the motivation to become proficient in using some of the elementary skills a mathematical or quantitative biologists would need to possess (e.g. diagram building, script writing/amending, elementary algebra and calculus, scientific writing).

The mathematical modeling competitions stemmed from the successful 24-hour Wisconsin Mathematical Modeling Challenge at UW-L, as well as the success of similar activities in other mathematical biology courses [8]. These competitions complement the individual, in-class quizzes by providing students with more open-ended modeling problems and a longer timespan to produce their solutions. These modeling problems can ofen be introduced with only a few paragraphs of text—with few or no equations. The students, in groups, then have 24 hours to come up with an appropriate model for this system, as well as answer the biological question posed. The group of students with the best solution is rewarded with perfect homework scores until the next modeling competition. The class has either an individual quiz or a modeling competition at the end of every other week for a total of three individual quizzes and three modeling competitions during the semester worth roughly 30 percent of each student's final grade.

Finally, the class concludes with a take-home final examination that the students have a week to complete. This final exam is a blend of routine modeling and analysis-type questions from the individual quizzes and open-ended modeling questions from the modeling competitions.

3.5 Assessment

The robust assessment of flipped classrooms is still an ongoing process, both for MTH 265 at UW-L and for educators in general. Because MTH 265 is only taught once a year at UW-L we were not able to cross-compare the performance of simultaneous MTH 265 sections taught via the inverted classroom and the traditional classroom simultaneously. However, we were able, through a series of CLASSE surveys [30], comments received by UW-L's Student Evaluation of Instruction (SEI) and informal and formal assessment of student work, to obtain a reasonable gauge on student perception of the course, as well as suggestions for improvement[3].

4 Results

The results of the CLASSE surveys, formal and informal student comments point to the flipped classroom environment eventually being successful in engaging students, while student performance results point us towards areas that need improvement. The responses to the CLASSE survey are summarized in Tables 1 and 2. Notice that many students in 2013 failed to take the end-of-semester CLASSE survey, possibly because they confused it with the SEIs they completed for all of their courses at the end of the semester. In 2014 the authors made an effort repeatedly remind the students to take the CLASSE, which lead to larger (although not perfect) participation in that year's end-of-semester survey.

Most students in the CLASSE survey indicated engagement levels in MTH 265 that were high (see Tables 1 and 2) and that they enjoyed the case study/group work format that the flipped-classroom model afforded them. For example, most students agreed that the course challenged them to amalgamate knowledge from other courses while doing assignments in MTH 265 (Table 2), and this agreement increased from the mid-semester surveys in 2013 and 2014 to the end-of-semester surveys in 2013 and 2014, respectively, suggesting that students were seeing the connections between the mathematical models and structures taught in MTH 265 with the objects they encountered in their life science courses. A student commented in the 2013 SEIs that they wished they could take or were looking forward to additional classes "taught in this manner", while one student in the 2014 SEI specifically said that the "flipped classroom style [the authors] used worked especially well for the content". In 2014, a student commented in the SEI that he or she found MTH 265 to be "by far, the most interesting math class [he or she has] ever taken". Another student commented that he or she "learned more in this class than any other math class". Additionally, many students also commented that, despite the difficulty of the course, they learned far more in MTH 265 than in any other math course they've taken. This level of engagement elicited class attendance and participation previously unseen by either of the authors: Zero students missed even one class period in the final eight weeks of the 2014 spring semester. This class attendance, although not awful, was not as robust in the spring of 2013. When this wonderful attendance was pointed out to the students, one of them remarked that the reason was that they realized that "[they] have a leg up on other students in our major, by adding an additional dimension to [their] skill set".

Initially some students are resistant to the flipped classroom environment. In both 2013 and 2014 about 17% (4 out of 24) of the class dropped the course within the first few

[3]The full results of the CLASSE survey are provided in the Supplemental Materials.

Engagement Activities

So far this semester, how often have you done each of the following in your MTH 265 class

	Survey	Never	1 or 2x	3 to 5x	> 5x	Mean
Came to your MTH 265 class without having completed readings or assignments	M2013	20 %	47 %	20 %	13 %	2.27
	E2013	20 %	40 %	20 %	20 %	2.40
	M2014	24 %	41 %	35 %	0 %	2.12
	E2014	8 %	54 %	15 %	23 %	2.54
Put together ideas or concepts from different courses when completing assignments or during class discussions in your MTH 265 class	M2013	13 %	27 %	40 %	20 %	2.67
	E2013	0 %	0 %	40 %	60 %	3.60
	M2014	0 %	0 %	41 %	59 %	3.59
	E2014	0 %	0 %	23 %	77 %	3.77

Cognitive Skills

So far this semester, how much of your coursework in your MTH 265 class emphasized the following mental activities?

	Survey	Very Little	Some	Quite a Bit	Very Much	Mean
Synthesizing and organizing ideas, information, or experiences into new, more complex interpretations and relationships	M2013	0 %	13 %	47 %	40 %	3.27
	E2013	0 %	40 %	20 %	40 %	3.00
	M2014	0 %	12 %	41 %	41 %	3.31
	E2014	0 %	0 %	46 %	54 %	3.54
Making judgments about the value of information, arguments, or methods, such as examining how others gathered and interpreted data and assessing the soundness of their conclusions	M2013	0 %	7 %	40 %	53 %	3.47
	E2013	20%	0 %	20 %	60 %	3.20
	M2014	0 %	24 %	18 %	53 %	3.31
	E2014	0 %	8 %	38 %	54 %	3.46
Applying theories or concepts to practical problems or in new situations	M2013	0 %	0 %	47 %	53 %	3.53
	E2013	0 %	0 %	60 %	40 %	3.40
	M2014	0 %	12 %	24 %	59 %	3.50
	E2014	0 %	0 %	38 %	62 %	3.62

Other Educational Practices

So far this semester:

	Survey	Never	Once	2x	> 2x	Mean
How often have you participated in a study partnership with a classmate in your MTH 265 class to prepare for a quiz or test?	M2013	40%	20 %	13 %	27 %	2.27
	E2013	20%	0 %	20 %	60 %	3.20
	M2014	44%	19 %	19 %	19 %	2.13
	E2014	15 %	8 %	23 %	54 %	3.15

Table 1: Above are example responses from the CLASSE survey given to students in MTH 265 during the spring semesters of 2013 and 2014 displaying how the course engaged students, developed their cognitive skills, and fostered interactions between the students. M2013 refers to the mid-semester survey for the spring semester of 2013, E2013 the end-of-semester survey for the spring semester of 2013, and so on. This survey was taken by 15 students in M2013, 5 students in E2013, 17 students in M2014, and 13 students in E2014.

Cognitive Skills

So far this semester, how much of your coursework in your MTH 265 class emphasized the following mental activities?

	Survey	Strongly Disagree	Disagree	Agree	Strongly Agree	Mean
I think I can be a more effective scientist because I took this course	M2013	0 %	0 %	53 %	47 %	3.47
	E2013	0 %	0 %	40 %	60 %	3.60
	M2014	6 %	0 %	69 %	25 %	3.13
	E2014	0 %	0 %	54 %	46 %	3.46
I feel the difference between the structure in this class and that of the traditional, lecture-style mathematics class	M2013	0 %	0 %	20 %	80 %	3.80
	E2013	0 %	0 %	0 %	100 %	4.00
	M2014	0 %	0 %	63 %	37 %	3.38
	E2014	0 %	0 %	23 %	77 %	3.77
This class has changed my idea of mathematics and mathematical modeling	M2013	0 %	7 %	33 %	60 %	3.53
	E2013	0 %	0 %	20 %	80 %	3.80
	M2014	0 %	6 %	69 %	25 %	3.19
	E2014	0 %	0 %	31 %	69 %	3.69
I learn well from the case studies we do during our class time together	M2013	0 %	7 %	33 %	60 %	3.53
	E2013	0 %	40 %	0 %	60 %	3.20
	M2014	0 %	6 %	56 %	38 %	3.31
	E2014	0 %	0 %	62 %	38 %	3.38
I am more likely to watch video lectures than I am to read a textbook	M2013	0 %	27 %	7 %	67 %	3.40
	E2013	0 %	20 %	0 %	80 %	3.60
	M2014	0 %	6 %	38 %	56 %	3.38
	E2014	8 %	0 %	38 %	54 %	3.38
I feel like I can translate what I learn in class examples to other problems outside of class	M2013	0 %	27 %	40 %	33 %	3.07
	E2013	0 %	0 %	40 %	60 %	3.60
	M2014	0 %	6 %	69 %	25 %	3.19
	E2014	0 %	0 %	77 %	23 %	3.23
Now I have learned mathematical modeling and how it can apply to science, I am better at performing mathematical tasks than I was before	M2013	0 %	20 %	40 %	40 %	3.20
	E2013	0 %	0 %	20 %	80 %	3.80
	M2014	0 %	6 %	69 %	25 %	3.19
	E2014	0 %	8 %	69 %	23 %	3.15
I make an effort to watch the video lectures	M2013	0 %	13 %	20 %	67 %	3.53
	E2013	0 %	20 %	0 %	80 %	3.60
	M2014	0 %	6 %	25 %	69 %	3.63
	E2014	0 %	0 %	23 %	77 %	3.77
I often rewatch the video lectures	M2013	13 %	33 %	33 %	20 %	2.31
	E2013	0 %	60 %	20 %	20 %	2.40
	M2014	13 %	56 %	25 %	6 %	2.31
	E2014	0 %	77 %	15 %	8 %	2.31

Table 2: Above are example responses from the CLASSE survey given to students in MTH 265 during the spring semesters of 2013 and 2014 displaying an overview of the students' general opinion of the course's ability to reach the instructor's goals. M2013 refers to the mid-semester survey for the spring semester of 2013, E2013 the end-of-semester survey for the spring semester of 2013, and so on. This survey was taken by 15 students in M2013, 5 students in E2013, 17 students in M2014, and 13 students in E2014.

weeks, often citing that the flipped classroom makes them uncomfortable, or that they wish the instructor would simply "tell them what to do", instead of "only using examples to illustrate the concept". Some of these students aired their disagreements at inapropriate times during the class period, which, while being common in flipped classrooms [44], was not anticipated by the authors. Some of these behavioral problems are unavoidable, as many of the video lectures simply tell the students "what to do in a given situation", doing exactly what the aforementioned student would like the instructor to do (only through a different medium). However, future iterations of this course need to provide the students with more of a rationale for the flipped-classroom environment—including the pedagogical research pointing to its success as well as its ability to increase the students' chances of being better scientists in the future. The authors, in an attempt to better motivate the flipped approach, provided the students with a letter titled "What MTH 265 is Like" at the beginning of the spring 2014 semester—which was an idea given by UW-L's Center for Advancement of Teaching and Learning[4]. While this did not decrease the number of drops from 2013 to 2014, the students that stayed in the 2014 course through its entire duration appeared to buy into the flipped environment more than those in the 2013 course, although the results of the CLASSE survey are inconclusive here (possibly due to small sample size).

Students also watched the video lectures frequently, with more than a fourth of the students in both 2013 and 2014 indicating they often rewatch the lectures if they didn't understand the material the first time (see Table 2). The CLASSE survey also indicated an overall improvement in the viewing of video lectures from 2013 to 2014, owing possibly to the insistence on shorter videos and a more fundamentalist stance against giving traditional lectures during class time by the instructor—leaving students with no choice but to view the video material outside of class. Student variability may the contributing factor to this change in behavior, or it could very well be that the class materials and instructor were more engaging the second time around. Additionally, students indicated that the breadth and depth of mathematical biology surprised them, and the class peaked their interests in subjects that they previously found boring. The flipped classroom's ability to expose the students to so many areas of mathematical biology no doubt contributes to this perception.

Despite the student's reported appreciation of the videos, the CLASSE survey does indicate that some students were unprepared for class a significant number of times (Table 1), and this number actually increased in 2014. While students being unprepared for class is not a new phenomenon, in the flipped classroom an unprepared student can present a unique challenge for his or her group members and the instructor. In the lecture format, and unprepared student is at least able to participate in the transmission phase of the learning process by taking notes. This is not the case in a flipped classroom, which usually means that a student has to follow along as his or her group members do most of the work on the in-class case studies or watch the video lectures, read the book or do the assigned homework during class time, and thus miss out on doing the case study. On one hand, a student's lack of preparation is usually exposed on the individual quizzes, which often motivates a student to actively participate in the process of group work. On the other hand, the presence of unproductive group members has the potential to discredit the idea of group work among the prepared students (although no one has expressed a concern about this thus far), and students watching video lectures during class time elicits the same feel as a traditional classroom, with the transmission phase done during class time. This dilemma serves as motivation for the authors to develop creative ways of making sure students are sufficiently prepared to fully participate in important classroom activities (using pre-class quizzes, for example [28]).

One additional problem that the students and instructor faced when attempting to accelerate student progress was a collective lack of algebra and calculus skills left over from previous coursework. Much of this is self-selection: many students taking a modeling course over a traditional second-semester calculus course probably because of an experience

[4]This document is also included as a part of the Supplementary Materials.

in algebra and calculus that was less than stellar. Some of this is also due to the fact that many students take MTH 265 after a significant amount of time off of mathematics (roughly 10 to 15 percent of the students in the class are seniors). Student frustration over insufficient algebra and calculus mastery may have indirectly caused some students to have negative feelings toward the flipped classroom at the beginning of the course. In the spring 2014 version of the course there were roughly 10 video lectures at the beginning of the class devoted to a review of calculus topics, but it's possible that more review is necessary for the students to be able to hit the ground running on some of the important course material.

In terms of student learning, we exposed the students to many different areas of mathematical biology that are not often reached in a traditional 14-week course. While we stress exposure, the assimilation of information is obviously the crucial goal of any course. Our informal observations through monitoring case studies and various informal observations of student learning suggest that the students in MTH 265 become more and more comfortable in mathematical modeling and dimensional analysis as the semester went on, which are two skills that are emphasized the least (if at all) in their undergraduate training ([20, 39, 21, 5]). At the beginning of the course students were hesitant even to start creating a model in any given situation, possibly because they were still struggling with prerequisite material. At the end of the semester, however, students were able to create multiple competing models for a given problem, and once his or her preferred model was selected, students were immediately focused on nondimensionalizing the model, if appropriate, and then on to the analysis of the model. Once enough problems were made simpler by scaling, the students appreciated what the extra algebra up front bought them, and were able to spend more time attempting to understand the biology they were modeling rather than the intricacies of the mathematics used. In our aforementioned comparison of MTH 265 with MTH 208 students, one of the initial in-class observations we had was that students in MTH 208 were spending the majority of time solving the math problems before attempting to interpret the results, while the students in MTH 265 were actually "guessing" what the results of the model were going to say biologically, in some sense using their mathematical analysis as a way of testing their hypothesis. This contrast was an unpredicted, and welcomed, biproduct of our initial course goals.

Student development was not as steep in computer programming, possibly due to the lack of training prior to the course. Many students commented on this, both informally and in SEIs, saying they would have either preferred a "crash course" at the beginning of the semester or a programming course as the prerequisite. One student, in 2014, specifically stated that he or she "was not aware the amount of computer programing that would be required" in his or her SEI. Nonetheless, by the end of the semester students, many of which have never programmed a computer before, were able to reproduce some of the results in the paper [45] with minimal help from their instructor, suggesting that a passible amount of coding was learned for their future careers as life science researchers. In future iterations of this course it may be beneficial to provide exercises inside and outside of class focused entirely on coding (there were only a few such in-class exercises in the first two iterations of the course).

Student performance on assigned work in the spring of 2014 points towards areas that need improvement in our future implementations of the flipped classroom. For example, student performance on the individual, in-class quizzes actually decreased as the semester went on (Median scores were 80 % for Quiz 1, 71% for Quiz 2 and 60 % for Quiz 3). Part of this decline can be attributed to an increase in the complexity of course material as the semester went on. However, this decline could possibly be due to the fact that much of the course is either group-based or untimed, causing the students' ability to perform assigned tasks by themselves and quickly to atrophy as the semester went on. A comparison of the scores for the individual and group projects also point to an overall weakness the students' ability to work independently versus working in groups, as 11 students (four groups) received scores above 90 percent for the group project, while only one student received such a score in the individual project[5]. In terms of the students' ability to work in a timely manner on mathematical biology problems, the take-home final exam, for which students were given a week to complete, had a median score of 91 percent, which is much higher than any of the scores for the timed, in-class quizzes discussed above. While collaboration and long-run diligence are probability more important for a scientist than the ability to do a task independently in a short period of time, future implementation of the flipped classroom needs to strike a better balance between collaboration and individual aptitude, as well as increase the number of skills each student can perform as "second nature". This can be achieved by implementing more "subproblems" in individual homework assignments, and using these problems as pre-class quizzes to assess student progress prior to class. These subproblems need to be carefully chosen so as not to bog the students down with mere "drill problems" in lieu of problems with genuine biological applications. Another possible way to strike this balance is to require students to work on the case studies alone for a significant portion of the class period, before coming together with their groups to finish the case study, which is often the way research in done collaboratively.

5 Discussion and Future Directions

The popularity and necessity of mathematical biology in today's scientific landscape make the way we quantitatively train life science majors an important pedagogical issue to consider. In this manuscript we motivated the need for and describe a flipped classroom for MTH 265, Mathematical Models in Biology, at the University of Wisconsin-La Crosse, as well as presented results pertaining to student engagement elicited by the approach. The course, which is mainly for life science majors specializing in biochemistry, is delivered via video lectures outside of class and well-constructed case studies during class, with student assessment executed using a combination of class projects, individual quizzes and group mathematical modeling competitions. Students by and large performed well in this course and their appreciation for the flipped classroom increased as the semester progressed, evidenced by both CLASSE Surveys, UW-L's Student Evaluations of Instruction and evaluation of student work (the mean and median final grade for the class in spring 2014 were 83% and 89%, respectively). Future, course-specific, work will focus on the continued refinement of course material (specifically video lectures) to meet the evolving needs of undergraduate students in the various life science majors, as well as a more robust set of tools for assessment of students using "just-in-time" teaching methods [28].

The success of the MTH 265 inverted classroom is part of an exciting movement on the University of Wisconsin-La Crosse campus which is a seeing a growing student interest in mathematical biology. For example, the first and second authors were recently the recipient of a UW-L Curricular Redesign Grant funding the formation of a minor in Mathematical Biology for biology majors, which will include creating a Biocalculus sequence [10], as well as an upper-division Mathematical Biology course springboarding from MTH 265. The authors hope that the formation of this minor will eventually lead to a major or emphasis in Mathematical Biology at UW-L. Additionally, the Center for the Advancement of Teaching and Learning at UW-L has begun giving three-week Blended Learning Instructor Training to faculty during winter and summer breaks in the hope that this will facilitate more flipped, inverted and blended classrooms on campus. This training was attended by the first author, and was very instrumental in improving the MTH 265 course from 2013 to 2014. The authors plan on using the principles of the flipped classroom while developing the mathematical biology curriculum at UW-L to continue to attack the aforementioned pedagogical challenges moving forward.

[5]Examples of student work for the group project are provided in the Supplemental Materials.

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