Modeling of Biological Systems

Applied Math (APMA) 1300
Fall 2017
Wilson Hall 309
Mon Wed Fri, 1:00 - 1:50pm
Canvas Homepage: https://canvas.brown.edu/courses/1300

Instructor: Veronica Ciocanel

Contact info:

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- You may expect to receive responses to email inquiries in to 2-3 days.

Office Hours: Wednesdays 3:30-5:30, and by appointment.

I **Course Description:**
Many problems in biology and neuroscience have benefited tremendously over the past decades from mathematical modeling. In this course, students will learn about a variety of biological fields where mathematical models and analysis have provided key insights. The increase in the availability of experimental data has led to both successful applications of existing mathematical techniques to improve understanding of biological systems and to novel mathematical analysis in fields such as linear algebra, dynamical systems, probability, scientific computing, and many more.

The goal of this course is to allow students interested in quantitative analysis and biological applications to discover how mathematics has furthered our understanding of critical questions in fields such as infectious disease spread, intracellular transport, cancer therapy, neural activity, and more. For example, what strategies work best for controlling gonorrhea incidence? What are the implications of single neuron dynamics to information processing in the brain? Students will review mathematical concepts needed for modeling complex biological problems and will learn how to analyze these models and interpret their results in the context of the application. They will gain practice with approaching biological problems from a quantitative modeling perspective through individual research projects. Pre-requisites for this course include courses in linear algebra and ordinary and partial differential equations. Familiarity with a programming language may be useful but is not required.

II **Course Goals and Learning Outcomes:**
By the end of the course, students will be able to:

- Formulate mathematical models that extend the class examples to address biological questions.
- Review linear algebra, differential equations, and probability techniques necessary to solve and analyze the mathematical models presented.
- Interpret the mathematical results in the context of the biological problems.
- Recognize situations where mathematical concepts can be applied to answer biological questions, and identify the techniques necessary to solve a specific problem.
- Prepare a mathematical report evaluating and extending an existing published mathematical model to improve biological understanding on a topic of choice.
- Communicate effectively with peers and collaborate with a group in preparing a mathematical biology project and report.

III **Course Materials:**
Dynamic Models in Biology
S.P. Ellner and J. Guckenheimer, published by Princeton University Press.
Obtaining the textbook is recommended.

IV **Course Requirements:**

Homework assignments (25%)

- Homework will be assigned most weeks on Wednesday and will be due Wednesday of the following week. The assigned homework problems will be available online on Canvas.
- The homework will occasionally include a reading component to get students comfortable with reading parts of research papers. These assignments will include short summaries of the paper conclusions/methods or filling in mathematical details.

Group problem sessions (15%)

- Throughout the course there will be several (3-4) class problem sessions. These consist of structured group assignments that should be completed during class time. These assignments will be exploratory allowing students to work in a group while learning a new mathematical technique or a new application through a hands-on approach.

Take-home midterm (25%)

- There will be one take-home exam roughly half-way through the semester. This exam will test the understanding of the modeling and mathematical techniques used to answer the biological problems explored in the first half of the course.
- Students will submit their exam in electronic form through Canvas.

Final Project (35%)

- A significant portion of the progress towards completion of the course goals will be evaluated through a modeling project. Groups of 2-3 students will select 1-2 research papers to carefully read, summarize and reproduce some of their results. They will also extend or modify the models proposed in the paper(s) to address an unexplored biological question or hypothesis.
- The final project consists of a proposal (10% of the grade) and a report submitted in two phases. The proposal will be 1-2 pages in length and will be a rough sketch of the topic the group selected. In addition to instructor feedback, students will provide and receive peer feedback on the proposal (5%). The report should be written in the form of a research article of roughly 10-15 pages including all mathematical details and figures illustrating results. The feedback from your peers' evaluation of your group's proposal should be considered for final submission of the report (20%).

More details on the final project are provided at the end of the syllabus.

V **Grading Policy:**

Graded work	Weight
Homework	25%
Group problem sessions	15%
Take-home midterm	25%
Final project	35%

Provisional grading scheme

Grade	Percentages to aim for
A	90 - 100%
B	80 - 89%
C	70 - 79%

The class may be taken pass/fail. In order to pass, students must aim for a 70% or more average grade in the course, and must not miss the final examination. Students will be awarded pass with distinction if they average 90% or more in the course. Note that the above grading scale is in accordance to the Brown University Grading System.

The grading scale above is subject to adjustment, especially in borderline cases; adjustments may take into account class and group problem session participation and improvements in performance over the semester. Minimum percentages for grade cut-offs will be approximately as (and no higher than) in the tentative scale above.

Plagiarized homework assignments will receive an automatic penalty grade of zero points.

VI **Policies and Expectations of Students:**

Homework:

- Late homework assignments will not be accepted. You will be given one limited free pass, but it is highly recommended (i.e., essential) that you work through all assignments to be able to keep up with the material.
- Students can collaborate on homework assignments: however, assignments must be written up separately and individually.

Take-home midterm:

- Students cannot discuss the midterm with others or work together on this summative assignment. They are encouraged to contact me for any questions about the midterm.

Group problem sessions:

- In group problem sessions, students will be divided into 3-person groups and work on practice problems, the details of a proof, or applications related to the concepts introduced that week.
- Attendance of the group problem sessions offered each week is required. It will provide extra preparation for assignments and exams, push your knowledge further, as well as help you make friends in the class. If for any reason you cannot attend a group problem session, notify me as early as possible so as to arrange a make-up assignment.
- You are expected to work on the problems with your group, and encouraged to use the board whenever needed. Make sure you understand all steps of the problems that you are solving with your group, and that you rotate the person summarizing the solution approach to the group in each problem/subproblem.

Final Project:

- Students are responsible for working in a group to complete this final project. After submission, they will be asked to fill out a form detailing their own and their group's contribution to the research and writing of the project.
- We will discuss organizing groups in class, based on interest in topics and your group preferences. We will cover how it may be beneficial to have at least one person with some programming experience in your group.
- If time allows, we will have informal presentations of the research projects at the end of the semester.

Software:

- For any work that requires the use of software such as Matlab or Mathematica, students may use their personal laptops or the computers available in the ETC Teaching Lab.
- Tutorials for these programs will be available on Canvas in advance of the problem sessions or assignments where they might be useful or needed.

VII Tentative Course Schedule

Week	Topic/Assignment
1	Introduction to searching for journal articles, Review of linear algebra HW (homework): Locate, download and summarize findings of a paper
2	Structured Population Models HW
3	Structured Population Models HW
4	Class problem session
5	Review of differential equations, Infectious disease dynamics HW
6	Simulation tools for solving differential equations, Infectious disease dynamics HW
7	Class problem session
8	Review/introduction of probability and stochastic methods, Mechanisms of intracellular transport Take-home midterm
9	Mechanisms of intracellular transport HW
10	Review/introduction of partial differential equations, Modeling dynamics by transport and diffusion HW
11	Modeling dynamics by transport and diffusion Final project proposal
12	Class problem session HW
13	TBD (student poll) Final project proposal peer review HW
14	TBD (student poll) HW
15	Final project due Informal presentations (time permitting) during reading period

VIII Accommodations for Students with Disabilities:

Brown University is committed to full inclusion of all students. Students who, by nature of a documented disability, require academic accommodations should contact me during office hours or by appointment, and we will determine a plan for completing their assignments throughout the semester. Students may also speak with Student and Employee Accessibility Services to discuss the process for requesting accommodations. Visit Student and Employee Accessibility Services (SEAS) for more information.

IX **Academic Support:**
TA Office Hours will be posted on the website. You are encouraged to take advantage of this resource available for the class.
The Math Resource Center hours are available at https://www.math.brown.edu/mrc/.

X **Inclusion and Diversity Statement:**
Brown University does not discriminate on the basis of sex, race, color, religion, age, disability, status as a veteran, national or ethnic origin, sexual orientation, gender identity, or gender expression in the administration of its educational policies, admission policies, scholarship and loan programs, or other school administered programs.

I intend to support an inclusive classroom environment where diverse perspectives are recognized, respected, and seen as a source of strength. I encourage you to learn from your fellow students, who may have a background in a range of different fields, as this will allow you to appreciate your new knowledge even more. I also recommend that you ask many questions, whether in the classroom or during office hours, to ensure that you understand the material throughout the semester.

XI **Academic Honesty:**
As mentioned in Brown University's Academic Code, "Academic integrity protects and promotes the University's pursuit of its academic mission. Membership in the Brown community thus carries with it a responsibility for upholding the University's principles. All members of the Brown community are expected to conduct themselves with integrity in their learning, teaching, research, and writing. It is also incumbent on those who know or suspect that someone else has violated Brown's academic code to report their knowledge or suspicions to the appropriate University authorities." Consult http://www.brown.edu/academics/college/degree/policies/academic-code for the full policies.

Final Project Proposal (10% **of course grade, 50 points)**

In the final project, you are asked to build on the skills developed throughout the course and prepare a well-written report where you summarize and reproduce the findings of an existing mathematical model addressing a biological problem. In addition, you are asked to extend this model to address a new/unexplored biological question or hypothesis arising from the model (See more information in the Final Project Assignment).

The final project proposal will consist of a 2-page sketch of the topic you choose to work on with your group. The proposal will help you settle on a biological application and paper(s) and will encourage your group to start brainstorming ideas for model extensions several weeks in advance of your final project. In addition, preparing this document will help you with organizing your work as a group and will give your practice with scientific writing. Feedback from your peers will be useful in understanding what aspects of your research project and writing could be clearer for your peer audience.

The project proposal should include the following:

- a brief introduction to the biological problem addressed by the paper(s) of your choosing (5 points),
- an overview of the mathematical model in the paper(s) (10 points),
- ideas for extending the model to answer a new question (10 points),
- the analytical and/or computational tools you plan to use (10 points), and
- a figure illustrating the biological context, the existing model, and/or the model extension (5 points).

Proposal structure and tools

You can edit the Latex files provided on Canvas, where you can find a sample structure for writing the proposal report; however, you can write the proposal in any other typesetting software such as Word, etc. If using computational tools in your final project, make sure you name the programming language that you plan to use. As seen in the Latex and pdf file examples, you must also include a short bibliography at the end that cites your group's chosen research paper(s).

Peer feedback

As part of your assignment, you will also provide feedback to another group's proposal (10 points). You will be assigned a sheet with questions about the clarity of the topic introduction, your understanding of the mathematical modeling involved, feedback on the proposed model extension and/or question to be answered, and on the scientific writing and formatting of the report. You will also be asked for a "muddiest point" of the report, which will be very useful to your peers in revising the clarity of their writing. Detailed answers to these questions will ensure the peer group will benefit from your feedback; sample answers and answer structures that would help their revision will be provided. If time allows, we will organize a feedback session where you can provide your feedback in person.

After receiving feedback from another group, you will have until the next class time to revise your report and submit the revised document. You will then receive written comments from me and may be asked to schedule an appointment to discuss the proposed project goals. Note that as in the case of the final project, you will be asked to fill out a Peer Evaluation Form for group work upon final submission.

Final Project Assignment (25% of course grade)

In the final project, you are asked to build on the skills developed throughout the course and prepare a well-written report where you summarize and reproduce the finding of an existing mathematical model addressing a biological problem. In addition, you are asked to extend this model to address a new/unexplored biological question or hypothesis arising from the model. In particular, you are asked to:

- Choose 1-2 published research papers that uses a dynamic model addressing a biological question.
- Discuss the context, the model, and the assumptions underlying it.
- Implement the model and reproduce the key analytical or computational results in the paper(s).
- Interpret the results in the context of the biological problem and explain the conclusions highlighted in the paper.
- Formulate one question or hypothesis that was not fully addressed in the paper. Modify or extend the model to address this question, and present your findings.

You should support all results and conclusions with arguments and well-chosen figures and make sure you properly and consistently cite any sources you used. With a small group of 2-3 students, submit a self-contained written report (aim at around 10-15 pages) that summarizes the original model, your model extension, and your conclusions. The intended audience for your report are your class peers. We will discuss organizing groups in class; keep in mind that it may be beneficial to have at least one person with some programming experience in your group. While the structure of your report may vary depending on the mathematical methods and application, make sure you include the following:

- Abstract (one paragraph)
- Introduction of biological problem/context
- Mathematical model
- Results (analysis/simulation and interpretation)
- Extension of the model and conclusions
- Outlook
- Reference list

Several examples of project reports and advice for scientific writing will be available on Canvas.

Presentations:

If time allows, we will have brief 8-10 minute presentations (5 slides maximum) during reading period. These presentations will not be part of the assessment of the final project but will serve to advertise your work to your peers in class.

Guide to identifying research papers:

The topic of the research paper does not need to be connected to anything we did in class. To find research papers and select a topic, browse the textbook for unexplored case studies or references, consider the case studies we explored in class and search for follow-up research papers using PubMed, Web of Science, or MathSciNet, or search these sources or journals such as Science, Nature, or PNAS (Proceedings of the National Academy of Sciences), Biophysical Journal, Journal of the Royal Society Interface if you have a specific topic in mind.

Additional topics to consider:

Here are some additional topics that you can consider in picking a research topic:

- Immunology: HIV, HPV, etc.
- Cancer: tumor growth, chemotherapy strategies
- Predator-prey models in ecology: insect pests, host-parasite interaction
- Neuroscience: integrate and fire neuron, neuronal networks, rhythmic dynamics
- Cell physiology: Hodgkin-Huxley model, intracellular calcium
- Pattern formation and social aggregation: zebrafish stripes, locusts, bird flocks
- Intracellular transport: interaction of molecular motor proteins and microtubules
- Circadian rhythms: biological clocks and rhythms

A grading rubric for this assignment is provided below.

	Outstanding	Competent	Developing
Report structure and organization	The paper has a clear introduction of the biological problem/context.	The report has an introduction of the biological problem and a conclusion.	The paper lacks an introduction and conclusion.
	The main points are clearly stated and well organized.	The paper lacks some organization.	The paper is poorly organized.
	There are clear conclusions summarizing the original research and the model extension.	Some main points from either the original paper or the model extension are not clear.	The main points and conclusions of the original paper or the model extension are not clear.
Mathematical and modeling content	The key results from the original paper(s) are clearly outlined and reproduced.	Some details are missing in reproducing the key results from the original paper(s).	The level of the writing does not match the audience.
	The mathematical techniques are used correctly.	The mathematical methods present only minor errors.	The mathematical methods present significant errors.
	The mathematical model proposed goes beyond the content of previous work and identifies an interesting unexplored question.	The mathematical model proposed goes beyond the content of previous work.	The mathematical model proposed does not go significantly beyond previous work.
Scientific writing	The figures/tables are clear and accurate, and well integrated into the report.	Figures/tables lack some clarity or are not integrated into the paper.	Figures/tables are unclear or are not included.
	The level of the writing is appropriate for the audience.	The level of the writing is almost always appropriate for the audience.	The level of the writing does not match the audience.
	Sources are properly and consistently cited and the bibliography is included.	Sources are cited and the bibliography is included.	No sources are given or the bibliography is missing.
	The report uses correct grammar and spelling.	The paper has only minor difficulties with grammar or spelling.	The paper has significant difficulties with grammar or spelling.