MATH 560 - Introduction to Mathematical Biology

Course overview Prerequisites Workload Weekly readings Project References Marking

Course overview

MATH 560 provides a broad overview of Mathematical Biology (obviously subject to the limitations of time and instructor knowledge and interests - this is a HUGE area of research). The course is organized around a sample of topics in biology that have seen a significant amount of mathematical modelling over the years. Currently, I'm including content from ecology, evolution and evolutionary game theory, epidemiology, biochemistry and gene regulation, cell biology, developmental biology, collective behaviour. However, this list changes gradually from year to year, to reflect students' and my own interests. The mathematical modelling methods and techniques covered are those that typically arise in the biological applications listed above. For example, I cover models using ordinary and partical differential equations, stochastic processes, agent-based models and using the methods of bifurcation theory, asymptotics, dimensional analysis, numerical solution methods, parameter estimation.

Prerequisites

The course does not have any official prerequisites listed on the UBC calendar but it is expected that students will have some experience with differential equations (acceptable: MATH 215, better: MATH 361 and/or MATH 316) and some familiarity with the ideas of probability and/or statistics (e.g. MATH 302 and/or STAT 200). If you aren't sure if you have the right background, come talk to me.

Workload

- **Three hours per week in class.** Roughly half the time will be me lecturing, a quarter students working on problems in class, and a quarter discussing papers.
- Reading papers. One paper will be assigned every week. With a partner, you will read
 and discuss each paper (outside of class) and write a short report on it. Every two
 weeks, we will discuss the most recent two papers in class.
- Written homework. I will give a small collection of practice exercises as a warm up / background to some of the papers (not weekly, maybe 4-5 throughout the term when the papers require it). If your background for the course is suitable, this will be light work.
- Project. See details below.

Learning goals

- Become comfortable reading papers on mathematical modelling in biology.
- Develop the ability to go from a question about a biological phenomenon observed or read about to building a modelling that can answer (part of) that question.
- Discern the best modelling framework (ODE, PDE, stochastic process, agent-based model etc.) for answering a particular biological question.
- Have an awareness of the analytical tools that might be required in formulating such answers (e.g. bifurcation theory, parameter estimation, matched asymptotics).

Weekly readings

Each week, there will be assigned readings. The "discussion" papers in the table below are to be read in preparation for our biweekly discussions. Together with a partner in the class, you are to hand in a report on the paper after reading and discussing it with your partner. You should focus on the structure of the paper as well as the content. Items to consider in your report:

- Structure of the paper How is the content organized? For example, <u>TAIMRD</u> is a common scientific format. Does any information seem out of place? What content is omitted or buried? For example, is all the mathematical analysis presented or in an appendix/ supplemental material section? Think about how different disciplines make these choices as we look at different papers.
- What is the scientific focus of the paper?
- What modeling formalism(s) is(are) used? (ODE numerics, PDE bifurcation theory, agent-based modeling...)
- How would you classify the model(s) in the paper with respect to the MAW classification (see Mogilner, Allard, and Wollman, Science 2012)? Plot the MAW axes with the paper marked as a point. Think about how you would tweak this classification scheme as we read different papers throughout the term.
- What are the main results? (mathematical and/or scientific)
- How are the main results dependent on the choice of modeling formalism? Could they have been achieved (better/worse) using other tools?
- How well are the main results highlighted and framed? That is, can you easily identify what the authors consider their most important contribution? And do they make a good case for the importance of those results?
- Who is the intended audience? Consider elements of your answer to "structure of the paper" and "highlighted and framed".

Sample paper report (von Dassow et al. 2000) - pdf, tex

Paper-discussion schedule:

TO BE UPDATED SOON FOR 2019

Date	Paper	
All term	<i>Cell polarity: quantitative modeling as a tool in cell biology.</i> Mogilner, Allard, Wollman. Science 336:175-179, 2012.	
Jan 5	<i>The segment polarity network is a robust developmental module.</i> von Dassow, Meir, Munro, Odell. Nature 406:188-192.	
Jan 12	Declining wild salmon populations in relation to parasites from farm salmon. Krkošek, Ford, Morton, Lele, Myers, Lewis. Science 318:1772-1775.	
Jan 19	A Simple Model for Complex Dynamical Transitions in Epidemics. Earn, Rohani, Bolker, Grenfell. Science 287:667-670, 2000.	
Jan 26	On the origin of species by sympatric speciation. Dieckmann, Doebeli. Nature 400:354-357, 1999.	
Feb 2	No paper discussion this week (guest lecture).	
Feb 9	The logic of animal conflict. Smith, Price. Nature 246:15-18, 1973.	
Feb 16	No paper discussion this week (Family Day catch-up).	
Feb 23	No paper discussion this week (reading break).	
Mar 2	Potential for Control of Signaling Pathways via Cell Size and Shape.	

	Meyers, Craig, Odde. Current Biology 16(17):1685-1693, 2006.	
Mar 9	<i>Thresholds in development.</i> Lewis, Slack, Wolpert. J Theo Bio 65:579-590, 1977.	
Mar 16	A Simple Model of Circadian Rhythms Based on Dimerization and Proteolysis of PER and TIM. Tyson, Hong, Thron, Novak. Biophys J 77:2411-2417, 1999.	
Mar 23	An agent-based model contrasts opposite effects of dynamic and stable microtubules on cleavage furrow positioning. Odell, Foe. J Cell Bio 183: 471–483, 2008.	
Mar 30	Resetting and annihilation of reentrant abnormally rapid heartbeat. Glass, Josephson. PRL 75(10):2059-2062, 1995.	
Apr 6	<i>Torque-speed relationship of the bacterial flagellar motor.</i> Xing, Bai, Berry, Oster. PNAS 103(5):1260-1265, 2006.	

Project

Description:

For this project, you will pick a paper (or a couple closely related papers) and consider the suitability of the modeling formalism used. Using an alternate formalism (or several), you will explore the impact this alternate choice has on (a subset of) the results in the paper(s). What can and what cannot be accomplished and why? For example, if the original paper carried out stability analysis and found a Turing instability, can you rediscover this using a numerical simulation approach or a stochastic treatment? The goal is to learn about the strengths and weaknesses of various formalisms. The project can be carried out in groups but groups are expected to address a few related papers and/or explore multiple alternate formalisms.

Timeline:

- Jan 20 Choose three papers to consider for the project.
- Jan 31 Submit a summary of your chosen paper(s) and a plan for the project.
- Feb 3-6 Meet with me to discuss your chosen paper and plan.
- Mar 6 Submit a report on your results. It should be in the TAIMRD format and roughly between 5-10 pages including any figures.
- Mar 13 Submit a plan for revising your work based on feedback on the report.
- Apr 3 Submit the final report.
- Apr (TBD) Presentations

Marking:

Given the typical wide range of backgrounds of students in this course, the marking is, to a large extent, on a relative scale. Along with your final report, you should submit a document a few paragraphs in length outlining your background for the course (your previous degree(s), relevant coursework, relevant research experience) and what aspects of the project you consider to represent new learning for you.

Papers:

This is a list of papers that you might want to consider for you project. Any of the "Discussion" papers above would also be acceptable.

Title	Author(s)	Journal info
A synthetic oscillatory network of transcriptional regulators.	Elowitz, Leibler.	Nature 403:335-338, 2000.
Thresholds in development.	Lewis, Slack, Wolpert.	J Theo Bio 65:579-590, 1977.
Dynamic instability of microtubules as an efficient way to search space.	Holy, Leibler.	PNAS 91:5682-5685, 1994.
Computer simulations reveal motor properties generating	Nedelec.	J Cell Bio 158(6):1005– 1015, 2002.

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stable antiparallel microtubule interactions.		
Sniffers, buzzers, toggles and blinkers: dynamics of regulatory and signaling pathways in the cell.	Tyson, Chen, Novak.	Current Opinion in Cell Biology 15:221–231, 2003
The Chemical Basis of Morphogenesis.	Turing.	Bull Math Bio 52(1):153- 197, 1952.

The reference textbook listed below by de Vries et al. has a collection of project ideas in "Part III" that would be appropriate for the project in this course. If you can't find a copy of that book, ask me about borrowing mine.

Here are some ideas that have some interesting interplay between different mathematical formalisms. You can look for your own paper or come talk to me for tips.

- Spiral waves using PDEs and cellular automata.
- Stochastic resonance noise near a Hopf bifurcation
 Turing instabilities or other patterning in a noisy environment PDEs, PDEs+noise, stochastic (e.g. using SMOLDYN)
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References

TO BE UPDATED SOON FOR 2019

Papers:

Relevant dates	Paper	
Jan 12	Variations and fluctuations of the number of individuals in animal species living together. Volterra. ICES Journal of Marine Science 3(1):3-51, 1928. DOI. Focus on pages 1-15.	
Jan 19	A contribution to the mathematical theory of epidemiology. Kermack, McKendrick. Proceedings of the Royal Society A 115(772):700-721, 1927.	
Jan 24	A General Method for Numerically Simulating the Stochastic Time Evolution of Coupled Chemical Reactions. Gillespie. J Comp Phys 22(4):403-434, 1976.	
Jan 24	<i>Exact stochastic simulation of coupled chemical reactions.</i> Gillespie. Phys Chem 81(25):2340-2361, 1977.	
Jan 24	Efficient formulation of the stochastic simulation algorithm for chemically reacting systems. Cao, Li, Petzold. J Chem Phys 121(9):4059-4067, 2004.	
Mar 26-28	A quantitative description of membrane current and its application to conduction and excitation in nerve. Hodgkin, Huxley. J Physiology 117: 500-544, 1952. Reprinted in Bull Math Bio 52(1):25-71, 1990.	
	Sniffers, buzzers, toggles, and blinkers: dynamics of regulatory and signaling pathways in the cell. Tyson, Chen, Novak. Curr Op in Cell Bio 15:221-231, 2003.	

Textbooks:

Relevant dates	Textbook	
Jan 8-26	<i>Mathematical models in population biology and epidemiology.</i> Brauer, Castillo-Chavez.	
Jan 8-26	A course in mathematical biology - quantitative modeling with mathematical and computational methods. de Vries, Hillen, Lewis, Müller, Schönfisch.	
Jan 22 - Feb 9	Evolutionary dynamics. Nowak.	
Lots	Mathematical models in biology. Edelstein-Keshet.	

Other (e.g. code):

Gillespie simulation code

My matlab code for simulating stochastic realizations, solution to the Kolmogorov equation and the logistic equation for the SIS model.

Lecture notes up to Jan 24

Marking

The marks in this course will be determined by three factors: (i) Participation in the weekly paper-discussions and the submitted summary (30%), (ii) the written homework (20%), (iii) written and oral project report (50%). The written report mark will have a self-evaluation component and the oral report will have a peer-evaluation component.