Evolutionary Systems Biology

Genetics 677-Sec11 410B Wendt Commons Fall 2016

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Office Hours
Tue 4:45pm-5:30pm
(or by appointment)

Course Times
Lecture: Tue 3:30pm-4:45pm
Lab: Thr 3:30pm-5:30pm

Course Numbers
Genetics: 55619
Medical Genetics: 55810

Course website: https://evosysbio-course.discovery.wisc.edu/

Mailing List: genetics677-11-f16@lists.wisc.edu (For EvoSysBio Students only)

Goal: To help you to build your own model of a small part of biology, incorporating aspects of the EvoSysBio perspective and using Evolvix, a programming language designed to make it easy to describe biological systems in mathematically accurate terms.

Overview and Purpose

Models are the maps of modern biology. Here you will learn to read and create them.

This course is about the bigger picture. We will build models to make connections that traverse the scale of organic life. Your interest and creativity will define the modeling possibilities, which may range from *molecules in cells* to *individuals in ecosystems* to *long-term evolution* itself.

You name it. You model it. You map it.

Evolutionary systems biology operates at the cutting edge of computational modeling, and building your own map of a small part of biology will develop your science skills like little else. By the course's conclusion, you will harness substantial analytical power, broadly transferable across scientific disciplines.

Some specific highlights:

- Hone your problem-solving skills in an active problem-based learning environment
- Form your own interdisciplinary student group and research topic
- Model a system of your choice, exploring its predictive power and limits
- Learn to use *Evolvix* to describe biological models with mathematical accuracy
- Receive one-on-one help from an expert with broad biological modeling skills
- Write a weekly Research Log (ReLog) that explains what you learned to your peers
- Write a research grant application, peer review others, and improve yours
- No exams! (instead you will continually improve your writing skills)

Take this course if you like …

- to solve challenging new problems to which no answer is known
- to connect to new disciplines and learn how they see the world and talk about it
- to get a taste of real-world research without having to redirect your career
- to think about the deep, inner meaning of things in order to make connections and achieve understandings that few others see
- to hone your writing abilities to become more skilled as a writer. (As some say: it takes 10,000 hours of practice to become really good at something, so you might as well get started in a course that emphasizes scientific writing)
- to learn a tool that helps you learn how to model Continuous Time Markov Chains (CTMCs)
- to take your first steps into a new field in relative privacy (a course is a safer way to dive into the vast ocean of scientific reality than starting a PhD program, only to decide that it wasn't a good idea after all!)

Do not take this course if you …

- prefer memorizing facts
- are uncomfortable with "the unknown" (and prefer to keep it that way)
- expect the instructor to always know the answer
- dislike peer reviewing and getting peer reviewed

Project Topics:

The group project is the core of this course, so choose it wisely in an area you are really interested in. If you already know your area of interest, speak with the Instructor to find a team of collaborators who share your interest. If you are unsure about your area of interest, you can always choose one of the available preselected topics.

You will only have about two (2) weeks to find your group and your project topic, so begin considering your team and project options immediately. You will need to present your tentative group project idea to the class at the end of Week 3.

Some project titles from previous groups:

"The Stag Hunt Game with Shirking: An Articulation, Analysis, and Application of a Model of Collective Action that Helps to Explain the Evolutionary Dynamics of Cooperation in Teams"

"Modeling the Process of Switching on ADH in the Human Liver"

"Construction of a Comprehensive Colon Cancer Signaling Network"

Prerequisites and Required Materials

Prerequisites:

An interest in interdisciplinary approaches to modeling in biology.

This is the central prerequisite for the course! Otherwise, enrollment is open. All undergraduate and graduate students are welcome from any field related to Biology, Medicine, Chemistry, Physics, Philosophy, Math, Stats, Computer Science, or Engineering.

Perhaps you are wondering why there are no prerequisites beyond being interested. How can one class accommodate such a wide range of students? Well….

- EvoSysBio builds on knowledge from diverse disciplines, but everything required from them will be covered in the course. EvoSysBio (and many other fields) depends on your willingness to interact with and learn from researchers in other disciplines. You do not need to master all disciplines to benefit from them or this course!
- Quantitative modeling is integral to EvoSysBio. In the course we will explore a very powerful standard modeling approach (known as Continuous Time Markov Chains, or 'CTMCs'), which is not only essential to EvoSysBio but also highly relevant to many disciplines. Centrally, students learn in this course how to turn the intuitive verbal models that often result from experimental work into computable models to predict time series which can be relevant in disciplines from biochemistry to ecology.
- The Evolvix[1] language used in the course provides an *easy*, user-friendly entry point for such modeling. Students can use Evolvix without needing to understand the details of its inner working, just as we can drive a car responsibly without knowing how to build one. This course will teach students how to 'drive' a CTMC model implemented in Evolvix to help them understand biology[2].
- Finally, previously acquired disciplinary expertise is relevant to the precise modeling questions chosen for the group project and the ReLog entries, both of which are integral to this course. In short, your diverse disciplinary backgrounds will make our questions, writing, and discussions more interesting and analytically rigorous!

The topics and skills learned in this course are highly relevant for understanding how many models are built in biology. They are not difficult to learn, but they will be immensely valuable.

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[1] Evolvix is being developed in the Evolutionary Systems Biology Group at the Laboratory of Genetics and the Wisconsin Institute for Discovery, UW-Madison. It has been designed by the course instructor for providing a reliable, research-quality platform that makes it easy to describe biological models in mathematically accurate terms. Evolvix drives a number of innovative modeling applications that are currently under development in the Loewe Lab.

[2] This course does not focus on the math, statistics, and computer science required for simulation. Students with the quantitative and formal expertise are welcome to employ their skills by extending Evolvix in a way that better meets the needs of their group project. Non-bio students are expected to learn some basic biology, just as bio students are expected to learn some basics about formal models – everyone is expected to contribute expertise to our interdisciplinary dialogue.

Required Materials:

- You will need a notebook computer in class each Thursday
- You will need a computer with an operating system capable of running Evolvix models:
    - Windows 7 – 10
    - Mac OSX 10.9 – 10.11
    - Linux (RedHat, Fedora, Ubuntu)
    - See http://evolvix.org for downloads and further details
- You must be able to:
    - Run Evolvix models on your own (at home or in the library)
    - Exchange modeling data within your research group (emails or USB stick); this will be essential during Thursday labs and to take group progress home for your own modeling work
    - Post to the group website (you will receive login information soon)

If you anticipate difficulty meeting these material requirements, you can work with another student and bring your data on a USB stick (or use some other work around). Please ask the instructor about your arrangement to ensure that it will work, as details may vary. You might also consider borrowing a computer from a campus library.

Course Website (https://evosysbio-course.discovery.wisc.edu/):

Since we will rely heavily on the course website this semester, some elements require explanation.

Login: You can only access the full website by logging in. The instructor will provide you with two user names at the beginning of the semester: (1) the "KnownName" acknowledges your identity and you will use it to post ReLog entries; (2) the "ReviewerName" is anonymous and you will use it to peer review your colleagues' written work. After establishing your user names, you will need to create two, distinct passwords. Since this site houses sensitive content, maintaining web security is essential. **Please ensure that you use https, rather than http, in the web address, and be sure that your passwords are at least 12 characters long and include at least one number and one symbol.** It is often helpful to use "passphrases" instead of passwords. For guidance on effective password creation refer to:

https://evosysbio-course.discovery.wisc.edu/how-to/choose-good-passwords

Course Tab: This page is the gateway to a series of explanations and descriptions that are more details than was possible in this syllabus. Some relevant resources include: the instructor's teaching philosophy, the course's learning goals, information on grading, expectations, and deadlines, and instructions for how to complete various course assignments. **Be sure to read and sign the Entry Agreement, which is a condition of enrollment.**

Timetable Tab: This page displays the course's progression, including deadlines.

How-To Tab: Refer to this page for assistance with the website, course assignments, and Evolvix.

Projects Tab: This is where you will develop your project proposal.

ReLogs and Feedback Tabs: These two pages are where you will develop your ReLogs and provide your peer reviews. Be sure to become acquainted with them early – much of your graded work will be developed on this page.

Readings:

Students will read a number of articles relevant to their project. **Graduate students are expected to complete a larger and/or more complex reading load than undergraduates**, reflecting their greater expertise. The instructor will know (or find out quickly) if you are engaging with interdisciplinary research or if you are simply rehashing what you already know..

The quality of your work and the broadening of your interdisciplinary horizon (and therefore your grade) will hinge on an earnest engagement with scientific literature from several disciplines. If you plan to avoid the difficulties posed by the unknown, well…is this course right for you?

There is no required book, though reading systems biology textbooks will help you navigate this course with greater ease. To explore a useful mix of topics, I recommend:

Klipp, E., et al. (2009) ***Systems Biology: A Textbook.*** *Wiley-Blackwell-VCH.*

Grading and Assignments

Grading in this course is intended to reflect research engagement, not memorization. What counts is the quality of: (1) your independently written ReLog entries; (2) your peer reviews (of your colleagues' ReLogs and project proposals); and (3) your contributions to the group project.
In your group, you will write a research grant application using preliminary modeling data to justify the theoretical or experimental work you propose.

This course is designed to provide a taste of what is important in the life of researchers (who do not take exams and, therefore, neither do you). Instead, **your grades will be based on how well you continually engage in your research through the course's duration**.

In a nutshell, there are three big tasks that you must make steady progress on:

1) Write (or re-write) a 500-word story for your ReLog each week
2) Peer review two ReLog entries each week
3) **Group project:** In your group, write a draft and two revisions of a grant application while adhering to the "Group Work" due dates listed in the Timetable Overview. The application's text should range between 3,000 and 10,000 words, though **concise prose** should take precedence over length. Avoid the fluff and make every word count!

Everything you write for this course will appear on the course website, and these entries will be the basis for your grades. Keep in mind that your texts are only visible to others in the course. Consider taking your drafts to UW's Writing Center, where trained professionals offer free editorial services:

The Writing Center
(608) 263-2992
http://www.writing.wisc.edu/

With your colleagues, you will exchange peer reviews that assess the quality of written work while providing **constructive** criticism. While these assessments are part of the learning experience (both for you and the reviewers), they are not your grades and only reflect how your fellow researchers see your work. **The instructor may or may not agree, and he will grade your work independently.**

Your **final course grade** will be based on the instructor's assessment of your overall performance as a researcher in the role of author, collaborator, and reviewer. Your major will also be taken into account.

The grade scale is:

30%	ReLog entries
20%	Peer reviews
40%	Group project
10%	Group collaboration

If you have questions, please ask the instructor.

Attention Graduate Students

Graduate students (particularly PhD students) will be held to **higher standards**. Both your quality of work and reading loads will be greater than those of your undergraduate peers.

In addition, you are required to write a 2000-word essay, due at the end of the semester, regarding the challenges of engaging other disciplines in an interdisciplinary research environment. This essay should assess the problems and strengths of interdisciplinary research and cross-discipline communication. The essay should end with recommendations for strategies to overcome these problems in your graduate research and beyond.

NSF Synergy

Students who plan to apply to the prestigious NSF Graduate Research Fellowship Program should alert the instructor early on to explore ways to integrate their research agenda in this course with their goals for the fellowship application. Doing so will take some experimenting, but students taking this course may benefit from discussions with an instructor who has secured an NSF award.

NSF Deadlines are in the 2nd half of October this year and depend on your discipline:

https://www.nsfgrfp.org/applicants/important_dates

Think about it. We will work something out if you are interested…

What Prior Students Have Said…

"It is precisely the way I think a college course should be taught: You allow students to articulate what they find interesting, then they pursue those projects, with assistance and instruction from you, the expert(s)."

"When we first got this project I thought it would be easy and then 2 months later I thought it would be impossible. Finally getting over the hurdles in this project was very empowering."

"I got a pretty good view on how a problem was approached in different manners from different mindsets. This meant that I expanded my vocabulary on words that I did not know had alternative meanings that are interpreted differently in different disciplines."

"[I enjoyed] Working with people from different disciplines and getting across the jargon barrier."

“This course developed my critical thinking skills in that I was challenged to think of a problem outside of my general science based approach. Having a small group of other disciplines made me think a bit differently than useful which was helpful.”

“I was introduced to, and learned a good deal about, mathematical techniques that will greatly enhance work in game theory that interests me.”

“Professor Loewe spent a lot of time working with us individually, was quick to respond to emails, and mentored us through the project. I have never had a class where I have gotten this much mentoring.”

“Learning more about how different disciplines approach a problem was definitely the number one thing I learned this semester.”

“I think going over parameter estimation was really helpful. It definitely put some things into perspective and made me understand biology a bit more from a mathematical point of view and let me see that everything is not as structured as it is made out in textbooks to be.”

“The research that I did for my project increased my understanding of cancer theories.”

“Going over deterministic and stochastic relationships also helped me to understand how random systems can be and how we can best model them to our particular needs.”

“The things that developed my critical thinking skills the most, were hitting roadblocks and getting swamped in papers that didn’t have the data we needed. This forced me to be creative with my solutions and try new approaches.”

“This course made me think hard about modeling and its relationship to reality. I greatly enjoyed learning about stochasticity and, above all else, nonlinear dynamics.”

“It was also useful to do more coding as I do not have a lot of computer science background so any experience is helpful.”

“[I was inspired] when Prof Loewe was talking about how things can frustrate you because you don’t know how to describe them. Once you are able to describe the thing you aren’t as bothered by it, you understand it. I find this is really true in many areas of life not just modeling systems biology.”

Fall 2016 Timetable Overview

The **"Group Work" column** specifies key events in the grant application submission process. Conform to this roadmap precisely if you want your grant application to be successful.

Deadlines are TBD, see course website. The final grant application deadline will be strict.

Day Week	Date 2015	Topic	Group Work
Tue 1	Lect 9/6	**Course overview. Why EvoSysBio?** Why trans-disciplinarity? Why problem-based learning? Why is modeling important for biology?	Meet fellow students.
Thur 1	Lab 9/8	Explanation of ReLogs, peer review, group projects. Bring your laptops each Thursday!	**Start to form your research group** *Many…*
Tue 2	Lect 9/13	**Intro to abstract populations, individuals, and actions:** from molecules in cells to organisms in ecosystems. *Reflect on the work of linking abstract math and messy biological reality by understandable names and InfoBlocks*	ReLog: explore topics for the group project; Begin considering potential research questions.
Thur 2	Lab 9/15	Install and run the Evolvix demo model on your laptop. Put your first ReLog on the course website.	**Form your research group; find topics** *…small steps…*
Tue 3	Lect 9/20	**Simple growing populations of bacteria** in Evolvix as 'zerodice' (deterministic) or 'manydice' (stochastic) models *Reflection on the roles of chance and necessity*.	ReLog: explore topics for your group project
Thur 3	Lab 9/22	**All Labs: bring your computer; sit with your group.** Re-run and explore models from lecture as needed; Work on your model(s) for group project, alone or in group; Ask other students or instructor for help as needed; Explain your project idea and where you need help.	**Decide to use your own or a default topic for the project?** *…very slowly…*
Tue 4	Lect 9/27	**Decaying population of radioactive material** recorded in Evolvix as a time series until amounts vanish. *Reflection on work with analytic and simulation models.*	**Finalize group.** ReLog on your part in the project.
Thur 4	Lab 9/29	Lab: Continue working on group project. **Today:** Groups present 2-3 min overview; adjust if needed.	**Present group area,** topics, rough plans. *…building on…*
Tue 5	Lect 10/4	**Birth, death, and extinction in cancer cell populations,** recorded by Evolvix as time series in a given time window. *Reflection on randomness and mean expectation in cancer.*	ReLog on your role in project.**Group** submit **title and work plan.**
5	10/6	Lab: Continue working on group project.	**Group research start!** *…top of each…*
Tue 6	Lect 10/11	**Reaction chains, waiting time & biopolymer synthesis,** recorded by Evolvix as time series of selected parts only. *Reflection on waiting, big data, and questions in models.*	ReLog on a question from your group work
6	10/13	Lab: Continue working on group project.	*… other can …*
Tue 7	Lect 10/18	**How carrying capacity limits can stabilize populations** in ecosystems, recorded in Evolvix as changes of density-dependent deaths over time. *Reflections on dynamic changes, differential equations and math's secret language*	ReLog on a question from your group work
7	10/20	Lab: Continue working on group project.	*… result in …*

Day Week	Date 2015	Topic	Group work
Tue 8	Lect 10/25	**How flux can stabilize populations of metabolites,** recorded in Evolvix as phase diagrams of amounts. *Reflect on dynamics, stationary flux-balance and Occam's razor.*	ReLog on a question from your group work
8	10/27	Lab: Continue working on group project.	*… incremental …*
Tue 9	Lect 11/1	**Oscillations in cell-virus, host-pathogen, predator-prey** simple systems, recorded in Evolvix as phase diagrams of fluxes, or other time series. *Reflection on the meaning of attraction and chaos in non-linear dynamics.*	ReLog on a question from your group work
9	11/3	Lab: Continue working on group project.	*… progress …*
Tue 10	Lect 11/8	**Stimulating and limiting kinetics of Michaelis & Menten** in degrading Alcohol, recorded in Evolvix as time series with varying precision. *Reflections on the differences between counts and concentrations.*	ReLog on a question from your group work
10	11/10	Lab: Continue working on group project.	*… that taken …*
Tue 11	Lect 11/15	**Molecular switches, Hill kinetics, and gene regulation,** recording the speed of a switch in Evolvix using time series. *Reflections on reversibility and irreversibility in biochemistry and ecology.*	ReLog on a question from your group work
11	11/17	Lab: Continue working on group project.	*… together …*
Tue 12	Lect 11/22	**Summary of Continuous Time Markov Chain** (CTMC) basics as used above, reviewing Evolvix syntax for easy CTMC modeling and clear mapping to math methods. *Reflection on danger analyzing models with only 1 method.*	ReLog on a question from your group work
12	11/24	Thanksgiving: No Lab	*… can be …*
Tue 13	Lect 11/29	**Directing experiments by sloppy CTMC models** with unknown parameters, using parameter sensitivity analyses and Approximate Bayesian Computation. *Reflection on the semantics of 'unknown' and 'verified' in biology and math.*	ReLog on a question from your group work
13	12/1	Lab: Finalize group project.	*… quite …*
Tue 14	Lect 12/6	**Using CTMCs in biology,** including biochemistry, cell biology, physiology, neurology, epidemiology, life-history, ecology, population genetics, evolution, and phylogeny.	ReLog on a question from your group work
14	12/8	**Presentations of work on group projects.**	*… impressive!* **Submit Grant Now!**
Tue 15	Lect 12/13	**Bringing it all together**. Using EvoSysBio, fitness landscapes and CTMCs to predict evolution. *Reflections on computing, reproducibility, and semantics in future biology.*	
Thr 15	12/15	**Presentations of work on group projects (end).** Open Discussion; Feedback.	
		No exam. Grades in: ReLogs, Group projects, Reviews.	