

BIOM 896 – Special Topics: Systems Bioengineering: multi-scale models in biology

Instructors: Shayn Peirce-Cottler and Jason Papin

Time: Tuesday & Thursday, 9:30am – 10:45am

Location: MR-5 room 2005

Pre-requisites

1. BIOM 601/602: Physiology (or equivalent)
2. One of the following courses in cellular and/or molecular biology:
 - . BIOM 204: Cell and Molecular Biology for Engineers
 - . BIOM 706: Genetic Engineering
 - . BIOM 823: Cell Mechanics, Adhesion, and Locomotion
 - . BIOM 891: Molecular Bioengineering
3. Programming experience in Matlab
4. SEAS graduate student status*
5. Or instructor permission

* Undergraduate students who have met pre-requisites #1, #2, and #3 and who are interested in taking this course *may* contact the instructors and obtain approval for enrollment on a case-by-case basis

Course Philosophy: The next generation of biomedical researchers has the opportunity to make a significant impact in biology and medicine through computational modeling, *but only* if they possess a quantitative mindset, critical thinking skills, hands-on programming experience, a baseline math competency, creativity, and an appreciation of the value and caveats associated with applying their techniques to biological questions. To this end, graduate students in this course will not only understand how and when different computational/mathematical modeling approaches can be used to address biological questions effectively, but they will also obtain hands-on experience in different simulation environments to fully appreciate the benefits and drawbacks of different techniques and how they compare to one another (a “learning through doing” approach). This is achieved through a combination of lectures, readings, discussions, and team projects, in which students apply their knowledge to real scientific questions by developing computational/mathematical models, producing results, verifying their results using published experimental data, and critically analyzing the validity, robustness, novelty, and utility of their models. This multi-faceted didactic approach will strengthen students’ quantitative capabilities, improve their critical analysis skills, and enable them to access a variety of different computational modeling tools, all of which will provide them with the skills necessary to create new computational/mathematical techniques and apply them in novel and useful ways to biomedical problem solving.

Course Description: This graduate level course introduces techniques for constructing mathematical and computational models of biological processes at many levels of organizational scale—from genome to whole-tissue. Students will rotate through several modules where they

will hear lectures, read literature, and participate in discussions focused on the various modeling techniques. In each module, students will learn:

- Which modeling techniques are best suited for addressing biological problems of different scales
- Quantitative characterization of biological properties (eg. robustness)
- What constitutes a valid assumption and how can complex problems in biology be simplified while maintaining biological relevance?

Specific modules will teach computational techniques for:

- 1) genome bioinformatics (e.g., genome-scale protein sequence comparisons),
- 2) genome network analysis (e.g., metabolic network reconstruction & analysis),
- 3) multi-cellular simulations (e.g., agent-based modeling of tissue patterning),
- 4) whole-organ analysis (e.g., finite element analysis of heart function).

Corresponding mathematical techniques will include:

- Partial Differential Equations
- Ordinary Differential Equations
- Linear Algebra

In each module, students will also work in teams to complete group modeling projects that utilize the modeling techniques specific to the particular module. This will provide students with hands-on experience in the different simulation environments while allowing them to address relevant biological problems of different length scales using appropriate modeling techniques. A pallet of possible projects will be provided by the Module Instructor on the first day of the module, and student teams will be invited to select a project from the pallet. Alternatively, students may define their own projects based on their familiarity with the modeling technique and their own research interests. Student teams, consisting of 3-5 students, will be assembled so that they maintain diversity with respect to computational, mathematical, and biological knowledge and skills, and therefore, students will also teach one another as they work together on their team to complete their projects. Although the detail and complexity of the models generated in each module may be very limited, the complete experience of identifying a problem, conceptual design of a model, execution of the design, and critical analysis will be beneficial in teaching students all of the components of the computational model-building process.

Students will present their projects to the class on the final day of the module. Throughout the module, peer critique of team projects will be encouraged in order to teach critical evaluation of computational models. Apart from the team projects in each module, there will be no additional homework assignments, other than reading assignments, and there will be no final project or exam. A sample timeline for a single module is provided below.

Grading

Class participation	2%
Reviewing Assignments (4)	2% each
Homework Assignments (2)	15% each
Group Projects (2)	30% each

TOTAL: 100%

Syllabus

WEEK 1

#1 Thu. Jan. 17 LECTURE: “Introduction to computational systems bioengineering”
by Dr. Peirce and Dr. Papin

WEEK 2

#2 Tue. Jan. 22 LECTURE: “Multiscale biology”
by Dr. Papin

#3 Thu. Jan. 24 LECTURE: “Appreciating the role of experimental data in modeling”
by Dr. Peirce

Reviewing Assignment #1: Read and summarize in a ½ page written review
the key points of 2 papers that will be assigned in class
(Due Thursday, Jan. 31)

WEEK 3

#4 Tue. Jan. 29 LECTURE: “Fundamentals of organ and tissue-level modeling”
by Dr. Peirce

Homework Assignment #1: FEA Model of Ischemia-Reperfusion Injury
(Due Thursday, Feb. 7)

#5 Thur. Jan. 31 DISCUSSION: ‘Current techniques in organ and tissue-level modeling’
by Dr. Peirce and Class

Reviewing Assignment #1 DUE

WEEK 4

#6 Tue. Feb. 5 LECTURE: “Fundamentals of multi-cell modeling (Part 1)”
by Dr. Peirce

Reviewing Assignment #2: Read and summarize in a ½ page written review
the key points of 2 papers that will be assigned in class
(Due Tuesday, Feb. 21)

Project Assignment #1: Meet with your assigned group and develop a
project idea, which you will present next Tuesday, Feb. 12th

#7 Thur. Feb. 7 LECTURE: “Fundamentals of multi-cell modeling (Part 2)”
by Dr. Peirce

Homework Assignment #1 *DUE*

WEEK 5

#8 Tue. Feb. 12 PROJECT DISCUSSION: “Preliminary project overview and brainstorming session”
by Dr. Peirce and Class

First Informal Team Presentations for Project #1

#9 Thur. Feb. 14 LECTURE: “Introduction to computational approaches for multi-cell modeling of biological phenomena”
by Dr. Peirce

WEEK 6

#10 Tue. Feb. 19 PROJECT DISCUSSION: “Project #1 progress report and troubleshooting session”
by Dr. Peirce and Class

Second Informal Team Presentations for Project #1

#11 Thu. Feb. 21 DISCUSSION: ‘Current techniques in multi-cell modeling’
by Dr. Peirce and Class

Reviewing Assignment #2 *DUE*

WEEK 7

#12 Tue. Feb 26 **Final Formal Team Presentations for Project #1 (half of the class)**

#13 Thu. Feb 28 **Final Formal Team Presentations for Project #1 (half of the class)**

WEEK 8

#14 Tue. Mar. 4 Spring Break: No Class

#15 Thu. Mar. 6 Spring Break: No Class

WEEK 9

#14 Tue. Mar. 11 LECTURE: “Quality control for ABM rules and integrating ABM with experiments for validation”
by Bryan Thorne and Alex Bailey

#15 Thu. Mar. 13 LECTURE: “Multiscale modeling in the heart”
by Dr. Jeff Saucerman

Project #1 Reports DUE

WEEK 10

#16 Tue. Mar. 18 LECTURE: “Fundamentals of genome bioinformatics”
by Dr. Papin

Reviewing Assignment #3: Read and summarize in a ½ page written review
the key points of 2 papers that will be assigned in class
(Due Tuesday, Mar. 25)

#17 Thu. Mar. 20 LECTURE: “Current techniques & tools for genome bioinformatics”
by Dr. Papin

Homework Assignment #2: Sequence and array analysis for identifying
genes and regulatory elements
(Due Tuesday, Apr. 1)

WEEK 11

#18 Tue. Mar. 25 LECTURE: “Analyzing expression array data”
by Dr. Papin

Reviewing Assignment #3 DUE

#19 Thu. Mar. 27 LECTURE: “Overview of network analysis challenges - defining system
boundaries; network reconstruction”
by Dr. Papin

Reviewing Assignment #4: Read and summarize in a ½ page written review
the key points of 2 papers that will be assigned in class
(Due Tuesday, Feb. 21)

Project Assignment #2: Meet with your assigned group and develop a
project idea, which you will present next *Tuesday, Feb. 12th*

WEEK 12

#20 Tue. Apr. 1 LECTURE: “Theory & numerical techniques for intracellular network
analysis; ODEs & PDEs of chemical reaction systems, Bayesian networks,
constraint-based modeling techniques – Part 1”
by Dr. Papin

Homework Assignment #2 DUE

#21 Thu. Apr. 3 PROJECT DISCUSSION: “Preliminary project overview and brainstorming session”
by Dr. Papin and Class

First Informal Team Presentations for Project #2

WEEK 13

#22 Tue. Apr. 8 LECTURE: “Theory & numerical techniques for intracellular network analysis; ODEs & PDEs of chemical reaction systems, Bayesian networks, constraint-based modeling techniques – Part 2”
by Dr. Papin

Reviewing Assignment #4 DUE

#23 Thu. Apr. 10 PROJECT DISCUSSION: “Project #2 progress report and troubleshooting session”
by Dr. Papin and Class

Second Informal Team Presentations for Project #2

WEEK 14

#24 Tue. Apr. 15 LECTURE: “ Theory & numerical techniques for intracellular network analysis; ODEs & PDEs of chemical reaction systems, Bayesian networks, constraint-based modeling techniques – Part 3”
by Dr. Papin

#25 Thu. Apr. 17 GUEST LECTURE: “Network models & bioengineering”
by TBA

WEEK 15

#26 Tue. Apr. 22 GUEST LECTURE: “Network models & bioengineering”
by TBA

#27 Thu. Apr. 24 **Final Formal Team Presentations for Project #1 (half of the class)**

WEEK 16

#28 Tue. Apr. 29

Final Formal Team Presentations for Project #1 (other half of the class)

Final Exam Time

#29 Date: TBA

LECTURE: “Wrap-up discussion; Future challenges of Systems Bioengineering”
by Dr. Papin

Project #2 Reports DUE
