PHOL 429: *Biophysical Modeling and Simulation of Cellular Transport*

Offered: Spring 2026

Lecture Program (1 credit): MWF 2:00-3:30 PM for 4 weeks
Mentored Research Program (2 credits): MF 2:00-2:50 PM

Lead instructor(s)

Course Director(s): Walter F. Boron, MD, PhD (walter.boron@case.edu)
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Format and Meeting times

This class will be offered as a two-module class/semester: a taught 4-week Lecture program, followed by a 11-week Research program. Students can take the class for either 1 credit hour ("Lecture Program") or 3 credit hours ("Lecture Program + Research Program").

Module I: Lecture Program (1 credit)

- **Meeting Times:** Mondays, Wednesdays, Fridays, 2:00-3:30 PM for 4 weeks
- **Format:** Live lectures with students attending the class in person. Participating faculty from UCSD and University of Auckland will deliver lectures via Zoom with students in the classroom. Each of these lectures will be followed by a small-group tutorial in which the teaching faculty and TAs will discuss the material covered in the preceding lecture. All lectures and tutorials will be recorded
- **Content overview:** Core Topics to provide the background knowledge on computational methods, Stimulating Peripheral Activity to Relieve Conditions (SPARC) resources, and epithelial transport physiology

Module II: Mentored Research Program (2 credits)

- **Meeting Times:** Mondays, Fridays, 2:00-2:50 PM in class tutorials/group discussions
- **Format:** Guided research and in class tutorials/group discussion of the assigned research projects. At the beginning of this module, students will receive a list of potential research projects. After a student chooses a project, the student will be paired with program faculty with relevant expertise for independent study under their guidance. Students generally will work in pairs on two parallel projects (so that each can still be first author on the term paper/publication plus, perhaps, a co-shared first authorship). Pairing of students will account for complementary expertise (e.g., a student with a more quantitative background will be paired with a student with a more biological background)

- **Content overview:** Tutorials covering examples of applications for the material learned in the previous module and discussion of research projects

Course description

This course is a graduate-level course designed to provide hands on experience in computational modeling of the neural regulation of digestive and renal epithelia through a lecture-based module and supervised modeling projects that make use of datasets, maps and models assembled and made available through the Stimulating Peripheral Activity to Relieve Conditions (SPARC) program of the National Institutes of Health (NIH). The SPARC program is a large NIH project aimed at understanding the anatomy and physiology of the autonomic nervous system (ANS) and its connections to develop new therapies based on the emerging science of neuromodulation.

The Lecture program will provide talks and small group tutorials introducing SPARC, concepts of open science, and modeling methodologies relevant to epithelial cells (including transporters & channels) and their control by the autonomic and enteric nervous systems. Students can take this first part as a 1 credit.

The Research program will provide students with a mentored experience in the development, testing, and textbook-linked publication of a Findable, Accessible, Interoperable, Reusable (FAIR) model that simulates epithelial transport. These models will use SPARC data and models, and leverage SPARC infrastructure. The Lecture program is a required pre-requisite for the research program.

The outcome of this reproducibility project will be submitted to an online repository. Students will be given the opportunity to publish their models in the *Physiome* journal (or another journal that publishes computational models). *Physiome* is an open access journal, launched by the International Union of Physiological Sciences (IUPS) that publishes reproducible and reusable mathematical models of physiological processes, where the experimental details and model validation have been published in a recognized 'primary' peer-reviewed journal. For the FAIR DOs ('Findable, Accessible, Interoperable, Reusable Development of Open Simulations') educational *Physiome* papers, the *Medical Physiology* textbook by Boron & Boulpaep will be regarded as the primary publication. Dr. Peter Hunter is the Editor-in-Chief of *Physiome* and Dr. Walter Boron is a co-editor of *Medical Physiology*. Drs. Nickerson & Occhipinti are members of the Editorial Board of *Physiome*.

Prerequisites and/or intended student population

There are no prerequisites for this course. This is a graduate-level class, and it is recommended that students have completed undergraduate-level biology, chemistry, mathematics, and physics courses appropriate for pre-medical or pre-dental programs.

Recommended and/or Required textbook(s) and/or other supplies

Textbook: "Medical Physiology", 3rd Edition, Boron & Boulpaep Eds (freely accessible online via ClinicalKey when students are connected to the Case network either on campus or via VPN).

SPARC resources are freely available from the website 'https://sparc.science'. Recommended and required reading will come from the online materials such as journal articles and e-textbooks freely available to all students at Case.

Learning objectives and Course Goals

Module I: Lecture Program

- Improved breadth of knowledge about computational methodologies, familiarity with the NIH SPARC effort and its resources, as well as a well-grounded working knowledge about epithelial transport physiology and control by the ANS.
- The Lecture program will cover five main Core Topics: (1) Biophysical modeling theory, (2) Biophysical modeling tools, (3) The NIH SPARC effort, (4) Neurophysiology review, (5) Computational knowledge management.
    1. Biophysical modeling theory (weeks 1, 2 & 3)
        - Introduction to bond graph modeling and its application to representing key processes in neurobiology such as the maintenance of membrane potential, receptor activation and membrane channel mechanisms;
        - Ordinary Differential Equation (ODE) modeling and its relationship with bond graphs. Worked examples for solute(s) movement across the cell membrane, including relationship between the relative ionic concentrations across the membrane with potential difference, simulation of action potential with focus on sodium- and calcium-mediated spikes relevant to neuron, secretory cell and smooth muscle signaling.

        After "Biophysical modeling theory", the student will be able to:
        - Understand solute transport across cell membranes;
        - Build a bond graph model of a simple transporter/channel/receptor mechanism;
        - Explain concepts of conservation of mass, charge and energy and appreciate that the bond graph formalism ensures conservation of mass, charge, and energy;
        - Understand the importance of consistent units in modeling and explain how to link unit consistency with bond graph formalism;
        - Use ODEs to model transporter processes and convert bond graphs to ODEs.
    2. Biophysical modeling tools (weeks 1, 2 & 3)
        - Reproducibility of simulation results, the *Physiome* journal, modular modeling and multiscale modeling;
        - CellML, OpenCOR and the Physiome Model Repository (PMR);
        - Online computational resources.

        After "Biophysical modeling tools", the student will be able to:

- Explain the importance of adopting community standards to ensure the reproducibility of computational models and how the *Physiome* journal is contributing to the development of a modular, standards-based, multiscale modeling framework;
- Understand the principles behind the development of CellML as a modeling standard, how to use CellML with the OpenCOR simulation environment and the PMR repository of CellML models; optional use of OpenCOR with o^2S^2PARC.

3. The SPARC effort (week 3)
   - The Portal;
   - Knowledge management;
   - FAIRness: Ensuring SPARC resources are findable, accessible, interoperable and reusable. Background on international FAIRness efforts will also be provided;
   - Data streams: Curation/segmentation/annotation examples for microscopy, neuron tracing, gene expression and electrophysiology experiments.

   After "the SPARC effort", the student will be able to:
   - Use the SPARC portal for browsing/searching SPARC datasets and simulations, navigating flatmaps, downloading and accessing data;
   - Be familiar with the theory and content of the SPARC Knowledge graph (SKG), reference ontologies, metadata and how to access the SKG;
   - Explain the FAIRness principles;
   - Understand data streams.
4. Neurophysiology Review (week 4)
   - The neurobiology of the pancreas (exocrine secretion), kidney (juxtaglomerular apparatus, renal tubular system, afferent/efferent arterioles), stomach (gastric glands), large intestine (colonic crypts and surface epithelium), gut immunity (spleen and Peyer's patches);
   - The biology of key transporter gene families in mammals.

   After "Neurophysiology review", the student will be able to:
   - Leverage the *Medical Physiology* textbook to navigate the salient concepts in transport physiology;
   - Navigate schematics that describe the physiological regulation of transport processes;
   - Familiarize with the notion of drug absorption, distribution, metabolism, and excretion (ADME).
5. Computational knowledge management (week 4)
   - ApiNATOMY flow scaffolds: linking advective and diffusive flows across multiple scales to map out flows of fluids and solutes;
   - Autonomic and enteric nervous system maps in SPARC: introduction and examples from stomach and colon.

   After "Computational knowledge management", the student will be able to:

- Experience the use of knowledge graphs to manage information about biological connectivity networks;
- Build schematics that describe the physiological regulation of transport processes by drawing knowledge from the *Medical Physiology* textbook and representing it using the ApiNATOMY formalism;
- Leverage ApiNATOMY to map out drug ADME processes in the context of whole-body transport thoroughfares.

Module II: Mentored Research Program

- Hands on experience with building a computational model in CellML including research, creation, execution and results analysis

Proposed Syllabus (subject to change):

Week	Date	Topic	Synopsis	Instructor
1	1/12	Course Introduction/ Biophysical Modeling Theory	Syllabus, rules, expectations, course structure, roadmap/ Physical units for physiology & introduction to multiscale modeling for physiology	Occhipinti/ Hunter
	1/14	Biophysical Modeling Theory/Tools	Physical laws and bond graphs/ Reproducibility, CellML, OpenCOR, PMR	Hunter/ Nickerson
	1/16	Biophysical Modeling Theory/Tools	Simple bond graph models	Hunter/ Nickerson
2	1/19	**Martin Luther King Jr. Holiday**		
	1/21	Biophysical Modeling Theory/Tools	Transport of small molecules across cell membranes (GLUT2, SGLT1)	Hunter/ Nickerson
	1/23	Biophysical Modeling Theory/Tools	ATPase pumps (NKE, SERCA, proton pump)	Hunter/ Nickerson
3	1/26	Biophysical Modeling Theory/Tools	Ion channels & action potentials	Hunter/ Nickerson
	1/28	Biophysical Modeling Theory/Tools	Cellular homeostasis: coupling protein models	Hunter/ Nickerson
	1/30	The SPARC Effort	Portal, knowledge management, FAIRness, data streams	Grethe/ Martone
4	2/2	Neurobiology of Transport I & II	Overview of transport concepts and tissue biology. Molecular biology of transport and drug ADME	de Bono

	2/4	Neurobiology of Transport II & III	Molecular biology of transport and drug ADME. Transport schematics in SPARC	de Bono
	2/6	Computational Knowledge Management	Knowledge graphs and ApiNATOMY modeling	de Bono
5	2/9	**Mini Exam**		Boron/ Moss
	2/13	Overview Research Program, Projects Presentations	Student pairing	Faculty
6	2/16	In class tutorial	Responsible Conduct of Research	Occhipinti
	2/20	Biophysical Modeling Theory/Tools	Cellular homeostasis: coupling protein models	Hunter
7	2/23	Biophysical Modeling Theory/Tools	Cellular homeostasis: coupling protein models	Hunter
	2/27	Group discussions		Faculty
8	3/2	In class tutorial	BG model parameterization	Ai
	3/6	In class tutorial		Faculty
9	3/9	**Spring Break**		
	3/13	**Spring Break**		
10	3/16	In class tutorial		Faculty
	3/20	Group discussions		Faculty
11	3/23	In class tutorial		Faculty
	3/27	In class tutorial		Faculty
12	3/30	In class tutorial		Faculty
	4/3	Group discussions		Faculty
13	4/6	In class tutorial	PMR & Physiome	Nickerson
	4/10	In class tutorial		
14	4/13	In class tutorial		Faculty
	4/17	Group discussions		Faculty
15	4/20	Presentation of final projects		Faculty
	4/24	Presentation of final projects		Faculty
	4/27	Presentation of final projects		Faculty
16	5/4	**Final Project due**	Term paper on research project	

Attendance Policy

This course is offered as a live course. Synchronous students are expected to attend all class meetings. Students may attend class synchronously on zoom if necessary.

Assessment and grading

For students enrolled in the full course (Lecture + Research Program, 3 credits), final grade will be based on class participation (10% = 3% Lecture Program +7% Research Program), homework (10%), mini-exam (10%), final presentation (10%) and project (60%).

For students enrolled in the Lecture Program only (1 credit), final grade will be based on class participation (10%), homework (30%) and mini-exam (60%).

Final Grading:

	Lecture Program (1 credit hr)	Lecture + Research Program (3 credit hr)
Participation:	10% of final score	10% of final score (3% Lect + 7% Res)
Homework:	30% of final score	10% of final score
In class Mini-Exam:	60% of final score	10% of final score
Final Presentation:	N/A	10% of final score
Final Project:	N/A	60% of final score
Grading Scale:	A: 85 - 100 B: 70 - 84 C: 60 - 69 D: 50 – 59 F: Below 50	

Homework: For students enrolled for 3-credit class, the homework will be 10% of final grade. For students enrolled for 1-credit class, the homework will account for 30% of final score. If a student is unable to submit the homework by the indicated time, the student should communicate the reason to the course directors to be justified. In the absence of a justification, homework submitted within 24 hours past the deadline will receive a max score of 50%; homework submitted between 24 and 48 hours past the deadline will receive a max score of 20%; homework submitted after 48 hours past the deadline will not be graded and will receive a 0 (zero).

Mini-Exam: For students enrolled for 3-credit class, the mini-exam will be 10% of final grade. For students enrolled for 1-credit class, the mini-exam will account for 60% of final score. All students will take their exams in-person during the scheduled class time in Canvas. If a student misses the mini-exam for a valid reason (documented illness, family emergency, etc.), the course director must be notified by noon-time on the missed day (at the latest) to provide an excused absence. Students will be allowed to make-up the mini-exam for excused absences only. The make-up mini-exam will be administered the week prior to Spring Break. Missed mini-exam for unexcused absences will result in a zero score.

Final Presentation & Final Project: The final project will consist of a paper article covering literature review, modeling procedures and results of reproducibility objectives. Students will be provided article

templates as guidelines. If a student is unable to submit the final project by the indicated time, the student should communicate the reason to the course directors to be justified. In the absence of a justification, final projects submitted within 24 hours past the deadline will receive a max score of 30%; final projects submitted between 24 and 48 hours past the deadline will receive a max score of 20%; final projects submitted after 48 hours past the deadline will not be graded and will receive a 0 (zero). If a student is unable to attend the final presentation for health reason or unexpected circumstance, the student is expected to communicate timely with the course directors, so that proper arrangements can be put in place for a presentation make-up.

Course specific guidelines/rules/policies

The students attending the course are expected to abide to proper ethical and professional conduct while in class and at the time of the exam and final presentation. No Cell Phone use is allowed in class, and the phones should be on vibrate to avoid disturbing the lecture. The use of tablets and PCs to follow Power Point presentation and note-taking is permitted. Use of Tablet or PC is allowed at the time of the exam to access Canvas. Phone should be on vibrate and placed at the front of the classroom, to be retrieved at the end of the exam. At the time of the exam, backpacks should be also placed at the front of the classroom, to be retrieved at the end of the exam.

No last minute contacting of the course director or block coordinator for grade change is acceptable. If a student is unable to attend class, the exam or final presentation for health reason or unexpected circumstance, the student is expected to communicate timely with the course director, so that proper arrangements can be put in place in case of the exam or final presentation.

Late arrival in class (more than 5 min since the start of class). If a student is unable to be in class on time, the student is expected to communicate in a timely manner to the course director no later than 30 minutes before the beginning of the lecture. If the student is late more than 5 min for more than 2 times during the Lecture Program and more than 5 times during the Research Program, 5% of the class participation for that module will count as a zero.

Resources available

Canvas course management system will be used for communication with the students, including posting of reading assignments, materials for in class work and grades.

Diversity and Inclusion

It is the intent that all students regardless of their background and perspective be well-served by this class. Further, we intend to present material whose content is respectful of diversity (gender identity, sexuality, disability, age, socioeconomic status, ethnicity, race, nationality, religion, and culture) and deliver it in a way that respects these differences as well. We expect that all students, instructors and guests will help foster an atmosphere of respect, trust and safety in the classroom. If you have suggestions for how to make the class content or environment more inclusive, or have specific incidents to report, please reach out to the instructor. If you are not comfortable reaching out to the instructor, feel free to reach out to someone else, such as the School of Medicine Graduate Education Office (som-

geo@case.edu) or the Office of Inclusion, Diversity and Equal Opportunity (OIDEO) (oideo@case.edu). More information on University policy and resources are available on OIDEO's website.

Disability Accommodations

In accordance with federal law, if you have a documented disability, you may be eligible to request accommodations from Disability Resources. In order to be considered for accommodations you must first register with the Disability Resources office. Please contact their office to register at 216.368.5230 or get more information on how to begin the process. Please keep in mind that accommodations are not retroactive.

Academic Integrity

Any violation of the University's Code of Ethics will not be tolerated. All forms of academic dishonesty including cheating, plagiarism, misrepresentation, and obstruction are violations of academic integrity standards and will result in a minimum penalty of receiving a zero for the assignment, the potential for failing the entire course. Cheating includes copying from another's work, falsifying problem solutions or laboratory reports, or using unauthorized sources, notes or computer programs. Plagiarism includes the presentation, without proper attribution, of another's words or ideas from printed or electronic sources. It is also plagiarism to submit, without the instructor's consent, an assignment in one class previously submitted in another. Misrepresentation includes forgery of official academic documents, the presentation of altered or falsified documents or testimony to a university office or official, taking an exam for another student, or lying about personal circumstances to postpone tests or assignments. Obstruction occurs when a student engages in unreasonable conduct that interferes with another's ability to conduct scholarly activity. Destroying a student's computer file, stealing a student's notebook, and stealing a book on reserve in the library are examples of obstruction.
In addition, the incident will be reported to the Dean of Undergraduate Studies and Academic Review Board for undergraduates or Senior Associate Dean of Graduate Studies, for Graduate Students. The CWRU Statement of Ethics for graduate students can be found here:
http://case.edu/gradstudies/about-the-school/policies-procedures/

We reserve the right to alter, change, or update this syllabus at any time without prior notice. Subsequent changes will be made known through Canvas announcements.