

Instructor Dr. Sorinel A. Oprisan
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Lecture time & place TR: 12:15pm - 1:30pm, RITA 375
Office hours TR in RITA 325, 4:00 P.M. -5:00 P.M. or by appointment

This is an introduction to basic biophysical models of excitable cells, i.e. cells that actively respond to an electric stimulus and their electrophysiology is primarily determined by both passive (electrical resistance and capacitance) and active (voltage-gated ionic channels) cell membrane properties. The course focuses on a widely-used class of mathematical models developed by Alan Hodgkin and Andrew Huxley for the squid's giant axon. Hodgkin and Huxley (HH) model is the "gold" standard for describing the behavior of excitable membranes. This course uses biophysical models for ionic diffusion across membrane, establishes quantitative relationships between resting membrane potential and ionic permeability, describes membrane excitation and recovery, and emphasizes the role of electrotonic interactions among excitable cells. This course emphasizes the effective use of computers in science, including searching neuroscience databases for experimental data regarding specific ionic currents, fitting experimental data with smooth analytic functions, integrating the membrane equations with freely available packages, e.g. Neuron and XPP, and the use of interactive graphics and virtual experiments on digital excitable cell models. Subject matter covers basic aspects of membrane morphology, passive and active electrical properties, electric currents involved in maintaining the activity of excitable cells, ionic channels, testing the existing computer implementations and developing new numerical simulations using freely available software packages.

Learning Outcomes

- Understand the historical context that lead to major advances in experimental and mathematical modeling of excitable cells.
- Develop a strong conceptual and quantitative understanding of the biophysics behind cellular excitability.
- Connect biophysical concepts, principals, and laws to biology and behavior by using mathematical concepts, equations, and computational tools.
- Understanding the connection between single-cell properties and the response of a large neural network.
- Develop the ability to search databases and summarize results in condensed mathematical and computational models with biophysical relevance.
- Enhance problem solving and computational skills.
- Augment investigative and observational skills.
- Broaden an appreciation for logical qualitative and quantitative reasoning.
- Enhance scientific communication skills.
- Present, in a concise manner, the results of an individual or group project.

- Write and/or debug computer code that mimics the activity of excitable cells.

Prerequisites

Physics section PHYS 396:

PHYS 111 & PHYS 112 or HONS 157 & HONS 158

and

BIOL 111 and BIOL 112

Biology section BIOL 396:

PHYS 101 & PHYS 102 or PHYS 111 & PHYS 112 or HONS 157 and HONS 158

and

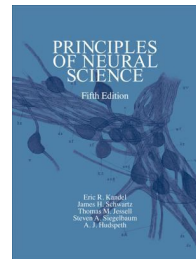
BIOL 111 and BIOL 112 and BIOL 211 and BIOL 212

or permission of the instructor.

Prior computer programming experience is desirable, but not required.

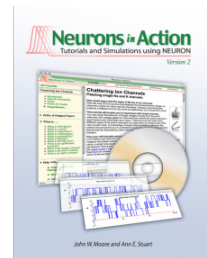
Recommended textbook and software packages

- Principles of Neural Science, E.R. Kandel, J.H. Schwartz, T.M. Jessell, 2005 (KSJ).
- Licensed software package “Neurons In Action 2: Tutorials and Simulations using NEURON”, J.W. Moore and A.E. Stuart, 2007 (MS).



Additional references

- Ionic Channels of Excitable Membranes, Third Edition. Bertil Hille. Sinauer Associates. Sunderland, MA. 2001 (H).
- Computational Cell Biology: An Introduction to Computer Modeling in Molecular Cell Biology. Chris Fall, Eric Marland, John Tyson, and John Wagner (editors). Springer-Verlag. New York, NY. 2002 (TW)



All books are available at College of Charleston library. The licensed software “Neurons In Action” (NIA) is installed on departmental computers. Both NIA and XPP software packages are freely available for all computer platforms. Course notes will be electronically distributed through our course management system.

Grading policy

Final exam	30%
Midterm exam	30%
Homework	25%
Quizzes	15%

Grading scale

Letter grade	A	A-	B+	B	B-	C+	C	C-	D+	D	D-	F
Quality	4.0	3.7	3.3	3.0	2.7	2.3	2.0	1.7	1.3	1.0	0.7	0.0

points												
Percentage	93.00	90.00	86.00	83.00	80.00	76.00	73.00	70.00	66.00	63.00	60.00	Bello
	-100	-	-	-	-	-	-	-	-	-	-	W
		92.99	89.99	85.99	82.99	79.99	75.99	72.99	69.99	65.99	62.99	60.00

Final exam

The final exam is comprehensive and is scheduled on Tuesday, December 11, 2017 between 12:00pm and 3:00pm in RITA 375.

An alternative format to the traditional written comprehensive final exam is the semester-long computational project related to biophysical modeling of excitable cells. The computational project could be your individual effort or a group project with no more than two members. To receive a grade for your computational project you must: (1) prepare a PowerPoint presentation and present it during the scheduled time at the end of the semester, and (2) submit an electronic final report (LaTeX preferred) no later than the final exam date to oprisans@cofc.edu. If you decide to complete a computational project, then you must submit an initial draft before the midterm, i.e. no later than the first week of October, containing the following items:

- a tentative title
- name(s) of the student(s) involved (no more than two per project)
- a short abstract (300-1000 words) describing the purpose of the project, required resources, cost of implementation, and expected results
- a timeline for your project with measurable milestones
- a preliminary list of references

The project title and the abstract are not final and you are free to alter them during the semester. Constantly inform me about your progress in order to make sure that the final presentation and written report are acceptable. The final presentation of your project should be short (15-20 minutes) and prepared in PowerPoint. A possible layout of the presentation is as follows:

- statement of the problem
- background and biomedical relevance and impact of the problem you addressed (because not everybody is familiar with the bibliography you read for this project and the importance of your biomedical application)
- methods and models
- results
- conclusions

The presentation and your final report will be made available through our course management system to all students. The final written report should be brief but self-consistent. The report should be organized as a research paper (LaTeX preferred). A possible layout of the presentation is as follows:

- Title
- Author(s)
- Abstract
- Introduction

- Methods
- Results
- Conclusions
- Acknowledgments
- References

If I found the project extensive enough to justify a group effort, and unless you decide to explicitly state the percent effort, I will assume that each member of the group contributed equally and will receive the same grade.

Midterm exam

There will be one in-class midterm test, which will consist of a mix of conceptual and quantitative problems. The concept questions will be similar to the concept questions solved in class or from your reading quizzes. The quantitative problems will be similar to the assigned homework problems, the examples given in your textbook(s), and the problems solved in class. No textbooks, notes, or any other kind of help is allowed during the midterm test and the final exam. During the semester, we will compile a short formula sheet that will be available to everyone during the tests.

Homework

Homework assignments will consist mostly of quantitative evaluations with the purpose of enhancing problem-solving and computational skills.

For computational assignments, both the source code and a printout are required. The entire assignment should be sent electronically as a single pdf file with the name Your LastName_HWK#x.pdf, e.g. Oprisan_HWK#2.pdf

Although not required, I strongly advise you to keep detailed solutions of the problems that you solved and bring them with you during office hours such that I have a clear understanding of your line of thought. Finally, a notebook containing detailed solutions to homework assignments will be an invaluable resource for your preparation for the midterm and final exams.

If a homework deadline overlaps with any C of C observed religious holidays the deadline is automatically extended to the first class after the holiday. In cases of illness or other personal emergencies you are responsible for requesting a deadline extension - a very brief email suffices. Any such requests must be made before the due date.

Reading assignments and quizzes

Reading assignments will be given regularly from the main textbook(s), additional references, and some recent research papers related to biophysical modeling of excitable cells. Quizzes may be administered at the beginning of class meetings. Any missed quiz receives zero points and there is no reading quiz make-up.

The following is a **tentative schedule** of our lectures and computational demos/activities. Both the topics and the test dates could change during the semester to accommodate unforeseen events.

Week 1

- Introduction to biophysics of excitable cells
- Individual reading assignments – review papers on introduction to excitable cells
- Computational demo: Windows/Mac OS X primer on operating systems

Week 2

- The brain and behavior (KSJ, chapter 1)
- Nerve cells and behavior (KSJ, chapter 2)
- Class presentations of review papers on introduction to excitable cells
- NIA2 hands-on computational activity: The Membrane

Week 3

- Ion channels (KSJ, chapter 6)
- Membrane potential (KSJ, chapter 7)
- NIA2 hands-on computational activity: The Membrane

Week 4

- Ionic basis of the membrane potential, Nernst & Goldman-Hodgkin-Katz equation
- NIA2 hands-on computational activity: Patch resting potential (MS)

Week 5

- Passive electrical properties of the cell membranes (KSJ, chapter 8)
- Propagating signaling: The action potential (KSJ, chapter 9)
- The superfamily of voltage-gated channels (H, chapter 3)
- NIA2 hands-on computational activity: Action potential (MS)

Week 6

- Hodgkin & Huxley biophysics of the squid giant axon (H, chapter 2)
- Dynamic Phenomena in Cells (TW, chapter 1)

Week 7

- Voltage-gated calcium channels (H, chapter 4)
- Potassium channels and chloride channels (H, chapter 5)
- Midterm exam

Week 8

- Numerical methods in biophysics (Taylor series, Euler and Runge-Kutta methods, and numerical errors)
- Overview of synaptic transmission (KSJ, chapter 10)
- XPP hands-on computational activity: Hodgkin & Huxley model implemented in XPP

Week 9

- Direct gating transmission (KSJ, chapter 11)
- Synaptic integration (KSJ, chapter 12)
- XPP hands-on computational activity: Hodgkin & Huxley model implemented in XPP (independent project based on a research paper)

Week 10

- Second messenger (KSJ, chapter 13)
- Mathematical modeling of synaptic transmission (electrical and chemical synapses, AMPA, GABBA, and NMDA)
- XPP hands-on computational activity: Multiple compartment models

Week 11

- Mathematical modeling of synaptic transmission (electrical and chemical synapses, AMPA, GABBA, and NMDA)
- Dopaminergic neurons, biological functions and their mathematical model
- XPP hands-on computational activity: Synaptic coupling models

Week 12

- Large scale neural networks, fronto-stratal loops
- Hands-on computational activity: Dopaminergic neuron/Time perception and neurodegenerative diseases

Week 13

- Large scale neural networks, the phase resetting approach
- Hands-on computational activity: Phase-locked modes in neural networks

Week 14

- Student presentations

Important dates (see the Registrar's Office academic calendar for a complete list)

- August 22, Fall full semester and Express I classes begin.
- October 1, Last day to submit an Undergraduate Application to Graduate in Fall 2017.
- October 16-17, Fall Break (SD*)
- October 20, Mid Term and Express I grades due at noon.
- November 22-26, Thanksgiving Holiday. No Classes. College Closed.
- December 4, Last day of full semester and Express II classes.
- December 5, Reading Day (SD*)
- December 13, Full semester and Express II final exams end.

Attendance and class participation

It is highly recommended that you attend all lectures and actively engage in material discussion and presentation. All concepts presented and all problems solved in class will be part of quizzes, tests, and the final exam.

Collaboration

I strongly encourage collaboration in and out of class. I recommend that you form small study groups (3-6 students) and work together on your homework assignments, hands-on computational activities and computational projects. Before working together or consulting others on any assignment, it pays to give yourself the opportunity to work on it alone. Activities for which collaboration is not permitted are: reading quizzes, in-class tests, and the final exam.

Class conduct

- Arrive on time to class to avoid disrupting the learning process.
- Refrain from talking out loud and/or inappropriately to the extent that it is disruptive to the learning process.
- There shall be no eating, drinking, or sleeping in the classroom.

- Do not leave trash behind (e.g., cups, containers, wrappers, etc.)
- Cell phones, beepers, headsets, iPods and any other electronic devices that may disrupt the class must be turned off and put away prior to class unless you have a job requiring them to be on for safety (firefighter, EMT, etc.)
- Computer use is limited to taking notes or participating in classroom activities.
- *Recording (video and/or audio) my lectures is allowed only with my written consent.*

See also Section 33 “Classroom Code of Conduct” of the Student Handbook (<http://studentaffairs.cofc.edu/honor-system/studenthandbook/index.php>).

Center for Student Learning (CSL) offers academic support services for assistance in study strategies, speaking & writing skills, and course content. They offer tutoring, Supplemental Instruction, study skills appointments, and workshops. The services are available to you at no cost. For more information regarding these services please visit their office in Addlestone Library, Room 116, check their website at <http://csl.cofc.edu>, or call (843) 953-5635.

The College will make reasonable accommodations for persons with documented disabilities. Students should apply for services at the Center for Disability Services/SNAP located on the first floor of the Lightsey Center, Suite 104. Students approved for accommodations are responsible for notifying me as soon as possible and for contacting me one week before the accommodation is needed.

“Accommodations will be determined on a case-by-case basis and are listed in the student’s Professor Notification Letter (PNL). It is the responsibility of the student to give the letter to their professors the first week of the semester. Students are not required to disclose their SNAP status to professors if they choose not to use accommodations in that professor’s class.” (<http://disabilityservices.cofc.edu/cds-resources/index.php>)
“Students are asked to sign up for their tests at The Center For Disability Services one week in advance. Professors are not required to accommodate students with extended time if they do not receive advance notice.” Please check the accommodations for testing at <http://disabilityservices.cofc.edu/cds-resources/alternate-testing-site-ats/index.php>.

Honor Code and Academic Integrity (from <http://academicaffairs.cofc.edu/documents/honor-code-language.pdf>)

“Lying, cheating, attempted cheating, and plagiarism are violations of our Honor Code that, when identified, are investigated. Each incident will be examined to determine the degree of deception involved. Incidents where the instructor determines the student’s actions are related more to a misunderstanding will be handled by the instructor. A written intervention designed to help prevent the student from repeating the error will be given to the student. The intervention, submitted by form and signed both by the instructor and the student, will be forwarded to the Dean of Students and placed in the student’s file. Cases of suspected academic dishonesty will be reported directly by the

instructor and/or others having knowledge of the incident to the Dean of Students. A student found responsible by the Honor Board for academic dishonesty will receive a XF in the course, indicating failure of the course due to academic dishonesty. This grade will appear on the student's transcript for two years after which the student may petition for the X to be expunged. The student may also be placed on disciplinary probation, suspended (temporary removal) or expelled (permanent removal) from the College by the Honor Board. Students should be aware that unauthorized collaboration -- working together without permission -- is a form of cheating. Unless the instructor specifies that students can work together on an assignment, quiz and/or test, no collaboration during the completion of the assignment is permitted. Other forms of cheating include possessing or using an unauthorized study aid (which could include accessing information via a cell phone or computer), copying from others' exams, fabricating data, and giving unauthorized assistance. Research conducted and/or papers written for other classes cannot be used in whole or in part for any assignment in this class without obtaining prior permission from the instructor. See also Section 9 (page 10) of the Student Handbook at <http://studentaffairs.cofc.edu/honor-system/studenthandbook/index.php>