

# Cellular Biophysics and Modeling — Fall 08

Prof. Gregory D. Smith

APSC 451 – Cross-listed as BIO 451

*Cellular Biophysics and Modeling* is an introduction to mathematical modeling in cellular physiology and neuroscience.

Topics covered include: membrane transport and diffusion, classical biophysics of the squid giant axon, the gating of voltage- and ligand-gated ion channels, metabotropic receptors, signal transduction, intracellular calcium responses, and plasma membrane and endoplasmic reticulum excitability, bistability, oscillations, and bursting.

Each topic will be studied from the perspective of nonlinear dynamics. Mathematical idealizations of each phenomena will be constructed and then analyzed using computer simulation (numerical integration) and graphical techniques (phase-plane analysis).



*Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting.* Eugene M. Izhikevich. 2006.

*Ionic Channels of Excitable Membranes.* Bertil Hille. 2001.

*Computational Cell Biology: An Introduction to Computer Modeling in Molecular Cell Biology.* Chris Fall et al., eds. 2002.



*Cellular Biophysics and Modeling* is a *Neuroscience* elective and a required course in the Applied Science *Theoretical Biology* minor.

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Prof. Gregory D. Smith (Applied Science)

APSC/BIO 451 — TR 3:30–4:50

## Catalog Description

An introduction to simulation and modeling of dynamic phenomena in cell biology and neuroscience. Topics covered include membrane transport and diffusion, the biophysics of excitable membranes, the gating of voltage- and ligand-gated ion channels, intracellular calcium signaling, and electrical bursting in neurons and other cell types.

Prerequisites: MATH111 and MATH112/113 (Calculus I & II); BIO203 (Principles of Biology: Molecules, Cells, and Development); or permission of instructor.

## Texts

- **Ionic Channels of Excitable Membranes**, Third Edition. Bertil Hille. Sinauer Associates. Sunderland, MA. 2001.
- **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.
- **Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting**. Eugene M. Izhikevich. The MIT Press. Cambridge, MA. 2006.

## Homework and Computer Laboratory

*Cellular Biophysics and Modeling* is a structured course with homework assignments. While some problem sets will be verbal and analytical in nature, others will involve computer modeling to be performed at home or in a computer laboratory using XPP (short for “X Phase Plane,” a freeware ordinary differential equation solver written by Bard Ermentrout, a computational neuroscientist at the University of Pittsburgh).

In order to maintain the accessibility of this class to upper-division biology majors, mathematical modeling techniques will be introduced in a manner that does not require ordinary differential equations or computer programming as a prerequisite. However, a basic understanding of cell and molecular biology and quantitative aptitude are essential.

## Exams

There will be three equally weighted exams. Each contributes 25% to your final grade. Homework contributes an additional 25%.

# Syllabus: Cellular Biophysics and Modeling

- **Membrane transport and diffusion**

Brownian motion, random walks, Fick's law, diffusion coefficients and the diffusion equation, electrodiffusion, equilibrium potentials and the Nernst equation, the Goldman-Hodgkin-Katz equation.

- **Classical biophysics of the squid giant axon**

Ohm's law, the resting membrane potential, the action potential, voltage clamp recording,  $\text{Na}^+$  and  $\text{K}^+$  currents in axons, activation and inactivation of  $\text{Na}^+$  currents, gating charge and gating currents.

An introduction to ordinary differential equations (ODEs), the electrical circuit model of the plasma membrane (PM), membrane conductance, capacitance, and time constants, solving and analyzing the passive membrane model using XPP, comparing numerical and analytical solutions to ODEs.

The Hodgkin-Huxley (HH) model of the action potential, current-voltage relations, the current balance equation, voltage-dependent variables of the HH model, the two kinetic processes that control  $\text{Na}^+$  conductances, and the "delayed rectifier"  $\text{K}^+$  conductance.

- **Voltage-and ligand-gated ionic currents, transporters, and pumps**

The superfamily of voltage-gated channels, voltage-gated  $\text{Ca}^{2+}$  channels, potassium channels and chloride channels, and ligand-gated channels of fast chemical synapses.

Mass action kinetics, transition-state diagrams and kinetic modeling of gating mechanisms, quasi-static approximation and simplification of kinetic models, derivation of HH-like gating variables.

- **Geometric analysis of plasma membrane electrical activity**

The Fitzugh-Nagumo model, the Morris-Lecar model, and phase-plane analysis of plasma membrane excitability, bistability, and oscillations. Anodal-break excitation, class 1 and 2 membranes, current-frequency relations, and spike-frequency adaptation.

- **Intracellular calcium signaling**

Confocal microfluorimetry and imaging of intracellular  $\text{Ca}^{2+}$ , ODEs for  $\text{Ca}^{2+}$  buffering, association and dissociation rate constants, equilibrium constants, equilibration times and conserved quantities.

The inositol 1,4,5-trisphosphate ( $\text{IP}_3$ ) receptor  $\text{Ca}^{2+}$  channel, the ryanodine receptor, single channel recording in planar lipid bilayers, the DeYoung-Keizer  $\text{IP}_3$  receptor model, a HH-like reduction of the DeYoung-Keizer model.

Compartmental models of  $\text{Ca}^{2+}$  handling,  $\text{Ca}^{2+}$  excitability, bistability, and oscillations, open versus closed cell models, total cell  $\text{Ca}^{2+}$  as a slow variable.

- **Electrical bursting,  $\text{Ca}^{2+}$ -activated  $\text{K}^+$  channels, and whole cell models**

Thalamic relay neurons, the T-type  $\text{Ca}^{2+}$  current and the low-threshold spike, post-inhibitory rebound bursting. Coupling of ER and PM dynamics in agonist-stimulated pituitary gonadotrophs and pancreatic beta cells. The classification of electrical bursters.