

Ion channels of excitable membranes *Spring 2013*

Course Number: 580.632/580.425

Instructor: Prof. David Yue (955-0078, dyue@jhmi.edu)

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Place: See postings on the web site.

Course web site: <http://web1.johnshopkins.edu/csl/academics/ionchannels/IonChannels.htm>

Time: W 3:30-5:00 pm, F 3:30-5:00 pm Talbot Library, Traylor Building 7th floor, SOM

Format: Problems sets about 1/week. Paper presentations required for 632 participants. Final exam.

Textbook: (required) Bertil Hille (2001) Ionic Channels of Excitable Membranes 3rd Edition, Sinauer (1st or 2nd edition will do); and (highly recommended) Johnston and Wu (1995) Foundations of Cellular Neurophysiology, MIT Press.

SYLLABUS

- 1/30 Course overview.
Ion channels 1-2-3: Extreme synthesis of HH view for cardiac action potential genesis.
Reading for week 1: Chapters 1-2 in Hille, Ion Channels 1-2-3.pdf, circuits chapter.pdf
- 2/1,6 OFF for Biophysical Society Meeting
- 2/8 In-class review of introductory problems.
- 2/13 Ch. 1 Classical view of permeation and gating: two important issues introduced by review of the Hodgkin-Huxley models of Na and delayed K currents. Explicit derivation of GHK current equation.
- 2/15,20 Ch. 2.1 – 2.3 The Big Deal About Single-Channel Info: Introduction of a state-diagram view of gating by way of a single-channel look at Na channel gating.
Ch. 2.4 – 2.5 Power of single-channel information and barebones continuous-time Markov processes.
- 2/22 Ch. 2.6 Lecture presentation of Aldrich, Corey, and Stevens (1983) A reinterpretation of mammalian sodium channel gating based on single channel recording. *Nature* 306:436-441.
- 2/27 Ch. 4.1 – 4.2 Markov models of ion channel gating I: Motivation from modern view of voltage-dependent activation and Ca²⁺ regulation of potassium channels. Relation to linear systems theory.
- 3/1,6,8 Ch. 4.3 – Markov models of ion channel gating I.
- 3/13 Jackie Niu. Paper presentation to illustrate application of Markov theory: Zagotta WN and Aldrich RW (1990) Voltage-dependent gating of Shaker A-type potassium channels in *Drosophila* muscle. *J. Gen. Physiol.* **95**:29-60.
- 3/15 Herzig et al. Boombim.
- 3/20,22 Hopkins Spring Break
- 3/27 Ch. 5 Markov models of ion channel gating II. Coverage of Colquhoun and Hawkes (1981) On the stochastic properties of single ion channels. *Proc R Soc Lond B* **211**:205-235. Equilibrium view of gating mechanisms: microscopic reversibility and the Boltzmann distribution.
- 3/29 Ch. 5 Markov models of ion channel gating II. (continued)
- 4/3 MATLAB expm cookbook session.

- 4/5 Paper presentation to illustrate application of Markov theory: Block analysis provides in depth understanding of local anesthetic action on Na channels:Gingrich, Beardsley, and Yue (1993) Ultra-deep blockade of Na channels by a quaternary ammonium ion: catalysis by a transition-intermediate state? J Physiol 471:319-341.
- 4/10 Noise analysis to infer single-molecule behavior from summed records from many molecules
- 4/12 Noise analysis (continued)
Paper presentation to illustrate use of noise analysis (student)
- 4/17 Optical FRET methods to understand molecular mechanisms of ion channels I
- 4/19 FRET meets chemical biology to understand molecular mechanisms of ion channels II
- 4/24 FRET/chemical biology paper presentation (student)
- 4/26 X-ray crystallographic methods to resolve ion channel structure I
- 5/1 X-ray crystallographic methods to resolve ion channel structure II
- 5/3 X-ray crystallographic insight into ion channel function (paper presentation)
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- 5/10 Final exam. Distributed 5/09, due at end of day on 5/10. 24 hours.