

Ion channels of excitable membranes *Spring 2007*

Course Number: 580.632/580.425

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

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Place: See postings on the web site.

Course web site: <http://webhost5.nts.jhu.edu/csl/academics/ionchannels/IonChannels.htm>

Time: Th 3:30-5p, F 2-3:30p

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

- 1/25 Organization meeting: *Course overview; Ion channels, why they are important; and Ion channel 1-2-3.*
Reading for week 1: Chapters 1-2 in Hille, optional Hodgkin AL and Huxley AF (1952) *J Physiol* **117**:500-544 (ignore sections on propagated action potentials).
- 2/1 *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. Reading for week 2: Johnston & Wu, Chapter 2, Chapter 3, Chapter 6 (pp 143-158).
- 2/2 *Macro-macroscopic context of ion channels: application to the EKG.*
- 2/8 *Elements of mathematical simulation of excitability based on classic views of permeation and gating.*
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, Readings: Chapter 2 of Scheaffer *Introduction to Probability*.
- 2/9 *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. [HW#1 due]
- 2/15-16 *Ch. 3. Single-channel insight visits other realms of biology—Lecture presentation of Liphardt et al (2001).*
Reversible Unfolding of Single RNA Molecules by Mechanical Force. *Science* **292**:733. [HW#2 due, 2/16]
- 2/22 *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.
- 2/23 *Ch. 4.3 – Markov models of ion channel gating I.* [HW#3 due]
- 3/1-3/2 *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. [HW#4 due]
- 3/8-3/9 MATLAB expm cookbook session.
- 3/15-16 *Spring break*
- 3/22 *Spring break, extended*
- 3/23 *2nd Paper presentation to illustrate application of Markov theory*: Herzig et al (1993) *Biophys J* **65**:1599 [HW#5 due]

- 3/29-3/30 *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. 3/30 [HW#6 due]
- 4/5 *Paper presentation to illustrate application of Markov theory: Block analysis provides in depth understanding of nicotinic acetylcholine receptor channel activation by ligand:* Neher and Steinbach (1978) Local anaesthetics transiently block currents through single acetylcholine-receptor channels. *J Physiol* 277:153-176.
- 4/6 *Paper presentation to illustrate application of Markov theory: Insight into calcium-channel modulation:* To be announced [HW#7 due]
- 4/12 *Ch. 6 (pp. 1 – 14) Gating-charge movement, another experimental clue as to gating.* Electrostatic derivation and lecture on first of two classic papers showing gating-charge immobilization of Na channels during inactivation, a phenomenon that also proves inconsistent with Hodgkin-Huxley gating models. Armstrong and Bezanilla (1974) Charge movement associated with the opening and closing of the activation gates of the Na channels. *J Gen Physiol* 63:533-552.
- 4/13 *Paper presentation to illustrate modern application of gating-charge approach.* Jones LP et al (1999) N-Type Calcium Channel Inactivation Probed by Gating-Current Analysis. *Biophys J* **76**:2530–2552. [HW#8 due]
- 4/19 *Optical FRET methods to understand molecular mechanisms of ion channels:*
- 4/20 *Optical FRET methods to understand molecular mechanisms of ion channels: Paper presentation of Erickson et al (2001) Neuron.* [HW#9 due]
- 4/26 *Ca²⁺ decoding by the CaM/VDCC complex—operational capabilities and biological impact*
- 4/27 *Mechanism of Ca²⁺ decoding by the CaM/VDCC complex* [HW#10 due]
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5/9 Final exam. Distributed 5/8, due at end of day on 5/9. 24 hours.