Foundation for Advanced Education in the Sciences
Graduate School at NIH

Biol 350: **Foundations of Cellular Neuroscience**
Spring 2018
Wednesdays, 5:30-8:30 pm, Building 10, B1C207

This course explores a wide range of cellular neuroscience, including: membrane biophysics and action potentials; ion channels; synaptic transmission and plasticity; dendritic integration and computation. Lectures also introduce techniques used to record and image activity and signaling in neurons, as well as quantitative methods used to analyze experimental data. In addition to lectures and exams, the course features in-depth discussions of classic and current literature, with problem sets to enhance comprehension of lecture material.

Course Director: Jeff Diamond, Ph.D., Senior Scientist, NINDS; diamond@ninds.nih.gov

Lecturers: John Ball, Ph.D. (NEI), Dahong Chen, Ph.D. (NIDDK), Jacob Gutzmann, Ph.D. (NICHD), Julia Bachman, Ph.D. (NIDCD), Ginger Hunter, Ph.D. (NINDS), Paul Kramer, Ph.D. (NINDS).

Text:

From Molecules to Networks: An Introduction to Cellular and Molecular Neuroscience
Elsevier. Edited by John H. Byrne and James L. Roberts
ISBN: 9780123971791
http://www.sciencedirect.com/science/book/9780123971791
Page references refer to the 3rd edition (available free online).

PDFs of handouts and papers available via Dropbox:
https://www.dropbox.com/sh/valb69ecg7dl9gl/AAC1_KRiXn1-sGRCvOs2tEm2a?dl=0

CLASS POLICIES:
Cell phones: If you need to call or text someone, please step outside the classroom.
Problem sets: Working together is encouraged, but submitted answers should reflect your own work.
Grading: 90%: successful completion of the problem sets (the 'A for effort' concept holds here). 10%: Journal club-style presentation of assigned paper.

NOTE: Each week includes material (in the red box) to be read ***before*** the class. This will *dramatically* enhance your comprehension and enjoyment of the week's lecture and paper presentation. It will also help you to get a head start on the problem set.

Syllabus

Jan. 31 *Cell Membranes and Membrane Potential* *Ball*

Read ***before*** class:

From Molecules to Networks:
Chapter 1: *Cellular components of nervous tissue.* (pp. 3 – 17)
Chapter 12: *Membrane potential and action potential* (pp. 351 – 358)

Other resources:

GHK/Nernst sim: http://www.nernstgoldman.physiology.arizona.edu/
Metaneuron: www.metaneuron.org
Physiologyweb.com introduction to & explanation of the reversal potential
http://www.scholarpedia.org/article/Electrical_properties_of_cell_membranes

Feb. 7 *Action Potentials* *Ball*

Read ***before*** class:

From Molecules to Networks:
Chapter 12: *Membrane potential and action potential* (pp. 358 – 366)
Chapter 13: *Biophysics of Voltage-Gated Ion Channels* (pp. 387-393)

Paper for discussion:

Curtis, H.J., and Cole, K.S. (1942) Membrane resting and action potentials from the squid giant axon. J Cell Comp Physiol **19**, 135-144. http://onlinelibrary.wiley.com/doi/10.1002/jcp.1030190202/epdf

Other resources:

Metaneuron: www.metaneuron.org
Hodgkin-Huxley model simulator: http://myselph.de/hodgkinHuxley.html
Helpful demonstrations on Wolfram.com (these require installation of "Wolfram CDF Player")
http://www.demonstrations.wolfram.com/NeuralImpulsesTheActionPotentialInAction/
http://demonstrations.wolfram.com/HodgkinHuxleyActionPotentialModel/
Nernst/GHK equation simulator: http://www.nernstgoldman.physiology.arizona.edu/

Feb. 14 *Electrophysiological Recordings* *Ball*

Read ***before*** class:

From Molecules to Networks:

Chapter 13: *Biophysics of Voltage-Gated Ion Channels* (pp. 393-400)

Chapter 14: Dynamic Properties of Excitable Membranes (pp. 409-412)

Paper for discussion:

Hodgkin, A.L., Huxley, A.F., and Katz, B. (1952). Measurement of current-voltage relations in the membrane of the giant axon of Loligo. *J. Physiol.* **116**, 424-448. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1392219/pdf/jphysiol01447-0057.pdf

Optional reading:

Chapter 14: *Dynamic Properties of Excitable Membranes* (pp. 412-end)

Huxley AF. Hodgkin and the action potential 1935-1952. (2002) *J. Physiol.* **538**, 2. http://www.ncbi.nlm.nih.gov/pubmed/11773311

Optional viewing:

Action Potentials from Squid featuring Alan Hodgkin

https://www.youtube.com/watch?v=k48jXzFGMc8

Feb. 21 *Ion Channels I: Diversity and Structure* *Gutzmann*

Read ***before*** class:

From Molecules to Networks:

Chapter 11: *Molecular Properties of Ion Channels*

Hille, B. (2001) *Ion Channels of Excitable Membranes* – Introduction

Paper for discussion:

Hamill, O.P., Marty, A., Neher, E., Sakmann, B., and Sigworth, F.J. (1981) Improved patch-clamp techniques for high-resolution current recording from cells and cell-free membrane patches. *Pflügers Arch* **391**, 85-100.

https://link.springer.com/content/pdf/10.1007%2FBF00656997.pdf

Feb. 28 *Ion Channels II: Kinetics, Analysis and Modeling* *Gutzmann*

Read ***before*** class:

From Molecules to Networks:

Chapter 13: *Biophysics of voltage-gated ion channels*

Paper for discussion:

Rosenmund C, et al. (1998) The Tetrameric Structure of a Glutamate Receptor Channel. *Science* **280**, 1596-1599.
http://science.sciencemag.org/content/sci/280/5369/1596.full.pdf

Optional Reading:

B Heitler: "How the Hodgkin-Huxley model for action potentials works – A text Tutorial" https://www.st-andrews.ac.uk/~wjh/hh_model_intro/

JR Banfelder: "Introduction to Markov Chains and Hidden Markov Models
http://physiology.med.cornell.edu/people/banfelder/qbio/resources_2016/S.1_markov.pdf

Mar. 7 *Synaptic Transmission I: Presynaptic Mechanisms* *Bachman*

Read ***before*** class:

From Molecules to Networks:

Chapter 15: *Release of Neurotransmitters* (pp. 443-470)
(stop at "The Standard Katz Model Does Not Always Apply")

Paper for discussion:

Deng, PY and Klyachko (2015) Genetic upregulation of BK channel activity normalizes multiple synaptic and circuit defects in a mouse model of fragile X syndrome. *Journal of Physiology* **594**, 83-97.
http://onlinelibrary.wiley.com/doi/10.1113/JP271031/epdf

Optional Reading:

Atwood HL and Karunanithi S. 2002. Diversification of synaptic strength: presynaptic elements. *Nat. Rev. Neurosci*. 3(7): 497-516.
https://www.nature.com/articles/nrn876

Ackermann F., Waites CL. And Garner CC. 2015. Presynaptic active zones in invertebrates and vertebrates. *EMBO Rep.* 16(8): 923-938.
http://embor.embopress.org/content/16/8/923.long

Mar. 14 *Synaptic Transmission II: Postsynaptic Mechanisms* *Bachman*

Read ***before*** class:

From Molecules to Networks:

Chapter 10: *Neurotransmitter Receptors*

pp. 285-294: stop at "Neuronal nAChRs Contain Two Types of Subunits."

pp. 297-312: start at "GABAA Receptors are Related in Structure to the nAChR but Exhibit an Inhibitory Function," stop at "Other Posttranslational Modifications are Required for Efficient GPCR Function."

Paper for discussion:

Hessler NA, Shirke, AM and Malinow R. 1993 The probability of transmitter release at a mammalian central synapse. *Nature* **366**, 569-572. https://www.nature.com/articles/366569a0

Optional Reading:

Sheng M and Kim E. 2011. The postsynaptic organization of synapses. *Cold Spring Harb Perspect Biol*. 3(12): 1-20. http://cshperspectives.cshlp.org/content/3/12/a005678.long

Ben-Ari Y. 2014. The GABA excitatory/inhibitory developmental sequence: a personal journey. *Neuroscience* 279: 187-219. http://www.sciencedirect.com/science/article/pii/S0306452214006411?via%3Dihub

Mar. 21 *Synaptic Transmission III: Diffusion, Uptake, etc.* *Bachman*

Read ***before*** class:

From Molecules to Networks:

Chapter 7: *Pharmacology and Biochemistry of Synaptic Transmission*

pp. 228-233: stop at "Why do Neurons have so many Transmitters?"

Chapter 9: *Connexin and Pannexin Based Channels in the Nervous System: Gap Junctions and More* (pp. 257-261): stop at "Connexins in CNS Ontogengy"

Random Walks in Biology (Berg): Chapter 1

Paper for discussion:

Tyzio R, et al. 2006. Maternal oxytocin triggers a transient inhibitory switch in GABA signaling in the fetal brain during delivery. *Science*. 314: 1788-92. http://science.sciencemag.org/content/314/5806/1788.long

Optional reading:

Barbour B. and Hausser M. 1997. Intersynaptic diffusion of neurotransmitter. *Trends Neurosci.* 20: 377-384 http://www.sciencedirect.com/science/article/pii/S0166223696200505?via%3Dihub

Mar. 28 *Microscopy and Imaging: Methods and Tools* *Hunter*

Read ***before*** class:

Imaging Neurons, Chapter 12:
Practical Limits to Resolution in Fluorescence Light Microscopy

Paper for discussion:

Apostolides, PF and Trussell, LO (2013) Regulation of interneuron excitability by gap junction coupling with principal cells. *Nat. Neurosci.* **16**, 1764-1774. https://www.nature.com/articles/nn.3569.pdf

Apr. 4 *Dynamics/Imaging of Ca Diffusion and Signaling* *Hunter*

Read ***before*** class:

Imaging in Neuroscience: A Laboratory Manual, Chapter 8:
Imaging Neuronal Activity with Genetically Encoded Calcium Indicators

Paper for discussion:

Chang, et al. (2017) Iterative Expansion Microscopy. *Nat. Methods* **14**, 593-599. https://www.nature.com/articles/nmeth.4261.pdf

Apr. 11 *Dendritic Integration I: Cable Theory, Modeling* *Chen*

Read ***before*** class:

From Molecules to Networks:
Chapter 17: *Cable Properties and Information Processing in Dendrites* (pp. 509-519)
Chapter 16: *Postsynaptic Potentials and Synaptic Integration* (pp. 495-501)

Paper for discussion:

De Juan-Sanz, et al. (2017) Axonal endoplasmic reticulum Ca^{2+} content controls release probability in CNS nerve terminals. *Neuron* **93**, 867-881.
http://www.cell.com/neuron/pdf/S0896-6273(17)30034-X.pdf

Optional reading:

http://www.scholarpedia.org/article/Rall_model

Other resources:

NEURON simulation software: https://www.neuron.yale.edu/neuron/
Metaneuron: http://www.metaneuron.org/

Apr. 18 *Dendritic Integration II: Membrane Mechanisms* *Chen*

Read ***before*** class:

From Molecules to Networks:
Chapter 17: *Cable Properties and Information Processing in Dendrites* (pp. 519-529)
Chapter 16: *Postsynaptic Potentials and Synaptic Integration* (pp. 504-507)

Paper for discussion:

Stuart, GJ and Spruston, N (1998) Voltage Attenuation in Neocortical Pyramidal Neuron Dendrites. *J. Neurosci.* **18**, 3501-3510.
http://www.jneurosci.org/content/18/10/3501.full.pdf

Optional reading:

From Molecules to Networks. (2nd edition):
Chapter 17: Information Processing in Complex Dendrites (pp. 479-497).
http://www.sciencedirect.com/science/article/pii/B9780121486600500184

Stuart, GJ and Spruston, N (2015) Dendritic Integration: 60 years of progress. *Nat. Neurosci*. **18**, 1713-1721.
http://www.nature.com/neuro/journal/v18/n12/full/nn.4157.html

Tran-Van-Minh, et al. (2015) Contribution of sublinear and supralinear dendritic integration to neuronal computations. *Front. Cell. Neurosci.*
http://journal.frontiersin.org/article/10.3389/fncel.2015.00067/full

Optional reading/viewing:

https://www.janelia.org/lab/spruston-lab/research/dendritic-integration/principles-dendritic-integration-ca1-pyramidal

Apr. 25 *GPCR Signaling and Modulation* *Kramer*

Read ***before*** class:

From Molecules to Networks:

Chapter 4: (pp. 119-132)

Chapter 18: *Synaptic Plasticity* (pp. 533-539)

Paper for discussion:

Magee, JC (1999) Dendritic Ih normalizes temporal summation in hippocampal CA1 neurons. Nat. Neurosci. **2**, 508-514. http://www.nature.com/neuro/journal/v2/n6/full/nn0699_508.html

Optional reading:

Bender, K.J., Ford, C.P. & Trussell, L.O. (2010). Dopaminergic Modulation of Axon Initial Segment Ca Channels Regulates Action Potential Initiation. *Neuron* **68**, 500-511.

Isaacson, J.S., Solis, J.M. & Nicoll, R.A. (1993). Local and diffuse synaptic actions of GABA in the hippocampus. *Neuron* **10**, 165-175.

Pitler, T.A. & Alger, B.E. (1992). Postsynaptic spike firing reduces synaptic GABAA responses in hippocampal pyramidal cells. *Journal of Neuroscience* **12**, 4122-4132.

Reviews

Katrich, V., Cherezov, V, & Stevens, R.C. (2012). Structure-function of the G protein-coupled receptor subfamily. *Ann. Rev. of Pharmacology and Toxicology* **53**, 531-556.

Lane, J.R., May, L.T., Parton, R.G., Sexton, P.M. & Christopoulosm A. (2017). A kinetic view of GPCR allostery and biased agonism. *Nature Chemical Biology* **13**, 929-937.

History

Gilman, A.G. (1894). G Proteins and Dual Control of Adenylate Cyclase. *Cell* **36**, 577-579.

DREADDs

Gomez, J.L., Bonaventura, J., Lesniak, W., Mathews, W.B., Sysa-Shah, P., Rodriguez, L.A., Ellis, R.J., Richie, C.T., Harvey, B.K., Dannals, R.F., Pomper, M.G., Bonci, A., & Michaelides, M. (2017). Chemogenetics revealed: DREADD occupancy and activation via converted clozapine. *Science* **357**, 503-507.

Mahler, S.V. & Aston-Jones, G. (2017). CNO Evil? Considerations for the use of DREADDs in Behavioral Neuroscience. *Neuropsychopharmacology*: AOP

May 2 *Presynaptic Plasticity* *Kramer*

Read ***before*** class:

From Molecules to Networks:

Chapter 18: *Synaptic Plasticity* (pp. 540-552)

Paper for discussion:

Courtney, N.A. & Ford, C.P. (2014). The timing of dopamine- and noradrenaline-mediated transmission reflects underlying differences in the extent of spillover and pooling. *Journal of Neuroscience* **34**, 7645-7656. http://www.jneurosci.org/content/jneuro/34/22/7645.full.pdf

Optional reading:

Dittman, J.S. & Regehr, W.G. (1998). Calcium dependence and recover kinetics of presynaptic depression at the climbing fiber to purkinje cell synapse. *Journal of Neuroscience* **18**, 6147-6162.

Midorikawa, M. & Sakaba, T. (2017). Kinetics of releasable synaptic vesicles and their plastic changes at hippocampal mossy fiber synapses. *Neuron* **96**, 1033-1040.

Rozov, A., Burnashev, N., Skamann, B. & Neher, N. (2001). Transmitter release modulation by intracellular Ca^{2+} buffers in facilitating and depressing nerve terminals of pyramidal cells in layer 2/3 of the rat neocortex indicates a target cell-specific difference in presynaptic calcium dynamics. *Journal of Physiology* **531**, 807-826.

Von Gerdorff, H., Schneggenburger, R., Weis, S.& Neher, E. (1997). Presynaptic depression at a calyx synapse: The small contribution of metabotropic glutamate receptors. *Journal of Neuroscience* **17**, 8137-8146.

Reviews

Jackman, S.L. & Regehr, W.G. (2017). The Mechanisms and Functions of Synaptic Facilitation. *Neuron* **94**, 447-464.

Zucker, R.S. & Regehr, W.G. (2002). Short-term synaptic plasticity. *Ann. Review of Physiology* **64**, 355-405.

History

Eccles, J.C., Eccles, R.M. & Magni, F. (1961) Central inhibitory action attributable to presynaptic depolarization produced by muscle afferent volleys. *Journal of Physiology* **159**, 147-166.

Read ***before*** class:

From Molecules to Networks:

Chapter 18: *Synaptic Plasticity* (pp. 533-539)

Paper for discussion:

Jackman, S.L., Turecek, J., Belinsky, J.E., & Regehr, W.G. (2016). The calcium sensor synaptotagmin 7 is required for synaptic facilitation. *Nature* **529**, 88-91. https://www.nature.com/articles/nature16507.pdf

Optional reading:

Dan, Y. & Poo, M.M. (2004). Spike timing-dependent plasticity of neural circuits. *Neuron* **44**, 23-30.

Dudeck, S.M. & Bear, M.F. (1992). Homeostatic long-term depression in area CA1 of hippocampus and effects of N-methyl-D-aspartate receptor blockade. *PNAS* **89**, 4363-4367.

Harnett, M.T., Bernier, B.E., Ahn, K.-C. & Morikawa, H. (2009). Burst-timing-dependent plasticity of NMDA receptor-mediated transmission in midbrain dopamine neurons. *Neuron* **62**, 826-838.

Isaac, J.T.R., Nicoll, R.A. & Malenka, R.C. (1995). Evidence for silent synapses: Implications for the expression of LTP. *Neuron* **15**, 427-435.

Liao, D., Hessler, N.A. & Malinow, R. (1995). Activation of postsynaptically silent synapses during pairing-induced LTP in CA1 region of hippocampal slice. *Nature* **375**, 400-404.

Reviews

Huganir, R.L. & Nicoll, R.A. (2013). AMPARs and Synaptic Plasticity: The Last 25 Years. *Neuron* **80**, 704-717.

Luscher, C. & Huber, K.M. (2010). Group I mGluR-Dependent synaptic long-term depression: Mechanisms and implications for circuitry and disease. *Neuron* **65**, 445-459.

Malenka, R.C. & Bear, M.F. (2004). LTP and LTD: An embarrassment of riches. *Neuron* **44**, 5-21.

History

Nicoll, R.A. (2017). A Brief History of LTP. *Neuron* **93**, 281-290.