NGG 575/ Biology 442/Psychology 421
Neurobiology of Learning and Memory
Fall Semester 2013
University of Pennsylvania

Syllabus

Professors:

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Meetings: Thursday 1:30-4:30 PM
Location: 10-100 Smilow

Office Hours:
Isabel Muzzio: By appointment.
Ted Abel: Thursdays, 10 am to 12 pm, Solomon B-1. Please contact Ted via email before coming to office hours.

Overview:

This course focuses on the current state of our knowledge about the neurobiological basis of learning and memory. A combination of lectures and discussions will explore the molecular and cellular basis of learning in invertebrates and vertebrates from a behavioral and neural perspective. This course is intended for upper level undergraduate and graduate students.

Prerequisites:

Biology 251 or permission of instructor.

Textbook and Readings:

Readings for this course will be drawn from several textbooks as well as the primary literature. All readings will be posted on the course Blackboard site (https://courseweb.library.upenn.edu/). It is critical that you do all the reading in timely fashion prior to class. Please consult textbooks and other sources as needed to fully understand the material.

Good sources for background reading include:

Kandel, E. R., Schwartz, J. H., Jessell, T. M., Siegelbaum, S. and Hudspeth A. J. (2012). Principles of Neural Science. New York, NY: McGraw-Hill.

Rudy, J. W. (2008). The Neurobiology of Learning and Memory. Sunderland, MA: Sinauer Associates.

Sweatt, J. D. (2003). Mechanisms of Memory. New York, NY: Elsevier Academic Press.

Carew, T. J. (2000). Behavioral Neurobiology: The Cellular Organization of Natural Behavior. Sunderland, MA: Sinauer Associates, Inc.

Dudai, Y. (1989). The Neurobiology of Memory: Concepts, Findings, Trends. New York, NY: Oxford University Press.

Lieberman, D. A. (1993). Learning: Behavior and Cognition. Pacific Grove, CA: Brooks/Cole Publishing Company.

Martinez, J. L., Jr., and Kesner, L. P. (eds.) (1998). Neurobiology of Learning and Memory. San Diego, CA: Academic Press.

Pearce, J. M. and Bouton, M. E. (2001). Theories of associative learning in animals. Annual Review of Psychology. 52: 111-139.

Shettleworth, S. J. (1998). Cognition, Evolution and Behavior. New York, NY: Oxford University Press.

Squire, L. R., and Kandel, E. R. (1999). Memory: From Mind to Molecules. New York, NY: Scientific American Library.

Course Format:

This course meets once per week. The first part of the class will be devoted to a lecture that will provide a general overview of the topic to be discussed and the approaches used in these studies. The second part of the class will be devoted to discuss the reading assignments in a debate format. For each class, there will be a list of two background readings and two assigned papers. The students should read the reviews and papers carefully to be able to comment about them during the following class. The discussions of the reviews will focus on the main issues rather than details, specially emphasizing the unresolved questions or the discrepancies in the field. The discussion of the assigned experimental papers will have two stages. During the first stage, students will be randomly called to explain Figures of a given paper. This part of the discussion will be aimed at summarizing the findings of the paper. During the second part of the discussion, the instructors will call members call students to discuss the strengths and weaknesses of the assigned paper. Prior to each class, students will be divided in a “pro”, and a “con” group. The “pro” group students should be prepared to discuss the uniqueness of experimental design and originality of the findings. The “con” group students should be able to point out the caveats, limitations, and alternative explanations of the findings. After this debate, there will be a brief class discussion to reach a conclusion about the assigned paper. Students will be evaluated based on their ability to present information, clarity of concepts, critical thinking, and participation. During presentations, all students are encouraged to ask questions and/or challenge the points presented by another student. Two experimental papers will be presented in each class and the

discussion of each article will take 15-20 min. Everyone is expected to participate in every class.

Readings:

Each week pdf files of background reading and papers to be discussed will be posted on the course site on Blackboard. It is mandatory that students read the first two papers of the background reading list each week. The third paper is recommended unless we specify otherwise. All lectures will precede paper discussions. Therefore, assignments for discussion will be given at least one week prior to the presentation. Exam questions will be taken from the assigned and background readings, class discussions, and lectures.

Grading:

For UNDERGRADUATES in the class, there will be three components that will be used in determining the grade for this course.

a. Class participation and presentations (50%): Ask critical questions and participate actively in the discussions

b. Take home midterm (25%): The questions will be given on October 3rd. The exam will be due October 24th.

c. Final Exam (25%): A take home final exam will be given out at noon (via email) on December 6th. This exam is due at noon (via email) on Dec 15^{h}.

For GRADUATE students in the class, there will be four components that will be used in determining the grade for this course:

a. Class participation and presentations (50%): Ask critical questions and participate actively in the discussions

b. Take home midterm (20%): The questions will be emailed on October 3rd. The exam will be due October 24th.

c. Final Exam (20%): A take home final exam will be given out at noon (via email) on December 6th. It is due at noon (via email) on Dec 15th.

d. For graduate students only: "News and Views" paper (10%): A short (5-7) page paper is due at noon via email on November 25th. The topic and format of this paper is described briefly below.

Midterm and Final Exams

The questions in the midterm and final exams will be essay format and may include additional papers to read and comment on. In many cases there may not be a correct answer; the most important thing is to demonstrate your ability to think about problems in the field of learning and memory. These exams are open book and open notes. You are welcome to refer to any written source, but your answers should not be plagiarized—you should clearly cite sources that you refer to that are not in the syllabus. Although the exam is open book you should not discuss your answers or your ideas with your classmates. All thinking and work must be your own.

Penn's Code of Academic Integrity (HYPERLINK "http://www.vpul.upenn.edu/osl/acadint.html" http://www.vpul.upenn.edu/osl/acadint.html). You are expected to follow Penn's Code of Academic Integrity in all of your work at Penn. All work should be your own and the work of others should be properly cited.

"News and Views" Article Assignment -**For graduate students only**
Due on November 25th.

Below are the guidelines for this article. These guidelines are a modification of what Nature sends to "News and Views" authors. We will hand out a sample "News and Views" so that you have an idea of what we are aiming for. (Actually, the sample will be a "Perspective," which is what Science calls its version of "News and Views.")

1. These articles inform readers about new scientific advances, as reported in recently published papers. The article should highlight the "news" presented in the research paper, provide the necessary scientific background to place this "news" in context and provide an outline of the future directions of the field. Two or three research papers will be handed out in class on October 17th one month before this assignment is due. Please choose ONE of these papers for your "News and Views."

2. "News and Views" articles should be within the length limits of 5 to 7 double-spaced typed pages in 12 point Times font (1500-2500 words). Writing a paper this short is a challenge and usually means starting with a paper that is much longer and working to sharpen and focus your arguments through multiple drafts.

3. The "news" should be mentioned in a succinct opening paragraph to attract the attention of those who are not experts in the field. This paragraph should explicitly refer to the paper under discussion and touch on the significance of the new work.

4. More detail, background and explanation should follow, including your own "views."

5. The article is often best rounded off with comment on the implications of the new work and on future research directions.

6. Most readers will have a general scientific background but specialized terminology should be avoided or clearly and concisely explained.

7. One or two diagrams should be used to explain the new points made or the background science to the new result, or to sketch out the future experiments proposed in the article.

8. References should be kept to a minimum, ideally fewer than ten. They should be cited in Author, Date format as used in the journal Cell. Be sure to include the title for all cited papers as in the reference format in the journal Cell. (Obviously, this is not included in Nature's advice to authors!)

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Lecture Schedule and Readings: The lectures about each topic will precede the paper discussions. Therefore, the papers assigned for discussion will be presented the week following each lecture.

August 29th: Introduction and Aplysia. Lecturer: Ted
Background reading
1. Dubnau, J., Chiang, A.-S. (2012). Systems memory consolidation in Drosophila. Current Opnion in Neurobiology, 23, 84-91.

2. Kandel, E. R. (2001). The molecular biology of memory storage: A dialogue between genes and synapses. Science. 294: 1030-1038.

Primary papers to be discussed on September 5th:

1. Majumdar, A., Cesario, W.C., White-Grindley, E., Jiang, H., Ren, F., Khan, M.R., Li, L., Choi, E.M., Kannan, K., Guo, F., Unruh, J., Slaughter, B., and Si, K. (2012). Critical role of amyloid-like oligomers of drosophila Orb2 in the persistence of memory, Cell, 148, 515-529.

2. Si, K. Choi' Y.-C, White-Grindley, E., Majumdar' A. and Kandel, E.R. (2010). *Aplysia* CPEB Can Form Prion-like Multimers in Sensory Neurons that Contribute to Long-Term Facilitation. Cell 140: 421-435.

September 5th: Spatial learning in the hippocampal formation. Lecturer: Isabel

Background reading:

1. Leutgeb, S., Leutgeb, J.K., Moser, M.B., Moser, E.I. (2005). Place cells, spatial maps and the population code for memory. Curr Opin Neurobiol 15:738-746.

2. Foster, D.J., Knierim, J. (2012). Sequence learning and the role of the hippocampus in rodent navigation. Current Opinion in Neurobiology, 22, 294-300.

Primary papers to be discussed on September 12th:

1. Macdonald CJ, Lepage KQ, Eden UT, Eichenbaum H. (2011). Hippocampal "time cells" bridge the gap in memory for discontiguous events. Neuron, 71:737-749.

2. Hafting T, Fyhn M, Molden S, Moser MB, Moser EI. (2005). Microstructure of a spatial map in the entorhinal cortex. Nature. 436: 801-806.

September 12th: Hippocampus: synaptic plasticity and genetic dissections. Lecturer: Ted
Background reading:

1. Havekes, R. and Abel, T. (2009). Genetic dissection of neural circuits and behavior in Mus musculus. *Advances in Genetics* 65: 1-38.

2. Nakazawa, K., McHugh, T. J., Wilson, M. A. and Tonegawa, S. (2004). NMDA receptors, place cells and hippocampal spatial memory. Nature Review Neuroscience. 5: 361-372.

Primary papers to be discussed September 19th:

1. Garner, A., R., Rowland, D.C., Hwang, S. Y., Baumgaertel, K., Roth, B.L., Kentros, C., and Mayford, M. (2012). Generation of a synthetic memory trace. Science, 335, 1513-1516. This paper should be compared with Ramirez et al. (2013) assigned on September 19th

2. Ramirez, S., Liu, X., Lin, P.-A., Suh, J., Pignatelli, M., Redondo, R.L., Ryan, T.J., and Tonegawa, S. (2013). Creating a false memory in the hippocampus. Science, 341, 387-391

September 19th: Amygdala—Emotional Memory. Lecturer: Ted

Background readings:

1. Johanssen, J.P., Cain, C.K., Ostroff, L.E., LeDoux, J.E. (2011). Molecular mechanisms of fear learning and memory, Cell, 147, 509-524.

2. Maren, S. and Quirk, G. J. (2004). Neuronal signalling of fear memory.
Nat. Rev. Neurosci. 5: 844-852.

Primary papers to be discussed September 26th:

1. Haubensak, W., Kunwar, P.S., Cai, H., Ciocchi, C., Wall, N.R., Ponnusamy, R., Biag, J., Ding, H.W., Deisseroth, K., Callaway, E.M., Fanselow, M.S., Luthi, A., Anderson, D.L. (2010). Genetic dissection of an amygdala microcircuit that gates conditioned fear. Nature, 468, 270-276.

2. Han JH, Kushner SA, Yiu AP, Hsiang HL, Buch T, Waisman A, Bontempi B, Neve RL, Frankland PW, Josselyn SA. (2009). Selective erasure of a fear memory. Science, 323(5920): 1492-1496.

September 26th. **Amygdala: Extinction and Reconsolidation. Lecturer: Isabel**

Background Readings:

1. Maren, S., Phan, K.L., and Liberzon, I. (2013). The contextual brain: Implications for fear conditioning, extinction and psychopathology. Nature Reviews in Neuroscience, 14, 417-428.

2. Lattal, K.M., Wood, M.A. (2013). Epigenics and persistent memory: Implications for reconsolidation and silent extinction beyond the zero. Nature Neuroscience, 16, 124-129.

Primary papers to be discussed October 3rd:

1. Monfils, M.H., Cowansage, K.K., Klann, K., LeDoux, J.E. . (2009). Extinction-reconsolidation boundaries: Key to persistent attenuation of fear memories. Science 324, 951:955.

2. Wan Lai, C.S., Franke, T.F., Gan, W.B. (2012). Opposite effects of fear conditioning and extinction on dendritic spine remodeling. Nature, 483, 88-91.

October 3rd: Epigenetics. **Lecturer: Ted**
Background reading

1. Zovkic, I.B., Guzman-Karlsson, M.C., Sweatt, J.D. (2013). Epigenetic regulation of memory formation and maintenance. Leraning and Memory, 20, 61-74.

2. Epigenetic targets of HDAC inhibition in neurodegenerative and psychiatric disorders. Abel T, Zukin RS. Curr Opin Pharmacol. 2008 Feb;8(1):57-64.

Papers to be discussed on October 17th:

1. McQuown SC, Barrett RM, Matheos DP, Post RJ, Rogge GA, Alenghat T, Mullican SE, Jones S, Rusche JR, Lazar MA, **Wood MA**. (2011) HDAC3 is a critical negative regulator of long-term memory formation. J Neurosci. 31(2):764-74.

2. **Miller** CA, **Sweatt** JD. (2007). Covalent modification of DNA regulates memory formation. Neuron. 53(6):857-69. Erratum in: Neuron. 2008 Sep 25;59(6):1051.

October 10th: No class Fall break

October 17th: Sleep and Memory. Lecturer: Isabel

Background readings (read all the papers):

1. Sinton, C. M. and McCarley, R. W. (2004). Neurophysiological mechanisms of sleep and wakefulness: a question of balance. Semin. Neurol. 24: 211-223.

2. Inostroza, M., Born, J. (2013). Sleep for preserving and transforming episodic memory. Annual Reviews in Neuroscience, 36, 79-102.

Primary papers to be discussed on October 31st:

1. Ngo, H.V., Martinetz, T., Born, J., Molle, M. (2013). Auditory closed-loop stimulation of the sleep slow oscillation enhances memory, Neuron, 78, 545-553.

2. Nakashiba T, Buhl DL, McHugh TJ, Tonegawa S. Hippocampal CA3 output is crucial for ripple-associated reactivation and consolidation of memory (2009). Neuron, 62:781-787.

October 24th: Learning and Memory in the Prefrontal cortex and beyond. Lecturer Isabel
Background readings:

1. Blumenfeld RS, Ranganath C. (2007). Prefrontal cortex and long-term memory encoding: an integrative review of findings from neuropsychology and neuroimaging. Neuroscientist, 13: 280-291.

2. D'Esposito M. (2007). From cognitive to neural models of working memory. Philos Trans R Soc Lond B Biol Sci.;362:761-72.

Primary papers to be discussed on November 7th:

1. Rigotti, M., Barak, O., Warden, M.R., Wang, X.J., Daw, N.D., Miller, E.K., Fusi, S. (2013). The importance of mized selectivity in complex xognitive tasks Nature, 497, 585-590.

2. Salazar, R.F., Dotson, N.M., Bressler, S.L., Gray, C.M. (2012) Content-specific fronto-parietal synchronization during visual working memory. Science, 338, 1097-1100.

October 31st. Memory maintenance and systems consolidation. Lecturer Isabel
Background readings:

1. Winocur, G., Moscovitch, M., Bontempi, B. (2010). Memory formation and long-term retention in human and animals: Convergence towards a transformation account of hippocampa-neocortical interactions. Neuropsychologia, 48, 2339-2356.

2. Wang, S.-H., Morris, R.G.M. (2010). Hippocampal neocortical interactions in memory formation, consolidation, and reconsolidation. Annual Reviews of Psychology, 61, 49-79.

Primary papers to be discussed on November 7th:

1. Tse, D., Takeuchi, T., Kakeyama, M., Kajii, Y., Okuno, H., Tohyama, C., Bito, H., Morris, R.G.M. (2011). Schema-dependnet gene activation and memory encoding in neocortex. Science, 333, 891-895.

2. Goshen, I., Brodsky, M., Prakash, R., Wallace, J., Gradinaru, V., Ramakrishnan, C., Deisseroth, K. (2011). Dynamics of retrieval strategies for remote memories. Cell, 147, 678-689.

November 7th. No class SFN

November 14th No class. SFN

November 21st. Neurogenesis and learning. **Lecturer Ted**
Background readings:

1. Gross, C. (2000). Neurogenesis in the adult brain: Death of a dogma. Nature Reviews Neuroscience. 1: 67-73.

2. Specter, M. (2001). Annals of science: Rethinking the brain. New Yorker. July 23: 42-53.

3. Aimone, J. B., Wiles, J. and Gage, F. H. (2006). Potential role for adult neurogenesis in the encoding of time in new memories. Nat. Neurosci. 9: 723-727.

Primary papers to be discussed on November 21st:

1. Sahay A, Scobie KN, Hill AS, O'Carroll CM, Kheirbek MA, Burghardt NS, Fenton AA, Dranovsky A, Hen R. (2011). Increasing adult hippocampal neurogenesis is sufficient to improve pattern separation. Nature 472, 466-470.

3. Nakashiba, T., Cushman, J.D., Pelkey, K. A., Buhl, D., McHugh, T.J., Rodriguez Barrera, V., et al. (2012). Young dentate granule cells mediate pattern separation, whereas old granule cells facilitate pattern completion. Cell, 149, 188-201.

November 26th: Aging and learning and memory. Lecturer Isabel. Note that this class in on Tuesday according to the SAS schedule. If BGS students have a problem with this class, it will be cancelled.
Background readings:
1. Burke, S.N., and Barnes, C.A. (2010). Senescent synapses and hippocampal circuit dynamics. TINS, 33, 153-161.

2. Morrison, J.H. and Baxter, M.G. (2012). The ageing cortical synapse: hallmarks and implications for cognitive decline. Nature reviews in Neuroscience, 13, 240-250.

Primary papers to be discussed on December 5th:

1. Johnson, S.C., Rabinovitch, P.S., and Kaeberlein, M. (2013). mTOR is a key modulator of ageing and age-related disease. Nature, 498, 338-344.

2. Peleg, S., Sananbenesi, F., et al. (2010). Altered histone acetylation is associated with age-dependent memory impairment in mice. Science, 428, 753-756.

December 5th. Final discussion. Interactions of Memory systems. Lecturer Isabel

Background readings:
1. Simons JS, Spiers HJ. (2003). Prefrontal and medial temporal lobe interactions in long-term memory. Nat Rev Neurosci., 4(8):637-648.

2. Hartley T, Burgess N. (2005) Complementary memory systems: competition, cooperation and compensation. Trends Neurosci., 28(4):169-170.