Biology 442/INSC 575/Psychology 421
Neurobiology of Learning and Memory
Fall Semester 2014
University of Pennsylvania

Syllabus

Professors:

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Meetings: Thursday 1:30-4:30 PM
Location: John Morgan 100

Office Hours:
Isabel Muzzio: By appointment.
Ted Abel: By appointment.

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 Canvas site (https://canvas.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. (2014). 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 discussing 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 carefully read the reviews and papers 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 on to explain figures and other details of a paper. This part of the discussion will be aimed at summarizing the findings of the paper and understanding details of the experimental design. During the second part of the discussion, the instructors will call on students to discuss the strengths and weaknesses of the assigned paper. 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, critical thinking, and participation. All students are encouraged to ask questions and/or challenge the points discussed by others. The discussion of each article will take about 30 min. Everyone is expected to participate in every class and in the discussion of every paper. The second part of the class will be devoted to a lecture that will provide a general overview of the topic to be discussed the following week.

Readings:

Each week pdf files of background reading and papers to be discussed will be posted on the course site on Canvas. It is mandatory that students read all the assigned papers. The lectures will focus on the topic assigned for the following week. Assignments for discussion will be given at least one week prior to the presentation. Exam questions will be based on 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 2nd. The exam will be due October 16th.

c. Final Exam (25%): A take home final exam will be given out at noon (via email) on December 4th. This exam is due at noon (via email) on Dec 16th.

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 2rd. The exam will be due October 16th.

c. Final Exam (20%): A take home final exam will be given out at noon (via email) on December 4th. It is due at noon (via email) on Dec 16th.

d. For graduate students only: "News and Views" paper (10%): A short (5-7) page paper is due at noon via email on November 26th. 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 (http://www.upenn.edu/academicintegrity/ai_codeofacademicintegrity.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 26th.

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.

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. The topic will be assigned 2-3 weeks prior the due date.

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 discussed the week following each lecture.

August 28th: Introduction, Aplysia and Drosophila. Lecturer: Ted
Background reading

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

2. Dubnau, J., Chiang, A.-S. (2012). Systems memory consolidation in Drosophila. Current Opnion in Neurobiology, 23, 84-91.

Primary papers to be discussed on September 4th:

1. 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.

2. 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.

September 4th: 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 11th:

1. Bjerknes, T.L., Moser, E.I., Moser, MB. (2014). Representation of geometric borders in the developing rat. Neuron. 82(1):71-8.

2. Bonnevie, T., Dunn, B., Fyhn, M., Hafting, T., Derdikman, D., Kubie, J., Roudi, Y. Moser, E.I., & Moser, M.B. (2013). Grid cells require excitatory drive from the hippocampus. Nat Neurosci., 16(3):309-17.

September 11th: 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 18th:

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.

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 18th: 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 25th:

1. 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.

2. Yiu, A.P., Mercaldo, V., Yan, C., Richards, A., Hsiang, H.L., Pressey, J., Mahadevan, V., Tran, M.M., Kushner, S.A., Woodin MA., Frankland, P.W., & Josselyn, S.A. (2014) Neurons Are Recruited to a Memory Trace Based on Relative Neuronal Excitability Immediately before Training. Neuron. 83(3):722-35.

September 25th. **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.
3. Besnard, A., Caboche, J., Laroche, S. (2012). Reconsolidation of memory: A decade of debate. Progress in Neurobiology, 99, 61-80.

Primary papers to be discussed October 2nd:

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 2nd: 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. Borelli, E., Nestler, E.J., Allis, D., and Sassone-Corsi, P. (2008). Decoding epigenetic language of neuronal plasticity. Neuron, 60, 961-974.

Papers to be discussed on October 16th:

1. Day JJ, Childs D, Guzman-Karlsson MC, Kibe M, Moulden J, Song E, Tahir A, Sweatt JD. (2013). DNA methylation regulates associative reward learning. Nat Neurosci.Oct;16(10):1445-52.

2. Rudenko A, Dawlaty MM, Seo J, Cheng AW, Meng J, Le T, Faull KF, Jaenisch R, Tsai LH. (2013). Tet1 is critical for neuronal activity-regulated gene expression and memory extinction. Neuron. 2013 Sep 18;79(6):1109-22.

October 9th: No Class Fall break

October 16th: Sleep and Memory. Lecturer: Isabel

Background readings (read all the papers):

1. Abel T, Havekes R, Saletin JM, Walker MP. (2013). Sleep, plasticity and memory from molecules to whole-brain networks. Curr Biol. 2013 Sep 9;23(17):R774-88.

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 23rd:

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 23rd: 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 October 30th:

1. Stujenske, J.M., Likhtik, E., Topiwala, M.A., & Gordon, J.A. (2014). Fear and Safety Engage Competing Patterns of Theta-Gamma Coupling in the Basolateral Amygdala. Neuron. 2014 Apr 2;82(1):71-8.

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 30th. 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 hippocampal-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 6th:

1. Tse, D., Takeuchi, T., Kakeyama, M., Kajii, Y., Okuno, H., Tohyama, C., Bito, H., Morris, R.G.M. (2011). Schema-dependent 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 6th. 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. TINS, 28(4):169-170.

Primary papers to be discussed on November 20th:

Siapas, A.G., Lubenov, E.V., Wilson, M.A. (2005). Prefrontal phase locking to hippocampal theta oscillations. Neuron, 46, 141-151.

Adhikari, A., Topiwala, M.A., Gordon, J.A. (2011). Single units in the medial prefrontal cortex with anxiety-related firing patterns are preferentially influenced by ventral hippocampal activity. Neuron, 71, 898-910.

November 13th No class SFN

November 20th. Neurogenesis and learning. **Lecturer Isabel**
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 25th:

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 25th: Tuesday corresponding to Thursday class schedule. NO CLASS Thanksgiving break

December 4th: Final discussion: Aging and learning and memory. Lecturer Isabel.

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: If there is no time for discussing these papers I will give an overview of the main findings

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.