Cellular Substrates of Learning and Memory (ME:440.702)

Johns Hopkins University School of Medicine
Department of Neuroscience
1/10/09 - 2/28/08

Class will meet on Thursdays from 2:30 PM to 5:30 PM in 811 Woods Basic Science Building. The instructor is David Linden (410-614-1529; dlinden@jhmi.edu, Office = 916 Hunterian Building).

Description: The search for the engram has proved to be one of the most fascinating and frustrating problems in contemporary biology. In this course we shall attempt to gain an understanding of the current state of the struggle through reading and discussion of the original literature. We shall examine attempts to find biochemical, electrophysiological and morphological changes in neural tissue during and following learning tasks, and attempts to interfere with or enhance learning and memory through genetic, electrophysiologic and pharmacologic manipulation. In addition, electrophysiological model systems of information storage such as long-term potentiation and long-term depression will be considered. Examples shall be taken from both the vertebrate and invertebrate literature.

Prerequisites: Prior coursework in electrophysiology is strongly recommended. Neuroscience and Cognition I (ME:440.811) is sufficient. Auditors are welcome with the permission of the instructor.

Grading: The goal of this class is to have an active, seminar-style discussion. There will be no exam and no final paper or project. Grades will be based solely on class participation. As a result, attendance is crucial. Students who miss one class meeting will be required to do a paper on the topic they missed. Students who miss two class meetings must withdraw from the course.

Organization: The first class meeting will be a lecture, and the subsequent 6 sessions will be seminar-style. The last session will be a free-form discussion about the future of research in learning and memory (wine and cheese provided). For each of the 6 seminar style meetings there will be a short (5–10 min) background talk given by the instructor at the outset, followed by the discussion of the papers. Each session will typically consider one review article (marked with an asterisk below) and three papers from the primary literature. You should read all of these **very** carefully and prepare notes to guide your discussion. *You should be prepared to discuss all aspects of all of the papers in any class meeting as students will be called upon randomly.*

Papers will be distributed as PDFs on a CD.

1/10/08 Introductory lecture: A Brief Overview of Learning and Memory.

*Linden, D. J. (2007). Learning, Memory and Human Individuality. In: *The Accidental Mind: How Brain Evolution has Given Us Love, Memory, Dreams and God*. Harvard/Belknap. Cambridge MA.

1/17/08 *Drosophila*

*Keene AC, Waddell S. Drosophila olfactory memory: single genes to complex neural circuits. Nat Rev Neurosci. 2007 May;8(5):341-54.

Qian M, Pan G, Sun L, Feng C, Xie Z, Tully T, Zhong Y. Receptor-like tyrosine phosphatase PTP10D is required for long-term memory in Drosophila. J Neurosci. 2007 Apr 18;27(16):4396-402.

Waddell, S., Armstrong, J. D., Kitamoto, T., Kaiser, K., and Quinn, W. G. (2000). The amnesiac gene product is expressed in two neurons in the Drosophila brain that are critical for memory. Cell *103*, 805-813.

Yu D, Akalal DB, Davis RL. Drosophila alpha/beta mushroom body neurons form a branch-specific, long-term cellular memory trace after spaced olfactory conditioning. Neuron. 2006 Dec 7;52(5):845-55.

1/24/08 Hippocampus I

*Malinow R. AMPA receptor trafficking and long-term potentiation. Philos Trans R Soc Lond B Biol Sci. 2003 Apr 29;358(1432):707-14.

Isaac, J. T., Nicoll, R. A., and Malenka, R. C. (1995). Evidence for silent synapses: implications for the expression of LTP. Neuron *15*, 427-434.

Hu H, Real E, Takamiya K, Kang MG, Ledoux J, Huganir RL, Malinow R. Emotion enhances learning via norepinephrine regulation of AMPA-receptor trafficking. Cell. 2007 Oct 5;131(1):160-73.

Whitlock JR, Heynen AJ, Shuler MG, Bear MF. Learning induces long-term potentiation in the hippocampus. Science. 2006 Aug 25;313(5790):1093-7.

1/31/08 Hippocampus II

*Kim SJ, Linden DJ. Ubiquitous plasticity and memory storage. Neuron. 2007 Nov 22;56(4):582-92.

Frick A, Magee J, Johnston D. LTP is accompanied by an enhanced local excitability of pyramidal neuron dendrites. Nat Neurosci. 2004 Feb;7(2):126-35.

Zhou, Q., Homma, K. J., and Poo, M.-m. (2004). Shrinkage of dendritic spines associated with long-term depression of hippocampal synapses. Neuron *44*, 749-757.

Park M, Salgado JM, Ostroff L, Helton TD, Robinson CG, Harris KM, Ehlers MD. Plasticity-induced growth of dendritic spines by exocytic trafficking from recycling endosomes. Neuron. 2006 Dec 7;52(5):817-30.

2/7/08 Amygdala

*Sigurdsson T, Doyère V, Cain CK, LeDoux JE. Long-term potentiation in the amygdala: a cellular mechanism of fear learning and memory. Neuropharmacology. 2007 Jan;52(1):215-27.

Tsvetkov, E., Carlezon, W. A. J., Benes, F. M., Kandel, E. R., and Bolshakov, V. Y. (2002). Fear conditioning occludes LTP-induced presynaptic enhancement of synaptic transmission in the cortical pathway to the lateral amygdala. Neuron *34*, 289-300.

Rumpel, S., LeDoux, J. E., Zador, A., and Malinow, R. (2005). Postsynaptic receptor trafficking underlying a form of associative learning. Science *308*, 83-88.

Shumyatsky GP, Malleret G, Shin RM, Takizawa S, Tully K, Tsvetkov E, Zakharenko SS, Joseph J, Vronskaya S, Yin D, Schubart UK, Kandel ER, Bolshakov VY. Stathmin, a gene enriched in the amygdala, controls both learned and innate fear. Cell. 2005 Nov 18;123(4):697-709.

2/14/08 Cerebellum I

*De Zeeuw CI, Yeo CH. Time and tide in cerebellar memory formation. Curr Opin Neurobiol. 2005 Dec;15(6):667-74.

Steinberg JP, Takamiya K, Shen Y, Xia J, Rubio ME, Yu S, Jin W, Thomas GM, Linden DJ, Huganir RL. Targeted in vivo mutations of the AMPA receptor subunit GluR2 and its interacting protein PICK1 eliminate cerebellar long-term depression. Neuron. 2006 Mar 16;49(6):845-60.

Jin Y, Kim SJ, Kim J, Worley PF, Linden DJ. Long-term depression of mGluR1 signaling. Neuron. 2007 Jul 19;55(2):277-87.

Koekkoek, S. K., Hulscher, H. C., Dortland, B. R., Hensbroek, R. A., Elgersma, Y., Ruigrok, T. J., and De Zeeuw, C. I. (2003). Cerebellar LTD and learning-dependent timing of conditioned eyelid responses. Science *301*, 1736-1739.

2/21/08 Cerebellum II

Koekkoek SK, Yamaguchi K, Milojkovic BA, Dortland BR, Ruigrok TJ, Maex R, De Graaf W, Smit AE, VanderWerf F, Bakker CE, Willemsen R, Ikeda T, Kakizawa S, Onodera K, Nelson DL, Mientjes E, Joosten M, De Schutter E, Oostra BA, Ito M, De Zeeuw CI. Deletion of FMR1 in Purkinje cells enhances parallel fiber LTD, enlarges spines, and attenuates cerebellar eyelid conditioning in Fragile X syndrome. Neuron. 2005 Aug 4;47(3):339-52.

Sdrulla AD, Linden DJ. Double dissociation between long-term depression and dendritic spine morphology in cerebellar Purkinje cells. Nat Neurosci. 2007 May;10(5):546-8.

Nelson, A. B., Krispel, C. M., Sekirnjak, C., and du Lac, S. (2003). Long-lasting increases in intrinsic excitability triggered by inhibition. Neuron *40*, 609-620.

Nelson, A. B., Gittis, A. H., and du Lac, S. (2005). Decreases in CaMKII activity trigger persistent potentiation of intrinsic excitability in spontaneously firing vestibular nucleus neurons. Neuron *46*, 623-631.

2/28/08 The future of learning and memory research

Come prepared to ponder and speculate (and sip and munch).