**PS504 Contemporary Trends in Neuroscience: Manipulating Memory Engrams**

Fall 2019

**Professor Steve Ramirez**

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Office Hours: Wednesday 1-2pm or Thursday 2-3pm, or send me an e-mail to arrange a time.

Note the class schedule for the Fall:



Class Prerequisites: CAS PS/NE202, CAS PS231, CAS PS/NE336 or 337, or CAS BI325, consent of instructor. Please read Class Preparation Section for more details regarding required background knowledge.

Course Description: Memories thread and unify our overall sense of being, as well as guide our decisions to interact with the world around us. The biological manifestation of a memory is termed an “engram.” This course aims to provide students with a modern understanding of the nature and organization of memory engrams at the neuroscience level by surveying the relevant literature in the form of primary research papers and reviews.

Course Materials. Required materials come from the following sources:  
Original scientific papers and review papers will be listed weekly on the Blackboard website, as well as TED talks, YouTube clips, and supplemental movie clips. There are no problem sets, quizzes, or exams.

Course Format and Requirements: The course format requires that students read the required readings or view the required media each week. The readings include both review articles and original papers. There is no textbook, but it is assumed that everyone has read at least one or two textbook chapters on memory in their prerequisite classes. During class, students are encouraged to ask questions about the lecture topic and the assigned reading material. I will normally lecture for about 10-15 minutes and then provide the remaining time for student presentations. **The primary goal of this course is to read, digest, and effectively communicate the science presented in the article chosen for that class.**

Students are required to attend classes and in keeping with BU policy attendance will be monitored at each class. I fully appreciate that unexpected events come up and therefore attendance won’t affect your overall grade directly, but I do expect you to be responsible for the material from missed classes (e.g. If you miss a class you are responsible for getting notes from a classmate).

Students are required to abide by the CAS Academic Conduct Code. Cases of academic misconduct, including cheating on exams, will be reported to the Dean of CAS and the Chairman of the Department of Psychological and Brain Sciences and the Director of the Undergraduate Program in Neuroscience.

**Grading criteria:** There are no fixed percentages of A grades, B grades, C grades etc. Grading will be broken down as follows:

* **40% Presentations (2 presentations per student group of 2-3 students; 20% of overall grade per presentation). First presentations will be graded more leniently than second, and I will give feedback for each presentation.**

For the last ~15 mins of each class in the beginning of the semester, I’ll provide background for the \*next\* paper so as to facilitate digesting some of the more complicated techniques and concepts we’ll cover.

PRESENTATION STYLE:

30 mins max: feel free to go into the most important figures (as opposed to copy and pasting every figure into a presentation). The presentation should include a brief Introduction on the topic, an overview of the Methods used, a Discussion of the key Figures, and an overall dialogue with the classroom. Please don’t feel the need to have to go over every detail of each paper—rather, feel free to call on students and myself to talk/think out loud on the key findings and figures themselves.

* **30% Discussion. As this is a discussion-heavy class, your contributions are essential to generate scientific and thought-provoking commentary and analyses of the paper presented each class. I’ll closely monitor in each class who contributes to discussion.**
* **30% Final Paper. Please pick 2-3 “engram” papers of your choice and provide a summary, a critique, and propose potential future directions for each in 2-3 pages or less. Please use 12pt Times New Roman font, 1 inch margins, single spaced.**

You will get the most out of this class if you have read the assigned readings and bring any relevant power point presentations to class. This will enable you to ask questions in class, follow the material as it is covered, and take part in the discussions. Please come to class with 2-3 questions on the assigned article to facilitate discussions.

The readings are available on the course website. Questions to keep in mind as you are reading these papers are: What is the main question the authors are trying to address? What is their central hypothesis? What did the experiment set out to test? How was this accomplished? What were the results, and how did the authors interpret these results? Are alternative outcomes or hypotheses provided? What do the authors conclude, and are follow up studies suggested? If you have read other studies that are related, are the findings between the studies consistent, or is there still an open debate? Are there studies that might solve this debate? If the weekly reading assignment includes a review paper, then you should be able to summarize the most important questions being addressed, which questions have been addressed in the previous studies (and how) and what areas are logical areas for follow up experiments.

**DATES, TOPICS, READINGS  
ALL REQUIRED READINGS ARE IN GREEN   
ALL OPTIONAL (BUT HIGHLY ENCOURAGED) ARE IN ORANGE**

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WEEK 1 January 22 and 24  
September 3, Lecture 1: An overview of the class and introduction to memory engrams  
  
September 5, Lecture 2: A brief discussion on memory engrams and the required reading below  
READING: Elizabeth Phelps, Memory editing from science fiction to clinical practice, *Nature,* 2019.  
  
YouTube Clip: Joshua Foer   
<https://www.ted.com/talks/joshua_foer_feats_of_memory_anyone_can_do?language=en>

WEEK 2  
September 10, Lecture 3: Isolating memories in the brain  
Reijmers, L. G., Perkins, B. L., Matsuo, N., & Mayford, M. (2007). Localization of a stable neural correlate of associative memory. *Science*, *317*(5842), 1230–1233. <https://doi.org/10.1126/science.1143839>  
  
September 12, Lecture 4: Isolating memories in the brain  
Han, J. H., Kushner, S. A., Yiu, A. P., Cole, C. J., Matynia, A., Brown, R. A., … Josselyn, S. A. (2007). Neuronal competition and selection during memory formation. *Science*, *316*(5823), 457–460. <https://doi.org/10.1126/science.1139438>  
  
OPTIONAL Reading: Reijmers, L., & Mayford, M. (2009). Genetic control of active neural circuits. *Frontiers in Molecular Neuroscience*, *2*(DEC), 1–8. https://doi.org/10.3389/neuro.02.027.2009

WEEK 3   
September 17, Lecture 5: Erasing Memories in the Brain  
Han, J. H., Kushner, S. A., Yiu, A. P., Hsiang, H. L., Buch, T., Waisman, A., … Josselyn, S. A. (2009). Selective erasure of a fear memory. *Science*, *323*(5920), 1492–1496. https://doi.org/10.1126/science.1164139  
  
September 19, Lecture 6: Erasing Memories in the Brain  
Schiller, D., Monfils, M. H., Raio, C. M., Johnson, D. C., Ledoux, J. E., & Phelps, E. A. (2010). Preventing the return of fear in humans using reconsolidation update mechanisms. Nature, 463(7277), 49–53. <https://doi.org/10.1038/nature08637>

OPTIONAL Reading: Josselyn, S. A. (2010). Continuing the search for the engram: Examining the mechanism of fear memories. Journal of Psychiatry and Neuroscience, 35(4), 221–228. https://doi.org/10.1503/jpn.100015

WEEK 4   
September 24, Lecture 7: Artificially Activating Memories  
Liu, X., Ramirez, S., Pang, P. T., Puryear, C. B., Govindarajan, A., Deisseroth, K., & Tonegawa, S. (2012). Optogenetic stimulation of a hippocampal engram activates fear memory recall. Nature, 484(7394), 381–385. https://doi.org/10.1038/nature11028

September 26, Lecture 8: Artificially Activating Memories  
Cowansage, K. K., Shuman, T., Dillingham, B. C., Chang, A., Golshani, P., & Mayford, M. (2014). Direct Reactivation of a Coherent Neocortical Memory of Context. Neuron, 84(2), 432–441. https://doi.org/10.1016/j.neuron.2014.09.022

OPTIONAL READING: Ramirez, S., Tonegawa, S., & Liu, X. (2014). Identification and optogenetic manipulation of memory engrams in the hippocampus. Frontiers in Behavioral Neuroscience, 7(January), 1–9. <https://doi.org/10.3389/fnbeh.2013.00226>

TED TALK: Shameful self-promotion <https://www.ted.com/talks/steve_ramirez_and_xu_liu_a_mouse_a_laser_beam_a_manipulated_memory/discussion>

WEEK 5   
October 1, Lecture 9: Artificially Inhibiting Memories  
Denny, C. A., Kheirbek, M. A., Alba, E. L., Tanaka, K. F., Brachman, R. A., Laughman, K. B., … Hen, R. (2014). Hippocampal memory traces are differentially modulated by experience, time, and adult neurogenesis. Neuron, 83(1), 189–201. <https://doi.org/10.1016/j.neuron.2014.05.018>  
  
October 3, Lecture 10: Artificially Inhibiting Memories  
Hsiang, H.-L., Epp, J. R., van den Oever, M. C., Yan, C., Rashid, A. J., Insel, N., … Josselyn, S. A. (2014). Manipulating a “Cocaine Engram” in Mice. Journal of Neuroscience, 34(42), 14115–14127. <https://doi.org/10.1523/JNEUROSCI.3327-14.2014>

OPTIONAL READING: Richards, B. A., & Frankland, P. W. (2013). The conjunctive trace. Hippocampus, 23(3), 207–212. https://doi.org/10.1002/hipo.22089

WEEK 6   
October 8, Lecture 11: Artificially Creating False Memories  
Ramirez, S. et al. Creating a false memory in the hippocampus. Science 341, 387–391 (2013).

October 10, Lecture 12: Artificially Creating False Memories  
Garner, A. R., Rowland, D. C., Hwang, S. Y., Baumgaertel, K., Roth, B. L., Kentros, C., & Mayford, M. (2012). Generation of a Synthetic Memory Trace. Neuron, 1513(March), 1513–1516. <https://doi.org/10.1126/science.1214985>

OPTIONAL READING: Denny, C. A., Lebois, E., & Ramirez, S. (2017). From Engrams to Pathologies of the Brain. Frontiers in Neural Circuits, 11(April), 1–20. https://doi.org/10.3389/fncir.2017.00023

WEEK 7  
October 15, NO CLASS Substitute Monday Schedule  
October 17, NO CLASS, Society for Neuroscience Meeting  
  
WEEK 8  
October 22, NO CLASS, Society for Neuroscience Meeting  
  
October 24, Lecture 13, Artificially Creating False Memories  
Ohkawa, N., Saitoh, Y., Suzuki, A., Tsujimura, S., Murayama, E., Kosugi, S., … Inokuchi, K. (2015). Artificial association of pre-stored information to generate a qualitatively new memory. Cell Reports, 11(2), 261–269. https://doi.org/10.1016/j.celrep.2015.03.017

WEEK 9   
October 29, Lecture 14: Updating the Contents of Memories   
Redondo, R. L., Kim, J., Arons, A. L., Ramirez, S., Liu, X., & Tonegawa, S. (2014). Bidirectional switch of the valence associated with a hippocampal contextual memory engram. Nature, 513(7518), 426–430. <https://doi.org/10.1038/nature13725>  
  
October 31, Lecture 15: Updating the Contents of Memories   
Nabavi, S., Fox, R., Proulx, C. D., Lin, J. Y., Tsien, R. Y., & Malinow, R. (2014). Engineering a memory with LTD and LTP. Nature, 511(7509), 348–352. https://doi.org/10.1038/nature13294  
  
OPTIONAL READING: Josselyn, S. A., Köhler, S., & Frankland, P. W. (2015). Finding the engram. Nature Reviews Neuroscience, 16(9), 521–534. https://doi.org/10.1038/nrn4000

WEEK 10   
November 5, Lecture 16: Bringing Memories Back from Amnesia  
Ryan, T. J., Roy, D. S., Pignatelli, M., Arons, A., & Tonegawa, S. (2015). Engram cells retain memory under retrograde amnesia. Science, 348(6238), 1007–1013. <https://doi.org/10.1126/science.aaa5542>  
  
November 7, Lecture 17: Bringing Memories Back from Amnesia  
Guskjolen, A., Kenney, J. W., de la Parra, J., Yeung, B. A., Josselyn, S. A., & Frankland, P. W. (2018). Recovery of “Lost” Infant Memories in Mice. Current Biology, 28(14), 2283-2290.e3. https://doi.org/10.1016/j.cub.2018.05.059

OPTIONAL READING: Hamidi, A. B., & Ramirez, S. (2018). Memory: The Majestic Case of an Amnestic Trace. Current Biology, 28(14), R784–R786. <https://doi.org/10.1016/j.cub.2018.06.007>

TED TALK: Tomas Ryan  
<https://www.tedmed.com/talks/show?id=624548>  
  
WEEK 11  
November 12, Lecture 18: Recoding Memories in the Brain  
Trouche, S., Perestenko, P. V., Van De Ven, G. M., Bratley, C. T., McNamara, C. G., Campo-Urriza, N., … Dupret, D. (2016). Recoding a cocaine-place memory engram to a neutral engram in the hippocampus. Nature Neuroscience, 19(4), 564–567. <https://doi.org/10.1038/nn.4250>  
  
November 14, Lecture 19: Recoding and Linking Memories in the Brain  
Cai, D. J., Aharoni, D., Shuman, T., Shobe, J., Biane, J., Song, W., … Silva, A. J. (2016). A shared neural ensemble links distinct contextual memories encoded close in time. Nature, 534(7605), 115–118. https://doi.org/10.1038/nature17955

OPTIONAL READING: Rogerson, T., Jayaprakash, B., Cai, D. J., Sano, Y., Lee, Y. S., Zhou, Y., … Silva, A. J. (2016). Molecular and cellular mechanisms for trapping and activating emotional memories. PLoS ONE, 11(8), 1–24. https://doi.org/10.1371/journal.pone.0161655

WEEK 12   
November 19, Lecture 20: Extinguishing Memories  
Khalaf, O., Resch, S., Dixsaut, L., Gorden, V., Glauser, L., & Gräff, J. (2018). Reactivation of recall-induced neurons contributes to remote fear memory attenuation. Science, 360(6394), 1239–1242. <https://doi.org/10.1126/science.aas9875>  
  
November 21, Lecture 21: Extinguishing Memories  
Lacagnina, A. F., Brockway, E. T., Crovetti, C. R., Shue, F., McCarty, M. J., Sattler, K. P., … Drew, M. R. (2019). Distinct hippocampal engrams control extinction and relapse of fear memory. Nature Neuroscience, 22(5), 753–761. https://doi.org/10.1038/s41593-019-0361-z

OPTIONAL READING: <https://science.sciencemag.org/content/360/6394/1186.long>

WEEK 13  
November 26, Lecture 22: Activating Memories in the Diseased State  
Perusini, J. N., Cajigas, S. A., Cohensedgh, O., Lim, S. C., Pavlova, I. P., Donaldson, Z. R., & Denny, C. A. (2017). Optogenetic stimulation of dentate gyrus engrams restores memory in Alzheimer’s disease mice. Hippocampus, 27(10), 1110–1122. <https://doi.org/10.1002/hipo.22756>  
  
November 28, NO CLASS Thanksgiving Break

OPTIONAL READING: Eichenbaum, H. (2016). Still searching for the engram. Learning and Behavior, 44(3), 209–222. <https://doi.org/10.3758/s13420-016-0218-1>

WEEK 14   
December 3, Lecture 23: STEVE AWAY (He’ll skype in and have a guest host in class):   
Making Memories without Experience  
Vetere, G., Tran, L. M., Moberg, S., Steadman, P. E., Restivo, L., Morrison, F. G., … Frankland, P. W. (2019). Memory formation in the absence of experience. Nature Neuroscience. <https://doi.org/10.1038/s41593-019-0389-0>  
  
December 5, Lecture 24: The molecular neuroscience of memory Engrams; Manipulating engrams to induce depression.

Student’s choice between one of the following:   
1) Zhang, T. R., Larosa, A., Raddo, M.-E. Di, Wong, V., Wong, A. S., & Wong, T. P. (2018). Negative memory engrams in the hippocampus enhance the susceptibility to chronic social defeat stress. BioRxiv, (July), 379669. <https://doi.org/10.1101/379669>  
  
2) Rao-Ruiz, P., Couey, J. J., Marcelo, I. M., Bouwkamp, C. G., Slump, D. E., Matos, M. R., … Kushner, S. A. (2019). Engram-specific transcriptome profiling of contextual memory consolidation. Nature Communications, 10(1), 1–14.

Week 15  
December 10, Lecture 25: STEVE AWAY, Skype in: Class Summary