BISC 462: Seminar in Optogenetics : reading and writing the neural code
Fall 2015 – revision 4 (8/24/15)

Over the last 20 years, optogenetic technology has transformed neuroscience research. Optogenetic observation tools (*e.g.* genetically-encoded calcium indicators) allow simultaneous observation of the activity of thousands of neurons with single-cell resolution in behaving animals. Optogenetic control tools (*e.g.* channelrhodopsin-2) allow optical control of the activity of neural circuits with single-action potential resolution.

This course covers 23 key papers on the development and application of optogenetics. Students will discover the historical foundation, design principles, molecular mechanisms and transformative applications of optogenetic techniques.

Each week two students will present a 1-2 papers each (2-3 papers per class). These students will be responsible for first framing the background that led to the publications, an explanation of the questions being addressed, the techniques/approaches being used, and an analysis of the results. Finally, the students will lead a discussion on the relative merits and importance of the paper. *Prior to class, every student* must email 2 questions about the paper to shires@usc.edu. These questions should demonstrate that the student read and tried to understand the paper. They will also guide discussion of the paper.

After the class works through discussion of all papers, each student will prepare a creative project proposal answering the question "*What would you investigate or create with optogenetic technology and how would you do it*?". For example, apply optogenetics to understand neural circuits of obesity, or create a new type of optogenetic tool to optically control gene expression. The first step of this proposal will be a 7 minute presentation of the idea to the class, followed by a class critique of the idea. The second step will be a written proposal (maximum of *2 pages* including any inset figures) that refines the idea based on class feedback. Final creative proposals are due at *midnight Sunday Dec. 6th*.

Course Coordinator:
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Office Hours: Tuesday 4 pm – 5 pm HNB 228

Textbook: None

Time and Place: Tuesday : 2 pm – 3:50 pm, HNB 120F

Grading: The grades for the course will be determined by the paper presentation (30%), creative proposal (30%), class participation (20%), and questions (20%).

Topics and Papers:

Fluorescent proteins

1) Extraction, purification and properties of aequorin, a bioluminescent protein from the luminous hydromedusan, Aequorea. SHIMOMURA O, JOHNSON FH, SAIGA Y. J Cell Comp Physiol. 1962 Jun;59:223-39.
2) Crystal structure of the Aequorea victoria green fluorescent protein. Ormö M, Cubitt AB, Kallio K, Gross LA, Tsien RY, Remington SJ. Science. 1996 Sep 6;273(5280):1392-5.
3) Improved monomeric red, orange and yellow fluorescent proteins derived from Discosoma sp. red fluorescent protein.Shaner NC, Campbell RE, Steinbach PA, Giepmans BN, Palmer AE, Tsien RY. Nat Biotechnol. 2004 Dec;22(12):1567-72. Epub 2004 Nov 21.

Cortical imaging

4) Photon upmanship: why multiphoton imaging is more than a gimmick. Denk W1, Svoboda K. Neuron. 1997 Mar;18(3):351-7.
5) Long-term in vivo imaging of experience-dependent synaptic plasticity in adult cortex. Trachtenberg JT, Chen BE, Knott GW, Feng G, Sanes JR, Welker E, Svoboda K. Nature. 2002 Dec 19-26;420(6917):788-94.

Genetically-encoded calcium indicators

6) Fluorescent indicators for Ca2+ based on green fluorescent proteins and calmodulin. Miyawaki A, Llopis J, Heim R, McCaffery JM, Adams JA, Ikura M, Tsien RY. Nature. 1997 Aug 28;388(6645):882-7.
7) Circular permutation and receptor insertion within green fluorescent proteins. Baird GS1, Zacharias DA, Tsien RY. Proc Natl Acad Sci U S A. 1999 Sep 28;96(20):11241-6.
8) Ultrasensitive fluorescent proteins for imaging neuronal activity. Chen TW, Wardill TJ, Sun Y, Pulver SR, Renninger SL, Baohan A, Schreiter ER, Kerr RA, Orger MB, Jayaraman V, Looger LL, Svoboda K, Kim DS. Nature. 2013 Jul 18;499(7458):295-300. doi: 10.1038/nature12354.

Genetically-encoded activity indicators

9) An optimized fluorescent probe for visualizing glutamate neurotransmission. Marvin JS1, Borghuis BG, Tian L, Cichon J, Harnett MT, Akerboom J, Gordus A, Renninger SL, Chen TW, Bargmann CI, Orger MB, Schreiter ER, Demb JB, Gan WB, Hires SA, Looger LL. Nat Methods. 2013 Feb;10(2):162-70. doi: 10.1038/nmeth.2333. Epub 2013 Jan 13.
10) Neural circuits. Labeling of active neural circuits in vivo with designed calcium integrators.Fosque BF1, Sun Y1, Dana H1, Yang CT1, Ohyama T1, Tadross MR1, Patel R1, Zlatic M1, Kim DS1, Ahrens MB1, Jayaraman V1, Looger LL1, Schreiter ER2. Science. 2015 Feb 13;347(6223):755-60. doi: 10.1126/science.1260922.

Imaging activity in virtual reality

11) Intracellular dynamics of hippocampal place cells during virtual navigation. Harvey CD1, Collman F, Dombeck DA, Tank DW. Nature. 2009 Oct 15;461(7266):941-6. doi: 10.1038/nature08499.
12) Emergence of reproducible spatiotemporal activity during motor learning. Peters AJ1, Chen SX1, Komiyama T2. Nature. 2014 Jun 12;510(7504):263-7. doi: 10.1038/nature13235. Epub 2014 May 4.

Light-gated ion channels & pumps

13) Channelrhodopsin-2, a directly light-gated cation-selective membrane channel. Nagel G, Szellas T, Huhn W, Kateriya S, Adeishvili N, Berthold P, Ollig D, Hegemann P, Bamberg E. Proc Natl Acad Sci U S A. 2003 Nov 25;100(24):13940-5. Epub 2003 Nov 13.
14) Millisecond-timescale, genetically targeted optical control of neural activity. Boyden ES, Zhang F, Bamberg E, Nagel G, Deisseroth K. Nat Neurosci. 2005 Sep;8(9):1263-8. Epub 2005 Aug 14.
15) Multimodal fast optical interrogation of neural circuitry. Zhang F1, Wang LP, Brauner M, Liewald JF, Kay K, Watzke N, Wood PG, Bamberg E, Nagel G, Gottschalk A, Deisseroth K. Nature. 2007 Apr 5;446(7136):633-9.

Cracking neural circuits

16) Deconstruction of a neural circuit for hunger. Atasoy D, Betley JN, Su HH, Sternson SM. Nature. 2012 Aug 9;488(7410):172-7. doi: 10.1038/nature11270.

17) Scalable control of mounting and attack by Esr1+ neurons in the ventromedial hypothalamus. Lee H1, Kim DW2, Remedios R3, Anthony TE3, Chang A3, Madisen L4, Zeng H4, Anderson DJ5. Nature. 2014 May 29;509(7502):627-32. doi: 10.1038/nature13169. Epub 2014 Apr 16.

Synthetic perception

18) Sparse optical microstimulation in barrel cortex drives learned behaviour in freely moving mice. Huber D1, Petreanu L, Ghitani N, Ranade S, Hromádka T, Mainen Z, Svoboda K. Nature. 2008 Jan 3;451(7174):61-4.

19) Neural coding during active somatosensation revealed using illusory touch. O'Connor DH, Hires SA, Guo ZV, Li N, Yu J, Sun QQ, Huber D, Svoboda K. Nat Neurosci. 2013 Jul;16(7):958-65. doi: 10.1038/nn.3419. Epub 2013 Jun 2.

Synthetic memory

20) Optogenetic stimulation of a hippocampal engram activates fear memory recall. Liu X1, Ramirez S, Pang PT, Puryear CB, Govindarajan A, Deisseroth K, Tonegawa S. Nature. 2012 Mar 22;484(7394):381-5. doi: 10.1038/nature11028.

21) Direct reactivation of a coherent neocortical memory of context. Neuron. 2014 Oct 22;84(2):432-41. doi: 10.1016/j.neuron.2014.09.022. Epub 2014 Oct 9. Cowansage KK1, Shuman T2, Dillingham BC3, Chang A1, Golshani P4, Mayford M5.

Total optical control

22) Simultaneous cellular-resolution optical perturbation and imaging of place cell firing fields. Rickgauer JP1, Deisseroth K2, Tank DW1. Nat Neurosci. 2014 Dec;17(12):1816-24. doi: 10.1038/nn.3866. Epub 2014 Nov 17.

23) Simultaneous all-optical manipulation and recording of neural circuit activity with cellular resolution in vivo. Packer AM1, Russell LE1, Dalgleish HW1, Häusser M1. Nat Methods. 2015 Feb;12(2):140-6. doi: 10.1038/nmeth.3217. Epub 2014 Dec 22.

Course Schedule

	Topic
25-Aug	***Welcome!***
1-Sep	***Fluorescent proteins***
8-Sep	***Cortical imaging***
15-Sep	***Genetically-encoded calcium indicators***
22-Sep	***Genetically-encoded activity indicators***
29-Sep	***Imaging activity & virtual reality***
5-Oct	***Optional discussion : Monday 2-4pm***
13-Oct	***Light-gated ion channels & pumps***
20-Oct	***Cracking neural circuits***
27-Oct	***Synthetic perception***
3-Nov	***Synthetic memory***
10-Nov	***Total optical control***
17-Nov	***Proposal presentations***
24-Nov	***Proposal presentations***
1-Dec	***Proposal presentations***
6-Dec	***Written proposal due***

Students with Disabilities: Students requesting academic accommodations based on a disability are required to register with Disability Services and Programs (DSP) each

semester. A letter of verification for approved accommodations can be obtained from DSP when adequate documentation is filed. Please be sure the letter is delivered to one of the instructors as early in the semester as possible. Disability Services and Programs is located in Student Union 301 and their phone number is (213) 740-0776.

Statement on academic integrity: USC seeks to maintain an optimal learning environment. General principles of academic honesty include the concept of respect for the intellectual property of others, the expectation that individual work will be submitted unless otherwise allowed by an instructor, and the obligations both to protect one's own academic work from misuse by others as well as to avoid using another's work as one's own. All students are expected to understand and abide by these principles. Scampus, the Student Guidebook, contains the Student Conduct Code in Section 11.00, while the recommended sanctions are located in Appendix A: http://www.usc.edu/dept/publications/SCAMPUS/gov/. Students will be referred to the Office of Student Judicial Affairs and Community Standards for further review, should there be any suspicion of academic dishonesty. The Review process can be found at: http://www.usc.edu/student-affairs/SJACS/.

Disclaimer: It may be necessary to make some changes in the syllabus during the semester.