Neuro109A
Precision Neuroscience:
Neural Circuits for Individuality

Harvard College/Graduate School of Arts and Sciences: 203341
Term: Fall 2016-2017
Exam Group: FAS12_B
Meeting Time: Thursday 7:00pm - 8:29pm

Course instructors:

Eva Aimable Naumann, PhD
Postdoctoral Fellow
510.646.3035
eva@mcb.harvard.edu
Location: Biological Laboratories 2074
Office hours: By appointment / TBA

Armin Bahl, PhD
Postdoctoral Fellow
arminbahl@fas.harvard.edu
Location: Biological Laboratories 2074
Office hours: By appointment / TBA

Course Description

How do neural circuits produce variability in the behavior of individuals? To understand how brains generate the behavioral differences that shape personality, we will study modern advances in neuroscience, from ion channels to whole-brain activity mapping. We will explore these ideas with a focus on the individual and will discuss the possibility of precision medicine applied to mental illness.

Prerequisites

LS 1a, MCB 80, and permission of Instructor

Course Objectives

Students will be given an overview of modern systems neuroscience in various model organisms and will learn how activity in neural circuits is thought to drive behavior. By the end of the course, students should have developed a strong grasp of what has motivated the recent NIH BRAIN Initiative. The course curriculum has been designed for students to:

(1) Develop a fundamental understanding of how neural circuits can drive behavior and how these circuits and behaviors may vary across individual animals
(2) Acquire the skills necessary to read, interpret, discuss, and present primary scientific literature on modern systems neuroscience.
(3) Gain a working understanding of statistical methods and their implementation in Matlab.

Assignments, Grading, and Workload

Assignment	% of Final Grade
Class Participation/ Assignments	**25%**
Weekly Paragraph Summary of Paper	15%
Class Presentations	25%
Matlab/ Statistics problem sets	10%
Final Project & Final presentation	25%

4-6 hours of workload per week

Style of instruction/ tutorial structure

In addition to teaching students how large data streams from individual animals are influencing modern systems neuroscience, a major goal of this tutorial will be to teach students how to critically analyze primary scientific literature and equip them with the practical statistical skills necessary to accurately assess the implications of scientific data. As programming proficiency in software like Matlab is quickly becoming a prerequisite for the modern biologist, we will also gently introduce students to data analysis in Matlab via problem sets that emphasize data visualization and statistics of large datasets.

In pursuit of these goals, each week students will be assigned to read at least one scientific publication (primary literature and or reviews) and write a summary paragraph to be submitted before class. In addition, students are expected to verbally summarize key figures and concepts (or communicate specific difficulties in understanding of findings or methods). Meetings will generally begin with either an instructor lecture or student presentation and will end with a class discussion or hands-on data analysis tutorial. To engage students, I will also offer ungraded, supplementary group meetings before class. In my experience, this has generally created an unusually active, collaborative, and engaged classroom for the duration of the semester.

A total of four Matlab problem sets will be assigned to familiarize students with real data analysis and visualization of both functional imaging and behavioral data. As a final project, students will choose from two options: (1) creating an interactive visualization of a dataset or (2) writing a mock grant proposal tailored to the NIH BRAIN initiative.

Materials

There is no required textbook for the course. All readings will be available online as PDFs.

Academic Integrity

Students are expected to be familiar with and adhere to the University's policies on academic integrity and plagiarism:
https://college.harvard.edu/academics/academic-integrity

All references and sources used in your assignments MUST be properly cited in accordance with Harvard guidelines. Instances of academic dishonesty may result in sanctions including but not limited to, failing grades being issued, and other consequences.

Schedule Fall 2016

Week	Date	Topic	Example Reading	Model organism
1	9/1	**Introduction, Twin Studies, lazy ants and what is Precision Neuroscience?**	(Freund et al., 2013)	Various
2	9/8	**Classic neural circuits** (Lecture and discussion)	(Fink et al., 2014)	Rodent
3	9/15	**Psychophysics and behavior** (Lecture and discussion)	(Newsome et al., 1989)	Primate, Rodent
4	9/22	**Modern neuroscience toolkit: Optogenetics** (Lecture and discussion)	(Otchy et al., 2015)(Lerner et al., 2016)	Mouse, Bird
5	9/29	**Matlab introduction** (Hands-on instruction, in class data collection)	TBA/ Instructor notes	Human, TBA
6	10/6	**Neuromodulation of behavioral states** (Lecture and discussion)	Gordus 2015, Flavell 2013	C. Elegans
7	10/13	**Variability in the Lobster stomach** (Lecture and discussion)	(Hamood and Marder, 2014)	Lobster, Crab
8	10/20	**Data and Image analysis** (Hands-on instruction)	TBA/ Instructor notes	Zebrafish, Human
9	10/27	**Neural circuits in Zebrafish** (Lecture and Laboratory tour)	(Pantoja et al., 2016) (Naumann et al.)	Zebrafish
10	11/3	**Modern statistical methods in neuroscience: Monte Carlo, bootstrap, etc.** (Hands-on instruction)	TBA/ Instructor notes	
11	11/10	**Modern neuroscience toolkit: Vision** (Lecture and discussion)	(Bahl et al., 2015)	Drosophila
12	11/17	**Modern neuroscience toolkit: Connectomics** (Lecture and discussion)	(Maisak et al., 2013) (Ohyama et al., 2015)	Drosophila
13	11/24	***-------Thanksgiving--------***		
14	**12/1**	**Student Project Presentations*/ Class dinner**	**Student assigned**	

Schedule Spring 2017

Week	Date	Topic	Example Reading	Model organism
1	1/26	**Animal personality, lazy ants, and cooperative meercats**	(Wolf and Weissing, 2012)	Various
2	2/2	**Behavioral idiosyncrasies in Drosophila** ***Ben de Blvort guest lecture***	(Ayroles et al., 2015; Kain et al., 2012)	Drosophila
3	2/9	**The power of habit: Plasticity** (Lecture and discussion)	(Chen et al., 2006) (Dulac, 2010) (Hofer et al., 2008)	Rodent
4	2/16	**Mental Disease Susceptibility** (Lecture and discussion)	(Casey and Lee, 2015)	Human, Rodent
5	2/23	**Epigenetics 1: Life experiences** (Lecture and discussion)	(Chattarji et al., 2015; Davidson and McEwen, 2012)	Rodent
6	3/2	**Epigenetics 2: Clones** (Lecture and discussion)	(Archer et al., 2003)	Pigs
7	3/9	**Computational models of neural circuits** (Lecture and hands-on instruction)	(Gao and Ganguli, 2015)	Zebrafish Lobster
8	3/16	***-------Springbreak--------***		

9	3/23	**Precision medicine: Oncology**	TBA	Human
10	3/30	**Measurements of individuality** (Lecture and Hands-on instruction)	(Berman et al., 2014)	Drosophila, Various
11	4/6	**Data visualization** (Lecture and Hands-on instruction)	(Tufte, 2001)	
12	4/13	**Blue Brain & Connectome** (Lecture and Discussion)	(Markram et al., 2015)	Silicon, Various
13	4/20	**Precision medicine for neuroscience? (**Excursion to MIT Broad institute)	(Jorgenson et al., 2015)	Various
14	**4/27**	Student Project Presentations/ Class dinner	**Student assigned**	

Note: Each student will be at least twice per semester be responsible to suggest and present articles for next session. This way they can incorporate material that is of interest to them as long as it is pertinent to the discussion/ topic of the week.

References

Archer, G.S., Friend, T.H., Piedrahita, J., Nevill, C.H., and Walker, S. (2003). Behavioral variation among cloned pigs. Appl. Anim. Behav. Sci. *81*, 321–331.

Ayroles, J.F., Buchanan, S.M., O'Leary, C., Skutt-Kakaria, K., Grenier, J.K., Clark, A.G., Hartl, D.L., and de Bivort, B.L. (2015). Behavioral idiosyncrasy reveals genetic control of phenotypic variability. Proc. Natl. Acad. Sci. U. S. A. *112*, 6706–6711.

Bahl, A., Serbe, E., Meier, M., Ammer, G., and Borst, A. (2015). Neural Mechanisms for Drosophila Contrast Vision. Neuron *88*, 1240–1252.

Berman, G.J., Choi, D.M., Bialek, W., and Shaevitz, J.W. (2014). Mapping the stereotyped behaviour of freely moving fruit flies. J. R. Soc. Interface R. Soc. *11*.

Casey, B.J., and Lee, F.S. (2015). Optimizing treatments for anxiety by age and genetics. Ann. N. Y. Acad. Sci. *1345*, 16–24.

Chattarji, S., Tomar, A., Suvrathan, A., Ghosh, S., and Rahman, M.M. (2015). Neighborhood matters: divergent patterns of stress-induced plasticity across the brain. Nat. Neurosci. *18*, 1364–1375.

Chen, Z.-Y., Jing, D., Bath, K.G., Ieraci, A., Khan, T., Siao, C.-J., Herrera, D.G., Toth, M., Yang, C., McEwen, B.S., et al. (2006). Genetic variant BDNF (Val66Met) polymorphism alters anxiety-related behavior. Science *314*, 140–143.

Davidson, R.J., and McEwen, B.S. (2012). Social influences on neuroplasticity: stress and interventions to promote well-being. Nat. Neurosci. *15*, 689–695.

Dulac, C. (2010). Brain function and chromatin plasticity. Nature *465*, 728–735.

Fink, A.J.P., Croce, K.R., Huang, Z.J., Abbott, L.F., Jessell, T.M., and Azim, E. (2014). Presynaptic inhibition of spinal sensory feedback ensures smooth movement. Nature *509*, 43–48.

Freund, J., Brandmaier, A.M., Lewejohann, L., Kirste, I., Kritzler, M., Krüger, A., Sachser, N., Lindenberger, U., and Kempermann, G. (2013). Emergence of individuality in genetically identical mice. Science *340*, 756–759.

Gao, P., and Ganguli, S. (2015). On simplicity and complexity in the brave new world of large-scale neuroscience. Curr. Opin. Neurobiol. *32*, 148–155.

Hamood, A.W., and Marder, E. (2014). Animal-to-Animal Variability in Neuromodulation and Circuit Function. Cold Spring Harb. Symp. Quant. Biol. *79*, 21–28.

Hofer, S.B., Mrsic-Flogel, T.D., Bonhoeffer, T., and Hübener, M. (2008). Experience leaves a lasting structural trace in cortical circuits. Nature *457*, 313–317.

Jorgenson, L.A., Newsome, W.T., Anderson, D.J., Bargmann, C.I., Brown, E.N., Deisseroth, K., Donoghue, J.P., Hudson, K.L., Ling, G.S.F., MacLeish, P.R., et al. (2015). The BRAIN Initiative: developing technology to catalyse neuroscience discovery. Philos. Trans. R. Soc. Lond. B. Biol. Sci. *370*.

Kain, J.S., Stokes, C., and de Bivort, B.L. (2012). Phototactic personality in fruit flies and its suppression by serotonin and white. Proc. Natl. Acad. Sci. U. S. A. *109*, 19834–19839.

Lerner, T.N., Ye, L., and Deisseroth, K. (2016). Communication in Neural Circuits: Tools, Opportunities, and Challenges. Cell *164*, 1136–1150.

Maisak, M.S., Haag, J., Ammer, G., Serbe, E., Meier, M., Leonhardt, A., Schilling, T., Bahl, A., Rubin, G.M., Nern, A., et al. (2013). A directional tuning map of Drosophila elementary motion detectors. Nature *500*, 212–216.

Marder, E., and Goaillard, J.-M. (2006). Variability, compensation and homeostasis in neuron and network function. Nat. Rev. Neurosci. *7*, 563–574.

Markram, H., Muller, E., Ramaswamy, S., Reimann, M.W., Abdellah, M., Sanchez, C.A., Ailamaki, A., Alonso-Nanclares, L., Antille, N., Arsever, S., et al. (2015). Reconstruction and Simulation of Neocortical Microcircuitry. Cell *163*, 456–492.

Naumann, E.A., Fitzgerald, J.E., Dunn, T.W., Rihel, J., Sompolinsky, H., and Engert, F. From whole-brain data to functional circuit models: the zebrafish optomotor response.

Newsome, W.T., Britten, K.H., and Movshon, J.A. (1989). Neuronal correlates of a perceptual decision. Nature *341*, 52–54.

Ohyama, T., Schneider-Mizell, C.M., Fetter, R.D., Aleman, J.V., Franconville, R., Rivera-Alba, M., Mensh, B.D., Branson, K.M., Simpson, J.H., Truman, J.W., et al. (2015). A multilevel multimodal circuit enhances action selection in Drosophila. Nature *advance online publication*.

Otchy, T.M., Wolff, S.B.E., Rhee, J.Y., Pehlevan, C., Kawai, R., Kempf, A., Gobes, S.M.H., and Ölveczky, B.P. (2015). Acute off-target effects of neural circuit manipulations. Nature *528*, 358–363.

Pantoja, C., Hoagland, A., Carroll, E.C., Karalis, V., Conner, A., and Isacoff, E.Y. (2016). Neuromodulatory Regulation of Behavioral Individuality in Zebrafish. Neuron.

Tufte, E.R. (2001). The Visual Display of Quantitative Information (Cheshire, Conn: Graphics Pr).

Wolf, M., and Weissing, F.J. (2012). Animal personalities: consequences for ecology and evolution. Trends Ecol. Evol. *27*, 452–461.