OEB 145 Genes and Behavior

Description of the course

This lecture course addresses causal links between genes and behavior, focusing on mechanisms by which gene products regulate behavioral outcomes. The course is organized into three parts.

Part I: Discoveries of genes related to brain disorders and psychiatric diseases.

Part II: Key research approaches to studying the genetic basis of behavior and brain functions.

Part III: Gene functions in common behavioral traits (olfaction, itch and pain, circadian rhythm, sexual behavioral, sleep, learning and memory).

General information

Lecturer:

Yun Zhang, Ph. D.
Professor
Department of Organismic and Evolutionary Biology
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Time and place:

Tuesday and Thursday 1:30pm – 2:45pm.
Northwest science building B108.

Class format

We will meet twice a week for 75 minutes each. In each week, the instructor will give a lecture in one class and the TF will lead a session in the other with one student presenting an assigned paper in each session. We will have a midterm exam in week 7 and a final exam at the end of the semester.

Outline of the class

Week	*Tuesday*	
1	09/03 Introduction lecture: class overview; Nature vs nurture in brain functions	
Week	**Thursday**	**Tuesday**
2	09/05 Lecture: Brain disorders I - Huntington disease	09/10 Session
3	09/12 Lecture: Brain disorders II - Alzheimer's disease and psychiatric disorders	09/17 Session
4	09/19 Lecture: Animal models and molecular genetics methods in neurobiology of behavior	09/24 Session
5	09/26 Lecture: Recording and manipulating neuronal activity	10/1 Session
6	10/03 Lecture: Olfaction in mammals	10/8 Session
7	10/10 Prepare for midterm exam	10/15 Midterm exam
8	10/17 Lecture: Olfaction in invertebrates	10/22 Session
9	10/24 Lecture: Circadian rhythms and sleep	10/29 Session
10	10/31 Lecture: Genetic basis for sexual behavior	11/05 Session
11	11/07 Lecture: Somatosensation (itch, pain)	11/12 Session
12	11/14 Lecture: Learning and memory I – synaptic plasticity	11/19 Session
13	11/21 Lecture: Learning and memory II – Learning and synaptic plasticity	11/26 Session
14	11/28 Thanksgiving	12/03 Prepare for final exam (Q&A)
Final Exam	Time and Place TBD	

Grading

The guideline for grading:
Class attendance --- 15%
Presentation – 15%
Homework assignments – 30%
Midterm --- 15%
Final exam ---25%

The letter grades:
A: 85%-100%;
B; 70%-84%;
C: 60%-69%;
Failed: < 60% or unexcused absence for >= 4 times

General Policy

<u>Class attendance</u> (15% of the final grade): All students are required to attend all classes.

(1) If a student cannot attend a class, they need to contact the instructor in advance to provide a notice. In this case, the student will make up the class by writing a 3-page single-spaced summary of the missed class. The student should contact the instructor or TF for instructions of the summary. If the student fails to submit the summary, they will lose 5 points from the final grade.
(2) If a student misses a class without a prior notice, they will not be allowed to submit a make-up summary and will lose 5 points from their final grade.

<u>Presentation</u> (15% of the final grade): Student presentations are critical components of the class. Students should not miss their assigned presentations. In the rare cases when a student had to miss their presentation, they should contact the instructor in advance and arrange a switch with another student. If a student misses an assigned presentation without arranging a switch, they will lose 15 points from their final grade.

<u>Homework</u> (30% of the final grade): Homework assignment for each week has two parts: a lecture assignment and a session assignment (15% of the final grade each). The lecture assignment contains several questions (usually multiple-choice) on lecture content. The session assignment contains several essay questions on the upcoming presentation paper (relates to the main question, background, discoveries, approaches, analyses and interpretation of the study). Students should answer each question with fewer than 200 words. Both assignments will be posted on Canvas after each lecture. Missing a homework deadline will result in a loss of 10 points out of 100 from that specific homework grade.

Syllabus

The syllabus was developed using the books and papers in the reading list or cited in *Principles of Neurobiology* by Liqun Luo as references.

<u>Week 1</u>
Lecture: Class overview

I. Class overview
II. Nature and Nurture in brain function and behavior

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 1, P1-5.

<u>Week 2</u>
Lecture: Genetic basis for brain disorders I

I. Genetics in human diseases
II. Single-gene effects in neurological diseases
III. Linkage study on Huntington disease using a Venezuelan HD pedigree.

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 12, P511-512.
2. Gusella et al (1984) DNA Markers for Nervous System Diseases. Science 225 (4668): 1320-1326.

<u>Paper for presentation</u>

3. The Huntington's Disease Collaborative Research Group (1993). A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. Cell 72:971–983.

Discussion session: TF will present the paper for this session.
Presentations will be assigned during Week 2.

Week 3
Lecture: Genetic basis for brain disorders II

I. The major risk factors for Alzheimer's disease
II. Many genes contribute to psychiatric disorders: schizophrenia, mood disorders, anxiety disorders, addiction.

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 12, P499-529.
2. Selkoe DJ (2021) Treatments for Alzheimer's disease emerge. Science 373(6555):624-626.

Paper for presentation

3. Haney MS et al. (2024) APOE4/4 is linked to damaging lipid droplets in Alzheimer's disease microglia. Nature 628(8006):154-161.

Discussion session: student presentation and discussion

Week 4
Lecture: Animal models and molecular genetics methods in neurobiology of behavior

I. Animal models in neurobiology research
II. Genetics and molecular methods: forward screen, reverse genetics, gene disruption, transgene expression, access to specific neuronal populations, RNA sequencing.

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 14, P591-612.
2. Fire A, Xu S, Montgomery MK et al. (1998) Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. Nature 391:806–811.
3. Brand AH & Perrimon N (1993) Targeted gene expression as a means of altering cell fates and generating dominant phenotypes. Development 118:401–415.
4. Gordon JW, Scangos GA, Plotkin DJ et al. (1980) Genetic transformation of mouse embryos by microinjection of purified DNA. Proc Natl Acad Sci USA 77:7380–7384.
5. Lander ES, Linton LM, Birren B et al. (2001) Initial sequencing and analysis of the human genome. Nature 409:860–921.
6. Cong L*, Ran FA*, Cox D, et al (2013) Multiplex genome engineering using CRISPR/Cas systems. *Science* 15;339(6121):819-23.

Paper for presentation

7. Jinek M, Chylinski K, Fonfara I, et al (2012) A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. Science. 337(6096):816-21.

Discussion session: student presentation and discussion

Week 5
Lecture: Recording and manipulating neuronal activity

Electrical recording, optical imaging, optogenetics

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 14, P625-642.
2. Miyawaki A, Llopis J, Heim R et al. (1997) Fluorescent indicators for Ca2+ based on green fluorescent proteins and calmodulin. Nature 388:882–887.
3. Ahrens MB, Li JM, Orger MB et al. (2012) Brain-wide neuronal dynamics during motor adaptation in zebrafish. Nature 485:471–477.
4. Boyden ES, Zhang F, Bamberg E et al. (2005) Millisecond-timescale, genetically targeted optical control of neural activity. Nat Neurosci 8:1263–1268.
5. Chen TW, Wardill TJ, Sun Y et al. (2013) Ultrasensitive fluorescent proteins for imaging neuronal activity. Nature 499:295–300.
6. Hamill OP, Marty A, Neher E et al. (1981) Improved patch-clamp techniques for high-resolution current recording from cells and cell-free membrane patches. Pflugers Arch 391:85–100.
7. Lima SQ & Miesenbock G (2005) Remote control of behavior through genetically targeted photostimulation of neurons. Cell 121:141–152.

Paper for presentation

8. Tomova L et al (2021). Acute social isolation evokes midbrain craving responses similar to hunger. Nature Neuroscience 23:1597-1605.

Discussion session: student presentation and discussion

Week 6

Lecture: Olfaction I: how do we sense odors?

I. Olfactory receptors and downstream signaling pathways
II. Combinatorial activation of olfactory receptors
III. Organization of odorant information in the brain
IV. Polymorphism in odorant receptors contributes to difference in odorant perception

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 6, P213-227.
2. Buck L & Axel R (1991) A novel multigene family may encode odorant receptors: a molecular basis for odor recognition. Cell 65:175–187.
3. Keller A, Zhuang H, Chi Q et al. (2007) Genetic variation in a human odorant receptor alters odour perception. Nature 449:468–472.
4. Malnic B, Hirono J, Sato T et al. (1999) Combinatorial receptor codes for odors. Cell 96:713–723.
5. Miyamichi K, Amat F, Moussavi F et al. (2011) Cortical representations of olfactory input by trans-synaptic tracing. Nature 472:191–196.

Paper for presentation

6. Lyons DB, Allen WE, Goh T et al. (2013) An epigenetic trap stabilizes singular olfactory receptor expression. Cell 154:325–336.

Discussion session: student presentation and discussion

Week 7

Thursday (10/10): Prepare for midterm exam
Tuesday (10/15): midterm exam

Week 8

Lecture: Olfaction II: how do worms and flies sense odors?

1. Sensory encoding of olfactory responses in *C. elegans.*
2. Transformation and processing of odorant inputs in the nervous system of *Drosophila*

3. The olfactory systems in insects and mammals share many similarities.

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 6, P227-237.
2. Troemel ER, Kimmel BE & Bargmann CI (1997) Reprogramming chemotaxis responses: sensory neurons define olfactory preferences in C. elegans. Cell 91:161–169.
3. Caron SJ, Ruta V, Abbott LF et al. (2013) Random convergence of olfactory inputs in the Drosophila mushroom body. Nature 497:113–117.
4. Jefferis GS, Potter CJ, Chan AM et al. (2007) Comprehensive maps of Drosophila higher olfactory centers: spatially segregated fruit and pheromone representation. Cell 128:1187–1203.

Paper for presentation

5. McBride CS, Baier F, Omondi AB et al. (2014) Evolution of mosquito preference for humans linked to an odorant receptor. Nature 515(7526):222-7.

Discussion session: student presentation and discussion

Week 9

Lecture: Circadian rhythms and sleep

1. Circadian rhythms are driven by an auto-inhibitory transcriptional feedback loop conserved from flies to mammals.
2. How is a circadian rhythm entrained?
3. The mammalian sleep–wake cycle is regulated by multiple neurotransmitter and neuropeptide systems.
4. Why do we sleep?

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 9, P394-408.
2. Konopka RJ & Benzer S (1971) Clock mutants of Drosophila melanogaster. Proc Natl Acad Sci USA 68:2112–2116.
3. Hunter-Ensor M, Ousley A & Sehgal A (1996) Regulation of the Drosophila protein timeless suggests a mechanism for resetting the circadian clock by light. Cell 84:677–685.
4. Lin L, Faraco J, Li R et al. (1999) The sleep disorder canine narcolepsy is caused by a mutation in the hypocretin (orexin) receptor 2 gene. Cell 98:365–376.
5. Rechtschaffen A, Gilliland MA, Bergmann BM et al. (1983) Physiological correlates of prolonged sleep deprivation in rats. Science 221:182–184.

Paper for presentation

6. Simon EB et al. (2019) Overanxious and underslept. Nature Human Behaviour 4:100-110.

Discussion session: student presentation and discussion

Week 10

Lecture: Genetic basis for sexual behavior

1. Drosophila courtship behavior is innate and genetically regulated.
2. Fruitless (Fru) is essential for many aspects of sexual behavior in fruit flies.
3. Sex-specific splicing of *Fru* and courtship behavior.
4. FruM neurons promote male courtship behavior.

Reading list:

1 Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 10, P411-423.

2 Demir E & Dickson BJ (2005) Fruitless splicing specifies male courtship behavior in Drosophila. Cell 121:785–794.
3 Kohl J, Ostrovsky AD, Frechter S et al. (2013) A bidirectional circuit switch reroutes pheromone signals in male and female brains. Cell 155:1610–1623.
4 Fan P, Manoli DS, Ahmed OM et al. (2013) Genetic and neural mechanisms that inhibit Drosophila from mating with other species. Cell 154:89–102.

Paper for presentation

5. Sten TH et al. (2021) Sexual arousal gates visual processing during Drosophila courtship. Nature 595:549-553.

Discussion session: student presentation and discussion

Week 11

Lecture: Somatosensation, how do we sense body movement, touch, temperature and pain?

1. Different types of sensory neurons respond to different somatosensory stimuli.
2. Mechanotransduction channel Piezo2.
3. TRP channels for sensing temperature, chemicals and pain
4. Pain sensation is subjected to peripheral and central modulation.

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 6: P260-274.
2. Caterina MJ, Schumacher MA, Tominaga M et al. (1997) The capsaicin receptor: a heat-activated ion channel in the pain pathway. Nature 389:816–824.
3. Coste B, Mathur J, Schmidt M et al. (2010) Piezo1 and Piezo2 are essential components of distinct mechanically activated cation channels. Science 330:55–60.
4. Usoskin D, Furlan A, Islam S et al. (2015) Unbiased classification of sensory neuron types by large-scale single-cell RNA sequencing. Nat Neurosci 18:145–153.

Paper for presentation

5. Han L, Ma C, Liu Q et al. (2013) A subpopulation of nociceptors specifically linked to itch. Nat Neurosci 16:174–182.

Discussion session: student presentation and discussion

Week 12

Lecture: Memory, learning and synaptic plasticity I

1. Hypotheses for learning and memory
2. Long-term potentiation (LTP)
3. LTP induction and expression: NMDAR, AMPAR and CaMKII

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 11: P445-456.
2. Bliss TV & Lomo T (1973) Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. J Physiol 232:331–356.
3. Giese KP, Fedorov NB, Filipkowski RK et al. (1998) Autophosphorylation at Thr286 of the alpha calcium-calmodulin kinase II in LTP and learning. Science 279:870–873.
4. Isaac JT, Nicoll RA & Malenka RC (1995) Evidence for silent synapses: implications for the expression of LTP. Neuron 15:427–434.
5. Morris RG, Anderson E, Lynch GS et al. (1986) Selective impairment of learning and blockade of long-term potentiation by an N-methyl-D-aspartate receptor antagonist, AP5. Nature 319:774–776.

Paper for presentation

6. Tullis JE et al (2023) LTP induction by structural rather than enzymatic functions of CaMKII. Nature, https://www.nature.com/articles/s41586-023-06465-y (Open Access).

Discussion session: student presentation and discussion

Week 13 and 14

Lecture (Nov. 21st): Memory, learning and synaptic plasticity II

1. Animals exhibit many forms of learning.
2. In rodents, spatial learning and memory depend on the hippocampus.
3. Many manipulations that alter hippocampal LTP also alter spatial memory.
4. Learning can induce LTP.

Reading list:

1. Principles of Neurobiology by Liqun Luo, 2nd edition, Chapter 11: P464-467, 477-482.
2. Tang YP, Shimizu E, Dube GR et al. (1999) Genetic enhancement of learning and memory in mice. Nature 401:63–69.
3. Whitlock JR, Heynen AJ, Shuler MG et al. (2006) Learning induces long-term potentiation in the hippocampus. Science 313:1093–1097.
4. Liu X, Ramirez S, Pang PT et al. (2012) Optogenetic stimulation of a hippocampal engram activates fear memory recall. Nature 484:381–385.

Paper for presentation

5. Kim WB and Cho J-H (2017) Encoding of Discriminative Fear Memory by Input-Specific LTP in the Amygdala. Neuron 95:1129-1146.

Discussion session (Nov. 26th): student presentation and discussion

Nov. 28th: Thanksgiving recess
Dec 3rd: Prepare for Final exam (Q&A)

Final Exam: time and place to be determined.