Sakaguchi et al (2018) eLIFE.

254C: Genetic Control of Morphogenesis and Neuronal Wiring in the Central Nervous System

Syllabus

Winter 2021

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Syllabus Table of Contents

(Hyperlinked for easy navigation)

Course Materials

Course CCLE Website:

All discussion papers *and supplemental information* will be available on the CCLE course site, at least 1 week before their discussion.

Useful Links for Accessing Papers Yourself:

PubMed: http://www.ncbi.nlm.nih.gov/pubmed

UCLA library system for epublications:

http://www.ncbi.nlm.nih.gov/sites/entrez?tool=cdl&holding=uclalib&otool=cdlotool

If you are using an off campus computer you will need to set up a VPN. Information can be found here at the UCLA Library's WI+RE tutorial site.

Recent papers from Elsevier (Cell, Molecular Cell) must be ordered from the library well ahead of your need for them due to the dispute between UC and the publisher. Go to the following link https://ucelinks.cdlib.org/sfx_local/cgi/core/citation-linker.cgi. The UCLA Interlibrary Loan Service may also be helpful.

One can also use Sci Hub to get PDFs, please use your own discretion when using this site.

Course Description

The MBIDP wants all of our graduate students to develop scientific analytical skills while working toward their Ph.D. We believe these skills are integral to your success in any scientific career. The 254 series is designed to strengthen your scientific thinking skills through practice and with guidance from faculty.

How can we develop scientific analytical skills? Evidence indicates that courses where students and instructors discuss primary literature can effectively couple the development of critical analytical skills with the communication of scientific thought and rationale. Such courses provide venues for acquiring foundational knowledge and engaging in collaborative problem solving, both of which are preparation for diverse scientific careers.

Topic Description. Our 254C segment focuses on neurogenetics. An explosion of new genetic technologies has enabled exploration of how specific genes and gene regulatory networks control fundamental aspects of the form and function of the nervous system, including (1) the placement and proliferation of neural progenitors in the early embryo and in adults, and (2) cellular events within the differentiating neurons that affect their wiring properties. Recent research publications that address the genetic mechanisms by which neurons are formed from proliferating progenitor cells in distinct locations will be considered. We will also explore recent literature

that addresses how neural circuits are established, and studies that address how neurons extend a neurite (axon) along a predetermined pathway, the mechanisms by which neurites build synapses, and how neurites engage in highly non-random interactions, "choosing" specific other neurons as pre- or postsynaptic partners. These attributes, or "wiring properties", of the large number of neurons engaging in a brain circuit define the function of that circuit. Finally, the course will examine publications highlighting how the above findings are providing new insight in neurologic diseases and potential treatment.

General 254 Learning Outcomes:

By the end of the course we hope you will be able to

1. Identify the primary question(s) addressed by each paper.
2. Evaluate the scientific background to assess the significance of the questions.
3. Identify and articulate the hypotheses being tested in each paper.
4. Correlate the data and methods with the authors' hypotheses and conclusions.
5. Evaluate the flow of information presented; can you sense the underlying logic of the order of presentation?
6. Evaluate the soundness of scientific arguments and conclusions.
7. Evaluate the significance of the findings in a research paper in light of the existing literature.
8. Devise and propose 'next step' experiments that could follow on from primary research papers.

Course-specific Learning Outcomes: *(Instructors add here based on content and delivery method of 254, examples below)*

1. Gain an appreciation for the major unanswered questions and current research within the field of neurogenetics.
2. Evaluate various experimental methods and model organisms used in neurogenetics for their strengths and limitations
3. Gain an appreciation for the breath of approaches used in this field, from "omics" to detailed analyses of the actions of individual genes.
4. Get experience relating the conclusions reached in one paper to those in other papers. This will not be possible for every paper given the breadth of this field, but the attempt to make connections will enhance your ability to identify significant knowledge gaps in a field of inquiry.
5. Develop confidence and skills in oral scientific presentation and visual design.

Commitment to Inclusivity

The MBIDP is committed to making our community a place where all scientists can succeed and achieve their goals. We will work with you to create an inclusive environment that promotes learning. We expect you to contribute to creating an environment where everyone is inspired to participate. We encourage you to discuss with us and each other how our environment can be inclusive. Concerns about inclusivity may also be discussed with us, with the 254 Organizers: Kathrin Plath (kplath@mednet.ucla.edu) and/or Siobhan Braybrook (siobhanb@ucla.edu), the MBIDP Director Hillary Coller (hcoller@ucla.edu), or one of the MBIDP Equity Advisors.

We hope you will communicate with us if you experience anything in this course that does not support an inclusive environment. However, you can also report any incidents of harassment or discrimination to the Office

of Equity, Diversity, and Inclusion on their website.

Course Structure

Student & Instructor Meetings: You will attend two meetings with us (instructors) per week (two hours each), for a total of five weeks. You will be expected to engage in discussions about the assigned research papers in these meetings. You will meet with one another on the day before each Student & Instructor meeting. The student assigned to the paper under discussion will present the general overview, including background, unanswered question addressed by the paper, and the hypothesis under investigation. In your meeting, you will decide as a group which students will present specific figures in the student + instruction session.

Student-only Meetings: You will meet to discuss the assigned paper as a group the day before each Student and Instructor meeting. You will organize the presentation for a specific paper in the Student-only meetings.

How to Succeed in this Course (Expectations we have of you)

The best way to succeed is to participate actively. To do this, you should read the papers ahead of your meeting as a student-only group so that you can be prepared to contribute to the development of the presentation and then to our joint discussions. Feel free to contact one of the instructors for guidance on your presentation. Ask and answer questions during our group discussions. None of us, including the instructors, are experts on these papers. But our collective experiences can bring us all to a better understanding. Form an opinion about the contribution of the paper under discussion to the field. Science is a collaborative process, so *it is important to participate beyond the presentation of your assigned figures*.

How to Succeed in this Course (Expectations you can have of us)

You are not required to consult your instructors about your in-class presentation, but you are welcome to do so. Just email one of us. You can expect us to participate fully in the discussions and to ask questions about each paper so that there will be opportunities to engage in spontaneous scientific discussions. We will do our best to provide continuous feedback to you. We welcome your suggestions on how to make this experience as enriching as possible.

How Your Learning Will Be Assessed (Grading Policy)

Our 254 Course Grading Policy does not have an enforced grade distribution or curve. We recognize that you are graduate students at an elite university. You are already motivated to do your best; we are not here to adhere to a rigid scheme. Nor will we be tabulating points every time you contribute to discussion. Fluency in critical analysis is not something you are born with—it is a skill that is learned through practice. Our goal is to provide opportunities that promote your personal development as a scientist and encouragement to work on areas where you or your instructors find the greatest room for growth as scientist. Therefore, we will provide feedback midcourse; we will also notify you if we feel that you are not achieving at the level that would earn you an A in this course; we will note improvement in assigning a final grade. Outstanding performance in one aspect of the course can offset challenges you face in another.

That said, we are required to present a grading scale and a rubric. As discussed, we will be flexible:

A+:	95-100%
A:	90 - 94%
B:	80 - 89.9%
C:	70 - 79.9%
D:	60 - 69.9%
F:	0 - 59.9%

Participating in Discussions (45%): Participation will be evaluated based on the aspects below. We will note and reward improvement over time.

1. Attendance. You must attend Student & Instructor and Student-only meetings consistently and arrive on time. Please notify us or a fellow student (student-only meetings) if you are going to miss a meeting. If necessary, an absence can be made up by providing a 2-page (double spaced) report on the missed paper. Please discuss with us if there is a reason why you will need to be consistently late.

2. Contribution. You should be willing to share your views on the papers. This contribution should go beyond the figure you are presenting. **Aim for at least one contribution beyond your presentation per session**. You should provide insights into the experimental implications and unanswered questions.

3. Inclusive Behavior. You should engage respectfully with each other in all meeting. Challenging each other's thinking is an essential part of the scientific process. However, we are together to learn from each other.

Presentation (40%):

1. Organization and Overview. When you are the assigned leader for a paper, you should be able to frame the background, the gap in knowledge addressed, and the overall approaches. You should be able to provide a succinct summary of the conclusions at the end of the presentation.

2. Communication. When you are not the assigned leader, you should be able to succinctly and accurately describe experiments and explain figures.

Feedback

By the fourth week (midcourse) we will provide you with individual feedback but feel free to ask any time. Our goal is to encourage your active participation in discussion, and to find out who we can help.

The Final (15%)

The final paper is meant to demonstrate that you've learned something with respect to the Learning Outcomes. As such, the final will be a mini-proposal based on a paper from the course list that we didn't discuss together in class.

Write a mini-proposal that explains the background, the unknown that was addressed and its significance to the field, and future experiment(s). Be sure to use proper citations for literature. The report should be no more than 3 pages, 1.5 or 2 line spacing, 1 inch page margins, font Arial & size 11. It should cover the following:

Section 1: Paper Discussion (2 pgs; 80 pts)

(1) Summarize the relevant background that leads to the work (20 pts).

(2) Summarize the main question(s) and key hypotheses addressed in this paper (20 pts).

(3) Describe the methodology and key finding(s) of the paper. Link the key findings to the question(s) you identified above and mention how the approaches used support (or do not) the conclusions (40 pts).

Section 2: Mini-proposal (1 pg; 70 pts) For this section develop a follow-on question and hypothesis from your chosen paper.

(4) Identify a follow-on question that interests you based on your reading of the paper you chose. This question will be unique to you and your interests – but try to think of something that moves the field forward, not that replicates done in the past.

(5) Provide an introductory paragraph to set up your question - Why is this a critical question (what gap in knowledge does it fill?). (30 pts)

(6) Transform your question into a Hypothesis and ideally, an Alternative Hypothesis. Describe what experiments you would undertake to discriminate between these; highlight possible outcomes and how each would affect your choice of the hypothesis vs the alternative. (40 pts).

The report should be submitted by email to the instructors by Feb 26. Each final will be evaluated by the two instructors. We will provide you with written feedback on your finals within 2 weeks of their receipt.

Course Schedule

This is a tentative schedule and subject to change, with schedule adjustments posted on CCLE announcements.

Week	Meeting No.	Date	Topic	Paper for Discussion
Week 1	1	Jan 12	Introductory lecture Neural Progenitors	None—but see review articles
	2	Jan 15	No class meeting-prepare for first paper	
Week 2	**3**	Jan 19	Lineage tracing in neurogenesis	Berg *et al* or Telley *et al*
	4	Jan 22	Mitochondrial control of neurogenesis	Iwata *et al* or Namba *et al*
Week 3	**5**	Jan 26	Quiescence and stem cell maintenance	Adusumilli *et a*l or Kalamakis *et al*
	6	Jan 29	Introductory lecture Neuronal Architecture and Connectivity	None—but see review articles
Week 4	**7**	Feb 2	Whole body gradients specify neuronal branching in C. elegans	Chen *et al.* or Zou *et al.*
	8	Feb 5	Dendritic Architecture in the Mouse Cerebellum	Lui *et al.* or Kawabata Galbraith *et al.*
Week 5	**9**	Feb 9	Setting Dendritic Branchpoints in Drosophila Sensory Neurons	Stürner *et al.* or Ziegler *et al.*
	10	Feb 12	Genes and Supercircuits: The Role of FOXP2 in Language	Kosubek-Langer *et al.* or Atkinson *et al. or* French *et al.* or Xu *et al.*
	N/A	Feb 26	**FINAL PROPOSAL DUE**	

READING LIST

Session 1 Introductory lecture: Neural progenitors

No assigned papers but read reviews

Reviews

Cellular and molecular introduction to brain development. Jiang X, Nardelli J.Neurobiol Dis. 2016 Aug;92(Pt A):3-17. doi: 10.1016/j.nbd.2015.07.007.

The role of cell lineage in the development of neuronal circuitry and function. Hartenstein V, Omoto JJ, Lovick JK.Dev Biol. 2020 Feb 1:S0012-1606(18)30265-3. doi: 10.1016/j.ydbio.2020.01.012.

Session 2: No meeting

Session 3 Lineage tracing in neurogenesis

Origins and Proliferative States of Human Oligodendrocyte Precursor Cells. Huang W, Bhaduri A, Velmeshev D, Wang S, Wang L, Rottkamp CA, Alvarez-Buylla A, Rowitch DH, Kriegstein AR. Cell. 2020 Aug 6;182(3):594-608.e11. doi: 10.1016/j.cell.2020.06.027.

Temporal patterning of apical progenitors and their daughter neurons in the developing neocortex. Telley L, Agirman G, Prados J, Amberg N, Fièvre S, Oberst P, Bartolini G, Vitali I, Cadilhac C, Hippenmeyer S, Nguyen L, Dayer A, Jabaudon D. Science. 2019 May 10;364(6440):eaav2522. doi: 10.1126/science.aav2522.

Review:

Neurogenesis From Embryo to Adult - Lessons From Flies and Mice. Mira H, Morante J. Front Cell Dev Biol. 2020 Jun 30;8:533. doi: 10.3389/fcell.2020.00533.

Session 4 Mitochondrial control of neurogenesis

Mitochondrial dynamics in postmitotic cells regulate neurogenesis. Iwata R, Casimir P, Vanderhaeghen P. Science. 2020 Aug 14;369(6505):858-862. doi: 10.1126/science.aba9760.

Metabolic Regulation of Neocortical Expansion in Development and Evolution. Namba T, Nardelli J, Gressens P, Huttner WB. Neuron. 2020 Dec 2:S0896-6273(20)30892-8. doi: 10.1016/j.neuron.2020.11.014.

Review

Metabolic regulation of neurodifferentiation in the adult brain. Maffezzini C, Calvo-Garrido J, Wredenberg A, Freyer C. Cell Mol Life Sci. 2020 Jul;77(13):2483-2496. doi: 10.1007/s00018-019-03430-9.

Session 5 Quiescence and stem cell maintenance

ROS Dynamics Delineate Functional States of Hippocampal Neural Stem Cells and Link to Their Activity-Dependent Exit from Quiescence. Adusumilli VS, Walker TL, Overall RW, Klatt GM, Zeidan SA, Zocher S, Kirova DG, Ntitsias K, Fischer TJ, Sykes AM, Reinhardt S, Dahl A, Mansfeld J, Rünker AE, Kempermann G. Cell Stem Cell. 2020 Nov 25:S1934-5909(20)30538-5. doi: 10.1016/j.stem.2020.10.019.

Quiescence Modulates Stem Cell Maintenance and Regenerative Capacity in the Aging Brain. Kalamakis G, Brüne D, Ravichandran S, Bolz J, Fan W, Ziebell F, Stiehl T, Catalá-Martinez F, Kupke J, Zhao S, Llorens-Bobadilla E, Bauer K, Limpert S, Berger B, Christen U, Schmezer P, Mallm JP, Berninger B, Anders S, Del Sol A, Marciniak-Czochra A, Martin-Villalba A. Cell. 2019 Mar 7;176(6):1407-1419.e14. doi: 10.1016/j.cell.2019.01.040.

Review

Quiescence of Adult Mammalian Neural Stem Cells: A Highly Regulated Rest. Urbán N, Blomfield IM, Guillemot F. Neuron. 2019 Dec 4;104(5):834-848. doi: 10.1016/j.neuron.2019.09.026.

Session 6 Introductory lecture: Neuonal Architecture and Connectivity

No assigned papers but read review

Review

Branching mechanisms shaping dendrite architecture. Lanoue V, Cooper HM. Dev Biol. 2019 Jul 1;451(1):16-24. doi: 10.1016/j.ydbio.2018.12.005.

Session 7 Whole body gradients specify neuronal branching in C. elegans

A Wnt-planar polarity pathway instructs neurite branching by restricting F-actin assembly through endosomal signaling. Chen CH[1], He CW[1], Liao CP[1], Pan CL[1]. PLoS Genet. 2017 Apr 6;13(4):e1006720. doi: 10.1371/journal.pgen.1006720. eCollection 2017 Apr.

A Dendritic Guidance Receptor Complex Brings Together Distinct Actin Regulators to Drive Efficient F-Actin Assembly and Branching. Zou W[1], Dong X[2], Broederdorf TR[3], Shen A[4], Kramer DA[3], Shi R[5], Liang X[2], Miller DM 3rd[6], Xiang YK[7], Yasuda R[8], Chen B[9], Shen K[10]. Dev Cell. 2018 May 7;45(3):362-375.e3. doi: 10.1016/j.devcel.2018.04.008.

Reviews:

Mechanisms that regulate morphogenesis of a highly branched neuron in C. elegans. Sundararajan L, Stern J, Miller DM 3rd.Dev Biol. 2019 Jul 1;451(1):53-67. doi: 10.1016/j.ydbio.2019.04.002.

Wnt signalling in the development of axon, dendrites and synapses. He CW, Liao CP, Pan CL.Open Biol. 2018 Oct 3;8(10):180116. doi: 10.1098/rsob.180116.

Wnt-signaling and planar cell polarity genes regulate axon guidance along the anteroposterior axis in C. elegans. Ackley BD. Dev Neurobiol. 2014 Aug;74(8):781-96. doi: 10.1002/dneu.22146.

Session 8 Dendritic Architecture in the Mouse Cerebellum

Lhx1/5 control dendritogenesis and spine morphogenesis of Purkinje cells via regulation of Espin. Lui NC[1], Tam WY[1], Gao C[1], Huang JD[2], Wang CC[3,4,5], Jiang L[1,6,7], Yung WH[4,8], Kwan KM[1,6,7]. Nat Commun. 2017 May 18;8:15079. doi: 10.1038/ncomms15079.

MTSS1 Regulation of Actin-Nucleating Formin DAAM1 in Dendritic Filopodia Determines Final Dendritic Configuration of Purkinje Cells. Kawabata Galbraith K[1], Fujishima K[2], Mizuno H[3], Lee SJ[4], Uemura T[4], Sakimura K[5], Mishina M[6], Watanabe N[7], Kengaku M[8]. Cell Rep. 2018 Jul 3;24(1):95-106.e9. doi: 10.1016/j.celrep.2018.06.013.

Session 9 Setting Dendritic Branchpoints in Drosophila Sensory Neurons

Transient localization of the Arp2/3 complex initiates neuronal dendrite branching in vivo. Stürner T, Tatarnikova A, Mueller J, Schaffran B, Cuntz H, Zhang Y, Nemethova M, Bogdan S, Small V, Tavosanis G. Development. 2019 Apr 4;146(7):dev171397. doi: 10.1242/dev.171397.

Cell-Autonomous Control of Neuronal Dendrite Expansion via the Fatty Acid Synthesis Regulator SREBP. Ziegler AB, Thiele C, Tenedini F, Richard M, Leyendecker P, Hoermann A, Soba P, Tavosanis G.Cell Rep. 2017 Dec 19;21(12):3346-3353. doi: 10.1016/j.celrep.2017.11.069.

Session 10 Genes and Supercircuits: The Role of FOXP2 in Language

Dynamic FoxP2 levels in male zebra finches are linked to morphology of adult-born Area X medium spiny neurons. Kosubek-Langer J, Scharff C.Sci Rep. 2020 Mar 16;10(1):4787. doi: 10.1038/s41598-020-61740-6.

No Evidence for Recent Selection at FOXP2 among Diverse Human Populations. Atkinson EG, Audesse AJ, Palacios JA, Bobo DM, Webb AE, Ramachandran S, Henn BM.Cell. 2018 Sep 6;174(6):1424-1435.e15. doi: 10.1016/j.cell.2018.06.048.

Differential effects of Foxp2 disruption in distinct motor circuits. French CA, Vinueza Veloz MF, Zhou K, Peter S, Fisher SE, Costa RM, De Zeeuw CI.Mol Psychiatry. 2019 Mar;24(3):447-462. doi: 10.1038/s41380-018-0199-x.

Foxp2 regulates anatomical features that may be relevant for vocal behaviors and bipedal locomotion. Xu S, Liu P, Chen Y, Chen Y, Zhang W, Zhao H, Cao Y, Wang F, Jiang N, Lin S, Li B, Zhang Z, Wei Z, Fan Y, Jin Y, He L, Zhou R, Dekker JD, Tucker HO, Fisher SE, Yao Z, Liu Q, Xia X, Guo X.Proc Natl Acad Sci U S A. 2018 Aug 28;115(35):8799-8804. doi: 10.1073/pnas.1721820115. Epub 2018 Aug 13.

Reviews

Insights into the Neural and Genetic Basis of Vocal Communication. Konopka G, Roberts TF.Cell. 2016 Mar 10;164(6):1269-1276. doi: 10.1016/j.cell.2016.02.039.

FOXP transcription factors in vertebrate brain development, function, and disorders. Co M, Anderson AG, Konopka G.Wiley Interdiscip Rev Dev Biol. 2020 Sep;9(5):e375. doi: 10.1002/wdev.375.

Additional Course Policies and UCLA Policies

Student Resources with Respect to Harassment:

Harassment and discrimination based on: race, ethnicity, ancestry, sex/orientation, gender, gender identity/expression, national origin/citizenship; religion; disability/medical condition, domestic partnership/marital status; age; or veteran status is not acceptable, may violate UCLA regulations, and will be addressed. Information on how to obtain redress or counseling can be found at https://equity.ucla.edu/report-anincident/ .

UCLA is bound by Title IX. Title IX prohibits gender discrimination, including sexual harassment, domestic and dating violence, sexual assault, and stalking. Students who have experienced sexual harassment or violence can receive confidential support at the CARE Advocacy Office for Sexual and Gender-Based Violence, 1st Floor Wooden Center West, CAREadvocate@caps.ucla.edu, (310) 206-2465. You can also report sexual violence or harassment to the University's Title IX Coordinator, 2241 Murphy Hall, titleix@conet.ucla.edu, (310) 206-3417.

Student Mental Health Resources:

Stress is a part of all of our daily lives and levels have been elevated by current events. It is normal for students to feel stress about courses. If you feel negative stress that impacts your mental health or your ability to focus on your education, there are many resources on campus for students that can help you including:

UCLA Behavioral Wellness Center For Graduate Students (https://medschool.ucla.edu/bwc), a student mental health center primarily for GPB graduate students, medical students, and medical residents; UCLA's Counselling and Psychological Services center (https://www.counseling.ucla.edu/), a mental health resource for students at UCLA; and The Bruin Resource Center (http://www.brc.ucla.edu/).

Support for Undocumented Students:

The MBIDP recognizes undocumented students as important members of our community. Resources and information can be found on the following websites: UCLA's Undocumented Students Program (https://www.usp.ucla.edu/) and UCLA's Office of Equity, Diversity, and Inclusion (https://equity.ucla.edu/know/immigration/).

Academic Accommodations Based on a Disability:

If you need academic accommodations based on a disability you should contact the Center for Accessible Education (CAE) at (310)825-1501 or in person at Murphy Hall A255. When possible, you should contact the CAE within the first two weeks of the term as reasonable notice is needed to coordinate accommodations. For more information visit www.cae.ucla.edu. If you require accommodations from us during meetings, please let us know so we can develop a plan together.