

NEURO 101V: Sculpting Activity: Neural Inhibition in Health and Disease

from molecular neurobiology to treatment of neuropsychiatric and neurodevelopmental disorders.....

Fall 2024

Class times	Tuesdays 3:00 -5:00 p.m.
Venue	Tba
Canvas page	https://canvas.harvard.edu/courses/135693
Instructor	Saad Hannan, Ph.D. Research Associate Hensch Lab Department of Molecular and Cellular Biology saadhannan@fas.harvard.edu
Office hours	Tuesdays 5:00 – 6:00 pm or by appointment, venue – Tba,

Course description: Although the vast majority of neurons in the mammalian brain are excitatory, inhibitory neurons working via GABA inhibition play a crucial role in normal brain function. Inhibition balances and shapes excitatory signals to maintain neural network stability and prevents excessive excitatory signaling that feature prominently in various psychiatric and neurological disorders such as anxiety and epilepsy. This course will explore molecular, cellular, physiological, circuit and behavioral mechanisms of GABAergic signaling that keep us healthy while covering neuropsychiatric and neurodevelopmental disorders that are caused due to dysfunctional GABA inhibition along with treatment strategies targeting this essential synapse.

Prerequisites: MCB/Neuro 80 (Neurobiology of Behavior) and permission of the instructor

Course goals: The overall objectives of this course are 1) to help students to gain an in-depth understanding of the function of inhibitory synapse at cellular, circuit and behavioral levels as well as the dysfunction that causes brain disorders and treatment strategies; 2) to learn about key neuroscience techniques used in neurosciences (e.g. molecular biology, electrophysiology, and cellular imaging) and help students learn to critically analyze experimental results in tutor-guided small group sessions; 3) to practice both reading scientific literature and communicating scientific results through presentations and brief digests.

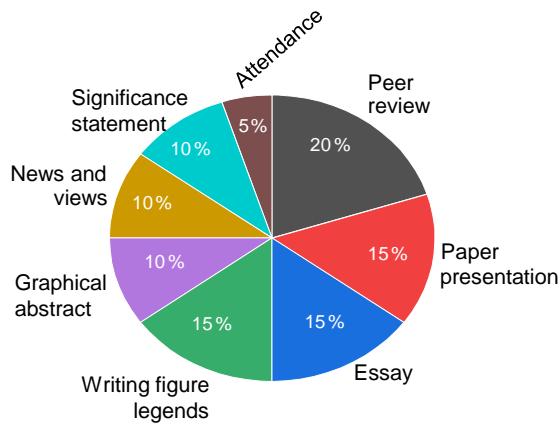
Required reading: Reading materials will include scientific literature in the form of original research paper and reviews. This course does not require textbooks. Required readings for each week will be posted on course website at least two to three weeks in advance of tutorial sessions.

Typical format: Each session will begin with a brief lecture component that will introduce the topic and paper of discussion along with addressing any unresolved issues from the previous week's tutorial. Next, the session will move onto discussing the contents of two papers chosen for the week by two or more students with help from the tutor. The introductory part should take around ~15 min while discussion on each paper should take roughly 45 min. The final few minutes will be used by the tutor to wrap up discussion and to briefly summarize how the chosen paper has extended our broader understanding of the area and what subsequent studies/ drug trials have revealed.

Typical workload: Typical workload will be approximately 3 to 5 hours a week. This will be spent on various assessments (see below) that will provide the students with ample opportunities in reading scientific literature and attaining high grades. While students are not expected to come up with a specific number of questions, the best tutorials are typified by high levels of student engagement and participation. Therefore, the expectation at the outset is that the students will ask questions to the tutor and each other. During the course, each tutee will pick at least one study and present to the group. Preparation for this may require an additional 1-2 hours. Needless to say, pre-presentation help and feedback will all be made available for all tutees.

Assessment: This course will provide tutees with multiple opportunities to improve their grades. The types of assignments chosen are deliberately diverse to equip tutees with a wide range of skills that are necessary not only in science but also related sectors in data analysis and presentation. Rubrics for grading for each assignment and feedback on progress will be provided at regular intervals. Feedback will also be provided on the essay assignment provided the tutee sends the essay no later than three weeks prior to the deadline.

The assignment breakdown for the course is as follows (pie chart shows summary):



Attendance – 5% of total

Assessment 1 – News and views (10% of total; due 01 Oct 2024)

Assessment 2 – Significance statement (10% of total; due 08 Oct 2024)

Assessment 3 – Paper presentation (15% of total; date to be chosen by tutees)

Assessment 4 – Writing figure legends (15% of total; due 15 Oct 2024)

Assessment 5 – Graphical abstract (10% of total; due 22 Oct 2024)

Assessment 6 – Essay (15% of total; due 05 Nov 2024)

Assessment 7 – Peer review (20% of total; due 03 Dec 2024)

Significance statement – tutees will write a 120-word significance statement on a seminal paper which was multiple firsts in neuroscience, molecular and cellular biology and pharmacology. So plenty to write about it.

News and views – here the tutees will write a 750 – 900 words summary on an inhibitory scaffold that is important for learning and memory. Detailed guidelines will be provided to students on how to approach this piece of coursework along with where to find numerous examples - on nature's website!

Guidance on how to write significance statements can be found at:

<https://neuronline.sfn.org/professional-development/how-to-write-an-accurate-concise-and-meaningful-significance-statement>

Course essay – three essay topics will be made available to tutees at the beginning of October with a deadline for submission five weeks later at the beginning of November. Tutees will write a 3000-word

essay on their topic of choice. This deadline has been chosen to give tutees ample time to work on the assignment. The essay should be a piece of original work on the core theme of inhibitory neurotransmission. Tutees are expected to read original research papers and reviews similar to those already covered in the course by that point and come up with their own assessment of their chosen topic. Feedback will be provided on the essay assignment provided the tutee sends the essay no later than 10 days prior to the deadline.

Figure legend writing – this exercise is aimed at giving students hands-on training on how to write figure legends. Three unpublished figures from one of my scientific studies will be provided and tutees will write the figure legends, the most likely statistical test used by analyzing the bar/ box plots and include n numbers where possible. The figures will be multi-panel and will be designed in a way so that the tutees appreciate the value of keeping the text succinct. This coursework is due on the week of tutorial 18 and by then the students should have a good foundation to take on such an exercise.

Additional details on format (from Nature): “Each figure legend should begin with a brief title for the whole figure and continue with a short description of each panel and the symbols used.... legends should not contain any details of methods. Legends should be fewer than 300 words each. All error bars and statistics must be defined in the figure legend.”

Graphical abstract – graphical depictions of scientific studies are rapidly gaining in popularity in various social media. Graphical abstracts are therefore powerful visual tools for reaching out to diverse audiences. This exercise is aimed at giving tutees the opportunity to gain hands-on experience of designing a graphical abstract while nurturing their artistic talents and receiving feedback from the tutor and the group.

The abstract will be prepared according to on the Cell Press format as follows:
https://www.cell.com/pb/assets/raw/shared/figureguidelines/GA_guide.pdf

The graphical abstract is due on the week of tutorial 8 and by then the tutees will have gained multiple exposure to papers with such abstracts as exemplars.

Seminar paper presentation - These will be informal presentations where the tutee will present findings, take questions from peers and guide/ moderate class discussion. Help and guidance will be provided during preparation stages as required.

Peer review - peer review of scientific papers and grants is an integral part of the scientific journey and this exercise will give tutees an opportunity to become an expert reviewer for a journal. An unpublished paper from the pre-print server bioRxiv containing materials covered on the course will be chosen. Tutees will be provided with guidelines on writing peer reviews and pointed to details of journals who publish peer review reports which can be used as examples. The final peer-review report does not have a word limit and will be excellent for honing critical thinking skills while analysing a real-world unpublished scientific paper.

Grading: Attendance, completion of writing and oral assignments, and thoughtful participation in class discussions will lead to an “A” grade. Letter grades will decrease due failure to complete assignments and low attendance.

Course timetable:

Week	Date	Topic
1	3 Sep 2024	<p>Course introduction – getting to know each other, what to expect from the course, dos and don'ts.</p> <p>Why is GABAergic signaling such an important drug target in the clinic?</p> <ul style="list-style-type: none"> • Structure of the GABAergic synapse • GABA_A receptors as ligand-gated ion channels – key targets for anxiolytics, antiepileptics, sedatives, hypnotics and general anesthetics • GABA_B receptors as Class C G-protein coupled receptors – targets for treatment of spasticity, addiction (nicotine, alcohol) and substance abuse
2	10 Sep 2024	Primer on essential techniques in neuroscience – brief introduction to electrophysiology, fluorescence imaging (wide-field, confocal, multiphoton), molecular biology, systems neuroscience and behavioral tests in rodents
3	17 Sep 2024	<p>Constructing inhibitory synapses – Birth of the synapse; how are synapses assembled? What keeps the synaptic machinery in place?</p> <p><i>Paper for news and views given out</i></p>
4	24 Sep 2024	Interneurons: the presynaptic viewpoint – diversity of interneurons, how do various types of interneurons find their targets? Interneuron dysfunction in psychiatric disorders.
5	1 Oct 2024	<p>Molecular pharmacology of GABA receptors – anxiolytics, anticonvulsants, anesthetics, antidepressants, neurosteroids and other ligands</p> <p><i>News and views due; Paper for significance statement and essay topics given out</i></p>
6	8 Oct 2024	<p>Phasic and tonic inhibition – two modes of inhibition - phasic and tonic are mediated by distinct receptor isoforms; role of tonic inhibition on sensory processing; role of phasic inhibition in brain oscillations</p> <p><i>Significance statement due; Figures for legend writing assessment given out</i></p>
7	15 Oct 2024	<p>GABA in development – there is more to GABA than inhibition; how GABA shapes critical periods during development</p> <p><i>Figure legends due; Paper for graphical abstract given out</i></p>
8	22 Oct 2024	<p>Epilepsy – genetic epilepsy due to GABA receptor variants (mutations); role of tonic inhibition in absence epilepsy - not all inhibition is the same when it comes to epilepsy.</p> <p><i>Graphical abstract due; Paper for peer review given out</i></p>
9	29 Oct 2024	Anxiety – synaptic GABA receptor levels determine extent of anxiety; brain circuit-specific coupling of GABA receptor signaling increases anxiety
10	5 Nov 2024	<p>Neurodegeneration and dementia – GABA_B-APP interactions as therapeutic targets in Alzheimer's disease</p> <p><i>Essay due for submission</i></p>
11	12 Nov 2024	Autism spectrum disorders – GABAergic signaling in sensory processing, sociability and repetitive behavior with particular emphasis on autism
12	19 Nov 2024	Rett syndrome – Rett phenotypes and their link to interneurons and GABAergic signaling
13	26 Nov 2024	Down syndrome – over-inhibition, cognition and a failed drug trial!
14	3 Dec 2024	Summary of the inhibitory synapse – general discussion
		<i>Peer review due</i>

Course Policies

Confidentiality

While most of the materials in the course are already in public domain, occasionally tutees may be given real-world unpublished results eg - figure legend writing assignment etc. Moreover, the peer-review assignment will be on an unpublished manuscript deposited in a pre-print server. I encourage all tutees to discuss their ideas and opinions with their peers and expect them to engage in these academic exercises with full vigour. However, due to the unpublished nature of some results, tutees are asked to refrain from disseminating contents of these assignments in the public domain. If you have any questions regarding this, then please feel free to get in touch.

Classroom Environment

Tutorials provide an excellent opportunity for students to iron out creases in their conceptual understanding of topics. Moreover, small group learning is ideal for student participation. Therefore, it is my expectation that the tutees will come to class prepared and actively participate in class discussions with respectful dialogue with classmates. Our classroom will be an inclusive environment that values diverse ideas which exists to support all students as they learn and grow throughout the year.

Attendance/Participation Policy

Students are expected to attend all classes and be an active participant in class. Three unexcused absences over the course of the school year will result in the drop of an entire letter grade. If you know that you are unable to attend class on a specific day, please contact the instructor as early as possible.

Feedback

Students will be continually provided feedback when sought. In addition, tutees will be provided with some opportunities to provide feedback at the end of tutorials to write down their views on content, format, or any other matter. These will be collected, reviewed and factored in to tailor the course to suit more to the needs of our pupils.

Late Work

Students are expected to turn in all work on time. Weekly assignments that are not turned in by 5 pm. on the day they are due will be assessed a 10% penalty for each day that it is late. If you have extenuating circumstances during the course, please speak with the instructor in advance of the assignment due date.

Academic Integrity and collaboration

Any written assignments that are submitted for evaluation are expected to be your own, independent work. Students are required to correctly cite literature (only books and peer reviewed journals allowed). Training will be provided during the course on how to cite correctly in scientific writing. Students must also acknowledge any assistance they received with their writing (e.g. feedback on drafts, etc.).

Course Schedule

The policies, schedule, or assignments described within this syllabus are subject to change during the course at the discretion of the instructor. Students will be notified of any changes to the schedule or readings/assignments at least one week ahead of time.

Use of artificial intelligence (AI)

We expect that all work students submit for this course will be their own. Students are discouraged from using ChatGPT or any other generative AI tools at all stages. We draw your attention to the fact that different classes at Harvard could implement different AI policies, and it is the student's responsibility to conform to expectations for each course.