Course goals:

We believe that having the â€œmeta-skillsâ€ of scientific logic, reasoning, and making intuitive leaps are necessary to be a successful scientist, and MCB 297 will try to hone those skills. We will help you gain a base intuition of scientific logic so you can plan an experimental program to gain clear insights into scientific questions, be they within your field or on topics outside your domain. 297 also serves as practice for your qualifying exam.

The course should teach you how to think like a scientist while learning some *neuroscience* in the process. We will achieve this by going over classic examples of how the scientific method has been applied to questions in neuroscience. This will involve 1) reading and discussing seminal papers that address important questions in the field so we can dissect the process of scientific discovery by examining the experimental logic, methods, and leaps of insight within these works. 2) You will be tasked with finding an unanswered question in the broad area of neuroscience, and design and defend experimental approaches to address aspects of that question.

Course format:

The class will meet each week on Wednesday from 12.45 to 2.45 p.m. in Northwest (room TBD).

297 consists of 2 components:

1) In-depth paper discussions

While we will be reading papers, this is NOT a traditional journal club; rather, we will have in-depth discussions in which we dissect the *logic* of how and why the assigned studies (many of them classics in the field) were designed and carried out and the *insights* that were gained in the processes.

We will discuss the historical context of the studies, the specific questions addressed, and why these were (or are) important questions. We will discuss the hypothesis space before the study (i.e., what were possible answers to the posed question) and how the experiments allowed the authors to effectively arbitrate between different hypotheses and arrive at conclusions. This will include discussing the specifics of the experimental strategy (choice of model system, techniques, and methods), their strengths and limitations, the degree to which the conclusions are supported by the data, and whether there may be alternate explanations to those offered by the author(s).

Expectations for paper discussions - While we will meet for 2 hours a week, we will be discussing these papers at a deep and involved level. Students are expected to be prepared for class by spending 10-15 hours by 1) reading the papers, 2) familiarizing themselves with the system and questions being addressed, 3) digging into the background and historical context of the questions, and 4) familiarize themselves with the techniques used in the studies. The overall goals are to understand A) the experimental logic of each step and what insights were gained by each, and B) why these experiments led to transformative insights. We will randomly call on participants during the meetings to facilitate the discussion. Grading for the discussions is based on preparation and involvement.

2) Topic proposal and defense

As part of the course, you will show your mastery of the scientific method by writing and orally defending a short proposal on a topic related to the class (i.e., neuroscience broadly construed). The scope of your proposed efforts will be on the order of the papers we have read, i.e., something you could accomplish on your own in a matter of a couple of years (not an NIH grant). Think of (and approach) this as a practice for your qualifying exam, similar to a â€œsecondary, off-topic examâ€ done by many PhD programs.

For this, look through the literature for a topic of your choice and find an *unanswered question* within that topic. We expect the question to be one that needs more than one possible answer, not a simple â€œyes or noâ€ question. Devise 2-3 aims to address this question, each aim consisting of one or more experiments to answer your question. Be sure to deeply research the background of the subfield, as well as the experimental methodologies you are proposing. Motivate why this is a question worth asking. Think through what the outcomes of each experiment will tell you, what the results can (and cannot) inform you of, and what other alternative approaches you could take if the experiments fail. Also, consider what alternative outcomes might occur, what alternative models/hypotheses this could generate, and how you might test them.

Written proposal on your topic

1. On 11/6: Turn in an initial small draft of the topic you have chosen, the question to be asked, and the aims you choose to propose to address this topic. (Â½ page). This will allow us to give you feedback to help hone your ideas.
2. On 11/13: Turn in a final Â½ page draft of the topic, question, and aims you are planning to address.
3. On 11/20: Turn in a complete proposal: 1-2 pages in length. This should include
    1. An introduction that explains the background of the topic, including what is known and not known, and why what you are proposing to address is worth knowing This should lead up to:
    2. A concise elaboration of the question you are addressing, a clear statement of the problem you are going to address, and a general description of how you will address it.
    3. Next, you will list each of your aims. Explain what the overall goal of each aim is, then detail what each experiment is within that aim and what each experiment will tell you, both if it is successful and unsuccessful.
    4. Finally, have a paragraph or two detailing what the combination of your experiments tells you and at what level they will address the question you proposed. Also, explain 1) what alternative experiments you could do if the proposed ones fail, 2) what alternative outcomes of the experiments would tell you, and 3) any other explanations/models that could explain the results of your experiments, be they successful or unsuccessful.

Oral exam

During the last week of class (12/2-12/6), you will give an oral defense of your proposal to two faculty in the same style and format as a qualifying exam. We expect a depth of knowledge on the biological system and the background of scientific studies on the topic, as well as an understanding of the techniques you are planning to use to address your question. Be prepared to explain and defend your aims, as well as address different outcomes for each aim, what those outcomes lead to in terms of understanding, and an idea of how one could address this with future experiments.

Grading:

50% - In-class discussions - being prepared and involved in discussions.

10% - Written Proposal (2% first draft, 2% second draft, 6% final draft).

40% - Oral exam.

Sample reading list:

(optional) *Indicate your sample reading list or upload the document to your course files and link to the file in this space*.

Enrollment cap, selection process, notification:

This course is designed for first-year graduate students in the MCO program but open to other graduate students and motivated undergraduates. However, for the discussions to be effective, we will cap enrollment. Please contact me by email (olveczky@fas.harvard.edu) if you are interested in taking the course and you are NOT a first-year MCO student.

Course schedule:

Course outline (subject to change, including the papers to be discussed. Iâ€™m very open to suggestions)

	date	**Topic**	**Assignments**	**Papers**
1	9/4/2024	**Intro class**	**n/a**	
		Action potentials and ionic		Hodgkin Huxley. 1938,

2	9/11/2024	conductances		1952
3	9/18/2024	Ion channels, stochasticity and noise		Sakmann and Neher, 1976. Mainen and Sejnowski, 1995.
4	9/25/2024	Neurotransmission		Fatt and Katz 1952 Castillo and Katz, 1954
5	10/2/2024	Neural circuits underlying behavior - Birdsong		Yu and Margoliahs 1996 Hahnloser and Fee, 2001
6	10/9/2024	Visual processing and perception		Standing 1973 Bays and Husain 2008
7	10/16/2024	Movement		Wolpert and Jordan 1995 Mazzoni and Krakauer 2006
8	10/23/2024	Joint with Ethanâ€™s class		tbd
9	10/30/2024	Algorithms for path integration		Wittlinger, Wehner, and Wolf. 2006 Srinivasan et al 1996.
10	11/6/2024	Papers TBD	Initial topic ideas and aims due.	
11	11/13/2024	Discussing and workshopping grant proposals	Final topic and aims due.	
12	11/20/2024	(No class)	Proposal due	
13	11/27/2024	Thanksgiving holiday (no class)		
	12/2-12/6	Oral Exams		