Molecular Neuroscience
NROC36H3F

University of Toronto Scarborough
Fall 2024
Wednesdays 3-5pm, SW319

_____

Instructor: **Maithe Arruda Carvalho** *(she/her)*   Email: m.arrudacarvalho@utoronto.ca

<u>Office hours</u>: Mondays 10am-12pm, SW533

_____

T.A.s: **Hanista Premachandran**   *E-mail*:* hanista.premachandran@mail.utoronto.ca

                 Anna Canella   *E-mail*:* a.canella@utoronto.ca

*Any questions referring to this course must be first addressed to the TAs.

_____

This course will provide students with a thorough background in the molecular and cellular mechanisms underlying neuronal communication in the central nervous system. We will explore concrete examples of that communication within the physiological (e.g. learning and memory) and pathological (e.g. neurodegenerative disorders) realms. We will start with the building blocks of synaptic communication, by learning about intracellular signalling, modulation of neuronal DNA and protein expression, and neurotransmitter systems. We will then use this knowledge to understand the specific molecular and cellular steps necessary for enabling neuronal communication. This will serve as a base to our understanding of how these mechanisms can be used in the brain to encode information in the form of synaptic plasticity in learning and memory. We will close by examining how these same mechanisms can be co-opted in pathological instances to impair cognitive and emotional function.

Course Learning Objectives

By the end of this course, students will:

- Understand the core principles underlying synaptic communication in the central nervous system, and how these mechanisms contribute to synaptic plasticity and learning
- Be provided with an overview of some of the main contemporary concepts and applications of molecular and cellular neuroscience
- Understand how molecular and cellular methods can be applied in research to address the latest challenges within the field
- Practice reading and analysing scientific articles relevant to the area
- Think critically and express themselves about unresolved questions in the field
- Gain the necessary background to critically evaluate the design, analysis, and conclusions of molecular neuroscience research
- Improve their oral and written communication skills through in-class discussions and feedback on written assignments and short-answer questions on exams

Course Materials

Students will be provided with complementary readings for each lecture, which will include textbook chapters and papers (see timetable). Mostly, this course will use selected chapters from two textbooks available online through the UTSC library website:

- **From molecules to networks: an introduction to cellular and molecular neuroscience = (MtN)** Edited by John H. Byrne, James L. Roberts.
  http://www.sciencedirect.com.myaccess.library.utoronto.ca/science/book/9780123971791

- **Principles of neural science = (PoN)**
  Edited by Eric R. Kandel et al.
  https://ebookcentral-proquest-com.myaccess.library.utoronto.ca/lib/utoronto/detail.action?pq-origsite=primo&docID=4959346

Additional material (including assigned papers) will be available through the *Library Reading List* link on Quercus.

Although not all content of textbook chapters will be covered in the lectures, it is **highly recommended** you read the accompanying chapter for each lecture. It will help your *understanding* of the topic and will *improve your performance* on the exams. You can also find any additional papers featured in the lectures (if they are not already available on course reserves) through a pubmed search - all references are on the lecture slides. Handouts of lecture slides will be posted on Quercus by midnight at the latest the night before the lecture.

Course Evaluation

<u>Summary of Evaluation:</u>

	Percent of final grade	Date
Writing assignment	15%	Nov 6th
Term tests 1 and 2	25% each	Oct 2nd and Nov 13th
Student generated MCQs	5%	Sep 13th, Sep 27th, Oct 18th, Nov 8th, Nov 29th
Final Exam	30%	Exam Period

<u>Description of evaluation components:</u>

1. *Writing Assignment (15%) – November 6th*

This assignment will consist of a critical review of an empirical research paper. You will be given a choice between two assigned papers. Papers will be assigned on October 2nd through an announcement on Quercus. Both the assigned papers have been submitted to Biorxiv without prior peer-review, which means you will be doing exactly what the reviewers of this manuscript will be doing when it is submitted to a neuroscience journal such as Journal of Neuroscience, etc – this is the real deal!

You will write a critique of the paper of your choice, which will be broken down in three sections:

1. Brief summary of results – In this 2-4 paragraph section you will briefly summarize the main rationale (what is the main goal of this paper? Which gap in knowledge are they trying to fill?), results and conclusions of the paper

2. Critical review – In this section you will evaluate this article in detail focusing on two parts: (i) its main strengths and (ii) its main weaknesses. This exercise is supposed to emulate the reviewing of a paper by a scientific journal. So think about the paper in terms of its conclusions and interpretations - Does the data support the conclusions? Are the experiments well designed and controlled? Are the techniques appropriate? Does this paper fill an important gap in knowledge? Does it answer the questions it set out to answer? Are you satisfied with the way they chose to answer those questions?

   You can explore the weaknesses of the manuscript in any way you prefer, but one suggestion is to frame your concerns relating to what you think the authors should do to improve the manuscript. This will strengthen your decision to recommend accepting or rejecting the manuscript (next section).

   Example (here in bullet points solely for illustration purposes):

   - Given that (i) estrous cycle blocks the behavioral deficits reported in this manuscript, (ii) TMX is an estrogen modulator and (iii) the known effects of estrogen on memory performance, estrogen seems a likely candidate to mediate the reported effects. Nevertheless, this possibility is not really discussed in the manuscript. Instead, the authors insist on comparing their data to ….
   - Several controls should be included to strengthen the conclusion that ….. Training data, anxiety and motor tests are the minimum necessary controls for these types of experiments, and are not present in this study.
   - It would be helpful for the reader if the authors described the drugs used in this study in the main text. As it stands no explanation or description is offered of their targets or function and of how they serve the described experiments.

3. Recommendation – In a few sentences, you will justify whether you would accept or reject this paper based on your critical evaluation in the last section. The options for the majority of journals include *accept, minor revisions, major revisions* or *reject*. State your recommendation and justify your choice!

This assignment will develop your critical and scientific writing skills. It will also give you a glimpse into the editorial process of any submitted manuscript to a journal. Importantly, you will receive feedback on your assignment identifying areas that require improvement.

The paper must be a <u>maximum of 5 pages, excluding references, double spaced, in Calibri font 11, with 1"</u> <u>margins</u>. In-text citations must follow the Journal of Neuroscience citation style. List all the references cited in the text in alphabetical order by first author's last name following Journal of Neuroscience citation style. Here is one example of Journal of Neuroscience citation style:

Drew MR, Denny CA, Hen R (2010) Arrest of adult hippocampal neurogenesis in mice impairs single- but not multiple-trial contextual fear conditioning. Behav Neurosci 124:446–454.

This assignment will be submitted through Quercus (with Turnitin). Submissions are due **by 11:59PM on November 6th**. Late submissions will be accepted with a **penalty of 10% for every day late**. To submit your assignment, click on Assignments: Writing assignment

2. Term Tests 1 and 2 (25% each) – October 2nd and November 13th, in class, 1h45m each

Tests will be based on the material covered on the lectures (Lectures 1-4 for term test 1, and lectures 5-8 for term test 2). Each term test will consist of multiple-choice and short answer questions. I will provide sample questions. Term tests will take place **in class** and will last 1h45m each.

3. Questions about lecture contents (5%) – Sep 13th, Sep 27th, Oct 18th, Nov 8th, Nov 29th

To help keep up with lecture content and allow the instructor an opportunity to check in with students more frequently, students are to submit 1 original question in multiple choice format (4-5 choices each) featuring content covered in each of the 10 lectures.

Example question:
Preventing the switch from GDP-to GTP-binding within a GPCR α subunit will lead to:

A. Dissociation of the α and $\beta\gamma$ subunit

B. A conformational change in the α subunit, activating its intrinsic GTPase activity

C. Lockdown of G protein activity to an inactive state

D. Recruitment of GTPase-activating proteins (GAPs) to replace GDP with GTP

Students will generate one question per lecture. Questions should cover topics explicitly featured in the respective lecture. The correct answer should be indicated in your submission. Try and be creative but fair, and avoid mere memorization questions (e.g. what is XYZ called, etc). The best questions may be shared (anonymously) with the class to help in their study preparation.

These questions will be submitted in pairs, with each submission featuring 2 lecture questions (one question for each covered lecture) for a 1% combined grade, on the following dates:

Lectures 1 and 2: Sep 13th by 11:59pm
Lectures 3 and 4: Sep 27th by 11:59pm
Lectures 5 and 6: Oct 18th by 11:59pm
Lectures 7 and 8: Nov 8th by 11:59pm
Lectures 9 and 10: Nov 29th by 11:59pm

The correct answer for each question must be indicated in your submission. Late submissions will be accepted with a **penalty of 10% for every day late**. To submit your questions, click on Assignments: Student Questions

I will post sample questions prior to each term test to further help with studying and keeping up with lecture content throughout the term.

4. Final Exam (30%) – Exam period

The final exam will be scheduled during the exam period and will be comprised of two sections:

Section 1 (12.5%)
Short answer and multiple choice questions spanning lectures 9 and 10

Section 2 (17.5%) – Research paper analysis
An empirical research paper will be posted 2 weeks prior to the final exam. Students should carefully read the paper in preparation for the exam. You will be required to answer questions assessing your understanding of the paper, its research topic, conceptual knowledge covered in the lecture materials, as well as providing a critical analysis of its content.

Overview of Course Schedule:

The following table presents the schedule of lectures and term tests as they will occur over the course of the term, and the due dates for the assignment.

Lecture	DATE	CONTENT	Recommended Reading	TO DO
1	Sep 4	Course Introduction and Recap of intracellular signaling	Excerpt from Molecular Biology of the cell (on course reserves)	
2	Sep 11	Regulation of Neuronal Gene Expression and Protein Synthesis	MtN chapter 5	Qs for lectures 1 and 2: Sep 13th
3	Sep 18	Neurotransmitter synthesis and removal	MtN chapter 7	
4	Sep 25	Neurotransmitter release	MtN chapter 15	Qs for lectures 3 and 4: Sep 27th
	Oct 2	**Term test 1**		Papers assigned
5	Oct 9	Neurotransmitter receptors I: Ionotropic Receptors	MtN chapter 10	
6	Oct 16	Neurotransmitter receptors II: Metabotropic Receptors	PoN chapter 11	Qs for lectures 5 and 6: Oct 18th
7	Oct 23	Molecular basis of implicit memory	PoN chapter 66	
	Oct 30	Reading Week		
8	Nov 6	Molecular basis of synaptic plasticity I	PoN chapter 67; Collingridge et al., Nat Rev Neuro 2004 and 2010; Henley and Wilkinson Nat Rev Neuro 2016	Writing assignment due Qs for lectures 7 and 8: Nov 6th
	Nov 13	**Term test 2**		
9	Nov 20	Molecular basis of synaptic plasticity II	MtN chapter 18; Lisman, Nat Rev Neuro 2002	
10	Nov 27	Molecular mechanisms of disease	MtN chapter 21	Qs for lectures 9 and 10: Nov 29th

Course Grading Scheme:
Following the University Assessment and Grading Practices Policy:
(http://www.governingcouncil.utoronto.ca/Assets/Governing+Council+Digital+Assets/Policies/PDF/grading.pdf;
http://www.artsci.utoronto.ca/newstudents/transition/academic/grading):

Letter Grade	Grade point value	Numerical Mark	Grade Definition
A+	4.0	90 - 100%	Excellent: Strong evidence of original thinking; good organization; capacity to analyze and synthesize; superior grasp of subject matter with sound critical evaluations; evidence of extensive knowledge base.

A	4.0	85 - 89%	Excellent
A-	3.7	80 - 84%	Excellent
B+	3.3	77 - 79%	Good: Evidence of grasp of subject matter; some evidence of critical capacity and analytic ability; reasonable understanding of relevant issues; evidence of familiarity with literature.
B	3.0	73 - 76%	Good
B-	2.7	70 - 72%	Good
C+	2.3	67 - 69%	Adequate: Student who is profiting from his/her university experience; understanding of the subject matter; ability to develop solutions to simple problems in the material.
C	2	63 - 66%	Adequate
C-	1.7	60 - 62%	Adequate
D+	1.3	57 - 59%	Marginal: Some evidence of familiarity with subject matter and some evidence that critical and analytic skills have been developed.
D	1.0	53 - 56%	Marginal
D-	0.7	50 - 52%	Marginal
F	0	0 - 49%	Inadequate: Little evidence of even superficial understanding of subject matter; weakness in critical and analytic skills; with limited or irrelevant use of literature.

Note: Consistently poor spelling/grammar will be penalized. Please make use of the resources available at the UTSC writing centre for additional help with writing: http://ctl.utsc.utoronto.ca/twc/.

DEPARTMENT OF PSYCHOLOGY POLICIES

Department of Psychology Missed Term Work Policy

For missed term work (assignments and term tests) due to illness, emergency, or other mitigating circumstances, please follow the procedure outlined below.

Procedure:

1. Complete the Request for Missed Term Work Accommodations Form ("MTW Form").

2. Email **BOTH** your MTW Form and Supporting Documentation to the TAs according to the instructions specified below.

Supporting Documentation Requirements and Deadlines:

Reason for Missed Work	Documentation required for a *first*	Documentation required for *subsequent absences* in	Deadline for submitting MTW form and

	absence in the term	the term	supporting documentation
Illness or Injury	ACORN Absence Declaration	UofT Verification of Illness Form	**WITHIN 2 BUSINESS DAYS** of the missed work
Bereavement	ACORN Absence Declaration	A death certificate or funeral announcement	**WITHIN 2 BUSINESS DAYS** of the missed work
University-sponsored athletic or artistic obligation at the varsity/provincial/national level	ACORN Absence Declaration	A note from a university staff member (advisor, coach, residence staff, etc.) who can substantiate the obligation, sent directly to the course email	**10 BUSINESS DAYS IN ADVANCE** of the missed deadline
Disability-related reasons for students registered with AccessAbility Services	For missed **TERM TESTS,** - **Contact your AccessAbility consultant** and have them write to the course email detailing the accommodations needed. For missed **ASSIGNMENTS,** - If your desired accommodation is **within the scope** of your Accommodation Letter (e.g. your letter includes "extensions of up to 7 days" and you need 3 days), send your **Accommodation Letter** to the course email and specify how many days extension you are requesting. - If your desired accommodation is **outside the scope** of your Accommodation Letter (e.g. your letter includes "extensions of up to 7 days" but you need more time than that), **contact your AccessAbility consultant** and have them write to the course email detailing the accommodations needed.		**PREFERABLY IN ADVANCE OF THE MISSED WORK, OR AS SOON AS POSSIBLE**
Academic Conflict (e.g. two midterms at the same time)	Screenshot from Quercus demonstrating the conflict.		**10 BUSINESS DAYS IN ADVANCE** of the missed work
Religious Conflict	None required		

Notes:

- The following reasons are not considered sufficient for missed term work: social activities, recreational travel, technological issues, avoidance of assessments or deadlines, work commitments
- Missed Final Exams are handled by the Registrar's Office and should be declared on eService.
- For ACORN absence declarations, the date you declare the absence is required to fall within the seven-day declaration period (i.e.) the absence cannot be submitted proactively or retroactively.
- Instructors cannot accept term work any later than five business days after the last day of class. Beyond this date, accommodations are only possible via the Registrar's Office petition process.

- If you are unable to submit your request within the specified number of business days, you must still email your instructor within that window to explain the nature of the delay. Exceptions to the deadlines are made only under exceptional circumstances.
- Multiple assignments due on the same day are <u>not</u> considered academic conflicts. Students are expected to manage their time effectively to meet assignment deadlines.
- Back-to-back tests/quizzes are <u>not</u> considered academic conflicts. Only overlapping activities are conflicts.
- Students are responsible for keeping their course timetables conflict-free. Students who register in two courses with overlapping lecture/tutorial/lab schedules will not be accommodated.

<u>**Next Steps:**</u>

After submitting your documentation, you will receive a response from your instructor or TA. The course instructor reserves the right to decide what accommodations will be made. Failure to adhere to any aspect of this policy may result in a denial of your request. **You are responsible for checking your official U of T email and Quercus course announcements daily**, as accommodations may be time-critical.

For missed assignments, **do not wait for the instructor's response to resume work on your assignment.** Extensions may be as short as one business day, depending on the nature of the illness/emergency. Complete your assignment as soon as you're able, and email it to your instructor.

If an accommodation is granted but a continued illness/emergency prevents you from meeting its requirements, you must <u>repeat</u> the missed term work procedure to request additional accommodations. **Please make it clear in your subject line that you are requesting a second accommodation.** Examples: If you were granted an extension for a paper but are still unable to meet the new deadline, or if you miss a <u>make-up</u> term test, you must submit *another* MTW form and supply documentation according to the "subsequent absences" column in the chart above. *Note: In the case of a missed make-up test, an opportunity to write a second make-up test may not necessarily be provided.

UTSC POLICIES

University's Plagiarism Detection Tool

Normally, students will be required to submit their course essays to the University's plagiarism detection tool for a review of textual similarity and detection of possible plagiarism. In doing so, students will allow their essays to be included as source documents in the tool's reference database, where they will be used solely for the purpose of detecting plagiarism. The terms that apply to the University's use of this tool are described on the Centre for Teaching Support & Innovation web site (https://uoft.me/pdt-faq).

Academic Integrity

The University treats cases of cheating and plagiarism very seriously. The University of Toronto's Code of Behaviour on Academic Matters (http://www.governingcouncil.utoronto.ca/policies/behaveac.htm) outlines the behaviours that constitute academic dishonesty and the processes for addressing academic offences.

Potential offences in papers and assignments include using someone else's ideas or words without appropriate acknowledgement, submitting your own work in more than one course without the permission of the instructor, making up sources or facts, obtaining or providing unauthorized assistance on any assignment.

On tests and exams, cheating includes using or possessing unauthorized aids, looking at someone else's answers during an exam or test, misrepresenting your identity, or falsifying or altering any documentation required by the University.

Equity, Diversity and Inclusion

The University of Toronto is committed to equity, human rights and respect for diversity. All members of the learning environment in this course should strive to create an atmosphere of mutual respect where all members of our community can express themselves, engage with each other, and respect one another's differences. U of T does not condone discrimination or harassment against any persons or communities.

The University of Toronto is a richly diverse community and as such is committed to providing an environment free of any form of harassment, misconduct, or discrimination. In this course, I seek to foster a civil, respectful, and open-minded climate in which we can all work together to develop a better understanding of key questions and debates through meaningful dialogue. As such, I expect all involved with this course to refrain from actions or behaviours that intimidate, humiliate, or demean persons or groups or that undermine their security or self-esteem based on traits related to race, religion, ancestry, place of origin, colour, ethnic origin, citizenship, creed, sex, sexual orientation, gender identity, gender expression, age, marital status, family status, disability, receipt of public assistance or record of offences.

University Land Acknowledgement

I wish to acknowledge this land on which the University of Toronto operates. For thousands of years, it has been the traditional land of the Huron-Wendat, the Seneca, and the Mississaugas of the Credit. Today, this meeting place is still the home to many Indigenous people from across Turtle Island and we are grateful to have the opportunity to work on this land.

Accommodations

Students with diverse learning styles and needs are welcome in this course. In particular, if you have a disability/health consideration that may require accommodations, please feel free to approach me and/or the AccessAbility Services Office as soon as possible.

AccessAbility Services staff (located in Rm AA142, Arts and Administration Building) are available by appointment to assess specific needs, provide referrals and arrange appropriate accommodations 416-287-7560 or email ability.utsc@utoronto.ca. The sooner you let us know your needs the quicker we can assist you in achieving your learning goals in this course.

Use of Generative Artificial Intelligence Tools

Students may use artificial intelligence tools, including generative AI, in this course as learning aids or to help produce assignments. However, students are ultimately accountable for the work they submit.

Students may not use artificial intelligence tools for taking tests, writing research papers, creating computer code, or completing major course assignments. However, these tools may be useful when gathering information from across sources and assimilating it for understanding.

The knowing use of generative artificial intelligence tools, including ChatGPT and other AI writing and coding assistants, for the completion of, or to support the completion of, an examination, term test, assignment, or any other form of academic assessment, may be considered an academic offense in this course.

Recording of Classroom Material by Students

Recording or photographing any aspect of a university course - lecture, tutorial, seminar, lab, studio, practice session, field trip etc. – without prior approval of all involved and with written approval from the instructor is not permitted.