BIPN 194/BGGN 284: Molecular Neuropharmacology
Winter 2022

Professor: Matthew Banghart (please contact via Canvas, not email)
Location: Biology Building Room 1138 (Muir College); Zoom: https://ucsd.zoom.us/j/95077833273
Time: Thursdays 11:00 – 12:20 pm
Website: Canvas
Office hours: by appointment only

Description: Pharmacology plays a fundamental role in neurobiology and its principles underlie the actions of therapeutic drugs. This course will address advanced concepts in neuropharmacology and explore the current state of neuropharmacology research through a critical reading of primary research publications.

Format: In-class group presentation and discussion of primary research literature and select background material (a review article). In week 1, Dr. Banghart will present foundational concepts in lecture format. In weeks 2-10, a primary research paper will be assigned for the entire class to read and understand (the pdf will be deposited on Canvas). Typically, one group of students will present the paper each week using slides. Each group member is required to equally contribute to the oral presentation. Non-presenters are required to submit a 1 page summary of the paper according to the provided guidelines. Supporting literature (typically a review article or two) will also be suggested to provide context. Only the presenting group is required to read the supporting literature, but it is highly recommended to all students. On occasion, a guest speaker who works at the forefront of neuropharmacological research at UCSD, typically a PhD student or postdoctoral fellow, will present a short lecture and guide the discussion. Each week, students will spend up to 4.5 hours reading and preparing for the in-class discussion, and 1.5 hours per week in class. All required and suggested papers are available in Canvas.

*Currently, the plan is to begin class on Zoom and then switch to in-person instruction a few weeks into the quarter. There will **NOT** be a hybrid option and class will not be recorded when on zoom.*

Guest speakers for WI22 include Dr. Lauren Faget, a postdoctoral fellow in the laboratory of Dr. Tom Hnasko (UCSD Neurosciences), and Jenny He, a PhD student in the laboratory of Dr. Banghart (UCSD Neurobiology/Biological Sciences). Dr. Faget has studied opioidergic and dopaminergic circuits for over a decade. Ms. He is preparing to defend her PhD thesis on molecular mechanisms of opioid receptor signaling in neurons.

Grading:	Attendance	10%
	Paper summaries	30%
	In-class participation	5%
	Group presentation	25%
	Final report	30%

*All assignments should be uploaded to Canvas using the assignment tool. Note that the portal closes at the time the assignment is due. Late submissions will be accepted with points deducted.

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Attendance: Attendance is mandatory and worth 10% of the total grade (1% per class). Absences must be pre-approved with Dr. Banghart or supported with a doctor's note. Some lenience will be granted given the ongoing pandemic. Please communicate early and openly. You will be supported.

Paper summaries: Students will be graded on their preparation for in class discussions, which will reflect their having read and understood the material. **By 9 pm on the Tuesday prior to each Thursday class,** students are required to submit a one-page summary, as well as a second page containing a list of at least three non-technical questions about the reading assignment (*i.e.* about the science, not simply the methods). Students should have a copy of their questions available in class to facilitate their participation in the discussion. Canvas submissions will close at 9 pm on Tuesdays. These summaries are worth 30% of the total grade (3.33% each for 9 papers during weeks 2-10). Students do not have to prepare summaries and questions when they are presenting. **See format guidelines at the end of this document.** A good overview of how to read scientific papers is provided in Canvas under syllabus.

In-class participation: Students are required to participate in discussions during the presentations. Minimally, this requirement can be met simply by asking at least one of the three pre-prepared questions during or after the presentation, although other forms of participation can supplant this option. Those who sit quietly all quarter will not receive full participation credit.

Group presentation: In weeks 2-10, students will take turns presenting the assigned primary research paper in small groups. Presentations should be ~45 minutes long to leave ample time for discussion. Each student will be a part of one group and present only once. Each group member is required to contribute equally to the oral presentation. Grades will be based on the overall quality of the presentation, adequate identification and discussion of the key scientific questions and key findings, correct interpretation of methods and data, and each individual's ability to answer questions posed by students and the instructor (presenters should take turns answering questions). Presenters should be prepared for an interactive discussion with interruptions for questions and discussions of key points. Each group should schedule a meeting with Dr. Banghart before their presentation (M-W) to address any questions about the paper or presentation. Final presentation files must be submitted to Dr. Banghart via Canvas, on the day of the presentation at the latest. **See detailed guidelines on format below.**

Students have been pre-assigned to groups according to this google document. Students must arrange any changes amongst themselves and obtain approval from Dr. Banghart.
https://docs.google.com/spreadsheets/d/1MM5Ddkk14zrzpEW3gNBRAbXJtBndjhI-PiqG-0i1HkA/edit?usp=sharing

Guidelines for giving oral scientific presentations in the form of a rubric are available in Canvas under Syllabus. The rubric, which is very thorough to a point beyond the scope of this course, will be roughly used for evaluation.

Final report: Students will be required to write a review-style research report that references primary research papers related to topics covered in class. Topics must be approved by the instructor to ensure appropriate scope and relevance. Grades will reflect the depth of understanding of concepts covered in class and the ability to conceptualize a relevant theme, as well as the appropriateness of the papers

chosen, and the ability to write and communicate effectively using appropriate technical terminology. Reports must be typed, single spaced with 1" margins, using 12 pt Times New Roman font. **Reports from undergraduate students enrolled in BIPN 194 should be 4-5 pages long, cover 3-4 primary research papers, and include 2 figures (~1/3 page max per figure). Reports from masters students enrolled in BGGN 284 should be 6-8 pages long, cover 6-8 primary research papers, and include 4 figures (~1/3 page max per figure).** The page requirements do not include references – these should be appended as a separate page. A conceptual figure similar to those found in review articles, presenting a model, scheme or possibly a flow-chart, must be created from scratch by the student and included in the report to obtain full credit. Minimally, the conceptual figure can be hand-drawn and photographed. Ideally, it will be constructed using drawing software (Inkscape is a free alternative to Adobe Illustrator with many great tutorials on Youtube). **Final reports are due on Thursday March 17 at 9:00 am (Finals Week). See guidelines on layout below.**

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Syllabus: (subject to change)

Class	Date	Topic (paper)	Presenter
1	1/6/22	Ligand-receptor interactions and GPCRs **(Wacker *et al.*, 2017)**	Dr. Banghart
2	1/13/22	A non-hallucinogenic psychedelic therapeutic **(Cameron *et al.*, 2021)**	Group A
3	1/20/22	Psilocybin causes dendritic spine growth in PFC **(Shao *et al.*, 2021)**	Group B
4	1/27/22	Serotonin in NAc rescues social deficits in autism **(Walsh *et al.*, 2018)**	Group C
5	2/3/22	Positive reinforcement in the absence of dopamine **(Zell *et al.*, 2020)**	Dr. Lauren Faget
6	2/10/22	Ketamine antidepressant action in the habenula **(Yang *et al.*, 2018)**	Group D
7	2/17/22	Ketamine causes spine growth in PFC via dopamine **(Wu *et al.*, 2021)**	Group E
8	2/24/22	Opioid side effects via receptor phosphorylation **(Kliewer *et al.*, 2019)**	Jenny He
9	3/3/22	mGluR NAMs as antidepressants **(Joffe *et al.*, 2020)**	Group F
10	3/10/22	Anthrax toxins for pain relief **(Yang *et al.*, 2021)**	Group G

Wacker, D., Stevens, R. C. and Roth, B. L. (2017) 'How Ligands Illuminate GPCR Molecular Pharmacology', Cell. pp. 414–427. doi: 10.1016/j.cell.2017.07.009.

Cameron, L. P. et al. (2021) 'A non-hallucinogenic psychedelic analogue with therapeutic potential', Nature. 589(7842), pp. 474–479. doi: 10.1038/s41586-020-3008-z.

Shao, L. X. et al. (2021) 'Psilocybin induces rapid and persistent growth of dendritic spines in frontal cortex in vivo', Neuron. 109(16), pp. 2535-2544.e4. doi: 10.1016/j.neuron.2021.06.008.

Walsh, J. J. et al. (2018) '5-HT release in nucleus accumbens rescues social deficits in mouse autism model', Nature. 560(7720), pp. 589–594. doi: 10.1038/s41586-018-0416-4.

Zell, V. et al. (2020) 'VTA Glutamate Neuron Activity Drives Positive Reinforcement Absent Dopamine Co-release', Neuron. 107(5), pp. 864-873.e4. doi: 10.1016/j.neuron.2020.06.011.

Yang, Y. et al. (2018) 'Ketamine blocks bursting in the lateral habenula to rapidly relieve depression', Nature. 554(7692), pp. 317–322. doi: 10.1038/nature25509.

Wu, M. et al. (2021) 'Ketamine Rapidly Enhances Glutamate-Evoked Dendritic Spinogenesis in Medial Prefrontal Cortex Through Dopaminergic Mechanisms', Biological Psychiatry. 89(11), pp. 1096–1105. doi: 10.1016/j.biopsych.2020.12.022.

Kliewer, A. et al. (2019) 'Phosphorylation-deficient G-protein-biased μ-opioid receptors improve analgesia and diminish tolerance but worsen opioid side effects', Nature Communications. 10(1), pp. 1–11. doi: 10.1038/s41467-018-08162-1.

Joffe, M. E. *et al.* (2020) 'mGlu2 and mGlu3 Negative Allosteric Modulators Divergently Enhance Thalamocortical Transmission and Exert Rapid Antidepressant-like Effects', *Neuron*. Cell Press, 105(1), pp. 46-59.e3. doi: 10.1016/j.neuron.2019.09.044.

Yang, N. J. et al. (2021) 'Anthrax toxins regulate pain signaling and can deliver molecular cargoes into ANTXR2+ DRG sensory neurons', Nature Neuroscience. pp. 1–12. doi: 10.1038/s41593-021-00973-8.

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Guidelines for Research Paper Summaries
Upload to Canvas BY 9 pm on Tuesday prior to class on Thursday.

Prepare a ~1 page summary (1" margins, 1.0 line spacing, 11-12 pt font) that addresses the following questions. Each question should be its own paragraph. Do not exceed 1 page. Do not write less than ¾ of a page.

1. What is the Big question? Broadly, what does the field need to know?
    a. Summarize the background in 5 sentences or less.
2. What is the specific question(s)?
    a. What focused question(s) does the study address?
    b. What were the underlying hypotheses?
3. What is the experimental approach?
    a. List the key methods (*e.g.* functional assays in cell culture, hot plate pain model in rats, etc.)
    b. Describe the key experimental workflow in ~5 sentences.
4. What are the key findings?
    a. Describe the key discoveries and explain why they are key.
    b. Are there any critical shortcomings that compromise their conclusions?
5. How do the findings advance the field?
    a. Address the specific questions.
    b. Address the Big question.

On page 2, include 3 non-technical questions about the study (*i.e.* about the science, not about the methods, not about definitions etc.).

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Guidelines for Group Presentations

Rely primarily on figures. Do not load slides with text (and read it to the audience). A picture is worth a thousand words.

Each slide should have a title that captures the message of the slide. Each slide should have a distinct message.

Do not over-crowd slides with images and data. Less is more. Only show the information that is required to convey the message of the slide. Not every data trace in the paper is critical.

When using images or data that do not come from the assigned paper, include the citation on the slide. This does not apply to random images borrowed from the internet – scientific content only.

Groups should split the presentation up evenly. One person can cover the intro while others split the results and conclusions. Or each person can cover sub-sections of results. This is up to the group. Everyone in the group will be equally graded on the quality of the slides and the material contained within. Individual grades will depend on the quality of individual contributions to the oral presentation.

Incorporate breaks into the presentation every 5-10 minutes to field questions from the class. Try to make these natural break points between topic transitions to facilitate discussion of prior slides. This is especially important for this remote version of the course to enable class participation, which is required from everyone for full credit. Do not simply blast through the presentation.

Structure

Intro – Gather material for the intro slides from the suggested review articles and any perspective pieces that accompany the primary research paper. Use their figures to convey critical concepts.

Begin with big picture background to place the research into context. What is the Big question? What is the premise? Why are people working on this problem? What is the relevance to society?

Provide a brief (1-3 slide) overview of critical scientific background information that is required to understand the detailed scientific question (*e.g.* key receptors, signaling pathways, brain regions, drugs etc.). Use diagrams freely. Sometimes a diagram from the end of a paper can be appropriate in the introduction.

Present the specific questions addressed by the study and any pertinent hypotheses. Justify the hypotheses in the context of the background material presented. Present more detailed background information here to make the specific questions clear. Showing data from previous papers can help set the stage for the questions being addressed.

Define the experimental approach. Explain key methods employed and their relevance to the study (e.g. behavioral assays, ligand binding assays, functional receptor assays etc.). These are often complicated and require diagrams or figures to explain clearly. Google is your friend.

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Be sure to define any key terms or abbreviations that are relied on in the text or presentation. Especially if they are novel and non-obvious to most Biology students (there will be many).

Results – Present the key data from the study that support the major findings. Only in rare cases should every single figure or figure panel be included. Consider incorporating select figures from the supporting information as well.

In general, presenting data in the same order in which it appears in the paper is fine, but feel free to mix things up if it helps tell the story better.

Dedicate a slide to each key figure. You can break up multipanel figures for clarity. Present the experiment, be sure to mention the method, explain the data clearly (do not just read the figure legend), and interpret the results (*e.g.* molecule X was more potent than the rest).

Be sure to minimally discuss control conditions and consider why the controls are appropriate (or why they may not be). Do not go overboard.

Statistics in scientific studies can be quite complicated. This is not a statistics course and you are not obligated to understand all of the analyses. Yet do recognize the meaning of a P value, and how the paper is using P values to justify their conclusions.

Be critical. What are the major assumptions going into an experiment? Are the assumptions valid? Did the authors overlook something? Is their data messy (and is that really even a problem)? Is the analysis clear? Did they omit a key control that would make their results more or less convincing?

Summary – Wrap up by summarizing the key findings, shortcomings and impact. More text is appropriate in this section in the form of concise bullet points. Diagrams (perhaps recycled from the intro) are very appropriate as well.

Did they answer the specific questions defined at the start? If so, what are the answers? If not, why not?

Were there any major problems, shortcomings, hang-ups etc.? Keep in mind that one paper cannot address everything and this is completely fine. It is a study based on experimental approaches available to the authors. Resources and time are not infinite. What did they NOT do that would have been helpful? This is not necessarily an attack on the authors or their science.

Were there any big surprises given the framework available going into the study?

How do the key findings advance the field? What issues have been resolved? What does it allow people to do in the future that they could not before? Often the answer to this question is that by solving one problem, people can now attend to another one…

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What are the likely next steps for future studies? What questions remain unresolved? Often impactful studies raise more questions than they answer, simply by finding something surprising. What would you want to do next if you were the authors?

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Guidelines for Final Reports

Final reports are due on Thursday March 17 at 9:00 am (Finals Week).

Final report should be based on a theme that is rooted in the concepts covered in class. There must be a strong common thread but students have great freedom to follow their interests. Students may also simply write about one of the exact topics from class using the papers provided. **Topics and papers must be cleared with Dr. Banghart by the end of Week 8 (Sun Feb 27) in order to obtain full credit for the paper.**

Themes should assimilate knowledge from a small body of work (a handful of related papers) from papers published primarily within the past 10 years. The theme should be anchored in a clearly defined Big question that is broad in scope, although the papers should address one or several closely related focused questions related to the Big question. Although including multiple papers from the same authors is fine, different research groups should be included to provide some breadth in perspective.

Ideas for themes can come from existing review papers that are broad in scope. Examples might include topics such as "Actions of anxiolytic drugs in reward circuits," "Allosteric modulators as antipsychotics," "Actions of cholinergics on glia in the brain," "Ligand bias at noradrenaline receptors," and so forth.

Themes can be built around an unresolved hypothesis that is currently being tested in the field (*e.g.* Are biased opioids the path to safer drugs?) – one might choose to discuss the open questions, what findings give rise to conflict, and what might be done to resolve the issue.

The overall structure should resemble what is commonly found in a review article. Many review articles are provided with the required primary research literature covered in class. The general sections are very similar to those used in the group presentation, but they will collect and organize information across multiple studies. Simply discussing studies individually back-to-back, is generally not a good approach, unless the studies build on each other (say multiple papers from the same group over several years). Organize the sub-themes topically and discuss the relevant findings from multiple studies within each sub-section. The general components are below:

Abstract
Begin with an abstract that concisely summarizes the major points. It should be 5-7 sentences long. It should state the Big problem and the specific questions addressed in your essay. It should state the major lines of research and the key findings, concisely, that support your stance. It should conclude with a forward-looking sentence on where the field is headed.

Background/Introduction
Spend a page or so on the Big question that all of the papers collectively address. Provide key definitions. Conceptual figures with schematics can be very helpful here (*e.g.* your original figure).

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Main Text

Use subheadings to organize your essay thematically. Discuss the key concepts you wish to convey and cite the primary research studies that support these ideas. Do not go into excessive experimental detail, but mentioning the methods employed is a very good idea (*e.g.* Using the SNI model of neuropathic pain in rats (Doe, J. *et al.*, 2008) and the CFA model of inflammatory pain in mice (Doe, J *et al.*, 2016), it has been shown that mu opioid receptors become less responsive to morphine in states of persistent or chronic pain).

Discuss not only the key findings but also and caveats or limitations to the studies (*e.g.* Although morphine efficacy is clearly reduced in multiple models, whether these findings apply to other opioid pain-killers such as fentanyl or other non-opioid analgesics remains to be determined.)

Use figures as appropriate to illustrate your points. Conceptual figures are always great, but a key panel from a primary paper (*i.e.* a single graph or two) can be very appropriate as well.

Tables can help organize information across multiple studies and facilitate key comparisons.

Conclusions

Finish your essay with a brief, 1-2 paragraph summary that re-iterates the material in the context of the Big question. Do not simply re-state the abstract or re-list the main ideas. This is the time to put the work into a broad context.

Be sure to spend at least a few sentences on where the field is headed next, what key questions remain unresolved, and why they are important to answer.

Citations and Bibliography (References, Works Cited)

Mendeley is a free online citation tool that lets you organize research literature and cite papers in programs such as Microsoft Word using an easy plugin. It also lets you choose formats for your bibliography. There are other similar programs out there. Please use a format that includes the Primary Author's last name and publication year in the text (Doe, J. *et al.*, 2020), and the full author list and title of the paper in the Bibliography section (as in your syllabus). Cell Press formats fit the bill.

In the Cell Press format, the bibliography typically lists the papers in alphabetical order by the last name of the primary author, as opposed to the order in which they are cited, which uses numbers in the text instead of the author name and year. Numerical citations are more difficult for the reader to follow but save precious space for text in premier journals such as Nature and Science.

Do not directly quote more than a few words from a primary publication. That is essentially lazy, transparent plagiarism and does not demonstrate comprehension. You will lose many points for this and it does not constitute independent writing. But do be sure to use citations appropriately. If you cite a paper at the beginning of a paragraph and continue to discuss information from that paper only, you do not have to cite it again and again at the end of every sentence. Once you change references, cite the new one, and go back to it, only then should you cite it again.