

ARTICLE**A Semester without Exams: Approaches in a Small and Large Course****Rachel C. Branco***Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN 46556.*

Exams carry pedagogical downsides: they can create stress, decrease intrinsic motivation, and tend to reduce opportunities for creative problem-solving. Exams are also difficult to administer when flexibility is paramount, such as during remote learning, when students have special testing conditions, or during a pandemic when a subset of students are sick or in quarantine. To account for these shortcomings, I designed and instituted two completely exam-free undergraduate Neuroscience and Behavior courses in the Spring of 2021, one a large introductory-level course and the other a small upper-level elective course. In the large introductory-level course, I used several methods including Gradescope and new roles for my Teacher's

Assistants to keep the grading load manageable. This exam-free approach was evaluated in four areas: creative thinking, interest in the material, stress level, and academic performance. Evaluation of success in these areas was completed via student feedback and by comparing final projects to final projects from previous semesters. The exam-free approach produced favorable or neutral results in every measured outcome. The framework for an exam-free course described here could be a useful starting point for other instructors who want to eliminate exams.

Key words: pedagogy; testing anxiety; undergraduate; assessment; course design

Exams are not always an appropriate pedagogical tool. Exams increase student stress (Sarason and Mandler, 1952; Liebert and Morris, 1967). This exam stress negatively correlates with intrinsic motivation, self-efficacy, and self-esteem (von der Embse et al., 2018) and can negatively impact student mental health (Putwain et al., 2021). Exams can be cumbersome for both students and professors when extra testing resources are necessary, when students are ill, or when dealing with a personal emergency. Frequent, low-stakes assessment is best for student learning (Roediger and Karpicke, 2006; Larsen et al., 2009), though frequent in-class assessments encroach on valuable class time. Exams are also not as effective as other methods for promoting creative thinking, writing, and problem-solving (Wideen et al., 1997). Lastly, when exams are moved into a virtual environment – as was done often during the COVID-19 pandemic – students still feel acute exam stress (Elsalem et al., 2020) and academic honesty is difficult to control with the same level of rigor as an in-person test (Dendir and Maxwell, 2020).

Because of these reasons, I completely eliminated in-class exams in two Neuroscience and Behavior lecture courses, one a small (33 person) upper-level elective and the other a large (154 person) introductory class. In the past, I had used exams to assess student learning in both of these classes. Originally, my pedagogical goal was to find a suitable replacement for exams in both of these courses. By eliminating exams completely, I was freed from finding a 'replacement' – indeed, most facsimiles of in-person exams fall short of the original experience. Instead, my goal with this alternative approach was to bolster the very things that are the weaknesses of an exam-based course. Namely, I aimed to: promote creative problem-solving, increase student interest, improve knowledge retention, and lower student stress.

The general structure was similar in both courses. Students completed graded, open-note, open-internet, unlimited time, unlimited attempt homework assignments

every two weeks. In the weeks between homework assignments, students would produce a creative written assignment connecting class material to the broader world, graded based on effort. The final project in both courses was a creative research project, with stepwise deadlines and class time devoted to completing this final research task. In this way, assignments acted as authentic assessments that encouraged real-world scientific thinking.

At the end of the semester, I surveyed students about their creative thinking, interest in the material, and stress level. I also collected open-ended student responses about the nature of the assessments in an exam-free course. To assess student learning, I compared the final projects from the exam-free semester to final projects from a previous semester. In all measures, I observed favorable or neutral outcomes, indicating that an exam-free course can be a useful framework for both large and small Neuroscience and Behavior classes. The methods described in this paper to establish an exam-free course represent a flexible, modifiable approach towards eliminating exams while improving creative problem-solving, student interest, student stress, and maintaining rigorous expectations of academic performance.

MATERIALS AND METHODS**Course descriptions and university context**

The current paper describes the assessment tools implemented during an exam-free semester in two in-person, three-credit hour lecture courses in the spring of 2021: Molecular Neuroscience (sophomore-level introductory course, 154 students) and Neuropharmacology (upper-level elective course, 33 students). These courses were taught at University of Notre Dame, a mid-sized Midwestern private institution with a 95% graduation rate. I was the sole instructor for both courses. Both courses are overwhelmingly populated with Neuroscience and Behavior majors, though each class had a small minority of students

from related majors. The content of Molecular Neuroscience focuses on the basic biochemical mechanisms of neuronal transmission, including electrical properties of neurons, chemical signaling, and synaptic plasticity. The content of Neuropharmacology focuses on the molecular, physiological, and subjective effects of psychoactive drugs. There are no laboratories associated with either course. Approximately 75% of students in both of these classes are interested in attending medical school after graduating.

Course Revisions

These course revisions were originally motivated by the necessity of a mid-pandemic classroom. With students sick or in quarantine so often, relying on infrequent, high-value exams was not optimal. The revisions were inspired by previous research showing the value of frequent, low-stakes authentic assessment (Roediger and Karpicke, 2006; Larsen et al., 2009, Wideen et al., 1997). I made modifications to these research methods to adapt to the learning goals of these specific classes, to encourage students' sense of self-efficacy, and to utilize reasonable, efficient, and fair grading practices.

Previously, both courses had three semi-cumulative exams which made up the majority of the final grade in each class. 20% of each exam's grade was a group portion of the exam where students had to collaborate to form a single answer. In the Neuropharmacology course, students also had to complete a final research project.

Overview of Grading Schema

Grades were calculated in an approximately similar manner in both Molecular Neuroscience and Neuropharmacology. In both cases, grades were based on: 1.) participation, 2.) creative writing assignments 3.) homework, and 4.) a final project.

Participation was ~10% of the final grade and graded based on in-class involvement and completion of feedback surveys. In Molecular Neuroscience, I used PollEverywhere to automate tracking of in-class involvement.

Creative writing assignments required students to connect the class material to the broader world. These assignments were due every two weeks, for a total of six assignments. Creative writing assignments were graded based on effort, where a good effort received full credit, a sub-optimal effort received half credit, and a missing assignment received no credit. The lowest of these assignments were dropped. These creative assignments accounted for <25% of the total grade.

Every two weeks, offset from the creative writing assignment, students completed a homework assignment that was graded for accuracy. These homework assignments essentially functioned as frequent, low-stakes, take-home quizzes. These homework assignments were open-note, open-internet, unlimited time, and unlimited attempts. In both courses, I used Gradescope Online Assessment tool to create and grade all homework. Gradescope is a platform that makes assessment building and grading much more speedy, easy, and equitable. Gradescope is helpful to use for many types of questions,

including multiple choice, multiple-multiple choice, drawing, showing calculations, short- or long-written answers. Additionally, Gradescope allowed me to provide quick, customized feedback to students. Homework assignments accounted for ~30% of their final grade.

Both courses had a creative final project. Intermediate deadlines were given (project proposal, draft) and included in the final project grade. The final project accounted for ~30% of the final grade.

Creative Writing Assignment for a Large, Intro-Level Class: Deep Dives

In Molecular Neuroscience, I called these creative assignments "Deep Dives". I had six undergraduate Teacher's Assistants (TAs), who each received two credits for their work. Before the semester started, I had each TA pick a topic in the field of Neuroscience that was interesting to them. They chose the topics of Vision, Neurodevelopment, Sleep, Food/Hunger, Depression/Anxiety, and Alzheimer's Disease. At the beginning of the semester, each student ranked the topics they were most interested in using Google Forms. I sorted each student into a 'Topic Group', such that every student was in one of their top three choices and each Topic Group contained approximately the same number of students. I performed this sorting using a simple homemade Python program that I would be happy to share upon request. Each TA became the leader of that Topic Group, providing background reading, answering topic-specific questions, and grading Deep Dives. TAs used Piazza to shepherd online discussions related to their topic. Deep Dive prompts were open-ended questions related to the class material from the preceding two weeks. These questions involved experimental design or drawing/explaining concepts. Students were expected to find research outside of class material in order to be able to complete the Deep Dive. TAs graded the Deep Dives for either full, half, or no credit based on effort and provided feedback where appropriate. Consistency was ensured between TAs via weekly group meetings with me. Because they were grading based on effort and each TA was only responsible for their own Topic Group, grading was completed quickly. I've included what I used as Deep Dive prompts for my Molecular Neuroscience class in Appendix 1.

Creative Writing Assignment for a Small, Upper-Level Class: Responses

In Neuropharmacology, I called these assignments "Responses". Responses had the following structure: the first paragraph was a Wikipedia-style explanation of a topic of their choice from class. In the second paragraph, the student connected that topic to something in their life or in the world. This connection did not necessarily have to be drawn from personal experience – students had the option of using material from broader culture (ex. a particular song, an event in history, a blog post, a book, a news article, a film, a TV show, or a Reddit thread, etc.). Students were asked to provide a way to read/experience the 'connection', if possible (i.e., provide a copy of an article, a link to a song, a Wikipedia overview of a book, etc.). These Responses were

graded based on effort for either full, half, or no credit.

Homework Assignment for a Large, Intro-Level Class

Every two weeks, students completed an open-note, open-internet, unlimited attempts, unlimited time Practice Problem set. These essentially functioned as take-home quizzes. Indeed, many questions for these homeworks were pulled from previous semesters' exams. Gradescope was used for all Problem Sets due to the ease of design and grading. Because the time and resources available to students, the questions were often quite difficult. However, because this class was so large, they needed to be easy to grade. Therefore, the questions were often multiple or multiple-choice questions, where the student was also required to explain their reasoning. This way, even if a student copied the correct multiple-choice response from a friend, they had to explain their answer in their own words. Zero credit was given if the reasoning was missing. I usually did not read all of the written reasoning unless it was clear there were common misunderstandings. By requiring a written reasoning, it was also easier to check for academic dishonesty by evaluating whether any wording was matching. To a lesser extent, these questions required students to perform calculations, provide an ultra-short written response, or draw a graph of expected data. Examples of some questions for these Practice Problems are in Appendix 2.

Homework Assignment for a Small, Upper-Level Class

Practice Problems for Neuropharmacology were identical to that for the large class with the exception of the nature of the questions. Because this class was smaller, the questions usually required in-depth written answers. Questions sought to mimic real-life research/clinical/moral problems in the field of Neuropharmacology. These questions often involved techniques, breakthroughs, or diseases that were not mentioned in class or in the book but were connected to a concept from class. Students were expected to perform some outside research in order to successfully complete these Practice Problems. Because of this expectation of some required research, these questions were not pulled from previous semesters' in-class exams. Some examples of these questions are in Appendix 3.

Final project for a Large, Intro-Level Class

For the final project, the students created a case study, an approach that has been useful in other Neuroscience classes (Bindelli et al., 2021). Students worked in groups of two due to the size of the class. They chose their own partner from within their Topic Group or had the option of being randomly sorted with a partner. The case study was required to include a coherent narrative, questions related to that narrative, the 'answer key' to those questions, and covering two out of the three units from the class (Electrical Transmission, Chemical Transmission, Plasticity). Students submitted a rough draft of their case study several weeks before the final due date. This rough draft was graded by their Topic Group leader based on effort and provided with detailed feedback. The TAs also shared with me their comments and expected letter grade for the drafts, to aid in

my grading of the final Case Studies at the end of the semester. I am planning on using some of the best of these Case Studies for use next time I teach this course. The rubric for the Case Study is in Appendix 4.

Final Project for a Small, Upper-Level Class

Students worked individually to create a final research poster on a topic of their choice relating to how drugs act on the nervous system. Students had several intermediate deadlines (topic proposal, rough draft) to incentivize starting work on their project early. Posters were displayed virtually using Google Drive such that students had a week to view and comment on their peers' posters.

Evaluation of Success of an Exam-Free Semester

In order to measure the success of these new methods, I solicited feedback from the students via surveys. The survey for the Neuropharmacology class asked students to rate their own interest in the subject matter, stress level, and confidence in creative problem-solving compared to what they think they would feel if the class included exams. Both Molecular Neuroscience and Neuropharmacology provided open-ended written feedback concerning their opinions of the assessments for the semester. I also compared the Neuropharmacology final project a previous semester's final project grades to determine if the level of learning was comparable. I did not do this final project comparison in the Molecular Neuroscience class because this was the first year that this class was taught to a large group of sophomores, so the student populations relative to previous semesters were not comparable.

RESULTS AND DISCUSSION

At the end of the semester, I asked students in the Neuropharmacology class about their creative thinking, interest in the material, and stress level. 28 out of the 33 students completed this survey. I also compared the final projects to final projects from a previous semester to assess student learning. In all measures, I observed positive outcomes. On a Likert scale from 1-7 where 1 represented "I learned less than if we had had tests" and 7 represented "I learned more than if we had had tests", students responded that they felt they learned more than if there had been tests (mean = 5.5, SEM = 0.23, Figure 1A). On a Likert scale from 1-7 where 1 represented, "these assessments made me less interested in the material," and 7 represented, "these assessments made me more interested in the material," students responded that they felt they had increased interest in the material (mean = 6.1, SEM = 0.18, Figure 1B). On a Likert scale from 1-7 in response to a prompt about creative problem-solving where 1 represented "I was less confident than I think I would have been if we had had tests" and 7 represented "I was more confident than I think I would have been if we had had tests" students responded that they felt they had increased confidence in creative problem solving (mean = 6.5, SEM = 0.12, Figure 1C). There was no evidence of a difference in final project scores for the Neuropharmacology final project between the Spring 2021 semester without exams and the Spring 2020 semester with exams (mean of 91.4% in Spring 2021, mean

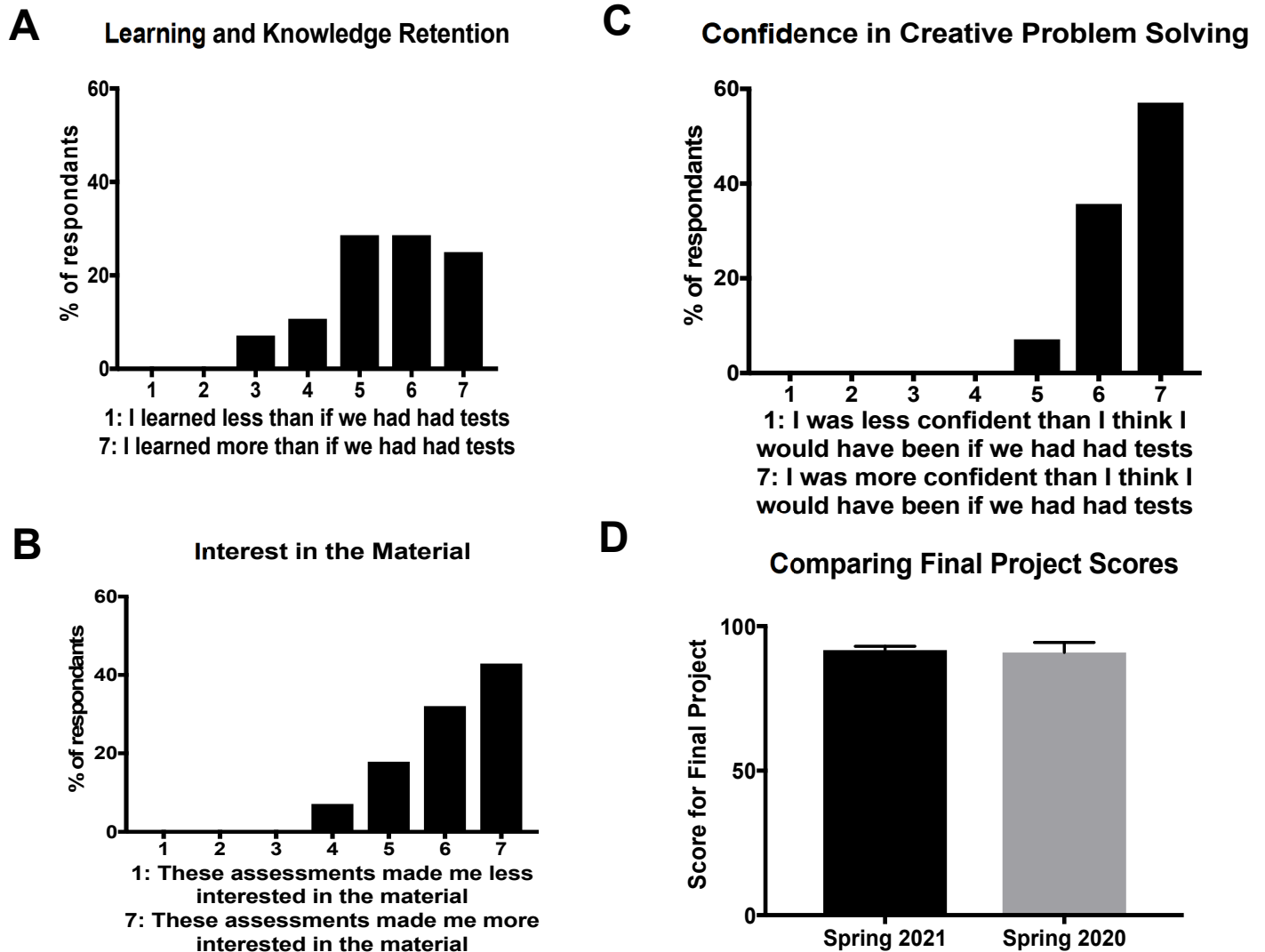


Figure 1. Results from a small, upper-level course. Student survey responses in the Neuropharmacology class regarding learning and knowledge retention (A), interest in the material (B), and confidence in creative problem solving (C). D shows final research project scores for Neuropharmacology in an exam-free semester (Spring 2021) and a semester with multiple exams (Spring 2020).

of 90.0% in Spring of 2020, $t(52) = 0.44$, $p = 0.70$, Figure 1D). In both classes, the median grade was an “A”, as has been the norm historically. The few students earning a “C” or below did so due to not turning in assignments.

Similarly, students in both classes provided written feedback regarding the nature of the assessments. 94% of Neuropharmacology students and 85% percent of Molecular Neuroscience students completed this open-ended survey. The relevant question in this survey was, “Please comment on how well the activities, readings, lectures, and assignments helped you learn in this course.” For the Molecular Neuroscience class, out of the 95 students who answered this part of the survey and specifically included their opinion of the assessments, 67 students had purely positive comments, 24 students offered mixed reviews, and 4 students had purely negative comments. The last student comment in Table 1 shows one of these negative comments, which is representative of the student critique of this course’s assessment. For the Neuropharmacology class,

out of the 15 students who answered this part of the survey and specifically included their opinion of the assessments, 13 students had purely positive comments, 1 student offered mixed reviews, and 1 student had purely negative comments. This feedback indicated that in general students enjoyed the creative nature of the assessments and thought it was an improvement compared to standard exams (Table 1).

Strengths of this Approach

I believe the exam-free approach described here represents an improvement over an exam-dependent semester. There are several aspects of this approach that are particularly helpful.

First, this approach allows the pedagogical focus to be on problem-solving over rote memorization. What makes professional Neuroscience researchers great is not the memorized facts about the subject, but the ability to use those facts to connect ideas, creatively solve problems, and

critically assess complex data. By making the assessments more like how real-world experts work within their fields, the students are growing in their abilities as scientists.

Second, this design offers a feasible way to implement frequent, low-stakes assessment. Frequent assessment is ideal for promoting student learning (Roediger and Karpicke, 2006; Larsen et al., 2009) but can be perceived as difficult to implement due to the class time constraints and the amount of grading required. This approach offers creative workarounds for both of these problems. By allowing the assessments to be take-home assignments, valuable class time is conserved. Indeed, by eliminating three days of exams compared to previous semesters, I was able to add class material. The burden of grading was also kept at a minimum by using Gradescope and TA effort-based grading. Even for the 154-person class, I found that with the help of Gradescope I could grade homework assignments within 30 mins to a few hours depending on the nature of the questions. By requiring students to explain their reasoning, I could make sure each student at least had to articulate their answer. Furthermore, by using TAs to grade the 154 Deep Dive writing assignments, I was also confident that academic dishonesty was kept to a minimum. Each TA only

read ~25 Deep Dives at a time, and each of those Deep Dives was restricted to the topic that the TA him/herself had selected. In this way, TAs became shepherds of their own topic area, and could recognize if sections were plagiarized between students. This also improved the TAs experience, since they were relatively autonomous and only grading on a topic that was interesting to them.

Third, the flexible nature of the assignments means that this approach can be adapted for a variety of classes. The difference between the “Deep Dives” (prompts relating mostly to experimental design) and the “Responses” (prompts asking students to connect class material with something in broader culture) are based on the learning goals of the class and level of student sophistication. A wide variety of similar short, creative assignments could fill this role. Indeed, many science teachers have already created such creative assignments, including editing Wikipedia articles (Burdo, 2012), writing blogs (Spix and Braiser, 2018), or team-authored research papers (Zwick, 2018).

Fourth, by incorporating the short creative writing assignment, the students were allowed to explore topics that were intrinsically interesting to them that still related to course content. From the feedback, I could see that

Neuropharmacology – Small Upper-Level Elective

I think that applying the material to problem sets really helped me to use my knowledge while enhancing my creative and analytical thinking, critical thinking skills, and helped me to adopt new perspectives on different topics. I think this was really great and likely helped me more than exams focused on retention of factual information would have.
I would like to really emphasize the no in-class tests. It not only reduced the stress level but I can 100% say I remember a LOT more because I wasn't just cramming forgetting cramming forgetting. I was able to simply enjoy and learn in the class.
The open-note problems sets really were a phenomenal learning activity and I would advocate that for their permanent inclusion. They replicate the type of learning that we will be asked to participate in out in the 'real world.' And, as occurred in problem set 5, they allow a much more uncertain/theoretical engagement with the field than a test that we all memorize content for would have. I really enjoyed the problem sets and found them a challenge, but in a way that pushed me to expand my comfort with the work.

Molecular Neuroscience – Large Introductory Required Course

The deep dives were one of my favorite parts of the course as I felt like they allowed me to actually pursue and learn more about a topic that was interesting to me. I learned a lot about "real life" issues and therefore I felt like this class equipped me with information I can use in my daily life and not just things I needed to know for future test-taking purposes.
The practice problems were actually very helpful for learning the course material, especially at the beginning of the semester when there were a lot of calculations. They kept me on track with the material. The deep dives and case study also helped me apply what I had learned to real world examples.
I liked that the structure of the class prioritized application over memorization. I liked that I didn't have to stress over timed exams but I could instead focus on learning and completing assignments to the best of my ability. The practice problems and deep dives both helped me to apply what I had learned.
I really liked how the emphasis in this course was on learning and not regurgitating information. I thought that the problem sets were helpful in getting me to think critically and apply the information we learned in lectures. I also really appreciated the deep dives because they allowed me to explore something I was interested in without the pressures of needing to be perfectly correct all the time.
I really enjoyed the problem sets and deep dives in this course. It allowed us to use what we have learned to real world problems and was good practice. Also not having a final or exams really helped relieve stress and make learning more interesting instead of stressful. I also enjoyed the end of class case studies we made.
The problem sets were crucial in learning to apply the concepts to scenarios we did not explicitly discuss in class. Moreover, the deep dives not only reviewed concepts we studied in class but encouraged us to engage with primary literature in neuroscience- an important skill to develop when entering the field of science.
Some of the problem sets were quite difficult given our understanding of the material from lectures. I understand that they are meant to challenge us, but when the problems were worded confusingly, I did not think that was an appropriate way to evaluate my understanding of the material.

Table 1. A sample of end-of-semester comments from students. Only comments regarding the exam-free nature of the course are included.

students appreciated guiding their own learning in this way.

Fifth, by allowing students to engage with class material creatively, I was also exposed to new content through student work. I plan on using some of the things I learned in

student responses in future semesters teaching these classes. The case studies in particular will be a useful resource for future semesters.

Lastly, a strength of this approach is the scheduled regularity for the students. From the students' perspective, they had something due every Thursday night (switching between the Problem Set and the short writing assignment every week). While the day of the week certainly isn't important, having a regular, repeated schedule meant that the rhythm of the class was quickly established. Compared to previous semesters, there were fewer student requests for late work. This also helped the TAs plan their review sessions.

Weaknesses of This Approach

This approach is not perfect, and I plan on continuing to get feedback from students and other teaching professionals on how to improve. There were a few weaknesses to be aware of.

First, it was critical to be precise regarding the level of difficulty and clarity of questions for the Practice Problem sets. Especially for the Molecular Neuroscience class, I have room for improvement regarding these Practice Problem set questions, as is reflected by some of the written student feedback. While some students found the Practice Problem sets too easy, most found them very difficult. Even knowing that they had unlimited time and resources, this was a source of stress for some students in the intro-level course. In the future, I need to be extremely careful in writing these homework questions, as any ambiguity ballooned into misunderstanding. I will also make sure to take time in class to lay out my expectations for how much outside research should be appropriate to answer homework questions. In my sophomore-level class, the students had not yet calibrated to college-level study habits or work expectations, and I hope future clarity will ameliorate stress borne from ambiguity.

Second, in the large, intro-level class, the assignments were only possible because I had six undergraduate TAs helping with grading. The TAs read, graded (based on effort), and provided feedback on each of the one-page Deep Dives and also provided valuable feedback and 'final grade estimation' for the final project. I would not have been able to even skim ~160 pages worth of Deep Dives every two weeks. I recognize that the availability of TAs is a limiting factor to instituting this course design in larger classes.

Third, I recognize that such an approach is not appropriate for all courses. In classes where the focus is on application and creative problem-solving, these methods could be useful. In courses that rely on in-person or timed exams to emulate real-life future application of material, traditional exams may be more appropriate. For example, I also teach a pre-medical Biochemistry class in which ~90% of the students go on to take the MCAT. As much as I would

love to take a more student-led, creative approach to my Biochemistry class, I will keep exams because I know that students benefit from practicing answering Biochemistry questions in a high-pressure, timed environment in preparation for the MCAT.

Fourth, while I did require students to explain their reasoning in Gradescope in the large class, I did not stringently check these short, written explanations for academic dishonesty. I believe this will be an area of growth as Gradescope moves out of the beta testing phase for this type of assessment.

Another weakness of this approach is that, depending on the nature of the creative written assignment, it requires some instructor expertise. For example, I was confident that I could pick up any Deep Dive from any Topic Group and could assess whether it was on the right track. However, if I were to implement such a system in my Biochemistry class, a discipline with which I am less familiar than Molecular Neuroscience, I would have to limit the possible Topics to those that I could reasonably and accurately assess.

CONCLUSION

High-value, infrequent exams are a mainstay of college-level science courses. However, relying on these exams can carry a host of unintended deleterious consequences. These weaknesses can be eliminated and turned to strengths by adopting an exam-free class structure with frequent, out-of-class, low-stakes authentic assessments like the approach described here. Furthermore, this approach can work at scale, even in a large, intro-level course. This scaled-up approach is dependent on outside tools, such as Gradescope for homeworks and use of TAs to shepherd specific topics. The framework described in this manuscript provides a reasonable alternative to exams while maintaining or improving pedagogical goals.

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APPENDIX 1: Deep Dive Prompts

Describe how and why resting membrane potential may be changed in your research topic. You may explain using a picture or write out your explanation.

Are action potentials or threshold affected by your research topic? Explain why or why not. You may use writing or pictures to answer.

Draw a presynaptic terminal with relevant cellular machinery (proteins, cellular structures, membranes, etc.). Highlight and explain where this presynaptic cellular machinery may be different as it relates to your topic.

You want to perform an experiment that tests how one of the neurotransmitters we discussed in class is important to your topic. Describe your experiment, making sure to include your hypothesis, experimental group(s), control group(s), methods, and a graph of your expected data if your hypothesis is correct.

Describe how a neuropeptide of your choosing relates to your topic of interest. Make sure to describe the relevant receptor, how it interacts with other neurotransmitters, and the effects on behavior. You may draw, use sentences, or sketch a concept map to illustrate your answer.

You hypothesize that synaptic plasticity plays a role in your topic of interest. Describe an experiment to test this hypothesis. Make sure to include your methods, control group(s), experimental group(s), and a graph of your expected data.

APPENDIX 2: Examples of Practice Problem Questions for a Large Intro-Level Class

These questions would not be included all in the same Practice Problem set.

1. If the gNa transiently and suddenly increased 100-fold, what would happen? Select all correct answers.

- the membrane would depolarize
- the membrane would hyperpolarize
- sodium would flood into the cell
- sodium would flood out of the cell
- sodium would stop passing through the cell membrane altogether
- sodium would travel across the cell membrane down its electrochemical gradient
- the current due to sodium would increase in magnitude
- the current due to sodium decrease in magnitude

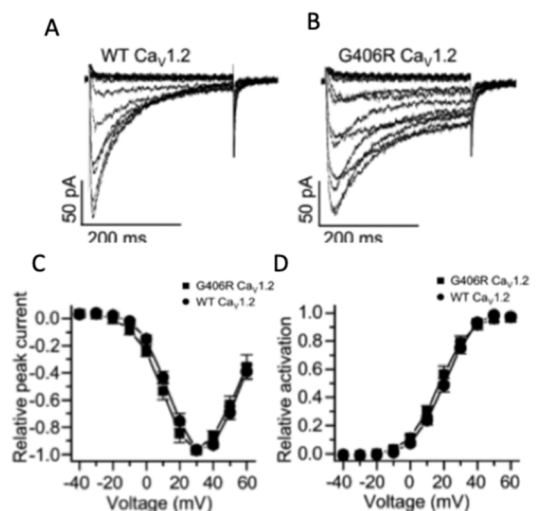
Explain your answer: _____

2. Sometimes experimenters will elicit action potentials in neurons by adding an extracellular solution high in potassium. Why does adding extracellular potassium elicit an action potential? Choose all statements that are true

- Extracellular potassium would make the reversal potential for potassium more positive
- Extracellular potassium would make the reversal potential for potassium more negative
- Using the Goldman or equivalence circuit equations, we know that the changed reversal potential of potassium would have a large effect on membrane potential
- The membrane potential would exceed threshold, triggering an action potential
- The membrane potential would approach but not reach threshold, triggering an action potential
- Extracellular potassium would disrupt the action of the sodium-potassium pump
- Extracellular potassium adds more positive charge to the extracellular environment, which causes the membrane to reach threshold
- Extracellular potassium changes the salt balance for all relevant ions, which together contribute to an altered membrane potential

Explain your answer: _____

3. Timothy syndrome (TS) is a rare genetic disorder caused by a mutation in the gene for voltage-gated calcium channels. This missense mutation, called G406R, results in a variety of abnormalities in multiple organ systems, and normally results in death due to heart failure before the age of three. Below is data showing the electrophysiological phenotype comparing normal neurons and neurons that have the G406R mutation. A and B show voltage-clamp recordings of the current through either a normal (WT) or Timothy syndrome (G406R) voltage-gated calcium channel in response voltage pulses ranging from -40 to +60 mV. (C) is an IV plot of maximum current through the calcium channel at various membrane potentials. (D) shows the likelihood of the voltage-gated calcium channels opening in response to various membrane potentials. Given the data below, how are a WT voltage-gated calcium channel and a G406R voltage-gated calcium channel similar? Choose all statements that are true. Modified from (Splawski et al., 2004)



- they both are gated by voltage
- they both produce an inward current when open
- they both produce an outward current when open
- they both are transmembrane proteins
- they both open at the same membrane potential
- they have the same peak current

- they both stay open for a similar length of time
- they both cause disease

4. Flunitrazepam (also known as Rohypnol) is a drug that acts on the GABA-A receptor that makes the receptor more easily able to bind its ligand, GABA. Draw a graph of the expected postsynaptic membrane potential response to GABA alone and the postsynaptic membrane potential response to GABA+flunitrazepam.

Explain your answer: _____

5. You are working with a newly discovered neuromodulator, Brancotonin (Br). A search of the literature suggests that Br does not work on a GPCR, but rather at a ligand-gated channel. You decide that you will be the first to ions pass through the Brancotonin receptor (BrR).
- a.) You first release Br onto a neuron that you know expresses BrR and record the change in the postsynaptic potential. You observe that the postsynaptic potential decreases when Br is applied. What does this tell you about the ion could be passing through BrR?
- the permeant ion is an anion
 - the permeant ion is a cation
 - the reversal potential of the permeant ion is lower than the resting membrane potential
 - the reversal potential of the permeant ion is higher than the resting membrane potential
 - the ion will flow out of the cell
 - the ion will flow into the cell
- b.) You decide to do an experiment to determine which ion is passing through BrR. What would be a reasonable experimental design?
- () Compare the effects of the neurotransmitter from 3.2 and Br on the membrane potential of a neuron expressing BrR
 - () Measure the intra- and extra-cellular concentrations of all the relevant ions before and after administering Br to a neuron expressing BrR
 - () Changing the extracellular concentration of relevant ions then administering Br to a neuron expressing BrR. Record which extracellular ion concentration change affects the change in membrane potential.

REFERENCES

Splawski I, Timothy KW, Sharpe LM, Decher N, Kumar P, Bloise R, Napolitano C, Schwartz PJ, Joseph RM, Condouris K, Tager-Flusberg H, Priori SG, Sanguinetti MC, Keating MT (2004). Ca(V)1.2 calcium channel dysfunction causes a multisystem disorder including arrhythmia and autism. *Cell* 119(1):19-31.

APPENDIX 3: Examples of Practice Problem Questions for a Small Upper-Level Class

The examples shown here would not all be in the same Practice Problem set.

1. Consider the following data:

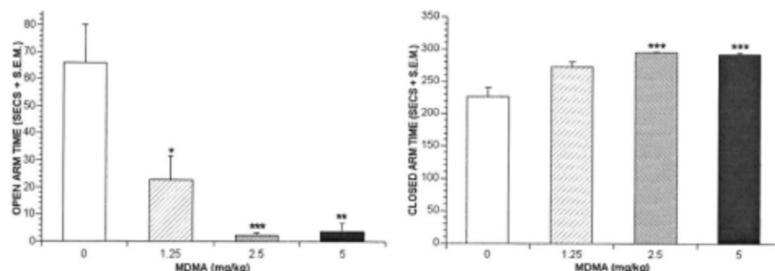


Fig. 1. Mean (+SEM) time spent in the open arms (left) and closed arms (right) of the elevated plus-maze by rats tested with MDMA or vehicle. * $P < 0.05$; ** $P < 0.01$, *** $P < 0.001$, relative to vehicle treatment, Mann-Whitney U -test.

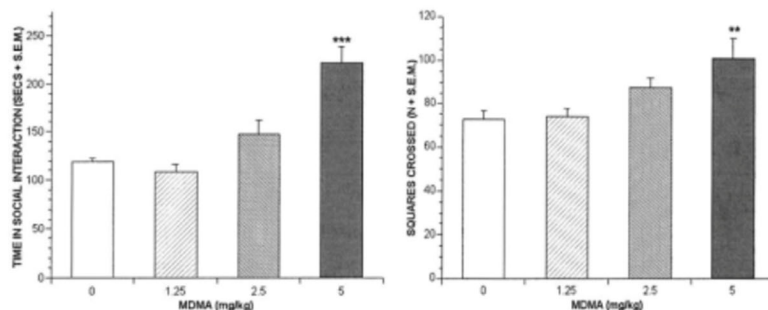


Fig. 2. Mean (+SEM) time spent in social interaction and mean (\pm SEM) number of squares crossed by rats tested with MDMA or vehicle. * $P < 0.01$, *** $P < 0.001$, relative to vehicle treatment, Bonferroni planned contrasts.

K.C. Morley, I.S. McGregor

(\pm)-3,4-Methylenedioxymethamphetamine (MDMA, 'Ecstasy') increases social interaction in rats
Eur. J. Pharmacol., 408 (2000), pp. 41-49

- What is the best conclusion from these data about how MDMA affects rats' behavior?
- What question(s) do you still have about the effects of MDMA after looking at these data?
- Propose an experiment to answer one of your questions. Be sure to state and justify your experimental question, model system, control group(s), experimental method(s). Draw a graph of what your data might look like.

2. For the next few questions, please reference the work done by Dr. Helen Mayberg, the leading researcher in deep-brain stimulation (DBS) for the treatment of depression.

- Dr. Mayberg's TedTalk: <https://www.youtube.com/watch?v=KwHFHV9Jfd8>
- Press release regarding recent research from the Mayberg lab: <https://www.mountsinai.org/about/newsroom/2019/long-term-follow-up-data-shows-deep-brain-stimulation-is-an-effective-treatment-for-treatment-resistant-depression>

- What are the relative advantages of traditional pharmacological treatments vs DBS for the treatment of depression? Name two advantages for each approach. (MAX 8 sentences, can be 4 listed points)

- b.) When thinking about the MECHANISM of how a treatment confers therapeutic benefit to depressed individuals, what are the similarities between pharmacological approaches and DBS? Name three similarities. (MAX three sentences or three listed points)

3. For the following questions, please reference the abstract below:

[Review](#) > [Neurosci Biobehav Rev.](#) 2016 Dec;71:657-670. doi: 10.1016/j.neubiorev.2016.10.017.

Epub 2016 Oct 20.

Pretreatment and prophylaxis against nerve agent poisoning: Are undesirable behavioral side effects unavoidable?

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Affiliations + expand

PMID: 27773692 DOI: [10.1016/j.neubiorev.2016.10.017](https://doi.org/10.1016/j.neubiorev.2016.10.017)

Abstract

The threat of chemical warfare agents like nerve agents requires life saving measures of medical pretreatment combined with treatment after exposure. Pretreatment (pyridostigmine) may cause some side effects in a small number of individuals. A comprehensive research on animals has been performed to clarify effects on behavior. The results from these studies are far from unambiguous, since pyridostigmine may produce adverse effects on behavior in animals in relatively high doses, but not in a consistent way. Other animal studies have examined the potential of drugs like physostigmine, galantamine, benactyzine, trihexyphenidyl, and procyclidine, but they all produce marked behavioral impairment at doses sufficient to contribute to protection against a convulsant dose of soman. Attempts have also been made to develop a combination of drugs capable of assuring full protection (prophylaxis) against nerve agents. However, common to all combinations is that they at anticonvulsant doses cause behavioral deficits. Therefore, the use of limited pretreatment doses may be performed without marked side effects followed by post-exposure therapy with a combination of drugs.

Keywords: Behavioral side effects; Enzymatic protection; Nerve agents; Pharmacological protection.

- a.) Pyrostigmine is a reversible AchE inhibitor. How would pyrostigmine pre-treatment ameliorate the effects of nerve agents, which are irreversible AchE inhibitors? Choose all that are true.

- pyrostigmine would occupy the binding site of AchE, such that a nerve agent would have a less severe effect
 pyrostigmine would permanently bind to AchE, such that AchE cannot be affected by a nerve agent
 pyrostigmine would block ChAT, reducing the amount of Ach available in the synapse, such that nerve agents have a reduced effect since there is less Ach present
 pyrostigmine would make someone sick and feel the effects of an overstimulated Ach system, so there would be no energy left to feel the effects once exposed to a nerve agent.

Briefly explain your rationale (2 sentences max):

- b.) Galantamine does not directly stimulate nAChRs. Instead, it increases the ability of the nAChR to bind to Ach. How would galantamine affect the dose-response curve of nAChR response vs Ach concentration?

- it would shift the curve to the left
 it would shift the curve to the right
 it would shift the curve up
 it would shift the curve down
 it would make the curve more steep
 it would make the curve more flat

Briefly explain your rationale (2 sentences max):

- c.) Given what we know about the unique nature of nAChRs, how does galantamine pretreatment confer protection against nerve agents? (3 sentences max, can also answer via a drawing if you prefer)
- d.) What behavioral effects would we expect from these pretreatments? Name three specific effects and explain why you would expect it given your knowledge of the cholinergic system. (Max 6 sentences or 3 bullet points with explanation)
- e.) Would nicotine be appropriate pre-treatment to protect against nerve agents? Why or why not? (max four sentences)
4. "Congenital insensitivity to pain" is a very rare genetic condition in which patients are able to perceive most sensory information but are unable to sense nociceptive inputs. Because of this, patients can sustain injuries without noticing, accidentally mutilating their own body. Patients often do not live to adulthood.
- a.) Patients with this disorder have a loss-of-function mutation in voltage-gated sodium channels that are expressed on nociceptors. Pick all choices that help explain how this mutation would lead to this unique sensory loss.
- the receptors within the pain pathways would not function correctly
 - the A δ and C fibers would not be able to send sensory information to the anterolateral pathway in the spine
 - the sensory-discriminative pain pathway would be silenced/reduced
 - affected neurons would not be able to fire action potentials
 - affected neurons would not be able to release neurotransmitter
- b.) Would patients with this disorder feel the effects of opiates?
- yes
 - no
- c.) Explain your reasoning (4 sentences MAX).
5. Read the following article: "What does dopamine mean" by Joshua Berke (Nature Neuroscience, 2018). ~4,700 words, expected read time of ~45 minutes. <https://www-nature-com.proxy.library.nd.edu/articles/s41593-018-0152-y>
- a.) Berke describes various techniques in this piece. For each method, give a one-sentence description of how it works/what information it gives and a one sentence description of how this technique contributed to our understanding of dopamine signaling.
- i. Microdialysis:
 - ii. Voltammetry (also called FSCV):
 - iii. Whole-cell electrophysiology (i.e., measuring frequency of firing in a cell):
- b.) How does Berke's description of the meaning of dopamine differ from the meaning of dopamine postulated in the 'dopamine hypothesis of addiction'? (four to eight sentences)
- c.) Berke does not mention addiction at all in this piece. How could his insights into the role of dopamine contribute to our understanding of drug-taking and addiction? (Six sentences max)

APPENDIX 4:

Rubric for Final Project: Creating a Case Study

You and a partner of your choosing from within your topical group will create a case study. The case study must include a coherent narrative, questions related to that narrative, the 'answer key' to those questions, and must cover two out of the three units from the class (Electrical Transmission, Chemical Transmission, Plasticity).

Final project – Total 110 points

20 points	Case Study Rough Draft (0, 10, 20 on effort)
10 points	Formatting, Grammar, and Spelling
20 points	Accuracy of content
20 points	Compelling and interesting narrative
40 points	Depth of content

****NOTE:** I will also ask you to assess your partner's contribution. If I determine that a partner relationship was unfair in any way, I reserve the right to adjust grades accordingly.

Formatting and content instructions:

- The audience for your case study is a sophomore Notre Dame NSBH major
- The case study should take the average Notre Dame NSBH major 30 minutes to an hour to complete.
- The case study should require critical thinking to complete.
- The case study should be no longer than 10 pages and no shorter than 4 pages. There is no 'right' length, as the length could be extremely variable depending on the story you want to tell, the use of images or figures, etc. The most important thing is that you cover the material in appropriate depth.
- Please use 12-point Ariel font, single spaced, with 1" margins on all sides. There should be a space between paragraphs. The Case Study should look visually pleasing and easy to read.
- Feel free to use figures, images, links to videos, etc. Please include the source of the image/figure directly under the figure.
- The main text of the Case study should be in black. You should also include answers to the questions you pose in your case study directly under the questions (as if you are answering the question). Your answers should be in red to indicate that it is the 'correct answer'. If there are multiple possible correct answers, describe what characteristics a correct answer would have.
- You can draw inspiration for your case study wherever you deem appropriate. I find it easiest to think about case studies as either "Medical" case studies or "Basic Science" case studies. In the former, the case study usually would start with symptom presentation and would lead towards thinking about how the biochemistry of the system contributes to disease presentation. "Basic Science" case studies are the opposite. In a 'Basic Science' case study, you could use an academic research article, graph, piece of data, or a problem about understanding mechanics of Molecular Neuroscience as the starting point, and generally moves toward apply that to a patient or population. You are welcome to blend these approaches or come up with something new entirely! You may also include other pieces of critical thinking that you think would be interesting/relevant to your case study (i.e., epidemiology, social justice, history, etc.).

Category	Top Marks	Low Marks
Formatting, Grammar, and Spelling	No or very few spelling or grammar mistakes. Follows formatting instructions. Pleasing to look at and easy to read. Answers are easily identifiable. Figures or images are cited.	Many spelling or grammar mistakes. Does not follow formatting guidelines. Visually confusing. Answers are not readily apparent.
Accuracy of content	All scientific information, including the answers, are accurate. The information that is related to the story you are trying to tell (i.e. creation of characters, hypothetical settings, etc.) can be made-up.	Scientific information is confusing, incomplete, misleading, or inaccurate.
Compelling and interesting narrative	The narrative is logical and interesting. There is a story arch (a beginning, middle, and end). There is/are clear problem(s) that must be solved. The questions in each section relate to the narrative portion immediately preceding.	Narrative is nonsensical, boring, disjointed, or missing. Questions seem to come out of nowhere and don't seem to relate to preceding section.
Depth of content	At least two of the three units are touched on in the case study (the three units are: Electrical Communication, Chemical Communication, and Plasticity). Completing the case study would take a ND NSBH student between 30 minutes – 1 hour to complete and would force that student to integrate and apply course material, potentially using help from the internet or notes. The case study sets the scene for a more in-depth understanding of Molecular Neuroscience content. Requiring the reader of the case study to draw from other classes or look up material outside of this course is okay.	The case study would take someone less than 30 minutes to complete or more than an hour to complete. Case study requires little critical thinking. Case study does not add much beyond what was explicitly covered in class.