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Sherlock Holmes and the Neurophysiologists: Unraveling the "Mystery" of Active Learning Success

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The Sherlock Holmes (SH) Project is a collaborative problem-solving activity in the form of a murder mystery that is a great resource for upper-level undergraduate courses in neurophysiology that emphasize synaptic transmission and neuromuscular communication. This project, originally described by Adler and Schwartz (2006), has become a central focus of the Neurophysiology course at Allegheny College, along with many complementary activities that work to reinforce the neuroscience material and skills such as creative experimental design and analysis. Active Learning research in advanced levels of undergraduate courses is rare in the pedagogy literature, and this paper adds to that body of research. Formal assessment of the course generally and the SH Project specifically support the hypothesis that the active learning pedagogical strategies employed foster a positive and successful learning environment.

Key words: active learning; Process Oriented Guided Inquiry Learning (POGIL); Neurophysiology; upper level; undergraduate course

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It is well documented that student-centered, active pedagogical strategies are more successful for all students' learning in undergraduate natural science classes, while more passive techniques such as pure lecture disproportionately disadvantage students from minoritized backgrounds (Theobald et al., 2020). Examples of such pedagogical approaches include problem-solving activities, research projects, and diverse methods of assessing student learning (oral presentations, written papers, in-class worksheets, discussions, in addition to more traditional exams). Providing students with a variety of ways to interact with class material increases engagement, application, and retention of knowledge (Haak et al., 2011; Freeman et al., 2014; Lombardi et al., 2021). Courses that involve elements that help to build a positive environment, such as structured organization, thoughtful collaboration, and frequent constructive instructor feedback help students to learn, while decreasing their stress and anxiety (Cooper et al., 2018; Downing et al., 2020).

The Sherlock Holmes Lab was developed by Adler and Schwartz (2006). It is an extended thought-experiment-based activity intended for upper-level neuroscience undergraduate courses covering electrophysiology and synaptic transmission. Students are presented with an introductory narrative based loosely on the structure of Sir Arthur Conan Doyle's famous detective novels, "The Case of the Four Toxins", in which some number of victims (equal to the number of 2-4 member student groups in the class) have been murdered by poison resulting in death from respiratory failure secondary to paralysis of the muscles of the chest and thorax. A vial of toxin was conveniently left at each crime scene. The police deduce that all the murders were committed by one person employing a single poisonous substance, while Sherlock Holmes hypothesizes that the same apparent results could be produced in different manners based on the function of various elements of the neuromuscular junction. The job of the intrepid neuroscientists is to discover specifically how their victim's toxin acts on the neuromuscular system by proposing experiments (in a written format) to test various questions about the toxin's actions. The instructor supplies the data the students' theoretical experiments would produce. The cycle of experiment proposal and data analysis continue until the students have sufficient evidence to explain their toxin's mechanism.

This project complements a neurophysiology course for a variety of reasons. First, experimental electrophysiology is highly technical and challenging. Mastering the techniques sufficiently for true data collection to occur takes a long time, and often more time than is practical for a typical undergraduate course. While some students may be able to conduct hypothesis-driven mini experiments within the structure of such a course, there is often not sufficient time for all students to be able to ask truly novel and thought-provoking questions. Using a thought experiment model like the Sherlock Holmes Lab gets around the need to physically master graduate-level techniques, not to mention the need for a vast array of expensive equipment and reagents. Therefore, another advantage of the SH Project is the fact that it has zero budgetary burden. It becomes practical for all students to get to work with the experimental design and data analysis part of laboratory research in a reasonable amount of time.

This paper represents the collaborative effort of an Allegheny College professor (LBF) and two former students. When first person is used, it is the voice of the lead author, who developed and teaches the Neurophysiology course. One Allegheny alumna author (MS), who took the course before the formal assessment process was employed, provided an account of her own experience. The other alumna author (MSR) was a neuroscience student who did not take the course but could speak to the organization and strategies from an outside perspective. All authors contributed to the pedagogy research, discussions of strengths and challenges of the SH Project, and ideas for future directions.

Description of SH Class Sessions

Neurophysiology 405 at Allegheny College is an upper-level course (for junior and senior undergraduate students) that blends both cellular and molecular neuroscience with the physiology of the nervous system. We discuss the structure and function of ion channels and receptors, and how signaling works in the nervous system. Weekly laboratory sessions focus on electrophysiology. Upon successful completion of this course, students are expected to be able to demonstrate the following (i.e., Student Learning Outcomes or SLOs): (1) a detailed understanding of signal propagation, ion channels, receptors, and synaptic transmission; (2) mastery of some basic electrophysiology techniques; (3) an understanding of experimental design, trouble shooting, and data analysis in neurophysiology; and (4) the ability to read critically and think independently about cellular and molecular neuroscience. The SH Project directly addresses all SLOs except number two, which is addressed by the lab portion of the course.

In the Neurophysiology course at Allegheny College, students are immediately drawn into the murder mystery project and have found the approach to be a two-way street in terms of learning neurophysiological concepts and applying them within the project and relating to the other class topics and activities. I have made a number of changes and additions to the original great idea detailed by Adler and Schwartz, such that the project has become central to my teaching of this course. For example, the project is conducted over the course of the entire semester, rather than the six-week module format described originally. I use a “flipped” model, where the majority of the active work is conducted within four of our three-hour lab sessions, instead of being assigned to be done outside of class. Although the flipped classroom model does not necessarily significantly improve student learning in and of itself (Lombardi et al., 2021), the process works well for the SH Project because it allows the instructor to actively engage the students in discussion as they work through experimental design- from developing a research question and hypothesis to the explanation of an appropriate technique and animal model, addressing SLO 3. The understanding of neurophysiology (i.e., SLO 1) develops from work among peers and with the faculty, involving direct interaction with data, hands-on experiences (lab- i.e., SLO 2; and SLO 3), and reading the existing literature (addressing SLO 4). This combination of approaches is well supported in the literature (Haak et al., 2011; Theobald et al., 2020 and Lombardi et al., 2021) as being successful with respect to student learning.

The Sherlock Holmes Project is itself a deep dive into the structure and function of the neuromuscular junction (NMJ), addressing SLO 1. The NMJ is the best understood synapse in the vertebrate nervous system, one of the most accessible synapses, and has served as the basis for learning about other synapses. Therefore, it seems appropriate to devote a significant amount of time and energy for students to learn about it in a neurophysiology course. The time devoted to the NMJ in this project frees up space in the rest of the course for other important topics and activities focused on cellular/molecular neuroscience.

The SH Project Introduction is the first lab session devoted to the project, which is generally the second lab meeting of the semester. The first lab meeting of the semester is focused on introducing electrophysiology equipment (e.g., amplifiers, electrodes and manipulators), and an overview discussion of basic electrophysiology techniques. In the SH Introduction period, we discuss the introductory narrative (Supplementary Material 1) document, which presents the story, goals, and timeline for the project across the semester. The document also explains the introductory assignment. Students in their lab groups research and write a brief overview of each of the following topics: the structure and function of the NMJ, extracellular recording, two-electrode voltage clamp, patch clamp, and a topic of their choosing that they think will support the project. The Google document they create in this opening session (and share with the instructor) serves as the running lab journal for the project, in which all notes, proposals and data are recorded.

The second SH lab session is focused on developing the students’ first experimental proposal (Supplementary Material 2). The premise is that they have a vial containing mystery toxin that killed their victim, and they have to “conduct” experiments on the NMJ to figure out how the toxin could cause paralysis. We have a meta-discussion of experimental design and different strategies for developing an effective research question- e.g., when a broad question versus a more narrowly focused question is appropriate. The students discuss options among themselves and then with the instructor. Once they have settled on a reasonable experimental question, they do research (in papers and textbooks) to figure out what techniques and animal models they should use. The students also think through what kind of results they might expect and what they would learn from them. They write their experimental plans and expected outcomes into their SH Project Journal documents.

In preparation for the third SH lab session, the instructor creates data to suit the experiments the students have proposed according to the identity of their mystery toxin. I aim to create figures that are close to what one would see upon actually conducting the experiment. Therefore, the first step for SH Day three is for the students to analyze their data and figure out whether their research question(s)/hypotheses were supported. Once they figure out and summarize what they have learned (or not), they develop a second experimental question/hypothesis and accompanying proposal as the next step toward identifying the lethal toxin’s mechanism. With a combination of strategic experimental planning and a little luck, many groups can determine the mechanism of their mystery toxin in two rounds of proposal and data-gathering. Some groups need or want to engage in an optional third round of "experimentation" (written outside of class) to confirm the toxin's mechanism.

The fourth and last SH Project lab session is devoted to data analysis and preparation of the final products of the Sherlock Holmes Project: a group presentation and write-up. Rather than taking the form of formal scientific talks/papers, the students are required to incorporate a creative element in order to tell the story of their victim, the details of the experiments they conducted and the data they received. To emphasize its importance, this creative aspect is one of the elements included in the rubric used to assess the final products (rubrics are available upon request). They conclude by predicting a possible toxin used in the crime, based on a thoroughly described mechanism of action they propose killed their victim. These projects most often incorporate a fictional narrative that shifts the scientific discussion from the world of solely technical jargon and acronyms to plain English explanation of what they did and what they discovered, which emphasizes scientific communication skills. The products have taken myriad forms over the years and are great fun for all involved such as plays, movies, board games and scavenger hunts, to name a few. The projects also encourage the students to use their brains differently than they typically might in a natural science course, which is yet another strategy to reinforce material.

The introductory assignment, as well as the experimental proposals can be written in their entirety within the three-hour lab sessions allotted. The only work the students do outside of the class sessions is typically to support the creative aspect of the project (e.g., filming a video in a specific location, gathering props) and/or to write an optional third experimental proposal.

Active learning strategies are most effective in helping students learn when they are used consistently and in a diverse range of formats (Theobald et al., 2020). Therefore, I have incorporated a variety of activities and assignments that complement the SH Project directly and reinforce the value in learning how to read about, design and analyze neuroscience experimental work. Perhaps most directly related and most important are the physical electrophysiology labs in which students learn several different recording techniques (such as extracellular recording, intracellular sharp electrode recording and two-electrode voltage clamp). The physical lab experiences inform the *in silico* ones they design and ideally help to stretch their imaginations and research skills to appreciate what questions can be pursued by studying electrical signals in biological preparations.

Other class activities that help to reinforce experimental design and interpretation include data interpretation/presentation, drawing synapses, explaining processes such as synaptic transmission with specific mutations (in writing and orally), and discussions of primary literature. I also make frequent use of multiple choice questions presented within the lecture slides, using voting cards (i.e., low-tech clickers- colored cards that can be folded to display A, B, C, or D), which can be used to assess student understanding and/or as the basis for in-class discussions. Students are also required to do short "Drug of the Week" presentations on a pharmacological compound (of their choosing) that interacts with the nervous system, with an emphasis on mechanism of action. These activities along with the SH Project share an emphasis on collaboration and allowing students the space and time to construct their own meaning from the class lecture material and reading assignments.

When using the broad and often vague term of "active learning", it is important to 1) define what specific activities one is using and 2) formally assess the course elements to help support the growing body of evidence-based pedagogical research and share beneficial resources among the community of educators (Lombardi et al., 2021). To support the involvement of the activities and projects described in this introduction, I conducted a formal assessment in order to test my hypothesis that the Sherlock Holmes Project is an effective way to learn advanced neurophysiology on its own, but especially in combination with other topics and activities to generate a positive learning experience. This course has been enjoyable and successful, supported by both anecdotal and quantitative data.

MATERIALS AND METHODS

Subjects

The subject population was Allegheny College upper class students (mostly juniors and seniors). The formal assessment consisted of surveys that were sent to the students in two successive offerings of the Neurophysiology course: Spring 2022 (22 students) and Spring 2023 (7 students). Students were told their participation was entirely voluntary, and they would receive no penalty for not participating. In order to preserve anonymity in the responses, the subjects generated their own unique identification code, which enabled pre- and post-survey comparisons, without attaching names to the data. A total of 27 students completed the initial pre-survey. Only data with both pre- and post- versions were included in the analysis, resulting in 18 total subjects. The study was approved by Allegheny's Institutional Review Board.

Assessment Instruments

The pre-survey (Supplementary Material 3) was administered as a Google Survey in the first week of classes, before the introduction of the Sherlock Holmes Project. It consisted of 5 questions asking about their level of understanding (on a likert scale where 1 indicates Disagree/Not at all and 5 indicates Agree/Very much so) with respect to Neurophysiology as a field (SLO 1), reading scientific papers with Neurophysiological techniques (SLO 4), the scientific experimental design process (SLO 3), experimental design as a creative endeavor (SLO 3) and how to analyze and solve a scientific problem (SLO 3/4). There was also a question as to whether they had any prior experience with experimental neurophysiological techniques and/or equipment. The post-survey (Supplementary Material 3) was administered as a Google Survey in the last week of classes, after the conclusion of the Sherlock Holmes Project. In addition to the same 5 likert scale-rated questions as in the pre-survey, there were 5 additional questions asking them to rate whether they enjoyed the project, whether it helped them understand neurophysiology (SLO 1), and whether it helped them understand 3 specific elements of the experimental design process (i.e., research question development, that an unsupported hypothesis is not necessarily bad news, and how to analyze experimental results; SLO 3). There were also two open-ended questions asking what suggestions they had for the course and what other elements of the course were supportive to their learning.

Data Analysis

The scores from all the likert scale questions were entered into the JMP statistical software to produce bar graphs displaying the descriptive statistics. The sample size was 18, and standard error of the mean was used to assess variability of the data. Comparisons of the pre- and post-scores of the 5 shared questions were performed with individual two-tailed paired t-tests at a significance level of 0.05 using an online calculator (https://www.socscistatistics.com/tests/ttestdependent/default2.aspx). Individual t-tests were used because the survey questions are independent of one another.

Educational materials supporting the SH Project (and this Neurophysiology course) are available on request via email with the corresponding author (LBF).

RESULTS

There was an increase in mean score from pre-survey to post-survey in all the shared questions, demonstrating an increased level of understanding in neurophysiology and experimental approaches (Figure 1). Paired t-tests showed that 4 questions had statistically significant increases ($p < 0.05$; Table 1): understanding of neurophysiology as a field, reading scientific papers, viewing experimental design as a creative process and analyzing experimental data. Only the question about the scientific experimental design process did not show a significant increase from pre- to post-survey scores.

Analysis of the Sherlock Holmes Project-specific question demonstrated an overwhelming positive response (Figure 2). The mean response ranged from 4.7 to 4.9, indicating the students enjoyed the project and that it helped them to understand neurophysiology generally and experimental elements specifically.

The qualitative data from the open-ended questions revealed that the students felt that many of the course elements were helpful to their learning. For example, in answer to the open-ended question about which class elements specifically helped them to learn about experimental neurophysiology, a large majority of students in the subject pool (10 out of 18) mentioned the Sherlock Holmes and/or the hands-on laboratory elements (i.e., SLO 2). Seven students listed the class activities and/or worksheets, and 4 named the study guides and/or review sessions as being supportive of their learning. Thirteen out of the 18 students indicated they had no suggestions for improvements to the course.

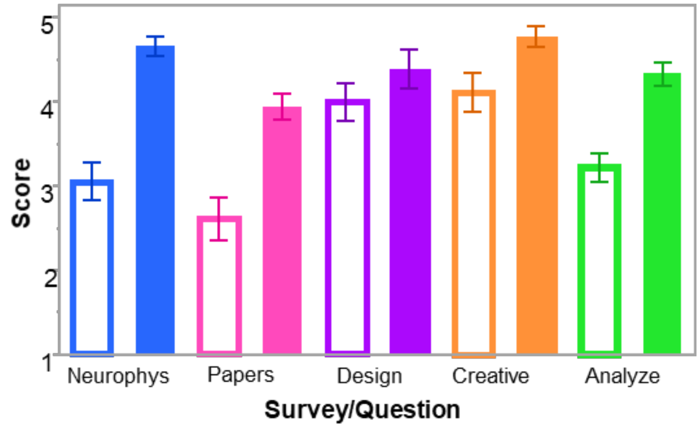

Figure 1. Comparison of Pre- and Post-Survey Question Scores. There were 5 questions that appeared in both the pre- and post-versions of the survey (see Methods for more detail). Open bars represent the pre-survey means; solid bars represent the post-survey means. Error bars are standard error of the mean; n= 18.

Question Subject	t value	p value
Neurophys	5.50	0.00004
Papers	4.41	0.00038
Design	1.16	0.26
Creative	3.37	0.0037
Analyze	4.89	0.00014

Table 1. T-test Results: Comparison of Pre- and Post-Survey Questions. Paired t-tests revealed that there were statistically significant increases from pre- to post-survey on 4 out of the 5 questions. There was no statistical difference between pre- and post-survey scores on the question about the experimental design process (Design- in red). See methods for more details on questions.

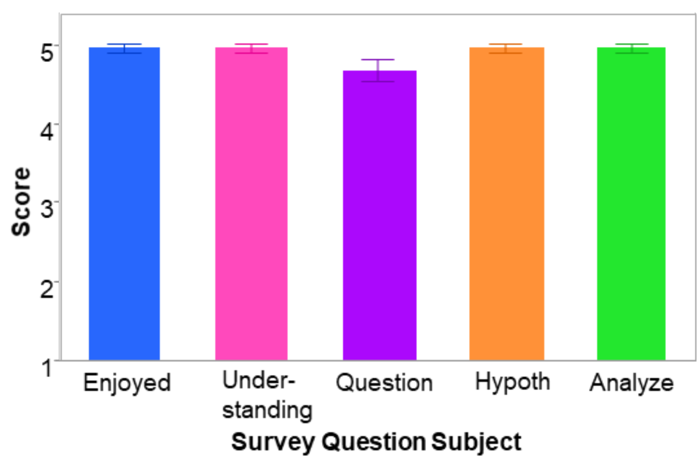

Figure 2. Overall SH Project Experience Post-Survey Question Scores. The scores of the 5 questions unique to the post-survey about how the students experienced the SH Project and how it impacted their learning (see methods for more details). Error bars are standard error of the mean; n= 18.

The only concrete suggestions offered in the surveys concerned timing of activities (e.g., starting the SH Project before doing any hands-on experiments) and a request for more lab experiments (notably this suggestion was from the class that was not able to conduct as many experiments as typical for the course due to Covid-19 panedemic-related supply chain issues that prevented the timely shipment of crayfish). Only a single survey respondent had any prior exposure to any experimental neurophysiological technique, and this experience was a demonstration of electroencephalogram recording shown to the student in a class.

DISCUSSION

The data from the assessment indicate that this neurophysiology course generally, and the Sherlock Holmes Project specifically, are successful in helping students learn about neurophysiology as a field, reading scientific papers involving neurophysiology techniques, discovering the creative aspect to experimental design and conducting data analysis (Figure 1). The students surveyed overwhelmingly enjoyed the Sherlock Holmes Project and felt it contributed significantly to their learning in the course (Figure 2). It cannot be ignored that the subject pool was small, and there could be a degree of self-selection occurring such that students who enjoyed the class/project were more likely to complete both survey intervals. It is also likely that the survey respondents were the students who engaged with the class and the project to the greatest degree. Therefore, although caution must be used in generalizing the results of the assessment, the perspective of this subject pool is still valid and important.

The question about the experimental design process was the only one on the paired surveys that did not show a significant increase from pre- to post- iteration (table 1). This lack of difference is likely due to the fact that experimental design is a process that is explored in many other courses in Allegheny College's natural science curricula, and therefore this element was likely not new to the majority of the students, thus explaining why the score for this element was so high on the pre-survey. Further, the project might have been too difficult if the students had never had any prior experience designing experiments. In the future, one way to potentially increase students' learning about the experimental design process might be to incorporate more meta-teaching to emphasize that the process they are using to develop their hypothetical experiment proposals could be directly applied to actual laboratory experiments given the appropriate time and resources. I also intend to continue the assessment process in future iterations of the course, and so it will be possible to see whether the data change with an increased sample size and as the course continues to evolve.

Qualitatively, I can report that the environment in the class is always energetic and positive on the Sherlock Holmes Project days, and the project and related activities have absolutely contributed greatly to my own enjoyment of teaching the course. The success of active problem-solving activities such as the ones used in this course (Figure 2) are well documented as universally supporting student learning in STEM courses (Freeman et al., 2014; Theobald et al., 2020). There are, however, specific elements of the broad range of active learning activities that have been recommended in the literature. For example, well-structured activities that involve collaboration among peers and frequent feedback from the instructor have been particularly helpful to student learning (Haak et al., 2011; Lombardi et al., 2021). The SH Project itself is a form of Process Oriented Guided Inquiry Learning (POGIL) in which students work in groups to solve a problem using the iterative process of posing questions (experiments), analyzing data and refining their understanding. This process also models the typical path of scientific discovery, further reinforcing the scientific method (Lombardi et al., 2021) and allowing students to incorporate their increasing body of knowledge about neurophysiology as the semester progresses.

During the in-class working sessions for the Sherlock Holmes Project, there is a lot of discussion among students and also with me. The flipped classroom approach is meant to maximize the active working time between professor and students, and also to minimize the amount of group work outside of our class meeting times. The most significant challenge for the students appears to be developing the first research question, which comes after the introductory session. The students commonly gravitate to more narrowly focused and complicated questions (e.g., testing individual channels or proteins) until I steer them to simpler more broadly focused questions (e.g., does the toxin produce spastic or flaccid paralysis; or is this a presynaptic or postsynaptic mechanism). We typically have discussions about the merits of designing a research question where any experimental result gives information (i.e., a "negative" result or lack of significant difference between control and experimental conditions is as informative as a "positive" result). The next step after articulating the research question is to plan out the methods, necessitating that the students search for papers, consult the textbook and/or review the lab activities they have performed. For example, in years that we can conduct the Crawdad (Wyttenbach et al., 2014) lab activities involving recording from crayfish motor nerves and muscle fibers, students often see how those very techniques (albeit in a vertebrate animal model) could be directly applied to test their "mystery toxin". Upon receiving their "synthetic" data, the students get to reinforce their developing skills at interpreting current or voltage vs. time traces. Creating data in this manner, in addition to resembling an "illicit" fun activity, also provides a learning opportunity for the instructor. The subsequent rounds of experimental development and analysis get progressively easier for the students; demonstrating the benefits of practice in an academic setting (Haak et al., 2011).

This process we follow in the SH Project is a direct application of the scientific method, allowing the students to determine their own path of discovery. Therefore, it makes sense that the project is successful in helping students to learn (Figure 1) about the creative aspect of experimental design, reading scientific literature and analyzing data. The extension of the project to encompass the entire semester allows it to dovetail with the rest of course, leading to increased learning about neurophysiology in general. The questions incorporated into the assessment instruments directly represent three out of four student learning objectives for the neurophysiology course (SLOs 1, 3 and 4- see introduction for specific wording). SLO 2, pertaining to laboratory experiments is referenced in one of the open-ended questions of the post-survey. Therefore this assessment provides evidence that the course as a whole has a positive effect on neuroscience students at Allegheny College, and supports their learning in addressing the course SLOs.

The SH Project is most successful (and enjoyable) when it can be coupled with in-person laboratory experiences. The Covid-19 pandemic provided an undesired “control” group- i.e., a year when laboratory experiments were not possible. While the students still succeeded at solving the mystery, and appeared to enjoy the process, it was clear that the absence of the hands-on experiments had a profound detrimental effect. Many of the students in the Fall 2020 iteration of the course (not included in the formal assessment) had never set foot in a physical college laboratory. They had never mixed chemicals, run physical equipment, and had never handled experimental animals. They could not visualize any of the techniques described in the papers they read. That semester required much more explanation on my part, and using pictures/videos as a substitute for the live experimentation. While it is definitely possible to manage a Sherlock Holmes Project under these conditions, it produced a dramatic comparison to see how much easier and more practical the entire process is when the laboratory exercises and the SH Project create a two-way street of knowledge and skill reinforcement.

The emphasis on creativity and breaking away from a traditional “IMRAD” (Introduction, Methods, Results and Discussion) lab report format puts an emphasis on explaining neurophysiological experiments in the students’ own words, in a way that highlights some of their talents outside of the neuroscience classroom. While some students immediately embrace the creative element of the project, others find themselves being drawn out of their comfort zones.

In the pedagogical literature, this type of assessment product that breaks away from more typical academic papers and exams is referred to as the “Unessay” (O’Donnell, 2012). Although originally more common in the Humanities disciplines (Sullivan, 2015), the use of this creative approach has become more common in the sciences as well (Aycock et al., 2019; Goodman, 2022; Wood and Stringham, 2022). With the freedom to choose how to finish their projects, the students all eventually find a means they can enjoy, further adding to the learning advantages of the project (Munakata and Doebel, 2021). I have been continually impressed by the students’ creations and ideas: there have been many dramatic portrayals of student-written narratives, board games, scavenger hunts and even an interactive choose-your-own adventure- type presentation.

The quantitative and qualitative data support the success of this course organization with the SH Project and complementary activities playing a major role. Therefore, in the future, it would be beneficial to further enhance the active learning aspects of the course to reinforce the successes and continue to improve the students’ experience. Specific modifications to the SH Project could include, for example, a model where a group of students, rather than the professor, provide the data for the experiments on the mystery toxins proposed by their peers. An additional element could be the creation of (modern day) backstories for the murder suspects to explore what practical (and nonlethal) uses there might be for the toxins, and also demonstrating professional directions for neuroscience majors with an interest in pharmacology. Further ties to the “non Sherlock Holmes” part of the course could be in the form of discussions of how antidotes to the mystery toxin might exert their effects (paralleling our existing discussions around drug design for diseases, such as Parkinson’s). In addition, students could write practice exam questions based on their own SH Project investigations, after which the groups could exchange questions and answer them.

The SH Project provides the opportunity for active application and reinforcement of much of the knowledge and skills used in other areas of the course, such as structure and function of the neuromuscular junction, the synaptic transmission process with and without pharmacological manipulation, interpreting current and voltage traces and reading scientific literature. The Neurophysiology course organization described in this paper, in which the SH Project plays a central role, is a form of what Theobald et al. (2020) describe as a “high intensity” active learning, which has been shown to improve all students’ learning and to narrow the achievement gap between over- and underrepresented student groups. The data suggest that this project and complementary activities support attainment of the course learning objectives while simultaneously creating a fun and supportive environment.

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