ARTICLE
A Course-Based Research Experience Using the Allen Brain Map: From Research Question to Poster Session

Jim Ryan[1], **Kaitlyn Casimo**[2]
[1]Biology Department, Hobart and William Smith Colleges, Geneva, NY 14456; [2]Allen Institute, Seattle, WA 98109.

San Francisco, CA A major challenge in implementing course-based undergraduate research experiences (CUREs) is for students to collect enough data for a robust analysis given the time and equipment available. One approach to mitigating this constraint in a CURE is to use massive open datasets such as those from the Allen Brain Map, produced by the Allen Institute for Brain Science. We describe a multi-week CURE module in which students generate a research question that can be addressed using at least two datasets of the Allen Brain Map, perform their analysis, and produce a conference-style poster detailing their findings. This article includes an adaptable CURE assignment, tutorials introducing students to selected datasets from the Allen Brain Map, and a summary of student outcomes.

Key words: CURE; Allen Institute; neuroanatomy; gene expression; poster presentation; student research

Course-based undergraduate research experiences (CUREs) can provide students with valuable practical skills in data collection, analysis, and presentation (Laursen et al., 2010; Makarevitch, et al., 2015; Shortlidge et al., 2017, and references therein). However, collecting sufficient quantity and quality of data for a robust project can be a challenge given constraints on lab access, available equipment and materials, and time. All of these restrictions are exacerbated under distance learning or socially distanced in-person conditions (Chandrasekaran, 2020; Ramos, 2020; Vasiliadou, 2020).

Using open online datasets as the basis for such student projects can enable students to concentrate on the elements of a research project that are feasible with limited or nonexistent lab access and facilities. Undergraduate neuroscience faculty can provide a meaningful research experience using the open resources from the Allen Brain Map (brain-map.org) as the basis for independent, student-led research projects spanning a full semester of work (Chu et al., 2015). The Allen Brain Map provides access to the open data resources and tools developed by the Allen Institute for Brain Science, a nonprofit biological sciences research organization that shares all of its work freely for use in research (Ramos et al., 2007; Jenks, 2009; Gilbert, 2018). These resources can also be leveraged to provide students access to types and quantities of high-quality data that would not otherwise be available to them (e.g., human tissue samples, whole-brain, whole-genome gene expression atlases).

Here we describe a month-long CURE-based curriculum module that can be used for either in-person or remote learning and directs students through an independent research project, from developing a research question to presenting their work to their classmates. Students use the data and resources at the Allen Brain Map portal to develop a research question that uses at least two different types of data, document their methods and findings, and present their work in a standard conference-style poster that introduces them to a common format of sharing work within the scientific community. The individualized nature of the research-based assignment and professional-style poster report can facilitate opportunities for students to pursue wider dissemination of their research beyond the course, deepening their relationship to the research work (Seraphin and Stock, 2020).

COURSE OUTINE

Biology 340 Neurobiology is a junior/senior-level undergraduate neurobiology course taught by author JR at Hobart and William Smith Colleges. The course was taught remotely after mid-March of 2020 due to Covid-19 and was taught in-person (with mask and class spacing restrictions) in the fall of 2020. Class size is typically 24 students, with two lab sections of 12 students each week. It uses experimental lab approaches such as electrophysiology and optogenetics in the first part of the semester and culminates with a four-week module utilizing Allen Brain Map open data resources (brain-map.org).

The learning objectives of the Allen Brain Map exercises were:

1) To understand the structure and function of mouse and human brains.
2) To learn about connections between important neural pathways in the brain.
3) To learn about gene expression patterns in the brain.
4) To use the Allen Brain Map resources along with the primary literature to develop research questions.
5) To gain experience presenting research in oral and poster forms.

At the beginning of the module, students are given the project assignment (Appendix). They are to develop a research question using Allen Brain Map resources, find and read key scientific papers on their topic, create a scientific poster, and present the poster orally to their peers in the course and others from the department who wish to attend.

The choice of research question is up to the students.

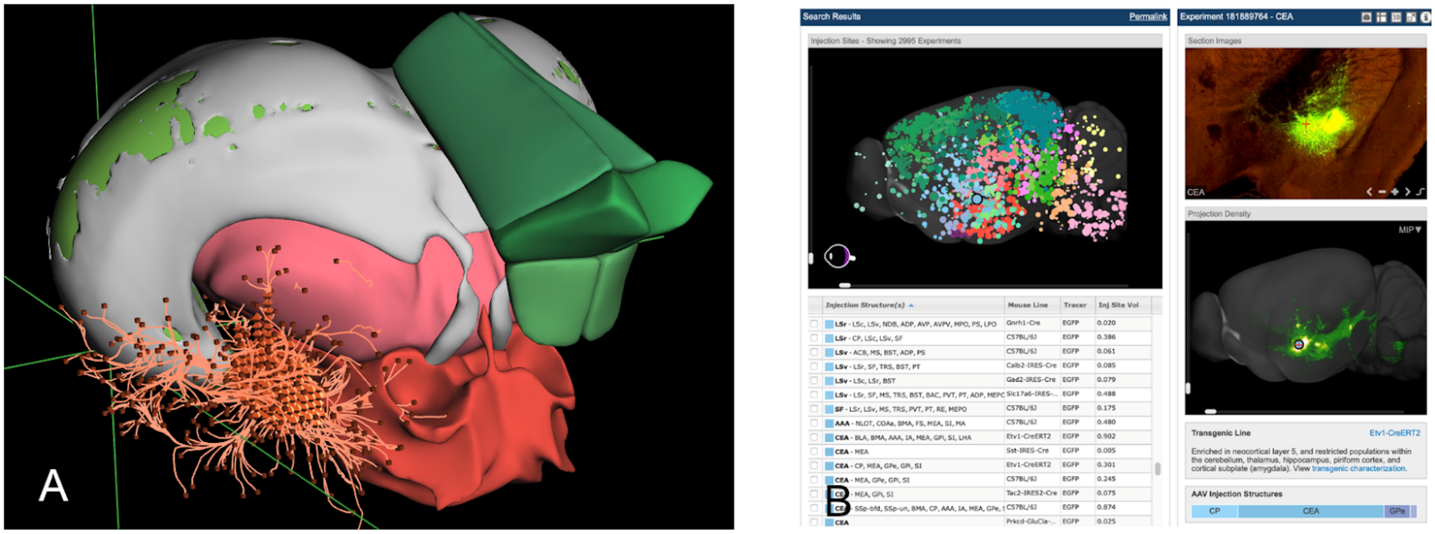

Figure 1. Data visualizations from the Allen Mouse Brain Connectivity Atlas, one of the resources students explore in the tutorials and may choose to use in their independent project. *(A)* Screenshot from the web-based Allen Brain Explorer of a 3D reconstruction of a portion of the mouse brain (solid shapes) with one virtual tractography of axonal projections (orange lines). *(B)* The search results window for one tract tracing experiment from the Mouse Brain Connectivity Atlas.

However, their project must use at least two different data resources from the Allen Brain Map. The topic must be approved by the instructor well in advance of the presentation and no two students may choose the same topic. Students are prompted with some general types of questions they may consider. For example, they might ask:

- What groups of genes are expressed in a specific brain region and why would that pattern of expression occur?
- Where in the brain is a specific gene of interest expressed and how can you explain that pattern?
- How does brain connectivity follow what we know about the function of those regions?
- What genes are correlated with a specific neurological or disease state?
- How does the pattern of gene expression change over developmental time?
- How much variation do we see in neuronal cell types in a specific brain region and in what way (properties) do they vary?

Prior to the first session in the module, students are required to view two videos that provide an overview of the Allen Institute for Brain Science mission and to read Gilbert (2018), an overview of the Allen Mouse Brain Atlas's applications for education, including sample research questions and an overview of the methods used in its development. In addition, they are given a pre-lab assignment that uses parts of the "Building Blocks of the Brain" lesson developed by KC at the Allen Institute (https://alleninstitute.org/about/education-outreach/).

In the first lab session, students receive an introduction to the methods and tools used to build the Allen Institute for Brain Science mouse brain reference atlas (Gilbert, 2018). Students then complete the first tutorial (Figure 1) using the Allen Mouse Brain Connectivity Atlas (Supplementary Material 1). Each tutorial walks students through how to use a particular atlas or database and asks them to complete several questions to check their understanding. After completing the tutorial students are asked to brainstorm potential research questions that might utilize this 3D resource. The second tutorial (Supplementary Material 2) introduces the gene expression data. This lab begins with an overview of how gene expression data are collected, analyzed, and displayed. After completing this tutorial, students are asked to find a gene of interest and explore it on the National Center for Biotechnology Information (NCBI) website (https://www.ncbi.nlm.nih.gov) and view its expression in the mouse brain. The third tutorial (Supplementary Material 3) introduces the Allen Human Brain Atlas (Figure 2). The introduction details how the human brain data were acquired using microarray to estimate relative quantity of RNA transcript on a region-by-region basis, z-scores, and heat maps. Students then complete the tutorial questions and use the remaining lab time to work on their own projects. Students must have an approved research question/topic by the end of the second week of the module, which gives them two weeks to complete their research, construct their poster, and hone their oral presentation. A sample of some of the research topics from fall 2020 is presented in Table 1.

Students were given a PowerPoint poster template to modify, guidelines for creating an informative and visually appealing poster, hints for effective public speaking, and an assessment rubric. The guidelines help students focus on the elements of a standard scientific conference poster/presentation. During the final week of lab, each student presented their research poster orally during the lab period. They were expected to talk for 12-15 minutes

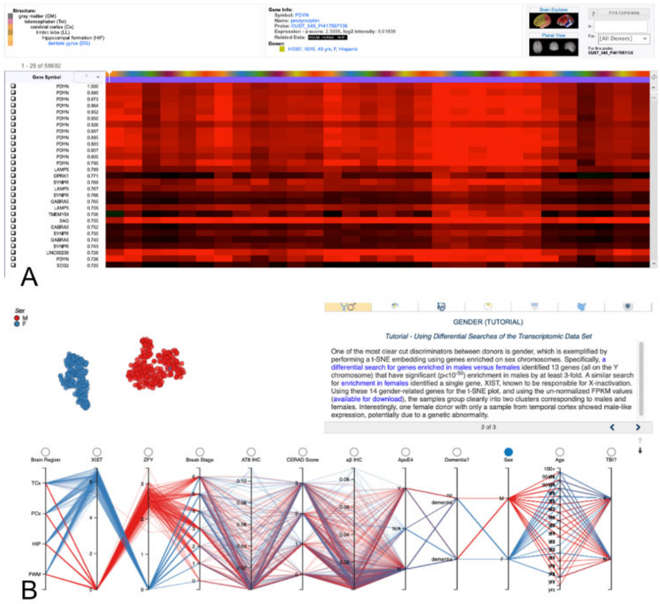

Figure 2. Data visualizations from two resources students explore in the tutorials and may choose to use in their independent project. *(A)* Screenshot of the heatmap data for the human prodynorphin gene (PDYN) from the Allen Human Brain Atlas. *(B)* Screenshot of the Allen Brain Map tutorial from the Aging, Dementia, and Traumatic Brain Injury dataset.

followed by a 2-5 minute question and answer period. Posters were projected onto a large screen and students could zoom in on the parts of the poster as they talked. For remote teaching, presenters shared their screen with the poster as they spoke. Students who were not presenting needed to develop a question for the presenter so that they actively participated in the process. Instructors may also find it useful to have non-presenting students assess their peers' presentations using the same rubric as the instructor, but not assign a "grade."

STUDENT OUTCOMES

No quantitative assessment was conducted due to the small sample size and disruptions due to COVID-19. However, students were asked to provide comments on each of the lab modules (electrophysiology, optogenetics, and Allen Brain project). These informal assessments at the end of the course revealed that students benefited and generally enjoyed these multi-week research projects. One student commented that, "I spent a lot of time researching the literature and accessing Allen Brain Map data for my research project, and I learned a lot about my topic." Another student added, "I felt like a real neuroscientist searching for answers to novel questions."

However, several students commented on being somewhat overwhelmed by the amount of data available on the Allen Brain Map portal. For example, one student commented that, "The hardest part was trying to come up with a good research question because there was so much data to choose from." The same student later added, "having to research my own topic gave me a sense of ownership and I felt proud of my final poster presentation."

Sonic Hedgehog Signaling Pathways in the Developing Brain
"Centriolopathy": ASPM, WDR62, and CPAP's Role in Microcephaly
How Olfaction Contributes to the Creation of Episodic Memories
Drug Addiction and the Mesolimbic Dopamine System
CRHR1 and Stress in Humans and NHP
The Role of *COMT* and *AKT1* Genes in Symptoms and Development of Schizophrenia
Location and Function of the 5-HT_{1B} Receptor
DAT-1 Role in the Substantia Nigra and ADHD
Two Critical Genes, BDNF and SYNE1, are Associated with the Increased Risk of Developing Bipolar Disorder (BD)
Endogenous Opioids, Exogenous Opioids, and Addiction Related Genes
Input of Theta Oscillations and Expression of CaMKII Isoforms in Hippocampal Formation
The Contribution of Gene, GRIN2A, in the Onset of Schizophrenia: The Glutamate Model Approach
Investigating the Expression of JOSD1 Gene in Relation to HTT Gene Significant to Huntington's Disease
FOXP2 Role in Language Development and Comprehension
Amyotrophic Lateral Sclerosis: Mutant $SOD1^{G93A}$
Hippocampal Formation: Patterns of Gene Expression and Effects of Aging
Examining the Expression of *GAD1* and its Association with Neurodevelopmental Psychiatric Disorders

Table 1. List of some of the titles for the Allen Brain Map poster project in fall 2020.

Some students reported technical difficulties with the web-based 3D Brain Explorer used to visualize the Allen Mouse Brain Connectivity Database, such as crashes or slow responsiveness. This can be a problem for students with computers that have older processors or limited RAM; potential solutions include using institutional computers if available or trying a different web browser. However, even students with these technical difficulties rated the project highly. Further, all other datasets from the Allen Brain Map use different online visualization tools with lower processing demands.

DISCUSSION

A typical CURE course has students address novel research questions or problems of general interest to a scientific field (e.g., neuroscience). Unlike a typical lab course, in CURE courses neither students nor faculty know the outcome of the research in advance. The Allen Brain Map exercises described here follow this CURE approach. Students generate new insights while also actively participating in the entire scientific process from the initial formulation of a research question to the presentation of results to the general public, further elevating the CURE with a non-disposable assignment (Seraphin and Stock, 2020). Additionally, our exercises can be completed in a laboratory setting or as a suite of remote (virtual) research exercises. This is especially important as many institutions move to virtual learning during the COVID-19 pandemic.

Previous research demonstrates that undergraduates who participate in research internships or research experiences report increased ability to think like a scientist and are more likely to pursue graduate education or careers in science (Auchincloss et al., 2014; Kardash, 2000; Lopatto, 2007). These positive outcomes of CUREs appear especially important for women and underrepresented minority students (Bangara and Brownell, 2014; Eagen, 2011).

Our tutorials also introduce students to the world of big data in neuroscience. Big data is now transforming neuroscience and today's undergraduates need to understand the approaches to mining these massive datasets (Landhuis, 2017; Sejnowski, 2014). For students without coding experience, gaining experience with these datasets before transitioning into using them as a basis for learning to code can provide an introduction to computer science in a scientific application-driven context. An example of how our tutorials could be expanded to introduce Python coding, Jupyter notebooks, and big data analyses are described in Juavinett (2020).

Finally, the scientific process is not complete until the results are shared with the scientific community and the general public. Through this assignment, students gain experience with a very common form of science communication, the conference poster, which requires them to synthesize their results and present them to their peers. Taking a research project from conception to data analysis to presentation prepares them to use their scientific knowledge of these common resources, their data analysis skills, and presentation skills as they advance into further research or other classes.

In conclusion, this lesson guides students through a transition from worksheet-based to project-based learning, supports them in developing independent research projects, provides a structure for learning broadly applicable data analysis skills, and develops science communication and presentation skills. The tutorials, independent research project, and poster presentation to their peers are all highly adaptable, thanks to their focus on developing students' research skills through the mechanism of open data. They can therefore be easily modified to suit the specific course needs, or directly applied from the provided materials (Appendix and Supplementary Materials 1-3).

APPENDIX AND SUPPLEMENTARY MATERIALS

Appendix: Project assignment description - student handout
S1: Allen Mouse Brain Atlas tutorial - student handout
S2: Allen Brain Map reference atlases tutorial - student handout
S3: Allen Human Brain Atlas tutorial - student handout

REFERENCES

Auchincloss LC, Laursen SL, Branchaw JL, Eagan K, Graham M, Hanauer DI, Lawrie G, McLinn CM, Pelaez N, Rowland S, Towns M, Trautmann NM, Varma-Nelson P, Weston TJ, Dolan EL (2014) Assessment of course-based undergraduate research experiences: a meeting report. CBE—Life Sci Educ 13(1):29–40.

Bangera G, Brownell SE (2014) Course-based undergraduate research experience.s can make scientific research more inclusive. CBE—Life Sci Educ 13(4):602–606.

Chandrasekaran AR (2020) Transitioning undergraduate research from wet lab to the virtual in the wake of a pandemic. Biochem and Molecular Biol Educ 48(5):436-438.

Chu P, Peck J, Brumberg JC (2015) Exercises in anatomy, connectivity, and morphology using neuromorpho.org and the allen brain atlas. J Undergrad Neurosci Educ 13(2):A95-A100.

Eagan MK, Sharkness J, Hurtado S, Mosqueda CM, Chang MJ (2011) Engaging undergraduates in science research: not just about faculty willingness. Res High Educ 52(2):151–177.

Gilbert TL (2018) The allen brain atlas as a resource for teaching undergraduate neuroscience. J Undergrad Neurosci Educ 16(3):A261–A267.

Grisham W, Brumberg JC, Gilbert T, Lanyon L, Williams R, Olivo R (2017) Teaching with big data: report from the 2016 society for neuroscience teaching workshop. J Undergrad Neurosci Educ 16(1):68–76.

Jenks BG (2009) A self-study tutorial using the allen brain explorer and brain atlas to teach concepts of mammalian neuroanatomy and brain function. J Undergrad Neurosci Educ 8(1):A21-5.

Juavinett A (2020) Learning how to code while analyzing an open access electrophysiology dataset. J Undergrad Neurosci Educ 19(1):A94-A104.

Kardash CM (2000) Evaluation of an undergraduate research experience: perceptions of undergraduate interns and their faculty mentors. J Educ Psychol 92:191–201.

Landhuis, E (2017) Neuroscience: big brain, big data. Nature 541(7638):559–561.

Laursen S, Hunter A-B, Seymour E, Thiry H, Melton G (2010) Undergraduate research in the sciences: engaging students in real science. San Francisco, CA: John Wiley & Sons.

Lopatto D (2007) Undergraduate research experiences support science career decisions and active learning. CBE Life Sci Educ 6(4):297– 306.

Makarevitch I, Frechette C, Wiatros N (2015) Authentic research experience and "big data" analysis in the classroom: maize response to abiotic stress. CBE Life Sci Educ 14(3):1–12.

Ramos RL (2020) Virtual was the reality in neuroscience education during the COVID-19 Pandemic. J Undergrad Neurosci Educ 19(1):E1-E2.

Ramos RL, Smith PT, Brumberg JC (2007) Novel *in silico* method for teaching cytoarchitecture, cellular diversity, and gene expression in the mammalian brain. J Undergrad Neurosci Educ 6(1):A8-A13.

Sejnowski TJ, Churchland PS, Movshon JA (2014) Putting big data to good use in neuroscience. Nat Neurosci 17(11):1440–1441.

Shortlidge EE, Bangera G, Brownell SE (2017) each to their own cure: faculty who teach course-based undergraduate research experiences report why you too should teach a CURE. J Microbiol Biol Educ 8(2):1-11.

Seraphin SB, Stock S (2020) Non-disposable assignments for remote neuroscience laboratory teaching using analysis of

human data. J Undergrad Neurosci Educ 19(1):A105-A112.
Vasiliadou R (2020) Virtual laboratories during coronavirus (covid-19) pandemic. Biochem and Molecular Biol Educ 48(5):482-483.

Received March 1, 2021; accepted April 2, 2021.

KC thanks the founder of the Allen Institute, Paul G. Allen, for his vision, encouragement, and support that enabled the open resources used in the lesson. We also thank Ron Hoy for reviewing an earlier draft of this manuscript and all the students in JR's Neurobiology classes at Hobart and William Smith Colleges.

Address correspondence to: Dr. Jim Ryan, Biology Department, Hobart & William Smith Colleges, 300 Pulteney Street, Geneva, NY 14456. Email: ryan@hws.edu

APPENDIX

NEUROBIOLOGY 340

POSTER PRESENTATION GUIDELINES

You will present a poster on your research question using the Allen Brain Map resources during the last two weeks of the semester. Your attendance at the poster session is required regardless of whether you are presenting that day or not.

Choosing a Poster Topic

The choice of research question is up to you. However, it must use at least 2 different databases from the Allen Brain Map (brain-map.org). Here are a few general suggestions:

- What groups of genes are expressed in a specific brain region and why would that pattern of expression occur?
- Where in the brain is a specific gene of interest expressed and how can you explain that pattern?
- How are specific brain regions connected? Does the connectivity pattern follow what we know about the function of those regions?
- What genes are correlated with a specific neurological or disease state? How might you explain the disease based on the genes that are associated with it?
- How does the pattern of gene expression change over developmental time?
- How much variation do we see in neuronal cell types in a specific brain region and in what way (properties) do they vary?

Feel free to use these as a starting point for your own more specific research question or come up with your own questions.

Some resources from the Allen Institute you may find useful as you develop your project include:

- Introduction to the Allen Brain Map tutorial: https://youtu.be/b_UvVjWydfo
- Additional tutorials on other resources: https://youtube.com/playlist?list=PLN-QyZNMh3PsJTFXvKmvSksTmHUbfcVL6
- Community forum for support and questions (search other questions or post your own): https://community.brain-map.org/

The purpose of a scientific poster

You have all seen poster sessions on campus and many of you have presented a poster before. For those who have not, the purpose of a scientific poster is to visually communicate your research to others. At scientific meetings, authors usually display and present their posters at an interactive poster session where interested audience members can listen and ask questions. Often posters are on display long after a poster session has ended. Therefore, a well-designed poster complements your presentation during a poster session and also contains enough information such that viewers can fully understand your presentation without your presence. In our case, we will have you present your poster orally and answer questions during the lab period.

Deadlines

April 10 - You must discuss your poster topic (research question) with me and get approval to proceed.

April 24 - First round of poster presentations in lab (I will randomly assign you to present on a given day)

May 1 - Second round or poster presentations in lab.

Missing deadlines will result in points being deducted from your poster project grade

Poster project is worth 100 points.

Important guidelines

- I will provide you with a poster template, which you will modify. Your poster should be a minimum of 36" wide by 24" high (template size).
- Your poster should contain elements of an Introduction, Goal/Hypothesis, Results, Summary, and Acknowledgements, even if these sections are not necessarily labeled as such.

General tips for preparing the poster

Here are some fundamental points to consider:

- The poster should be a **succinct**, **clear**, and **self-explanatory** presentation of your research.
- Your poster should allow you to present your findings in a **concise**, **visual** form.
- Your figures should be crafted to communicate your central results and ideas.
- Your poster should present a narrative that is capable of being understood without the author.
- Walk through the halls of the science center to find examples of different poster styles and formats.
- Posters are typically about 40% graphics and 60% text.