Connectomics in the classroom: Introducing students to neuroscientific principles using the *Drosophila* Female Adult Fly Brain electron microscopy data set.

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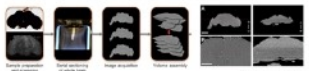
Abstract

Neuroscience students at undergraduate institutions and high schools benefit from access to a diverse array of laboratory experiences that highlight key neuroscientific principles while also providing practical insights into the research process and career paths in neuroscience. Unfortunately, the ability to provide these laboratory opportunities often requires significant investment in hardware and instrumentation, which can preclude adoption of these experiences in classrooms or institutions where resources are limited. Moreover, the COVID-19 pandemic laid bare the need for laboratory exercises that can be implemented in a remote setting. We set out to design *in silico* active-learning laboratory modules that introduce students to key neuroscience concepts, situated within the context of connectomics. Connectomics is a burgeoning subfield of neuroscience where researchers are endeavoring to create comprehensive maps of synaptic connectivity within the nervous system to provide the anatomical framework in which to understand brain circuitry and function. Using a complete serial section electron microscopy volume of a Female Adult Fly Brain (FAFB) and the Collaborative Annotation Toolkit for Massive Amounts of Image Data (CATMAID) software platform, we have designed active-learning modules that teach students how to navigate within a connectomics dataset while teaching fundamental neuroscience concepts. These modules were implemented in undergraduate and high school lab courses at four institutions across the United States. Initial assessment indicates that student acquisition of fundamental neurobiological concepts was enhanced and that students experienced a deepened connection to the research process. Future efforts will be dedicated towards developing new active-learning modules that highlight other neuroscientific concepts, creating scalable opportunities for authentic research experiences for undergraduates and high school students, and improving infrastructure to facilitate widespread dissemination of these materials to classrooms around the world.

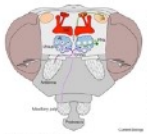
Generation of EM Volume



Zheng et al., 2018

The FAFB data set consists of ~21 million images of >7000 serial thin sections through the *Drosophila* brain.

Drosophila olfactory system



Perisse et al., 2013

The FAFB data set has allowed circuit mapping of the *Drosophila* olfactory system.

Our laboratory modules ask students to explore the anatomy and connectivity of the olfactory circuit using analysis of published neuron annotations.

Methods

CATMAID active learning modules were implemented in high school and undergraduate classrooms at:

- Ector County Independent School District: Neuroscience course (22 high school students)
- UC-Santa Barbara: Research for Undergraduates: Molecular Biology Experience (RUMBLE) (40 first year biology students)
- Appalachian State University: Introductory-level neuroscience course (30 Biology/Psychology majors)
- Mount Holyoke College: Upper-level neuroscience course (10 Neuroscience majors)

Active Learning Modules

Neuroanatomy Module

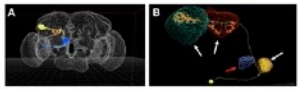


Figure 1. Representative images module-specific neurons visualized within the CATMAID 3D volumetric viewer to highlight neuroanatomical features. (A) An olfactory projection neuron color-coded along the anterior (blue) – posterior (yellow) axis situated within the entire brain volume. (B) An olfactory projection neuron (yellow) is visualized with the sub-regions that it innervates (white arrows), along with other sub-regions that it does not innervate (red arrow).

Cytology Module

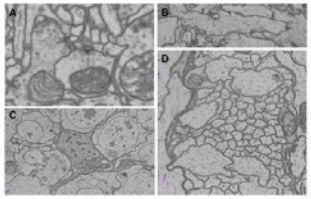


Figure 2. Representative electron microscopic images of cytological structures that students are guided to locate and identify. (A) synapse featuring pre-synaptic T-bar, synaptic vesicles and post-synapse dendrites; (B) microtubules running longitudinally in an axon; (C) glial cell contacting several neurons; (D) axonal tracts in cross section.

Connectivity Module

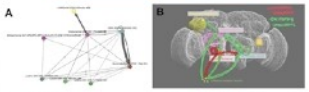


Figure 3. (A) Representative connectivity plot from the CATMAID Connectivity widget showing the extent to which eight neurons are synaptically connected. This analysis is by students to identify circuit motifs like lateral inhibition. (B) Student-generated graphical summary of excitatory and inhibitory neurons that control sensory information flow within the olfactory system.

Tracing Module

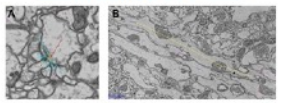


Figure 4. (A) Synapses are identified and labeled in CATMAID with post-synaptic partners identified with blue arrows and the pre-synaptic neuron with a red arrow. The yellow synaptic connector is placed at the T-bar. (B) Students learn how to place nodes at the center of mass of neurons of interest. The green node in the middle is active, and axon, in transverse is connected with other nodes in yellow.

Students who completed FAFB/CATMAID lab modules reported improved understanding of neurobiology concepts

My understanding of the following neuroscientific principles was enhanced by using the Connectome Laboratory modules:

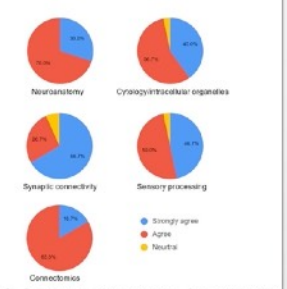
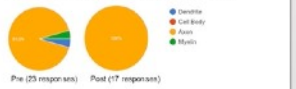


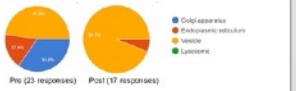
Figure 5. Post-semester survey responses from undergraduate neurobiology students at Appalachian State University and Mount Holyoke College who completed FAFB/CATMAID laboratory modules (n = 30)

Students who completed a neurobiology course using FAFB/CATMAID lab modules showed improved performance on neurobiology concepts inventory

Action potentials travel along which part of the neuron before arriving at the terminal and evoking neurotransmitter release?



What is the name of the cellular organelle that contains neurotrans mitter waiting to be released?



The diagram below (not shown) depicts a neural circuit in the retina. In this circuit horizontal cells receive excitatory synapses from photoreceptor cells and in turn send inhibitory synapses to multiple neighboring photoreceptors. What is this an exemple of?

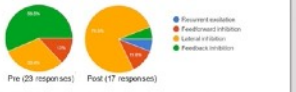


Figure 6. Pre- and post-semester content inventory responses from undergraduate neurobiology students at Appalachian State University who completed FAFB/CATMAID laboratory modules

Survey responses suggest that students who used FAFB/CATMAID lab materials developed a deeper connection to science

High School Student Feedback:

"Overall this class made me feel like I was part of something bigger, rather than just another high school students in a regular science class."

"I never believed in cells. I could never understand something I could not see. I did not understand how something so small could have organelles inside it that even smaller and everything is actively working together. CATMAID completely changed my perspective because the visuals convinced me that our body really is complex at the cellular level too."

"Taking this course did change how I felt about science because I had felt before that science was not for me but after this course I realized that I did enjoy participating in this field."

College Student Feedback:

"I think it was nice to see EM images of neurons, and not the standard cookie cutter drawings from text books."

"It really gave me an appreciation for the people who spend their time doing this type of research. It is crazy how long it takes to trace just a super tiny section of one neuron in the fruit fly brain."

"I really enjoyed the software that we used to look at the fly brain, it was fascinating to me. I thought it was really cool and I even showed it to some of my friends and family."

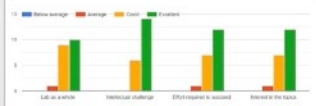


Figure 7. Post-semester survey responses from high school neuroscience students at George H.W. Bush New Tech Odessa in Ector County Independent School District, Odessa Texas when asked to rate the FAFB/CATMAID laboratory modules (n=22)

Conclusions and Lessons Learned

1. We developed a series of four active-learning lab modules that use the FAFB dataset and CATMAID interface to teach undergraduate and high school students neurobiology fundamentals and connectomics.
2. The laboratory modules have undergone pilot implementation at three undergraduate institutions and one high school, with ~100 students participating.
3. Pilot assessment data suggests that students advanced their neurobiology content learning, self-reported understanding of neurobiology concepts, and personal connection to science.

Future Goals

1. We will use our assessment data to guide refinement and expansion of our existing laboratory modules.
2. We hope to expand our connections to additional partner institutions and classrooms to disseminate these materials and tools.
3. We will collect additional assessment data to measure student learning outcomes and students' connection to the process of scientific research.
4. Develop a framework for students to use these tools to pursue independent studies and capstone projects after the conclusion of the course.
5. Through continued user experience, contribute recommendations for ongoing enhancements to the user interface.

References and Acknowledgements

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Perisse, Emmanuel et al. "Shocking revelations and saccharin sweetness in the study of Drosophila olfactory memory." *Current biology : CB* vol. 23,17 (2013): R752-63. doi:10.1016/j.cub.2013.07.060

Zheng, Zhihao et al. "A Complete Electron Microscopy Volume of the Brain of Adult Drosophila melanogaster." *Cell* vol. 174,3 (2018): 730-743.e22. doi:10.1016/j.cell.2018.06.019