Exploring Descending Neurons within the Brain

Matthew Q. Clark
0000-0002-1113-9388

matthew.clark@bucknell.edu

assets/catmaid/Add Neurons from your Lineage to the Selection Table.mp4
(a) Add Neurons from your Lineage to the Selection Table

assets/catmaid/Display Network of Connectivity.mp4
(b) Display Network of Connectivity

assets/catmaid/Display your neuron.mp4
(c) Display your neuron

assets/catmaid/Export a Movie.mp4
(d) Export a Movie

assets/catmaid/Rotate View Turn on z Plane.mp4
(e) Rotate View Turn on z Plane

assets/catmaid/Show a Connectivity Graph.mp4
(f) Show a Connectivity Graph

assets/catmaid/Show Pre Post Sites.mp4
(g) Show Pre Post Sites

assets/catmaid/Show Table of Synaptic Partners.mp4
(h) Show Table of Synaptic Partners

Figure 1: How-to videos for CATMAID

0.1 Goal

The goal of this lab is to understand how neural lineages help to build functional circuitry. Though the function of some of these neurons isn't completely understood, having a connectivity map can help us generate hypotheses about circuit function and also learn about the developmental origins of these circuits.

CATMAID (Instructions for Tracing Neurons)

With a stable internet connection open CATMAID to access the L1 brain.

Schneider-Mizell et al. (2016) is an early paper that described the utility of platform

For how-to movies see here

To do a screenshot in windows check here

For a copy of today's talk click here

For this module you can work in pairs!

0.2 Part I: Exploring the connections between neurons in a known circuit

0.2.1 We will be working with neurons:

1. MDNa_left; pair 1 left
2. MDNa_right; pair 2 right
3. MDNb_right; pair 1 right
4. MDNb_left; pair 2 left

0.2.2 Display your neuron:

1. Click on the widget that looks like a neuron  and then press the / on your keyboard
2. Type in the "annotated" neuron box "DNs from Brain Akira" and change to show 100 entries instead of 50
3. Select the boxes that say MDNa_left; pair 1 left, MDNa_right; pair 2 right, MDNb_right; pair 1 right, and MDNb_left; pair 2 left
4. Open the 3D viewer and click append (make sure the box next to append says Neuron Search 1)
5. Within the 3D viewer press view settings

1. Find the drop down that says volume and then click the box next to CNS
2. Press the check mark next to floor to get rid of the grid on the 3D view screen

6. Now press View within the 3D viewer and then press the box that says ZX to get it in the correct orientation

0.2.3 Show a presynaptic site (red points): receiving information

1. In the 3D viewer go to view setting
2. In the box next to Node handle scaling - increase the number until the red dots on the neurons are clearly visible

Where are the red points mainly located? The VNC or the cerebral hemispheres?

0.2.4 Show a postsynaptic site (cyan points): putting out information

1. In the box next to link site scaling, increase the number until the blue dots on the neuron are clearly visible.

Where are the blue points located on the neuron? Are there more on the VNC or in the cerebral hemispheres?

0.2.5 Show table of synaptic partners:

Click on this widget:

0.2.5.1 Display network of connectivity:

Click on this widget:

1 Connectivity of Carreira-Rosario et al. (2018)

1. Go back to the neuron search window and in the annotated section copy and past Carreira-Rosario et al. (2018) and press submit
2. Open the 3D viewer and click append (make sure the box next to append says Neuron Search 1)
3. Show table of synaptic partners:
   1. Click on the widget

1.1 Part II: Exploring the connections between neurons in an unknown circuit

1.1.1 Key links:

SEZ from brain DN from brain

1. Find a bilateral pair of neurons from either powerpoint linked above (SEZ or DN from brain) of the DN's from the Brain Akira.
   1. Make sure the neurons you select are similar in some way, this could be by their name, how far they venture into the VNC, all ipsilateral or contralateral, etc.
2. Follow the similar workflow that was used for the MDNs to **display your neurons, show a table of synaptic partners, and display network of connectivity.** Since there is likely to be a long list of connected neurons, focus on the top 5 upstream and downstream partners shown in the table of synaptic partners. Please show the morphology of the upstream and downstream partners.
3. For next week's lab update, please share with us your selected DNs, the morphology of the top upstream inputs and downstream outputs, and the connectivity diagram of inputs and outputs of your DNs.

1.1.2 Useful widgets:

- shows keyboard shortcuts
- neuron search ('/' also opens this widget)
- 3D viewer of selected skeletons (use this in conjunction with the widget to manage list of skeletons)

1.1.3 Fun search terms:

- "Whole motor neurons at A1 segment akira"
- "DNs from Brain akira"
- "DNs from SEZ akira"
- et al

1.1.4 Papers to explore neural circuits:

- Zwart et al. (2016)
- Masson et al. (2020)
- Burgos et al. (2018)
- Eschbach et al. (2020)
- Carreira-Rosario et al. (2018)
- Miroschnikow et al. (2018)
- Zarin, Mark, Cardona, Litwin-Kumar, & Doe (2019)
- Mark et al. (2021)
- Berck et al. (2016)
- Eichler et al. (2017)
- Andrade et al. (2019)
- Larderet et al. (2017)
- Ohyama et al. (2015)
- Jovanic et al. (2016)

- Schlegel et al. (2016)
- Jovanic et al. (2019)
- Fushiki et al. (2016)
- Takagi et al. (2017)
- Tastekin et al. (2018)
- Imambocus et al. (2022)
- Kohsaka et al. (2019)
- Heckscher et al. (2015)
- Gerhard, Andrade, Fetter, Cardona, & Schneider-Mizell (2017)

Bibliography

Andrade, I. V., Riebli, N., Nguyen, B.-C. M., Omoto, J. J., Cardona, A., & Hartenstein, V. (2019). Developmentally Arrested Precursors of Pontine Neurons Establish an Embryonic Blueprint of the Drosophila Central Complex. *Current Biology*, *29*(3), 412–425. https://doi.org/10.1016/j.cub.2018.12.012

Berck, M. E., Khandelwal, A., Claus, L., Hernandez-Nunez, L., Si, G., Tabone, C. J., … Cardona, A. (2016). The wiring diagram of a glomerular olfactory system. *Elife*, *5*. https://doi.org/10.7554/elife.14859

Burgos, A., Honjo, K., Ohyama, T., Qian, C. S., Shin, G. J.-e., Gohl, D. M., … Grueber, W. B. (2018). Nociceptive interneurons control modular motor pathways to promote escape behavior in Drosophila. *Elife*, *7*. https://doi.org/10.7554/elife.26016

Carreira-Rosario, A., Zarin, A. A., Clark, M. Q., Manning, L., Fetter, R. D., Cardona, A., & Doe, C. Q. (2018). MDN brain descending neurons coordinately activate backward and inhibit forward locomotion. *Elife*, *7*. https://doi.org/10.7554/elife.38554

Eichler, K., Li, F., Litwin-Kumar, A., Park, Y., Andrade, I., Schneider-Mizell, C. M., … Cardona, A. (2017). The complete connectome of a learning and memory centre in an insect brain. *Nature*, *548*(7666), 175–182. https://doi.org/10.1038/nature23455

Eschbach, C., Fushiki, A., Winding, M., Schneider-Mizell, C. M., Shao, M., Arruda, R., … Zlatic, M. (2020). Recurrent architecture for adaptive regulation of learning in the insect brain. *Nature Neuroscience*, *23*(4), 544–555. https://doi.org/10.1038/s41593-020-0607-9

Fushiki, A., Zwart, M. F., Kohsaka, H., Fetter, R. D., Cardona, A., & Nose, A. (2016). A circuit mechanism for the propagation of waves of muscle contraction in Drosophila. *Elife*, *5*. https://doi.org/10.7554/elife.13253

Gerhard, S., Andrade, I., Fetter, R. D., Cardona, A., & Schneider-Mizell, C. M. (2017). Conserved neural circuit structure across Drosophila larval development revealed by comparative connectomics. *Elife*, *6*. https://doi.org/10.7554/elife.29089

Heckscher, E. S., Zarin, A. A., Faumont, S., Clark, M. Q., Manning, L., Fushiki, A., … Doe, C. Q. (2015). Even-Skipped+ Interneurons Are Core Components of a Sensorimotor Circuit that Maintains Left-Right Symmetric Muscle Contraction Amplitude. *Neuron*, *88*(2), 314–329. https://doi.org/10.1016/j.neuron.2015.09.009

Imambocus, B. N., Zhou, F., Formozov, A., Wittich, A., Tenedini, F. M., Hu, C., … Soba, P. (2022). A neuropeptidergic circuit gates selective escape behavior of Drosophila larvae. *Current Biology*, *32*(1), 149–163. https://doi.org/10.1016/j.cub.2021.10.069

Jovanic, T., Schneider-Mizell, C. M., Shao, M., Masson, J.-B., Denisov, G., Fetter, R. D., … Zlatic, M. (2016). Competitive Disinhibition Mediates Behavioral Choice and Sequences in Drosophila. *Cell*, *167*(3), 858–870. https://doi.org/10.1016/j.cell.2016.09.009

Jovanic, T., Winding, M., Cardona, A., Truman, J. W., Gershow, M., & Zlatic, M. (2019). Neural Substrates of Drosophila Larval Anemotaxis. *Current Biology*, *29*(4), 554–566. https://doi.org/10.1016/j.cub.2019.01.009

Kohsaka, H., Zwart, M. F., Fushiki, A., Fetter, R. D., Truman, J. W., Cardona, A., & Nose, A. (2019). Regulation of forward and backward locomotion through intersegmental feedback circuits in Drosophila larvae. *Nature Communications*, *10*(1). https://doi.org/10.1038/s41467-019-10695-y

Larderet, I., Fritsch, P. M., Gendre, N., Neagu-Maier, G. L., Fetter, R. D., Schneider-Mizell, C. M., … Sprecher, S. G. (2017). Organization of the Drosophila larval visual circuit. *Elife*, *6*. https://doi.org/10.7554/elife.28387

Mark, B., Lai, S.-L., Zarin, A. A., Manning, L., Pollington, H. Q., Litwin-Kumar, A., … Doe, C. Q. (2021). A developmental framework linking neurogenesis and circuit formation in the Drosophila CNS. *Elife*, *10*. https://doi.org/10.7554/elife.67510

Masson, J.-B., Laurent, F., Cardona, A., Barré, C., Skatchkovsky, N., Zlatic, M., & Jovanic, T. (2020). Identifying neural substrates of competitive interactions and sequence transitions during mechanosensory responses in Drosophila. *PLOS Genetics*, *16*(2), e1008589. https://doi.org/10.1371/journal.pgen.1008589

Miroschnikow, A., Schlegel, P., Schoofs, A., Hueckesfeld, S., Li, F., Schneider-Mizell, C. M., … Pankratz, M. J. (2018). Convergence of monosynaptic and polysynaptic sensory paths onto common motor outputs in a Drosophila feeding connectome. *Elife*, *7*. https://doi.org/10.7554/elife.40247

Ohyama, T., Schneider-Mizell, C. M., Fetter, R. D., Aleman, J. V., Franconville, R., Rivera-Alba, M., … Zlatic, M. (2015). A multilevel multimodal circuit enhances action selection in Drosophila. *Nature*, *520*(7549), 633–639. https://doi.org/10.1038/nature14297

Schlegel, P., Texada, M. J., Miroschnikow, A., Schoofs, A., Hückesfeld, S., Peters, M., … Pankratz, M. J. (2016). Synaptic transmission parallels neuromodulation in a central food-intake circuit. *Elife*, *5*. https://doi.org/10.7554/elife.16799

Schneider-Mizell, C. M., Gerhard, S., Longair, M., Kazimiers, T., Li, F., Zwart, M. F., … Cardona, A. (2016). Quantitative neuroanatomy for connectomics in Drosophila. *Elife*, *5*. https://doi.org/10.7554/elife.12059

Takagi, S., Cocanougher, B. T., Niki, S., Miyamoto, D., Kohsaka, H., Kazama, H., … Nose, A. (2017). Divergent Connectivity of Homologous Command-like Neurons Mediates Segment-Specific Touch Responses in Drosophila. *Neuron*, *96*(6), 1373–1387. https://doi.org/10.1016/j.neuron.2017.10.030

Tastekin, I., Khandelwal, A., Tadres, D., Fessner, N. D., Truman, J. W., Zlatic, M., … Louis, M. (2018). Sensorimotor pathway controlling stopping behavior during chemotaxis in the Drosophila melanogaster larva. *Elife*, *7*. https://doi.org/10.7554/elife.38740

Zarin, A. A., Mark, B., Cardona, A., Litwin-Kumar, A., & Doe, C. Q. (2019). A multilayer circuit architecture for the generation of distinct locomotor behaviors in Drosophila. *Elife*, *8*. https://doi.org/10.7554/elife.51781

Zwart, M. F., Pulver, S. R., Truman, J. W., Fushiki, A., Fetter, R. D., Cardona, A., & Landgraf, M. (2016). Selective Inhibition Mediates the Sequential Recruitment of Motor Pools. *Neuron*, *91*(3), 615–628. https://doi.org/10.1016/j.neuron.2016.06.031