Math 568 project: proposal

Michael Ivanitskiy, Aakash Patel, Connor Puritz

October 9, 2019

Recently, the connectome of both sexes of *C. elegans* has been mapped throughout its development [4] [2] [6]. The pathways governing synaptogenesis throughout development are always well studied in the organism [1]. These combined make *C. elegans*, with only 302 neurons, an excellent organism for *in silico* studies of synaptogenesis.

For our project, we aim to build a network-scale model of synaptogenesis with a focus on replicating chemotaxic behavior. Such a model is important to understand both decision-making at the primitive level that it occurs in *C. elegans* [5] [3], as well as as a precursor to features like long-term memory in more complex organisms. To build such a model, we will initially simply hard-code many features, notably growth cone initiation and axon guidance molecule emission (as a function of neural activity) based on data from studies of *C. elegans*.

To test our model, we will start with a C. elegans connectome from early in development, and try to mimic synaptic growth by releasing the appropriate amounts of neurotrophins by the correct neurons. We will also simulate the electrical activity in the connectome throughout the growth period for a variety of stimuli, as these can play a role in synaptogenesis. After some time, we will compare the structure and function of the resulting network to the actual connectome of adult C. elegans.

In our project, we aim to determine:

- can synaptogenesis in *C. elegans* be effectively modelled *in silico*?
- to what extent do external stimuli play a role in connectome development of in silico C. elegans, and how well do these results match those done in vivo?

References

- [1] Andrew D Chisholm, Harald Hutter, Yishi Jin, and William G Wadsworth. The genetics of axon guidance and axon regeneration in caenorhabditis elegans. *Genetics*, 204(3):849–882, 2016.
- [2] Steven J Cook, Travis A Jarrell, Christopher A Brittin, Yi Wang, Adam E Bloniarz, Maksim A Yakovlev, Ken CQ Nguyen, Leo T-H Tang, Emily A Bayer, Janet S Duerr, et al. Whole-animal connectomes of both caenorhabditis elegans sexes. *Nature*, 571(7763):63, 2019.
- [3] Travis A Jarrell, Yi Wang, Adam E Bloniarz, Christopher A Brittin, Meng Xu, J Nichol Thomson, Donna G Albertson, David H Hall, and Scott W Emmons. The connectome of a decision-making neural network. *Science*, 337(6093):437–444, 2012.
- [4] Marcus Kaiser. Mechanisms of connectome development. Trends in Cognitive Sciences, 21(9):703-717, 2017.
- [5] Linjiao Luo, Quan Wen, Jing Ren, Michael Hendricks, Marc Gershow, Yuqi Qin, Joel Greenwood, Edward R Soucy, Mason Klein, Heidi K Smith-Parker, et al. Dynamic encoding of perception, memory, and movement in a c. elegans chemotaxis circuit. *Neuron*, 82(5):1115–1128, 2014.
- [6] Laura Pereira, Florian Aeschimann, Chen Wang, Hannah Lawson, Esther Serrano-Saiz, Douglas S Portman, Helge Grosshans, and Oliver Hobert. Timing mechanism of sexually dimorphic nervous system differentiation. *Elife*, 8:e42078, 2019.