State-Dependent Modulation of Neuronal Circuits in *C. elegans* Sleep

Thesis by
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Preface

> "You have brains in your head. You have feet in your shoes.
> You can steer yourself any direction you choose. You're on your
> own. And you know what you know. And YOU are the one
> who'll decide where to go…"
>
> — Doctor Seuss, *Oh the Places You'll Go*

It is always a joy to start something new. There is nothing like the initial excitement of getting a machine to work for the first time or the gratification of being surprised by the result of an experiment. It is the promise of something novel: another puzzle to solve.

In contrast, the real work is staying the course and finishing the story. Although I have provided most of the labor for the work shown here, its existence has to be attributed to others: partly to Paul who used both carrot and stick to drive me through my graduate career, partly to Michael who showed me how to start being an adult, and to my father who taught me responsibility. I hope that I'm not too far from the mark.

I am not sure how to feel about the end result, but there were definitely a lot of surprises along the way. It is shocking how four pairs of neurons and one question can elude a person for several years. Three hundred and two will take over your life... ask Paul.

ABSTRACT

C. elegans is a compact system of 302 neurons with identifiable and mapped connections that makes it ideal for systems analysis. This work is a demonstration of what I have been able to learn about the nature of state-specific modulation and reversibility during a state called lethargus, a sleep-like state in the worm. I begin with a description about the nervous system of the worm, the nature of sleep in the worm, the questions about its behavior and apparent circuit properties, the tools available and used to manipulate the nervous system, and what I have been able to learn from these studies. I end with clues that the physiology helps teach us about the dynamics of state specific modulation, what makes sleep so different from other states, and how we can use these measurements in understanding which modulators, neurotransmitters, and channels can be used to create different dynamics in a simple model system.

for my parents

and maybe Paul…

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