**Caenorhabditis elegans Movement Project Summary and Funding Proposal**

Anthony Gualandri, Sarah Hunt, Scott Page, Steven Rotter

Caenorhabditis elegans roundworms have been the focus of neurological research for several decades because their genomic makeup is similar to that of humans, yet simple enough to produce a connectome and complete neurological map of all 302 of its neurons. The aim of such research is to better understand how certain neurons in the brain affect certain behavioral actions. Investigations to date have not been able to provide a complete or cohesive understanding of what characterizes sequential, repeated worm movement and posture based behaviors, or demonstrate that such patterns of behavior even exist for this species as observed in human and other mammalian behavior.

The objective of this proposal is to design, implement, and evaluate a set of modeling approaches that seek to explicitly understand the behavioral patterns of C. elegans over time and the interrelationships between such behaviors. The value in this objective is to provide biologists and neuroscientists with a way to differentiate between C. elegans mutant types in order to better understand how certain neural connections relate to specific changes in behavioral patterns. Our hypothesis, based on our own preliminary findings and that of other researchers, is that there are a distinct yet shared set of behavioral patterns between worms at various time granularities and that modeling them will enable scientists to better understand how mutated worm behavior differs from non-mutated worm behavior. To test our hypothesis we propose the following two specific aims:

**Aim 1: Develop a modeling approach to map locomotive trajectory behavior.** Current research understands that macro level worm behavior falls into three general categories: (a) exploration, (b) exploitation, and (c) satiation or rest. Exploration is largely characterized by longer periods of travel, with more forward movement behaviors, to find new locations of food. Exploitation is largely characterized by shorter periods of travel, usually through the use of frequent turning movement behaviors, to exploit a specific area in search of food. One of the challenges to modeling such behavioral patterns is to make worm movement aligned on a comparable scale both in terms of time duration, but also direction, since the specific section of the agar plate the worm is traveling to and coming from is random and unimportant. To address this challenge and to model such behaviors, we propose to: (1) determine a fixed time interval and transform the data within each interval to always start at the same point and end on the positive X axis, (2) using these comparable trajectories a method for performing k-means clustering on longitudinal data known as KLM3D will be used to discover the appropriate number of observable locomotive trajectories, and (4) these locomotive states will be sequentially modeled using a Hidden Markov Model to form a new understanding of the worm’s trajectorial decision processes.

**Aim 2: Develop a modeling approach to map more fine grained, posture based movement behavior.** While locomotive trajectory is more intuitive and pronounced, especially to the unaided eye, following recent research and our own preliminary findings we hypothesize that there also exists a set of behavioral patterns that might not be captured entirely by a trajectorial change, but are expressed more in terms of how the worm’s body position or pose changes over time as it moves through its surroundings in search of food. The challenge in modeling this type of behavior is that scientists do not know a correct or complete set of such fine grained behavioral patterns or what posture based movements comprise them. To address this kind of challenge we propose to: (1) prepare a set of images extracted from video recordings suitable for modeling such behavioral patterns, (2) deploy a state-of-the-art unsupervised learning algorithm known as a Beta Process Hidden Markov Model (BP-HMM) to discover both a shared and unique set of behavioral states between both wildtype and mutated worms, and (3) model the output of the BP-HMM as a probabilistic graphical model using another state-of-the-art technology known as a Continuous Time Bayesian Network (CTBN), to learn the conditional dependency structure of one behavioral state over another as well as to learn the amount of time a worm spends in one behavioral state before transitioning to another.