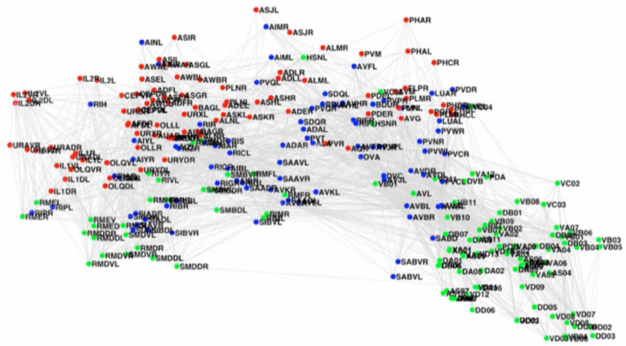

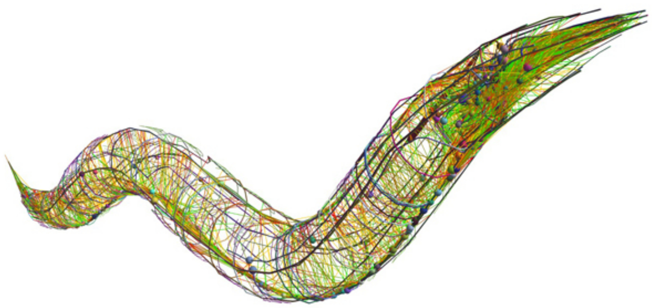

A Learning Connectome

Research Proposal

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Table of Contents

I. INTRODUCTION

Caenorhabditis elegans is one of the most researched model organisms for biological and neural network development. C. elegans is among one of the simplest organisms having nine-hundred cells and a nervous system, which is comprised of approximately three-hundred static neurons that have been mapped into a connectome, or wiring diagram detailing how each neuron connects to another. A connectome can be described as a map of neural connections whether it is an organism's brain or nervous system. The term is mainly used in scientist's efforts in capturing, mapping and understanding the organization of the neural interactions that exist.

Many companies, public and private, in addition to government organizations are working towards modelling the human brain connectome in attempt to build unparalleled thinking machines, also known as artificial intelligences. Companies, such as Open Worm, are using the wiring diagram for C. elegans as a map to write software and this software they have placed in a Lego robot. Open Worm has one goal in mind, and that goal is to understand the human brain and, in the future, to build a computer model of the worm, C. elegans, with the hope that if Scientists are able to understand the worm's brain, this could lead to monumental discoveries in how diseases like Alzheimer's and Parkinson's originate and progress.

There are many applications of understanding and applying the connectome, or wiring diagram for C. elegans. As mentioned previously, it could lead to further work in building the connectome of a human brain. While the human brain is much more complex, the basic building blocks are essentially the same. The main structure that exists in the nervous system is the neuron. Neurons communicate with one another, depending on their role and function, and different types of neurons include motor neurons (which control movement), sensory neurons (which collects environmental information such as temperature) and interneurons (neurons that exists between the sensory and motor neurons).

Neurons communicate with other neurons via electrical signals which travel in a space between the neurons called a synapse. That space will also be the home of certain neurotransmitters, or brain chemicals, which can alter the behavior of these signals in the organism. In the case of C. elegans scientists were able to map out all 302 neurons and label them as what type of neuron it was. Unfortunately, there are limitations to what a connectome can help research. There is still no viable way to see how neurons behave in real time or how neurons regulate one another.

Some early research findings were discovered by scientists destroying certain neurons one by one to determine if abilities in C. elegans were retained or lost. In the 1980’s a postdoctoral student was able to use this method to accurately map out the specific neural circuits responsible for C. elegans’ ability to wriggle backward when poked on the head and move forward when touched on the tail. In future research involving a connectome of a human brain, similar methods can be utilized however the human brain is much more complex as neurons use the flexibility of altering their synaptic strength or signal strength of their connections to allow for memory and learning.

Our research objectives will explore this subject further. We will build the C. elegans connectome in C++ and message passing interface employing the parallelism of the software library and its parallelism. Will the connectome behave like the real worm when stimulated? Can this connectome be trained to solve a machine learning problem? If so, what algorithms can be applied to stimulate neuron growth, and which results in higher accuracy?

This study will help build more of an understanding how the connectome works, as well as if it exhibits behaviors similar to the living worm. Furthermore, this will explore the connectome and its ability to be used in problem solving.

II. RELATED WORK

Studies involving C. elegans and its use to study biological functions can be traced back to the 1960’s and 1970’s. In 1974, Sydney Brenner published his paper, The Genetics of Caenorhabditis elegans, in which he makes the argument for and establishes the nematode as a model not only for developmental biology from a genetic level, but for neurobiology as well. Brenner began to assemble the first connectome by hand by tracing electron micrographs of the body cross sections.

Later he began to write software that would attempt to reconstruct the cell morphologies from sequential micrographs. It would not be until 1986 structure of the neural network would be determined for the hermaphrodite by the use of electron micrographs. “The hermaphrodite nervous system has a total complement of 302 neurons, which are arranged in an essentially invariant structure.” (PMID: 22462104, DOI: 10.1098). As a eutelic organisms they have a fixed number of cells when they reach maturity, the number is invariant for any particular species.

In our study we will be creating a computational model of the C. elegans connection using C/C++ and Argonne National Labs, message passing interface MPICH. This was developed as open source software in a partnership with the University of Chicago and the United States Government. This software provides synchronized communications between processes in a logical graph-like topology. Additionally, it allows for the combination of partial results as they become available using gather and reduce operations, and synchronization of nodes through barrier operations. Because by their nature networks are constructs in which many neurons can operate in parallel we have elected to build a computational cluster based on a low priced on commodity the Raspberry Pi 2 developer board.

III. GOALS & OBJECTIVES

A connectome is meant to map the neural pathways of an actual organism. Our research is intended to focus on how close the behaviors of the software actually are to that a living entity. The goal of this research project is to further our understanding of machine learning and how living organisms think and learn. Specifically, over the next several weeks we hope to accomplish several objectives:

1) Assess the current behavior of connectome and its similarities and differences to C. elegans.
2) Test the learning capability and limitations of connectome.
3) Analyze patterns that emerge and identify what/if any algorithms can improve Connectome's performance and learning capabilities
4) Test how some algorithms improve/reduce capabilities and alter behavior.

Within time frame of this study we should be able to determine if connectome is actually moving towards truly mimicking a living organism. Primarily work will focus on the first, and time permitting we will explore the others. Additional goals will attempt to explore if this can be translated to any immediate use outside of attempting to replicate how a living organism thinks.

IV. BACKGROUND

A connectome can be thought of as a map, in this case it is a map of neural connections and can also be thought of synonymously with a wiring diagram. In the field of neurobiology, a connection is a mapping of all the neural connections within an organism's nervous system. In most scientific efforts the term connectome is used when capturing, mapping and attempting to understand how neural interactions exist. The study of said connectomes and how neurons, synapses and how they interact within a nervous system is called connectomics and this area of neurobiology. Research involving *Caenorhabditis elegans* has been a huge success for connectomes and the future of connectomics. Our research will be focusing on the connectome of *C. elegans* and after recreating the connectome we will pursue the answers to the question of will our connectome behave like a real roundworm when stimulate and can a connectome of *C. elegans* be trained to solve a machine learning problem.

The roundworm may not be large however the existing connectome, created in the 1970's, has led to discoveries of great significance. For example, in 2002 the Nobel Prize was awarded in the area of Physiology or Medicine for "discoveries concerning genetic regulation of organ development and programmed cell death." (The Nobel Prize in Physiology or Medicine 2002, n.d.) In 2006 the Nobel Prize was awarded in the same discipline for "discovery of RNA interference – gene silencing by double-stranded RNA." (The Nobel Prize in Physiology or Medicine 2006, 2016) Both of these discoveries were assisted by knowledge and research into *C. elegans,* however connectomes have more to do with neurobiology than genetics. Mapping a connectome and building a functional connectome is a step forward in understanding how neurons and different type of neurons interact with one another. The OpenWorm Project has already succeeded in putting a "[w]orm's [m]ind in [a] Lego [b]ody" (Black, 2014) by utilizing different algorithms to have the neurons interact. This was done using a robot built using Lego Mindstorms and software can be implanted and utilized on different platforms such as Raspberry Pi's as in our research case.

The ability of being able to model and simulate a whole organism inside a computer has many applications. The research that connectomics extends to has a greater reach than just understanding how neurons interact with one another. Neurons interact and synapses fire in order to produce behaviors and analysis of these behaviors may be able to answers questions in the fields of biology, synthetic biology, and pharmaceuticals and also push forward in the fields of artificial intelligence. The first question in this activity will be to determine if the software implanted on a computer to simulate the organism *C. elegans* will behave as expected when stimulated. To prove this, we will utilize known data about expected behaviors of C. elegans and which neural pathways are being activated. In the 1980's, a postdoctoral student was able to explain a specific C. elegans behavior using a wiring diagram. The specific neural circuits were discovered and mapped for "the worm's tendency to wriggle backward when poked on the head and to squirm forward when touched on the tail." (Jabr, 2012) Behaviors of C. elegans,such as this, that are known and have neural circuits already mapped can be used to verify and answer our question.

So far, the connectome has been used to discover and research C. elegans behaviors and activities, but as the OpenWorm project shows "[w]ith the worm's nose neurons replaced by a sonar sensor and the motor neurons running down both sides of the worm replicated on the left and right motors of the Lego bot, the robot could emulate the worm's biological wiring." (Shadboldt, 2015). This brings up another question, however, as the connectome can now respond to stimuli can the connectome be taught to solve a problem? Algorithms can be written, in this case C or C++ using a Raspberry Pi cluster. Studying the scientific possibility opens up many possible applications of connectomes such as: artificial intelligence, synthetic biology, and even studies into mental illnesses. Out of what was mentioned, artificial intelligence can be considered a concern ethically as there are a range of applications which can also be taken advantage of and used unethically.

V. ETHICAL CONCERNS

Artificial Intelligence has has existed in our minds due mainly to science fiction. For example, the Terminator series introduced us to Skynet and the intelligence killing machines, but science fiction also gave us a friendlier form of artificial intelligence with Data on Star Trek: The Next Generation whose quest to understand was displayed as innocent curiosity. However, there are many questions that come with advances in the areas of A.I. In Star Trek, Data struggled with the label of "android" and discussion of whether or not he was, in fact, a sentient being. These questions will also appear in our own development and research into A.I.

While it is true that there are small groups, businesses and individuals researching and experimenting with this type of technology, it is the domain of the giant technology companies. Facebook, Google, IBM, and Amazon among many are investing and spending Millions if not Billions of dollars in a race to build the best systems and reach the ultimate goal of a general purpose artificial intelligence, a machine capable of thinking at a level equivalent to that of a human, or perhaps even beyond.

One question that must be asked and reflected upon is a connectome, a mapping of the neurons in the brain of a living animal, when recreated in code if it exhibits similar or identical behaviors to the living entity alive? What if its reset, or switched off?

More machines are also appearing in everyday life, automation is entering the workforce and this causes more and more people to be displaced as their jobs are replaced by a robot. Writing code for a machine to perform the same task over and over again without fatigue or need to take a lunch is, perhaps, economically better. However, as mentioned, this displaces workers and forces them to seek new employment. Perhaps we must reanalyze and perhaps restructure our human societal constructs, perhaps by implementing a universal income for all to ensure a balance among the corporations that own these machines, and regular citizenry.

In the future with a successful mapping of a human brain connectome, would this be a considered a breach of privacy? Although the diagram will just be a road map of an individual's neural pathways, those pathways are that individual's memories and who they are. As in any field of science, consent is always requested and required for most procedures and activities however many brain disorders rob individuals of that right to make informed decisions. Brain disorders such as dementia and Alzheimer's break down a person's memory and cognitive abilities, would would a connectome look like for that individual?

Hopefully, research into a connectome would yield results and advances in knowledge into such brain disorders and this can lead to advances in medications and treatment options. However as promising as this may be, just as the debate in Parkinson's treatment using Deep Brain Stimulation or DBS, are we doing more harm than good? At one point lobotomy was a very viable and sought out treatment for many diseases. In hindsight our knowledge has taught us that there are better treatment options, however will treatment's based on connectome research be viewed similarly years from now?

VI. DESIGN

- Build eleven computer cluster with Arch Linux ARM
- Configure Network
- Write Software using C/ C++ using Argonne National Lab's MPICH library.
- Test connectome for touch response shown in *The Neural Circuit for Touch Sensitivity in Caenorhabditis elegans.*

VII. ANTICIPATED RESULTS

Since our project is purely research based, we do not know what our definitive results will be. We will be taking research that has already been performed, and what is being learned, and extending our knowledge to perform a neural network with using a different language. We will be exploring new territory and hope our final results end with a connectome learning an algorithm.

VIII. PERSONAL STATEMENT

This project is very interesting for me; it involves a lot of fields of study that I personally find fascinating. Science was never a strong subject for me so applying a subject that I do know such as Computer Science to a topic in the neurobiology field is very exciting. I work in the Medical Manufacturing field where the company I work for produces Spinal Cord Stimulators for pain management and we are also entering the Deep Brain Stimulation market for treatment of Parkinson's disease. I recently was offered a position as a Software Engineer where I will be programming Clinician Programmers on the DBS (Deep Brain Stimulation) platform. It is very exciting and also fulfilling to know that I am contributing to a a product that can potentially increase the quality of life of a patient who has this debilitating disease.

The impact that a connectome can have on future Scientific discovers has a huge potential. I grew up with a lot of science fiction and my family is full of Engineers so scientific and technical advances were what we discussed. In the future I would absolutely like to stay in the field of Medical Manufacturing, even if I move away from DBS there are still advances being made in the areas of cardiology (pacemakers) and pain management as well. I have a personal friend whose mother is actually implanted with one our SCS products and it helped decrease the massive amount of painkillers and additional back surgeries she might have required for her pain. I think in the future as we study neural networks and impacts on behavior or pain we can make better devices and better treatments.

IX. BUDGET

QTY	Description of Item	Total Cost
11	Raspberry Pi 2 Model B Project Board - 1GB RAM	$416.90
11	3ft Cat6 Snagless Ethernet	$19.80

11	Kingston Digital 16GB microSDHC Class 10	$64.02
1	100 Pack M2.5 Nylon Hex 12mm Standoff	$10.49
2	8 ½ x 11 Inch Acrylic Sheet ⅛ inch thickness	$4.00
8	M2.5 Steel Nuts	$2.40
4	M2.5 Steel Screws	$1.20
1	Sabrent USB 2.0 Ethernet Adapter	$14.99
24	Dupont Male to Female 2.54mm Jumper Cable	$3.60
2	Breadboard Power Rail	$2.00
1	MeanWell Switching Power Supply RT-50C	$20.12
1	D-Link 16-Port Gigabit Switch (DGS-1016A)	$67.02
	TOTAL	**$626.54**

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