

Analysis of the *C. Elegans* Neuronal Network

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Abstract

By studying the neuronal network of the *C. Elegans*, where the possibility of a complete analysis exists due to its simplicity, one can further understand more complicated neuronal networks. To simplify the study of a complicated network it is necessary to find what distinguishes a simple network from a random one. Through this process, we have found several parameters that are necessary to the characterization of the *C. Elegans* neuronal network.

1. Introduction

The study of the *C. Elegans* neuronal network is preparatory work for the Brain Networks Laboratory (BNL). The goals of the BNL include imaging the mouse brain at a neuronal level, constructing a web based representation of the mouse brain neuronal network, and discovering the circuits of the mouse brain. The results that are found through studying the *C. Elegans* network will be used to better understand the neuronal network of a mouse. It will lay a foundation for the visualization and analysis of the mouse brain.

To begin the analysis of the *C. Elegans* neuronal network it is necessary to apply existing and new visualization techniques. There are many different ways to visualize a network so we must find which technique is best for seeing the different characteristics. This will be helpful because networks have several characteristics that are can be enumerated, i.e. the number of connections, nodes, the in and out degree of each node, etc. Having numerous ways to categorize each network makes it simple to graph the networks in a variety of styles where each one can display a different characteristic.

The methods used include generating different random networks that satisfied different parameters. By comparing each random network to the *C. elegans* network and using different visualization tools we were able to narrow down what makes the *C. elegans* network unique. It was found that the in and out degree of a network is one way to characterize a network, and motif analysis can set the *C. elegans* network apart from a random network.

2. Background

The *C. elegans* is the most primitive organism that exists which shares many of the biological characteristics of mammals. In addition, the *C. elegans* neuronal network only

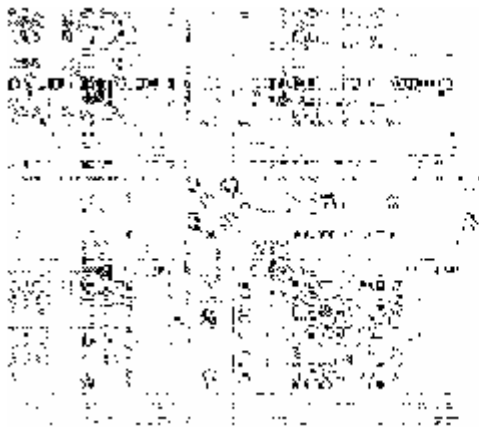
has about three hundred neurons and four thousand connections, which makes it possible to do many useful things. For example, make a complete listing of every node, every connection, and construct an html based representation of the neuronal network. The simplicity of the network makes it simple to analyze, and its similarities to a mammal brain makes it easy to use the gathered information to simplify the analysis of the mouse brain.

3. Proposed Method

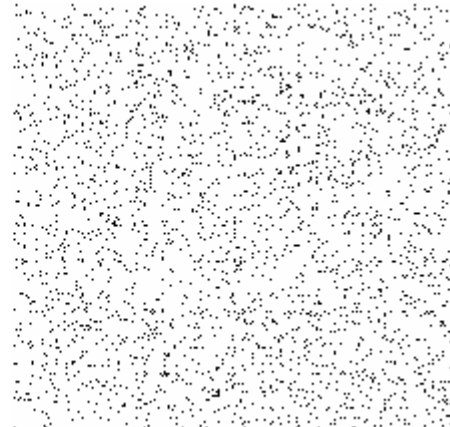
Through the use of tools such as Octave, Walrus, and MFinder a more thorough analysis of the *C. elegans* network can be achieved. Octave will be used to generate a completely random matrix, and an Octave script written by Perry Evans was used to create the parametrically random matrix. The tool Walrus by CAIDA was used to visualize the networks in three dimensions. After the use of other graphing tools in Octave, MFinder will be used to do motif analysis.

4. Experimental Results

Our goal is to analyze the *C. elegans* network for distinguishing characteristics compared to random networks. In order to do this we began with a random network where restrictions were only placed on the number of connections and nodes. After constructing this network, we began with a visual representation of the two network's adjacency matrices:



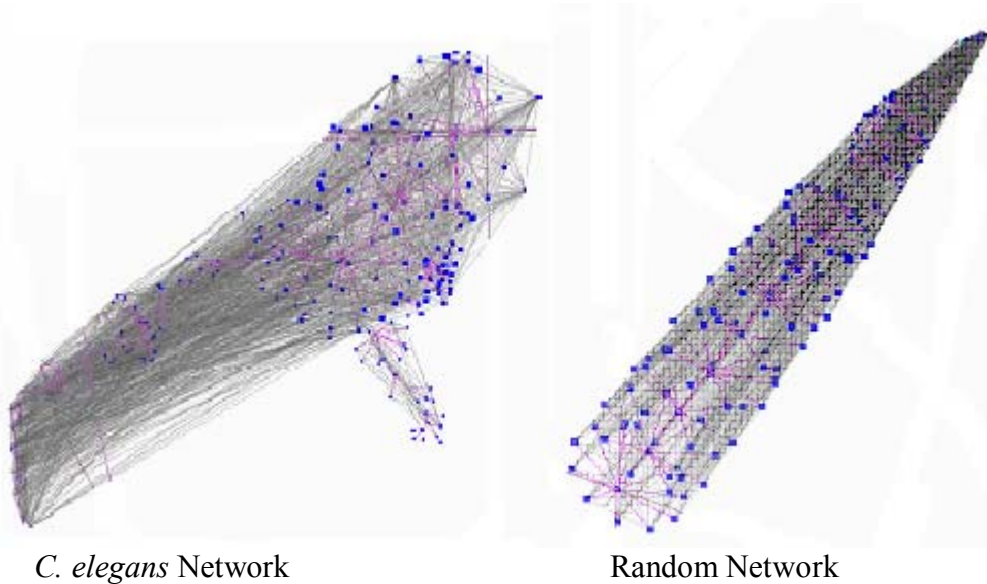
C. Elegans network



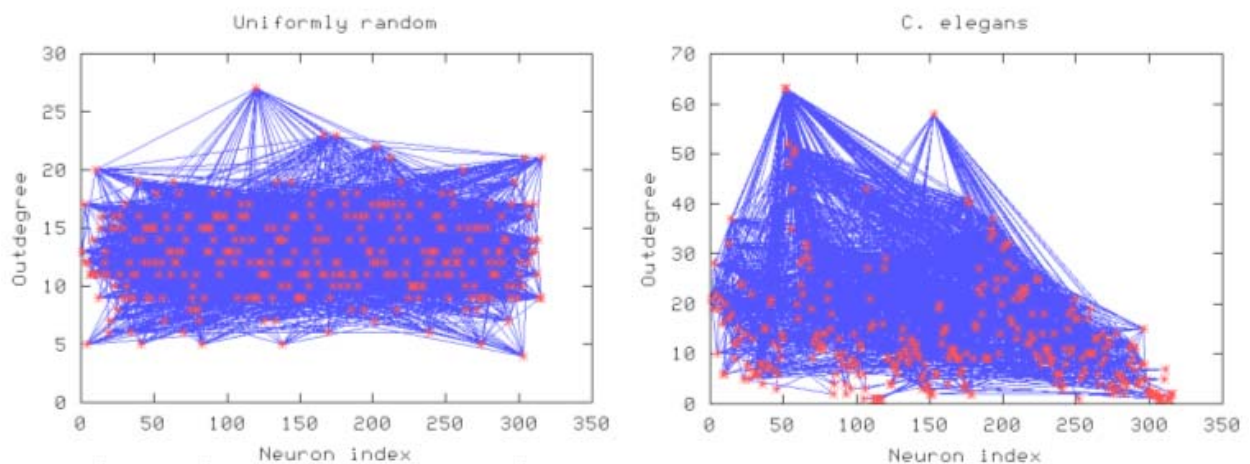
Random Network

Each of these dots represents a connection in the respective network. If there is a dot in the matrix at position (x,y) it means that there is a connection from x to y . From the above matrices you can see that the random network is evenly distributed while the *C. elegans* network is not. Looking at the *C. elegans* network you can see that there are visible lines in the graph, these occur when there is a hub in the network. Hubs exist in any natural network; there are always those nodes that have more incoming or outgoing connections. There are also nodes that do not have many connections; these are those rows that are nearly completely clear.

From studying these graphs we know there is a difference in distribution. This prompted viewing the networks using a different visualization style. Using the tool Walrus¹, which uses a spanning tree to generate a three dimensional graph of the given network, we generated the following:



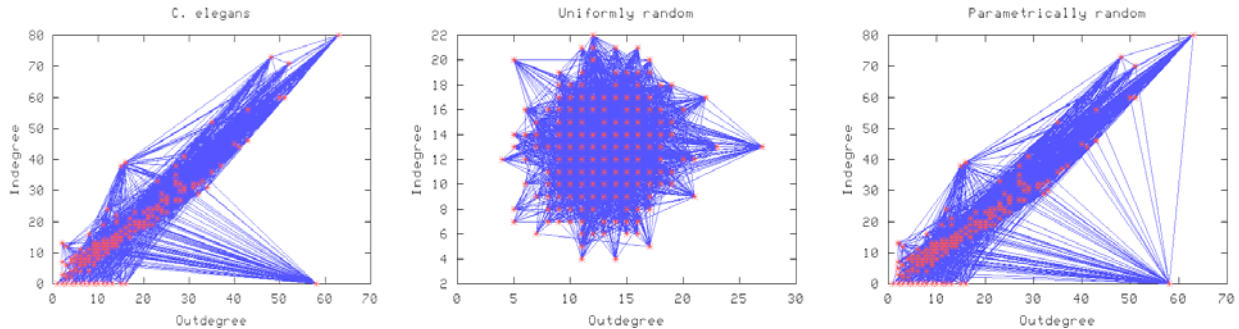
Using Walrus, the two networks appear to be fairly similar. Again, the random network has a very even distribution of the nodes. The *C. elegans* network has areas where there is a high concentration of nodes, while there are also areas that have very few nodes. One major difference is the small appendage in the *C. elegans* graph. This is caused by the pharyngeal neurons in the *C. elegans* network that are their own subsection. There is only one neuron connecting the pharyngeal neurons to the rest of the network. Since the two graphs have the same cylindrical shape it is necessary to graph the networks based on different information.



From this perspective the two networks are vastly different. The every node in the uniformly random network has an out degree ranging from five to about 25. Yet the nodes in the *C. elegans*

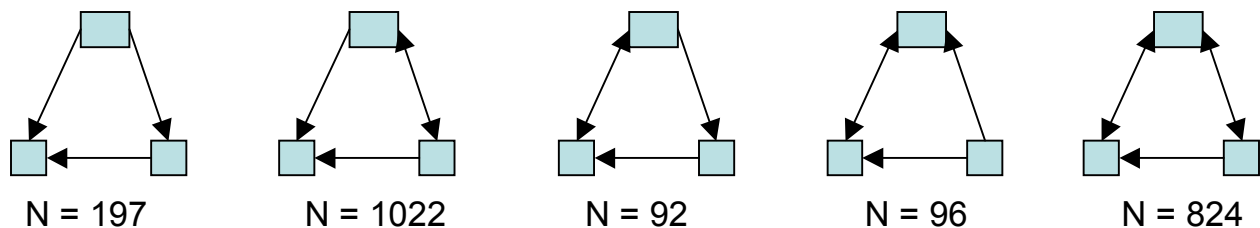
network have an out degree ranging from zero to about 65. In comparison these ranges are vastly different. In the *C. elegans* graph you can see the hubs toward the top of the graph. The uniformly random network does not have any hubs, nor does it have any nodes without any outgoing connections. From these graphs it is clear that the number of outgoing connections is important in a network.

The next logical step was to generate a random network where the parameters were the number of nodes and the preservation of the in and out degree of the *C. elegans* network.



By looking at the above graphs it is clear that the random network that preserves the in and out degree of the *C. elegans* network is very similar to the actual network. In the *C. elegans* network the nodes near the bottom left corner represent the anterior of the nematode. In the parametrically random network the distribution is exactly the same, and only differs in the bottom right corner. There are a lot of connections that go from this node to the nodes at the upper right corner, this doesn't happen in the *C. elegans* network due to anatomical reasons, connections go from the head to the tail, not vice versa.

After being able to generate a random network that is this similar to the actual network it is necessary to find other ways that the *C. elegans* network is unique. The next step involves the use of MFinder to conduct motif analysis.



The above motifs were the most common three hop motifs found in the *C. elegans* network. The second one from the left is the most interesting because it occurred the most frequently. Another student in the research group studied a natural network that involved bands and their musical influences; this motif was also the most prevalent. Further research in this area will need to be done in the future.

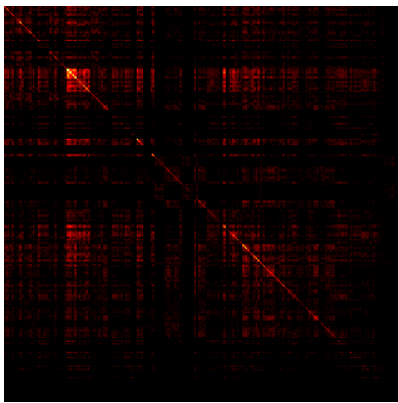
5. Related Work

The *C. Elegans* neuronal network is very simple; as a result many efforts have been made to construct a complete mapping of it. The paper “The Structure of the nervous system of the nematode *C.elegans*”² contains data about each nodes individual position in the *C. elegans* neuronal network. The data from this paper along with data from "The pharynx of *Caenorhabditis elegans*"³ was used to write "*C. elegans* synaptic connectivity data"⁴ which is a complete catalog of every synapse in the *C. elegans* neuronal network. This data was essential to our research in that we used this list to visualize and study the network.

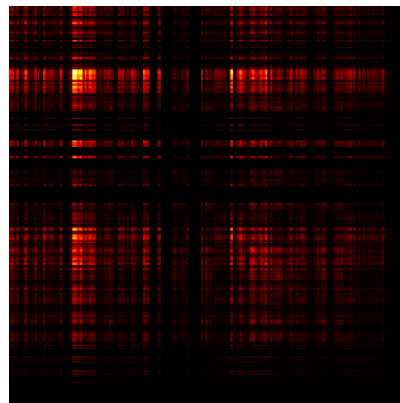
The article “Network Motifs: Simple Building Blocks of Complex Networks”⁵ provides reasons for motif analysis. Alon, an author of the article, also developed a tool called MFinder, which takes a network as input and as output gives an analysis of the motifs based upon certain specifications given in the command. The tool was used to find the motifs in the *C. elegans* network, and the article was used to understand the significance of the output.

6. Future Work

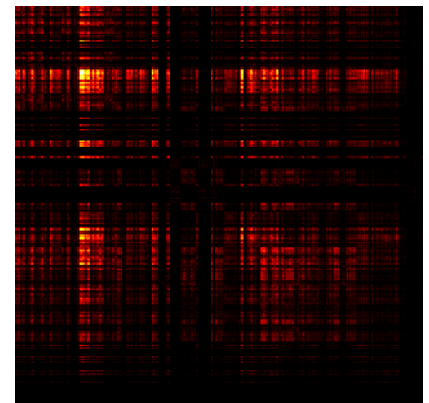
It is necessary to continue on with the motif analysis. First it is necessary to do motif analysis through the motif size of six. After that is complete it would be interesting to do motif analysis for higher order adjacency matrices.



ci^2

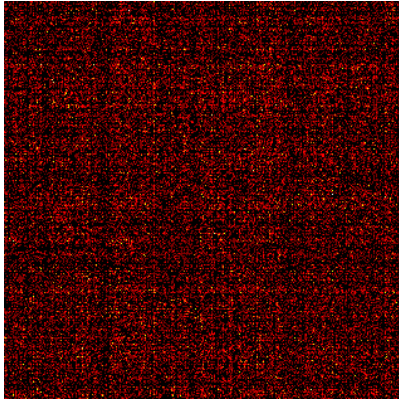


ci^3

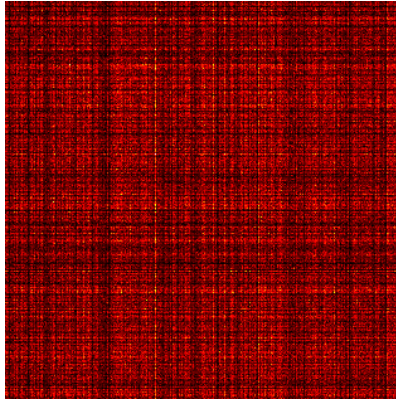


ci^4

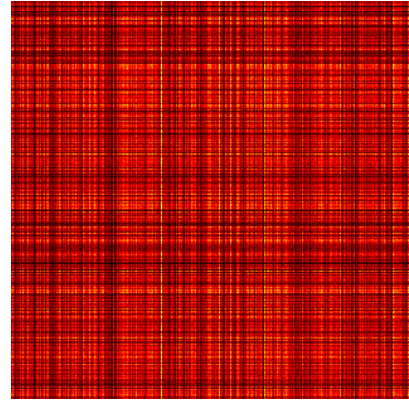
The above illustrations are the graphs of the adjacency matrices for the higher order powers. The one on the left is the *C. elegans* adjacency matrix to the second power; the one in the middle is the adjacency matrix to the third power; the one on the right is the adjacency matrix to the fourth power. As the powers increase the images of the adjacency matrices begin to look increasingly similar.



r^2

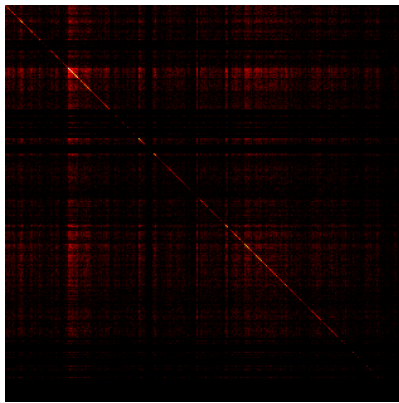


r^3

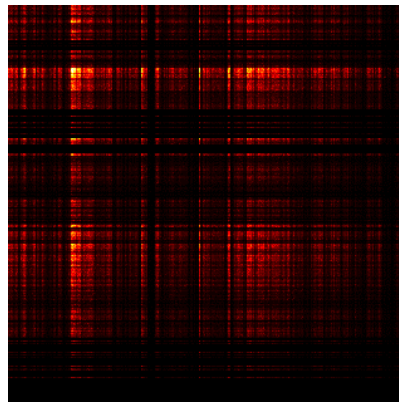


r^4

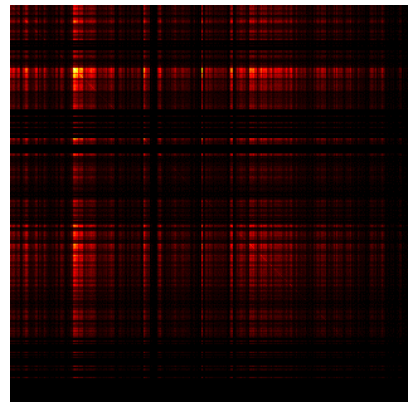
The above pictures are visualizations of the adjacency matrices of the random network that was not bounded by any parameters other than the number of connections and the number of nodes in the network.



pr^2



pr^3



pr^4

The above pictures are visualizations of the adjacency matrices of the parameterized random network.

¹ Walrus Visualization Tool. [www.caida](http://www.caida.org)

² White, J. G., Southgate, E., Thomson, J. N. & Brenner, S.
"The structure of the nervous system of the nematode *Caenorhabditis elegans*." *Phil. Trans. R. Soc. Lond. B* 314, 1-340 (1986).

³ Albertson, D. G., & Thomson, J. N.
"The pharynx of *Caenorhabditis elegans*." *Phil. Trans. R. Soc. Lond. B* 275, 299-325 (1976).

⁴ K. Oshio, S. Morita, Y. Osana and K. Oka;

"C. elegans synaptic connectivity data," Technical Report, CCEP, Keio Future No. 1 (1998)

⁵ R. Milo, S. Shen-Orr, S. Itzkovitz, N. Kashtan, D. Chklovskii, and U. Alon; "Network Motifs: Simple Building Blocks of Complex Networks." www.sciencemag.org. (October 25, 2002).