EN.580.694: Statistical Connectomics
Final Project Report

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Clustering and inferring the *C. elegans* glia network

Opportunity The idea of including non-neuronal cell types in Connectomics have been posed by some authors, who claim that the exclusion of glia from the BRAIN Initiative makes the quest of Connectomics of understanding the brain futile [1]. These same authors have proposed the use of the *C. elegans* connectome data as starting point for the inclusion of glia in cell wiring studies. However, no action has been taken in the matter, and it remains uncertain whether their claims are valid or not. Do glia play a role in the *C. elegans* connectome? Are their roles important enough to consider them in connectivity studies? Does their exclusion make current Connectomics studies unvalid? How are they organized? Many questions remain unanswered.

Challenge The precise *C. elegans* glia-glia wiring has never been investigated, which in terms slows down the study of the interactions of glial cells. However, the WormAtlas Project [2] does report a detailed neuron-glia adjacency list (with images included) and neuron-neuron connectivity data, from which the glia-glia network can be inferred.

Action The glia-glia adjacency matrix was inferred from the data available at the 'WormAtlas Project' site; the hermaphrodite neuron-neuron adjacency list and neuron-glia adjacency list were used. The glia-glia (GG) adjacency list was constructed under the assumption that glial cells connected to neuron A are connected to glial cells connected to neuron B given that neuron A and neuron B are connected to each other. Additionally, the glia-glia network (GG) was added to the neuron-neuron (NN) adjacency list and the neuron-glia (GN) adjacency list to create the matrix named 'Total', which we call the 'Worm Glia+Neuron Connectome' because it includes all types of connections between the two cell types. The full matrices for glia glia, neuron glia, neuron neuron glia and neuron neuron connections were constructed too. We then performed kmeans and hierarchical clustering on the 'Total' matrix, the Glia-glia matrix and on 'GN' (the glia-neuron matrix) for comparison.

Resolution The matrices obtained are shown on the Images section.The glia population in the neuron neuron glia matrix appear to be clustered in a small community, with glial members that interact with the neurons interacting little with other glial cells (see glia neuron matrix for comparison). Both and hierarchical clustering on the Glia+Neuron Connectome appear to have grouped neurons and glia on separate clusters when k=2, and when k=3, the communities appear to be 'neurons that connect to neurons', 'glia that only connect to glia' and 'glia that connect both to glia and neurons'.

Future Work Statistical analysis must be performed on the inferred networks to determine whether or not their structure is product of assumptions made when constructing the network, or errors in the algorithm used to produce the data. Additionally, permutation testing should be carried out to determine whether the observed structure in communities can be obtained by chance. We hope that this first step in computing the glial connectivity data can help to answer the questions posed above.

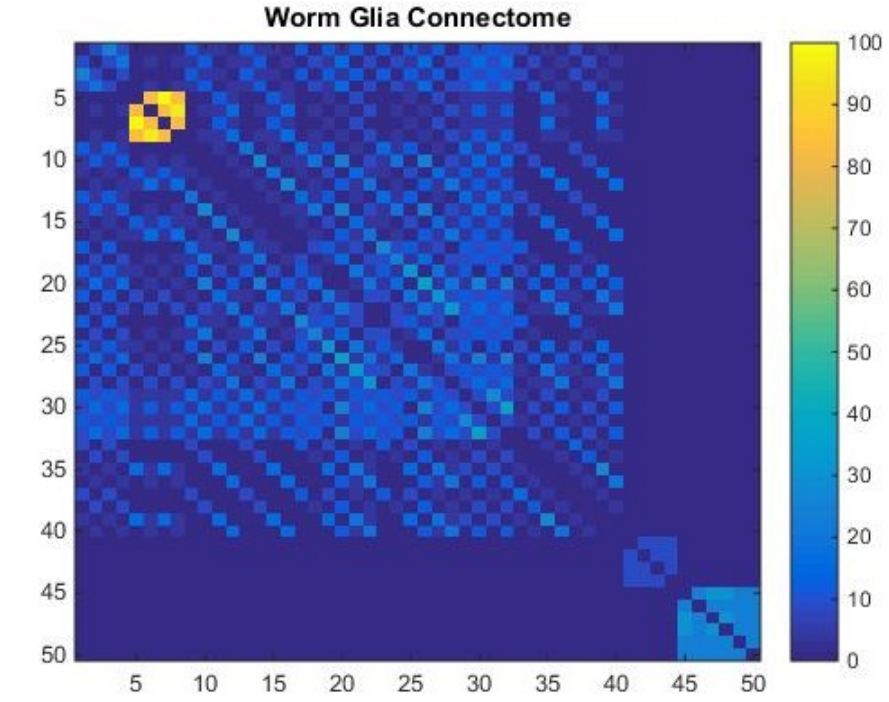
Bibliography

1. Nature 501, 2527 (05 September 2013), doi:10.1038/501025a

2. WormAtlas, Altun, Z.F., Herndon, L.A., Crocker, C., Lints, R. and Hall, D.H. (ed.s) 2002-2015. http://www.wormatlas.org/neuronalwiring.html

3. Mutant sensory cilia in the nematode C. elegans. L.A. Perkins et al. Dev. Biol. (1986) 117:456-487; link: http://www.wormatlas.org/ver1/handbook/hypodermis/gliatable.htm

1 Images


Worm Glia Connectome
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15
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25
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5 10 15 20 25 30 35 40 45 50
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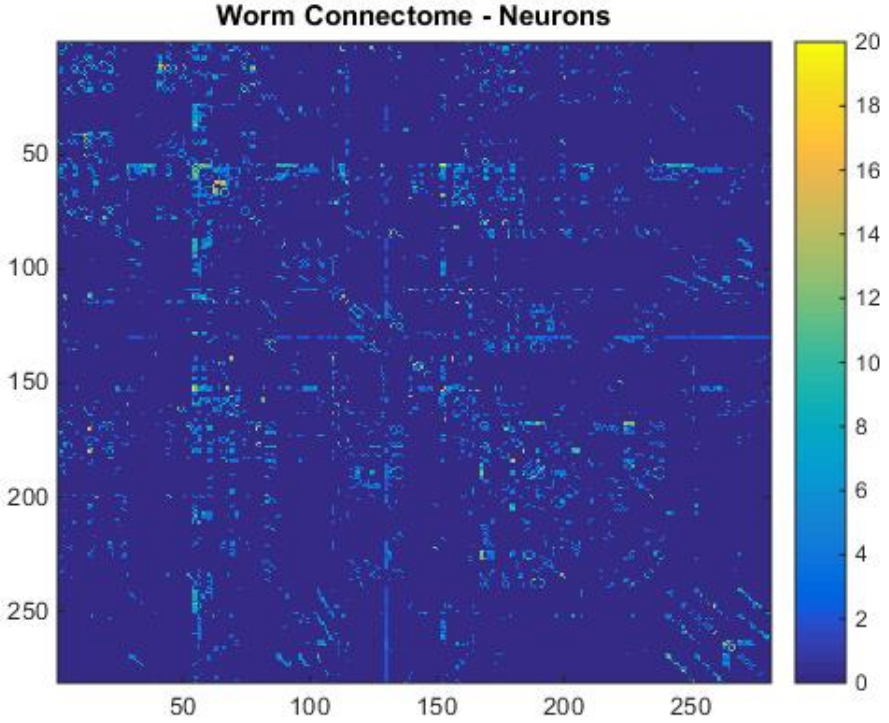
30
20
10
0


Worm Connectome - Neurons
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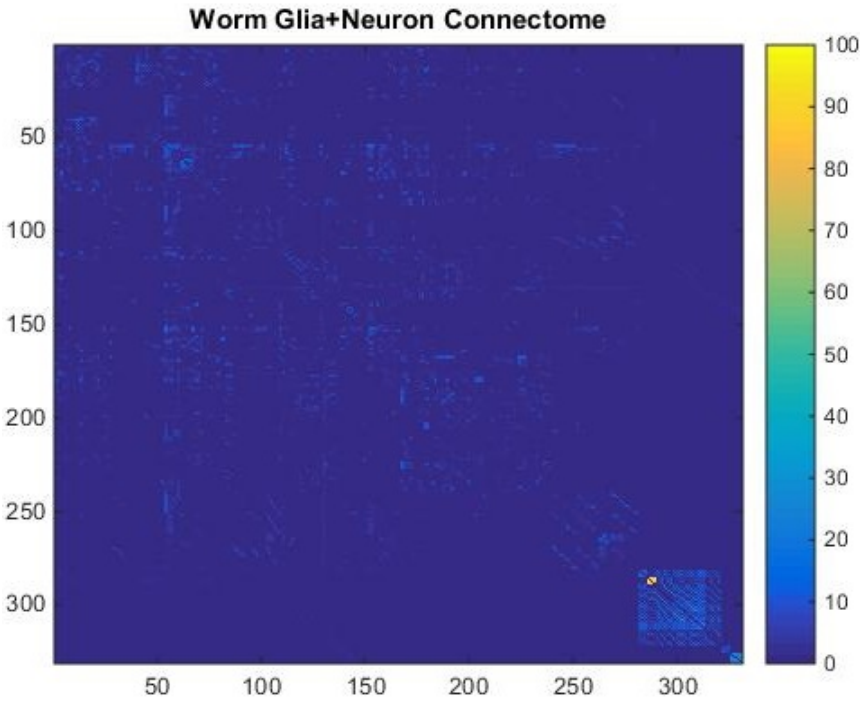
100
150
200
250
50 100 150 200 250
20
18
16
14
12
10
8
6
4
2
0


Worm Glia+Neuron Connectome
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30
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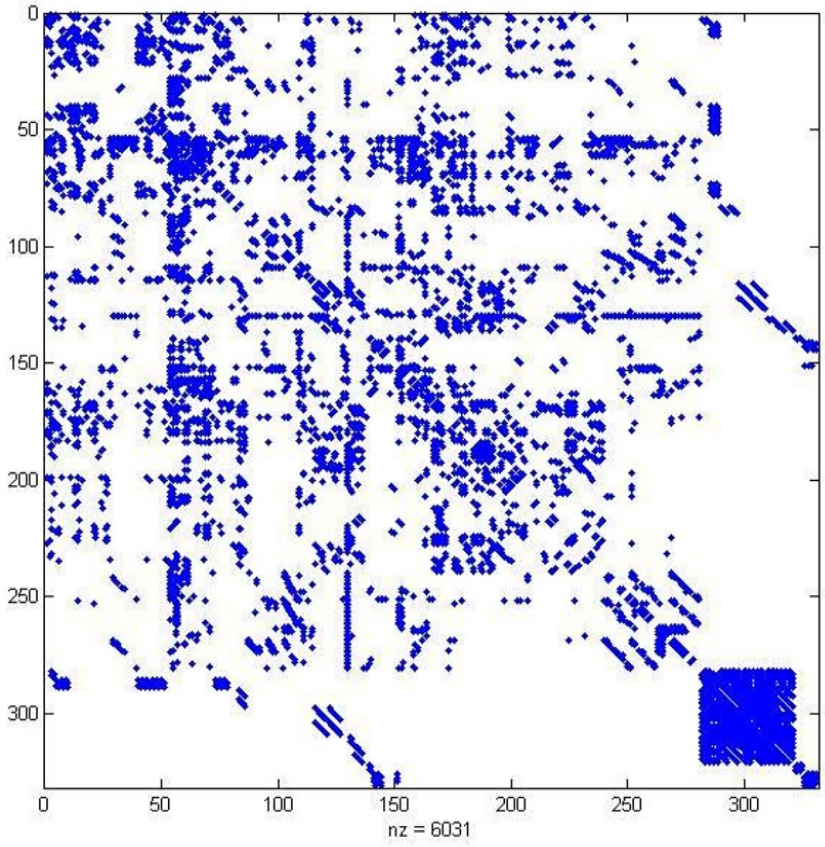
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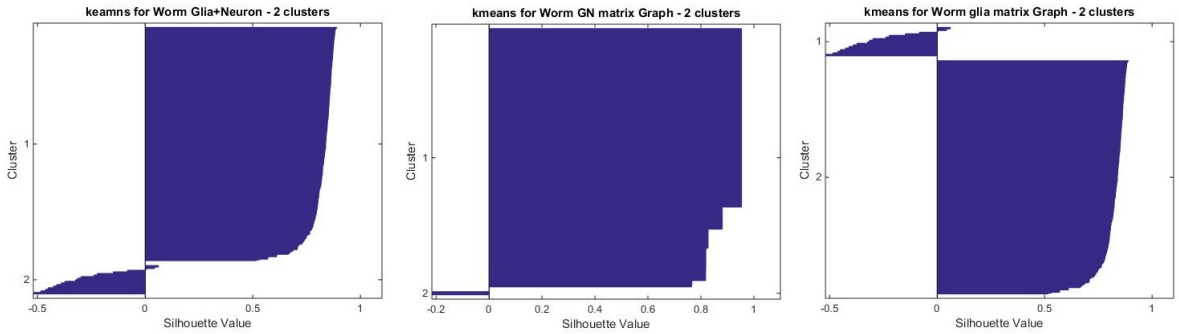
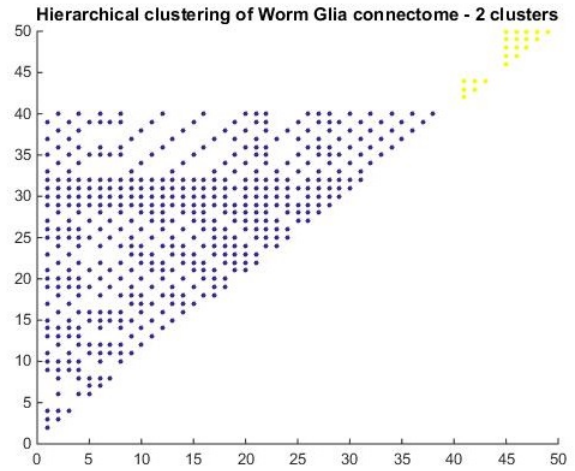
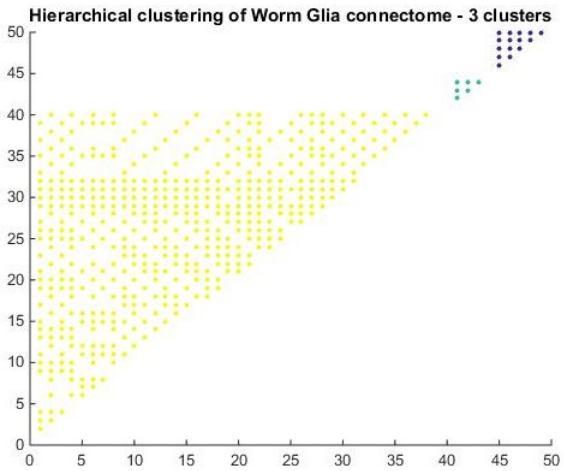
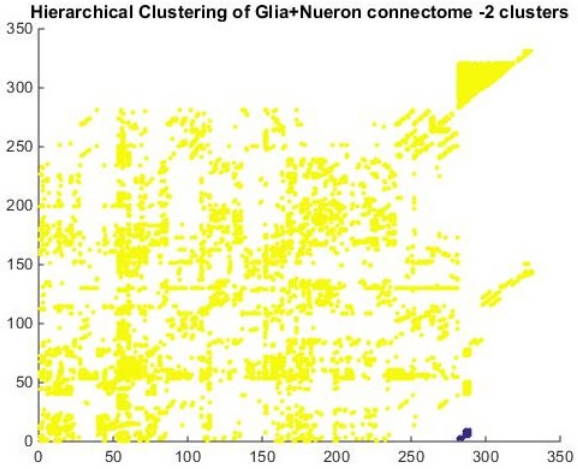
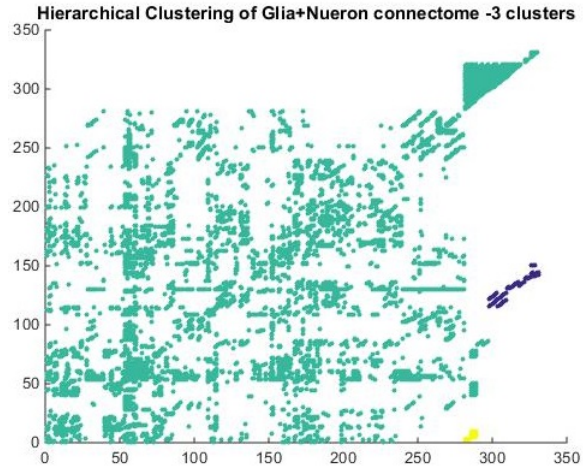
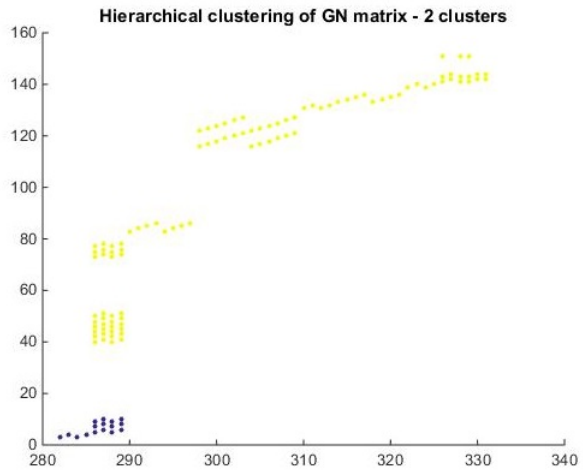

keamns for Worm Glia+Neuron - 2 clusters
Cluster
Silhouette Value
kmeans for Worm GN matrix Graph - 2 clusters
Cluster
Silhouette Value
kmeans for Worm glia matrix Graph - 2 clusters
Cluster
Silhouette Value


Hierarchical clustering of Worm Glia connectome - 2 clusters


Hierarchical clustering of Worm Glia connectome - 3 clusters


Hierarchical Clustering of Glia+Nueron connectome -2 clusters


Hierarchical Clustering of Glia+Nueron connectome -3 clusters


Hierarchical clustering of GN matrix - 2 clusters
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280
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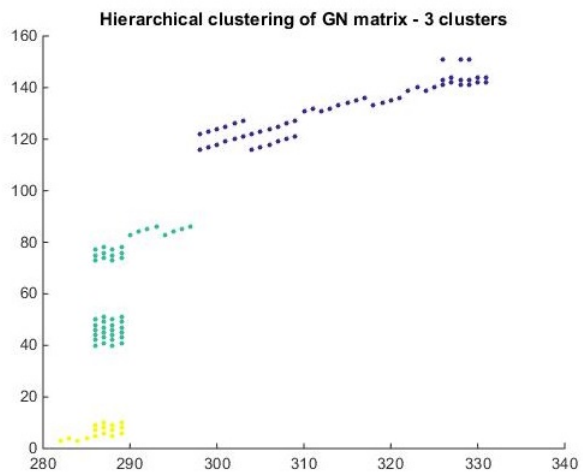
300
310
320
330
340


Hierarchical clustering of GN matrix - 3 clusters
160
140
120
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