Exploration of the Human Connectome

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CIS 397

Background:

A connectome is a network where each node represents a neuron and each edge represents a fiber connection. This means the network more accurately represents structural connections rather than functional connections. The specific connectome I am looking at in the exploration is from a Human. The data was collected from a diffusion mri, a Diffusion-weighted magnetic resonance imaging (DWI or DW-MRI) is the use of specific MRI sequences as well as software that generates images from the resulting data that uses the diffusion of water molecules to generate contrast in MR images. It allows the mapping of the diffusion process of molecules, mainly water, in biological tissues, in vivo and non-invasively. Molecular diffusion in tissues is not random, but reflects interactions with many obstacles, such as macromolecules, fibers, and membranes. Water molecule diffusion patterns can therefore reveal microscopic details about tissue architecture, either normal or in a diseased state. In the context of the human connectome we are able to reveal the synaptic connections between neurons.

** Edit ** Human Connectome was too big to analize in the time frame of this project so the Macque Rhesus Brain (Monkey) was used instead

Goals:

1. Explore the nodal and network properties of the connectome and relate them to neuroscience.
    - Why is this important?
        - Having a decent understanding of graph theory and network analysis will allow us to notice properties that stand out to us, the purpose of this section is to explore the meaning of these properties in a neuroscience context.
    - Methods:
        - average degree - average number of physical connections
        - histogram of degree distribution
        - betweenness - how many shortest paths from one neuron to another pass through this neuron
        - Participation coefficient - how many communities node is directly connected to
        - Identify hubs by aggCent

        - Identify bridges - important neurons that would create a disconnected network if lesioned
        - Find network density
        - Find Louvain communities
        - Rich club subgraph visualization
2. Does PageRank accurate describe hubness in a connectome?
    - Why is this important?
        - By understanding how the metrics we use to describe a "good" webpage in a search algortihm apply to neurons can give us insight to what exactly a "good" neuron is in the context of PageRank.
    - Methods:
        - Convert to Directed Graph
        - Run PageRank
        - Compare and Contrast with CentAgg hubs identified in step 1
3. Which theory better enables a complete infection of the network, constant remodeling of synaptic edges vs stable edges.
    - Why is this important?
        - Neuroplasticity is the ability of the brain to change in structure or function in response to experience. We can be 100% sure our brains are at least a little plastic, if not we would not be able to learn anything new. A study found that during human development, the 100 trillion synapses in the human cortex are forming at a rate of 10,000 every 15 minutes. The question I am asking at this point in my research is: "Does the amount of plasticity have an effect on how easily action potential can propagate through the network?". I am going to be testing two hypotheses: 1) the plasticity is happening at a rate so small relative to action potential propagation that plasticity will have no effect (stable edges), 2) the plasticity is happening so rapidly it will always have a chance to reconfigure edges before a neuron can excite its neighbor (constant remodeling). I will also be investigating how the start node affects
    - Methods:
        - Simulate Epidemic for test cases
        - Store the boolean representing if all nodes we excited in a dataframe
        - Compare the efficacy of the test cases / influcence on total "infection"
4. Explore which Neurons are critical in the prevention of Alzheimer's Disease or Schitzaphernia
    - Why is this important?
        - By understanding which nodes are integral to maintaining small world and non-random properties of the network, we can better understand and diagnose connectivity based disorders/diseases.

- Methods:
  - add relevant attributes to nodes (brainAttributes())
  - convert to dataframe
  - sort dataframe by aggCent value, highest to lowest.
  - remove or 'lesion' the top 10 nodes 1 by 1, checking each time if isSmallWorld is true and print the result

Datasets: HUMAN-JUNG2015-M87101234 MACAQUE-RHESUS-BRAIN-1

Sources: https://networkrepository.com/bn-human-Jung2015-M87101234.php https://networkrepository.com/bn-macaque-rhesus-brain-1.php

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title={The Network Data Repository with Interactive Graph Analytics and Visualization}, author={Ryan A. Rossi and Nesreen K. Ahmed}, booktitle={AAAI}, url={https://networkrepository.com}, year={2015}

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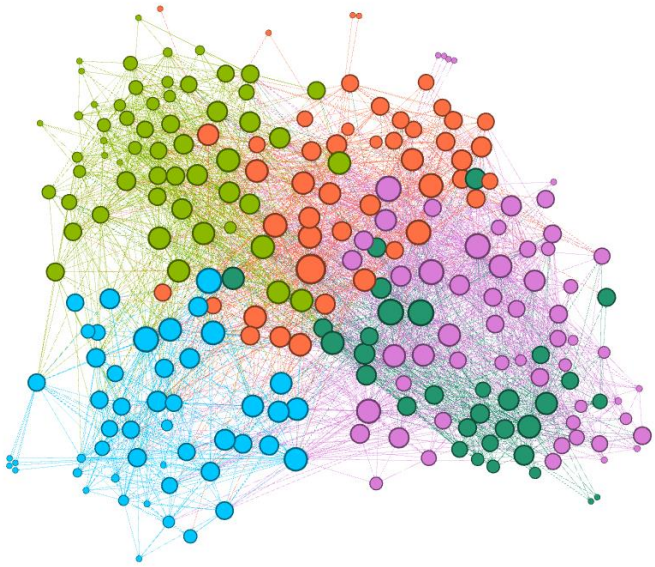
1) Explore the nodal and network properties of the connectome and relate them to neuroscience

Our first step is to identify the hubs of the network. Hubs are nodes that have a high degree or high betweenness centrality, indicating they are important for the overall connectivity of the network. We will also calculate the participation coefficient for each node, which measures the diversity of the connections of a node to different modules of the network. This will give us a more nuanced understanding of the role each node plays in the network.

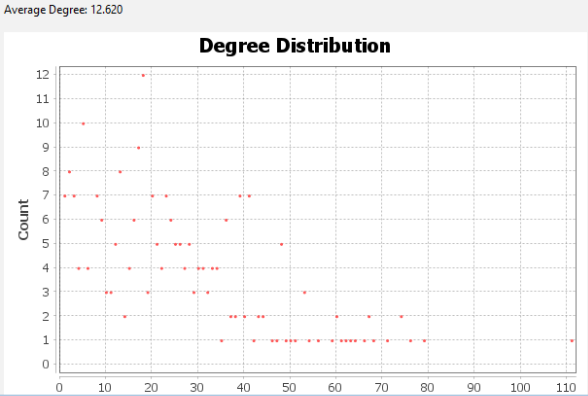
This Network has a total of 242 nodes and 3054 edges. The Network has a denisty of 0.105. A dense graph would have an edge value closer to N^2 where n in the number of nodes. Since we have less than 58,000 edges we can say that out graph is sparce.



mod_sized_by_centagg.png

This is a visualization of the Macque Rhesus Connectome. The nodes are sized by a centrality aggregate function that is the sum of degree, betweenness and particpation coeffcient. The nodes are colored by louvain community. In the undirected graph, 5 communities were discorved. This could reflect the 4 lobe model we use for humans, we recognize the Frontal, Parietal, Occipital and Temporal lobes as distinct communities. The extra group could be the parts of the brain that are not represented by these lobes like the medulla etc.

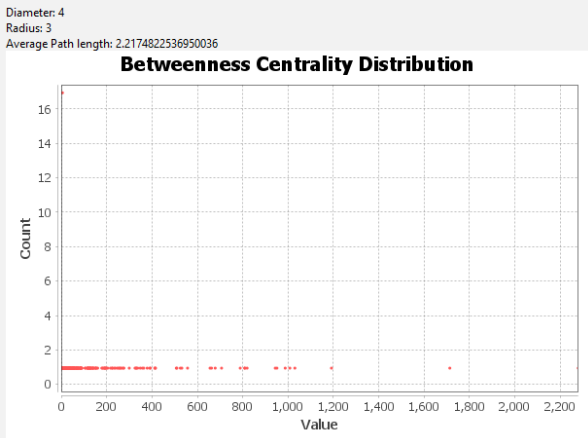
Degree - tells us how many physical connections a neuron has



avgDegreeDistrobution.png

In this network, a neuron has on average 13 connections. We see a non-gaussian distribution of degree, we expect to see this in a small world network

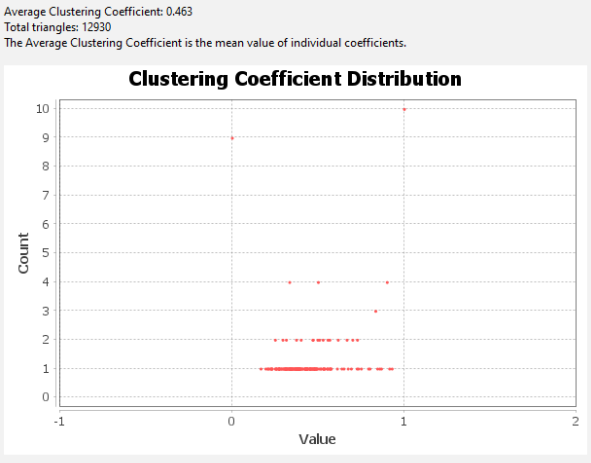
Betweenness - how many shortest paths from one neuron to another will travel through this neuron



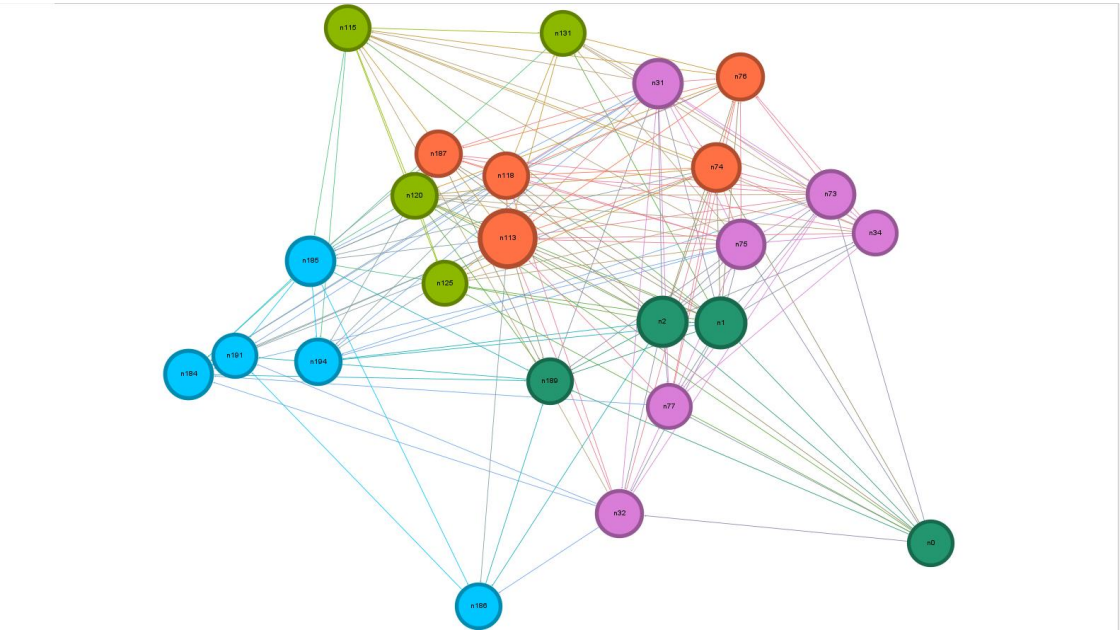
BetweennessDistorbution.png

The diameter of our network is 4. The average path length is 2.71, this is also consistent with a small world network.

Clustering Coefficient - this tells us how connected a neurons neighbors are, describing the local density of connections.



ClusteringDistrobution.png



top10%bycentagg.png

I decided to take a look at the 10% of nodes with the highest centrality aggreate values

Nodes pictured: n186, n32, n0, n77, n189, n2, n1, n75, n73, n34, n74, n113, n125, n194, n191, n184, n185, n120 ,n187, n118, n76, n31, n131, n115

Total nodes: 24

There seems to be 4-6 nodes from every community, implying that it is a helpful for a community to have a few high degree nodes that participate in many communities.

2) Does PageRank accurate describe hubness in a connectome?

3) Which theory better enables a complete infection of the network, constant remodeling of synaptic edges vs stable edges

We will use an epidemic model to simulate the propagation of action potentials in the network. This will help us understand how information may flow through the network and identify potential bottlenecks or vulnerabilities in the network structure. I will also be testing to see if synaptic restructering happens at a rate non-relevant to action potential propagtion (stable edges) or if synaptic restructuing happens at a rate of once per activation. After initially trying to model this with a cascade, I found that for a few reasons an epidemic was better fitting. First off, a neuron does not get one and only one chance to excite its neighbors. An epidemic allows us to give it a chance to excite it neighbors multiple times. An epidemic also allows us to model the state of the ion chanels in a SIRS type model.

Here we propose an epidemic model of action potential propagation in a network of neurons. This model is inspired by models of infectious disease spread in social networks, where an “infection” can spread from one individual to another across the connections in the network. In our model, an “infection” corresponds to a neuron being in an excited state, meaning it has recently fired an action potential.

A critical feature of our model is that it includes a refractory period for each neuron: after firing an action potential, a neuron becomes temporarily less likely to fire again. This is modeled by reducing the “infection rate”, or excitability, for a certain period of time after a neuron fires. This feature captures a key property of real neurons: their refractory period due to the time it takes for ion channels to reset.

Our model also takes into account the strength of synaptic connections between neurons, which can vary greatly in a biological neural network. Stronger connections are more likely to result in an action potential in the receiving neuron. We model this by assigning a random strength to each synaptic connection, and using this strength to determine the likelihood of an action potential propagating across the connection.(It is assigned a random arbitrary value to simulate differences in strength but does not accurately represent strength)

My code will run a set amount of steps in the epidemic, it will return true if at some point in the epidemic every node had fired. They do not need to be consequtive fires. If I had more time, I would add code that adds each step to a dataframe so I can visualize the propagation of action potential.

Unfortunately, I was unable to run the epidemic simulation in time. If I were to continue the research I would check my code for correctness and make sure I care about the answer being computed by my epidemic function, then try to get time to run the epidemics on a better computer. I would want to run each test a few times, the first few with the epidemic starting at my hub nodes, then the page rank nodes, then starting at a randomly selected set of nodes. I will then keep the results of these trials in a dataframe and compare which set of nodes was able to get the most true values returned. In my

2) Does PageRank accurate describe hubness in a connectome?

understanding of this problem it would signify and better suited network for propagating action potential.

4) Explore which Neurons are critical in the prevention of Alzheimer's Disease or Schitzaphernia

After identifying the hubs and nodes with high PageRank, we will perform a lesioning experiment to test the resilience of the network. We will remove the hubs, high PageRank nodes, and some random nodes and measure how the network maintains its complex small world properties. A loss of these properties is indicative of Alzheimer's disease or Schizophrenia, so this experiment can help us understand how the network may be affected in those conditions.

Unfortunately, I was not able to evaulate the effect of lesioning the network. From steps 1 and 2, I was able to identify my nodes of intrest and I have code that will create subgraphs of G with a singular node removed and evaluate the small world coeefcient of the resulting subgraph. I am doing this with the nx.sigma function. On my laptop I was running the sigma function overnight and I was not able to get a result. I played with the parameter to make it as quick as possible but it yet to return. In future research I would like to run my code for every node of interest and look at the resulting small world coefficient. This would allow me to compare the hub nodes and pagerank nodes to random and see if there is a statistically significant difference for lesioning those nodes or if any node could potentially cause a loss of these features.