MATH472 Final Presentation

Motifs and scale-free properties of connectivity networks across species

Brandon Barton, Lowell Kalman

Mathematical and Computational Neuroscience
Colorado School of Mines

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Network Neuroscience

- Our project is distinct from network models we have discussed so far
- Network science and graph analytic approach
  - This approach focuses on representing connectivity in large networks
  - Challenging to capture the dynamics of single neuron spiking
  - Better at representing network as a whole

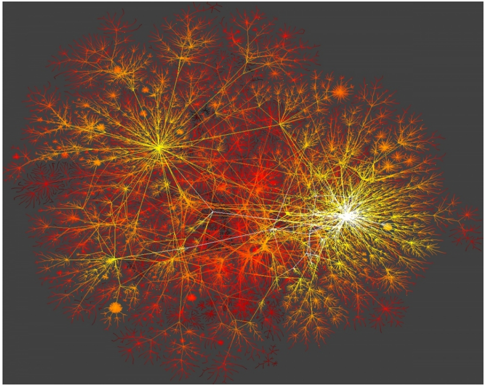
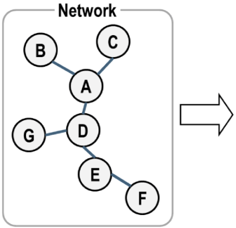


Figure: The Topology of the Internet [2]

Brain Network Representation

- Given a graph $G = (N, E)$
- We can represent neurons as nodes (N), and synaptic connections as edges (E)
- **Recall:** Connectivity/ Adjacency Matrix $\mathbf{A}$
- The element A_{ij} in $\mathbf{A}$ represents a connection between the nodes in the i^{th} row, and j^{th} columns



Connectivity Matrix

	A	B	C	D	E	F	G
A	0	1	1	1	0	0	0
B	1	0	0	0	0	0	0
C	1	0	0	0	0	0	0
D	1	0	0	0	1	0	1
E	0	0	0	1	0	1	0
F	0	0	0	0	1	0	0
G	0	0	0	1	0	0	0

Figure: Example of a Connectivity/ Adjacency Matrix [6]

Connectivity in Brain Networks

- How is brain connectivity measured?
  1. Anatomical connectivity - voxels of gray matter, connections of dense axonal bundles
  2. Functional connectivity - fMRI analysis shows temporal connection between brain regions [8]
- Challenging to measure single neuron connections
  - Human brain $\mathbf{A}$: (N $=$ 1 Billion, E $=$ Many Trillions) $\rightarrow$ 1,250,000,000 TB
- Connectivity at varying resolution
  - Neuron-to-neuron connections
  - Brain region-to-region

Network Motifs

- What is a network motif?
  - Let H = (N, E) be the host graph
  - A subgraph $G = (N', E') \in H$
- A motif is simply a statistically significant subgraph existing in the larger complex network
- Motifs can represent recurring interactions of circuitry in the brain

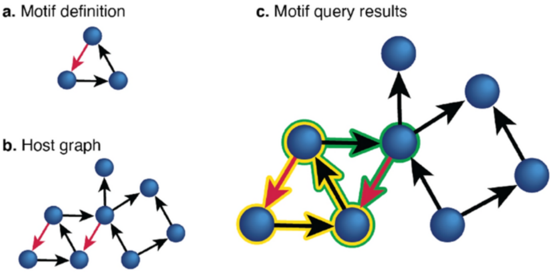


Figure: Depiction of motif query [5]

The Degree Distribution of a Network

- $p(k)$ = The probability of a randomly selected node having k connections
- Gives insight into the overall structure of a network

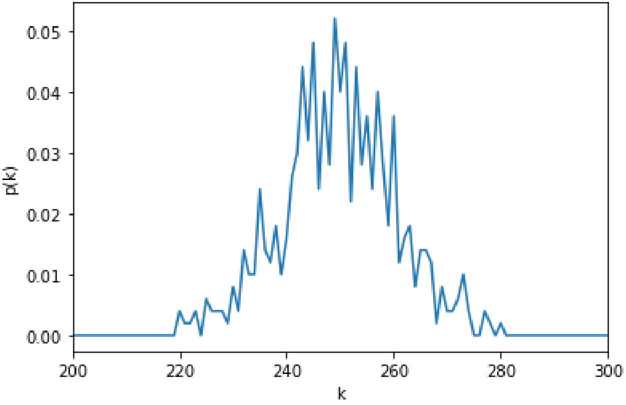


Figure: Binomial degree distribution for a random graph

Motivating Questions

1. Do the building blocks of network interactions (motifs) provide insight into how the complex brain network is formed fundamentally?
2. Do motif concentrations follow similar distributions in networks of differing scales?
3. Are there any striking differences between the connectomes of different animals?

Data Gathering Techniques

- Drosophila: Electron Microscopy
- Mouse: Enhanced Green Fluorescent Protein
- Cat: Tract Tracing
- Macaque: Retrograde Tracing

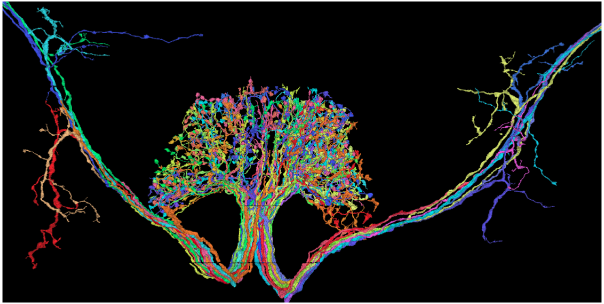


Figure: Display of Fly Brain [7]

Connectivity Data Across Species

- We investigated networks of varying **size** and **resolution**

Network	Nodes (N)	Edges (E)	Density (ρ)	Rel. Density (ρ_r)	Avg Degree (k_{avg})
Drosophila	1780	17417	0.006	0.007	20
Mouse	213	21807	0.483	0.576	205
Cat	65	1139	0.274	0.326	35
Macaque	91	628	0.077	0.091	14

Table: Network attributes and summary statistics

Motifs

- What network motifs are useful for brain networks?
- What network motifs *can* we search for?
- Subgraph monomorphism task is computationally intensive, (NP-Complete) [3, 5, 9]
- DotMotif uses a variation of the VF2 algorithm [5]

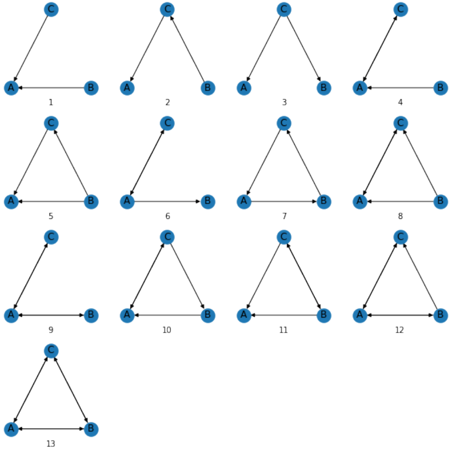
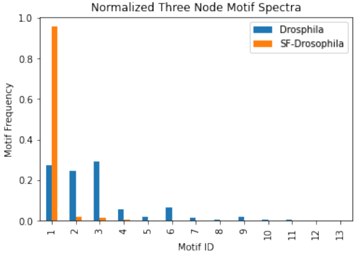


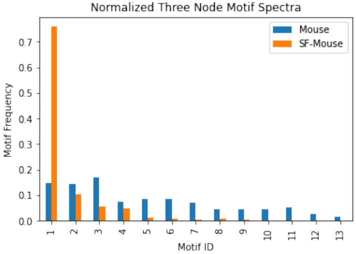
Figure: Set of three node (n=3) directed motifs.

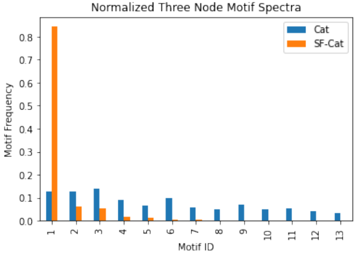
Stochastic Graph Generation

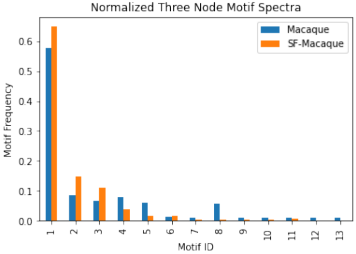
- We generated canonical random networks using NetworkX graph generators. [4]
- Barabási–Albert (BA) model [1]
  - Adds nodes one-by-one
  - Preferential attachment
- Scale-free (SF) Model
  - Variation of the BA model, with additional parameters
- We stochastically generated two graphs for each animal network
  1. BA networks with Nodes (N) and average degree (k_{avg}) from the animal brain networks.
  2. Directed scale-free (SF) networks with vertices (V)

Motif Concentrations









Discussion - Motifs

- All networks show high concentrations of simple three node motif structures
  - Unidirectional
- As complexity of motif relationships increases, motif frequency decreases across all networks.
  - SF and real networks are most similar in this regard
  - Directed network relationships are important
- The macaque network is highly similar to the SF generated network, while other networks differ significantly

Degree Distributions of Mouse, Cat, and Macaque

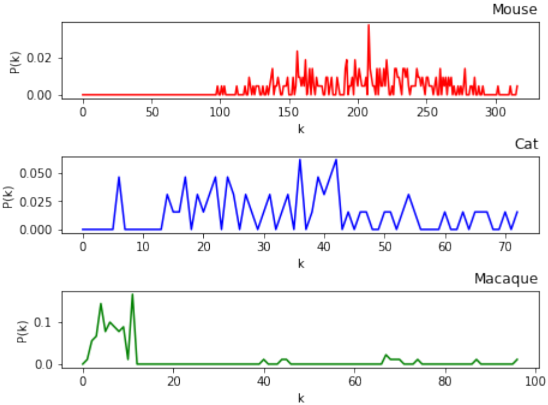


Figure: Degree Distributions for Real Networks

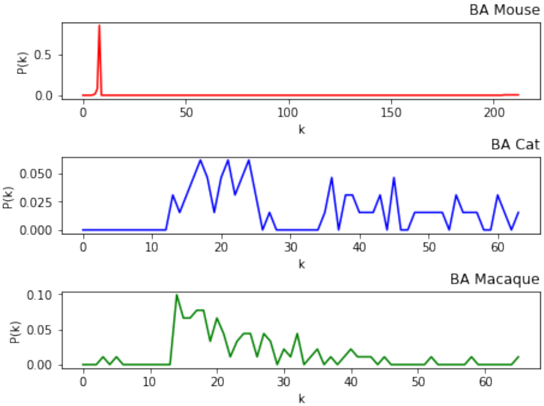


Figure: Degree Distributions for Barabasi-Albert Networks

Degree Distribution of the Drosophila

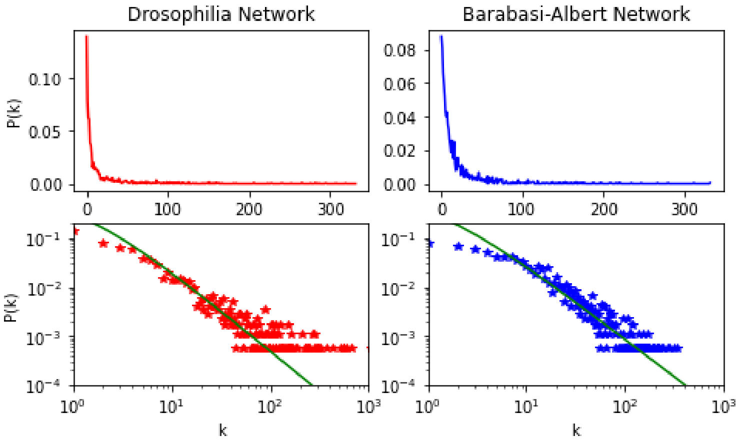


Figure: Linear and Loglog representations of the Drosophila Degree Distribution vs BA Random Network

Implications of the Degree Distributions and Scale-Free Networks

- The Drosophila network follows a power law degree distribution
  - $p(k) = k^{-\gamma}$
  - "Scale-Free": Fractal structure in the network, presence of hubs
  - Calculating γ can give more insight, but it is not trivial [2]
  - Drosophila is the network with the highest resolution: connections between individual neruons
- Mouse, Cat, and Macaque do not have a clearly distinguishable degree distribution
  - This suggests information is lost in the lower resolution connectomes
  - Could also result from having less nodes

Future Research

- Gathering data of other animals at a neuron to neuron resolution
  - It would be expected that the scale-free property emerges
- Compare networks to other random graph models
  - Sub-linear preferential attachment (limits of neuronal attachment)
- Examine relevant motifs per brain region

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[3] L. P. Cordella, P. Foggia, C. Sansone, and M. Vento. A (sub)graph isomorphism algorithm for matching large graphs. *IEEE Transactions on Pattern Analysis and Machine Intelligence*, 26(10):1367–1372, 2004.

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