

# CSCI 598 Final Presentation

Brain Network Motifs and Graph Properties of *C. Elegans* Through Development

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# 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 [4]
- Challenges of network approach
  - Challenging to capture the dynamics of single neuron spiking
  - Human brain **A**: ( $N = 1$  Billion,  $E = \text{Many Trillions}$ )  $\rightarrow 1,250,000,000$  TB
  - However, better at representing network as a whole
- Connectivity at varying resolution
  - Neuron-to-neuron connections
  - Brain region-to-region

# C. elegans

- *Caenorhabditis elegans* (aka *C. elegans*) are a small nematode worm
- Well-studied
  - Short life-span
  - Feed on bacteria
  - Relatively small neuronal network
- Connectome is fully mapped
  - Larval stages of development → to adulthood
  - Snap-shots of multiple networks

# C. elegans Development Phases

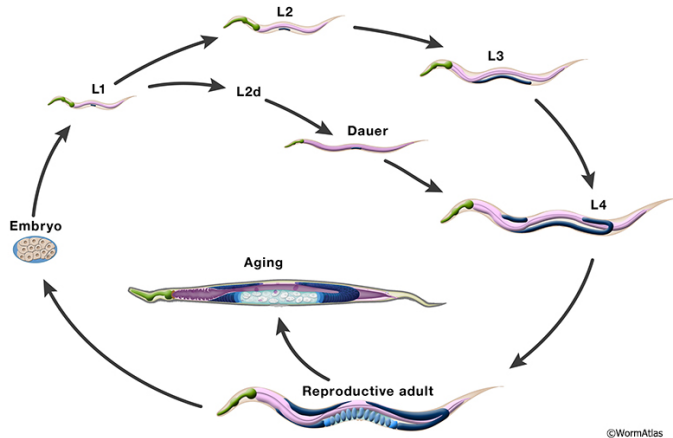


Figure: C. elegans developmental cycle

# Network Development

Dataset	Nodes (N)	Edges (E)	Density ( $\rho$ )
Witvliet 2020 1	187	849	0.024
Witvliet 2020 2	194	1095	0.029
Witvliet 2020 3	198	1101	0.028
Witvliet 2020 4	204	1324	0.040
Witvliet 2020 5	211	1763	0.037
Witvliet 2020 6	216	1707	0.050
Witvliet 2020 7	222	2450	0.051
Witvliet 2020 8	219	2416	0.077

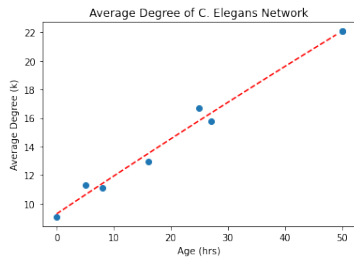
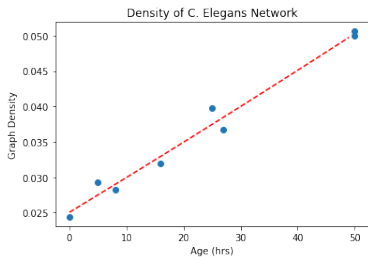
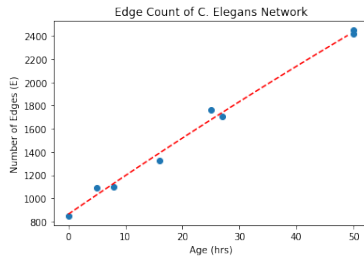
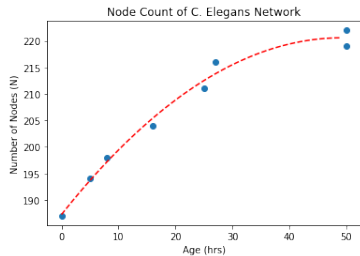
Table: Network attributes and summary statistics

# Chemotaxis

- How do neurons form connections?
  - Axonal projections search for chemical traces in the cerebral spinal fluid
  - Similar to white blood cell following traces of inflammation

► Axon Guidance

# Graph Properties of C. Elegans

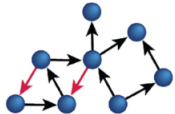


# Motifs

a. Motif definition



b. Host graph



c. Motif query results

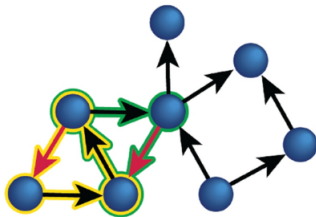


Figure: Depiction of motif query [3]

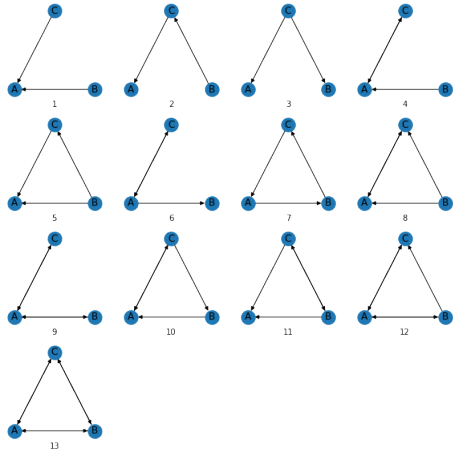


Figure: Set of three node motifs



# Counting Motifs

- Extension of the graph isomorphism problem  $\rightarrow$  Subgraph isomorphism problem
- Given graphs  $G = (V_1, E_1)$  and  $H = (V_2, E_2)$ , we say  $G$  is isomorphic to  $H$  if there exists a bijection  $f : V_1 \rightarrow V_2$
- A subgraph isomorphism exists between  $G$  and  $H$  *iff* there exists a subgraph  $G'$  of  $G$  such that  $G'$  is isomorphic to  $H$ .
- Monomorphism loses the bijection requirement to simply an injection
  - This means that the match can have other edges

# Counting Motifs

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**Algorithm 1:** Our approach: Subgraph search

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**Input** : A small motif graph  $M$

**Input** : An arbitrarily large host graph  $H$

Initialize an empty results set  $R$ ;

Initialize an empty task queue  $Q$ ;

Add the empty candidate mapping ( $\{\}$ ) to  $Q$ ;

**while**  $Q$  is non-empty **do**

    Pop a new candidate  $B$  from  $Q$ ;

    Identify  $m_1$  the most interesting node in motif  $M$  that does not yet have a mapping assigned in  $B$ ;

    Identify all nodes that are valid mappings from the candidate to  $m_1$  (based upon degree, attributes, etc.);

**if** *multiple nodes are valid candidates* **then**

        Add each new candidate to  $Q$ ;

**else**

        (All nodes in  $M$  have a valid mapping in  $B$  to  $H$ );

        Add the mapping to the results set  $R$ ;

**end**

**end**

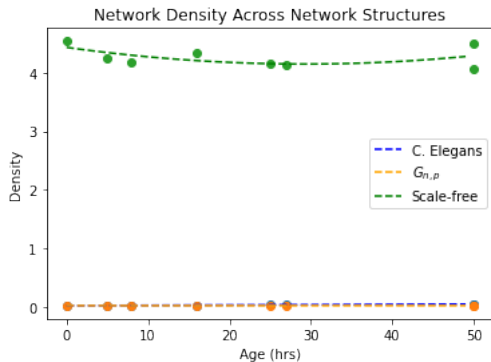
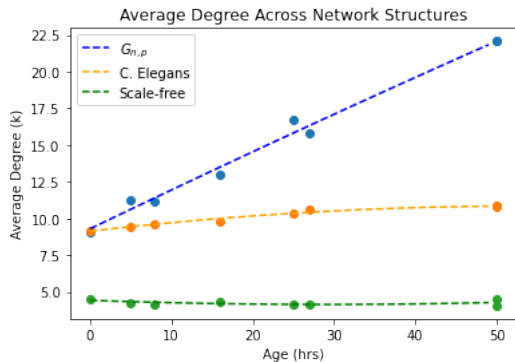
**Result:** The set  $R$  of resultant mappings from nodes in  $M$  to IDs in  $H$

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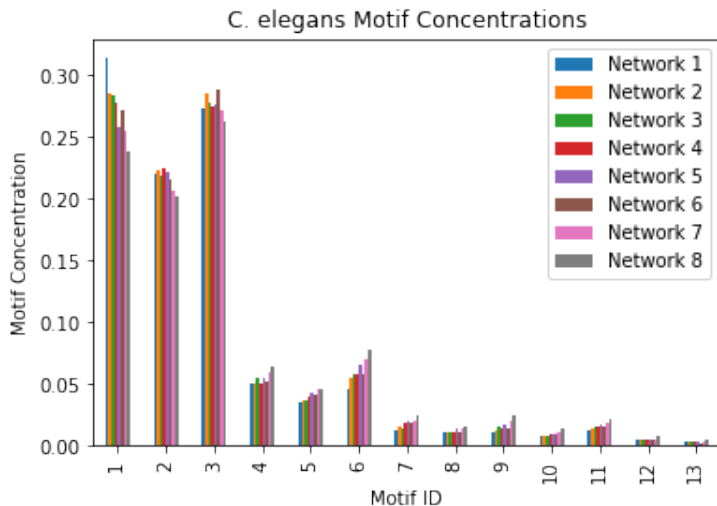
# Random Graph Generation

- Generated random graphs using NetworkX graph generators. [2]
- Directed Erdős-Rényi (aka  $G_{n,p}$ ) graphs
  - variation of the BA model
- Scale-free (SF) Model
  - Directed variation of the BA model
  - Adds nodes iteratively
  - Preferential attachment [1]
- Fitting the random graphs to simulate C. elegans
  1. SF: nodes N
  2.  $G_{n,p}$ : nodes N, random seed, and fine tuning the  $p$  parameter

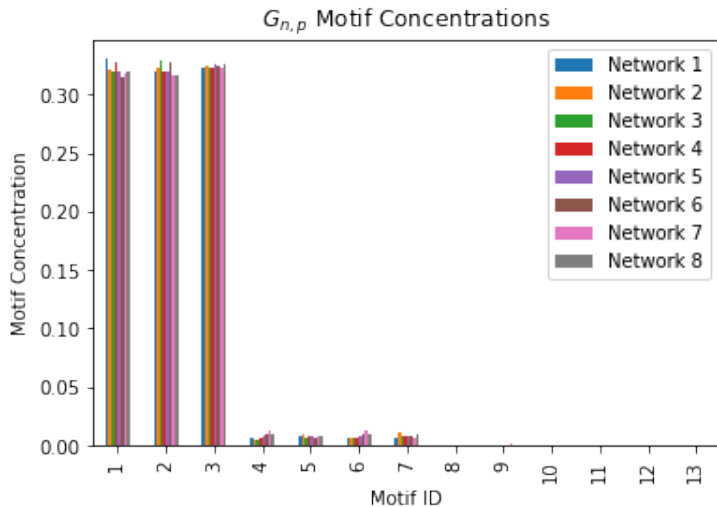
# Graph Properties Across Network Structures



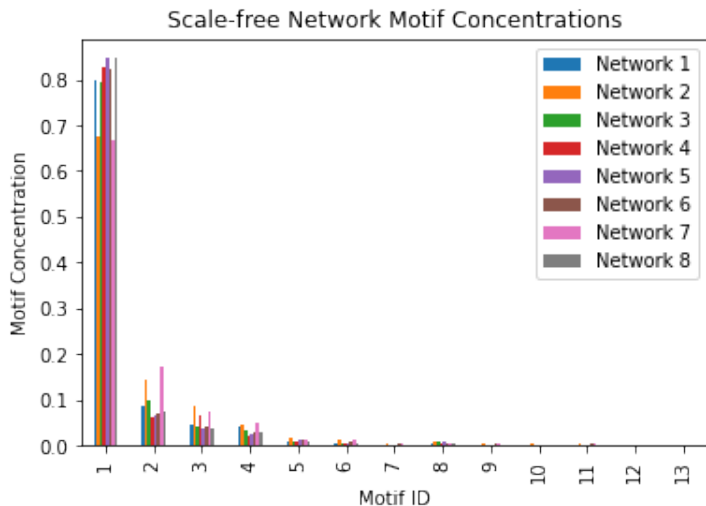
# Motif Concentrations - C. elegans



# Motif Concentrations - $G_{n,p}$

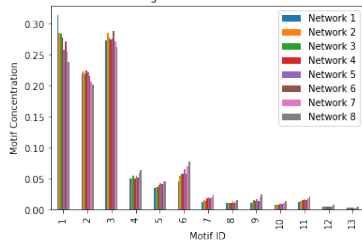


# Motif Concentrations - Scale-free

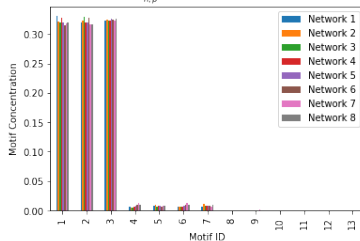


# Combined Results

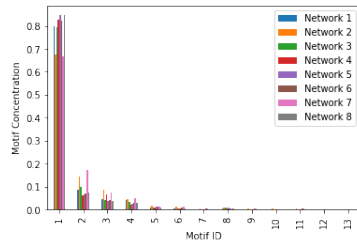
*C. elegans* Motif Concentrations



$G_{n,p}$  Motif Concentrations



Scale-free Network Motif Concentrations





# Future Work

- Gathering data of other animals at a neuron to neuron resolution
  - Investigate motif spectra of neuronal networks of differing scale
- Compare networks to other random graph models
  - Sub-linear preferential attachment (limits of neuronal attachment)
- Examine relevant motifs per brain region
- Implement directed Small-World network generator
- Speed up graph isomorphism search algorithm

# References

- [1] A.-L. Barabási and R. Albert. Emergence of scaling in random networks. *Science*, 286(5439):509–512, 1999.
- [2] A. Hagberg, P. Swart, and D. S Chult. Exploring network structure, dynamics, and function using networkx. Technical report, Los Alamos National Lab.(LANL), Los Alamos, NM (United States), 2008.
- [3] J. K. Matelsky, E. P. Reilly, E. C. Johnson, J. Stiso, D. S. Bassett, B. A. Wester, and W. Gray-Roncal. DotMotif: an open-source tool for connectome subgraph isomorphism search and graph queries. *Scientific Reports*, 11(1):1–14, 2021.
- [4] Q. K. Telesford, S. L. Simpson, J. H. Burdette, S. Hayasaka, and P. J. Laurienti. The Brain as a Complex System: Using Network Science as a Tool for Understanding the Brain. *Brain Connectivity*, 1(4):295–308, 2011.