# Caenorhabditis Elegans Connectome

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CS 590 – Complex Networks

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# Background & Motivation

Caenorhabditis elegans (C. elegans)

- Nematode about 1mm in length
- Only organism to have complete "connectome" available

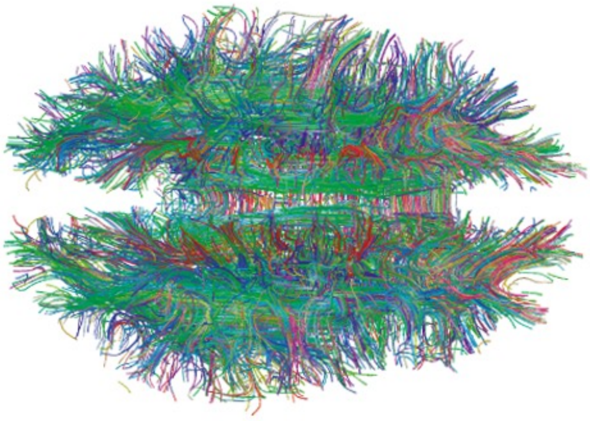
Connectomes

- Full neuron connection mappings in the nervous system
- C. Elegans ~300 neurons total.
  - Flies have ~100 thousand neurons.
  - Mice have ~100 million.
  - Humans have ~100 billion!

Compare Against Generated Networks

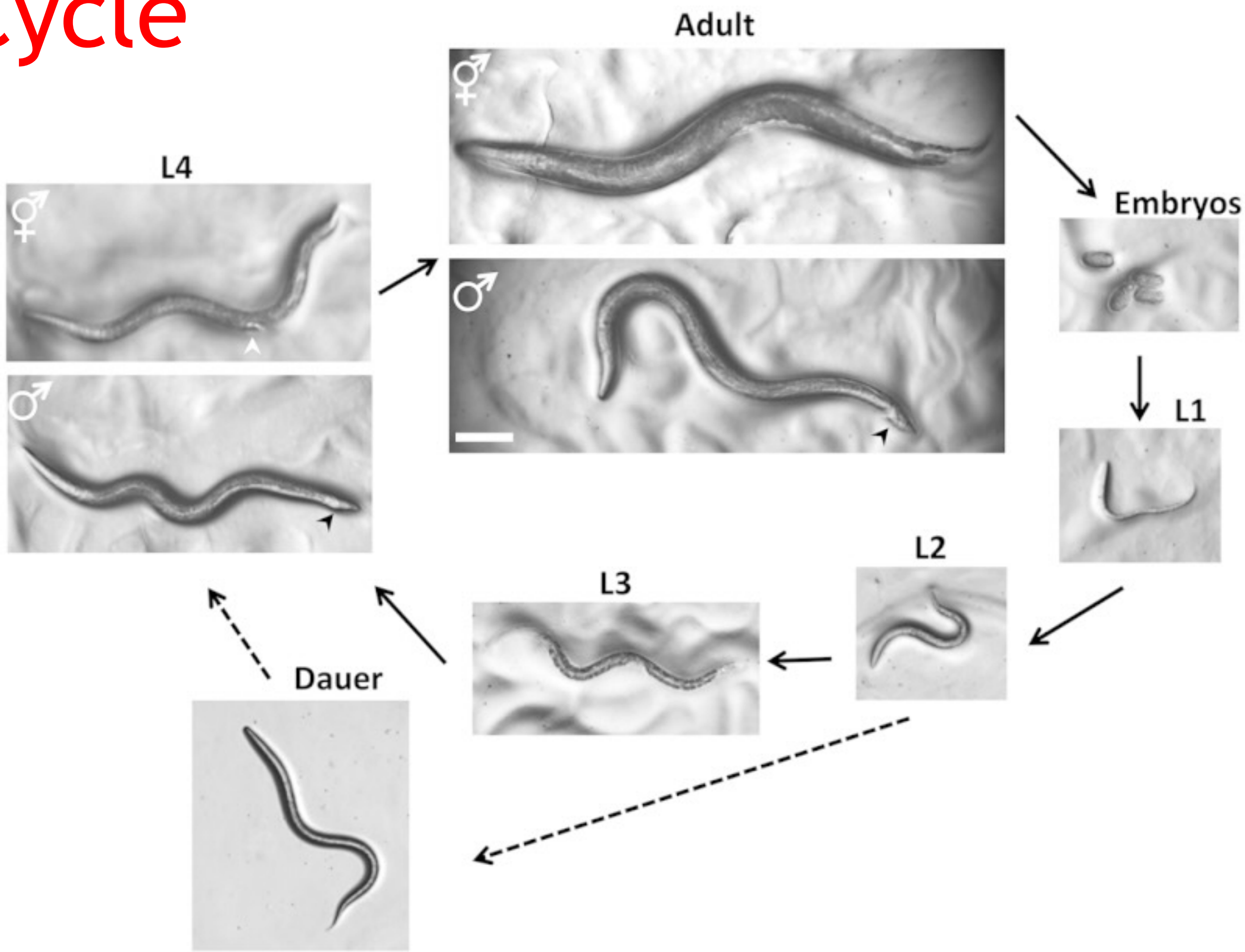
- Erdos-Renyi
- Barabasi-Albert
- …

https://bio.unc.edu/faculty-profile/goldstein/



doi:10.1371/journal.pone.0004006

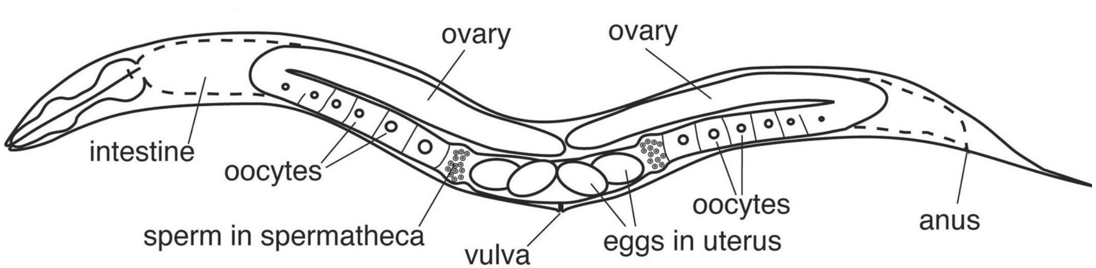
# Life Cycle



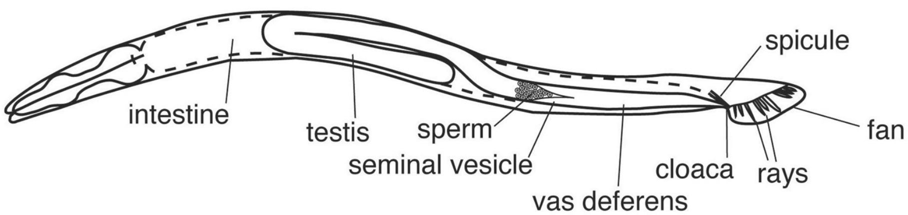

Lifespan: ~18-20 days. Birth Cycle: ~3 days
https://www.ncbi.nlm.nih.gov/books/NBK299460/figure/celegansintro_figure2/

# Sexual Dimorphism

XX Hermaphrodite
- 302 neurons
- 8 sex-specific neurons
- More than 99% naturally
- Can birth clones



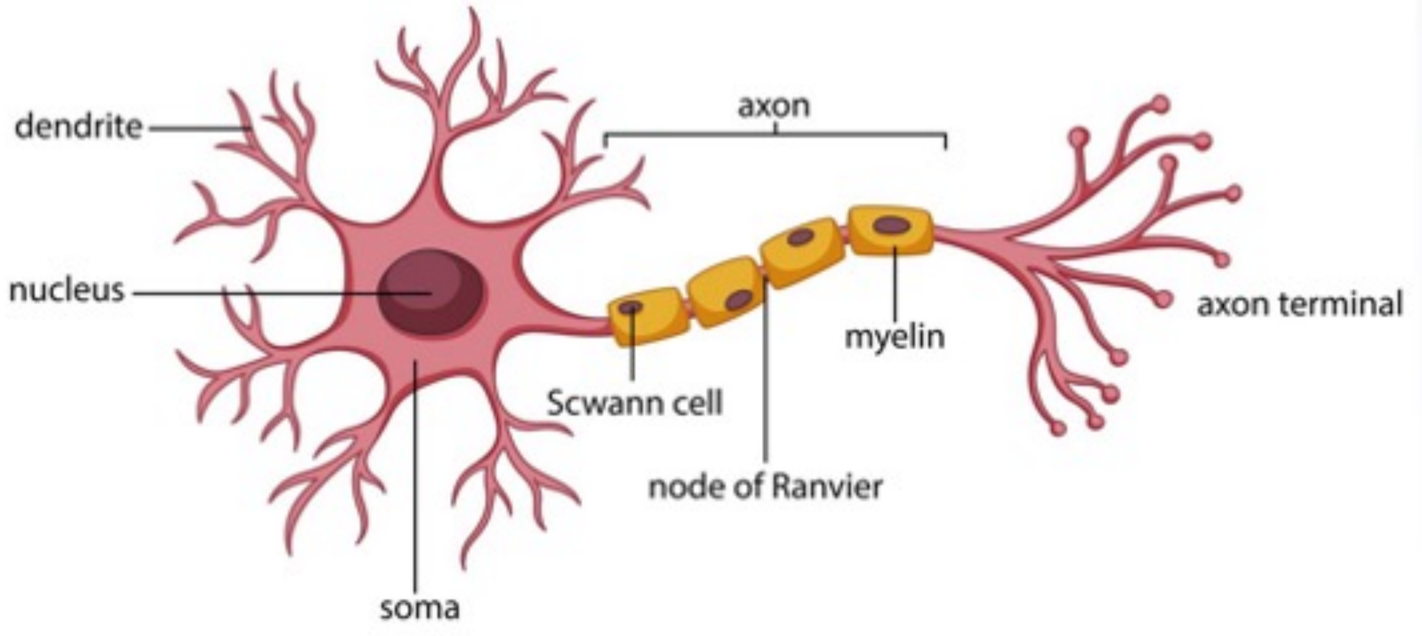

XO Male
- 385 neurons
- 91 sex-specific neurons
- Increased complexity near spicules for reproduction




http://wormbook.org/chapters/www_somaticsexdeterm/somaticsexdetfig1.jpg

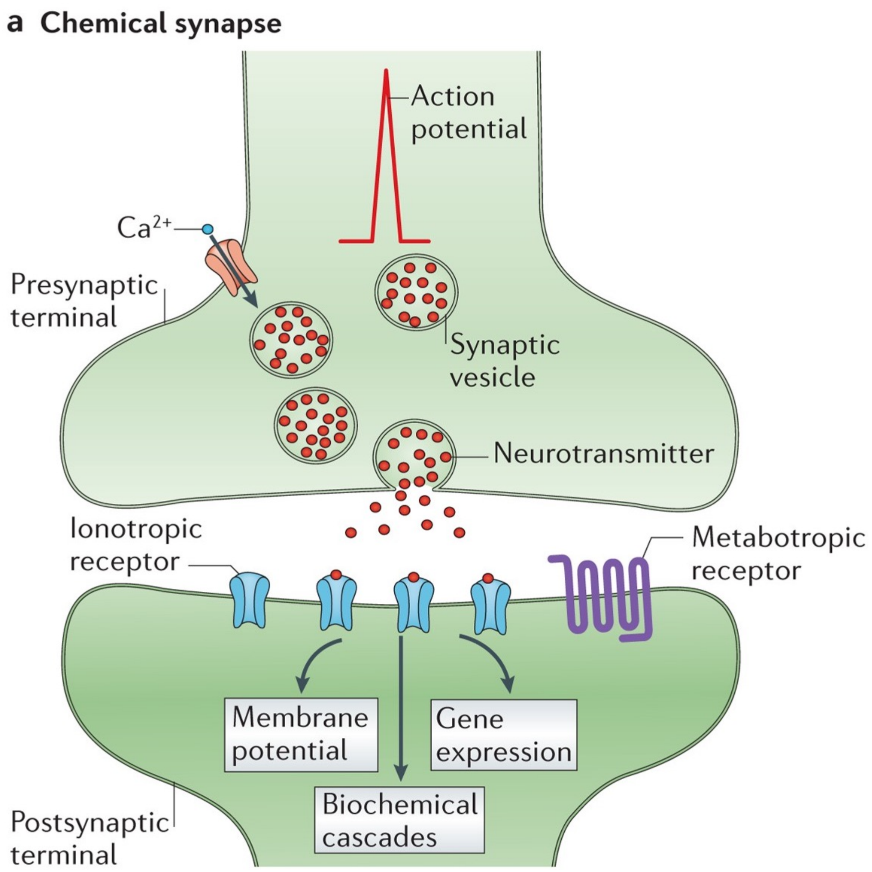
# Neurons

- Axons (exit edges) and Dendrites (enter edges)
- "Activated" neurons will send small electrical signals down axons to receiving neurons' dendrites
- Various reactions based in part by dendrite signals determines if a neuron will "activate"




https://www.vecteezy.com/vector-art/358962-diagram-of-neuron-anatomy

# Types of Directed, Weighted, Edges




NOTE: Symmetric and Asymmetric variations of Electrical Synapses!
https://www.nature.com/articles/nrn3708

# Data

| | I1L | I1R | I2L | I2R | I3 | I4 | I5 | I6 | M1 | M2L | M2R | M3L | M3R | M4 | M5 | MCL | MCR | MI | NSML | NSMR | pm1 | pm2D | pm2VL | pm3D | pm3VL | pm3VR | pm4D | pm4VL | pm4VR | pm5D | pm5VL | pm5VR | pm6D | pm6VL | pm6VR | pm7D | pm7VR | mc2DL | mc2DR | mc2V | mc3V | e3D | e3VL | e3VR | g1p | g1AL | g1AR | g2L | g2R | bm | ASIL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| I1L | | | 10 | | 3 | | 2 | 1 | | 3 | | 8 | 2 | | | 2 | 2 | 2 | 3 | | 2 | | | | 7 | | 1 | 2 | | | | | | | | | | | | | | | | | | | | | | | |
| I1R | | | | 6 | 1 | | 2 | | 1 | 1 | 3 | 1 | 6 | | | 3 | 4 | 1 | 1 | 2 | 2 | | | 2 | | 5 | 1 | | 2 | 2 | | 1 | | | | | | | | | | | | | | | | | | | |
| I2L | 2 | | | 3 | | 13 | 2 | 2 | 1 | | | | 3 | 4 | | | | | 14 | 24 | | | | | 1 | | | 2 | | 1 | 2 | 1 | | | | | | | | | | | 1 | | | | | | | | |
| I2R | | 1 | 3 | | | 20 | 2 | 3 | 3 | | 2 | | 2 | 3 | | 1 | | | 34 | 7 | 1 | | | | | 1 | 2 | 1 | | | 1 | 4 | | | | | | | | | | | | 1 | | | | | | | |
| I3 | 1 | 1 | | | | | 2 | 1 | 2 | 2 | | 2 | 2 | 2 | | 1 | 2 | 1 | | 2 | | | | | | | 2 | | | 4 | | | | | | | | | | | | | | | | | | | | | |
| I4 | | | | 7 | | | 2 | | | 5 | | 6 | 22 | | | | | 1 | 8 | 15 | | | | | | | 1 | | | | 11 | 2 | | | | | | | | | | | | | | | | | | | |
| I5 | 2 | | 3 | 1 | 1 | 7 | | | 3 | 4 | | 4 | 2 | 19 | 2 | | | 4 | 1 | 5 | | | | | | | | | | | 4 | 14 | | 1 | | | | | | | | | | | | 9 | 6 | | | | |
| I6 | | 1 | 1 | 4 | 12 | | | | | | | 10 | | 15 | | | | | 24 | 23 | | | | | | | | | | 13 | | | | | | | | | | | | | | | 2 | | | | | 2 | |
| M1 | | 1 | 3 | 2 | 8 | 1 | 2 | | | | | | | 1 | 1 | | | 6 | 2 | | | 1 | 1 | | 1 | | 1 | | | 3 | | | | | | | | | | | | 3 | 1 | | 5 | | | | | | |
| M2L | | | | | 2 | 8 | 2 | | | | | 3 | 1 | | | | | | | | | | | | | | 3 | 9 | | 2 | 21 | | | | | | | | | | | | | | | 8 | | | | | |
| M2R | | | | | | 1 | 3 | | | | | 2 | 1 | | | | | | | 1 | | | | | | | 3 | | 3 | | | 12 | | | | | | | | | | | | | | | 3 | | | | |
| M3L | | | | | | | | | | | | | | | | | | | 1 | | | | | | | | 17 | 6 | | 4 | 2 | | | | | | | | | | | | | | | | | | | | |
| M3R | | | | | | | | | | | | | | 2 | | | | | | | | | | | | | 6 | | 1 | | | | | | | | | | | | | | | | | | 3 | | | 1 | |
| M4 | | | | | | 5 | 1 | | | 1 | | 1 | | 15 | | 1 | | | | | | | | | | | | | 1 | 69 | 50 | 72 | | | | | | | | | | | | | 46 | 43 | 49 | 3 | | | |
| M5 | | | | | | | 1 | | 1 | | | | | | | | | | | | | | | | | | | | | | 1 | 3 | 2 | 2 | 2 | 3 | 2 | | | | 4 | | | | | 3 | 1 | 2 | 1 | | |
| MCL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 7 | 13 | | | | | | | | | | | |
| MCR | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 6 | 4 | 11 | | | | | | | | | | | |
| MI | 1 | | | | 2 | 1 | | | 7 | 3 | 2 | 2 | 2 | | | 3 | | | 1 | 2 | | | | | | | 2 | 1 | 7 | 5 | | | | | | | | | | | | | | | | | | | | | |
| NSML | | | | | | 1 | | 1 | | | | 21 | 1 | 13 | | | | | | 7 | | | | | | | | 2 | | 38 | 63 | 8 | | | | | | | | | | | | | | | | | | 88 | |
| NSMR | | | 1 | 1 | | 3 | | 4 | | | | | 24 | | | | | | | | | | | | | | 3 | | | 9 | 1 | 53 | | | | | | | | | | | | | | | | | | 72 | |
| ASIL | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

https://www.wormwiring.org/pages/adjacency.html

[SI 5 Connectome adjacency matrices, corrected July 2020.xlsx] complete-data — view c-elegans-hermaphrodite-complete.csv — 115×32

```
,I1L,I1R,I2L,I2R,I3,I4,I5,I6,M1,M2L,M2R,M3L,M3R,M4,M5,MCL,MCR,MI,NSML,NSMR,pm1,pm2D,pm2VL,pm3D,pm3V
,pm4VL,pm4VR,pm5D,pm5VL,pm5VR,pm6D,pm6VL,pm6VR,pm7D,pm7VR,mc2DL,mc2DR,mc2V,mc3V,e3D,e3VL,e3VR,g1p,g
,g2R,bm,ASIL,ASIR,ASJL,ASJR,AWAL,AWAR,ASGL,ASGR,AWBL,AWBR,ASEL,ASER,ADFL,ADFR,AFDL,AFDR,AWCL,AWCR,A
L,ASHR,ADLL,ADLR,BAGL,BAGR,URXL,URXR,ALNL,ALNR,PLNL,PLNR,SDQL,SDQR,AQR,PQR,ALML,ALMR,AVM,PVM,PLML,P
R,DVA,PVDL,PVDR,ADEL,ADER,PDEL,PDER,PHAL,PHAR,PHBL,PHBR,PHCL,PHCR,IL2DL,IL2DR,IL2L,IL2R,IL2VL,IL2V
,CEPVL,CEPVR,URYDL,URYDR,URYVL,URYVR,OLLL,OLLR,OLQDL,OLQDR,OLQVL,OLQVR,IL1DL,IL1DR,IL1L,IL1R,IL1VL
INR,AIML,AIMR,RIH,URBL,URBR,RIR,AIYL,AIYR,AIAL,AIAR,AUAL,AUAR,AIZL,AIZR,RIS,ALA,PVQL,PVQR,ADAL,ADA
DUL,BDUR,PVR,AVFL,AVFR,AVHL,AVHR,PVPL,PVPR,LUAL,LUAR,PVNL,PVNR,AVG,DVB,RIBL,RIBR,RIGL,RIGR,RMGL,RM
RICL,RICR,SAADL,SAADR,SAAVL,SAAVR,AVKL,AVKR,DVC,AVJL,AVJR,PVT,AVDL,AVDR,AVL,PVWL,PVWR,RIAL,RIAR,RI
AVER,RMFL,RMFR,RID,AVBL,AVBR,AVAL,AVAR,PVCL,PVCR,RIPL,RIPR,URADL,URADR,URAVL,URAVR,RMEL,RMER,RMED,
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vBWMR2,vBWMR3,vBWMR4,vBWMR5,vBWMR6,vBWMR7,dBWML8,dBWML9,dBWML10,dBWML11,dBWML12,dBWML13,dBWML14,dB
,dBWML17,dBWML18,dBWML19,dBWML20,dBWML21,dBWML22,dBWML23,dBWML24,dBWMR8,dBWMR9,dBWMR10,dBWMR11,dBW
dBWMR14,dBWMR15,dBWMR16,dBWMR17,dBWMR18,dBWMR19,dBWMR20,dBWMR21,dBWMR22,dBWMR23,dBWMR24,vBWML8,vBW
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BWMR9,vBWMR10,vBWMR11,vBWMR12,vBWMR13,vBWMR14,vBWMR15,vBWMR16,vBWMR17,vBWMR18,vBWMR19,vBWMR20,vBWM
BWMR23,vBWMR24,CEPshDL,CEPshDR,CEPshVL,CEPshVR,GLRDL,GLRDR,GLRL,GLRR,GLRVL,GLRVR,CANL,CANR,exc_cel
hyp,int,mu_intL,mu_intR,mu_anal,mu_sph,HSNL,HSNR,VC01,VC02,VC03,VC04,VC05,VC06,vm2AL,vm2AR,vm1AL,v
1PR,vm2PL,vm2PR$
I1L,,,10,,3,,2,1,,3,,8,2,,,2,2,2,3,,2,,,,7,,1,2,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,
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# Data Translation

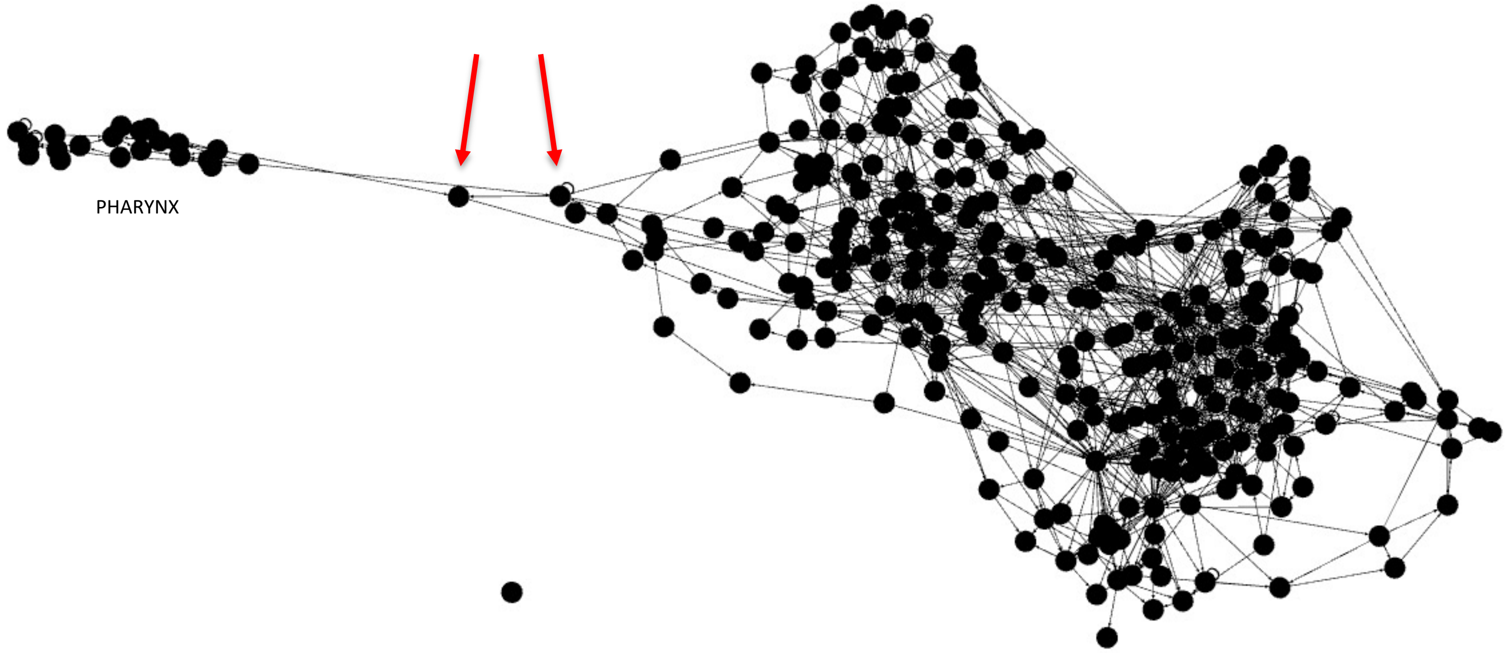
Six data sets based on sex and synapse type

```
david@Davids-Mac-mini complete-data % ls -l *csv
-rw-r--r--@ 1 david  staff  146249 Nov 26 21:15 c-elegans-hermaphrodite-chemical.csv
-rw-r--r--@ 1 david  staff  227444 Nov 26 23:00 c-elegans-hermaphrodite-gapjn-asymmetric.csv
-rw-r--r--@ 1 david  staff  229118 Nov 26 23:03 c-elegans-hermaphrodite-gapjn-symmetric.csv
-rw-r--r--@ 1 david  staff  231818 Nov 27 11:56 c-elegans-male-chemical.csv
-rw-r--r--@ 1 david  staff  352654 Nov 27 17:02 c-elegans-male-gapjn-asymmetric.csv
-rw-r--r--@ 1 david  staff  354799 Nov 27 17:03 c-elegans-male-gapjn-symmetric.csv
david@Davids-Mac-mini complete-data % python3 c-elegans-parse.py
Data options for C. Elegans Connectome:
 1. Hermaphrodite - Chemical
 2. Hermaphrodite - Neuromuscular Gap Junction - Asymmetric
 3. Hermaphrodite - Neuromuscular Gap Junction - Symmetric
 4. Hermaphrodite - ALL 3
 5. Male - Chemical
 6. Male - Neuromuscular Gap Junction - Asymmetric
 7. Male - Neuromuscular Gap Junction - Symmetric
 8. Male - ALL 3
 9. Both sexes - NOT IMPLEMENTED YET!
Your choice (number only then press enter):
1
Total detected neurons in file(s):  302
Total neurons added to graph:  302
Total number of edges added to graph:  3709
Average Degree:  24.56291390728477
david@Davids-Mac-mini complete-data %
```

# Homework-Style Data

## Important nodes

- RIPL and RIPR (Ring Interneuron P)

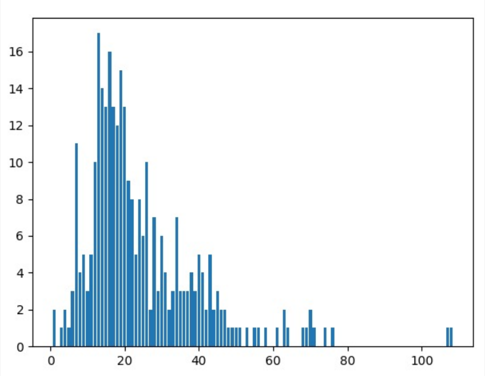
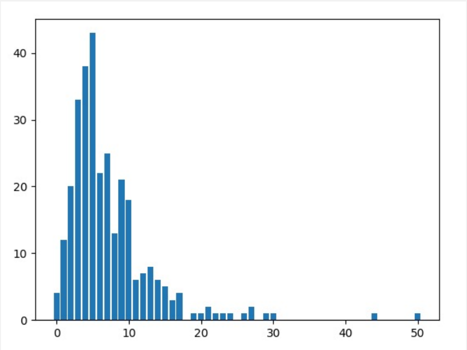
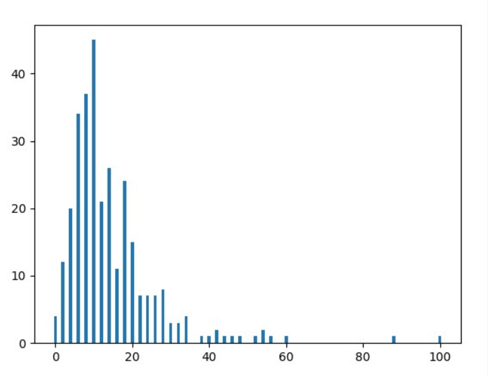
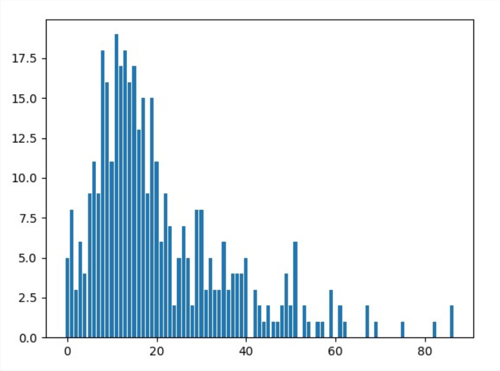
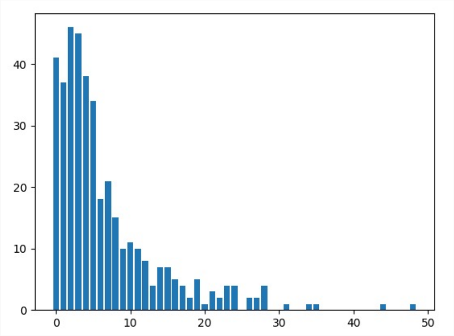
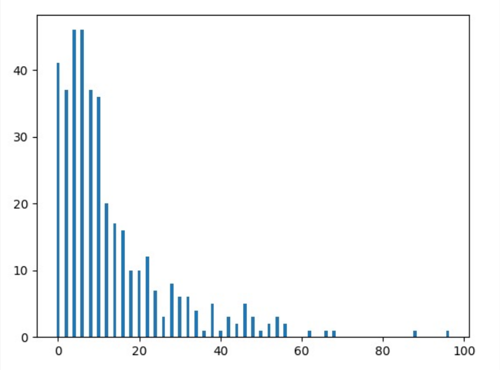



https://www.wormatlas.org/neurons/Individual%20Neurons/Neuronframeset.html

# Homework-Style Data

| Sex | Chemical | Electrical Asymmetric | Electrical Symmetric |
|---|---|---|---|
| XX | Number of nodes: 302<br>Number of edges: 3709<br>Mean degree: 24.562<br>Median degree: 20.0<br>Min Degree: 1<br>Max Degree: 108<br>Average clustering coefficient: 0.2436<br>Min clustering coefficient: 0<br>Max clustering coefficient: 1.0<br>Mean betweenness centrality: 0.00632<br>Median betweenness centrality: 0.0032<br>Min betweenness centrality: 0.0<br>Max betweenness centrality: 0.088<br>Number of disconnected nodes: 0 | Number of nodes: 302<br>Number of edges: 1105<br>Mean degree: 7.3178<br>Median degree: 6.0<br>Min Degree: 0<br>Max Degree: 50<br>Average clustering coefficient: 0.1085<br>Min clustering coefficient: 0<br>Max clustering coefficient: 0.5<br>Mean betweenness centrality: 0.0018<br>Median betweenness centrality: 0.000<br>Min betweenness centrality: 0.0<br>Max betweenness centrality: 0.039<br>Number of disconnected nodes: 0 | Number of nodes: 302<br>Number of edges: 2196<br>Mean Degree: 14.5430<br>Median degree: 10.0<br>Max Degree: 100<br>Min Degree: 0<br>Mean clustering coefficient: 0.21705<br>Min clustering coefficient: 0<br>Max clustering coefficient: 1.0<br>Mean betweenness centrality: 0.00863<br>Median betweenness centrality: 0.00364<br>Max betweenness centrality: 0.1494<br>Min betweenness centrality: 0.0<br>Number of disconnected nodes: 4 |
| XO | Number of nodes: 391<br>Number of edges: 4055<br>Mean degree: 20.7416<br>Median degree: 16<br>Max Degree: 86<br>Min Degree: 0<br>Mean clustering coefficient: 0.2376<br>Max clustering coefficient: 1.0<br>Min clustering coefficient: 0<br>Mean betweenness centrality: 0.00558<br>Median betweenness centrality: 0.00246<br>Min betweenness centrality: 0.0<br>Max betweenness centrality: 0.0731<br>Number of disconnected nodes: 5 | Number of nodes: 395<br>Number of edges: 1313<br>Mean degree: 6.64810<br>Median degree: 4<br>Min Degree: 0<br>Max Degree: 48<br>Average clustering coefficient: 0.09472<br>Min clustering coefficient: 0<br>Max clustering coefficient: 0.5<br>Mean betweenness centrality: 0.00097<br>Median betweenness centrality: 6.98954e-05<br>Min betweenness centrality: 0.0<br>Max betweenness centrality: 0.01794<br>Number of disconnected nodes: 41 | Number of nodes: 395<br>Number of edges: 2604<br>Mean degree: 13.18481<br>Median degree: 8<br>Min Degree: 0<br>Max Degree: 96<br>Average clustering coefficient: 0.1894<br>Min clustering coefficient: 0<br>Max clustering coefficient: 1.0<br>Mean betweenness centrality: 0.0052<br>Median betweenness centrality: 0.0011<br>Min betweenness centrality: 0.0<br>Max betweenness centrality: 0.0878<br>Number of disconnected nodes: 41 |

# Homework-Style Data

| Sex | Chemical | Electrical Asymmetric | Electrical Symmetric |
|---|---|---|---|
| XX |  |  |  |
| XO |  |  |  |

Degree Distributions

# Comparisons (pt. 1)

Generated Graphs per Sex/Synapse Combination

- Erdos-Renyi
- Gilbert
- Watts Stroggatz
- Barabasi-Albert

Generated X number of each graph and averaged values

- Used 10 by default but is configurable

# Comparisons (pt. 2)

Hermaphrodite – Chemical

| Deltas from Generated vs. C. Elegans | Erdos-Renyi | Gilbert | Watts Strogattz | Barabasi-Albert |
|---|---|---|---|---|
| Degree Mean | 24.562 | 24.670 | 12.0 | 3.973 |
| Degree Max | 39.9 | 38.3 | 17.3 | 45.4 |
| Degree Min | 12.4 | 12.7 | 7.5 | 1.8 |
| Clustering Mean | 0.081 | 0.081 | 0.254 | 0.059 |
| Clustering Max | 0.140 | 0.137 | 0.565 | 1.0 |
| Clustering Min | 0.035 | 0.031 | 0.049 | 0.0 |
| Betweenness Mean | 0.003 | 0.003 | 0.005 | 0.008 |
| Betweenness Max | 0.008 | 0.008 | 0.016 | 0.310 |
| Betweenness Min | 0.008 | 0.008 | 0.016 | 0.310 |

Deltas from 10 instances of each generated models averaged together

# Comparisons (pt. 3)

## Hermaphrodite – Electrical Asymmetric

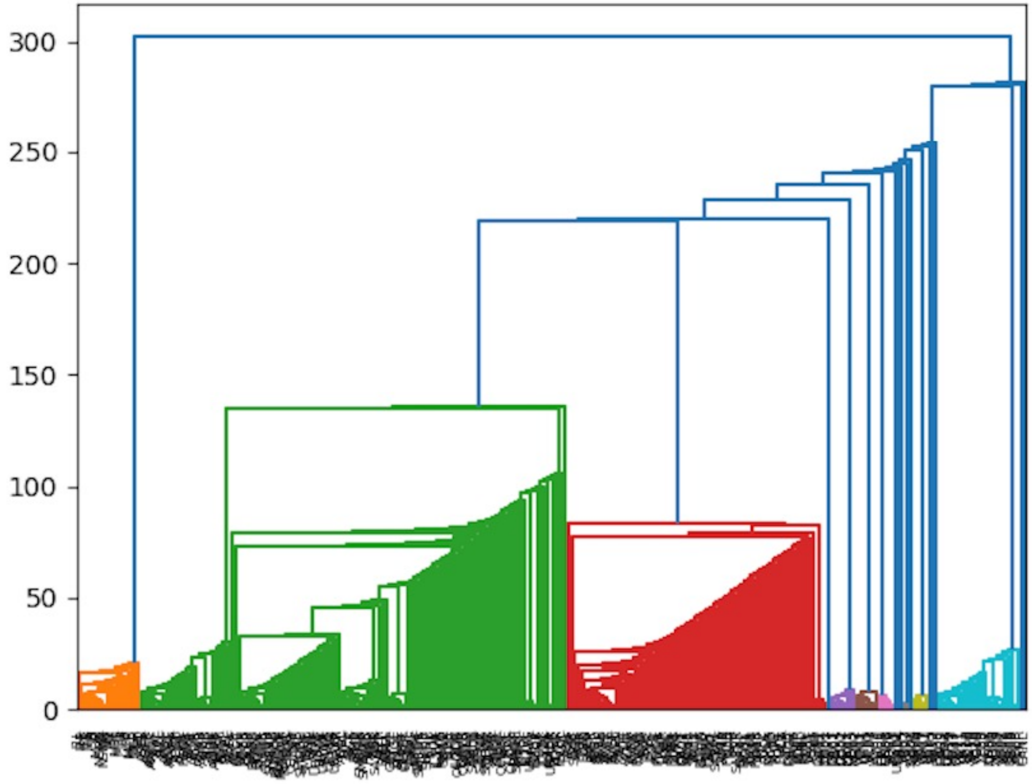
| Deltas from Generated vs. C. Elegans | Erdos-Renyi | Gilbert | Watts Strogattz | Barabasi-Albert |
|---|---|---|---|---|
| Degree Mean | 7.317 | 24.851 | 12.0 | 3.973 |
| Degree Max | 15.4 | 39.2 | 17.1 | 44.8 |
| Degree Min | 0.8 | 12.5 | 7.7 | 1.9 |
| Clustering Mean | 0.023 | 0.082 | 0.251 | 0.057 |
| Clustering Max | 0.373 | 0.132 | 0.576 | 1.0 |
| Clustering Min | 0.0 | 0.034 | 0.048 | 0.0 |
| Betweenness Mean | 0.006 | 0.003 | 0.005 | 0.008 |
| Betweenness Max | 0.026 | 0.008 | 0.016 | 0.294 |
| Betweenness Min | 2.194 | 0.000 | 0.000 | 0.0 |

Deltas from 10 instances of each generated models averaged together

# Clustering (pt. 1)

Hermaphrodite Chemical Synapses using Girvan-Newman

How many clusters/classes would you predict from this?



# Clustering (pt. 2)

Real World Comparison: The neurons in the hermaphrodite have been assigned to 118 distinct classes according to their topology and synaptic connection patterns (White et al., 1986).

Adjacency matrix input data is available via this class organization as well!

# Clustering (pt.3)

## Clustering – troubleshooting other synapse types

```
partitions = nx.community.girvan_newman(G)

node_groups = []
node_groups_hashes = [[]]

partition_counter = 0
for partition in partitions:
    node_groups_hashes.append([])
    node_groups.append(list(partition))
    for community in list(partition):
        node_groups_hashes[partition_counter].append(hash(frozenset(community)))
    partition_counter += 1

print('Number of disconnected nodes: ',len(disconnected_nodes))

for i in range(0,len(node_groups)):
    print('length of iteration ',i,',: ' ,len(node_groups[i]))
```

```
Number of disconnected nodes:  0
length of iteration  0 ,:  2
length of iteration  1 ,:  3
length of iteration  2 ,:  4
length of iteration  3 ,:  5
length of iteration  4 ,:  6
```

```
length of iteration  297 ,:  299
length of iteration  298 ,:  300
length of iteration  299 ,:  301
length of iteration  300 ,:  302
```

# Resilience and Spreading

The RIPL and RIPR neurons are critical due to their high betweenness of the pharynx and somatic clusters. If targeted by attack, could be quite deleterious. Also makes them key spreaders/activators.

Nodes within the somatic and pharynx sections are not as susceptible to attacks due to their higher clustering coefficients.

# Conclusions and Next Steps

More analysis needed to determine “extra” neurons assigned to the male nematode

Additional debugging and code refactoring needed

Resiliency and Spreading analysis needs to be updated

The C. elegans connectome is scale-free!

Combine certain synapse types into unified dataset for ease of use and aggregation of results

# Thank You!

# Questions?

# Related Resources

- The Genetics of Caenorhabditis Elegans – S. Brenner - 1973
- The pharynx of Caenorhabditis elegans – Albertson and Thomson – 1976
- The Structure of the Nervous System of the Nematode Caenorhabditis elegans (The Mind of a Worm) – White et. al – 1986
- Structural Properties of the Caenorhabditis elegans Neuronal Network – Varshney et. al - 2011
- The Connectome of a Decision-Making Neural Network – Jarrel et. al – 2012

- https://www.wormatlas.org/
- https://wormwiring.org/