

ILLINOIS TECH

| College of Computing

Research Collaboratorium

C. elegans neural network dynamics

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Applied Math

10-16-24

Math biology Math neuroscience

Mathematical models for
biological systems

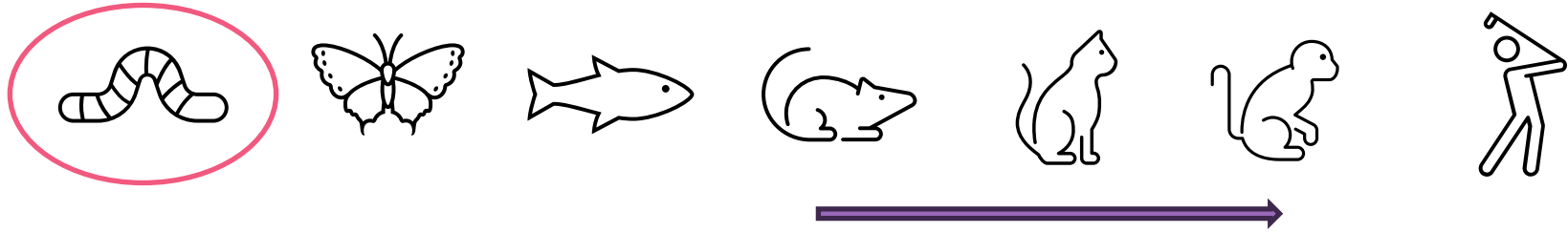
How do biological networks...

- perform computations?
- make decisions?
- integrate sensory input?
- coordinate behavior?

Why make math models of neurons?

- It's nice to have rules for how things work
- Computer simulations can replace experiments
- Models can help aid in drug development
- Models can help us engineer neural networks

Neuroscience model organisms

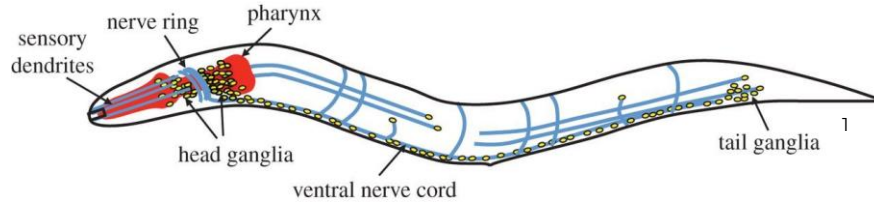


Complex organisms
modeling limitations:

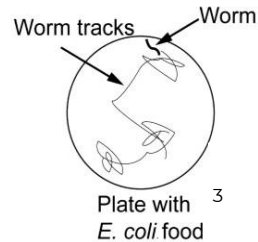
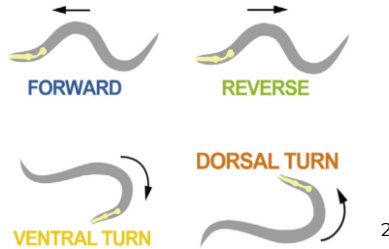
- Limited data
- Many complex functions, large search space
- Computational limitations

C. elegans nervous system and behavior

- ~1 mm
- Soil dwelling
- Moves by contracting muscles
- 302 neurons



Basic behaviors

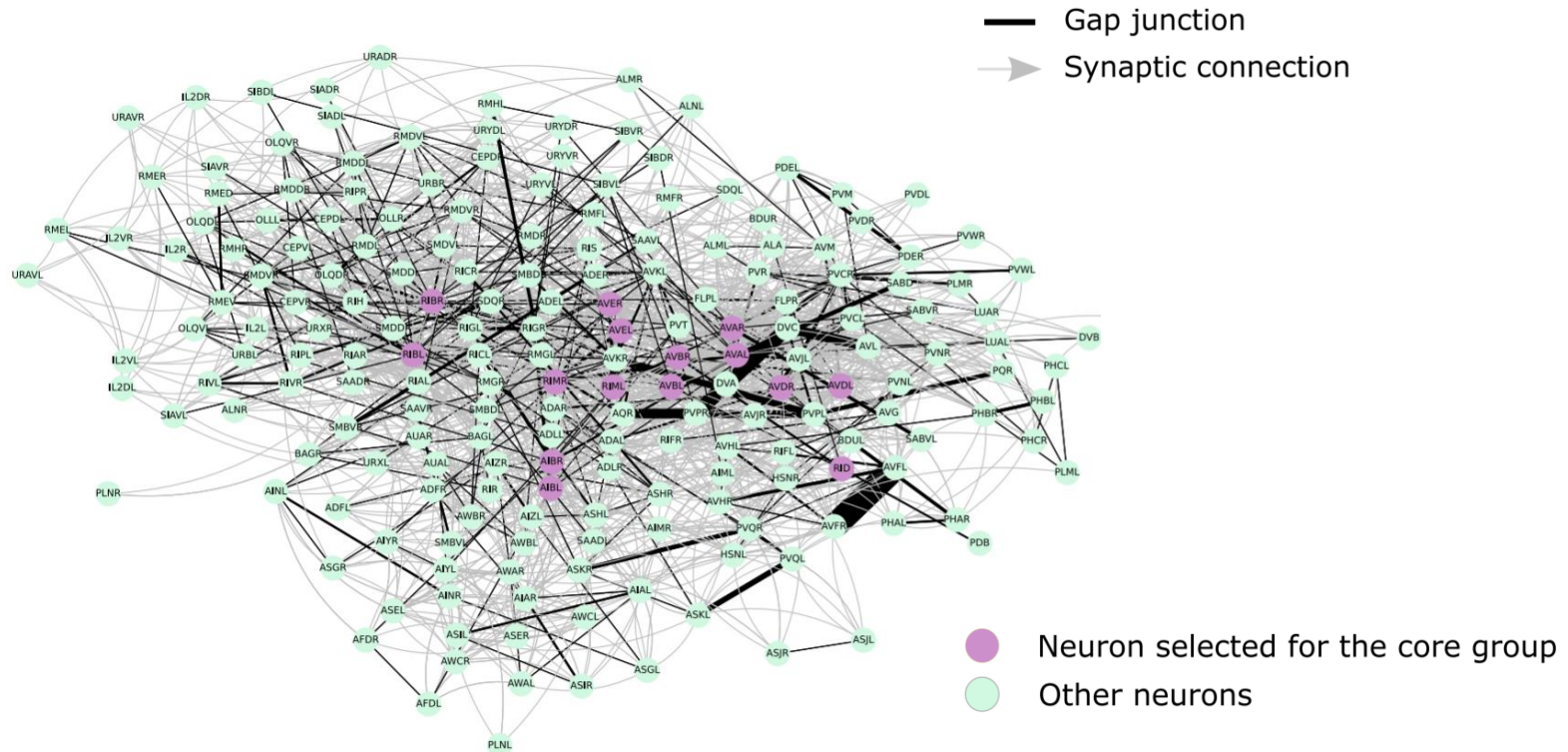


Complex behaviors

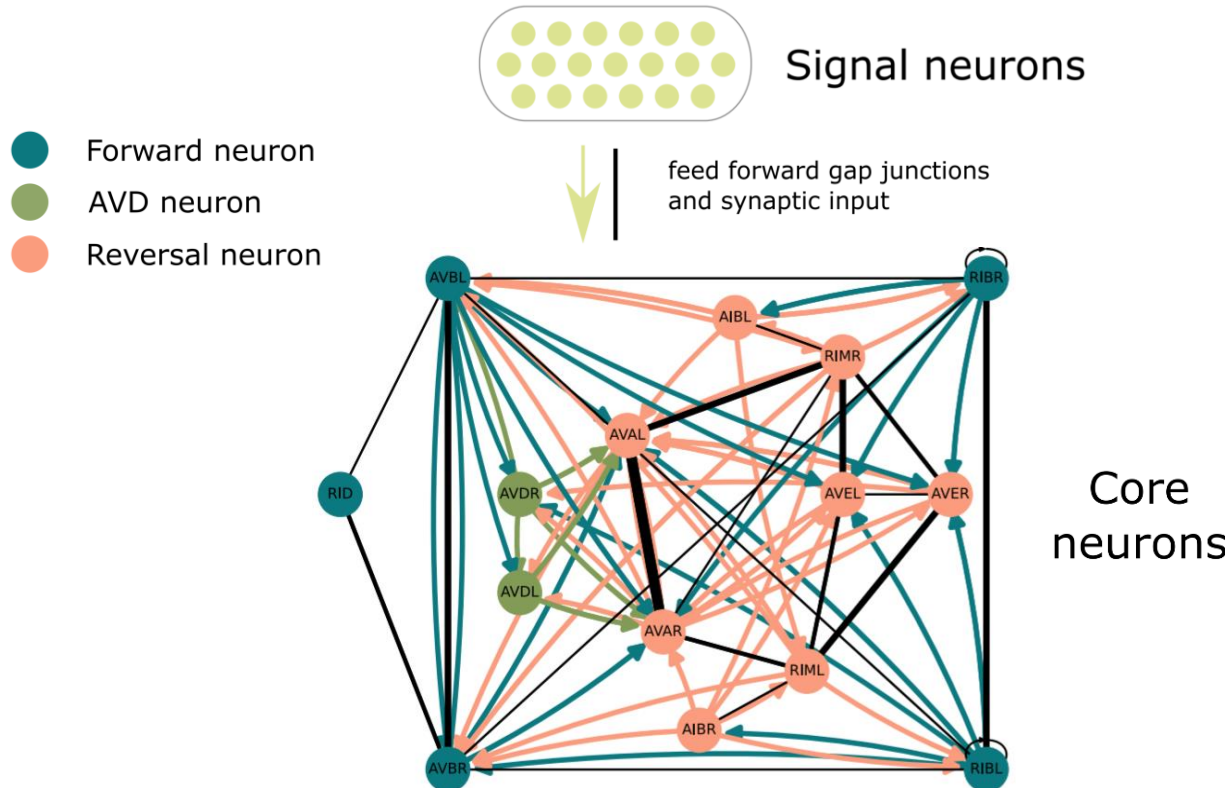
- Foraging for food
- Escaping predators
- Following a gradient
- Forming social aggregates

1. Fang-Yen, C., Alkema, M. J., & Samuel, A. D. (2015)
2. Kato, S., Kaplan, H. S., Schrödel, T., Skora, S., Lindsay, T. H., Yemini, E., ... & Zimmer, M. (2015)
3. Pokala, N., & Glater, E. E. (2018)

Partial connectome



Proposed premotor network model



Network dynamics

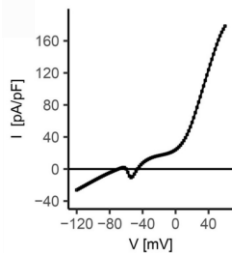
Model neurons $\mathbf{x} = [x_1, \dots, x_{15}]^T$
 Signal neurons $[x_{16}, \dots, x_N]^T$

1. Posit general model
2. Fit the parameters using data

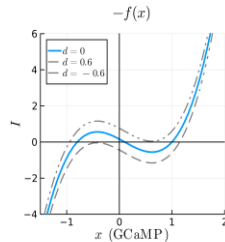
Model Neurons

$$\tau \frac{dx_i}{dt} = \underbrace{f(x_i) + d_i}_{\text{intrinsic dynamics}} + \beta \sum_{j=1}^N \underbrace{\mathbf{W}_{ij}}_{\text{gap junctions (electrical)}} (x_j - x_i) + \sum_{j=1}^N \underbrace{\mathbf{A}_{ij}}_{\text{synaptic connections (chemical)}} \sigma(x_j)$$

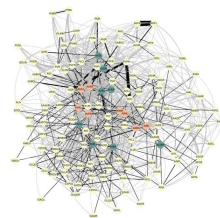
Voltage clamp



Intrinsic dynamics

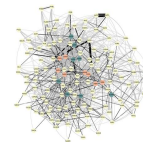


Connectome

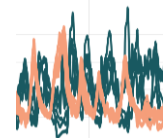


Regression analysis

Connectome

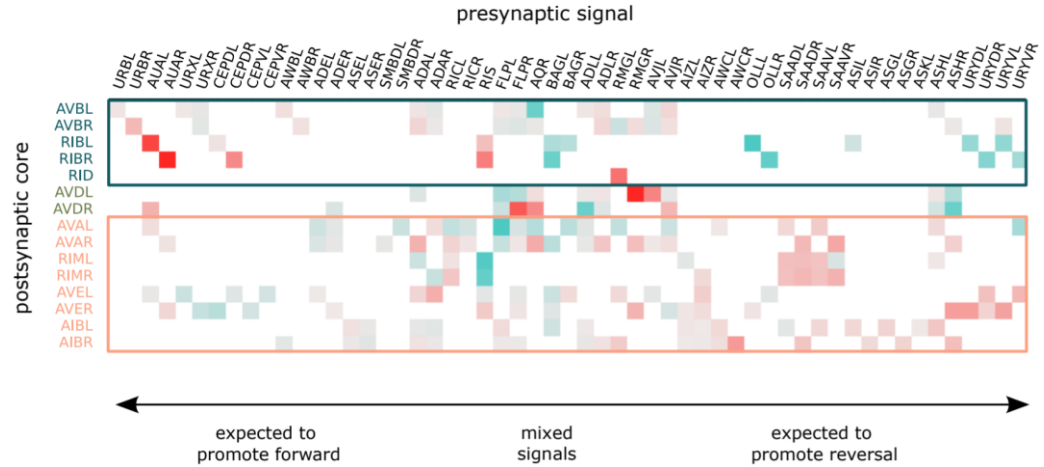
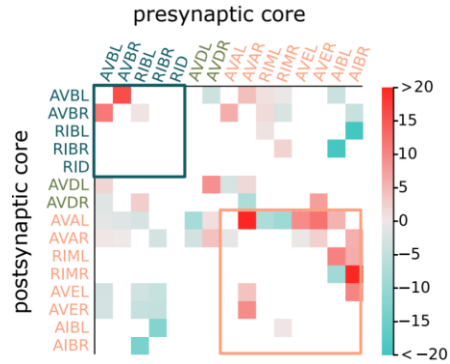
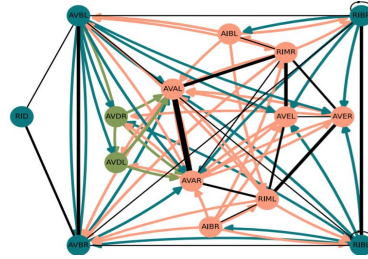


Whole-brain calcium imaging



Synaptic weights

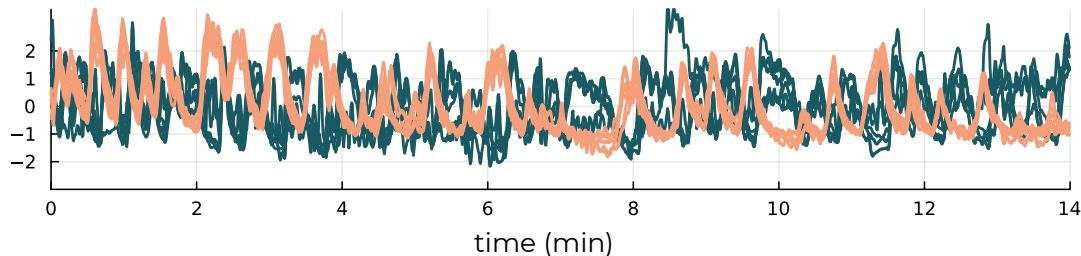
■ forward cluster
■ AVD
■ reversal cluster



Simulation reproduces network activity

How can we compare real data to simulation output?

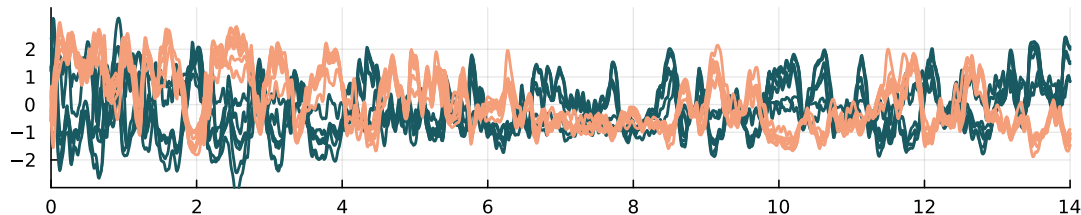
Calcium imaging
data:
2023-01-23-15



forward
neurons

reversal
neurons

Simulation
timeseries



Data
behavior



Simulation
behavior

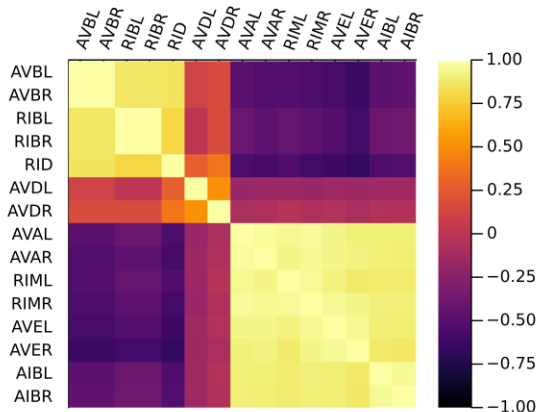


forward

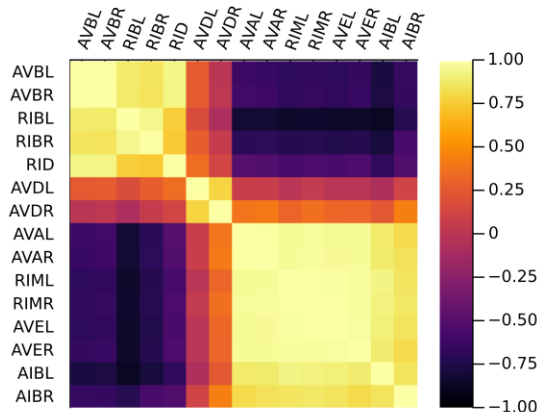
reversal

Simulation reproduces search activity in neural network

Data
correlations



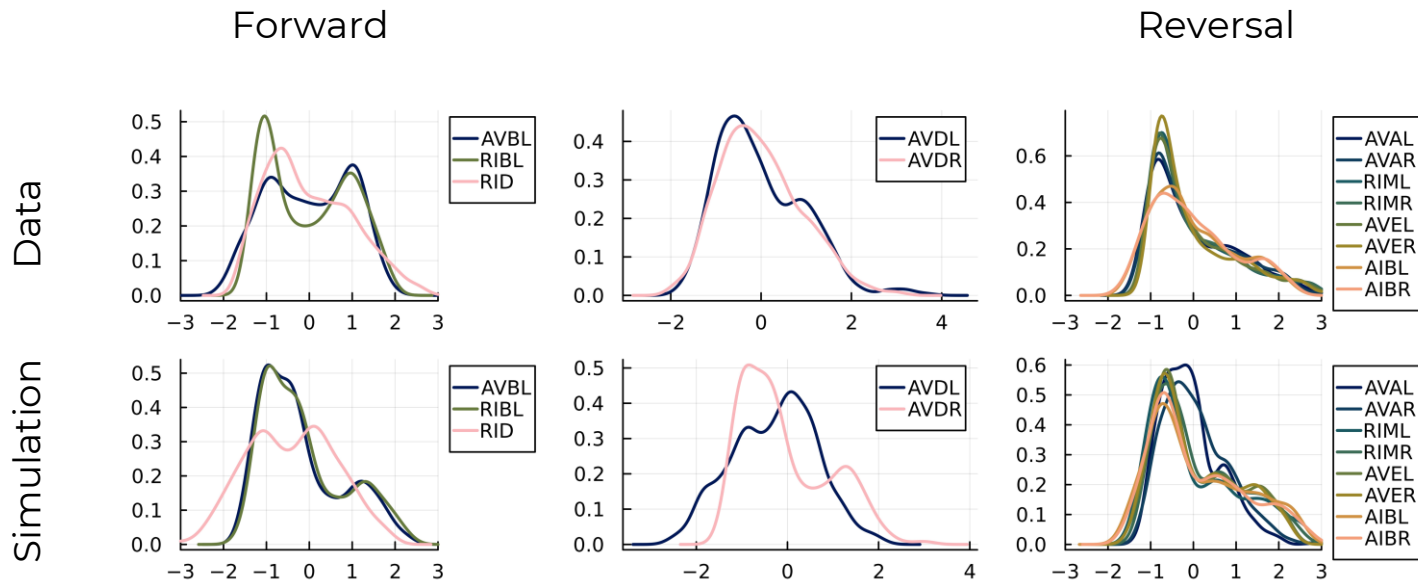
Simulation
correlations



- Correlation matrices are similar
- Forward neurons are highly correlated
- Reversal neurons are highly correlated
- Forward and reversal are anti-correlated

Simulation reproduces search activity in neural network

Individual neuron distributions are similar



Input signals induce different long-lasting behaviors

■ forward
■ reversal

Frequent switching - “dwelling”

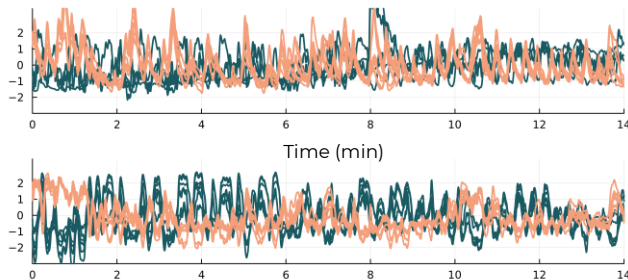
Sustained behavior - “roaming”

Neural activity

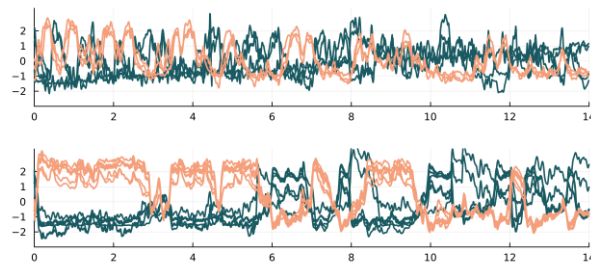
calcium imaging data

simulation

dataset: 2023-01-09-22



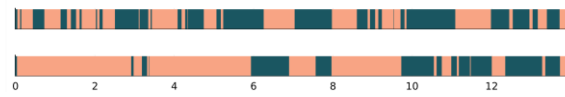
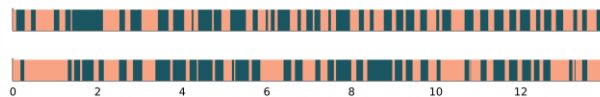
dataset: 2023-201-09-08



Behavior

data

simulation



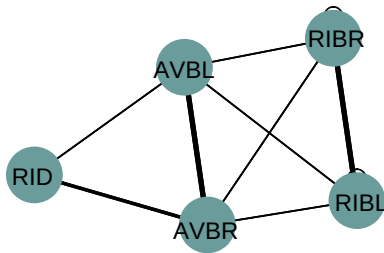
Gap junctions versus synaptic connections

Forward neurons

— AVBR
— RIBL
— RIBR
— AVBL
— RID

Forward cluster

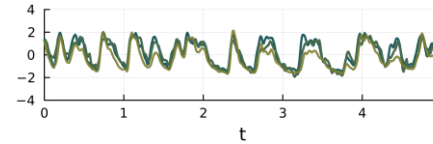
Model neurons



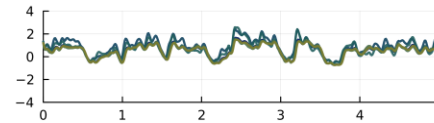
Signal neurons

AVJ
AWB
URB
RIM
URY
⋮

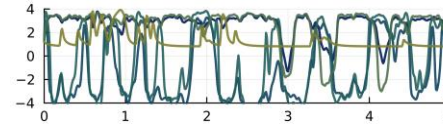
Calcium imaging data: Dataset 2023-01-23-15



Simulation – only gap junctions

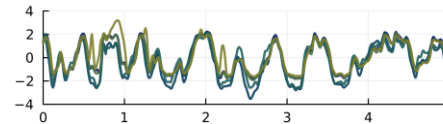


Simulation – only synapses



Take out one type of connection

Simulation – gap junctions and synapses



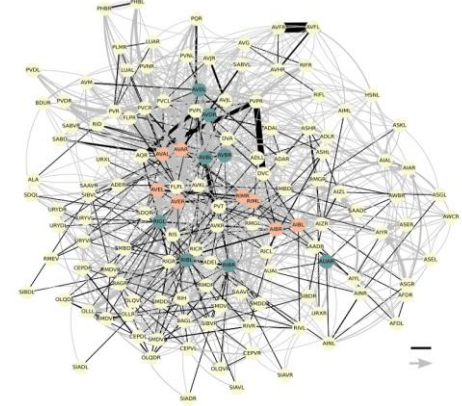
Challenges

Prevalent in math biology,
exemplified in *C. elegans*

- Building data-driven models with **datasets** that are ***disparate***, ***partial***, and ***descriptive***
- Create models that go ***beyond reproducing phenomena*** under a set of constraints

Summary

- We model the *C. elegans* premotor network as a **driven network dynamical system**
- We use different types of data to construct a single **general model**
- Our model reproduces the **higher-order statistics** of premotor neural activity
- Our model can be used to analyze how **structure supports behavior**



Open problems

Moving forward...

- How well can a toy model network be fit using various amounts of data? (A little versus a lot of data)
- How much data is necessary for a fit model to be useful?
- What is the purpose of redundant/ highly correlated neurons?

Student projects

Projects

- Synaptic sign identification in toy network models
- The predictive ability of driven dynamical systems breaks down as network size increases – explore this phenomena in toy models

Student projects

Prerequisites and skills

- Coding experience, familiar with using Python or Julia
- Familiar with working with datasets
- Familiar with networks and using graph structures
- Courses in differential equations and statistics
- Basic courses in biology and neuroscience