A Joint Graph Inference Case Study: the *Caenorhabditis elegans* Neural Networks

Li Chen

Applied Mathematics and Statistics
Johns Hopkins University,
Baltimore, MD 21218

*lichen87@jhu.edu*

Joint work with Joshua Vogelstein and Carey Priebe

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Overview

1. The Roundworm Nervous System
2. Brief Intro to Networks
3. Seeded Graph Matching
4. Joint Vertex Classification
The *Caenorhabditis* Neural Network

**The *C. elegans* neural network**

- The *C. elegans* is a non-parasitic and transparent roundworm.
- 253 neurons. Each neuron belongs to exactly one neuron type: motor (43.5%), interneurons (30%), and sensory (26.5%).
- Two types of synaptic connections: chemical $A_c$ and electrical $A_g$. They result in a pair of neural networks.

*Figure:* An image of the *Caenorhabditis elegans* (*C. elegans*) roundworm.
Graphs

Making inferences about graphs

- Graph $G = (V, E)$ consists of vertices and edges. Adjacency matrix $A$ for undirected graph $G$.
- Vertex based inferences: clustering, classification, nomination, matching, ...

Figure: (Left) Chemical synaptic neural network $A_c$. (Right) Electrical synaptic neural network $A_g$. **Red**: motor. **Green**: inter. **Blue**: sensory.
Statistical Models for Graphs

Random Graph Models

- **Erdos-Renyi Graph**: each edge is present independently with equal probabilities.
- **Stochastic Blockmodel**: each vertex is a member of one block. The block membership of a pair of vertices determine their edge presence probabilities.
- **Latent Position Models**: each vertex has latent attributes. Edge probabilities are based on a link function.
Stochastic Blockmodel (SBM)

**Definition**

- $K$: number of blocks.
- $B$: $K \times K$ symmetric matrix specifying the probability of block connectivities.
- $\pi$: a length $K$ block membership probability vector.
- $Y$: block membership of each vertex, given by $Y : \pi \rightarrow [K]$.

Then $A \sim SBM([n], B, \pi)$ if the edge probabilities are conditionally independent given the block memberships, and determined by entries of $B$ given the memberships.

**Model Dimension**

The SBM is $d$-dimensional if $\text{rank}(B) = d$. 

The block-structure of the neural network

**Figure**: The adjacency matrices of the *C. elegans* neural networks $A_c$ and $A_g$. 
Low rank eigen-structure of the neural network

Figure: The low-rank eigen-structure of the *C. elegans* neural network.
Inference on single networks

Vertex classification [1], [5], vertex clustering [4], vertex nomination [3].
Joint Graph Inference Framework

Joint inference on a pair of networks

We focus on two aspects of joint graph inference:

- Seeded graph matching - finding the correspondence of vertices across the pair of *C. elegans* neural network.
- Joint vertex classification - predicting the class membership of a vertex using information from the joint graph space.
Seeded Graph Matching

The Problem of Graph Matching

- Given two adjacency matrices \( A, B \).
- Objective: minimize the number of edge disagreements.

\[
\arg\min_{P \in \mathcal{P}} f(P) = \arg\min_{P \in \mathcal{P}} \| A - PBP^T \|_F = \arg\max_{P \in \mathcal{P}} \text{tr}(APBP^T).
\]

(1)

- Tool: Frank-Wolfe Algorithm.

The Problem of Seeded Graph Matching

- Seeds: vertices whose true alignments are known.
- Addition of seeds improves accuracy.
- Small change to graph matching algorithm.
Neurological Motivation for applying SGM on *C. elegans* neural network

- In neuroscience, it is interesting to compare brains both within and across species.
- The extent of graph heritability with a species remains an open question.
- Compare graphs across species to enable comparative connectomics.

All of these basic science questions benefit from graph matching methods!

*Figure*: An visualization of the SGM procedure.
Finding the Correspondence between the Chemical and the Electrical Synapses

![Graph showing seeded graph matching accuracy for C. elegans synapses. The graph compares matching accuracies for barycenter, RCM, and chance methods.](image)
Finding the Correspondence between the Chemical and the Electrical Synapses

C. elegans seeded graph matching
Ag matching Ac

Matching Accuracy

0 0.04 0.08 0.12 0.16 0.2

0 20 40 60 80 100 120 140 160 180

Number of Seeds m

Bary center
RCM
Chance
Motivation of Joint Vertex Classification on the *C. elegans* Neural Network

**Statistical Motivation**

The result of SGM on the *C. elegans* Neural Network suggests that inference must proceed in the joint space.

**Neurological Motivation**

We intend to understand the significance of the coexistence of the chemical and electrical connections.
Joint Classification on the Pair of Neural Networks

**Algorithm 1** Joint Vertex Classification [2]

**Goal:** Classify the neuron $v$ in $G_1$ whose neuron type is $Y$.

**Input:** A pair of the neural networks, $\{G_1, G_2\}$. A specified dissimilarity measure $D$.

1. **Compute the dissimilarities of $G_1$ and $G_2$ using $D$**
2. **Compute the Omnibus matrix $M$**

   \[
   M = \begin{pmatrix}
   D_1 & \Lambda \\
   \Lambda & D_2
   \end{pmatrix} \in \mathbb{R}^{2n \times 2n}.
   \]  

3. **Embed** The omnibus matrix $M$ into $d$-dimensional Euclidean space using classical multidimensional scaling. $U = \begin{bmatrix} U_1 \\ U_2 \end{bmatrix} \in \mathbb{R}^{2n \times d}$. $U_1 \in \mathbb{R}^{n \times d}$ is the joint embedding corresponding to $G_1$, and $U_2 \in \mathbb{R}^{n \times d}$ to $G_2$.

4. **Train** on $T_{n-1} = U_1[1 : (n-1), :] \in \mathbb{R}^{(n-1) \times d}$ and **classify** $v$. 


Algorithm 1 Flow Chart

\[ \begin{pmatrix} D_1 & \Lambda \\ \Lambda & D_2 \end{pmatrix} \xrightarrow{2n} \begin{bmatrix} U_1 \\ U_2 \end{bmatrix} \xrightarrow{d} U_1 \xrightarrow{d} U_1[1 : (n - 1), :] \]

Train

Test

\[ U_1[n, :] \]
Joint Classification on the Pair of Neural Networks

**Algorithm 2** Joint Vertex Classification [2]

**Goal**: Classify the neuron \( v \) in \( G_1 \) whose neuron type is \( Y \).

**Input**: A pair of the neural networks, \( \{ G_1, G_2 \} \).

1. **Compute the dissimilarities of** \( G_1 \) **and** \( G_2 \).
2. **Compute the Omnibus matrix** \( M \)

\[
M = \begin{pmatrix} D_1 & \Lambda \\ \Lambda & D_2 \end{pmatrix} \in \mathbb{R}^{2n \times 2n}.
\] (3)

3. **Embed** The omnibus matrix \( M \) into \( d \)-dimensional Euclidean space using classical multidimensional scaling. \( U = \begin{bmatrix} U_1 \\ U_2 \end{bmatrix} \in \mathbb{R}^{2n \times d} \). \( U_1 \in \mathbb{R}^{n \times d} \) is the joint embedding corresponding to \( G_1 \), and \( U_2 \in \mathbb{R}^{n \times d} \) to \( G_2 \).

4. **Train** on \( \mathcal{T}_{n-1} = U_2[1 : (n - 1), :] \in \mathbb{R}^{(n-1) \times d} \) and **classify** \( v \)
Algorithm 2 Flow Chart

\[
\begin{pmatrix}
D_1 & \Lambda \\
\Lambda & D_2
\end{pmatrix}
\rightarrow
\begin{bmatrix}
U_1 \\
U_2
\end{bmatrix}
\]

Train

Test

\[U_2[1 : (n-1), :]
\]

\[U_1[n, :]
\]
Compare the performance of joint vertex classification and separate vertex classification: Classification on $A_c$.
More distances

Joint classification vs single classification on Ac
Distance measure: ASE_L1

Joint classification vs single classification on Ac
Distance measure: ASE_L2

Joint classification vs single classification on Ac
Distance measure: shortest paths

Joint classification vs single classification on Ac
Distance measure: involweighted
Compare the performance of joint vertex classification and separate vertex classification: Classification on $A_g$
More distances

Joint classification vs single classification on Ag
Distance measure: ASE_L1

Joint classification vs single classification on Ag
Distance measure: ASE_L2

Joint classification vs single classification on Ag
Distance measure: shortest paths

Joint classification vs single classification on Ag
Distance measure: involweighted
Understanding the Coexistence of the Chemical and the Electrical Synapses

**Implication of the Joint Classifier**

- The classifier using the joint information from both networks performs better than the classifier using the information from the network separately.
- The improvement in classification indicates significance of the coexistence of the chemical and the electrical synapses.
- This discovery deserves further investigation in both the neuroscience and the statistics fields.
Li Chen, Joshua Vogelstein, and Carey Priebe.
Robust vertex classification.

Li Chen, Joshua Vogelstein, and Carey Priebe.

Donniell Fishkind, Vince Lyzinski, Henry Pao, Li Chen, and Carey Priebe.
Vertex nomination schemes for membership prediction.

Vince Lyzinski, Daniel Sussman, Minh Tang, Avanti Athreya, and Carey Priebe.
Perfect clustering for stochastic blockmodel graphs via adjacency spectral embedding.

Daniel L Sussman, Minh Tang, Donniell E Fishkind, and Carey E Priebe.
A consistent adjacency spectral embedding for stochastic blockmodel graphs.

Lav R Varshney, Beth L Chen, Eric Paniagua, David H Hall, and Dmitri B Chklovskii.
Structural properties of the *caenorhabditis elegans* neuronal network.
Thank you!