A correlation-based motif search algorithm for biological network graph models

JENNA JABOURIAN[1], Sharmila Venugopal[2]
[1]BIG Summer Program, Institute for Quantitative and Computational Biosciences, UCLA
[2]Department of Neurology, David Geffen School of Medicine, UCLA

Introduction

Brain functions are orchestrated by causal interactions between diverse biomolecules. Currently, there is a lack of systematic approaches to assemble interactions derived from disparate experimental datasets. We recently developed a workflow to gather evidence-based interactions focusing on neuronal functions. We created a novel directed network graph with neurotransmitters, neuroproteins and nucleic acids as nodes with edges representing pairwise causal associations. Here, we implemented a Python software module for network analysis. The network was modeled as a connectivity matrix in which nodes were denoted by row and column numbers, and positive or negative causal effects were modeled as weighted integers with zero being no association. Iterative reordering revealed subspaces with highly correlated nodes (corr. coeff. ≥ 0.5). For proof-of-concept, counts of 3-node motifs were searched. Ongoing work is automating statistical significance tests for network structure in order to predict novel motifs of multicellular signaling relevant to neuroinflammation and neural excitability functions.

Materials and Methods

Fig. 1

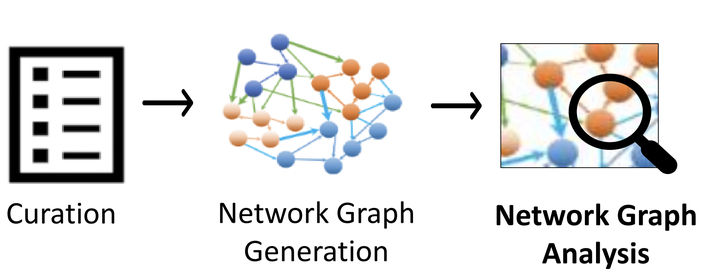

Fig. 2

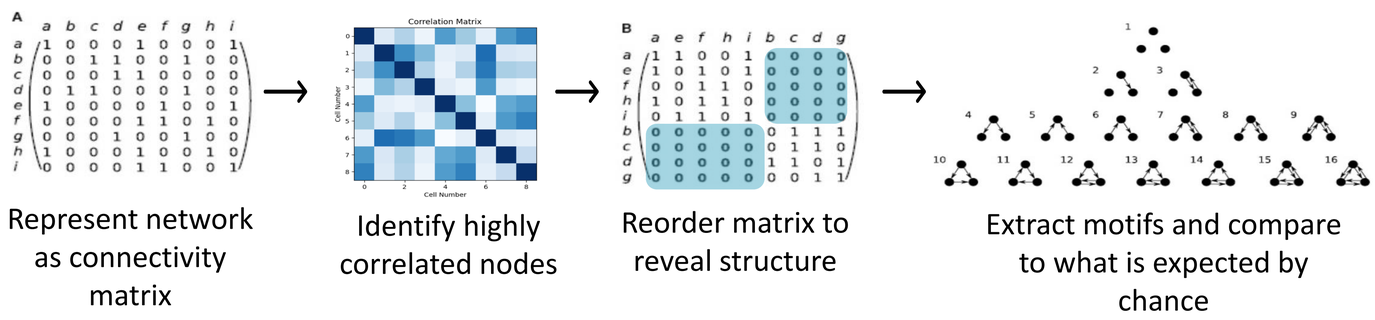

Fig. 1 Workflow diagram of curation of association studies relevant to various neuronal functions. Generation of network graph where nodes represent neurotransmitters, neuroproteins, and nucleic acids and directed, weighted edges represent pairwise causal associations.[1,2]

Fig. 2 Workflow diagram of approach/methodology. Network represented as connectivity matrix where rows/columns represent nodes and matrix entries represent causal effects.[3]

Results

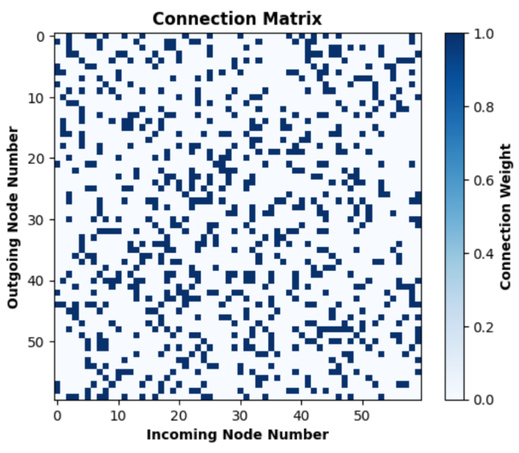

Fig. 3 Generate connectivity matrix where rows represent outgoing connections and columns represent incoming connections

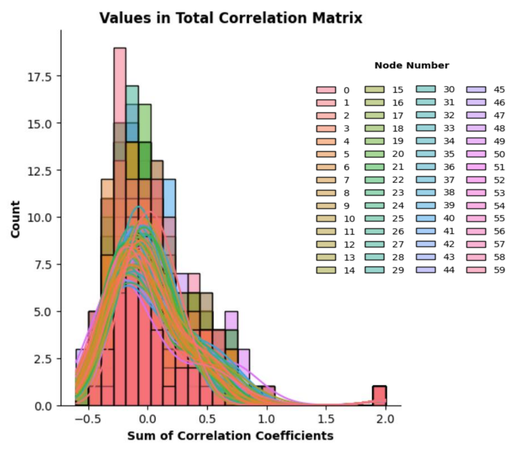

Fig. 4 Histogram of total correlation coefficients, bimodality indicates clustering

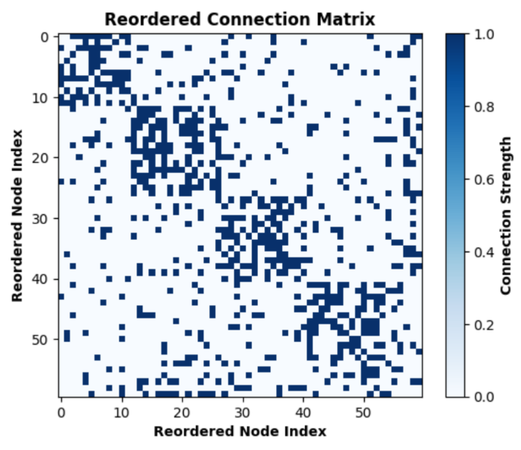

Fig. 5 Reordering outputs list of reorganized nodes, axes of reordered matrix correspond to node index

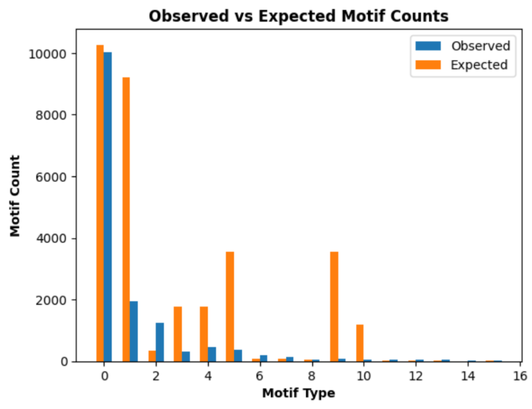

Fig. 6 Bar plot of observed vs. expected motif counts for each 3-node motif type based on probability of connection types

Conclusions

- By representing a network graph as a matrix and reordering the matrix based on highly correlated nodes, we were able to reveal hidden structures, extract 3-node motifs, and compare our observed motif count to what was expected by chance.
- A limitation of this project was identifying a standard threshold for nodes to be considered highly correlated, since a threshold too low groups nodes that may not be associated while a threshold too high may not identify nodes that are correlated.
- The next steps of this project involve the development of a more extensive threshold as well as automation of statistical significance tests for motif prediction.
- This algorithm can then be applied to our directed network graph to identify novel motifs between associated biomolecules in the brain involved in neuroinflammation and neural excitability functions.

References

1. Automated development of novel functional interactomes across brain scales, D Takher, S Kadadi, S Venugopal, SACNAS National Diversity in STEM (NDiSTEM) Conference, Oct, 2023, in Portland, Oregon.
2. Constructing a novel functional interactome to study the dynamic crosstalk between neuroinflammation and neural excitability, JV Morgenland, A Allahverdian, R Knorr, S Venugopal, 50th Society for Neuroscience Meeting, Nov 2021, (Virtual).
3. Miller, P. (2018).”Connections between Neurons.” *An Introductory Course in Computational Neuroscience.* The MIT Press. Chapter 5.

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