Pipeline to Infer Functional Brain Connectivity Networks from fMRI Data

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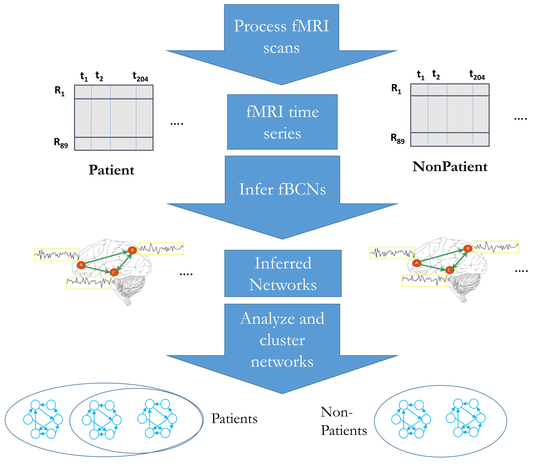
Introduction

Information about the functional connectivity of the brain has been shown to have potential clinical value. Through a comparison amongst functional brain connectivity networks (fBCNs) from a population with a brain disorder and fBCNs from a control population, it is possible to develop rich and sensitive markers of diseases [1]. One procedure for finding functional connections involves analyzing fMRI scans, which indirectly identify the activation of neurons by measuring the fluctuation of blood oxygenation in different regions of the brain over time [5]. Developing network inference methods for fMRI data is thus an important step towards identifying underlying brain connectivity networks.

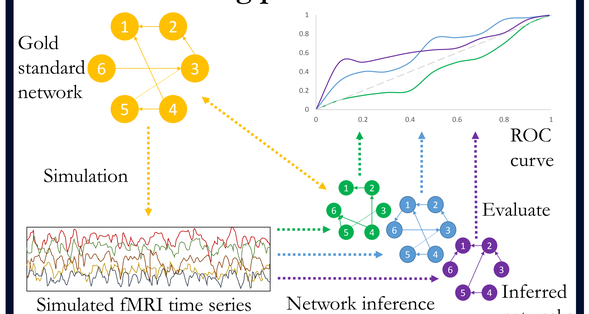


Objectives

1. Create a pipeline for inferring fBCNs from fMRI data.
2. Benchmark network inference methods from neuroscience [6] and molecular biology [2] & [3] using random and scale-free *in silico* networks.
3. Verify whether combining network inference methods to build a consensus fBCN will return better results than using the methods individually, a "wisdom of crowds" approach inspired from lessons learned by the molecular biology network inference community [4].

Methods

- **Benchmarking process**



Benchmarking process done using the MULAN software package

- **Gold standard networks**

Network type	Nodes	Networks	Simulations
Barabási–Albert scale-free network	50	100	100
Erdős–Rényi random network	50	100	100

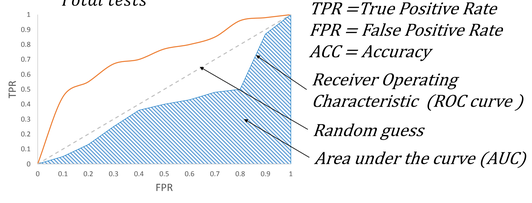
  - Scale-free dynamics have been observed in many biological systems including fBCNs
  - Random networks included to test the general robustness of the methods

- **Evaluating performance**

$$TPR = \frac{TP}{TP + FN} \qquad FPR = \frac{FP}{FP + TN}$$

$$ACC = \frac{TP + TN}{Total\ tests}$$

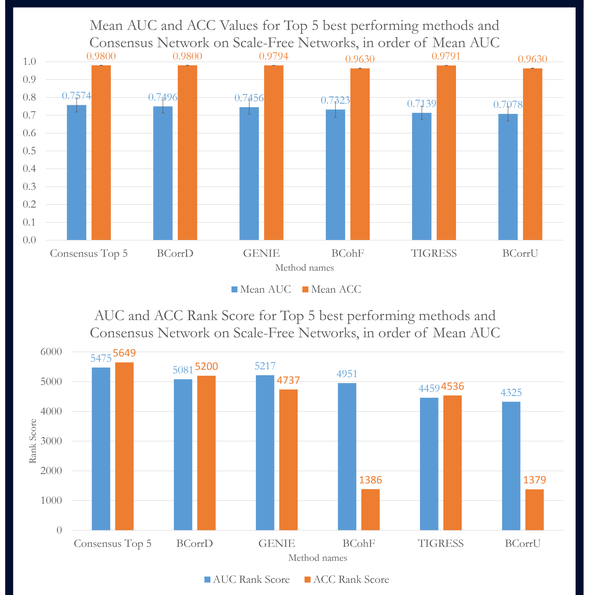
TP = True Positive
FP = False Positive
TN = True Negative
FN = False Negative
TPR =True Positive Rate
FPR = False Positive Rate
ACC = Accuracy

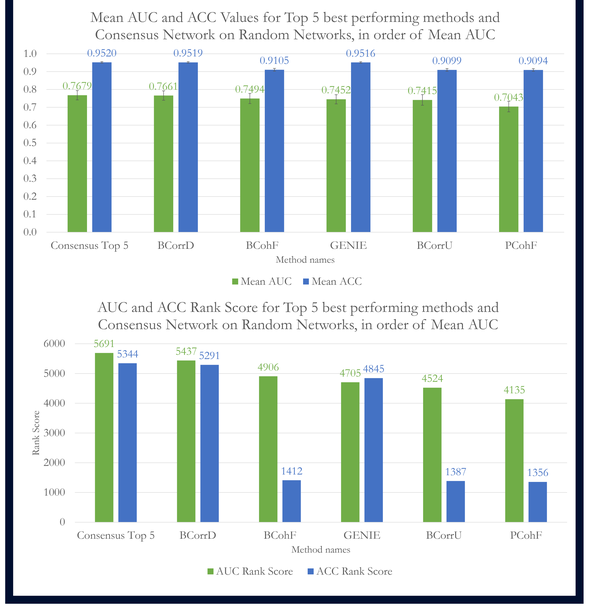


- **Consensus networks**

Each network inference method returns, per edge, a probability value for such an edge being present in the network. We built a consensus network from multiple network inference methods by assigning to each edge the mean probabilities assigned by the constituent methods.

Results



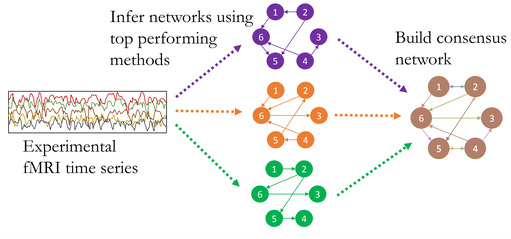


Discussion

- Across mean AUC, mean ACC, AUC rank score, and ACC rank score, we identified several methods that consistently performed in the top five: For random networks, these methods were BCorrD and GENIE. For scale-free networks, these methods were BCorrD, GENIE, and TIGRESS.
- Thus, the molecular biology network inference methods performed very well with fMRI data.
- Combining the best methods through consensus networks performs better than any of those methods individually.
- This is true for the top five methods ranked by mean AUC, mean ACC, AUC rank score, and ACC rank score for both random networks and scale-free networks.

Conclusion

A systematic *in silico* benchmarking of network inference methods for fBCNs is an important step to adequately select the most appropriate methods. Through our *in silico* benchmarking process we have shown that the networks inferred from combining the top 5 performing methods outperform any of the individual methods. From these results, we propose the following pipeline to infer fBCNs :



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Acknowledgements

Funded by National Science Foundation award #1460967