Adaptive Thresholding for Graph-Theoretical Analysis in Network Neuroscience

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INTRODUCTION

Connectivity analyses of brain networks (BNs) play a key role in our understanding of activity in the brain. Functional and structural connectivity analyses provide insights into time-varying activity in different 'regions of interest'. BNs have several clinical applications - evaluation of brain disease vulnerability, neurosurgical planning, and diagnosis of psychiatric illnesses.

BNs are studied using graph-theoretical metrics in a network where the connection strength is a statistical correlation metric representing phase/amplitude synchronization features between brain regions. Some common approaches to generate these graphs include, but are not limited to:

1) fMRI (BOLD)
   a) Pearson Correlation
   b) Spearman Correlation
2) Electroencaphalography (EEG)
   a) Amplitude Coupling
   b) Phase Coupling
   c) PLI - Phase Lag Index
   d) dPLI - directed Phase Lag Index

For the purpose of the preliminary testing of the proposed algorithm, we utilized amplitude coupling as a metric in the EEG source space, with roughly 72 regions of interest.

AIM

Evidence shows that filtering spurious connections is based on arbitrary choices, which can yield incongruous network parameters.

Thresholding, the method responsible, currently lacks standardization and a systematic method to discern meaningful connections. Arbitrarily chosen thresholds, both absolute and proportional, vary greatly between studies, often leading to distorted results.

We propose a novel and robust approach based on an adaptive threshold with a higher likelihood of yielding reliable results. We aim to develop greater insights into the impact of thresholding on network propertie, in hopes of encouraging standardization of this step in BN analysis.

METHOD

This approach generates a threshold based on (1) the stabilization of the average connectivity in a given set of networks and (2) the proportional impact of each edge weight relative to the weighted node degree.

Initial graphs were generated from source space EEG data that had been preprocessed to remove noisy channels and artefacts.

The Algorithm

Given a set of graphs $\boldsymbol{G}$

- Iterate over a range of threshold (a_j) values
- Discard the weakest a edges in all $g \subseteq \boldsymbol{G}$
- Calculate the global average connectivity (C_{glob}), as well as the global average change in connectivity (δ_{glob}) from the previous α

$$C_{glob}(\alpha_j) = \frac{1}{|G|} \sum_{g_i}^{g_i \subseteq G} C(g_i(\alpha_j))$$

$$\delta_{glob}(\alpha_j) = \frac{1}{|G|} \sum_{g_i}^{g_i \subseteq G} C(g_i(\alpha_{j+1})) - C(g_i(\alpha_j))$$

This effectively creates a threshold-connectivity cost function, which can be used to determine a threshold where the network structure stabilizes.

Stability is inferred from the minimal change in average connectivity when alpha is adjusted. The value at which the average change of connectivity across all graphs is minimized is used as the threshold globally.

It is important to note that while applying a threshold (a), each edge weight is evaluated relative to the weighted node degree.

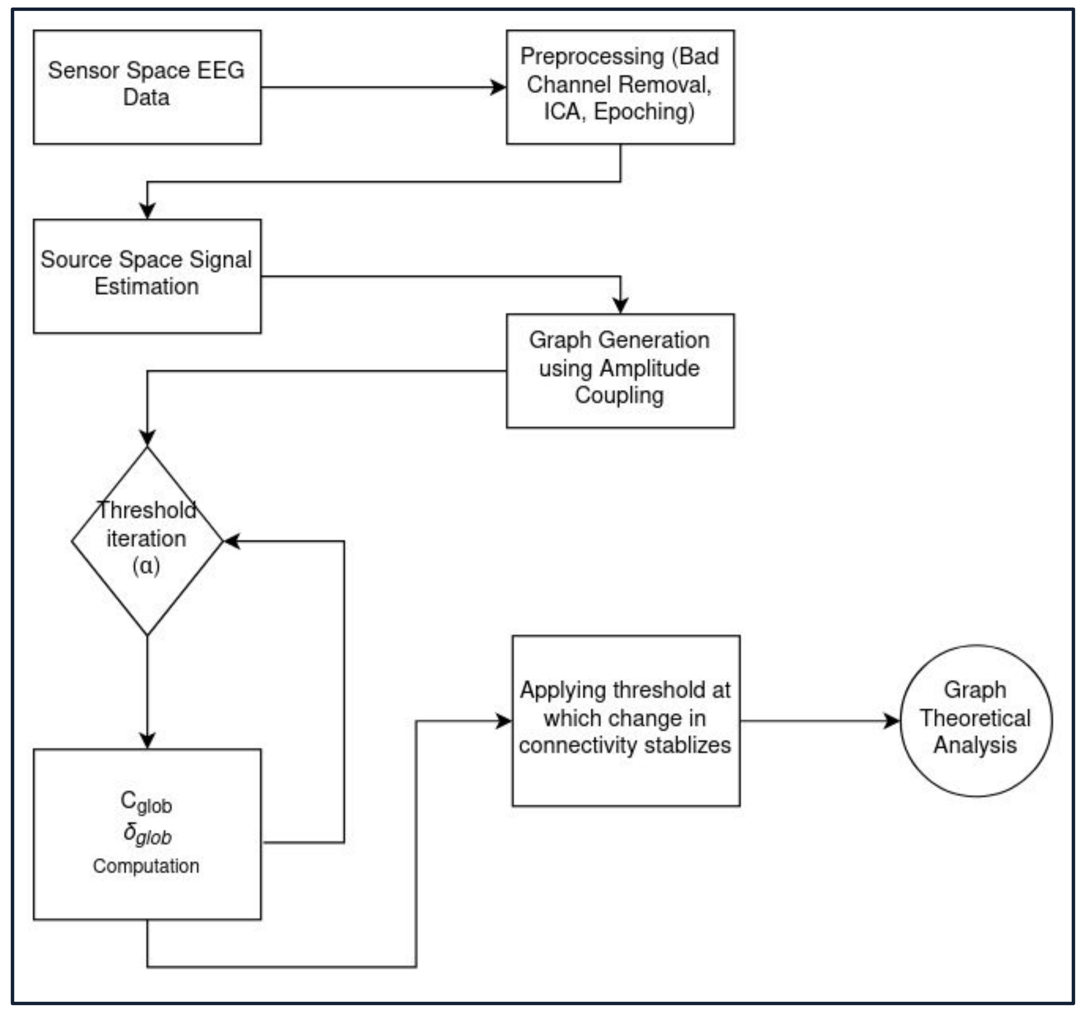

Fig 2. Flowchart for thresholding operations

EXPECTED RESULTS

Threshold-Connectivity cost function
We expect to see an inverse relationship between α and the Global Connectivity.

As for the global average change in connectivity, we expect to see some sort of bell distribution - since eliminating weaker connections will have a smaller impact on the change in connectivity, and the impact of removing the small number of extremely strong connections, is small compared to the contributions to connectivity made by the numerous mid-strength connections. Additional evidence about the modularity of the brain, which suggests small-world characteristics, should support this hypothesis.

Using a point of global stability, effectively where δ_{glob} is minimized, should give us an optimal threshold.

The assumption is that edges contributing to stable average connectivity are likely to be relevant and meaningful in understanding network structure - and finding the point of minimal change should help retain meaningful connections.

Preliminary testing was performed on BNs constructed from amplitude coupling metrics from the EEG source space. Future work would involve testing inter-metric and inter-modal performance.

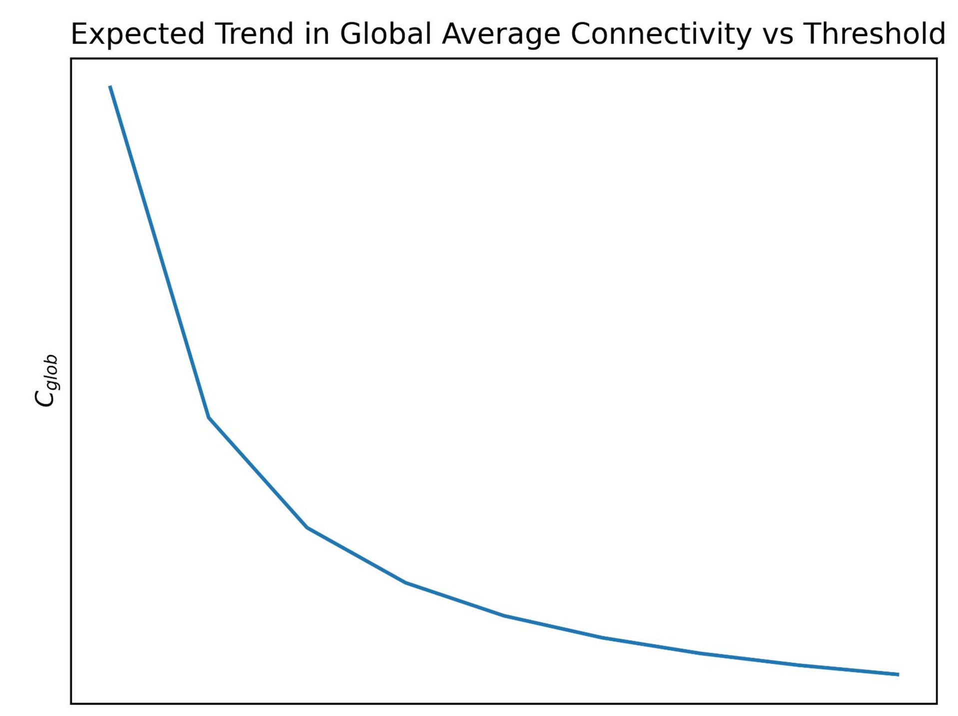

Fig 2. Expected trend for C_{glob} vs α

Possible Concerns
Iterating over α can prove to be computationally expensive. Preliminary results indicate that the point of most stability lies within the range of 0.001 = 0.1, however further testing is needed.

Additionally, this approach seems to be better suited towards eliminating weak spurious edges, as opposed to unwanted stronger 'static' edges - caused due to artefacts like channel noise. These hazards can be mitigated at pre-processing stages, however an optimal network-based approach for eliminating stronger "noisy" edges is yet to be found.

FUTURE DIRECTIONS

Validating the robustness and consistency of this approach is essential to standardization in preprocessing techniques used in functional and structural analysis of BNs.

Different metrics provide insights into different information (time, phase, space, etc) . Therefore, we expect to see differences while evaluating thresholded networks derived from different metrics. Studying the distribution of connectivity measures, as well as final graph measures, across networks generated using different metrics, as suggested by Adamovich, T., Zakharov, I., Tabueva, A. et al. offers a robust way to account for these differences.

CONCLUSION

While not yet completely validated, improving our understanding of such data-driven approaches can lead to greater standardization in the construction and analyses of BNs, promoting stable and reliable results, potentially increasing their utility in clinical and non-clinical settings.

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