Large-Scale Neural Connectivity Analysis using Graph Theory

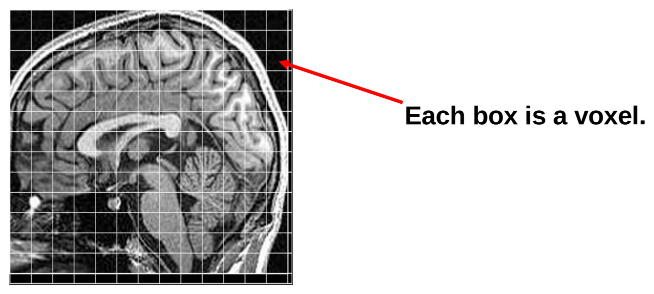
[1]Devdutta Warhadpande, [2,3]Patrick C. M. Wong, [2]Tyler Perrachione, and [4]Ji-Ping Wang
[1]Computation Biology and Bioinformatics, Northwestern University, [2]The Roxelyn and Richard Pepper Department of Communication Sciences & Disorders, Northwestern University , [3]Northwestern University Institute for Neuroscience, [4]Department of Statistics, Northwestern University

Abstract

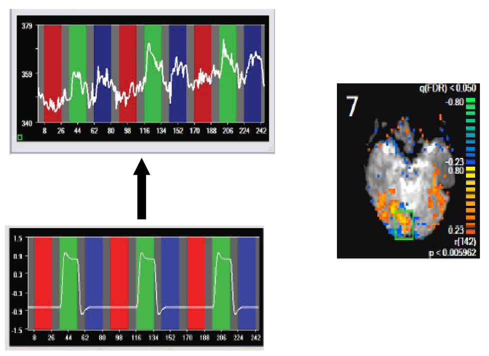
Functional magnetic resonance imaging (fMRI) detects regional changes in blood flow to identify brain regions "activated" by a given task. Traditional analysis methods of fMRI data, while effective at localizing regions of increased neural activity, are unable to reveal large-scale patterns of neural connectivity. In this study, we are using graph theory methods to characterize these patterns. The use of pair-wise correlations to generate a functional neural network has been previously validated (Eguiluz et al. 2005). We employed the same technique on fMRI data from a prior study of auditory perception expertise (Margulis et al. 2007) to generate a connectivity network. Preliminary results show a non-random connectivity relationship and suggest that experts' brains have different connectivity patterns from non-experts.

Introduction

•Basics of fMRI:
- A technique used to map brain activity
- Measures contrast between oxygenated and deoxygenated blood
- Voxel: basic unit of an MRI image (3D pixel)

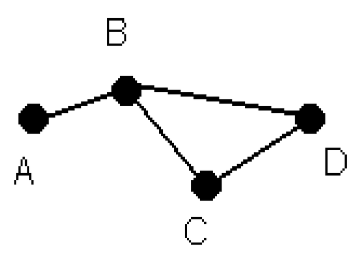


•Traditional methods:
- General Linear Model (GLM): shows activation intensity of a region relative to others



•Our method:
- Considers the whole brain
- Relatively few assumptions about hemodynamic response

•Graph Theory:
- Graphs: set of nodes and edges (connections)



- Nodes (A, B, C, D)
- Edges (AB, BC, BD)
- Degree: number of connections for a given node (e.g., A = 1, B = 3, C = D = 2)
- Cluster: total connections between adjacent nodes relative to the possible connections between them
- Path Length: the distance between one node to another (e.g., ABC, ABD, ABCD)
- Networks (e.g. airports)

•Graph theory methods can be used to analyze networks.
•Brain can be thought of as a network with many regions connected to each other and its connectivity pattern can be analyzed using graph theory.

Methods

•Experiment:
- Consisted of violinists and flutists listening to violin and flute music (stimuli)
- There were two conditions – expert and non-expert.
  - Violinists listening to violin or flutists listening to flute – expert.
  - Violinists listening to flute or flutists listening to violin – non-expert.
- Both stimuli were presented randomly and mixed with each other and were interspersed with rest periods.
- The subjects' response was to click a clicker after a given stimulus.

•Data:
- Preprocessing was done on the images (motion correction, spatial smoothing, detrending).
- We chose only those voxels that corresponded to the grey matter for all subjects .
- The data was separated by condition and adjusted for lag.
- Voxel-by-voxel pair-wise correlations were calculated for all voxels.

$$r(x_1, x_2) = \frac{\langle V(x_1,t)V(x_2,t)\rangle - \langle V(x_1,t)\rangle\langle V(x_2,t)\rangle}{\sigma(V(x_1))\sigma(V(x_2))}$$

Eq. 1 (Eguiluz, 2005)

- We selected thresholds (e.g., 0.7)
  - If correlation coefficient, r, was greater than threshold then voxels were assumed to be functionally connected (r=1); if r was less than threshold, then voxels were assumed to be not connected (r=0).
- This gave a binary connection matrix.

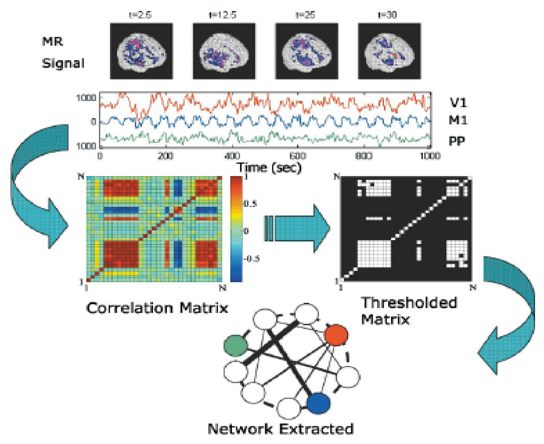


Figure 1 (Eguiluz, 2005)

•Calculate number of connections for each voxel (degree)
•Plot the degree vs the degree frequency.
•Project the degrees back to the brain

Preliminary Results

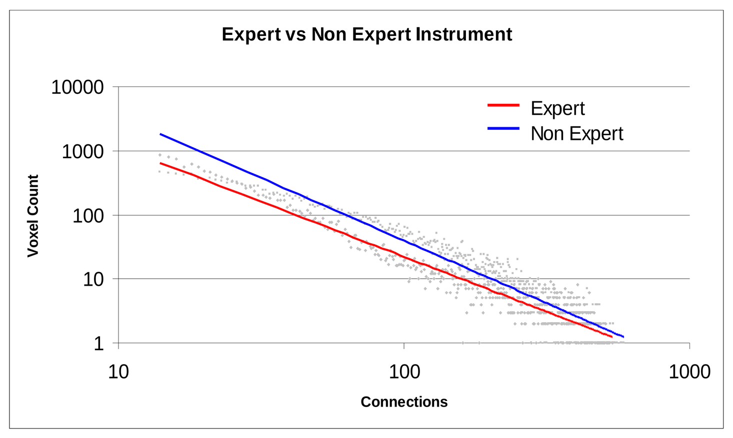
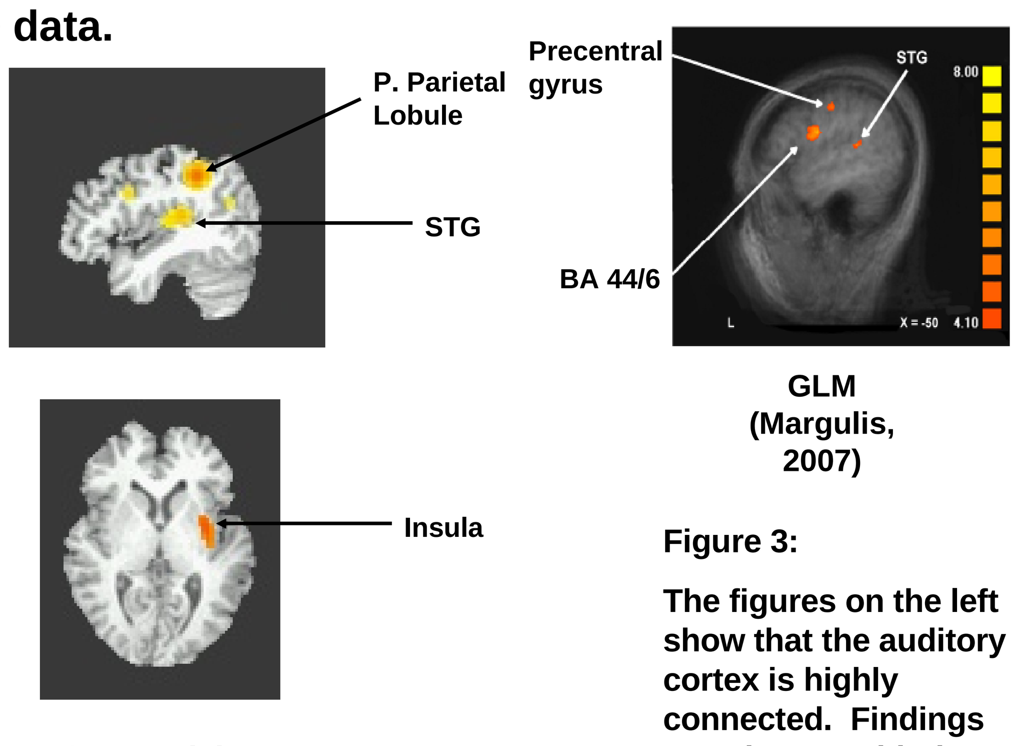


Figure 2: Degree Distribution for experts and non experts.

•Both expert and non-expert plots show power law relationship – a characteristic of scale-free networks. It is a non-random relationship.
•The expert line is shifted lower than the non-expert.

•The data was projected back to the brain to ascertain the validity.

•We compared it to the analysis done in the previous study on the same data.



Connectivity Analysis

GLM (Margulis, 2007)

Figure 3:

The figures on the left show that the auditory cortex is highly connected. Findings corroborate with the previous analysis done on this data (right).

•The color scale in connectivity set of images indicate the connectivity of the indicated voxels. The redder it is, the more highly connected it is.
•The scale in the GLM image indicates the strength of activation.
•The connectivity analysis identified similar regions as the GLM analysis. It also identified some areas that were not shown in the GLM analysis.

Discussion

•We were able to use graph theory methods to analyze fMRI data.
•Plotting degrees verses their frequencies revealed a power law relationship. This is a property of scale-free networks.
•The method was able to differentiate connectivity patterns between different auditory behaviors (expert vs. non-expert)
•Projecting back to the brain provided converging evidence for the areas of activation (e.g., STG) identified using GLM, BUT:
- Also revealed additional areas that showed increased connectivity.

•Future work:
- We are currently working on cluster analysis, as well as path length analysis. Cluster analysis will identify areas of high interaction where as path length analysis will identify whether the discovered network has small-world properties.
- Currently, the generated network is an unweighted network. We intend to generate a weighted network from the same data and compare it to the unweighted graph.
- Another possible avenue to explore is directionality.

Selected References

Margulis, E.H., Mlsna, L.M., Uppunda, A.K., Parrish, T.B. & Wong, P.C.M. Selective Neurophysiologic Responses to Music in Intrumentalists with Different Listening Biographies. (in press). *Human Brain Mapping*.

Sporns, O., Chialvo, D., Kaiser, M., and Hilgetag, C.C. (2004) Organization, development and function of complex brain networks. Trends in Cognitive Sciences 8, 418-425.

Victor M. Egui´luz, Dante R. Chialvo, Guillermo A. Cecchi, Marwan Baliki, and A. Vania Apkarian (2005). *Scale-Free Brain Functional Networks.*