



Analysis of brain activity as a massively interconnected dynamical network

V. Eguíluz¹, G. Cecchi², M. Baliki³, D.R. Chialvo^{1,3}, A. Apkarian³

¹Physics, IMEDEA, CSIC & University of the Balearic Islands, Mallorca, Spain.

²IBM Research, Yorktown Heights, NY, USA.

³Physiology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA.

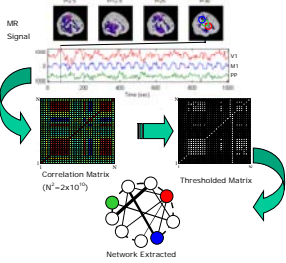
TH 272

INTRODUCTION

This work is driven by: A) recent theoretical developments in the area of nonlinear complex networks. It has been documented that disparate networks of interacting elements obey similar organizational principles. For example, in metabolic networks, it is shown that, despite a wide variation in constituents and pathways, they share topological scaling properties that are similar to the organization of complex non-biological systems, such as the Internet.

The approach is also driven by: B) the large body of electrophysiological evidence indicating that adequate understanding of the dynamics of information processing in the brain must take into account interactions between neurons. Therefore, we combine A and B to examine brain information processing from the viewpoint of a fully connected dynamical system. fMRI data is used to this end.

Standard analysis of network properties of brain fMRI involves two steps: (I) regions involved in a given task are identified by relating individual voxel activity to the timings of task presentation. (II) The inter-relationship between the identified regions are then analyzed based on their cross-covariance matrix. Here we extend connectivity analysis of fMRI by studying connectivity across all brain voxels.



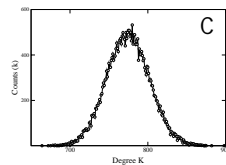
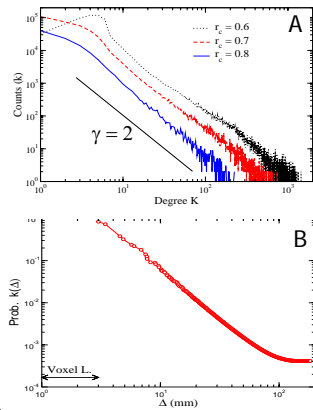
Analysis of the brain full correlation matrix was done on fMRI data collected in rest-state and during various tasks, on a 3 Siemens Trio (TR = 2500, data acquired for 400 TRs).

The correlation matrix was then collapsed to an adjacency matrix, where the link between two voxels was set to 1 if the correlation was above a threshold, 0 otherwise. The thresholded matrix describes an undirected graph, that represents the network of brain voxels with mutual correlation throughout the duration of the task.

The method allows for a collective view of brain functional networks. In particular, we asked:

- What is their prevailing topology?
- What are their statistical regularities?
- Are the networks functionally relevant?

Brain functional networks are scale-free



Distribution of links: how many voxels (nodes hereafter) have so many links with other nodes.

We found that, consistent across subjects and tasks, the link distribution is scale-free, as represented in panel A (average of 22 fMRI scan sets in 7 subjects). Panel B depicts the probability of having a link between two nodes as a function of their distance, and also shows a scale-free behavior. Panel C shows the link distribution for the null hypothesis, where volumes were randomized.

Brain functional networks have small-world features

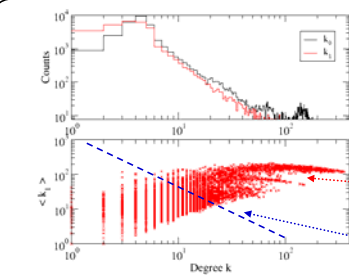
r_c	N	C	L	$\langle k \rangle$	γ	C_{rand}	L_{rand}
0.6	31503.2	0.144	11.42	13.41	2.0	4.3×10^{-4}	3.9
0.7	17174.6	0.127	12.95	6.29	2.1	3.7×10^{-4}	5.3
0.8	4891.3	0.156	5.96	4.12	2.2	8.9×10^{-4}	6.0

Network	N	C	L	$\langle k \rangle$	γ	C_{rand}	L_{rand}
C. Elegans	282	0.28	2.65	14	.	0.025	2.1
Macaque VC	32	0.55	1.77	9.85	.	0.318	1.5
Cat Cortex	65	0.54	1.87	17.48	.	0.273	1.4

Networks topological measures: N is the number of nodes. Clustering C measures the number of first neighbors of a node that are mutually connected (i.e. how many "triangulations" there are), and average minimal length L measures the average number of steps needed to connect any two nodes in the network. Small-world networks are those whose L is similar to that of a random network (i.e., $L \sim L_{rand}$), but whose clustering is much larger (i.e., $C \gg C_{rand}$). ($\langle k \rangle$ is the average number of links and γ the scaling exponent of the degree distribution).

We show, for the first time, that brain networks possess a small-world structure; a property shown previously in communication networks, including gene networks, linguistic networks and the Internet.

Brain functional networks seem non-hierarchical

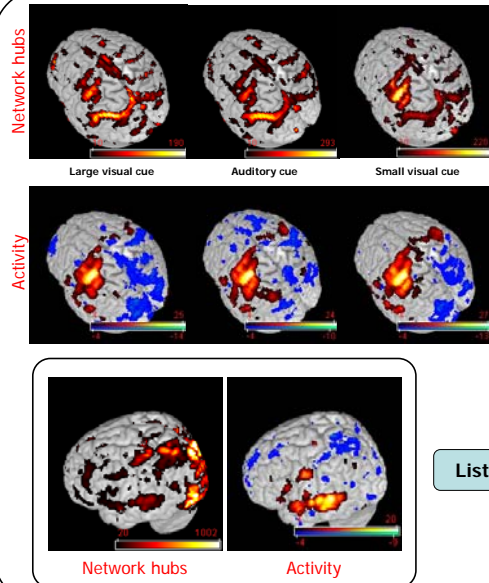


Some networks show hierarchy, where nodes with high connectivity link to many nodes with only a few connections (---), as in gene networks and airlines routes. We found, however, that brain networks are non-hierarchical, i.e. highly connected nodes link to well connected ones (xxx).

Functional brain networks

Hierarchical networks

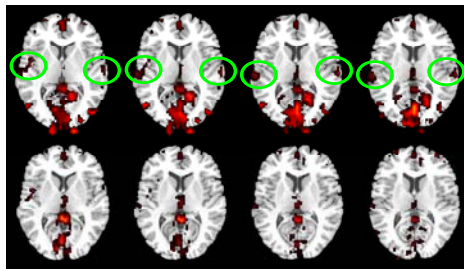
The networks are functional



A comparison between the network hubs and the conventional activity/rest analysis shows that both methods identify similar but not identical networks. The basic task is finger-tapping, with three different cue conditions. However, a music-listening task shows the full power of this unsupervised method, where a much larger network is uncovered, encompassing that found by the conventional stimulus-driven approach.

Listening to music

Brain functional networks show sensitivity to instruction set

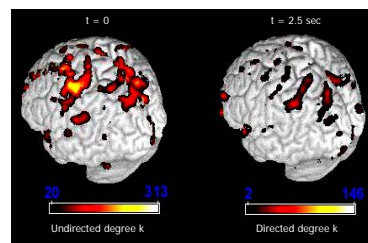


Finger Tapping task

The figure shows, color-coded, the locations of those voxels with relatively large number of connections, averaged over 5 subjects. The condition is a finger-tapping motor task, interleaved with rest.

Top row is for the motor task when the cue to start and stop is auditory. Bottom row is for scans when the cue is visual. Four consecutive slices are shown. Auditory cortex regions showing high connectivity are encircled.

Higher-order temporal correlations



The approach can be extended to include delayed correlations. The figure shows the comparison between the zero-delay correlation hubs and those corresponding to a lag of 2.5 secs (=TR) for the finger tapping task. The networks revealed correspond to functional areas, and they also display similar scale-free properties (not shown).

CONCLUSIONS

We demonstrate how studying the full connectivity of functional brain states one extracts different information than traditional stimulus-driven methods. The networks identified by the methods parallel to brain areas consistent with the tasks investigated, and seem to provide additional information regarding sensory-motor transformation integrated by connectivity through regions involved in attention.

The extracted networks have topological properties shared with many biological and technological communication networks, as they show a *Scale-free, Non-hierarchical, Small-world* organization. It is the first time these properties have been characterized in brain activity networks.

This unsupervised method can be a powerful window into the brain in particular when no clear external correlators can be identified. The possibility of discriminating different brain states by means of global topological measures based on this approach (e.g. scaling) is the subject of current work; it remains an open question what the precise experimental paradigms are that could profit the most from these methods.