Brain Oscillatory and Network Activity During Resting States

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Abstract
In this project, we aimed to analyse and compare two EEG datasets corresponding to two resting states. They are recorded from 64 electrodes with a subject at rest in eyes-open and eyes-closed during resting states. We performed several analyses including spectral analysis and network analysis in order to understand brain connectivity estimation and information flows between brain regions. We also detected some motifs over the networks and practiced the clustering algorithms for a similar purpose.
We used the Python high-level programming language[2] and various packages specific to network and connectivity analysis and clustering. (see included Jupyter Notebook for list of packages and references).
Keywords: Neuroscience, Graph Theory, Brain connectivity

Introduction
For the study of network activity during resting state, we used the Electroencephalography (EEG) data. EEG is an electrophysiological monitoring method to record electrical activity of the brain.[3] The main advantages of EEG can be listed as follows: 1) EEG has the high temporal resolution on the order of milliseconds, 2) EEG setups are portable and thus usable in realistic situations and 3) EEG can be used in subjects who are incapable of making a motor response. The data are from PhysionNet, "EEG Motor Movement/Imagery Dataset"[4]. From the entire dataset, we selected subject S002 and its first two runs R01 (recorded during eyes-open), and R02 (recorded during eyes-closed). Previously, human brain networks have been studied in resting state with EEG and according to these studies, abnormalities and changes can provide important insights.

We performed several analyses in order to achieve our aim. We tried to choose the best options between existing analysis techniques. These analyses are respectively on; spectral analysis, connectivity graph, graph theory indices, motif analysis and community detection.

Graph theory is used in neuroscience to analyse; 1) Structural connectivity which describes the anatomical connections linking a set of neural elements, and 2) Functional connectivity which describes patterns of statistical dependence among neural elements. With regards to network (graph) theory in neuroscience, we can analyse a network in different scales. Firstly, we can analyse node indices (such as degree and betweenness centralities). Secondly, we can analyse different motifs and modularity which are constructed by a few subset of nodes. Finally, we can also analyse more general properties of a network such as average path length, clustering coefficient which all help to make different comments about the network.

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[2] https://www.python.org
[3] https://en.wikipedia.org/wiki/Electroencephalography
[4] https://physionet.org/physiobank/database/eegmmidb/ and http://www.schalklab.org/research/bci2000

Analyses

1) *Spectral Analysis*

In statistical signal processing, the goal of spectral density estimation (SDE) is to estimate the spectral density (also known as the power spectral density) of a random signal from a sequence of time samples of the signal.[5] Intuitively speaking, the spectral density characterizes the frequency content of the signal. One purpose of estimating the spectral density is to detect any periodicities in the data, by observing peaks at the frequencies corresponding to these periodicities.[6] There are many techniques for spectral estimation to mitigate the disadvantages of the basic periodogram. We can divide them as non-parametric and parametric methods.

For this study, we used two different techniques. The first one is a non-parametric methods named as "Welch's method". This method is based on the concept of using periodogram spectrum estimates, which are the result of converting a signal from the time domain to the frequency domain.[7] The second one is a parametric method named as "Autoregressive Model (AR)". This model is generally used to describe time varying random processes in economics and natural sciences. To estimate the parameters in AR, there are many different methods but in this study we use the Yule-Walker equation.

In order to estimate PSD, we need to choose one relevant channel. Since the occipital lobe is responsible for processing visual stimuli, we can choose one of the occipital positioned channels, O1, O2, Oz. We chose Oz instead of O1, O2 because Oz is closer to the primary visual cortex. Figure 1.1 shows us PSD with Welch's method for both datasets. And Figure 1.2 shows us PSD with AR method for both datasets.

2) *Connectivity Graph*

The term of connectivity used in graph theory of neuroscience, has two different definitions as anatomical and functional. In this study, we are dealing with functional connectivity which means the existence of temporal relation between the activity recorded in different cerebral sites. If we describe the brain connectivity as information flows between different brain regions, we need to construct a graph to follow brain connectivity. In this way we can understand the network organisation, quantify brain connectivity properties and look for markers based on connectivity.

We decided to use Partial Directed Coherence (PDC) to estimate brain connectivity. PDC is based on MVAR model. Higher performances when the aim is to accurately reconstruct the exact pattern of interactions between signals and distinguish the direct influence from those mediated by other signals. PDC was introduced by Baccala and Sameshima[8] in the form:

$$P_{ij}(f) = \frac{A_{ij}(f)}{\sqrt{\mathbf{a}_j^*(f)\mathbf{a}_j(f)}}$$

where, $A_{ij}(f)$ is an element of A(f) - a Fourier transform of MVAR model coefficients A(t), where $a_j(f)$ is j-th column of A(f) and the asterisk denotes the transpose and complex conjugate operation.[9]

[5] Porat, B. (1994). *Digital processing of random signals: theory & methods*. Prentice Hall.
[6] https://en.wikipedia.org/wiki/Spectral_density_estimation#Frequency_estimation
[7] https://en.wikipedia.org/wiki/Welch%27s_method
[8] Baccala, L. A.; Sameshima, K. (2001). *Partial directed coherence: A new conception in neural structure determination*. Biol Cybern. 84 (6): 463–474.
[9] https://en.wikipedia.org/wiki/Brain_connectivity_estimators#cite_note-PDC-25

For the estimation the brain connectivity among 64 channels with PDC, we chose 11Hz as a relevant frequency value because at this point we saw the biggest peak in the spectral analysis. 11Hz falls into the alpha band, where we expected to see high power density when eyes are closed and low power density when eyes are open. We also applied a threshold to have binary connectivity matrices that have network densities equal to 1%, 5%, 10%, 20%, 30% and 50%. The graphical representation of the binary adjacency matrix for each density is in Annex of this paper (see Figures 2.1, 2.2, 2.3, 2.4, 2.5, 2.6 respectively). Additionally, we put a topological representation of the networks with 5% density (see Figure 2.7). In our last connectivity analysis, we performed PDC again but with a different EEG rhythm which is delta. We chose 1Hz as a relevant frequency value as there was a relative peak at that position. Figure 2.8 represents delta wave connectivity matrices with 20% density.

3) *Graph Theory Indices*

Graph indices provide many facilities in order to interpret the basic structural elements of a graph. There are global and local features. We compute two binary global indices: Clustering Coefficient = 0.4674 and Path Length = 2.4018. The highest 10 channels for local graph indices (degree, in degree and out degree) are listed in Table 3.1. Figure 3.1 presents the behaviour of global graph indices for the network densities (1%, 5%, 10%, 20%, 30%, 50%). Figure 3.2 presents a topographical representation of local indices.

4) *Motif Analysis*

A network motif is defined as "patterns of interconnections occurring in complex networks at numbers that are significantly higher than those in randomized networks".[10] These patterns help us to encode basic interconnection properties of complex networks in nature. Counting how many times a motif appears in a given network yields a frequency spectrum that contains important information on the network basic building blocks. We can divide the motifs in two as: functional motifs and structural motifs. A structural motif of size M is comprised of a specific set of M vertices that are linked by edges. The functional motifs form a set of sub-graphs of a given structural motif. All such functional motifs consist of the original M vertices of the structural motif to which they belong, but contain only a subset of its edges. The motifs can appear because of constraints in the way the network was developed, thus being related to the evolution of the whole complex system or they can appear in relation to the classes of networks based on types of motifs found.

Some studies have also considered anti-motifs: subgraphs which are significantly underrepresented compared to randomized versions of the network. To use a sampling method to find anti- motifs, it might be more fruitful to sample initial subgraphs from the random ensemble rather than the network being studied. Anti-motifs will be more prevalent in the ensemble than in the target network, and thus are more likely to be discovered by sampling from the ensemble.[11]

Finding the motifs is a computationally hard task. As the size of the motifs increases, the time needed to calculate them grows exponentially. For example, while there are13 different isomorphic types of 3-node connected subgraph, it is 199 for 4-node subgraphs and 9364 for 5-nodes subgraphs. In this study, we will use only 3-node and 4-node subgraphs motifs. We got all motifs configurations that exist for 3-node subgraphs and 198 of motifs for 4-node subgraphs motifs for our strongly connected graph.

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[10] Milo R, Shen-Orr SS, Itzkovitz S, Kashtan N, Chklovskii D, Alon U (2002). *Network motifs: simple building blocks of complex networks*. Science. 298 (5594): 824–827.

[11] Grochow J. A., Kellis M. (2007). *Network motif discovery using subgraph enumeration and symmetry-breaking.* Computer Science and AI Laboratory, M.I.T. Broad Institute of M.I.T. and Harvard.

Table 4.1 presents all the motifs found for 3-node subgraphs and their z-scores. Refer to the included Jupyter Notebook to view all 4 node subgraph motifs. Figure 4.2 shows us a topographical representation of the networks considering only the connections involved in A→B←C configuration. Figure 4.3 shows the motifs involve for Poz (Parieto-occipital midline) channel.

5) *Community Detection*

Communities are subsets of vertices within which vertex–vertex connections are dense, but between which connections are less dense. Community detection based on a quantitative criterion to assess the goodness of a graph partition. A quality function is a function that assigns a number to each partition of a graph. In this way one can rank partitions based on their score given by the quality function. There are several algorithms to detect communities. We choose Louvain Algorithm to apply because it is easy to implement, extremely fast and it has no resolution limit problem.

Louvain Algorithm is divided in two phases that are repeated iteratively. In first part of algorithm, we calculate the gain of modularity. We calculate this by considering each node i and its neighbours j. If removing i from its community and placing it in the community of j gives us a positive number, node i is placed in the community for which this gain is maximum. The gain of modularity is equal to;

$$\Delta Q = \left[\frac{\Sigma_{in} + k_{i,in}}{2m} - \left(\frac{\Sigma_{tot} + k_i}{2m}\right)^2\right] - \left[\frac{\Sigma_{in}}{2m} - \left(\frac{\Sigma_{tot}}{2m}\right)^2 - \left(\frac{k_i}{2m}\right)^2\right]$$

Where Σ_{in} is sum of all the weights of the links inside the community i is moving into, Σ_{tot} is the sum of all the weights of the links to nodes in the community, k_i is the weighted degree of i, $k_{i,in}$ is the sum of the weights of the links between i and other nodes in the community, and m is the sum of the weights of all links in the network.

In the second phase of the algorithm, it groups all of the nodes in the same community and builds a new network where nodes are the communities from the previous phase. Any links between nodes of the same community are now represented by self-loops on the new community node and links from multiple nodes in the same community to a node in a different community are represented by weighted edges between communities. Once the new network is created, the second phase has ended and the first phase can be re-applied to the new network.[12]

List 5.1 shows the number and name of nodes for each Louvain cluster. Figure 5.1 presents a representation of Louvain clusters. Figure 5.2 shows a graphical representation of the community structure in both rest conditions. Lastly, we would like to compare the community structure obtained by means of two different methods (modularity-based vs information theory-based approaches). We used Spinglass Algortihm, Infomap Clustering Algorithm, Edge Betweenness Algorithm. You can find comparison of these clustering algorithm in Figure 5.3.

Conclusion

Network analysis has emerged as a crucial tool to understand anatomical and functional brain connectivity. We performed a collection of analysis that quantify complex brain networks. The accompanying brain connectivity toolbox allows researchers to start exploring network properties of complex structural and functional datasets. Louvain clustering especially gives more significant results.

[12] https://en.wikipedia.org/wiki/Louvain_Modularity

Annex

Table 0: List of task chosen for this study

TASK	CLASS
1.1	Mandatory
1.2	B
2.1	Mandatory
2.3	A
2.5	C
2.6	B
3.1	Mandatory
3.4	C
3.5	B
4.1	Mandatory
4.2	C
4.3	C
4.4	E
5.1	Mandatory
5.2	B
5.3	C

1. Spectral Analysis

Figure 1.1: PSD with Welch's method for both datasets

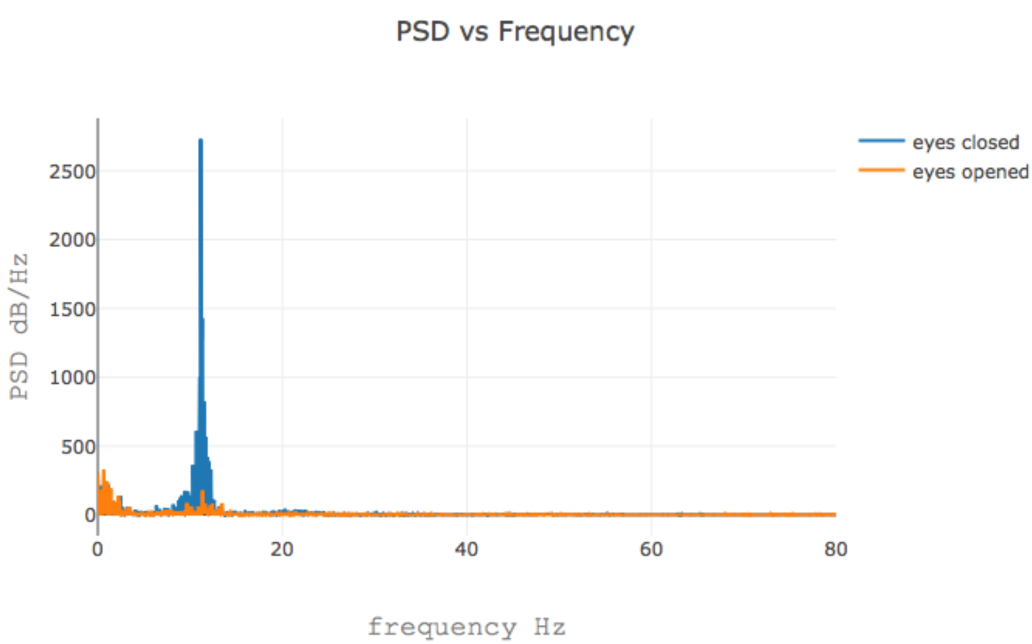
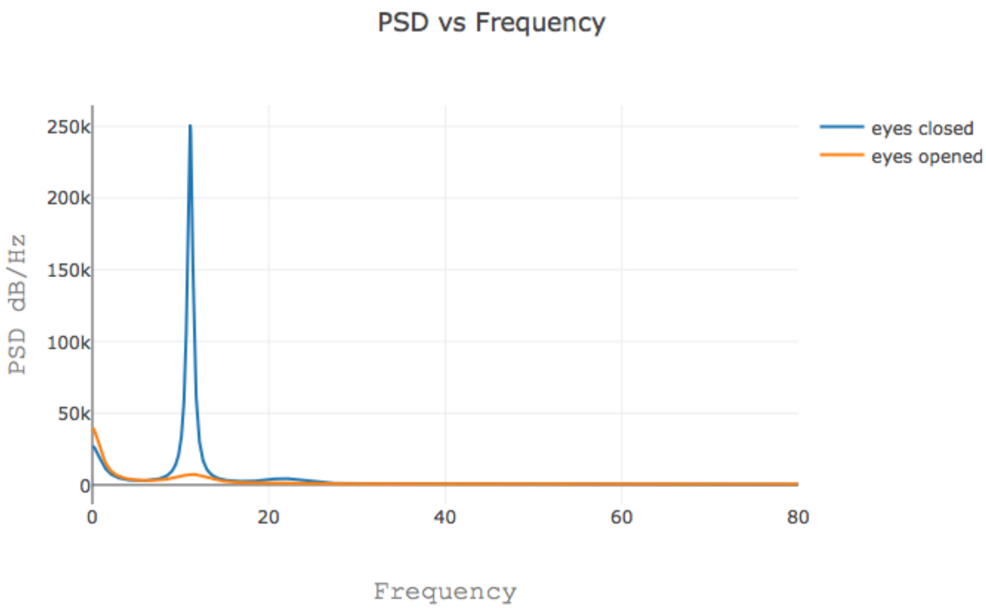


Figure 1.2: PSD with AR method for both datasets



2. Connectivity Graph

Figure 2.1: The graphical representations of the binary adjacency matrices (Density 1%)

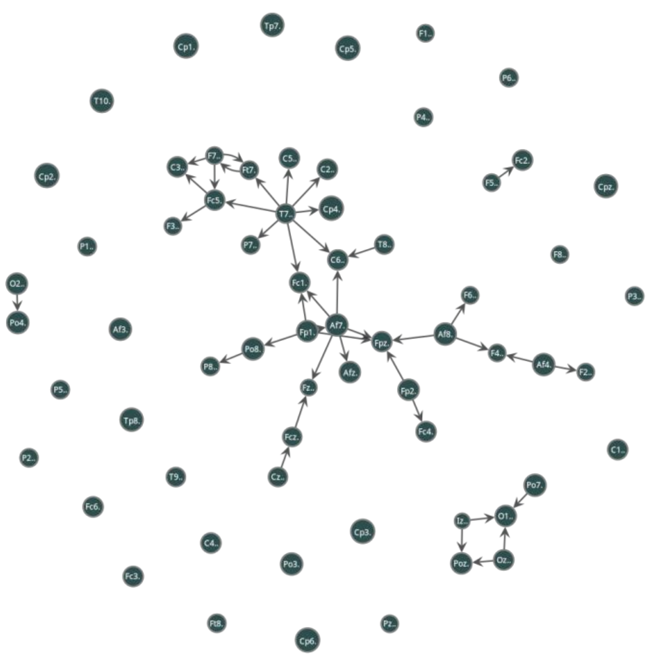


Figure 2.2: The graphical representations of the binary adjacency matrices (Density 5%)

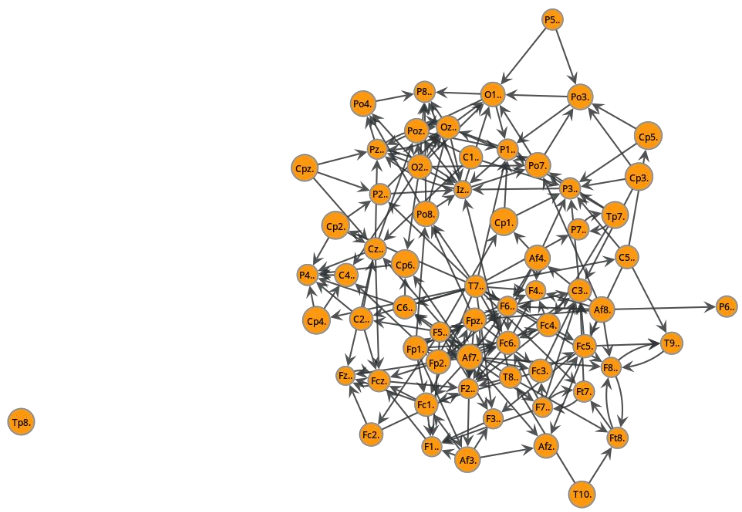


Figure 2.3: The graphical representations of the binary adjacency matrices (Density 10%)

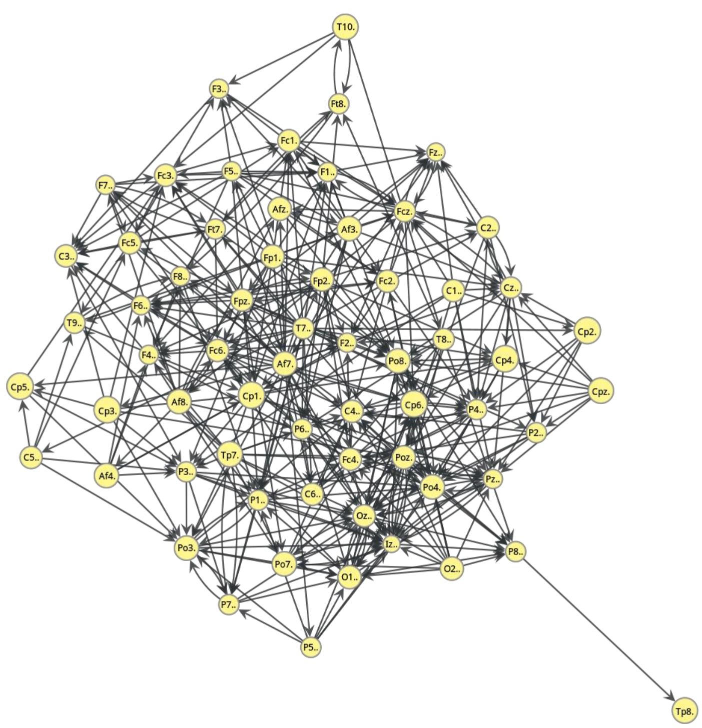


Figure 2.4: The graphical representations of the binary adjacency matrices (Density 20%)

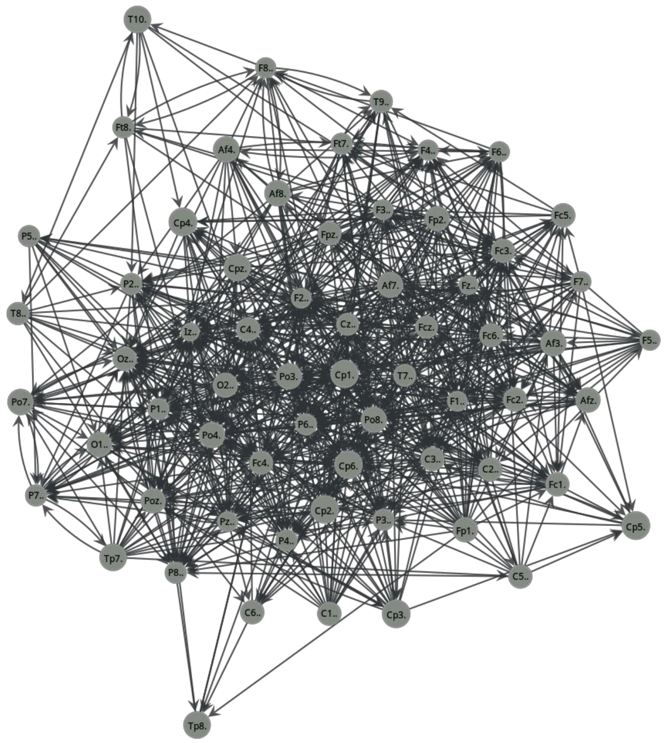


Figure 2.5: The graphical representations of the binary adjacency matrices (Density 30%)

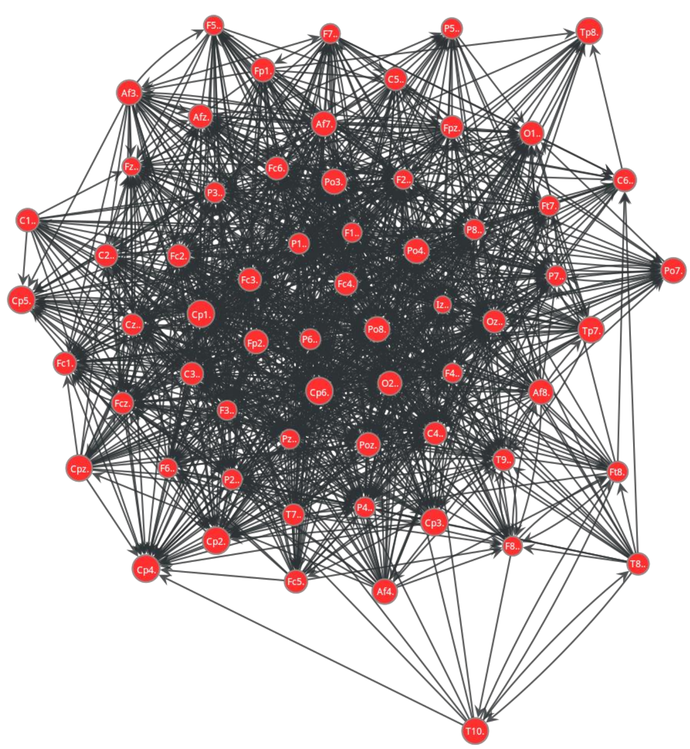


Figure 2.6: The graphical representations of the binary adjacency matrices (Density 50%)

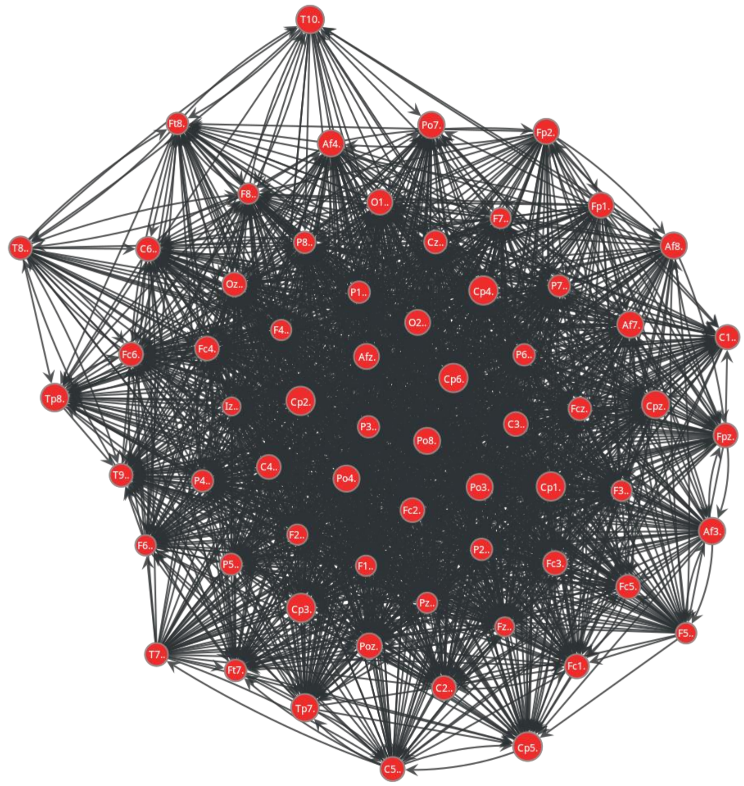


Figure 2.7: The topological representation of the networks with 5% density

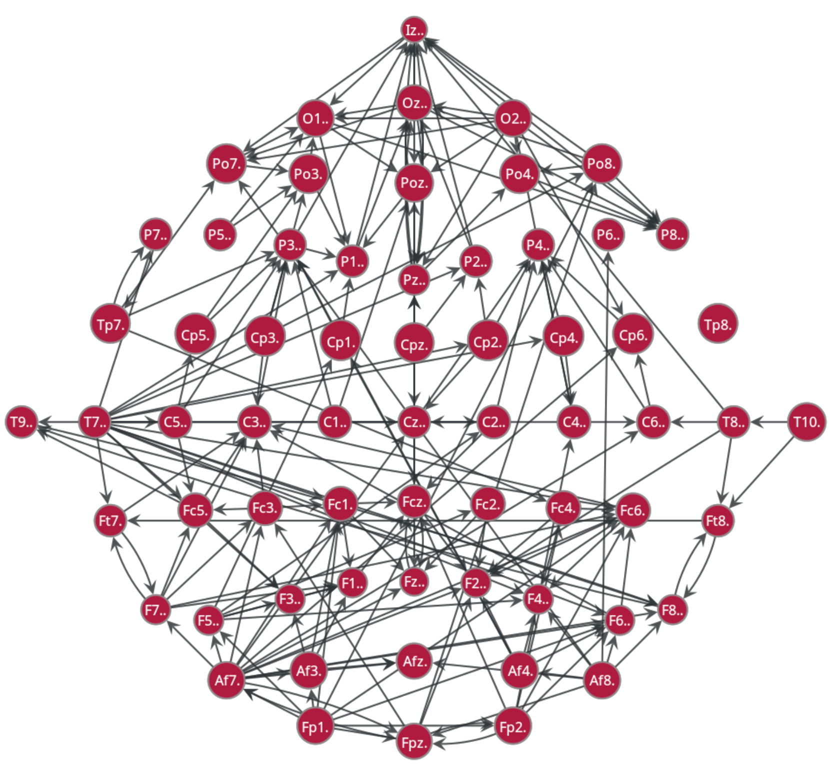
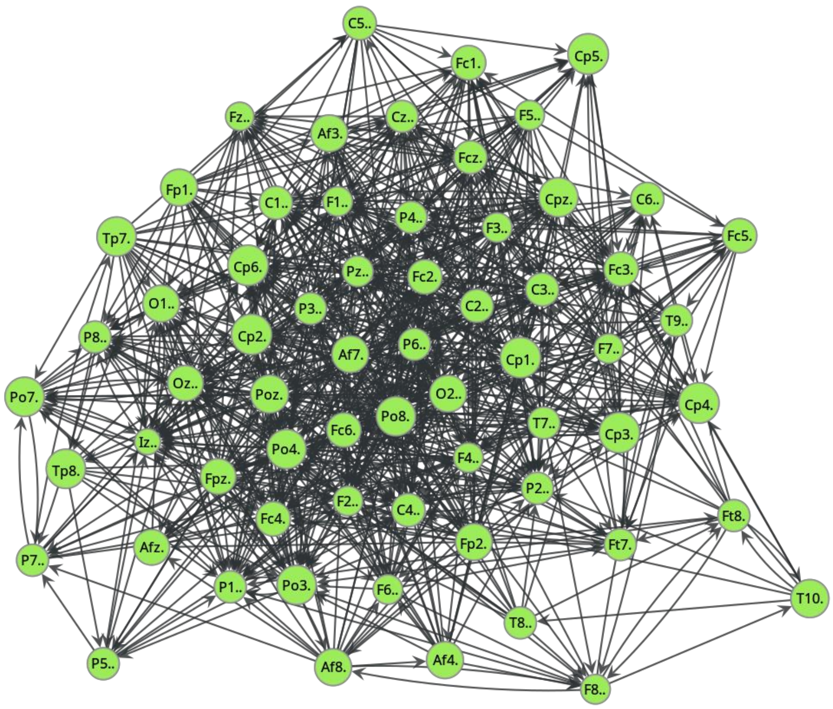


Figure 2.8: The delta waves connectivity matrices with 20% density



3. Graph Theory Indices

Table 3.1: List of the highest 10 channels for local indices

	Degree	**In Degree**	**Out Degree**
1	Po8.	Po8.	Af7.
2	Po4.	Po4.	T7..
3	Iz..	Iz..	Fp2.
4	Oz..	C4..	Fp1.
5	P6..	Cp6.	Cpz.
6	Cp1.	P6..	Af3.
7	C4..	Oz..	Cz..
8	Af7.	Cp1.	Af8.
9	Cp6.	F2..	Fpz.
10	Po3.	Po3.	C1..

Figure 3.1: The behaviour of global graph indices for the network densities (1%, 5%, 10%, 20%, 30%, 50%)

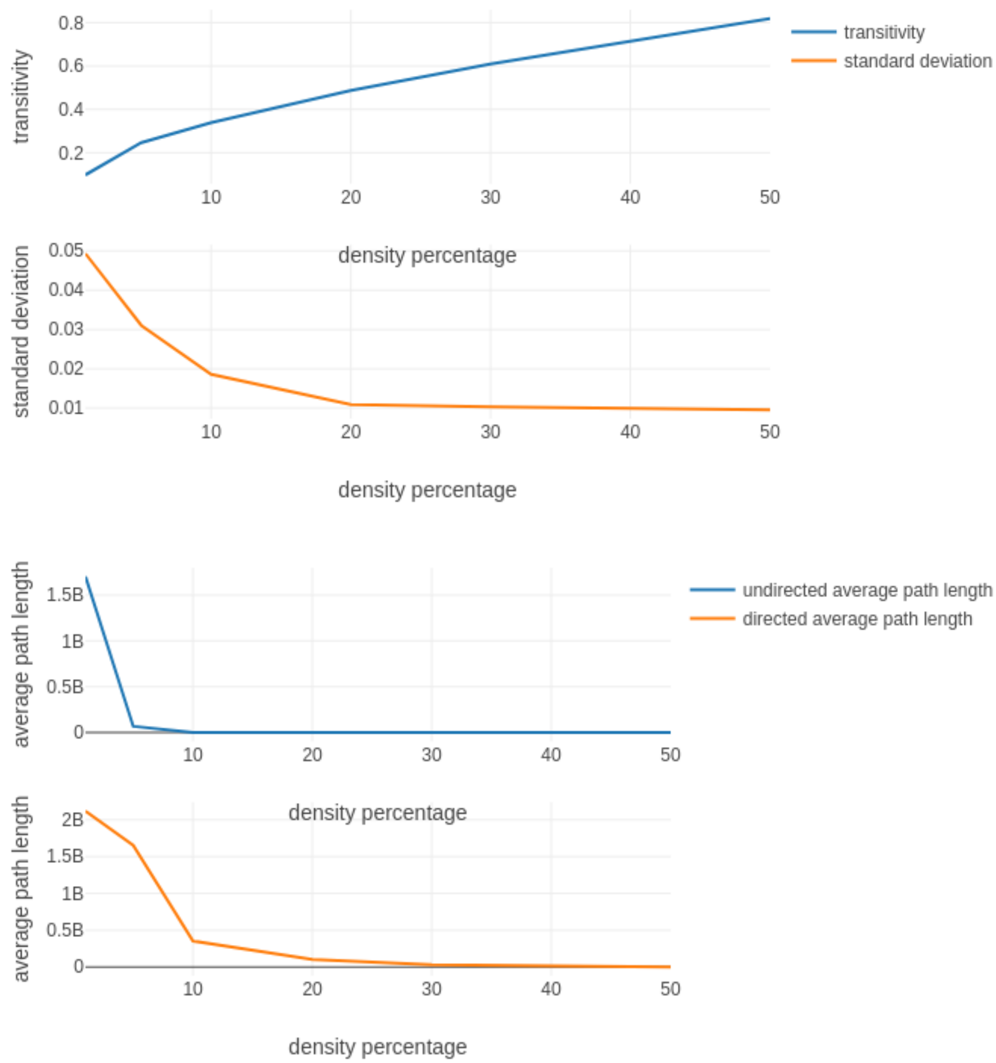
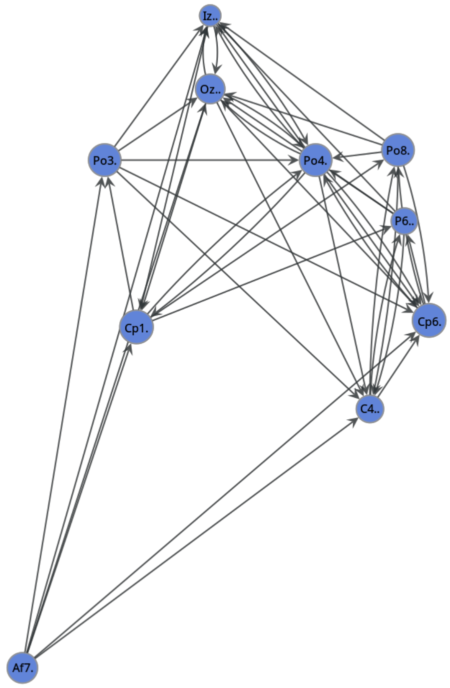
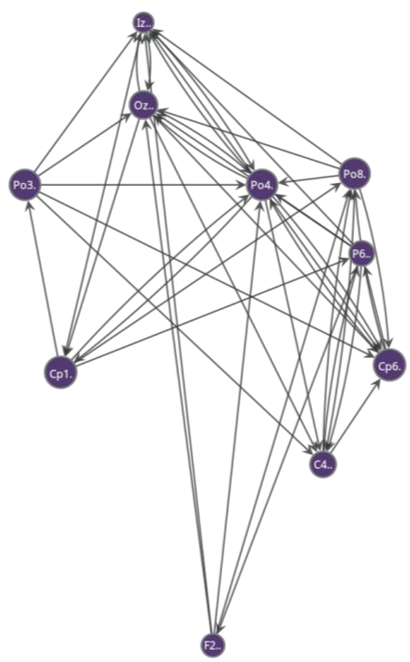


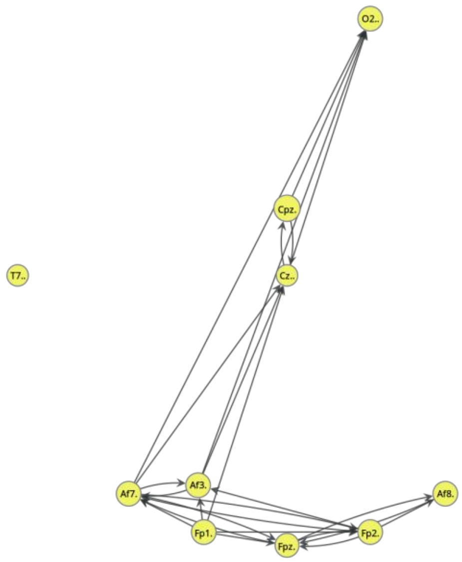
Figure 3.2: Topographical representation of local indices



DEGREE



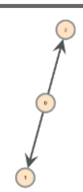
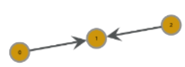
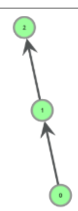
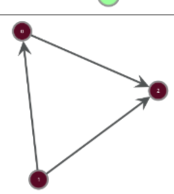
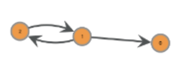
IN-DEGREE



OUT-DEGREE

4. **Motif Analysis**

Table 4.1: The motifs found for 3-node subgraphs and their z-scores

Motifs	Number of appear	Z-Scores
	1890	-6.863248291513048
	3376	-4.549343428734371
	2571	-3.047290642769208
	1725	-1.2871773348159827
	541	-0.22637518653727623

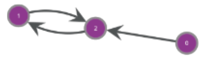
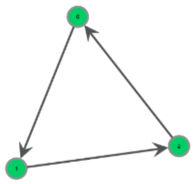
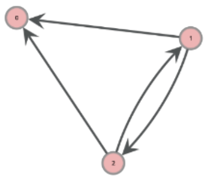
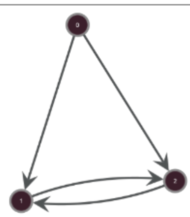
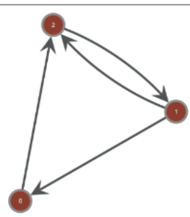
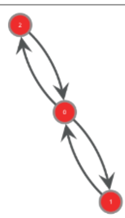
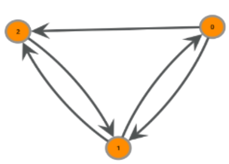
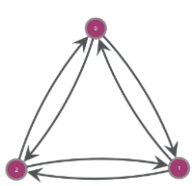
	1192	0.8291706351318426
	74	-4.674857482039854
	264	8.147845978655566
	397	2.7372709970498827
	179	-2.1822642386170745
	61	-1.5245465402106784
	147	5.716304151546676
	31	12.663737716796886

Figure 4.2: The topographical representation of the networks considering only the connections involved in A→B←C configuration

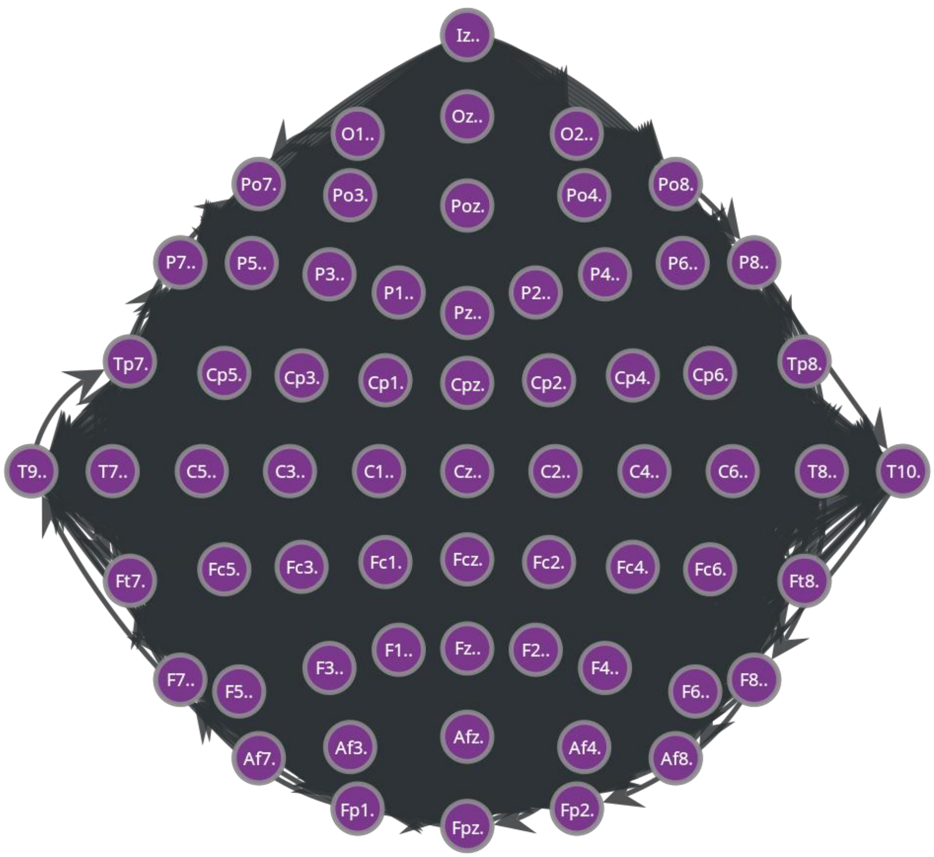
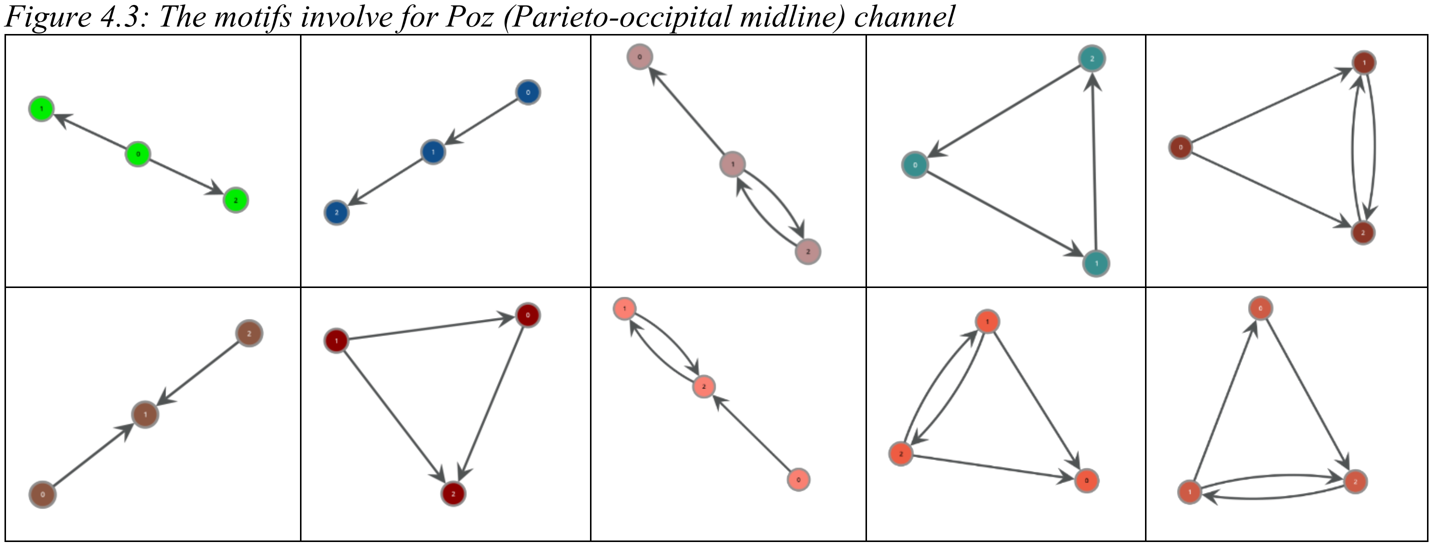
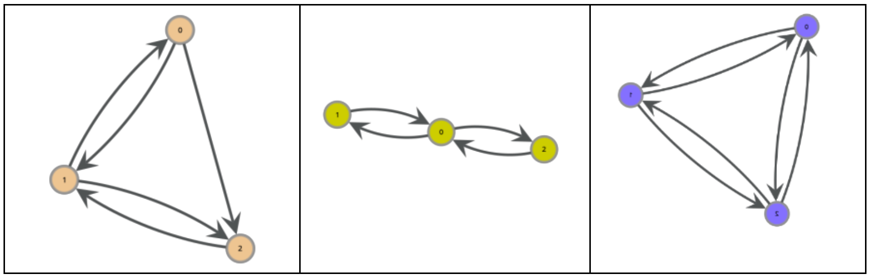


Figure 4.3: The motifs involve for Poz (Parieto-occipital midline) channel





5. Community Detection

List 5.1: The number and name of nodes for each Louvain cluster

Cluster	Size	Composition
1	30	'Fc5.', 'Fc3.', 'Fc1.', 'Fcz.', 'Fc2.', 'Fc6.', 'C5..', 'C3..', 'Cp5.', 'Fp1.', 'Fpz.', 'Fp2.', 'Af7.', 'Af3.', 'Afz.', 'Af4.', 'Af8.', 'F7..', 'F5..', 'F3..', 'F1..', 'Fz..', 'F2..', 'F4..', 'F6..', 'F8..', 'Ft7.', 'T7..', 'T9..', 'P6..'
2	19	'Fc4.', 'Cp3.', 'Cp1.', 'Tp7.', 'Tp8.', 'P7..', 'P5..', 'P3..', 'P1..', 'Pz..', 'P8..', 'Po7.', 'Po3.', 'Poz.', 'Po4.', 'O1..', 'Oz..', 'O2..', 'Iz..'
3	15	'C1..', 'Cz..', 'C2..', 'C4..', 'C6..', 'Cpz.', 'Cp2.', 'Cp4.', 'Cp6.', 'Ft8.', 'T8..', 'T10.', 'P2..', 'P4..', 'Po8.'

Figure 5.1: The graphical representation of Louvain clusters

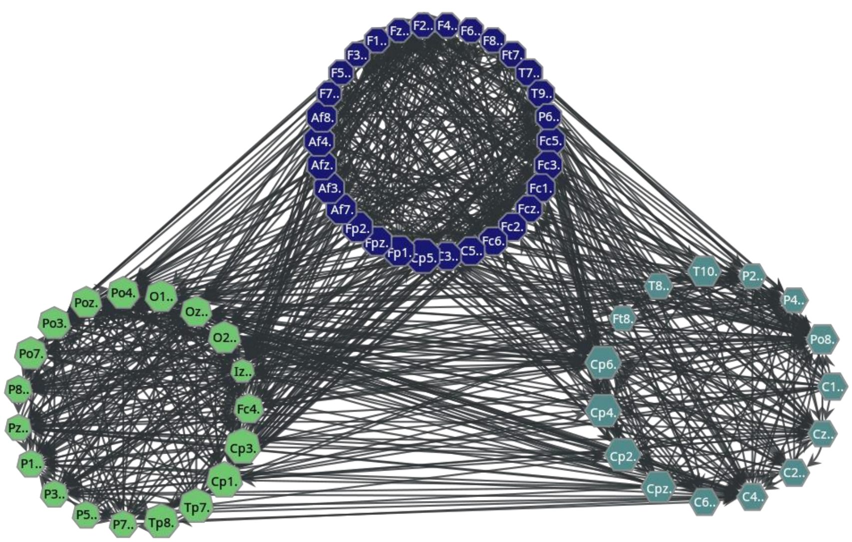


Figure 5.2: The graphical representation of the community structure in both rest conditions

Eyes-Closed

Eyes-Opened

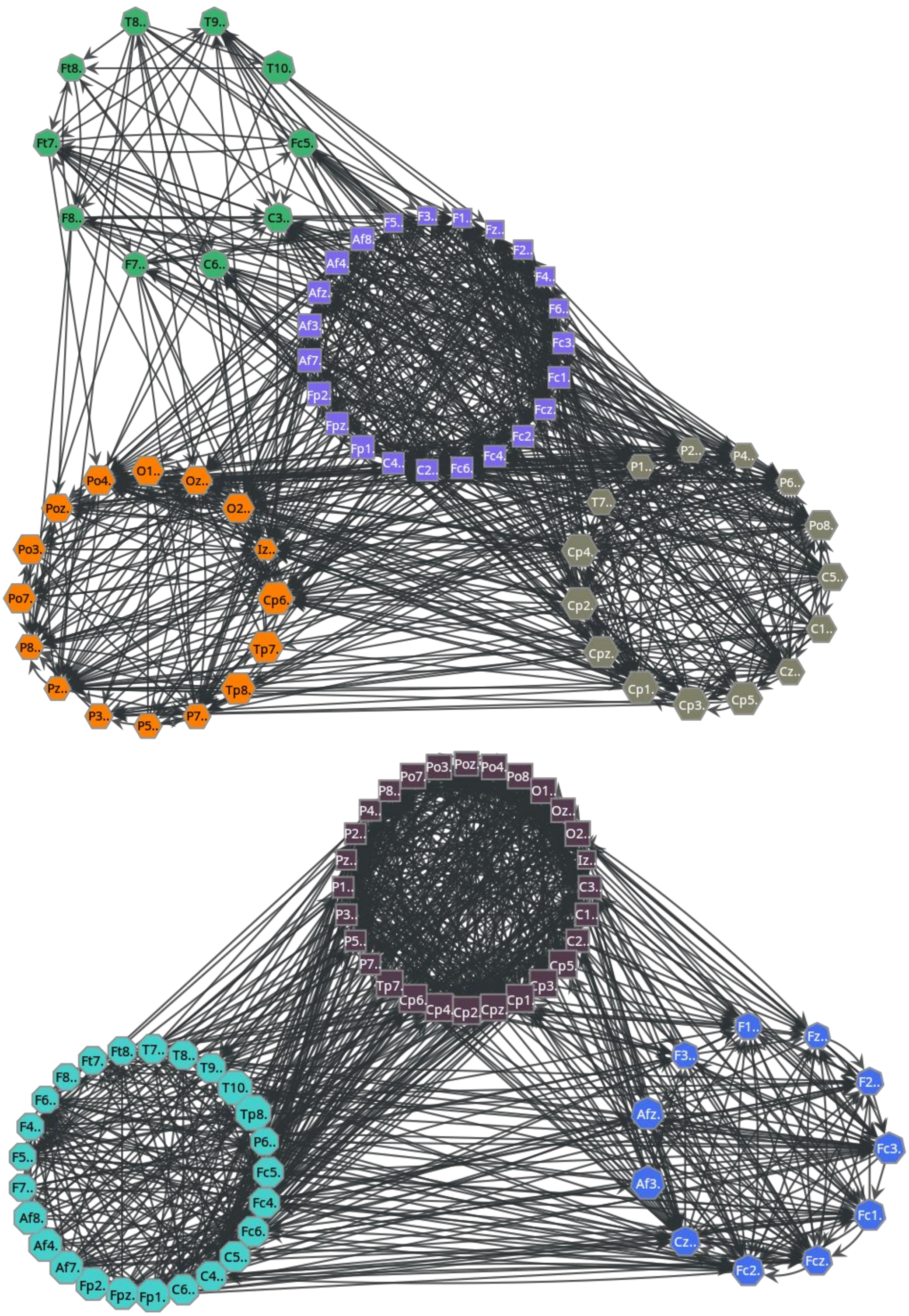
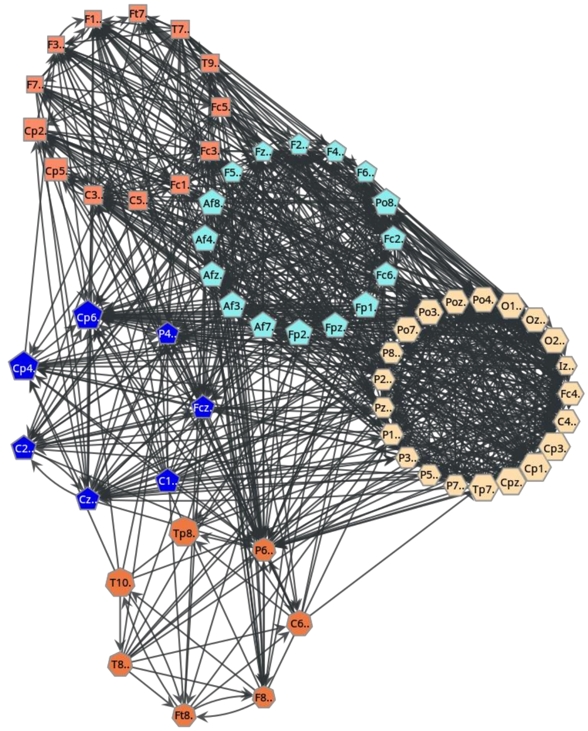
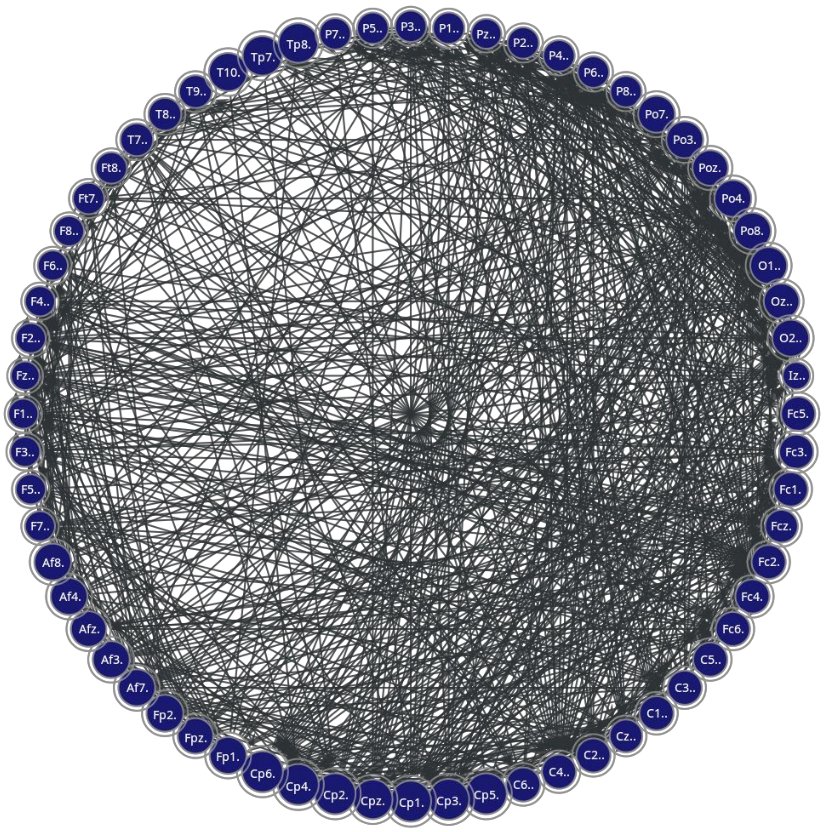


Figure 5.3: The community structure obtained from two different methods (modularity-based vs information theory-based approaches) (Spinglass Clustering Algoritm, Informap Clustering Algorithm, Edge Betweenness Clustering Algorithm)

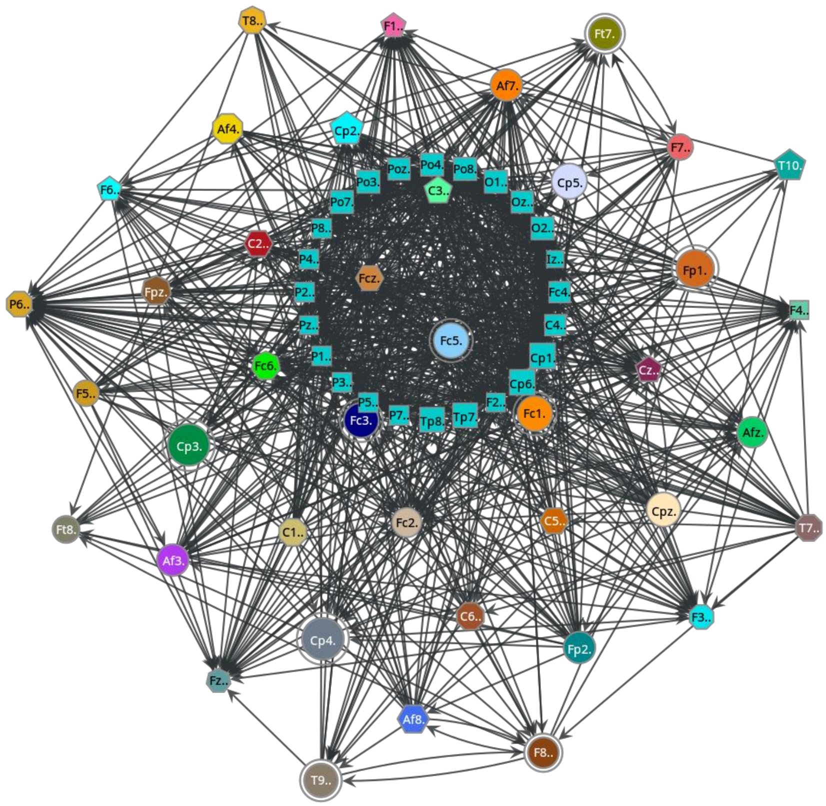


Spinglass Clustering Algorithm



Infomap Clustering Algorithm

Edge Betweenness Clustering Algorithm



See the output folder in the included archive file to see large versions of the graph outputs and further graph representations.