Springer Proceedings in Complexity

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Complex Networks XIV

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Editors
Andreia Sofia Teixeira
Faculty of Sciences
University of Lisbon
Lisbon, Portugal

José Fernando Mendes
Department of Physics
University of Aveiro
Aveiro, Portugal

Giuseppe Mangioni
Department of Electrical, Electronic
and Computer Engineering
University of Catania
Catania, Italy

Federico Botta
Department of Computer Science
University of Exeter
Exeter, UK

Ronaldo Menezes
Department of Computer Science
University of Exeter
Exeter, UK

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Contents

Brain's Dynamic Functional Organization with Simultaneous EEG-fMRI Networks

Francisca Ayres-Ribeiro[1,2,3](✉), Jonathan Wirsich[4], Rodolfo Abreu[5,6],
João Jorge[7,8], Andreia Sofia Teixeira[3], Alexandre P. Francisco[2],
and Patrícia Figueiredo[1]

[1] ISR-Lisboa and Department of Bioengineering, Instituto Superior Técnico,
Universidade de Lisboa, Lisboa, Portugal
`francisca.ayres.ribeiro@tecnico.ulisboa.pt`
[2] INESC-ID and Instituto Superior Técnico, Universidade de Lisboa,
Lisboa, Portugal
[3] LASIGE, Faculdade de Ciências, Universidade de Lisboa, Lisboa, Portugal
[4] EEG and Epilepsy Unit, Department of Clinical Neurosciences,
University of Geneva, Geneva, Switzerland
[5] Coimbra Institute for Biomedical Imaging and Translational Research (CIBIT),
Universidade de Coimbra, Coimbra, Portugal
[6] Institute for Nuclear Sciences Applied to Health (ICNAS),
Universidade de Coimbra, Coimbra, Portugal
[7] Laboratory for Functional and Metabolic Imaging,
École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland
[8] Swiss Center for Electronics and Microtechnology (CSEM), Systems Division,
Neuchâtel, Switzerland

Abstract. The brain's functional networks can be assessed using imaging techniques like functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). Recent studies have suggested a link between the dynamic functional connectivity (dFC) captured by these two modalities, but the exact relationship between their spatiotemporal organization is still unclear. Since these networks are spatially embedded, a question arises whether the topological features captured can be explained exclusively by the spatial constraints. We investigated the global structure of resting-state EEG and fMRI data, including a spatially informed null model and found that fMRI networks are more modular over time, in comparison to EEG, which captured a less clustered topology. This resulted in overall low similarity values. However, when investigating the community structure beyond spatial constraints, this similarity decreased. We show that even though EEG and fMRI functional connectomes are slightly linked, the two modalities essentially capture different information over time, with most but not all topology being explained by the underlying spatial embedding.

Keywords: EEG-fMRI · Connectomics · dFC · Community analysis

1 Introduction

Brain activity is believed to be organized into functional networks, reflecting the dynamic coupling between brain regions and the continuous exchange of infor-

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mation throughout the whole brain [19]. This coupling is known as functional connectivity. Characterizing the dynamic behaviour of these networks and their topology might be key to increase the understanding of the brain's complex activity, its spatiotemporal organization and, possibly, provide biomarkers for neurological and psychiatric diseases [9,29].

These functional networks can be defined using different imaging techniques like functional Magnetic Resonance Imaging (fMRI) and electroencephalography (EEG), that allow the characterization of time-varying activity in the whole brain. However, these techniques have distinct temporal and spatial resolution and are sensitive to different physiological changes associated with neuronal activity [21]. FMRI measures brain activity indirectly and is based on changes in the blood flow, consisting in a blood-oxygen-level-dependent (BOLD) signal. These changes, however, come slow and with a significant delay [28]. In contrast, EEG allows the direct measurement of transient brain electrical dipoles generated by neuronal activity [21] - with the use of scalp electrodes -, having high temporal precision. Even though both reveal the brain's dynamic behaviour, it is still not entirely known how the two are correlated, i.e., what is the relationship between the hemodynamic response and electric neuronal activity, and whether they capture the same information or not [24].

In recent years, several studies have analysed functional connectivity by combining simultaneously acquired EEG-fMRI recordings, in resting-state, with the objective of establishing a correlation or link between the two and also to take advantage of their complementarity [1,8,26,33,38]. Moreover, this type of analysis can provide richer characterization of the spatiotemporal organization of the brain activity. However, it is still missing a comparative analysis between these two modalities functional networks by investigating their topology over time. Such analysis can be done considering a graph theory framework that allows the brain functional systems to be modeled as complex networks [9]. In this context, the functional networks and their dynamic topology can be studied by analysing their global properties, such as their community structure [5,18], which looks at the organization of the network into modules reflecting coherent activity between different brain regions.

Furthermore, since these networks are spatially embedded, the question arises whether the topological features captured can be explained by impositions determined by the brain's underlying structure [31], in order to minimize energy costs of maintaining such connections [32], or if there is still some functional synchronization deviating from these proximity constraints. Some studies have explored this spatial effect in structural networks [31,32] and, more recently, in the community structure of functional networks, distinguishing the influence of short- and long-distance connections [16].

Therefore, this study intends to fill the gap in the present literature by performing a comparative network analysis with EEG and fMRI dynamic functional connectivity (dFC) data, on a global level, by means of a community analysis. For that, several established approaches were used, such as the Louvain algorithm [6] for the extraction of modules of coordinated activity, as well as its multiplex version [25], here applied to find partitions combining EEG and fMRI for the first time. Moreover, with hopes of exploring the influence of space in the topology, it was investigated the functional networks topology beyond these spatial constraints. Hence, a new approach was applied - a modified version of the Louvain algorithm [11], that includes a degree constrained spatial null model in the modularity definition.

2 Materials and Methods

2.1 Data Acquisition and Preprocessing

The dataset used in this work consists in simultaneous EEG-fMRI recordings acquired during rest in the scope of a previous project [20], using a 7T MRI scanner along with a 64-channel EEG system, involving 9 healthy subjects (4F, 22–26 yrs). The data preprocessing and brain segmentation was done according to [35]. Moreover, the BOLD timeseries were bandpass-filtered at 0.009–0.08 Hz, while the EEG signals were filtering at 0.3–70 Hz and segmented as a multiple of the Repetition Time (TR) of the fMRI acquisition (TR 1s).

2.2 Construction of Functional Networks

In order to analyse and compare the EEG and fMRI functional networks' topology, a graph representation was used. The nodes were set as 68 regions of interest defined by the Desikan(-Killiany) atlas [14], for both modalities. This parcellation was chosen considering the number of EEG channels and the optimal parcellation size to capture independent EEG signals according to [17]. Moreover, to guarantee this spatial alignment between modalities, the EEG data was subjected to a source reconstruction procedure, using the Tikhonov-regularized minimum norm [2], as described in [35].

The edges, on the other hand, were defined by functional connectivity matrices obtained for each time point (TR) using phase coherence for fMRI and imaginary part of coherency for EEG [27]. The first constitutes an instantaneous connectivity measure, based on phase synchronization, which was estimated using an adaptation of Cabral et al.'s implementation[1] [10], while the second was obtained using the Brainstorm function *bst_ cohn.m* (according to the Brainstorm 2018 implementation, 'icohere' measure[2]) as described in [35]. Furthermore, the imaginary part of coherency estimation was averaged for the 5 canonical frequency bands: delta δ (1–4 Hz), theta θ (4–8 Hz), alpha α (8–12 Hz), beta β (12–30 Hz), gamma γ (30–60 Hz).

To guarantee temporal equivalence between EEG and fMRI functional networks, a motion scrubbing step was taken, excluding, for both modalities, the time points where excessive motion was detected on the EEG data. In addition, as the BOLD time-series have an intrinsic delay with respect to the EEG data

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[1] https://github.com/juanitacabral/LEiDA.

[2] http://neuroimage.usc.edu/brainstorm.

due to the different nature of the two signals, this temporal shift was estimated and taken into account in aligning the two modalities' networks. This was done using a resting-state hemodynamic response function (HRF) deconvolution toolbox[3] [37], leading to 3–4seconds delay, depending on the subject.

Finally, to remove any spurious connectivity arising from noise or artifacts typical on this type of dataset, the functional networks were thresholded. The choice of an adequate proportional threshold was made using a data-driven percolation approach [7], i.e., by finding the percentage of edges necessary for each time point to avoid the collapse of the giant component, which guarantees the network's structure integrity. Expecting fluctuations in activity over time, resulting in more or less structured networks [5], it was selected the median value of said percentage of edges to be kept, resulting in the following threshold values: 11%, 7.5%, 6.6%, 7.0%, 6.1%, 7.0% and 6.5% for fMRI and EEG delta, theta, alpha, beta and gamma frequency bands, respectively.

2.3 Community Analysis

Community analysis was performed to characterize both EEG and fMRI functional networks on a macro-scale, to explore their potential similarity over time and also to investigate the possible influence of the proximity constraints in the modular structure captured.

Global Structure Statistical Significance. First, the global topology of these functional networks was analysed over time, in comparison to a rewiring null model, using three metrics: clustering coefficient, average path length and modularity (computed using NetworkX's functions). This allowed for the selection of time instances associated to functional networks whose global structure was statistically significant. In concrete, this statistical testing step was done for all metrics by generating 100 surrogates for each corresponding network and selecting the time instances with $p < 0.05$. Subsequently, the selection of time points was intersected with respect to the three metrics and for both modalities, considering each frequency band independently. This led to a unique set of time instances corresponding to statistically significant structured networks, for EEG and fMRI simultaneously. Moreover, since the topology observed may be due to spatial constraints, this analysis was performed again with respect to a degree constrained spatial null model [11], resulting in a second set of time points deviating from what was expected by the influence of space.

Louvain Algorithm. With the goal of identifying modules of synchronized activity, potentially similar between modalities, the community structure of these functional networks was analysed. This was done using the Louvain algorithm for the set of time points previously selected with respect to the rewiring null model. To explore the potential correlation between the two modalities regarding to the modular structure captured, the communities extracted were compared

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[3] https://github.com/compneuro-da/rsHRF.

for all selected time points, using the Normalized Mutual Information (NMI) metric, with values between 0 and 1.

Modified Louvain Algorithm. Considering the influence of the spatial constraints in the functional networks topology, it was desirable to check if some modular configuration present emerged from functional necessity and not just as a consequence of space proximity. With this objective, the community structure beyond these spatial constraints was investigated. This was done using the modified Louvain algorithm[4] [11], for all selected time points obtained previously with respect to the degree constrained spatial null model. Additionally, the communities extracted with and without the spatial influence were compared over time using the NMI metric. Finally, the EEG and fMRI communities extracted while regressing out the influence of space were compared for all time points, again using the NMI metric. This was done to distinguish and quantify the influence of the spatial constraints in the alignment of the two modalities and also to verify if there was still some similarity beyond that, reflecting the underlying synchronous activity captured by the two.

Multiplex Louvain Algorithm. To investigate if combining EEG and fMRI information would lead to new and improved results, a multilayer version of the Louvain algorithm [25] was used to extract communities common to both modalities (using i-graph's louvain package *find_partition* function), for all time points selected using the rewiring null model. This algorithm was applied as a multiplex case, i.e., where all the layers share the same node set, since there is a spatial equivalence between EEG and fMRI networks. With this, the improved modularity was estimated for the combined multiplex EEG-fMRI network, for each frequency band. In parallel, it was computed the modularity associated to these communities when isolating the two layers, to check if this optimization procedure led to different partitions than the ones obtained as described in Sect. 2.3). Additionally, these values were compared with the equivalent ones for the degree constrained spatial null model of both modalities.

3 Results and Discussion

3.1 Global Structure Statistical Significance

The global structure of EEG and fMRI functional networks was analysed, comparing global metrics values with a rewiring and a spatial null model. Fig. 1 illustrates the temporal variation of the modularity values (chosen between the three metrics computed as they showed similar behaviour) in comparison to each null model. Table 1 summarizes the percentage of time points deviating from these null models, averaging for all subjects.

From these results, it is noticeable an oscillation over time, for both modalities, which is not surprising considering that brain functional connectivity tends

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[4] https://github.com/Yquetzal/spaceCorrectedLouvainDC.

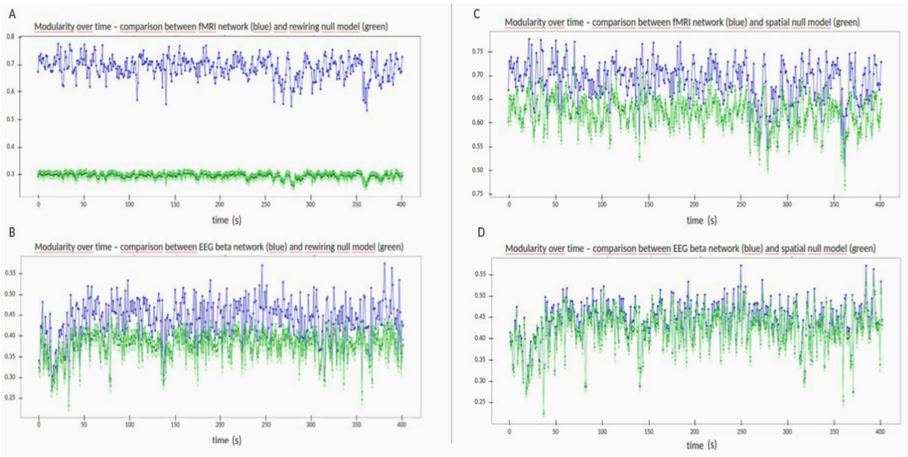

Fig. 1. Temporal variation of modularity (blue) for fMRI (A, C) and EEG beta (B, D), in comparison to the rewiring null model (green, A, B) and to the degree constrained spatial null model (C, D), for arbitrary subject. (Color figure online)

Table 1. Percentage of time points for which both modalities functional networks reflect a clustered structure in comparison to both rewiring and degree constrained spatial null model - for each frequency band, averaged for all subjects.

Percentage (%)	delta	theta	alpha	beta	gamma
Rewiring	60.6±6.5	56.8±5.3	59.1±5.3	59.5±7.1	65.3±11.4
Spatial	12.9±3.5	7.0±2.0	9.1±1.2	7.2±1.9	9.9±4.0

to oscillate between segregated and integrated states [4,5,15]. Besides this, there is a significant difference between fMRI and EEG functional networks, as the first one appears to possess a more clustered structure. This resulted in the selection of time points for both modalities being almost entirely constrained by the EEG. Furthermore, the degree constrained spatial null model presents a somewhat clustered topology, suggesting an important contribution of the spatial constraints for the structure observed. This is not surprising, since it has been reported a general tendency for the clusters, in functional networks, to be composed by regions that are near one another [3]. In particular, the spatial null model's global metrics appear to be almost identical to the EEG functional networks', suggesting that the topology detected for this modality might be a result of the spatial constraints imposed. This points to a higher susceptibility of the EEG's connectivity to these proximity constraints, which might result from its intrinsic lower spatial resolution as well as to its low signal-to-noise ratio (SNR). Nevertheless, there was still statistically significant structure being detected for some time points, specially for the delta frequency band, supposedly due to its ability to capture synchronized oscillations between brain regions at a longer distance than higher frequencies [13,22].

Table 2. Median modularity values associated to the communities extracted for fMRI and EEG frequency bands over time using the Louvain algorithm, averaged for all subjects. These values were computed considering each set of selected time points, using the rewiring null model, for every EEG-fMRI pair, for all frequency bands.

Modularity (Q)	delta	theta	alpha	beta	gamma
Q_{EEG}	0.455±0.004	0.466±0.002	0.447±0.003	0.465±0.010	0.428±0.015
Q_{fMRI}	0.700±0.004	0.700±0.005	0.697±0.005	0.699±0.004	0.699±0.015

3.2 Louvain Algorithm

The overall results of the community analysis with the Louvain algorithm, using the time points selected with the rewiring null model, are reported hereafter, for both EEG and fMRI functional networks. Table 2 summarizes the median modularity obtained for each modality, averaging for all subjects. Fig. 2 represents the range of modularity and NMI values obtained from the comparison of the community structure of both functional networks. Figure 3 shows the correlation over time between the two modalities, for arbitrary frequency band and subject.

In line with the previous observations, the fMRI functional networks show a more modular configuration than the EEG, which is also in accordance with previous dFC studies [33]. The less modular topology retrieved for the EEG might be due: i) to a worse quality of the data collected, as it is more affected by artifacts [30]; ii) to lack of sensibility of the technique to capture the topology of the underlying functional networks [23]; or iii) due to the difficulty in performing an accurate source reconstruction, specially for resting-state data [12].

Regarding the comparison between the two modalities' captured topology, it was found a low-to-moderate similarity, as it can be observed from the NMI results, which is in line with previous reports comparing EEG and fMRI static connectomes [35] for the same dataset. These results are also in accordance to studies examining dFC with both modalities, reporting a link between the two [1,8,13,34]. Nevertheless, this similarity is not particularly high, which might be due to the lack of modular topology for the EEG networks, as discussed. It might also be that this modality captures different interactions, leading to a more integrated topology instead of the segregated one found for the fMRI networks. In fact, it has been shown in [26] that EEG functional connectivity clusters into groups of brain regions differently than the fMRI functional connectivity and that these clusters appear to be extended in space, with a lower connectivity within modules than between them. Moreover, from the coloured NMI arrays, it is noticeable an oscillation in similarity over time, which was found to be specific to each frequency band. This not surprising considering past studies reporting a different contribution of each EEG frequency band to the BOLD connectivity dynamics [13,38], that varies across space [36], with a more local topology captured for higher frequency bands, such as the gamma band, and a more global connectivity for lower ones, like the delta band [22,34].

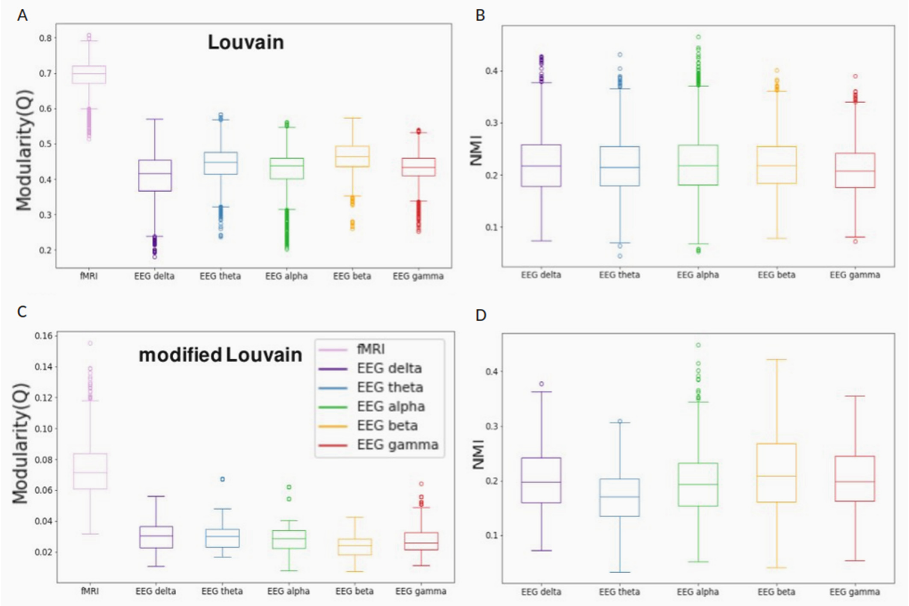

Fig. 2. Range of modularity for both EEG and fMRI networks (A, C), for all frequency bands, as well as range of NMI values (B, D) regarding the comparison of both modalities' communities obtained over time, with the Louvain algorithm (A, B) and with modified Louvain algorithm (C, D), for all subjects.

3.3 Modified Louvain Algorithm

To further analyse the spatiotemporal organization and contemplate its spatial embedding, the community analysis was performed with the modified Louvain algorithm, using the time points selected with the spatial null model. Table 3 summarizes the median modularity obtained for each modality, averaging for all subjects. Figure 2 shows the similarity between EEG and fMRI networks still arises beyond the influence of space, for all frequency bands, while Fig. 4 shows the comparison between the communities obtained over time with and without the spatial constraints, for arbitrary frequency band and subject.

Spatial constraints seem to explain the majority of the topology observed in EEG and fMRI functional networks, as observed in Sect. 3.1. Nevertheless, it was still possible to retrieve some significant community structure beyond these expectations, despite being associated to quite low modularity values (Table 3). When comparing the communities obtained with the regular and modified version of the Louvain algorithm, it was found an overall high similarity, but not a complete match. This points to the existence of relevant spatial patterns that arise out of functional necessity and not just as a consequence of space, even if not to a great extent. Furthermore, these similarity values are lower for the EEG, implying that, on top of not having a clear modular structure as the fMRI networks, the spatial effects have a higher impact in EEG networks' topology.

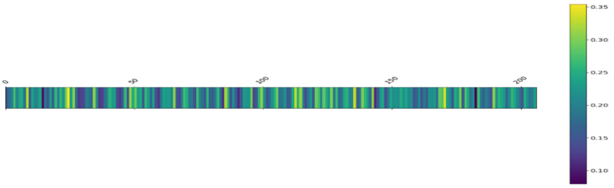

Fig. 3. NMI coloured array regarding the comparison of the communities obtained over time with the Louvain algorithm, between fMRI and EEG alpha band, for arbitrary subject. (Color figure online)

Table 3. Median modularity values associated to the communities extracted for fMRI and EEG frequency bands over time using the modified Louvain algorithm, averaged for all subjects. These values were computed considering each set of selected time points, using the degree constrained spatial null model, for every EEG-fMRI pair, for all frequency bands.

Modularity (Q)	delta	theta	alpha	beta	gamma
Q_{EEG}	0.036±0.003	0.034±0.002	0.034±0.001	0.032±0.002	0.033±0.002
Q_{fMRI}	0.072± 0.002	0.071± 0.005	0.073± 0.003	0.072± 0.004	0.071± 0.003

Comparing the two modalities community structure beyond the spatial constraints, an overall lower similarity was obtained, in comparison to the one presented in Sect. 3.2 (see Fig. 2). This suggests that part of the similarity between the two is guaranteed by the underlying spatial embedding. Even so, it was still retrieved a partially similar modular configuration beyond that, which supports a link between the EEG and fMRI dFC. However, it is important to take into consideration that this analysis was done only for the few time points deviating from the spatial null model (around 9%).

3.4 Multiplex Louvain Algorithm

Since it was not found a total match between the topology captured by two modalities on a global level, one can speculate that these complementary techniques capture different information regarding the underlying neuronal activity and its functional organization. The improved median modularity resulting from the multiplex Louvain algorithm analysis is reported in Table 4, as well as the individual values obtained for each modality.

One can immediately notice that the individual modularity values obtained are lower than the single-layer ones reported in Sect. 3.2. Meaning that the multilayer approach finds clusters common to both modalities that were not captured previously, as these partitions possessed too low modularity to be selected by the community detection procedure. This suggests that using EEG and fMRI together allows the capture of modules of synchronised activity that otherwise would not be found if looking at each functional network individually. These findings are in line with two previous studies that performed a joint-analysis of

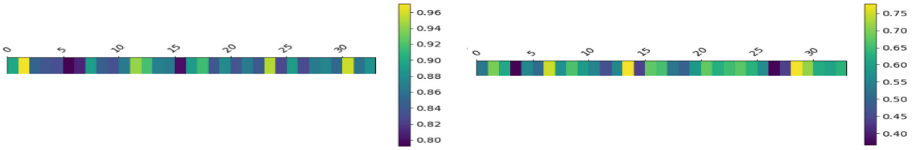

Fig. 4. NMI coloured arrays regarding the comparison of the communities obtained over time with and without the spatial constraints, between fMRI and EEG theta band, respectively, for arbitrary subject. (Color figure online)

Table 4. Median modularity (Q) values associated to the common communities extracted from both fMRI and EEG frequency bands over time using the multiplex Louvain algorithm, averaged for all subjects. These values were computed considering each set of selected time points, using the rewiring null model, for every EEG-fMRI pair, for all frequency bands.

Modularity (Q)	delta	theta	alpha	beta	gamma
$Q_{multiplex}$	0.747±0.004	0.752±0.004	0.748±0.005	0.755±0.005	0.751±0.005
Q_{EEG}	0.091±0.009	0.123±0.009	0.105±0.005	0.148±0.011	0.102±0.014
Q_{fMRI}	0619±0.011	0.591±0.010	0.603±0.009	0.571±0.009	0.615±0.007

these modalities, by means of a hybrid independent component analysis [33] and by building a multimodal graph, joining the EEG and fMRI nodes into a single network [38] to identify new connectivity structure. Furthermore, the modularity found was statistically significant in comparison to a multiplex spatial null model for most time points, implying that it is not just the spatial embedding that leads to the common partitions found.

4 Conclusions

From this work it is possible to draw several conclusions. First of all, the EEG and fMRI functional connectivity seem to capture different information on a global level. FMRI networks showed more modular configuration, consistent over time, while EEG ones captured a less clustered topology, with each frequency band capturing a slightly different structure oscillating across time. Moreover, when combining the two modalities, significant communities were extracted that would not be captured otherwise. Secondly, both functional networks' organization is mostly explained by the spatial embedding, giving preference to close connections. Nevertheless, relevant communities were still obtained beyond those constraints, for both fMRI and EEG, in particular for the delta, alpha and gamma bands. Finally, despite the differences reported, there is a similarity between the modalities' topology over time, again mostly explained by the spatial embedding. Nonetheless, when regressing out the influence of space, a small similarity was still retrieved for a set of time points. Therefore, it is possible to conclude that, even though fMRI and EEG functional connectomes are slightly linked, the two