Nodal equivalence relation for brain connectivity analysis

Relation d'équivalence par statistiques nodales pour l'analyse de la connectivité cérébrale

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Résumé – Dans les réseaux, l'importance des rôles des nœuds peut être cruciale dans différents domaines d'application. En neurosciences, par exemple, dans les réseaux de connectivité cérébrale fonctionnelle, l'organisation en hub révèle les changements dans différents états de conscience. Cependant, la comparaison de graphes, en tenant compte du rôle des sommets, reste largement inexplorée. Pour cela, nous définissons une relation d'équivalence sur les nœuds d'un graphe associée à une collection de statistiques nodales (une fonction sur l'ensemble de sommets) qui nous permet d'identifier les rôles des sommets. Ainsi, nous identifions la partition induite par cette relation avec le motif structurel du graphe et nous introduisons une nouvelle méthode pour comparer des graphes en fonction de la correspondance de ces motifs. Nous appliquons notre méthode à des données réelles ce qui révèle des scores de correspondance élevés chez la population de sujet sains et permet de différencier les patients comateux.

Abstract – In networks, the importance of node roles can be crucial in different application domains, such as social science or neurosciences. For instance, in functional brain connectivity networks, hub organization reveals the changes in different consciousness states. However, the comparison of multiple networks instances, by taking into account their respective node roles, remains largely unexplored. Inspired by the concept of node equivalent, we define an equivalence relation on graph nodes associated with any collection of nodal statistics (i.e. any functions on the node-set). This allows us to identify node roles with the equivalence classes of the partition induced by our relation. Thus, we identify such partition with the graph structural pattern and introduce a new method to compare graphs by the correspondence of their structural patterns. We apply our method to real data concerning human brain functional connectivity, which reveals high correspondence scores among the healthy population and differentiate at the nodal level comatose patients from healthy controls.

1 Introduction

In network science, the notion of node roles has proven to be important in various applications [11, 5]. This concept has been introduced in social science [4] with at least two different conceptions: nodal structural equivalence and nodal structural isomorphism. According to the former, nodes are equivalent if they share exactly the same neighbors. For the latter, nodes are equivalent if there exists an automorphism that maps the first node to the second and *vice versa*. In this work, we consider this latter conception and show how node roles can be used for human brain functional connectivity network comparison.

Functional networks provide a natural model to represent communication among brain regions in a given period of time. In this graph model, network units correspond to brain regions and edges indicate the presence of a pairwise connection between them. Individual connectivity networks may evolve depending on various factors, notably the presence of neurological disease. Being able to distinguish between normal versus pathological networks is highly valuable in neuroscience and clinical applications. However, there is no clear evidence of the best measure to be used to discriminate between networks representative of different brain states [14, 10].

In recent years, nodes organization has proven to be critical in functional connectivity analysis, for instance to differentiate various consciousness states [2, 7] or degenerative dementias [18]. Motivated by these reasons, we have lately proposed a new framework to compare graph instances based on a new similarity score that evaluates the node roles' correspondence [8]. With respect to other proposed graph similarities based on Graph Neural Networks, our method defines a new way to consider regional information without the permutation-invariance assumption. Hence, the graph similarity score takes into account regional node labeling when comparing networks through their local information (nodal-statistics). This is especially suitable for our neuroscience application, where brain regions are not exchangeable.

Here, we propose to use such a framework for the discrimination task of comatose patients from healthy controls. In this task, classical graph metrics analysis was found not to be significant in the discrimination, while dissimilarity in the nodal organization was determined through the definition of a hand-crafted disruption index [2].

2 Nodal-statistics-based equivalence relation

2.1 Single undirected unweighted graph

First, we propose a new way to determine node role in a single undirected unweighted graph. In particular, we define the graph structural pattern as the equivalence classes of an original equivalence relation. The traditional structural equivalence definition identifies two nodes as automorphically equivalent if it exists a node permutation preserving the adjacency matrix (an automorphism) which maps the first node to the second and *vice versa* [13].

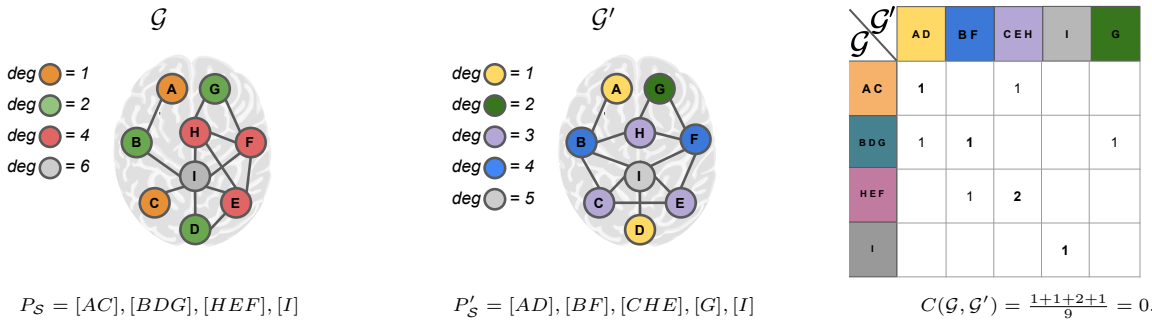

Figure 1 – Left: Visualization of the structural pattern associated with the Degree statistics in two graphs, $\mathcal{G}$ and $\mathcal{G}'$. Nodes with the same structural role have the same color. Right: computation of the correspondence structural pattern score. Adapted from Brain Design by A.S. Adije licensed under CC, retrieved from Creative Fabrica.

Here, we propose to relax the automorphic equivalence definition, by considering an equivalence relation associated with one or more nodal statistics, i.e. any map on the node set $s : \mathcal{V} \to s(\mathcal{V})$ which is a function of the adjacency matrix, i.e. node degree, clustering coefficient of a node, centrality measures, etc. We observe that for every pair of automorphically equivalent nodes $u, v \in \mathcal{V}$, any nodal statistics s is preserved. Therefore, we define the equivalence relation $\sim_s$, associated with the statistics s, on the nodes set $\mathcal{V}$ of a graph as follows:

$$v \sim_s u \iff s(u) = s(v). \tag{1}$$

When the nodal statistics have as $s(\mathcal{V})$ a dense and continuous subset of $\mathbb{R}$, the equivalence is defined up to a fixed positive small ϵ: $v \sim_s u \iff |s(u) - s(v)| \leq \epsilon$). As $\sim_s$ is an equivalence relation on $\mathcal{V}$, it is possible to find its induced partition P on $\mathcal{V}$,

$$P_s := \frac{\mathcal{V}}{\sim_s} = \{[a]_{l,\sim_s} \quad \forall l \in s(\mathcal{V})\}, \tag{2}$$

which we name the structural pattern of $\mathcal{G}$ associated with the statistics s, and whose elements are the classes of equivalence $[a]_l, \forall l \in s(\mathcal{V})$,

$$[a]_{l,\sim_s} = [a] = \{b \in \mathcal{V} | a \sim_s b \iff s(a) = s(b) = l\}. \tag{3}$$

Each equivalence class identifies a node role.
Subsequently, we extend the equivalence relation associated with one statistics to any statistics collection $\mathcal{S} = \{s_i\}_{i=1,..,n}$, requiring that:

$$a \sim_{\mathcal{S}} b \iff a \sim_{s_1} b, a \sim_{s_2} b, \ldots, a \sim_{s_n} b. \tag{4}$$

Again, we can determine $P_{\mathcal{S}} := \{[a]_{\sim_{\mathcal{S}}}\}$ the induced partition by $\sim_{\mathcal{S}}$ on $\mathcal{V}$ as the intersection of each class of the considered $\{s_i\}_{i=1,..,n}$. The possibility of combining more nodal statistics allows for refining the structural pattern of a graph at different granularities. A visualization of the partitions associated with the degree statistics is shown in Fig. 1.

2.2 Graph Collection

As it happens in our application, we consider graphs that have the same node-set. In this case, we propose to compare each graph pair by evaluating the correspondence between their structural patterns. Note that the node set constraint can be easily circumvented when two graphs do not share all the nodes, by including all nodes in the graph vertex sets and allowing the considered networks to be composed of more connected components. Indeed, each network can be seen as the union of one strongly-connected component with as many single disconnected vertices as needed.
Hence, we define the structural pattern comparison as follows. Let $\mathcal{G}, \mathcal{G}'$ be two graphs having same vertices $\mathcal{V}$ and let $\mathcal{S}$ be a statistics collection whose associated partitions are $P_{\mathcal{S}}, P'_{\mathcal{S}}$ on $\mathcal{G}, \mathcal{G}'$ respectively. Given the bijective mappings from $P_{\mathcal{S}}, P'_{\mathcal{S}}$ to an initial segment of the natural numbers as enumerations, and given $c(v_i), c'(v_i)$ be the enumeration of the classes of node v_i, the correspondence structural pattern score between $\mathcal{G}, \mathcal{G}'$ is defined as:

$$C(\mathcal{G}, \mathcal{G}') := \max_{\pi \in \Pi} \frac{1}{|\mathcal{V}|} \sum_{i=1}^{|\mathcal{V}|} \mathcal{X}\left(\pi\left(c(v_i)\right) = c'(v_i)\right) \tag{5}$$

where Π is the set of all coupling between the elements in $P_{\mathcal{S}}$ and the elements in $P'_{\mathcal{S}}$ and $\mathcal{X}$ is the indicator function.
A possible implementation of $C(\mathcal{G}, \mathcal{G}')$ in polynomial time is given by the Hungarian algorithm ([15]) for assignment problems with a complexity $\mathcal{O}(\max\{|P_{\mathcal{S}}|, |P'_{\mathcal{S}}|\}^3) \leq \mathcal{O}(|\mathcal{V}|^3)$.
The correspondence structural pattern score can be applied to evaluate graph similarity based on their structural pattern similarity. An example of the structural pattern computation is shown on the right of Fig. 1. $C(\mathcal{G}, \mathcal{G}')$ takes values in $]0, 1]$. If for every class in $P_{\mathcal{S}}$ there exists one class of $P'_{\mathcal{S}}$ having all and only its elements, then $P_{\mathcal{S}} = P'_{\mathcal{S}}$ and $C(\mathcal{G}, \mathcal{G}') = 1$. The opposite is also true: the same partitions determine a correspondence structural pattern score equal to 1.
For a more complete description of this theoretical framework, please refer to our previous work published in Physical Review E [8].

3 Application in human brain functional connectivity

3.1 Data

We apply our framework for the comparison of brain functional connectivity networks. We consider 200 networks built from resting-state functional magnetic resonance imaging (RS-fMRI) of healthy subjects (HC) available through Human Connectome Project (HCP) [22, 20] and a smaller dataset including 20 healthy subjects and 17 comatose patients (CO)

[2]. The brain is parcelled in ninety regions (AAL90 atlas) [21], corresponding to the vertices of our network. For each region, a unique time-series signal was determined by averaging the RS-fMRI time-series over all voxels, weighted by the gray matter proportion. Then, wavelet correlation [6] among regional time-series was estimated at the frequency scale just below 0.1Hz [17, 9, 19]. Finally, we threshold our correlation matrices to extract unweighted graphs at a specific sparsity ratio (the ratio of observed edges over the total number of possible edges) [12, 3]. Particularly, we select a sparsity of 0.1 which guarantees that each extracted network belongs to a small-world regime corresponding to global and local efficiencies comprised between the ones of Erdős-Rényi graphs and ones of the complete graphs [1, 16].

3.2 Experiments

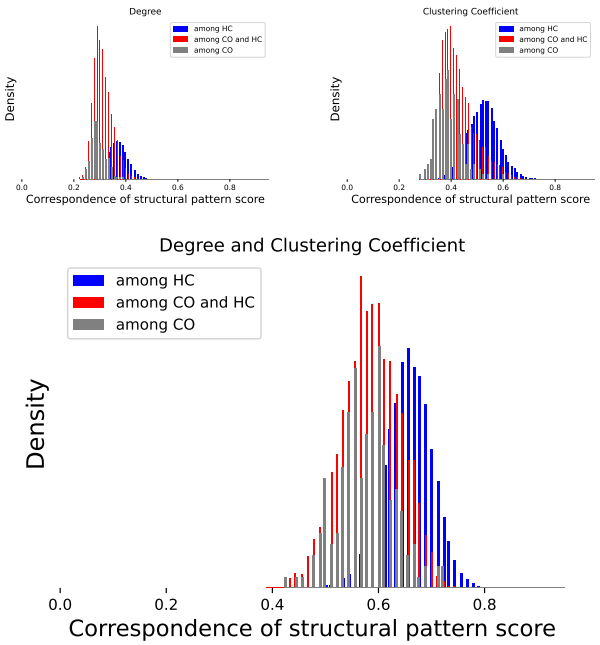

Figure 2 – Distribution of correspondence structural patterns score in the dataset

First, we determine the distribution of the correspondence structural pattern score associated with different nodal statistics in three different groups: a group of only healthy controls, a group including all the comatose and healthy controls, and a smaller group including all the comatose patients. Next, we train an SVM which employs the correspondence structural pattern score as a kernel function to discriminate comatose networks from healthy controls networks.

3.3 Results

In Figure 2, we report the distribution of the structural pattern scores in the three groups of interest. Results are shown for the equivalence relation associated with the degree and the clustering coefficient in combination or as single statistics. For the three equivalence relations, we can notice how the healthy controls and the comatose patients distributions are separated; the healthy controls group showing a higher correspondence. This separation was found statistically significant under the Z-test with a p-value < 0.001 for the three cases. Significant difference was also observed in the distributions of the entire dataset (CO+HC) and HC. No significant difference was found when comparing CO+HC and CO using the clustering coefficient associated structural pattern, while it was found in the other nodal statistics combinations. Indeed, the correspondence between comatose subjects is similar to the value obtained when they are pooled with HC, revealing a high inhomogeneity in the CO group when considering the clustering coefficient.

Moreover, we can appreciate the benefit of combining together more nodal statistics for the identification of finer structural patterns. Thus, structural pattern scores vary from 0.2 to 0.5 when considering only the degree and 0.4 to 0.8 when degree and clustering coefficient are used. At the same time, the significant difference between comatose and healthy controls is maintained.

Finally, in Figure 3, we plot the results of the discrimination between comatose patients and healthy controls when considering the structural pattern associated with degree and clustering coefficient. The discrimination reaches a perfect score in a 5-cross-validation procedure.

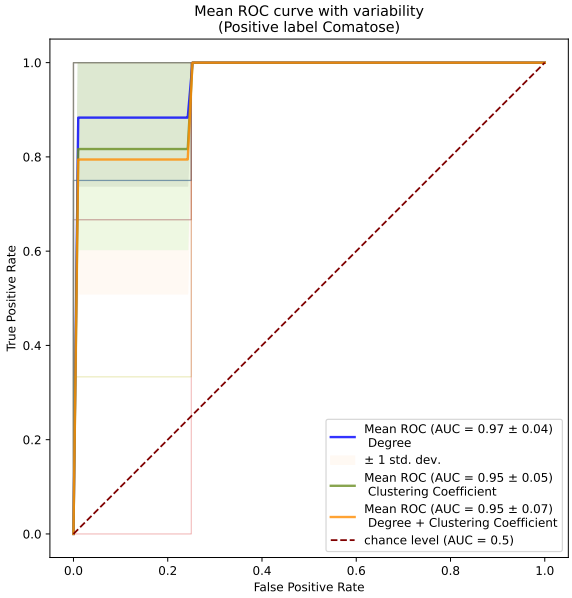

Figure 3 – Roc curve of discrimination between comatose network and healthy controls in a 5 cross-validation considering structural pattern associated with degree, clustering coefficient and their combinations.

4 Conclusion

To conclude, we have proposed a mathematical framework with the specific purpose of comparing networks by preserving the nodal structural organization. Our method defines a new nodal statistics-based equivalence relation that allows combining nodal statistics for single graph structural pattern detection

in an original way. This definition relaxes the automorphically equivalence definition but can retrieve it when considering an infinity set of nodal statistics.
In this work, we apply our developed tools for human brain functional connectivity networks. We report high correspondence scores among networks of healthy controls, validating the existence of a nodal organization signature in healthy subjects. Moreover, we reach perfect discrimination scores between comatose patients and healthy controls. These results not only validate that our proposed structural pattern comparison can capture the nodal structural organization but is also highly valuable in this specific application where no significant difference was obtained in a classical metric analysis framework.

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