# Graph matching of structural and functional brain networks

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# GRAPH MATCHING OF STRUCTURAL AND FUNCTIONAL BRAIN NETWORKS

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## ABSTRACT

By subdividing the cortex into regions according to a given atlas, we assume that all the regions match across different subjects. However, because of inter-subject variability, it may not be possible to produce a single brain atlas for all subjects. Previous works have proposed to use structural connectomes constructed from diffusion magnetic resonance imaging tractography to align brain regions across a group of subjects, leading to an improved similarity of connectomes. In this work, we propose to simultaneously exploit structural and functional information in the alignment process. This allows us to explore multiple perspective of brain networks. Our results show the permutations induced by one type of connectivity (structural, functional) are not always supported by the other connectivity network, but when considering combined alignment, it is possible to find permutations of regions which are supported by both connectome modalities, leading to an increased similarity of functional and structural connectivity across subjects.

***Index Terms*—** Brain network, Brain connectivity, Structure-Function, Graph matching

## 1. INTRODUCTION

Due to the large number of neurons in the brain [1], detecting all of their individual activation patterns responsible for human behavior is technically impossible. A reasonable approach consists in subdividing the gray matter surface into homogeneous neuronal areas [2]. The regions and their relationships can be represented as a graph, with the regions being the nodes and the connectivity between them being the edges [3, 4, 5]. The connectivity, corresponding to the edges of the graph, is usually represented as a square matrix called a connectome [3], of dimensions $N \times N$, with $N$ being the number of brain regions. In our case, we consider symmetric connectome matrices. It is generally assumed that the regions of connectomes correspond across subjects, meaning regions with the same label are expected to have the same structural and functional roles in the brain network. However, spatial organization of both cortex and white matter is shaped by environmental and genetic factors [6]. This leads to spatial neuronal inter-subject variability and consequently in structural and functional variability. As a result, it is challenging to produce a single brain atlas for all subjects [7]. The inter-subject variability can be observed during neurosurgery, where patients undergo highly invasive awake-surgery with electrical cortical stimulation to precisely localize given functional areas [8]. The problem of producing a single brain atlas is exacerbated for atlases with very small regions, as the spatial variability across subjects may be larger than the region size [9]. In particular, it is problematic when we want to carry out group-level analysis or modeling of brain networks, because a particular label of the chosen atlas may not represent the same neuronal structure across subjects [10], therefore limiting the specificity of the results. A previous approach used connectivity fingerprint to find a matching of regions [11]. Another one [12] proposes to increase the similarity between graphs of structural connectivity across subjects, computed from diffusion magnetic resonance imaging (dMRI) tractography, by allowing permutations of regions (the nodes of the graph). Two subject's brain atlas can be aligned by selecting the connectome of a subject as the reference to align the other subject's connectome. A matching of the regions across subjects is found by maximizing the graph similarity, a process known as graph alignment [13]. Graph alignment was shown to improve the inter-subject similarity, as it captures the inter-subject variability of connectivity in insect brains [14]. It was observed that brain function connectivity often differs spatially across subjects [15], but the previous approach has only been tested using structural connectomes (SCs) and never on functional connectomes (FCs) derived from resting-state functional MRI (rs-fMRI). In this work, we present the results of graph matching using both structural and functional networks. More specifically, we investigate whether it is possible to find permutations that are consistent in structural and functional graphs, resulting in an improvement of similarity for both SCs and FCs across subjects.

## 2. MATERIALS AND METHODS

### 2.1. Network alignment, FAQ algorithm

As mentioned previously, the regions of an atlas may not be mapped coherently from one subject to another. To find the

mismatched regions, we can compare the connectivity of regions of the atlas to the rest of the cortex, i.e. one row of the symmetric structural connectome, across subjects. We will then permute the labels of the regions if the permutation increases the similarity of the region connectivity with respect to the reference graph. More precisely, for a given subject, a region labeled $l_a$ is permuted with a region labeled $l_b$ if the permuted connectome is more similar to the connectome of reference. Finding the optimal permutation, i.e. finding the permutation matrix that maximizes the similarity between two graphs is formulated mathematically as:

$$\underset{P \in \mathscr{P}}{\text{minimize}} \quad \|PCP^T - C^{\text{ref}}\|_{\mathcal{F}}^2 \,, \tag{1}$$

where $P$ is a permutation matrix belonging to the permutation group $\mathscr{P} = \{P \in \{0,1\}^{n \times n} : P^T\mathbf{1} = P\mathbf{1} = \mathbf{1}\}$ and induces a permutation of rows and columns of the connectome $C$ to align it with the reference connectome $C^{ref}$. The similariry of the connectomes is based on the Frobenius norm $\|.\|_{\mathcal{F}}$. Unfortunately, solving this problem is NP-hard. The Fast Approximate Quadratic Assignment Problem (FAQ) algorithm [16] tackles this difficulty by solving a relaxed version of the above optimization problem: $P$ is allowed to be in the set of bistochastic matrices instead of just the set of permutation matrices to enable optimization by gradient descent. The obtained bistochastic matrix is then projected onto the set of permutation matrices [17], yielding an approximate solution to Eq. (1). The gradient descent is initialized as the bistochastic projection of the adjacency matrix of the spatially adjacent regions of the atlas, as it was shown to be the best choice for initializing the algorithm [12] by favoring local permutations.

To combine the information of two brain networks coming from different modalities, we modified the FAQ algorithm such that it solves the optimization problem

$$\begin{aligned}\underset{P \in \mathscr{P}}{\text{minimize}}\ \alpha \, \|PC_AP^T - C_A^{\text{ref}}\|_{\mathcal{F}}^2 \\ + \ (1-\alpha) \, \|PC_BP^T - C_B^{\text{ref}}\|_{\mathcal{F}}^2\end{aligned} \tag{2}$$

with $C_A$ and $C_B$ being the symmetric connectomes of modality A and B, and $C_A^{\text{ref}}$ and $C_B^{\text{ref}}$ the corresponding reference connectomes. The same permutation matrix $P$ is applied to both connectomes. The weight term $\alpha$ is used to favor one modality over the other. Indeed, if one modality is more noisy than the other, we may disfavor it with respect to the less noisy one. Specific cases are $\alpha = 1$, which corresponds to an alignment with modality A only and $\alpha = 0$ for an alignment considering only modality B. Both are equivalent to the original FAQ algorithm of Eq. (1) for $C_A$ or $C_B$ respectively. We kept the same initialisation depicted above as a starting point.

In the work of [12], the FAQ algorithm is applied on structural connectomes, and shows significant alignment of structural networks. In our work, $C_A$ will correspond to SC and $C_B$ to FC. The connectomes of references $C_A^{\text{ref}}$ and $C_B^{\text{ref}}$ are the Fréchet means of the SCs and FCs of the cohort. Using Frobenius distance, the Fréchet mean corresponds to the connectome that minimizes the sum of the variance to all the other connectomes [18].

Note that the network alignment is carried out on the left and right hemisphere of the brain independently. Otherwise the algorithm would be very likely to permute regions across hemispheres because of relative symmetry of the brain, which is undesirable.

### 2.2. MRI acquisition and preprocessing, HCP data

In this work, we consider 1050 subjects of the HCP diffusion MRI and resting-state MRI young-adults dataset. For each subject, 288 dMRI volumes have been acquired: 18 volumes at b-value 0 s/mm$^2$, 90 volumes at b-values 1000 s/mm$^2$, 90 volumes at b-values 2000 s/mm$^2$, and 90 volumes at b-values 3000 s/mm$^2$. Each volume is composed of 145 × 174 × 145 voxels with a resolution of 1.25 × 1.25 × 1.25 mm$^3$. Diffusion data has been preprocessed according to the Minimal Preprocessing HCP pipeline [19], including EPI distortion and eddy-current correction. Functional data are originated from FIX-Denoised (Extended) rs-fMRI dataset of HCP [20]. The rs-fMRI data is rescaled in MNI space.

### 2.3. Data processing

#### *2.3.1. fMRI*

To filter out irrelevant parts of the BOLD signal, we used a Butterworth bandpass filter of order 8 and with cut-off frequencies of 0.06 and 0.125 Hz [21]. The processed BOLD signals are averaged over the regions of a multimodal atlas, and their respective temporal mean of every region averaged signal is removed. The correlation matrix is computed on processed BOLD signals using Pearson's coefficient. Regarding the atlas, we chose a multimodal atlas [22] with the FreeSurfer surface of subjects registered in the MNI space. The subcortical region of the hippocampus has been removed, leading to 179 regions per hemisphere. Because FCs are correlation matrices, there are by definition symmetric.

#### *2.3.2. dMRI*

We used the TractoFlow [23] pipeline to reconstruct tractograms from preprocessed dMRI. Spherical harmonics of order 10 maximum are fitted to the preprocessed dMRI data. Then, 120 seeds per voxels at the intersection of the gray matter and white matter are positioned as starting points of streamlines. The streamlines are reconstructed using a step size for Particle Filter Tracking (PFT) of 0.3125 mm. Only valid streamlines with a length ranging from 20 to 300 mm are kept. The other parameters of TractoFlow script are set to their default values. The structural connectome is constructed

by counting the number of streamlines included in the tractogram that connects the two regions of the given matrix entry [4]. A local search is performed to find the closest cortical region to the endpoints of the streamline, with a upper bound distance of 5.0 mm. The same atlas as for the FC is used, but with the FreeSurfer surface of subjects in the original space. The connectomes are symmetrized by adding their transpose and dividing by 2. Then they are normalized such that they become dimensionless and have the same Frobenius norm as the FC of the same subject.

## 3. RESULTS AND DISCUSSION

Our implementation of the FAQ algorithm, sometimes, does not find a permutation matrix that increases the connectome similarity with respect to the reference connectomes. It then returns the identity matrix, meaning no permutations. Moreover, the permutation matrix may increase the similarity of one connectome modality, but not the similarity of the other. A relevant criterion to evaluate the performance of our algorithm is, therefore, the percentage of subjects in the dataset where the connectome similarity strictly increased with respect to the respective references for both structural and functional modality.

### 3.1. Hyperparameter alpha

To empirically find the $\alpha$ value, we track the percentage of subjects whose connectomes are more similar to the Frechet mean connectomes after the permutation, for the SCs and FCs (See Fig. 1).

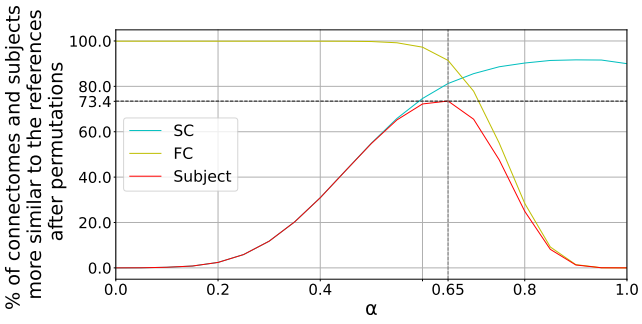



**Fig. 1**. The percentage of subjects where the connectome similarity increased after graph matching, depending on the hyperparameter $\alpha$. The percentage of SC (blue curve) increases, whereas the percentage of FC (yellow curve) decreases with $\alpha$ because the alignment on SCs is favored. The red curve represents the percentage of subjects who have both their SC and FC more similar to the respective references with the alignment. The highest percentage of subjects is reached for $\alpha = 0.65$, and is equal to 73.4%.

The percentage of subjects that have an increased similarity after graph matching depends on the value of the hyperparameter $\alpha$ (See Fig. 1). Recall that the particular cases where $\alpha = 0$ and $\alpha = 1$ correspond to aligning the FCs and SCs independently. We observe that matching networks using only one modality ($\alpha$ = 0 or 1) does not improve the connectome similarity of the other modality. However, there is a trade-off for $\alpha = 0.65$, where we improve the structural and functional similarity in more than 73% of the subjects. This result shows that it is possible to find a permutation matrix that strictly increases the similarity for both structural and functional brain networks for a majority of subjects.

### 3.2. Comparison of alignment on SC, on FC, and on combined SC-FC

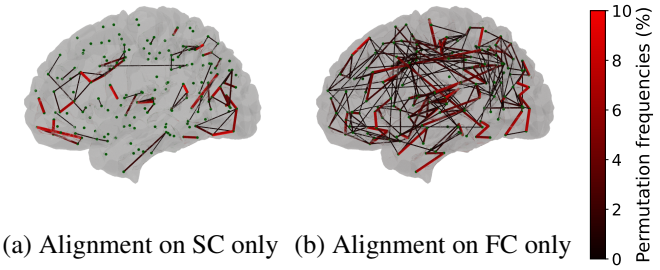
We take a particular look at the specific cases where we align only on SC ($\alpha = 1$) or only on FC ($\alpha = 0$). Indeed, those two specific cases give very different results on the set of permutations, which explains why alignment with SC does not align properly the FCs and conversely. On average, over the 1050 subjects, 18.5% of labels have been permuted with the alignment on SC only ($\alpha = 1$) and 61.3% of labels have been permuted with the alignment on FC only ($\alpha = 0$), but only 15.6% of the labels are permuted for a combined alignment with $\alpha = 0.65$. Moreover, 57.7% of the permutations (projection of one label onto another) from the alignment with $\alpha = 0.65$ are either given by the alignment of SC ($\alpha = 1$) or by the alignment of FC ($\alpha = 0$). More precisely, 42.7% of the permutations for the combined alignment are shared with the alignment on SC and only 16.3% are shared with the alignment on FC. The numbers of permutations given by the 3 approaches (3 values of $\alpha$) averaged per subject are illustrated in Fig.2d.

The permutations can be illustrated as edges on the brain cortex networks, linking two regions of the atlas when they are permuted. Those edges are weighted by their frequencies of permutations in the dataset of 1050 subjects (See Fig.2a-c).

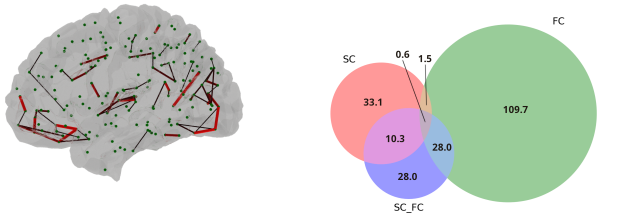
The alignments on SC only (Fig.2a) or FC only (Fig.2b) induce many permutations throughout the cortical surface. Most of them are discarded in the combined alignment (Fig.2c). We observe that the combined alignment shares more permutations with the SC alignment than with the FC alignment (Fig.2b,d). The edges are mostly located in the frontal and in the occipital lobes.

The alignment on FC gives more permutations than the alignment on SC because FCs represent statistical correlation of BOLD signals which contains a non-negligible level noise, leading to quite similar connectivity profiles across the regions, that can be permuted without a great change in the FC.

One important feature of the permutations to notice is that they are almost all short-range permutations, which we explicitly favored with the initialization based on the adjacency matrix. This is consistent with the fact that it is very unlikely




(a) Alignment on SC only (b) Alignment on FC only




(c) Alignment on SC and FC (d) Relationship of permutations

**Fig. 2**. Distribution of permutations for alignment on SC (a) ($\alpha = 1$), FC (b) ($\alpha = 0$) and combined alignment (c) ($\alpha = 0.65$) in the left hemisphere. The gravity centers of the atlas regions are represented by green dots. The width of the edges represents the frequency of permutations of the two nodes that are incident with the given edge.
(d) presents a Venn diagram, showing the total amount and overlap of permutations that are common in the 3 cases (averaged over left and right hemispheres).

to have distant matching regions across subjects. Moreover, a lower number of permutations is provided by the FAQ algorithm when considering SC and FC together, than when considering only one modality. This suggests that irrelevant permutations are removed by the addition of one modality. Those irrelevant permutations proposed in the one-modality alignment might be the results of remaining noise, artifacts or lack of information.

Interestingly, Fig.2a shows permutations which agreed with the variability in the left-hemisphere of language areas in the meta-analysis of Vigneau et al. [9]

The permutations localized in the visual cortex are unexpected because of the strong assumptions about their spatial organization. Indeed, those suggested permutations supported by both structural and functional connectivity information might occur due to the similar connectivity of the visual regions to the rest of the cortex and may only align remaining noise. This needs further investigation. A confidence index might be used on the permutations, such as the connectivity variability of the permuted regions of the same subject. If two permuted regions have similar connectivity profile on the same subjects (as for the regions in the visual cortex) we are less confident in the permutation as for permuted regions that present weak connectivity similarity.

Often, two regions would not be entirely mislabeled, but their boundaries might be rotated, shrunk or shifted in certain directions and thus do not really delineate a homogeneous neuronal region, and overlap more of another region than the one it is supposed to delineate. In that case, the permutation of labels is a way to partially improve the similarity across subjects of regions with same labels.

## 4. CONCLUSION

In this work, we propose a method which improved the alignment of atlas regions, incorporating functional connectivity information. We modified the FAQ algorithm in order to find a single permutation matrix that aligns the brain atlas using both structural and functional connectivity. Using only structural connectivity entails permutations often not consistent in the functional data, whereas using only functional connectivity seems noisy and suggests a lot of irrelevant permutations. Our novel approach of aligning the cortex regions across subjects finds permutations of regions that remain consistent both in structural and functional networks. Our results suggest that, before any group processing of brain networks, this alignment step should be performed to avoid consideration of mismatched regions across subjects.

## 5. COMPLIANCE WITH ETHICAL STANDARDS

This research study was conducted retrospectively using human subject data made available in open access by the Human Connectome Project Dataset [20]. Ethical approval was not required as confirmed by the license attached with the open access data.

## 6. ACKNOWLEDGMENTS

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