



HAL
open science

BRAIN NETWORK ALIGNMENT USING STRUCTURAL AND FUNCTIONAL CONNECTIVITY WITH ANATOMICAL CONSTRAINTS

Yanis Aeschlimann, Anna Calissano, Théodore Papadopoulo, Samuel
Deslauriers-Gauthier

► **To cite this version:**

Yanis Aeschlimann, Anna Calissano, Théodore Papadopoulo, Samuel Deslauriers-Gauthier. BRAIN NETWORK ALIGNMENT USING STRUCTURAL AND FUNCTIONAL CONNECTIVITY WITH ANATOMICAL CONSTRAINTS. 2025. hal-04387986v2

HAL Id: hal-04387986

<https://hal.science/hal-04387986v2>

Preprint submitted on 17 Jan 2025

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

BRAIN NETWORK ALIGNMENT USING STRUCTURAL AND FUNCTIONAL CONNECTIVITY WITH ANATOMICAL CONSTRAINTS

Y. Aeschlimann* A. Calissano† T. Papadopoulo* S. Deslauriers-Gauthier*

* Université Côte d’Azur, Inria, France

† Department of Mathematics, Imperial College, London

ABSTRACT

Brain research often segments the cortex into regions based on an atlas, assuming a perfect matching of the regions across different subjects. However, due to genetic and environmental factors, inter-subject variability makes it challenging to produce a single brain atlas with a perfect correspondence of region labels across subjects, especially at a fine-grained scale. Previous work has proposed to use structural connectomes constructed from diffusion magnetic resonance imaging to permute brain regions across subjects and align the cortical regions from one subject to another, leading to an improved similarity of connectomes across subjects. In this work, we propose a multimodal approach to exploit simultaneously structural and functional connectivity information in the alignment process. Spatial constraints are included to prevent unlikely permutations between remote regions. Experimental results show the validity of the approach and the effectiveness of the constraint.

Index Terms— graph alignment, inter-subject variability, structural connectivity, functional connectivity, cortical atlas

1. INTRODUCTION

Due to the billions of cells in the brain, current imaging techniques cannot capture the activity of every single neuron. A general and feasible approach is to subdivide the cortex into regions, and then assess activity per region. Those regions are assumed to be homogeneous in terms of structural connectivity or functional connectivity and ideally both. However, the cortex and white matter are shaped by environmental and genetic factors [1] and therefore differ between subjects. Spatial inter-subject variability of brain activity has been the topic of numerous studies, e.g. [2]. For instance, it has been shown that activation peaks for language areas have a standard deviation reaching 19.5 mm [3]. Nonetheless, brain atlases generally do not account for inter-individual variability. Especially at a fine-grained level, labels of tiny brain regions probably do not correspond from one subject to another. One approach to make the structural and functional connectivity correspond across subjects is to permute the region labels to increase the similarity of brain regions across

subjects. In our context, connectivity strengths between regions are stored in a connectome, represented as a $N \times N$ matrix, with N being the number of regions. The permutations of regions is a graph alignment problem, it boils down to permuting the rows and columns of a subject connectome matrix to match the connectome of another subject (Fig.1). The alignment of the brain regions has been shown to improve the similarity of structural connectomes (SC) [4] computed from diffusion Magnetic Resonance Imaging (MRI) but has never been tested on functional connectomes (FC) computed from functional MRI (fMRI). This paper proposes a simultaneous alignment of structural and functional connectomes. Moreover, we add a regularization term to favor permutations of local regions rather than remote ones. We show that it is possible to identify permutations that simultaneously align structural and functional connectomes while respecting plausible anatomical constraints.

2. MATERIALS AND METHODS

2.1. Network alignment, FAQ algorithm

Finding the permutation matrix that maximizes the similarity between two connectomes is formulated as:

$$\min_{P \in \mathcal{P}} \|PCP^T - C_r\|_{\mathcal{F}}^2, \quad (1)$$

where P is a permutation matrix belonging to the permutation group $\mathcal{P} = \{P \in \{0,1\}^{N \times N} : P^T \mathbf{1} = P \mathbf{1} = \mathbf{1}\}$ inducing a permutation of rows and columns of the connectome C to align it with the reference connectome C_r . The similarity of the connectomes is based on the Frobenius norm $\|\cdot\|_{\mathcal{F}}$. Solving this problem is NP-hard. The Fast Approximate Quadratic Assignment Problem (FAQ) algorithm [5] tackles this difficulty by solving a relaxed version of the above optimization problem by allowing P to be in the space of bistochastic matrices to enable optimization by gradient descent. The obtained matrix is then projected onto the set of permutation matrices, yielding an approximate solution to Eq.(1). The optimization is initialized as the identity matrix, as we suppose it is a close approximation of the resulting permutation.

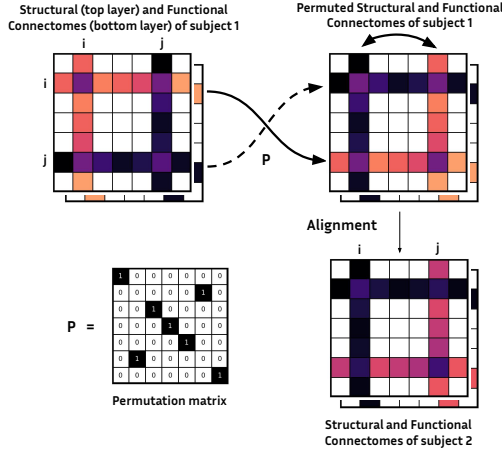


Fig. 1. Example of alignment of regions using permutations of rows and columns on a pair of subject’s connectomes from a given subject 1 to a given subject of reference 2.

To combine the information of two brain networks coming from different modalities, we modified the FAQ algorithm to minimize the criterion

$$L_1(P) = \alpha \|PSP^T - S_r\|_{\mathcal{F}}^2 + (1 - \alpha) \|PFP^T - F_r\|_{\mathcal{F}}^2 \quad (2)$$

with S and F being respectively the symmetric SC and resting-state FC (rs-FC) of a given subject, and S_r and F_r the corresponding connectomes of a subject chosen as reference. The same permutation matrix P is applied to both connectome’s modalities, as we suppose the regions to have the same role in the brain from both structural and functional perspectives. The weighting term α taking values between 0 and 1, balances the two modalities in the optimization. Specific cases are $\alpha = 0$ or 1, corresponding to respectively an alignment of rs-FC or SC only, as in Eq.(1).

To incorporate spatial information in the alignment optimization, we add a regularization term:

$$L_2(P) = L_1(P) - \lambda \text{Trace}(P^T R). \quad (3)$$

The regularization term, weighted by the hyperparameter λ requires a binary regularization matrix R . We construct R so that the entry at row i and column j is 1 if we allow the permutation from region i to j . This regularization term is minimized if the entries of the permutation matrix P are 1 where the entries of R are also 1, in which case $\text{Trace}(P^T R) = N$. The regularization term behaves similarly in the bistochastic matrix space, as any matrix that minimizes the regularization term is a permutation matrix. For a sufficiently large value of λ , the regularization term will thus be constant and minimal (equals to $-\lambda N$), therefore only containing permutations allowed by R .

In this work, we propose 3 different optimization strategies:

- Hemispheric Alignment (HA), performed separately on the two connectomes restricted to left and right hemispheres, neglecting the inter-hemispheric information. The left and right permutation matrices of shape $\frac{N}{2} \times \frac{N}{2}$ are computed using $L_1(P)$ and recombined in a $N \times N$ permutation matrix;
- Whole-brain Alignment (WBA), P is the min argument of $L_2(P)$ with permutations restricted to regions within the same hemisphere, allowing to use the inter-hemispheric information of whole-brain connectomes;
- Whole-brain Alignment with Neighborhood Constraints (WBANC), P is the min argument of $L_2(P)$ with permutations restricted to neighbor regions and forbidding inter-hemispheric permutations.

2.2. Assessment of identified permutations

To validate the permutations, the following error criterion is computed:

$$\|C - C_r\|_{\mathcal{F}} - \|PCP^T - C_r\|_{\mathcal{F}} \quad (4)$$

which is the difference between the connectomes’ distances C and C_r before and after the permutations of the rows and columns using P . The matrices P are identified on each pair of subjects for each optimization strategy, for α from 0 to 1 with a step size of 0.1 and $\lambda = 1000$ (determined experimentally).

A Wilcoxon test is used to assess the significance of our results. A statistically significant result indicates that the distribution of the distance’s differences is statistically greater than a distribution symmetric about 0, which is equivalent to testing whether the distribution of the distances after alignment is statistically lower than the distribution of the distances before the alignment.

2.3. Data processing

We selected the first 200 subjects from the Human Connectome Project (HCP) S1200 release. The images included resting-state fMRI (rs-fMRI), diffusion MRI (dMRI), and task-evoked fMRI (t-fMRI) for motor, language, social, gambling, emotion, relational, and working memory tasks. The imaging protocols have been described in detail in [6].

The fine-grained atlas of 1000 regions proposed by [7] is used to produce symmetric connectomes. The pipeline of connectome generation is as follows.

Rs-fMRI data originate from the “FIX-Denoised (Extended)” dataset of HCP in 4D volumetric format. The time series of rs-fMRI of left-right and right-left phase encoding are concatenated along the time axis. Irrelevant parts of the BOLD signal are removed with a bandpass filter with cut-off frequencies of 0.06 and 0.125 Hz. The processed BOLD signals are averaged over the regions of the atlas. The correlation matrix is computed on processed BOLD signals using

Pearson’s coefficient. The previous pipeline is applied to the two runs of resting-state separately, leading to two rs-FC per subject. Task-evoked functional images were preprocessed through the HCP Minimal Preprocessing Pipeline (MPP) [8] and the same pipeline is applied on the seven t-fMRI concatenated along the time axis, leading to a single task-state-FC [9] (ts-FC), averaging the seven tasks.

Diffusion images are preprocessed through MPP [8]. We used the TractoFlow pipeline [10] to reconstruct tractograms from preprocessed dMRI, with spherical harmonics of order 10 maximum fitted to the preprocessed dMRI data. The streamlines are reconstructed using a step size for Particle Filter Tracking of 0.3125 mm with 120 seeds per voxel at the intersection between white and gray matter. Streamlines from 20 to 300 mm are kept. The other parameters of the TractoFlow script are set to their default values. We construct streamline count connectomes. Each SC is symmetrized and normalized to have the same Frobenius norm as the FC of the same subject.

The rs-FC from the first run and the SC will be used in the optimizations, considered as “training” connectomes. The “validation” connectomes, rs-FC from the second run, and the ts-FC of the concatenated 7 tasks are used to test the robustness of the identified permutations.

3. RESULTS AND DISCUSSION

The distributions of the differences of Eq.(4) are illustrated in Fig.2. Statistically significant results are presented with one ($p < 0.005$) or two ($p < 0.001$) stars. For $\alpha = 1$ (right column in Fig.2, alignment on SC only) the distributions of the difference of distances after and before the alignment of SC (red) are significantly positive. This means we can find permutations for every optimization (HA, WBA, WBANC) that reduce the distance between the SC matrices. Conversely, for $\alpha = 0$ (left column, alignment on run 1 of rs-FC only) the distances between the rs-FC (run 1) (dark green) always decreased thanks to the alignment (distributions of the differences shifted above 0).

We also observe that permutations do not always generalize to other connectome modalities. In other words, the permutations identified on one type of connectome, do not always allow to also decrease the connectome’s distances of other types of connectomes (distributions sometimes shifted below 0). However, for multimodal alignments (α between 0 and 1 excluded), particularly for $\alpha = 0.5$, the distributions of the differences of distances for SC (red) and run 1 of rs-FC (dark green) are both shifted to the right for every method. We conclude that our algorithm can find permutations that simultaneously align SC and rs-FC matrices. Note that when including the first run of rs-FC in the alignment optimization (first 3 columns, $\alpha \neq 1$), the identified permutations decrease the distances between the rs-FC of the second run (light green), even if not used in the optimization. We can

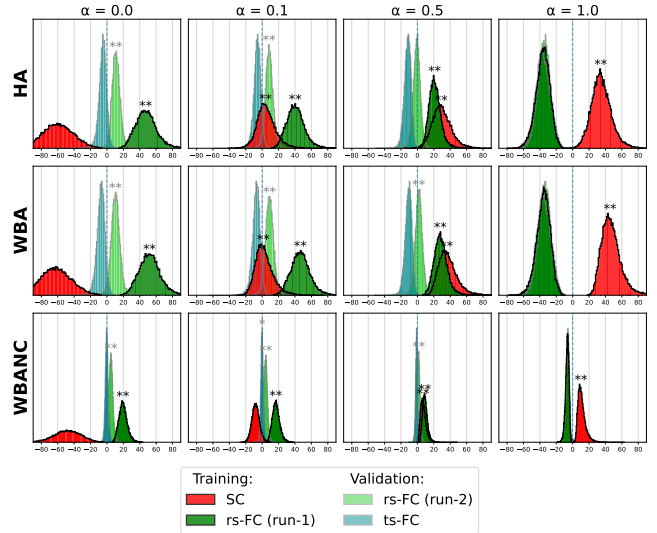


Fig. 2. Distributions of the differences of the distances between connectomes after and before alignment, for the three methods: HA (first row), WBA (middle row), WBANC (last row) and for different values of α .

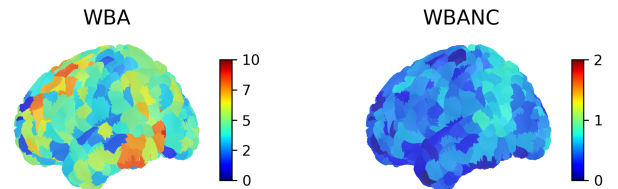


Fig. 3. Distances between permuted regions on average for WBA and WBANC methods and $\alpha = 0.5$. Distance is calculated as the minimum number of regions in between two permuted regions.

say that permutations generalize to the rs-FC of the second run.

Comparing the HA and WBA optimizations (first and second rows), we observe that the distributions of SC for $\alpha = 1$ (red distribution in right column) and rs-FC (run 1) for $\alpha = 0$ (dark green in left column) are more shifted to the positive using WBA than HA. This means that the inter-hemispheric connectivity improves the alignment.

The WBANC optimization (last row) has a weaker effect on the shift of the distributions because we are restricting the set of possible permutations. However, restricting the permutations to neighboring regions still allows us to identify permutations that decrease the connectomes distances. In addition, it is the only optimization that generalizes to ts-FC at $\alpha = 0.1$ (blue distribution at the third row and second column), because when applied to ts-FC, the connectomes’ dis-

tances decrease.

Our results show that the regularization term acts almost as a constraint because, in the WBA alignment, 99.9% of the permutations concern regions within the same hemispheres, and in the WBANC alignment 99.9% of the permutations are restricted to neighboring regions. Fig.3 shows for each region on a brain map the distance to its permuted regions over all the subject's alignment, for WBA and WBANC methods, and $\alpha = 0.5$. A distance between two permuted regions is calculated as the minimum number of regions in between. The permutation distance for a region not permuted in a subject's alignment is thus 0.

4. CONCLUSION

Our framework of brain alignment shows that it is possible to simultaneously align structural and functional connectomes from resting-state fMRI. Moreover, permutations also generalize to resting-state connectomes not used during the alignment optimization. The inter-hemispheric connectivity informs the alignment. The restriction to local permutations has a less significant effect on the decrease of the distances between the connectomes but induces permutations probably more robust because it generalizes to task functional connectomes.

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. Ethical approval was not required as confirmed by the license attached with the open access data.

6. ACKNOWLEDGMENTS

This research is partially funded by the Department of Mathematics of the Imperial College London via Chapman Fellowship funding scheme.

The authors are grateful to the OPAL infrastructure from Université Côte d'Azur for providing resources and support.

Data were provided by the Human Connectome Project, WU-Minn Consortium (Principal Investigators: David Van Essen and Kamil Ugurbil; 1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University.

7. REFERENCES

- [1] P.M. Thompson, T.D. Cannon, K.L. Narr, T. Van Erp, V. Poutanen, M. Huttunen, J. Lönqvist, C. Standertskjöld-Nordenstam, J. Kaprio, M. Khaledy, et al., "Genetic influences on brain structure," *Nature neuroscience*, vol. 4, no. 12, pp. 1253–1258, 2001.
- [2] Mohamed L Seghier and Cathy J Price, "Interpreting and utilising intersubject variability in brain function," *Trends in cognitive sciences*, vol. 22, no. 6, pp. 517–530, 2018.
- [3] M. Vigneau, V. Beaucousin, P. Hervé, H. Duffau, F. Crivello, O. Houde, B. Mazoyer, and N. Tzourio-Mazoyer, "Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing," *Neuroimage*, vol. 30, no. 4, pp. 1414–1432, 2006.
- [4] Anna Calissano, Theodore Papadopoulo, Xavier Pennec, and Samuel Deslauriers-Gauthier, "Graph alignment exploiting the spatial organization improves the similarity of brain networks," *Human Brain Mapping*, vol. 45, no. 1, pp. e26554, 2024.
- [5] J.T. Vogelstein, J.M. Conroy, V. Lyzinski, L.J. Podrazik, S.G. Kratzer, E.T. Harley, D.E. Fishkind, R.J. Vogelstein, and C.E. Priebe, "Fast approximate quadratic programming for graph matching," *PLOS one*, vol. 10, no. 4, pp. e0121002, 2015.
- [6] D.C. Van Essen, K. Ugurbil, E. Auerbach, D. Barch, T.E.J. Behrens, R. Bucholz, A. Chang, L. Chen, M. Corbetta, S.W. Curtiss, S. Della Penna, D. Feinberg, M.F. Glasser, N. Harel, A.C. Heath, L. Larson-Prior, D. Marcus, G. Michalareas, S. Moeller, R. Oostenveld, S.E. Petersen, F. Prior, B.L. Schlaggar, S.M. Smith, A.Z. Snyder, J. Xu, and E. Yacoub, "The human connectome project: A data acquisition perspective," *NeuroImage*, vol. 62, no. 4, pp. 2222–2231, 2012.
- [7] Alexander Schaefer, Ru Kong, Evan M Gordon, Timothy O Laumann, Xi-Nian Zuo, Avram J Holmes, Simon B Eickhoff, and BT Thomas Yeo, "Local-global parcellation of the human cerebral cortex from intrinsic functional connectivity mri," *Cerebral cortex*, vol. 28, no. 9, pp. 3095–3114, 2018.
- [8] M.F. Glasser, S.N. Sotiropoulos, J.A. Wilson, T.S. Coalson, B. Fischl, J.L. Andersson, J. Xu, S. Jbabdi, M. Webster, J.R. Polimeni, et al., "The minimal preprocessing pipelines for the human connectome project," *Neuroimage*, vol. 80, pp. 105–124, 2013.
- [9] Xin Zhang, Lei Guo, Xiang Li, Tuo Zhang, Dajiang Zhu, Kaiming Li, Hanbo Chen, Jinglei Lv, Changfeng Jin, Qun Zhao, Lingjiang Li, and Tianming Liu, "Characterization of task-free and task-performance brain states via functional connectome patterns," *Medical Image Analysis*, vol. 17, no. 8, pp. 1106–1122, Dec. 2013.
- [10] Guillaume Theaud, Jean-Christophe Houde, Arnaud Boré, François Rheault, Felix Morency, and Maxime Descoteaux, "Tractoflow: A robust, efficient and reproducible diffusion mri pipeline leveraging nextflow & singularity," *NeuroImage*, 2020.