

Joint Spectral Decomposition for the Parcellation of the Human Cerebral Cortex Using Resting-State fMRI

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Abstract. Identification of functional connections within the human brain has gained a lot of attention due to its potential to reveal neural mechanisms. In a whole-brain connectivity analysis, a critical stage is the computation of a set of network nodes that can effectively represent cortical regions. To address this problem, we present a robust cerebral cortex parcellation method based on spectral graph theory and resting-state fMRI correlations that generates reliable parcellations at the single-subject level and across multiple subjects. Our method models the cortical surface in each hemisphere as a mesh graph represented in the spectral domain with its eigenvectors. We connect cortices of different subjects with each other based on the similarity of their connectivity profiles and construct a multi-layer graph, which effectively captures the fundamental properties of the whole group as well as preserves individual subject characteristics. Spectral decomposition of this joint graph is used to cluster each cortical vertex into a subregion in order to obtain whole-brain parcellations. Using rs-fMRI data collected from 40 healthy subjects, we show that our proposed algorithm computes highly reproducible parcellations across different groups of subjects and at varying levels of detail with an average Dice score of 0.78, achieving up to 9% better reproducibility compared to existing approaches. We also report that our group-wise parcellations are functionally more consistent, thus, can be reliably used to represent the population in network analyses.

1 Introduction

The human cerebral cortex is assembled into subregions that interact with each other in order to coordinate the neural system. Identification of these subregions is critical for a better understanding of the functional organization of the human brain and to reveal the connections of underlying subsystems [19]. Functional connectivity studies have identified several subsystems, each of which is spanned across different cortical areas and associated with a specific functional ability [16]. This has further advanced the analysis of the functional architecture of the brain by constructing graphical models of the connections within individual subsystems and their interactions with each other at different levels of detail [14, 25]. Analysis of these networks is also important for

deriving biomarkers of neurological disorders such as Alzheimer’s disease [20] and schizophrenia [1].

In this paper, our main motivation is to identify functionally homogeneous and spatially continuous cortical subregions which can be used as the network nodes for a whole-brain connectivity analysis. In a typical network analysis, nodes are usually represented by the average signal within each cortical subregion, which is further beneficial to improve the SNR [9]. A good parcellation framework should be capable of grouping cortical regions with similar functional patterns together, thus the average signal can effectively represent each part of the subregion. It is also highly critical to generate a reliable group-wise representation that reflects the common functional characteristics of the community, yet is tolerant to changes in the functional organization at the single-subject level that may emerge due to functional and anatomical differences across subjects.

Our proposed method is based on connectivity patterns captured from resting-state functional magnetic resonance imaging (rs-fMRI) data. Rs-fMRI records neurocognitive activity by measuring the fluctuations in the blood oxygen level signals (BOLD) in the brain while the subject is at wakeful rest. Since the brain is still active in the absence of external stimuli, these fluctuations can be used to identify the cerebral functional connections [4]. On the other hand, task-based fMRI parcellations driven by neuropsychological studies, e.g. language task [12], target specific subregions in the cortex in order to investigate their functional organization, but ignores the activation from the non-target areas, which makes them incapable for the whole-brain network analyses. Similarly, anatomical parcellations generated from cytoarchitectonic atlases [22] are not able to capture the functional organization of the brain. This can be attributed to the fact that cytoarchitecture of the cerebral cortex does not necessarily require to be consistent with the functional connectivity patterns [12,21] and arbitrary parts of the same cytoarchitectonic region can exhibit structural and functional variability [6]. Nevertheless, parcellating the cerebral cortex based on resting-state correlations can potentially identify functional organization of the cerebral cortex without the knowledge of the cytoarchitecture and an external stimulus or a cognitive process [18].

The rs-fMRI-based cortical parcellation literature consists of methods that subdivide the cerebral cortex into different number of subregions according to the requirements of the applications and topological network features across the cerebral cortex [15]. These methods are based on but not limited to independent component analysis (ICA) [2], region growing [5,24], spectral graph theory [6,14,17], boundary mapping [9], k-means clustering [3,8] and hierarchical clustering [11,23]. Some of these techniques [2,3,14,25] parcellate the cortex at a very coarse level (less than hundred subregions), with the aim of identifying resting-state networks spanning across the cortex or some fractions of it. Because of the aforementioned risks of having non-uniform functional patterns within subregions, these parcellations cannot be reliably used for network node identification. Other methods typically generate a few hundred clusters without losing the ability of representing the functional organization of the cortex.

The most critical issue that is not addressed by these techniques is the adaptability of group representation to individual single subjects. The group-wise parcellations generated from a set of subjects are generally assumed to represent the whole group. However, due to functional and structural variations at the single-subject level, it is very unlikely that a group parcellation would highly match with single-level parcellations [9].

We address this problem and introduce a new parcellation framework which is capable of both generating group-wise and single-level parcellations from a joint graphical model. To this end, we make use of spectral graph decomposition techniques and represent the population in a multi-layer graph which effectively captures the fundamental properties of the whole group as well as preserves individual subject characteristics. We show that the parcellations obtained in this setting are (a) more reproducible across different groups of subjects and (b) better reflect functional and topological features shared by multiple subjects in the group compared to other parcellation methods. These aspects of the proposed method differentiate it from the previous parcellation algorithms and constitute our main contributions in this paper. Finally, our framework can be used to generate parcellations with different number of subregions, allowing users to conduct a network analysis at different levels of detail.

2 Methodology

2.1 Data Acquisition and Preprocessing

We evaluate our algorithm using data from the WU-Minn Human Connectome Project (HCP). We conducted our experiments on the rs-fMRI datasets, containing scans from 40 different unrelated subjects (22 female, 18 male healthy adults, ages 22–35). The data for each subject was acquired in two sessions, divided into four runs of approximately 15 min each. During the scans, subjects were presented a fixation crosshair, projected against a dark background, which prevented them from falling asleep. The dataset was preprocessed and denoised by the HCP structural and functional minimal preprocessing pipelines [7]. The final result of the pipeline is a standard set of cortical time courses which have been registered across subjects to establish correspondences. This was achieved by mapping the cortical gray matter voxels to the native cortical surface and registering them onto the 32k standard triangulated mesh. Following the preprocessing step, each time course was temporally normalized to zero-mean and unit-variance. We concatenated the time courses of each scan, obtaining an almost 60-minute rs-fMRI data for each of the 40 subjects and used them to evaluate our approach.

2.2 Joint Spectral Decomposition

We propose a clustering approach based on spectral decomposition to identify whole-cortex parcellations that can effectively capture the functional associations

across multiple subjects. At the single-subject level, the cerebral cortex is represented as an adjacency matrix, in which the functional correlations are encoded as edge weights. Each adjacency matrix is transformed to the spectral domain via an eigenspace decomposition. The corresponding eigenvectors are combined into a multi-layer graph, which is capable of representing the fundamental properties of the underlying functional organization of individual subjects. Similar to the single-level graph decomposition, this joint multi-layer graph can then be decomposed into its eigenvectors, creating a feature matrix in the spectral domain that can be fed into a clustering algorithm, e.g. k -means, for grouping each vertex into a subregion, hence producing the final parcellations. A visual summary of the approach is given in Fig. 1.

Sparse Adjacency Matrix. The cerebral cortex of the brain is represented as a smooth, triangulated mesh with no topological defects. We model the mesh vertices and their associations as a weighted graph $G = (V, E)$, where V is the set of vertices (nodes) and E is the set of edges connecting them. Here we enforce a spatial constraint and construct an edge between two vertices if and only if they are adjacent to each other. This spatial constraint results in a sparse adjacency matrix with two benefits: (a) it ensures that resulting clusters are spatially continuous and (b) it reduces the computational overhead during the spectral decomposition of the graph. Finally, the edge weights between the adjacent vertices are set to the Pearson product-moment correlation coefficients of their rs-fMRI time courses (after discarding negative correlations and applying Fisher’s z -transformation) and represented as an $n \times n$ weighted adjacency matrix W , where n is the number of vertices on the cortex.

Spectral Decomposition. Given the adjacency matrix W , the graph Laplacian can be computed as $L = D - W$, where $D = \text{diag}(\sum_j w_{ij})$ is the degree matrix of W . L is a diagonalizable matrix which can be factorized as $L = U\Lambda U^{-1}$, where $U = (u_1, u_2, \dots, u_n)$ is the eigensystem, with u_i representing each eigenvector and Λ is a diagonal matrix that contains the eigenvalues, represented as $\Lambda_{ii} = \lambda_i$. Eigenvectors are powerful tools in terms of encapsulating valuable information extracted from the decomposed matrix in a lower dimension. In particular, after sorting the eigenvalues as $0 = \lambda_1 \leq \lambda_2 \leq \dots \leq \lambda_n$ and organizing the corresponding eigenvectors accordingly, the first k eigenvectors denoted as the *spectral feature matrix* $F = (u_1, u_2, \dots, u_k)$ are capable of representing the most important characteristics of the decomposed matrix. Thus, each vertex on the cortical surface can be represented by its corresponding row in F , without losing any critical information.

Spectral Matching. The idea of spectral matching is finding the closest vertex pairs in two eigensystems by comparing their eigenvectors in the spectral feature matrices [13]. The observations on the cortical surfaces transformed to the spectral domain revealed that eigenvectors show very similar characteristics across

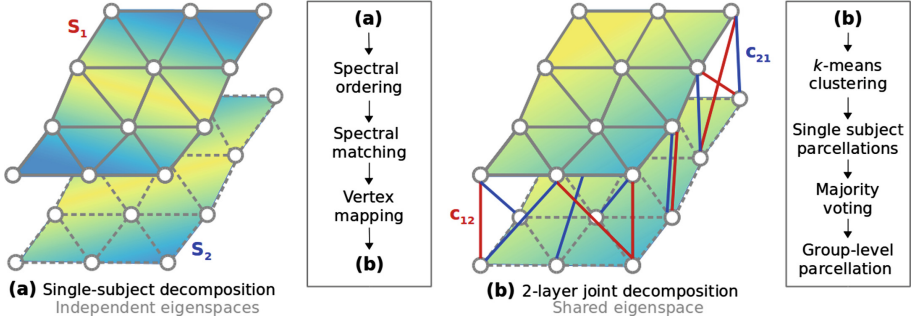


Fig. 1. Visual representation of the parcellation pipelines with an emphasis on (a) single-subject and (b) joint spectral decomposition, illustrated on the patches cropped from the cortical surfaces S_1 and S_2 . The red and blue edges correspond to the mappings c_{12} and c_{21} , obtained by matching the closest vertices in S_1 and S_2 , respectively (Color figure online).

subjects. This attribute can be utilized to obtain a common eigensystem that reflects structural and functional features shared by the subjects in the group, while also preserving individual subject characteristics.

Notably, the same cortical information represented with the eigenvector u_i in F_1 can be decoded in the eigenvector u_j in F_2 , without the necessity of being in the same order or having the same sign. Therefore, an additional correction must be carried out in order to find the corresponding eigenvectors on both cortical surfaces before applying spectral matching. To this end, we make use of a simple spectral ordering technique, where for each eigenvector u_i in F_1 we compute its closest eigenvector u_j in F_2 using Euclidean distance and if $i \neq j$ we mark u_j for re-ordering. We then take another iteration and repeat the same process after flipping the signs of each eigenvector in F_2 and if a closer match is found, the new eigenvector is marked and its new sign is preserved throughout the sequential processes. Finally, the marked eigenvectors in F_2 are re-ordered accordingly.

After spectral ordering, we use only the first 8 eigenvectors for spectral matching, since our experiments showed that increasing the number of eigenvectors do not change the mappings between corresponding vertices, thus has no effect on the final parcellations. The spectral matching problem can be solved by mapping the closest vertices x and y on cortex S_1 and cortex S_2 with respect to their re-ordered spectral feature matrices F_1 and F_2 as illustrated in Fig. 1. The mappings $c_{12} : x_i \mapsto y_{c_{12}(i)}$ and $c_{21} : y_i \mapsto x_{c_{21}(i)}$ for $i = 1, \dots, n$ can be identified with a nearest-neighbor search applied on F_1 and F_2 .

Multi-layer Correspondence Graph. The use of spectral matching to find the mappings between pairs of cortical surfaces can be extended to generate a multi-layer correspondence graph for representing the whole group of subjects. The most critical part in such a setting is the definition of edge weights that

constitute the connections between the mapped vertices. Using the correlations of rs-fMRI time courses for this purpose is not sensible, since the mapped vertices do not belong to the same cortex. Instead, we use the correlations of the connectivity fingerprints, computed by correlating the rs-fMRI time courses of each vertex with the rest of the vertices on the cortical surface (after Fisher’s z-transformation). Connectivity fingerprints effectively reflect the functional organization of the cerebral cortex and intuitively, we expect two fingerprints in different cortices to be similar if they are matched with each other in spectral domain.

We define the multi-layer correspondence graph $\mathbb{W} = (W_{ij} \mid \forall i, j \in [1, N])$ as a combination of weighted adjacency matrices, where $W_{ii} = W_i$ and W_{ij} ($i \neq j$) is the set of edges between cortical surfaces S_i and S_j with respect to their mappings c_{ij} and c_{ji} , weighted by the connectivity fingerprint correlations. \mathbb{W} is an N -layer graph, with a size of $(n \times N) \times (n \times N)$ where N is the number of subjects in the group. A small patch taken from a 2-layer graph is illustrated as an example in Fig. 1(b).

Generation of Group-wise and Single Subject Parcellations. The spectral decomposition of \mathbb{W} is performed similarly as described in the Spectral Decomposition section. The corresponding eigenvectors provide us with a shared feature matrix \mathbb{F} , representing every subject in the group with a combined parametrization. That is, each eigenvector can be separated into sub-vectors and used to characterize the underlying subjects. Similarly, each row in \mathbb{F} can be used to describe its corresponding cortical vertex, thus can be used in a clustering setting. Here, we use k -means clustering for its simplicity and applicability, however it can be replaced by any other technique. We set the number of eigenvectors k to the desired number of subregions K , into which we would like to parcellate the cortical surfaces.

The output of the clustering approach is a label vector \mathbb{L} of length $n \times N$ that assigns a parcel to each vertex on all cortical surfaces used to define \mathbb{W} . By dividing \mathbb{L} into sequential sub-vectors of length n , we can obtain a parcellation for each subject. A simple majority voting across the single parcellations can then be used to generate the group parcellation. Hence, our method is capable of computing both a group-wise parcellation and single subject parcellations from the same graphical model.

3 Results

We compare our algorithm with a state-of-the-art parcellation approach based on spectral clustering [6]. This method decomposes subject specific adjacency matrices and makes use of the corresponding eigenvectors to obtain single-level parcellations with the help of normalized cut clustering. In order to be consistent in comparisons, we used the same adjacency matrices initially computed in our approach. The single level clustering is followed by a second level clustering, in which a coincidence matrix is computed [10]. This is a special adjacency matrix where an edge between two vertices is weighted by the number

of times they appear in the same parcel across all individual parcellations and used to obtain a group-level parcellation. Alternatively, a group-wise parcellation can be performed by averaging the individual adjacency matrices (after Fisher’s z-transformation) and then submitting the average to the normalized cut clustering algorithm. These methods will be referred as two-level and group-mean clustering, respectively, throughout the rest of the paper.

We assess the performance of the methods in two ways: (a) parcellation reproducibility across different groups of subjects and (b) functional consistency between single-level parcellations and the group-wise parcellation.

3.1 Reproducibility

We measure the reproducibility using the Dice similarity measure [5, 17]. We first identify overlapping parcels in two parcellations and compute their Dice scores. The overlapping parcels with the highest Dice score constitute a match and both are excluded from the parcellations. The algorithm iteratively continues to match the remaining parcels until all overlapping pairs are identified. The average Dice score of all pairs is used to measure the reproducibility of the parcellations. We also include overlap scores of 0 for non-matching parcels to the average calculation in order to penalize parcellations with non-overlapping parcels.

We present the group-wise reproducibility results obtained by our proposed algorithm as well as the comparison methods in Fig. 2. In this experiment, we separated all subjects in the dataset into two equally-sized, mutually exclusive groups by random selection and computed group-level parcellations for each group by running the algorithms separately on the left and right hemispheres. This process was repeated for 10 times, each time setting new groups and

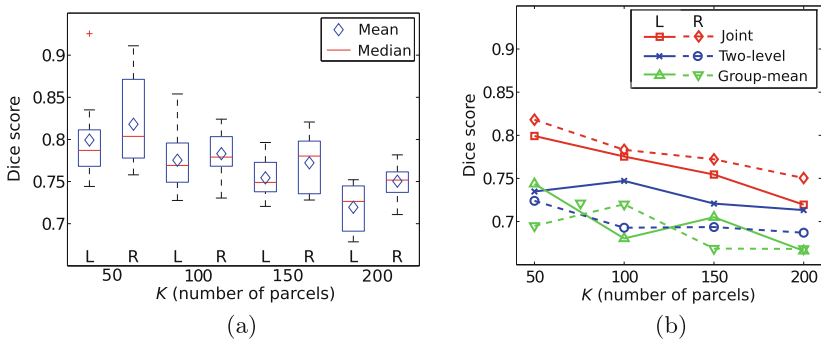


Fig. 2. Group-wise parcellation reproducibility results for different number of parcels obtained on different groups of subjects by running each method separately on the left and right hemispheres (indicated by L and R, respectively). (a) Dice scores of the proposed method, boxes indicating the range within different runs. (b) Dice scores of each method, averaged across all runs.

generating the corresponding group-wise parcellations for each method. Results indicate that our joint spectral decomposition approach is able to obtain more reproducible parcellations at each level of resolution, with at least an average Dice score of 0.72. The right hemisphere is slightly more reproducible than its left conjugate, which can be attributed to the topological differences between two hemispheres. There is a general decreasing trend in all methods with the increasing parcellation resolution. Dice scores for $K > 200$ were even lower, which might indicate that larger resolutions are not appropriate for parcellation. This can be attributed to the fact that, as K gets larger, the functional variability across subjects gets more prominent, thus, reducing the similarity between the common characteristics within different groups and leading to less reproducible group parcellations.

In Fig. 3, we present the group-wise parcellations obtained by our approach from one group of 20 randomly selected subjects with different number of parcels and visualize the reproducibility of each group-level parcel across single subject parcellations. Cross-subject reproducibility is measured by the same Dice similarity based method. For each group-level parcel we find its match in a single-level parcellation and record their Dice score. We repeat the same process for all subjects and average the Dice scores to get the reproducibility measure for that group-parcel. Darker colors indicate a high reproducibility across single-subject parcellations. Due to high functional inter-variability between different individuals and the varying levels of SNR in the rs-fMRI data, it is not possible to obtain high Dice scores for each part of the cerebral cortex [9]. Nevertheless, our approach is robust enough to achieve an average Dice score of at least 0.5 for each group-wise parcel.

3.2 Functional Consistency

Another critical performance measure for group-wise parcellations is their ability to represent individual subjects in terms of functional consistency. We expect the variability in functional evaluation measures to be consistent and minimal in order to reliably use the group-wise representation in place of each subject in the group. To this end, we evaluate functional consistency by computing (a) the change in parcel homogeneities and (b) the difference across functional connectivity networks, when we replace a single-level parcellation with its corresponding group-wise parcellation without changing the underlying rs-fMRI data. Both measurements were computed with respect to 20 different group-level parcellations obtained by randomly selected groups of 20 subjects. We excluded the group-mean method from this experiment, since it does not provide individual subject parcellations.

In Fig. 4(a), we present the whole-brain homogeneity changes for different number of parcels. Homogeneity of a parcel is measured by summing the Euclidean distances between the constituent rs-fMRI time courses and their average. A homogeneous parcellation consists of subregions with alike time courses, thus the sum of distances is expected to be low across the parcellated brain. The results indicate that the homogeneity levels between group- and single-level

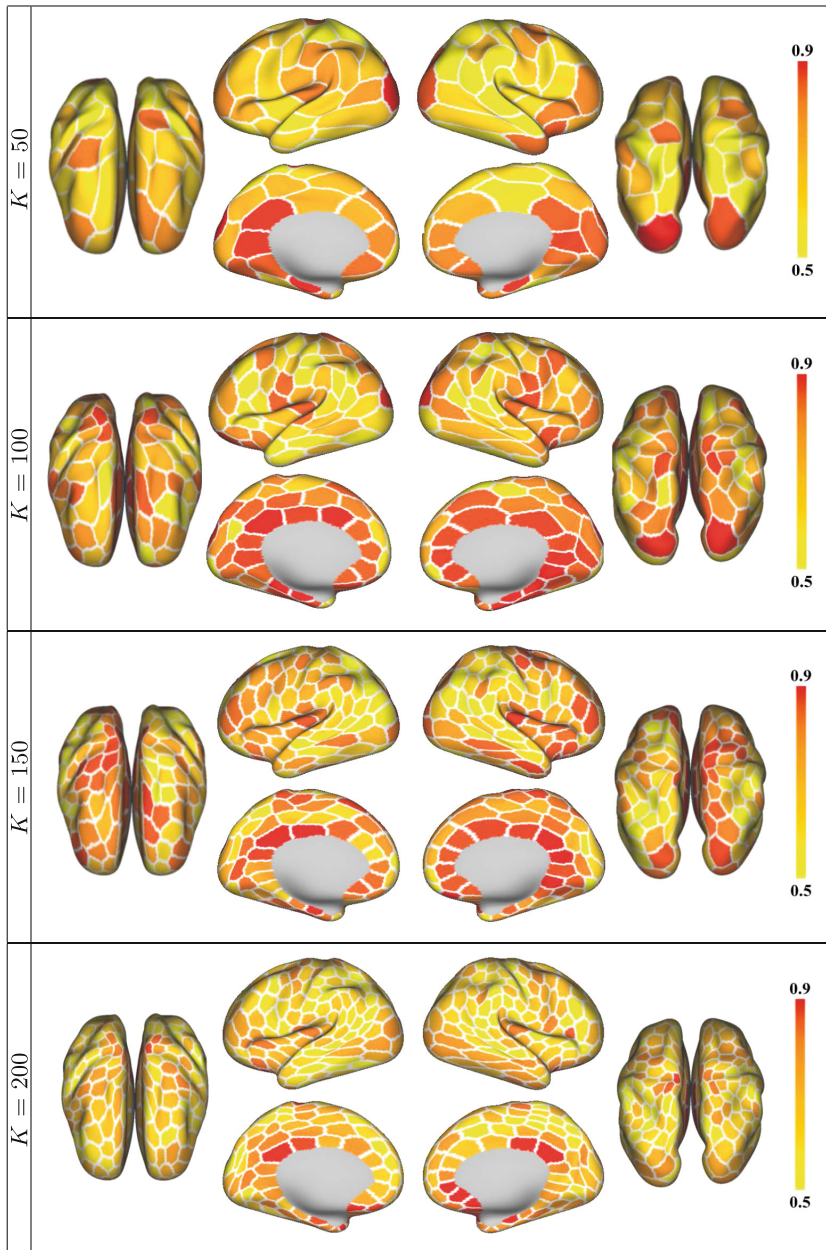


Fig. 3. Group-wise whole-brain parcellations obtained by the joint spectral decomposition method, run on each hemisphere separately for the number of parcels $K = 50$, 100, 150, and 200. The color of the parcellations indicates the average reproducibility score of each parcel across single-level parcellations (Color figure online).

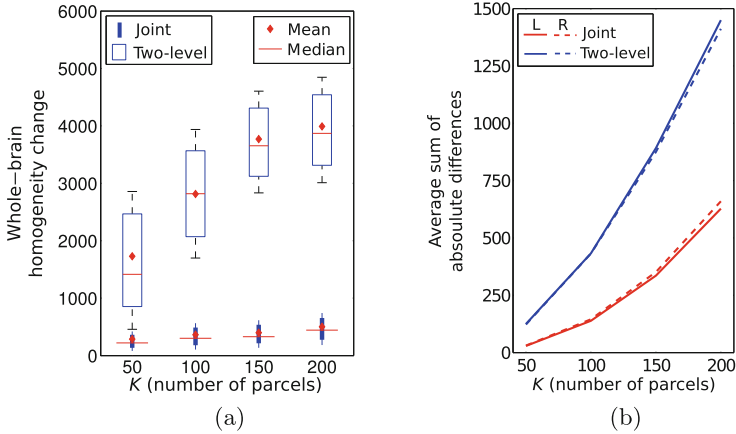


Fig. 4. Functional consistency results of the proposed and two-level method computed for 20 different group-level parcellations obtained by randomly selected groups of 20 subjects at different resolution levels. (a) The change in parcel homogeneities averaged throughout the whole brain, boxes indicating the range across different groups. (b) The sum of absolute differences (SAD) between the functional connectivity networks obtained by the individual parcellations and their group-wise representations, averaged across all runs. Left and right hemispheres are indicated by L and R, respectively.

parcellations obtained by our approach are highly consistent across different runs and at varying levels of detail compared to the other approach, which performs even worse for higher number of parcels.

In Fig. 4(b), we present the average sum of absolute differences (SAD) between the functional connectivity networks obtained by the individual parcellations and their group-wise representations. A functional connectivity network is computed by cross-correlating parcels, each of which is represented by its average time course. In order to compare two networks, we first match the single- and group-level parcellations using the Dice similarity method and exclude the non-matching parcels from the comparison in order to allow an objective comparison of both methods. SAD results show a similar pattern as the homogeneity results, with our approach producing more consistent networks compared to the two-level clustering.

4 Conclusions

We presented a spectral graph decomposition approach to parcellate the entire human cerebral cortex using resting-state fMRI data. Our experiments demonstrated that the proposed algorithm can produce robust parcellations with higher reproducibility and can better reflect functional and topological features shared by multiple subjects compared to other parcellation methods. The functional

consistency of our parcellations can be attributed to the graphical model we propose, which combines individual functional features with the general functional tendency of the group. Group-wise parcellations obtained by our approach can be reliably used to represent the individual subjects in the group as well as to identify the nodes in a network analysis. In order to show the effectiveness of our approach, a planned future work is to conduct a network analysis using parcellations derived from different age groups and demonstrate how connectivity changes though aging.

One bottleneck of the proposed approach is the high computational space and time requirements in order to decompose the multi-layer graph. To overcome this, we are working on an initial clustering stage for grouping highly correlated and spatially close vertices into pre-parcels represented by their average time course, thus reduce the dimensionality of the graph and improve the SNR levels across the cerebral cortex.

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