GRAPH SLEPIANS TO PROBE INTO LARGE-SCALE NETWORK ORGANIZATION OF RESTING-STATE FUNCTIONAL CONNECTIVITY

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ABSTRACT

Functional magnetic resonance imaging (fMRI) is providing large amounts of data about brain function. Measuring correlations between spontaneous activity time courses from resting-state fMRI has revealed large-scale network organization. In the graph-based approach for functional connectivity analysis, a graph is built where nodes are brain regions and edge weights are pairwise correlations between the associated time courses. Here, we propose to apply recent approaches from graph signal processing to analyze fMRI data. First, the graph is constructed from structural connectivity, then, the corresponding graph spectrum is obtained such that the graph Slepian design can be deployed. In particular, graph Slepians are band-limited (i.e., using only graph Laplacian eigenvectors with lowest eigenvalues) with optimal energy concentration in predefined subgraphs. The subgraphs selected here are default-mode network (DMN) and fronto-parietal network (FPN), known as task-negative and -positive networks, respectively. While their activity appears anti-correlated during resting-state, a much more complicated interplay has been suggested recently using dynamic and time-resolved approaches. Preliminary results using data from the Human Connectome Project show that the proposed framework can direct the analysis to specific parts of the network and bring to light interactions between local and global aspects of network organization that were hidden before.

Index Terms— fMRI, functional imaging, Slepian, graph analysis, brain networks.

1. INTRODUCTION

Functional magnetic resonance imaging (fMRI) is a non-invasive technique that measures a hemodynamic proxy of neural activity, and that has allowed to extensively map brain functions [1]. Consecutive volumes of the brain are acquired either in the presence or absence of stimuli or tasks, to elicit a specific brain system (task-based fMRI) or record spontaneous fluctuations of activity (resting-state fMRI), respectively. Functional connectivity (FC) investigates the statistical inter-dependencies between the fMRI signals at different brain locations. In particular, resting-state FC has revealed that spatially distant regions organize in large-scale networks, which are consistent across subjects and can reveal meaningful information about the individual [2]. Graph-based approaches are commonly adopted to explore how FC is organized. First, the brain is parcellated into a number of regions (nodes) and then pairwise correlations between the fMRI timecourses of these regions are computed (edge weights). This leads to so-called functional connectomes, that can be analysed in terms of graph properties and compared across subjects [3]. For instance, spectral graph methods have been used to analyze graph clustering and community structure of such brain connectomes [4].

The default-mode network (DMN) is a prominent network of resting-state with its core region being the posteromedial cortex. DMN activity is thought to be stronger during resting-state than during engagement into tasks, which makes it task-negative as opposed to, for instance, the fronto-parietal network (FPN), that is task positive. The anticorrelation pattern that emerges between these networks during a resting-state run (e.g., when building a correlation map for a seed in the posterior cingulate cortex) can be interpretated as activity is alternating, but recent evidence points towards a much more complex and dynamic interplay [5, 6]. In particular, the anticorrelation pattern is supported by subsystems of the networks rather than by activity of the complete networks. Therefore, there is a need for more sophisticated, time-resolved, techniques to observe and characterize these network interactions [7].

In this work, we are going to apply recent advances from graph signal processing [8, 9] that has introduced graph Slepians, which generalize the joint space-frequency localization theory of Slepian and colleagues [10, 11] to graphs [12]. In particular, we will define the graph based on structural brain connectivity derived from diffusion-weighted MRI, and then analyze fMRI as graph signals. The Slepian design will allow to focus the analysis to specific parts of the graph, under a graph bandwidth constraint. More specifically, to study the interactions between DMN and FPN, we will deploy the "augmented" criterion [13], that allows us to select DMN and FPN as two opposing networks. The bandwidth setting controls the global-vs-local trade-off. At very high bandwidth, the approach becomes equivalent to completely separating the

selected subgraph. Therefore, low to intermediate settings of the bandwidth appear more interesting as they allow to explore the transition from local to global organization. We will demonstrate that the graph Slepian basis reveals interesting information for both resting-state and task fMRI data, and might be another promising approach to analyze brain dynamics in a framework that considers both structure and function.

2. METHODS

2.1. MRI Data and Preprocessing Pipeline

Structural, diffusion-weighted, and functional MRI of healthy subject #100307 from the Human Connectome Project (HCP) were considered. We used the Craddock atlas where the original 950 regions were reduced to $N = 715$ by excluding regions with insufficient fMRI signal as well as cerebellar ones. A structural connectome characterized by a weighted adjacency matrix $\mathbf{A}$ was obtained using the MRItrix toolbox; i.e., multi-shell multi-tissue response function estimation, spherical deconvolution, tractogram generation with 10^7 output streamlines.

For the fMRI data, we used both a working-memory task session and a resting-state one. The fMRI volumes were preprocessed using a standard pipeline that included: realignment, regression of baseline, linear and quadratic trends, average white matter and cerebrospinal fluid signals, motion scrubbing with cubic spline interpolation [14]. Then, data was regionally averaged in the 715 ROIs derived from Craddock atlas. The working-memory task consisted of alternating blocks of fixation and image presentation (faces, places, tools or body parts), in 0-back or 2-back fashion [15].

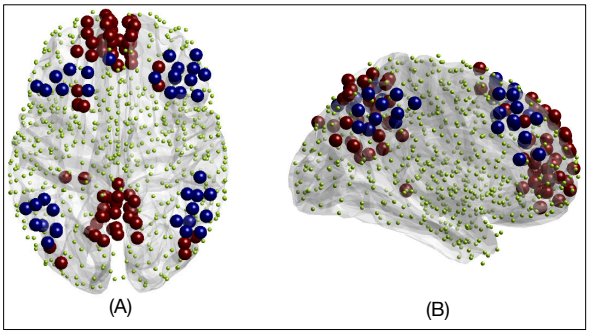

Fig. 1. Nodes belonging to positive (in red, default mode network, DMN) and negative (in blue, fronto-parietal network, FPN) subgraph selection used for Slepian design. (A) Axial and (B) sagittal views.

2.2. Graph Slepians of the Brain

The graph Slepian with the augmented criterion was adopted here and applied to the $N \times N$ weighted adjacency matrix $\mathbf{A}$ that represents the brain's structural connectome. We define the graph spectral domain from the eigendecomposition of the graph Laplacian $\mathbf{L} = \mathbf{D} - \mathbf{A}$, where $\mathbf{D}$ is the diagonal degree matrix; in particular, we have eigenvectors $\mathbf{u}_i$ with associated eigenvalues λ_i that satisfy

$$\mathbf{L}\mathbf{u}_i = \lambda_i \mathbf{u}_i, \quad i = 1, \ldots, N. \tag{1}$$

By convention, eigenvectors are ordered according to ascending eigenvalues. The graph Fourier transform (GFT) of a graph signal represented by a vector $\mathbf{x}$ of length N is then obtained as $\hat{\mathbf{x}} = \mathbf{U}^T\mathbf{x}$, where $\mathbf{U}$ is an $N \times N$ matrix with all eigenvectors u_i in its columns.

Spectral band limitation was achieved by selecting the first $W = 180$ eigenvectors with smallest eigenvalues, and considering the $N \times W$ truncated GFT matrix $\mathbf{U}_W$. Then, we constructed the diagonal selection matrix $\mathbf{S}$ that put a weight $+1$ on the nodes of the DMN ($71/715$ nodes), a weight -1 on the nodes of the FPN ($39/715$ nodes), and 0 otherwise; see Fig. 1. The eigendecomposition of the $W \times W$ concentration matrix $\mathbf{C} = \mathbf{U}_W^T\mathbf{S}\mathbf{U}_W$ then leads to the spectral coefficients of graph Slepians that are bandlimited with maximal energy concentration in the DMN and minimal concentration in the FPN; i.e., we have

$$\mathbf{C}\hat{\mathbf{s}}_j = \mu_j \hat{\mathbf{s}}_j, \quad j = 1, \ldots, W, \tag{2}$$

where the eigenvalues μ_j of $\mathbf{C}$ represent the difference of energy concentrations in two subgraphs, respectively. The graph-domain Slepians can be retrieved as linear combinations of the Laplacian eigenvectors:

$$\mathbf{s}_j = \mathbf{U}_W\hat{\mathbf{s}}_j, \quad j = 1, \ldots, W. \tag{3}$$

All graph Slepians can be stacked together in the $N \times W$ Slepian matrix $\mathbf{Slep}$. A few example graph Slepians are shown in Fig. 2. The preprocessed task-based and resting-state fMRI timecourses are then organized in the matrices $\mathbf{X}_{\text{task}}$ and $\mathbf{X}_{\text{rest}}$, respectively, that have N rows and as many columns as the number of timepoints. The projection of the data in the Slepian space is then obtained as

$$\tilde{\mathbf{X}}_{\text{task}} = \mathbf{Slep}^T\mathbf{X}_{\text{task}} \tag{4}$$

$$\tilde{\mathbf{X}}_{\text{rest}} = \mathbf{Slep}^T\mathbf{X}_{\text{rest}} \tag{5}$$

Similarly, the data was also projected on the truncated GFT as

$$\hat{\mathbf{X}}_{\text{task}} = \mathbf{U}_W^T\mathbf{X}_{\text{task}} \tag{6}$$

$$\hat{\mathbf{X}}_{\text{rest}} = \mathbf{U}_W^T\mathbf{X}_{\text{rest}} \tag{7}$$

Notice that both projections are in principle lossy for bandwidth $W < N$.

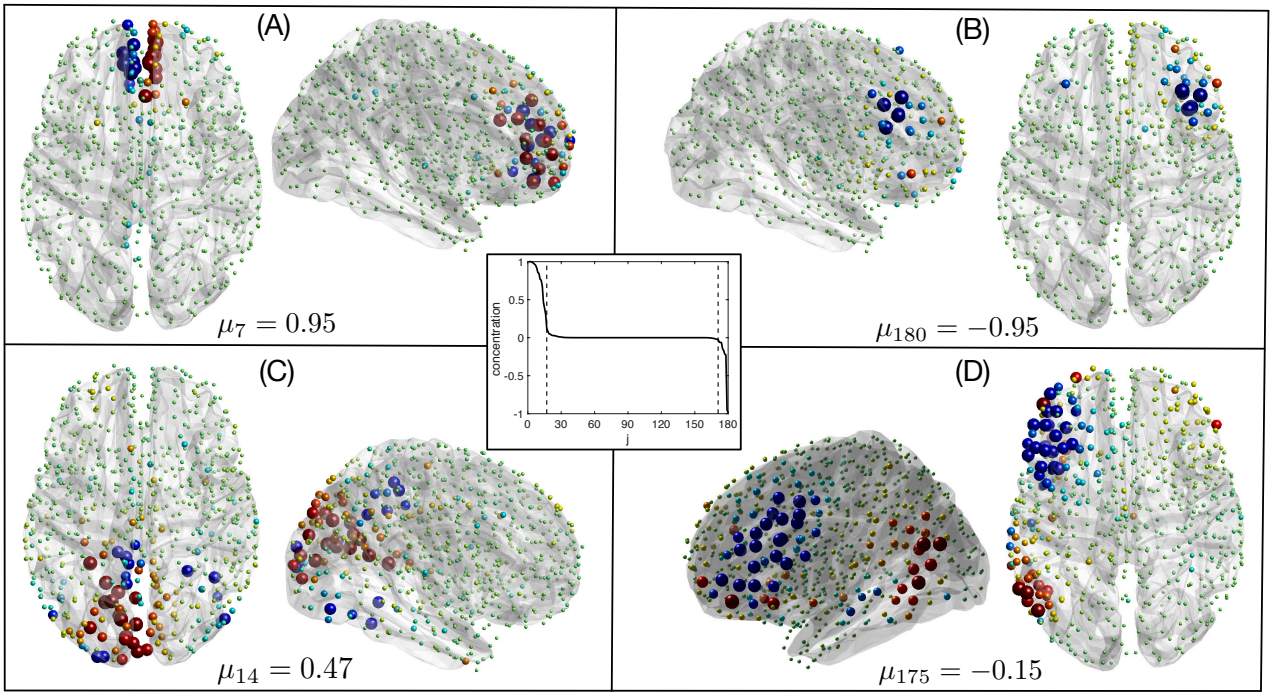

Fig. 2. Graphs Slepians for $W = 180$ with their concentration energy μ. (A) and (B) are strongly localized on the selection subgraphs (DMN and FPN, respectively), while for (C) and (D) an intermediate concentration allows to take into account other networks in the brain. In the middle, the concentration energy plot is reported and dashed vertical lines indicate the Shannon numbers for the two selections.

3. RESULTS AND DISCUSSION

The choice of the bandwidth parameter is an important handle to control the trade-off between local and global network organization in the Slepian design. For bandwidth $W = 180$, the Shannon number of classical Slepian function indicates $180 \times 71/715 = 17.9$ for the positive DMN selection, and $180 \times 39/715 = 9.9$ for the FPN selection. For a regular graph, these would be the number of graph Slepians that are well concentrated in each subgraph.

A few example Slepians are showed in Fig. 2, for the selected bandwidth $W = 180$. It is possible to notice that the Slepians that have high energy concentrations (i.e., in DMN or FPN) are localized on parts of these subgraphs, with no interaction with the rest of the graph (Fig. 2 A-B). Interestingly, the Slepian graph focused on the frontal DMN (Fig. 2 A) splits left and right hemispheres, shown with opposite signs, while the one focused on the frontal FPN includes mostly nodes of the right hemisphere (Fig. 2 B). A more interesting view on connectivity is offered by the moderately concentrated Slepians (in the so-called "phase transition" range), showing interactions between within-subgraph and whole-brain nodes; e.g., Fig. 2 C-D. In Fig. 2 C, for instance, only the dorsal portion of the posteromedial DMN is depicted (in blue), together with additional occipital and temporal regions, while Fig. 2-D shows the frontal part of FPN together with prefrontal cortex opposed to temporal regions. This goes in line with the more recent studies reporting a complex dynamic interplay between functional networks, which are composed by different subgraphs possibly acquiring different functional roles and continuously evolving in time [6, 5, 16].

When projecting task-based fMRI data onto the Slepian basis, we can notice how these coefficients nicely reveal switches between task-positive and task-negative patterns w.r.t. to the experimental paradigm (see Fig. 3). On the contrary, the Laplacian framework based on the same structural backbone does not clearly capture these temporal features of functional data although the same linear subspace is spanned.

When projecting the resting-state fMRI data, the obtained time-dependent coefficients cannot be compared against a paradigm, but we have computed the correlation matrices; see Fig. 4. Clearly, the first graph Slepians, which are strongly localized in the DMN, show positive correlation while being mostly anti-correlated with Slepians that have low energy concentration in the DMN, including those that are localized in the FPN. Again, the Laplacian eigenbasis does not provide this insight.

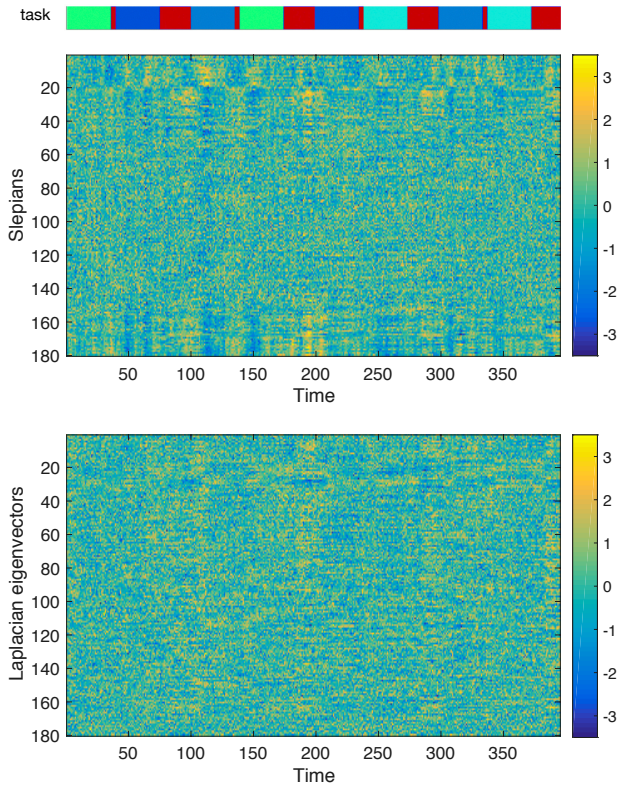

Fig. 3. Working memory task-based fMRI data projected onto Slepian basis (top panel) and onto the Laplacian basis (bottom panel). On the top, the task paradigm is illustrated along time, with the following color code for the type of visual stimulus: red = fixation, dark blue = tools, light blue = faces, turquoise = body, green = places.

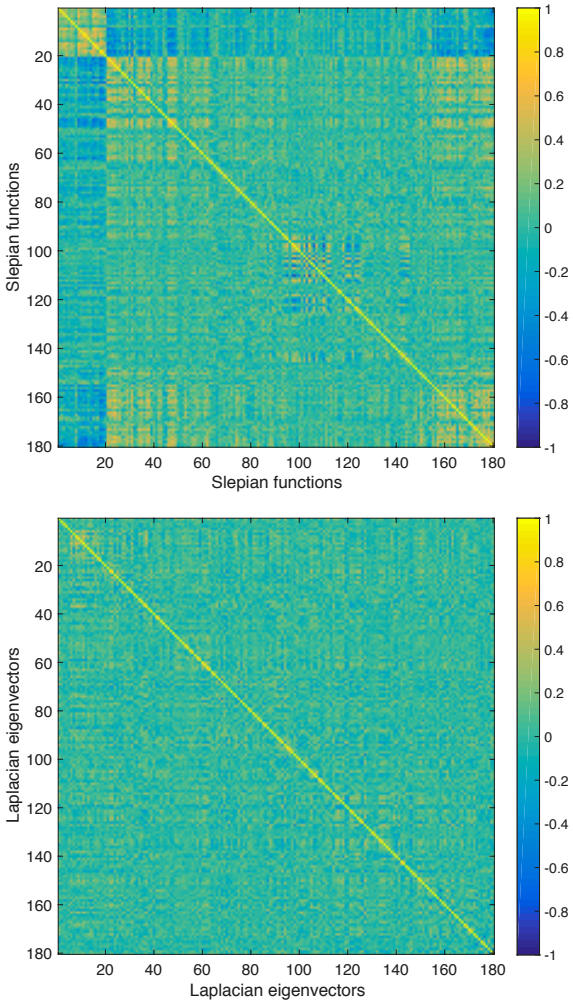

Fig. 4. Correlation matrix between timecourses of Slepian (top) and Laplacian (bottom) coefficients obtained from resting-state fMRI data.

4. CONCLUSION

We showed that recent advances in graph signal processing, and graph Slepian designs, in particular, can be applied to brain network analysis. Structural connectivity from diffusion-weighted MRI provides the information for the graph structure, while functional signals are analyzed on top of this backbone. While the Laplacian eigenvectors of the graph capture main modes of structural organization, the Slepian concept then allows to inject prior knowledge about functional network organization and, in particular, study how brain structure supports interactions between task-positive and task-negative networks, for instance. As a proof-of-principle, we showed for a single subject from the HCP dataset that this leads to new representations of fMRI data that are potentially useful both for task and resting-state.

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