Graph signal processing for identifying structure-function coupling using multimodal brain imaging with fMRI and MEG

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***Abstract*— Understanding how brain dynamics emerge from and are constrained by the underlying neuronal connectivity structure is a central question in neuroscience. Graph harmonic analysis has been used to quantify the coupling between the structural connectome and slow (0.01-1 Hz) brain activity fluctuations measured with functional magnetic resonance imaging (fMRI), revealing a macroscale gradient of the structure-function coupling that aligns with the unimodal-transmodal cortical organization. Magnetoencephalography (MEG) yields access to millisecond-resolution brain dynamics, enabling the spectral characterization of fast (1-100 Hz) neuronal oscillations. Neuronal oscillations are fundamental for healthy brain function, providing a temporal clocking mechanism for neuronal communication. Yet, how the rich spatiotemporal patterns of oscillation dynamics are related to the brain's structural connectome has remained poorly understood. To address this knowledge gap, we implemented the graph harmonic analysis to investigate how MEG oscillatory activities are constrained by the structural connectome and to evaluate their similarities with fMRI. Our results demonstrate that graph harmonic analysis can be used to quantify frequency-dependent MEG structure-function relationships. Furthermore, we show a partial similarity between MEG and fMRI imaging modalities and their relation to the structural network, particularly in neural oscillations between 10-20hz. This work characterizes how neural oscillations flow on top of the structural network.**

Keywords*— *Graph harmonic analysis, structure-function coupling, MEG, fMRI

I. Introduction (*Heading 1*)

In neuroscience, the structure-function coupling (SFC) refers to the relationship between white matter structural pathways (i.e., the brain structural connectome (SC)) and the time-dependent activity of neural populations [1]. Investigating the SFC is of primary importance to understanding how functional brain networks emerge from the structural topology [2]. The SFC has been studied using different methods, including statistical models correlating functional and structural connectivity patterns, linear regression models predicting functional connectivity from a set of structural-derived predictors, and biophysical models simulating functional activity of structurally connected neural populations [1], [3]. In recent years, the SFC in the human brain has been investigated using graph signal processing (GSP) methods, in particular, graph harmonic analysis [4], [5]. In neuroscience, GSP is appealing due to the modeling of the macroscale brain structure as a graph (with brain regions representing graph nodes and their inter-areal structural connections representing graph edges), on top of which neural signals flow. Thus, GSP methods are particularly useful to resolve the relationship between brain structure and function. Here, using the eigendecomposition of the structural graph Laplacian, we decomposed neural functional activity as the linear combination of SC harmonics (Fig. 1) [5].

Using graph harmonic analysis, neural activity is decomposed into two distinct components and indexed by the Structural Decoupling Index (SDI), a nodal measure quantifying the SFC [5]. The first component represents the portion of regional activity aligned with the structural connectome, henceforth referred to as 'coupled'. This coupled part indicates a similar activity pattern across structurally connected regions. The second component corresponds to the part of the signal exhibiting sharp variations between topological neighbors, henceforth termed 'decoupled'. The ratio of the decoupled to coupled signal components - the SDI - directly quantifies the degree of SFC of a brain region in terms of the amount of signal being (un)constrained by the SC [5], [6], [7]. Previous studies using graph harmonic analysis on fMRI data showed that the brain SFC is regionally heterogeneous, with stronger correspondence in unimodal (sensory) cortices and weaker correspondence in transmodal (associative) cortices [3], [5]. Compared to fMRI,

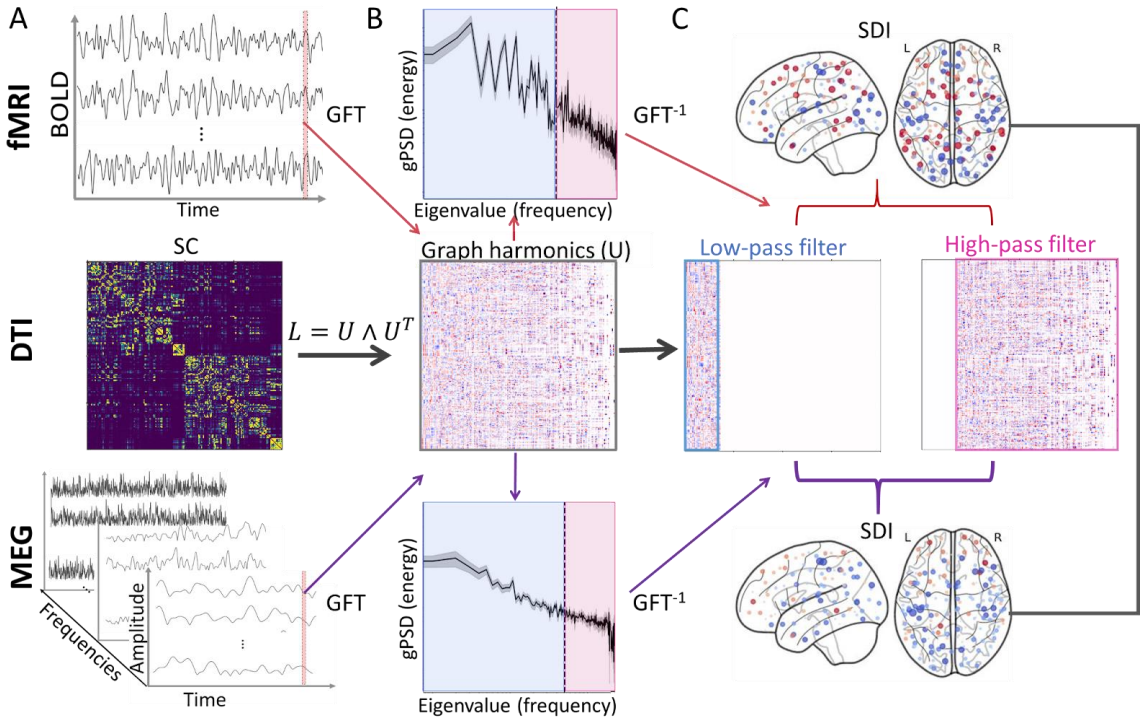

Figure1. Workflow of decomposition of fMRI and MEG functional signals with respect to the structural network. The workflow is the same for both imaging modalities, but is implemented independently. Note that the lower part of B) and C) exemplified only one MEG frequency at 10 Hz. **A)** Structural and functional data modalities and Graph Fourier transform (GFT). For each time frame, the vector of the BOLD activity (top) or amplitude envelope (bottom) across brain regions was projected into the eigenvectors (graph harmonics, U) of the structural connectivity (SC) graph Laplacian (L) (middle), producing the Fourier coefficients of the signal. **B)** The graph power spectrum density (gPSD) plots show the spectral energy distribution across graph frequencies. A cut-off (dashed vertical line in gPSD plots) splitting the total energy across graph frequencies in half was used to split harmonics into low-frequency (LF) and high-frequency (HF) harmonics. **C)** Inverse graph Fourier transform (GFT^{-1}) and structural decoupling index (SDI). By projecting the Fourier coefficients in LF or HF harmonics (low and high filters, respectively), it is possible to reconstruct the signal in two different components: one corresponding to the part of the signal that is constrained by the SC (coupled); the second corresponding to the part of the signal that is unconstrained by the SC (decoupled). The structural decoupling index (SDI) is the ratio between the norms across time of decoupled and coupled signals for each brain region. The SDI represents the coupling (blue nodes in brain plots) or decoupling (red nodes in brain plots) between a brain region and the SC. Finally, we correlated the fMRI and MEG frequency-specific SDI patterns.

electrophysiological methods track neuronal activity with millisecond precision, allowing for the mapping of the spectral frequency content of neuronal signals. In humans, non-invasive magneto- and electro-encephalography (M/EEG), especially MEG, when combined with source reconstruction, yields spatially precise information [8]. These data capture neuronal activity characterized by rhythmic excitability fluctuations—neuronal oscillations—which are abundant across the brain's hierarchy and spatiotemporal scales and are thought to play a fundamental role in the dynamic routing of neuronal signaling [9]. Yet, in contrast to fMRI, there is a scarce understanding of how oscillation dynamics emerge from the underlying brain structural connectome.

In the present study, our aim was to analyze the SFC in the rich spectral dynamics of MEG data and its similarity to the SFC in fMRI. To do so, we implemented the graph harmonic decomposition using structural, hemodynamic, and electrophysiological data from N = 75 healthy participants. First, we filtered source-reconstructed MEG data into narrowband time series using 40 Morlet wavelets with center frequencies spanning between 1-96 Hz. Next, we assessed SFC across MEG frequencies and BOLD time courses from fMRI. Finally, we evaluated the correspondence in the SFC between MEG and fMRI (Fig. 1). Our findings suggested that the SFC in MEG is frequency-dependent and that the SFC observed in MEG and fMRI is also correlated in a frequency-specific manner.

II. Methods

A. Participants

Brain structural and functional data were recorded from 75 subjects (45 males, 29 females, 1 unreported gender) with a mean age of 31.89 years, ranging from 18 to 62 years. This study was conducted in accordance with the Declaration of Helsinki. All procedures were approved by the Ethical Committee of the Helsinki and Uusimaa Hospital District. All participants gave written informed consent before participating in the study.

B. MRI acquisition and fMRI

T1-weighted MRI diffusion-weighted imaging (DWI) and 15-minute eyes-open resting state (RS) fMRI scans were obtained with a 3 Tesla MRI scanner (Magnetom Skyra, Siemens, Munich, Germany) at AMI Centre, Aalto University, using a 32-channel head coil. T1-weighted MRI was recorded using an MP-RAGE protocol with a resolution of 1×1×1. DWI data were recorded with a resolution of 3.0×3.0×3.0 mm, repetition time of 4100 ms, and echo time of 105 ms. Additionally, T2*-weighted images were obtained to optimize brain parcellation and co-registration. The fMRI

measurements were taken with 3mm isometric resolution with a TR = 1.25 seconds and echo time = 30ms.

Functional time courses were obtained after preprocessing with fMRIprep, which included slice-time correction, resampling onto native space, co-registration to the T1w reference, and nuisance regression (DVARS, white matter, CSF, and global signals). Component-based noise correction (CompCor), and high-pass filtering were also applied. Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardized DVARS were annotated as motion outliers and regressed from the final time series.

After preprocessing, subject-level BOLD time series for 200 cortical brain regions from the Schaefer atlas were obtained and z-scored across time.

C. MEG data acquisition, preprocessing, and source reconstruction

15-minute eyes-open resting-state MEG data were recorded with 306-channel MEG (Megin Oy, Helsinki) either at BioMag laboratory in the Helsinki University Hospital or at MEG Core in Aalto University. Data preprocessing and source reconstruction were performed with the MNE-python software (https://mne.tools/stable/index.html) [10]. Temporal signal space separation (tSSS) was used to suppress extracranial noise from MEG sensors, interpolate bad channels, and compensate for head motions. Independent components analysis (ICA) was used to remove artifacts related to ocular, heartbeat, and muscle.

MNE software was used for MEG–MRI colocalization and for preparing forward and inverse operators for source reconstruction. Noise covariance matrices (NCM) were obtained from preprocessed data filtered to 151 – 249 Hz. Source reconstruction was performed with minimum norm estimation (MNE) using dynamic statistical parametric maps (dSPM). The source models had dipole orientations fixed to pial-surface normals. Source vertices were collapsed into 200 parcels of the Schaefer atlas by using fidelity-weighted collapsing operators. Broadband parcel time series were then filtered into narrowband time series by convolution with 40 Morlet wavelets at center frequencies spanning from 2 to 96 Hz in log-linear space. Node (parcel)-level oscillation amplitudes were z-scored across time for each frequency.

D. Structural connectivity

Subject-level structural connectomes (SC) were constructed from individual DWI data such that edges corresponded to the number of white matter connections between parcels of the Schaefer atlas. For subsequent analysis, a group-averaged SC was computed as the average of the subjects' SC.

E. Graph signal decomposition and structural decoupling index

Brain regions' functional data (either BOLD activity or MEG frequency-specific amplitudes) were expressed as the weighted linear combination of the eigenvectors (also called graph harmonics, U) of the group structural connectivity graph Laplacian (L) (Fig. 1A). The graph eigenvectors are the analog in a graph of the Fourier basis in classical signal processing. Therefore, the graph Fourier transform (GFT) of the signal produces the graph Fourier coefficients associated with each harmonic:

$$\hat{x}(t)=U^{T}x(t) \quad (1)$$

The total amount of energy in each graph frequency (Fig. 1B, see graph power spectrum density (gPSD) plots) corresponds to the square of its Fourier coefficient averaged across time. A subject-specific cut-off splitting the total energy across graph frequencies in half was used to divide the harmonics into two sets [5]. Graph harmonics below the cut-off represent global patterns of smooth variation across topological neighbors and were labeled low-frequency (LF) harmonics. Complementary, high-frequency (HF) harmonics, above the cut-off, denote sharp variation across neighbors. LF and HF harmonics were used as spectral filters U_L and U_H (Fig. 1C). U_L corresponds to a matrix with the same dimensions as U, retaining LF harmonics and zeros everywhere else, and U_H corresponds to a matrix with only HF harmonics and zeros everywhere else (Fig. 1C). By multiplying the Fourier coefficients with these spectral filters (inverse graph Fourier transform), we obtained, in the spatial domain, the coupled and decoupled components of the original signal, such as:

$$x_c(t)=U_L\hat{x}(t) \quad (2)$$

$$x_d(t)=U_H\hat{x}(t) \quad (3)$$

Then, the structural decoupling index (SDI) was computed for each brain region as the ratio between the l2- norm across time of x_d and x_c (Fig. 1C) [5]. This metric quantifies the (de)coupling between the regional activity and the underlying SC. For visualization purposes, SDI values are log2 transformed, so negative values are associated with a higher SFC, and positive values with a lower SFC.

F. Statistical analysis

To estimate the significance of our results, we created two types of surrogate data [5] [11]. First, to test the significance of the whole-brain frequency-dependent pattern of SDI (see result section 'Structure-function coupling in MEG'), we compared the parcel-level SDI values with those of 100 surrogates, which were generated by shuffling the signs of the brain harmonics with their respective Fourier coefficients. This allowed for the comparison of observed SDI values against the SDI from surrogate signals with an altered structure-function relationship, but the same energy distribution across harmonics as the observed signal.

Second, to assess the significance of the SDI frequency-dependent correlation pattern between MEG-frequencies and fMRI (see result section 'SDI correlation fMRI-MEG'), we compared the observed fMRI-MEG SDI correlation with the correlation between observed MEG SDI and a 1000 surrogates fMRI SDI obtained from the projection of the observed fMRI signal in a randomized structural connectome [11]. By correlating these surrogates with the observed SDI values in MEG, we assessed whether the observed fMRI-MEG correlation was explained by a trivial correspondence between MEG amplitude and BOLD signals.

III. Results

A. Structure-function coupling in fMRI

Across participants, the cut-off splitting harmonics in low-frequency (LF) and high-frequency HF ranged from 25 to 42 (median value across participants = 35), corroborating that the graph spectral energy distribution in fMRI is higher in LF compared to HF harmonics [5]. In fMRI, we found that the negative SDI values corresponding to the strongest SFC were in parcels of the visual and somatomotor networks. Conversely, positive SDI values corresponding to the decoupled regions were primarily found in parcels of the control, dorsal, and ventral attention networks, while the default mode network appeared halfway between coupling and decoupling (Fig. 2A).

B. Structure-function coupling in MEG

In the MEG data, the cut-off splitting harmonics in LF and HF varied across frequencies and subjects (Fig. 2B). At lower MEG frequencies, from the delta to theta bands (1–7 Hz), the median cut-off across subjects gradually decreased from 67 to 57. It reached a minimum value of 53 in the low alpha band (8–12 Hz), then increased progressively in the beta band (13–30 Hz) from 55 to 68. Finally, it reached a plateau in the gamma band (40–96 Hz) with a cut-off equal to 73.

The negative SDI values corresponding to the coupled areas were widespread over the cortex, particularly in somatomotor and visual networks, while the positive SDI values corresponding to decoupled areas were found mostly in the prefrontal cortex (Fig. 2C). The parcel-SDI values across MEG frequencies were highly correlated (Spearman correlation test, mean across frequencies r = 0.89), except for alpha frequency (8-12Hz) in which the correlations with other frequencies were relatively smaller but still significant (Fig. 2D).

To assess the whole-brain tendency of MEG oscillations to be coupled or decoupled with the SC, the SDI was averaged across parcels, showing that MEG activity across frequencies tend to be coupled with the SC (Fig. 2E). Furthermore, similar to the cut-off values distribution across frequencies, the whole-brain SDI showed a peak in the alpha band, corresponding to a higher global coupling in the brain (peak in negative SDI) compared to other MEG frequencies. The whole-brain decoupling was significantly different from the surrogate data, specifically between 10-20 Hz (Fig. 2E) (see methods). Importantly, our results are unlikely to be explained by the higher power in the alpha band since time-course amplitudes were z-scored across time, thereby normalizing the power across MEG frequencies. Furthermore, the absence of alpha peaks in surrogate signals indicates a genuine specificity of SFC in the alpha frequency band.

C. Correlation of SDI between fMRI and MEG

To assess the correspondence between the SFC across brain imaging modalities, we computed the correlation between the fMRI and MEG frequencies of the parcel-level SDI values (Fig. 3A). The correlation values were stronger compared to the surrogate data for all frequencies. Moreover, the correlation peaked in the alpha band, which had the lowest SDI values, i.e., the strongest coupling (r = 0.28 at 10 Hz). When detailing the parcel-level characteristics in the correlation of SDI values between 10 Hz and BOLD, we found a strong average correlation (r = 0.53), with a higher correspondence in unimodal regions, including visual and somatomotor networks (Fig. 3B).

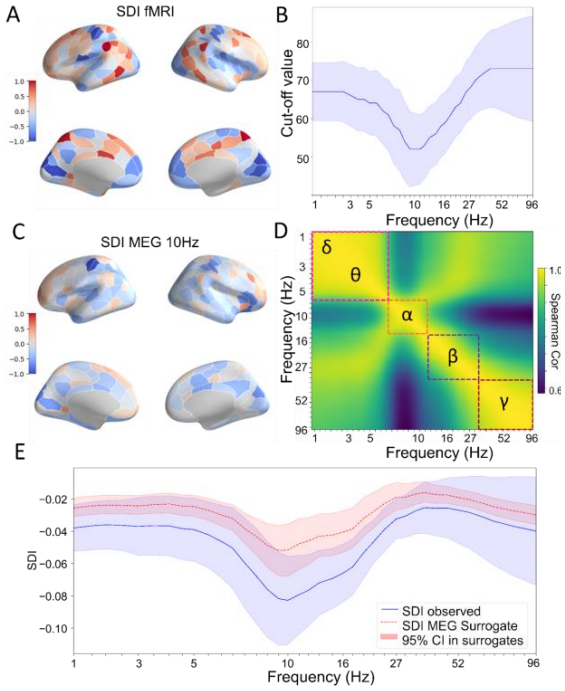

Figure 2. Structural decoupling index (SDI) in fMRI and MEG. A) The cortical pattern of fMRI SDI values in the 200 parcels of the Schaefer atlas. SDI values are log2 transformed, so blue corresponds to coupling and red to decoupling. B) Cut-off values across MEG frequencies splitting the total spectral energy across harmonics in half. C) SDI pattern across brain parcels for the MEG frequency with the lowest cutoff (10Hz). D) Spearman correlation across MEG frequency bands for parcel-level SDI values. E) Whole-brain average over 200 parcels of the log2 transformed SDI values across MEG frequency bands. The blue line indicates the observed SDI value from N = 75 participants, and the red dashed line indicates the mean SDI across surrogates (SDI_sur_MEG). Shaded areas represent 95% confidence intervals.

IV. Discussion

In the present study, using graph harmonic decomposition, we investigated the SFC in fMRI and MEG in terms of the smoothness of hemodynamic or electrophysiological brain activity on top of the structural network. To quantify the SFC, we used the structural decoupling index (SDI) [5], which assesses whether brain signals (in the present work either BOLD activity or brain oscillations) change progressively (coupled), contrary to sharply (decoupled) across structurally connected brain regions.

Our findings reveal how the rich spectrotemporal patterns of MEG data relate to the SC in a frequency-specific manner. The lowest cut-off values across frequencies were observed in the alpha band, with LF harmonics exhibiting more energy than HF harmonics, suggesting a tendency for alpha oscillations to be more constrained by the SC. This was paralleled by a negative peak at around 10 Hz in the whole-brain SDI and a significant SFC from 10-26 Hz, demonstrating higher SFC in the alpha-beta frequencies compared to other frequency bands.

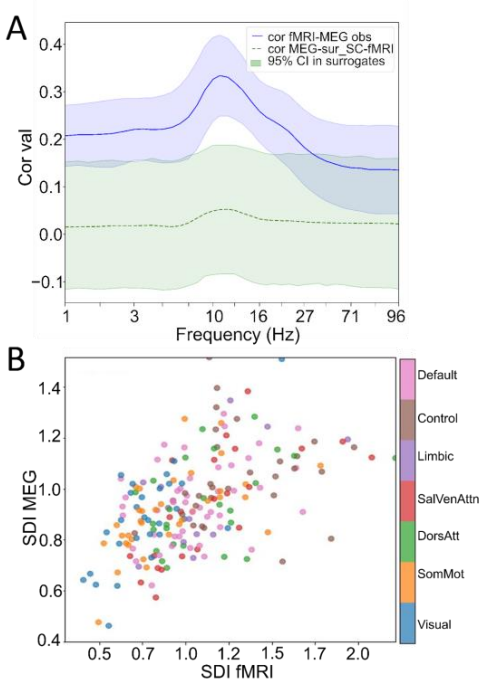

Figure 3. A) Correlation of the parcel-level SDI values between fMRI and MEG frequencies showing a significant correlation between 1-20 Hz. The blue line indicates the average correlation across subjects for each MEG frequency, and the green dashed line corresponds to the surrogate mean SDI obtained from the projection of the observed fMRI signal in a randomized structural connectome. Shaded areas represent 95% confidence intervals. B) Parcel-level SDI correlation between fMRI and MEG at 10Hz. Nodes are colored according to the Yeo 7 Networks.

This is in partial accordance with previous investigations examining the global similarity between SC and MEG frequencies, which showed higher correspondence between the SC and the beta band functional network [12], [13]. Here, we found a higher SFC (negative SDI) in the high-alpha to beta frequency range (10-26 Hz). Methodological differences to compute the whole-brain SFC could explain the discrepancy in the results. In this study, we measured SFC based on the smoothness of the signal across topological neighbors rather than calculating the correlation between structural and functional connectivity matrices, as in [12] and [13]. Furthermore, as shown in previous implementations of GSP on electrophysiological data, the SDI pattern across brain regions was highly similar across MEG frequency bands [7], [14], indicating that the specificity in alpha is due to an increased magnitude in the SFC across brain regions. The highest SFC in the alpha-beta band is intriguing since decades of research have associated these oscillations with global brain resting rhythms [15].

Consistent with the frequency-dependent SFC results, MEG SDI in the 10–20 Hz range showed the strongest correlation with fMRI SDI. This indicates that both BOLD activity and MEG amplitude in the alpha-beta band are similarly influenced by the underlying structural network. These results are in line with previous investigations correlating fMRI and MEG functional connectivity matrices [13], [16]. Importantly, the overall low correlation values in our results indicate that even though there are similarities in the SFC between fMRI and MEG signals, a large part of these signals arises via independent mechanisms, which is expected given the different nature of the brain signals (hemodynamic vs. neural activity).

In summary, we employed graph signal processing to investigate the SFC, utilizing graph harmonic analysis in MEG and fMRI data recorded from the same participants. Our results highlight a particular trimodal correspondence between oscillations in the alpha-to-beta band, BOLD activity, and the structural connectome.

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