Brain activation mapping based on Regional Synchronization of fMRI signals embedded in Graph Eigenmodes

Zhenyu Tang[1], Yu Zhao[2⋆], Yang Yang[1], Xiaoyu Liu[3], and Jingyong Su[1⋆]

[1] Harbin Institute of Technology, Shenzhen
[2] Department of Radiology, West China Hospital of Sichuan University
[3] University of Pennsylvania
sujingyong@hit.edu.cn, zhaoyu.mri@wchscu.cn

Abstract. Functional magnetic resonance imaging (fMRI) analysis models the detected temporal signals as a superposition of linear hemodynamic responses (HDR) to task-related stimuli, yielding spatial maps of brain function. However, recent studies have demonstrated that neural responses exhibit significant nonlinearity, challenging the validity of such linear models. In this work, we propose a novel mathematical framework, Regional Synchronization based on Graph Eigenmodes (RS-GEm), to analyze fMRI data and localize brain activation without relying on the linear assumptions of traditional models. Using Laplacian Eigenmaps (LEM), we capture the graph structure of the brain and derive its eigenmodes. These eigenmodes characterize possible spatial organizations of neural activity across different hierarchical levels of the human brain. By computing the regional synchronization of fMRI signals embedded in the eigenmode space and employing clustering metrics, we extract task-relevant eigenmodes to identify task-evoked activation regions. Validations on the Human Connectome Project (HCP) dataset demonstrate that our method can map task-evoked brain activations without the linear assumptions. The proposed approach offers a novel methodological framework for elucidating understudied aspects of brain function featured with nonlinear HDRs, thereby facilitating a more complete understanding of brain dynamics.

Keywords: fMRI · Brain activation mapping · Laplacian Eigenmaps · Nonlinear hemodynamic response · General linear model

1 Introduction

Functional magnetic resonance imaging (fMRI) is an important non-invasive tool for investigating the mechanisms of brain neural activity. fMRI captures temporal signals through the neurovascular coupling effect, which is considered as the linear superposition of predetermined hemodynamic responses to specific condition stimuli in fMRI tasks [3]. Based on this linear assumption, researchers can

⋆ Corresponding author.

use a general linear model to fit fMRI signals in the time domain and localize brain activity related to specific tasks or behaviors [13]. Widely used analysis tools, such as Statistical Parametric Mapping (SPM), are based on the general linear model. However, increasing evidence shows that the nonlinearity of neurovascular coupling [2, 19], along with spatial variations of brain hemodynamics[7, 9], challenging the linear assumption, leading to insufficient or inappropriate mapping of brain activation [12, 14]. Therefore, the development of a data-driven method without linear assumptions is essential for improving the detection capability of neural activity and advancing our understanding of the human cognitive neural architecture.

The human brain is an immense network composed of intricate neural circuits, capable of interacting with its complex surrounding environment. During the brain's neural computations, both local and long-range neurons coordinate and integrate their activities, resulting in the spatial organization of neural activity [8, 23]. This perspective offers novel insights for studying task-evoked neural activations in the human brain. In the emerging field of neural manifolds, neurobiological observations across different spatial scales have revealed that the brain exhibits a set of latent activity patterns [4, 15, 16]. These patterns encapsulate the coordinated behaviors of large populations of neurons. Furthermore, recent studies [1, 6, 11] suggest that the brain's neural dynamics can be understood through intrinsic spatial modes, which represent the system's fundamental resonance patterns. Among these approaches, Laplacian Eigenmaps (LEM) effectively exploit the graph-structured nature of brain networks, decomposing functional connectivity into distinct spatial eigenmodes. The coordinated excitation of these eigenmodes forms the foundation of the brain's spatiotemporal dynamics. From this perspective, we aim to characterize neural activity by identifying which spatial eigenmodes are activated in the human brain, extracting deep information embedded within these modes to detect task-related neural activations.

Inspired by the capacity of the Laplacian Eigenmaps (LEM) method to capture regional patterns of neural activity, we propose a novel framework, Regional Synchronization based on Graph Eigenmodes (RS-GEm), for detecting task-induced neural activation. In this framework, we first construct a brain graph that reflects the brain's intrinsic functional organization, derived from functional connectivity data. By applying the graph Laplacian operator, we decompose this graph structure and derive eigenmodes across different gradients. These eigenmodes uncover the deep connectivity structures of the brain, revealing neural coordination states across multiple hierarchical levels. Functional information within the local neighborhood of each voxel is derived from these eigenmodes and subsequently integrated using Principal Component Analysis (PCA) to compute the regional synchronization of voxels. This metric quantifies the degree of coordination between a voxel and its functionally related neighbors under task-induced conditions. By analyzing the clustering scores of regional synchronization across eigenmodes, we identify task-relevant eigenmodes and generate brain activation maps. Our method achieves accurate detection of task-induced activations at the individual level and identifies eigenmodes specifically associated with task stimulation, providing a novel perspective for analyzing brain dynamics.

2 Materials and Methods

2.1 Data Acquisition and Preprocessing

This work primarily utilized the preprocessed fMRI data from the Human Connectome Project (HCP) acquired on a 3T scanner, including resting-state fMRI (rfMRI) data from a subset of 800 participants and task-based fMRI (tfMRI) data from 100 unrelated adult participants [18, 20]. To assess within-subject reproducibility, HCP test-retest data from 45 participants were also incorporated.

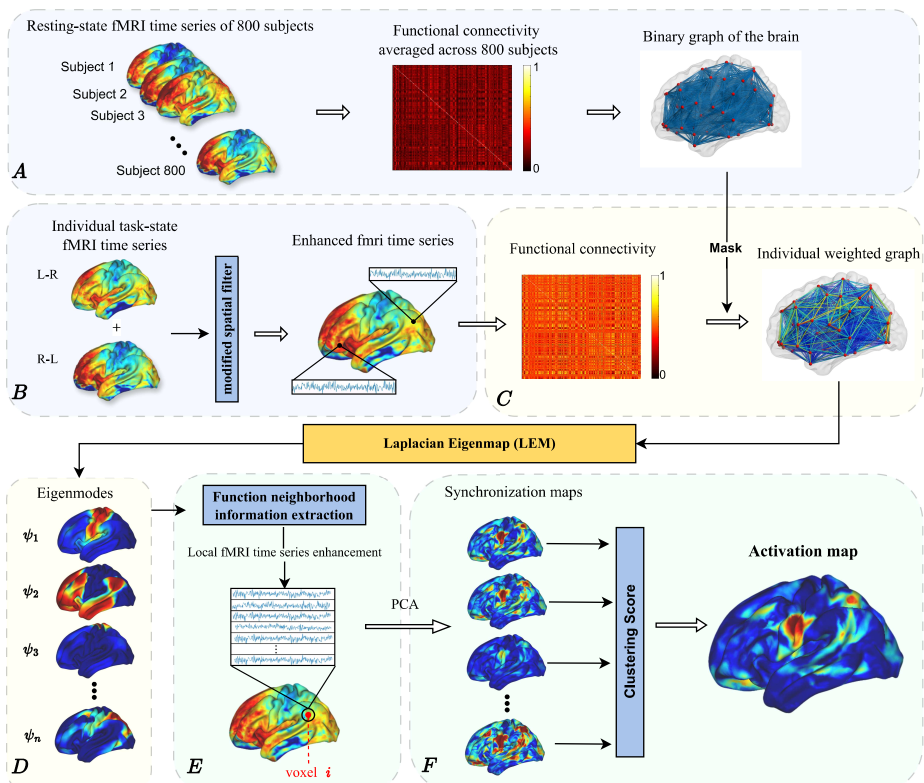

Fig. 1. The overall architecture of our proposed RS-GEm. (A, C) Group-level and individual-level brain graph construction. (B) Individual-level fMRI data processing. (D) Eigenmodes of the brain. (E) Regional Synchronization computation. (F) Task-related eigenmodes extraction and activation mapping.

We conducted additional processing on the preprocessed HCP data to enhance the quality of individual-level fMRI data characterized by a low signal-to-noise ratio (Fig. 1B). Based on the different phase-encoding directions in magnetic resonance imaging, the fMRI data were divided into two groups: from left to right (LR) and from right to left (RL). By integrating normalized LR and RL signals, we generated a new fMRI signal with an extended temporal dimension to improve voxel signal robustness and enhance the correlation of activated voxels [5]. Furthermore, we filtered the extended fMRI signal using a modified spatial filter linked to brain structure. Compared to traditional isotropic Gaussian filters, this filter leverages brain structural information to more accurately denoise and enhance the signal.

2.2 Individual Graph Construction and Eigenmodes

Laplacian Eigenmap (LEM) projects complex, high-dimensional brain signal data into a lower-dimensional space while preserving the intrinsic topological structure by maintaining the regional connectivity of the graph [10, 17]. To achieve this, we first construct a functional connectivity (FC) graph for the brain in the task state. Since individual-level signals often contain noise that disrupts graph structure, we calculate a group-level resting-state FC (rsFC) graph as a stable backbone (Fig. 1A) and integrate individual task-state FC data into this framework (Fig. 1C). This ensures stability while embedding individual-specific information.

The brain's communication structure is represented as a graph $\mathcal{G} = (\mathcal{V}, \mathcal{E})$, where $\mathcal{V}$ denotes the voxels sampled from the gray matter cortical surface as nodes ($n = 59,412$ in this work), and $\mathcal{E}$ represents edges based on correlations in the functional connectivity (FC) matrix. The adjacency matrix $\mathbf{A}$ is constructed from resting-state FC (rsFC) data by assigning edges ($a_{ij} = 1$) for the top k strongest correlations for each node, ensuring symmetry (with $k = 300$ in this work). This process results in a sparse, binary adjacency matrix $\mathbf{A}$, where $a_{ij} = 1$ if the correlation c_{ij} is among the k largest values in row i of the dense FC matrix, and $a_{ij} = 0$ otherwise.

To incorporate individual-specific information, task-state FC data are normalized and assigned as weights to the edges in $\mathbf{A}$, producing an individual-level weighted adjacency matrix $\mathbf{B}$. The graph Laplacian $\mathbf{L}_\mathcal{G}$ is then defined as the difference between the degree matrix $\mathbf{D_B}$ and the weighted adjacency matrix $\mathbf{B}$, *i.e.*, $\mathbf{L}_\mathcal{G} = \mathbf{D_B} - \mathbf{B}$. Here, the degree matrix $\mathbf{D_B}$ is a diagonal matrix where each diagonal element is the sum of the weights of all edges connected to the node.

The eigenfunctions $\Psi = \{\psi_1, \psi_2, \cdots, \psi_n\}$ are computed by solving the eigenvalue problem:

$$\mathbf{L}_\mathcal{G}\psi_i = \lambda_i \psi_i,\ i \in \{0, 1, \cdots, n\}. \tag{1}$$

The resulting eigenvectors Ψ represent the spatial activation patterns of the brain under different gradients, revealing the coordinated states of nodes in the graph (Fig. 1D). Nodes with similar eigenvector values tend to co-activate and participate in specific tasks or functional activities. Each eigenvector ψ_i corresponds to a unique spatial mode of brain organization, referred to as an eigenmode. These patterns project high-dimensional FC data into a lower-dimensional space, uncovering the hierarchical and distributed organization of brain function, analogous to harmonics in signal resonance [6].

2.3 Functional Similarity and Synchronization

These eigenmodes specifically reflect the coordination strength among voxels (*i.e.*, graph vertices) under a particular feature mode, indicating the synchronization level of voxel responses to task stimuli. Based on these eigenmodes, we further identified functional neighborhoods and analyzed regional functional characteristics of the voxels (Fig. 1E).

Specifically, if voxels i and j have similar values under an eigenmode ψ_m, they are considered to share similar functional roles and belong to the same functional neighborhood. For each voxel, we define its functional neighborhood $\mathcal{N}_r^m$, which consists of the r closest voxels in the eigenmode ψ_m. The similarity between voxels is quantified by a Gaussian kernel weight matrix $\mathbf{W}$, defined as:

$$W_{ij} = \exp\left(-\frac{d_{ij}^2}{2\sigma^2}\right), \tag{2}$$

where d_{ij} is the Euclidean distance between voxel i and voxel j in the eigenmode ψ_m, and σ controls the range of similarity.

Using the computed weight matrix $\mathbf{W}$, we construct the locally enhanced fMRI data matrix $\mathbf{X}_{W_i}$ for each voxel i, defined as:

$$\mathbf{X}_{W_i} = \mathbf{W}_{i\cdot} \cdot \left[\mathbf{x}_i, \mathbf{x}_1, \mathbf{x}_2, \cdots, \mathbf{x}_r\right], \tag{3}$$

where $\mathbf{W}_{i\cdot}$ is the weight vector for voxel i, and $\mathbf{x}_i, \mathbf{x}_1, \cdots, \mathbf{x}_r$ are the fMRI signals of voxel i and its functional neighbors. This matrix provides a weighted aggregation of fMRI signals within the functional neighborhood of voxel i, capturing its regional functional characteristics.

Next, we perform PCA on $\mathbf{X}_{W_i}$ and compute the contribution of the first principal component. To quantify this, we define a synchronization metric (Syn) as follows:

$$\mathrm{Syn}(m, i) = \frac{\lambda_0}{\sqrt{\lambda_0^2 + \lambda_1^2 + \lambda_2^2 + \cdots + \lambda_r^2}}, \tag{4}$$

where $\lambda_0, \lambda_1, \cdots, \lambda_r$ are the eigenvalues obtained from PCA on $\mathbf{X}_{W_i}$, sorted in descending order, and m corresponds to the eigenmode ψ_m. The contribution of the first principal component reflects the linear correlation and consistency of the locally enhanced fMRI data [24], indicating the spatial coordination of signals within the functional neighborhood.

This synchronization metric captures the dynamic changes in fMRI data under various eigenmodes ψ_m, providing a quantitative measure of the coordinated activation of voxels in response to task stimuli. Specifically, it reflects the extent to which functionally related voxels exhibit synchronized responses under external task-driven conditions. By emphasizing the contribution of the first principal component, the metric highlights the dominant mode of regional coordination, effectively characterizing the cooperative activation of voxels.

2.4 Clustering Score and Activation Map

To evaluate the functional significance of eigenmodes, we introduce a clustering score to quantify the regional coherence of synchronization values within each eigenmode (Fig. 1F). Unlike the functional neighborhood $\mathcal{N}_r^m$, which is based on feature similarity, the clustering score uses the spatial neighborhood $\mathcal{N}_s$ derived from anatomical proximity. The clustering score is defined as:

$$\text{Clustering Score} = \sum_{i=1}^{n} \frac{1}{1 + \left(\text{Syn}(m,i) - \frac{1}{k_i} \sum_{j \in \mathcal{N}_s(i)} \text{Syn}(m,j)\right)^2}, \tag{5}$$

where $\text{Syn}(m,i)$ is the synchronization metric for voxel i, $\mathcal{N}_s(i)$ represents the spatial neighborhood of voxel i, k_i is the number of neighbors in $\mathcal{N}_s(i)$, and n is the total number of voxels. The clustering score evaluates the intensity of synchronization changes between a voxel and its spatial neighbors, which reflects the regional coherence of each eigenmode. This allows us to identify eigenmodes most relevant to task stimuli, as task-related patterns tend to exhibit higher regional consistency.

By calculating the clustering score, we identify the top four eigenmodes most relevant to task stimuli, where the brain exhibits stronger coordination under these eigenmodes. This provides a systematic method to link deep functional gradients to task-specific neural mechanisms. Finally, we compute the average synchronization map across these four eigenmodes to generate the final activation map of the task-related voxels.

3 Experimental Results

3.1 Activation Detection on Motor task

Based on the RS-GEm framework, we conducted an in-depth analysis of brain activity using the tfMRI data from the HCP dataset, focusing on the detection of task-related voxels. Taking the motor execution task as an example, the HCP dataset divides this task into 10 blocks (Fig. 2A), each consisting of a visual cue (3 seconds) followed by 10 motor trials (12 seconds). The motor task involves five types of movements: right hand, left hand, right foot, left foot, and tongue.

By analyzing the fMRI time series within each block, the RS-GEm method successfully captured high-intensity signals from functional subregions of the primary motor cortex (Fig. 2B). Furthermore, the neural activation regions induced by different motor subtasks corresponded, with fine granularity, to the functional body control map established in behavioral neuroscience (Fig. 2C). In the activation maps, we also observed minor neural activations that were not directly related to motor execution, which likely reflect background neural activity of the participants. At the individual level, the proposed method demonstrated exceptional accuracy in identifying task-related activation regions.

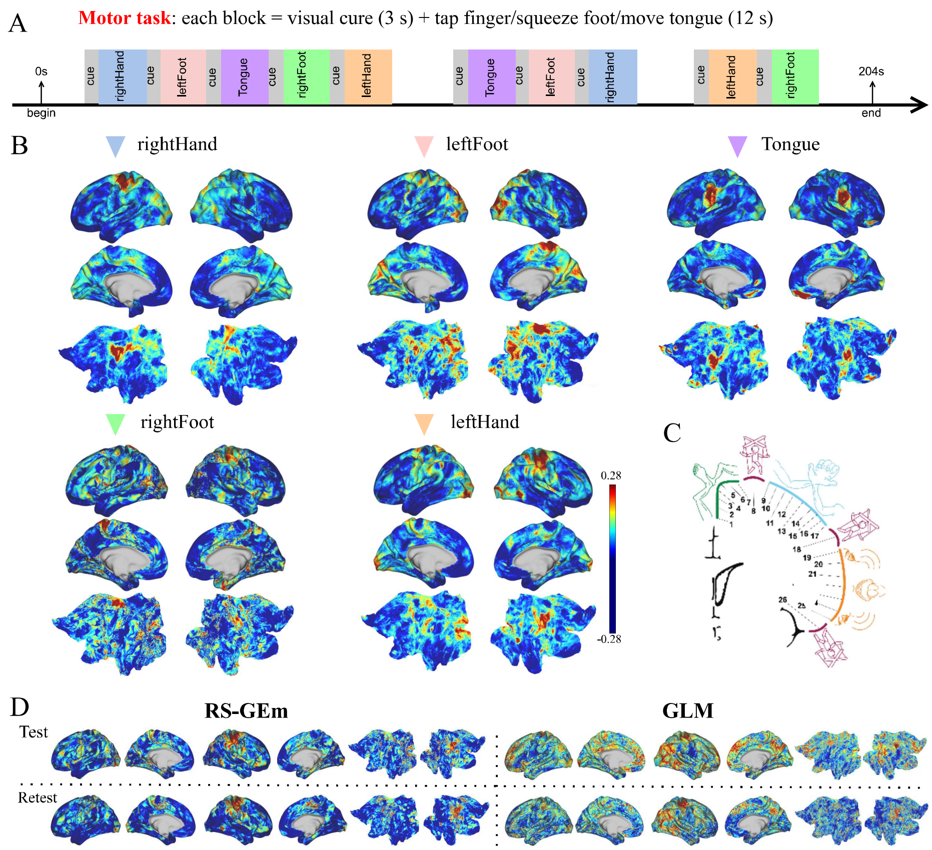

Fig. 2. Brain activation mapping for HCP motor task. (A) The diagram of the HCP motor task. (B) Activation maps in HCP motor task generated using RS-GEm. (C) Functional map of the human body control. (D) Activation maps for the left-hand motor task in the test-retest dataset generated using the RS-GEm and GLM methods.

The test-retest dataset provided by HCP was used to evaluate the within-subject reproducibility of the proposed method in detecting brain neural activations. This dataset includes 45 participants, each of whom underwent two repeated fMRI scans. We tested the activation maps associated with the left-hand motor task using both the RS-GEm method and the traditional GLM method within this dataset (Fig. 2D). The results show that, compared to the GLM, the

RS-GEm method demonstrates superior spatial consistency between test and retest data, underscoring its enhanced robustness and reliability in identifying neural activations.

3.2 Eigenmodes Analysis in Brain Activity

Distinct brain regions coordinate through synchronous fluctuations to achieve complex functions [21, 22]. Specific eigenmodes reveal the functional working modes of brain activity in different subdomains, where neurons collaborate with specific regions to perform specialized tasks under certain eigenmodes. The brain accomplishes specific tasks under the combined influence of multiple eigenmodes. Consequently, synchronization maps derived from different eigenmodes reflect the degree of voxel-level coordination within specific functional modes.

Using the Clustering Score, eigenmodes with higher neural synchrony during task states can be identified, as these eigenmodes contribute more effectively to task performance. For the motor execution task, we observed that the top four eigenmodes with the highest scores across various motor subtasks consistently corresponded to the same eigenmodes (Fig. 3A), with Clustering Scores significantly exceeding those of subsequent eigenmodes. In the group-level analysis of resting-state data, these four eigenmodes exhibited high coordination in the motor cortex regions (Fig. 3B), further validating the practical significance and effectiveness of the eigenmodes in analyzing neural activity.

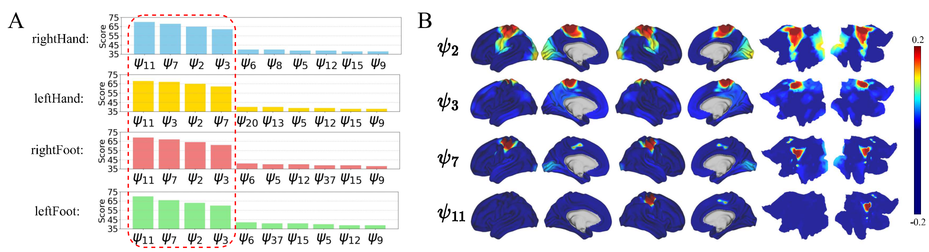

Fig. 3. Task-relevant eigenmodes identified using the Clustering Score. (A) The top four eigenmodes with the highest Clustering Scores during the motor execution task. (B) Four eigenmodes show high coordination in motor cortex regions.

4 Conclusion

In this study, we proposed RS-GEm, a novel framework that leverages graph eigenmodes to detect brain activity. By constructing individualized weighted brain networks and deriving distinct eigenmodes through Laplacian Eigenmaps, RS-GEm quantifies regional synchronization to reliably identify task-evoked activations. Our findings demonstrate that RS-GEm achieves high sensitivity at the individual level and exhibits strong stability in detecting task-induced activations. Furthermore, the extracted eigenmodes provide valuable insights into hierarchical neural coordination, revealing that brain activation arises from the complex interplay of distributed functional regions. This framework offers a powerful and flexible tool for analyzing neural activity, with the potential for application to the study of neurological and psychiatric disorders. Future work will focus on integrating multimodal data and exploring condition-specific paradigms to further validate the robustness of RS-GEm and deepen our understanding of large-scale brain dynamics.

Acknowledgments. This work was supported by National Natural Science Foundation of China (grant No. 62376068, U24A20340, 32361143787, 82302167), by Guangdong Basic and Applied Basic Research Foundation (grant No. 2023B1515120065), by Guangdong S&T programme (grant No. 2023A0505050109), by Shenzhen Science and Technology Innovation Program (grant No. JCYJ20220818102414031).

Disclosure of Interests. The authors have no competing interests to declare that are relevant to the content of this article.

References

1. Atasoy, S., Donnelly, I., Pearson, J.: Human brain networks function in connectome-specific harmonic waves. Nature Communications **7**(1), 10340 (2016)
2. Chuang, K.H., Li, Z., Huang, H.H., Khorasani Gerdekoohi, S., Athwal, D.: Hemodynamic transient and functional connectivity follow structural connectivity and cell type over the brain hierarchy. Proceedings of the National Academy of Sciences **120**(5), e2202435120 (2023)
3. Cohen, M.S.: Parametric analysis of fMRI data using linear systems methods. NeuroImage **6**(2), 93–103 (1997)
4. Cunningham, J.P., Yu, B.M.: Dimensionality reduction for large-scale neural recordings. Nature Neuroscience **17**(11), 1500–1509 (2014)
5. Finn, E.S., Shen, X., Scheinost, D., Rosenberg, M.D., Huang, J., Chun, M.M., Papademetris, X., Constable, R.T.: Functional connectome fingerprinting: identifying individuals using patterns of brain connectivity. Nature Neuroscience **18**(11), 1664–1671 (2015)
6. Glomb, K., Kringelbach, M.L., Deco, G., Hagmann, P., Pearson, J., Atasoy, S.: Functional harmonics reveal multi-dimensional basis functions underlying cortical organization. Cell Reports **36**(8) (2021)
7. Gonzalez-Castillo, J., Saad, Z.S., Handwerker, D.A., Inati, S.J., Brenowitz, N., Bandettini, P.A.: Whole-brain, time-locked activation with simple tasks revealed using massive averaging and model-free analysis. Proceedings of the National Academy of Sciences **109**(14), 5487–5492 (2012)
8. Leergaard, T.B., Bjaalie, J.G.: Atlas-based data integration for mapping the connections and architecture of the brain. Science **378**(6619), 488–492 (2022)
9. Lindquist, M.A., Loh, J.M., Atlas, L.Y., Wager, T.D.: Modeling the hemodynamic response function in fMRI: efficiency, bias and mis-modeling. NeuroImage **45**(1), S187–S198 (2009)

10. Ortega, A., Frossard, P., Kovačević, J., Moura, J.M., Vandergheynst, P.: Graph signal processing: Overview, challenges, and applications. Proceedings of the IEEE **106**(5), 808–828 (2018)
11. Pang, J.C., Aquino, K.M., Oldehinkel, M., Robinson, P.A., Fulcher, B.D., Breakspear, M., Fornito, A.: Geometric constraints on human brain function. Nature **618**(7965), 566–574 (2023)
12. Polimeni, J.R., Lewis, L.D.: Imaging faster neural dynamics with fast fMRI: A need for updated models of the hemodynamic response. Progress in Neurobiology **207**, 102174 (2021)
13. Poline, J.B., Brett, M.: The general linear model and fMRI: does love last forever? NeuroImage **62**(2), 871–880 (2012)
14. Robson, M.D., Dorosz, J.L., Gore, J.C.: Measurements of the temporal fMRI response of the human auditory cortex to trains of tones. NeuroImage **7**(3), 185–198 (1998)
15. Seelig, J.D., Jayaraman, V.: Neural dynamics for landmark orientation and angular path integration. Nature **521**(7551), 186–191 (2015)
16. Shine, J.M., Breakspear, M., Bell, P.T., Ehgoetz Martens, K.A., Shine, R., Koyejo, O., Sporns, O., Poldrack, R.A.: Human cognition involves the dynamic integration of neural activity and neuromodulatory systems. Nature Neuroscience **22**(2), 289–296 (2019)
17. Shuman, D.I., Narang, S.K., Frossard, P., Ortega, A., Vandergheynst, P.: The emerging field of signal processing on graphs: Extending high-dimensional data analysis to networks and other irregular domains. IEEE Signal Processing Magazine **30**(3), 83–98 (2013)
18. Smith, S.M., Beckmann, C.F., Andersson, J., Auerbach, E.J., Bijsterbosch, J., Douaud, G., Duff, E., Feinberg, D.A., Griffanti, L., Harms, M.P., et al.: Resting-state fMRI in the human connectome project. NeuroImage **80**, 144–168 (2013)
19. Tang, L., Avison, M.J., Gore, J.C.: Nonlinear blood oxygen level-dependent responses for transient activations and deactivations in v1—insights into the hemodynamic response function with the balloon model. Magnetic Resonance Imaging **27**(4), 449–459 (2009)
20. Van Essen, D.C., Smith, S.M., Barch, D.M., Behrens, T.E., Yacoub, E., Ugurbil, K., Consortium, W.M.H., et al.: The wu-minn human connectome project: an overview. NeuroImage **80**, 62–79 (2013)
21. Varela, F., Lachaux, J.P., Rodriguez, E., Martinerie, J.: The brainweb: phase synchronization and large-scale integration. Nature Reviews Neuroscience **2**(4), 229–239 (2001)
22. Vincent, J.L., Patel, G.H., Fox, M.D., Snyder, A.Z., Baker, J.T., Van Essen, D.C., Zempel, J.M., Snyder, L.H., Corbetta, M., Raichle, M.E.: Intrinsic functional architecture in the anaesthetized monkey brain. Nature **447**(7140), 83–86 (2007)
23. Yuste, R.: From the neuron doctrine to neural networks. Nature Reviews Neuroscience **16**(8), 487–497 (2015)
24. Zhao, Y., Gao, Y., Zu, Z., Li, M., Schilling, K.G., Anderson, A.W., Ding, Z., Gore, J.C.: Detection of functional activity in brain white matter using fiber architecture informed synchrony mapping. NeuroImage **258**, 119399 (2022)