Atlas-Free Functional Brain Connectome Analysis via Task-Driven Parcellation

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CODE

Summary

Selecting a suitable brain atlas for node definition is a critical yet challenging step in functional connectome analysis. A mismatched atlas can obscure subtle topographies and undermine the subsequent analysis. In this work, we propose an Atlas-Free functional brain CONnectome analysis (AFCON) that bypasses atlas selection by jointly optimizing an adaptive parcellation module and a graph-based connectome analysis module. Unlike classical methods reliant on fixed, predefined atlases, AFCON adaptively generates task-specific, individualized parcellations from fMRI data, which better aligns with the prediction task and offers enhanced interpretability. Besides, we introduce two neurobiologically-informed regularizers to ensure plausible parcellations: a balanced distribution regularizer to mitigate extreme parcel size imbalances and a spatial compactness regularizer to promote anatomical coherence. Experiments on ADHD and ADNI datasets demonstrate that AFCON outperforms atlas-based baselines in predictive accuracy while identifying disease-relevant brain regions, enhancing both interpretability and clinical relevance. Notably, this work focuses on the cerebral cortex, serving as an initial step towards potential whole brain connectivity analysis in the future for more robust clinical utility.

Framework

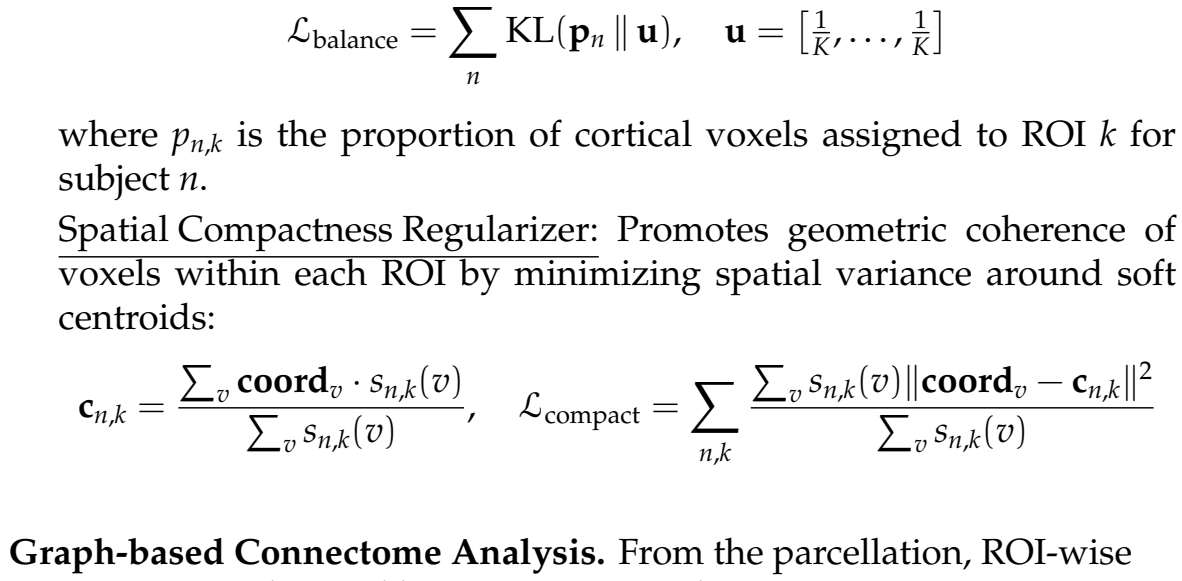


Figure: The overall framework of AFCON.

Adaptive Brain Parcellation. We apply a 3D U-Net to generate voxel-wise soft assignments of cortical voxels into K ROIs. During training, Gumbel-Softmax enables differentiable one-hot assignments; during inference, Argmax is used for deterministic parcellation.

To enhance biological plausibility, we introduce two regularizers:

Balanced Distribution Regularizer: To prevent extreme imbalances of ROIs sizes, we penalize deviation from a uniform volume distribution:

$$\mathcal{L}_{\text{balance}} = \sum_n \mathrm{KL}(\mathbf{p}_n \,\|\, \mathbf{u}), \quad \mathbf{u} = \left[\tfrac{1}{K}, \ldots, \tfrac{1}{K}\right]$$

where $p_{n,k}$ is the proportion of cortical voxels assigned to ROI k for subject n.

Spatial Compactness Regularizer: Promotes geometric coherence of voxels within each ROI by minimizing spatial variance around soft centroids:

$$\mathbf{c}_{n,k} = \frac{\sum_v \mathbf{coord}_v \cdot s_{n,k}(v)}{\sum_v s_{n,k}(v)}, \quad \mathcal{L}_{\text{compact}} = \sum_{n,k} \frac{\sum_v s_{n,k}(v) \|\mathbf{coord}_v - \mathbf{c}_{n,k}\|^2}{\sum_v s_{n,k}(v)}$$

Graph-based Connectome Analysis. From the parcellation, ROI-wise time series are obtained by averaging voxel time courses. We compute functional connectivity matrices $\mathbf{C}_n$ using Pearson correlation and retain the top 10% positive connections to form sparse brain networks $\mathbf{A}_n \in \mathbb{R}^{K \times K}$. We adopt a Graph Convolutional Network (GCN) to predict target labels:

$$\hat{y}_n = \mathrm{GCN}(\mathbf{A}_n, \mathbf{H}_n)$$

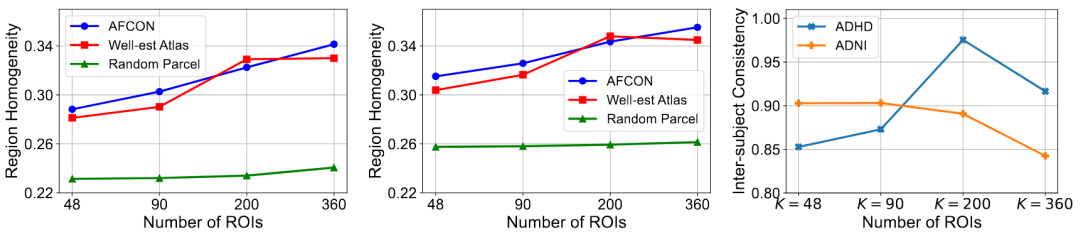
where $\mathbf{H}_n$ is the connection profile node feature matrix (i.e., rows of $\mathbf{C}_n$).

Experiments

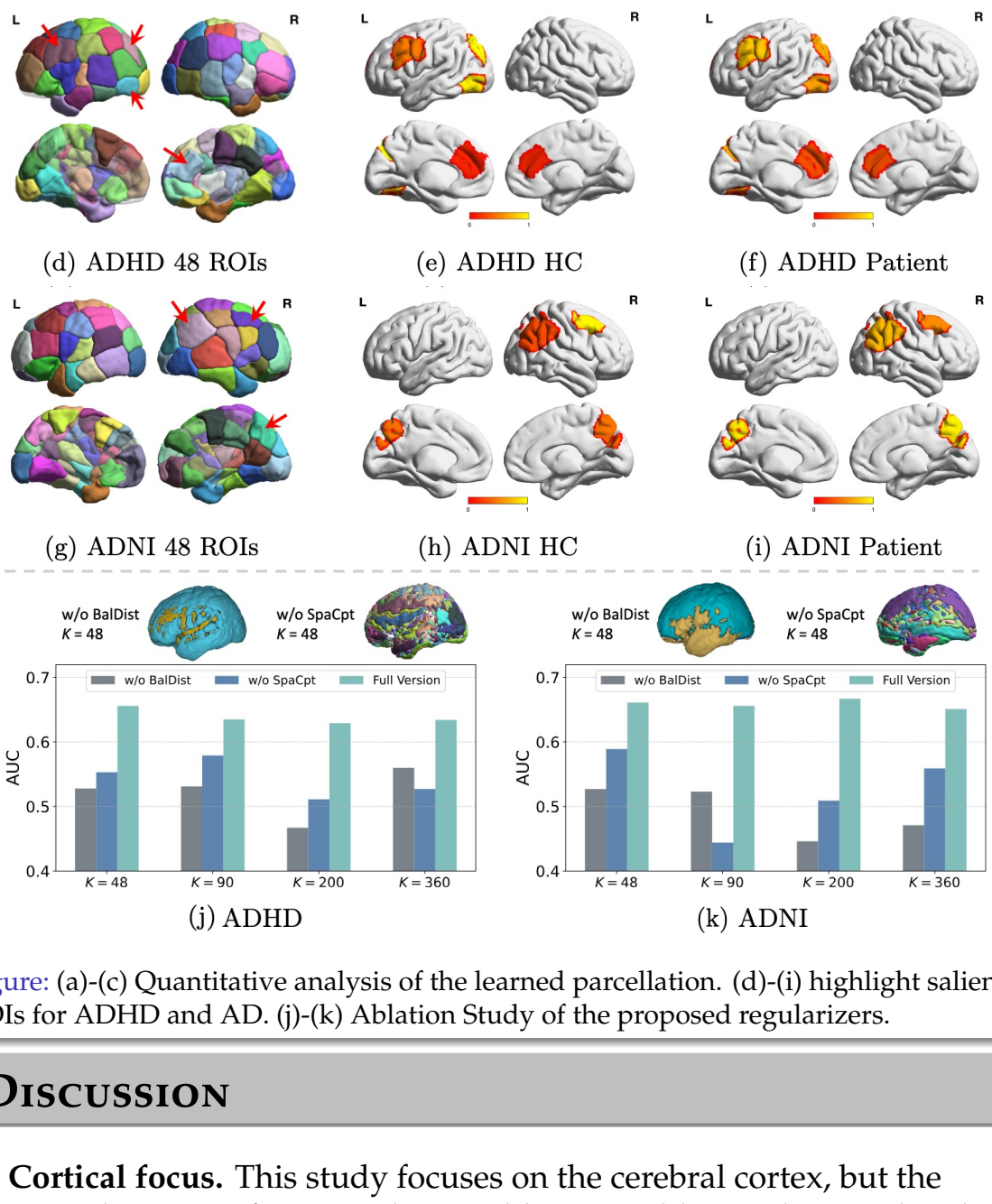
Datasets. Two rs-fMRI datasets: *ADHD-200* (569 subjects; 43.2% ADHD; 64 timepoints) and *ADNI* (200 subjects balanced between AD and HC; 197 timepoints), both preprocessed using fMRIPrep.

Table: Overall Prediction performance (mean±std, %).

Model	ADHD			ADNI		
	ACC↑	AUC↑	F1↑	ACC↑	AUC↑	F1↑
GCN	$59.7_{\pm 6.2}$	$63.2_{\pm 6.9}$	$48.3_{\pm 12.7}$	$60.5_{\pm 9.1}$	$65.7_{\pm 9.2}$	$63.4_{\pm 8.3}$
GAT	$57.7_{\pm 2.9}$	$60.3_{\pm 3.7}$	$53.6_{\pm 10.0}$	$56.0_{\pm 2.5}$	$59.4_{\pm 9.1}$	$55.4_{\pm 5.7}$
BrainGNN	$53.2_{\pm 3.8}$	$55.2_{\pm 3.7}$	$50.3_{\pm 7.0}$	$51.0_{\pm 5.4}$	$52.3_{\pm 6.3}$	$53.2_{\pm 5.5}$
BrainNetCNN	$56.0_{\pm 3.3}$	$58.7_{\pm 6.4}$	$52.1_{\pm 6.7}$	$58.5_{\pm 4.6}$	$65.9_{\pm 7.8}$	$53.6_{\pm 19.1}$
BrainGB	$56.7_{\pm 2.7}$	$58.3_{\pm 4.4}$	$46.0_{\pm 6.1}$	$56.5_{\pm 5.8}$	$59.7_{\pm 4.9}$	$58.2_{\pm 7.2}$
BrainNetTF	$59.8_{\pm 5.4}$	$63.8_{\pm 7.7}$	$45.0_{\pm 22.8}$	$59.5_{\pm 5.3}$	$62.3_{\pm 3.8}$	$59.7_{\pm 8.6}$
NeuroGraph	$56.5_{\pm 5.4}$	$59.4_{\pm 4.3}$	$57.6_{\pm 4.7}$	$56.5_{\pm 8.5}$	$57.6_{\pm 8.2}$	$58.9_{\pm 11.1}$
AFCON (K=48)	$63.2_{\pm 2.7}$	$65.6_{\pm 2.1}$	$56.8_{\pm 3.5}$	$62.5_{\pm 6.5}$	$66.1_{\pm 7.3}$	$62.6_{\pm 5.7}$
AFCON (K=90)	$60.0_{\pm 4.9}$	$63.5_{\pm 3.1}$	$50.7_{\pm 12.0}$	$61.5_{\pm 4.1}$	$65.6_{\pm 5.6}$	$61.5_{\pm 5.9}$
AFCON (K=200)	$61.8_{\pm 0.9}$	$62.9_{\pm 2.0}$	$47.9_{\pm 6.8}$	$62.0_{\pm 5.1}$	$66.7_{\pm 4.2}$	$59.8_{\pm 7.5}$
AFCON (K=360)	$61.1_{\pm 3.9}$	$63.4_{\pm 5.7}$	$49.8_{\pm 11.6}$	$59.5_{\pm 3.3}$	$65.1_{\pm 2.7}$	$55.1_{\pm 6.8}$

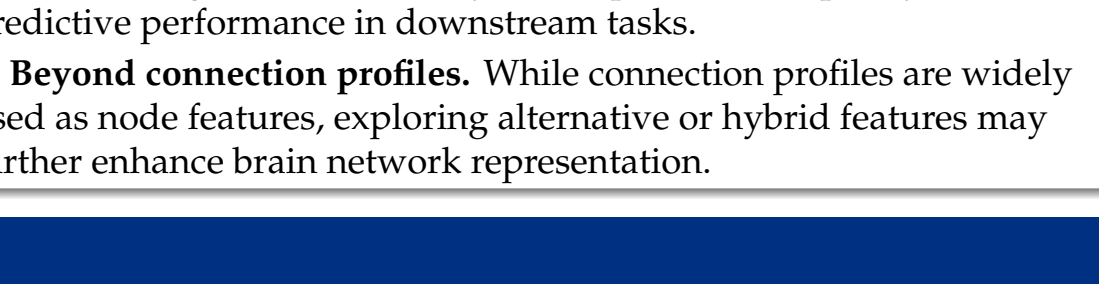


(a) Region Homogeneity on ADHD (b) Region Homogeneity on ADNI (c) Inter-subject Consistency



(d) ADHD 48 ROIs (e) ADHD HC (f) ADHD Patient

(g) ADNI 48 ROIs (h) ADNI HC (i) ADNI Patient



(j) ADHD (k) ADNI

Figure: (a)-(c) Quantitative analysis of the learned parcellation. (d)-(i) highlight salient ROIs for ADHD and AD. (j)-(k) Ablation Study of the proposed regularizers.

Discussion

1. Cortical focus. This study focuses on the cerebral cortex, but the proposed AFCON framework is readily extensible to subcortical and cerebellar regions for full-brain modeling.

2. Multimodal integration. Incorporating additional imaging modalities (e.g., sMRI, DTI) may enrich parcellation quality and boost predictive performance in downstream tasks.

3. Beyond connection profiles. While connection profiles are widely used as node features, exploring alternative or hybrid features may further enhance brain network representation.