A Deep Biclustering Framework for Brain Network Analysis

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Abstract

Brain functional connectivity (FC) analysis has emerged as a compelling quest to understand human brain dynamics and clarify disorder-related aberrations. Typically, FC can be portrayed as a graph of brain components (nodes) and their functional links (edges) known as the brain network (BN). The brain operates as a modular unit, with different regions forming semantically cohesive submodules to execute essential neuronal processing. Identifying these granules can provide insights into the underlying neurobiological mechanisms. Consequently, substantial research efforts have been directed toward clustering the constituents of brain networks. However, the inherent subject heterogeneity in the biological population and the wide spectrum of brain disease manifestation significantly impede cluster generalization. Thus, it often delivers a suboptimal solution and misses insightful nuances of neural systems. Therefore, we propose a deep neural network (DNN) framework for a more granular subgrouping of brain networks by simultaneously stratifying subjects and feature dimensions. The framework adapts discrete learning of BN edges and jointly optimizes instance and feature assignment probability distributions for a novel bicluster retrieval. Extensive experiments on multiple neuroimaging datasets show our model outperforms state-of-the-art biclustering methods. In addition, the extracted biclusters render more modular and semantically meaningful communities in the brain network highlighting significant neuroscientific relevance.

1. Introduction

Brain network analysis (BNA) has become the fundamental avenue for understanding the human brain and its enigmatic facets. The human brain is a modular unit; with distinct parts forming connected communities to carry out brain functionalities [10, 52]. and regular cognition [52]. Modern neuroscience models this neural organization as a graph known as the brain network [5, 25]. Nodes are defined as the anatomic regions of interest (ROIs), and edges are the functional connectivity between those ROIs. The connection between two ROIs is mechanistically measured through statistical dependence (correlation) or causal inference [6]. Comprehending the brain's network architecture—how its various regions communicate and coordinate—is crucial for unraveling the mysteries of cognition, behavior, and neurological disorders [5, 25]. Human brain functions emerge from the coordinated activity of diverse brain network components. Brain disorders influence such systems and are hypothesized to be delineated from disruptions in brain connectivity [66]. Studying brain networks and finding their concerted submodules potentially shed light on understanding cognitive processes such as memory, attention, and decision-making [11]. In clinical neuroscience, this provides insights into brain connectivity alteration due to neuropsychiatric conditions such as Alzheimer's disease, schizophrenia, and depression [32].

Multi-disciplinary methods have been deployed to uncover the ensembles of brain network constituents [16, 47, 58, 61]. However, the majority of BNA frameworks dissect the brain network into a set of nodes and probes to learn the node-level representations. Then, run a clustering heuristics to implement node (ROIs) clustering [16, 36, 46]. The widespread graph neural network (GNN) based approaches also optimize the node representations and generate clusters of nodes [14, 35, 37, 43, 75] by treating each node as a discrete data point for a canonical clustering setting. Network neuroscience demonstrates nodes - anatomical regions in the brain - are often connected to different neural submodules (clusters) via distinct edges [3, 19]. The submodules are intrinsically associated with different brain functions and cognitive activities [54]. Hence, clustering nodes obviate their functional diversity and ubiquitousness limiting the granularity in the subgrouping. So, in this study, we opt for clustering the edges (functional connections) evidently, the most volatile parts of the brain network. The edge clustering provides a coarser subgrouping of neural communication in the brain network. Additionally, a subgroup of nodes can be inferred from a cluster of edges by disentangling the vertices. That node cluster can be treated as a submodule governed by this set of connections. Moreover, this approach allows a single node cluster representing different

edge clusters with distinct connectivity profiles providing a more plausible understanding of brain networks.

Another aspect of clustering-based approaches is they explore only the feature dimension for co-regulated communities in the brain networks. Inherent subject variability in the biological population limits the generalization of the extracted subgroupings significantly. Also, heterogeneity in disease symptoms, progression, and effects instantiate disparate disease subtypes that require discrete attention to design effective medication [22, 31, 74]. As such, active brain network harmony becomes intractable in a whole-population analysis. Therefore, simultaneous stratification of the subject and feature dimension through a biclustering framework is imperative to delve into the smaller subpopulations for meaningful connectivity patterns. However, a single end-to-end DNN framework for feature learning and biclusters modeling is challenging and less explored in the literature. Existing DNN-based biclustering models are either not end-to-end - segregated steps for feature learning and biclustering [63] or dependent on an off-the-shelf clustering algorithm for the bicluster assignment task [68]. Due to the lack of such an optimization framework, many useful constraints that field experts are keen to impose for meaningful biclustering are hard to execute. For instance, semantic locality constraint is substantial for neuroimaging data since brain activations (captured by neuroimaging technologies e.g., MRI) are expected to be semantically coherent with distinct cognitive functions. Also, in region-based correspondence in 3D shape matching, spatial integrity is cardinal [18]. Given a flexible DNN architecture, these constraints could be easily transformed into differentiable functions to regulate the convergence of a DNN model. Thus, we propose a lightweight deep neural network (DNN) model for feature learning and biclustering brain networks. The model outperforms diverse BNA schemes on bicluster quality, pattern modularity, and semantic consistency Fig. 3.

2. Related Works

The broad subcategory of BNA methods is governed by the graph neural network (GNN). GNN-based methods have been tremendously effective for graph-structured data analysis. To this end, there is BrainTGL [45] for dynamic brain graph learning, BrainGNN [44] for utilizing functional information in brain networks, IBGNN [15] for enhanced interpretability, BN-GNN [75] GNN reinforcement learning, and FBNetGen [35] a generative model for learning brain networks has been introduced. Another modern subcategory is transformer-based methods leveraging self-attention to learn an informative representation of the brain networks [16, 36] and cluster-friendly projection. There is also a plethora of studies on the brain's functional connectivity (FC) analysis [17, 20, 28, 69, 72, 73]. These studies use one-dimensional clustering k-means to generate FC states. However, the biclustering brain network data has not been carried out to our knowledge. The most recent biclustering algorithms are based on the concepts of treating the data matrix as a bipartite graph [24, 53, 64], binarizing the matrix [60] for well-defined biclusters. GAEBic uses a Gaussian mixture model (GMM) to perform the cluster assignment task [68]. Also, there is a significant number of co-clustering methods introduced for simultaneously clustering the sample and features [23, 49, 71]. However, co-clustering clusters instances and features simultaneously into two different sets of clusters using distinct model order. On the other hand, biclustering clusters instances and features simultaneously into k (model order) clusters based on their co-regulation. We propose a DNN-based end-to-end biclustering model applied to brain network functional links.

3. Brain Network Construction

The aforementioned BNA methods use ROI-based atlas for brain network construction. The ROI atlas implicitly operates under the assumption that the functional connectivity profile within each anatomically defined region remains stable over time and consistent across individuals. However, research studies have consistently identified variations in the spatial patterns of functional entities, both between individuals and within individuals over time, challenging this assumption [33]. In this study, we adapt intrinsic connectivity networks (ICN) based parcellation of the brain - seemingly more robust than static ROI and captures nuanced patterns in brain imaging data [27, 40]. ICN allows for spatial overlap, consistency, and dynamics in functional connectivity. Furthermore, multiple studies have shown that ICNs are more informative and interpretable building blocks of the human brain [41, 42]. Therefore, we run spatially constrained group ICA (gICA) from the NeuroMark [21] pipeline on the functional magnetic resonance imaging (fMRI) volumes. We use NeuroMark spatial templates (presented in the supplementary) to guide gICA that decomposes the images into intrinsic connectivity networks (ICNs) which can be treated as ROIs (nodes). NeuroMark gICA generates 53 ICNs and their corresponding time courses (TCs). The ICNs are grouped into seven functional brain domains [26, 59] namely subcortical (SC), auditory (AU), visual (VS), sensorimotor (SM), cognitive control (CC), default mode (DM), and cerebellum (CB). The functional connections (edges) are usually estimated using the Pearson correlation between ICNs over time. The mean across the time course generates a 53×53 symmetric square matrix popularly known as static functional network connectivity (sFNC) [34]. The sFNC matrix is essentially an adjacency matrix for the brain network (more detail in supplementary).

4. Proposed Method

4.1. Problem Definition

Given brain network (i.e., sFNC in our case) $G \in \mathbb{R}^{N\times(V\times V)}$, where N is the number of samples and V is the number of nodes (ICNs). After feature engineering, $G = \{X : X \in \mathbb{R}^{N\times M}\}$, where M is the number of unique connections. Our model primarily learns two assignments $P_{ft}^{M\times K}$ and $H_{sub}^{N\times K}$ for the features and subjects in the data matrix. Finally, our model generates bicluster assignment $B : b^1, b^2, ..., b^K$ where $b^i = \{(x, y) : x \subset M, y \subset N\}$.

4.2. Brain Network Biclustering

The majority of modern BNA methods use the whole adjacency matrix as input data where the edges are redundant and shifted across the diagonal (due to the symmetry of correlation). Here, we use only the lower/upper triangle of the adjacency matrix delineating unique edges in the brain network. We skip the diagonal entries with 1's prompted by the correlation between the identical nodes. To this end, we propose a simple yet effective DNN framework coined as 'BnBiC' for discrete learning of edge features and joint optimization of the probability distribution for a novel biclustering retrieval. The input triangles are flattened for training purposes. Note that the vector representation loses the functional connectivity semantics. Therefore, BnBiC appends learnable positional encoding for the edges. Fig. 1 illustrates the proposed BnBiC framework built on an autoencoder (AE) architecture equipped with biclustering regularization. The architectural design is motivated to facilitate the biclustering approach using a bottleneck layer where the size of the bottleneck (i.e., the number of neurons in the hidden layer) is provided by the number of expected biclusters (K). The bottleneck potentially captures the information flow from a sample and feature for a given downstream task. Sun et al., use the bottleneck layer and the weight matrix to estimate the contributions of samples and features within hidden neurons [63].

Let the data matrix be $X : N \times M$, N number of samples, and M features. We leverage the weight matrix $W \in \mathbb{R}^{M\times K}$ and hidden activation $Z \in \mathbb{R}^{K\times 1}$ to configure the probability distribution of cluster assignments for samples and features. The model is pre-trained over a prediction task and input reconstruction, fine-tuned using bicluster-oriented constraints. The reconstruction error (L_r) is computed on the output from the decoder and binary cross-entropy loss (L_c) for the subject's disease label classification. Cluster projection is regularized by transforming the $W_1^{M\times K}$ and $Z^{K\times 1}$ to the soft assignment for features and instances respectively and minimizing the distance between target auxiliary distributions. In the inference, relevant subjects and features are selected using the meta-heuristic (Sec. 4.2) on the hidden activation and weight matrix.

$$L_r = \frac{1}{NM}\sum_{N}^{n=1}\sum_{M}^{m=1} ||X_{n,m} — f_\phi(X_{n,m})||^2 \quad (1)$$

where $f_\phi(X_{n,m})$ is the autoencoder's reconstruction of the input $X_{n,m}$ and $\|.\|$ is the Euclidean norm. The average cross-entropy for N samples is given by (2),

$$L_c = -\frac{1}{N}\left[\sum_{N}^{n=1}\left[t_n \log(p_n) + (1—t_n)\log 1 - p_n\right]\right] \quad (2)$$

where t_n is the true label and p_n is the Softmax probability for n^{th} sample.

For a biclustering regularization, we formalize a constraint based on the feature clustering projection and the subject assignment distribution. We transform the W matrix into soft assignments for features by applying Softmax across the last dimension. We consider $P_{ft} = [p_{ik}]^{M\times K}$ as the distribution of assignment of all the features where p_{ik} is denoted by (3).

$$p_{ik} = \frac{e^{W_{ik}}}{\sum_{j=1}^{K} e^{W_{ij}}} \quad (3)$$

As described in the deep embedded clustering (DEC) [70] method, cluster learning can be refined from their high-confidence assignments. We can optimize P_{ft} by learning from the high-confidence assignments illustrated as a target distribution $Q_{ft} = [q_{ik}]$ [71].

$$q_{ik} = \frac{q_{ik}^2/\sum_u q_{uk}}{\sum_e (q_{ie}^2/\sum_u q_{ue})} \quad (4)$$

The distribution of subject assignment (soft) can be computed using Z. Given, a batch of b subjects, the soft assignments $H_{sub} = [h_{ik}]^{b\times K}$

$$h_{ik} = \frac{e^{Z_{ik}}}{\sum_{j=1}^{K} e^{Z_{ij}}} \quad (5)$$

Similarly, the target distribution $L_{sub} = [l_{ik}]$ is denoted by (6)

$$l_{ik} = \frac{h_{ik}^2/\sum_u h_{uk}}{\sum_e (h_{ie}^2/\sum_u h_{ue})} \quad (6)$$

Finally, we minimize KL-divergence between the source and target distributions described in (7),

$$L_{bic} = KL(P_{ft}||Q_{ft}) + KL(H_{sub}||L_{sub}) \quad (7)$$

Moreover, we impose a sparsity constraint on the weight matrix to avoid bias from larger weights to help better reconstruct the features. We use a revised $L1$ norm on the W

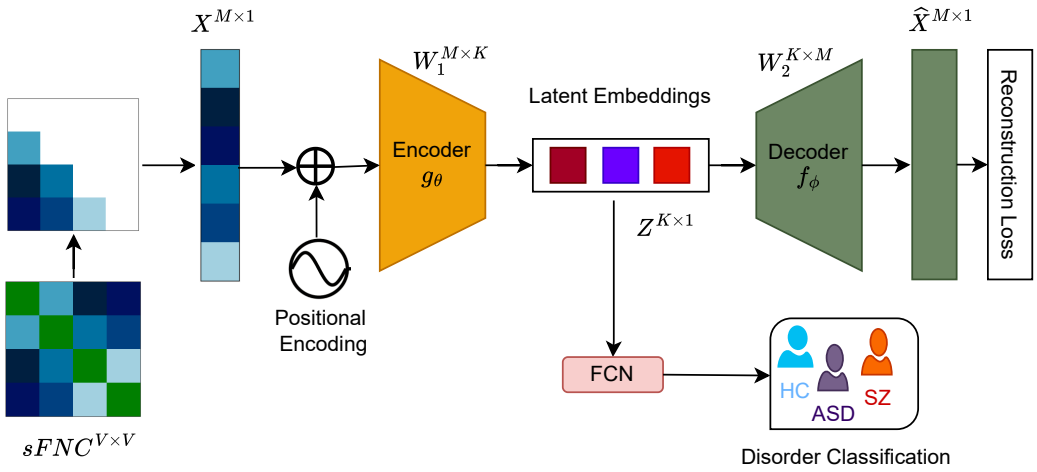

Figure 1. Our proposed brain network biclustering (BnBiC)architecture.

matrix for the sparsity. Rationally, since we adjust the sparsity on primary neuroimaging data through gICA, we prune the sparsity constraint lower than the standard $L1$ norm.

$$L_s = \sqrt{\|W\|_1} \tag{8}$$

The combined objective function using pre-training and fine-tuning constraints can be formulated as,

$$L_{opt} = \mu(L_r + L_c) + (1—\mu)(\delta L_{bic} + \gamma L_s) \tag{9}$$

where δ and γ are non-negative and control the regularization by different penalty terms. μ helps train the model by balancing the load between feature learning and cluster-oriented loss. In the inference phase, the weight $|W_{f,k}|$ determines the contribution of the f^{th} feature to the k^{th} bicluster, similarly, $Z_s^{(k)}$ decides for s^{th} subject. The meta-heuristic for bicluster's inclusion criteria is,

- Subject selection: Pick any subject s with $|Z_s^{(k)}| > \beta(\beta \in (0,1))$
- Feature selection: Pick any feature f with $|W_{f,k}| > \alpha(\alpha \in (0,1))$

4.3. Model Training

The training scheme is divided into two phases. Firstly, we pre-train the autoencoder framework using the reconstruction error described in (1) and the classification loss (2). Then, we fine-tune using the biclustering and sparsity constraints described in (7) and (8) respectively. The optimization is accomplished by minimizing the objective function defined in (9). Initially, it sets a comparatively large value for μ to allow more pre-training errors until the model achieves reasonable stability in recovering the input. Then, we reduce μ to enable the cluster-oriented losses to make more impacts on the latent space. We run the model for 200 epochs using the Adam optimizer with a learning rate of 10^{-4} in Pytorch.

5. Experiments

5.1. Datasets

We run experiments on two real resting-state fMRI (rs-fMRI) datasets. The first one is a combination of three studies, COBRE [51], fBIRN [39], and MPRC [2]. The combined dataset has 437 subjects with 275 healthy control (HC) and 162 schizophrenic (SZ) subjects. The rationale behind selecting this dataset is it's a well-researched schizophrenia and healthy subject collection. Also, it provides the harmonized cognitive and symptom scores for the participating subjects useful for our bicluster analysis. We use another publicly available benchmark dataset Autism Brain Imaging Data Exchange (ABIDE) [12]. The dataset includes rs-fMRI volumes from 17 international sites and consists of 1112 subjects, with 539 being Autism spectrum disorder (ASD) and the remaining typical control. The data is completely anonymized. Both of these datasets are pre-processed using standard NeuroMark [21] pipelines.

5.2. Experimental Settings

We use a multi-layer perception (MLP) for both encoder and decoder models. We empirically determine the size of the bottleneck and set it to $k = 5$ for the experiments. We primarily create 2 random data splits for the training (70%) and evaluation (30%). Then, from the evaluation split we use random 40% for validation and the remaining 60% for testing. The batch size is kept at 32 for the experiments. The hyperparameters sensitivity study is added in the supplementary material (sec. 3). To compare the performance, we include a baseline k-means, two empirical biclustering

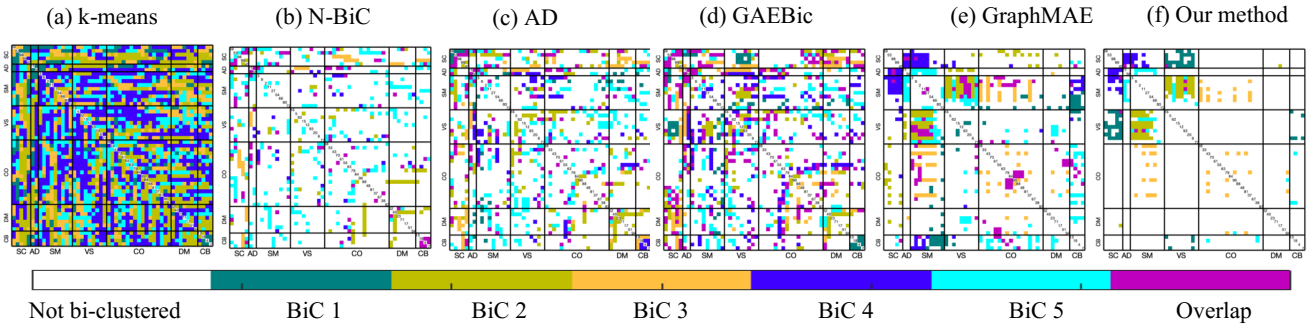

Figure 2. The grouping of edges evaluated by comparing methods on combined dataset. The biclusters are visualized on a standard brain network (input matrix) annotated by brain regions to explain the partitioning in neuro-connectivity semantics. Compared to other methods, we observe fewer overlaps and modular structures in the bi-clustered patterns in BnBiC.

Table 1. Performance comparison with different baselines. The highlighted row is our method BnBiC presents the best performances

	Combined			ABIDE		
Method	MSR	APCC	FCO	MSR	APCC	FCO
k-Means	0.681±0.05	0.277±0.04	0.319±0.05	0.713±0.06	0.267±0.03	0.331±0.05
N-BiC	0.531±0.05	0.381±0.05	0.387±0.06	0.651±0.04	0.336±0.03	0.362±0.03
FABIA	0.420±0.04	0.365±0.05	0.412±0.07	0.421±0.05	0.441±0.04	0.383±0.05
AD	0.412±0.04	0.440±0.02	0.465±0.04	0.480±0.03	0.415±0.03	0.491±0.02
GAEBic	0.460±0.03	0.375±0.02	0.446±0.02	0.603±0.05	0.346±0.04	0.435±0.04
GraphMAE	0.320±0.04	0.476±0.05	0.601±0.06	0.412±0.04	0.467±0.03	0.513±0.04
BCOT	0.305±0.06	0.510±0.05	0.608±0.07	0.396±0.07	**0.493±0.03**	0.521±0.04
BnBiC	**0.301±0.05**	**0.538±0.07**	**0.623±0.04**	**0.378±0.06**	0.492±0.05	**0.545±0.08**
Ablation 1	0.367±0.02	0.491±0.06	0.534±0.07	0.402±0.07	0.447±0.07	0.463±0.07
Ablation 2	0.318±0.05	0.515±0.06	0.612±0.06	0.375±0.06	0.467±0.03	0.533±0.04
Ablation 3	0.347±0.07	0.512±0.08	0.564±0.07	0.417±0.05	0.455±0.09	0.483±0.04

methods FABIA [29] and N-BiC [57]. Then, we incorporate DNN models Auto Decoder (AD) [63]. For a more comprehensive comparison, we included the GNN-based method GAEBiC [68], and GraphMAE [30]. Also, we include a concurrent model on optimal transport-based bipartite graph partitioning BCOT [24]. Moreover, we add three ablation studies to evaluate the influence of the proposed constraints. Ablation 1 is without propagating biclustering penalty in (7), ablation 2 is without sparsity loss (8), and ablation 3 removes the classification pre-training. We run the models for 50 repetitive iterations and present the (mean ± standard deviation) of the performances across the runs.

5.3. Performance Evaluation

We don't have any ground truth biclustering partition for the brain network data. So, we introduce a metric based on functional connectedness [65] to measure coherence among the biclusters. We also adapt two more biclustering metrics mean square residue (MSR) [9] and average Pearson correlation coefficients (APCC) [55] for comparing our model's performance with analogous methods.

Functional Coherence (FCO) FCO compares the strength of the connectivity among the attributes within a bicluster and the interactions with the other parts of the system. In brain dynamics, it's a measure of the interaction among a subset of brain networks and their communication with the rest of the brain. Given the brain networks, to evaluate a bicluster partitioning B, we can measure the inter and intra connectedness (C) of a bicluster b as follows,

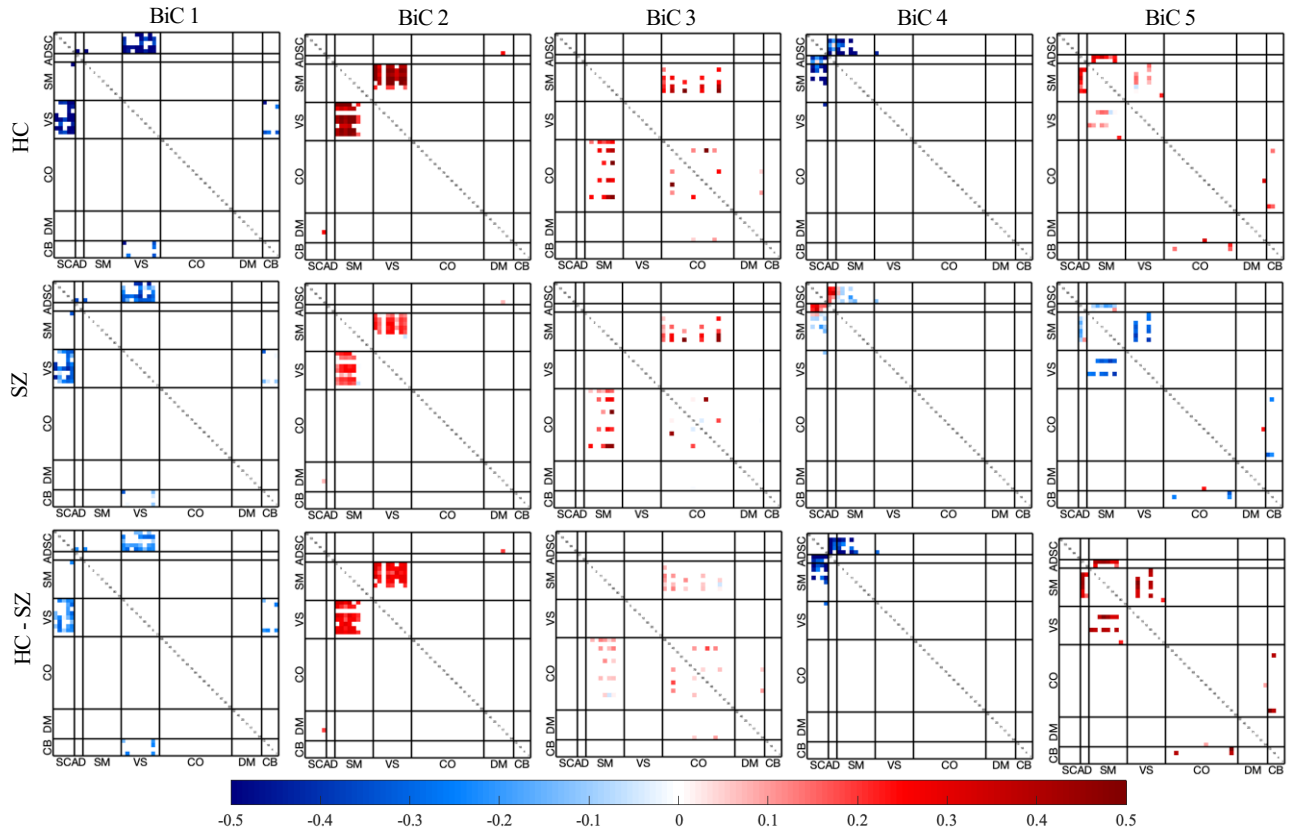

Figure 3. Edge biclusters of Brain network from the combined dataset. The top row is computed by averaging the HC subjects within a bicluster, the middle row for SZ, and the bottom HC-SZ difference. The color bar represents the strength of the connection.

$$C_{intra}(b) = \frac{1}{|b|} \sum_{i \in b} \sum_{j \in b} X_{ij} \tag{10}$$

$$C_{inter}(b) = \frac{1}{|b'|} \sum_{i \in b} \sum_{j \notin b} X_{ij} \tag{11}$$

where b' is the set of connections made by the community b with the rest of the system. We formulate functional coherence (FCO) for a biclustering run B as in the equation (12).

$$FCO(B) = \frac{1}{\sum_{b \in B} |b|} \sum_{b \in B} (C_{intra}(b) - C_{inter}(b)) \tag{12}$$

We also define the functional clustering index (CI) to approximate the functional consistency in the grouped instances.

$$CI(b) = \frac{C_{intra}(b)}{C_{inter}(b)} \tag{13}$$

5.4. Performance Analysis

Figure 2 shows the biclusters estimated by a subset of comparing methods. This figure summarizes the performances highlighting the overlaps and functional modularity in biclustering results from distinct methods. Our method provides a more disjoint and functionally modular subgroup of instances. For most approaches, the bi-clustered elements are more diffused and spread across wide areas of the brain connectivity dynamic. Also, the overlaps between the biclusters are substantial (violet color). The overlaps hinder the interpretation of the bicluster as a close community and link with specific cognitive functionalities. Moreover, the modularity in the subgroups aids in investigating precise neurobiological processes potentially associated with the connectivity patterns. Table 1 shows the performance comparison between our model and different state-of-the-art biclustering methods. Our proposed method outperforms various baselines and yields competitive performance in some cases. We vary the regularizers for biclustering constraint, sparsity, and classification to check the performance of each ablated variant of BnBiC. The ablation study confirms the incremental improvements in performance corresponding to different components of the BnBiC model.

5.5. Bicluster Analysis

We visualize the brain network edge biclusters in figure 3. The bi-clustered connections are more modular and localized in functional domains. Brain network elements (nodes/edges) belonging to the same functional modules often share similar behaviors regarding activations and deactivations in response to various external stimulations [7]. So, these patterns increase the chance of conducting coherent neural activity such as motor, visual, and auditory responses. Bicluster (BiCs) 1, 2, 4, and 5 show significant group (HC/SZ) connectivity differences in visual (VS), subcortical (SC), and sensorimotor (SM). Prior studies have identified these domains to be associated with schizophrenia dysfunction and social impairments [48]. Reduced connectivity strength (BiC 2) or inverse connectivity (BiC 5) between SM and VS is potentially liable for difficulty in social cognition and mentalization [1, 48]. The bi-clustered connections in BiC 4 and 5 show opposite directionality in HC and SZ groups. It indicates the relevant cognition driven by these connected communities is divergent which may justify the cognitive differences between the subject groups.

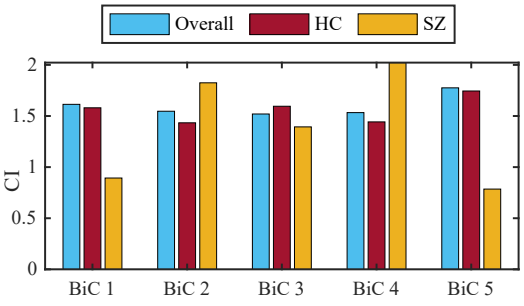

Figure 4. Functional Clustering Index (CI) for extracted connectivity biclusters of the brain network.

5.5.1 Functional Clustering

We utilize the functional clustering index (CI) described in equation (13) to experiment with the bi-clustered sFNC elements for functional connectedness. We can check if the community forms a functional cluster or not using their intra and inter-connectivity. In brain dynamics, a functional cluster can be defined as a subset of neural elements that are strongly interactive among themselves but weakly interactive with the rest of the system. A CI value near 1 indicates a homogeneous system, while a high cluster index indicates that a subset of brain regions forms a functional cluster. All the biclusters exhibit a CI greater than 1 indicating the formation of a functional cluster and a homogeneous community in Figure 4. In other words, the components of the bicluster are functionally cohesive. However, in BiC 1 and 5 the CI in SZ community is less than 1 which denotes the loss of functional connectedness in the diseased population.

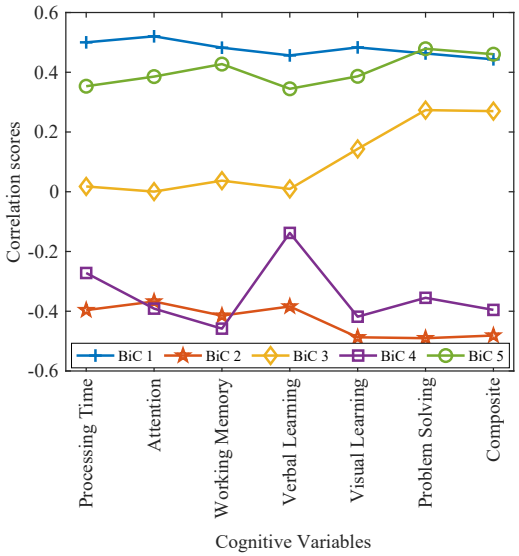

Figure 5. Correlation between bi-clustered edges of brain network with distinct cognitive variables.

5.5.2 Association with Cognitive Scores

Figure 5 shows the association of connectivity submodules of the brain network with multiple cognitive measures. The design of cognitive tests and acquisition of cognitive scores for the datasets are described in these studies [56, 62]. The cognitive batteries utilized in this project are CMINDS [67] and MCCB [4]. Also, we run standard data harmonization to ensure the consistency of the scores across the datasets. We observe that BiC 1 shows a significantly higher correlation with all the cognitive measures that evident the necessity of interactions between SC and VS to perform these tasks. That also holds for BiC 5 demonstrating SM to auditory (AD) and VS connections. BiC 2 (VS-SM connectivity) also shows a strong negative association with cognitive measures. Especially, for the problem-solving task it shows a significant inverse correlation. That characterizes the relatedness with the inverse directional flow necessary for specific cognitive tasks. Overall, the sensorimotor and visual domain is liable for performing diverse motor and visual processing which are imperative for the cognitive tasks in our experiment [1, 13]. BnBiC estimates convergent submodules (clusters) of the brain network exhibiting coordination between sensorimotor, visual, and auditory regions. These regions of the human brain mostly process sensor simulations and generate cognitive responses. Thus these

submodules and their connectivity profiles are significantly insightful for understanding regular cognition and disease-related deficits.

5.5.3 Association with SZ Symptom Scores

We examine the association of bi-clustered connectivity with SZ symptom scores measured by positive and negative syndrome scale (PANSS) [38] in figure 6. BiC 1 and 5 show a similar link with the PANSS scores; a higher correlation with general and strong anti-correlation with negative and positive symptoms. The connections are between VS, SM, AD, and SC domains which are found to be akin to SZ symptoms [8, 50]. These substantial associations with symptom scores indicate clustered connectivity patterns are informative about the disorder and further experiments are required to determine the absolute linkage which can potentially help design personalized medicine in schizophrenia.

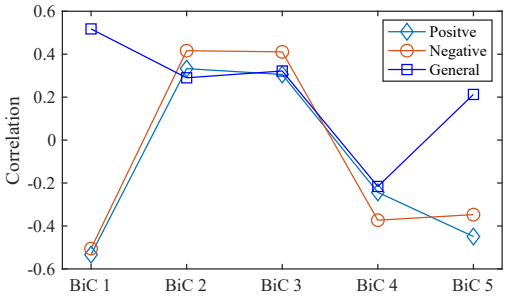

Figure 6. Correlation between mean edge value (average functional connectivity strength) across the schizophrenia subjects included in a bicluster and the corresponding schizophrenia symptom scores.

6. Conclusion

In this paper, we develop a deep biclustering model to learn the edge features of brain network and produce semantically coherent substructures of connectivity. It also harness the diversity in the sample dimension by generating homogeneous subgroups of subjects and edges. The biclusters allow delving into a constrained and meaningful subspace of neuroimaging data that are significantly informative about the underlying neural mechanisms and the disorder. The joint optimization of instance and feature assignment distribution regulates the biclusters from multiple perspectives thus revealing modular communities in the brain network. The experiments demonstrate their association with cognitive performance and how the connectivity patterns differ in patients and healthy controls. The performance analysis on two substantial neuroimaging datasets validates our method for a better subgrouping framework with a significant improvement in biclusters' quality. The model is robust to any neuroimaging modalities (EEG, MEG) and brain network construction techniques. Moreover, this framework is extendable to multi-modal data and multi-omics clusters which might provide inter-modality biclusters for exploring homogeneity across multiple physiological sources.

7. Acknowledgments

This work is supported by the National Institute of Health (NIH) under the grant number NIH R01MH118695 and the National Science Foundation with grant number NSF 2112455.

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