
Modeling Human Brain Connectomes using Structured Neural Networks

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Abstract

Generalizations of neural network architectures to arbitrarily structured data, e.g. graphs, have opened new opportunities for applying data-driven learning to novel scientific domains, in particular brain network analysis. While classical approaches have relied on hand-engineering statistical descriptors from structural or functional connectomes of human brains to build predictive models, there is growing interest in leveraging deep learning techniques. Though the human connectome is often viewed as a graph defined with each node indicating to a brain region, and the edges representing neural connections, we argue that existing graph neural network solutions, that are built on the assumption of information diffusion, are not directly applicable. Consequently, we develop a structured network architecture that uses the connectome to constrain the message passing between two network layers representing edges and nodes respectively. Using connectomes from the Human Connectome Project (HCP), we show that proposed approach can effectively predict meta-information such as age and gender, and accurately recover the volumes of different brain regions, which are known to be encoded in the connectomes.

1 Introduction

Inspired by the effectiveness of deep learning methods in vision, speech and language processing, there is growing interest in extending those techniques to high-impact application domains such as healthcare. While much of demonstrated success has been on dealing with clinical images/volumes and textual reports, more recent efforts have focused on challenging data sources including multi-modal health records, knowledge graphs etc. These efforts have relied on generalizing the foundational formalisms such as convolutional neural nets to arbitrarily structured data. For example, graph neural networks (GNNs) [15] are known to have strong expressive capability with graph-structured data, and have been found to be highly effective with population graphs in clinical diagnosis, e.g. autism [1].

In this paper, we study the use of deep neural networks for analyzing brain connectomes, which is a comprehensive map of neural connections in the human brain. Recently, the Human Connectome Project (HCP) [14] has made significant strides in producing elaborate structural and functional connectivity of neural pathways in the brain. By leveraging the corresponding neuroimaging data of a human subject, it is now possible to construct a connectivity matrix encoding the neural connections (e.g. number of fibers) between brain regions. Commonly referred to as the *structural connectome*, this connectivity matrix is known to contain signatures relevant to population characteristics such as gender and age [3], and more importantly, information pertinent to determining the volumes of different brain regions. For the first time, we propose to utilize deep neural networks to directly process the structural connectome and test the hypotheses on the predictability of population characteristics and region-specific volumes. This study is a critical first step towards building predictive models from functional connectomes that can reliably predict behavioral traits and cognitive states.

*This work was performed while in Lawrence Livermore National Labs, and with equal contribution

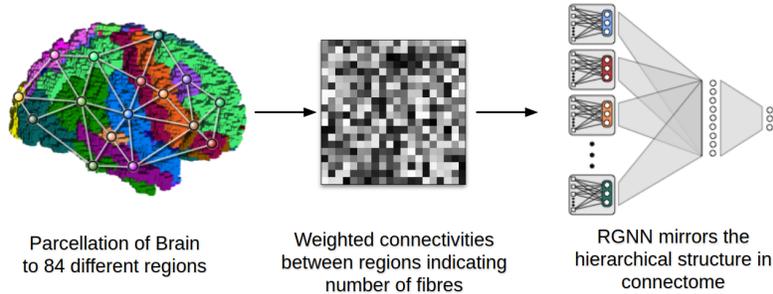


Figure 1: An overview of the proposed approach. The T1 scans are parcellated to 84 different regions in the brain, on which, tractography is performed to compute the weighted matrix representing the structural connectome. Our RGNN model is used to process the connectome for prediction tasks.

Though it seems natural to interpret the structural connectome for each subject as a graph, and employ off-the-shelf graph processing tools, there is a fundamental difference between the connectome and conventional graph datasets such as social networks. With information diffusion-style networks that we typically deal with in practice, an edge between two nodes indicates the likelihood of information exchange between those two nodes. However, even if two nodes are not directly connected by an edge, information exchange can still happen through diffusion from related nodes. In contrast, connectomes encode neural connections as a relational structure and does not allow information diffusion [16]. In other words, a missing edge indicating the absence of connections between two brain regions is a neurological pattern. Consequently, we require network architectures that can directly utilize the connectome as a structural prior and infer mappings to the target variables. Similar ideas have been explored in the context of relational reasoning and causal processes [9, 5].

We develop relational graph neural network (RGNN) that is designed to incorporate the relational structure of the neural connections and infer effective latent representations for the connectomes. First, we utilize the edge attribute (e.g. number of fibers) as the input edge feature, and construct node representations through constrained message passing with learnable weights. More specifically, we design two network layers that explicitly correspond to the edges and nodes, and constrain the message passing between the two layers using the connectome. In other words, the representation for each node can only depend on the edges involving that node. Interestingly, this architecture is effective for even densely connected graphs. Another interesting feature of our approach is that we can produce interpretable explanations (e.g. Shap analysis [7]) both at the coarse-grained node level and the fine-grained edge level simultaneously.

From our experiments, we find that state-of-the-art approaches including GNN and random walk-based embedding techniques such as *DeepWalk* are very ineffective at recovering the region-specific volumes. Surprisingly, even a simple fully connected network on the edge attributes outperforms the graph network baselines. In comparison, the proposed RGNN accurately estimates the region-specific volumes as well as summary quantities such as total gray matter and total white matter. Furthermore, our prediction results on gender prediction strongly corroborates with the findings in the neuroscience community [3]. This clearly evidences the effectiveness of RGNN as a learning strategy for connectomes, and we believe this can be suitable for studying functional connectomes.

2 Human Connectome Data

We used data from the Human Connectome Project - Young Adult dataset², which included about 900 subjects. In order to generate the structural connectome for each subject, we performed the following steps: First, we segmented the T1 images into five tissue types (MRtrix³ command `5ttgen`) [10]. Then we used the diffusion MRI data along with the tissue segmented volume to produce tissue-specific response functions (MRtrix command `dwi2response`) [4]. Subsequently, this response was used to construct fiber orientation distributions using the spherical deconvolution (MRtrix command `dwi2fod`) [13] and tractography was carried out using the iFOD2 technique (MRtrix command `tckgen`) [12]. Finally, we employed the SIFT2 method to compute streamline weights (MRtrix

²<https://www.humanconnectome.org/study/hcp-young-adult>

³MRtrix version 3.0, <https://www.mrtrix.org>

command `tcksift2`) [11], and the weighted streamline counts were used along with the Desikan parcellation to compute the connectome matrix (MRtrix command `tck2connectome`) [2].

3 Approach

We describe the RGNN architecture that leverages the relational structure of connectomes. Though the focus of this paper is on structural connectomes, our approach applies to functional connectomes as well. Our approach uses constrained message passing kernels, with learnable parameters, on the connectome edges to obtain node (region) representations. To this end, we design two neural network layers: the first layer representing the neuron connections takes as input the vectorized set of edge weights of size $N \times N$, where N is the total number of regions in the connectome. The second layer corresponds to the N nodes (or regions). The relational structure from the connectome is directly used to construct messaging passing kernels between the two layers. In other words, the feature for each node in the second layer should depend only on the edges involving that node, i.e.,

$$\mathbf{h}_i = \sigma\left(\sum_{j=1}^n W_{ij}\theta_j\right), \quad (1)$$

where \mathbf{h}_i is the learned representation for node i , W_{ij} is the connectome edge weight between node i and j , $\theta_i = [\theta_1, \theta_2 \dots \theta_N]^T$ are the learnable parameters of the kernel associated with node i , and σ is a non-linearity function (e.g. ReLU).

From another perspective, we pool all information from the edges involving a node to constructing its representation. Furthermore, we allow the use of multiple kernels for the same node, akin to multiple heads in attention models, we refer to this as the pooling size p . In the case of multiple kernels, we concatenate the p representations for each node, thus producing a graph level feature of effective size $N \times p$.

$$\tilde{\mathbf{h}}_i = \parallel_{k=1}^p \mathbf{h}_i^{(k)} \quad \text{and} \quad \tilde{\mathbf{H}} = \parallel_{i=1}^N \tilde{\mathbf{h}}_i$$

Though the constrained message passing kernel can be implemented in different ways, we adopt a simple strategy where a fully connected layer is used to produce a weighted sum of edge connectivities and the network parameters are optimized using backpropagation. Note, we use different kernels for each of the nodes, and their weights are not shared. Finally, we pass the node representations $\tilde{\mathbf{h}}_i$ through a classifier or a regressor implemented using additional fully connected layers. All volume estimation models are trained with the mean squared error loss, while the age/gender prediction uses the binary cross entropy loss.

4 Empirical Validation

We validate the suitability of RGNN to analyze connectomes by attempting to estimate the region-specific volumes in different parts of the brain and predict meta-information, such as age and gender, directly based on the neural connections. This empirical study was motivated by existing works in the neuroscience literature, which have hypothesized that specific signatures, that can predict the volume statistics and gender/age information, are encoded in the connectome. Consequently, we expect an appropriate neural network architecture to adhere to these hypotheses.

In all experiments with RGNN, we set the pooling size to 5 and the hidden layer size at 16. For comparison, we consider the following popularly adopted solutions:

a) FCN: In this simple baseline, we ignore the network structure and simply vectorize the connectivity matrix for each subject to produce a feature vector of 7056 dimensions (84×84). Subsequently, we build a fully connected network with a single hidden layer of 16 units and ReLU non-linearity.

b) DeepWalk [8]: For this random-walk baseline, we first build a supra graph, whose adjacency is constructed by stacking the connectomes as block diagonals. We run the DeepWalk algorithm on this supra graph and extract 64-d features for each node. Note, for better results, we sparsified each connectome by retaining only the top 75% values. Finally, the representation for each connectome is obtained by concatenating all its node embeddings and the prediction is carried out using XGBoost.

c) Message Passing GCN [6]: By treating each connectome as a graph, we build a 2-layer GCN model based on weighted message passing. Since the nodes do not have explicit attributes, the

Table 1: Estimating region-specific volumes using the structural connectome. For each case, we report the R^2 / **Pearson correlation coefficient** metrics.

Region	DeepWalk	GCN	FCN	RGNN
Total gray matter	0.4444 / 0.675	-0.0116 / 0.1829	0.6515 / 0.8197	0.7219 / 0.8577
Total white matter	0.3753 / 0.62	-0.0132 / 0.1459	0.7011 / 0.8559	0.8029 / 0.9078
Left hemisphere cortical white matter	0.3849 / 0.6281	-0.0133 / 0.1561	0.7022 / 0.8572	0.8027 / 0.9082
Right hemisphere cortical white matter	0.3731 / 0.6173	-0.0132 / 0.1351	0.6967 / 0.8534	0.7975 / 0.9047
Left hemisphere cortical gray matter	0.4342 / 0.6688	-0.0102 / 0.1092	0.6231 / 0.8017	0.6987 / 0.8449
Right hemisphere cortical gray matter	0.4525 / 0.6817	-0.0114 / 0.2206	0.6491 / 0.8159	0.7172 / 0.8580
Intracranial	0.3627 / 0.6084	-0.0175 / 0.1469	0.5987 / 0.7920	0.6652 / 0.8239

message passing with edge weights do not produce meaningful features and hence the performance of GCN is poor on regression experiments compared to DeepWalk. We experimented with different initializations for the node attributes, including a constant attribute at each node and the eigenfunctions. Finally, we concatenate the transformed node features to obtain the connectome representation and utilize a fully connected layer for the actual prediction.

Volume Estimation: In this experiment, we considered the prediction of volumes in the following regions: cortical white matter and cortical gray matter volumes in the left and right hemispheres of the brain, and finally the summary total gray matter and total white matter volumes. Table 1 reports the performance of the volume estimation experiment. All the results reported were obtained using a 80% – 20% train-test split of 900 subjects and by aggregating the performance from 20 random trials. We use the R^2 statistic and the Pearson correlation coefficient as performance metrics. As it can be observed, RGNN consistently outperforms all baseline methods by a significant margin, and more importantly, the GCN based on a diffusion-network assumption fails completely. In comparison, even the naïve FCN baseline produces meaningful estimates. This clearly demonstrates the need for specific architectures that can leverage the relational structure of connectomes.

Methods	Gender	Age
DeepWalk	77.09% (± 2.46)	43.10% (± 3.85)
GCN	81.33% (± 2.36)	40.08% (± 3.12)
FCN	89.80% (± 2.94)	44.72% (± 3.96)
RGNN	92.75% (± 1.70)	47.19% (± 3.06)

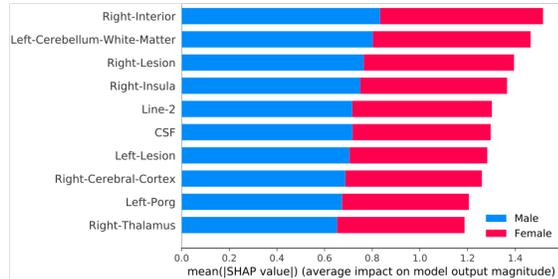


Figure 2: Node importances from SHAP analysis of age prediction model.

Predicting Age/Gender: In this experiment, we use RGNN to identify patterns from the connectome that can effectively discriminate subjects by their gender or age characteristics. Following the observation in [3], we find that RGNN can effectively predict the meta-information based on the structural connectome. Further, we perform sensitivity analysis (using SHAP), Fig. 2 shows node-level importance and so the regions corresponding to the *Right* part of the brain carry crucial information. Edge-level sensitivity analysis indicates that, within hemispheric connectivities are of importance for gender prediction and our results corroborates with the findings in [3]. Similarly, with age prediction (Table 3), RGNN produces highly accurate predictions compared to baseline methods.

These two empirical studies clearly establish RGNN as a potential choice for processing structural and functional connectomes, in order to perform more challenging tasks, such as predicting behavioral traits and cognitive states.

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