REVIEW ARTICLE

Modeling Brain Functional Networks Using Graph Neural Networks: A Review and Clinical Application

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Abstract

The integration of graph neural networks (GNNs) with brain functional network analysis is an emerging field that combines neuroscience and machine learning to enhance our understanding of complex brain dynamics. We first briefly introduce the fundamentals of brain functional networks, followed by an overview of Graph Neural Network principles and architectures. The review then focuses on the applications of these networks and address current challenges in the field, such as the need for interpretable models and effective integration of multi-modal neuroimaging data. We also highlight the potential of GNNs in clinical areas such as perimenopausal depression research, demonstrating the broad applicability of this approach. The review concludes by outlining future research directions, including the development of more sophisticated architectures for large-scale, heterogeneous brain graphs, and the exploration of causal inference in brain networks. By synthesizing recent advances and identifying key research directions, this review aims to summarize the focal points of brain functional network analysis and GNNs, explore the potential of their integration, and provide a reference for advancing this interdisciplinary field.

Keywords: graph neural networks, brain functional networks, neuroimaging analysis.

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1 Introduction

Brain functional networks represent the complex patterns of neural interactions that underlie cognitive processes and behavior [1]. These networks are typically derived from neuroimaging data, such as functional magnetic resonance imaging (fMRI) or electroencephalography (EEG), which capture the temporal correlations between different brain regions [2]. Understanding these networks is crucial for unraveling the intricacies of brain function in both health and disease [3].

Graph-based approaches have emerged as powerful tools for modeling and analyzing brain functional networks. By representing brain regions as nodes and their interactions as edges, these methods can capture the topological properties of neural systems [4]. These functional network analyses have shown promising potential in contributing to

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disease prediction and risk assessment across various neurological and psychiatric conditions [5, 6]. For example, graph theory provides a rich set of metrics to quantify network characteristics, such as modularity, efficiency, and hub structures, offering insights into brain organization and function [7]. Network theory researches on complex networks have also revealed novel principles of network resilience, such as cascading failures and recovery processes, potentially offering valuable insights into the robustness and adaptive mechanisms of brain functional networks in response to perturbations [8, 9].

Recent advances in machine learning have led to the development of graph neural networks (GNNs), a class of deep learning models specifically designed to operate on graph-structured data. GNNs also emerged as a powerful tool in neuroscience for analyzing brain networks. They process graph-structured spatio-temporal signals, combining structural and functional neuroimaging data. GNNs have already shown promise in applications like disease classification [10] and causal inference [11] in brain networks. These studies highlight GNNs' potential to enhance our understanding of brain function and neurological disorders.

This review aims to provide an overview of the concept and application of GNNs in modeling brain functional networks. We will explore:

1. The fundamentals of brain functional networks and their graph-theoretic representations.
2. The principles and architectures of GNNs.
3. Current applications of GNNs in analyzing brain functional networks.
4. Challenges and future directions in this rapidly evolving field.

2 Brain Functional Network

2.1 Measure Brain Functional activity and Establish brain network

Functional Magnetic Resonance Imaging (fMRI) is a non-invasive technique used to measure brain activity by detecting changes in blood oxygenation and flow, referred to as the Blood Oxygen Level Dependent (BOLD) signal [12]. This process works by capturing the fluctuations in oxygen levels that occur when active neurons increase their consumption of oxygen, which is subsequently replenished by increased blood flow. These shifts in deoxyhemoglobin concentrations are what fMRI scans detect as changes in the BOLD signal.

From the temporal correlations of BOLD signals across different brain regions, researchers can determine functional connectivity. This connectivity reflects synchronized activity patterns between regions, indicative of network-level communication. By leveraging this data, fMRI enables the detailed mapping of functional networks, which provides crucial insights into how various parts of the brain interact during tasks or in resting states.

Electroencephalography (EEG) is a non-invasive technique used to record electrical activity in the brain by measuring voltage fluctuations from neurons. EEG offers a significant advantage in functional connectivity studies due to its high temporal resolution, capturing rapid neuronal oscillations with millisecond precision. This is particularly useful for investigating real-time dynamics of brain networks, as described by Kim et al. [13]. However, its spatial resolution is more limited compared to techniques like fMRI.

Magnetoencephalography (MEG), which records magnetic fields generated by neural activity, complements EEG by providing similarly high temporal resolution with better spatial localization, as outlined by da Silva [14]. Together, EEG and MEG allow for the detailed analysis of oscillatory synchronization and functional connectivity, critical for understanding the rapid temporal dynamics of brain networks. Additionally, the integration of EEG and fMRI data provides a more comprehensive view of brain function, combining EEG's high temporal precision with fMRI's superior spatial mapping. Zhang et al. [15] demonstrated this in their study, where they used simultaneous EEG-fMRI to reveal the spatiotemporal dynamics of brain activity during covert and overt speech. This combination enables researchers to explore both the timing and location of brain processes more effectively, offering deeper insights into network-level communication and function.

2.2 Graphical Theory and Metrics of Network

Graph theory provides a mathematical framework for analyzing complex brain systems [16]. In this context, nodes represent brain regions or sensors, while edges depict functional connections between them. The network structure is mathematically represented by an adjacency matrix. Graphs can be categorized as weighted (edges have associated strengths) or unweighted (edges simply indicate connection presence), and as directed (edges have directionality) or undirected. These concepts allow for a comprehensive representation and analysis of brain network organization and dynamics.

Graph theory provides a robust framework for analyzing the structure and function of brain networks by offering a variety of metrics. These metrics help characterize network properties, shedding light on how different regions of the brain interact.

One key metric is modularity, which quantifies the extent to which a network is divided into distinct communities or modules. According to Girvan et al. [17], modularity provides insights into the community structure of complex networks, helping identify clusters of brain regions that function together.

Centrality measures identify important nodes within a network. Barthelemy [18] explored betweenness centrality, which determines how often a node acts as a bridge along the shortest path between other nodes. This metric highlights regions that play a crucial role in connecting different parts of the brain network. Additionally, Ravasz et al. [19] examined **hierarchical organization** in complex networks, showing how centrality can help elucidate the multi-level organization of brain networks, revealing the presence of hubs and their connectivity patterns.

The concept of small-worldness is another critical feature of brain networks. Bassett et al. [20] revisited the small-world characteristics of brain networks, demonstrating that the human brain exhibits both high clustering and short path lengths, indicating an efficient balance between local specialization and global integration. Further, Heuvel et al. [21] discussed scale-free organization, showing that brain networks exhibit a few highly connected nodes (hubs), akin to a scale-free topology, which has implications for the brain's resilience and efficiency.

To facilitate the analysis of these complex network properties, several software tools have been developed. For instance, GAT (Graph Analysis Toolbox), introduced by Hosseini et al. [22], is designed for analyzing group differences in structural and functional brain networks. This toolbox is particularly useful for comparing brain networks across different populations or conditions.

GRETNA (Graph Theoretical Network Analysis), described by Wang et al. [23], is another toolbox that allows for comprehensive graph-theoretical analyses of brain connectomics. It offers a wide range of metrics to assess brain network properties, making it a versatile tool for imaging connectomics research.

Finally, GraphVar, developed by Kruschwitz et al. [24], provides an easy-to-use platform for performing graph analyses on functional brain connectivity data. This toolbox enables researchers to conduct in-depth graph analyses, visualize network metrics, and perform statistical tests on brain connectivity data.

Together, these metrics and tools enable researchers to explore the complex structure and function of brain networks, providing valuable insights into how the brain's architecture supports cognitive processes and behaviors.

3 Graph Neural Network (GNN)

3.1 Overview of GNN

Graph Neural Networks (GNNs) emerged as an extension of neural networks to handle graph-structured data. GNNs excel at capturing complex relationships and interdependencies in graph-structured data, making them particularly effective for tasks involving relational information and network analysis. The fundamental principle of GNNs lies in their ability to learn representations of nodes, edges, and graphs through an iterative process of information propagation and aggregation. The fundamental workflow of GNNs can be described as follows:

Initialization: The process begins with the initialization of node features.

Message Passing and Aggregation: Through multiple iterations, each node engages in a message-passing mechanism, receiving information from its neighboring nodes.

Iterative Update and Convolution: After receiving and aggregating messages, each node updates its own representation through a learnable function, typically combining the aggregated information with the node's previous state. The message passing, aggregation, and update steps are repeated multiple times, enabling the propagation of information across the entire graph structure.

Pooling and Readout: For graph-level tasks, an additional pooling or readout step is performed to obtain a comprehensive graph representation.

3.2 GNN Initialization

In the context of functional network analysis, initialization plays a crucial role in determining the initial representation of brain regions (nodes) and their connections (edges). Feature initialization refers to using specific attributes like regional labels or physical properties to define these initial node states. In their study, Cui et al. [25] introduced Braingb, a benchmark designed for brain network analysis using graph neural networks (GNNs). This benchmark allows for the comparison of different GNN models in terms of their ability to capture brain network features, emphasizing the importance of initialization strategies for nodes and edges. The authors highlight how feature initialization can impact the ability of GNNs to model brain connectivity and how using appropriate initial features is vital for achieving accurate analysis.

When no prior information is available for initialization, random methods are often employed. Abboud et al. [26] explored the surprising effectiveness of random node initialization in GNNs. Their study revealed that even without explicit prior knowledge, random initialization can yield strong performance across various tasks. This finding challenges traditional approaches that emphasize the need for carefully designed initial representations, suggesting that randomness can still lead to meaningful learning in GNNs.

Furthermore, Li et al. [27] conducted an in-depth analysis of different initialization strategies for GNNs, focusing on how these strategies influence model convergence and performance. Their research demonstrates that the choice of initialization has a significant impact on GNNs, particularly in complex networks such as brain functional networks. They show that careful consideration of initialization techniques can lead to better model performance, emphasizing the importance of selecting an appropriate method for specific tasks.

These studies collectively highlight the critical role that initialization plays in functional network analysis with GNNs. Whether using feature-based or random initialization, the way in which nodes and edges are represented initially can significantly affect the outcome of the analysis.

3.3 GNN Aggregation and Pooling

Aggregation and pooling are fundamental operations in GNNs, crucial for processing brain network data effectively.

Aggregation combines information from a node's neighborhood, capturing local structure information around each brain region. Various aggregation schemes have been proposed, from simple mean or sum operations to more sophisticated attention-based mechanisms. For instance, GraphSAGE introduced trainable aggregation functions [28], while Graph Attention Networks (GATs) assign different importance to different neighboring regions [29]. Pooling serves two main purposes in GNNs: reducing the graph size for hierarchical representation learning and generating graph-level embeddings [30]. This is particularly useful for analyzing brain networks at different scales or for tasks requiring a single representation of the entire brain state.

Global pooling methods (e.g., mean, sum, or max of node features) are commonly used to obtain fixed-size representations of the entire brain network. Hierarchical pooling methods, such as DiffPool [31] and SAGPool [32], learn a coarsened graph structure, allowing the model to capture multi-scale properties of brain organization.

Recent advancements in graph neural network pooling techniques have significantly improved the stability and expressiveness of models used for brain network analysis. Mesquita et al. [30] rethought traditional pooling strategies, proposing new methods to better preserve structural information. Ying et al. [31] introduced hierarchical graph representation learning through differentiable pooling. Lee et al. [32] focused on self-attention mechanisms to enhance pooling. Meanwhile, Zhang et al. [33] developed multi-view pooling techniques for structure learning, and Ranjan et al. [34] proposed adaptive pooling strategies tailored to hierarchical graph representations. Together, these innovations enable more nuanced and accurate analyses of brain function across various scales and modalities.

3.4 GNN Convolution

Graph convolution is a fundamental operation in graph neural networks (GNNs) that generalizes the concept of convolution, traditionally used in grid-like data (such as images), to irregular graph-structured data. In standard convolutional neural networks (CNNs), the convolution operation extracts features by applying filters to local neighborhoods of pixels, capturing spatial relationships. Similarly, in GNNs, graph convolution aggregates information from neighboring nodes in a graph to capture both local and global structural patterns. This operation is crucial for analyzing functional brain networks, where nodes represent different brain regions and edges represent connections or interactions between these regions.

The key idea behind graph convolution is that it iteratively updates the representation of each node by aggregating information from its neighbors. This allows the network to build hierarchical representations of the graph, progressively capturing more complex relationships. The process typically involves two main steps: aggregation, where the node's neighbors' features are combined using a function such as summation or averaging, and transformation, where the aggregated features are passed through a learnable weight matrix (often followed by a non-linear activation function).

Graph convolution is particularly useful in brain network analysis because brain regions are interconnected in complex ways that don't follow a regular grid structure. By applying graph convolutions, GNNs can effectively learn patterns of connectivity that are crucial for understanding brain function and dysfunction. The ability to capture both local interactions (e.g., between closely connected brain regions) and global patterns (e.g., broader network-wide properties) makes graph convolution a powerful tool for tasks such as disease diagnosis, brain state classification, and network comparison across individuals.

Graph convolution operations can be classified into two main approaches: spectral-based and spatial-based methods [36]. Spectral methods operate in the frequency domain of graph Laplacian eigenvectors, capturing global graph structure by applying filters in the spectral domain. While these methods offer strong theoretical foundations and global insights, they are computationally expensive and difficult to generalize across different graphs. The need for eigen-decomposition of the Laplacian matrix makes them impractical for large graphs, and their specificity to individual graphs limits their transferability.

In contrast, spatial-based methods perform convolution directly in the graph's vertex domain by aggregating information from local neighborhoods around each node. These methods are more scalable and flexible, making them well-suited for large graphs. However, they focus on local node interactions, potentially missing out on global patterns. A significant development in the field is the Graph Convolutional Network (GCN) [37], which approximates spectral convolutions using local operations. GCNs balance computational efficiency and expressiveness, but they tend to rely on shallow architectures and can suffer from over-smoothing when extended to deeper networks. Overall, GCNs strike a middle ground, combining the strengths of both spectral and spatial approaches.

4 Combine Brain Functional Network and GNN

As shown in Figure 1, GNNs integration with brain functional network analysis has emerged as a powerful approach to understanding complex brain dynamics and neurological disorders. This fusion has significantly advanced neuroscience research in several key areas, offering potential for more precise and individualized assessments of brain health.

In brain state classification, GNN models have demonstrated remarkable performance. A local-to-global graph neural network was developed for classifying brain disorders in resting-state functional magnetic resonance imaging (rs-fMRI). This method enhanced classification accuracy by capturing brain functional connectivity patterns at different spatial scales [38]. Another study empirically evaluated EEG-based graph neural network classification of Alzheimer's disease, comparing the effectiveness of various functional connectivity methods. This research not only showcased GNN's potential in processing EEG data but also provided guidance for selecting appropriate functional connectivity methods [39]. Furthermore, a graph neural network approach using imaging of effective brain connectivity successfully achieved dementia classification, demonstrating GNN's advantages in handling complex brain connectivity patterns [40].

In the field of biomarker identification, GNN models have shown exceptional capabilities. A graph neural network method for interpreting task-fMRI biomarkers was proposed, which not only improved prediction accuracy but also enhanced the interpretability of results [41]. A comprehensive review explored the use of GNNs in discovering robust biomarkers of neurological disorders from functional MRI, highlighting the growing importance of this approach in neuroscience research [42]. Additionally, a pooling regularized graph neural network for fMRI biomarker analysis was developed, addressing the challenge of extracting meaningful features from complex brain network data [43]. In the context of autism spectrum

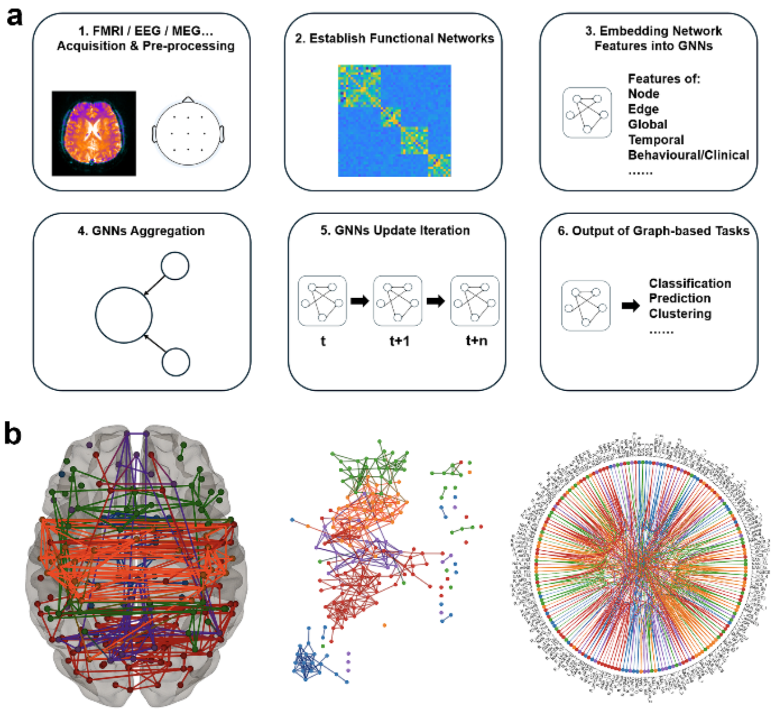

Figure 1. (a) Workflow of applying graph neural networks (GNNs) to brain functional network analysis. (b) An example of brain functional connectivity in brain anatomy, graph, and circular views.

disorder diagnosis, a graph attention network based on spatial-constrained sparse functional brain networks was employed, showcasing the potential of GNNs in analyzing specific neurological conditions [44].

Specialized GNN architectures have been employed to model dynamic functional connectivity, providing insights into how brain function evolves over time. A graph-generative neural network for EEG-based epileptic seizure detection was developed, which discovered dynamic brain functional connectivity patterns. This approach demonstrated the potential of GNNs in capturing the temporal aspects of brain function, particularly in the context of neurological disorders [45].

The versatility of GNNs extends to multi-modal integration, combining functional connectivity data with other types of information, such as structural connectivity. A study on joint embedding of structural and functional brain networks with GNNs for mental illness diagnosis showcased this capability. This comprehensive approach allows for a deeper understanding of brain organization and function by leveraging complementary information from different neuroimaging modalities [46].

As the field progresses, there is a growing focus on developing interpretable GNN models, aiming to provide not just accurate predictions but also insights into the biological basis of their decisions [47]. This trend towards interpretability is crucial for bridging the gap between machine learning models and clinical applications, potentially leading to more informed decision-making in neurological and psychiatric care.

5 Discussion and Outlook

This review has illuminated the remarkable strides made in applying GNNs to various facets of brain network analysis. From brain state classification to biomarker identification and dynamic functional connectivity analysis, GNNs have demonstrated their potential to revolutionize our understanding of the brain's complex network dynamics.

GNNs have shown exceptional prowess in detecting subtle network topology differences that often elude traditional methods [54]. This capability is paramount for distinguishing healthy from diseased brain states, offering a level of precision that was previously unattainable. The power of GNNs lies not just in their ability to classify states, but in their capacity to identify discriminative subnetworks and node properties. This granular level of analysis paves the way for more precise and personalized brain health assessments, potentially transforming how we approach neurological and psychiatric disorders.

The application of GNNs to dynamic functional connectivity analysis represents a significant leap forward in our ability to understand the brain's ever-changing landscape. By capturing the temporal evolution of brain function, its response to stimuli, and its alterations in neurological disorders, GNNs offer a window into the brain's adaptive processes that was previously obscured. This dynamic perspective could be instrumental in unraveling the complexities of disorders characterized by altered brain dynamics, such as epilepsy or schizophrenia.

Table 1. GNNs application examples in brain functional networks.

Applications	Innovations	References
Brain State Classification	Hierarchical architecture; Effective connectivity; EEG-based graphs	[38], [39], [40]
Neurological Disorder Diagnosis	Interpretable biomarkers; Pooling regularization; Spatial-constrained networks	[41], [42], [43], [44]
Dynamic Functional Network	Graph-generative models; Spatio-temporal attention	[45], [48]
Longitudinal Brain Analysis	Temporal GNN; Brain tokenization	[49], [50]
Cross-modal Integration	Joint embedding; Cross-modal learning	[46], [51]
Causal Inference	Causal discovery; Interpretable GNN; Multimodal coarsening	[11], [47], [52], [53]

As shown in Table 1, the application of GNNs to dynamic functional connectivity analysis represents a significant leap forward in our ability to understand the brain's ever-changing landscape. By capturing the temporal evolution of brain function, its response to stimuli, and its alterations in neurological disorders, GNNs offer a window into the brain's adaptive processes that was previously obscured. This dynamic perspective could be instrumental in unraveling the complexities of disorders characterized by altered brain dynamics, such as epilepsy or schizophrenia.

1. Interpretable GNNs: While the predictive power of GNNs is impressive, their 'black box' nature often hinders their adoption in clinical settings. Developing GNN architectures that not only make accurate predictions but also provide insights into the biological mechanisms underlying their decisions is paramount [55]. For example, GNNs provide clinically relevant insights into the neurobiological basis of ASD, potentially informing diagnosis and treatment strategies [56]. Future research could focus on developing attention mechanisms or saliency maps specifically tailored to brain network data, allowing for more intuitive interpretation of GNN decisions.

2. Longitudinal Studies: The brain is not a static entity but a dynamic system that changes over time. Applying GNNs to longitudinal neuroimaging functional data holds immense promise for understanding brain development, aging, and disease progression [49, 50]. This approach could reveal temporal patterns in brain network evolution that are invisible in cross-sectional studies. Moreover, it could lead to early detection methods for neurodegenerative diseases, potentially allowing for intervention before significant symptoms manifest.

3. Large-scale, Heterogeneous Graph Datasets: As our ability to collect and store neuroimaging data grows, so does the complexity of our datasets. Deep learning-based methods will face more challenges in handling diverse datasets with uncertain information [57]. GNNs will need to evolve to handle these large-scale, heterogeneous brain graphs that incorporate multiple types of nodes and edges [58]. This challenge is not just about computational efficiency, but about developing models that can meaningfully integrate diverse data types – from functional connectivity to structural connectivity, and even genetic information. Success in this area could lead to more holistic models of brain function that account for the multi-faceted nature of neural systems.

4. Causal Inference: While current GNN models excel at finding correlations in brain network data, the holy grail of neuroscience is understanding causation. Developing GNN models that can infer causal relationships in brain networks could revolutionize our understanding of how activity propagates through the brain and how interventions affect neural dynamics [11]. This could have far-reaching implications, from optimizing neurostimulation therapies to designing more targeted pharmacological interventions.

5. Clinical Translation: Translating GNN insights into clinical practice represents both a significant challenge and an exciting opportunity. For instance, in the realm of perimenopausal depression, GNNs could help

unravel the complex interactions between hormonal changes, brain network alterations, and depressive symptoms [59]. By modeling how menopausal hormonal fluctuations causally influence brain network properties, such as functional connectivity in emotion regulation circuits [60], we could gain new insights into the neurobiological underpinnings of mood disorders in this population. Similarly, like Alzheimer's disease, GNNs can be applied to model disease progression [39], aiding in early diagnosis and help tailor interventions based on individual patient profiles.

As we look to the future, the integration of GNNs with other cutting-edge technologies presents intriguing possibilities. For instance, combining GNNs with advanced neuroimaging techniques like high-field MRI or novel PET tracers could provide unprecedented resolution in mapping brain networks. Similarly, integrating GNNs with techniques from the burgeoning field of computational psychiatry could lead to more sophisticated models of mental illness that account for both neural network dynamics and cognitive processes.

6 Conclusion

In this extensive review, we delved into the landscape of Graph Convolutional Networks (GCNs) and their growing relevance in the analysis of graph-structured data. Beginning with a discussion of foundational concepts, we distinguished between the two main categories of convolution operations—spectral-based and spatial-based methods. Spectral-based methods leverage graph Laplacian eigenvectors to operate within the frequency domain, capturing the global structure of graphs. On the other hand, spatial-based methods aggregate information from a node's immediate neighbors, offering advantages in terms of computational scalability and efficiency. Each approach brings distinct strengths, and the development of GCNs has been pivotal in balancing the expressiveness of spectral methods with the scalability of spatial techniques, especially in the context of large-scale graphs.

Looking ahead, the future of GCNs hinges on overcoming several key challenges that are central to advancing their practical applications. First and foremost, improving model interpretability is a critical issue. GCNs, like other complex machine learning models, often operate as "black boxes," making their decision-making processes opaque. This lack of transparency poses significant risks, particularly in sensitive areas such as healthcare and finance, where high-stakes decisions require a clear understanding of the underlying rationale. In applications such as diagnosing diseases or making financial forecasts, the ability to interpret a model's outputs is crucial for building trust and ensuring accountability. As such, future research must prioritize developing more interpretable GCN models, enabling users to better understand, verify, and trust their predictions.

Second, scalability and computational efficiency are persistent challenges as the complexity of both models and data continues to increase. Real-world data, particularly in fields like neuroscience, is often heterogeneous and multi-modal, comprising diverse sources such as imaging modalities, temporal data, and connectomic information. In the study of Brain Functional Networks, for example, researchers must integrate fMRI, EEG, and other neuroimaging data types to create a comprehensive model of brain activity. Effectively managing this level of complexity without sacrificing computational efficiency remains a major challenge. Innovations in GCN architectures must focus on handling this diversity of data while maintaining the ability to perform large-scale, efficient computations. Successfully achieving this will be instrumental in advancing not only brain research but also the broader application of GCNs to other complex systems.

Lastly, the integration of causal inference mechanisms into GNN frameworks represents a promising direction for future research. Causal inference allows for the identification of cause-and-effect relationships, a crucial capability for understanding the interactions and dependencies within complex systems such as brain networks or social ecosystems. In the study of brain networks, where neural activity is influenced by both external stimuli and internal states, understanding the causal pathways behind observed behaviors can lead to more effective interventions, particularly in the realm of mental health and neurological disorders. Similarly, in social science, incorporating causal inference can yield deeper insights into how social interactions shape behavior, providing valuable data for policy-making and educational reform. By integrating these mechanisms, GCNs will enable a more nuanced analysis of dynamic, interconnected systems, thereby pushing the boundaries of what is possible in data-driven research.

In summary, the continued advancement of GCNs will depend on our ability to overcome these challenges. By improving interpretability, enhancing scalability and efficiency, and incorporating causal inference, GCNs have the potential to unlock new frontiers in data analysis across a wide array of fields. From revolutionizing the way we understand the brain to providing more reliable models for financial forecasting, GCNs are poised to have a transformative impact. As these models evolve, their applications will extend far beyond their current capabilities, driving innovation and fostering deeper insights across industries such as healthcare, finance, and social science. The future of GCNs is rich with potential, and by addressing these pressing issues, researchers will pave the way for more accurate, efficient, and impactful analyses of complex data.

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Not applicable.

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Conflicts of Interest

The authors declare no conflicts of interest.

Ethical Approval and Consent to Participate

Not applicable.

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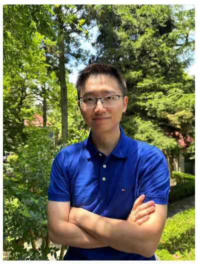

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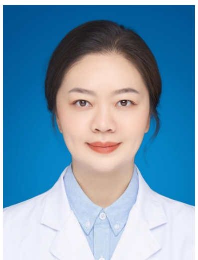

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