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Hypergraph Neural Networks for Brain Tumor Analysis and Medical Image Understanding: A Review

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Abstract: Medical image analysis plays a critical role in modern clinical diagnosis and treatment planning. While deep learning, particularly convolutional neural networks, has achieved remarkable success, conventional models struggle to capture the complex high-order relationships inherent in anatomical structures and pathological patterns. Hypergraph neural networks (HGNNs), which generalize standard graphs by allowing hyperedges to connect multiple nodes, have emerged as a powerful paradigm for modeling such high-order interactions. This review provides a systematic overview of hypergraph learning techniques for medical image analysis. We first introduce the mathematical foundations of hypergraphs and categorize existing hypergraph construction methods into similarity-based, topology-based, and learning-based approaches. We then review state-of-the-art hypergraph neural network architectures, including dynamic hypergraph neural networks, hypergraph transformers, and over-smoothing mitigation strategies. Subsequently, we survey key applications in brain tumor classification, functional brain network analysis, medical image segmentation, and survival prediction. Finally, we discuss open challenges and promising future directions, including multi-modal fusion, model interpretability, computational efficiency, and domain generalization. This review aims to provide researchers with a comprehensive understanding of hypergraph learning for medical imaging and to inspire further advancements in this rapidly evolving field.

Keywords: Hypergraph neural network, Medical image analysis, Brain tumor classification, High-order relationships, Dynamic hypergraph, Topological data analysis.

1. Introduction

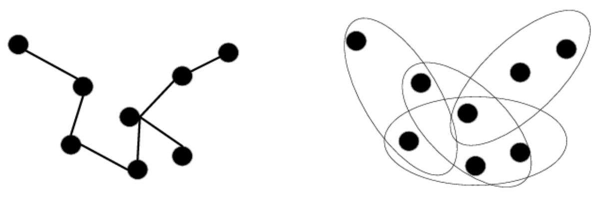
Medical imaging technologies, particularly magnetic resonance imaging (MRI), computed tomography (CT), and histopathology imaging, have become indispensable tools for disease diagnosis, prognosis assessment, and treatment planning [1]. Among various clinical applications, brain tumor analysis—especially glioma characterization—remains particularly challenging due to the complex morphology, heterogeneous composition, and infiltrative nature of these lesions [2].

In response to these challenges, deep learning has been extensively adopted to automate and enhance medical image interpretation. Deep learning, especially convolutional neural networks (CNNs), has revolutionized medical image analysis over the past decade [3]. CNNs excel at learning hierarchical representations from raw pixel data, achieving human-level performance in tasks ranging from pneumonia detection to diabetic retinopathy screening [4]. However, CNNs suffer from inherent limitations when applied to medical images: (i) they operate on fixed regular grids, failing to capture the irregular spatial relationships between anatomical structures; (ii) they rely on local receptive fields, struggling to model long-range dependencies across distant image regions; and (iii) they treat image patches independently, ignoring the rich contextual information that clinicians naturally integrate [5].

To address these limitations, researchers have turned to graph-based representations. Graph neural networks (GNNs) and graph convolutional networks (GCNs) model medical images as graphs where nodes represent image patches or anatomical regions, and edges capture pairwise relationships [6]. GNNs have shown promise in applications such as brain network analysis, tumor segmentation, and disease classification [7].

Despite their success, standard GNNs are fundamentally limited to pairwise relationships—they can only model interactions between two nodes at a time. However, medical images often contain high-order interactions that extend beyond pairwise connections. For example, in a brain tumor MRI, the coordinated characteristics of multiple regions—the necrotic core, peritumoral edema, and enhancing tumor margin—collectively determine tumor grade and prognosis. These relationships cannot be fully captured by binary edges [8].

Hypergraph neural networks (HGNNs) overcome this limitation by generalizing the notion of edges to hyperedges, each of which can connect an arbitrary number of nodes [9]. As illustrated in Figure 1, a hyperedge can simultaneously link multiple image regions that share semantic or pathological relevance, enabling direct modeling of high-order relationships without decomposing them into pairwise approximations.



(a)Graph (b)Hypergraph

Figure 1. Comparison between standard graph and hypergraph for medical image representation

Although several existing surveys have explored hypergraph learning in general application domains [10], a comprehensive review that specifically focuses on hypergraph learning in the field of medical image analysis is still lacking. Current review works either concentrate on the theoretical fundamentals of hypergraph learning or target general computer vision applications, leaving a noticeable research gap in the medical imaging literature.

To address this gap, this review systematically organizes the relevant literature from three interrelated perspectives: hypergraph construction methods, which explore how hypergraphs are constructed from medical images; network architectures, which investigate how hypergraph neural networks (HGNNs) are designed and optimized for various medical tasks; and clinical applications, which summarize scenarios where HGNNs have shown promising performance [11].

The key contributions of this review are as follows. First, it proposes a structured taxonomy of hypergraph construction methods specially adapted for medical images. Second, it systematically reviews the architectural progress of HGNNs, including developments in dynamic hypergraphs, hypergraph transformers, and strategies for alleviating over-smoothing issues. Third, it summarizes empirical results across representative clinical applications, with a particular focus on brain tumor analysis. Finally, it identifies current open challenges in this field and puts forward specific and feasible directions for future research.

2. Hypergraph Construction Methods for Medical Images

The construction of hypergraphs from raw medical images is a critical design choice that fundamentally affects model performance. Based on a systematic analysis of the literature, we propose a taxonomy consisting of three categories: similarity-based, topology-based, and learning-based dynamic methods. Table 1 compares the characteristics of the three hypergraph construction paradigms.

Table 1. Comparison of hypergraph construction methods for medical images

Aspect	Similarity-based	Topology-based	Learning-based
Construction basis	Feature distance	Persistent homology	Learnable prototypes / Attention
Adaptivity	Static	Static	Dynamic
Topological awareness	Low	High	Medium
Computational cost	Low	High	Medium
Interpretability	High	Medium	Low
Parameter sensitivity	k or ε	Persistence threshold	Number of prototypes, top-k
Best suited for	Large-scale, local patterns	Structure-rich, global morphology	Task-specific grouping

2.1. Similarity-based Construction

Similarity-based methods are the most straightforward and widely adopted approach, constructing hyperedges based on distances or similarities in the feature space. For k-Nearest Neighbor (KNN) hypergraphs, each node (typically representing an image patch or superpixel) identifies the k most similar nodes in the feature space and forms a hyperedge containing the center node and its k neighbors [12], with similarity commonly measured using Euclidean distance, cosine similarity, or Gaussian kernel functions; in contrast, ε-neighborhood hypergraphs connect all nodes within a distance threshold ε of the center node [13], adapting to local density but requiring careful threshold selection. These methods offer key advantages: they are simple to implement and computationally efficient, and they perform well when feature-space distances correlate with semantic relationships, but they also have notable limitations: they are sensitive to hyperparameters (k or ε), cannot capture global or topological structures, and produce static graphs that remain fixed during training. In medical imaging applications, KNN hypergraphs have been successfully applied to brain tumor segmentation [14] and histopathology image analysis [15], where local feature similarity correlates reasonably with pathological relationships. Figure 2 illustrates the process of similarity-based hypergraph construction, where each node connects to its k-nearest neighbors in the feature space.

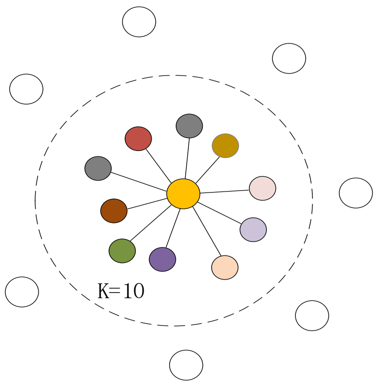


Figure 2. Similarity-based Construction

2.2. Topology-based Construction

Recognizing that similarity-based methods overlook global structural information, researchers have introduced topological data analysis (TDA) into hypergraph construction, with a core technique in this category being persistent homology, which tracks the emergence and disappearance of topological features—such as connected components, loops, and voids—across a filtration process [16].

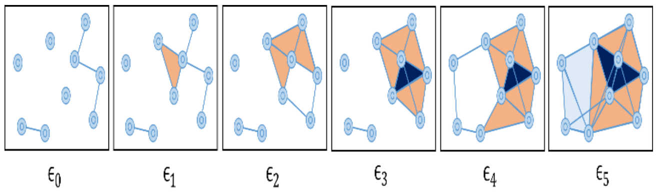


Figure 3. The process of VR-filtration

Given a set of nodes in feature space, a Vietoris-Rips complex is constructed at increasing scale parameters ε, and the "persistence" of each topological feature—its lifetime, calculated as the difference between its death and birth scales—indicates its structural significance: long-lived features are considered salient, while short-lived features are treated as noise. The Vietoris-Rips filtration process for topological feature extraction is shown in Figure 3, where the scale parameter ε increases from left to right. To integrate this with hypergraph learning, salient topological features are used to define hyperedges, where for each persistent feature, node pairs whose distances fall within the corresponding persistence interval are connected, and these topology-informed edges are then combined with local KNN edges to form a hybrid hypergraph that captures both local geometry and global topology. This approach offers several advantages: it captures multi-scale structural patterns, is robust to noise (as short-lived features are filtered out), and provides theoretically grounded topological guarantees, but it also has notable limitations: it is computationally expensive (the Vietoris-Rips complex scales poorly with data size), threshold selection for determining feature saliency remains challenging, and the resulting graph is still static after construction. In medical imaging applications, topology-aware hypergraph construction has been applied to brain tumor MRI classification [17], where tumor morphology exhibits characteristic topological signatures that can distinguish high-grade from low-grade gliomas.

2.3. Learning-based Dynamic Construction

To overcome the static nature of pre-constructed hypergraphs, recent works have introduced learning-based methods that adaptively build hypergraph structures during training, with one prominent approach being attention-guided hypergraph construction, which introduces learnable hyperedge prototypes (embeddings) that represent latent high-order semantic patterns [18]; for each node, attention scores are computed between the node feature and all hyperedge prototypes, the top-k prototypes with the highest attention scores are selected, and the normalized attention weights form a soft incidence matrix, with the hyperedge prototypes crucially updated via gradient descent to enable the hypergraph structure to co-evolve with node representations. A related strategy involves clustering-based dynamic hypergraphs, which use differentiable clustering to group nodes into hyperedges [19], where node features are clustered at each layer and the resulting clusters serve as hyperedges for subsequent convolution, naturally adapting the hypergraph to the evolving feature space. These methods offer several key advantages: they are task-adaptive, as the hypergraph structure is optimized directly for the objective function; they can capture task-specific high-order relationships; and the soft assignment mechanism provides full differentiability, allowing for smooth gradient flow through the graph construction process, but they also present notable limitations: they incur increased computational cost, require careful regularization to avoid trivial or degenerate solutions, and remain sensitive to hyperparameters such as the number of prototypes or the top-k selection value. In medical imaging applications, dynamic hypergraph construction has demonstrated superior performance on brain tumor classification [20] and medical image segmentation, where the optimal grouping of image regions depends heavily on the specific pathological context.

The choice of construction method involves trade-offs between computational cost, structural expressiveness, and adaptivity. Similarity-based methods are suitable for large-scale applications where local patterns are sufficient; topology-based methods are preferred when global structural information is discriminative; and learning-based dynamic methods are most appropriate when the optimal grouping is not known a priori and can be learned from data.

3. Hypergraph Neural Network Architectures for Medical Image Analysis

After constructing a suitable hypergraph structure, the design of hypergraph neural network (HGNN) architectures plays an equally important role in achieving high performance in medical image analysis. Different from simple graph neural networks, HGNNs need to effectively propagate and aggregate high-order information via hyperedges.

In this section, we review mainstream architectural designs of HGNNs, including spectral and spatial convolution, dynamic hypergraph networks, hypergraph transformers, strategies for over-smoothing mitigation, and lightweight or hybrid structures tailored for medical imaging tasks. Table 2 provides a comparative summary of different HGNN architectures, highlighting their core mechanisms, advantages, and limitations.

Table 2. Summary of hypergraph neural network architectures for medical image analysis.

Architecture	Core Mechanism	Key Advantage	Limitation
Spectral HGNN	Laplacian eigen-decomposition	Theoretically solid	High computation
Spatial HGNN	Two-stage message passing	Flexible, efficient	Lack global context
Dynamic HGNN	Structure co-evolves with features	Task-adaptive	Extra computation
Hypergraph Transformer	Hyperedge-guided attention	Long-range modeling	High memory cost
Over-smoothing Mitigation	Residual, routing, DropEdge	Enables deep networks	Architectural complexity
Lightweight HGNN	CNN-HGNN hybrid, sparse ops	Edge-deployable	Potential performance drop

3.1. Spectral and Spatial Hypergraph Convolution

Hypergraph convolution can be roughly divided into two categories: spectral-based methods and spatial-based methods. Spectral hypergraph convolution is derived from hypergraph signal processing, which defines convolution operations by performing eigen-decomposition on the hypergraph Laplacian matrix, achieving feature smoothing and transformation in the frequency domain.

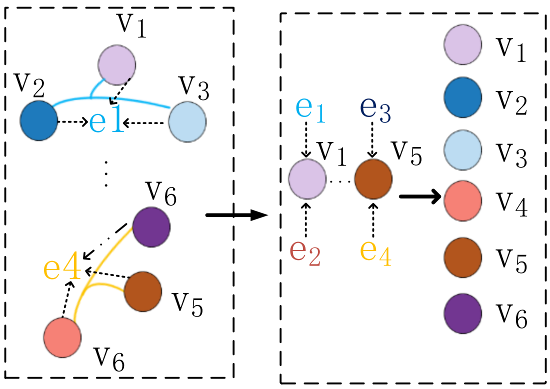


Figure 4. Schematic diagram of hypergraph convolution

The two-stage message passing mechanism of hypergraph convolution is illustrated in Figure 4. Such methods have solid theoretical support and can explicitly model global signal variations, making them suitable for medical image analysis tasks that require stable topological constraints. For instance, the pioneering HGNN framework proposed by Feng et al. [21] adopts spectral convolution to realize hypergraph feature learning, which has been widely applied in brain network analysis and pathological image recognition. However, spectral methods rely on fixed hypergraph structures and suffer from high computational complexity when dealing with large-scale medical image data, such as high-resolution whole-slide pathological images and volumetric MRI data [22]. In contrast, spatial hypergraph convolution directly defines information propagation rules on the hypergraph topology, following the node-to-hyperedge aggregation and hyperedge-to-node distribution mechanism. This two-stage message-passing mechanism is more flexible and can be easily combined with convolutional neural networks to extract multi-scale medical image features. For example, HGNN+ [23] extends spatial convolution to support multi-modal data fusion, which has achieved good results in multi-modal brain tumor image analysis. Moreover, spatial convolution can be integrated with attention mechanisms to dynamically adjust the aggregation weights of nodes and hyperedges, further enhancing the model's ability to capture discriminative pathological features [24]. Due to these advantages, spatial hypergraph convolution has become the mainstream design in medical imaging applications, especially for tasks such as brain tumor segmentation and classification that require efficient feature fusion and adaptive information propagation.

3.2. Dynamic Hypergraph Neural Networks

Static hypergraphs constructed in advance cannot adapt to the changing feature distributions during network training, especially for heterogeneous medical images such as brain tumors and pathological slices, where the relationships between regions are complex and diverse [25]. Dynamic hypergraph neural networks address this issue by updating the hypergraph structure synchronously with feature learning. During each iteration or network layer, the incidence matrix, hyperedge weights, or node connections are adjusted according to the current feature representations, enabling the model to capture adaptive high-order relationships [26]. In medical image analysis, dynamic HGNNs can automatically perceive lesion boundaries, aggregate multi-region pathological features, and suppress noise interference from non-target tissues. For example, Li et al. [27] first proposed a dynamic hypergraph neural network that updates the hypergraph structure during training, which effectively improves the accuracy of disease classification. In brain tumor MRI analysis, dynamic HGNNs can adaptively adjust the connections between tumor regions, edema areas, and normal tissues, thereby more accurately modeling the heterogeneous characteristics of gliomas [28]. In addition, dynamic hypergraphs combined with attention mechanisms can further enhance the model's ability to capture key pathological features. For example, the attention-guided dynamic hypergraph construction method proposed in this study can automatically learn hyperedge prototypes and adjust node-hyperedge connections, which has achieved excellent performance in brain tumor classification [29]. Compared with static hypergraphs, dynamic HGNNs have stronger adaptability and robustness, and are more suitable for complex medical image analysis tasks with high heterogeneity and variability.

3.3. Hypergraph Transformers

Benefiting from the strong long-range dependency modeling ability of Transformers, hypergraph transformers integrate hypergraph structures into the self-attention mechanism to further enhance high-order semantic modeling. This architecture uses hyperedges to guide the generation of attention matrices, reducing redundant calculations while focusing on clinically meaningful region combinations. Traditional Transformers lack explicit structural modeling capabilities and often treat image patches as independent individuals, ignoring the topological relationships between anatomical and pathological regions [30]. Hypergraph transformers solve this problem by introducing hypergraph structure information into the attention calculation, enabling the model to capture both global long-range dependencies and high-order structural relationships. For medical images with complex spatial distributions and large field-of-view demands, such as whole-slide pathological images and brain MRI volumes, hypergraph transformers can effectively model long-distance interactions between lesions and normal tissues, fuse global and local information, and achieve performance breakthroughs in high-precision clinical tasks. For example, Li et al. [31] proposed a hypergraph transformer neural network that combines hypergraph convolution with Transformer, which has achieved advanced results in brain network analysis and disease classification. In brain tumor analysis, hypergraph transformers can capture the long-range semantic dependencies between different sub-regions of gliomas, thereby improving the accuracy of tumor grading and prognosis prediction [32]. In addition, hypergraph transformers can be combined with multi-scale feature learning mechanisms to adapt to the multi-scale characteristics of pathological structures, further enhancing the model's feature expression ability [33].

3.4. Over-smoothing Mitigation in HGNNs

With the increase of network layers, HGNNs face the over-smoothing problem similar to traditional graph neural networks, that is, node features tend to be homogenized and lose discriminability, which seriously affects the characterization of subtle pathological differences [34] This problem is more prominent in medical image analysis, because the subtle differences between lesion and normal tissues, as well as between different grades of tumors, are crucial for accurate diagnosis. To alleviate this issue, researchers have proposed a variety of strategies. First, residual connections and dense connections are introduced into hypergraph convolution to retain shallow local features while deepening the network, preventing excessive homogenization of node features [35]. For example, the topology-aware routing hypergraph convolution module proposed in this study uses adaptive residual connections to effectively alleviate over-smoothing and achieve deep network training [36]. Second, adaptive hyperedge weights are used to control the information transmission range, avoiding excessive aggregation of irrelevant features and maintaining the discriminability of node representations [37]. Third, multi-branch structures are designed to maintain feature diversity, and different branches capture different scales and types of structural features, reducing the risk of over-smoothing [38]. In addition, methods such as feature normalization and DropEdge can also be used to relieve over-smoothing in HGNNs [39]. For example, Chen et al. [40] proposed a method to prevent over-smoothing in hypergraph neural networks from a topological perspective, which has achieved good results in medical image analysis. These methods effectively maintain the differentiation of node representations, enabling deep HGNNs to be better applied in medical image analysis with high requirements for detail perception.

3.5. Hybrid and Lightweight HGNN Architectures

In clinical scenarios, medical image analysis models often need to meet the requirements of low latency and high efficiency, especially for edge deployment and real-time diagnosis applications [41]. Hybrid architectures that combine CNNs and HGNNs have become a practical solution, where CNNs are used to extract local visual features from images, and HGNNs are responsible for modeling high-order topological relationships between regions [42]. This hybrid structure takes advantage of the powerful feature extraction ability of CNNs and the high-order relationship modeling ability of HGNNs, achieving a balance between performance and efficiency. For example, in brain tumor image analysis, CNNs are used to extract the texture and shape features of tumor regions, and HGNNs model the relationships between different tumor sub-regions, significantly improving the accuracy of tumor classification and segmentation [43]. In addition, lightweight HGNN designs simplify hypergraph convolution operations, reduce the number of hyperedges and learnable parameters, and maintain performance while improving inference speed [44]. For example, the adaptive multi-scale residual feature learning module proposed in this study uses lightweight Inception-ResNet structure to reduce model complexity while ensuring multi-scale feature extraction ability [45]. Moreover, lightweight HGNNs combined with attention mechanisms can further improve computational efficiency by focusing on key pathological regions and reducing redundant calculations [46]. Such structures are suitable for clinical deployment, real-time diagnosis and other practical medical applications, promoting the clinical transformation of hypergraph neural network technology.

4. Clinical Applications of Hypergraph Neural Networks in Medical Image Analysis

Benefiting from powerful high-order relationship modeling capabilities, hypergraph neural networks have been widely and successfully applied in various medical image analysis tasks. In this section, we summarize the representative clinical applications, with a particular emphasis on brain tumor analysis, including brain tumor classification, brain tumor segmentation, and survival prediction. We also introduce applications in functional brain network analysis, histopathological image analysis, and other medical image computing tasks. An overview of representative clinical applications of HGNNs is presented in Figure 5, covering brain tumor analysis, functional brain network analysis, histopathology, and survival prediction.

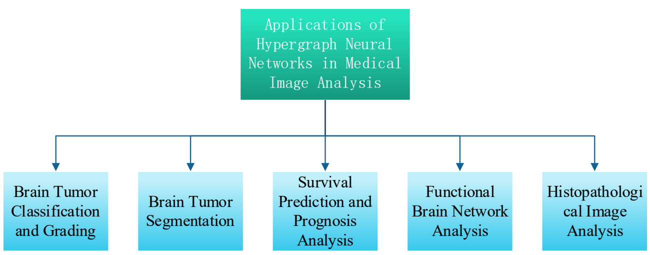


Figure 5. Applications of Hypergraph Neural Networks in Medical Image Analysis

4.1. Brain Tumor Classification and Grading

Brain tumor grading, especially for gliomas, is one of the most important and widely explored applications of hypergraph learning in medical imaging. Due to the high heterogeneity, complex morphology, and infiltrative structure of gliomas, modeling high-order relationships among tumor subregions is critical for accurate classification. Hypergraph neural networks provide a natural way to capture the joint interactions among necrotic core, solid tumor, edema, and enhanced regions, which significantly improves grading accuracy. Similarity-based hypergraphs have been used to model local patch similarities for brain tumor subtype classification [47]. Topology-aware hypergraphs further integrate persistent homology to capture global morphological features, enabling better discrimination between low-grade and high-grade gliomas [48]. Learning-based dynamic hypergraphs achieve the best performance by adaptively optimizing hyperedge connections during training, focusing on discriminative pathological regions. Recent studies also combine hypergraphs with transformers to model long-range dependencies in multi-modal MRI, further boosting classification performance [49].

4.2. Brain Tumor Segmentation

Segmentation of brain tumors, including whole tumor, core tumor, and enhanced tumor regions, is essential for surgical planning and prognosis assessment. Traditional CNN-based methods struggle to capture global spatial relationships between disconnected tumor regions. Hypergraph neural networks overcome this limitation by connecting semantically related regions with hyperedges. Many methods use hypergraph convolution to propagate contextual information among multi-scale image patches, improving the integrity and continuity of segmentation results [50]. Dynamic hypergraphs can adaptively adjust the connectivity between tumor regions during training, reducing false positives and enhancing segmentation accuracy in heterogeneous areas. Some hybrid models combine CNNs and hypergraphs to use local texture features and global high-order relationships simultaneously, achieving state-of-the-art performance on public brain tumor datasets such as BraTS [51].

4.3. Survival Prediction and Prognosis Analysis

Survival prediction and gene status estimation for glioma patients provide important references for clinical treatment. Hypergraph models can integrate multi-modal data, including MRI, genomic data, and clinical information, to construct comprehensive high-order relationships for prognosis analysis. Hypergraphs are used to fuse high-dimensional features from different modalities, modeling complex interactions between imaging phenotypes and molecular characteristics [52]. By using hyperedge learning to mine prognostic biomarkers, these methods can effectively predict overall survival and progression-free survival. Topological hypergraphs further enhance prognostic feature representation by capturing stable structural patterns in multi-modal data [53].

4.4. Functional Brain Network Analysis

Functional brain networks derived from fMRI and DTI contain complex high-order interactions among brain regions that cannot be fully represented by traditional graphs. Hypergraph neural networks become a natural tool for modeling brain functional connectivity. Hyperedges are used to represent joint activation patterns among multiple brain regions, enabling more accurate analysis of brain connectivity and disease classification [54]. Hypergraph attention networks further enhance the modeling of key brain region connections, improving the performance of neurological disease diagnosis.

4.5. Histopathological Image Analysis

Histopathological images are characterized by complex cell layouts and heterogeneous tissue structures. Hypergraphs can model spatial relationships among multiple cells, glands, and pathological regions. Similarity and dynamic hypergraphs are widely used to cluster and classify pathological patches, improving the accuracy of cancer diagnosis and grading. Hypergraph convolution helps aggregate contextual information among spatially distributed nuclei and tissues, which is beneficial for nuclear segmentation, cancer detection, and biomarker discovery [55].

5. Open Challenges and Future Directio

Despite the rapid progress and encouraging achievements of hypergraph neural networks in medical image analysis, several critical challenges still restrict their further development and clinical translation. These challenges mainly involve multi-modal data fusion, model interpretability, over-smoothing in deep networks, computational efficiency, domain generalization, and clinical practicability. In this section, we elaborate on these open issues and propose corresponding future research directions, aiming to provide clear and valuable guidance for subsequent research. The key open challenges of hypergraph neural networks in medical image analysis are illustrated in Figure 6, including multi-modal fusion, model interpretability, over-smoothing mitigation, computational efficiency, domain generalization, and clinical integration.

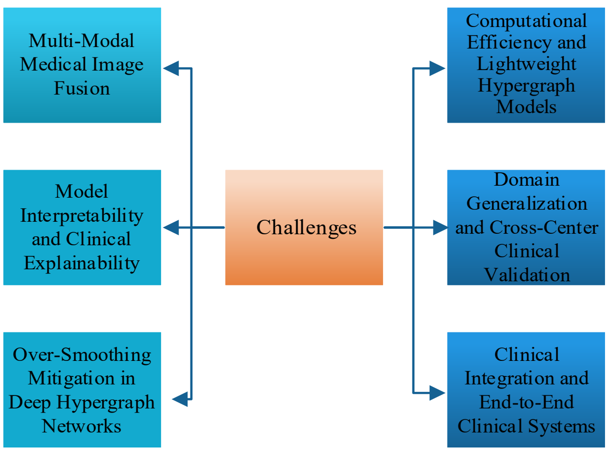


Figure 6. Schematic diagram of hypergraph convolution

5.1. Multi-Modal Medical Image Fusion

In clinical practice, accurate diagnosis of brain tumors and other diseases usually depends on comprehensive information from multiple modalities, such as multi-sequence MRI, CT, PET, histopathology, and even genomic data [56]. However, most existing hypergraph models are designed for single-modal images and lack effective mechanisms to fuse heterogeneous features. Multi-modal data differ significantly in spatial resolution, distribution, structural topology, and information dimension, making it difficult to construct a unified high-order hypergraph structure [57]. In addition, how to weigh the contributions of different modalities and avoid noise interference remains unresolved. Future research should focus on cross-modal hypergraph construction, adaptive hyperedge alignment, and dynamic hypergraph fusion frameworks to integrate complementary information across modalities [58]. It is also necessary to explore hypergraph structures that can simultaneously model intra-modal and inter-modal high-order relationships, thereby improving the robustness and accuracy of complex disease diagnosis.

5.2. Model Interpretability and Clinical Explainability

Although hypergraph neural networks achieve high performance in various medical image tasks, they are still regarded as black-box models with poor interpretability [59]. The interaction mechanism between nodes and hyperedges is complex and difficult to visualize, and clinicians cannot clearly understand which regions or structural features dominate the final decision. This lack of transparency seriously hinders clinical trust and practical deployment. In the future, interpretable hypergraph learning should be developed by combining visualization tools, causal inference, and prior clinical knowledge. For example, using Grad-CAM, t-SNE, or topological visualization to highlight key hyperedges and pathological regions can help verify whether model decisions conform to clinical logic [60]. In addition, structurally constrained hyperedge learning and clinically annotated hypergraph regularization are expected to make the model more transparent and reliable.

5.3. Over-Smoothing Mitigation in Deep Hypergraph Networks

With the increase of network depth, hypergraph neural networks still suffer from the over-smoothing problem, which makes node features increasingly homogeneous and loses discriminative pathological details [61]. This problem is more critical in medical image analysis, where subtle differences between tumor subtypes and normal tissues determine diagnostic accuracy. Although residual connections, adaptive weights, and dense connections have been used to alleviate over-smoothing, most methods lack theoretical support for medical images [62]. Future research can combine topological data analysis to design topology-guided hypergraph convolution and persistent homology regularization to maintain structural discrimination during deep propagation. Adaptive routing mechanisms, dynamic hyperedge adjustment, and multi-branch structure design are also effective ways to suppress over-smoothing.

5.4. Computational Efficiency and Lightweight Hypergraph Models

High-resolution medical images (such as whole-slide pathology images and 3D MRI volumes) lead to huge computational and memory costs in hypergraph construction and convolution [63]. Many hypergraph models cannot meet the real-time requirements of clinical diagnosis, limiting their practical application. Future research should explore sparse hypergraph optimization, lightweight hyperedge generation, and simplified hypergraph convolution. Hybrid structures combining CNNs and hypergraphs can reduce redundant calculations while maintaining high-order modeling capabilities. In addition, efficient Transformer–hypergraph fusion models and dynamic sparse attention mechanisms are expected to achieve a better balance between performance and speed [64].

5.5. Domain Generalization and Cross-Center Clinical Validation

Medical image data vary significantly among different hospitals, scanners, acquisition protocols, and patient groups. Most hypergraph models are trained and tested on single datasets, resulting in poor generalization ability. In real clinical scenarios, model performance may drop sharply due to domain shift. Future research should focus on domain-adaptive hypergraph learning, cross-center structure alignment, and generalized hypergraph construction strategies. It is also necessary to conduct large-scale multi-center clinical validation to improve the stability and reliability of hypergraph models [65].

5.6. Clinical Integration and End-to-End Clinical Systems

To realize real clinical value, hypergraph models must be integrated into the actual clinical workflow, including tumor diagnosis, segmentation, surgical planning, survival prediction, and automatic report generation. However, most existing methods only focus on a single task and lack end-to-end clinical systems [66]. Future research should build a unified hypergraph framework that can simultaneously complete segmentation, classification, prognosis, and biomarker mining. Such systems can provide comprehensive and accurate auxiliary diagnosis for clinicians and promote the practical application of hypergraph learning in intelligent medicine.

6. Conclusion

In conclusion, hypergraph learning has the potential to significantly impact the accuracy and reliability of medical image analysis, especially for brain tumor diagnosis and characterization. The benefits of hypergraph neural networks in this field are substantial, ranging from effectively modeling high-order relationships among anatomical and pathological regions to capturing complex structural interactions that conventional CNNs and GNNs cannot fully represent. Hypergraph construction strategies, advanced network architectures, dynamic structure learning, and topological information integration have collectively contributed to improved performance in brain tumor classification, segmentation, survival prediction, and functional brain network analysis.

However, it is essential to acknowledge the existing challenges and limitations associated with hypergraph learning in medical imaging. These challenges include the difficulty of fusing multi-modal medical data within a unified hypergraph framework, the limited interpretability of complex node–hyperedge interactions, over-smoothing in deep network structures, high computational complexity on large-scale high-resolution images, poor domain generalization across centers and devices, and the lack of end-to-end clinical deployment systems. Addressing these challenges is crucial to maximize the benefits of hypergraph learning and ensure that it remains an effective and trustworthy tool for enhancing clinical diagnosis, prognosis, and personalized treatment planning.

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