ISSN: 2710-0588

Graph-Based Learning for Ophthalmic Image Analysis: Models, Methodologies, and Future Directions

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Abstract

Ophthalmic imaging serves as a cornerstone for the diagnosis and management of ocular diseases, capturing intricate anatomical structures and relational patterns that are not fully characterized by conventional convolutional neural networks operating on Euclidean grids. Graph-based learning offers a powerful paradigm to overcome this limitation by representing images as graphs, where nodes correspond to anatomical units and edges encode structural, spatial, or semantic relationships. This review provides a systematic and critical synthesis of graph-based methodologies applied to ophthalmic image analysis. It examines fundamental graph construction strategies-including node representation, edge formulation, and topological design-tailored to the hierarchical and relational nature of retinal structures. We further survey the evolution of graph learning models, from early graphical approaches to modern graph neural networks (GNNs) and their attention-based, diffusion-aware, and higher-order extensions. The discussion extends to learning strategies optimized for ophthalmic data challenges such as annotation scarcity, class imbalance, and domain shift. Clinically, we summarize representative applications across major imaging modalities, including fundus photography and optical coherence tomography, highlighting how graph-based frameworks advance tasks such as glaucoma assessment, diabetic retinopathy grading, vessel segmentation, and layered tissue analysis. Despite promising progress, critical challenges remain in robust and anatomically consistent graph construction, computational scalability, cross-domain generalization, and clinical interpretability. Future directions emphasize adaptive and uncertainty-aware graph building, scalable GNN architectures, integration of hypergraph representations for group-wise interactions, and unified multi-modal and longitudinal modeling. Through a structured analysis of models, methodologies, and applications, this review aims to guide the translation of graph-based learning into reliable and interpretable clinical tools for precision ophthalmology.

Keywords

Graph-based Learning, Graph Neural Networks, Ophthalmic Image Analysis, Retinal Imaging, Structural Representation, Medical Image Computing, Clinical Applications, Deep Learning in Ophthalmology.

1. Introduction

Ophthalmic imaging constitutes a cornerstone of modern ophthalmology, providing indispensable visual evidence for the diagnosis, monitoring, and management of a spectrum of ocular pathologies, including glaucoma, diabetic retinopathy, and age-related macular degeneration[1]. Advancements in imaging modalities-such as fundus photography and optical coherence tomography (OCT)-have enabled the acquisition of high-resolution, anatomically detailed representations of retinal structures[2]. These images are inherently rich in spatial,

ISSN: 2710-0588

relational, and hierarchical information, capturing complex interactions among retinal regions, vascular networks, and layered tissues.

The advent of artificial intelligence (AI), particularly deep convolutional neural networks (CNNs), has catalyzed significant progress in ophthalmic image analysis.[3] CNNs have demonstrated remarkable efficacy in tasks ranging from disease classification and lesion detection to tissue segmentation. However, their architectural design, rooted in operations on regular Euclidean grids, presents fundamental limitations[4]. CNNs primarily rely on local receptive fields and struggle to explicitly model long-range dependencies, non-local interactions, and the topological organization that are intrinsic to ophthalmic anatomy[5]. Critical clinical structures-such as the relational geometry between the optic disc and cup, the connectivity patterns of retinal vasculature, or the inter-layer correlations in OCT scans-cannot be fully characterized through convolutional filters alone, as they extend beyond local spatial adjacency[6].

These limitations underscore the need for learning frameworks that can explicitly represent and reason about structural relationships[1]. Graph-based learning emerges as a potent paradigm in this context, extending deep learning to non-Euclidean domains by representing images as graphs. In such representations, nodes correspond to pixels, regions, or anatomical constituents, while edges encode spatial, feature-based, or anatomical relationships. This formulation enables the explicit modeling of structural dependencies and relational reasoning, aligning naturally with the organized and connective nature of ophthalmic data[7].

The adoption of graph-based learning in ophthalmology is motivated by two principal factors. First, many ocular diseases manifest through subtle alterations in structural relationships-such as changes in retinal layer geometry, vascular connectivity, or optic disc configuration-rather than isolated local anomalies[8]. Graph representations provide a natural mechanism to encapsulate these relational patterns, facilitating context-aware feature aggregation and integrative analysis. Second, clinical ophthalmic datasets are often characterized by limited annotations and substantial heterogeneity across imaging devices and populations[9]. Graph-based models, by leveraging structural priors and relational constraints, offer enhanced robustness against overfitting and improved generalization under such challenging data conditions, addressing key barriers to real-world clinical deployment[10].

Among graph-based methodologies, graph neural networks (GNNs) and their variants have garnered increasing attention. Through message-passing or diffusion mechanisms, GNNs propagate information across graph nodes, integrating both local and global contextual cues[11]. Attention-based extensions further refine this process by adaptively weighting inter-node interactions, thereby accentuating clinically salient structures[12]. Recently, higher-order graph representations, such as hypergraphs, have been explored to model complex group-wise relationships among multiple anatomical elements, offering a promising avenue for capturing sophisticated retinal interactions, though their application in ophthalmology remains nascent[13].

Despite growing interest, the field of graph-based ophthalmic image analysis remains fragmented. Studies exhibit considerable variation in graph construction strategies, model architectures, learning paradigms, and evaluation protocols, often focusing on specific tasks or datasets[14]. This fragmentation impedes a unified understanding of methodological trends and comparative performance. Moreover, persistent challenges-including reliable graph construction from noisy clinical images, scalability to high-resolution data, interpretability of learned graph representations, and generalization across diverse devices and populations-represent critical open questions that must be addressed to advance the field toward robust clinical integration[15].

ISSN: 2710-0588

1.1. Scope and Contributions

This review provides a structured and critical synthesis of graph-based learning methods applied to ophthalmic image analysis. Distinct from general surveys of AI in ophthalmology, this work focuses specifically on graph-centric modeling strategies, emphasizing their role in addressing the unique structural characteristics of ophthalmic data. The principal contributions are threefold:

1) We systematically analyze and categorize graph modeling strategies for ophthalmic images, including node representation schemes, edge construction mechanisms, and topological designs.

2) We present a structured taxonomy of graph-based learning models, spanning traditional graphical models, modern GNNs, and emerging higher-order extensions, discussing their applicability and limitations in ophthalmic contexts.

3) We synthesize key clinical applications, identify persistent methodological and practical challenges, and articulate promising future research directions to guide the translation of graph-based learning into clinically impactful tools.

1.2. Review Organization

The remainder of this review is organized as follows. Section 2 details graph modeling strategies tailored to ophthalmic images. Section 3 reviews the evolution of graph-based learning models, from traditional methods to contemporary GNN architectures. Section 4 discusses learning strategies and optimization considerations specific to ophthalmic data. Section 5 surveys major application domains across different imaging modalities. Finally, Section 6 outlines current challenges and proposes future research trajectories to advance the field.

2. Graph Modeling for Ophthalmic Images

Graph modeling constitutes the methodological foundation of graph-based learning for ophthalmic image analysis, as it defines how raw image data are abstracted into structured representations amenable to relational reasoning[16]. Unlike grid-based formulations, graph representations require explicit design choices regarding node definition, edge construction, and overall topology[4]. Given the strong anatomical organization inherent in ophthalmic images, effective graph modeling should preserve clinically meaningful structures while maintaining computational efficiency.

2.1. Node Representation Strategies

Node representation determines the basic semantic units of a graph and directly influences both modeling capacity and computational complexity. Early studies predominantly adopted pixel-level representations, treating individual pixels as graph nodes[17]. This fine-grained strategy preserves detailed spatial information and enables precise modeling of local anatomical structures, making it suitable for tasks such as retinal layer boundary detection in OCT images. However, pixel-level graphs scale poorly with image resolution, resulting in prohibitively large graphs for high-resolution ophthalmic data[18].

To address this limitation, region-based node representations have been widely explored. In this paradigm, visually homogeneous regions-typically obtained through superpixel segmentation or region proposal techniques-serve as graph nodes. By aggregating local pixel information into compact and semantically coherent units, region-level graphs significantly reduce graph size while retaining essential structural cues[19]. This strategy achieves a practical balance between representational expressiveness and computational efficiency and has been successfully applied to disease classification and lesion analysis tasks[20].

ISSN: 2710-0588

More recent approaches incorporate ophthalmic domain knowledge by constructing anatomy-aware graphs, in which nodes explicitly correspond to clinically meaningful structures such as retinal vessels, optic disc and cup components, or retinal layers[21]. These representations enhance interpretability and align model reasoning with established anatomical concepts. However, their effectiveness depends on the reliability of upstream anatomical extraction procedures, and errors introduced during preprocessing may propagate through subsequent graph learning stages[22].

2.2. Edge Construction and Graph Topology

While node representations define the entities being modeled, edge construction determines how relational information is encoded and propagated[23]. The most commonly adopted strategy relies on spatial adjacency, connecting neighboring nodes to preserve local continuity and anatomical coherence[24]. Such spatially constrained graphs provide stable and interpretable structures but are inherently limited in capturing long-range dependencies across anatomically distant regions[25].

To overcome this limitation, feature similarity-based connectivity has been introduced, linking nodes with similar visual or learned representations regardless of spatial proximity. This strategy facilitates global information exchange and enables the modeling of distributed pathological patterns[26]. However, feature-based edges are sensitive to noise and representation quality, necessitating careful feature design and regularization to ensure stability.

Incorporating anatomical priors into edge construction further improves clinical relevance and structural consistency. Examples include enforcing vessel connectivity patterns or layer ordering constraints in OCT images. While anatomically informed graph topologies enhance interpretability, they often require reliable prior knowledge and may reduce flexibility when applied to heterogeneous imaging conditions or unseen data distributions[3].

2.3. Graph Construction Paradigms

From a methodological perspective, graph construction strategies can be broadly categorized into fixed, adaptive, and multi-scale paradigms. Fixed graph construction relies on predefined rules to generate graph topology prior to training, offering simplicity and stability but limited adaptability to task-specific patterns. In contrast, adaptive graph construction allows edge weights or connectivity patterns to be optimized jointly with model parameters, enabling task-driven structural refinement during learning[27]. While adaptive graphs improve modeling flexibility, they introduce additional complexity and potential challenges related to training stability and interpretability.

Multi-scale graph construction has emerged as an effective strategy for capturing structural information at different levels of abstraction. By integrating graph representations across multiple resolutions, multi-scale approaches can simultaneously encode fine-grained local details and global anatomical organization, which is particularly beneficial for ophthalmic image analysis[28]. Within this context, hypergraphs represent a higher-order extension of conventional graphs by modeling group-wise relationships among multiple nodes. Although hypergraph-based approaches remain relatively underexplored in ophthalmic imaging, they offer a promising framework for representing complex anatomical interactions beyond pairwise relationships.

3. Traditional Graph-Based Models

Following graph construction, graph learning models aim to exploit structured representations to perform effective feature propagation and relational reasoning. Over time, graph-based learning for ophthalmic image analysis has evolved from traditional probabilistic models with

ISSN: 2710-0588

handcrafted potentials to modern graph neural networks capable of end-to-end representation learning[29]. This section reviews representative graph learning models, emphasizing their methodological characteristics and suitability for ophthalmic imaging tasks.

3.1. Traditional Graph-Based Models

Early graph-based approaches in ophthalmic image analysis predominantly relied on probabilistic graphical models and energy-based optimization frameworks. Markov Random Fields (MRFs) and Conditional Random Fields (CRFs) were widely adopted to encode local dependencies among neighboring pixels or regions, enforcing spatial smoothness and structural consistency. These properties made them particularly effective for tasks such as retinal layer segmentation, vessel extraction, and anatomical boundary delineation[30].

Graph cut-based methods further advanced traditional graph modeling by formulating image analysis tasks as global energy minimization problems. Through carefully designed unary and pairwise potentials, graph cut frameworks enabled efficient optimization with theoretical guarantees[31]. In ophthalmic imaging, such methods were successfully applied to optic disc segmentation and retinal structure extraction, benefiting from their robustness and interpretability.

Despite these advantages, traditional graph-based models are limited by their reliance on handcrafted features and predefined potentials. Their fixed representational capacity restricts adaptability to complex pathological variations and heterogeneous imaging conditions. These limitations motivated the transition toward learning-based graph models that jointly optimize feature representations and relational reasoning.

3.2. Graph Neural Networks

Graph neural networks (GNNs) represent a fundamental shift from handcrafted graph models to data-driven learning on graph-structured representations. Through iterative message-passing mechanisms, GNNs aggregate and transform information from neighboring nodes, enabling node representations to be learned in an end-to-end manner[32]. This learning paradigm allows both structural relationships and feature embeddings to be optimized simultaneously, making GNNs well suited for modeling complex ophthalmic anatomy.

GNN architectures can be broadly categorized into spectral-based and spatial-based approaches. Spectral-based GNNs define convolution operations in the graph spectral domain and are grounded in graph signal processing theory. However, their dependence on graph-specific eigen-decompositions limits scalability and transferability across varying graph structures, which constrains their practical applicability in large-scale ophthalmic image analysis[33].

Spatial-based GNNs operate directly in the node domain by aggregating information from local neighborhoods. Their flexibility and scalability have made them the dominant choice in ophthalmic applications, including fundus image analysis and OCT-based modeling. By explicitly propagating information across graph neighborhoods, spatial-based GNNs effectively integrate local anatomical coherence with broader contextual information.

Nevertheless, standard GNN architectures exhibit inherent limitations. As network depth increases, repeated neighborhood aggregation may lead to over-smoothing, where node representations become increasingly indistinguishable. In addition, fixed aggregation schemes may inadequately capture heterogeneous or long-range dependencies present in complex ophthalmic structures[34]. These limitations have motivated the development of enhanced graph learning mechanisms, as discussed below.

ISSN: 2710-0588

3.3. Attention, Diffusion, and Higher-Order Extensions

To improve the expressive power of standard GNNs, recent studies have explored advanced graph learning extensions that address their inherent limitations. Graph Attention Networks (GATs) introduce attention mechanisms into message passing, allowing models to assign adaptive importance weights to neighboring nodes[35]. This selective aggregation is particularly advantageous in ophthalmic image analysis, where not all anatomical relationships contribute equally to disease characterization. Attention-based GNNs enhance both modeling flexibility and interpretability by highlighting clinically relevant structures.

Diffusion-based graph learning extends message passing by modeling information propagation across multiple steps or scales. Rather than limiting aggregation to immediate neighborhoods, diffusion mechanisms enable the integration of long-range contextual information, which is essential for capturing global anatomical patterns and disease-related structural changes[36]. In ophthalmic imaging, diffusion-based approaches have been employed to enhance contextual awareness across distant retinal regions, complementing local neighborhood modeling.

Beyond pairwise relationships, hypergraph-based learning introduces higher-order interactions by allowing hyperedges to connect multiple nodes simultaneously. This formulation enables the modeling of group-wise anatomical relationships, such as coordinated changes across retinal layers or collective behavior of vascular segments[6]. Although hypergraph-based approaches remain relatively underexplored in ophthalmic image analysis, they offer a promising framework for capturing complex structural dependencies that are difficult to represent using conventional graphs. However, challenges related to hypergraph construction, computational complexity, and data availability continue to limit their widespread adoption[37].

4. Learning Strategies and Optimization

Beyond graph construction and model architecture, learning strategies and optimization techniques critically influence the performance and reliability of graph-based models for ophthalmic image analysis[38]. Given the practical constraints of ophthalmic datasets, including limited annotations, class imbalance, and cross-device variability, effective training paradigms and optimization strategies are essential for achieving robust and clinically meaningful results.

4.1. Learning Paradigms

Most existing graph-based approaches in ophthalmic image analysis adopt supervised learning paradigms, where models are trained using manually annotated labels for classification, segmentation, or regression tasks. While supervised learning remains effective, its reliance on large-scale, high-quality annotations limits scalability in clinical practice due to the cost and variability of expert labeling[39].

To alleviate this limitation, semi-supervised and weakly supervised learning strategies have been increasingly explored. By leveraging unlabeled or partially labeled data, these paradigms reduce annotation requirements while maintaining competitive performance[8]. Graph-based models are particularly amenable to such settings, as relational structures facilitate information propagation from labeled nodes to unlabeled ones, enhancing learning efficiency under limited supervision.

In addition, domain generalization and cross-device learning have emerged as important considerations. Ophthalmic images acquired from different devices or clinical centers often exhibit variations in resolution, illumination, and noise characteristics[40]. Training strategies that incorporate domain adaptation, data augmentation, or graph-level regularization have been investigated to improve robustness across heterogeneous data sources, thereby enhancing the practical applicability of graph-based models.

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4.2. Loss Functions and Regularization

Loss function design plays a central role in guiding graph-based models toward clinically meaningful predictions. Standard task-driven losses, such as cross-entropy for classification and Dice-based losses for segmentation, are widely adopted. However, severe class imbalance is common in ophthalmic image analysis, particularly when pathological regions occupy only a small fraction of the image[41]. To address this issue, weighted loss functions and focal loss variants have been employed to emphasize hard or minority-class samples.

Beyond task-specific objectives, structural regularization has been incorporated to enforce consistency among graph-connected nodes and preserve anatomical coherence. Smoothness constraints encourage similar predictions for neighboring regions, while topology-aware regularization promotes anatomically plausible structures, such as continuous vessels or ordered retinal layers. These regularization strategies contribute to improved training stability and reduced overfitting, especially in noisy or low-data regimes.

Multi-task learning provides an additional optimization strategy by jointly training graph-based models on complementary tasks, such as segmentation and disease classification[42]. Shared graph representations enable efficient knowledge transfer across tasks, improving overall performance and robustness while aligning with clinical workflows that integrate multiple diagnostic cues.

4.3. Interpretability and Clinical Trust

Interpretability is an important consideration for the clinical adoption of graph-based learning models. By explicitly modeling relationships among anatomical structures, graph-based frameworks offer opportunities to enhance transparency beyond conventional deep learning approaches[10]. Visualization of node relevance, edge weights, or attention scores provides insights into how structural context influences model predictions[1].

Attention-based graph models and explainable graph learning techniques have been increasingly employed to highlight influential nodes or subgraphs associated with disease-related patterns. In ophthalmic image analysis, such interpretability mechanisms facilitate clinical validation by enabling alignment between model reasoning and established anatomical knowledge[43]. These capabilities support clinician trust and promote the responsible integration of graph-based models into clinical decision-making processes.

5. Applications in Ophthalmic Image Analysis

Building upon the graph modeling strategies and learning mechanisms discussed in the previous sections, graph-based learning has been increasingly applied to a broad range of ophthalmic image analysis tasks. Rather than reiterating methodological principles, this section synthesizes representative applications across major imaging modalities, emphasizing how graph-based representations are instantiated in practice to address modality-specific clinical objectives[44].

Overall, existing applications can be broadly categorized according to imaging modality, including fundus photography, optical coherence tomography (OCT), and emerging multi-modal and longitudinal analysis settings. Across these domains, graph-based learning serves as a unifying framework for integrating anatomical structures, relational context, and task-specific objectives[45].

5.1. Fundus Imaging-Based Applications

Fundus photography remains one of the most widely explored modalities in graph-based ophthalmic image analysis due to its clear anatomical landmarks and rich structural

ISSN: 2710-0588

information. In this context, graph-based learning has been primarily applied to disease diagnosis, lesion analysis, and vascular structure modeling.

For glaucoma assessment, graph representations are commonly constructed around optic disc and optic cup regions, enabling explicit modeling of disc–cup geometry and spatial relationships. Such formulations support more sensitive characterization of structural changes relevant to glaucoma diagnosis[46]. In diabetic retinopathy and related retinal diseases, graph-based approaches focus on modeling interactions among lesion regions, retinal vasculature, and surrounding tissue, facilitating context-aware disease grading and severity assessment. Additionally, graph-based vessel analysis methods encode vascular connectivity and branching topology, supporting anatomically consistent vessel segmentation and structural characterization.

5.2. Fundus Imaging-Based Applications

OCT imaging provides high-resolution cross-sectional views of retinal microstructures, where layered anatomical organization plays a central role in clinical interpretation. Graph-based learning has therefore been extensively applied to OCT-based analysis, particularly for retinal layer segmentation and structural abnormality assessment[9].

In retinal layer segmentation tasks, graph representations typically model pixels, regions, or layer-specific components as nodes, with edges encoding spatial adjacency and anatomical ordering relationships. This design promotes structural coherence and continuity across layers, improving robustness to noise and imaging artifacts[47]. Beyond segmentation, graph-based approaches have been employed to analyze disease-related structural alterations by modeling inter-layer relationships, enabling the detection of subtle morphological changes associated with conditions such as age-related macular degeneration and neurodegenerative disorders

5.3. Multi-Modal and Longitudinal Applications

Recent studies have extended graph-based learning to multi-modal ophthalmic image analysis, where complementary information from different imaging modalities, such as fundus photography and OCT, is jointly exploited. In these settings, graph-based frameworks facilitate the integration of heterogeneous data by constructing modality-specific subgraphs and modeling cross-modal interactions, supporting more comprehensive disease characterization.

Graph-based learning has also been explored in longitudinal analysis, where temporal relationships among imaging sessions are incorporated into graph structures. By jointly modeling spatial and temporal dependencies, these approaches provide a principled framework for disease progression analysis, particularly for chronic conditions such as glaucoma[7]. Emerging work further investigates patient-specific graph representations for personalized risk assessment and monitoring, highlighting the potential of graph-based learning for precision ophthalmology.

As illustrated by the above applications and summarized in Table 1, graph-based learning has been successfully instantiated across diverse ophthalmic imaging modalities and clinical tasks, with consistent design patterns emerging in node representation, relational modeling, and learning strategies. Rather than replacing conventional deep learning approaches, graph-based frameworks complement them by providing explicit mechanisms for modeling anatomical structures and relational context. At the same time, the diversity of application settings highlights practical challenges related to scalability, robustness, and generalization, which motivate the discussion of open issues and future research directions in the following section.

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Table 1. Representative Clinical Applications of Graph-Based Learning in Ophthalmic Image Analysis

Imaging Modality	Clinical Task	Node Representation	Edge / Relation Modeling	Graph Learning Model	Clinical Objective
Fundus	Glaucoma diagnosis	Optic disc / cup regions	Spatial adjacency, morphological similarity	GNN, GAT	Disc–cup relationship modeling
Fundus	Diabetic retinopathy grading	Lesion regions / superpixels	Feature similarity, spatial proximity	GNN	Context-aware lesion aggregation
Fundus	Retinal vessel segmentation	Vessel segments / pixels	Vessel connectivity, topology constraints	GNN, Graph Cut	Anatomically consistent vessel extraction
OCT	Retinal layer segmentation	Pixels / layer-specific regions	Spatial adjacency, layer ordering priors	GNN, CRF-GNN	Preserving layered anatomical structure
OCT	Structural abnormality analysis	Retinal layers / regions	Inter-layer relational modeling	Diffusion-based GNN	Detection of disease-related morphological changes
Fundus + OCT	Multi-modal diagnosis	Modality-specific regions	Cross-modal relational links	Multi-graph GNN	Holistic disease characterization
Fundus / OCT	Longitudinal progression analysis	Temporal region representations	Temporal adjacency, diffusion relations	Temporal GNN	Disease progression modeling
Fundus / OCT	Personalized risk assessment	Patient-specific anatomical regions	Individualized structural relations	Adaptive GNN	Precision ophthalmology

6. Challenges and Future Directions

Despite the growing adoption of graph-based learning in ophthalmic image analysis, several fundamental challenges continue to limit its scalability, robustness, and clinical translation. Addressing these challenges requires not only incremental methodological improvements but also a shift toward more principled, anatomically grounded, and clinically oriented graph learning frameworks.

6.1. Robust and Anatomically Consistent Graph Construction

Reliable graph construction remains a critical bottleneck for ophthalmic applications. Many existing approaches depend on preprocessing steps such as segmentation or region partitioning, making graph topology sensitive to image noise, artifacts, and device-specific variations. Errors introduced at this stage may propagate through subsequent learning processes and undermine model stability.

Future research should focus on developing graph construction strategies that are both robust to imaging variability and consistent with ophthalmic anatomy. Promising directions include anatomy-aware adaptive graph construction, uncertainty-aware edge modeling, and joint optimization of graph topology and representation learning. Such approaches have the potential to reduce sensitivity to preprocessing errors while improving anatomical plausibility and clinical reliability.

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6.2. Scalability and Generalization

Scalability remains a major challenge as ophthalmic imaging moves toward higher resolutions, larger datasets, and population-level analysis. Large and densely connected graphs impose substantial computational and memory burdens, limiting their applicability in real-world clinical environments.

In parallel, achieving robust generalization across imaging devices, clinical centers, and patient populations remains an open problem. Although graph-based learning emphasizes relational information, current models still exhibit performance degradation under domain shifts. Future work should explore scalable graph learning architectures, efficient sampling and sparsification strategies, and domain-robust training paradigms, including self-supervised and cross-domain graph representation learning.

6.3. Toward Advanced Graph Learning

Beyond addressing existing limitations, advances in graph learning methodologies offer opportunities to expand the scope of ophthalmic image analysis. Higher-order graph representations, such as hypergraphs, provide a principled means of modeling group-wise anatomical interactions that extend beyond pairwise relationships. While still underexplored, such formulations may be particularly valuable for capturing coordinated changes across retinal layers or vascular networks.

Another promising direction lies in integrated multi-modal and longitudinal graph learning, where spatial, temporal, and cross-modal relationships are jointly modeled within unified graph frameworks. These approaches align closely with clinical practice, which often relies on complementary imaging modalities and longitudinal follow-up. Realizing this potential will require advances in adaptive graph construction, scalable learning, and clinically interpretable modeling.

Overall, graph-based learning represents a powerful and flexible paradigm for ophthalmic image analysis. Continued progress in robust graph construction, scalable learning, and integrated modeling will be essential for translating methodological advances into clinically impactful tools.

Conflicts of Interest

The authors declare that they have no known competing financialinterests or personal relationships that could have appeared to influencethe work reported in this paper.

Acknowledgments

We are grateful to our colleagues at the School of Software, Henan Polytechnic University, for their constructive discussions and technical support, which were invaluable during the research and writing process.

Furthermore, we acknowledge the contributions of the broader research community, including the developers of open-source tools and the custodians of publicly available ophthalmic image datasets, whose work provides the essential foundation for reproducible and collaborative research in this field.

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