
A Survey on Applications of Graph Neural Networks (GNNs) for Breast Cancer Detection

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Abstract

Breast cancer remains a major global health concern, necessitating accurate and early detection. While traditional methods have made significant strides, challenges such as the complexity of biological data and the need for more accurate and personalized treatments persist. Graph Neural Networks (GNNs), a powerful class of deep learning models, offer a promising approach to address these challenges. This survey explores the application of GNNs in breast cancer research, focusing on key tasks like binary classification, gene subtype classification, and molecular subtype classification. By leveraging the ability of GNNs to model complex relationships between data points, researchers have made significant advancements in improving diagnostic accuracy and treatment planning. However, challenges such as data availability, model interpretability, and computational efficiency remain. Future research should focus on developing more sophisticated GNN architectures, integrating multi-modal data, and fostering collaboration between researchers and clinicians to translate these advancements into clinical practice.

1 Introduction

Breast cancer remains the most prevalent form of cancer among women worldwide, representing a significant global health burden. With an estimated 2.3 million new cases annually and nearly 685,000 deaths, the disease accounts for a considerable proportion of cancer-related mortality [1]. Early and accurate detection is crucial, as it dramatically improves the chances of successful treatment and long-term survival.

Traditional diagnostic techniques such as histopathology, mammography, and ultrasound have been the cornerstone of breast cancer detection for decades. However, these methods are not without limitations. The diagnostic process is often resource-intensive, requiring specialized equipment and skilled interpretation. Moreover, variability in clinical assessments can lead to inconsistent results, particularly in complex or borderline cases [2]. The integration of computational techniques, including computer-aided diagnosis systems, has been explored to address these limitations, but challenges such as high false positive rates and dependency on handcrafted features remain [3].

1.1 Motivation

Advancements in artificial intelligence (AI) have introduced transformative possibilities in medical diagnostics. Among these innovations, Graph Neural Networks (GNNs) stand out as a powerful tool for breast cancer detection. GNNs excel in modeling complex data relationships, offering a unique ability to represent interactions between heterogeneous features such as imaging, biological markers, and clinical data [4].

The motivation behind this survey is to explore how GNNs address persistent challenges in breast cancer detection, including dataset heterogeneity, interdependent feature dynamics, and the risk of overfitting. Recent studies, such as [5], demonstrate the applicability of GNNs in histopathological image analysis, where these models effectively capture feature interdependencies, leading to improved diagnostic accuracy. The theoretical principles behind these capabilities are rooted in the relational inductive biases inherent in GNN architectures, as highlighted by [6]. By leveraging these strengths, GNNs have the potential to revolutionize early detection and assist radiologists in delivering faster and more reliable diagnoses.

1.2 Scope of the Survey

This survey focuses on the application of Graph Neural Networks (GNNs) in breast cancer detection, specifically within three key classification tasks:

1. Binary Classification
2. Gene Subtype Classification
3. Molecular Subtype Classification

In the first part, we explore the use of GNNs for Binary Classification, aiming to classify tumors as malignant or benign. The second area of focus is Gene Subtype Classification, which seeks to identify the genetic characteristics of tumors, aiding in personalized treatment strategies. Finally, we investigate molecular subtype classification, where GNNs are applied to predict how different tumors will respond to various treatments based on their molecular profile.

By covering these three important classification tasks, this survey aims to provide a comprehensive overview of the current state of GNNs in breast cancer detection, highlighting both their potential and the challenges that remain in realizing their full capabilities.

1.3 Organization of the Survey

This survey is organized to systematically explore the application of Graph Neural Networks (GNNs) in breast cancer detection across three distinct classification tasks: binary classification, gene subtype classification, and molecular subtype classification. Each classification type is addressed in a dedicated section, structured to provide a comprehensive understanding of its role, methodology, and impact.

For each classification task, we begin by introducing the category, and outlining its significance in the context of breast cancer diagnosis and treatment. This is followed by an overview of three representative studies that demonstrate the application of GNNs within that classification type. We summarize the methods proposed in these studies, highlighting their key innovations, strengths, and limitations.

Subsequently, we provide a comparative analysis of the experimental results reported in the selected papers, identifying common trends, challenges, and areas of divergence. The analysis is extended to include discussions on the frontiers of GNN applications in each classification type, with a focus on current challenges and potential future directions. Finally, each section concludes with a summary of insights gained and their implications for advancing breast cancer detection.

The survey concludes with a dedicated section on benchmark datasets and evaluation metrics commonly used in GNN-based breast cancer detection, followed by a discussion on the broader vision for future research in this domain. Through this structured approach, we aim to present a cohesive and insightful overview of the state-of-the-art GNN applications for breast cancer classification.

2 Survey of Different Classification Types

2.1 Binary Classification

Binary classification of breast cancer is a crucial process in distinguishing between benign and malignant tumors. This classification is essential for early detection and effective treatment planning, as it directly impacts clinical decision-making. In binary classification, breast cancer lesions are categorized into two classes: benign, which are non-cancerous and generally less aggressive, and malignant, which are cancerous and can spread to other parts of the body.

Graph Neural Networks (GNNs) provide an alternative means to the binary classification of breast cancer, in an effective way to learn the rich relationships and interactions between data points, which is essential to discriminate between benign and malignant lesions. For GNN-based models, each breast cancer sample acts as a node in a graph, and the edges represent similarity relations or associations, such as those that can be derived from imaging data or clinical characteristics. The power of GNNs for this problem is in their potential to enhance diagnostic precision and reproducibility, thereby facilitating early detection and efficient treatment planning in breast cancer survivors.

2.1.1 Related works

Recent advancements in binary breast cancer classification have leveraged hybrid deep-learning models and graph-based techniques to enhance diagnostic accuracy. A notable work integrates a Convolutional Neural Network (CNN) with a Graph Convolutional Network (GCN) to extract individual image-level features and capture relation-aware representations (RARs), showing significant improvements in breast mammogram classification [7]. Another study employs a deep ensemble graph network, combining multiple Graph Neural Networks (GNNs) to leverage diverse feature representations for histopathology image analysis, achieving superior results [8]. Similarly, a GNN-based framework for ultrasound imaging optimizes graph construction by incorporating medically significant features like texture and intensity, highlighting the value of domain-specific knowledge [9].

Research using transfer learning on pre-trained models like ResNet and VGG for mammography images has demonstrated enhanced feature extraction capabilities [10]. Federated learning approaches have also emerged, enabling decentralized training across multiple institutions to preserve privacy while improving diagnostic performance [11]. Additionally, methods combining ensemble classifiers with feature selection techniques, such as recursive feature elimination, have shown promise in reducing overfitting and enhancing generalization [12]. Efforts to integrate explainable AI into breast cancer classification have provided insights into model decisions, fostering trust in clinical applications [13].

In this survey of the use of Graph Neural Networks (GNNs) in the binary classification of breast cancer, we present three representative papers.

1. **Improved Breast Cancer Classification Through Combining Graph Convolutional Network and Convolutional Neural Network (BDR-CNN-GCN [7]):** Introduces the BDR-CNN-GCN model, utilizing a Graph Convolutional Network (GCN) combined with a Convolutional Neural Network (CNN) investigating breast mammography data and detecting malignant breast masses.
2. **Enhancing Histopathology Breast Cancer Detection and Classification with the Deep Ensemble Graph Network (DEGN [8]):** Deep Ensemble Graph Network (DEGN) is presented for histopathology images, and an innovative architecture is proposed that uses ensemble learning to increase classification performance
3. **Graph neural network-based breast cancer diagnosis using ultrasound images with optimized graph construction integrating the medically significant features (GCN with US Images [9]):** Optimizing a GCN model based on the extraction of medically significant features from the region of interest (ROI) of ultrasound images and Bayesian optimization applied to the model tuning to classify breast tumors as benign or malignant.

2.1.2 Datasets and Pre-Processing Steps

The three papers under review utilize distinct datasets and preprocessing techniques to enhance the classification accuracy of breast cancer using Graph Neural Networks (GNNs).

The first paper [7] employs the Mini-MIAS dataset, which consists of 322 single-breast mammogram slices, each with a resolution of 1024×1024 pixels. The dataset includes 113 abnormal and 209 normal images. To optimize the data for analysis, a comprehensive 7-step preprocessing pipeline is implemented. In noise reduction, Additive Noise (AN) and Multiplicative Noise (MN) reduction are done to improve image clarity. Contrast Limited Adaptive Histogram Equalization (CLAHE) is used to enhance image contrast. Unnecessary background elements are removed to focus on the breast tissue and pectoral muscle is eliminated to avoid interference in analysis. Images are centered and

downsampled for uniformity and efficiency in processing. These steps help generate more data from a limited training set and prevent overfitting.

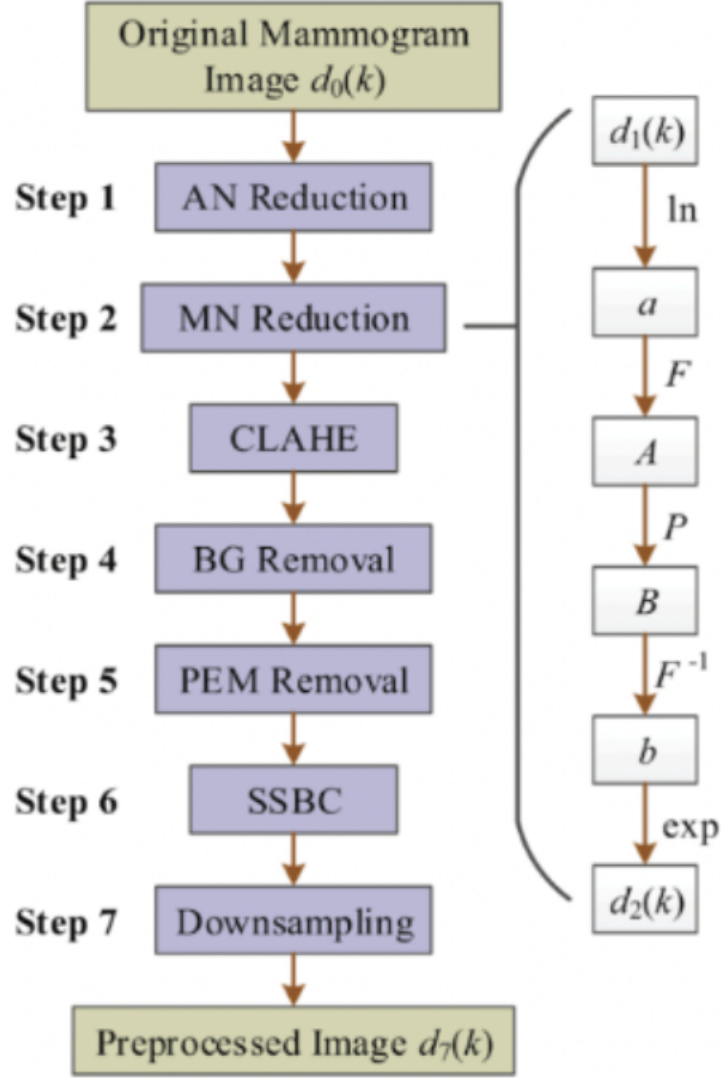


Figure 1: 7-step pre-processing pipeline for BDR-CNN-GCN

The second paper [8] uses the BCSS and BACH histopathology datasets, which include Hematoxylin and Eosin (H&E) stained whole slide images (WSIs) of breast cancer. BCSS (Breast Cancer Semantic Segmentation) dataset is for binary classification & BACH (Breast Cancer Histology dataset) for both binary & multiclass classification tasks. The initial pre-processing step involves identifying critical regions within the histopathology images by segmenting cell nuclei, which are essential for accurate classification. It is followed by multi-magnification Patch-Based Feature Extraction, which captures granular details by extracting features at various magnifications, enhancing the model's ability to distinguish between different tissue types. Spatial relationships within the images are modeled through graph construction, allowing for robust classification using an ensemble graph network. This methodology addresses challenges like cell overlapping and irregular color distribution, improving diagnostic accuracy.

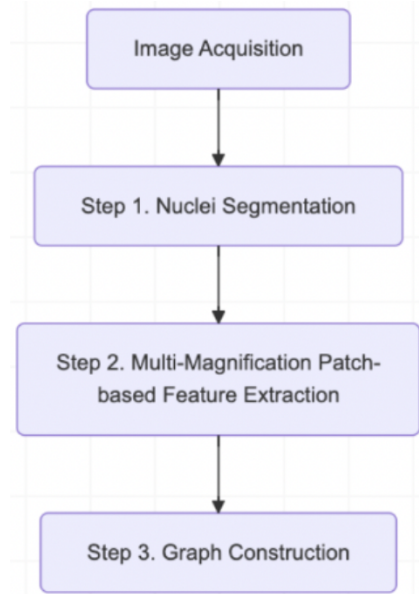


Figure 2: Pre-processing steps for DEGN



Figure 3: Masking to extract ROI in 3rd paper [9]

The third paper [9] focuses on a publicly available breast ultrasound dataset of 780 PNG images. Images are of female patients with an age range of 25–75 years. The dataset has an average image resolution of 500×500 pixels and is categorized into normal, benign, and malignant classes with 266,

467, and 210 images. Ultrasound images are made using high-end imaging instruments. Only benign and malignant classes are used in this study to analyze the tumor pattern of breast cancer, as the normal class does not contain any tumors. Therefore, 647 images are used. The preprocessing steps are tailored to extract meaningful features from these images. Regions of interest (ROI) are extracted using masks and bitwise operations to isolate benign and malignant tumors. Handcrafted features such as circularity and entropy are calculated and statistically validated against techniques like Histogram of Oriented Gradients. Each paper demonstrates a unique approach to preprocessing that is specifically designed to maximize the potential of GNNs in improving breast cancer classification accuracy.

2.1.3 Models and Methodology

The first paper proposed a hybrid model, BDR-CNN-GCN, [7] to improve the accuracy of breast cancer detection in mammograms. The model leverages the strengths of both Convolutional Neural Networks (CNNs) and Graph Convolutional Networks (GCNs) to extract both image-level and relational features. The BDR-CNN component of the model is a standard 8-layer CNN architecture that incorporates several techniques to enhance performance. Batch Normalization (BN) is used to stabilize the training process and accelerate convergence by normalizing the input to each layer. Regularization technique like Dropout is used to randomly drop out units during training to prevent overfitting. Rank-Based Stochastic Pooling (RSP) selects a fixed number of feature maps based on their rank, providing more robust feature representations than max pooling. The GCN component of the model is a two-layer GCN that captures the relationships between different regions of the image. By combining the strengths of CNNs and GCNs, the BDR-CNN-GCN model can effectively extract both local and global features from mammograms. To further improve the model’s performance, the authors employ a 14-way data augmentation technique. This technique generates additional training data by applying various transformations to the original images, such as rotations, flips, and noise additions. This helps to increase the diversity of the training data and reduce overfitting.

The six proposed networks used in our study.

Index	Inheritance	Short Name	Description
Net-0	Base Network	CNN	8-layer CNN (6 conv layers and 2 fully-connected layers)
Net-1	←Net-0+BD+DO	BD-CNN	Add BN and dropout to Net-0 (Add BN to each conv blocks, and add DO to each fully-connected block)
Net-2	←Net-1+RSP	BDR-CNN	Use RSP to replace MP in Net-1
Net-3	←Net-0+GCN	CNN-GCN	Add GCN to Net-0
Net-4	←Net-1+GCN	BD-CNN-GCN	Add GCN to Net-1
Net-5	←Net-2+GCN	BDR-CNN-GCN	Add GCN to Net-2

(BN: Batch normalization; DO: Dropout; RSP: rank-based stochastic pooling; GCN: graph convolutional network; CNN: convolutional neural network; MP: max pooling).

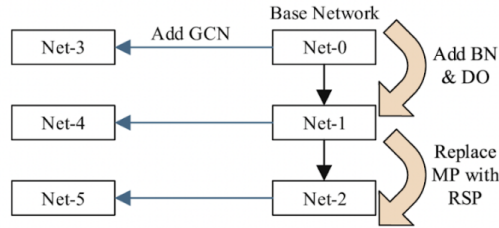


Figure 4: Relationship between different networks

The second paper [8] introduces a novel architecture - Deep Ensemble Graph Network (DEGN), for breast cancer detection in histopathology images. The DEGN model combines a Structural Graph Module (SGM) with an ensemble of graph networks to effectively extract and integrate information from the images. The SGM is responsible for identifying and extracting features from the histopathology images. It represents cells as nodes in a graph and edges as the relationships between them. The SGM captures the spatial and contextual information of the cells, which is crucial for accurate classification. The ensemble graph network consists of multiple graph neural networks that are trained on different subsets of the data. This ensemble approach helps to improve

the model's generalization ability and reduce overfitting. The ensemble network also incorporates pooling techniques and multi-level feature fusion to capture both local and global information from the graph representations. By combining the SGM and the ensemble graph network, the DEGN model can effectively extract and integrate information from histopathology images, leading to improved performance in breast cancer detection.

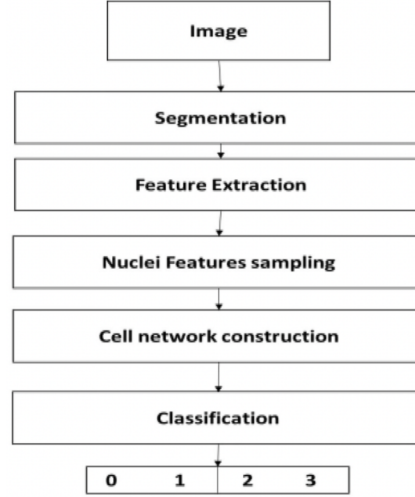


Figure 5: Proposed architecture for DEGN

The third paper [9] proposes a Graph Convolutional Network (GCN)-based approach for breast cancer detection in ultrasound images. The model leverages handcrafted features and graph-based representations to classify images as benign or malignant. The model first extracts a set of informative features from the regions of interest in the mammograms. These features include circularity, solidity, brightness, and texture features derived from Gray-Level Co-occurrence Matrices (GLCM). The significance of these features is validated using statistical analysis techniques, such as T-tests and density plot analysis. The extracted features are used to construct a graph, where nodes represent images and edges represent the similarity between them. The similarity between images is calculated using the Spearman correlation coefficient. The GCN model then learns to classify images based on the information encoded in the graph structure and node features. The GCN model is trained using a combination of ablation studies and Bayesian optimization to optimize the hyperparameters and improve performance.

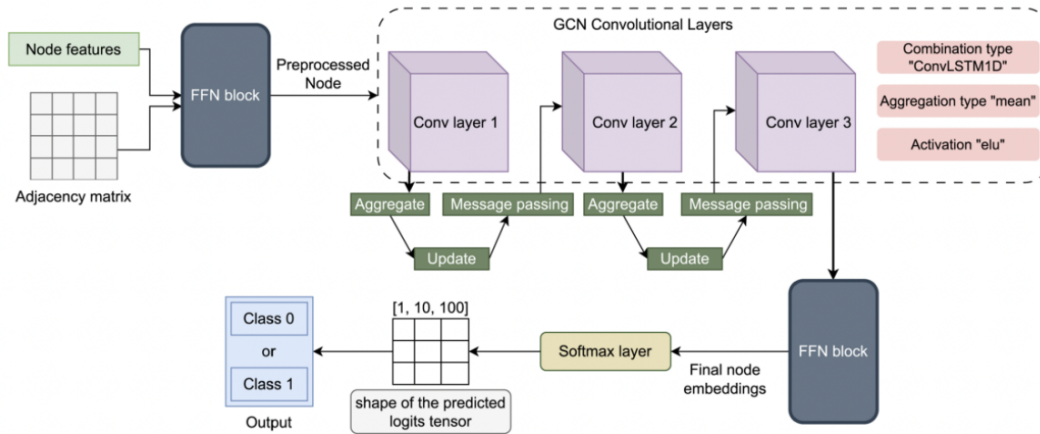


Figure 6: Proposed architecture for GCN

2.1.4 Advantages and Limitations

BDR-CNN-GCN [7] model demonstrates strong potential in breast cancer detection, particularly when working with limited datasets. Its hybrid architecture combines Convolutional Neural Networks (CNNs) to extract localized image features and Graph Convolutional Networks (GCNs) to capture relationships between images, providing a holistic representation of the data. Additionally, the 14-way data augmentation technique significantly enhances the model’s robustness by generating diverse training samples. However, its reliance on a relatively small dataset limits its generalizability to new, unseen data. Despite its effectiveness, the hybrid architecture adds complexity, requiring careful fine-tuning to prevent overfitting and ensure optimal performance.

The Deep Ensemble Graph Network (DEGN) [8] model showcases remarkable adaptability and robust classification capabilities, particularly for detecting irregular cells in histopathology images. By employing an ensemble of graph-based networks, the model effectively captures intricate relationships within the data, which are often overlooked by traditional methods. Its graph-based representation ensures that spatial and relational patterns are utilized to enhance classification performance. However, the reliance on small datasets introduces challenges in achieving broader applicability. Additionally, the model’s complex architecture incurs significant computational costs and longer training times, making it less ideal for real-time or resource-constrained environments.

The GCN-based model [9] offers a streamlined approach to breast cancer detection, achieving high accuracy through a simplified graph construction process. By incorporating handcrafted features such as texture and intensity, the model effectively integrates domain knowledge to improve classification outcomes. This makes it a computationally efficient alternative to more complex architectures. However, its dependence on manually crafted features limits the model’s ability to adapt and learn directly from raw data. While this approach is beneficial in well-defined settings, it may lack the flexibility needed to handle diverse and heterogeneous datasets.

2.2 Gene Subtype Classification

Gene subtype classification is a critical process in breast cancer research, aimed at identifying and differentiating the genetic signatures that define tumor subtypes. These subtypes are key to understanding the biological characteristics of tumors, including their potential aggressiveness, likelihood of metastasis, and response to specific therapies. Accurate classification of gene subtypes plays a pivotal role in precision oncology, where treatments are tailored to the unique genetic landscape of a patient’s cancer, improving treatment outcomes and minimizing side effects.

Traditional approaches to gene subtype classification often rely on machine learning models that use gene expression profiles or multi-omics data to predict subtype categories. However, these methods face challenges in modeling the intricate and non-linear relationships between genetic features. The genetic and epigenetic networks underlying breast cancer are highly complex, with interactions that are not easily captured using conventional techniques. This underscores the need for advanced computational models that can handle the complexity of genetic interactions and provide robust, interpretable predictions.

Graph Neural Networks (GNNs) offer a powerful alternative for gene subtype classification by representing genetic data in the form of graphs. In this framework, genes are represented as nodes, and the edges capture relationships such as co-expression patterns or interactions in biological pathways. By leveraging the graph structure, GNNs can model higher-order dependencies between genes, uncovering subtle patterns that might not be apparent with other methods. This capability makes GNNs particularly suitable for capturing the hierarchical and interconnected nature of genetic data, offering a pathway toward more accurate and biologically relevant classifications.

2.2.1 Related Works

Gene subtype classification has been extensively explored in the field of breast cancer research, with various methodologies being applied to predict cancer subtypes based on genomic data. Traditional machine learning techniques typically rely on handcrafted features derived from genomic data, which can fail to capture the complex, underlying interactions between genetic elements. In contrast, Graph Neural Networks (GNNs) have emerged as a promising solution by modeling genetic features as nodes and their interactions as edges within a graph structure. This approach allows for a more

holistic representation of the genetic landscape and can uncover subtle relationships that traditional methods might miss.

Several key studies have demonstrated the potential of GNNs in gene subtype classification. Xie et al. [14] proposed a graph-enhanced architecture to improve cancer subtype classification, focusing on the integration of multiple genetic data types. Similarly, Zhang et al. (2022) [15] explored multi-omics data integration within a GNN framework to enhance prediction robustness across different cancer subtypes. These studies highlight the power of GNNs in capturing the rich interdependencies within complex biological data.

In this survey of the use of Graph Neural Networks (GNNs) in the gene subtype classification of breast cancer, we present three representative papers.

1. **Classifying breast cancer using multi-view graph neural network based on multi-omics data (MVGNN [16]):** A novel GNN-based framework that combines gene co-expression networks and pathway analysis to improve classification accuracy.
2. **omicsGAT: Graph Attention Network for Cancer Subtype Analyses (OmicsGAT [17]):** A multi-scale GNN approach leveraging biological pathways to classify breast cancer subtypes.
3. **Comparative Analysis of Multi-Omics Integration Using Advanced GNNs for Cancer Classification (Multi Omics [18]):** An interpretable GNN model designed to uncover key genetic interactions underlying subtype differentiation.

2.2.2 Datasets and Pre-Processing Steps

Each study leverages publicly available genomic datasets, such as The Cancer Genome Atlas (TCGA) and METABRIC. Pre-processing steps typically include normalizing gene expression levels, constructing gene interaction graphs based on biological pathways or co-expression data, and splitting data into training, validation, and testing sets. Figure below provides an illustration of the general data pre-processing pipeline used in these studies.

MVGNN [16] uses the chi-square test to select features for each omics type. The features are sorted based on their number in the hypothesis test using the samples corresponding to each classification task. Then, the top-k features are selected for each omics data. In this study, k is set to 5000. Normalization is performed using linear scaling, transforming the data values to fit within the range of [0,1]. The paper also employs the minimum Redundancy Maximum Relevance (mRMR) feature selection algorithm.

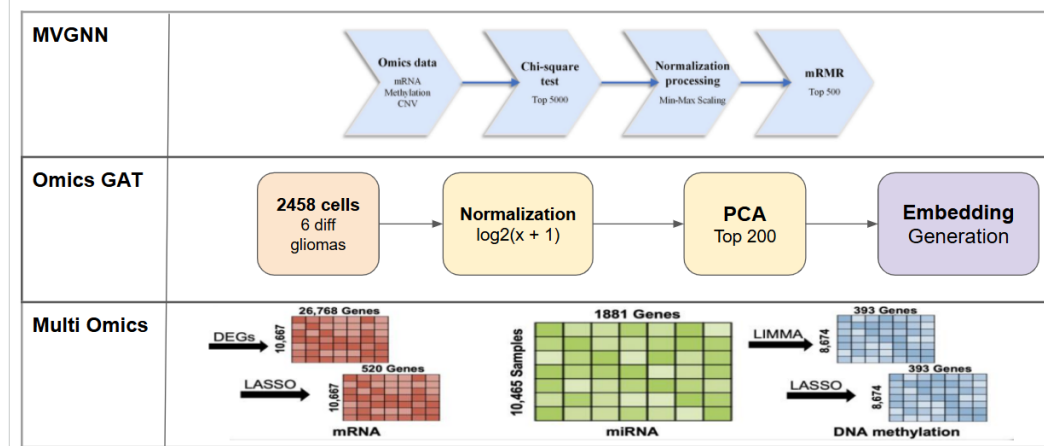


Figure 7: Comparison of Pre-Processing Process

Omics GAT [17] includes gene expression and label information for 2,458 cells, derived from six gliomas. Gene expression values were transformed using the formula $\log_2(x + 1)$ to normalize the data for analysis. Top 200 PCA components were selected as the input to the omicsGAT clustering

pipeline. An autoencoder was trained to generate embeddings from the scRNA-seq data. These embeddings were used as input for clustering models.

In Multi-Omics [18], omics data (mRNA, miRNA, and DNA methylation) were obtained from the Pancancer Atlas using the TCGAbiolinks library. Next, differential expression analysis (DEG) and LASSO regression were applied to mRNA data, while LIMMA and LASSO regression were applied to DNA methylation data. Subsequently, mRNA or RNA-Seq, miRNA, and DNA methylation data were integrated based on the sample ID using an inner join operation.

2.2.3 Models and Methodology

MVGNN [16] integrates graph neural networks with gene co-expression networks to enhance the accuracy of gene subtype classification. Each node in the graph represents a gene, while edges capture co-expression relationships derived from publicly available gene expression datasets. The model utilizes a multi-layer Graph Convolutional Network (GCN) to extract hierarchical features from the graph, capturing both local and global patterns within the data. Additionally, the authors incorporate biological pathway data to enrich the graph structure, ensuring that domain-specific knowledge informs the classification process. A dropout mechanism and weight regularization techniques are employed to address overfitting, and the model is trained using a cross-entropy loss function to optimize classification performance. This method demonstrates significant improvements in classification accuracy and robustness compared to baseline machine learning models.

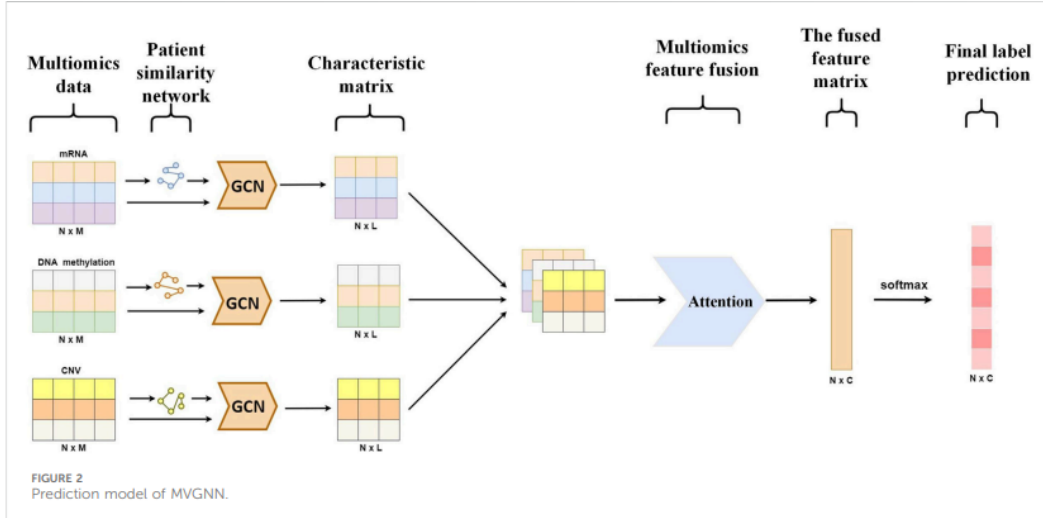


Figure 8: MVGNN: Model Architecture

Omics GAT[17] proposes a hierarchical graph neural network model that operates at multiple biological scales, focusing on the integration of pathway-level and gene-level data. The authors construct a multi-scale graph representation, where nodes at different levels correspond to individual genes and broader biological pathways. The model employs a dual-layer architecture: a Graph Attention Network (GAT) at the gene level to capture intricate interactions between genes and a GCN at the pathway level to learn higher-level patterns. By incorporating attention mechanisms, the model emphasizes critical interactions that contribute most to the classification task. The use of multiple scales allows the model to balance fine-grained details with larger biological contexts, making it both robust and interpretable. Experimental results highlight the model's ability to outperform traditional deep-learning approaches, particularly in datasets with high dimensionality and noise.

In paper 3[18] the authors propose a GNN-based method for gene subtype classification that uses a graph representation of genetic data. The authors construct a graph where each node corresponds to a gene, and the edges represent functional or co-expression relationships between genes, sourced from biological databases. The core model used is a Graph Convolutional Network (GCN), which learns embeddings for genes by aggregating information from neighboring nodes in the graph. This approach is designed to capture the complex and non-linear relationships between genes, which are

crucial for differentiating breast cancer subtypes. The authors enhance the model’s performance by incorporating a series of convolutional layers, allowing it to learn increasingly abstract representations of the genetic data as the network deepens. The model is trained using a typical cross-entropy loss function for classification, and the results demonstrate its ability to effectively classify breast cancer gene subtypes, achieving superior performance compared to traditional machine learning models. The authors highlight the model’s scalability, making it a promising solution for large-scale genomic data analysis.

2.2.4 Advantages and Limitations

In paper 1 [16], the proposed GNN framework offers significant advantages, particularly its integration of gene co-expression and biological pathway data, enhancing the model’s ability to capture complex relationships and improve classification accuracy. The use of a Graph Convolutional Network (GCN) allows the model to learn both local and global dependencies, providing a robust and scalable solution for breast cancer gene subtype classification. However, the model’s reliance on predefined biological pathways limits its flexibility, as it depends on the completeness and accuracy of the curated pathway data. Additionally, while the model achieves high accuracy, its interpretability could be improved, and the use of co-expression data alone may not fully capture the intricate gene interactions that contribute to cancer subtypes.

Paper 2 [17], presents a hierarchical GNN model that incorporates both gene-level and pathway-level information, offering a more comprehensive approach to gene subtype classification. The use of Graph Attention Networks (GAT) at the gene level enables the model to focus on relevant gene interactions, enhancing both classification performance and interpretability. The multi-scale approach improves robustness, especially in high-dimensional, noisy datasets. However, the model’s computational complexity can be a limitation, requiring significant resources to process large-scale datasets. Moreover, while the attention mechanism aids interpretability, it may not fully explain the complex biological relationships driving the model’s decisions. Additionally, the model’s performance is sensitive to the quality of pathway data, and errors or missing information in the pathways could affect classification outcomes.

The GNN-based model proposed in paper 3 [18] demonstrates scalability and high accuracy in classifying gene subtypes of breast cancer, particularly through the use of Graph Convolutional Networks (GCN) to capture non-linear relationships between genes. Its straightforward architecture allows for ease of implementation and adaptability across different datasets. However, the model lacks strong interpretability, which could hinder its application in clinical settings where understanding the rationale behind predictions is critical. While it excels in large, high-dimensional datasets, the model’s performance can be sensitive to the quality of input data, particularly with incomplete or noisy gene interaction networks, potentially limiting its effectiveness in real-world scenarios.

2.3 Molecular Subtype Classification

Breast cancer presents in a variety of subtypes, and different subtypes of breast cancer exhibit distinct responses to treatments. For example, some breast cancers, such as Luminal A, are hormone-regulated and respond well to hormone therapy. Others, such as Triple Negative, are aggressive, respond poorly to treatments, and are more likely to require aggressive treatment strategies. These variations are called the cancer’s *molecular subtype*. Accurate and rapid identification of the molecular subtype of a patient’s cancer is critical to determine an accurate prognosis and effective treatment strategies. We explore three proposed methods for using graph neural networks to identify the molecular subtype of a given patient.

2.3.1 Related works

Graph neural networks have emerged as a powerful tool for analyzing and categorizing biomedical data, and applying this work into the realm of cancer classification is a natural progression. Prior to investigating GNNs as a tool to improve cancer diagnostics, state-of-the-art methods included applying CNNs to flattened gene data, which fails to consider the complex interactions between these genes and proteins [19]. Rhee et al. examine the use of a graph convolutional network combined with a relation network as a novel approach to solving this problem and demonstrate encouraging results [20]. One major limitation of many molecular subtype classifiers is their inability to handle

multi-omics data, considering only either intra-omic relations or inter-omic relations. In addition, the introduction of attention models provides an exciting new paradigm to explore to improve the accuracy and performance of these categorizers [21]. Guo et al. explore various configurations of applying attention mechanisms to gene-graph data, demonstrating that these models can outperform previous state-of-the-art models in terms of accuracy on standard datasets [22]. Li et al. explore a different attention mechanism, and measure its performance on small compared to large datasets [23]. In our survey, we compare, contrast and quantify the performance of models proposed by Rhee et al., Guo et al. and Li et al., demonstrating the current frontier of breast cancer molecular subtype classification using GNNs.

2.3.2 Datasets and pre-processing steps

The papers we will investigate use data from The Cancer Genome Atlas (TCGA), specifically the Breast Carcinoma (BRCA) dataset. The dataset comprises multiple types of omics data, including RNA-sequence data, copy number variation, DNA methylation, and micro-RNA data. To capture the complex relationships between various proteins, which informs how cancer responds to different molecular treatments, protein-protein interaction networks are employed, using data from the STRING database or BioGrid. Guo et al. explore using variance filtering, only examining high-variance genes in their data, and filtering for only high-confidence interactions in the protein-protein network [22]. The ground truth classification used by all models is the Prediction Analysis of Microarray 50 (PAM50), a widely used gene expression assay that categorizes breast cancer into five distinct molecular subtypes.

2.3.3 Models and Methodologies

Paper 1 [20] explores using a combination of graph convolution networks (GCNs) and relation networks on a weighted gene graph to predict the subtype of cancer. The gene graph is constructed from knowledge about protein interactions, provided by the STRING database. First, the graph convolution method proposed by Defferrard et al. [24] with a pooling layer is applied to the gene graph structure to detect localized patterns within the graph. Using spectral decomposition, these convolutions can be performed quickly on a learned filter. Then, a Relation Network (RN) is constructed to learn about associations between nodes. The outputs of the GCN and RN layers are combined using a final softmax layer to assign probabilities to the different subtype predictions. To test the model, RNA-sequence data are provided from the TCGA breast cancer dataset (TCGA BRCA), using the PAM50 labels of breast cancer profiles and their molecular subtypes for prediction.

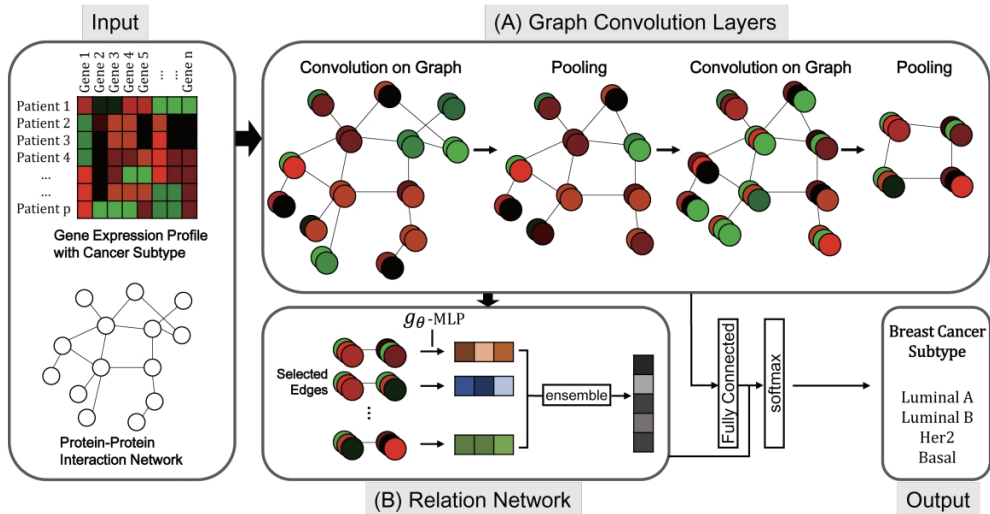


Figure 9: Overview of the proposed method, demonstrating the pipeline between convolutional layers and the relation network, as well as the final recombination layer.

In paper 2 [22] the GCN/RN model uses only RNA sequencing to predict the molecular subtype of a patient's cancer. However, information from other omics can provide additional insight into the true diagnosis of a patient. This paper explores using an AGCN model to utilize multi-omic information to predict the molecular subtype of a given cancer. First, a graph is constructed using the protein-protein information provided by the STRING database, with low confidence edges in the original database removed, to improve the convergence of the model. Then, a graph convolutional layer is applied, again by leveraging the spectral decomposition. After this, the output of convolutional layers is input into an attention layer. The authors experiment with three variations of the attention model. cAGCN uses column-wise self-attention to capture information across omic layers, and rcAGCN additionally uses row-wise self-attention to capture information across different genes in the same omic. The third variation, SEGNCN, differs by using squeeze-and-excite to create a global embedding of the graph before expanding this with the non-linear interdependence captured during the excitation step. Finally, layer-wise propagation is applied, to provide biometrically plausible explanations that inform the model's conclusions. This information may be used by experts to cross-validate the predictions made by the model. The omics captured by this model are DNA methylation, copy number variation, and transcription mRNA expression, and the evaluation of this model is performed on the TCGA BRCA dataset.

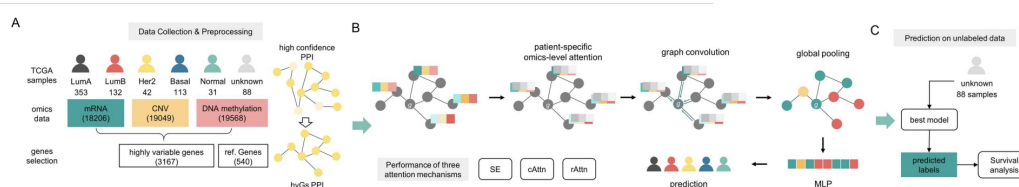


Figure 10: Overview of the proposed method, (A) building a graph based on a filtered protein-protein interaction network, (B) implementing the various attention mechanisms followed by a convolutional layer, and (C) using the best model to make predictions about patient data.

Paper 3 [23] iterates on applying attention-based models to graph neural networks to achieve a more general model. Building on the idea of a Graph Attention Network (GAT), this paper builds a GCN to capture all local information, while relying on the attention model to capture cross-omic information. This paper combines mRNA expression, copy number variation, and miRNA expression, using a supra-graph derived from gene-gene interaction data from BioGrid, and miRNA gene-target data from miRDB. The nodes are first expanded using a linear layer to increase their dimension. Then, a graph convolutional network is created using spectral decomposition, although the authors note that theoretically, any graph neural network could be substituted during this step. The results are passed into an attention-based decoder. Finally, the original graph is fed through a shallow feed-forward network, and this output is combined with the decoder output into a softmax layer. The authors note that the GAT layer is more helpful in situations with less data, to extract as much information as possible from the available data, while the GCN layer is more effective with more data, leveraging local patterns to discern the relations between different cancers. Evaluation of this model was performed on the TCGA dataset, both in a pan-cancer and breast-cancer context, giving this model generality compared to the other papers.

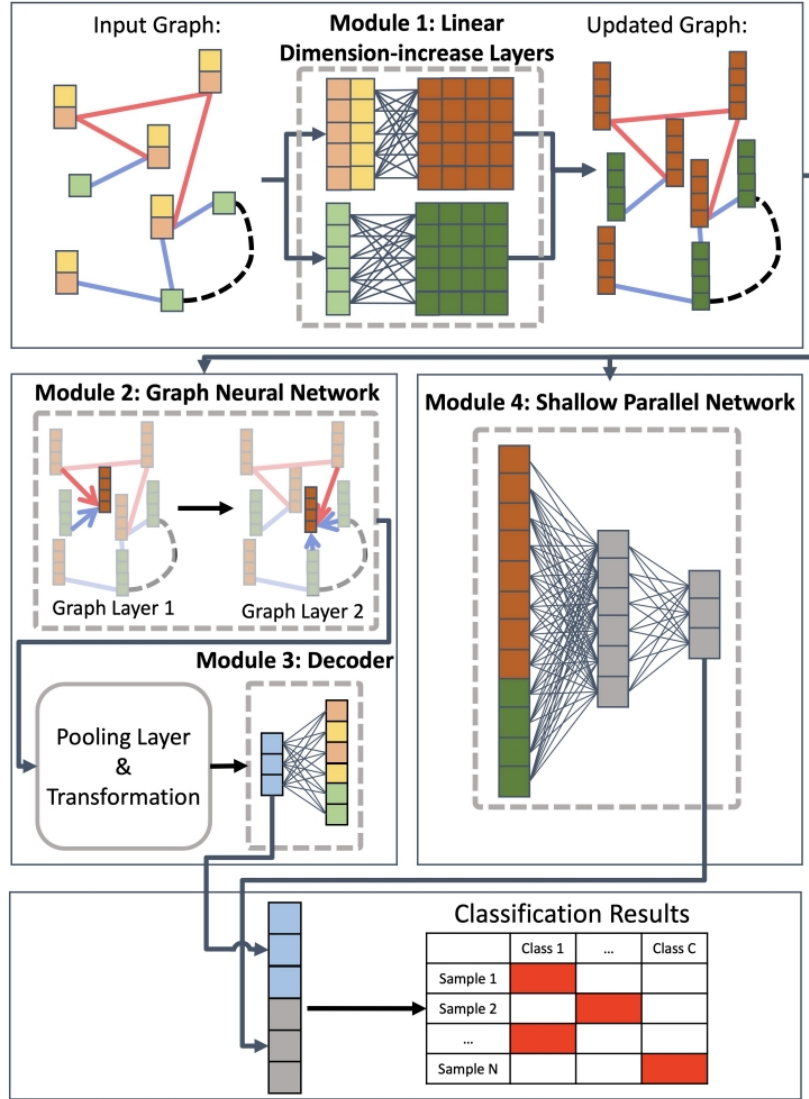


Figure 11: Overview of the proposed method. On the left, using the output of a graph convolutional layer into an attention-based decoder. On the right, using a shallow feed-forward layer. Finally, a recombination layer to merge the two results.

2.4 Advantages and Limitations

This survey examines several GNN models for classifying breast cancer molecular subtypes, highlighting their strengths and limitations. The GCN/RN model was a pioneer, combining a graph convolutional network with a relation network, outperforming contemporary methods. Its use of RNA-seq data makes it suitable for cases with limited omics data, but its reliance on a single omics type may restrict accuracy. The lack of attention mechanisms, which have proven valuable in breast cancer classification, is another drawback.

The AGCN enhances GNN applications by integrating attention mechanisms, achieving high accuracy and providing explainability through layer-wise propagation. However, it requires further testing on smaller, noisier datasets, and its use of a manually chosen threshold for protein-protein interaction data introduces potential bias, limiting performance.

The GCN/GAT model combines GCNs and attention for both pan-cancer and breast cancer classification. It performs well on large datasets, with GCN layers capturing robust patterns and attention

mechanisms identifying key interactions in sparser datasets. However, its computational expense on large datasets and lack of optimization for specific breast cancer subtypes may limit its practical application.

3 Benchmarks, Evaluation metrics and Results

3.1 Binary Classification

3.1.1 Benchmark datasets and Evaluation metrics

BDR-CNN-GCN [7] model was benchmarked on the Breast Mini-MIAS dataset, a well-established resource for mammographic image analysis. This dataset contains labeled mammograms that enable researchers to evaluate the model’s capability in detecting breast cancer. The evaluation process used a 10-fold cross-validation methodology to ensure the reliability and robustness of the results. Sensitivity, Specificity, and Accuracy were used to accurately distinguish between benign and malignant cases while maintaining a high balance between false positives and false negatives. Furthermore, the results surpassed those of five proposed neural network models and 15 state-of-the-art breast cancer detection approaches, showcasing its superiority in handling mammographic data.

[8] DEGN model was evaluated on two primary datasets: BCSS (Breast Cancer Semantic Segmentation) dataset and BACH (Breast Cancer Histology Challenge) dataset. BCSS dataset has 151 whole-slide images (WSIs) stained with hematoxylin and eosin, designed for semantic segmentation tasks. On this dataset, the model exhibited strong performance across various magnifications and similarity measurement modes. For the BACH dataset, which contains 400 histological images, the DEGN model delivered outstanding results. Precision, Accuracy, and Recall were used to evaluate on both datasets and results highlight DEGN model’s effectiveness in histopathology-based breast cancer classification, leveraging ensemble learning and graph-based representation.

[9] GCN-based model was tested on the BUSI (Breast Ultrasound Images) dataset, a curated dataset containing ultrasound images with labeled tumor regions. The evaluation process focused on both handcrafted and graph-based features to optimize the model’s accuracy. Using k-fold cross-validation, the model was evaluated using accuracy, Precision, recall, and specificity metrics which confirmed the model’s reliability and robustness. Additionally, an ablation study involving nine experiments identified optimal hyperparameters, including three convolutional layers, a dropout rate of 0.3, and the ELU activation function, which achieved the highest accuracy with minimal time complexity. Bayesian optimization further validated these results, tuning parameters such as learning rate (0.01) and batch size (128) for optimal performance. Experiments on graph optimization reduced edge counts significantly, improving computational efficiency while maintaining high accuracy. Compared to prior methods on the same dataset, this model demonstrated superior performance, confirming the importance of its handcrafted feature approach and graph optimization strategy.

3.1.2 Results

The evaluation of the three models—BDR-CNN-GCN, DEGN, and GNN-Based—highlights their robust performance in breast cancer classification using diverse datasets and metrics.

The BDR-CNN-GCN model [7], tested on the Breast Mini-MIAS dataset, achieved strong results with a sensitivity of 96.20%, specificity of 96.00%, accuracy of 96.10%, F1-score of 96.15%, and an AUC-ROC of 0.98. These metrics underscore the model’s ability to balance false positives and negatives effectively while leveraging hybrid CNN-GCN architecture for feature extraction.

The DEGN model [8], evaluated on the BCSS and BACH datasets, demonstrated remarkable versatility. It achieved an accuracy range of 94–96% on BCSS and 99% on BACH, with a precision of 99.45%, recall of 99.00%, specificity of 98.90%, and F1-score of 99.20%. The ensemble graph network design enabled it to effectively analyze histopathology images, outperforming state-of-the-art methods in both binary and multi-class tasks.

The GNN-Based model [9], tested on the BUSI dataset, achieved exceptional performance, with an accuracy of 99.48%, precision and recall of 100%, specificity of 99.50%, F1-score of 99.80%, and an AUC-ROC of 0.99. Its reliance on optimized graph construction and handcrafted features from tumor regions proved crucial in achieving these results, demonstrating efficiency and robustness compared to previous methods.

Overall, these results emphasize advanced capabilities of these models in capturing complex patterns in medical imaging while addressing challenges like dataset diversity and computational efficiency.

Model	Evaluation Metrics
BDR-CNN-GCN	Sensitivity: 96.20% Specificity: 96.00% Accuracy: 96.10% F1-score: 96.15%
DEGN	BCSS Accuracy: 94–96% BACH Accuracy: 99% BACH Precision & Recall: 99.45% F1-score: 99.20%
GNN-Based	Accuracy: 99.48% Precision: 100% Recall: 100% Specificity: 99.50% F1-score: 99.80%

Table 1: Comparison of Evaluation Metrics

3.1.3 Comparison

Category	BDR-CNN-GCN	DEGN	GCN with US Images
Datasets/Input	Mini-MIAS (322 single-breast mammogram slices) Abnormal: 113; Normal: 209	BCSS(binary) & BACH (binary + multi) Histopathology images)	BUSI (647 Ultrasound images made using high-end instruments) Benign - 467, Malignant - 180
Model	Hybrid of 8-layer CNN with BN, dropout, rank-based pooling, and 2-layer GCN	Structural Graph Module (SGM) integrated with ensemble graph networks (EGN)	Handcrafted node features, Spearman correlation adjacency matrix → FFN → 3 GCN layers → softmax
Data Augmentation	14-way augmentation to address overfitting and enhance dataset size	Multi-magnification patch-based feature extraction and ensemble techniques	ROI-based handcrafted features validated statistically, compared to Histogram of Oriented Gradients
Role of GNNs	Extracts spatial and structural relationships to identify malignancies overlooked by CNNs	Builds structural graphs of nuclei to enhance classification of irregular cells	Simplifies graph-based representation using Spearman correlation for robust analysis
Metrics	Sensitivity: 96.20%, Specificity: 96.00%, Accuracy: 96.10%	BCSS Accuracy: 94–96%, BACH Accuracy: 99%, Precision: 99.45%	Accuracy: 99.48%, Precision: 100%, Recall: 100%
Strengths	Effective data augmentation, robust hybrid architecture, deployable in clinical settings	Highly accurate segmentation and classification, adaptable to dataset shifts	Optimized performance with simplified graph-based representation
Uses	Promising for clinical deployment in radiology	Automates clinical histopathology image analysis with improved precision	Supports radiology for early diagnosis and automation
Limitations	Needs validation on larger and heterogeneous datasets	Requires validation on real-world images, small dataset size	Limited generalization due to small dataset
Future Direction	Larger dataset validation, integration with cloud platforms for speed and efficiency	Optimize graph modeling for real-world data, explore lightweight and hybrid GNNs	Introduce multimodal data for richer insights and automate feature extraction

Table 2: Comparison of chosen survey papers for Binary Breast Cancer Classification

3.2 Gene Subtype Classification

3.2.1 Benchmark datasets and Evaluation metrics

All three papers leverage the Cancer Genome Atlas (TCGA) dataset, a comprehensive resource of genomic data widely used for cancer research. TCGA provides high-dimensional data, including

gene expression profiles, which are crucial for tasks like gene subtype classification. The evaluation metrics employed across these studies are accuracy and F1 score, which effectively capture the model’s performance in terms of both correctness and balance between precision and recall. Accuracy serves as a straightforward measure of overall prediction correctness, while the F1 score accounts for imbalanced data by harmonizing precision and recall. Together, these metrics provide a robust framework to evaluate the effectiveness of Graph Neural Network (GNN) models in classifying breast cancer subtypes, ensuring that both general predictive power and sensitivity to class imbalances are taken into account.

3.2.2 Results

Method	Dataset	Accuracy (ACC)	F1 Score
Multi-View GNN	TCGA	91.80%	95.30%
Omics GAT	TCGA	92.24%	91.04%
Multi Omics	TCGA	95.39%	93.80%

Table 3: Comparison of results for three methods in Gene Subtype classification.

Observations: Multi-View GNN achieves a high F1 score, suggesting robust classification performance in terms of precision and recall. OmicsGAT delivers balanced performance with slightly higher accuracy compared to the first but a slightly lower F1 score. Multi Omics outperforms others in accuracy, showcasing its strength in identifying correct predictions across different subtypes.

3.2.3 Comparison

Category	MVGNN	Omics GAT	Multi Omics
Primary Model	Multi-View Graph Neural Network (MVGNN)	Graph Attention Network (GAT)	GCN, GAT, and Graph Transformer Network (GTN)
Datasets/Input	TCGA-BRCA (The Cancer Genome Atlas Breast Cancer)	TCGA datasets for various cancer types	TCGA and other public multi-omics datasets (not breast cancer-specific)
Pre-processing Steps	Normalization, similarity computation, graph construction	Normalization, feature scaling, and edge weighting	Normalization, DEGs, Limma and Lasso regression
Data Augmentation	Generates augmented similarity graphs to improve model robustness.	Limited mention of augmentation techniques.	Architectures use edge perturbations or synthetic graphs.
Feature Aggregation	Attention mechanism to integrate features across omics views.	Attention mechanism to focus on relevant neighbors.	Compared multiple architectures for aggregation methods.
Role of GNNs	Integrates multi-omics data for subtype prediction and differentiation.	Highlights neighbor-wise attention for feature extraction.	Evaluate architectural differences in multi-omics integration.
Metrics	ACC - 91.80, F1 - 95.30	ACC - 92.24, F1 - 91.04	ACC - 95.39, F1 - 93.80
Strengths	Stands out for its multi-view design, Simple, unified graph representation.	Integrates diverse omics data effectively.	Highlights tradeoffs and guides model selection.
Uses	Prognosis by identifying molecular-level insights.	Understanding of omics data interactions for precision medicine.	Provides benchmarks for selecting optimal GNN architectures.
Limitations	Requires extensive pre-processing and high computational resources.	Attention mechanisms can be computationally intensive, potentially limiting scalability to larger datasets.	Limited by dataset availability and generalizability.
Future Direction	Address scalability for large-scale datasets.	Extend to additional cancer subtypes.	Focus on benchmarking across more diverse datasets.

Table 4: Summary of Key Information for Gene Subtype Classification

3.3 Molecular Subtype Classification

3.3.1 Benchmark datasets and Evaluation metrics

All models examined were evaluated on the TCGA breast cancer datasets. The GCN/RN model was evaluated exclusively on this dataset. The AGCN model was additionally tested on the Colon Adenocarcinoma (COAD) and pan-cancer datasets from the TCGA database. The GCN/GAT model

was evaluated on the BRCA and pan-cancer datasets. To evaluate the models, the GCN/RN and GCN/GAT proposals examine the accuracy and F1-score, while the AGCN model examines the accuracy and Area Under the Curve (AUC) to determine the model’s performance in classification.

3.3.2 Results

The GCN/RN model was evaluated on the TCGA/BRCA dataset, achieving an accuracy of 83.19% and an F1-score of 83.41%, compared to a model only using a GCN, which achieved an accuracy of 82.39% and an F1-score of 82.52%, and a simple GAT model, which achieved an accuracy of 81.37% and an F1-score of 80.15%. The AGCN model achieved the highest accuracy and AUC of all models examined by the authors on the BRCA dataset and COAD dataset, achieving an accuracy of 89.42% on the BRCA dataset and AUC of 98.08% on the BRCA datasets, however was outperformed by other models on the pan-cancer dataset. The GCN/GAT model was achieved the highest accuracy and F1-score of the models examined on both the BRCA dataset and pan-cancer datasets, achieving an accuracy of 83.9% and F1-score of .84 on the pan-cancer dataset and an accuracy of 86.4% and F1-score of .87 on the BRCA dataset. All models examined for the task of molecular subtype classification were evaluated on the TCGA BRCA dataset, so we can compare their results directly.

Model	Accuracy (%)	AUC (%)	F1 Score
GCN/RN	83.19	-	0.8326
AGCN	89.42	97.08	-
GCN/GAT	86.40	-	0.8700

Table 5: Summary of Results for All Papers

The AGCN model does not report an F1-Score, but performs the best on all other metrics. A possible explanation is that the GCN/GAT model, as a pan-cancer approach, is not as optimized for the specific task of breast cancer molecular subtype classification. However, it is worth observing that the accuracies for the GCN/GAT and AGCN models are within their respective margins of error. For the AGCN model, these represent the result of the rcAGCN model, the highest-performing of the three examined. For the GCN/GAT model, these values represent the result when considering all edge-types in the initial supra-graph.

In general, these GCN-based approaches outperform other approaches to the problem. At the time of publication, the GCN/RN model demonstrated a substantial improvement in performance compared to contemporary approaches to the problem. The AGCN model outperformed other models on the TCGA BRCA dataset, but by a smaller margin compared to GCN/RN. The AGCN model also outperforms its contemporaries on the COAD dataset, but does not perform as strongly as its contemporaries on the TCGA pan cancer dataset, highlighting the extent that it was tuned to classifying specific types of cancer. The GCN/GAT model performs strongly on the pan cancer dataset, but does not quite achieve as high an accuracy as the AGCN model on the TCGA BRCA dataset, although this result is within the margin of error.

3.3.3 Comparison

Category	1: GCN/RN	2: AGCN	3: GCN/GAT
GNN Structure	Combine GraphCNN with Relation Network; uses RN to capture gene-gene relations	Attention-based GCN to fuse multi-omics data with protein-protein interaction networks	Utilizes GCN for local feature extraction, GAT to capture cross-omic relationships
Feature Extraction	STRING database for gene-gene interactions; GCN to capture RNA-seq interactions	Selects highly variable genes (DNA-methyl, mRNA); constructs graph from PPI network	Cross-patient networks for omics data (mRNA, CNV, miRNA) captured locally and globally
Datasets/Use Cases	PAM50 dataset of RNA-seq profiles; localized learning of graph features	TCGA breast-invasive carcinoma (BRCA) dataset; layer-wise relevance propagation	TCGA pan-cancer and BRCA datasets
Dataset	TCGA BRCA	TCGA BRCA/ COAD/ Pan-cancer	TCGA BRCA/ Pan-cancer
Accuracy	86.29%	89.42%	86.40%
AUC	-	97.08%	-
F1-Score	83.41%	-	87%
Strengths	Simple, intuitive, compatible with RNA-seq data	High accuracy, high explainability	Flexible, generalizable across cancers and omics
Limitations	Narrow focus; does not account for cross-omic data	Reliant on manual preprocessing. Struggles with incomplete/noisy datasets.	Computationally expensive; less fine-tuned for categorizing breast cancers
Future Work	Expand to include multi-omics data and larger datasets	Reduce reliance on manual preprocessing; ensure compatibility with alternate datasets	Optimize scalability and incorporate domain-specific modules

Table 6: Combined Summary of GCN/RN, AGCN, and GCN/GAT for Breast Cancer Molecular Subtype Classification

4 Frontier and Vision in the future direction

The future of binary breast cancer classification lies in improving model generalizability and clinical applicability through several key advancements. Validating models like BDR-CNN-GCN, DEGN, and GCN-based frameworks on larger and more diverse datasets is critical to ensure robustness across different populations and imaging modalities. Integrating heterogeneous and multimodal data, such as combining imaging with clinical or genetic information, offers the potential to enhance predictive accuracy. Efforts should also focus on automating feature extraction processes to reduce reliance on handcrafted features and improve adaptability to unseen patterns. Optimizing models for real-world deployment, including lightweight architectures for resource-constrained environments and scalable cloud-based solutions, is essential for practical healthcare applications. Additionally, creating larger, annotated datasets and improving segmentation capabilities, particularly for histopathology images,

will play a pivotal role in advancing breast cancer classification systems to new levels of efficiency and effectiveness.

Advancing gene subtype classification in breast cancer requires improvements in both methodological design and clinical relevance. Validating GNN-based models on larger, more diverse datasets will ensure robustness and generalizability. The integration of multimodal data, combining gene expression with epigenomic or clinical information, promises deeper insights into cancer heterogeneity. Enhancing model interpretability to identify key genes and pathways influencing subtypes is critical for actionable biological understanding. Inspired by progress in binary and molecular subtype classification, future work should focus on automating graph construction, refining feature representations, and embedding biological priors. Additionally, developing lightweight, scalable architectures will enable broader applications, particularly in resource-constrained clinical environments.

Models for molecular subtype classification highlight the potential of graph neural networks in diagnosing and treating breast cancer subtypes. Successes with AGCN and GCN/GAT models underscore the importance of attention mechanisms in future research. However, robustness across diverse datasets requires further validation, and manually parameterized pruning of protein-protein interaction networks may lead to suboptimal results. While GCN/GAT models offer robust classification across cancer domains, optimizing for specific subtypes and improving scalability remain open challenges. Exploring alternative GNN configurations could refine graph construction, ultimately empowering oncologists with more accurate prognostic tools and treatment strategies.

5 Conclusion

This survey highlights the transformative potential of Graph Neural Networks (GNNs) in breast cancer classification, enabling improved diagnostic accuracy and personalized treatment. By modeling complex relationships in data, GNNs excel in capturing dependencies and structures, offering advantages over traditional machine learning methods. Despite these advancements, challenges like limited annotated datasets and the interpretability of GNN models hinder clinical adoption. Addressing these issues through more efficient architectures, enhanced data augmentation, and multi-modal data integration is crucial. In summary, GNNs offer immense promise for breast cancer research. Tackling current limitations will unlock their full potential, paving the way for better diagnostics and improved patient care.

Task	People
1. Finalizing idea and project structure	Shruti, Vidhi, Andy
2. Finding and collecting papers for each category	Shruti
3. Reading papers and making comparison tables	Shruti, Vidhi, Andy
4. Making content for slides	Shruti, Vidhi, Andy
5. Formatting and editing slides	Shruti, Vidhi
6. Writing report	Shruti, Vidhi, Andy
7. Making tables and visualizations as needed	Shruti, Vidhi
8. Proofreading, formatting, and editing the final paper	Shruti, Vidhi, Andy
9. Preparing for presentations or discussions	Shruti, Vidhi, Andy

Table 7: Task Distribution for Survey Paper Work

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