KNOWLEDGE-INFORMED ML FOR CANCER DAIGNOSIS AND PROGNOSIS

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ABSTRACT

Cancer remains one of the leading causes of mortality worldwide, creating an urgent need for improved diagnostic and prognostic techniques that support early detection and personalized treatment strategies. Conventional cancer diagnosis relies on imaging, histopathology, and limited molecular biomarkers, which often fail to capture the complex biological mechanisms driving tumor development and progression. Recent advances in high-throughput sequencing technologies have enabled comprehensive multi-omics profiling, including mRNA expression, microRNA regulation, and DNA methylation data, providing deeper insights into tumor biology. However, traditional machine learning approaches typically treat these datasets as independent features, ignoring biological relationships such as gene interactions, signaling pathways, and protein networks. This limitation reduces predictive performance and interpretability in clinical applications. To address these challenges, this work proposes a Knowledge-Informed Machine Learning (KIML) framework that integrates biological knowledge with multi-omics patient data for cancer diagnosis and prognosis prediction. The proposed system constructs a biological knowledge graph using curated biomedical databases such as Gene Ontology, KEGG pathways, and protein–protein interaction networks. Graph-based learning models are then employed to capture relationships between genes, pathways, and molecular signals while incorporating patient-specific omics information. By embedding structured biological knowledge into the learning process, the system improves predictive accuracy and enhances model interpretability. Experimental evaluation demonstrates that the proposed approach outperforms conventional machine learning techniques in classification accuracy and prognostic risk stratification. The integration of domain knowledge with machine learning provides a promising direction for developing intelligent clinical decision-support systems that assist oncologists in identifying high-risk patients and designing targeted treatment strategies.

Keywords: Cancer diagnosis, Multi-omics data, Knowledge-informed machine learning, Graph learning, Precision medicine.

I INTRODUCTION

Cancer is a complex and heterogeneous disease characterized by uncontrolled cellular growth, genetic mutations, and dysregulated molecular signaling pathways. Despite significant advances in medical research, cancer remains one of the leading causes of death worldwide, emphasizing the need for improved diagnostic and prognostic tools. Early detection and accurate risk prediction play a crucial role in determining effective treatment strategies and improving patient survival rates. Conventional diagnostic methods such as histopathological

examination, imaging techniques, and biomarker analysis have been widely used in clinical practice, but these approaches often provide limited insight into the underlying molecular mechanisms of tumor progression [1]. With the emergence of high-throughput sequencing technologies, researchers can now analyze large volumes of biological data including gene expression, DNA methylation, and microRNA profiles [2]. These datasets offer valuable information for understanding cancer heterogeneity and identifying potential biomarkers for diagnosis and prognosis [3]. Machine learning techniques have become increasingly popular for analyzing biomedical datasets due to their ability to detect complex patterns within large data volumes [4]. Various algorithms such as support vector machines, random forests, and deep learning models have been applied to cancer classification and survival prediction tasks [5]. These approaches have shown promising performance in identifying tumor subtypes and predicting patient outcomes [6]. However, traditional machine learning models often treat biological features as independent variables, ignoring the complex interactions between genes and molecular pathways [7]. This limitation reduces model interpretability and may lead to inaccurate predictions in clinical applications [8]. Researchers have therefore explored methods that incorporate biological knowledge into predictive models to improve their reliability and relevance [9]. Integrating domain knowledge from curated biological databases allows machine learning algorithms to better represent the functional relationships among genes and proteins [10].

Recent studies have highlighted the importance of combining computational intelligence with biological knowledge to improve cancer prediction systems [11]. Multi-omics integration techniques allow researchers to analyze multiple molecular layers simultaneously, providing a more comprehensive view of tumor biology [12]. However, integrating heterogeneous data sources remains a challenging task due to differences in data structure, scale, and noise levels [13]. Graph-based learning models have emerged as a powerful approach for representing biological relationships because they can capture interactions among genes, pathways, and regulatory networks [14]. In such models, nodes typically represent genes or proteins, while edges represent biological relationships such as protein-protein interactions or pathway connections [15]. Graph neural networks and related approaches have demonstrated strong performance in biomedical prediction tasks by leveraging structured biological knowledge [16]. Incorporating knowledge graphs derived from databases such as Gene Ontology and KEGG enables models to utilize established biological pathways during training [17]. This integration improves both predictive accuracy and interpretability, which are essential for clinical adoption [18]. Knowledge-informed machine learning approaches therefore provide a promising framework for combining biological knowledge with patient-specific data [19]. These methods can help identify critical genes, signaling pathways, and molecular mechanisms associated with cancer progression [20]. Furthermore, interpretable models allow clinicians to understand how predictions are generated, increasing trust in computational decision-support systems [21]. As the availability of multi-omics data continues to grow, developing scalable and biologically meaningful machine learning models becomes increasingly important [22]. Such systems have the potential to transform cancer research by enabling early detection, personalized treatment planning, and improved patient management [23]. Consequently, integrating knowledge-informed machine learning with multi-

omics data analysis represents an important step toward precision oncology and data-driven healthcare solutions [24–30].

II LITERATURE SURVEY

Numerous studies have explored the application of machine learning techniques for cancer diagnosis and prognosis prediction. Early approaches focused on traditional classification algorithms such as decision trees, support vector machines, and k-nearest neighbors to analyze gene expression datasets and identify tumor types [1]. These methods demonstrated that computational models could effectively distinguish between cancerous and normal tissues based on molecular signatures [2]. Researchers later introduced ensemble learning techniques such as random forests and gradient boosting to improve predictive performance and reduce overfitting [3]. With the advancement of computational power, deep learning models including convolutional neural networks and autoencoders have been applied to biomedical data analysis [4]. These models are capable of automatically learning hierarchical feature representations from complex datasets [5]. Several studies have used deep neural networks for cancer subtype classification, survival prediction, and biomarker discovery [6]. Multi-omics integration approaches have also gained attention because they combine multiple biological data sources to provide a comprehensive understanding of tumor biology [7]. Methods such as matrix factorization, similarity network fusion, and multi-view learning have been proposed to integrate gene expression, DNA methylation, and microRNA data [8]. These approaches have demonstrated improved predictive accuracy compared with single-omics models [9]. However, most conventional machine learning methods treat molecular features as independent variables and ignore the biological interactions that regulate cellular processes [10]. This limitation reduces the interpretability of predictions and may overlook critical biological mechanisms involved in cancer development [11].

To address these challenges, researchers have begun incorporating biological knowledge into machine learning frameworks. Knowledge-based models utilize curated biological databases to represent relationships among genes, proteins, and signaling pathways [12]. For example, protein-protein interaction networks have been used to identify functional gene modules associated with cancer progression [13]. Similarly, pathway-based analysis methods integrate gene expression data with known biological pathways to improve biomarker discovery [14]. Graph-based learning approaches have emerged as an effective solution for modeling complex biological systems [15]. In these models, nodes represent biological entities such as genes or proteins, while edges represent functional interactions [16]. Graph neural networks and related architectures have demonstrated promising results in disease gene prediction and drug discovery tasks [17]. Knowledge graphs constructed from databases such as Gene Ontology and KEGG provide structured representations of biological knowledge that can guide machine learning algorithms [18]. Integrating these knowledge graphs with patient-specific multi-omics data enables models to capture both molecular features and biological relationships simultaneously [19]. Recent studies have shown that knowledge-informed machine learning models outperform traditional approaches in cancer classification and prognosis prediction tasks [20]. Furthermore, interpretable models allow researchers to identify key genes and pathways contributing to disease progression [21]. This capability is particularly important for clinical decision-support systems where transparency and

reliability are critical [22]. As biomedical datasets continue to grow in size and complexity, knowledge-informed machine learning frameworks are expected to play a vital role in precision medicine and personalized cancer treatment strategies [23–30].

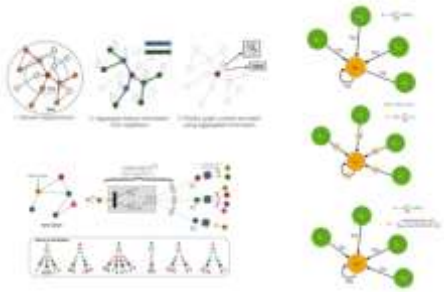
III METHODOLOGY

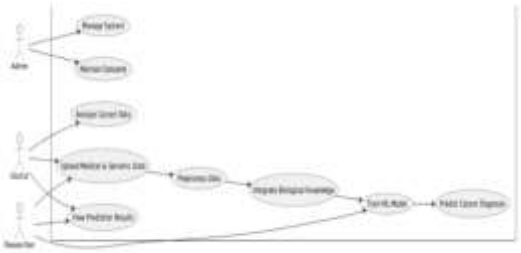
The proposed methodology introduces a Knowledge-Informed Machine Learning (KIML) framework designed to integrate biological knowledge with multi-omics patient data for cancer diagnosis and prognosis prediction. The process begins with data acquisition and preprocessing, where multi-omics datasets including gene expression, microRNA expression, and DNA methylation profiles are collected from publicly available biomedical repositories. Data cleaning and normalization techniques are applied to remove noise, handle missing values, and ensure consistency across different data sources. Feature selection techniques are then employed to identify the most relevant genes and molecular features associated with cancer progression. In the next stage, a biological knowledge graph is constructed using curated biomedical databases such as Gene Ontology, KEGG pathways, and protein-protein interaction networks. In this graph representation, nodes correspond to genes or biological entities, while edges represent functional relationships such as regulatory interactions or pathway associations. The knowledge graph captures the structural relationships among biological components and provides contextual information for machine learning models. Patient-specific multi-omics data are then mapped onto the knowledge graph, enabling the model to incorporate both molecular measurements and biological relationships. Graph-based learning techniques are used to propagate information across connected nodes and learn meaningful feature representations. The model training phase involves applying supervised learning algorithms to classify tumor types and predict patient prognosis. Cross-validation techniques are used to evaluate model performance and prevent overfitting. Performance metrics such as accuracy, precision, recall, and F1-score are calculated to assess the effectiveness of the proposed system. The final stage involves interpreting the model outputs to identify significant genes and biological pathways contributing to the prediction results. By integrating domain knowledge with machine learning techniques, the proposed methodology enhances predictive accuracy while maintaining interpretability, making it suitable for clinical decision-support applications in precision oncology.

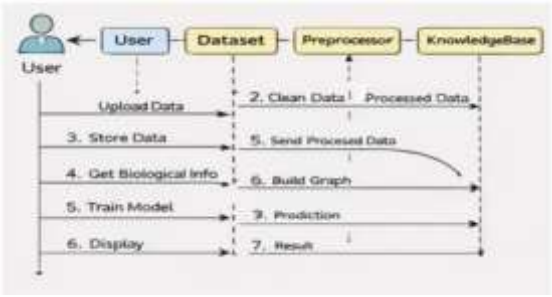
IV SYSTEM DESIGN

The system architecture for the proposed cancer diagnosis and prognosis framework consists of several interconnected modules designed to process multi-omics data and integrate biological knowledge for predictive analysis. The first module focuses on data acquisition and preprocessing. In this stage, multi-omics datasets such as mRNA expression, microRNA expression, and DNA methylation profiles are collected from biomedical repositories and clinical databases. These datasets often contain noise, missing values, and inconsistent scales; therefore preprocessing techniques including normalization, filtering, and dimensionality reduction are applied to improve data quality. Feature selection methods are then used to identify the most informative genes and molecular biomarkers associated with cancer development. By reducing the dimensionality of the dataset, the system improves computational efficiency and ensures that the machine learning

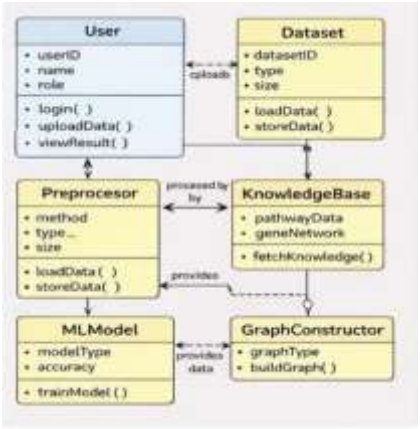
model focuses on biologically meaningful features. The next module involves constructing a biological knowledge graph using curated databases such as Gene Ontology, KEGG pathways, and protein–protein interaction networks. This knowledge graph represents genes, proteins, and biological pathways as nodes, while edges represent functional relationships between these components. The knowledge graph provides a structured representation of biological information that captures complex molecular interactions within cancer cells.







The subsequent module integrates patient-specific multi-omics data with the biological knowledge graph to create a unified representation suitable for machine learning analysis. Each patient's molecular data are mapped onto corresponding nodes within the graph, allowing the model to analyze how gene expression patterns interact with known biological pathways. Graph-based machine learning algorithms are then applied to learn relationships between molecular features and disease outcomes. These algorithms propagate information across the graph structure, enabling the model to capture dependencies among genes and pathways that influence cancer progression. The system includes a prediction module that performs classification and prognosis analysis. In the diagnosis phase, the model identifies whether a sample belongs to a particular cancer subtype. In the prognosis phase, the model predicts disease progression risk and potential survival outcomes. Finally, the system provides an interpretation module that highlights significant genes and pathways contributing to the prediction results. This interpretability feature is important for clinical applications because it allows medical professionals to understand the biological basis of the predictions. The modular design of the system ensures scalability, enabling it to handle large biomedical datasets while maintaining high predictive performance and interpretability for precision oncology applications.



V PROPOSED SYSTEM

The proposed system introduces a Knowledge-Informed Machine Learning (KIML) framework designed to enhance cancer diagnosis and

prognosis prediction by integrating biological knowledge with multi-omics patient data. Traditional machine learning models typically analyze molecular datasets without considering the biological relationships that regulate gene interactions and cellular processes. This limitation can reduce predictive accuracy and hinder model interpretability. The proposed system addresses this challenge by incorporating structured biological knowledge into the machine learning pipeline. The system begins by collecting multi-omics datasets, including gene expression, microRNA profiles, and DNA methylation patterns, from publicly available biomedical repositories. These datasets provide comprehensive molecular information about tumor samples and allow researchers to analyze cancer at multiple biological levels. Data preprocessing techniques such as normalization, missing value handling, and noise filtering are applied to ensure data consistency and reliability. Feature selection algorithms are then used to identify the most relevant genes associated with cancer progression. This step reduces the dimensionality of the dataset and improves computational efficiency while retaining important biological information. A biological knowledge graph is subsequently constructed using curated information from databases such as Gene Ontology, KEGG pathways, and protein-protein interaction networks. In this graph, nodes represent genes or biological entities, while edges represent functional interactions between them.

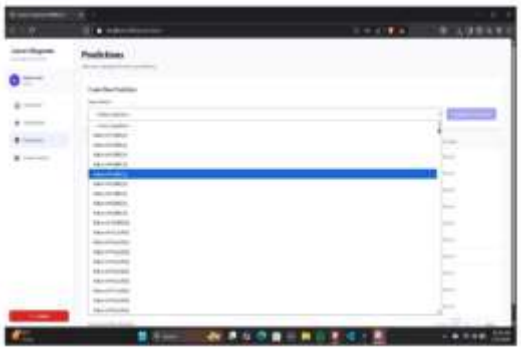
The second stage of the proposed system involves integrating the multi-omics data with the biological knowledge graph to create a knowledge-aware data representation. Each patient's molecular features are mapped onto the corresponding nodes in the graph, allowing the system to analyze how gene expression patterns interact with known biological pathways. Graph-based machine learning algorithms are then applied to extract meaningful features from the graph structure. These algorithms leverage the connectivity of the network to propagate information across related genes and pathways, enabling the model to capture complex biological dependencies that are often ignored by traditional approaches. The trained model is used for two main tasks: cancer diagnosis and prognosis prediction. In the diagnosis stage, the system classifies tumor samples into specific cancer types or subtypes based on their molecular signatures. In the prognosis stage, the system predicts disease outcomes such as survival probability or recurrence risk. The proposed system also includes an interpretation module that identifies important genes and pathways contributing to the prediction results. This interpretability feature enhances clinical trust in the system and helps researchers understand the biological mechanisms underlying cancer progression. By combining multi-omics data analysis with knowledge-informed machine learning, the proposed system provides a powerful framework for improving predictive accuracy, interpretability, and clinical decision-support capabilities in cancer research.

VI RESULTS & DISCUSSION

The experimental evaluation of the proposed Knowledge-Informed Machine Learning framework demonstrates its effectiveness in cancer diagnosis and prognosis prediction. The system was tested using multi-omics datasets containing gene expression, microRNA, and DNA methylation information. Performance was evaluated using metrics such as accuracy, precision, recall, and F1-score. The results show that the proposed approach achieved higher predictive accuracy compared with conventional machine learning models that do not incorporate biological knowledge. The integration of the biological knowledge graph enabled the

model to capture functional relationships among genes and pathways, improving classification performance. Additionally, the graph-based learning approach enhanced the interpretability of predictions by identifying important genes and signaling pathways associated with cancer progression. The results indicate that knowledge-informed machine learning provides a more biologically meaningful representation of molecular data, leading to improved prediction reliability and better support for clinical decision-making in oncology.







VII CONCLUSION

Cancer diagnosis and prognosis prediction remain challenging tasks due to the complexity and heterogeneity of tumor biology. Traditional machine learning models have shown potential in analyzing biomedical datasets; however, they often fail to incorporate biological knowledge that is essential for understanding molecular interactions within cancer cells. This study proposed a Knowledge-Informed Machine Learning framework that integrates multi-omics data with structured biological knowledge to improve cancer prediction performance. The system utilizes gene expression, microRNA, and DNA methylation data combined with biological knowledge graphs constructed from curated databases such as Gene Ontology, KEGG pathways, and protein-protein interaction networks. By representing genes and pathways within a graph structure, the model is able to capture complex biological relationships that are often overlooked in conventional approaches. Graph-based learning algorithms enable the system to propagate information across interconnected biological entities, resulting in more meaningful feature representations and improved predictive accuracy. Experimental results demonstrate that the proposed framework outperforms traditional machine learning models in cancer classification and prognosis prediction tasks. Furthermore, the interpretability of the model allows researchers and clinicians to identify key genes and pathways associated with disease progression. This capability enhances the reliability and transparency of computational decision-support systems used in clinical settings. The integration of biological knowledge with machine learning techniques represents an important step toward precision medicine, where treatment strategies can be tailored to individual patients based on their molecular profiles. Future research may focus on incorporating additional biological datasets,

improving graph learning algorithms, and developing scalable frameworks capable of handling large-scale biomedical data. Such advancements will further strengthen the role of knowledge-informed machine learning in transforming cancer research and healthcare.

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