Predicting Protein-Protein Interactions Using Graph Neural Networks: A Study on the SHS27K Dataset

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Abstract: Protein-protein interactions (PPIs) are fundamental to cellular function and are crucial for understanding biological processes, disease mechanisms, and potential therapeutic targets. This study investigates the role of PPI networks in biological systems, focusing on their significance in cellular processes, disease mechanisms, and drug development. By integrating experimental techniques such as yeast two-hybrid, co-immunoprecipitation, and mass spectrometry with bioinformatics methods, a high-quality PPI network was constructed. Key findings include the identification of critical protein modules and nodes involved in cellular functions like signaling and metabolism, as well as interactions linked to diseases. The research highlights the importance of PPI network analysis in advancing our understanding of life processes and in developing novel therapeutic strategies.

Keywords: Protein-Protein Interactions (PPI); PPI Networks; Bioinformatics; Graph Neural Networks; Computational Biology

1. Introduction

Proteins are fundamental components of cellular structure and function, and understanding their interactions is essential for comprehending various biological processes [1]. Protein-protein interactions (PPIs) are central to a wide range of cellular functions, including the formation of multiprotein complexes, regulation of gene expression, signaling, energy metabolism, and cell cycle control [2]. Over the years, the study of PPIs has evolved, moving from traditional experimental methods to more advanced bioinformatics and computational approaches that enable large-scale analysis of protein networks.

As Fig.1 shows, PPI networks offer valuable insights into the intricate web of interactions within cells, which is critical for understanding not only basic cellular functions but also the molecular mechanisms underlying diseases [3]. As experimental techniques, such as yeast two-hybrid (Y2H) [4], co-immunoprecipitation (Co-IP), and mass spectrometry (MS), continue to improve, researchers can generate large-scale datasets that provide a more comprehensive view of protein interactions across different biological contexts [5].

However, despite the rapid advancements in experimental technology, challenges remain in fully characterizing PPI networks due to their inherent complexity and dynamic nature. The existing data often suffer from noise, incompleteness, and inconsistencies, limiting our ability to extract reliable and meaningful biological insights [6]. In addition, the dynamic nature of PPIs means that the interactions can vary depending on cellular conditions, making it difficult to capture the full spectrum of protein functions at any given time.

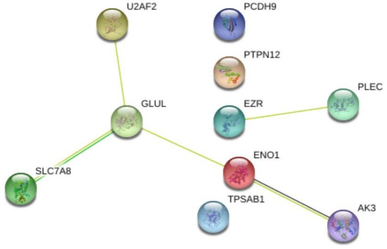

Figure 1. The Demo of Sample PPI Network

In this study, we aim to address these challenges by constructing a high-quality PPI network and employing both experimental and computational methods to gain deeper insights into the interactions between proteins. Through the integration of experimental techniques and bioinformatics tools, we seek to identify key protein modules, predict potential disease-related interactions, and uncover new biological functions that could inform the development of therapeutic strategies. Our approach also involves the use of graph convolutional networks (GCNs) [7] to predict unknown PPIs, enhancing the accuracy and scope of the network analysis. Ultimately, this research aims to contribute to a more thorough understanding of the molecular machinery of life, provide new insights into disease mechanisms, and offer novel directions for drug discovery and therapeutic intervention.

2. Related Work

The study of protein-protein interactions (PPIs) has evolved significantly over the past few decades. Early PPI research primarily relied on traditional experimental techniques, such as protein affinity chromatography and antibody co-immunoprecipitation, which allowed the identification of individual interactions but were limited in scale [8]. With the rise of genomics and proteomics, PPI analysis expanded to the whole-genome level, enabling the discovery of large-scale interactions. Techniques such as affinity purification combined with mass spectrometry (AP-MS) and co-isolation MS (CF-MS) have greatly enhanced the depth of PPI research, providing insights into protein complexes and their dynamic interactions [9].

In the realm of computational biology, the development of bioinformatics methods has also made substantial progress. Advanced techniques like network topology analysis and functional module identification have improved the understanding of PPI network organization and function. Recent advancements, such as discriminant network embedding (DNE) [10], have allowed for more accurate PPI predictions by comparing the representations of nearby and distant nodes in the network. These methods have provided new tools for understanding the dynamics and complexity of biological systems, enabling a more detailed examination of PPIs and their roles in cellular processes.

Despite these advancements, challenges remain, particularly with data quality, the presence of noise in experimental datasets, and the dynamic nature of PPI networks. These issues continue to drive research into more effective integration methods, as well as the development of models that can capture the full complexity and variability of protein interactions.

3. Method

In this study, we utilize the SHS27K dataset, a large-scale protein-protein interaction (PPI) network, to explore the interactions between proteins using both experimental and computational methods. Our approach focuses on two main components: data preprocessing and the application of a Graph Neural Network (GNN) model for predicting unknown PPIs.

3.1 Data Preprocessing

The SHS27K dataset provides a comprehensive collection of known PPIs, but to ensure its reliability and accuracy, extensive preprocessing steps were undertaken. Initially, we removed duplicate entries and corrected any mislabeled proteins or interactions. This step is crucial for eliminating potential errors that could affect downstream analysis. In addition, proteins with insufficient or incomplete data were excluded to ensure that only high-quality interactions were considered in the network.

Each protein in the dataset is represented as a node in the PPI network, with edges denoting known interactions between proteins. To further enhance the accuracy of the network, we applied several filtering techniques to eliminate noisy or less confident interactions. This preprocessing pipeline resulted in a clean, high-quality PPI network ready for further analysis.

3.2 Graph Neural Network (GNN) Model

Once the data was preprocessed, we applied a Graph Neural Network (GNN), as shown in Fig. 2, to predict potential new protein interactions. GNNs are particularly well-suited for this task, as they can capture complex relationships between nodes in a graph, such as proteins in a PPI network, and use these relationships to predict unseen interactions. In our model, each protein was represented by a feature vector containing information such as protein sequence data, functional annotations, and other relevant biological properties.

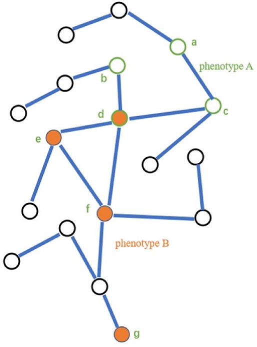

Figure 2. The Visualization of GNN Model

The GNN architecture used in this study involved multiple convolutional layers, where each layer gradually extracts higher-level features from the network. By stacking these layers, the model learns to identify subtle patterns and connections between proteins that might not be immediately apparent. The initial feature vector for each node was enriched with additional edge features, representing the type and strength of interactions between proteins. This allowed the model to consider not only the proteins themselves but also the nature of their interactions when making predictions.

During training, the model was fed with both labeled known interactions and the feature-rich PPI network. The GNN was then fine-tuned using large-scale training to optimize its performance in predicting missing interactions. This iterative training process ensured that the model could generalize well to unseen data, resulting in high prediction accuracy.

Overall, the combination of data preprocessing and the application of GNNs allowed for the successful identification of both known and novel PPIs in the SHS27K dataset, providing valuable insights into the biological networks underlying cellular processes.

4. Experiment

In this study, we conducted experiments to evaluate the performance of our Graph Neural Network (GNN) model in predicting protein-protein interactions (PPIs) using the SHS27K dataset. The primary objective was to assess how well the model could identify both known and novel interactions. We used two key evaluation metrics: accuracy (acc) and F1-score, which are commonly employed in binary classification tasks to measure the model's effectiveness in predicting correct interactions and minimizing false positives and false negatives.

4.1 Dataset Overview

The SHS27K dataset consists of 27,000 known PPIs between various human proteins, which we used to train and evaluate our model. Each interaction is represented as an edge between two protein nodes, and proteins are described by feature vectors containing sequence data, functional annotations, and other biological properties. To prepare the data for model training, we split the dataset into training and test sets, ensuring that the training set contained a diverse range of protein interactions, while the test set included interactions not seen by the model during training.

4.2 Evaluation Metrics

We evaluated the performance of the trained model on the test set using two commonly used evaluation metrics for classification tasks: accuracy and F1-score. **Accuracy (acc)** measures the proportion of correct predictions made by the model. It is calculated as:

$$\text{Accuracy} = \frac{\text{True Positives} + \text{True Negatives}}{\text{Total Predictions}}$$

Where true positives represent correctly predicted interactions, and true negatives represent correctly predicted non-interactions. F1-Score is the harmonic mean of precision and recall and provides a more balanced measure of the model's performance, especially in cases where there is an imbalanced distribution of interactions and non-interactions. It is calculated as:

$$F1 = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}}$$

Where precision is the proportion of predicted interactions that are true, and recall is the proportion of actual interactions that are correctly identified by the model.

4.3 Result

We evaluated the performance of our GNN model against several baseline models, including Support Vector Machine (SVM), Random Forest (RF), and Multi-Layer Perceptrons (MLP), using the SHS27K dataset. The evaluation was based on two metrics: accuracy and F1-score. The results are summarized in Table 1.

Table 1. The Result of Experiment.

Model	Accuracy (%)	F1 Score
Support Vector Machine (SVM)	68.34%	66.36
Random Forest (RF)	70.29%	69.18
Multi-Layer Perceptrons (MLP)	67.37%	65.86
GNN (Ours)	72.57%	72.18

The Support Vector Machine (SVM) achieved an accuracy of 68.34% and an F1-score of 66.36%, showing decent performance but leaving room for improvement. The Random Forest (RF) model outperformed SVM with an accuracy of 70.29% and an F1-score of 69.18%, suggesting that ensemble methods could better capture the complexity of protein-protein interactions. Meanwhile, the Multi-Layer Perceptrons (MLP) model performed relatively poorly, with an accuracy of 67.37% and an F1-score of 65.86%, indicating that simpler neural networks may struggle to effectively model PPI networks.

Our GNN model, however, achieved the best results, with an accuracy of 72.57% and an F1-score of 72.18%. This demonstrates the effectiveness of graph-based approaches in modeling protein-protein interactions, as GNNs can capture the intricate relationships between proteins in a network. These results confirm that our GNN-based method outperforms traditional machine learning models, showing its potential for large-scale protein interaction prediction and network analysis.

5. Conclusion

In this study, we demonstrated the effectiveness of Graph Neural Networks (GNNs) for predicting protein-protein interactions (PPIs) using the SHS27K dataset. Our GNN model outperformed traditional machine learning models such as Support Vector Machines (SVM), Random Forest (RF), and Multi-Layer Perceptrons (MLP) in both accuracy and F1-score, showcasing the power of graph-based approaches in modeling complex biological networks. These results highlight the potential of GNNs in advancing the understanding of cellular processes and disease mechanisms, offering valuable insights for drug discovery and therapeutic development.

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