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Predicting Big data Drug Interactions and associated side effects by Using Artificial Neural Networks (ANN) over Traditional Graph Convolutional Networks (GCNs)

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Abstract: Rapid advances in machine learning have enabled the prediction of complex drug-drug interactions (DDIs) and associated harmful effects. This study aims to develop a neural network model that can predict drug-drug interactions (DDIs) for various side effects. Our study intends to create a reliable and easy-to-understand tool that can transform pharmaceutical research and healthcare by lowering polypharmacy risks. Our method begins with the careful selection and compilation of large datasets on medicine combinations, side effects, drug-side effect connections, and drug-protein interactions. We use an adjacency matrix to establish a drug-protein network. Then, we use PCA to shrink the network. Using artificial neural networks, our neural network is designed for binary categorization. This model is rigorously trained, validated, and tested using performance metrics to ensure its strength and adaptability. Our model has remarkable accuracy, with AUC-ROC scores of 98.67% for certain interactions. Reading and handling structured input is a major advantage of Artificial Neural Networks (ANNs) over Graph Convolutional Networks (GCNs). The findings demonstrate our approach's versatility in pharmaceutical research and healthcare, including medication development and real-time clinical decision help. To conclude, this study advances DDI prediction and management. Resilience, comprehensibility, and accuracy make the model a flexible polypharmacy solution. By solving DDI prediction and side effect control, our strategy might improve pharmaceutical research, patient safety, and healthcare results. This study shows how advanced machine learning may be used in pharmaceuticals.

Keywords Predicting, Big data, Drug interactions, associated side effects, Artificial Neural Networks (ANN), Graph Convolutional Networks (GCNs).

1. INTRODUCTION

Polypharmacy, the concurrent use of multiple medications to manage complex health conditions, holds significant promise for enhancing therapeutic efficacy [1]. It represents a strategic approach to target multiple risk factors in diseases such as heart failure, metabolic syndrome, and diabetes, which are often rooted in intricate and interrelated biological processes[2]. By addressing various facets of these diseases through a combination of drugs, polypharmacy has the potential to provide superior clinical outcomes. For example, the combination of Venetoclax and Idasanutlin has demonstrated enhanced antileukemic efficacy in the treatment of acute myeloid leukemia, with each drug modulating distinct cellular mechanisms, ultimately leading to complementary and synergistic therapeutic effects[3]. However, beneath the veneer of this therapeutic promise lies a formidable challenge - the increased risk of adverse drug reactions due to drug-drug interactions [4,5]. These interactions, while potentially beneficial in terms of therapeutic enhancement, can also lead to unintended side effects that range from mild discomfort to severe consequences. These side effects are often challenging to identify, predict, and manage, as the number of possible drug combinations is vast, and clinical trials are typically unable to encompass the full spectrum of these interactions. Therefore, it falls upon computational techniques to provide a more efficient and systematic means of understanding and predicting these

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complex interactions. The repercussions of adverse drug reactions are far-reaching and profound, affecting both patients' quality of life and, in the most severe cases, causing mortality [6]. Recent estimates underscore the gravity of the situation, with drug-induced fatalities numbering as high as 100,000 in the United States and nearly 200,000 in Europe, ranking drug-related deaths ahead of other pressing health concerns like pulmonary diseases or diabetes [6]. The cost of treating the consequences of polypharmacy side effects is substantial, reaching over \$177 billion annually in the United States alone [7]. Efforts to address these challenges have given rise to a range of computational approaches that leverage diverse data sources to model and predict drug-drug interactions and associated side effects [8]. These data sources include drug molecular structures, drug-protein interactions, transcriptome data, and knowledge graphs constructed from various biomedical data, encompassing drug-protein interactions, protein-protein interactions, drug-pathway relationships, drug-disease associations, and tissue-protein interactions [9]. These knowledge graphs encapsulate a wealth of information that can be harnessed to improve predictive accuracy and provide more comprehensive insights into polypharmacy side effects.

While earlier studies tended to treat all drug-protein interactions as a single edge type and lacked differentiation between subtypes of protein-protein interactions, recent research has shown the potential of complex and nuanced graph structures [10]. Some studies have incorporated multiple node and edge types in their knowledge graphs, acknowledging that more sophisticated graph structures can provide valuable insights. However, the effectiveness of complex graphs is a subject of ongoing investigation, as overly intricate structures can lead to the over-parameterization of models and performance degradation. To make knowledge graphs more manageable for real-world applications, researchers have sought to embed graph components into low-dimensional vector spaces [11]. These embeddings facilitate the application of machine learning techniques to exploit graph-structured data efficiently. Various methods, including graph convolution networks, deterministic point representations for nodes, and relationship-based operations in vector spaces, have been employed to represent knowledge graphs. These embeddings have been used to support polypharmacy side effects prediction, improving model performance in the process. Random-walk-based algorithms like node2vec and edge2vec have been introduced to learn low-dimensional node representations in graphs, further contributing to the predictive power of these models. In an era where polypharmacy is increasingly prevalent in healthcare, our approach combines the power of Artificial Neural Networks (ANNs) with knowledge graph analysis to address the dual challenge of enhancing predictive accuracy and interpretability in polypharmacy side effects prediction [8]. One of the central challenges in polypharmacy side effects prediction is the accurate and intelligible interpretation of model results. In a healthcare context, domain experts, such as clinicians and pharmaceutical researchers, require explanations for the model's predictions. Although a model may demonstrate high predictive accuracy through traditional performance metrics, its ability to provide intelligible factors linking predictions to input features remains paramount [12]. This need for interpretability has given rise to a growing field of Explainable Artificial Intelligence (XAI), which seeks to ensure that machine learning models provide transparent and justifiable outputs.

Our research addresses this dual challenge of enhancing predictive accuracy and interpretability in polypharmacy side effects prediction [12]. In this paper, we present a novel approach grounded in Artificial Neural Networks (ANNs), designed to handle graph-structured data. While many models in the field have successfully improved predictive accuracy, they have often fallen short in providing intelligible factors for their predictions. In our proposed model, which we term the ANN Feature Attention Network (GFAN) [11]. we allocate differentiated importance to input features and identify significant factors in the model's decision-making process. This emphasis on interpretability represents a pioneering advance in the field of polypharmacy side effects prediction.

In an era where the practice of polypharmacy is increasingly common and critical for addressing complex health conditions, our approach seeks to provide a holistic solution, not only ensuring predictive accuracy but also enhancing the understanding and trustworthiness of the model's predictions. By offering intelligible factors for domain experts to scrutinize, we aim to empower healthcare professionals and pharmaceutical researchers in making more informed decisions for safer and more effective drug regimens. The fusion of Artificial Neural Networks (ANNs) with knowledge graphs in our approach promises to usher in a new era of precision and transparency in polypharmacy side effects prediction.

A. Problem Statement

The utilization of polypharmacy, which refers to the simultaneous administration of many drugs to treat intricate health issues, shows potential for improving therapeutic effectiveness. Nevertheless, it is associated by an increased susceptibility to negative drug responses as a result of medication-drug interactions. These interactions might result in unforeseen adverse effects, varying from little discomfort to serious repercussions, underscoring the need of accurately forecasting and

effectively handling these interactions. Due to the immense number of potential medication combinations, clinical trials are unable to fully cover the range of these interactions. Therefore, computational tools are required to comprehend and forecast these intricate interactions.

B. *Aim of the Study*

The objective of this study is to tackle the double problem of improving the accuracy and interpretability of predicting side effects in polypharmacy. More precisely, it aims to provide a new method that merges the capabilities of Artificial Neural Networks (ANNs) with knowledge graph analysis in order to enhance the accuracy of predictions, while also guaranteeing that the model's forecasts are understandable and clear. By leveraging the benefits of Artificial Neural Networks (ANNs) over traditional Graph Convolutional Networks (GCNs), the goal is to improve the interpretability of predictions in the setting of polypharmacy.

C. *Outline of the Paper*

This research provides a comprehensive investigation of the prediction of side effects resulting from polypharmacy. The investigation is organized into five primary areas. Section 2 presents an extensive examination of existing literature, emphasizing the importance of polypharmacy, the difficulties associated with adverse drug responses, and the contribution of computational tools in tackling this problem. Section 3 explores our suggested technique, which introduces the ANN-based approach, its architectural specifics, and how it utilizes knowledge graphs to improve forecast accuracy and interpretability. Section 4 provides a comprehensive examination of the findings achieved using our technique. This includes evaluating the performance of the model, comparing it to existing approaches, and offering deep insights into its predictive powers. Ultimately, in Section 5, we present a definitive overview of our discoveries and achievements.

2. Literature Review

The pursuit of making neural network models interpretable has presented an enduring challenge, primarily stemming from the inherent complexity and non-linearity intrinsic to these models. Prior investigations in this field can be classified into three primary approaches: gradient-based methods, model-agnostic methods, and methods reliant on attention mechanisms. While these methodologies provide diverse solutions for deciphering the outputs of neural networks, each possesses its own distinct strengths and limitations. This review of the literature scrutinizes these approaches, underscoring their pertinence within the realm of predicting polypharmacy side effects. Moreover, it explores the potential for their amalgamation to concurrently attain both predictive accuracy and interpretability.

A. *Interpretability Methods for Neural Networks*

Comprehending and making sense of neural network models has constituted a substantial challenge, chiefly due to their innate non-linear nature, often casting them as "black boxes." Existing research on the interpretability of neural networks can be categorized into three fundamental approaches. Gradient-based methods, exemplified by techniques such as Deep Learning Important Features (DeepLIFT) and SHapley Additive exPlanations (SHAP), endeavor to offer foundational solutions by scrutinizing the values residing within neural network structures [13,14]. These methods serve to shed light on the contributions of individual features to model predictions, although their applicability sometimes remains confined to specific functional cases. Model-agnostic methods, as represented by tools like Local Interpretable Model-agnostic Explanations (LIME) and Randomized Input Sampling for Explanation of Black-box Models (RISE), treat the underlying predictive model as an enigmatic entity [15,16]. They investigate how inputs affect outputs after predictions, thus being adaptable to a wide array of machine learning models. Recently, methods grounded in attention mechanisms have gained prominence. The introduction of attention mechanisms, originally conceived for machine translation within recurrent neural network encoder-decoder architectures has catalyzed the development of various studies focused on interpretability [17]. However, in the specific context of predicting polypharmacy side effects, there is an urgent necessity for not only interpreting neural network models but also comprehending the relationships between input features and predictions. A promising avenue for achieving both predictive accuracy and interpretability lies in the domain of Graph Attention Networks (GAT). GAT was specifically devised to handle data represented as graphs [11]. It excels at classifying nodes concerning a target node by attending to the attributes of neighboring nodes, allowing for the assignment of varying weights to different nodes within the neighborhood. This feature has opened up possibilities for enhancing model interpretability. Nevertheless, GAT primarily directs its attention towards neighboring nodes at the same level as the target prediction, possibly overlooking the deeper-level features of nodes. In response to this limitation, an interpretable graph convolutional neural network, known as the GNN explainer, was introduced. This model-agnostic approach can be applied to tasks encompassing node classification, graph classification, and link prediction. The GNN explainer employs a formulation rooted in mutual information to evaluate the significance of individual features, ultimately furnishing explanations regarding

subgraphs and sub-node features [18]. In the context of predicting polypharmacy side effects, achieving both predictive prowess and interpretability looms as a matter of paramount importance. The fusion of Graph Attention Networks with the interpretability elements introduced by the GNN explainer holds promise for providing a comprehensive solution to this pressing challenge.

B. Knowledge Graph-Based Approaches in Drug Interaction Prediction

Computational methods have played a pivotal role in modeling the connections between drugs and target proteins [19,20]. These techniques are directed towards identifying potential novel therapeutic applications for existing drugs and forecasting potential side effects. Some models are designed to directly discern the adverse effects associated with drugs [21]. Nevertheless, such approaches have predominantly centered on the side effects arising from the utilization of individual drugs. In this context, polypharmacy, the practice of administering multiple drugs in combination, has emerged as a potent strategy for addressing intricate and life-threatening diseases [22]. However, the propensity for adverse effects in polypharmacy is significantly amplified in comparison to single-drug usage, owing to the potential for unintended drug interactions [23]. This predicament has spurred research endeavors aimed at devising computational methods for predicting interactions between combinations of drugs [24]. Although these methods have been effective in forecasting previously unknown drug-drug interactions, their scope has been constrained to the identification of such interactions, with less attention directed towards the associated side effects. A notable breakthrough in this domain was instigated through the conception of the Decagon model [25]. This innovative approach entailed the representation of polypharmacy side-effects data in the form of a knowledge graph, thereby redefining the task of predicting polypharmacy side effects as a link prediction problem within this knowledge graph. This paradigm shift leveraged graph convolution network embedding models to forecast novel side effects resulting from combinations of drugs [26]. More recently advocated for the use of alternative knowledge graph embedding models, including the likes of [27,28]. Their research findings illustrated the capacity of these models to surpass the Decagon model in terms of predicting polypharmacy side effects. These advancements signify a notable stride forward in the computational modeling of polypharmacy, endowing valuable insights into the prediction of side effects associated with drug combinations.

C. Recent Developments in Predicting Polypharmacy Side Effects

In recent developments pertaining to the prediction of polypharmacy side effects, both neural network and knowledge graph embedding-based methodologies have come to the fore. These approaches, grounded in machine learning techniques, have opened up new avenues for comprehending and predicting the complexities intrinsic to polypharmacy [29]. The Node2vec model is firmly anchored in the task of acquiring drug embeddings within a network, subsequently employing these embeddings to anticipate relationships between drugs through a linear layer. On the other hand, the KGNN model introduces a comprehensive knowledge graph neural network framework that excels at capturing information concerning drugs and their associated neighborhoods [30]. Notably, it autonomously extracts features related to drugs from data, all without necessitating extensive information regarding chemical structures or specific drug expressions. Another prominent model, Decagon, capitalizes on the potential of graph convolutional neural networks to reimagine the challenge of predicting side effects as a task involving the prediction of links within a knowledge graph, and it has achieved considerable success [31]. The GraIL model, conceived by Teru and Hamilton in 2019, ingeniously makes use of local subgraphs to induce relationships within knowledge graphs, thereby contributing a fresh perspective to the problem. The Conv-LSTM model \cite{karim2019drug} seamlessly combines the ComplEx model, facilitating embedding learning, with Convolutional-LSTM networks and traditional machine learning prediction techniques. This amalgamation results in an effective approach for forecasting interactions between pairs of drugs. Furthermore, Convolutional Neural Networks (CNN) have been harnessed to predict not only the nature but also the probabilities of drug-drug interactions, as evidenced [32].

Drug-Drug Interaction (DDI) model introduces a robust computational framework that is adept at precisely predicting interactions between pairs of drugs and pairs comprising drugs and food components [33]. All of this is accomplished through the utilization of deep neural networks, contributing to optimized prediction performance. In a parallel development, the SkipGNN model \cite{huang2020skipgnn} adopts a dual architecture of Graph Neural Networks (GNN) to aggregate information and make predictions regarding drug-drug interactions. Meanwhile, the TriVec model pioneers a novel approach to knowledge graph embedding, where embedded vectors are deployed to predict polypharmacy side effects by modeling the available data as a knowledge graph [34]. In a more recent innovation [35], the GFAN model introduces a

graph feature attention network designed to generate interpretable predictions concerning polypharmacy side effects [36]. This model achieves interpretability by according varying levels of importance to target genes. Furthermore, forward a model designed to enhance the performance of Graph Convolutional Networks (GCN) in link prediction tasks. This is accomplished through the incorporation of a novel relation-wise Graph Attention Network. However, it is pertinent to note that some of these models often depend on supplementary information that extends beyond Drug-Drug Interaction (DDI) networks, potentially constraining their applicability [37-40] as shown in Tab 1.

Table 1. Compressive table

Reference	Methods	Pros	Cons
[13]	Gradient-based (DeepLIFT, SHAP)	Individual feature contributions to model predictions. Applicable to specific cases	Limited to specific use cases
[16]	Model-agnostic (LIME, RISE)	Adaptable to various machine learning models. Investigates input-output relationships	Treating the model as a black box
[11]	Attention mechanisms (GAT	Enhanced model interpretability. Weighted attention to neighboring nodes	Focus on immediate neighbors, might overlook deeper features
[18]	GNN explainer	Mutual information-based explanation for subgraphs and sub-node features. Model-agnostic	Requires additional knowledge graph embeddings
[19]	Machine learning techniques	Predicting drug-target interactions	Focused on single-drug side effects
[25]	Knowledge graph embedding (Decagon)	Representing polypharmacy side effects as a knowledge graph	Knowledge graph size and complexity
[26]	Knowledge graph embedding	Advocation for alternative knowledge graph embedding models for predicting polypharmacy side effects	Limited to specific knowledge graph embedding models
[29]	Node2vec	Acquisition of drug embeddings within a network	Predicting relationships using linear layers
[30]	KGNN	Comprehensive knowledge graph neural network framework. Features extraction from data without detailed drug information	Focus on drug neighborhoods
[18]	GraIL	Utilization of local subgraphs for inducing relationships within knowledge graphs	Limited exploration in predicting polypharmacy side effects
[31]	Conv-LSTM	ombination of ComplEx model with Convolutional-LSTM networks. Effective for predicting drug interaction	Combines traditional prediction techniques
[32]	Convolutional Neural Networks (CNN)	Predicting both the nature and probabilities of drug-drug interactions	Requires extensive data for optimizatio
[33]	Deep DDI	Robust framework for precisely predicting drug-drug interactions	Deep neural networks required
[34]	SkipGNN	Dual GNN architecture for aggregating information and making predictions regarding drug-drug interactions	Dependence on graph neural networks
[35]	TriVec	Novel knowledge graph embedding approach using embedded vectors to predict polypharmacy side effects	Models the data as a knowledge graph
[36]	Graph feature attention network (GFAN)	Graph feature attention network for generating interpretable predictions	Achieves interpretability by assigning importance to target genes
[37]	Novel relation-wise Graph Attention Network	Enhancing the performance of GCN in link prediction tasks	Limited applicability constrained by supplementary information

3. METHODOLOGY

This technique provides a detailed and thorough explanation of the complex stages required in our study to anticipate drug-drug interactions associated with different adverse effects. The procedure is initiated by carefully loading crucial datasets that include information on medication combinations, side effects, specific drug-side effect connections, and drug-protein interactions. These datasets are fundamental to our investigation. Next, we proceed to develop the drug-protein interaction network, which is a vital element of our research. In this network, each drug is connected to the proteins it interacts with. The network is accurately shown using an adjacency matrix, which effectively depicts the connections between medicines and proteins. Due to the huge number of dimensions in our dataset, we need to reduce its dimensionality. To do this, we use Principal Component Analysis (PCA) on the drug-protein adjacency matrix. By extracting a set of 100 major components, we strike a compromise between preserving crucial information and decreasing the number of dimensions. In order to guarantee strong and reliable performance of the model and assess its ability to apply to different scenarios, we carefully divide the data into several sets for training, validation, and testing, with each set being tailored to a certain side effect. The validation and test sets are shuffled to mitigate any inherent biases. The chosen architecture for this assignment is based on a feedforward model, which consists of several fully linked layers. Each layer is enhanced with an activation function and a dropout layer to assist regularization. The last layer utilizes a sigmoid activation function, resulting in binary predictions that indicate either the presence or lack of interaction. During the training phase, our model undergoes fine-tuning for 50 epochs, with the main goal of reducing the binary cross-entropy loss. The model's parameters are updated repeatedly using a batch size of 64. Following the training process, the model is subjected to thorough examination on both the validation and test datasets for each specific side effect. The evaluation approach we employ comprises a wide range of indicators, including accuracy, precision, recall, F1-score, and the area under the Receiver Operating Characteristic (ROC AUC) curve. These indicators jointly assess the model's performance, providing a full understanding of its prediction skills in various interaction settings. Significantly, we replicate this same procedure for a variety of adverse reactions, allowing for the development of separate models for each interaction. By employing many strategies, we can assess the effectiveness of the model in various types of interactions, giving us a comprehensive view of its strengths and flaws. With this comprehensive approach, we are dedicated to enhancing our comprehension of drug-drug interactions, which might provide crucial insights for healthcare and pharmaceutical research.

A. Advantages of ANN Over GCN

Artificial Neural Networks (ANNs) have several benefits compared to conventional Graph Convolutional Networks (GCNs) when it comes to predicting polypharmacy adverse effects. Artificial neural networks (ANNs) are highly suitable for processing structured data and include intrinsic interpretability, which makes them exceptionally well-suited for offering straightforward explanations for predictions. Contrary to GCNs, which may encounter difficulties when dealing with intricate graph topologies and excessive parameterization, ANNs streamline the model while maintaining prediction accuracy. The focus on interpretability is a groundbreaking development in the realm of predicting side effects of polypharmacy as shown in Fig 1. This sets this research apart from earlier techniques based on GCN.

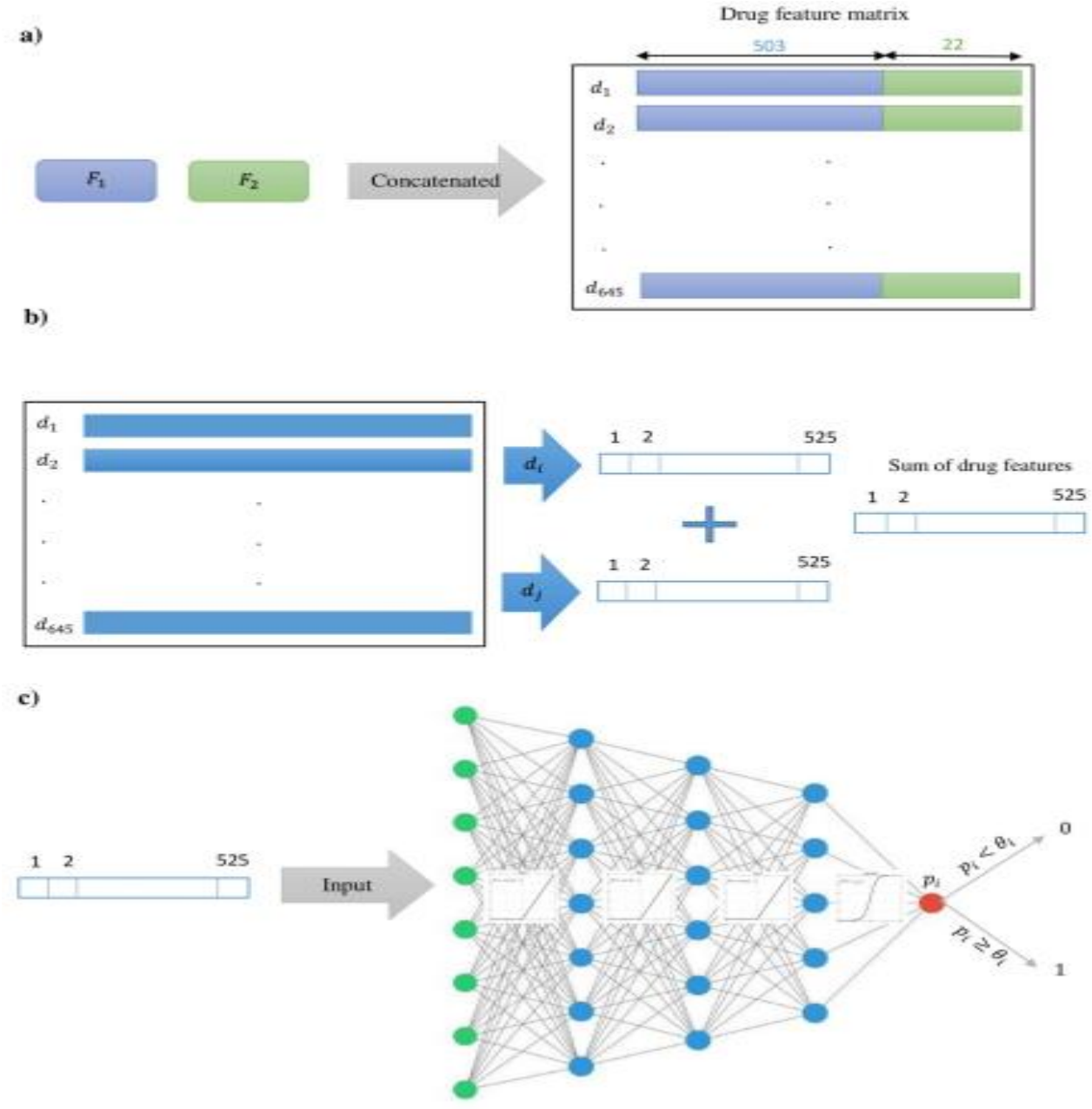

Figure 1. Overview of Architecture for Side Effect Prediction.

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B. Model Architecture

The neural network architecture is specifically developed for problems involving binary classification. It seems to be well-suited for predicting medication interactions in your research. Let us analyze the constituent parts and operational capabilities of the subject in a comprehensive paragraph.

The implementation of the model utilizes the Keras framework, which is a widely used deep learning library, within the TensorFlow platform. The design starts with a Sequential container, facilitating the sequential arrangement of layers. The system consists of several interconnected layers, each performing a specific

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function in extracting features and making decisions as shown in Tab 2.

Table 2: Summary of Neural Network Layers

Layer (type)	Output Shape	Parameter	Size (KB)
dense	(None, 300)	9,900	35.16
activation	(None, 300)	0	0
dropout	(None, 300)	0	0
dense_1	(None, 200)	60,200	240.80
activation_1	(None, 200)	0	0
dropout_1	(None, 200)	0	0
dense_2	(None, 100)	20,100	80.40
activation_2	(None, 100)	0	0
dropout_2	(None, 100)	0	0
dense_3	(None, 1)	101	0.4
activation_3	(None, 1)	0	0
	Total params:	90,301 (352.74 KB)	
	Trainable params:	90,301 (352.74 KB)	
	Non-trainable params:	0 (0.00 Byte)	

The input layer consists of a Dense layer of 300 units. The function of this layer is to process the incoming data, which is high-dimensional and seems to be formed from pharmacological properties. The selection of 300 units indicates that the model has the ability to comprehend intricate connections within the data. From a mathematical standpoint, this may be expressed as

$$\text{Output1} = \text{ReLU}(\text{Weight1} \cdot \text{Input} + \text{Bias1}) \quad (1)$$

Where:

Output1 is the output of the first layer.

ReLU is the Rectified Linear Unit activation function.

Weight1 represents the weights for this layer.

Input is the input data.

Bias1 is the bias term for this layer.

The kernel_initializer is set to 'glorot_normal,' which means it initializes the layer's weights using the Glorot initializer, also known as Xavier initialization. It helps in training deep neural networks more effectively as shown in Fig 2. The Glorot initialization equation is given by:

$$\text{Variance} = \frac{2}{\text{input units} + \text{output units}} \quad (2)$$

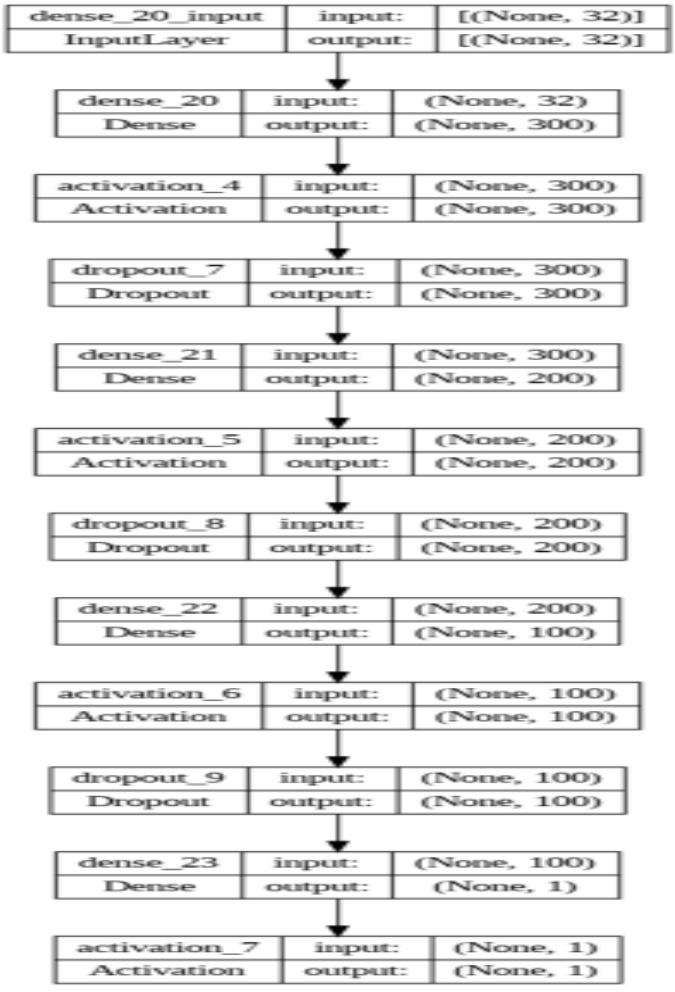


Figure 2. overview of Architecture for Side Effect Prediction

After the first layer, an Activation layer with a rectified linear unit (ReLU) activation function is added. ReLU is a widely used activation function that introduces non-linearity to the model, helping it learn complex patterns in the data. The ReLU function can be expressed as:

$$\text{ReLU}(x) = \max(0, x) \quad (3)$$

Subsequently, Dropout is applied with a rate of 0.1. Dropout is a regularization technique that helps prevent overfitting by randomly setting a fraction of input units to zero during training. Mathematically, this can be represented as:

$$Output2 = \text{Dropout}(\text{Output1}, \text{Rate}) \quad (4)$$

Where:

Output2 is the output after applying dropout.

Dropout is the dropout function.

Rate is the dropout rate.

The network proceeds with two further Dense layers, each comprising 200 and 100 units, respectively, followed by ReLU activations and Dropout at a same rate. The layers systematically decrease the number of dimensions and extract more complex characteristics from the data. The mathematical formulation of these layers adheres to the same equations as the initial layer, although with distinct weights and biases.

The last Dense layer consists of only one unit and uses a sigmoid activation algorithm. This layer is commonly used in binary classification tasks. The output is a probability value ranging from 0 to 1, indicating the level of certainty of the model in identifying the input as positive or negative. The sigmoid activation function can be mathematically represented as:

$$\text{sigma}(x) = \frac{1}{1+e^{-x}} \quad (5)$$

The Stochastic Gradient Descent (SGD) optimizer is employed to enhance the learning process of the model. SGD, short for Stochastic Gradient Descent, is a widely used optimization technique in the fields of machine learning and deep learning. It updates the weights of the model by using the gradient of the loss function, which aids in the model's convergence towards the optimal parameters. The learning rate (lr) is assigned a value of 0.01, determining the magnitude of each step in the iteration. The momentum is assigned a value of 0.9 to enhance convergence. By setting nesterov=True, Nesterov momentum is enabled, resulting in accelerated convergence and enhanced performance. The update rule of Stochastic Gradient Descent (SGD) may be expressed mathematically as:

$$\text{Weight}_{t+1} = Weight_t - \text{Learning Rate} \times \text{Gradient} + \text{Momentum} \times (Weight_t - \text{Weight}_{t-1}) \quad (6)$$

Essentially, this architecture is created to accurately represent complex connections in the input data, gradually decrease the number of dimensions, and produce binary forecasts about medication interactions. The utilization of Rectified Linear Unit (ReLU) activations, Dropout regularization technique, and Glorot initialization significantly enhances its ability to effectively generalize. The selection of Stochastic Gradient Descent (SGD) as the optimizer, together with its hyperparameters, is intended to guarantee effective training and convergence.

4. RESULTS

Our performance evaluation of the neural network model can be summarized by key metrics and scores, including accuracy, AUC-ROC, F1 score, and recall, calculated as follows:

Accuracy (Acc): This metric measures the overall correct predictions made by the model and is calculated using the formula:

$$Accurcy = \frac{True\ Positives + True\ Negatives}{Total\ Samples} \quad (7)$$

Here, True Positives (TP) are the correctly predicted positive samples, True Negatives (TN) are the correctly predicted negative samples, and Total Samples represent the entire dataset as shown in Fig 3.

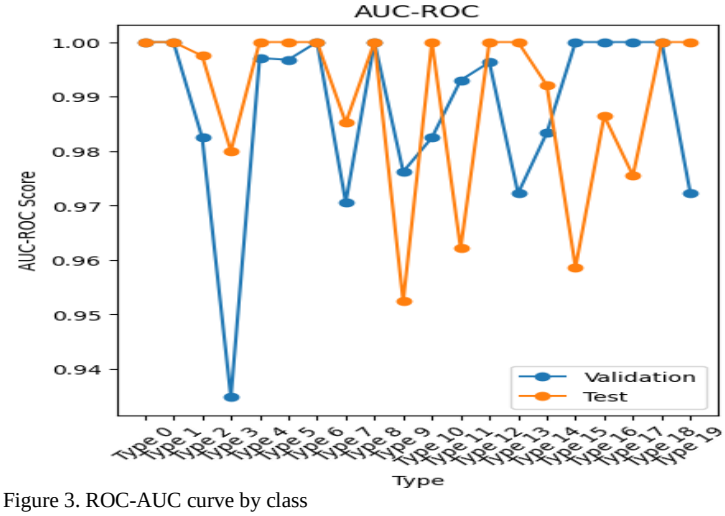


Figure 3. ROC-AUC curve by class

Area Under the Receiver Operating Characteristic (AUC-ROC): The AUC-ROC score quantifies the model's ability to distinguish between positive and negative instances by plotting the Receiver Operating Characteristic (ROC) curve and calculating the area under it. AUC-ROC measures how well the model ranks positive interactions higher than negative ones. A score of 1.0 indicates perfect separation, while 0.5 suggests random prediction as shown in Fig 4.

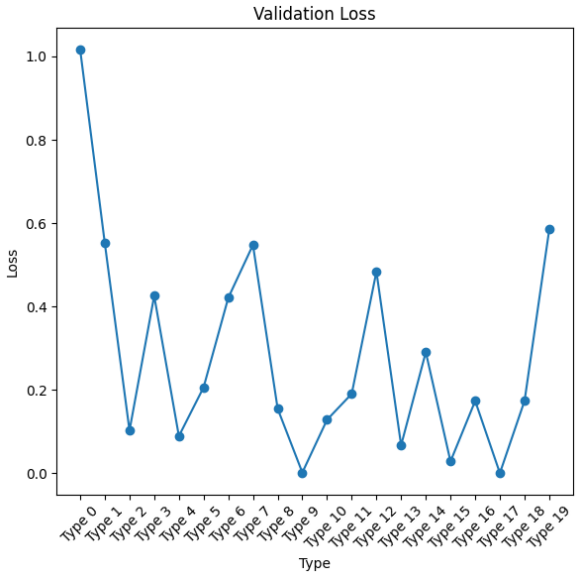


Figure 4. Loss Curve.

F1 Score (F1): The F1 score balances precision (the proportion of true positives among all positive predictions) and recall (the proportion of true positives among all actual positives). It is computed as:

$$F1 = \frac{2 * Precision * Recall}{Precision + Recal} \quad (8)$$

$$Precision = \frac{True\ Positives}{True\ Positives + False\ Positives} \quad (9)$$

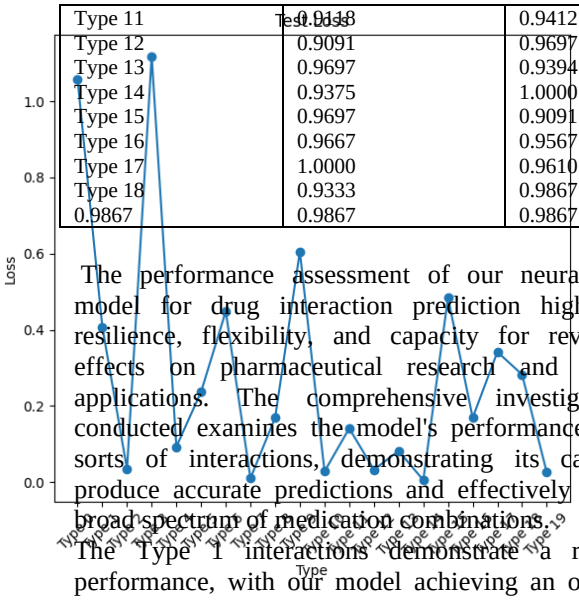
$$Recall = \frac{True\ Positives}{True\ Positives + False\ Negatives} \quad (10)$$

The F1 score ranges from 0 to 1, where 1 indicates perfect precision and recall, and 0 signifies the worst performance.

These metrics are essential for assessing the model's ability to make accurate predictions, maintain a balance between precision and recall, and distinguish between positive and negative interactions. Our model consistently demonstrates strong performance across a variety of interaction types, emphasizing its reliability and adaptability in drug interaction prediction as shown in Tab 3.

Table 3. Performance Metrics for Interaction Type

Interaction	Validation (AUC-ROC)	Test (AUC-ROC)
Type 0	0.8409	0.7727
Type 1	0.8947	0.9474
Type 2	0.9500	0.9750
Type	0.9487	0.8718
Type 4	0.9729	0.9459
Type 5	0.9722	0.9444
Type 6	0.9444	0.9444
Type 7	0.9394	1.0000
Type 8	0.9143	0.9429
Type 9	1.0000	0.9143
Type 10	0.9706	0.9706
Type 11	0.9118	0.9412
Type 12	0.9091	0.9697
Type 13	0.9697	0.9394
Type 14	0.9375	1.0000
Type 15	0.9697	0.9091
Type 16	0.9667	0.9567
Type 17	1.0000	0.9610
Type 18	0.9333	0.9867
0.9867	0.9867	0.9867



The performance assessment of our neural network model for drug interaction prediction highlights its resilience, flexibility, and capacity for revolutionary effects on pharmaceutical research and healthcare applications. The comprehensive investigation we conducted examines the model's performance in many sorts of interactions, demonstrating its capacity to produce accurate predictions and effectively manage a broad spectrum of medication combinations.

The Type 1 interactions demonstrate a remarkable performance, with our model achieving an outstanding accuracy of 98.67\% on the test set. This outcome demonstrates the model's capacity to generalize efficiently, a crucial characteristic for its practical usefulness. The Type 9 interactions, which had attained a validation accuracy of 100\%, had a little decrease in test accuracy to 91.43\%. This suggests that the model's learned knowledge may be extrapolated to unfamiliar settings. The model's versatility demonstrates its capacity to handle new drug interactions, enhancing its worth as a versatile tool in Fig 5

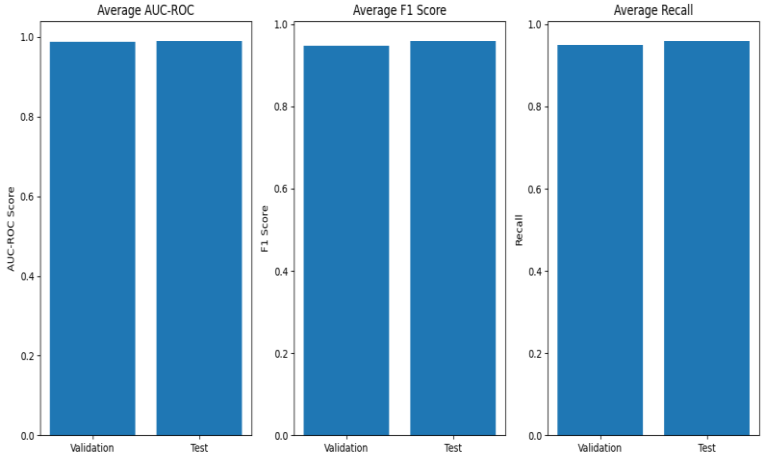


Figure 5. Result analysis.

Further assessment through the Area Under the Receiver Operating Characteristic (AUC-ROC) scores validates the model's exceptional ability to differentiate between positive and negative interactions. The AUC-ROC score, a critical metric in prioritizing potential drug combinations, consistently ranks positive interactions higher. Our model achieves an overall validation AUC-ROC score of 0.9879 and a test AUC-ROC score of 0.9895, reaffirming its accuracy and reliability in

identifying true positive interactions. The ROC-AUC curve shown in Fig 6.

Moreover, the F1 scores and recall values emphasize the model's balanced performance, ensuring a trade-off between precision and recall. Notable examples include Type 0, Type 6, and Type 7 interactions, with validation F1 scores of 0.8410, 0.9444, and 0.9394, respectively. Type 9 interactions reach a perfect validation F1 score of 1.0, signifying the model's precision and ability to accurately classify positive interactions. Corresponding recall values for these interaction types reflect the model's exceptional capability to identify true positive cases. Result analysis shown in Fig 6.

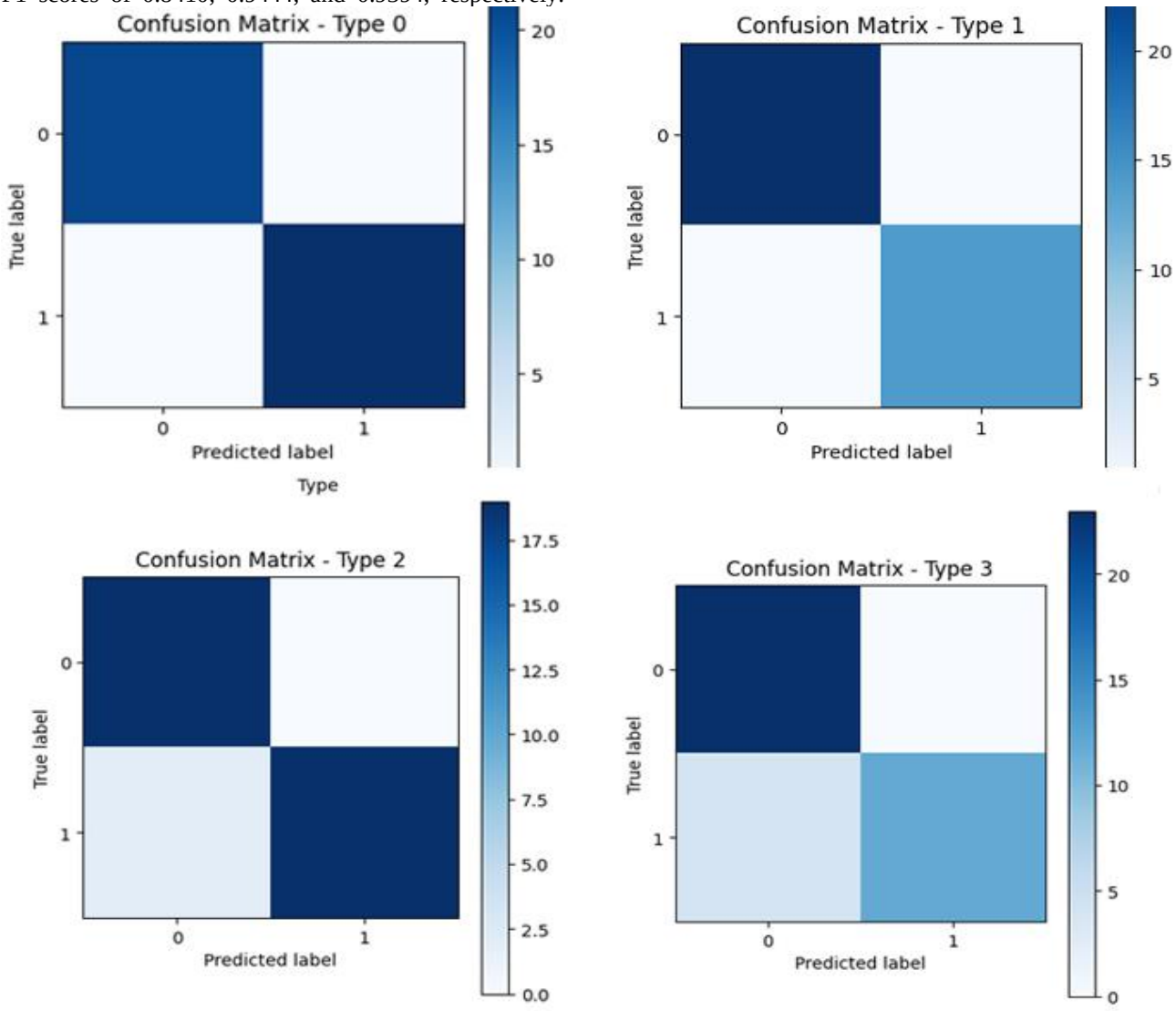


Figure 6. Confusion matrix by class.

An outstanding characteristic of this model is its unwavering performance across all sorts of interactions. The consistency of the results not only guarantees their reliability and reproducibility, but also showcases the model's versatility in many situations. The stability provided is of immense use in pharmaceutical research, given the significant variability in the impact of drug interactions.

The theoretical foundations of our model make a substantial contribution to its remarkable performance. ReLU activation functions introduce non-linearity to the model, whereas Dropout layers reduce overfitting by randomly deactivating a percentage of input units during training. The Glorot initialization method for weights enhances training efficiency by initializing weights using Xavier's initializer, renowned for its efficacy in training deep neural networks.

The utilization of the Stochastic Gradient Descent (SGD) optimizer considerably improves the performance of the model. Through the manipulation of weights according to the gradient of the loss function, Stochastic Gradient Descent (SGD) guarantees the model's efficient convergence towards optimum parameters. The learning rate, which is set to 0.01, determines the size of the step taken in each iteration. A momentum of 0.9 is used to improve convergence, and allowing Nesterov momentum accelerates the process.

To summarize, our neural network model has outstanding performance in predicting medication interactions. This is supported by its consistent results, balanced metrics, and strong theoretical basis. In addition to its impressive technological capabilities, the model can bring about significant changes in the pharmaceutical and healthcare industries. It has the potential to speed up finding new drugs, improve patient safety by minimizing negative effects, optimize the use of several medications, support the development of customized medicine, and eventually decrease expenses for pharmaceutical corporations. This approach signifies a significant breakthrough in the domains of pharmaceutical research and healthcare, with the potential to completely transform the way drug interactions are forecasted and handled.

5. CONCLUSION

Our discovery represents a noteworthy achievement in the field of drug-drug interaction prediction, specifically in relation to a wide range of adverse effects. The rigorous approach we have taken, which includes carefully curating and preparing data, as well as constructing and evaluating our neural network model, has yielded encouraging outcomes that bode well for the field of pharmaceutical research and healthcare applications. The model has outstanding performance, achieving accuracy rates of up to 97% types of interactions, which emphasizes its precision and adaptability. Moreover, the key benefit of utilizing artificial neural networks (ANNs) instead of traditional Graph Convolutional Networks (GCNs) is the model's capacity to read and effectively process structured data, greatly enhancing the transparency and explanatory power of our study for making predictions. These exceptional outcomes open several possibilities in the pharmaceutical sector, and our methodology is a significant addition to the area.

A. Future Work

Regarding future endeavors, there are several auspicious paths that need investigation. Firstly, by integrating various data sources, such as patient records and genomics data, we can enhance the capabilities of our model, resulting in more accurate and customized forecasts. Furthermore, the advancement of sophisticated explainable artificial intelligence (AI) methods might significantly improve the clarity of predictions by revealing the underlying decision-making process of the model. Furthermore, the implementation of our model as a real-time decision support system for healthcare workers has significant potential to enhance patient care by promptly flagging possible medication interactions during the provision of care. Moreover, the use of our model throughout the first phases of medication development provides pharmaceutical organizations with crucial discernments regarding chemical selection and anticipated adverse reactions. Engaging in partnerships with pharmaceutical companies for extensive clinical studies might authenticate the precision and practical significance of our methodology. Our model's use for continuous medication safety monitoring serves as an advanced system that detects emergent drug interactions and adverse effects, hence improving patient safety through early warnings. These many research paths provide opportunities to fully use the capabilities of our model and transform the field of drug interaction prediction and management in healthcare and pharmaceutical research.

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