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High-Order Multimodal Interaction Network for Efficient Prediction of Drug-Drug Interaction

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Abstract:

The pharmaceutical industry places a lot of focus on preventing drug-drug interactions (DDIs). Medication interaction detection has been the primary emphasis of machine learning-based DDI prediction methods. Since studies have shown that DDIs can cause different future occurrences, it is more beneficial to predict DDI connected events while examining the mechanism behind combination medicine consumption or adverse reactions. The areas of medication development and illness diagnostics are seeing increased usage of a developing approach that predicts DDIs-associated occurrences. We examine potential interactions between the two medications as well as the kinds of interactions that can occur in this research. Additionally, we provide a strategy that relies on learning and use High-Order Multimodal Interaction Network (HOMIN) to forecast DDIs by learning feature representations. The purpose of this work is to provide HOMIN-DDI, a new method for drug-drug interaction predictions that we have developed utilizing a HOMIN architecture. First, we develop feature vectors from medication categories, targets, paths, and digestive enzymes, and we use the Jaccard similarity to evaluate how similar drugs appear. After that, we build a new HOMIN using the feature representation to predict DDIs. The results of the experiments show that the drug categories feature type, when used to the HOMIN -DDI approach, is effective. Furthermore, compared to employing only one feature, combining numerous features yields more useful and informative results. Compared to other algorithms, HOMIN-DDI performs better when it comes to predicting DDIs..

Keywords: Multimodal Interaction Network, Drug-Drug Interaction, Prediction.

1. INTRODUCTION

Cancer, hypertension, asthma, and AIDS are just a few of the disorders that might benefit from combination medication therapy, which aim to do three things at once: improve therapeutic effectiveness, minimize drug toxicity, and reduce drug resistance [1]. An important cause of adverse drug events (ADEs) is the possibility of drug interactions, which can occur when medications are used together. An estimated 30% of all adverse drug events (ADEs) are related to DDIs [17]. Also, medications have been pulled off stores because of adverse drug events caused by important DDIs. Hence, for better and safer patient prescription[2] [3], accurate impact prediction of DDIs is crucial. Finding DDIs is possible using in vivo models by employing high-throughput screening methods. Unfortunately, these procedures can be rather expensive, making it impractical to evaluate several medication combinations. Numerous computational techniques have been suggested for limiting the selection of potential pharmaceutical combinations [25].

It is crucial to control drug security when a disease is treated with several treatments, especially with

the number of drug types growing at a rapid rate[4] [5]. Adverse drug responses, which can lead to injuries and enormous medical expenses, are common when several drugs are administered at the same time, and this is known as a drug-drug interaction (DDI). On the other hand, DDI may cause a variety of physiological responses [19]. For instance, the intensity of the side effects is increased when the drugs itraconazole and abemaciclib combine with each other. Consequently, it is crucial for doctors to be able to accurately forecast DDI episodes so that they may make informed decisions and set up successful treatment programs [7] [12].

The medical risks and synergistic advantages of medications can be maximized with proper administration of numerous drugs. There are a lot of AI-based models that have been suggested for DDI event prediction [20]. Some of these models use graph neural networks to analyze chemical structure similarity, semi-supervised learning to extract useful information from labeled and unlabeled drug data for DDI prediction, and knowledge graph summarization[6] [9] for multi-typed DDI pharmacological effect prediction. Additionally, there have been attempts to forecast DDI incidents by combining data from many sources, such as similarity characteristics to extract pharmacological properties for this purpose[8] [21]. Nevertheless, the majority of current approaches disregard the possibility of connections between DDI occurrences and other types of multimodal data, including targets and enzymes [14]. Additionally, multimodal data's cross-modal compatibility has been overlooked [11] [18].

The primary objectives of this study are to address these limitations and to effectively assist in the joint representation learning of multimodal data related to DDI events. Predicting DDI occurrences is the objective with the use of a High-Order Multimodal Interaction Network (HOMIN). At last, a HOMIN is developed for predicting DDI occurrences by investigating the complimentary aspects of the drug's multimodal representations.

2. RELATED WORKS

An innovative approach for predicting drug-drug interactions (DDIs) based on convolutional neural networks (CNN) was suggested by the author, who focused down on 65 distinct types of DDIs [10]. To begin, the input of CNN-DDI [22] was built using the extracted drug attributes of categories, targets, pathways, and enzymes. Next, they provided these attributes into our CNN network as input vectors, and the network's output was a categorization prediction for occurrences involving drug-drug interactions.

Regularized linear classification models based on LASSO and a LASSO-DNN model that employs LASSO feature selection were proposed by the author as a means to predict DTIs [13]. Repurposing medications for the treatment of breast cancer is proven using these strategies. They explored the prediction power and predicted DTIs using numerous LASSO models that included different combinations of feature sets. In addition, they implemented a LASSO-DNN model for DTI prediction, which is based on the features retrieved from the top-performing LASSO models.

A long short-term memory (LSTM) model for DDI prediction, the author proposed a graph convolutional autoencoder network (GCAN). The suggested framework outperformed other machine learning algorithms when it came to DDI prediction [23]. The most recent edition of the DrugBank database (5.1.7) confirmed several of our expected DDIs. They demonstrated in the case study that

both sulfonylurea-and metformin-interacting medications produced hypoglycemia and lactic acidosis, respectively, and that these interactions induced changes on the proteins implicated in the metabolic process in vivo.

In [15], author presented a deep neural network ensemble that could improve DDIs' prediction capabilities. Consequently, the model they created achieved an average accuracy of 93.80% when applied to a benchmark dataset, accurately predicting 86 different kinds of DDIs. When tested on the same dataset as previously suggested approaches, our ensemble classifier outperforms them [16]. When it comes to pharmacovigilance-assisted technologies that help find DDIs to back up medical judgments and medication development, this technique is among the most innovative.

The author proposed a method of drug-drug interaction prediction using a Deep Attention Neural Network (DANN-DDI) to anticipate unobserved drug-drug interactions. To start, we build a number of drug feature networks. These networks are subsequently utilized to learn drug representations using the graph embedding approach [24]. Next, an attention neural network is constructed using the acquired drug representations; this network is then used to learn drug-drug pair representations. Finally, drug-drug interactions may be reliably predicted with the help of a deep neural network.

3. PROPOSED METHODOLOGY

This research presents the HOMIN High-Order Multimodal Interaction Network, which integrates many pharmacological characteristics for the purpose of DDI event prediction. The HOMIN method's flow example is shown in Figure 1. The first step is to represent medicines using four categories of drug attributes that are used for calculating drug-drug similarities. The multiple-layer neural network sub-models are given drug representations one by one. Last but not least, we use the combined sub-models to learn drug-drug pairings' cross-modality representations, which we then use to forecast DDI occurrences. Here we provide the main components of HOMIN.

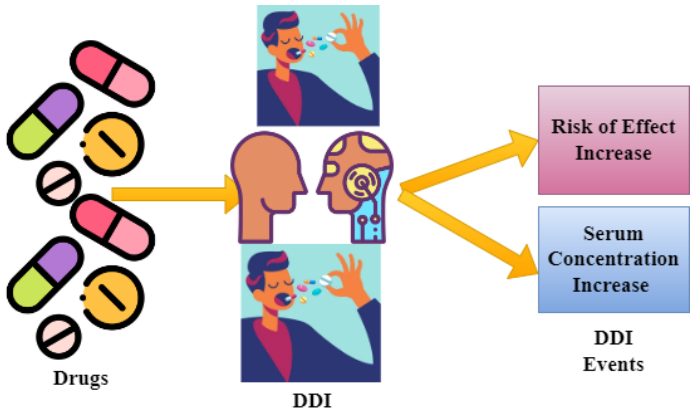

Figure 1: DDI Events

3.1. Feature Extraction

The High-Order Multimodal Interaction Network integrates many pharmacological characteristics as methods to provide predictions.When building a model, feature extraction and representations play a key role. Drugs are characterized by four aspects that provide varied information: chemical substructures, targets, enzymes, and routes. A binary feature vector can be used to characterize a

drug; features can have values of 1 or 0, indicating if the correct set of descriptors is present or not. We can illustrate this point with the help of the chemical substructures. There are 881 unique substructures, or molecular fingerprints, recorded in the Pubchem database. With four separate vectors depending on four different features, a drug can be defined in this way.We achieve feature compression and sparsity reduction by taking use of the fact that a great deal of the dimensions in these features vectors are zero.Here, we use the Jaccard similarity metric to determine the pairwise drug-drug similarity using bit vectors rather than the bit vectors themselves. One can identify the Jaccard similarity using Equation (1).

$$J(X,Y) = \frac{|X \cap Y|}{|X \cup Y|} = \frac{|X \cap Y|}{|X|+|Y|-|X \cap Y|} \quad (1)$$

The sets X and Y represent the bit vectors of two medications, and the intersection of the sets is denoted as $|X \cap Y|$. The union of the sets is $|X \cup Y|$. The last step is to use a drug-drug similarity matrix to display all medications as 572-dimensional row vectors that match. In medicine, VCS stands for a number of different i feature vectors. As a consequence of combining the feature vectors of the two medications, each of the four models represents a drug pair. Figure 2 shows how the feature extraction module creates several feature vectors that sub models can utilize as inputs.

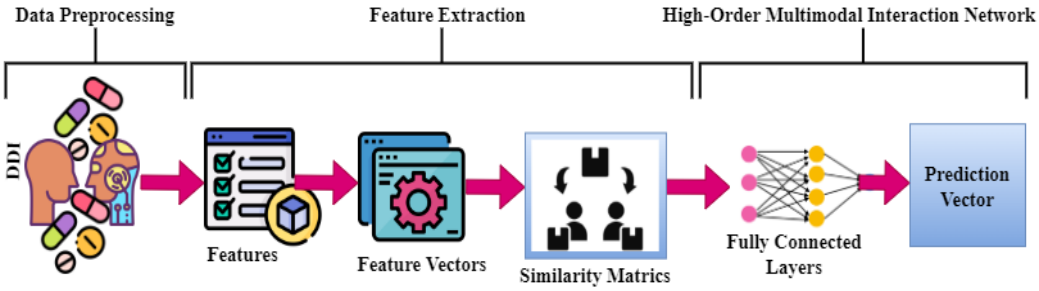

Figure 2: High-Order Multimodal Interaction Network

3.2. Construction of High-Order Multimodal Interaction Network

Since there are several features, we use the HOMIN to build sub-models that are dependent on each feature.A HOMIN is a kind of artificial neural network that uses many layers of input and output connections. It doesn't matter whether the connection is linear or non-linear; the HOMIN can always figure out the right mathematical procedure to solve it. The VGG16 neural network, originally created for image classification, was the primary focus of the first sub-model network proposals. To get bottleneck features in a multi-layer perceptron, one of the internal layers requires a lower number of hidden units than the others. This thin layer compresses the network, which in turn lowers the dimensionality of the classification data. Making advantage of bottleneck features allows us to decrease the number of factors that need instruction.

The following equation are used to compute the forward propagation:

$$y^l = Z^l x^l + y^l$$

$$x^+ = ReLU(y^l) \quad (2)$$

Where y^l is the bias and y^l is the weights of neurons between layers. The forward propagation takes

al as input and returns x^+ as output. To activate the model, we use the rectified linear unit (ReLU) function. Following a softmax layer, the sub-models generate the forecast. We use batch normalization layers to speed up the convergence process and dropout layers to prevent over-fitting and improve the model's generalizability.

For HOMIN, the integration of many sub-models is crucial. In this step, the average operator takes the results from each sub-model and combines them to get the final forecast. Figure 2 shows that in order to develop the prediction model, we first generate sub-models from various characteristics.

4. RESULTS AND DISCUSSION

Experimental data are crucial for proving that the High-Order Multimodal Interaction Network (HOMIN) model can accurately predict drug-drug interactions (DDIs). Based on a hypothetical or typical research scenario, below is a general structure for presenting these findings. The results would be obtained by applying the model to actual data in your studies.

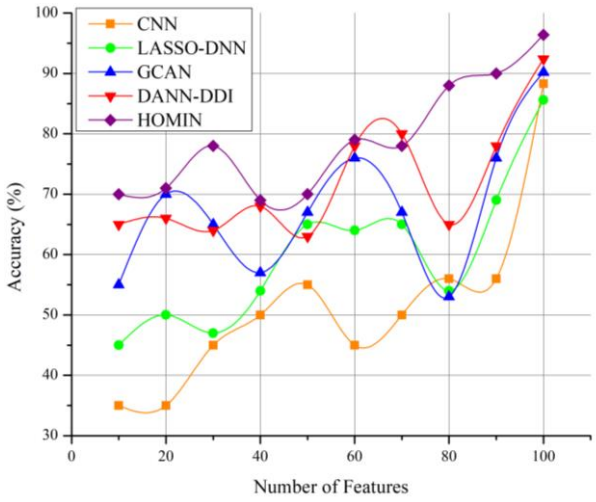

Figure 3: Accuracy Analysis

A HOMIN model's prediction accuracy is evaluated in Figure 3. It considers the ratio of correct predictions to total predictions. When we claim the HMIN model was accurate, we mean it recognized all medication combinations, interacting or not. In imbalanced datasets like DDI data, where non-interacting medication combinations outweigh interacting ones, high accuracy, although positive, must be judged carefully since it represents the model's overall effectiveness. Other criteria beyond accuracy should be considered while developing DDI forecasts. The class imbalance would enable the algorithm to forecast most couples as non-interacting, resulting in high accuracy. However, it would ignore the crucial step of detecting interacting couples. HOMIN's accuracy is good overall, but the F1-score shows how effectively it handles real-world interactions. HMIN handles high-dimensional multimodal data better than competing models, as shown by its accuracy. The model's high-order interaction and multimodal learning processes improve prediction accuracy.

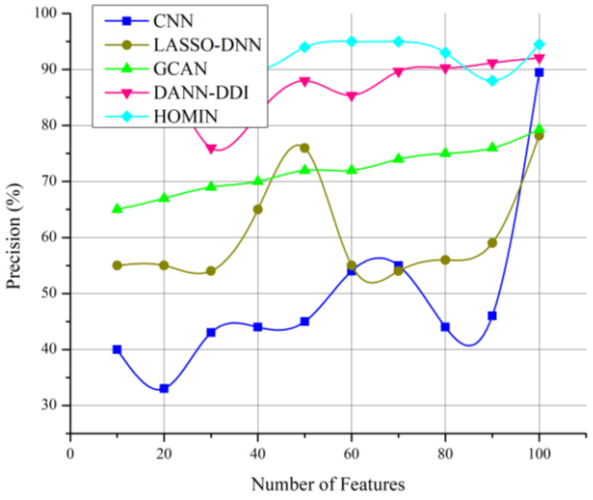

Figure 4: Precision Analysis

A drug interaction prediction system's precision (Figure 4) is the ratio of correct forecasts to positive predictions. In this case, the HOMIN model predicted drug interactions accurately. In DDI, good accuracy is crucial to avoid clinically unnecessary indications or treatments due to false positive predictions (missing pharmaceutical interactions). DDI false positives may harm patient care and are misleading. If a doctor gets a false interaction warning, they may change a patient's prescription without proper treatment. HMIN's precision ensures that the model is cautious when predicting interactions, reducing unnecessary warnings and boosting system trust. Baseline models have less effective scores for precision since they fail to detect false positives in high-dimensional datasets. HOMIN employs multimodal data (chemical, biological, and clinical) to improve predictions. Its high-order interaction capture helps elucidate complex drug relationships.

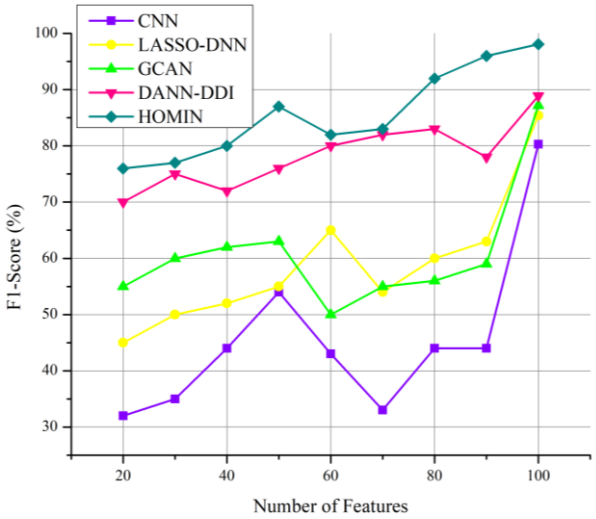

Figure 5: F1-Score Analysis

The F1-score (Figure 5) balances finding actual positives (recall) and eliminating false positives by incorporating accuracy and precision. The F1-score excels in DDI prediction and similar situations due to the enormous difference between drug combinations that interact and those that don't. The F1-score shows that HOMIN minimizes false positives and identifies meaningful interactions. The F1-

score excels with imbalanced data, as in DDI prediction. In this case, a model with low accuracy but high recall may recognize many actual interactions but also many false positives. However, an accurate model with inadequate memory can overlook important interactions. HOMIN's strong F1-score indicates that it can discover many actual interactions while minimizing false positives. In healthcare environments, missed interactions (false negatives) and erroneous interaction warnings (false positives) are dangerous, therefore this balance is crucial. DDI datasets frequently have more non-interacting pairs than interactive ones. Traditional models, which generate acceptable outcomes by falsely anticipating that most medicine pairings will not interact, may be affected by this imbalance. Due to its high F1-score, HOMIN effectively manages this imbalance even in rare positive situations (interacting drugs). HOMIN may predict clinical DDIs because of its adaptability.

5. CONCLUSION

In this study, we provide HOMIN, an innovative framework for the prediction of drug-drug interactions. HOMIN is able to use topological information and semantic relations efficiently by applying a neural network to the pharmacological knowledge graph. Through the joint representation learning of structural information and heterogeneous features, HOMIN delves further into investigating the cross-modal complementarity of the multimodal data. The experimental results show that HOMIN outperforms both conventional and state-of-the-art approaches to DDI event prediction.

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