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A Critical Review On Predicting Drug-Drug Reactions Using Machine Learning Techniques

Research Article

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Abstract

Drug-Drug interaction (DDI) refers to change in the reaction of a drug when the person consumes other drug. It is the main cause of avertable bad drug reactions, causing major issues on the patient's health and the information systems. Many computational techniques have been used to predict the adverse effects of drug-drug interactions. However, these methods do not provide adequate information required for the prediction of DDI. Machine learning algorithms provide a set of methods which can increase the accuracy and success rate for well-defined issues with abundant data. This paper provides a comprehensive survey on most popular machine learning and deep learning algorithms used by the researchers to predict DDI. In addition, the advantages and disadvantages of various machine learning approaches have also been discussed here.

Keywords: Domestic Violence; Violence Exposure; Ptsd; Sexual Assault; Mental Health And Violence.

Introduction

Adverse drug reactions (ADR) are the major source of medical issues and adverse drug reactions are determined to be the major cause of death in many countries ahead of pulmonary disease, diabetes, AIDS and pneumonia [1]. Estimates of the number of patients suffered due to drug-drug interactions vary from 5-8% of all complication errors within healthcare centers. Also, the fusion of various drugs may results in interaction between drugs, which is a major cause of detrimental drug events. It is very difficult to find out the DDI during various clinical examinations. Detection of drug-target interactions is very important to both new drug discovery process and old drug repositioning. Computational methods always require a vast amount of data for optimization. Also, the large gap between familiar and unfamiliar drug-target pairs has paved the way for prediction of various drug interactions. The easiest way to explore a large number of drug combinations for detecting interactive drugs is through machine learning and deep learning methodologies [14].

Machine learning is the process which involves combination of algorithms to analyze the data, learn from it and then make a future prediction for any given new data sets. Machine learning techniques can be broadly classified into four categories namely supervised learning, unsupervised learning, Semi-supervised learning and Reinforcement learning. In Supervised learning, the output or result for the given input is known previously and the model should be able to assign the given new input to the correct output. The model must be trained before the test samples are given to it in order to the correct output [2, 17].

In unsupervised learning, the result or output for the given inputs is unknown and here the input data is given before and the model is run on it. Semi-supervised learning technique falls in-between the supervised and unsupervised learning algorithms. It makes use of unlabeled datasets for training process, usually a less amount of datasets containing a combination of labeled and unlabeled data. Semi-supervised learning plays a vital role in the classification of real world problems. In reinforcement learning, the model is trained to make a sequence of actions. Here the agent takes a suitable action in a complex environment to achieve the goal [3, 16].

Currently many machine learning methodologies including the deep learning techniques which allow multiple layers of data representation with many levels of abstraction have brought developments in various fields of education and industry such as speech synthesis and recognition, disease prediction, image classification

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and bioinformatics. A large group of machine learning algorithms and applications on large-sized datasets are now possible with the help of Graphics Processing Unit (GPU). Also, many machine learning techniques have been found and applied successfully in bioinformatics field for efficient detection and discovery process. It is very important to have knowledge about the current scenario of machine learning methodologies in the pharmaceutical drugs reaction discovery field in-order to discover the various adverse drug-drug interactions and their results [4, 15].

Literature Survey

Manfred K. Warmuth [5] used Support vector machine (SVM) for the drug discovery process. SVM is one of the widely used supervised machine learning techniques which has been repeatedly applied in the process of drug-drug interaction discovery. SVM is based on the idea of finding a maximum margin separating hyper plane in order to classify the given dataset. Also, the dataset showed that how SVM's can be used in partitioning the fruitful data from useless data. It is also true for active learning scenarios, where the used data were replaced during the analysis to increase the accuracy of results.

Geonhee Lee [6] proposed a deep learning framework to forecast the results of DDIs with high accuracy. The proposed methodology used a combination of auto-encoders and a deep feed-forward neural network which are trained by using a combination of structural similarity profiles (SSP), Gene Ontology (GO) term similarity profiles (GSP) and target gene similarity profiles (TSP) of known drugs combination to find out the pharmacological effects of many DDIs. The results showed that use of SSP alone increases the prediction accuracy of GSP and TSP and the auto-encoder is more effective than PCA for minimizing the dimensions of each profile. The model also showed good results than the available existing methods and discovered a number of novel DDIs which are useful for the present research.

Reza Ferdousi [7] used a computational method for predicting DDI's based on functional similarity of all drugs. The proposed model was set based on a number of key biological elements namely carriers, enzymes, transporters and targets (CETT). The proposed model was tested for 2189 approved drugs in which the corresponding CETT's are collected and their corresponding binary vectors were designed to find the DDIs. Many similarity measures was performed, in which inner product-based similarity measures (IPSMs) provided high prediction values to detect DDIs. Totally 2,394,767 potential drug pairs interactions are evaluated and more than 250,000 unknown potential DDIs were detected. The major drawback of this method was unavailability of drugs data which leads to inaccurate all possible pairs of DDIs detection. Guy Shtar [8] used a combination of computational techniques namely artificial neural network and graph node factor propagation methods like adjacency matrix factorization (AMF) and adjacency matrix factorization with propagation (AMFP) for predicting the interaction between drugs. The model was trained by using Drug-bank database which consists of 1,142 drugs and 45,297 drug-drug. The trained model was evaluated using the latest version of drug bank with 1,442 drugs and 248,146 drug-drug interactions. Also ensemble-based classifier using AMF, AMFP are created and the results were evaluated based on receiver operating characteristic (ROC) curve. The results showed that proposed ensemble based classifier gives critical data for drug development and gives noisy data for drug prescription. Also, the drug embedding's have been made public which was created during the training of models using interaction network. Andy W. Chen [9] proposed a predictive model to predict Adverse Drug Reactions (ADR). The predictive model is a combination of Support Vector Machine, Logistic Regression, random forest and Gradient Boosted Tree. Two datasets are used in this model namely DEMO dataset which includes attributes like patient's age, weight, sex and DRUG dataset which contains attributes like drug's name, role and dosage. The dataset includes 46% males and 54% females. The built model shows good prediction rate for balanced set of samples. Also the results showed that the proposed model gives high accuracy only for large sample of datasets. Achille Fokoue [10] proposed a framework called as Tiresias for detecting Drug-drug Interactions (DDI). Tiresias framework takes as input, a large sources of drug-related information and gives DDI predictions as end results. The DDI detection methodology starts with semantic integration of the input data which results in a knowledge graph representing drug attributes and relationships with various related objects such as enzymes, chemical structures, and pathways. Several similarity measures between all categories of drugs are calculated using knowledge graph in a scalable and distributed environment. A large scale logistic regression prediction model is built using the computed the similarity metrics to predict the DDI's. The results showed that Tiresias framework is effective in finding the new interactions among currently available drugs and also among newly designed and existing drugs. A drawback of the proposed Tiresias model is the requirement of large scaled drug information which leads to high cost of the developed model. Xinyu Hou [11] proposed a model using deep neural network architecture to predict the adverse drug events because of Drug-drug interactions. The proposed model uses the codes of 5000 drugs that are downloaded from Drug Bank. The proposed model finds out 80 types of DDI's using the calculated features. The model is also built using Tensor Flow-GPU which takes 4432 drug features as input. The trained model gives an accuracy of 88% in predicting the reactions of inflammatory bowel disease (IBD) drugs. The results also showed that the model works better only for large sample of datasets. Andrej Kastrin [12] used statistical learning methodologies to predict the potential Drug-drug interactions (DDI). DDI is represented as intricate network in which the nodes represent drugs and the links represent their possible interactions. Link prediction process is represented as a binary classification job on networks of DDI's. A massive DDI databases are arbitrarily chosen to predict the unknown drug interactions. Various supervised and unsupervised machine learning techniques including support vector machine, classification tree, boosting and random forest are used for link prediction in various DDI networks. The supervised link prediction approach produced promising results when compared with unsupervised techniques. The proposed methodology requires Unified Medical Language System (UMLS) filtering to detect the link between the drugs which created a problem for the researchers. Also the proposed system considers only the static network snapshots which creates a problem for DDI's system as it is a dynamic system. Chi-Shiang [13] Wang proposed a deep neural network model to detect Adverse Drug Reactions (ADR). The model uses the synthetical, biological and biomedical knowledge of drugs to predict ADRs. The model also used the drug data from SIDER databases. Target drug representations were distributed in a vector space to find the relationship between drugs using word-embedding approach

which helped to improve the proposed system performance. The main problem with proposed system is, it works better only for the standard SIDER databases.

Conclusion

In this review paper, a detailed study was performed on the various methods and techniques used for the prediction of various DDI's. Each of the machine learning methodologies has its own pros and cons. In particular, we focus on combining several machine learning techniques to create an ensemble classifiers to predict the DDI's. Machine Learning techniques provides a promising results in the detection of DDI's in near future when the volume of data is tremendous.

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