

A Systematic Literature Review on Drug Synergy Prediction Techniques

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Abstract:

Synergistic combinations of drugs are extensively utilized for cancer treatment. However, prediction of drug synergy is defined as an ill-posed problem. Because manual testing is only implementable on small group of drugs. Recently, many researchers have utilized machine and deep learning models for drug synergy prediction. The main objective of this paper is to systematically review the drug synergy prediction techniques. We have considered some recently designed machine and deep learning-based drug synergy prediction techniques. Thereafter, we have reviewed these papers and compared some of them with each other based upon certain characteristics. From, this systematic literature review, it has been found that the prediction of drug synergy using machine and deep learning is still an open area of research. The techniques applied so far suffer from hyper-parameters tuning issue. Finally, we have discussed some future scope to improve the drug synergy prediction techniques

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INTRODUCTION

Even though many tools are available to predict the cancer in human beings, but development of an anti-cancer treatments is still a challenging issue [1]. Generally, cancer patients need an efficient combination of various drugs so called drug synergy [2]. However, prediction of an efficient drug combination is still a challenging issue. Recently many researchers have designed various machine and deep learning techniques to overcome this issue [3]. However, each technique has its own inherent issues. Therefore, in this paper, we have studied these techniques and try to find the limitation of these techniques. The main objective is to present future direction for efficient prediction of drugs.

An efficient combination has a huge impact on cancer patients through the fusion of various drug-combinations [4]. The drug synergy combinations help cancer patients against cancer pathogens attacking the body [5] like viruses [6] and bacteria [7] in different ways [8]. The specific drug

targets specific intrusive pathogens and provides resistance to the host from the specific antigen [9]. The knowledge of drug synergy prediction can be implemented for the diagnostics of cancer patients [10]. It is therefore of interest to develop improved methods for predicting drug synergy in an efficient manner [11]. Therefore, drug synergy prediction becomes a significant issue [12]. Researchers have devoted great efforts to drug synergy prediction techniques by using machine learning techniques in the past decade [13]. Ensembling based machine learning models can be efficiently used to predict the drug synergy prediction [14].

Figure 1 shows a typical layout of drug synergy prediction model based upon the neural networks [1].

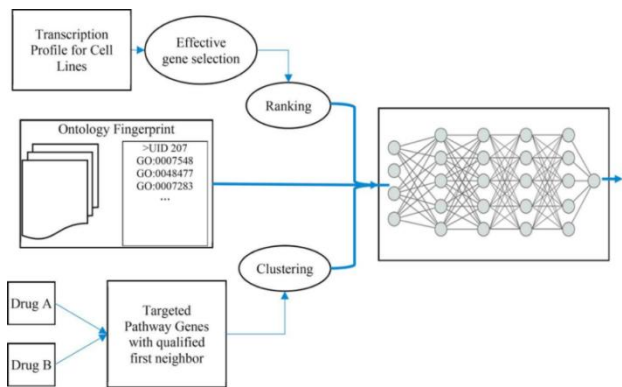


Figure 1: Drug synergy prediction model

Figure 2. shows compound descriptor array-based machine learning model to predict drug interactions. In the training step, compound descriptor arrays are obtained for drugs [2].

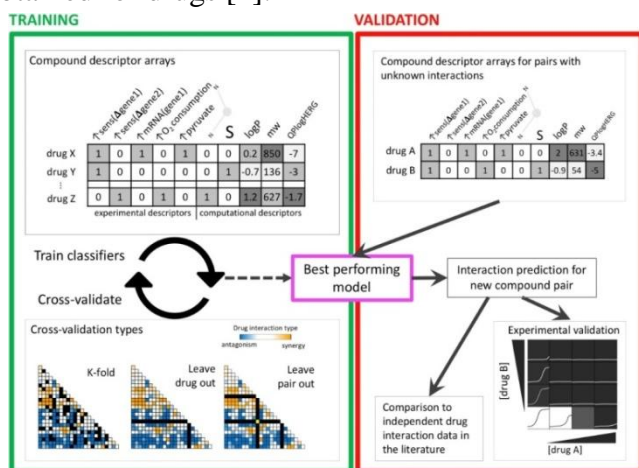


Figure 2: Compound descriptor array-based drug synergy prediction

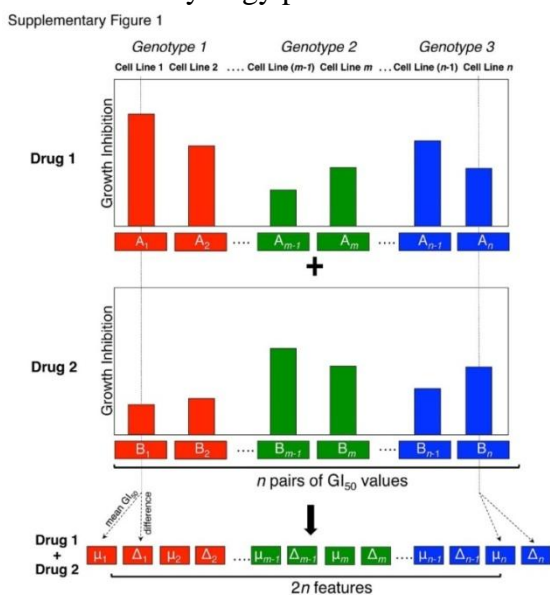


Figure 3: Diagrammatic view of the drug synergy evaluation

Figure 3 shows the diagrammatic view of the drug synergy evaluation. It clearly shows the obtained drug has features of both input drugs. Therefore, it will have more potential against cancer patients [3]. The overall objective of this paper is to systematically review the drug synergy prediction techniques. 68 papers related to machine and deep learning-based drug synergy prediction are considered for comparative analysis. Thereafter, we have reviewed these papers and compared some of them with each other based upon certain characteristics. From, this systematic literature review, it has been found that the prediction of drug synergy using machine and deep learning is still an open area of research. The techniques applied so far suffer from hyper-parameters tuning issue. Finally, we have discussed some future scope to improve the drug synergy prediction techniques.

The remaining paper is organized into following sections. Competitive techniques and their comparative analysis are presented in Section II. Future scope is demonstrated in Section III. Finally, conclusion is presented in Section IV.

II. COMPETITIVE TECHNIQUES

In this section, a review of some competitive machine learning techniques is presented. These techniques are utilized in the literature to predict the drug synergy.

Initially, we will discuss the general flow of the drug synergy prediction model (see Figure 4 [4]). However, our main concentration is on drug synergy prediction techniques only.

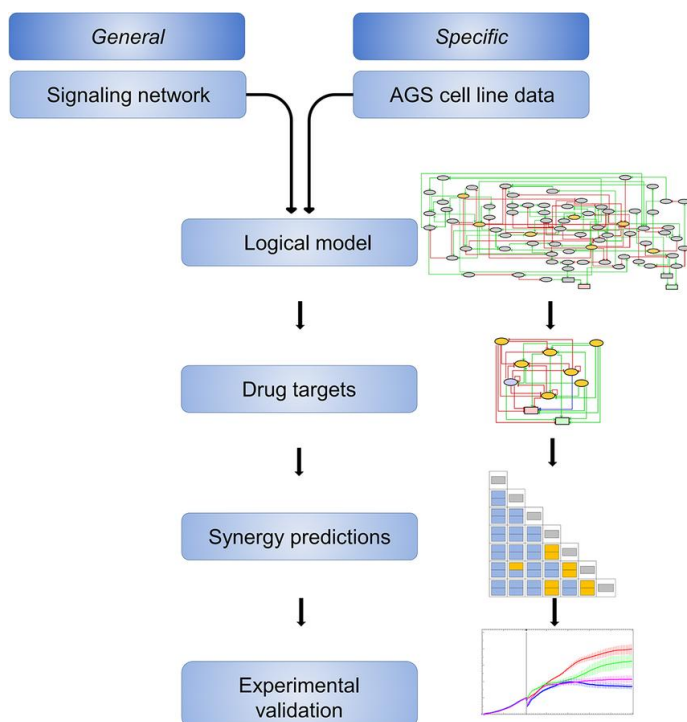


Figure 4 Drug synergy prediction model

Singh et al. designed a novel machine learning based drug synergy prediction model. Ensemble based differential evolution has been utilized to tune the hyper-parameters of support vector machine. It has been shown that the efficient tuning of hyper-parameters of machine learning models can efficiently improve the prediction accuracy [15]. Shin et al. implemented a deep learning-based model to predict the drug synergy. It has shown remarkable performance over the existing techniques, but it suffers from the hyper-parameter tuning issue [16]. More et al. has shown that the cellular network architecture can be used to monitor the efficient combination of drugs. It has shown remarkable results at good computational speed. However, due to its complex behaviours some time it may stuck in local optima [17].

Zhang et al. (2019) discussed the use of synergistic drug combinations for cancer patients. A computational model so called SyFFM, has been implemented. SvFFM utilizes pharmacological data and implements field-aware factorization machines to approximate potential synergistic drug combinations [18]. Chen et al. (2018) implemented a novel MCDC model which combines different

drugs by considering the proteins and diseases. MCDC combines drug details such as chemical structure, target profile, disease phynotype, together with their interactions to build a two-layer heterogeneous network. MCDC then predicts synergy score for each disease using a link prediction algorithm [19].

Kaur et al. (2018) prediction of drug synergy plays a significant role for cancer patients treatments. an efficient differential evolution based multinomial random forest has been implemented to improve the results further [20]. Deac et al (2019) discussed a drug-drug interactions and its significant for cancer patients treatments. It has been found that the machine learning based models has an ability to predict the drug synergy score [21]. Chen et al. (2016) designed a network-based Laplacian regularized least square based drug synergy score prediction. It has shown a remarkable improvement over the competitive drug synergy prediction techniques [22]. Li et al. (2016) utilized various machine learning models to predict drug-drug interaction score. It has been found that designing and efficient drug synergy score is still an open area of research [23].

III. FUTURE SCOPE

From the existing literature, it has been found that existing machine learning models implemented for drug synergy prediction suffer from at least one of the following issues: -

1. **Feature selection:** - Majority of existing researchers have neglected the effect of feature selection techniques during the training and testing time. It has been observed from the literature that an efficient feature selection technique has an ability to improve the performance of machine learning models.
2. **Ensembling:** - Most existing researchers have neglected the use of optimistic ensembling approaches to improve the performance of existing machine learning models for B-cell epitope prediction.

3. Parameters tuning: - Parameters tuning is another major gap found in the existing literature. An efficient tuning of parameters has ability to improve the performance further.

4. Meta-heuristic techniques: - It has been observed that majority of existing researchers have focused on designing heuristic machine learning model for drug synergy prediction.

Therefore, in near future someone may focus on the aforementioned issues to design a more efficient drug synergy prediction techniques.

IV. CONCLUSIONS

Predicting the drug synergy combination is found to be challenging issue. We have reviewed some recently designed and implemented drug synergy prediction techniques using machine and deep learning models. Comparative analysis has shown that the techniques applied so far suffer from hyper-parameters tuning issue. The issue considered in this paper, helps to predict the efficient combination of drugs for cancer patients. By conducting the review of existing research on drug synergy prediction technique. We have found that majority of existing researcher have neglected the use of feature selection, parameter tuning and ensembling techniques etc. The researchers who have focused some of these issues have not considered the prediction of drug synergy. Also, parameter tuning is still an ill-post problem. Therefore in near future, we will design a novel machine learning technique for drug synergy prediction by modifying a well-known NSGA-III algorithm to tune the required parameters for a given model in a more efficient manner. Also, ensembling approach will be improved by considering bias theorem to prioritize selected machine learning models for ensembling.

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