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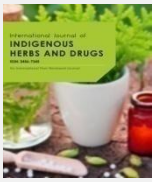

PREDICTING ENCOUNTERS WITH ARTIFICIAL INTELLIGENCE

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Abstract

Over the past decade, polypharmacy the concurrent use of multiple medications to treat patients with complex or multiple health conditions has become increasingly common. While necessary, this practice elevates the risk of drug-drug interactions (DDIs), which can result in serious adverse drug events (ADEs). Artificial intelligence (AI) has emerged as a promising tool for predicting DDIs, helping clinicians make more informed pharmacotherapy decisions. AI can process vast datasets and identify patterns that may not be immediately apparent to human experts, offering valuable support in medication management. However, one of the primary challenges limiting the widespread adoption of AI in clinical settings is the lack of transparency in many models, often referred to as "black-box" systems. These models provide predictions without clearly explaining how those predictions were made, reducing trust among healthcare providers. To address this, explainable AI (XAI) techniques have been introduced to improve model interpretability, enabling clinicians to understand and validate the reasoning behind AI-generated insights. In addition to predicting DDIs, AI is being developed to forecast interactions involving food, excipients, and the human microbiome further enhancing its utility in personalized medicine. Machine learning models that incorporate drug similarity, molecular structure, and the activity of metabolic enzymes such as cytochrome P450 have shown significant progress in predicting complex interactions. This review explores key methodologies, databases, and algorithms in DDI prediction, emphasizing AI's expanding role in improving clinical decision-making and patient safety, while reinforcing the importance of transparency through the integration of XAI techniques.

Keywords Drug; Drug–Drug Interaction; Database; Web Server; Computational Model.

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Introduction

Drug-drug interactions (DDIs) can lead to adverse drug events (ADEs), increasing patient risks, especially in polypharmacy cases. Traditional experimental methods for detecting DDIs are slow and resource-intensive. Artificial intelligence (AI) offers faster, data-driven predictions but often operates as a "black-box," limiting interpretability. AI is also used to analyze drug-food-microbe interactions, improving treatment safety. Despite advancements, AI models typically predict single interactions rather than complex, multi-drug interactions seen in clinical settings. Future research should focus on holistic AI models capable of providing comprehensive insights into drug therapies, enhancing drug safety and treatment optimization in healthcare [1-3].

Algorithms commonly used machine learning methods

Machine learning (ML) is a broad term encompassing a category of algorithms capable of extracting hidden patterns from extensive recorded data and utilizing them for prediction or computation. The ML workflow involves data acquisition, data preprocessing, algorithm selection, model training, evaluation using a test dataset, parameter optimization, and model deployment. In recent years, ML techniques for computational prediction have gained significant popularity, assisting researchers in handling large datasets, identifying patterns, and forecasting unknown challenges.

K-nearest neighbor

The K-nearest neighbor (KNN) algorithm is a supervised learning technique suitable for classification tasks with limited prior data knowledge. It requires minimal preprocessing, no distinct training phase, and is

robust against outliers. KNN excels in large-scale categorization
but has drawbacks like lazy learning and high computational demands. Jiang et al. used KNN to predict drug-target interactions, outperforming traditional methods like logistic regression with faster data processing [4-6].

Decision tree

The Decision Tree (DT) framework is a hierarchical model used for classification a forecasting without requiring data preprocessing. It processes quantitative and qualitative data, making it ideal for categorization and regression tasks. Ng et al. utilized DT to assess drug-drug interaction data in pharmaceutical documentation, aiding in evaluating drug guidelines and references efficiently [7].

Random forest

Random Forest (RF) is an ensemble learning technique that combines multiple Decision Trees (DT) to handle large datasets efficiently. Javed et al. used RF, Naïve Bayes, and J48 for Drug-Drug Interaction classification, with RF achieving a 0.99 accuracy. RF offers high precision, fast training, and efficient parallel processing [8]..

Naive Bayes

Naive Bayes (NB) is a supervised classification algorithm based on probability theory, excelling with small datasets and independent features. Though it struggles with correlated data, NB is faster than SVM and RF. Researchers have successfully applied NB in drug discovery, achieving AUC scores of 75–100% in predicting drug targets and DDIs [9-10].

- **Support Vector Machin:**
  Support Vector Machine (SVM) is a supervised learning algorithm that constructs an optimal hyperplane for classification. It excels in both linear and nonlinear tasks by mapping data into higher dimensions using kernel functions. Chao et al. developed an effective SVM model for drug interaction prediction using an RBF kernel. (11).
- **Extreme gradient boosting:**
  Extreme Gradient Boosting (XGBoost) is a high-performance ensemble method for classification and regression, excelling in accuracy and handling missing data. Wu et al. used XGBoost to classify CYP450 inhibitors, achieving 90.4% accuracy, outperforming deep learning models and other ensemble techniques in drug I nteraction prediction. (12).
- **Logistic regression:**
  Logistic Regression (LR) is a simple yet interpretable classification method suited for binary problems. It struggles with nonlinearity, multicollinearity, and imbalanced data.
  Wang et al. used LR to analyze drug interactions in China, identifying 1,979 cases. Feature selection techniques like GBDT can enhance LR's effectiveness in complex datasets. (13)
- Gradient boosting decision treeGradient Boosting Decision Trees (GBDT) use loss function gradients to fit regression trees, offering high accuracy and handling

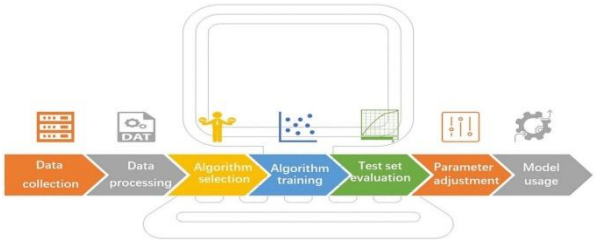


Fig:1 The ML workflow

nonlinear data well. Xuan et al. developed DTIDBGT, a GBDT-based model for predicting drug–target interactions. It reduces class imbalance effects and outperforms other advanced methods in interaction prediction (14)

The process of ML includes data collection, data processing, algorithm selection, algorithm training, test set evaluation, parameter tuning and model usage.

3. Data sets

To support drug-drug interaction (DDI) prediction, databases like DDI Extraction 2011, DDI Extraction 2013, and DrugBank provide essential drug properties and DDI events. These datasets enable AI-driven identification of interactions, typically using binary values—1 for interaction and 0 for no known interaction. [15]

4. Deep learning-based prediction model

Deep learning (DL) is increasingly used for drug-drug interaction (DDI) prediction due to its ability to process complex relationships. Unlike traditional machine learning (ML), which relies on manual feature engineering, DL performs data representation and prediction simultaneously. Its superior classification performance drives its growing application in DDI extraction and prediction tasks. [16]

- **Artificial neural network (ANN):**
  Artificial Neural Networks (ANNs) identify hidden patterns in data through interconnected neurons, solving linear and nonlinear problems. ANN models have been used for DDI prediction, including two-layer models, feed-forward networks with ReLU activation, and propagation methods over DDI graphs. XGBoost classifiers further enhance classification accuracy by predicting drug interactions. [17]
- Convolutional neural network (CNN): ConvolutNeural Networks (CNNs), inspired by the animal visual cortex, process grid-like data by extracting spatial features through convolution and pooling layers. CNNs are well-suited for DDI prediction due to their feature-learning capabilities and scalability. Activation functions like sigmoid and softmax are used for binary and multiclass classification, respectively.
- Conventional CNN: Chen et al. used CNNs in a bi-levelmodel to extract local and global features for DDI prediction. Wu et al. combined CNNs, pooling, and attention-based RNNs to classify interactions.

Quan et al. utilized CNNs with word embeddings, max pooling for feature reduction, and a SoftMax layer for classification. [18]

- Dependency-based CNN: Traditional CNNs strugglewith long-distance word relationships in DDI instances, leading to data sparsity. Dep-CNN addresses this by using dependency parsing trees to capture dependencies. Liu et al.'s Dep-CNN model includes a look-up table, convolution, max-pooling, and SoftMax layers to extract features and classify DDIs effectively.

Deep CNN:

Considering various properties in texts, the successful application of Deep CNN (DCNN) in identifying complex patterns of image and video in computer vision suggested its application in DDIs extraction task. Sun et al. proposed a DCNN model which utilized a small convolution architecture to operate directly at the word level of the raw biomedical text input to get the embedding-based convolutional features. Then, the SoftMax classifier will be used to operate these features and extract DDIs from biomedical literature. [19]

Graph convolutional neural network (GCNN): GCNNs are used in DDI prediction to analyze drug molecular structures and interactions in non-Euclidean spaces. They represent drugs as nodes and interactions as edges. Models like SC-DDIS and GOGNN enhance feature extraction using graph-based learning, improving DDI prediction by capturing complex relationships between drug structures and interactions.

Recurrent neural network: RNNs, particularly LSTM and GRU, are widely used in DDI extraction tasks due to their memory mechanism for handling sequential data. Models like BiLSTM, hierarchical RNN, and skeleton-LSTM enhance DDI prediction by leveraging sentence structures, dependency paths, and attention mechanisms to extract meaningful relationships from biomedical texts and transcriptome data.[20]

Machine learning Methods

AI and ML methods predict interactions across domains like social networks, chemistry, and DDIs by processing large datasets and uncovering complex patterns. These approaches enhance predictive accuracy in fields such as NLP, biological systems, and recommender systems, offering insights that would be challenging or time-consuming for humans to deduce.

Supervised Learning:

Supervised learning models are trained using labeled data, where the input data is paired with the corresponding output (e.g., the presence or absence of an interaction). These models learn to predict interactions by identifying patterns in the labeled training data.

Common Methods in Predicting Interactions: Support Vector Machines (SVM): SVM is used for binary classification tasks (e.g., predicting if two drugs will interact or if two users will engage in a particular behavior). SVMs create a hyperplane that best separates data points from different classes. In the case of predicting interactions, it finds a decision boundary between interacting and non-interacting entities.

Application:

Predicting drug-drug interactions or social media interactions.

- Logistic Regression: Logistic regression is a statistical model often used for binary classification tasks, where the goal is to predict the probability of an interaction occurring. It is used for predicting whether two entities (e.g., users, drugs, products) will interact in a specific way.

Application:

Predicting social interactions or predicting whether two drugs might interact in the body.

- **Neural Networks (Feedforward and Recurrent):** Neural networks, particularly deep neural networks (DNNs), are used to predict interactions between entities by learning complex, nonlinear relationships from large datasets. Recurrent neural networks (RNNs) are particularly useful when the prediction depends on sequence-based data (e.g., time series interactions, user behavior over time).

Application:

Predicting dynamic interactions in recommender systems or social media platforms.

- **Unsupervised Learning:** Unsupervised learning involves finding patterns or relationships in data that is not labeled. This is particularly useful in domains where labeled interaction data is sparse or unavailable. Unsupervised learning can help identify new types of interactions that were not previously known.

Common Methods: Clustering Algorithms (e.g., k-Means, DBSCAN):

Application: Identifying clusters of similar products or drugs that might interact similarly, or detecting communities within social networks.

- **Reinforcement Learning (RL):** Reinforcement Learning (RL) is a method where agents learn to interact with an environment by taking actions and receiving feedback in the form of rewards or penalties. RL is useful for predicting interactions that involve decision-making, where the outcome is dependent on a series of actions and feedback.
- **Common Methods:** Q-Learning: In the context of predicting interactions, Q-learning can be used to predict the optimal sequence of interactions, such as the best series of user actions on a platform or the best set of drug interactions to maximize efficacy while minimizing harm.

Application:

Predicting user interactions in social media platforms or optimizing therapeutic strategies involving drug

combinations.[21]

- Ensemble Methods: Ensemble methods combine multiple machine learning models to improve the accuracy of predictions. These methods are especially useful in DDI prediction and other interaction-based applications, as they can combine the strengths of various models to reduce overfitting and bias.

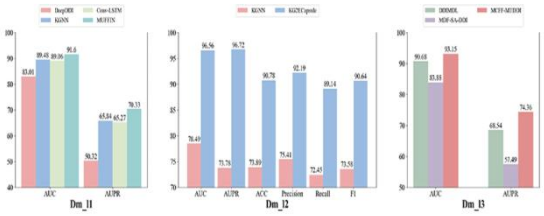
  Common Methods: Boosting: Boosting algorithms, like AdaBoost or Gradient Boosting, iteratively improve the predictions by adjusting weights on misclassified samples. These methods can be effective when predicting interactions that involve highly complex relationships between entities.

  Application: Predicting DDIs, where the interaction between drugs may depend on subtle, nonlinear relationships.
- **Bagging:** Bootstrap Aggregating, creates multiple models from different subsets of the training data. It can help to increase the robustness and reduce variance in interaction prediction tasks.

  Application: Social network analysis, where I nteractions are dynamic and complex, bagging can predict future interactions based on historical data

Challenges and Opportunities

Although excellent results have been achieved using deep learning and knowledge graph for DDI prediction, there are still some issues that need to be resolved, which aresummarized as follows



Performance evaluation under multi-label task

Future perspectives

The future perspectives of AI predicting interactions, particularly in areas like communication, human behavior, and decision-making, are vast and evolving. Here are a few key areas where AI is expected to significantly influence interactions:

- Personalized User Experiences: AI will continue to improve its ability to predict and understand individual preferences, behaviors, and needs. By analyzing past interactions, AI systems can tailor responses, recommendations, and experiences in real-time across various platforms, including social media, e-commerce, and entertainment.

  Examples:

  Personalized content feeds (like Netflix or YouTube), targeted marketing strategies, AI-driven customer service that predicts your needs before you even ask.
- **Human-AI Collaboration:**

  In the future, AI could work alongside humans to predict the flow of conversations, collaboration dynamics, and even emotional responses. This could lead to more seamless communication and enhanced collaboration in both professional and personal settings.

  Examples:

  Virtual assistants that predict and manage your work tasks, AI in team settings that can anticipate your needs, assist with brainstorming, and adjust based on group dynamics.
- **Human Behavior Modeling for Conflict Resolution**:

  AI could predict how individuals or groups will respond to different conflict resolution strategies, making it a powerful tool in areas like negotiation, diplomacy, or even social work.[22]

  Examples: AI predicting outcomes of diplomatic negotiations, AI-backed tools for conflict resolution, or algorithms that forecast interpersonal disputes based on historical data and personality traits.
- **Real-Time Predictive Analytics:**

  AI will allow organizations to predict human behavior in real-time. This will open the door for more dynamic and responsive systems in marketing, retail, customer service, and even security.

  Examples:

  Predicting a customer's next purchase based on browsing habits, or anticipating when an employee may need a break to prevent burnout.
- **AI in Autonomous Systems**:

  In fields like autonomous vehicles, drones, or robotics, AI's ability to predict human actions (such as pedestrian movements or the actions of other vehicles) will be crucial for ensuring safety and efficiency.

  Examples:

  Self-driving cars predicting the behavior of pedestrians, drones anticipating the movement of objects in their path, or robots that work alongside humans without colliding.
- Advancements in Natural Language Understanding: Future AI systems will improve their understanding of context, tone, and subtleties in human language. This means more fluid and natural conversations with AI, and the ability to predict what kind of communication will be effective in various situations.

Examples:

AI acting as a mediator in sensitive conversations, translating languages while maintaining cultural nuances, or using conversational AI to help in legal, psychological, or medical fields.

Conclusion

This study reviews AI models for predicting drug-drug interactions (DDIs), categorizing them into undirected prediction, drug interaction events, and asymmetric prediction. It highlights progress in the field, discusses commonly used datasets, and identifies model interpretability as a challenge. The paper advocates incorporating Explainable AI (XAI) and offers guidance for model selection and future research directions to enhance clinical relevance.

Author contribution

All authors are contributed equally

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Declaration of Competing Interest

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Reference

1. Askari M, Eslami S, Louws M, Wierenga PC, Dongelmans DA, Kuiper RA, Abu-Hanna A. Frequency and nature of drug-drug interactions in the intensive care unit. Pharmacoepidemiology and drug safety. 2013 Apr;22(4):430-7. https://doi.org/10.1002/pds.3415
2. Cohen AL, Budnitz DS, Weidenbach KN, Jernigan DB, Schroeder TJ, Shehab N, Pollock DA. National surveillance of emergency department visits for outpatient adverse drug events in children and adolescents. The Journal of pediatrics. 2008 Mar 1;152(3):416-21. https://doi.org/10.1016/j.jpeds.2007.07.041
3. Chen S, Li T, Yang L, Zhai F, Jiang X, Xiang R, Ling G. Artificial intelligence-driven prediction of multiple drug interactions. Briefings in bioinformatics. 2022 Nov;23(6):bbac427. https://doi.org/10.1093/bib/bbac427
4. Ehsani R, Drabløs F. Robust distance measures for k NN classification of cancer data. Cancer informatics. 2020 Oct;19:1176935120965542. 1176935120965542. https://doi.org/10.1177/1176935120965542
5. Asikainen AH, Ruuskanen J, Tuppurainen KA. Performance of (consensus) kNN QSAR for predicting estrogenic activity in a large diverse set of organic compounds. SAR and QSAR in Environmental Research. 2004 Feb 1;15(1):19-32. https://doi.org/10.1080/10629360320001696 42
6. Lee JY, Styczynski MP. NSkNN: a modified k-nearest neighbors approach for imputing metabolomics data. Metabolomics. 2018 Dec;14:1-2. https://doi.org/10.1007/s11306-018-1451-8
7. Borenstein E. Computational systems biology and in silico modeling of the human microbiome. Briefings in bioinformatics. 2012 Nov 1;13(6):769-80. https://doi.org/10.1093/bib/bbs022
8. Bielza, C., & Larranaga, P. (2014). Discrete Bayesian network classifiers: A survey. ACM Computing Surveys (CSUR), 47(1), 1-43. https://doi.org/10.1145/2576868
9. Sun H. A naive Bayes classifier for prediction of multidrug resistance reversal activity on the basis of atom typing. Journal of Medicinal Chemistry. 2005 Jun 16;48(12):4031-9. https://doi.org/10.1021/jm050180t
10. Pang, X., Fu, W., Wang, J., Kang, D., Xu, L., Zhao, Y., ... & Du, G. H. (2018). Identification of estrogen receptor α antagonists from natural products via in vitro and in silico approaches. Oxidative medicine and cellular longevity, 2018(1), 6040149. https://doi.org/10.1155/2018/6040149
11. Huang MW, Chen CW, Lin WC, Ke SW, Tsai CF. SVM and SVM ensembles in breast cancer prediction. PloS one. 2017 Jan 6;12(1):e0161501. https://doi.org/10.1371/journal.pone.0161501
12. Sheridan RP, Wang WM, Liaw A, Ma J, Gifford EM. Extreme gradient boosting as a method for quantitative structure–activity relationships. Journal of chemical information and modeling. 2016 Dec 27;56(12):2353-60. https://doi.org/10.1021/acs.jcim.6b00591
13. Stoltzfus JC. Logistic regression: a brief primer. Academic emergency medicine. 2011 Oct;18(10):1099-104. https://doi.org/10.1111/j.1553-2712.2011.01185.x
14. Xuan P, Sun C, Zhang T, Ye Y, Shen T, Dong Y. Gradient boosting decision tree-based method for predicting interactions between target genes and drugs. Frontiers in genetics. 2019 May 31;10:459. https://doi.org/10.3389/fgene.2019.00459
15. Li T, Yang K, Stein JD, Nallasamy N. Gradient boosting decision tree algorithm for the prediction of postoperative intraocular lens position in cataract surgery. Translational Vision Science & Technology. 2020 Dec 1;9(13):38-. https://doi.org/10.1167/tvst.9.13.38
16. Wishart DS, Knox C, Guo AC, Shrivastava S, Hassanali M, Stothard P, Chang Z, Woolsey J. DrugBank: a comprehensive resource for in silico drug discovery and exploration. Nucleic acids research. 2006 Jan 1;34(suppl_1):D668-72. https://doi.org/10.1093/nar/gkj067
17. Wang Y, Sohn S, Liu S, Shen F, Wang L, Atkinson EJ, Amin S, Liu H. A clinical text classification paradigm using weak supervision and deep representation. BMC medical informatics and decision making. 2019 Dec;19:1-3. https://doi.org/10.3390/make5020036
18. Kumar Shukla P, Kumar Shukla P, Sharma P, Rawat P, Samar J, Moriwal R, Kaur M. Efficient prediction of drug–drug interaction using deep learning models. IET Systems Biology. 2020 Aug;14(4):211-6. https://doi.org/10.1049/iet-syb.2019.0116
19. Sejnowski TJ. The unreasonable effectiveness of deep learning in artificial intelligence. Proceedings of the National Academy of Sciences. 2020 Dec 1;117(48):30033-8. https://doi.org/10.1073/pnas.1907373117
20. Esteva A, Robicquet A, Ramsundar B, Kuleshov V, DePristo M, Chou K, Cui C, Corrado G, Thrun S, Dean J. A guide to deep learning in healthcare. Nature medicine. 2019 Jan;25(1):24-9. https://doi.org/10.1038/s41591-018-0316-z
21. Hou WJ, Ceesay B. Extraction of drug–drug interaction using neural embedding. Journal of

bioinformatics and computational biology. 2018 Dec 19;16(06):1840027. **https://doi.org/10.1142/S0219720018400279**

22. Hwisa NT, Gindi S, Rao CB, Katakam P, Rao Chandu B. Evaluation of Antiulcer Activity of Picrasma Quassioides Bennett Aqueous Extract in Rodents.

Vedic Res. Int. Phytomedicine. 2013;1:27. **https://www.researchgate.net/publication/248995990**