International Research Journal of Advanced Engineering and Science
ISSN (Online): 2455-9024

DDI Event Prediction via Graph Convolutional Network with Agent Attention Mechanism

Jiayi Zhong[1]
[1]Department of Computer Science, Qufu Normal University, Rizhao,Shandong, China, 276800

***Abstract*—*DDI event prediction can reduce the risks of combination therapy and has become a research focus in public health security and medical safety monitoring. To address the problem of excessive computational complexity in the contrast module of existing multi-scale contrastive learning architectures for DDI event prediction, this paper proposes a DDI event prediction method based on graph convolutional neural network fused with Agent Attention Mechanism. Meanwhile, the TopK method is adopted to generate agent tokens for the agent attention mechanism, so as to construct the corresponding attention model. Experiments show that the proposed model can maintain stable performance while effectively reducing computational cost, and achieves competitive prediction results on standard datasets.*

***Keywords*—** *DDI event prediction; Graph Convolutional Neural Network; Agent Attention Mechanism; TopK method.*

I. INTRODUCTION

In recent years, combination therapy using multiple drugs simultaneously has become a promising strategy for treating patients with complex diseases[1]. In the field of deep learning, the development of DDI event prediction methods has mainly progressed through convolutional neural network (CNN)-based[2] and graph convolutional neural network (GCN)-based[3] approaches. However, neural networks often face data bottlenecks when processing complex data. Thus, using only the above models may lead to limited information capture and expression, resulting in data loss. Recently, with the advancement of deep learning research, neural networks based on attention mechanisms[4] have also become a research hotspot.

Aiming at the problem of high computational complexity in computing intra-layer and inter-layer substructure relationships at different scales in the existing fused multi-scale contrastive learning method for DDI event prediction, this study develops a graph convolutional neural network fused with Agent Attention Mechanism to maintain stable model performance while effectively reducing computational complexity. It explores the TopK method to select the most important nodes and generate agent tokens A for Agent Attention, constructing the Agent Attention quadruple (Q, A, K, V). Finally, DDI event prediction is realized to effectively respond to DDI risks.

II. MATERIALS AND BACKGROUND

A. Adoption of Graph Convolutional Neural Network

The core of GCN is to extend the convolution operation of CNN to graphs. It uses the node feature matrix and adjacency matrix of the graph to obtain the connection relationships and weights between nodes, and captures information between nodes and their neighbors through convolution to achieve feature extraction. Xuan Lin et al. from Hunan University proposed KGNN[5], a knowledge graph-based graph neural network, which can effectively capture drugs and their potential neighborhood entity information by mining knowledge graphs (KG). The DDI-CGN[6] model by Zuquan Weng's team from Fuzhou University demonstrated advanced prediction performance on an independent hold-out set and provided visualization of DDI-related structural features to help study potential mechanisms, providing references for this model. The MSResG model[7] proposed by Lin Guo's team from Shaanxi Normal University addressed the issue of balancing different drug features in DDI event prediction by calculating similarity scores through averaging. It then integrated the comprehensive similarity network with the drug interaction network and encoded and decoded it using a graph autoencoder based on residual graph convolutional networks. Encoding learns latent feature vectors of drugs containing similarity and interaction information, while decoding reconstructs the network to predict unknown drug-drug interactions. This proves the potential and value of GCN-based DDI event prediction.

B. Adoption of Agent Attention Mechanism

Agent Attention Mechanism[8], proposed by Dongchen Han et al. from Tsinghua University, is an attention mechanism integrating Softmax Attention and Linear Attention, with advantages of stable performance and high efficiency. It innovatively introduces agent token A to form the quadruple attention mechanism (Q, A, K, V). As an agent of Q, A aggregates information from K and V and broadcasts it back to Q. Since the dimension of A is n×d and Q is N×d ($n \ll N$), Agent Attention enables global information modeling at low computational cost. Fusing Agent Attention into GCN can effectively extract node information and greatly reduce computational complexity while ensuring model performance.

C. Neural Network Prediction Method Fused with Attention Mechanism

Park et al. proposed AGCN method[9], namely attention-based GCN, and put forward a novel attention-based pruning strategy to optimize information usage and ignore irrelevant information, so as to solve the problem that although existing DDI extraction methods mainly focus on the context or structural information of sentences with complementary effects, previous studies did not even utilize the full knowledge of input sentences, which might lead to the loss of key clues. Dongjiang Niu et al. from Qingdao University proposed a DDI prediction model SRR-DDI based on substructure refined representation learning via self-attention mechanism[10], so as to improve the robustness of substructure features that determine drug properties and further enhance the performance of DDI

Jiayi Zhong, "DDI Event Prediction via Graph Convolutional Network with Agent Attention Mechanism," *International Research Journal of Advanced Engineering and Science*, Volume 11, Issue 2, pp. 57-60, 2026.

International Research Journal of Advanced Engineering and Science
ISSN (Online): 2455-9024

prediction. This provides a feasible direction for the development of neural network models fused with attention mechanism.

III. Research Methods

A. Graph Convolutional Neural Network Fused with Agent Attention Mechanism

In view of this, this study uses the latest theoretical and technological achievements of graph convolutional neural network, Agent Attention and other aspects to fuse them into a new prediction model. The drug molecular structure information collected from TCMdatabase, DrugBank and other databases is taken as input, and node update is realized by aggregating the information of each hop neighbor node to extract drug molecular features and realize DDI event prediction (see Fig.1).

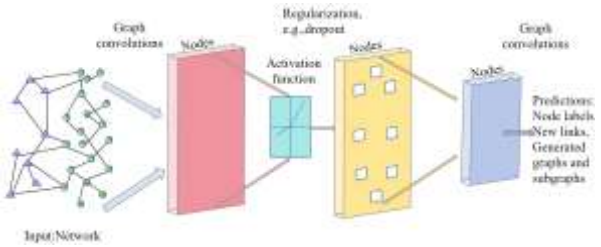

Fig. 1. GCN model diagram.

Different from traditional attention mechanisms such as Softmax Attention, this study uses a new attention mechanism called Agent Attention Mechanism, which integrates Softmax Attention and Linear Attention and introduces a set of agent tokens A. The newly introduced agent token A can be regarded as an "agent" of the query token Q, which aggregates information from K and V and then broadcasts the information back to Q. The dimension of A is n×d, and n is much smaller than N. The dimension of Q and K is reduced through matrix multiplication with A, thereby reducing the amount of calculation and achieving a good balance between computational efficiency and representation ability. Thus, it can solve the problem of excessive computation of drug node comparison in the study of DDI event prediction.

First, define the basic operation of the graph convolutional neural network, where $\tilde{D}^{-\frac{1}{2}}\tilde{J}$ is the normalized adjacency matrix, $\tilde{J} = J + I$ is the original adjacency matrix plus the identity matrix to include self-connections, and $\tilde{D}$ is the degree matrix of $\tilde{J}$. The node feature matrix X is updated to $H^{(l)}$ through graph convolution operation, where $W^{(l)}$ is the weight matrix of the l-th layer:

$$H^{(l)} = \sigma(\tilde{D}^{-\frac{1}{2}}\tilde{J}\tilde{D}^{-\frac{1}{2}}XW^{(l)}) \tag{1}$$

$$\alpha_{ij} = \frac{\exp(Leaky\,\mathrm{Re}\,LU(\alpha^T[Wh_i, Wh_j]))}{\sum_{k\in N_i}\exp(Leaky\,\mathrm{Re}\,LU(\alpha^T[Wh_i, Wh_j]))} \tag{2}$$

where h_i and h_j are the feature vectors of node i and node j respectively, and N_i is the neighbor set of node i. In this way, the model can adaptively assign different weights to each neighbor node, so as to better capture the complex relationship between nodes.

B. Generating Agent Tokens Based on TopK Method

In the Agent Attention Mechanism model, its agent token A is generated through a pooling operation. The TopK method is a method that efficiently finds the top K most important or highest-ranked elements by using techniques such as sorting, heap sorting, and quick selection. This method does not need to process the entire dataset, has no large number of learnable parameters, and can effectively reduce computation time and memory requirements.

In view of this, this study adopts TopK pooling to find the top K most important or highest-ranked nodes from a large number of drug molecular nodes, generate the corresponding agent token A for Agent Attention, and then use the Agent Attention Mechanism combined with Softmax Attention and Linear Attention to reduce the computational complexity (see Fig.2). After that, the importance of each substructure is calculated to highlight important substructures instead of emphasizing secondary substructures for DDI prediction, so as to model substructure-substructure interactions and complete the prediction of DDI events (see Fig.3).

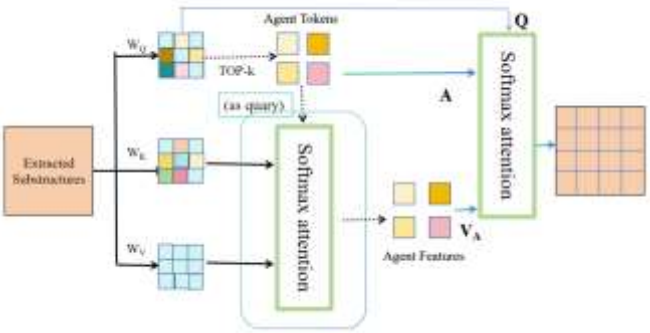

Fig. 2. Agent Attention model structure.

Define the number of agent tokens as n. The agent token A can be generated by applying TopK pooling operation to the input feature matrix X. The specific formula is as follows:

$$A = TopK(X, n) \tag{3}$$

This formula means selecting the most important feature vectors from the feature matrix as agent tokens.

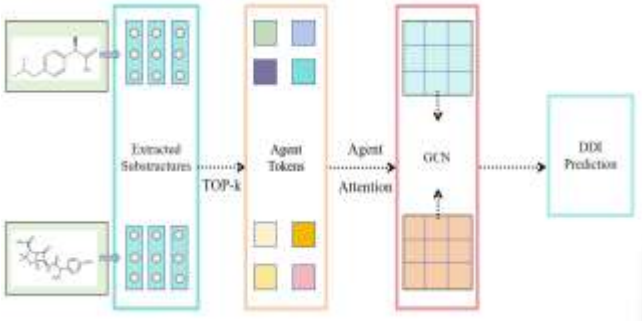

Fig. 3. Framework of DDI event prediction model.

Jiayi Zhong, "DDI Event Prediction via Graph Convolutional Network with Agent Attention Mechanism," *International Research Journal of Advanced Engineering and Science*, Volume 11, Issue 2, pp. 57-60, 2026.

IV. Experimental Results and Analysis

A. Datasets

In order to effectively deal with the challenges of DDI event prediction and verify the accuracy and efficiency of the model, this study collected different datasets. It not only focuses on the widely recognized data resources in academia, but also deeply explores professional drug data information. This study mainly uses Deng's dataset and DrugBank dataset. Deng's dataset has high authority and popularity in the field of drug prediction and contains rich drug interaction information. As a comprehensive drug database, DrugBank covers basic information such as drug molecular structure, mechanism of action and interaction between drugs, which is of great significance for in-depth understanding of DDI mechanism and improving the generalization ability of the prediction model.

B. Evaluation Indicators

Common classification evaluation indicators such as Accuracy (ACC), Recall (Rec), F1-score, and Precision (Prec) are adopted. Accuracy, as a basic indicator to measure the classification correctness of the model, reflects the overall classification performance of the model on all samples. However, since DDI event prediction usually involves unbalanced datasets (i.e., the number of positive samples and negative samples is quite different), the accuracy may be disturbed to a certain extent.

Therefore, this study combines other classification evaluation indicators to conduct a comprehensive evaluation of the model. Recall, also known as completeness, measures the proportion of positive samples (i.e., real DDI events) that can be correctly identified by the model. In DDI event prediction, high recall means that the model can identify more real DDI events, which is crucial for the evaluation of drug safety.

Precision measures the proportion of actual positive samples in the samples predicted as positive by the model. High precision indicates that the prediction results of the model are more reliable and can reduce false positives. In DDI event prediction, high precision helps to reduce unnecessary drug safety warnings, thereby improving the efficiency of clinical decision-making.

F1-score is the harmonic mean of precision and recall, which comprehensively considers the performance of the model in terms of accuracy and recall. The higher the F1-score, the better balance the model achieves between accuracy and recall. In DDI event prediction, a high F1-score means that the model can identify as many real DDI events as possible while ensuring the prediction accuracy.

To sum up, the comprehensive use of various evaluation indicators can comprehensively and objectively evaluate the model performance, so as to optimize the model in a timely manner.

C. Analysis of Model Evaluation Results

In this study, the existing models (such as DeepDDI, TrimeNet-DDI, SSI-DDI, MRCGNN, DGNN-DDI, etc.) and the model proposed in this study were evaluated on Deng's dataset and DrugBank dataset, and the generated data were extensively tested and fully compared with existing methods.

Experimental results show that on Deng's dataset, our model is significantly better than other existing models in accuracy, F1-score, precision and recall, especially the significant improvement in recall and F1-score, indicating that the model performs well in identifying real DDI events. On DrugBank dataset, our model also achieves excellent performance in accuracy, AUC, F1-score, precision and recall. The model also performs well in AUPR and AP indicators, further proving its advantages in dealing with unbalanced datasets and evaluating model ranking performance.

Through experiments on multiple model architectures, it is proved that this study has a very large room for improvement in reducing computational complexity and enhancing model expression ability. It shows great potential in capturing nodes and hidden information more accurately, effectively reducing computational complexity, and realizing reasonable prediction of DDI events.

TABLE I. Comparative evaluation on Deng's dataset.

	ACC	F1	Prec	Rec
DeepDDI	0.7807	0.6055	0.6611	0.5839
TrimNet-DDI	0.8570	0.6548	0.7046	0.6363
SSI-DDI	0.7866	0.4216	0.5139	0.3896
MRCGNN	0.8979	0.7791	0.8101	0.7688
DGNN-DDI	0.8921	0.8953	0.8699	0.9222
AGCA-TopK(ours)	0.9011	0.9024	0.8715	0.9347

TABLE II. Performance comparison on the DrugBank dataset.

	ACC	AUC	F1	Prec	Rec	AUPR	AP
MR-GNN	0.9323	0.9731	0.9339	0.9114	0.9576	0.9410	0.9645
SSI-DDI	0.9449	0.9838	0.9265	0.9509	0.9770	0.9814	0.9611
GMPNN-CS	0.9530	0.9846	0.9360	0.9360	0.9722	0.9785	0.9794
SA-DDI	0.9623	0.9880	0.9629	0.9502	0.9759	0.9834	0.9836
DGNN-DDI	0.9609	0.9894	0.9616	0.9472	0.9788	0.9863	0.9846
SRR-DDI	0.9667	0.9905	0.9672	0.9528	0.9824	------	0.9874
AGCA-TopK(ours)	0.9672	0.9910	0.9685	0.9550	0.9810	0.9880	0.9880

V. Conclusion and Prospect

A. Challenges and Deficiencies

This study focuses on DDI event prediction. The core innovation lies in the combination of agent attention mechanism and graph convolutional neural network. This method can effectively represent the interaction between drugs and reduce computational complexity. Experimental results show that the model performance is significantly improved, and the accuracy and precision achieve excellent results. In addition, the study also uses the TopK method to generate agent tokens for the agent attention mechanism, which further optimizes the model construction and achieves more accurate prediction of DDI events.

The integration of attention mechanism and graph convolution proposed in this study also has certain difficulties. The attention mechanism focuses on capturing key information of data, while graph convolution focuses on extracting local features of graph information. How to effectively integrate the two and make good use of both local and global information is a technical problem.

Since this study is proposed based on the method of using graph convolutional neural network to predict DDI events, the computing resources itself will be limited. When processing

Jiayi Zhong, "DDI Event Prediction via Graph Convolutional Network with Agent Attention Mechanism," *International Research Journal of Advanced Engineering and Science*, Volume 11, Issue 2, pp. 57-60, 2026.

large-scale data graphs, graph convolutional neural networks consume a lot of computing resources and memory due to complex node and edge information and convolution operations, which also restricts its application in large-scale datasets.

In addition, the TopK method has its own problems. Sorting all data during sorting wastes a lot of sorting time. In quick sorting, the TopK method cannot guarantee good complexity either.

B. Reflection and Improvement

In view of the problems in the research process, we can further study the basic principles and algorithms of graph convolutional neural network and explore more efficient network architectures, such as sparse graph convolution, hierarchical graph convolution and other methods, to reduce computational complexity and memory usage. Or consider introducing distributed computing and parallel processing technology to split large-scale graph data into multiple subgraphs and perform convolution operations respectively to improve computing efficiency.

In addition, for the limitations of the TopK method itself, more efficient TopK search algorithms can be studied, such as heap sorting, quick selection algorithm, etc., to reduce sorting time and improve the efficiency of the TopK method.

REFERENCES

[1] Bansal M, Yang J, Karan C. A community computational challenge to predict the activity of pairs of compounds[J]. Nature Biotechnology, 2014, 32(12): 1213-1222.

[2] LeCun Y, Boser B, Denker JS. Backpropagation applied to hand-written zip code recognition[J]. Neural Computation, 1989, 1(4): 541-551.

[3] Kipf TN, Welling M. Semi-Supervised Classification with Graph Convolutional Networks[C]. In: Proceedings of the International Conference on Learning Representations (ICLR), 2016.

[4] Tsotsos JK, Culhane SM, Wai WYK. Modeling visual attention via selective tuning[J]. Artificial Intelligence, 1995, 78(1-2): 507-545.

[5] Lin X, Quan Z, Wang Z. KGNN: knowledge graph neural network for drug-drug interaction prediction[C]. In: Proceedings of the International Joint Conference on Artificial Intelligence (IJCAI), 2020: 2739-2745.

[6] Yi Z, Zheng B, Chen X. DDI-GCN: Drug-drug interaction prediction via explainable graph convolutional networks[J]. Artificial Intelligence in Medicine, 2024, 144: 102640.

[7] [7] Lin G, Lei X, Chen M. MSResG: Using GAE and Residual GCN to Predict Drug-Drug Interactions Based on Multi-source Drug Features[J]. Computational Life Sciences, 2023, 15(2): 171-188.

[8] Han D, Ye T, Han Y. Agent Attention: On the Integration of Softmax and Linear Attention[J]. ArXiv, 2023, 2312.08874.

[9] Park C, Park J, Park S-H. AGCN: Attention-based graph convolutional networks for drug-drug interaction extraction[J]. Expert Systems with Applications, 2020, 159: 113538.

[10] Niu D, Xu L, Pan S. SRR-DDI: A Drug-Drug Interaction Prediction Model with Substructure Refined Representation Learning based on Self-Attention Mechanism[J]. Knowledge-Based Systems, 2024, 285: 111337.