Predicting Drug-Target Interactions Using a Bipartite Graph Model and Local-k-Dimensional Weisfeiler-Lehman Neural Machine (BG-δ-k-WLNM)

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INTRODUCTION

- Drug–target Interaction (DTI) prediction is a crucial task in drug discovery and drug repositioning.
- Traditional experimental methods are expensive and inefficient, making computational approaches a practical alternative.
- Recent advancements in Deep Neural Network (DNN) architectures have significantly impacted computational DTI prediction.
- Semi-supervised DNNs address the challenge of limited labeled data by leveraging unlabeled information and discovering latent patterns.
- A semi-bipartite graph is constructed using known DTIs and drug-drug/protein-protein similarities to provide richer structural context.
- Recently, Weisfeiler-Lehman Neural Machine (WLNM) has been proposed for link prediction on complex networks
- In this poster, we propose a supervised learning heuristic that employs WLNM combined with DNN on DTI Bipartite Graph (BG-δ-k-WLNM).
- The model applies graph labeling and vertex ordering to preserve structural roles before encoding subgraphs into embeddings.

OBJECTIVE

- Develop a novel deep learning framework (BG-δ-k-WLNM) for predicting drug–target interactions using bipartite graph structures.
- Capture higher-order topological patterns through local-k-dimensional WL refinement of 2-tuples.
- Improve prediction accuracy by encoding subgraph patterns into embeddings and learning them via a neural network.

DATASET

Statistics	Drugs	Targets	Known Interactions
NR	54	26	90
GPCR	223	95	635
IC	210	204	1476
Enzyme	445	664	2926

Table. 1. *D*atasets specification

METHODS

To capture the topological structure of drug-target relationships, we represent the interaction network as a semi-bipartite graph defined as: G =< D, T, E>

Step 1) Extract k-Tuples

- We generate all possible k-tuples of nodes, where k defines the number of nodes in each tuple
- The k-tuples serve as local structural units
- The number of k-tuples of size K follows the combinatorial pattern

$$\text{Number of k-tuples} = \binom{K}{k} \times k!$$

Step 2) Pattern Encoding of the Extracted

- We apply local δ-k WL color refinement to assign labels
- While K=2, then each tuple represents a drug-target, drug-drug, or target-target pair.

Step 3) Aggregate Tuple Features

- After labeling all k-tuples, we map them to a numeric form using integer encoding: a low-dimensional vector

Step 4) Learning phase by neural network

- The encoded vectors are used to train the DNN
- Fully-connected layers with 32, 32, and 16 hidden neurons
- 10-fold cross-validation
- Activation layer: Rectified Linear Unit (ReLU)
- A SoftMax layer is used as the output layer

Experiments: AUROC

- Area under TPR and FPR

$$TPR = \frac{TP}{TP + FN}$$

$$FPR = \frac{FP}{FP + TN}$$

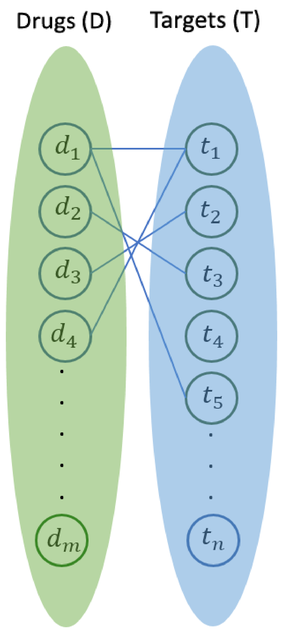


Fig. 1. *The drug-target* semi-bipartite graph structure.

RESULTS

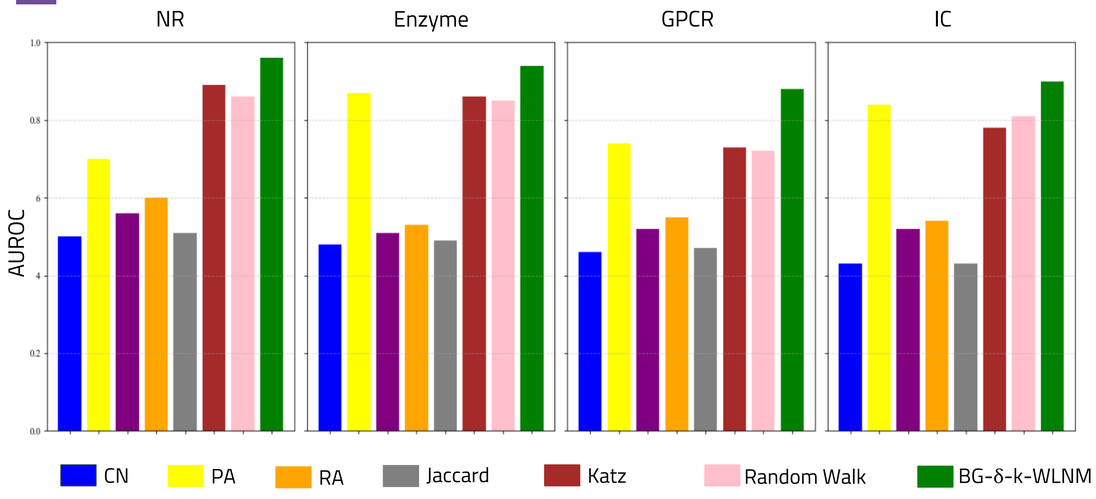


Fig. 2. Comparing the AUROC performance metric of our method (BG-δ-K-WLNM) with others for four datasets.

RESULTS

- BG-δ-k-WLNM outperformed all baseline methods (heuristic and WL-based) across four benchmark datasets (NR, GPCR, IC, Enzyme) in terms of AUROC
- Incorporating drug-drug and protein-protein similarities improved prediction accuracy by 14–18%
- An18.5% AUROC gain on the NR dataset compared to existing WL-based methods.

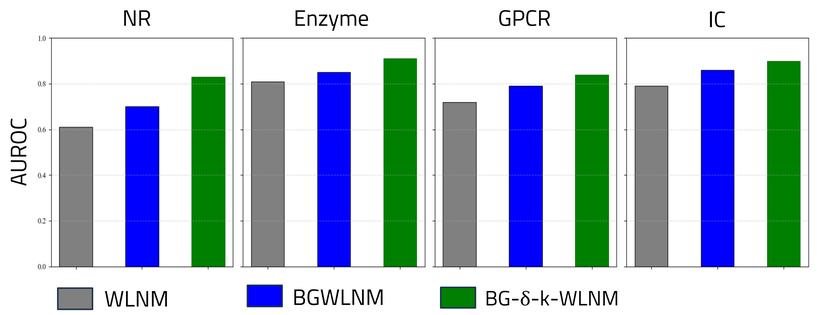


Fig. 3. Comparing the AUROC performance metric of our method (BG-δ-K-WLNM) with other WL-based methods for four datasets.

DISCUSSION AND CONCLUSION

- We propose BG-δ-k-WLNM, a deep learning framework for predicting drug–target interactions using bipartite graph structures.
- Experimental results confirm that our method outperforms traditional heuristics and existing WL-based approaches.
- By applying local-k-dimensional WL refinement on 2-tuples, our model captures complex topological patterns.
- It effectively integrates similarity data and subgraph embeddings to enhance prediction accuracy.

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