HiGraphDTI: Hierarchical Graph Representation Learning for Drug-Target Interaction Prediction–Supplementary Materials

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1 Comparing Baseline Models

DeepDTA [6] is a deep-learning model that leverages only the sequence information of drugs and targets to predict drug-target binding affinity. It utilizes a convolutional neural network to encode SMILES and amino acid sequences separately, followed by concatenation after max-pooling. Then, the concatenated vector is input into a fully connected layer to output the predicted probabilities. To adapt DeepDTA, a drug-target affinity prediction model, to the DTI prediction task, we replace the loss function in its last layer with binary cross-entropy loss.

DeepConv-DTI [5] utilizes convolution on amino acid subsequences of varying lengths to capture local residue patterns in proteins, obtaining feature representations for targets. Additionally, it employs fully connected layers on drug fingerprints to acquire feature representations for drugs. The drug and target features are concatenated and passed through a fully connected layer for prediction.

MolTrans [4] develops a substructure mining algorithm for extracting substructure properties in DTI and efficiently leverages a substantial amount of unlabeled data. The algorithm decomposes drugs and targets into sets of subsequences to build feature representations, encoding by the Transformer encoder. Ultimately, CNNs are applied to capture higher-order interactions from the feature representations for DTI prediction.

TransformerCPI [2] leverages graph neural networks and convolutional neural networks to extract features for drugs and targets. The target features serve as the output of the Transformer encoder, while the drug features serve as the input to the Transformer decoder, facilitating interaction. The resulting interactive features are utilized for DTI prediction.

IIFDTI [3] comprises four feature components: target features extracted by convolutional neural networks, drug features extracted by graph attention networks, and two interaction features obtained from the Transformer. The two interaction features refer to the target features with aggregated drug information

and the drug features with aggregated target information. These four feature components are concatenated for Drug-Target Interaction (DTI) prediction.

DrugBAN [1] employs graph convolutional neural networks and convolutional neural networks to extract feature representations for drugs and targets, respectively. Additionally, it utilizes a bilinear attention network module to capture local interactions between drugs and targets for DTI prediction. Its paper mentions two different experimental setups:in-domain and cross-domain. Based on our experimental data, we chose the in-domain experimental setup for comparison.

2 Detailed Experimental Results

The detailed comparative experiments for each dataset are shown in the following tables, with the highest scores highlighted in bold.

Table 1. Comparison results on human dataset

Methods	AUC(Std)	AUPR(Std)	Precision(Std)	Recall(Std)
DeepDTA	0.972 (0.001)	0.973 (0.002)	0.938 (0.012)	0.935 (0.017)
DeepConv-DTI	0.967 (0.002)	0.964 (0.004)	0.939 (0.018)	0.907 (0.023)
MolTrans	0.974 (0.002)	0.976 (0.003)	**0.955 (0.012)**	0.933 (0.022)
TransformerCPI	0.970 (0.006)	0.974 (0.005)	0.911 (0.021)	0.937 (0.011)
IIFDTI	0.984 (0.003)	0.985 (0.003)	0.946 (0.017)	0.947 (0.017)
DrugBAN	0.984 (0.001)	0.981 (0.001)	0.941 (0.006)	0.943 (0.008)
Ours	**0.985 (0.001)**	**0.988 (0.001)**	0.944 (0.006)	**0.952** (0.007)

Table 2. Comparison results on *C.elegans* dataset

Methods	AUC(Std)	AUPR(Std)	Precision(Std)	Recall(Std)
DeepDTA	0.983 (0.001)	0.984 (0.007)	0.970 (0.011)	0.960 (0.010)
DeepConv-DTI	0.983 (0.002)	0.985 (0.001)	0.954 (0.006)	0.936 (0.008)
MolTrans	0.982 (0.003)	0.982 (0.003)	**0.971 (0.007)**	0.963 (0.012)
TransformerCPI	0.984 (0.002)	0.983 (0.003)	0.949 (0.011)	0.948 (0.012)
IIFDTI	0.991 (0.002)	0.992 (0.003)	0.954 (0.010)	**0.971 (0.011)**
DrugBAN	0.989 (0.001)	0.990 (0.002)	0.968 (0.003)	0.963 (0.002)
Ours	**0.993 (0.001)**	**0.993 (0.001)**	0.954 (0.007)	0.959 (0.008)

Table 3. Comparison results on BindingDB dataset

Methods	AUC(Std)	AUPR(Std)	Precision(Std)	Recall(Std)
DeepDTA	0.934 (0.007)	0.934 (0.008)	0.858 (0.021)	0.860 (0.023)
DeepConv-DTI	0.922 (0.003)	0.921 (0.004)	0.835 (0.024)	0.846 (0.031)
MolTrans	0.899 (0.006)	0.897 (0.010)	0.826 (0.021)	0.768 (0.019)
TransformerCPI	0.933 (0.011)	0.934 (0.015)	0.840 (0.023)	0.891 (0.022)
IIFDTI	0.944 (0.003)	0.945 (0.004)	0.879 (0.011)	0.873 (0.013)
DrugBAN	0.945 (0.007)	0.944 (0.005)	0.852 (0.018)	**0.893 (0.023)**
Ours	**0.954 (0.003)**	**0.955 (0.003)**	**0.913 (0.025)**	0.853 (0.034)

Table 4. Comparison results on GPCR dataset

Methods	AUC(Std)	AUPR(Std)	Precision(Std)	Recall(Std)
DeepDTA	0.776 (0.006)	0.762 (0.015)	0.713 (0.014)	0.712 (0.015)
DeepConv-DTI	0.752 (0.011)	0.685 (0.010)	0.695 (0.020)	0.713 (0.021)
MolTrans	0.807 (0.004)	0.788 (0.009)	0.699 (0.007)	0.762 (0.014)
TransformerCPI	0.842 (0.007)	0.837 (0.010)	0.755 (0.013)	0.796 (0.015)
IIFDTI	0.845 (0.008)	0.842 (0.007)	**0.766 (0.009)**	0.783 (0.017)
DrugBAN	0.837 (0.010)	0.823 (0.013)	0.699 (0.023)	**0.893 (0.023)**
Ours	**0.858 (0.004)**	**0.850 (0.003)**	0.754 (0.006)	0.791 (0.014)

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