

DeepPurpose: a Deep Learning Library for Drug-Target Interaction Prediction and Applications to Repurposing and Screening

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Abstract

Accurate prediction of drug-target interactions (DTI) enables drug discovery tasks, including virtual screening and drug repurposing, which can shorten the time to identify promising drug candidates and provide cures to patients. Recently, there is a growing number of research that developed deep learning (DL) models for DTI. Despite their superior performance, these research models are difficult to use in real drug discovery practice due to the complexity of deploying the research code as well as the restricted data formatting, model capacity, and evaluation setting. We present DeepPurpose, a comprehensive and easy-to-use software toolkit for DL based DTI prediction with applications to drug screening and repurposing. The unique feature of DeepPurpose is that it enables non-computational drug development scientists to identify drug candidates based on five pre-trained DL models with only a few lines of codes. Further, computer scientists can use DeepPurpose to train customized DTI prediction models with 15 drug and target encodings and 50+ novel DL architectures. To tackle method development challenges, DeepPurpose also supports various data split settings and preloads five benchmarking datasets. We demonstrated that DeepPurpose allows users to obtain state-of-the-art prediction performance on several benchmark datasets. We also presented several case studies, including a study on drug repurposing for COVID-19, where promising drug candidates currently investigated in clinical trials are ranked high in DeepPurpose’s predictions.

Introduction

Drug-target interactions (DTI) characterize the binding of drug molecules to the protein targets, Accurate identification of DTI is fundamental for drug dis [1–4]. Among others, drug screening and repurposing are two main applications based on DTI. Drug screening helps identify ligand candidates that can bind to the protein of interest [5], whereas drug repurposing finds new therapeutic purposes for existing drugs [6–8]. Both tasks can alleviate time-consuming and labor-intensive processes in drug development, which are especially important for finding effective and safe treatments for emerging pathogens, such as COVID-19 [9].

Deep learning (DL) has recently demonstrated superior performance than traditional computational methods because of the expressive power of deep neural networks in extracting, processing, and extrapolating complex patterns in molecular data [10–13]. For example, an existing study shows they quickly found a drug candidate that could act against an untreatable strain of bacteria with DL [14]. There are many DL models designed for DTI prediction [12, 13, 15], which can be used for drug repurposing and virtual screening. However, to generate predictions, deploy predictive models in practice, test and evaluate model performance, and understand model robustness to missing and incomplete data, one needs to have considerable programming skills and extensive biochemical knowledge [16, 17]. Many existing tools [12, 13, 15, 18] are designed for computer scientists and are challenging to use by domain researchers with limited experience in training and deploying deep learning models. Furthermore, each open-sourced tool has a different programming interface and is coded differently, which prevents easy integration of outputs from a variety of methods and construction of multi-model ensembles [19].

In this work, we break the technical barrier by introducing DeepPurpose, a powerful Python toolkit that can recommend most likely drug candidates. Using only a few code lines that specify the target amino acid sequences and the drug candidates, DeepPurpose loads and processes input molecular data, feeds the data into multiple state-of-the-art deep learning models pre-trained on the large BindingDB-Kd datasets [20] with different drug and target encoders. DeepPurpose aggregates prediction results and generates a descriptive ranked list in which drug candidates with the highest predicted binding scores are placed at the top. This list can then be examined by domain scientists who inspect the top-ranked drug candidates for downstream experimental validation.

In addition to the design mentioned above for helping domain scientists, DeepPurpose also offers a flexible framework for computer scientists to innovate new models for drug-target interaction prediction, expediting repurposing, and screening. In particular, DeepPurpose includes multiple molecular encoders, including deep neural networks on classic molecular descriptors from computational biology and cheminformatics [21–26], a convolutional neural network (CNN) [27], a convolutional recurrent neural network (CNN-RNN) [28, 29], Transformer encoders [30], and Message-Passing Neural Network (MPNN) [31]. In total, DeepPurpose combines seven encoders for proteins and eight encoders for drugs and offers over 50 predictive models. To the best of our knowledge, most encoders and models are novel approaches for drug interaction prediction. Further, DeepPurpose allows rapid prototyping of new methods by offering a ten-line programming framework that unlocks new models with a variety of robust settings for performance evaluation and rigorous method benchmarking provided by dataset loaders with fixed training/testing splits.

Finally, we conducted extensive experiments to demonstrate that models implemented in DeepPurpose achieve competitive performance compared to state-of-the-art baselines. Further, we provided case studies on repurposing for COVID-19, where DeepPurpose generates promising drug candidates investigated in clinical trials.

Related Works

Drug Target Interaction Prediction

Computational methods for DTI prediction have received considerable attention in recent literature. Similarity-based methods, such as kernel regression [32] and matrix factorization [33], infer new DTI relations by exploiting existing DTI's drug-target similarity information. Feature-based methods first generate numerical descriptors for

drugs [21, 34, 35] and proteins [23, 25, 26] and then feed them into downstream prediction classifiers. The typical classifiers include gradient boosting [36] and random forest [37]. Recently, DL based methods [12, 13, 15, 38] have achieved strong performance because they can capture intricate non-linear molecular patterns. Notably, DeepDTA uses a CNN to encode drugs and proteins, and GraphDTA uses graph neural networks to learn powerful drug encodings.

We formulate deep learning methods for DTI prediction as an encoder-decoder framework [39], which covers a variety of DTI models, including most of the previous works. That means that each method has two key components. First, the encoder component specifies a deep transformation function that maps drugs and proteins to points in an embedding space, where the structure of the embedding space is optimized to reflect the structure of the input data. Second, the decoder component takes the learned drug and protein embeddings and combines them to output the final interaction activity scores. The encoder-decoder framework is a unifying mathematical formulation of deep learning methods for DTI prediction. Unlike previous toolkits that only use one type of encoder for drugs and proteins, DeepPurpose adopts the unifying formulation. Because of that, DeepPurpose can implement a flexible deep learning framework integrating 15 encoders, unlocking state-of-the-art methods for DTI prediction.

Deep Learning Libraries for Drug Discovery and Development

Next, we briefly review existing deep learning libraries developed to assist in a variety of drug discovery and development tasks. Most notably, DeepChem [40] provides a general framework for life science tasks. MoleculeNet [41] offers a benchmark for drug property prediction. Similarly, GuacaMol [42] designs a benchmark for de novo molecule generation and a related library OpenChem (<https://github.com/MarieWelt/OpenChem>) is designed for modeling molecules. More relevant to DeepPurpose is a library called DeepScreening [43] that provides a web interface for in silico drug efficacy screening using RNN/DNN encoders for drugs. Concurrently, kGCN [44] constructs a GCN-based framework for DTI prediction. In contrast, DeepPurpose is more powerful since it not only provides 15 encoders for both drugs and proteins but also presents a user-friendly interface for both domain researchers and computer scientists.

Design and Implementation

Overview of DeepPurpose

DeepPurpose uses an encoder-decoder framework for drug-target interaction prediction (Fig 1). Drug repurposing and screening are two important applications of DTI prediction. DeepPurpose will take the drug's simplified molecular-input line-entry system (SMILES) string and target amino acid sequence pair (Fig 2) as input, and output a score indicating the binding activity of the drug target pair.

Encoders

DeepPurpose provides 8 drug encoders and 7 protein target encoders, ranging from classic chemical fingerprints to various deep neural networks, each with a variety of customizable parameters. DeepPurpose feeds the embeddings, returned by the drug and target encoders into a decoder to produce the final prediction score. As such, DeepPurpose has a uniquely appealing property in a sense that the user can easily switch encoders. By specifying the name of the encoder of interest, DeepPurpose automatically switches to the appropriate model and connects the encoder with the relevant decoder for prediction.

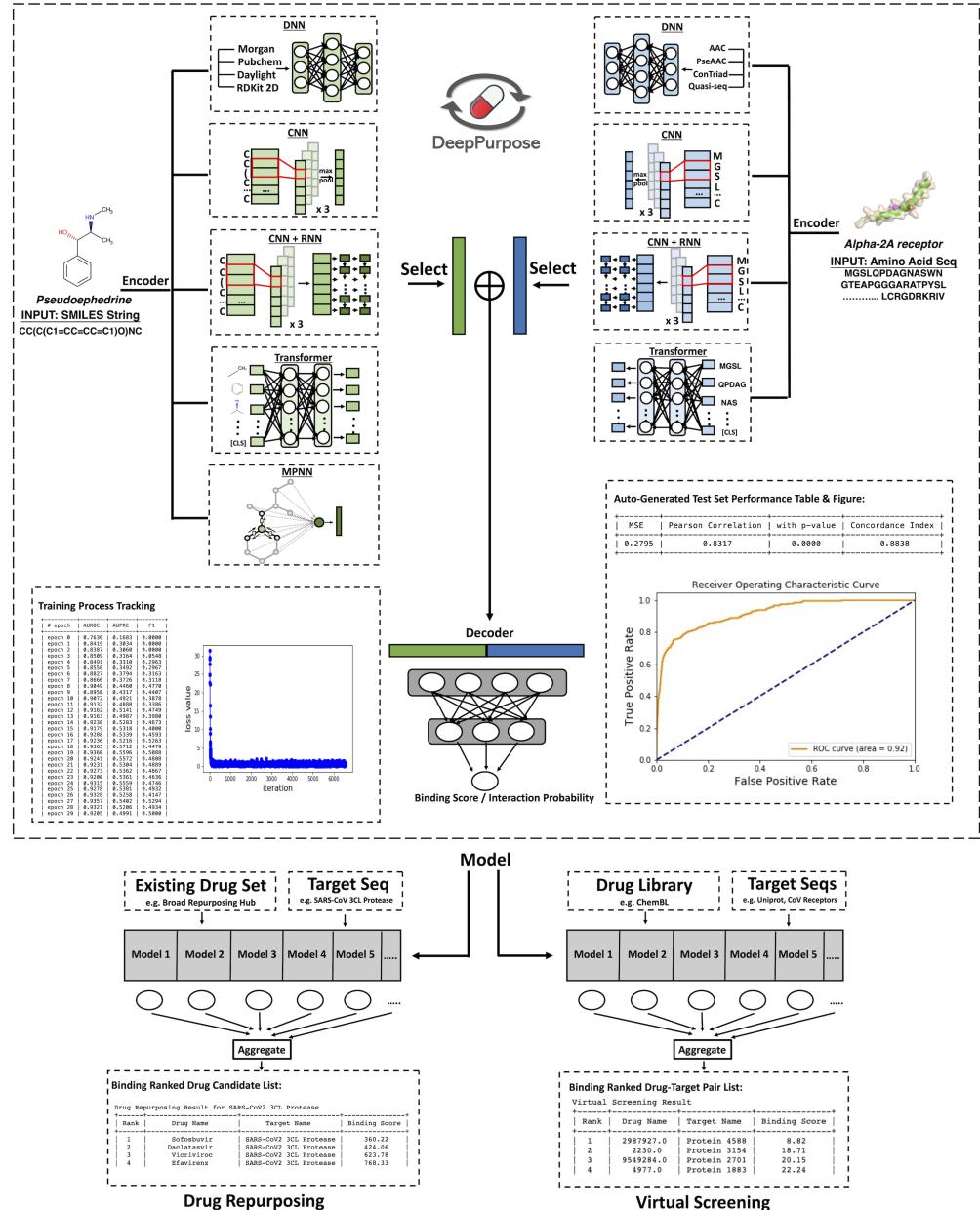


Fig 1. DeepPurpose method overview. DeepPurpose takes the accessible drug's SMILES string and target's amino acid sequence and encodes them through one of the selected 15+ encoder models. Then, the latent representations are concatenated and fed into a decoder to classify. The model is trained end-to-end and the training process, along with the test set performance is automatically-generated and reported. For drug repurposing and virtual screening, given a drug library and a new target of interest or new drug-target pairs of interest, DeepPurpose feeds them into five pretrained models and the predictions are aggregated and ranked to generate a drug-target list. This list can then be used for wet-lab validation. This entire process can be done using one line of code in DeepPurpose.

Drug Encoders

The input molecule is represented by the SMILES fingerprint [45, 46] corresponding to the relevant molecular graph. DeepPurpose supports the following types of drug

Ritonavir: CC(C)C1=NC(=CS1)CN(C)C(=O)NC(C(C)C)C(=O)NC(CC2=CC=CC=C2)CC(C(CC3=CC=CC=C3)NC(=O)OCC4=CN=CS4)O

SARS-CoV2-3CL Protease: SGFRKMAFPKGVEGCMVQVTCGTTLNGLWDDVYCPRHVICTEDMLNPNEYEDLLIRKSNNHNFLVQA
GNVQLRVIGHSMQNCVVLKLKVDTANPKTPKYKFVRIQPQQTFSVLACYNGSPSGVYQCAMRPNFTIKGSFLNGSCGSVGFNIDYDCVSFCYMH
MELPTGVHAGTDLEGNFYGPVDRQTAQAAGTDTTITVNVLAWLYAAVINGDRWFLNRFTTLNDFNLVAMKYNYEPLTQDHVDILGPLSAQTG
IAVLDMCASLKEELLQNGMNGRTILGSALLEDEFTPFDVVVRQCSGVTFQ

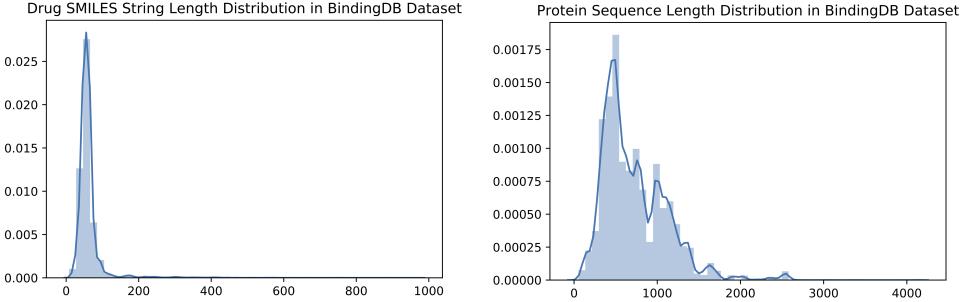


Fig 2. Input visualization. Drug is represented as a SMILES string and target is represented as an amino acid sequence. The length distribution of the input is provided.

embeddings that are inferred from the input SMILES fingerprints.

1. **Morgan** [21] Fingerprint is a 1024-length bits vector that encodes circular radius-2 substructures. A multi-layer perceptron is then applied to the fingerprint vector.
2. **Pubchem** [22] is an 881-length bits vector, where each bit corresponds to an expert hand-crafted substructure. A multi-layer perceptron is then applied on top of the vector.
3. **Daylight**¹ is a 2048-length vector that encodes path-based substructures. A multi-layer perceptron is then applied on top of the vector.
4. **RDKit-2D**² is a 200-length vector that describes the global pharmacophore property. It is normalized to make the range of the features on the same scale using cumulative density function fit given a sample of the molecules.
5. **CNN** [27] is a multi-layer 1D convolutional neural network. The SMILES characters are first encoded with an embedding layer and then fed into the CNN convolutions. A global max-pooling layer is then attached, and an embedding describing the drug is generated.
6. **CNN+RNN** [28, 29] attaches a bidirectional recurrent neural network (GRU or LSTM) on top of the 1D CNN output to leverage the more global temporal dimension of the drug. The input is also the SMILES character embedding.
7. **Transformer** [30] uses a self-attention based transformer encoder that operates on the sub-structure partition fingerprint [43].
8. **MPNN** [31] is a message-passing graph neural network that operates on the drug molecular graphs. It transmits latent information among the atoms and edges, where the input features incorporate atom/edge level chemical descriptors such as atom/bond type, formal charge, chirality and etc. A readout function (mean/sum) is used to obtain a molecular graph-level embedding vector.

¹Daylight chemical information systems: <https://www.daylight.com/>

²<https://github.com/bp-kelley/descriptastorus>

Protein Encoders

The input targets are proteins represented by amino acid sequences. DeepPurpose uses protein sequence information to infer protein embeddings with any of the following protein encoders:

1. **AAC** [23] is an 8,420-length vector where each position corresponds to an amino acid k-mers, which is an amino acid subsequence of length k. The k is up to 3.
2. **PseAAC** [24] is a 30-length vector that includes the protein hydrophobicity and hydrophilicity patterns information in addition to the composition.
3. **Conjoint Triad** [25] is a 343-length descriptor that uses the continuous three amino acid frequency distribution from a hand-crafted 7 classes (AGV, ILFP, YMTS, HNQW, RK, DE, C) according to their dipoles and volumes of the side chains.
4. **Quasi Sequence** [26] takes account of the sequence order effect using a set of sequence-order-coupling numbers. Combination of sequence composition and correlation of physicochemical properties such as hydrophobicity, hydrophilicity, polarity, and side-chain volume.
5. **CNN** [27] is a multi-layer 1D convolutional neural network. The target amino acid is decomposed to each individual character and is encoded with an embedding layer and then fed into the CNN convolutions. It follows a global max-pooling layer.
6. **CNN+RNN** [29,39] attaches a bidirectional recurrent neural network (GRU or LSTM) on top of the 1D CNN output to leverage the sequence order information.
7. **Transformer** [30] uses a self-attention based transformer encoder that operates on the sub-structure partition fingerprint [47] of proteins. Since the transformer's computation time and memory is quadratic on the input size, it is computationally infeasible to treat each amino acid symbol as a token. The partition fingerprint decomposes amino acid sequence into protein substructures of moderate-sized such as motifs and then each of the partitions is considered as a token and fed into the model.

Decoders, Objective functions, and Model Inference

The generated drug and protein embeddings will be fed into a multi-layer perceptron decoder. There are two classes of tasks/datasets in DTI prediction. The label can be either continuous binding scores, including Kd and IC50, or a binary output indicating whether they can bind. DeepPurpose can automatically detect whether the task is a regression for continuous label or classification for the binary label by counting the number of unique labels in the data. For binding affinity score prediction, the training uses mean squared error (MSE) loss; for binary interaction prediction, it uses binary cross-entropy (BCE) loss:

$$\mathcal{L}_{MSE} = \frac{1}{n} \sum_{i=1}^n (y_i - \hat{y}_i)^2, \quad (1)$$

$$\mathcal{L}_{BCE} = \frac{1}{n} \sum_{i=1}^n y_i \log(\hat{y}_i) + (1 - y_i) \log(1 - \hat{y}_i), \quad (2)$$

where y_i is the true label and \hat{y}_i is the predicted label for i-th drug-target pair. For evaluation, the following metrics are included: MSE, Concordance Index, and Pearson Correlation for continuous regression and Receiver Operating Characteristics-Area Under the Curve (ROC-AUC), Precision Recall-Area Under the Curve (PR-AUC) and F1 score at threshold 0.5 for binary classification. During inference, given new targets or new drugs, the model prediction is used as the predicted binding score/interaction probability.

Applications to Drug Repurposing and Drug Efficacy Screening

After the models are trained from the DTI prediction datasets, they can be used to do drug repurposing and screening since the model is able to capture the chemical knowledge to infer a new drug-target pair's binding affinity. For drug repurposing, given a new target protein and a drug repurposing library, which is an array of approved drugs, DeepPurpose replicates the target and form drug-target pairs, which are then fed into the model for inference. In the case of drug efficacy screening, given many drug-target pairs, we directly feed them into the model, which, in turn, produces output prediction scores.

Pretrained Models and Prediction Aggregation

DeepPurpose includes over 20 pre-trained models. This is important because deep learning models require considerable computational resources for training. Thus, providing a pre-trained model that does not need to be trained from scratch can significantly reduce the time and resources needed for deploying the model in a real-world application. Using a pre-trained model is also desirable for a new target with a low amount of training data since it could benefit from the knowledge transferred via models learned from massive data [48]. Unlike most previous works that mainly rely on a single model for prediction, DeepPurpose integrates many encoders in one framework and ensemble multiple models for repurposing and virtual screening. Such an multi-model approach can greatly reduce the limitation and bias brought forward by any individual model, albeit a well-performing approach. DeepPurpose includes three aggregation strategies: mean, max, and the average of mean and max. The mean measures the overall performance across models, while the max favors the most reliable signals across all models. To leverage both approaches, we also include an aggregation scheme that takes the average of mean and max. For the one-line default mode for domain scientists, we use the latter option.

One-Line Mode for Drug Repurposing and Screening

For biomedical scientists, DeepPurpose provides a one-line mode that only requires the target protein amino acid sequences and the drug candidates' inputs. Then, DeepPurpose uses five pretrained models trained on large BindingDB datasets and applies a mean-max aggregation scheme to ensemble the prediction result. The result binding scores are ranked, and the top drug-target pairs are retrieved. The entire pipeline happens in one line. A sample code is illustrated in Fig 3.

The five pretrained models defined in the default One-Line mode are listed below:

1. MPNN for drugs and CNN for proteins;
2. CNN for drug and CNN for proteins;
3. Daylight for drugs and AAC for proteins;
4. Morgan fingerprint for drugs and AAC for proteins;

```

A. [-----]
>>> from DeepPurpose import oneliner
>>> from DeepPurpose.dataset import *
>>>
>>> oneliner.repurpose(*read_file_target_sequence('target.txt'), \
    *read_file_repurposing_library('repurpose.txt'))

[-----]
>>> from DeepPurpose import oneliner
>>> from DeepPurpose.dataset import *
>>>
>>> oneliner.virtual_screening(['MKK...LIDL', ...], ['CC1=C...C4)N', ...])
[-----]

B. [-----]
>>> from DeepPurpose import models
>>> from DeepPurpose.utils import *
>>> from DeepPurpose.dataset import *
>>>
>>> X_drug, X_target, y = load_process_DAVIS(SAVE_PATH, binary=False)
>>>
>>> drug_encoding, target_encoding = 'CNN', 'CNN'
>>> train, val, test = data_process(X_drug, X_target, y, drug_encoding, \
    target_encoding, split_method='random', \
    frac=[0.7, 0.1, 0.2], random_seed = 1)
>>>
>>> config = generate_config(drug_encoding, target_encoding, \
    cls_hidden_dims = [1024,1024,512], \
    train_epoch = 100, LR = 0.001, batch_size = 256, \
    cnn_drug_filters = [32,64,96], \
    cnn_drug_kernels = [4,8,12], \
    cnn_target_filters = [32,64,96], \
    cnn_target_kernels = [4,8,12])
>>>
>>> model = models.model_initialize(**config)
>>> model.train(train, val, test)
[-----]

```

Fig 3. DeepPurpose programming framework illustration. A. Generate a drug candidate list using a one-line mode for non-computational researchers. B. A 10-lines framework for machine learning method researchers.

5. Morgan fingerprint for drugs and CNN for proteins.

The above-pretrained model architectures are selected based on the following principles.

- The pretrained models should have literature support, i.e., GraphDTA [15] (Graph Neural Network+CNN) for model 1 and DeepDTA [12] (CNN+CNN) for model 2;
- The models should include classic informatics embedding since they sometimes contain more global information that deep learning-based methods may miss [19] (Morgan+AAC, Daylight+AAC) as model 3 and model 4;
- A hybrid model between DL based method and classic embeddings (Morgan+CNN) as model 5. We omit transformers and CNN-RNN based methods due to the consideration that pretrained models need to be relatively lightweight for deployment.

Framework for Drug-Target Interaction Prediction

For computer scientists, DeepPurpose provides a 10-lines framework that accepts user-customized information to conduct method research. For example, it enables easy

switching of different encoders, supports customized data split such as cold drug setting, and allows almost any model parameters or optimizer hyperparameters. A sample code is illustrated in Fig 3.

Additional Functionalities

DeepPurpose provides several additional functions that can aid users in drug repurposing and virtual screening. First, DeepPurpose provides many types of data: public large binding affinity dataset such as BindingDB-Kd [20], KIBA [36], DAVIS [49]; bioassay data such as AID1706 for SARS-CoV 3CL Protease; repurposing library such as Broad Repurposing Hub [50], antiviral drugs; target proteins such as SARS-CoV2 3CL Protease, Helicase, endoRNase, etc. This can save users valuable time since the data sources are scattered and information to process the raw data is limited online. With one line of code, DeepPurpose downloads and preprocesses the dataset to downstream models' compatible input. We also provide data loading functions from users' txt files. Second, binding affinity scores such as K_d , IC_{50} is recorded in the nM unit. However, the label distribution is very skewed. Hence, DeepPurpose also provides a convert unit function that can transform the label unit to log-scale for easy regression and also convert back when doing repurposing and virtual screening. Third, some classic encoders require some preprocessing time. DeepPurpose provides a reference time to help users estimate the computing hours. Fourth, DeepPurpose supports Bayesian Optimization hyperparameter tuning. Fifth, DeepPurpose takes the input of only one drug to model screening data for a target that does not have protein sequence format, such as bacteria.

Results

We conduct three experiments to evaluate DeepPurpose.

Predictive Performance on Drug-Target Interaction Prediction

First, we demonstrate that various models in DeepPurpose achieve competitive performance against state-of-the-art DL models for DTI prediction tasks on two benchmark datasets, DAVIS [49], and KIBA [36]. We compare it with DeepDTA [12], GraphDTA [15], two state-of-the-art DL models, and KronRLS [32], a classic method. Since DAVIS and KIBA are binding scores, the evaluation metric is MSE and Concordance Index. We use 7:1:2 train: validation: test splits. Dataset statistics are provided in Table 1.

Table 1. Data Statistics.

Dataset	Num. of Drugs	Num. of Proteins	Num. of Interactions
DAVIS [49]	68	379	30,056
KIBA [36]	2,068	229	118,254
BindingDB-Kd [20]	13,349	1,658	74,641

We report the performances of seven DeepPurpose models and three state-of-the-art models for DTI prediction on DAVIS and KIBA in Table 2. We find that DeepPurpose achieves competitive performance on all metrics on both datasets, confirming its powerful performance. Specifically, we find using MPNN for drugs and AAC for target proteins achieve the best result in both datasets. It has 7.6% increase in MSE, 1.3% increase in concordance index for DAVIS dataset and 2.8% increase in MSE, 1.2% increase in concordance index for KIBA dataset over the best baseline.

Table 2. Drug target interaction predictive performance on benchmark datasets. The bottom seven methods are from DeepPurpose. Results reported with five dataset splits average and standard deviation. Note that all models including the baselines run on the same five data splits to ensure fair comparison.

Dataset 1: DAVIS			
	Model	MSE	Concordance Index
Baselines	KronRLS	0.329 (0.019)	0.847 (0.006)
	GraphDTA	0.263 (0.015)	0.864 (0.007)
	DeepDTA	0.262 (0.022)	0.870 (0.003)
DeepPurpose	CNN+CNN	0.254 (0.018)	0.879 (0.011)
	MPNN+CNN	0.271 (0.012)	0.858 (0.007)
	MPNN+AAC	0.242 (0.009)	0.881 (0.005)
	CNN+Trans	0.282 (0.009)	0.852 (0.006)
	Morgan+CNN	0.271 (0.012)	0.858 (0.007)
	Morgan+AAC	0.258 (0.012)	0.861 (0.008)
	Daylight+AAC	0.277 (0.014)	0.861 (0.008)
Dataset 2: KIBA			
	Model	MSE	Concordance Index
Baselines	KronRLS	0.852 (0.014)	0.688 (0.003)
	GraphDTA	0.183 (0.003)	0.862 (0.005)
	DeepDTA	0.196 (0.008)	0.864 (0.002)
DeepPurpose	CNN+CNN	0.196 (0.005)	0.856 (0.004)
	MPNN+CNN	0.222 (0.006)	0.825 (0.003)
	MPNN+AAC	0.178 (0.002)	0.872 (0.001)
	CNN+Trans	0.240 (0.013)	0.818 (0.004)
	Morgan+CNN	0.229 (0.008)	0.825 (0.004)
	Morgan+AAC	0.233 (0.009)	0.823 (0.004)
	Daylight+AAC	0.252 (0.014)	0.808 (0.008)

Prediction Evaluation for Pretrained Models in One-Line Mode

Second, we observe that DAVIS and KIBA are high throughput screening data, and the unique number of proteins and targets is small. Due to the small size, models trained on these two datasets are not ideal for generalization over unseen drugs and proteins, especially for what we need for the one-line pretrained model. We thus use pre-trained models that are trained on a large BindingDB-Kd dataset, which consists of 1,413 proteins and 10,665 drugs. To evaluate the predictive efficacy of each pre-training model used in the one-line mode, we report the predictive performance on the test set in Table 3. We see all five models achieve high performance on all metrics in the test set for the BindingDB-Kd dataset.

Table 3. Predictive performance of pretraining models on the BindingDB-Kd dataset. Five fold average and standard deviation of the test set performance is reported.

DeepPurpose Model	MSE	Concordance Index
MPNN+CNN	0.635 (0.014)	0.841 (0.004)
CNN+CNN	0.600 (0.007)	0.857 (0.003)
Morgan+CNN	0.631 (0.002)	0.846 (0.005)
Morgan+AAC	0.629 (0.034)	0.848 (0.005)
Daylight+AAC	0.649 (0.014)	0.841 (0.004)

In many cases, the users may use drug-target pairs that are different from the training dataset. To test the model’s generalizability, we test on the DAVIS dataset, which has zero overlaps with the pretraining BindingDB-Kd dataset. We then sample 1,000 unseen drug-target pairs from DAVIS and feed them into the pretrained models and report the Pearson correlation between the true and predicted binding scores. We find the predicted Kd values of DeepPurpose are highly correlated with the true values with Pearson correlation **0.7789** (Fig 4), indicating the reliable predictions from DeepPurpose, even on new data. This result suggests the high-quality prediction for unseen data, making the pretrained models ideal for one-line default usage.

Performance on UNSEEN DAVIS dataset:

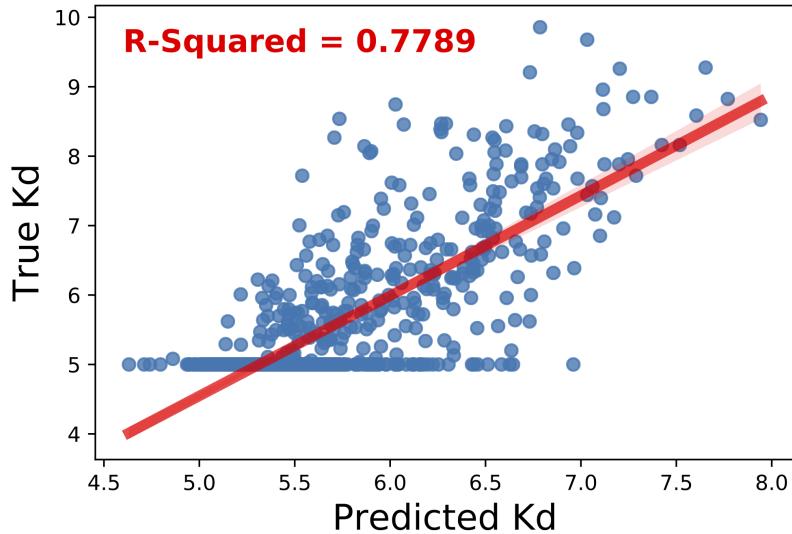


Fig 4. DeepPurpose pretrained models aggregation are able to generalize over unseen dataset. This finding validates that one-line pre-trained models can be used by drug developers to quickly generate a list of potential drug candidates.

Case Study on Drug Repurposing for COVID-19

Third, we conduct two case studies to showcase the easy usage of DeepPurpose for biomedical researchers. In the first case, suppose a biomedical researcher wants to identify which existing antiviral drugs can be repurposed to target SARS-CoV2 3CL Protease (3CLPro). With only one line of code, DeepPurpose aggregates multiple pretrained models and outputs top-ranked antiviral drug candidates. We present the results in Fig 5. Out of the 81 antiviral drugs in the library, DeepPurpose recommends 13 potentially active drugs that have Kd values within 500 [51] units. We conduct a literature search for the 13 drugs and find that Ritonavir, Darunavir, Lopinavir are three of a few drug candidates that are currently undergoing clinical trials for SARS-CoV2-3CLPro [52–54]. The top recommended drug Sofosbuvir is an anti-HCV protein inhibitor and is currently undergoing many in-vitro investigations for its potential usage for COVID19 [55]. Some other molecular docking studies also reported the potential efficacy of Simeprevir [56] and Amantadine [57]. Overall, 6 recommendations out of 13 have promising evidence based on literature or clinical trials, which confirms the potential of DeepPurpose for suggesting high-quality repurposing candidates.

Next, we illustrate the flexibility of DeepPurpose for a more customized biomedical use case. We still consider the 3CL Protease for repurposing for COVID-19. However, in

Case Study: Drug Repurposing for 3CLPro				
	Rank	Drug Name	Target Name	Binding Score
	1	* Sofosbuvir	SARS-CoV2 3CL Protease	190.25
	2	Daclatasvir	SARS-CoV2 3CL Protease	214.58
	3	Vicriviroc	SARS-CoV2 3CL Protease	315.70
* Supported by other Literature Evidence	4	* Simeprevir	SARS-CoV2 3CL Protease	396.53
	5	Etravirine	SARS-CoV2 3CL Protease	409.34
	6	* Amantadine	SARS-CoV2 3CL Protease	419.76
+ Undergo Clinical Trial for COVID-19	7	Letermovir	SARS-CoV2 3CL Protease	460.28
	8	Rilpivirine	SARS-CoV2 3CL Protease	470.79
	9	+ Darunavir	SARS-CoV2 3CL Protease	472.24
	10	+ Lopinavir	SARS-CoV2 3CL Protease	473.01
	11	Maraviroc	SARS-CoV2 3CL Protease	474.86
	12	Fosamprenavir	SARS-CoV2 3CL Protease	487.45
	13	+ Ritonavir	SARS-CoV2 3CL Protease	492.19

Fig 5. DeepPurpose identifies drug candidates in ongoing clinical trials for COVID-19. Using one line of code, given the amino acid sequence of SARS-CoV2-3CLPro target, and a list of SMILES strings of an antiviral drug library, DeepPurpose aggregates from five pretrained models and generates a ranked list, where drugs that have top predicted binding scores are displayed. We conduct literature search and discover that the top ranked drugs are in ongoing clinical trials for COVID-19. Note that DeepPurpose only uses the chemical structures of target and drugs, without any information about existing ongoing clinical trials. The clinical trials information is only used to validate the utility of our methods.

this case, a biomedical scientist wants to train a deep learning model from past bioassay data such as high throughput screening (HTS) assay on SARS-CoV 3CL Protease [34], which conserves large portion of the gene with SARS-CoV-2. This is potentially a better training dataset than the general BindingDB-Kd dataset for COVID-19. Specifically, DeepPurpose takes the customized training dataset as input and trains multiple DL models using this assay data to score drug candidates from the antiviral library or any proprietary data. This resulting candidate list has support from the literature. We find that most of them are protein synthesis inhibitors, which is consistent with the general 3CLPro inhibition mechanism. Specifically, in addition to Ritonavir, it surprisingly outputs Remdesivir with high confidence, which is a star candidate for COVID19 by blocking the RNA polymerase and has shown initial clinical effects [58]. There are also initial literature evidence or clinical trials for Tipranavir [59], Methisazone [60], Baloxavir [61], Indinavir [60] to tackle COVID-19. Since this bioassay has a binary label, DeepPurpose automatically switches from regression for binding affinity to binary classification by using different loss functions. The use case is illustrated in Fig 6.

Availability and Future Works

All scripts, datasets, and models are described and open-sourced online at <https://github.com/kexinhuang12345/DeepPurpose>. The related documentation is located at <https://deeppurpose.readthedocs.io/en/latest/>. We also provide numerous tutorials, demos, and blogs to aid user usage in the repository.

DeepPurpose is a python package with a Jupyter Notebook interface. It can run locally to ease the concern of processing proprietary drug data. It can also run on the

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target.txt

SARS-CoV2_3CL_Protease SGF...TFQ

repurpose.txt

Rufloxacin CN1...2=O
Sparfloxacin C[C...C]C
...

train.txt

SGFKK...VGGVRLQ
CCOC1...C=CC=N4 0
CC1=C...C=CC=C2 1
...

Rank	Drug Name	Target Name	Interaction	Probability
1	+ Remdesivir	SARS-CoV 3CL Protease	YES	0.99
2	Efavirenz	SARS-CoV 3CL Protease	YES	0.98
3	Vicriviroc	SARS-CoV 3CL Protease	YES	0.98
4	* Tipranavir	SARS-CoV 3CL Protease	YES	0.96
5	* Methisazone	SARS-CoV 3CL Protease	YES	0.94
6	Letermovir	SARS-CoV 3CL Protease	YES	0.88
7	Iodoxuridine	SARS-CoV 3CL Protease	YES	0.77
8	Loviride	SARS-CoV 3CL Protease	YES	0.76
9	+ Baloxavir	SARS-CoV 3CL Protease	YES	0.74
10	Ibacitabine	SARS-CoV 3CL Protease	YES	0.70
11	Taribavirin	SARS-CoV 3CL Protease	YES	0.65
12	* Indinavir	SARS-CoV 3CL Protease	YES	0.62
13	Podophyllotoxin	SARS-CoV 3CL Protease	YES	0.60
14	Zanamivir	SARS-CoV 3CL Protease	YES	0.59
15	+ Ritonavir	SARS-CoV 3CL Protease	YES	0.58
16	Doravirine	SARS-CoV 3CL Protease	YES	0.57
17	Elvitegravir	SARS-CoV 3CL Protease	YES	0.50

* Supported by other Literature Evidence

+ Undergo Clinical Trial for COVID-19

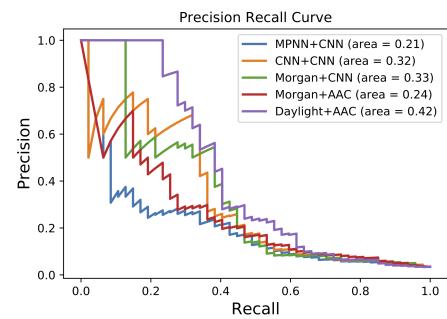
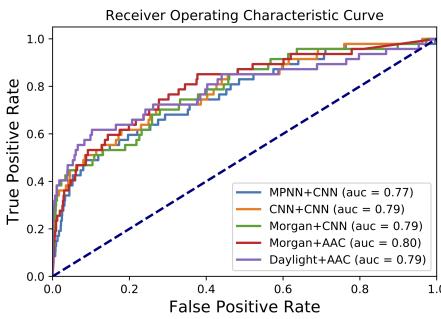


Fig 6. Repurposing using customized training data in one line of code .

Still using one line of code, DeepPurpose is able to take in customized training data, such as AID1706 bioassay data in this case and train five new models to generate a drug candidate list. The ROC-AUC and PR-AUC curves are automatically generated and they compare different training model's predictive performance.

cloud, which alleviates the computational resource burdens faced by some users. DeepPurpose is OS-agnostic.

In the future, we plan to increase its capabilities by potentially including more models, adding more functionalities such as interpretability, and expanding to more biomedical therapeutic entities such as antibody.

Discussion

DeepPurpose has several advantages over other DTI prediction pipelines. First, DeepPurpose is user-friendly. DeepPurpose is a python package with a Jupyter Notebook interface. It can run locally to ease the concern of processing proprietary

drug data. It can also run on the cloud, which alleviates the computational resource burdens faced by some users. For biomedical researchers, it allows one line of code to unlock state-of-the-art deep learning and apply it to any target protein of interest for drug repurposing and virtual screening. For computer scientists, DeepPurpose provides a 10-line programming framework that can be adapted to any neural architecture and can expedite the development of new computational methods. We also provide tutorials, demos, and documentation to aid user usage. It also bears different user demands and has a variety of features, including model robustness evaluation by cold-drug/target splits, customized training datasets such as high throughput screening data, and screening for non-protein targets such as bacteria.

Second, DeepPurpose is powerful. It incorporates 7 encoders for proteins, 8 encoders for drugs, over 50 state-of-the-art deep learning models, over 20 pre-trained models trained on large benchmark datasets, and over 5 benchmark datasets loaders. By implementing them in the same framework, DeepPurpose also allows flexibility in using different encoders algorithms (i.e., input representations). This could broaden the search horizons and catch drugs that were missed by existing works due to the bias from only using one particular encoder model.

Conclusion

We propose a powerful, user-friendly, and general framework for drug-target interaction prediction. We envision that DeepPurpose will increase the accessibility of deep learning for drug discovery and create valuable insights that can benefit patients. DeepPurpose is an open-source project, and we call for both domain scientists and computational researchers to contribute to it.

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