Protocol Capture

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1 Prerequisites

1.1 Datasets

High quality datasets from [1, 2] are used for the experiments. See original papers for details of datasets.

Datasets can be downloaded from `https://figshare.com/articles/dataset/Well-curated_QSAR_datasets_for_diverse_protein_targets/20539893`

Decompress the downloaded file, to get .sdf files.

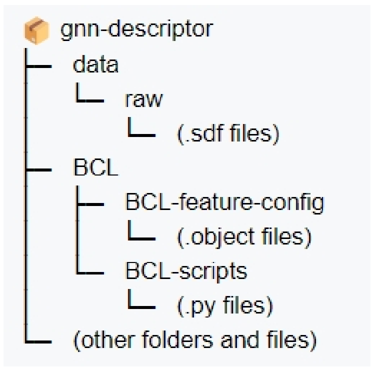
1.2 Creating BCL Features

This section will process the datasets described in the previous section into BCL features. The output of this section is a new folder named BCL-feats and BCL features are stored in (dataset-BCL-feat.csv) in that folder.

BCL can be downloaded at `https://github.com/BCLCommons/bcl/`. See `https://www.frontiersin.org/articles/10.3389/fphar.2022.833099/full` for an introduction of BCL. The following scripts assume the *bcl.exe* command points to a working BCL program.

After downloading the scripts (.py) and configuration files (.obejct) from `https://github.com/meilerlab/gnn-descriptor/BCL`, place them according to Fig. 1.

When at the BCL folder, execute the following commands step by step to generate BCL features:



```
gnn-descriptor
├── data
│   └── raw
│       └── (.sdf files)
├── BCL
│   ├── BCL-feature-config
│   │   └── (.object files)
│   └── BCL-scripts
│       └── (.py files)
└── (other folders and files)
```

Figure 1: In order to run the codes, the files should be named and placed according to this diagram. The datasets (.sdf files) should be placed under *raw* folder. The BCL configuration files (.object) should be placed under *BCL-feature-config* folder. The BCL-scripts should be placed under *BCL-scripts* folder. All the other files and folders from the github repository are placed as they are in the gnn-descriptor folder.

```
python BCL-scripts/1_combine_sdf.py # This combines active and inactive SDF files into one SDF file.
```

```
python BCL-scripts/2_add_id_to_sdf.py # This will add IDs to the header of each molecule in the SDF. So it is easy to identify which molecules are filtered out in the later steps.
```

```
python BCL-scripts/3_filter.py # Add hydrogen, neutralize molecules and filter out molecules that do not have simple atoms (C, O, N, S, P, F, Cl, Br, I)
```

```
python BCL-scripts/4_data_preparation.py  # This creates the BCL features and stores that in the BCL-feats folder.
```

```
python BCL-scripts/5_count_unmatched.py # This counts how many molecules are filtered out.
```

```
python BCL-scripts/6_clean_intermediate.py  # This cleans up the generated intermediate files to save hardware space. ‘
```

2 Running the Codes

2.1 General Instructions

Install the following python library:

- pytorch 2.0.1
- torch-geometric 2.3.0
- pytorch-scatter 2.1.2
- rdkit 2023.9.1
- tqdm
- pandas 2.1.2
- numpy 1.26.1

All necessary scripts can be downloaded at `https://github.com/meilerlab/gnn-descriptor`

To run the codes, the first thing is to set the running parameters as a .cfg file in the config folder. Below, an example of a GCN configuration file is shown as *GCN.cfg*

```
[GENERAL]
seed = 1
num_workers = 12

[DATA]
dataset_name = 1798
root = data
split_scheme = random1_IAratio100_cv0

[TRAIN]
num_epochs = 50
batch_size = 32
warmup_iterations = 2000
peak_lr = 1.4e-4
end_lr = 1e-9


[MODEL]
model_type = gcn # all model names should be lowercased
in_channels = 28
hidden_channels = 32
num_layers = 4
with_bcl = False
bcl_dim = 391
```

The experiments in the main texts used split_scheme = ['random1_IAratio100_cv0', 'random1_IAratio100_cv1', 'random1_IAratio100_cv2'] and mode_type = ['mlp', 'gcn', 'schnet', 'spherenet']

Example command:

```
python main --config config/GCN.cfg --no_train_eval --test
```

The *GCN.cfg* should be replaced with a configuration file specified by the user.

–*config* is a required flag and it specifies the configuration file.

–*no_train_eval* is an optional flag. When the flag is added, the training evaluation is skipped.

–*test* is an optional flag. When the flag is added, the training is skipped and a saved model (in *saved_model* folder) is directly evaluated at the testing set.

2.2 Use Cases

Use User-Specified Data

Place the .sdf files in the *raw* folder in Fig. 1. There should also be a file specifying how the data is split into train and test. The split file is put into *split* folder. The split file is a .pt file that contains a python dictionary. The dictionary has two keys, 'train' and 'test'. The value for either key is a list of index numbers of the data.

A example split.pt file: {'train':[1,3,8,...2943], 'test':[2,4,5,6,7, 2944]}

Train a Model

To train the model scratch, first set the model.cfg configuration file and placing that in the *config* folder as shown in Sec. 2.1, you can train the model with

```
python main --config config/model.cfg
```

*If you do not want to see the evaluation metrics during metrics, –*no_train_eval* flag can be used to speed up the training.

Test a Pre-trained Model

First, place the pre-trained model in the *saved_model* folder. Then the model can be run with the test model with the following command:

```
python main --config config/model.cfg --test
```

The –*test* flag helps to skip the training process and directly evaluate the model

References

[1] Butkiewicz, M., Lowe Jr, E. W., Mueller, R., Mendenhall, J. L., Teixeira, P. L., Weaver, C. D., and Meiler, J. (2013). Benchmarking ligand-based virtual high-throughput screening with the pubchem database. *Molecules*, 18(1):735–756.

[2] Butkiewicz, M., Wang, Y., Bryant, S. H., Lowe Jr, E. W., Weaver, D. C., and Meiler, J. (2017). High-throughput screening assay datasets from the pubchem database. *Chemical informatics (Wilmington, Del.)*, 3(1).