ProteinLigandBenchmarks Documentation

plbenchmark

Apr 20, 2022

CONTENTS:

CHAPTER

ONE

INSTALLING THE PROTEIN LIGAND BENCHMARK SET

The Protein Ligand Benchmark Set is currently only installable from source.

1.1 Installation from Source

The repository uses git-lfs (large file storage) for the storage of all the data file. Ideally git-lfs is installed first before cloning the repository.

```
conda create -n plbenchmark python=3.7 git-lfs
conda activate plbenchmark
git lfs clone https://github.com/openforcefield/protein-ligand-benchmark.git
cd protein-ligand-benchmark
conda env update --file environment.yml
pip install -e .
```

CHAPTER

TWO

EXAMPLE NOTEBOOK: PROTEIN-LIGAND-BENCHMARK

[1]:
```
from plbenchmark import targets
from IPython.core.display import HTML
```

```
Warning: Unable to load toolkit 'OpenEye Toolkit'. The Open Force Field Toolkit does not␣
↪require the OpenEye Toolkits, and can use RDKit/AmberTools instead. However, if you␣
↪have a valid license for the OpenEye Toolkits, consider installing them for faster␣
↪performance and additional file format support: https://docs.eyesopen.com/toolkits/
↪python/quickstart-python/linuxosx.html OpenEye offers free Toolkit licenses for␣
↪academics: https://www.eyesopen.com/academic-licensing
```

2.1 Get the whole set of targets in the dataset

[2]:
```
# it is initialized from the `plbenchmark/sample_data/targets.yml` file
target_set = targets.TargetSet()
# to see which targets are available, one can get a list of names
target_set.get_names()
```

[2]:
```
['mcl1_sample']
```

The `TargetSet` is a `Dict`, but can be converted to a `pandas.DataFrame` or a `html` string via `TargetSet.get_dataframe(columns=None)` or `TargetSet.get_html(columns=None)`. The default `None` for `columns` means that all columns are printed. One can also define a subset of columns as a `list`:

[3]:
```
HTML(target_set.get_html(columns=['name', 'fullname', 'pdb', 'references', 'numLigands',
↪'minDG', 'maxDG', 'associated_sets']))
```

```
/home/dhahn3/miniconda3/envs/plbenchmark/lib/python3.9/site-packages/pandas/core/dtypes/
↪cast.py:1638: UnitStrippedWarning: The unit of the quantity is stripped when␣
↪downcasting to ndarray.
  result[:] = values
```

[3]:
```
<IPython.core.display.HTML object>
```

A `target` can be accessed with its name in two ways

[4]:
```
mcl1 = target_set['mcl1_sample']
mcl1_2 = target_set.get_target('mcl1_sample')
```

2.2 The Target class

contains all the available information about one target of plbenchmark. It also has two member variables, _ligand_set and _edge_set, which contain the information about the available ligand and edges of the respective target. A Target can either be accessed from the TargetSet (see cell before) or initialized using its name via

[5]:
```
mcl1 = targets.Target('mcl1_sample')
# The data in the column is stored in a pandas.Series and can be accessed via
mcl1.get_dataframe(columns=None)
```

```
/home/dhahn3/miniconda3/envs/plbenchmark/lib/python3.9/site-packages/pandas/core/dtypes/
↪cast.py:1638: UnitStrippedWarning: The unit of the quantity is stripped when␣
↪downcasting to ndarray.
  result[:] = values
```

[5]:
```
associated_sets                                    [Schrodinger JACS]
comments            hydrophobic interactions contributing to binding
date                                                       2020-08-21
fullname           Induced myeloid leukemia cell differentiation ...
id                                                                 99
ligands            [lig_23, lig_26, lig_27, lig_28, lig_29, lig_3...
name                                                      mcl1_sample
netcharge                                                          xx
pdb                                                              4HW3
references         {'calculation': ['10.1021/ja512751q', '10.1021...
numLigands                                                         15
maxDG                                       -6.1 kilocalorie / mole
minDG                                       -9.0 kilocalorie / mole
std(DG)                                      0.9 kilocalorie / mole
calculation        REP1http://dx.doi.org/10.1021/ja512751qREP2Wan...
pdblinks           REP1http://www.rcsb.org/structure/4HW3REP24HW3...
dtype: object
```

Access to the EdgeSet and LigandSet in different formats is achieved by

[6]:
```
mcl1_ligands = mcl1.get_ligand_set()
mcl1_ligands_df = mcl1.get_ligand_set_dataframe()
HTML(mcl1.get_ligand_set_html(columns = ['name', 'ROMol', 'measurement',
↪'DerivedMeasurement']))
```

[6]:
```
<IPython.core.display.HTML object>
```

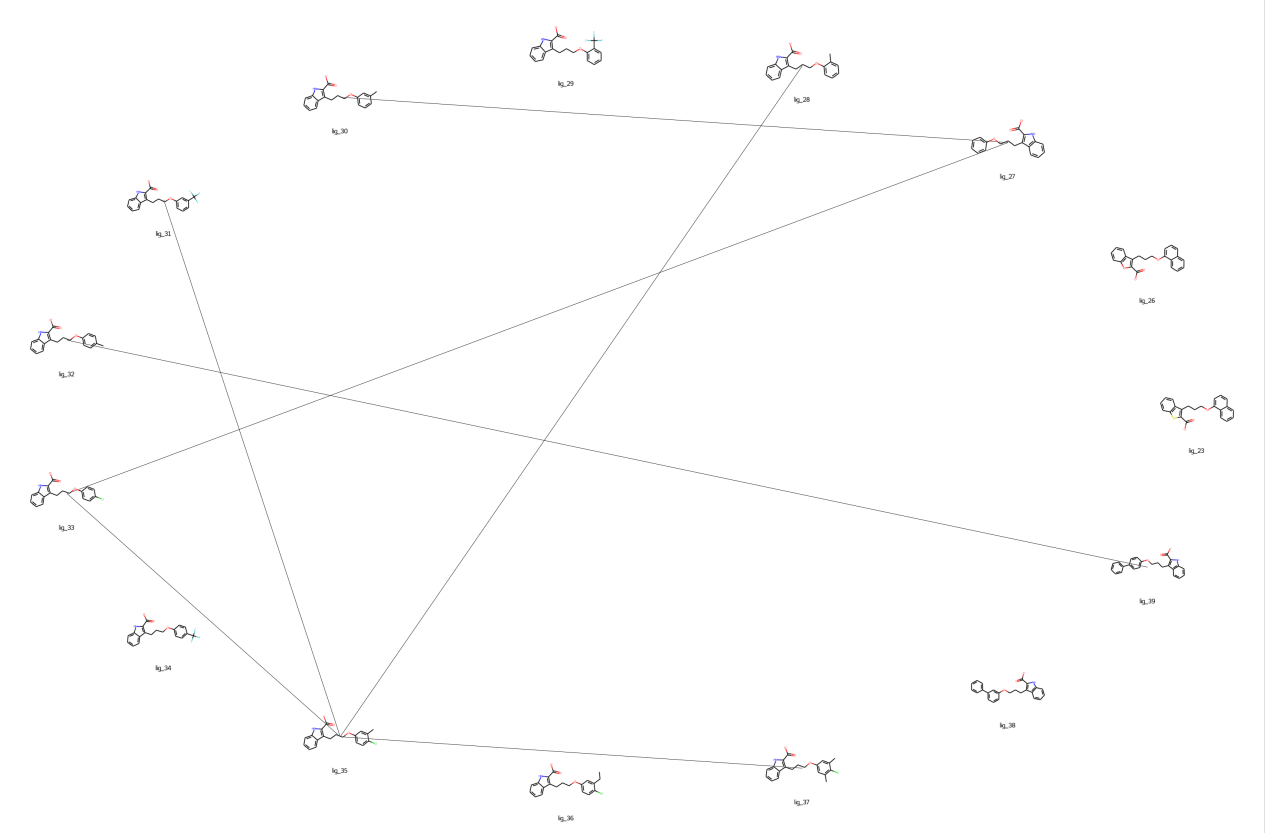
[7]:
```
mcl1_edges = mcl1.get_edge_set()
mcl1_edges_df = mcl1.get_edge_set_dataframe()
HTML(mcl1.get_edge_set_html())
```

```
/home/dhahn3/miniconda3/envs/plbenchmark/lib/python3.9/site-packages/pandas/core/dtypes/
↪cast.py:1638: UnitStrippedWarning: The unit of the quantity is stripped when␣
↪downcasting to ndarray.
  result[:] = values
```

[7]:
```
<IPython.core.display.HTML object>
```

Finally, the set out of ligands and edges can be visualized in a graph:

[8]:
```
graph = mcl1.get_graph()
```



2.3 The LigandSet and Ligand class

The LigandSet consists of a Dict of Ligands which are availabe for one target. It is accessible via Target.get_ligand_set(), but can also be initialized directly.

[9]:
```
from plbenchmark import ligands
```

[10]:
```
mcl1_ligands = ligands.LigandSet('mcl1_sample')
HTML(mcl1_ligands.get_html())
```

```
/home/dhahn3/miniconda3/envs/plbenchmark/lib/python3.9/site-packages/pandas/core/dtypes/
↪cast.py:1638: UnitStrippedWarning: The unit of the quantity is stripped when␣
↪downcasting to ndarray.
  result[:] = values
```

[10]:
```
<IPython.core.display.HTML object>
```

The Ligand classes can be accessed from the LigandSet by their name. Each Ligand has information about experimental data, references, SMILES string and SDF file path of the docked structure. Additionally, there are functions to derive and process the primary data, which is then added to the pandas.Series as a new entry.

[11]:
```
lig_30 = mcl1_ligands['lig_30']
lig_27 = mcl1_ligands.get_ligand('lig_27')
```

2.4 The EdgeSet and Edge class

The EdgeSet contains a dict of Edges which are availabe for one target. It is accessible via Target.get_edge_set(), but can also be initialized directly.

[12]:
```
from plbenchmark import edges
```

[13]:
```
mcl1_edges = edges.EdgeSet('mcl1_sample')
HTML(mcl1_edges.get_html())
```

```
/home/dhahn3/miniconda3/envs/plbenchmark/lib/python3.9/site-packages/pandas/core/dtypes/
↪cast.py:1638: UnitStrippedWarning: The unit of the quantity is stripped when␣
↪downcasting to ndarray.
  result[:] = values
```

[13]:
```
<IPython.core.display.HTML object>
```

[14]:
```
mcl1_edges.keys()
```

[14]:
```
dict_keys(['edge_28_35', 'edge_30_27', 'edge_31_35', 'edge_33_27', 'edge_35_33', 'edge_
↪35_37', 'edge_39_32'])
```

The Edge classes can be accessed from the EdgeSet by their name. They are lightweight and provide only access to a pandas.DataFrame and a Dict:

[15]:
```
edge_30_27 = mcl1_edges.get_edge('edge_30_27')
df = edge_30_27.get_dataframe()
edge_30_27.get_dict()
```

[15]:
```
{'ligand_a': 'lig_30',
 'ligand_b': 'lig_27',
 'name': 'edge_30_27',
 'Mol1': <rdkit.Chem.rdchem.Mol at 0x7f1a3046e8e0>,
 'Smiles1': '[H]c1c(c(c2c(c1[H])C(=C(N2[H])C(=O)[O-
↪])C([H])([H])C([H])([H])C([H])([H])Oc3c(c(c(c(c3[H])C([H])([H])[H])[H])[H])[H])[H])[H]
↪',
 'Mol2': <rdkit.Chem.rdchem.Mol at 0x7f1a30460700>,
 'Smiles2':
↪'[H]c1c(c(c(c(c1[H])[H])OC([H])([H])C([H])([H])C([H])([H])C2=C(N(c3c2c(c(c(c3[H])[H])[H])[H])[H])C(=O
↪])[H])[H]',
 'exp. DeltaG [kcal/mol]': 1.73 <Unit('kilocalorie / mole')>,
 'exp. Error [kcal/mol]': 0.22 <Unit('kilocalorie / mole')>}
```

[ ]:

CHAPTER

THREE

DATA

3.1 Data file tree and file description

The data is organized as follows:

```
data
├── targets.yml                                # list of all targets and their directories
├── <date>_<target_name_1>                     # directory for target 1
    ├── 00_data                                #     metadata for target 1
        ├── edges.yml                          #         edges/perturbations
        ├── ligands.yml                        #         ligands and activities
        └── target.yml                         #         target
    ├── 01_protein                             #     protein data
        ├── crd                                #         coordinates
            ├── cofactors_crystalwater.pdb     #             cofactors and cyrstal waters
            └── protein.pdb                    #             aminoacid residues
        └── top                                #         topology(s)
            └── amber99sb-star-ildn-mut.ff     #             force field spec.
                ├── cofactors_crystalwater.top#                 Gromacs TOP file of␣
↪cofactors and crystal water
                ├── protein.top                #                 Gromacs TOP file of␣
↪amino acid residues
                └── *.itp                      #                 Gromacs ITP file(s) to␣
↪be included in TOP files
    └── 02_ligands                             #     ligands
    ├── lig_<name_1>                           #          ligand 1
        ├── crd                                #              coordinates
            └── lig_<name_1>.sdf               #                  SDF file
        └── top                                #              topology(s)
            └── openff-1.0.0.offxml            #                  force field spec.
                ├── fflig_<name_1>.itp         #                      Gromacs ITP file :␣
↪atom types
                ├── lig_<name_1>.itp           #                      Gromacs ITP file
                ├── lig_<name_1>.top           #                      Gromacs TOP file
                └── posre_lig_<name_1>.itp     #                      Gromacs ITP file :␣
↪position restraint file
    ├── lig_<name_2>                           #         ligand 2
    ...
    └── 03_hybrid                              #    edges (perturbations)
    ├── edge_<name_1>_<name_2>                 #         edge between ligand 1 and ligand␣
↪2
```

(continues on next page)

(continued from previous page)

```
│   │   └── water                          #             edge in water
│   │       ├── crd                        #                 coordinates
│   │       │   ├── mergedA.pdb            #                     merged conf based on␣
↪coords of ligand 1
│   │       │   ├── mergedB.pdb            #                     merged conf based on␣
↪coords of ligand 2
│   │       │   ├── pairs.dat              #                     atom mapping
│   │       │   └── score.dat              #                     similarity score
│   │       └── top                        #                 topology(s)
│   │           └── openff-1.0.0.offxml    #                     force field spec.
│   │               ├── ffmerged.itp       #                         Gromacs ITP file
│   │               ├── ffMOL.itp          #                         Gromacs ITP file
│   │               └── merged.itp         #                         Gromacs ITP file
│   ...
├── <date>_<target_name_2>                 # directory for target 2
...
```

CHAPTER

FOUR

CONTRIBUTIONS

- **Authors** David Hahn
- **Data Contributors The authors of the following publications, especially Vytautas Gapsys and Christina E. M. Schindler.**
  - V. Gapsys et al., Large scale relative protein ligand binding affinities using non-equilibrium alchemy, Chem. Sci., 2020,11, 1140-1152
  - Christina E. M. Schindler et al., Large-Scale Assessment of Binding Free Energy Calculations in Active Drug Discovery Projects, J. Chem. Inf. Model. 2020, 60, 11, 5457–5474
  - Laura Perez Benito et al., Predicting Activity Cliffs with Free-Energy Perturbation, J. Chem. Theory Comput. 2019, 15, 3, 1884–1895
- **Discussions and Suggestions** Christopher I. Bayly, Marko Breznik, Hannah E. Bruce Macdonald, John D.Chodera, Katharina Meier, Antonia S. J. S. Mey, David L. Mobley, Laura Perez Benito, Gary Tresadern, Gregory L. Warren and all members of the Open Force Field Initiative
- **Code review and discussions** Matt Thompson, Jeffrey Wagner

CHAPTER

FIVE

API DOCUMENTATION

5.1 Targets

5.2 Ligands

5.3 Edges

5.4 Utils

utils.py Contains utility functions

plbenchmark.utils.**convert_error**(*error_value*, *value*, *original_type*, *final_type*, *temperature=300.0*, *out_unit=None*)

Converts an experimental value into another derived quantity with specified unit.

Parameters

- **error_value** – float, error of val, numerical value
- **value** – float, numerical value
- **original_type** – string, code for the original observable. Can be *dg*, *ki*, *ic50*, *pic50*
- **final_type** – string, code for the desired derived quantity. Can be *dg*, *ki*, *ic50*, *pic50*
- **temperature** – float, temperature in kelvin
- **out_unit** – unit of type `pint`, output unit of final_type, needs to fit to the requested final_type

Returns `pint.Quantity` with desired unit

plbenchmark.utils.**convert_value**(*value*, *original_type*, *final_type*, *temperature=300.0*, *out_unit=None*)

Converts an experimental value into another derived quantity with specified unit.

Parameters

- **value** – float, numerical value
- **original_type** – string, code for the original observable. Can be *dg*, *ki*, *ic50*, *pic50*
- **final_type** – string, code for the desired derived quantity. Can be *dg*, *ki*, *ic50*, *pic50*
- **temperature** – float, temperature in kelvin

- **out_unit** – unit of type pint, output unit of final_type, needs to fit to the requested final_type

Returns pint.Quantity with desired unit

plbenchmark.utils.**find_doi_url**(*doi*)

Finds the links to a digital object identifier (doi).

Parameters **doi** – string

Returns string compiled string including the urls to the publication

plbenchmark.utils.**find_pdb_url**(*pdb*)

Finds the links to a pdb or a list of pdb codes.

Parameters **pdb** – string or list of strings

Returns string compiled string including the urls to the pdb entries

CHAPTER

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- modindex
- search

PYTHON MODULE INDEX

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