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>
```

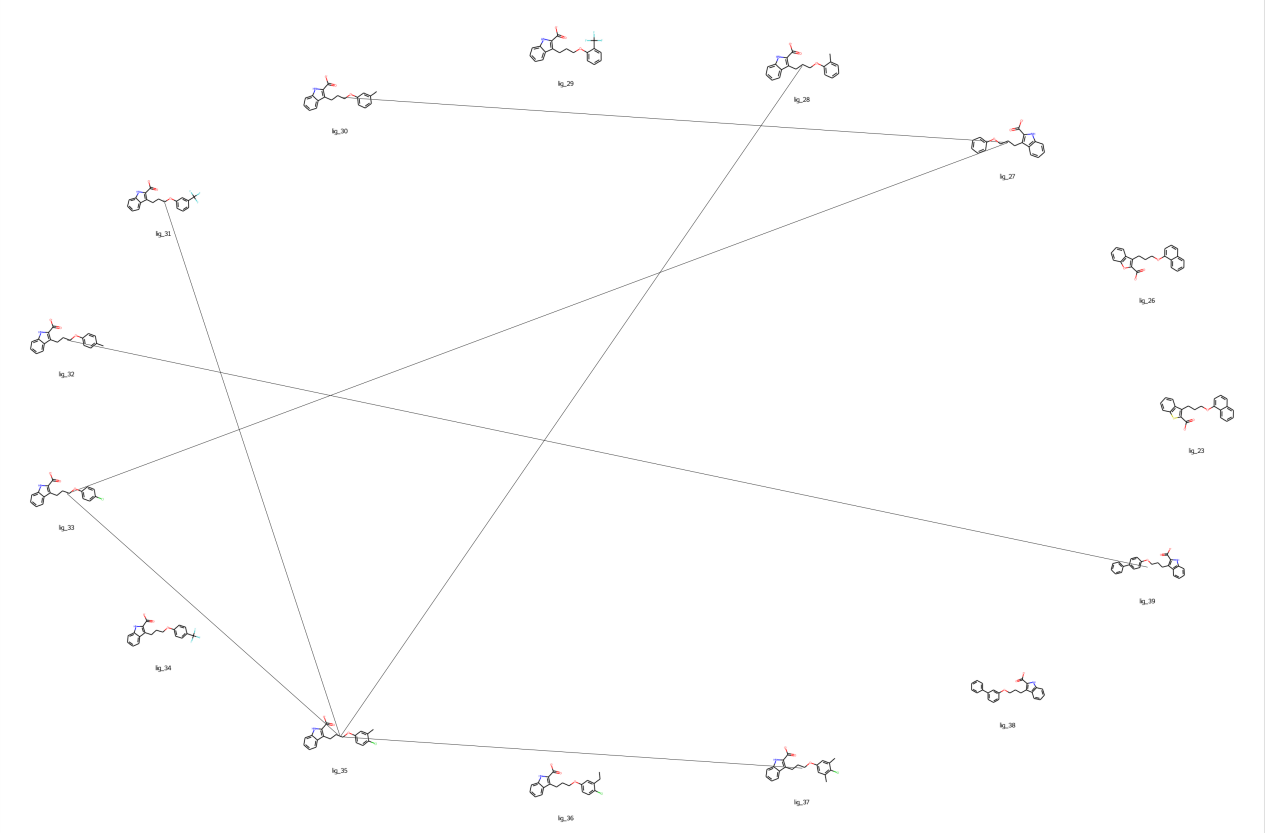
[7]:
```
mcl1_edges = mcl1.get_edge_set()
mcl1_edges_df = mcl1.get_edge_set_dataframe()
HTML(mcl1.get_edge_set_html())
```

```
/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

targets.py Functions and classes for handling the target data.

class plbenchmark.targets.**Target**(*name: str*)

Class to store the data of one target.

add_ligand_data()

Adds data from ligands to `plbenchmark.targets.target`. Molecule images and the minimum and maximum affinity are added.

Returns None

find_links()

Processes primary data to have links in the html string of the target data

Returns None

get_dataframe(*columns=None*)

Access the target data as a `pandas.DataFrame`

Parameters **cols** – `list` of columns which should be returned in the `pandas.DataFrame`

Returns `pandas.DataFrame`

get_edge_set()

Get `plbenchmark:edges:edgeSet` associated with the target

Returns `plbenchmark:edges:edgeSet` object

get_edge_set_dataframe(*columns=None*)

Get `plbenchmark:edges:edgeSet` associated with the target as a `pandas.DataFrame`

Parameters **columns** – list of columns which should be returned in the `pandas.DataFrame`

Returns `plbenchmark:edges:edgeSet` object

get_edge_set_html(*columns=None*)

Get `plbenchmark:edges:edgeSet` associated with the target in a html string

Parameters **columns** – `list` of edge which should be returned

Returns html string

get_graph()

Get a graph representation of the ligand perturbations associated with the target in a `matplotlib.figure`

Returns `matplotlib.figure`

get_ligand_set()

Get `ligandSet` associated with the target

Returns `plbenchmark.ligands.ligandSet` object

get_ligand_set_dataframe(*columns=None*)

Get `ligandSet` associated with the target in a `pandas.DataFrame`

Parameters **columns** – `list` of columns which should be returned in the `pandas.DataFrame`

Returns `pandas.DataFrame`

get_ligand_set_html(*columns=None*)

Get `ligandSet` associated with the target in a html string

Parameters **columns** – list of columns which should be returned

Returns html string

get_name()

Access the name of the target.

Returns name as a string

class plbenchmark.targets.**TargetSet**(**arg*, ***kw*)

Class inherited from dict to store all available targets in plbenchmark.

get_dataframe(*columns=None*)

Convert targetSet class to `pandas.DataFrame`

Parameters **columns** – `list` of columns which should be returned in the `pandas.DataFrame`

Returns `pandas.DataFrame`

get_html(*columns=None*)

Access the `plbenchmark:targets:targetSet` as a HTML string

Parameters **cols** – `list` of columns which should be returned in the `pandas.DataFrame`

Returns HTML string

get_names()

Get a list of available target names

Returns `list` of strings

get_target(*name*)

Accesses one target of the targetSet

Parameters **name** – string name of the target

Returns `plbenchmark.targets.target` class

plbenchmark.targets.**get_target_data_path**(*target*)

Gets the file path of the target data

Parameters **target** – string with target name

Returns list of directories (have to be joined with '/' to get the file path relative to the plbenchmark repository)

plbenchmark.targets.**get_target_dir**(*target*)

Gets the directory name of the target

Parameters **target** – string with target name

Returns string with directory name

plbenchmark.targets.**set_data_dir**(*path='/home/docs/checkouts/readthedocs.org/user_builds/plbenchmarks/checkouts/0.1.2/plb*

Gets the directory name of the target

Parameters **path** – string with path to data directory

5.2 Ligands

ligands.py Functions and classes for handling the ligand data.

class plbenchmark.ligands.**Ligand**(*d: dict*, *target: Optional[str] = None*)

Store and convert the data of one ligand in a pandas.Series.

add_mol_to_frame()

Adds a image file of the ligand to the pandas.Dataframe

Returns None

derive_observables(*derived_type='dg'*, *destination='DerivedMeasurement'*, *out_unit=None*)

Derive observables from (stored) primary data, which is then stored in the pandas.DataFrame

Parameters

- **derived_type** – type of derived observable, can be any of 'dg' 'ki', 'ic50' or 'pic50'
- **destination** – string with column name for 'pandas.DataFrame' where the derived observable should be stored.
- **out_unit** – unit of type pint unit of derived coordinate

Returns None

find_links()

Processes primary data to have links in the html string of the ligand data

Returns None

get_coordinate_file_path()

Get file path relative to the plbenchmark repository of the SDF coordinate file of the docked ligand

Returns file path as string

get_dataframe(*columns=None*)

Access the ligand data as a pandas.Dataframe

Parameters **columns** – list of columns which should be returned in the pandas.Dataframe

Returns pandas.Dataframe

get_html(*columns=None*)

Access the ligand as a HTML string

Parameters **columns** – list of columns which should be returned in the pandas.Dataframe

Returns HTML string

get_image()

Creates a molecule image.

Returns PIL.Image object

get_molecule()

Get molecule object with coordinates of the docked ligand

Returns file path as string

get_name()

Access the name of the ligand.

Returns name: string

class plbenchmark.ligands.**LigandSet**(*target*, **arg*, ***kw*)

Class inherited from dict to store all available ligands of one target.

get_dataframe(*columns=None*)

Access the ligandSet as a pandas.Dataframe

Parameters **columns** – list of columns which should be returned in the pandas.Dataframe

Returns pandas.Dataframe

get_html(*columns=None*)

Access the plbenchmark:ligands.ligandSet as a HTML string

Parameters **columns** – list of columns which should be returned in the pandas.Dataframe

Returns HTML string

get_ligand(*name*)

Accesses one ligand of the ligandSet

Parameters **name** – string name of the ligand

Returns plbenchmark.ligands.ligand class

get_list()

Returns list of ligands

Returns list of ligand names

get_molecules()

Returns a dict with names as keys and values as py:class:*openforcefield:topology:Molecule* objects

Returns dict

5.3 Edges

edges.py Functions and classes for handling the perturbation edges.

class plbenchmark.edges.**Edge**(*d: dict*)

Store and convert the data of one perturbation ("edge") in a pandas.Series.

Parameters **d** – dict with the edge data

Returns None

add_ligand_data(*ligand_set*)

Adds data from ligands to edge. Molecule images and the affinity difference are added.

Parameters **ligand_set** – plbenchmark:ligands:ligandSet class of the same target

Returns None

get_dataframe(*columns=None*)

Access the edge data as a pandas.DataFrame

Parameters **cols** – list of columns which should be returned in the pandas.DataFrame

Returns pandas.DataFrame

get_dict()

Access the edge data as a dict which contains the name of the edge as key and the names of the two ligands as list.

Returns dict

get_name()

Access the name of the edge.

Returns name as string

class plbenchmark.edges.**EdgeSet**(*target*, **arg*, ***kw*)

Class inherited from dict to store all available edges of one target.

get_dataframe(*columns=None*)

Access the plbenchmark:edges.edgeSet as a pandas.DataFrame

Parameters **cols** – list of columns which should be returned in the pandas.DataFrame

Returns pandas.DataFrame

get_dict()

Access the plbenchmark:edges.edgeSet as a dict which contains the name of the edges as key and the names of the two ligands in a list as items.

Returns dict

get_edge(*name*)

Accesses one edge of the plbenchmark.edges.edgeSet

Parameters **name** – string name of the edge

Returns plbenchmark:edges:edge class

get_html(*columns=None*)

Access the plbenchmark:edges.edgeSet as a HTML string

Parameters **cols** – list of columns which should be returned in the pandas.DataFrame

Returns HTML string

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

SIX

INDICES AND TABLES

- genindex
- modindex
- search

PYTHON MODULE INDEX

p

INDEX

L

M

P

S

T