ProDy

Protein Dynamics & Sequence Analysis

Structure Analysis

Release 1.5.1

Ahmet Bakan

December 24, 2013

CONTENTS

CHAPTER

ONE

INTRODUCTION

This tutorial shows how to various ProDy features for managing, handling, and analyzing protein structures.

1.1 Required Programs

Latest version of ProDy[1] and Matplotlib[2] are required.

1.2 Recommended Programs

IPython[3] is strongly recommended.

1.3 Getting Started

To follow this tutorial, you will need the following files:

```
There are no required files.
```

We recommend that you will follow this tutorial by typing commands in an IPython session, e.g.:

```
$ ipython
```

or with pylab environment:

```
$ ipython --pylab
```

First, we will make necessary imports from ProDy and Matplotlib packages.

```
In [1]: from prody import *

In [2]: from pylab import *

In [3]: ion()
```

We have included these imports in every part of the tutorial, so that code copied from the online pages is complete. You do not need to repeat imports in the same Python session.

[1] http://prody.csb.pitt.edu
[2] http://matplotlib.org
[3] http://ipython.org

CHAPTER

TWO

PDB FILES

This examples demonstrates how to use the flexible PDB fetcher, `fetchPDB()`. Valid inputs are PDB identifier, e.g 2k39[1], or a list of PDB identifiers, e.g. `["2k39", "1mkp", "1etc"]`. Compressed PDB files (`pdb.gz`) will be saved to the current working directory or a target folder.

2.1 Fetch PDB files

2.1.1 Single file

We start by importing everything from the ProDy package:

```
In [1]: from prody import *
```

The function will return a filename if the download is successful.

```
In [2]: filename = fetchPDB('1p38')
```

```
In [3]: filename
Out[3]: '1p38.pdb'
```

2.1.2 Multiple files

This function also accepts a list of PDB identifiers:

```
In [4]: filenames = fetchPDB(['1p38', '1r39', '@!~#'])
```

```
In [5]: filenames
Out[5]: ['1p38.pdb', '1r39.pdb', None]
```

For failed downloads, `None` will be returned (or the list will contain `None` item).

Also note that in this case we passed a folder name. Files are saved in this folder, after it is created if it did not exist.

ProDy will give you a report of download results and return a list of filenames. The report will be printed on the screen, which in this case would be:

[1] http://www.pdb.org/pdb/explore/explore.do?structureId=2k39

```
@> 1p38 (./1p38.pdb.gz) is found in the target directory.
@> @!~# is not a valid identifier.
@> 1r39 downloaded (./1r39.pdb.gz)
@> PDB download completed (1 found, 1 downloaded, 1 failed).
```

2.2 Parse PDB files

ProDy offers a fast and flexible PDB parser, `parsePDB()`. Parser can be used to read well defined subsets of atoms, specific chains or models (in NMR structures) to boost the performance. This example shows how to use the flexible parsing options.

Three types of input are accepted from user:

- PDB file path, e.g. `"../1MKP.pdb"`
- compressed (gzipped) PDB file path, e.g. `"1p38.pdb.gz"`
- PDB identifier, e.g. 2k39[2]

Output is an `AtomGroup` instance that stores atomic data and can be used as input to functions and classes for dynamics analysis.

2.2.1 Parse a file

You can parse PDB files by passing a filename (gzipped files are handled). We do so after downloading a PDB file (see *Fetch PDB files* (page 2) for more information):

```
In [6]: fetchPDB('1p38')
Out[6]: '1p38.pdb'

In [7]: atoms = parsePDB('1p38')

In [8]: atoms
Out[8]: <AtomGroup: 1p38 (2962 atoms)>
```

Parser returns an `AtomGroup` instance.

Also note that the time it took to parse the file is printed on the screen. This includes the time that it takes to evaluate coordinate lines and build an `AtomGroup` instance and excludes the time spent on reading the file from disk.

2.2.2 Use an identifier

PDB files can be parsed by passing simply an identifier. Parser will look for a PDB file that matches the given identifier in the current working directory. If a matching file is not found, ProDy will downloaded it from PDB FTP server automatically and saved it in the current working directory.

```
In [9]: atoms = parsePDB('1mkp')

In [10]: atoms
Out[10]: <AtomGroup: 1mkp (1183 atoms)>
```

[2] http://www.pdb.org/pdb/explore/explore.do?structureId=2k39

2.2.3 Subsets of atoms

Parser can be used to parse backbone or Cα atoms:

```
In [11]: backbone = parsePDB('1mkp', subset='bb')

In [12]: backbone
Out[12]: <AtomGroup: 1mkp_bb (576 atoms)>

In [13]: calpha = parsePDB('1mkp', subset='ca')

In [14]: calpha
Out[14]: <AtomGroup: 1mkp_ca (144 atoms)>
```

2.2.4 Specific chains

Parser can be used to parse a specific chain from a PDB file:

```
In [15]: chA = parsePDB('3mkb', chain='A')

In [16]: chA
Out[16]: <AtomGroup: 3mkb_A (1198 atoms)>

In [17]: chC = parsePDB('3mkb', chain='C')

In [18]: chC
Out[18]: <AtomGroup: 3mkb_C (1189 atoms)>
```

Multiple chains can also be parsed in the same way:

```
In [19]: chAC = parsePDB('3mkb', chain='AC')

In [20]: chAC
Out[20]: <AtomGroup: 3mkb_AC (2387 atoms)>
```

2.2.5 Specific models

Parser can be used to parse a specific model from a file:

```
In [21]: model1 = parsePDB('2k39', model=10)

In [22]: model1
Out[22]: <AtomGroup: 2k39 (1231 atoms)>
```

2.2.6 Alternate locations

When a PDB file contains alternate locations for some of the atoms, by default alternate locations with indicator `A` are parsed.

```
In [23]: altlocA = parsePDB('1ejg')

In [24]: altlocA
Out[24]: <AtomGroup: 1ejg (637 atoms)>
```

Specific alternate locations can be parsed as follows:

```
In [25]: altlocB = parsePDB('1ejg', altloc='B')

In [26]: altlocB
Out[26]: <AtomGroup: 1ejg (634 atoms)>
```

Note that in this case number of atoms are different between the two atom groups. This is because the residue types of atoms with alternate locations are different.

Also, all alternate locations can be parsed as follows:

```
In [27]: all_altlocs = parsePDB('1ejg', altloc=True)

In [28]: all_altlocs
Out[28]: <AtomGroup: 1ejg (637 atoms; active #0 of 3 coordsets)>
```

Note that this time parser returned three coordinate sets. One for each alternate location indicator found in this file (A, B, C). When parsing multiple alternate locations, parser will expect for the same residue type for each atom with an alternate location. If residue names differ, a warning message will be printed.

2.2.7 Composite arguments

Parser can be used to parse coordinates from a specific model for a subset of atoms of a specific chain:

```
In [29]: composite = parsePDB('2k39', model=10, chain='A', subset='ca')

In [30]: composite
Out[30]: <AtomGroup: 2k39_A_ca (76 atoms)>
```

2.2.8 Header data

PDB parser can be used to extract header data in a `dict`[3] from PDB files as follows:

```
In [31]: atoms, header = parsePDB('1ubi', header=True)

In [32]: list(header)
Out[32]:
['A',
 'sheet',
 'classification',
 'reference',
 'title',
 'polymers',
 'resolution',
 'space_group',
 'chemicals',
 'experiment',
 'helix',
 'version',
 'authors',
 'identifier',
 'deposition_date',
 'biomoltrans']

In [33]: header['experiment']
```

[3]http://docs.python.org/library/stdtypes.html#dict

```
Out[33]: 'X-RAY DIFFRACTION'

In [34]: header['resolution']
Out[34]: 1.8
```

It is also possible to parse only header data by passing *model=0* as an argument:

```
In [35]: header = parsePDB('1ubi', header=True, model=0)
```

or using `parsePDBHeader()` function:

```
In [36]: header = parsePDBHeader('1ubi')
```

2.3 Write PDB file

PDB files can be written using `writePDB()` function. This example shows how to write PDB files for `AtomGroup` instances and subsets of atoms.

2.3.1 Write all atoms

All atoms in an `AtomGroup` can be written in PDB format as follows:

```
In [37]: writePDB('MKP3.pdb', atoms)
Out[37]: 'MKP3.pdb'
```

Upon successful writing of PDB file, filename is returned.

2.3.2 Write a subset

It is also possible to write subsets of atoms in PDB format:

```
In [38]: alpha_carbons = atoms.select('calpha')

In [39]: writePDB('1mkp_ca.pdb', alpha_carbons)
Out[39]: '1mkp_ca.pdb'

In [40]: backbone = atoms.select('backbone')

In [41]: writePDB('1mkp_bb.pdb', backbone)
Out[41]: '1mkp_bb.pdb'
```

CHAPTER

THREE

BLAST SEARCH PDB

This example demonstrates how to use Protein Data Bank blast search function, `blastPDB()`.

`blastPDB()` is a utility function which can be used to check if structures matching a sequence exist in PDB or to identify a set of related structures for *Ensemble Analysis*[1].

We will used amino acid sequence of a protein, e.g. `ASFPVEILPFLYLGCAKDSTNLDVLEEFGIKYILNVTPNLPNLF...YDIVKM`

The `blastPDB()` function accepts sequence as a Python `str()`[2].

Output will be `PDBBlastRecord` instance that stores PDB hits and returns to the user those sharing sequence identity above a user specified value.

3.1 Blast search

We start by importing everything from the ProDy package:

```
In [1]: from prody import *
```

Let's search for structures similar to that of MKP-3, using its sequence:

```
In [2]: blast_record = blastPDB('''ASFPVEILPFLYLGCAKDSTNLDVLEEFGIKYILNVTPNL
   ...:  PNLFENAGEFKYKQIPISDHWSQNLSQFFPEAISFIDEAR
   ...:  GKNCGVLVHSLAGISRSVTVTVAYLMQKLNLSMNDAYDIV
   ...:  KMKKSNISPNFNFMGQLLDFERTL''')
   ...:
```

`blastPDB()` function returns a `PDBBlastRecord`. It is a good practice to save this record on disk, as NCBI may not respond to repeated searches for the same sequence. We can do this using Python standard library `pickle`[3] as follows:

```
In [3]: import pickle
```

Record is save using `dump()`[4] function into an open file:

```
In [4]: pickle.dump(blast_record, open('mkp3_blast_record.pkl', 'w'))
```

Then, it can be loaded using `load()`[5] function:

[1] http://prody.csb.pitt.edu/tutorials/ensemble_analysis/index.html#pca
[2] http://docs.python.org/library/functions.html#str
[3] http://docs.python.org/library/pickle.html#pickle
[4] http://docs.python.org/library/pickle.html#pickle.dump
[5] http://docs.python.org/library/pickle.html#pickle.load

```
In [5]: blast_record = pickle.load(open('mkp3_blast_record.pkl'))
```

3.2 Best match

To get the best match, `PDBBlastRecord.getBest()` method can be used:

```
In [6]: best = blast_record.getBest()

In [7]: best['pdb_id']
Out[7]: '1mkp'

In [8]: best['percent_identity']
Out[8]: 100.0
```

3.3 PDB hits

```
In [9]: hits = blast_record.getHits()

In [10]: list(hits)
Out[10]: ['1mkp']
```

This results in only MKP-3 itself, since percent_identity argument was set to 90 by default:

```
In [11]: hits = blast_record.getHits(percent_identity=50)

In [12]: list(hits)
Out[12]: ['1m3g', '2hxp', '3lj8', '3ezz', '1mkp']

In [13]: hits = blast_record.getHits(percent_identity=40)

In [14]: list(hits)
Out[14]: ['3lj8', '1mkp', '1zzw', '2g6z', '2hxp', '3ezz', '1m3g', '2oud']
```

This resulted in 7 hits, including structures of MKP-2, MKP-4, and MKP-5 More information on a hit can be obtained as follows:

```
In [15]: hits['1zzw']['percent_identity']
Out[15]: 49.27536231884058

In [16]: hits['1zzw']['align-len']
Out[16]: 138

In [17]: hits['1zzw']['identity']
Out[17]: 68
```

3.4 Download hits

PDB hits can be downloaded using `fetchPDB()` function:

```
filenames = fetchPDB(hits.keys())
filenames
```

CHAPTER

FOUR

BUILDING BIOMOLECULES

Some PDB files contain coordinates for a monomer of a functional/biological multimer (biomolecule). ProDy offers functions to build structures of biomolecules using the header data from the PDB file. We will use PDB file that contains the coordinates for a monomer of a biological multimeric protein and the transformations in the header section to generate the multimer coordinates. Output will be an `AtomGroup` instance that contains the multimer coordinates.

We start by importing everything from the ProDy package:

```
In [1]: from prody import *

In [2]: from pylab import *

In [3]: ion()
```

4.1 Build a Multimer

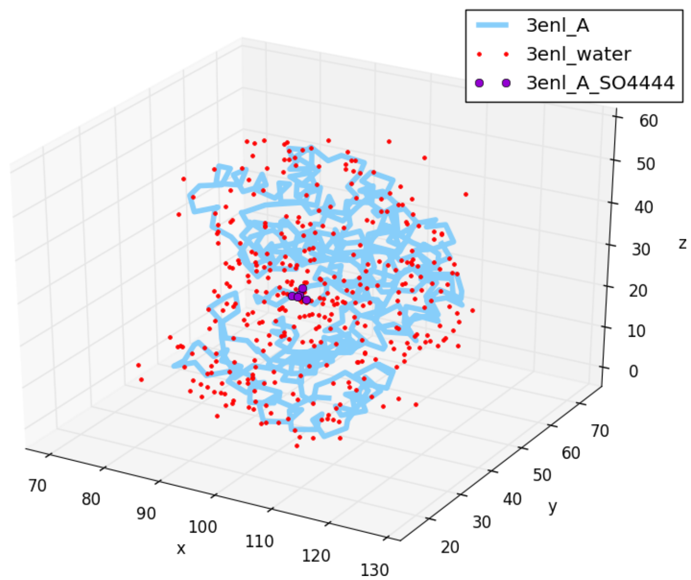
Let's build the dimeric form of 3enl[1] of enolase[2]:

```
In [4]: monomer, header = parsePDB('3enl', header=True)

In [5]: monomer
Out[5]: <AtomGroup: 3enl (3647 atoms)>
```

Note that we passed `header=True` argument to parse header data in addition to coordinates.

```
In [6]: showProtein(monomer);

In [7]: legend();
```

[1]http://www.pdb.org/pdb/explore/explore.do?structureId=3enl
[2]http://en.wikipedia.org/wiki/enolase



Let's get the dimer coordinates using `buildBiomolecules()` function:

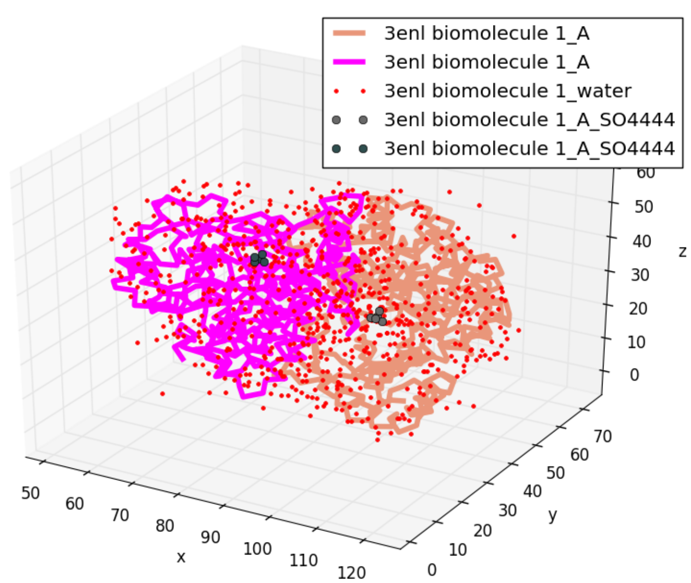
```
In [8]: dimer = buildBiomolecules(header, monomer)
```

```
In [9]: dimer
Out[9]: <AtomGroup: 3enl biomolecule 1 (7294 atoms)>
```

This function takes biomolecular tarnsformations from the *header* dictionary (item with key `'biomoltrans'`) and applies them to the *monomer*.

```
In [10]: showProtein(dimer);
```

```
In [11]: legend();
```



The *dimer* object now has two chains:

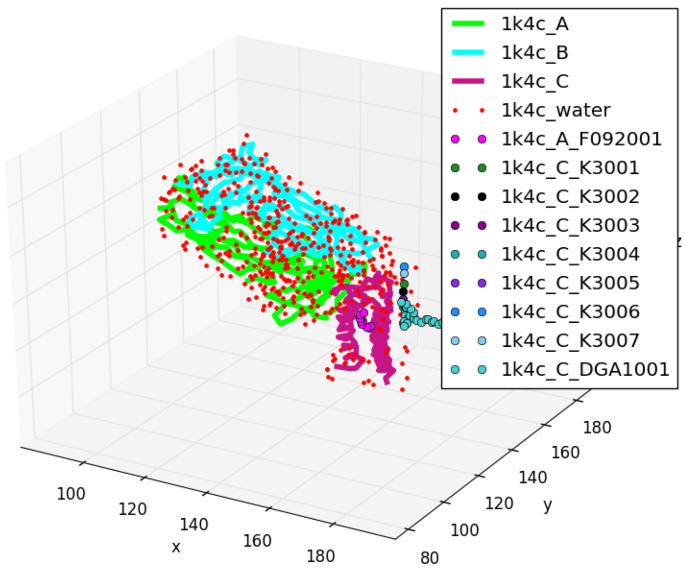
```
In [12]: list(dimer.iterChains())
Out[12]:
```

```
[<Chain: A from Segment A from 3enl biomolecule 1 (790 residues, 3647 atoms)>,
 <Chain: A from Segment B from 3enl biomolecule 1 (790 residues, 3647 atoms)>]
```

4.2 Build a Tetramer

Let's build the tetrameric form of 1k4c[3] of KcsA_potassium_channel[4]:

```
In [13]: monomer, header = parsePDB('1k4c', header=True)

In [14]: monomer
Out[14]: <AtomGroup: 1k4c (4534 atoms)>

In [15]: showProtein(monomer);

In [16]: legend();
```



Note that we do not want to replicate potassium ions, so we will exclude them:

```
In [17]: potassium = monomer.name_K

In [18]: potassium
Out[18]: <Selection: 'name K' from 1k4c (7 atoms)>

In [19]: without_K = ~ potassium

In [20]: without_K
Out[20]: <Selection: 'not (name K)' from 1k4c (4527 atoms)>

In [21]: tetramer = buildBiomolecules(header, without_K)

In [22]: tetramer
Out[22]: <AtomGroup: 1k4c Selection 'not (name K)' biomolecule 1 (18108 atoms)>
```

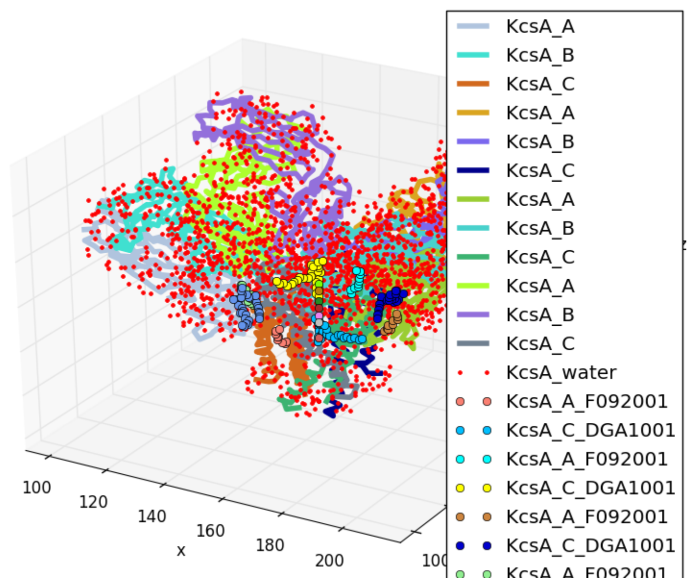
[3] http://www.pdb.org/pdb/explore/explore.do?structureId=1k4c
[4] http://en.wikipedia.org/wiki/KcsA_potassium_channel

Now, let's append potassium ions to the tetramer:

```
In [23]: potassium.setChids('K')

In [24]: kcsa = tetramer + potassium.copy()

In [25]: kcsa.setTitle('KcsA')
```

Here is a view of the tetramer:

```
In [26]: showProtein(kcsa);

In [27]: legend();
```



Let's get a list of all the chains:

```
In [28]: list(kcsa.iterChains())
Out[28]:
[<Chain: A from Segment A from KcsA (426 residues, 1822 atoms)>,
 <Chain: B from Segment A from KcsA (417 residues, 1851 atoms)>,
 <Chain: C from Segment A from KcsA (162 residues, 854 atoms)>,
 <Chain: A from Segment B from KcsA (426 residues, 1822 atoms)>,
 <Chain: B from Segment B from KcsA (417 residues, 1851 atoms)>,
 <Chain: C from Segment B from KcsA (162 residues, 854 atoms)>,
 <Chain: A from Segment C from KcsA (426 residues, 1822 atoms)>,
 <Chain: B from Segment C from KcsA (417 residues, 1851 atoms)>,
 <Chain: C from Segment C from KcsA (162 residues, 854 atoms)>,
 <Chain: A from Segment D from KcsA (426 residues, 1822 atoms)>,
 <Chain: B from Segment D from KcsA (417 residues, 1851 atoms)>,
 <Chain: C from Segment D from KcsA (162 residues, 854 atoms)>,
 <Chain: K from KcsA (7 residues, 7 atoms)>]
```

You see that chain identifiers are preserved within monomers, and monomers have different segment names. To get chain B from first monomer with segment name A, we would do the following:

```
In [29]: kcsa['A', 'B']
Out[29]: <Chain: B from Segment A from KcsA (417 residues, 1851 atoms)>
```

CHAPTER

FIVE

ALIGNMENTS

AtomGroup instances can store multiple coordinate sets, i.e. multiple models from an NMR structure. This example shows how to align such coordinate sets using alignCoordsets() function.

Resulting AtomGroup will have its coordinate sets superposed onto the active coordinate set selected by the user.

5.1 Parse an NMR structure

We start by importing everything from the ProDy package:

```
In [1]: from prody import *

In [2]: from pylab import *

In [3]: ion()
```

We use 1joy[1] that contains 21 models homodimeric domain of EnvZ protein from E. coli.

```
In [4]: pdb = parsePDB('1joy')

In [5]: pdb.numCoordsets()
Out[5]: 21
```

5.2 Calculate RMSD

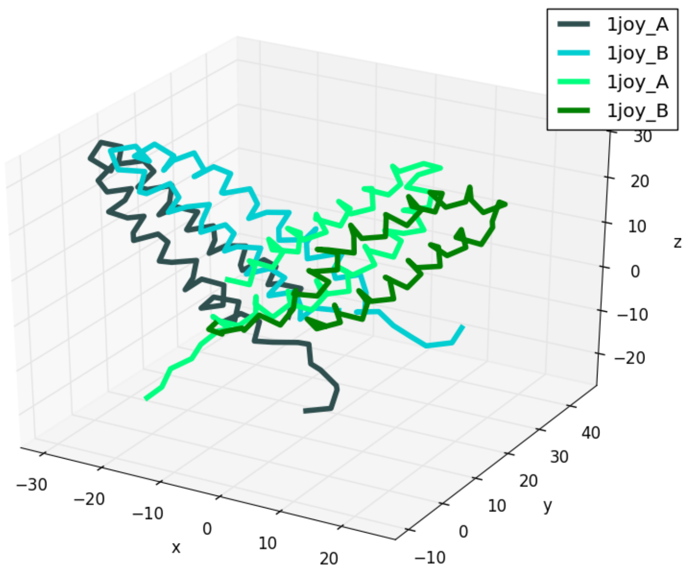
```
In [6]: rmsds = calcRMSD(pdb)

In [7]: rmsds.mean()
Out[7]: 37.506911678400989
```

This function calculates RMSDs with respect to the active coordinate set, which is the first model in this case.

```
In [8]: showProtein(pdb);

In [9]: pdb.setACSIndex(1) # model 2 in PDB is now the active coordinate set

In [10]: showProtein(pdb);
```

[1] http://www.pdb.org/pdb/explore/explore.do?structureId=1joy

```
In [11]: legend();
```



5.3 Align coordinate sets

We will superpose all models onto the first model in the file using based on Cα atom positions:

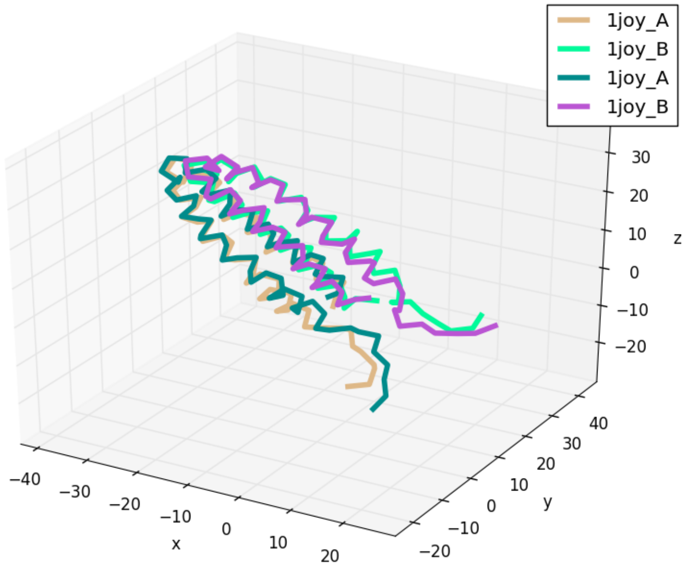
```
In [12]: pdb.setACSIndex(0)

In [13]: alignCoordsets(pdb.calpha);
```

To use all backbone atoms, `pdb.backbone` can be passed as argument. See *Atom Selections*[2] for more information on making selections.

Coordinate sets are superposed onto the first model (the active coordinate set).

```
In [14]: rmsds = calcRMSD(pdb)

In [15]: rmsds.mean()
Out[15]: 3.2768912151768554

In [16]: showProtein(pdb);

In [17]: pdb.setACSIndex(1) # model 2 in PDB is now the active coordinate set

In [18]: showProtein(pdb);

In [19]: legend();
```

[2] http://prody.csb.pitt.edu/manual/reference/atomic/select.html#selections



5.4 Write aligned coordinates

Using `writePDB()` function, we can write the aligned coordinate sets in PDB format:

```
In [20]: writePDB('1joy_aligned.pdb', pdb)
Out[20]: '1joy_aligned.pdb'
```

CHAPTER

SIX

STRUCTURE COMPARISON

This section shows how to find identical or similar protein chains in two structures files and align them.

`proteins` module contains functions for matching and mapping chains. Results can be used for RMSD fitting and PCA analysis.

Output will be `AtomMap` instances that can be used as input to ProDy classes and functions.

6.1 Match chains

We start by importing everything from the ProDy package:

```
In [1]: from prody import *

In [2]: from pylab import *

In [3]: ion()
```

Matching chains is useful when comparing two structures. We will find matching chains in two different HIV Reverse Transcriptase[1] structures.

First we define a function that prints information on paired (matched) chains:

```
In [4]: def printMatch(match):
   ...:     print('Chain 1     : {}'.format(match[0]))
   ...:     print('Chain 2     : {}'.format(match[1]))
   ...:     print('Length      : {}'.format(len(match[0])))
   ...:     print('Seq identity: {}'.format(match[2]))
   ...:     print('Seq overlap : {}'.format(match[3]))
   ...:     print('RMSD        : {}\n'.format(calcRMSD(match[0], match[1])))
   ...:
```

Now let's parse bound RT structure 1vrt[2] and unbound structure 1dlo[3]:

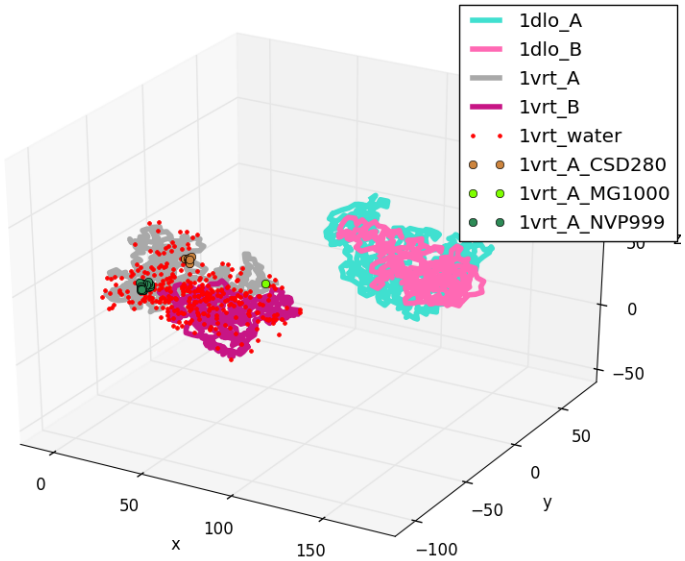
```
In [5]: bound = parsePDB('1vrt')

In [6]: unbound = parsePDB('1dlo')
```

Let's verify that these structures are not aligned:

[1]http://en.wikipedia.org/wiki/Reverse Transcriptase
[2]http://www.pdb.org/pdb/explore/explore.do?structureId=1vrt
[3]http://www.pdb.org/pdb/explore/explore.do?structureId=1dlo

```
In [7]: showProtein(unbound, bound);
```

```
In [8]: legend();
```



We find matching chains as follows:

```
In [9]: matches = matchChains(bound, unbound)
```

```
In [10]: for match in matches:
   ....:     printMatch(match)
   ....:
Chain 1     : AtomMap Chain B from 1vrt -> Chain B from 1dlo
Chain 2     : AtomMap Chain B from 1dlo -> Chain B from 1vrt
Length      : 400
Seq identity: 99.2518703242
Seq overlap : 96
RMSD        : 110.45149192

Chain 1     : AtomMap Chain A from 1vrt -> Chain A from 1dlo
Chain 2     : AtomMap Chain A from 1dlo -> Chain A from 1vrt
Length      : 524
Seq identity: 99.0458015267
Seq overlap : 94
RMSD        : 142.084163869
```

This resulted in two matches. Chains A and B of two structures are paired. These chains contain only Cα atoms:

```
In [11]: match[0][0].iscalpha
Out[11]: True
```

```
In [12]: match[0][1].iscalpha
Out[12]: True
```

For a structural alignment based on both chains, we merge these matches as follows:

```
In [13]: bound_ca = matches[0][0] + matches[1][0]
```

```
In [14]: bound_ca
```

```
Out[14]: <AtomMap: (AtomMap Chain B from 1vrt -> Chain B from 1dlo) + (AtomMap Chain A from 1vrt -> C

In [15]: unbound_ca = matches[0][1] + matches[1][1]

In [16]: unbound_ca
Out[16]: <AtomMap: (AtomMap Chain B from 1dlo -> Chain B from 1vrt) + (AtomMap Chain A from 1dlo -> C
```

Let's calculate RMSD:

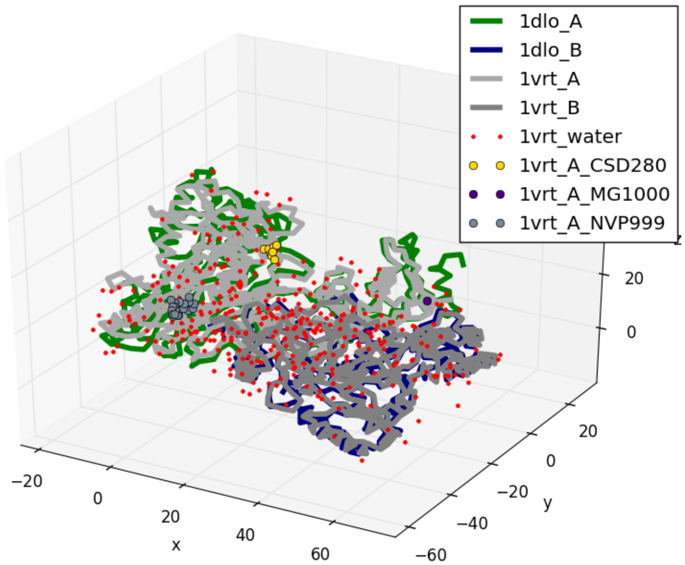
```
In [17]: calcRMSD(bound_ca, unbound_ca)
Out[17]: 129.34348658001386
```

We find the transformation that minimizes RMSD between these two selections and apply it to unbound structure:

```
In [18]: calcTransformation(unbound_ca, bound_ca).apply(unbound);

In [19]: calcRMSD(bound_ca, unbound_ca)
Out[19]: 6.0020747465625393
```

Let's see the aligned structures now:

```
In [20]: showProtein(unbound, bound);

In [21]: legend();
```



By default, `matchChains()` function matches Cα atoms. *subset* argument allows for matching larger numbers of atoms. We can match backbone atoms as follows:

```
In [22]: matches = matchChains(bound, unbound, subset='bb')

In [23]: for match in matches:
   ....:     printMatch(match)
   ....:
Chain 1     : AtomMap Chain B from 1vrt -> Chain B from 1dlo
Chain 2     : AtomMap Chain B from 1dlo -> Chain B from 1vrt
Length      : 1600
Seq identity: 99.2518703242
Seq overlap : 96
```

```
RMSD        : 1.71102621571

Chain 1     : AtomMap Chain A from 1vrt -> Chain A from 1dlo
Chain 2     : AtomMap Chain A from 1dlo -> Chain A from 1vrt
Length      : 2096
Seq identity: 99.0458015267
Seq overlap : 94
RMSD        : 7.78386812028
```

Or, we can match all atoms as follows:

```
In [24]: matches = matchChains(bound, unbound, subset='all')

In [25]: for match in matches:
   ....:     printMatch(match)
   ....:
Chain 1     : AtomMap Chain B from 1vrt -> Chain B from 1dlo
Chain 2     : AtomMap Chain B from 1dlo -> Chain B from 1vrt
Length      : 3225
Seq identity: 99.2518703242
Seq overlap : 96
RMSD        : 2.20947196284

Chain 1     : AtomMap Chain A from 1vrt -> Chain A from 1dlo
Chain 2     : AtomMap Chain A from 1dlo -> Chain A from 1vrt
Length      : 4159
Seq identity: 99.0458015267
Seq overlap : 94
RMSD        : 7.83814068858
```

6.2 Map onto a chain

Mapping is different from matching. When chains are matched, all matching atoms are returned as `AtomMap` instances. When atoms are mapped onto a *chain*, missing atoms are replaced by dummy atoms. The length of the mapping is equal to the length of *chain*. Mapping is used particularly useful in assembling coordinate data in analysis of heterogeneous datasets (see *Ensemble Analysis*[4]).

Let's map bound structure onto unbound chain A (subunit p66):

```
In [26]: def printMapping(mapping):
   ....:     print('Mapped chain     : {}'.format(mapping[0]))
   ....:     print('Target chain     : {}'.format(mapping[1]))
   ....:     print('Mapping length   : {}'.format(len(mapping[0])))
   ....:     print('# of mapped atoms: {}'.format(mapping[0].numMapped()))
   ....:     print('# of dummy atoms : {}'.format(mapping[0].numDummies()))
   ....:     print('Sequence identity: {}'.format(mapping[2]))
   ....:     print('Sequence overlap : {}\n'.format(mapping[3]))
   ....:

In [27]: unbound_hv = unbound.getHierView()

In [28]: unbound_A = unbound_hv['A']

In [29]: mappings = mapOntoChain(bound, unbound_A)
```

[4] http://prody.csb.pitt.edu/tutorials/ensemble_analysis/index.html#pca

```
In [30]: for mapping in mappings:
   ....:     printMapping(mapping)
   ....:
Mapped chain      : AtomMap Chain B from 1vrt -> Chain A from 1dlo
Target chain      : AtomMap Chain A from 1dlo -> Chain B from 1vrt
Mapping length    : 556
# of mapped atoms: 524
# of dummy atoms : 32
Sequence identity: 99
Sequence overlap : 94
```

`mapOntoChain()` mapped only Cα atoms. *subset* argument allows for matching larger numbers of atoms. We can map backbone atoms as follows:

```
In [31]: mappings = mapOntoChain(bound, unbound_A, subset='bb')
```

```
In [32]: for mapping in mappings:
   ....:     printMapping(mapping)
   ....:
Mapped chain      : AtomMap Chain B from 1vrt -> Chain A from 1dlo
Target chain      : AtomMap Chain A from 1dlo -> Chain B from 1vrt
Mapping length    : 2224
# of mapped atoms: 2096
# of dummy atoms : 128
Sequence identity: 99
Sequence overlap : 94
```

Or, we can map all atoms as follows:

```
In [33]: mappings = mapOntoChain(bound, unbound_A, subset='all')
```

```
In [34]: for mapping in mappings:
   ....:     printMapping(mapping)
   ....:
Mapped chain      : AtomMap Chain B from 1vrt -> Chain A from 1dlo
Target chain      : AtomMap Chain A from 1dlo -> Chain B from 1vrt
Mapping length    : 4370
# of mapped atoms: 4159
# of dummy atoms : 211
Sequence identity: 99
Sequence overlap : 94
```

CHAPTER

SEVEN

INTERMOLECULAR CONTACTS

This examples shows how to identify intermolecular contacts, e.g. protein atoms interacting with a bound inhibitor. A structure of a protein-ligand complex in PDB format will be used. Output will be `Selection` instances that points to atoms matching the contact criteria given by the user. `Selection` instances can be used as input to other functions for further analysis.

7.1 Simple contact selections

We start by importing everything from the ProDy package:

```
In [1]: from prody import *

In [2]: from pylab import *

In [3]: ion()
```

ProDy selection engine has a powerful feature that enables identifying intermolecular contacts very easily. We will see this by identifying protein atoms interacting with an inhibitor.

We start with parsing a PDB file that contains a protein and a bound ligand.

```
In [4]: pdb = parsePDB('1zz2')
```

1zz2[1] contains an inhibitor bound p38 MAP kinase structure. Residue name of inhibitor is B11[2]. Protein atoms interacting with the inhibitor can simply be identified as follows:

```
In [5]: contacts = pdb.select('protein and within 4 of resname B11')

In [6]: repr(contacts)
Out[6]: "<Selection: 'protein and wit... of resname B11' from 1zz2 (50 atoms)>"
```

`'protein and within 4 of resname B11'` is interpreted as select protein atoms that are within 4 A of residue whose name is B11. This selects protein atoms that within 4 A of the inhibitor.

7.2 Contacts between different atom groups

In some cases, the protein and the ligand may be in separate files. We will imitate this case by making copies of protein and ligand.

[1] http://www.pdb.org/pdb/explore/explore.do?structureId=1zz2
[2] http://www.pdb.org/pdb/ligand/ligandsummary.do?hetId=B11

```
In [7]: inhibitor = pdb.select('resname B11').copy()

In [8]: repr(inhibitor)
Out[8]: "<AtomGroup: 1zz2 Selection 'resname B11' (33 atoms)>"

In [9]: protein = pdb.select('protein').copy()

In [10]: repr(protein)
Out[10]: "<AtomGroup: 1zz2 Selection 'protein' (2716 atoms)>"
```

We see that inhibitor molecule contains 33 atoms.

Now we have two different atom groups, and we want protein atoms that are within 4 Å of the inhibitor.

```
In [11]: contacts = protein.select('within 4 of inhibitor', inhibitor=inhibitor)

In [12]: repr(contacts)
Out[12]: "<Selection: 'index 227 230 2... 1354 1356 1358' from 1zz2 Selection 'protein' (50 atoms)>"
```

We found that 50 protein atoms are contacting with the inhibitor. In this case, we passed the atom group *inhibitor* as a keyword argument to the selection function. Note that the keyword must match that is used in the selection string.

7.3 Composite contact selections

Now, let's try something more sophisticated. We select Cα atoms of residues that have at least one atom interacting with the inhibitor:

```
In [13]: contacts_ca = protein.select(
   ....:     'calpha and (same residue as within 4 of inhibitor)',
   ....:     inhibitor=inhibitor)
   ....:

In [14]: repr(contacts_ca)
Out[14]: "<Selection: 'index 225 232 2... 1328 1351 1359' from 1zz2 Selection 'protein' (20 atoms)>"
```

In this case, `'calpha and (same residue as within 4 of inhibitor)'` is interpreted as select Cα atoms of residues that have at least one atom within 4 A of any inhibitor atom.

This shows that, 20 residues have atoms interacting with the inhibitor.

7.4 Spherical atom selections

Similarly, one can give arbitrary coordinate arrays as keyword arguments to identify atoms in a spherical region. Let's find backbone atoms within 5 Å of point (25, 73, 13):

```
In [15]: sel = protein.select('backbone and within 5 of somepoint',
   ....:                         somepoint=np.array((25, 73, 13)))
   ....:
```

7.5 Fast contact selections

For repeated and faster contact identification `Contacts` class is recommended.

We pass the protein as argument:

```
In [16]: protein_contacts = Contacts(protein)
```

The following corresponds to `"within 4 of inhibitor"`:

```
In [17]: contants = protein_contacts.select(4, inhibitor)

In [18]: repr(contacts)
Out[18]: "<Selection: 'index 227 230 2... 1354 1356 1358' from 1zz2 Selection 'protein' (50 atoms)>"
```

This method is 20 times faster than the one in the previous part, but it is limited to selecting only contacting atoms (other selection arguments cannot be passed). Again, it should be noted that `Contacts` does not update the KDTree that it uses, so it should be used if protein coordinates does not change between selections.

CHAPTER

EIGHT

LIGAND EXTRACTION

This example shows how to align structures of the same protein and extract bound ligands from these structures.

`matchAlign()` function can be used for aligning protein structures. This example shows how to use it to extract ligands from multiple PDB structures after superposing the structures onto a reference. Output will be PDB files that contain ligands superposed onto the reference structure.

8.1 Parse reference and blast search

We start by importing everything from the ProDy package:

```
In [1]: from prody import *

In [2]: from pylab import *

In [3]: ion()
```

First, we parse the reference structure and blast search PDB for similar structure:

```
In [4]: p38 = parsePDB('1p38')

In [5]: seq = p38['A'].getSequence()

In [6]: blast_record = blastPDB(seq)
```

It is a good practice to save this record on disk, as NCBI may not respond to repeated searches for the same sequence. We can do this using Python standard library `pickle`[1] as follows:

```
In [7]: import pickle
```

Record is save using `dump()`[2] function into an open file:

```
In [8]: pickle.dump(blast_record, open('p38_blast_record.pkl', 'w'))
```

Then, it can be loaded using `load()`[3] function:

```
In [9]: blast_record = pickle.load(open('p38_blast_record.pkl'))
```

[1] http://docs.python.org/library/pickle.html#pickle
[2] http://docs.python.org/library/pickle.html#pickle.dump
[3] http://docs.python.org/library/pickle.html#pickle.load

8.2 Align structures and extract ligands

Then, we parse the hits one-by-one, superpose them onto the reference structure, and extract ligands:

```
In [10]: for pdb_id in blast_record.getHits():
   ....:     # blast search may return PDB identifiers of deprecated structures,
   ....:     # so we parse structures within a try statement
   ....:     try:
   ....:         pdb = parsePDB(pdb_id)
   ....:         pdb = matchAlign(pdb, p38)[0]
   ....:     except:
   ....:         continue
   ....:     else:
   ....:         ligand = pdb.select('not protein and not water')
   ....:         repr(ligand)
   ....:         if ligand:
   ....:             writePDB(pdb_id + '_ligand.pdb', ligand)
   ....:
```

```
In [11]: !ls *_ligand.pdb
1a9u_ligand.pdb  2baj_ligand.pdb  3d7z_ligand.pdb  3gcv_ligand.pdb  3lfa_ligand.pdb  3ody_ligand.pdb
1bl6_ligand.pdb  2bak_ligand.pdb  3d83_ligand.pdb  3gfe_ligand.pdb  3lfb_ligand.pdb  3odz_ligand.pdb
1bl7_ligand.pdb  2bal_ligand.pdb  3ds6_ligand.pdb  3gi3_ligand.pdb  3lfc_ligand.pdb  3oef_ligand.pdb
1bmk_ligand.pdb  2baq_ligand.pdb  3dt1_ligand.pdb  3ha8_ligand.pdb  3lfd_ligand.pdb  3p5k_ligand.pdb
1di9_ligand.pdb  2ewa_ligand.pdb  3e92_ligand.pdb  3hec_ligand.pdb  3lfe_ligand.pdb  3p78_ligand.pdb
1ian_ligand.pdb  2fsl_ligand.pdb  3e93_ligand.pdb  3heg_ligand.pdb  3lff_ligand.pdb  3p79_ligand.pdb
1kv1_ligand.pdb  2fsm_ligand.pdb  3fc1_ligand.pdb  3hl7_ligand.pdb  3lhj_ligand.pdb  3p7a_ligand.pdb
1kv2_ligand.pdb  2fso_ligand.pdb  3fi4_ligand.pdb  3hll_ligand.pdb  3mgy_ligand.pdb  3p7b_ligand.pdb
1m7q_ligand.pdb  2fst_ligand.pdb  3fkl_ligand.pdb  3hp2_ligand.pdb  3mh0_ligand.pdb  3p7c_ligand.pdb
1ouk_ligand.pdb  2gfs_ligand.pdb  3fkn_ligand.pdb  3hp5_ligand.pdb  3mh1_ligand.pdb  3pg3_ligand.pdb
1ouy_ligand.pdb  2ghl_ligand.pdb  3fko_ligand.pdb  3hrb_ligand.pdb  3mh2_ligand.pdb  3qud_ligand.pdb
1ove_ligand.pdb  2ghm_ligand.pdb  3fl4_ligand.pdb  3hub_ligand.pdb  3mh3_ligand.pdb  3que_ligand.pdb
1oz1_ligand.pdb  2gtm_ligand.pdb  3fln_ligand.pdb  3huc_ligand.pdb  3mpa_ligand.pdb  3rin_ligand.pdb
1r39_ligand.pdb  2gtn_ligand.pdb  3flq_ligand.pdb  3hv3_ligand.pdb  3mpt_ligand.pdb  3roc_ligand.pdb
1r3c_ligand.pdb  2i0h_ligand.pdb  3fls_ligand.pdb  3hv4_ligand.pdb  3mvl_ligand.pdb  3s3i_ligand.pdb
1w7h_ligand.pdb  2npq_ligand.pdb  3flw_ligand.pdb  3hv5_ligand.pdb  3mvm_ligand.pdb  3s4q_ligand.pdb
1w82_ligand.pdb  2puu_ligand.pdb  3fly_ligand.pdb  3hv6_ligand.pdb  3mw1_ligand.pdb  3u8w_ligand.pdb
1w83_ligand.pdb  2qd9_ligand.pdb  3flz_ligand.pdb  3hv7_ligand.pdb  3new_ligand.pdb  3uvp_ligand.pdb
1w84_ligand.pdb  2rg5_ligand.pdb  3fmh_ligand.pdb  3hvc_ligand.pdb  3nnu_ligand.pdb  3uvq_ligand.pdb
1wbn_ligand.pdb  2rg6_ligand.pdb  3fmj_ligand.pdb  3iph_ligand.pdb  3nnv_ligand.pdb  3uvr_ligand.pdb
1wbo_ligand.pdb  2yis_ligand.pdb  3fmk_ligand.pdb  3itz_ligand.pdb  3nnw_ligand.pdb  3zs5_ligand.pdb
1wbs_ligand.pdb  2yiw_ligand.pdb  3fml_ligand.pdb  3iw5_ligand.pdb  3nnx_ligand.pdb  3zsg_ligand.pdb
1wbt_ligand.pdb  2yix_ligand.pdb  3fmm_ligand.pdb  3iw6_ligand.pdb  3nww_ligand.pdb  3zsh_ligand.pdb
1wbv_ligand.pdb  2zaz_ligand.pdb  3fmn_ligand.pdb  3iw7_ligand.pdb  3o8p_ligand.pdb  3zsi_ligand.pdb
1wbw_ligand.pdb  2zb0_ligand.pdb  3fsf_ligand.pdb  3iw8_ligand.pdb  3o8t_ligand.pdb  3zya_ligand.pdb
1yqj_ligand.pdb  2zb1_ligand.pdb  3fsk_ligand.pdb  3k3i_ligand.pdb  3o8u_ligand.pdb  4a9y_ligand.pdb
1yw2_ligand.pdb  3bv2_ligand.pdb  3gc7_ligand.pdb  3k3j_ligand.pdb  3obg_ligand.pdb  4aa0_ligand.pdb
1ywr_ligand.pdb  3bv3_ligand.pdb  3gcp_ligand.pdb  3kf7_ligand.pdb  3obj_ligand.pdb  4aa4_ligand.pdb
1zyj_ligand.pdb  3bx5_ligand.pdb  3gcq_ligand.pdb  3kq7_ligand.pdb  3oc1_ligand.pdb  4aa5_ligand.pdb
1zz2_ligand.pdb  3c5u_ligand.pdb  3gcs_ligand.pdb  3l8s_ligand.pdb  3ocg_ligand.pdb  4aac_ligand.pdb
1zzl_ligand.pdb  3ctq_ligand.pdb  3gcu_ligand.pdb  3l8x_ligand.pdb  3od6_ligand.pdb  4dli_ligand.pdb
```

Ligands bound to p38 are outputted. Note that output PDB files may contain multiple ligands.

The output can be loaded into a molecular visualization tool for analysis.

Acknowledgments

Continued development of Protein Dynamics Software *ProDy* is supported by NIH through R01 GM099738 award. Development of this tutorial is supported by NIH funded Biomedical Technology and Research Center (BTRC) on *High Performance Computing for Multiscale Modeling of Biological Systems* (MMBios[4]) (P41 GM103712).

[4]http://mmbios.org/