Afpdb - An Efficient Protein Structure Manipulation Python Package

Yingyao Zhou

https://github.com/data2code/afpdb

Last updated: October 15, 2024



Contents

[Introduction 4](#_Toc179893019)

[Installation 4](#_Toc179893020)

[Demo 4](#_Toc179893021)

[Fundamental Concepts 7](#_Toc179893022)

[Internal Data Structure 7](#_Toc179893023)

[Data Members 7](#_Toc179893024)

[Illustration 8](#_Toc179893025)

[Example 9](#_Toc179893026)

[Contig 13](#_Toc179893027)

[Single Residue 13](#_Toc179893028)

[Single Fragment 14](#_Toc179893029)

[Multiple Same-Chain Fragments 14](#_Toc179893030)

[Multiple Fragments 14](#_Toc179893031)

[Special Keywords 15](#_Toc179893032)

[Note 15](#_Toc179893033)

[inplace 15](#_Toc179893034)

[Clone 15](#_Toc179893035)

[Selection 17](#_Toc179893036)

[Atom Selection 17](#_Toc179893037)

[Residue Selection 19](#_Toc179893038)

[Residule List 22](#_Toc179893039)

[Casting 25](#_Toc179893040)

[Read/Write 27](#_Toc179893041)

[Sequence & Chain 30](#_Toc179893042)

[Extraction 30](#_Toc179893043)

[Missing Residues 30](#_Toc179893044)

[Length 31](#_Toc179893045)

[Search 32](#_Toc179893046)

[Mutagenesis 32](#_Toc179893047)

[Mutation 33](#_Toc179893048)

[Chain Name and Order 34](#_Toc179893049)

[Residue Labeling 36](#_Toc179893050)

[Residue Renumbering 37](#_Toc179893051)

[Merge & Split Chains 38](#_Toc179893052)

[Geometry, Measurement, and Visualization 41](#_Toc179893053)

[Select Neighboring Residues 41](#_Toc179893054)

[Display 43](#_Toc179893055)

[B-factors 44](#_Toc179893056)

[PyMOL Interface 46](#_Toc179893057)

[Distance 48](#_Toc179893058)

[RMSD 50](#_Toc179893059)

[Solvent-Accessible Surface Area (SASA) 52](#_Toc179893060)

[Secondary Structures - DSSP 54](#_Toc179893061)

[Internal Coordinate 55](#_Toc179893062)

[Protein Object Manipulation 57](#_Toc179893063)

[Move Objects 57](#_Toc179893064)

[Align 58](#_Toc179893065)

[Align Sequences 60](#_Toc179893066)

[Split & Merge Objects 60](#_Toc179893067)

[Parsers for AI Models 63](#_Toc179893068)

[Parse AlphaFold Output 63](#_Toc179893069)

[Parse ColabFold Output 63](#_Toc179893070)

[Parse ESMFold Output 64](#_Toc179893071)

[Parse ProteinMPNN Output 64](#_Toc179893072)

[Parser LigandMPNN Output 64](#_Toc179893073)

[Protein AI Design Use Cases 66](#_Toc179893074)

[Handle Missing Residues in AlphaFold Prediction 66](#_Toc179893075)

[Structure Prediction with ESMFold 67](#_Toc179893076)

[Create Side Chains for de novo Designed Proteins 68](#_Toc179893077)

[Binding Score for EvoPro 70](#_Toc179893078)

[Developer's Note 72](#_Toc179893079)

[Installation 72](#_Toc179893080)

[Selection 73](#_Toc179893081)

[Change in residue/chain 73](#_Toc179893082)

[Residue Identifier 73](#_Toc179893083)

[inplace 73](#_Toc179893084)

[Extract Atom Coordinates 73](#_Toc179893085)

[Extract Atom Pair Coordinates 74](#_Toc179893086)

[Caution 75](#_Toc179893087)

# Introduction

The emergence of AlphaFold and subsequent protein AI models has revolutionized protein design. To maximize the probability of success, the AI-driven protein design process involves analyzing thousands of protein structures. This includes handling structure file read/write operations, aligning structures and measuring structural deviations, standardizing chain/residue labels, extracting residues, identifying mutations, and creating visualizations. However, existing programming packages do not fully address these challenges. To bridge this gap, we introduce the Afpdb module. Built upon AlphaFold’s NumPy architecture and leveraging the intuitive contig syntax proposed by RFDiffusion, Afpdb streamlines structure analyses. While supplementing Biopython with dozens of methods commonly used in protein AI design but not readily available elsewhere; it also offers a user-friendly interface that seamlessly integrates with PyMOL’s visualization capabilities.

This document is a tutorial on Afpdb. Throughout this tutorial, we will use two example antigen-antibody complex structures: 5cil.pdb and fake.pdb. 5cil.pdb contains three chains, L and H chains for the antibody light chain and heavy chain, respectively, and P chain for the antigen. fake.pdb contains two short chains, the L chain contains 4 residues including two with insertion codes and 3 missing residues, and the H chain contains two residues.

The best way to learn Afpdb is to open the Jupyter Notebook in Google Colab and play with the examples. This PDF is meant to clone the content of the Jupyter Notebook for the convenience of offline reading. The Jupyter Notebook does not export nicely into a PDF file, we therefore decided to recreate the content. As the Jupyter Notebook is frequently updated, this PDF version only served as a snapshot in time for user’s learning purpose, therefore, the content may become outdated. If you use a Linux environment, however, we expect the notebook can run in other platforms if Afpdb has been installed.

## Installation

To install the Afpdb package:

pip install git+https://github.com/data2code/afpdb.git

To enable PyMOL-dependent features

conda install conda-forge::pymol-open-source

To assign secondary structures:

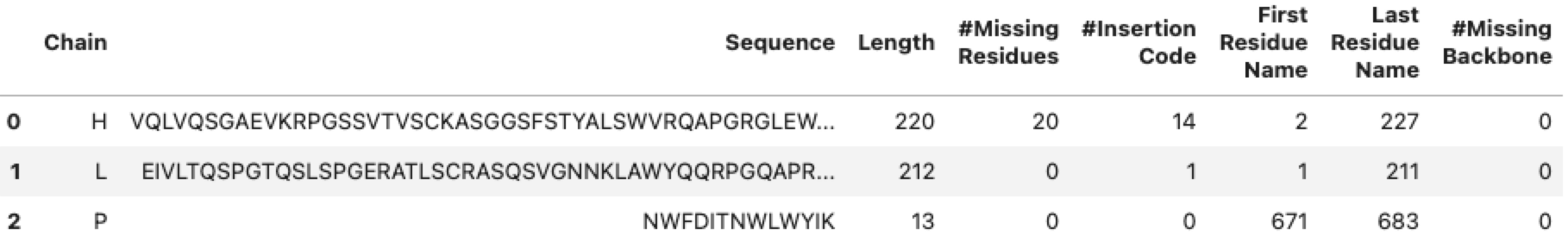
conda install sbl::dssp

The Notebook contains more detailed codes for the Colab environment and for developers.

## Demo

To convince you Afpdb is effective and elegant, let us look at the following example, where we first identify contact residues in the antibody-antigen interface and then extract those residues into a separate PDB file. The structure display confirms the extraction was correct. These manipulations are not so straightforward using PyMOL or Biopython.

# load the ab-ag complex structure using PDB code name  
p=Protein("5cil")  
# show key statistics summary of the structure  
p.summary()



Notice that residue names do not start from "1" for chain "H" and chain "L" (see column "First Residue Name"), some residues in the CDR regions have insertion code (see column "#Insertion Code"), so that residue numbering goes from 1 to 211 for 212 residues on chain "L". It is good that learn that all residues have the complete set of backbone atoms "N,CA,C,O".

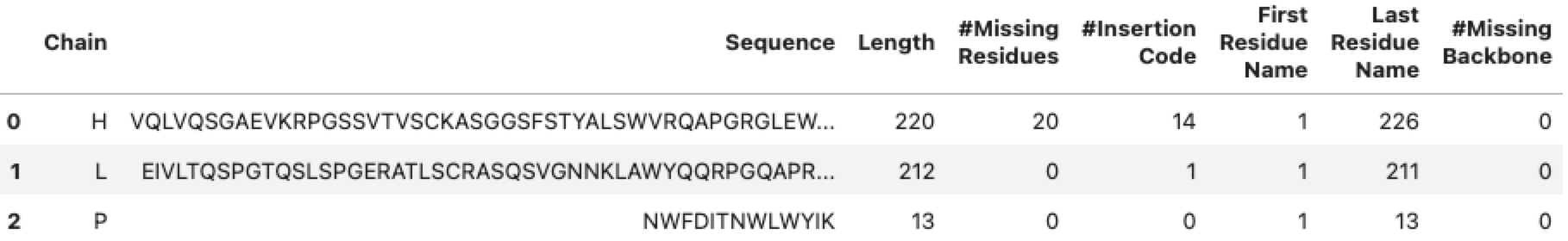
We can standardize residue naming (we use blue fonts for outputs):

print("Old P chain residue numbering:", p.rs("P").name(), "\n")

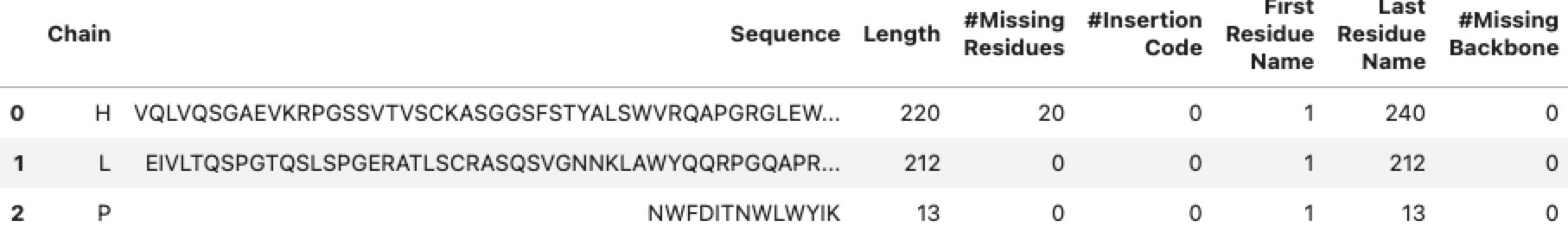
Old P chain residue numbering: ['671', '672', '673', '674', '675', '676', '677', '678', '679', '680', '681', '682', '683']

q, old\_num=p.renumber("RESTART")  
print("New P chain residue numbering:", q.rs("P").name(), "\n")  
  
New P chain residue numbering: ['1', '2', '3', '4', '5', '6', '7', '8', '9', '10', '11', '12', '13']

q.summary()



# We can further remove the insertion code by  
# renumber() returns a tuple, (Protein obj, old numbers)  
q=p.renumber("NOCODE")[0].renumber("RESTART")[0]  
q.summary()

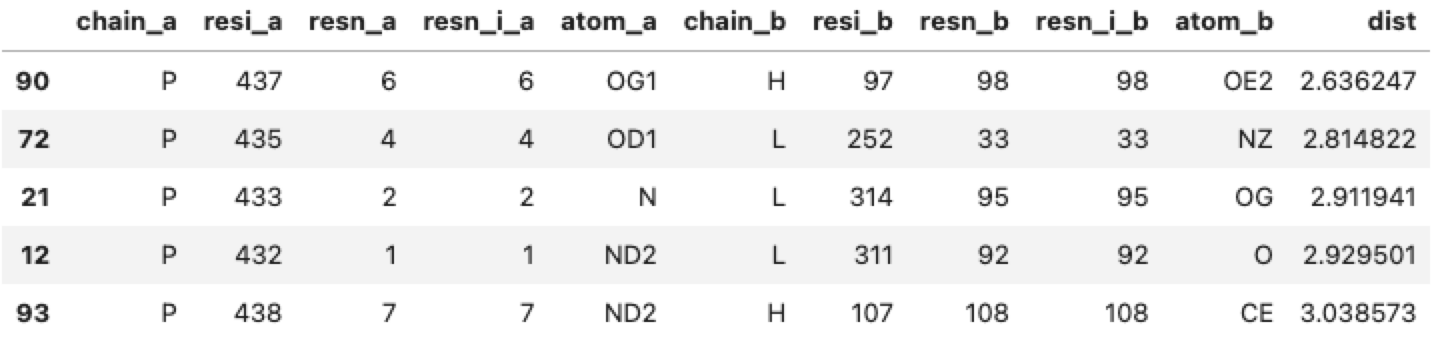


To predict the structure with AlphaFold, we can replace missing residues with glycines. Notice we refer to missing residues within a single chain, not using glycines to connect different chains.

print("Sequence for AlphaFold modeling, with the 20 missing residues replaced by Glycine:")  
print(">5cil\n"+p.seq(gap="G")+"\n")

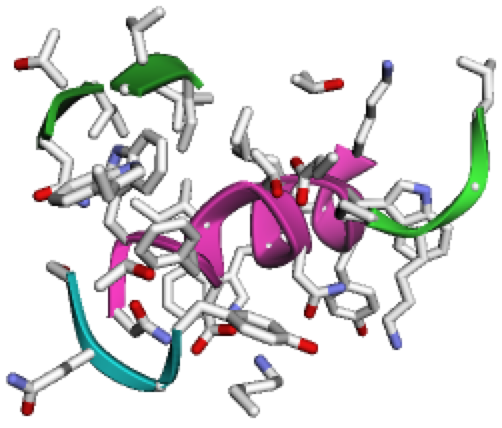
Sequence for AlphaFold modeling, with the 20 missing residues replaced by Glycine:  
>5cil  
VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSSASTKGPSVFPLAPSGGGGGGGGGTAALGCLVKDYFPEPVTVGSWGGGGNSGALTSGGVHTFPAVLQSGSGLYSLSSVVTVPSSSLGTGGQGTYICNVNHKPSNTKVDKKGGVEP:EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR:NWFDITNWLWYIK

# identify H,L chain residues within 4A to antigen P chain  
binder, target, df\_dist=p.rs\_around("P", dist=4)  
# show the distance of binder residues to antigen P chain  
df\_dist[:5]



# create a new PDB file only containing the antigen and binder residues  
p=p.extract(binder | "P")  
# save the new structure into a local PDB file  
p.save("binding.pdb")

# display the PDB struture, default is show ribbon and color by chains.  
p.show(show\_sidechains=True)



The above script shows a few strengths of Afpdbs:

* User friendly: We use Protein() to create a protein object, use '''save()''' to create a PDB file. We will explain both methods can accommodate multiple formats.
* Residue selection: We use "H:L" and "P" to select all Ab and Ag residues, we use binder | "P" to Boolean combine selections. Afpdb supports a "contig" syntax to select residues with their human readable labels.
* Visualization: We here show how a protein object can be visualized within Jupyter Notebook. We will explain how Afpdb integrates with PyMOL for more powerful 3D visualization and transfer the residues selections from Afpdb into PyMOL.
* AI ready: Afpdb was created to meet our own protein AI design needs. We show a brief example of how Afpdb prepares an input for AlphaFold, and we will show more sophisticated AI use cases.

# Fundamental Concepts

## Internal Data Structure

### Data Members

From the demo, we see how fast Afpdb analyses are, which is because Afpdb uses NumPy arrays for storing protein structure data, which is very different from most existing packages relying on the model-chain-residue-atom tree structure.

To better understand why **Afpdb** can manipulate protein structures efficiently, it is helpful to first discuss how the structure data in a PDB file is stored within the AlphaFold's Protein class. The following descriptions are mostly taken from DeepMind’s alphafold/common/protein/protein.py file.

  # Cartesian coordinates of atoms in angstroms. The atom types correspond to  
  # residue\_constants.atom\_types, i.e. the first three are N, CA, C.  
  atom\_positions: np.ndarray  # [num\_res, num\_atom\_type, 3]  
  
  # Amino-acid type for each residue represented as an integer between 0 and  
  # 20, where 20 is 'X'.  
  aatype: np.ndarray  # [num\_res]  
  
  # Binary float mask to indicate presence of a particular atom. 1.0 if an atom  
  # is present and 0.0 if not. This should be used for loss masking.  
  atom\_mask: np.ndarray  # [num\_res, num\_atom\_type]  
  
  # Residue index as used in PDB. It is not necessarily continuous or 0-indexed.  
  residue\_index: np.ndarray  # [num\_res]

We modified residue\_index to dtype "<U6" in order to be able to store residue id with possible insertion code. A residue\_index was an integer in AlphaFold, in our extension, residue\_index can include insertion code, e.g., "121", "122A", "112B". The maximum residue id can be 9999 if we allow insertion codes with two letters, otherwise, 99999 if all insertion codes are single letters.

  # 0-indexed number corresponding to the chain in the protein that this residue  
  # belongs to.  
  chain\_index: np.ndarray  # [num\_res]  
  
  # B-factors, or temperature factors, of each residue (in sq. angstroms units),  
  # representing the displacement of the residue from its ground truth mean  
  # value.  
  b\_factors: np.ndarray  # [num\_res, num\_atom\_type]  
  
  # Chain names - this is added by us. DeepMind's original code does not memorize the chain  
 # name in the PDB file  
  
  # chain names became A, B, C, etc. afpdb keeps the original chain names in the PDB file  
  chain\_id: np.ndarray # [num\_chains]

## Illustration

A diagram of a diagram of a diagram

Description automatically generated

Notice the first axis of all NumPy arrays are the number of residues. The second axis can be either one or the number of possible non-hydrogen atom types (which is 37).

The above is AlphaFold's Protein class, developers access this data via Afpdb's Protein class, which is a wrapper of AlphaFold's protein class.

In Afpdb's Protein class, it contains an attribute called data, which points to an AlphaFold's Protein instance.

from afpdb.afpdb import Protein

p=Protein(fk)

# p.data points to AlphaFold's Protein object

print(p.data.atom\_positions[:, 1])  
  
# outputs  
# [[  6.30200005 -14.27600002 -18.36100006]  
#  [  9.34000015 -16.29100037 -17.33600044]  
#  [  9.67800045 -16.51799965 -13.59899998]  
#  [ 16.89500046 -17.8920002   -7.03000021]  
#  [ 25.96999931   6.87099981 -19.03800011]  
#  [ 25.11199951   9.9829998  -16.98600006]]  
  
print(p.res\_map)  
  
# outputs  
# {'L5': 0, 'L6A': 1, 'L6B': 2, 'L10': 3, 'H3': 4, 'H4': 5}

In the example above, we obtain the (X, Y, Z) coordinates of the CA atoms (i.e., we specify 1 for the 2nd axis of atom\_positions) corresponding to the first six residues via accessing p.data.

To further speed up structure manipulations, Afpdb's Protein class maintains a dictionary called res\_map, which maps the full residue id, in the format of {chain}{residue\_index}, into its residue position. {chain}{residue\_index} is the user-friendly format for identifying a specific residue, e.g., "C122A" is the residue index "122A" on chain "C". This residue corresponds to an integer index in the NumPy arrays internally. Developers should remember to call self.\_make\_res\_map() to update this mapping dictionary, if a method requires the underlying mapping to be refreshed after changing the positions/types of residues for any location. The example above shows how the six full residue names are mapped to the NumPy arrays.

For the rest of the tutorial, when we use the term "Protein" class, we refer to Afpdb's Protein class, which can be imported using from afpdb.afpdb import Protein. We will no longer mention AlphaFold's Protein class to avoid confusion, infact, users do not need to directly access p.data, only developers need to be aware that p.data points to multiple NumPy arrays behind the scenes.

### Example

Let us further explain the previous example and examine p.data NumPy arrays using fake.pdb.

The following is the fake.pdb file, which contains 4-residue chain L and a 2-residue chain H.

MODEL     1  
ATOM      1  N   GLU L   5       5.195 -14.817 -19.187  1.00  1.00           N  
ATOM      2  CA  GLU L   5       6.302 -14.276 -18.361  1.00  1.00           C  
ATOM      3  C   GLU L   5       7.148 -15.388 -17.731  1.00  1.00           C  
ATOM      4  CB  GLU L   5       5.794 -13.368 -17.248  1.00  1.00           C  
ATOM      5  O   GLU L   5       6.658 -16.231 -17.006  1.00  1.00           O  
ATOM      6  CG  GLU L   5       6.934 -12.664 -16.494  1.00  1.00           C  
ATOM      7  CD  GLU L   5       6.461 -11.817 -15.327  1.00  1.00           C  
ATOM      8  OE1 GLU L   5       7.282 -11.138 -14.677  1.00  1.00           O  
ATOM      9  OE2 GLU L   5       5.243 -11.804 -15.070  1.00  1.00           O  
ATOM     10  N   ILE L   6A      8.444 -15.321 -17.934  1.00  1.00           N  
ATOM     11  CA  ILE L   6A      9.340 -16.291 -17.336  1.00  1.00           C  
ATOM     12  C   ILE L   6A      9.657 -15.849 -15.925  1.00  1.00           C  
ATOM     13  CB  ILE L   6A     10.604 -16.433 -18.162  1.00  1.00           C  
ATOM     14  O   ILE L   6A     10.192 -14.739 -15.685  1.00  1.00           O  
ATOM     15  CG1 ILE L   6A     10.228 -16.847 -19.590  1.00  1.00           C  
ATOM     16  CG2 ILE L   6A     11.540 -17.469 -17.523  1.00  1.00           C  
ATOM     17  CD1 ILE L   6A     11.401 -17.319 -20.426  1.00  1.00           C  
ATOM     18  N   VAL L   6B      9.339 -16.725 -14.982  1.00  1.00           N  
ATOM     19  CA  VAL L   6B      9.678 -16.518 -13.599  1.00  1.00           C  
ATOM     20  C   VAL L   6B     11.024 -17.188 -13.330  1.00  1.00           C  
ATOM     21  CB  VAL L   6B      8.569 -17.028 -12.666  1.00  1.00           C  
ATOM     22  O   VAL L   6B     11.242 -18.372 -13.679  1.00  1.00           O  
ATOM     23  CG1 VAL L   6B      8.960 -16.919 -11.194  1.00  1.00           C  
ATOM     24  CG2 VAL L   6B      7.268 -16.234 -12.927  1.00  1.00           C  
ATOM     40  N   GLN L  10      15.587 -17.776  -7.649  1.00  1.00           N  
ATOM     41  CA  GLN L  10      16.895 -17.892  -7.030  1.00  1.00           C  
ATOM     42  C   GLN L  10      16.721 -18.330  -5.569  1.00  1.00           C  
ATOM     43  CB  GLN L  10      17.616 -16.572  -7.093  1.00  1.00           C  
ATOM     44  O   GLN L  10      16.270 -17.557  -4.746  1.00  1.00           O  
ATOM     45  CG  GLN L  10      17.963 -16.094  -8.483  1.00  1.00           C  
ATOM     46  CD  GLN L  10      18.781 -14.822  -8.460  1.00  1.00           C  
ATOM     47  NE2 GLN L  10      20.052 -14.951  -8.083  1.00  1.00           N  
ATOM     48  OE1 GLN L  10      18.284 -13.727  -8.786  1.00  1.00           O  
ATOM    862  N   LEU H   3      27.368   6.440 -19.107  1.00  1.00           N  
ATOM    863  CA  LEU H   3      25.970   6.871 -19.038  1.00  1.00           C  
ATOM    864  C   LEU H   3      25.761   7.794 -17.840  1.00  1.00           C  
ATOM    865  CB  LEU H   3      25.089   5.647 -18.873  1.00  1.00           C  
ATOM    866  O   LEU H   3      25.979   7.398 -16.661  1.00  1.00           O  
ATOM    867  CG  LEU H   3      25.225   4.606 -19.964  1.00  1.00           C  
ATOM    868  CD1 LEU H   3      24.282   3.430 -19.748  1.00  1.00           C  
ATOM    869  CD2 LEU H   3      24.962   5.190 -21.355  1.00  1.00           C  
ATOM    870  N   VAL H   4      25.291   9.008 -18.090  1.00  1.00           N  
ATOM    871  CA  VAL H   4      25.112   9.983 -16.986  1.00  1.00           C  
ATOM    872  C   VAL H   4      23.672  10.399 -16.963  1.00  1.00           C  
ATOM    873  CB  VAL H   4      25.976  11.257 -17.222  1.00  1.00           C  
ATOM    874  O   VAL H   4      23.143  10.875 -17.973  1.00  1.00           O  
ATOM    875  CG1 VAL H   4      25.686  12.319 -16.177  1.00  1.00           C  
ATOM    876  CG2 VAL H   4      27.466  10.902 -17.258  1.00  1.00           C  
TER     877      VAL H   4  
ENDMDL  
END

We first read in fake.pdb, there is a warning indicating there are residues with insertion codes: 6A and 6B. This alerts users that there may be duplicates in the integer portion of the residue ID, so it is a good habit not to rely on the assumption that residue integer IDs are all unique. AlphaFold’s original code did not support insertion codes. **Afpdb** made modifications to eliminate this limitation.

p=Protein(fk)  
print(p.data.warning(), "\n")

{'renamed\_res': [], 'insertion\_res': [('L6A', 'ILE'), ('L6B', 'VAL')], 'unknown\_res': []}

# show the sequences by chain  
print(p.seq\_dict())  
  
{'L': 'EIVXXXQ', 'H': 'LV'}

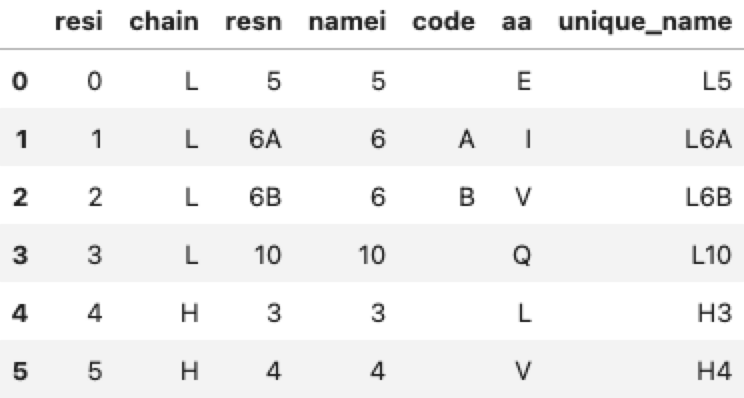
# print the total number of residues  
print("Total length:", len(p), "\n")

Total length: 6   
  
print("Residue labels:", p.rs().name(), "\n")  
  
Residue labels: ['5', '6A', '6B', '10', '3', '4']

print("Their chain labels:", p.rs().chain())

Their chain labels: ['L', 'L', 'L', 'L', 'H', 'H']

Here p.rs() is a "residue selection" that points to all residues. The residue selection, to be explained later, can be used to fetch the metadata for residues (their labels, chain names, amino acid types, etc). The most convenient way to access residue identifiers as a DataFrame object is to use its df() method.



Our protein object p contains an attribute data, which points to AlphaFold's NumPy arrays. First, any warnings during the parsing of the PDB file can be extracted using p.data.warning(), which includes unrecognized residues, special forms that are renamed, and residues with an insertion code.

Let us examine the backend NumPy data within p.data. Here p.rs() is a "residue selection" that points to all residues. The residue selection, to be explained later, can be used to fetch the metadata for residues (their labels, chain names, amino acid types, etc.).

g=p.data  
# we used p.rs() to select ALL residues  
# we used p.rs().name() to get all residue labels, which is stored in g.residue\_index  
print(g.residue\_index, "\n")

['5' '6A' '6B' '10' '3' '4']

# p.res\_map maps each unique residue label to their row indices in the NumPy arrays.  
print(p.res\_map, "\n")

{'L5': 0, 'L6A': 1, 'L6B': 2, 'L10': 3, 'H3': 4, 'H4': 5}

# we used p.rs().chain() to get the chain name of each residue  
# chain information is stored in g.chain\_index  
print(g.chain\_index, "\n")

[0 0 0 0 1 1]

# To obtain the list of chain names in the order of their appearance in the PDB file,  
# we should use the chain\_id() method instead  
print(p.rs().chain(), "\n")

['L', 'L', 'L', 'L', 'H', 'H']

print(p.chain\_id())

['L', 'H']

g.chain\_index shows the first 4 residues belong to chain index 0, and the next 2 residues belong to chain index 1. AlphaFold uses Biopython to parse PDB files, Chains are numbered in the order of their appearance in the PDB file, so chain L is indexed as chain 0 and chain H is indexed as chain 1. It is important to remember that the best practice is to access data without assuming how chains appear in a certain order in the PDB or in Protein objects. It is safer to access structure or sequence data by their chain names.

What are the chain names for 0 and 1? AlphaFold’s original code did not store chain names and chains were named as A, B, C, etc. Afpdb has improved AlphaFold's code to add a new data member chain\_id() into its Protein class.

Array aatype stores the identity of amino acids as defined in alphafold.common.residue\_constants.py:

restypes = ['A', 'R', 'N', 'D', 'C', 'Q', 'E', 'G', 'H', 'I', 'L', 'K', 'M', 'F', 'P', 'S', 'T', 'W', 'Y', 'V']

So index 6 translates into “E”.

There are a total of 6 residues. By assuming residues are numbered sequentially, we imply three residues (7, 8, and 9) are missing in the PDB file. Missing residues are not stored in the NumPy arrays; they can only be inferred based on the gaps in the integer portion of the residue IDs.

# afres contains protein structure constants defined by AlphaFold  
import afpdb.myalphafold.common.residue\_constants as afres  
print(g.aatype, "\n")

[ 6 9 19 5 10 19]

[ afres.restypes[x] for x in g.aatype ]

['E', 'I', 'V', 'Q', 'L', 'V']

Users do not have to use afres, residue types can be extracted with the residue selection object:

# Notice three missing residues are represented as 3 "X", but they are not there in the protein structure  
# notice sequences from different chains are separated by ":"  
print(p.seq(), "\n")  
  
EIVXXXQ:LV  
  
# retrieve sequence information via residue selection  
p.rs().aa()

['E', 'I', 'V', 'Q', 'L', 'V']

There are different types of metadata for residues. In Afpdb, we use the following convention:

* **resn** refers to the residue\_index, a string with an optional insertion code without chain name.
* **resi** refers to the internal numpy array indices, e.g., the resi for resn = '6A' is 1.
* **resn\_i** refers to the integer portion of the resn, resn\_i for residue 6B is integer 6. p.res\_map maps the unique residue name, (chain + **resn**), into **resi**.

Note: Early Afpdb users use p.data\_prt, although this is still supported for now, please switch to use p.data going forward.

There are a total of 37 possible atom types when all 20 amino acid types are combined (not counting hydrogens), AlphaFold uses an array of 6 x 37 to store atom 3D coordinates (we have 6 residues in this example). Therefore, the atom\_positions is a 3-dimensional NumPy array, where the last dimension is for (X, Y, Z) coordinates:

g.atom\_positions.shape

(6, 37, 3)

No residue will have all 37 atoms, they all have N, CA, C, and O, but do not necessarily have CB, CG, etc. Therefore, AlphaFold's code uses slightly more memory than needed to store the coordinates. As PDB data are small, trading extra memory to gain convenience and speed with NumPy arrays is wise. This is why implementing new computations in Afpdb can be done quickly, as no boilerplate loops are required to navigation the model/chain/residue/atom tree to access coordinate data, like what is the required for using the Biopython API.

As not all array members are used, we thus need to know what atoms in the atom\_positions array contain real data using a binary array atom\_mask:

print(ATS.i('CA'), "\n")

1  
  
print(g.atom\_mask[:, ATS.i('CA')], "\n")  
  
[1. 1. 1. 1. 1. 1.]

print(g.atom\_positions[:, ATS.i('CA')], "\n")

[[ 6.30200005 -14.27600002 -18.36100006]

[ 9.34000015 -16.29100037 -17.33600044]

[ 9.67800045 -16.51799965 -13.59899998]

[ 16.89500046 -17.8920002 -7.03000021]

[ 25.96999931 6.87099981 -19.03800011]

[ 25.11199951 9.9829998 -16.98600006]]

print(g.atom\_mask[:, ATS.i('CG')], "\n")

[1. 0. 0. 1. 1. 0.]

print(g.atom\_positions[:, ATS.i('CG')], "\n")

[[ 6.93400002 -12.66399956 -16.49399948]

[ 0. 0. 0. ]

[ 0. 0. 0. ]

[ 17.96299934 -16.09399986 -8.4829998 ]

[ 25.22500038 4.60599995 -19.9640007 ]

[ 0. 0. 0. ]]

str(~ p.ats('CA'))

'N,C,CB,O,CG,CG1,CG2,OG,OG1,SG,CD,CD1,CD2,ND1,ND2,OD1,OD2,SD,CE,CE1,CE2,CE3,NE,NE1,NE2,OE1,OE2,CH2,NH1,NH2,OH,CZ,CZ2,CZ3,NZ,OXT'

We refer to an atom with its name instead of memorizing its index in the arrays. ATS is the atom selection class to be introduced later. ATS.i method converts an atom name into its integer index. We also show a simple "~" operator to demonstrate selection objects can be Boolean manipulated.

We see that all six residues have CA (Cα) atom, but only the 1st, 4th, and 5th residues (E, Q, L) have (Cγ). So the coordinates for those atoms within atom\_positions array, but with corresponding atom\_mask set to 0 should be ignored (these atoms are not present in the PDB structure). Although atoms with coordinates at the origin are likely masked-out atoms, we should not rely on that assumption. In fact, when AlphaFold2 prediction starts, all atoms are placed at the origin -- so-called black hole conformation. Therefore, we should rely on the atom\_mask array to determine the presence of atoms and assume the coordinates of masked out atoms can be any garbage numbers.

You might worry that the extra array elements for masked atoms will create computational overhead. In the Developers' Note section, we will explain methods that convert this sparse coordinate NumPy array into a dense coordinate NumPy array. Indeed, eliminating non-existing atoms further accelerate the computation and that is used in Afpdb's analyses.

Lastly and similarly, b\_factors are also stored in an array at the atom level. Only elements with atom\_mask equaling 1 have meaningful b factors.

g.b\_factors.shape

(6, 37)

To summarize, for a given Afpdb Protein object p, we store all key PDB information into a few NumPy arrays: atom\_positions, atom\_mask, residue\_index, chain\_index, b\_factors, and chain\_id within p.data. We also have a helper dictionary p.res\_map.

These arrays make structure manipulations a breeze. End users do not need to access these NumPy arrays, the architecture is for developers to understand.

## Contig

Based on how Afpdb uses NumPy arrays to store structure data, we can access a few residues and a few atoms is as easily as accessing certain rows and columns in these NumPy arrays. To specify what residues are of interest, we use a string format called **contig**. Contig is a string format introduced by recent protein AI packages such as RFDiffusion and ProteinMPNN, we adopt and slightly improve the syntax as detailed below.

### Single Residue

RESIDUE = CHAIN RESIDUE\_INDEX without a space in between

In PDB, each residue is assigned an integer id. In some cases, a residue label (RESIDUE\_INDEX) can be followed by an insertion code, which is an alphabet letter (two letters in very rare cases). This is because when insertions were made to a residue, such as residue 100 in the antibody CDR loops, people prefer to call the new residues 100A and 100B so that the rest of the residues do not need to be renumbered.

The residue label alone without the chain name is not unique, because the same residue label can appear on different chains. Therefore, to fully specify a residue, we include their chain name. For example, a single residue contig can be H99, H100A. Remember p.res\_map maps a residue contig into its internal array index.

Note: Contig syntax cannot handle negative residue index. Residue index should not contain a negative integer. Afpdb still can read such PDB files, but we should renumber the residues (introduced later) if we want to use the more advanced contig syntax.

### Single Fragment

FRAGMENT = CHAIN[START ID][-][END ID]

To specify a continuous range of residues, we specify the start and end residues without the need to enumerate all residues in between. The chain name only occurs once in the beginning. The following are all valid contigs: H1-98, H-98, H98-, H, H98-100A, H98-100B, etc. H stands for the whole chain. H-98 has the start residue ID omitted, which means it starts from the first residue (which is not necessarily residue 1, as the numbering can start, e.g., from 5 in the PDB file fk.pdb). H98- covers 98 to the last residue. H98-100A does not include 100B. H98-100B includes both 100A and 100B. A single residue contig is a special fragment contig.

A chain can contain missing residues, e.g., the PDB structure may contain residues 92, 93, 98, 99, 100A, 100B, and 101, where the integer portion of the residue labels jumps from 93 to 98. We, therefore, assume residues 94-97 are missing. H92-99 will select all residues including 92, 93, 98, and 99, i.e., the contig is not broken simply because there maybe missing residues implied.

### Multiple Same-Chain Fragments

To specify multiple fragments within the same chain:

IN-CHAIN\_FRAGMENTS = FRAGMENT[,[START ID][-][END ID]]\*

Chain letter should only appear once. E.g., H-5,10-15 covers residues from the beginning to residue 5 on chain H, followed by residue 10 to residue 15 on the same chain.

Note: Fragments may overlap, however, the only the unique residues end up in the residue selection object to be introduced later. We should avoid overlap, as it makes the contig string confusing.

### Multiple Fragments

CONTIG = IN-CHAIN\_FRAGMENTS[:[IN-CHAIN\_FRAGMENTS]]\*

We can specify multiple same-chain fragments by concatenating them with ":". An example contig is H-98:L:P2-5, which specifies the whole L chain, H residues from the beginning to residue ID 98, and includes residues in the P chain from 2 to 5. You can certainly describe same-chain fragments using the general contig syntax, e.g., H-5,10-15:L-10 is equivalent to H-5:H10-15:L-10. In the Demo section, we use "H:L" to specify the whole Ab chains and "P" to select the whole antigen chain. Those are valid contig strings.

If there are multiple fragments within a chain, we advise to keep them together, so that these segments are not separated by segments from other chains for better clarity. As mentioned later, align(), and rmsd() do not reorder the underlying residue selections in its arguments, as these methods requires the one-to-one residue mapping of the two lists of input residues. extract() methods do not reorder residues specified in the contig, however, it requires the all residues of the same chain stay together and ordered ascendingly in the contig string, otherwise, it will generate an error. This is because **Afpdb** makes a heavy use of a method called chain\_pos, which assumes all residues colocated on the same chain appear sequentially. Do not worry too much as **Afpdb** code validates the input contig. Contig strings can be canonicalized, which is described later. When a protein is constructed based on a PDB input, Afpdb makes sure residues are ordered correctly, even if they are ordered incorrected in the source file.

### Special Keywords

None, "ALL" match all residues. "", "NONE", and "NULL" matches no residue.

### Note

As mentioned above, there are multiple ways of describing the same set of residues. Contig strings can be canonicalized using the \_\_str\_\_ method of a residue selection object. Print(rs) or str(rs) will implicitly call the \_\_str\_\_ method.

p=Protein(fk)  
str(p.rs("L6B,5:L-6B"))

'L5-6B'

## inplace

Many methods support a boolean argument called inplace, this is a practice copied from the well-known Python packaged called **Pandas**. inplace=True will modify the original protein object without allocating new memory, while inplace=False will leave the original object unmodified and return the modified structure as a new object.

Developers should stick to to the practice and set False as the default value, whenever inplace is used as the argument.

p=Protein(fn)  
# inplace=False by default  
print(p.chain\_id())

['L', 'H', 'P']

# q has the two chains switched  
q=p.extract("H:L")  
print(p.chain\_id()[:2], q.chain\_id(), p==q, "\n")  
  
['L', 'H'] ['H' 'L'] False

# p is modified if inplace=True  
q=p.extract("H:L", inplace=True)  
print(p.chain\_id(), q.chain\_id(), p==q)

['H' 'L'] ['H' 'L'] True

## Clone

If a method does not support inplace and you would like to keep the original object unmodified, you can first clone a copy:

p=Protein(fn)  
print(p.chain\_id(), "\n")

['L', 'H', 'P']

q=p.clone()  
# we modify q in place  
q.extract("P", inplace=True)  
# q is modified  
print(q.chain\_id(), "\n")

['P']

# p is untouched  
print(p.chain\_id())

['L', 'H', 'P']

# Selection

Selection is a powerful concept in PyMOL and we support both atom selections and residue selections. We consider the concept of selection a major feature missing in Biopython, which led to tedious residue/atom enumerations and made the code less readable and more error prone. **Afpdb** stores residues as rows and atoms as columns in the first two axes of the NumPy arrays, a residue selection contains the row indices as its data member and an atom selection contains a column index as its data member. Therefore, a residue selection and an atom selection can be used to form a new NumPy array with two axes. Notice the same atom selection is shared by all residues, which greatly simplify the usage and backend implementation. We do not support the selection that combines Ca from residue 1 and Cb from residue 2. We do not see this as a limitation in our practice.

## Atom Selection

**Afpdb** provides a class named ATS for an atom selection. ATS has an attribute data, which is a NumPy array storing the atom column indices.

There are 37 unique atoms across all 20 amino acids. The syntax for users to select atoms is by providing an atom list, or as a comma-separate string. use either "N,CA,C,O" or ["N","CA","C","O"] for backbone atoms. All atom names are in upper case only.

Internally, atom\_positions and atom\_mask have 37 elements in their axis=1 dimension, one per atom type. Therefore, the atom list is represented as a NumPy integer array internally. For "N,CA,C,O", they are represented as ats.data = np.array([0, 1, 2, 4)]), so atom\_positions[:, ats.data] will select the atom coordinates for the 4 backbone atoms. This is a key benefit of using NumPy to store PDB structural data.

Note: We often use "ats" for an atom selection object, since the word "as" is a reserved word in python.

print(ATS("N,CA,C,O"), "\n")

N,CA,C,O

print("ATS data member:", ATS("N,CA,C,O").data, "\n")

ATS data member: [0 1 2 4]

# Atoms are reordered in the selection object  
print(ATS(["CA","C","N","O"]), "\n")

N,CA,C,O

# Atoms are deduplicated in the selection object  
print(ATS("CA,CA"), "\n")

CA

# special keywords  
print("ALL", ATS("ALL"), "\n")

ALL N,CA,C,CB,O,CG,CG1,CG2,OG,OG1,SG,CD,CD1,CD2,ND1,ND2,OD1,OD2,SD,CE,CE1,CE2,CE3,NE,NE1,NE2,OE1,OE2,CH2,NH1,NH2,OH,CZ,CZ2,CZ3,NZ,OXT

print(None, ATS(None), np.all(ATS(None).data==ATS().data), "\n")

None N,CA,C,CB,O,CG,CG1,CG2,OG,OG1,SG,CD,CD1,CD2,ND1,ND2,OD1,OD2,SD,CE,CE1,CE2,CE3,NE,NE1,NE2,OE1,OE2,CH2,NH1,NH2,OH,CZ,CZ2,CZ3,NZ,OXT True

print("Empty string, NONE, NULL", ATS("").data, ATS("NONE").data, ATS("NULL").data, "\n")

Empty string, NONE, NULL [] [] []

As shown above, the order of the atoms does not matter, and duplicates are removed and column indices are sorted. We have also special keywords: None and "ALL" for selecting all atoms, "", "NONE", and "NULL" for an empty selection. You can also initialize an ATS object with a set/list/tuple/pandas.Series of atom strings, a NumPy array, another ATS object. If a single integer is provided, it is treated as one atom index. Basically, ATS supports all sensible input formats.

If a method expects an ATS object as an argument, we can provide the value using any of the format that can be used to initialize an ATS object. For developers, the first thing the method should do is to cast the input argument into an ATS object using the following idiom:

ats=ATS(ats)

We consider it is a good practice to create an ATS object from a Protein object using p.ats(), so that we can avoid explicitly using the ATS class (one less class to memorize):

p=Protein()  
ats=p.ats("N,CA,C,O")  
print(ats, "\n")

N,CA,C,O

print(p.ats([0,1,2,3]), "\n")

N,CA,C,CB

print(len(ats), "\n")

4

# not\_full can be empty or less than 37 atoms  
print(ats.is\_empty(), ats.is\_full(), ats.not\_full(), "\n")

False False True

# method i() converts an atom name into its integer index  
print(ATS.i("CA"), ATS.i("CB"), "\n")

1 3

# in operator  
print("N" in ats, "CB" in ats, 2 in ats, "\n")

True False True

print(p.ats\_not("N,CA,C,O"), "\n")

CB,CG,CG1,CG2,OG,OG1,SG,CD,CD1,CD2,ND1,ND2,OD1,OD2,SD,CE,CE1,CE2,CE3,NE,NE1,NE2,OE1,OE2,CH2,NH1,NH2,OH,CZ,CZ2,CZ3,NZ,OXT

print(p.ats2str(ATS("N,C,CA,O")), "the same as", str(ATS("N,C,CA,O")), "\n")

N,CA,C,O the same as N,CA,C,O

We also support the set operations &, |, ~ (not), + (the same as |), - (a-b means in a but not in b). We strongly recommend to use these Boolean operators as they make the code easier to read:

ats1=ATS("N,CA,C,O")  
ats2=ATS("C,O,CB")  
print("or:", ats1 | ats2, "\nsame as +:", ats1+ats2, "\n")

or: N,CA,C,CB,O   
same as +: N,CA,C,CB,O

print("and:", ats1 & ats2, "\n")

and: C,O

print("minus:", ats1 - ats2, "\n")

minus: N,CA

print("not:", ~ats1, "\nnot not:", ~~ats1, "\n")

not: CB,CG,CG1,CG2,OG,OG1,SG,CD,CD1,CD2,ND1,ND2,OD1,OD2,SD,CE,CE1,CE2,CE3,NE,NE1,NE2,OE1,OE2,CH2,NH1,NH2,OH,CZ,CZ2,CZ3,NZ,OXT

not not: N,CA,C,O

## Residue Selection

We use a contig string previously described to select residues. To create a residue selection use the RS class or preferrably the p.rs() method. A residue selection object contains a data member, which is literally an integer numpy.ndarray. E.g., rs.data=np.array([0,1,9]). Therefore, atom\_positions[rs.data][ ATS('N,CA,C,O').data] will capture the 3D coordinates of the 4 backbone atoms for residue 1st, 2nd, and 10th.

For developers, atom\_positions[rs.data, ATS('N,CA,C,O').data] does not work, as it pairs the residue id with the corresponding atom id. We could do atom\_positions[np.ix\_(rs.data, ATS('N,CA,C,O').data)] to select the subarray.

The following is an example where we only extract the backbone atoms from chain H and L and save them into a new PDB file.

p=Protein(fn)  
p.extract("H-5:L-5", ats="C,CA,N,O", inplace=True)  
p.save("bb.pdb")  
print("\n".join(util.read\_list("bb.pdb")[:15])+"\n...\n")

HEADER AFPDB PROTEIN 10-Jun-24 XXXX

MODEL 1

ATOM 1 N VAL H 1 32.582 3.997 -22.715 1.00 1.00 N

ATOM 2 CA VAL H 1 31.113 4.261 -22.594 1.00 1.00 C

ATOM 3 C VAL H 1 30.727 4.737 -21.206 1.00 1.00 C

ATOM 4 O VAL H 1 30.948 4.033 -20.247 1.00 1.00 O

ATOM 5 N GLN H 2 30.105 5.899 -21.101 1.00 1.00 N

ATOM 6 CA GLN H 2 29.676 6.451 -19.826 1.00 1.00 C

ATOM 7 C GLN H 2 28.215 6.827 -20.036 1.00 1.00 C

ATOM 8 O GLN H 2 27.888 7.435 -21.037 1.00 1.00 O

ATOM 9 N LEU H 3 27.368 6.440 -19.107 1.00 1.00 N

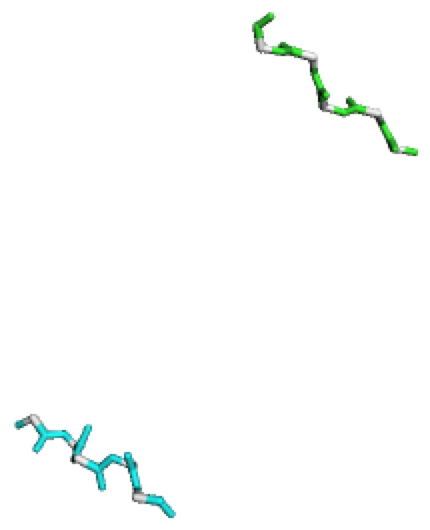
ATOM 10 CA LEU H 3 25.970 6.871 -19.038 1.00 1.00 C

ATOM 11 C LEU H 3 25.761 7.794 -17.840 1.00 1.00 C

ATOM 12 O LEU H 3 25.979 7.398 -16.661 1.00 1.00 O

ATOM 13 N VAL H 4 25.291 9.008 -18.090 1.00 1.00 N

p.show(style="stick", show\_sidechains=True)



Because we only have backbone atoms, all residues (except Gly, which fake.pdb does not have) have missing atoms.

# no residue has missing backbone atoms  
print("Missing backbone:", p.rs\_missing\_atoms(ats="N,CA,C,O"), "\n")  
  
Missing backbone:

# they all have missing side chain atoms, ats defaults to None -- all atoms  
print("Missing side chain:", p.rs\_missing\_atoms(), "\n")

Missing side chain: H:L

Similar to ATS, RS can be initialized by a contig str or special keywords (None, "ALL" for all residues and "", "NONE", "NULL" for an empty selection). RS can also be initialized with a set/list/tuple/pandas.Series, a numpy array, another RS object or RL object (explained later). If a single integer is provided, it is treated as one residue index. Basically, RS supports all sensible input formats.

If a method expects an RS object as an argument, we should implement it in a way that users can provide the selection object using any of the data format that can be used to initialize an RS object. E.g., we can write p.extract("H"), p.extract([0,1,2,3]), p.extract(np.array([2,4,6])), p.extract((2,4,6)), or p.extract(p.rs("H")), etc. The contig is the most popular format we strongly recommend, as it is the most readable and error-proof. For developers, the first thing the method should do is to cast the input argument into an RS object using the following idiom:

rs=RS(self, rs)

Unlike ATS, RS requires a Protein object as its first argument in the initialization, as a residue selection will not be meaningful without being tied to a protein structure. For this reason, we often create an RS object from a Protein object using p.rs() instead of using RS(protein\_obj, selection\_data)

# residue selections  
p=Protein(fn)  
rs1=RS(p, "H1-3")  
rs2=RS(p, "H3-5:L-3")  
print("1st rs:", rs1)

1st rs: H1-3

print("2nd rs:", rs2, "\n")

2nd rs: L1-3:H3-5

# however, we prefer to create an RS object using Protein.rs() method  
rs1=p.rs("H1-3")  
rs2=p.rs("H3-5:L-3")  
print("1st rs:", rs1)

1st rs: H1-3

print("2nd rs:", rs2, "\n")

2nd rs: L1-3:H3-5

# Protein also provides set operations on rs objects, however, try not the use these, as the Boolean operators (shown in the next cell) make the code easier to read  
print("and:", p.rs\_and(rs1, rs2), "\n")

and: H3

print("or:", p.rs\_or(rs1, rs2), "\n")  
or: L1-3:H1-5

# as we not H:L, the only residues left are P chain residues  
print("not:", p.rs\_not("H:L"), p.data.chain\_index[p.rs\_not("H:L").data], "\n")

not: P [2 2 2 2 2 2 2 2 2 2 2 2 2]

# we can specify the residue universe using full\_set, this can reduce the size of rs\_not  
# in the example below, we restrict the not selection within chain L  
print("not with full set:", p.rs\_not("L-100", rs\_full="L"), "\n")

not with full set: L101-111

print("notin:", p.rs\_notin(rs1, rs2), "\n")

notin: H1-2

print(p.rs2str(p.rs\_or(rs1, rs2)))

L1-3:H1-5

In Afpdb, our convention is any method name starts with rs\_ is expected to return an RS object and any argument named rs or starts with rs\_ should take any residue selection formats whenever possible. The exception is rs\_seq() returns a list of RS objects.

Residue selection behaves like a set, where residue indices within rs.data are deduplicated and sorted. All sensible set operations apply, therefore, instead of using p.rs\_or, p.rs\_and, we prefer to use set operators directly as shown below:

p=Protein(fn)  
# an unusal selection  
rs1=p.rs("H1-3")  
rs2=p.rs("H3-5:L-3")  
print("and:", rs1 & rs2, "\n")

and: H3

print("or:", rs1 | rs2, "same as", rs1+rs2, "\n")

or: L1-3:H1-5 same as L1-3:H1-5

print("not:", ~ p.rs("H:L"), "\n")

not: P

# ~ cannot take additional argument, so we need to use \_not(), if rs\_full needs to be specified  
print("not with full set:", p.rs("L-100").\_not(rs\_full="L"), "\n")

not with full set: L101-111

print("notin:", rs1-rs2, "\n")

notin: H1-2

# inplace operations  
rs1+=rs2  
print(rs1, "\n")

L1-3:H1-5   
  
rs1-=rs2  
print(rs1, "\n")

H1-2

# more  
p=Protein(fn)  
print(p.rs("").is\_empty(), "\n")

True

print(p.rs("ALL").is\_full(), "\n")

True

print(p.rs(None).is\_empty(), p.rs(None).is\_full(), "\n")

False True

print(p.rs("H").is\_full(), p.rs("H").is\_empty(), "\n")

False False

# to combine a list of selections  
rs1=p.rs("H1-3")  
rs2=p.rs("H3-5:L-3")  
rs3=p.rs("H:P")  
rs\_list=[rs1, rs2, rs3]  
print(RS.\_or(\*rs\_list), "\n")

L1-3:H:P

# AND on the list  
print(RS.\_and(\*rs\_list), "\n")  
  
H3

# only the first element of the list needs to be an RS object, the rest can be any format  
# we need to extract the Protein object from the first RS object  
print(RS.\_or(rs1, "H", "P"), "\n")

H:P  
  
# residue lookup, convert a residue name to its internal AlphaFold residue order number  
print(RS.i("GLY"), RS.i("Gly"), RS.i("G"), "\n")

7 7 7

## Residule List

Residue indices within a RS object, rs.data, are unique and sorted. We sometimes need duplicate residue indices or require indices to be in specific order. Residule List (RL) class is the parent class of RS, which serves the purpose.

p=Protein(fn)  
rl=p.rl("H3-5:L-3:H1-3")  
print("Not sorted and not unique:", rl.data, "\n")

WARNING> contig should keep the segments for the same chain together H1-3, if possible!

Not sorted and not unique: [113 114 115 0 1 2 111 112 113]

# compared to residue list  
rs=p.rs("H3-5:L-3:H1-3")  
print("Unique and ordered:", rs.data, "\n")

WARNING> contig should keep the segments for the same chain together H1-3, if possible!

Unique and ordered: [ 0 1 2 111 112 113 114 115]

# cast between RS and RL  
# notice we need to provide a protein object as the first arugment, when we use RS or RL to create the object  
print(RS(rl.p, rl), "\n")

L1-3:H1-5  
  
print("Sorted and unique:", p.rs(rl).data, "\n")  
print(p.rl(p.rs("H3-5:L-3:H1-3")).data, "\n")

Sorted and unique: [ 0 1 2 111 112 113 114 115]

WARNING> contig should keep the segments for the same chain together H1-3, if possible!

[ 0 1 2 111 112 113 114 115]

When printed as a string, RL is shown as a compact contig format.

print(p.rl("H3-5:L-3:H1-3"), "\n")  
  
H3-5:L1-3:H1-3  
  
print(p.rl("H:H:H"))

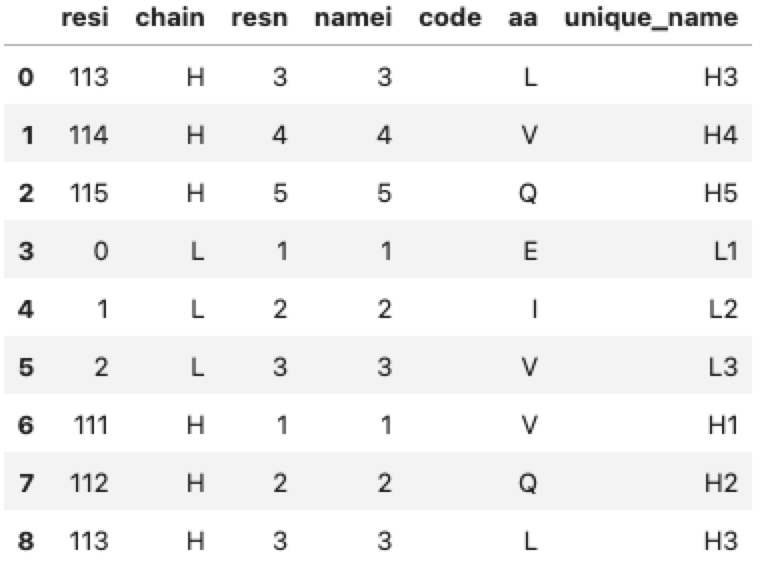
H:H:H

Residue list is handy for extracting key annotations for the residues, as demonstrated before:

p=Protein(fk)  
rl=p.rl("H:L:H")  
df=pd.DataFrame({"resi": rl.data})  
df['chain']=rl.chain()  
df['resn']=rl.name()  
df['resni']=rl.namei()  
df['aa']=rl.aa()  
df['unique\_name']=rl.unique\_name()  
df



This can be simplified with the df() method.



In the above example, we introduce a few terms:

* resi: the internal integer residue index used as the row index of backend numpy arrays
* chain: the chain name of the residue
* resn/name: the residue index, may include an insertion code, such as "6A" and "6B" in this example.
* resni: the integer part of the residue index without insertion code. This is integer type and can be used for sorting.
* Code: insertion code
* aa: amino acid letter
* unique\_name/contig: the unique residue name: {chain}{residue\_index}

Later we will see residue list is also used in aligning two structures, as we would like to present the one-to-one mapping between residues.

Boolean operations of RL objects. Residues in a RL object are ordered and can be duplicated, therefore, set operations such as AND/OR are not well defined. Nevertheless, it is convenient to provide some basic operations on RL.

rl\_h=p.rl("H")  
rl\_l=p.rl("L")  
# + and | both means concatenation of the two selections  
print(rl\_h + rl\_l, "\n")

H:L

print(rl\_h | rl\_l | rl\_h, "\n")

H:L:H

# to concatenate multiple RL objects  
print(RL.\_or(rl\_h, rl\_l, rl\_h, rl\_l), "\n")

H:L:H:L

# - mean remove any residues in the first RL that appear in the second RL  
print(rl\_h + rl\_h - p.rl("H3"), "\n")  
  
H4:H4

We may notice the contig representation for two H4 residues is "H4:H4" instead of "H4,4". They are equivalent. In fact, to programmatically construct a contig str for a RL or RS object, is it often convenient to simply ":"-join residues' unique names:

rl=p.rl("H3:L6A-10")  
print(rl.data)

[4 1 2 3]

print(":".join(rl.unique\_name()))

H3:L6A:L6B:L10

## Casting

Unless we are sure two proteins have the identical sequences, including how their chains are ordered, Boolean operation between RS/RL of two protein objects should be avoided! This is because RS/RL uses the internal indices of residues, these indices lose their meaning when they are used in the context of a different protein.

p=Protein(fk)  
print(p.chain\_id())

['L', 'H']

# object q arranges chains in a different order  
q=p.extract("H:L")  
print(q.chain\_id())

['H', 'L']

print(p.rs("L").name(), "\n")

['5', '6A', '6B', '10']

# the following is wrong, as it use selections of two different objects, the ouput misses residue L5  
print(p.rs("L") & q.rs("L"), "\n")

L6B-10

print((p.rs("H") & q.rs("H")).is\_empty(), "\n")

True

When we know two proteins share the same sequence(s), we can first align their chains and residues:

# first, let's creat two proteins with different chain names and chain orders  
p=Protein(fk)  
q=p.rename\_chains({'H':'A', 'L':'B'})  
q=q.extract('A:B')  
print(p.seq(), "\n")

EIVXXXQ:LV

print(q.seq(), "\n")

LV:EIVXXXQ

# to align these two proteins, we rename the chains in q and reorder them according to object p  
q=q.rename\_reorder\_chains(p, {'A':'H', 'B':'L'})  
print(q.seq())

EIVXXXQ:LV

However, the recommended approach to transfer a selection to another object is to cast, which internally uses contig strings to make sure the "meaning" of the selection is transferred.

p=Protein(fk)  
print(p.chain\_id())

['L', 'H']

# object q arranges chains in a different order  
q=p.extract("H:L")  
print(q.chain\_id())

['H' 'L']

rs\_a=p.rs("L")  
# L chain are in the first 4 positions of object p  
print(rs\_a.data, "\n")  
  
[0 1 2 3]

# once casted into object q, the "L" selection of object q are the last 4 positions  
rs\_b=rs\_a.cast(q)  
# rs\_b now belongs to object q  
print(rs\_b.p == q, "\n")

True

print(rs\_b.data, "\n")

[2 3 4 5]

print(rs\_b.name())

['5', '6A', '6B', '10']

# Read/Write

One of our philosophies in designing Afpdb is to reduce the number of methods and arguments to bare minimum to reduce the burden of memorization. The convenience of Afpdb can be demonstrated by how we read/write protein structures. Regardless of what format a protein structure is represented, we use Protein() to create and use save() to export.

p=Protein(fn)  
print(p.chain\_id())

['L', 'H', 'P']

p.save("test.pdb")  
out=util.unix("ls -l test.pdb")

-rw-r--r-- 1 zhoyyi1 staff 155520 Jun 10 19:40 test.pdb

The constructor can optionally take a contig string if you want to only read in a subset of the structure:

p=Protein(fn, contig="H:L")  
print(p.chain\_id(), "\n")

['H' 'L']

p=Protein(fn, contig="H-5:L-10")  
print(p.seq(), "\n")

VQLVQ:EIVLTQSPGT

# however, for clarity, we recommend to separate the two operations, use contig in the extract() method explicitly.  
p=Protein(fn)  
print(p.extract("H:L").chain\_id(), "\n")

['H' 'L']

p=Protein(fn)  
print(p.extract("H-5:L-10").seq(), "\n")

VQLVQ:EIVLTQSPGT

The first argument in Protein() constructor can be quite flexible. Just be aware that only the first model is read, if the PDB file contains multiple models. AlphaFold was not designed to handle multiple conformations, afpdb can be made much more efficient by assuming only one conformation is being manipulated.

Below are a few examples:

print("Load a local PDB file")  
# support both .pdb and .ent extensions  
print(fn)  
p=Protein(fn)  
print(p.chain\_id(), "\n")

Load a local PDB file

/Users/zhoyyi1/afpdb/tutorial/example\_files/5cil.pdb

['L', 'H', 'P']

print("Create Protein from another afpdb.Protein object")  
q=Protein(p)  
print(q.chain\_id(), "\n")  
  
Create Protein from another afpdb.Protein object

['L' 'H' 'P']

print("Create Protein from an afpdb.Protein.data object")  
q=Protein(p.data)  
print(q.chain\_id(), "\n")  
  
Create Protein from an afpdb.Protein.data object

['L' 'H' 'P']

print("Create Protein from a BioPython Structure object")  
b=p.to\_biopython()  
print(type(b))  
q=Protein(b)  
print(q.chain\_id(), "\n")

Create Protein from a BioPython Structure object

<class 'Bio.PDB.Structure.Structure'>

['L', 'H', 'P']   
  
print("Create Protein from a str containing the content of a PDB file")  
s=p.to\_pdb\_str()  
print("\n".join(s.split("\n")[:5])+"\n...")  
q=Protein(s)  
print(q.chain\_id())

Create Protein from a str containing the content of a PDB file

HEADER AFPDB PROTEIN 10-Jun-24 XXXX

MODEL 1

ATOM 1 N GLU L 1 5.195 -14.817 -19.187 1.00 1.00 N

ATOM 2 CA GLU L 1 6.302 -14.276 -18.361 1.00 1.00 C

ATOM 3 C GLU L 1 7.148 -15.388 -17.731 1.00 1.00 C

...

['L', 'H', 'P']

# more examples ...  
print("Save as .cif, save Protein into a .cif file\n")  
p=Protein(fn)  
p.save("test.cif")

Save as .cif, save Protein into a .cif file

print("Create Protein from a local .cif file")  
p=Protein("test.cif")  
print(p.chain\_id(), "\n")

Create Protein from a local .cif file

['L' 'H' 'P']

print("Create with a PDB 4-letter code, fetch structure from PDB online.")  
p=Protein("1crn")  
print(p.seq(), "\n")

Create with a PDB 4-letter code, fetch structure from PDB online.

--2024-06-10 19:40:31-- https://files.rcsb.org/download/1crn.pdb1.gz

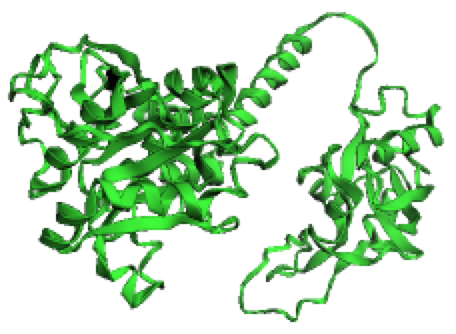
TTCCPSIVARSNFNVCRLPGTPEAICATYTGCIIIPGATCPGDYAN

print("Create with a EMBL AlphaFold model code, fetch structure from EMBL online.")  
p=Protein("Q2M403")  
print(p.seq())  
p.show()

Create with a EMBL AlphaFold model code, fetch structure from EMBL online.

Saving to: ‘AF-Q2M403-F1-model\_v3.pdb’

MVVVSLQCAIVGQAGSSFDVEIDDGAKVSKLKDAIKAKNATTITGDAKDLQLFLAKQPVEDESGKEVVPVYRPSAEEMKEESFKWLPDEHRAALKLVEGESDDYIHALTAGEPILGSKTLTTWFYTKNNMELPSSEQIHVLVVVPDGAGGSASDTSRMDRLFDKVDKVYEHTVLSKRTRYVHSEMNSAKGNILLNDLKIRISPVDTVKFAGGVPTPAKEFKWKSDRTEEQQKEPYREYVVANIGDVLTNNKLCVVGVEKGANILTVEVPGRDIVLAGRTDMIVLSDIAQKFPHYLPHLPGVRMLIEVKKVVTTASEFQALSELIALDIIVTESVMALLTNLTNHWQFFWVSRKSDDRVIIETTTLIAPGEAFAVIRTLLDQSPSAGAEVSLPCFEKPVKRQKLSQLLPSISEASGSSGIRESIERYYDIASMLGPDLEMARAVASQVARSIPTLSYF

****

# Sequence & Chain

## Extraction

p=Protein(fn)  
p.seq()

'EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV:VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS:NWFDITNWLWYIK'

Notice the sequences from different chains are concatenated by colon (color in red) into one line:

EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLS  
TFGQGTKVEVKRTV**:**VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLEL  
NSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS**:**NWFDITNWLWYIK

This is a standard format used to provide multimer sequence inputs to ColabFold and AlphaFold for protein structure prediction.

Here the order of the chain sequences is the same as how they occur in the PDB file. However, it is always safer to assume that chain order may change when we convert objects among different formats. Therefore, we strongly recommend users tie chain names with their sequences by using seq\_dict() method instead:

p.seq\_dict()

{'L': 'EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV',

'H': 'VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS',

'P': 'NWFDITNWLWYIK'}

## Missing Residues

When there are missing residues in the structure, they will be represented as "X" in the sequence string:

p=Protein(fn)  
q=p.extract("H1-10:H21-30")  
print(len(q.data.residue\_index), q.data.residue\_index, "\n")

20 ['1' '2' '3' '4' '5' '6' '7' '8' '9' '10' '21' '22' '23' '24' '25' '26'

'27' '28' '29' '30']

print("Number of residues in numpy arrays:", q.data.atom\_positions.shape, "\n")  
print(q.seq(), "\n")

Number of residues in numpy arrays: (20, 37, 3)

VQLVQSGAEVXXXXXXXXXXCKASGGSFST

print(q.seq\_dict(gap="."), "\n")

{'H': 'VQLVQSGAEV..........CKASGGSFST'}

print(q.seq().replace("X", "G"), "\n")

VQLVQSGAEVGGGGGGGGGGCKASGGSFST

print(q.seq(gap="G"), "\n")

VQLVQSGAEVGGGGGGGGGGCKASGGSFST

The number of missing residues is determined based on residue numbering. Users shoudl be aware that the SEQRES section in the PDB file is not used to determine missing residues. In the above example, we first create a new object by taking the first ten residues from chain H, skipping 10 residues, then take another 10 residues. In the resultant object q, the 10-residue gap is preserved (residue index jumps from 10 to 21). Although the 10 missing residues have no corresponding elements in the internal NumPy array representation or in the saved PDB file (the array only contains 20 residues in total, the discontinuity in the residue index allows us to figure out that 10 residues are missing). Therefore, seq() and seq\_dict() outputs ten "X". You can change the display of "X" by the gap argument or suppress gap by "". For protein structure prediction, we often replace the missing residues by Glycine "G". If somehow you want to ignore missing residues, set gap=''.

p=Protein(fk)  
print(p.data.residue\_index, "\n")

['5' '6A' '6B' '10' '3' '4']   
  
print(p.seq\_dict(), "\n")

{'L': 'EIVXXXQ', 'H': 'LV'}

print(p.seq\_dict(gap=""))

{'L': 'EIVQ', 'H': 'LV'}

When we determine missing residues, only the integer part of the residue ID is considered. In the above example, residue index 6 appears twice as 6A and 6B, followed by residue 10. We assume residues 7, 8, and 9 are missing.

Note: Missing residues at the N or C terminals cannot be recovered. In addition, if the residue numbering in the full structure is not numerically continuous, e.g., both residues "6A" and "6B" were removed, we can only infer that one residue "6" is missing:

p=Protein(fk)  
q=p.extract("L5,10:H")  
print(q.data.residue\_index, "\n")

['5' '10' '3' '4']

print(q.seq(), "\n")

EXXXXQ:LV

## Length

The get the total number of residues (not counting missing residues), i.e, the number of rows in the backend numpy arrays, use:

p=Protein(fn)  
print("Total residue counts:", len(p), "\n")

Total residue counts: 250

print("Residue counts per chains:", p.len\_dict())

Residue counts per chains: {'L': 111, 'H': 126, 'P': 13}

q=Protein(fk)  
# missing residues are not counted as part of the length  
print(q.seq(), "\n")

EIVXXXQ:LV

print(q.len\_dict(), "\n")

{'L': 4, 'H': 2}

## Search

When we have a sequence fragment and would like to locate where it came from, use:

p=Protein(fn)  
out=p.rs\_seq('LTI')  
for i,m in enumerate(out):  
    print(f"Matched #{i+1}, location: {m}, sequence: {m.seq()}")

Matched #1, location: L74-76, sequence: LTI  
Matched #2, location: H54-56, sequence: LTI

The name rs\_seq() suggests the method performs sequence search and return residue selection (RS) objects. Since there can be multiple matches, it returns a list of RS objects. We will explain residue selection objects later, for now, we just need to know that a residue selection object can be printed as a contig string and its seq() method returns the corresponding sequence.

The two matches are in bold below:

EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFT**LTI**SRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV:VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPL**LTI**TNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS: NWFDITNWLWYIK

If we are only interested in sequence search within a list of chains, provide the chain name(s) list:

out=p.rs\_seq('LTI', in\_chains="H")  
print(len(out), out[0], "\n")  
  
1 H54-56

The sequence search pattern can be a regular expression, e.g., to match all charged residues:

out=p.rs\_seq(r'[RHKDE]')  
# concatenate the list of matched residue selection objects into one RS object, RS.\_or() will be explained later.  
m=RS.\_or(\*out)  
print(m)

L1,17-18,24,33,40,46,55,61-62,71,78,80,82-83,104,106,108-109:H9,11-12,22,37,42,45,62,66,72-73,81,86,88-89,97-98,103,105,108,115:P4,13

print(m.seq())

EERRKRRRDRDREEDKEKREKRKRRERRDREREDREDDKHDK

## Mutagenesis

To perform mutagenesis on a structure, we thread a new sequence onto an existing Protein object. As this method requires the installation of PyMOL, it throws an exception if PyMOL is not found.

When we specify the new sequence, we only specify the new residues for which there is coordinate information, i.e., missing residues should not occur in the new sequence. Chain L's sequence was EIVXXXQ, the target sequence is AIVD instead of AIVXXXD.

The following example requires PyMOL to be installed. The installation can take some time in Google Colab.

install\_pymol()  
p=Protein(fk)  
print(p.seq(), "\n")  
  
EIVXXXQ:LV

p.thread\_sequence({"L":"AIVD", "H":"LG"}, "m.pdb")

###JSON STARTS

{"output\_pdb": "m.pdb", "ok": true, "output\_equal\_target": false, "input": {"L": "EIVQ", "H": "LV"}, "output": {"H": "LG", "L": "AIVXXXD"}, "target": {"L": "AIVD", "H": "LG"}, "relax": false, "residues\_with\_missing\_atom": "", "mutations": [["L", 5, "GLU", "ALA"], ["L", 10, "GLN", "ASP"], ["H", 4, "VAL", "GLY"]]}

###JSON END

{'output\_pdb': 'm.pdb',

'ok': True,

'output\_equal\_target': False,

'input': {'L': 'EIVQ', 'H': 'LV'},

'output': {'H': 'LG', 'L': 'AIVXXXD'},

'target': {'L': 'AIVD', 'H': 'LG'},

'relax': False,

'residues\_with\_missing\_atom': '',

'mutations': [('L', 5, 'GLU', 'ALA'),

('L', 10, 'GLN', 'ASP'),

('H', 4, 'VAL', 'GLY')]}

From the output JSON data, we see L5 was "E" and it is replaced with "A". L6A-L6B was not changed, therefore, their side chain coordinates remain the same. L10 is replaced by "D". On the chain H, H6 was "G" and is replaced by "V".

The new mutated residues have their side chain torsion angles generated by PyMOL. Therefore, it generally makes sense to relax the side chain, for example, with Amber. Relax is not supported by Afpdb due to its dependency on Amber. TODO: we might investigate this more.

## Mutation

If a chain name is in two proteins and the chain has the same number of residues, we can identify mutated residues by a residue-by-residue comparison. The example below identifies three mutated residues:

p=Protein(fk)  
# m.pdb was produced with the previous thread\_seq() example  
q=Protein("m.pdb")  
print(p.seq(), q.seq(), "\n")

EIVXXXQ:LV LG:AIVXXXD   
  
print(p.rs\_mutate(q))

L5,10:H4

## Chain Name and Order

In the fn PDB file, chains go from L, to H, to P. chain\_id() will return chain names in the same order. p.data.chain\_index stores the chain index. **Afpdb** expects all residues belong to the same chain are stored together without being interrupted by another chain.

p=Protein(fn)  
print(p.chain\_id(), "\n")

['L', 'H', 'P']

print(p.data.chain\_index, "\n")

[0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0

0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0

0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0

1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1

1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2]

Although we should not rely on the exact order of chains in the PDB file, we can nevertheless reorder chains, if we wish:

p=Protein(fn)  
q=p.data  
print("Original chain order:", p.chain\_id(), "\n")

Original chain order: ['L', 'H', 'P']

print(p.seq(), "\n")

EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV:VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS:NWFDITNWLWYIK

# notice the last 20 residues belong to chain L, then chain P in the q.chain\_index NumPy array  
print(q.chain\_index[-20:], "\n")

[1 1 1 1 1 1 1 2 2 2 2 2 2 2 2 2 2 2 2 2]

print(q.residue\_index[-20:], "\n")  
  
['120' '121' '122' '123' '124' '125' '126' '1' '2' '3' '4' '5' '6' '7' '8'

'9' '10' '11' '12' '13']

p.reorder\_chains(["P","L","H"])  
q=p.data  
print("After chain reorder:", p.chain\_id(), "\n")

After chain reorder: ['P', 'L', 'H']

print(p.seq(), "\n")

NWFDITNWLWYIK:EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV:VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS

# after ordering, notice the last 20 residues belong to chain H in the q.chain\_index NumPy array  
print(q.chain\_index[-20:], "\n")

[2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2]

print(q.residue\_index[-20:], "\n")

['107' '108' '109' '110' '111' '112' '113' '114' '115' '116' '117' '118'

'119' '120' '121' '122' '123' '124' '125' '126']

# The method reorder\_chains() is no longer needed, as we can use extract():  
p=Protein(fn)  
p.extract("P:L:H", inplace=True)  
q=p.data  
print("After chain reorder:", p.chain\_id(), "\n")

After chain reorder: ['P' 'L' 'H']   
  
print(p.seq(), "\n")

NWFDITNWLWYIK:EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV:VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS

print(q.chain\_index[-20:], "\n")

[2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2]   
  
print(q.residue\_index[-20:], "\n")

['107' '108' '109' '110' '111' '112' '113' '114' '115' '116' '117' '118'

'119' '120' '121' '122' '123' '124' '125' '126']

Notice after reordering, the chain\_index array goes from 0 to 2, and the chain\_id list has also been updated.

The extract() method will error if the selection list contains duplicates or residues of the same chain are not ordered.

p=Protein(fn)  
try:  
    p.extract("H:H:L")  
except Exception as e:  
    print(e)

There are duplicate residues: [111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128

129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146

147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164

165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182

183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200

201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218

219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236]

try:  
    p.extract("H5-:H1")  
except Exception as e:  
    print(e)  
  
Residues within chain H are not sorted in order.

WARNING> contig should keep the segments for the same chain together H2, if possible!

try:  
    p.extract("H1:L:H2")  
except Exception as e:  
    print(e)  
  
Residues for chain ['H'] are not grouped together.

Treat as residue selection ...

WARNING> contig should keep the segments for the same chain together H2, if possible!

# as\_rl=False, all examples are fine, b/c the contig selection will be cast into an unordered/non-redundant residue selection  
print("Treat as residue selection ...\n")  
q=p.extract("H:H:L", as\_rl=False)  
q=p.extract("H5-:H1", as\_rl=False)  
q=p.extract("H1:L:H2", as\_rl=False)

Treat as residue selection ...

As a shortcut, we can rename and reorder chains in one method. In the example below, the original chain names are L:H:P, AlphaFold's corresponding modeling output has the chain named as A:B:C. We can prepare both objects as chain H:L:P with the following:

p=Protein(fn)  
int(p.chain\_id())

['L', 'H', 'P']

print(q.chain\_id())

['A', 'B', 'C']

p=p.extract("H:L:P")  
q.rename\_reorder\_chains(p, {"A":"L", "B":"H", "C":"P"}, inplace=True)  
print(p.seq() == q.seq())

True

# although we don't recommend this, since two objects have exact the same sequence, RS/RL objects can be used across  
print(p.rs("H35-50") & q.rs("H40-45"), "\n")

H40-45

# the recommended way is to use cast  
print(p.rs("H35-50") & q.rs("H40-45").cast(p))

H40-45

## Residue Labeling

The method chain\_pos() is an important utility method. It returns the start and end NumPy indices of each chain, which can be used to access the corresponding numpy arrays. For our example structure, the complex consists of 3 chains. The array residue\_index has 250 elements. The residues in chain L are stored as the first 111 elements in the numpy arrays, in Python, the indices are from 0 to 110.

Many methods relies on chain\_pos to accelerate the computation, this is the reason why **Afpdb** assumes all residues of the same chain should be stored together within the backend numpy arrays. If they are not in the PDB file, their order will be fixed by Apfdb during the protein object creation.

p=Protein(fn)  
print(p.chain\_pos(), "\n")

{'L': [0, 110], 'H': [111, 236], 'P': [237, 249]}

q=p.data  
print(q.residue\_index[108:114], "\n")

['109' '110' '111' '1' '2' '3']

print(q.chain\_index[108:114])  
  
[0 0 0 1 1 1]

# we should avoid using p.data, all can be done by residue selection  
rs=p.rs(list(range(108, 115)))  
print(rs.name(), "\n")

['109', '110', '111', '1', '2', '3', '4']   
  
print(rs.chain())

['L', 'L', 'L', 'H', 'H', 'H', 'H']

The chain\_index for element 110 is the last residue of chain L, its residue name is '111' and chain id is 0, i.e., resn="111", resi=110, resn\_i=111. Element 111 is the first residue of chain H. Its residue name is '1' and chain id is 1, i.e., resn="1", resi=111, resn\_i=1.

If we only want to extract the coordinates for the 13 residues of chain P, we will use:

q.atom\_positions[237:250].shape

(13, 37, 3)

## Residue Renumbering

Residue index can be modified. There are a number of renumbering modes:

    None: keep original numbering unmodified.  
    RESTART: 1, 2, 3, ... for each chain  
    CONTINUE: 1 ... 100, 101 ... 140, 141 ... 245  
    GAP200: 1 ... 100, 301 ... 340, 541 ... 645 # mimic AlphaFold gaps  
    You can define your own gap by replacing GAP200 with GAP{number}, e.g., GAP10  
    NOCODE: remove insertion code, residue 6A and 6B becomes 6, 7

p=Protein(fk)  
q=p.data  
print(q.chain\_index, "\n")  
  
[0 0 0 0 1 1]

p.renumber(None, inplace=True)  
print(q.residue\_index, "\n")

['5' '6A' '6B' '10' '3' '4']

p.renumber('RESTART', inplace=True)  
print(q.residue\_index, "\n")

['1' '2A' '2B' '6' '1' '2']

p.renumber('CONTINUE', inplace=True)  
print(q.residue\_index, "\n")

['1' '2A' '2B' '6' '7' '8']

p.renumber('GAP200', inplace=True)  
print(q.residue\_index, "\n")  
  
['1' '2A' '2B' '6' '207' '208']

p.renumber('GAP10', inplace=True)  
print(q.residue\_index, "\n")  
  
['1' '2A' '2B' '6' '17' '18']

p.renumber('NOCODE', inplace=True)  
print(q.residue\_index)

['1' '2' '3' '7' '8' '9']

NOCODE is used to remove insertion code, in case we need to feed a structure into a tool that cannot deal with insertion code. Notice "2A" and "2B" are renamed to "2" and "3" to avoid the collision, then residue "6" is renamed to "7" to preserve the three missing residues in the original naming.

By default, renumber() returns a tuple (p\_object, old\_number). inplace=False is the default, i.e., the input object is not modified.

If we need a custom naming, e.g., we really want to remove the gaps for missing residues, we can provide our own custom list of residue names, using resn(). Without any argument, resn() is a read method that returns the current residue names. If providing an argument as a list or NumPy array, its length should match the number of residues.

p=Protein(fk)  
q, old\_resn=p.renumber("RESTART")  
print("Old Name:", old\_resn, "New Name:", q.resn(), "\n")

Old Name: ['5' '6A' '6B' '10' '3' '4'] New Name: ['1' '2A' '2B' '6' '1' '2']

# restore the old residue names  
q.resn(old\_resn)  
print(q.resn(), "\n")

['5' '6A' '6B' '10' '3' '4']

# set custom residue names, we create new residue names as a continous integer without gap  
q.resn([str(x) for x in range(1, len(q)+1)])  
print(q.resn())

['1' '2' '3' '4' '5' '6']

Be aware that resn() modifies the object in place. If we only want to rename a few residues, we can use a RL object to specify the target residues.

p=Protein(fk)  
print(p.resn())

['5' '6A' '6B' '10' '3' '4']

p.resn(["6", "7"], "L6A-6B")  
print(p.resn())

['5' '6' '7' '10' '3' '4']

## Merge & Split Chains

Before AlphaFold Multimer was created, we had to use AlphaFold monomer model to predict multimer structures. The hack is to merge chains into one single chain, where we introduce a 200 gap in the residue indices between the original chain junctions to keep AlphaFold from treating the previous C- and the next N-terminals of two contiguous chains from being mistakenly treated as neighboring residues. This could be achieved by:

p=Protein(fn)  
q, c\_pos=p.merge\_chains(gap=200, inplace=False)  
print(q.seq\_dict(gap="."), "\n")  
  
{'L':'EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV........................................................................................................................................................................................................VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS........................................................................................................................................................................................................NWFDITNWLWYIK'}

print(c\_pos, "\n")

{'L': [0, 110], 'H': [111, 236], 'P': [237, 249]}

r=q.split\_chains(c\_pos, inplace=False)  
print(r.seq\_dict())

{'L':'EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV',

'H':'VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSS',

'P': 'NWFDITNWLWYIK'}

As chains got merged into a single change, 200-residue gaps were introduced and shown as "." in the sequence output. We notice there is only one chain, where the first chain name in the original PDB file was used. The method returns the original c\_pos object, which memorizes the chain structure before the merge.

After AlphaFold predicts the structure as a monomer, the output PDB file can then be used by split\_chains to restore the original trimer structure. Here c\_pos guides the method to split the monomer chain and restores the naming of the original chains.

If we send one sequence to AF without residue indices, we would actually need to replace the gap with glycines. The predicted structure will contain extra glycine linkers, those need to be removed before we can split\_chains(). The extra glycines can be identified with q.rsi\_missing() or pred.rs\_insertion(), as demonstrated later in the first AI use case. The idea is outlined below:

p=Protein(fn)  
# for the sake of saving paper space, we use a gap of 20 residues  
q, c\_pos=p.merge\_chains(gap=20, inplace=False)  
seq=q.seq(gap="G")  
# obtain the positions for the glycine linkers  
linker\_pos=q.rsi\_missing()  
print("Chain breaks:", c\_pos, "\n")

Chain breaks: {'L': [0, 110], 'H': [111, 236], 'P': [237, 249]}

print("Position of G:", linker\_pos, "\n")

Position of G: [111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128

129 130 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272

273 274 275 276]

print("Send the following fasta sequence to AlphaFold monomer model for prediction:\n")  
  
Send the following fasta sequence to AlphaFold monomer model for prediction:

print(">af\_pred\n"+seq, "\n")  
  
>af\_pred  
EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTVGGGGGGGGGGGGGGGGGGGGVQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCAREGTTGDGDLGKPIGAFAHWGQGTLVTVSSGGGGGGGGGGGGGGGGGGGGNWFDITNWLWYIK

print("AF prediction, generate pred.pdb ...\n")  
print("Read the predicted structure:")  
print("    pred=Protein('pred.pdb')\n")  
print("Remove glycine linkers:")  
print("    pred.extract(~ RS(pred, linker\_pos), inplace=True)\n")  
print("Restore three chains:")  
print("    pred.split\_chains(c\_pos)\n")

AF prediction, generate pred.pdb ...  
Read the predicted structure:  
 pred=Protein('pred.pdb')  
Remove glycine linkers:  
 pred.extract(~ RS(pred, linker\_pos), inplace=True)  
Restore three chains:  
 pred.split\_chains(c\_pos)

The hack for merging chains is no longer needed with AlphaFold Multimer, this is required for using ESMFold web service. Also replacing missing residues within a chain by Glycine is a common practice.

# Geometry, Measurement, and Visualization

## Select Neighboring Residues

For a given residue selection, rs\_around selects neighboring residues, where their closest distance is within the specified dist argument. In the example below, we find all residues that are within 3.5Å around P chain residues. AlphaFold's NumPy arrays do not contain hydrogens. We compute distances among all possible atom pairs and use the minimum atom-atom distance as the final distance between two residues. In this example, it identifies 5 residues on chain L and 8 residues on chain H. The method does not consider intra-selection distances, i.e., it will not include residues that are already part of the seed selection. If you want to include seed residues, just use "or" operator to combine two residue selections.

There are three returned values, the first is a new residue selection of the neighboring residues and second is a residue selection of the seed residues (i.e., source residues that have a neighbor), the third is a DataFrame object. The DataFrame object provides the details about all residue pairs, the source is marked as "a" (chain P here) and the target is marked as "b" (chain H or L). resn\_ stands for residue name, resn\_i\_ is for the integer part of the residue names without the insertion code and it is an integer type. resi\_ is for the internal Numpy array index (i.e., residue selection rs.data). The shortest distance between two residues is listed under the dist column and the atom pair that contributes to this shortest distance is listed as atom\_a and atom\_b. The DataFrame is sorted by descending dist values.

p=Protein(fn)  
rs\_nbr, rs\_seed, t=p.rs\_around("P", dist=3.5)  
print("Neighbors:", rs\_nbr.name(), "\n")

Neighbors: ['33', '92', '93', '94', '95', '30', '56', '58', '98', '106', '107', '108', '109']

print("Seeds:", rs\_seed.name(), "\n")

Seeds: ['1', '2', '3', '4', '6', '7', '10']

t  


To include the seed residues in the selection, use the following idiom:

# p.rs(t.resi\_a) select all seed residues appears in the neighbor table  
# resi\_a contains the residue IDs for those on the P chain that interact with rs\_nbr  
rs\_both = rs\_nbr | rs\_seed  
print(rs\_both)

L33,92-95:H30,56,58,98,106-109:P1-4,6-7,10

The distance table contains all residues pairs between seeds and their neighbors. If we only want to see one seed per neighbor, we define drop\_duplicates = True:

rs\_nbr, rs\_seed, t2=p.rs\_around("P", dist=3.5, drop\_duplicates=True)  
print(rs\_seed, "\n")

P1-4,6-7,10

print(rs\_nbr)  
t2

L33,92-95:H30,56,58,98,106-109

By default, the DataFrame object only keep one atom pair per residue pair. If we want to access all atom pairs within the specified distance, use keep\_atoms = True.

The reason we provide resn\_i is to enable us to filter the output DataFrame. The data type for resn is a string, as resn could contain insertion codes. If we are interested in rows corresponding to residues within H95-106, we cannot use the resn column for filtering. Instead, we can accomplish this with the resn\_i column:

print("resn cannot be used for filtering, as it's string type, str greater than '95' will be all less than '116'")  
t2=t[(t.chain\_b=="H")&(t.resn\_b>="95")&(t.resn\_b<="106")]  
t2

resn cannot be used for filtering, as it's string type, str greater than '95' will be all less than '116'



print("resn\_i is an integer column")  
t2=t[(t.chain\_b=="H")&(t.resn\_i\_b>=95)&(t.resn\_i\_b<=106)]  
t2

resn\_i is an integer column



By default, all residue atoms are considered. However, we can restrict the distance measurement using an atom selection. We can also restrict the target residues using a residue selection rs\_within.

p=Protein(fn)  
rs=p.rs("P")  
# select residues on chain H that have CA-CA distance within 8A.  
rs\_nbr, rs\_seed, t=p.rs\_around(rs, dist=8, rs\_within="H", ats="CA")  
print(rs\_nbr)

H30-32,51,58,108-111

t



## Display

To visualize a structure, please save it to a PDB file and use PyMOL. If you prefer to display the structure in an HTML file, use util.save\_string("my\_protein.html", p.html()) and open it in a browser.

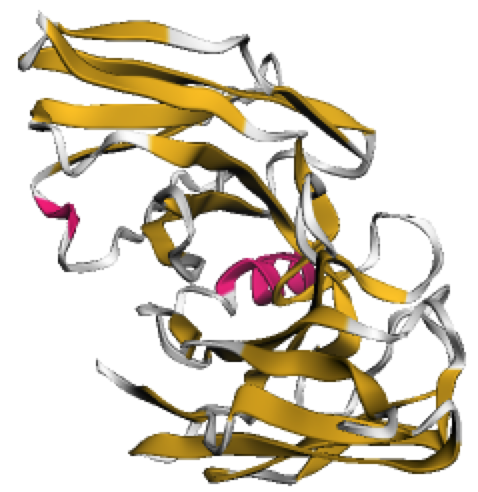
Within Jupyter Notebook, p.show() will display the structure as we do throughout this notebook.

The arguments for show() and html() are the same. show\_sidechains=False, show\_mainchains=False, color="chain", style="cartoon", width=320, height=320)

color can be: "chain", "lDDT", "b", "spectrum", "ss". style can be: "cartoon", "stick", "line", "sphere", "cross".

If colored by lDDT, the b-factors should be in the range of [0, 100]. If colored by "b", b-factors should be normalized to [0, 1].

p=Protein(fn)  
util.save\_string("my\_protein.html", p.html())  
print("You can also open my\_protein.html in a browser to view the protein structure.")  
print("We display the protein within Jupyter notebook below")  
p.show(style="cartoon", color="ss")



## B-factors

B-factor is an embedded attribute that can be repurposed to store other computation results. E.g., AlphaFold uses b-factors to store pLDDT for the structure prediction confidence. we can use b-factors to flag the CDR loop residues. PyMOL can then color residues by b-factors, which enables us to visualize the computational results in their structural context. In Afpdb, we currently read/write b-factors at the residue level, i.e., all atoms in a residue share the same b-factor value, as we have not yet encountered the need for displaying b-factors at the atom level.

p=Protein(fk)  
# read b\_factors as a numpy array  
print(p.b\_factors())

[1. 1. 1. 1. 1. 1.]

# set b\_factors by providing a numpy array  
import numpy as np  
p.b\_factors(np.random.random((len(p))), "\n")

[0.0668895 0.31111105 0.04879224 0.51323109 0.13960504 0.86005201]

To color by b-factors, set color = "b" in the show() method. However, please normalize b-factor NumPy array to be within [0, 1] to get the expected coloring effect (although show() method will clip the values, it does not normalize them).

p=Protein(fn)  
n=len(p)  
p.b\_factors(np.sin(np.arange(n)/n\*np.pi))  
p.show(style="cartoon", color="b")



It may be more convenient to get or set b-factors for each chain using b\_factors\_by\_chain() method.

# in this example, we color residues based on how far they are from the P chain  
p=Protein(fn)  
rs, rs\_seed, dist=p.rs\_around("P", dist=1e8)  
# important to sort the residues by their internal indices, so that the order of distance matches the internal b-factor array  
# we use drop\_duplicates to make sure each residue only occur once (to its nearest seed residue)  
dist.drop\_duplicates("resi\_b", inplace=True)  
dist.sort\_values("resi\_b", inplace=True)  
assert len(dist)==len(p.rs("H:L"))  
d\_min,d\_max=dist.dist.min(), dist.dist.max()  
# b factors should be in [0, 1], if we want to color by b-factos.  
dist["dist"]=(dist["dist"]-d\_min)/(d\_max-d\_min)  
b={"P":0, "H":dist[dist.chain\_b=="H"].dist.values, "L":dist[dist.chain\_b=="L"].dist.values}  
# set b\_factors  
p.b\_factors\_by\_chain(b)  
p.show(color="b")



We can also provide a residue selection for b\_factors().

# Use b-factor to mimic color by chain  
p=Protein(fn)  
# provide b-factors as an array  
p.b\_factors(np.zeros(len(p.rs("H"))), rs="H")  
# a number is considered a special case  
p.b\_factors(0.5, rs="L")  
p.b\_factors(1, rs="P")  
p.show(color="b")



# visualize CDRs  
p=Protein(fn)  
# CDR sequence (Chothia definition) light chains followed by heavy chain  
CDR\_L=['RASQSVGNNKLA', 'GASSRPS', 'QQYGQSLST']  
CDR\_H=['GGSFSTY', 'IPLLTI', 'EGTTGDGDLGKPIGAFAH']  
# color the framework resdues  
p.b\_factors(1, "H")  
p.b\_factors(0.9, "L")  
p.b\_factors(0.8, "P")  
for i,(seq,chain) in enumerate(zip(CDR\_L+CDR\_H, ["L"]\*3+["H"]\*3)):  
    b=i/20  
    # we select the CDR fragment by sequence search  
    # as rs\_seq returns a list of RS, we take the first element  
    rs\_cdr=p.rs\_seq(seq, in\_chains=[chain])[0]  
    p.b\_factors(b, rs=rs\_cdr)  
p.show(color="b")



We can leverage PyMOL to create more powerful visualizations, which will be described next.

## PyMOL Interface

PyMOL is a power structure visualization tool. **Afpdb** provides efficient and convenient programming interface for structure computation. An easy-to-use interface between Afpdb and PyMOL can help combine the strenght of both tools covering both structure analysis and visualization. The PyMol() method fills this role.

The method returns a PyMOL object, which has a run method enabling us to run any PyMOL commands.

# create a new PyMOL engine  
pm=Protein().PyMOL()  
pm.cmd(f"load {fn}, myobj")  
p=Protein(fn)  
rs\_binder, rs\_seed, t = p.rs\_around("P", rs\_within="H:L", dist=4)  
# selecting all interface residues  
rs\_int = rs\_binder | rs\_seed  
# convert Afpdb residue selection to a PyMOL selection command, where the selection object is named "myint"  
rs\_str = rs\_int.str(format="PYMOL", rs\_name="myint")  
print(rs\_str, "\n")

select myint, (chain L and resi 33+92-95+97) or (chain H and resi 30+32+46+49-51+54+56-58+98+106-109) or (chain P and resi 1-7+9-10)

# We can also control the selection to CA only  
print(rs\_int.str(format="PYMOL", rs\_name="myint\_ca", ats="CA"), "\n")  
  
select myint\_ca, ((chain L and resi 33+92-95+97) or (chain H and resi 30+32+46+49-51+54+56-58+98+106-109) or (chain P and resi 1-7+9-10)) and name CA

pm.run(f"""  
# color by chain  
as ribbon, myobj  
util.cbc  
# defines a selection named myint  
{rs\_str}  
show sticks, myint  
# focus on the selection  
zoom myint  
""")  
pm.run("""deselect; save mypm.png; save mypm.pse""")  
# dispose the PyMOL object to save system resource  
pm.close()

PyMOL>load /Users/zhoyyi1/afpdb/tutorial/example\_files/5cil.pdb, myobj

CmdLoad: "" loaded as "myobj".

PyMOL># color by chain

PyMOL>as ribbon, myobj

PyMOL>util.cbc

util.cbc: color 26, (chain H)

util.cbc: color 5, (chain L)

Executive: Colored 939 atoms.

util.cbc: color 154, (chain P)

Executive: Colored 844 atoms.

Executive: Colored 130 atoms.

PyMOL># defines a selection named myint

PyMOL>select myint, (chain L and resi 33+92-95+97) or (chain H and resi 30+32+46+49-51+54+56-58+98+106-109) or (chain P and resi 1-7+9-10)

Selector: selection "myint" defined with 245 atoms.

PyMOL>show sticks, myint

PyMOL># focus on the selection

PyMOL>zoom myint

PyMOL>deselect; save mypm.png; save mypm.pse

Ray: render time: 0.31 sec. = 11623.1 frames/hour (0.31 sec. accum.).

Save: Please wait -- writing session file...

ScenePNG: wrote 640x480 pixel image to file "mypm.png".

Save: wrote "mypm.pse".

The generated mypm.pse is a PyMOL session file to visualize the binding interface in 3D.

We here also automatically save the image into a PNG file as below.

A close up of a structure

Description automatically generated with medium confidence

As shown in this example, we can send any PyMOL commands via the run method. The input can be a single line or multiple lines. We can use # to add comments. The computation, i.e., the identification of the interface residues, can be done in **Afpdb** using rs\_around. A residue selection object's str method casts the selection into a PyMOL selection command:

rs\_str = rs\_int.str(format="PYMOL", rs\_name="myint")

turns the interface residues into the command that defines a selection object named "myint":

select myint, (chain L and resi 33+92-95+97) or (chain H and resi 30+32+46+49-51+54+56-58+98+106-109) or (chain P and resi 1-7+9-10)

If we only want to select CA atoms, we can do:

rs\_str = rs\_int.str(format="PYMOL", rs\_name="myint", ats="CA")

This will produce:

select myint, ((chain L and resi 33+92-95+97) or (chain H and resi 30+32+46+49-51+54+56-58+98+106-109) or (chain P and resi 1-7+9-10)) and name CA

When there are multiple objects in the PyMOL session, the argument obj\_name can constrain the selection to that object.

PyMOL command show sticks, myint and zoom myint shows the interface residues as sticks and zoom in to focus on them. We can also provide multiple PyMOL commands into one line with ";" as the concatenator. The example line is:

deselect; save mypm.png; save mypm.pse

Users can use all the PyMOL command they are already familiar with, but use **Afpdb** for the computational tasks that are not straightforward to do in PyMOL. Destroy the PyMOL() instance with close(), when it is no longer needed to save resource.

Note: If we already have PyMOL commands saved into a text file, we can also use pm.script(script\_file\_name) to execute it.

## Distance

In a previous example, rs\_around method already uses the distance measurement method rs\_dist internally.

Given two residue groups, rs\_a and rs\_b, rs\_dist computes the distance between all residue pairs. The distance is determined based on the two closest atoms. The output dataframe is sorted by distance and indicates which atom pair contributes to the distance measure.

p=Protein(fk)  
print(p.seq\_dict())  
print(p.rs().name(), "\n")  
  
t=p.rs\_dist('L', 'H')  
t



# we restricted the distance measurement to CA-CA distance, notice the distance are now longer  
t=p.rs\_dist('L', 'H', ats='CA')  
t

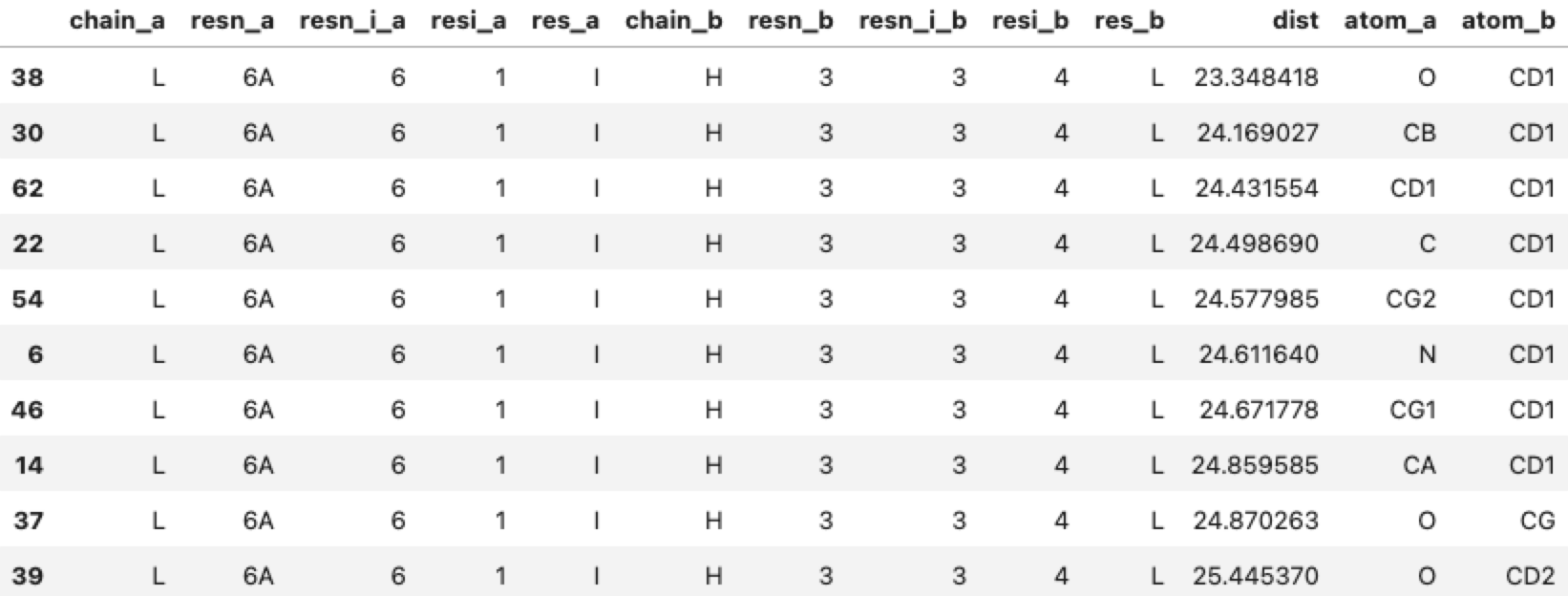


Instead of residue distance, we can also measure the distance between all-atom combinations. Our aim in the future is to add a column for interaction types, such as clash, electrostatic, hydrogen bonds, etc. Please contact us, if you have the knowledge in how to classify the interaction type of each atom pair.

# We list distances between all atom pairs of two residues  
p=Protein(fk)  
t=p.atom\_dist('L6A', 'H3')  
print(f"\n... total rows: {len(t)}\n")

... total rows: 64

t[:10]

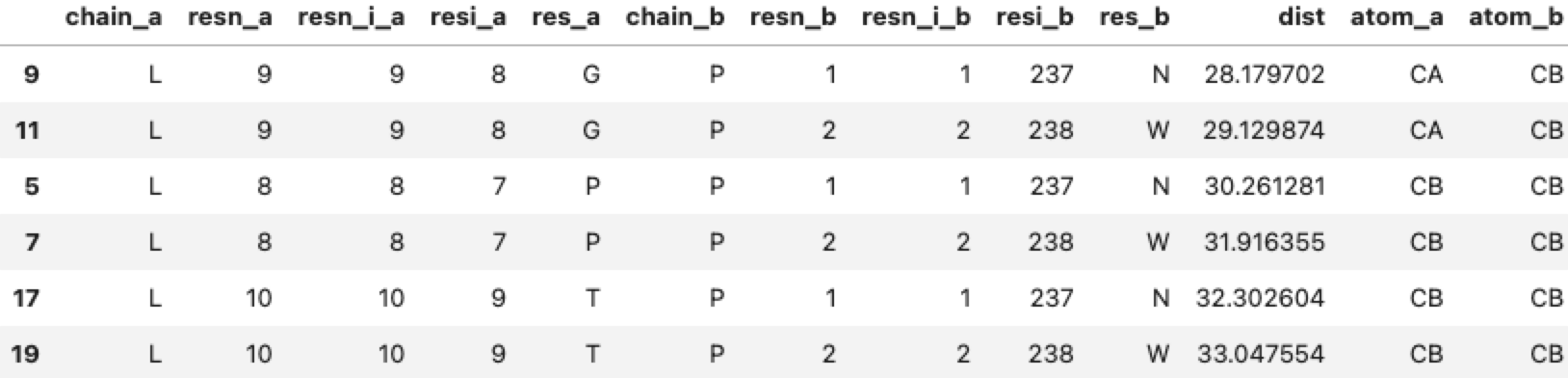


# We list distances between all backbone atom pairs of two residues  
t=p.atom\_dist('L6A', 'H3', ats=['CA','C','N','O'])  
t



Sometimes we compute inter-residue distance as distances between CB atoms, however, since Glyine does not have CB atom, special care needs to bee taken. We can compute distances among both CA and CB, then remove records associated with non-G CA atoms.

p=Protein(fn)  
t=p.atom\_dist("L8-10", "P1-2", ats="CA,CB")  
bad\_entry=((t.res\_a!="G")&(t.atom\_a=="CA"))|((t.res\_b!="G")&(t.atom\_b=="CA"))  
t=t[~ bad\_entry]  
t



This logic is implemented in method cb\_dist().

## RMSD

To measure the root mean square deviation (RMSD) between two residue selections, we first translate one molecule by 5Å, then call rmsd(). The method rmsd() takes a target object, source residue list, target residue list, and optionally an atom selection.

p=Protein(fk)  
q=p.translate([3.0,4.0,0.0], inplace=False)  
print("Translation:", p.center(), q.center(), q.center()-p.center(), "\n")

Translation: [ 15.54949999 -8.0205001 -15.39166681] [ 18.54949999 -4.0205001 -15.39166681]

[3. 4. 0.]

# consider all matched atoms, rs='ALL' or rs=None mean all residues  
print(q.rmsd(p, None, None), "\n")

5.0

# consider CA only  
print(q.rmsd(p, ats='CA'))

5.0

The two selections should have the same number of residues, unless one selection has only one residue. Otherwise, it will error. Make sure the order of residues in the two selections is what you want, as the distance is computed for each residue pairwise in order. If two residues are of different types, only the common atoms are used, which is enforced by the atom\_mask array. If we have different residue types, we recommend users use ats to explicitly restrict the computation to the backbone atoms only, e.g., "N,CA,C,O" or "CA".

rmsd() and align() are two methods where the order of the residues in the input matters, therefore, argument rl\_a and rl\_b are Residue Selection (RL) instead of RS. The following example shows why it is important to make sure the residue orders should match:

p=Protein(fn)  
print(p.chain\_id(), "\n")

['L', 'H', 'P']

# protein p and q have different chain orders  
q=p.extract("P:H:L")  
print(q.chain\_id(), "\n")

['P' 'H' 'L']

# The default behavior of using Residue List returns the right answer  
print(p.rmsd(q, "H:L", "H:L", ats="CA"), "\n")  
  
0.0

# However, if you pass in residue select, the result is wrong in this case, as residues in the RS# has been reordered  
print(p.rmsd(q, p.rs("H:L"), q.rs("H:L"), ats="CA"), "\n")

29.09069364318863

# this is because in object p, p.rs("H:L") standarize the residue index and put L residues in  
# front of H residue  
# in object q, p.rs("H:L") keeps H residues in front of L residues.  
# Therefore, residue selection breaks the one-to-one mapping relationship between the  
# two residue lists.  
# This example is created to demonstrate why we need to be careful, if we use RS objects for  
# the RL argument in rmsd() and align().

We often need to align the two structures first, before we take RMSD measurement. If we pass align=True into rmsd(), object p will then be first aligned to q, RMSD is then calculated. The align() method will be explained later.

DockQ

To compare how well a modeling/AI tool can accurately dock one protein against another in the binder-target problem, one can align the target structures and compute RMSD of the binder models. However, a popular metric in the literature is to compute DockQ score. Before using the dockQ static method, we need to make sure both proteins have the same corresponding chain names, and they are ordered the same. In the example below, the experimental chains are L, H, and P, but chains are numbered as A, B, and C in AlphaFold prediction. We first use rename\_reorder\_chains to rename chains in the predicted object q, and reorder its chains according to experimental object p.

The dockQ methods takes four arguments. The first two are experimental and prediction objects, where the order matters. The next two are chain contig strings that points to the two parts, where DockQ computes the interface. The method returns many fields reproducing the DockQ package (<https://github.com/bjornwallner/DockQ>), however, the main field is 'DockQ'.

# experimental structure

p=Protein(fn)

print(p.len\_dict(), "\n")

{'L': 111, 'H': 126, 'P': 13}

# AlphaFold prediction

q=Protein(str(fn).replace('.pdb', '\_AF.pdb'))

print(q.len\_dict(), "\n")

{'A': 111, 'B': 126, 'C': 13}

# make sure both structures have the same chain names and in the same order

q.rename\_reorder\_chains(p, {'A':'L', 'B':'H', 'C':'P'}, inplace=True)

print(q.len\_dict(), "\n")

{'L': 111, 'H': 126, 'P': 13}

# in dockQ method, the first object is exp obj, and the second is the prediction

# we assess the docker of P onto H:L, so using Ab and Ag as two parts

Protein.dockQ(p, q, "H:L", "P")

{'fnat': 1.0,

'fnonnat': 0.07272727272727275,

'nat\_correct': 51,

'nat\_total': 51,

'nonnat\_count': 4,

'model\_total': 55,

'clashes': 0,

'len1': 237,

'len2': 13,

'F1': 0.9622641509433962,

'class1': 'receptor',

'class2': 'ligand',

'LRMSD': 0.45316338508343096,

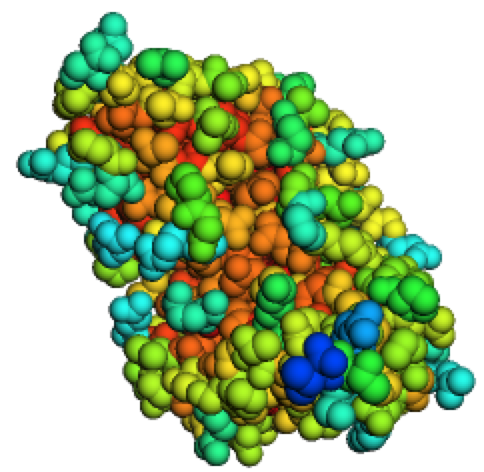
'iRMSD': 0.35339803042511503,

'DockQ': 0.9815259926329158}

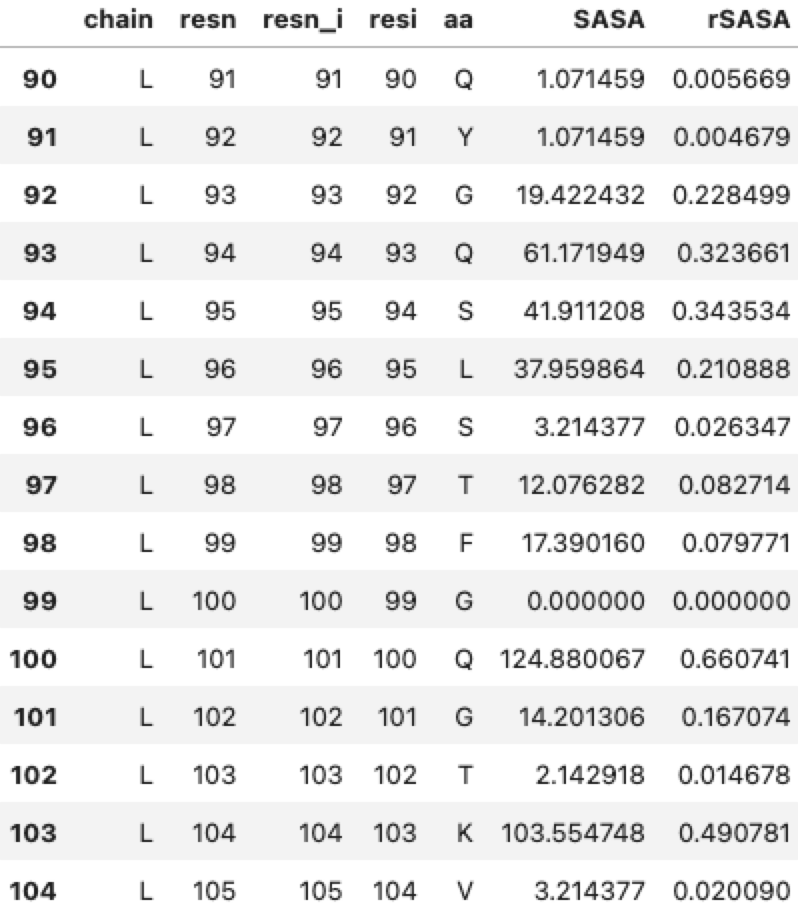
## Solvent-Accessible Surface Area (SASA)

We often would like to exclude some chains during the surface area computation. Although we can use extract() to take the chains we like, the in\_chains argument provides more convenience. For example, if all chains are included in the antibody-antigen complex, CDR binding residues will not be accessible to water. But if the antigen chain is excluded, contact CDR residues will be exposed. Computing the different of SASA values with different in\_chains is another popular way of identifying interface residues in addition to using rs\_around.

p=Protein(fn)  
# consider all chains, H:L:P, so the interface residues between H:L and P are mostly buried with low SASA values  
t\_HLP=p.sasa()  
sasa=p.sasa().SASA.values  
p.b\_factors(sasa/sasa.max())  
p.show(style="sphere", color="b")



# Get residue surface of a few L-chain residues  
t\_all=t\_HLP[(t\_HLP.chain=="L")][90:105]  
t\_all

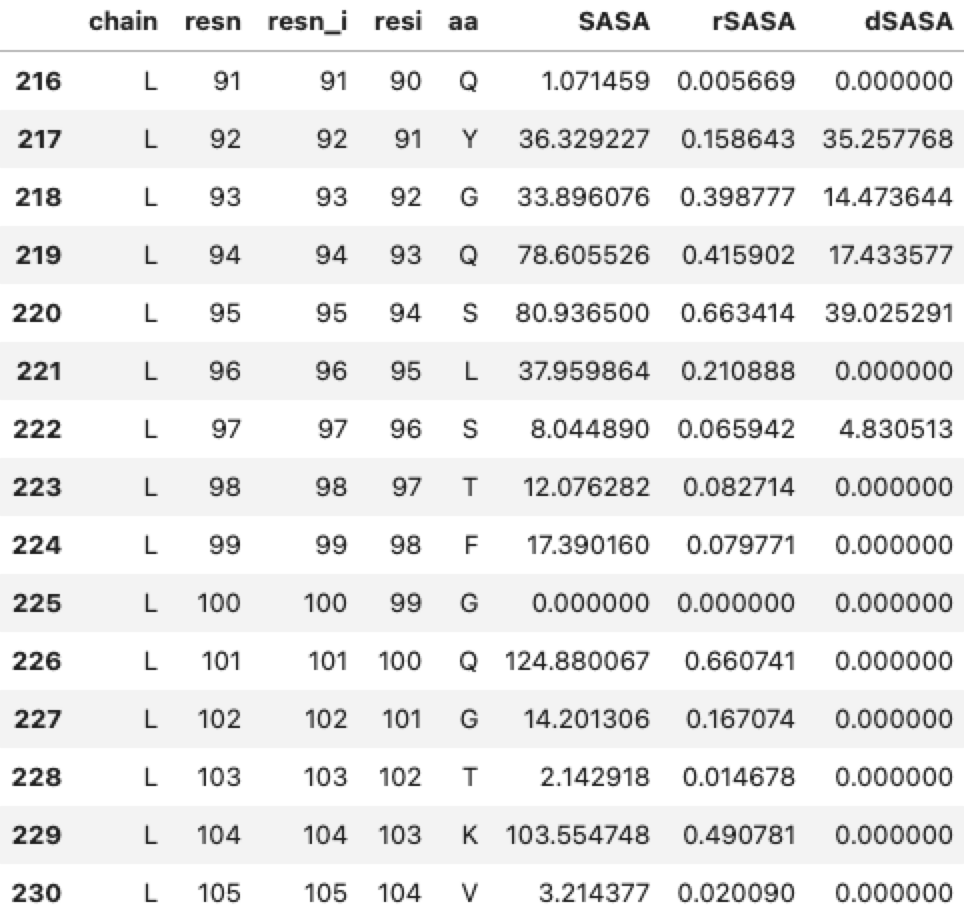


rSASA is defined as the relative SASA, i.e., SASA of each residue is normalized by its maximum possible surface area as defined in the G-X-G peptide: SASA/MaxResidueSASA. We use the values defined in the paper: [https://arxiv.org/pdf/1211.4251](https://www.google.com/url?q=https%3A%2F%2Farxiv.org%2Fpdf%2F1211.4251)

print("\nnotice residue L92 only has a small surface area 1.071459\n")  
# ignore antigen, CDR contact residues are now exposed with high SASA values  
t\_HL=p.sasa("H:L")  
t\_ag=t\_HL[(t\_HL.chain=="L")][90:105]  
t\_ag



print("\nnotice residue L92 now has a large surface area 36.3292\n\n")  
t\_ag['dSASA']=t\_ag['SASA'].values-t\_all['SASA'].values  
t\_ag



binder, rs\_seed, t=p.rs\_around(p.rs("P"), rs\_within="L", dist=4)  
print("Interface residues can also be identified with rs\_around directly:", binder, "\n")  
# the two methods are quite consistent with each other

Interface residues can also be identified with rs\_around directly: L33,92-95,97

Since we often need to compute the delta in SASA, there is a method dsasa() specifically defined for doing all steps shown above. The example below uses dsasa() to identify the Ab-Ag interface residues using the ideas outlined in the previous example.

p=Protein(fn)  
# compute the delta SASA for the interface formed between H:L and P  
t=p.dsasa("H:L", "P")  
p.b\_factors(1-t.drSASA.values)  
p.show(color="b")  
  
# this is mostly equivalent to finding interface residues with rs\_around  
rs\_L, rs\_seed,\_ = p.rs\_around("P", rs\_within="L", dist=4)  
# Let's display the result for residues on the L residues in the L-P interface  
t[t.resi.isin(rs\_L.data)]

This demonstrates that we can either use rs\_around to select interface residues, or calculate ΔASAS. The dsasa() method not only compute the SASA changes in the normalized scale drSASA, it also classify the types of residues according to [https://doi.org/10.1016/j.jmb.2010.09.028](https://www.google.com/url?q=https%3A%2F%2Fdoi.org%2F10.1016%2Fj.jmb.2010.09.028).

rSASAm is the rSASA when the two components are separated ("m" stands for monomer). rSASAc is when the two components for a complex ("c" stands for complex). Based on these two values and drSASA (rSASAm - rSASAc), residues can be classified into:

* iterior residues: No change between rSASAm and rSASAc, never accessible.
* surface residues: No change bewteen rSASAm and rSASAc, always accessible.
* core interface residues: accessible in rSASAm but inaccessible in rSASAc.
* rim interface residues: reduced SASA in the complex, but remain accessible in the complex.
* support interface residues: reduced SASA in the complex, but inaccessible in the monomer.

A diagram of a protein structure

Description automatically generated with medium confidence

## Secondary Structures - DSSP

Method dssp is a wrapper on BioPython's Bio.PDB.DSSP API, which requires the pre-installation of the DSSP package as described in [https://en.wikipedia.org/wiki/DSSP\_(algorithm)](https://www.google.com/url?q=https%3A%2F%2Fen.wikipedia.org%2Fwiki%2FDSSP_%28algorithm%29).

We can install DSSP with:

conda install sbl::dssp

The secondary structure codes are:

* G = 3-turn helix (310 helix). Min length 3 residues.
* H = 4-turn helix (α helix). Minimum length 4 residues.
* I = 5-turn helix (π helix). Minimum length 5 residues.
* T = hydrogen bonded turn (3, 4 or 5 turn)
* E = extended strand in parallel and/or anti-parallel β-sheet conformation. Min length 2 residues.
* B = residue in isolated β-bridge (single pair β-sheet hydrogen bond formation)
* S = bend (the only non-hydrogen-bond based assignment).
* C = coil (residues which are not in any of the above conformations).

In the simplified mode, we map the codes into a - alpha helix, b - beta sheet, and c - coil.

# BioPython relies on DSSP command line program to compute secondary structures  
if IN\_COLAB:  
    if not os.path.isfile("INSTALL\_DSSP"):  
        ! conda install sbl::dssp  
        ! touch INSTALL\_DSSP  
  
p=Protein(fn)  
# Biopython relies on command line DSSP program, it does not automatically detect the version, so we provides a locate\_dssp() method  
# locate\_dss() does this for us  
dssp\_settings=Protein.locate\_dssp()  
print("DSSP command line and its version:", dssp\_settings)  
ss=p.dssp(simplify=True, \*\*dssp\_settings)  
print(ss, "\n")

DSSP command line and its version: {'DSSP': '/Users/zhoyyi1/anaconda3/bin/mkdssp', 'dssp\_version': '4.2.2.1'}

{'L': '---bb-cccbbbb-cc--bbbbbbbccPPaaa-bbbbbb-ccc--bbbbbcccb--ccc-ccbbbbbbccbbbbbbcc--aaa-cbbbbbb-cccc-bb---bbbbb----', 'H': '-bbbbPPPbbb-cc--bbbbbbbbcc-cccc-bbbbbb-ccc-bbbbbbbbaaacbbbb-aaacccbbbbbbccccbbbbbb-c--aaa-bbbbbbbbbbccccccc-bbbbbbbb---bbbbb--', 'P': '-aaaaaaaaaaa-'}

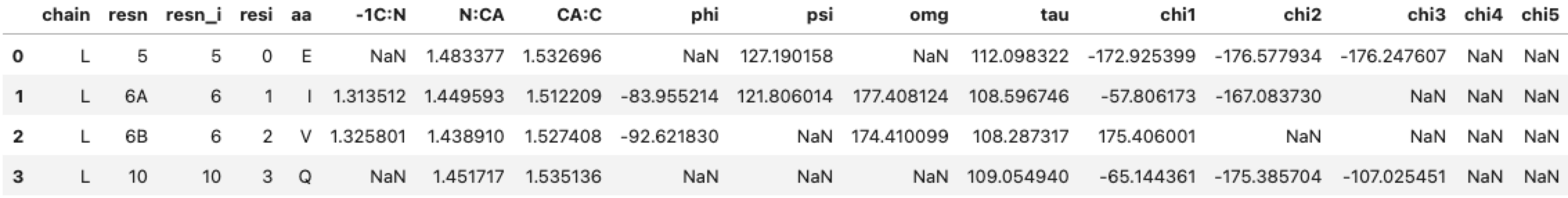
# set helix to 1, otherwise 0  
for k,v in ss.items():  
    b=np.zeros(len(v))+0.5 # default to turns  
    b[np.array(list(v))=="a"]=0  
    b[np.array(list(v))=="b"]=0.8  
    b[np.array(list(v))=="c"]=0.3  
    ss[k]=b  
p.b\_factors\_by\_chain(ss)  
p.show(color="b")



## Internal Coordinate

To obtain the bond length (for backbone) and bond angles:

p=Protein(fk)  
t=p.internal\_coord(rs="L")  
t

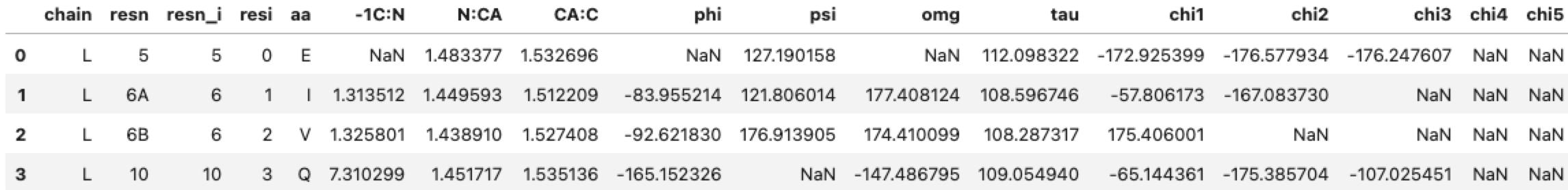


resi is the internal residue\_index, and resn is residue name. The bond lengths are "-1C:N" (previous C to current N), N-CA, and CA-C, followed by all bond angles.

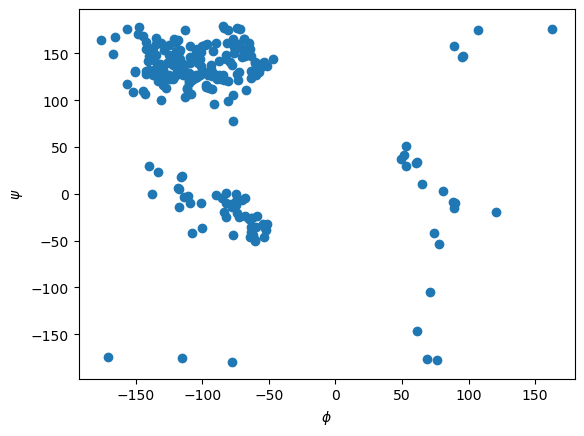
Notice ϕ and ω angle for the first residue is NaN, as there is no peptide bond for the first residue. Similarly, ψ angle is not defined for the last residue.

The peptide bond length is NaN between residues 6B and 10, as there are missing residues. If we do want to know how far these two residues are, we can modify the default MaxPeptideBond from 1.4 to a bigger value (which can be useful for imperfect structures output by diffusion methods):

p=Protein(fk)  
t=p.internal\_coord(rs="L", MaxPeptideBond=1e6)  
t



To run the example below, make sure you have matplotlib installed. If not, run in the shell:

pip install matplotlib  
  
p=Protein(fn)  
t=p.internal\_coord()  
#t.display()  
from matplotlib import pyplot as plt  
plt.scatter(t.phi, t.psi)  
plt.xlabel('$\\phi$')  
plt.ylabel('$\\psi$')  
print("Ramachandran Plot")  
  
#TODO: add the boundaries for popular engles, similar to the countours in https://www.mathworks.com/help/bioinfo/ref/ramachandran.html

# Protein Object Manipulation

## Move Objects

We can recenter, translate, and rotate an object.

p=Protein(fk)  
print("Original center:", p.center(), "\n")

Original center: [ 15.54949999 -8.0205001 -15.39166681]

q=p.center\_at([3.0,4.0,5.0])  
print("New center after recentering:", q.center(), "\n")

New center after recentering: [3. 4. 5.]

q=p.translate([1.,0.,-1.])  
print("New center after translate:", q.center(), "\n")

New center after translate: [ 16.54949999 -8.0205001 -16.39166681]

# rotate 90 degrees around axis [1,1,1]  
print("RMSD before rotation:", q.rmsd(p, None, None, "CA"), "\n")

RMSD before rotation: 1.4142135623730951

# we only rotate 5 degrees  
q=p.rotate([1,1,1], 5)  
print("Old center:", p.center(), "New center:", q.center(), "\n")

Old center: [ 15.54949999 -8.0205001 -15.39166681] New center: [ 15.10944354 -6.44301224 -16.52909822]

print("RMSD after rotation:", q.rmsd(p, ats="CA"), "\n")

RMSD after rotation: 2.190194408912404

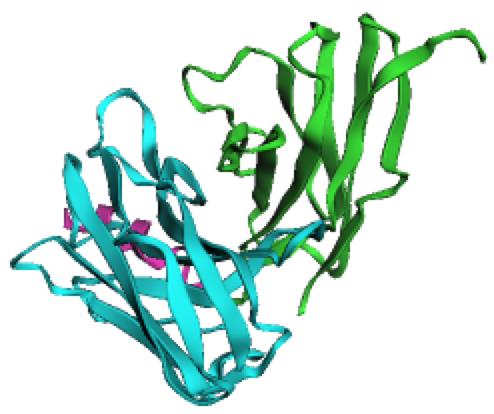
# Warning, rotate is done using the origin as the center, that's why the rotation dramatically increase RMSD in the example above.  
# most of the time, it's only meaningful if we center the molecule before rotation  
rc=p.center()  
q=p.center\_at([0,0,0])  
# rotate 5 degrees  
q.rotate([1,1,1], 5, inplace=True)  
# restore the center to the old center  
q.center\_at(rc, inplace=True)  
# now the RMSD is much smaller  
print("RMSD (center before rotate):", q.rmsd(p, None, None, "CA", align=True), "\n")

RMSD (center before rotate): 1.926437630612445e-12

To reset the position of an object, use reset\_pos(). This will place the object center at the origin, as well as align its three PCA axes along Z, X, and Y axis, respectively.

p=Protein(fn)  
print("Old center:", p.center(), "\n")  
  
Old center: [ 20.15256404 -5.12843199 -15.77199195]

# rotation around a random axis direction with a random angle  
p.rotate(np.random.random(3), np.random.random()\*180)  
p.show()

  
p.reset\_pos()  
p.show()

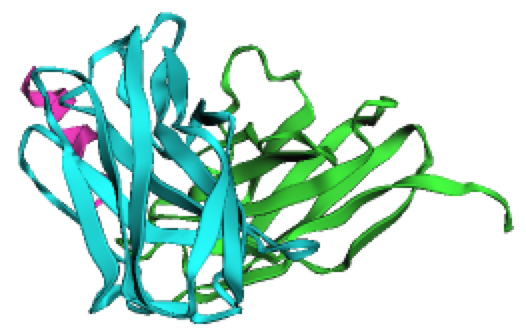
  
print("New center:", p.center())

New center: [-9.80548975e-15 -2.61479727e-15 7.52908846e-15]

## Align

It makes sense to align two objects before making RMSD measurement. Align method takes two residule lists (not residue selection) as it arguments. The default value is None, which refers to all residues.

p=Protein(fn)  
q=p.translate([3.,4.,0.], inplace=False)  
q.rotate([1,1,1], 90, inplace=True)  
p.show()  
  
  
q.show()

  
print("RMSD before alignment:", q.rmsd(p, "ALL", "ALL", ats='CA'))

RMSD before alignment: 45.854280383656324

R,t=q.align(p, ats="CA")  
q.show()

  
print("RMSD after alignment:", q.rmsd(p, ats='CA'))  
print("Rotation matrix:\n", R, "\n")  
print("Translation vector:", t)

RMSD after alignment: 2.470821699978209e-07

Rotation matrix:

[[ 0.33333331 -0.24401692 0.91068361]

[ 0.91068361 0.33333331 -0.24401693]

[-0.24401692 0.91068361 0.33333331]]

Translation vector: [[-3.00000031e+00 -3.99999992e+00 3.11646732e-07]]

RMSD usually requires a pre-alignment, therefore, we can combine the two into one by providing align=True to rmsd(). Notice the coordinates of object p is changed as the side effect!

p=Protein(fn)  
q=p.translate([3.,4.,0.], inplace=False)  
q.rotate([1,1,1], 90, inplace=True)  
print("RMSD without alignment:", p.rmsd(q), "\n")

RMSD without alignment: 45.98047321761866

print("RMSD with built-in alignment:", p.rmsd(q, align=True), "\n")  
# The side effect is p has been changed by align=True

RMSD with built-in alignment: 2.493618546797601e-07

print("RMSD without alignment on the new p object:", p.rmsd(q), "\n")

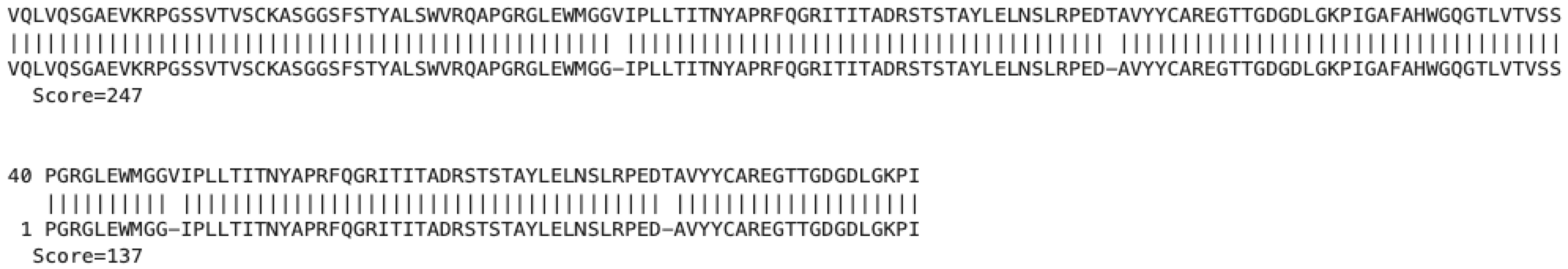
RMSD without alignment on the new p object: 2.493618546797601e-07

## Align Sequences

Both align() and rmsd() requires a pair of pre-aligned RL objects. If two proteins share the same sequence or a few spot mutations, the whole sequence can be used as the RL arguments. However, where there are insertions and deletions, it can be tedious to construct the RL pairs manually. This can happen even when we compare an experimental structure to its predicted structure, because modeling software may not be able to handle some non-canonical residues and resulting missing residues in the models. Afpdb can programmatically align two sequences and extract the aligned subset of residues as a RL pair.

We first create two proteins, one with two missing residues:

p=Protein(fn)  
# create q with two deletions  
q=p.extract(~ p.rs("H50,90"))  
# by default the two sequences are algined using Biopython global alignment  
x, a, b=Protein.find\_aligned\_positions(p.rs("H").seq(), q.rs("H").seq())  
print(x[1], "\n")  
#If the second sequence is a truncation of the first one, local alignment generally works better (no penalty for ends)  
x, a, b=Protein.find\_aligned\_positions(p.rs("H").seq(), q.rs("H40-110").seq(), is\_global=False)  
print(x[1])



The method find\_aligned\_positons is a low-level debugging method, we generally use a higher-level method rl\_align instead.

rl\_q, rl\_p=q.rl\_align(p)

print(rl\_p, "\n")

L:H1-49:H51-89:H91-126:P

print(rl\_q)

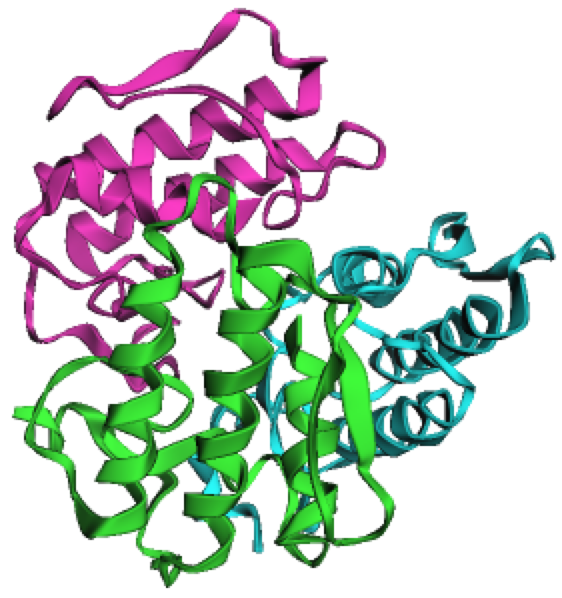
L:H:P

rl\_algin uses is\_global = True by default and one can adjust some scores to fine tune the alignment algorithm. In the above example, rl\_align() returns a pair of RL object for all aligned residue pairs. Here since object q has H50 and H100 removed, we can see these two residues are not in the rl\_p object. All residues in object q are used, therefore, its contig is L:H:P. The resultant RL object can then be used in the align() or rmsd() methods.

## Split & Merge Objects

To split an object into multiple objects, just use extract. To merge multiple structure objects into one, use merge.

# 1a3d.pdb is a three-chain homotrimer.  
p=Protein(pwd / "example\_files/1a3d.pdb")  
print(p.seq\_dict(), "\n")  
p.show()

  
  
# Extract each chain into a new object  
Q=[ p.extract(x, inplace=False) for x in p.chain\_id() ]  
print("Object 1:", Q[0].seq\_dict(), "\n")

Object 1: {'A': 'NLYQFKNMIKCTVPSRSWWDFADYGCYCGRGGSGTPVDDLDRCCQVHDNCYNEAEKISGCWPYFKTYSYECSQGTLTCKGDNNACAASVCDCDRLAAICFAGAPYNDNNYNIDLKARCQ'}

#for object 2 & 3, computer RMSD, then align them against object 1 and print RMSD after alignment  
for i,q in enumerate(Q[1:]):  
    # we intentionally rename chains to A for all object, the merge method will be able to auto rename chains  
    q.rename\_chains({'B':'A', 'C':'A'})  
    print(f"Object {i+2}:", q.seq\_dict())  
    print("RMSD to Object 1:", q.rmsd(Q[0], None, None, ats='N,CA,C,O'), "\n")  
    q.align(Q[0], ats='N,CA,C,O')  
    q.translate(np.random.random(3)\*1.5) # add a small jitter, so that we can later see there are three objects overlaid  
    print("RMSD after align:", q.rmsd(Q[0], None, None, ats='N,CA,C,O'), "\n")  
  
Object 2: {'B': 'NLYQFKNMIKCTVPSRSWWDFADYGCYCGRGGSGTPVDDLDRCCQVHDNCYNEAEKISGCWPYFKTYSYECSQGTLTCKGDNNACAASVCDCDRLAAICFAGAPYNDNNYNIDLKARCQ'}

RMSD to Object 1: 29.520795074060185

RMSD after align: 1.01025425274622e-14

Object 3: {'C': 'NLYQFKNMIKCTVPSRSWWDFADYGCYCGRGGSGTPVDDLDRCCQVHDNCYNEAEKISGCWPYFKTYSYECSQGTLTCKGDNNACAASVCDCDRLAAICFAGAPYNDNNYNIDLKARCQ'}

RMSD to Object 1: 29.520795074060185

RMSD after align: 1.061576257419e-14

q=Protein.merge(Q)  
print(q.seq\_dict())

{'A':'NLYQFKNMIKCTVPSRSWWDFADYGCYCGRGGSGTPVDDLDRCCQVHDNCYNEAEKISGCWPYFKTYSYECSQGTLTCKGDNNACAASVCDCDRLAAICFAGAPYNDNNYNIDLKARCQ',

'B':'NLYQFKNMIKCTVPSRSWWDFADYGCYCGRGGSGTPVDDLDRCCQVHDNCYNEAEKISGCWPYFKTYSYECSQGTLTCKGDNNACAASVCDCDRLAAICFAGAPYNDNNYNIDLKARCQ',

'C':'NLYQFKNMIKCTVPSRSWWDFADYGCYCGRGGSGTPVDDLDRCCQVHDNCYNEAEKISGCWPYFKTYSYECSQGTLTCKGDNNACAASVCDCDRLAAICFAGAPYNDNNYNIDLKARCQ'}

q.show()



# Parsers for AI Models

Afpdb also provides some utility classes to parse output of AlphaFold, ColabFold, ESMFold, ProteinMPNN, and LigandMPNN. Since these utilities do not take a protein structure object as either its input or output, they are not part of the Afpdb's Protein class, but are provided in the afpdb.aiparser module. Due to file size constrains, we do not include the output files from these models, but instead show the example code and their abbreviated output.

## Parse AlphaFold Output

import afpdb.util

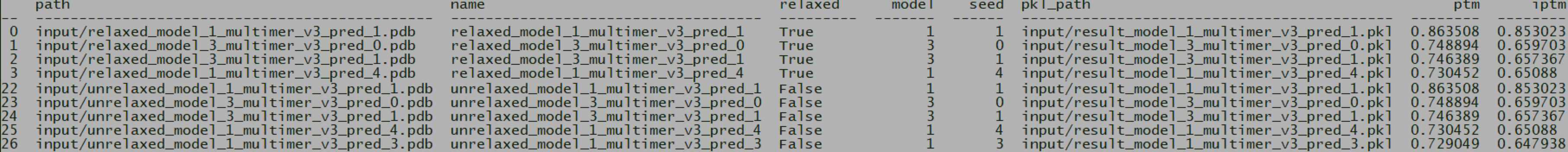
from afpdb.aiparser import AlphaFoldParser

# points the parser to the model output folder (which should contain .pdf and .pkl files)

x=AlphaFoldParser('af\_output')

# x.data is a DataFrame listing all predictions and their key metrics

x.data.display()



As shown, the parser compiles all the .pdb files, listing the relaxed model (if available) first. The model’s ptm, iptm, and corresponding pickle files (.pkl) are included. The .pkl file contains pLDDT and PAE information. pLDDT is also embedded in the .pdb files as b-factors. Predictions are ranked by relaxed status, then by iPTM and PTM.

print(x.get\_pdb())  
  
input/relaxed\_model\_1\_multimer\_v3\_pred\_1.pdb

print(x.get\_ptm())

0.8635075964711556

print(x.get\_iptm())

0.8530234098434448

print(x.get\_plddt().shape)

(554,)

print(x.get\_plddt()[:5])

[76.5977254 91.16503033 95.96849556 97.97122074 98.53807982]

print(x.get\_pae().shape)

(554, 554)

The get\_\* methods extract the corresponding properties. Both get\_plddt and get\_pae return Numpy array objects. These method takes an optional idx argument, default to 0, indicating the row index of the prediction user is interested in (idx = 0 is the best prediction listed in x.data).

The usage of other parsers is quite similar, therefore we simply outline the code and skip their outputs.

## Parse ColabFold Output

from afpdb.aiparser import ColabFoldParser

x=ColabFoldParser('cf\_output')

x.data.display()

print(x.get\_pdb())

print(x.get\_ptm())

print(x.get\_iptm())

print(x.get\_plddt())

pae=x.get\_pae()

print(pae.shape)

## Parse ESMFold Output

from afpdb.aiparser import ESMFoldParser

from afpdb.afpdb import Protein

from afpdb import util

x=ESMFoldParser('esmfold\_output')

x.data.display()

print(x.get\_plddt())

data=(x.get\_pae())

print(data.shape)

p=Protein(x.get\_pdb())

print(p.len\_dict())

## Parse ProteinMPNN Output

from afpad.aiparser import ProteinMPNNParser

from afpdb import util  
x=ProteinMPNNParser('mpnn\_output')

# results are sorted by score

x.data.display()

path name sample score global\_score T seq\_recovery seq

-- ------------------------ ------- -------- ------- -------------- --- -------------- --------------------------------------------

6 mpnn\_output/seqs/1crn.fa 1crn.fa 7 1.1493 1.2145 0.1 0.5238 TVCCPSSLSEYLSCLSSGTPSSSCASETGCIIISGSSCPSSY

3 mpnn\_output/seqs/1crn.fa 1crn.fa 4 1.1639 1.206 0.1 0.5476 TVCCPSPLSSYLSCRSSGRPDSECAKLTGCIIISGSTCPSSY

7 mpnn\_output/seqs/1crn.fa 1crn.fa 8 1.1695 1.2297 0.1 0.5238 TVCCPSSLSSFLACLSSGTPVEECCKETGCIVISGSTCPSSY

8 mpnn\_output/seqs/1crn.fa 1crn.fa 9 1.1747 1.2383 0.1 0.5238 TVCCPSSLSDYLNCLSSGTPTSICAKETGCIVISGSNCSSDY

9 mpnn\_output/seqs/1crn.fa 1crn.fa 10 1.1962 1.2587 0.1 0.4762 TVCCPSPLSEYLECLSSGKPPEECCKETGCIIISGSSCPSSY

5 mpnn\_output/seqs/1crn.fa 1crn.fa 6 1.1966 1.2474 0.1 0.5714 TVCCPSPLSEYLACRSSGTPDSLCALATGCIIISGSSCPSDY

2 mpnn\_output/seqs/1crn.fa 1crn.fa 3 1.1978 1.242 0.1 0.5238 TICCPSPRSEYESCLSSGTPPSSCCEETGCIIISGSTCPSSF

4 mpnn\_output/seqs/1crn.fa 1crn.fa 5 1.1978 1.2609 0.1 0.5476 TVCCPSPLSEYLQCLSSGTPPEECAKATGCIIISGSTCPASY

0 mpnn\_output/seqs/1crn.fa 1crn.fa 1 1.1982 1.2612 0.1 0.5 TICCPSPLEEYLSCLSSGTPPEECCEETGCIIISGSSCPSDY

1 mpnn\_output/seqs/1crn.fa 1crn.fa 2 1.2151 1.2849 0.1 0.5476 TVCCPSPLAEYLECLSSGTPPEECAKATGCIIISGSTCPSDY

# to produce structures with side chains

# produce .pdb files named output\_folder/sample1.pdb, output\_folder/sample2.pdb, ...

# Since Afpdb does not include Amber, the structures are not relaxed.  
x.make\_structure('template.pdb', 'output\_folder')

## Parser LigandMPNN Output

Side chain conformations are generated by LigandMPNN, therefore, ```make\_structure()``` method is not provide.

from afpad.aiparser import LigandMPNNParser

from afpdb import util

x=LigandMPNNParser('mpnn\_output')

# results are sorted by overall\_confidence

x.data.display()

path name id T seed overall\_confidence ligand\_confidence seq\_rec seq

-- ------------------------ ------- ---- --- ------ -------------------- ------------------- --------- -------------------------- 0 mpnn\_output/seqs/1BC8.fa 1BC8.fa 5 0.1 111 0.4074 0.4074 0.4731 GKSSMSLHEFLLKLLSDPKYADII

1 mpnn\_output/seqs/1BC8.fa 1BC8.fa 1 0.1 111 0.4073 0.4073 0.5054 GTSKISLWEFLLELLSDPKYKDYI

2 mpnn\_output/seqs/1BC8.fa 1BC8.fa 4 0.1 111 0.404 0.404 0.5161 GKSKISLHEFLLKLLSDPKYADYI

3 mpnn\_output/seqs/1BC8.fa 1BC8.fa 2 0.1 111 0.3969 0.3969 0.4516 GHSHMSLHEFILSLLSKPEYDDYI

4 mpnn\_output/seqs/1BC8.fa 1BC8.fa 3 0.1 111 0.3831 0.3831 0.4839 GTSKMSLYEFLLELLSDPKYNDII

# Protein AI Design Use Cases

One effective AI protein design strategy involves generating hypothetical binder backbone structures based on a target protein (e.g., using RFDiffusion), followed by using inverse folding AI models to create binder sequences (e.g., using ProteinMPNN). These designs can then be validated using structure prediction models like AlphaFold. In order to achieve successful designs, thousands of protein structures need to be manipulated within a project. **Afpdb** aims to increase the productivity for such large-scale AI protein design efforts.

In this section, we demonstrate a few real use cases on how **Afpdb** tools help in AI protein design processes.

## Handle Missing Residues in AlphaFold Prediction

In evaluating protein structure prediction models such as AlphaFold, the true experimental structure p\_exp may contain missing residues. We often replace missing residues with glycine for AlphaFold modeling. When align the predicted structure p\_af against p\_exp, we need to exclude those added G residues, as they do not exist in p\_exp.

The example below first created a fake experimental p\_exp with five missing residues, and a fake AF-predicted p\_af with five extra Glycines. p\_exp contains 106 residues with L15-19 missing. p\_af contains 111 residues with five extra Gs.

From p\_exp, rsi\_missing() returns a residue selection object that can be used to point at the extra G residues in p\_af. Methods align and rmsd can then be done with those extra residues excluded.

p**=**Protein(fn)

miss\_residues**=**"L15-19"

*# create an experimental structure for chain L with residues L15-19 missing*

p\_exp**=**p**.**extract( **~** p**.**rs(miss\_residues) **&** "L")

print(p\_exp**.**seq(), "\n")

EIVLTQSPGTQSLSXXXXXTLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV

print("Notice five residues XXXXX corresponds to position 15-19\n")

Notice five residues XXXXX corresponds to position 15-19

af\_seq**=**p\_exp**.**seq(gap**=**"G")

print(af\_seq, "\n")

EIVLTQSPGTQSLS**GGGGG**TLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV

print("We run AlphaFold prediction using af\_seq, i.e., replacing missing residues with Gly ...\n")

We run AlphaFold prediction using af\_seq, i.e., replacing missing residues with Gly ...

*# Create a fake AlphaFold predicted structure, by changing the missing residues to Glycine*

p\_af**=**p**.**extract("L") *# extract chain L*

rs**=**p\_af**.**rs(miss\_residues)

print(rs)

L15-19

p\_af**.**data**.**aatype[rs**.**data]**=**RS**.**i("G") *# set residue type to Gly*

*# np.ix\_ select all rows in rs.data and all columns in ~ATS("N,CA,C,O")).data*

p\_af**.**data**.**atom\_mask[np**.**ix\_(rs**.**data, (**~**ATS("N,CA,C,O"))**.**data)]**=**0 *# Gly does not have side chain atoms*

print("Pretend p\_af is the output of AlphaFold prediction\n")

Pretend p\_af is the output of AlphaFold prediction

print("Verify the missing resiudes are not missing in p\_af, they are Gs:\n")

print(p\_af**.**seq(), "\n")

Verify the missing resiudes are not missing in p\_af, they are Gs:

EIVLTQSPGTQSLSGGGGGTLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV

print(f"# of residues: p\_exp={len(p\_exp)}, p\_af={len(p\_af)}")

# of residues: p\_exp=106, p\_af=111

print("AlphaFold predicted structure has 5 more residues, which needs to be excluded for alignment purpose.\n")

AlphaFold predicted structure has 5 more residues, which needs to be excluded for alignment purpose.

*# we now need to align the common residues, excluding the inserted G residues as they do not exist in p\_exp*

*# the above is equivalent to first find the missing residue indices, notice rsi\_missing returns an array*

*# rsi=p\_exp.rsi\_missng()*

*# warning: do not use rsi on p\_exp, as rsi contains non-existing residue indices!!!*

*# cast rsi into a RS object for object p\_af*

*# rs\_miss=RS(p\_af, rsi)*

*# The shortcut is to find the inserted residues in p\_af with respect to p\_exp*

rs\_miss**=**p\_af**.**rs\_insertion(p\_exp)

*# now rs\_miss is meaningful, as they point to the 5 Gs*

print(rs\_miss, rs\_miss**.**seq(), "\n")

L15-19 GGGGG

*# now align the two structure and measure RMSD*

print(p\_exp**.**rmsd(p\_af, rl\_b**=~**rs\_miss, ats**=**"CA", align**=True**), "\n")

5.956938906837272e-15

## Structure Prediction with ESMFold

We provide a fold() method, which uses Meta's free EMSFold web service to predict protein structures. Our method support multiple chains, as well as missing residues. The multi-chain support was based on the idea outlined in the "Merge & Split" section, i.e., by default we concatenate chains by 50 glycine residues (gap=50 can be modified) into one chain. Missing residues are replaced by glycine just as we did in the above AlphaFold example.

Please be aware that ESMFold generally produces less accurate results compared to AlphaFold. The web service limits the intermediate sequence length to maximally 400 residues. Connection can fail after a few continuously predicted, as this public resource is protected from being overused. fold() is a quick way of occasionally turning a sequence into a structure.

We here provide an example of predicting the antibody structure of 5CLI.

Let us try the Ab-Ag complex, which ESMFold failed to prediction.

p=Protein(fn)

exp=p.extract("H:L")

try:

pred=Protein.fold(exp.seq())

print(pred.rmsd(exp, ats="N,CA,C,O", align=True))

exp.b\_factors(0.2)

q=Protein.merge([exp, pred])

q.show(color="b")

#q.save(pwd / "example\_files/esmfold.pdb")

except Exception as e:

print(e)

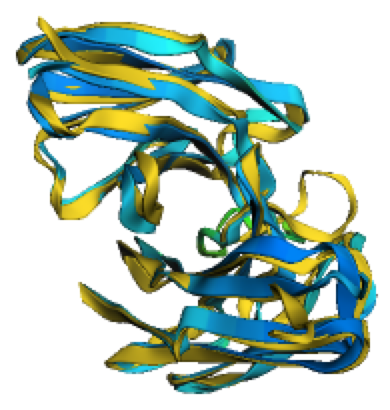
print("ESMFold service is not always stable. If you see error, try again!\n")

print("We show results from a previous successful run:\n")

p=Protien(pwd / "example\_files/esmfold.pdb")

p.show(color="b")

2.4554355609575724



p=Protein(fn)

exp=p.extract("H:L:P")

try:

pred=Protein.fold(exp.seq())

# algin by Ab only

# predicted chains are A, B, C

pred.rename\_chains({"A":"H", "B":"L", "C":"P"})

pred.align(exp, "H:L", "H:L", ats="N,CA,C,O")

# print RMSD of antigens

print(pred.rmsd(exp, "P", "P", ats="N,CA,C,O"))

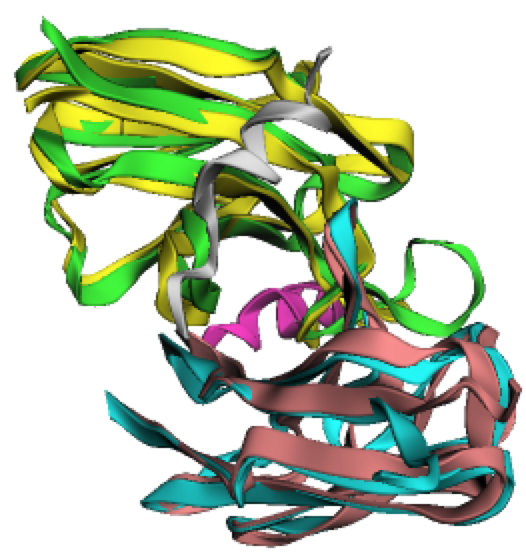
Protein.merge([exp, pred]).show(color="chain")

except Exception as e:

print(e)

print("ESMFold service is not always stable. If you see error, try again!")

41.00484574766786



We can see that ESMFold predicts the antibody structure well, however, it got the antigen binding mode wrong. Instead of binding to the CDR loops, it places antigen on the other end. Ab-Ag complex prediction is an extremely difficult problem, the prediction accuracy was improved in the latest AlphaFold3 model.

## Create Side Chains for de novo Designed Proteins

In the current AI-based protein design, RFDiffusion only generates a protein backbone. The output PDB file only contains coordinates for N, CA, C, O atoms. Often, RFDiffusion works on an input template and was used to design only part of the structure (known as inpainting). For example, in an antibody design application, RFDiffusion may be only used to redesign the CDR loops, while leaving the framework residues and structures untouched. In the example below, we use RFDiffusion to design CDR H3 loops with the rest of the antibody sequence fixed. For convenience, let us refer to those fixed residues approximately as framework residues and the CDR H3 loop as CDR residues without creating confusion.

In the output PDB file generated by RFDiffusion, no sidechain atom exists, even for those framework residues. The generated CDR H3 backbone are represented by glycine residues. ProteinMPNN will preserve the identities of the input framework residues, while proposing CDR H3 residues to replace those glycines. In order to visualize the full-atom model of the design antibody-antigen complex structure, we can use AlphaFold to predict the structure from the ProteinMPNN sequences. However, AlphaFold prediction is time consuming, and the predicted structure can be very different from the desired PDB structure due to the limited prediction accuracy on Ab-Ag complexes.

The method thread\_sequence() helps us rapidly create a full-atom structure by threading the ProteinMPNN-generated sequence onto the RFDiffusion backbone-only structure. When the ProteinMPNN sequence is threaded onto the PDB backbone template, the side chain coordinates of those framework residues are now generated by PyMOL, which are sampled from their most frequent torsion angles and can be very different from their original known coordinates. For this reason, thread\_sequence() takes an additional argument side\_chain\_pdb, which specifies the original PDB file that contains the side chain atoms for the framework residues (this is the PDB file used as the input for RFDiffusion). With this additonal input, the side chain coordinates for framework residues in the original PDB structure will be used instead of relying on PyMOL generation. Argument seq2bfactor=True maps the upper/lower-case of the input sequence onto b-factors (1.0/0.5), so that we can use b-factor to distinguish the redesigned residues (lower case) from those framework residues (upper case) preserved from the input template.

There are details inside the method that make use of several other **Afpdb** methods. For example:

The predicted structure needs to be aligned with the side\_chain\_pdb first, before we are able to clone the coordinates of the side chain atoms. This is because the original PDB structure and the RFDiffusion-generated structure are not aligned by default.

When RFDiffusion generates its output, chains are named A, B, C, etc. with the original chain names lost. As RFDiffusion can hallucinate new chains that do not exist in the original structure, it may not be able to preserve the original chain names even if it likes to. For this reason, we also need to provide a chain\_map argument, so that the threading code knows how to map the wild-type chain names into the RFDiffusion chain names in order to align them correctly.

Side chain coordinate cloning for the framework residues were done by manipulating the backend NumPy arrays.

# we first mimic a backbone-only structure, by changing all residues to Gly

q=Protein(pwd / "example\_files/5cil\_rfdiffuse\_H3.pdb")

# rs\_missing\_atoms returns all residues where their sidechain atoms are missing

no\_sc=q.rs\_missing\_atoms()

print("All non-Gly residues have missing side-chain atoms:", util.unique(no\_sc.seq()), "\n")

All non-Gly residues have missing side-chain atoms: ['T', 'E', 'R', 'N', 'K', 'Y', 'F', 'P', 'V', 'Q', 'S', 'D', 'W', 'A', 'I', 'M', 'L', 'C']

seq\_MPNN={  
'A':'EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV', 'B':'NWFDITNWLWYIK', 'C':'VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCARhlvrtvgsgsnpemgdvvWGQGTLVTVSS'}

# we thread seq\_MPNN onto RFDiffusion output structure q

# output a new PDB file: test.pdb

# copy sidechains of framework residues from template fn

# map the A/B/C chain names in the RFDiffusion structure to the L/P/H chains in the template fn

# seq2bfactor=True means we assign b-factor of value 0.5 for lower-cased seq\_MPNN residues (those are CDR H3 residues redesigned)

# framework residues (upper case) have b-factor of value 1.0.

q.thread\_sequence(seq\_MPNN, 'test.pdb', seq2bfactor=True, side\_chain\_pdb=fn, chain\_map={"H":"C", "L":"A", "P":"B"})

###JSON STARTS

{"output\_pdb": "test.pdb", "ok": true, "output\_equal\_target": true, "input": {"A": "EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV", "B": "NWFDITNWLWYIK", "C": "VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCARGGGGGGGGGGGGGGGGGGWGQGTLVTVSS"}, "output": {"A": "EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV", "B": "NWFDITNWLWYIK", "C": "VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCARHLVRTVGSGSNPEMGDVVWGQGTLVTVSS"}, "target": {"A": "EIVLTQSPGTQSLSPGERATLSCRASQSVGNNKLAWYQQRPGQAPRLLIYGASSRPSGVADRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGQSLSTFGQGTKVEVKRTV", "B": "NWFDITNWLWYIK", "C": "VQLVQSGAEVKRPGSSVTVSCKASGGSFSTYALSWVRQAPGRGLEWMGGVIPLLTITNYAPRFQGRITITADRSTSTAYLELNSLRPEDTAVYYCARhlvrtvgsgsnpemgdvvWGQGTLVTVSS"}, "relax": false, "residues\_with\_missing\_atom": "", "mutations": [["C", 98, "GLY", "HIS"], ["C", 99, "GLY", "LEU"], ["C", 100, "GLY", "VAL"], ["C", 101, "GLY", "ARG"], ["C", 102, "GLY", "THR"], ["C", 103, "GLY", "VAL"], ["C", 105, "GLY", "SER"], ["C", 107, "GLY", "SER"], ["C", 108, "GLY", "ASN"], ["C", 109, "GLY", "PRO"], ["C", 110, "GLY", "GLU"], ["C", 111, "GLY", "MET"], ["C", 113, "GLY", "ASP"], ["C", 114, "GLY", "VAL"], ["C", 115, "GLY", "VAL"]]}

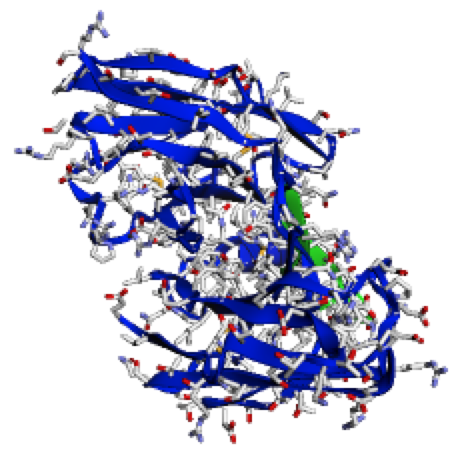
###JSON END

q=Protein("test.pdb")

print("\nResidues with missing atoms:", q.rs\_missing\_atoms(), "\n")

Residues with missing atoms:

q.show(color="b", show\_sidechains=True)



In the RFDiffusion output file 5cil\_rfdiffuse\_H3.pdb, all 250 residues have missing atoms due to their missing side chains. After threading using the wild-type PDB 5cil.pdb as the template, we copy the side chain coordinates for all upper-case residues except the lower-case residues in the H3 CDR loop. The side chain atoms for the H3 loop are generated by PyMOL by replacing Glycine with corresponding ProteinMPNN-generated residues. At the end, the final output test.pdb contains all atoms, therefore, no residue has missing atoms. The framework residues are colored in blue and the redesigned CDR H3 loop is colored in green.

## Binding Score for EvoPro

EvoPro is a de novo protein design framework that iteratively evolutes protein binder sequences (<https://doi.org/10.1073/pnas.2307371120>). EvoPro starts from a pool of binder sequences; it uses AlphaFold to predict complex structures and then ranks the candidates by their EvoPro scores. A new canidate pool is generated with genetic algorithm based on a few top-scoring sequences. This process iterates until sequences of good scores are found.

We here demonstrate how EvoPro score, as described in the publication can be implemented straightforwardly with Afpdb. The score is the sum of three scores. The first is the placement confidence score that is the total number of interface residue pairs, weighted by AlphaFold PAE scores. The second is the fold confidence score based on AlphaFold's pLDDT scores. The third is the conformal stability score based on the RMSD between the binder structures as a monomer and as the binder of the complex.

The implementation is shown below:

# We score 5cli

# Ab-Ag predicted complex structure

p\_complex = Protein(pwd / "example\_files/5cil\_AF.pdb")

p\_complex.rename\_chains({"A":"L", "B":"H", "C":"P"})

# load the PAE score generated by AF, PAE is the pairwise uncertainty in inter-residue distance

import json

pae = np.array(json.loads(util.read\_string(pwd / "example\_files/5cil\_AF.json"))['pae'])

# AF uses b-factors to store pLDDT

plddt=p\_complex.b\_factors()

# Antibody predicted as a monomer

p\_ab = Protein(pwd / "example\_files/5cil\_ab\_AF.pdb")

p\_ab.rename\_chains({"A":"L", "B":"H"})

# Compute placement confidence

# identify all contact residue pairs

rs\_ab, rs\_ag, dist = p\_complex.rs\_around("P", rs\_within="H:L", dist=4)

# extract PAE for contact residue pairs

# each row in dist DataFrame is one residue pair, they are weighted by PAE

# if PAE is small, we are more confident that the contact pair is real

pae\_xy=pae[dist.resi\_a.values, dist.resi\_b.values]

pae\_yx=pae[dist.resi\_b.values, dist.resi\_a.values]

# add negative, b/c the lower the score, the better

placement\_score = -np.sum(((35-pae\_xy) + (35-pae\_yx))/70)

# Compute fold confidence

# pLDDT score is [0-100], scale it by ten

fold\_score = -np.mean(plddt)/10

# Compute conformational stability score

# The argument is if the binder does not change its conformation after binding,

# it is more likely to bind

stability\_score = p\_ab.rmsd(p\_complex, "H:L", "H:L", align=True)\*5

# the lower the better

overall\_fitness = placement\_score + fold\_score + stability\_score

print(f"Fitness: {overall\_fitness:.2f}")

print(f"Placement: {placement\_score:.2f}")

print(f"Fold: {fold\_score:.2f}")

print(f"Stability: {stability\_score:.2f}")

Fitness: -39.96

Placement: -31.51

Fold: -9.73

Stability: 1.28

# Developer's Note

## Installation

TODO: When the package is considered stable, we need to publish afpdb into pypi, it then simply "pip install afpdb".

The instructions below are for users who would like to install **Afpdb** locally and for developers.

Python

If you do not have Python installed, follow the instructions on <https://docs.anaconda.com/free/miniconda/> to install the latest miniconda. Type command python should launch the Python programming shell, if it is installed successfully.

Install Afpdb

pip install git+https://github.com/data2code/afpdb.git

Jupyter Notebook (optional)

To view and run this tutorial, Jupyter should be installed:

pip install notebook

Type command jupyter notebook to launch the Jupyter Notebook, if it is installed successfully.

This is no longer needed. However, if the embedded protein structures do not display in Jupyter after rerun the cell, install the required plugin:

jupyter labextension install jupyterlab\_3dmol

PyMOL (optional)

PyMOL is the preferred application for visualizing protein structures. It is required by examples using thread\_sequence() or PyMOL(). To install the open source PyMOL:

conda install conda-forge::pymol-open-source

In Colab, we also need to run:

conda install conda-forge::openssl=3.2.0

DSSP (optional)

Required for the secondary structure assignment with method dssp().

conda install sbl::dssp

There are multiple options, sbl::dssp suits Apple Silicon.

matplotlib (optional)

Required for the Ramachandra plot example

pip install matplotlib

Install pytest as a developer:

pip install pytest

Type command pytest within the root folder of the Afpdb package, you will run all test examples in tests\test\_all.py.

For developers, after we fixed the bugs and passed pytest, we run pip install . to update the package under the conda installation.

## Selection

When creating a method that takes a selection argument named 'rs', the first step is to convert it into an internal selection object using: rs = self.rs(rs), this will convert the argument into a RS object, which has its data member storing the residue indices. Similarly, if we have an atom selection argument named 'ats', do ats=self.ats(ats). Similarly, if we take a residue list object, we do rl=self.rl(rl). When we use a residue/atom selection to index atom\_positions or atom\_mask, check if the selection is empty/full with ats.is\_empty() and ats.is\_full(). Empty selection often implies an error on the users' side, a full selection means you can skip the indexing, as the original array is already good.

Please use extract() as an example to see how we support selection arguments.

## Change in residue/chain

The Protein class contains a data structure called res\_map, which is a dictionary that maps a full residue name "{chain}{residue\_id}{code}" into its internal ndarray index. A few methods rely on this mapping. Therefore, whenever a method renames a chain, changes chain orders, mutates a residue, or changes the full residue name and its internal index, self.\_make\_res\_map() should be called at the end. This is also needed in extract() as the underlying arrays have been changed.

## Residue Identifier

When outputting a dataframe containing a residue, our recommendation is to provide all residue ID formats. This includes chain, resn, resn\_i, resi. Please use rs\_dist as an example. We often use the resi column to create a Residue List object, then use its name, namei, chain, aa methods to add additional residue annotation data. See the example under rs\_dist().

## inplace

To support inplace, the idiom is to use: obj = self if inplace else self.clone(), then use obj to manipulate the structure. Please set inplace=False as the default, so that users do not have to memorize what the default is.

## Extract Atom Coordinates

p.data.atom\_positions contains non-existent atoms. It is often faster to compute distances between two residue sets, if we only keep the coordinates for real atoms. This is done with \_get\_xyz() method, which returns three variables: (residue\_indices, atom\_indices, XYZ\_array).

In [2]:

p=Protein(fk)

rs\_i, atom\_i, xyz=p.\_get\_xyz(p.rs("H"), p.ats("N,CA"))

print("Residue ID:", rs\_i, p.rl(rs\_i).name(), "\n")

print("Atom ID:", atom\_i, [str(p.ats(x)) for x in atom\_i], "\n")

print("XYZ:", xyz)

Residue ID: [4 4 5 5] ['3', '3', '4', '4']

Atom ID: [0 1 0 1] ['N', 'CA', 'N', 'CA']

XYZ: [[ 27.36800003 6.44000006 -19.10700035]

[ 25.96999931 6.87099981 -19.03800011]

[ 25.29100037 9.00800037 -18.09000015]

[ 25.11199951 9.9829998 -16.98600006]]

Note: To extract a rectangular subarray of rows and columns, we need to use np.ix\_.

p=Protein(fk)

# the followin is an error, as the row indice have two residues, column indices have 4 atoms

# NumPy tries to pair the indices

try:

p.data.atom\_mask[np.array([2,3]), ATS("N,CA,C,O,CB,CG").data]

except Exception as e:

print(e)

shape mismatch: indexing arrays could not be broadcast together with shapes (2,) (6,)

# The correct way is to generate a mesh indices

print("\n")

x=p.data.atom\_mask[np.ix\_(np.array([2,3]), ATS("N,CA,C,O,CB,CG").data)]

print(x.shape, "\na", x, "\n")

(2, 6)

a [[1. 1. 1. 1. 1. 0.]

[1. 1. 1. 1. 1. 1.]]

# or

print(p.data.atom\_mask[np.array([2,3])][:, ATS("N,CA,C,O,CB,CG").data])

[[1. 1. 1. 1. 1. 0.]

[1. 1. 1. 1. 1. 1.]]

## Extract Atom Pair Coordinates

For align and rmsd, we need to extract atom coordinates in pairs, we can use \_get\_xyz\_pair.

Note: If two residues have different types (their side chain atoms are different), only the common atoms are included.

p=Protein(fk)

# move X by 1, Y/Z remains the same

q=p.translate(np.array([1,0,-1]), inplace=False)

rs\_i, atom\_i, rs\_j, atom\_j, xyz\_i, xyz\_j=p.\_get\_xyz\_pair(q, p.rs("H"), q.rs("H"), ATS("N,CA"))

print("Protein i\n")

print("Residue ID:", rs\_i, p.rl(rs\_i).name(), "\n")

print("Atom ID:", atom\_i, [str(p.ats(x)) for x in atom\_i], "\n")

print("XYZ:", xyz\_i)

Protein i

Residue ID: [4 4 5 5] ['3', '3', '4', '4']

Atom ID: [0 1 0 1] ['N', 'CA', 'N', 'CA']

XYZ: [[ 27.36800003 6.44000006 -19.10700035]

[ 25.96999931 6.87099981 -19.03800011]

[ 25.29100037 9.00800037 -18.09000015]

[ 25.11199951 9.9829998 -16.98600006]]

print("\n\n")

print("Protein j\n")

print("Residue ID:", rs\_j, p.rl(rs\_j).name(), "\n")

print("Atom ID:", atom\_j, [str(p.ats(x)) for x in atom\_j], "\n")

print("XYZ:", xyz\_j)

Protein j

Residue ID: [4 4 5 5] ['3', '3', '4', '4']

Atom ID: [0 1 0 1] ['N', 'CA', 'N', 'CA']

XYZ: [[ 28.36800003 6.44000006 -20.10700035]

[ 26.96999931 6.87099981 -20.03800011]

[ 26.29100037 9.00800037 -19.09000015]

[ 26.11199951 9.9829998 -17.98600006]]

## Caution

When we add a new method, please keep in mind that the residue index may not start from 1, a residue index may contain insertion code, there can be gaps in the residue index (missing residues), the integer part of the residue index may not be unique within a chain (e.g. 6A and 6B). You should use the file "fk" to test your method. Please also add a corresponding test method into tests/test\_all.py.