a6

February 19, 2025

1 Assignment 6

1.1 Steve Cheney

1.1.1 RBIF110

[ ]:
```
import os
#os.rename("pymol-edu-license.lic", "license.lic")
```

[ ]:
```
!curl -L -o smina.static https://sourceforge.net/projects/smina/files/smina.
↪static/download
```

```
  % Total    % Received % Xferd  Average Speed   Time    Time     Time  Current
                                 Dload  Upload   Total   Spent    Left  Speed

  0     0    0     0    0     0      0      0 --:--:-- --:--:-- --:--:--     0
100   585  100   585    0     0   2253      0 --:--:-- --:--:-- --:--:--  2276

100   327  100   327    0     0    673      0 --:--:-- --:--:-- --:--:--   673
100   327  100   327    0     0    673      0 --:--:-- --:--:-- --:--:--     0

100 9622k  100 9622k    0     0  7275k      0  0:00:01  0:00:01 --:--:-- 7275k
```

[ ]:
```
!python --version

!mamba --version
```

```
Python 3.11.11

2.0.5
```

[ ]:
```
import subprocess
import sys
import shutil
import tqdm.notebook as tqdm

# Define function to install packages
def install_package(command, progress, step):
    try:
        subprocess.run(command, shell=True, check=True)
```

```
        progress.update(step)
    except subprocess.CalledProcessError as e:
        print(f"Error installing {command}: {e}")

# Initialize progress bar
total_steps = 100
with tqdm.tqdm(total=total_steps) as pbar:

    # Ensure conda is available
    if not shutil.which("mamba"):
        print("Mamba is not installed. Please install it first.")

    install_package("conda install -c conda-forge libnetcdf -y", pbar, 10)

    # Install PyMOL
    install_package("mamba install -c schrodinger pymol-bundle --yes", pbar, 10)

    install_package("conda install -c conda-forge gemmi -y", pbar, 10)

    # Install mols2grid
    install_package("mamba install -c conda-forge mols2grid --yes", pbar, 20)

    # Install RDKit
    install_package("mamba install -c conda-forge rdkit --yes", pbar, 20)

    # Install py3Dmol
    install_package("mamba install -c conda-forge py3Dmol --yes", pbar, 30)

print("All packages installed successfully.")
```

```
  0%|          | 0/100 [00:00<?, ?it/s]
All packages installed successfully.
```

[ ]:
```
#import some cheminformatics packages and data processing packages
import rdkit
from rdkit import Chem

import py3Dmol
import mols2grid

import numpy as np
import pandas as pd

import shutil
import os

# Define paths
```

```
license_src = os.path.abspath("license.lic")  # Path to your existing license file
pymol_license_dir = os.path.expanduser("~/.pymol")  # Default PyMOL license directory

# Ensure the directory exists
os.makedirs(pymol_license_dir, exist_ok=True)

# Copy license file to the expected location
shutil.copy(license_src, os.path.join(pymol_license_dir, "pymol.lic"))

os.environ["PYMOL_LICENSE_FILE"] = os.path.join(pymol_license_dir, "pymol.lic")
```

[ ]:
```
import os
import gemmi
import pandas as pd

# Directory containing .cif files
cif_dir = "./a6_files"

# List to store extracted data
summary_data = []

# Process each .cif file
for cif_file in os.listdir(cif_dir):
    if cif_file.endswith(".cif"):
        file_path = os.path.join(cif_dir, cif_file)

        # Read CIF file using gemmi
        cif_doc = gemmi.cif.read(file_path)  # Read mmCIF file
        block = cif_doc.sole_block()  # Get the first block

        # Extract PDB ID (cleaned)
        pdb_id = cif_file.replace(".cif", "").replace("_updated", "")

        # Extract resolution safely
        resolution = None
        res_value = block.find_value('_refine.ls_d_res_high')
        if res_value and res_value.replace('.', '', 1).isdigit():  # Check if res_value is not None and numeric
            resolution = float(res_value)

        # Extract ligand information
        ligands = set()
        structure = gemmi.make_structure_from_block(block)  # Convert to gemmi Structure
```

```
        for model in structure:
            for chain in model:
                for res in chain:
                    if res.subchain:  # Ligands typically have a non-empty␣
 ↪subchain
                        ligands.add(res.name)

        # Only add structures that have at least one ligand
        if ligands:
            summary_data.append({
                "PDB_ID": pdb_id,
                "Resolution (Å)": resolution,
                "Ligands": ", ".join(ligands)
            })

# Convert to DataFrame
df = pd.DataFrame(summary_data)

# Sort by resolution (lower = better), ignoring NaN values
df_sorted = df.sort_values(by="Resolution (Å)", ascending=True,␣
 ↪na_position='last')

# Display the filtered DataFrame (top 10 results)
print(df_sorted.head(10).to_string(index=False))  # Prints formatted table
```

```
PDB_ID  Resolution (Å)
Ligands
  7mzy           1.500      SER, GLY, ALA, PHE, ACT, ILE, HOH, GLN, TRP, TYR,
ASN, VAL, CYS, ASP, LYS, ARG, PRO, THR, GLU, HIS, MET, LEU
  4z55           1.550 SER, GLY, ALA, PHE, ILE, 4LO, HOH, GLN, TRP, TYR, ASN,
VAL, CYS, ASP, LYS, ARG, GOL, PRO, THR, GLU, HIS, MET, LEU
  9gbe           1.580    SER, GLY, ALA, PHE, ILE, HOH, GLN, TRP, TYR, A1IJ8,
ASN, VAL, CYS, ASP, LYS, ARG, PRO, THR, GLU, HIS, MET, LEU
  5a9u           1.600      SER, GLY, ALA, PHE, ILE, HOH, GLN, TRP, TYR, ASN,
VAL, CYS, ASP, LYS, ARG, PRO, THR, 5P8, GLU, HIS, MET, LEU
  8arj           1.645      SER, GLY, ALA, NRR, PHE, ILE, HOH, GLN, TRP, TYR,
ASN, VAL, CYS, ASP, LYS, ARG, PRO, THR, GLU, HIS, MET, LEU
  4clj           1.660      SER, GLY, ALA, PHE, ILE, HOH, GLN, TRP, TYR, ASN,
VAL, CYS, ASP, LYS, ARG, PRO, THR, 5P8, GLU, HIS, MET, LEU
  2yfx           1.700      SER, GLY, ALA, VGH, PHE, ILE, HOH, GLN, TRP, TYR,
ASN, VAL, CYS, ASP, LYS, ARG, PRO, THR, GLU, HIS, MET, LEU
  5aac           1.700      SER, GLY, ALA, VGH, PHE, ILE, HOH, GLN, TRP, TYR,
ASN, VAL, CYS, ASP, LYS, ARG, PRO, THR, GLU, HIS, MET, LEU
  4foc           1.700      SER, GLY, ALA, PHE, ILE, HOH, OUU, GLN, TRP, TYR,
ASN, VAL, CYS, ASP, LYS, ARG, PRO, THR, GLU, HIS, MET, LEU
  5ftq           1.700 SER, GLY, ALA, PHE, ILE, HOH, U4W, GLN, TRP, TYR, ASN,
VAL, CYS, ASP, LYS, ARG, GOL, PRO, THR, GLU, HIS, MET, LEU
```

[ ]:
```
# Define the CIF file path
cif_file = "./a6_files/4z55_updated.cif"

# Read the CIF file
cif_doc = gemmi.cif.read(cif_file)
block = cif_doc.sole_block()

# Extract PDB ID
pdb_id = "4Z55"

# Extract resolution
resolution = None
res_value = block.find_value('_refine.ls_d_res_high')
if res_value and res_value.replace('.', '', 1).isdigit():
    resolution = float(res_value)

# Extract protein and ligand details
structure = gemmi.make_structure_from_block(block)

ligands = set()
chains = set()

for model in structure:
    for chain in model:
        chains.add(chain.name)  # Collect chain names
        for res in chain:
            if res.subchain:  # Ligands typically have a non-empty subchain
                ligands.add(res.name)

# Generate a structured report
report = f"""
# Structural Report: {pdb_id}

## General Information:
- **PDB ID:** {pdb_id}
- **Resolution:** {resolution} Å
- **Number of Chains:** {len(chains)}
- **Chains Present:** {', '.join(sorted(chains))}

## Ligand Information:
- **Bound Ligands:** {', '.join(ligands) if ligands else "None"}

## Summary:
PDB structure {pdb_id} has a resolution of {resolution} Å and contains␣
 ↪{len(chains)} chains.
The structure includes the following bound ligands: {', '.join(ligands) if␣
 ↪ligands else "None"}.
```

```
This makes it a suitable candidate for further **virtual screening**.

"""

# Save the report to a text file
output_report = "./4z55_report.txt"
with open(output_report, "w") as f:
    f.write(report)

# Print confirmation
print(f"Report generated: {output_report}")
```

```
Report generated: ./4z55_report.txt
```

2 Structural Report: 4Z55

2.1 General Information:

- **PDB ID:** 4Z55
- **Resolution:** 1.55 Å
- **Number of Chains:** 1
- **Chains Present:** A

2.2 Ligand Information:

- **Bound Ligands:** LEU, ILE, THR, TYR, PRO, GLN, HIS, PHE, GLY, ARG, 4LO, HOH, VAL, SER, TRP, ALA, ASP, ASN, CYS, MET, GOL, LYS, GLU

2.3 Summary:

PDB structure 4Z55 has a resolution of 1.55 Å and contains 1 chains. The structure includes the following bound ligands: LEU, ILE, THR, TYR, PRO, GLN, HIS, PHE, GLY, ARG, 4LO, HOH, VAL, SER, TRP, ALA, ASP, ASN, CYS, MET, GOL, LYS, GLU. This makes it a suitable candidate for further **virtual screening**.

[ ]:
```
#Test to make sure pymol is working lets download melatonin receptor and display
from pymol import cmd
from IPython.display import Image
cmd.reinitialize()
cmd.fetch("4Z55")
cmd.orient("4Z55")
cmd.rotate("z","270")
cmd.png("4Z55.png") #In order to display in our python notebook we need to make␣
 ↪a temp image called image.png
Image(filename = "4Z55.png", unconfined=True)
```

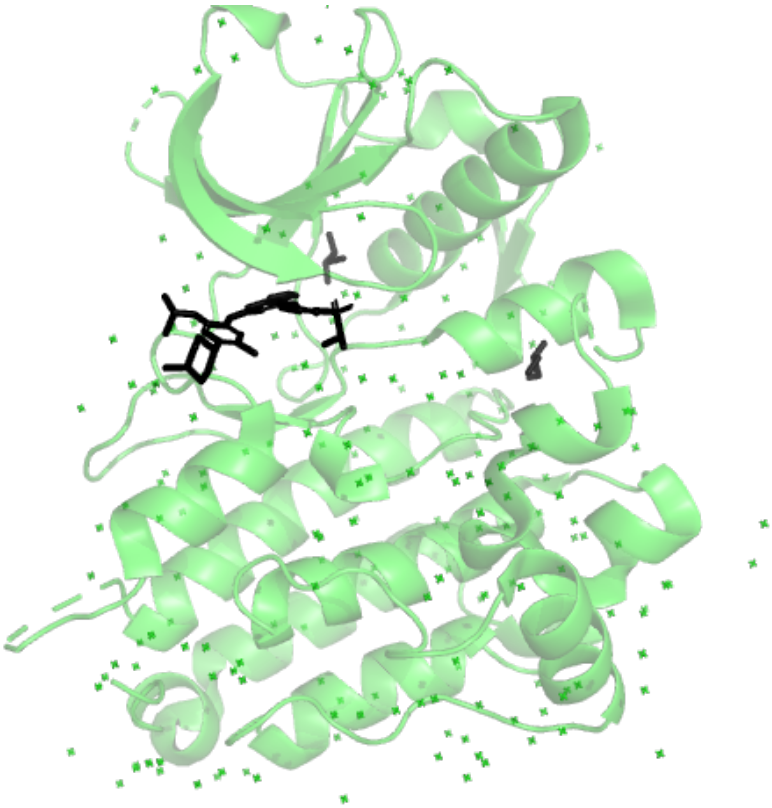
[ ]:

[ ]:
```
#There are likely multiple chains here, so we need to check that (CBC = Color␣
 ↪By Chain)
cmd.util.cbc()
cmd.png("4Z55.png")
Image(filename = "4Z55.png", unconfined=True)
```

[ ]:

[ ]:
```
cmd.color("black","organic")
cmd.set("cartoon_transparency",0.5)
cmd.png("4Z55.png")
Image(filename = "4Z55.png", unconfined=True)
```

[ ]:



Observation: By coloring the organic structures black, and reducing the cartoon transparency, we can see that there are two replicate chains in the crystal structure, but we will only need one for the docking experiment.

[ ]:
```
import gemmi

# Load the CIF file
cif_file = "./a6_files/4z55_updated.cif"
cif_doc = gemmi.cif.read(cif_file)
block = cif_doc.sole_block()

# Extract structure
structure = gemmi.make_structure_from_block(block)

# Define ligand interaction distance cutoff (e.g., 5.0Å)
interaction_distance = 5.0

# Define the target ligand ("4LO") from RCSB: https://www.rcsb.org/structure/
↪4z55
ligand_name = "4LO"
```

```
# Define the target protein chain (A)
target_chain = "A"

# List of standard amino acids
standard_amino_acids = {
    "ALA", "ARG", "ASN", "ASP", "CYS", "GLN", "GLU", "GLY",
    "HIS", "ILE", "LEU", "LYS", "MET", "PHE", "PRO", "SER",
    "THR", "TRP", "TYR", "VAL"
}

# Step 1: Identify 4LO ligand atoms
ligand_atoms = []
for model in structure:
    for chain in model:
        for res in chain:
            if res.name == ligand_name:  # Look for 4LO
                for atom in res:
                    ligand_atoms.append(atom.pos)  # Store 4LO atom positions

# Step 2: Find only **unique** protein residues near 4LO
binding_residues = set()  # Use a **set** to avoid duplicates

for model in structure:
    for chain in model:
        if chain.name == target_chain:  # Only process Chain A
            for res in chain:
                if res.seqid.num:  # Ensure residue has a valid ID
                    if res.name in standard_amino_acids:  # Ensure it's a␣
 ↪protein residue
                        # Check if **any** atom in this residue is within the␣
 ↪threshold distance of 4LO
                        for atom in res:
                            if any(atom.pos.dist(lig_atom) <=␣
 ↪interaction_distance for lig_atom in ligand_atoms):
                                binding_residues.add((res.name, res.seqid.num,␣
 ↪chain.name))  # Store unique residues
                                break  # Avoid duplicates

# Step 3: Print the refined 4LO-binding residues
if binding_residues:
    print(f" {len(binding_residues)} Unique Protein Residues Interacting with␣
 ↪4LO in Chain {target_chain} ( {interaction_distance}Å):")
    for res in sorted(binding_residues, key=lambda x: x[1])[:50]:  # Print␣
 ↪first 50 for readability
        print(f"- **Residue:** {res[0]} (ID: {res[1]}), Chain: {res[2]}")
else:
```

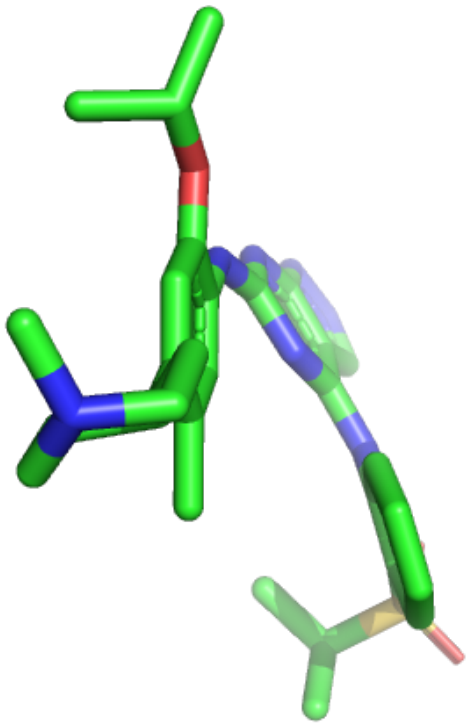
```
    print(f"  No protein residues found within {interaction_distance}Å of 4LO.")
```

```
 25 Unique Protein Residues Interacting with 4LO in Chain A ( 5.0Å):
- **Residue:** LEU (ID: 1122), Chain: A
- **Residue:** GLY (ID: 1123), Chain: A
- **Residue:** HIS (ID: 1124), Chain: A
- **Residue:** GLY (ID: 1125), Chain: A
- **Residue:** ALA (ID: 1126), Chain: A
- **Residue:** VAL (ID: 1130), Chain: A
- **Residue:** GLU (ID: 1132), Chain: A
- **Residue:** ALA (ID: 1148), Chain: A
- **Residue:** LYS (ID: 1150), Chain: A
- **Residue:** VAL (ID: 1180), Chain: A
- **Residue:** LEU (ID: 1196), Chain: A
- **Residue:** GLU (ID: 1197), Chain: A
- **Residue:** LEU (ID: 1198), Chain: A
- **Residue:** MET (ID: 1199), Chain: A
- **Residue:** ALA (ID: 1200), Chain: A
- **Residue:** GLY (ID: 1201), Chain: A
- **Residue:** GLY (ID: 1202), Chain: A
- **Residue:** ASP (ID: 1203), Chain: A
- **Residue:** SER (ID: 1206), Chain: A
- **Residue:** GLU (ID: 1210), Chain: A
- **Residue:** ARG (ID: 1253), Chain: A
- **Residue:** ASN (ID: 1254), Chain: A
- **Residue:** LEU (ID: 1256), Chain: A
- **Residue:** GLY (ID: 1269), Chain: A
- **Residue:** ASP (ID: 1270), Chain: A
```

[ ]:
```
#Now we need to split the above into a ligand and a receptor file
cmd.select("4Z55-ligand", "resn 4LO") #Create a selection called 4Z55-ligand␣
 ↪from the ligand
cmd.select("4Z55-receptor", "4Z55 and not 4Z55-ligand")  #Select all that is␣
 ↪not the ligand, and make that the protein
cmd.save("4Z55-ligand.pdb", "4Z55-ligand")
cmd.save("4Z55-receptor.pdb", "4Z55-receptor")
```

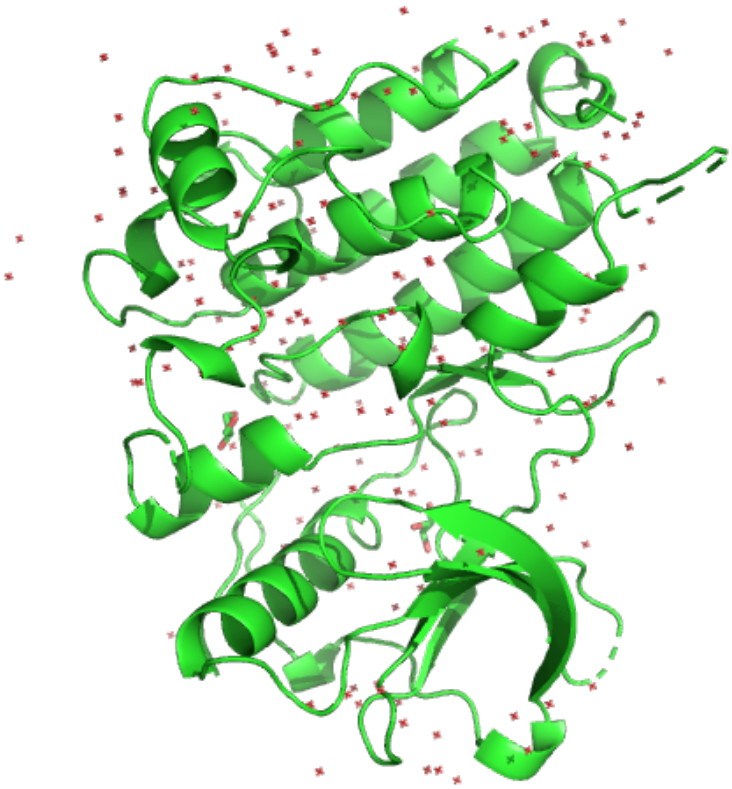
[ ]:
```
#Now lets look at the individual files -first the ligand
cmd.reinitialize() #Wipe the pymol memory and create an empty workspace
cmd.load("4Z55-ligand.pdb")
cmd.png("ligand.png")
Image(filename = "ligand.png", unconfined=True)
```

[ ]:



[ ]:
```
#Now the receptor
cmd.reinitialize() #Wipe the pymol memory and create an empty workspace
cmd.load("4Z55-receptor.pdb")
cmd.orient("4Z55-receptor")
cmd.rotate("z","270")
cmd.png("receptor.png")
Image(filename = "receptor.png", unconfined=True)
```

[ ]:



[ ]:
```
#Lets look at the smina program - you can get a list of possible commands and␣
↪switches by just running the program with no arguments
!wsl ./smina.static
```

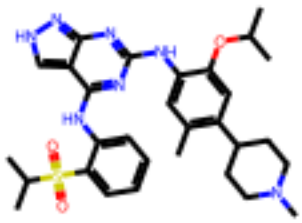
```
Missing receptor.

Correct usage:

Input:
  -r [ --receptor ] arg         rigid part of the receptor (PDBQT)
  --flex arg                    flexible side chains, if any (PDBQT)
  -l [ --ligand ] arg           ligand(s)
  --flexres arg                 flexible side chains specified by comma
                                separated list of chain:resid or
                                chain:resid:icode
  --flexdist_ligand arg         Ligand to use for flexdist
  --flexdist arg                set all side chains within specified distance
                                to flexdist_ligand to flexible

Search space (required):
  --center_x arg                X coordinate of the center
```

```
  --center_y arg                Y coordinate of the center
  --center_z arg                Z coordinate of the center
  --size_x arg                  size in the X dimension (Angstroms)
  --size_y arg                  size in the Y dimension (Angstroms)
  --size_z arg                  size in the Z dimension (Angstroms)
  --autobox_ligand arg          Ligand to use for autobox
  --autobox_add arg             Amount of buffer space to add to auto-generated
                                box (default +4 on all six sides)
  --no_lig                      no ligand; for sampling/minimizing flexible
                                residues

Scoring and minimization options:
  --scoring arg                 specify alternative builtin scoring function
  --custom_scoring arg          custom scoring function file
  --custom_atoms arg            custom atom type parameters file
  --score_only                  score provided ligand pose
  --local_only                  local search only using autobox (you probably
                                want to use --minimize)
  --minimize                    energy minimization
  --randomize_only              generate random poses, attempting to avoid
                                clashes
  --minimize_iters arg (=0)     number iterations of steepest descent; default
                                scales with rotors and usually isn't sufficient
                                for convergence
  --accurate_line               use accurate line search
  --minimize_early_term         Stop minimization before convergence conditions
                                are fully met.
  --approximation arg           approximation (linear, spline, or exact) to use
  --factor arg                  approximation factor: higher results in a
                                finer-grained approximation
  --force_cap arg               max allowed force; lower values more gently
                                minimize clashing structures
  --user_grid arg               Autodock map file for user grid data based
                                calculations
  --user_grid_lambda arg (=-1)  Scales user_grid and functional scoring
  --print_terms                 Print all available terms with default
                                parameterizations
  --print_atom_types            Print all available atom types

Output (optional):
  -o [ --out ] arg              output file name, format taken from file
                                extension
  --out_flex arg                output file for flexible receptor residues
  --log arg                     optionally, write log file
  --atom_terms arg              optionally write per-atom interaction term
                                values
  --atom_term_data              embedded per-atom interaction terms in output
                                sd data
```

```
Misc (optional):
  --cpu arg                     the number of CPUs to use (the default is to
                                try to detect the number of CPUs or, failing
                                that, use 1)
  --seed arg                    explicit random seed
  --exhaustiveness arg (=8)     exhaustiveness of the global search (roughly
                                proportional to time)
  --num_modes arg (=9)          maximum number of binding modes to generate
  --energy_range arg (=3)       maximum energy difference between the best
                                binding mode and the worst one displayed
                                (kcal/mol)
  --min_rmsd_filter arg (=1)    rmsd value used to filter final poses to remove
                                redundancy
  -q [ --quiet ]                Suppress output messages
  --addH arg                    automatically add hydrogens in ligands (on by
                                default)

Configuration file (optional):
  --config arg                  the above options can be put here

Information (optional):
  --help                        display usage summary
  --help_hidden                 display usage summary with hidden options
  --version                     display program version
```

[ ]:
```
#So now we need to make a new file, that has a "pure" unbiased version of the ligand - so lets create it directly from SMILES
#We can get the ligand information here: https://www.rcsb.org/ligand/4LO
# CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[S](=O)(=O)C(C)C)c5c[nH]nc5n3
from rdkit import Chem
from rdkit.Chem import Draw

size = (120, 120)

lig = Chem.MolFromSmiles("CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[S](=O)(=O)C(C)C)c5c[nH]nc5n3")
img = Draw.MolToImage(lig, size=size)
img
```

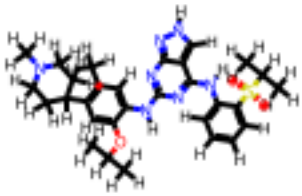
[ ]:



This is a 2D structure without 3D coordinates. SMINA needs a 3D structure - we can only get that by minimizing to the nearest energy minima. Thankfully RDKit has a minimizer

[ ]:
```
lig = Chem.AddHs(lig, addCoords=True) #We need to add hydrogens to the new
 ↪ligand
Draw.MolToImage(lig, size=size)
```

[ ]:



[ ]:
```
#Now to minimize to a 3D structure using the AllChem Module
import py3Dmol
from rdkit.Chem import AllChem
AllChem.EmbedMolecule(lig)
AllChem.MMFFOptimizeMolecule(lig)


#Display the result using py3Dmol
mblock = Chem.MolToMolBlock(lig)

view = py3Dmol.view(data=mblock, style={"stick": {}, "sphere": {"scale": 0.3}})
view.zoomTo()
```

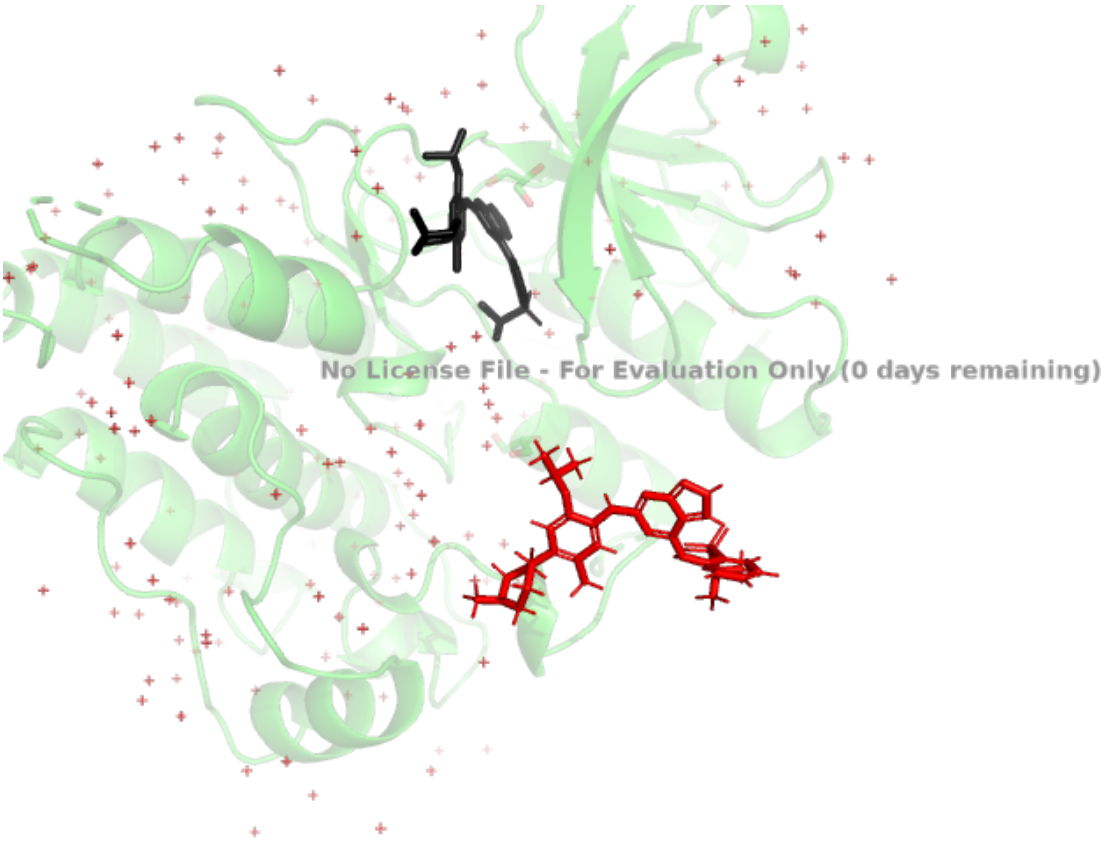
[ ]:
```
<py3Dmol.view at 0x233151143d0>
```

[ ]:
```
#Allright now we have the molecule converted to 3D - sae it as a new sdf
file = Chem.SDWriter('newligand_1.sdf') #create the file
file.write(lig) #write the 3d ligand to the file
```

[ ]:
```
#Lets check the new ligand - so the new ligand should be assigned random␣
 ↪coordinates in space. If we load this new one into our previous PDB file, we␣
 ↪will see it's somewhere random
cmd.reinitialize() #Wipe the pymol memory and create an empty workspace
cmd.load("4Z55-receptor.pdb")
cmd.load("4Z55-ligand.pdb")
cmd.color("black","4Z55-ligand")
cmd.load("newligand_1.sdf")

print(cmd.get_object_list())



cmd.color("red","newligand")
cmd.set("cartoon_transparency",0.6)
cmd.select("ligands", "organic")
cmd.zoom("ligands")
#cmd.rotate("z","270")
cmd.png("receptor.png")
Image(filename = "receptor.png", unconfined=True)
```

```
['4Z55-receptor', '4Z55-ligand', 'newligand_1']
```

[ ]:



Observation We can see the new minimized ligand is not even in the protein - so we need to use smina to "dock" the ligand back into the protein.

[ ]:
```
#OK - so now we have the ligand and receptor in separate files, lets see if␣
 ↪smina can redock the ligand into the receptor
#The autobox command tells smina to focus docking around the cognate ligand and␣
 ↪create a "box"
!wsl ./smina.static -r  4Z55-receptor.pdb -l newligand_1.sdf --autobox_ligand␣
 ↪4Z55-ligand.pdb -o 4Z55-ligand-poses.sdf
```

```
 _______  _______ _________ _        _______
(  ____ \(       )\__   __/( (    /|(  ___  )
| (    \/| () () |   ) (   |  \  ( || (   ) |
| (_____ | || || |   | |   |   \ | || (___) |
(_____  )| |(_)| |   | |   | (\ \) ||  ___  |
      ) || |   | |   | |   | | \   || (   ) |
/\____) || )   ( |___) (___| )  \  || )   ( |
\_______)|/     \|\_______/|/    )_)|/     \|
```

```
smina is based off AutoDock Vina. Please cite appropriately.
```

```
Weights      Terms
-0.035579    gauss(o=0,_w=0.5,_c=8)
-0.005156    gauss(o=3,_w=2,_c=8)
0.840245     repulsion(o=0,_c=8)
-0.035069    hydrophobic(g=0.5,_b=1.5,_c=8)
-0.587439    non_dir_h_bond(g=-0.7,_b=0,_c=8)
1.923        num_tors_div

Using random seed: -595611308

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
1       -10.3      0.000      0.000
2       -9.9       1.390      2.441
3       -9.5       1.990      3.441
4       -9.4       2.282      4.174
5       -9.3       2.402      3.120
6       -9.3       1.243      2.854
7       -9.1       2.763      5.118
8       -8.7       2.858      4.747
9       -8.7       3.817      9.221
Refine time 17.012
Loop time 17.480

==============================
*** Open Babel Warning  in Init
  Unable to open data file 'space-groups.txt'
==============================
*** Open Babel Warning  in Init
  Cannot initialize database 'space-groups.txt' which may cause further errors.
```

[ ]:
```
#Ok lets look at the sdf that was generated
from rdkit.Chem import PandasTools

dockedposes = PandasTools.LoadSDF("4Z55-ligand-poses.sdf")
```

```
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
```

```
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:24:11] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
```

[ ]:
```
dockedposes
```

[ ]:

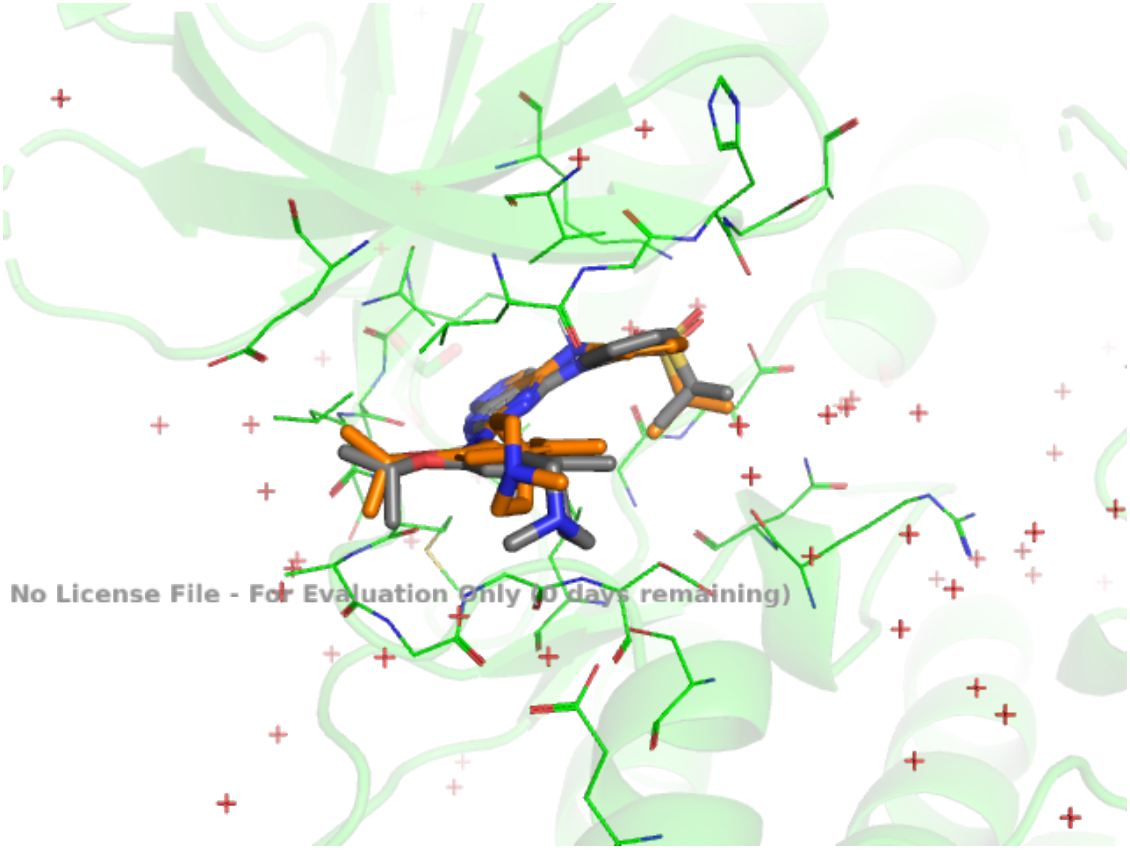
	minimizedAffinity	ID	ROMol
0	-10.31775		<rdkit.Chem.rdchem.Mol object at 0x00000233151…
1	-9.88187		<rdkit.Chem.rdchem.Mol object at 0x00000233151…
2	-9.50745		<rdkit.Chem.rdchem.Mol object at 0x00000233151…
3	-9.37844		<rdkit.Chem.rdchem.Mol object at 0x00000233151…
4	-9.34420		<rdkit.Chem.rdchem.Mol object at 0x00000233151…
5	-9.32954		<rdkit.Chem.rdchem.Mol object at 0x00000233151…
6	-9.12522		<rdkit.Chem.rdchem.Mol object at 0x00000233151…
7	-8.69728		<rdkit.Chem.rdchem.Mol object at 0x00000233151…
8	-8.67304		<rdkit.Chem.rdchem.Mol object at 0x00000233151…

Observation We can see the list of poses, with the lowest energy pose at the top of the list. This lowest energy pose should be closest to the real binding pose of the compound in the receptor. Lets look at it.

[ ]:
```
#Wipe the memory and load into the workspace
cmd.reinitialize()
cmd.load("4Z55-receptor.pdb")
cmd.load("4Z55-ligand.pdb")
cmd.load("4Z55-ligand-poses.sdf")


cmd.color("green","4Z55-receptor") #color the protein cyan
cmd.color("grey", "4Z55-ligand") #Color the original pose grey
cmd.color("orange", "4Z55-ligand-poses")

#We will cerate a selection sphere around the ligand and show the residues
cmd.select("pocketresidues", "byres (all within 5 of 4Z55-ligand)&polymer.
 ↪protein")
cmd.show("line","pocketresidues")
cmd.set("ray_shadow",0)
cmd.set("cartoon_transparency", 0.8)
cmd.util.cnc()
cmd.zoom("pocketres") #zoom in on only the pocket
cmd.rotate("z","90")
```

```
camera = cmd.get_view() #save the camera viewpoint sometimes it can get reset␣
 ↪so we will enforce the same

#display the best pose
camera = cmd.get_view()
cmd.png("pose.png")
Image(filename = "pose.png", unconfined=True)
```

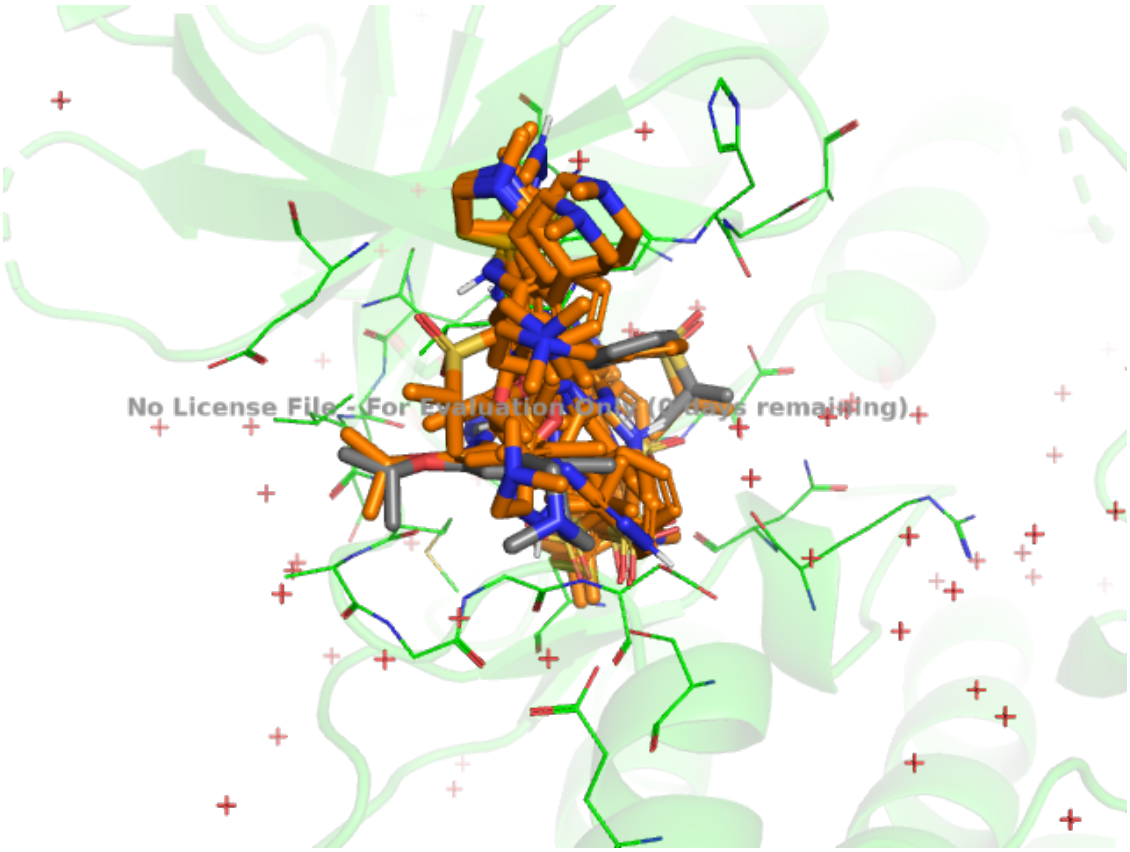
[ ]:



Observation: We can see that the best smina docked pose is reasonably close to the original crystallographic pose. But lets look at all the poses and some higher energy poses.

[ ]:
```
#show all the poses
cmd.set("all_states", 1)
cmd.set_view(camera)
cmd.png("pose.png")
Image(filename = "pose.png", unconfined=True)
```

[ ]:



[ ]:
```
#we can also get individual poses by splitting the poses into individual
cmd.set("all_states",0)
cmd.split_states("4Z55-ligand-poses")
cmd.get_names()
```

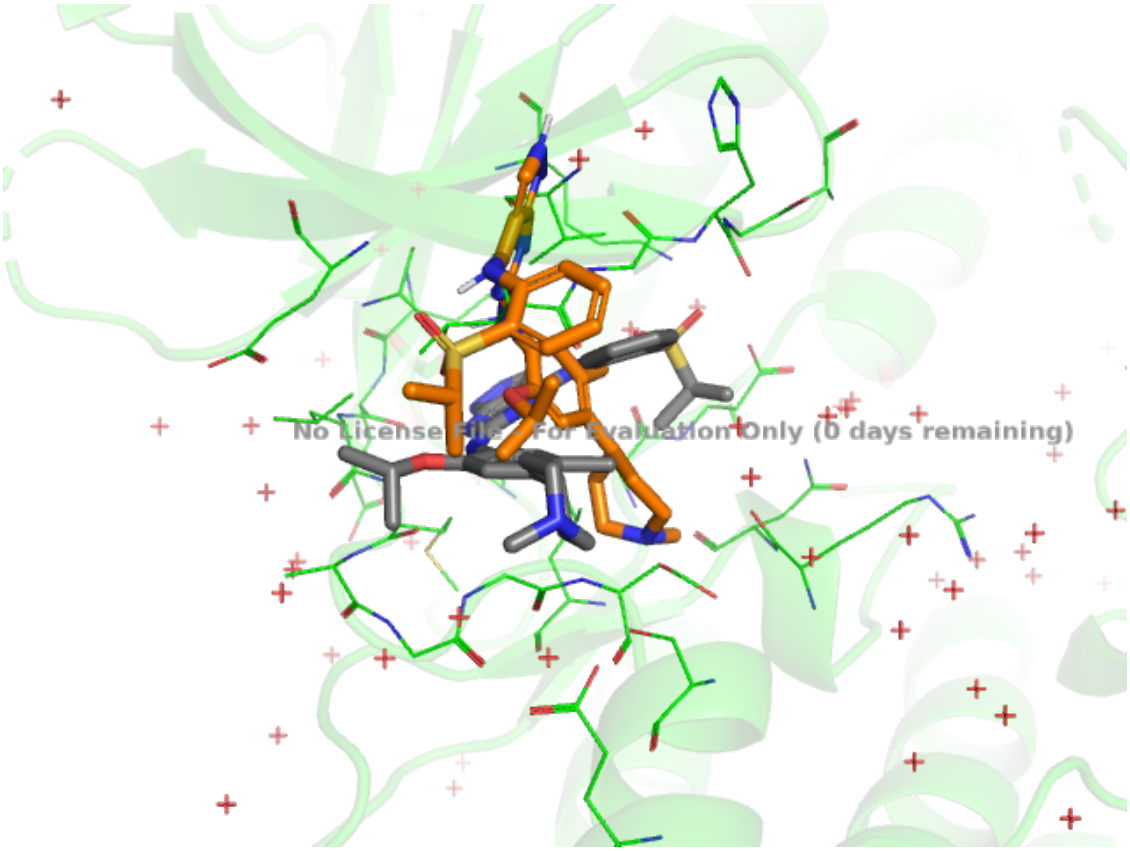
[ ]:
```
['4Z55-receptor',
 '4Z55-ligand',
 '4Z55-ligand-poses',
 '4Z55-ligand-poses_0001',
 '4Z55-ligand-poses_0002',
 '4Z55-ligand-poses_0003',
 '4Z55-ligand-poses_0004',
 '4Z55-ligand-poses_0005',
 '4Z55-ligand-poses_0006',
 '4Z55-ligand-poses_0007',
 '4Z55-ligand-poses_0008',
 '4Z55-ligand-poses_0009']
```

[ ]:
```
cmd.get_names()[-1]  #The last one in this list is the highest energy
```

[ ]:
```
'4Z55-ligand-poses_0009'
```

[ ]:
```
cmd.hide("everything","4Z55-ligand-poses*") #hide all the poses
worst = cmd.get_names()[-1]
cmd.show("stick",worst)  #Get the last pose, which should be the worst (highest␣
↪energy)

cmd.set_view(camera)

cmd.png("pose.png")
Image(filename = "pose.png", unconfined=True)
```

[ ]:



Observation Now we can see that the worst energy ligand pose is very far from the original ligand pose

Dock a library of ligands

Now lets look at some random ligands, and some true positives and conduct a virtual screen

We will get some positives from ChEMBl that are known to bind to the receptor (but not necessarily this site - for this exercise we will assume that they do). For negatives,

we can either pick true negatives from ChEMBL, but we can make the assumption that a random ligand will not posess the correct combination of interatomic interactions and conformational complementarity to bind very well to the receptor.

[ ]:
```
import requests

CHEMBL_API_URL = "https://www.ebi.ac.uk/chembl/api/data/activity.json"

def fetch_alk_binders(max_ic50_um = 15, chembl_api = CHEMBL_API_URL):
    ic50_molar = max_ic50_um * 1e-6
    pchembl = -np.log10(ic50_molar)
    params = {
        "target_chembl_id": "CHEMBL4247",
        "standard_type": "IC50",
        "pchembl_value__gte": pchembl,
        "limit": 1000
    }
    response = requests.get(chembl_api, params=params)
    if response.status_code == 200:
        data = response.json()
        if "activities" not in data:
            print("No data found.")
            return None
        compounds = [
            {
                "ChEMBLID": entry["molecule_chembl_id"],
                "Canonical SMILES": entry.get("canonical_smiles", "N/A"),
                "IC50 (uM)": float(entry["standard_value"]) / 1000 if entry.
 ↪get("standard_units") == "nM" else entry.get("standard_value", "N/A"),
                "Standard Value (nM)": entry["standard_value"],
                "pChEMBL Value": entry.get("pchembl_value", "N/A"),
                "Target ChEMBL ID": entry["target_chembl_id"],
            }
            for entry in data["activities"]
        ]
        chembl_df = pd.DataFrame(compounds)
        return chembl_df

alk_binders_df = fetch_alk_binders()
```

ChEMBL simplifies activity values to a "pChembl" value - which is meant to represent the pIC50, or pEC50 etc. To simplify things, we will jus take rows that have pChembl > 8 as being "active"

[ ]:
```
for col in alk_binders_df.columns:
    print(col)
```

```
ChEMBLID
Canonical SMILES
```

```
IC50 (uM)
Standard Value (nM)
pChEMBL Value
Target ChEMBL ID
```

[ ]:
```
#Take only rows with pChembl > 8
alk_binders_df = alk_binders_df.rename(columns={"Canonical SMILES": "Smiles"})
alk_binders_df["pChEMBL Value"] = pd.to_numeric(alk_binders_df["pChEMBL␣
 ↪Value"], errors='coerce')

actives=pd.DataFrame(alk_binders_df.loc[alk_binders_df['pChEMBL Value'] >␣
 ↪8]['Smiles'])
cognate=pd.DataFrame({"Smiles":
 ↪["CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[S](=O)(=O)C(C)C)c5c[nH]nc5n3"]})␣
 ↪#4LO

actives=pd.concat([actives,cognate]) # Make sure that we add the cognate ligand␣
 ↪to the actives list


#Lets also compare the similarity with the cognate ligand
from rdkit import DataStructs

fpgen = AllChem.GetMorganGenerator()
query = Chem.
 ↪MolFromSmiles('CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[S](=O)(=O)C(C)C)c5c[nH]nc5n3')
queryfp = fpgen.GetFingerprint(query)

sim=[]
for x in actives.Smiles:
  target = Chem.MolFromSmiles(x)
  targetfp = fpgen.GetFingerprint(target)
  s=DataStructs.TanimotoSimilarity(targetfp,queryfp)
  sim.append(s)

actives = pd.DataFrame(actives)
actives["Active"]="True"
actives["Sim"]=sim
actives = actives.rename(columns = {'Smiles':'smiles'}) #adjust capitalization␣
 ↪of name
actives=actives.sort_values("Sim",ascending=False)
actives=actives.drop_duplicates(subset='smiles', keep="first")
actives
```

[ ]:

	smiles	Active	Sim
0	CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[…	True	1.000000
507	Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)C(C)C)n2)c…	True	0.552000

```
509  Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)C(C)C)n2)c…   True  0.524590
878  Cc1cc(Nc2ncc(Cl)c(Nc3cn(C)nc3S(=O)(=O)C(C)C)n2…   True  0.468750
894  Cc1cc(Nc2ncc(Cl)c(Nc3cn(C)nc3S(=O)(=O)C(C)C)n2…   True  0.389706
..                                                 …     …       …
982  CCc1cc2c(cc1C1=CCN(C(=O)C3COCCN3)CC1)C(C)(C)c1…   True  0.077778
969  CCc1cc2c(cc1-c1cnn(CC(N)=O)c1)C(C)(C)c1[nH]c3c…   True  0.076923
229  Cn1cc(/C=C2\C(=O)NN=C2c2nccs2)c2c(OCc3c(F)cccc…   True  0.076923
968  CCc1cc2c(cc1-c1cnn(CC(=O)N(C)C)c1)C(C)(C)c1[nH…   True  0.075581
100  CCN(CC)CCOc1ccc2c(c1)C(C)(C)c1[nH]c3cc(C#N)ccc…   True  0.068323

[211 rows x 3 columns]
```

Negatives For negatives we can visit this site created by Dr. Irwin at UCSF - a tremendous resource for virtual screening. Chemical space is very large, and downloading all of these could take a serious amount of time. We will just take a small random sample ###https://zinc.docking.org/tranches/home/#

[ ]:
```python
import requests

# Define file URLs and names
ligand_urls = {
    "sample_one.smi": "http://files.docking.org/2D/CD/CDAC.smi",
    "sample_two.smi": "http://files.docking.org/2D/EF/EFEA.smi",
    "sample_three.smi": "http://files.docking.org/2D/HJ/HJAB.smi"
}

# Download each file
for filename, url in ligand_urls.items():
    try:
        response = requests.get(url, stream=True)
        response.raise_for_status()  # Raise error if request fails
        with open(filename, "wb") as file:
            file.write(response.content)
        print(f" Successfully downloaded: {filename}")
    except requests.exceptions.RequestException as e:
        print(f" Failed to download {filename}: {e}")
```

```
 Successfully downloaded: sample_one.smi
 Successfully downloaded: sample_two.smi
 Successfully downloaded: sample_three.smi
```

[ ]:
```python
#OK lets load all of them into a single dataframe
frames = [pd.read_csv('sample_one.smi', sep=" "),
          pd.read_csv('sample_two.smi', sep=" "),
          pd.read_csv('sample_three.smi', sep=" ")]
randoms = pd.concat(frames,ignore_index=True)
```

[ ]:
```
smiles_randoms = randoms.copy()
randoms
```

[ ]:
```
                                                  smiles    zinc_id
0                          O=C(NCCN1CCC(O)CC1)OCc1ccccc1  306320515
1                 CC(C)(C)OC(=O)N1CCC2(CC1)C[C@@H](N)CCO2   91303585
2                           O=C(Cc1ncon1)Nc1ccc(F)c(F)c1F      93298
3                      Cc1cc(F)c(B(O)OC(C)(C)C(C)(C)O)cc1C  200317185
4                       CCOC(=O)[C@]1(C)Oc2cc(Cl)ccc2NC1=O   26340455
…                                                     …        …
91268  Cc1nc([C@H]2CCN(CC3CCCCC3)C2)nc(C)c1CC(=O)Nc1c…  257287581
91269  CC[C@@H]1CSC2=N[C@@H](c3ccccn3)[C@H](c3cccn3-c…  260780925
91270  CC[C@H](C)OC(=O)CN1C(=O)S/C(=C/c2ccc(-c3ccc(F)…  408600907
91271  Cc1ccc(C)c(NC(=O)CSc2nnc(COc3ccc4c(c3)CCCC4)o2)c1  409008213
91272         COC(=O)c1c(NC(=O)CSCc2cccc(Cl)c2)sc2c1CCCC2  409121891

[91273 rows x 2 columns]
```

[ ]:
```
randoms.head()
```

[ ]:
```
                                     smiles    zinc_id
0            O=C(NCCN1CCC(O)CC1)OCc1ccccc1  306320515
1   CC(C)(C)OC(=O)N1CCC2(CC1)C[C@@H](N)CCO2   91303585
2            O=C(Cc1ncon1)Nc1ccc(F)c(F)c1F      93298
3       Cc1cc(F)c(B(O)OC(C)(C)C(C)(C)O)cc1C  200317185
4        CCOC(=O)[C@]1(C)Oc2cc(Cl)ccc2NC1=O   26340455
```

[ ]:
```
#Calculate the similarity of the random mols to 4LO
randoms=pd.DataFrame(randoms['smiles'])
randoms=randoms.sample(300)

sim=[]
for x in randoms.smiles:
  target = Chem.MolFromSmiles(x)
  targetfp = fpgen.GetFingerprint(target)
  s=DataStructs.TanimotoSimilarity(targetfp,queryfp)
  sim.append(s)

randoms["Active"]="False"
randoms["Sim"]=sim
randoms=randoms.sort_values("Sim", ascending=False)
randoms.head()
```

[ ]:
```
                                                  smiles Active       Sim
63531  Cc1cc(C)cc(Nc2nc(NC[C@@H]3CCCO3)nc3c2cnn3-c2cc…  False  0.175676
25355   Cc1ccc(S(=O)(=O)N2CCCCCC2)cc1C(=O)Nc1ccccc1C(C)C  False  0.165468
73030   CCn1c2ccccc2c2cc(NC(=O)c3ccccc3S(=O)(=O)CC)ccc21  False  0.157143
```

```
26827  COC(=O)c1cc2ccccc2cc1NC(=O)c1cc(C(C)C)nc2c1c(C…  False  0.151724
60173  COc1cc(C(F)(F)F)ccc1C(=O)Nc1ccccc1C(=O)N1CCCC[…  False  0.148649
```

Observation: We can see that the random molecules are very dissimilar from the cognate ligand.

[ ]:
```
#For our positives, we will take the 10 most similar rows to the cognate ligand.
 ↪ The assumption here
#is that similar ligands could potentially bind to the same site
activesample=actives.sort_values("Sim", ascending=False)[0:3]
print(activesample)
```

```
                                                 smiles Active      Sim
0     CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[…   True  1.00000
507   Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)C(C)C)n2)c…   True  0.55200
509   Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)C(C)C)n2)c…   True  0.52459
```

[ ]:
```
## OK - we have negatives (random molecules) as sdf, and then some positives as␣
 ↪smiles. Lets make a uniform dataframe as all smiles
## We will make a dataframe of 3 positives, and 7 randoms
import random
import numpy as np
vsmols = pd.concat([activesample,randoms.sample(7)])
#Ok now we have a dataframe with some actives and some negatives. Last thing to␣
 ↪do is to create a unique ID
number=np.arange(0,len(vsmols)).astype('str')
vsmols["ID"]=np.char.add('Molecule_',number)
```

[ ]:
```
vsmols.head(10)
```

[ ]:
```
                                                 smiles Active       Sim  \
0      CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[…   True  1.000000
507    Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)C(C)C)n2)c…   True  0.552000
509    Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)C(C)C)n2)c…   True  0.524590
45961    C[C@H](NC(=O)CSc1nncn1-c1ccccc1F)c1cccc2ccccc12  False  0.100629
45255   CCc1ccccc1NC(=O)c1cccc(S(=O)(=O)Nc2cccc(Cl)c2)c1  False  0.100671
7216        CC(C)(C)c1cnc(N2CCN(c3ccc(O)nc3)CC2)c(C#N)c1  False  0.077465
55458  O=C(c1cccc(Cl)c1)N1CCC(F)(F)[C@]2(CCN(c3cccc(F…  False  0.070968
70763       CCn1c(COc2cccc(C)c2C)nnc1SCC(=O)Nc1ccc(C)cc1  False  0.110390
91131  CCc1ccc(-c2csc(NC(=O)[C@@H](C)Sc3nnc(C4CC4)o3)…  False  0.096154
21804       Cc1nc(Oc2ccccc2F)nc(C)c1NC(=O)COc1ccc(Cl)cc1  False  0.125874

                ID
0       Molecule_0
507     Molecule_1
509     Molecule_2
45961   Molecule_3
45255   Molecule_4
```

```
7216   Molecule_5
55458  Molecule_6
70763  Molecule_7
91131  Molecule_8
21804  Molecule_9
```

[ ]:
```
#Ok now we need to convert all these SMILES into 3d structures

#write a conversion function to convert SMILES to a 3D structure
def Convert3D(molsmile):
  mol = Chem.MolFromSmiles(molsmile)
  mol = Chem.AddHs(mol, addCoords=True)
  AllChem.EmbedMolecule(mol)
  AllChem.MMFFOptimizeMolecule(mol)
  return mol
```

[ ]:
```
minim=[]
for x in vsmols.smiles:
  minim.append(Convert3D(x))
```

[ ]:
```
#add the column of minimized structures to our dataframe
vsmols["minim"]=minim
```

[ ]:
```
vsmols.head(10)
```

[ ]:
```
                                                 smiles Active       Sim  \
0      CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[…   True  1.000000
507    Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)C(C)C)n2)c…   True  0.552000
509    Cc1cc(Nc2ncc(Cl)c(Nc3ccccc3S(=O)(=O)C(C)C)n2)c…   True  0.524590
45961    C[C@H](NC(=O)CSc1nncn1-c1ccccc1F)c1cccc2ccccc12  False  0.100629
45255   CCc1ccccc1NC(=O)c1cccc(S(=O)(=O)Nc2cccc(Cl)c2)c1  False  0.100671
7216        CC(C)(C)c1cnc(N2CCN(c3ccc(O)nc3)CC2)c(C#N)c1  False  0.077465
55458  O=C(c1cccc(Cl)c1)N1CCC(F)(F)[C@]2(CCN(c3cccc(F…  False  0.070968
70763       CCn1c(COc2cccc(C)c2C)nnc1SCC(=O)Nc1ccc(C)cc1  False  0.110390
91131  CCc1ccc(-c2csc(NC(=O)[C@@H](C)Sc3nnc(C4CC4)o3)…  False  0.096154
21804       Cc1nc(Oc2ccccc2F)nc(C)c1NC(=O)COc1ccc(Cl)cc1  False  0.125874

                ID                                                 minim
0      Molecule_0  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
507    Molecule_1  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
509    Molecule_2  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
45961  Molecule_3  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
45255  Molecule_4  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
7216   Molecule_5  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
55458  Molecule_6  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
70763  Molecule_7  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
91131  Molecule_8  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
```

```
21804  Molecule_9  <rdkit.Chem.rdchem.Mol object at 0x0000023315F…
```

[ ]:
```
#Write the minimized 3D structures to a file for Smina to dock

PandasTools.WriteSDF(vsmols, out="dockingligands.sdf",
                     molColName='minim',
                     idName='ID',
                     properties=None,
                     allNumeric=False,
                     forceV3000=False)
```

[ ]:
```
#Allright now lets dock the sdf to the receptor, with maximum speed␣
 ↪(exhaustiveness = 1), and accept only 1 pose per ligand (num_modes = 1)
#Docking speed usually depends on the number of rotatable bonds, with more␣
 ↪taking longer to sample and "fit" to the protein
#Colab pro may have access to faster CPUs
!wsl ./smina.static -r  4Z55-receptor.pdb -l dockingligands.sdf␣
 ↪--autobox_ligand 4Z55-ligand.pdb -o output.sdf --exhaustiveness 1␣
 ↪--num_modes 1 -q
```

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0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 11.9095

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Refine time 16.3233

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Refine time 10.3503

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Refine time 4.09458

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Refine time 3.58637

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```

```
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Refine time 2.4278

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Refine time 2.36599

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Refine time 6.31235

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Refine time 4.30381

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**************************************************
Refine time 3.81312
Loop time 70.0558

==============================
*** Open Babel Warning  in Init
  Unable to open data file 'space-groups.txt'
==============================
*** Open Babel Warning  in Init
  Cannot initialize database 'space-groups.txt' which may cause further errors.
```

[ ]:
```
#now load the results
vsresults = PandasTools.LoadSDF("output.sdf")

merged=vsmols.merge(vsresults, left_on="ID",right_on="ID")
merged=merged[['ID','Active','Sim','minimizedAffinity']] #We can clean up a few␣
  ↪of the columns
merged=merged.sort_values('minimizedAffinity', ascending=True)
merged
```

```
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
```

```
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
[22:28:09] Warning: molecule is tagged as 2D, but at least one Z coordinate is
not zero. Marking the mol as 3D.
```

[ ]:

	ID	Active	Sim	minimizedAffinity
0	Molecule_0	True	1.000000	-10.33072
5	Molecule_5	False	0.077465	-7.28969
7	Molecule_7	False	0.110390	-7.86899
9	Molecule_9	False	0.125874	-8.00171
8	Molecule_8	False	0.096154	-8.08743
1	Molecule_1	True	0.552000	-8.14979
6	Molecule_6	False	0.070968	-8.62694
3	Molecule_3	False	0.100629	-9.10356
4	Molecule_4	False	0.100671	-9.24877
2	Molecule_2	True	0.524590	-9.94205

[ ]:

```
#Something looks wrong here - have to make sure that the score column
(MinimizedAffinity is treated as a number)
merged['minimizedAffinity']=merged['minimizedAffinity'].astype('float64')
merged=merged.sort_values('minimizedAffinity', ascending=True)
merged
```

[ ]:

	ID	Active	Sim	minimizedAffinity
0	Molecule_0	True	1.000000	-10.33072
2	Molecule_2	True	0.524590	-9.94205
4	Molecule_4	False	0.100671	-9.24877
3	Molecule_3	False	0.100629	-9.10356
6	Molecule_6	False	0.070968	-8.62694
1	Molecule_1	True	0.552000	-8.14979
8	Molecule_8	False	0.096154	-8.08743
9	Molecule_9	False	0.125874	-8.00171
7	Molecule_7	False	0.110390	-7.86899
5	Molecule_5	False	0.077465	-7.28969

Observation: We can see that 2/3 of the true positives were pushed to the top of the list (meaning Smina thought they were good binders). Lets calculate a ROC plot to measure performance.

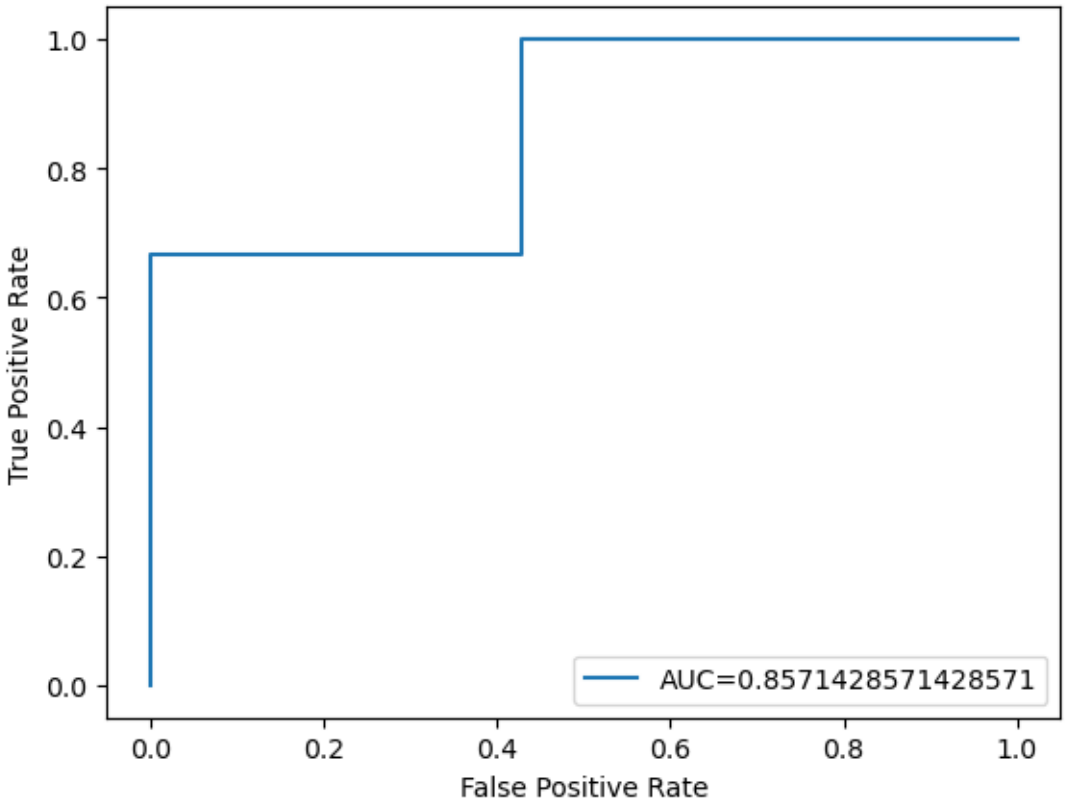
[ ]:
```
from sklearn import metrics
import matplotlib.pyplot as plt

#convert Actie = True False to 1 or 0
merged.replace({"False": 0, "True": 1}, inplace=True)


#define metrics
fpr, tpr, _ = metrics.roc_curve(merged['Active'], ␣
 ↪-merged['minimizedAffinity']) #Use the negative of the score here to rank␣
 ↪more negative scores better
auc = metrics.roc_auc_score(merged['Active'],  -merged['minimizedAffinity'])␣
 ↪#Also invert the score here too

#create ROC curve
plt.plot(fpr,tpr,label="AUC="+str(auc))
plt.ylabel('True Positive Rate')
plt.xlabel('False Positive Rate')
plt.legend(loc=4)
plt.show()
```

```
C:\Users\Stephen\AppData\Local\Temp\ipykernel_344\102533532.py:5: FutureWarning:
Downcasting behavior in `replace` is deprecated and will be removed in a future
version. To retain the old behavior, explicitly call
`result.infer_objects(copy=False)`. To opt-in to the future behavior, set
`pd.set_option('future.no_silent_downcasting', True)`
  merged.replace({"False": 0, "True": 1}, inplace=True)
```



####**Observation** Intuitively this ROC plot makes sense. We can see the docking experiment enriched true actives somewhat toward the top of the list, meaning that the true positives were ranked highly most of the time.

[ ]:
```
#Wipe the memory and load into the workspace
cmd.reinitialize()
cmd.load("4Z55-receptor.pdb")
cmd.load("4Z55-ligand.pdb")
cmd.load("virtualscreen.sdf")


cmd.color("green","4Z55-receptor") #color the protein cyan
cmd.color("grey", "4Z55-ligand") #Color the original pose grey
cmd.color("orange", "virtualscreen")

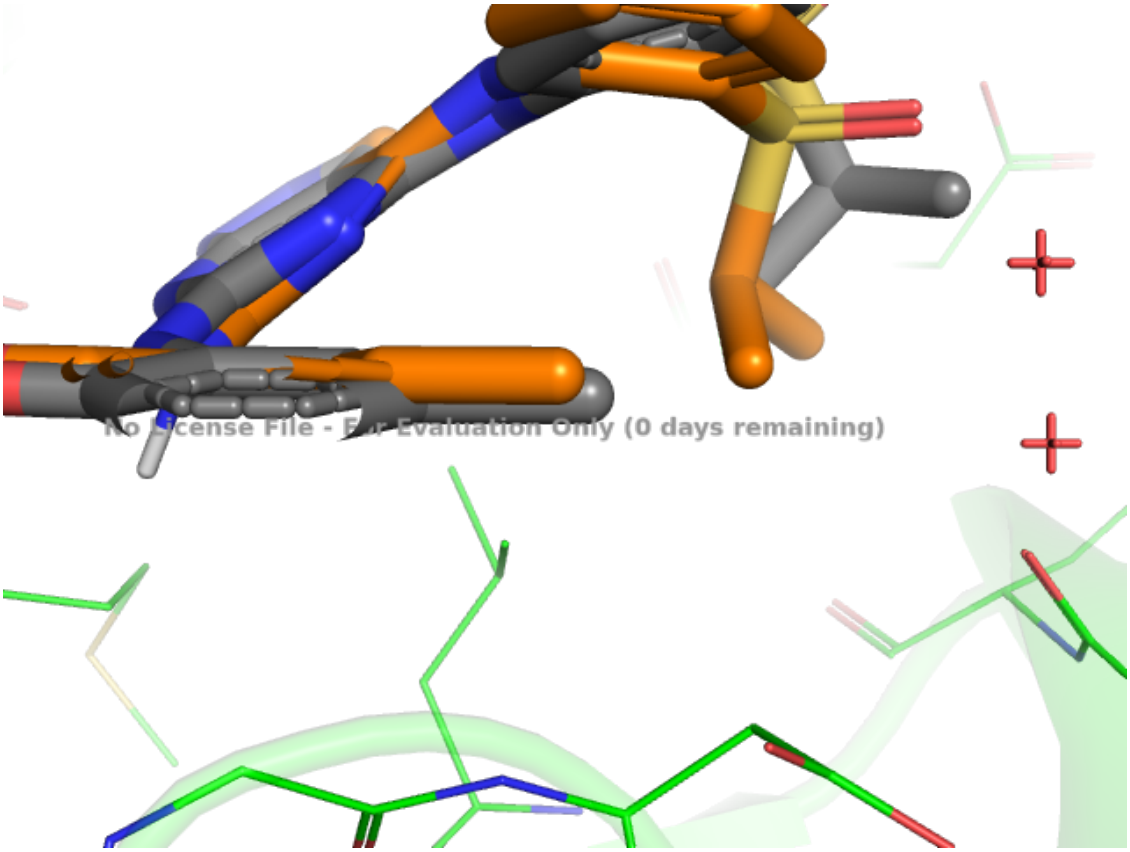
#We will cerate a selection sphere around the ligand and show the residues
cmd.select("pocketresidues", "byres (all within 5 of 4Z55-ligand)&polymer.
 ↪protein")
cmd.show("line","pocketresidues")
cmd.set("ray_shadow",0)
cmd.set("cartoon_transparency", 0.8)
```

```
cmd.util.cnc()
cmd.zoom("pocketres") #zoom in on only the pocket
cmd.rotate("z","90")
camera = cmd.get_view() #save the camera viewpoint sometimes it can get reset␣
↪so we will enforce the same

#ok lets split the states and show the first docked ligand
cmd.split_states("virtualscreen")
cmd.remove("virtualscreen")
cmd.hide("stick","Molecule_*")
cmd.show("stick","Molecule_0")

cmd.png("pose.png")
Image(filename = "pose.png", unconfined=True)
```

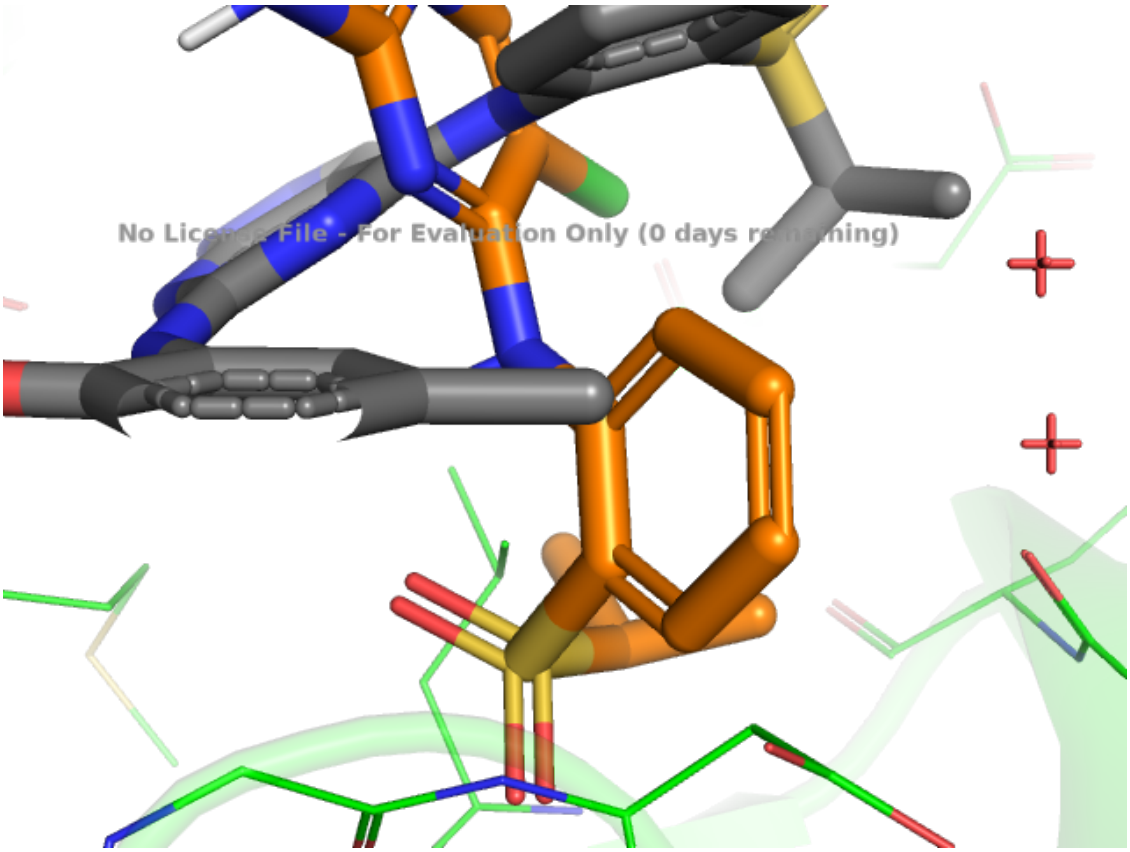
[ ]:



[ ]:
```
cmd.hide("stick","Molecule_*")
cmd.show("stick","Molecule_1")

cmd.png("pose.png")
Image(filename = "pose.png", unconfined=True)
```

[ ]:



Observation We can see that while some of the similar aromatic rings got placed near the original pose (grey) there are quite a few differences. Analyze the rest of the dataset!

[ ]:
```
import random
from rdkit import Chem
from rdkit.Chem import SDWriter, FilterCatalog
from rdkit.Chem.FilterCatalog import FilterCatalogParams
from rdkit import RDLogger
RDLogger.DisableLog('rdApp.*')  # Suppress all RDKit warnings

# Load the SDF file
sdf_file = "Week6-VirtualLibrary.sdf"
suppl = Chem.SDMolSupplier(sdf_file)

# Convert to list and filter valid molecules
mols = [mol for mol in suppl if mol is not None]

# Load PAINS filter from RDKit
pains_catalog = FilterCatalog.FilterCatalogParams()
pains_catalog.AddCatalog(FilterCatalogParams.FilterCatalogs.PAINS_A)
```

```
pains_catalog.AddCatalog(FilterCatalogParams.FilterCatalogs.PAINS_B)
pains_catalog.AddCatalog(FilterCatalogParams.FilterCatalogs.PAINS_C)
pains_filter = FilterCatalog.FilterCatalog(pains_catalog)

# Filter molecules: Remove PAINS compounds
filtered_mols = [mol for mol in mols if not pains_filter.HasMatch(mol)]

# Select 10 random non-PAINS molecules
random_subset = random.sample(filtered_mols, min(200, len(filtered_mols)))

# Add hydrogens to each selected molecule
mols_with_h = [Chem.AddHs(mol) for mol in random_subset]

# Write to new SDF file
output_sdf = "filtered_no_PAINS.sdf"
writer = SDWriter(output_sdf)

for mol in mols_with_h:
    writer.write(mol)

writer.close()

print(f" Successfully created {output_sdf} with 200 non-PAINS ligands␣
 ↪(Hydrogens Added)")
```

```
 Successfully created filtered_no_PAINS.sdf with 200 non-PAINS ligands
(Hydrogens Added)
```

[ ]:
```
!wsl ./smina.static -r  4Z55-receptor.pdb -l filtered_no_PAINS.sdf␣
 ↪--autobox_ligand 4Z55-ligand.pdb -o full_data.sdf --exhaustiveness 1␣
 ↪--num_modes 1 -q
```

```
0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.06848

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Refine time 1.34682

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Refine time 3.95764
```

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Refine time 2.86541

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Refine time 1.66891

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Refine time 1.70605

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Refine time 2.39363

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Refine time 4.38033

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Refine time 4.84023

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Refine time 2.30205

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Refine time 2.26581

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Refine time 2.10021

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Refine time 8.6511

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Refine time 4.28233

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Refine time 1.33798

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Refine time 2.1342

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Refine time 2.42409

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Refine time 5.40383

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Refine time 1.48576

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Refine time 4.88193

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Refine time 2.27197

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Refine time 3.98507

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Refine time 2.74933

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Refine time 2.10946

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Refine time 3.11234

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Refine time 3.46621

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Refine time 2.1003

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Refine time 2.87556

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Refine time 5.75495

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Refine time 2.63829

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Refine time 2.95702

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Refine time 5.72505

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Refine time 6.02204

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Refine time 7.9826

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Refine time 2.03759

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Refine time 8.91963

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Refine time 4.38147

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Refine time 1.4715

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Refine time 2.23171

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Refine time 4.61533

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Refine time 3.59871

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Refine time 2.27115

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Refine time 1.32403

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Refine time 3.5861

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************************************************
Refine time 4.3693

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Refine time 1.3289

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Refine time 1.25021

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Refine time 1.87188
```

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Refine time 1.79304

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Refine time 4.83326

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Refine time 1.87913

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Refine time 2.24531

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Refine time 2.1163

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Refine time 1.60391

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Refine time 1.06853

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Refine time 4.8251

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.99935

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.66264

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.6958

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.76227

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.05838

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 0.965582

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 6.69913

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.52983

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.17983

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.12616

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.66814

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 3.18285

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 1.72333

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 18.3431

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.34952

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 5.22357

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 1.95775

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.96942

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.54587

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.99302

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.19025
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0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.37092

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.49719

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.6889

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 5.53493

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.51727

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.66004

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.7612

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.11463

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.03765

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.16008

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.21726

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.16683

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.6016

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.87191

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 7.34611

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.17604

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.26818

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.60638

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.48255
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0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.95804

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.51079

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.52298

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.77492

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.50414

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.56105

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.05681

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 3.42251

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.20672

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.33397

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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Refine time 2.04822

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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Refine time 4.26632

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.49613

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.34635

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 2.72585

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.71409

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.52324

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 6.25742

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.78923

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 2.80875

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.5881

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 3.78149

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.36685

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.46601

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.88332

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 1.3558

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.9371

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 2.41958

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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Refine time 5.03597
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0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 3.41168

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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Refine time 5.17556

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.21629

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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Refine time 2.95003

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.37305

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.79296

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 5.30288

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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Refine time 2.04892

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.15611

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 5.82362

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.70134

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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Refine time 1.53852

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 3.22696

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.33299

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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Refine time 3.89117

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 2.26816

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.01078

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
************************************************
Refine time 3.3632

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 4.81109
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0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 2.01089

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.82071

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.45513

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 6.31936

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.82473

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.68496

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.34095

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.85058

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.37159

0%   10   20   30   40   50   60   70   80   90   100%
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Refine time 1.63571

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.58787

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.20797

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.10095

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.01583

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.80696

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.70336

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.8371

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.99077

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.93367

0%   10   20   30   40   50   60   70   80   90   100%
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**************************************************
Refine time 3.39601

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 5.0865

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.09656

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.11837

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.29786

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.66865

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.71301

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.61486

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 0.905272

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.82517
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0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.53077

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.90645

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.36207

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.06057

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.18787

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.19352

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.23089

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.46969

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.65659

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
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**************************************************
Refine time 4.05325

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.40089

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.34966

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 12.0299

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.52266

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.8575

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.63999

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.22836

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.83706

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.85211
```

```
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.68522

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 3.98085

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 2.1154

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.84371

0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**************************************************
Refine time 1.33038
Loop time 699.212

==============================
*** Open Babel Warning  in Init
  Unable to open data file 'space-groups.txt'
==============================
*** Open Babel Warning  in Init
  Cannot initialize database 'space-groups.txt' which may cause further errors.
```

[ ]:
```python
subset_results= PandasTools.LoadSDF("full_data.sdf")
filter_no_pains = PandasTools.LoadSDF("filtered_no_PAINS.sdf")
print(subset_results.columns)
print(filter_no_pains.columns)

merged=filter_no_pains.merge(subset_results, left_on="ID",right_on="ID")
merged=merged[['ID','minimizedAffinity']] #We can clean up a few of the columns
merged['minimizedAffinity']=merged['minimizedAffinity'].astype('float64')
merged=merged.sort_values('minimizedAffinity', ascending=True)

subset_results = subset_results[["ID", "ROMol"]]
# Merge to add ROMol from subset_results into merged DataFrame
merged = merged.merge(subset_results, on="ID", how="left")
merged["SMILES"] = merged["ROMol"].apply(lambda mol: Chem.MolToSmiles(mol) if␣
 ↪mol is not None else None)
```

```
merged
```

```
Index(['minimizedAffinity', 'ID', 'ROMol'], dtype='object')
Index(['identifier', 'ID', 'ROMol'], dtype='object')
```

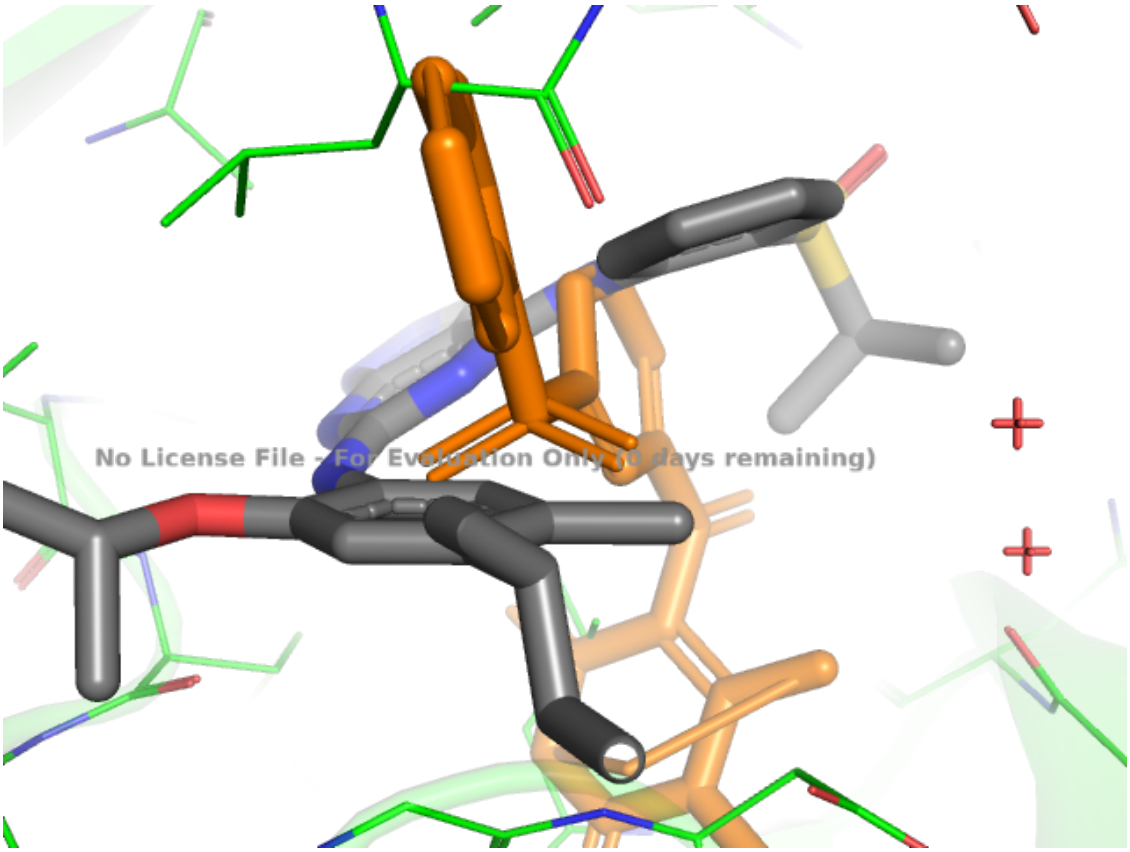
[ ]:

	ID	minimizedAffinity	ROMol	SMILES
0	ZINC000003328706	-9.91545	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	Cn1c(N)c(C(=O)c2cccc(S(=O)(=O)N3CCc4ccccc43)c2…
1	ZINC000016248871	-9.29532	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	C[C@H]1c2cccc(O)c2C(O)=C2C(=O)[C@]3(O)C(=O)C(C…
2	ZINC000000788703	-9.17463	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	[H]/N=c1\c(C(=O)NC)cc2c(=O)n3cccc(C)c3nc2n1CCC…
3	ZINC000019961074	-9.06716	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	O=C1C[C@H](C(=O)Nc2ccccc2[N+](=O)[O-])c2c(nc(N…
4	ZINC000012823896	-8.97571	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	Cn1c(=O)c2c(ncn2CC(=O)OCC(=O)NC(=O)c2ccccc2)n(…
..	…	…	…	…
195	ZINC000008777097	-5.83903	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	C#CCNS(=O)(=O)c1cn(C)c(=O)n(C)c1=O
196	ZINC000079387582	-5.69655	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	CCO/C(=C/C(=O)C(F)(F)F)N1CC[NH+](C)CC1
197	ZINC000073373064	-5.63793	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	C=CC/[NH+]=C(/NCCN1CCOCC1)NC[C@H](C)Cn1cccn1
198	ZINC000253387604	-5.55237	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	CCOC(=O)[C@]1(C#N)[C@H](c2cccc(Cl)c2)[C@H](C(N…
199	ZINC000116334711	-4.33152	<rdkit.Chem.rdchem.Mol object at 0x000002337D3…	C#CCOCCOCCOCCOCCOCCOCCOCCOCC[NH3+]

[200 rows x 4 columns]

[ ]:
```
#Wipe the memory and load into the workspace
cmd.reinitialize()
cmd.load("4Z55-receptor.pdb")
cmd.load("4Z55-ligand.pdb")
cmd.load("full_data.sdf")


cmd.color("green","4Z55-receptor") #color the protein cyan
cmd.color("grey", "4Z55-ligand") #Color the original pose grey
cmd.color("orange", "full_data")

#We will cerate a selection sphere around the ligand and show the residues
cmd.select("pocketresidues", "byres (all within 5 of 4Z55-ligand)&polymer.
 ↪protein")
cmd.show("line","pocketresidues")
cmd.set("ray_shadow",0)
cmd.set("cartoon_transparency", 0.8)
cmd.util.cnc()
cmd.zoom("pocketres") #zoom in on only the pocket
cmd.rotate("z","90")
camera = cmd.get_view() #save the camera viewpoint sometimes it can get reset␣
 ↪so we will enforce the same

# Split docked ligands into individual molecules
cmd.split_states("full_data")
cmd.remove("full_data")  # Remove the original multi-state object

# Hide all docked ZINC ligands
cmd.hide("stick", "ZINC*")

# Ensure only ZINC000003328706 is shown
cmd.show("stick", "ZINC000003328706")
cmd.color("orange", "ZINC000003328706")

# Clean up unwanted molecules
cmd.remove("not (4Z55-receptor or 4Z55-ligand or ZINC000003328706)")

# Select pocket residues (within 5Å of original ligand)
cmd.select("pocketresidues", "byres (all within 5 of 4Z55-ligand) & polymer.
 ↪protein")
cmd.show("line", "pocketresidues")

cmd.png("pose.png")
Image(filename = "pose.png", unconfined=True)
```

[ ]:



[ ]:
```
#Wipe the memory and load into the workspace
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cmd.load("4Z55-receptor.pdb")
cmd.load("4Z55-ligand.pdb")
cmd.load("full_data.sdf")


cmd.color("green","4Z55-receptor") #color the protein cyan
cmd.color("grey", "4Z55-ligand") #Color the original pose grey
cmd.color("orange", "full_data")

#We will cerate a selection sphere around the ligand and show the residues
cmd.select("pocketresidues", "byres (all within 5 of 4Z55-ligand)&polymer.
 ↪protein")
cmd.show("line","pocketresidues")
cmd.set("ray_shadow",0)
cmd.set("cartoon_transparency", 0.8)
cmd.util.cnc()
cmd.zoom("pocketres") #zoom in on only the pocket
cmd.rotate("z","90")
```
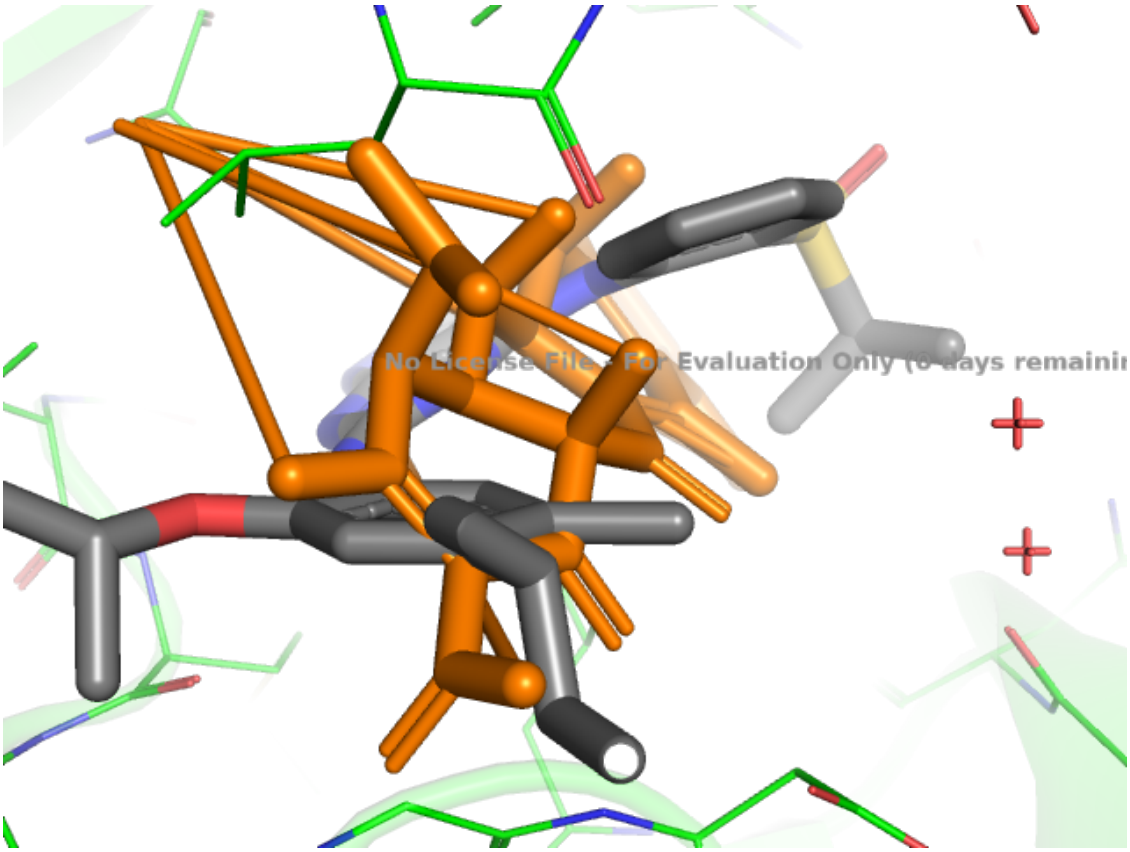

```
camera = cmd.get_view() #save the camera viewpoint sometimes it can get reset␣
 ↪so we will enforce the same

# Split docked ligands into individual molecules
cmd.split_states("full_data")
cmd.remove("full_data")  # Remove the original multi-state object

# Hide all docked ZINC ligands
cmd.hide("stick", "ZINC*")

# Ensure only ZINC000016248871 is shown
cmd.show("stick", "ZINC000016248871")
cmd.color("orange", "ZINC000016248871")

# Clean up unwanted molecules
cmd.remove("not (4Z55-receptor or 4Z55-ligand or ZINC000016248871)")

# Select pocket residues (within 5Å of original ligand)
cmd.select("pocketresidues", "byres (all within 5 of 4Z55-ligand) & polymer.
 ↪protein")
cmd.show("line", "pocketresidues")

cmd.png("pose.png")
Image(filename = "pose.png", unconfined=True)
```

[ ]:



[ ]:
```
fpgen = AllChem.GetMorganGenerator()
query = Chem.
  ↪MolFromSmiles('CC(C)Oc1cc(C2CCN(C)CC2)c(C)cc1Nc3nc(Nc4ccccc4[S](=O)(=O)C(C)C)c5c[nH]nc5n3')
queryfp = fpgen.GetFingerprint(query)

sim=[]
for x in merged.SMILES:
  target = Chem.MolFromSmiles(x)
  targetfp = fpgen.GetFingerprint(target)
  s=DataStructs.TanimotoSimilarity(targetfp,queryfp)
  sim.append(s)


merged["Sim"]=sim
merged
```

[ ]:
```
                   ID  minimizedAffinity  \
0    ZINC000003328706           -9.91545
1    ZINC000016248871           -9.29532
2    ZINC000000788703           -9.17463
```

```
3    ZINC000019961074           -9.06716
4    ZINC000012823896           -8.97571
..                …                …
195  ZINC000008777097           -5.83903
196  ZINC000079387582           -5.69655
197  ZINC000073373064           -5.63793
198  ZINC000253387604           -5.55237
199  ZINC000116334711           -4.33152

                                                    ROMol  \
0    <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
1    <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
2    <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
3    <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
4    <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
..                                                 …
195  <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
196  <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
197  <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
198  <rdkit.Chem.rdchem.Mol object at 0x000002337D3…
199  <rdkit.Chem.rdchem.Mol object at 0x000002337D3…

                                                  SMILES       Sim
0    Cn1c(N)c(C(=O)c2cccc(S(=O)(=O)N3CCc4ccccc43)c2…  0.118421
1    C[C@H]1c2cccc(O)c2C(O)=C2C(=O)[C@]3(O)C(=O)C(C…  0.063291
2    [H]/N=c1\c(C(=O)NC)cc2c(=O)n3cccc(C)c3nc2n1CCC…  0.144654
3    O=C1C[C@H](C(=O)Nc2ccccc2[N+](=O)[O-])c2c(nc(N…  0.119497
4    Cn1c(=O)c2c(ncn2CC(=O)OCC(=O)NC(=O)c2ccccc2)n(…  0.107383
..                                                 …       …
195                C#CCNS(=O)(=O)c1cn(C)c(=O)n(C)c1=O  0.095238
196            CCO/C(=C/C(=O)C(F)(F)F)N1CC[NH+](C)CC1  0.061069
197      C=CC/[NH+]=C(/NCCN1CCOCC1)NC[C@H](C)Cn1cccn1  0.099338
198  CCOC(=O)[C@]1(C#N)[C@H](c2cccc(Cl)c2)[C@H](C(N…  0.089172
199                C#CCOCCOCCOCCOCCOCCOCCOCCOCC[NH3+]  0.025210

[200 rows x 5 columns]
```