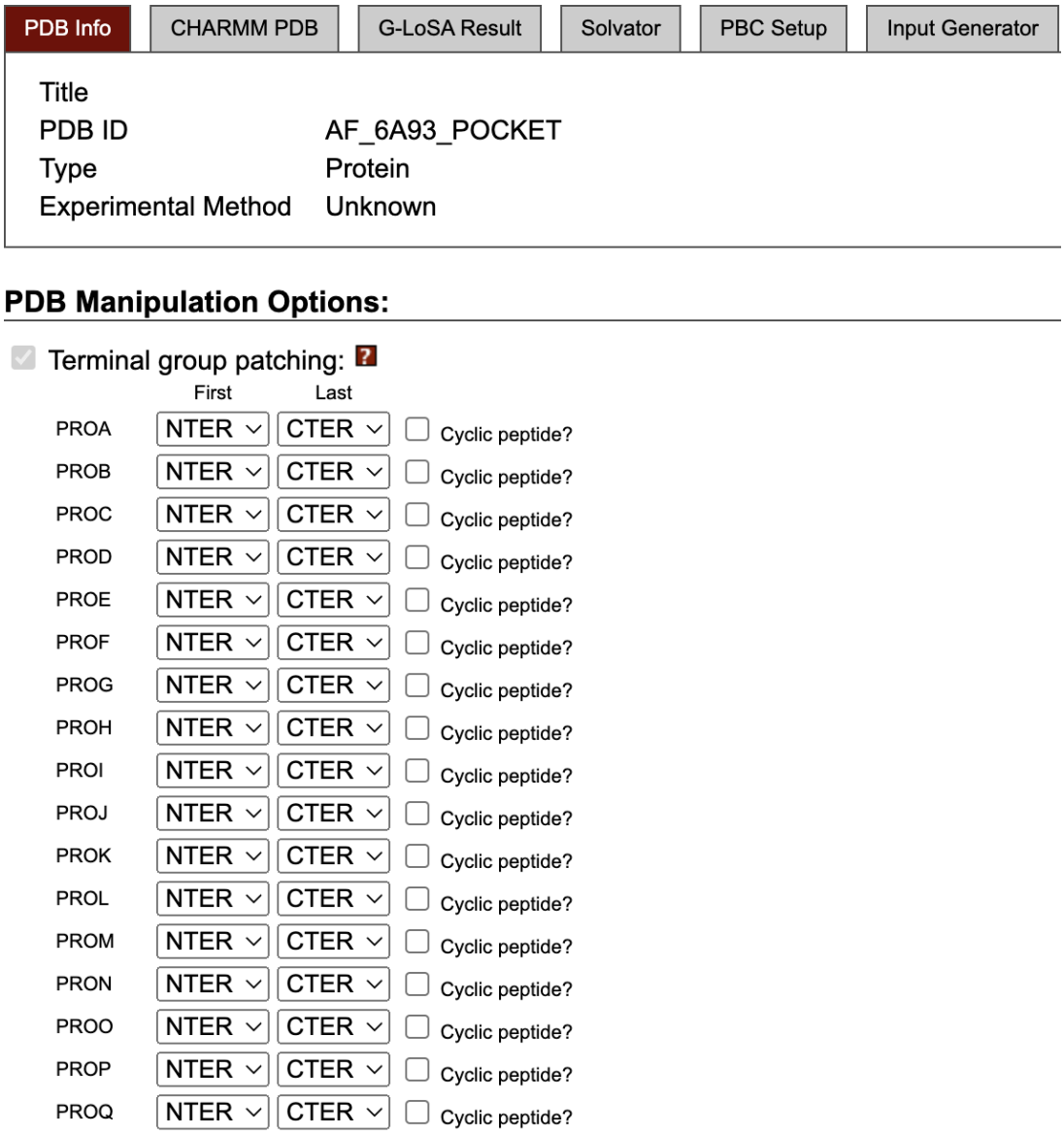
Using Charmm-GUI LBS with OpenMM

Charmm-GUI is an online interface containing a ligand binding site (LBS) using G-LoSA. It is essentially the same idea as G-LoSA search with added steps in preparing the templates to be used in MD simulations. It is quite striaghtforward to go through the Charmm-GUI process, but here are some explanations for each step.

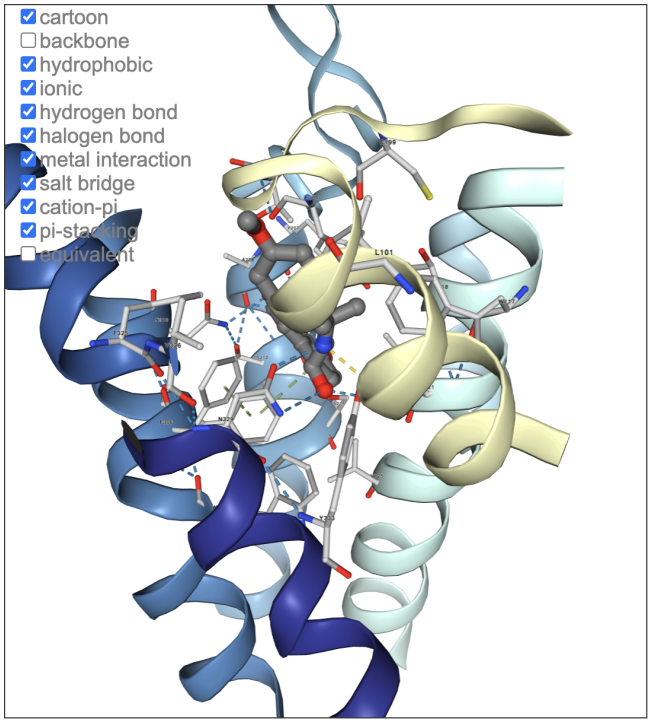
1. Uploading and formatting PDB
    a. Upload a PDB file or fetch it from RCSB PDB
    b. Chain Separation and PDB Manipulation
        i. Choose all Chains that are detected. There may be many chains detected as the pocket may be composed of many non-adjacent residues
        ii. Manipulation options are available. For most cases, just continue with Terminal group patching.



c. Submit email to run G-LoSA search.

2. G-LoSA Run

a. Selecting Top Templates. G-LoSA will output the Top 10 templates as well as the Top 10 Clusters (templates it deems similar will be clustered). Select the desired template to derive MD restraints with.



Top10 | Top10 Cluster

Select	Rank	PDB ID	Ligand	Sequence Identity	TM-score	GA-score
☑	1	2y02B	WHJ	40	0.44	0.81
☐	2	2YCZA	I32	40	0.45	0.81
☐	3	5tudA	ERM	38	0.36	0.81
☐	4	4ldlA	XQC	24	0.29	0.78
☐	5	3A0Hh	BCR	no fasta	0.36	0.77
☐	6	3HRMB	CSO	33	0.29	0.76
☐	7	3A0BH	BCR	0	0.36	0.76
☐	8	2HZTC	CSU	20	0.36	0.75
☐	9	2HZTD	CSU	20	0.37	0.75
☐	10	3O1FA	SME	0	0.40	0.74

3. Choosing MD Parameters
    a. Fit waterbox to protein size
    b. Include NaCl ions at 0.15 concentration
    c. Calculate distant restraints on α carbons only
    d. Follow the default system size settings and force field settings
4. Generating Input
    a. Download the .tgz folder to get the MD input settings and continue to OpenMM
5. Installing OpenMM
    a. Create a conda environment and follow installation instructions at http://docs.openmm.org/latest/userguide/application/01_getting_started.html#installing-openmm
6. Running OpenMM with Charmm-GUI output
    a. Locate the README C shell in the Charmm output folder, found at `/openmm/README` in the Charmm folder
    b. Run the script with `csh README` in the conda environment
    c. Load the final .dcd file into PyMol to see the states of the simulation