

Molecular Docking

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I. Preparing the protein

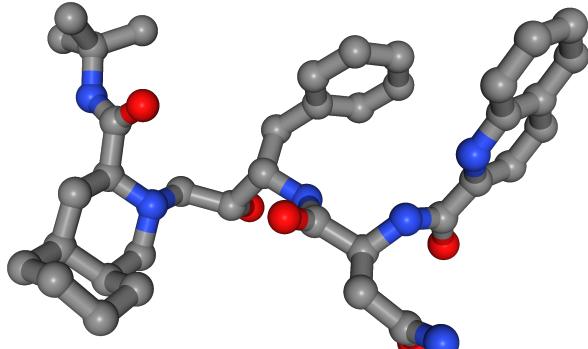


Figure 1: Saquinavir

II. Selecting a ligand with the best fit

I used a python script to parse the qvina output files and extract the most negative binding affinity score for each ligand out of 2116 tested. This involved identifying lines containing the "REMARK VINA RESULT" and capturing the first numerical value (the binding affinity score).

The top 10 best ligands selected can be seen in the Table 1. The two top ones are just Saquinavir with some additional hydrogens. I decide to select the ligand with the third lowest binding affinity score was named fda_1700 and it can be seen in Figure 2. Its structure is somewhat similar to Saquinavir which is not surprising. It's almost identical to fda_554 which has one missing hydrogen atom. The ligand's binding affinity score was -11.1 kcal/mol which is slightly less than Saquinavir's -11.4 kcal/mol.

Ligand	Model									min
	1	2	3	4	5	6	7	8	9	
fda_553	-11.4	-10.4	-10.4	-9.7	-9.6	-9.5	-9.3	-9.3	-8.9	-11.4
fda_554	-11.4	-10.8	-10.4	-10.1	-10.0	-9.9	-9.9	-9.5	-9.0	-11.4
fda_1700	-11.1	-10.2	-10.1	-9.9	-9.9	-9.8	-9.7	-9.6	-9.6	-11.1
fda_1755	-11.0	-10.8	-10.7	-10.4	-10.1	-10.0	-10.0	-10.0	-9.9	-11.0
fda_871	-11.0	-11.0	-10.8	-10.7	-10.6	-10.1	-9.9	-9.8	-9.8	-11.0
fda_872	-11.0	-11.0	-10.8	-10.6	-10.5	-10.5	-10.1	-9.6	-9.5	-11.0
fda_1829	-10.9	-10.9	-10.6	-10.6	-10.2	-10.2	-10.1	-10.1	-10.0	-10.9
fda_95	-10.8	-10.4	-10.4	-9.8	-9.7	-9.6	-9.3	-9.3	-8.7	-10.8
fda_161	-10.8	-9.7	-9.5	-9.5	-9.5	-9.2	-9.2	-9.1	-8.9	-10.8
fda_160	-10.7	-9.9	-9.7	-9.6	-9.6	-9.5	-9.4	-9.2	-8.8	-10.7

Table 1: Top 10 ligands with the lowest minimal (out of all models tested) binding affinity score

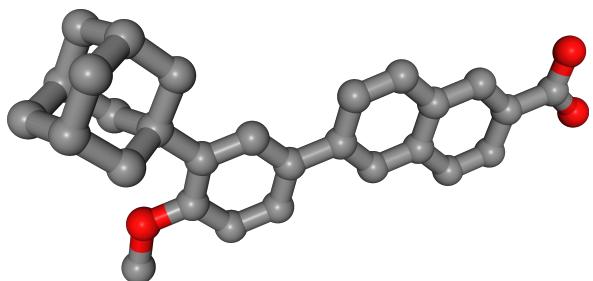


Figure 2: Ligand with name fda_1700 which reached the third lowest binding affinity score of -11.1 kcal/mol out of 2116 ligands tested.

III. MD

In this section I outline the sequence of computational steps taken to prepare a molecular system for dynamic simulation using GROMACS.

Initially, I converted ligand's structural data from PDBQT to PDB format with *Open Babel*, separating molecules and adding of hydrogens. Next, *Antechamber* was used to gener-

ate a MOL2 file, calculating AM1-BCC charges and setting the net charge and multiplicity. The `parmchk2` command then created a force field modification file for missing parameters. With `tleap`, I prepared the system using the `ff14SB` force field, incorporating ligand parameters. The final step involved the `parmed_amber2gmx.py` script (see `scripts` folder) to convert AMBER files to GROMACS format. Following the successful setup of the ligand, I applied `tleap` and `parmed_amber2gmx.py` steps to prepare the protein component.

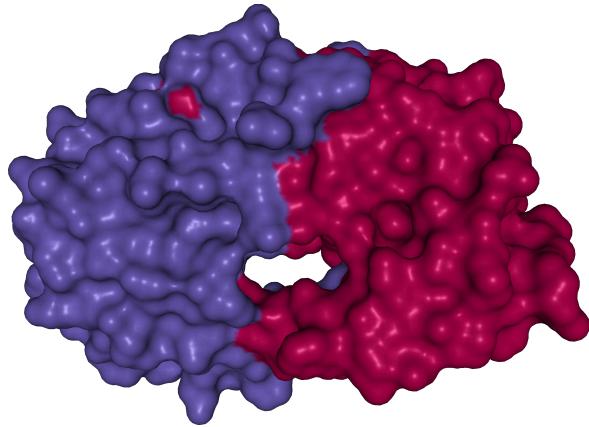


Figure 3: HIV-1 protease variant G48T/L89M

IV. MD Trajectory Analysis