**Curso Introducción al Diseño de Fármacos**

**Guía de ejercicios 2: Docking Molecular**

Perform molecular re-docking of molecule sulfonamide pyrrolidine to progesterone (PRGR) protein. Redocking of PDB ligands to its protein structure allows you to evaluate your system preparation and docking protocol, previously to run a high-throughput docking campaign.

Required software: ICM, OpenBabel (http://openbabel.org/wiki/Category:Installation), Auto

Dock Vina (http://vina.scripps.edu/download.html), AutoDockTools

(<http://mgltools.scripps.edu/downloads>)

1. System preparation:
   1. Open pdb “3kba” in ICM to visualize the system. Convert the structure to ICM format. Delete water molecules and co-factors, keep one chain of the protein and the ligand.
   2. Visualize Histidine, Asparagine and Glutamine residues in the binding pocket. Use the function Sphere.
   3. Save the ligand as .mol2 and the protein as .pdb.
   4. Find and write down the 3D coordinates of the center of mass of the

ligand. Use Xyz(...) and Mean(…) ICM functions. These coordinates will serve

as the center of the docking box. The size of the box should be around 20Å.

You may use AutoDockTools to visualize the box.

* 1. Docking box: Using AutoDockTools save the receptor and ligand in .pdbqt

format. Then, visualize the box around the ligand using the coordinates of the

center of mass previously recorded. Adjust the size of the box if needed. Write down the final values of the box.

1. Docking calculation:
   1. Write the config file for Auto Dock Vina. You may use an exhaustiveness value of 12 for better accuracy (8 is default).
   2. Perform molecular docking with Vina. You will need the vina.exe, ligand,

protein and config files in the same directory. (Command: vina --config

config.txt --ligand ligand.pdbqt --out out\_dir.pdbqt --log log\_dir.log)

* 1. Export the docked poses (in .pdbqt format) to sdf (.mol) or mol2 using

OpenBabel. Visualize the docking results.

1. Results analysis:
   1. Inspect all the docking poses. Do all lie within the binding site?
   2. For the first pose (the lowest energy one), visualize the docked pose and the interactions with the protein (take a picture, which shows the relevant

interactions between ligand and protein). Note particularly, hydrogen bonds,

hydrophobic interactions, and other interactions you find relevant.

* 1. The first approach to evaluate the quality of a docked pose, particularly when

re-docking the crystal structure pose, is by visual inspection. Do the atoms of

the ligands in the docked pose coincide with the ligand atoms in the crystal

structure? Compare the results of the docking program with the available

crystal structure. Did the docking program do a good job? Was it able to find a

reasonable ligand pose compared to what was determined in the crystal

structure? (There should be good overlap, but this is not always the case.) If

there is a good pose, is it the top-ranked pose?

* 1. The quantitative way to gauge re-docked quality is done using the root-mean-

square-deviation (RMSD) of the atomic positions between the ligand and the

docked pose. An RMSD value of 0 (zero) means the pose is identical to the

crystal structure. Normally, anything below 2Å is acceptable, but of course, the lower the better. Calculate the RMSD.