



Docking: general rules

1. Getting the ligand structure.

- Find the molecule in [PubChem](#) and download the 3D structure. You can search the molecule by SMILES.
- If you don't know its SMILES, you can obtain it drawing its chemical structure [here](#).
- If the molecule is not in PubChem, you can directly use [obabel](#) to obtain the 3D structure from the SMILES string. Remember to add the `--gen3d` tag.



Later for ligand parametrization, each atom of the ligand should have a unique name (C1, C2...)

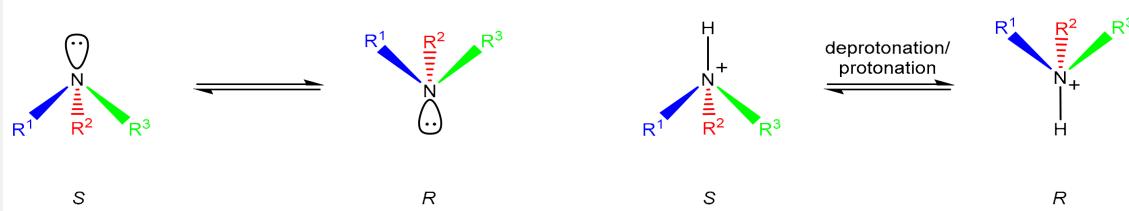
2. Protonating the ligand.

- For docking, it is fundamental that the ligand is correctly protonated. Fast protonation at physiological pH (7.4) can be done with obabel.

```
# Protonate  
obabel lig.sdf -O lig_prot.sdf -p  
  
# Add all hydrogens  
obabel lig.sdf -O lig_prot.sdf -h
```



Sometimes protonating a nitrogen creates an asymmetric center. Make sure that you are selecting the most reasonable stereoisomer for the active center of your receptor.



3. Preparing the receptor.

- The receptor must be protonated. See:

[Building a system: general rules](#)

- A short energy minimization on the receptor will remove unfavorable crashes and make the docking more effective. This can be done in Chimera. Before doing this, make sure again that the receptor structure has been correctly prepared (disulfide bonds, histidines, etc.)

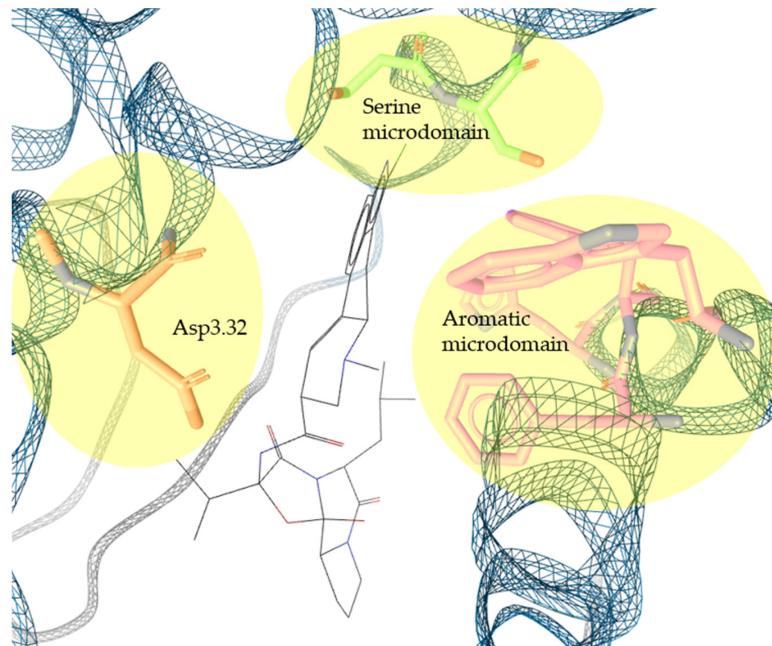
4. Docking with Vina.

- Follow the tutorial:

Basic docking — Autodock Vina 1.2.0 documentation

 https://autodock-vina.readthedocs.io/en/latest/docking_basic.html

- As they recommend, it is better to provide your own protonation for the receptor rather than using the `prepare_receptor -h` option.
- For me, using the **scoring function from AutoDock4 (ad4)** worked a lot better at ensuring that the salt bridge between the ligand and Asp3.32. This interaction is fundamental in some aminergic GPCRs, like D2R.



- Look in the bibliography for other canonical interactions that are important for ligand-protein binding.