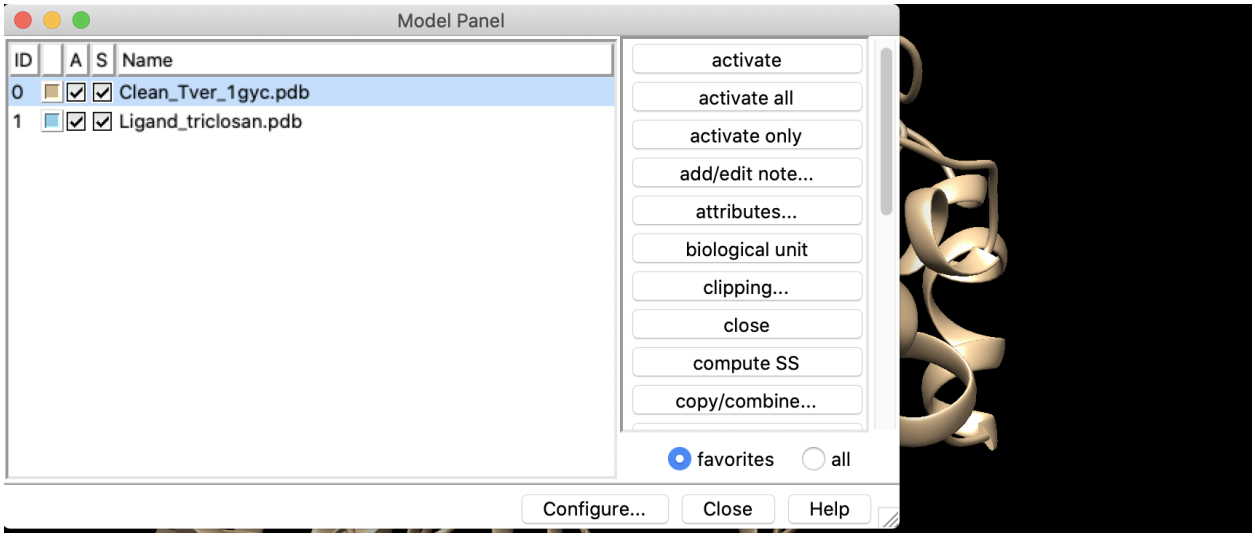
Step 1: Docking of ligand in active site

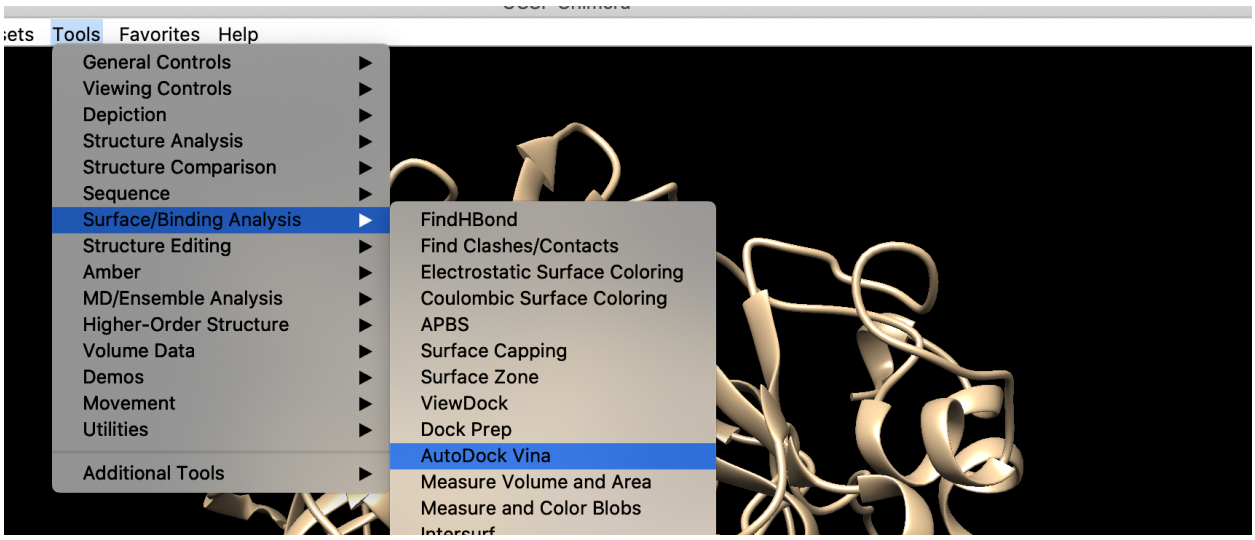
Autodock Vina + Chimera

Learned from https://www.youtube.com/watch?v=cLGQ-951FDk

1. First, download UCSF Chimera and autodock vina.
    a. If you are on a Mac, you have to go into security to allow your mac to run vina since it's from an unidentified developer from the internet
    b. Note the path of vina - it will look something like autodockvina/bin/vina. You will need this in the future
2. Get PDBs of your receptor and your ligand. Open both your receptor and your ligand in one chimera window. You can check this by going to favorites > model panel, and you should get the following window:

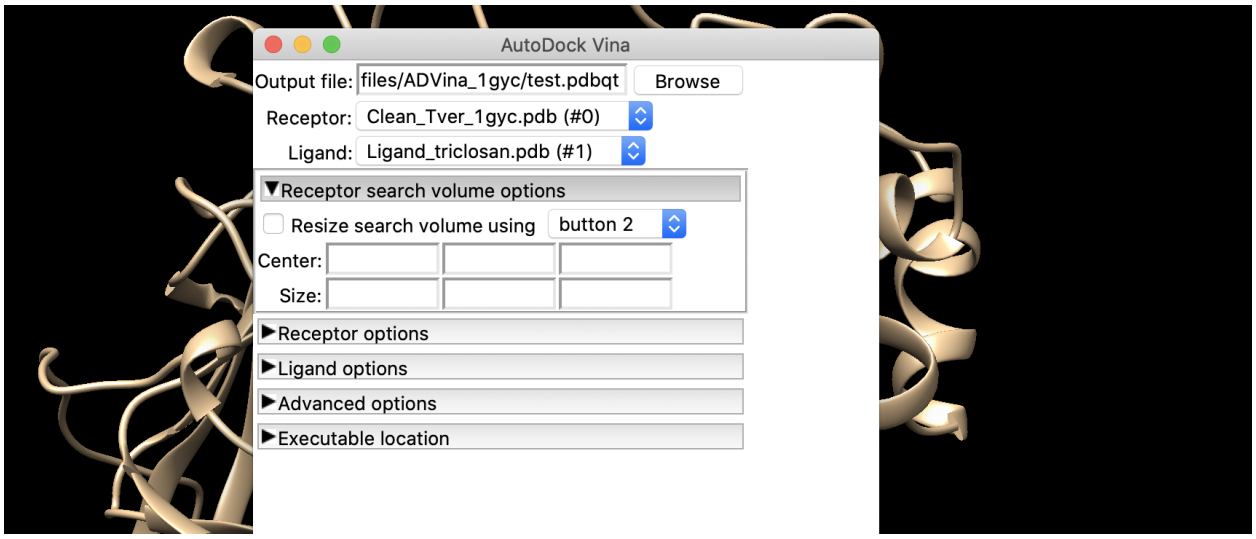


3. Navigate to tools>Surface/Binding Analysis>Autodock Vina.

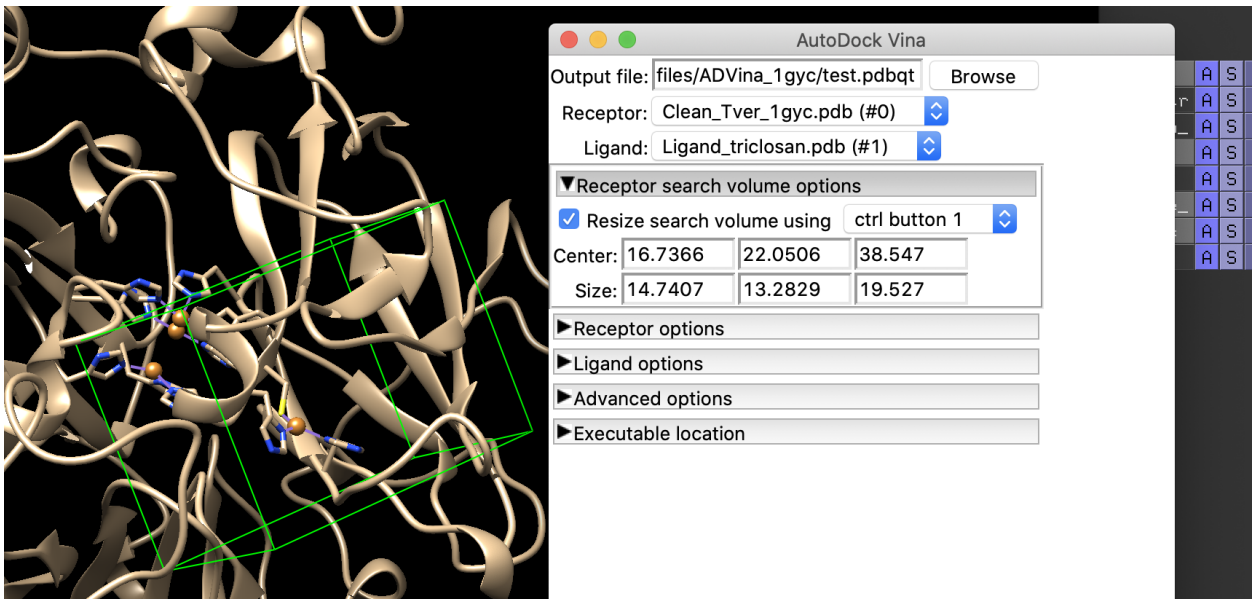


4. In the resulting window, specify the output file path via the browse button. It is advisable to create a new folder for each docking, because ADVina will generate many files. Select your receptor and ligand.

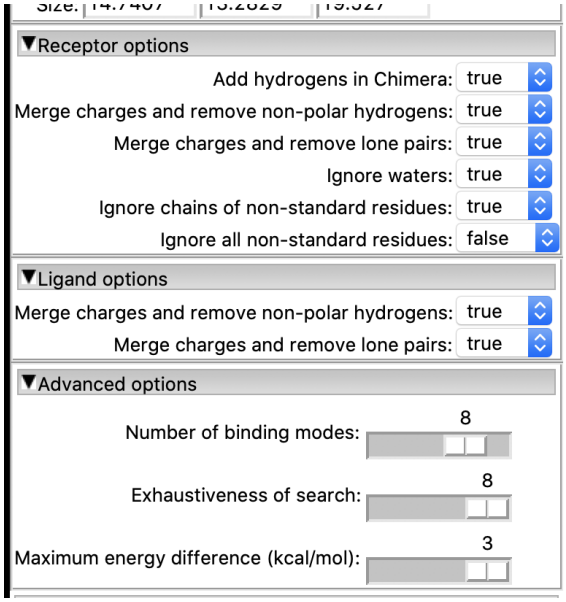
    Specifying the output file path is important, it's not enough to just type in a file name. Not sure why, but just typing in a file name without clicking the "Browse" button prevents the program from working. It throws Error 30 - something about a read only file.



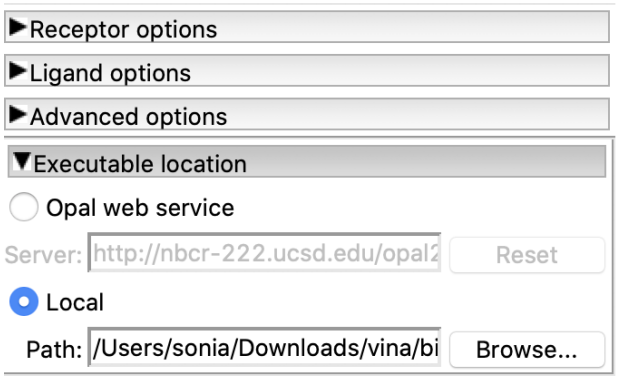
5. Check the "resize search volume…" button, and configure which button you want to press. I used control + b. Draw a box around the active site. Be sure to rotate the molecule around to check box size, and see box dimensions. Typical box sizes are 20x20x20. The larger the box, the longer the program has to run.



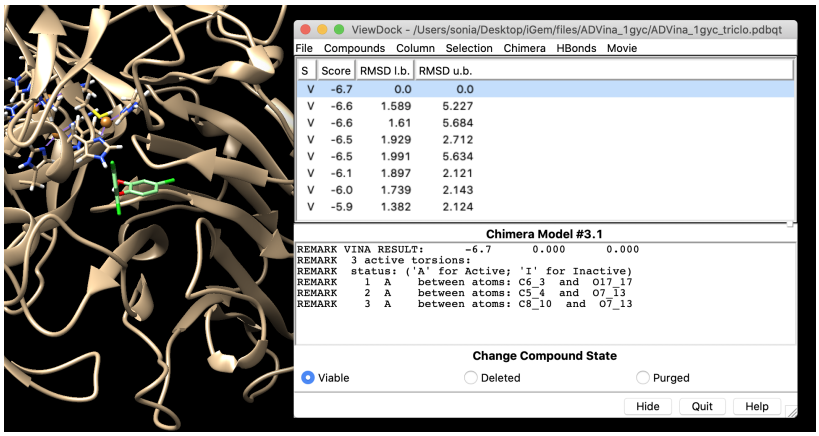
6. (optional) Receptor + ligand + advanced options can all be kept at default, but it's good to know what each category means. Or I guess they're all pretty intuitive - if you want to speed up the simulation run time then you can decrease binding mods + exhaustiveness of search.



7. Under executable location, make sure local is selected. There used to be an option to run docking on a remote web server, but [as of 2020 that has been deactivated](). Set that path in local to be the path to your vina program, as noted in step 1a.



8. Select ok. Wait a few moments, and the ligand should appear in the active site, along with a Viewdock module that shows the number of binding modes and corresponding energies. A more negative number means a better thermodynamic model



    a. Even if a binding mode is better thermodynamically, it is best to confirm the docking conformation with literature. If it's a difference of .something, then there isn't a big difference between each mode and the conformation that is most consistent with literature is best. In this example (1gyc + triclo), the version with -6.1 is best because the hydrogen is coordinated by histidine, which is what the electron transfer requires
9. In Chimera, click file>Save PDB. Specify save file path, and check "save multiple models as one PDB". Leave everything else as default
10. Open the saved PDB with multiple models in Pymol. At the bottom right corner of the screen, there is a section called "states", with an index such as 1/10 next to it. These are all the possible binding states that ADVina found. Use the buttons next to this section to run through and rewind through all possible states. You will notice a few things:
    a. The first state is just your receptor with no ligand.
    b. The next states show the ligand jumping around, but no protein is in sight
    c. The ligand may look very strange - select the ligand and show as spheres
11. To address 5.a and 5.b, add your input protein to Pymol and align it with the first state of ADVina. Now, as you move through all the states, the protein is still in view
12. Select the best state and same as a PDB. This is your final docked product. Congratulations!