<https://dock.compbio.ucsf.edu/>

<https://www.youtube.com/watch?v=m4ZI-UUwoyk>

Based on [this tutorial](https://ringo.ams.stonybrook.edu/index.php/2018_DOCK_tutorial_1_with_PDBID_2NNQ#I._Introduction)

The files you are looking for are located in $DOCK\_HOME/parameters/ (running echo $DOCK\_HOME will show you the full path).

**Prepping Files** (local)

**Checking the structure** (local)

1. Read the article related to the PDB file to understand protonation states, charges, environmental conditions and other important information regarding the receptor and the ligand.
2. Open the pdb file through chimera and look at the structure. Identify the main components of the model (receptor, ligand, solvent, surfactants, metal ions)
3. Carefully look to identify if there are any missing residues or missing loops. (This particular PDB file didn't contain any missing loops or missing residues)
   1. To fix missing sections (dashed lines): Tools → Surface Editing → Model/Refine Loops
      1. Loop modeling protocol: DOPE-HR
      2. non-terminal missing structure
   2. Save model as new PDB file

**Preparation of receptor** (local)

1. Isolate the receptor using the select tool and delete tool in Chimera/ChimeraX
2. Save the isolated receptor as a mol2 file.
   1. 2nnq\_rec\_noH.mol2
3. Open 2nnq\_rec\_noH.mol2
4. DockPrep each file: Tools -> Structure/Binding Analysis -> DockPrep
   1. Or do the following:
      1. Tools -> Structure Editing -> Add H (To add Hydrogen atoms)
      2. Tools -> Structure Editing -> Add Charge (To add the charge use the latest AMBER force field available for standard residues. Here we used AMBER ff14SB)
5. Save as mol2 file
   1. 2nnq\_rec\_withH.mol2

**Preparation of ligand** (local)

1. Open the PDB file via Chimera/ChimeraX
2. Using Chimera, isolate the ligand
3. add H atoms
4. add charge
5. save it as a mol2 file by following the same steps followed for the receptor
   1. 2nnq\_lig\_withH.mol2

**Generating receptor surface and spheres** (local+server/cluster)

**Preparation of DMS file** (local)

1. Open receptor with noH file with Chimera
2. Action -> Surface -> Show
3. Select the whole thing
4. Tools -> Structure Editing -> Write DMS
5. Save as 2nnq\_rec\_noH.dms into 2.surface\_spheres folder

**Generating spheres** (On Server/Cluster)

1. cd 2.surface\_spheres (folder)
2. Type vim INSPH
3. Type the following lines:

2nnq\_rec\_noH.dms

R

X

0.0

4.0

1.4

2nnq\_rec.sph

* 1. Note: The first line 2nnq\_rec\_noH.dms specifies the input file. R indicates that spheres generated will be outside of the receptor surface. X specifies all the points will be used. 0.0 is the distance in angstroms and it will avoid steric clashes. 4.0 is the maximum surface radius of the spheres and 1.4 is the minimum radius in angstroms.The last line 2nnq\_spheres.sph creates the sph file that contains clustered spheres.

1. Push “esc” to switch to normal mode
2. Type :wq + “enter” saves changes and quits Vim
   1. You will notice that the there is a file called “INSPH” now created
3. Generate spheres: sphgen -i INSPH -o OUTSPH
4. If successful, the output file should be created (2nnq\_spheres.sph)

**Selecting Spheres**

1. sphere\_selector 2nnq\_rec.sph /home/sjt3532/dockTutorial/tutorial1/1.dockprep/2nnq\_lig\_withH.mol2 10.0
   1. This command will select all of the spheres within 10.0 angstroms of the ligand and output them to selected\_spheres.sph. Visualize the selected spheres using Chimera to make sure the correct spheres are selected. Notice that, spheres around the ligand binding site are kept and all the other spheres are deleted in the image below.

**Generating box and grid**

**Generating box**

1. Create showbox.in file using nano in 3.boxgrid directory
2. Write the following in the file:

Y

8.0

/home/sjt3532/dockTutorial/tutorial1/2.surface\_spheres/selected\_spheres.sph

1

2nnq.box.pdb

* 1. Each line does the following:
  2. We intend to generate a box
  3. The box length should be 8 Angstroms
  4. Use the selected\_spheres file in the designated location
  5. Cluster #
  6. The name of the pdb output file that contains the generated box.

1. Generate the box: showbox < showbox.in
2. If successful, output file should be created (2nnq.box.pdb)
3. Create grid.in file using nano
   1. Enter the information in this file into the [grid.in file](https://docs.google.com/document/d/1LUbeJKJYVeIXs_4sxgA3WiDJzWxe8RtvZx11oEcIMQY/edit)
   2. Change what is highlighted in yellow
4. **Added step:** move vdw\_AMBER\_parm99.defn and chem.defn to working directory
5. Generate the grid: grid -i grid.in -o gridinfo.out
   1. Files generated (gridinfo.out, grid.nrg, grid.bmp)
   2. Note: Go through gridinfo.out file to make sure all the information about the receptor in the file matches with the original information of the receptor. (Eg:- Total charge, residues and their charges) If the information doesn't match, that means you have made an error in one of the steps that you followed so far.
6. If successful, output files should be created (gridinfo.out, grid.nrg, grid.bmp)

**Docking a single molecule for pose reproduction**

**Energy minimization**

1. cd 4.dock
2. Create min.in file using nano
   1. Enter the information in this file into the [min.in file](https://docs.google.com/document/d/1tK__xOYFuivCRtZlbipcA82apB9522KHiSTSQqPfbrY/edit)
   2. Change what is highlighted in yellow
3. dock6.mpi -i min.in
4. If successful, output file should be created (2nnq.lig.min\_scored.mol2)

**Complete one of the docking (Rigid, Fixed Anchor, or Flexible)**

**Rigid Docking**

1. Create rigid.in file using nano
   1. Enter the information in this file into the [rigid.in](https://docs.google.com/document/d/18ETU9Bzjt5LNZbAIrkPTKtt4uPH_U4pFsih0q_w4Hvc/edit), [RGD.in](https://docs.google.com/document/d/1pLnFX9dJDfrqG_X6QEMUedlr-zT6LqD7HWcy-u5fViM/edit)
   2. Change what is highlighted in yellow
2. dock6.mpi -i rigid.in
3. If successful, output file should be created (rigid.out\_scored.mol2)

**Fixed Anchor Docking**

1. Create fixed.in file using nano
   1. Enter the information in this file into the [fixed.in](https://docs.google.com/document/d/1CIjeYT9ET9RyGRXPRffQnr5dBM2q66RW5OVMUStStkM/edit), [FAD.in](https://docs.google.com/document/d/18voUdKIBQS85XyMFJgQE7hjZ0Vk36I4KavOaDE67Drc/edit)
   2. Change what is highlighted in yellow
2. dock6.mpi -i fixed.in
3. If successful, output file should be created (2nnq\_fad\_scored.mol2)

**Flexible Docking**

1. Create flex.in file using nano
   1. Enter the information in this file into the [flex.in](https://docs.google.com/document/d/1kcYuPitHpTBFGIYfXIsradznwCulbRVsuQGQz29bU2A/edit), [FLX.in](https://docs.google.com/document/d/1wdWobgTdBypkw4Qc6DOlBiXvfjB5KDWv8zDa9jfNHW4/edit)
   2. Change what is highlighted in yellow
2. dock6.mpi -i flex.in
3. If successful, output file should be created (flex.out\_scored.mol2)
   1. flex.out\_conformers.mol2 contains all of the poses, ranked

**Checking Docking Output**

1. Check output file (flex.out\_scored.mol2, rigid.out\_scored.mol2, 2nnq\_fad\_scored.mol2) using Chimera
   1. Open Chimera
   2. File -> Open -> 2nnq\_rec\_withH.mol2
   3. File -> Open -> 2nnq\_lig\_withH.mol2
   4. Tools -> Surface/binding Analysis -> ViewDock -> Select the Flexible Dock output file. (flex.out\_scored.mol2)
   5. In the loaded dialog box select Dock4,5 or 6
   6. Go to ViewDock window
      1. Column -> Show -> gridscore
      2. Column -> Show -> HA\_RMSDs
      3. Follow the same steps to get all the properties

**Molecular Footprint**

1. Cd 6.footprint
2. Create footprint.in file using nano
   1. Enter the information in this file into the [footprint.in](https://docs.google.com/document/d/1mof5ibShp9dUFJGGBd5GkJicdLBNsmAE3FOyymngB-Q/edit)
   2. Change what is highlighted in yellow
3. dock6.mpi -i footprint.in
4. If successful, the output files should be created (footprint.out\_footprint\_scored.txt, footprint.out\_hbond\_scored.txt, footprint.out\_scored.mol2)
5. Use [python script](https://ringo.ams.stonybrook.edu/~rizzo/StonyBrook/downloads/plot_footprint_single_magnitude.py) to visualize the molecular footprint: [plot\_footprint\_script.py](https://docs.google.com/document/d/11ukltFVnidUaS3teBA50Iww1kZuz-Pe0y6_n8WfSKao/edit)
6. Run the script python plot\_footprint\_script.py footprint.out\_footprint\_scored.txt 50

**Virtual Screen**

1. Cd 7.virtual\_screen
2. Create virtual.in file using nano
   1. Enter the information in this file into the [virtual.in](https://docs.google.com/document/d/17763ayLp_A6FybWYRT7I41tpi7aDE0gftlAzK2WxaLo/edit)
   2. Change what is highlighted in yellow
3. dock6.mpi -i virtual.in

**Notes:**

* For “Write DMS” ensure that you select the molecules before writing DMS

**Problems**