Ensemble Docking Project

Receptor Ensemble Preparation

1) Login to the Linux partition using previous directions.
2) Install software
    a. Go to http://mgltools.scripps.edu/downloads
    b. Download mgltools_i86Linux2_1.5.6.tar.gz
    c. Open a terminal
        ~> tar xzvf mgltools_i86Linux2_1.5.6.tar.gz
        ~> cd mgltools_i86Linux2_1.5.6
        ~> ./install.sh
3) Get files needed for project
    a. Click on terminal icon on top left of the screen
    b. In terminal type
        ~> wget http://cmb.ornl.gov/~sek/kraken_project.tgz
        ~> tar xzvf kraken_project.tgz
        ~> cd ~/kraken_project
        ~> ls

4) Change script to point to installed software from step 1. gedit is a regular text editor. Call it from the command line with the name of the script you need to change. Adding the & sign allows for you to continue using the terminal with gedit open. Save file after changes are made.

    ~> gedit scripts/prep_receptors.py &

    scroll to the second occurrence of **projectDir+'scripts**
    and change to

    '/home/bcmb422/mgltools_i86Linux2_1.5.6/bin

5) Go to the following website in order to extract snapshots:
    http://nbcr-222.ucsd.edu/opal2/dashboard?command=serviceList

6) Click on GROMOS Clustering
    a. Enter your email address
    b. Select trajectory file 2src-vmd-H-wb-delBwat-0.1M-pro-out-step100ps-100ns-superposed.pdb.gz
    c. Select binding site file src_binding_site.pdb.gz
    d. Choose between gromos (0.2 or 0.175 cut-off) and linkage (0.15 or 0.14 cut-off) clustering methods

e. When complete, open the clusterid file and record the id numbers

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f. Use the back arrow key on the browser and click on the cluster_frames directory link
g. Click on each file to download
h. Move the files to the project directory

~> mkdir pdb
~> mv ~/*frame_* pdb

7) Prepare pdbqt files

~> cd pdb
~> python ../scripts/prep_receptors.py

this should have made a directory called receptors which contains the pdbqt files for each pdb file

~> cd ../receptors
~> ls

we also want to include the crystal structure

~> mv ../src.pdbqt .

8) Create the receptors.txt parameter file. In order to do this, we need a method for selecting the box center. We will use four different atoms on different sides of the cocrystalized ligand.

VAL 281 CG1
LEU 393 CD1
GLN 275 O
MET 341 N

We also need to select the box size. The cocrystalized ligand measures over 18 Å in length. Therefore, we will use a box that just fits the ligand and one with a little extra room: 20 Å and 30 Å.

Use your set of parameters as input for the script as follows:

~> python ../scripts/make_rec_param.py VAL_281_CG1 30

replace the last two parameters with your assigned values (make sure to use underscores in the atom parameter and not spaces).

~> cd ..
~> less receptors.txt

9) Put files needed for Kraken in a directory, archive it and save to a USB or email to self. We will have to log back into Windows to transfer files to Kraken since you do not have direct ssh access.

   ~> mkdir src_screen
   ~> mv receptors/ src_screen/
   ~> mv receptors.txt src_screen/
   ~> tar czvf src_screen.tgz src_screen/

   Now save to USB or email to self. Also, email to sellings@utk.edu (this will be part of your grade).

Setting-up and Starting Job on Kraken

1) Upload src_screen.tgz to your scratch space on Kraken. (directions to transfer files are on the class website http://cmb.ornl.gov/~sek/bcmb422.html)

   ~> cd $CUE_SCRATCH
   ~> tar xzvf src_screen.tgz
   ~> cd src_screen

2) Get ligands files for the screen

   ~> cp /lustre/scratch/proj/bcmb422/kraken_project/src/ligands.tgz .
   ~> cp /lustre/scratch/proj/bcmb422/kraken_project/src/ligands_sort.txt .
   ~> tar xzvf ligands.tgz

3) Get submission file for job

   ~> cp /lustre/scratch/proj/bcmb422/kraken_project/src/submit_job.pbs .
   ~> vi submit_job.pbs

   a. press i to go into insert mode
   b. if you have a 10 snapshot screen instead of a 4 snapshot screen, increase the number of processors, use arrow keys to navigate cursor to size=1800 and replace 1800 with 3600
   c. scroll down with the arrow keys, delete my email address and replace with yours
   d. if you changed the number of processors in b. change the –n flag for aprun from 300 to 600
   e. if you have 11 receptors in your screen (10 snapshots plus the crystal structure) then change the number of receptors parameter from 5 to 11

f. press esc key and type :wq

4) Submit job

~> qsub submit_job.pbs

5) When you receive an email from root@kraken.nics.utk.edu notifying you that your job completed, forward to sellings@utk.edu.

6) When the job is complete, archive the files

~> tar czvf out.tgz out/

7) Download out.tgz and save to USB

Analyzing Results

1) Save out.tgz (from a file browser) to the kraken_project directory and unarchive

~> cd ~/kraken_project
~> tar xzvf out.tgz

2) Create a sorted list of all of the results

~> cd out
~> python ../scripts/postdocking_vina.py
~> less sorted_results

3) Make enrichment documents for each receptor in the screen

~> cd ..
~> mkdir analysis
~> mv out/sorted_results analysis/
~> cd analysis/
~> python ../scripts/enrichment_all.py ../src_screen/receptors.txt
~> ls

4) Make the enrichment graph

a. Open the file ~/kraken_project/scripts/plots in a text editor and change the file names to the ones for your screen and add entries if you had a larger screen

~> gnuplot ../scripts/plots

b. In a file browser, navigate to ~/kraken_poject/analysis/ and double click on

src_screen.eps to open in a viewer.

PowerPoint Slides

Put your src_screen.eps graph in a powerpoint slide. Include on your slide your name, clustering method, cut-off value, atom at center of box, and size of box. On a second slide add your interpretation of the results.

Send slides to me by email at sellings@utk.edu before April 26th at 11:59 pm.