Tutorial: Advanced docking and scoring

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Freeware programs:
Autodock Vina: http://vina.scripps.edu/
Autodock Tools: http://mgltools.scripps.edu/

Advice and Tutorials:
https://pymolwiki.org/

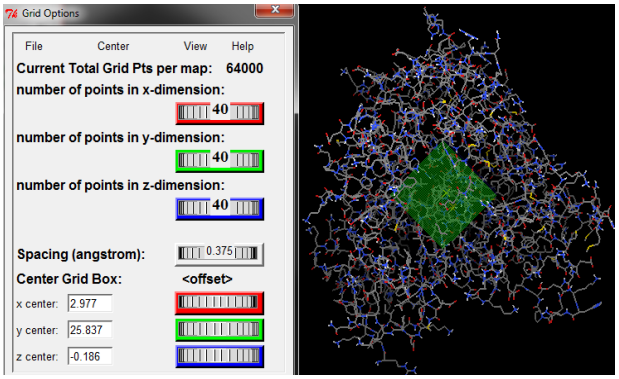
Task: Dock tetra-brominated inhibitor into casein kinase II enzyme

Preparation for Docking in PyMOL

Step	Menu	Command line
Load Structure		
1	File/Save Session As (.pse)	File/Log – Save (.pml)
2	Plugin/PDB Loader Service – Code 1J91	fetch 1J91
3	Sequence (S bottom right corner), Scroll to ligand	
4	Left/right mouse click – zoom	zoom organic
5	-- show/sticks	show sticks, organic
Analyze Structure	Wizard/Measurement – Polar Neighbors/In All Objects	
6	Selecting (bottom right corner):Atoms vs. Residues	
7	Click on ligand and waters around/Done	
Save Receptor		
8	Drag/Scroll over protein sequence	select **prot**, resi x-y **(prot=name of variable)**
9	File/Save molecule/sele > 1J91_prot.pdb	save 1J91_prot.pdb, sele **(sele = name of selection)**
Protonate and Save Ligand		
10	Console (Top righ corner)/Builder/AddH	
11	Select ligand on Sequence, File/Save Molecule sele > 1J91_lig.pdb	save 1J91_lig.pdb, resn ligand
Saving Work		
	File/Save Session As (.pse)	File/Close Log View .pml in WordPad

Preparation for Docking in AutoDock Tools
http://autodock.scripps.edu/

Protein preparation (with and without Wat 339* as part of receptor*)
Start/All Programs/MGL Tools/AutoDockTools
File >> Read Molecule >> 1J91_prot.pdb
Edit >> Hydrogens >> Add >> Polar Only
Grid >> Macromolecule >> Choose >> 1J91_prot >> Select
Save 1J91_prot.pdbqt
Ligand >> Input > Open (All Files) > 1J91_lig.pdb



Adjust grid size (!numbers may differ!)
Grid >> Grid Box
Column L: unclick (hide) prot
Number of points: 50, 50, 50
Spacing: 1.0
Center Grid Box: 4.5; -2.944; -5.25
File/Close Saving Current

Ligand preparation
Reset View (5th icon, top left corner)
Check rotatable torsions
Ligand >>Torsion Tree >> Choose Torsions…
Shift click to change status
Revert to two RotBonds
Done
Ligand >> Output >> Save as pdbqt

Docking with Autodock Vina
http://vina.scripps.edu/manual.html#contents

Copy **vina.exe** into the same directory as both pdbqt files *(e.g. Desktop)*
Open **cmd** program *(type cmd into the search field in Windows start panel)*
Go to directory with files *(e.g. cd Desktop)*
Other commands *("cd .." means go directory up; "dir" means list entries in directory)*
Type **vina.exe** to see help *(Tab key will fill up name of file)*
Either it is possible to fill in all parameters in one long line or within config file *(config.txt)*

Docking parameters file – config.txt
#Inputs
```
receptor = ./1J91_prot.pdbqt
ligand = ./1J91_lig.pdbqt
```
#Outputs
```
out    = 1J91-nowat-Vina.pdbqt
log    = 1J91-nowat-Vina.log
```
#Box center
```
center_x = 4.500
center_y = -2.944
center_z = -5.250
```
#Box size
size_x = 50
size_y = 50

size_z = 50
#Parameters
exhaustiveness = 8
seed = 123456

Autodock Vina Docking
Go to working directory using **cmd** program
Run command: **"vina.exe --config config.txt"**
Docking should take ca. 10 s *(Progress is shown with stars)*
Predicted affinity and RMSD to the first predicted pose are printed *(same info is in log file)*

Analyse results in PyMol
File/Open (All Files) vina.pdbqt
Arrows (bottom right corner) to scroll through poses

View the .log file
- Scores as affinity estimation
- RMSD as geometric criteria of similarity

Questions:
1) Which pose is the closest to the crystal (visual inspection)
2) What is its score?
3) How many groups of docking solutions are there?
4) What distinguishes them?

--- Docking with halogen bond (workaround): change the sign of partial charges of bromine atoms in lig.pdbqt to positive
--- Flexible docking – allow protein side chain move
Compare poses with the native binding mode