



## Computer Lab, Session 7





Download Thrombin\_VS.tar.gz from course website to Lab7 folder.

Unzip and untar file:

tar zxf Thrombin\_VS.tar.gz

Change into Thrombin\_VS folder:

cd Thrombin\_VS

and open all mol2 files in PyMOL:

pymol \*.mol2

Generate ligand library (as in Lab6):

AutoDockVina → Export ligand library and save as *Thrombin\_VS* library

Next, perform docking with similar settings as in Lab6 (use again Lab6 0.pse file for protein template):





		AutoDockVina Plugin	×						
		Choose target protein and ligand library for AutoDock simulation							
Project definition name									
Base directory		/home/student/Desktop/CADD_Lab/Lab8	Browse						
Project subdire	ctory:	project_VS							
Ligand library									
Path to ligand library:									
But in a lasting	,								
Protein selection									
Protein from file	Protein from file [PDB,MOL2,MOL]								
Path to protein file:	Path to protein file: Full path to protein file Sea								
File containing multiple protein structures [NMR-PDB]									
Path to protein file:	Full pa	th to protein file	arch and Import						
Trajectory from	Amber -								
Path to topology file:	Full	path to .top file	Search and Import						
Path to trajectory file	: Full	path to .trj file	Search and Import						
→ Protein in current PyMol session —									
Objects to select from: • 1 MU6									
Protoin propagation									
Protein preparation Let autodock change protonation states									
		OK Cancel							





			Αι	utoDoo	:kVina	Plugin					
earch volume   Fle	exible re:	sidues	Outpu	ut settin	gs						
Center of box											
— Definition based o	n x,y,z	coordina	tes —								
_						17.1					
Center (x):	-10.0		0.0		10.0		20.0		30.0		
-	-10.0			13.7	10.0	•	20.0		30.0		
Center (y):				13.7							
	-30.0	-2	0.0	-10	.0	0.0		10.0		20.0	
							23.1				_
Center (z):	-10.0	п	1.0	10.	n	20.0		30.0		40.0	
	Selection	n  sele			Det	termine i	iew box	coordir	iates		
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Size of box ———————————————————————————————————	0.0 0.0	10.0	23.0 20.0 19.0 20.0	30.0	40.0	50.0	60.0	70.0	80.0	90.0	
Size of box  Definition based o  Box length (x):  Box length (y):	on x,y,z o	coordina 10.0 10.0	23.0 20.0 19.0 20.0	30.0	40.0	50.0	60.0	70.0	80.0		
Size of box —  Definition based of Box length (x):  Box length (y):  Box length (z):  Definition based of	0.0 0.0	10.0 10.0 10.0 selection	23.0 20.0 19.0 20.0 18.0 20.0	30.0 30.0 30.0	40.0	50.0 50.0	60.0	70.0 70.0 70.0	80.0 80.0	90.0	
Size of box  Definition based o  Box length (x):  Box length (y):  Box length (z):	0.0 0.0	10.0 10.0 10.0 selection	23.0 20.0 19.0 20.0 18.0 20.0	30.0 30.0 30.0	40.0	50.0 50.0	60.0	70.0 70.0 70.0	80.0 80.0	90.0	ensions
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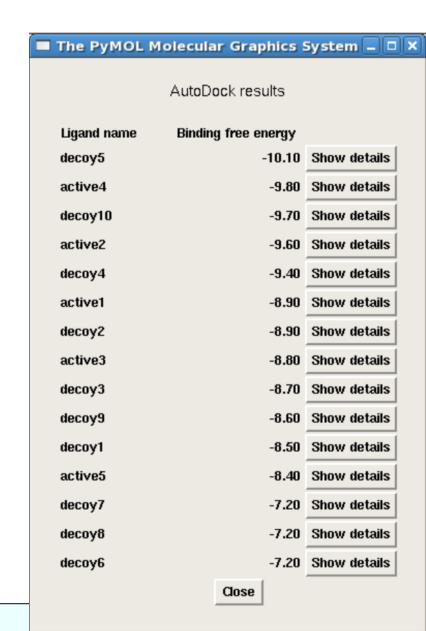




After docking simulations are finished import results:

AutoDockVina → Import results select Monitor.aut in folder project VS client

For statistical analysis: Open Excel
Create Excel table with the following
format using the AutoDock Results
dialog:



MCMP 690 5





#### Excel table:

Active or decoy in ranked list	Rank %	Actives found at rank %	Ideal	Random
	0	0	0	0
0	6.666666	=# of actives in first column*100/5	20	6.666666
1	13.33333		40	13.33333
0	20.00000		60	20.00000

Plot "Actives found at rank %", "Ideal", "Random" as a function of "Rank %" and compute enrichment factor at 0, 6.66666%, 13.3333%, ...



#### Discussion



#### Case study (**Use software from course**):

Based on the crystal structure of a thrombin-ligand complex (1mu6) you have virtually screened a library of 10000 compounds using Autodock Vina with a single solution as output. You want to identify possible new lead structures and optimize their binding affinity.

Please, discuss the following issues:

- 1. Propose ideas to validate the outcome of your screen; in particular, how can you decide how many compounds from the top-ranked list you should consider as possible active compounds? How can you refine the outcome of the screen?
- 2. Plan a possible strategy to optimize the affinity of the lead compound using discussed software. Take into consideration a reasonable balance between accuracy and efficiency.