Autodock Vina tutorial

Master Bioinformática Universidad de Valencia
13-05-2013

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Hands on...

- We will :
  - Predict the binding site for a given protein structure.
    - Using Metapocket2 .
  - Dock a small molecule (inhibitor) into the predicted binding site.
    - Using Autodock Vina.
  - Visualize the ligand POSE. Creating a complex with the inhibitor and the protein.

https://www.dropbox.com/s/96xrk0vy6s0658e/valencia_docking.tar.gz

First steps...

- Visualize the protein structure with pymol.

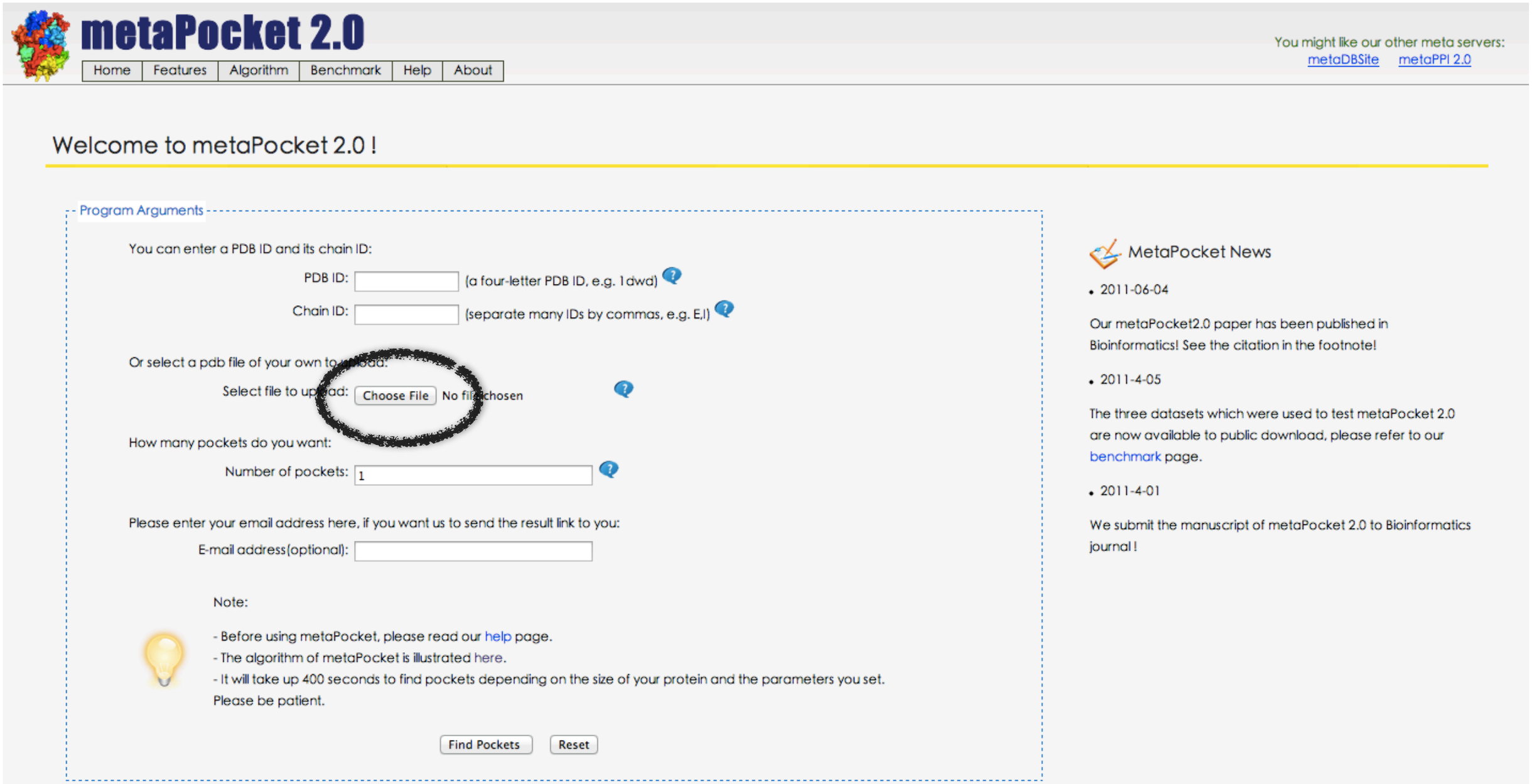
```
>pymol /path_to_directory/receptor.pdb
```

- Show the structure as cartoons. (With secondary structure representation). In Pymol.

show as -> cartoon.

- Is there a putative binding pocket?

Predicting the binding



Retrieving the top predicted binding site...

4. Potential ligand binding sites HELP

The potential 1 ligand binding sites in your protein:

HEADER binding site ID: 1

RESI	ILE_A^203^	PRO_A^205^	GLY_A^206^	LEU_A^207^	GLY_A^208^
RESI	TYR_A^202^	LEU_A^204^	ASP_A^209^	MET_A^142^	ASN_A^198^
RESI	ALA_A^210^	GLY_A^201^	ALA_A^144^	GLY_A^211^	LYS_A^200^
RESI	ALA_A^81^	PRO_A^141^	ARG_A^80^	THR_A^145^	ARG_A^105^
RESI	ASP_A^140^	ILE_A^143^	VAL_A^113^	MET_A^117^	LEU_A^79^
RESI	PHE_A^215^	ALA_A^146^	THR_A^148^	LYS_A^111^	GLU_A^112^
RESI	GLY_A^110^	SER_A^147^	GLU_A^107^	ASP_A^109^	ILE_A^78^
RESI	ALA_A^103^	PRO_A^114^	VAL_A^108^	MET_A^149^	TYR_A^122^
RESI	SER_A^104^	VAL_A^119^	ASP_A^116^	VAL_A^106^	ASP_A^118^
RESI	GLY_A^102^	ILE_A^101^	ASN_A^199^		

Download files of potential binding sites:

A python script to visualize the protein structure and potential binding sites using PyMOL.

(**Note: Please make sure to download all the following files to the same folder before to run this script.)

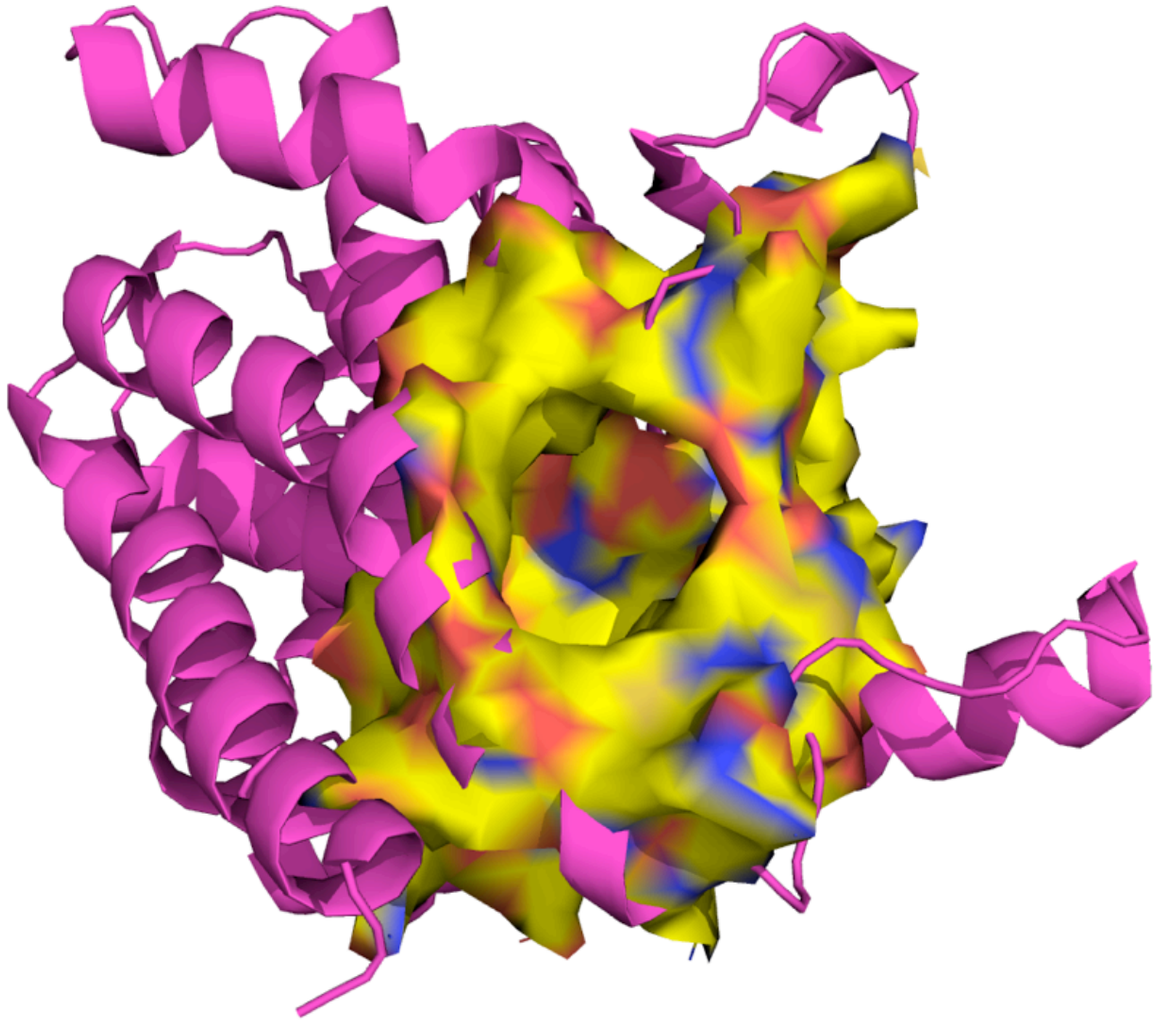
The potential binding atoms of top 1 binding sites (PDB format).

The potential binding atoms of all the binding sites (PDB format).

The potential binding residues of top 1 binding sites (PDB format).

The potential binding residues of all the binding sites (PDB format).

Visualizing predicted binding site + protein structure



Getting the binding site Center of Mass

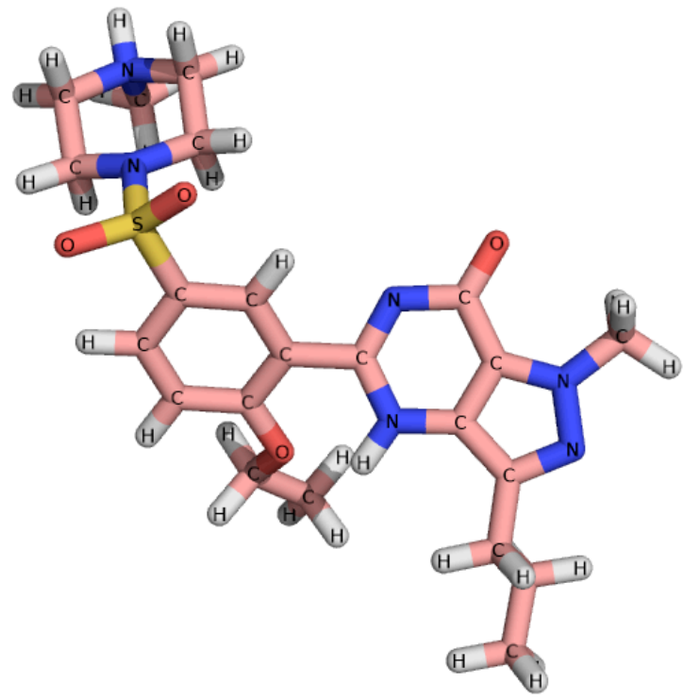
- In pymol there is a plugin that calculates the CoM of an certain region.
http://www.pymolwiki.org/index.php/Center_of_mass

- In our case, the plugin is not installed but the point is :

X: 28.035454 Y:119.400581 Z:9.578382

Exploring the ligand...

- Visualize the ligand in pymol.
- File -> open -> ligand.mol2
- Show as -> sticks.
- Label -> Atom name.



Preparing the ligand for docking...

- Open Autodock Tools.
- Ligand -> Input -> Open -> ligand.mol2
- Ligand -> Torsion Tree -> Choose Torsion (Default).
- Save the *.pdbqt file in your working directory.
- **Remember!**, we have to measure the ligand size.
- Display -> Measure -> Distance. (~15 Å).

Preparing the receptor...

- Grid -> macromolecule -> Open -> receptor.pdb
- Save the *.pdbqt file in your working directory.
- Visualize as ribbons.
- Grid center: Center of Mass.
- Grid -> Grid Box.

X: 28.035454 Y:119.400581 Z:9.578382

- Grid size : double of the ligand size. (~30 Å).

Setting the config file for vina...

receptor = path_to_receptor.pdbqt
ligand = path_to_ligand.pdbqt
out= path_to_out_file.pdbqt
log= path_to_log_file.txt
center_x= X
center_y = Y
center_z= Z

num_models = Num_models
exhaustiveness= 8

size_x = 30
size_y = 30
size_z = 30

```
>vina --help_advanced
```

```
fran@davide-desktop:~/Documents/master_valencia$ ./vina --help_advanced
Input:
  --receptor arg        rigid part of the receptor (PDBQT)
  --flex arg            flexible side chains, if any (PDBQT)
  --ligand arg          ligand (PDBQT)

Search space (required):
  --center_x arg        X coordinate of the center
  --center_y arg        Y coordinate of the center
  --center_z arg        Z coordinate of the center
  --size_x arg          size in the X dimension (Angstroms)
  --size_y arg          size in the Y dimension (Angstroms)
  --size_z arg          size in the Z dimension (Angstroms)

Output (optional):
  --out arg             output models (PDBQT), the default is chosen based on
                        the ligand file name
  --log arg             optionally, write log file

Advanced options (see the manual):
  --score_only                                score only - search space
                                              can be omitted
  --local_only                                do local search only
  --randomize_only                            randomize input, attempting
                                              to avoid clashes
  --weight_gauss1 arg (=-0.035579)            gauss_1 weight
  --weight_gauss2 arg (=-0.005156)            gauss_2 weight
  --weight_repulsion arg (=0.84024500000000002)     repulsion weight
  --weight_hydrophobic arg (=-0.035069000000000003) hydrophobic weight
  --weight_hydrogen arg (=-0.58743900000000004)     Hydrogen bond weight
  --weight_rot arg (=0.058459999999999998)          N_rot weight

Misc (optional):
  --cpu arg                   the number of CPUs to use (the default is to try to
                              detect the number of CPUs or, failing that, use 1)
  --seed arg                  explicit random seed
  --exhaustiveness arg (=8)   exhaustiveness of the global search (roughly
                              proportional to time): 1+
  --num_modes arg (=9)        maximum number of binding modes to generate
  --energy_range arg (=3)     maximum energy difference between the best binding
                              mode and the worst one displayed (kcal/mol)

Configuration file (optional):
  --config arg          the above options can be put here

Information (optional):
  --help                display usage summary
  --help_advanced       display usage summary with advanced options
  --version             display program version
```

Run Vina!!

```
>vina --config=/path_to_config_file/config.txt
```

```
fran@davide-desktop:~/Documents/master_valencia$ ./vina  --config=config_2.txt
###############################################################
# If you used AutoDock Vina in your work, please cite:        #
#                                                             #
# O. Trott, A. J. Olson,                                      #
# AutoDock Vina: improving the speed and accuracy of docking  #
# with a new scoring function, efficient optimization and     #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                     #
#                                                             #
# DOI 10.1002/jcc.21334                                       #
#                                                             #
# Please see http://vina.scripps.edu for more information.    #
###############################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1305734982
Performing search ...
0%   10   20   30   40   50   60   70   80   90   100%
|----|----|----|----|----|----|----|----|----|----|
**********************************
```

Analyze the output...

>more log_file.txt

```
#################################################################
# If you used AutoDock Vina in your work, please cite:          #
#                                                               #
# O. Trott, A. J. Olson,                                        #
# AutoDock Vina: improving the speed and accuracy of docking    #
# with a new scoring function, efficient optimization and       #
# multithreading, Journal of Computational Chemistry 31 (2010)  #
# 455-461                                                       #
#                                                               #
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#                                                               #
# Please see http://vina.scripps.edu for more information.      #
#################################################################

WARNING: The search space volume > 27000 Angstrom^3 (See FAQ)
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1305734982
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -9.4      0.000      0.000
   2         -9.3      1.716      2.266
   3         -9.1      4.545      8.194
   4         -9.1      6.205      8.979
   5         -9.1      3.806      8.467
   6         -9.0      3.756      7.807
   7         -8.9      2.479      4.540
   8         -8.9      2.492      3.125
   9         -8.8      2.300      3.561
  10         -8.7      8.711     11.420
  11         -8.7      1.843      2.343
  12         -8.6      4.321      8.198
  13         -8.6      2.421      3.471
  14         -8.6      2.246      3.591
  15         -8.4      5.066      8.604
  16         -8.4      2.579      3.888
  17         -8.0      2.929      4.943
  18         -7.9      2.722      4.951
Writing output ... done.
```
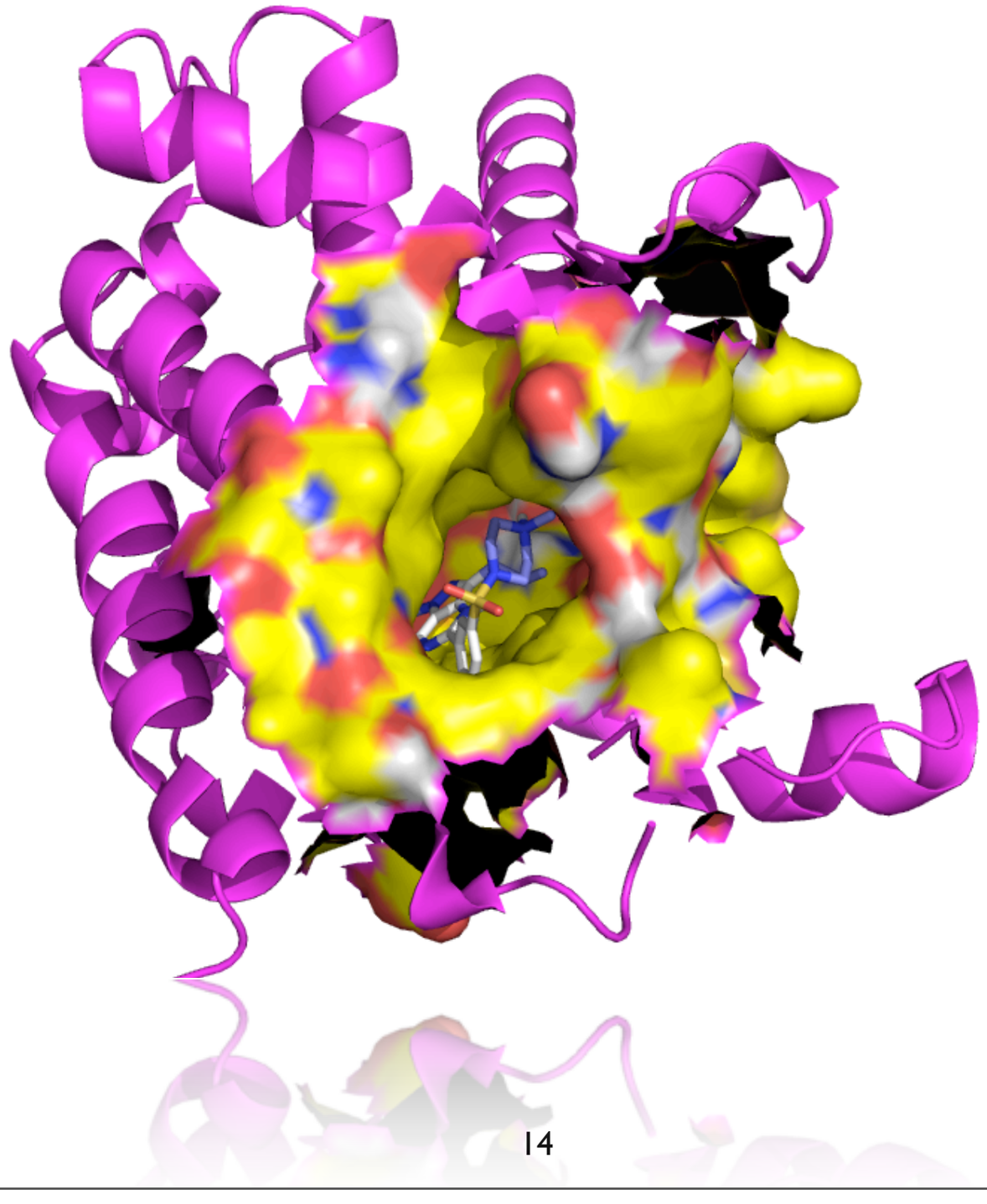
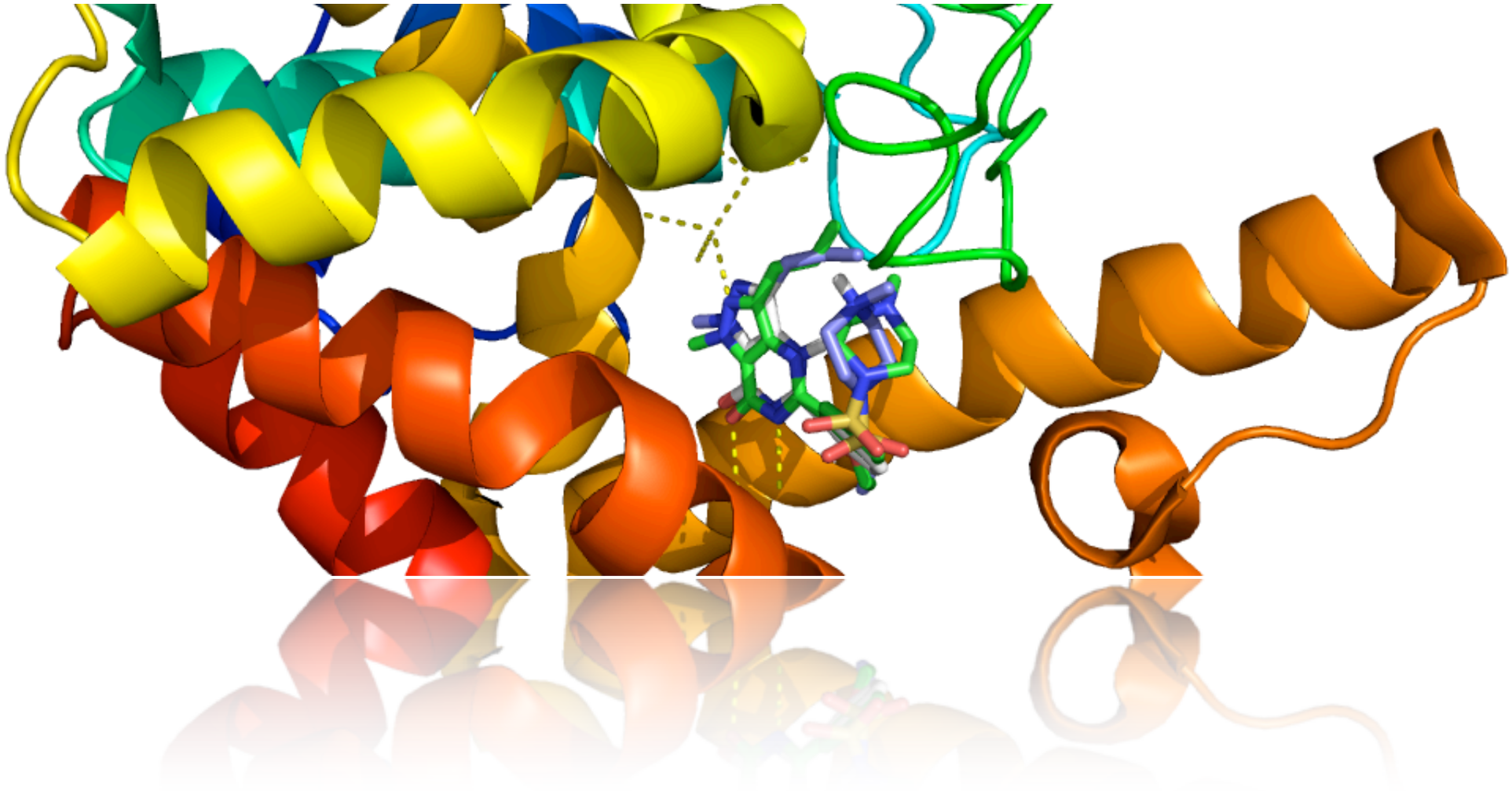

Visualize the output...

```
>pymol receptor.pdb out_docking.pdbqt
```



How good are our solutions?

```
pymol - Open -> Solutions/receptor_ligand.pdb
```



But... What is our complex?

Let´s figure it out !

:)