Hands-on tutorials of AutoDock 4 and AutoDock Vina

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AutoDock

http://autodock.scripps.edu

AutoDock is a suite of automated docking tools. It is designed to predict how small molecules, such as substrates or drug candidates, bind to a receptor of known 3D structure.

AutoDock 4.2

Morris, G. M., Huey, R., Lindstrom, W., Sanner, M. F., Belew, R. K., Goodsell, D. S. and Olson, A. J. (2009) Autodock4 and AutoDockTools4: automated docking with selective receptor flexiblity. *J. Computational Chemistry* 2009, **16**: 2785-91.

AutoDock 3 & 4

Morris, G. M., Goodsell, D. S., Halliday, R.S., Huey, R., Hart, W. E., Belew, R. K. and Olson, A. J. (1998), Automated Docking Using a Lamarckian Genetic Algorithm and and Empirical Binding Free Energy Function *J. Computational Chemistry*, **19**: 1639-1662.

AutoDock 4 Scoring Function

Huey, R., Morris, G. M., Olson, A. J. and Goodsell, D. S. (2007), A Semiempirical Free Energy Force Field with Charge-Based Desolvation *J. Computational Chemistry*, **28**: 1145-1152.

AutoDock 2.4

Morris, G. M., Goodsell, D. S., Huey, R. and Olson, A. J. (1996), Distributed automated docking of flexible ligands to proteins: Parallel applications of AutoDock 2.4 *J. Computer-Aided Molecular Design*, **10**: 293-304.

AutoDock 1

Goodsell, D. S. and Olson, A. J. (1990), Automated Docking of Substrates to Proteins by Simulated Annealing *Proteins:Structure, Function and Genetics.*, **8**: 195-202.

AutoDock 4 is free and is available under the GNU General Public License.

AutoDock Vina

http://vina.scripps.edu/

AutoDock Vina: Improving the Speed and Accuracy of Docking with a New Scoring Function, Efficient Optimization, and Multithreading

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Department of Molecular Biology, The Scripps Research Institute, La Jolla, California

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Published online 4 June 2009 in Wiley InterScience (www.interscience.wiley.com).

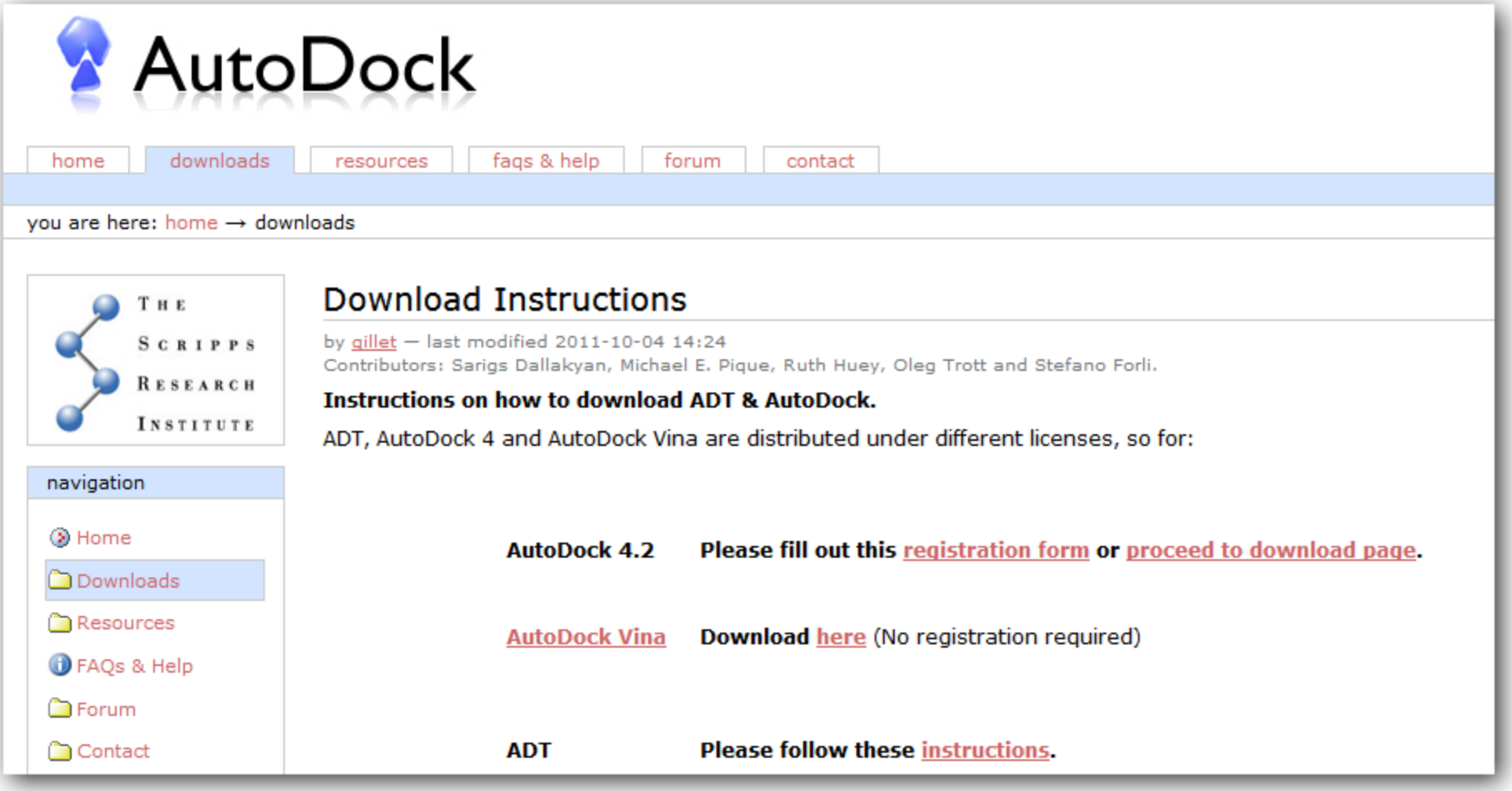
Abstract: AutoDock Vina, a new program for molecular docking and virtual screening, is presented. AutoDock Vina achieves an approximately two orders of magnitude speed-up compared with the molecular docking software previously developed in our lab (AutoDock 4), while also significantly improving the accuracy of the binding mode predictions, judging by our tests on the training set used in AutoDock 4 development. Further speed-up is achieved from parallelism, by using multithreading on multicore machines. AutoDock Vina automatically calculates the grid maps and clusters the results in a way transparent to the user.

 J Comput Chem 31: 455–461, 2010

Because the scoring functions used by AutoDock 4 and AutoDock Vina are different and inexact, on any given problem, either program may provide a better result.

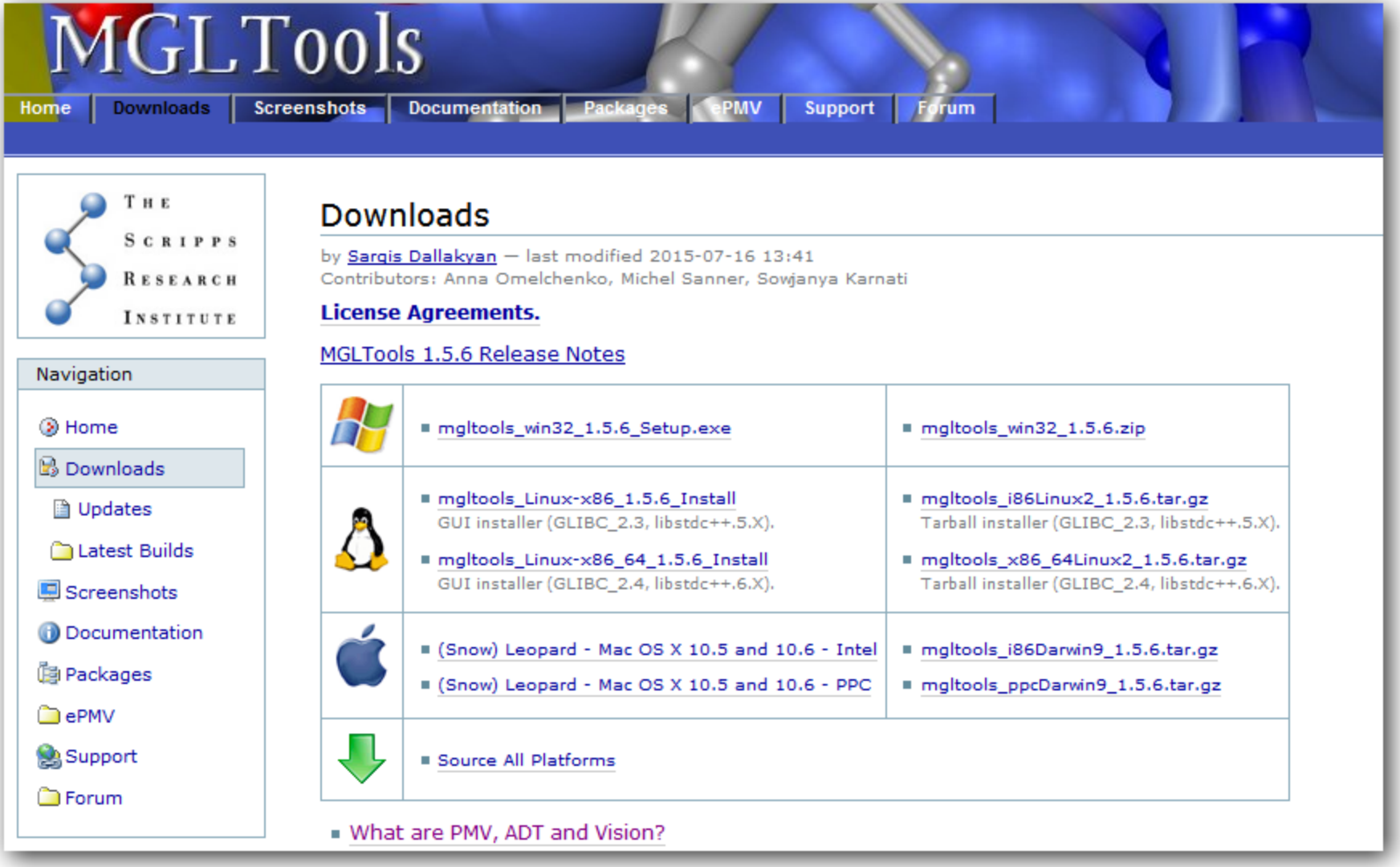
AutoDock Vina is available under the Apache license, allowing commercial and non-commercial use and redistribution.

http://autodock.scripps.edu/downloads



These programs were installed on VM.

http://mgltools.scripps.edu/



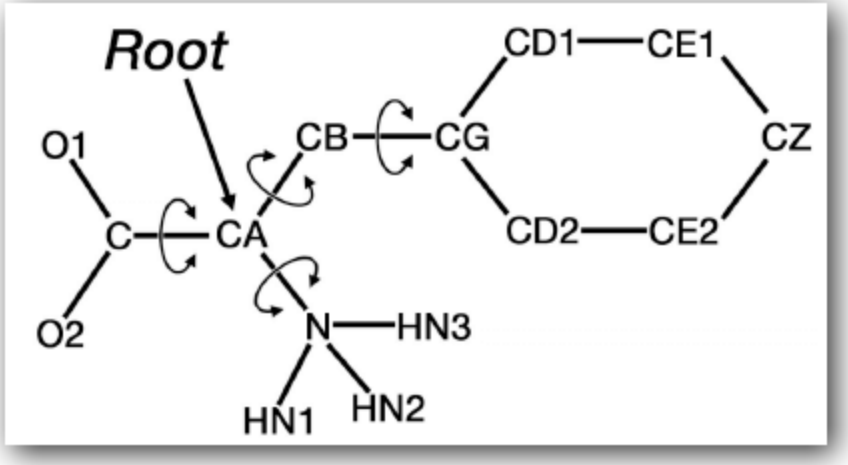
AutoDockTools (ADT) is developed to help set up the docking. ADT is included in **MGLTools** packages.

In general, each docking (AutoDock 4 and/or AutoDock Vina) requires:

1. structure of the receptor (protein), in pdbqt format
2. structure of the ligand (small molecule, drug, etc.) in pdbqt format
3. docking and grid parameters (search space)

PDBQT format is very similar to PDB format but it includes **partial charges** ('Q') and AutoDock 4 (AD4) **atom types** ('T').

- Preparing the ligand involves ensuring that its atoms are assigned the correct AutoDock4 atom types, adding Gasteiger charges if necessary, merging non-polar hydrogens, detecting aromatic carbons if any, and setting up the 'torsion tree'.
- Preparing the receptor involves ensuring that its atoms conform to the AutoDock4 atom types by adding Gasteiger charges if necessary, merging non-polar hydrogens and detecting aromatic carbons.



Sample PDBQT file

```
REMARK  4 active torsions:
REMARK  status: ('A' for Active; 'I' for Inactive)
REMARK    1  A    between atoms: N_1  and  CA_5
REMARK    2  A    between atoms: CA_5  and  CB_6
REMARK    3  A    between atoms: CA_5  and  C_13
REMARK    4  A    between atoms: CB_6  and  CG_7
ROOT
ATOM      1  CA  PHE A   1      25.412  19.595  12.578  1.00 12.96     0.287 C
ENDROOT
BRANCH   1   2
ATOM      2  N   PHE A   1      25.225  18.394  13.381  1.00 13.04    -0.065 N
ATOM      3  HN3 PHE A   1      25.856  17.643  13.100  1.00  0.00     0.275 HD
ATOM      4  HN2 PHE A   1      25.558  18.517  14.337  1.00  0.00     0.275 HD
ATOM      5  HN1 PHE A   1      24.247  18.105  13.350  1.00  0.00     0.275 HD
ENDBRANCH   1   2
BRANCH   1   6
ATOM      6  CB  PHE A   1      26.873  20.027  12.625  1.00 12.45     0.082 C
BRANCH   6   7
ATOM      7  CG  PHE A   1      27.286  20.629  13.923  1.00 12.96    -0.056 A
ATOM      8  CD2 PHE A   1      27.470  22.001  14.050  1.00 12.47     0.007 A
ATOM      9  CE2 PHE A   1      27.877  22.571  15.265  1.00 13.98     0.001 A
ATOM     10  CZ  PHE A   1      28.108  21.754  16.360  1.00 13.84     0.000 A
ATOM     11  CE1 PHE A   1      27.919  20.380  16.242  1.00 13.77     0.001 A
ATOM     12  CD1 PHE A   1      27.525  19.821  15.027  1.00 11.32     0.007 A
ENDBRANCH   6   7
ENDBRANCH   1   6
BRANCH   1  13
ATOM     13  C   PHE A   1      25.015  19.417  11.141  1.00 13.31     0.204 C
ATOM     14  O2  PHE A   1      24.659  20.534  10.507  1.00 12.12    -0.646 OA
ATOM     15  O1  PHE A   1      25.024  18.283  10.608  1.00 13.49    -0.646 OA
ENDBRANCH   1  13
TORSDOF 4
```

http://autodock.scripps.edu/faqs-help/faq/what-is-the-format-of-a-pdbqt-file

Both ligand and receptor PDBQT files used for the standard AutoDock 4 force field have additional requirements:

- Gasteiger PEOE partial charges.
- A united-atom representation (i.e. only polar hydrogens). A united atom representation can be obtained by first computing the partial charges for an all-hydrogen model of the molecule. Then, for each non-polar heavy atom that has any hydrogens bonded to it, the partial charge of the hydrogen should be added to that of the bonded heavy atom, then this hydrogen atom can be deleted.

Ideally, the structure of protein and ligand should already have all hydrogens added.

Most structures were solved by X-ray so the protons are missing in the PDB file.

Add hydrogens and/or charges to the structure

- **UCSF Chimera**

- **Open Babel**
  Open Babel is a chemical toolbox, which can be used for converting files, molecular searching, hydrogen addition and deleting, Gasteiger-Marsili partial charge calculation, etc.
  http://openbabel.org

- **pdb2pqr**
  pdb2pqr prepares structures for further calculations by reconstructing missing atoms, adding hydrogens, assigning atomic charges and radii from specified force fields, and generating PQR files. PQR files are PDB files where the occupancy and B-factor columns have been replaced by per-atom charge and radius.
  http://www.poissonboltzmann.org
  http://nbcr-222.ucsd.edu/pdb2pqr_2.1.1 (web server)

PDB2PQR Server

Currently using PDB2PQR Version 2.1.1

Return to the PDB2PQR homepage.

This server enables a user to convert PDB files into PQR files. PQR files are PDB files where the oc
B-factor columns have been replaced by per-atom charge and radius.

pKa calculations are performed by PROPKA.

For more information on PDB2PQR please see the:

- Home Page
- Register (and help suport PDB2PQR & APBS)
- User Guide
- Examples
- Release Notes

If you use the PDB2PQR service in a publication, please cite:

> *Dolinsky TJ, Nielsen JE, McCammon JA, Baker NA. PDB2PQR: an automated pipeline for the s
> execution, and analysis of Poisson-Boltzmann electrostatics calculations. Nucleic Acids Resear
> W665-W667 (2004). [Link]*

Note: In order to distribute server load, the PDB2PQR server currently is limited to a maximum siz
atoms per protein. If you are interested in using PDB2PQR for larger proteins, you are encouragec
command line version of PDB2PQR from the PDB2PQR download page. For additional limitations
PDB2PQR user guide

Note: This server uses automatic refreshing to update the status of your PDB2PQR submission. D
back button on your browser while the server is running.

Please enter either:

- ◉ *a PDB ID:* [ ]
- ○ *upload a PDB file:* [Browse...] No file selected.

Pick a forcefield to use:

- ○ *AMBER*
- ○ *CHARMM*
- ◉ *PARSE*
- ○ *PEOEPB*
- ○ *SWANSON*
- ○ *TYL06*
- ○ *User-defined forcefield (help):* [Browse...] No file selected.
  User-defined names (help): [Browse...] No file selected.
  ** If you select user-defined forcefield, you also need to specify a user-defined .names file.*

Pick an output naming scheme to use (help):

- ◉ *Internal naming scheme (What's this?)*
- ○ *AMBER*
- ○ *CHARMM*
- ○ *PARSE*
- ○ *PEOEPB*
- ○ *SWANSON*
- ○ *TYL06*

Available options:

- ☑ *Ensure that new atoms are not rebuilt too close to existing atoms*
- ☑ *Optimize the hydrogen bonding network*
- ☐ *Assign charges to the ligand specified in a MOL2 file:* [Browse...] No file selected.
- ☑ *Create an APBS input file (this also enables the option to run APBS and visualize your results through the web interface, if it has been installed)*
- ☐ *Add/keep chain IDs in the PQR file*
- ☐ *Insert whitespaces between atom name and residue name, between x and y, and between y and z*
- ☐ *Create Typemap output*
- ☐ *Make the protein's N-terminus neutral (requires PARSE forcefield)*
- ☐ *Make the protein's C-terminus neutral (requires PARSE forcefield)*

pKa Options*:

Use pH [7]

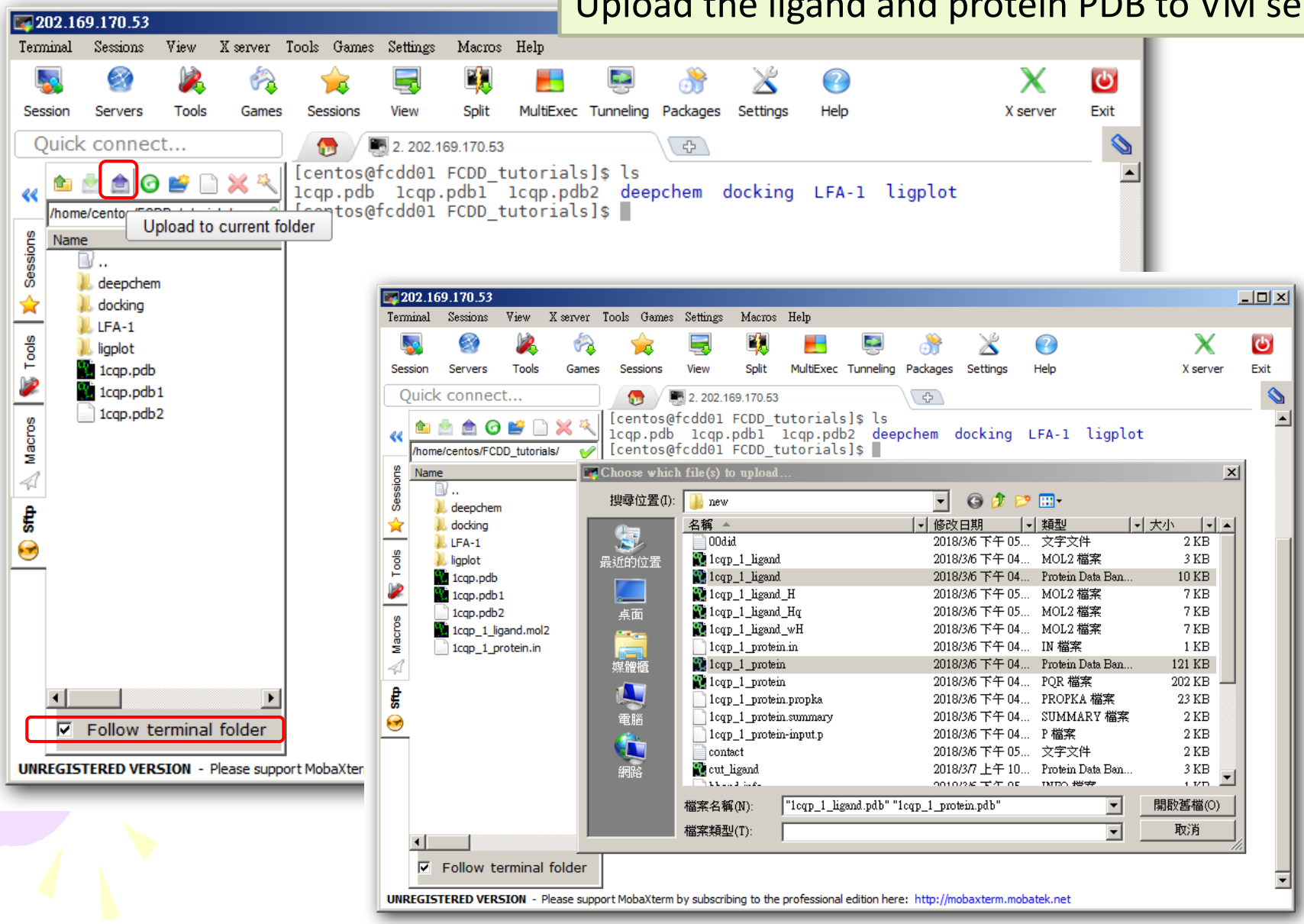
- ○ *No pKa calculation*
- ◉ *Use PROPKA to assign protonation states at provided pH*
- ○ *Use PDB2PKA to parametrize ligands and assign pKa values (requires PARSE forcefield) at provided pH*

** Warning: PDB2PKA is currently experimental and the process can take a very long time. The webserver will kill any jobs that last longer than one week. See the Release Notes for changes since the last version.*

[Submit]

```
$cd ~/FCDD_tutorials
$ls
```

Upload the ligand and protein PDB to VM server.



Prepare structure files

```
$cd ~/FCDD_tutorials/docking
$mkdir 1_preparation
$cp 1cqp_1_protein.pdb 1cqp_1_ligand.pdb ./1_preparation
$cd 1_preparation


$obabel -ipdb 1cqp_1_ligand.pdb \
          -omol2 -O 1cqp_1_ligand_wH.mol2 -p 7.4


$/opt/pdb2pqr/pdb2pqr  --with-ph=7.4 \
        --ph-calc-method=propka --apbs-input \
        --ff=amber --ffout=amber --verbose --summary \
        1cqp_1_protein.pdb 1cqp_1_protein.pqr


## use scripts from ADTools to prepqre pdbqt file
$prepare_ligand4.py -l 1cqp_1_ligand_wH.mol2 -v -o ligand.pdbqt
$prepare_receptor4.py -r 1cqp_1_protein.pqr -v -o receptor.pdbqt
```

http://autodock.scripps.edu/faqs-help/how-to/how-to-prepare-a-ligand-file-for-autodock4

http://autodock.scripps.edu/faqs-help/how-to/how-to-prepare-a-receptor-file-for-autodock4

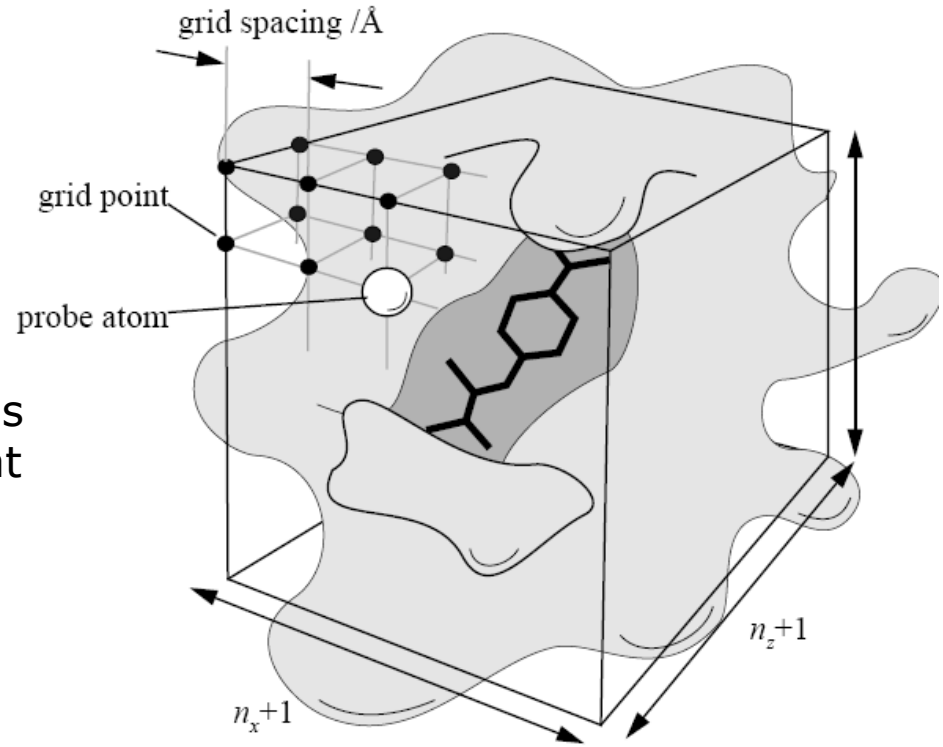
```
prepare_ligand4.py -l filename

    Description of command...
         -l     ligand_filename

    Optional parameters:
        [-v]    verbose output
        [-o pdbqt_filename] (output filename)
        [-d]    dictionary to write types list and number of active torsions
        [-A]    type(s) of repairs to make:
                 bonds_hydrogens, bonds, hydrogens
        [-C]    do not add charges
        [-p]    preserve input charges on atom type, eg -p Zn
        [-U]    cleanup type:
                 nphs_lps, nphs, lps, ''
        [-B]    type(s) of bonds to allow to rotate
        [-R]    index for root
        [-F]    check for and use largest non-bonded fragment (Fals
        [-M]    interactive (default is automatic)
        [-I]    string of bonds to inactivate composed of
                   of zero-based atom indices eg 5_13_2_10
                   will inactivate atoms[5]-atoms[13] bond
                                and atoms[2]-atoms[10] bond
                      (default is '')
        [-Z]    inactivate all active torsions
                      (default is leave active)
```

```
prepare_receptor4.py -r filename
    Description of command...
         -r   receptor_filename
    Optional parameters:
        [-v]  verbose output (default is minimal output)
        [-o pdbqt_filename]  (default is 'molecule_name.pdbqt')
        [-A]  type(s) of repairs to make:
             'bonds_hydrogens': build bonds and add hydrogens
             'bonds': build a single bond from each atom with no bonds to its closest neighbor
             'hydrogens': add hydrogens
             'checkhydrogens': add hydrogens only if there are none already
             'None': do not make any repairs
             (default is 'None': do not to make any repairs)
        [-C]  preserve all input charges ie do not add new charges
             (default is addition of gasteiger charges)
        [-p]  preserve input charges on specific atom types, eg -p Zn -p Fe
        [-U]  cleanup type:
             'nphs': merge charges and remove non-polar hydrogens
             'lps': merge charges and remove lone pairs
             'waters': remove water residues
             'nonstdres': remove chains composed entirely of residues of
                      types other than the standard 20 amino acids
             'deleteAltB': remove XX@B atoms and rename XX@A atoms->XX
             (default is 'nphs_lps_waters_nonstdres')
        [-e]  delete every nonstd residue from any chain
              'True': any residue whose name is not in this list:
                   ['CYS', 'ILE', 'SER', 'VAL', 'GLN', 'LYS', 'ASN',
                    'PRO', 'THR', 'PHE', 'ALA', 'HIS', 'GLY', 'ASP',
                    'LEU', 'ARG', 'TRP', 'GLU', 'TYR','MET']
              will be deleted from any chain. NB: there are no
              nucleic acid residue names at all in the list.
             (default is False which means not to do this)
        [-M]  interactive
             (default is 'automatic': outputfile is written with no further user input)
```

Search Space

- center (X, Y, Z coordinate of the center)
- dimension (size in the X, Y, Z dimension)

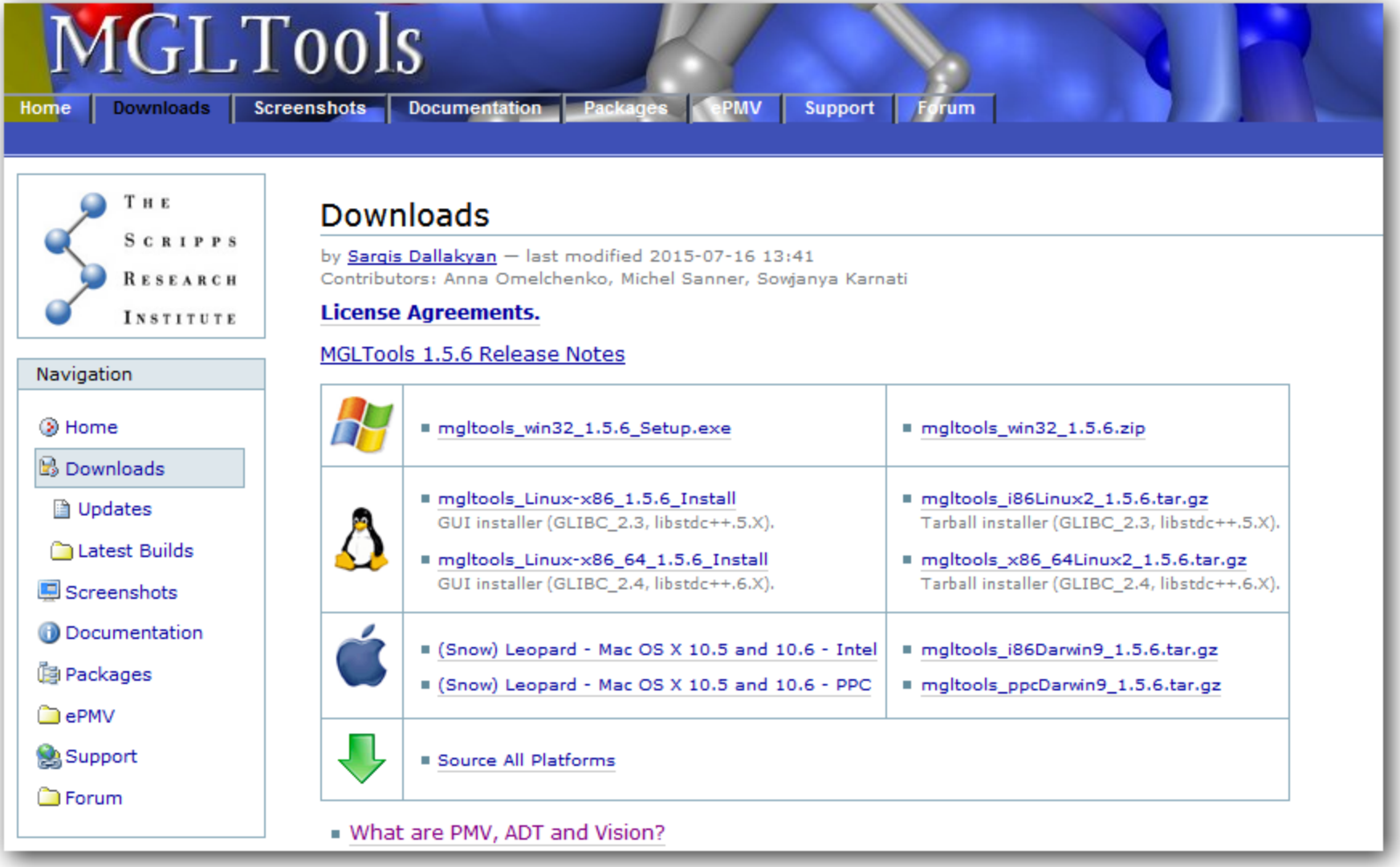
AutoDock 4 performs the docking of the ligand to a set of grid maps describing the target protein. These grids are pre-calculated by autogird4. The search space is defined by these grids in terms of grid points, grid spacing, and grid center.



AutoDock Vina does not require pre-calculating grid maps. Instead, it calculates the grids internally, for the atom types that are needed, and it does this virtually instantly. The search space is defined by the dimension in Angstrom and the center coordinates.

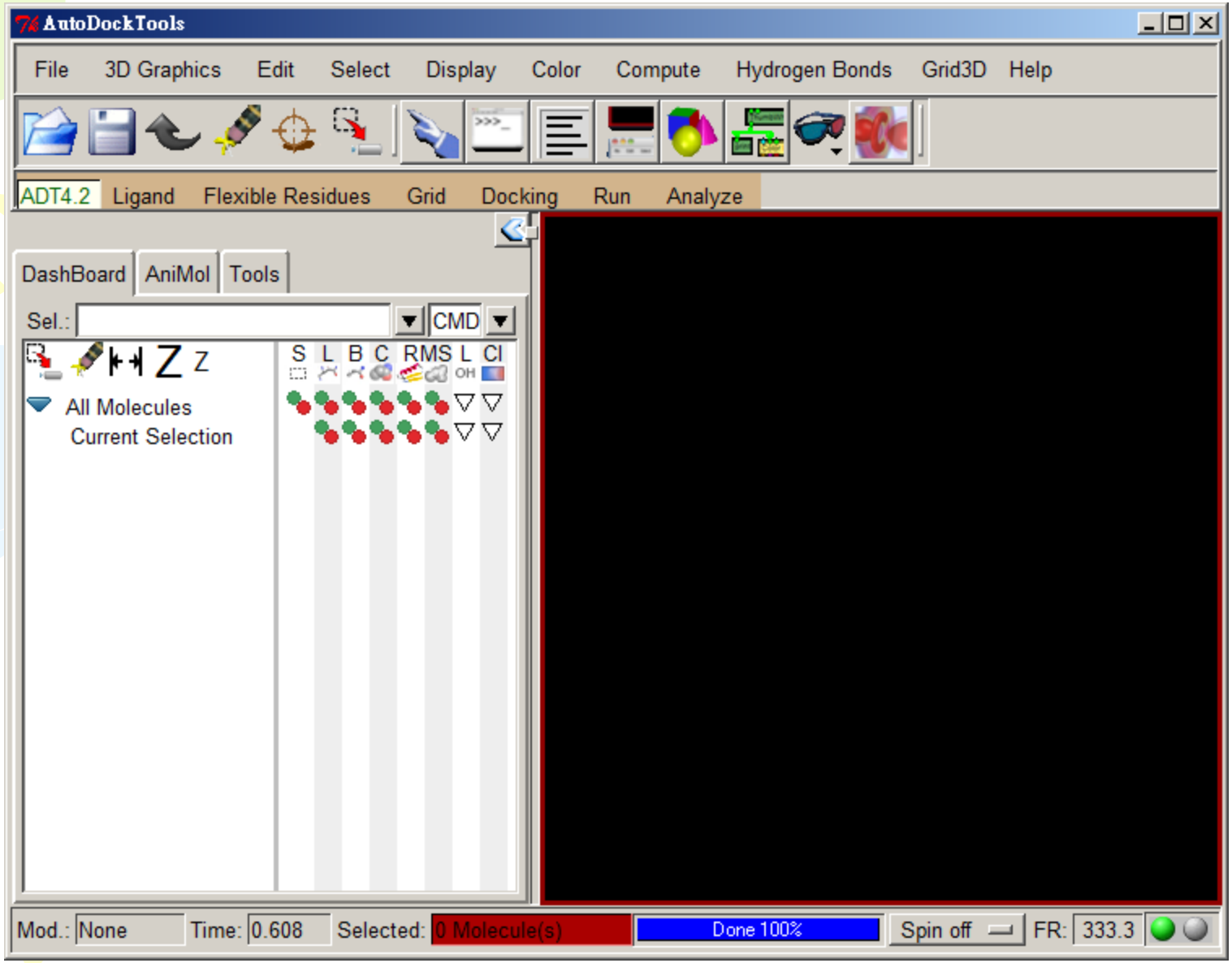
dimension (Å) = grid spacing x (number of grid points – 1)

http://mgltools.scripps.edu/

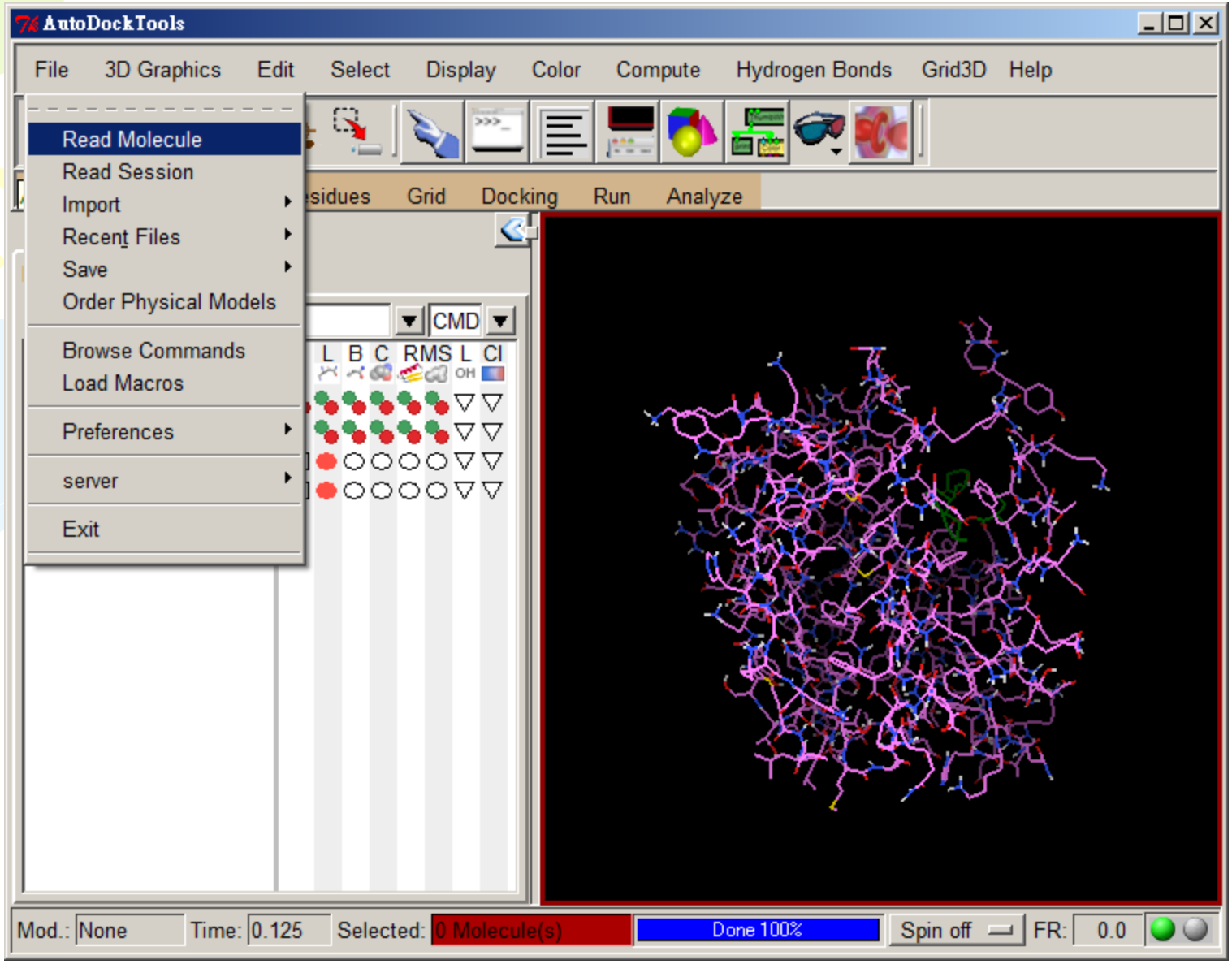


AutoDockTools (ADT) is developed to help set up the docking. ADT is included in **MGLTools** packages.

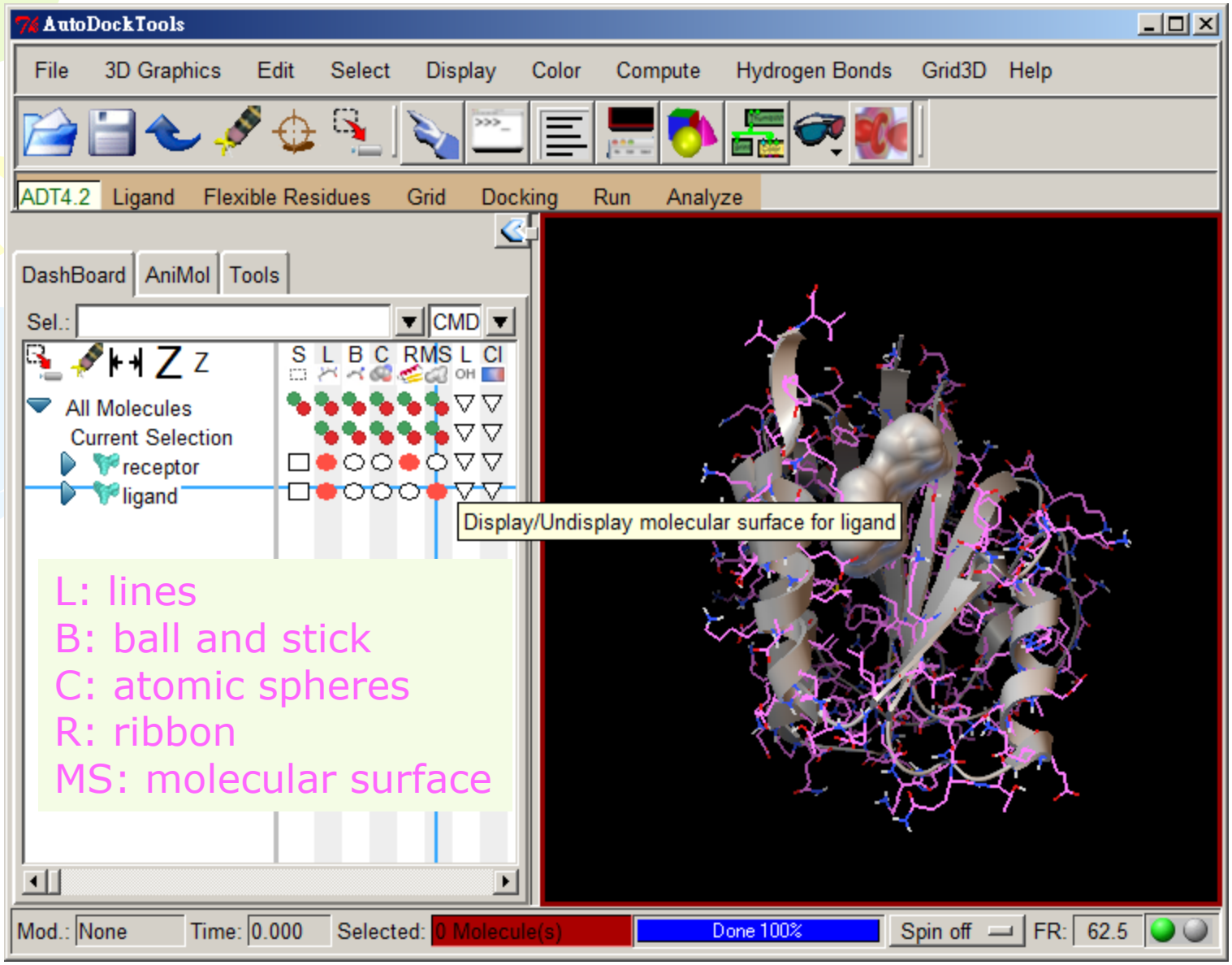
Launching AutoDockTools



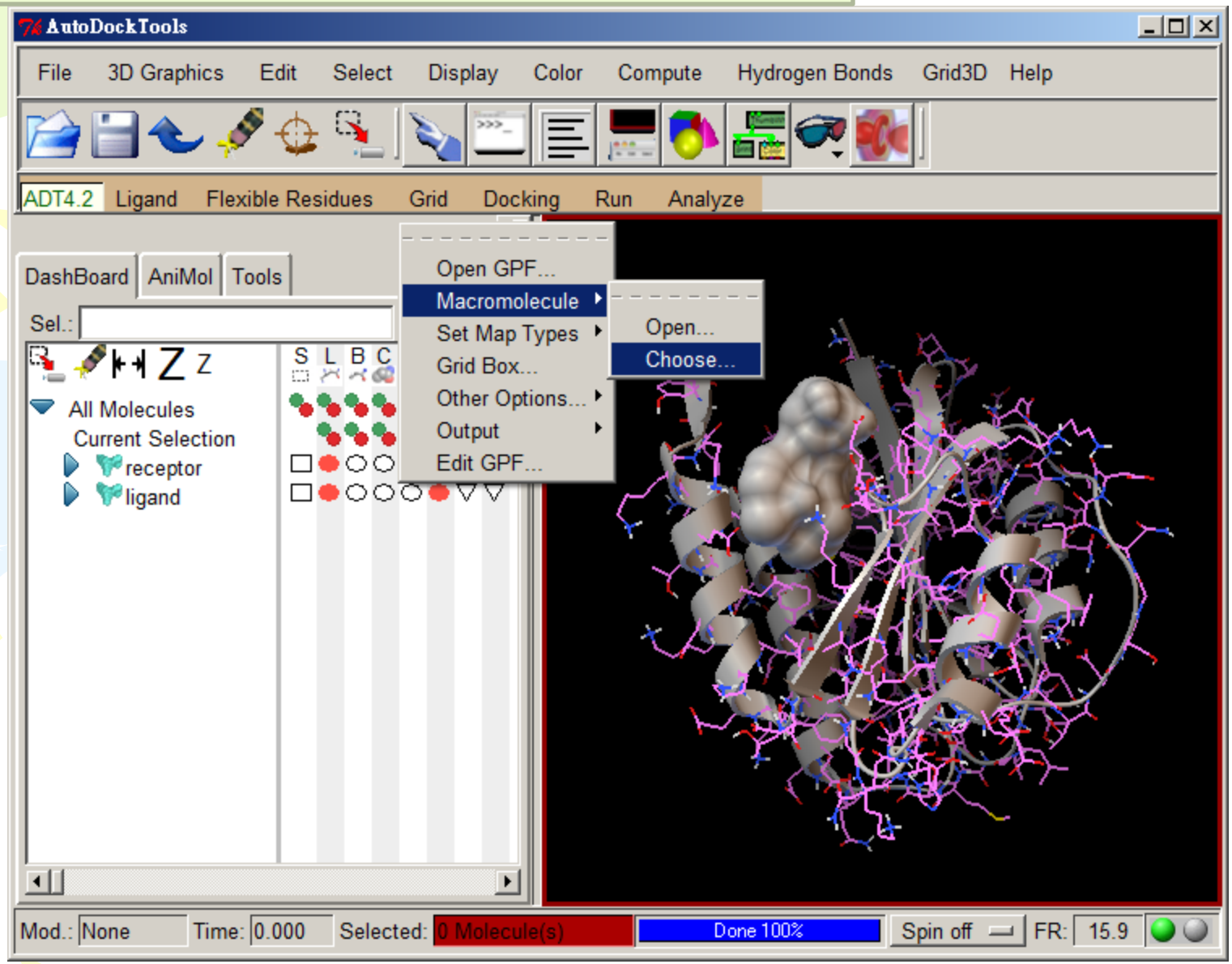
read in receptor.pdbqt and ligand.pdbqt



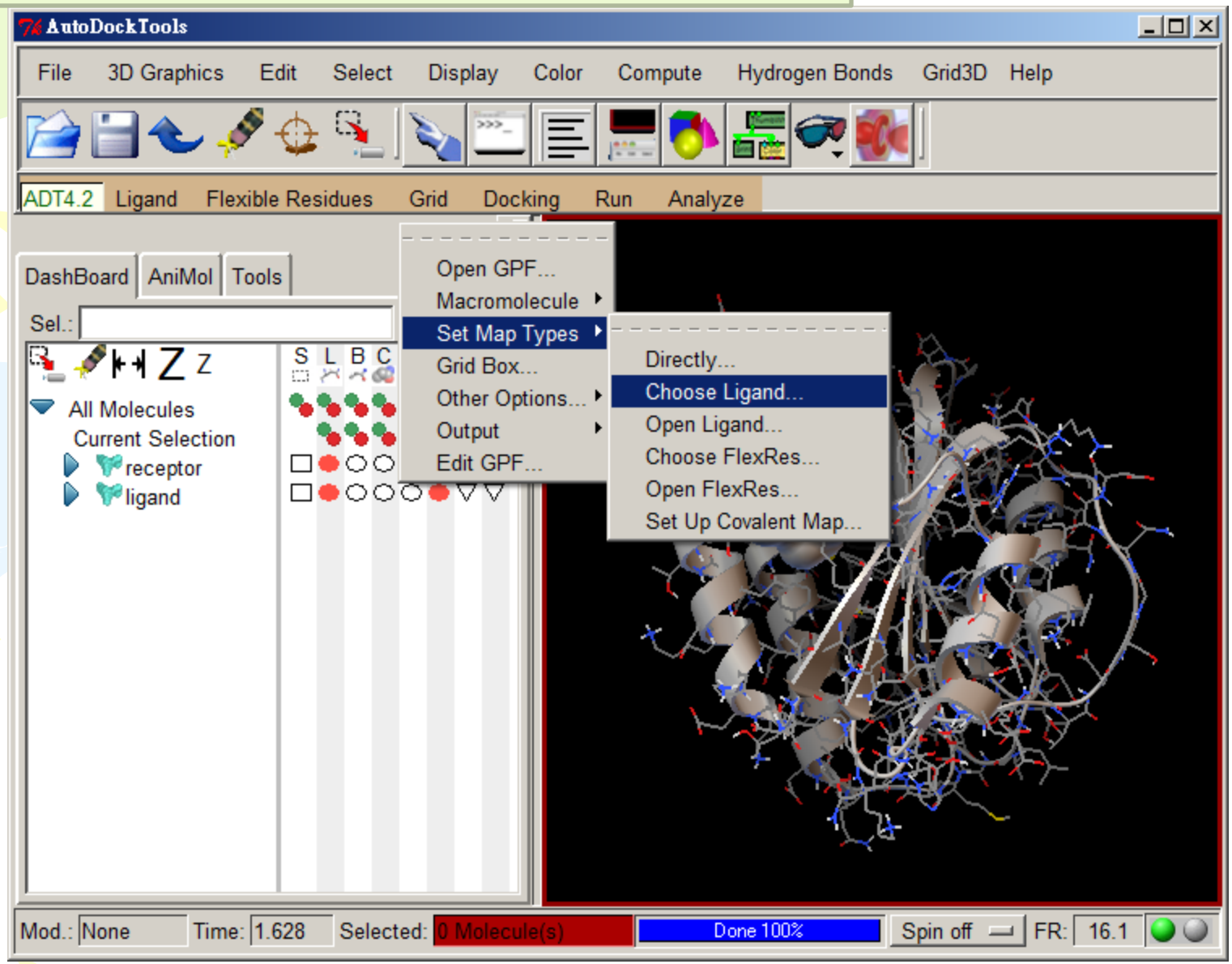
change the presentation of molecules



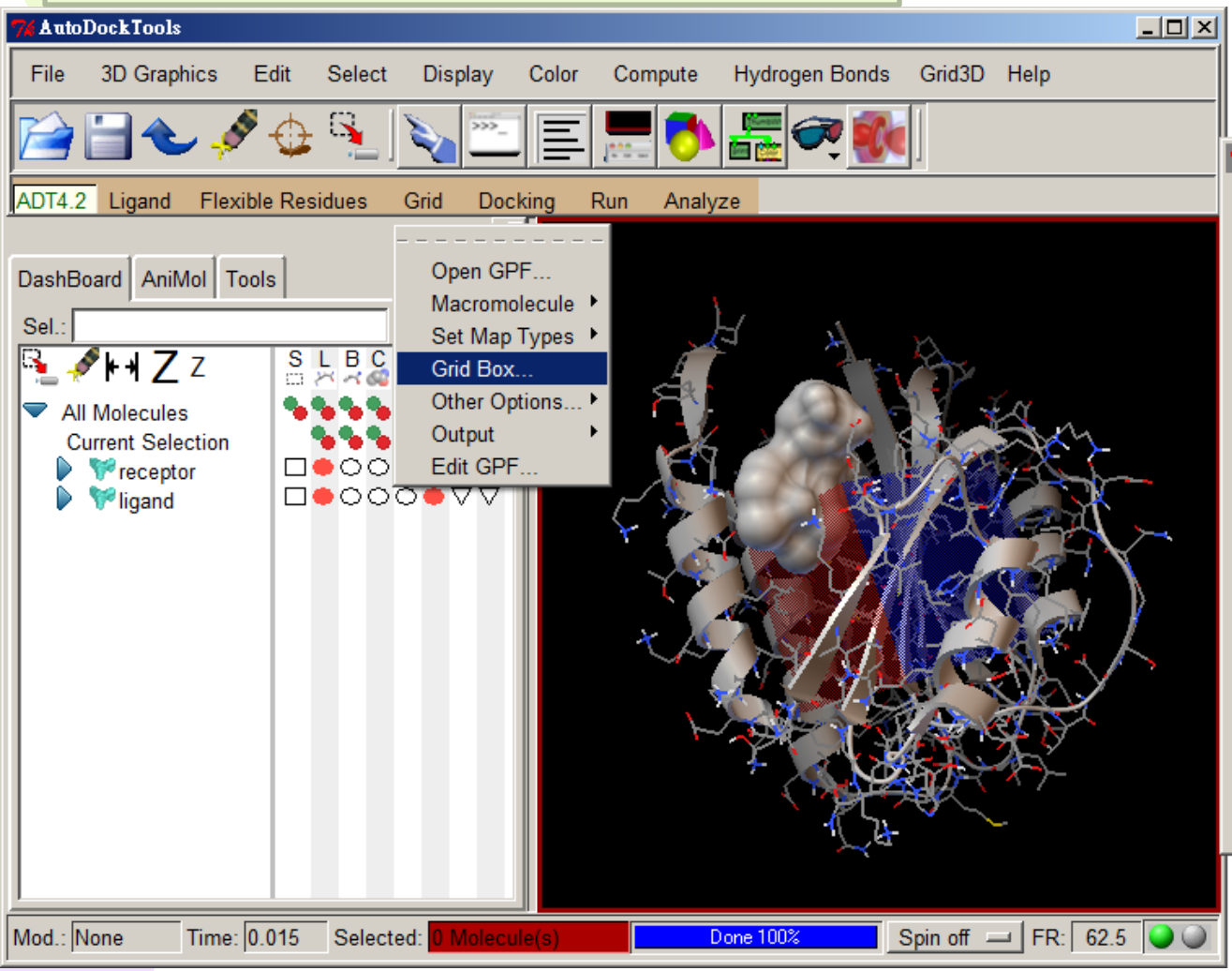
Choose **Grid** → **Macromolecules** → **Choose**

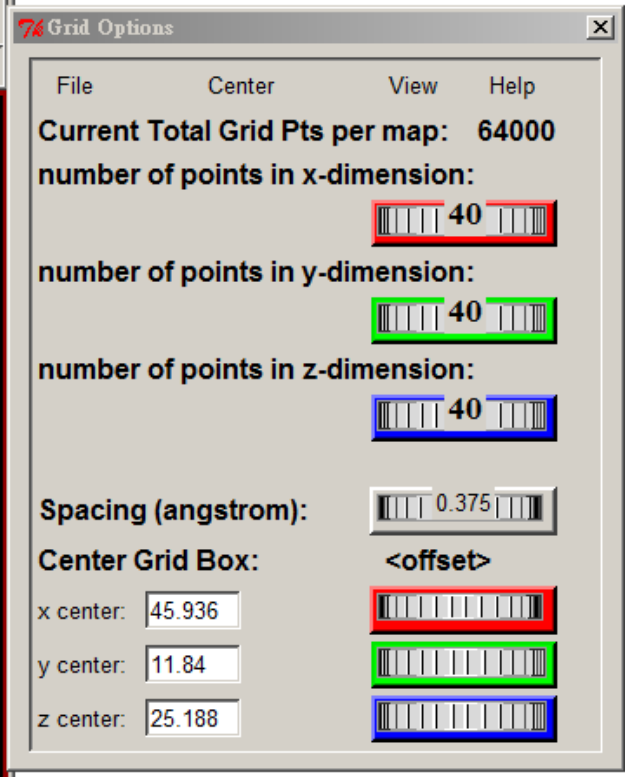


Choose **Grid** → **Set Map Types** → **Choose Ligand**

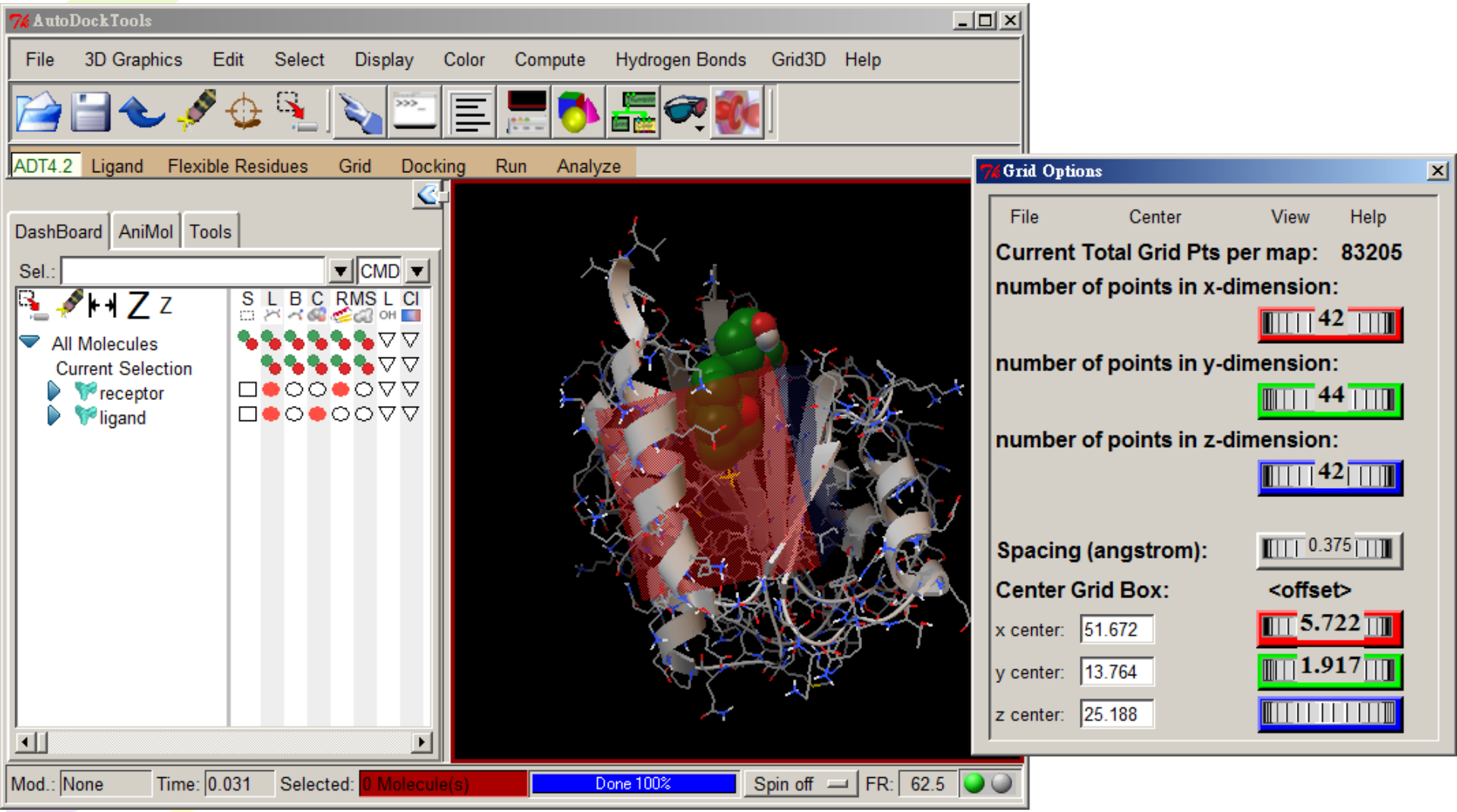


Choose **Grid** → **Grid Box**



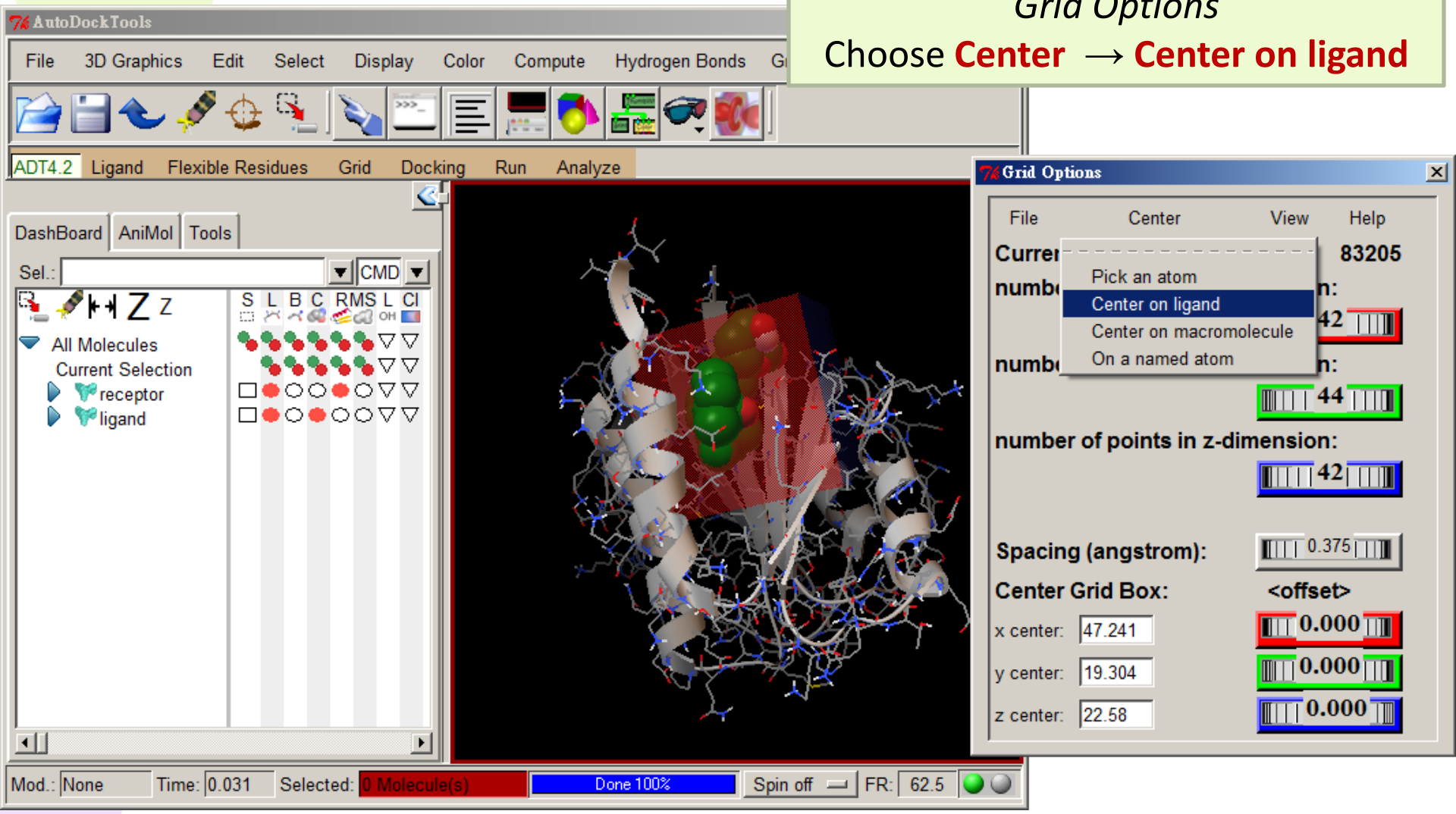


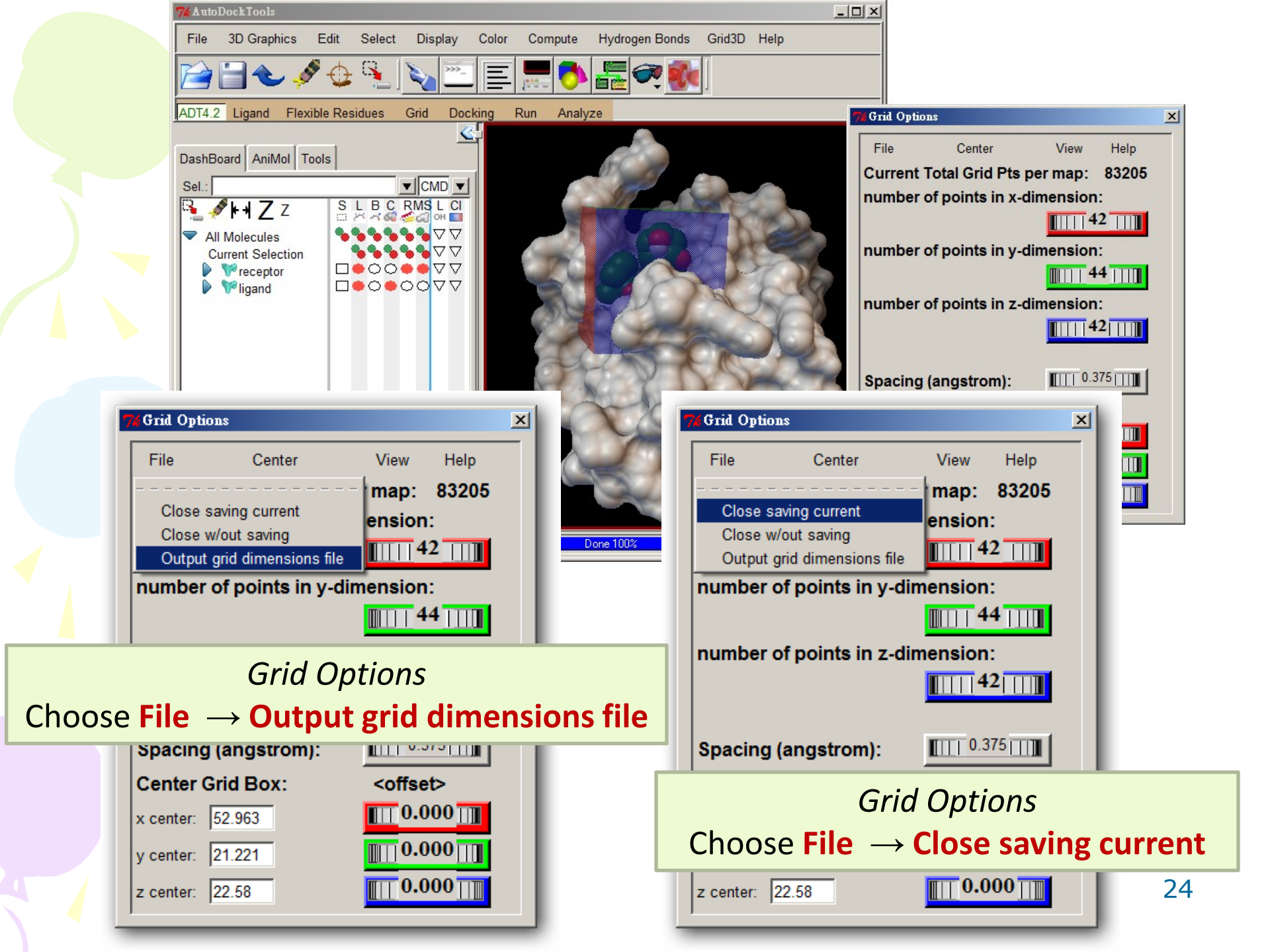
Adjust grid parameters to make sure the grid box can cover the entire ligand and the binding pocket.



Grid Options

Choose **Center** → **Center on ligand**




AutoDockTools
File 3D Graphics Edit Select Display Color Compute Hydrogen Bonds Grid3D Help
ADT4.2 Ligand Flexible Residues Grid Docking Run Analyze
DashBoard AniMol Tools
Sel.: CMD
All Molecules
Current Selection
receptor
ligand
Done 100%
Grid Options
File Center View Help
Current Total Grid Pts per map: 83205
number of points in x-dimension: 42
number of points in y-dimension: 44
number of points in z-dimension: 42
Spacing (angstrom): 0.375
Close saving current
Close w/out saving
Output grid dimensions file
Center Grid Box: <offset>
x center: 52.963 0.000
y center: 21.221 0.000
z center: 22.58 0.000
Grid Options
Choose File → Output grid dimensions file
Grid Options
Choose File → Close saving current

Search Space

AutoDock 4

spacing 0.375
npts 42 44 42
center 52.963 21.221 22.580

AutoDock Vina

0.375x41=15.375
0.375x43=16.125
dimensions 15.375 16.125 15.375
center 52.963 21.221 22.580

Docking with Autodock4

```
$pwd
$cd ..
$mkdir 2_docking
$cd 2_docking
$mkdir autodock4 autodock_vina
$cd autodock4
$cp ../../1_preparation/*.pdbqt ./

##prepare grid parameter and docking parameter files
$prepare_gpf4.py -l ligand.pdbqt -r receptor.pdbqt
$prepare_dpf4.py -l ligand.pdbqt -r receptor.pdbqt
##edit grid parameter file (receptor.gpf)
$vi receptor.gpf
##edit docking parameter file (ligand_receptor.dpf)
$vi ligand_receptor.dpf

## generate grid maps
$autogrid4 -p receptor.gpf -l receptor.glg
## perform docking
$autodock4 -p ligand_receptor.dpf -l ligand_receptor.dlg
```

AutoDock 4

spacing 0.375
npts 42 44 42
center 52.963 21.221 22.580

AutoDock4 Grid Parameter File: GPF

The grid parameter file specifies an AutoGrid calculation, including the size and location of the grid, the atom types that will be used, the coordinate file for the rigid receptor, and other parameters for calculation of the grids.

Sample Grid Parameter File (from tutorial)

```
npts 60 60 60                          # num.grid points in xyz
gridfld 1hsg.maps.fld                  # grid_data_file
spacing 0.375                          # spacing(A)
receptor_types A C HD N OA SA          # receptor atom types
ligand_types A C NA OA N HD            # ligand atom types
receptor 1hsg.pdbqt                    # macromolecule
gridcenter 2.5 6.5 -7.5                # xyz-coordinates or auto
smooth 0.5                             # store minimum energy w/in rad(A)
map 1hsg.A.map                         # atom-specific affinity map
map 1hsg.C.map                         # atom-specific affinity map
map 1hsg.NA.map                        # atom-specific affinity map
map 1hsg.OA.map                        # atom-specific affinity map
map 1hsg.N.map                         # atom-specific affinity map
map 1hsg.HD.map                        # atom-specific affinity map
elecmap 1hsg.e.map                     # electrostatic potential map
dsolvmap 1hsg.d.map                    # desolvation potential map
dielectric -0.1465                     # <0, AD4 distance-dep.diel;>0,
                                       constant
```

AutoDock4 Docking Parameter File: DPF

```
autodock_parameter_version 4.2       # used by autodock to validate parameter set
outlev ADT                             # diagnostic output level
seed pid time                        # seeds for random generator
unbound_model bound                  # state of unbound ligand

ligand_types A C NA OA N HD          # atoms types in ligand
fld 1hsg.maps.fld                    # grid_data_file
map 1hsg.A.map                       # atom-specific affinity map
map 1hsg.C.map                       # atom-specific affinity map
map 1hsg.NA.map                      # atom-specific affinity map
map 1hsg.OA.map                      # atom-specific affinity map
map 1hsg.N.map                       # atom-specific affinity map
map 1hsg.HD.map                      # atom-specific affinity map
elecmap 1hsg.e.map                   # electrostatics map
desolvmap 1hsg.d.map                 # desolvation map
move ind.pdbqt                       # small molecule
about 0.3689 -0.2148 -4.9865         # small molecule root center

tran0 random                         # initial coordinates/A or random
quaternion0 random                   # initial orientation
dihe0 random                         # initial dihedrals (relative) or random

ga_pop_size 150                      # number of individuals in population
ga_num_evals 2500000                 # maximum number of energy evaluations
ga_num_generations 27000             # maximum number of generations
ga_elitism 1                         # top individuals to survive to next generation
ga_mutation_rate 0.02                # rate of gene mutation
ga_crossover_rate 0.8                # rate of crossover
set_ga                               # set the above parameters for GA or LGA

sw_max_its 300                       # iterations of Solis & Wets local search
sw_max_succ 4                        # consecutive successes before changing rho
sw_max_fail 4                        # consecutive failures before changing rho
sw_rho 1.0                           # size of local search space to sample
sw_lb_rho 0.01                       # lower bound on rho
ls_search_freq 0.06                  # probability of performing local search
set_psw1                             # set the above pseudo-Solis & Wets parameters

ga_run 10                            # do this many hybrid GA-LS runs

rmstol 2.0                           # cluster_tolerance/A
analysis                             # perform a ranked cluster analysis
```

The docking parameter file specifies the files and parameters for an AutoDock calculation, including the map files that will be used for the docking, the ligand coordinate files, and parameters for the search.

http://autodock.scripps.edu/faqs-help/manual

AutoDock 4.2 User Guide

http://autodock.scripps.edu/faqs-help/how-to

How to prepare a grid parameter file for AutoGrid 4

How to prepare a docking parameter file for AutoDock4

How to prepare a flexible residue file for AutoDock4

http://autodock.scripps.edu/faqs-help/tutorial

Using AutoDock 4 with AutoDockTools

Using AutoDock 4 for Virtual Screening

Water, metal ion, covalent bond involved?

- Hydrated ligand docking
- AutoDock force field for ZN metalloproteins
- AutoDock4 covalent docking

##results
$**vi ligand_receptor.dlg**

```
Number of distinct conformational clusters found = 3,  out of 10 runs,
Using an rmsd-tolerance of 2.0 A


        CLUSTERING HISTOGRAM
        ____________________

_____|_____________|_____|_____________|_____|_____________________________________
Clus | Lowest      |     | Mean        | Num |
-ter | Binding     | Run | Binding     | in  | Histogram
Rank | Energy      |     | Energy      | Clus|    5    10   15   20   25   30   35
_____|_____________|_____|_____________|_____|____:____|____:____|____:____|____:___
   1 |      -9.28  |   3 |      -9.05  |   6 |######
   2 |      -8.84  |   7 |      -8.71  |   3 |###
   3 |      -8.29  |   5 |      -8.29  |   1 |#
_____|_____________|_____|_____________|_____|_____________________________________
```

Rank	Sub-Rank	Run	Binding Energy	Cluster RMSD	Reference RMSD	Grep Pattern
1	1	3	-9.28	0.00	2.22	RANKING
1	2	4	-9.13	1.10	2.02	RANKING
1	3	2	-9.03	1.83	2.72	RANKING
1	4	10	-9.01	1.95	2.82	RANKING
1	5	9	-8.96	1.99	2.93	RANKING
1	6	6	-8.87	0.65	2.22	RANKING
3	1	5	-8.29	0.00	2.62	RANKING

$**grep "RANKING" ligand_receptor.dlg > ranking.txt**

Estimated Free Energy of Binding in **kcal/mol**
Estimated Inhibition Constant(Ki)

```
MODEL        3
USER    Run = 3
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 6
USER
USER    RMSD from reference structure       = 2.224 A
USER
USER    Estimated Free Energy of Binding    =   -9.28 kcal/mol  [=(1)
USER    Estimated Inhibition Constant, Ki   =  158.19 nM (nanomolar)
```

get conformation of the lowest energy ligand
$**write_lowest_energy_ligand.py -f ligand_receptor.dlg**

convert pdbqt to pdb
$**pdbqt_to_pdb.py -f ligand_BE.pdbqt**

get conformations from docking result (dlg) file
$**write_conformations_from_dlg.py -d ligand_receptor.dlg**
$**mkdir poses**
$**mv ligand_*.pdbqt poses**

make complexes structure
$**write_all_complexes.py -d ligand_receptor.dlg -r receptor.pdbqt**
$**mkdir complexes**
$**mv receptor_ligand_*.pdbqt complexes**

Docking with Autodock Vina

```
$cd ../autodock_vina
$cp ../../1_preparation/*.pdbqt ./

##perform docking
$vina --receptor receptor.pdbqt --ligand ligand.pdbqt  \
      --center_x 52.963 --center_y 21.221 --center_z 22.58 \
      --size_x 15.375 --size_y 16.125 --size_z 15.375 \
      --out vina_out.pdbqt --log vina.log

##put some parameters in the config.txt file
$vi config.txt
$vina --config config.txt --log vina.log
```

AutoDock Vina
dimensions 15.375 16.125 15.375
center 52.963 21.221 22.580

```
receptor = receptor.pdbqt
ligand = ligand.pdbqt
center_x = 52.963
center_y = 21.221
center_z = 22.58
size_x = 15.375
size_y = 16.125
size_z = 15.375
out = out.pdbqt
```

```
$vina –-config configB.txt –-ligand ligandB.pdbqt  \
      --out outB.pdbqt –log vinaB.log
```

```
receptor = receptor.pdbqt
center_x = 52.963
center_y = 21.221
center_z = 22.58
size_x = 15.375
size_y = 16.125
size_z = 15.375
```

http://vina.scripps.edu/tutorial.html

https://youtu.be/-GVZP0X0Tg8

http://vina.scripps.edu/download.html

Download:

The current version is 1.1.2 (May 11, 2011).

Windows	autodock_vina_1_1_2_win32.msi	(0.5 MB)	Compatibility, installation and usage notes
Linux	autodock_vina_1_1_2_linux_x86.tgz	(1.2 MB)	Compatibility, installation and usage notes
MacOSX	autodock_vina_1_1_2_mac.tgz	(0.9 MB)	Compatibility, installation and usage notes
Source	autodock_vina_1_1_2.tgz (browse)	(0.1 MB)	Building from source

See also: GUIs, web interfaces, etc. | Old versions | History of changes

```
REMARK VINA RESULT:      -8.1      0.000      0.000
REMARK VINA RESULT:      -6.8      1.671      3.283
REMARK VINA RESULT:      -6.7      1.866      7.035
REMARK VINA RESULT:      -6.6      1.858      6.818
REMARK VINA RESULT:      -6.6      2.237      5.650
REMARK VINA RESULT:      -6.6      1.969      4.588
REMARK VINA RESULT:      -6.5      1.464      4.336
REMARK VINA RESULT:      -6.4      1.946      3.985
REMARK VINA RESULT:      -6.4      2.037      4.066
```

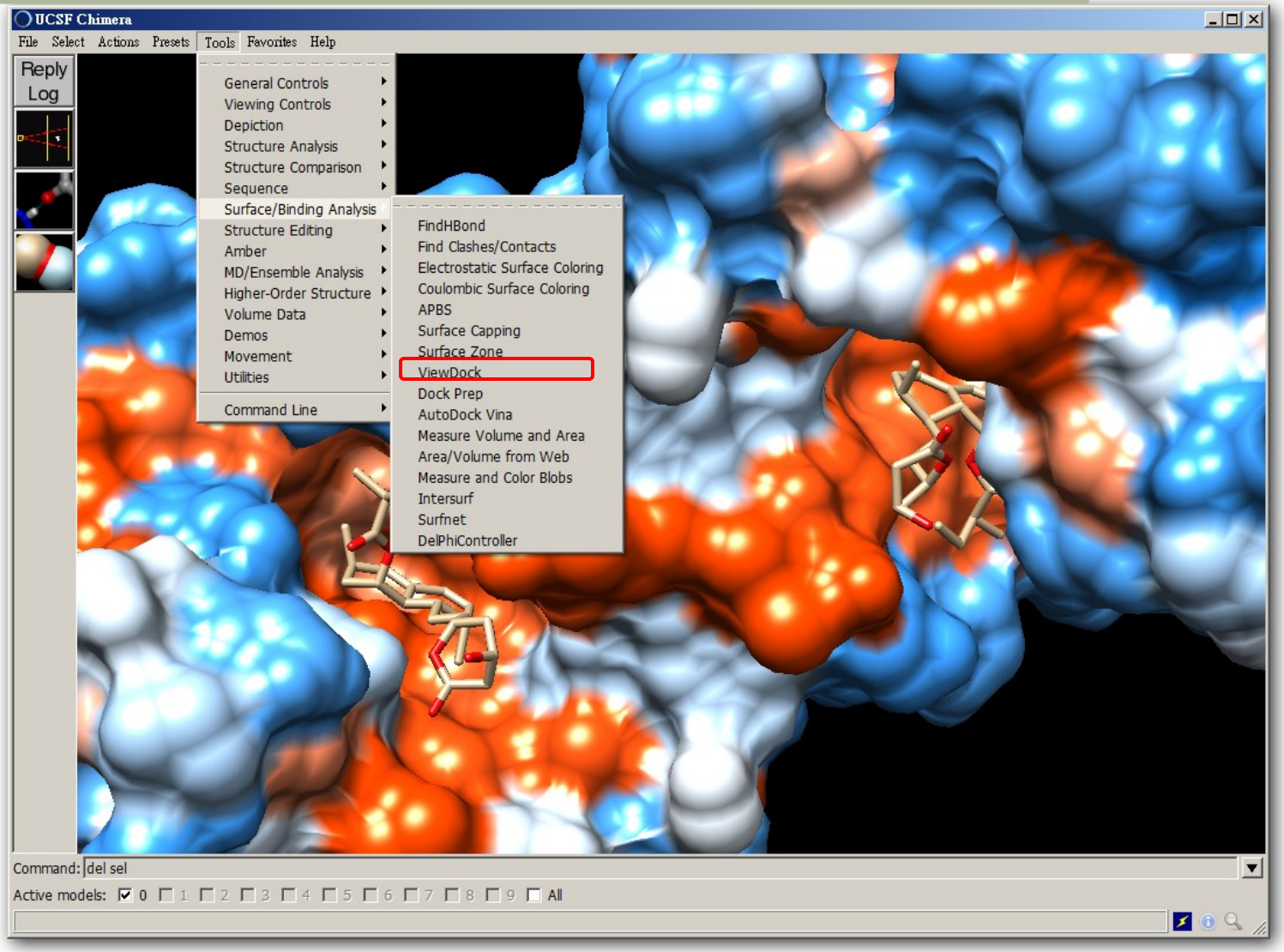
The predicted binding affinity is in kcal/mol.

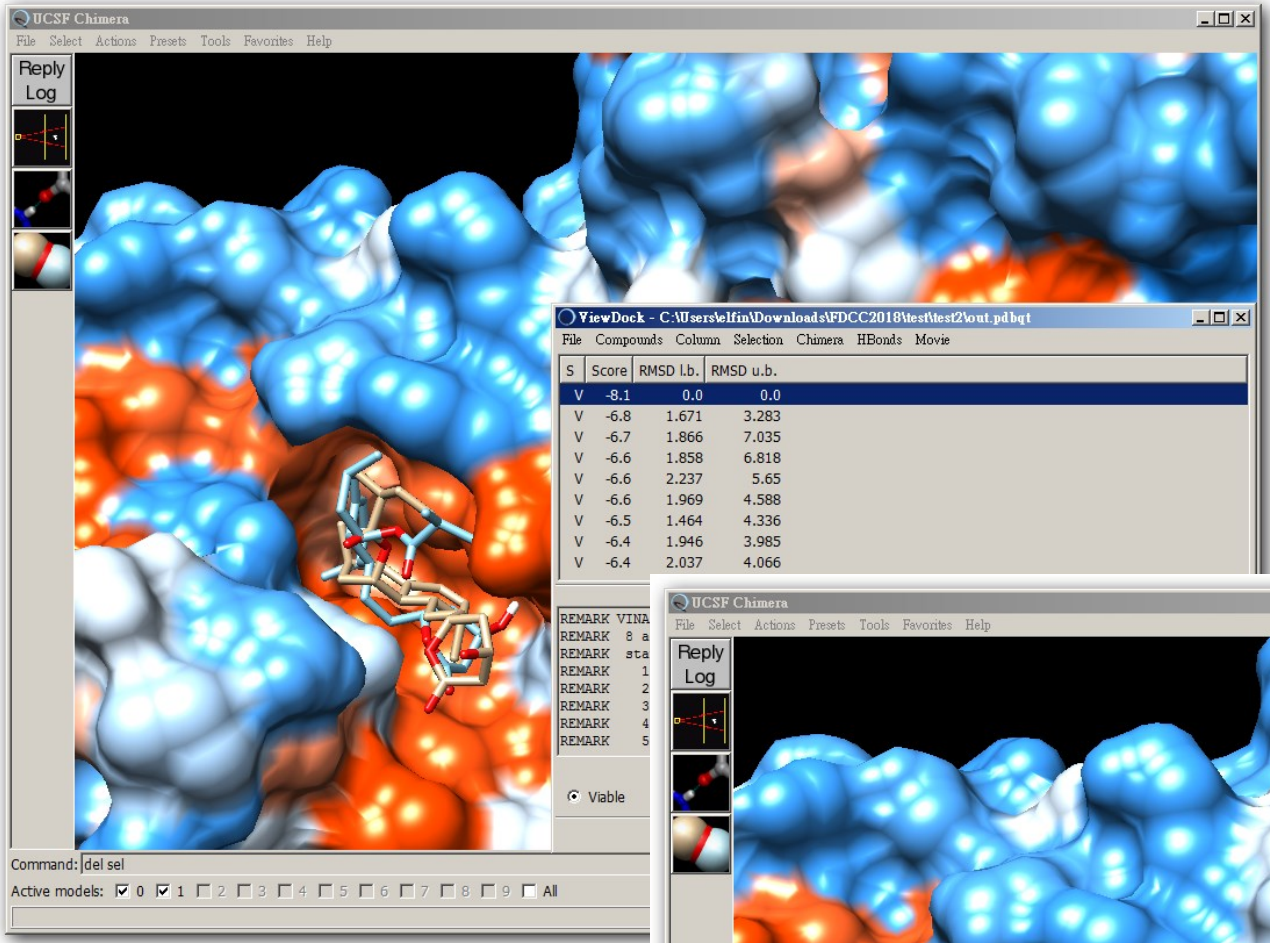
```
##results
$vi out.pdbqt

$grep "REMARK VINA RESULT" out.pdbqt

## get conformations from outout.pdbqt
$/opt/autodock_vina/bin/vina_split --input out.pdbqt \
                                   --ligand vinaDock_

$pdbqt_to_pdb.py -f vinaDock_1.pdbqt
$mkdir poses
$mv vinaDock_*.pdbqt poses
```

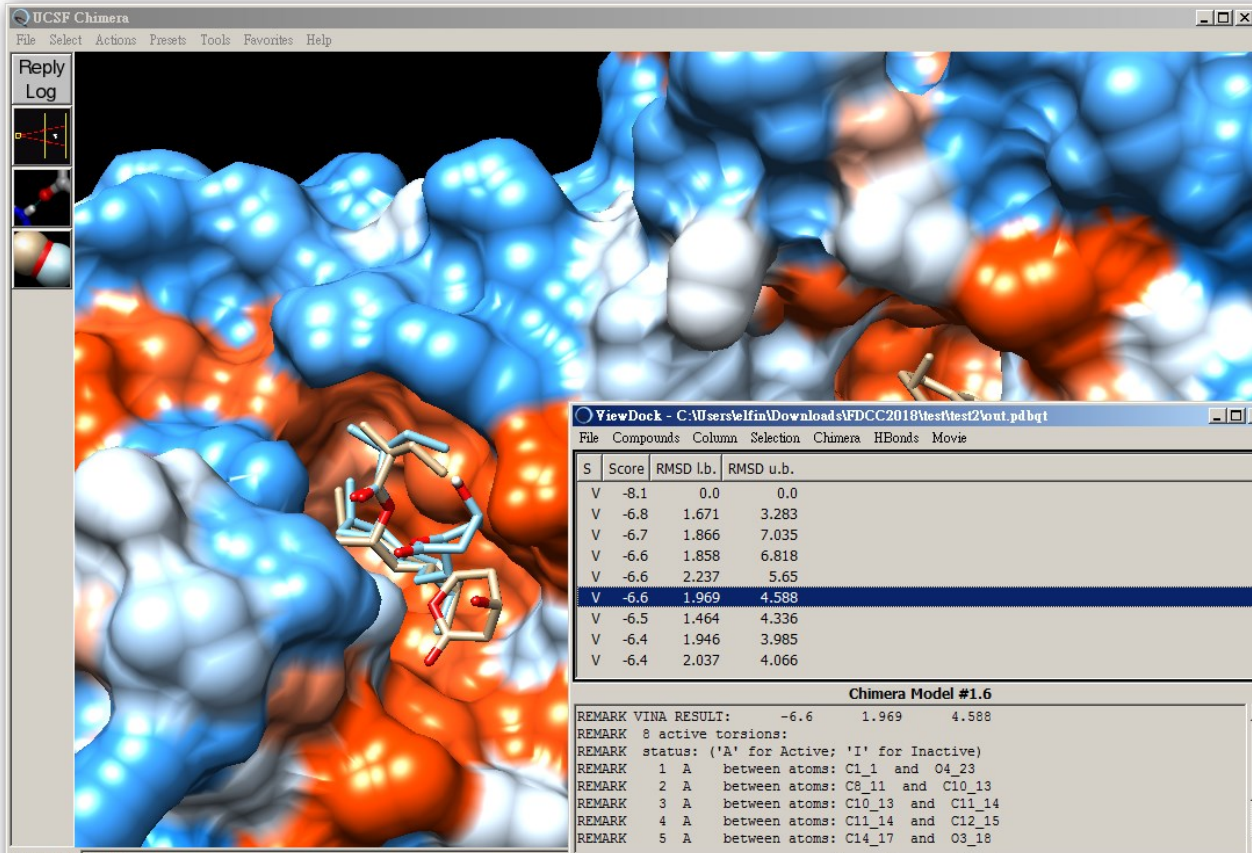
```
vinaDock_1.pdb    vinaDock_3.pdbqt  vinaDock_6.pdbqt  vinaDock_9.pdbqt
vinaDock_1.pdbqt  vinaDock_4.pdbqt  vinaDock_7.pdbqt
vinaDock_2.pdbqt  vinaDock_5.pdbqt  vinaDock_8.pdbqt
```

Download docked poses (AutoDock4 and AutoDock Vina)
Use chimera to view the protein structure and the docked poses

Choose **Tools** → **Surface/Binding Analysis** → **ViewDock**




UCSF Chimera
File Select Actions Presets Tools Favorites Help
Reply Log
ViewDock - C:\Users\elfin\Downloads\FDCC2018\test\test2\out.pdbqt
File Compounds Column Selection Chimera HBonds Movie
S Score RMSD l.b. RMSD u.b.
V -8.1 0.0 0.0
V -6.8 1.671 3.283
V -6.7 1.866 7.035
V -6.6 1.858 6.818
V -6.6 2.237 5.65
V -6.6 1.969 4.588
V -6.5 1.464 4.336
V -6.4 1.946 3.985
V -6.4 2.037 4.066
REMARK VINA
REMARK 8 a
REMARK sta
REMARK 1
REMARK 2
REMARK 3
REMARK 4
REMARK 5
Viable
Command: del sel
Active models: 0 1 2 3 4 5 6 7 8 9 All


UCSF Chimera
File Select Actions Presets Tools Favorites Help
Reply Log
ViewDock - C:\Users\elfin\Downloads\FDCC2018\test\test2\out.pdbqt
File Compounds Column Selection Chimera HBonds Movie
S Score RMSD l.b. RMSD u.b.
V -8.1 0.0 0.0
V -6.8 1.671 3.283
V -6.7 1.866 7.035
V -6.6 1.858 6.818
V -6.6 2.237 5.65
V -6.6 1.969 4.588
V -6.5 1.464 4.336
V -6.4 1.946 3.985
V -6.4 2.037 4.066
Chimera Model #1.6
REMARK VINA RESULT: -6.6 1.969 4.588
REMARK 8 active torsions:
REMARK status: ('A' for Active; 'I' for Inactive)
REMARK 1 A between atoms: C1_1 and O4_23
REMARK 2 A between atoms: C8_11 and C10_13
REMARK 3 A between atoms: C10_13 and C11_14
REMARK 4 A between atoms: C11_14 and C12_15
REMARK 5 A between atoms: C14_17 and O3_18

Virtual Screening with Autodock Vina

One receptor and a set of search space
Many small molecules

```
## prepare small molecules
## downlod dbfda-interesting.sdf from ZINC15
$mkdir mol2 pdbqt
$cd mol2
$obabel -isdf ../dbfda-interesting.sdf -omol2 -Ofda_.mol2 \
        -p 7.4 --append zinc_id -m
$cd ../
$obabel -isdf dbfda-interesting.sdf -osmi -O dbfda.smi \
        --append zinc_id –addoutindex

$sh prepare_ligand.sh
```

```
#! /bin/bash
cd mol2
for f in fda_*.mol2; do
    b=`basename $f .mol2`
    echo Processing ligand $f $b.pdbqt
    prepare_ligand4.py -l $f -o $b.pdbqt
    mv $b.pdbqt ../pdbqt
done
```

perform docking for each small molecules

$**vi configB.txt**

$**sh vina_screen.sh**

```
receptor = receptor.pdbqt
center_x = 52.963
center_y = 21.221
center_z = 22.58
size_x = 15.375
size_y = 16.125
size_z = 15.375
```

```
#! /bin/bash

mkdir dock
cd pdbqt
for f in fda_*.pdbqt; do
    b=`basename $f .pdbqt`
    echo Processing ligand $b
    mkdir -p ../dock/$b
    /opt/autodock_vina/bin/vina --config ../configB.txt --ligand $f \
                                --out ../dock/${b}/${b}_docked.pdbqt \
                                --log ../dock/${b}/log.txt

    /opt/autodock_vina/bin/vina_split \
                               --input   ../dock/${b}/${b}_docked.pdbqt \
                               --ligand ../dock/${b}/${b}_vd

done
```

perform docking for each small molecules

$**cd dock**

$**grep "VINA RESULT" */fda_*vd*.pdbqt | sort -k4 -r | sed -e 's/:REMARK VINA RESULT://g' > sum.txt**

```
[centos@fcdd01 dock]$ cat sum.txt
fda_998/fda_998_vd1.pdbqt       -7.1      0.000      0.000
fda_998/fda_998_vd2.pdbqt       -7.0      1.735      2.548
fda_998/fda_998_vd3.pdbqt       -6.9      1.446      1.973
fda_998/fda_998_vd5.pdbqt       -6.8      2.981      5.422
fda_998/fda_998_vd4.pdbqt       -6.8      2.652      4.736
fda_998/fda_998_vd7.pdbqt       -6.6      2.564      5.110
fda_998/fda_998_vd6.pdbqt       -6.6      2.526      4.902
fda_998/fda_998_vd8.pdbqt       -6.5      2.273      4.856
fda_996/fda_996_vd1.pdbqt       -6.5      0.000      0.000
fda_998/fda_998_vd9.pdbqt       -6.4      3.529      6.321
fda_996/fda_996_vd2.pdbqt       -6.4      2.380      6.550
fda_999/fda_999_vd1.pdbqt       -6.4      0.000      0.000
fda_997/fda_997_vd1.pdbqt       -6.4      0.000      0.000
```

Databases for virtual Screening

- ZINC

  A free database of commercially-available compounds for virtual screening. ZINC contains over 230 million purchasable compounds in ready-to-dock, 3D formats. ZINC also contains over 750 million purchasable compounds you can search.
  http://zinc15.docking.org/
  http://zinc.docking.org/pdbqt/

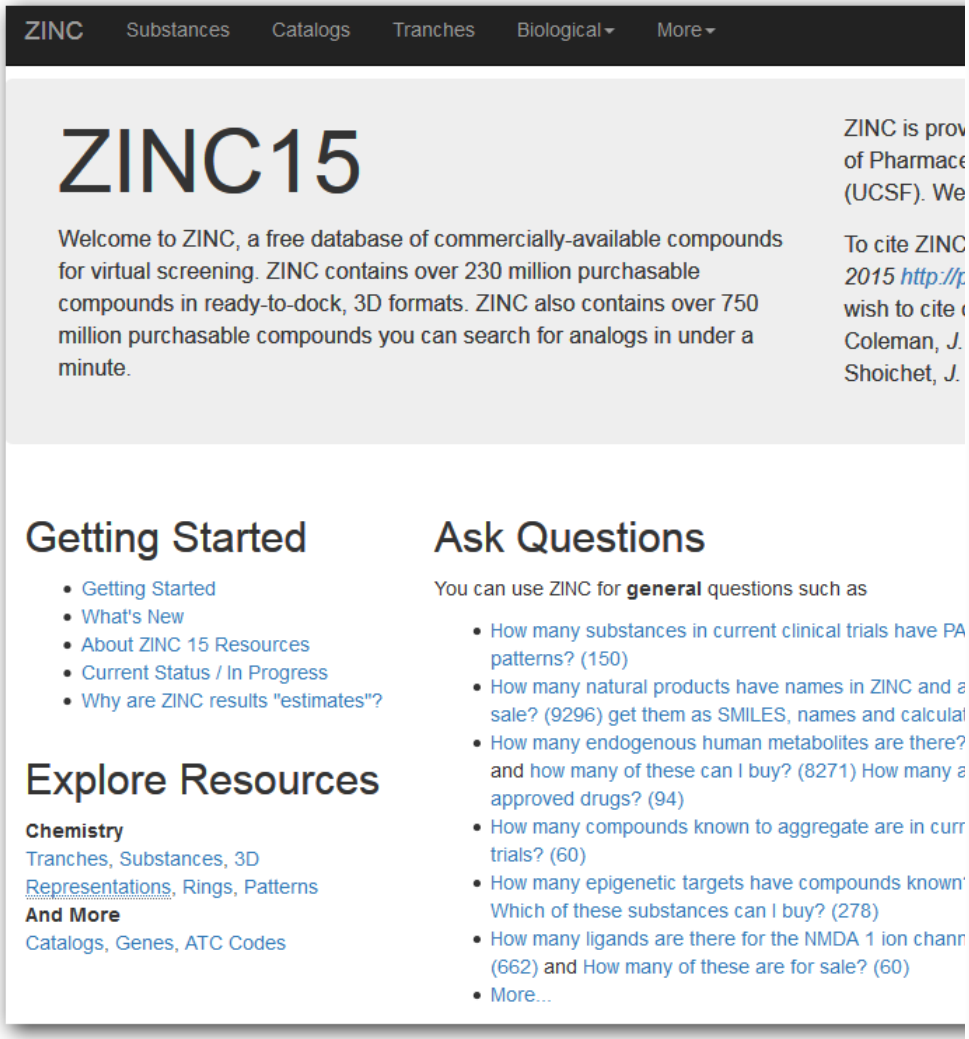
- NCI Diversity Set

  https://wiki.nci.nih.gov/display/NCIDTPdata/Compound+Sets

- PDBbind

  http://www.pdbbind.org
  http://www.pdbbind.org.cn/

http://zinc15.docking.org/



http://zinc.docking.org/pdbqt/