

Autodock tutorial

VINA with UCSF Chimera

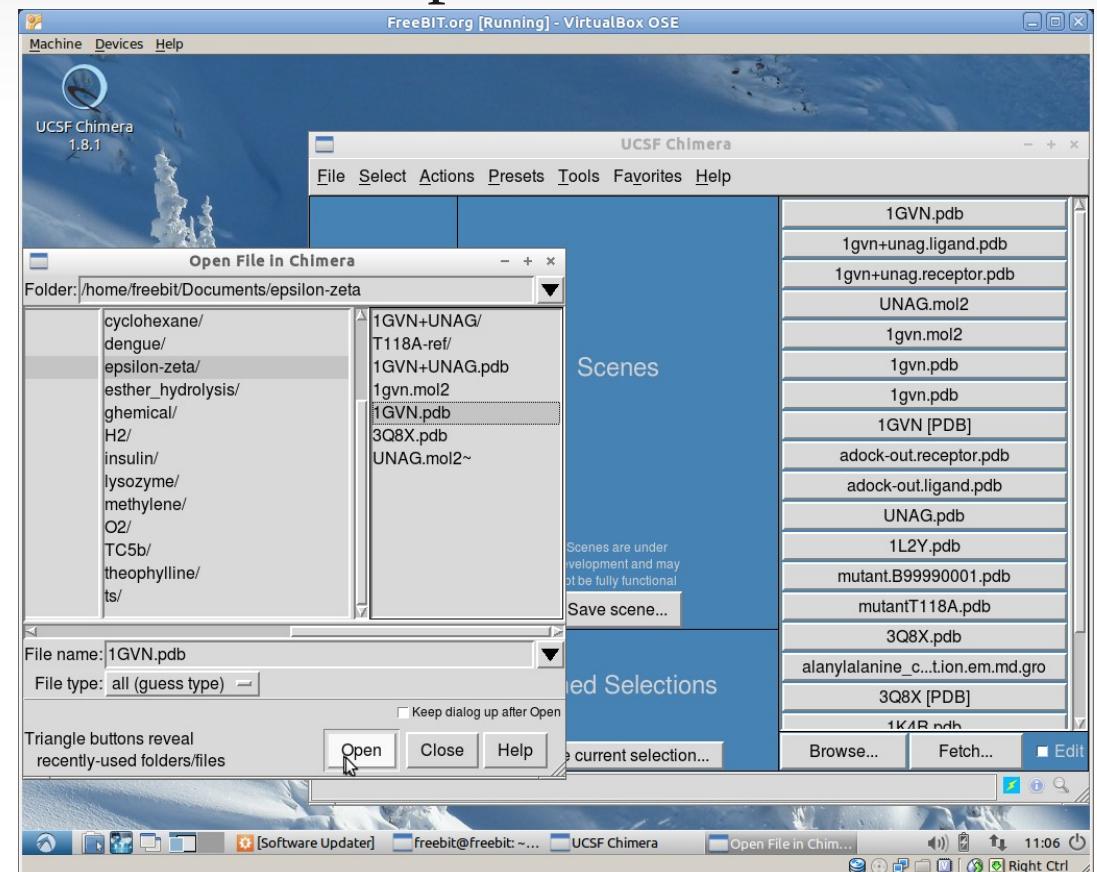
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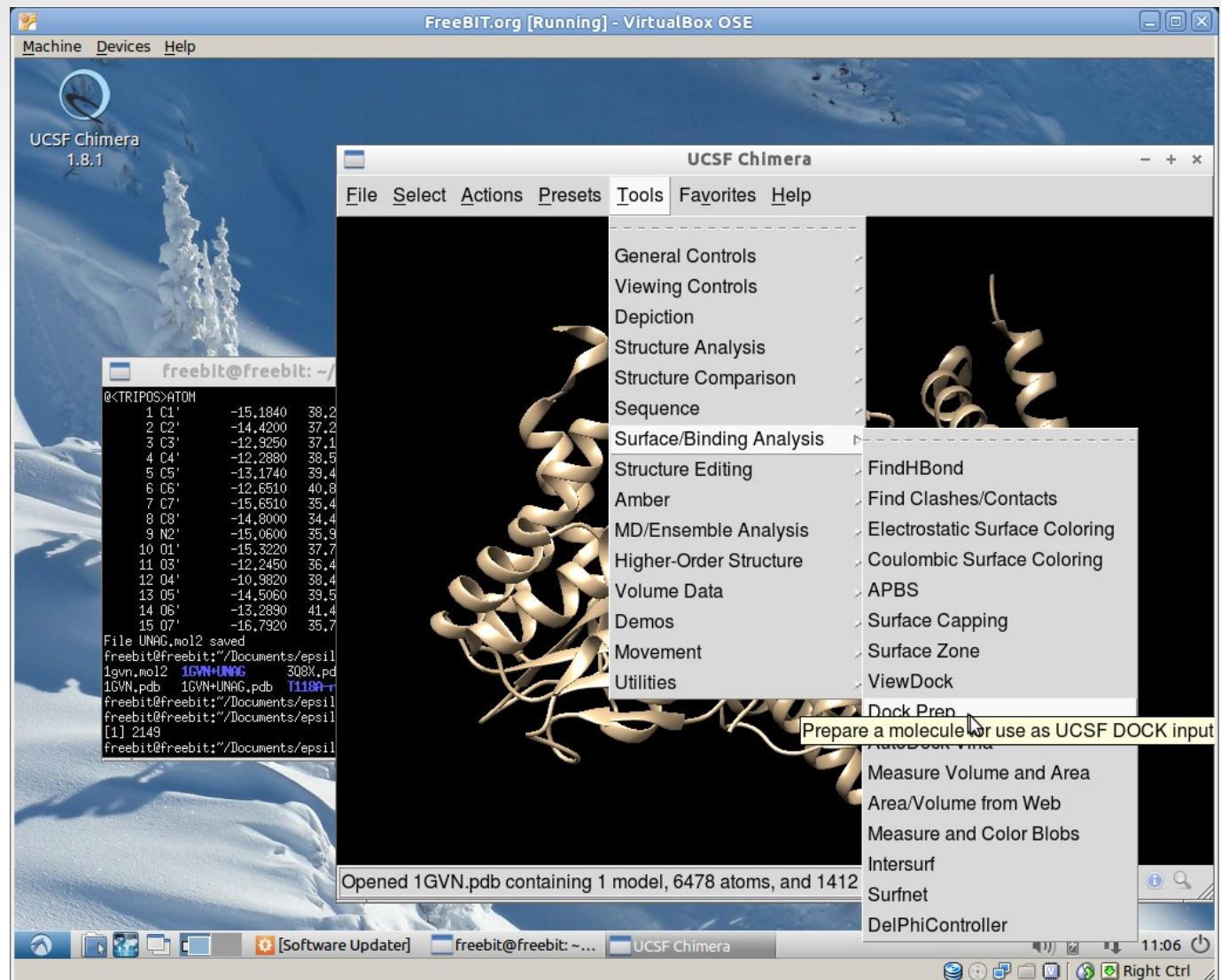
Loading the receptor

- Open UCSF Chimera and then load the protein:
 - File → Open
 - Documents/epsilon-zeta/1GVN.pdb



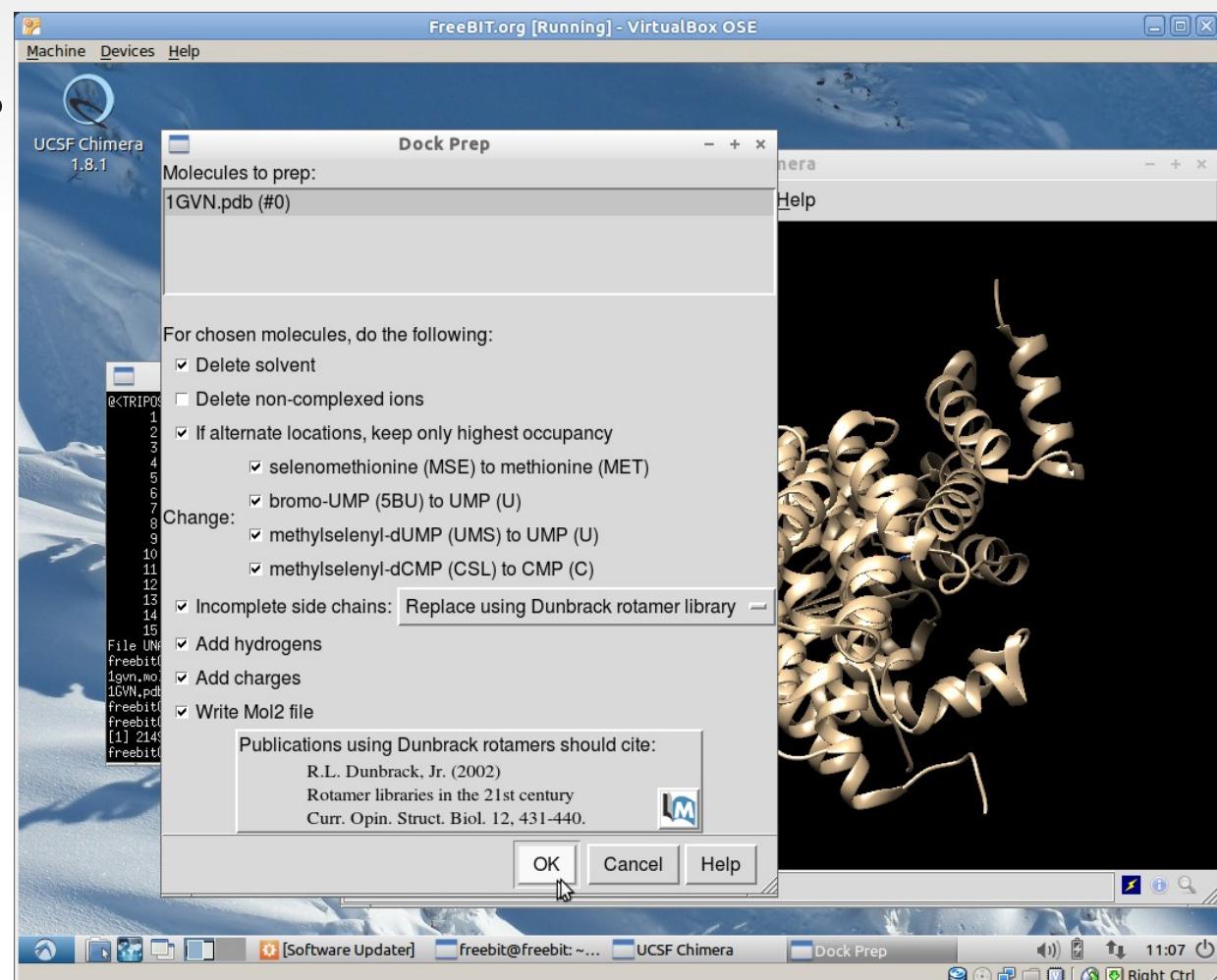
Preparing the receptor

- Tools → Surface/Binding Analysis → DockPrep



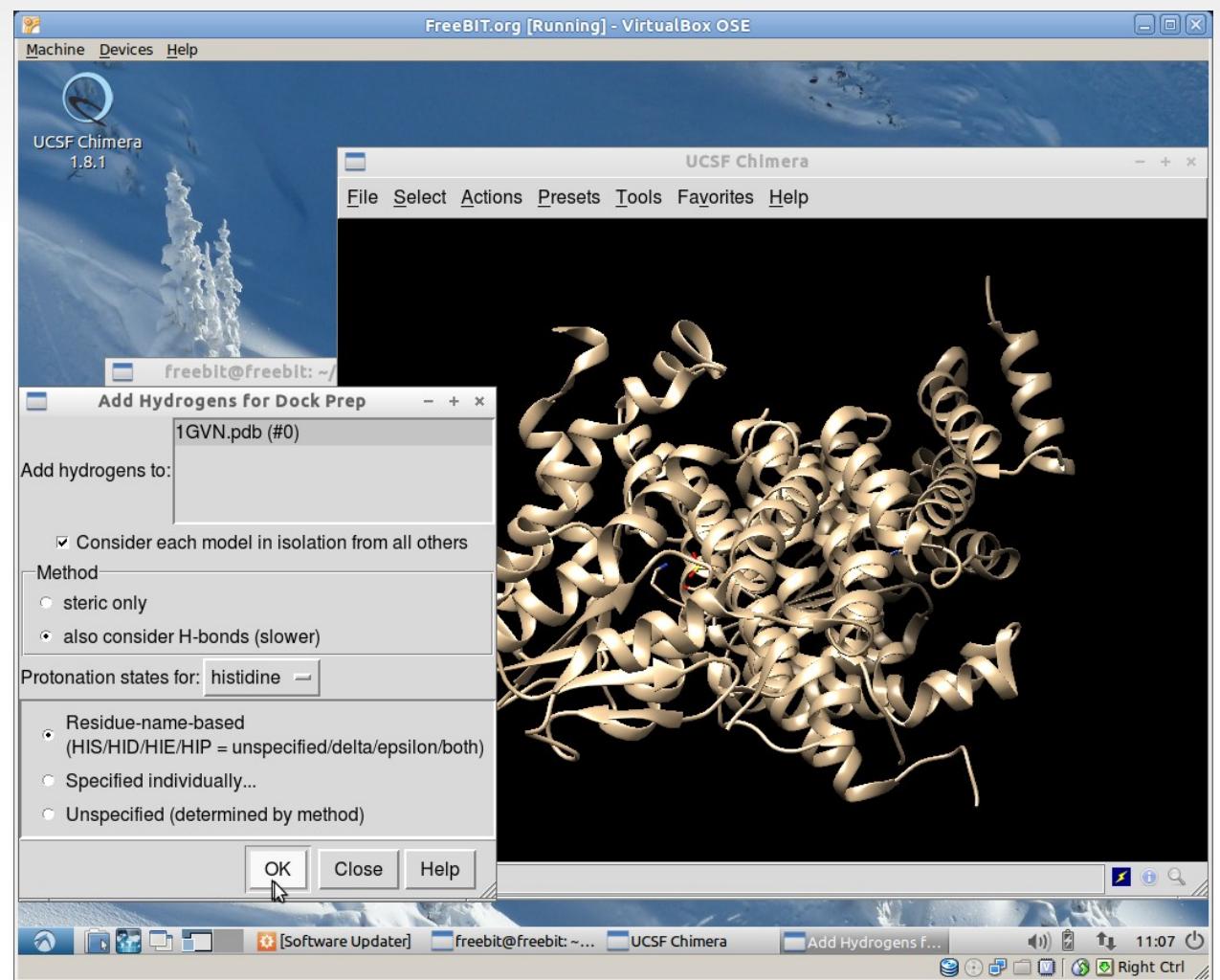
Clean Up the structure

- Remove solvent and fix non-standard residues used for crystallization
- Add H and charges



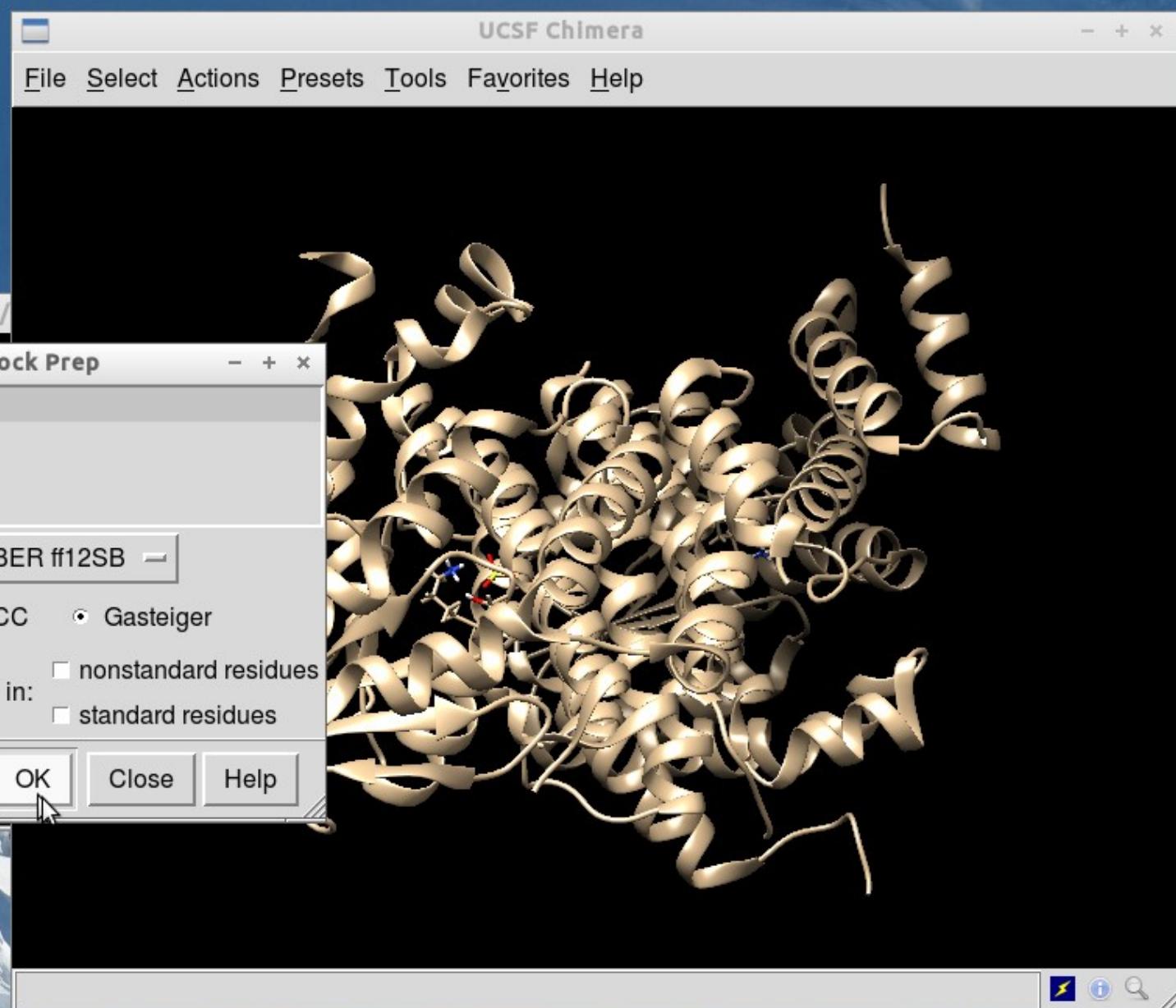
Adding Hydrogens

- Note that you can specify the protonation state for specific residues if needed



Assigning charges

- Protein charges are assigned using an AMBER forcefield
- AMBER does not contain charges for most non-protein atoms:
 - AM1-BCC (semi-empirical quantum mechanics, accurate but slow)
 - Gasteiger (empirical rules, fast)

[Machine](#) [Devices](#) [Help](#)UCSF Chimera
1.8.1freebit@freebit: ~/
DRAFTING ATOMS

[Software Updater]

freebit@freebit: ~....

UCSF Chimera

Assign Charges f...



11:07

Specify net charges

- For non-protein molecules in the model (if included)
 - Specify expected net charge of the whole molecules
 - Specify how to compute the charges for each atom in the molecules
- Generally (for *protein residues* and *non-protein molecules*) Chimera will check that the sum of atomic charges leads to an integer matching the expected summary charge.

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1.8.1

freebit@freebit: ~/

Specify Net Charges

Residue	Net Charge
SO4	-2

Please specify the net charges for the above residues so that their atomic partial charges can be computed.

Charge method: AM1-BCC Gasteiger

Charges are computed using ANTECHAMBER.

Publications using ANTECHAMBER charges should cite:

Wang, J., Wang, W., Kollman, P.A., and Case, D.A. (2006)

Automatic atom type and bond type perception in molecular mechanical calculations

Journal of Molecular Graphics and Modelling, 25, 247-260.



OK

Cancel

Help



[Software Updater]

freebit@freebit: ~...

UCSF Chimera

Specify Net Charges



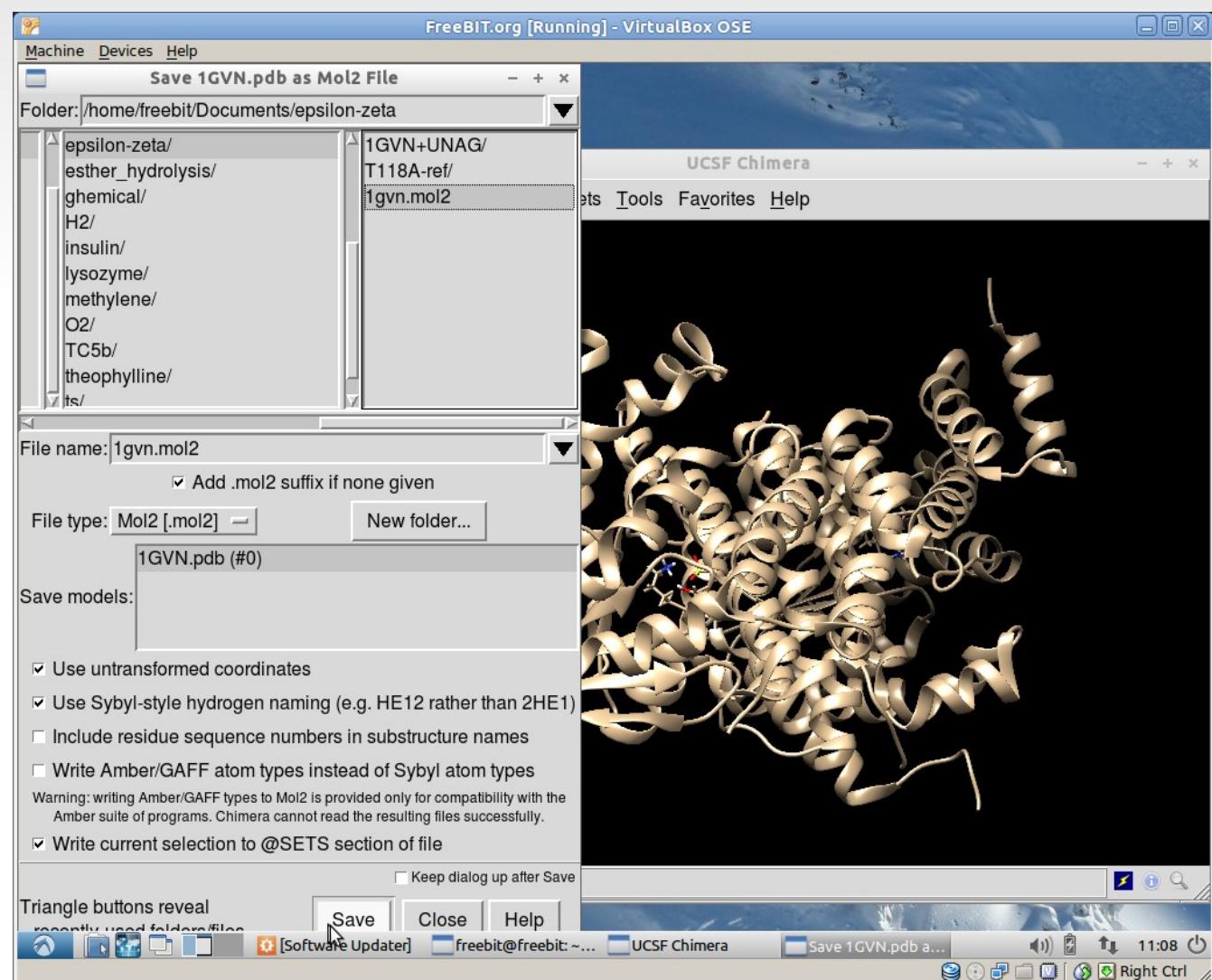
11:08



Right Ctrl

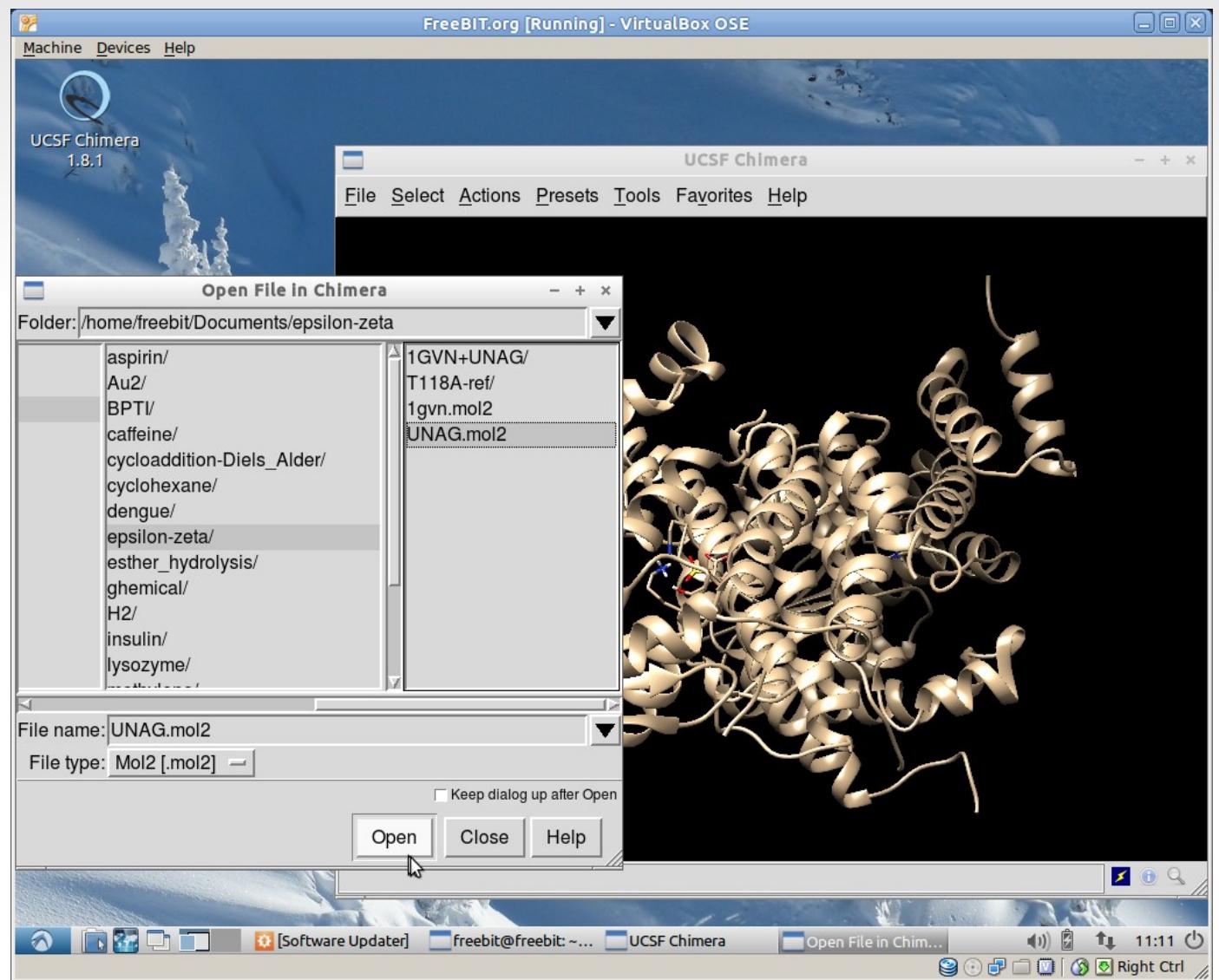
Wait and save results

- Save the “clean” receptor as a “MOL2” file
 - 1gvn.mol2



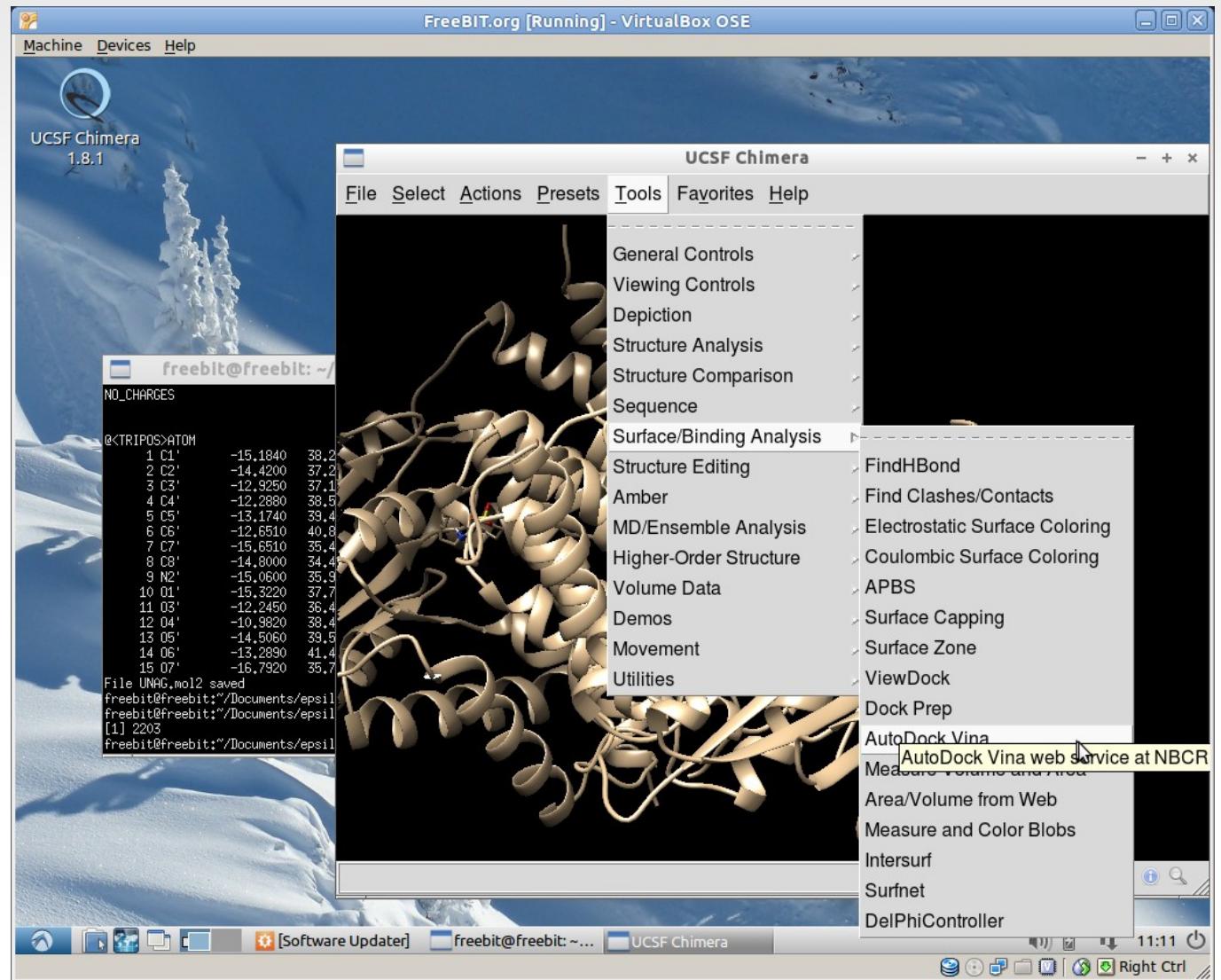
Open the ligand

- File → Open → UNAG.mol2



Prepare the docking job

- Tools → Surface/Binding Analysis → AutoDock Vina



Select molecules and site

- Give a “base” name for all job-generated files
 - e.g.: 1gvn+unag
- Specify receptor and ligand
 - Receptor: 1GVN
 - Ligand: UNAG
- Select area to explore: a parallelepiped boundary for the search grid
 - Enclose the active site using the mouse
 - Center: 15 – 35 – 60
 - Size: 20 – 20 – 20



UCSF Chimera

1.8.1

AutoDock Vina

Output file: 1gvn+unag

Receptor: 1GVN.pdb (#0)

Ligand: 1GVN.pdb (#0)

▼ Receptor search volume options

Resize search volume using

Center: -15 35 60

Size: 20 20 20

► Receptor options

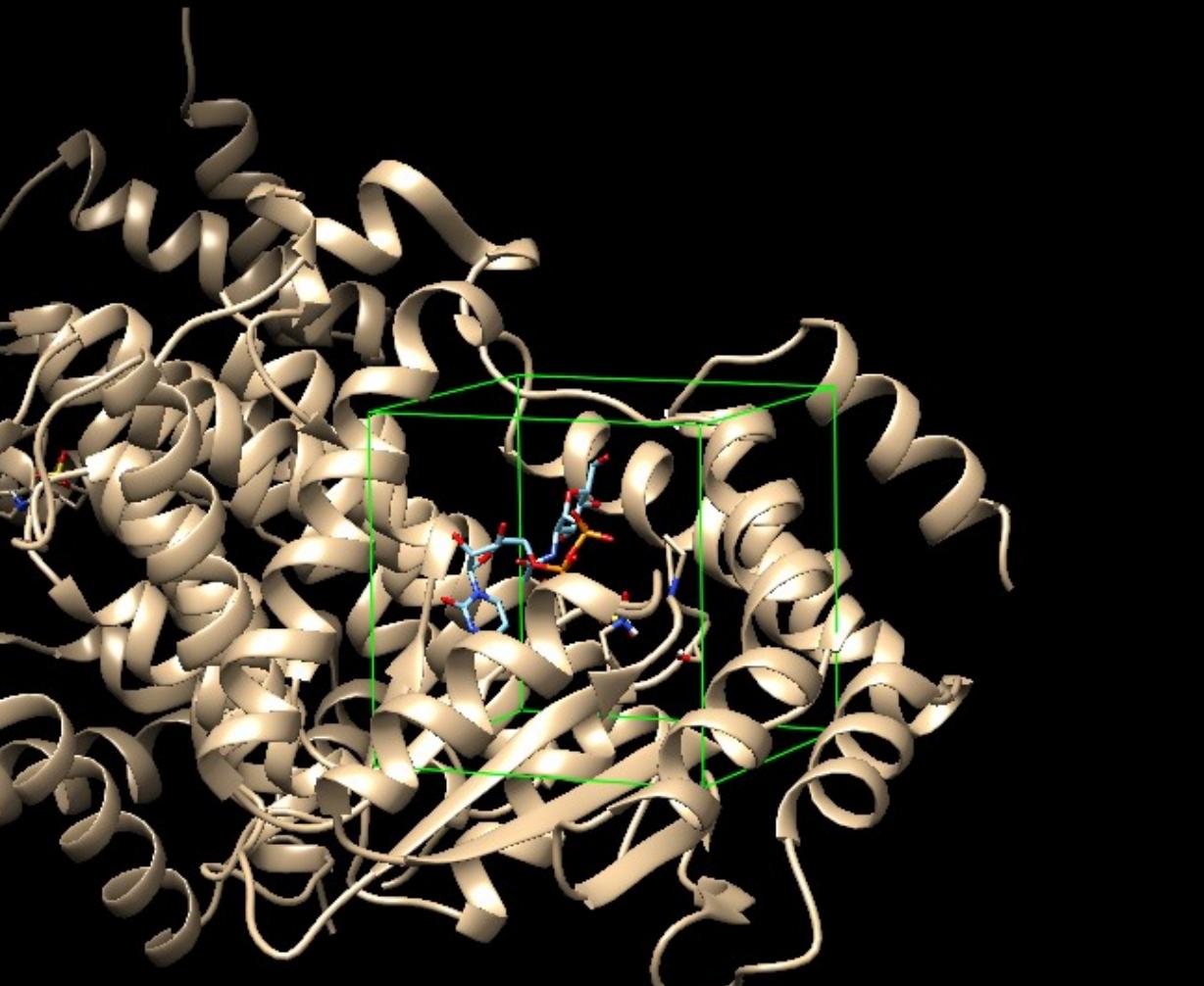
► Ligand options

► Advanced options

► Executable location

UCSF Chimera

Actions Presets Tools Favorites Help

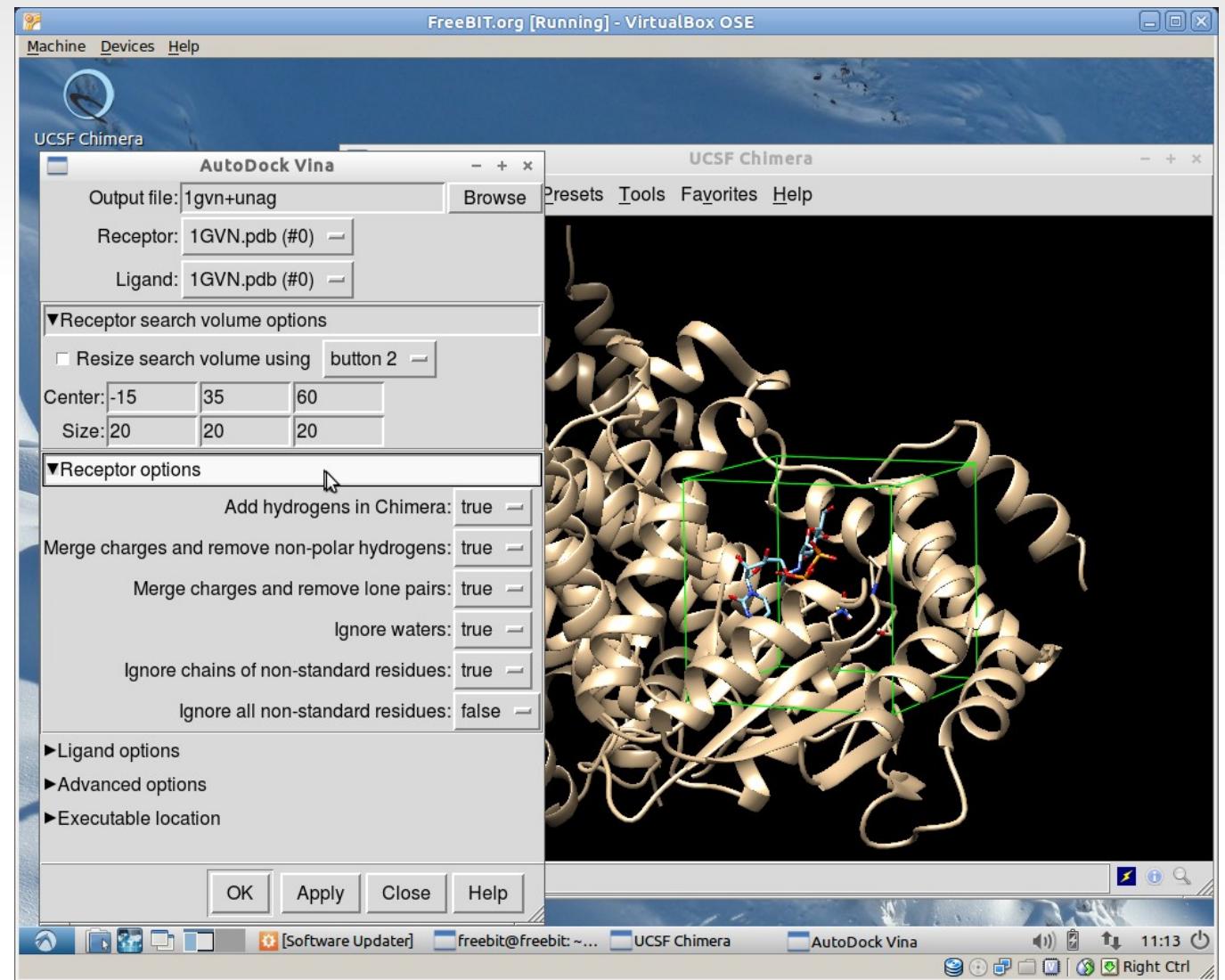


```
freebit@freebit:~/Documents/epsil  
freebit@freebit:~/Documents/epsil  
[1] 2203  
freebit@freebit:~/Documents/epsil
```



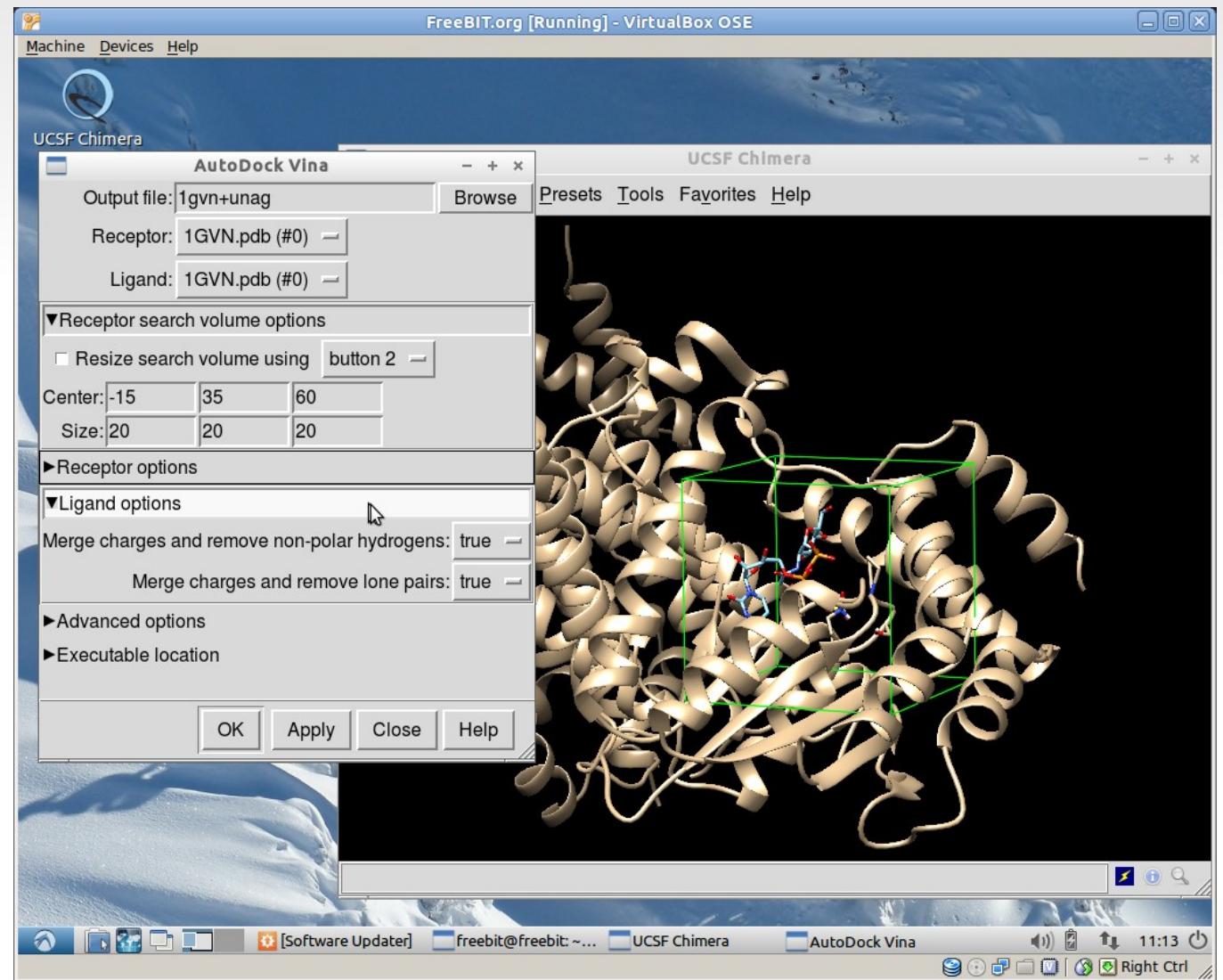
Set receptor options

- Expand/close the section as needed



Set ligand options

- Expand/close the section as needed



Select the precision

- Click on “Advanced options”
 - Select the number of binding modes to generate (9)
 - Select the thoroughness of the search: lower values will run faster but be less accurate.
 - Since we cannot wait, we'll use the fastest setting (1)
 - You will normally use the slowest one – 8
 - Select the report threshold (poses not scoring within these kcal/mol of the best will be discarded)



UCSF Chimera

AutoDock Vina

Output file: 1gvn+unag

Receptor: 1GVN.pdb (#0)

Ligand: 1GVN.pdb (#0)

▼ Receptor search volume options

Resize search volume using

Center: -15 35 60

Size: 20 20 20

► Receptor options

► Ligand options

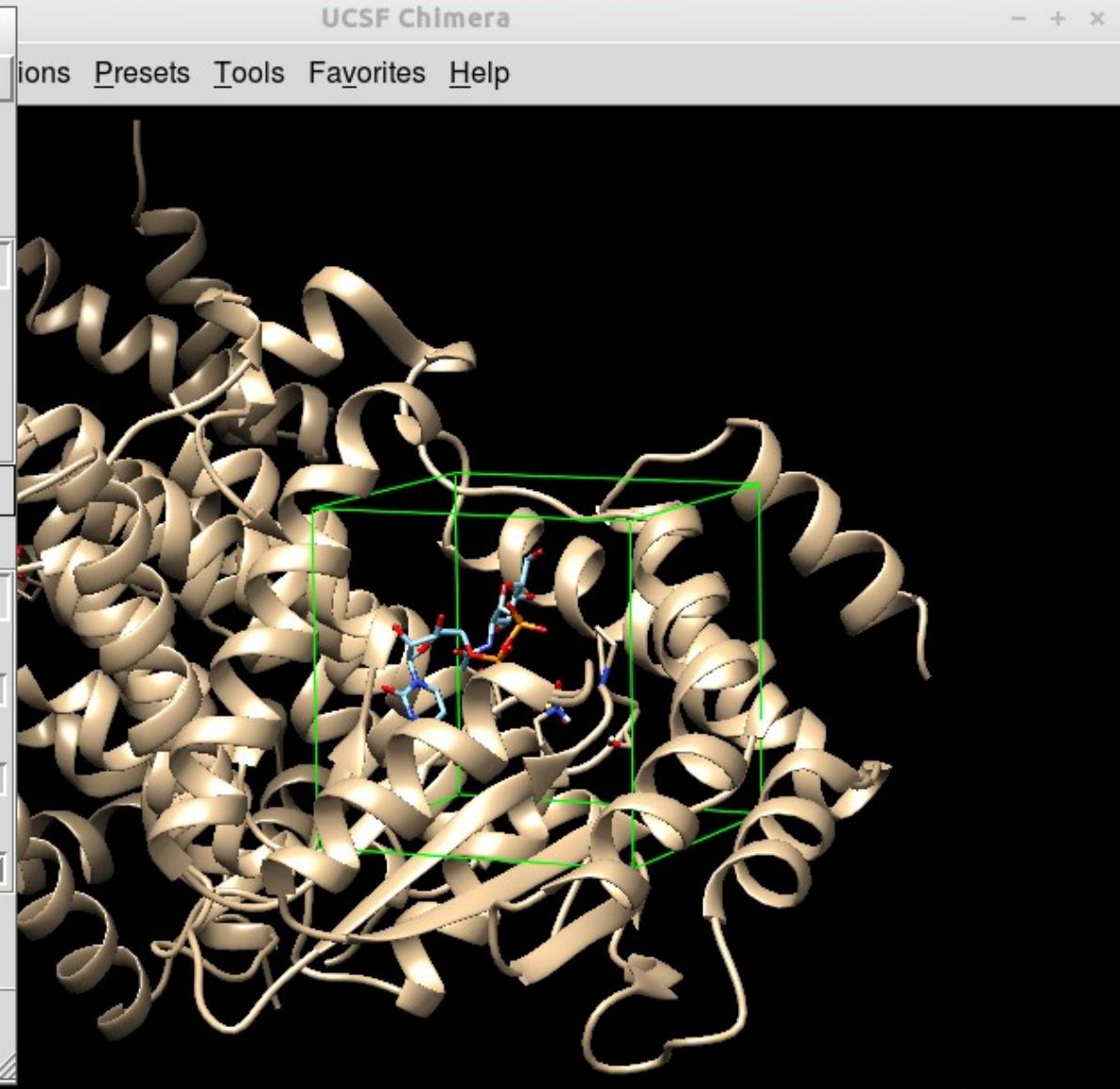
▼ Advanced options

Number of binding modes: 9

Exhaustiveness of search: 1

Maximum energy difference (kcal/mol): 3

► Executable location



Select executable

- You can run VINA remotely on a public web service or locally
 - The remote server is shared with other users
 - Local runs require that you have VINA installed
- We do not want to overload the server with a tutorial
 - Select “Local”
 - Set the executable to “**/usr/bin/vina**”



UCSF Chimera

AutoDock Vina

Output file:

Receptor:

Ligand:

▼ Receptor search volume options

Resize search volume using

Center:
Size:

► Receptor options

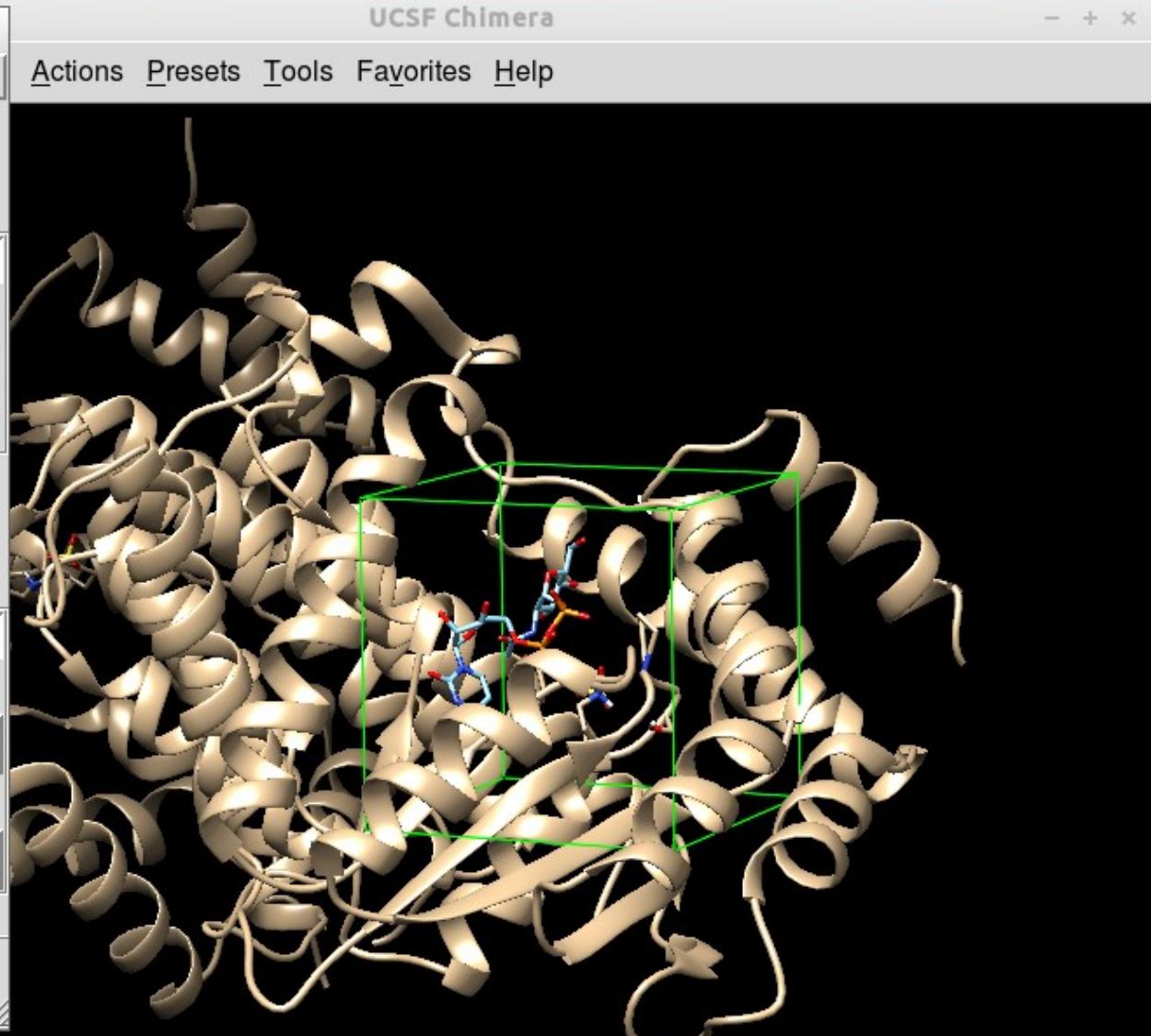
► Ligand options

► Advanced options

▼ Executable location

Opal web service
 Local

Server:
Path:



Check

- Ensure that everything is OK:
 - Receptor is “1GVN”, Ligand is “UNAG”
 - The green grid box fully encloses the active site
 - The receptor and ligand options are correct
 - The precision, threshold and poses requested are what you want
 - The correct executable has been chosen
- Click on “OK”

[Machine](#) [Devices](#) [Help](#)

AutoDock Vina

Output file: [Browse](#)

Receptor:

Ligand:

▼ Receptor search volume options

Resize search volume using [button 2](#)

Center:
Size:

► Receptor options

► Ligand options

► Advanced options

▼ Executable location

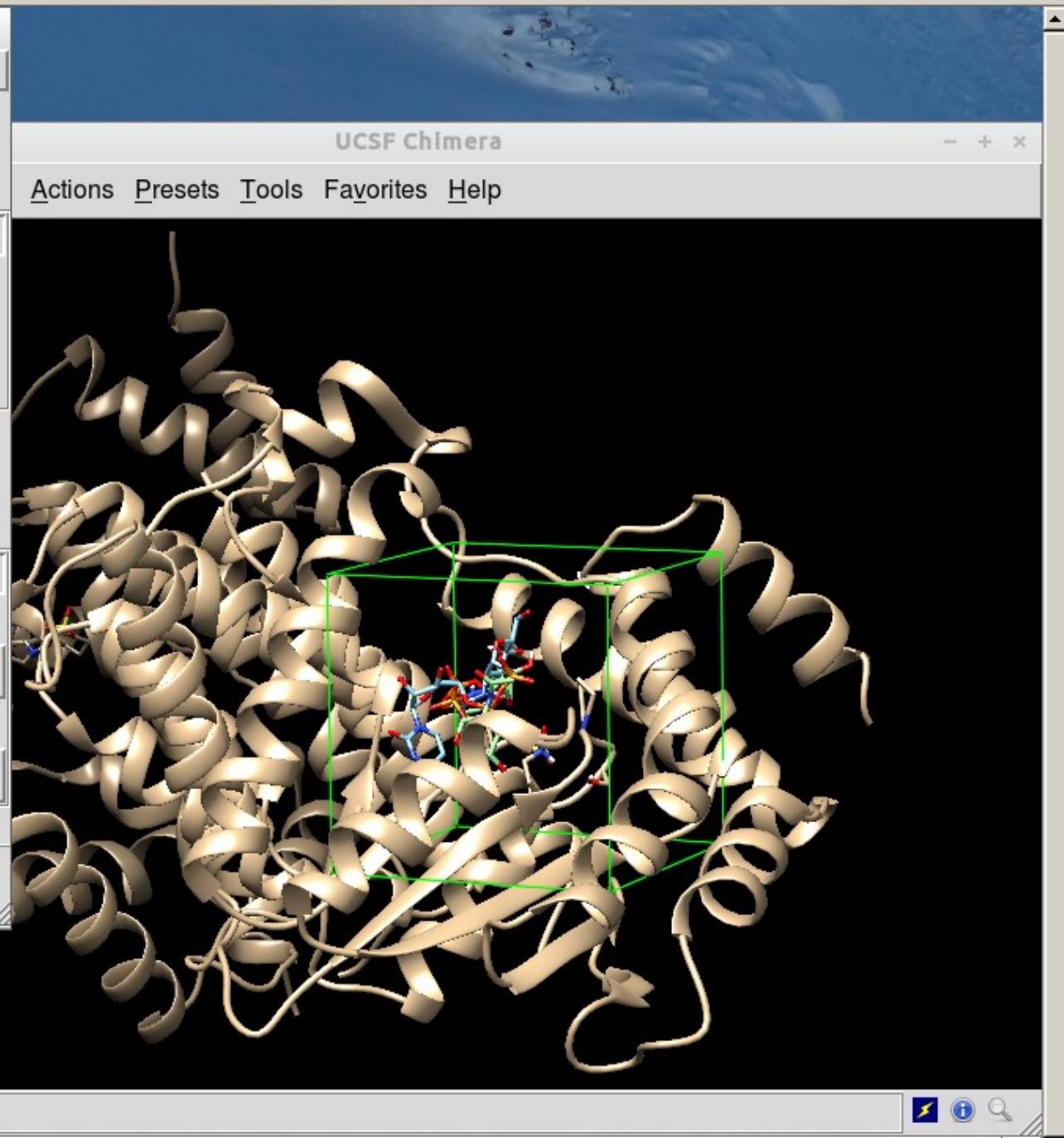
Opal web service

Server: [Reset](#)

Local

Path: [Browse...](#)

[OK](#) [Apply](#) [Close](#) [Help](#)

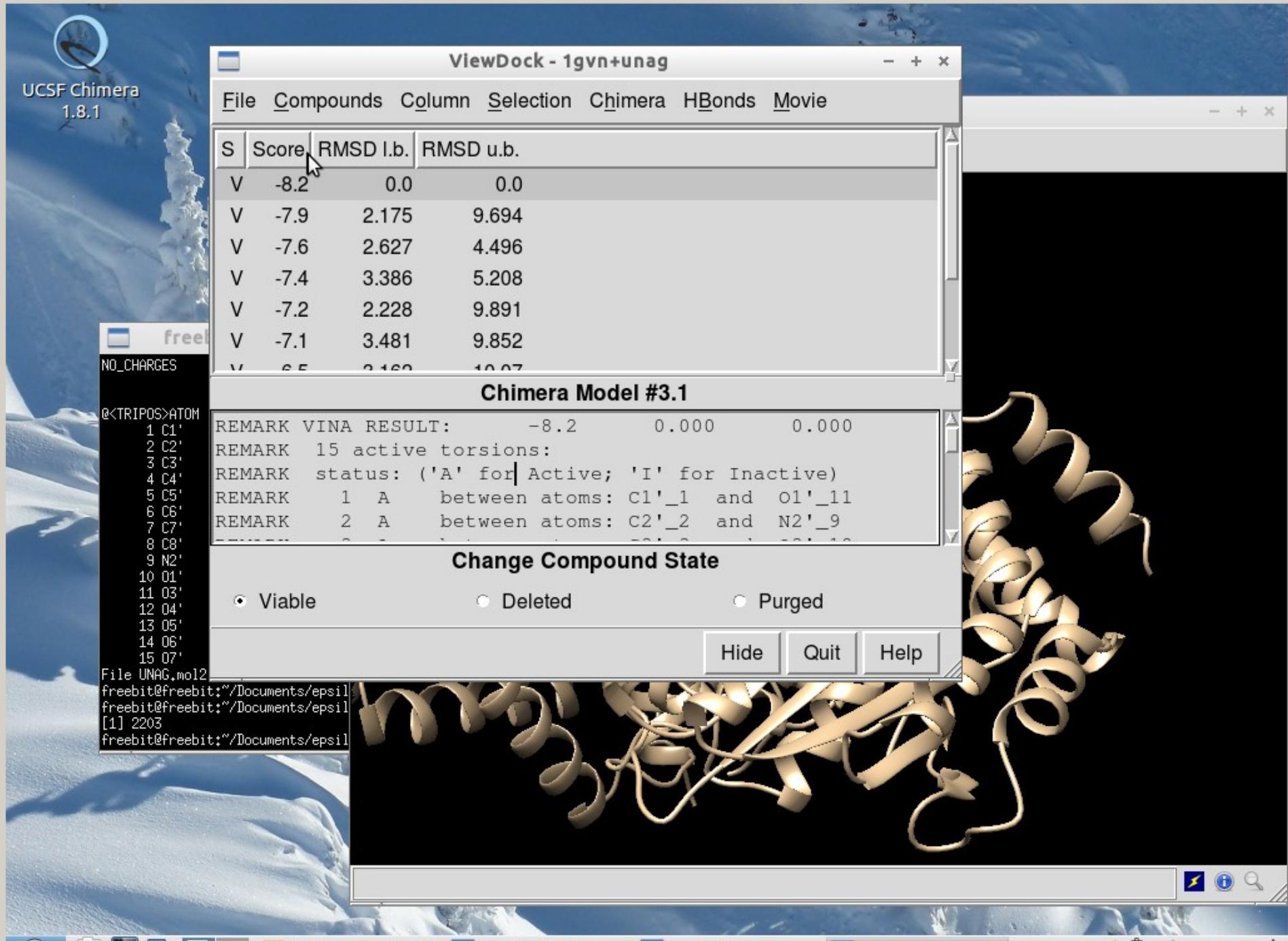


Wait

Wait

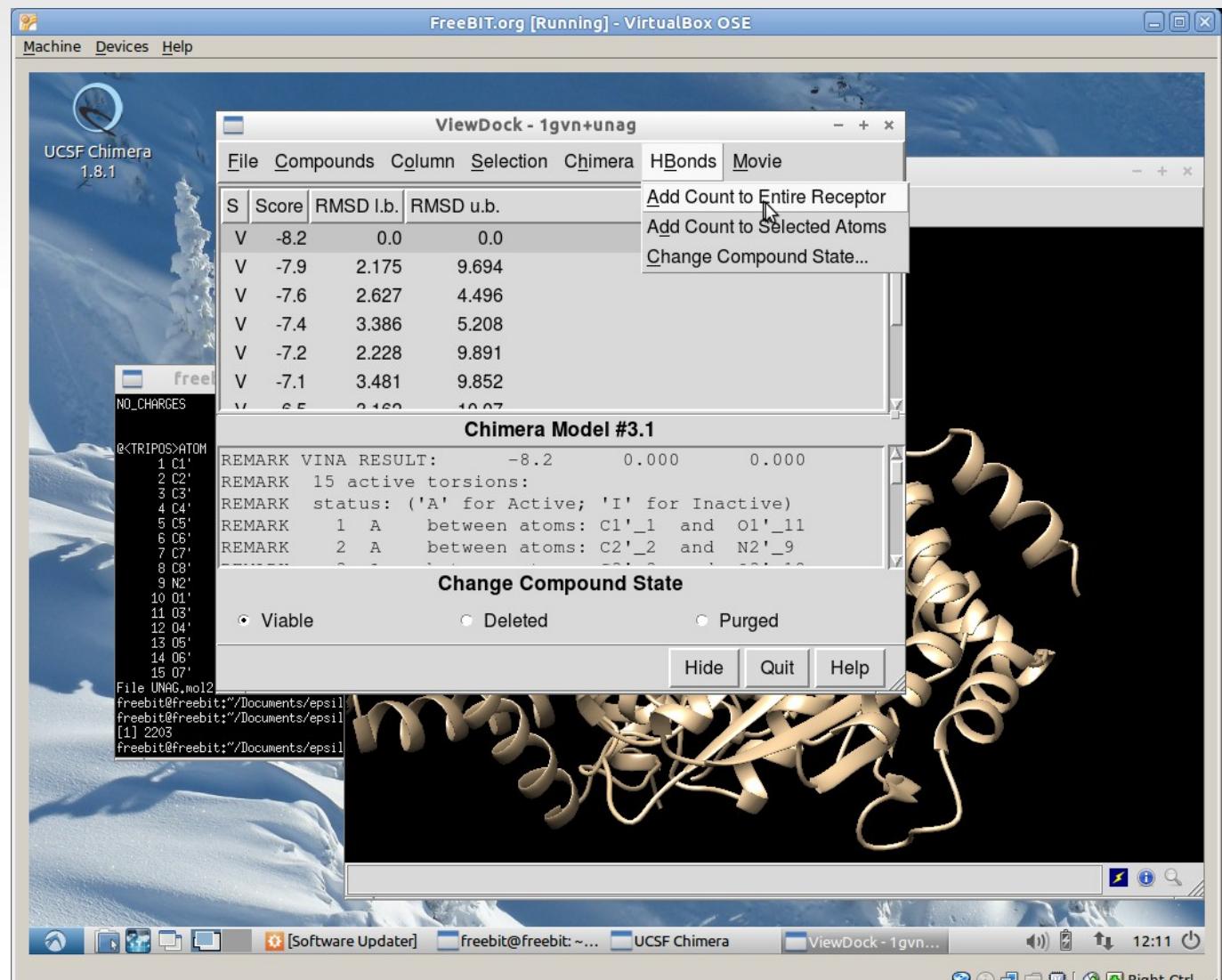
Inspect results

- After it is done, UCSF Chimera will open the “ViewDock” interface
 - Tabular list of poses selected
 - You can change sort order clicking on column headers
 - You can compute properties and add them to the table
 - You can organize poses:
 - Viable
 - Deleted
 - Purged



Compute H-Bonds

- Hbonds → Add count to entire receptor



Choose H-bonds

- We only want H-bonds between ligand and receptor
 - Inter-model
- We want to distinguish “inexact” h-bonds
 - Color H-bonds not meeting precise criteria differently
- We do not want intra-molecule or intra-residue bonds
- We want to see them all
 - If endpoint atom hidden, show endpoint residue



```
Free
NO_CHARGES
@<TRIPOS>ATOM
 1 C1'
 2 C2'
 3 C3'
 4 C4'
 5 C5'
 6 C6'
 7 C7'
 8 C8'
 9 N2'
10 O1'
11 O3'
12 O4'
13 O5'
14 O6'
15 O7'
File UNAG.mol2
freebit@freebit:~/Documents/epsil
freebit@freebit:~/Documents/epsil
[1] 2203
freebit@freebit:~/Documents/epsil
```

S	Score	RMSD l.b.	RMSD u.b.
V	-8.2	0.0	0.0
V	-7.9	2.175	9.694
V	-7.6	2.627	4.496
V	-7.4	3.386	5.208
V	-7.2	2.228	9.891
V	-7.1	3.481	9.852
V	-6.5	2.160	10.07

Chimera

```
REMARK VINA RESULT:      -8.2
REMARK 15 active torsions:
REMARK status: ('A' for Acti
REMARK      1   A    between ato
REMARK      2   A    between ato
```

Change Cor

Viable

Deleted

H-Bond Parameters

H-bond color: cyan

Line width: 1.0

Label H-bond with distance

Relax H-bond constraints

Relax constraints by: 0.4 angstroms
20.0 degrees

Color H-bonds not meeting precise criteria differently: orange

Restrict to models...

Only find H-bonds with at least one end selected

Include intra-molecule H-bonds

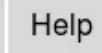
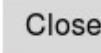
Include intra-residue H-bonds

If endpoint atom hidden, show endpoint residue

Retain currently displayed H-bonds

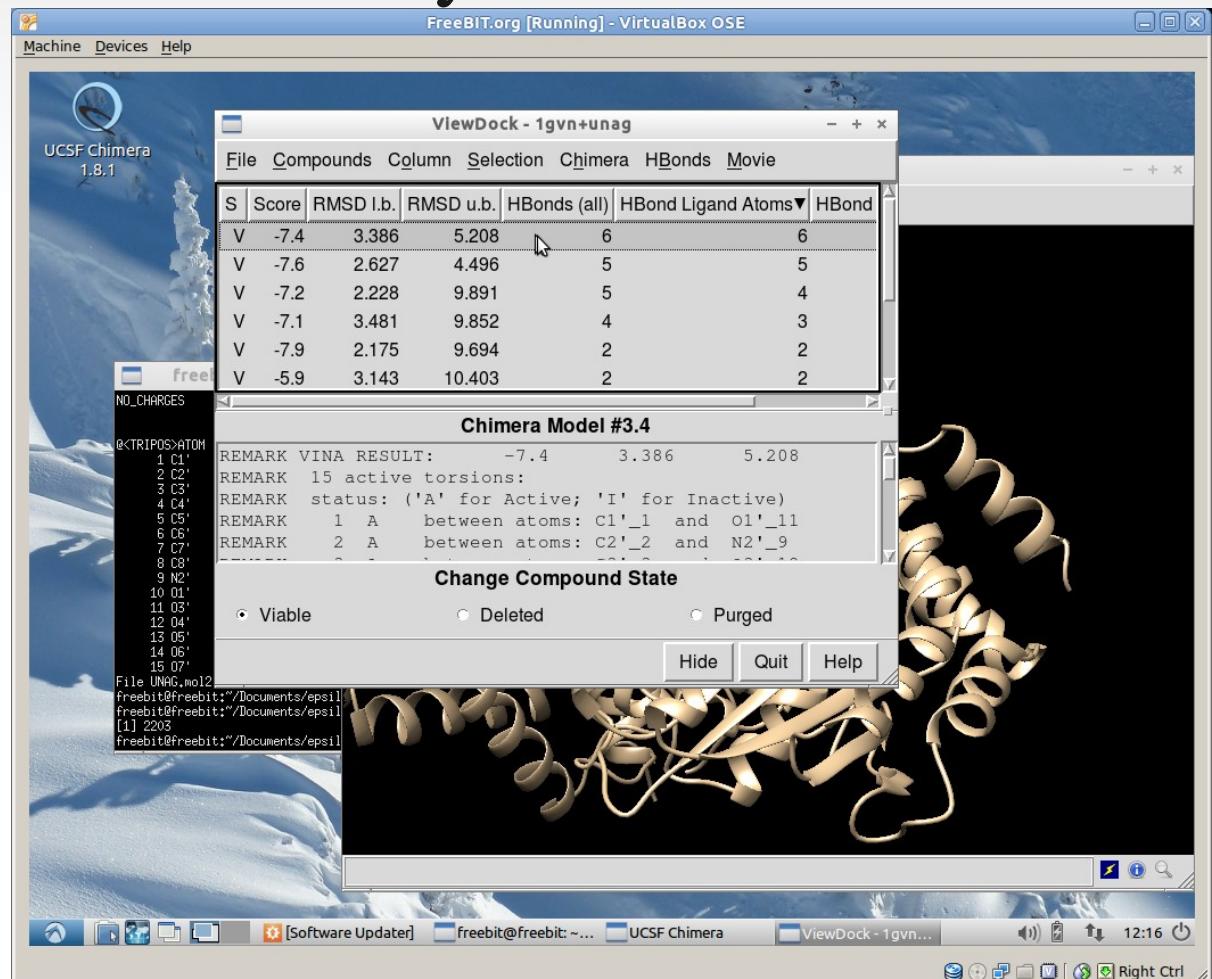
Write information to file

Write information to reply log



Inspect H-bonds

- H-bonds contribute significantly to stability
- You can sort the conformers by H-bonds formed



Too much clutter?

- Bring up the “Model Panel”
 - Tools → Model Panel
- You can activate/deactivate which models are shown
- Play with selections to show only relevant information
- Select the reference ligand and give it a special color
- Play with UCSF Chimera...

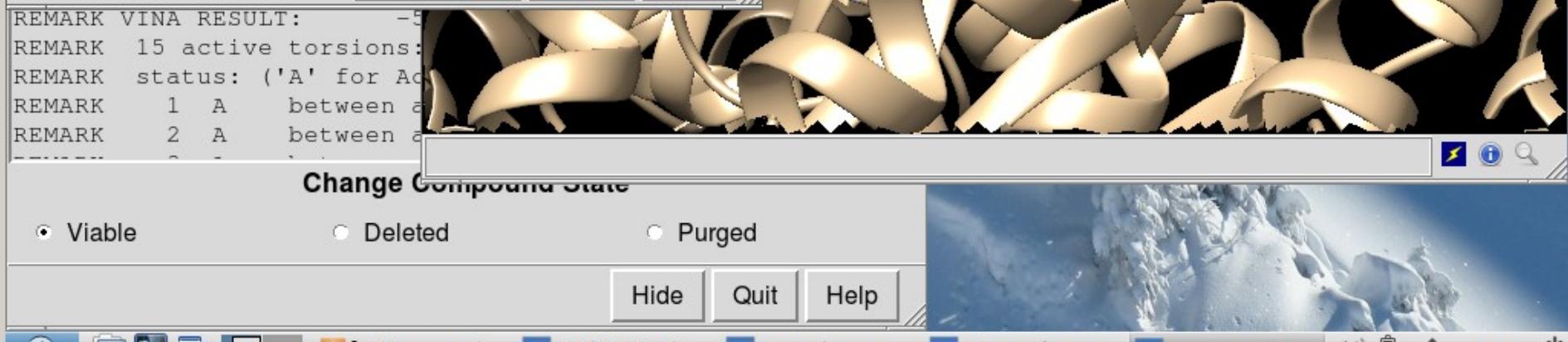


Model Panel

ID	A	S	Name
0	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	1GVN.pdb
1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	UNAG
2	<input checked="" type="checkbox"/>	<input type="checkbox"/>	AutoDock Vina Search
3.1...3.10	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	1gvn+unag

activate
activate all
activate only
add/edit note...
attributes...
biological unit
clipping...
close
 favorites all

Configure... Close Help



[Software Upd...

freebit@freebi...

UCSF Chimera

ViewDock - 1g...

Model Panel



12:22

That was all folks!