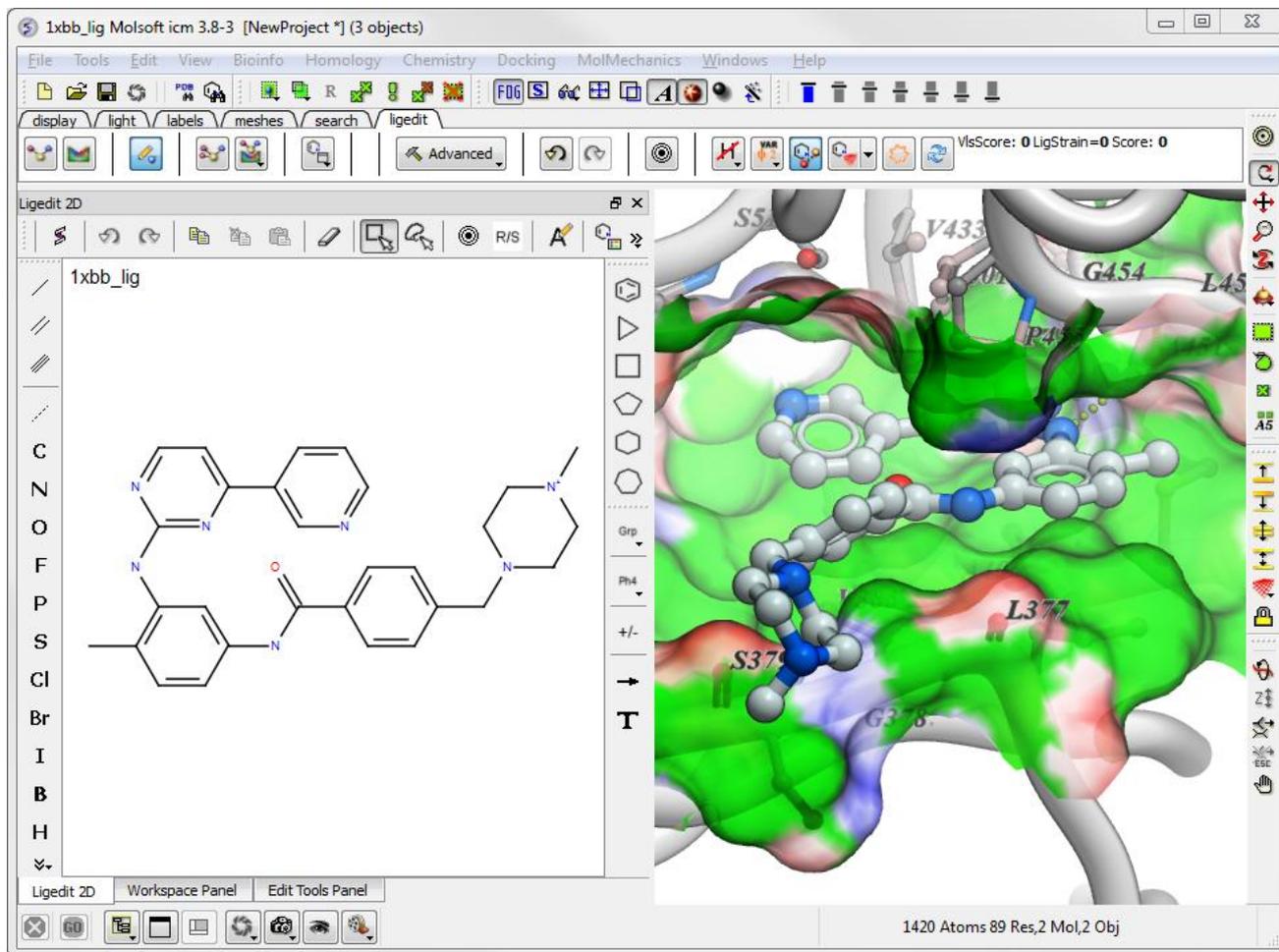


# ICM Interactive Ligand Editor Getting Started Guide

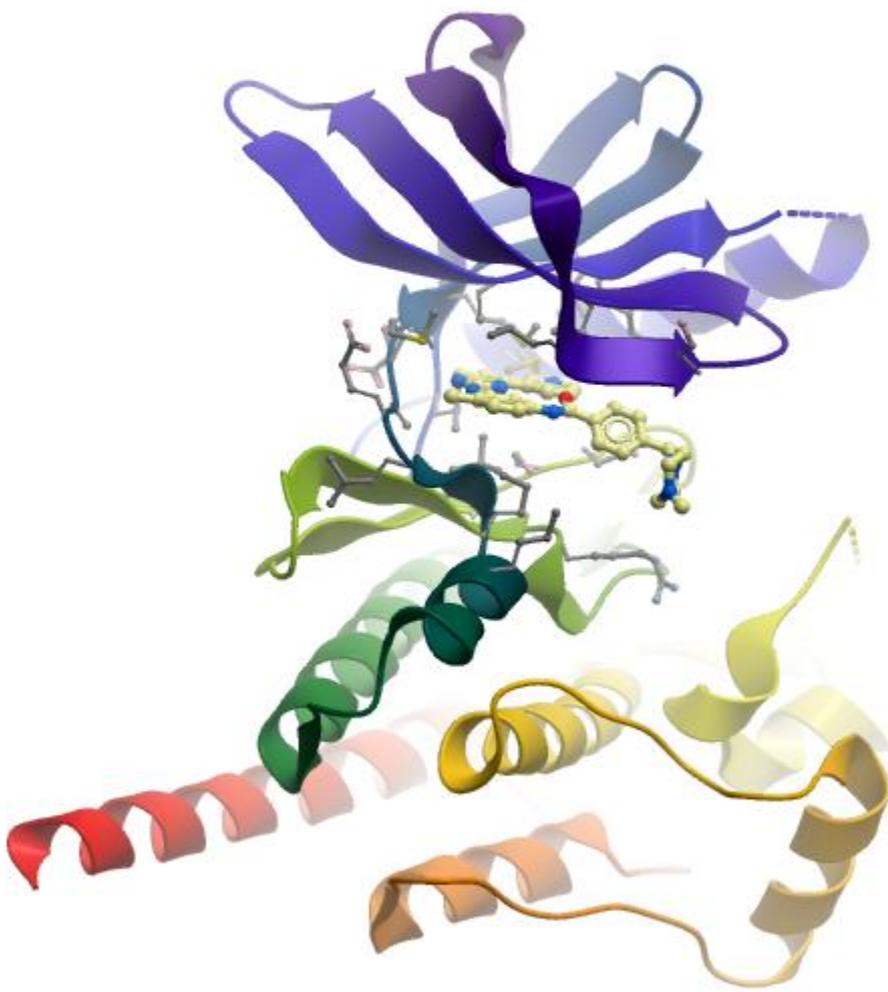


# Reading in a PDB file and Setting up the Ligand and Receptor

Read in a PDB file (File/Open) OR use the PDB search tab.

File/Open

PDB Search Tab  
enter string e.g.  
PDB code "1xbb"



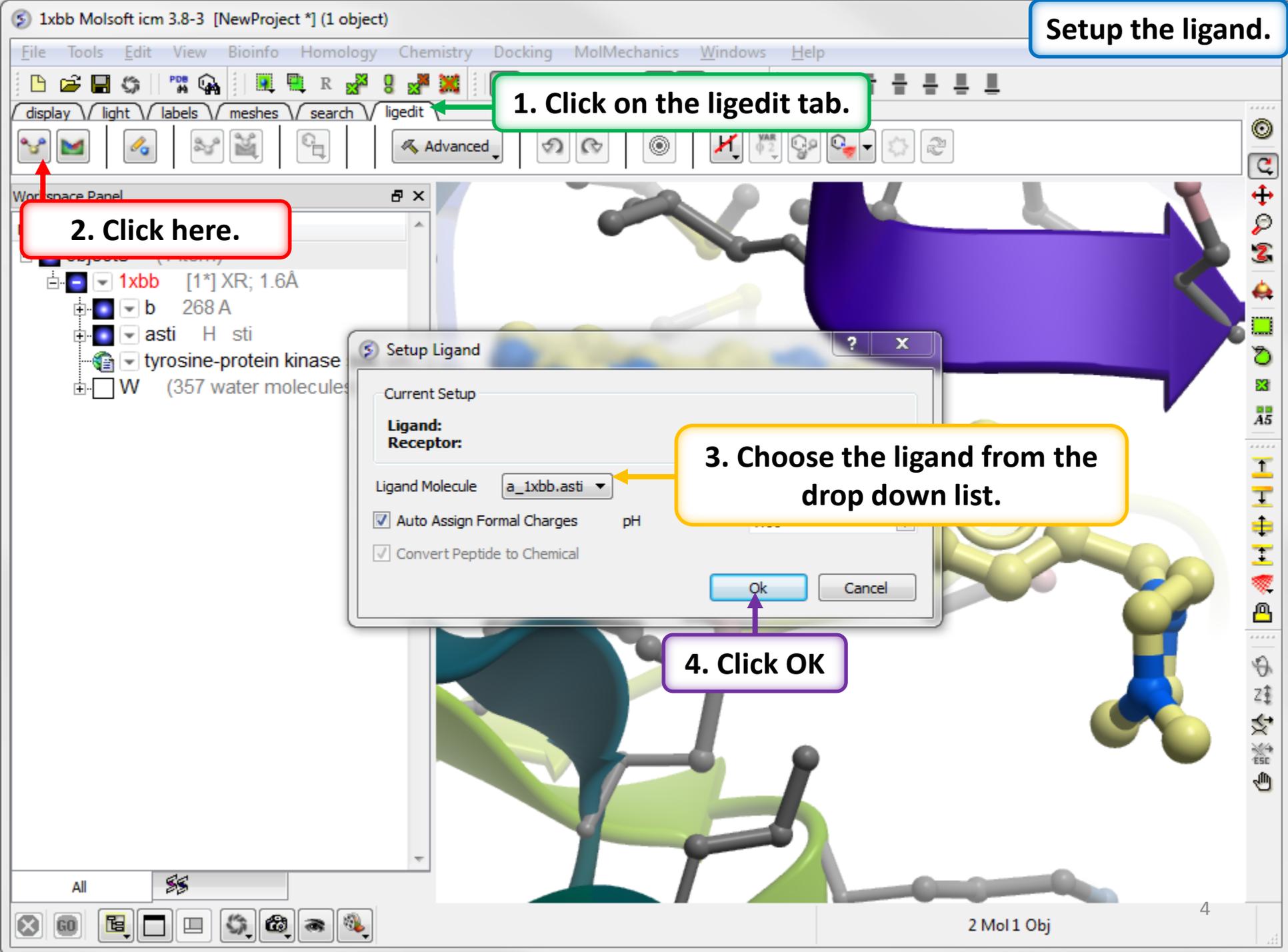
Setup the ligand.

1. Click on the ligedit tab.

2. Click here.

3. Choose the ligand from the drop down list.

4. Click OK



Setup the receptor.

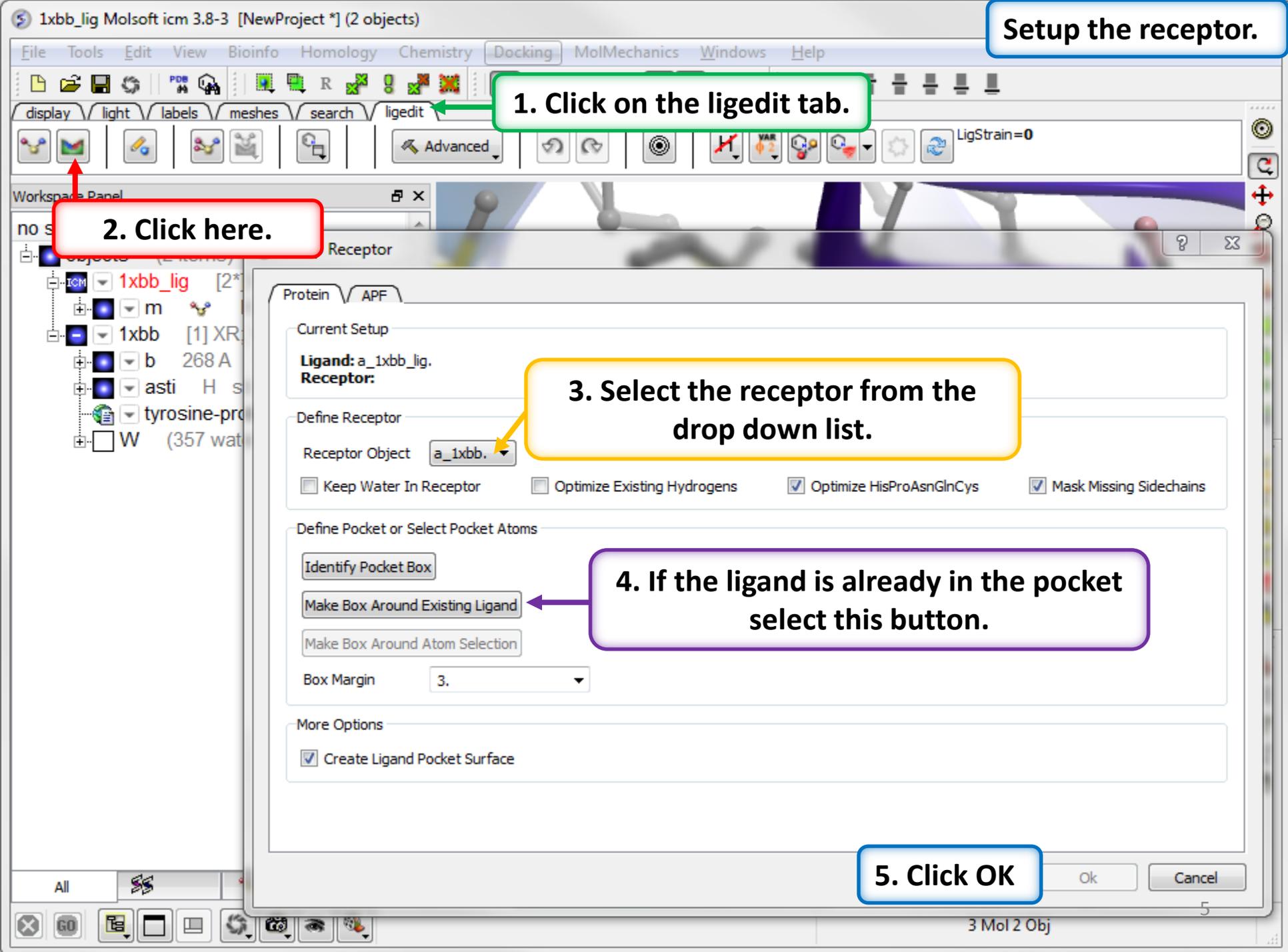
1. Click on the ligedit tab.

2. Click here.

3. Select the receptor from the drop down list.

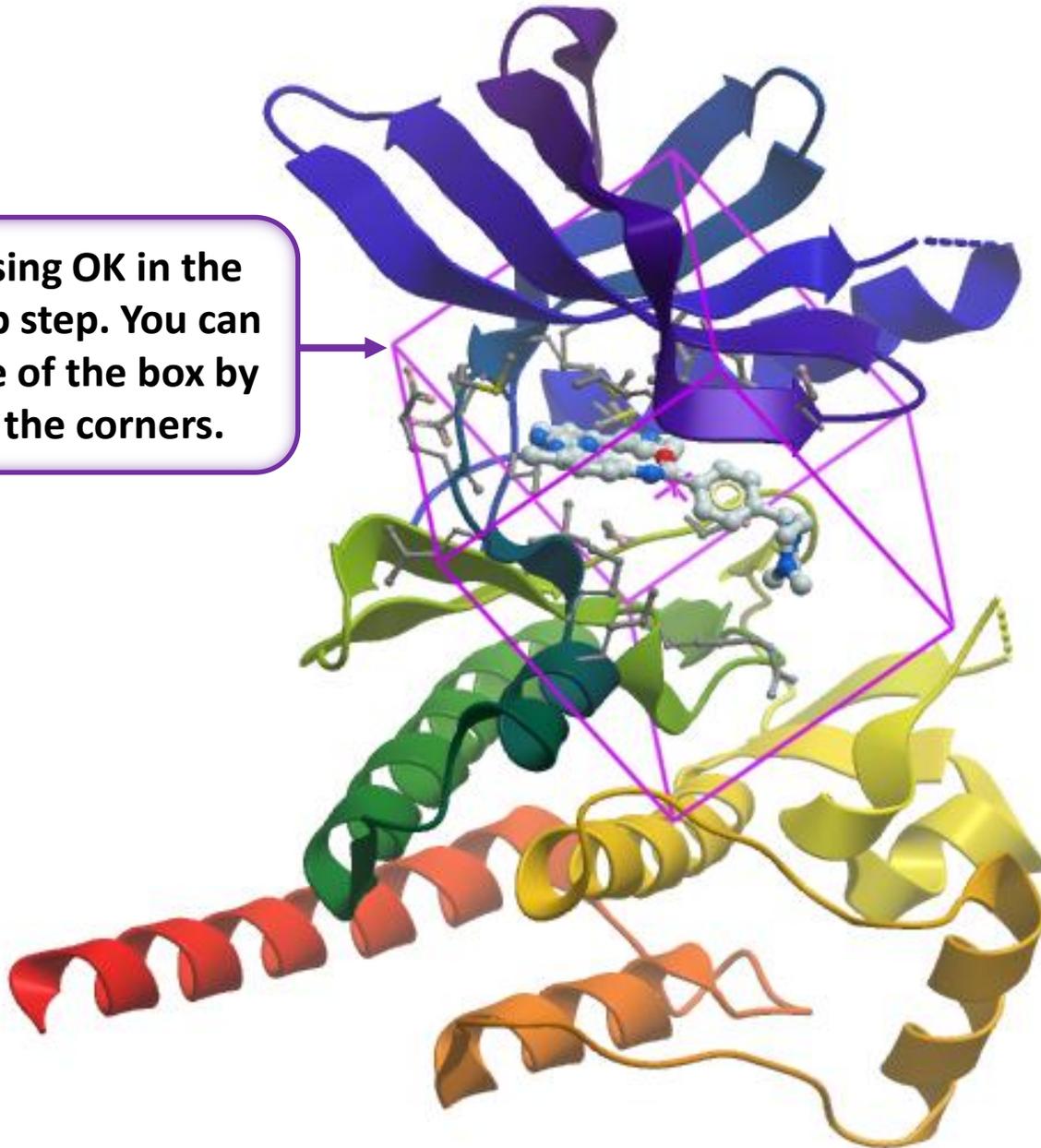
4. If the ligand is already in the pocket select this button.

5. Click OK

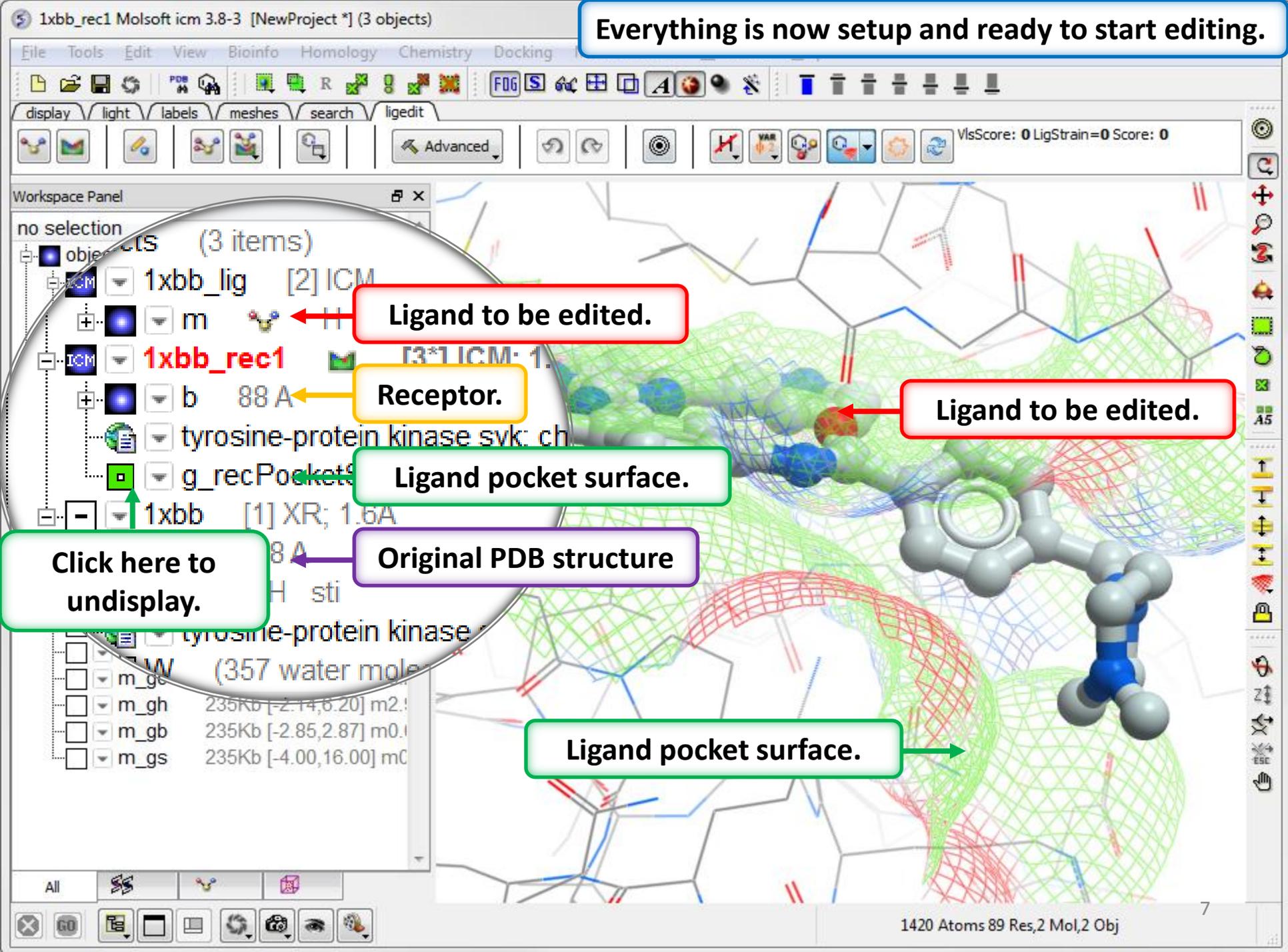


The energy maps are made inside the purple box.

Prior to pressing OK in the receptor setup step. You can adjust the size of the box by dragging on the corners.



Everything is now setup and ready to start editing.



Ligand to be edited.

Receptor.

Ligand to be edited.

Ligand pocket surface.

Click here to undisplay.

Original PDB structure

Ligand pocket surface.

# Ligand Editing in 2D

Select the 2D editing button in the edit tools panel.

1. Open the edit tools panel.

2. Click on the 2D editing button.

The image shows the Molsoft ICM 3.8-2 software interface. The top toolbar includes buttons for 'display', 'light', 'labels', 'meshes', 'search', and 'ligedit'. The 'ligedit' button is highlighted with a red arrow. Below the toolbar is the 'Edit Tools Panel', which contains various editing tools. A yellow circle highlights the '2D editing' button (represented by a pencil icon) in the 'Edit Tools Panel', with a yellow arrow pointing to it. The main workspace displays a 3D molecular model of a protein-ligand complex. The protein backbone is shown in grey, and the ligand is shown in blue and red. Several residues are labeled: E81, G85, D84, K89, V18, K33, G11, I10, Q130, and D86. The bottom status bar shows '2 ICM Obj' and the page number '9'.

# Edit the ligand in the 2D editor and apply changes to 3D.

The screenshot displays a molecular modeling software interface. At the top, a menu bar includes 'File', 'Tools', 'Edit', 'View', 'Bioinfo', 'Homology', and 'Chemistry'. Below the menu is a toolbar with various icons for file operations and editing. A secondary toolbar contains 'display', 'light', 'labels', 'meshes', 'search', and 'ligedit' tabs. The 'ligedit' tab is active, showing a 'Commit changes to 3D' button highlighted in a green box. A red arrow labeled '2D' points from the 2D editor to a 3D view labeled '3D'. The 2D editor shows a chemical structure with a pyridine ring, a benzene ring, and a piperidine ring. The 3D view shows the same molecule docked into a protein binding pocket, with the protein surface colored in green, red, and blue. The protein residues S5, V433, G454, L45, P45, S379, L377, and G378 are labeled. The status bar at the bottom right indicates '1420 Atoms 89 Res, 2 Mol, 2 Obj'.

1xbb\_lig Molsoft icm 3.8-3 [NewProject \*] (3 objects)

File Tools Edit View Bioinfo Homology Chemistry

display light labels meshes search ligedit

Advanced

VisScore: 0 LigStrain=0 Score: 0

Ligedit 2D

Commit changes to 3D

2D 3D

S5 V433 G454 L45 P45 S379 L377 G378

Ligedit 2D Workspace Panel Edit Tools Panel

1420 Atoms 89 Res, 2 Mol, 2 Obj

Change default behavior  
Advanced/Preferences

The 2D ligand editor panel can be docked into the  
GUI or dragged out.

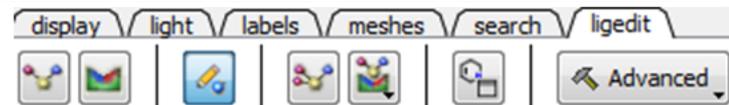
Drag window out  
by clicking here.

Toggle between edit tools, ICM  
workspace and 2D editor here.

The image shows a software interface for molecular docking. At the top, there is a toolbar with various icons, including one labeled 'Advanced'. Below the toolbar is a 'Ligedit 2D' panel. This panel has a vertical toolbar on the left with icons for different elements (C, N, O, F, P, S, Cl, Br, I, B, H) and a central workspace showing a 2D chemical structure of a ligand. To the right of the 2D editor is a 3D molecular model of a protein-ligand complex. The protein is shown as a grey ribbon structure with a green surface representation. The ligand is shown as a ball-and-stick model. Labels for amino acid residues are visible, such as S5, V433, G454, L45, P45, S379, L377, and G378. At the bottom of the interface, there are tabs for 'Ligedit 2D', 'Workspace Panel', and 'Edit Tools Panel'. A red arrow points to the 'Edit Tools Panel' tab.

# Ligand Editing in 3D

Select the modification you want to make from the panel below and then click on the ligand in the 3D display. One or more substituents can be screened.



Click to display

Change Atom Type

Change Charge

Change Torsions

Buttons for atom types: C, N, O, F, H, P, S, Cl, Br, I, More...

Buttons for charge: +, -

Buttons for torsions: Set distance restraints, Set tethers

← Set distance restraints

← Set tethers

← Move atoms

← Set fragments

BondType

BondType buttons: single, double, triple, aromatic, R/S, E/Z, wedged, hashed, plain

Add new substituents to table

Buttons: Add New, O, F, Cl, Br, I, Erase

Edit in 2D

Buttons: Cis/Trans Switch, Stereo Switch


Select one or more substituents ( ICM will dock on the fly).

# Select multiple substituents to test

1. Click here to see the edit panel

2. Single click to select or unselect one or more substituents.

3. Click on the atom you wish to modify.

4. A table of results will be displayed.

The screenshot displays the Molsoft ICM 3.8-2 software interface. At the top, the title bar reads "biotin Molsoft icm 3.8-2 [NewProject \*] (3 objects 1 table)". The main window shows a 3D ribbon representation of a protein structure with a ligand (biotin) docked in a binding pocket. The protein backbone is grey, and the biotin molecule is shown with pink and blue spheres. Residues are labeled: N2, L25, S27, V47, A50, G48, N49, D128, S88, L110, and A86. Distances are indicated: 2.11 Å between N2 and L25, and 1.97 Å between G48 and N49. The "Edit Tools Panel" is open, showing a grid of substituents. A red arrow points from the "1. Click here to see the edit panel" callout to the "Edit Tools Panel" icon in the top toolbar. A yellow arrow points from the "3. Click on the atom you wish to modify." callout to a green atom in the biotin molecule. A red arrow points from the "2. Single click to select or unselect one or more substituents." callout to a substituent in the grid. A green arrow points from the "4. A table of results will be displayed." callout to the results table at the bottom. The table has columns for "mol", "group", "smiles", "Score", "VlsScore", "Strain", "MolCoP", and "Mol". The first row shows a substituent with SMILES "[\*][H]" and a Score of -41.77. The bottom status bar shows "2 ICM Obj" and "14".

All modifications to the ligand can be undone or redone.

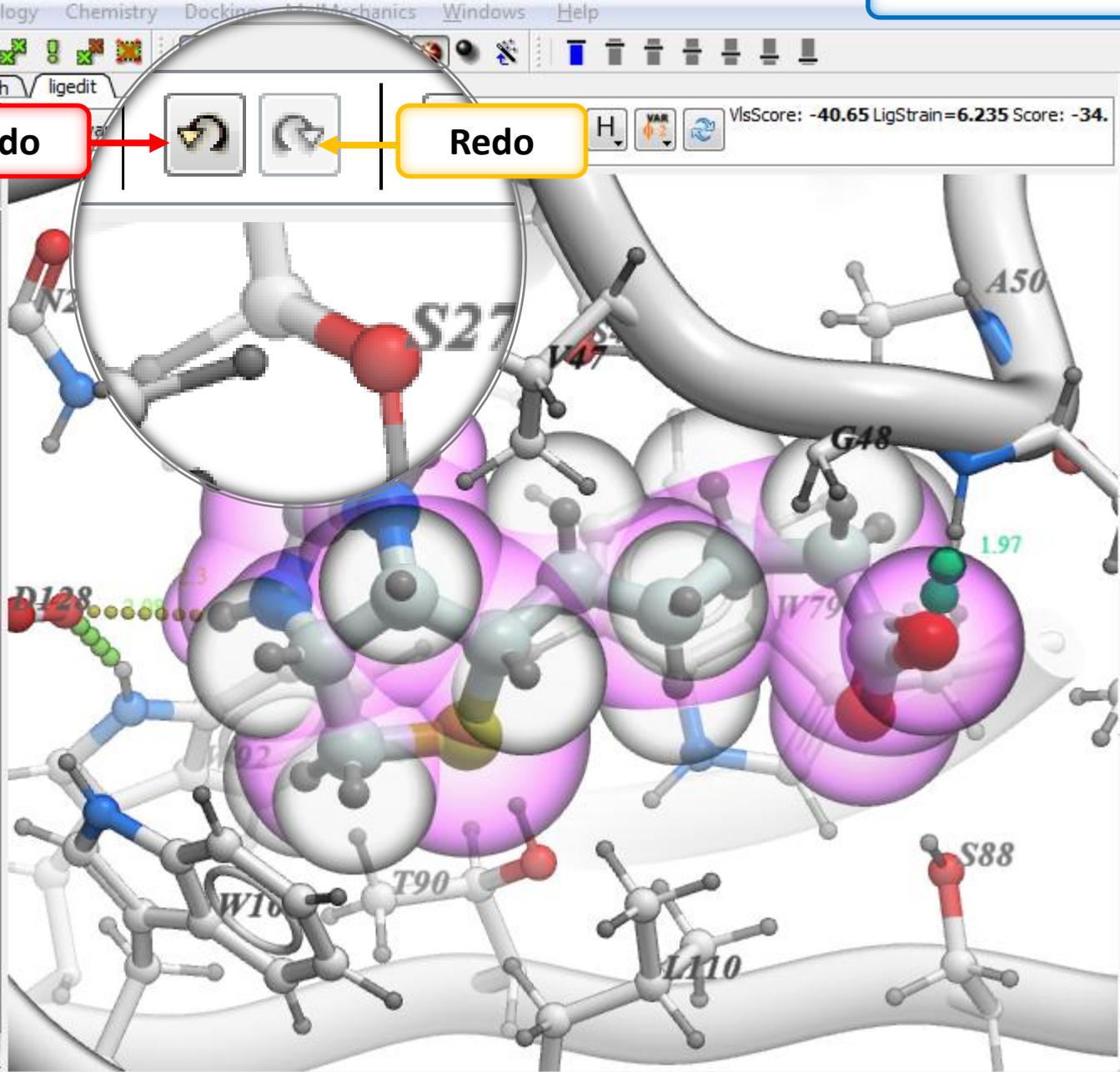
Undo

Redo

Workspace Panel

no selection

- 3D labels (1 item)
- ligandhbonds (6 hydro)
- objects (3 items)
  - ICM biotin [1\*] ICM; 2.6Å
    - biotin H btn
    - streptavidin complex
  - ICM rec\_rec1 [3] IC
    - a 45 A
    - ICM rec [2] ICM; 1.8Å; stre
      - a 116 A
- meshes (1 item)
  - g\_recPocketSurface
- maps (7 items)
  - m\_gc\_simple 102Kb
  - m\_ge 102Kb [-36.00
  - m\_gl 102Kb [-6.23,6
  - m\_gc 102Kb [-3.66,
  - m\_gh 102Kb [-1.74,
  - m\_gb 102Kb [-2.79,
  - m\_gs 102Kb [-4.00,



VlsScore: -40.65 LigStrain=6.235 Score: -34.

If you like a modification you can store it in a chemical spreadsheet and load it again later.

Modifications can be saved directly to a chemical spreadsheet and tagged if needed.

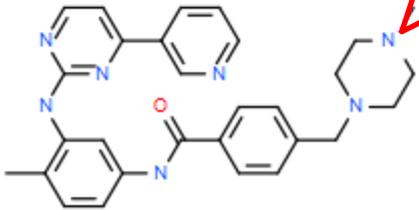
Single click to add to spreadsheet.  
Click and Hold to tag.

Enter tag name.

Add Current Ligand to T...

Molecule Tag

Ok Cancel

N	mol	3D	tag	RecConf	rec	Molecule Name	L	Score	VlsScore	Strain	Steric
1			Series 1	1xbb_rec1:1	1xbb_rec1	1xbb_lig		-27.47	-30.31	2.841	-32.22

Evaluate how well the modifications fit into the pocket. The lower the score the better the predicted fit.

To evaluate the Score and Strain.

1. Edit and Minimize or Dock the Ligand.

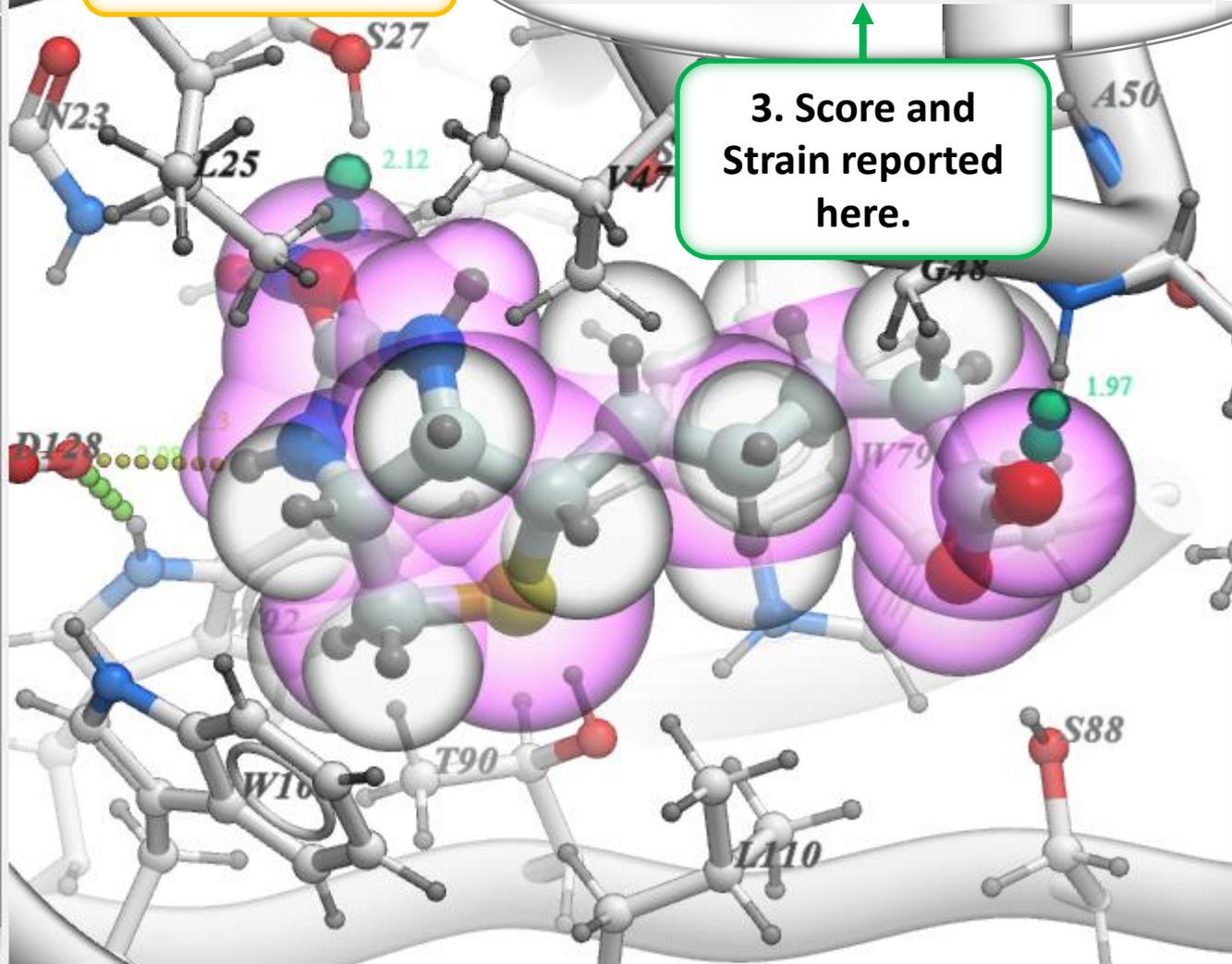
2. Single click here.

VlsScore: -40.65 LigStrain=6.235 Score: -34.

3. Score and Strain reported here.

Workspace Panel

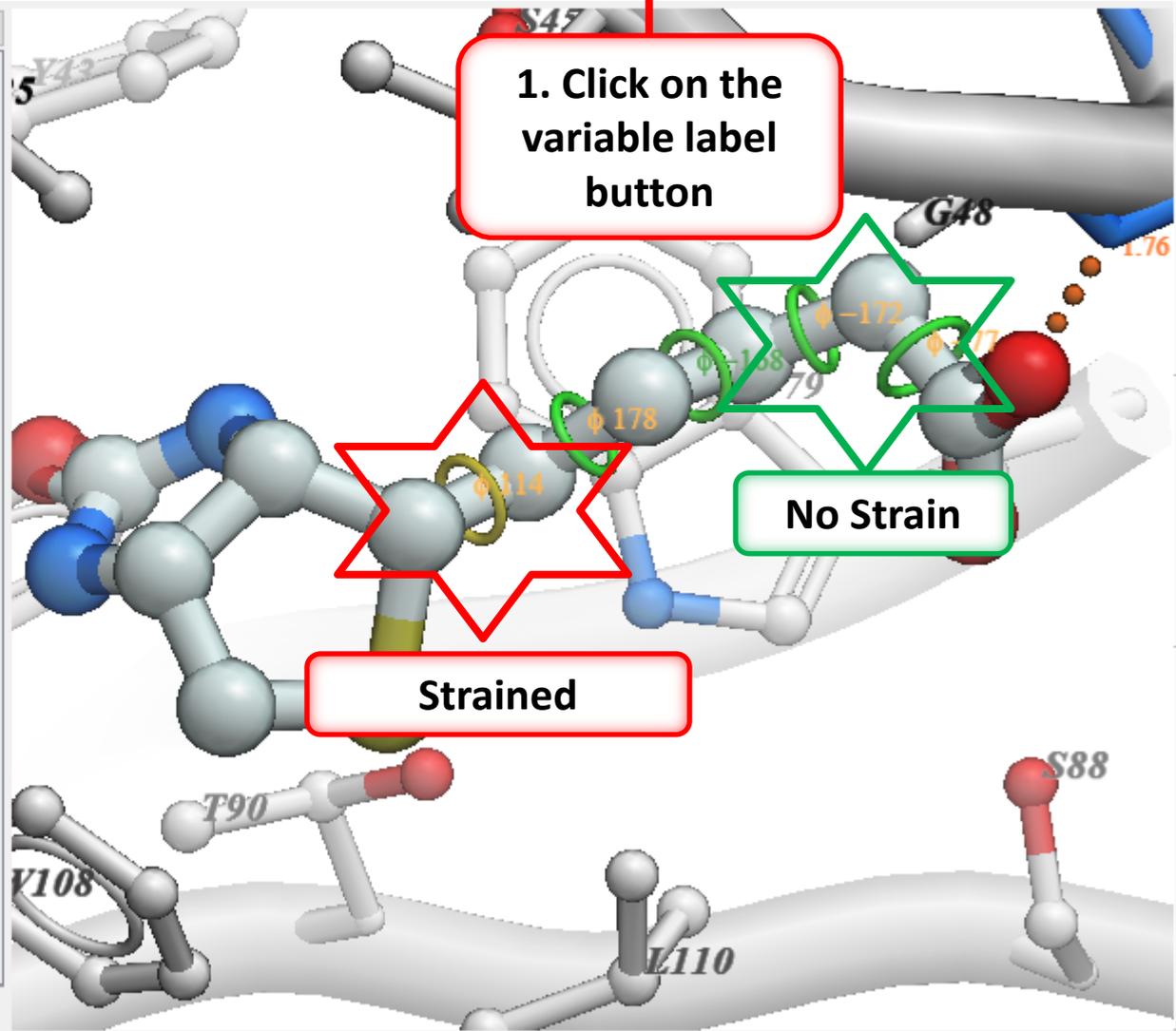
- no se
- biotin
- streptavidin complex
- ICM rec\_rec1 [3] IC
- ICM a 45 A
- ICM rec [2] ICM; 1.8Å; stre
- ICM a 116 A
- meshes (1 item)
- g\_recPocketSurface
- maps (7 items)
- m\_gc\_simple 102Kb
- m\_ge 102Kb [-36.00
- m\_gl 102Kb [-6.23,6
- m\_gc 102Kb [-3.66,
- m\_gh 102Kb [-1.74,
- m\_gb 102Kb [-2.79,
- m\_gs 102Kb [-4.00,



Workspace Panel

no selection

- 3D labels (1 item)
- ligandhbonds (2 hydrogen bonds)
- objects (3 items)
  - ICM biotin [1\*] ICM; 2.6Å
    - biotin H btn
    - streptavidin complex with biotin
  - ICM rec\_rec1 [3] ICM; 1.8Å
    - a 45 A
    - rec [2] ICM; 1.8Å; streptavidin
      - a 116 A
- meshes (1 item)
  - g\_recPocketSurface v=3494
- maps (7 items)
  - m\_gc\_simple 102Kb [-2.36,4.00] m4
  - m\_ge 102Kb [-36.00,36.00] m4
  - m\_gl 102Kb [-6.23,6.20] m4
  - m\_gc 102Kb [-3.66,6.20] m3
  - m\_gh 102Kb [-1.74,6.20] m3
  - m\_gb 102Kb [-2.79,2.81] m0
  - m\_gs 102Kb [-4.00,16.00] m0



1. Click on the variable label button

No Strain

Strained