



ICM-Chemist-Pro How-To Guide

Version 3.6-1h

Last Updated 12/29/2009

ICM-Chemist-Pro

ICM 3D LIGAND EDITOR: SETUP

1. Read in a ligand molecule or PDB file.

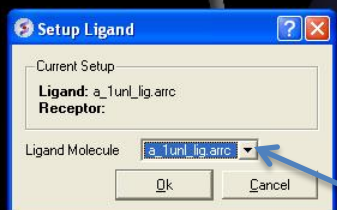
How to setup the ligand in the ICM 3D Ligand Editor.

2. Click on the "ligand" tab

3. Click here

5. This symbol means that this molecule has been setup as a ligand

4. Enter the name of the ligand using ICM selection language or use the drop down button to find it.



```
icm/lun1> LIGAND.info = "<no info>"
icm/lun1> as_out = a_lun1.arcc & a *.H
icm/lun1> if ( Nof( Obj( as_out ) ) > 1 ) Askg(" Warning: More than one object in input selection.", "OK", simple )
icm/lun1> if ( Nof( Obj( as_out ) ) > 1 ) as_out = as_out & Obj( as_out )[1]
icm/lun1> e3dSetLigand as_out yes
icm/lun1_lig>
```

How to setup the receptor in the ICM 3D Ligand Editor.

1. Click here

3a. Identify Pocket Box:
This option will run the icmPocketFinder macro. A table of pockets will be displayed – click on the binding pocket in the output table to select it.

3b. Make Box Around Existing Ligand: If you already have a ligand inside the binding pocket then this is a good option to choose.

2. Select the name of the receptor from the drop down list.

3c. Make Box Around Atom Selection. Use the selection tools to select the residues around the ligand binding pocket.

Setup Receptor

Current Setup
Ligand: a_1unl_lig.arc
Receptor: a_1unl_rec.

Define Receptor
Receptor Object: a_1unl

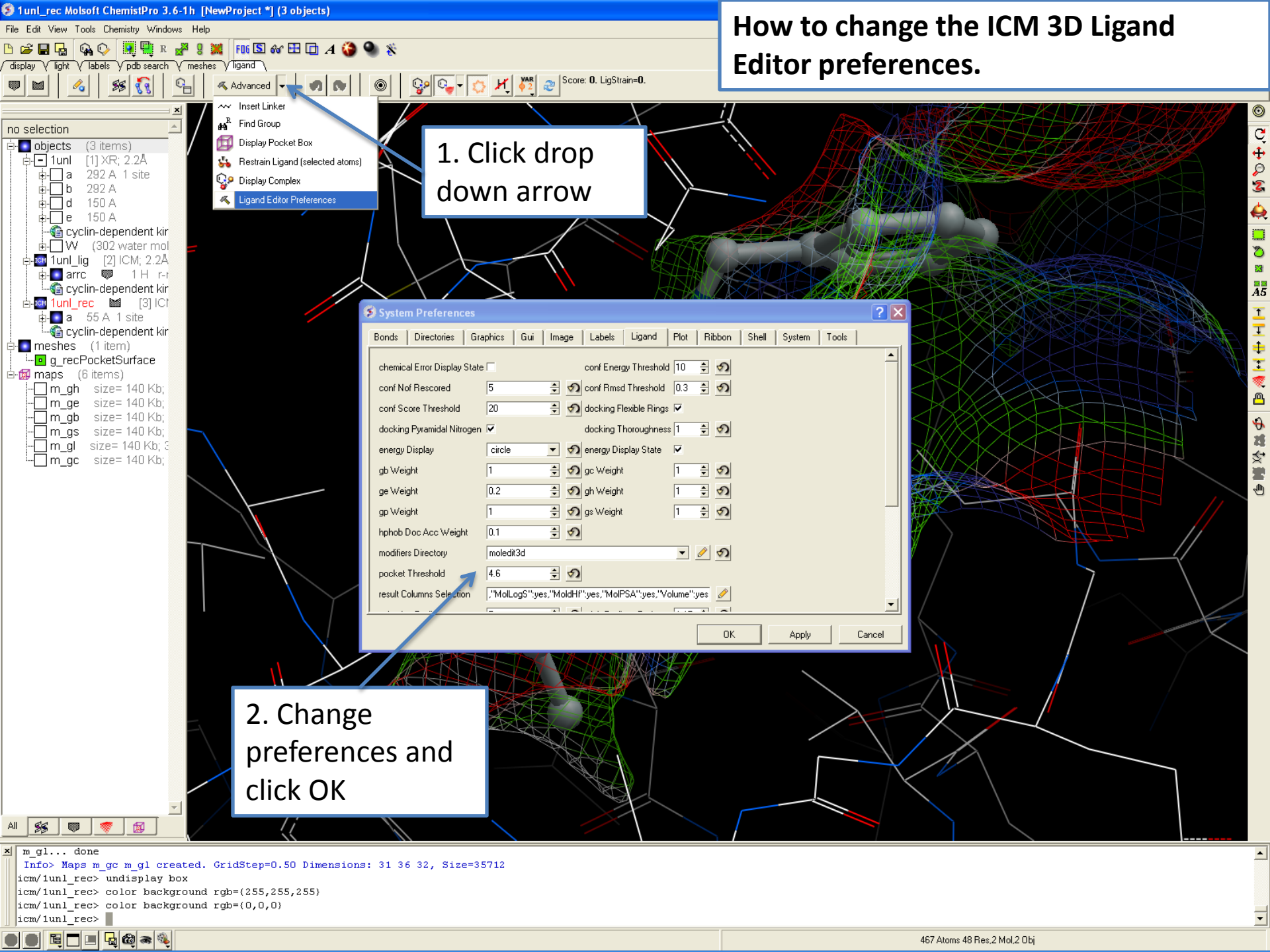
Keep Water In Receptor Optimize Existing Hydrogens Optimize HisProAsnGlnCys

Define Pocket or Select Pocket Atoms
Identify Pocket Box
Make Box Around Existing Ligand
Make Box Around Atom Selection

Box Margin: 3

More Options
 Create Ligand Pocket Surface

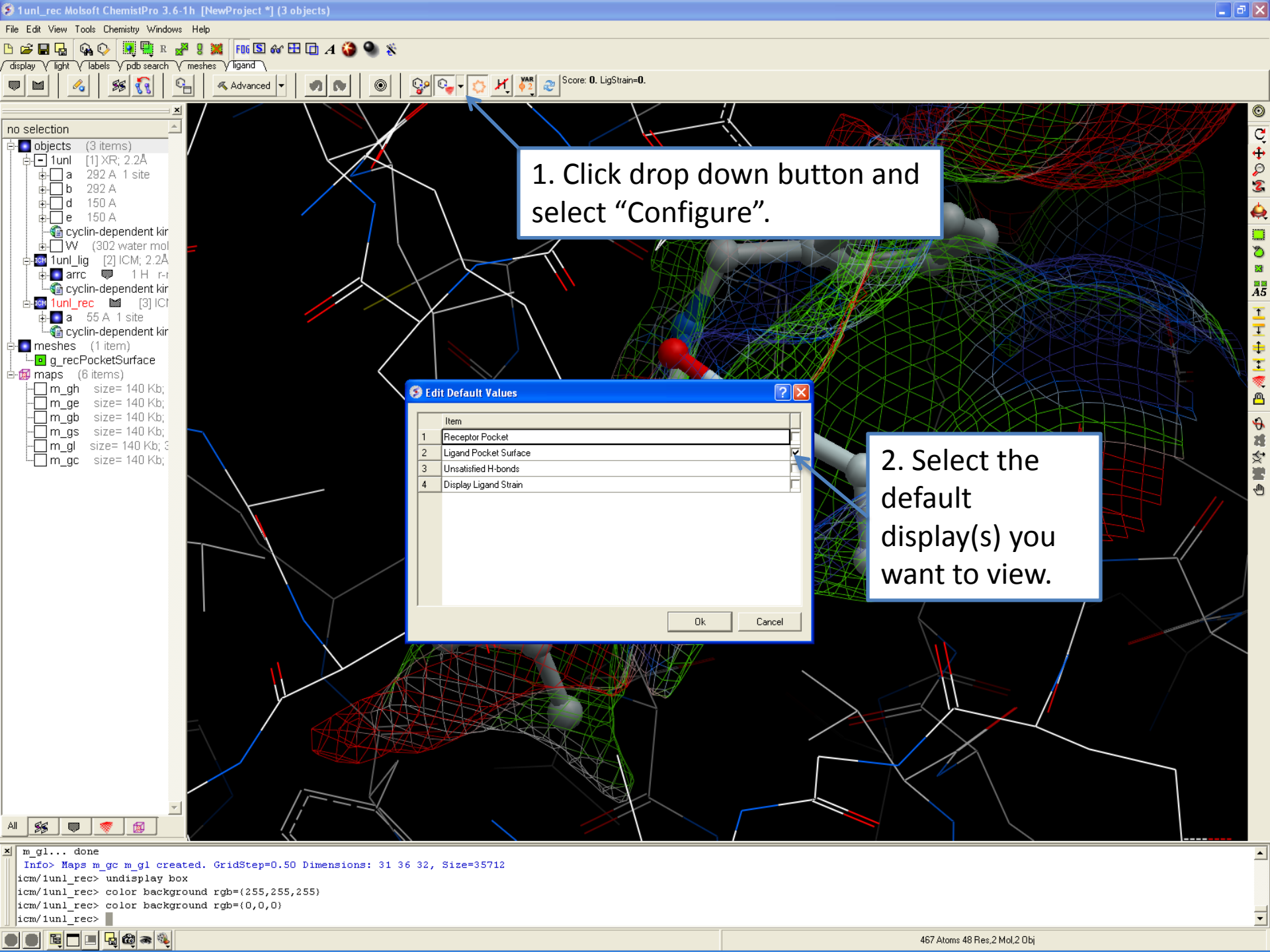
How to change the ICM 3D Ligand Editor preferences.



1. Click drop down arrow

2. Change preferences and click OK

```
m_gl... done
Info> Maps m_gc m_gl created. GridStep=0.50 Dimensions: 31 36 32, Size=35712
icm/1unl_rec> undisplay box
icm/1unl_rec> color background rgb=(255,255,255)
icm/1unl_rec> color background rgb=(0,0,0)
icm/1unl_rec>
```



1. Click drop down button and select "Configure".

2. Select the default display(s) you want to view.

Dialog box titled "Edit Default Values" with a table of items and checkboxes.

Item	
1 Receptor Pocket	<input type="checkbox"/>
2 Ligand Pocket Surface	<input checked="" type="checkbox"/>
3 Unsatisfied H-bonds	<input type="checkbox"/>
4 Display Ligand Strain	<input type="checkbox"/>

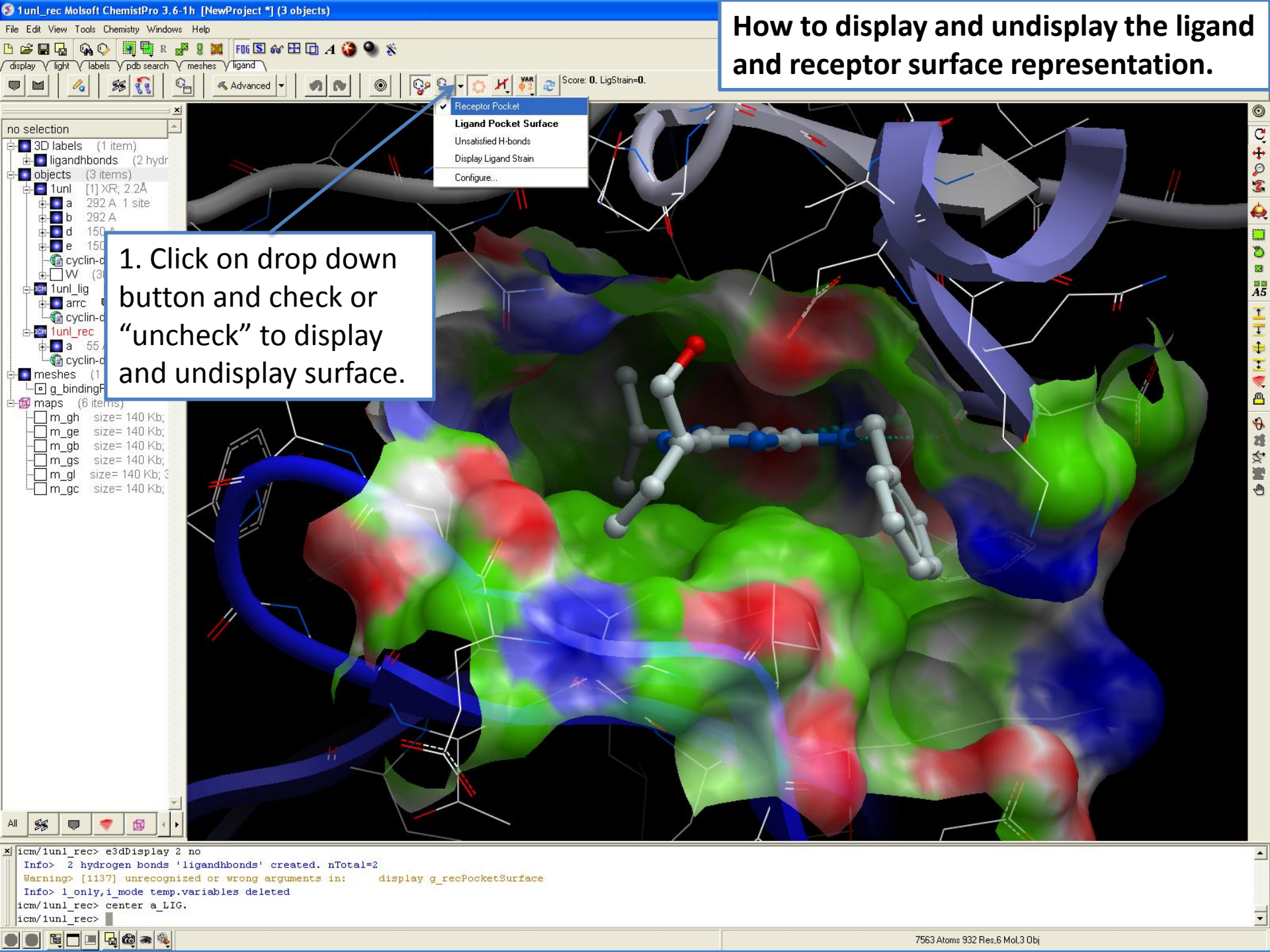
Buttons: Ok, Cancel

```
m_gl... done
Info> Maps m_gc m_gl created. GridStep=0.50 Dimensions: 31 36 32, Size=35712
icm/1unl_rec> undisplay box
icm/1unl_rec> color background rgb=(255,255,255)
icm/1unl_rec> color background rgb=(0,0,0)
icm/1unl_rec>
```

ICM-Chemist-Pro

ICM 3D LIGAND EDITOR: DISPLAY

How to display and undisplay the ligand and receptor surface representation.



no selection

- 3D labels (1 item)
- ligandhbonds (2 hydr)
- objects (3 items)
 - 1unl [1] XR; 2.2Å
 - a 292 A 1 site
 - b 292 A
 - d 150 A
 - e 150 A
 - cyclin-d
 - W (3)
- 1unl_lig
 - arrc
- 1unl_rec
 - a 55
- cyclin-d
- meshes (1)
- g_bindingF
- maps (6 items)
 - m_gh size= 140 Kb;
 - m_ge size= 140 Kb;
 - m_gb size= 140 Kb;
 - m_gs size= 140 Kb;
 - m_gl size= 140 Kb; 3
 - m_gc size= 140 Kb;

- Receptor Pocket
- Ligand Pocket Surface
 - Unsatisfied H-bonds
 - Display Ligand Strain
 - Configure...

```
icm/1unl_rec> e3dDisplay 2 no
Info> 2 hydrogen bonds 'ligandhbonds' created. nTotal=2
Warning> [1137] unrecognized or wrong arguments in: display g_recPocketSurface
Info> i_only,i_mode temp.variables deleted
icm/1unl_rec> center a_LIG.
icm/1unl_rec>
```


How to display and undisplay hydrogen bonds.

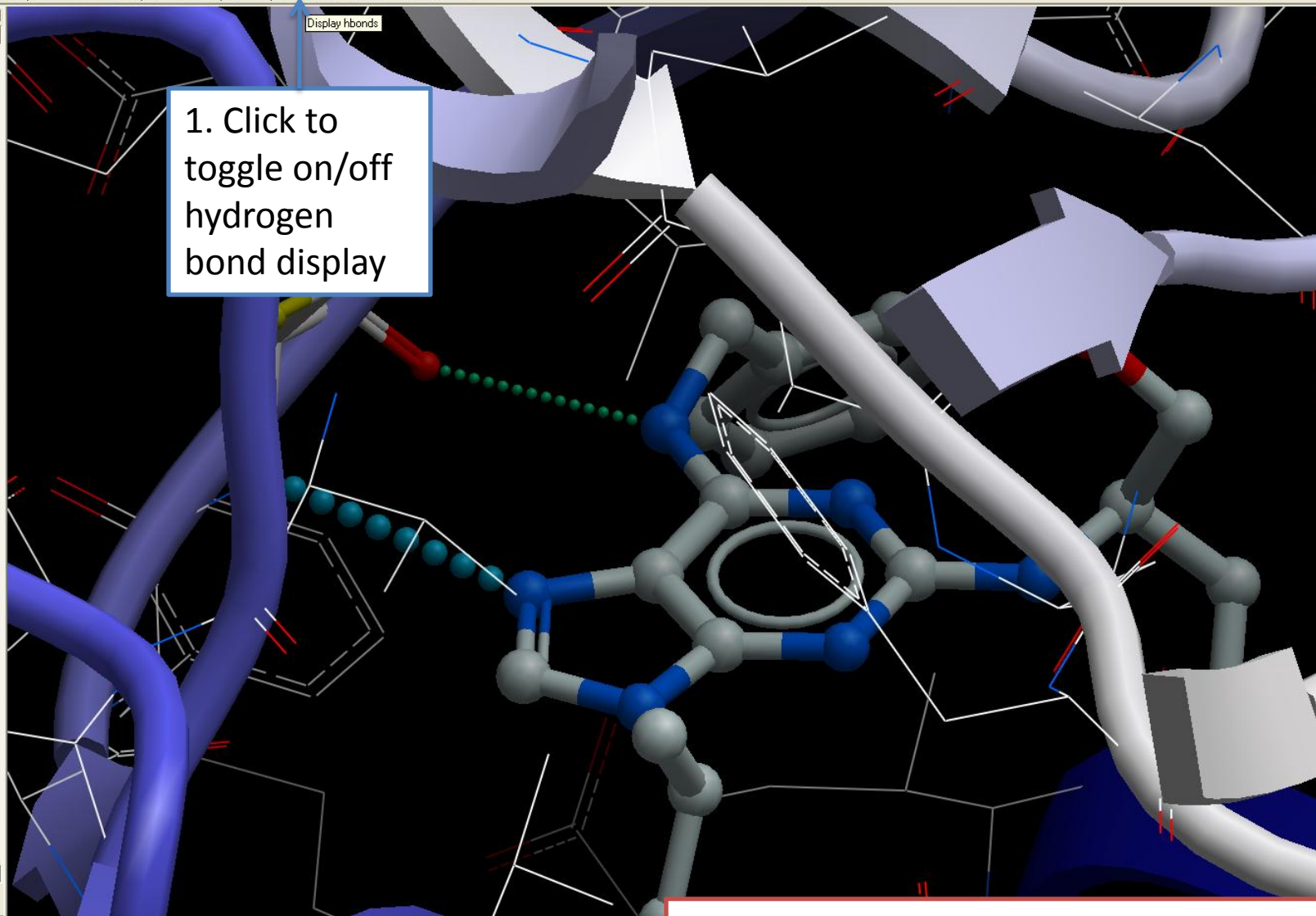
no selection

- 3D labels (1 item)
- ligandhbonds (2 hydr)
- objects (3 items)
 - 1unl [1] XR; 2.2A
 - a 292 A 1 site
 - b 292 A
 - d 150 A
 - e 150 A
 - cyclin-dependent kir
 - W (302 water mol)
 - 1unl_lig [2] ICM; 2.2A
 - arrc 1 H r-r
 - cyclin-dependent kir
 - 1unl_rec [3] ICT
 - a 55 A 1 site
 - cyclin-dependent kir
- maps (6 items)
 - m_gh size= 140 Kb;
 - m_ge size= 140 Kb;
 - m_gb size= 140 Kb;
 - m_gs size= 140 Kb;
 - m_gl size= 140 Kb;
 - m_gc size= 140 Kb;

All

1. Click to toggle on/off hydrogen bond display

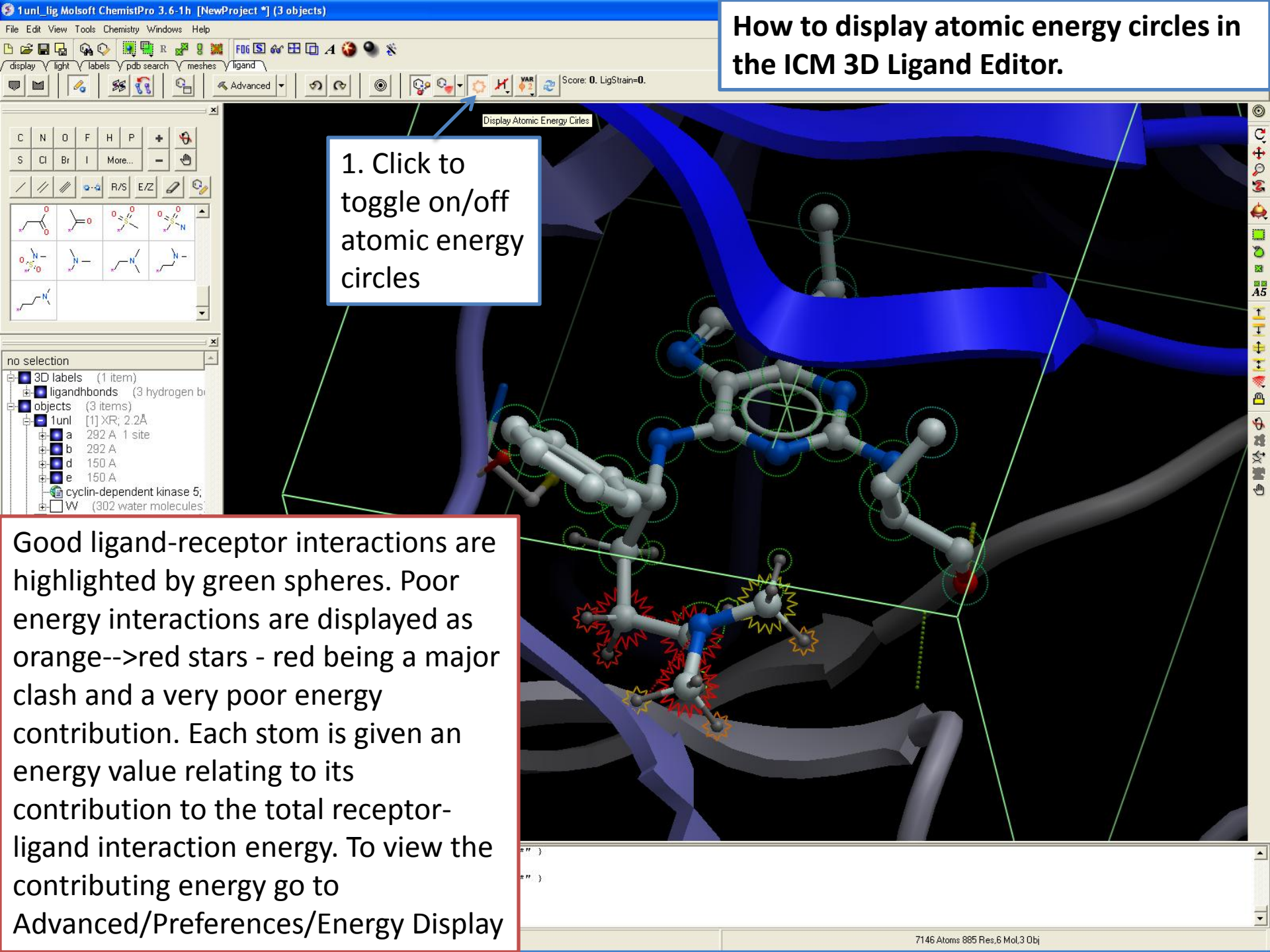
Display hbonds



The coloring of the H-bonds are red (strong - thick spheres) to blue (weak - thin spheres).

```
Warning> [1137] unrecognized or wrong arguments in: display g_recPocketSurface
Info> i_only,i_mode temp.variables deleted
icm/1unl_rec> center a_LIG.
icm/1unl_rec> delete g_bindingPocket
icm/1unl_rec> center static as_graph
icm/1unl_rec>
```

How to display atomic energy circles in the ICM 3D Ligand Editor.



1. Click to toggle on/off atomic energy circles

Good ligand-receptor interactions are highlighted by green spheres. Poor energy interactions are displayed as orange-->red stars - red being a major clash and a very poor energy contribution. Each atom is given an energy value relating to its contribution to the total receptor-ligand interaction energy. To view the contributing energy go to **Advanced/Preferences/Energy Display**

1. Click and hold here

- Score: 0. LigStrain=0.
- No Hydrogens
 - PH Polar Hydrogens
 - H All Hydrogens
 - LH Ligand All, Rec Polar
 - Display Formal Charges
 - Ribbon+CPK
 - Ligand+Ribbon
 - Atoms
 - Chemical
 - Undisplay Beyond Selection
 - Elegant Ribbon+Ligand Sketch
 - Green Wireframe

Element selection panel:

C N O F H P +
S Cl Br I More... -

Chemical structure icons:

no selection

objects (3 items)

- 1un1 [1] XR; 2.2Å
 - a 292 A 1 site
 - b 292 A
 - d 150 A
 - e 150 A
- cyclin-dependent kinase 5;
 - WV (302 water molecules)
- 1un1_rec [2] ICM; 2.2Å
 - a 55 A 1 site
- cyclin-dependent kinase 5;
- 1un1_lig [3] ICM; 2.2Å
 - arrc 1 H r-roscovit
- cyclin-dependent kinase 5;
- maps (6 items)
 - m_gh size= 140 Kb; 32*(36°)
 - m_ge size= 140 Kb; 32*(36°)
 - m_gb size= 140 Kb; 32*(36°)
 - m_gs size= 140 Kb; 32*(36°)
 - m_gl size= 140 Kb; 32*(36°)
 - m_gc size= 140 Kb; 32*(36°)

How to display and undisplay hydrogen atoms.

```
icm/1un1_lig> delete ligandhbonds
icm/1un1_lig> GRAPHICS.hydrogenDisplay=2
icm/1un1_lig> display hydrogen
icm/1un1_lig> GRAPHICS.hydrogenDisplay=4
icm/1un1_lig> display hydrogen
icm/1un1_lig>
```

How to display unsatisfied hydrogen bonds.

1. Click drop down arrow and select "Unsatisfied Hydrogen Bonds"

Unsatisfied hydrogen bond donors displayed as blue sphere

Unsatisfied hydrogen bond acceptors displayed as red sphere

The screenshot shows the Chem3D software interface. The main window displays a protein-ligand complex. The protein backbone is shown as a grey ribbon, and the ligand is shown as a ball-and-stick model. Several unsatisfied hydrogen bonds are highlighted: donors are shown as blue spheres and acceptors as red spheres. A blue arrow points to the 'Unsatisfied Hydrogen Bonds' option in the 'Advanced' menu. A red box highlights the blue spheres, and another red box highlights the red spheres. The command window at the bottom shows the following commands:

```
icm/1un1_lig> GRAPHICS.hydrogenDisplay=4  
icm/1un1_lig> display hydrogen  
icm/1un1_lig> GRAPHICS.hydrogenDisplay=3  
icm/1un1_lig> display hydrogen  
icm/1un1_lig> dsUnsatHbonds yes  
icm/1un1_lig>
```

The left sidebar shows a tree view of the objects, including the protein (cyclin-dependent kinase 5), water molecules, and the ligand (1un1_lig). The bottom status bar indicates the system is at 7137 Atoms, 885 Res, 6 Mol, 3 Obj.

How to center on the ligand.

The screenshot shows the Chem3D software interface. The main window displays a protein structure (grey ribbon) with a ligand (white sticks) and its electron density map (colored mesh). The top toolbar contains various icons for file operations, display settings, and navigation. A blue arrow points to the 'center' icon (a circle with a dot) in the top toolbar. A white callout box with a blue border contains the text '1. Click here'.

1. Click here

Chemical structure editor toolbar with buttons for element selection (C, N, O, F, H, P, S, Cl, Br, I, More...), bond types (single, double, triple), and functional groups (aldehyde, ketone, amine, amide, nitrile).

Object list panel showing a tree view of the current scene:

- no selection
- objects (3 items)
 - 1unl [1] XR; 2.2Å
 - a 292 A 1 site
 - b 292 A
 - d 150 A
 - e 150 A
 - cyclin-dependent kinase 5;
 - WV (302 water molecules)
 - 1unl_rec [2] ICM; 2.2Å
 - a 55 A 1 site
 - cyclin-dependent kinase 5;
 - 1unl_lig [3] ICM; 2.2Å
 - arrc 1 H r-roscovit
 - cyclin-dependent kinase 5;
- meshes (1 item)
 - g_recPocketSurface v=5776
- maps (6 items)
 - m_gh size= 140 Kb; 32*(36°)
 - m_ge size= 140 Kb; 32*(36°)
 - m_gb size= 140 Kb; 32*(36°)
 - m_gs size= 140 Kb; 32*(36°)
 - m_gl size= 140 Kb; 32*(36°)
 - m_gc size= 140 Kb; 32*(36°)

```
icm/1unl_rec> display g_recPocketSurface wire
icm/1unl_rec> center static a_LIG.I
icm/1unl_rec> dsUnsatHbonds no
icm/1unl_rec> undisplay xstick Res(a_*.//DD)
icm/1unl_rec> cool a_1unl_lig.arrc
icm/1unl_rec>
```

ICM-Chemist-Pro

ICM 3D LIGAND EDITOR: EDIT LIGAND

1. Click here to display the Edit panel.

File Edit View Tools Chemistry

display light labels pdb

Advanced

Score: 0. LigStrain=0.

Atoms/Bonds

Erase

Add New

O	F	Cl
Br	I	

Substituents

no selection

objects (3 items)

- 1unl [1] XRF; 2.2Å
- a 292 Å 1 site

Substituents

- W (302 water molecules)
- 1unl_rec [2] ICM; 2.2Å
- a 55 Å 1 site
- cyclin-dependent kinase 5;
- 1unl_lig [3] ICM; 2.2Å
- arrc 1 H r-roscovit
- cyclin-dependent kinase 5;
- meshes (1 item)
- g_recPocketSurface v=5776
- maps (6 items)
- m_gh size= 140 Kb; 32*(36°)
- m_ge size= 140 Kb; 32*(36°)
- m_gb size= 140 Kb; 32*(36°)
- m_gs size= 140 Kb; 32*(36°)
- m_gl size= 140 Kb; 32*(36°)
- m_gc size= 140 Kb; 32*(36°)

```
icm/1unl_rec> display g_recPocketSurface wire
icm/1unl_rec> center static a_LIG.I
icm/1unl_rec> dsUnsatHbonds no
icm/1unl_rec> undisplay xstick Res(a_*.//DD)
icm/1unl_rec> cool a_1unl_lig.arrc
icm/1unl_rec>
```

Click on the atom where you want to make an edit.

How to Undo/Redo Edits

The screenshot displays the Molsoft Chem3D Pro 3.6-1h software interface. The main window shows a 3D molecular model of a protein-ligand complex. The protein is represented by a grey ribbon, and the ligand is shown as a white ball-and-stick model. The protein surface is overlaid with a green mesh, and the ligand is surrounded by a red mesh. A blue ribbon highlights a specific part of the protein structure. A callout box with a white background and black border points to the Undo and Redo buttons in the top toolbar. The text inside the callout box reads: "Undo and Redo all your edits by clicking here." The software interface includes a menu bar at the top (File, Edit, View, Tools, Chemistry, Windows, Help), a toolbar with various icons, and a command line at the bottom. The command line shows the following commands:

```
icm/lun1_rec> display g_recPocketSurface wire  
icm/lun1_rec> center static a_LIG.I  
icm/lun1_rec> dsUnsatHbonds no  
icm/lun1_rec> undisplay xstick Res(a_*.//DD)  
icm/lun1_rec> cool a_lun1_lig.arcc  
icm/lun1_rec>
```

Undo and Redo all
your edits by clicking
here.

- no selection
- objects (3 items)
 - 1unl [1] XR; 2.2Å
 - a 292 A 1 site
 - b 292 A
 - d 150 A
 - e 150 A
 - cyclin-dependent kinase 5;
W (302 water molecules)
 - 1unl_rec [2] ICM; 2.2Å
 - a 55 A 1 site
 - cyclin-dependent kinase 5;
1unl_lig [3] ICM; 2.2Å
 - arcc 1 H r-roscovit
 - cyclin-dependent kinase 5;
- meshes (1 item)
 - g_recPocketSurface v=5776
- maps (6 items)
 - m_gh size= 140 Kb; 32*(36°
 - m_ge size= 140 Kb; 32*(36°
 - m_gb size= 140 Kb; 32*(36°
 - m_gs size= 140 Kb; 32*(36°
 - m_gl size= 140 Kb; 32*(36°
 - m_gc size= 140 Kb; 32*(36°

```
icm/lun1_rec> display g_recPocketSurface wire  
icm/lun1_rec> center static a_LIG.I  
icm/lun1_rec> dsUnsatHbonds no  
icm/lun1_rec> undisplay xstick Res(a_*.//DD)  
icm/lun1_rec> cool a_lun1_lig.arcc  
icm/lun1_rec>
```


1. Click here to see the Edit panel.

The Edit panel shows a grid of chemical substituents. A blue arrow points to the 'Add New' button. Below the grid is a list of objects:

- objects (3 items)
 - 1unl [1] XR; 2.2Å
 - a 292 A 1 site
 - b 292 A
 - d 150 A
 - e 150 A
 - cyclin-dependent kinase 5;
 - W (302 water molecules)
 - 1unl_rec [2] ICM; 2.2Å
 - a 55 A 1 site
 - cyclin-dependent kinase 5;
 - 1unl_lig [3] ICM; 2.2Å
 - arrc 1 H r-roscovit
 - cyclin-dependent kinase 5;

meshes (1 item)

 - g_recPocketSurface v=5776

maps (6 items)

 - m_gh size= 140 Kb; 32*(36°)
 - m_ge size= 140 Kb; 32*(36°)
 - m_gb size= 140 Kb; 32*(36°)
 - m_gs size= 140 Kb; 32*(36°)
 - m_gl size= 140 Kb; 32*(36°)
 - m_gc size= 140 Kb; 32*(36°)

2. Choose the substituent or atom you want to use for your edit

Click on the atom where you want to add the substituent

```
icm/1unl_rec> display g_recPocketSurface wire
icm/1unl_rec> center static a_LIG.I
icm/1unl_rec> dsUnsatHbonds no
icm/1unl_rec> undisplay xstick Res(a_*./DD)
icm/1unl_rec> cool a_1unl_lig.arrc
icm/1unl_rec>
```

How to sample more than one substituent at a time.

The screenshot shows the Molsoft Chem3D Pro 3.6.1h interface. At the top, the title bar reads "1 un1_lig Molsoft Chem3D Pro 3.6.1h [NewProject *] (3 objects 1 table)". The menu bar includes File, Edit, View, Tools, Chemistry, Windows, and Help. The toolbar contains various icons for file operations, display settings, and molecular editing. The main window displays a 3D ball-and-stick model of a ligand bound to a protein, with a green and red mesh overlay. A substituent selection table is visible on the left, and a table of substituent properties is at the bottom.

1. Click the substituents you want to sample. Grey background means selected. Click again to unselect.

2. Click on the position you would like to sample the substituents

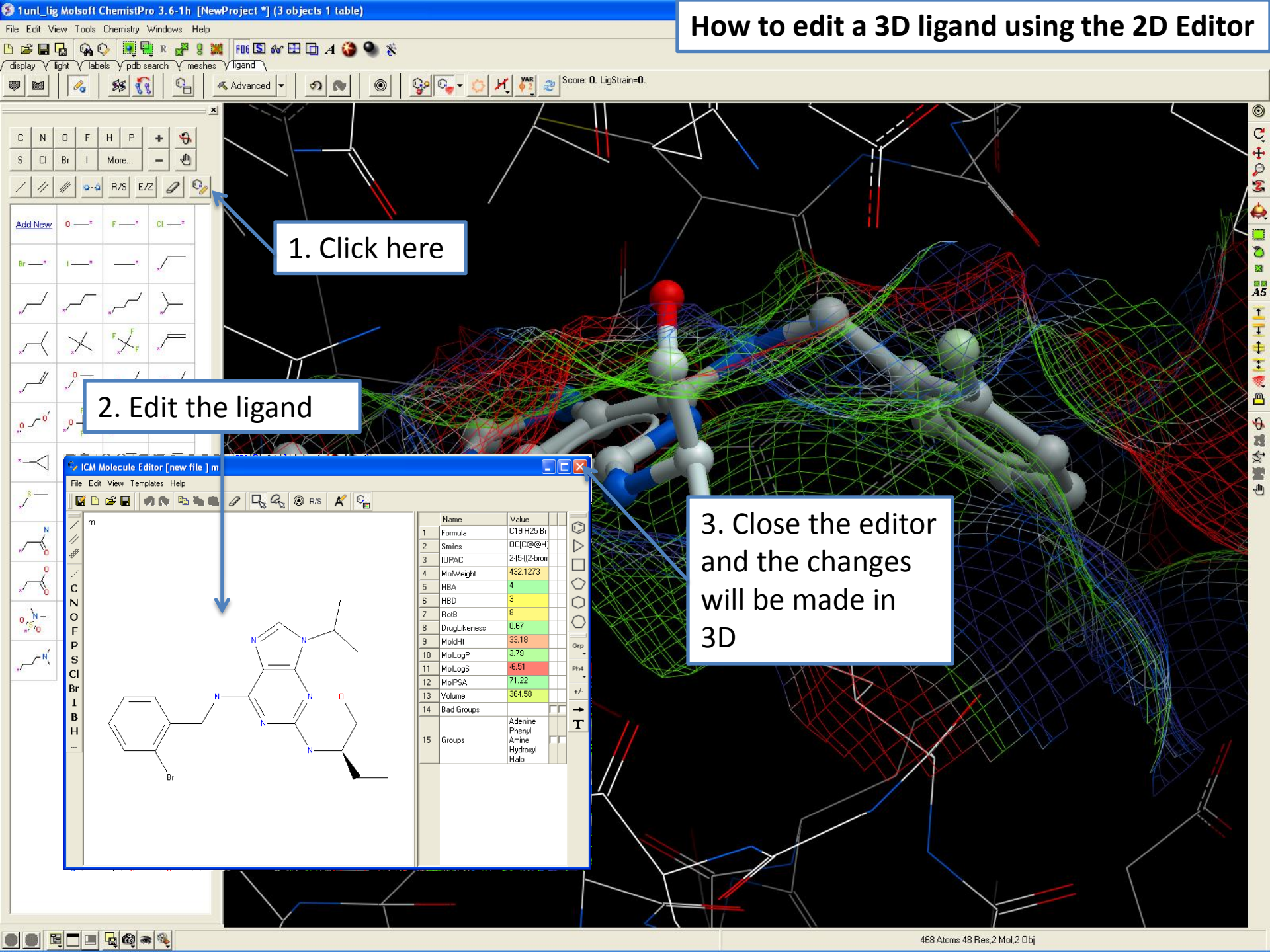
3a. A table with the substituents and their Score and Substructure Score will be displayed

3b. Click here to display the substituent

3c. Double click here to load the full ligand

mol	L	group	smiles	SubstScore	Score	Strain	MolLogP	MolLogS	MoldHf
1	chiral,3D		F*	-2.668	-18.89	2.468	3.211	-6.082	-18.03
2	chiral,3D		[Cl]*	-1.304	-5.128	11.93	3.656	-6.552	21.85
3	chiral,3D		*c1ccccc1	-2.995	-4.385	12.12	3.343	-6.074	20.27

How to edit a 3D ligand using the 2D Editor



1. Click here

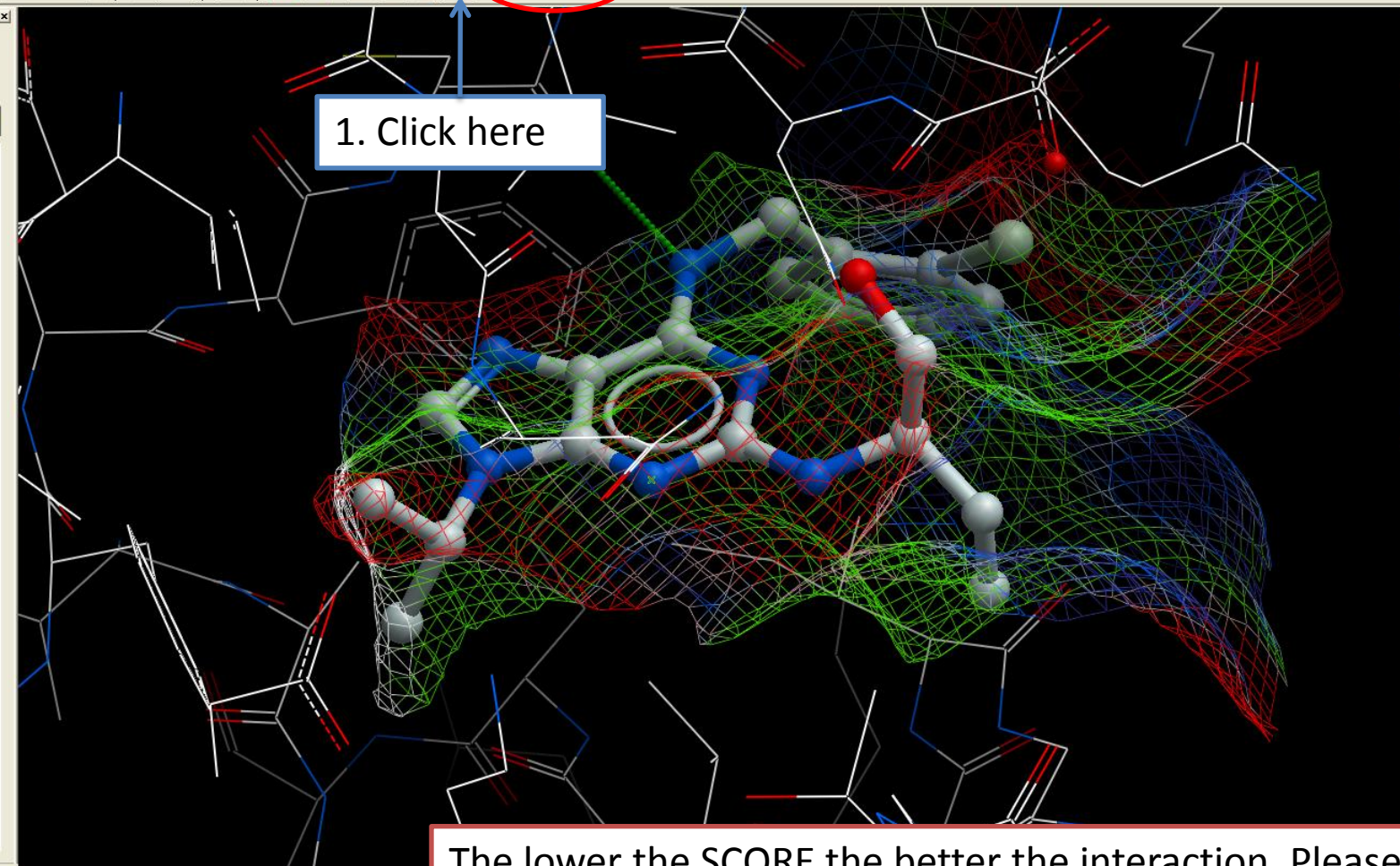
2. Edit the ligand

3. Close the editor and the changes will be made in 3D

ICM Molecule Editor [new file] m

File Edit View Templates Help

Name	Value
1 Formula	C19 H25 Br
2 Smiles	CC(C)C@OH
3 IUPAC	2-[5-[(2-bromophenyl)amino]imidazole-2-yl]propan-1-ol
4 MolWeight	432.1273
5 HBA	4
6 HBD	3
7 RotB	8
8 DrugLikeness	0.67
9 MolHI	33.18
10 MolLogP	3.79
11 MolLogS	-6.51
12 MolPSA	71.22
13 Volume	364.58
14 Bad Groups	
15 Groups	Adenine Phenyl Amine Hydroxyl Halo



1. Click here

How to evaluate the SCORE and ligand strain.

The lower the SCORE the better the interaction. Please see: Totrov M, Abagyan R. *Derivation of sensitive discrimination potential for virtual ligand screening*. Proceedings of the third annual international conference on Computational molecular biology 1999, Lyon, France; 312-320.

LIGANDS

N	mol	rec	NAME	L	Score	Strain	Steric	Tors
1		chiral,3D	1unl_rec 1unl_lig		-12.59	2.685	-31.01	

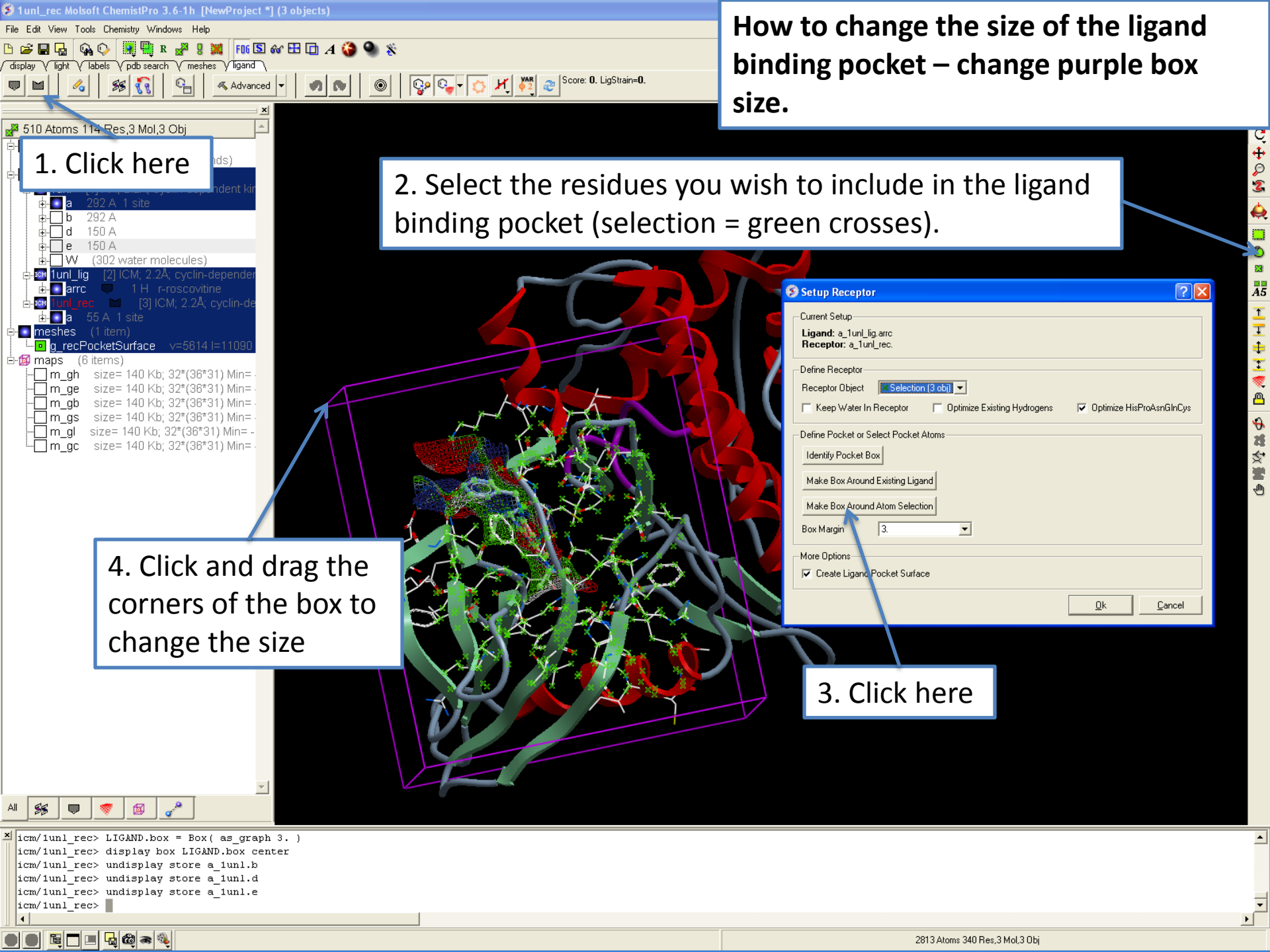
How to add an edited ligand to a chemical spreadsheet (table).

1. Click here to save the edited ligand in a chemical spreadsheet.

The screenshot displays the Molsoft Chem3D Pro 3.6.1h software interface. The main window shows a 3D ball-and-stick model of a ligand (white and blue) bound to a protein (grey) within a mesh representation of the protein's surface. The ligand is highlighted with a blue selection box. A callout box points to a button in the 'LIGANDS' table at the bottom of the interface, with the text '1. Click here to save the edited ligand in a chemical spreadsheet.' The 'LIGANDS' table is a spreadsheet with columns for various properties of the ligand. The first row contains the following data:

N	mol	rec	NAME	L	Score	Strain	Steric	Torsion	Electro	Hbond	Hydroph	Surface	MolLogP	MolLogS	MolHf	MolPSA	Volume	Comment
1	chiral,3D	1unl_rec	1unl_lig		-12.59	2.685	-31.01	7	14.21	-2.119	-8.149	17.3	3.793	-6.513	33.18	71.22	364.6	

The left sidebar contains a 'LIGANDS' library with various chemical structures. The bottom status bar shows '468 Atoms 48 Res,2 Mol,2 Obj'.



How to change the size of the ligand binding pocket – change purple box size.

1. Click here

2. Select the residues you wish to include in the ligand binding pocket (selection = green crosses).

Setup Receptor

Current Setup
Ligand: a_1unl_lig_arc
Receptor: a_1unl_rec.

Define Receptor
Receptor Object: Selection (3 obj)

Keep Water In Receptor Optimize Existing Hydrogens Optimize HisProAsnGlnCys

Define Pocket or Select Pocket Atoms
Identify Pocket Box
Make Box Around Existing Ligand
Make Box Around Atom Selection

Box Margin: 3

More Options
 Create Ligand Pocket Surface

Ok Cancel

4. Click and drag the corners of the box to change the size

3. Click here

```
icm/1unl_rec> LIGAND.box = Box( as_graph 3. )
icm/1unl_rec> display box LIGAND.box center
icm/1unl_rec> undisplay store a_1unl.b
icm/1unl_rec> undisplay store a_1unl.d
icm/1unl_rec> undisplay store a_1unl.e
icm/1unl_rec>
```

ICM-Chemist-Pro

ICM 3D LIGAND EDITOR: MINIMIZATION AND DOCKING

After making a small edit to a ligand a minimization will remove any clashes or bad geometry.

1. Click here to perform a minimization step.

C	N	O	F	H	P		
S	Cl	Br	I	More...	-		

Add New

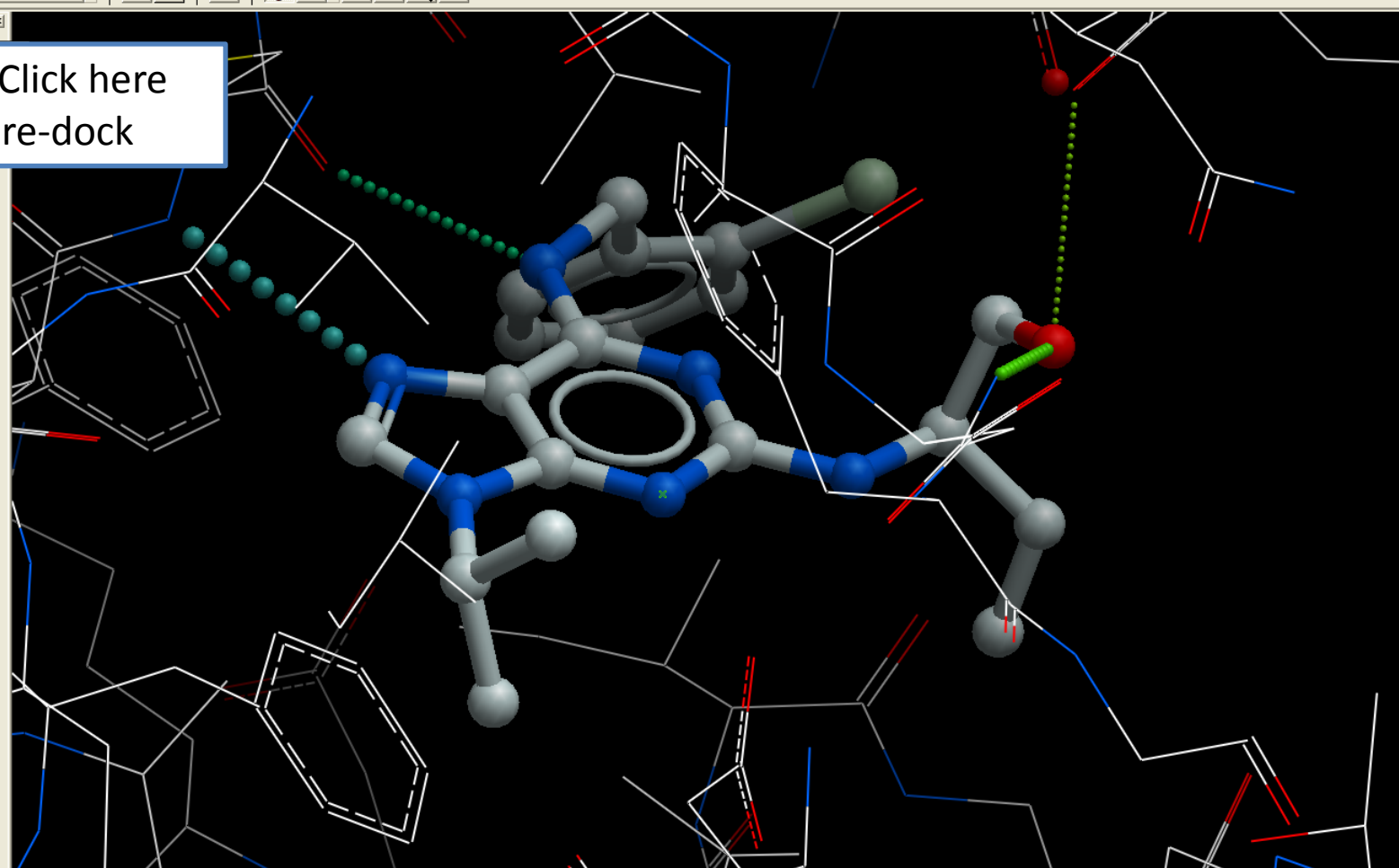
Br

LIGANDS

N	mol	rec	NAME	L	Score	Strain	Steric	Torsion	Electro	Hbond	Hydroph	Surface	MolLogP	MolLogS	MolHf	MolPSA	Volume	Comment	
1	chiral,3D	1unl_rec	1unl_lig		-12.59	2.685	-31.01		7	14.21	-2.119	-8.149	17.3	3.793	-6.513	33.18	71.22	364.6	

How to re-dock a ligand in the ICM 3D Ligand Editor.

1. Click here to re-dock



Click here to display conformation

2. Best energy pose will be displayed by default. The stack of other conformations are listed here.

ConNum	L	Score	Strain	Steric	Torsion	Electro	Hbond	Hydroph	Surface
1	<input checked="" type="checkbox"/>	-27.91	4.484	-37.1	7	8.222	-4.637	-8.363	16.56
2	<input type="checkbox"/>	-21.17	3.395	-33.75	7	10.89	-3.956	-8.221	17.75
3	<input type="checkbox"/>	-15.01	6.021	-30.19	7	8.541	-2.757	-8.228	15.75

C N O F H P
S Cl Br I More...

R/S E/Z

Add New

Br

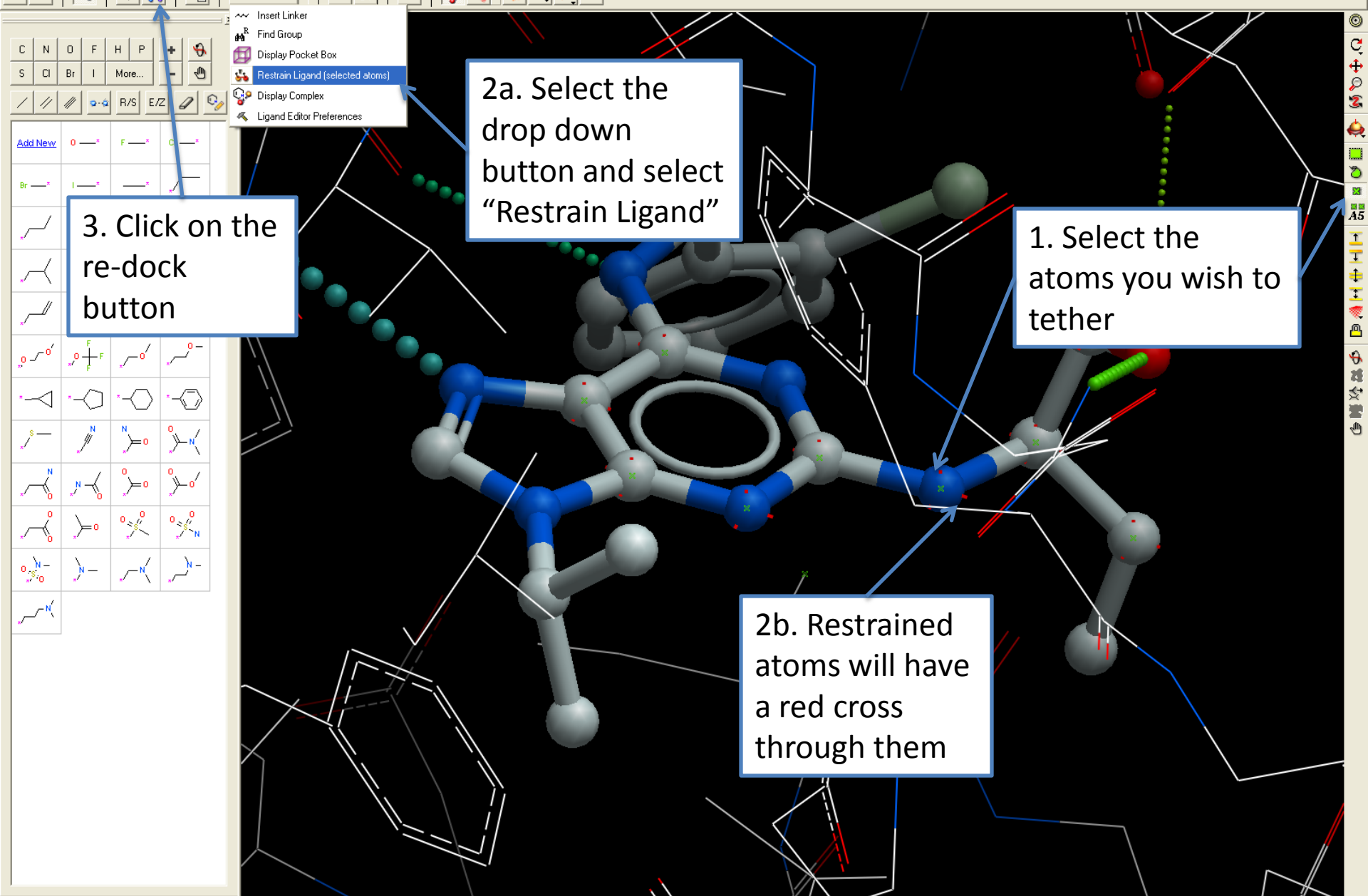
3. Click on the re-dock button

2a. Select the drop down button and select "Restrain Ligand"

1. Select the atoms you wish to tether

2b. Restrained atoms will have a red cross through them

How to restrain (tether) atoms during docking.



How to screen a database of substituents.

1. Select one hydrogen (or other terminal) atom . You may use the “atom pick” button.

2. Click on the “Advanced” drop down button and select “Find Group”

3. Select whether you want to calculate a Score for the substituent or the whole database.

4. Use the in-built ICM database of substituents or use your own external table

5a. A table with the substituents and their Score and Substructure Score will be displayed

5b. Click here to display the substituent

3c. Double click here to load the full ligand

Find Best Replacement Group For Selected Atoms

Calculate Substituent Score Only Calculate Full Binding Score

Use System Modifiers List Use External Table

R-group Table: [Dropdown]

Hint
Select one hydrogen (or other terminal) atom to find substituents.
You may use 'atom pick' tool.

Ok Cancel

mol	group
1	chiral_3D

chiral_3D

chiral_3D

594 Atoms 48 Res, 2 Mol, 2 Obj

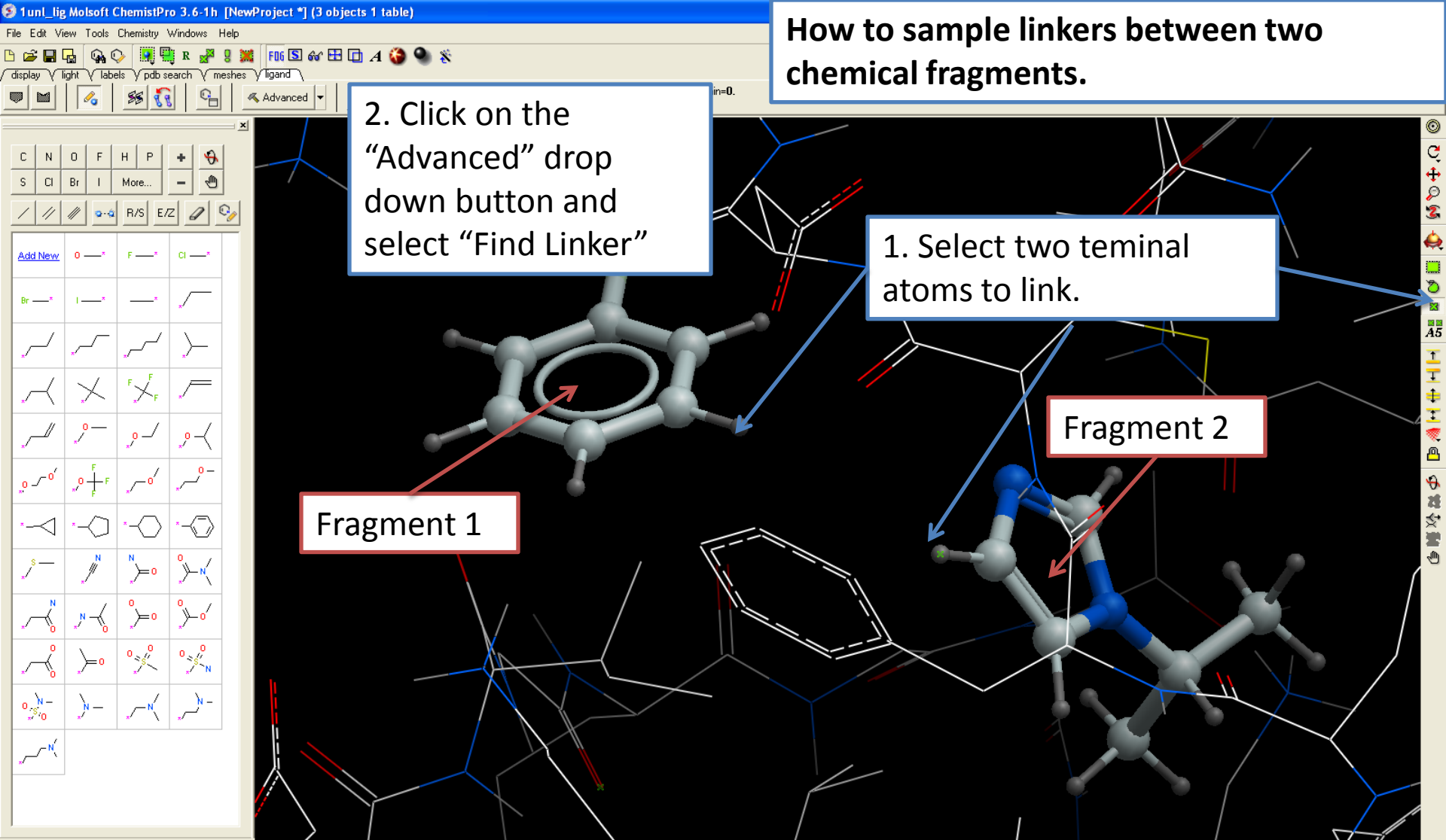
How to sample linkers between two chemical fragments.

2. Click on the "Advanced" drop down button and select "Find Linker"

1. Select two terminal atoms to link.

Fragment 1

Fragment 2



mol	L	group	smiles	SubstScore	Score	Strain	MolLogP	MolLogS	MolHf	MolPSA	Volume
1			*C=C	-4.704	0	5.63	4.466	-6.895	53.31	70.81	401.8
			*C	-4.162	0	3.808	4.369	-6.59	28.28	70.81	381.5

ICM-Chemist-Pro

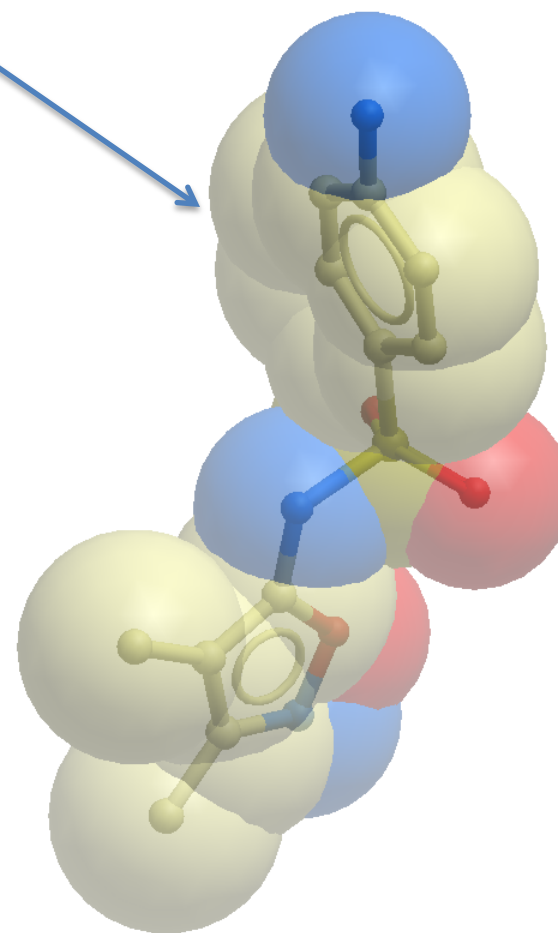
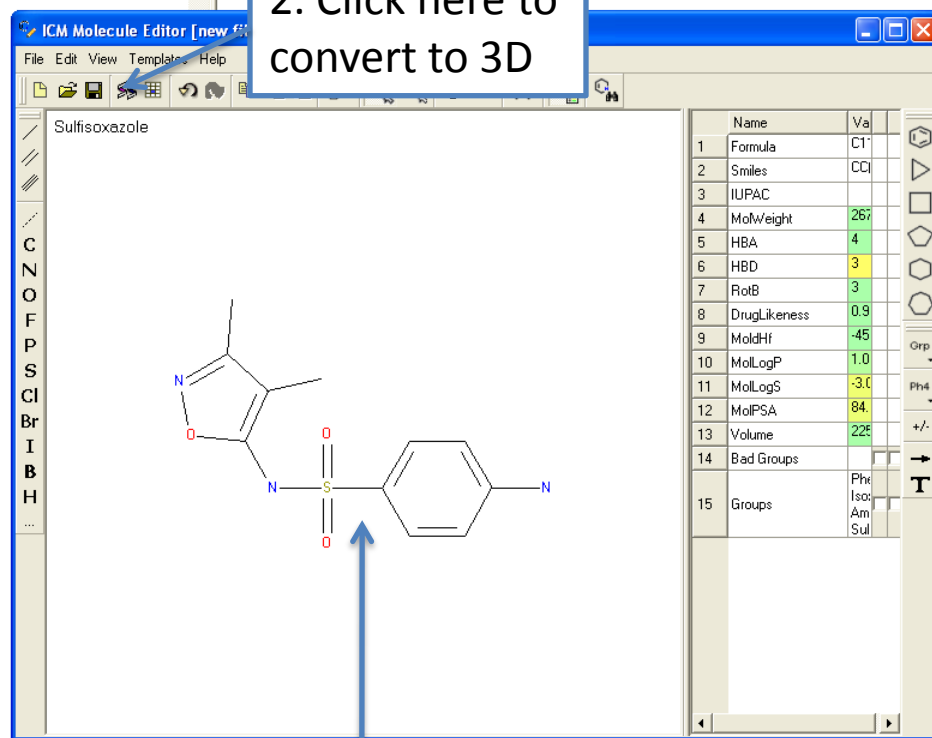
ICM 3D LIGAND EDITOR: CONVERT CHEMICALS TO 3D

How to convert 2D sketches in the molecule editor into 3D.

3. 3D molecule will be displayed and listed in the ICM Workspace

2. Click here to convert to 3D

1. Sketch the molecule



```
Info> 127 colors and 17 graphic modes read from C:/Program Files/Molsoft LLC/Molsoft ICM-Chemist_3/icm.cir
icm/Sulfoxazole> color background rgb=(100,255,0)
icm/Sulfoxazole> color background rgb=(255,255,255)
icm/Sulfoxazole> display cpk Res(a_*/DD)
icm/Sulfoxazole> GRAPHICS.hydrogenDisplay=3
icm/Sulfoxazole> display hydrogen
icm/Sulfoxazole>
```

How to convert 2D chemical sketches to 3D.

The screenshot shows the Molsoft ICM-Chemist software interface. The main window displays a table with 6 rows of chemical structures. The first row is highlighted in blue. A blue box with the text "1. Read in chemical spreadsheet (mol sdf format)" points to the first row. A second blue box with the text "2. Chemistry/Convert to 3D" points to the "Convert To 3D..." option in the "Chemistry" menu. A third blue box with the text "3. Convert a local table or in batch mode" points to the "Convert To 3D" dialog box. The dialog box shows "Local Tables" and "Files" tabs, with "Molecular Table" set to "ricinLigands2D". The "Options" section has "Keep Hydrogens" and "In Place" checked, and "Fix Amide Bonds" also checked. The command-line window at the bottom shows the following commands:

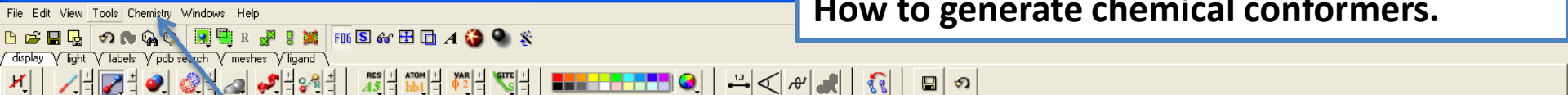
```
icm/Sulfisoxazole> delete all
icm/def> undisplay window
icm/def> s_currentProject = ""
icm/def> openFile "C:\\Program Files\\Molsoft LLC\\Molsoft ICM-Chemist_3\\ricinLigands2D.sdf" 0 yes no no no ""
Info> table 'ricinLigands2D' ( 0 headers, 1 arrays[7]) created
icm/def> delete ricinLigands2D.NAME_
icm/def>
```

1. Read in chemical spreadsheet (mol sdf format)

2. Chemistry/Convert to 3D

3. Convert a local table or in batch mode

How to generate chemical conformers.



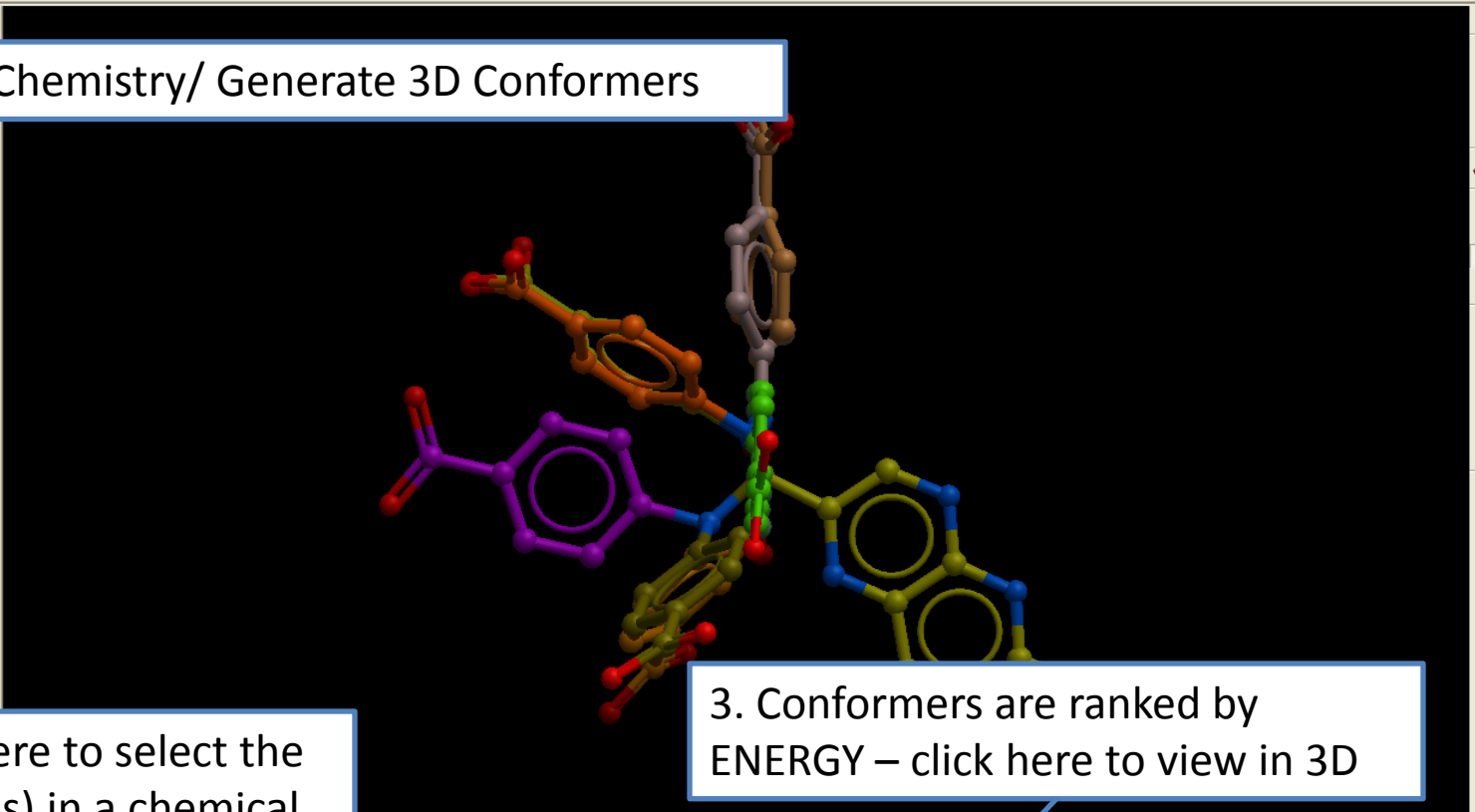
2. Chemistry/ Generate 3D Conformers

1. Click here to select the chemical(s) in a chemical spreadsheet

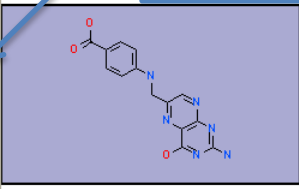
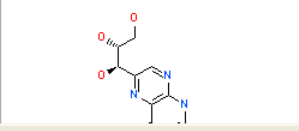
3. Conformers are ranked by ENERGY – click here to view in 3D

no selection

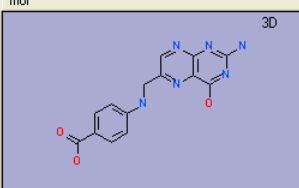
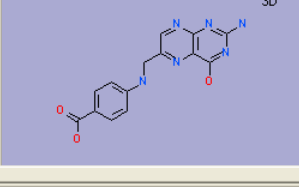
- objects (9 items)
 - conformers_1 [1] XR; 0.0Å
 - m 1 H C14H12N6O33d
 - conformers_2 [2] XR; 0.0Å
 - m 1 H C14H12N6O33d
 - conformers_3 [3] XR; 0.0Å
 - m 1 H C14H12N6O33d
 - conformers_4 [4] XR; 0.0Å
 - m 1 H C14H12N6O33d
 - conformers_5 [5] XR; 0.0Å
 - m 1 H C14H12N6O33d
 - conformers_6 [6] XR; 0.0Å
 - m 1 H C14H12N6O33d
 - conformers_7 [7] XR; 0.0Å
 - m 1 H C14H12N6O33d
 - conformers_8 [8] XR; 0.0Å
 - m 1 H C14H12N6O33d
 - conformers_9 [9] XR; 0.0Å
 - m 1 H C14H12N6O33d
- tables (2 items)
 - ricinLigands2D 7 rows 2 cols 0 headers
 - conformers 9 rows 7 cols 2 headers



ricinLigands2D

mol	N
1	
2	chiral
3	

conformers

mol	L	NAME	MOL NUM	CONF NUM	ENERGY
1		C14H12N6O33d	1	1	0
2		C14H12N6O33d	1	2	0.2469

ICM-Chemist-Pro

ICM 3D LIGAND EDITOR: CHEMICAL SUPERPOSITION

How to perform rigid and flexible chemical substructure superposition.

The screenshot shows the ICM software interface. The 'Chemistry' menu is open, and 'Rigid Substructure Superimpose...' is highlighted. The 'objects' list on the left shows several chemical structures, with 'C10H11' selected. The 'Flexible Substructure Superimpose...' option is also visible below the rigid option.

1. Select the chemicals you wish to superimpose.

2. Chemistry/Rigid (or Flexible) Superimpose

The dialog box for 'Flexible chemical superimposition' is shown. It has a 'template' dropdown menu set to 'a_C18H25N2O5'. There is a checkbox for 'Use Largest Fragment Only' which is currently unchecked. The 'Ok', 'Cancel', and 'Help' buttons are at the bottom.

3. Use the drop down arrow to select the superposition template.

```
icm/C9H9N2O4> antiSuper a_C18H25N2O5. Real( 2. )
antiSuper> xm = 8.294854 ym = 8.216468 win_asp = 1.318088 nr = 3 nc = 4
Info> ym,xm,win_asp,tmp,r_margin,os_template,nr,nob,nc,mol_asp,iy0,iy,ix0,ix,iob,i_template temp.variables deleted
icm/C9H9N2O4> color xstick Res(a_*/./DD) & a_*/./c* & a_*/./!P molecule
icm/C9H9N2O4> color background rgb=(255,255,255)
icm/C9H9N2O4>
```

How to use Atomic Property Fields for Chemical Superposition.

The screenshot shows the main menu of the software. The 'Flexible APF Superposition to Template...' option is highlighted in blue. Other options include 'Rigid Substructure Superimpose...', 'Flexible Substructure Superimpose...', 'Multiple APF Alignment...', and 'Arrange as Grid...'. The 'objects' list on the left shows a hierarchy of objects including '1f8d', 'mman', 'a', 'ynag', 'xnag', 'x', 'xman', 'ynag2', 'm', 'm2', 'mman', 'W', 'super_1f8d', and 'm'.

1. Load a 3D template to superimpose onto

3. Chemistry/Flexible APF Superposition to Template

4. Fill in dialog box

The dialog box 'Flexible APF Superposition to Template' is shown. It has the following fields and options:

- Chemical Table: LIGANDS
- template: a_1f8d_ligand.mman
- thoroughness: 1.
- Sample Rings:
- Sample CisTrans:
- Weight Atoms by Occupancy:
- Report APF Score:
- Multiple Poses:
- Buttons: Ok, Cancel, Help

```
Info> file 'C:\DOCUME~1\ANDREW~1\LOCALS~1\Temp\super tmp out.sdf' removed
icm> 1f8d> dsChemTemp new
icm> tmpmol> dsChemLock new
icm> super_1f8d_ligand_22
icm> super_1f8d_ligand_22
icm> super_1f8d_ligand_22
```

2. Load a table of chemicals to superimpose

5. Results table – click here to display 3D structure

The screenshot shows the 'LIGANDS' table with two columns: 'mol' and 'NAME'. The first row shows '1' in the 'mol' column and 'ara2' in the 'NAME' column. A second row shows '1' in the 'mol' column and 'chiral' in the 'NAME' column. A 3D structure of a molecule is displayed in the 'chiral,3D' view. A red circle highlights the 'super_1f8d_ligand' entry in the table, and a blue arrow points to a small green square icon next to it, indicating the button to click to display the 3D structure.

ICM-Chemist-Pro

ICM 3D LIGAND EDITOR: QUANTITATIVE STRUCTURE ACTIVITY RELATIONSHIP (QSAR)

How to build a QSAR prediction model.

1. Predict IC50 based on 2D sketch

2. Tools/ Table/ Build Prediction Model

3. Fill in dialog box – choose algorithm etc...

Model saved in the ICM Workspace

Learn Options

Table: Column:

Model name:

Algorithm:

Algorithm parameters: Try to estimate Number of latent vectors: to

No free term constraint: f(0) = 0

Descriptors:

- the "mol" column and all numerical columns except "IC50"
- the selected columns only
- the mol column only

Chemical Fingerprints:

Type: Binary Counted

Length: Auto

Minimal chain length Maximal chain length

lev	Atom properties	Bond properties
1	1 atom number,nHydrogens	
2	2 atom number,nHydrogens	bond order
3	3 atom number,nHydrogens	bond order

Test:

cross-validation, nof groups =

hold-out the selected rows

bootstrapping, nof repetitions =

```
Info> 15: R2(1.0000,1.0000) RMSE(2.589e-015,1.695e-015) MAE(2.422e-015,1.454e-015) in 0.02s (mem: 4MB)
Info> Optimal number of latent vectors: 5
Info> plsRegression model for property 'IC50' built for 64 records. Corr_R2=1.00 (CV=1.00), rmsError=0.01 (CV=0.01)
Info> FP statistics: maxatw=0.375510 minatw=0.018556
icm/def> delete compounds
icm/def>
```

How to apply a QSAR prediction model.

2. Tools/Table/Predict

1. Predicting IC50 based on 2D sketch using IC50pred model generated in previous example.

3. Choose table you would like to make the prediction on

5. New column added to table with prediction

4. Enter name of model

Predict Options

Table: binding_data_assay2
Model: IC50pred
Type: plsRegression

Name	Value
Type	plsRegression
No of latent vectors	5
Dimensionality	1024
Fingerprint max chain length	3
self: R2	0.999889
self: RMSE	0.00743199
self: MAE	0.00597391
self: Spearman	0.998443
test: R2	0.999787
test: RMSE	0.0103798

Color atoms by contribution red/black/blue

Required columns
mol

Predict Cancel Help

```
icm/def> delete compounds
icm/def> openFile "V:\\training course\\icm-chemist-pro-webinar\\qsar.icb"
Info> 7 shell objects read (skipped 1) from V:\\training course\\icm-chemist-pro-webinar\\qsar.icb
icm/def> predict binding_data_assay2 IC50pred
Info> property 'IC50pred' predicted by 'plsRegression' model for 23 objects.
icm/def>
```