

Read into ICM multiple receptor conformations of your receptor.

Multiple conformations of this loop region.

#### NOTES:

- A built in stack can be used.
- Superimpose the receptor pocket.

The screenshot displays the Molsoft ICM software interface. The title bar reads "1pwm\_conf3 Molsoft icm 3.7-2c [NewProject \*] (5 objects 1 table)". The menu bar includes File, Edit, View, Bioinfo, Tools, Homology, Chemistry, Docking, and MolMechanics. The toolbar contains various icons for file operations, display settings, and search functions. The Workspace Panel on the left shows a tree view with "no selection" and a list of objects: "objects (6 items)" containing "1pwm\_conf1 [1] ICM; 0.9Å", "1pwm\_conf2 [2] ICM; 0.9Å", "1pwm\_conf3 [3\*] ICM; 0.9Å", "1pwm\_conf3\_conf4 [4] ICM", and "1pwm\_conf3\_conf5 [5] ICM", along with "sites (1 item)" and "tables (1 item)". The main 3D view shows a protein structure in yellow ribbon representation with a small molecule in the center. A blue callout box points to a specific loop region. The Terminal at the bottom shows the following commands: "icm/1pwm\_conf3> copy a\_Name(a\_) [1]+ \"\_conf5\" delete display", "Info> copying object 'a\_1pwm\_conf3.' to 'a\_1pwm\_conf3\_c", "icm/1pwm\_conf3> color Res(a\_\*.//DD) object ribbon", and "icm/1pwm\_conf3>".

Setup the ligand in the ligedit tab.

1. Select the ligedit tab

2. Click on the "Setup Ligand" button.

3. Select a ligand from one of the objects in the ligand binding pocket.

The image shows the ChimeraX software interface. The 'ligedit' tab is selected in the top toolbar. A 'Setup Ligand' dialog box is open, showing the 'Ligand Molecule' dropdown set to 'a\_1pwm\_conf1.afid'. The 'Auto Assign Formal Charges' checkbox is checked, and the 'pH' is set to 7.00. The 'Ok' button is highlighted. In the background, a 3D molecular model is visible. At the bottom, a terminal window shows the following commands:

```
icm/1pwm_conf3> copy a_Name(a_)[1]+ "_conf5" delete display  
Info> copying object 'a_1pwm_conf3.' to 'a_1pwm_conf3_conf5.'  
icm/1pwm_conf3> color Res(a_*/DD) object ribbon  
icm/1pwm_conf3>
```

The status bar at the bottom right indicates '6 Mol 5 Obj'.

Setup the multiple receptors and setup the receptor.

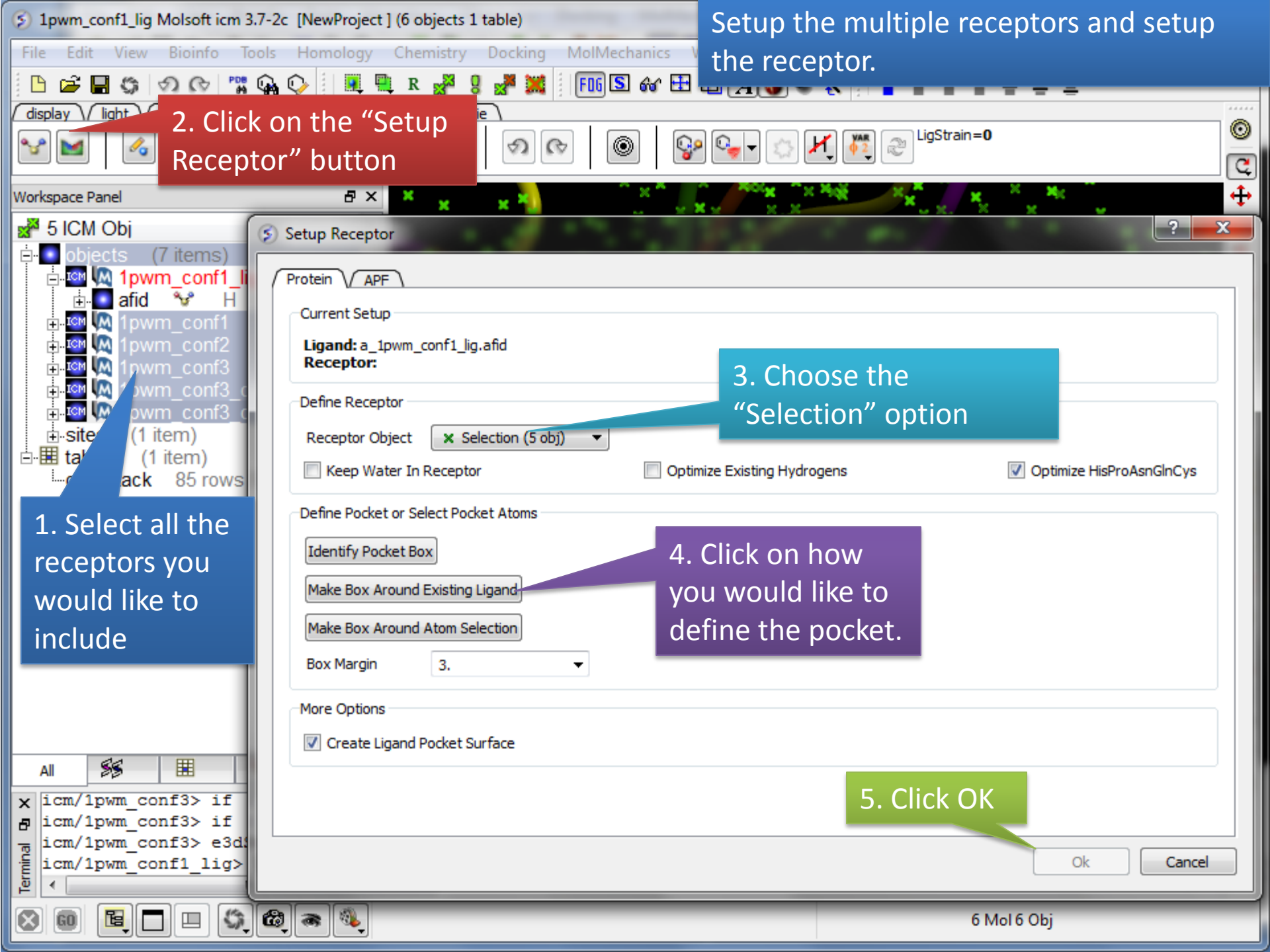
2. Click on the "Setup Receptor" button

1. Select all the receptors you would like to include

3. Choose the "Selection" option

4. Click on how you would like to define the pocket.

5. Click OK



Observe the 4D maps have been made and are located in the ICM Workspace.

The screenshot displays the ICM (Interchangeable Conformations Method) software interface. The main window shows a 3D molecular model with several 4D maps overlaid, represented as semi-transparent meshes in various colors (red, green, blue, orange). The Workspace Panel on the left lists the objects in the workspace:

- 5 ICM Obj
  - aria H (2S,4S)-Z-arr
  - 1pwm\_conf1\_rec1
  - 1pwm\_conf2\_rec1
  - 1pwm\_conf3\_rec1
  - 1pwm\_conf3\_conf4\_rec1
  - 1pwm\_conf3\_conf5\_rec1
  - 1pwm\_conf1 [1] ICM; 0.9Å
  - 1pwm\_conf2 [2] ICM; 0.9Å
  - 1pwm\_conf3 [3] ICM; 0.9Å
  - 1pwm\_conf3\_conf4 [4] IC
  - 1pwm\_conf3\_conf5 [5] IC
- sites (1 item)
- meshes (1 item)
  - g\_recPocketSurface v=3263
- tables (1 item)
  - confStack 85 rows 5 cols 4 head
- maps (6 items)
  - m\_gh 4D 398Kb [-1.96,6.20]
  - m\_ge 4D 398Kb [-36.00,36.00]
  - m\_gb 4D 398Kb [-2.82,2.87]
  - m\_gs 4D 398Kb [-4.00,0.00]
  - m\_gl 4D 398Kb [-6.19,6.20]
  - m\_gc 4D 398Kb [-3.77,6.20]

The 'maps' section is circled in red. The terminal at the bottom shows the following commands:

```
icm/1pwm_conf1_rec1> display m_gh
Info> default colors { 1 2 3 4 0 5 6 7 8 } [0 is transparent]
icm/1pwm_conf1_rec1> undisplay store m_gh
icm/1pwm_conf1_rec1>
```

The status bar at the bottom right indicates '6 ICM Obj'.

Note you can toggle between the multiple receptor conformations.

```
f1_rec1> e3dLoad4DRecConf 3
```

```
f1_rec1> e3dLoad4DRecConf 5
```

```
f1_rec1> e3dLoad4DRecConf 3
```

```
f1_rec1>
```

VisScore: 0 LigStrain=0 Score: 0

1pwm\_conf3\_rec1:1  
1pwm\_conf1\_rec1:1  
1pwm\_conf2\_rec1:1  
1pwm\_conf3\_rec1:1  
1pwm\_conf3\_conf4\_rec1:1  
1pwm\_conf3\_conf5\_rec1:1

1. Click and select conformation. Each conformation is colored uniquely.

Re-dock ligand to multiple receptor conformations.

The screenshot displays the Molsoft icm 3.7-2c software interface. The main window shows a 3D molecular model of a protein-ligand complex. The protein is represented by a grey wireframe, and the ligand is shown as a white ball-and-stick model. A semi-transparent mesh is overlaid on the protein, representing the docking site. The interface includes a menu bar (Bioinfo, Tools, Homology, Chemistry, Docking, MolMechanics, Windows, Help), a toolbar with various icons, and a command line at the bottom.

A context menu is open over the docking button, showing two options:

- Redock in Current Receptor
- Redock in Multiple Receptors (4D)

A blue callout box points to the docking button with the text: "1. Click and hold on the docking button".

The command line at the bottom shows the following commands:

```
f1_recl> e3dLoad4DRecConf 3  
f1_recl> e3dLoad4DRecConf 5  
f1_recl> e3dLoad4DRecConf 3  
f1_recl>
```

The status bar at the bottom right indicates "2 ICM Obj".

These signs indicate the 4D docking is running.

The screenshot displays the Molsoft ICM 3.7-2c software interface. The main window shows a 3D molecular model of a protein-ligand complex. The protein is represented by a grey wireframe, and the ligand is shown as a ball-and-stick model with white, blue, and red atoms. The ligand is docked within a mesh representation of the protein's binding pocket, which is colored in red, green, and blue. The interface includes a menu bar (File, Edit, View, Bioinfo, Tools, Homology, Chemistry, Docking, MolMechanics), a toolbar with various icons, and a Workspace Panel on the left. The Terminal window at the bottom shows the following commands and output:

```
icm/lpwm_conf1_rec1> e3dLoad4DResConf 3  
icm/lpwm_conf1_rec1> processLigandICM a_LIG.I "redock" Sarray(1,"4D")  
Info> 4D grid docking option is enabled
```

The status bar at the bottom indicates "Running: 4D Docking in Multiple Receptors" and "2 ICM Obj".

Best docked ligand conformation is listed in a table ranked by Score.

Workspace Panel

- 5 ICM Obj
  - 1pwm\_conf1\_rec1
  - 1pwm\_conf2\_rec1
  - 1pwm\_conf3\_rec1
  - 1pwm\_conf3\_conf4\_rec1
  - 1pwm\_conf3\_conf5\_rec1
  - 1pwm\_conf1 [1] ICM; 0.9Å
  - 1pwm\_conf2 [2] ICM; 0.9Å
  - 1pwm\_conf3 [3] ICM; 0.9Å
  - 1pwm\_conf3\_conf4 [4] IC
  - 1pwm\_conf3\_conf5 [5] IC
  - 1pwm [12] XR; 0.0Å
  - m H 1pwm

Tables

ConfNum	L	Score	VlsScore	Strain	RecConf	Steric	Torsion	Electro	Hbond	Hvdrooph	Surface
1	14	-4.268	-15.61	11.34	1pwm_conf1_rec1:1	-14.4	1	3.216	-3.671	-3.729	10.47
2	2	-4.008	-22.89	18.88	1pwm_conf1_rec1:1	-25.52	1	1.871	-2.887	-3.333	13.78
3	12	-1.764	-15.32	13.55	1pwm_conf1_rec1:1	-18.18	1	4.072	-3.654	-3.406	14.8
4	13	1.824	-11.06	12.88	1pwm_conf1_rec1:1	-20.53	1	4.881	-0.4725	-3.77	12.5
5	11	6.257	6.952	12.21	1pwm_conf1_rec1:1	10.70	1	10.76	0.7644	2.875	12.80

Terminal

```
icm/1pwm_conf1_lig> updateLigandScore a_LIG.I 0. 0. yes  
icm/1pwm_conf1_lig> e3dLoad4DRecConf 1  
icm/1pwm_conf1_lig> updateLigandScore a_LIG.I 0. 0. yes  
icm/1pwm_conf1_lig>
```

1. Click here to display the ligand.

5 Obj [3 non-IC



Toggle through each conformation and calculate the score.

1. Toggle through each conformation here.

2. Click here to calculate the score.

Score	Strain	RecConf	Steric	Torsion	Electro	Hbond	Hvdrohp	Surface
-15.61	11.34	1pwm_conf1_rec1:1	-14.4	1	3.216	-3.671	-3.729	10.47
-12.89	18.88	1pwm_conf1_rec1:1	-25.52	1	1.871	-2.887	-3.333	13.78
-15.32	13.55	1pwm_conf1_rec1:1	-18.18	1	4.072	-3.654	-3.406	14.8
-11.06	12.88	1pwm_conf1_rec1:1	-20.53	1	4.881	-0.4725	-3.77	12.5
-15.057	12.21	1pwm_conf1_rec1:1	-19.70	1	10.76	0.7644	2.875	12.80

```
dateLigandScore a_LIG.I 0. 0. yes
dLoad4DRecConf 1
dateLigandScore a_LIG.I 0. 0. yes
```

5 Obj [3 non-ICM]