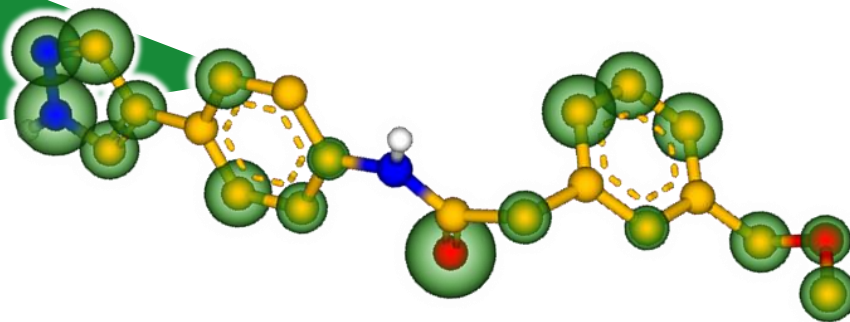




BioSolveIT
expect actives!

SeeSAR

Beginner's Guide
Version 13 - Midas



**Time to start an interactive dialog with
your compound!**

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0. Before you start

The screenshot displays a molecular docking software interface. The main window shows a 3D ribbon representation of a protein (blue) with a ligand (grey sticks) docked in its binding site. A data panel on the left lists proteins, with 'SOJE' selected. A '2D' view of the ligand structure is shown in the bottom-left corner, labeled 'VSK_A_401'. The structure features an indole ring system, a chiral center with an NH_3^+ group, and a piperazine ring system. Two analysis windows are open: 'N1, VSK_A_401' showing a Hydrated Binding Energy (Hyde) of -3.4 kJ/mol, and 'C10 - C9, VSK_A_401' showing a Torsion angle of 63°. The torsion plot is a histogram with a vertical line at 63 degrees. The bottom of the interface shows a 'Sequence View' with a protein sequence from residue 1 to 38, including residues like SER1, THR2, GLY3, ASP11, ALA16, THR17, ILE18, THR19, PRO20, VAL21, GLN22, ILE23, GLY24, THR25, PRO26, ALA27, GLN28, THR29, LEU30, ASN31, LEU32, ASP33, PHE34, ASP35, THR36, GLY37, and SER38.

Category	Lig	Rec
Hyde	-3.4 kJ/mol	
Desolvation	6.8	2.4
Interaction	-7.9	-4.8

Torsion Angle (°)	Frequency
-180	1.0
-90	0.5
0	0.2
63	1.0
90	0.5
180	1.0

Welcome to
SeeSAR 13.0
fast • visual • easy Midas



Continue
Previous Project

Continue with your last project.



New
Project

Start your drug discovery project here.



Start SeeSAR
Tour

Find an introduction to SeeSAR's interface.

The screenshot displays the SeeSAR software interface. At the top center, the SeeSAR logo is highlighted with a red box. On the right side, the 'Appearance' menu is open, and the 'Color blindness' section is highlighted with a red box. This section shows two options: 'Green - Red' (selected) and 'Blue - Red'. A green callout box on the left contains the text: 'SeeSAR comes with a "Color blindnes" mode. It can be turned on in the "Appearance" menu.'

PDB code or keyword

Data

Paste protein from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar

2D


Sequence View








Show binding site only

Name (e.g. gly)

No protein selected

No molecule selected



Data

Proteins

1

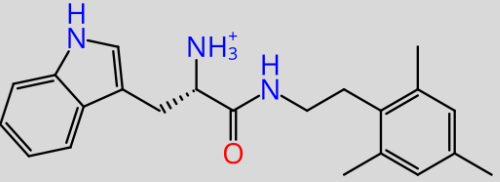
Lost your compound? Zoomed out too far?
 Focus the view on the compound with the space bar.

Ligand for 5OJE

Name	Estimated Affinity			
	pM	nM	μM	mM
VSK_A_401				

2D

VSK_A_401



Sequence View

Show Binding Site Only

Name (e.g. gly)

1 5 10 15 20 25 30 35

all SOJE SER1 THR2 GLY3 SER4 ALA5 THR6 THR7 THR8 PRO9 ILE10 ASP11 SER12 LEU13 ASP14 ASP15 ALA16 TYR17 ILE18 THR19 PRO20 VAL21 GLN22 ILE23 GLY24 THR25 PRO26 ALA27 GLN28 THR29 LEU30 ASN31 LEU32 ASP33 PHE34 ASP35 THR36 GLY37 SER38

SOJE VSK_A_401

Use the "L" hot key for labeling. SeeSAR allows you to label a lot of molecules to provide you with interesting details on individual contributions of atoms to the overall binding affinity, molecular torsions, and much more.

N1, VSK_A_401
 Hyde: -3.4 kJ/mol

	Lig	Rec
Desolvation	6.8	2.4
Interaction	-7.9	-4.8

C10 - C9, VSK_A_401
 Torsion: 63°

2D
 VSK_A_401

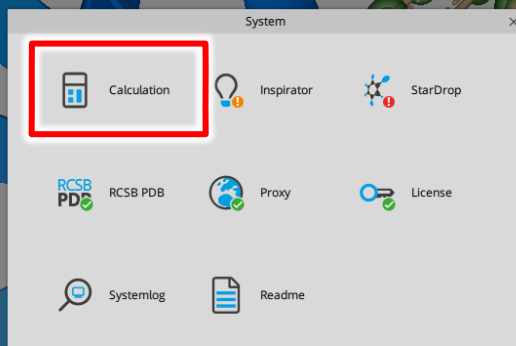
Sequence View

1 5 10 15 20 25 30 35

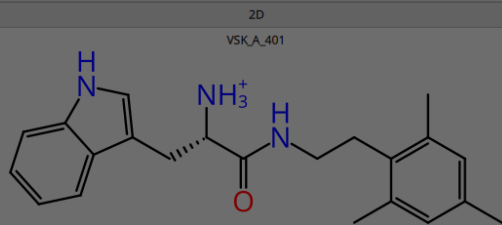
SOJE SER1 THR2 GLY3 SER4 ALA5 THR6 THR7 THR8 PRO9 ILE10 ASP11 SER12 LEU13 ASP14 ASP15 ALA16 TYR17 ILE18 THR19 PRO20 VAL21 GLN22 ILE23 GLY24 THR25 PRO26 ALA27 GLN28 THR29 LEU30 ASN31 LEU32 ASP33 PHE34 ASP35 THR36 GLY37 SER38

SOJE VSK_A_401

To save computational time and resources, it is possible to select what parameters are calculated once a molecule is added to one of SeeSAR'S modes. Got to "System" and select "Calculation".



The image shows a 'System' dialog box with several options. The 'Calculation' option, represented by a calculator icon, is highlighted with a red box. Other options include Inspirator, StarDrop, RCSB PDB, Proxy, License, Systemlog, and Readme.



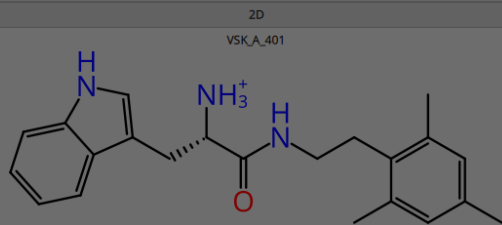
In the table, select which parameters are to be calculated for the respective modes.

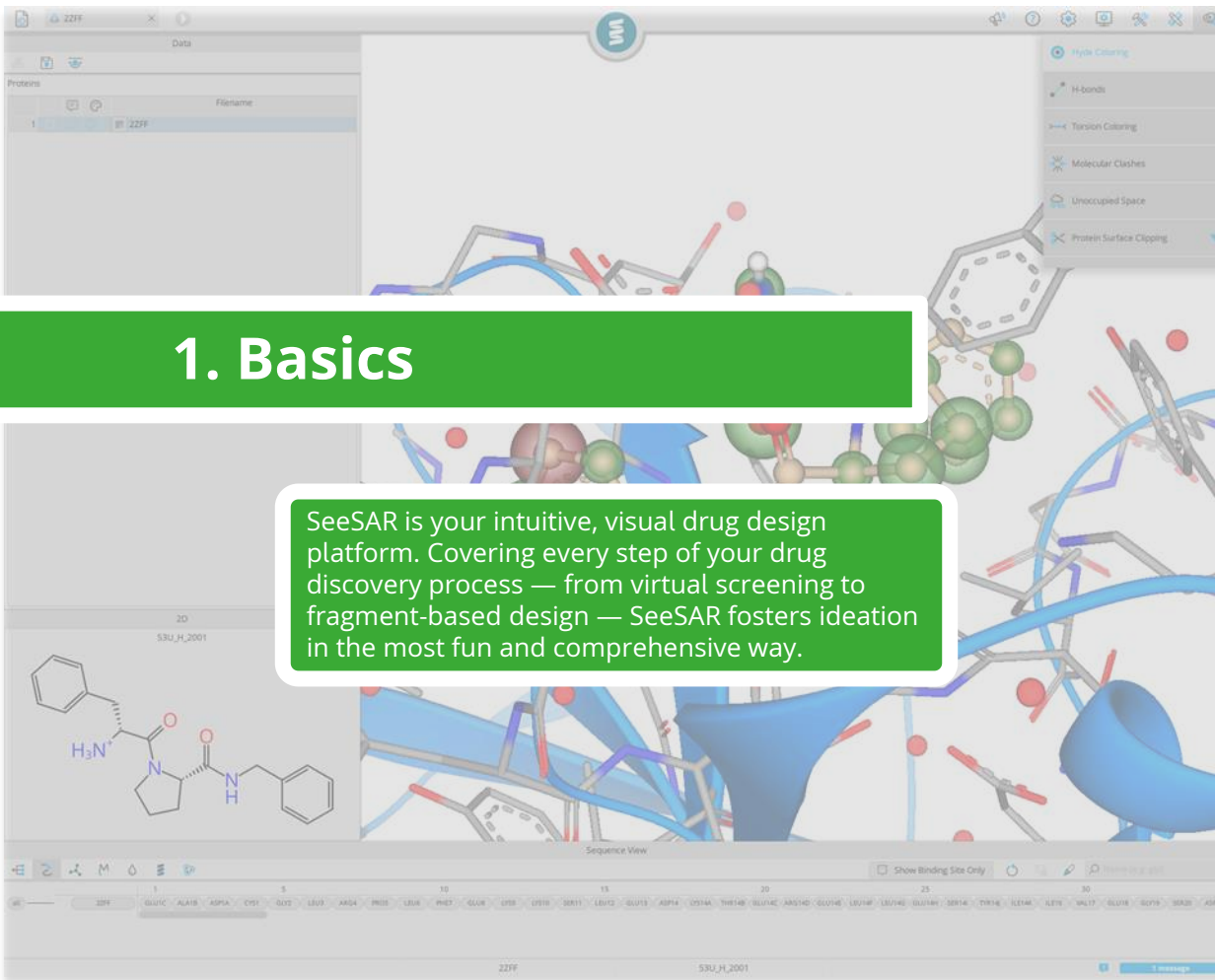
System

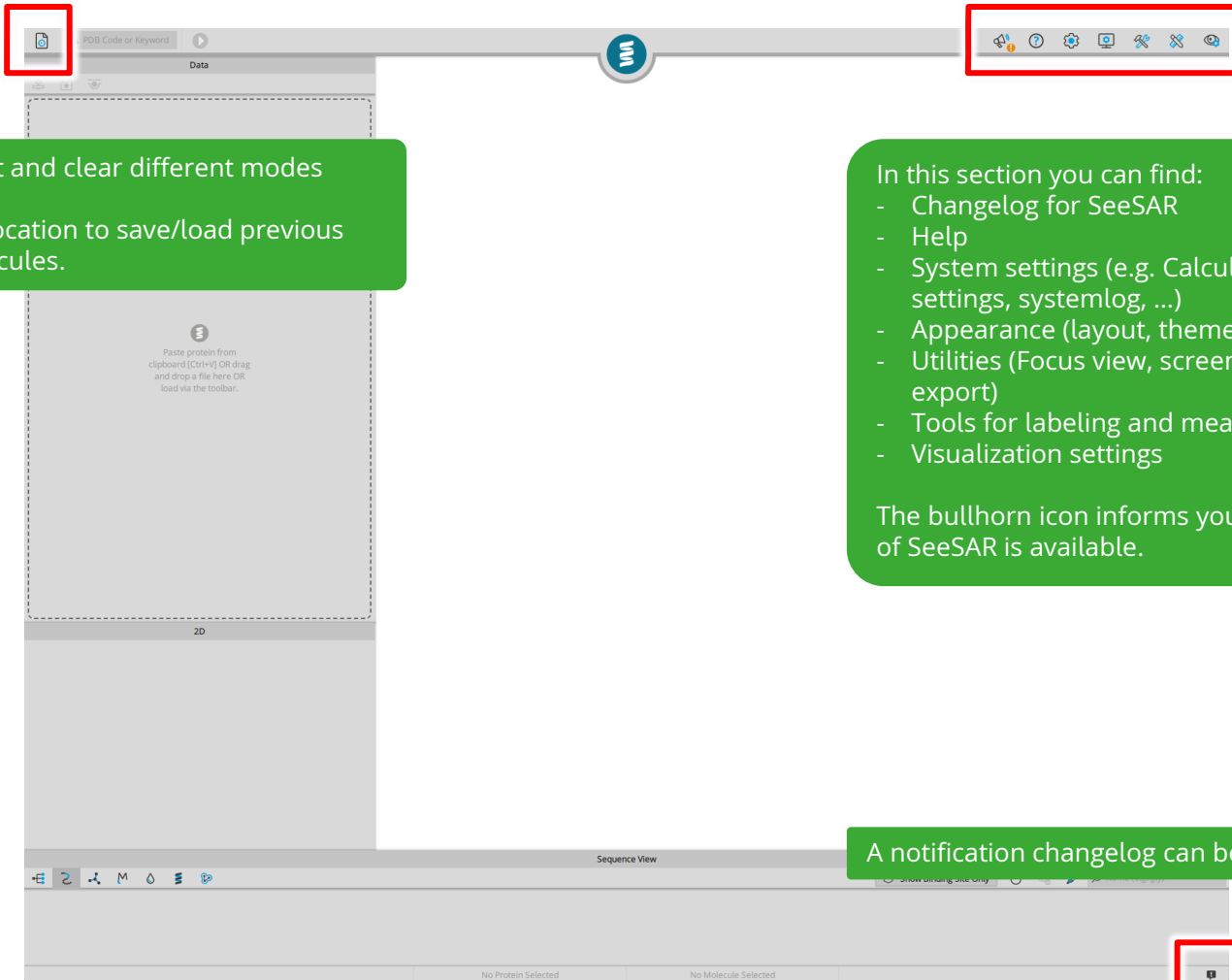
Calculation - Define which calculations should run automatically in often used workflows.

	Load Molecules from File	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Load Proteins	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Save Editor Molecules to Table	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	Save Inspirator Molecules to Table	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
	Generate Docking Poses	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
	Generate Similarity Scanner Poses	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Back Apply







Start new project and clear different modes here.
This is also the location to save/load previous projects or molecules.

In this section you can find:

- Changelog for SeeSAR
- Help
- System settings (e.g. Calculations, licence settings, systemlog, ...)
- Appearance (layout, theme)
- Utilities (Focus view, screenshots, 3D scene export)
- Tools for labeling and measurement
- Visualization settings

The bullhorn icon informs you if a new version of SeeSAR is available.

A notification changelog can be found here.

The image shows a screenshot of a web-based protein structure viewer. At the top, a search bar contains the text '2ZFF' and is highlighted with a red rectangle. Below the search bar, a green callout box contains the text: 'Type a pdb code in the search box and press enter to download a protein directly from the pdb. For this guide we will use 2ZFF as example.' Below this, another green callout box contains the text: 'Note: You can also load your protein from a file, via the file menu button.' The interface includes a top navigation bar with a '100' logo and various icons. The main area is currently empty, with a '2D' label at the bottom. The bottom toolbar includes icons for navigation and a 'Show Binding Site Only' button. The status bar at the very bottom shows 'No Protein Selected' and 'No Molecule Selected'.

The screenshot shows the Z2FF software interface. At the top, a play button icon is highlighted with a red box and labeled '2.'. Below it, a table titled 'Extract Your Ligand' is shown, with a red box around the first two rows and labeled '1.'. The table has columns for 'Name' and 'Estimated Affinity' (with sub-columns for pM, nM, μM, mM). The first row is labeled 'not extract a ligand' and the second row is labeled 'H₂O'. To the right of the table is a 3D ribbon diagram of a protein structure in blue, with a red line indicating a binding site. At the bottom, a 'Sequence View' panel shows a protein sequence with residues 1 through 30, including Z2FF, GLU1C, ALA1B, ASP1A, CYS1, GLY2, LEU3, ARG4, PRO5, LEU6, PHE7, GLU8, LYS9, LYS10, SER11, LEU12, GLU13, ASP14, LYS14A, THR14B, GLU14C, ARG14D, GLU14E, LEU14F, LEU14G, GLU14H, SER14I, THR14J, ILE14K, ILE16, VAL17, GLU18, GLY19, SER20, and ASP21.

	Name	Estimated Affinity			
		pM	nM	μM	mM
1	not extract a ligand				
2	H ₂ O				

Note:
If you are not sure what name contains which molecule, click on the name and have a look at the 2D structure below.

The screenshot displays a software interface for protein-ligand analysis. On the left, a 'Data' panel lists proteins, with '53U_H_2001' highlighted in a red box. Below this, a 'Ligand for 2ZFF' table shows the selected ligand. A green arrow points from the ligand name to a 2D chemical structure window. The main 3D view shows a blue protein ribbon structure with a red ligand molecule and orange spheres representing atoms within a 6.5 Å radius. A green text box explains this selection process. At the bottom, a 'Sequence View' panel shows the protein's amino acid sequence.

2ZFF

Data

Proteins

Filename
1 2ZFF

Ligand for 2ZFF

Name	Estimated Affinity
53U_H_2001	

2D

53U_H_2001

Sequence View

Show Binding Site Only

Name (e.g. gly)

1 5 10 15 20 25 30

all 2ZFF 53U_H_2001

GLU1C ALA1B ASP1A CYS1 GLV2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14 THR14 ILE14K ILE14L VAL17 GLU18 GLY19 SER20 ASP21

2ZFF 53U_H_2001 1 message

After ligand selection, all residues within a 6.5 Angstrom radius around it are automatically selected and presented in the model.

Click on the ligand. Its structure will be presented in the 2D window.

22FF

Data

Proteins

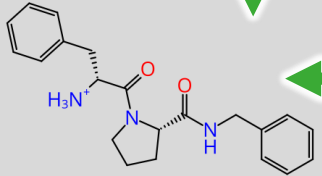
Filename
1 22FF

Ligand for 22FF

Name	Estimated Affinity
	pM nM μ M mM
53U_H_2001	

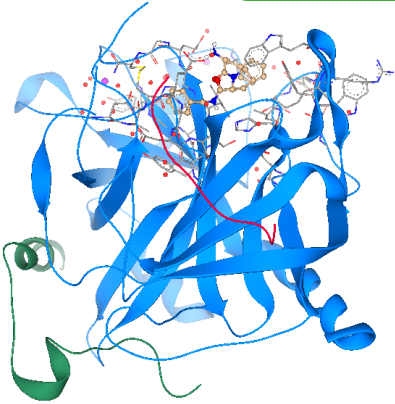
2D

53U_H_2001



3D-viewer:

- right-click to rotate
- mouse-wheel to zoom
- middle-click to shift



Tables:

- drag rim to re-size
- click entries to select

Sequence View

Show Binding Site Only

Name (e.g. gly)

1	5	10	15	20	25	30
22FF	GLU1C ALA1B ASP1A CYS1	GLY2 LEU3 ARG4 PRO5	LEU6 PHE7 GLU8 LYS9	LYS10 SER11 LEU12	GLU13 ASP14 LYS14A	THR14B GLU14C ARG14D
				GLU14E LEU14F LEU14G	GLU14H SER14	THR14 ILE14K ILE14L
				VAL17	GLU18	GLY19 SER20
				ASP21		

22FF

53U_H_2001

1 message

The screenshot displays the SeeSAR software interface. On the left, there are panels for 'Data' (showing protein 2ZFF), 'Ligand for 2ZFF' (showing 53U_H_2001), and '2D' (showing the chemical structure of 53U_H_2001). The main area shows a 3D ribbon representation of the protein (blue) with the ligand (green) bound. On the right, a settings menu is open, highlighting the 'Background' section. This menu includes options for 'Change Color', 'Layout', 'Theme' (Dark/Light), 'Label Size' (a slider), and 'Color Blindness' (Green-Red/Blue-Red). Green callout boxes with arrows point to these settings, explaining their functions. A larger green callout box at the bottom right provides instructions on how to access these settings.

Adjust background color

Change the table layout

Switch between dark and light theme

Adjust lable size

Switch to color blindness mode

If you want to customize the layout of SeeSAR, click on the 'appearance' button in the top right toolbar. For this guide will use the light one, but please feel free to use whatever you prefer!

Note that you are in the **Protein mode**. The mode switch button shows in which mode you are and allows you to change the mode as well. Hover over it so see your options.

Ligand for 2ZFF	
Name	Estimated Affinity
	pM nM μ M mM
53U_H_2001	

2D
53U_H_2001

C1CCN(C1)C(=O)C(C2=CC=CC=C2)C(=O)NCC3=CC=CC=C3

Sequence View

Show Binding Site Only

1 5 10 15 20 25 30

2ZFF GLU1C ALA18 ASP14 CYS1 GLU2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14 THR14 ILE14K ILE14L VAL17 GLU18 GLY19 SER20 ASP21

2ZFF 53U_H_2001 1 message



Proteins



In the Proteins mode you can load and superpose proteins.



Similarity Scanner



Binding Site



The Binding Site mode sets the reference pocket.

Editor



Protein Editor



The Protein Editor mode is for editing side chains, deleting waters or buffers, or search for similar binding sites.



Docking



The Analyzer mode is for filtering molecule sets, hit triaging etc.



Analyzer



Similarity Scanner



The Molecule Editor mode is for designing new molecules in 3D.



Molecule Editor



The Inspirator mode helps you to generate new ideas.



Inspirator

In the Docking mode you can generate poses for new molecules.



Docking



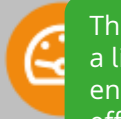
Proteins



Binding Site



Protein Editor



The Similarity Scanner is a ligand-based mode enabling fast and efficient 3D alignment of a set of input molecules on a template molecule.



Molecule Editor



Inspirator



Docking



Similarity Scanner

22FF

Data

Proteins

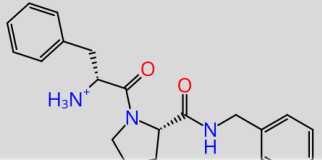
Filename
1 22FF

Ligand for 22FF

Name	Estimated Affinity
	pM nM μ M mM
53U_H_2001	

2D

53U_H_2001



3D visualization of protein 22FF (blue ribbon) with ligand 53U_H_2001 (red sticks) bound to it.

As the 3D view can easily get busy, let's customize the visualization.

Sequence View

Show Binding Site Only

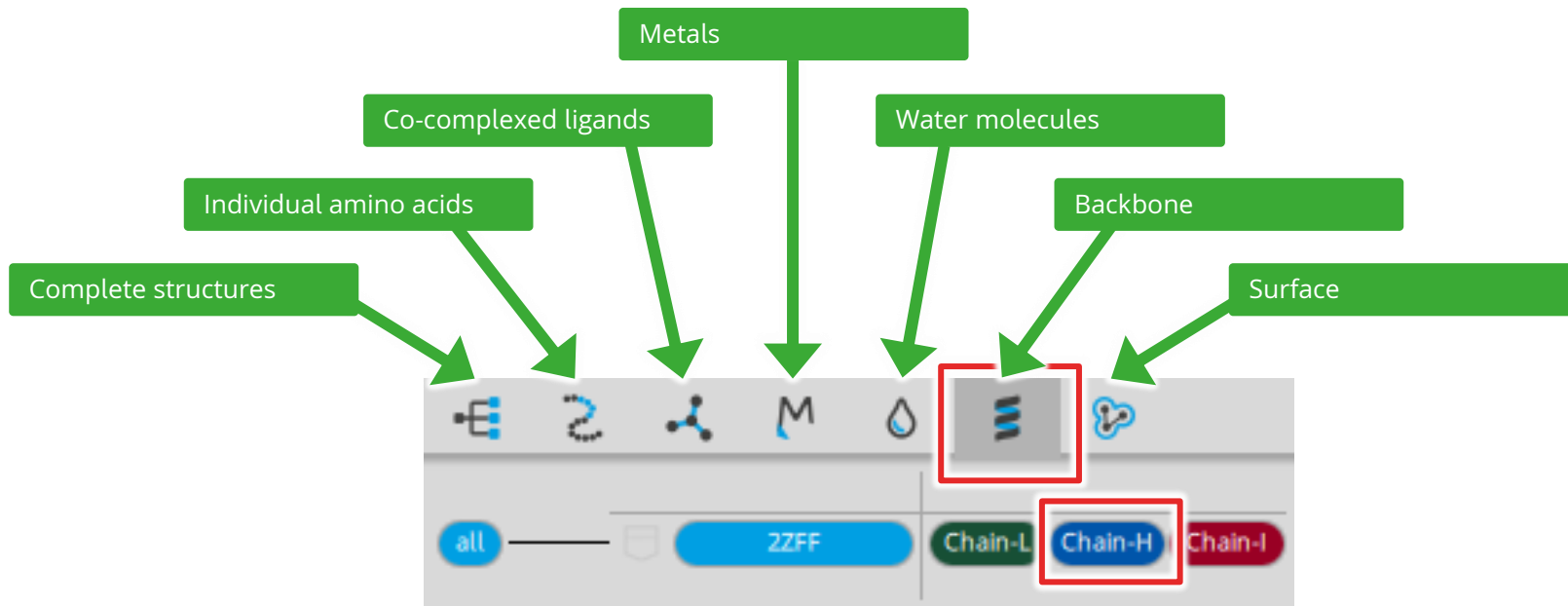
Name (e.g. gly)

1	5	10	15	20	25	30
22FF	GLU1C ALA1B ASP1A CYS1	GLV2 LEU3 ARG4 PRO5	LEU6 PHE7 GLU8 LYS9	LYS10 SER11 LEU12	GLU13 ASP14 LYS14A	THR14B GLU14C ARG14D
				GLU14E LEU14F LEU14G	GLU14H SER14	THR14 ILE14K ILE16
					VAL17	GLU18 GLY19
						SER20 ASP21

22FF 53U_H_2001

1 message

The view controls let you toggle on/off:



Let's hide the secondary structure, by clicking on the "Chain-H" button in the backbone tab. Upon clicking it turns grey (deactivated)

Note:
All buttons are clickable, so that you can hide all parts of one protein in one click (useful with several proteins).

The screenshot displays a molecular docking software interface. On the left, a sidebar contains several panels: 'Data' at the top, 'Proteins' with a table listing '1' and '2ZFF', 'Ligand for 2ZFF' with a table listing '53U_H_2001' and a context menu, and '2D' showing the chemical structure of '53U_H_2001'. The context menu is open, with 'Add to Binding Site Mode' highlighted in a red box. Other menu items include 'Add to Molecule Editor', 'Add to Inspirator', 'Add to Docking Mode', and 'Add to Similarity Scanner'. The main window shows a 3D ribbon representation of a protein in blue with a ligand in green. At the bottom, a 'Sequence View' panel shows the protein chain '2ZFF' and '53U_H_2001'.

Filename
1 2ZFF

Name	Estimated Affinity			
	pM	nM	µM	mM
53U_H_2001				

2D
53U_H_2001

Sequence View

Show Binding Site Only

Name (e.g. gly)

2ZFF Chain1 Chain1 Chain1

2ZFF 53U_H_2001

1 message

If you want to add or remove individual amino acids after the automatic selection of residues for the binding site, right click your ligand and add it to Binding Site mode.

22FF - Define Your Binding Site
 30 residues are currently selected for the binding site.
 You can modify the binding site selection, or **confirm with the green button above.**

Name	# Residues
53U_H_2001	30

Pocket ID	# Residues	DoGSiteScore	# Donors	# Acceptors

Sequence View

Show Binding Site Only

1 5 10 15 20 25 30

22FF GLU1C ALA18 ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I THR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

22FF No Molecule Selected 1 message

You are now in the **Binding Site mode**.

Residues already included in the binding site are highlighted in pink.



22FF - Define Your Binding Site

30 residues are currently selected for the binding site.
You can modify the binding site selection, or **confirm with the green button above**.

Molecules	
Name	# Residues
53U_H_2001	30

Unoccupied Pockets				
Pocket ID	# Residues	DoGSiteScore	# Donors	# Acceptors

Here you can search for unoccupied binding pockets.

Sequence View

Show Binding Site Only

22FF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14 THR14 ILE14K ILE14L VAL17 GLU18 GLY19 SER20 ASP21

22FF No Molecule Selected 1 message

22FF - Define Your Binding Site

30 residues are currently selected for the binding site.
You can modify the binding site selection, or **confirm with the green button above.**

Molecules

Name	# Residues
22FF	30

Unoccupied Pockets

Pocket ID	# Residues	DoGSiteScore	# Donors	# Acceptors
1	56	0.53	39	45
2	19	0.28	11	8
3	16	0.20	7	10
4	12	0.12	7	10

2D

3D

Sequence View

Show Binding Site Only

Name (e.g. gly)

22FF

No Molecule Selected

1 message

Unoccupied pockets are listed and presented with their respective color in 3D.

You can add or remove binding pockets and residues in 3D with the key combination ctrl + right left click.
To display all residues, toggle the residue selection in the visualization bar (1.)
Confirm your selection (2.)

Go back to the Protein mode to inspect the binding mode of the ligand inside the binding site.

Name	Estimated Affinity
	pM nM μ M mM
53U_H_2001	

2D
53U_H_2001

C1CCN(C1)C(=O)C(C2=CC=CC=C2)C(=O)NCC3=CC=CC=C3

Sequence View

Show Binding Site Only

Name (e.g. gly)

1 5 10 15 20 25 30

GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

Z2FF 53U_H_2001

1 message

For the next step make sure that 'Hyde Coloring' is turned on. You can do that in the 'Visualization' menu.

The screenshot displays a molecular visualization software interface. On the left, there are panels for 'Data', 'Proteins', 'Ligand for Z2FF', and '2D' (showing the chemical structure of 53U_H_2001). The main window shows a 3D model of a protein (blue ribbon) with a ligand (53U_H_2001, shown as a ball-and-stick model) bound to it. The protein is colored by 'Hyde Coloring', showing a gradient from blue to red. A 'Visualization' menu is open on the right, with 'Hyde Coloring' selected. The bottom of the interface shows a 'Sequence View' with a list of amino acids and their positions.

Name	Estimated Affinity
53U_H_2001	

Sequence View: 1 5 10 15 20 25 30
Z2FF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

The colored spheres depict the contributions of each atom to the estimated binding affinity. Red means unfavorable contribution, green a favorable contribution and the bigger the sphere is, the stronger is the effect. No sphere means that such atom is not estimated to have a significant impact on the binding affinity. To find out more about each Hyde sphere activate the label function and click on one atom.

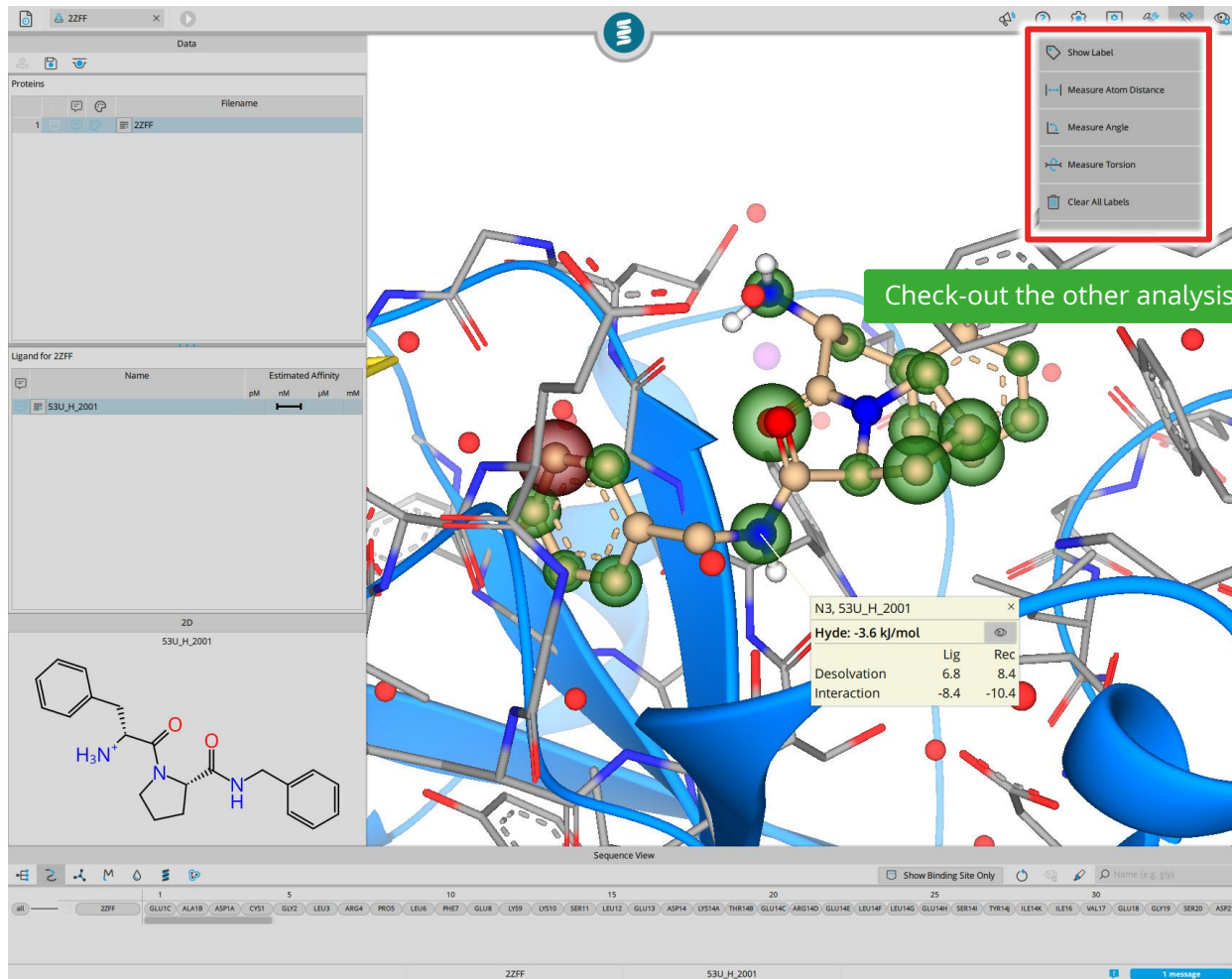
Note:
You can use the shortcut key 'L' + left click to label your atoms.

N3, 53U_H_2001
Hyde: -3.6 kJ/mol

	Lig	Rec
Desolvation	6.8	8.4
Interaction	-8.4	-10.4

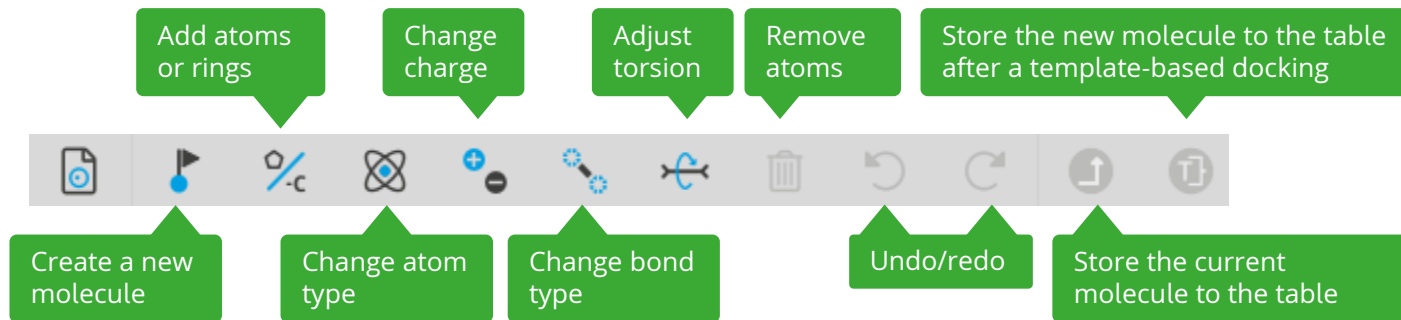
Sequence View
Show Binding Site Only

22FF 53U_H_2001 1 message



The screenshot displays a molecular docking software interface. On the left, a 'Data' panel shows a table with one entry for 'Z2FF'. Below it, a 'Ligand for Z2FF' panel lists '53U_H_2001' with a red box highlighting the 'Add to Molecule Editor' option. The main 3D view shows a protein structure in blue and a ligand in stick representation. A green callout box contains the text: 'Add to Molecule Editor' is accessible with a right-click on the table entry. This copies the molecule into the mode and automatically switches to that mode. At the bottom, a 'Sequence View' panel shows the protein sequence: 1 5 10 15 20 25 30
Z2FF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

The editor-menu will appear on the top left.
There you can:



To edit a molecule ALWAYS:

1. **select** (atoms or bonds)
2. **modify** (using the function of choice from above)

Note that many editor functions have shortcut-keys.
E.g. select a bond and type 1, 2 or, 3 on the keyboard,
or select an atom and type the element (C, N, O, ...).

As an exercise, we add an amino group to the ring by selecting the Hydrogen in meta-position and changing its element type to "N".

Note:
During editing you see all hydrogens but no estimated affinity and no Hyde spheres.
To see them, 1st add the edited ligand to the table (with the green button) and 2nd select the new entry in the table!

Molecules (# 1)				
Name	Estimated Affinity			
	pM	nM	µM	mM
1	53U_H_2001			

2211 No Molecule selected 1 message

The screenshot displays a molecular docking software interface. The main view shows a protein structure in blue and a ligand in stick representation. A data table in the top-left corner lists molecules with their estimated affinities and related coronas. A 2D chemical structure of the ligand is shown in the bottom-left corner. A play button is highlighted in the bottom-right corner of the main view.

	pM	nM	µM	mM
1				
2				

2D
53U_H_2001_1

Sequence View

Show Binding Site Only

Name (e.g. gly)

22FF

53U_H_2001_1

1 message

If you click on the molecule entry you see the estimated affinity and related coronas, but only polar Hydrogens. The editor menu is locked now.

To continue editing, click on the 'Resume' button in the center!

Now let's add a methyl group in the *meta* position. Again, storing this in the table, we see a further increased affinity estimate.

If you are running out of ideas: try the Inspirator mode. To get your molecule there select it with the checkbox at the front of every row and add it to the Inspirator mode. It will help you to replace parts of the molecule, further grow the molecule or merge molecules.

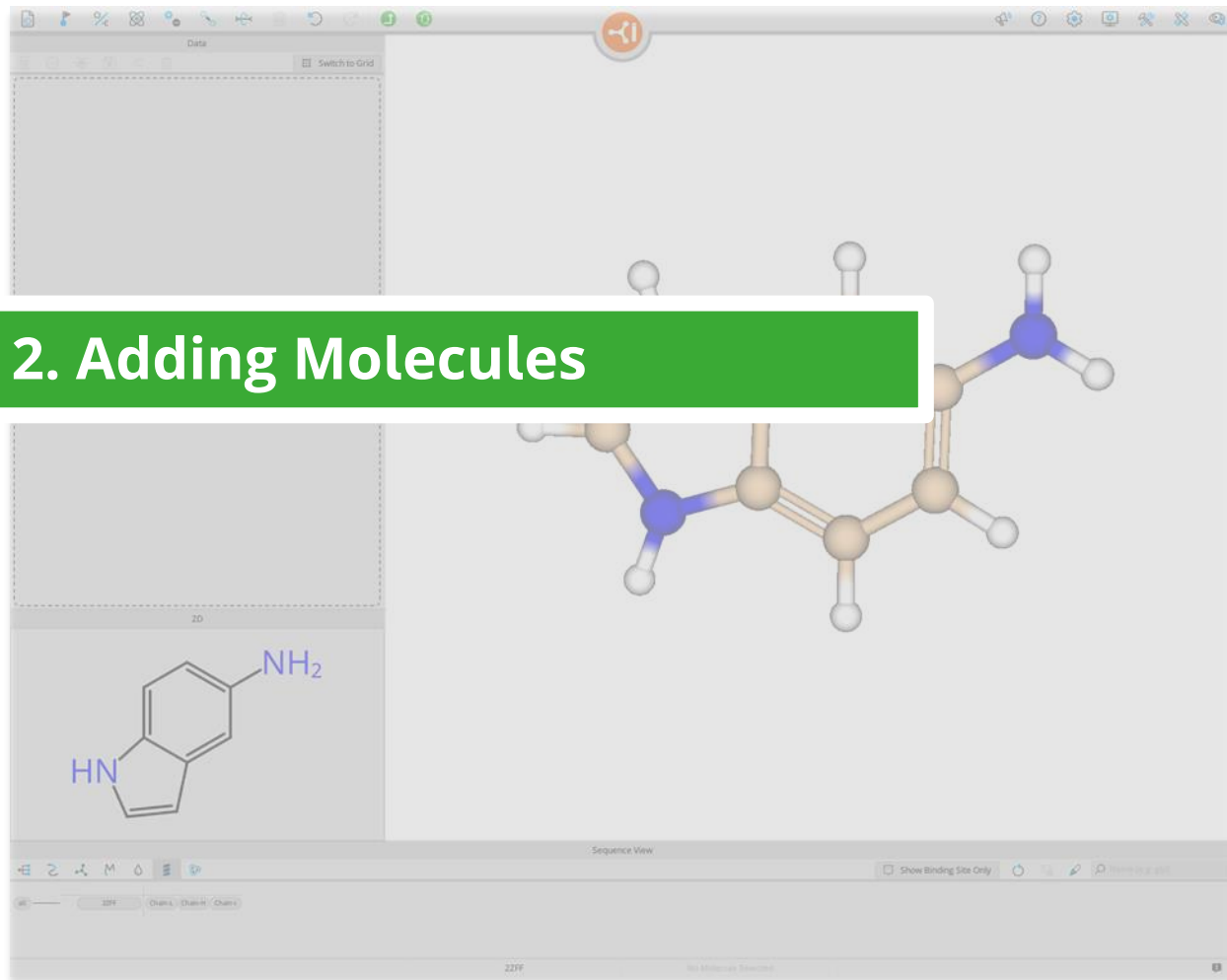
	pM	nM	µM	mM
1				
2				
3				

2D
53U_H_2001_1_3

22FF

53U_H_2001_1_3

1 message



Paste molecule from clipboard (Ctrl+V) OR drag and drop a file here OR load via the toolbar.

2Z

2ZFF

Sequence View

Show Binding Site Only

Name (e.g. gly)

1 5 10 15 20 25 30

GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

2ZFF No Molecule Selected

If you want to add your own molecules to a SeeSAR-session: Use e.g. your favorite drawing tool and save the molecules as sdf-, smiles-, or mol2-file.

Switch to the **Analyzer mode** in SeeSAR and add your molecules via the load button or copy/paste them to the input library field.

Paste molecule from clipboard (Ctrl+V) OR drag and drop a file here OR load via the toolbar.

Alternatively, copy/paste (ctrl + c/ctrl + v) your molecules (as smiles or sdf) here. For example, copy the three molecules below, to change their names:

```
O=C(N1CCCC1)c2c3c(NC=C3)ccc2  
O=C(N1CCOCC1)c2c3c(NC=C3)ccc2  
O=C(N1c2c(c(N)ccc2)CC1)c3c4c(NC=C4)ccc3
```

Sequence View

Show Binding Site Only

Name (e.g. gly)

2ZFF

1 5 10 15 20 25 30

GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14 THR14 ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

2ZFF No Molecule Selected

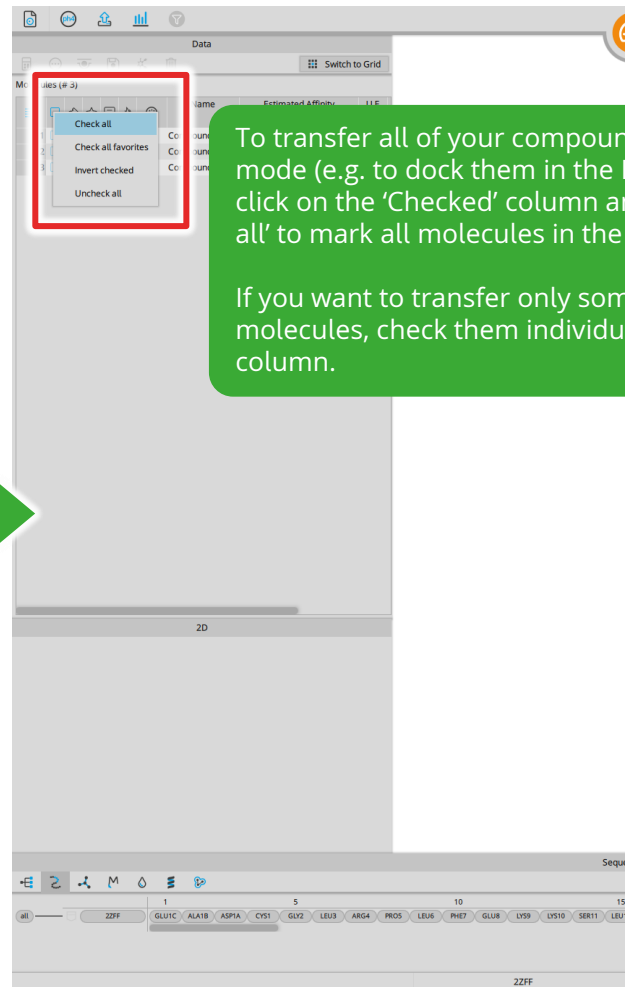
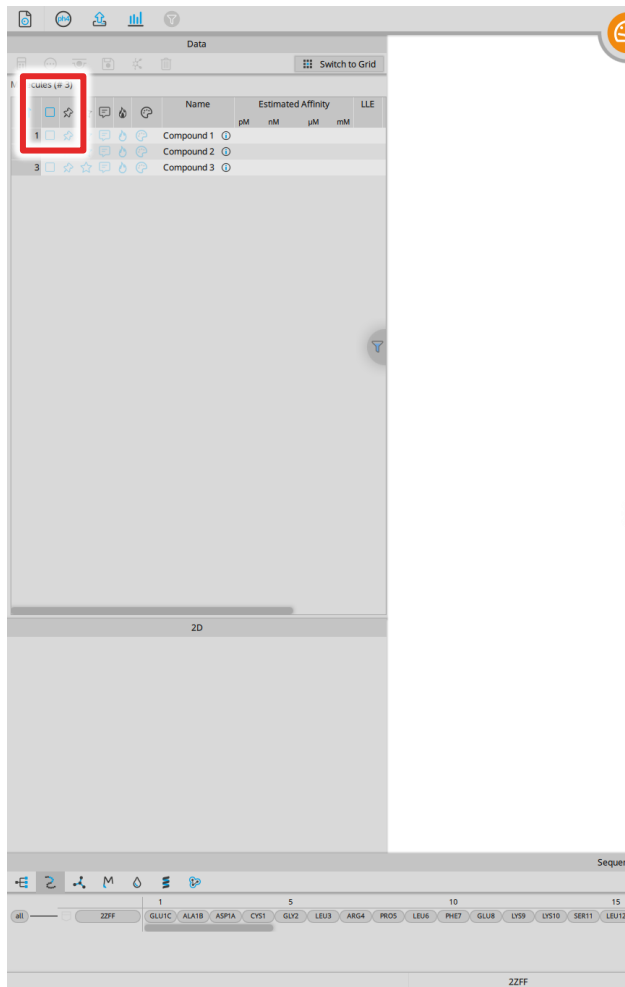
The screenshot displays a molecular docking software interface. At the top, there is a toolbar with various icons. Below it, a 'Data' panel contains a table of molecules. A red box highlights the 'Name' column of this table. The main workspace shows a 3D ribbon representation of a protein structure in blue, with a red ligand molecule docked in its binding site. At the bottom, a 'Sequence View' panel shows the amino acid sequence of the protein, with the binding site residues highlighted.

	Name	Estimated Affinity			
		pM	nM	μM	mM
1	no name				
2	no name				
3	no name				

Sequence View: 2ZF (No Molecule Selected)

Sequence: 1 5 10 15 20 25 30
 GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

Double click on the molecule name ('no name' in this case) to change it. Confirm the change with the enter key.



The screenshot shows a software interface with a protein structure (blue ribbon) and a molecule list. The molecule list has three entries, with the second entry, 'Add molecules to Docking mode', highlighted by a red box. A green callout box contains the following text:

Click on 'Add checked molecules to mode' and select the mode of your choice to work with the molecules. Since we want to dock them, we will select the **Docking mode**.

The docking procedure is explained in Section 3 (Docking).

The interface also shows a 'Data' panel at the top left, a 'Sequence View' panel at the bottom, and a '2D' panel on the left side. The protein structure is shown in a 3D view, and the molecule list is shown in a table format.

		Estimated Affinity	LLE	
		nM	μM	nM
1				
2	Add molecules to Docking mode			
3				

The screenshot displays a software interface for molecular modeling. On the left is a large 2D workspace with a dashed border and a central instruction: "Paste molecule from clipboard (Ctrl+V) OR drag and drop a file here OR load via the toolbar." Below this workspace is a label "2D". On the right is a 3D view of a protein structure, primarily blue with a red ribbon and a green helix. The top toolbar contains several icons, with a blue square icon and an orange circular icon with a white arrow highlighted by red boxes. The bottom toolbar includes a "Sequence View" section with a search bar "Name (e.g. gly)" and a list of amino acid residues: 1 Z2FF, 2 GLU1C, 3 ALA1B, 4 ASP1A, 5 CYS1, 6 GLY2, 7 LEU3, 8 ARG4, 9 PRO5, 10 LEU6, 11 PHE7, 12 GLU8, 13 LYS9, 14 LYS10, 15 SER11, 16 LEU12, 17 GLU13, 18 ASP14, 19 LYS14A, 20 THR14B, 21 GLU14C, 22 ARG14D, 23 GLU14E, 24 LEU14F, 25 LEU14G, 26 GLU14H, 27 SER14I, 28 THR14J, 29 ILE14K, 30 ILE16, 31 VAL17, 32 GLU18, 33 GLY19, 34 SER20, 35 ASP21. At the bottom center, it says "22FF" and "No Molecule Selected".

You can also create new molecules in the Molecule Editor mode.

The screenshot displays a molecular modeling software interface. On the left, a menu titled 'Create New Molecule' is open, showing options for 'Create New Ring' and 'Custom SMILES'. Under 'Create New Ring', a list of rings is shown, with 'Benzene' selected. The main workspace shows a protein structure in blue ribbon representation, with a benzene ring highlighted in red. A green text box on the right contains instructions: 'Let's start with a benzene ring. Once you clicked on 'Benzene' a ring will appear. Zoom in on the ring with the space bar or via 'Utilities' → 'Focus View'.' The bottom of the interface shows a 'Sequence View' with a list of amino acids: 1 Z2FF, 2 GLU1C, 3 ALA1B, 4 ASP1A, 5 CYS1, 6 GLY2, 7 LEU3, 8 ARG4, 9 PRO5, 10 LEU6, 11 PHE7, 12 GLU8, 13 LYS9, 14 LYS10, 15 SER11, 16 LEU12, 17 GLU13, 18 ASP14, 19 LYS14A, 20 THR14B, 21 GLU14C, 22 ARG14D, 23 GLU14E, 24 LEU14F, 25 LEU14G, 26 GLU14H, 27 SER14I, 28 THR14J, 29 ILE14K, 30 ILE16, 31 VAL17, 32 GLU18, 33 GLY19, 34 SER20, 35 ASP21. The bottom status bar shows '2ZFF' and 'No Molecule Selected'.

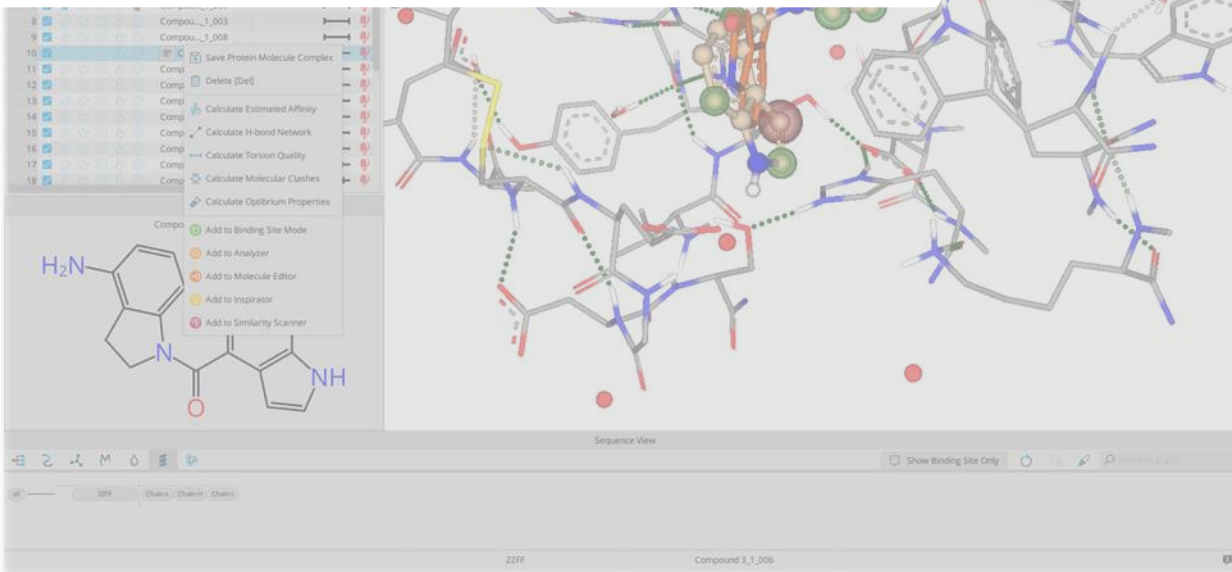
The screenshot displays a software interface for molecular modeling. On the left, a vertical panel is divided into two sections: the top section is a 2D workspace with a dashed border and a text prompt "Paste molecule from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar.", and the bottom section shows a 2D skeletal structure of a benzene ring. On the right, a 3D ball-and-stick model of the same benzene ring is shown. A green callout box is positioned to the right of the 3D model, containing text about editing molecules in 2D and 3D. At the top, a toolbar contains various icons, with a red box highlighting a subset of them. At the bottom, a "Sequence View" panel shows a single residue labeled "2ZF" and a status bar at the very bottom indicates "2ZF" and "No Molecule Selected".

You can modify your molecule in the 2D and 3D window.
In 2D you can add rings and change the bond type.
In 3D it is also possible to select the hydrogen atoms and replace them with 'Change element' icon. You can also use hot keys for elements, e.g. use 'C' to change an atom to a carbon or 'N' to change it to a nitrogen.

The screenshot displays a software interface for molecular modeling. On the left, a 'Data' panel contains a 2D chemical structure of tryptophan, labeled '2D'. The structure is a benzene ring fused to an indole ring, with an amino group (-NH₂) attached to the benzene ring. Below the 2D structure is a 'Sequence View' panel showing the residue '22FF' and its chain information. On the right, a 3D ball-and-stick model of the tryptophan molecule is shown, with carbon atoms in orange, nitrogen in blue, and hydrogen in white. A green callout box with white text is positioned above the 3D model, stating: 'Once you are finished, export the molecule to the table with 'Save edited molecules to table''. The top toolbar of the software includes a red-bordered icon with a green plus sign, which is highlighted.



3. Docking



The screenshot displays a software interface for molecular docking. A red square highlights a circular icon in the top toolbar. On the left, a 'Docking Library (# 3)' table lists three compounds with columns for Name and Estimated Affinity (pM, nM, uM, mM). Below it is a 'Generated Poses (# 0)' section. The main area shows a 3D molecular model of a protein with several small molecules docked. At the bottom, a 'Sequence View' shows the protein chain '2ZFF'.

Docking Library (# 3)	
Name	Estimated Affinity
	pM nM uM mM
1 Compound 1	
2 Compound 2	
3 Compound 3	

Generated Poses (# 0)		
Name	Estimated Affinity	LLS
	pM nM uM mM	

Sequence View

2ZFF Chain-L Chain-H Chain-I

2ZFF No Molecule Selected

The **Docking mode** is used to place (= dock) molecules at the targets binding site.

You need ligands to dock them. See Section 2 (Adding Molecules) on how to add molecules to the docking library.

Note: ALL molecules in the 'Docking library' will be docked if they are added.

The screenshot shows a molecular docking software interface. At the top, a toolbar contains several icons, with a green 'S' icon highlighted by a red box. Below the toolbar, the interface is divided into several panels. On the left, there is a 'Docking Library (# 3)' panel with a table of compounds and their estimated affinities. Below that is a 'Generated Poses (# 0)' panel. The main central area displays a 3D molecular model of a protein with a ligand docked. At the bottom, there is a 'Sequence View' panel showing the protein sequence for chain 2ZFF.

	Name	Estimated Affinity			
		pM	nM	µM	mM
1	Compound 1				
2	Compound 2				
3	Compound 3				

	Name	Estimated Affinity				LLE
		pM	nM	µM	mM	
Generated Poses (# 0)						

To start your docking, press the 'Standard docking: Generate poses' button.

At most 10 poses per molecule are generate this way, as we have left the docking settings on default.

The next slide will explain how to adjust docking parameters to refine your docking results.

The screenshot shows the SeeSAR docking software interface. A red box highlights the settings panel on the left, which includes three sliders: 'Maximum Number of Poses' (set to 10), 'Clash Tolerance' (set to Standard), and 'Allowed Ring Conformations' (set to Standard). A callout box on the right explains these settings. The main window shows a 3D molecular model of a protein-ligand complex.

Maximum Number of Poses
10

Clash Tolerance
Standard Medium High

Allowed Ring Conformations

Generated Poses (# 0)

Sequence View

Show Binding Site Only

Name (e.g. gly)

all 22FF Chain-L Chain-H Chain-I

22FF No Molecule Selected

'Maximum Number of Poses' defines the highest possible number of poses that will be generated for each molecule. SeeSAR generates 10 poses per default.

'Clash Tolerance' defines how SeeSAR handles clashes between ligand and target during docking. For tight binding sites increase of the tolerance to 'Medium' or 'High' may improve the results.

'Allow Ring Conformations' can be used to allow energetically unfavorable ring conformations (twist, boat).

The 'Generated Poses' table will be populated with generated poses of the ligands from 'Docking Library'.

To assess the affinity of the generated poses check all poses with the 'Checked' column and 'Check all'.

Docking Library (# 3)	
Name	Estimated Affinity
	pM nM μ M mM
1	Compound 1
2	Compound 2
3	Compound 3

Generated Poses (# 30)		
Name	Estimated Affinity	LLE
	pM nM μ M mM	
1	Compou..._1_001	<input type="checkbox"/>
2	Compou..._1_002	<input type="checkbox"/>
3	Compou..._1_003	<input type="checkbox"/>
4	Compou..._1_004	<input type="checkbox"/>
5	Compou..._1_005	<input type="checkbox"/>
6	Compou..._1_006	<input type="checkbox"/>
7	Compou..._1_007	<input type="checkbox"/>
8	Compou..._1_008	<input type="checkbox"/>
9	Compou..._1_009	<input type="checkbox"/>
10	Compou..._1_010	<input type="checkbox"/>
11	Compou..._1_001	<input type="checkbox"/>
12	Compou..._1_002	<input type="checkbox"/>
13	Compou..._1_003	<input type="checkbox"/>
14	Compou..._1_004	<input type="checkbox"/>
15	Compou..._1_005	<input type="checkbox"/>
16	Compou..._1_006	<input type="checkbox"/>
17	Compou..._1_007	<input type="checkbox"/>
18	Compou..._1_008	<input type="checkbox"/>

The screenshot displays the HYDE software interface. On the left, a sidebar menu is visible with 'Estimated Affinity' highlighted in a red box. Below this, a table lists 'Generated Poses (# 30)' with columns for Name, Estimated Affinity (pM, nM, μM, mM), and LLE. The table contains 22 rows of data, each representing a different compound pose. The main window shows a 3D molecular model of a protein-ligand complex, with the protein backbone in grey and the ligand in blue and red. The bottom of the interface shows the 'Sequence View' section with the protein name '2ZFF' and a 'Show Binding Site Only' button.

	Name	Estimated Affinity				LLE
		pM	nM	μM	mM	
5	Compou..._1_005					
6	Compou..._1_006					
7	Compou..._1_007					
8	Compou..._1_008					
9	Compou..._1_009					
10	Compou..._1_010					
11	Compou..._1_001					
12	Compou..._1_002					
13	Compou..._1_003					
14	Compou..._1_004					
15	Compou..._1_005					
16	Compou..._1_006					
17	Compou..._1_007					
18	Compou..._1_008					
19	Compou..._1_009					
20	Compou..._1_010					
21	Compou..._1_001					
22	Compou..._1_002					

Then go to 'Calculations for checked molecules' and select 'Estimated Affinity'.

Note:
You may restrict the HYDE-calculation to a pre-selected set of checked molecules.

The screenshot displays a molecular docking software interface. At the top, a 'Data' panel shows a 'Docking Library (# 3)' with three compounds. Below it, a 'Generated Poses (# 30)' panel is highlighted with a red box, showing a table of 30 generated poses. The table has columns for 'Name' and 'Estimated Affinity' (pM, nM, μM, mM). The 'Estimated Affinity' column headers are highlighted in red. Below the table, the chemical structure of 'Compound 1_1_003' is shown. The main 3D view displays a protein structure with a ligand bound in the binding site, and a 'Sequence View' panel at the bottom.

Name	Estimated Affinity			
	pM	nM	μM	mM
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
15				
16				
17				
18				

Chemical structure of Compound 1_1_003: C1CCCN1C(=O)c2ccc3c(c2)c[nH]3

Now the estimated affinities appear as a range on the **logarithmic scale**.

Clicking on a column header sorts according to this value.

The screenshot displays a molecular docking software interface. The central 3D view shows a grey protein structure with a red and white ligand docked in its binding site. The interface includes several panels:

- Dock Library (# 3):** A table listing three compounds with their estimated affinities in pM, nM, μM, and mM. A red box highlights the 'Dock' icon in the top-left corner.
- Generated Poses (# 30) (Checked (# 30)):** A table listing 30 generated poses for Compound 3. Two poses are highlighted with red boxes. A context menu is open over the second pose, listing analysis options: Calculate Estimated Affinity, Calculate H-bond Network, Calculate Torsion Quality, Calculate Molecular Clashes, and Calculate Optimum Properties.
- Bottom Panel:** A 'Sequence View' section with a 'Show Binding Site Only' checkbox and a search bar. Below it, a chemical structure of a protein residue is shown with labels for H₂N and NH groups.

To inspect multiple poses in comparison, toggle the permanent visibility by marking a molecule as reference. Now stay visible as you select other molecules. You can even color each molecule to differentiate them.

You can calculate more pose assessment parameters with a right click on a molecule, or using the method describe in the previous slides to calculate them for all checked molecules.

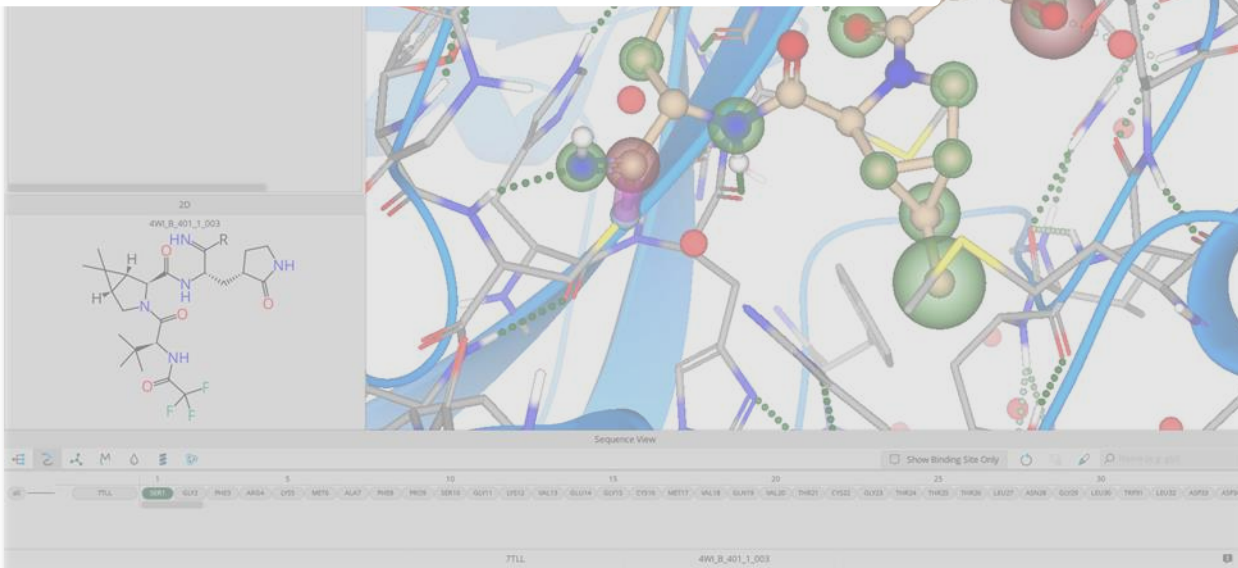
The image shows a screenshot of a molecular docking software interface. A red box highlights a toolbar with several icons. Callouts in green boxes explain the functions of these icons:

- 3D visibility:** Points to the 3D view icon (a blue cube).
- Add anotation:** Points to the speech bubble icon.
- Molecule color:** Points to the palette icon.
- Mark as favorite:** Points to the star icon.
- Mark as active/inactive:** Points to the flame icon.

A separate callout box in the upper right states: "You can add notes and descriptors in the molecule table window." The interface includes a "Docking Library (# 3)" table with columns for "Name" and "Estimated Affinity" (pM, nM, μM, mM). A 2D chemical structure of a molecule is visible at the bottom left.



4. Covalent Docking



7TLL

Data

7TLL - Extract Your Ligand

Hetero Groups

LOI	Name	Estimated Affinity
		μM nM μM mM
1	Do not extract a ligand	
2	4WL_A_401	
3	4WL_B_401	

Covalently bound

2D

Sequence View

Show Binding Site Only

Name (e.g. gly)

1 5 10 15 20 25 30

7TLL SER1 GLY2 PHE3 ARG4 LYS5 MET6 ALA7 PHE8 PRO9 SER10 GLU11 LYS12 VAL13 GLU14 GLY15 CYS16 MET17 VAL18 GLN19 VAL20 THR21 CYS22 GLY23 THR24 THR25 THR26 LEU27 ASN28 GLY29 LEU30 TRP31 LEU32 ASP33 ASP34

7TLL 4WL_B_401

You can perform covalent docking at any PDB protein structure. PDB files that contain a covalent ligand provide this information upon loading within the info icon.

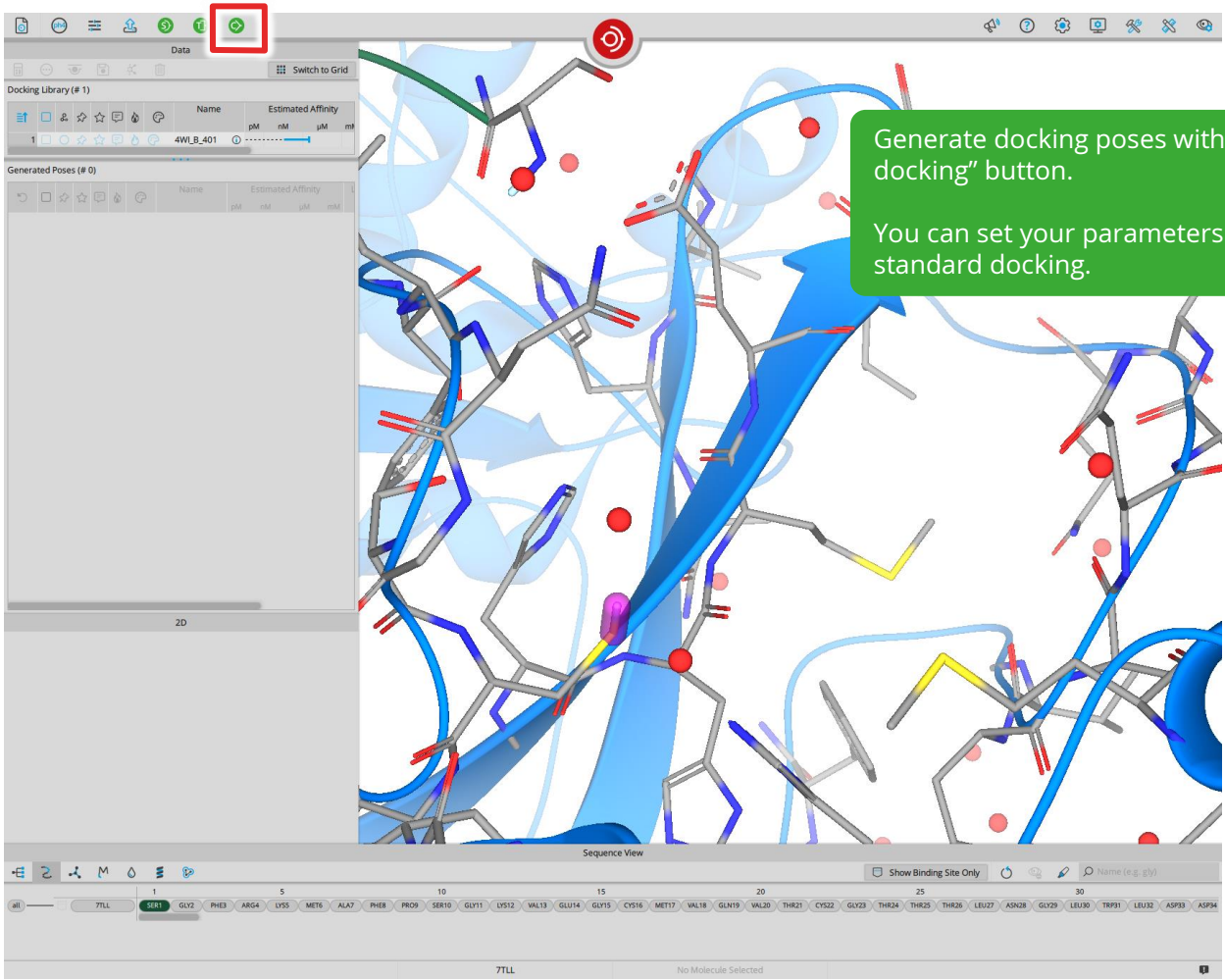
For this example, we will use the PDB 7TLL.

The linking point is represented as R in the 2D structure.

The screenshot displays a molecular docking software interface. The main window shows a protein structure in blue ribbon representation with a ligand molecule (4WI_B_401) docked in the binding site. The ligand is shown in stick representation with green and red spheres. A green callout box with a white arrow points to the ligand and contains the text: "After defining your ligand transfer it to the Docking Mode."

The interface includes several panels:

- Data Panel:** Shows the protein name "7TLL".
- Proteins Panel:** Lists the protein "7TLL".
- Ligand for 7TLL Panel:** Contains a table with columns for Name, Estimated Affinity (pM, nM, μM, mM), and a list of actions. The "Add to Docking Mode" action is highlighted with a red box.
- 2D Panel:** Shows the chemical structure of the ligand 4WI_B_401.
- Sequence View Panel:** Shows the protein sequence with residues 1 to 30 visible, including SER1, GLY2, PHE3, ARG4, LYS5, MET6, ALA7, PHE8, PRO9, SER10, GLU11, LYS12, VAL13, GLU14, GLY15, CYS16, MET17, VAL18, GLN19, VAL20, THR21, CYS22, GLY23, THR24, THR25, THR26, LEU27, ASN28, GLY29, LEU30, TRP31, LEU32, ASP33, and ASP34.



Generate docking poses with the “Covalent docking” button.
You can set your parameters the same as for standard docking.

The screenshot displays a molecular docking software interface. The main view is a 3D representation of a protein (blue ribbon) with a ligand (grey sticks) docked in its binding site. The protein is shown in a semi-transparent blue surface. The ligand is shown in grey sticks with red, blue, and green spheres representing oxygen, nitrogen, and carbon atoms, respectively. A red box highlights a specific atom in the ligand, which is also highlighted in the 2D chemical structure view below. The 2D structure shows a complex molecule with a central nitrogen atom and various side chains, including a fluorinated group. The interface includes a 'Data' panel at the top left, a 'Docking Library (# 1)' panel, and a 'Generated Poses (# 10)' table. The table lists 10 generated poses with their names and estimated affinities in pM, nM, μM, and mM. The 'Generated Poses' table is highlighted with a red border. The 'Sequence View' at the bottom shows the protein sequence from residue 1 to 30, with the binding site residues highlighted in grey. The sequence is: 1 SER1, 2 GLY2, 3 PHE3, 4 ARG4, 5 LYS5, 6 MET6, 7 ALA7, 8 PHE8, 9 PRO9, 10 SER10, 11 GLU11, 12 LYS12, 13 VAL13, 14 GLU14, 15 GLY15, 16 CYS16, 17 MET17, 18 VAL18, 19 GLN19, 20 VAL20, 21 THR21, 22 CYS22, 23 GLY23, 24 THR24, 25 THR25, 26 THR26, 27 LEU27, 28 ASN28, 29 GLY29, 30 LEU30, TRP31, LEU32, ASP33, ASP34.

Generated Poses (# 10)		
	Name	Estimated Affinity
		pM nM μM mM
1	4WL_001	0
2	4WL_002	0
3	4WL_003	0
4	4WL_004	0
5	4WL_005	0
6	4WL_006	0
7	4WL_007	0
8	4WL_008	0
9	4WL_009	0
10	4WL_010	0

2D
4WL_B_401_1_003

Sequence View
Show Binding Site Only
Name (e.g. gly)

7TL 7TL 4WL_B_401_1_003

Your results will be displayed in the "Generated Poses" table.

If you have selected several residues as potential targets you can switch between them by clicking on the anchor point.

If no covalent linking point of the structure is defined, you can introduce it in the **Protein Editor Mode**.

Select the atom of the target residue (e.g. cys, lys, ser) which will be replaced with the ligand.

The interface includes a top toolbar with a circular icon highlighted in red. A data panel on the left shows the filename '7TLL' and description 'STRUCTURE OF SARS-COV-2 MPR...'. A 2D chemical structure of a thiol group is shown in the bottom left. The bottom sequence viewer shows residues from MET6 to CYS38, with MET17 highlighted in green.

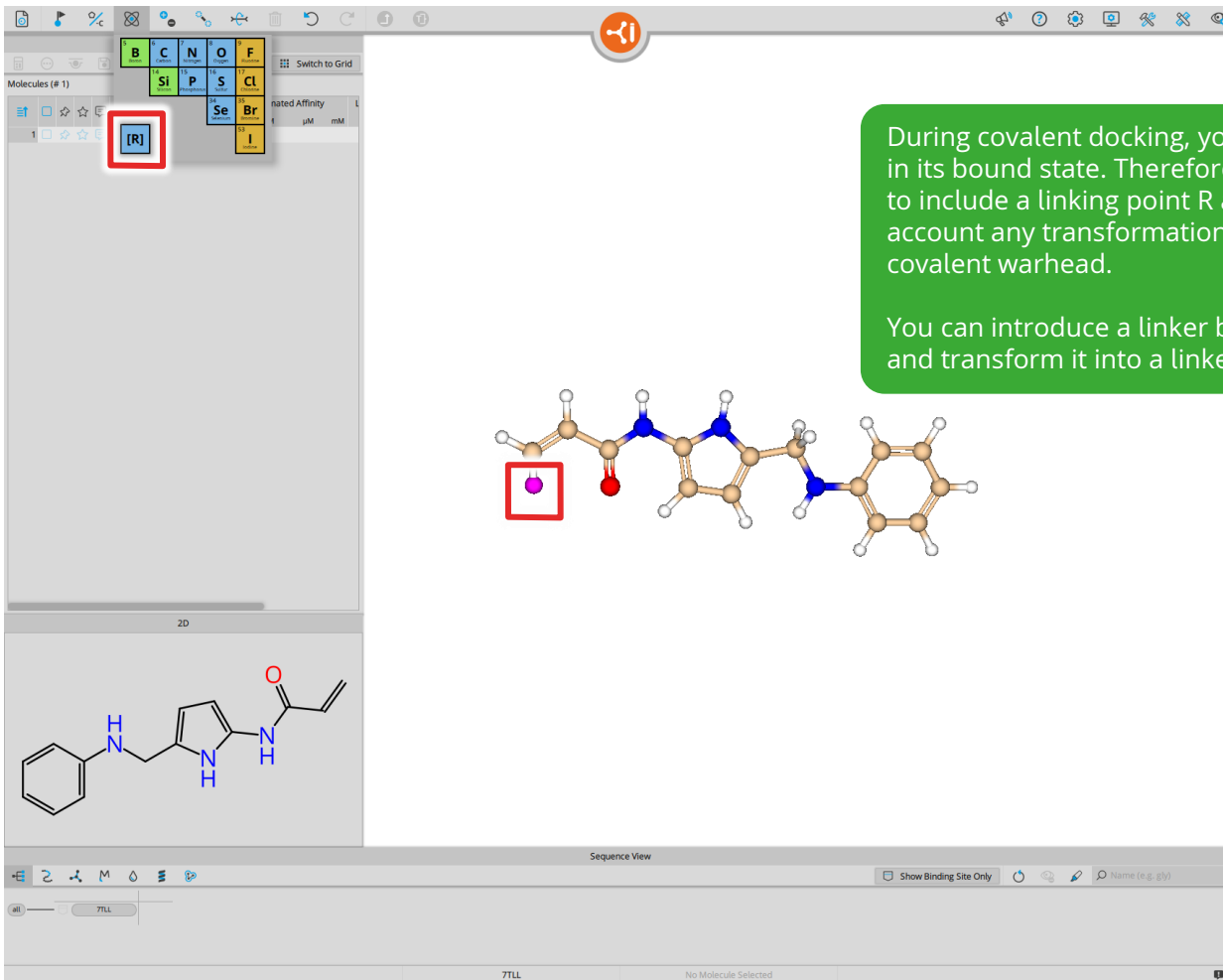
The screenshot displays a molecular docking software interface. At the top, a toolbar contains various icons, with a green box highlighting the 'Change element' icon (a green 'E' in a square). Below the toolbar is a periodic table of elements, with a red box highlighting the element '[R]' (representing a generic atom). The main 3D view shows a protein structure in green ribbon representation with a yellow and blue ball-and-stick model of a linker atom positioned near a binding site. A 2D chemical editor at the bottom left shows a chemical structure with a carbonyl group (C=O), an amine group (NH), and a sulfur atom (S), with 'R' groups indicating attachment points. The sequence view at the bottom shows a protein sequence with residue 16 highlighted in green, labeled 'New'. The interface also includes a 'Data' panel, a 'Filename' field, and a 'Sequence View' panel.

Use the "Change element" icon and select "[R]" or use "R" on your keyboard to introduce a linker in that position.

Export the modified protein back to the Protein Mode. Be sure, that your target residue is part of the binding site.

Note:
The position of the linker atom is important for the outcome of the docking. Please check the elaborated and comprehensive Covalent Docking Guide on our website for more details:

[Covalent Docking Guide](#)



During covalent docking, your ligand is docked in its bound state. Therefore, your structure has to include a linking point R and take into account any transformations that occur at the covalent warhead.

You can introduce a linker by selecting an atom and transform it into a linker.

The screenshot shows a software interface for molecular docking. On the left, a 'Data' table lists molecules. The main area displays a 3D ball-and-stick model of a ligand. Below it, a 2D chemical structure is shown, with a red box highlighting an acrylamide group (CH₂=CH-C(=O)-R). The interface includes a top toolbar, a 'Sequence View' at the bottom, and a status bar at the very bottom.

Molecules (# 2)		Name	Estimated Affinity			
			pM	nM	μM	mM
1		Create...cufe_1				
2		Create...cufe_2				

Sequence View

Show Binding Site Only

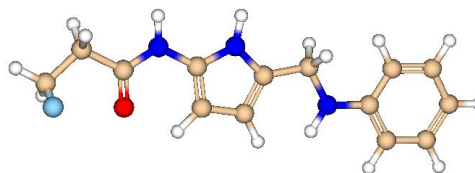
Name (e.g. gly)

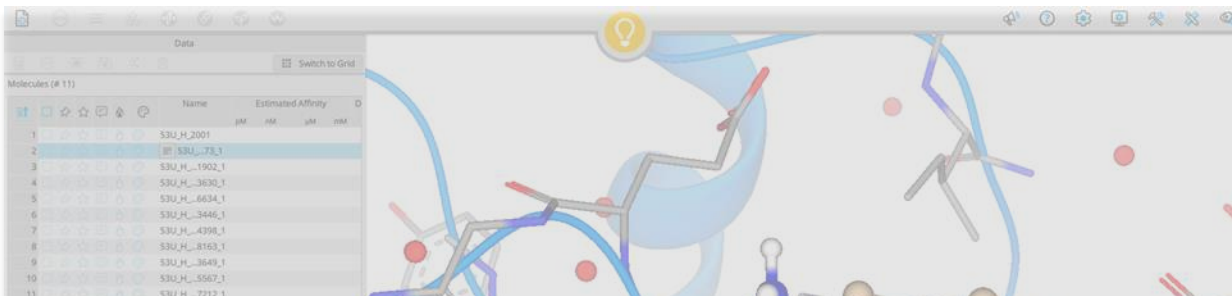
7LL

No Molecule Selected

You can introduce a linker atom to your SMILES string with [R*].

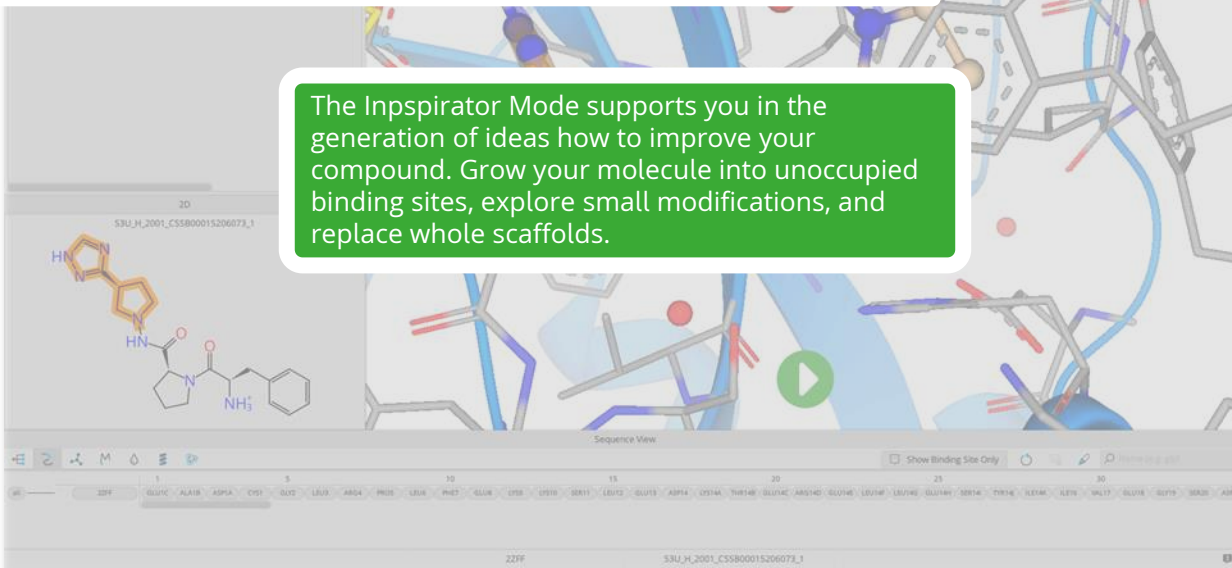
In this example we have transformed an acrylamide warhead to its bound form to prepare the ligand for covalent docking.





5. Inspirator

The Inspirator Mode supports you in the generation of ideas how to improve your compound. Grow your molecule into unoccupied binding sites, explore small modifications, and replace whole scaffolds.



2ZFF

ata

2ZFF - Extract Your Ligand

Hetero Groups

	LOI	Name	Estimated Affinity			
			pM	nM	µM	mM
1		Do not extract a ligand				
2		53U_H_2001				

2D

53U_H_2001

Sequence View

Show Binding Site Only

Name (e.g. gly)

1 5 10 15 20 25 30

2ZFF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14 THR14 ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

2ZFF 53U_H_2001



For this guide we will use PDB 2ZFF as example.
Load it in the **Protein Mode** and select a ligand to work with.



The screenshot displays a molecular docking software interface. On the left, a sidebar contains several panels: 'Data' at the top, 'Proteins' with a table listing '1' and 'Z2FF', 'Ligand for Z2FF' with a table listing '53U_H_201' and a context menu where 'Add to Inspirator' is highlighted with a red box, and a '2D' panel showing the chemical structure of '53U_H_2001'. The main workspace shows a 3D ribbon representation of a protein in blue with a grey ball-and-stick model of a ligand docked in its binding site. A green callout box in the upper right corner contains the text 'Transfer your ligand to the Inspirator Mode.' At the bottom, a 'Sequence View' panel shows the amino acid sequence of the protein, with 'Z2FF' and '53U_H_2001' highlighted.

Protein	Filename
1	Z2FF

Name	Estimated Affinity
	pM nM μ M mM
53U_H_201	

2D
53U_H_2001

Sequence View

Show Binding Site Only

Name (e.g. gly)

1	5	10	15	20	25	30
GLU1C	ALA1B	ASP1A	CYS1	GLY2	LEU3	ARG4
PRO5	LEU6	PHE7	GLU8	LYS9	LYS10	SER11
LEU12	GLU13	ASP14	LYS14A	THR14B	GLU14C	ARG14D
GLU14E	LEU14F	LEU14G	GLU14H	SER14I	TYR14J	ILE14K
ILE16	VAL17	GLU18	GLY19	SER20	ASP21	

Z2FF 53U_H_2001

Transfer your ligand to the Inspirator Mode.

The Inspirator Mode features several tools and applications to generate ideas how to improve your compound or to find novel scaffolds.

Linking&Merging:
Connects two fragments

MedChemesis:
Creates a series of analogs

ReCore:
Replaces scaffolds

FastGrow:
Grows into binding pockets

Name	Estimated Affinity			
	pM	nM	μM	mM
1				

Sequence View

Show Binding Site Only

Name (e.g. gly)

1 5 10 15 20 25 30

22FF GLU1C ALA18 ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

22FF No Molecule Selected

Nc1ccc(cc1)CNC(=O)[C@@H]2CCCN2C(=O)[C@H](c3ccccc3)N

The screenshot shows the SeeSAR software interface. On the left, there is a 'Molecules (# 1)' table with one entry: 'S3U_H_2001'. Below this is a 2D chemical structure of a molecule. The main window displays a 3D protein structure with a ligand. A 'System' menu is open in the center, with 'Inspirator' highlighted by a red box. Other options in the menu include Calculation, StarDrop, RCSB PDB, Proxy, License, Systemlog, and Readme. At the bottom, there is a 'Sequence View' showing a protein sequence with residues 1 through 30 listed.

Name	Estimated Affinity			
	pM	nM	µM	nM
S3U_H_2001				

2D
S3U_H_2001

Sequence View

1 5 10 15 20 25 30
22FF GLU1C ALA1B ASP1A CYS1 GLU2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I THR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

ReCore:

This tool screens millions of molecular fragments to find replacements for a 3D scaffold. To use the tool, you need to download and add a ReCore index (= fragment library) to SeeSAR.

ReCore indices can be accessed and downloaded directly from SeeSAR or from our website:

Download more libraries

Got to "System" and select "Inspirator".

System

Core indices and fragment growing files for inspirator mode.

ReCore Indices

- magicrings3D_2022-05
- Inspirator_CSD_2022-05
- recore
- PDB-ReCore-L_90218-seesar

Fragment Growing Files

- FastGrowDB_...20k_2023-03

A valid ReCore index is selected.

Apply

2D

S3U_H_2001

Sequence View

Show Binding Site Only

Name (e.g. 6S)

22FF

1 5 10 15 20 25 30

GLUTC ALA18 ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G LEU14H SER14 THR14 ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

22FF No Molecule Selected

Here you can download and add ReCore indices to SeeSAR. Once you are done adding your indices, confirm everything with "Apply". Then you can close the window.

Click on bonds to set constraints (= exchange vectors) at your molecule. You can do this in 2D or 3D.

Subsequent click on the same bond changes the direction of the vector (= what part should remain and what part is to be replaced). A third click removes the vector.

With at least two cutting points ReCore becomes available. Push the "Core replacement" button to generate results. Your active ReCore index will be used for this. If you want to use another one, go back to "System" → "Inspirator" to change the index.

Saturated part of the molecule will remain

Grey-out part of the molecule will be replaced

Sequence View

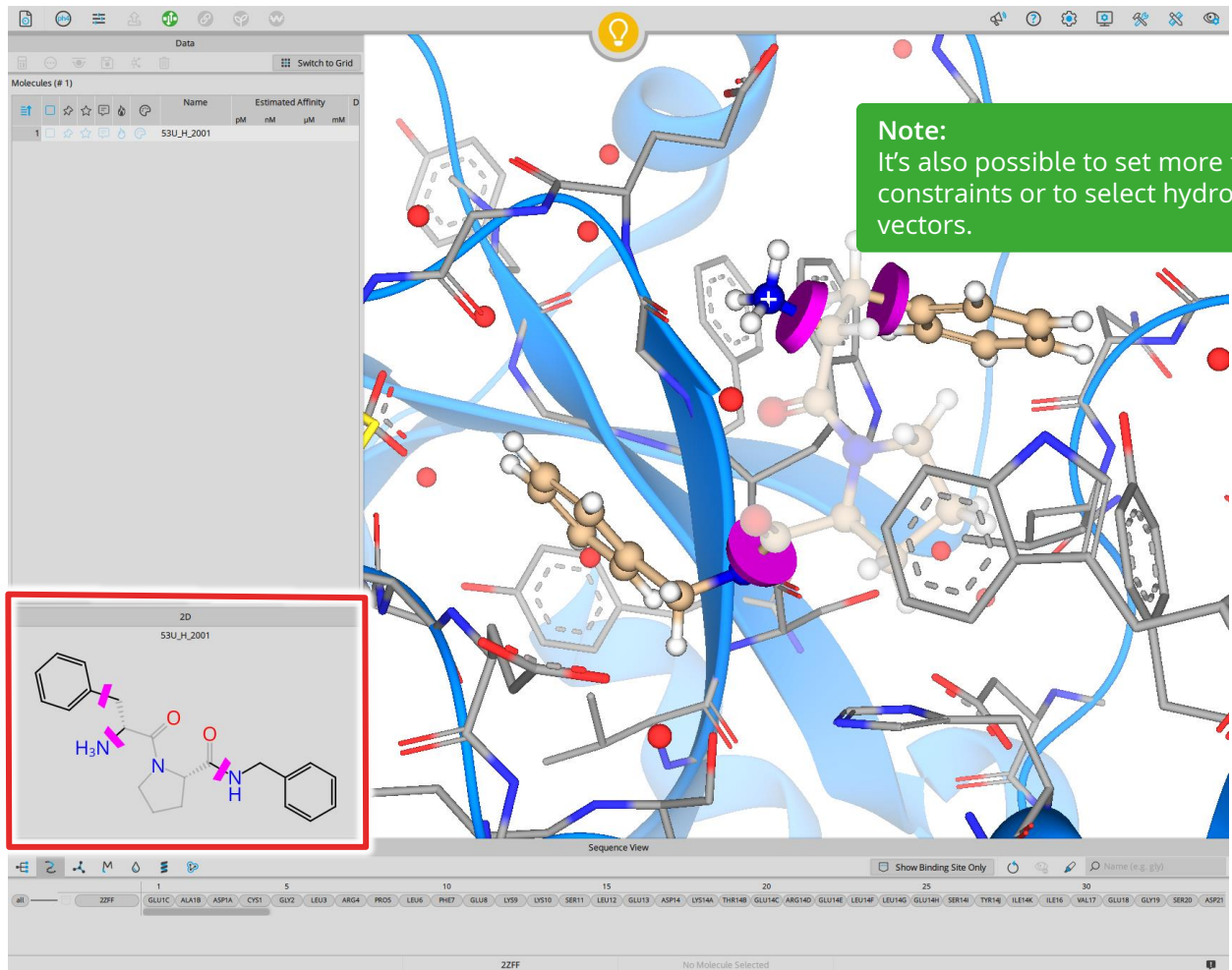
Show Binding Site Only

Name (e.g. gly)

10 15 20 25 30

G4 PROS LEUE PHE7 GLUR LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

2ZF No Molecule Selected



FastGrow:
 To grow into a binding site, select a bond in 2D or 3D to select which part of the molecule should be kept. Only one selection is required to perform growing.

Once you made a selection, the "Growing" button will become active. Push it to generate results.

Saturated part of the molecule will remain

Grey-out part of the molecule will be replaced

2ZFF

1 20 25 30
 GLU1C ALA1B ASP1A CYS1 ASP14 LYS14A THR14B GLU14C ARG14D LEU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

No Molecule Selected

The screenshot displays a molecular docking software interface. On the left, a 'Molecules (# 11)' table lists 11 molecules with their names and estimated affinities. The second molecule, 'S3U_H_73_1', is highlighted in blue. Below the table, a 2D chemical structure of the selected molecule is shown, featuring a benzimidazole ring system connected to a cyclopentane ring and a primary amine group. The main 3D view shows the molecule docked into a protein's binding site, with the protein backbone in light blue and the molecule in a stick representation. A green play button is visible in the 3D view. At the bottom, a 'Sequence View' shows the protein sequence: 22FF, 1 GLU1C, 4 ALA18, 5 ASP1A, 6 CYS1, 7 GLY2, 8 LEU3, 9 ARG4, 10 PRO5, 11 LEU6, 12 PHE7, 13 GLU8, 14 LYS9, 15 LYS10, 16 SER11, 17 LEU12, 18 GLU13, 19 ASP14, 20 LYS14A, 21 THR14B, 22 GLU14C, 23 ARG14D, 24 GLU14E, 25 LEU14F, 26 LEU14G, 27 GLU14H, 28 SER14, 29 THR14, 30 ILE14K, 31 ILE16, 32 VAL17, 33 GLU18, 34 GLY19, 35 SER20, 36 ASP21.

Name	Estimated Affinity			
	pM	nM	µM	mM
1 S3U_H_2001				
2 S3U_H_73_1				
3 S3U_H_1902_1				
4 S3U_H_3630_1				
5 S3U_H_6634_1				
6 S3U_H_3446_1				
7 S3U_H_4398_1				
8 S3U_H_8163_1				
9 S3U_H_3649_1				
10 S3U_H_5567_1				
11 S3U_H_7212_1				

2D
S3U_H_2001_CSSB00015206073_1

Sequence View
Show Binding Site Only

Results will be added to the molecule table. The grown part is highlighted, and the respective name of the used fragment is added to the molecule name.

Note:
It is also possible to grow from a hydrogen in 3D.

Data

	Name	Estimated Affinity			
		pM	nM	µM	mM
1	S3U_H_2001				
2	S3U_H_73_1				
3	S3U_H_1902_1				
4	S3U_H_3630_1				
5	S3U_H_6634_1				
6	S3U_H_3446_1				
7	S3U_H_4398_1				
8	S3U_H_8163_1				
9	S3U_H_3649_1				
10	S3U_H_5567_1				
11	S3U_H_7212_1				

2D

S3U_H_2001_CSSB00015206073_1

NC(=O)C1CCCN1C(=O)C2=CC=CC=C2

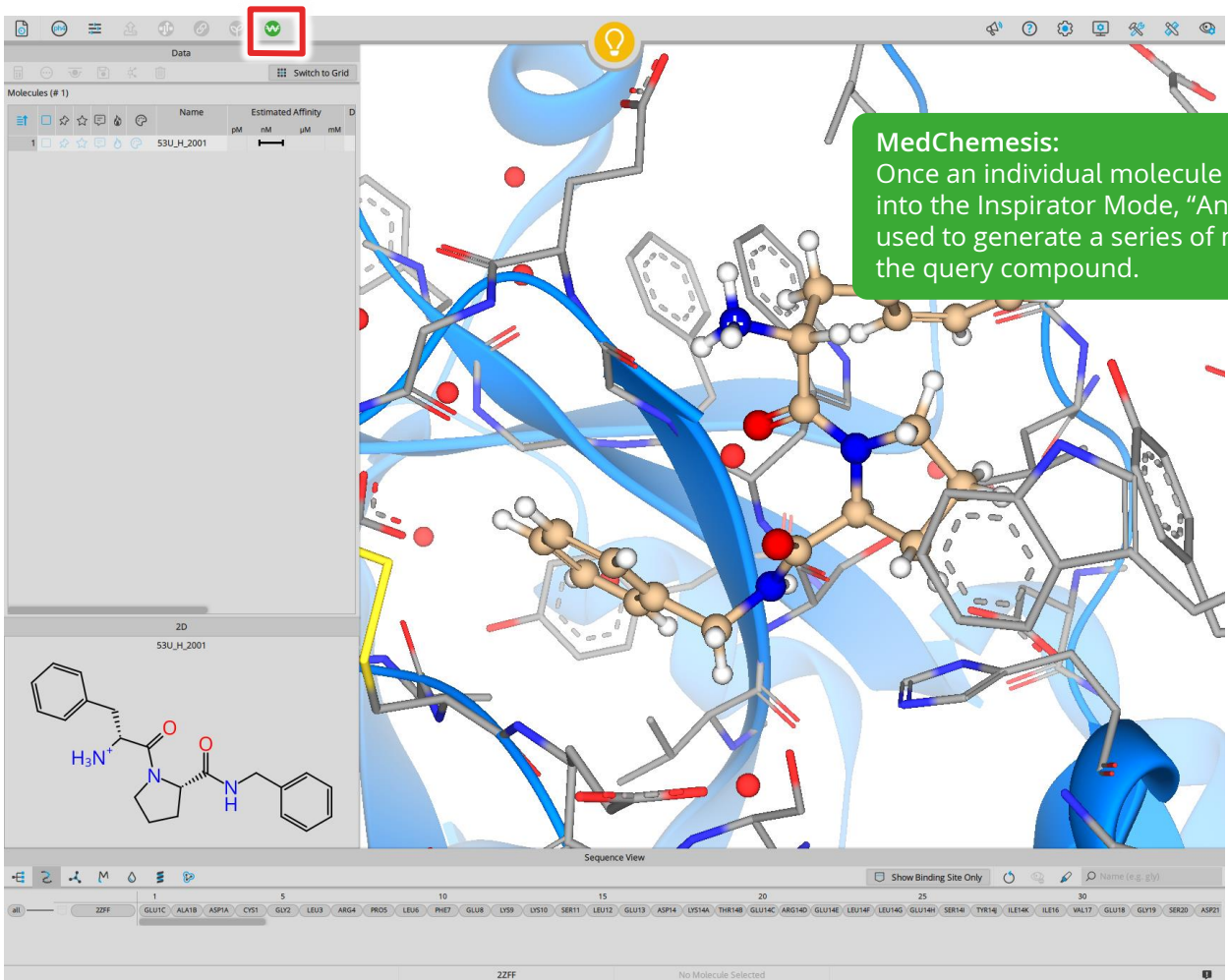
Sequence View

Show Binding Site Only

22FF S3U_H_2001_CSSB00015206073_1

SeeSAR comes with a growing library featuring over 12 thousand fragments. A larger library featuring over 120 thousand fragments can be downloaded for free from our website:

[Download more libraries](#)



The screenshot displays a molecular docking software interface. On the left, a table lists 11 molecules with their names and estimated affinities in pM, nM, and μM. The main window shows a 3D model of a protein (blue ribbon) with a ligand (grey sticks) docked in its binding site. A 2D chemical structure of the ligand is shown at the bottom left, with a red box highlighting a specific group. A green callout box explains that results will be added to the molecule table and the transformed part of the molecule will be highlighted.

Molecules (# 11)	Checked (# 11)	Name	Estimated Affinity
			pM nM μM
1	<input checked="" type="checkbox"/>	S3U_H_2001	
2	<input checked="" type="checkbox"/>	S3U_H_1,2	
3	<input checked="" type="checkbox"/>	S3U_H_2,2,2	
4	<input checked="" type="checkbox"/>	S3U_H_3,3,2	
5	<input checked="" type="checkbox"/>	S3U_H_~xy,4,2	
6	<input checked="" type="checkbox"/>	S3U_H_~do,5,2	
7	<input checked="" type="checkbox"/>	S3U_H_~xy,6,2	
8	<input checked="" type="checkbox"/>	S3U_H_~N,7,2	
9	<input checked="" type="checkbox"/>	S3U_H_~2,8,2	
10	<input checked="" type="checkbox"/>	S3U_H_~do,9,2	
11	<input checked="" type="checkbox"/>	S3U_H_~2,10,2	

2D
S3U_H_2001_add_nitrogen_1,2

Sequence View

Show Binding Site Only

Name (e.g. gly)

22FF S3U_H_2001_add_nitrogen_1,2

Results will be added to the molecule table. The transformed part of the molecule will be highlighted and the applied medicinal chemistry transformation is added to the molecule name.

H₂N

The image shows a screenshot of a molecular docking software interface. On the left, a sidebar titled 'Data' contains a 'Molecules' list with several options. The option 'Add molecules to Inspirator' is highlighted with a red box. Below this, a 2D chemical structure window displays two molecules: one with a carboxylic acid group and an ammonium group, and another with a primary amine group. The main window shows a 3D representation of a protein binding site with a ligand. The protein is shown as a blue ribbon structure, and the ligand is shown as a stick model with orange, white, and red atoms. A sequence view at the bottom shows the amino acid sequence: 1 5 10 15 20 25 30
22FF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14I TYR14J ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21
22FF No Molecule Selected

Linking & Merging:
If you want to connect two different fragments/molecules you need to load both of them to the Inspirator Mode simultaneously.

To do so check both molecules and select "Add molecules to Inspirator".

The screenshot displays a molecular docking software interface. The main window shows a 3D representation of a protein (blue ribbon) with a ligand (orange and white ball-and-stick model) docked in its binding site. The interface includes a top toolbar with a green 'Linking & Merging' button highlighted by a red box. On the left, a 'Molecules (# 2)' table lists two molecules:

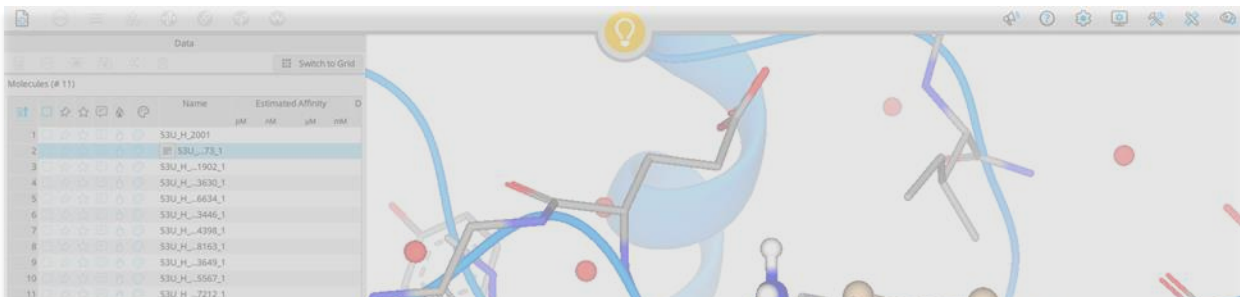
	Name	Estimated Affinity		
		pM	nM	µM
1	S3U_H_2001_1			
2	S3U_H_2001_2			

Below the table is a 2D chemical structure editor. Two chemical structures are shown, each with a red box around a specific atom: a carbonyl oxygen (C=O) and a nitrogen atom (H₃N). The bottom of the interface shows a 'Sequence View' with a protein sequence: 1 5 10 15 20 25 30
22FF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G GLU14H SER14 THR14 ILE14K ILE16 VAL17 GLU18 GLY19 SER20 ASP21

Set the vectors to connect both molecules. You can also replace undesired parts in the process leading to a fragment merging.

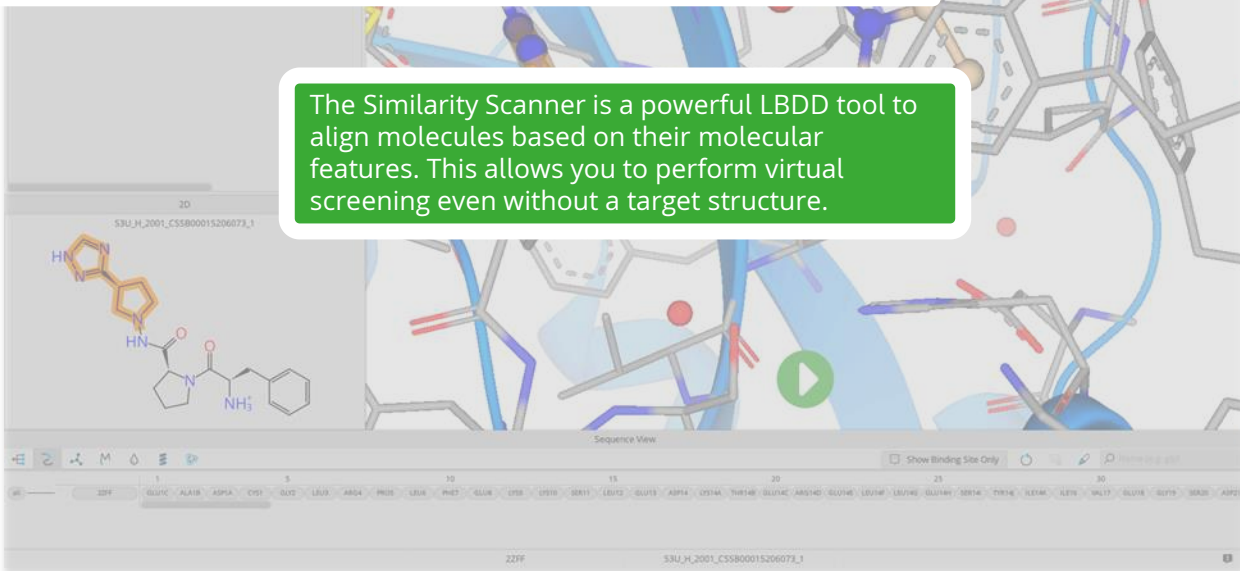
Once at least two vectors were set, the "Linking&Merging" button will become active. Press it to generate results.

Note: Linking&Merging applies the current active ReCore index. You can change the used fragment set in "System" → "Inspirator".



6. Similarity Scanner

The Similarity Scanner is a powerful LBDD tool to align molecules based on their molecular features. This allows you to perform virtual screening even without a target structure.



The Similarity Scanner can be used for ligand-based drug discovery. You can add molecules as SMILES by copy-and-paste those with [Ctrl + V] or load those via the toolbar.

For this example, we will work with two compounds:

```
O=C1Nc2ccc(Cl)cc2[C@@](C#CC2CC2)(C(F)(F)F)O1 Efavirenz
Cc1cc(C#N)cc(C)c1Oc1nc(Nc2ccc(C#N)cc2)nc(N)c1Br Etravirine
```

Data	
Switch to Grid	
Molecules (# 2)	
Name	Tor. Intra-class
1 Efavirenz	
2 Etravirine	

Generated Poses (# 0)

2D
Efavirenz

Sequence View
Show Binding Site Only

No Protein Selected Efavirenz

The screenshot displays a molecular docking software interface. On the left, the 'Molecules (# 2)' panel lists 'Efavirenz' and 'Etravirine', with a play button icon highlighted by a red box. Below this, the 'Generated Poses (# 0)' panel is empty. At the bottom left, a 2D chemical structure of Efavirenz is shown. On the right, a 3D ball-and-stick model of the ligand is displayed. Two green callout boxes provide instructions: the top one says 'Select a ligand (in this case Efavirenz) as a template in the molecule window. Generate alignment poses with the play button.' and the bottom one says 'You can add pharmacophore constraints and adjust the screening parameters as well.' The interface includes a top toolbar with a play button, a central search icon, and a bottom toolbar with a 'Show Binding Site Only' button. The status bar at the bottom indicates 'No Protein Selected' and 'Efavirenz'.

The screenshot displays a molecular docking software interface. At the top, a toolbar contains various icons for file operations and settings. Below the toolbar, the 'Data' panel shows a list of molecules:

	Name	Tor.	Intra-clash
1	Efavirenz		
2	Etravirine		

The 'Generated Poses (# 1)' panel, highlighted with a red border, shows a table of generated poses:

	Name	Similarity Rating	Tor.	Intra-clash
1	Etrav_e_1_1	★★★★		

To the right of the interface is a 3D ball-and-stick model of a molecule, showing a complex structure with orange, blue, and red atoms. Below the interface is a 2D chemical structure of Etravirine_1_1, which is a pyrimidopyrimidinone derivative with a bromine atom, an amino group, and a cyano group.

At the bottom of the interface, the 'Sequence View' panel shows 'No Protein Selected' and 'Etravirine_1_1'. The status bar at the very bottom indicates 'No Protein Selected' and 'Etravirine_1_1'.

Generated poses will receive an alignment score which can be used to rank the compounds.



**Have fun and enjoy your
interactive drug discovery
journey with SeeSAR!**

**If you have any problems,
please reach out to us:
support@biosolveit.de**