

BioSolveIT
expect actives!

SeeSAR

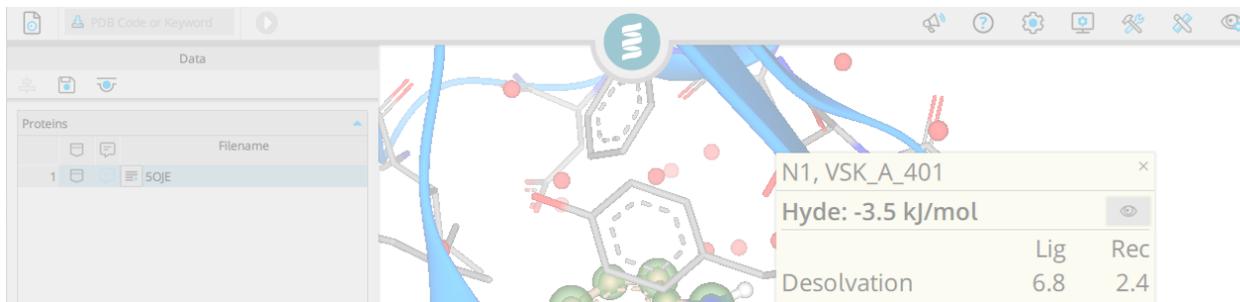
Beginner's Guide
Version 14 - Atlas

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

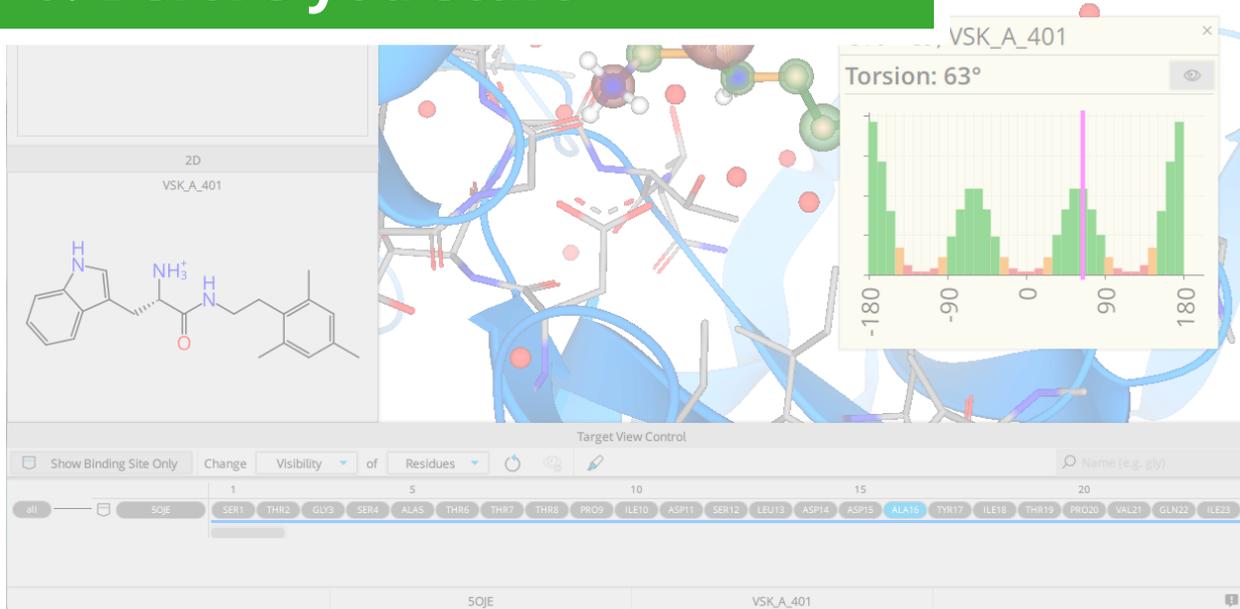
Click on the section
you are interested in

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0. Before you start



Welcome to SeeSAR 14.0

fast • visual • easy

Atlas



Continue
Previous Project

Continue with your last project.



New
Project

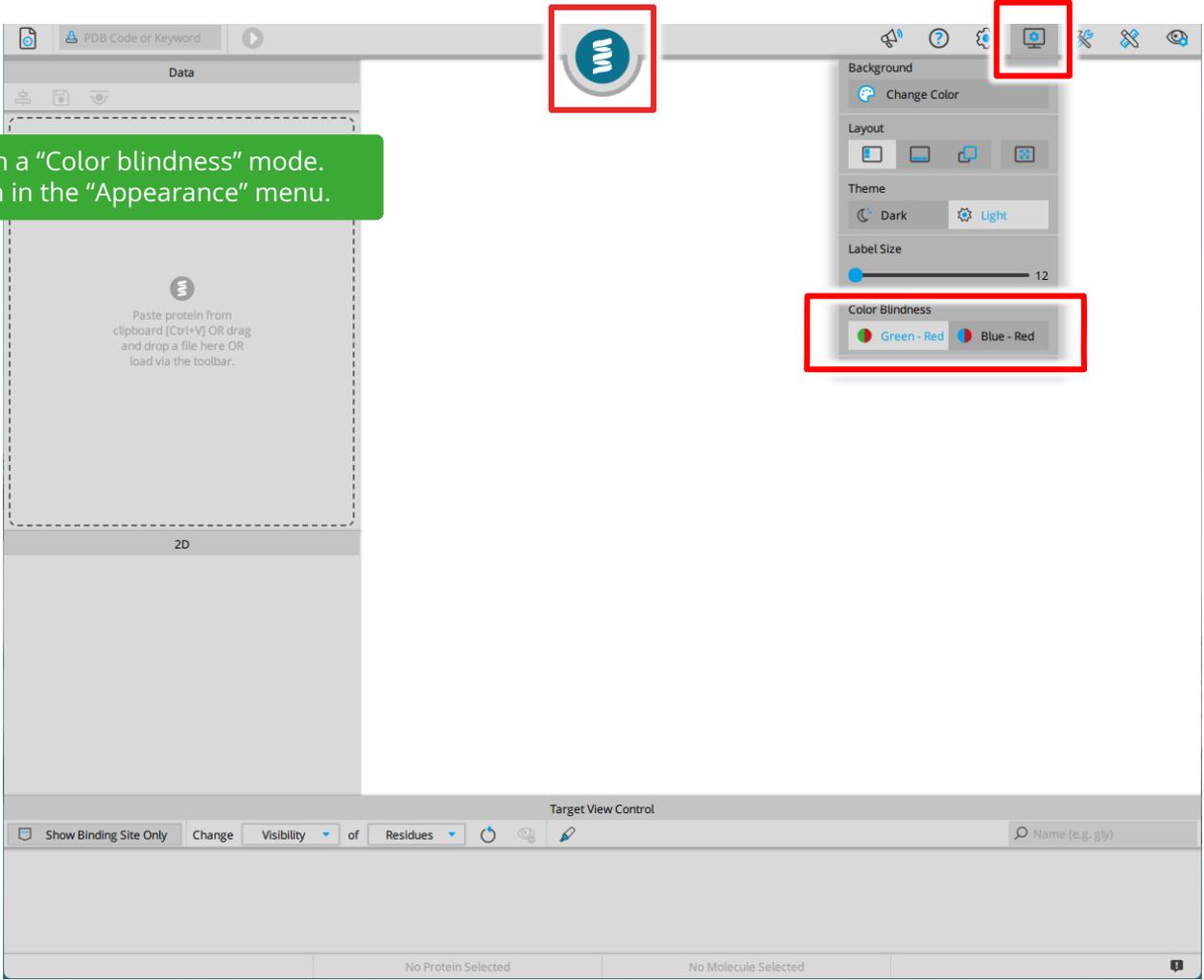
Start your drug discovery project here.



Start SeeSAR
Tour

Find an introduction to SeeSAR's interface.

SeeSAR comes with a "Color blindness" mode. It can be turned on in the "Appearance" menu.



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

The screenshot displays a molecular visualization application. At the top, there is a toolbar with icons for search, help, settings, and other functions. Below the toolbar, the 'Data' panel shows protein information. The 'Ligand for 5OJE' table lists the bound ligand:

Name	Estimated Affinity			
	pM	nM	μM	mM
VSK_A_401				

The '2D' panel shows the chemical structure of VSK_A_401, which is a tryptophan derivative with a complex side chain. The main 3D view shows a protein structure with a small blue molecule (the ligand) bound to it. At the bottom, the 'Target View Control' panel allows users to show the binding site and select specific residues. The residue list includes: SER1, THR2, GLY3, SER4, ALAS, THR6, THR7, THR8, PRO9, ILE10, ASP11, SER12, LEU13, ASP14, ASP15, ALA16, TYR17, ILE18, THR19, PRO20, VAL21, GLN22, ILE23. The 'ALA16' residue is currently selected.

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

The screenshot displays the SeeSAR software interface. The central 3D view shows a protein structure in blue ribbon representation with a ligand molecule (VSK_A_401) in stick representation. The interface includes several panels and windows:

- Data Panel (Top Left):** Shows the PDB Code or Keyword and a search icon.
- Ligand for 5OJE (Middle Left):** A table listing the ligand VSK_A_401 with an estimated affinity range from pM to mM.
- 2D Structure (Bottom Left):** A 2D chemical structure of VSK_A_401.
- Target View Control (Bottom):** A sequence viewer showing residues from 1 to 23, with VSK_A_401 highlighted in blue.
- Analysis Windows (Right):** Two windows provide detailed energy and torsion data:
 - N1, VSK_A_401:** Shows a hydride energy of -3.5 kJ/mol and a table of contributions:

	Lig	Rec
Desolvation	6.8	2.4
Interaction	-7.9	-4.8
 - C10 - C9, VSK_A_401:** Shows a torsion angle of 63° and a histogram of the torsion angle distribution from -180° to 180°.

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 screenshot displays the SeeSAR software interface. At the top right, a red box highlights a gear icon in the toolbar. A central 'System' dialog box is open, with a red box highlighting the 'Calculation' option, which is represented by a calculator icon. Other options in the 'System' menu include HPSee, Inspirator, License, Proxy, RCSB PDB, Readme, Systemlog, and StarDrop. The background shows a 3D molecular model of a protein-ligand complex. On the left, a 'Ligand for 5OJE' table lists 'VSK_A_401' with an estimated affinity range from pM to mM. Below the table is a 2D chemical structure of VSK_A_401. At the bottom, a 'Target View Control' bar shows a sequence of residues from 1 to 20, with 'ALA16' highlighted in blue.

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

The screenshot shows a molecular docking software interface. A 'System' dialog box is open, displaying a table for defining automatic calculations. The table has columns for different calculation modes, indicated by icons: a file folder, a protein, a save icon, a yellow question mark, a red target, and a purple target. The rows list various calculation tasks, and the table cells contain green checkmarks or red 'X' marks to indicate which modes are selected for each task.

Calculation	File	Protein	Save	Question Mark	Red Target	Purple Target
Load Molecules from File	X	X	X	X	X	X
Load Proteins	✓	✓	X	X	X	X
Save Editor Molecules to Table	✓	✓	X	X	X	X
Save Inspirator Molecules to Table	✓	✓	X	X	X	X
Generate Local Docking Poses	✓	✓	✓	X	X	X
Generate External Docking Poses	✓	✓	✓	X	X	X
Generate Similarity Scanner Poses	X	X	X	X	X	X

The screenshot displays the SeeSAR software interface. On the left, a 'Data' panel shows a message: 'ZZFF - Define Your Binding Site' and '56 residues are currently selected for the binding site. You can modify the binding site selection, or confirm with the green button above.' Below this is a table of molecules:

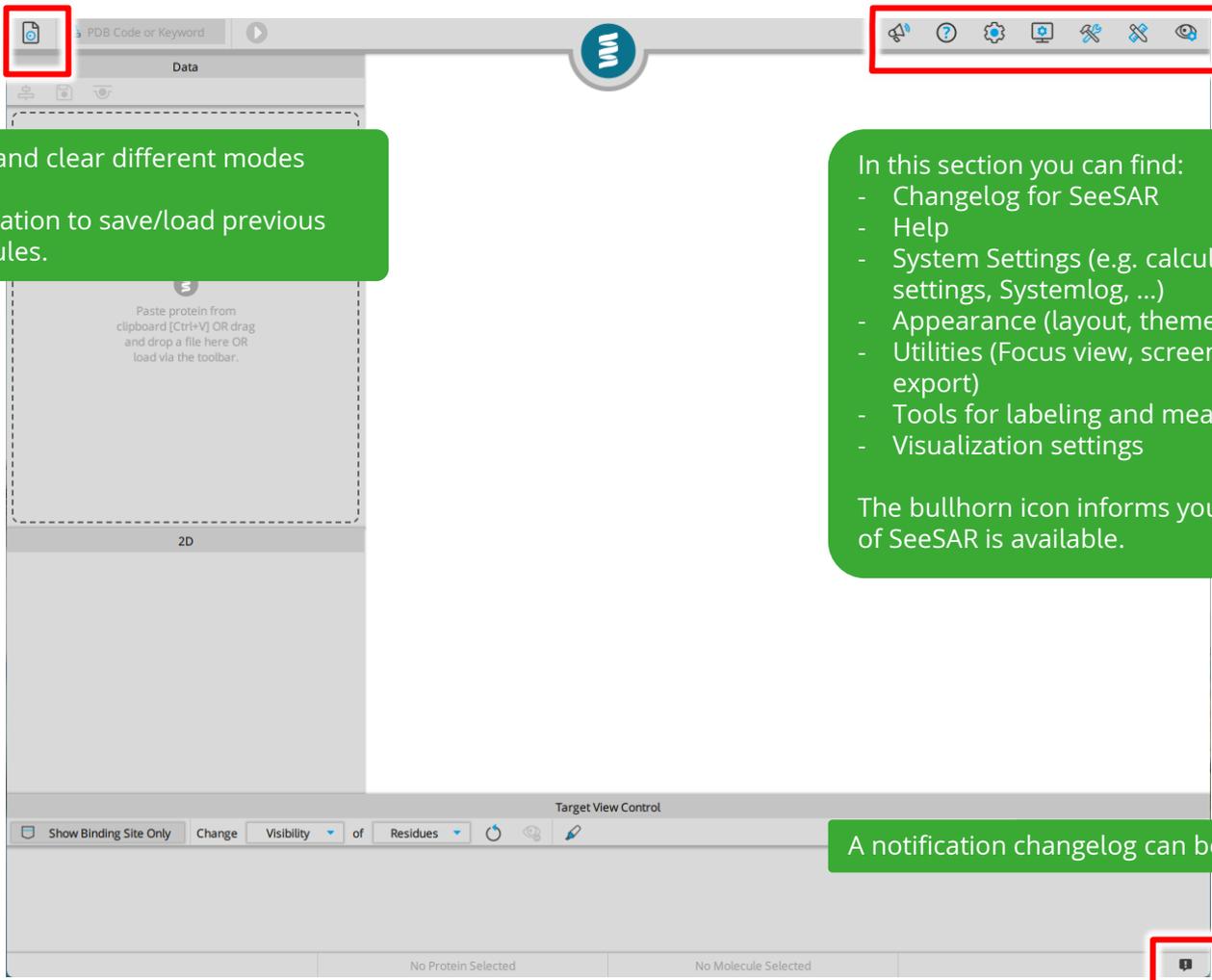
Molecules	Name	# Residues
	53U_H_2001	30

On the right, a 3D ribbon diagram of a protein structure is shown with a yellow highlighted binding site. A green callout box contains the text: 'SeeSAR is your intuitive, visual drug design platform. Covering every step of your drug discovery process — from virtual screening to fragment-based design — SeeSAR fosters ideation in the most fun and comprehensive way.'

At the bottom, a sequence viewer shows a protein sequence with a 'Target' dropdown menu. The sequence includes residues: 190 (ILE162, VAL163, ILLU164, ARG165, PRO166, VAL167, CYS168, LYS169, ASP170, ...), 195 (ASP170, ...), 205 (THR177, ASP178, ASN179, MET180, PHE181, CYS182, ALA183, GLY184), and 210. A '2D' view is also visible.

1. Basics

SeeSAR is your intuitive, visual drug design platform. Covering every step of your drug discovery process — from virtual screening to fragment-based design — SeeSAR fosters ideation in the most fun and comprehensive way.



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, license 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.

2ZFF

RCSB PDB (1 hits)

2ZFF Exploring Thrombin S1-pocket

Type a PDB code in the search box (or the name of the protein) and press enter to download a protein directly from the RCSB PDB. For this guide we will use 2ZFF as example.

Note:
You can also load your protein from a file, via the file menu button.

2D

Target View Control

Show Binding Site Only Change Visibility of Residues 🔍 Name (e.g. gly)

No Protein Selected No Molecule Selected

2ZFF - Extract Your Ligand

Hetero Groups

LOI	Name	Estimated Affinity			
		pM	nM	µM	mM
1	Do not...ligand				
2	53U_H_2001		—		

The protein is loaded and all molecules, buffers, co-factors etc. will be listed. Please (1.) select the ligand or chose to not extract a ligand and (2.) press the "Apply" button.

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

Target View Control

Show Binding Site Only Change Visibility of Residues

all 2ZFF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F

2ZFF No Molecule Selected

Warning sign appears if the structure has missing segments. It is visualized in 3D via a yellow/black line, or if it occurs within binding sites, as a red/black line.

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.

The screenshot displays a molecular docking software interface. At the top, a 'Proteins' table lists '2ZFF' with a warning icon and a tooltip that reads 'Structure contains unresolved segments'. Below this, a 'Ligand for 2ZFF' table lists '53U_H_2001' with a red box around its name. A 3D ribbon model of the protein is shown on the right, with a yellow/black line indicating unresolved segments. A 2D chemical structure of the ligand '53U_H_2001' is shown in the bottom left. The bottom of the interface features a 'Target View Control' panel with a 'Show Binding Site Only' button and a 'Residues' list including GLU17C, ALA18B, ASP1A, CYS1, GLY2, LEU3, ARG4, PRO5, LEU6, PHE7, GLU8, LYS9, LYS10, SER11, LEU12, GLU13, ASP14, LYS14A, THR14B, GLU14C, ARG14D, GLU14E, and LEU14F. A '1 message' button is visible in the bottom right corner.

The screenshot displays a software interface for molecular docking. On the left, there are two tables: 'Proteins' and 'Ligand for 2ZFF'. The 'Proteins' table has a red box around its collapse arrow. The 'Ligand for 2ZFF' table lists '53U_H_2001' with a red box around its collapse arrow. Below these is a 2D chemical structure of the ligand, 53U_H_2001, with a green double-headed arrow indicating its relationship to the 3D view. The 3D view on the right shows a blue protein structure with a red ligand bound to it. A green box on the right provides instructions for the 3D viewer. At the bottom, a 'Target View Control' panel shows a sequence of residues from 1 to 20, with '2ZFF' selected. A message bar at the bottom right indicates '1 message'.

Tables:

- Collapse and re-open
- Drag rim to re-size
- Click entries to select

3D-viewer:

- Right-click to rotate
- Mouse-wheel to zoom
- Middle-click to shift

Change the table layout

Adjust label size

Adjust background color

Switch between dark and light theme

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, feel free to use whatever you prefer!

2ZFF

53U_H_2001

Name	Estimated Affinity
53U_H_2001	pM nM μM mM

2D
53U_H_2001

Target View Control

Show Binding Site Only Change Visibility of Residues

all 2ZFF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F

2ZFF 53U_H_2001 1 message

Note that you are in **Protein mode**. The mode switch button indicates your current mode and also allows you to change modes. Hover over it to view your options.

Target View Control

all — 2ZFF of Residues 1 5 10 15 20

GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F

2ZFF 53U_H_2001 1 message

Detailed description: The image shows a software interface for molecular docking. At the top, a red box highlights a circular icon with a blue 'M' and a white ribbon, representing the 'Protein mode' button. Below this, a green text box provides instructions. The main window displays a 3D ribbon model of a protein (blue) with a ligand (red) bound to its active site. On the left, a 'Data' panel shows 'Proteins' and 'Ligand for 2ZFF'. The 'Ligand' table lists '53U_H_2001' with an estimated affinity range from pM to mM. Below the table is a '2D' view of the ligand, showing its chemical structure with a benzyl group, a pyrrolidine ring, and a benzylamide group. At the bottom, a 'Target View Control' panel shows a sequence of residues from 1 to 20, with '2ZFF' selected. A message bar at the bottom right indicates '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.



Protein Editor



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



Docking



Space 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

In the Docking mode, you can generate poses for new molecules through molecular docking. It includes two sub-modes: dock in local machine and external server.



Inspirator



The Inspirator mode helps you to generate new ideas.

Hover over icon from the left for local machine.



From the right for the external server.



Docking



Space Docking



The Space Docking Mode was added in Version 14 of SeeSAR. It has its own dedicated section in this guide.

[Jump to section](#)



Proteins



Binding Site



Protein Editor



Inspirator



Docking



Space Docking

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



Similarity Scanner

2ZFF

Data

Proteins

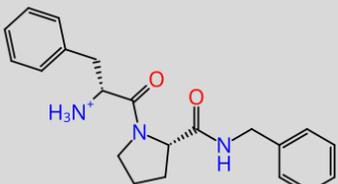
Filename
1 2ZFF

Ligand for 2ZFF

Name	Estimated Affinity			
	pM	nM	μM	mM
53U_H_2001	-----			

2D

53U_H_2001



3D visualization of protein 2ZFF (blue ribbon) with ligand 53U_H_2001 (red stick) bound to the active site. The protein structure is shown in blue, and the ligand is shown in red sticks with green and red atoms.

As the 3D view can easily get busy, let's customize the visualization in the "Target View Control" window.

Target View Control

Show Binding Site Only Change Visibility of Residues

all 2ZFF

1	5	10	15	20
GLU1C	ALA1B	ASP1A	CYS1	GLY2
LEU3	ARG4	PRO5	LEU6	PHE7
GLU8	LYS9	LYS10	SER11	LEU12
GLU13	ASP14	LYS14A	THR14B	GLU14C
ARG14D	GLU14E	LEU14F		

2ZFF 53U_H_2001 1 message

Choose one of the options to display

Show Binding Site Only

OR

Show Whole Protein

Change Visibility of Residues

Targets

- ✓ Residues
- Molecules
- Metals
- Waters
- Chains
- Surfaces

Reset user settings

Identify the components that are most similar or different from each other, when multiple structures are loaded.

similar ————— 0.0 Å different

Show only interacting components

The view controls let you toggle on/off. All buttons are clickable, so that you can hide all parts of one protein in one click

all — 2ZFF

1 5 10

GLU39 LEU40 LEU41 CYS42 HIS57 TYR60A TRP60D LYS60F ARG73 GLU97A A

Example:
 To visualize surface, select Change "Visibility" of "Surfaces" and toggle on the PDB code.
 To adjust this surface visibility, set Change "Color" of "Surfaces" and right-click on PDB code to explore the options.

The screenshot displays a molecular docking software interface. On the left, a 'Data' panel shows a list of proteins with '2ZFF' selected. Below it, a 'Ligand for 2ZFF' panel lists '53U_H_2001'. A context menu is open over the ligand entry, with 'Add to Binding Site Mode' highlighted in a red box. The main 3D view shows a blue protein structure with a red ligand molecule bound to its surface. At the bottom, a 'Target View Control' panel shows a sequence of residues from 1 to 20, with 'LEU14E' highlighted. A green callout box on the right contains the following text:

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.

2ZFF - 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

2D

Target View Control

Show Binding Site Only Change Visibility of Residues

Name (e.g. gly)

all 2ZFF 1 5 10 15 20

GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F L

2ZFF No Molecule Selected 1 message



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

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

2ZFF - 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

Unoccupied Pockets

Pocket ID	# Residues	DoGSiteScore	# Donors
-----------	------------	--------------	----------

2D

Target View Control

Show Binding Site Only Change Visibility of Residues

Name (e.g. gly)

all 2ZFF 1 5 10 15 20

GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F L

2ZFF No Molecule Selected 1 message

Here you can search for unoccupied binding pockets.

ZZFF - Define Your Binding Site

56 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
1	56	0.53	39	45
2	19	0.28	11	8
3	16	0.20	7	10
4	12	0.12	7	10

Add Residue to Binding Site

190 195 205 210

all 22FF 1161 ILE162 VAL163 GLU164 ARG165 PRO166 VAL167 CYS168 LYS169 ASP170 SER171 THR172 ARG175 ILE176 THR177 ASP178 ASN179 MET180 PHE181 CYS182 ALA183 GLY184

22FF No Molecule Selected 1 message

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

You can select desired binding pockets by clicking on the colored pockets on 3D or right-click on the table entry.

To add residues: in 3D, use Ctrl + left click to select. In the sequence view, right-click on a residue to access the option.

Finally, confirm your selection by clicking on the top green play button.

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

To adjust the view, click on "Show Binding Site Only". Make sure to set the selection at Change "Visibility" of "Residues". Now toggle your cursor and click on the PDB code below.

Proteins	
Filename	
2ZFF	

Ligand for 2ZFF	
Name	Estimated Affinity
53U_H_2001	pM nM μM mM
	┌───┐

Target View Control

Show Binding Site Only Change Visibility of Residues

all 2ZFF GLU1C ALA1B ASP1A CYS1 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F L

2ZFF 53U_H_2001 1 message

You should now be able to see the binding site residues. Click on the ligand and hit the space bar to zoom in.

The screenshot displays a molecular docking software interface. The main window shows a protein structure (blue ribbon) with a ligand (ball-and-stick model) docked in its binding site. The interface is divided into several panels:

- Data Panel:** Contains a 'Proteins' list with one entry: '2ZFF'.
- Ligand for 2ZFF Panel:** Contains a table with the following data:

Name	Estimated Affinity			
	pM	nM	µM	mM
53U_H_2001				
- 2D Panel:** Shows the chemical structure of the ligand, 53U_H_2001, with the SMILES string: C1CCN(C1)C(=O)C(Cc2ccccc2)C(=O)NCC3=CC=CC=C3.
- Target View Control Panel:** Shows a residue list for the protein 2ZFF, with residues 1 through 20 visible. The residues are: GLU39, LEU40, LEU41, CYS42, HIS57, TYR60A, TRP60D, LYS60F, ARG73, GLU97A, ASN98, LEU99, TRP141, GLY142, ASN143, GLN151, PRO152, LEU160, SER171, THR172, ILE174, ALA183, GLY184.

Click on the "Visualization" menu. Make sure the "Hyde Coloring" is selected. Additionally, Hydrogen bonds, Torsion Coloring, Molecular Clashes can also be kept on.

Ligand for 2ZFF				
Name	Estimated Affinity			
	pM	nM	µM	mM
53U_H_2001	[Bar]			

2D
53U_H_2001

C1CCN(C1)C(=O)C[C@H](Cc2ccccc2)C(=O)NCC3=CC=CC=C3

Target View Control

Show Whole Protein Change Visibility of Residues

all 2ZFF 1 5 10 15 20

GLU39 LEU40 LEU41 CYS42 HIS57 TYR60A TRP60D LYS60F ARG73 GLU97A ASN98 LEU99 TRP141 GLY142 ASN143 GLN151 PRO152 LEU160 SER171 THR172 ILE174 ALA183 GLY184

2ZFF 53U_H_2001 1 message

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

The screenshot displays a molecular docking software interface. The main window shows a 3D representation of a protein (blue ribbon) with a ligand (green and orange spheres) docked in its binding pocket. A red box highlights a menu with the following options: Show Label, Measure Atom Distance, Measure Angle, Measure Torsion, and Clear All Labels. A green callout box points to this menu with the text "Check-out the other analysis options!".

The left sidebar contains a "Data" panel with a "Proteins" table and a "Ligand for 2ZFF" table. The "Ligand for 2ZFF" table is as follows:

Name	Estimated Affinity			
	pM	nM	µM	mM
53U_H_2001		█		

Below the ligand table is a "2D" section showing the chemical structure of 53U_H_2001. The structure is a piperidine ring substituted with a benzyl group, a methylamino group, and a benzylamino group.

The bottom of the interface features a "Target View Control" panel with a "Show Whole Protein" button, a "Change Visibility" dropdown, and a "Residues" dropdown. A sequence viewer shows residues 1 to 20, with 2ZFF and 53U_H_2001 highlighted. A "1 message" button is visible in the bottom right corner.

Check-out the other analysis options!

The screenshot displays a molecular docking software interface. The main window shows a protein structure (blue ribbon) with a ligand (green and orange spheres) docked in its binding site. A context menu is open over the ligand entry '53U_H_2001' in the 'Ligand for 2ZFF' table. The menu items are: Copy to Clipboard [Ctrl+C], Calculate Estimated Affinity, Add to Binding Site Mode, Add to Analyzer, Add to Molecule Editor (highlighted with a red box), Add to Inspector, Add to Docking Mode, Add to Similarity Scanner, and Use as Template. A green text box explains that 'Add to Molecule Editor' is accessible via a right-click and automatically switches the mode. The interface also includes a 'Data' panel, a 'Target View Control' bar, and a residue list at the bottom.

2ZFF

Data

Proteins

Filename
1

'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.

Ligand for 2ZFF

Name	Estimated Affinity			
	pM	nM	µM	mM
53U_H_2001				

- Copy to Clipboard [Ctrl+C]
- Calculate Estimated Affinity
- Add to Binding Site Mode
- Add to Analyzer
- Add to Molecule Editor**
- Add to Inspector
- Add to Docking Mode
- Add to Similarity Scanner
- Use as Template

Target View Control

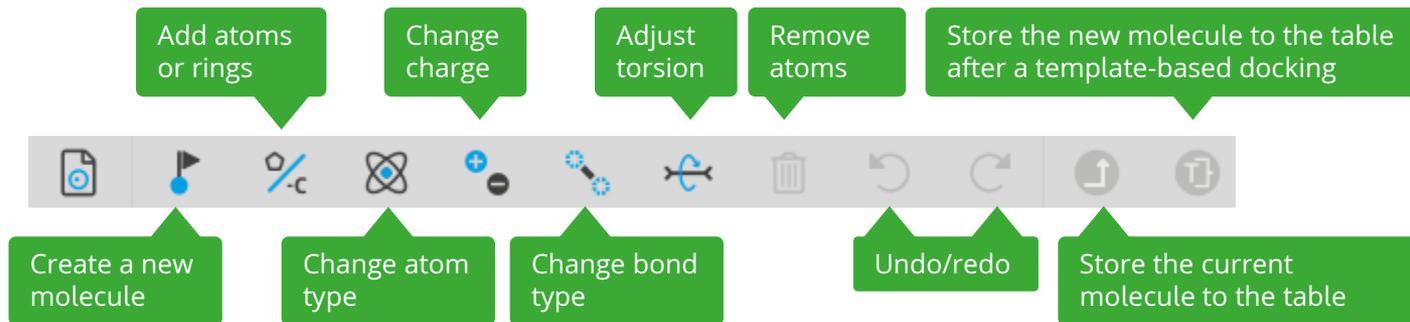
Show Whole Protein Change Visibility of Residues

all 2ZFF 1 5 10 15 20

GLU39	LEU40	LEU41	CYS42	HIS57	TYR60A	TRP60D	LYS60F	ARG73	GLU97A	ASN98	LEU99	TRP141	GLY142	ASN143	GLN151	PRO152	LEU160	SER171	THR172	ILE174	ALA183	GLY184
-------	-------	-------	-------	-------	--------	--------	--------	-------	--------	-------	-------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------

2ZFF 53U_H_2001 1 message

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, ...).

The screenshot shows a molecular modeling software interface. At the top, a toolbar contains a green button with a downward arrow, highlighted by a red box. A green callout bubble points to this button with the text: "Click this button to save the edited molecule." Below the toolbar is a "Data" panel with a table of molecules. The table has columns for "Name" and "Estimated Affinity" (with sub-columns for pM, nM, μM, and mM). Two entries are listed: "53U_H_2001" and "53U_H_2001_1". A green callout bubble points to the table with the text: "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'." The main 3D view shows a complex molecular structure with a red dashed box highlighting a specific hydrogen atom. A green callout bubble points to this area with the text: "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!" At the bottom, a "Target View Control" panel shows a dropdown menu set to "Whole Protein" and a "Chain-H" button, both highlighted by a red box. A green callout bubble points to this area with the text: "Additionally toggle off visibility of chains to avoid clutter." The interface also shows a 2D view of a benzene ring with an amino group (H₂N) and a hydrogen atom (H) at the meta position.

	Name	Estimated Affinity			
		pM	nM	μM	mM
1	53U_H_2001				
2	53U_H_2001_1				

The screenshot displays a molecular docking software interface. At the top, a toolbar contains various icons for navigation and editing. Below the toolbar, a 'Data' panel shows a table of molecules. The table has columns for 'Name' and 'Estimated Affinity', with sub-columns for pM, nM, μM, and M. Two molecules are listed: '53U_H_2001' and '53U...01_1'. A red box highlights the table. Below the table, a green text box contains the following text:

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!

Below the text box, a '2D' panel shows the chemical structure of '53U_H_2001_1'. The structure is a complex molecule with a central pyrrolidine ring, a benzamide group, and a benzylammonium group. A red box highlights a green play button icon in the 3D molecular model area. At the bottom, a 'Target View Control' panel shows 'Show Whole Protein' and 'Change Visibility of Chains' options. The bottom status bar shows '2ZFF' and '53U_H_2001_1'.

	Name	Estimated Affinity			
		pM	nM	μM	M
1	53U_H_2001				
2	53U...01_1				

2D
53U_H_2001_1

Target View Control

Show Whole Protein Change Visibility of Chains

all 2ZFF Chain-H Chain-I

2ZFF 53U_H_2001_1 1 message

The screenshot displays a molecular docking software interface. On the left, a 'Data' panel shows a table of molecules and their estimated affinities. A red box highlights the table. Below the table is a 2D chemical structure of a molecule with an amino group (H₂N) and a hydroxyl group (HO). The main window shows a 3D ball-and-stick model of a protein-ligand complex, with a red box highlighting a specific hydroxyl group on the ligand. A green play button icon is visible in the 3D view. At the bottom, a protein sequence is shown with residues 25 to 30 highlighted: LYS185, PRO186, GLY186C, LYS186D, ARG187, GLY188, ASP189, ALA190, CYS191, and GLU192. The bottom status bar shows the PDB ID 2ZFF, the molecule name 53U_H_2001_4, and a '1 message' button.

	Name	Estimated Affinity			
		pM	nM	μM	m
1	53U_H_2001				
2	53U_H_2001_1				
3	53U_...01_4				

2D
53U_H_2001_4

all Show Whole

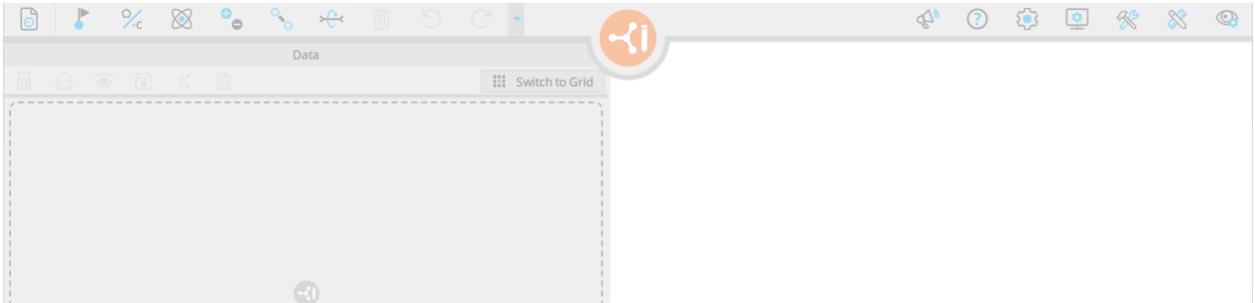
Name (e.g. gly)

25 30
LVS185 PRO186 GLY186C LYS186D ARG187 GLY188 ASP189 ALA190 CYS191 GLU192

2ZFF 53U_H_2001_4 1 message

Now let's add a hydroxy 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.



2. Adding Molecules

The screenshot shows the software interface with a 2D view of a benzene ring and a 3D ball-and-stick model of a molecule. The 3D model consists of orange spheres representing carbon atoms, white spheres representing hydrogen atoms, and a double bond between two carbon atoms. The interface includes a 'Target View Control' section at the bottom with a search bar and a list of residues.

Target View Control

Show Whole Protein Change Visibility of Residues

all — 2ZF

1	5	10	15	20																		
GLU39	LEU40	LEU41	CYS42	HIS57	TYR60A	TRP60D	LYS66F	ARG73	GLU97A	ASN98	LEU99	TRP141	GLY142	ASN143	GLN151	PRO152	LEU160	SER171	THR172	ILE174	ALA183	GLY184

2ZF No Molecule Selected 1 message

The screenshot shows the SeeSAR software interface. The top menu bar includes options like 'New', 'Clear Analyzer', 'Load Project...', 'Load Molecules...', 'Save Project', 'Save Project as...', and 'About SeeSAR'. The 'Load Molecules...' option is highlighted with a red box. A green callout box contains the following text:

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.

The main window displays a 3D molecular model of a protein-ligand complex. The bottom panel shows the 'Target View Control' with a sequence viewer for protein 2ZFF. The sequence viewer shows residues from 1 to 20, with the following amino acids: 1: all, 2: 2ZFF, 3: GLU39, 4: LEU40, 5: LEU41, 6: CYS42, 7: HIS57, 8: TYR60A, 9: TRP60D, 10: LYS66F, 11: ARG73, 12: GLU97A, 13: ASN98, 14: LEU99, 15: TRP141, 16: GLY142, 17: ASN143, 18: GLN151, 19: PRO152, 20: LEU160, SER171, THR172, ILE174, ALA183, GLY184.

The screenshot displays a molecular visualization software interface. The main window shows a 3D ribbon representation of a protein structure. On the left, a 2D panel is highlighted with a red border, containing a text box that reads: "Paste molecule from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar." Below this panel, the text "2D" is visible. At the bottom of the interface, there is a "Target View Control" section with a "Show Whole Protein" button and a "Change Visibility of Residues" dropdown menu. A sequence of residues is shown below, including 2ZFF, GLU39, LEU40, LEU41, CYS42, HIS57, TYR60A, TRP60D, LYS66F, ARG73, GLU97A, ASN98, LEU99, TRP141, GLY142, ASN143, GLN151, PRO152, LEU160, SER171, THR172, ILE174, ALA183, and GLY184. The status bar at the bottom indicates "2ZFF", "No Molecule Selected", and "1 message".

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
```

The screenshot displays a molecular docking software interface. At the top, a toolbar contains various icons for navigation and manipulation. Below the toolbar, a 'Data' panel is visible. A red box highlights the 'Molecules (# 3)' table, which lists three molecules. The first molecule is named 'Compd' and has an estimated affinity of 0. The second and third molecules are named 'no name' and also have an estimated affinity of 0. Below the table, a 2D chemical structure of the first molecule is shown, labeled 'no name'. The structure consists of a pyrrolidine ring connected to a carbonyl group, which is further connected to a benzimidazole ring system. To the right of the 2D structure is a 3D ball-and-stick model of the protein-ligand complex. The protein is shown in a light gray color, and the ligand is shown in a darker gray color. At the bottom of the interface, a 'Target View Control' panel is visible, showing a sequence of residues from 1 to 20. The residues are labeled as follows: 1 (GLU39), 2 (LEU40), 3 (LEU41), 4 (CYS42), 5 (HIS57), 6 (TYR60A), 7 (TRP60D), 8 (LYS60F), 9 (ARG73), 10 (GLU97A), 11 (ASN98), 12 (LEU99), 13 (TRP141), 14 (GLY142), 15 (ASN143), 16 (GLN151), 17 (PRO152), 18 (LEU160), 19 (SER171), 20 (THR172). The interface also shows a search bar for the target name (e.g., gly) and a '1 message' button.

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

2D
no name

Target View Control

Show Whole Protein Change Visibility of Residues

1 5 10 15 20

all 22FF GLU39 LEU40 LEU41 CYS42 HIS57 TYR60A TRP60D LYS60F ARG73 GLU97A ASN98 LEU99 TRP141 GLY142 ASN143 GLN151 PRO152 LEU160 SER171 THR172 ILE174 ALA183 GLY184

22FF no name 1 message

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 table of molecules and a 2D chemical structure. The table has columns for Name, Estimated Affinity (pM, nM, μM, mM), LLE, and Tor. The molecules listed are Compound1, Compound2, and Compound3. A red box highlights the 'Molecules (# 3)' panel on the left, which contains a list of molecules with checkboxes and icons. Below the table is a 2D chemical structure of Compound1, which is a benzimidazole derivative with a pyrrolidine ring attached to the imidazole ring.



The screenshot shows the same software interface as the left one, but with a context menu open over the 'Molecules (# 3)' panel. The menu options are: Check all, Check all favorites, Invert checked, and Uncheck all. A green callout box is overlaid on the right side of the interface, containing text. Below the table is a 2D chemical structure of Compound1, which is the same as in the left screenshot. The 'Target View Control' at the bottom shows a protein sequence with residues 1 to 10 highlighted.

To transfer all of your compounds to another mode (e.g. to dock them in the Docking mode), click on the 'Checked' column and select 'Check all' to mark all molecules in the list.

If you want to transfer only some of the molecules, check them individually in the column.

Data

Molecules (Add molecules to Binding Site mode)

Add molecules to Molecule Editor Affinity LLE Tor. Intra-clash Inter-clash

1 Add molecules to Inspiration

2 Add molecules to Docking on Your Local Machine

3 Add molecules to Docking on Your Local Machine

2D
Compound1

Target View Control

Show Whole Protein Change Visibility of Residues Name (e.g. gly)

all 1 5 10 15 20

GLU39 LEU40 LEU41 CYS42 HIS57 TYR60A TRIP60 LYS60F ARG73 GLU97A ASN98 LEU99 TRIP141 GLY142 ASN143 GLN151 PRO152 LEU160 SER171 THR172 ILE174 ALA183 GLY184

2ZFF Compound1 1 message

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 on local machine.

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

The screenshot displays a software interface for molecular visualization. At the top, a toolbar contains several icons, with a play button and a circular icon containing three connected nodes highlighted by red boxes. Below the toolbar, the interface is split into two main areas. On the left is a 2D workspace with a dashed border and a central text prompt: "Paste molecule from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar." Below this workspace is a "2D" label. On the right is a 3D view of a protein structure, rendered in a stick representation with atoms colored by element (carbon in grey, oxygen in red, nitrogen in blue). A green callout box with white text is overlaid on the 3D view, stating: "You can also create new molecules in the Molecule Editor mode." At the bottom of the interface is a "Target View Control" panel. It includes a "Show Whole Protein" button, a "Change Visibility of Residues" dropdown menu, and a search bar labeled "Name (e.g. gly)". Below these controls is a sequence viewer showing a protein sequence from residue 1 to 20. The sequence is: 1: all, 2: 2ZFF, 3: GLU39, 4: LEU40, 5: LEU41, 6: CYS42, 7: HIS57, 8: TYR60A, 9: TRIP60D, 10: LYS60F, 11: ARG73, 12: GLU97A, 13: ASN98, 14: LEU99, 15: TRIP141, 16: GLY142, 17: ASN143, 18: GLN151, 19: PRO152, 20: LEU160, SER171, THR172, ILE174, ALA183, GLY184. At the very bottom, there is a status bar with "2ZFF", "No Molecule Selected", and a "1 message" button.

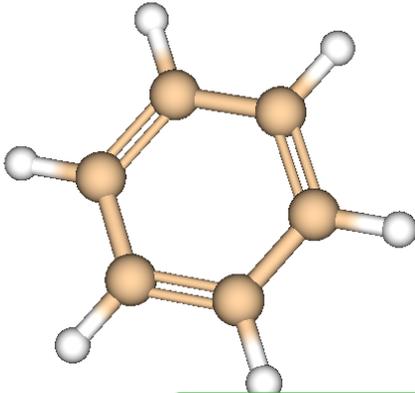
The screenshot shows a molecular modeling software interface. On the left, a 'Create New Ring' menu is open, listing options: Cyclopropane, Cyclobutane, Cyclopentane, Cyclopentadiene, Cyclohexane, and Benzene. The 'Benzene' option is highlighted. Below the menu, there is a text box: 'Paste molecule from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar.' The main workspace displays a 2D representation of a protein structure with various residues colored in blue, red, and yellow. At the bottom, there is a 'Target View Control' panel with a sequence viewer showing residues from 1 to 20, including GLU39, LEU40, LEU41, CYS42, HIS57, TYR60A, TRP60D, LYS60F, ARG73, GLU97A, ASN98, LEU99, TRP141, GLY142, ASN143, GLN151, PRO152, LEU160, SER171, THR172, ILE174, ALA183, and GLY184. The status bar at the bottom indicates '2ZFF', 'No Molecule Selected', and '1 message'.

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 screenshot displays a software interface for molecular modeling. At the top, a toolbar contains several icons, with a red box highlighting the 'Change element' icon (a blue circle with a white 'C'). Below the toolbar, the main workspace is divided into two sections. The upper section is a 2D view showing a benzene ring (a hexagon with an inscribed circle) and a text prompt: "Paste molecule from clipboard [Ctrl+V] OR drag and drop a file here OR load via the toolbar." The lower section is a 3D view showing a ball-and-stick model of the same benzene ring. At the bottom of the interface, there is a "Target View Control" panel with a sequence of residues: "all", "2ZFF", "GLU39", "LEU40", "LEU41", "CYS42", "HIS57", "TYR60A", "TRP60D", "LYS60F", "ARG73", "GLU97A", "ASN98", "LEU99", "TRP141", "GLY142", "ASN143". The status bar at the very bottom shows "2ZFF", "No Molecule Selected", and "1 message".

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.

Once you are finished, export the molecule to the table with 'Save edited molecules to table'.

2D

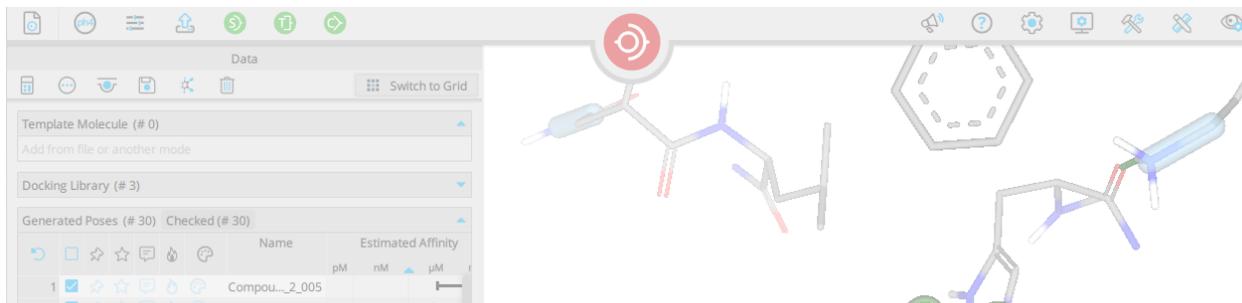
Target View Control

Show Whole Protein Change Visibility of Residues

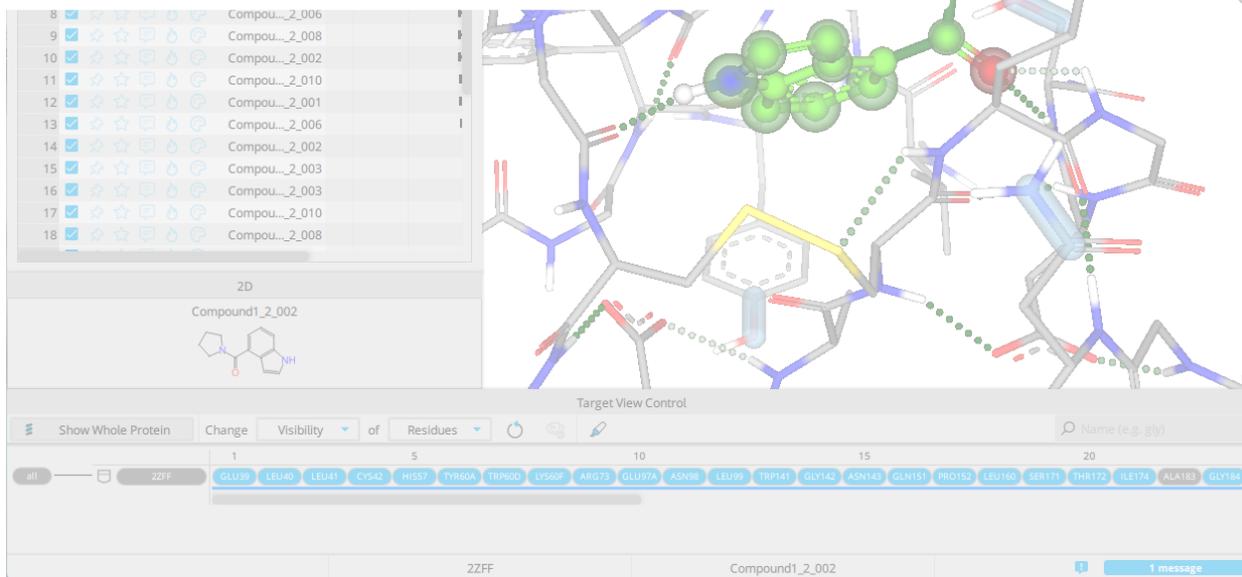
all — 2ZFF

1	5	10	15	20																		
GLU39	LEU40	LEU41	CYS42	HIS57	TYR60A	TRP60D	LYS60F	ARG73	GLU97A	ASN98	LEU99	TRP141	GLY142	ASN143	GLN151	PRO152	LEU160	SER171	THR172	ILE174	ALA183	GLY184

2ZFF No Molecule Selected 1 message



3. Docking



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.

Docking Library (# 3)							
	Name	Estimated Affinity				LLE	T
		pM	nM	μM	mM		
1	Compound1						
2	Compound2						
3	Compound3						

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

Target View Control

Show Whole Protein Change Visibility of Residues

all — 22FF

1 5 10 15 20

GLU39 LEU40 LEU41 CYS42 HIS57 TYR60A TRP60D LYS66F ARG73 GLU97A ASN98 LEU99 TRP141 GLY142 ASN143 GLN151 PRO152 LEU160 SER171 THR172 ILE174 ALA183 GLY184

22FF No Molecule Selected 1 message

Standard docking: Generate poses

Template Molecule (# 0)
Add from file or another mode

Docking Library (# 3)

	Name	Estimated Affinity				LLE	T
		pM	nM	μM	mM		
1	Compound1						
2	Compound2						
3	Compound3						

Generated Poses (# 0)

	Name	Estimated Affinity				LLE	Tor.
		pM	nM	μM	mM		

2D

Target View Control

Show Whole Protein Change Visibility of Residues

all 22FF

1	5	10	15	20																		
GLU39	LEU40	LEU41	CYS42	HIS57	TYR60A	TRP60D	LYS66F	ARG73	GLU97A	ASN98	LEU99	TRP141	GLY142	ASN143	GLN151	PRO152	LEU160	SER171	THR172	ILE174	ALA183	GLY184

22FF No Molecule Selected 1 message

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 displays the SeeSAR software interface. On the left, a settings panel is highlighted with a red box, containing the following options:

- Maximum Number of Poses:** A slider set to 10.
- Clash Tolerance:** A slider set to the 'Standard' position, with 'Medium' and 'High' also visible.
- Allowed Ring Conformations:** A slider set to the left, with a 'boat' conformation icon below it.
- Allow Stereo Center Flipping:** A slider set to the left, with 'Off', 'R/S', 'E/Z', and 'Both' options below it.
- Flexible Covalent Attachment:** A green toggle switch.

The main window shows a 3D molecular model of a protein-ligand complex. At the bottom, the 'Target View Control' panel shows a sequence of residues from 1 to 20, with a search bar for 'Name (e.g. gly)' and a '1 message' button.

'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).

'Allow Stereo Center Flipping' can be used to automatically flip R/S or E/Z or both stereo centers during docking.

The screenshot displays a molecular docking software interface. On the left, a panel titled 'Generated Poses (# 30)' is highlighted with a red border. It contains a table with columns for Name, Estimated Affinity (pM, nM, μM, mM), LLE, and Tor. The table lists 18 poses, with the first 18 rows showing various compound names and their estimated affinities. A green callout box on the right contains the text: 'The 'Generated Poses' table will be populated with generated poses of the ligands from 'Docking Library'.' The main area shows a 3D molecular model of a protein (2ZFF) with several ligands docked into its binding pocket. The protein is shown in a grey ribbon representation, and the ligands are shown in stick representation with different colors (blue, red, yellow, green). At the bottom, there is a 'Target View Control' section with a 'Show Whole Protein' button and a 'Change Visibility of Residues' dropdown menu. The residue list includes: 1, 5, 10, 15, 20, 2ZFF, GLU39, LEU40, LEU41, CYS42, HIS57, TYR60A, TRP60D, LYS66F, ARG73, GLU97A, ASN98, LEU99, TRP141, GLY142, ASN143, GLN151, PRO152, LEU160, SER171, THR172, ILE174, ALA183, GLY184.

ID	Name	Estimated Affinity				LLE	Tor.
		pM	nM	μM	mM		
1	Compou..._1_001					→	⚙️
2	Compou..._1_002					→	⚙️
3	Compou..._1_003					→	⚙️
4	Compou..._1_004					→	⚙️
5	Compou..._1_005					→	⚙️
6	Compou..._1_006					→	⚙️
7	Compou..._1_007					→	⚙️
8	Compou..._1_008					→	⚙️
9	Comp..._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					→	⚙️

Estimated Affinity

H-bond Network

Torsion Quality

Molecular Clashes

Optirium Properties

	Checked (# 30)	Estimated Affinity	LLE	Tor.	
		pM	nM	µM	mM
1	<input checked="" type="checkbox"/>				
2	<input checked="" type="checkbox"/>				
3	<input checked="" type="checkbox"/>				
4	<input checked="" type="checkbox"/>				
5	<input checked="" type="checkbox"/>				
6	<input checked="" type="checkbox"/>				
7	<input checked="" type="checkbox"/>				
8	<input checked="" type="checkbox"/>				
9	<input checked="" type="checkbox"/>				
10	<input checked="" type="checkbox"/>				
11	<input checked="" type="checkbox"/>				
12	<input checked="" type="checkbox"/>				
13	<input checked="" type="checkbox"/>				
14	<input checked="" type="checkbox"/>				
15	<input checked="" type="checkbox"/>				
16	<input checked="" type="checkbox"/>				
17	<input checked="" type="checkbox"/>				
18	<input checked="" type="checkbox"/>				

2D

Target View Control

Show Whole Protein Change Visibility of Residues

Name (e.g. gly)

all 2ZFF

1 5 10 15 20

GLU39 LEU40 LEU41 CYS42 HIS57 TYR60A TRP60D LYS60F ARG73 GLU79A ASN98 LEU99 TRP141 GLY142 ASN143 GLN151 PRO152 LEU160 SER171 THR172 ILE174 ALA183 GLY184

2ZFF No Molecule Selected 1 message

If your poses did not generate affinity automatically, check all poses with the 'Checked' column and 'Check all'.

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. On the left, a panel titled "Generated Poses (# 30)" contains a table of results. The "Estimated Affinity" column header is highlighted with a red box. The table lists 18 poses, each with a name, a numerical affinity value, and a "Tor." icon. The 3D view on the right shows a protein structure with a purple sphere representing a binding site and several ligand molecules in various colors (blue, red, yellow, grey) docked within it. At the bottom, a "Target View Control" bar shows a sequence of residues from 1 to 20, with "2ZFF" selected. A status bar at the very bottom indicates "2ZFF", "No Molecule Selected", and "1 message".

	Name	Estimated Affinity	LLE	Tor.
1	Compou...1_001	-5.8		
2	Compou...1_002	-5.8		
3	Compou...1_003	-5.8		
4	Compou...1_004	-5.8		
5	Compou...1_005	-5.8		
6	Compou...1_006	-5.8		
7	Compou...1_007	-5.8		
8	Compou...1_008	-5.8		
9	Comp...009	-5.8		
10	Compou...1_010	-5.8		
11	Compou...1_001	-5.8		
12	Compou...1_002	-5.8		
13	Compou...1_003	-5.8		
14	Compou...1_004	-5.8		
15	Compou...1_005	-5.8		
16	Compou...1_006	-5.8		
17	Compou...1_007	-5.8		
18	Compou...1_008	-5.8		

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. On the left, a panel titled "Generated Poses (# 30)" contains a table with columns for "Name", "Estimated Affinity" (with sub-columns for pM, nM, μM, mM), and "LLE". The table lists several compounds, with "Compo..._002" highlighted. A context menu is open over "Compo..._002", listing various actions such as "Calculate Estimated Affinity", "Calculate H-bond Network", "Calculate Torsion Quality", "Calculate Molecular Clashes", and "Calculate Optibrium Properties". The main 3D view shows a protein structure with a ligand (green spheres) docked in its binding site. A "Target View Control" bar at the bottom shows a sequence of residues from 1 to 20, with "GLU39" selected. The bottom status bar indicates "2ZFF" and "Compound1_2_002".

ID	Name	Estimated Affinity				LLE
		pM	nM	μM	mM	
1	Compo..._2_005					
	Compo..._2_001					
	Compo..._002					
5	Compo..._003					
6	Compo..._004					
7	Compo..._005					
8	Compo..._006					
9	Compo..._007					
10	Compo..._008					
11	Compo..._009					
12	Compo..._010					
13	Compo..._011					
14	Compo..._012					
15	Compo..._013					
16	Compo..._014					
17	Compo..._015					
18	Compo..._016					

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 screenshot displays a molecular docking software interface. On the left, a table lists 30 generated poses with columns for name, estimated affinity (pM, nM, μM, mM), LLE, Tor., and Intra-clash. A red box highlights a 'Properties' dialog box with the following options:

- Checked
- Visibility in 3D
- Favorite
- Annotation
- Active Status
- Molecule Color
- Name
- Optimization State
- Src
- Estimated Affinity
- LLE

The 3D view shows a protein structure with a green molecule docked. The protein sequence viewer at the bottom shows residues 1 to 20, with 22FF highlighted. The molecule is labeled 'Compound1_2_002'.

To change table properties, scroll horizontally to the last column header and click on it. This will provide options to choose which columns to display.

The screenshot shows a molecular docking software interface. On the left, there is a 'Docking Library' table with columns for 'Name', 'Estimated Affinity', and 'pM', 'nM', 'uM'. A red box highlights the top row of icons in this table. A larger red box highlights a 'Molecule' toolbar with various icons. Green callout boxes provide descriptions for these icons: '3D visibility', 'Add anotation', 'Molecule color', 'Mark as favorite', and 'Mark as active/inactive'. A green callout box at the top right states: 'You can add notes and descriptors in the molecule table window.' The interface also shows a 3D molecular model of a ligand bound to a protein target.

You can add notes and descriptors in the molecule table window.

3D visibility

Add anotation

Molecule color

Mark as favorite

Mark as active/inactive

Name	Estimated Affinity	pM	nM	uM
mpou..._2_005				
mpou..._2_001				
Comp..._002				

The screenshot shows a software interface with a 'Data' panel on the left. It contains a table of 'Generated Poses (# 20)'. The table has columns for Name, Estimated Affinity (pM, nM, μM, mM), LLE, Tor., Intra-clash, and Inter-clash. The first two rows are visible:

	Name	Estimated Affinity	LLE	Tor.	Intra-clash	Inter-clash
		pM	nM	μM	mM	
1	4WL_B_7_001	----->	●	●	●	
2	4WL_B_401_7_003	----->	●	●	●	

To the right of the table is a 3D ball-and-stick model of a ligand bound to a protein structure.

4. Covalent Docking

The screenshot shows a software interface with a 'Data' panel on the left. It contains a table of 'Generated Poses (# 20)'. The table has columns for Name, Estimated Affinity (pM, nM, μM, mM), LLE, Tor., Intra-clash, and Inter-clash. The first two rows are visible:

	Name	Estimated Affinity	LLE	Tor.	Intra-clash	Inter-clash
		pM	nM	μM	mM	
9	4WL_B_401_7_006	----->	●	●	●	
10	Example...1_7_008	----->	●	●	●	
11	4WL_B_401_7_005	----->	●	●	●	
12	4WL_B_401_7_008	----->	●	●	●	
13	Example_1_7_001	----->	●	●	●	

Below the table is a '2D' view of the chemical structure of the ligand, labeled '4WL_B_401_7_001'. The structure is a complex heterocyclic molecule with a fluorinated group.

To the right of the 2D structure is a 3D ball-and-stick model of the ligand covalently bound to a protein structure. The covalent bond is highlighted with a red line.

At the bottom of the interface is a 'Target View Control' panel. It shows a protein sequence with residues 7TLL, PRO52, TYR54, PHE140, LEU141, ASN142, GLY143, SER144, CYS145, GLY146, HIS163, HIS164, MET165, GLU166, LEU167, PRO168, VAL171, HIS172, ALA173, PHE181, VAL186, ASP187, ARG188, and GLN189. The residue 4WL_B_401_7_001 is highlighted in blue.

7TLL

Data

7TLL - Extract Your Ligand

Hetero Groups

	LOI	Name	Estimated Affinity			
			pM	nM	μM	mM
1	<input type="radio"/>	Do not extract a ligand				
2	<input type="radio"/>	4WL_A_401				
3	<input checked="" type="radio"/>	4WL_B_401				

Covalently bound

2D

4WL_B_401

R

Target View Control

Show Binding Site Only Change Visibility of Residues

1 5 10 15 20

all 7TLL SER1 GLV2 PHE3 ARG4 LYSS MET6 ALA7 PHE8 PRO9 SER10 GLY11 LYS12 VAL13 GLU14 GLY15 CYS16 MET17 VAL18 GLN19 VAL20 THR21 CYS22 GLV23

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.

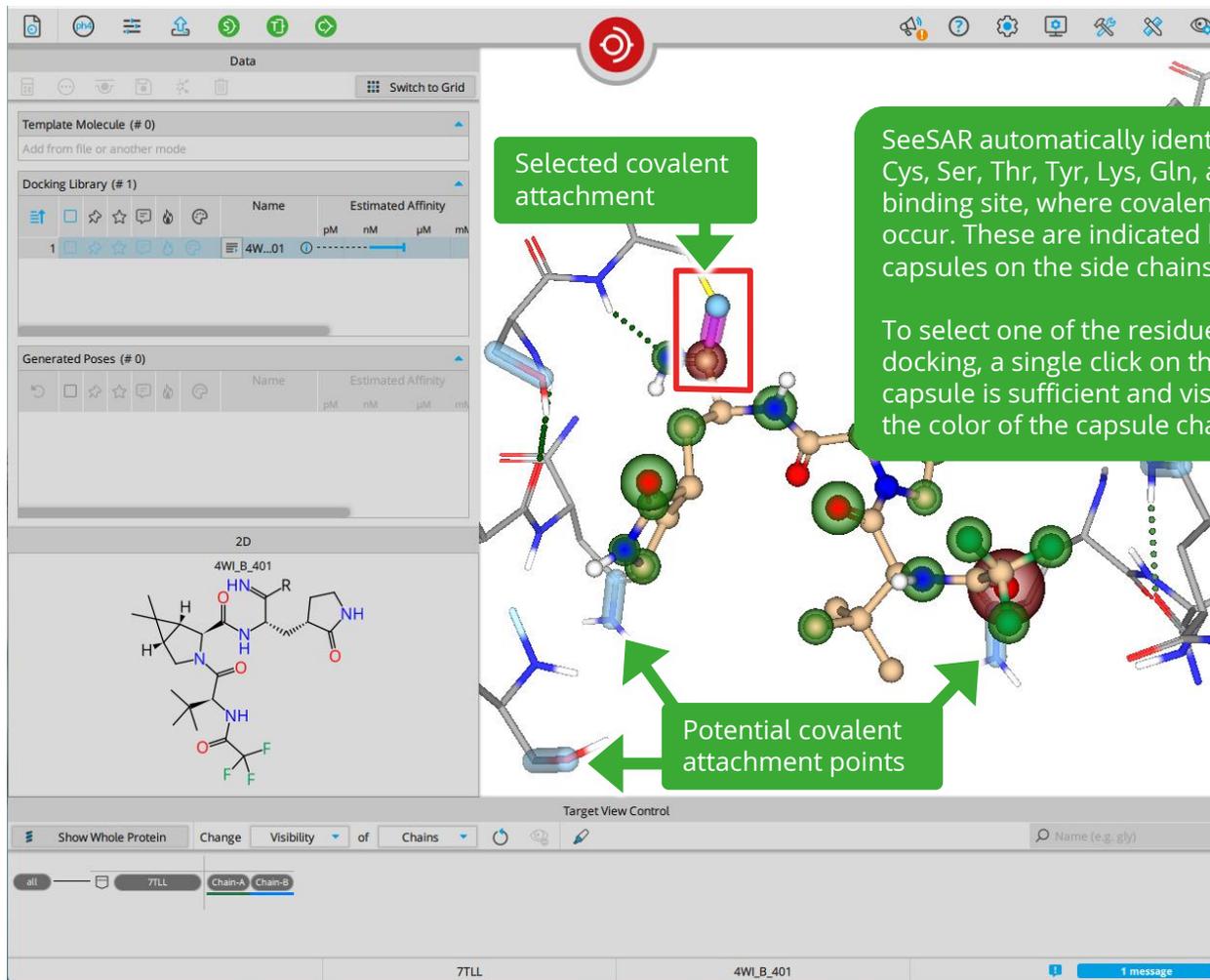
For this example, we will use the PDB 7TLL.

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

The screenshot displays a software interface for molecular docking. On the left, a 'Proteins' panel lists '7TLL'. Below it, a 'Ligand for 7TLL' panel shows '4WI_B_401' with a '2D' chemical structure view. A context menu is open over the 3D protein-ligand complex, with 'Add to Docking Mode' and 'on Your Local Machine' highlighted in red. The 'Target View Control' at the bottom shows a sequence of residues from 1 to 23, with 'SER1' selected. A green callout box on the right contains text explaining the docking mode and providing a reference for external docking.

After defining your ligand, transfer it to the Docking Mode.

This demo covers docking on a local machine. For external docking, follow similar steps and additionally refer the external docking section for details on usage.



	Name	Estimated Affinity				LLE	Tor.	Intra-clash	Inter-clash	FU
		pM	nM	µM	mM					
1	4WL_B_401									
2	Example									

Molecules without linker attachments can still be directly loaded into the docking library. Covalent docking automatically identifies warheads and modifies the ligands to attach a covalent linker.

In this demo, an example molecule with an acrylamide reactive group, without a linker, is loaded into the docking library.

For details on which reactive groups are transformed, refer the FlexX guide.

[Link to FlexX Guide](#)

The screenshot displays the docking software interface. A red box highlights the parameter settings panel on the left, which includes:

- Maximum Number of Poses: 10
- Clash Tolerance: Standard
- Allowed Ring Conformations: Standard
- Allow Stereo Center Flipping: Off
- Flexible Covalent Attachment:

The interface also shows a docking library, generated poses, and a 3D molecular model of the target protein and ligand. The target view control at the bottom indicates the binding site is shown for chain 7TLL.

The pharmacophore and docking parameters can be adjusted as usual. For covalent docking, the parameter "Flexible Covalent Attachment" becomes relevant. This allows the user to choose whether the terminal bond of the residue involved in covalent attachment should be rotatable. By default, it is set to flexible.

Once all the parameters are set, click the third green docking button for Covalent Docking to initiate the process.

Data

Switch to Grid

Template Molecule (# 0)

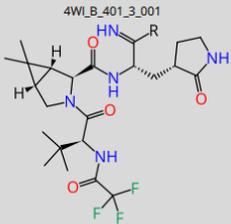
Docking Library (# 2)

Generated Poses (# 40)

	Name	Estimated Affinity				LLE	Tor.	Intra-clash	Inter-clash
		pM	nM	µM	mM				
1	4WL_B_3_001	----->	----->	----->	----->	👁	🟢	🟢	
2	4WL_B_401_4_001	----->	----->	----->	----->	👁	🟢	🟢	
3	4WL_B_401_3_003	----->	----->	----->	----->	👁	🟢	🟢	
4	4WL_B_401_4_003	----->	----->	----->	----->	👁	🟢	🟢	
5	4WL_B_401_3_004	----->	----->	----->	----->	👁	🟢	🟢	
6	4WL_B_401_4_004	----->	----->	----->	----->	👁	🟢	🟢	
7	4WL_B_401_3_009	----->	----->	----->	----->	👁	🟢	🟢	
8	4WL_B_401_4_009	----->	----->	----->	----->	👁	🟢	🟢	
9	4WL_B_401_3_002	----->	----->	----->	----->	👁	🟡	🟢	
10	4WL_B_401_4_002	----->	----->	----->	----->	👁	🔴	🟢	
11	4WL_B_401_3_006	----->	----->	----->	----->	👁	🔴	🟢	
12	4WL_B_401_4_006	----->	----->	----->	----->	👁	🔴	🟢	
13	4WL_B_401_3_005	----->	----->	----->	----->	👁	🟢	🟢	

2D

4WL_B_401_3_001



Target View Control

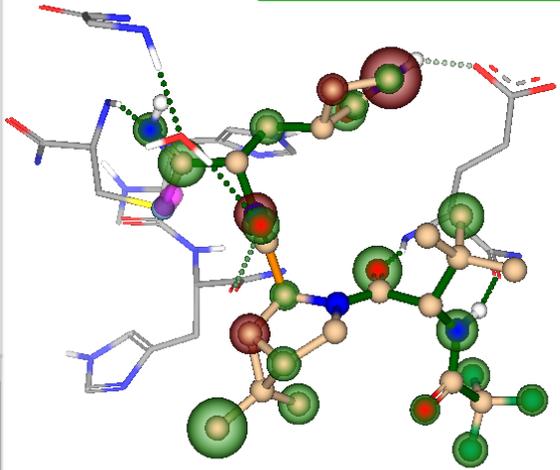
Show Whole Protein Change Visibility of Residues

Name (e.g. gly)

all 7TL 1 SER1 THR26 LEU27 PRO39 HIS41 CYS44 MET49 PRO52 TYR54 PHE140 LEU141 ASN142 GLY143 SER144 CYS145 GLY146 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 VAL171

7TL 4WL_B_401_3_001

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



Data

Switch to Grid

Template Molecule (# 0)

Docking Library (# 2)

Generated Poses (# 40)

		Name	Estimated Affinity				LLE	Tor.	Intra-clash	Inter-clash
			pM	nM	μM	mM				
14	<input type="checkbox"/>	4WI_B_401_4_005	-----	-----	-----	-----				
15	<input type="checkbox"/>	4WI_B_401_3_008	-----	-----	-----	-----				
16	<input type="checkbox"/>	4WI_B_401_4_008	-----	-----	-----	-----				
17	<input type="checkbox"/>	4WI_B_401_3_007	-----	-----	-----	-----				
18	<input type="checkbox"/>	4WI_B_401_4_007	-----	-----	-----	-----				
19	<input checked="" type="checkbox"/>	Exam..._008	-----	-----	-----	-----				
20	<input type="checkbox"/>	Example..._2_3_001	-----	-----	-----	-----				
21	<input type="checkbox"/>	Example..._1_4_006	-----	-----	-----	-----				
22	<input type="checkbox"/>	Example..._1_3_004	-----	-----	-----	-----				
23	<input type="checkbox"/>	Example..._1_3_008	-----	-----	-----	-----				
24	<input type="checkbox"/>	Example..._1_3_003	-----	-----	-----	-----				
25	<input type="checkbox"/>	Example..._1_4_005	-----	-----	-----	-----				
26	<input type="checkbox"/>	Example..._1_4_004	-----	-----	-----	-----				

2D

Example_Allylamide_UnsaturatedCarbons_1_4_008

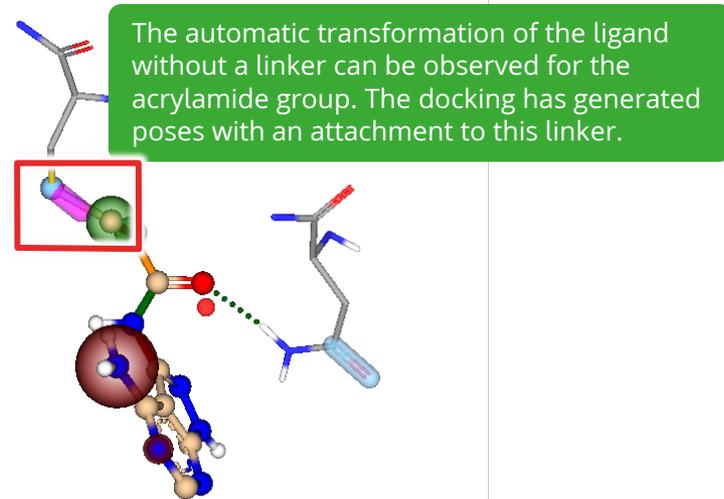
Target View Control

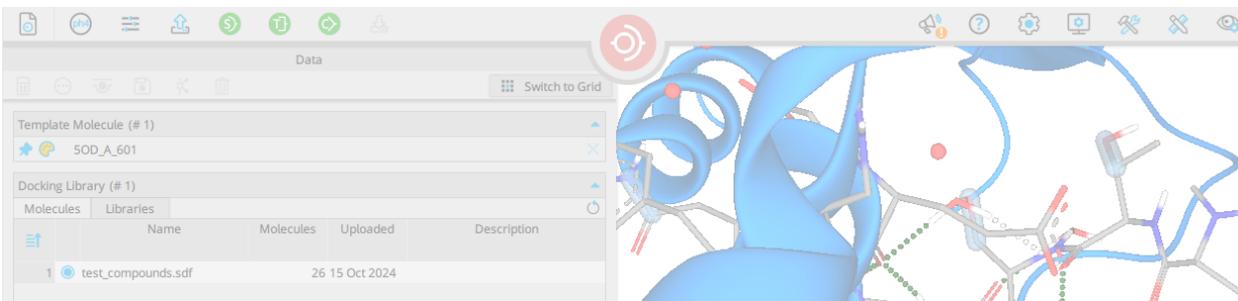
Show Whole Protein Change Visibility of Residues

Name (e.g. gly)

all 7TLL LEU141 ASN142 GLY143 SER144 CYS145 GLY146 HIS163 HIS164 MET165 GLU166 LEU167 PRO168 VAL171 HIS172 ALA173 PHE181 VAL186 ASP187 ARG188 GLN189 THR190 ALA191 GLN192

7TLL Example_Allylamide_UnsaturatedCarbons_1_4_008





5. External Docking

In this section, we present a new feature, a possibility to perform remote docking. For users who prefer not to run docking on their local machines, HPSee (a platform for High-Performance Computing, know more [here](#)) allows you to link SeeSAR to a remote high-performance computing system. Using this mode, you can initiate docking locally from SeeSAR and once completed, review and inspect the top results locally for visualization.

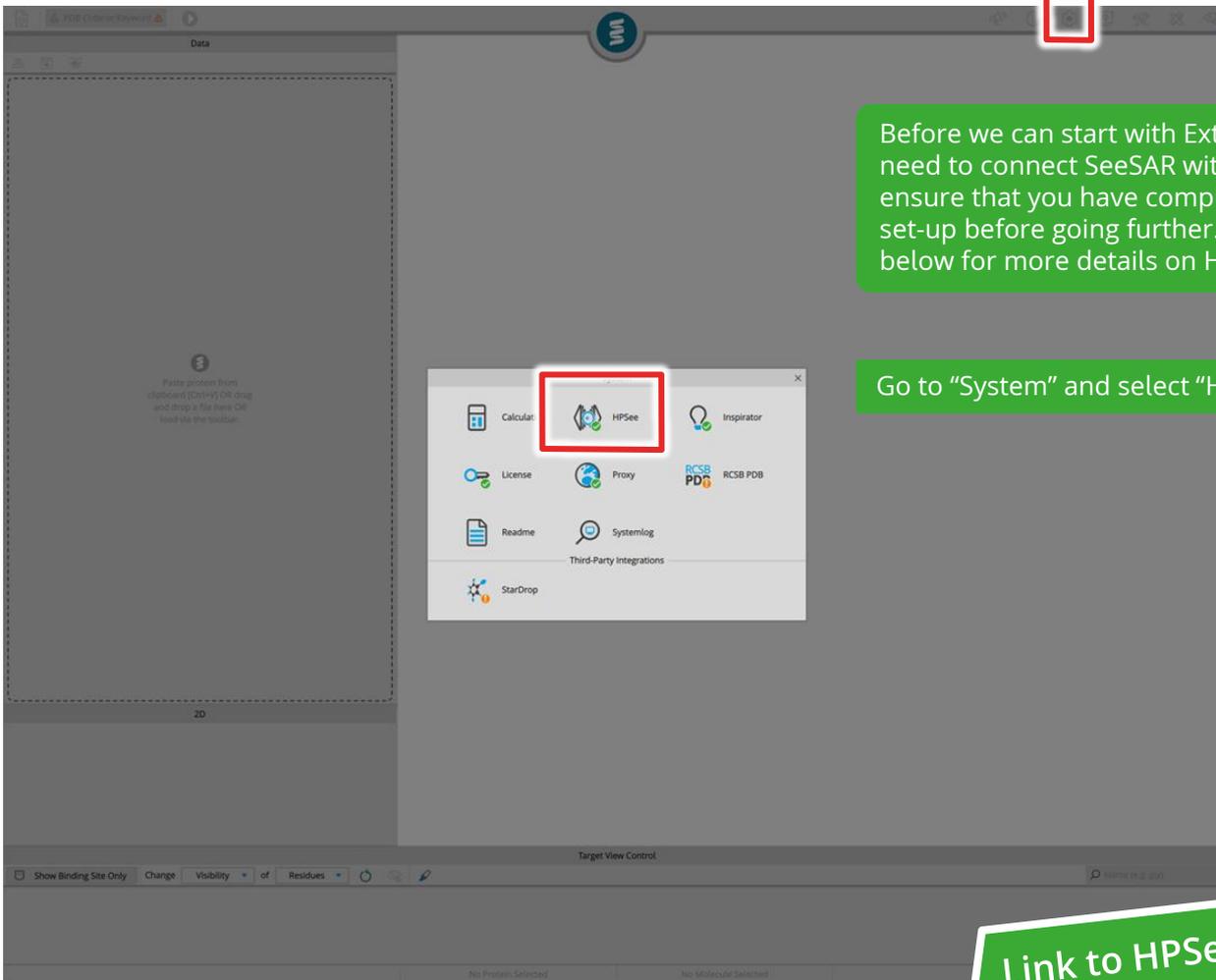
Name	Molecules	Uploaded	Description
Example 30_4_01			
Example 30_4_02			
Exam			
Exam			
6_4_0			
6_4_0			
Exam			

Target View Control

Show Binding Site Only Change Visibility of Residues Name (e.g. gly)

all SEHR ARG4 ARG5 TRP6 PHE7 HIS8 PRO9 ASN10 ILE11 THR12 GLY13 VAL14 GLU15 ALA16 GLU17 ASN18 LEU19 LEU20 LEU21 THR22 ARG23 GLY24 VAL25 ASP26

SEHR SHP099-1/Example 7_4_01 2 messages



Before we can start with External Docking, we need to connect SeeSAR with HPSee. Please ensure that you have completed your HPSee set-up before going further. Refer to the guide below for more details on HPSee.

Go to "System" and select "HPSee".

[Link to HPSee guide](#)

Type in your machine's hostname and port that you used while installing HPSee.

Provide user details. It must be previously created using the admin dashboard.

Test

Test to check validity of server and login credentials.

Successful

Click Apply.

Server version: 2.1.0
Server tools: **All tools are compatible with this SeeSAR version**
Licenses: **All licenses are valid**
User authentication: **Login successful.**

Successful

Server tools: **All tools are compatible with this SeeSAR version**
Licenses: **All licenses are valid**
User authentication: **Login successful.**

Successful

Servername: http://<hostname>
Port: <port>
Username: user1
Password:

Allow connections to insecure servers
 Save password

Back Apply

Back Apply

Back Apply

5EHR

Data

5EHR - Extract Your Ligand

Hetero Groups

	LOI	Name	Estimated Affinity			
			pM	nM	μ M	mM
1	<input type="radio"/>	Do not extract a ligand				
2	<input checked="" type="radio"/>	5OD_A_601		█		
3	<input type="radio"/>	PO4_A_602				
4	<input type="radio"/>	PO4_A_603				
5	<input type="radio"/>	PO4_A_604				
6	<input type="radio"/>	5OD_B_601				
7	<input type="radio"/>	PO4_B_602				
8	<input type="radio"/>	PO4_B_603				
9	<input type="radio"/>	PO4_B_604				

2D

5OD_A_601

Nc1nc(N2CCN(C)CC2)c3cc(Cl)c(Cl)cc13

Target View Control

Show Binding Site Only Change Visibility of Residues

Name (e.g. gly)

1 5 10 15 20

all SEHR ARG4 ARG5 TRP6 PHE7 HIS8 PRO9 ASN10 ILE11 THR12 GLY13 VAL14 GLU15 ALA16 GLU17 ASN18 LEU19 LEU20 LEU21 THR22 ARG23 GLY24 VAL25 ASP26

5EHR 5OD_A_601

To demonstrate External Docking, we will use the PDB 5EHR.

Extract 5OD_A_601 ligand from Chain A to define the binding site automatically.

The screenshot shows the SEHR software interface. A dropdown menu is open, listing several tools: Proteins, Binding Site, Protein Editor, Analyzer, Molecule Editor, Inspirator, Docking on an external server, and Space Docking. The 'Docking on an external server' option is highlighted with a red box and a mouse cursor. A green callout box on the right contains the text: "Access external docking mode by moving the cursor to the right on the 'Docking' mode icon until it displays 'on an external server.'" The background shows a 3D protein structure in blue with a red ligand docked in the binding site. The interface includes a 'Data' panel on the left with 'Proteins' and 'Ligand for SEHR' sections, and a 'Target View Control' panel at the bottom with a sequence viewer.

Proteins	Filename
1	SEHR

Ligand for SEHR	Name	Estimated Affinity
		pM nM μ M
1	SOD_A_601	

Target View Control

Show Binding Site Only Change Visibility of Residues

all SEHR ARG4 ARG5 TRP6 PHE7 HIS8 PRO9 ASN10 ILE11 THR12 GLY13 VAL14 GLU15 ALA16 GLU17 ASN18 LEU19 LEU20 LEU21 THR22 ARG23 GLY24 VAL25 ASP26

SEHR No Molecule Selected 1 message

The screenshot displays the SeeSAR software interface. The main window shows a protein structure in blue ribbon representation. On the left, there is a 'Data' panel with a 'Docking Library (# 0)' section highlighted by a red box. This section contains two sub-sections: 'Molecules' and 'Libraries'. Below these are two tables for 'Generated Poses (# 0)'. The bottom of the interface features a 'Target View Control' panel with a sequence viewer for protein 5EHR.

Molecules		Libraries		Name	Estimated Affinity				LLE	Tor.	Intra-clash
					pM	nM	µM	mM			

Generated Poses (# 0)		Name	Estimated Affinity				LLE	Tor.	Intra-clash
			pM	nM	µM	mM			

Target View Control

Show Binding Site Only | Change | Visibility | of | Residues | Name (e.g. gly)

all | SEHR | 1 | ARG4 | ARG5 | TRP6 | PHE7 | HIS8 | PRO9 | ASN10 | ILE11 | THR12 | GLY13 | VAL14 | GLU15 | ALA16 | GLU17 | ASN18 | LEU19 | LEU20 | LEU21 | THR22 | ARG23 | GLY24 | VAL25 | ASP26

5EHR | No Molecule Selected

The window resembles the local docking mode, but now the "Docking library" has two sections: "Molecules" and "Libraries."

"Molecules" refers to those molecules you load locally in SeeSAR, but you intend to start docking in the remote machine.

"Libraries" refers to the molecule library already uploaded to the HPSee server.

The pharmacophore and docking parameters can be modified as usual, with an additional docking parameter called "Maximum Number of Solutions." This defines how many top poses you wish to retrieve from the docking experiment.

Setting it to a specific number X will return the top X poses, while selecting "Max" retrieves up to 50 thousand poses, which is the maximum capacity allowed by the SeeSAR table.

The screenshot displays the HPSee software interface. On the left, a 'Data' panel contains a 'Docking Library (# 1)' table, which is highlighted with a red box. The table has columns for 'Name', 'Molecules', and 'Uploaded'. Below it is a 'Generated Poses (# 0)' table with columns for 'Name', 'Estimated Affinity', 'LLE', 'Tor.', and 'in clash'. The main area shows a 3D protein structure in blue ribbon representation with a red molecule docked in its binding site. At the bottom, a 'Target View Control' panel shows a sequence of residues from 1 to 26, with 'SEHR' selected at position 1. The status bar at the bottom indicates 'SEHR' and 'No Molecule Selected'.

Name	Molecules	Uploaded
test_compounds.sdf		26 15 Oct 2024

Name	Estimated Affinity	LLE	Tor.	in clash
------	--------------------	-----	------	----------

Target View Control

all — SEHR ARG4 ARG5 TRP6 PHE7 HIS8 PRO9 ASN10 ILE11 THR12 GLY13 VAL14 GLU15 ALA16 GLU17 ASN18 LEU19 LEU20 LEU21 THR22 ARG23 GLY24 VAL25 ASP26

SEHR No Molecule Selected

For this experiment, we will perform docking using the library already uploaded to the HPSee server.

Instructions on how to upload a library to HPSee are provided in the HPSee Guide

The screenshot displays the SEHR software interface. At the top, a red box highlights a circular icon with a stylized 'M' and 'S' inside. The main window is divided into several panels. On the left, the 'Proteins' panel shows a table with one entry: 'SEHR'. Below it, the 'Ligand for SEHR' panel shows a table with one entry: 'SOD_A_601'. A context menu is open over this entry, listing various actions such as 'Copy to Clipboard [Ctrl+C]', 'Calculate Estimated Affinity', 'Add to Binding Site Mode', 'Add to Analyzer', 'Add to Molecule Editor', 'Add to Inspirator', 'Add to Docking Mode', 'Add to Similarity Scanner', 'Use as Template', 'In Local Docking Mode', 'In External Docking Mode', 'In Space Docking Mode', and 'In Similarity Scanner'. Below the 'Ligand for SEHR' panel, a 2D chemical structure of the ligand is shown, featuring a benzene ring with two chlorine atoms, a pyridine ring, and a piperidine ring with a protonated nitrogen atom (NH₃⁺). On the right side of the interface, a 3D ribbon representation of the protein SEHR is shown in blue, with the ligand SOD_A_601 docked in its binding site, shown in green and red. A green callout box on the right contains the following text: 'You have the option to perform template docking by adding a template molecule. In this case, we'll use the co-crystallized ligand as the template. To do this, return to Proteins mode, right-click on the ligand, and select "Use as Template" and "in External Docking Mode."'.

The screenshot shows a software interface for molecular docking. A 'System' dialog box is open, titled 'Calculation - Define automatic calculations in frequently used workflows'. It contains a table of calculation options with checkboxes for each. The 'Generate External Docking Poses' option is highlighted with a red box and has all checkboxes checked and green. Other options include 'Load Molecules from File', 'Load Proteins', 'Save Editor Molecules to Table', 'Save Inspirator Molecules to Table', and 'Generate Similarity Scanner Poses'. The background shows a 3D molecular model of a protein and a docking library table.

Calculation	✓	✓	✓	✓	✓
Load Molecules from File	✗	✗	✗	✗	✗
Load Proteins	✗	✗	✗	✗	✗
Save Editor Molecules to Table	✗	✗	✗	✗	✗
Save Inspirator Molecules to Table	✗	✗	✗	✗	✗
Generate External Docking Poses	✓	✓	✓	✓	✓
Generate Similarity Scanner Poses	✗	✗	✗	✗	✗

Before starting the docking process, decide what type of results you would like to retrieve from the server: FlexX (docking only) or HYDE (docking and scoring).

Navigate to "System" and click on "Calculation." The "Generate External Docking Poses" option can be adjusted based on your preference. If you only want docking results, uncheck the boxes.

In this demo, we will retrieve both docked and scored results, so the check marks are enabled and green. Finally, click "Apply."

Template docking:
Generate poses based on template molecule

Template Molecule (# 1)
5OD_A_601

Docking Library (# 1)

Molecules	Libraries	Name	Molecules	Uploaded	Description
1	<input checked="" type="radio"/>	t_compounds.sdf		26 15 Oct 2024	

Estimated Affinity: μM LLE Tor. In clash

Target View Control

Show Binding Site Only Change Visibility of Residues

all SEHR ARG4 ARG5 TRP6 PHE7 HIS8 PRO9 ASN10 ILE11 THR12 GLY13 VAL14 GLU15 ALA16 GLU17 ASN18 LEU19 LEU20 LEU21 THR22 ARG23 GLY24 VAL25 ASP26

SEHR No Molecule Selected

At this stage, ensure you “Save” the SeeSAR project file before initiating docking.

Once the run begins, you may close the SeeSAR project and later reopen to monitor the progress or download the results.

Once the template and all parameters are set, and the docking library is selected using the radio button, click the second green docking button: Template Docking.

This will initiate the process, and the progress can be tracked in SeeSAR via the progress bar.

Docking in Progress (33%)

Download and delete results from server

Template Molecule (# 1)
5OD_A_601

Docking Library (# 1)

Molecules	Libraries	Name	Molecules	Uploaded	Description
1		test_compounds.sdf		26 15 Oct 2024	

Generated Poses (# 0)

Name	Estimated Affinity	LLE	Tor.	in clash
	pM nM μ M mM			

2D

Target View Control

Show Binding Site Only Change Visibility of Residues Name (e.g. gly)

all SEHR ARG4 ARG5 TRP6 PHE7 HIS8 PRO9 ASN10 ILE11 THR12 GLY13 VAL14 GLU15 ALA16 GLU17 ASN18 LEU19 LEU20 LEU21 THR22 ARG23 GLY24 VAL25 ASP26

SEHR No Molecule Selected 1 message

When the run is finished, the "Download Results" button will appear. Be aware that you can only download your results once, and after downloading, all results on the server will be deleted. Click the button to proceed.

The screenshot displays a molecular docking software interface. On the left, there is a sidebar with several panels:

- Data**: Contains a "Template Molecule (# 1)" section with "SOD_A_601" and a "Docking Library (# 1)" section with a table of molecules.
- Generated Poses (# 250)**: A table listing 11 poses with columns for Name, Estimated Affinity (pM, nM, μM, mM), LLE, Tor., and In clash.
- 2D**: Shows a chemical structure for "SHP099-1/Example 7_4_01".
- Target View Control**: A sequence viewer showing residues from 1 to 26, with "SEHR" highlighted.

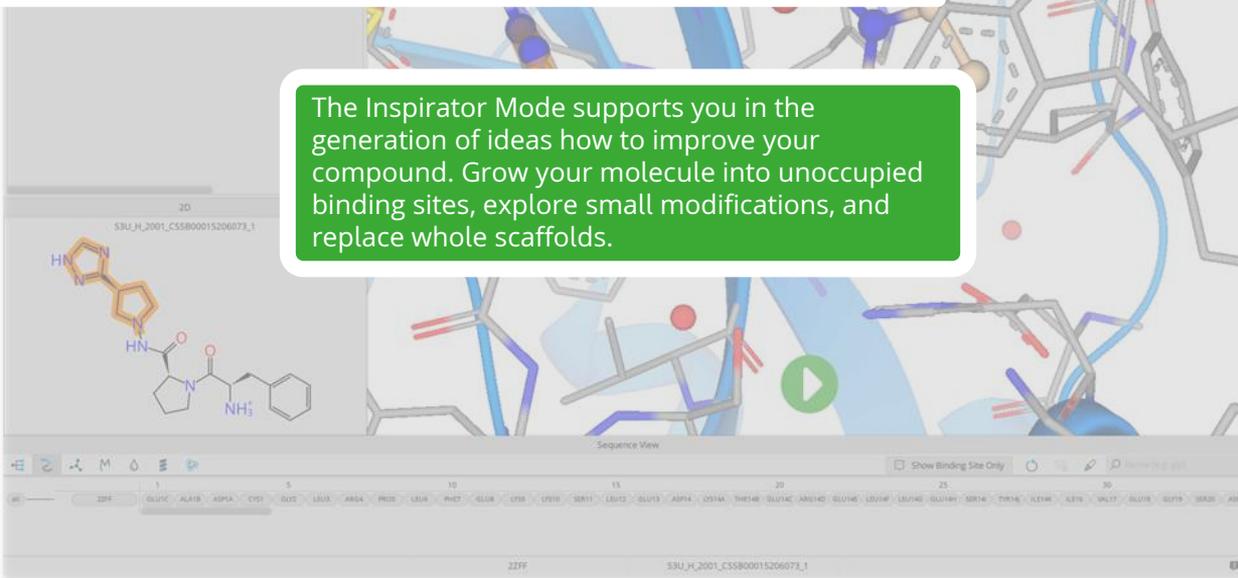
The main window shows a 3D visualization of a protein structure (blue ribbon) with a docked ligand (green and yellow spheres). A green callout box on the right contains the text: "The visualization options for poses are similar to those in local docking mode. You can color the molecules, including the template, or move the poses to Analyzer mode."

Another green callout box at the bottom right contains the text: "The External mode also supports standard and covalent docking. Similar procedures can be followed for these types of docking."



6. 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

2ZFF - Extract Your Ligand

Hetero Groups

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

2D

53U_H_2001

Sequence View

Show Binding Site Only

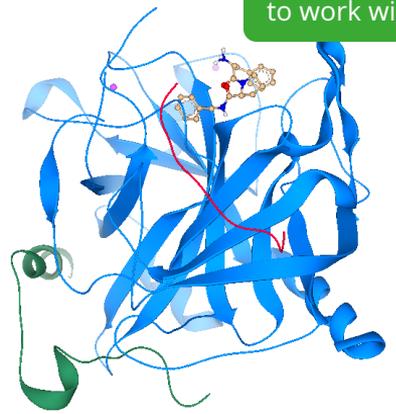
Name (e.g. gly)

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 '2D' showing the chemical structure of '53U_H_2001'. The main window shows a 3D ribbon representation of a protein in blue with a ligand in orange and red sticks. 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: 1 Z2FF, 5 GLU1C ALA1B ASP1A CYS1, 10 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11, 15 LEU12 GLU13 ASP14 LYS14A THR14B ARG14C ARG14D, 20 GLU14E LEU14F LEU14G LEU14H SER14, 25 TYR14 ILE14K ILE16, 30 VAL17 GLU18 GLY19 SER20 ASP21. The bottom status bar shows 'Z2FF' and '53U_H_2001'.

Protein	Filename
1	Z2FF

Ligand	Name	Estimated Affinity
		pM nM μ M mM
53U_H_201	Calculate Estimated Affinity	
	Add to Binding Site Mode	
	Add to Analyzer	
	Add to Molecular Editor	
	Add to Inspirator	
	Add to Docking Mode	
	Add to Similarity Scanner	

2D
53U_H_2001

Sequence View
Show Binding Site Only

1 Z2FF 5 GLU1C ALA1B ASP1A CYS1 10 GLY2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 15 LEU12 GLU13 ASP14 LYS14A THR14B ARG14C ARG14D 20 GLU14E LEU14F LEU14G LEU14H SER14 25 TYR14 ILE14K ILE16 30 VAL17 GLU18 GLY19 SER20 ASP21

Z2FF 53U_H_2001

Transfer your ligand to the Inspirator Mode.

The screenshot displays the BioSolveIT software interface. At the top, a toolbar contains several icons, with a red box highlighting a group of four icons: a vertical bar with an upward arrow, a chain link, a plant, and a green 'W' in a circle. A large green callout box on the right states: "The Inspirator Mode features several tools and applications to generate ideas how to improve your compound or to find novel scaffolds." Below this, four smaller green callout boxes point to specific icons in the toolbar: "Linking&Merging: Connects two fragments" points to the chain link icon; "MedChemesis: Creates a series of analogs" points to the plant icon; "ReCore: Replaces scaffolds" points to the vertical bar with an upward arrow icon; and "FastGrow: Grows into binding pockets" points to the green 'W' icon. The main workspace shows a 3D molecular model of a protein-ligand complex. At the bottom, a 2D chemical structure of the ligand is shown, and a sequence view of the protein is visible at the very bottom.

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

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, 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 amino acid residues from 1 to 30.

Name	Estimated Affinity			
	pM	nM	µM	mM
S3U_H_2001				

2D
S3U_H_2001

Sequence View

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 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. gln)

22FF

1 5 10 15 20 25 30

GLU1C ALA1B ASP1A CYS1 GLU2 LEU3 ARG4 PRO5 LEU6 PHE7 GLU8 LYS9 LYS10 SER11 LEU12 GLU13 ASP14 LYS14A THR14B GLU14C ARG14D GLU14E LEU14F LEU14G LEU14H SER14I THR14J 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

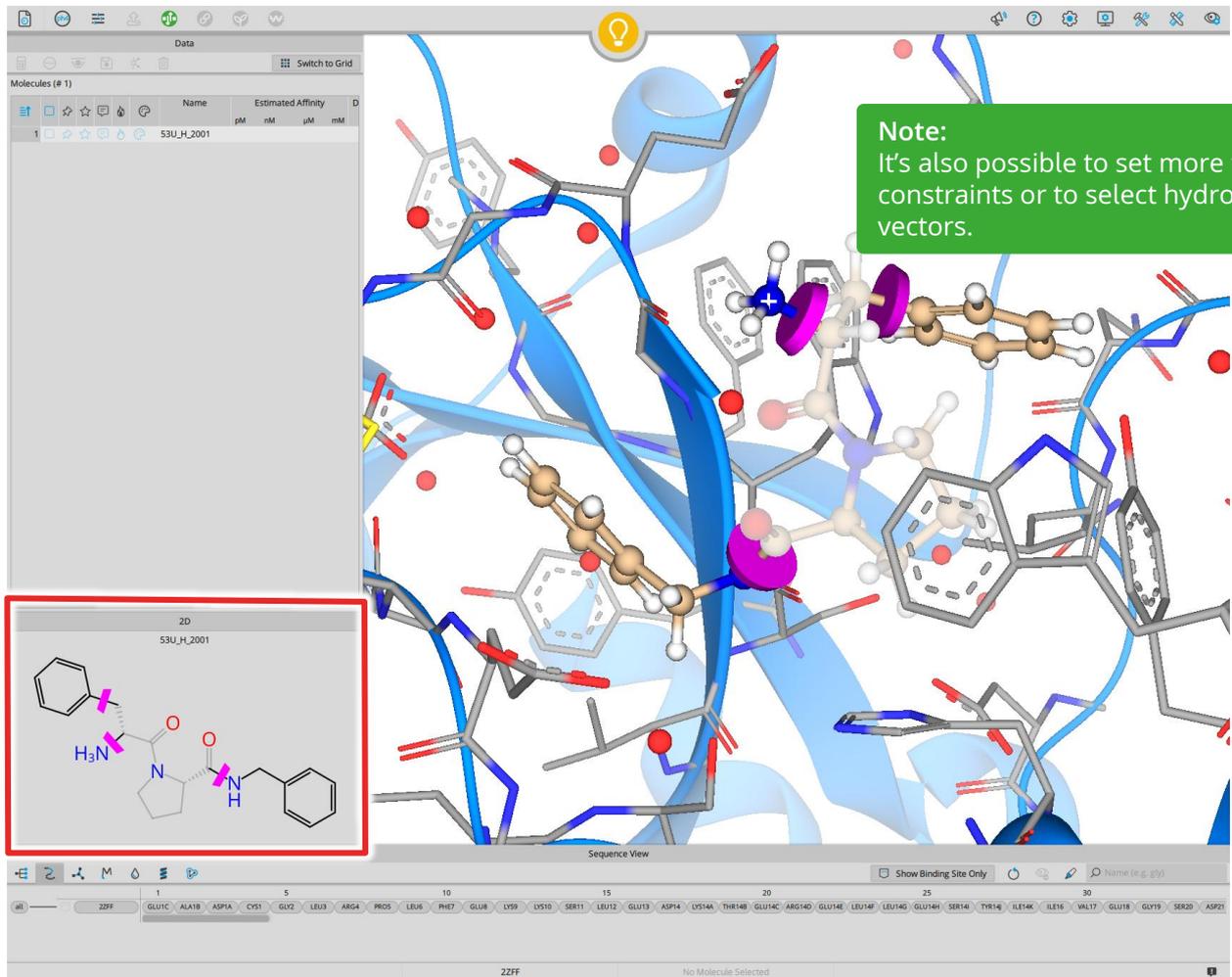
Show Binding Site Only

Name (e.g. gly)

10 15 20 25 30

G4 PROS 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

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
 ASP14 LYS146 THR148 GLU148 ARG140 LEU148 LEU148 LEU148 LEU148 SER148 TYR148 ILE148 ILE16 VAL17 GLU18 GLY19 SER20 ASP21

No Molecule Selected

The screenshot displays a molecular docking software interface. On the left, a 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 S3U_H_2001_CSSB00015206073_1 is shown, featuring a quinoline ring system connected to a piperidine ring, which is further linked to a benzamide derivative. The main 3D view shows a protein binding site (blue ribbon) with a ligand (orange and blue sticks) docked inside. A green play button is visible in the 3D view. At the bottom, a sequence viewer 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, 37 22FF, 38 S3U_H_2001_CSSB00015206073_1.

	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.

The screenshot displays the SeeSAR software interface. The main window shows a 3D molecular docking simulation of a ligand (orange and blue) bound to a protein (blue ribbon). The interface includes several panels:

- Molecules (# 11) Table:** A table listing 11 molecules with their names and estimated affinities. The table is highlighted with a red border.
- 2D Panel:** Shows the chemical structure of the selected molecule, S3U_H_2001_CSSB00015206073_1.
- Sequence View:** Shows the protein sequence with residues 1 to 30 visible.

Molecules (# 11)

ID	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

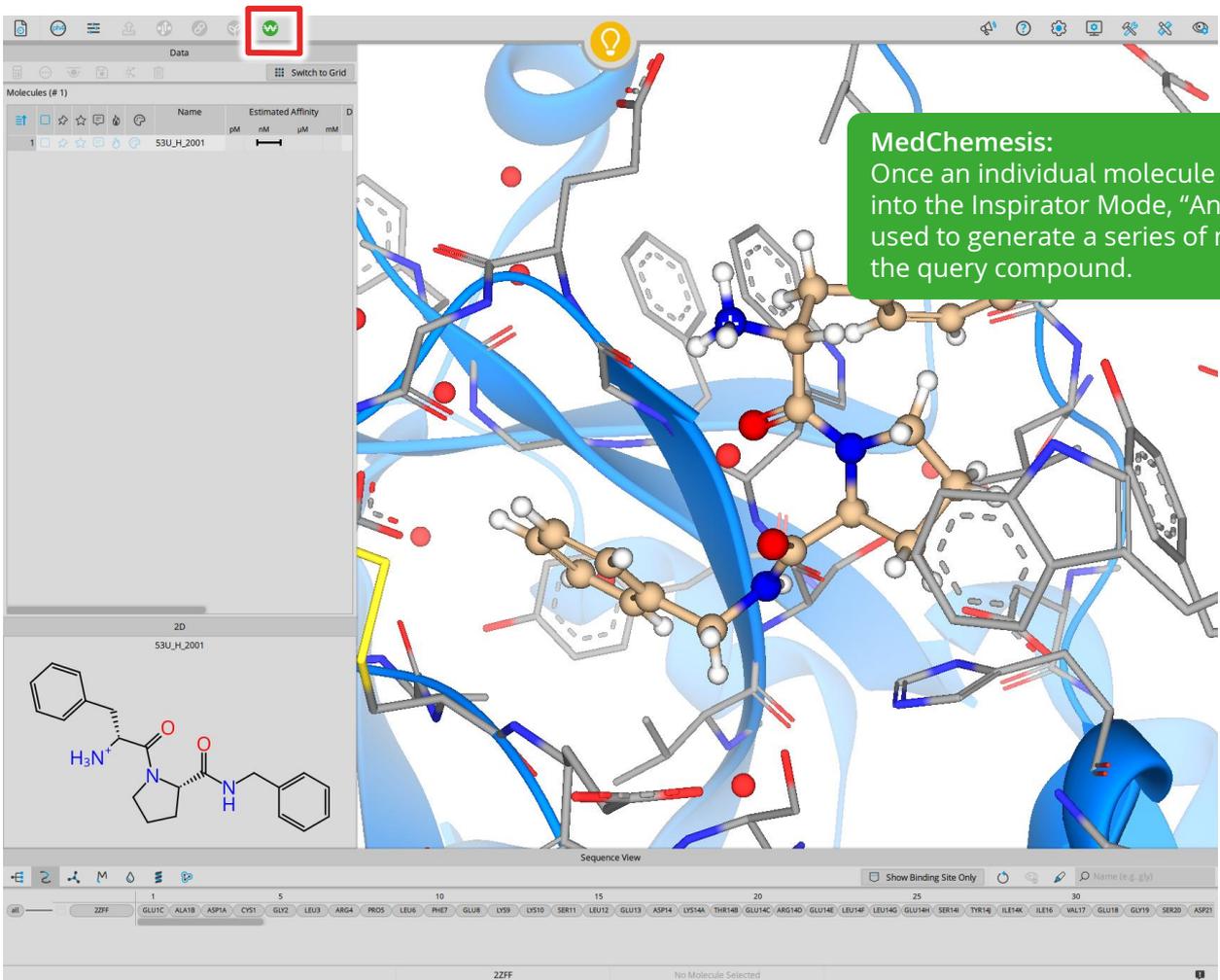
Show Binding Site Only

2ZF

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](#)



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.

Molecules (# 11)		Checked (# 11)		Switch to Grid	
	Name	Estimated Affinity			D
		pM	nM	μM	mM
1	S3U_H_2001				
2	S3U_H_1_2				
3	S3U_H_2_2_2				
4	S3U_H_3_3_2				
5	S3U_H_4_4_2				
6	S3U_H_5_5_2				
7	S3U_H_6_6_2				
8	S3U_H_7_7_2				
9	S3U_H_8_8_2				
10	S3U_H_9_9_2				
11	S3U_H_10_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

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".

2D chemical structures shown:
NC(Cc1ccccc1)C(=O)O
NCCc1ccccc1

Sequence View: 22FF, 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

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 (O) and a nitrogen atom (N) labeled '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".

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
```

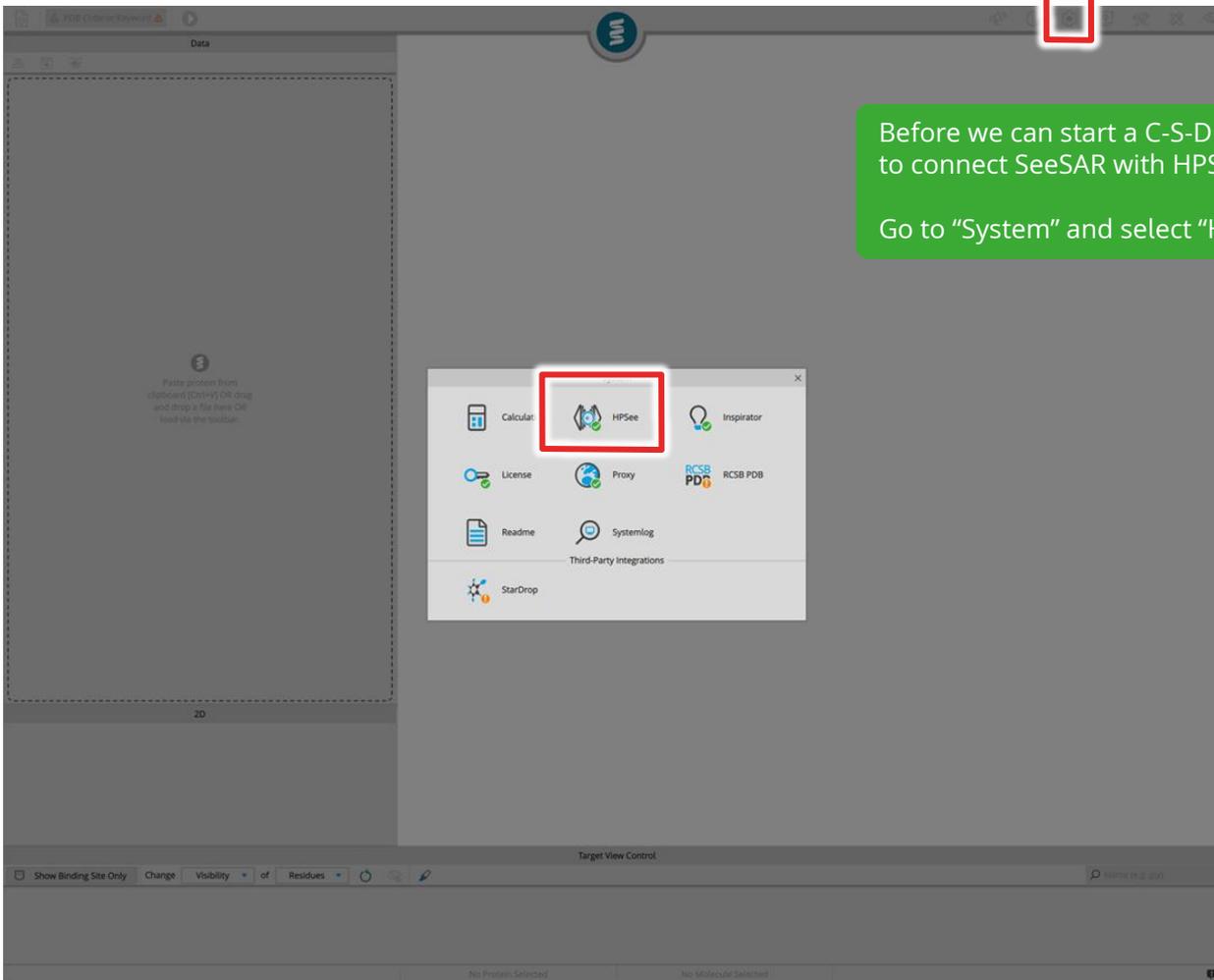
The screenshot displays a molecular docking software interface. On the left, the 'Molecules (# 2)' panel lists 'Efavirenz' and 'Etravirine', with 'Efavirenz' selected. A red box highlights a play button icon in the top toolbar. Below the molecule list, the 'Generated Poses (# 0)' panel is empty. At the bottom left, a 2D chemical structure of Efavirenz is shown. The main workspace features a 3D ball-and-stick model of the Efavirenz molecule, with a red box highlighting a play button icon in the top toolbar. Two green callout boxes provide instructions: the first points to the play button and says 'Select a ligand (in this case Efavirenz) as a template in the molecule window. Generate alignment poses with the play button.'; the second points to the 3D model and says 'You can add pharmacophore constraints and adjust the screening parameters as well.'

Select a ligand (in this case Efavirenz) as a template in the molecule window. Generate alignment poses with the play button.

You can add pharmacophore constraints and adjust the screening parameters as well.

The screenshot displays a software interface for molecular docking. At the top, a 'Data' panel lists two molecules: Efavirenz and Etravirine. Below it, a 'Generated Poses (# 1)' panel is highlighted with a red border, showing a single pose named 'Etrav-e_1_1' with a similarity rating of four stars. To the right, a 3D ball-and-stick model of the Etravirine molecule is shown. At the bottom, a 'Sequence View' panel displays the chemical structure of Etravirine_1_1. The interface includes various toolbars and a status bar at the bottom indicating 'No Protein Selected' and 'Etravirine_1_1'.

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



Before we can start a C-S-D workflow, we need to connect SeeSAR with HPSee.

Go to "System" and select "HPSee".

Type in your machine's hostname and port that you used while installing HPSee.

Provide user details. It must be previously created using the admin dashboard.

Test

Test to check validity of server and login credentials.

Server version: 2.1.0

Server tools: **All tools are compatible with this SeeSAR version**

Licenses: **All licenses are valid**

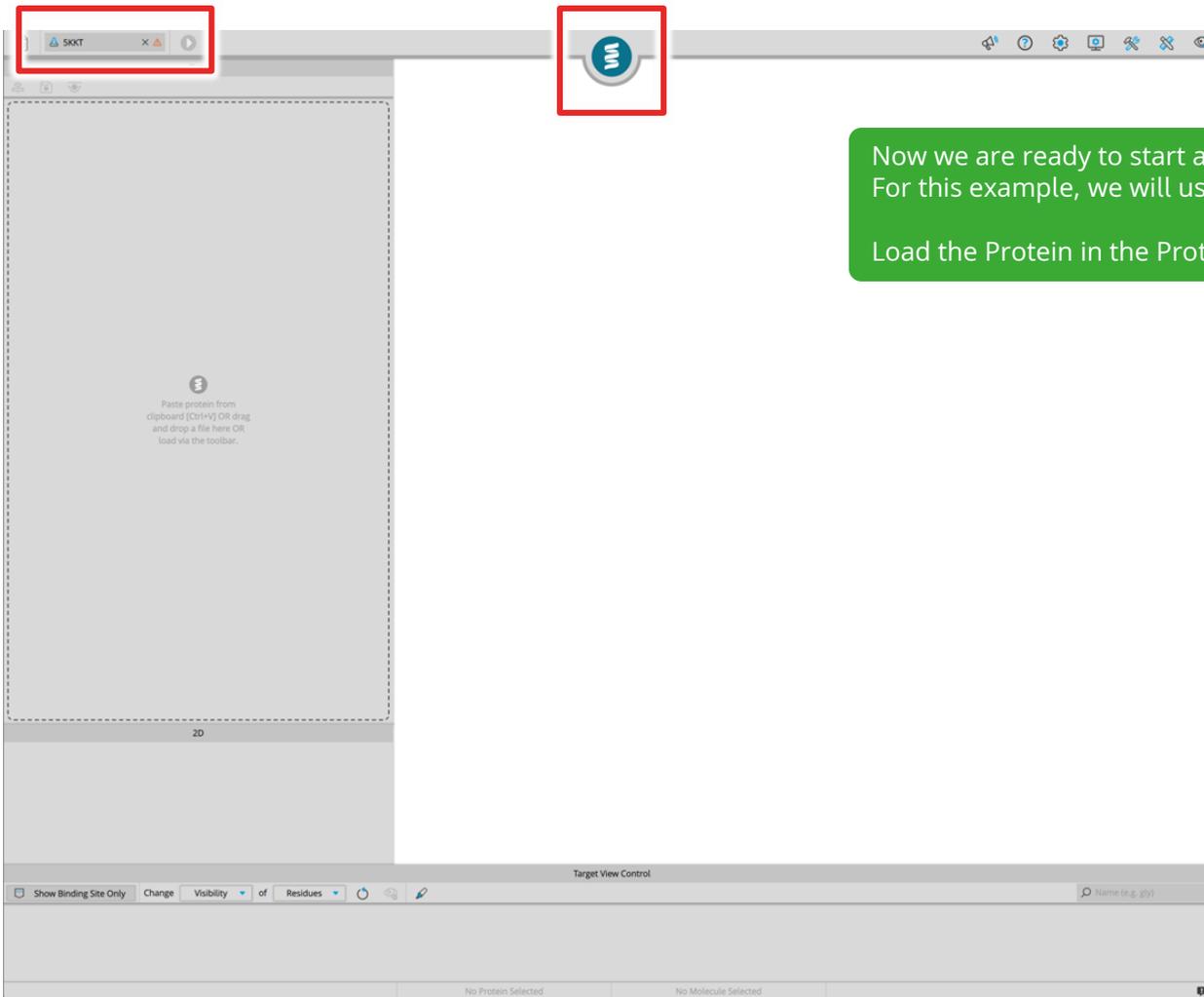
User authentication: **Login successful.**

Successful Back Apply

Successful Back Apply

Click Apply.

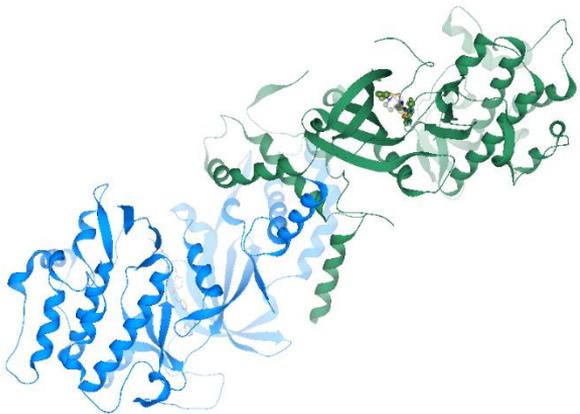
The image shows a software configuration window titled "HPSee - Server Connectivity" with a "User Authentication" tab. It contains input fields for "Servername" (http://<hostname>), "Port" (<port>), "Username" (user1), and "Password" (masked with dots). There are two checked checkboxes: "Allow connections to insecure servers" and "Save password". A "Test" button is located to the right. Below the form, a success message is displayed in a light gray box with a green bar at the bottom that says "Successful". This message includes the text: "Server version: 2.1.0", "Server tools: All tools are compatible with this SeeSAR version", "Licenses: All licenses are valid", and "User authentication: Login successful." Below the message are "Back" and "Apply" buttons. A red box highlights the success message area. Green callout boxes provide instructions and feedback. One callout points to the "Test" button, another points to the "Apply" button, and a third points to the success message. The background shows a blurred interface with a "Data" tab and a "Show Binding Site Only" checkbox.



Now we are ready to start a C-S-D run.
For this example, we will use 5KKT as PDB.
Load the Protein in the Protein Mode.

SKKT - Extract Your Ligand

EPN	Name	Estimate of Affinity
1	Do not extract a ligand	
2	6U2_A_501	
3	6U2_A_501	



2D
6U2_A_501

C1CCN(C1)CCOC2=CC=C(C=C2)CC(=O)Nc3nc4c(ncn4)C5=CC=CC=C53

Target View Control

Show Binding Site Only Change Visibility of Residues

1 5 10 15 20 25 30

SKKT SKR1 PHE7 GLU8 THR8 ARG10 PHE11 GLU12 LYS13 MET14 ASP15 ASN16 LEU17 LEU18 ARG18 ASP20 PRO21 LYS22 SER23 GLU24 VAL25 ASN26 SER27 ASP28 CYS29 LEU30 LEU31 ASP32 GLY33 LEU34 ASP35 ALA36 LEU37 VAL38 TYR39

SKKT 6U2_A_501

Select the first ligand and confirm your binding site.

The screenshot displays the SKKT software interface. A menu overlay is visible, listing various tools: Proteins, Analyzer, Similarity Scanner, Binding Site, Molecule Editor, Protein Editor, Inspirator, Docking, and Space Docking. The 'Space Docking' option is highlighted with a green callout box that says "Switch to Space Docking Mode." The background shows a protein structure in blue and green ribbon representation. The interface includes a 'Data' panel on the left with a 'Proteins' table and a 'Ligand for SKKT' table. The 'Target View Control' panel at the bottom shows a sequence of residues from 1 to 30.

Filename
SKKT

Name	Estimated Affinity		
	pM	nM	pM
EU2_A_501			

Target View Control

Show Binding Site Only | Change | Visibility | of | Residues |

1 5 10 15 20 25 30

SKKT SKN PHE7 GLU8 THR8 ARG10 PHE11 GLU12 LYS13 MET14 ASP15 ASN16 LEU17 LEU18 ARG18 ASP20 PRO21 LYS22 SER23 GLU24 VAL25 ASN26 SER27 ASP28 CYS29 LEU30 LEU31 ASP32 GLY33 LEU34 ASP35 ALA36 LEU37 VAL38 TYR39

SKKT No Molecule Selected 1 message

The screenshot shows a molecular docking software interface. At the top, there is a 'Data' panel with a dropdown menu labeled 'Template or Reference Molecule (# 0)' and the text 'Add from file or another mode'. A red box highlights this dropdown, and a green arrow points to it. The main view shows a protein structure in green and blue, with a molecule in grey and red. At the bottom, there is a 'Target View Control' panel with a search bar and a sequence viewer showing residues from 1 to 20. The sequence viewer shows residues: SIKT, SER6, PHE7, GLU8, THR9, ARG10, PHE11, GLU12, LYS13, MET14, ASP15, ASN16, LEU17, LEU18, ARG19, ASP20, PRO21, LYS22, SER23, GLU24, VAL25, ASN26, SER27, ASP28.

You now have a choice to either perform "Template CSD" or a "Standard CSD".

- "Template CSD" will place the anchor fragment in reference to the "Template Molecule".
- "Standard CSD" explores the binding site freely to find the best possible pose to bind the anchor fragments.

If you choose to perform a "Standard CSD", skip the next slide and continue the demo. If you choose to perform a "Template CSD", the next slide shows how to add one.

"Template Docking"

The extracted ligand from PDB can be used as a "Template Molecule" in this demo.

Go to "Protein Mode" and right-click on the ligand and choose the option "Use as Template in Space Docking Mode".

You could also load an SDF directly in 'Space Docking' mode.

Ligand for SKKT				
Name	Estimated Affinity			
	pM	nM	µM	mM
6U2_A_501				

2D
6U2_A_501

Target View Control

Show Binding Site Only Change Visibility of Residues

1 5 10 15 20 25 30

SKKT SKKT 6U2_A_501

"Template Docking"

Template or Reference Molecule (# 1)
6U2_A_501

You should see your "Template Molecule" in this box, if you decide to perform a "Template CSD".

"Template Molecule is displayed in 3D after its import to the Space Docking Mode. You can remove visibility or change color using from the table.

Target View Control

Show Binding Site Only Change Visibility of Residues Name (e.g. gly)

all	1	5	10	15	20																		
SKKT	SER6	PHE7	GLU8	THR9	ARG10	PHE11	GLU12	LVS13	MET14	ASP15	ASN16	LEU17	LEU18	ARG19	ASP20	PRO21	LVS22	SER23	GLU24	VAL25	ASN26	SER27	ASP28

5KKT ROCK1-test-space No Molecule Selected 2 messages

"Template Docking"

You can remove the "Template Molecule" here.

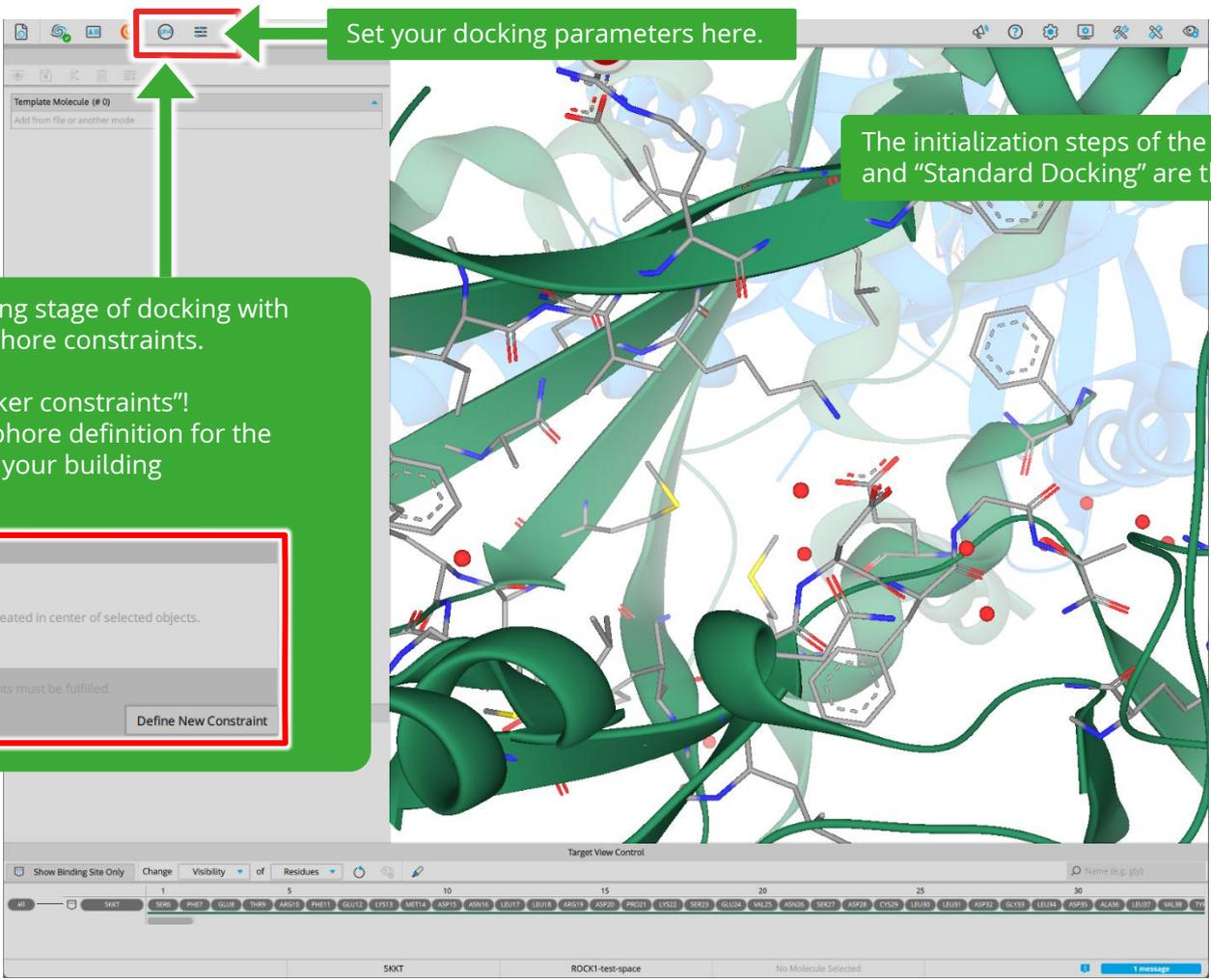
If you want to continue with the "Template Molecule", keep it in the table and continue with the next slides of "Standard Docking".

Target View Control

Show Binding Site Only Change Visibility of Residues Name (e.g. gly)

1	5	10	15	20
all	SKKT	SER6 PHE7 GLU8 THR9 ARG10 PHE11 GLU12 LYS13 MET14 ASP15 ASN16 LEU17 LEU18 ARG19 ASP20 PRO21 LYS22 SER23 GLU24 VAL25 ASN26 SER27 ASP28		

SKKT ROCK1-test-space No Molecule Selected 2 messages



Set your docking parameters here.

The initialization steps of the "Template Docking" and "Standard Docking" are the same.

Guide your Anchoring stage of docking with desired pharmacophore constraints.

Hint: Check out "linker constraints"!
This is a pharmacophore definition for the extension vector of your building blocks/synthons.

Define Pharmacophore

New spheres will be created in center of selected objects.

At least 0 optional constraints must be fulfilled.

Define New Constraint

Start Anchoring step of CSD.

- \$ button lets you perform a standard docking of anchors in CSD.
- T button can be used for template-based docking in anchoring step of CSD.

This guide will follow a standard CSD.

Target View Control

Show Binding Site Only Change Visibility of Residues Name (e.g. gly)

1	5	10	15	20
all	SKKT	SER6 PHE7 GLU8 THR9 ARG10 PHE11 GLU12 LYS13 MET14 ASP15 ASN16 LEU17 LEU18 ARG19 ASP20 PRO21 LYS22 SER23 GLU24 VAL25 ASN26 SER27 ASP28		

SKKT ROCK1-test-space No Molecule Selected 2 messages

Terminate a running workflow.

Please ensure you "Save" the SeeSAR project file after initiating CSD.

Once the run begins, you may close the SeeSAR project and later reopen to monitor the progress or download the results to proceed to next steps.

Important hint

Progress bar at top can be used to monitor.

Docking in Progress (16%)

After the run is complete, click on 'View Results' to access Anchoring results.

View Results

The screenshot displays the SeeSAR software interface. At the top, a toolbar contains a progress bar labeled 'Anchoring' with a play button and a red box around it. Below the progress bar, a status box shows 'Docking in Progress (37%)' with a red 'X' icon. A green arrow points from the 'Terminate a running workflow.' text to this status box. In the center, a 3D molecular model shows a protein structure in green and blue, with a ligand molecule in grey and red. A green box with a red border highlights the 'Docking in Progress (16%)' progress bar at the top. Another green box with a red border highlights the 'View Results' button at the bottom. Below the molecular model, the 'Target View Control' panel is visible, showing a residue list with columns for residue number (1, 5, 10, 15, 20) and residue name (SER6, PHE7, GLU8, THR9, ARG10, PHE11, GLU12, LYS13, MET14, ASP15, ASN16, LEU17, LEU18, ARG19, ASP20, PRO21, LYS22, SER23, GLU24, VAL25, ASN26, SER27, ASP28). The bottom status bar shows '5KKT', 'ROCK1-test-space', 'No Molecule Selected', and '2 messages'.

The screenshot shows a software interface for molecular docking. On the left, a table lists fragments with their estimated affinities. A green arrow points to the '+' icon next to fragment #E26_4. Below the table is a 2D chemical structure of a pyrazole ring with an 'R' group. The main part of the interface is a 3D visualization of a protein (green ribbon) with a ligand (grey sticks) and a light-blue dummy atom (a cluster of green spheres). A red box highlights this dummy atom. At the bottom, a 'Target View Control' bar shows a sequence of residues: SKKT, SER6, PHE7, GLU8, THR9, ARG10, PHE11, GLU12, LYS13, MET14, ASP15, ASN16, LEU17, LEU18, ARG19, ASP20, PRO21, LYS22, SER23, GLU24, VAL25, ASN26, SER27, ASP28.

Torsion and clash filters are applied automatically. The results are sorted based on LE.

Click "+" to select fragments for the Extension step.

Visualize your anchor fragment to the right in 3D. Optionally compare it with respect to your "Template Molecule".

For this run, 142 poses were generated. Visually assess them for their binding modes. Keep in mind that the **light-blue dummy atom** is the **extension vector** for this synthon: All built-up molecules will grow from it. If it points towards an undesired area (e.g., solvent-exposed lumen or a binding site you do not want to fill), do not pick this pose for the next step.

Important hint

Change filters as desired.

Visualization shows feasible extension directions from the linker atom of the fragments in the next step.

Target View Control

all — SKKT — SER6 — PHE7 — GLU8 — THR9 — ARG10 — PHE11 — GLU12 — LYS13 — MET14 — ASP15 — ASN16 — LEU17 — LEU18 — ARG19 — ASP20 — PRO21 — LYS22 — SER23 — GLU24 — VAL25 — ASN26 — SER27 — ASP28

SKKT ROCK1-test-space #E15_3 3 messages

Data

Template or Reference Molecule (# 1)
6U2_A_501

Fragments on Server: (# 113) Results on Server (# 0)

	Name	Estimated Affinity				LLE
		pM	nM	μM	mM	
13	#E17_5					
14	#E15_3					
15	#E29_5					
16	#E7_2					
17	#E29_3					
18	#E13_3					
19	#E16_2					

1 / 2

Fragments: (# 4)

	Name	Estimated Affinity				LLE	Tc
		pM	nM	μM	mM		
1	#E21_2						
2	#E23_2						
3	#E26_4						
4	#E15_3						

2D

#E15_3

RNc1ccc(R)cc1

After selection of the desired fragments, start the extension step by clicking this button.

The screenshot displays a molecular docking software interface. The main view shows a protein structure in green ribbon representation with a ligand molecule docked in a binding pocket. The interface includes a 'Data' panel on the left with two tables of fragment information, a 'Target View Control' at the bottom, and a '2D' view of a selected fragment.

Table 1: Fragments on Server (# 142)

#	Name	Estimated Affinity	LLE	Tor.	Intra-clash	Inter-clash
		pM	nM	μM	mM	
21	#E31_3					
22	#E29_1					
23	#E29_3					
24	#E51_5					
25	#E51_3					
26	#E51_1					
27	#E43_2					

Table 2: Fragments (# 6)

#	Name	Estimated Affinity	LLE	Tor.	Intra-clash	Inter-clash	M
		pM	nM	μM	mM		
1	#E48_4						11
2	#E30_2						11
3	#E49_3						11
4	#E45_2						11
5	#E51_5						11
6	#E43_2						11

2D View: #E43_2
C1=CN=C(C=C1)R

Target View Control: Show Binding Site Only | Change Visibility of Residues | 1 5 10 15 20 25 30 | SKKT SRP PHE7 GLU8 THR8 ARG10 PHE11 GLU12 LYS13 MET14 ASP15 ASN16 LEU17 LEU18 ARG18 ASP20 PRO11 LYS22 SER23 GLU24 VAL25 ASN26 SER27 ASP28 CYS29 LEU30 LEU31 ASP32 GLY33 LEU34 ASP35 ALA36 LEU37 VAL38 TYR39

Selected fragments are moved to this table. You can also remove no longer desired fragments to exclude them from the next steps.

The screenshot displays a molecular docking software interface. On the left, there are two tables of fragments. The top table, 'Fragments on Server: (# 158) Results on Server (# 9)', lists fragments #E155_1 through #E305_3. The bottom table, 'Fragments: (# 10)', lists fragments #E163_1 through #E66_1. Below these tables is a 2D chemical structure of fragment #E152_4, which is a benzothiazole derivative with an R group. The main window shows a 3D view of a protein (green ribbon) with a ligand (grey sticks) docked in its binding site. A red box highlights the 'Extension 2' button in the top toolbar. At the bottom, a 'Target View Control' bar shows the protein sequence from residue 1 to 30, with residues SKT, SRP, PHE7, GLU8, THR8, ARG10, PHE11, GLU12, LYS13, MET14, ASP15, ASN16, LEU17, LEU18, ARG18, ASP20, PRO21, LYS22, SER23, GLU24, VAL25, ASN26, SER27, ASP28, CYS29, LEU30, LEU31, ASP32, GLY33, LEU34, ASP35, ALA36, LEU37, VAL38, and TYR39. The bottom status bar shows 'SKT', 'ROCK1-test-space', '#E152_4', and '3 messages'.

The procedure for the next step remains the same. You will receive full/complete molecules and fragments, that can be further extended.

Select the fragments you want to grow and continue with the extension.

Your results may differ!

The molecules produced depend on the fragments you chose to extend.

The screenshot displays the SeeSAR software interface. The main window shows a 3D molecular docking simulation of a ligand (represented by a ball-and-stick model) bound to a protein (represented by a green ribbon structure). The protein's binding site is highlighted in light blue. A green callout box on the right contains the text: "Select your final molecules. At this stage, you can save your SeeSAR project and return to it whenever you wish."

The interface includes several panels:

- Data Panel (Top Left):** Shows a list of molecules on the server (# 330) and a list of molecules (# 10) selected for further analysis. The selected molecules are ranked by estimated affinity.
- Molecules on Server (# 330) Table:**

Name	Estimated Affinity	LLE	Tor.	Intra-clash	Inter-clash
	pM	nM	pM	nM	
18 rxn501___A1_4		⊕	●	●	●
19 rxn501___A3_3		⊕	●	●	●
20 rxn501___A5_5		⊕	●	●	●
21 rxn501___A5_4		⊕	●	●	●
22 rxn501___A5_3		⊕	●	●	●
23 rxn501___A5_5		⊕	●	●	●
24 rxn501___A1_4		⊕	●	●	●
- Molecules (# 10) Table:**

Name	Estimated Affinity	LLE	Tor.	Intra-clash	Inter-clash	MF
	pM	nM	μM	mM		
1 rxn5___A5_5		⊕	●	●	●	37
2 rxn501___A5_2		⊕	●	●	●	36
3 rxn501___A5_1		⊕	●	●	●	36
4 rxn501___A5_2		⊕	●	●	●	42
5 rxn501___A5_1		⊕	●	●	●	34
6 rxn501___A5_2		⊕	●	●	●	32
7 rxn501___A5_5		⊕	●	●	●	32
8 rxn501___A1_1		⊕	●	●	●	36
9 rxn501___A1_1		⊕	●	●	●	36
10 rxn501___A1_2		⊕	●	●	●	36
- 2D View (Bottom Left):** Shows the chemical structure of the selected molecule, rxn501b_mod___C2___B3___A5_5.
- Target View Control (Bottom):** Shows the protein sequence with residues 1-30 visible. The selected molecule is shown bound to the protein.

The screenshot displays a molecular docking software interface. The main view shows a protein structure in green ribbon representation with a ligand molecule docked in a grey stick representation. A red box highlights a dropdown menu with the following options: Anchoring, Extension 1, Extension 2, and Result (checked). A green callout box with arrows pointing to the 'Result' dropdown and the main interface contains the text: "This page shows all the full molecules. You can go to any of the steps and re-run the calculations." Below the main view is a table of results for 10 molecules, and a 2D chemical structure of the selected molecule.

Name	Estimated Affinity	LLE	Tor.	Intra-clash	Inter-clash	MF
	µM	mM	µM	mM		
1 rxn5_AS_5						37
2 rxn501_AS_2						36
3 rxn501_AS_1						36
4 rxn501_AS_2						42
5 rxn501_AS_1						34
6 rxn501_AS_2						32
7 rxn501_AS_5						32
8 rxn501_A1_1						36
9 rxn501_A1_1						36
10 rxn501_A1_2						36

2D
rxn501b_mod__C2__B3__A5_5

Target View Control

Show Binding Site Only Change Visibility of Residues

1 5 10 15 20 25 30

SKT SRP PHE7 GLU8 THR8 ARG10 PHE11 GLU12 LYS13 MET14 ASP15 ASN16 LEU17 LEU18 ARG18 ASP20 PRO21 LYS22 SER23 GLU24 VAL25 ASN26 SER27 ASP28 CYS29 LEU30 LEU31 ASP32 GLY33 LEU34 ASP35 ALA36 LEU37 VAL38 TYR39

SKT ROCK1-test-space rxn501b_mod__C2__B3__A5_5 4 messages

The screenshot displays the CSD software interface. A red box highlights the 'Terminate' button in the top toolbar. The main window shows a 3D molecular model of a protein-ligand complex. On the left, there are two tables of molecules. The top table, 'Molecules on Server: (# 330)', lists molecules with columns for Name, Estimated Affinity (pM, nM), LLE, Tor., Intra-clash, and Inter-clash. The bottom table, 'Molecules: (# 10)', lists 10 molecules with columns for Name, Estimated Affinity (pM, nM, μM, mM), LLE, Tor., Intra-clash, Inter-clash, and MF. Below the tables is a 2D chemical structure of a molecule labeled 'rxn501b_mod__C2__B3__A5_5'. At the bottom, there is a 'Target View Control' section with a residue list and a search bar.

Alternatively, you have the option to 'Terminate' the CSD workflow.

The "Terminate" button will only show the full molecules that are selected below, into a Results page. All remaining intermediate fragments/molecules will be deleted. You can no-longer navigate to any of the previous steps after you 'Terminate'.

The screenshot displays a molecular docking software interface. On the left, a table lists 10 molecules with their names, estimated affinity, and various quality metrics. The main window shows a 3D visualization of a protein (green ribbon) with several ligands (stick models) docked in its binding site. A green callout box on the right contains congratulatory text. At the bottom, a residue list is visible, and a 2D chemical structure of the selected molecule is shown in the bottom-left corner.

Molecules: (# 10)		Estimated Affinity			LLE	Tor.	Intra-clash	Inter-clash	MF
	Name	pH	mM	μ M	mM				
1	rxn501___A5_5	1				☒	●	●	37
2	rxn501___A5_2					☒	●	●	36
3	rxn501___A5_1	1				☒	●	●	36
4	rxn501___A5_2					☒	●	●	42
5	rxn501___A5_1					☒	●	●	34
6	rxn501___A5_2					☒	●	●	32
7	rxn501___A5_5					☒	●	●	32
8	rxn501___A1_1					☒	●	●	36
9	rxn501___A1_1					☒	●	●	36
10	rxn501___A1_2					☒	●	●	36

2D
rxn501b_mod___C1___B3___A5_2

Target View Control

Show Binding Site Only Change Visibility of Residues

1 5 10 15 20 25 30

SKT SKR PHE7 GLU8 THR8 ARG10 PHE11 GLU12 LYS13 MET14 ASP15 ASN16 LEU17 LEU18 ARG18 ASP20 PRO1 LYS22 SER23 GLU24 VAL25 ASN26 SER27 ASP28 CYS29 LEU30 LEU31 ASP32 GLY33 LEU34 ASP35 ALA36 LEU37 VAL38 TYR39

SKT No Space Selected rxn501b_mod___C1___B3___A5_2 4 messages

This is the final page with all selected full-molecules so far.

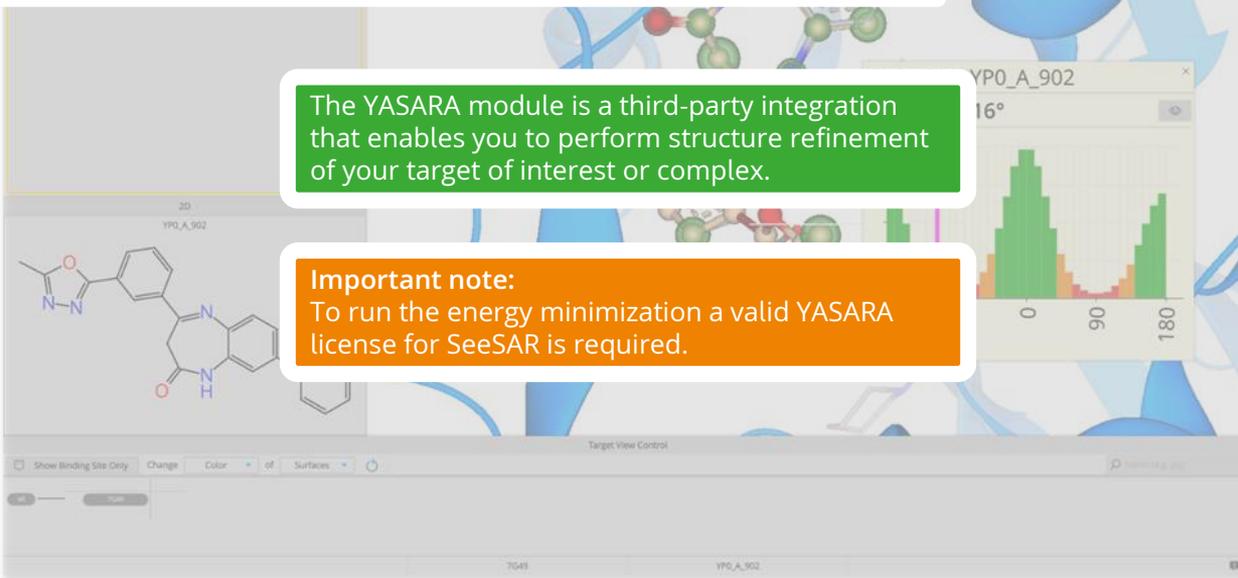
Congratulations! You finished your first C-S-D run!



9. Energy Minimization

The YASARA module is a third-party integration that enables you to perform structure refinement of your target of interest or complex.

Important note:
To run the energy minimization a valid YASARA license for SeeSAR is required.



7G49

2.

1.

7G49 - Extract Your Ligand

Hetero Groups	LOI	Name	Estimated Affinity
			pM nM μ M mM
<input type="checkbox"/>		Do not extract a ligand	
<input type="checkbox"/>	2	MES_A_901	
<input checked="" type="checkbox"/>	3	YPO_A_902	
<input type="checkbox"/>	4	CLA_907	
<input type="checkbox"/>	5	NAG_B_1	

2D

YPO_A_902

Cc1nc2c(c1)oc3ccccc32C4=NC(=O)N(C4)c5ccc(cc5)C6=CC=C(C=C6)F

Target View Control

Show Binding Site Only Change Color of Surfaces

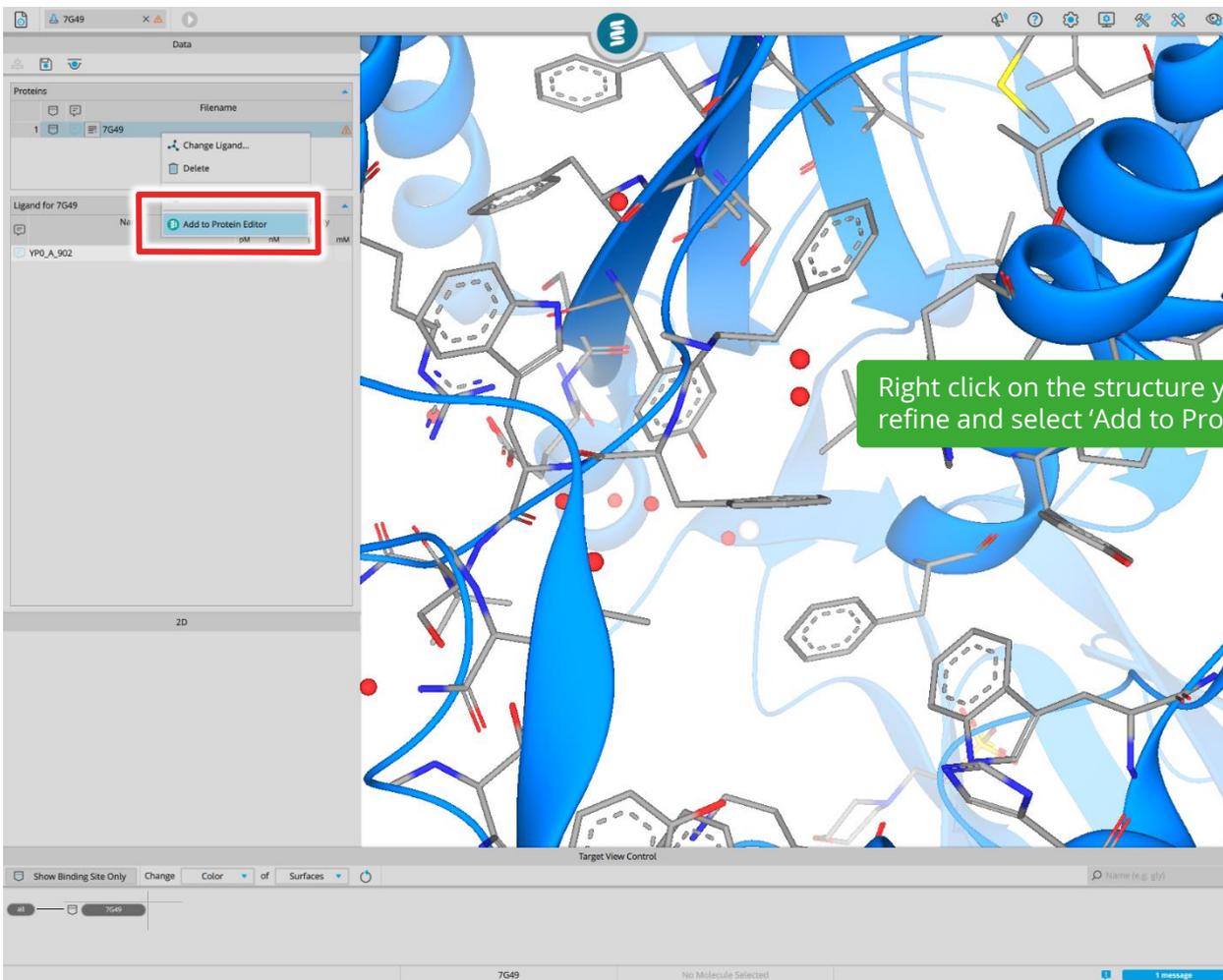
7G49

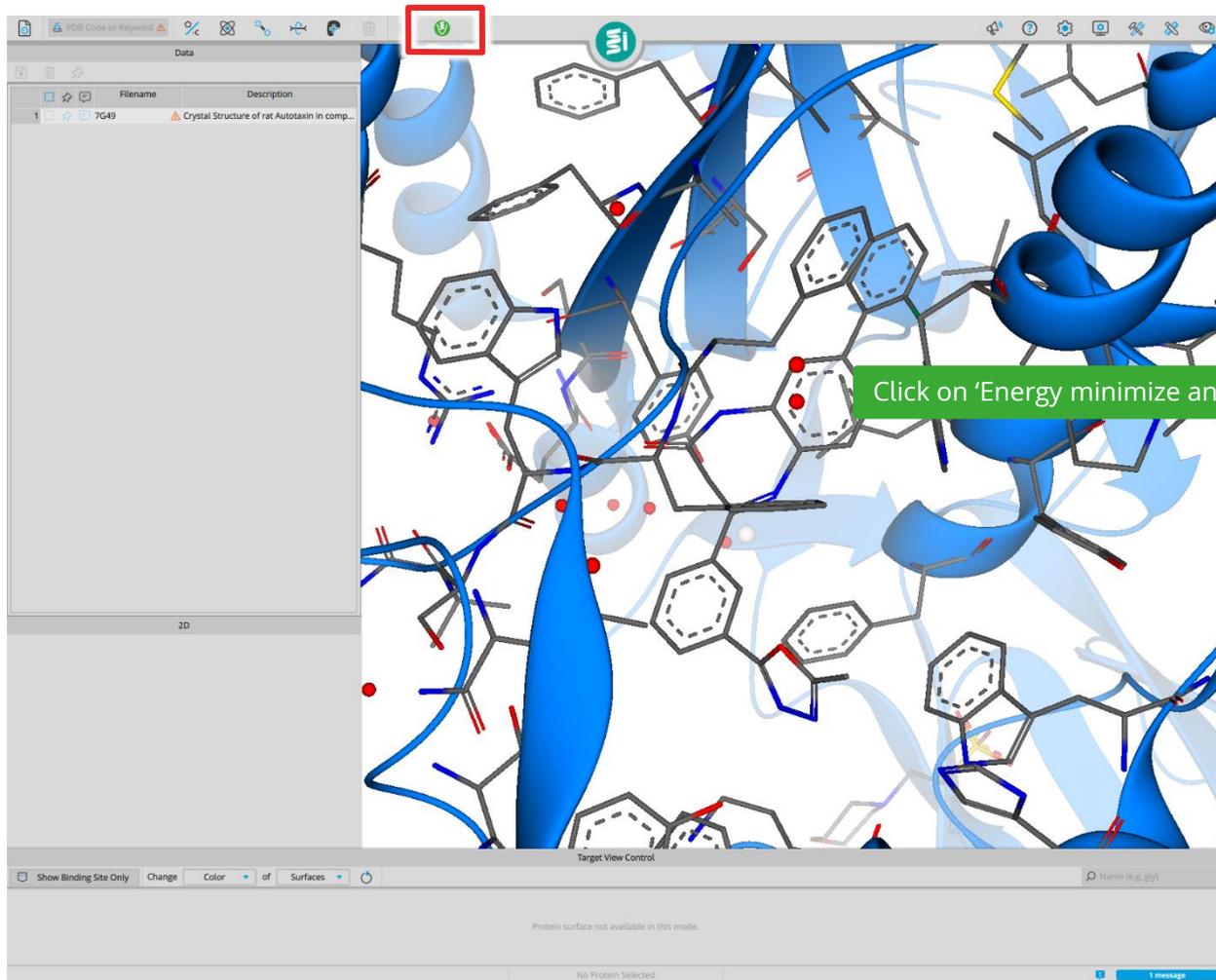
7G49 YPO_A_902

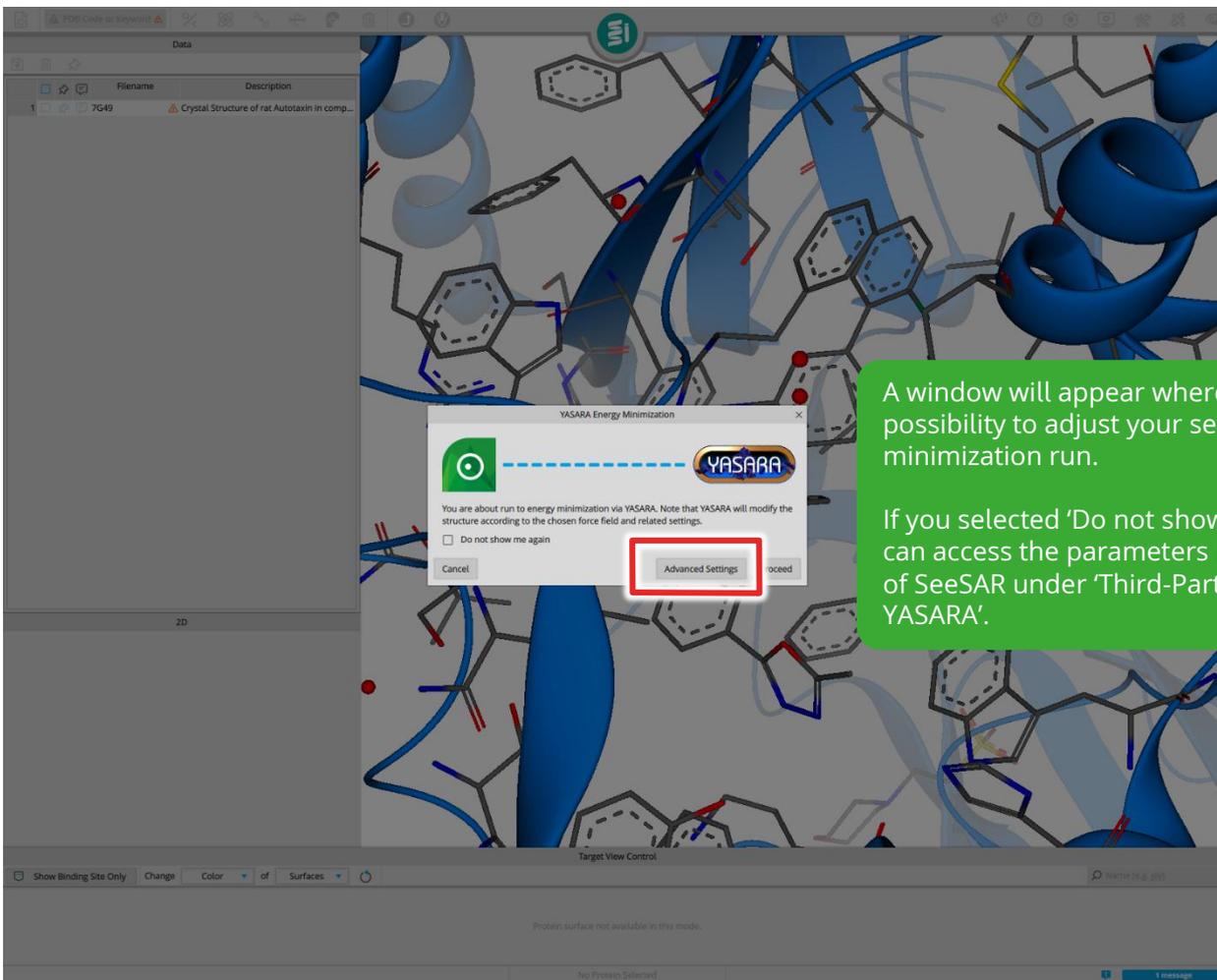
C16 - C19, YPO_A_902
Torsion: -116°

In order to perform an energy minimization, we will load PDB 7G49. This complex contains a ligand with an unfavorable torsion.

Load the PDB and select YPO as the ligand to define the binding site.

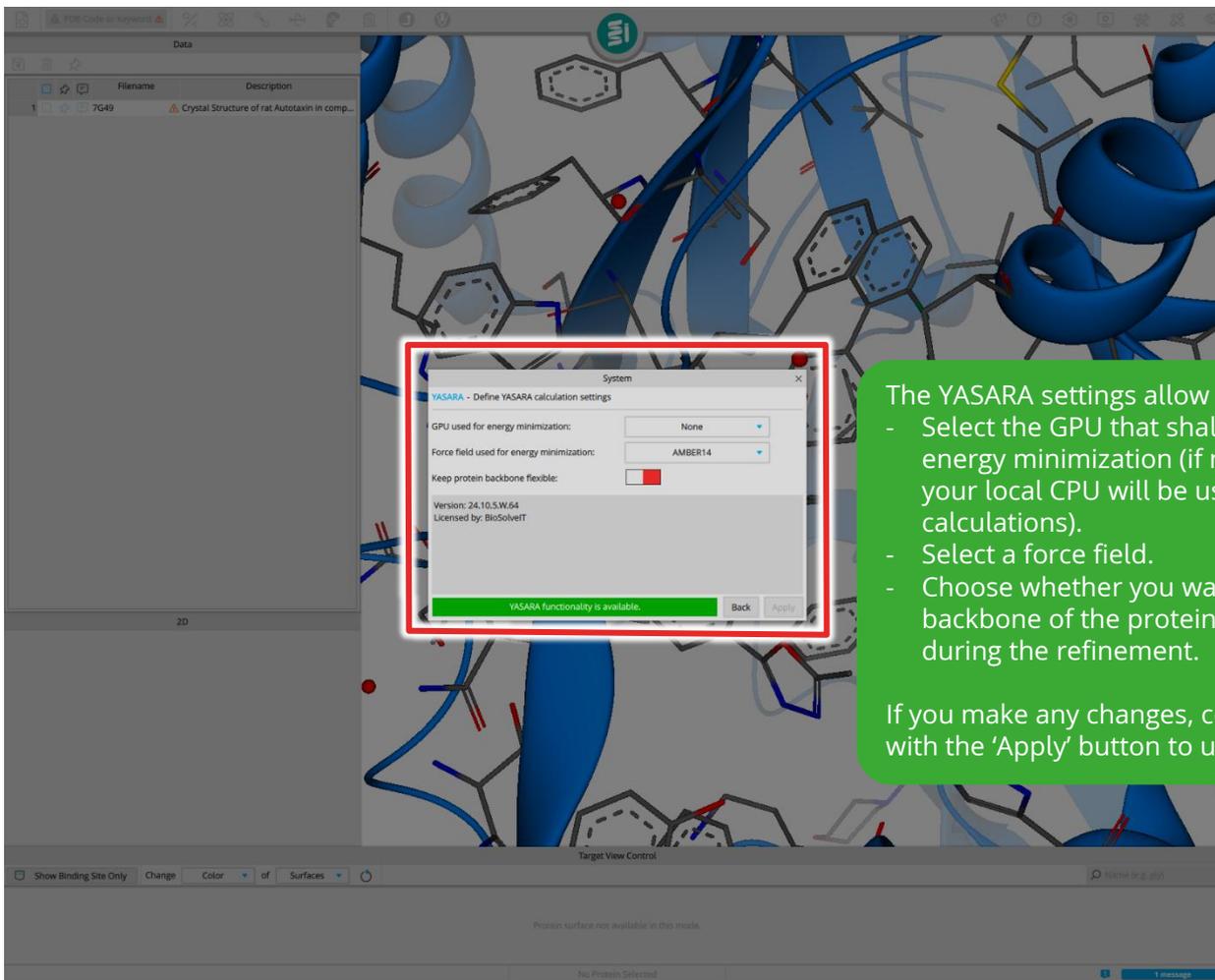






A window will appear where you will have the possibility to adjust your settings or start the minimization run.

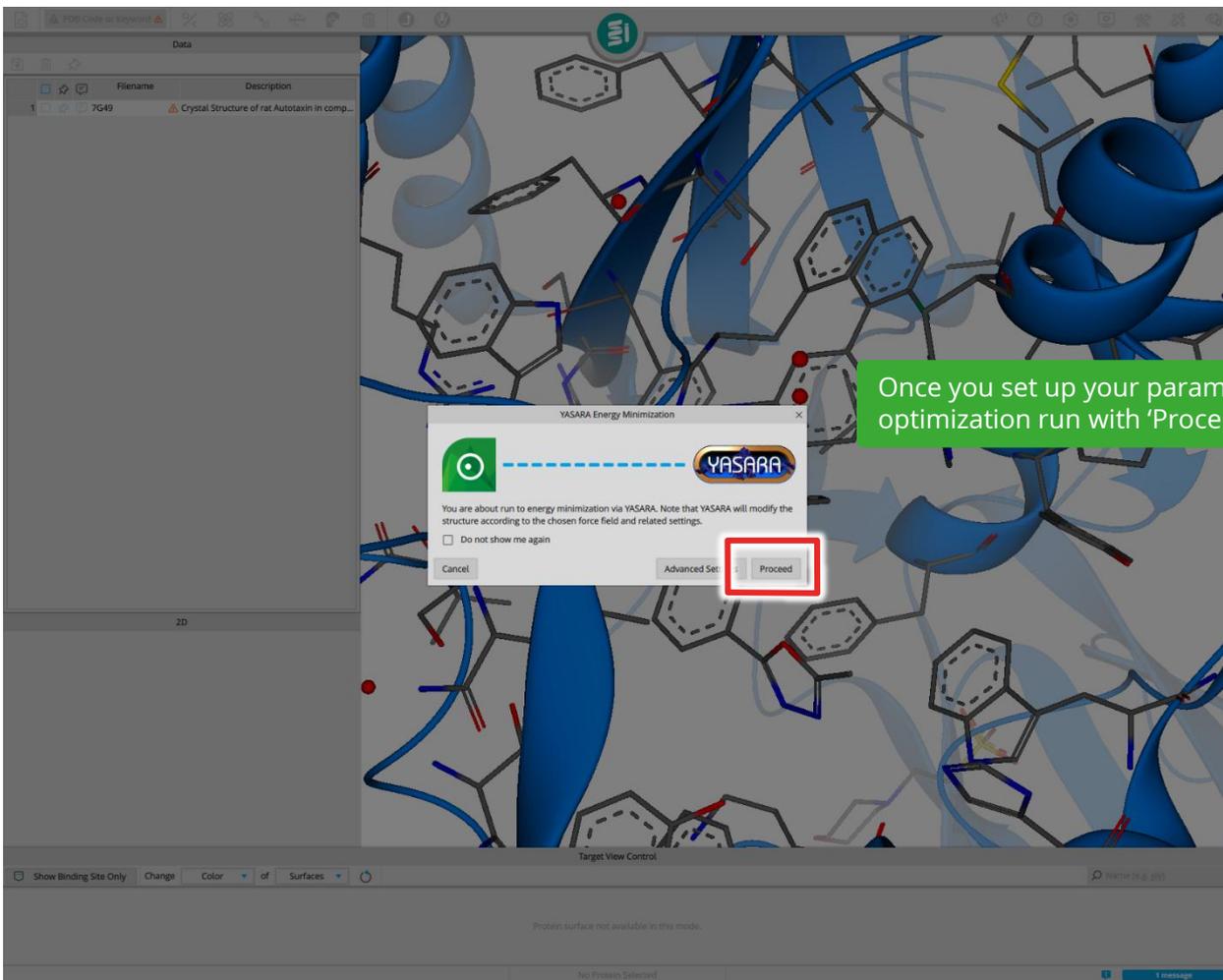
If you selected 'Do not show me again', then you can access the parameters in the 'System' menu of SeeSAR under 'Third-Party Integrations → YASARA'.



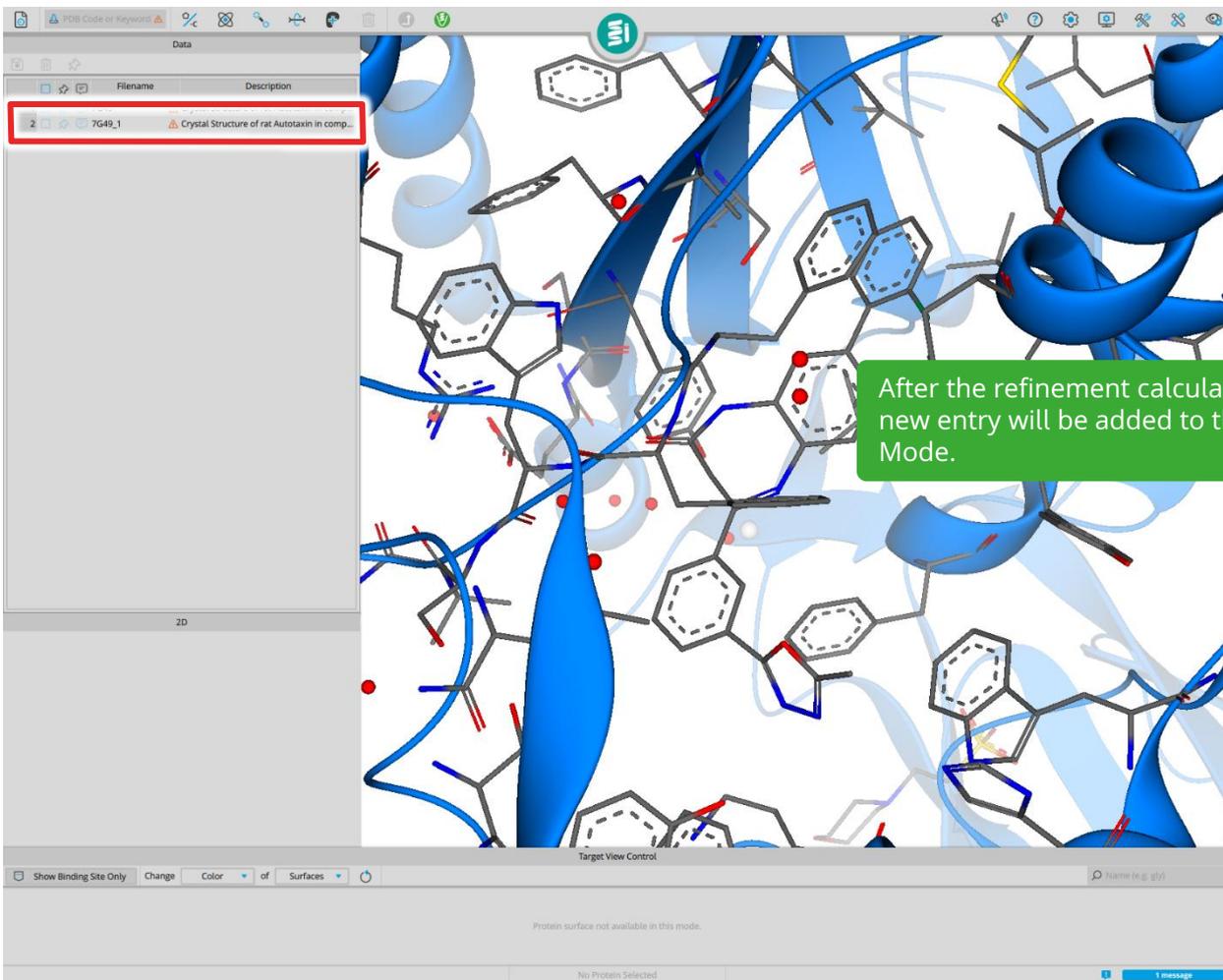
The YASARA settings allow you to:

- Select the GPU that shall be used for the energy minimization (if no GPU is selected, your local CPU will be used for the calculations).
- Select a force field.
- Choose whether you want to keep the backbone of the protein flexible or rigid during the refinement.

If you make any changes, confirm the settings with the 'Apply' button to use them.



Once you set up your parameters, start the optimization run with 'Proceed'.



After the refinement calculation has finished, a new entry will be added to the Protein Editor Mode.

2.

1.

Filename	Description
7G49	Crystal Structure of rat Autotaxin in comp...
7G49_1	Crystal Structure of rat Autotaxin in comp...

From here on, you can export the refined structure or continue working with it.

For export, check the refined structure and click on 'Save proteins'. All checked proteins will be exported to your selected folder.

If you are working with several structures, make sure to rename them (by double clicking on the name in the 'Filename' column).

Target View Control

Show Binding Site Only Change Color of Surfaces

Name (e.g. gly)

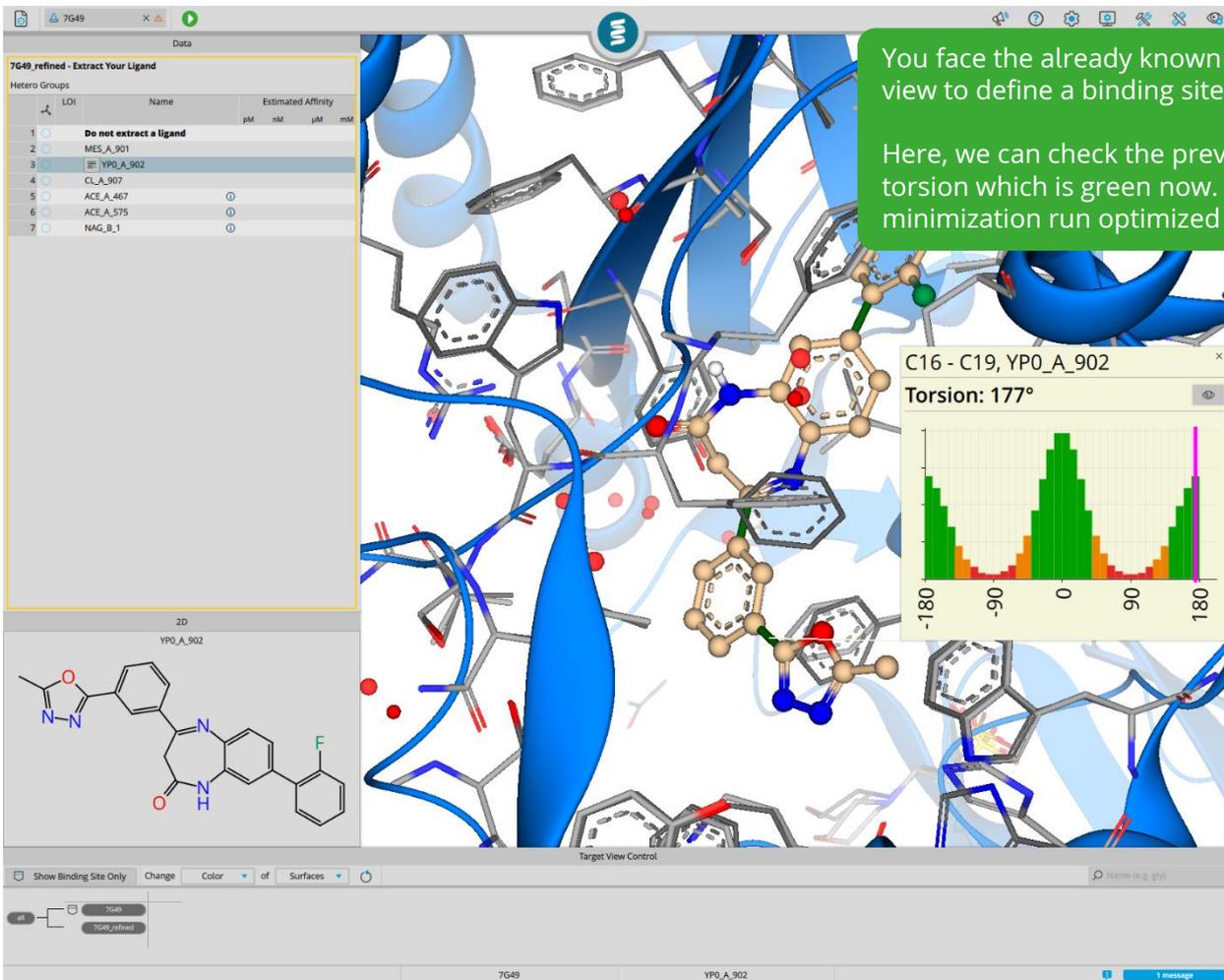
Protein surface not available in this mode.

No Protein Selected

1 message

The image shows a screenshot of a molecular modeling software interface. On the left, a 'Data' panel is visible, containing a table with columns for 'Filename' and 'Description'. Two entries are listed, both with the filename '7G49' and description 'Crystal Structure of rat Autotaxin in comp...'. Below the table, a red rectangular box highlights two buttons: 'Add to Protein Mode' and 'Add to Protein Editor'. The main area of the interface displays a 3D molecular model of a protein structure, represented by blue ribbons, with a complex organic molecule (ligand) bound to it. The ligand is shown in a stick representation with various atoms colored (grey for carbon, red for oxygen, blue for nitrogen). At the bottom of the interface, there is a 'Target View Control' section with options like 'Show Binding Site Only', 'Change Color of Surfaces', and a search bar for 'Name (e.g. gly)'. A message at the bottom center states 'Protein surface not available in this mode.' The bottom status bar shows '7G49_refined' and '1 message'.

To continue working on a structure, right click on it and select 'Add to Protein Mode'.



You face the already known ligand selection view to define a binding site.

Here, we can check the previously red colored torsion which is green now. The energy minimization run optimized the strained torsion.



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

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