

# Introduction to the Schrodinger Bioluminate package

## Session 1: Maestro

## **Learning goals:**

By the end of this workshop, participants will be able to:

- Know where to find additional resources for learning about Schrodinger functionality.
- Know where to find and how to use the commands for selecting, editing, and rendering molecules.
- Import and prepare a protein for further analysis.
- Create new macromolecules using the Maestro interface.

## **Contents:**

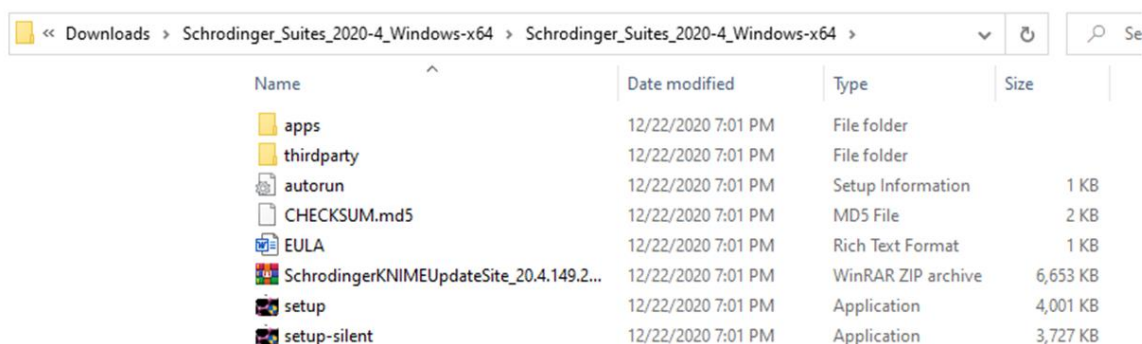
1. Intro to Schrodinger
2. Schrodinger resources: Where to find them and how to use them
3. Learn the Maestro interface:
  - a. Demonstration of importing pdbs + user interface
  - b. Try it yourselves
  - c. Demonstration of protein preparation & analysis
  - d. Try it yourselves
4. Evaluation

## Download and Install Bioluminate

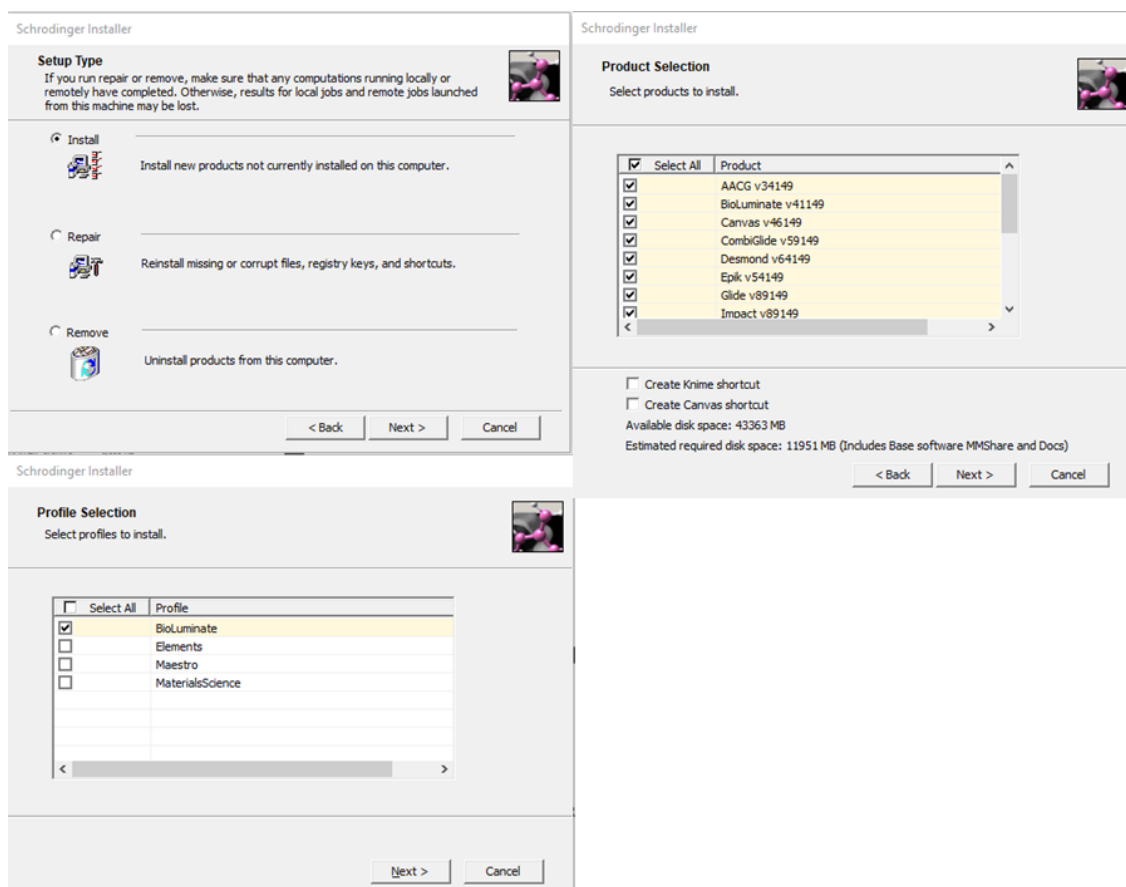
1. Go to [www.schrodinger.com](http://www.schrodinger.com) and create an account.
2. Click the download button in the top menu.
3. Choose the latest version and your operating system. Check the license agreement (EULA) box and click **DOWNLOAD**. You will need at least 6 GB of free disk space to download the full suite.
4. When the download is done, double-click the downloaded package to extract the software.

The screenshot shows the Schrodinger website's 'Download Releases' page. At the top is the Schrodinger logo and a navigation bar with links: ABOUT, PLATFORM, PIPELINE, USER EVENTS, CAREERS, and INVESTORS. Below this is a sub-navigation bar with 'Download Releases' (highlighted in orange), 'Other Downloads', 'KNIME Workflows', and 'Free Maestro'. The main heading is 'Download Releases'. Below it, a prompt says 'Please choose the version of the release you'd like to download:' followed by a 'Version:' label and a dropdown menu showing 'Release 2020-4' with a plus icon. A blue button labeled 'VIEW LIST OF NEW FEATURES' is below the dropdown. Then, a prompt says 'Please choose your OS:' followed by three radio button options: Linux (with a penguin icon), Windows 64-bit (with a Windows logo icon), and Mac (with an Apple logo icon). Below these are three links: 'Click here to view a list of supported platforms for Release 2020-4.', 'Click here to view any Known Issues for the current release.', and 'Click here to view a list of upcoming infrastructure projects that may require changes from your IT team.' Another link says 'Download KNIME Workflows here (see a complete list on the KNIME workflows page)'. A checkbox is present with the text: 'By downloading our software, you are agreeing to the terms set forth in our End User License Agreement (EULA), please confirm that you have read the EULA, and agree to the terms. \*'. At the bottom is a large blue button labeled 'DOWNLOAD'.

5. Enter the extracted folder and double-click the setup file to start the installation.



6. Choose the Install option and select the products to install.



You will need almost 12GB of disk space to install the whole package. If you don't have enough free space you can install Maestro (4.3GB) for now.

Quick guide to other useful Schrodinger packages we will be using in other sessions:

Canvas	Tools for chem/bioinformatics. For finding and building libraries of substructures.
Desmond	Molecular dynamics simulation engine
Epik	pKa predictions
Glide	Molecular docking
Jaguar	Ab initio Quantum mechanics
Macromodel	Force-field based molecular modeling
Prime	Homology modelling

# The Maestro interface

The screenshot shows the Maestro BioLuminate interface. The main workspace displays a green ribbon representation of a protein structure. On the left, the Workspace Navigator shows the ENTRY LIST and STRUCTURE HIERARCHY. The top of the interface features a menu bar (File, Edit, Select, Workspace, Scripts, View, Window, Help) and a toolbar with various icons. Below the toolbar is a shortcut bar. The bottom of the interface has a footer bar displaying the protein sequence (1:1Q4G\_A, 1:1Q4G\_B) and a command line. Labels on the right side of the image identify the 'The Toolbar', 'Shortcut bar', 'Workspace', 'Footer bar', and 'Protein sequence'.

This screenshot shows the 'Select/Picker' menu, which is accessed by clicking the 'R' icon in the toolbar. The menu lists several selection options: Atoms, Residues (which is currently selected with a checkmark), Chains, Molecules, Entries, and Secondary Structure.

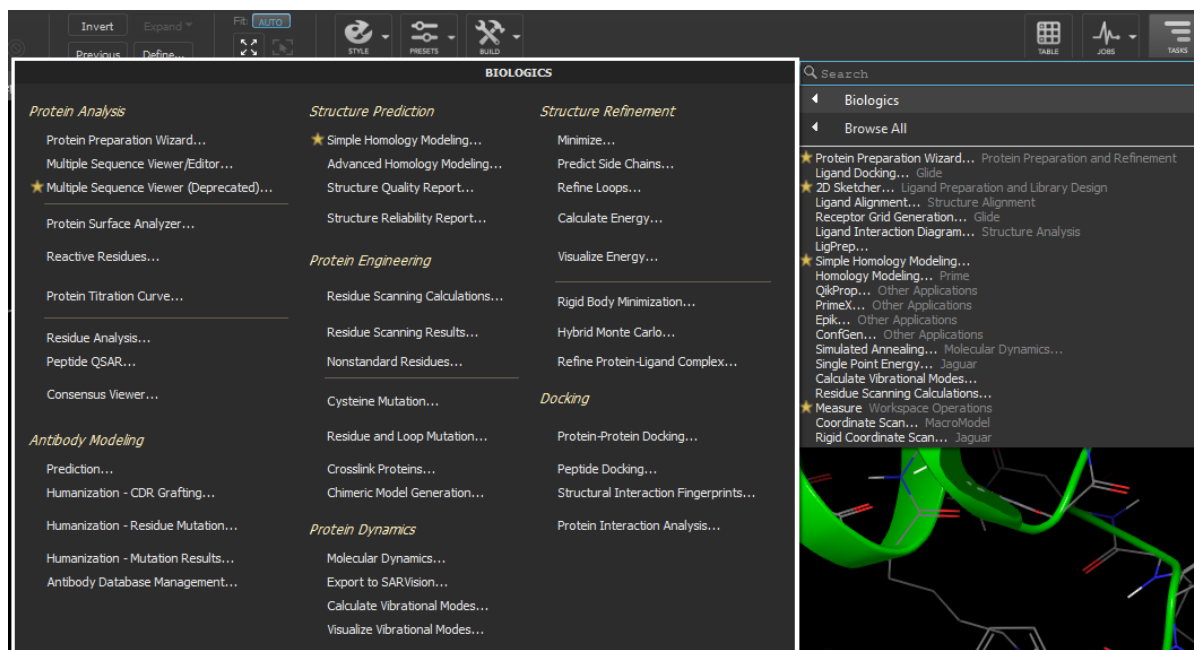
Select/Picker

This screenshot shows the 'Apply styles' menu, which is accessed by clicking the 'S' icon in the toolbar. The menu includes options for Style, Presets, and Build. Below these are various style icons for atoms, bonds, and surfaces. There are also sections for 'Color Atoms' (Element + Color, Carbons), 'Apply Labels', and 'Ribbons'.

Apply styles

This screenshot shows the 'Builder/edit structures' menu, which is accessed by clicking the 'B' icon in the toolbar. The menu includes a '3D Builder' section with various building tools like 'Add Fragments' and 'Draw'. Below this is a 'Organic' section with a grid of chemical structures (including water, ammonia, and formaldehyde) and a 'Metal Centers' section. At the bottom, there is a 'Create Enumerated Entries...' button.

Builder/edit structures



Tasks finder & Search bar

Project Table --- Scratch Project

File Table Data Select Window ePlayer

Import Export 3D Viewer Plot Sort Find/Replace Show Props Color Rows Calculator

Columns Tree Show Show Family 2D Structure Hide Family

Row	In	Title	Stars	Entry ID	Date Added	Date Modified	PDB TITLE	PDB ID	PDB RESOLUTION	PDB EXPDTA	PDB EXPDTA TEMPERATURE	PDB EXPDTA PH	Source Path	Source File	Source File Index	prepared
1	<input type="radio"/>	1Q4G	☆☆☆☆	1	16:08	16:23	2.0 ANGS...	1Q4G	2.000	X-RAY DIFFRA...	180.000	6.700	C:\Users\Y...	1q4g.pdb	1	<input type="checkbox"/>
2	<input checked="" type="radio"/>	1Q4G - preprocessed	☆☆☆☆	2	16:25	16:40	2.0 ANGS...	1Q4G	2.000	X-RAY DIFFRA...	180.000	6.700	C:\Users\Y...	1q4g.pdb	1	<input checked="" type="checkbox"/>

Entries: 2 total, 1 selected, 1 included Groups: 0 total, 0 selected Properties: 37 total, 14 shown

Project table

## The basics

Using the mouse:

Left click: Pick atoms/residues

Shift + left click: Pick atoms inside the formed box

Scroll: Adjust the pane clipping

Middle click + move mouse: Translate the view

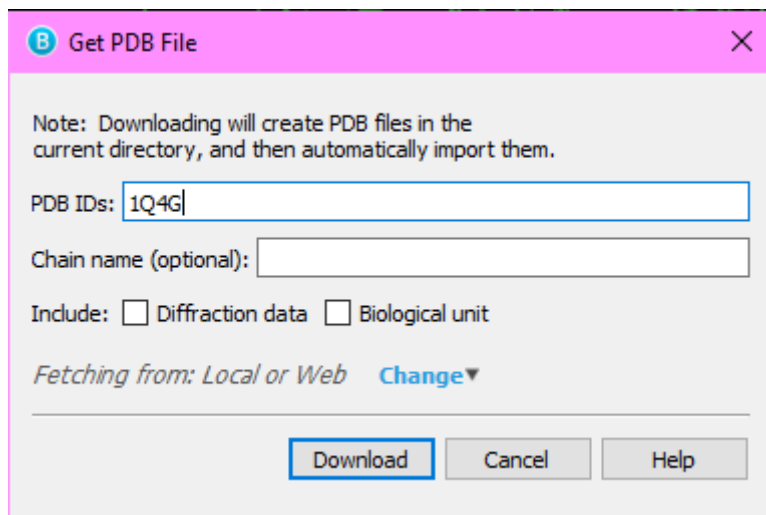
Right click: Opens menu options for the clicked structure

Right click + move mouse: Zoom

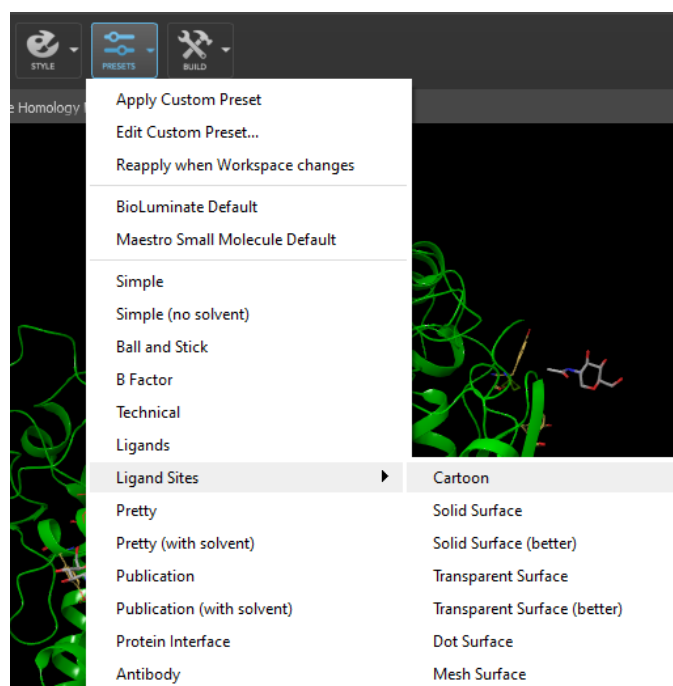
**What do combinations of left, middle and right clicking and movements do?**

## Get to know the Maestro user interface

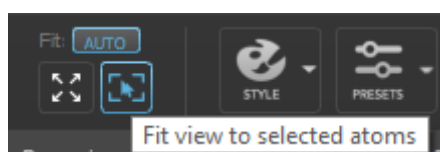
1. Create a directory on your desktop and change the working directory to it (File -> Change Working directory).
2. Import the 1Q4G structure (File -> Get PDB).



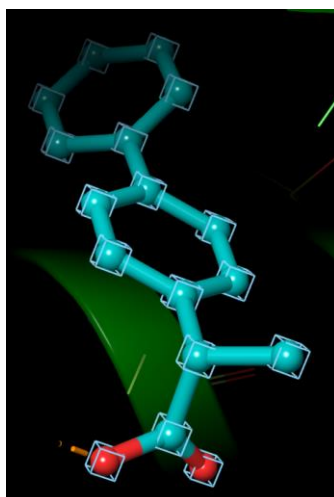
3. Change the look of the protein using the presets. Try out different ones until you find something that you like.



4. Find a ligand, select it and fit the view on it (see previous page for mouse controls).



5. Change the color and line thickness of the ligand.



6. Use the search bar to find the measurement tool. Measure the distance between the carboxylate oxygens and the Arginine nitrogen. **Which other measurements can you make using this menu?**

SEARCH BAR: measure

VIEW RESULTS FOR: measure

DISPLAYING 1-10 of 11 RESULTS

- ★ Measure Workspace Operations
- Planar Angle Measurement... Workspace Operations
- View Measurements... Workspace Operations
- Binding Site Detection... Structure Analysis
- Structure Reliability Report...
- Structure Quality Report...
- Simulation Interactions Diagram... Molecular Dynamics...
- Simulation Quality Analysis... Molecular Dynamics...
- Hydrogen Bond Basicity... Jaguar
- Protein Reliability Report... Structure Analysis

7. You can see all your measurements if you click the three dots above the measurement icon (the ruler). Delete a measurement.

MEASUREMENTS

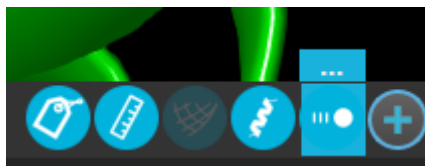
Distance Angle Dihedral

Atom1	Atom2	Distance
N:10962	O:14814	2.95
N:10965	O:14815	3.13
O:14814	C:14274	8.31

ENTRIES 2  
CHARGE -3



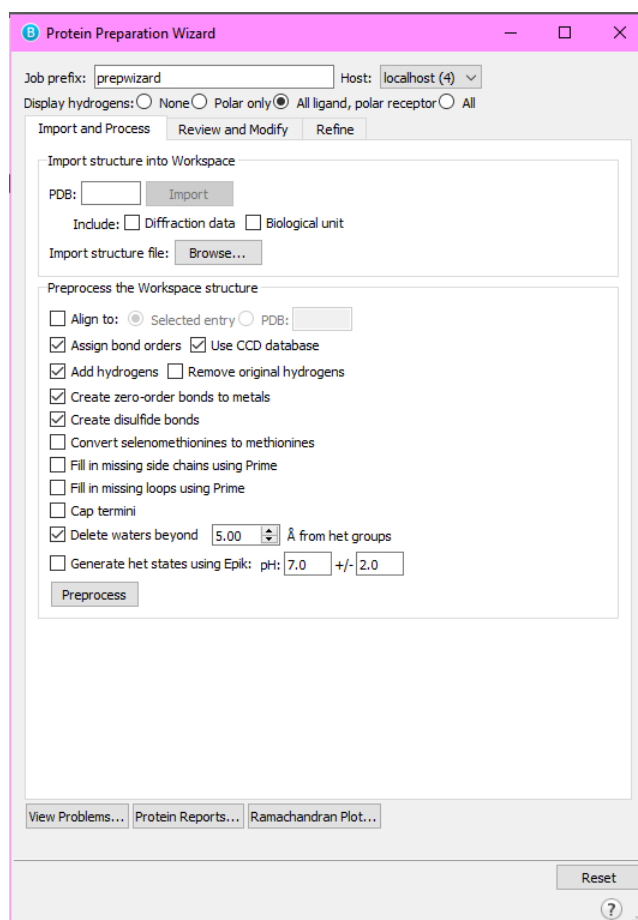
8. Try the interactions toggle to see if the ligand has any interactions with the surrounding protein. Clicking the three dots above the toggle will open a window that tells you what kind of interactions this ligand has. **What kind of interactions does it have? What kind of intramolecular interactions does it have?**



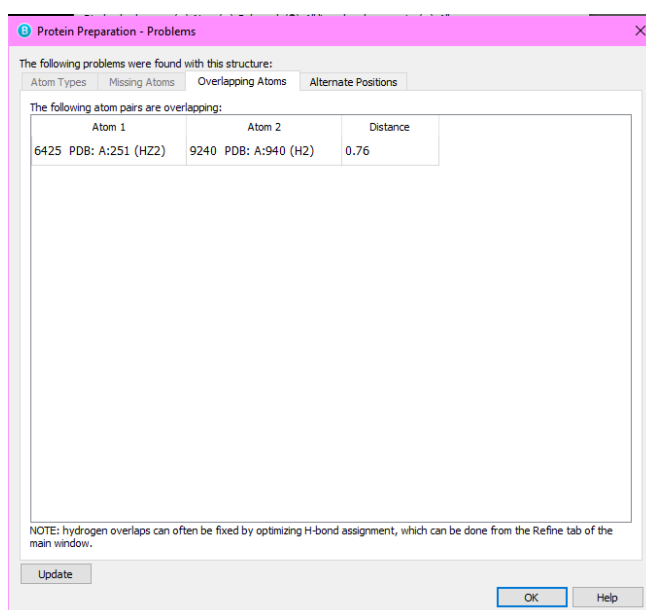
9. If you have time left: explore the workspace and click at random buttons to see what they do!

## Prepare the structure with prepwizard

1. Search for the prepwizard in the Tasks menu and start it. If you haven't installed the Epik package, uncheck the "Generate het states using Epik" box. Then click Preprocess.

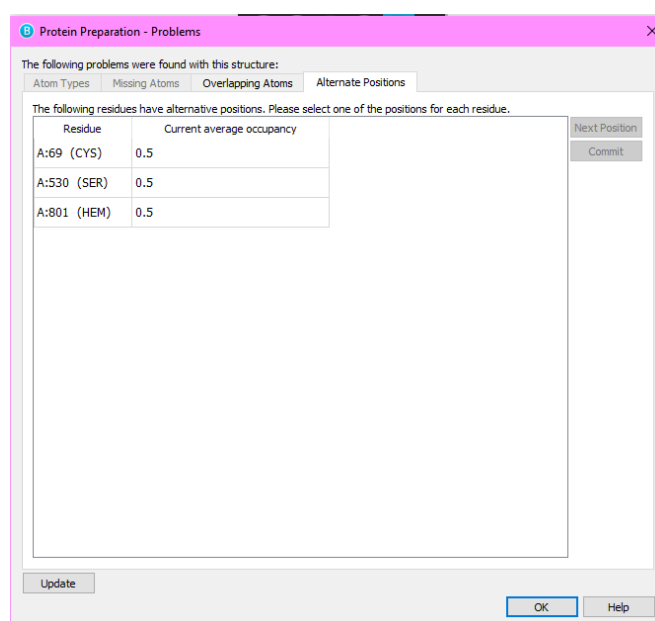


2. Fix the problem that came up by double-clicking the row and see what's wrong in the workspace.

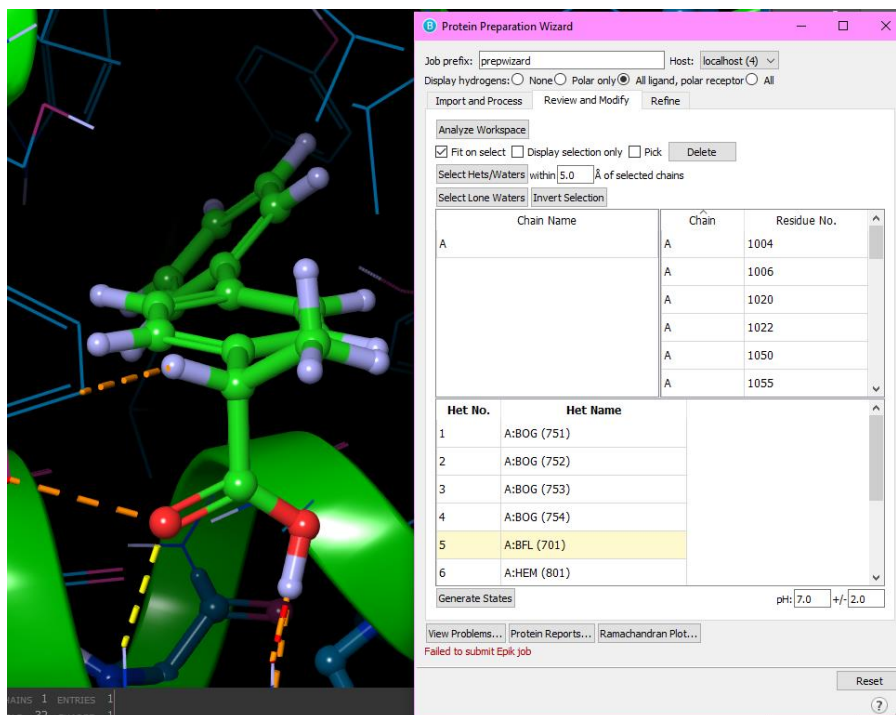


When you have fixed the problem, go back to the problem window and click Update to see if it was resolved.

3. Move on to the alternate positions tab in the same window. These residues have at least two different orientations. Decide which one is the most appropriate orientation and click the Commit button on the right-hand side. When there are no more issues, click the OK button.



- Go back to the Protein Preparation Wizard window and click the Review and Modify tab. Take a look at BFL. This molecule is supposed to have a deprotonated carboxylate with a negative charge. Use the build menu to fix it. Don't forget to choose the right picker!



- Check that your ligand has the correct charge by labelling it according to its formal charge. (Try right-click)
- Go back to the Protein Preparation Wizard window and choose the Refine tab. Click Optimize. While the job is running (ca 2 min), monitor the output by going to the Monitor pane.

The screenshot shows the Protein Preparation Wizard window in the Refine tab. The window contains various settings for H-bond assignment, water removal, and restrained minimization.

Job prefix: prepwizard Host: localhost (4)

Display hydrogens: ☐ None ☐ Polar only ☒ All ligand, polar receptor ☐ All

Import and Process Review and Modify Refine

H-bond assignment

☒ Sample water orientations

☐ Use crystal symmetry

☐ Minimize hydrogens of altered species

☒ Use PROPKA pH: 7.0 ☐ Label pKas

☐ Use simplified rules pH: ☐ Very low ☐ Low ☒ Neutral ☐ High

Optimize

Interactive Optimizer...

Remove waters

Remove waters ☒ Beyond hets 3.0 Å

☐ With fewer than 3 H-bonds to non-waters

Restrained minimization

Converge heavy atoms to RMSD: 0.30 Å

☐ Hydrogens only

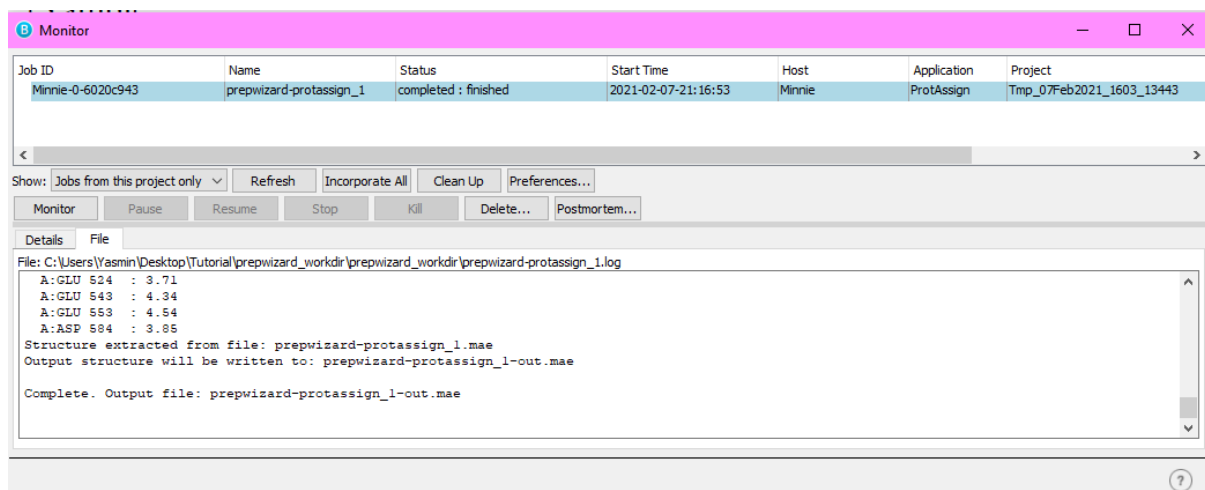
Force field: OPLS3e

Minimize

View Problems... Protein Reports... Ramachandran Plot...

Optimize H-bond job incorporated.

Reset



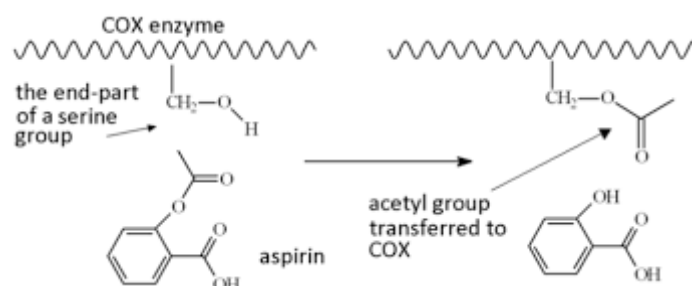
**What did optimization do to the structure? Do you agree with the changes?**

To compare more easily when moving between different entries, you can save the current view by going to the main menu (View -> Save Camera View). To restore the view go to View -> restore camera view.

7. Convert the neutral Glutamate to a charged one.

Create an acetylated COX-1 in complex with salicylic acid from 1Q4G

1. COX is irreversibly acetylated by aspirin, which acetylates Ser530 and results in salicylic acid. **Build the new complex based on the current structure. Don't forget the hydrogens!**



2. Export your new complex using the name AcetylatedCOX-1.mae