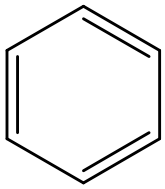
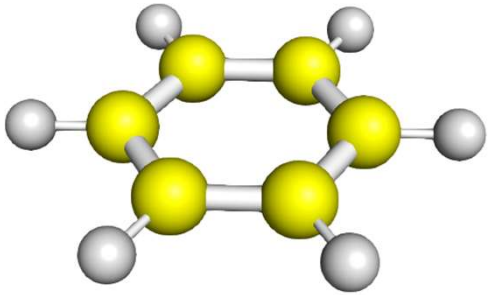
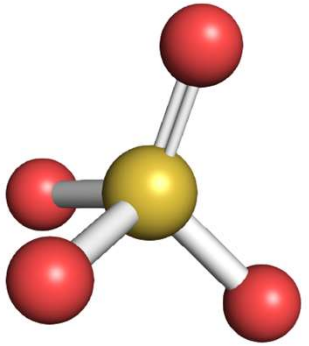
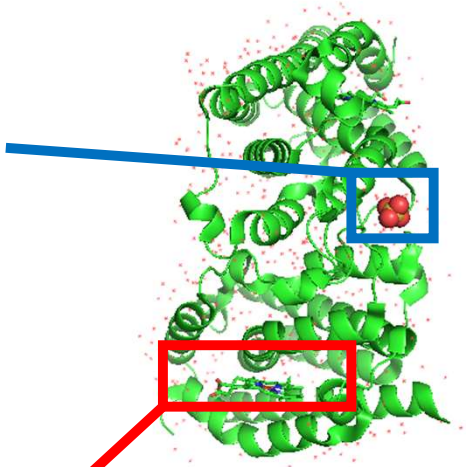
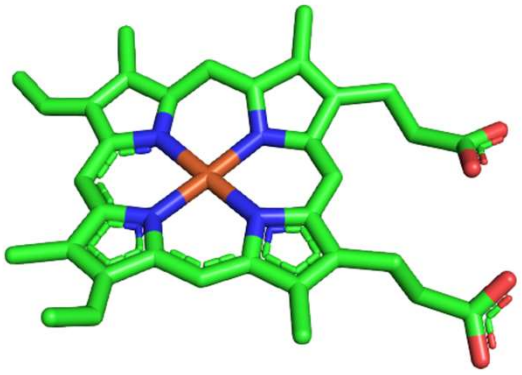
ChemDraw and PyMOL: Interacting with molecules in 2 dimensions and 3 dimensions











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October 8, 2024
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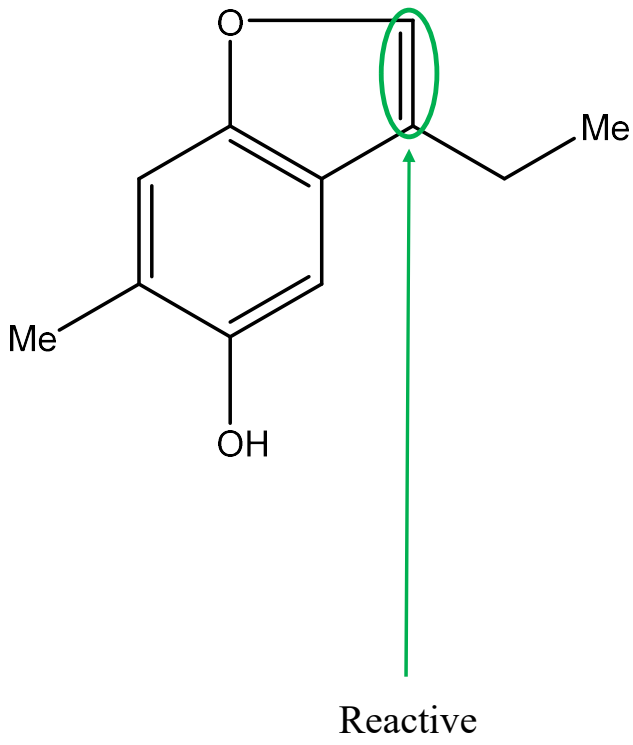
Boston University Chemistry

- **Chemists are able to deduce physical properties, spectroscopic properties, and reactivity of molecules by simply looking at the 2-Dimensional representation of the molecule.**
- ChemDraw is the standard tool used by chemists to draw moleulces in 2 Dimensions and to disseminate their work in peer-reviewed journals.
- ChemDraw is also used as a plugin in many online tools such as SciFinder and CSD.



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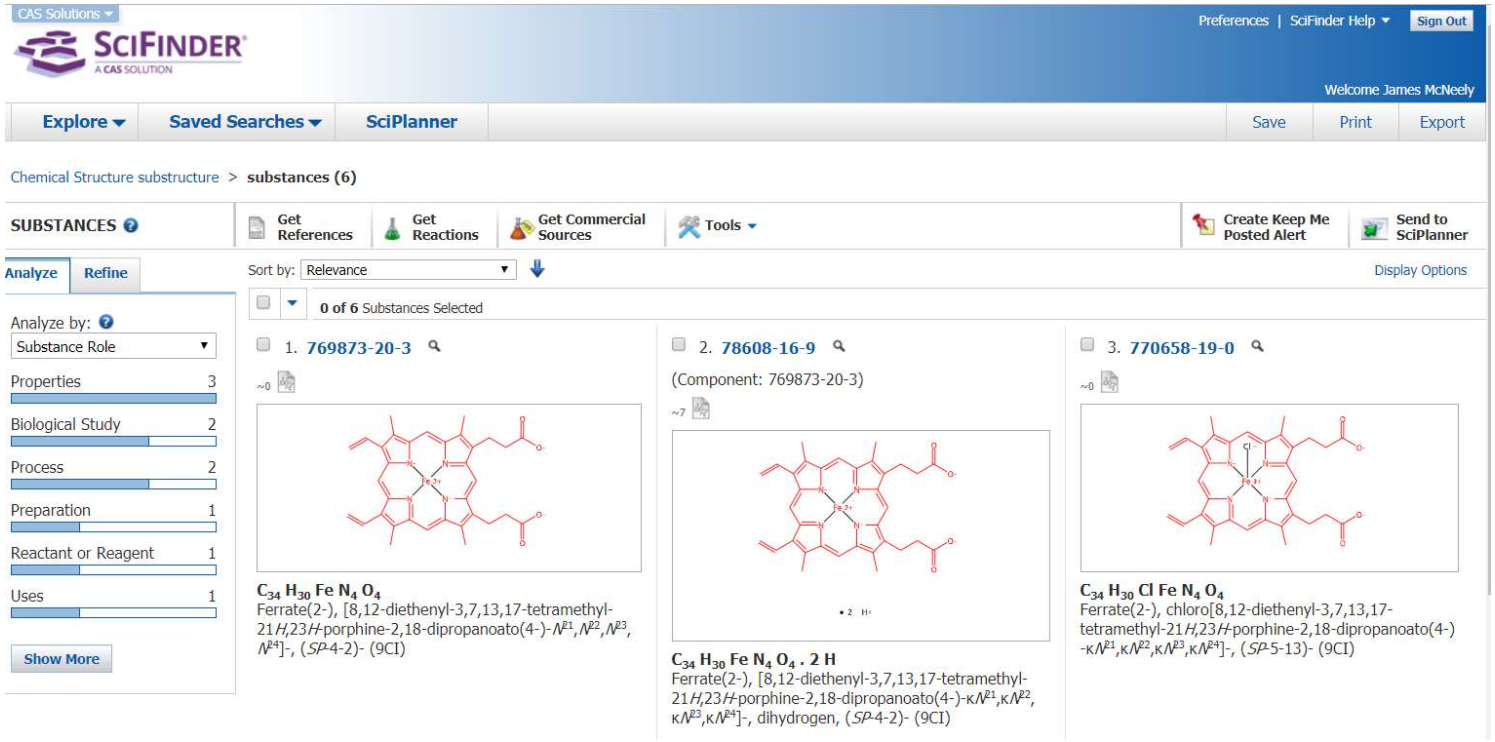
From the American Chemical Society Author Guidelines:

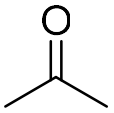
Prepare chemical structures according to the guidelines below. These parameters are specifically for ChemDraw (make sure to use the ACS-1996 document settings); authors using other drawing packages should adapt these parameters to their systems.

Item	Settings
chain angle	120 degrees
bond spacing	18% of width
fixed length	14.4 pt (0.2 in.)
bold width	2.0 pt (0.0278 in.)
line width	0.6 pt (0.0083 in.)
margin width	1.6 pt (0.0222 in.)
hash spacing	2.5 (0.0345 in.)

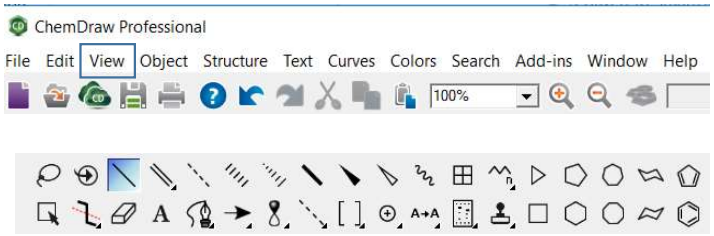
- **ChemDraw also has a SciFinder plugin that allows a user to perform a "structural" literature search.**



Tutorial 1. Drawing a Structure

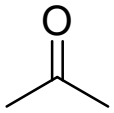


- Make sure the main toolbar is displayed by going to “View” and checking to make sure that “Show Main Toolbar” is checked.
- Select the solid bond icon in the main toolbar.
- Add a bond to the drawing area by clicking once.
- To add a second bond, click on the right end of the bond you just created.
- Click the double-bond icon in the main toolbar (directly next to the solid bond icon).

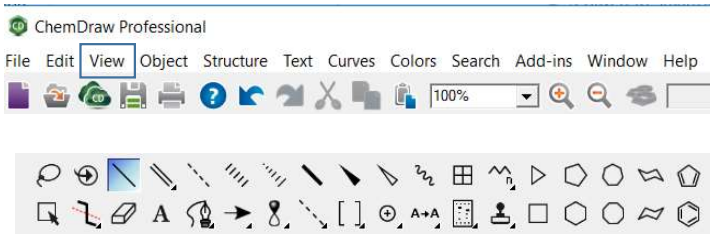


If you make a mistake, you can delete an atom or bond by clicking the select icon, click the mistake, and then hit delete on the keyboard.

Tutorial 1. Drawing a Structure (cont'd)



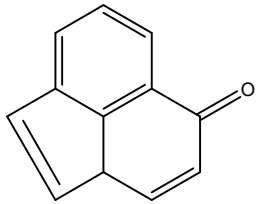
- Click the vertex of the bonds you've already drawn to add a double bond.
- Move your mouse cursor over the terminal carbon of the double bond.
- Type 'o' on your keyboard while the cursor is over the atom you want to change.
- Name the structure by selecting the molecule (ctrl-a on PC, cmd-a on Mac) and going to "Structure – Convert Structure to Name"
- Save the structure as an .sdf (3000) and a .cdx file.



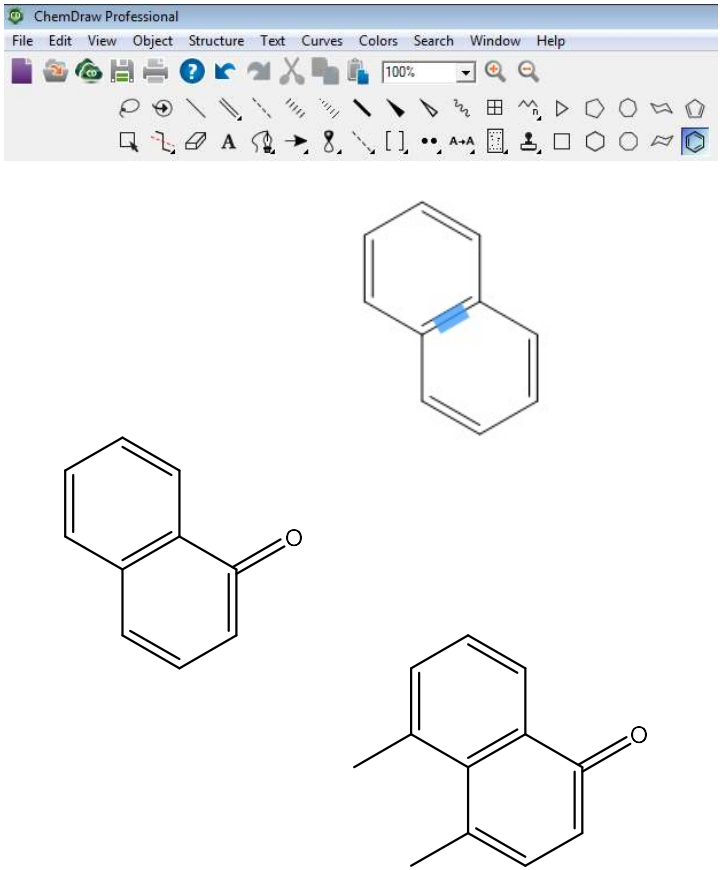
If you make a mistake, you can delete an atom or bond by clicking the select icon, click the mistake, and then hit delete on the keyboard.

Pressing the <esc> key on your keyboard will close a text box.

Tutorial 2. Drawing Rings

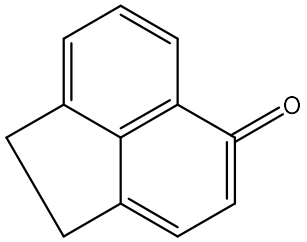


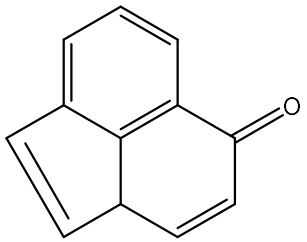
- Click the Benzene icon in the main toolbar, and click once in the drawing area.
- With the benzene icon still selected, hover your mouse/trackpad cursor over the lower right bond in the benzene you just added and click again.
- Add a double bond to the naphthyl fragment at the position shown above, and change the label for the terminal carbon from C to O.
- Add single bonds to the naphthyl fragment at the positions shown above.



Tutorial 2. Drawing Rings (cont'd)

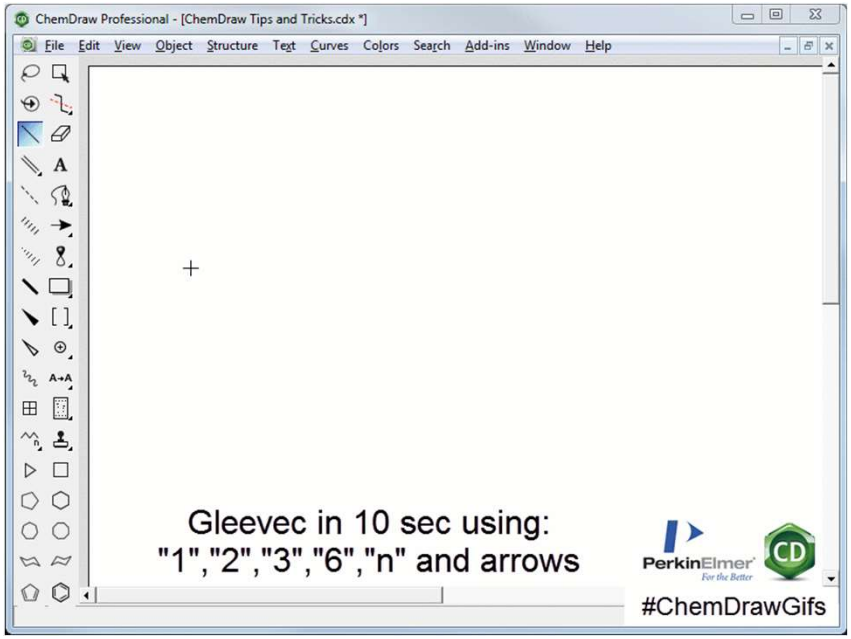
- Add a bond between the terminal carbons by clicking and dragging between the two atoms with the solid bond icon selected.
- Now change the bond order to match the structure shown to the right in one of two ways.
  1. Hover your mouse/trackpad cursor over a bond and hit '1' on your keyboard to change to a single bond. Hit '2' to change to a double bond.
  2. Right click on a bond and select the bond type from the list.





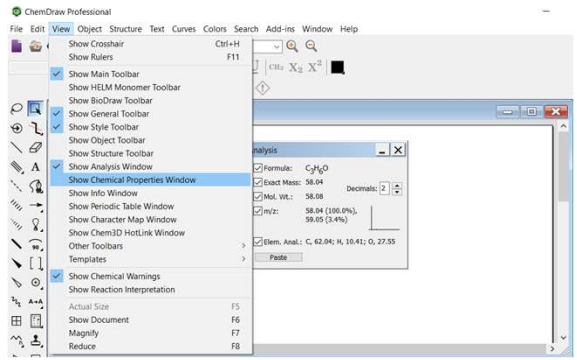
Additional Tools: Hotkeys

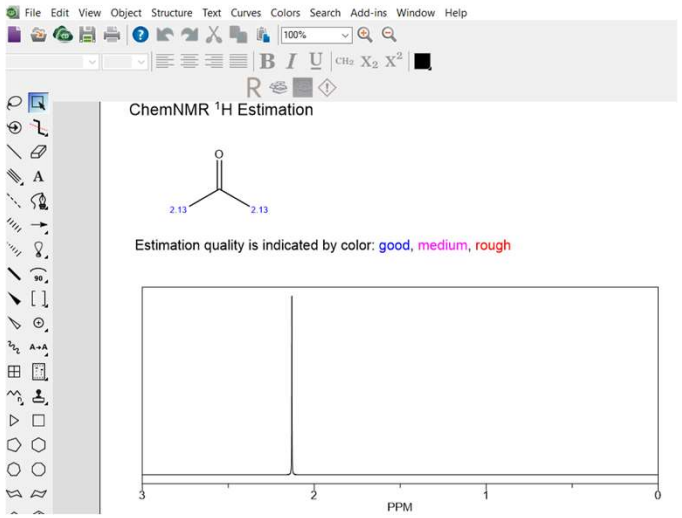
- Hotkeys are serious timesavers … they are keyboard shortcuts for building structures in ChemDraw.
- You can find a list of Hotkeys by going to “Help” – “Hotkeys Cheat Sheet”.



Additional Tools: Chemical Properties and NMR Spectra

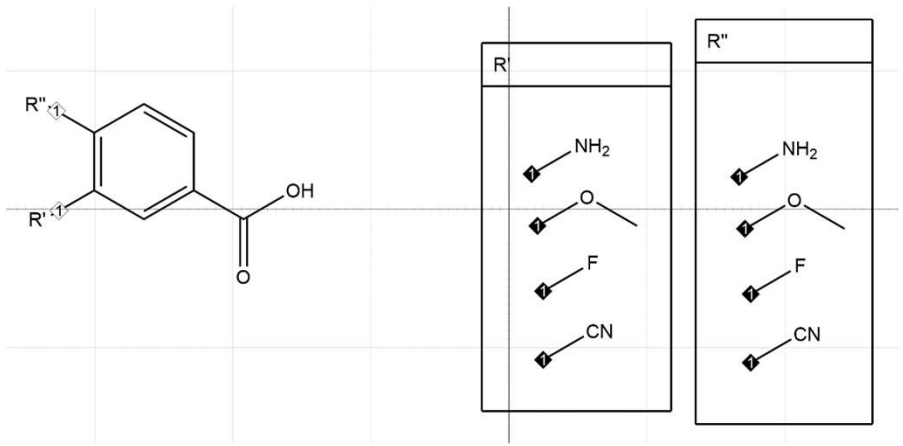
- Go to one of the structures you previously built and press ctrl/cmd-a (Win/Mac).
- Go to “View” – “Show Chemical Properties Window”
- Go to “View” – “Show Analysis Window”
- Go to “Structure” – “Predict ^{1}H-NMR Shifts”





Additional Tools: Generic Structures (contd)

- Add the following substituents to each: amino, methoxy, fluoro, cyano.
  - See live demo for instructions on how to do this.

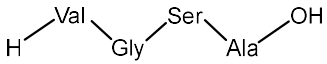


- Now select everything and go to “Structure” – “Expand Generic Structure”

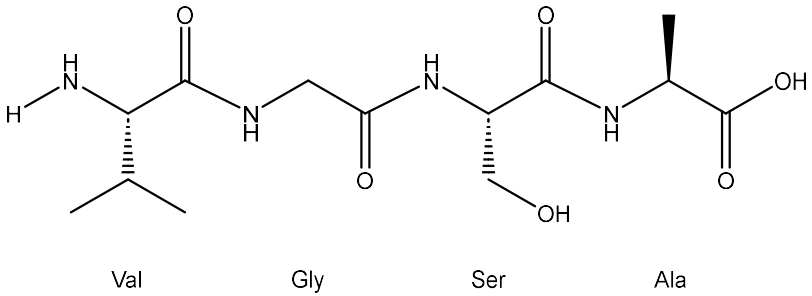
Additional Tools: Building Peptides

- Chemdraw contains a lot of tools to assist biochemists.
- One “easy” way to build peptides is to first draw an alkyl chain:

- Then replace the Carbons with the three-letter amino acid code, and the termini for the terminal residues



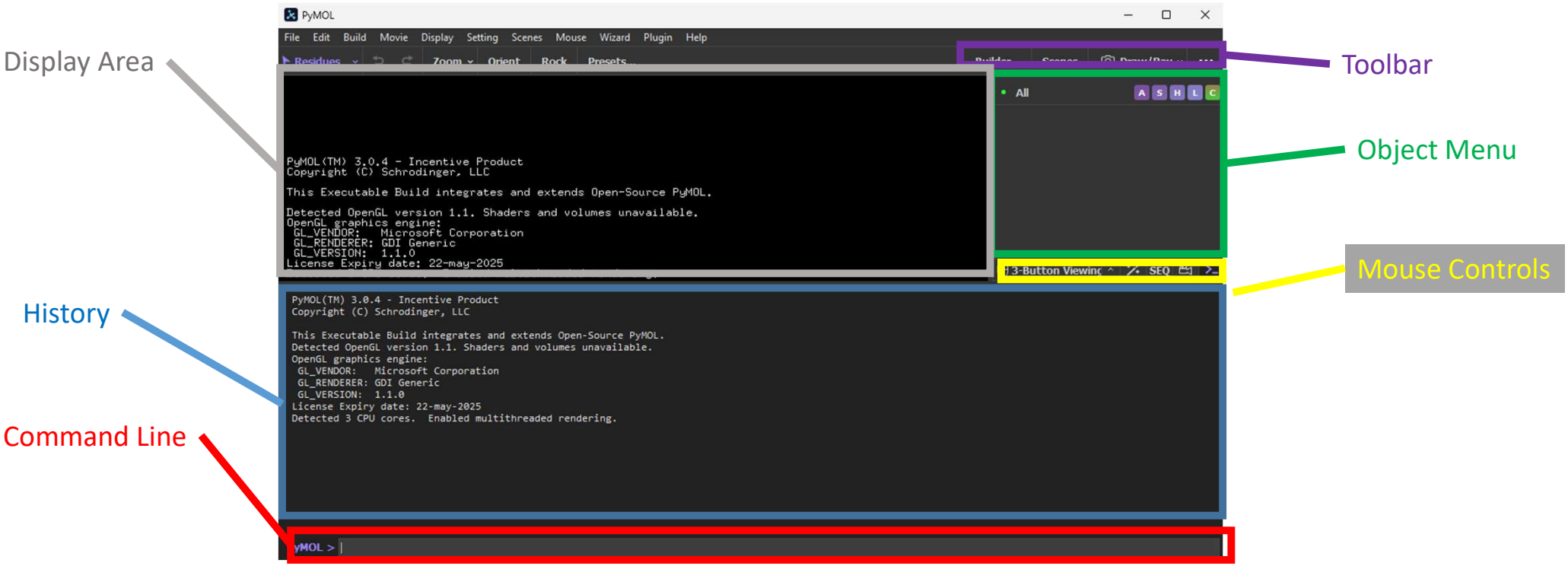
- Then select the structure, and go to “Structure”-“Expand Label”



Or just Copy/Paste the SMILES string!!

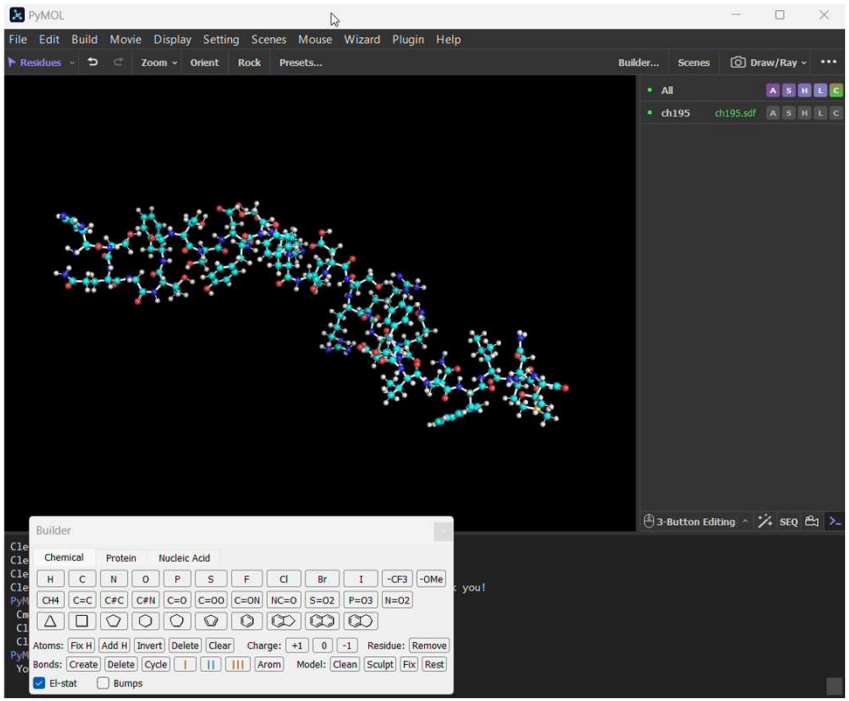
PyMOL: The Basics

- PyMOL is a powerful utility for studying molecules via interacting with the 3D representation(s) of the molecule(s).
  - Particularly suited for the study of biomolecules.



PyMOL: Tutorial 1 – Import From ChemDraw

- Build Glucagon with ChemDraw, and save it as an SDF.
- Open this file with PyMOL
- Click the builder button, and then click the ‘Add H’ button.
- Now click the ‘Clean’ button.



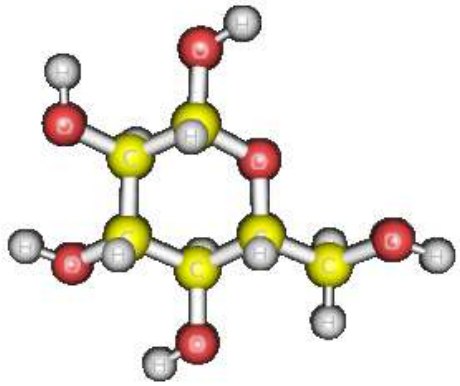
PyMOL: Tutorial 2 – Making Movies

- The PyMOL GUI has a set of tools to make simple but high-quality movies that can be exported to powerpoint.
  - There are countless other options when you use the command line to make the movie!
  - https://pymol.org/tutorials/moviemaking/
- In this simple example we will Zoom In on a inhibiting ligand for a protein

- Type the following in the command line:
  - mset 1x60
  - fetch 1t46
  - cmd.show_as("cartoon")
  - scene 001, store
  - show sticks, organic
  - orient organic
  - scene 002, store
  - mview store, 1, scene=001
  - mview store, 30, scene=002
  - mplay

PyMOL: Tutorial 3

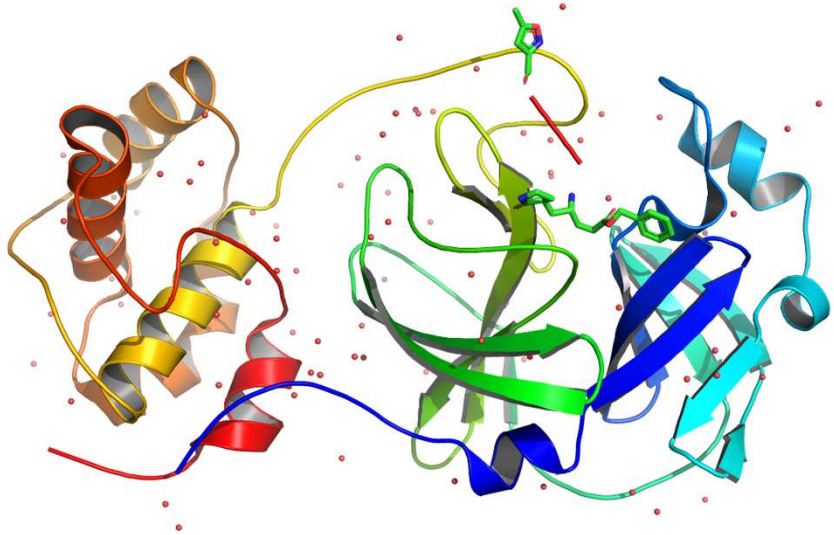
- Try to fetch and display β-glucose as shown to the right using only the command line:
  - Note … β-Glucose has a PDB code "BGC"
- One extra note … when loading/saving files from your computer, in general you should use the complete file path.
  - MAC: The complete file path for:
    - Dropbox: "/Users/*UserName*/Dropbox", etc…
  - WINDOWS: The complete file has the form:
    - "C:\Users*UserName*\Documents\", etc…



- fetch *code*: downloads a file from the internet.
- center *ObjName*: Centers the molecule in the display.
- orient *ObjName*: Lines the molecule's principle axes with the screen axes.
  - Z: out-of-plane
  - X: Right-to-Left
  - Y: Up-to-Down
- rotate *axis*, *degrees*: Rotates the molecule along the defined axis.
- clean *ObjName*: cleans the geometry with the MMFF94 force field.
- zoom: Auto-zooms the molecule.
- preset.ball_and_stick(selection='*ObjName*', mode=1): Changes the molecular representation to ball and stick.
- util.cba*x*: Change the color scheme, here *x* refers to the color of the Carbon atoms (g green, y yellow, etc…)
- save *filename.ext*: Saves the file
- ray: Generates a ray for your molecule.
- png *filename*, width=300,dpi=300, ray=1: Saves the previously generate ray to a file.

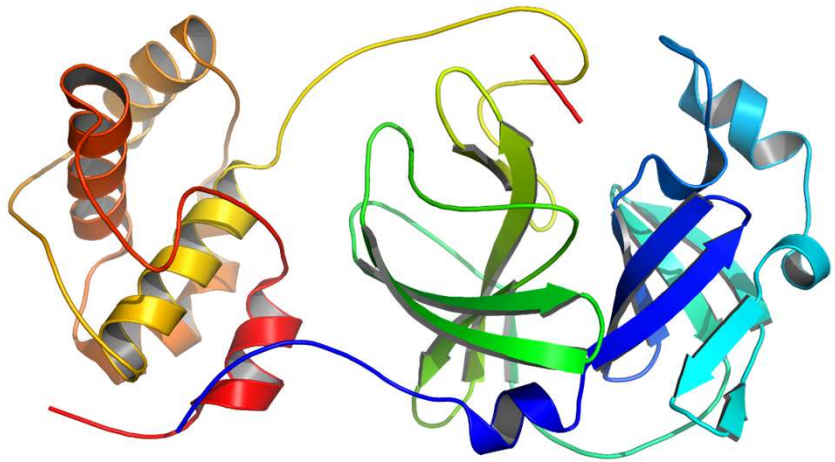
PyMOL: Loading PDBs

- PyMOL has a very useful Protein Data Bank (PDB) importer to ease the visualize and exploration of proteins.
- First, pick a protein, any protein!
  - Go to www.rcsb.org/pdb/home/sitemap.do
  - In the search bar, type in the name of your protein.
- A list will show up that contains the PDB code for different forms of your protein.
- Now go to "File" – "Get PDB…" and enter the code. Shown to the right is the results for getting 6LU7 (SARS-CoV-2).
  - Or you can type fetch 6LU7
  - Shown to the right is the Publication with solvent preset style



PyMOL: Macromolecule Representations

- There are many different "styles" to represent large macromolecules such as proteins. We will focus on three of the major options.
  - On the previous slide, we used a hybrid style that contained two of the three base styles.
  - **Base Style 1: CARTOON**
  - Base Style 2: STICKS
  - Base Style 3: SPHERES



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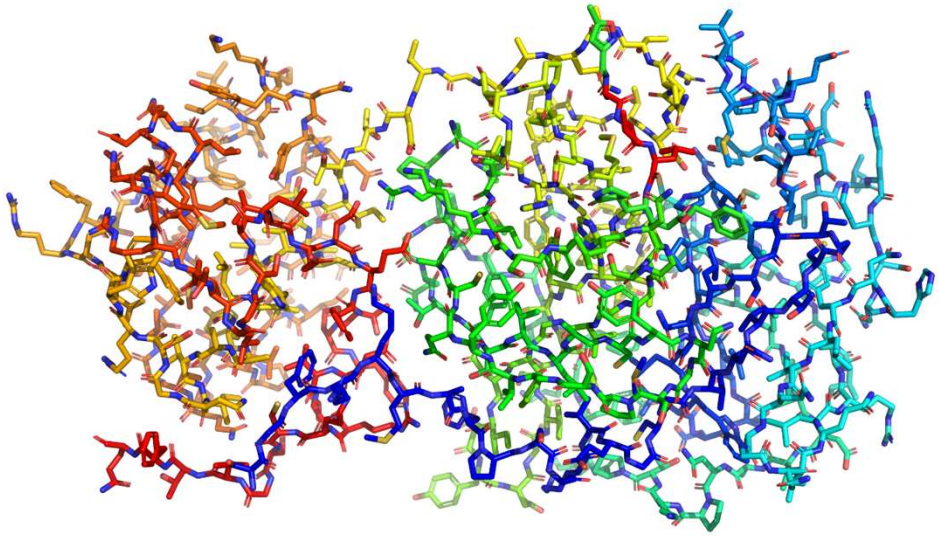

Try Out The Slab Viewing Function!
Hit scroll your scroll-wheel!

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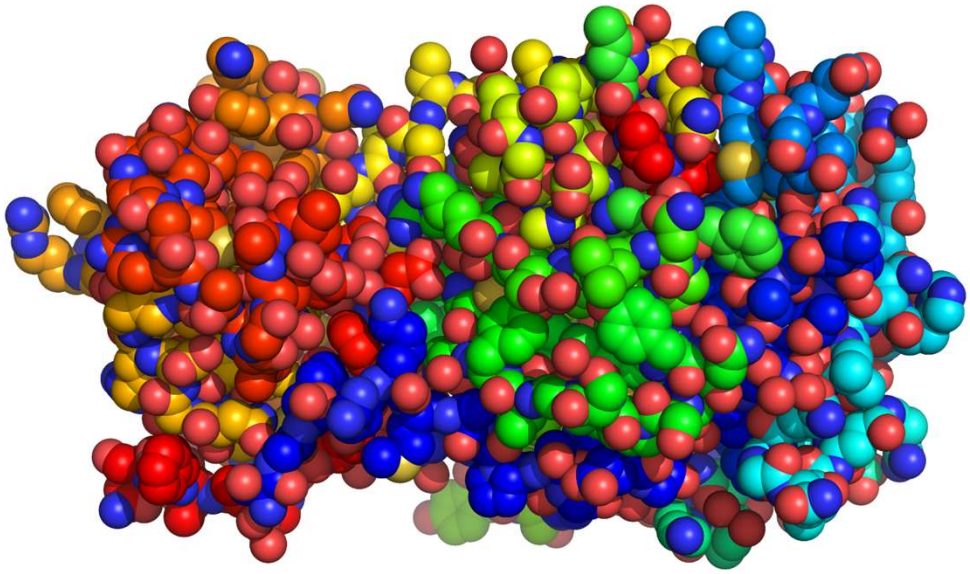

PyMOL: Scripting Library

- There are a lot of PyMOL users who have published some custom scripts!
  - https://www.pymolwiki.org/index.php/Category:Script_Library (old)
  - https://github.com/Pymol-Scripts/Pymol-script-repo (more modern)