Spring School on Digital Chemistry Applied to Drug & Crop Protection Discovery

Les Diablerets, 16.-20. April 2023

Beyond software: CADD behind the scenes

Wednesday, 19.04.2023, 14:00-18:30

In contrast to the other sessions, where you learned about different concepts & technologies and how to apply them in a CADD setting, we will focus now on the discussion of results you obtain from those tools in a concrete project-like setting. Nowadays, computational tools have evolved a lot in the sense, that their application is often just a button click away, and by keeping "standard settings" almost everybody can retrieve some "computational results/ predictions" on their target. But actually, that's only when the work of a CADD scientists starts: We will have different examples ready to analyse those initial results, which aspects could be considered or discussed in depth and how to derive working hypotheses from them.

Installations

Please install **PyMol**:

Follow the instructions here:

Linux: https://pymolwiki.org/index.php/Linux_Install

MAC: https://pymolwiki.org/index.php/MAC_Install

Windows: https://pymolwiki.org/index.php/Windows_Install

download the exact files mentioned under “Example of filenames 2023-01-12”:

- pymol_launcher-2.5-cp311-cp311-win_amd64.whl
- pymol-2.6.0a0-cp311-cp311-win_amd64.whl
- numpy-1.22.4+mkl-cp311-cp311-win_amd64.whl

AND (Win)**Coot**:

https://www2.mrc-lmb.cam.ac.uk/personal/pemsley/coot/binaries/release/

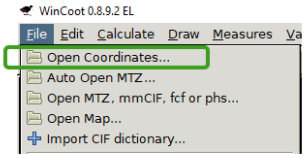
OR: http://bernhardcl.github.io/coot/wincoot-download.html

Introduction to Coot

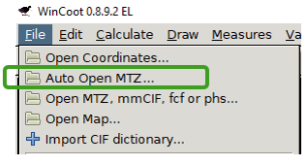
Mini intro Coot 1

Coot displays maps and models

- Open your .pdb file (coordinates):
  File → Open Coordinates…



- Open your .mtz file (reflection data from the xray experiment):
  File → Auto Open MTZ…



This will automatically create the 2FoFc and the FoFc maps. By default the contour level for sigma is 1.5 for 2FoFc and ±3.0 for FoFc maps.

Literature:

- Coot website
- Acta Crystallographica Section D66, 2010, 486-501, P. Emsley et al.: "Features and development of Coot"

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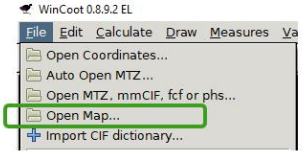
Mini intro Coot 2

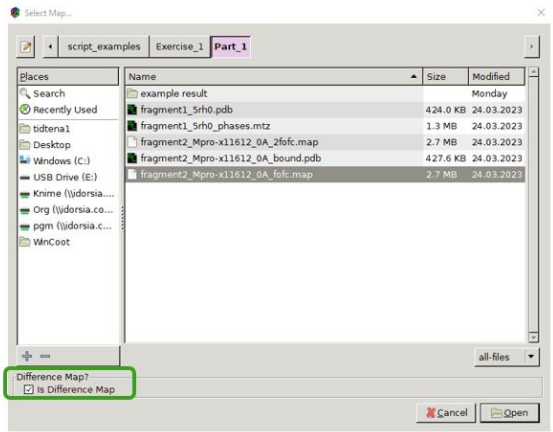
In case you don't have the .mtz

- Open your .map files (2FoFc and FoFc maps):
  File → Open Map…



Make sure to tick the box for the FoFc map in the next dialog.

By default the contour level for sigma is 1.5 for 2FoFc and ±3.0 for FoFc maps.



Literature:

- Coot website
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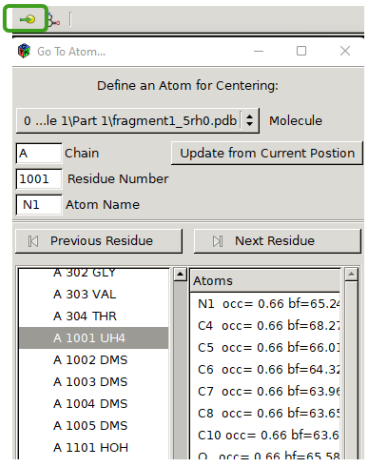
Mini intro Coot 3

How to navigate

- Jump to your ligand in the viewer:
  - ➢ click the little symbol for "Go To Atom"  or press F6
  - ➢ in the new window "open" the chains by clicking on the triangle and scroll down through the residues. Click on the residue that is the ligand (hint: usually the ligand comes after all amino acids and before solvents/ions)
  - ➢ in the viewer window the center will jump to the selected molecule
- Rotate: Hold the left mouse button and move
- Zoom: Hold the right mouse button and move
- Jump: Middle-button-click on an atom and the viewer center will jump
- Drag: Hold the middle mouse button and move



Literature:

- Coot website
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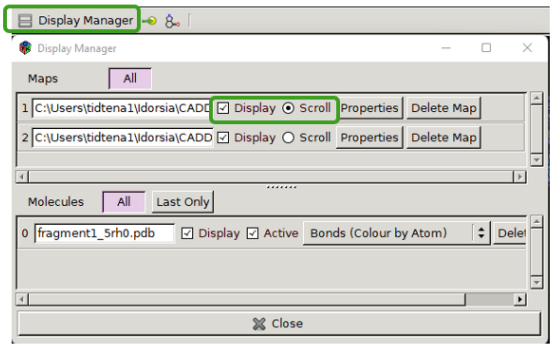
Mini intro Coot 4

How switch objects on and off, scroll through sigma contour levels

- Open the Display Manager (shortcut F7)
- All opened maps and coordinate files are listed and can be switched on and off (tick or untick the "Display" box)
- Only one map at a time can be selected for scrolling through sigma contour levels
- Scroll: use the mouse wheel
  (the sigma level will be displayed on the top of the viewer window)



Literature:

- Coot website
- Acta Crystallographica Section D66, 2010, 486-501, P. Emsley et al.: "Features and development of Coot"

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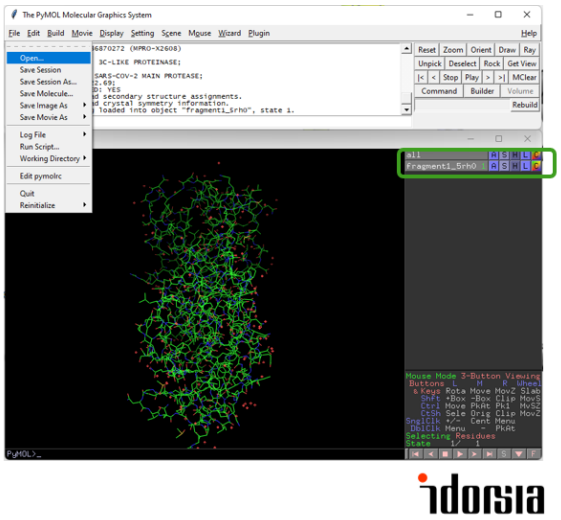
Introduction to PyMol

Mini intro PyMol 1

PyMOL is a user-sponsored molecular visualization system on an open-source foundation, maintained and distributed by Schrödinger.

- PyMol has 2 windows (viewer & commands menu)
- File → Open… and select your .pdb file
- A new object appears on the object panel
- Switch the object on and off in the viewer by clicking on it in the object panel
- Click on the "S" (show) next to the object to change visualization styles (lines, sticks, cartoon, surface…)
- Click on the "H" (hide) to remove visualization styles
- Click on the "C" (color) to change coloring. If you select "by element" only carbons will be colored differently.



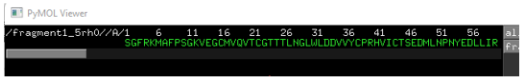
Literature:

- PyMol website

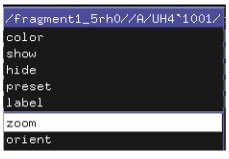
Mini intro PyMol 2

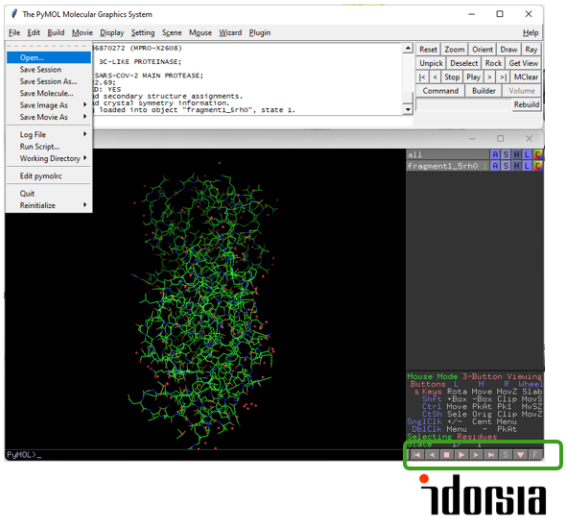
PyMOL is a user-sponsored molecular visualization system on an open-source foundation, maintained and distributed by Schrödinger.

- Zoom: Hold the right mouse button and move
- Mouse wheel: change the depths of your view
- Rotate: Hold the left mouse button and move
- Jump: middle-button-click on atom
- "S" on the far bottom right in the viewer window displays the sequence of your visible objects. It will be shown in the top of the viewer window:



scroll it to the right, right-click on the ligand, "zoom" to the ligand



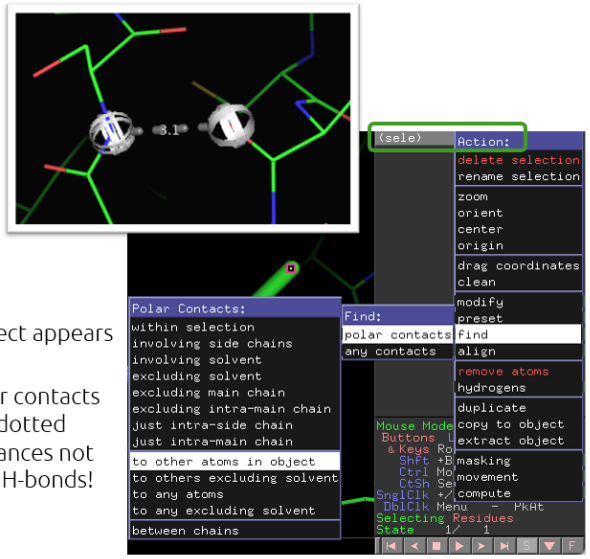


Literature:

- PyMol website

Mini intro PyMol 3

PyMOL is a user-sponsored molecular visualization system on an open-source foundation, maintained and distributed by Schrödinger.



- Measure distances between 2 atoms:
  - Ctrl + middle-button-click on 2 atoms: a dotted line will be shown labeled with the distance in Å
  - save it as object: type “dist” into the bottom line of either of the 2 windows) and press Enter
  - Remove atom markers: Ctrl + middle-button-click into the background
- Find polar contacts:
  - left-click on ligand (it will be selected: “(sele)”-object appears on the right)
  - Click on “A” next to the sele-object → find → polar contacts → to other atoms in object: a new object with all dotted lines will be created. **Caveat**: it just considers distances not angles – not all of these dotted lines will be good H-bonds!

Literature:

- PyMol website

Mini intro PyMol 4

PyMOL is a user-sponsored molecular visualization system on an open-source foundation, maintained and distributed by Schrödinger.

- Align two protein structures on their Cα:
  - Type “align” into the bottom line of the window:


```
align object-name, reference-object-name ↵
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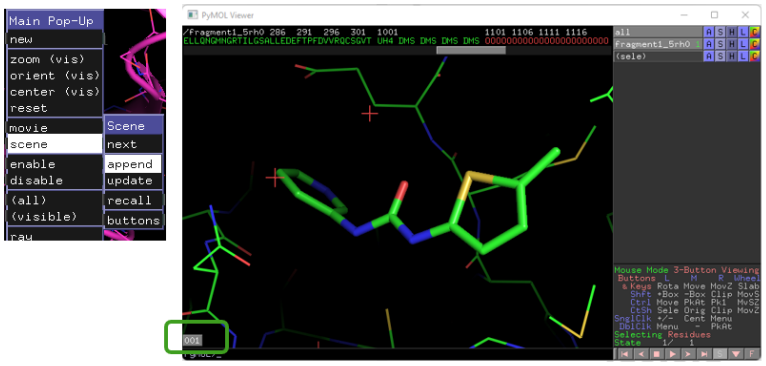
- Scenes: Save a particular view as a scene
  - Right click into the background → scene → append
  - A scene “001” will be saved in the bottom left of the viewer
  - Right click on it an rename or update it (in case of changes)
  - Left click on it to see your pre-defined view



Literature:

- PyMol website

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