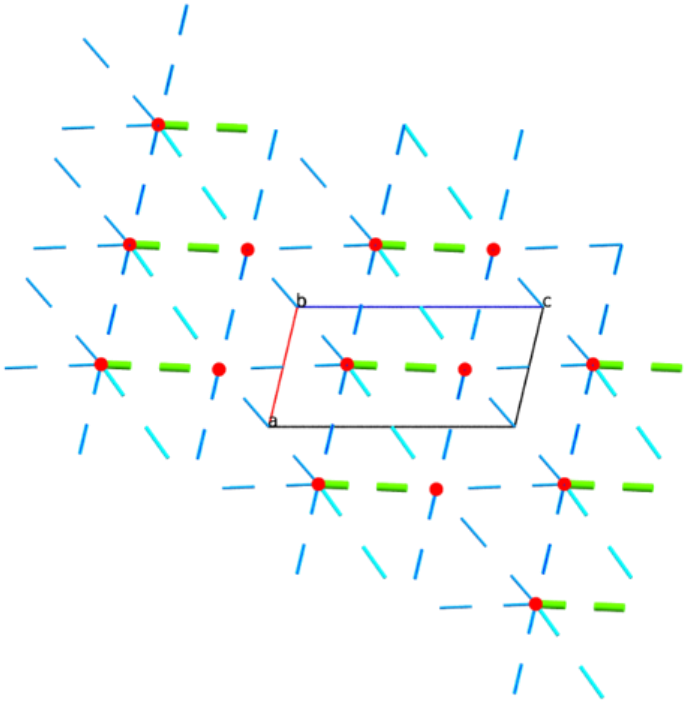
Interaction Network Analysis with Mercury

Developed using 2026.1 CSD release



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Introduction

This workshop will focus on the Interaction Networks tool in Mercury. Interaction Networks make use of *force field*-based calculations to provide information that may be useful for understanding interactions in crystal structures. The tool calculates and displays *Periodic Bond Chains* (PBCs) which are chains of repeating strong interactions that can be used to explain the relationship between crystal structure and crystal growth or to aid the interpretation of other properties of a crystal structure.

Learning Outcomes

At the end of this workshop, you will be able to:

- Calculate PBCs in Mercury using the Interaction Networks tool and interpret the results
- Visualise and rationalise the morphology of a crystal using the BFDH model

This workshop will take approximately **25 minutes** to be completed. The words in *Blue Italic* in the text are linked and reported in the Glossary at the end of this handout.

Prerequisite Skills

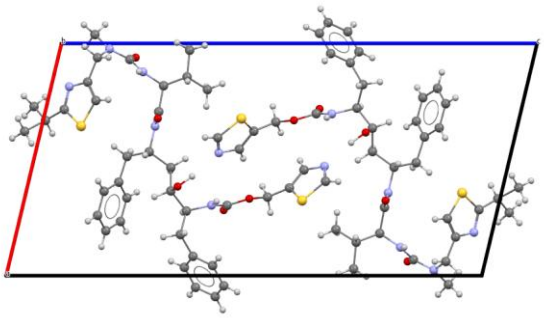
Familiarity with the Mercury interface is desirable but not essential. You may find the free course https://www.ccdc.cam.ac.uk/community/training-and-learning/csdu-modules/visualization-101/ helpful if you are not already familiar with Mercury.

Materials

No additional materials are required.

Example: Calculating Periodic Bond Chains in Mercury

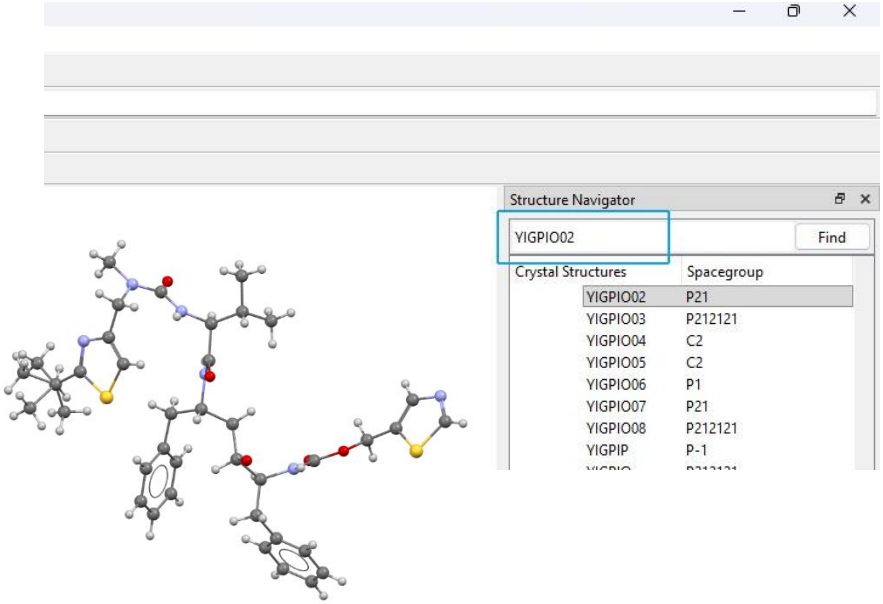
In this example, we will use the Interaction Networks tool in Mercury to calculate the periodic bond chains (PBCs) of a *polymorph* of ritonavir (Form I, CSD refcode YIGPIO02) and explore whether they might help explain the observation of a rod-like habit for crystals of this form. [1]



Ritonavir, Form I, CSD refcode YIGPIO02

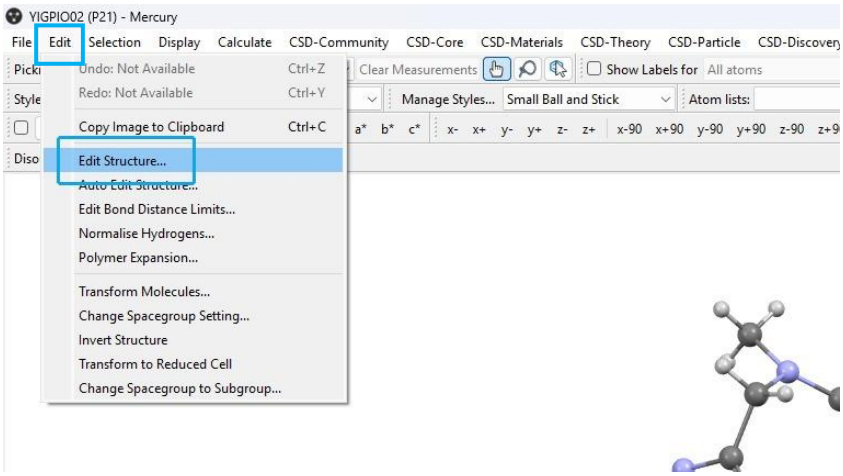
Preparing the Structure

1. In the Structure Navigator, type "YIGPIO02". The structure of the Form I polymorph of ritonavir will be loaded in the visualiser.

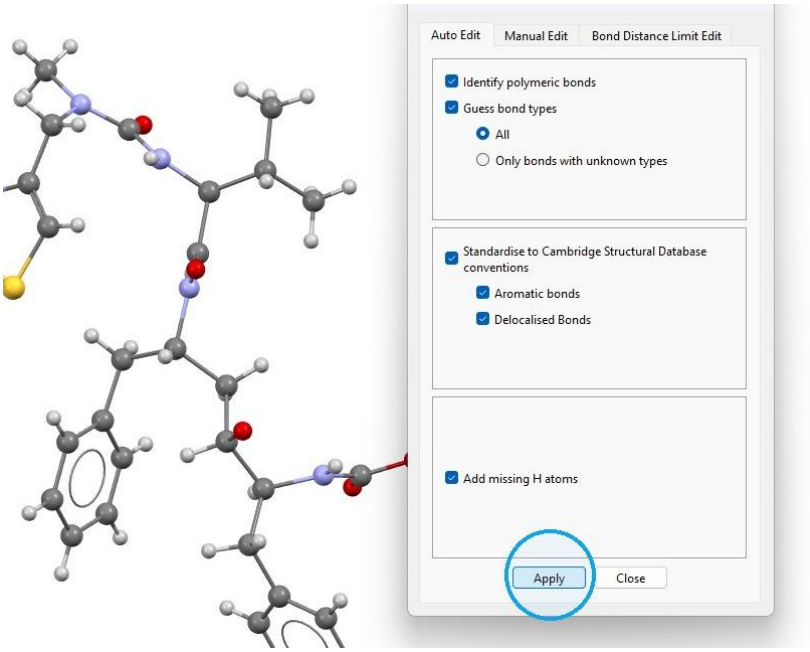


[1] J. Baur, S. Spanton, R. Henry, J. Quick, W. Dziki, W. Porter and J. Morris, *Pharm. Res.*, 2001, **18**, 895–866 DOI: 10.1023/A:1011052932607

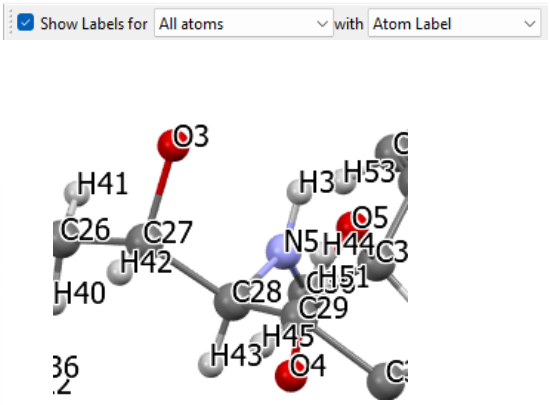
2. From the top menu, go to **Edit > Edit Structure** to open the structure editing tool.



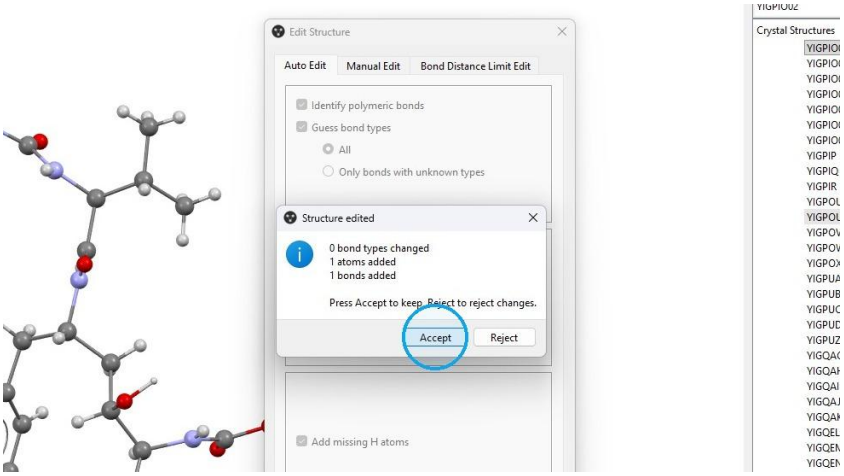
3. One alcohol group is missing a hydrogen atom. The missing atom can be added to the structure in Mercury. Click on the **Auto Edit** tab, make sure **Add missing H atoms** is ticked, then click **Apply**. You can also edit the structure manually if you prefer, using the tools in the Manual Edit tab.



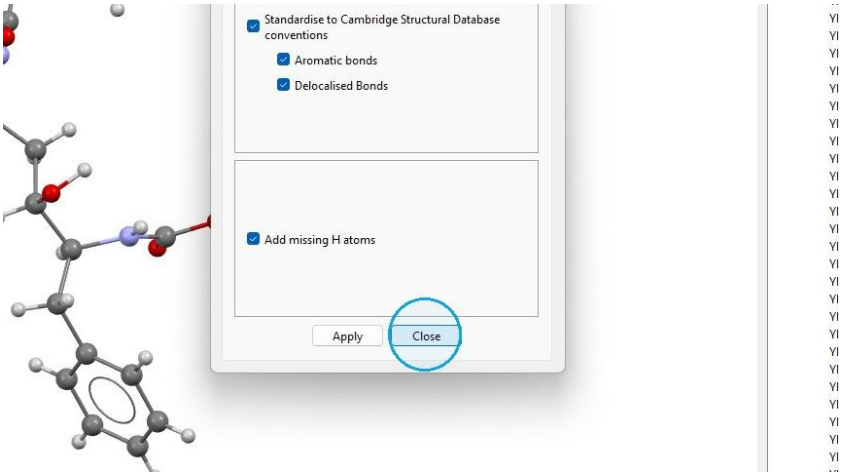
Tip: if you tick Show Labels for *All atoms* with *Atom Label*, the affected oxygen atom is **O3**.



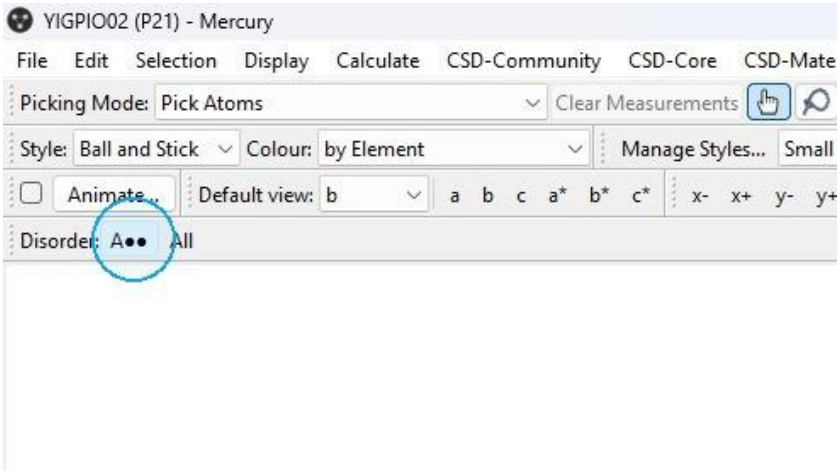
4. Check that the hydrogen atom has been added as expected, then click **Accept**.



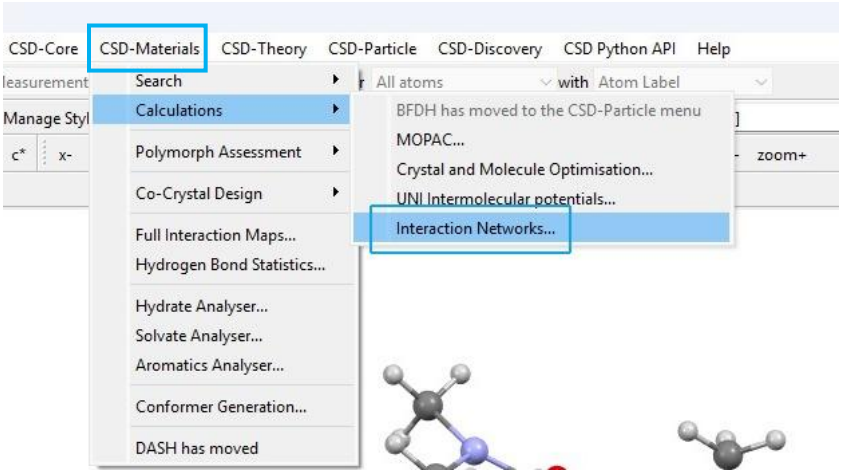
5. Click **Close**.



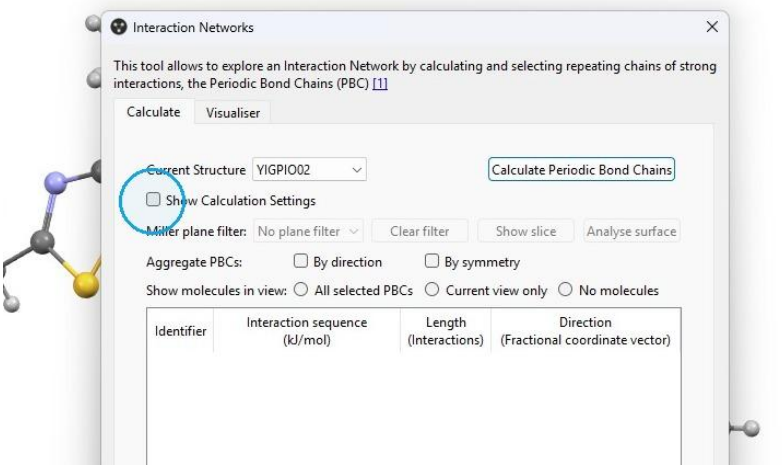
6. YIGPIO02 has a disordered isopropyl group. Click "A●●" to select the first disorder group of the disorder assembly.



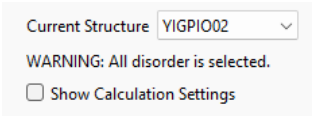
7. From the **CSD-Materials** menu, select **Calculations > Interaction Networks**.



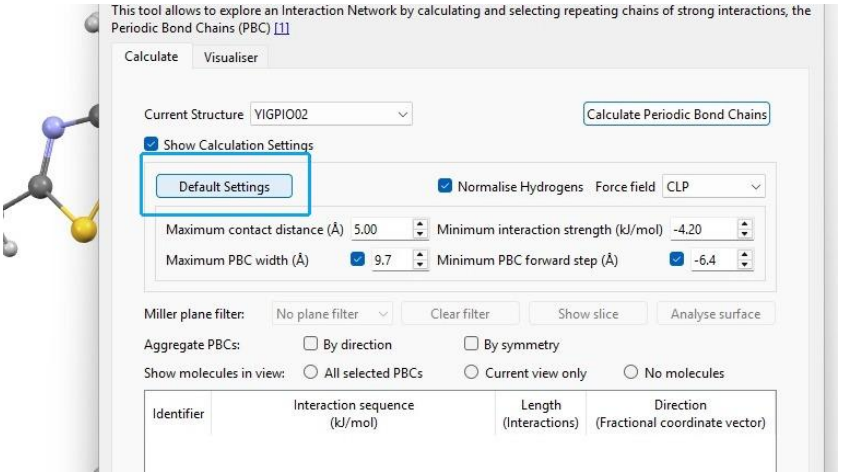
8. In the Interaction Networks tool, click **Show Calculation Settings**.



Tip: if you have not edited the structure or selected a disorder group, a warning may be displayed. You will need to complete these steps to proceed.



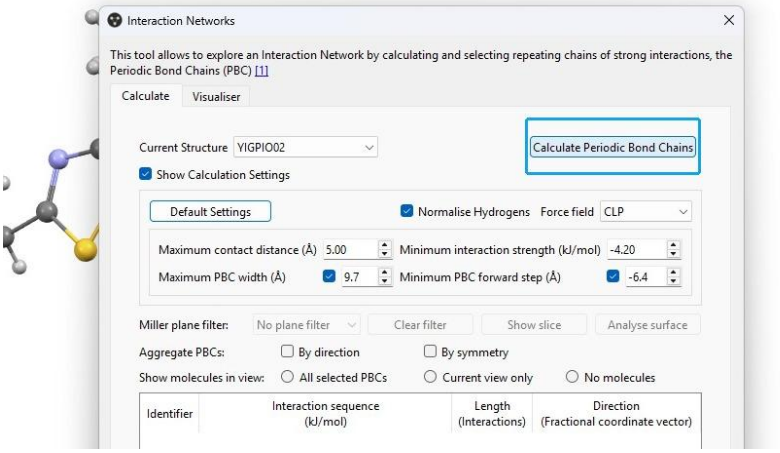
9. Click **Default Settings**.



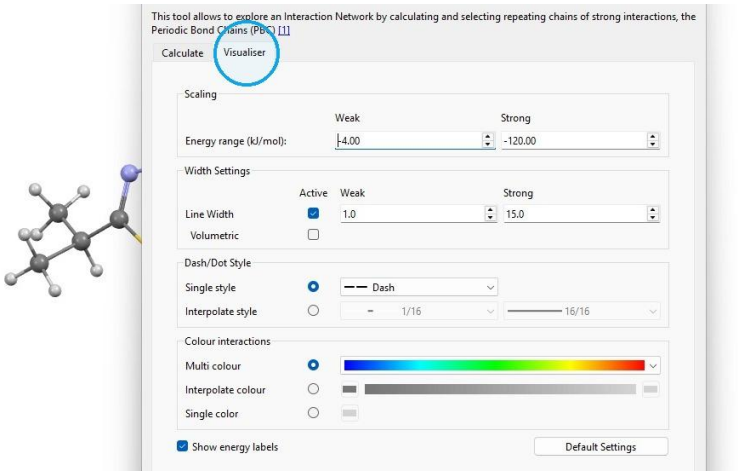
Tip: The forcefields available in Interaction Networks are CLP, UNI and CSD-OPCS16.

Further details on the settings can be found here.

10. Click **Calculate Periodic Bond Chains**.

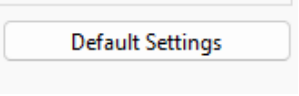


11. Click on the **Visualiser** tab and ensure that the settings are as shown below. Click **Default Settings**, then tick the box next to **Line Width** in the Width Settings area (see 11a and 11b).

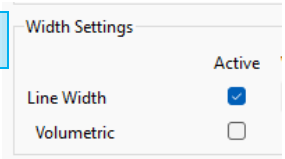


Tip: The appearance of the PBCs is highly customisable. Feel free to explore different styles but note that your view may not match that shown later in the handout if you do.

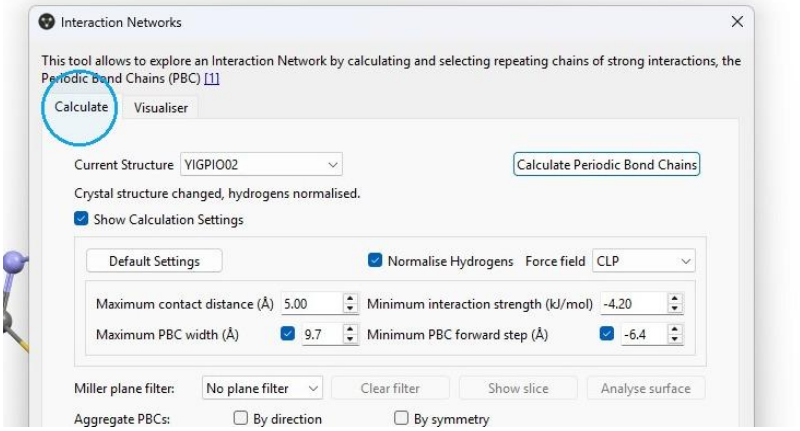
11a



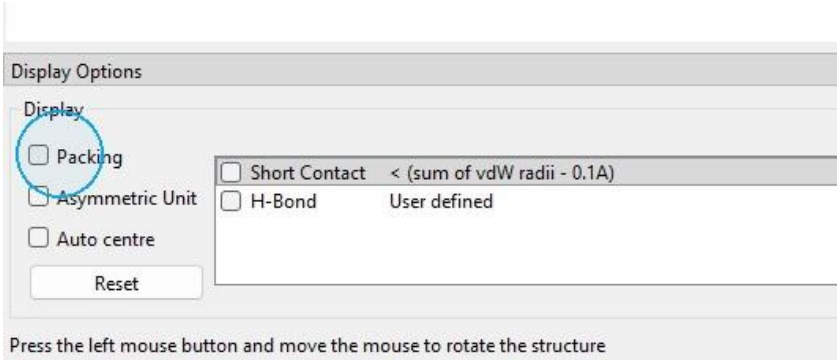
11b



12. Click on the **Calculate** tab to return to the calculation results.

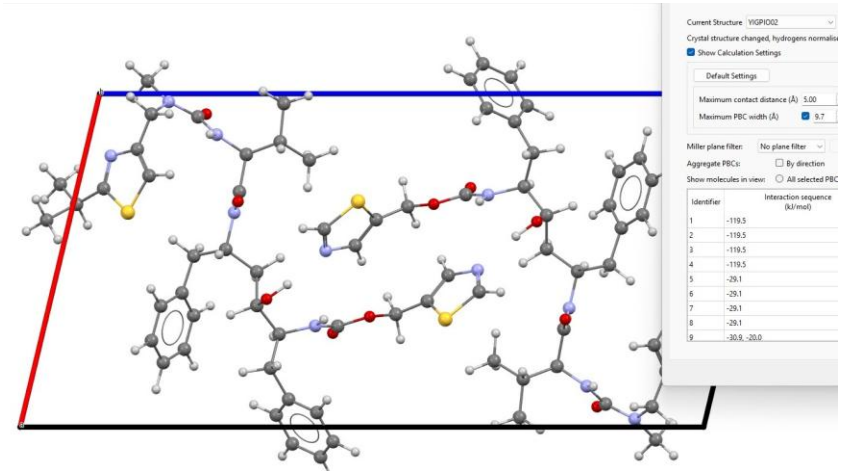


13. Enable **Packing** in the Display Options toolbar.

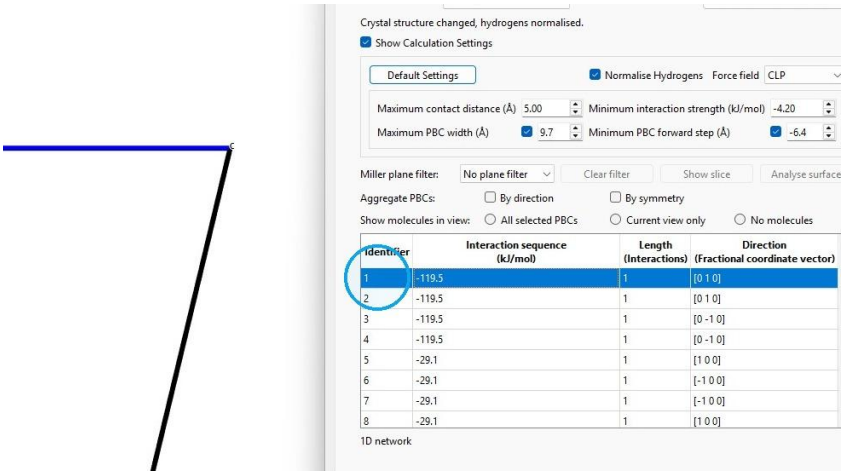


Tip: If you want finer control of the packing display, go to **Calculate > Packing/Slicing** to view more options.

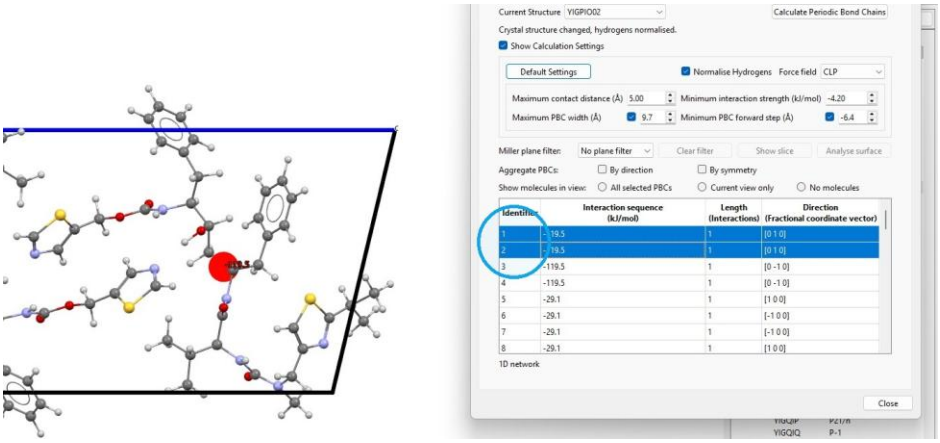
14. You may need to zoom in/out to get a good view of the structure. You can hold down the right-hand mouse button while moving up/down with the mouse to do that.



15. Click on the rows in the table to show the selected periodic bond chain (PBC) in the visualiser.

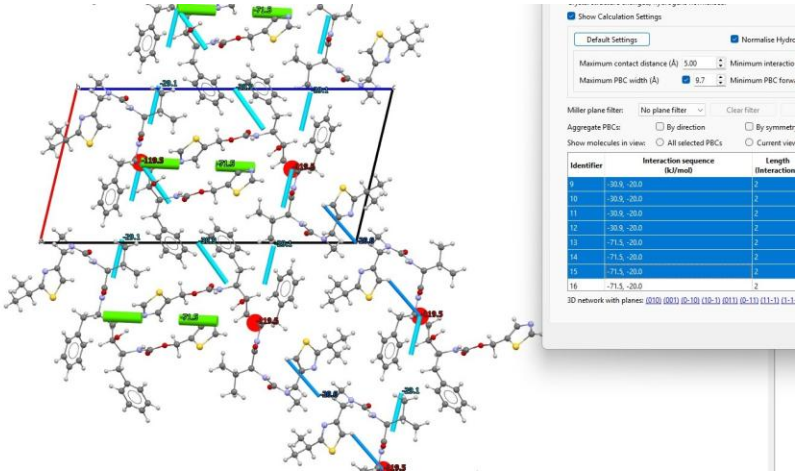


16. Hold down Ctrl whilst clicking on rows to add multiple PBCs to the display.

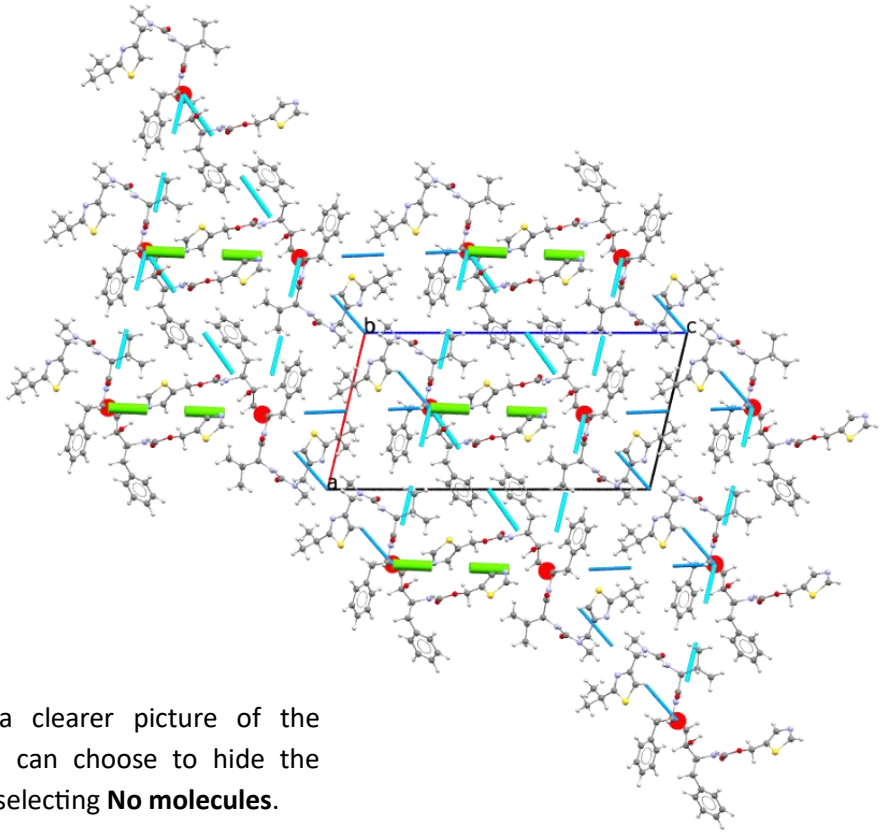


Tip: To reduce the number or rows visible in the table, you can enable to Aggregate PBCs by direction, by symmetry, or both.

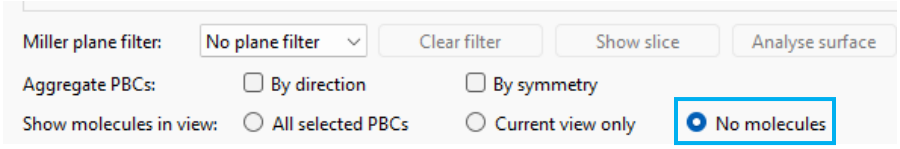
17. As you continue to add periodic bond chains, you will gain a picture of the interaction networks in the structure, and you can identify the directions of strong interactions by the colour and thickness of the lines, if you have these options enabled.

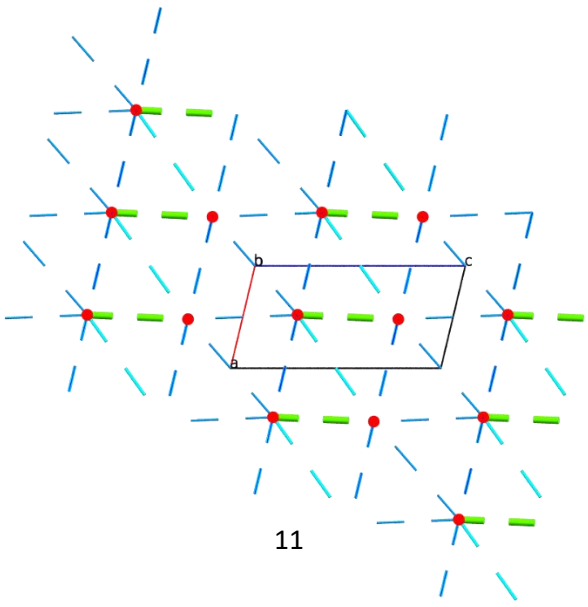


18. To select all the PBCs, click a row in the table, then press Ctrl + A. Take some time to explore the different PBCs and their arrangement and note if there are any particular directions with strongly stabilising PBCs. You should see that there are columns of strong (red) interactions interlinked by medium strength (green) interactions. The remaining interactions (blue) are considerably weaker.

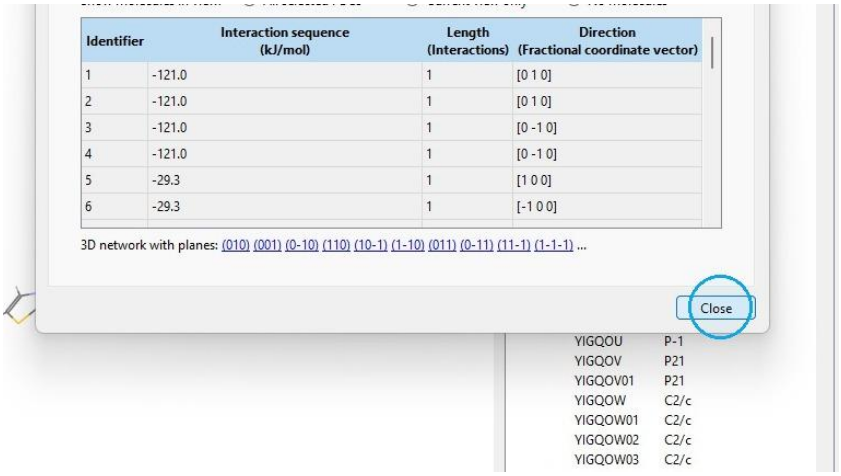


Tip: To get a clearer picture of the networks you can choose to hide the molecules by selecting **No molecules**.

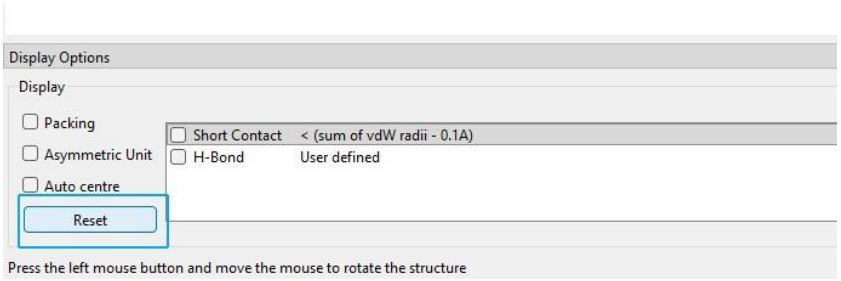




19. Click **Close** in the Interaction Networks tool.

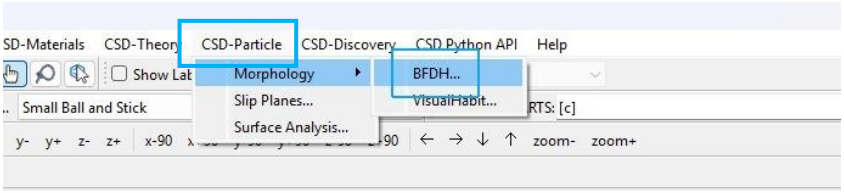


20. Click **Reset** in the Display Options toolbar.

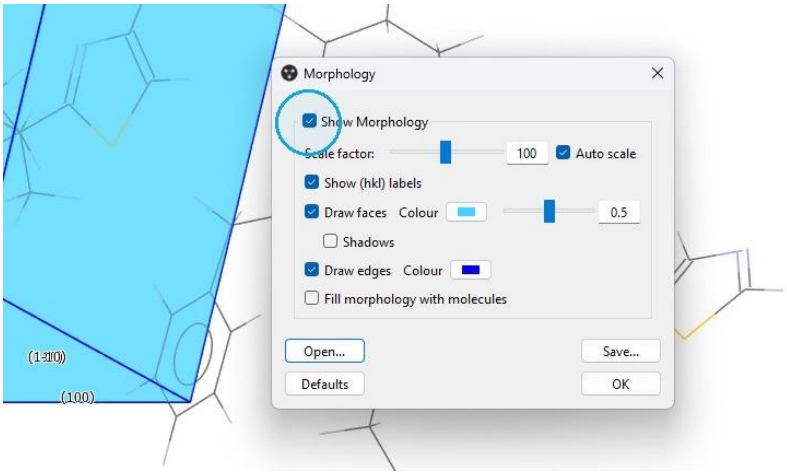


We will proceed to visualise the morphology of the crystal using the Bravais, Friedel, Donnay and Harker (BFDH) method in Mercury.

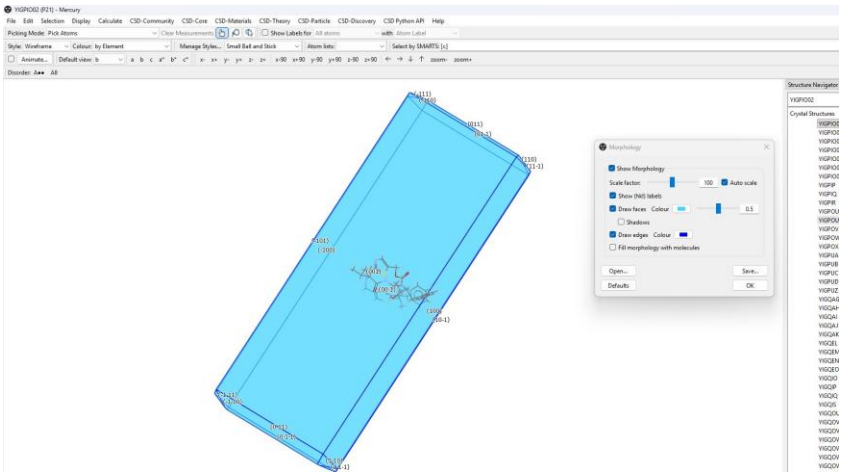
21. From the **CSD-Particle** menu, select **Morphology > BFDH**.



22. The morphology should be displayed automatically. If it is not, make sure that **Show Morphology is ticked**.

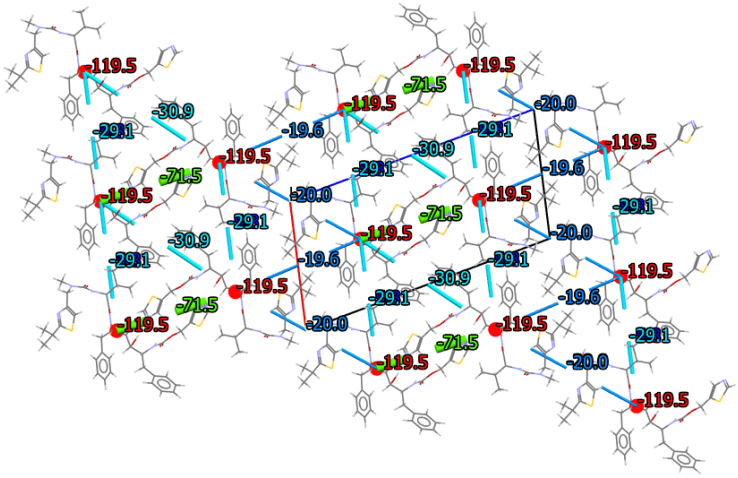


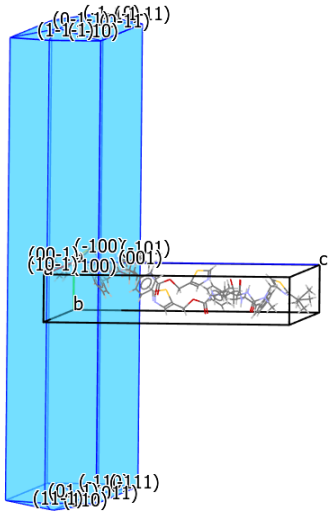
23. You should find that the morphology has a rod-like shape.



Conclusions

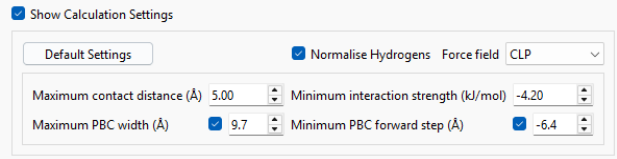
In this example we have used the Interaction Networks tool to calculate the periodic bond chains in a polymorph of ritonavir. We have found that there are strongly stabilising PBCs running in parallel columns (along the [0 1 0] and [0 -1 0] directions) throughout the structure (red) and that the columns are linked either by moderate strength (green) or low strength (blue) interactions, as shown below. In the process of crystal growth, this may lead to preferential attachment of molecules in the [0 1 0] direction which could ultimately be expressed in the morphology. The simulated BFDH morphology of the YIGPIO02 matches experimentally observed ones reasonably well (see Figure 1 of this paper). Cases where this happens suggest an implicit correspondence between the strength of intermolecular interactions and the unit cell dimensions (the *b* axis is considerably shorter than the *a* and *c* axes in this structure). In this particular case, it may be that the strong interactions parallel to [0 1 0] relate to the short *b* axis, hence fast growth and relatively smaller faces in this direction.





Notes on Interaction Networks Settings

Some further details on the settings for calculating Periodic Bond Chains.



- **Normalise Hydrogens** applies a correction before the optimisation to all C-H, N-H and O-H bond lengths, moving the H atom along the bond vector to make the bond length equal to the average neutron diffraction value.
- **Force Field** allows you to select from the implemented force fields in Mercury, which include UNI, CLP and CSD-OPCS16.
- **Maximum contact distance** sets the maximum distance between the closest atoms of two molecules for an interaction to be explored.
- **Minimum interaction strength** sets the least attractive interaction in a chain which will lead to a PBC being listed. This is constrained to be ≤ 0.00, as more attractive interactions have more negative energies of interaction.
- **Maximum PBC width** sets the maximum diameter of a cylinder containing the chain of interactions for that chain to be listed as a PBC.
- **Minimum PBC forward step** defines the minimum progress limit for any step in a chain, in order for the chain to be listed as a PBC. This is used to prevent large backwards steps against the overall chain direction, and defaults to -2/3 of the maximum PBC width.

Summary

In this workshop we have demonstrated Interaction Networks tool in Mercury. You should now be able to:

- Calculate the PBCs in a crystal structure using Interaction Networks and interpret the results
- Calculate the BFDH morphology of a crystal in Mercury

For your reference, you can find the user manual here https://www.ccdc.cam.ac.uk/media/mercury-1.pdf.

Next Steps

If you have found the tools shown in this workshop useful, you might like to try some of our other self-guided workshops from the CSD-Materials and CSD-Particle areas, where you can explore other tools to study intermolecular interactions and morphology.

https://www.ccdc.cam.ac.uk/community/training-and-learning/workshop-materials/csd-materials-workshops/

https://www.ccdc.cam.ac.uk/community/training-and-learning/workshop-materials/csd-particle-workshops/

How to cite these tools

Mercury: C. F. Macrae, I. Sovago, S. J. Cottrell, P. T. A. Galek, P. McCabe, E. Pidcock, M. Platings, G. P. Shields, J. S. Stevens, M. Towler and P. A. Wood, *J. Appl. Cryst.*, **53**, 226–235, 2020 DOI: 10.1107/S1600576719014092

A comparison of the force fields implemented in Crystal Optimiser can be found in this paper: L. M. Hunnisett, P. Sacchi and A. G. P. Maloney, *Struct. Chem.*, 2026, **37**, 1063–1067 DOI: https://doi.org/10.1007/s11224-025-02715-z

Glossary

Disorder

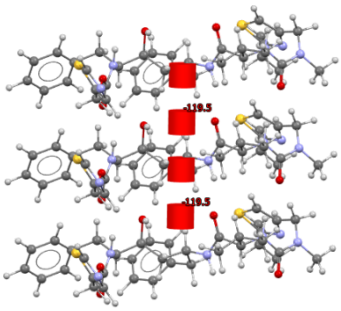
A disorder assembly is a cluster of atoms that show long range positional disorder but are locally ordered. A disorder groups consists of the atoms in the assembly that are linked by occupancy. E.g. an isopropyl group disordered over two sites has one disorder assembly and two disorder groups.

Force field

A parameterised mathematical model used to calculate the potential energy of a crystal structure from atomic positions, enabling estimation of lattice energies and crystal packing interactions. Mathematical descriptions of the force fields implemented in Crystal Optimiser can be found here.

Periodic Bond Chain

Periodic Bond Chains (PBCs) were first introduced by Hartman and Perdok as a way to find a connection between crystal structure and crystal morphology, as described in their series of articles published in 1955.[2,3,4] According to Hartman and Perdok's theory, PBCs can help to identify directions of preferential growth of a crystal by considering uninterrupted chains of strong bonds (or intermolecular interactions) between the crystal's building units, which can be atoms or, molecules. Each PBC is identified with a vector indicating its direction, as well as information about the molecules that form part of the PBC.



A periodic bond chain in CSD entry YIGPIO02

Polymorphs

Polymorphism is the occurrence of two or more crystalline forms of the same substance. Where available, polymorph information can be displayed for Cambridge Structural Database (CSD) structures. Structures known to be polymorphic contain comments which include the word polymorph (when reported by the author), e.g., non-triboluminescent polymorph. There is also a CSD subset of polymorphic structures.

[2] P. Hartman and W. G. Perdok, *Acta Cryst.*, 1955, **8**, 49–52 DOI: 10.1107/S0365110X55000121
[3] P. Hartman and W. G. Perdok, *Acta Cryst.*, 1955, **8**, 521–524 DOI: 10.1107/S0365110X55001679
[4] P. Hartman and W. G. Perdok, *Acta Cryst.*, 8, 1955, **8**, 524–525 DOI: 10.1107/S0365110X55001680

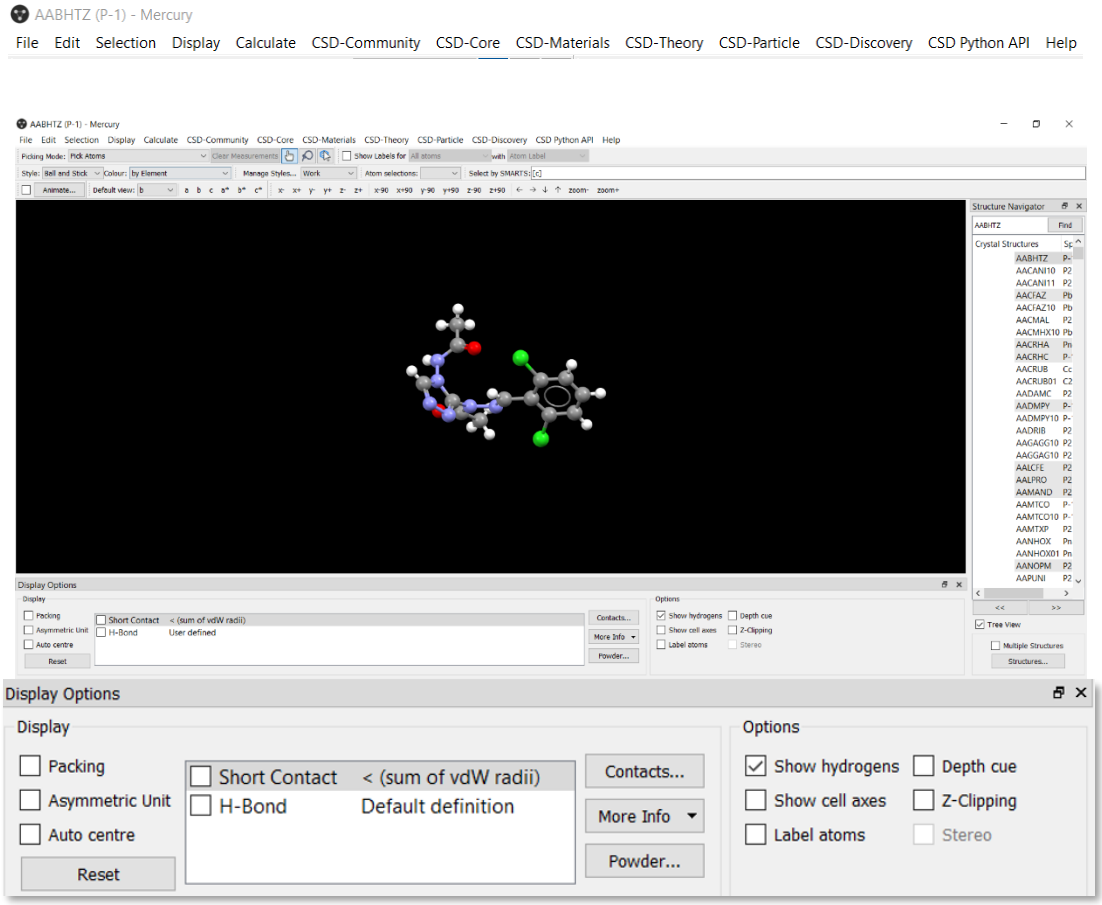
Basics of Mercury Visualization

Mercury is the CCDC's visualization software to view 3D structures of small molecules, generate images, and animations of molecules

In the following we will see some of the basics of navigation and visualization in Mercury that you will find helpful to support your analysis. You can also find an extensive range of video resources here.

In the **Mercury interface** we find:

- **At the top**: list of menus from which we can access visualization and analysis options, and other CSD components such as CSD-Materials.
- **On the right-hand side**: the **Structure Navigator**, with the database loaded (depending on your licence). The Structure Navigator allows you to select a refcode to visualize in the main Mercury window.
- **Beneath the main display window: Display options toolbar.** You can quickly view a packing diagram, display Hydrogen bonding and detailed information about the molecule using the More Info option.



Using the **mouse to enhance visualization**:



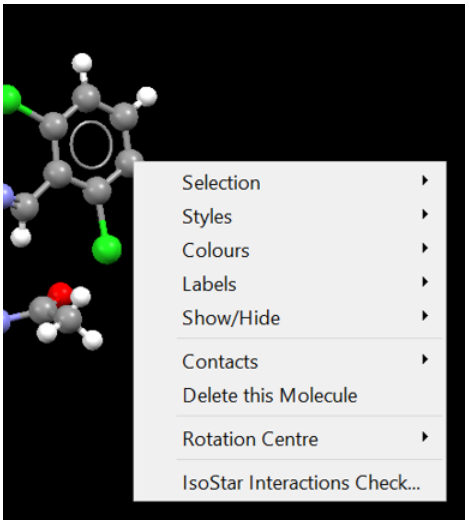
- Left mouse button and move – rotate molecules.
- Middle Mouse wheel – move molecules up and down.
- Right mouse button and move up and down – zoom in and out of molecules.
- Shift + Left mouse button and move - rotate in the plane molecules.
- Ctrl + Left mouse button and move - translate molecules.

Additional gestures may be available with trackpads.

Right click:

a) Near a molecule and
b) Away from a molecule

a



b



