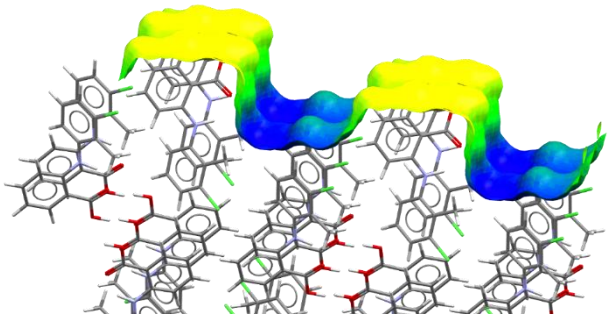
Surface Analysis with CSD-Particle Tools in Mercury (PAR-001)

Developed using
2025.1 CSD Release

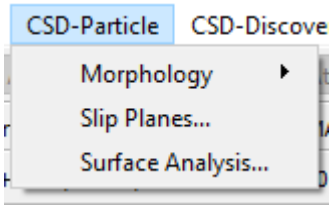


advancing structural science

Table of Contents

Introduction

This workshop shows you how to use functionality from the CSD-Particle suite to visualize and analyse the mechanical and chemical properties of molecular crystals. It uses quick computational models and algorithms, alongside data from the Cambridge Structural Database (CSD), to provide both qualitative and quantitative analyses of particle shape as well as surface and bulk properties. Such features are found under the CSD-Particle menu in Mercury.

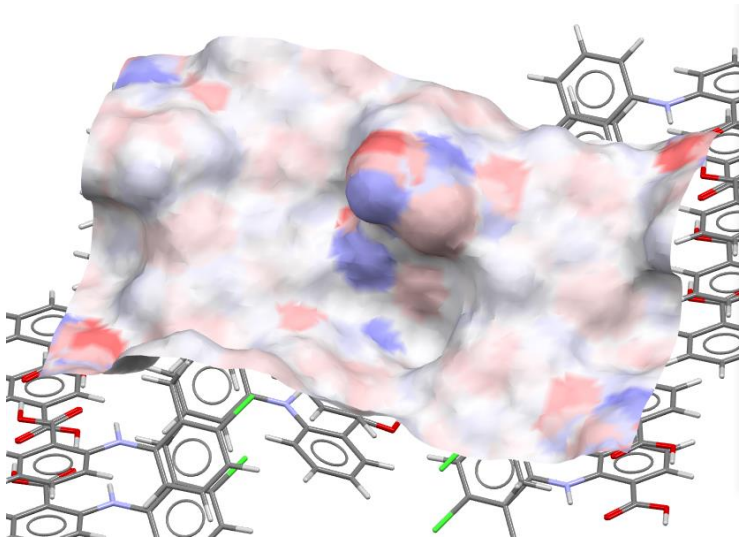


Before beginning this workshop, ensure that you have a registered copy of CSD-Materials or CSD-Enterprise installed on your computer. Please contact your site administrator or workshop host for further information.

Learning Outcomes

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

- Analyse particle surfaces.
- Calculate Full Interaction Maps on surfaces.



Note: The words in *Blue Italic* in the text are reported in the Glossary at the end of this handout. The exercise in this handout will take approximately ***45 minutes*** to be completed.

Pre-required Skills

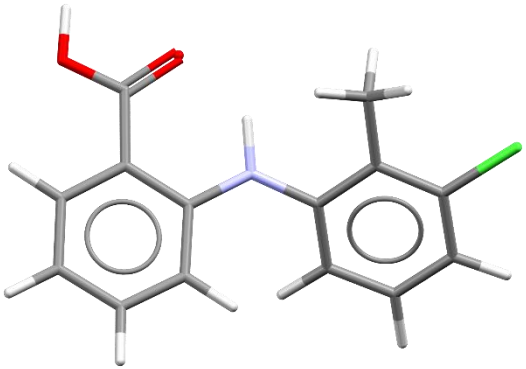
The following exercises assume you have a working knowledge of the basics of visualizing structures with Mercury, namely, how to display and manipulate structures from a 3D coordinates file. Familiarity with Full Interaction Maps (FIMs) would also be helpful (See FIMs workshop MER-002 and CSDU module).

Materials

There are no additional materials required for this workshop.

Example 1. Surface Analysis

In this example, we will employ tools from the *Surface Analysis* feature in CSD-Particle to investigate two different surfaces of a 2-(3-chloro-2-methylanilino)benzoic acid crystal. The two surfaces under investigation are the (110) and the (020). By calculating these two surfaces and analysing their properties and the chemistry on each surface, we will learn more about their activities.



CSD Entry KAXXAI10 2-(3-chloro-2-methylanilino)benzoic acid

1. Open Mercury by double-clicking the Mercury icon on the desktop.

2. In the **Structure Navigator** toolbar type the refcode KAXXAI10.

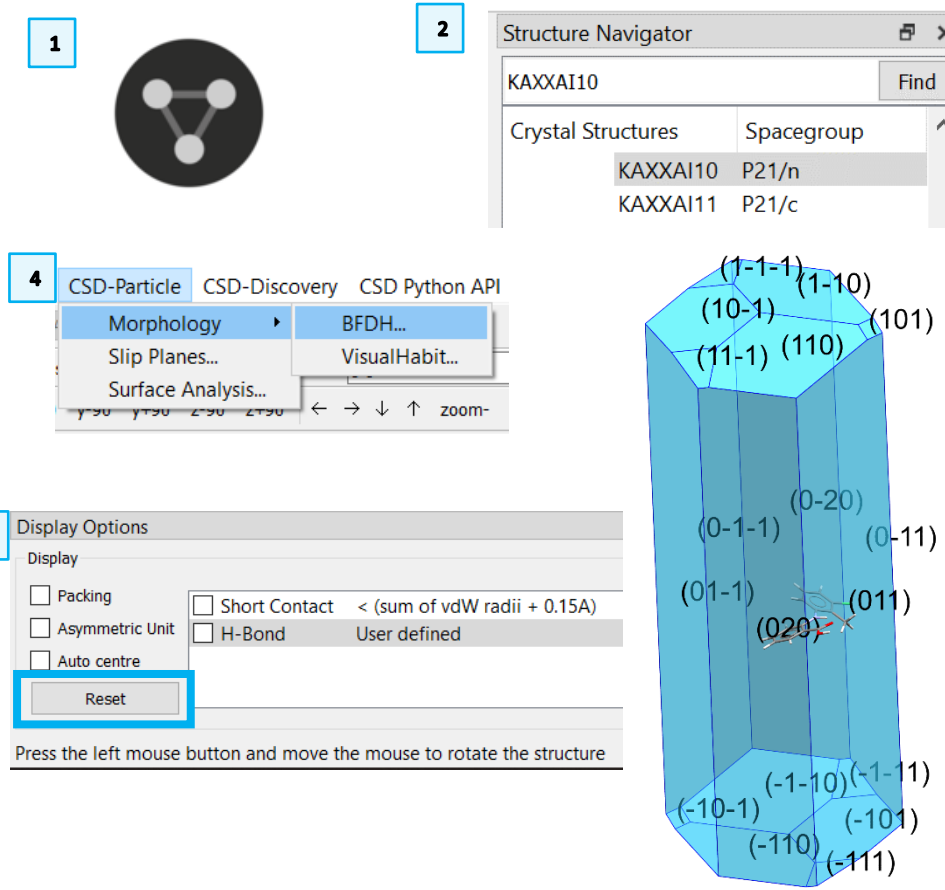
BFDH Morphology

3. We want to identify facets of interest in this morphology. We will first create the morphology using the *BFDH morphology* feature.

4. From the top-level menu select **CSD-Particle > Morphology > BFDH…** to generate the morphology. BFDH morphology uses the unit cell to create the morphology you see, therefore it does not account for the chemistry of the structure.

5. Rotate the structure to view the various facets that have been generated. For this exercise, we will explore two facets: (020) and (110). If you wish, explore options in the *Morphology* menu. Once you are ready to continue, close the *Morphology* menu and click the Reset button from the *Display Options* menu to return to the structure view.

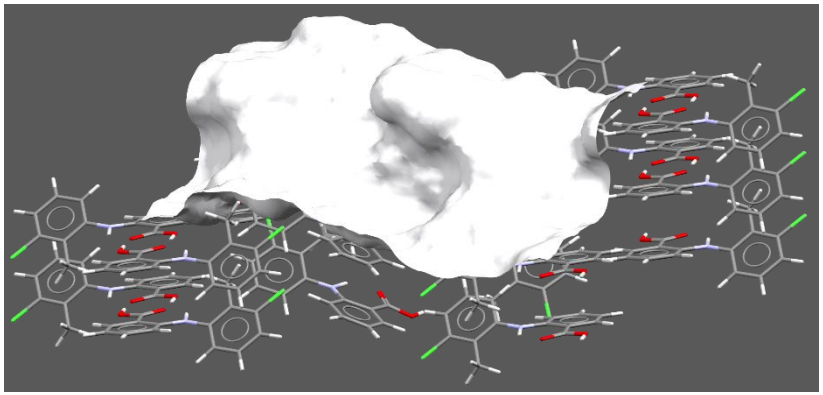
6. The first surface that we will explore is the (110) facet.



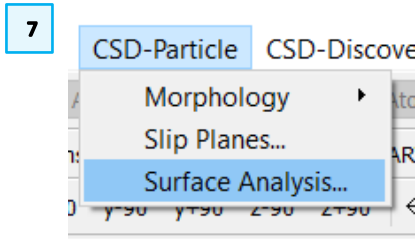
Surface Analysis

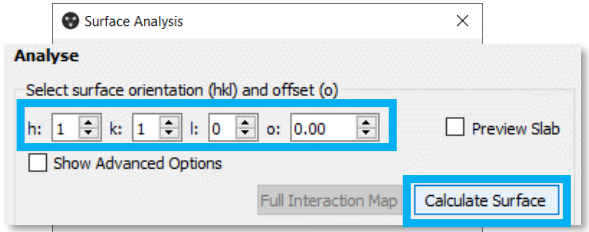
7. From the top-level menu select **CSD-Particle > Surface Analysis…** to open the Surface Analysis dialog. Since we are interested in the (110) surface, we want to enter those values in the *Select surface orientation (hkl) and offset (o)* section. Change the value for *h* and *k* to 1, and leave *l* and *o* as 0, then click **Calculate Surface**.

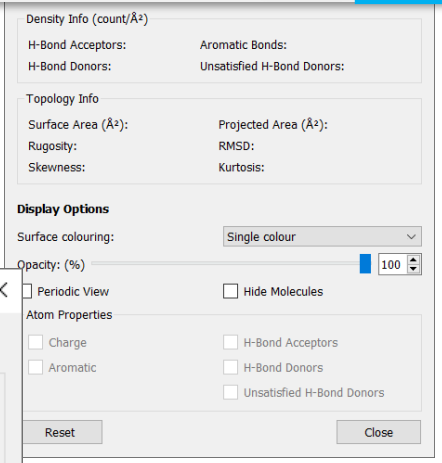
8. You will notice that a surface has been generated and the *Results* section of the *Surface Analysis* dialog has been populated. Let us go through the sections to understand what they mean.

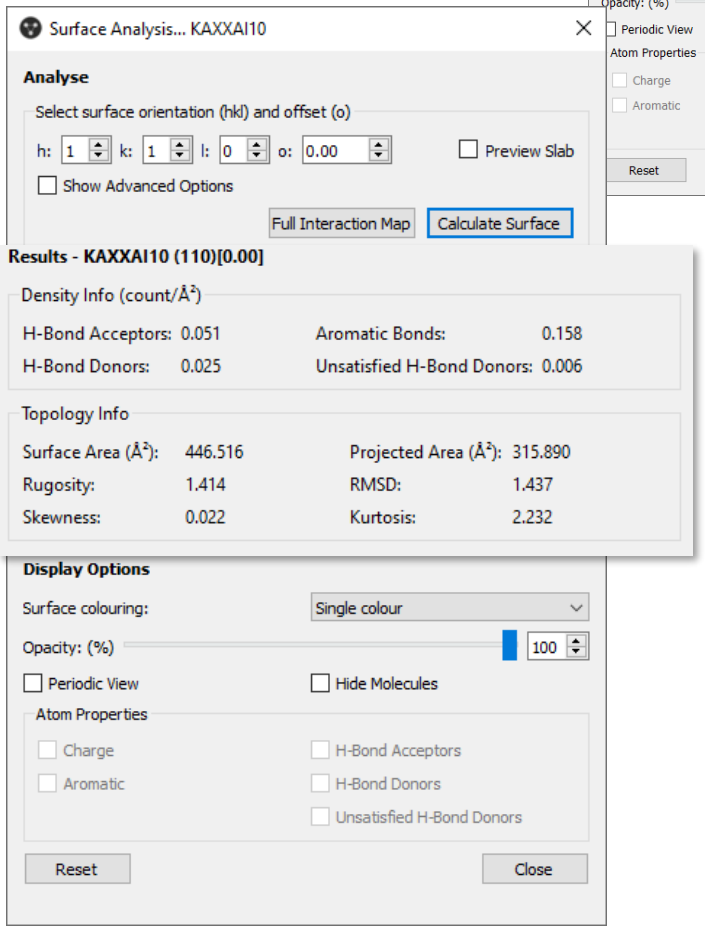


9. The *Results* section begins with the structure refcode and the surface generated as (orientation)[offset], here KAXXAI10(110)[0.00]. The ***Density Info (count/Å²)*** portion tells us about the chemistry on the surface that is in contact with the topology (the white surface that has been generated). The density of hydrogen bond acceptors is higher than hydrogen bond donors on the surface. Observe that the density of *Unsatisfied H-Bond Donors* is lower than the density of hydrogen bond donors as they are a subset of this group. You can then rotate the surface to view the aromatic bonds in contact with the surface.
   The ***Topology Info*** section describes the physical roughness of the generated surface. The *Rugosity* is the ratio of the surface area to the projected area, and *RMSD* is the root mean squared deviation of the height from the mean plane. *Skewness* describes whether the surface is dominated by peaks (value higher than 0) or by valleys (lower than 0). Finally, *Kurtosis* describes the









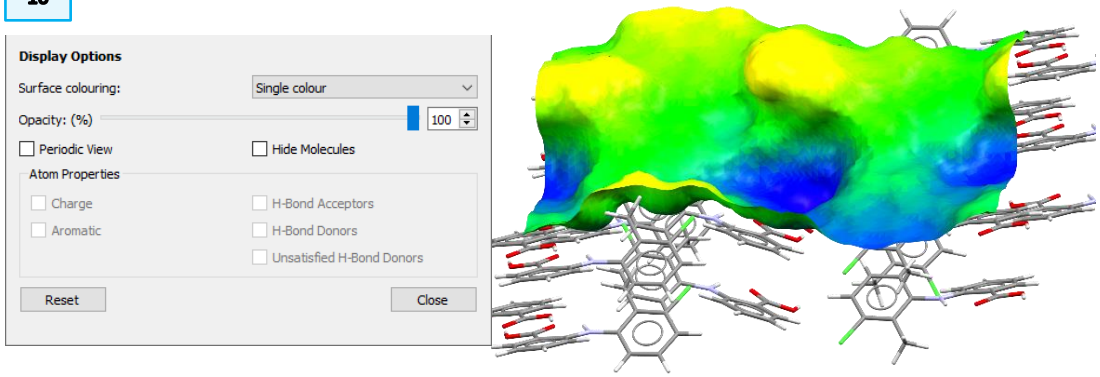
sharpness of the peak: values smaller than 3 signify a step-height change and values higher than 3 hint at a sharp peak.

10. The *Display Options* section of the **Surface Analysis** dialog allows us to generate more dynamic views of the surface. We will adjust the values here to change the surface views.

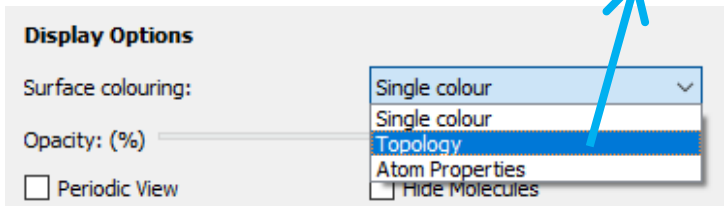
11. First, we will change the *Surface colouring* from *Single Colour* to *Topology* to get a better view of the height map of the surface. The areas closer to red are the peaks (note that in this case, we see a maximum of yellow), while the blue-purple areas are the valleys.

12. Next, select *Atom Properties* from the Surface Colouring menu. You will see that the surface is back to white and that it is now possible to tick the *Atom Properties* options below to visualize where specific chemistry is found on the surface. Explore the options to learn more about the surface. Tick H-Bond Acceptors (coloured red), H-Bond Donors (blue) and Aromatic (orange). We notice that what we observe on the surface is in line with the descriptors explored before. If some areas show both red and blue, the dominant colour will be hydrogen bond acceptors. To get a better view of which atoms are contributing to the maps, you can reduce the opacity.

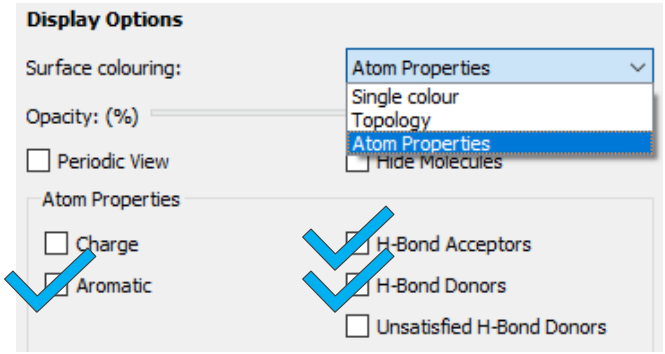
10

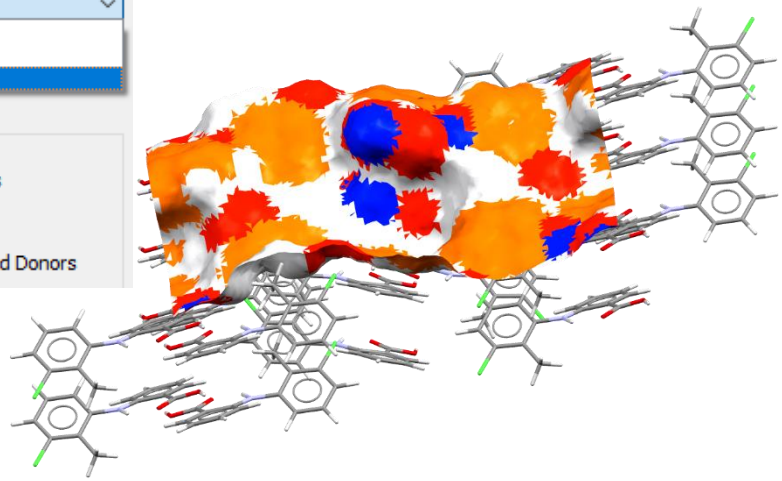


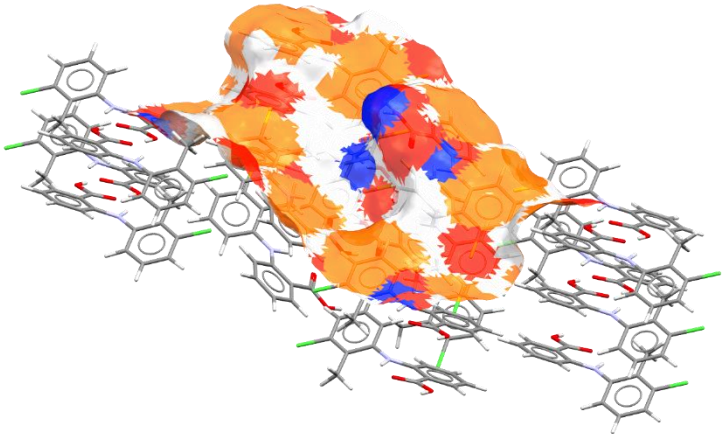
11



12





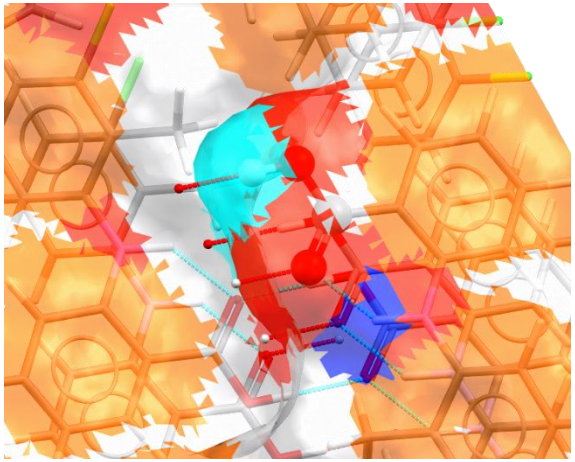


13. We will now visualize where hydrogen bond donors and acceptors are located by turning on H-Bonds in the *Display Options* box at the bottom of the Mercury interface.

14. The next atom property to investigate is the *Unsatisfied H-Bond Donors*. Tick the corresponding box in the *Atoms Properties* section of the **Surface Analysis** dialog to colour the matching areas in teal (light blue shade).

15. Observe that not all the H-bond donors (blue) areas became teal, as some of the donors are satisfied. As an example, observe the hydrogen bond donors in the images on the side and on your structure: you will notice that (a) is protruding out of the surface and has a hydrogen to donate hence it is unsatisfied, while (b) is part of a dimer and the hydrogen donor is satisfied within the structure. This is important because it allows us to explore which hydrogens are available for donation, for incoming molecules for example, and which donors are not available as they are already involved in hydrogen bonds with the bulk of the surface.

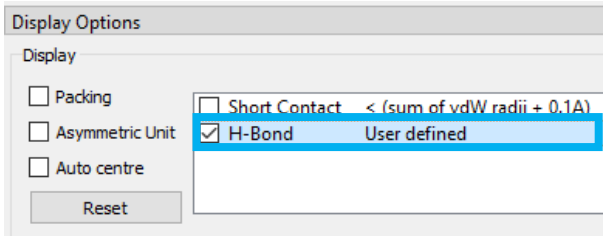
15a



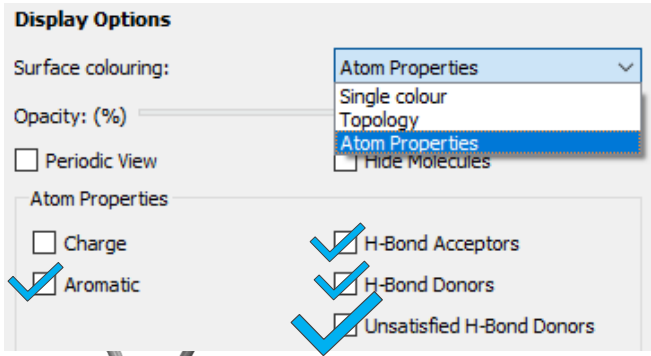
16. At the end of the analysis, turn off the hydrogen bonds by unticking the H-Bond box (opposite of **Step 13**).

17. The last atom property that we will see in this example is the charge. In the *Atoms Properties* section of the **Surface Analysis** dialog, untick all the properties that you currently have on and tick only *Charge*.

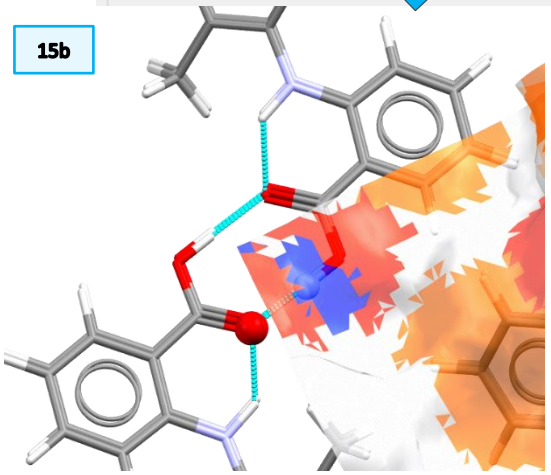
13



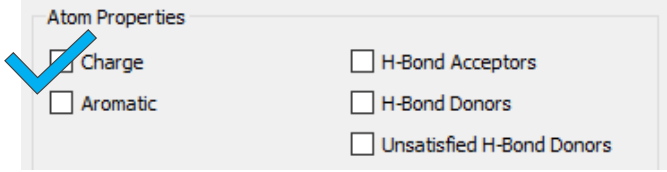
14



15b

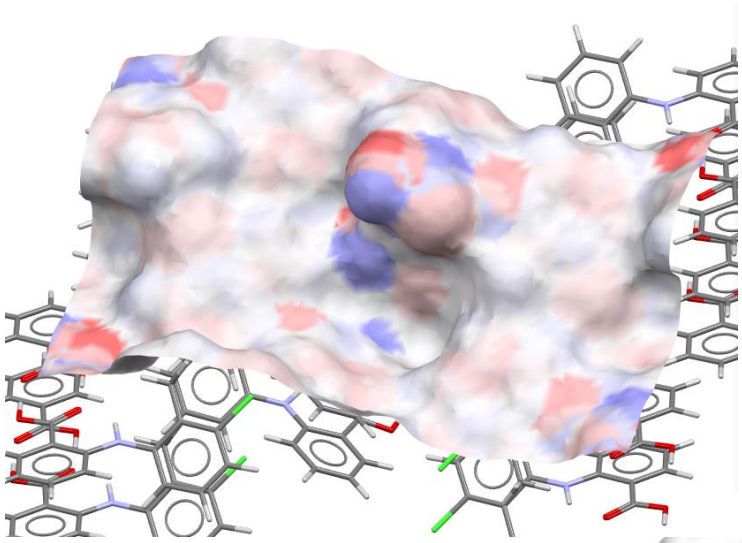


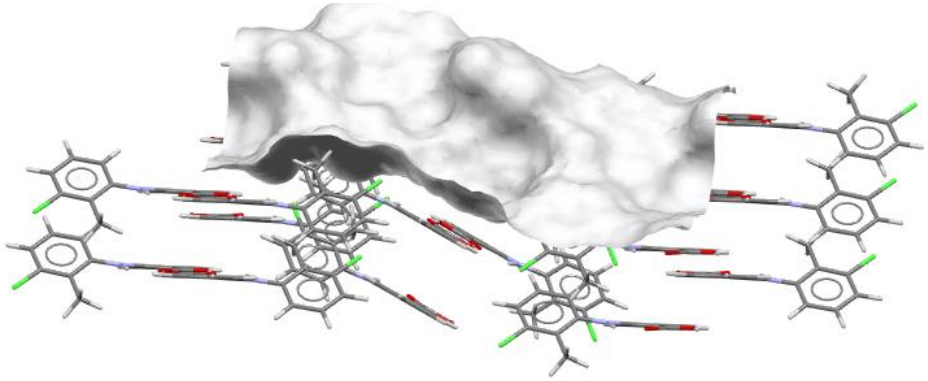
17



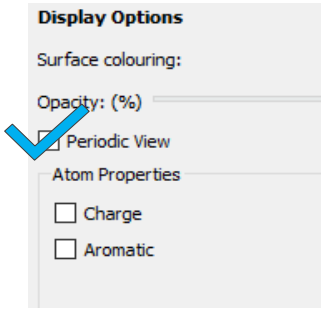
18. The surface is now coloured representing the *Gasteiger charges*. You can observe areas of positive charge (blue) and negative charge (red). **Bonus tip**: if you have calculated your own charges, you can import them into a mol2 file by modifying the charges column and when you do the surface analysis, it will overlay the charges that you have given.

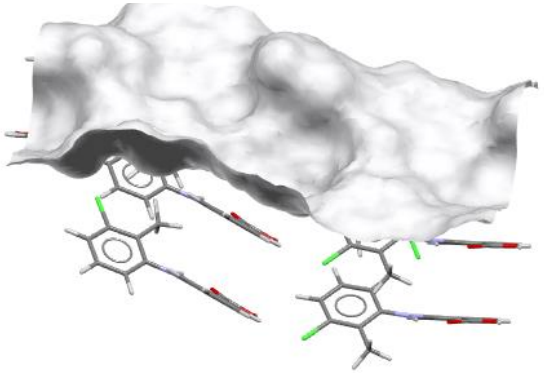
19. **Bonus tip**: If you tick the box next to *Periodic View* in the **Surface Analysis** dialog, you will only see the molecules that are within the bounding box of the surface. You may export this representation for further calculations, for example with Molecular Dynamics, Quantum Mechanics, or other computational techniques.





19



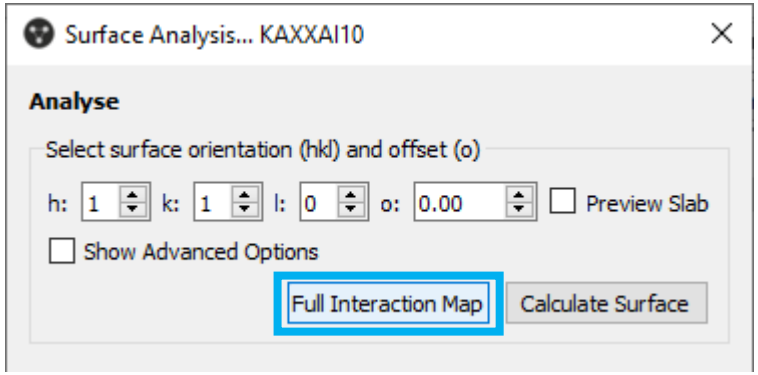


FIMs on Surface

20. For the next part, we will study the Full Interaction Maps (FIMs) on Surface. We will start with the same surface analysed in the previous part of this example.

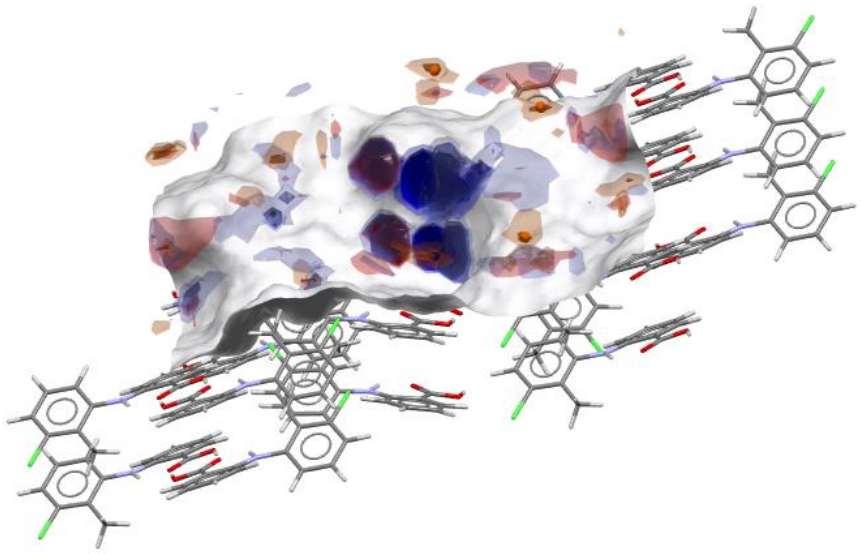
21. For this example, we will first untick all the options in the *Atom Properties* section of the **Surface Analysis** dialog. Then, click the **Full Interaction Map** button at the top of the **Surface Analysis** dialog.

21



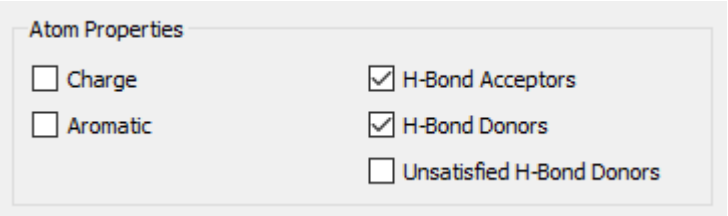
22. This will bring up the **Full Interaction Maps on Surface** window. For this example, we will keep the default settings and additionally, we will tick the *Generate hotspots in the map* box, and also select in the probes *Water Oxygen*. Then, click **Calculate Surface Maps**. A progress bar will appear.

23. FIMs have been generated on the surface and they show the likelihood of finding interactions of the selected probes on this surface. We can see maps and hotspots.

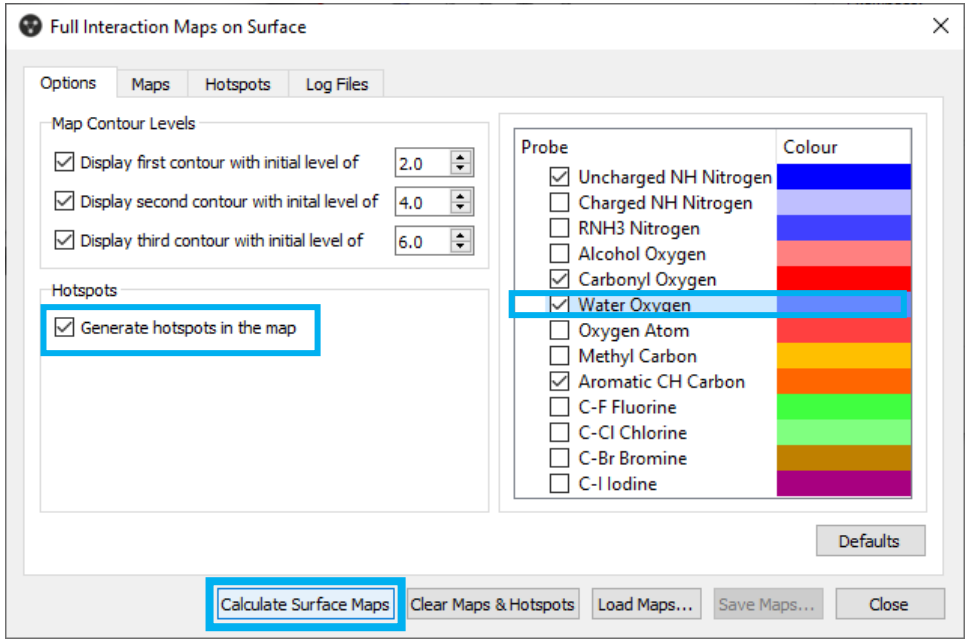


24. Let us investigate the maps. For ease of visualization, turn off the hotspots by going in the *Hotspots* tab and untick *All* above the *Visible* column.

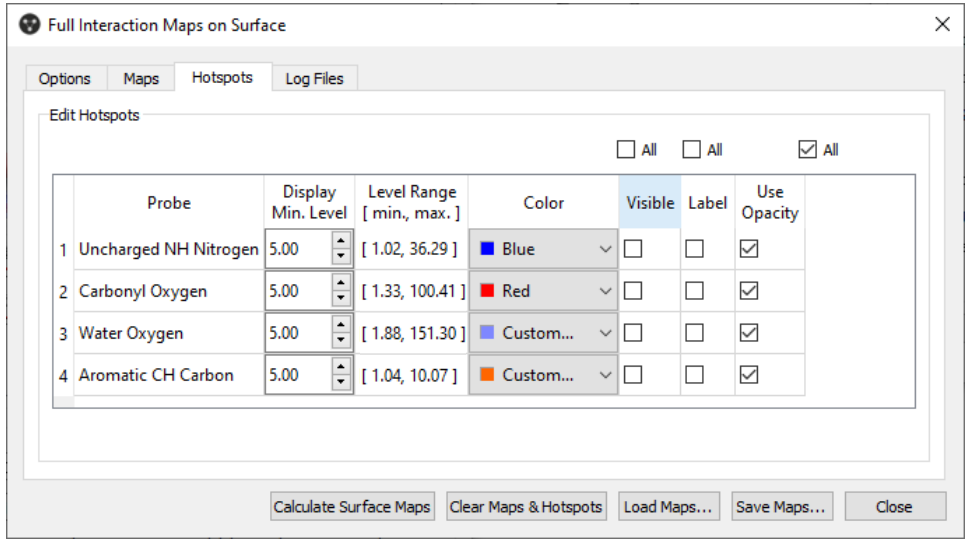
25. Then, in the **Surface Analysis** dialog, tick again the atom properties *H-Bond Acceptors* and *H-Bond Donors*.



22



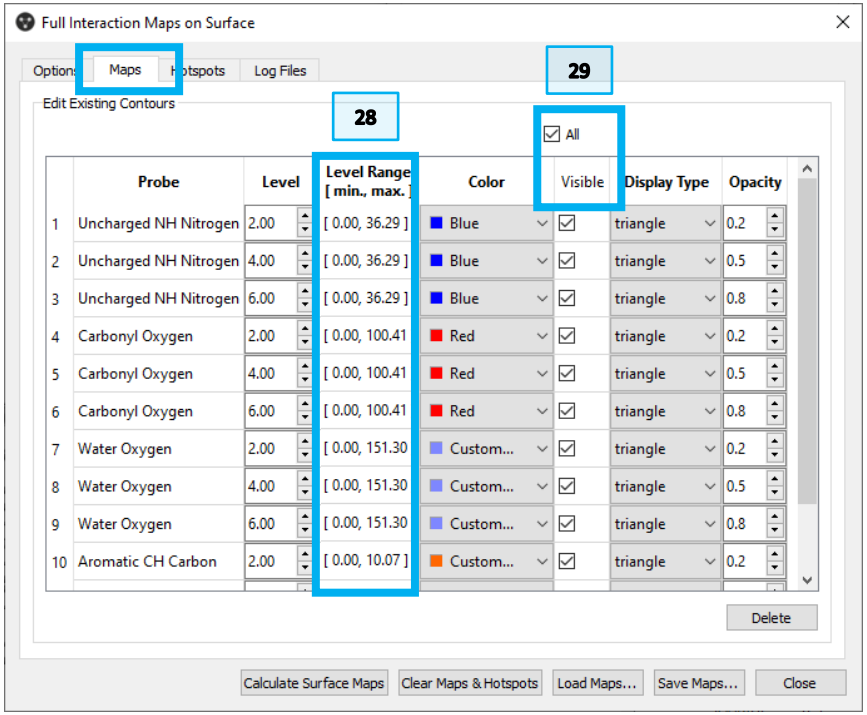
24



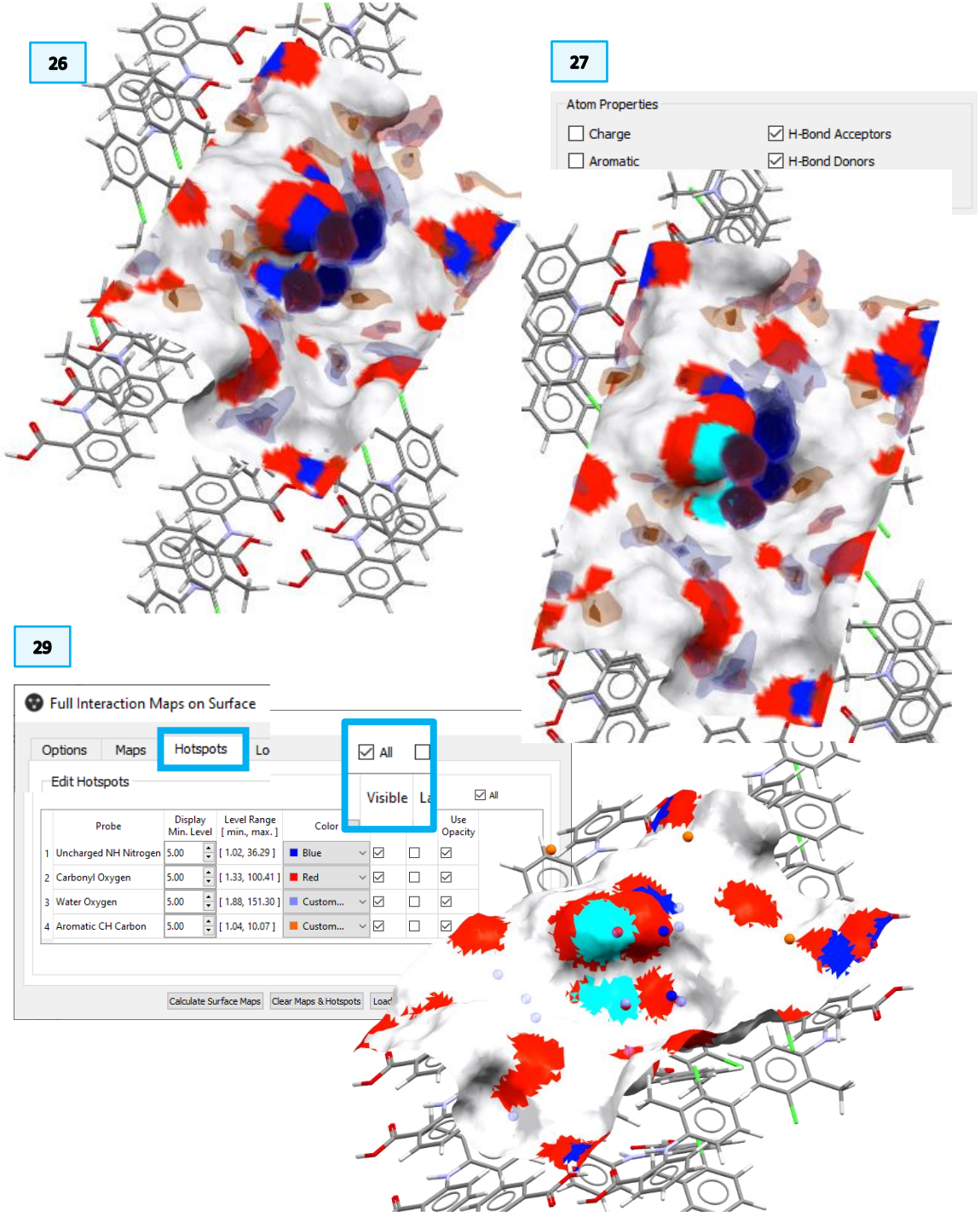
26. Observe that red areas on the surface (H-bond acceptors) match blue areas in the FIMs (NH Nitrogen, H-bond donors), while blue areas on the surface (H-bond donors) correspond to red areas in the FIMs (Carbonyl Oxygen, H-bond acceptors). **Hint**: Turn on and off parts of the plot for better visibility.

27. You can continue the analysis by turning on the *Unsatisfied H-Bond Donors* property for the surface. You will see that the unsatisfied hydrogen bond donors have a likely acceptor area on the maps, while satisfied donors do not as having already formed a H-bond in the surface would make the formation of any other hydrogen bond at an unlikely angle.

28. We can then explore FIMs numerically. Go to the *Maps* tab and observe the values in the *Level Range* column. These values express how likely over random it is to find such interaction.



29. We can now look in more detail at the *hotspots*. For ease of visualization, turn off the maps by unticking *All* above the *Visible* column. Then, move to the *Hotspots* tab and tick *All* above the *Visible* column.



30. As hotspots represent the areas of the highest likelihood of interactions, observe where they are located on the surface and which atom properties they correspond to. What do you observe?

Comparison of different surfaces

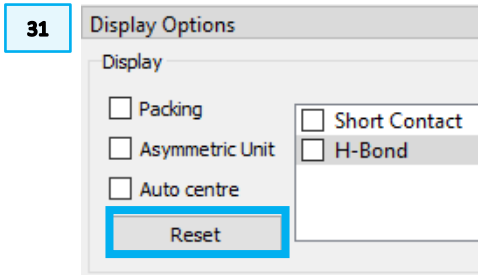
31. Click **Clear Maps and Hotspots,** then close the **Full Interaction Maps on Surface** window and click the **Reset** button in the *Display Options* menu at the bottom of the Mercury interface.

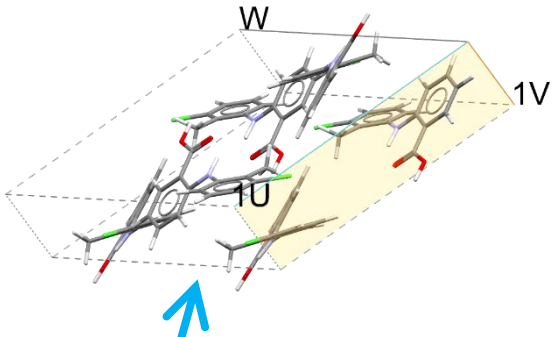
32. Since we are now interested in the (020) facet, in the **Surface Analysis** dialog we want to enter those values in the *Select surface orientation (hkl) and offset (o)* section. Change the value for *h* and *l* to 0, for *k* to 2, and leave *o* as 0.

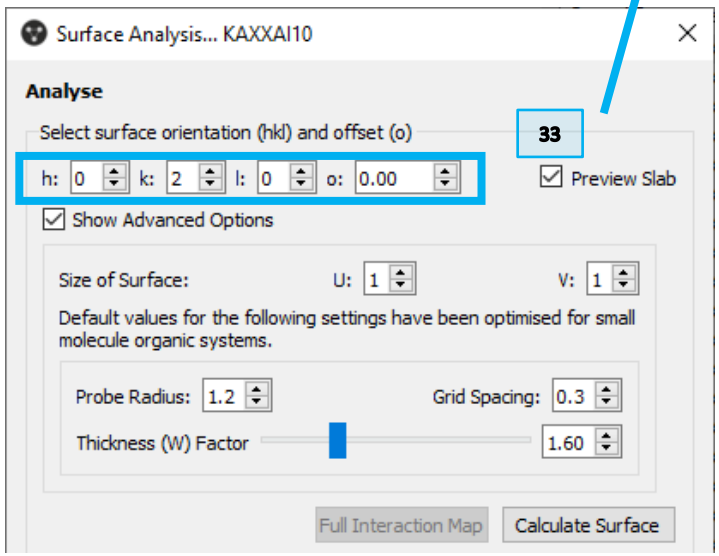
33. Before calculating the slab, it is possible to preview it by ticking the *Preview Slab* option. You can tick *Show Advanced Options* to explore different visualization options, for example by changing *U* and *V* to 2 to obtain a 2x2 surface. Observe the surface, then untick both *Preview Slab* and *Show Advanced Options*.

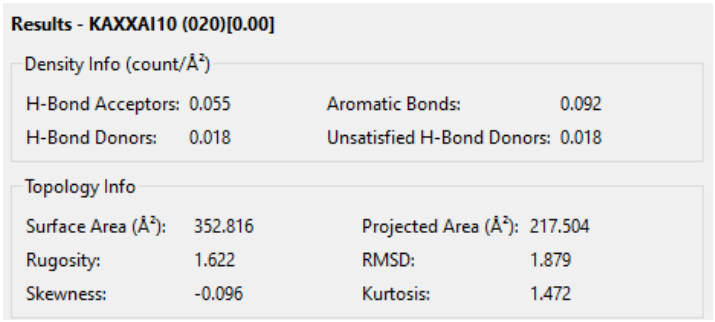
34. Now click **Calculate Surface** as in **Step 7**.

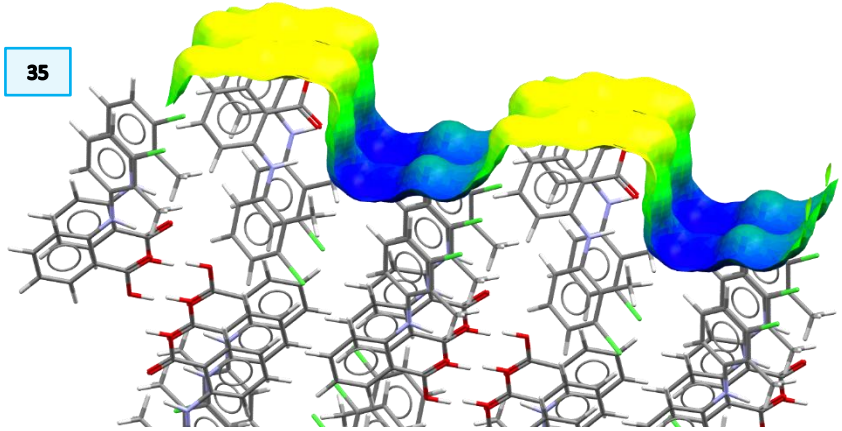
35. At the bottom of the **Surface Analysis** dialog select *Topology* from the Surface Colouring menu. We can observe how the surface is different from the previous one; this is reflected also in the topology values. Compare these with the results obtained in **Step 9** for surface (110). In particular, we observe a







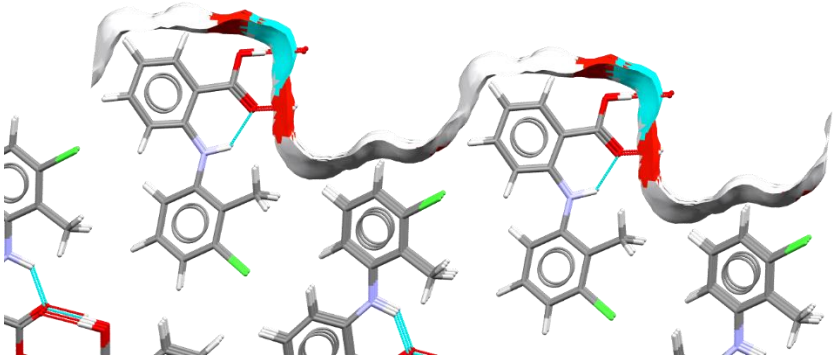




negative value of the *Skewness* and a lower *Kurtosis* value, meaning that we have a surface resembling more a step function rather than a round peak.

36. Next, select *Atom Properties* from the Surface Colouring menu. Tick H-Bond Acceptors, H-Bond Donors, and Unsatisfied H-Bond Donors. Also, observe the *Density Info* values in the dialog (**Step 35**) and compare them with **Step 9** for surface (110). In particular, we observe that all the hydrogen bond donors are unsatisfied in this case; moreover, the unsatisfied H-bond donors count per Å^2 is higher than for the (110) surface, while the aromatic bonds density is lower.

37. Now turn on the hydrogen bonds as in **Step 13** to observe where potential hydrogen bonds could be formed on the surface.

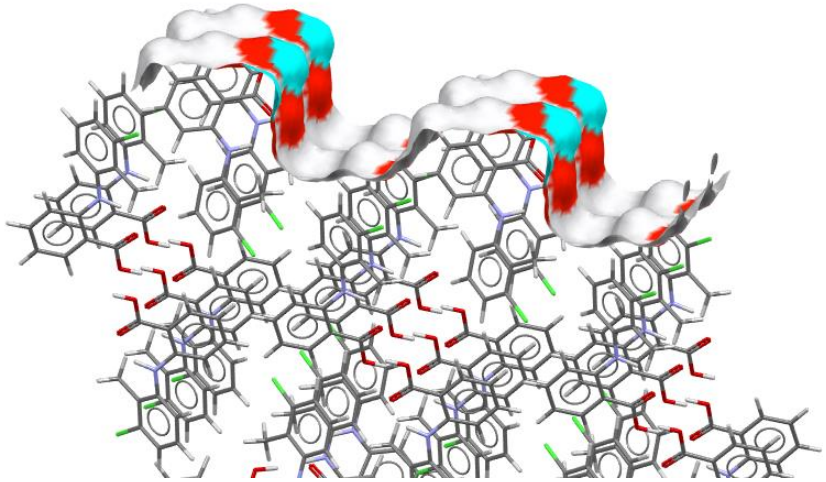


38. You may also observe the Gasteiger charges as in **Step 17** above.

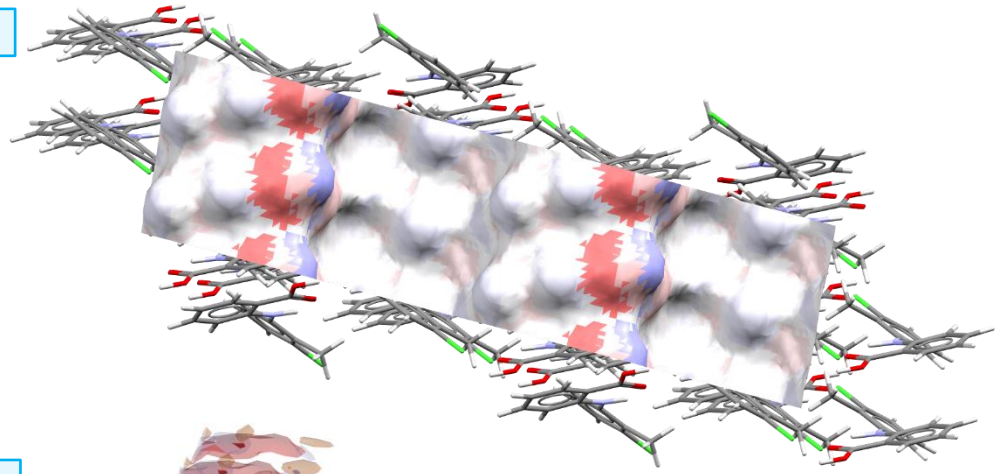
39. Next, we will generate FIMs on Surface, following **Steps 21 to 23** above.

40. Then, compare the values in the *Level Range* column of the table in the *Maps* tab with the ones obtained for surface (110) at **Step 28**. You will notice that in this case the values of the water oxygen and carbonyl oxygen are lower than in the previous case, suggesting a lower likelihood of interaction.

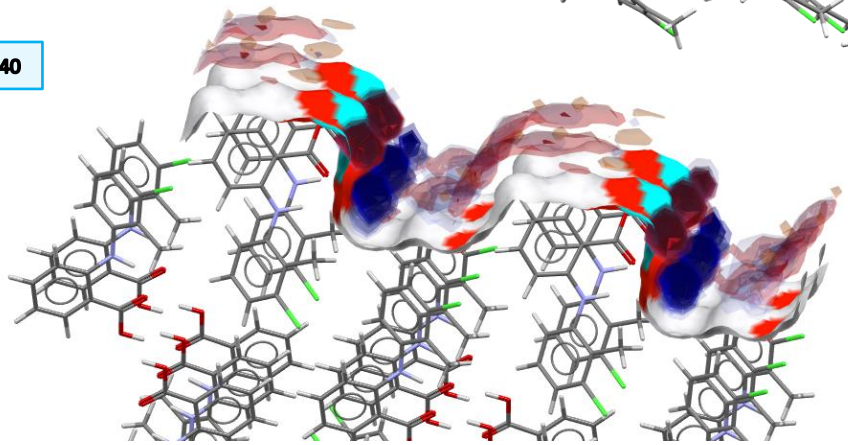
36



38



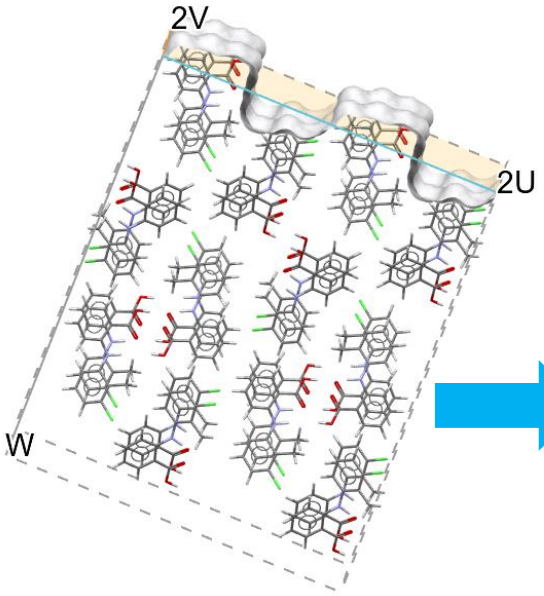
40



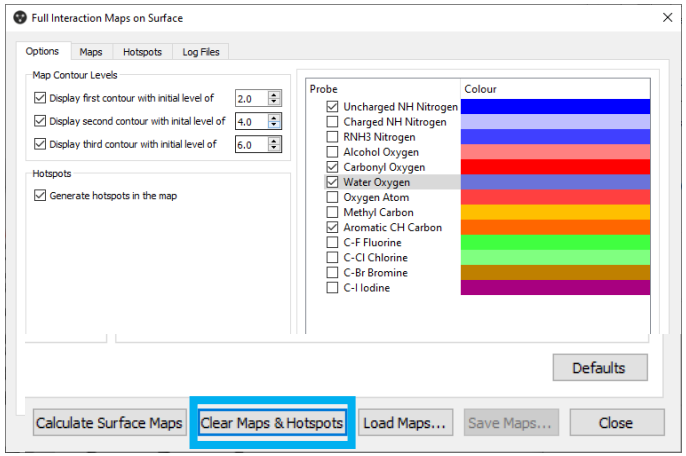
Exercise

41. Clear the maps and close the **Full Interaction Maps on Surface** window.

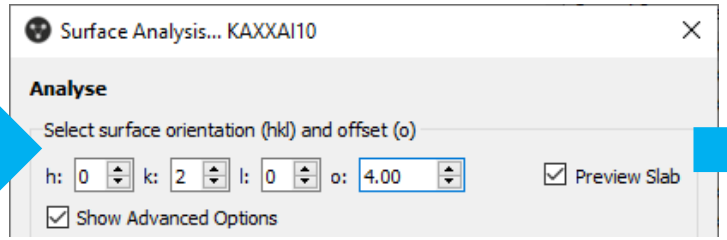
42. Bring up again the preview slab, as done in **Step 33**. This time, change the offset to observe how that impacts the surface terminations. We set the offset to 4 Å.

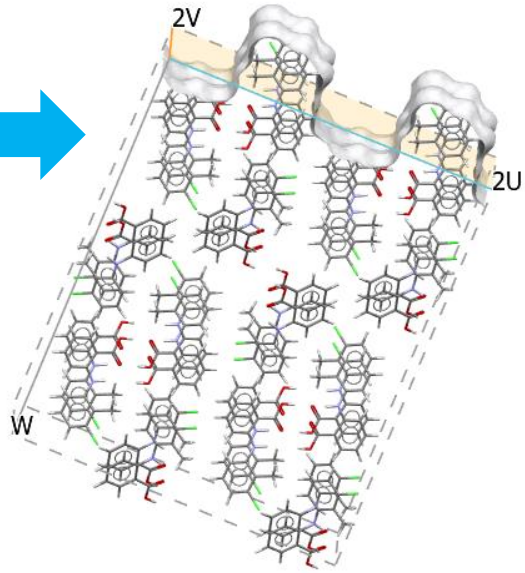


41



42





43. Click **Calculate Surface** to generate the surface and observe how its properties differ from the one without offset.

44. Observe the chemistry and the properties: how does changing the terminations impact the properties of the surface? What does it mean?

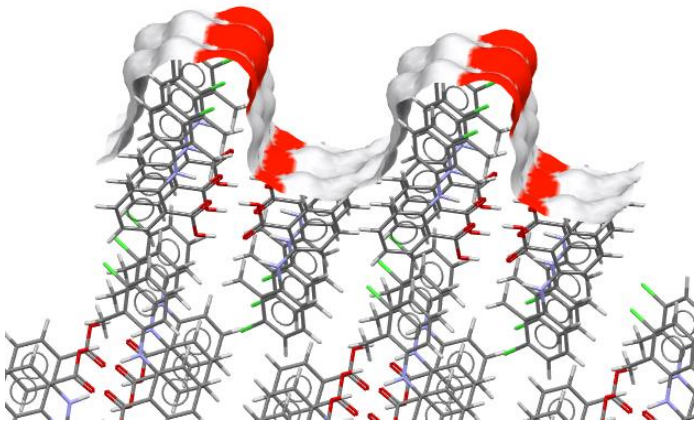
Results - KAXXAI10 (020)[4.00]

Density Info (count/Å²)

H-Bond Acceptors:	0.037	Aromatic Bonds:	0.129
H-Bond Donors:	0.018	Unsatisfied H-Bond Donors:	0.000

Topology Info

Surface Area (Å²):	421.063	Projected Area (Å²):	217.504
Rugosity:	1.936	RMSD:	2.727
Skewness:	0.041	Kurtosis:	1.425



Conclusion

In this example, we saw in more detail how to use tools from *Surface Analysis* from CSD-Particle to analyse two *hkl* surfaces, namely the (110) and the (020), of a 2-(3-chloro-2-methylanilino)benzoic acid crystal. For each, we learnt how to investigate the chemistry and the topology of the surface and how to visualize such properties in the 3D visualizer in Mercury. We have also generated FIMs on each surface: FIMs allow us to quickly analyse where likely interactions are expected on the surface and which kind of chemistry we could expect. Changing the offset of the calculated surface also allows us to investigate how the activity of a surface would change.

Summary

After this workshop you should now be able to:

- Calculate *hkl* surfaces and investigate their chemical and topological properties.
- Display different properties on the generated surface to visualize its potential activity and personalise the surface view to enhance clarity.
- Calculate Full Interaction Maps on such a surface to quickly identify likely interactions.
- Visualize hydrogen bonds in Mercury.

Next Steps

After this workshop, you can explore more exercises in the self-guided workshops available in the CSD-Particle workshops area on our website and the Surface Analysis CSDU module. We suggest trying the Investigation of Plastic and Elastic Properties with CSD-Particle Tools workshop.

Feedback

We hope this workshop improved your understanding of Surface Analysis Tools in Mercury and you found it useful for your work. As we aim to continuously improve our training materials, we would love to hear your feedback. Follow the link on the workshop homepage or click on this link to a survey, it will take less than **5** minutes to complete. The feedback is anonymous. You will be asked to insert the workshop code, which for this self-guided workshop is PAR-001. Thank you!

Reading suggestions

You might find the following publications of interest:

- "Particle Informatics": Advancing Our Understanding of Particle Properties through Digital Design, ***Cryst. Growth Des.***, 2019, **19**, 9, 5258–5266 - https://doi.org/10.1021/acs.cgd.9b00654
- Elastically flexible molecular crystals, ***Chem. Soc. Rev.***, 2021, **50**, 11725-11740 - https://doi.org/10.1039/D1CS00469G

Glossary

BFDH Morphology

Simulation of morphology using the Bravais Friedel Donnay Harker (BFDH) method. BFDH crystal morphology is an approximation based on crystallographic geometrical considerations. For a given structure, the BFDH algorithm will predict the habit or shape of a crystal using the corresponding unit cell and symmetry operator information.

Gasteiger Charges

Gasteiger charges refer to partial charges calculated with the Marsili-Gasteiger method.

In Mercury, for atoms in a molecule increasing red colour represents an increasing positive charge and increasing blue colour represents an increasing negative charge. For surfaces instead, colouring by Charge colours the surface with a continuous scale from negative (red) to positive (blue).

Hotspots

Hotspots represent the positions of the highest local density for each contour.

Hydrogen Bonds

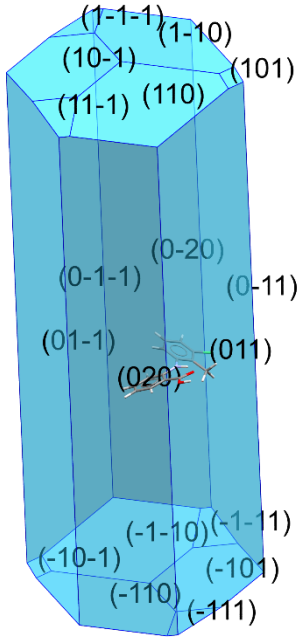
Hydrogen bonding occurs between donor-acceptor interactions involving hydrogen atoms. The H-bond interactions are classified as: strong (mostly covalent), moderate (mostly electrostatic) and weak (electrostatic). Their strength is observed to be between 12 and 30 kJ/mol.

Kurtosis

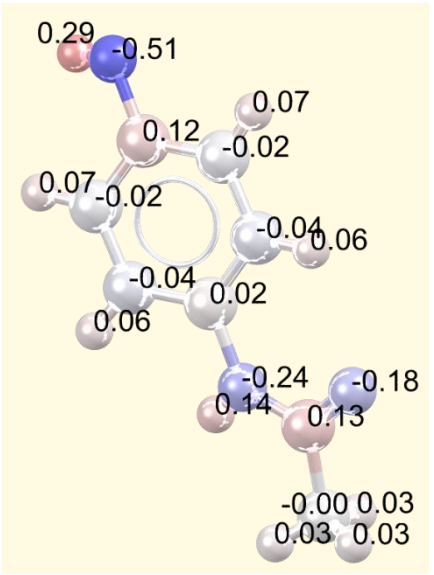
Kurtosis is a statistical characterisation of a dataset, such as surface topology, which measures the sharpness of height distribution and has a value of zero for a normal distribution. Positive values indicate a distribution with a sharp peak and long, “thick” tails. Negative values indicate a rounded peak with short, “thin” tails.

Minimum Slab Separation

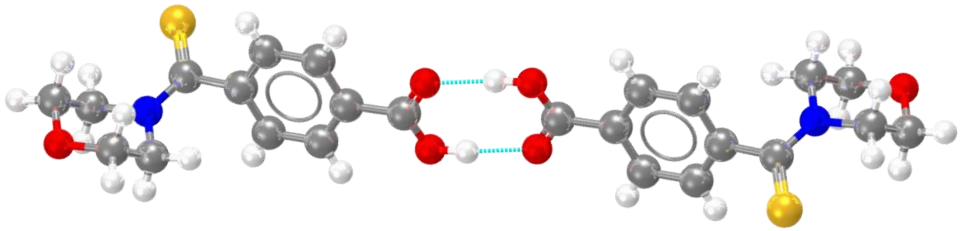
Potential slip planes will only be shown if the slab separation value is greater than the minimum slab separation which is 0 Å. The slab distance is the shortest distance between slabs of molecules on either side of this slip plane (Å).



Example of BFDH Morphology for CSD Entry KAXXAI10.



Molecule of paracetamol (CSD Entry HXACAN) with atoms coloured by Gasteiger charge, also expressed in the label.



In light blue, example of hydrogen bonds for refcode MULWIC.

Offset
This is the value in Å of the distance to the calculated surface from the parallel Miller plane.

Perpendicular Planes
The *Perpendicular Planes* column in the Slip Planes table contains a list of any potential slip planes >45° from the given plane.

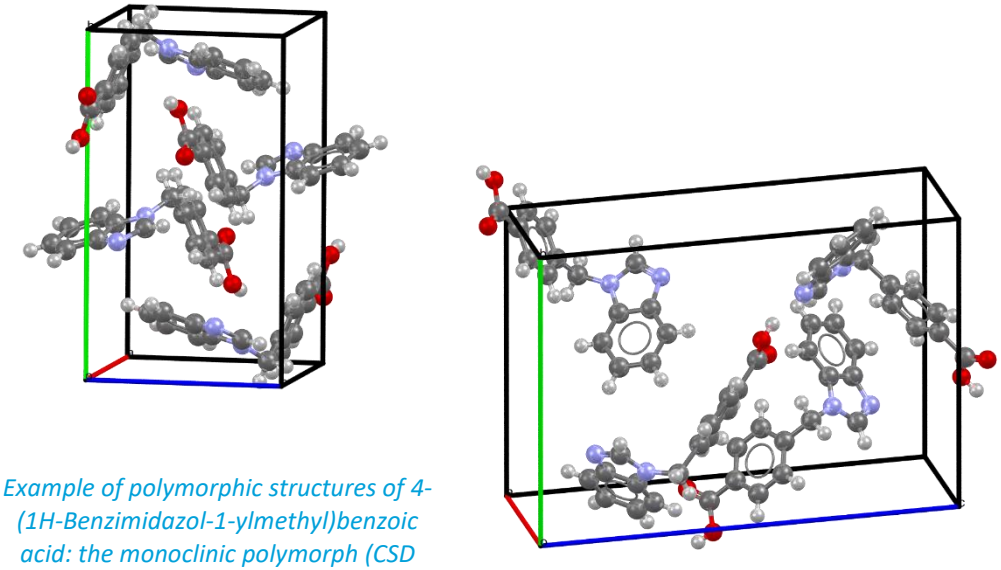
Polymorph
Polymorphism is the occurrence of two or more crystalline forms of the same substance. Where available, polymorph information can be displayed for Cambridge Structural Database (CSD) structures. Structures known to be polymorphic contain comments which include the word polymorph (when reported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

Rugosity
Rugosity is used to describe the roughness of the surfaces and is calculated as the surface area divided by the projected area.

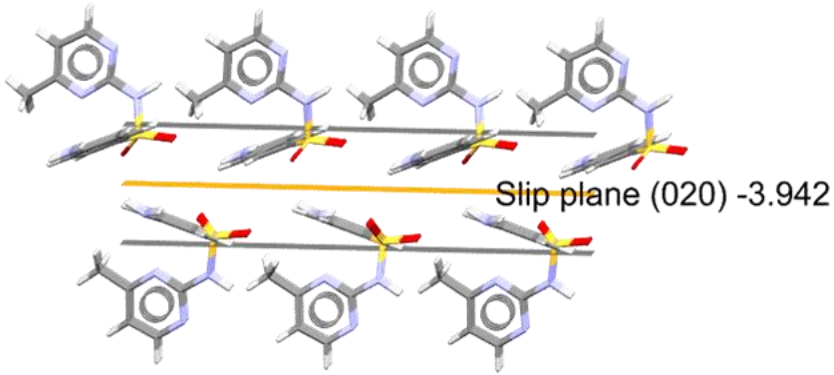
Skewness
Statistical characterisation of a dataset, such as surface topology. Skewness measures the lack of symmetry, so in the case of surface topology, equal peaks and valleys would have a skewness of 0. If the surface was mostly valleys, then the skewness would be a negative value close to -1 and if the value is higher than 0, then the surface was mostly dominated by peaks.

Slip Planes
Slip planes represent planes in a crystal structure along which a slip can take place.
Please note that in CSD-Particle, the Slip Planes functionality identifies potential slip planes in a crystal structure.

Root Mean Square Deviation (RMSD)
The root mean square deviation (RMSD) is a commonly used measure of the difference between two sets of values (usually comparing observed data to



Example of polymorphic structures of 4-(1H-Benzimidazol-1-ylmethyl)benzoic acid: the monoclinic polymorph (CSD Entry ABADIS) at the top, and the orthorhombic polymorph (CSD Entry ABADIS01) on the right.

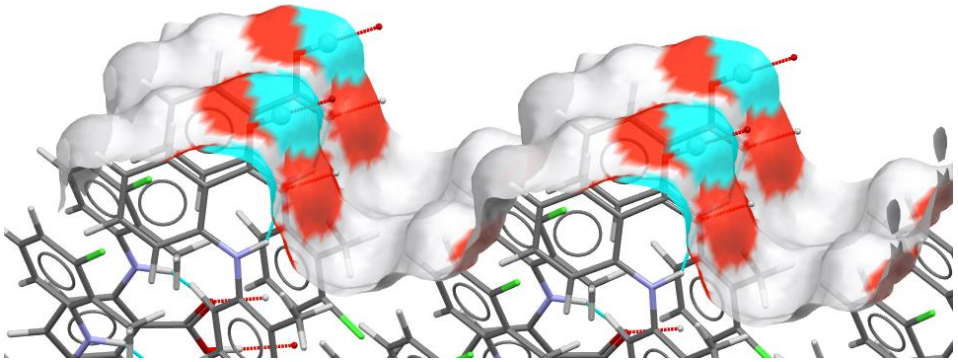


Example of potential slip plane in CSD Entry SLFNMA02.

estimated data). The RMSD is defined as the square root of the mean squared error. In Mercury this is used to measure the geometric difference between packing features or packing patterns in crystal structures.

Unsatisfied Hydrogen Bonds

Unsatisfied hydrogen bond donors are defined as those whose hydrogen atom is surface-terminating and not being used in an existing hydrogen bond. They are reported as unsatisfied hydrogen bond donor density (count/Å^2).



Example of unsatisfied H-bond donors on the (020) surface of CSD Entry KAXXAI10.

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.

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.

Right click:
a) Near a molecule and
b) Away from a molecule