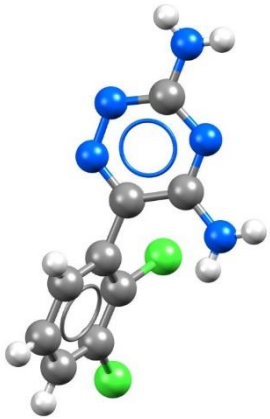
Solvate Analyser

(MAT-003)

2023.3 CSD Release



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Introduction

This tutorial will introduce you to the *Solvate Analyser* in *CSD-Materials*.

The Solvate Analyser tool in Mercury provides the user with the ability to quickly investigate complex solvated structures.

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

Learning Outcomes

After completing this workshop, you should be able to:

- Explore visualisation options.
- Select a solvent and conduct space calculation.
- Investigate hydrogen bonding motifs in solvate structures.
- Analyse disordered solvents.

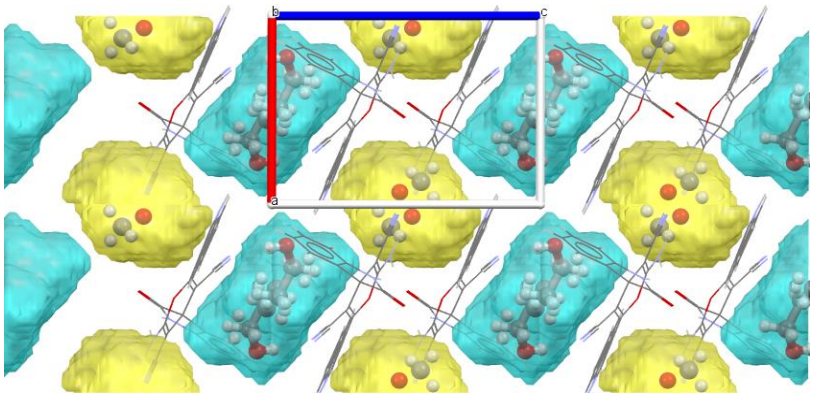
This workshop will take approximately 45 minutes to be completed.

Pre-required Skills

Familiarity with the Mercury interface is important; you can access the Visualization in Mercury self-guided workshop on this page. You can find other CSD-Materials self-guided workshops here.
https://www.ccdc.cam.ac.uk/community/training-and-learning/workshop-materials/

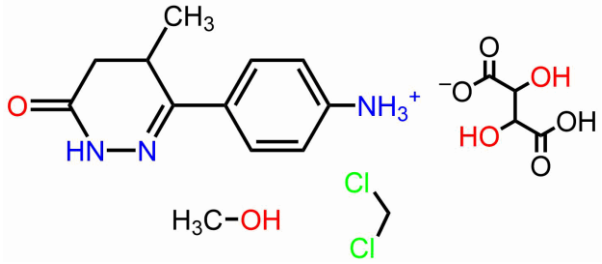
Materials

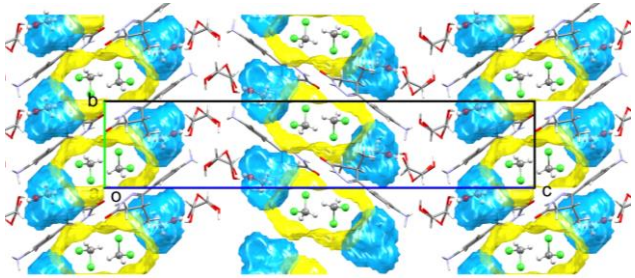
There are no additional materials required for this workshop.



Example 1. Analysing a solvate structure.

The physicochemical properties of crystalline materials, such as pharmaceutical compounds and excipients, can be considerably influenced by the presence of solvent molecules within the crystal structure. Solvents are frequently found in the crystal structures of pharmaceutical compounds, either interacting directly with the host compound or simply filling gaps in the structure. Understanding the behaviour of solvents in these structures is of great importance in pharmaceutical industry since this can lead to further understanding and improvement of the crystallization process.
This example shows how to assess solvate structures using the Solvate Analyser within CSD-Materials. The case studies illustrate how to quickly investigate complex solvated structures, including structures with more than one solvent, a mixture of solvents, co-formers and counter-ions or even disordered solvate structures.





6-(4-Ammoniophenyl)-4,5-dihydro-5-methyl-3(2H)-pyridazinone (-)-tartrate dichloromethane methanol solvate salt
CSD refcode ***HAVKIY***

Solvent selection and space calculation

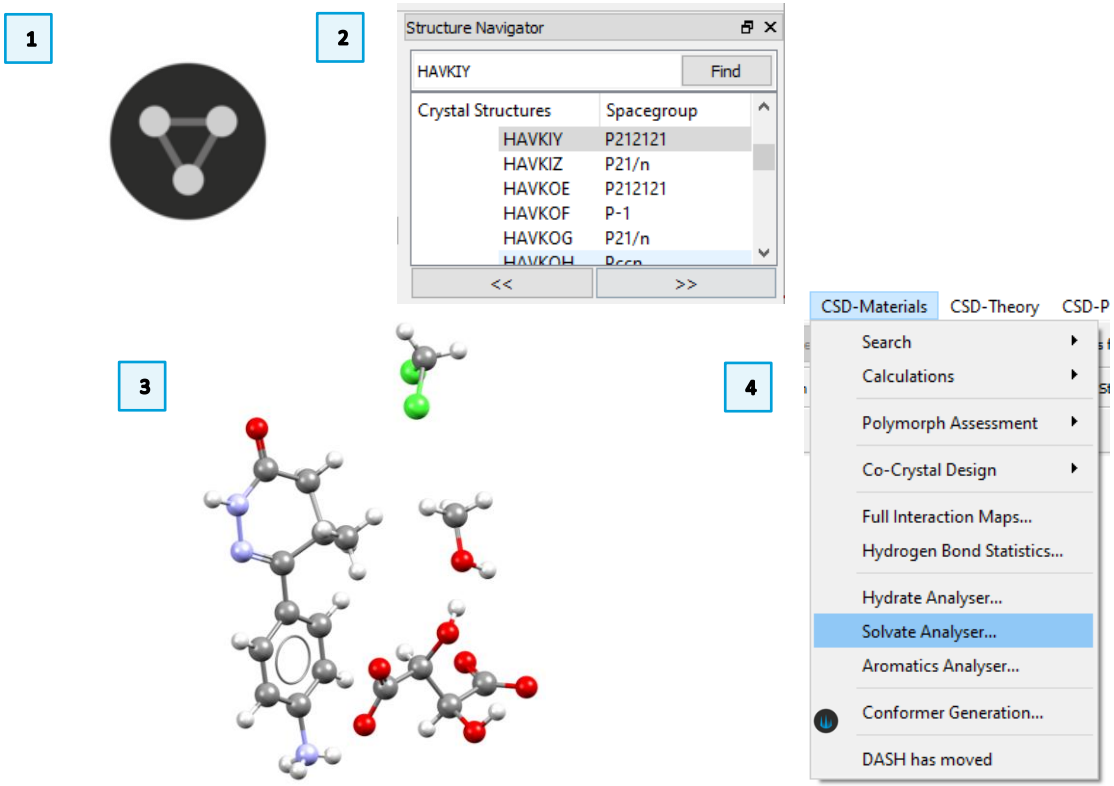
In this section, you will learn how to generate and manipulate solvent space in a salt containing a mixture of solvents.

1. Open Mercury by clicking the desktop icon, or launching from the Start menu (Windows), Launchpad (macOS) or command line (Linux).

2. In the **Structure Navigator** window, type the refcode *HAVKIY*, to bring up the structure of 6-(4-Ammoniophenyl)-4,5-dihydro-5-methyl-3(2H)-pyridazinone (-)-tartrate dichloromethane methanol solvate.

3. The structure will be displayed in the 3D visualiser.

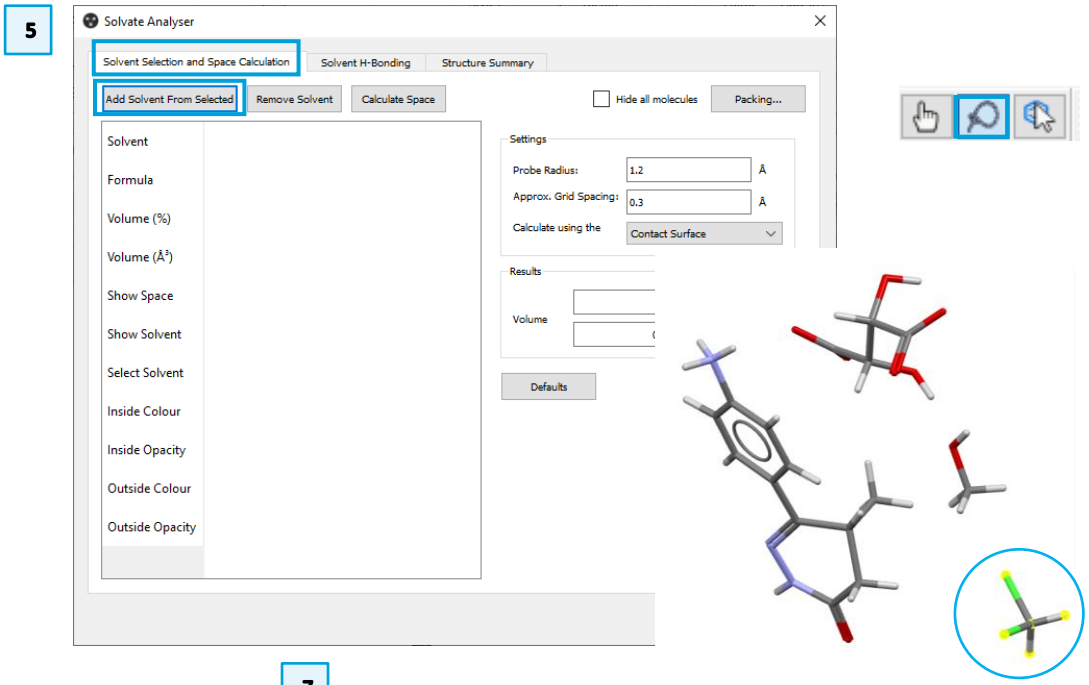
4. From the top-level menu select **CSD-Materials > Solvate Analyser**….

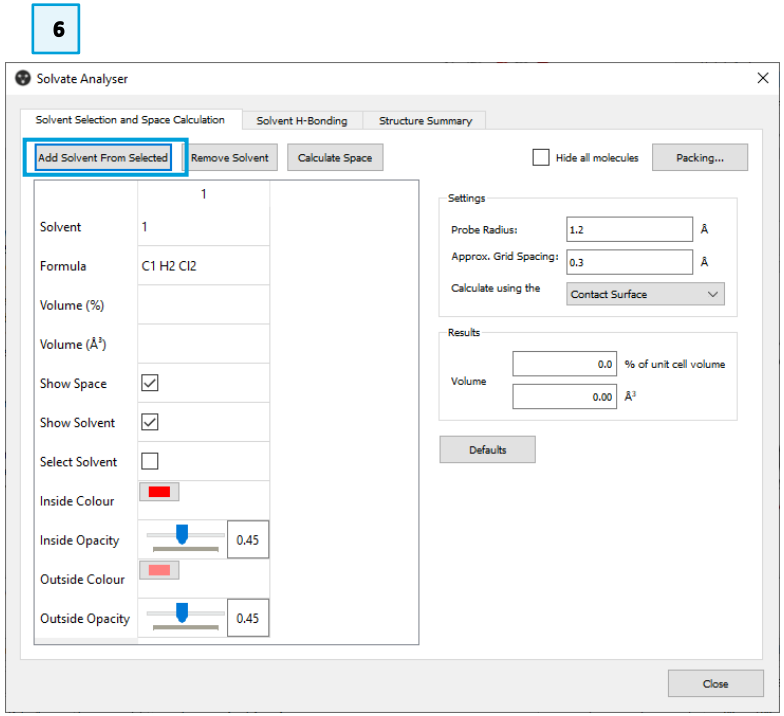


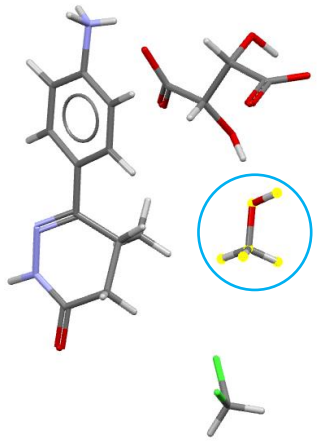
5. The *Solvate Analyser* contains 3 tabs with different functionality options. In the **Solvent Selection and Space Calculation** tab you can individually select different solvent molecules within the structure and analyse them independently. Hold shift and click on the dichloromethane in the 3D visualiser. Alternatively, you can select the molecule by using the **Lasso selection mode** from the top-level toolbar. With the dichloromethane molecule selected, click on **Add Solvent From Selected** button to register that group of atoms as a specified solvent.

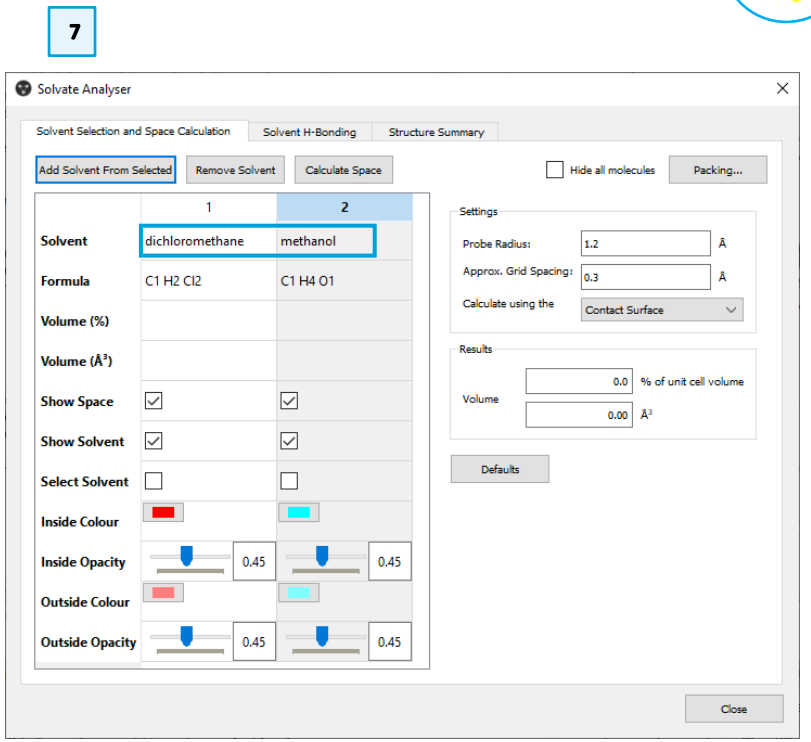
6. Information is now displayed in the table for dichloromethane. Repeat the same steps for methanol: select the molecule and click **Add Solvent From Selected**.

7. Methanol information is now added in second column of the table. Double-click on each cell in the **Solvent** row, which is interactive, and add the names for each solvent.









8. You can make the solvents easier to see by clicking on the **Select Solvent** boxes and change the *Style* to **Ball and Stick** from the top-level Mercury toolbar. Click **Calculate Space** to generate the solvent space using the default parameters. This will automatically create a 1x1x1 packing and display the space occupied by solvents or structural voids.

9. You can change the inside and outside colour of the solvent space. For instance, click on the **Inside Colour** of dichloromethane and select the deep yellow, then click on the **Outside Colour** and select light yellow.

10. To further explore the location of the solvent space click the **Packing…** button**.** Enter 0.0 to 2.0 for *a* axis and -0.5 to 2.0 for *b* and *c* axes to obtain a more complete picture of the voids. Click **OK** and then **Calculate Space**. Click *b* axis from the top-level toolbar to view along it. Note that the dichloromethane solvent forms channels along the *a* axis, while the methanol solvent is located in discrete pockets. Select the view along *a* axis. A double column of dichloromethane molecules is filling the channel space and one methanol molecule is occupying the discrete pockets.

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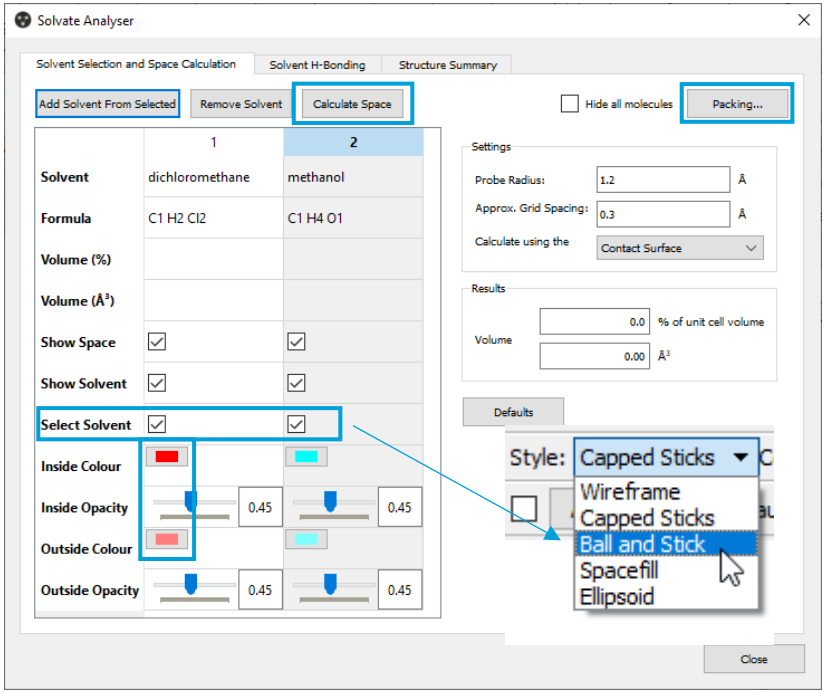

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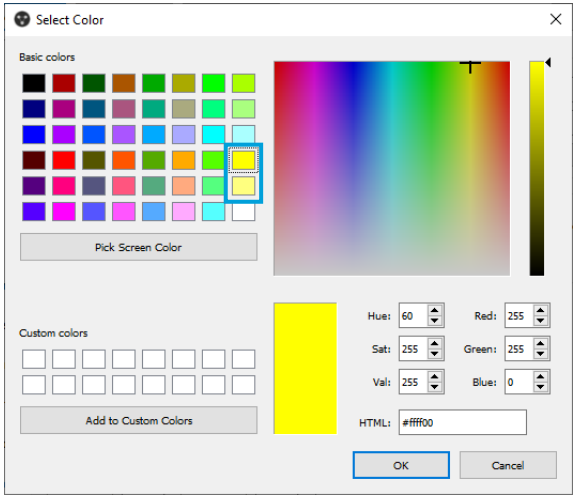

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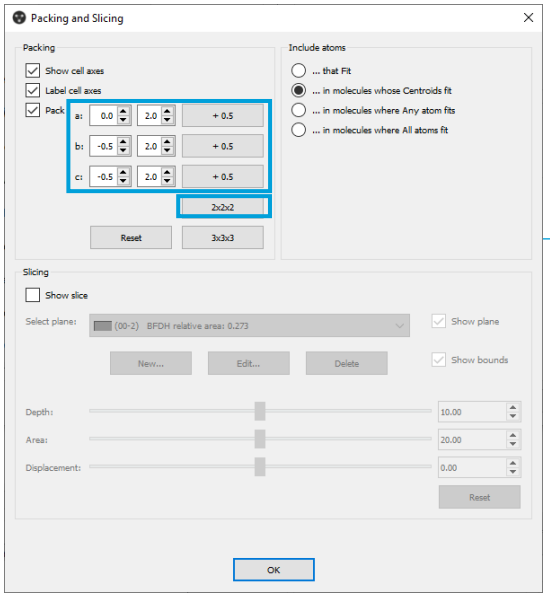

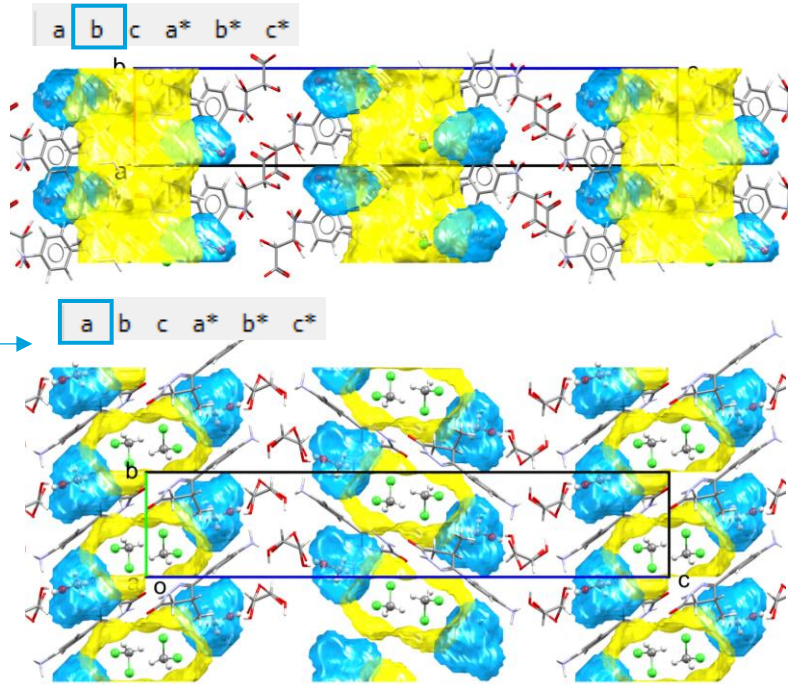

Investigating H-bonding

In this section you will learn how to quickly analyse solvent H-bonding motifs. To go back to the initial view click **Reset** in the *Display Options* area of the Mercury interface.

11. Check on the **Solvent H-Bonding** tab. This shows an automated analysis of the H-bonding environments of the solvate molecule(s). This is a quick way to investigate the H-bonding in complex solvate structure. The methanol molecule is involved in two H-bond interactions with the tartrate. There is one donation and one acceptance each from O8 of the methanol molecule.

12. To identify the atoms involved in H-bond interactions toggle on the **H-Bond** check box in the *Display Options* dialogue box.

13. Display the atoms labels and expand the contacts by clicking on the hanging atoms (red dotted line).

Generating summary reports

14. To generate solvent analysis reports, select **Structure Summary** tab in the *Solvent Analyser* dialogue box. You can customise the information that is displayed in this tab and output in your report by using the **Configure…** button. Once you are happy click on **Save As…** button to save a report in Word (DOC) or HTML format.

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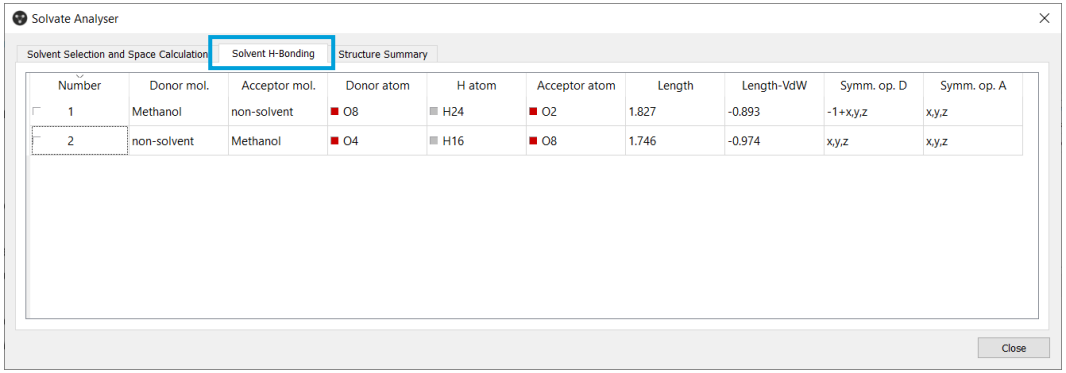

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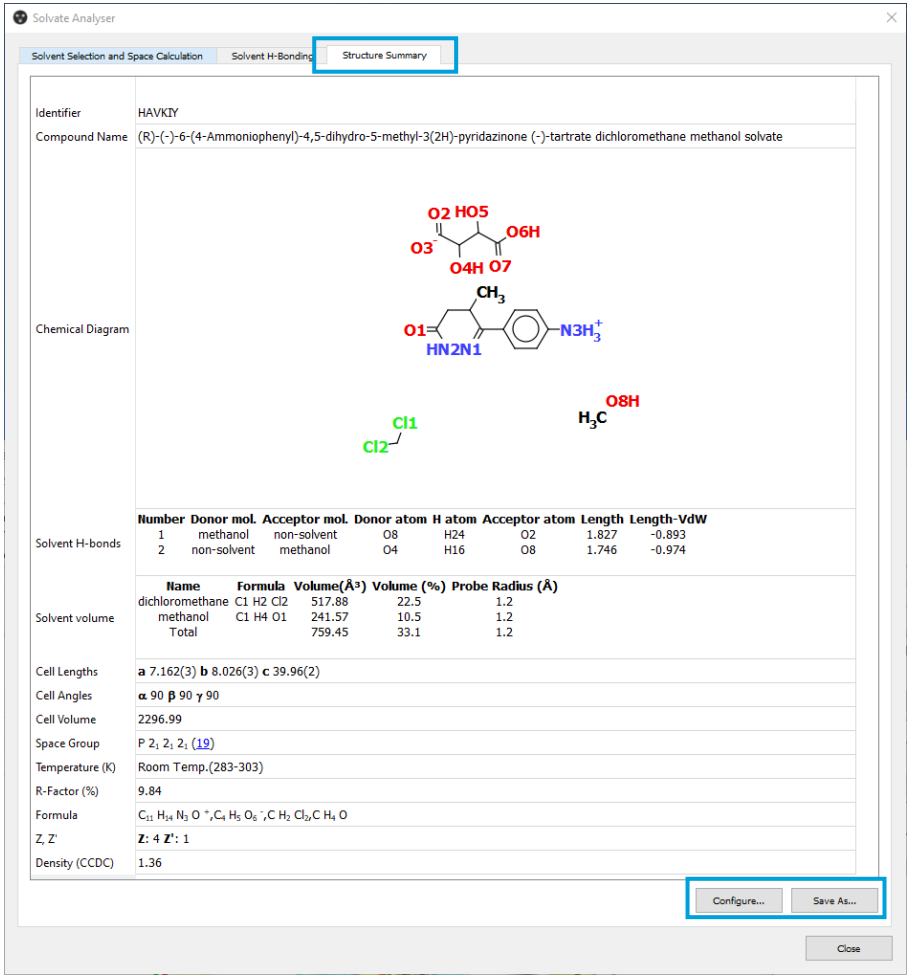

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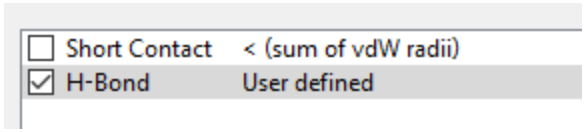

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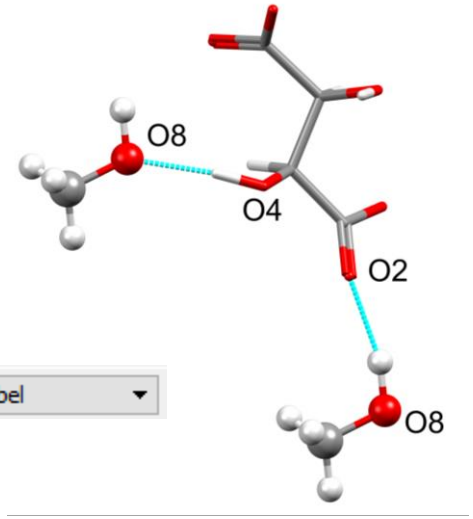
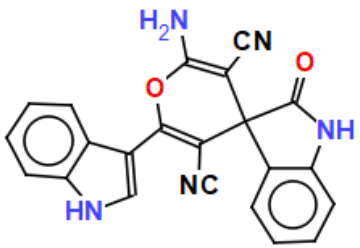
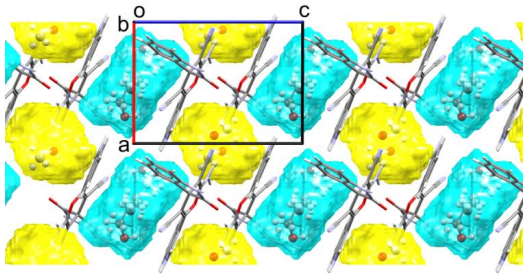


Example 2. Exploring disordered solvate structures.

One advantage of using the Solvate Analyser tool is the ability to quickly generate solvent space for complex, disordered solvents.

In this example you will learn how to display solvent space for disordered structures.





*2'-(indol-3-yl)-2-oxospiro(indoline-3,4'-pyran) derivative ethanol methanol solvate **PACMIR***

1. Open Mercury by clicking the desktop icon, or launching from the Start menu (Windows), Launchpad (macOS) or command line (Linux).

2. In the **Structure Navigator** window, type the refcode *PACMIR*, to bring up the solvated disordered structure.

3. From the top-level menu select **CSD-Materials>Solvate Analyser**….

4. In the 3D visualiser select all the methanol atoms using the lasso tool then click on **Add Solvent From Selected.**

5. Repeat the same steps for the ethanol molecule again using the lasso tool**.**

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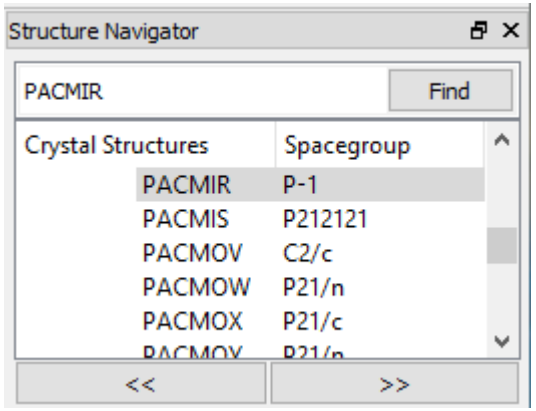

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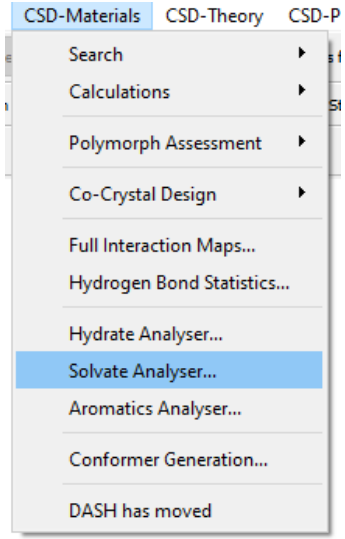

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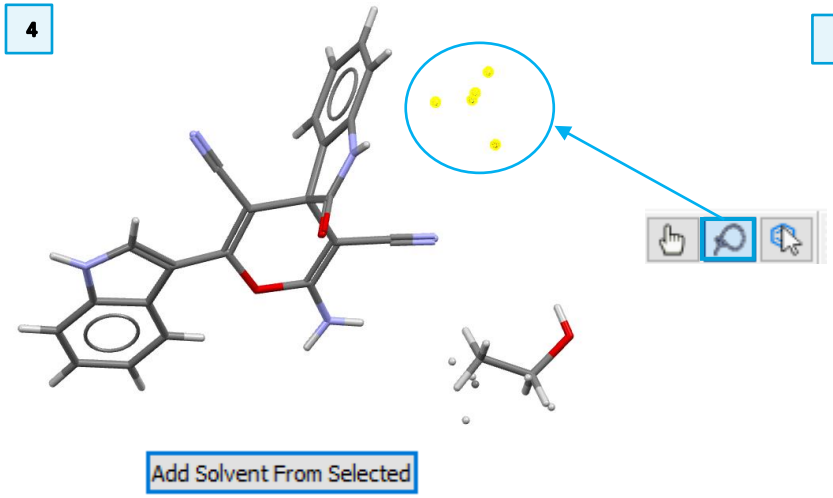

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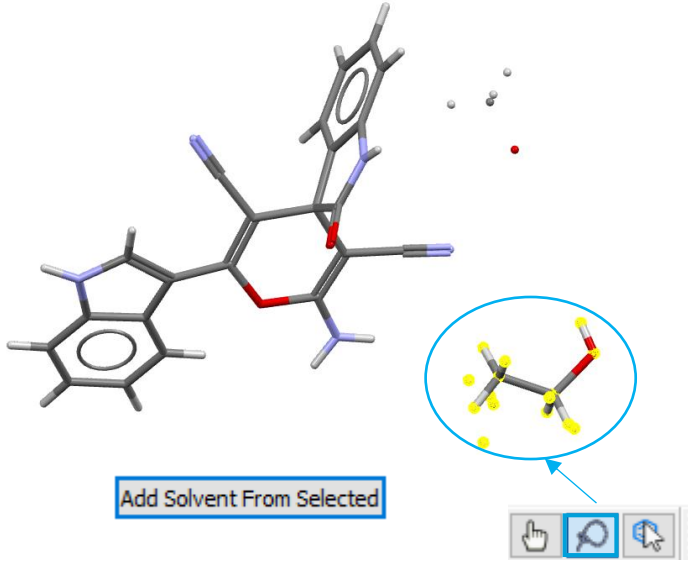

6. Type the solvent names into the **Solvent** row. Toggle on the **Select Solvent** check boxes and change the *Style* to **Ball and Stick** from the top-level toolbar. Click on **Calculate Space** to generate the solvent spaces in the crystal lattice.

7. To further explore the location of the solvent space click the **Packing…** button. Enter 0.0 to 2.0 for *a* and *b* axes and -0.6 to 2.0 for *c* axis. Click **OK** and then **Calculate Space**. Click *b* axis from top-level toolbar to view along it.

8. *How many molecules of methanol and ethanol occupy the pockets?*

9. *How does the solvent space of the two different molecules intercalate with the parent molecule within the crystal lattice?*

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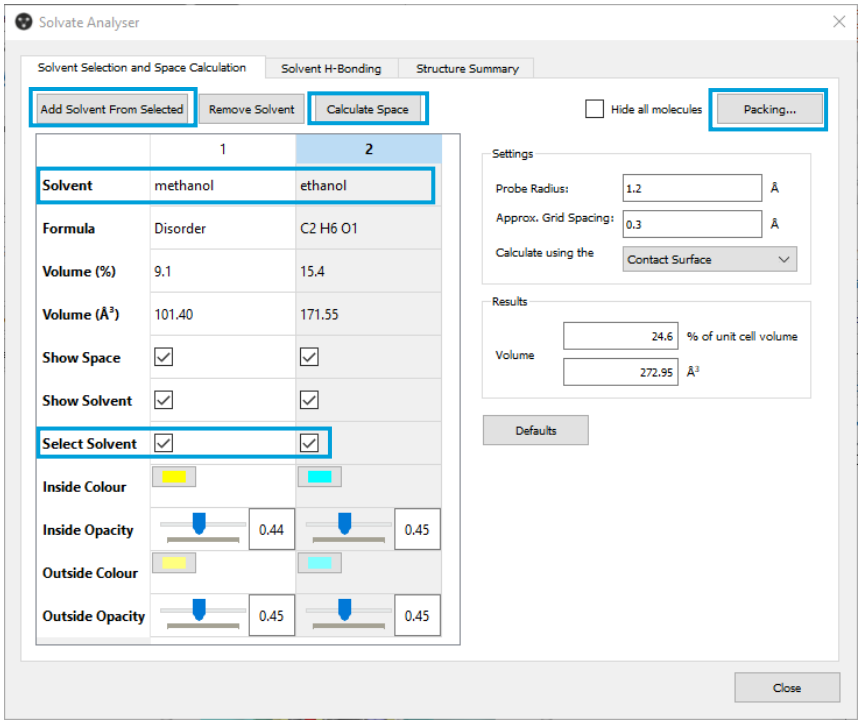

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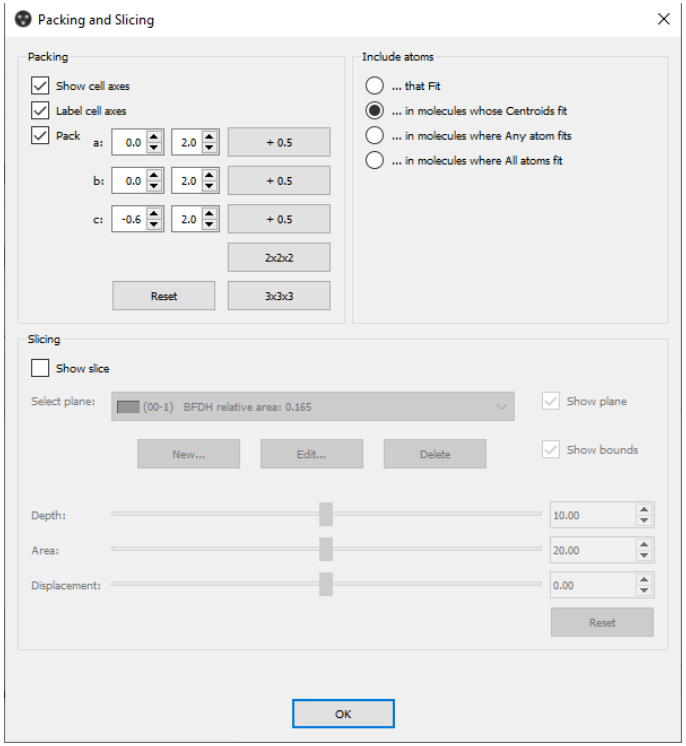

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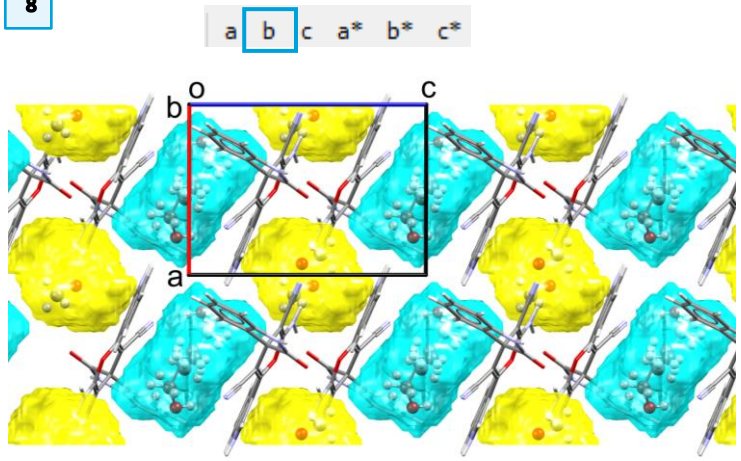

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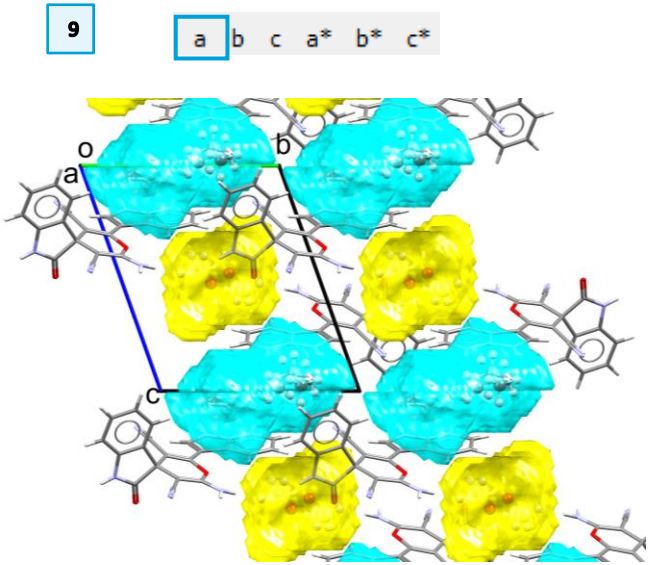

Conclusion

In this example, we have explored how to generate solvent space for complex, disordered solvents. By selecting all ethanol disorder sites, the generated solvent space reflects the available space rather than the space that could be occupied concurrently. Since the disorder sites for ethanol are not occupied at the same time selecting only one set of atoms at a time leads to 0 for the calculated space. This should be kept in mind when using the tool on disordered solvents.

Summary

We have applied the *Solvate Analyser* tool for several structures, including systems with a mixture of solvents and disordered solvent. You should now be able to:

- Select a solvent and calculate the solvent space.
- Change the colour of the solvent space.
- Investigate hydrogen bonding motifs.
- Generate a summary report.
- Explore disordered solvate structures.

Next Steps

Hydrogen bonding was briefly mentioned in this workshop; to further explore hydrogen bonding networks, we recommend working through our workshops on using the Hydrogen Bond Propensity tool in Mercury that is available from the CSD-Materials workshops page: (https://www.ccdc.cam.ac.uk/community/training-and-learning/workshop-materials/csd-materials-workshops/). Other analyses tools in the CSD-Materials suite that can offer more insights into your structures are the Aromatics Analyser and Hydrate Analyser tools. You can find self-guided workshops on these tools also in the CSD-Materials workshops page.

Feedback

We hope this workshop improved your understanding of the *Solvate Analyser* and you found it useful for your work. As we aim to continuously improve our training materials, we would love to hear your feedback. Click on this link to a survey (link also available from workshops webpage), 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 MAT-003. Thank you!