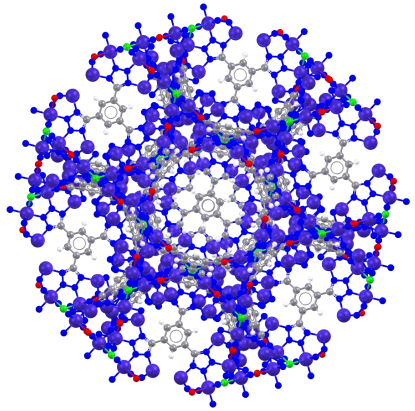
REC

Advanced Functionality for Visualization and Analysis of Structures in Mercury

CCDC Virtual Workshop

30th April 2024

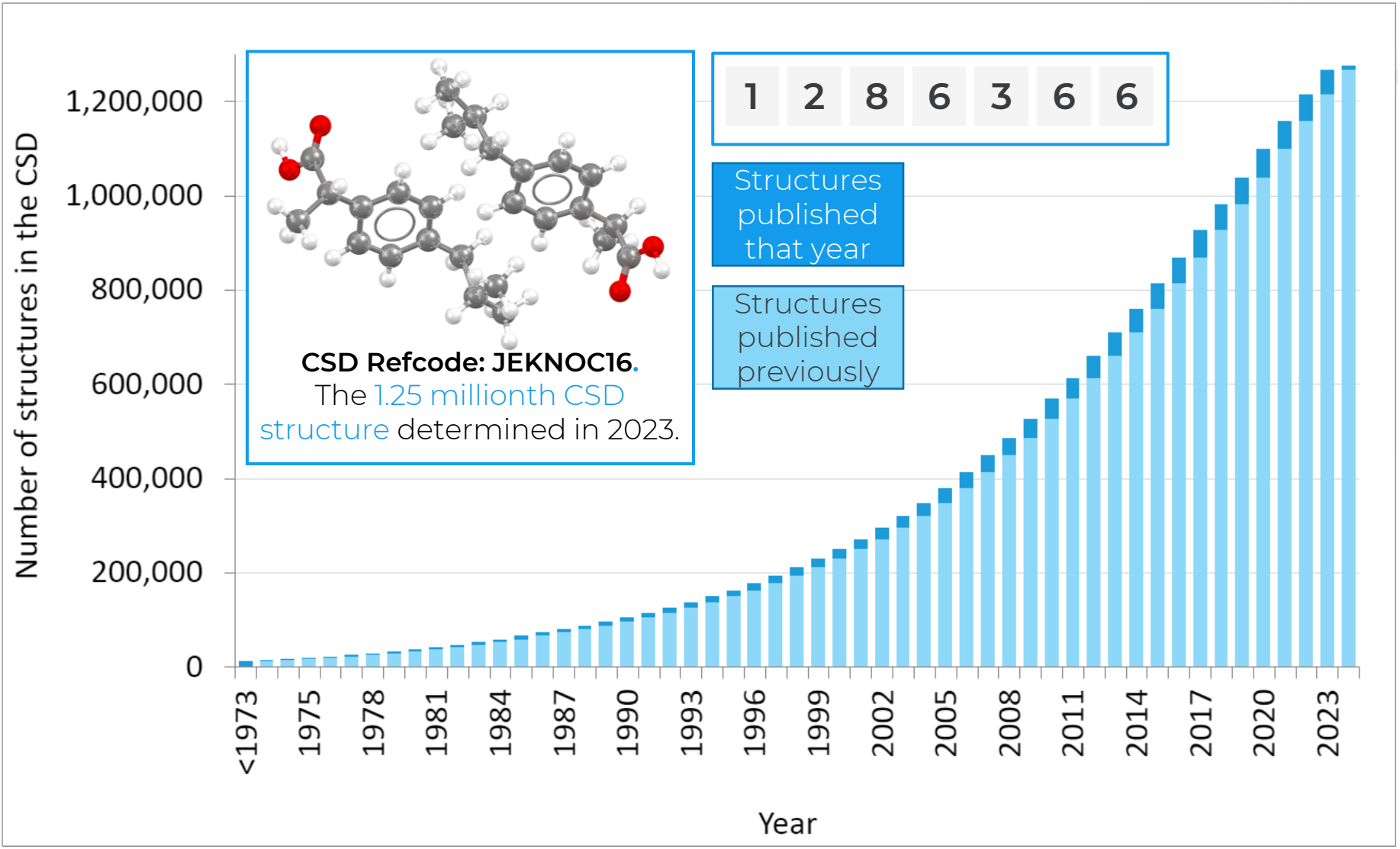


CCDC
advancing structural science

Learning outcomes for today

- Understand more about the advanced functionality in Mercury and how it can be used to visualise, analyse and compare solid forms effectively, including guidance on:
  - Applications of the new disorder visualization feature.
  - Edit structures, select, hide or delete parts of the structure and create your own style!
  - Structure and molecule overlay, for comparing crystal structures packing and molecular conformations and stereochemistry.
  - Visualize a slice of the crystal packing along BFDH planes.
  - Conformer generator for generating plausible conformers of compounds of interest.
  - Programmatic access though CSD Python API menu - no need for coding with the pre-loaded functionality!
- Learn tips and tricks for using a range of tools effectively to save you time and help you advance your research
- Gain confidence in the functionality used today so you can apply the techniques on your own systems/structures.

The Cambridge Structural Database



- Every published structure
  - Inc. ASAP & early view
  - *CSD Communications*
  - Patents
  - University repositories
  - Thesis
- Every entry enriched and annotated by experts
- Discoverability of data and knowledge
- Sustainable for over 58 years
- A trusted CoreTrustSeal repository

Certified as Trustworthy by CoreTrustSeal

Inside the Cambridge Structural Database

The CSD is a database of all the published organic and metal-organic experimental crystal structures

Organic
45%

Metal-Organic
55%

At least one transition metal, lanthanide, actinide or any of Al, Ga, In, Tl, Ge, Sn, Pb, Sb, Bi, Po

Not Polymeric
89%

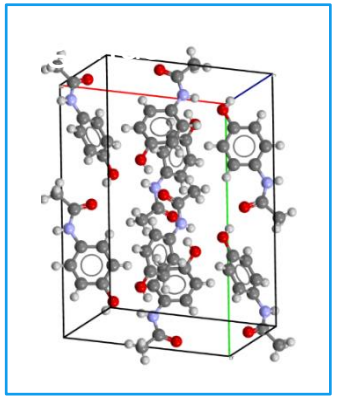
Polymeric: 11%

Single Component
58%

Multi Component
42%

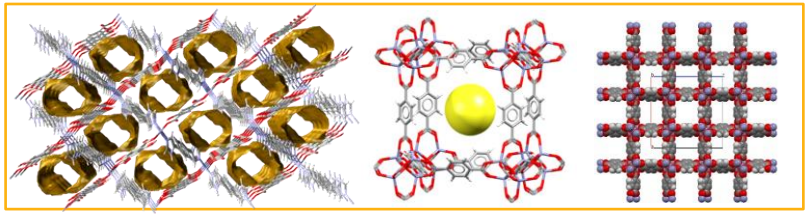
Organic

- Drugs
- Agrochemicals
- Pigments
- Explosives
- Protein ligands



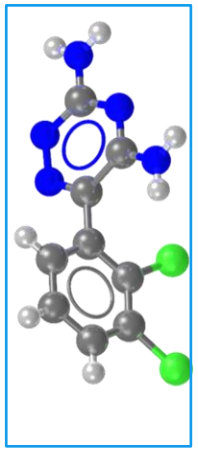
Metal-Organic

- Metal Organic Frameworks
- Models for new catalysts
- Porous frameworks for gas storage
- Fundamental chemical bonding



Additional data

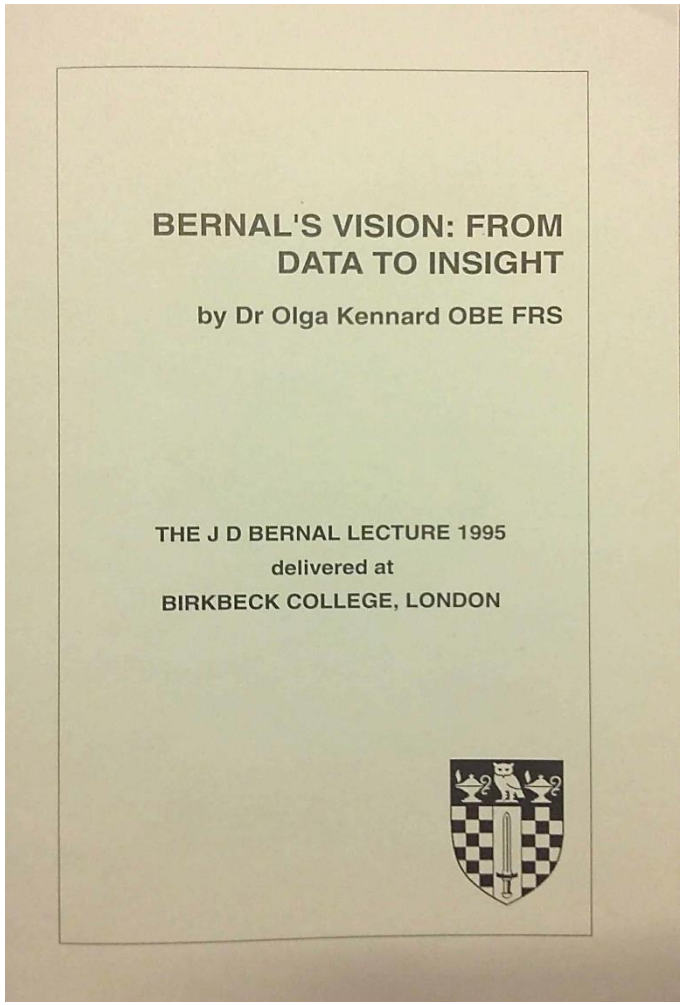
- 13,478 polymorph families
- 174,987 melting points
- 1,075,904 crystal colours
- 951,746 crystal shapes
- 30,275 bioactivity details
- 13,641 natural source data
- > 350,000 oxidation states



Links and subsets

- DrugBank
- Druglike
- MOFs
- PDB ligands
- PubChem
- ChemSpider
- Pesticide PDB

The vision


BERNAL'S VISION: FROM DATA TO INSIGHT

by Dr Olga Kennard OBE FRS

THE J D BERNAL LECTURE 1995
delivered at
BIRKBECK COLLEGE, LONDON

We clearly recognised even in those early days, that data banks have three principal functions. Firstly they must gather together existing knowledge and make it readily available to the scientific community. Secondly they can be used to reduce a large number of observations to a small set of constants and rules, and in this way transform a data base to a knowledge base. Such a knowledge base may obviate the need for further individual experiments in specific areas. Thirdly, they facilitate the comparison and collective analysis of individual results to gain insight into new or as yet unexplained phenomena. These ideas have been at the heart of the work of the Cambridge Crystallographic Data Centre and the driving force for improving methods of data collection, storage and dissemination. Most importantly they influenced development of computer programs and methodologies which are needed for the analysis and transformation of the accumulated information. (5)

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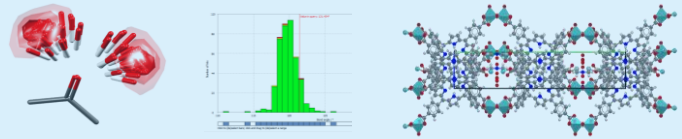
The CSD Portfolio today

CSDCore.

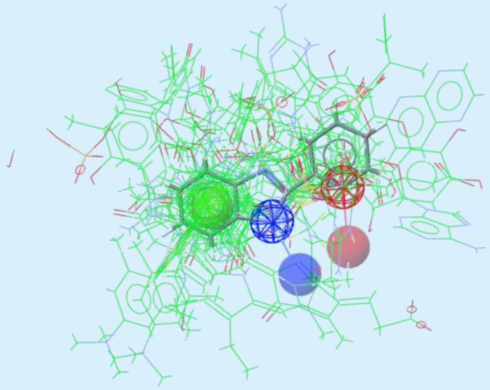
Search, visualise, analyse and communicate structural data

Insights into molecular and crystal shape and interactions



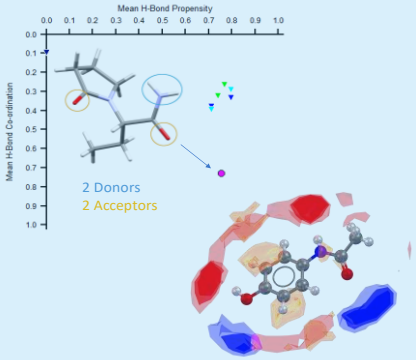
CSDDiscovery.

Design of new molecules



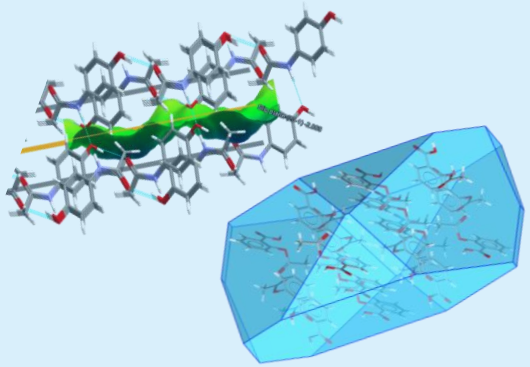
CSDMaterials.

Assessment of solid form stability and properties



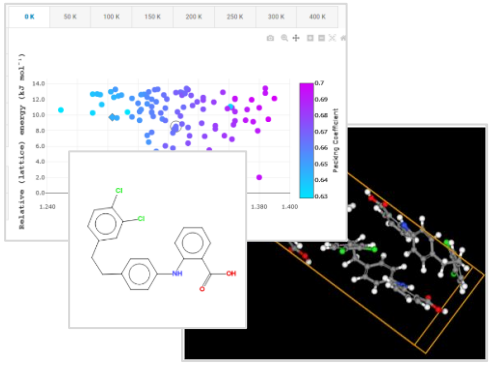
CSDParticle.

Anticipate particle properties and behaviour



CSDTheory.

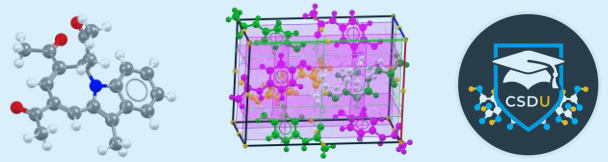
Insights from predicted structure landscapes



CSDCommunity.

Deposit, publish, access and visualise structural data

Free functionality to share and learn from structures



Medicinal & Computational Chemists ♦ Crystallographers & Structural Biologists ♦ Solid Form & Crystallisation Scientists ♦ Functional Materials Scientists ♦ Educators ♦ Industry and Academia

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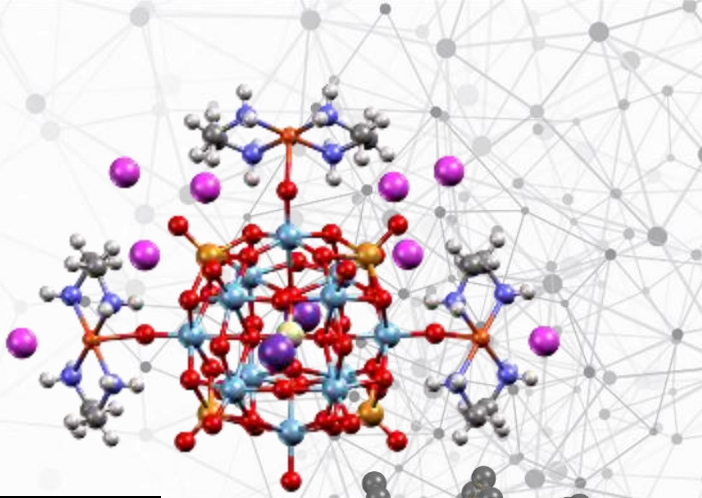
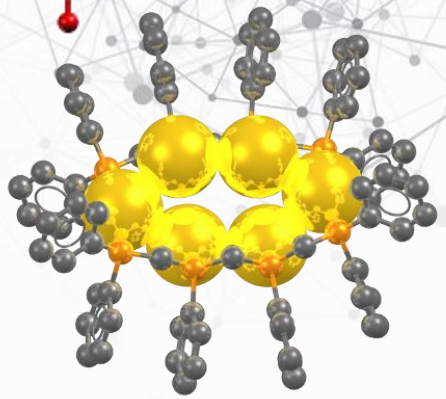
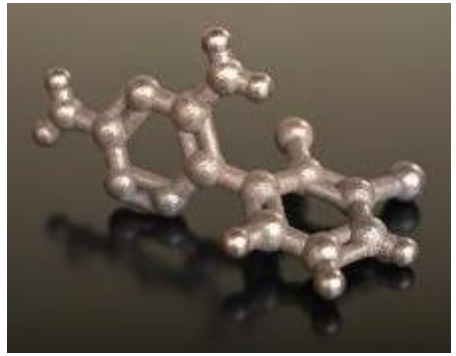
Mercury – Structure visualisation

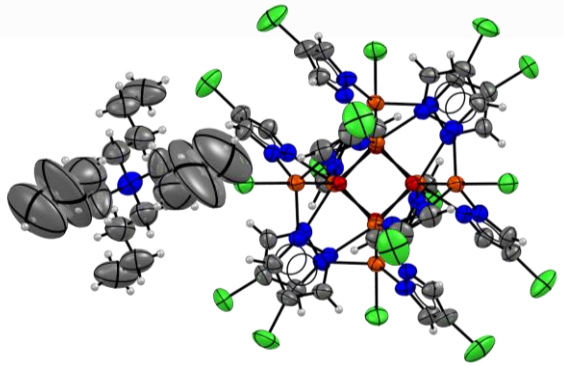
With Mercury you can:

- Explore crystal structures, molecular conformations, crystallographic planes and simulated morphologies
- Generate high quality structural images for effective scientific communication
- Output model files for 3D printing
- Analyse geometries, interactions and the packing inside structures









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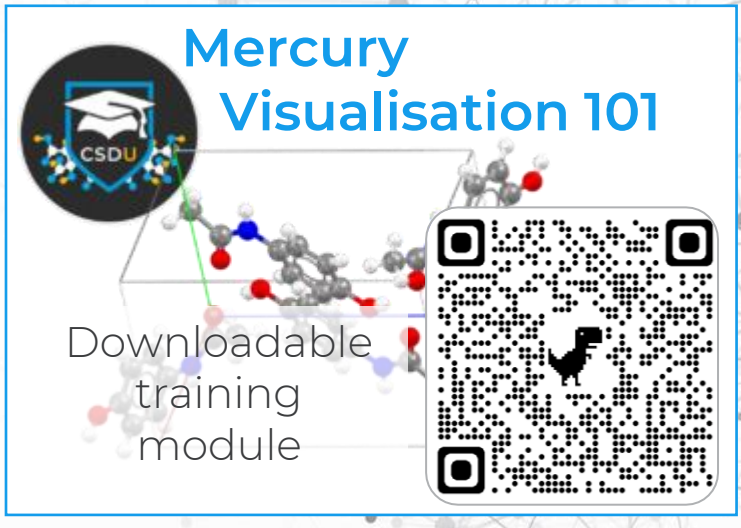
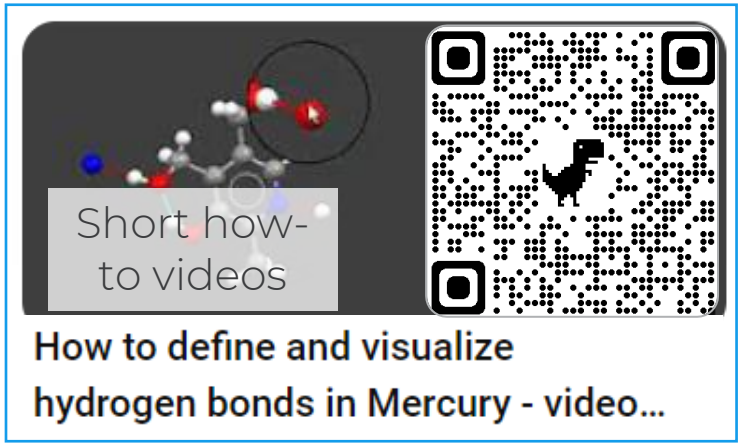
Structure visualisation – Basics

What have we learnt in previous workshops and resources?

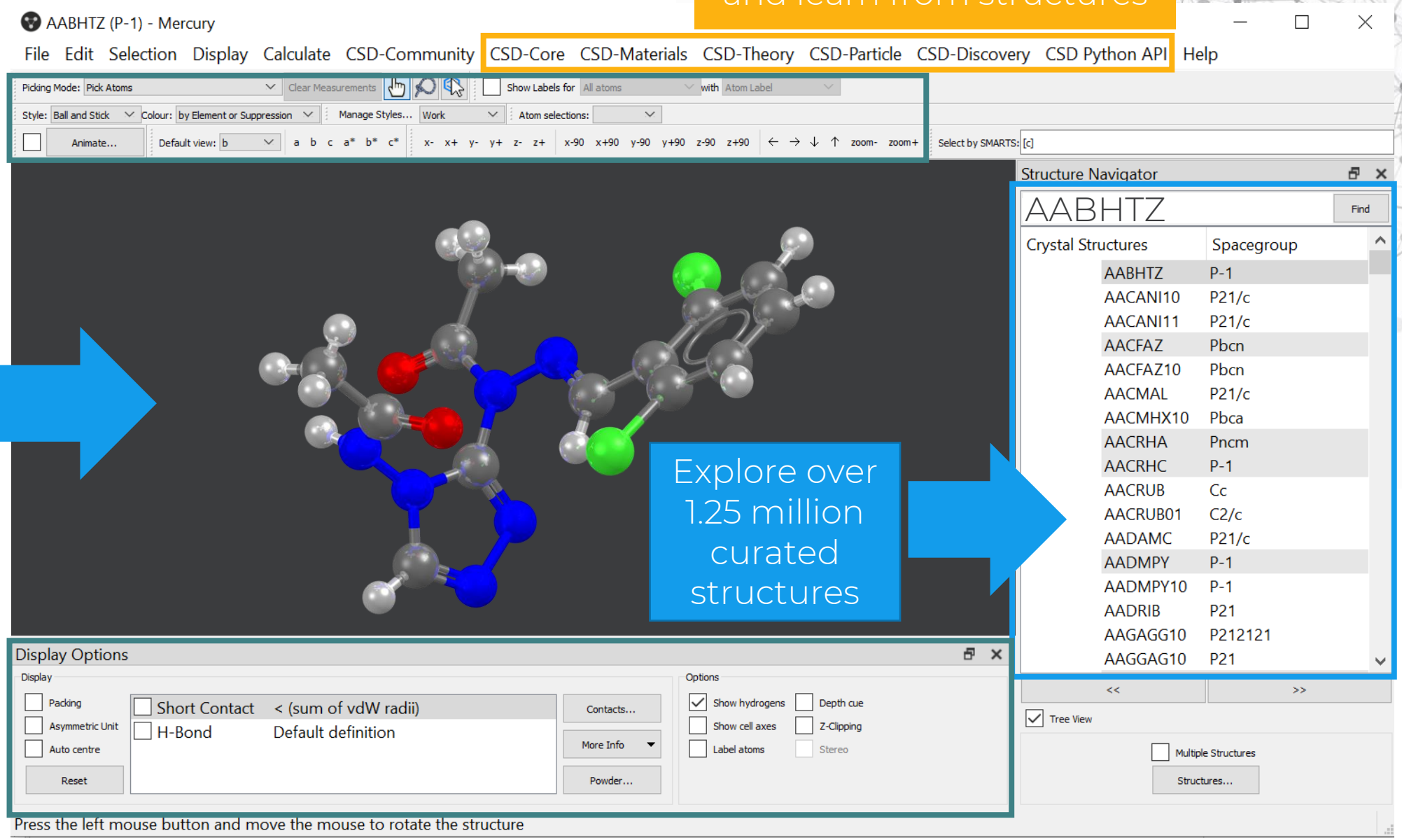
- The basics of the Mercury interface.
- Basic options to visualise small molecule crystal structures.
- Analysis and visualisation of Hydrogen bonds.
- Visualisation of the packing and basic symmetry.
- Creation of high-resolution publication ready images.





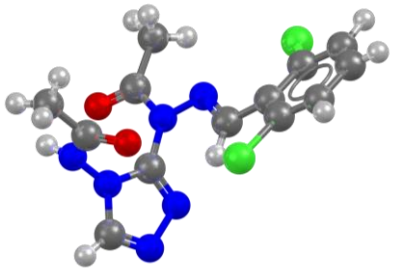
Mercury Overview

More advanced functionality to analyse and learn from structures



Display options to visualise and navigate structures

CSD Refcodes



CSD Refcode - AABTHZ

What is AABHTZ?

- A CSD Refcode
- A database reference code
- Containing 6-8 characters
- Used to identify entries in the CSD

Refcode families

- The same substances are assigned the *same* 6 letter code plus an additional 2 numbers
  - Polymorphs
  - New determinations or re-refinements of the same substance
  - Determinations at different temperatures/pressures
- Stereoisomers or different solvates, co-crystals, etc are assigned *different* refcode families

Some of my favourite refcodes are: KITTEN, BATMAN, DISNEY, GAUTAM, GLYCIN

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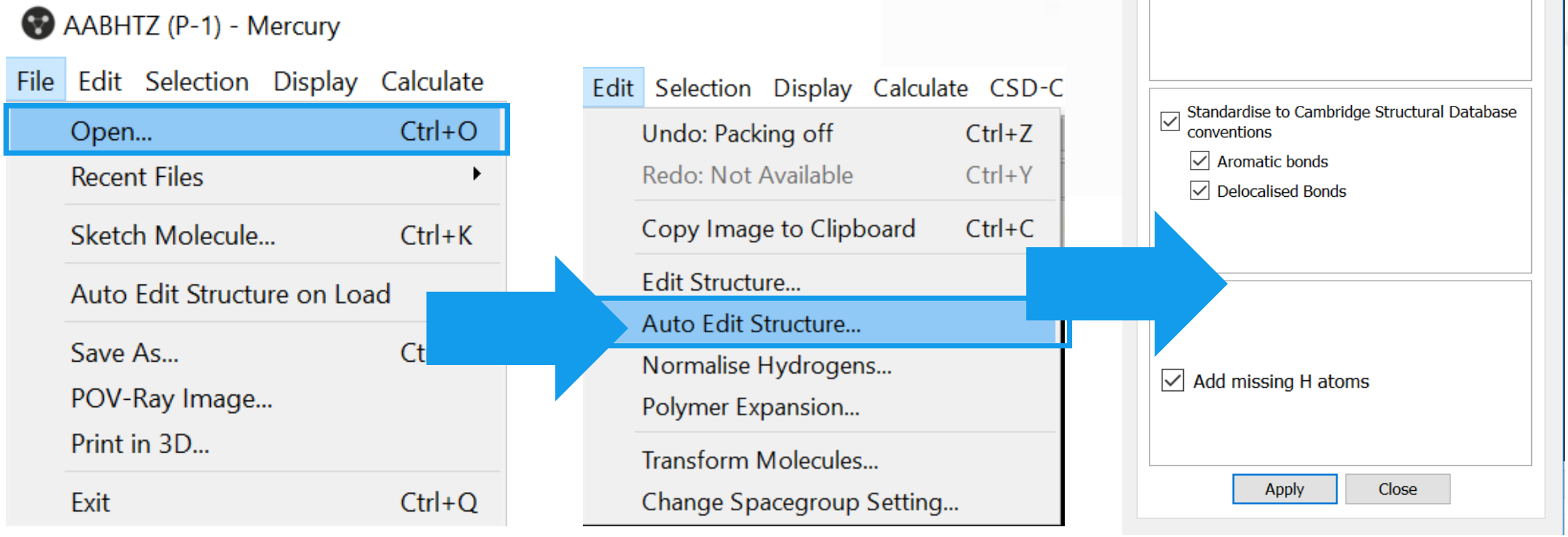
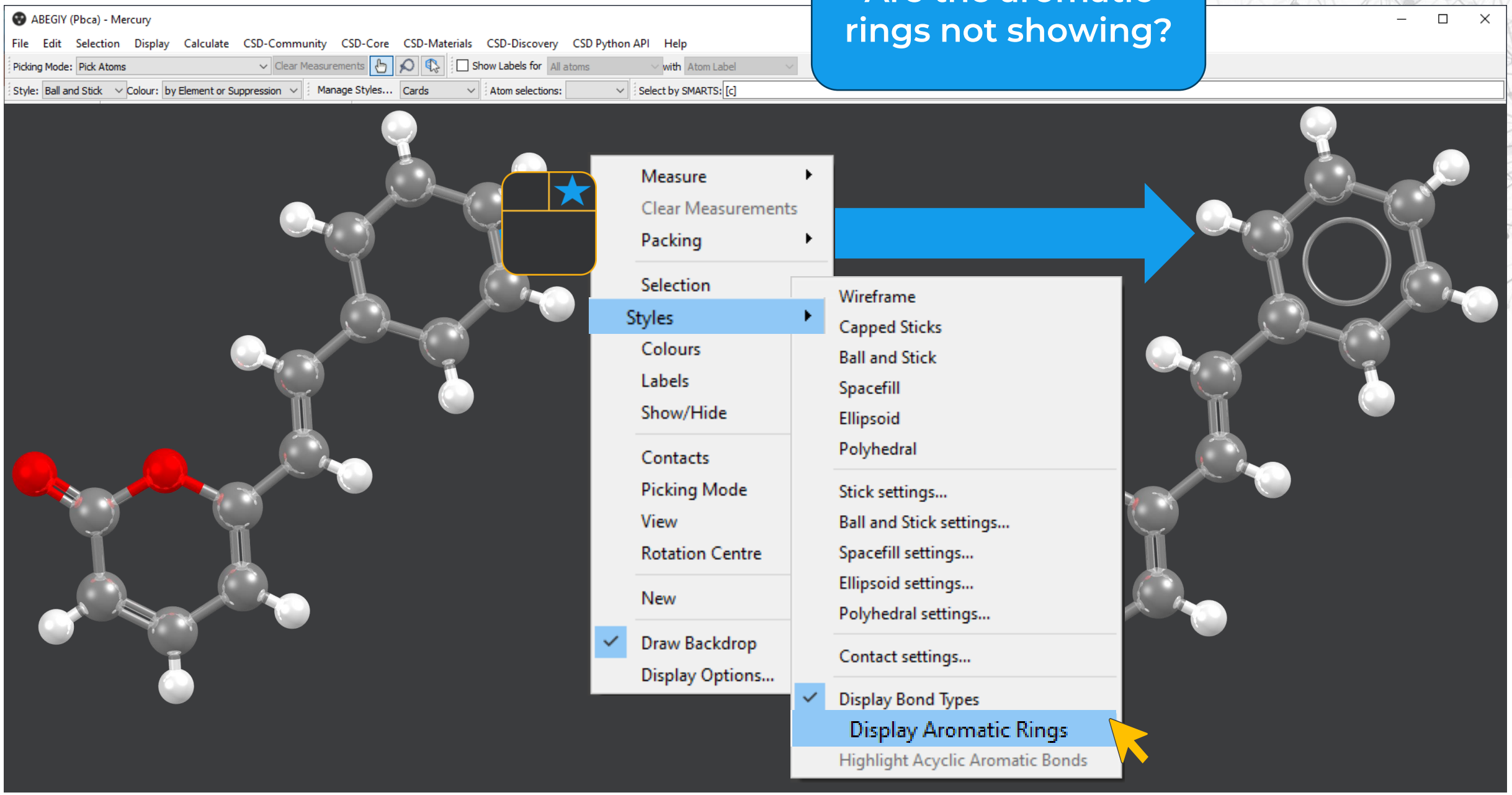
Visualise your own structures

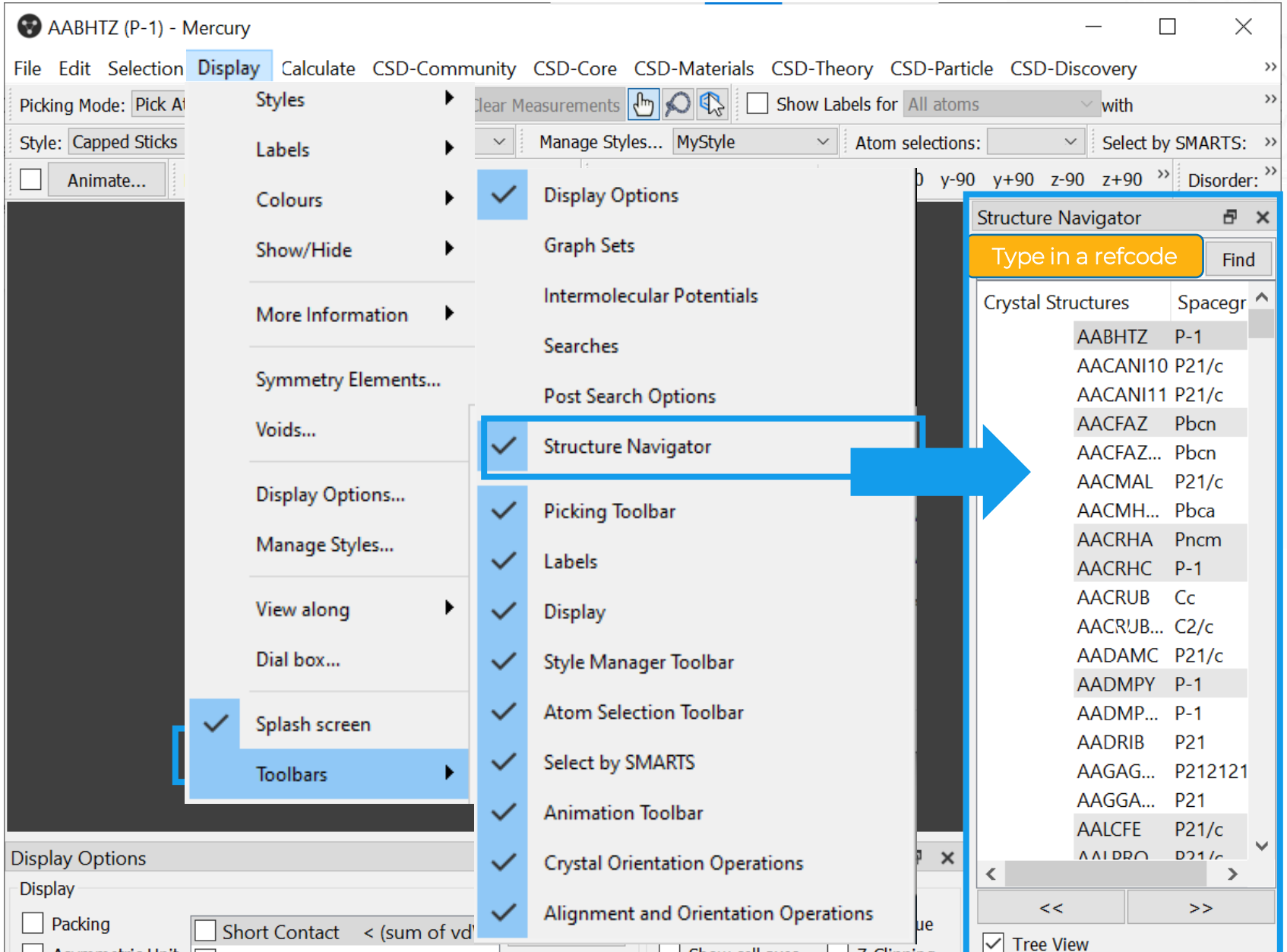
Import and assign bond types and missing hydrogens (optional)

- File > Open – to open one of your own files for example a CIF
- Edit > Auto Edit Structure to assign bond types
- File > Auto Edit Structure on Load to automate



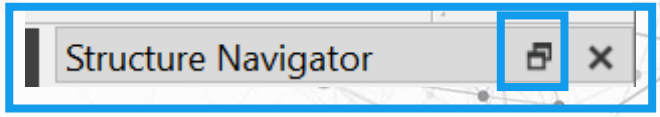

Are the aromatic rings not showing?
ABEGIY (Pbca) - Mercury
File Edit Selection Display Calculate CSD-Community CSD-Core CSD-Materials CSD-Discovery CSD Python API Help
Picking Mode: Pick Atoms
Clear Measurements
Show Labels for
All atoms
with
Atom Label
Style: Ball and Stick
Colour: by Element or Suppression
Manage Styles...
Cards
Atom selections:
Select by SMARTS: [c]
Measure
Clear Measurements
Packing
Selection
Styles
Colours
Labels
Show/Hide
Contacts
Picking Mode
View
Rotation Centre
New
Draw Backdrop
Display Options...
Wireframe
Capped Sticks
Ball and Stick
Spacefill
Ellipsoid
Polyhedral
Stick settings...
Ball and Stick settings...
Spacefill settings...
Ellipsoid settings...
Polyhedral settings...
Contact settings...
Display Bond Types
Display Aromatic Rings
Highlight Acyclic Aromatic Bonds

Lost toolbars?



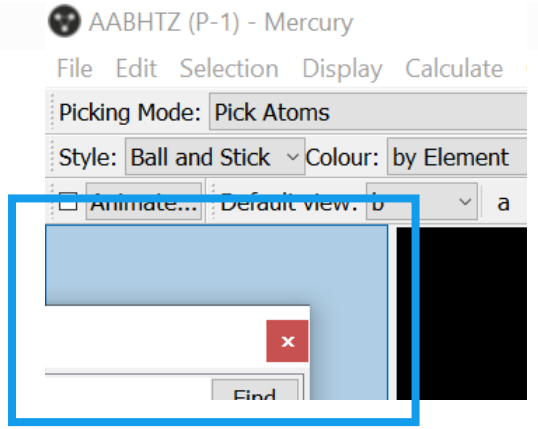
Extra Tip

Click on the resize icon or drag the top to pop the toolbar out.



Extra Tip

To pop the toolbar back in drag it to the area you want it.



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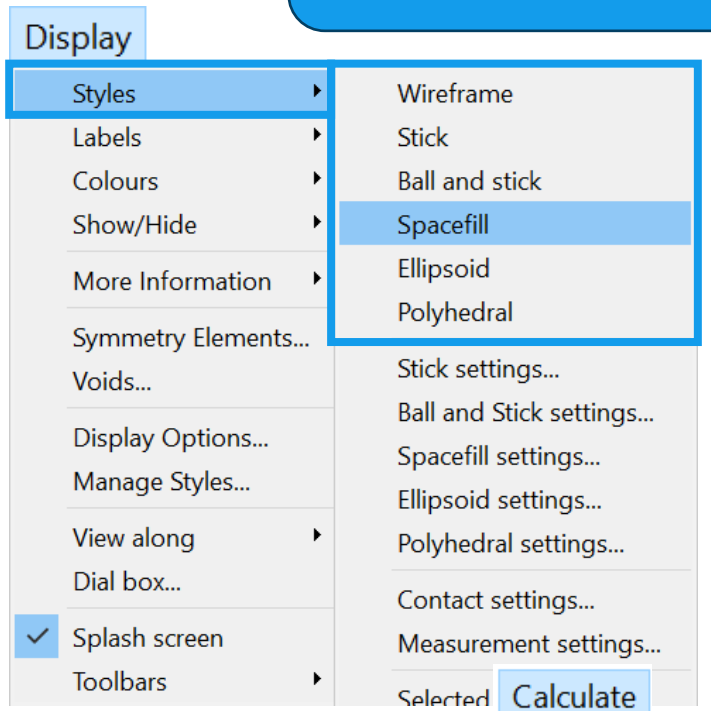
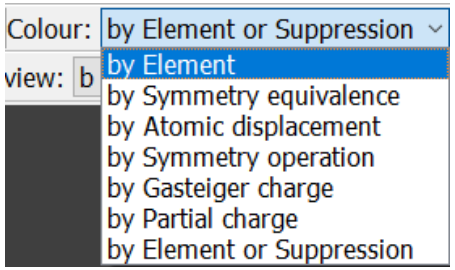
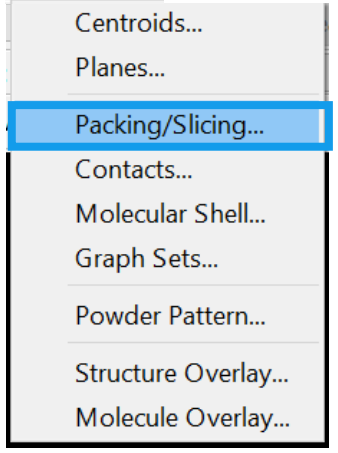
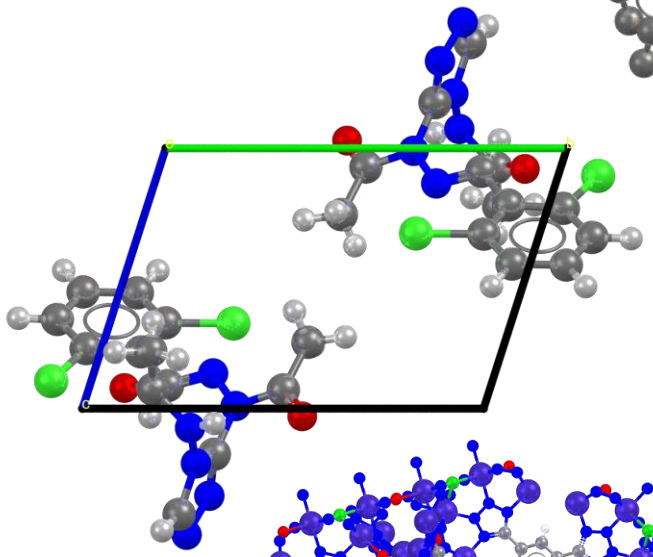
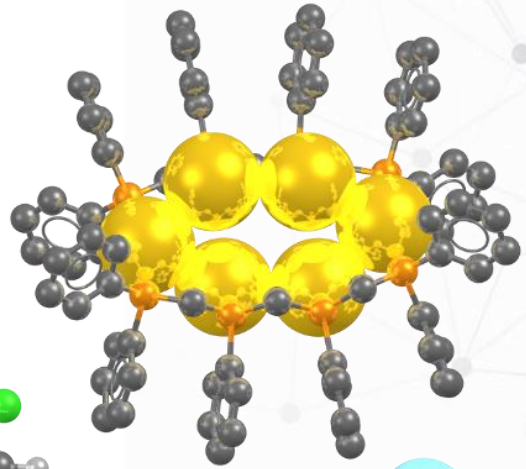
Improve visualization with lots of display options!

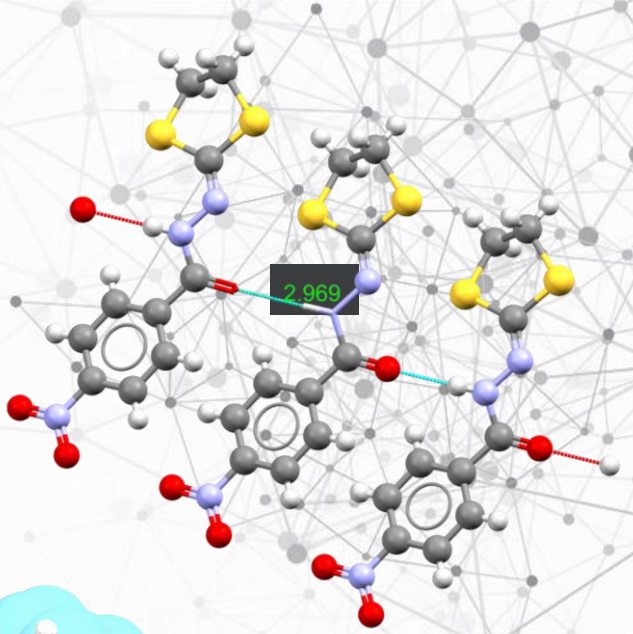


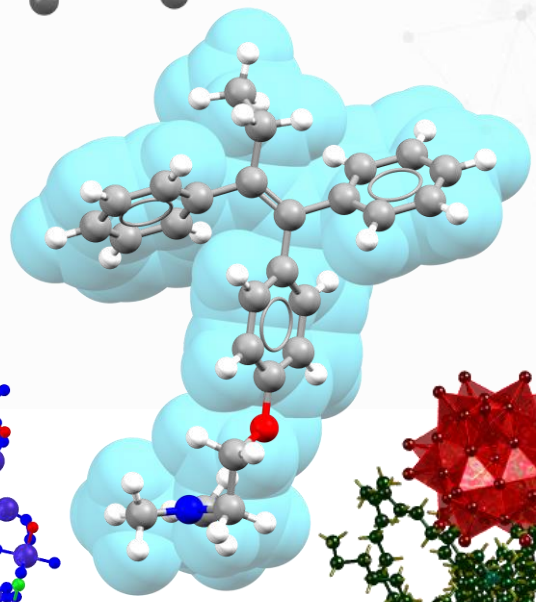


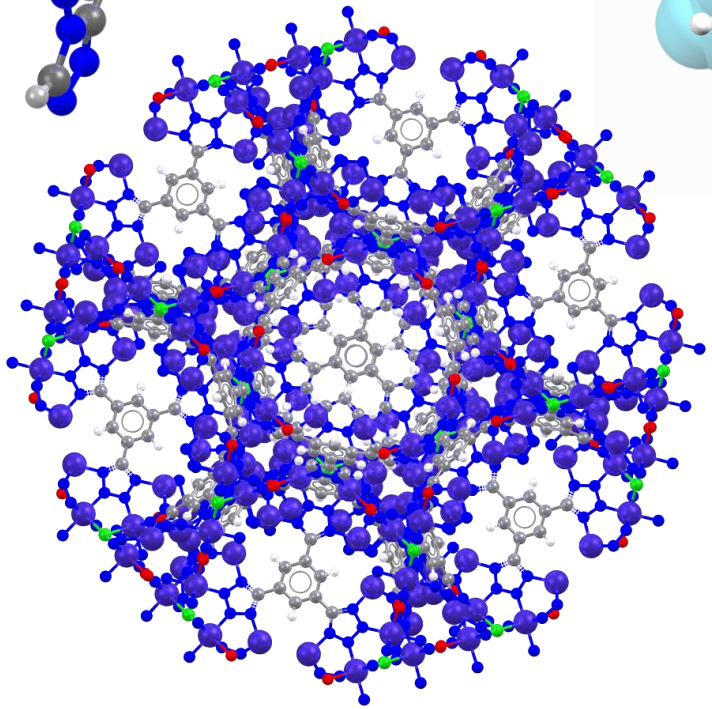


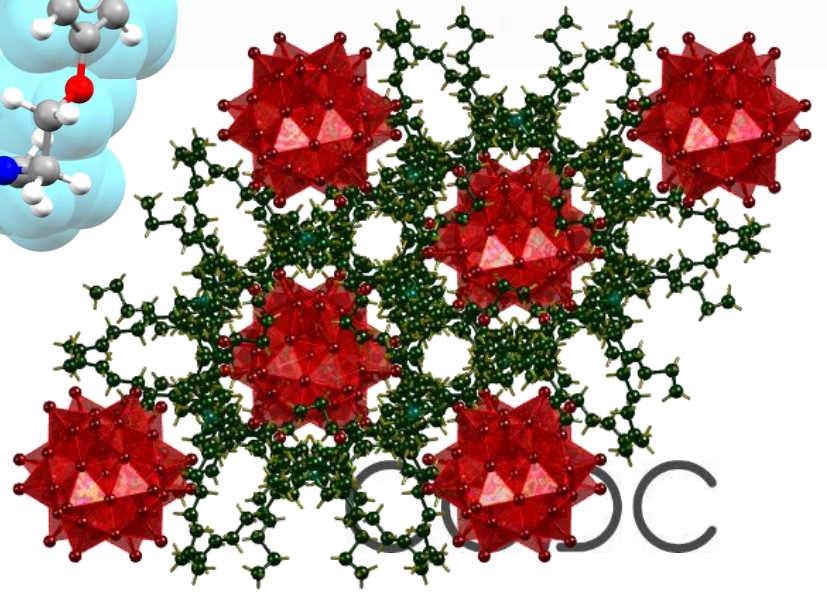




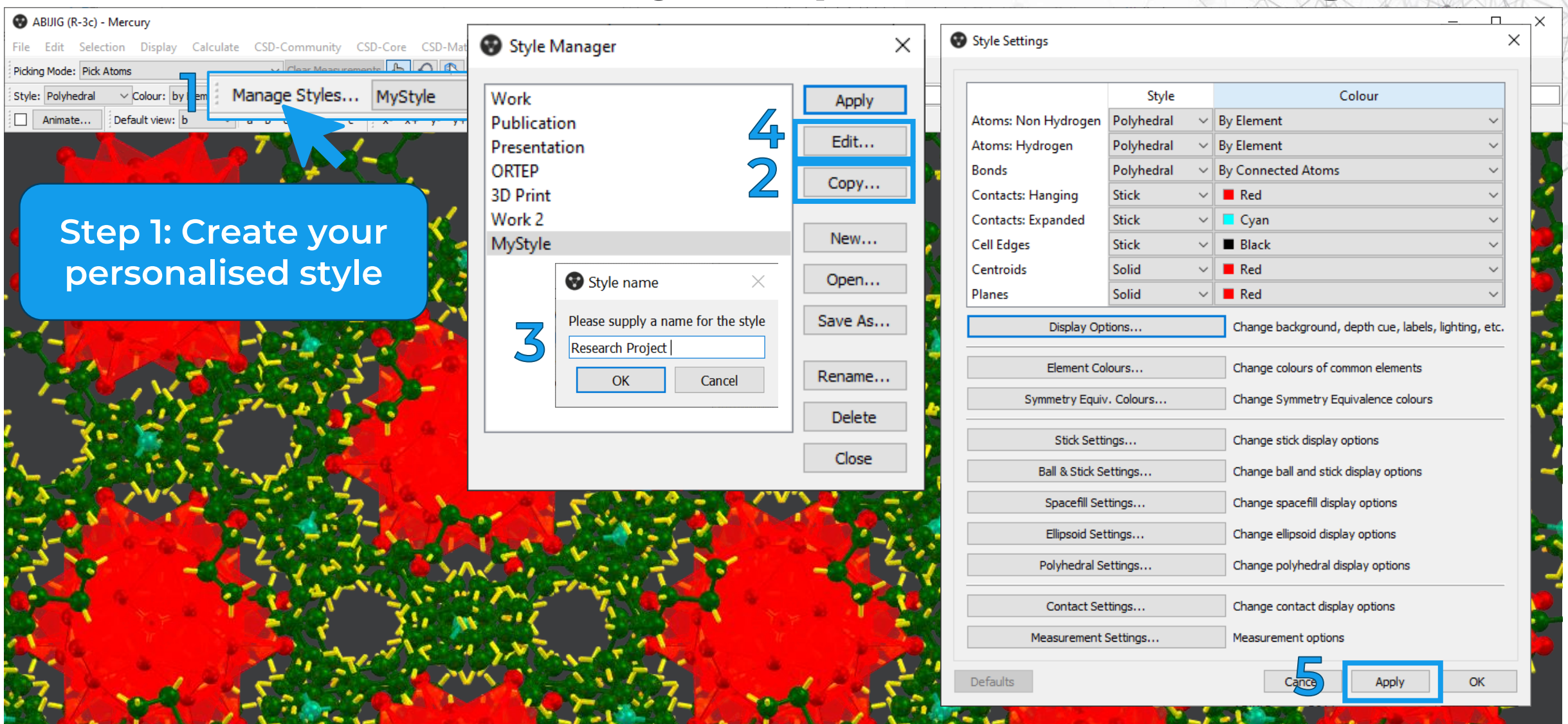




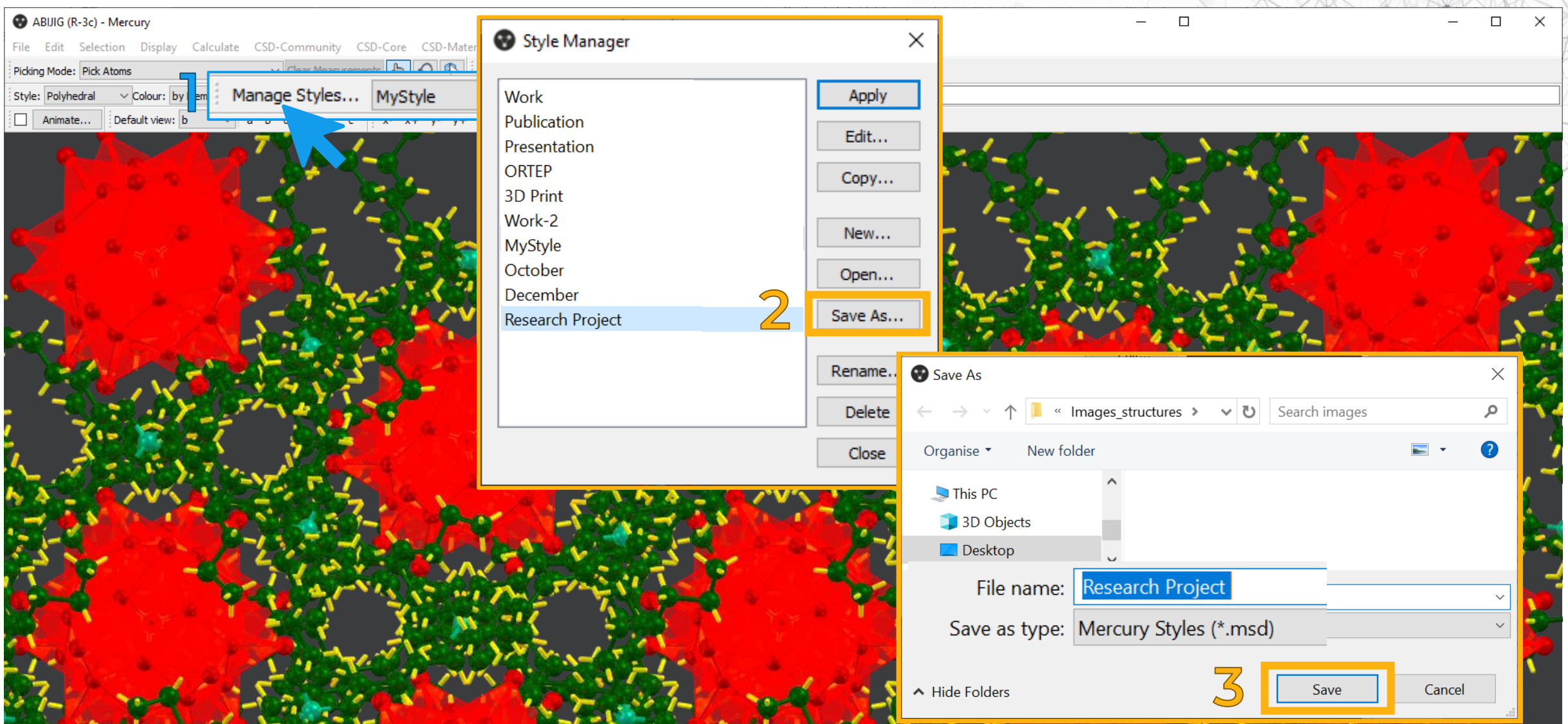




Working with colleagues and want consistent look of your publication images?

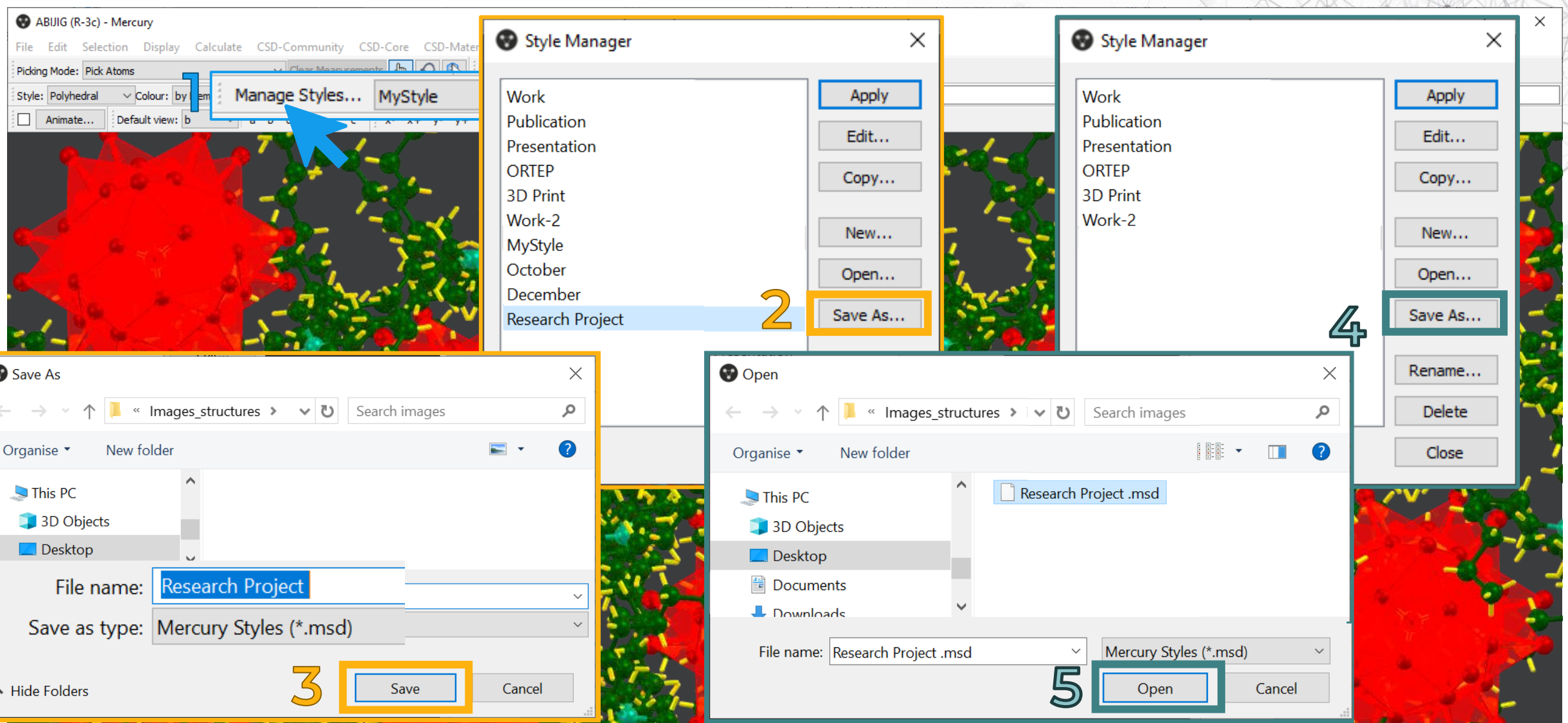


Step 2: Save it and share it with your collaborators



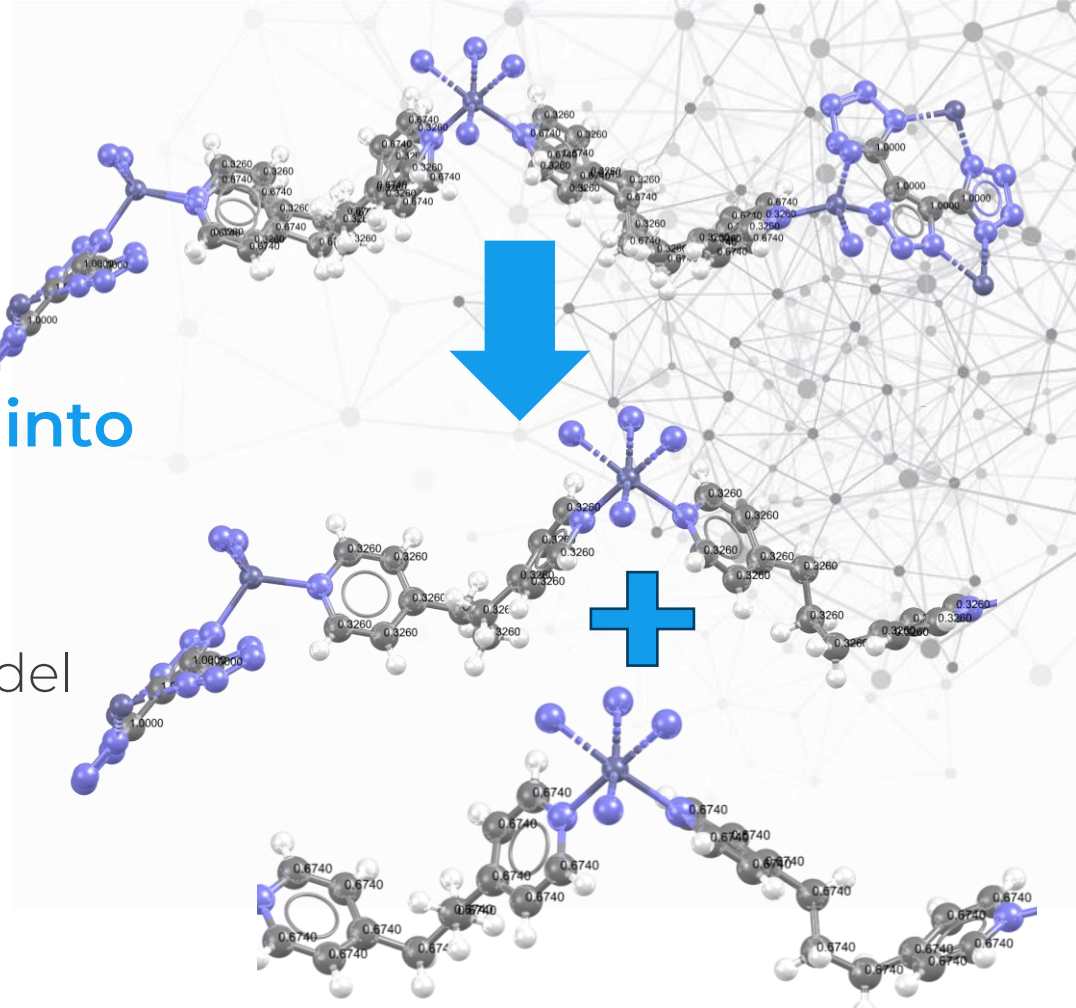
Step 2: Save it and share it with your collaborators

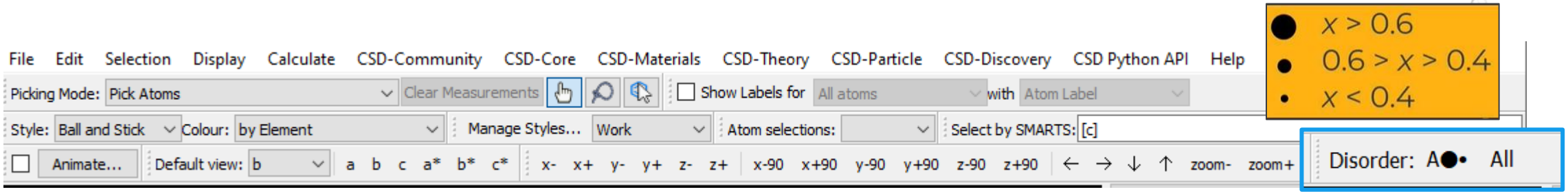
Step 3: Your collaborators can then open and save your new style.



Visualizing disorder

- New functionality when you **load a CIF into Mercury:**
  - Visualise the different disorder models
  - Visualize the contacts for each disorder model
  - Visualize the voids for each disorder model
  - Available from July 2023 onwards
- More disorder work planned.





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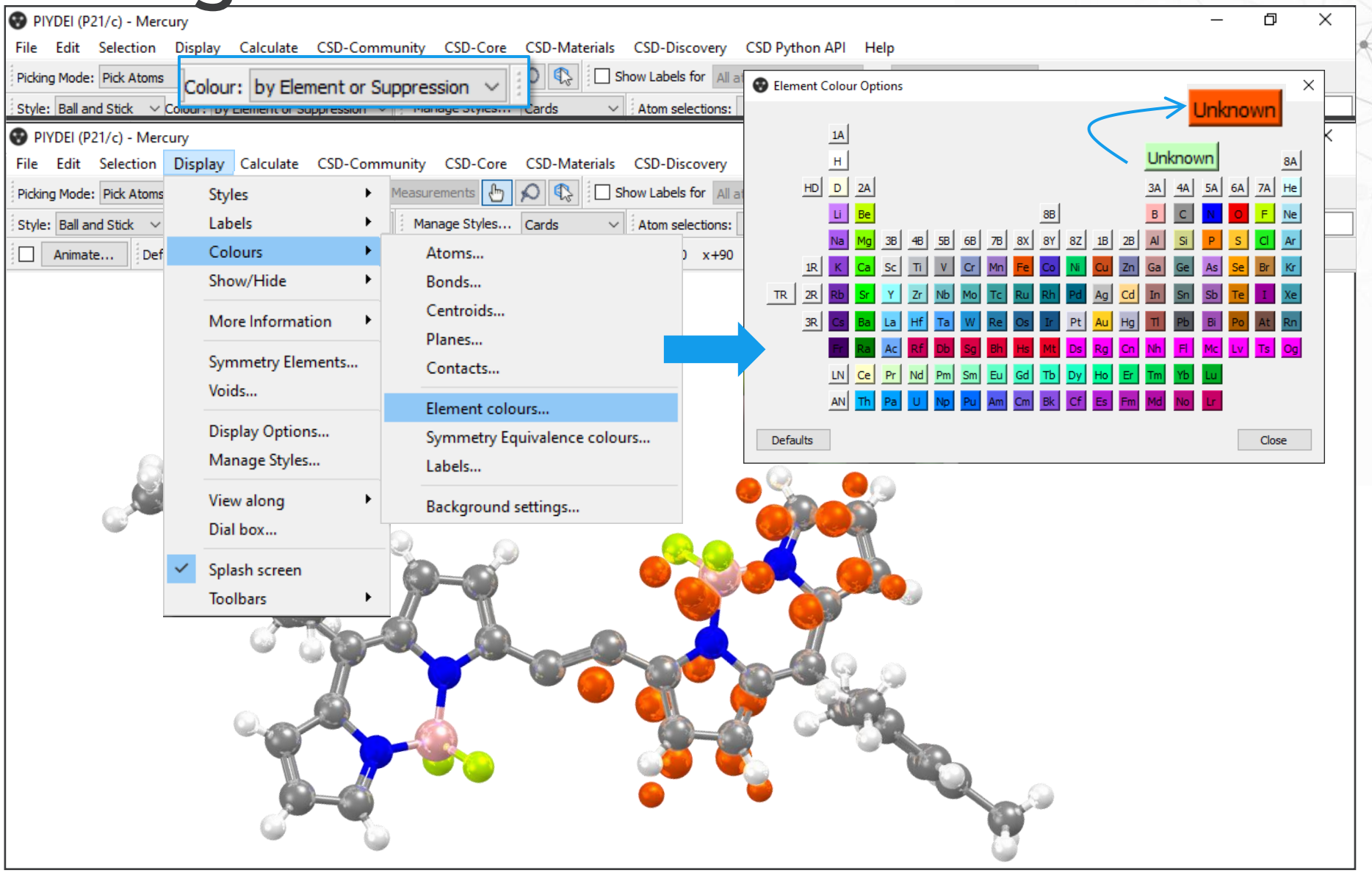
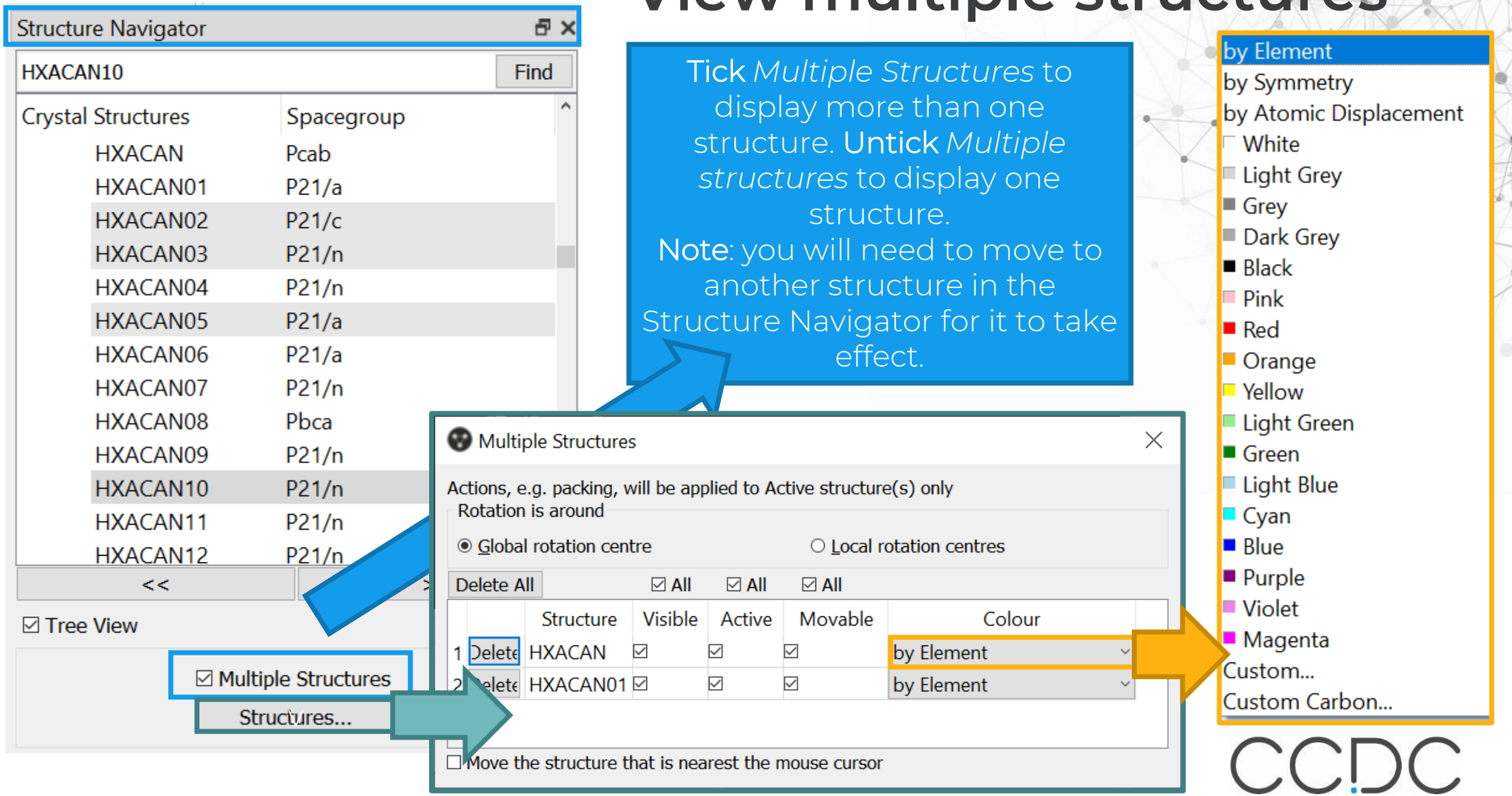
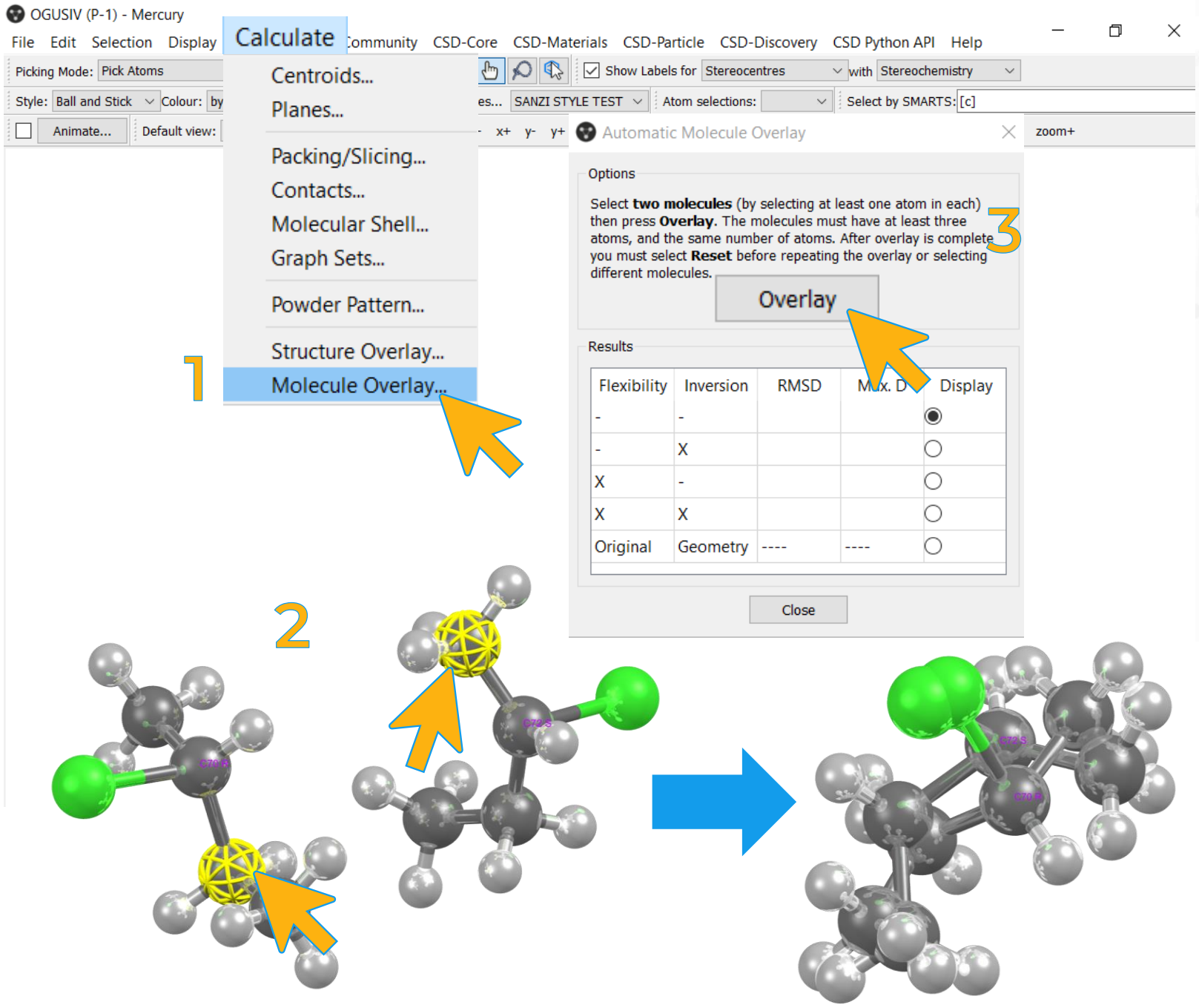
Change disordered atoms colours



CCDC

View multiple structures





Molecule Overlay

When to use:

- To compare the chirality of stereochemistry of molecules.
- To compare conformers.

What is does:

- Uses inversion and flexibility to calculate overlays.

What you can use it on:

- 2 molecules in different structures
- Or 2 molecules in a single structure.
- On identical or non-identical molecules.

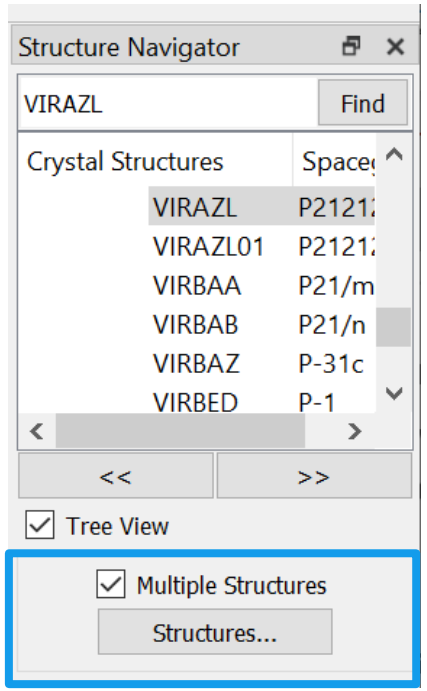
Tip

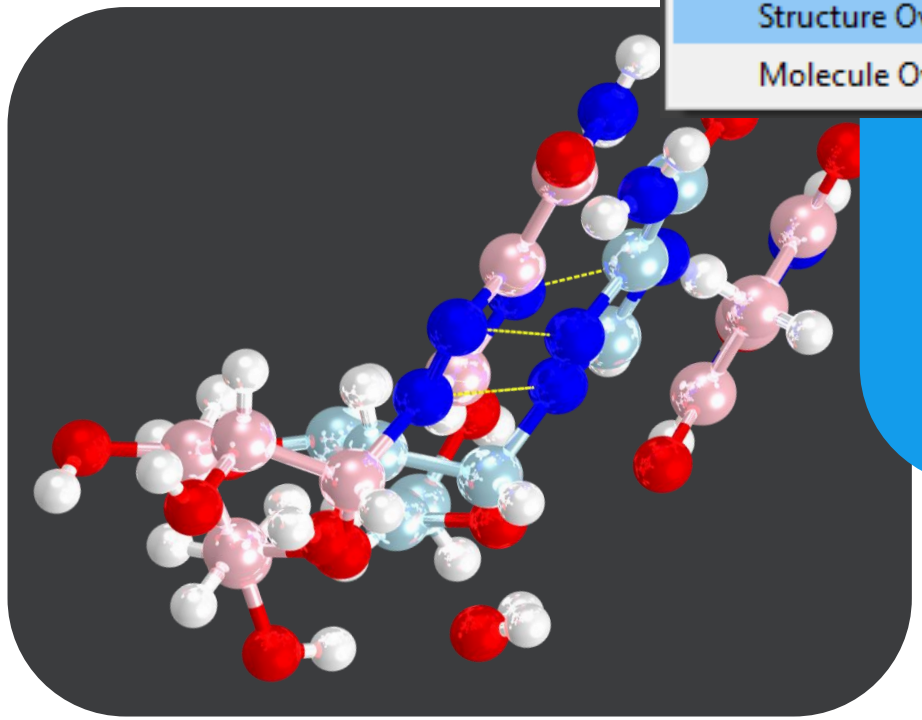
- If the reported RMSD for the overlay is quite low, but the Max. D value is large, it may be an indication that the molecules are quite similar, except for a localised area.
- For example, a comparison of cis and trans geometries may result in a low RMSD but high Max. D.

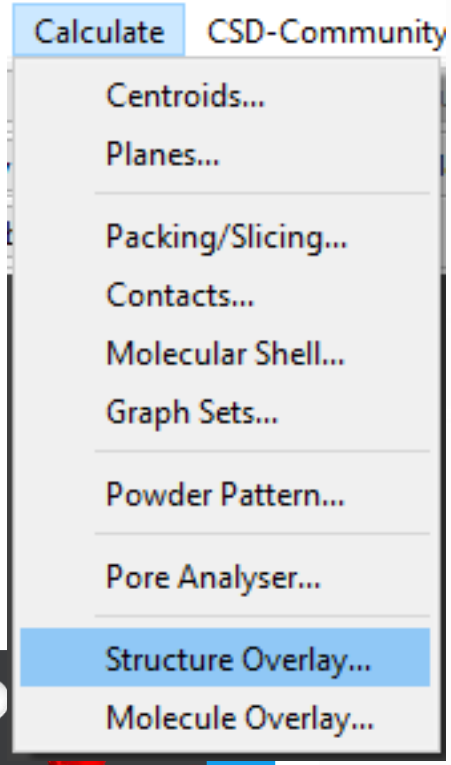
Structure Overlay

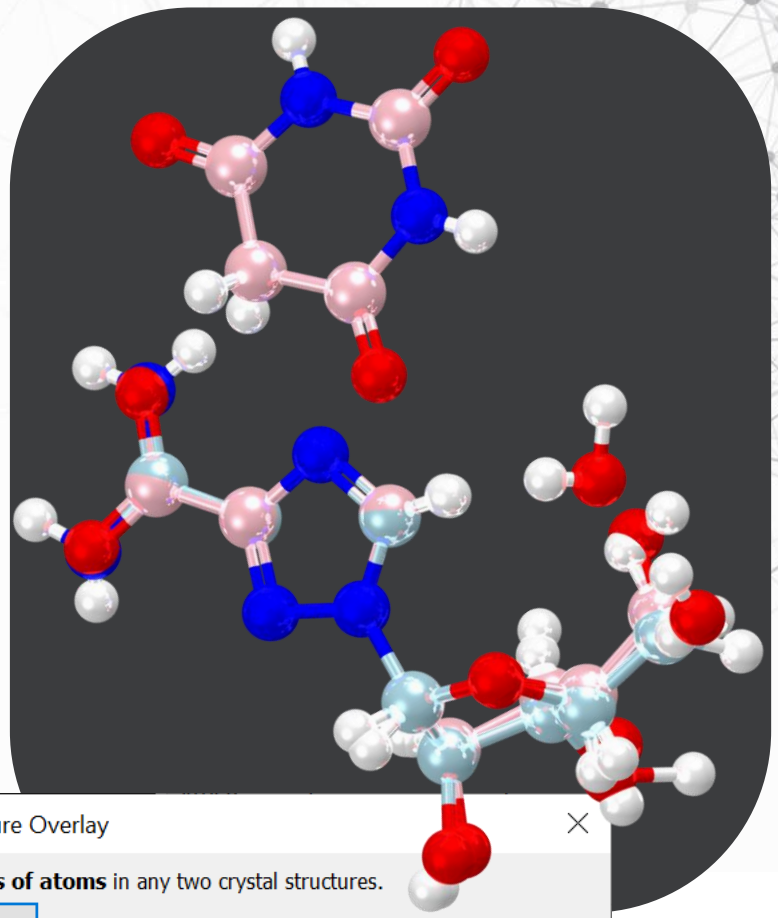
Tick Multiple structures to load more than one structure

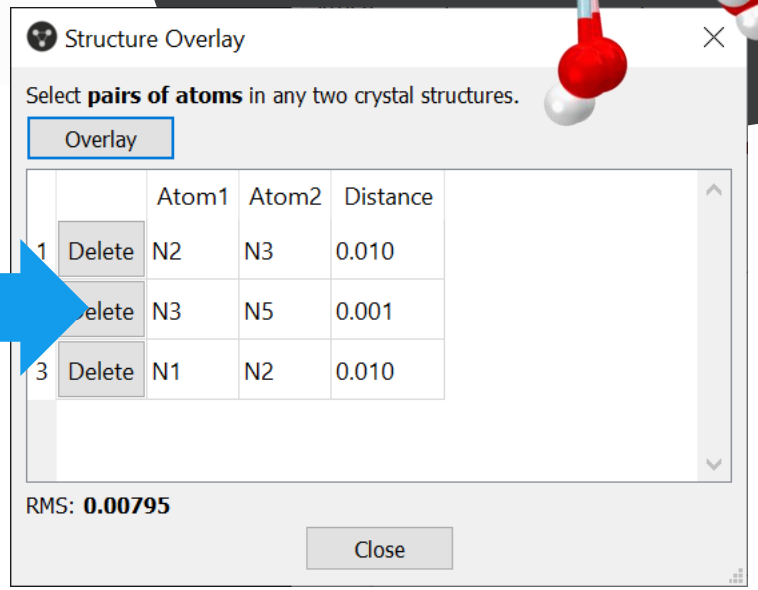
CSD Refcodes: VIRAZL, FOQROU (light blue – pink)

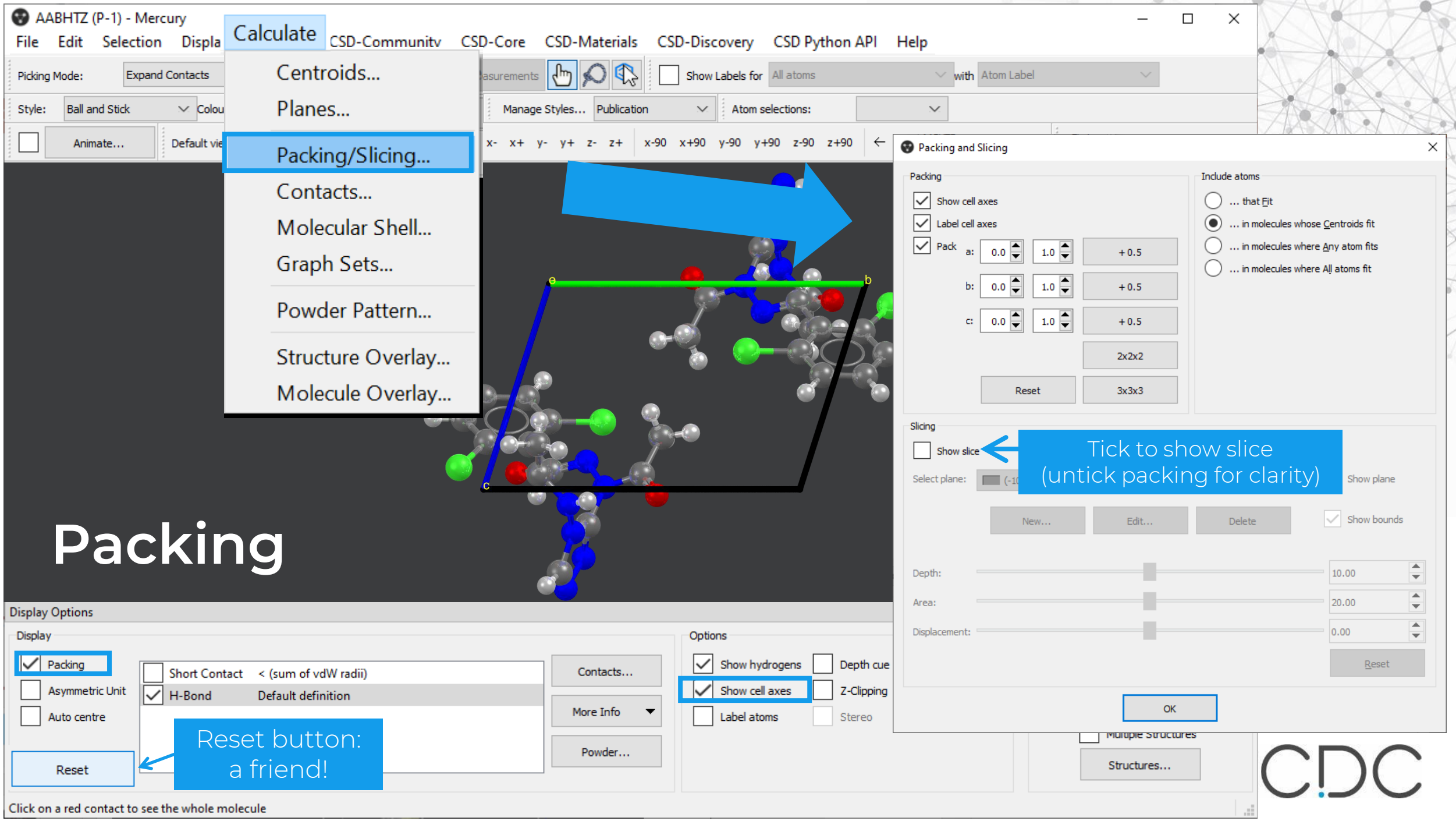






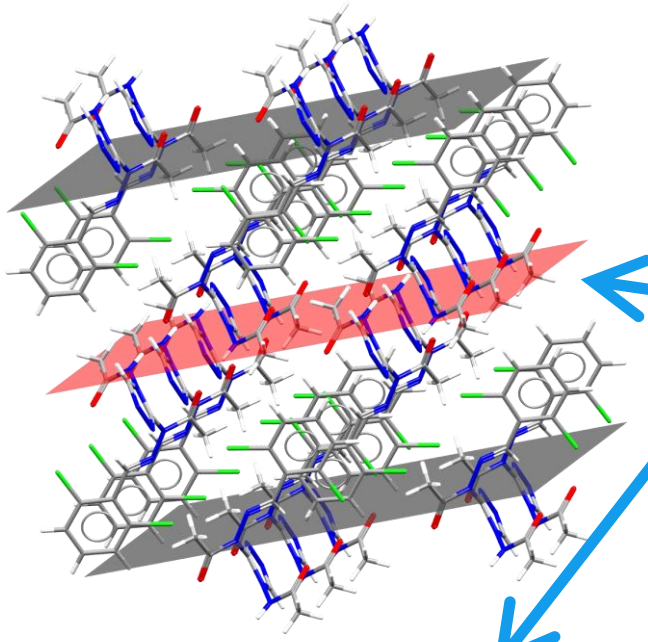


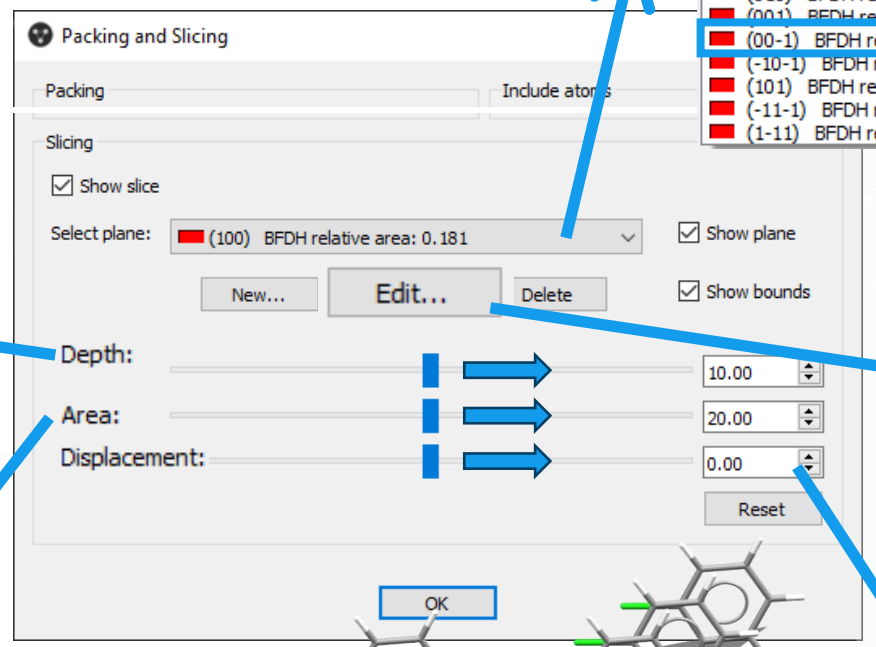


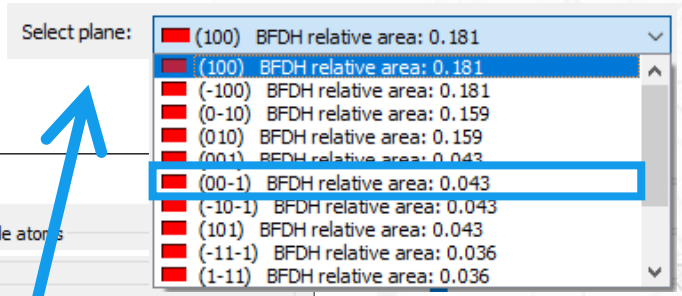

AABHTZ (P-1) - Mercury
File Edit Selection Displa
Calculate
CSD-Community CSD-Core CSD-Materials CSD-Discovery CSD Python API Help
Centroids...
Planes...
Packing/Slicing...
Contacts...
Molecular Shell...
Graph Sets...
Powder Pattern...
Structure Overlay...
Molecule Overlay...
Picking Mode: Expand Contacts
Show Labels for All atoms with Atom Label
Style: Ball and Stick
Manage Styles... Publication
Atom selections:
Animate...
Packing
Packing and Slicing
Packing
Show cell axes
Label cell axes
Pack
Include atoms
... that Fit
... in molecules whose Centroids fit
... in molecules where Any atom fits
... in molecules where All atoms fit
Reset
3x3x3
2x2x2
Slicing
Show slice
Tick to show slice
(untick packing for clarity)
Select plane:
Show plane
New...
Edit...
Delete
Show bounds
Depth:
Area:
Displacement:
OK
Display Options
Display
Packing
Asymmetric Unit
Auto centre
Short Contact < (sum of vdW radii)
H-Bond Default definition
Reset
Reset button:
a friend!
Contacts...
More Info
Powder...
Options
Show hydrogens
Depth cue
Show cell axes
Z-Clipping
Label atoms
Stereo
Structures...
Click on a red contact to see the whole molecule

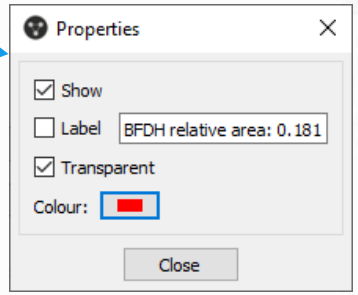
Packing

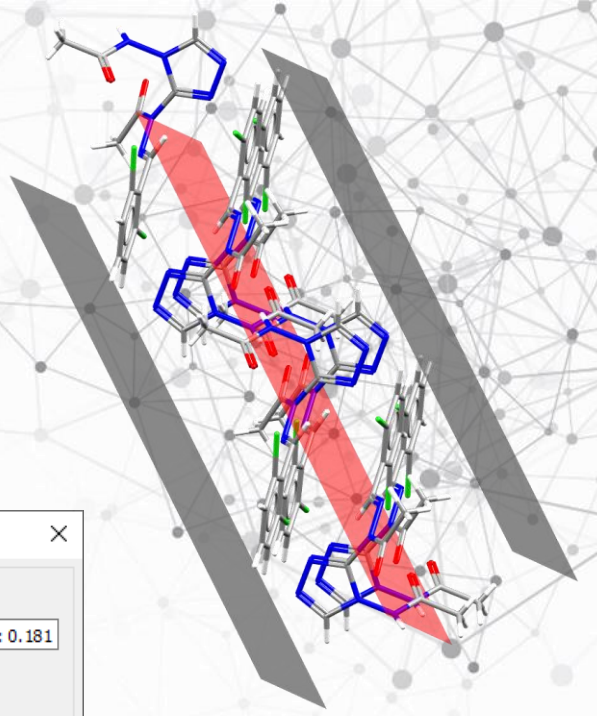
Slicing

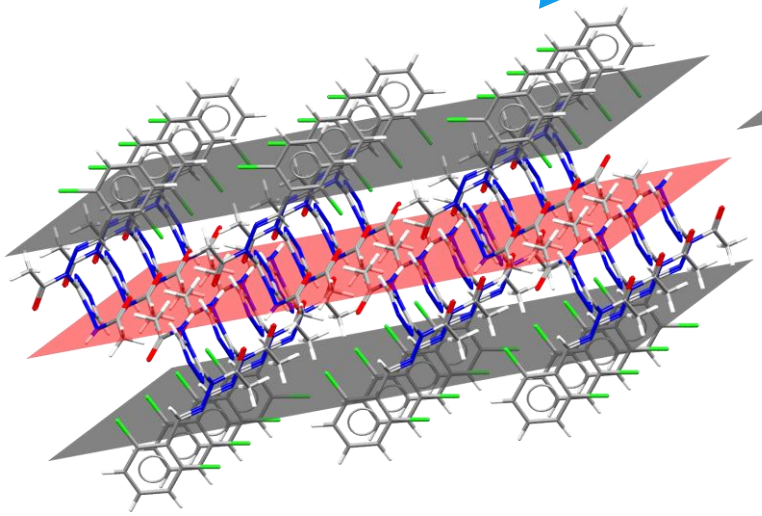


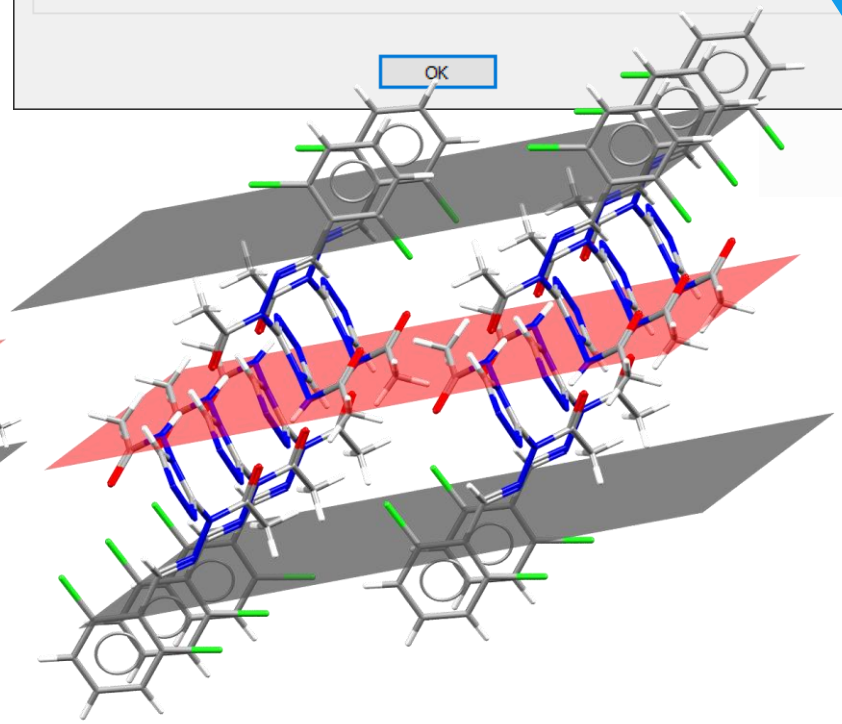


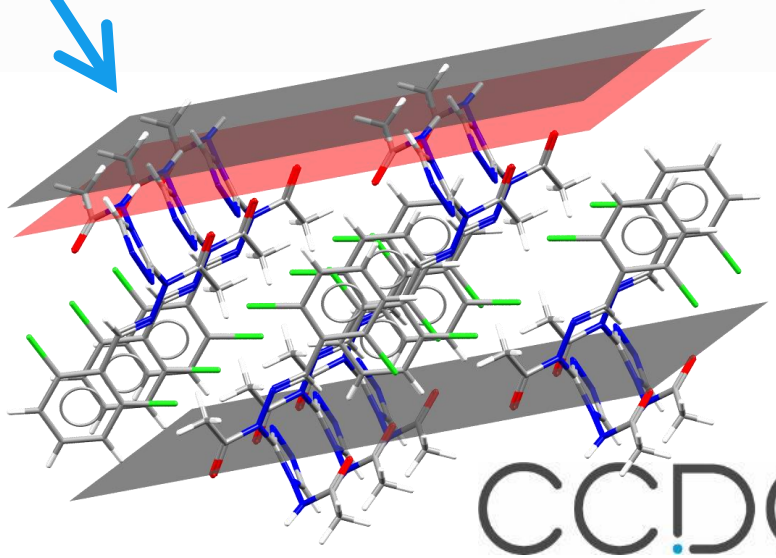






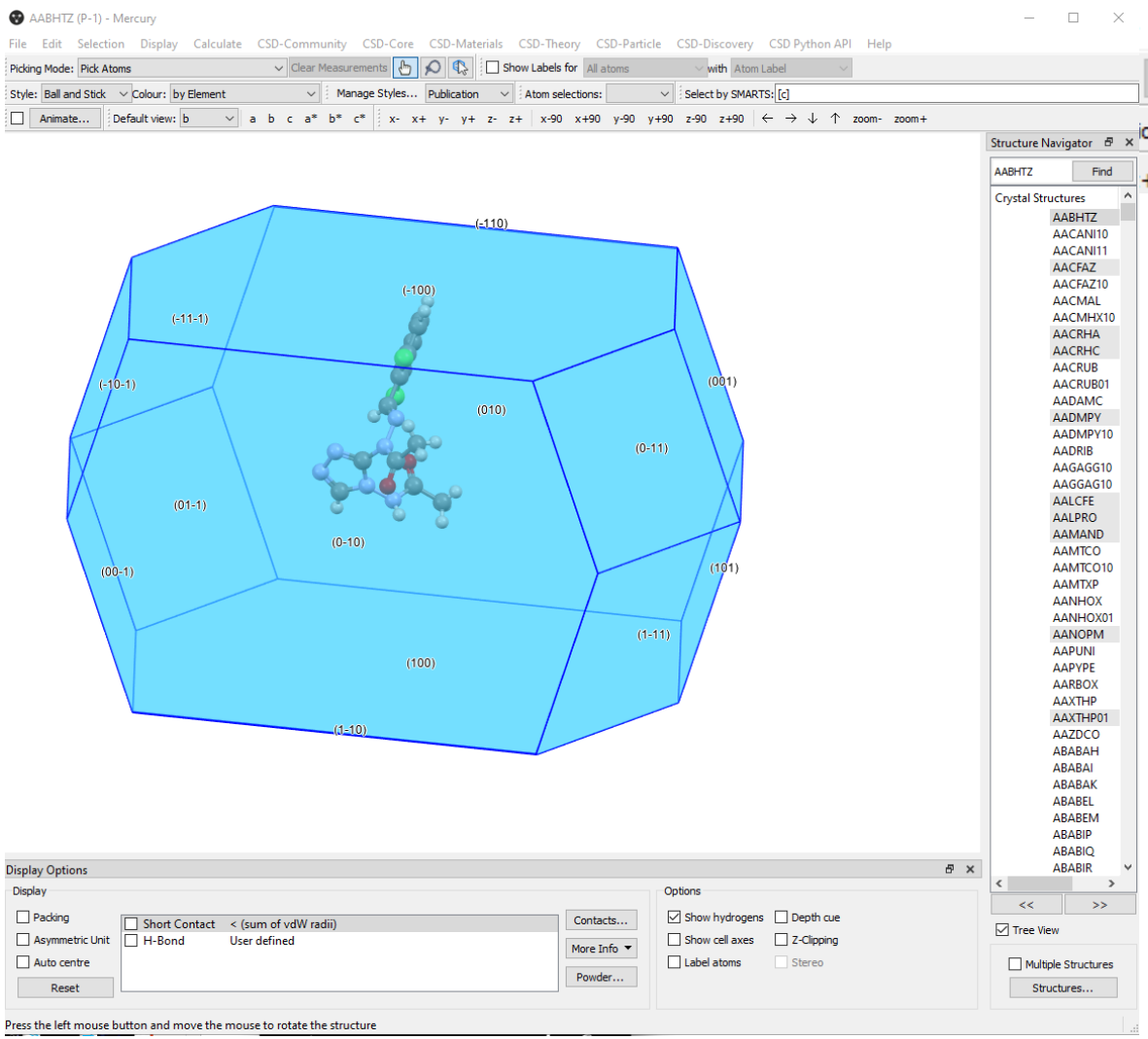


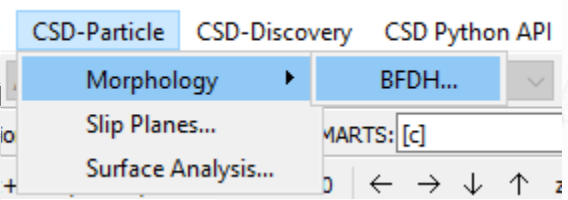




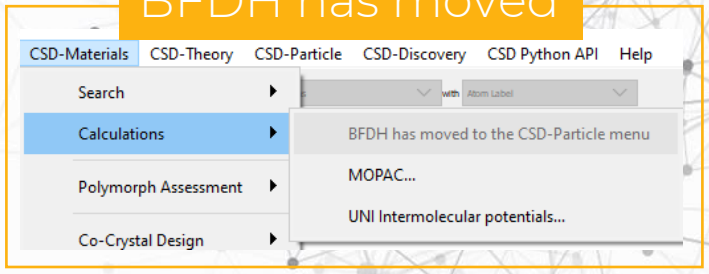
CCDC

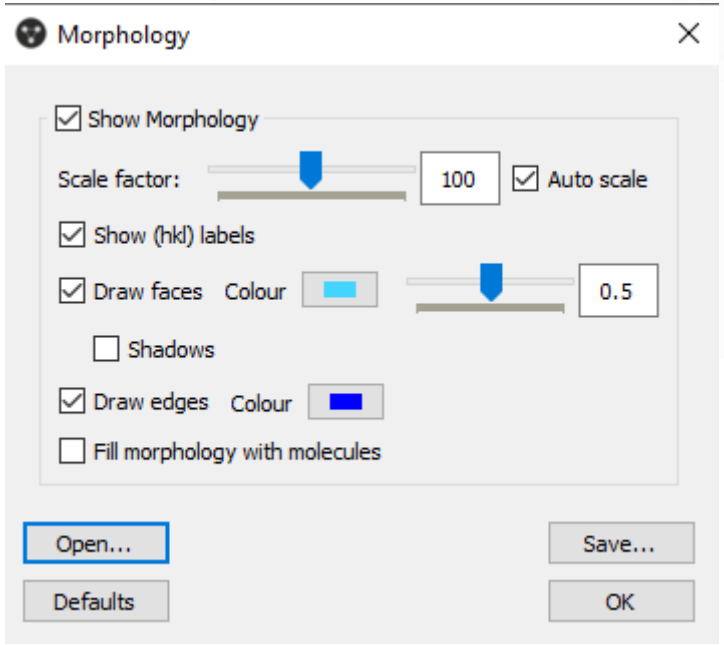
A reminder: BFDH Morphology





BFDH has moved



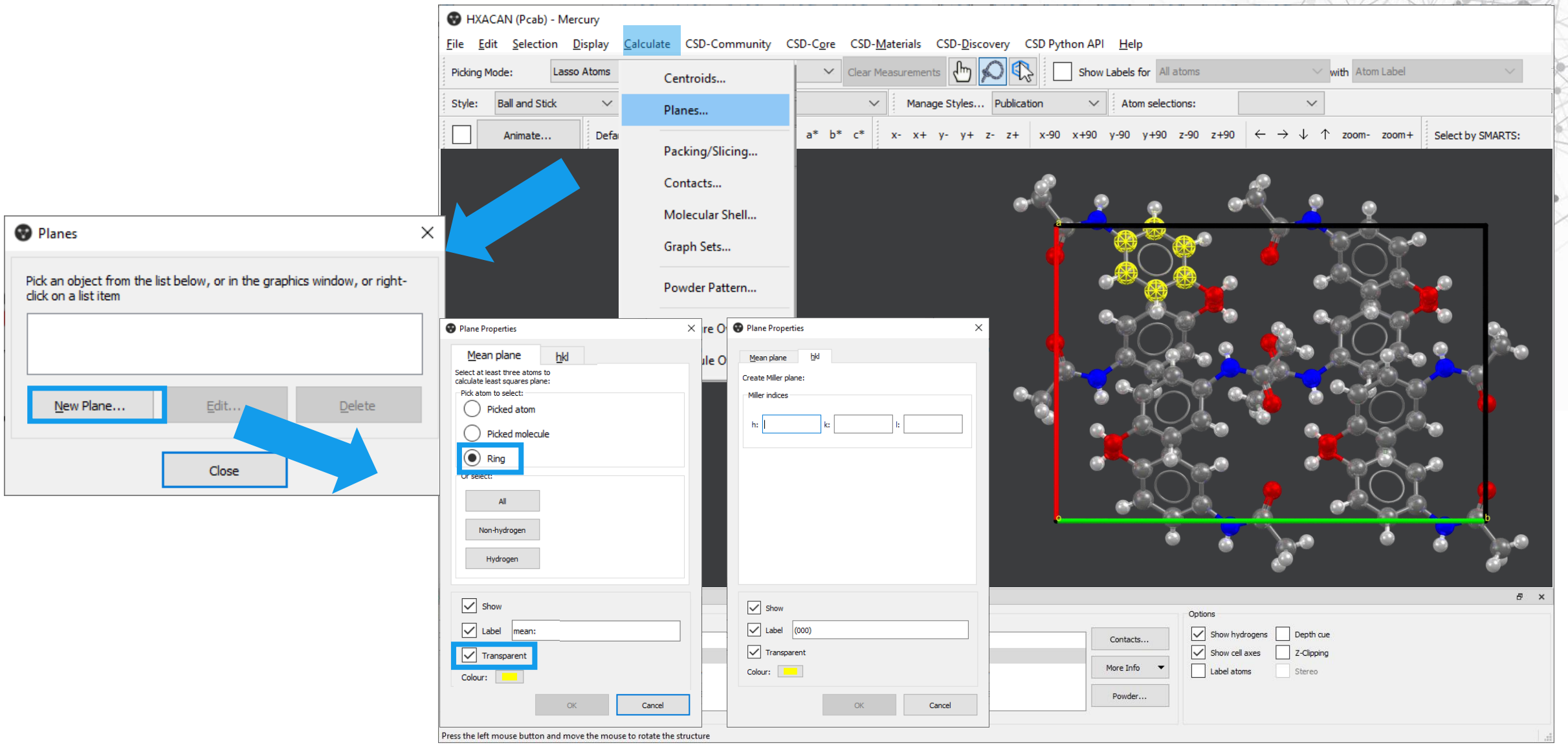


Display Options

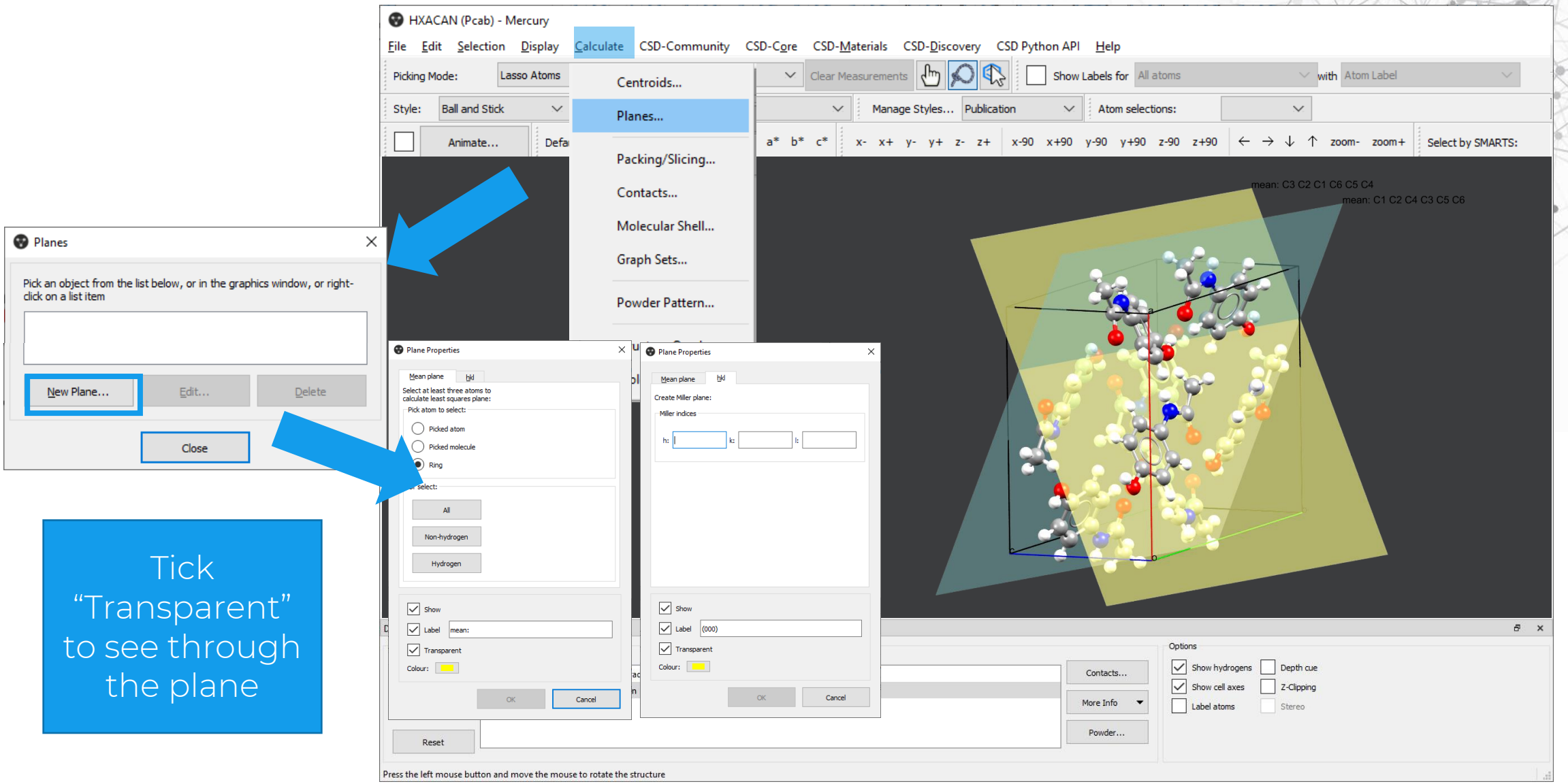
Save and Load

CCDC

Calculating planes



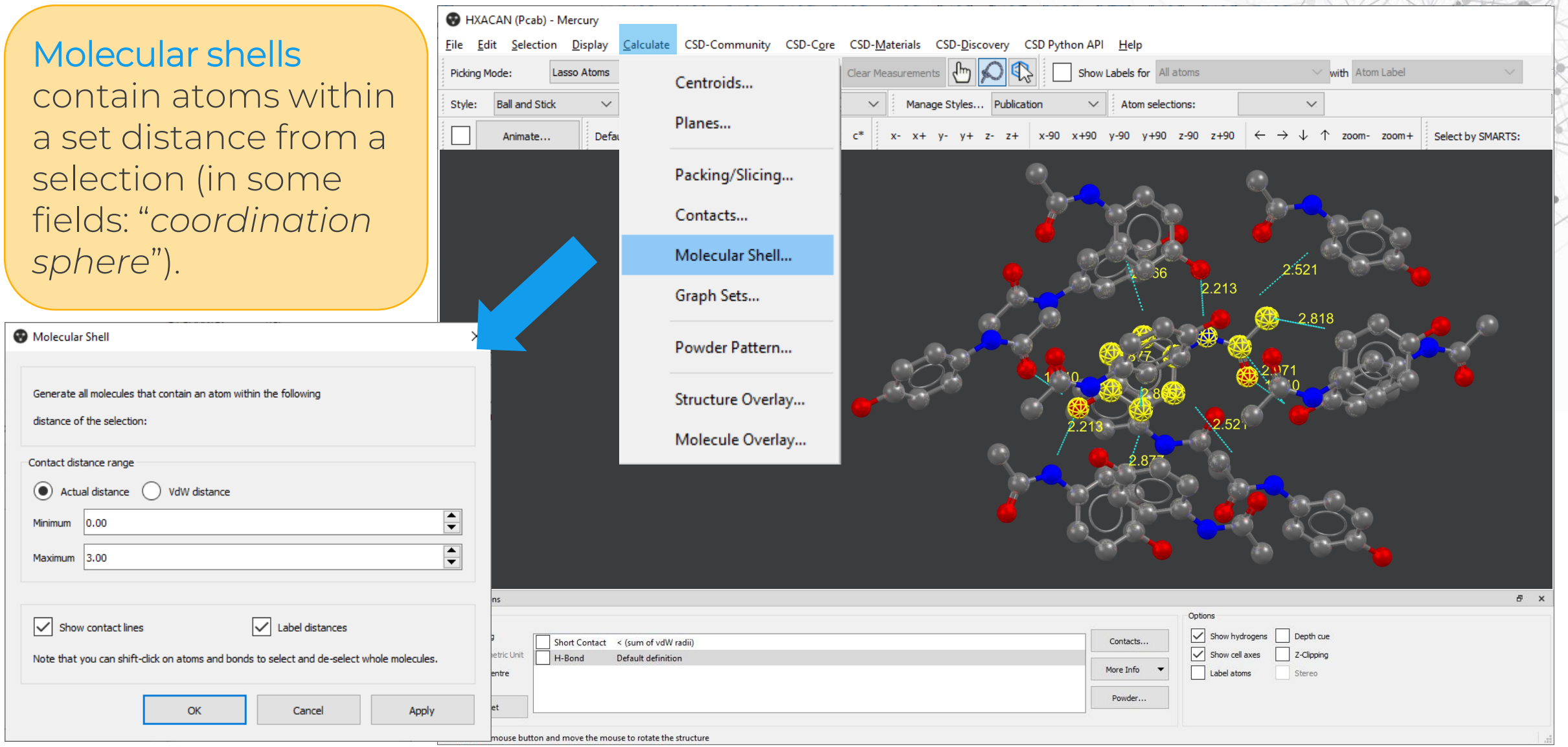
Calculating planes



Tick "Transparent" to see through the plane

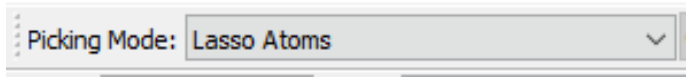
Exploring Molecular Shells

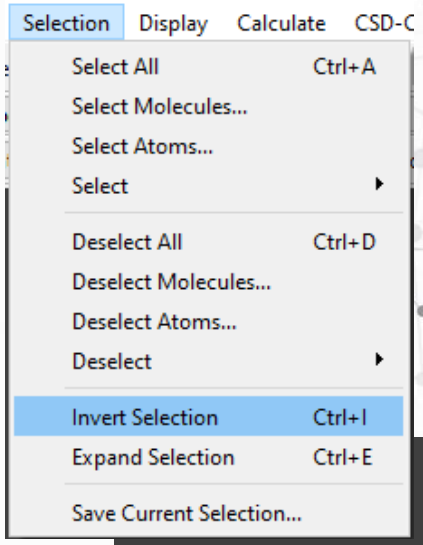
Molecular shells contain atoms within a set distance from a selection (in some fields: "*coordination sphere*").

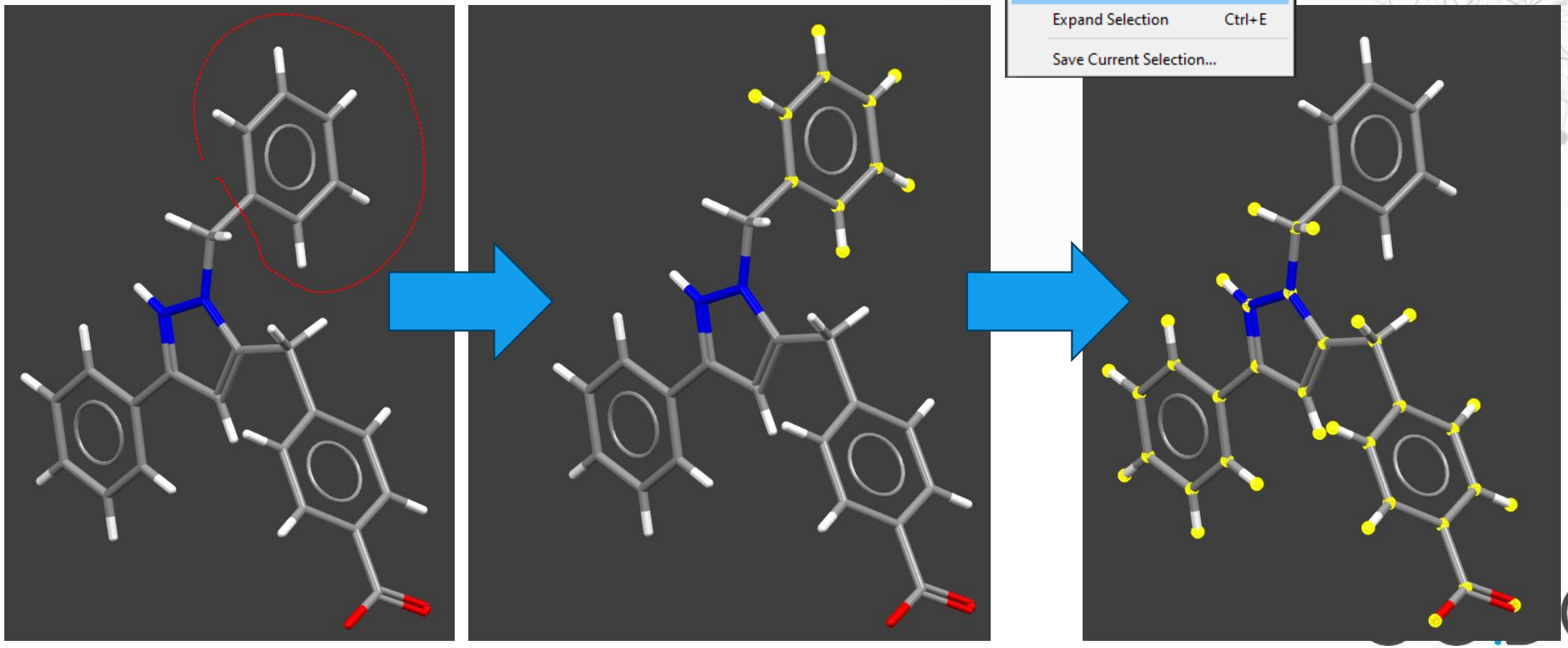


Select tips

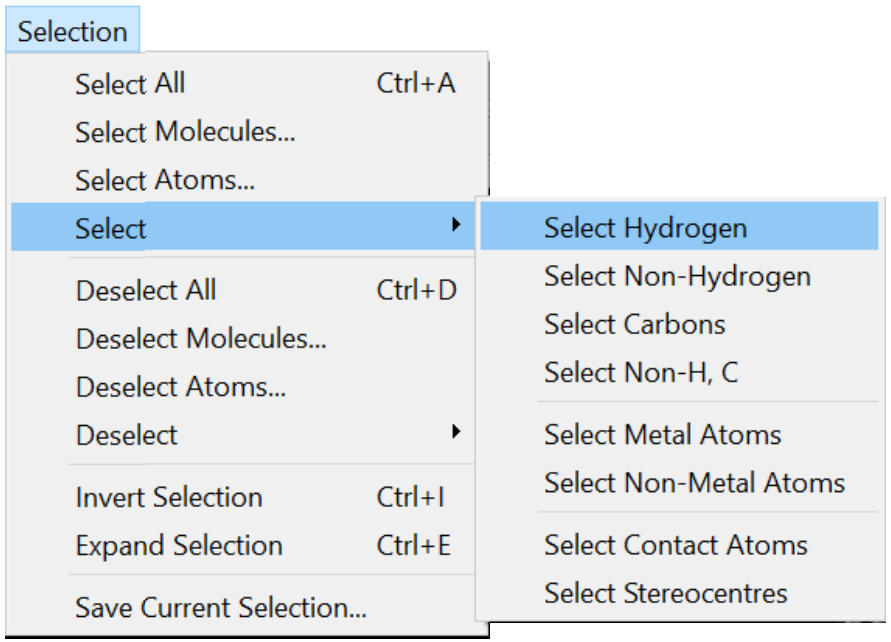
CSD Refcode
FOQQOT

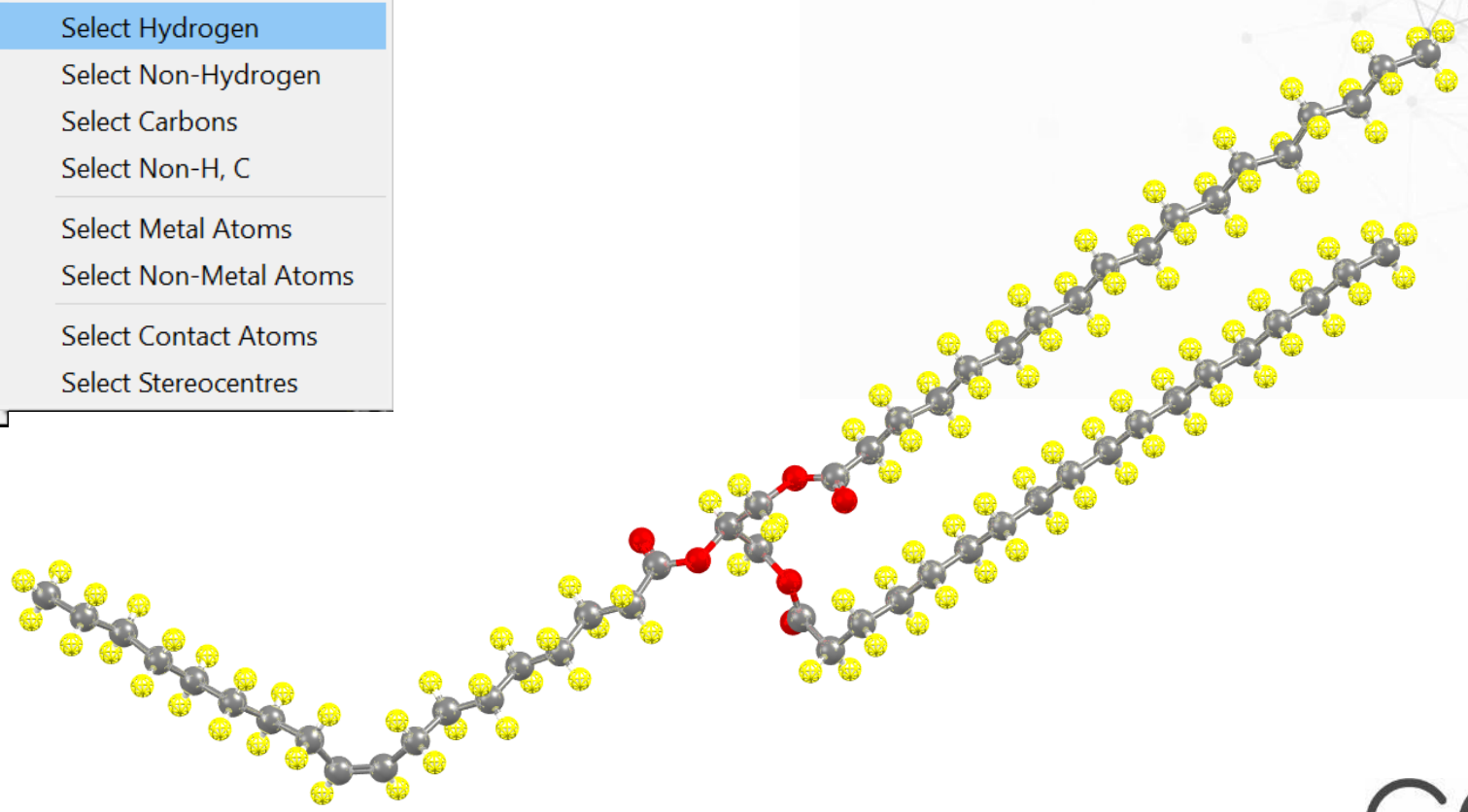




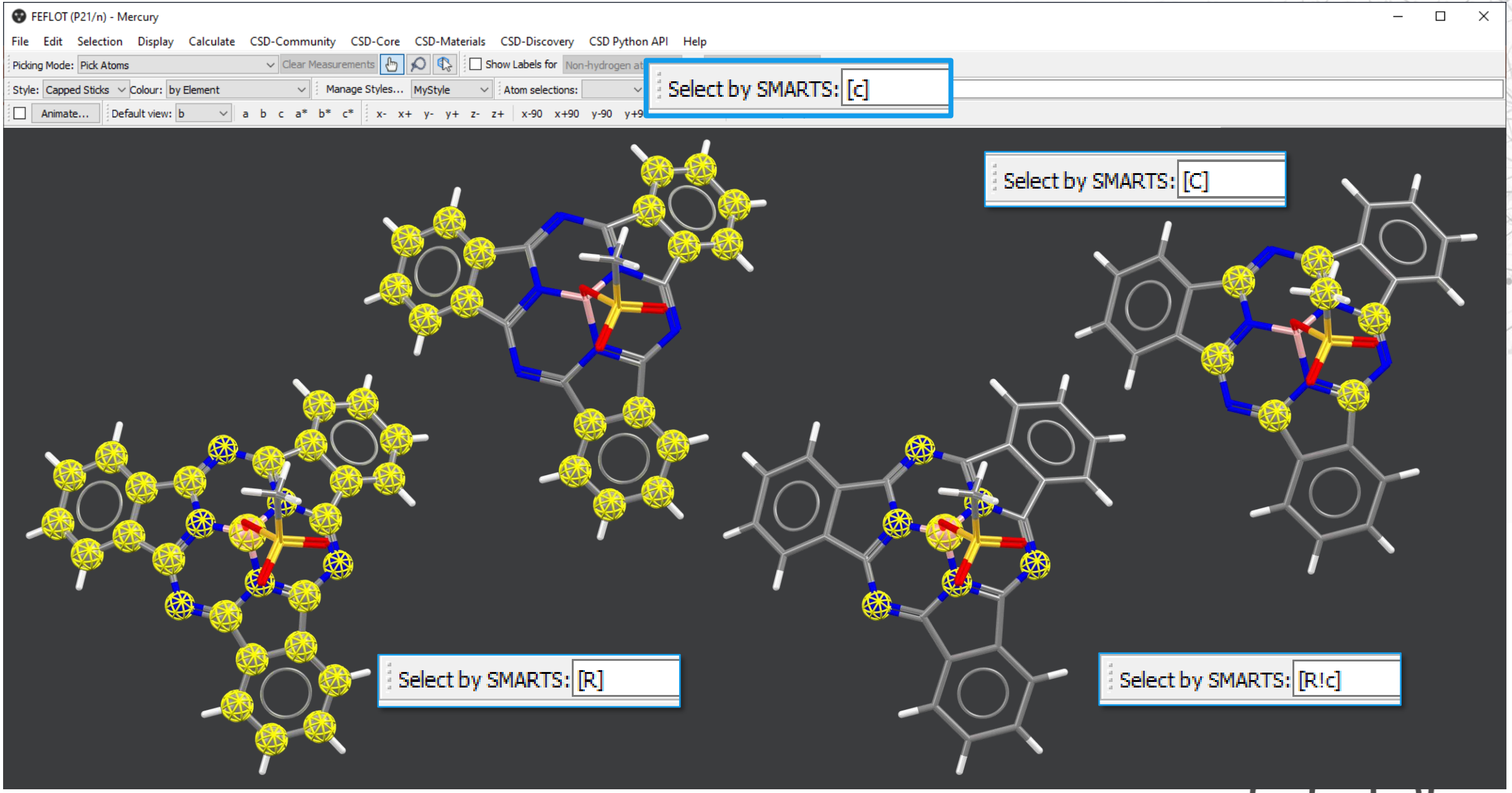


Select Tips





CCDC


FEFLOT (P21/n) - Mercury
File Edit Selection Display Calculate CSD-Community CSD-Core CSD-Materials CSD-Discovery CSD Python API Help
Picking Mode: Pick Atoms
Clear Measurements
Show Labels for
Style: Capped Sticks
Colour: by Element
Manage Styles...
MyStyle
Atom selections:
Animate...
Default view: b
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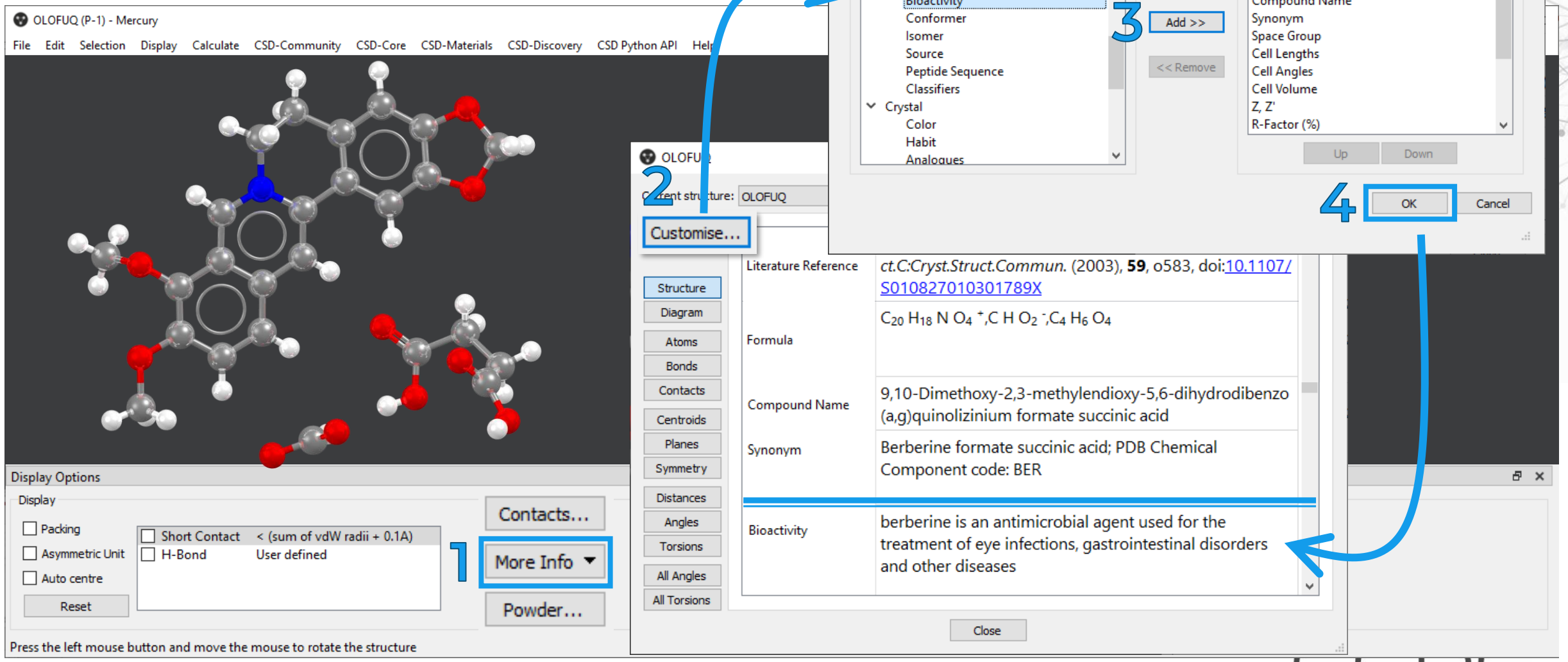
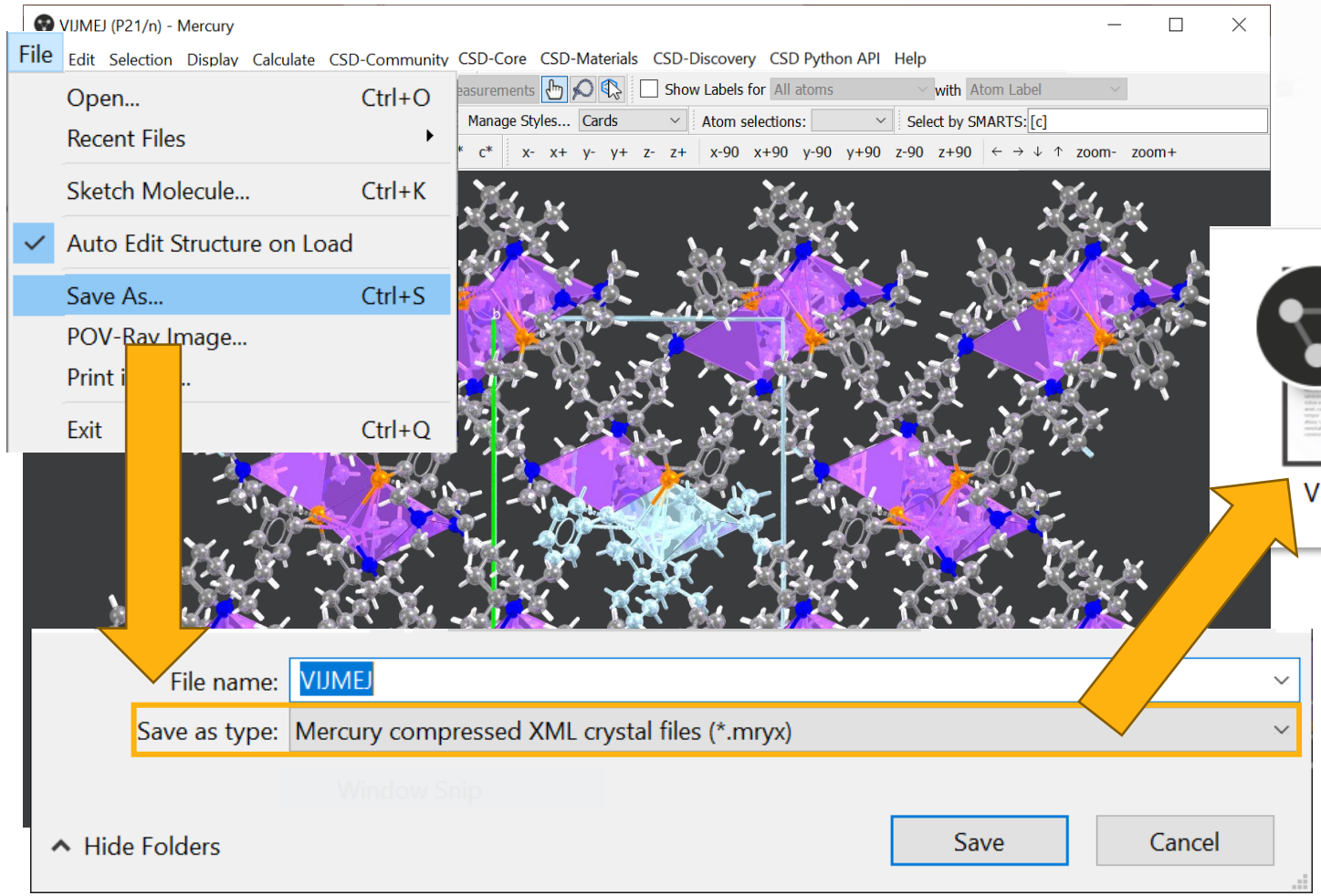
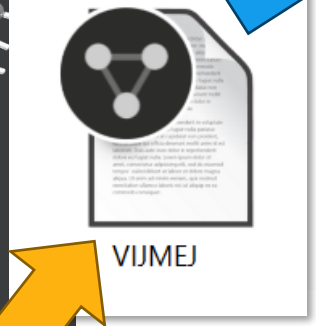
Select by SMARTS: [R!c]

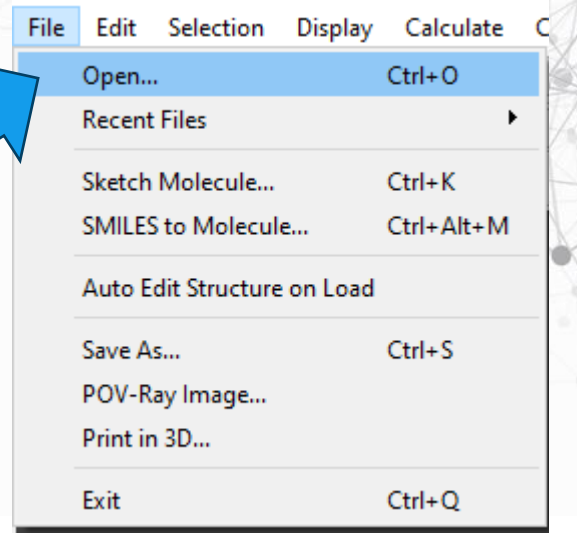
Missing information?



Save your current display







... and reopen it later!

CCDC

CSD-Conformer Generator

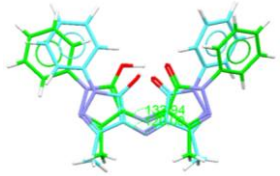
Mogul can display distributions of important molecular geometries based on the bond lengths, angles, ring geometries, and torsions of the expertly curated structures in the CSD.

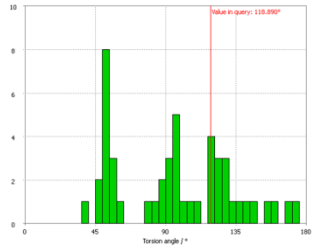
- Part of CSD-Discovery, CSD-Materials and CSD-Enterprise suites
- The starting point are Mogul data libraries with some changes and improvements to tailor them to conformer generation
- 2022.1 release of Conformer Generator version: improved handling of flexible ring systems
    - Using Mogul templates for isolated, fused, spiro-linked and bridged rings
    - If no template available, then generated on the fly with cyclic bond rotamer distributions
- Fast & chemically plausible conformations
- Initial optimisation step also useful to prepare compound libraries before virtual screening

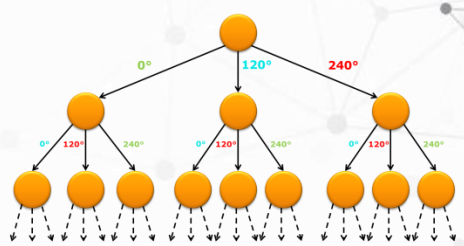
Knowledge-Based Conformer Generation Using the Cambridge Structural Database.
Cole J. C., *et al. J. Chem. Inf. Model.* (2018), **58**, 615-629.

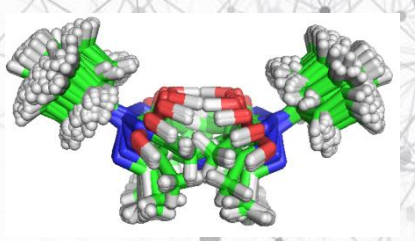
CCDC

CSD-Conformer Generator: Methodology

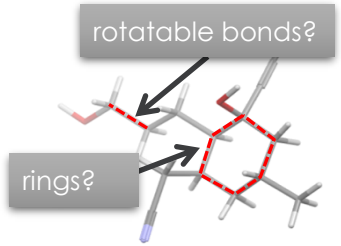


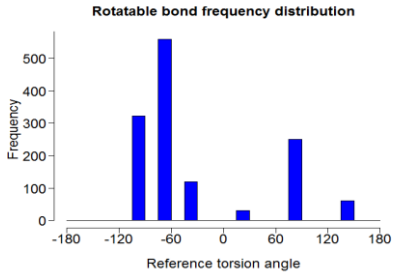


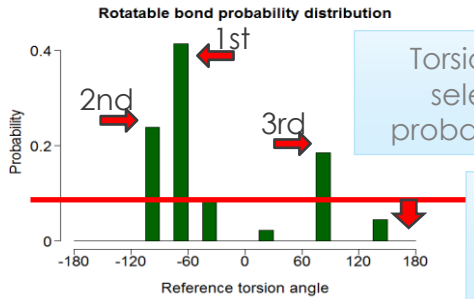




molecule → (optimise) → get rotamer and ring distributions → sample and score conformers → select diverse subset

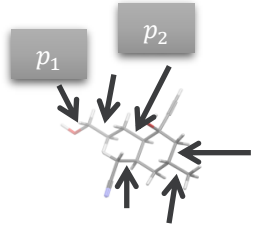






Torsion angles selected in probability order

Unusual threshold to reduce conf space



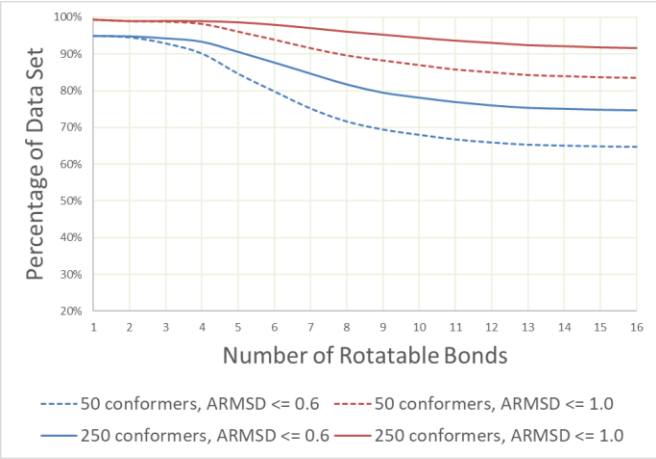
Overall conf prob (score) $p = p_1\, p_2 \cdots p_n$

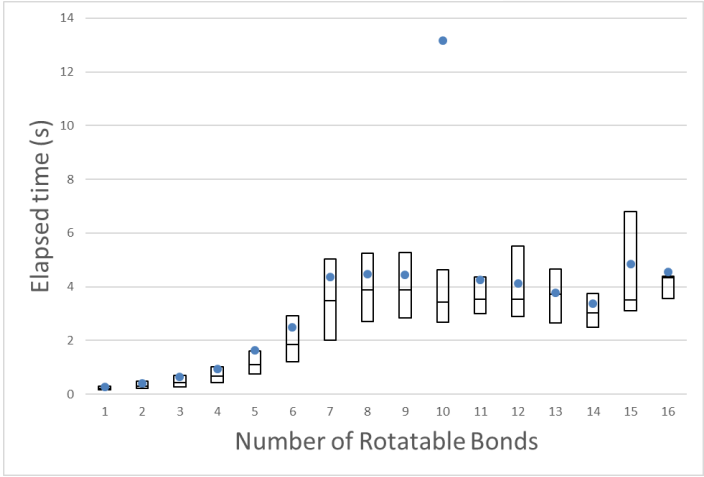
CCDC

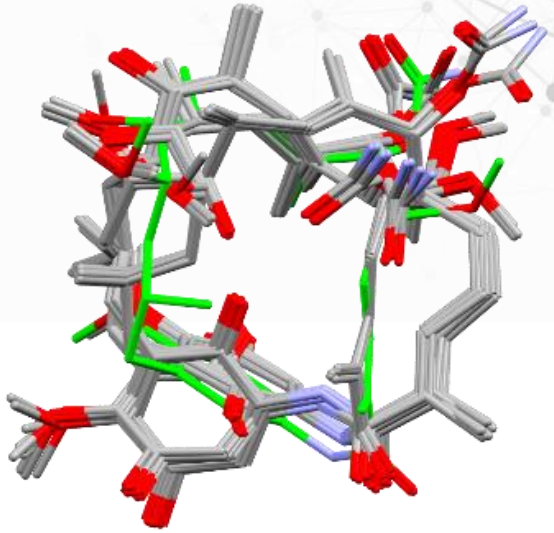
CSD-Conformer Generator: Latest validation

- Performance evaluated against the Platinum* diverse data set → get fast & chemically plausible conformations

	Top n conformers		
n	1	50	250
least ARMSD < 0.5 Å (%)	18	57	66
least ARMSD < 1.0 Å (%)	39	84	92
mean ARMSD		0.59	0.48



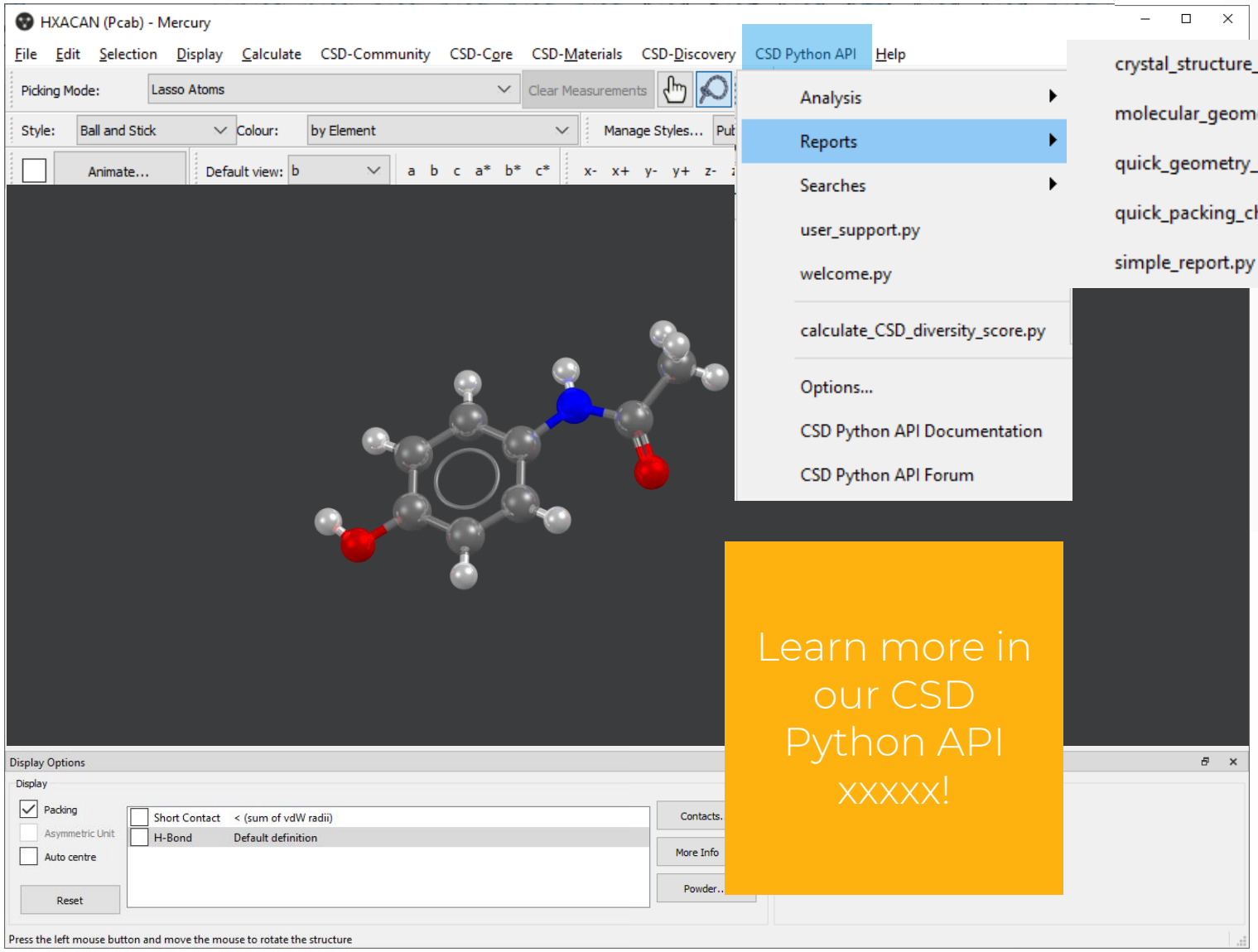




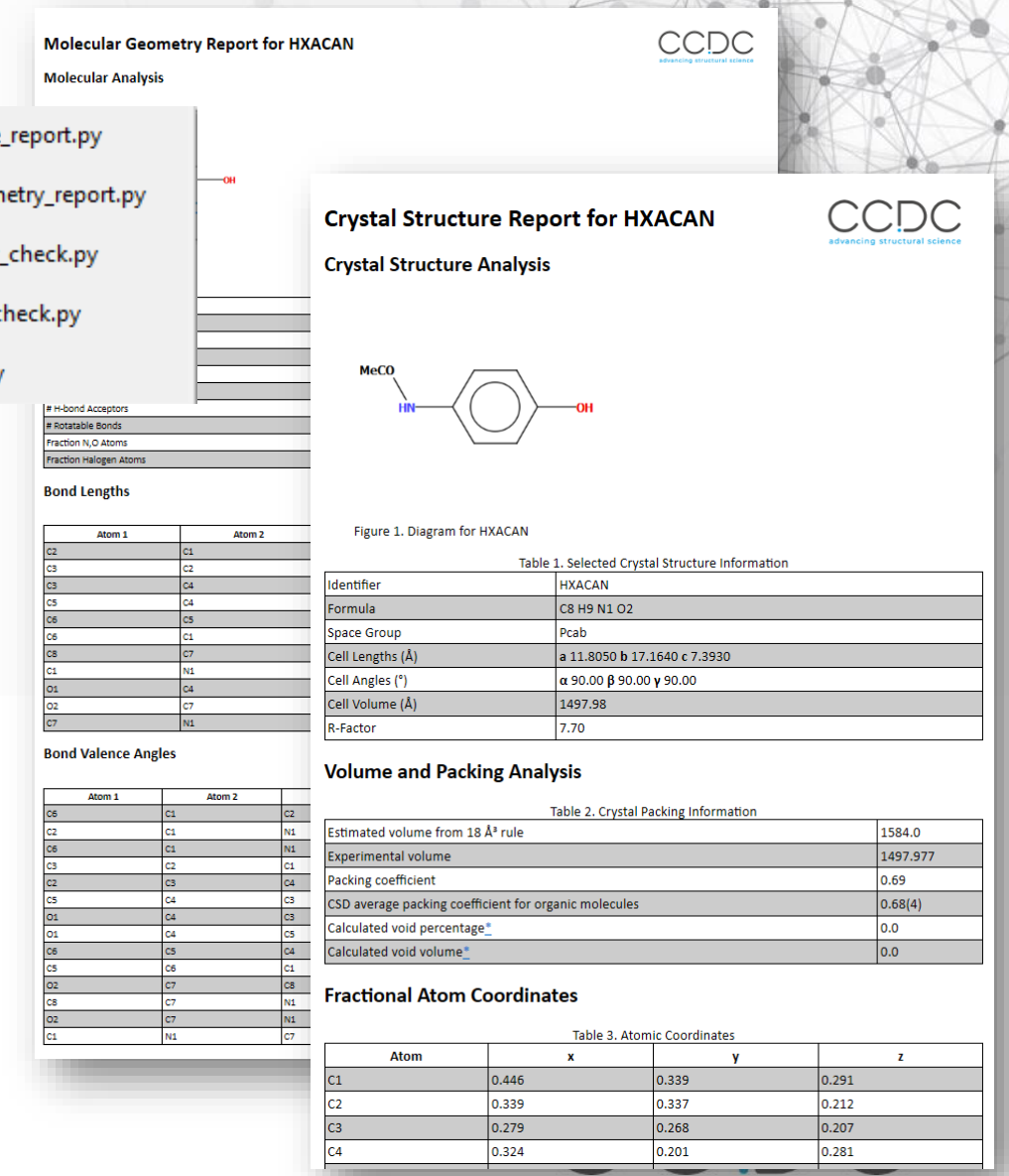
Geldanamycin, 19 atoms in ring (PDB 3C11): top 50 conformers, least AMRSD = 0.95 Å

Benchmarking Commercial Conformer Ensemble Generators
Friedrich N.-O., *et al. J. Chem. Inf. Model.* (2017), **57**, 2719–2728.

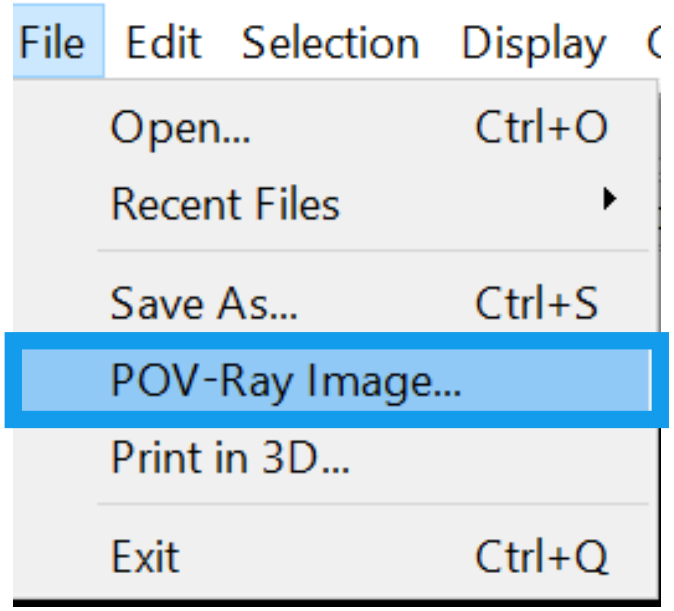
No Coding? No problem!

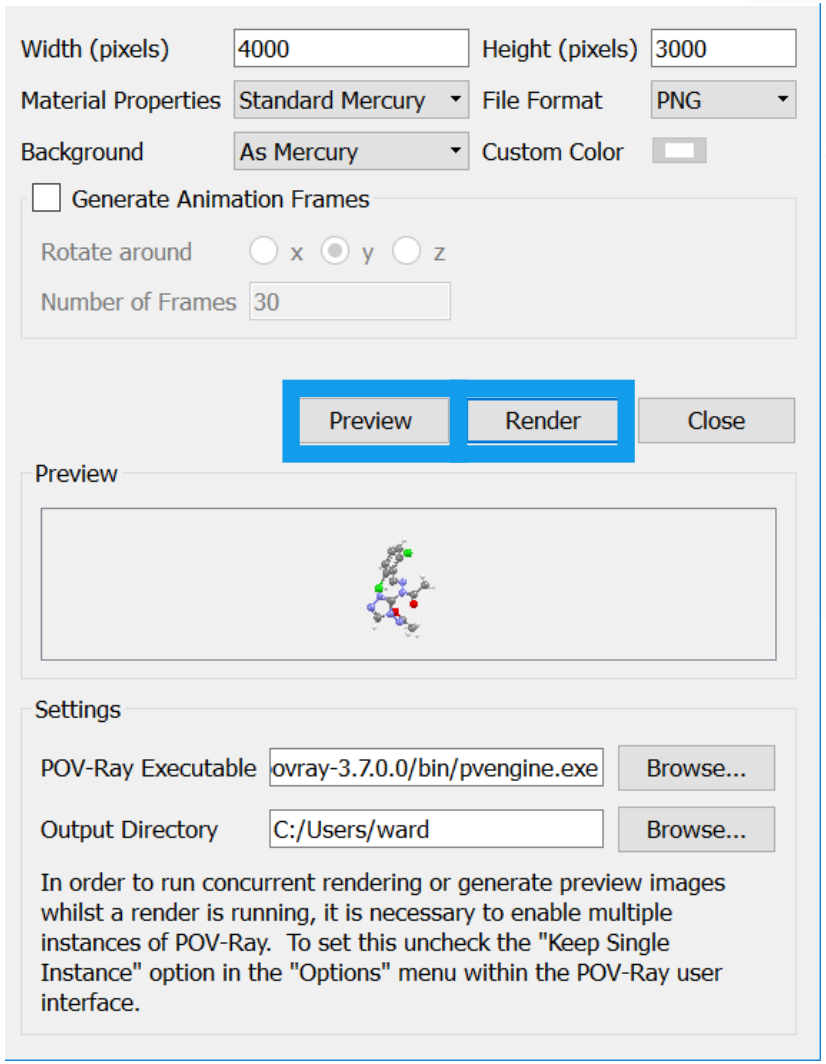


Learn more in our CSD Python API xxxxx!



Generating high quality images





File > POV-Ray Image

Change Resolution

Width = 4000

Height = 3000

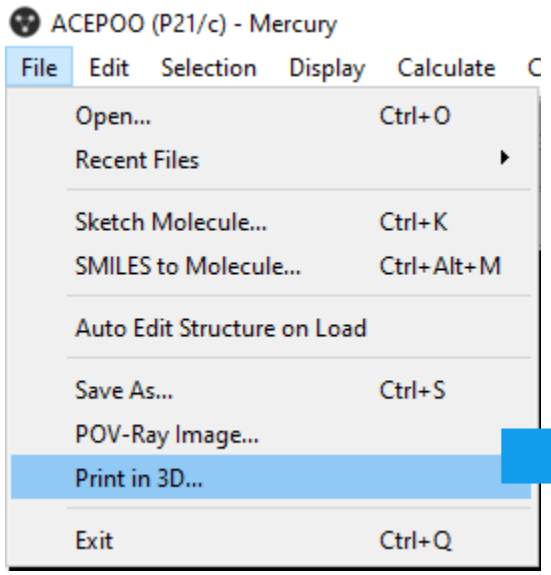
Change ‘Material Properties’ to ‘Metallic’

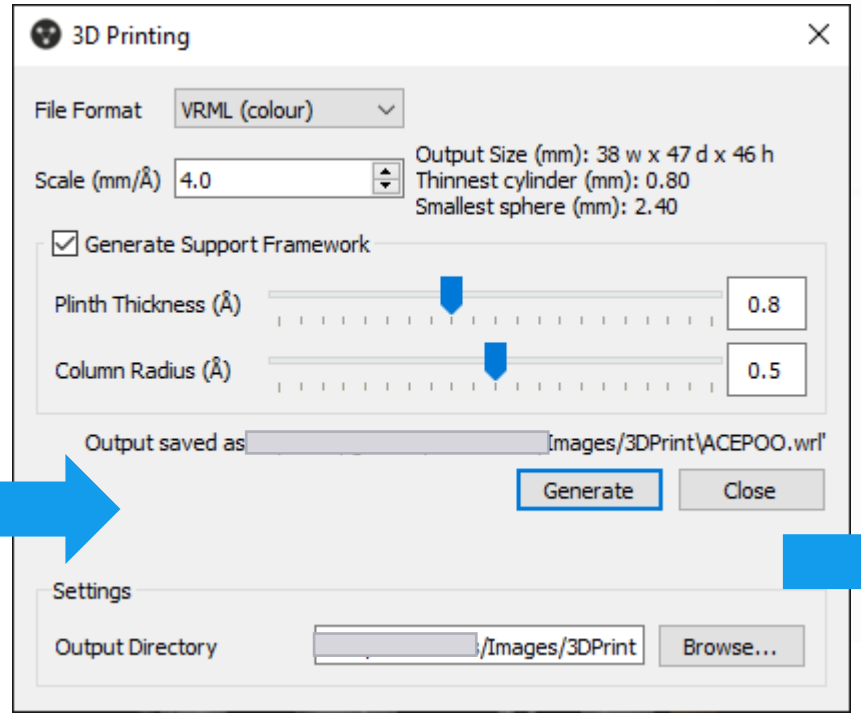
Set ‘Background’ to ‘Transparent’

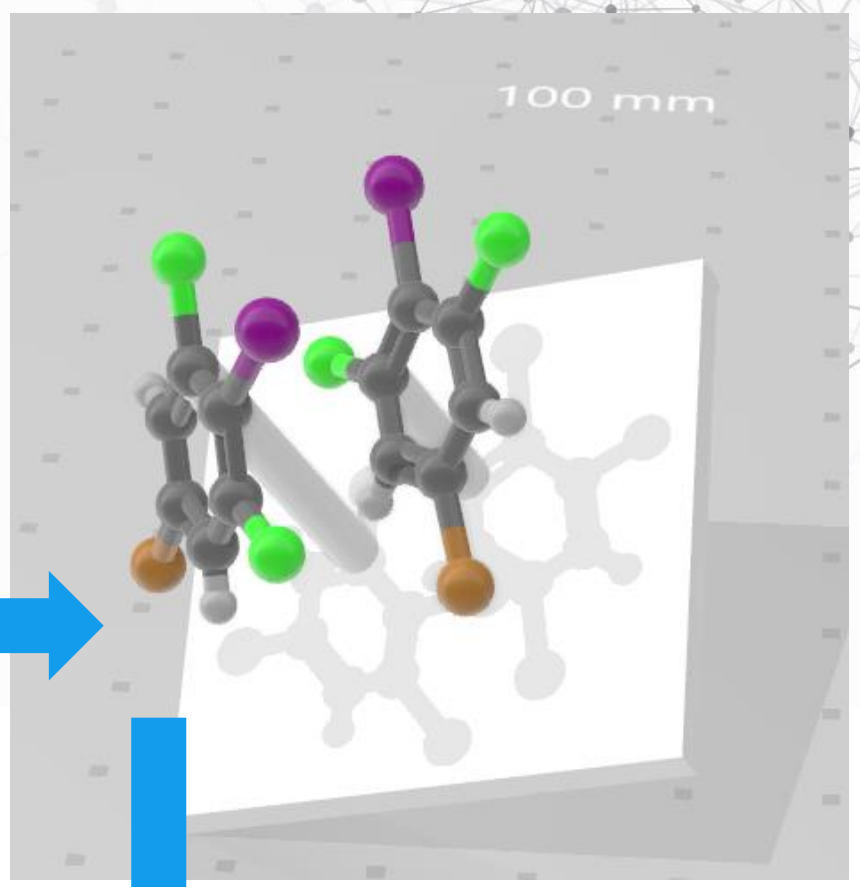
Press ‘Preview’

CCDC

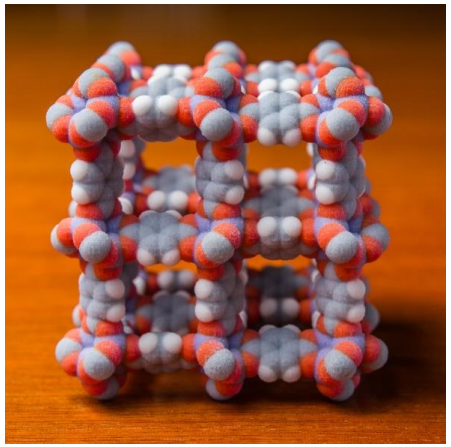
3D printing







Print with your 3D printer
or at a 3D printing service!

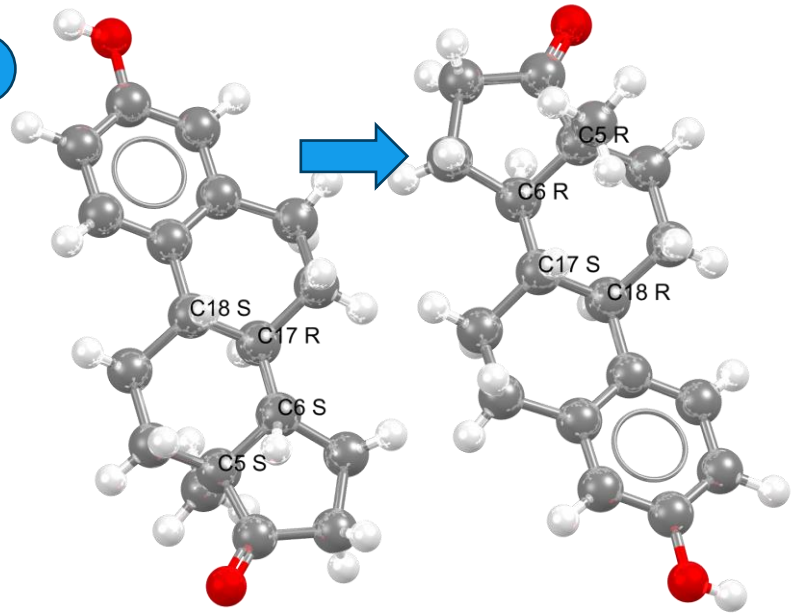


Example of 3D printed structure of
CSD Refcode SAHYIK

CCDC

Advanced Edit Features

3



Edit | Selection | Display | Calculate | CSD-Commu

Undo: Not Available Ctrl+Z
Redo: Not Available Ctrl+Y

Copy Image to Clipboard Ctrl+C

Edit Structure...
Auto Edit Structure...
Edit Bond Distance Limits...
Normalise Hydrogens...
Polymer Expansion...

1 Transform Molecules...
2 Change Spacegroup Setting...
3 Invert Structure
4 Change Spacegroup to Subgroup...

1

Transform Molecules

Active Structure: FAZHET01

Transform | Copy | Close

Symmetry Operators

Choose an operator below and click Transform to move all molecule(s), or click Copy to create a transformed copy of all molecule(s). Or select an atom in one or more molecules to apply the transformation to those particular molecules.

Crystal Symmetry Operators | Inversion & Translation

x,y,z
1/2-x,-y,1/2+z
-x,1/2+y,1/2-z
1/2+x,1/2-y,-z

Unit Cell Translations

a 0 b 0 c 0 Reset to Zero

Reset unit cell translations to zero automatically after copying or transforming

2

Change Spacegroup Setting

Entry: FACROQ

Space group Setting: 1: Hexagonal Axes (R-3)

1: Hexagonal Axes (R-3)
2: Rhombohedral Axes (R-3)

Standardise | OK | Cancel

4

Change Spacegroup to Subgroup

Entry: ESTRON10

Current Spacegroup: P 2_1 2_1 2_1 (19) setting 1

Available Subgroups: P 1 1 21 (4) setting 2 [1/4,0,0]

P 1 1 21 (4) setting 2 [1/4,0,0]
P 21 (4) setting 1 [0,0,1/4]
P 21 1 1 (4) setting 3 [0,1/4,0]

OK | Close | Apply

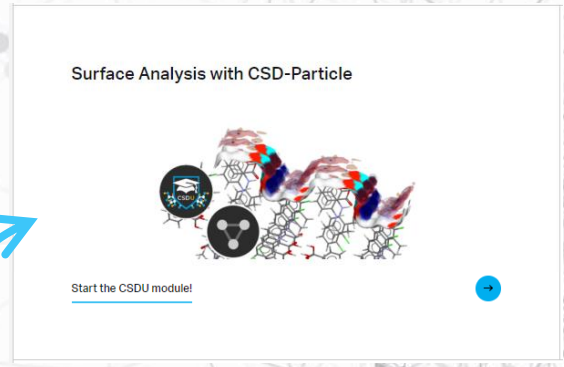
Want to explore more?

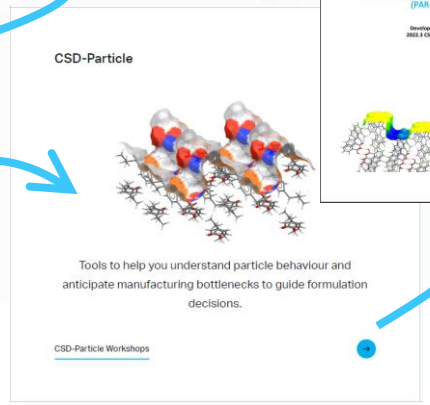
On-demand training resources

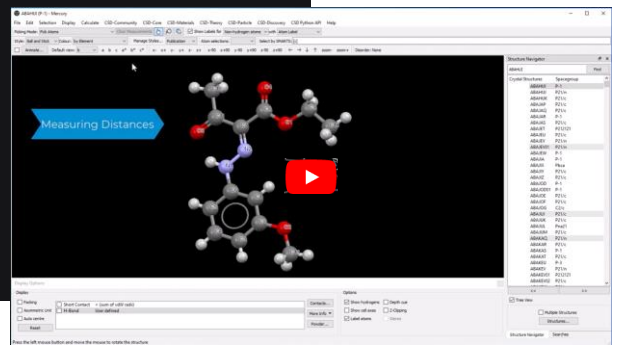
Solutions | Community | Discover | Consultancy

- Access/Deposit Structures
- CCDC for the Community
- Education and Outreach
- Events
- Free Products
- Training and Learning

- Free Online Courses
- Self-Guided Workshops
- Training and Support Videos







CCDC

Free online training courses

With completion certificates!

CSDU

On-demand modules to learn how to use the CSD software at your own pace.

UWatch — UTry — UTest

Mercury

Python API

WebCSD

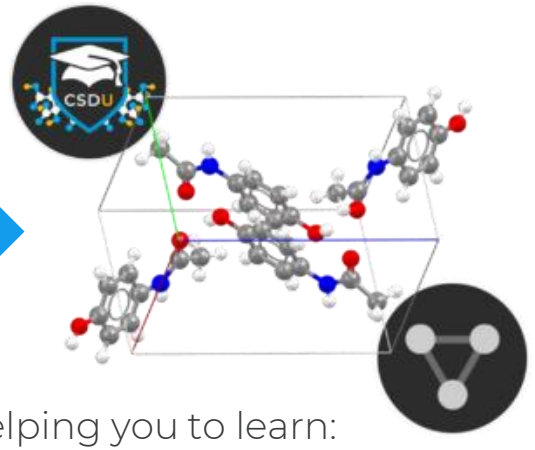
GOLD Docking

Mogul

FIMs

Particle

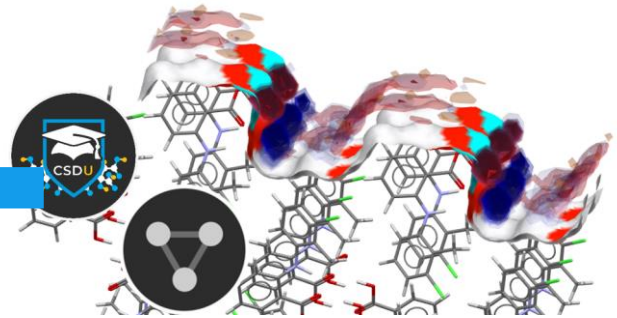
Visualization 101



Helping you to learn:

- The basics of Mercury software.
- How to explore and pack structures.
- How to create high resolution images.

Surface analysis



Helping you to learn:

- The basics of CSD-Particle.
- How to perform a surface analysis.
- How to visualise likely interactions with the surface using Full Interaction Maps (also a CSDU course!).

https://www.ccdc.cam.ac.uk/community/training-and-learning/csdu-modules/

Upcoming Virtual Workshops & Events

CCDC

VIRTUAL WORKSHOP

In-Depth Comparison of Polymorphic Structures Using Mercury

Tuesday, 14th May
10 am (BST)

REGISTER NOW

And more!!

CCDC

Innovation in Discovery Science

UGM 2024

Virtual
Thursday 9th May
9:30am-3:30pm BST

REGISTER TODAY

CCDC **discovery science** software users and non-users will collectively discuss the latest trends and advancements in the industry, including the rise of **AI and machine learning**.

Use cases will be presented and common challenges discussed.

https://www.ccdc.cam.ac.uk/community/events/

CCDC