How to visualise and analyse surfaces using Mercury

CCDC Virtual Workshop

Alex Moldovan, Ilaria Gimondi, Pietro Sacchi, Suzanna Ward, Andy Maloney

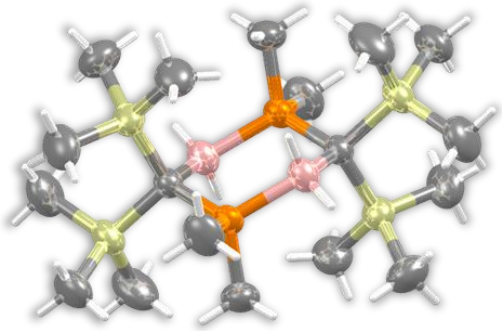
October 2022

CCDC
advancing structural science

Learning outcomes for today

- Learn how informatics and data-driven approaches can be used to understand particle properties.
- Familiarise yourself with what tools are available in the CSD-Particle suite and what they can be used to do.
- Learn how to use Surface Analysis and Slip Planes to identify key particle properties.

The Cambridge Structural Database



CSD Refcode ELOFUJ
The 1.1 millionth CSD structure
A *CSD Communication*
determined by Bill Clegg

- 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 57 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
43%

Metal-Organic
57%

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

Not Polymeric
89%

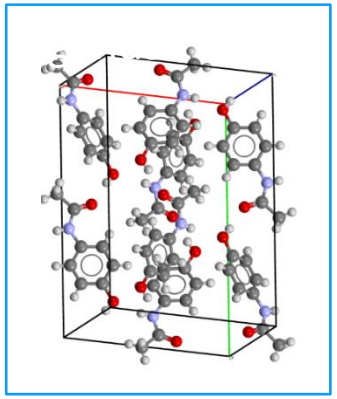
Polymeric: 11%

Single Component
56%

Multi Component
44%

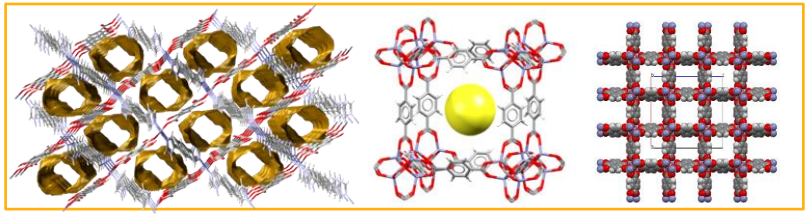
Organic

- Drugs
- Agrochemicals
- Pigments
- Explosives
- Protein ligands



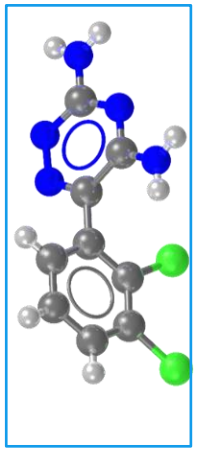
Metal-Organic

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



Additional data

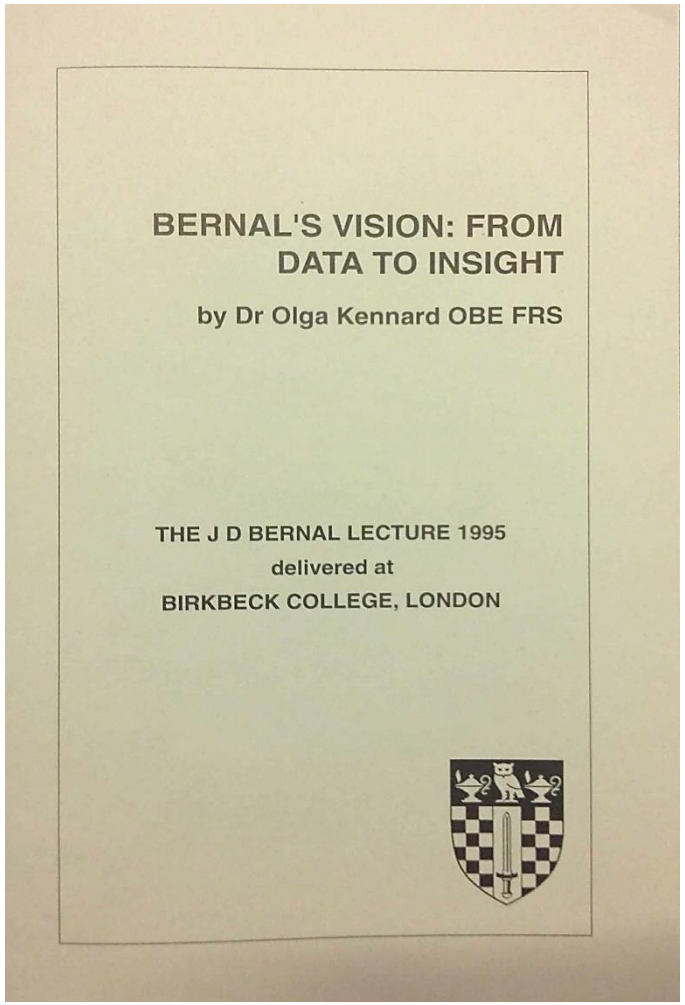
- 11,525 polymorph families
- 171,683 melting points
- 909,992 crystal colours
- 778,663 crystal shapes
- 24,916 bioactivity details
- 11,387 natural source data
- > 250,000 oxidation states



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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Software to gain new insights

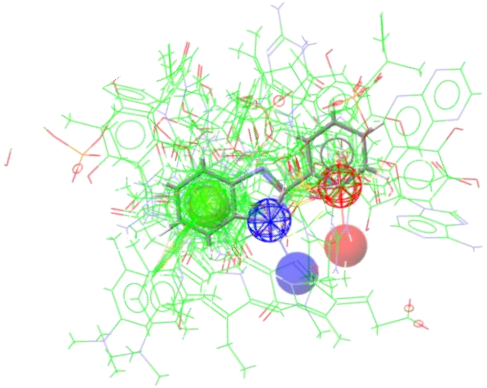
CSDCore.

Search, visualise, analyse and communicate structural data

Insights into molecular and crystal shape and interactions

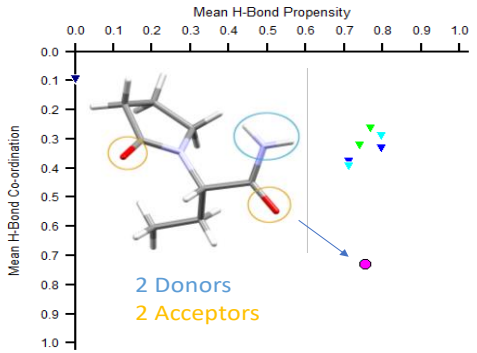
CSDDiscovery.

Design of new molecules



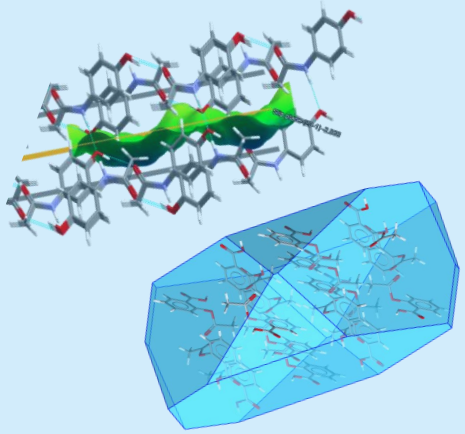
CSDMaterials.

Assessment of solid form stability and properties



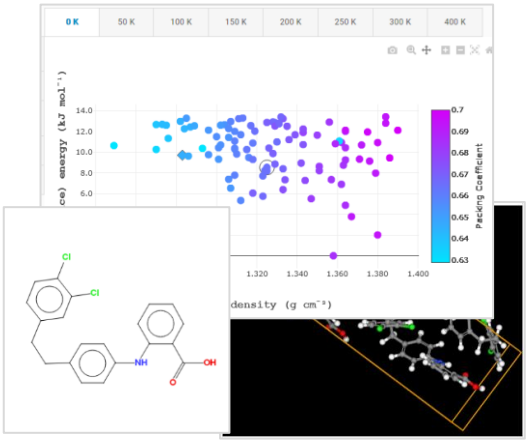
CSDParticle.

Anticipate particle properties and behaviour



CSDTheory.

Insights from predicted structure landscapes



Medicinal & Computational Chemists ♦ Crystallographers & Structural Biologists ♦ Solid Form & Crystallisation Scientists

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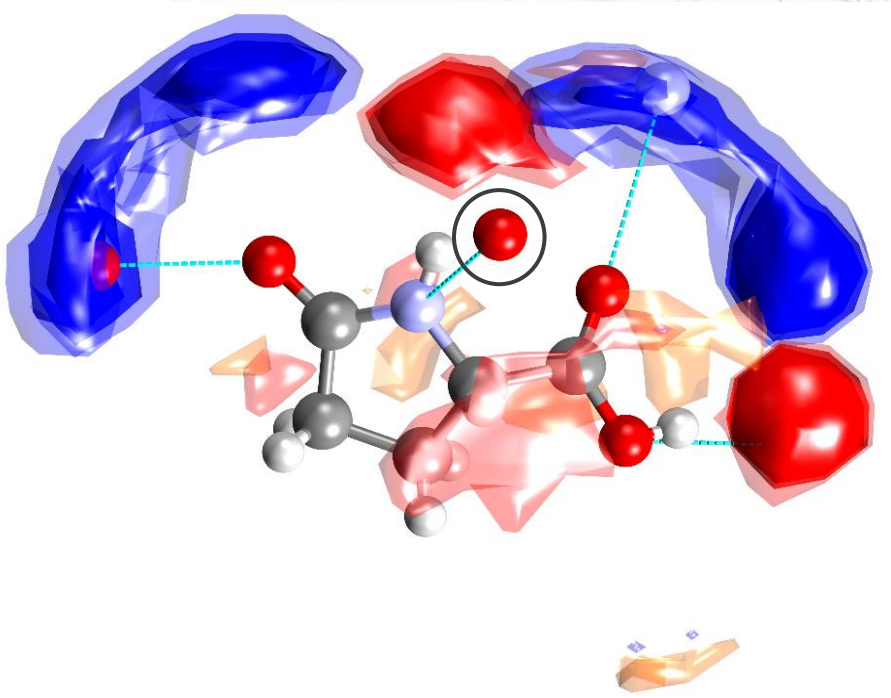
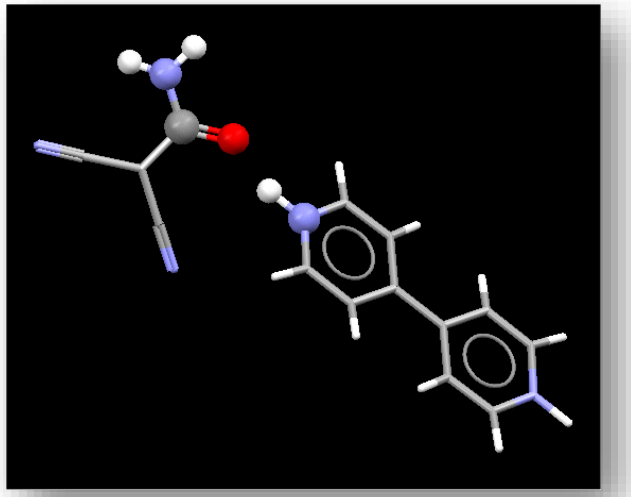
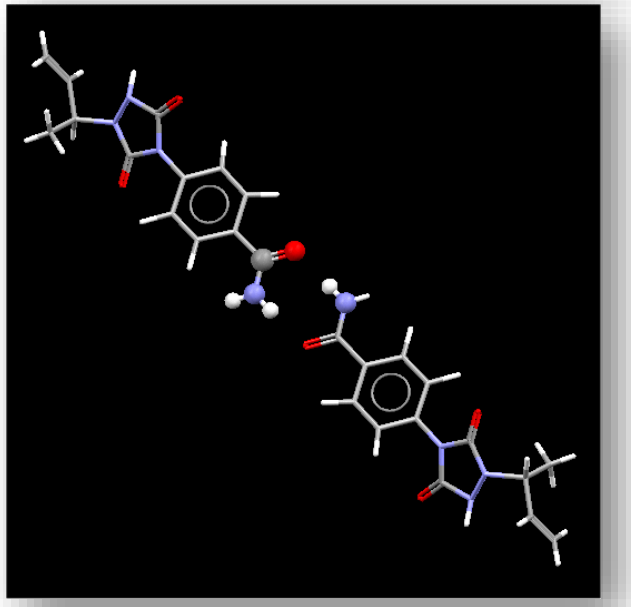
Key concepts - Full Interaction Maps

- Map interaction preferences around complete molecules in a crystal structure
- Visualise observed atom-atom contacts with respect to likely geometries in 3D space
- Identify interaction hot-spots around chemical groups



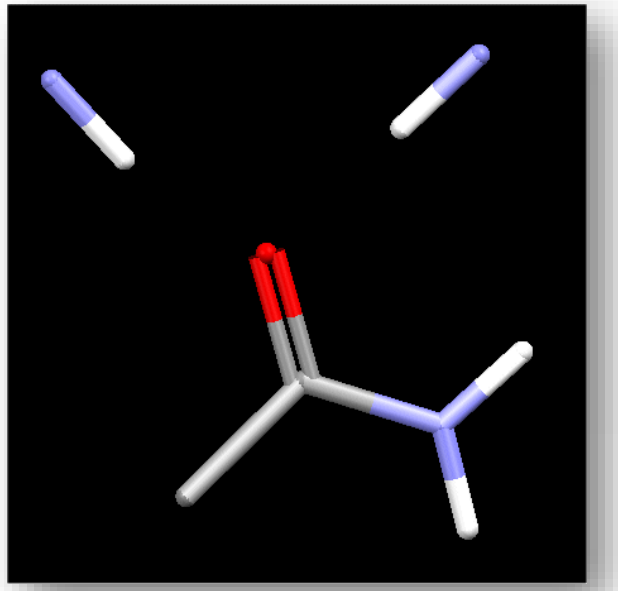
Key concepts - Full Interaction Maps

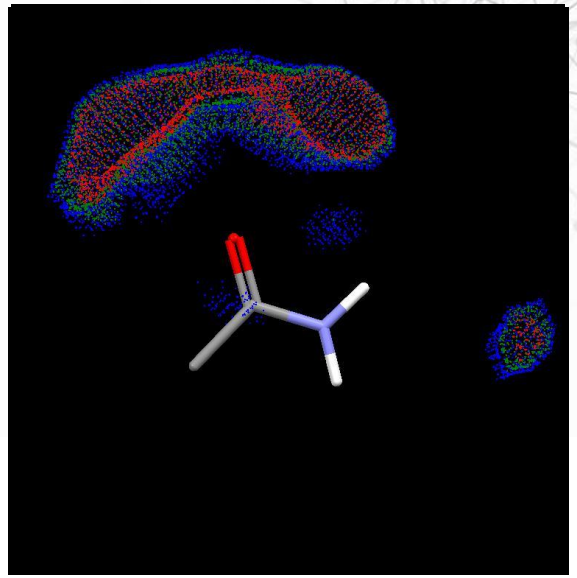




central group: -$CONH_2$

contact group: NH





Search for structures containing desired contact

Superimpose hits and display as scatterplots or contour plots

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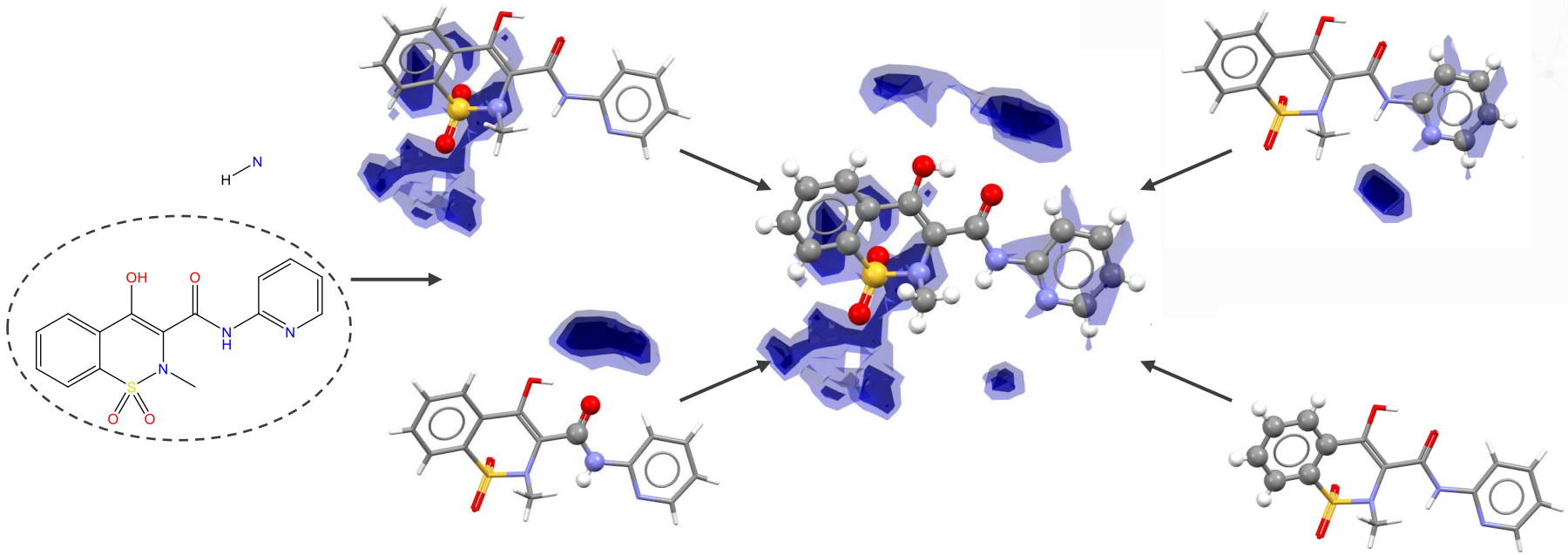
Key concepts - Full Interaction Maps

- Molecule is broken down into fragments
- IsoStar maps for each fragment are combined to give the Full Interaction Map



- Multiple maps can be generated for different probes

P. A. Wood *et al.*, *CrystEngComm* (2013), **15**, 65–72

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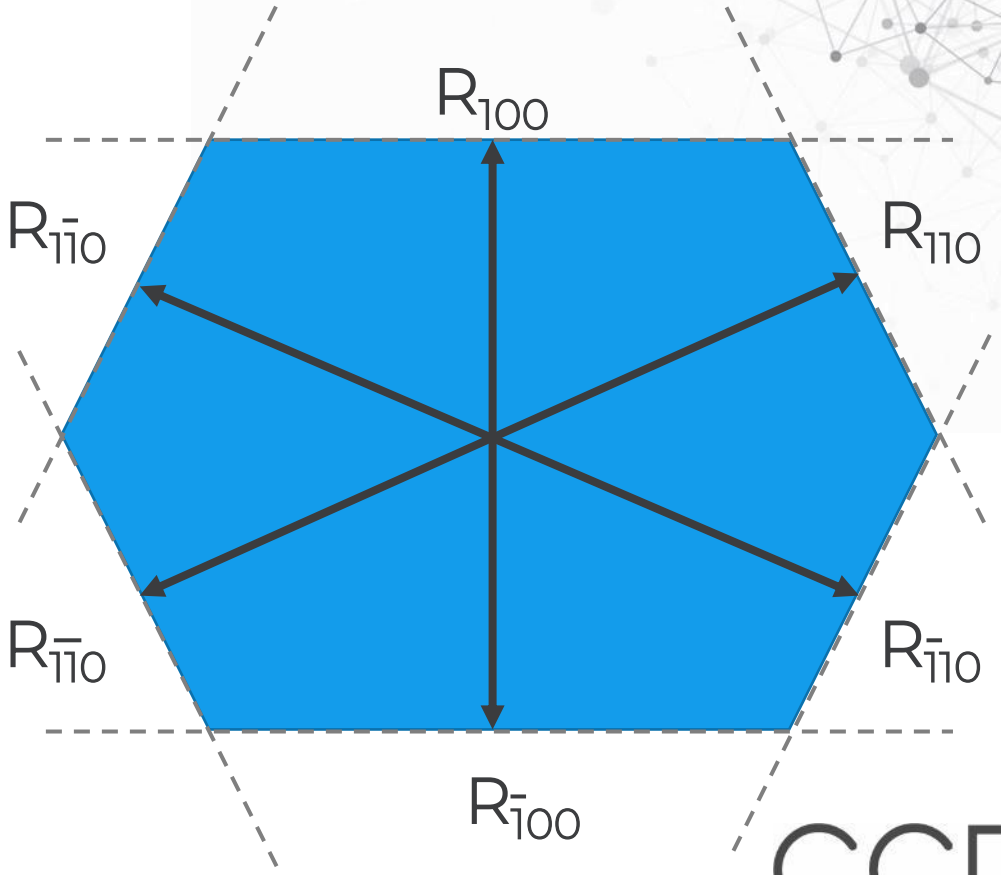
Key concepts - How do crystals grow?

- Depends on relative growth rates
  - R_{hkl}
  - *Faster* growing faces are *smaller*
- Growth rates are dependent on many things
  - Supersaturation
  - Solvents
  - Impurities



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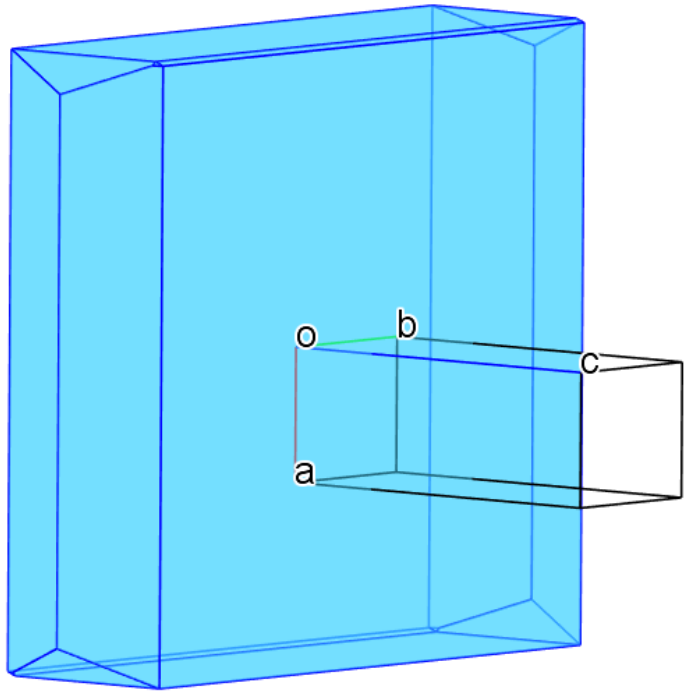
Key concepts – BFDH morphologies

- Simplest morphology model
  - Essentially based on unit cell
- Point molecules
- Growth rates inversely proportional to distance between Miller planes
- Layer-on-layer growth
- Independent of growth environment



A. Bravais, *Études Crystallographiques*, Gauthier-Villars, Paris, (1866)

M.G. Friedel *Bull. Soc. Franc. Miner.* (1907), 9, 326-455.

J.D. Donnay, D. Harker, *Amer. Min.* (1937), 22, 446-467.

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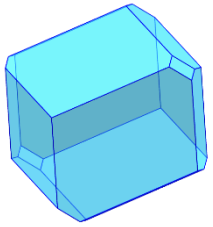
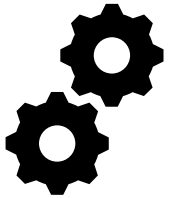
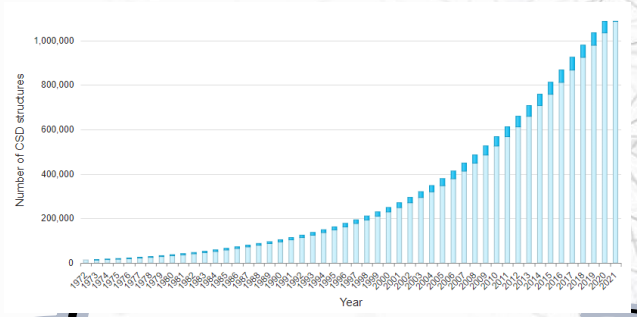
The field



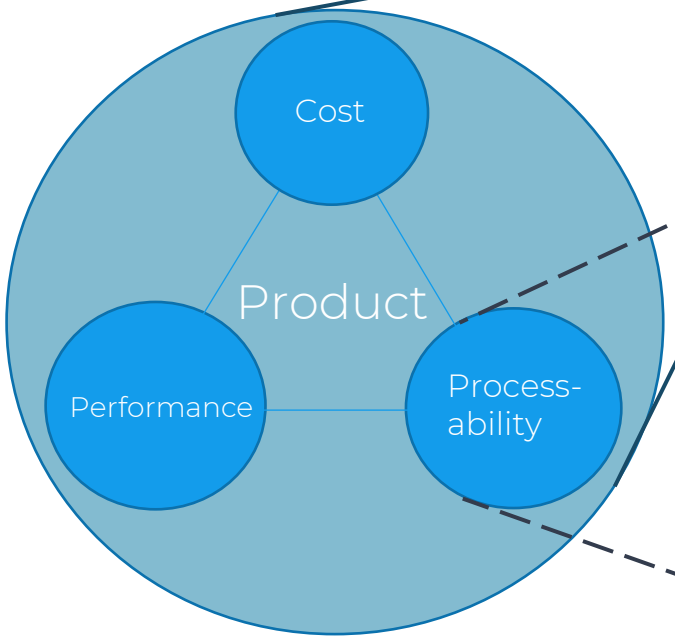
Particle

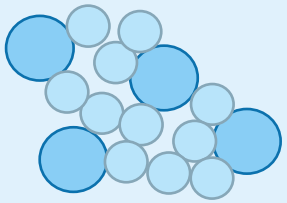


Product

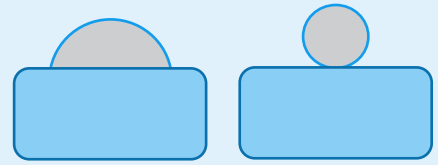


CSD

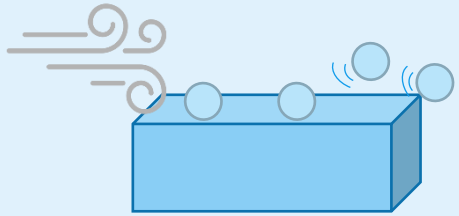


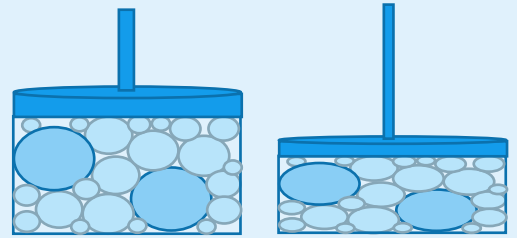


Particle Sticking &
Flowability

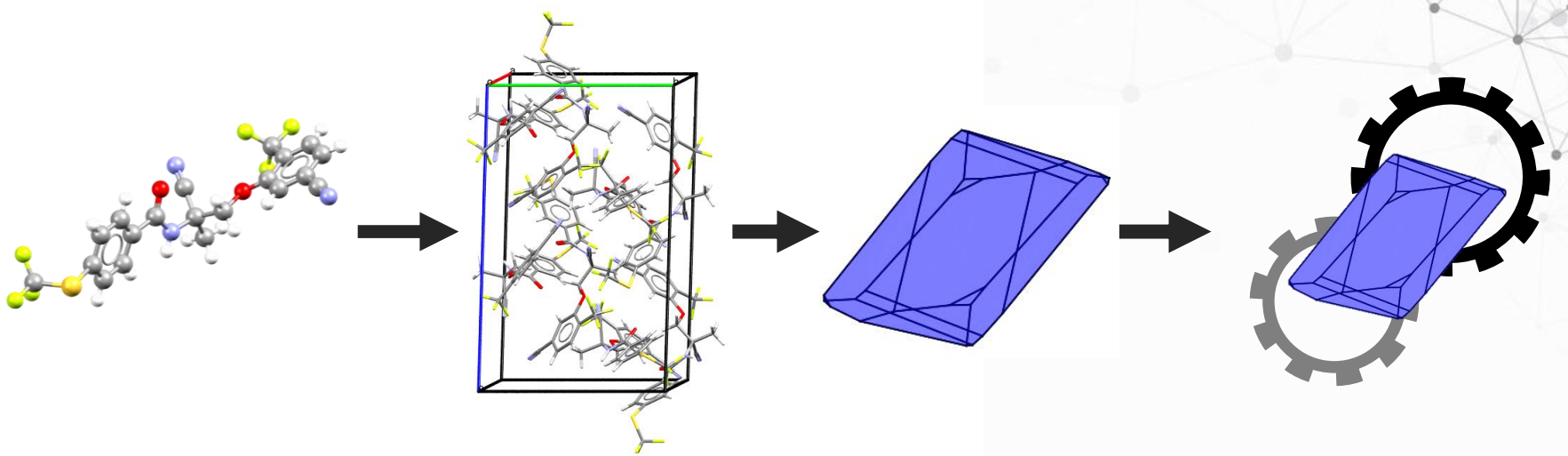


Wettability &
Compaction





From Solid Form to Particle Properties



Molecule Form Particle Properties

Solid Form Informatics

Particle Informatics

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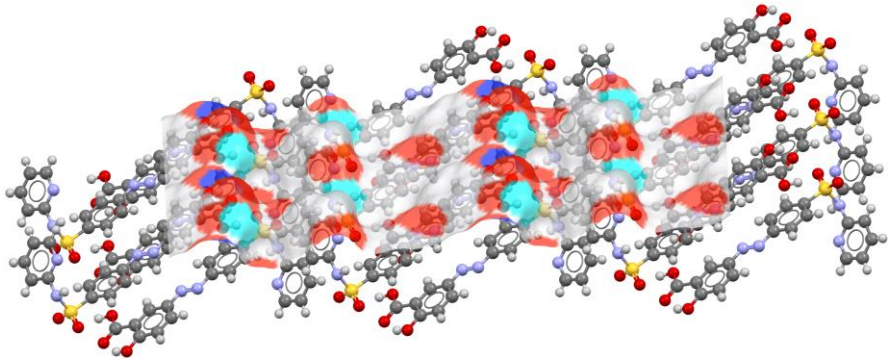
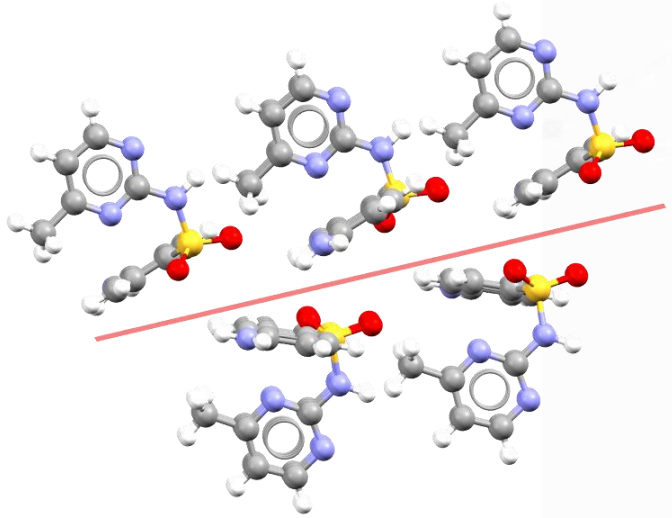
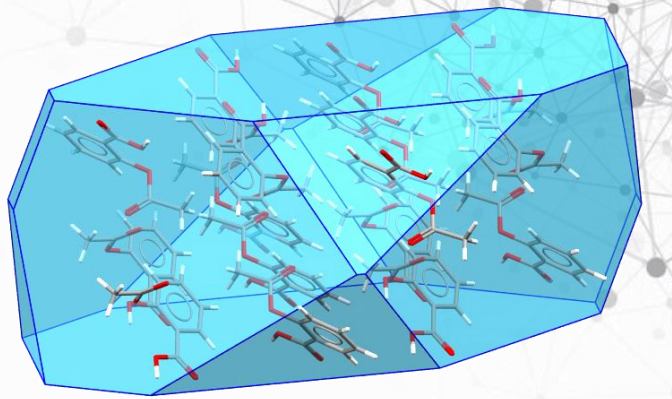
Particle Informatics



Visualisation and analysis of surface properties



Identification and analysis of potential slip planes



Morphology calculations

- Ongoing research projects into particle and surface phenomena are developing our understanding of formulation and manufacturing processes
- Application of rapid, informatics-based approaches to understand the link between crystal structure and properties that influence downstream behaviour

M. J. Bryant *et al.*, *Cryst. Growth Des.* (2019), **19**, 9, 5258-5266

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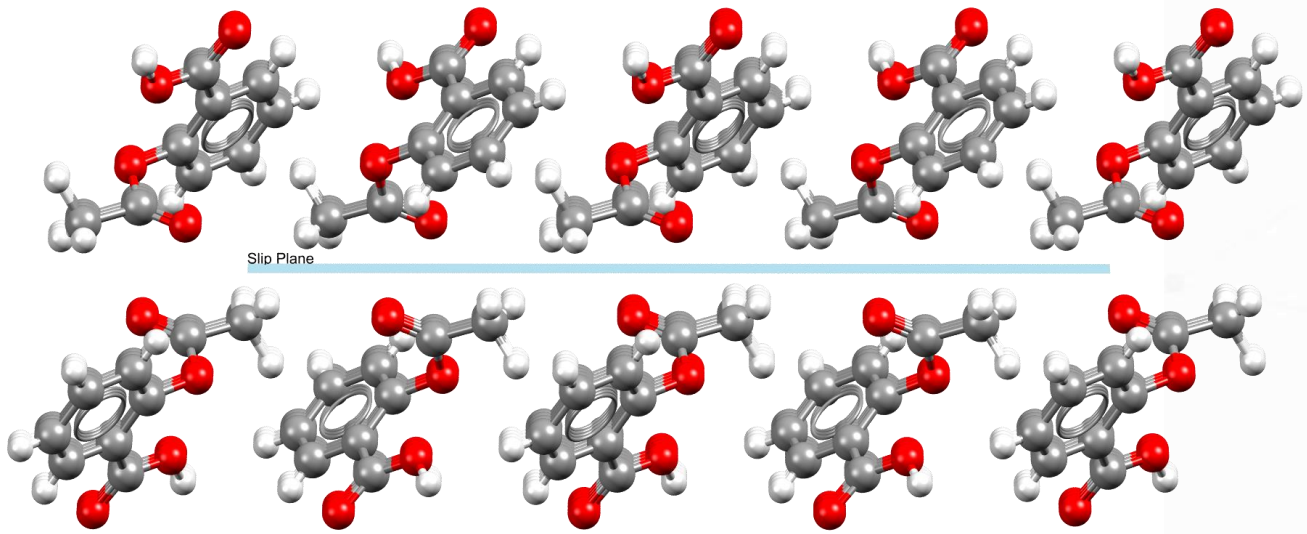

Slip Planes

- Identification of Potential Slip Planes
- Analysis of Structure Hydrogen Network

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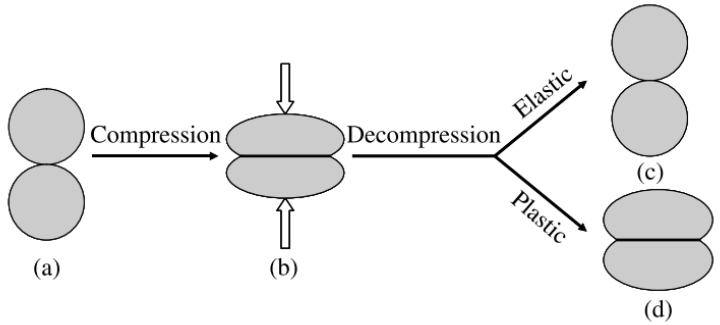
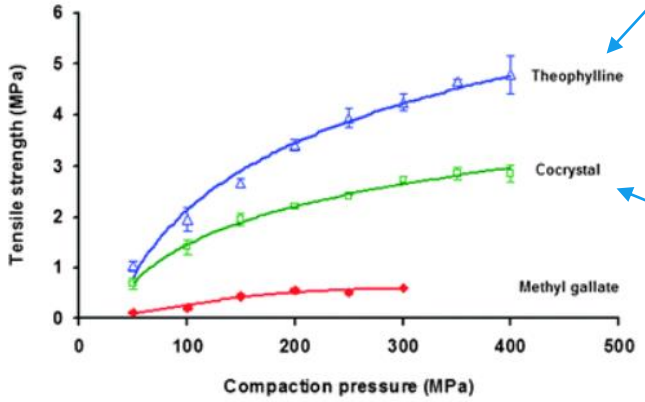
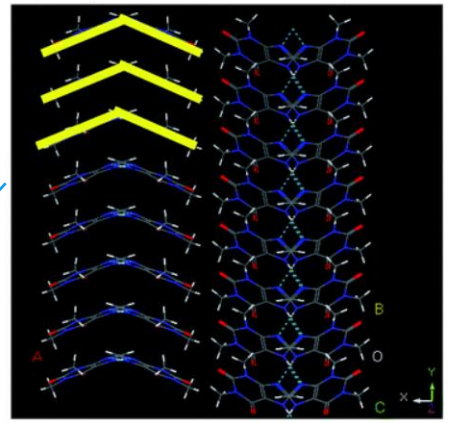
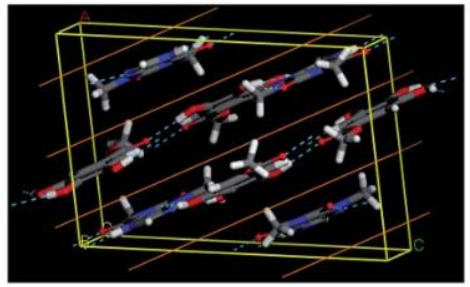
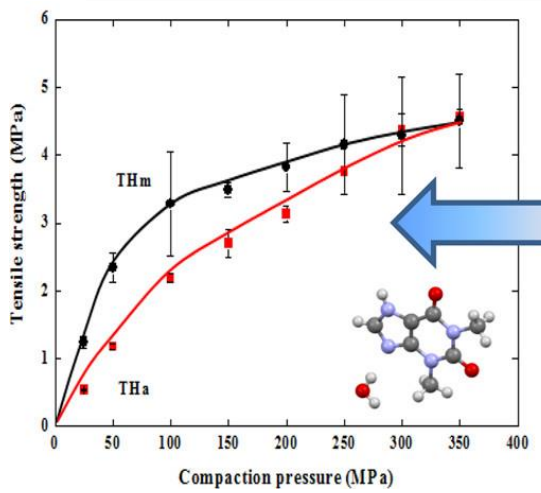
Compaction and Bending

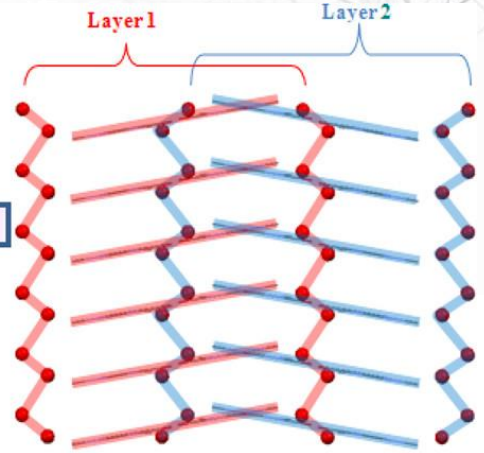








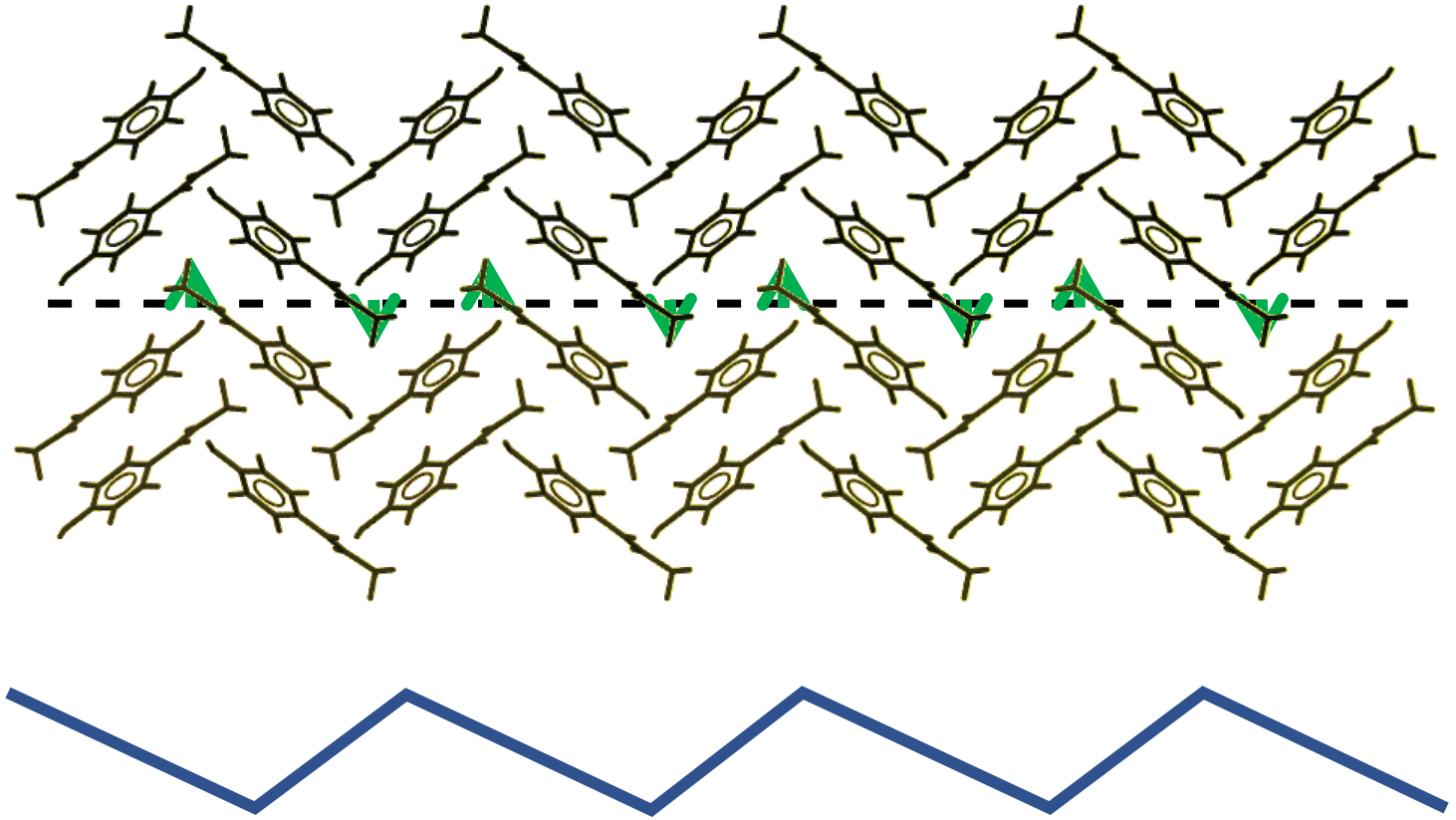




S. Chang and C. C. Sun *Molecular Pharmaceutics* 2017 14 (6), 2047-2055 10.1021/acs.molpharmaceut.7b00124

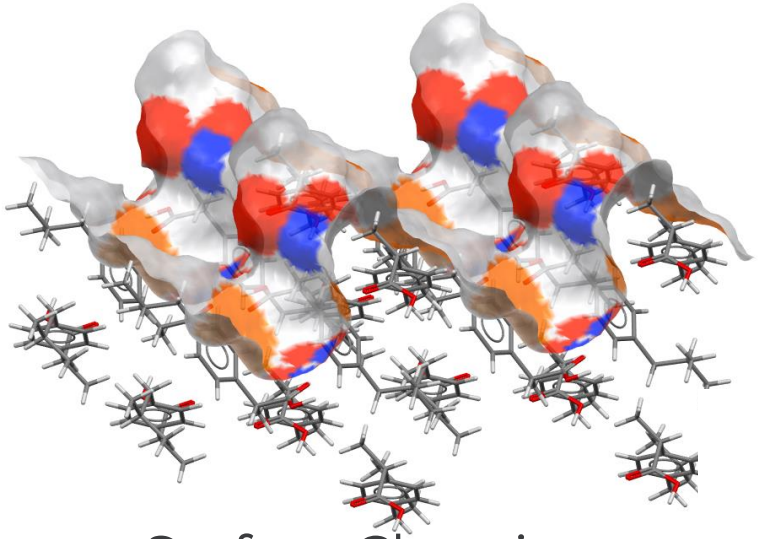
S. Chattoraj, L. Shi, C.C. Sun *CrystEngComm*, 2010,12, 2466–2472 | 2467 10.1039/C000614A

Predicting slip planes

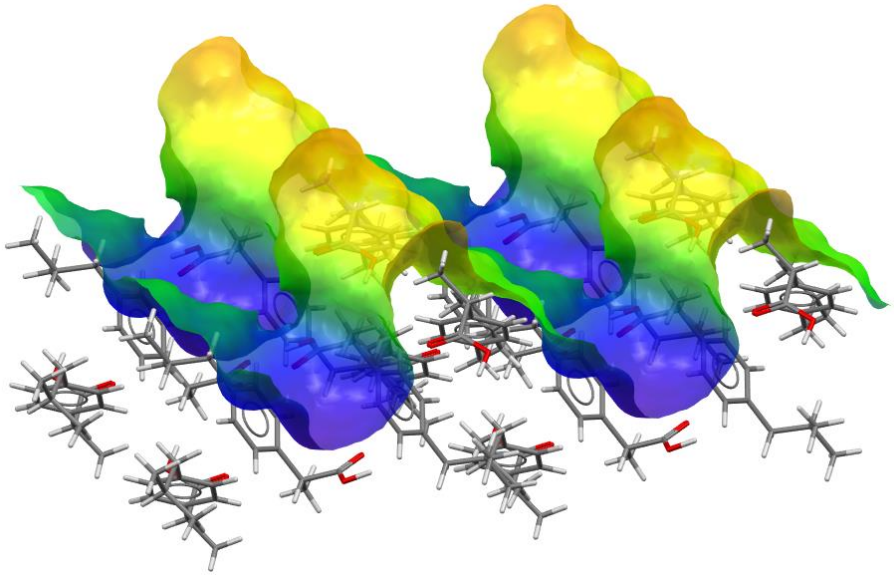


M. J. Bryant *et al.*, *CrystEngComm* (2018), **20**, 2698-2704

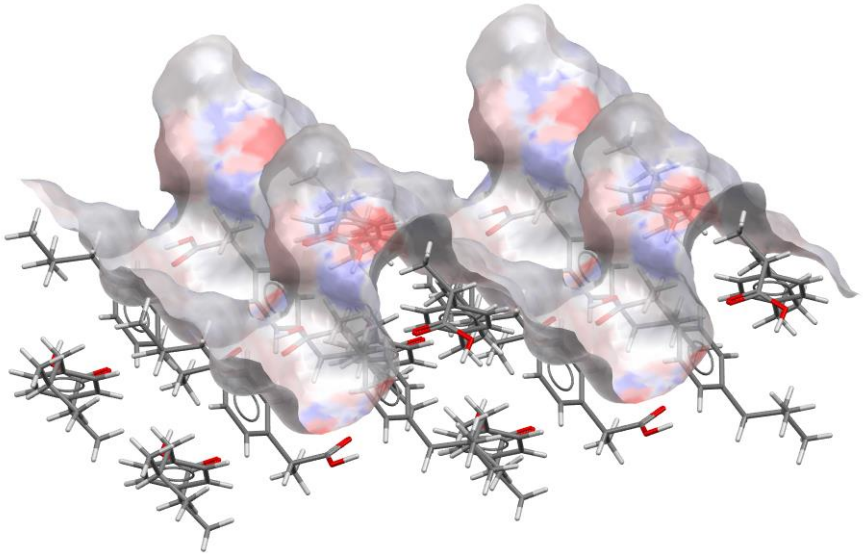
Surface Analysis



Surface Chemistry



Surface Roughness



Surface Charge

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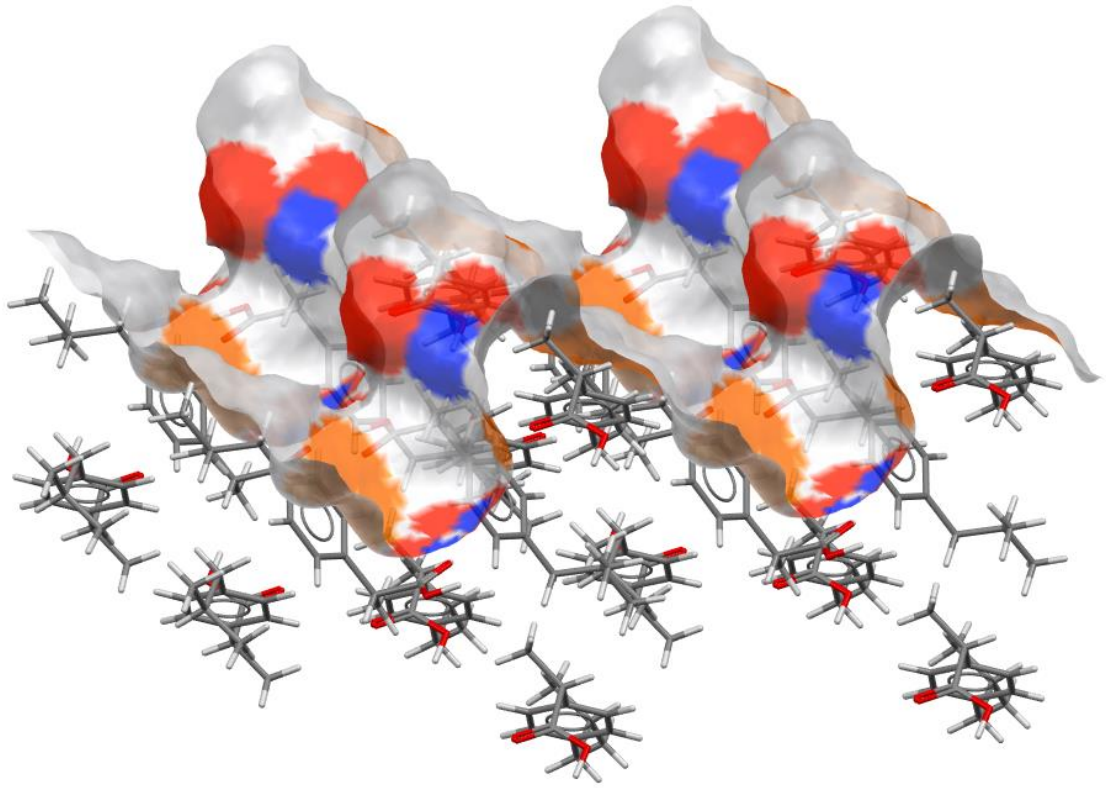
Surface Analysis



Descriptors	
Physical	Chemical
Reticular Surface Area	Hydrogen Bond Donor/Acceptor Density
Rugosity	Aromatic Bond Density
RMSD, Skewness, and Kurtosis	
Statistically Derived Interaction Data	

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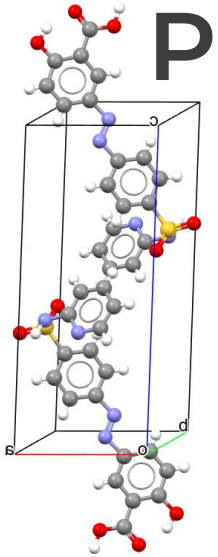
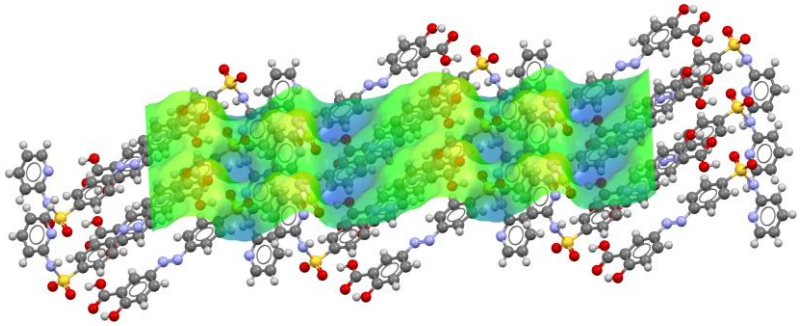
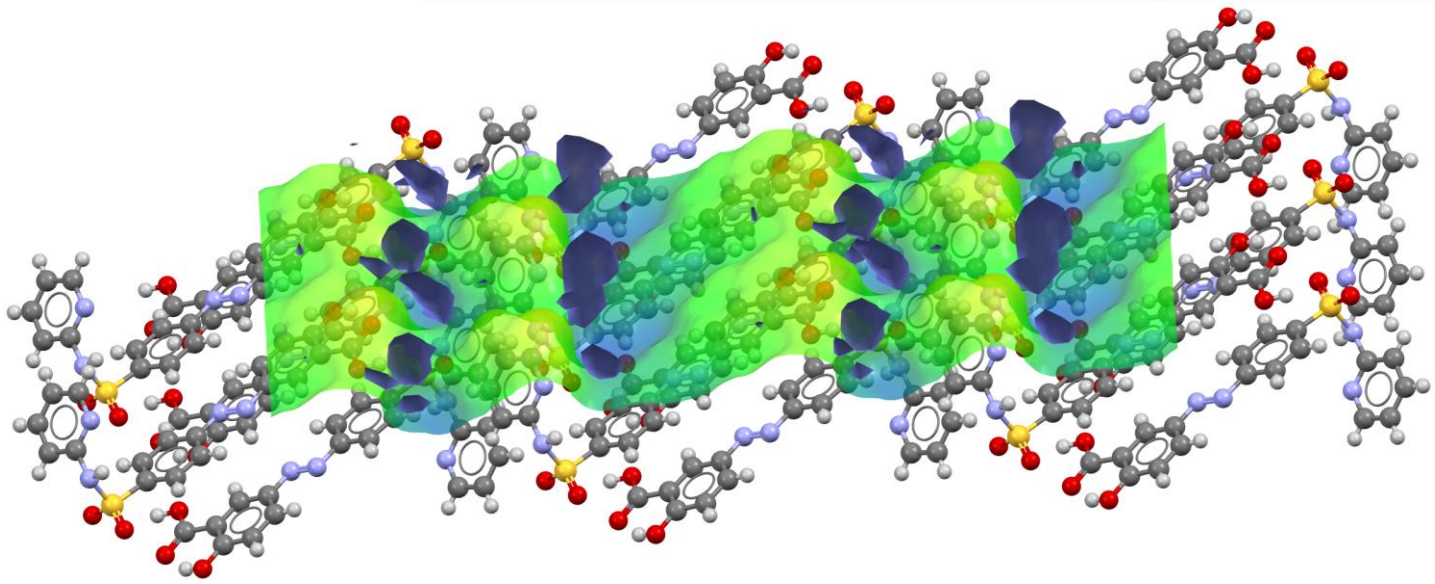
Particle Informatics



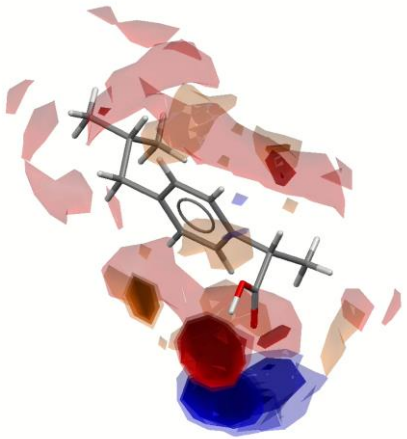




Descriptors	
Physical	Chemical
Reticular Surface Area	Hydrogen Bond Donor/Acceptor Density
Rugosity	Aromatic Bond Density
RMSD, Skewness, and Kurtosis	

FIMs on Surface

FIMs on Surface



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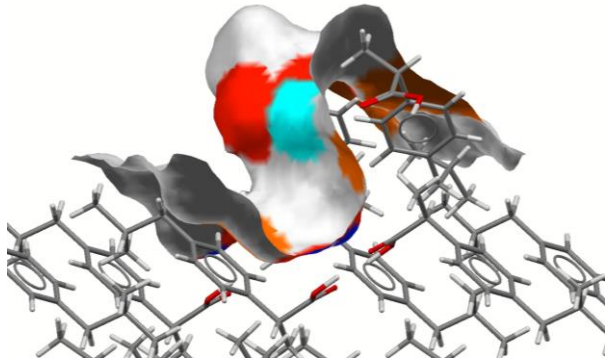

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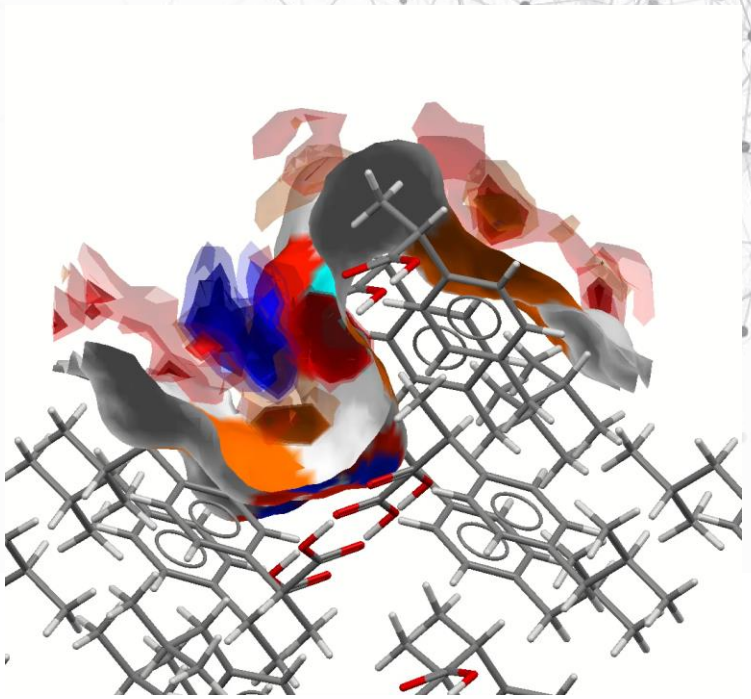
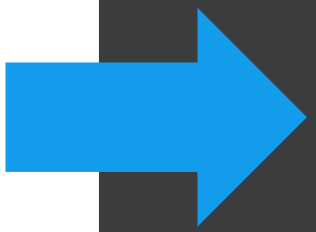


FIM on Surface

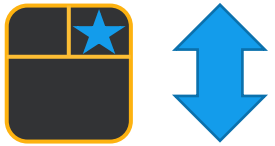
Accessing CSD-Particle through Mercury



Reminder: Basic navigation in Mercury

- Left mouse button and move – rotate molecules

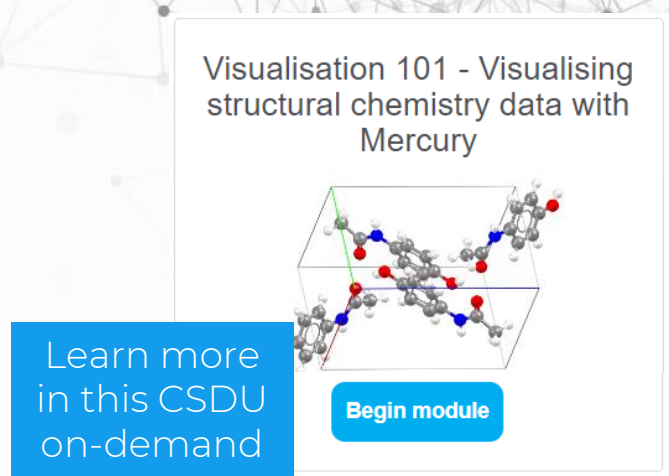
- Middle Mouse wheel – move molecules up and down



- 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

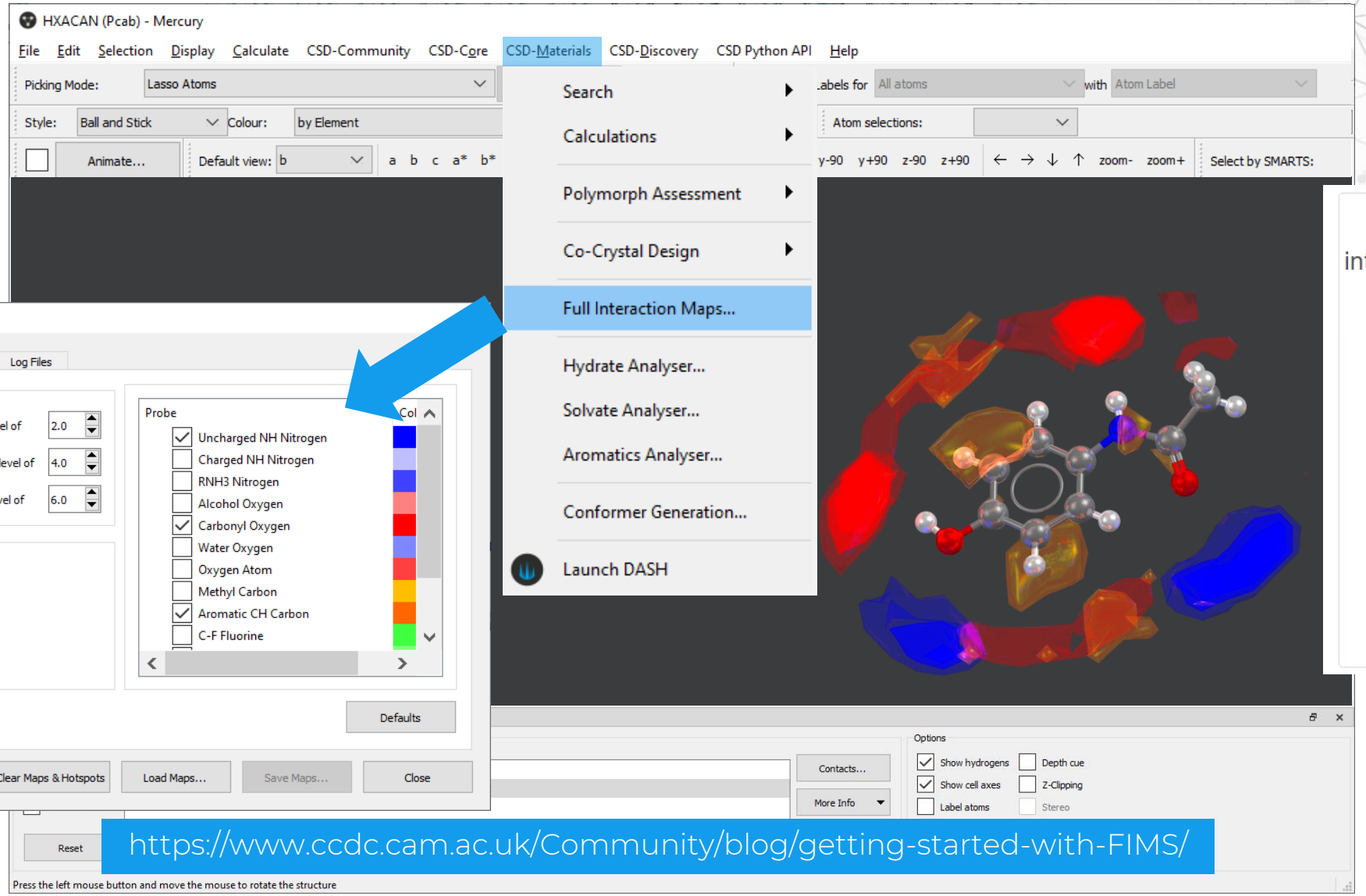
- Ctrl + Left mouse button and move - translate molecules



Learn more in this CSDU on-demand course

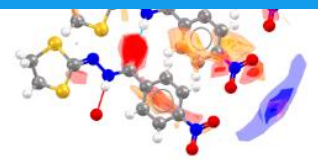
CCDC

Creating a Full Interaction Map



Analysing intermolecular interactions 101 - Full Interaction Maps

Learn more in this CSDU on-demand course

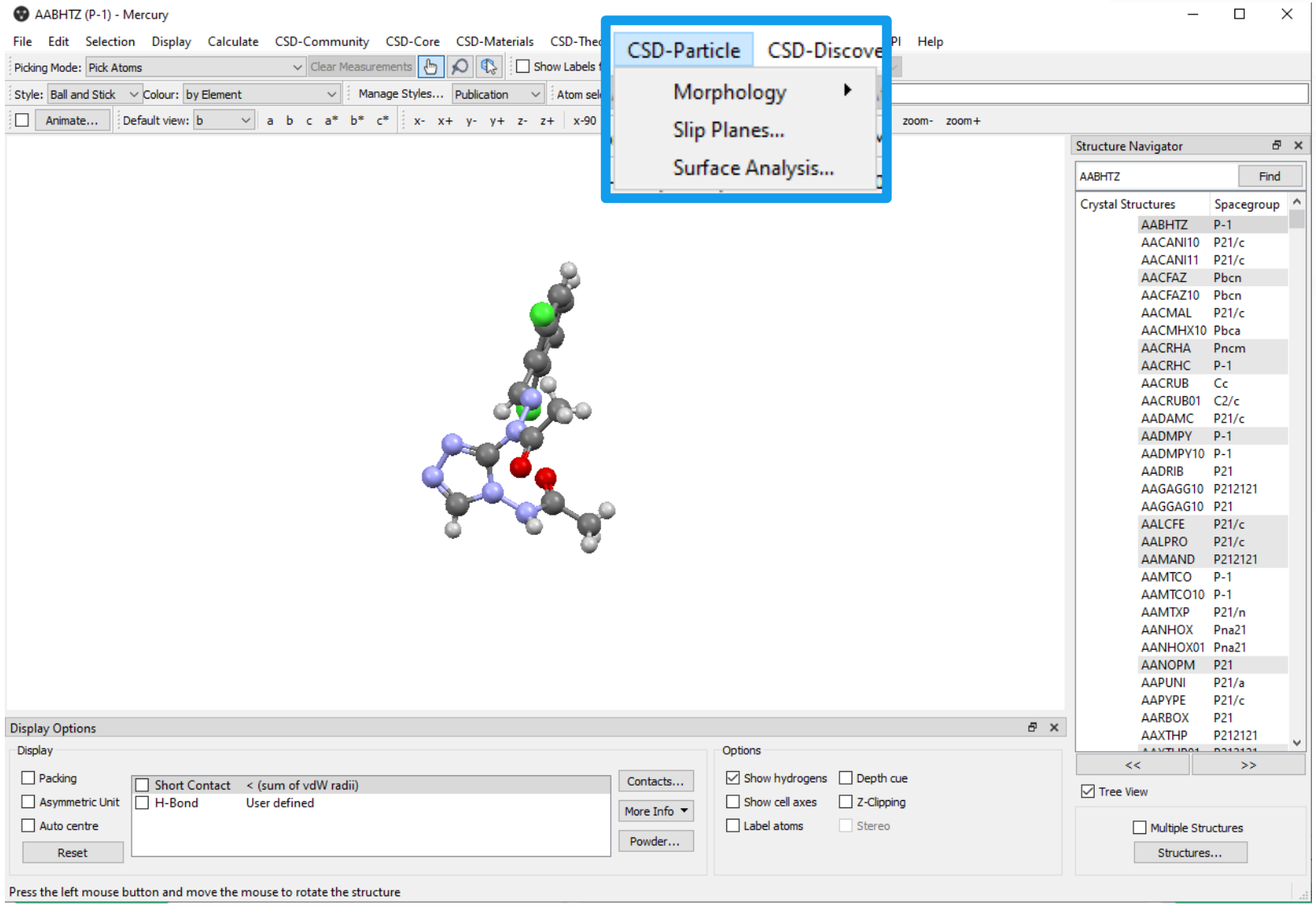


Begin module

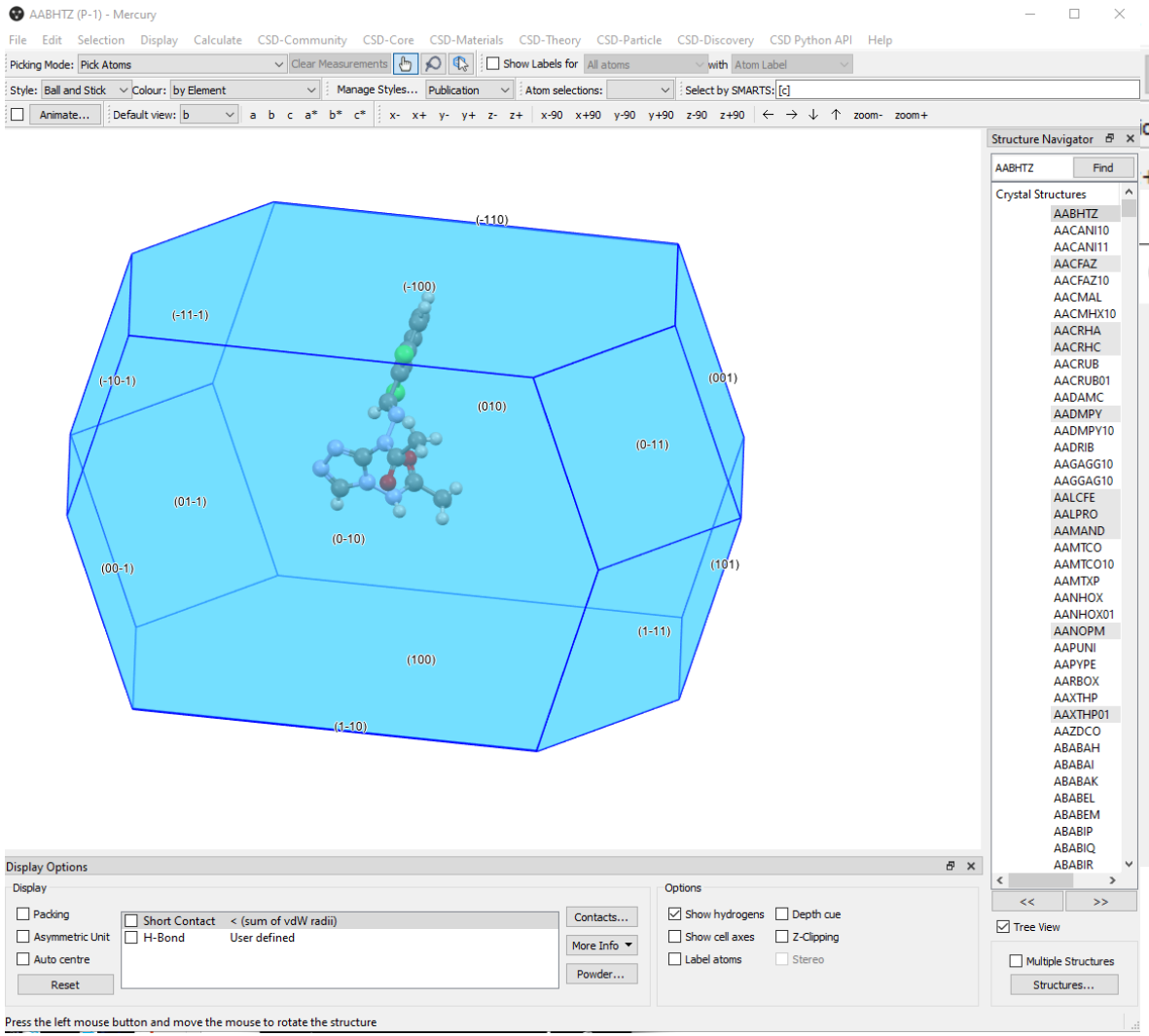
https://www.ccdc.cam.ac.uk/Community/blog/getting-started-with-FIMS/

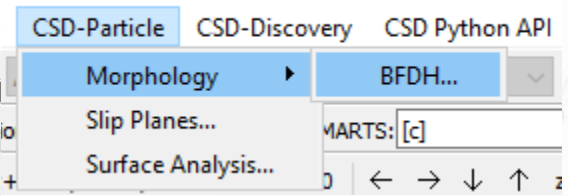
CCDC

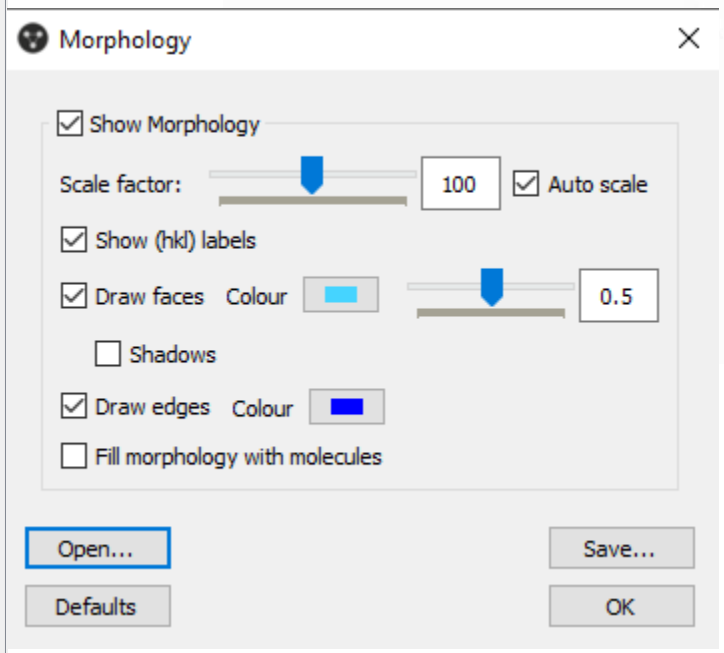
CSD-Particle Menu



CSD-Particle – Morphology - BFDH





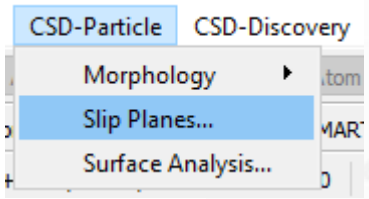


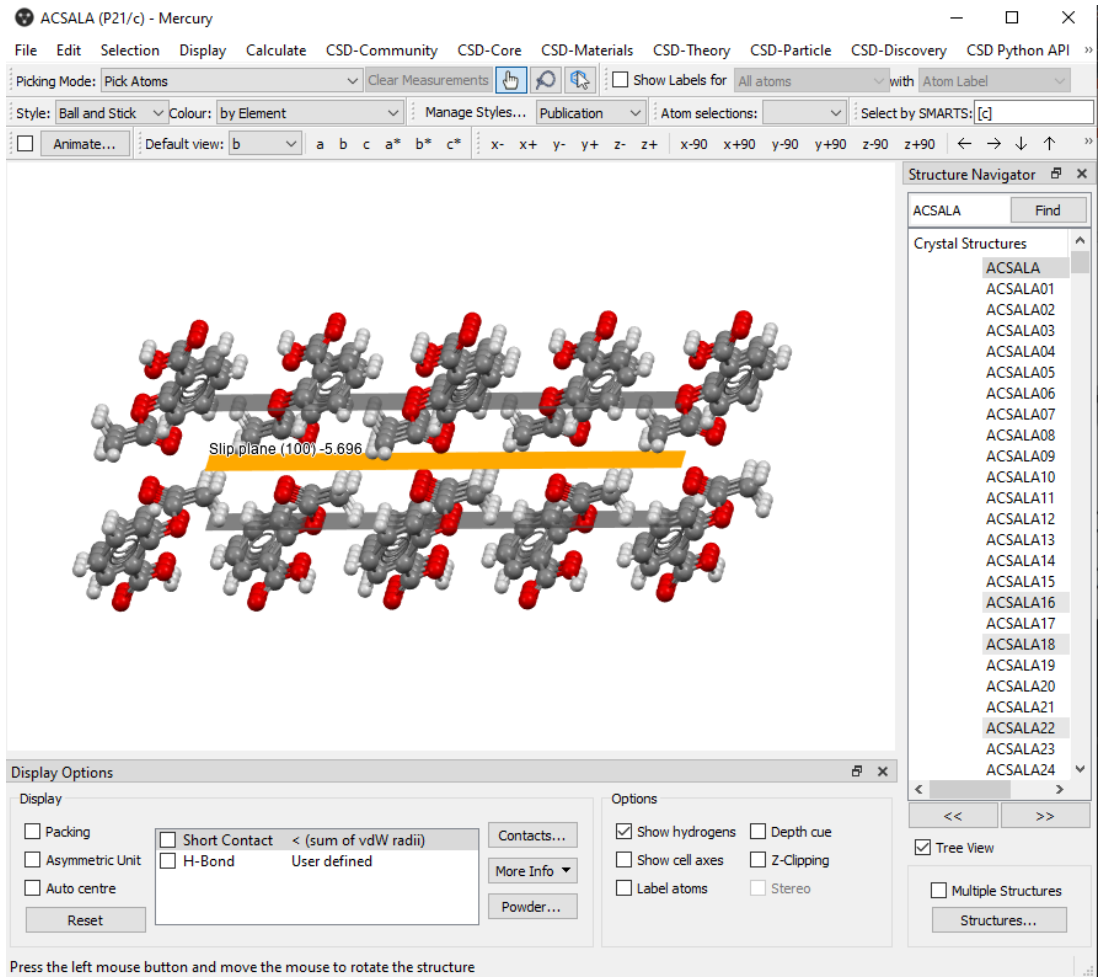
Display Options

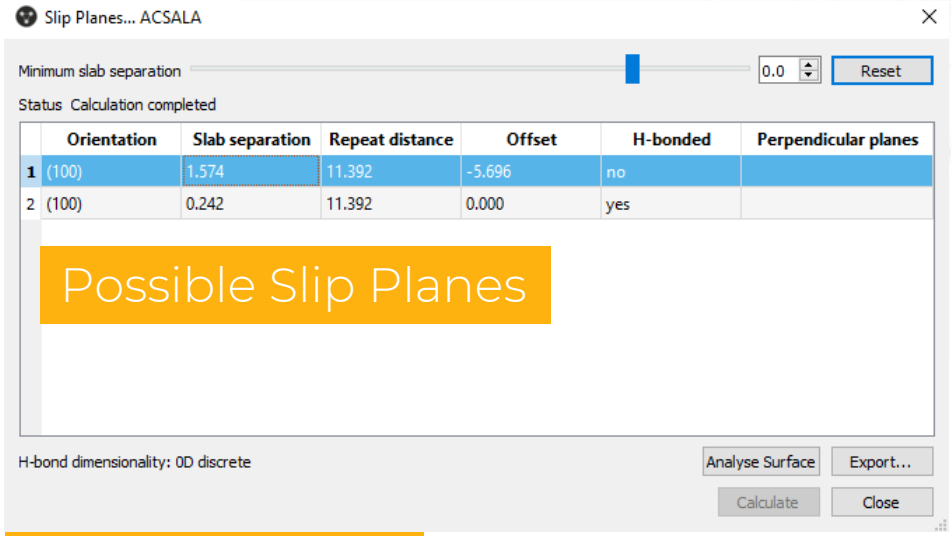
Save and Load

Learn more on BFDH Morphology in the *Glossary* in the handout.

CSD-Particle – Slip Planes







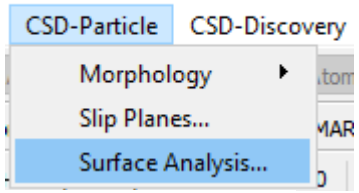
Possible Slip Planes

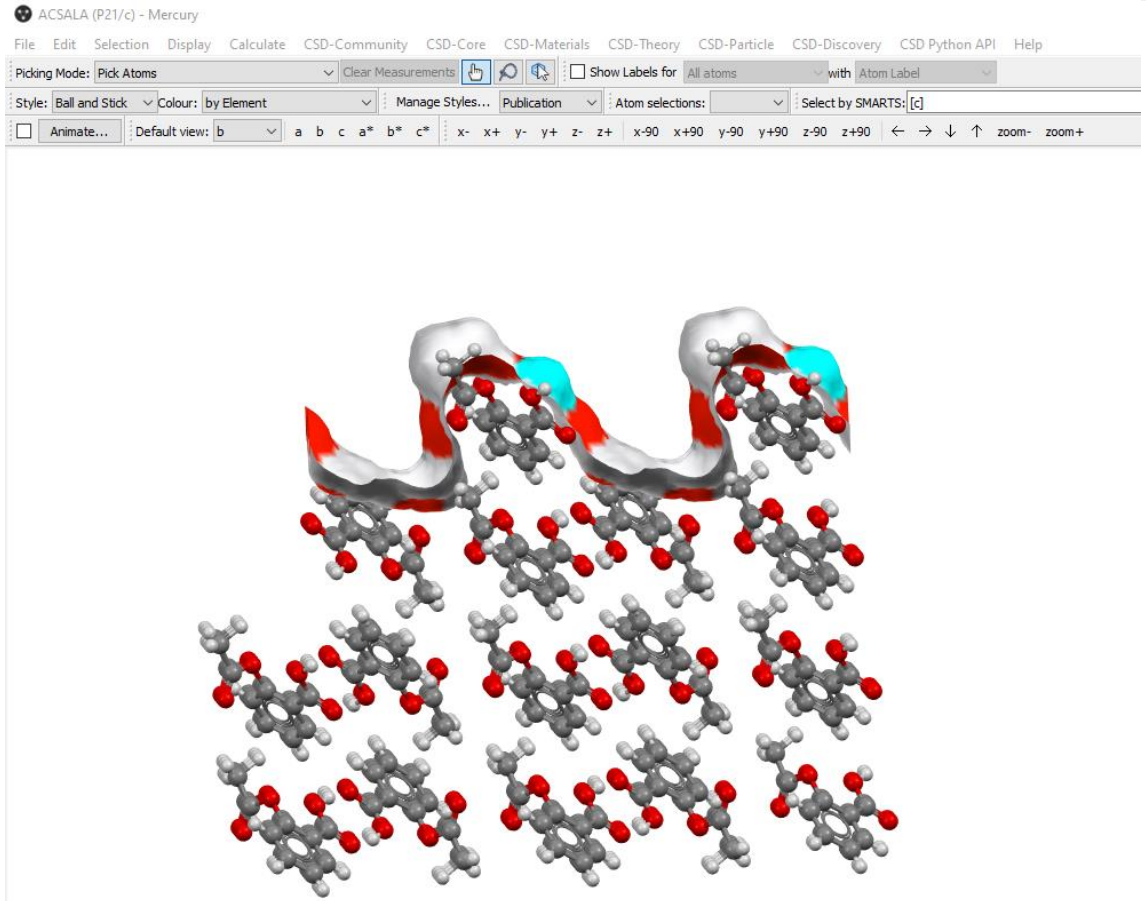
Export Table

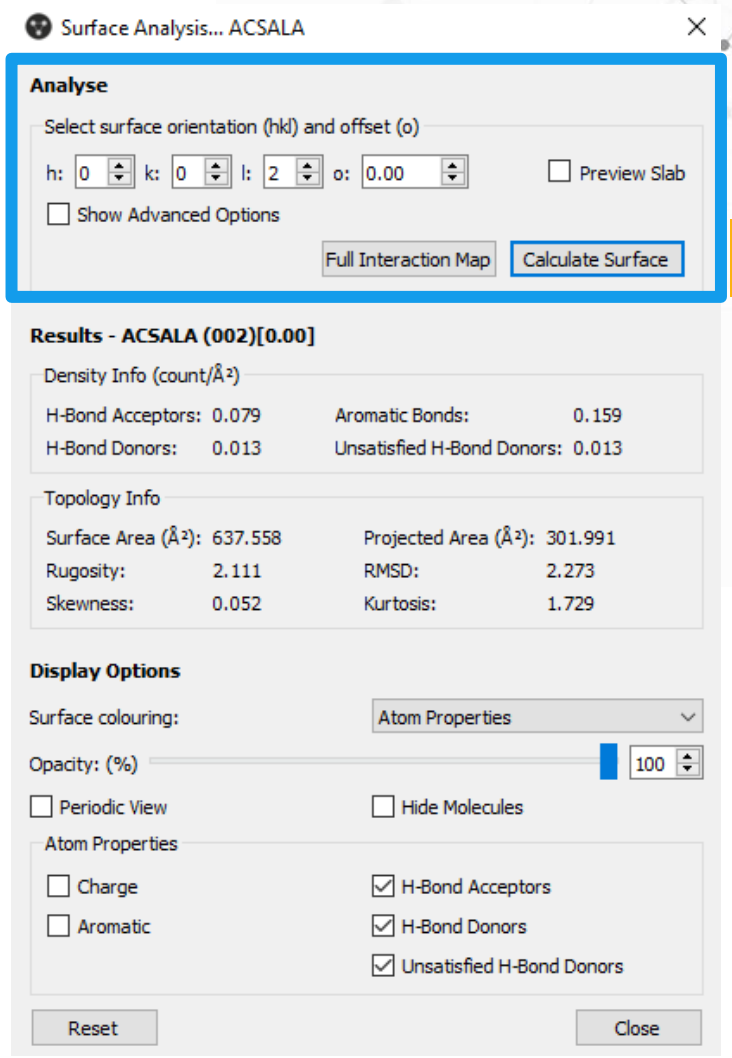
H-Bond System

Learn more on Slip Planes in the *Glossary* in the handout.

CSD-Particle – Surface Analysis

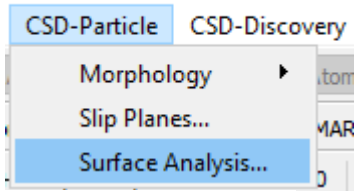


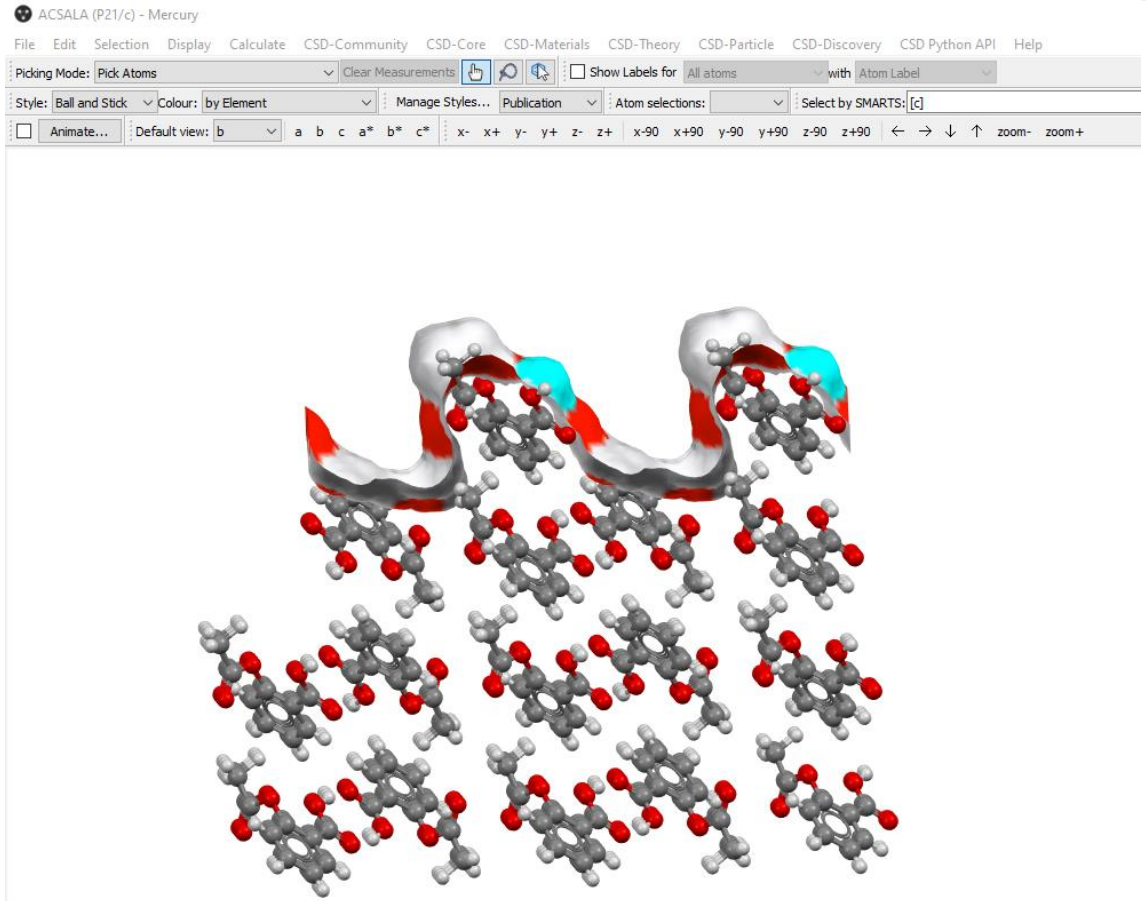


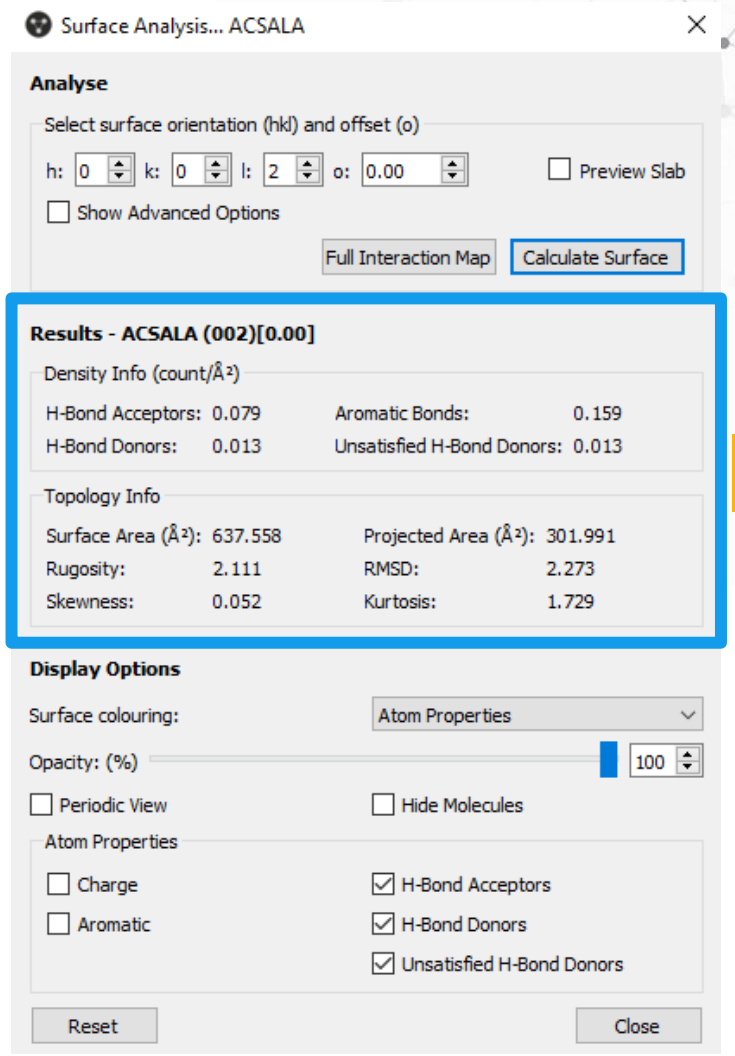


Input

CSD-Particle – Surface Analysis



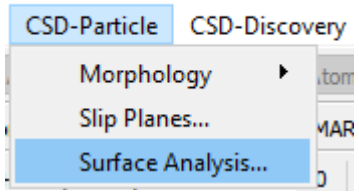


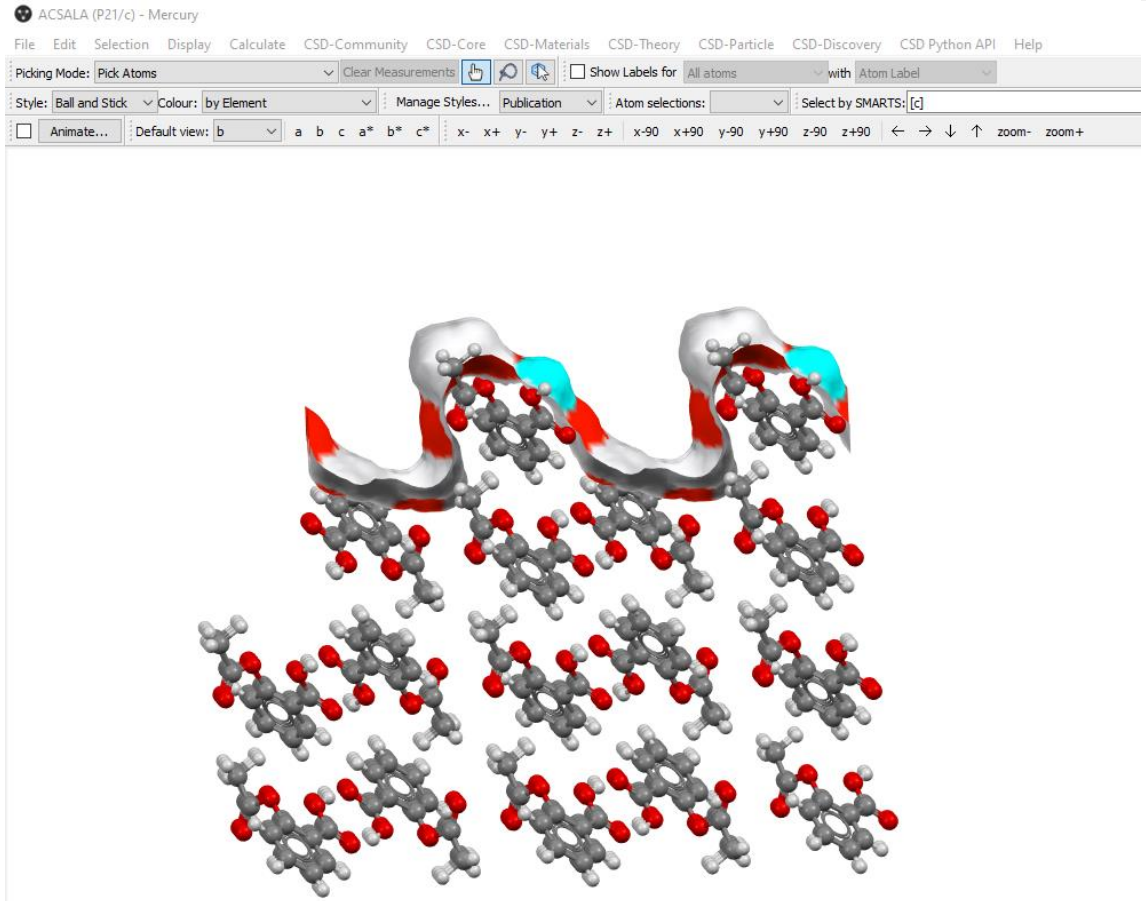


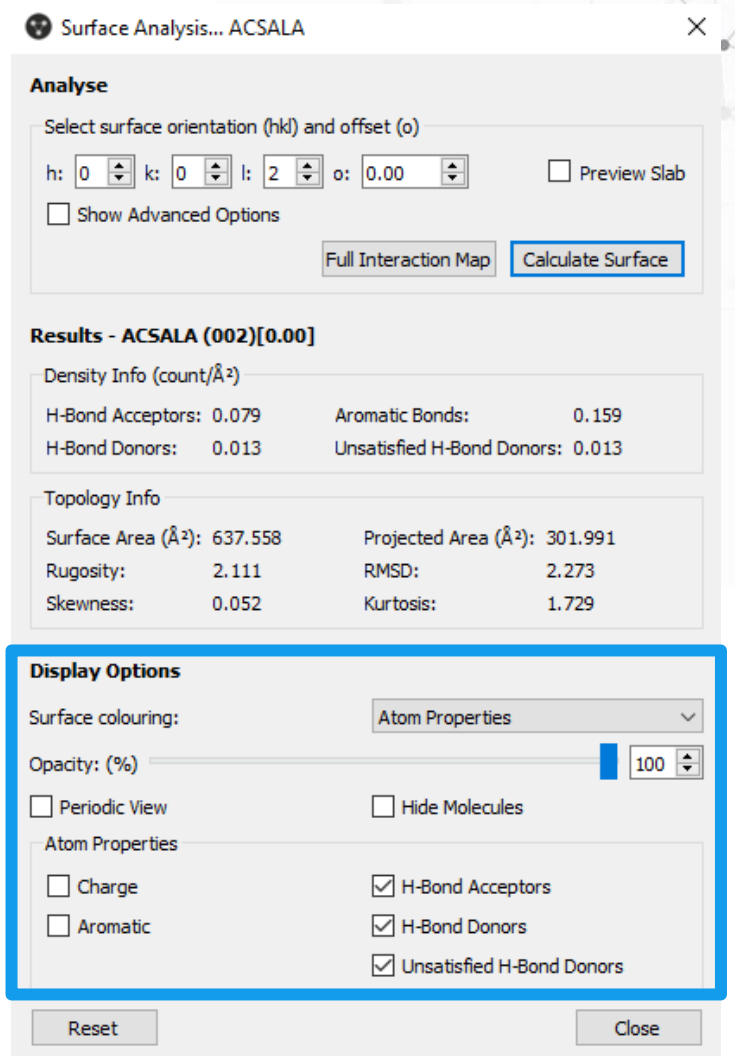
Results

Learn more about these parameters in the *Glossary* in the handout.

CSD-Particle – Surface Analysis



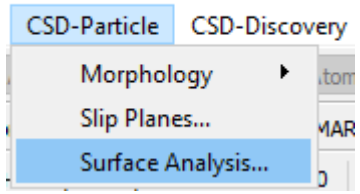


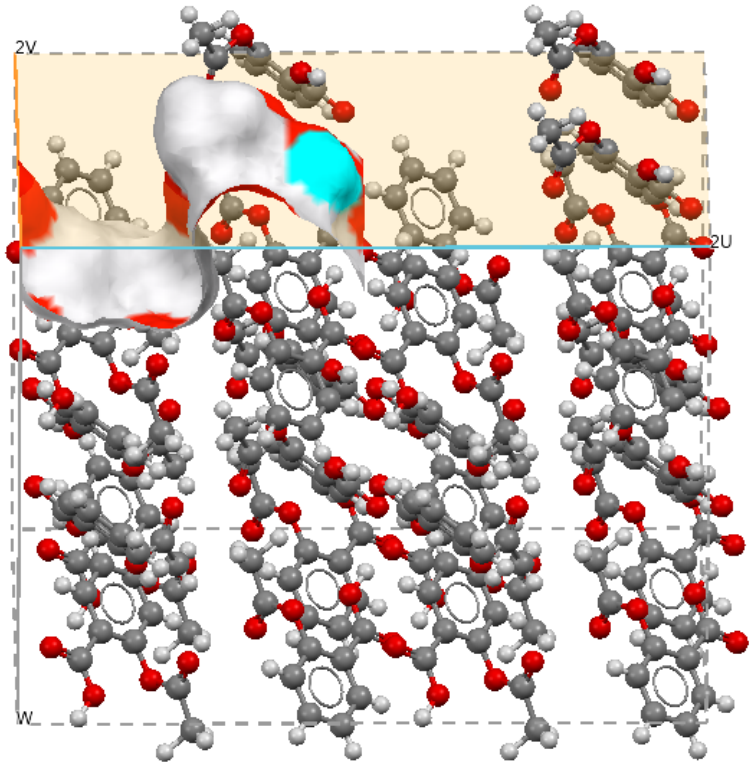


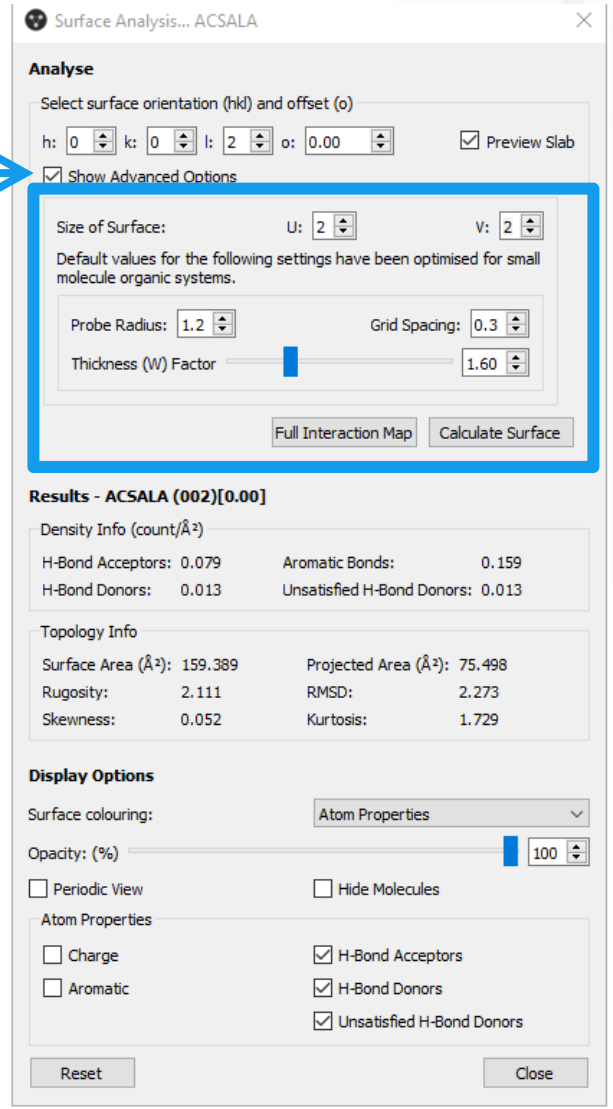
Display Options

CCDC

CSD-Particle – Surface Analysis



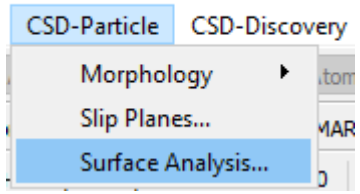


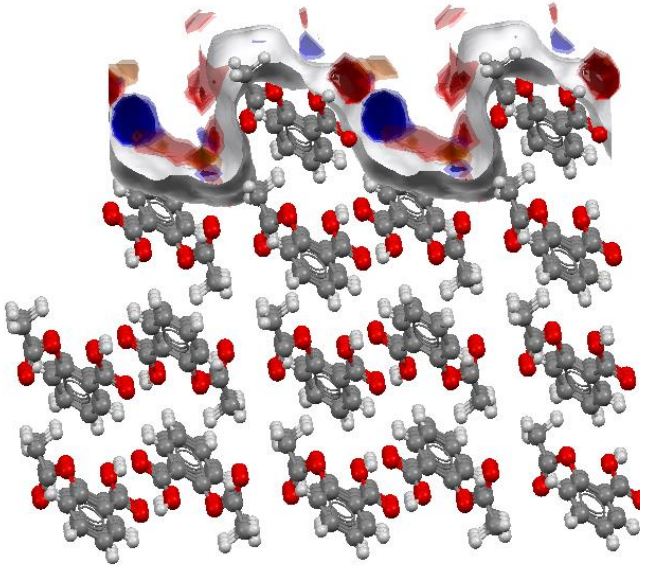


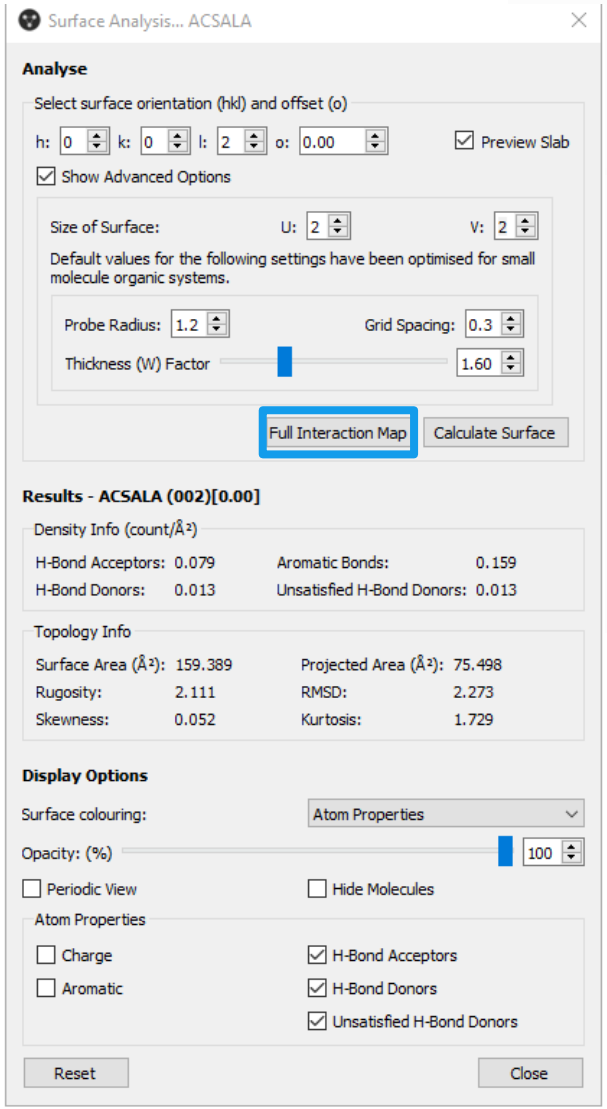
Advance Options

CCDC

CSD-Particle – FIMs on Surface



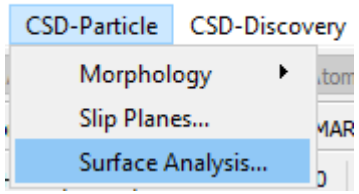


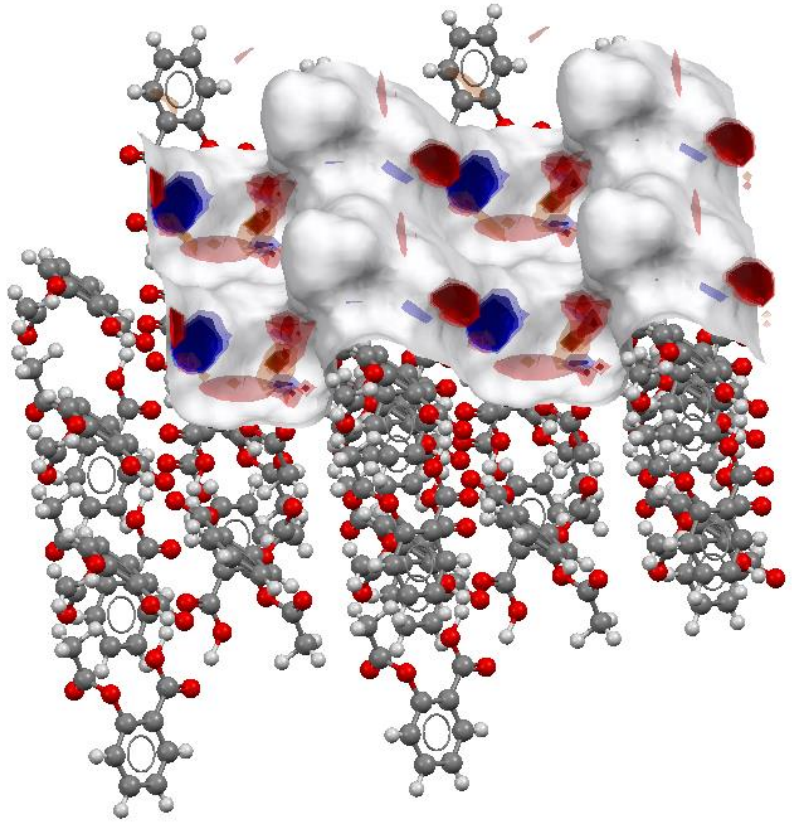


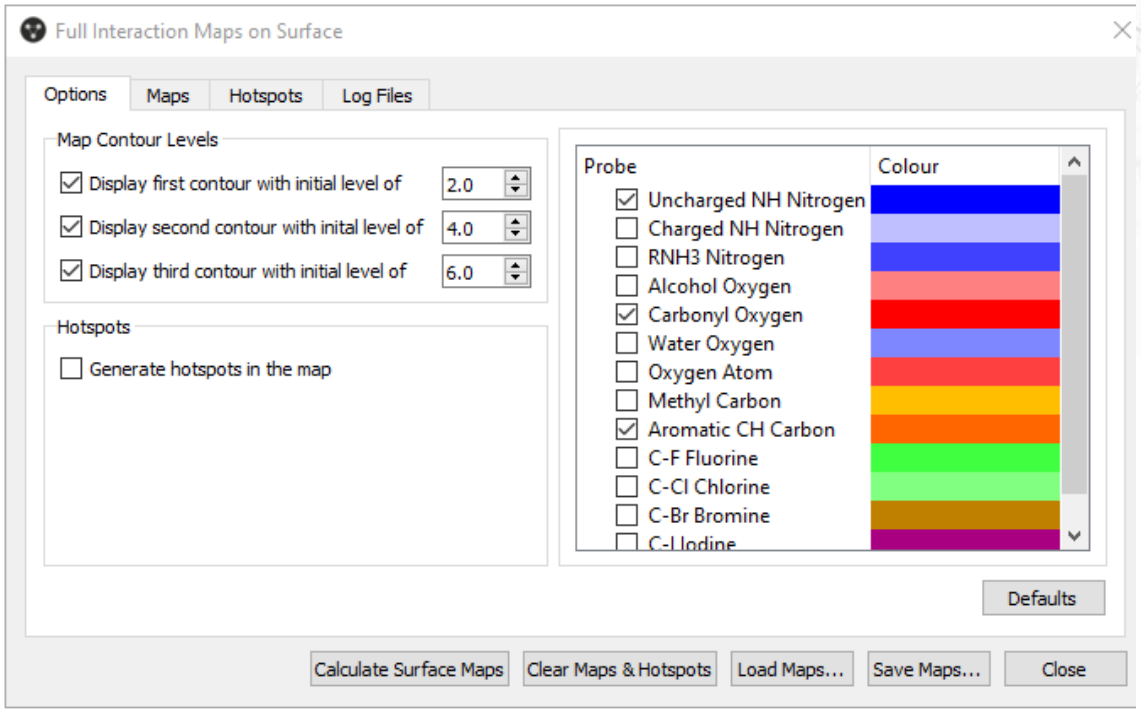
Full Interaction Map on Surface

CCDC

CSD-Particle – FIMs on Surface







https://www.ccdc.cam.ac.uk/Community/educationalresources/

Want to explore more?

Training and Educational Resources

The wealth of information contained within the Cambridge Structural Database (CSD) extends far beyond a collection of crystal structures. Knowledge derived from these materials informs much of chemistry, biochemistry, and biology. Chemical and structural concepts are often difficult to grasp without real world, interactive examples for students to explore.

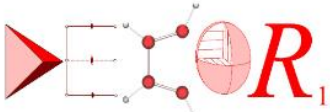
The CCDC and our colleagues continually produce educational materials for use in classroom and computer lab settings, or as independent study modules. Many of these materials make use of the Teaching Subset - a freely available set of over 750 structures that can be investigated with the free version of our Mercury visualisation and analysis program. Of course, our database of over one million entries are available for free through our Access Structures portal.

If you are an educator looking for supplementary teaching materials, find out more about the Teaching Database **here**. If you have developed your own modules using the CSD and would like to share them with the broader community, please contact us at education@ccdc.cam.ac.uk.

To keep up to date with the latest news from education and outreach at the CCDC, sign up for the Education and Outreach Newsletter **here**.

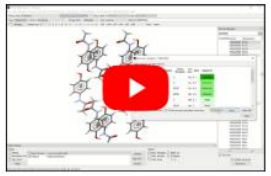
Information on the Teaching Subset

Access a series of teaching modules for use in the classroom



DECOR: Educational Resources for Teaching Crystallography

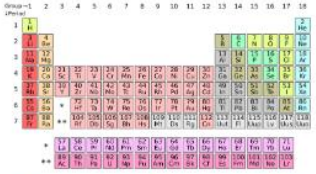
Download a series of self-guided workshop materials for CCDC tools and features



Watch software training and support videos

CSDU modules - Explore our on-demand training courses

Access fun science activities for kids through the CCDC Home learning page



Explore the Periodic Table through Crystal Structures

Bound! a Protein-Drug matching card game

Register for E&O newsletter

On-demand modules with completion certificate

Self-guided workshops

YouTube and LabTube channels

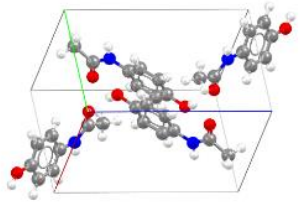
A new docking card game

CSDU

- On-demand modules to learn how to use the CSD Software at your own pace.
- Completion certificate after a final quiz!

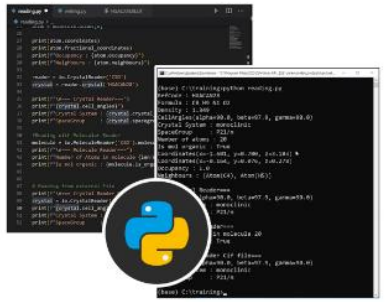
UWatch ••• UTry ••• UTest

Visualisation 101 - Visualising structural chemistry data with Mercury



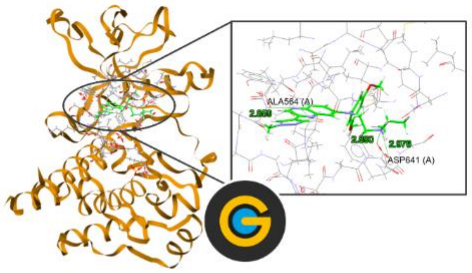
Begin module

Programmatic access to the CSD 101 – CSD Python API



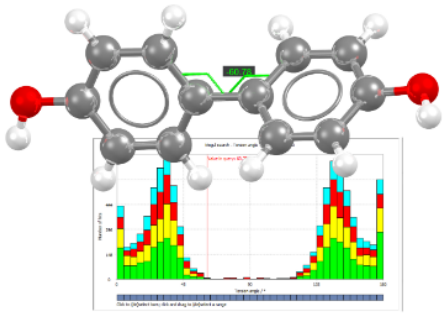
Begin module

Protein-ligand docking 101 - Running a simulation in GOLD



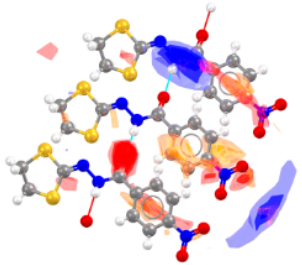
Begin module

Analysing molecular geometries 101 - basics of Mogul



Begin module

Analysing intermolecular interactions 101 - Full Interaction Maps



Begin module

https://www.ccdc.cam.ac.uk/Community/educationalresources/CSDU/

CCDC

CCDC Engagement Grants

Engage, inspire, share!

- Do you wish to inspire others with your love of crystallography or structural science?
- CCDC Engagement Grants cover costs for you to produce resources or activities to increase schools and public engagement in crystallography and structural science.

https://www.ccdc.cam.ac.uk/Community/awardsandsponsorship/ccdc-engagement-grants/

CCDC