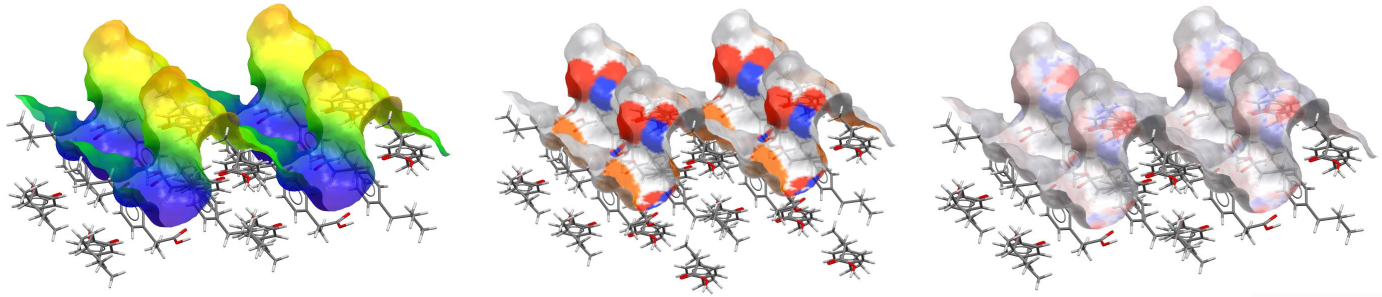


How to visualise and analyse surfaces
Using CSD-Particle in Mercury

CCDC Virtual Workshop

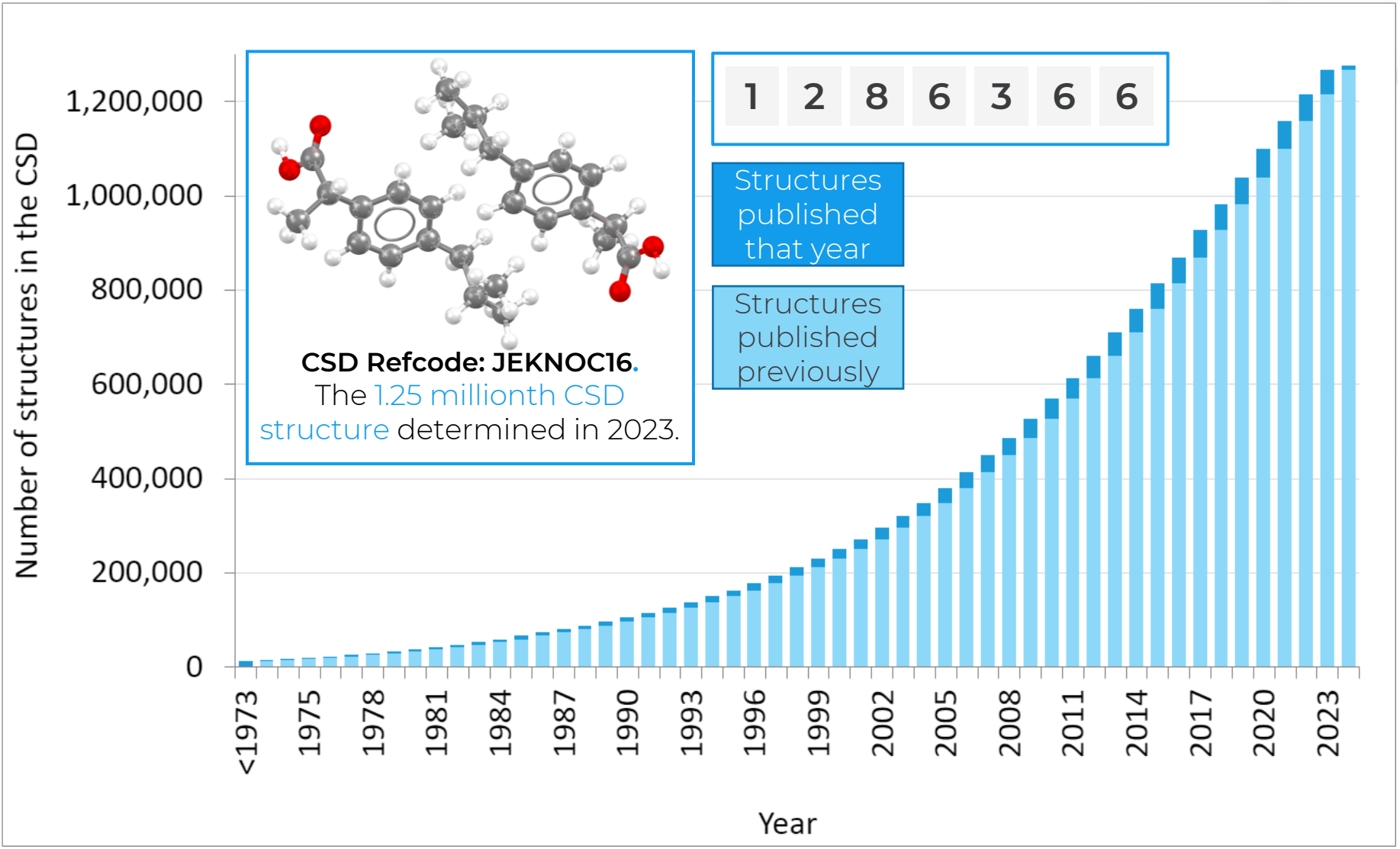
16th April 2024

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 the Surface Analysis and Slip Planes tools to identify key particle properties.

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%

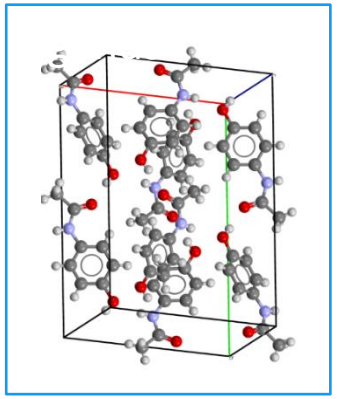
Polymeric: 11%

Single Component
58%

Multi Component
42%

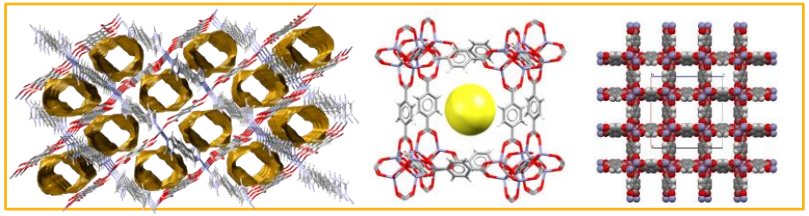
Organic

- Drugs
- Agrochemicals
- Pigments
- Explosives
- Protein ligands



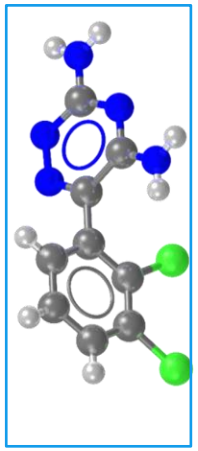
Metal-Organic

- 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



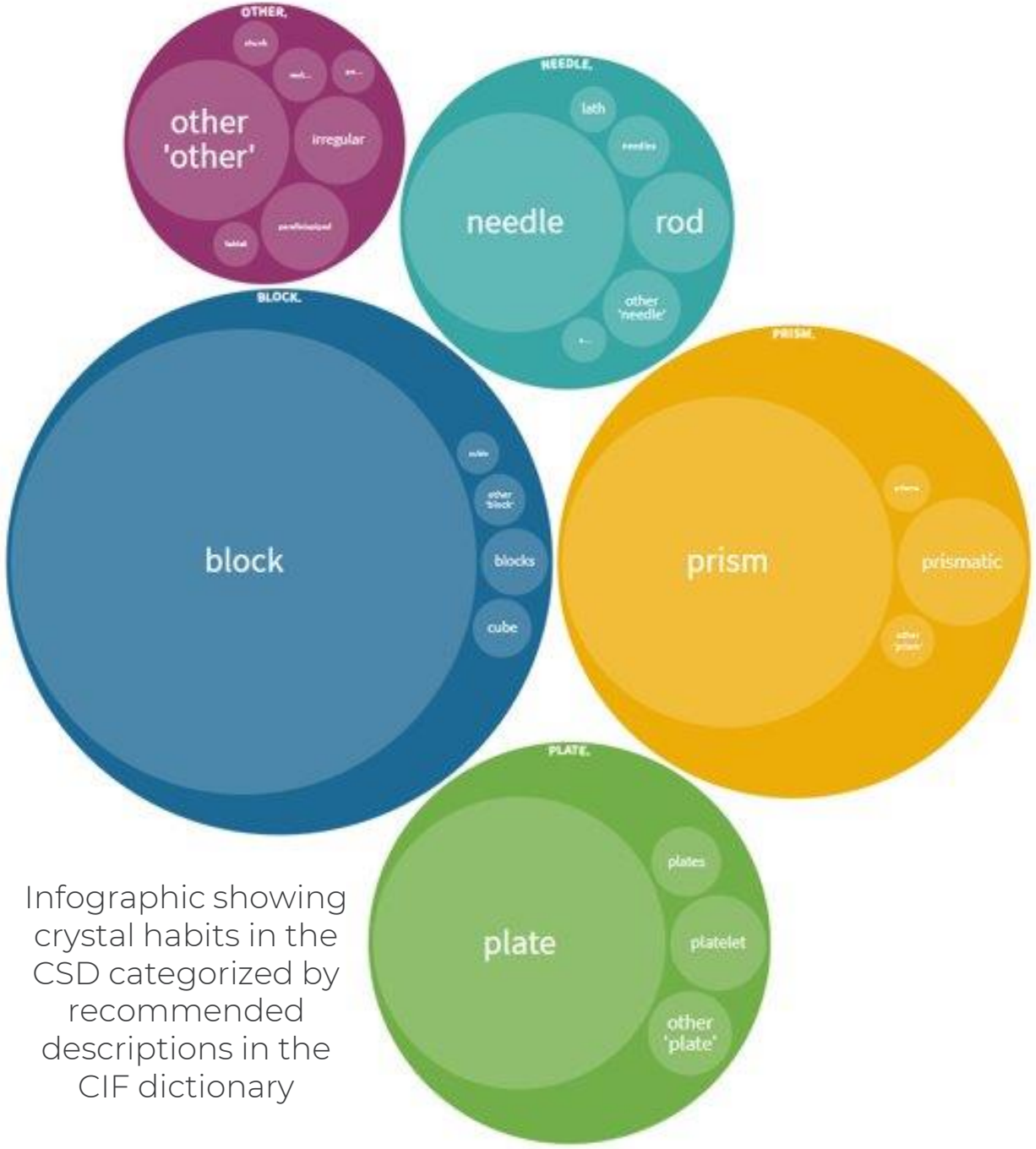
Links and subsets

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

Exploring the CSD

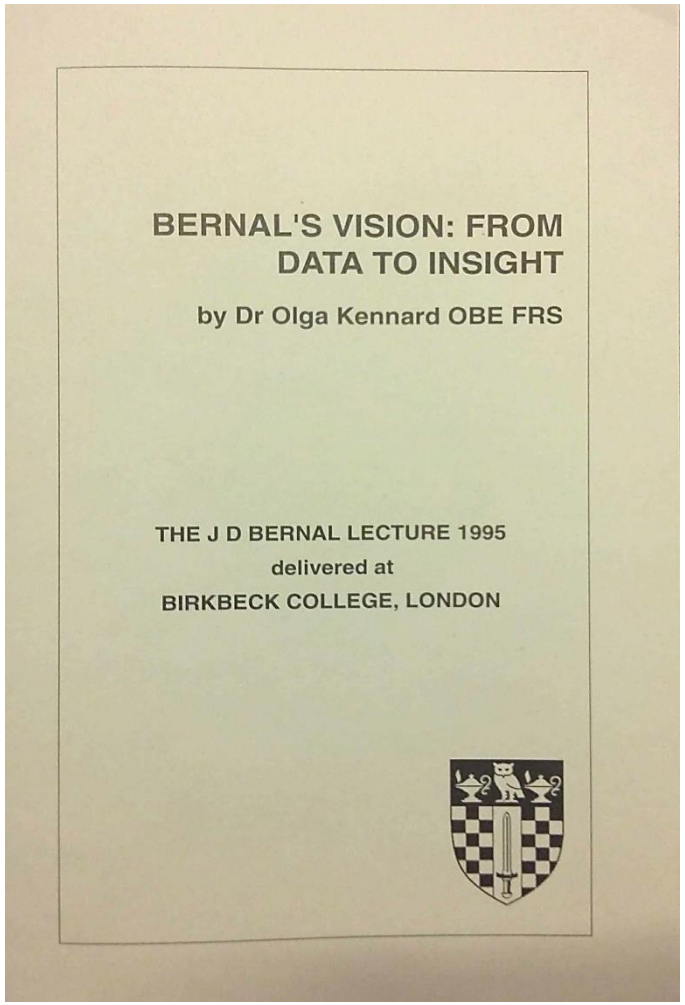
- >900,000 experimental crystal habits
- > 1 million structures
  - >94M 3D coordinates
- > 28 million bond lengths
  - >2M unique distributions
- > 40 million valence angles
  - >3M unique distributions
- > 14 million torsion angles
  - >800K unique distributions
- > 2 million rings
  - >400K unique distributions

Image created using the CSD Python API and Flourish



Infographic showing crystal habits in the CSD categorized by recommended descriptions in the CIF dictionary

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

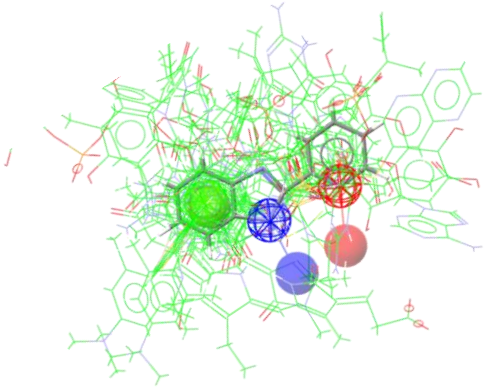
CSDCore.

Search, visualise, analyse and communicate structural data

Insights into molecular and crystal shape and interactions

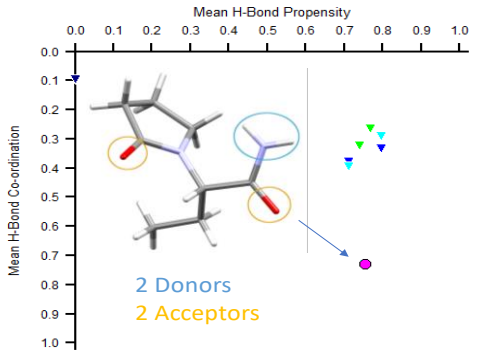
CSDDiscovery.

Design of new molecules



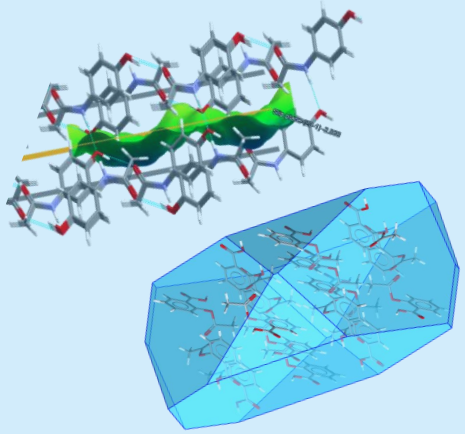
CSDMaterials.

Assessment of solid form stability and properties



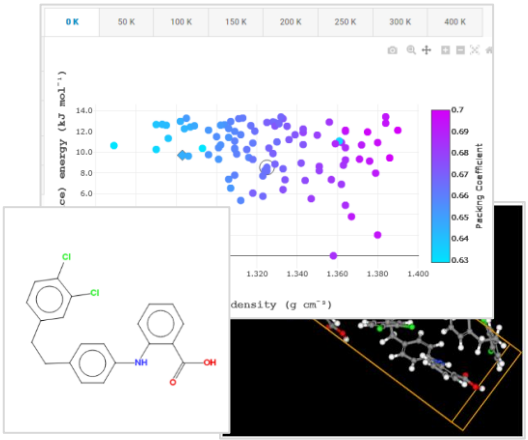
CSDParticle.

Anticipate particle properties and behaviour



CSDTheory.

Insights from predicted structure landscapes

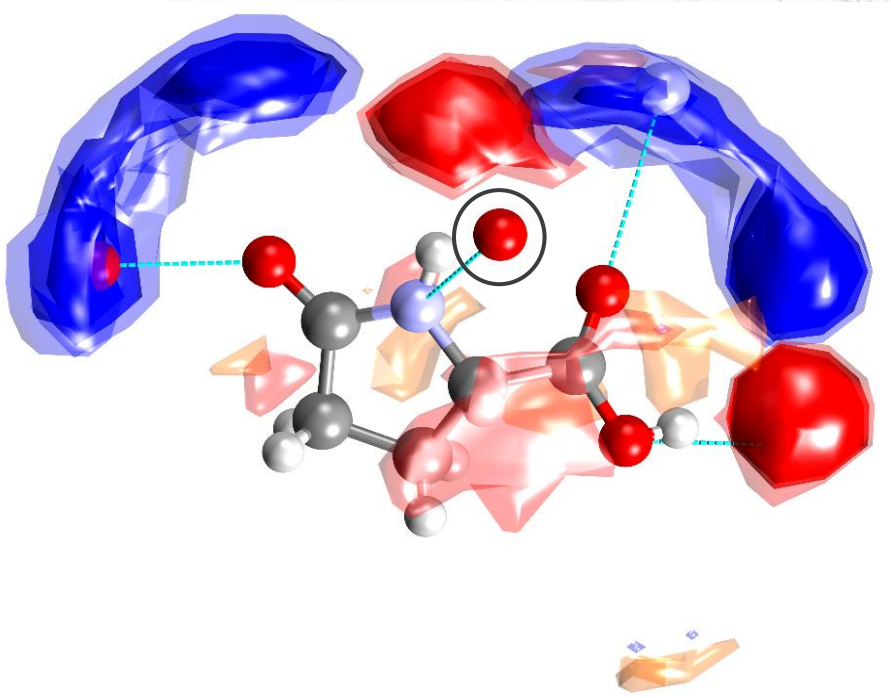


Medicinal & Computational Chemists ♦ Crystallographers & Structural Biologists ♦ Solid Form & Crystallisation Scientists

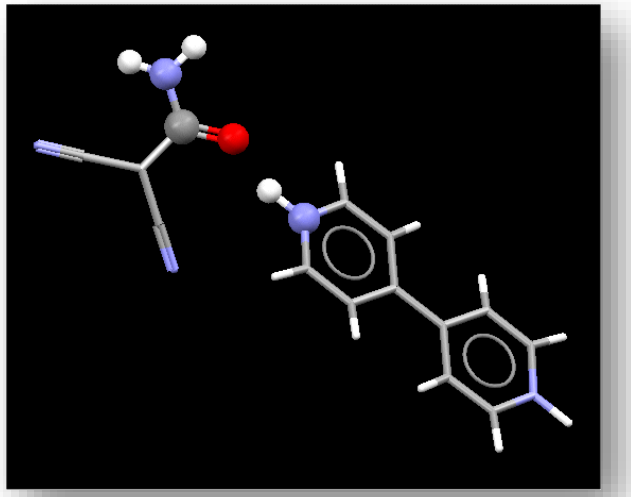
CCDC

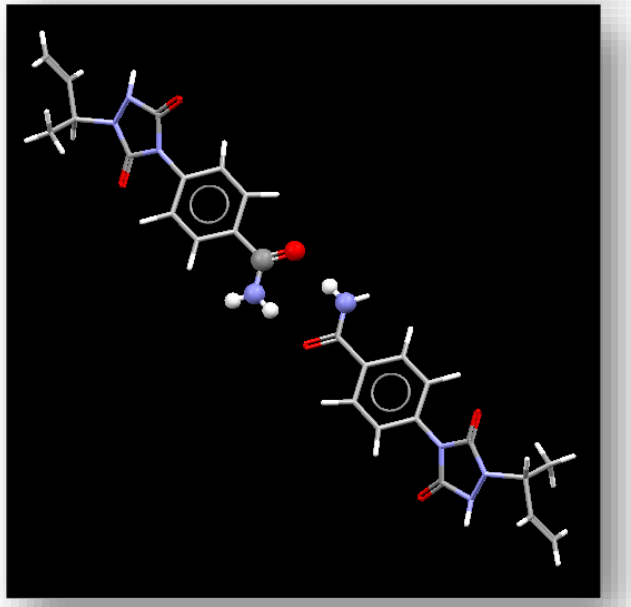
Key concepts - Full Interaction Maps

- 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



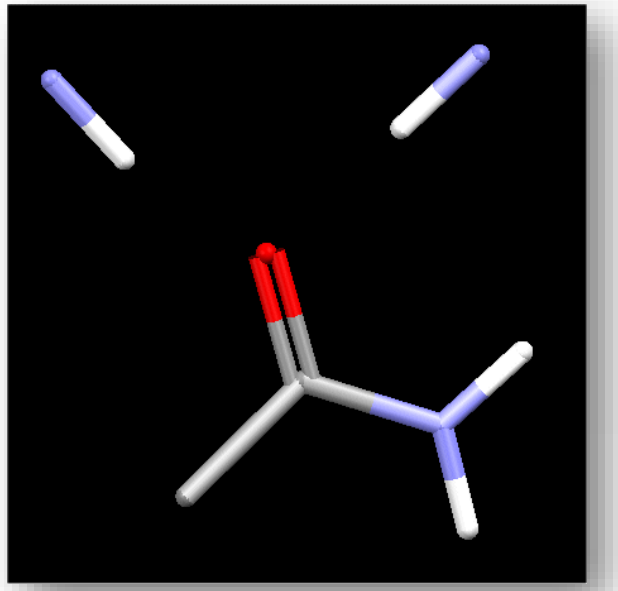
Key concepts - Full Interaction Maps

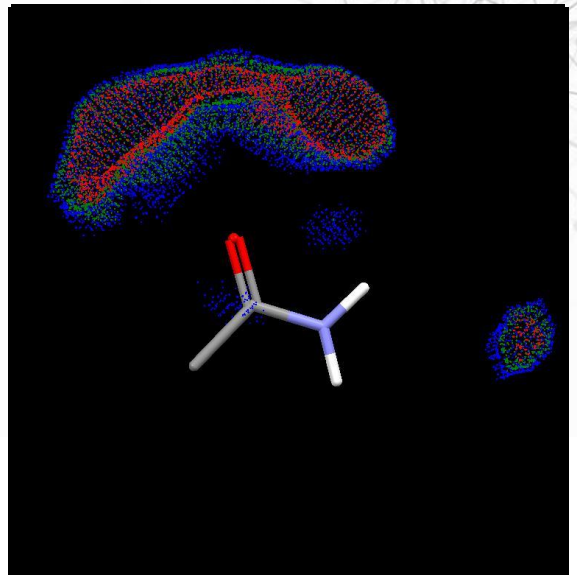




central group: -$CONH_2$

contact group: NH





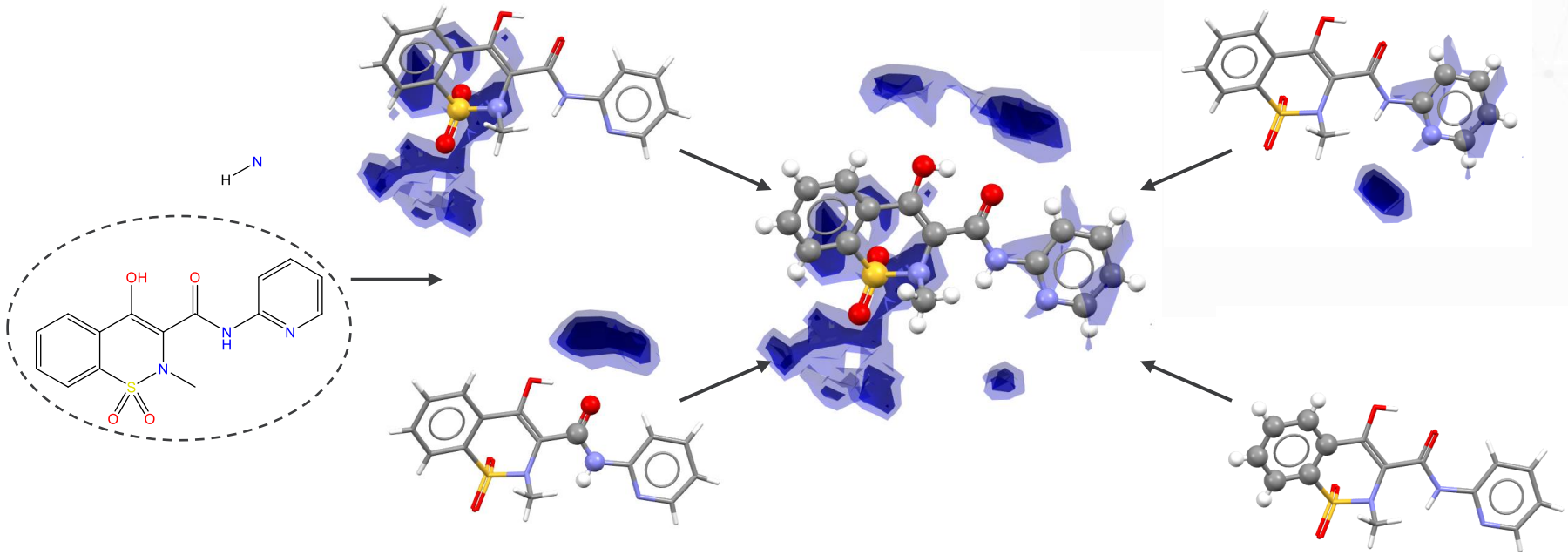
Search for structures containing desired contact

Superimpose hits and display as scatterplots or contour plots

CCDC

Key concepts - Full Interaction Maps

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



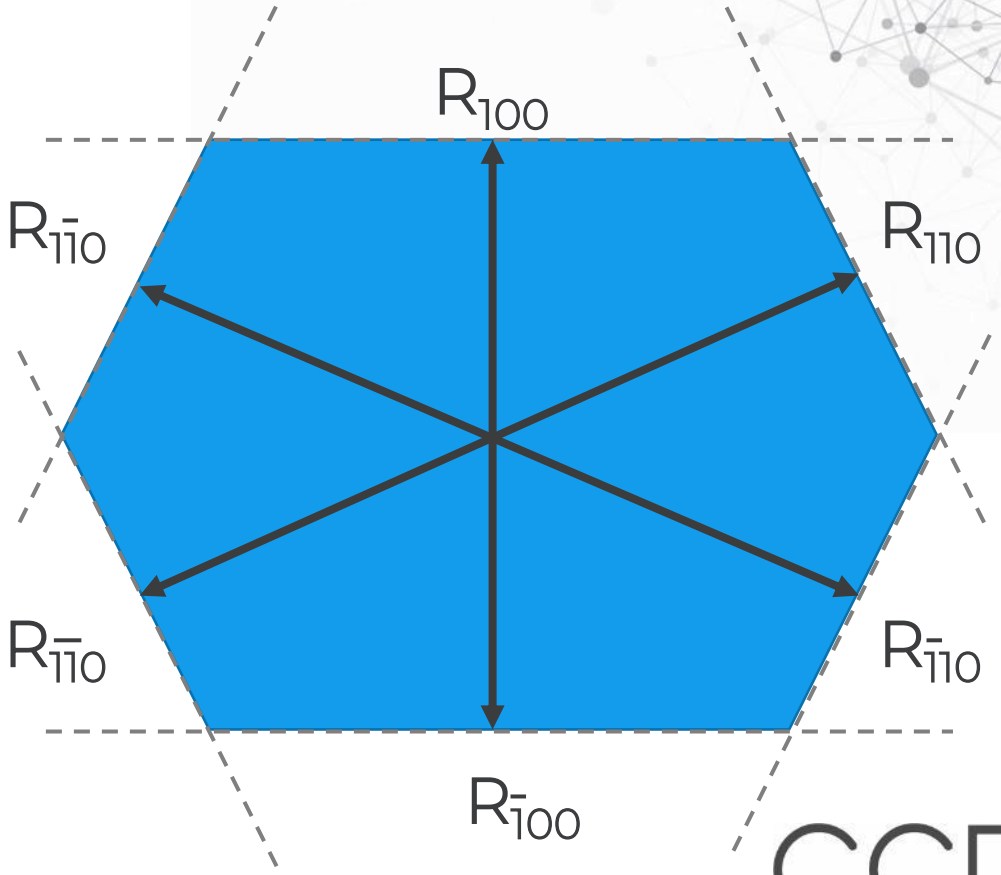
- Multiple maps can be generated for different probes

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

CCDC

Key concepts - How do crystals grow?

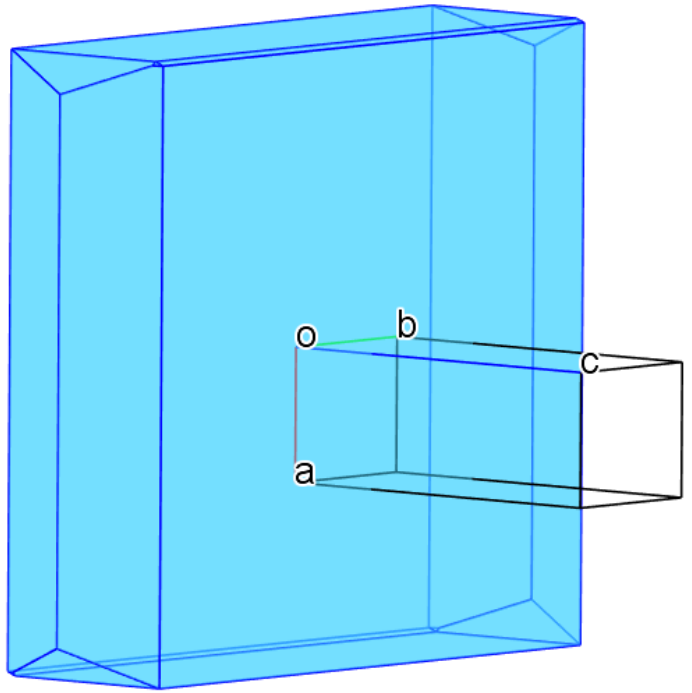
- Depends on relative growth rates
  - R_{hkl}
  - *Faster* growing faces are *smaller*
- Growth rates are dependent on many things
  - Supersaturation
  - Solvents
  - Impurities



CCDC

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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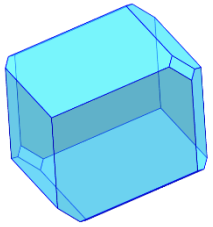
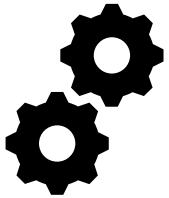
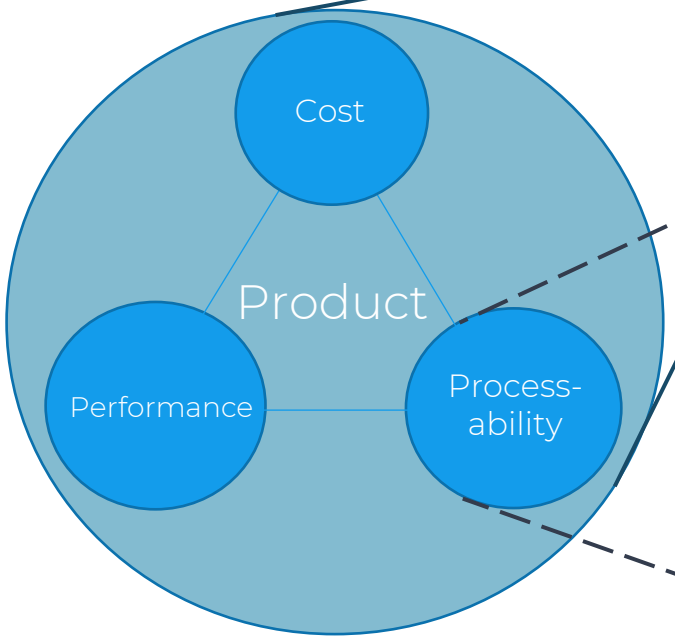
The field

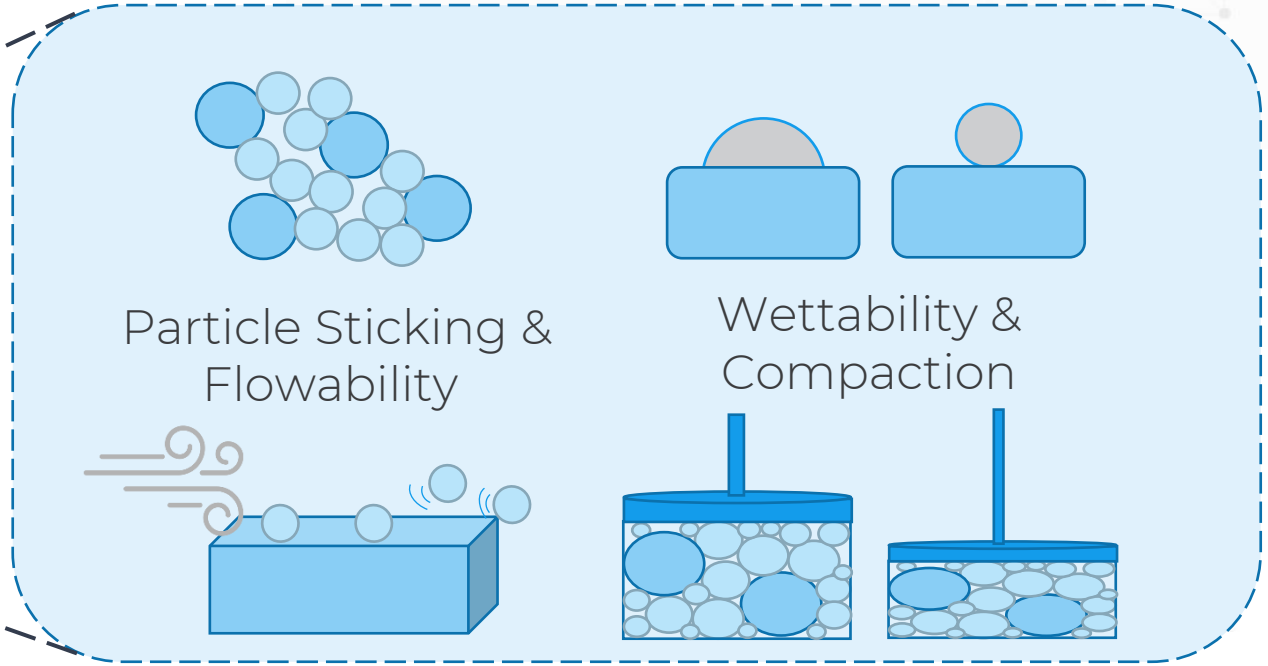


Particle

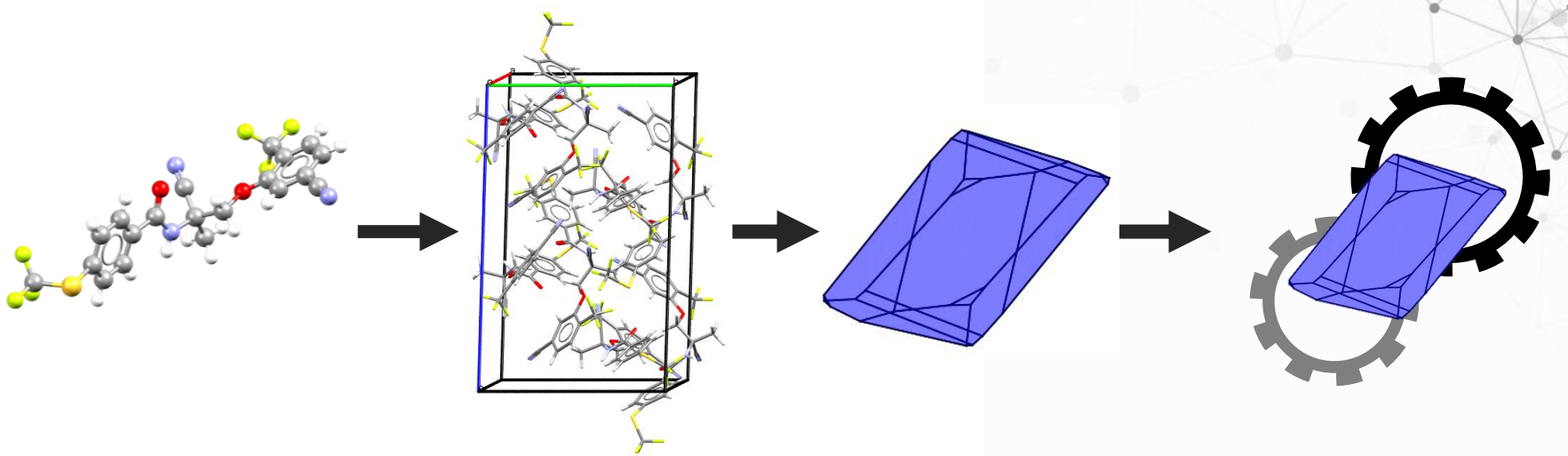


Product





From Solid Form to Particle Properties



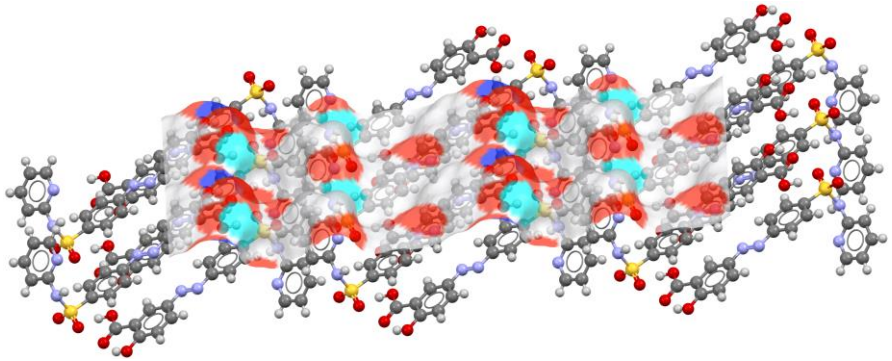
Molecule Form Particle Properties

Solid Form Informatics

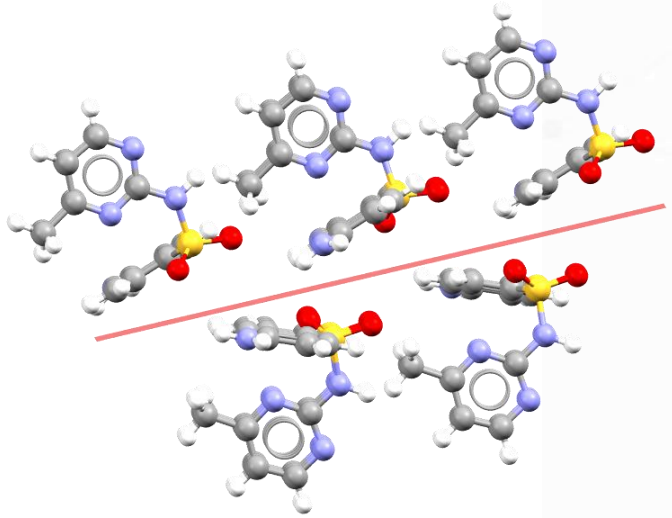
Particle Informatics

CCDC

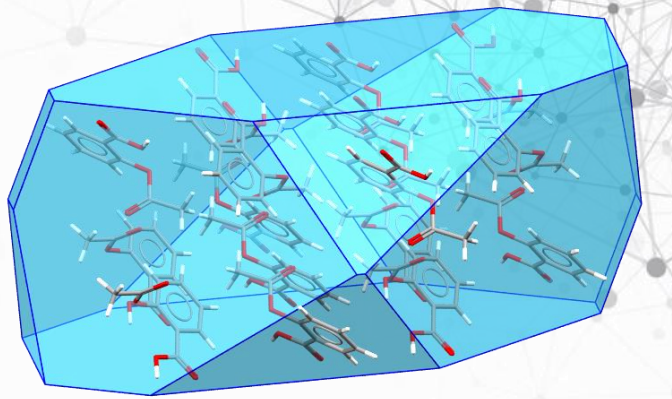
Particle Informatics



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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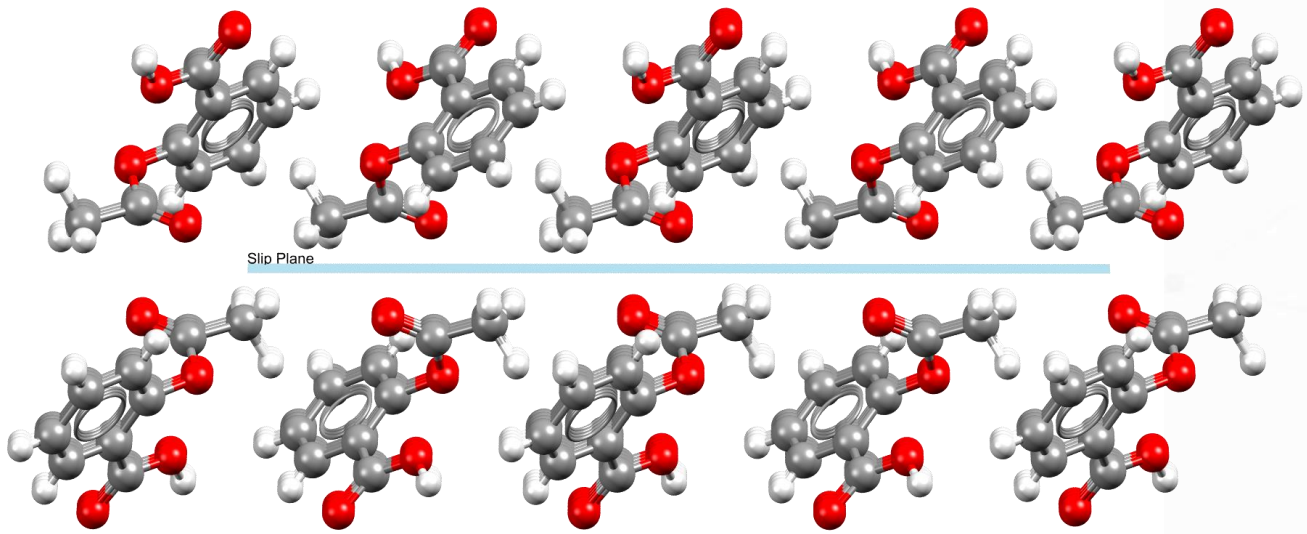
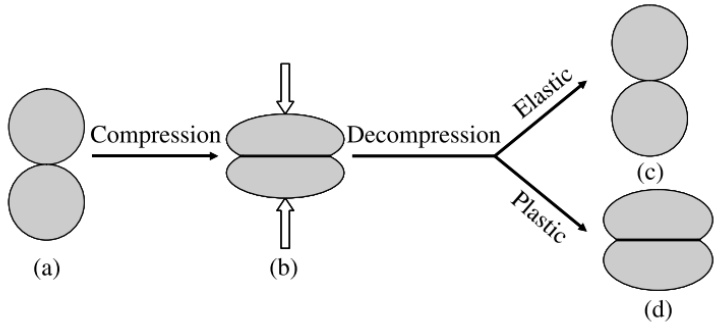


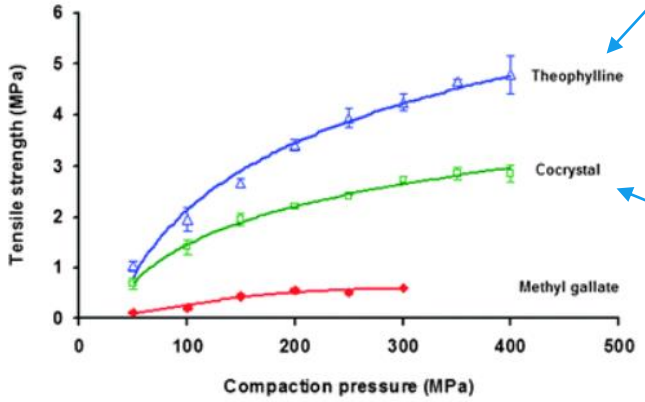
Slip Planes

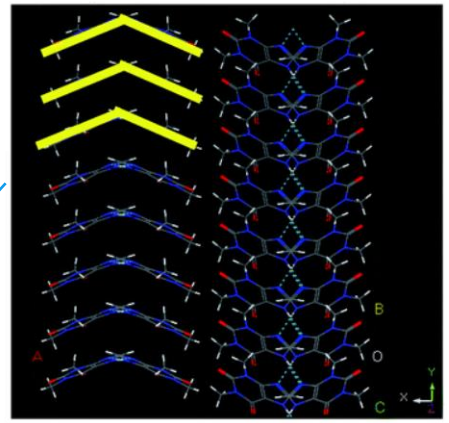
- Identification of Potential Slip Planes
- Analysis of Hydrogen Bonding Network

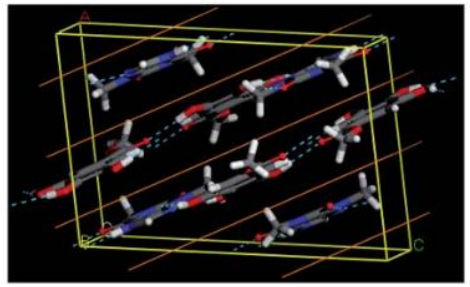
CCDC

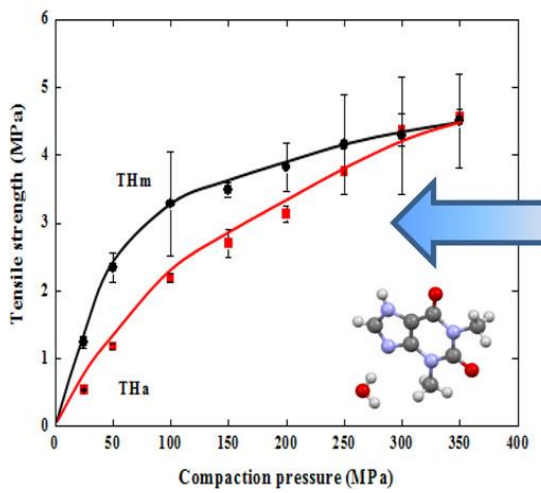
Compaction and bending

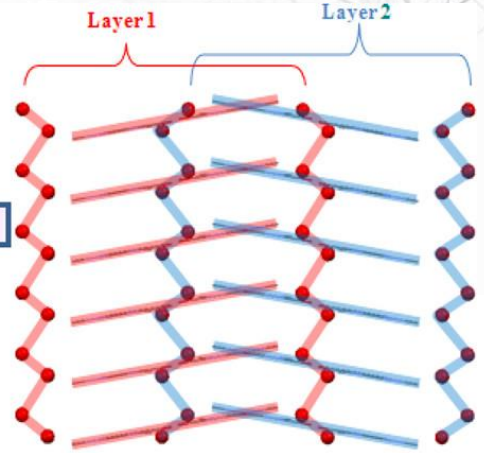








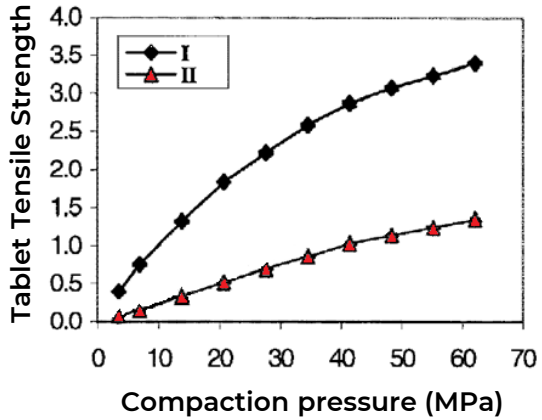


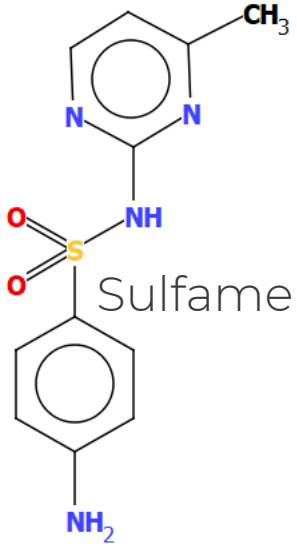


S. Chang and C. C. Sun *Molecular Pharmaceutics* 2017 14 (6), 2047-2055 10.1021/acs.molpharmaceut.7b00124

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

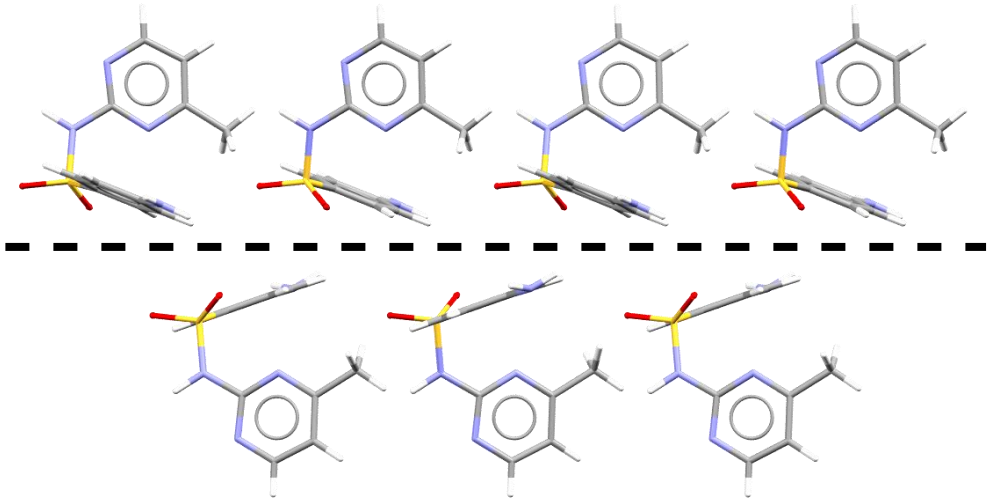
Compression and slip planes



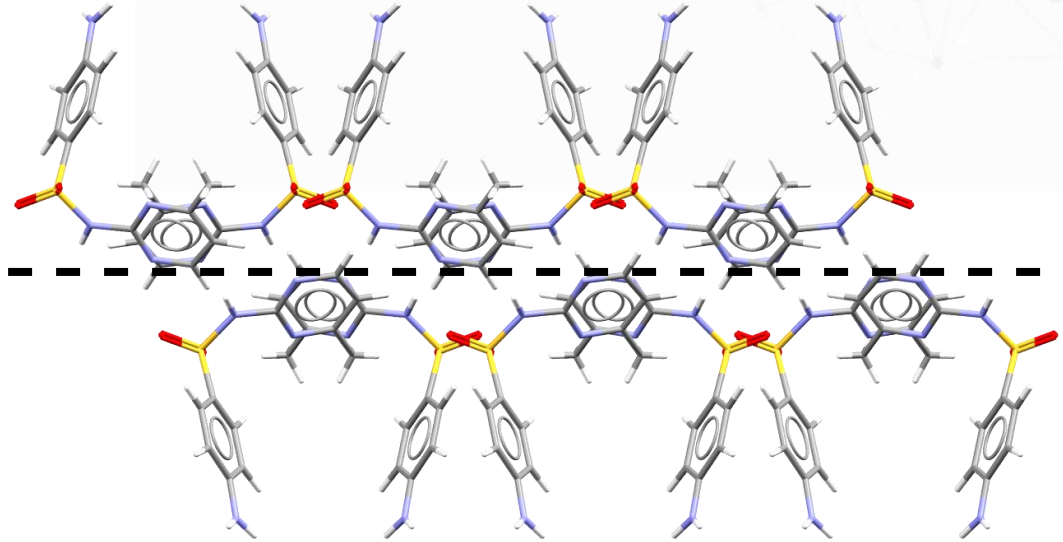


Sulfamerazine

Form I



Form II



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

C.C. Sun, *J. Adhes. Sci. Technol.* (2011), **25**, 483 - 499

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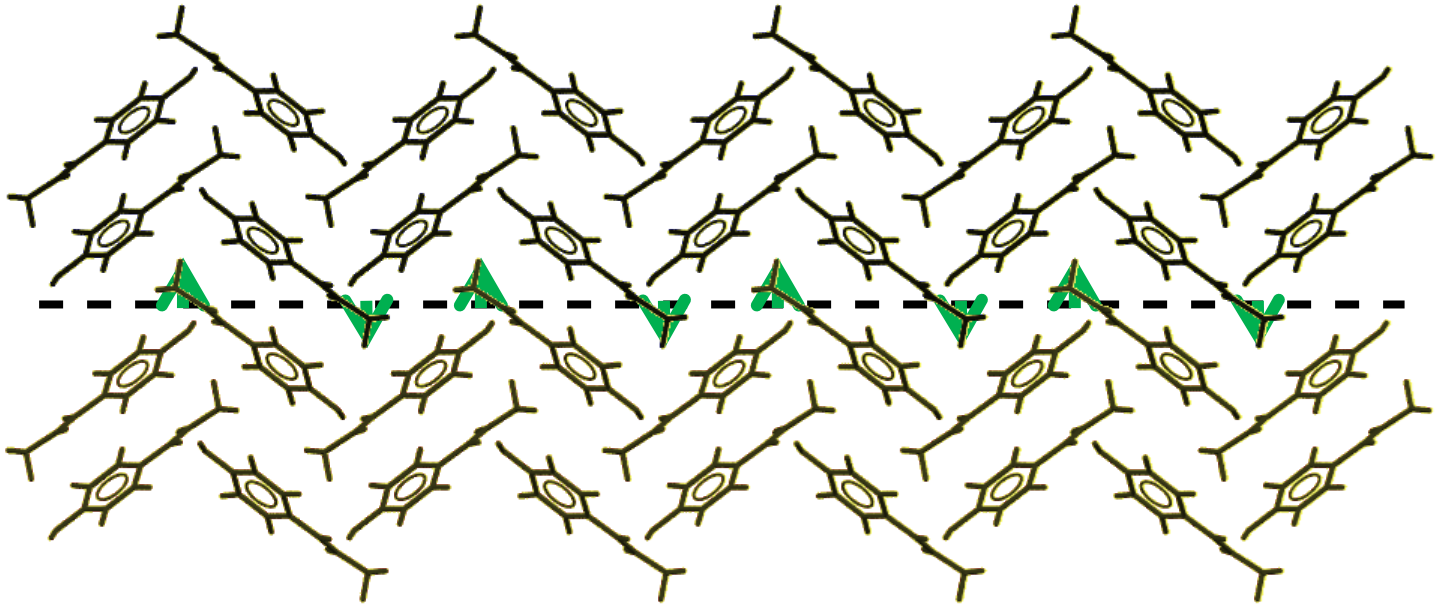
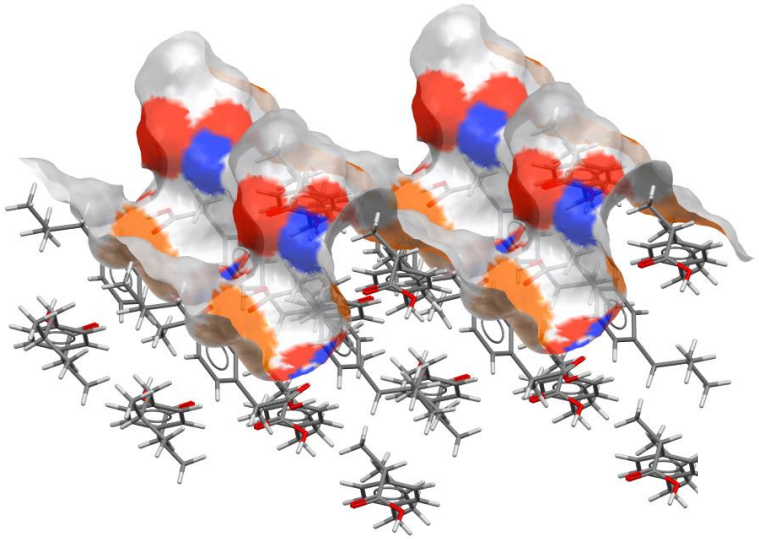
Predicting slip planes

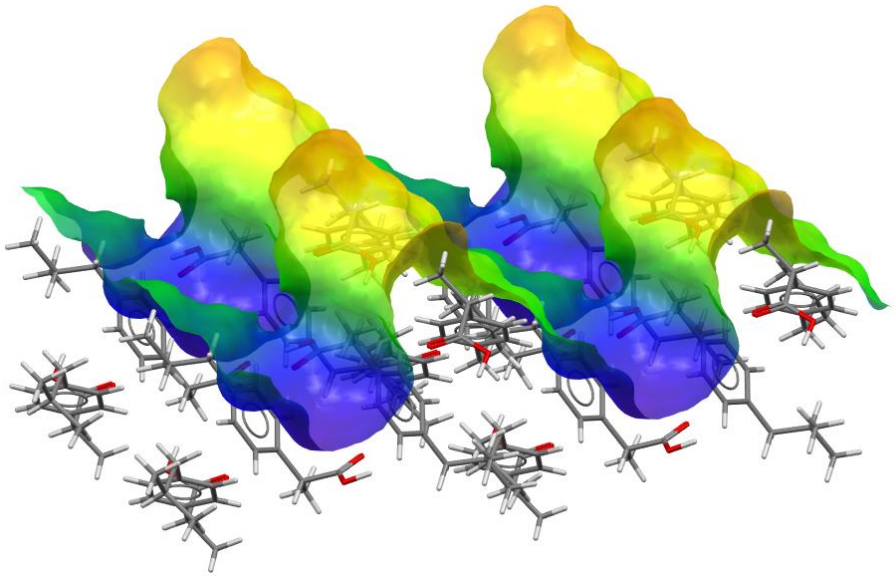


M. J. Bryant *et al.*, *CrystEngComm* (2018), **20**, 2698-2704

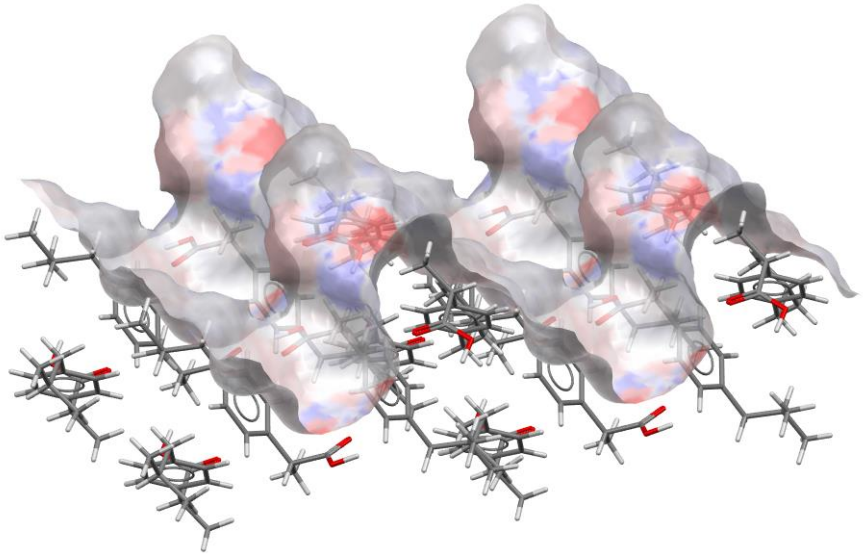


Surface Chemistry

Surface Analysis



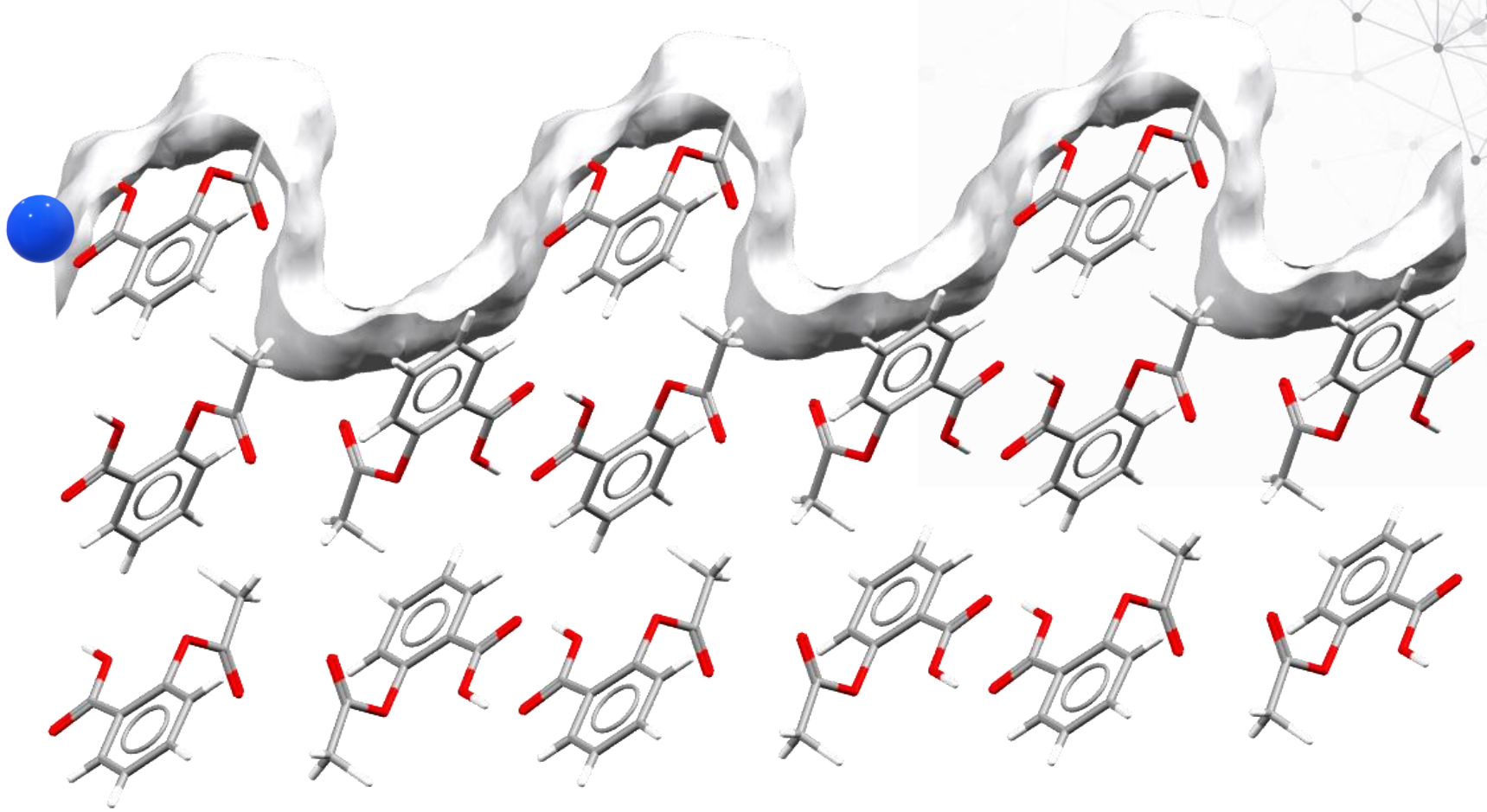
Surface Roughness



Surface Charge

CCDC

Surface Analysis



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

A. A. Moldovan and A. G. P. Maloney, *Submitted*

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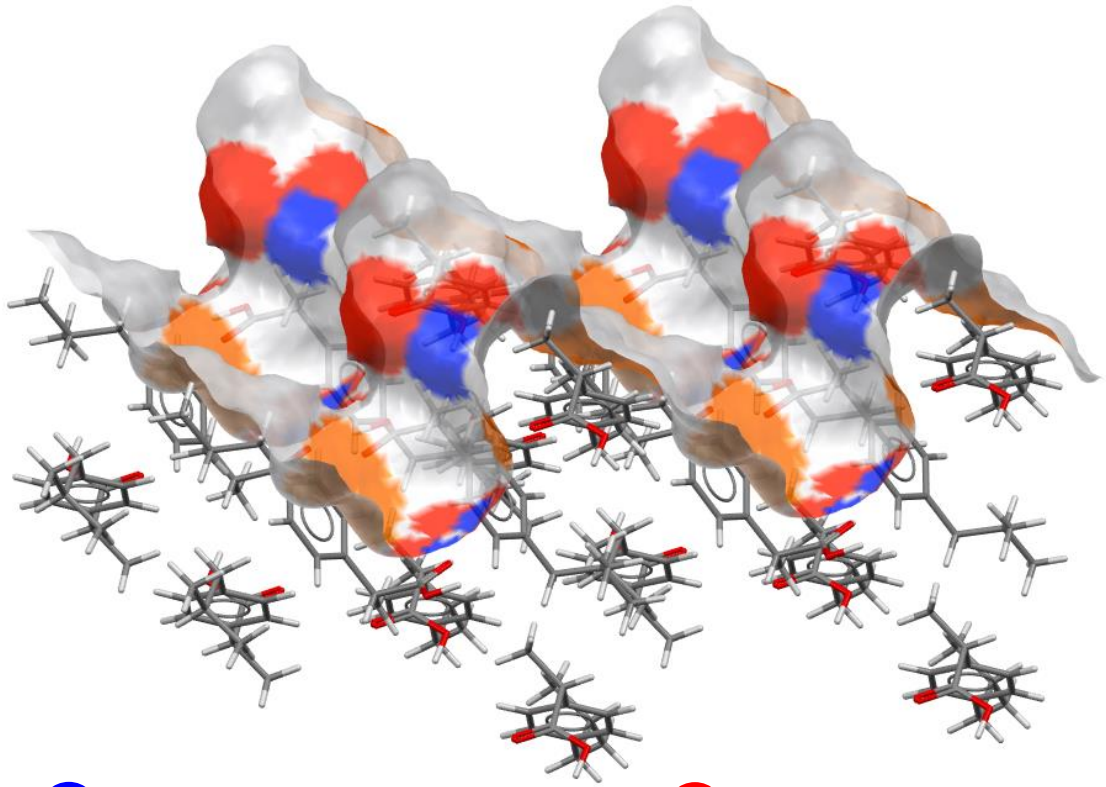
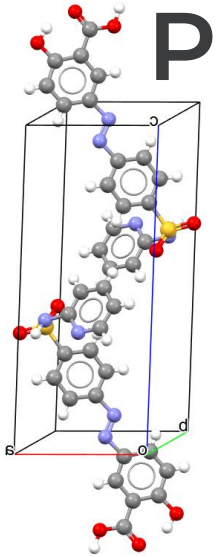
Surface Analysis

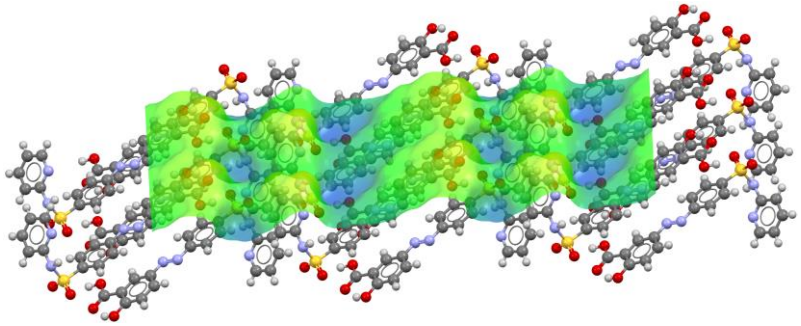


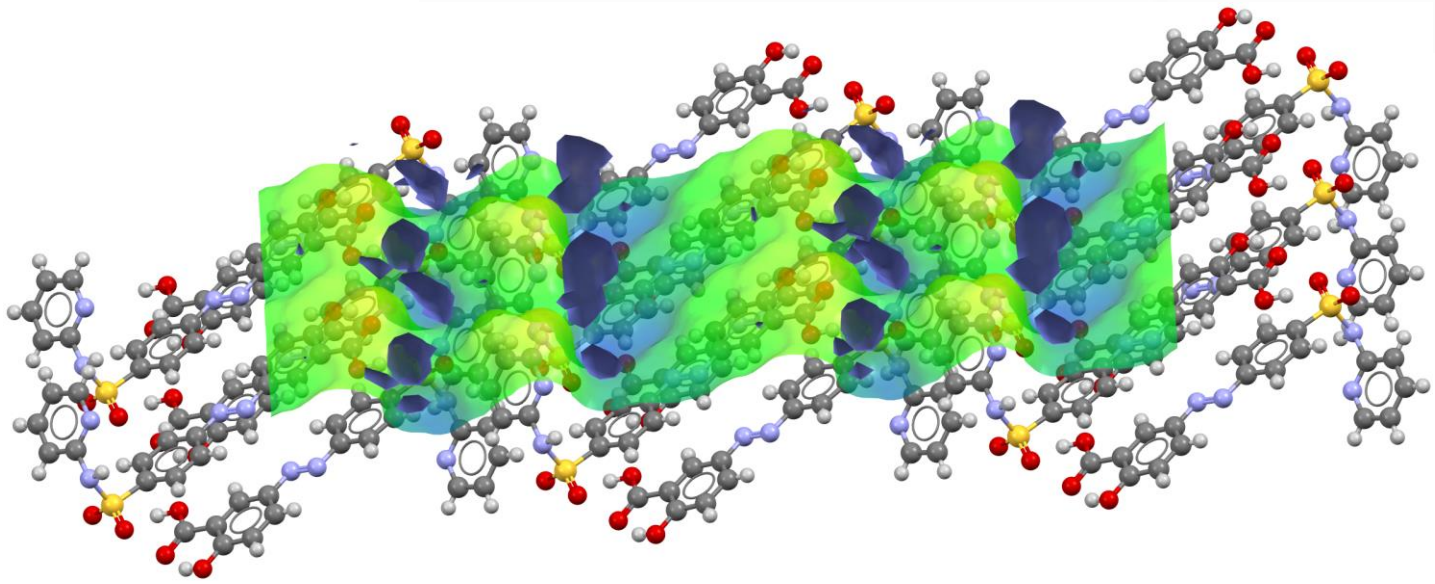
Descriptors	
Physical	Chemical
Reticular Surface Area	Hydrogen Bond Donor/Acceptor Density
Rugosity	Aromatic Bond Density
RMSD, Skewness, and Kurtosis	
Statistically Derived Interaction Data	

CCDC

Particle Informatics



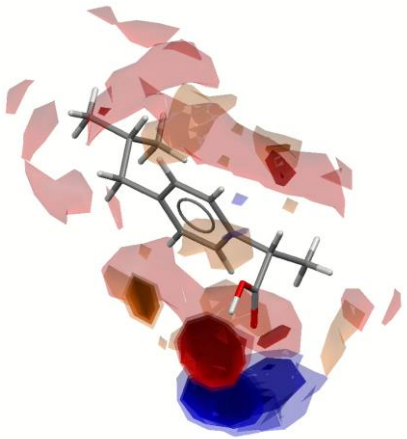




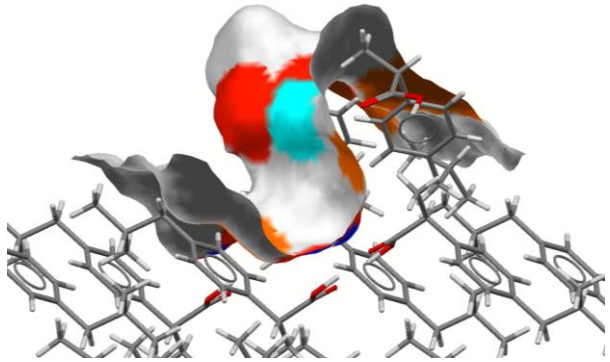
Descriptors	
Physical	Chemical
Reticular Surface Area	Hydrogen Bond Donor/Acceptor Density
Rugosity	Aromatic Bond Density
RMSD, Skewness, and Kurtosis	

FIMs on Surface

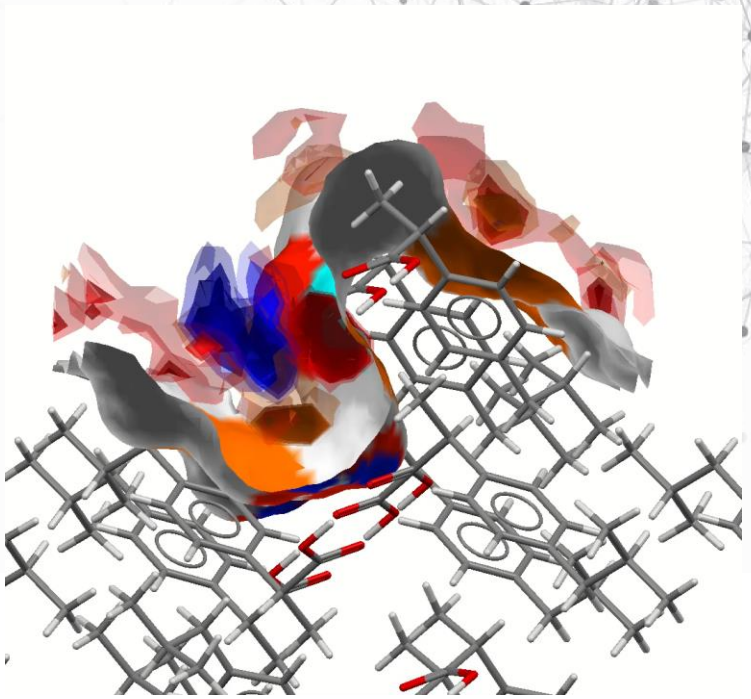
FIMs on Surface



FIM

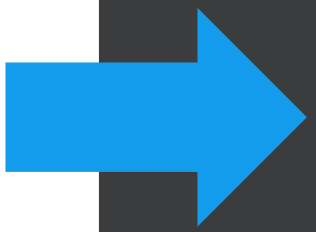


Surface



FIM on Surface

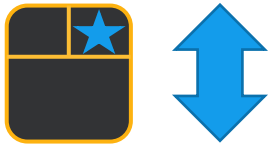
Accessing CSD-Particle through Mercury



Reminder: Basic navigation in Mercury

- Left mouse button and move – rotate molecules

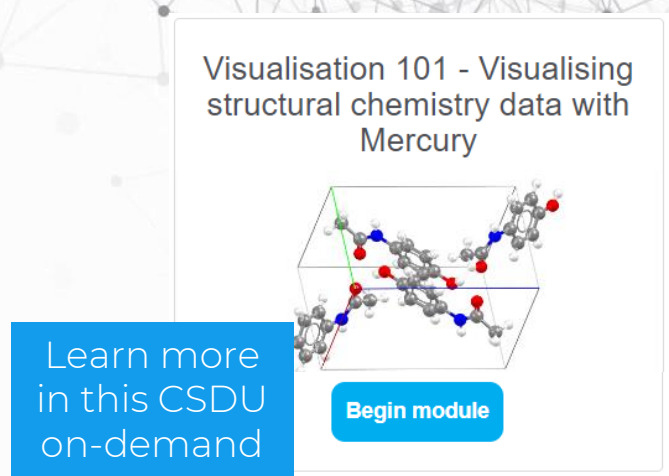
- Middle Mouse wheel – move molecules up and down



- 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

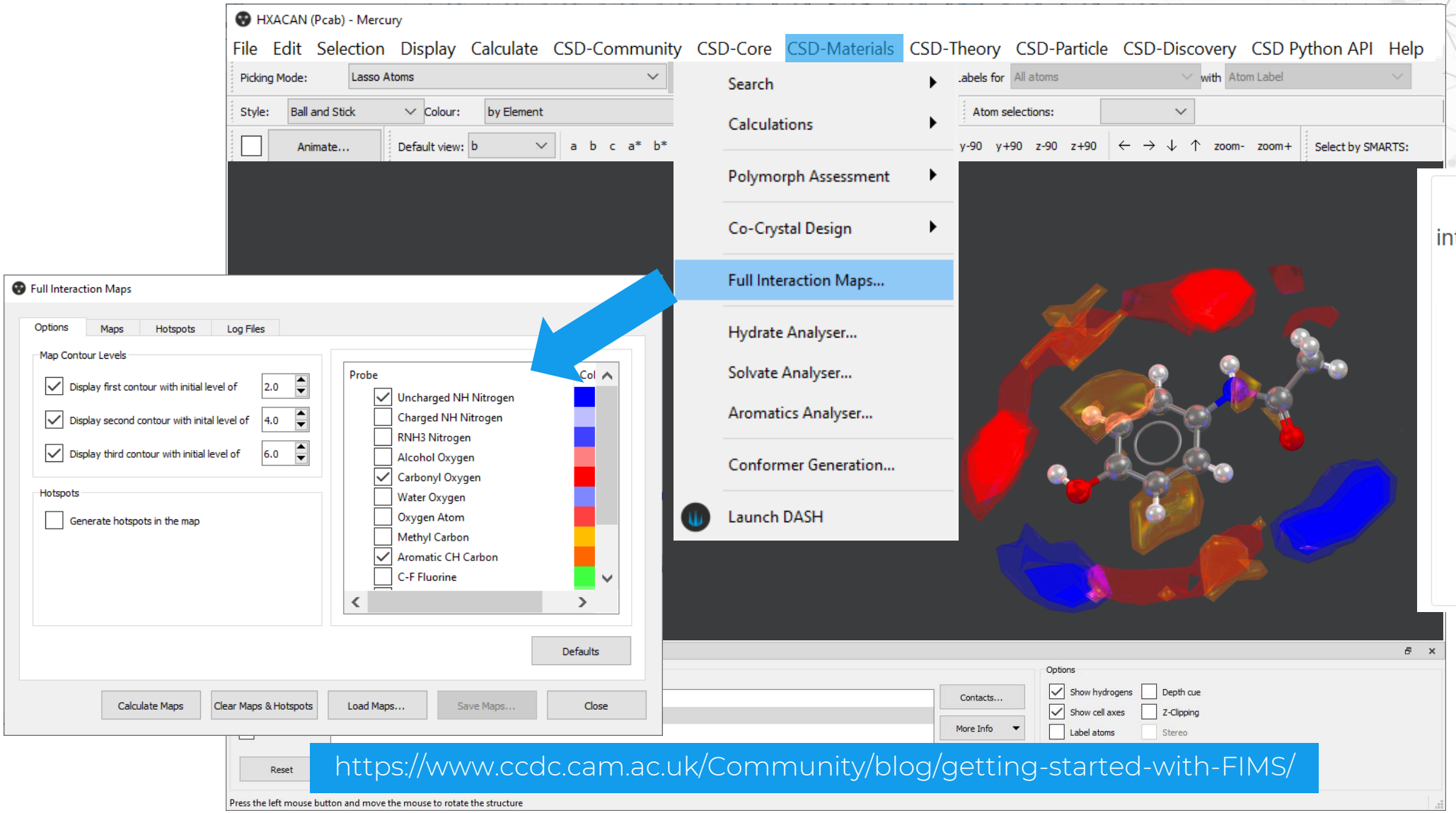
- Ctrl + Left mouse button and move - translate molecules



Learn more in this CSDU on-demand course

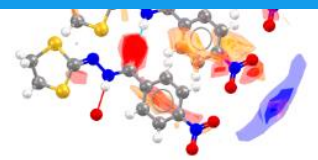
CCDC

Creating a Full Interaction Map



Analysing intermolecular interactions 101 - Full Interaction Maps

Learn more in this CSDU on-demand course

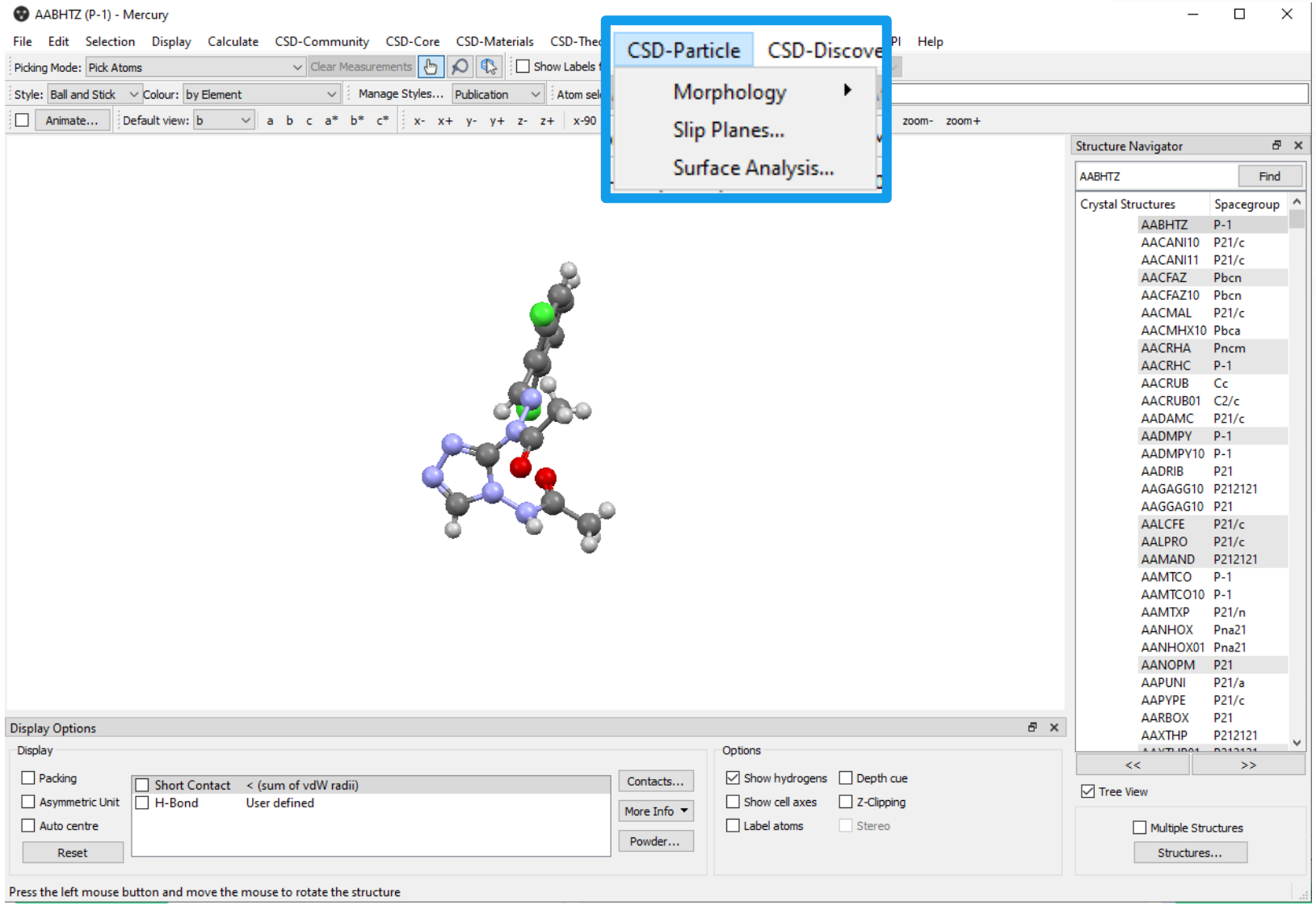


Begin module

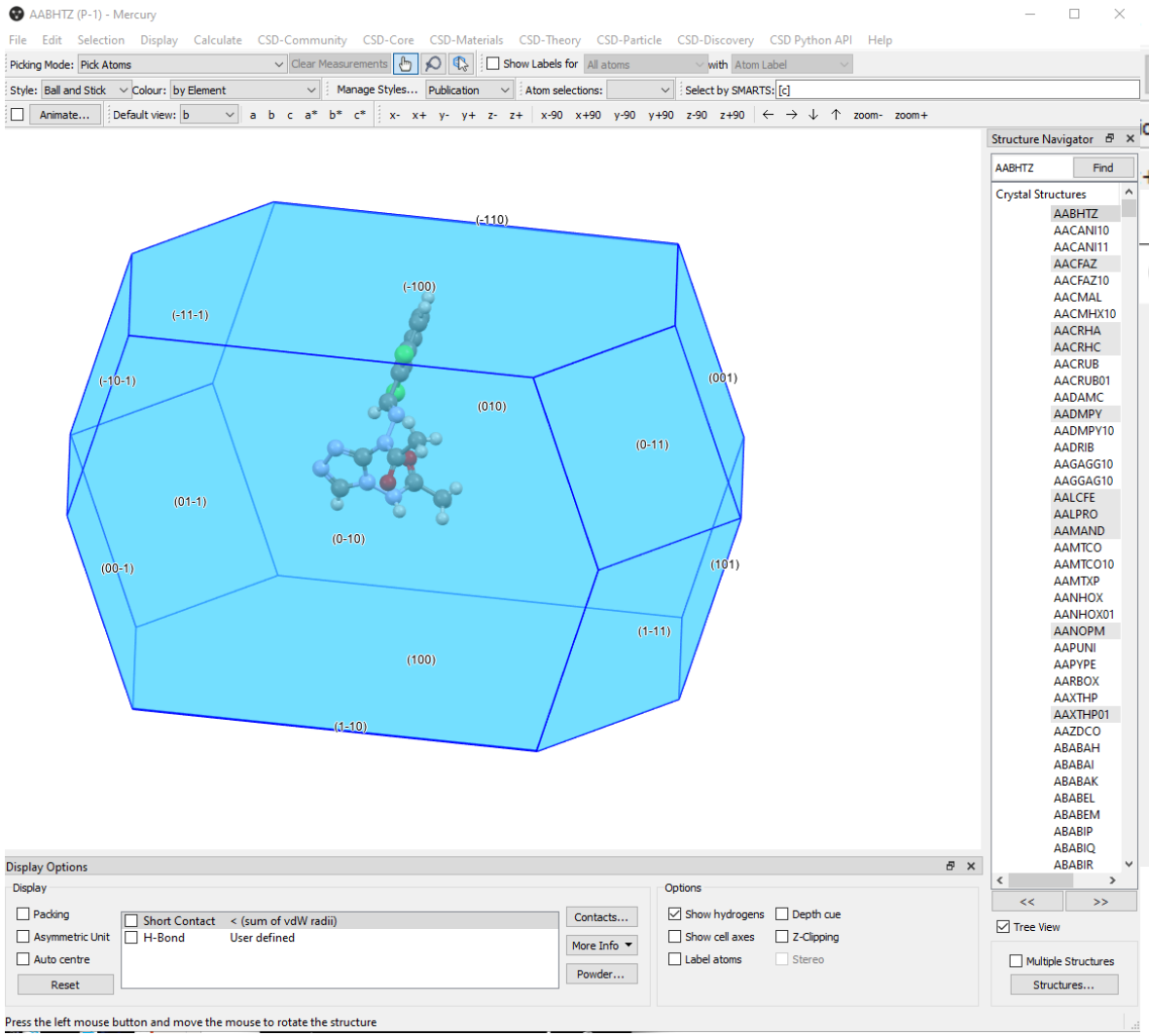
https://www.ccdc.cam.ac.uk/Community/blog/getting-started-with-FIMS/

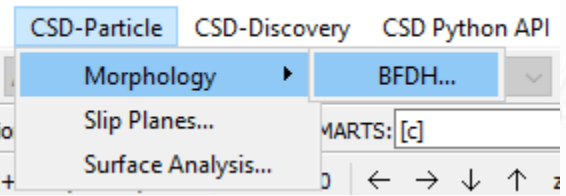
CCDC

CSD-Particle Menu

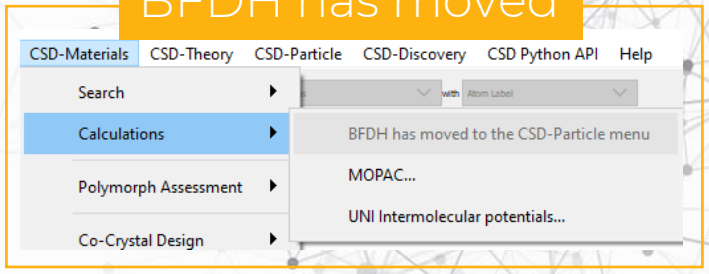


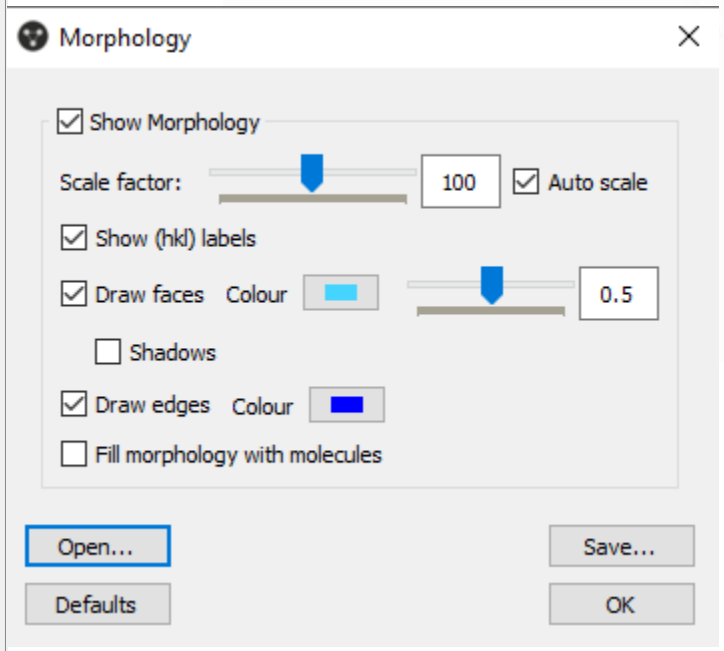
CSD-Particle – Morphology - BFDH





BFDH has moved



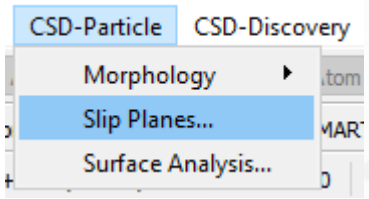


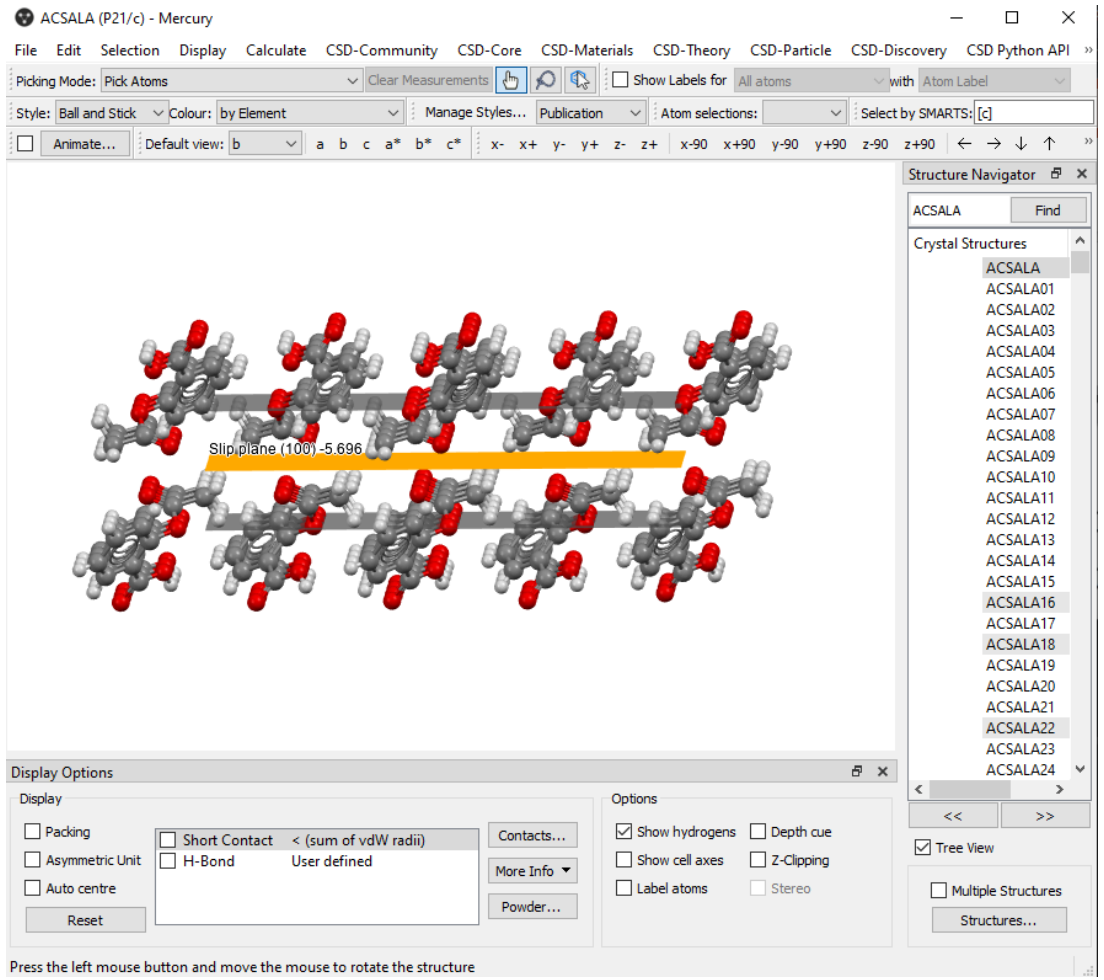
Display Options

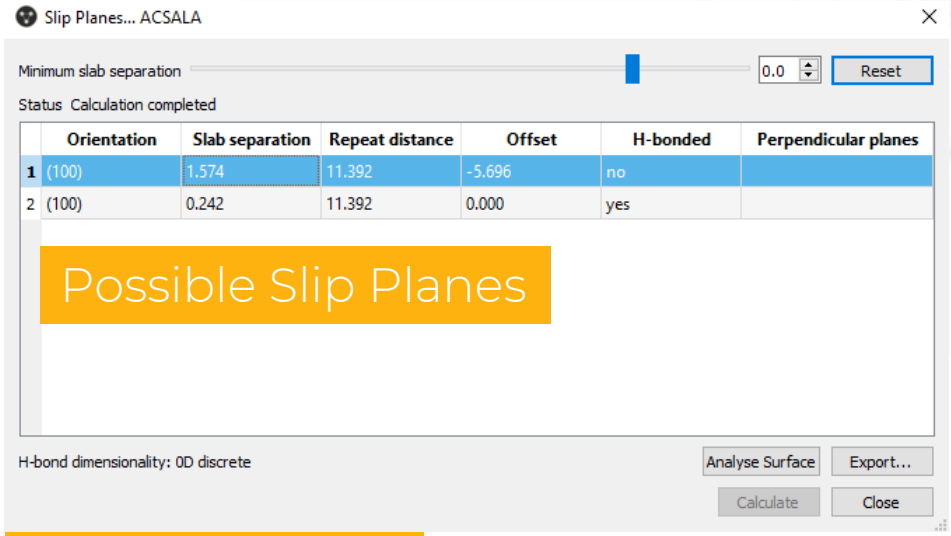
Save and Load

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

CSD-Particle – Slip Planes







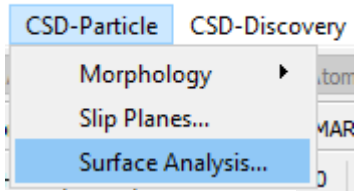
Possible Slip Planes

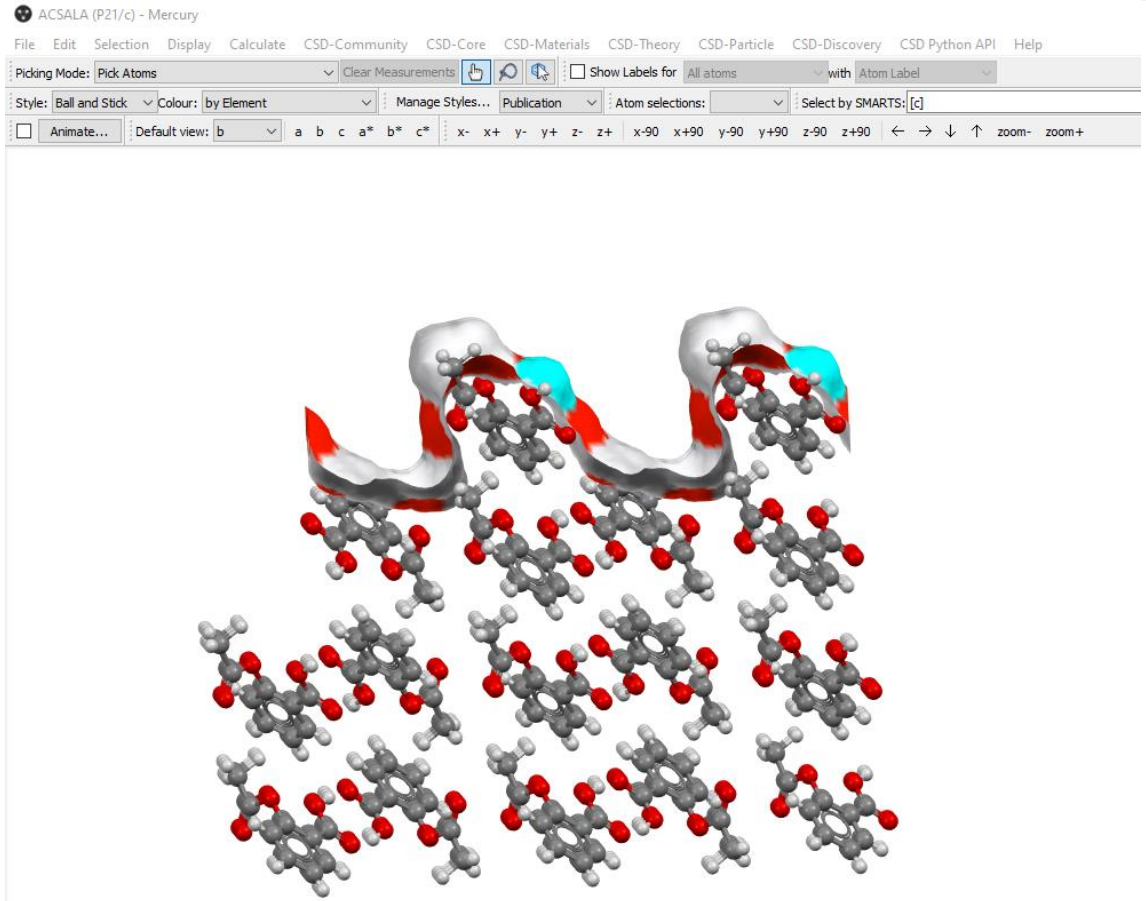
Export Table

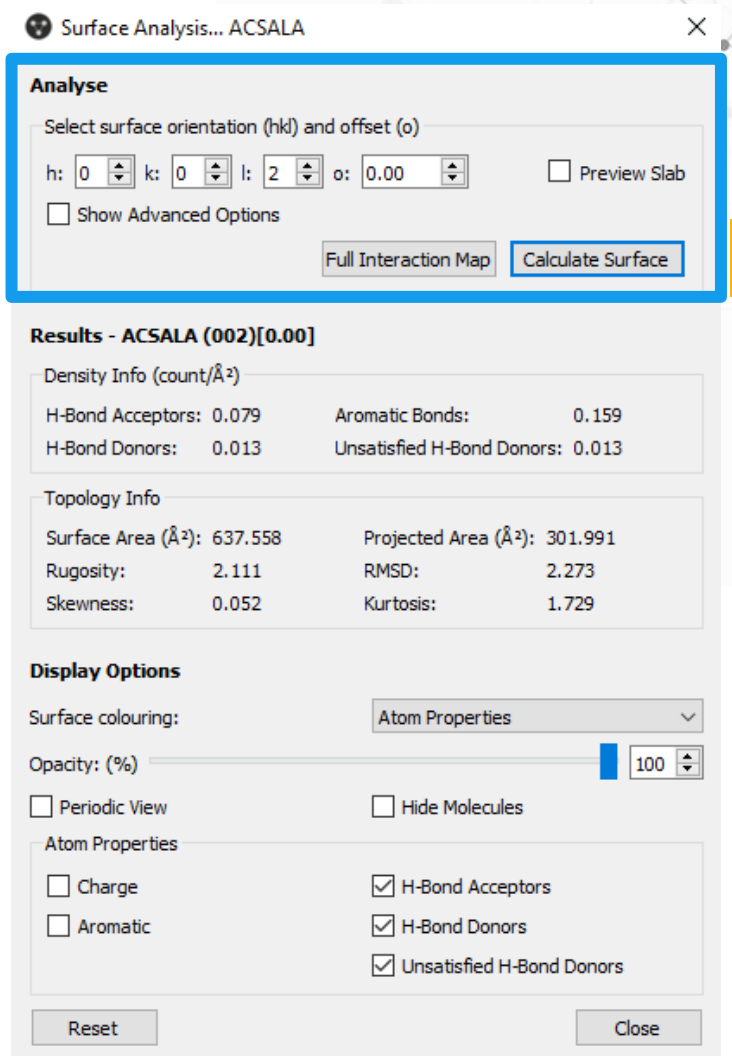
H-Bond System

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

CSD-Particle – Surface Analysis

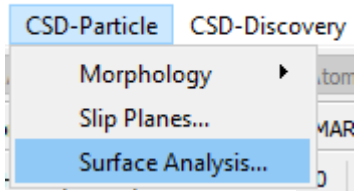


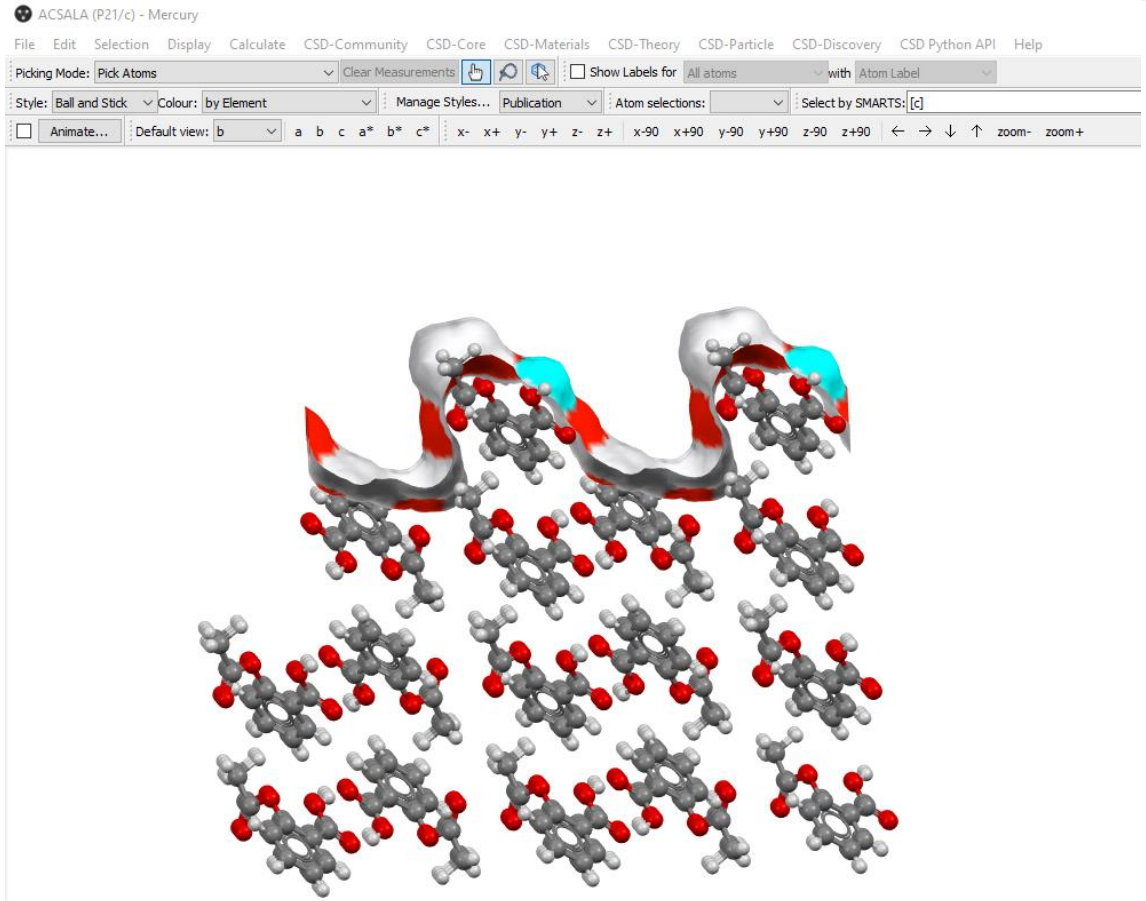


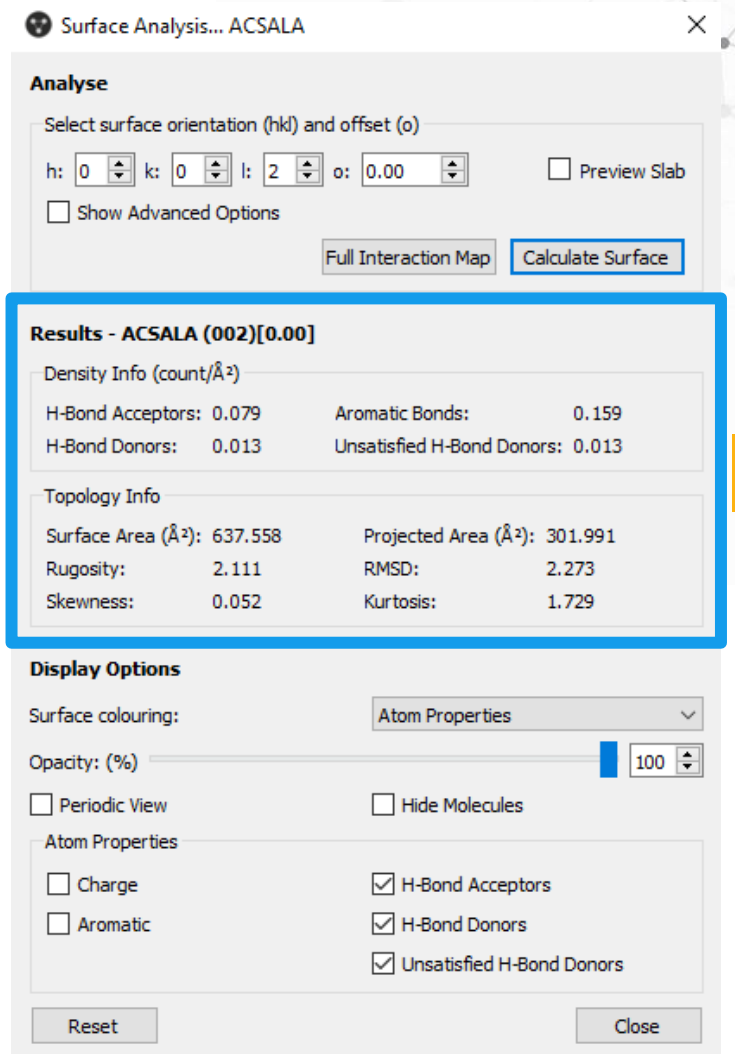


Input

CSD-Particle – Surface Analysis



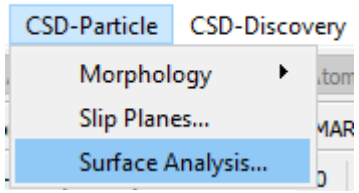


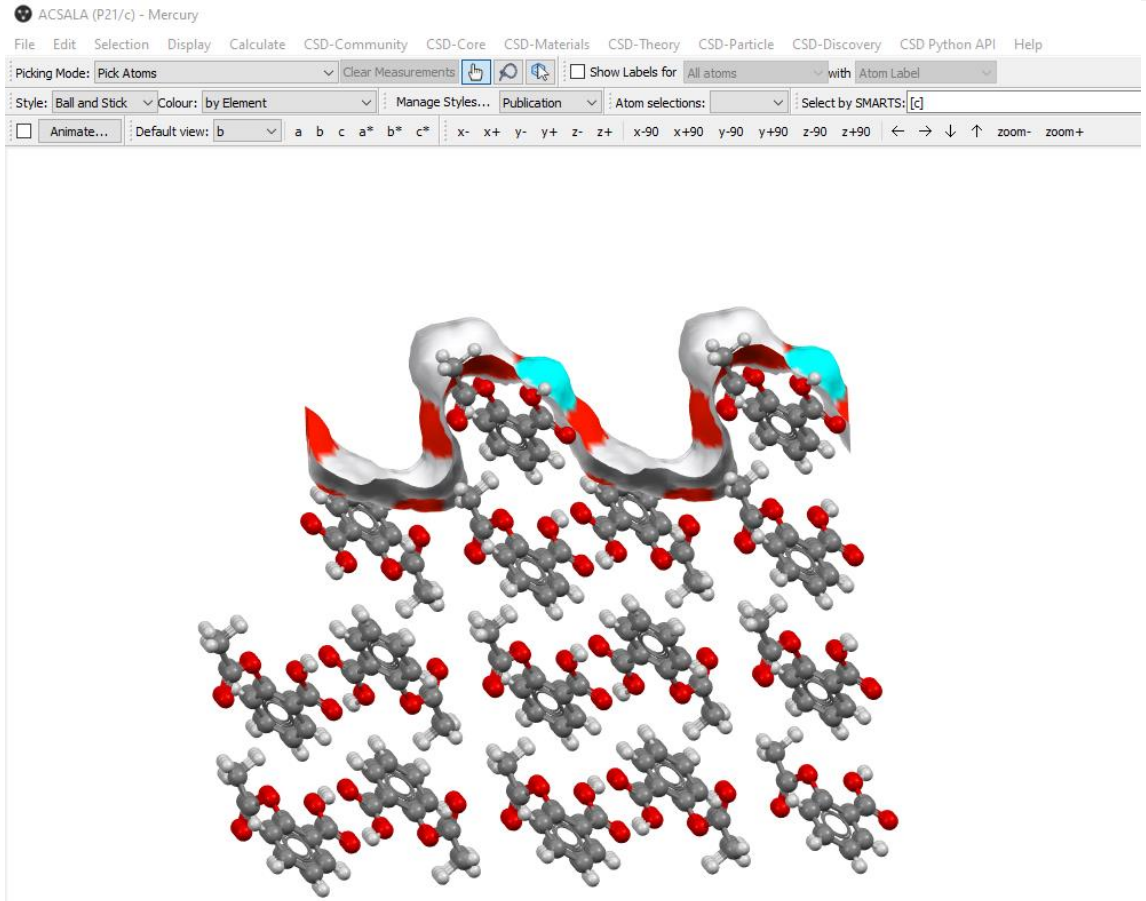


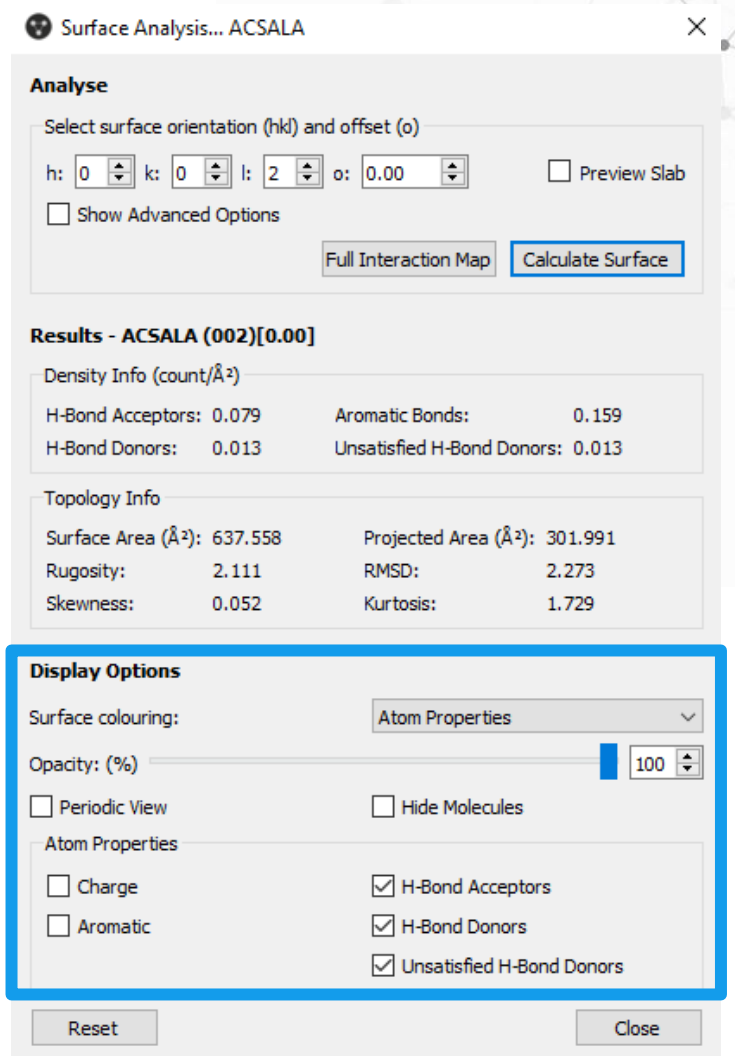
Results

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

CSD-Particle – Surface Analysis



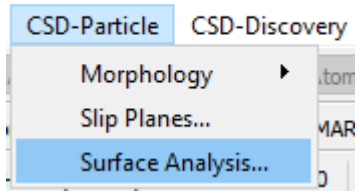


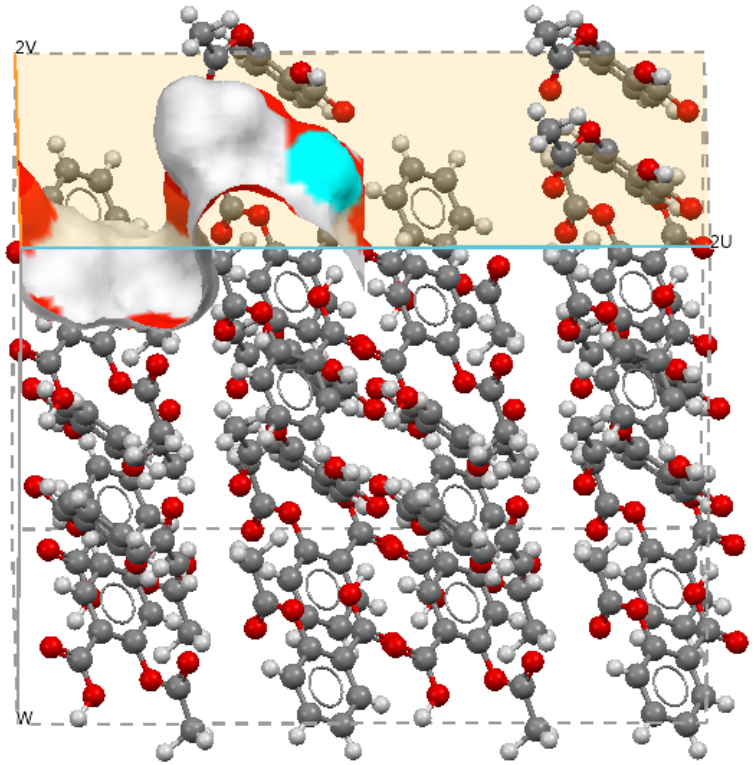


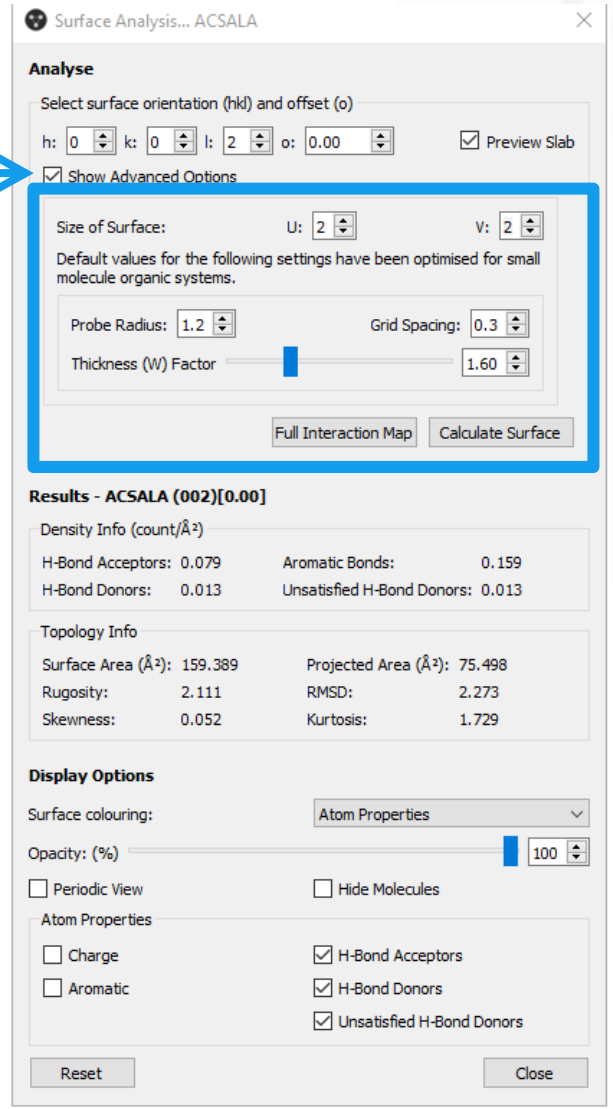
Display Options

CCDC

CSD-Particle – Surface Analysis







Advanced Options

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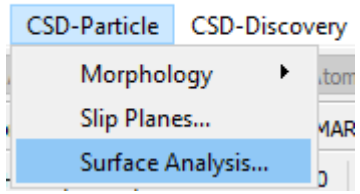
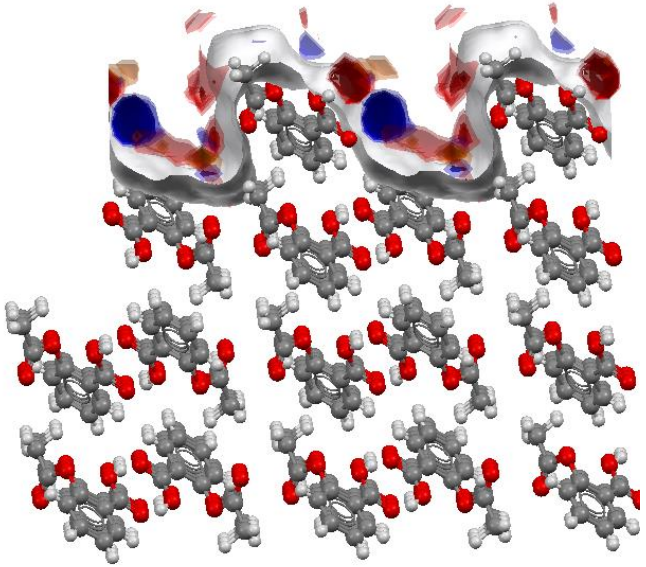
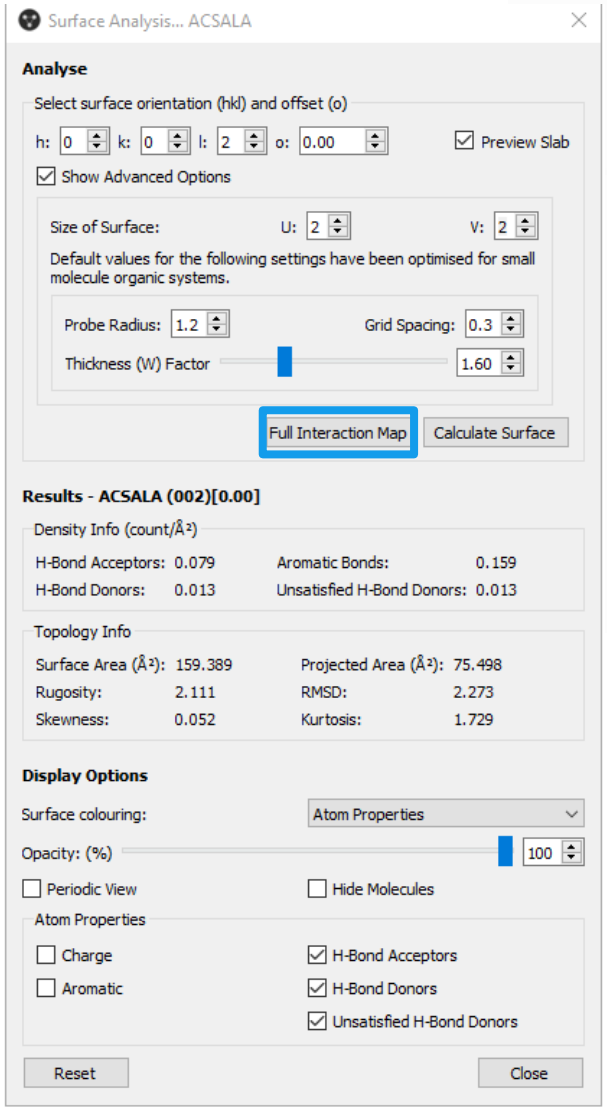
CSD-Particle – FIMs on Surface







Full Interaction Map on Surface

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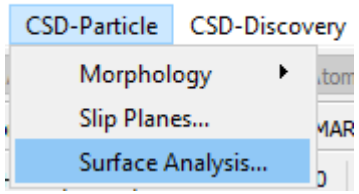
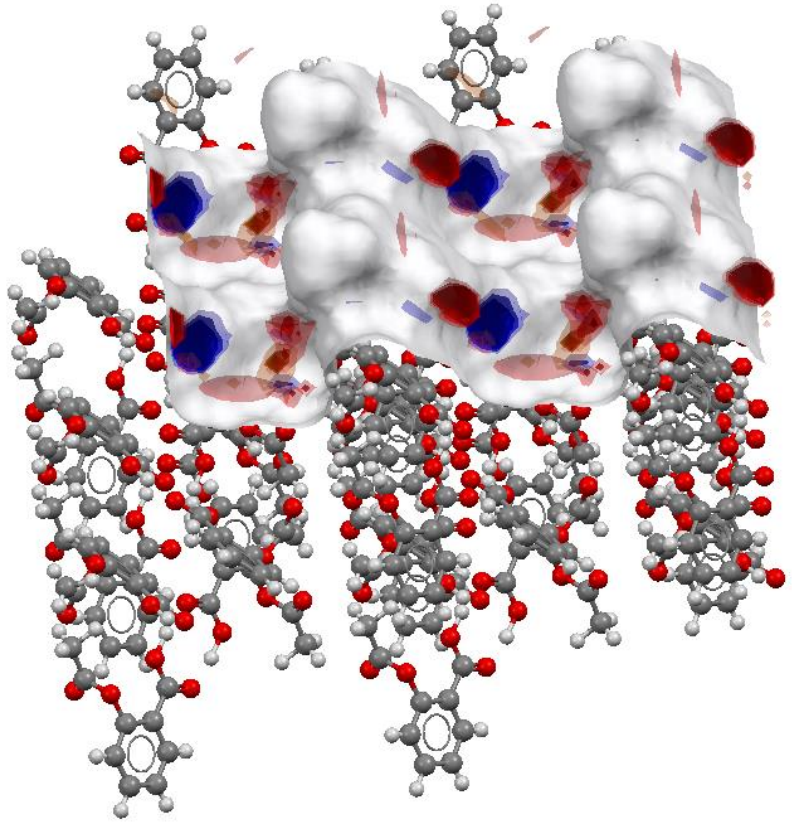
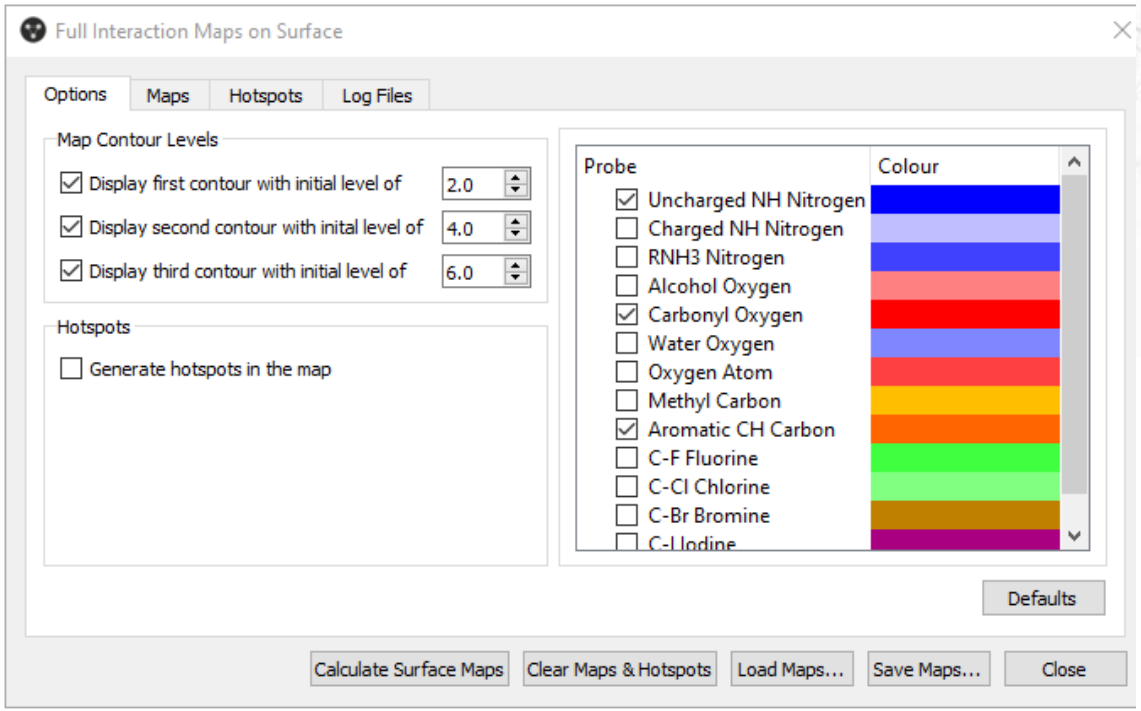
CSD-Particle – FIMs on Surface







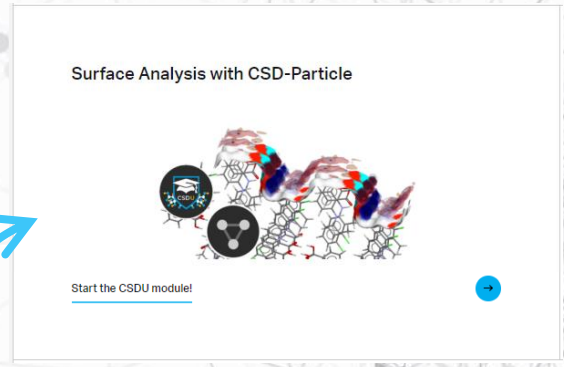
Want to explore more?

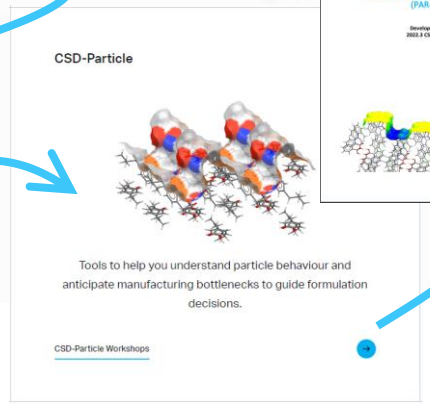
On-demand training resources

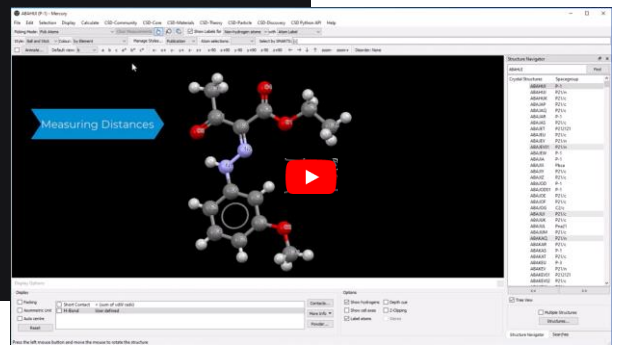
Solutions | Community | Discover | Consultancy

- 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







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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

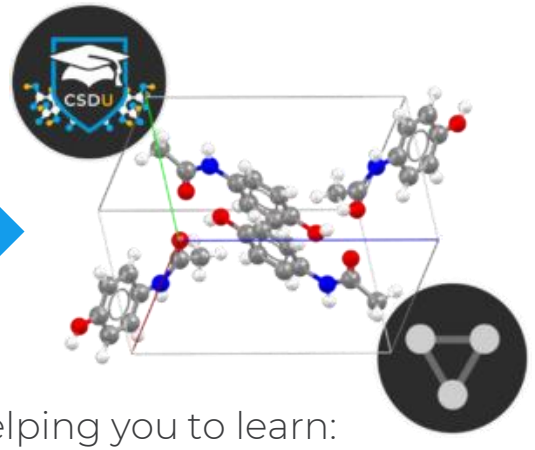
GOLD Docking

Mogul

FIMs

Particle

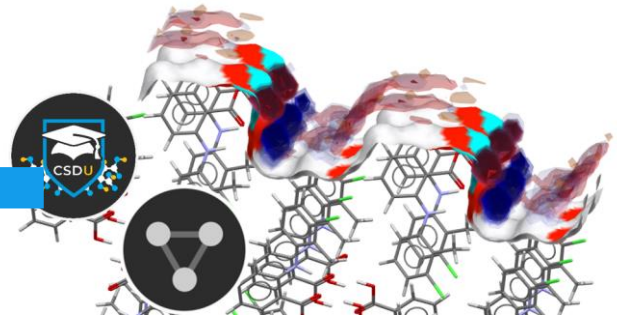
Visualization 101



Helping you to learn:

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

Surface analysis

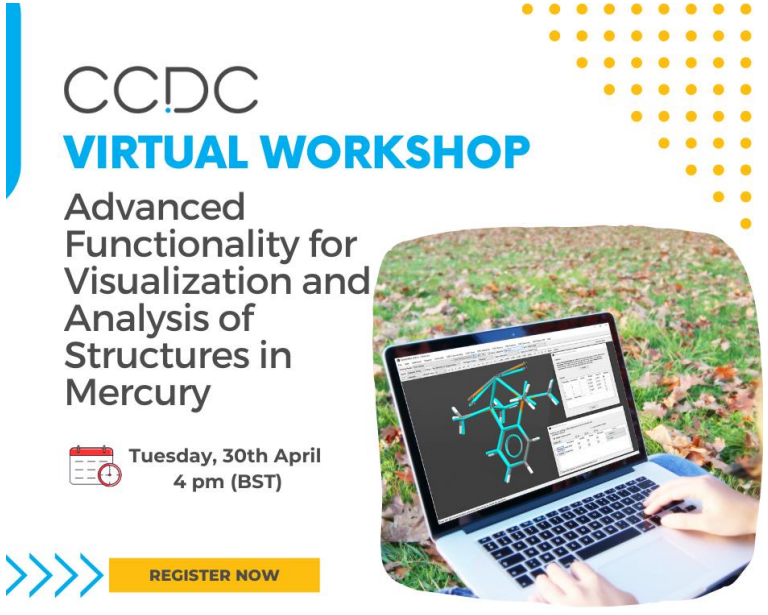


Helping you to learn:

- 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



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

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