

How to visualise and analyse surfaces

Using CSD-Particle in Mercury

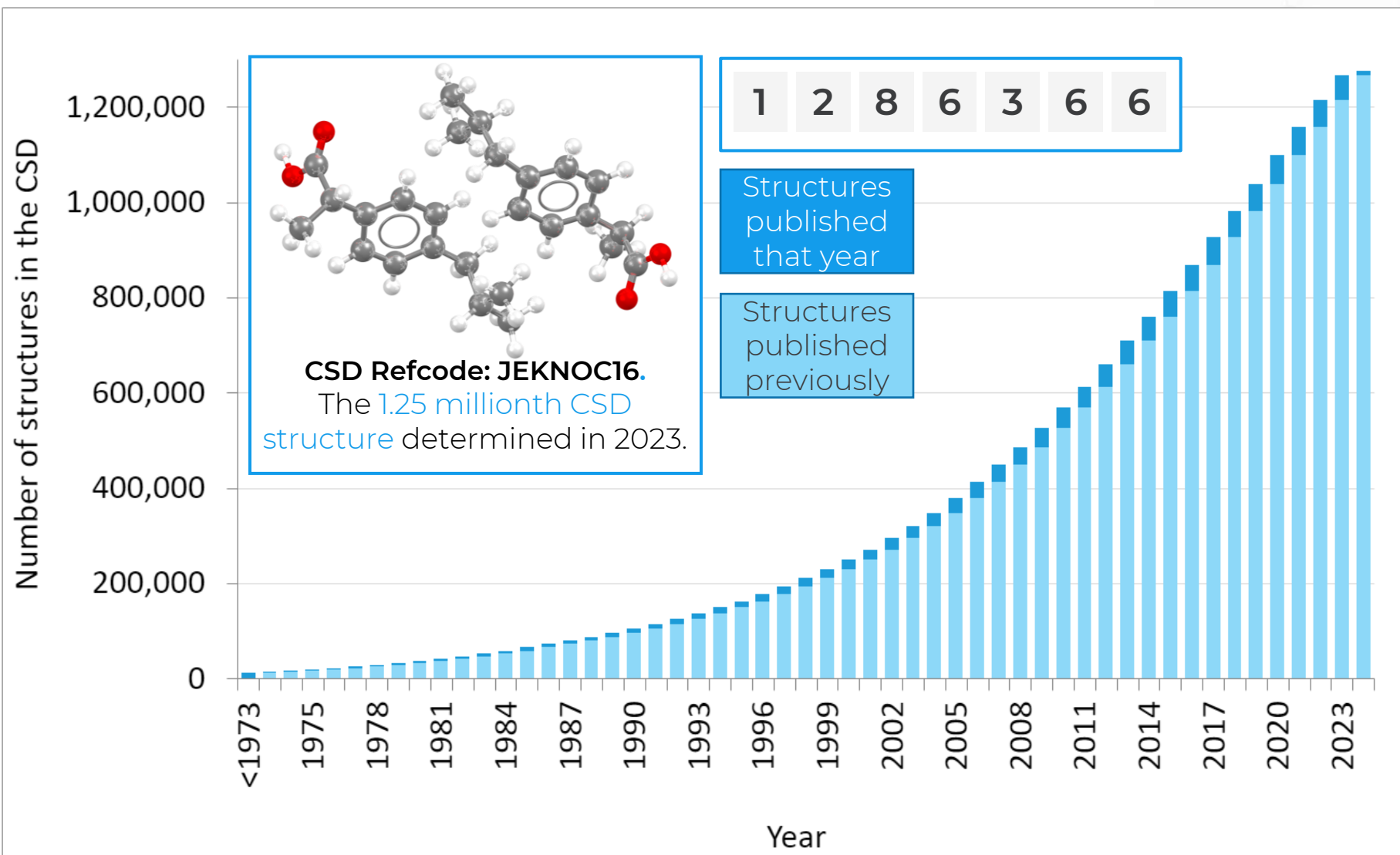
CCDC Virtual Workshop

16th April 2024

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

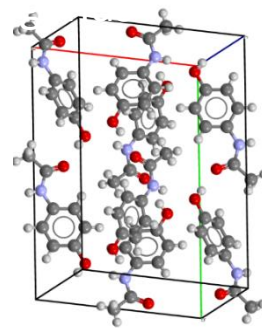
Organic
45%

Metal-Organic
55%

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

Organic

- Drugs
- Agrochemicals
- Pigments
- Explosives
- Protein ligands



Additional data

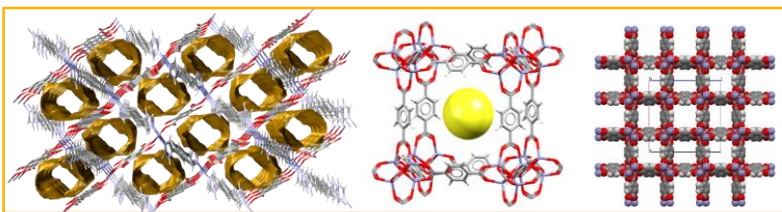
- 13,478 polymorph families
- 174,987 melting points
- 1,075,904 crystal colours
- 951,746 crystal shapes
- 30,275 bioactivity details
- 13,641 natural source data
- > 350,000 oxidation states

Not Polymeric
89%

Polymeric: 11%

Metal-Organic

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

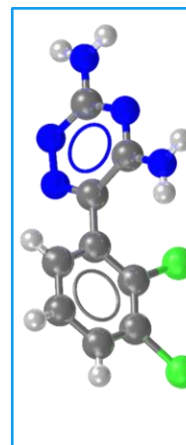


Single
Component
58%

Multi
Component
42%

Links and subsets

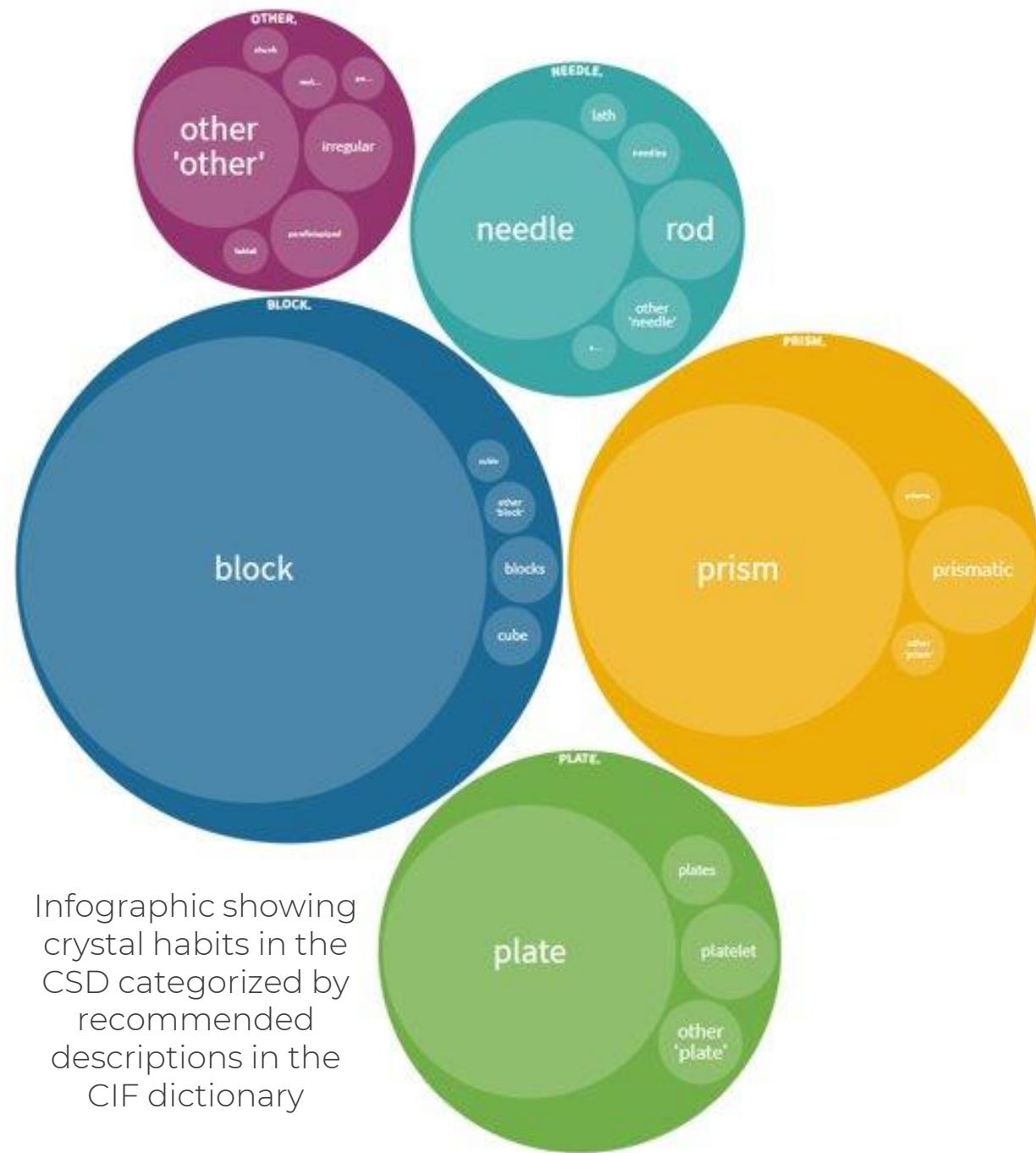
- DrugBank
- Druglike
- MOFs
- PDB ligands
- PubChem
- ChemSpider
- Pesticide PDB



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



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



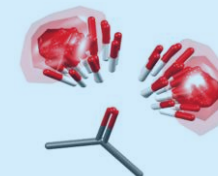
We clearly recognised even in those early days, that data banks have three principal functions. Firstly they must gather together existing knowledge and make it readily available to the scientific community. Secondly they can be used to reduce a large number of observations to a small set of constants 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)

Software to gain new insights



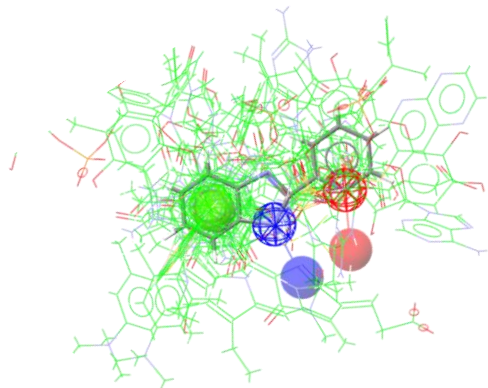
CSDCore.

Search, visualise, analyse and communicate structural data
Insights into molecular and crystal shape and interactions



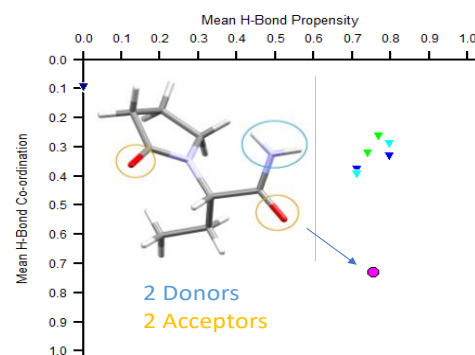
CSDDiscovery.

Design of new molecules



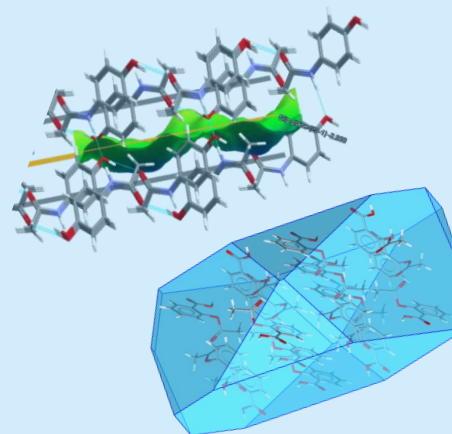
CSDMaterials.

Assessment of solid form stability and properties



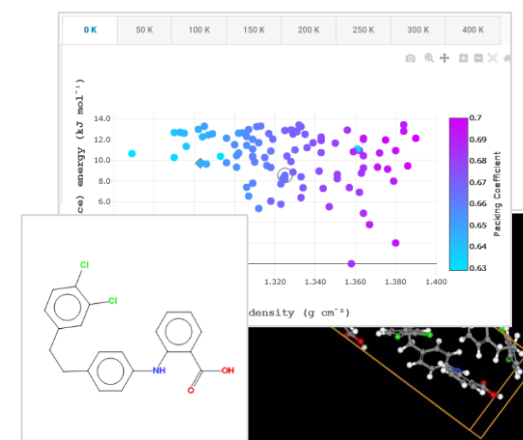
CSDParticle.

Anticipate particle properties and behaviour



CSDTheory.

Insights from predicted structure landscapes

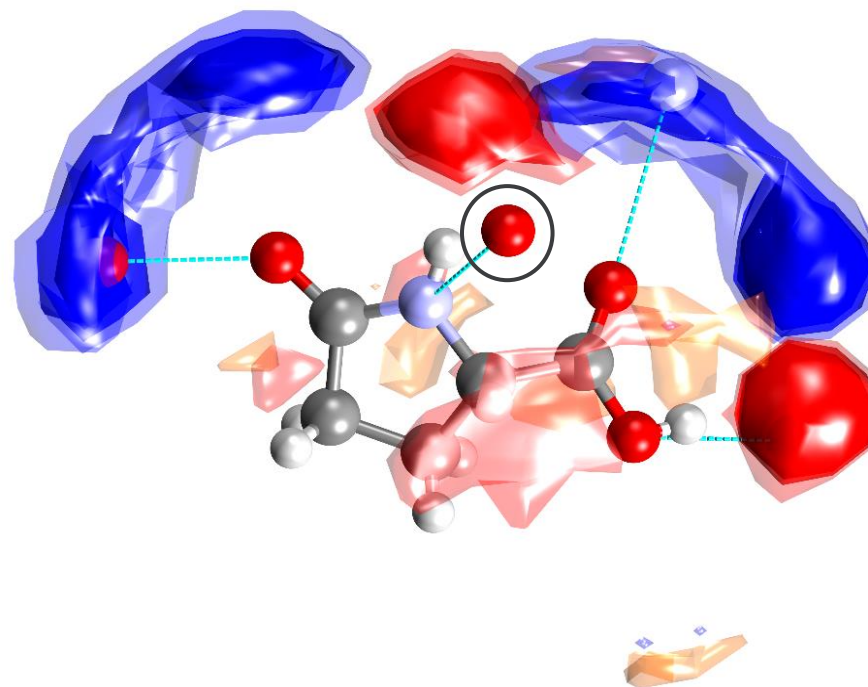


Medicinal & Computational Chemists ♦ Crystallographers & Structural Biologists ♦ Solid Form & Crystallisation Scientists

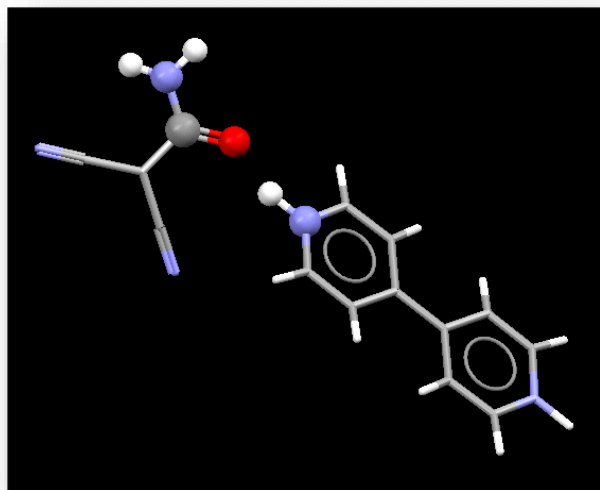
CCDC

Key concepts - Full Interaction Maps

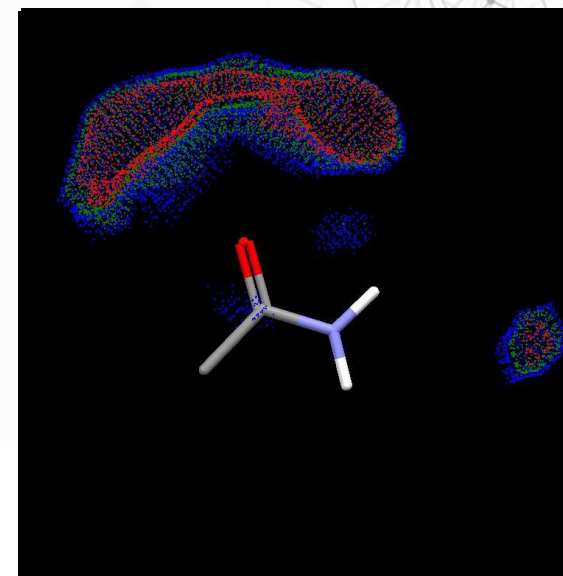
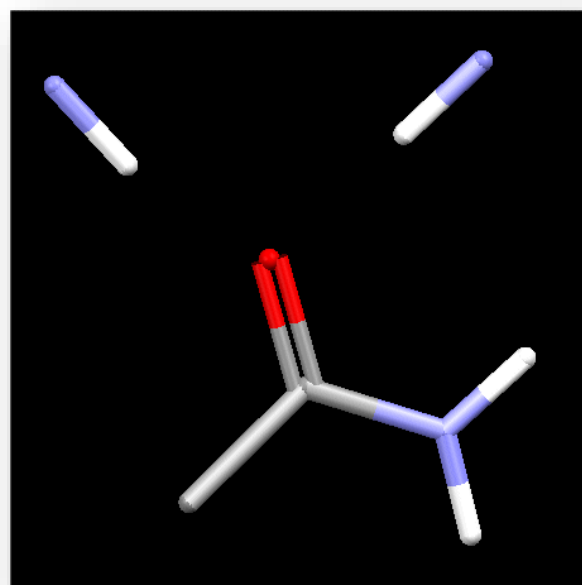
- Map interaction preferences around complete molecules in a crystal structure
- Visualise observed atom-atom contacts with respect to likely geometries in 3D space
- Identify interaction hot-spots around chemical groups



Key concepts - Full Interaction Maps



central group: -CONH_2
contact group: NH



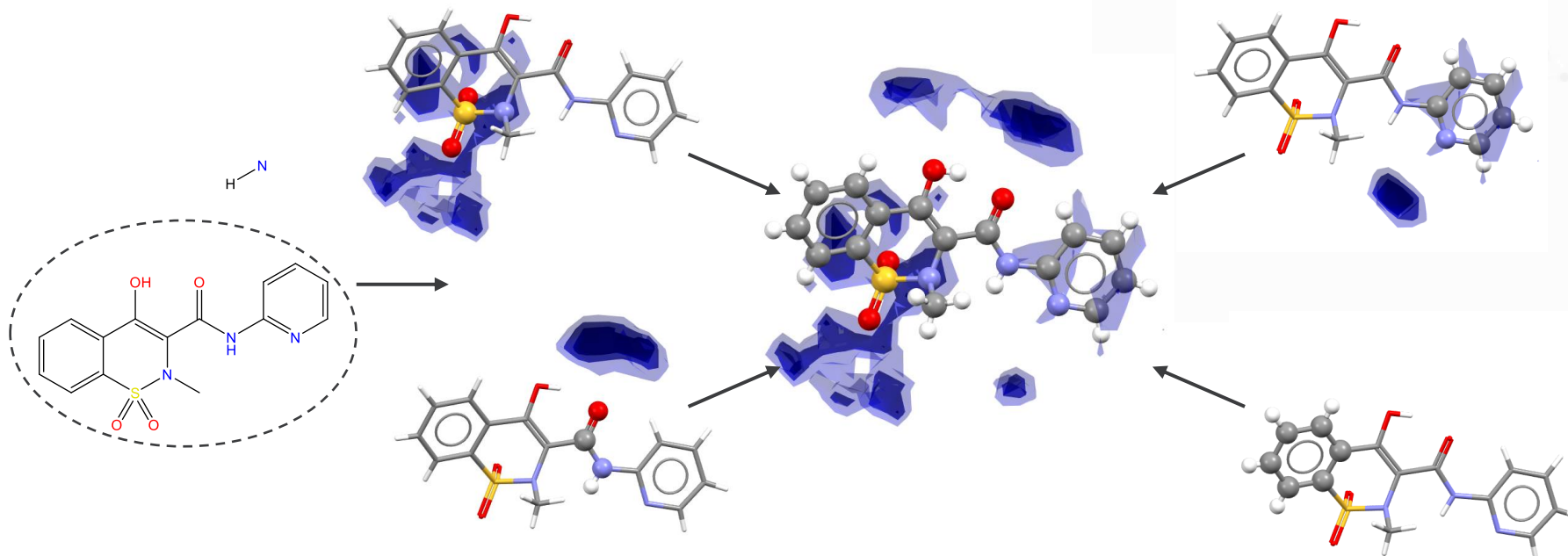
Search for structures containing desired contact

Superimpose hits and display as scatterplots or contour plots

CCDC

Key concepts - Full Interaction Maps

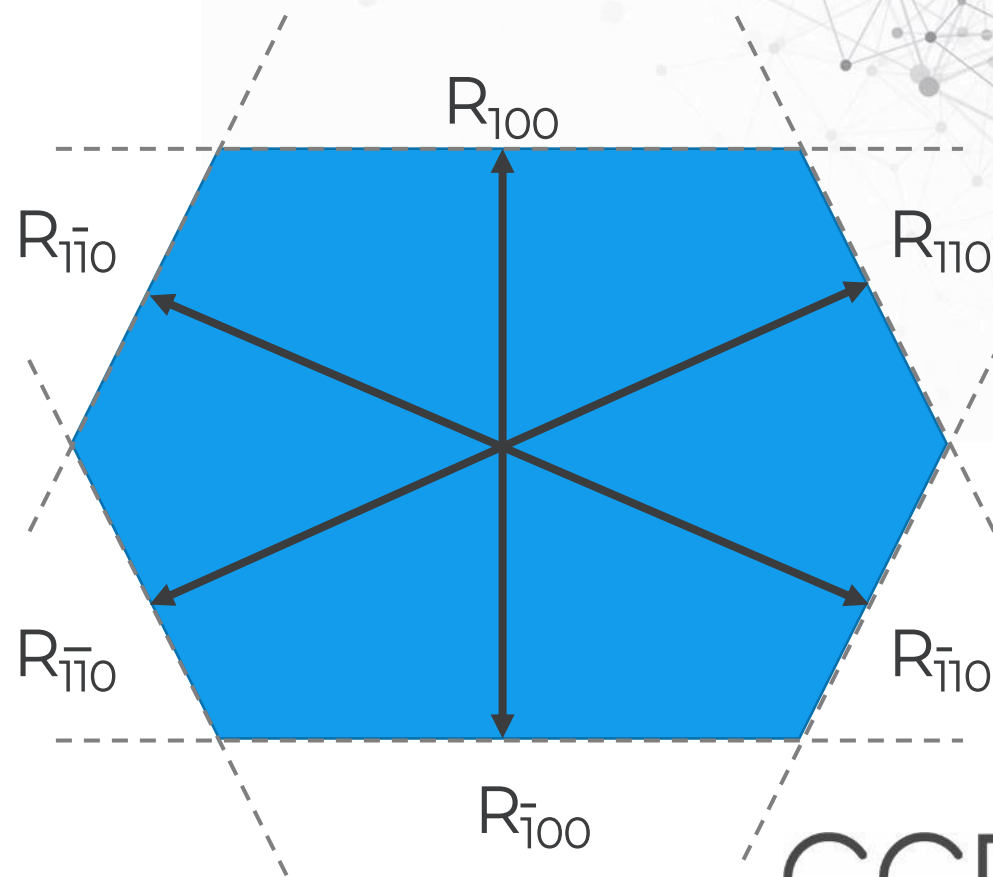
- Molecule is broken down into fragments
- IsoStar maps for each fragment are combined to give the Full Interaction Map



- Multiple maps can be generated for different probes

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



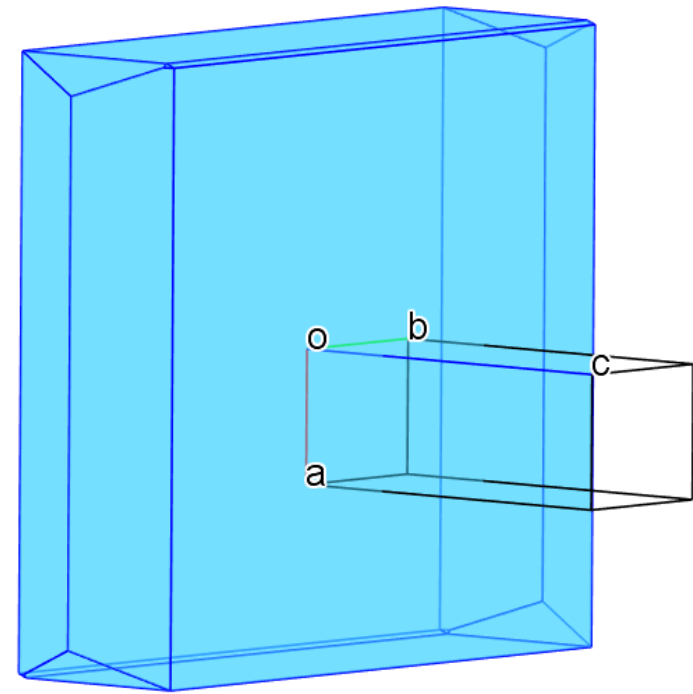
Key concepts – BFDH morphologies

- 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

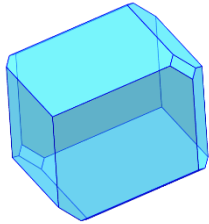
A. Bravais, *Études Crystallographiques*, Gauthier-Villars, Paris, (1866)

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

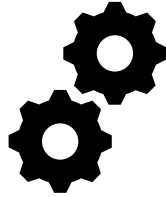
J.D. Donnay, D. Harker, *Amer. Min.* (1937), 22, 446-467.



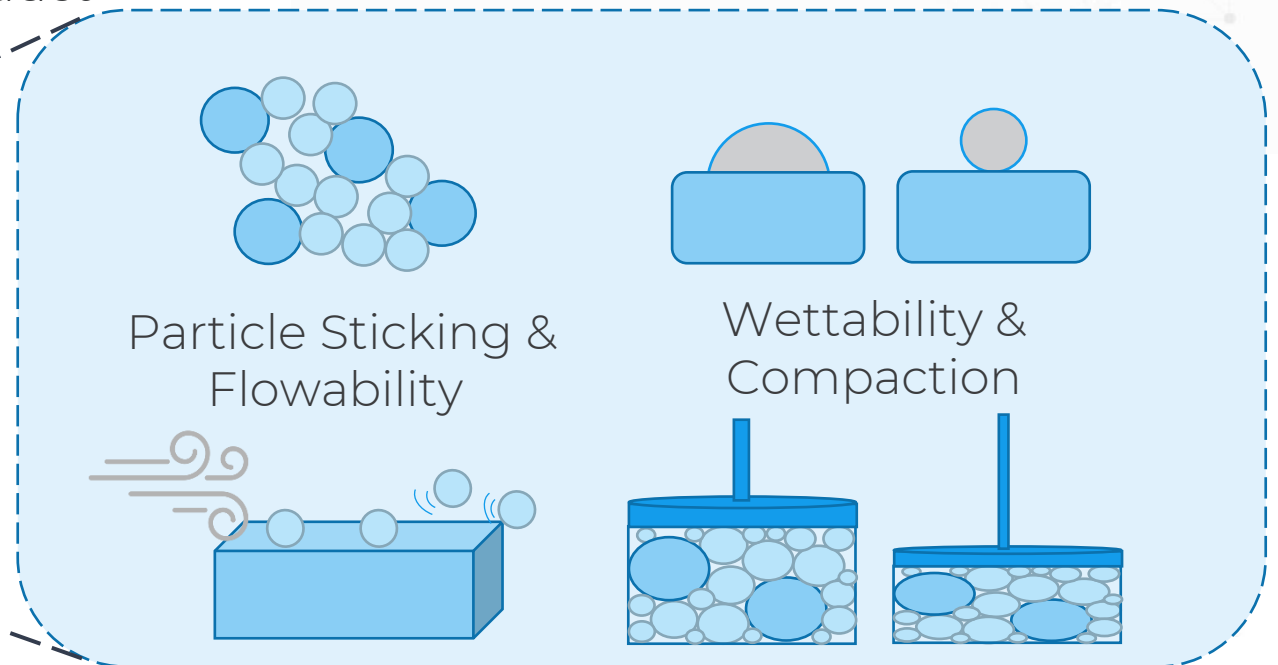
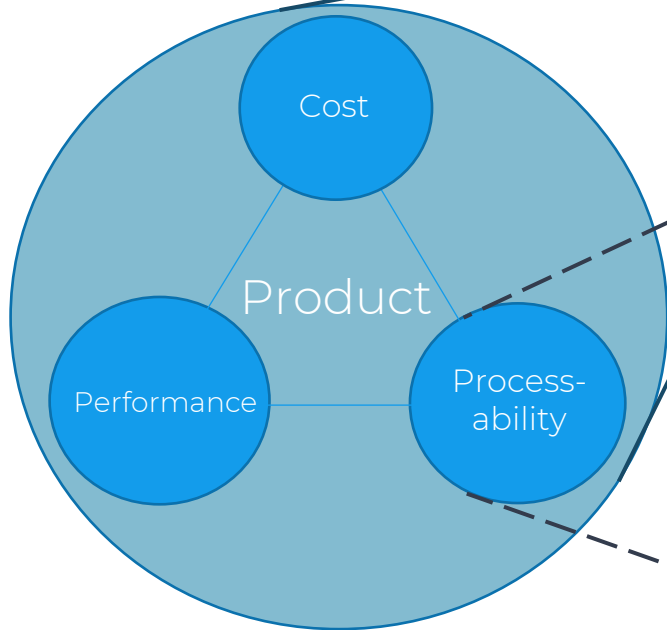
The field



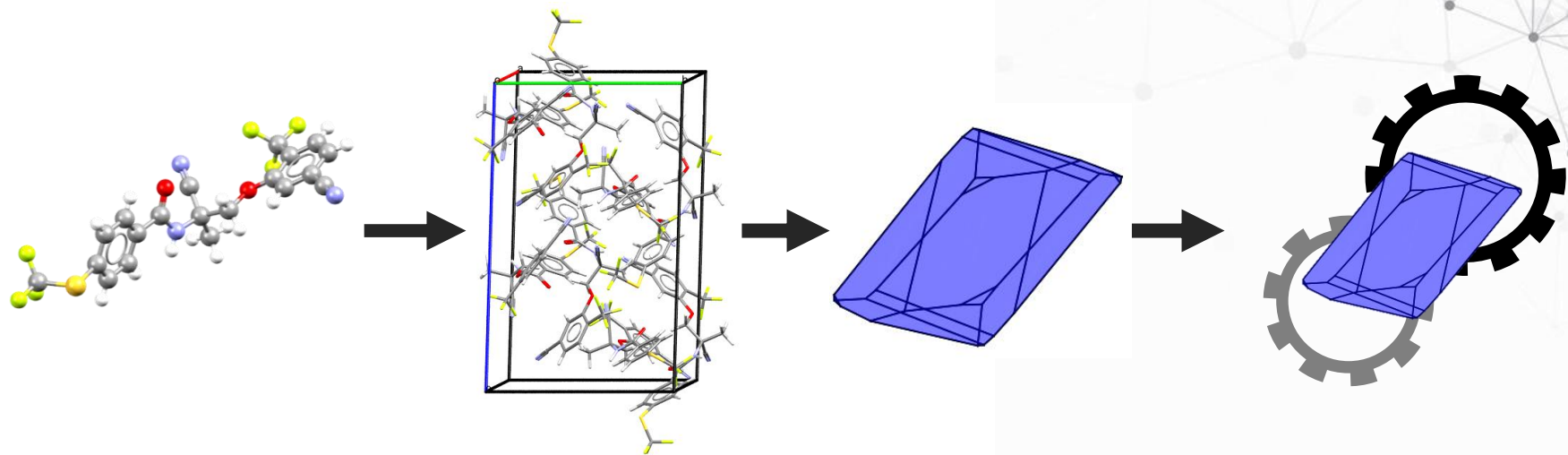
Particle



Product



From Solid Form to Particle Properties



Molecule

Form

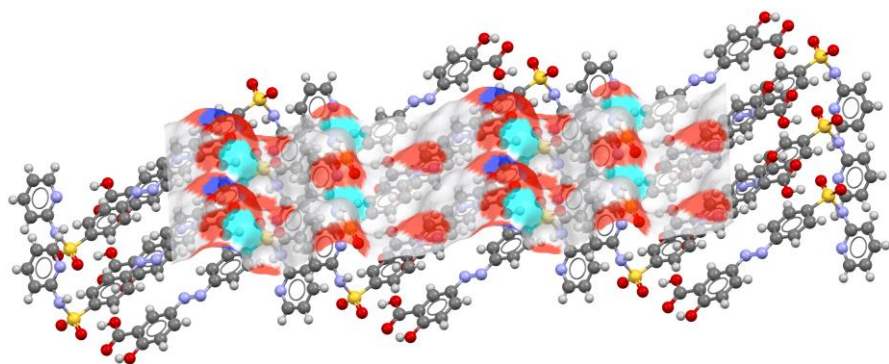
Particle

Properties

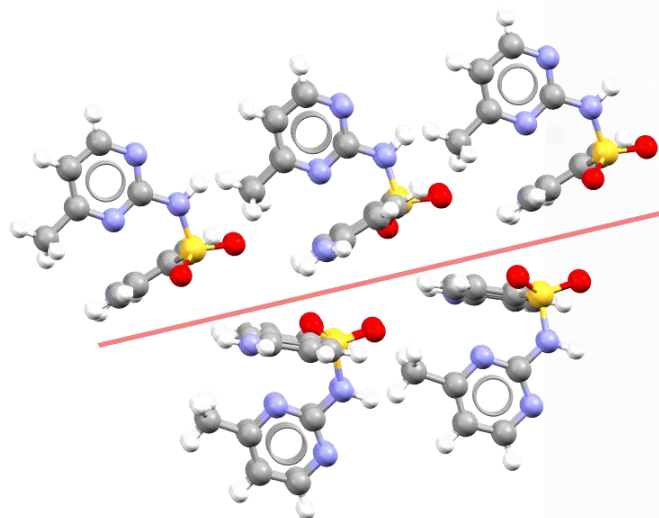
Solid Form Informatics

Particle Informatics

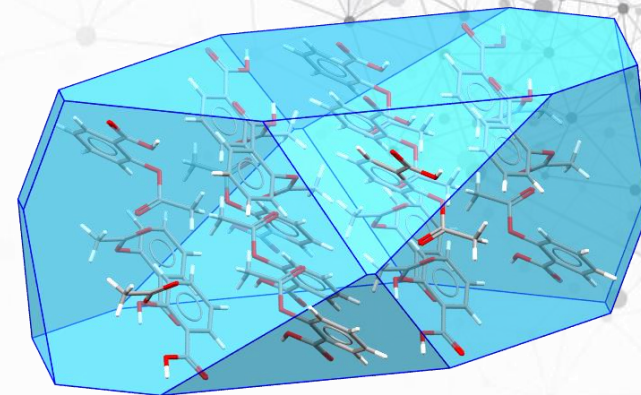
Particle Informatics



Visualisation and analysis
of surface properties

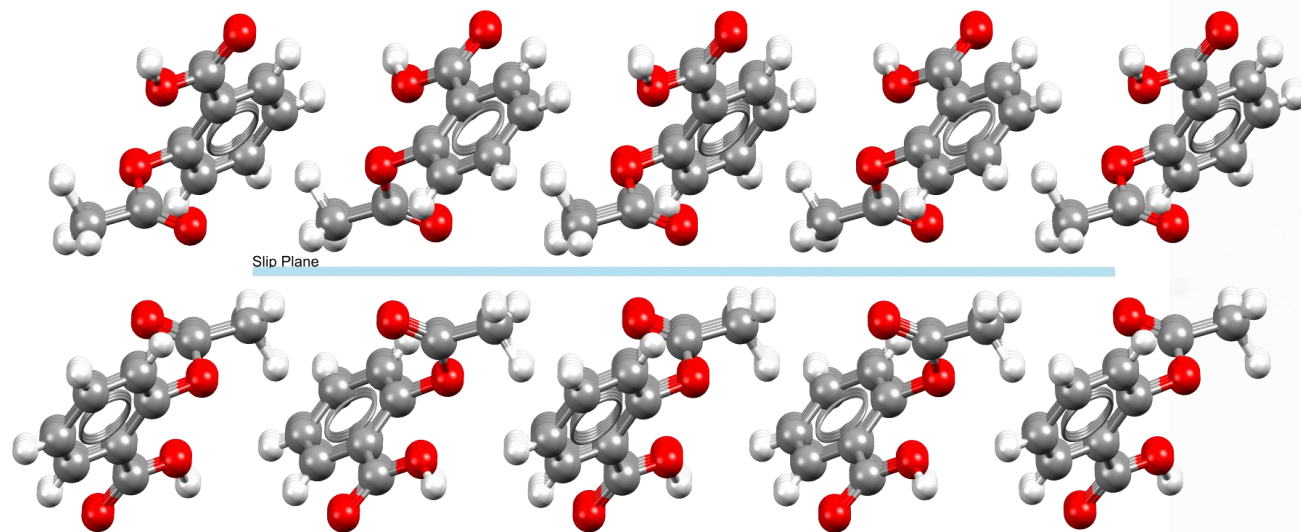


Identification and analysis of
potential slip planes



Morphology calculations

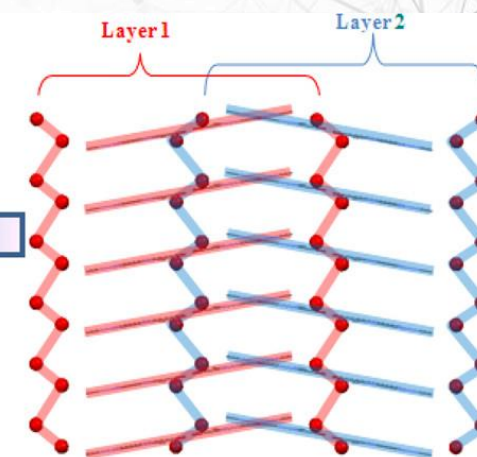
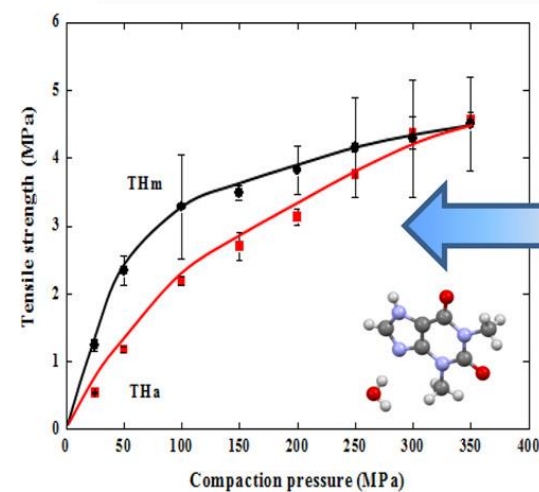
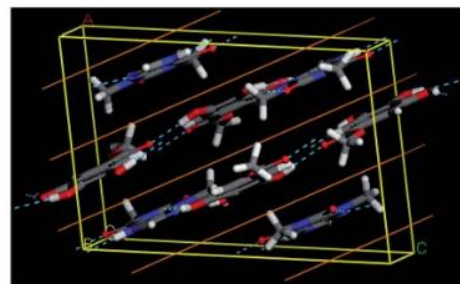
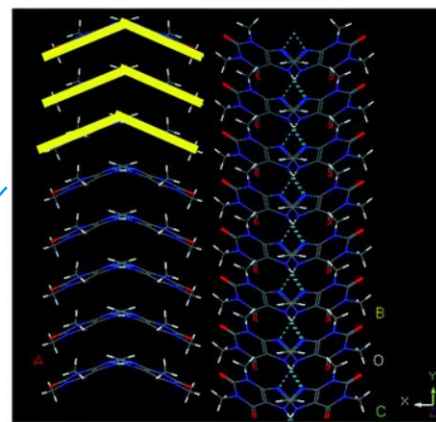
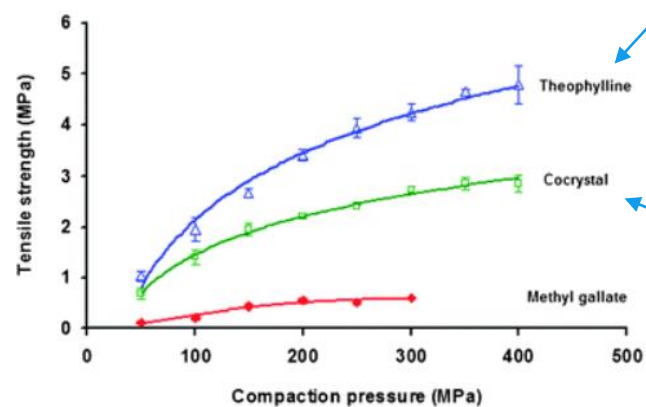
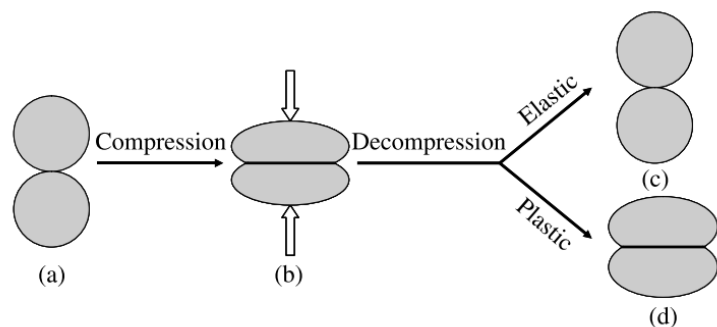
- Ongoing research projects into particle and surface phenomena are developing our understanding of formulation and manufacturing processes
- Application of rapid, informatics-based approaches to understand the link between crystal structure and properties that influence downstream behaviour



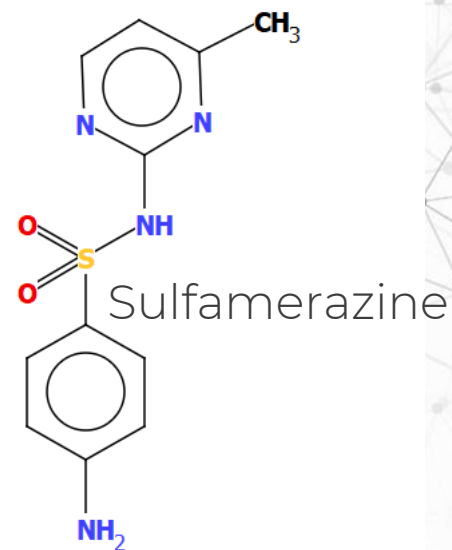
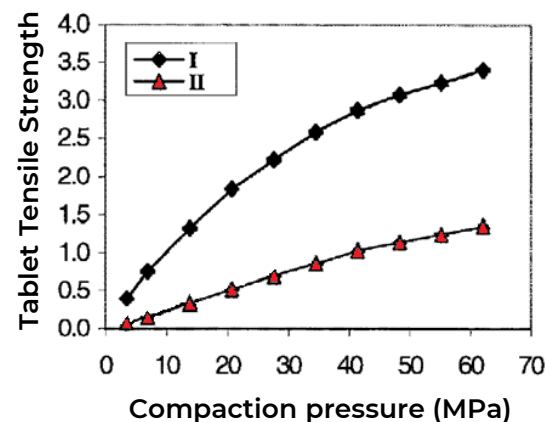
Slip Planes

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

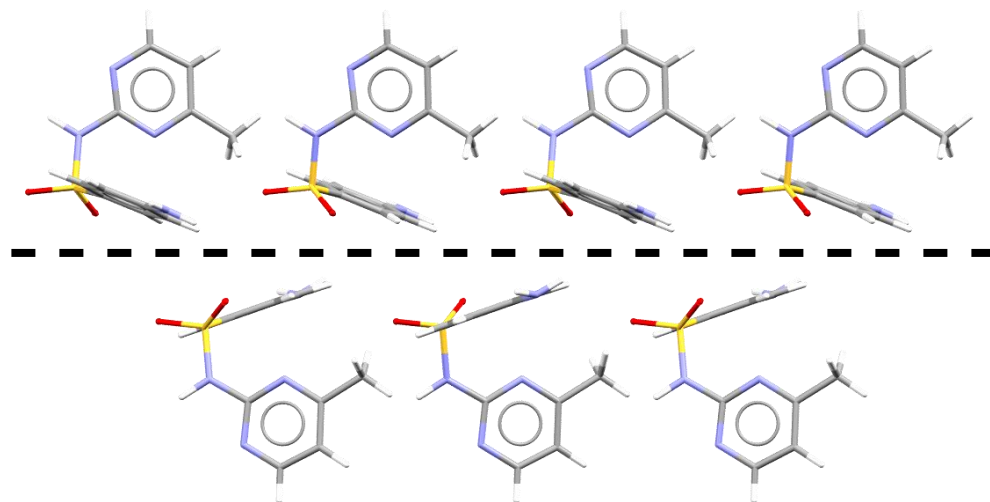
Compaction and bending



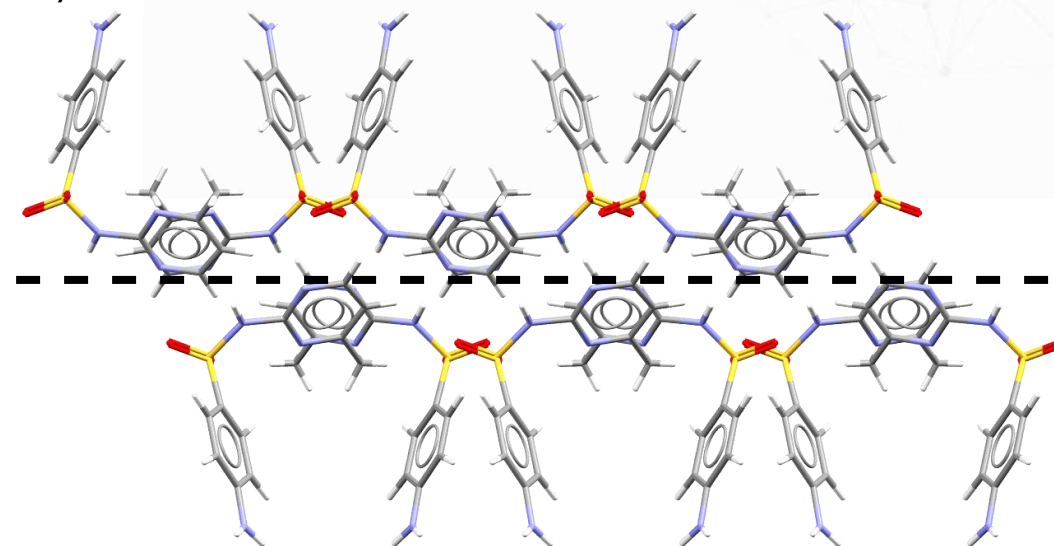
Compression and slip planes



Form I



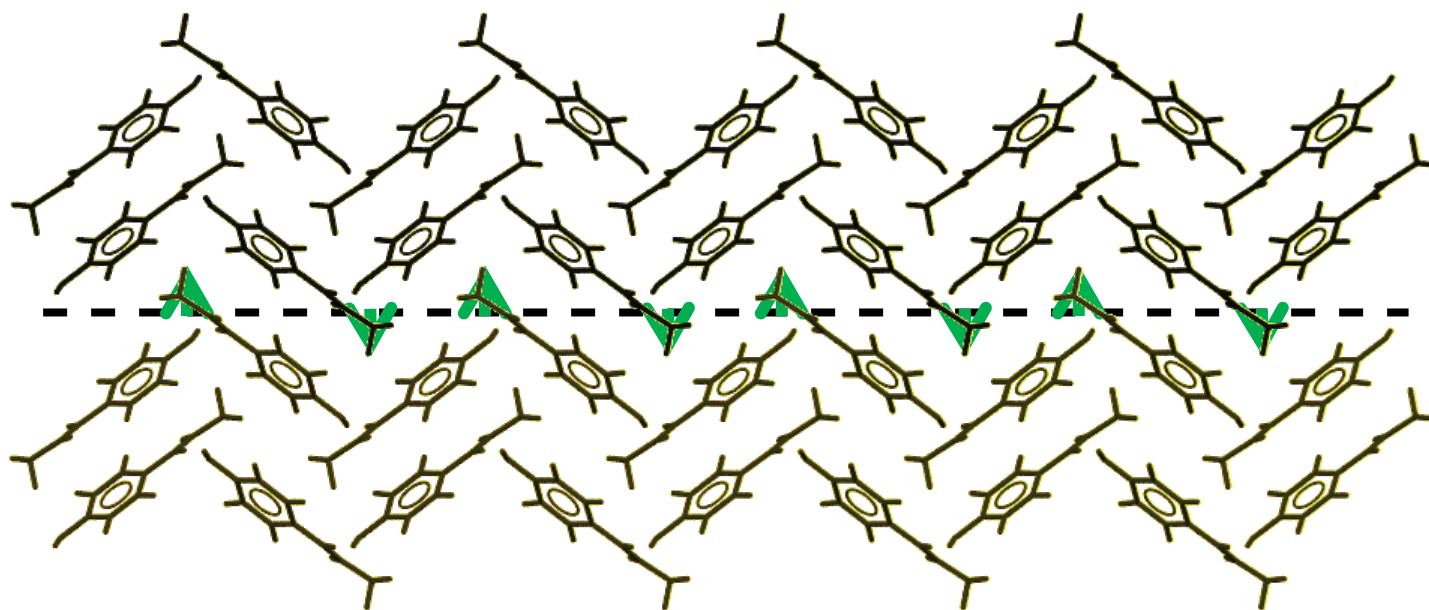
Form II



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

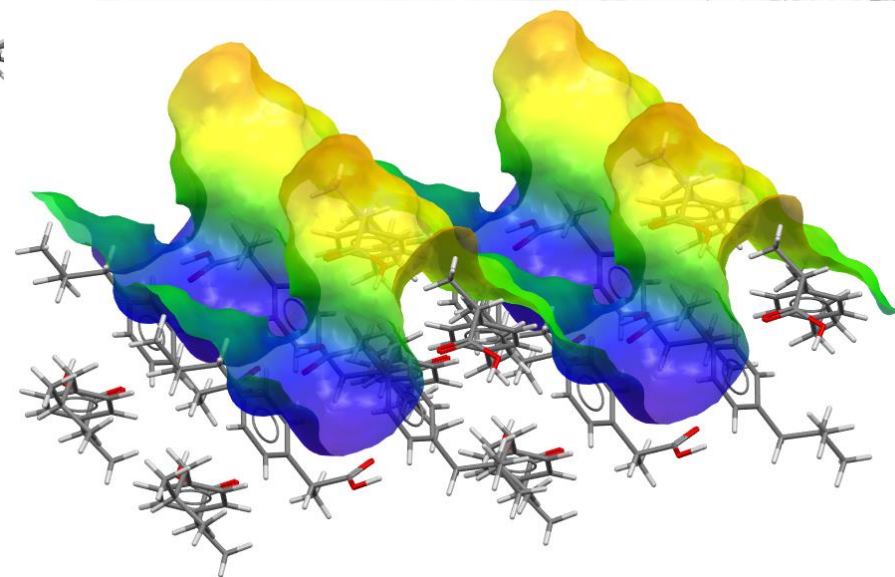
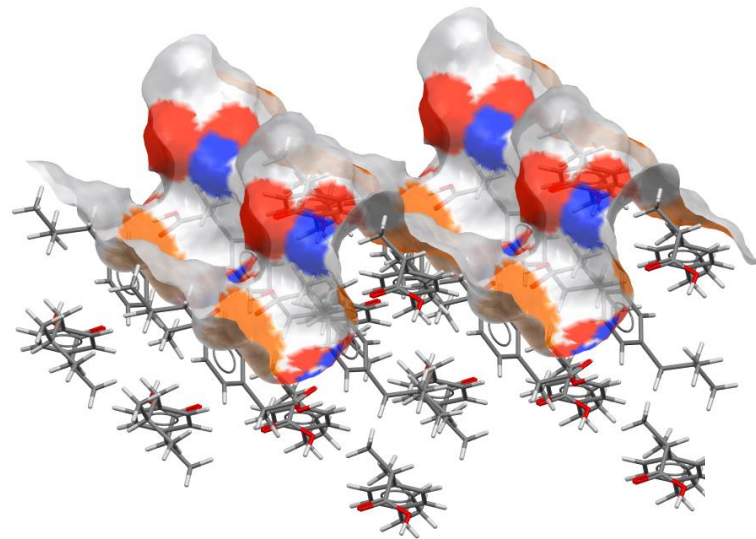
C.C. Sun, *J. Adhes. Sci. Technol.* (2011), 25, 483 - 499

Predicting slip planes

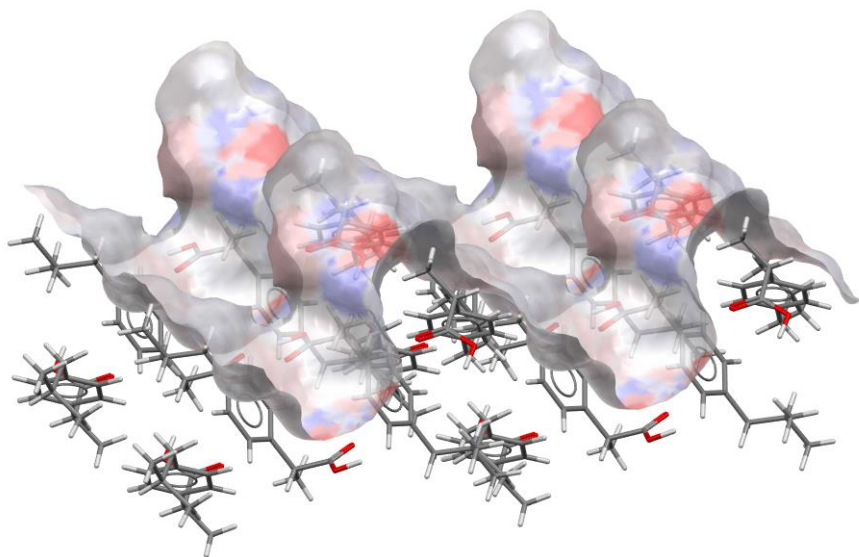


Surface Analysis

Surface Chemistry

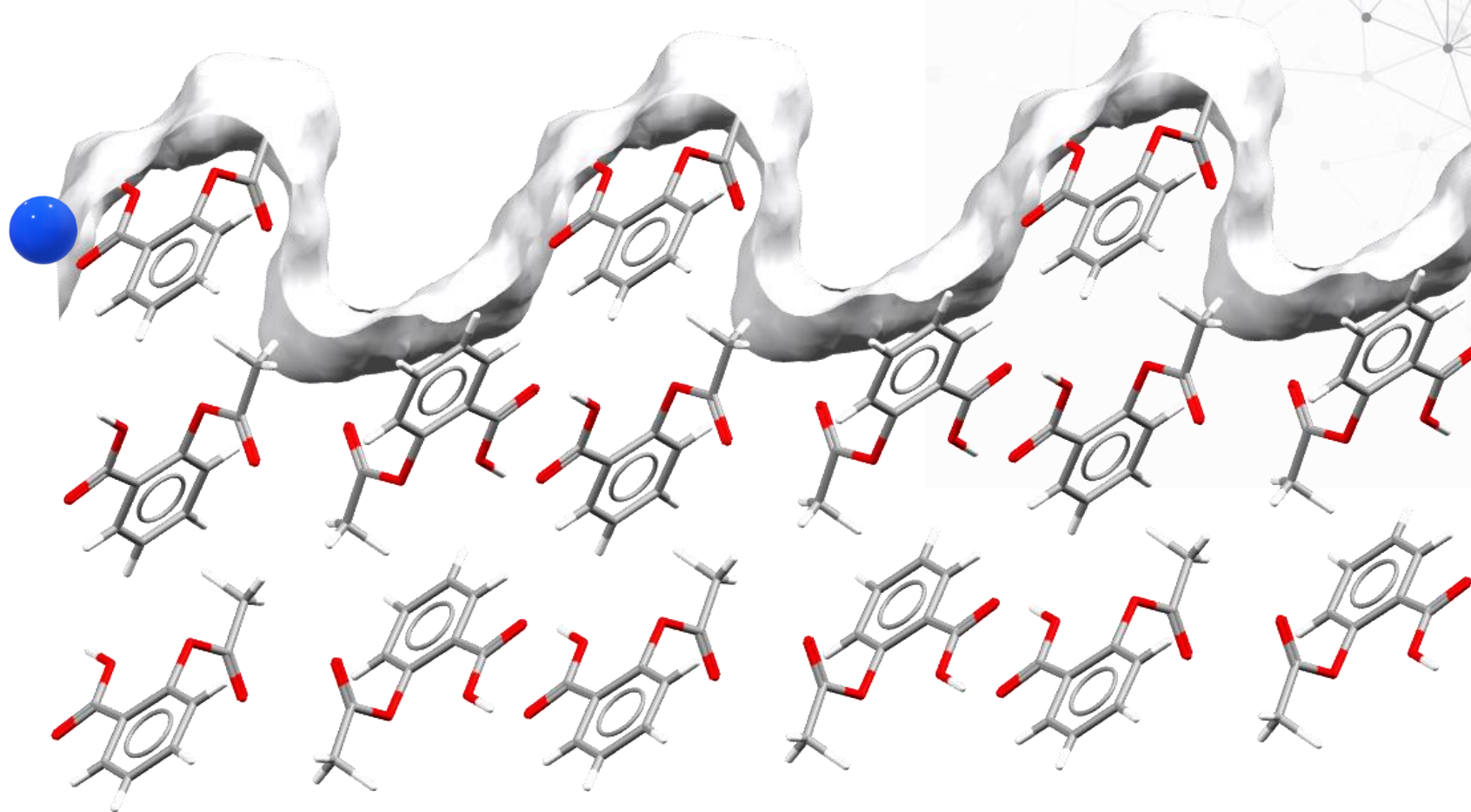


Surface Roughness



Surface Charge

Surface Analysis

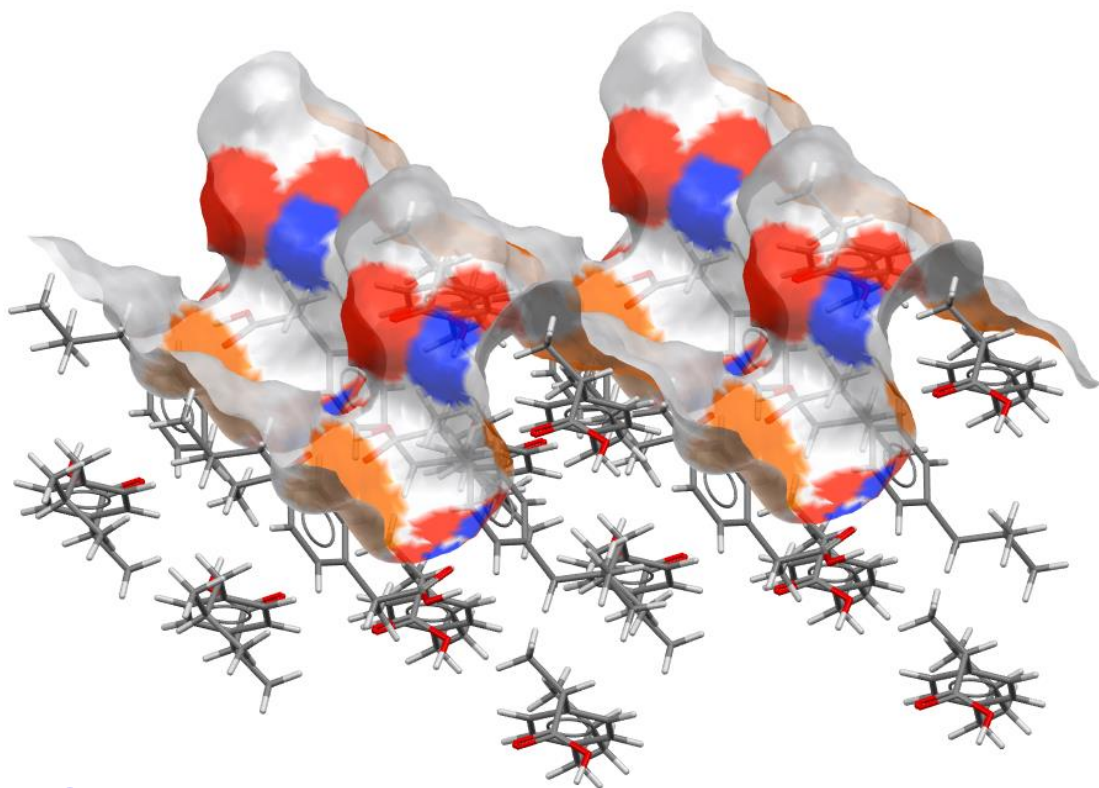


M. J. Bryant *et al.*, *Cryst. Growth Des.* (2019), **19**, 9, 5258-5266

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

CCDC

Surface Analysis



H-bond donor



H-bond acceptor

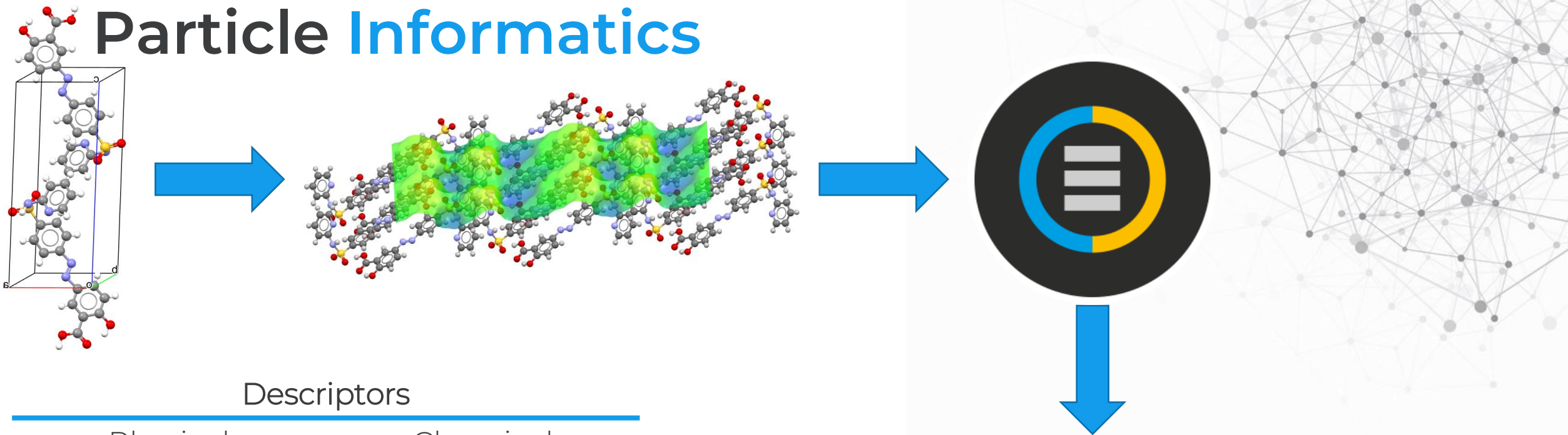


Aromatic bond

Descriptors

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

Particle Informatics



Descriptors

Physical

Reticular Surface
Area

Rugosity

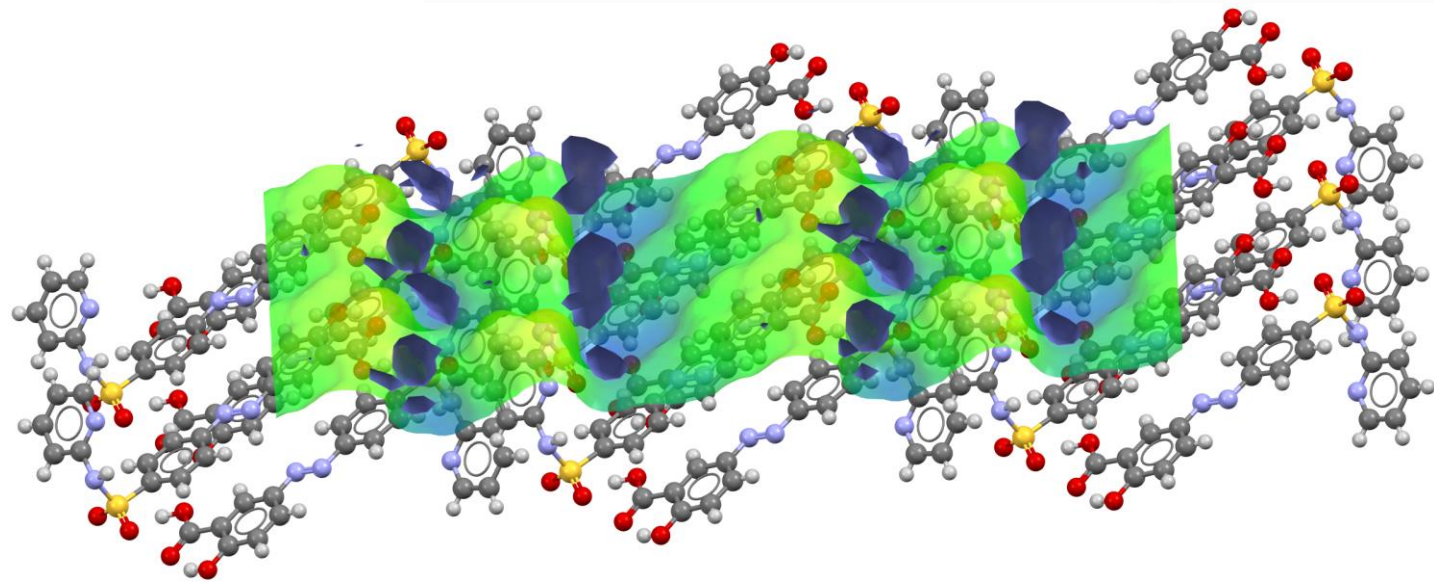
RMSD, Skewness,
and Kurtosis

Chemical

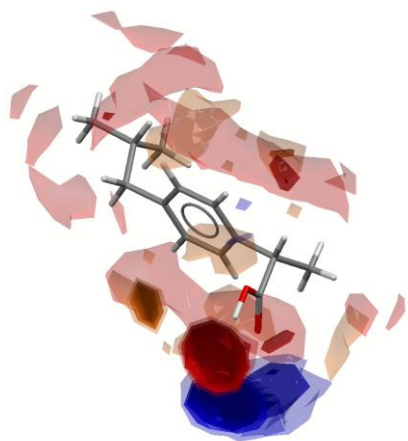
Hydrogen Bond
Donor/Acceptor
Density

Aromatic Bond
Density

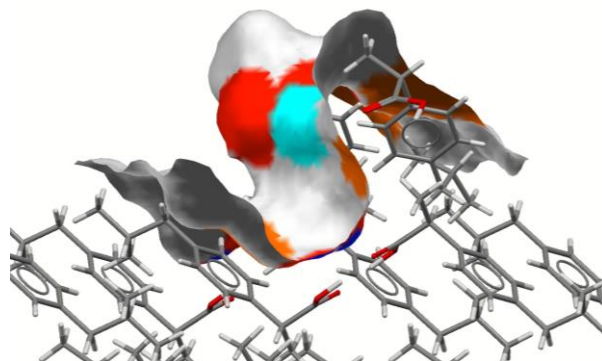
FIMs on Surface



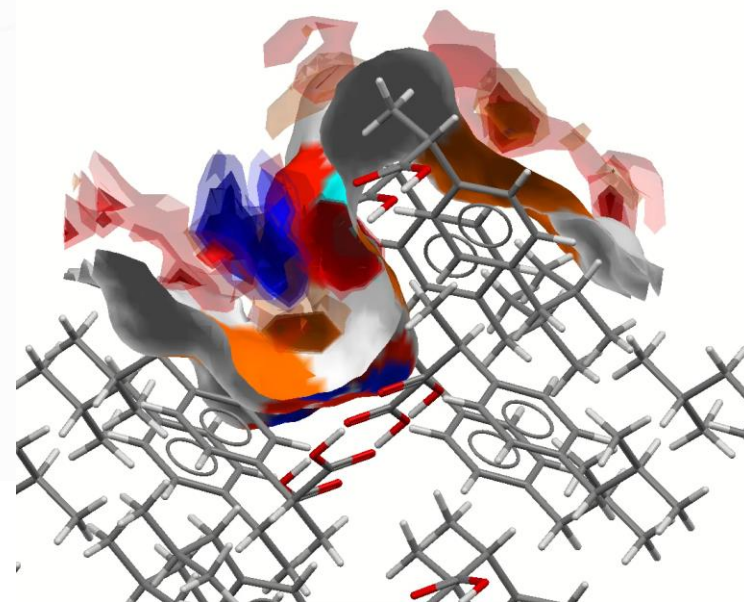
FIMs on Surface



FIM



Surface



FIM on Surface

Accessing CSD-Particle through Mercury



AABHTZ (P-1) - Mercury

File Edit Selection Display Calculate CSD-Community CSD-Core CSD-Materials CSD-Theory CSD-Particle 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... Work Atom selections:

Animate... Default view: b a b c a* b* c* x- x+ y- y+ z- z+ x-90 x+90 y-90 y+90 z-90 z+90 Select by SMARTS: [c]

Structure Navigator

AABHTZ Find

Crystal Structures	Spacegroup
AABHTZ	P-1
AACANI10	P21/c
AACANI11	P21/c
AACFAZ	Pbcn
AACFAZ10	Pbcn
AACMAL	P21/c
AACMHX10	Pbca
AACRHA	Pncm
AACRHC	P-1
AACRUB	Cc
AACRUB01	C2/c
AADAMC	P21/c
AADMPY	P-1
AADMPY10	P-1
AADRIB	P21
AAGAGG10	P212121
AAGGAG10	P21

Display Options

Display

☐ Packing ☐ Short Contact < (sum of vdW radii) ☐ Asymmetric Unit ☐ H-Bond Default definition ☐ Auto centre

Reset

Contacts... More Info Powder...

Options

☒ Show hydrogens ☐ Depth cue ☐ Show cell axes ☐ Z-Clipping ☐ Label atoms ☐ Stereo

Tree View ☐ Multiple Structures Structures...

Press the left mouse button and move the mouse to rotate the structure

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

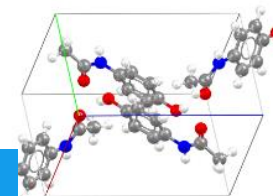


- Shift + Left mouse button and move – rotate in the plane molecules



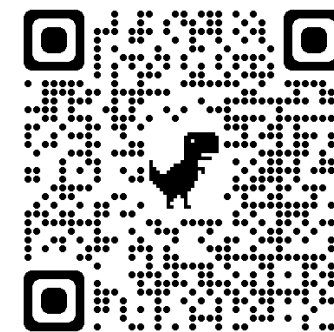
- Ctrl + Left mouse button and move – translate molecules

Visualisation 101 - Visualising structural chemistry data with Mercury

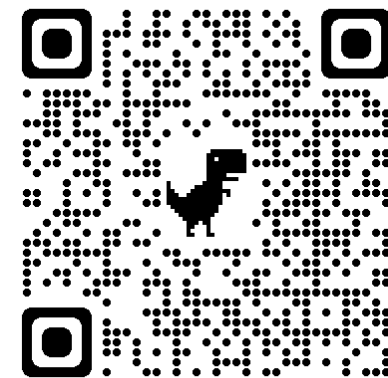


Learn more
in this CSDU
on-demand
course

Begin module

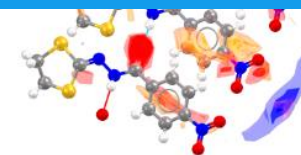


Creating a Full Interaction Map



Analysing intermolecular interactions 101 - Full Interaction Maps

Learn more in this CSDU on-demand course



Begin module

CCDC

A screenshot of the Mercury software interface. The main window shows a molecular structure with interaction maps. A sidebar on the left contains a menu with options like 'Search', 'Calculations', 'Polymorph Assessment', 'Co-Crystal Design', 'Full Interaction Maps...', 'Hydrate Analyser...', 'Solvate Analyser...', 'Aromatics Analyser...', 'Conformer Generation...', and 'Launch DASH'. The 'Full Interaction Maps...' option is highlighted. A blue arrow points from this menu item to the 'Full Interaction Maps' dialog box. The dialog box has tabs for 'Options', 'Maps', 'Hotspots', and 'Log Files'. The 'Options' tab is active, showing 'Map Contour Levels' (Display first, second, and third contours) and 'Hotspots' (Generate hotspots in the map). The 'Maps' tab shows a 'Probe' list with checkboxes for various interaction types (Uncharged NH Nitrogen, Charged NH Nitrogen, RNH3 Nitrogen, Alcohol Oxygen, Carbonyl Oxygen, Water Oxygen, Oxygen Atom, Methyl Carbon, Aromatic CH Carbon, C-F Fluorine) and a color scale. The 'Log Files' tab shows a list of log files. The bottom of the dialog box has buttons for 'Calculate Maps', 'Clear Maps & Hotspots', 'Load Maps...', 'Save Maps...', and 'Close'. The main window also has a 'Contacts...' button and a 'More Info' dropdown. The bottom of the main window has a 'Reset' button and a URL: <https://www.ccdc.cam.ac.uk/Community/blog/getting-started-with-FIMS/>. The bottom left of the main window has a note: 'Press the left mouse button and move the mouse to rotate the structure'.

CSD-Particle Menu

AABHTZ (P-1) - Mercury

File Edit Selection Display Calculate CSD-Community CSD-Core CSD-Materials CSD-Theo PI Help

Picking Mode: Pick Atoms Clear Measurements Show Labels

Style: Ball and Stick Colour: by Element Manage Styles... Publication Atom sel

Animate... Default view: b a b c a* b* c* x- x+ y- y+ z- z+ x-90

zoom- zoom+

CSD-Particle CSD-Discover PI Help

- Morphology
- Slip Planes...
- Surface Analysis...

Structure Navigator

AABHTZ Find

Crystal Structures	Spacegroup
AABHTZ	P-1
AACANI10	P21/c
AACANI11	P21/c
AACFAZ	Pbcn
AACFAZ10	Pbcn
AACMAL	P21/c
AACMHX10	Pbca
AACRHA	Pnmc
AACRHC	P-1
AACRUB	Cc
AACRUB01	C2/c
AADAMC	P21/c
AADMPY	P-1
AADMPY10	P-1
AADRIB	P21
AAGAGG10	P212121
AAGGAG10	P21
AALCFE	P21/c
AALPRO	P21/c
AAMAND	P212121
AAMTCO	P-1
AAMTCO10	P-1
AAMTXP	P21/n
AANH0X	Pna21
AANH0X01	Pna21
AANOPM	P21
AAPUNI	P21/a
AAPYPE	P21/c
AARBOX	P21
AAXTHP	P212121

Display Options

Display

☐ Packing ☐ Short Contact < (sum of vdW radii) ☐ Asymmetric Unit ☐ H-Bond User defined ☐ Auto centre

Reset

Contacts... More Info... Powder...

Options

☒ Show hydrogens ☐ Depth cue ☐ Show cell axes ☐ Z-Clipping ☐ Label atoms ☐ Stereo

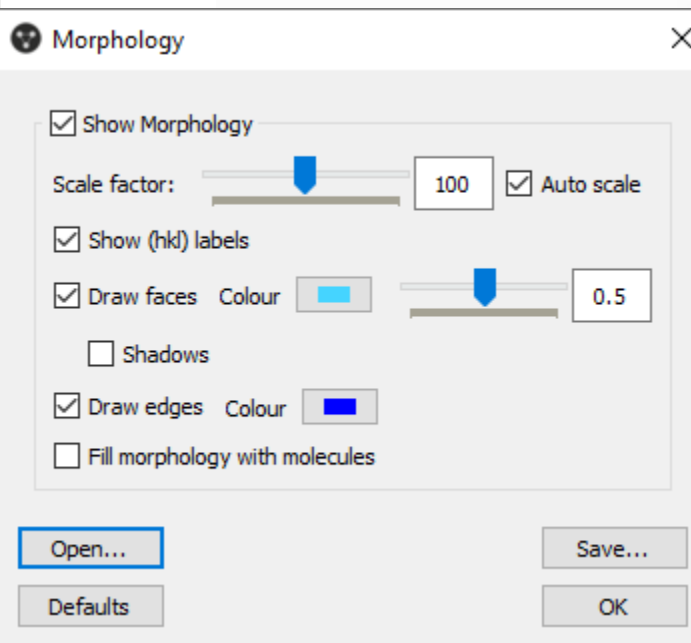
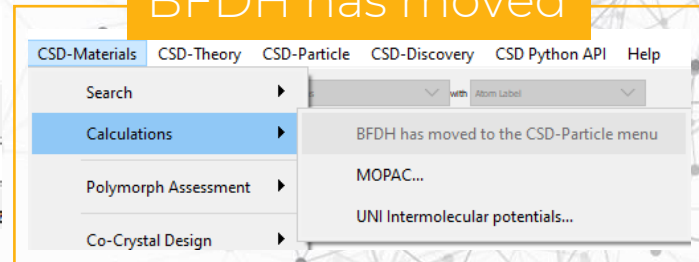
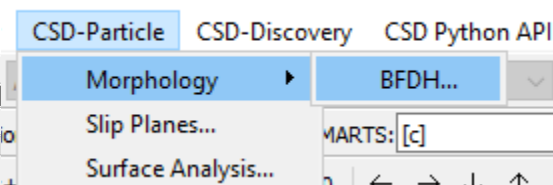
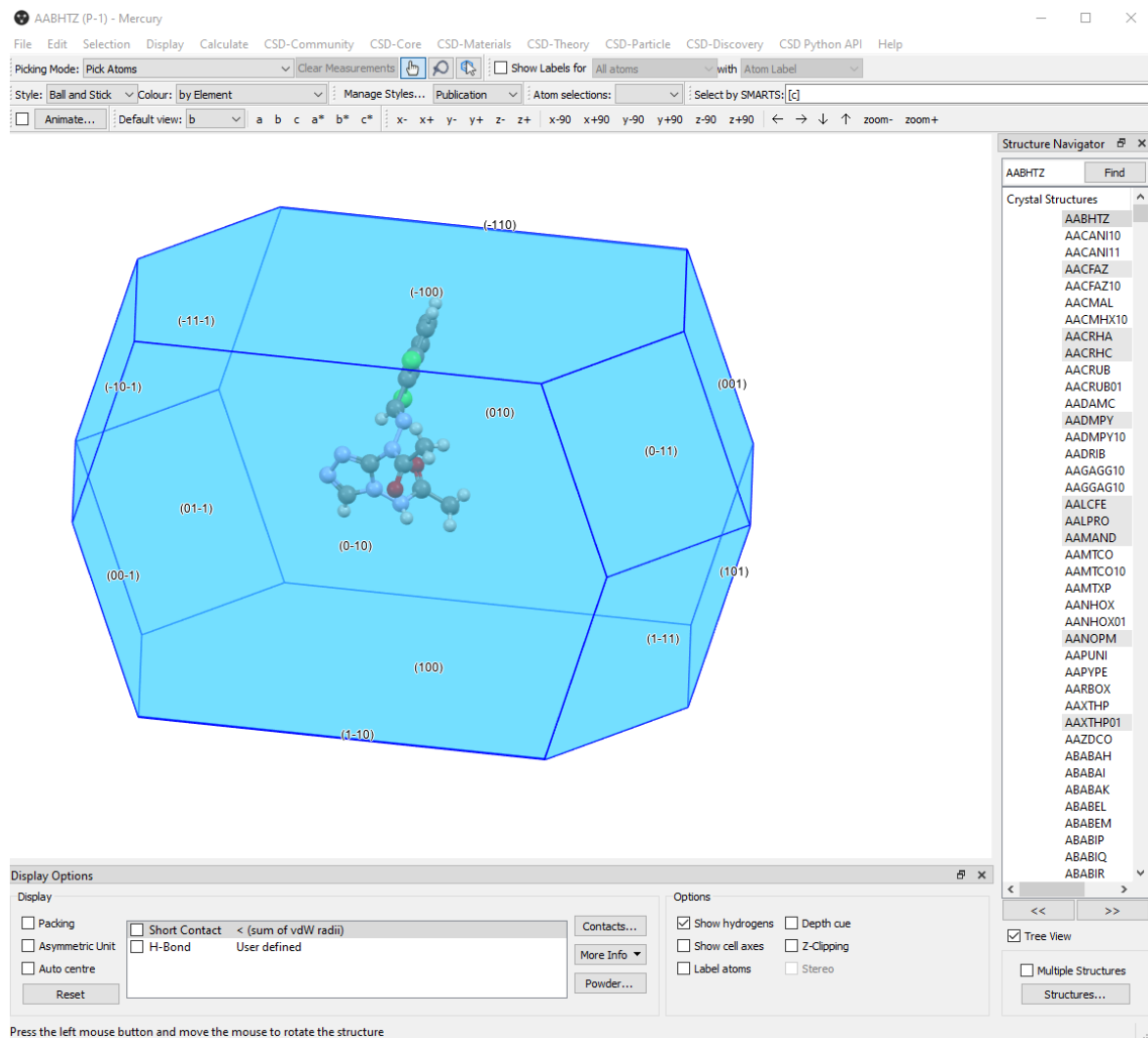
Tree View

Multiple Structures Structures...

Press the left mouse button and move the mouse to rotate the structure

CSD-Particle – Morphology - BFDH

BFDH has moved

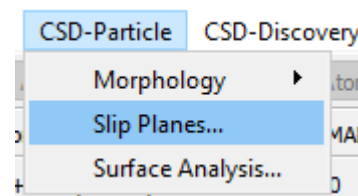
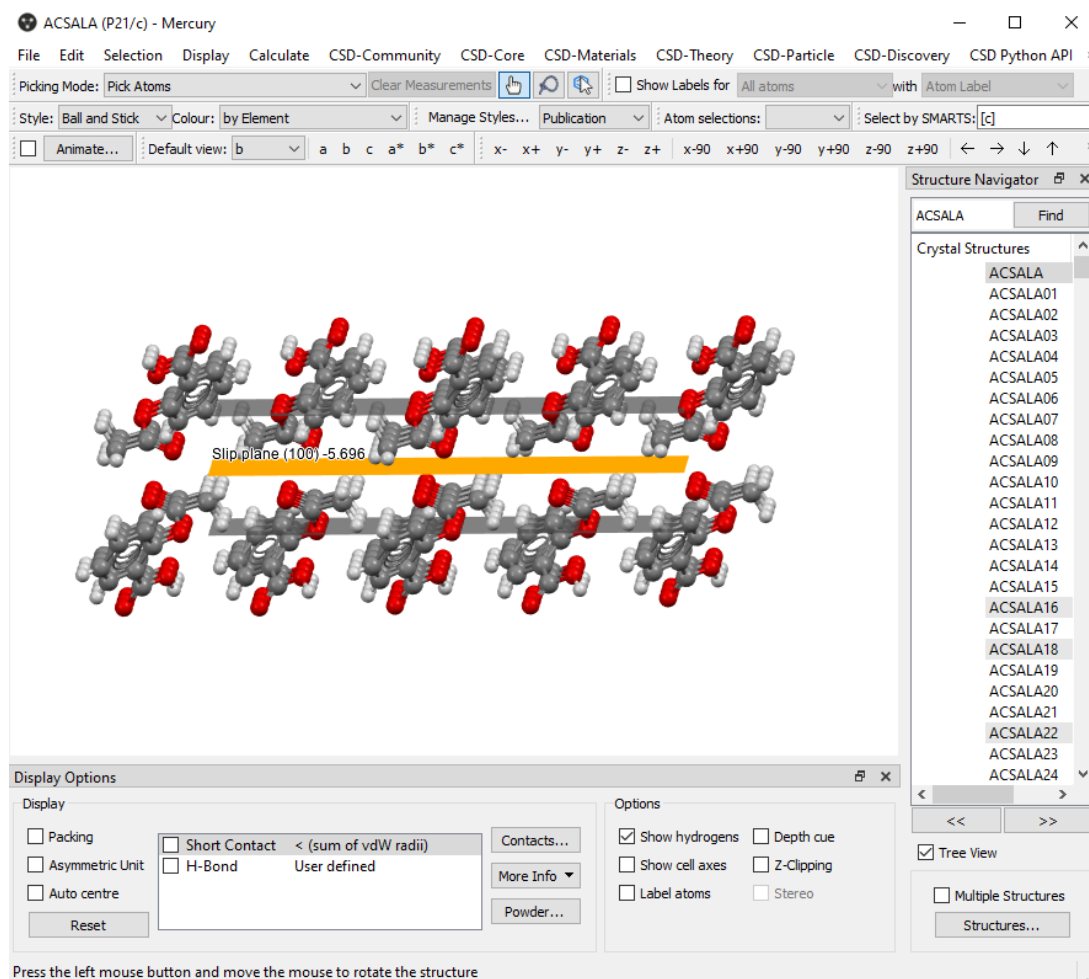


Display Options

Save and Load

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

CSD-Particle – Slip Planes



Slip Planes... ACSALA

Minimum slab separation 0.0 Reset

Status: Calculation completed

	Orientation	Slab separation	Repeat distance	Offset	H-bonded	Perpendicular planes
1	(100)	1.574	11.392	-5.696	no	
2	(100)	0.242	11.392	0.000	yes	

H-bond dimensionality: 0D discrete

Analyse Surface Export... Calculate Close

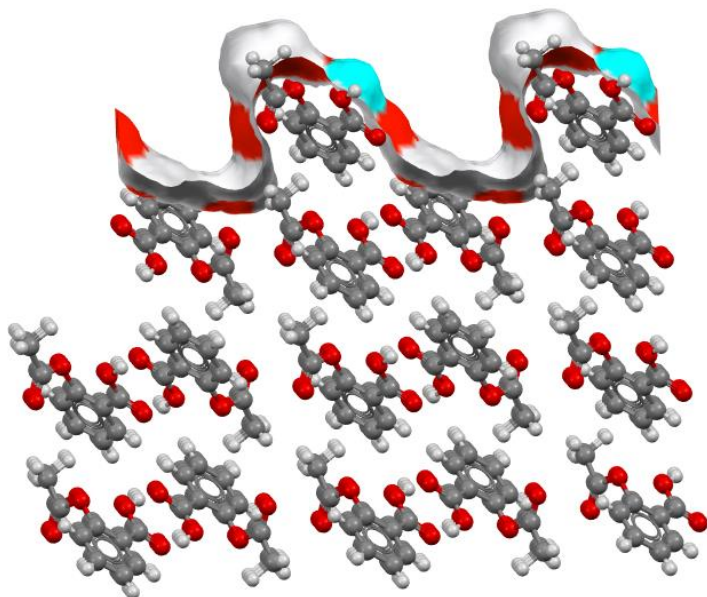
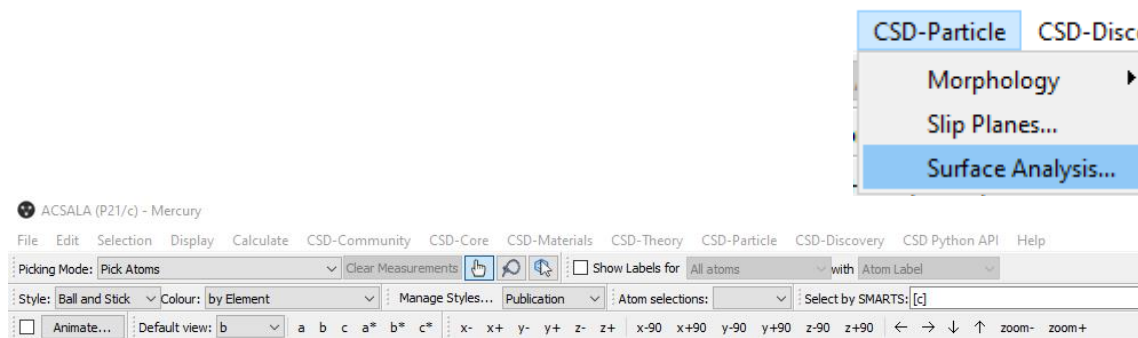
Possible Slip Planes

H-Bond System

Export Table

Learn more on
[Slip Planes](#)
in the *Glossary* in
the handout.

CSD-Particle – Surface Analysis



Surface Analysis... ACSALA

Analyse

Select surface orientation (hkl) and offset (o)

h: 0 k: 0 l: 2 o: 0.00

☐ Preview Slab

☐ Show Advanced Options

Full Interaction Map

Calculate Surface

Input

Results - ACSALA (002)[0.00]

Density Info (count/Å²)

H-Bond Acceptors: 0.079

Aromatic Bonds: 0.159

H-Bond Donors: 0.013

Unsatisfied H-Bond Donors: 0.013

Topology Info

Surface Area (Å²): 637.558

Projected Area (Å²): 301.991

Rugosity: 2.111

RMSD: 2.273

Skewness: 0.052

Kurtosis: 1.729

Display Options

Surface colouring:

Atom Properties

Opacity: (%)

100

☐ Periodic View

☐ Hide Molecules

Atom Properties

☐ Charge

☒ H-Bond Acceptors

☐ Aromatic

☒ H-Bond Donors

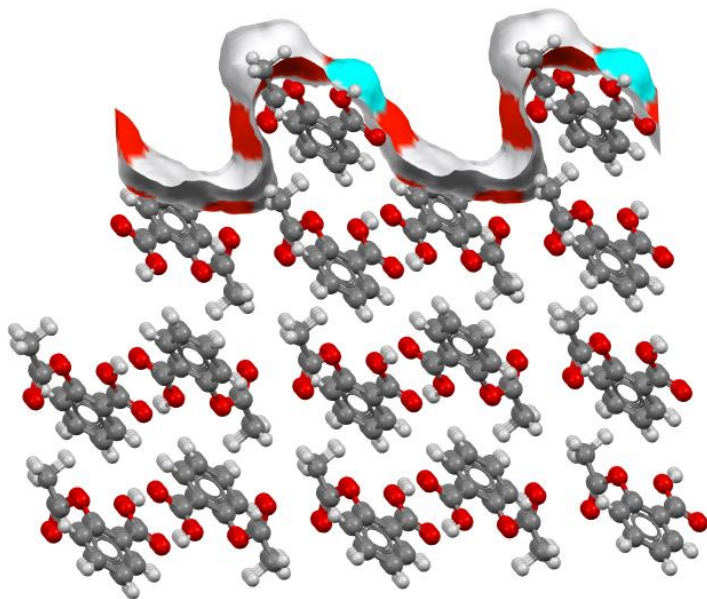
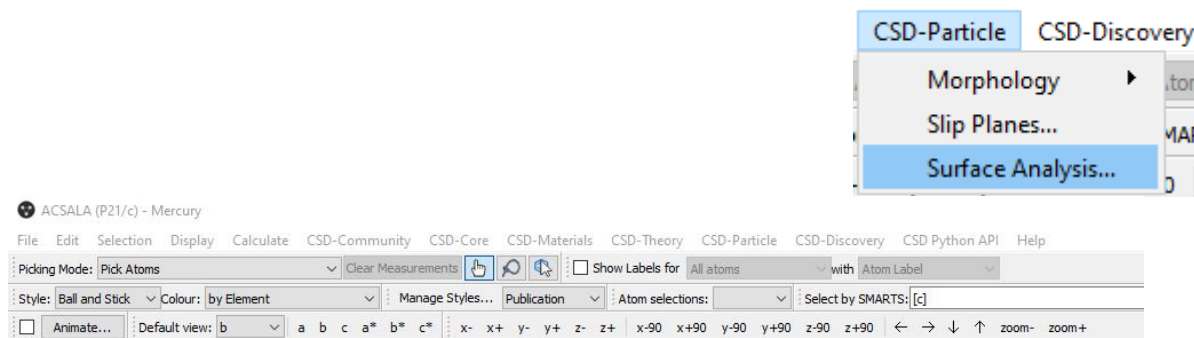
☒ Unsatisfied H-Bond Donors

Reset

Close

CCDC

CSD-Particle – Surface Analysis



Surface Analysis... ACSALA

Analyse

Select surface orientation (hkl) and offset (o)

h: 0 k: 0 l: 2 o: 0.00 ☐ Preview Slab

☐ Show Advanced Options

Full Interaction Map Calculate Surface

Results - ACSALA (002)[0.00]

Density Info (count/Å²)

H-Bond Acceptors:	0.079	Aromatic Bonds:	0.159
H-Bond Donors:	0.013	Unsatisfied H-Bond Donors:	0.013

Topology Info

Surface Area (Å ²):	637.558	Projected Area (Å ²):	301.991
Rugosity:	2.111	RMSD:	2.273
Skewness:	0.052	Kurtosis:	1.729

Display Options

Surface colouring: Atom Properties

Opacity: (%) 100

☐ Periodic View ☐ Hide Molecules

Atom Properties

☐ Charge ☒ H-Bond Acceptors

☐ Aromatic ☒ H-Bond Donors

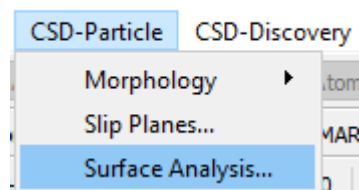
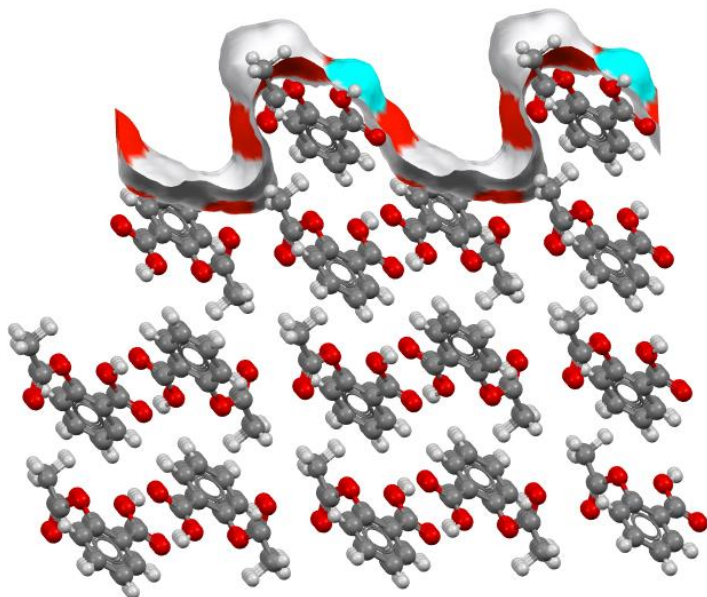
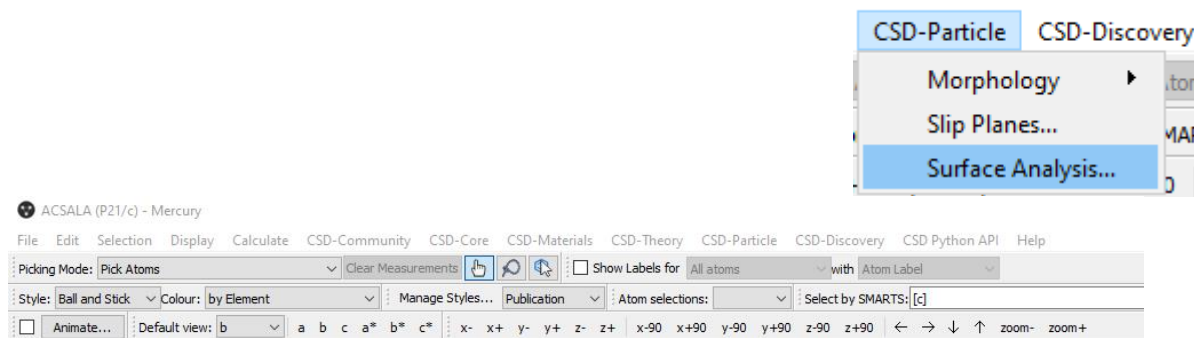
☒ Unsatisfied H-Bond Donors

Reset Close

Results

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

CSD-Particle – Surface Analysis



Surface Analysis... ACSALA

Analyse

Select surface orientation (hkl) and offset (o)

h: 0 k: 0 l: 2 o: 0.00 ☐ Preview Slab

☐ Show Advanced Options

Full Interaction Map Calculate Surface

Results - ACSALA (002)[0.00]

Density Info (count/Å²)

H-Bond Acceptors:	0.079	Aromatic Bonds:	0.159
H-Bond Donors:	0.013	Unsatisfied H-Bond Donors:	0.013

Topology Info

Surface Area (Å ²):	637.558	Projected Area (Å ²):	301.991
Rugosity:	2.111	RMSD:	2.273
Skewness:	0.052	Kurtosis:	1.729

Display Options

Surface colouring: Atom Properties

Opacity: (%) 100

☐ Periodic View ☐ Hide Molecules

Atom Properties

☐ Charge ☒ H-Bond Acceptors

☐ Aromatic ☒ H-Bond Donors

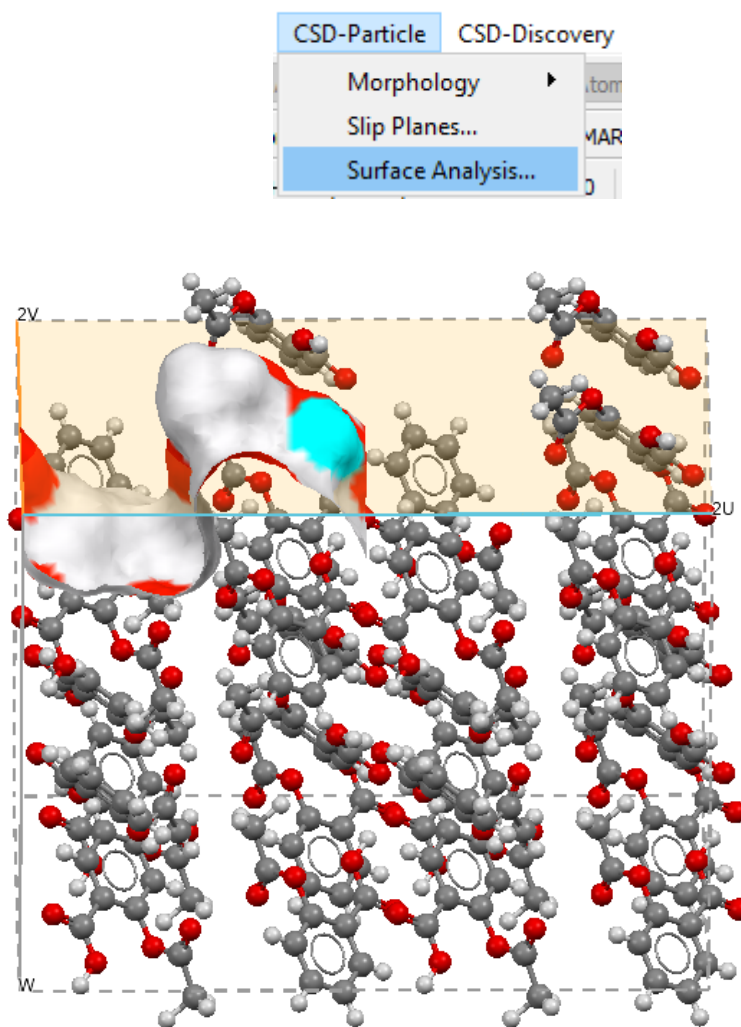
☒ Unsatisfied H-Bond Donors

Reset Close

Display Options

CCDC

CSD-Particle – Surface Analysis



The screenshot shows the 'Surface Analysis... ACSALA' dialog box. The 'Advanced Options' section is highlighted with a blue box. The 'Analyse' section includes fields for 'h', 'k', 'l', and 'o', and a 'Preview Slab' checkbox. The 'Advanced Options' section includes fields for 'Size of Surface' (U, V), 'Probe Radius', 'Grid Spacing', and 'Thickness (W) Factor'. The 'Results - ACSALA (002)[0.00]' section displays density information and topology data. The 'Display Options' section includes checkboxes for 'Periodic View', 'Hide Molecules', 'Atom Properties', 'Charge', 'Aromatic', 'H-Bond Acceptors', 'H-Bond Donors', and 'Unsatisfied H-Bond Donors'.

Analyse

Select surface orientation (hkl) and offset (o)

h: 0 k: 0 l: 2 o: 0.00 ☒ Preview Slab

☒ Show Advanced Options

Size of Surface: U: 2 V: 2

Default values for the following settings have been optimised for small molecule organic systems.

Probe Radius: 1.2 Grid Spacing: 0.3

Thickness (W) Factor: 1.60

Full Interaction Map Calculate Surface

Results - ACSALA (002)[0.00]

Density Info (count/Å³)

H-Bond Acceptors: 0.079	Aromatic Bonds: 0.159
H-Bond Donors: 0.013	Unsatisfied H-Bond Donors: 0.013

Topology Info

Surface Area (Å ²): 159.389	Projected Area (Å ²): 75.498
Rugosity: 2.111	RMSD: 2.273
Skewness: 0.052	Kurtosis: 1.729

Display Options

Surface colouring: Atom Properties

Opacity: (%) 100

☐ Periodic View ☐ Hide Molecules

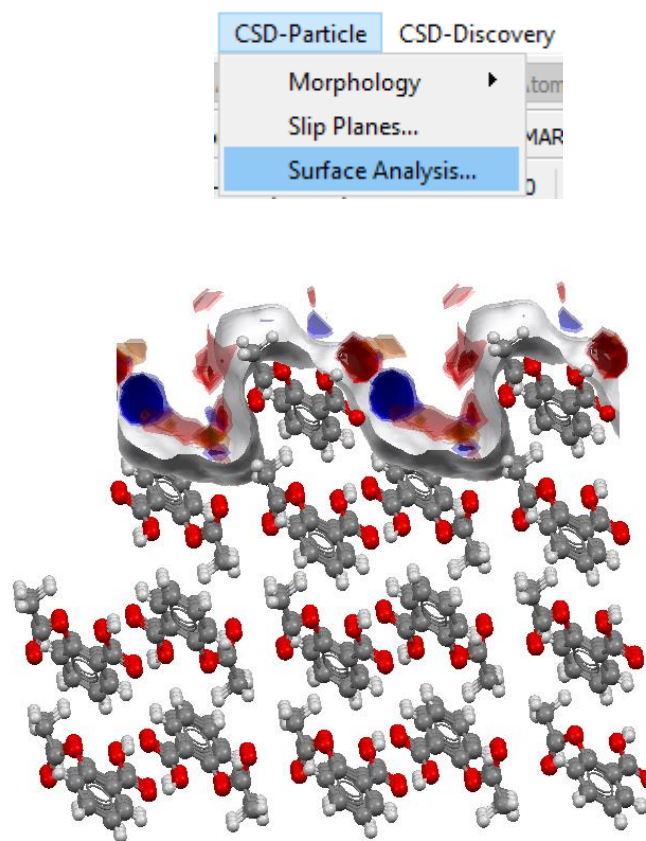
Atom Properties

☐ Charge	☒ H-Bond Acceptors
☐ Aromatic	☒ H-Bond Donors
	☒ Unsatisfied H-Bond Donors

Reset Close

Advanced Options

CSD-Particle – FIMs on Surface



Surface Analysis... ACSALA

Analyse

Select surface orientation (hkl) and offset (o)

h: 0 k: 0 l: 2 o: 0.00 ☒ Preview Slab

☒ Show Advanced Options

Size of Surface: U: 2 V: 2

Default values for the following settings have been optimised for small molecule organic systems.

Probe Radius: 1.2 Grid Spacing: 0.3

Thickness (W) Factor 1.60

Results - ACSALA (002)[0.00]

Density Info (count/Å²)

H-Bond Acceptors: 0.079	Aromatic Bonds: 0.159
H-Bond Donors: 0.013	Unsatisfied H-Bond Donors: 0.013

Topology Info

Surface Area (Å ²): 159.389	Projected Area (Å ²): 75.498
Rugosity: 2.111	RMSD: 2.273
Skewness: 0.052	Kurtosis: 1.729

Display Options

Surface colouring: Atom Properties

Opacity: (%) 100

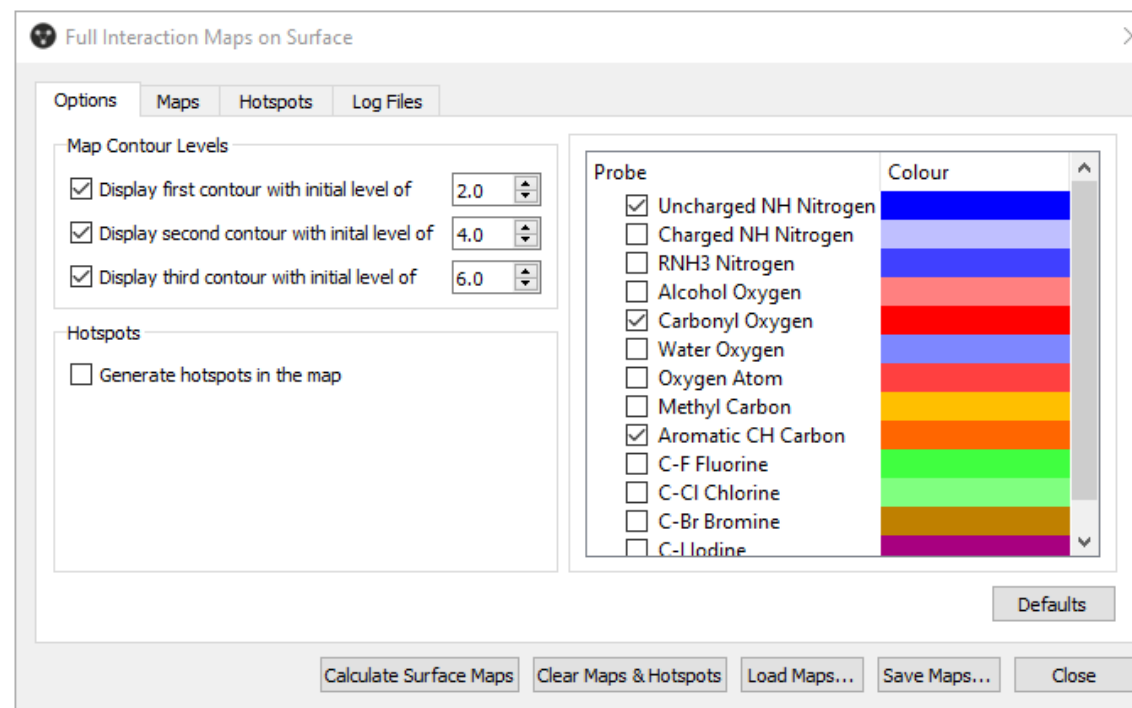
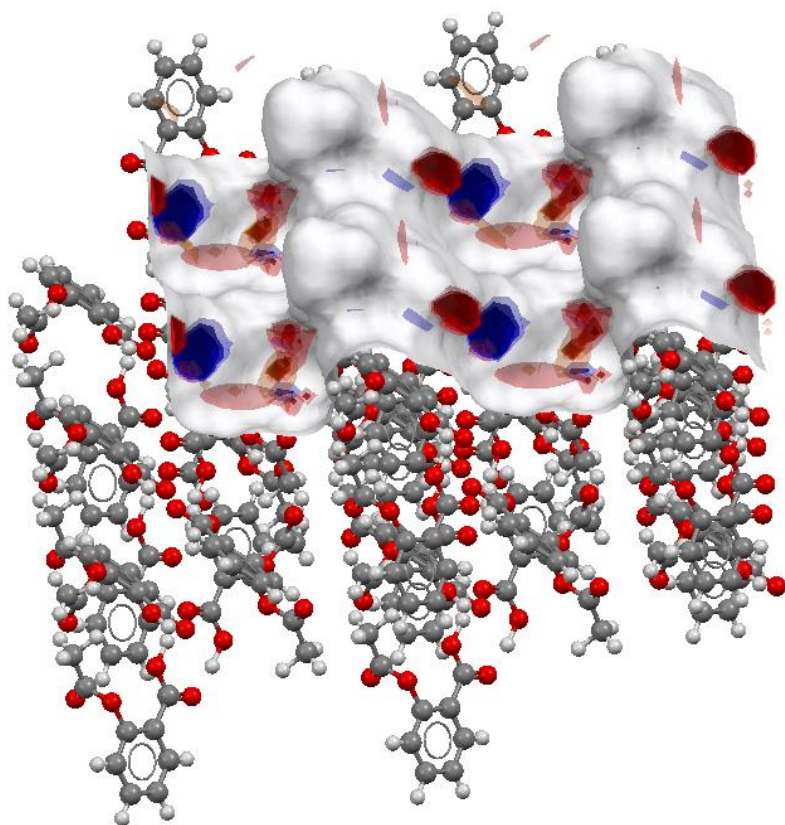
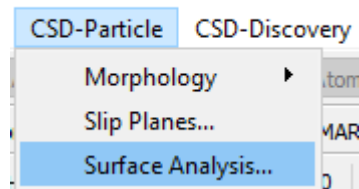
☐ Periodic View ☐ Hide Molecules

Atom Properties

☐ Charge	☒ H-Bond Acceptors
☐ Aromatic	☒ H-Bond Donors
	☒ Unsatisfied H-Bond Donors

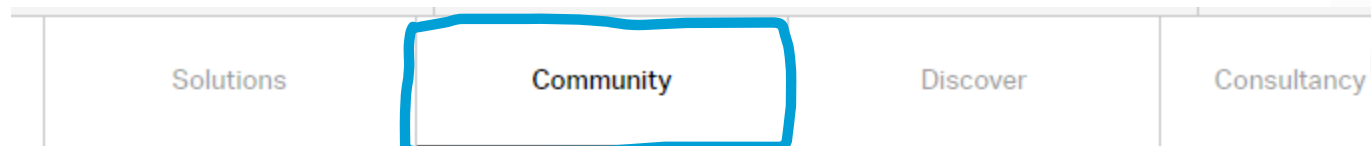
Full Interaction Map on Surface

CSD-Particle – FIMs on Surface



Want to explore more?

On-demand training resources



Access/Deposit Structures

CCDC for the Community

Education and Outreach

Events

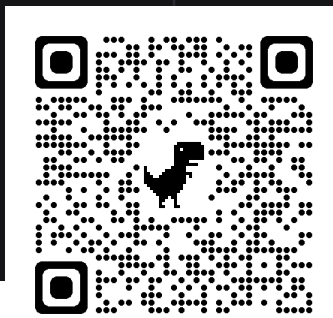
Free Products

Training and Learning

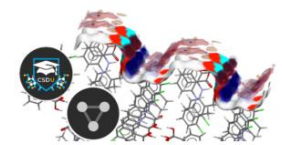
Free Online Courses

Self-Guided Workshops

Training and Support Videos

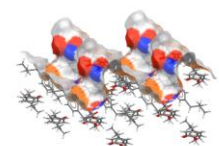


Surface Analysis with CSD-Particle



Start the CSDU module!

CSD-Particle

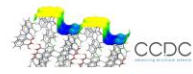


Tools to help you understand particle behaviour and anticipate manufacturing bottlenecks to guide formulation decisions.

CSD-Particle Workshops

Investigation of Plastic and Elastic Properties with CSD-Particle Tools in Mercury (PAR-002)

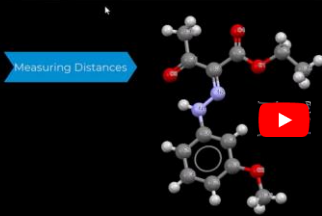
Developed using 2023.3 CSD Mercury



CCDC

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Example 1: Slip plane analysis to investigate elastic properties	3
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Hydrogen bonds analysis	5
Expanding more potential slip planes	7
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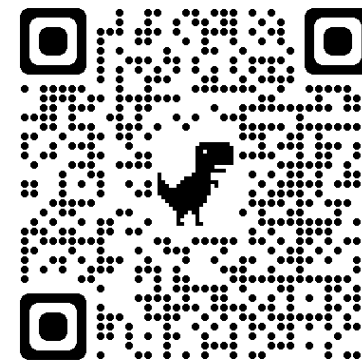
Measuring Distances



Measuring Distances



Free online training courses



With completion certificates!



CSDU

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



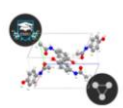
UWatch



UTry



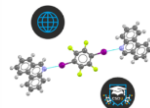
UTest



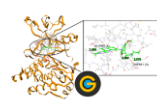
Mercury



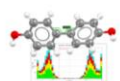
Python
API



WebCSD



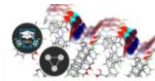
GOLD
Docking



Mogul

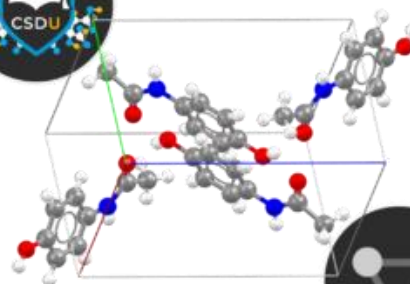


FIMs



Particle

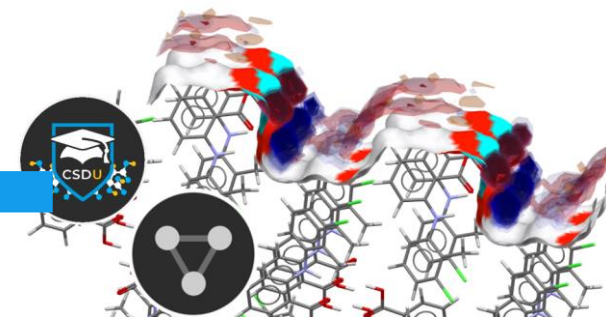
Visualization 101



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

Advanced
Functionality for
Visualization and
Analysis of
Structures in
Mercury



Tuesday, 30th April
4 pm (BST)



REGISTER NOW



CCDC VIRTUAL WORKSHOP

In-Depth
Comparison of
Polymorphic
Structures Using
Mercury



Tuesday, 14th May
10 am (BST)



REGISTER NOW



WEBINAR

Drug Design Inspiration from
Torsional Data Mining

Speaker: Gilles Ouvry, NRG Therapeutics
24 April - 3 p.m. (BST)



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

CCDC