CSD-Core for Medicinal Chemists – Resources and Helpful Information

The **Cambridge Structural Database** (CSD) is a global resource of crystallographic data, widely used by medicinal chemists for its insights into molecular geometries, interactions, and properties crucial in drug design and development.

Capabilities of CSD-Core include:

- Powerful search, advanced 2D/3D visualisation and flexible results analysis
- Conformation analysis
- Fragment interaction maps
- CSD Python API (Applications Programming Interface)

Summary:

CSD-Core supports medicinal chemists by providing a toolkit for analysing, validating, and visualising molecular structures, which are essential to drug discovery and design. The software leverages the Cambridge Structural Database (CSD) to facilitate in-depth understanding of molecular geometries, enabling chemists to predict and optimize interactions between potential drugs and biological targets.

Through tools like Mogul and IsoStar, chemists can assess bond angles, torsions, and intermolecular interactions, refining ligand structures to enhance binding affinity and specificity in structure-based drug design. Additionally, CSD-Core aids in fragment-based drug design by offering libraries and data for assembling small, bioactive molecular fragments into larger therapeutic compounds.

This document aims to support those working in medicinal chemistry by highlighting relevant resources, documentation and literature to assist in their efforts.

Introductory Training Materials & CCDC Resources

Training documentation:

- Structure Visualisations with Mercury - HG-Visualisations-Core.pdf
- An Introduction to ConQuest - Introduction-to-ConQuest.pdf
- An Introduction to IsoStar - Introduction-to-IsoStar.pdf
- An Introduction to Hermes - Introduction-to-Hermes.pdf
- An Introduction to Mogul - HG-Mogul-Intro-MOG-001.pdf
- Using 3D Information in Searches with ConQuest - 3D-information-searches-ConQuest.pdf
- Analysing Molecular Geometries with ConQuest & Mercury - Molecular-geometry-ConQuest-Mercury.pdf

- In-depth Mogul Geometry Analysis - HG-Mogul-Intermediate.pdf
- Advanced training – how to search the CSD with the Python API - Advanced-search-with-API.pdf

Guided Training Videos:

- Guided Video – How to Substructure Search with 3D data - How to: Substructure Search with 3D data
- Guided Video – How to use CSD Subsets in ConQuest - How to use CSD Subsets in ConQuest
- How to measure distances, angles and torsions in Hermes - How to measure distances, angles and torsions in Hermes
- How to visualise proteins in Hermes - How to visualise proteins in Hermes

CCDC Case Studies:

- Mogul in Action - Mogul in Action: Structural Validation of Isoflavones | CCDC; ref ***CrystEngComm***, 2022,**24**, 4731-4739 https://doi.org/10.1039/D2CE00169A
- Mogul in Action (2021) - Mogul in Action: Astex Pharmaceuticals. Protein–Ligand Complex Analysis to Identify Unusual Torsional Geometry in Drug Candidates | CCDC; ref ***J. Med. Chem.***, 2021, **64**, 11, 7533−7543. https://doi.org/10.1021/acs.jmedchem.1c00228

CCDC Webinars:

- Drug Design Inspiration from Torsional Data Mining with Giles Ouvry, NRG Tx - Watch on demand here
- CCDC Webinar: Accelerated, Accurate Drug Discovery using Enhanced Torsion Distributions - Watch on demand here
- User Webinar: How Rapid Assessment of Molecular Geometries Can Help the Structure-Based Drug Designer - Watch on demand here
- Webinar: Using Crystallographic Structures and Data-Driven Solutions to Advance Drug Design - Watch on demand here
- Webinar: How To Get Started With IsoStar, and Tips and Tricks To Work With Hermes - Watch on demand here

CCDC Blogs Posts:

- How Torsional Data Can Inspire Drug Design - How Torsional Data Can Inspire Drug Design | CCDC

- Identifying Unusual Features – Mogul Identifying Unusual Features in Structure-Based Drug Design | CCDC

Additional journal references – med chem related:

J. Chem. Inf. Model. 2019, 59, 10, 4195–4208 (**Torsional Strain in Crystal Structures of Small Molecules and Protein–Ligand Complexes)** **https://doi.org/10.1021/acs.jcim.9b00373**

Liebeschuetz, J. et al. J Comput Aided Mol Des 26, 169–183 (2012). (**The good, the bad and the twisted: a survey of ligand geometry in protein crystal structures**) https://doi.org/10.1007/s10822-011-9538-6

Liebeschuetz, J, J. Med. Chem. 64, 7533–7543 (2021). **(The Good, the Bad, and the Twisted Revisited: An Analysis of Ligand Geometry in Highly Resolved Protein–Ligand X-ray Structures)** https://doi.org/10.1021/acs.jmedchem.1c00228

J. Med. Chem. 2010, 53, 14, 5061–5084 (A Medicinal Chemist's Guide to Molecular Interactions) https://pubs.acs.org/doi/10.1021/jm100112j

Cole JC, Wiggin S, Stanzione F. **New insights and innovation from a million crystal structures in the Cambridge Structural Database**. *Struct Dyn*. 2019;6(5):054301. Published 2019 Aug 28. https://doi.org/10.1063/1.5116878

J. Med. Chem. 2010, 53, 6, 2601–2611. (**Intramolecular Hydrogen Bonding in Medicinal Chemistry)** https://doi.org/10.1021/jm100087s

Joanna, Bojarska & Breza, Martin & Borowiecki, Paweł & Madura, Izabela & Kaczmarek, Krzysztof & Ziora, Zyta & Wolf, Wojciech. (2024) **An experimental and computational investigation of the cyclopentene-containing peptide-derived compounds: focus on pseudo-cyclic motifs via intramolecular interactions** **http://dx.doi.org/10.1098/rsos.240962**

Customer Testimonials:

- "Time and time again, going back to actual conformational data derived from small molecule Xray has helped me interpret structure activity relationships" – Dr Giles Ouvry, ***NRG Therapeutics*.**
- "The breadth and depth of CSD data is enormous today. It covers a lot of space of interest to medicinal chemistry" – Dr Martin Stahl, CSO, ***LifeMine Therapeutics*.**

- “Mogul is an excellent tool for identifying crystallographic problems with ligands in protein-ligand crystal structures” – Dr John Liebeschuetz, Computational Chemist, ***Astex Pharmaceuticals*.**