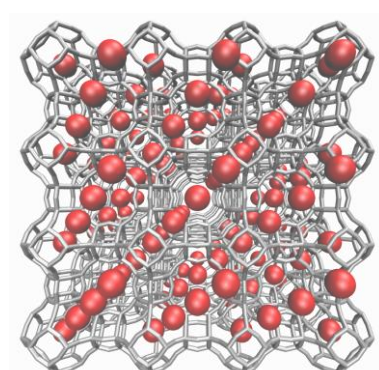


CRYSTALLINE SPONGES: CRYSTALLISING THE UNCRYSTALLISABLE

Robert C. Carroll, Simon J. Coles

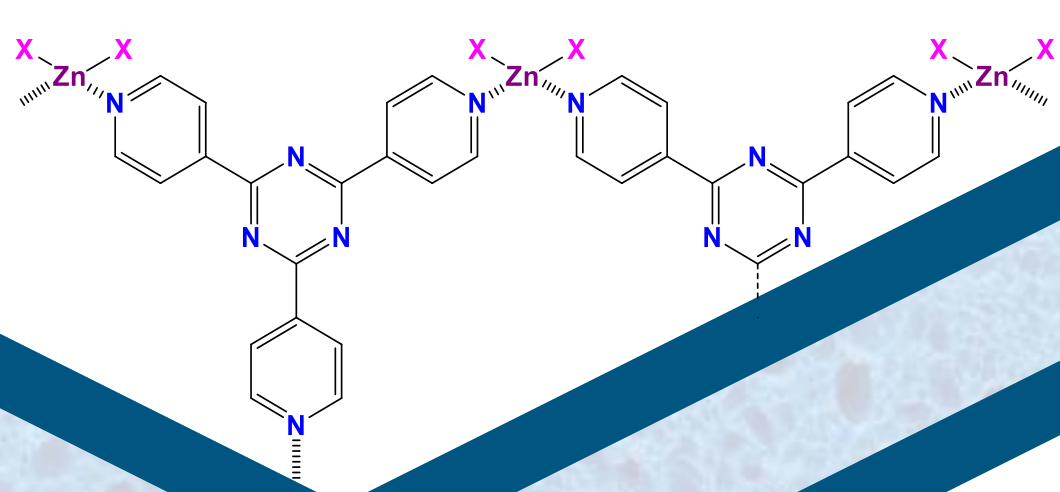
POROUS MATERIALS



Porous solids can be used for gas storage, drug delivery, and **analysis of drugs!** [1]

Metal Organic Frameworks (**MOFs**) are some of the **most diverse** porous materials available to researchers

Smaller building units bond together to form **infinite networks** with accessible **pores** and **cavities**



CRYSTALLINE SPONGES

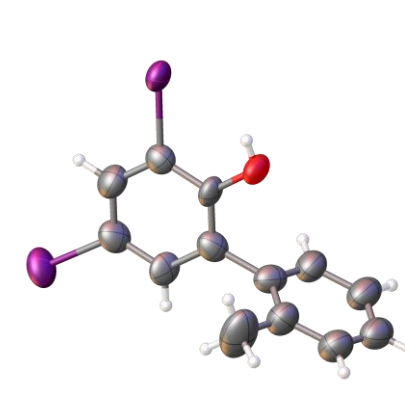
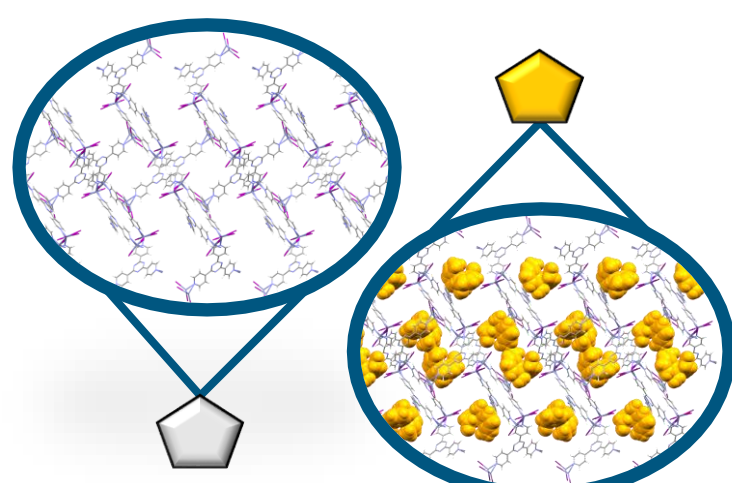


Crystalline Sponges (CS) aid **analysis of drugs**

They are **molecular scaffolds** which **soak-up** small molecules and hold them in place for study with X-rays! [2]



Oily Product



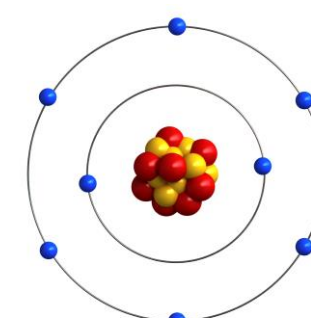
Atomic Structure

Drugs which were **previously impossible** to analyse with X-ray diffraction are now compatible!

X-RAY DIFFRACTION



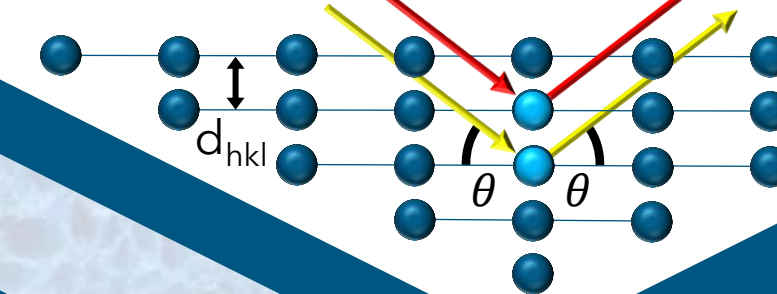
"**Gold standard**" for molecular structure analysis and provides us with atomic level details!



XRD probes electron density and helps to determine **shape** of molecules and the **element types** present

However, the technique is **limited** by the need for **high-quality single crystals** which many drugs can't form!

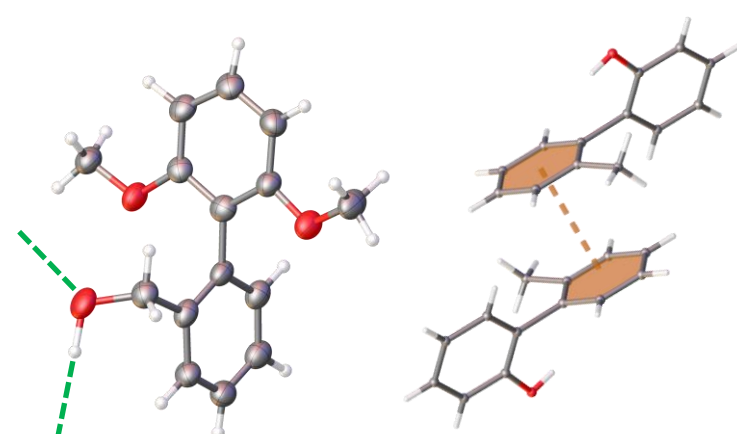
Atoms scatter X-rays at incident angles



DRUG INTERACTIONS

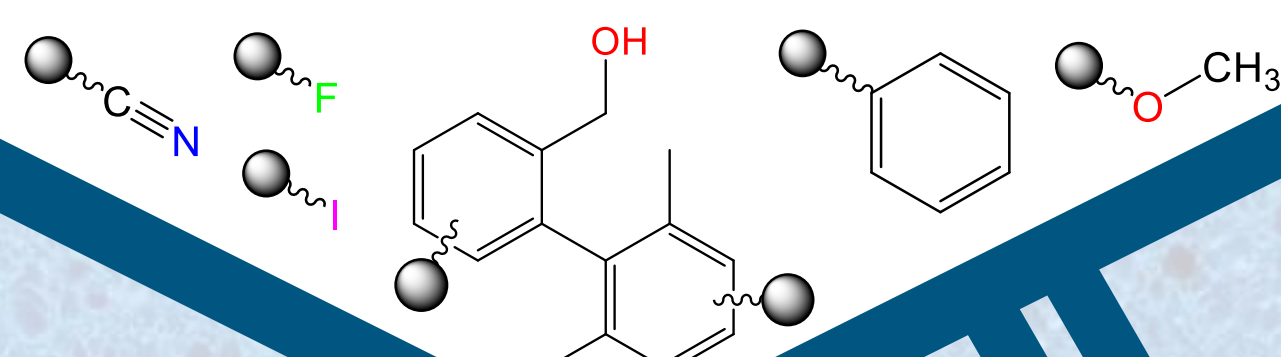
Intermolecular interactions guide how drugs arrange on the atomic scale

Type of contact depends on the atoms present and influences if treatments are provided to patients as **tablets** or **injections**



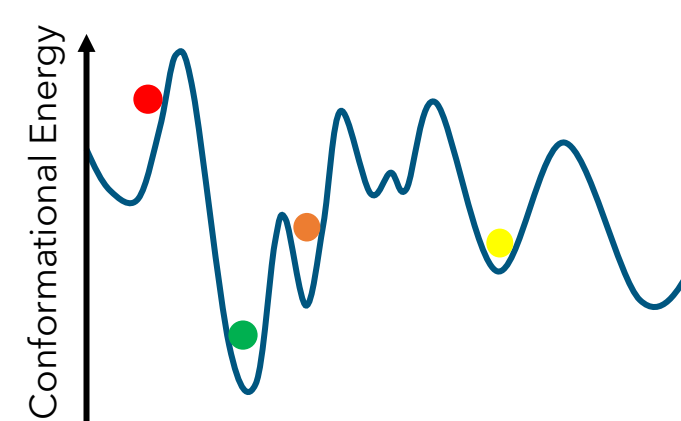
Analysing a family of molecules with a range of chemical functionalities enabled study of **host-guest interactions**

Small structural changes had a big influence, we could rationalise which drugs would work well with CS in future!



DRUG 3D SHAPE

Drug 3D shape determines how molecules **interact with enzymes** in the body



It can be **extremely difficult** to determine molecular geometry for liquids and oils!

Our study compared CS with **gas**, **liquid**, and **solid** forms to construct a spectrum of conformational flexibility

Some guests had relaxed '**liquid-like**' shapes and shows CS can offer even more insight for **pharmaceuticals!**

CRYSTAL SERVICE

The **National Crystallography Service (NCS)** has been in Southampton since 1997 and operating since 1980

Home to some of the **most powerful** lab-based X-ray diffractometers in the world and **100+ years** of experience!



Data was collected on **ADA**, one of our copper source instruments

In 2023 **Newcastle University** was incorporated into the NCS, adding more expertise to the service!

CONCLUSIONS

Small structural changes impact **interactions** with the CS host and informed us which drugs will be **compatible!**

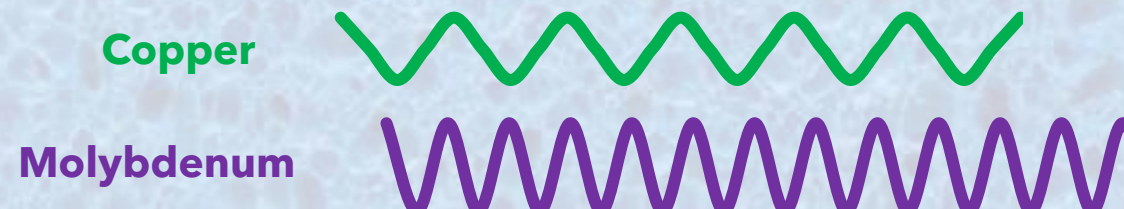
Relaxed guest molecules offer insights into '**liquid**' conformations, vital for understanding how drugs behave!

Advancements made in **methodology** can now be used by other researchers to find **new crystalline sponges!**

- [1] H. Furukawa *et al.* *Science* **2013**, 341, 1230444
- [2] Y. Inokuma *et al.* *Nature* **2013**, 495, 461 - 46
- [3] R. C. Carroll *et al.* *IUCrJ* **2023**, 10, 497 - 508

We thank EPSRC for funding this project, as well as the NCS and Merck Crystal-Do teams for support throughout the work.

Different metals produce X-rays with different wavelengths!



For scale, rhinos are ~1000x larger than squirrels!



NANOCRYSTALS

Launched in 2023 the **National Electron Diffraction Facility (NEDF)** will complement XRD analysis at the NCS

CS research has improved analysis of liquids, but the **size of crystals** has also been challenging researchers

Combining CS and NEDF aims to improve **quality** of results and develop **new hosts!**



Electrons enable analysis of crystals **1000x smaller** than X-rays due to stronger interactions with matter!