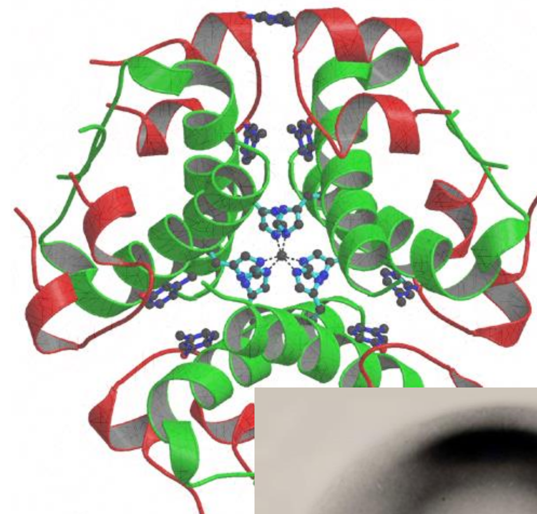
Crystallography with non-crystalline materials

Literature Presentation
22.10.13

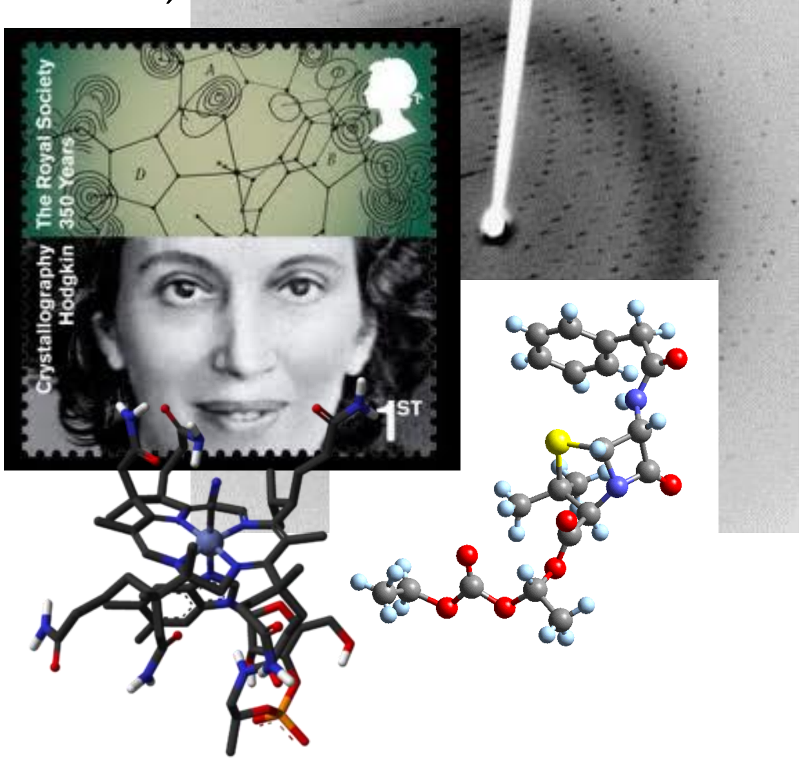
Jacqueline Habegger

Importance of crystallography

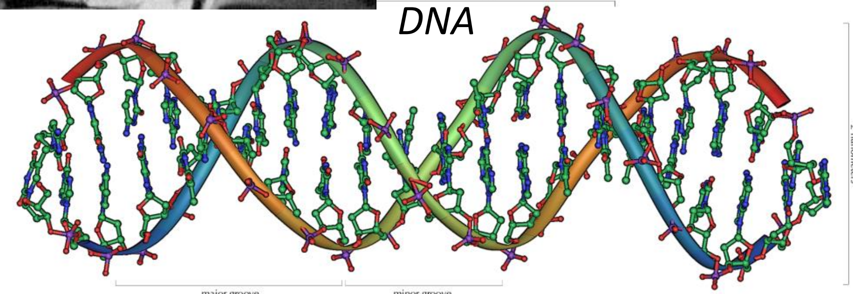
- Direct structural information at the atomic level
- Most reliable structure determination
- Determination of absolute stereochemistry
- Valuable for protein structure determination



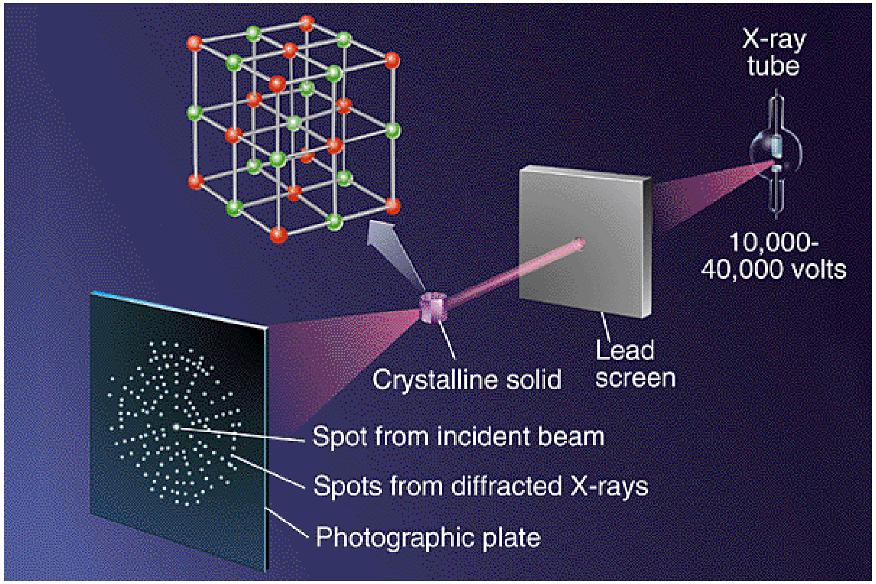
Dorothy Hodgkins
Penicillin, Vitamine B12



Rosalind Franklin
DNA

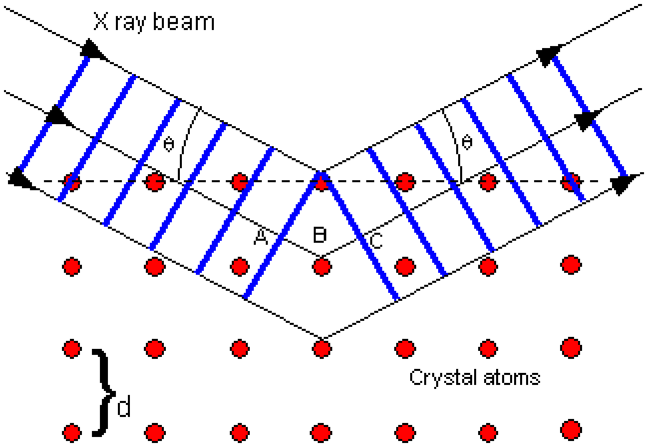


Experimental technique



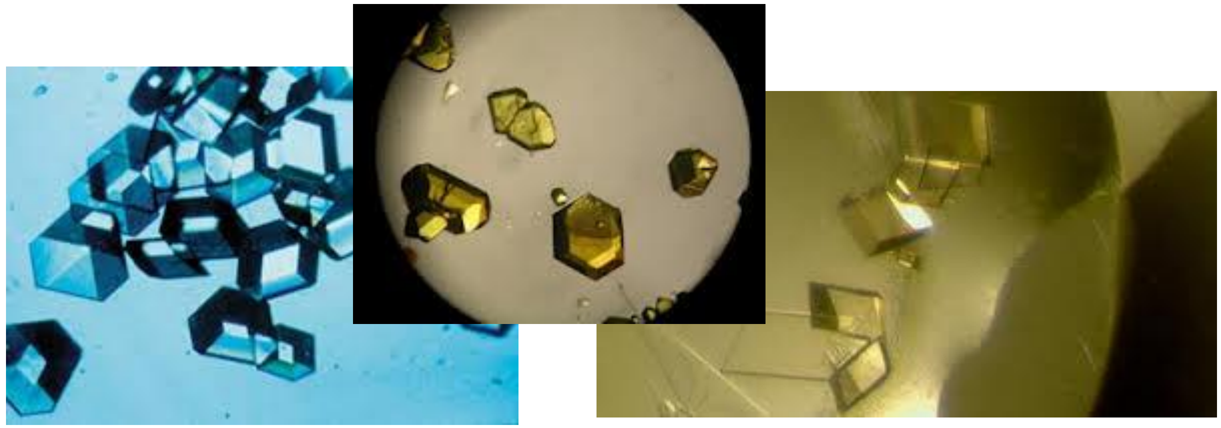
- X-rays are diffracted by electrons
- Interference of scattered X-rays produces diffraction pattern
- Crystalline sample is required in order to amplify the signals

- Many improvements over the decades
- Better X-ray sources (e.g. synchrotron)
- Better detectors
- Computer programs to solve structures



Bottleneck: Crystallisation

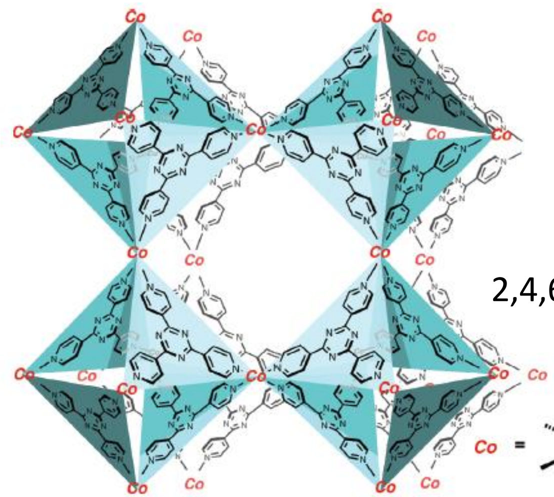
- **Material must be crystalline!**

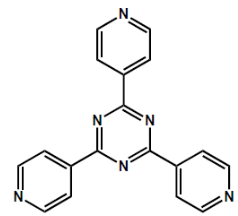


- Crystallising material can take long times
- Requires relatively large amounts of material
- Some solids just do not form crystals
- Oils and liquids can not be crystallised

How else can we get ordered systems?

Metal-organic frame works





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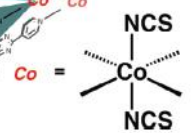
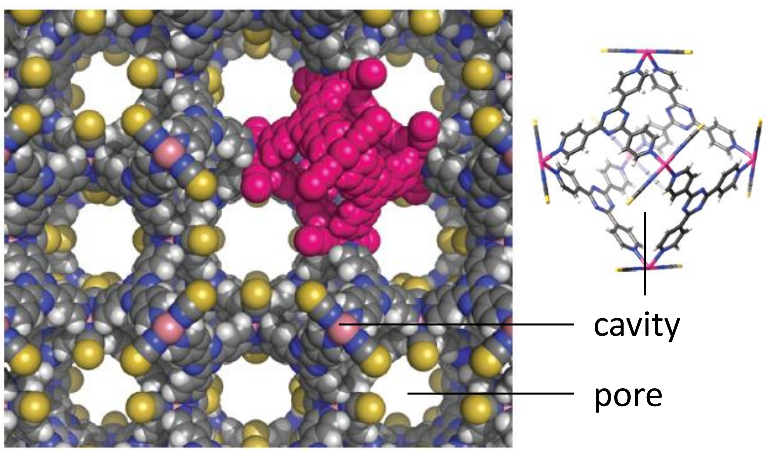
2,4,6-tris(4-pyridyl)triazine (TPT)

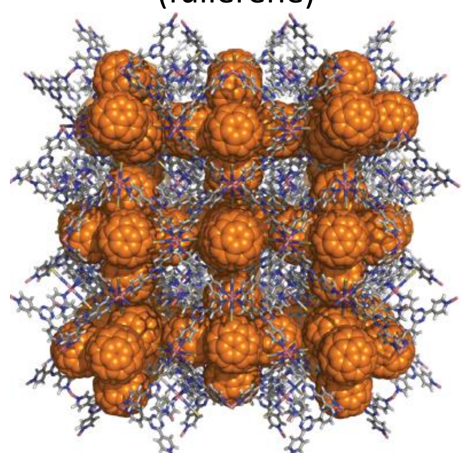


$\{[(Co(NCS)_2)_3(\mathbf{1})_4] \bullet x(\text{solvent})\}_n$

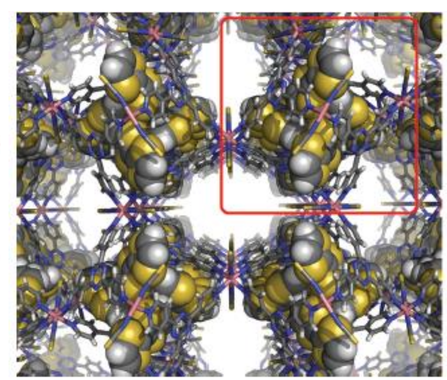
- Crystalline porous network cages
- Developed as host systems
- Most guest/host systems do not show guests in X-ray (disorder)
- Fujita observed that in their cages guests do show in X-ray
  → **Imposing order on guest systems?**



Pores filled (fullerene)



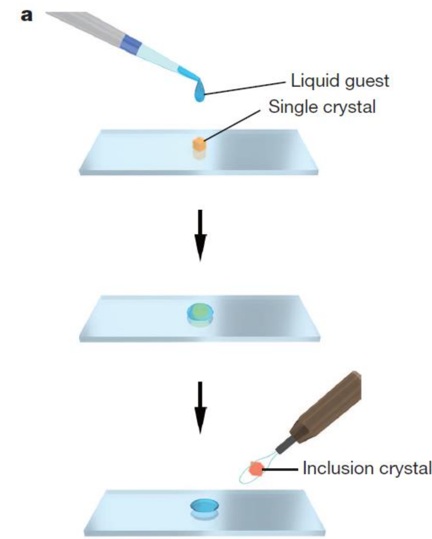
Cavities filled (tetrathiafulvalene)



Fujita, *Nat. Chem.* **2010**, 780
Fujita, *Angew. Chem. Int. Ed.* **2002**, 3392

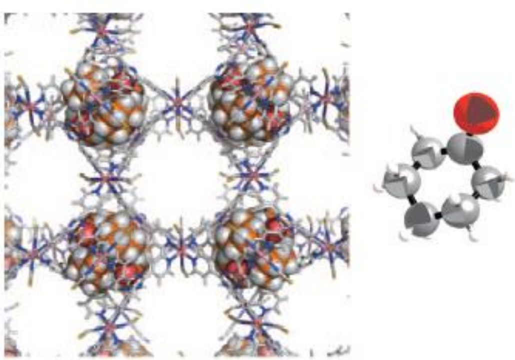
Crystalline sponges for X-ray

- Molecular recognition ability of pores
- Strong host/guest interaction due to panel ligand
- Balance between promiscuity and selectivity
- Voids of sponges contains solvent molecules → wet cavities
- Guest can exchange solvent molecules
- Equilibration process takes place under thermodynamic control

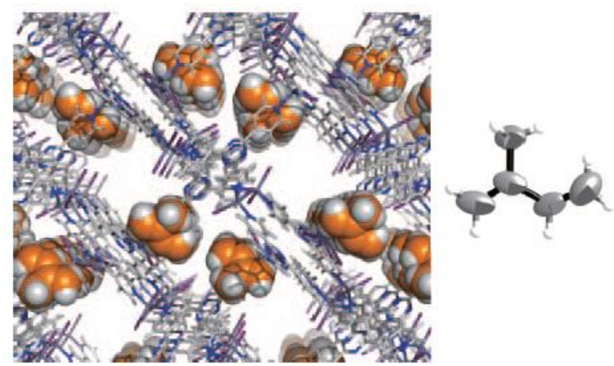


Liquid guest molecules:

Cyclohexanone

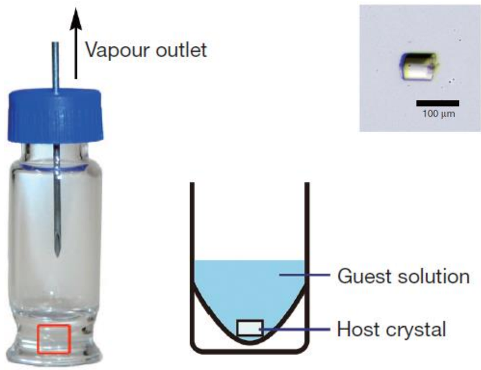


Isoprene



Fujita, *Nature* **2013**, 461

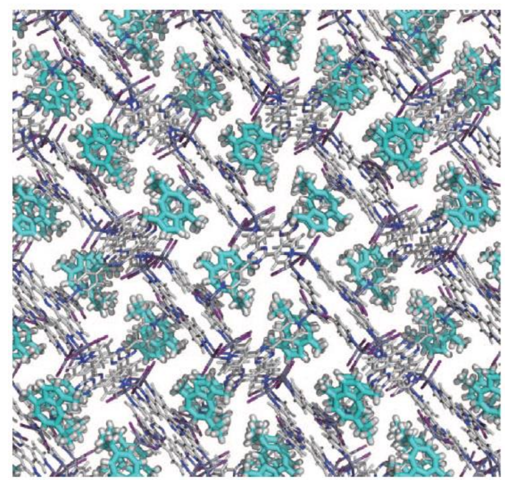
Microanalysis: Sample preparation



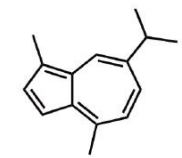
- So far: Large excess of guest molecules
- Only one tiny crystal required for analysis
  → **sample amount estimated in ng-µg order**

Example:

- 500 ng guaiazulene in 5 µl DCM
- Added to host crystal in 45 µl cyclohexane
- Slow evaporation of solvents over 2 d
- Colourless crystal gradually turned blue
- Crystal directly mounted onto diffractometer
- Sample size further reduced to 80 ng (!)



Guaiazulene in host crystal



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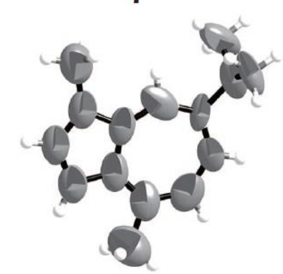


Fujita, *Nature* **2013**, 461

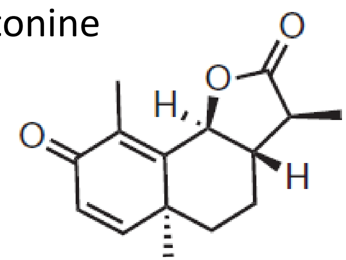
Absolute structure determination

- Usually, chemical introduction of heavy elements is necessary for absolute stereochemistry determination

- Host frame work contains heavy atoms (Co/Zn, I)

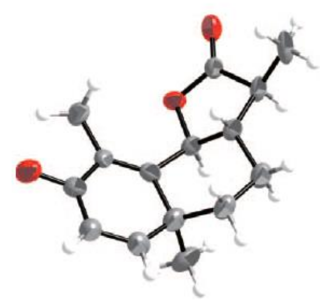
  → **Determination of absolute stereochemistry**!

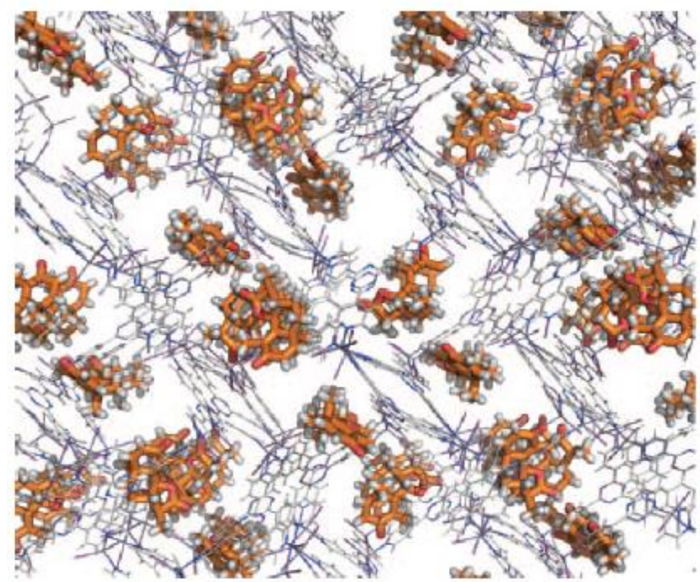
Example: trace amount (5 µg) of santonine



- Coordination network has achiral space group (C2/c)

- Space group changed to chiral ($P2_1$)upon treatment with santonine





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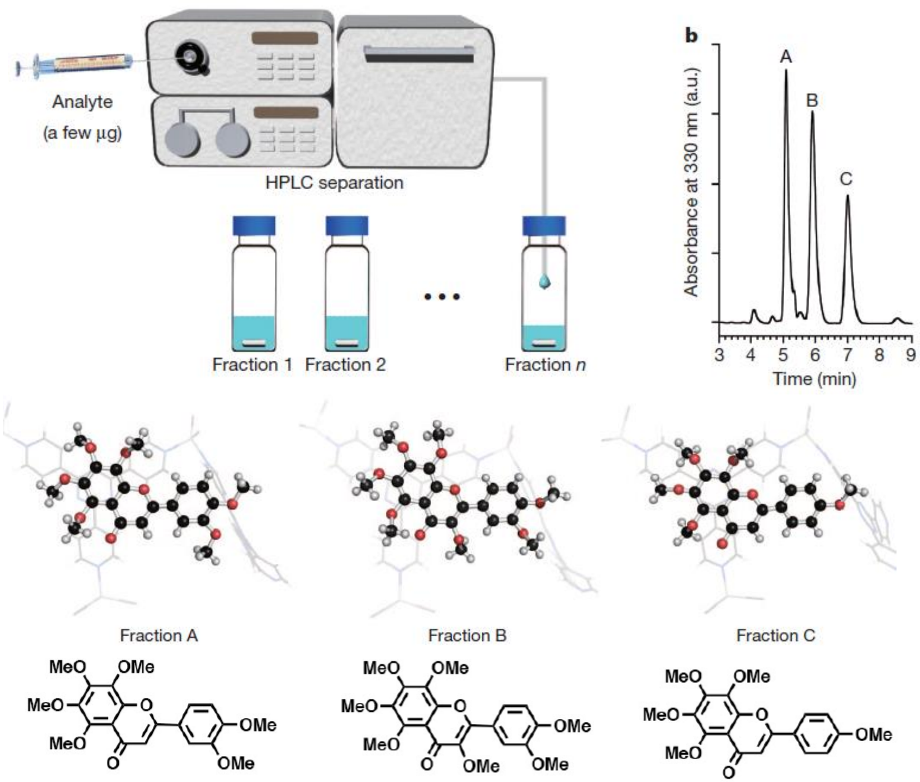
LC-SCD analysis

- Requisite guest amount (micrograms) matches separation scale of HPLC

  → Combination of liquid chromatography and single crystal diffraction LC-SCD



- Trace amount of sample mixture sparated by HPLC

- Each fraction is directly treated with crystalline sponge

Example:

- Crude mixture of polymethoxyflavones (PMFs, ~30 µg) extracted from orange peel

- Three main fractions A (6 µg), B (7 µg) and C (5 µg)

- Structures are in good accordance with MS

Fujita, *Nature* **2013**, 461

Impact and Limitations

- Crystal structures of non-crystalline materials (liquids, oils etc.)
- Microanalysis of small sample mixtures (e.g. natural product mixtures from natural sources)
- Quicker and easier X-ray diffraction
- Future of crystallography: Test different sponges instead of different crystallisations

- Pore size limits size of guest molecule (proteins for example, can not be measured)
  → Synthesis/design of a variety of porous crystals for different purposes
- Scope needs to be examined (how broadly applicable is technique?)