

Chemical Crystallography and Structural Chemistry

(VO 270287)

5th March 2020

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- personal Homepage: <https://homepage.univie.ac.at/tim.gruene/>
- Consultation hours: Thursdays, 12pm-1pm (after lecture), or by appointment

Course Details

5 March	lecture N° 1	19 March	lecture N° 2
26 March	lecture N° 3	2 April	exercise N° 1
23 April	lecture N° 4	30 April	lecture N° 5
7 May	lecture N° 6	14 May	exercise N° 2
28 May	lecture N° 7	4 June	lecture N° 8
25 June	lecture N° 9	18 June	exercise N° 3

- Group exercises: same place, same time
- Lecture notes and exercises will be made available online
- <https://homepage.univie.ac.at/tim.gruene/teaching/chemcryst>

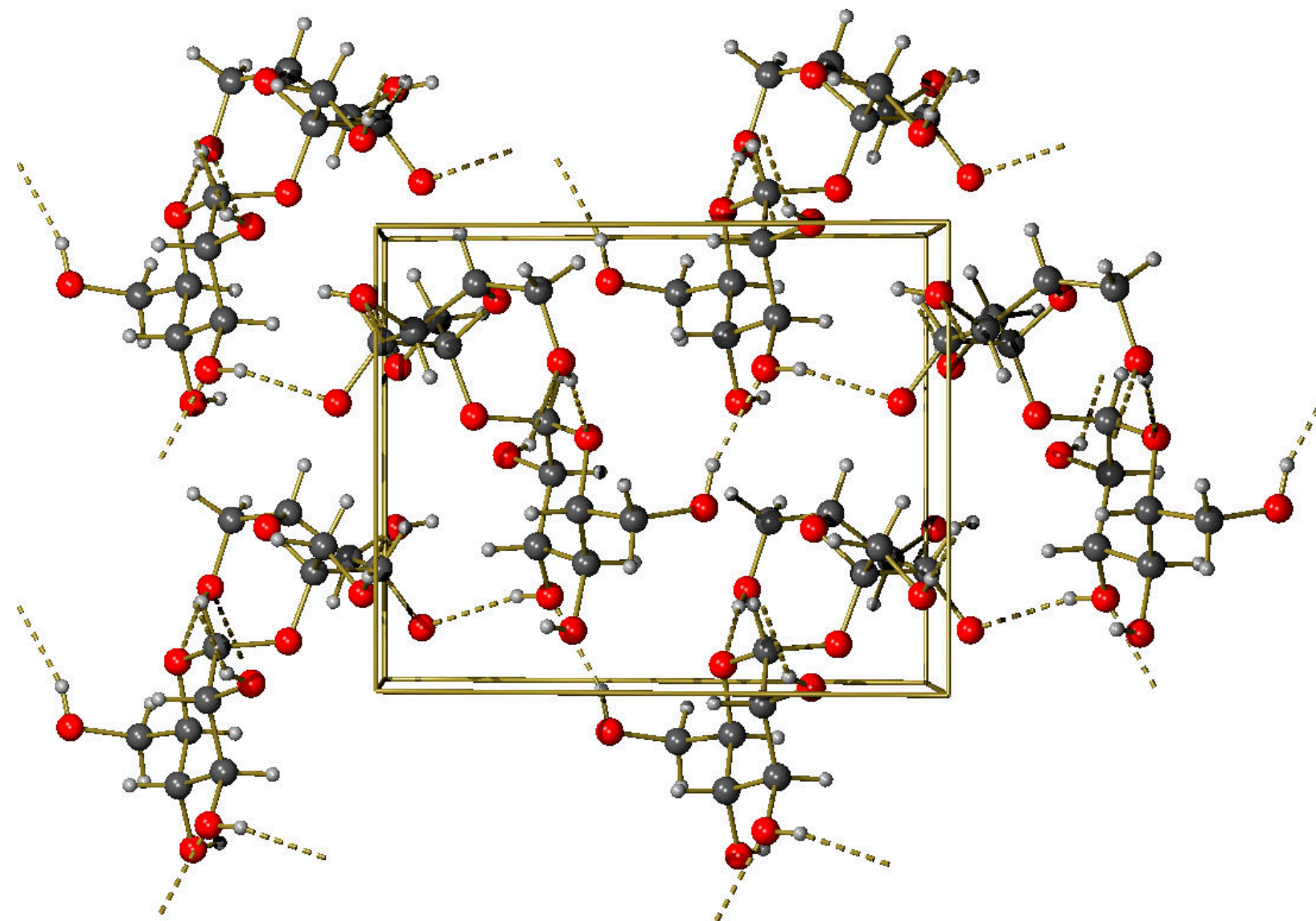
Examination

There will be an **oral** exam.

Course Objective

Chemical Crystallography:

Determination of the 3-dimensional structure of chemical compounds with single crystal diffraction



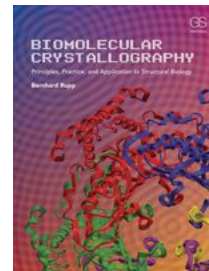
Crystal structure of sucrose, with hydrogen bonds

- what do we learn from a crystal structure?
- what are the **limits** of crystallography

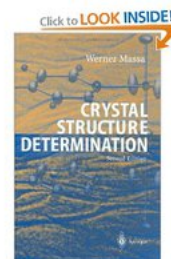
Content of today's Lecture

1. (Teaching) Resources for crystallography
2. (public) data bases for crystallography
3. what are crystals
4. X-rays and X-ray diffractometers
5. Conducting a diffraction experiment

Resources: Literature for Crystallography



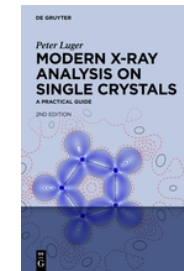
B. Rupp, *Biomolecular Crystallography*, Garland Science



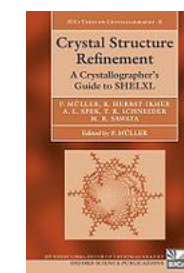
W. Massa, *Crystal Structure Determination*, Springer



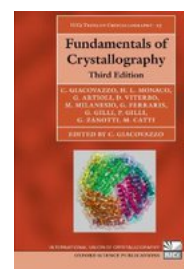
International Tables of Crystallography
A–F <http://www.iucr.org>



P. Luger “Modern X-Ray Analysis on Single Crystals” De Gruyter

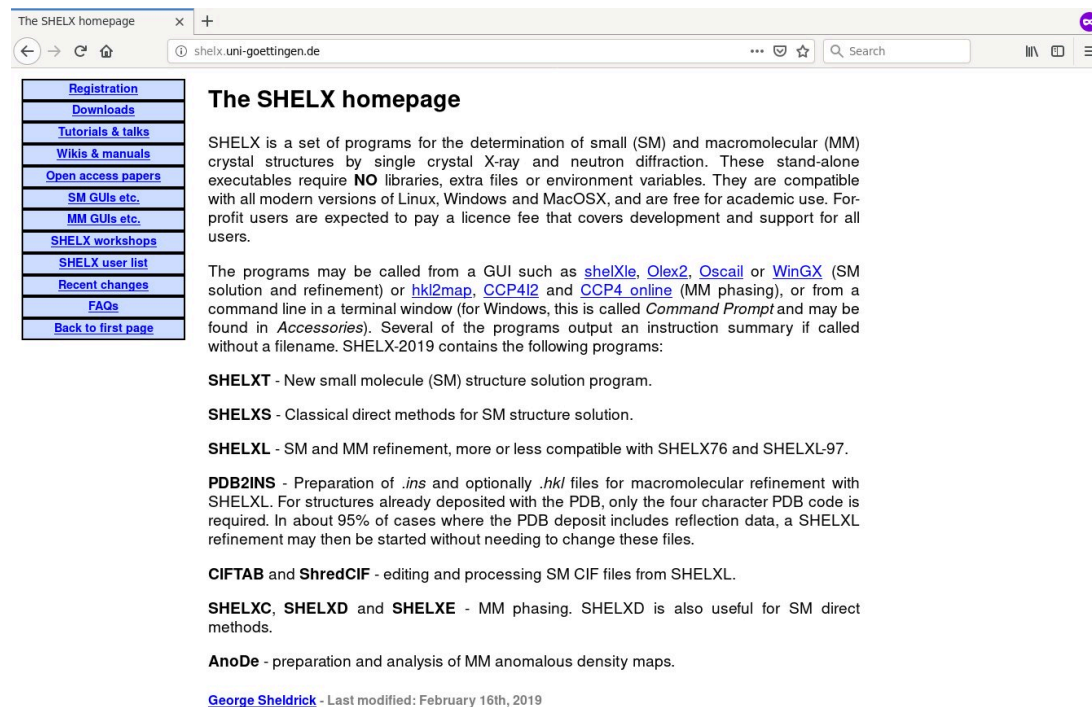


P. Müller *et al.*, “Crystal Structure Refinement — A Crystallographer’s Guide to SHELXL” Oxford University Press



C. Giacovazzo *et al.*, *Fundamentals of Crystallography*, Oxford Science Publications

Online Resources



The SHELX homepage

SHELX is a set of programs for the determination of small (SM) and macromolecular (MM) crystal structures by single crystal X-ray and neutron diffraction. These stand-alone executables require **NO** libraries, extra files or environment variables. They are compatible with all modern versions of Linux, Windows and MacOSX, and are free for academic use. For-profit users are expected to pay a licence fee that covers development and support for all users.

The programs may be called from a GUI such as [shelXle](#), [Olex2](#), [Oscail](#) or [WinGX](#) (SM solution and refinement) or [hkl2map](#), [CCP412](#) and [CCP4 online](#) (MM phasing), or from a command line in a terminal window (for Windows, this is called *Command Prompt* and may be found in *Accessories*). Several of the programs output an instruction summary if called without a filename. SHELX-2019 contains the following programs:

SHELXT - New small molecule (SM) structure solution program.

SHELXS - Classical direct methods for SM structure solution.

SHELXL - SM and MM refinement, more or less compatible with SHELX76 and SHELXL97.

PDB2INS - Preparation of *.ins* and optionally *.hkl* files for macromolecular refinement with SHELXL. For structures already deposited with the PDB, only the four character PDB code is required. In about 95% of cases where the PDB deposit includes reflection data, a SHELXL refinement may then be started without needing to change these files.

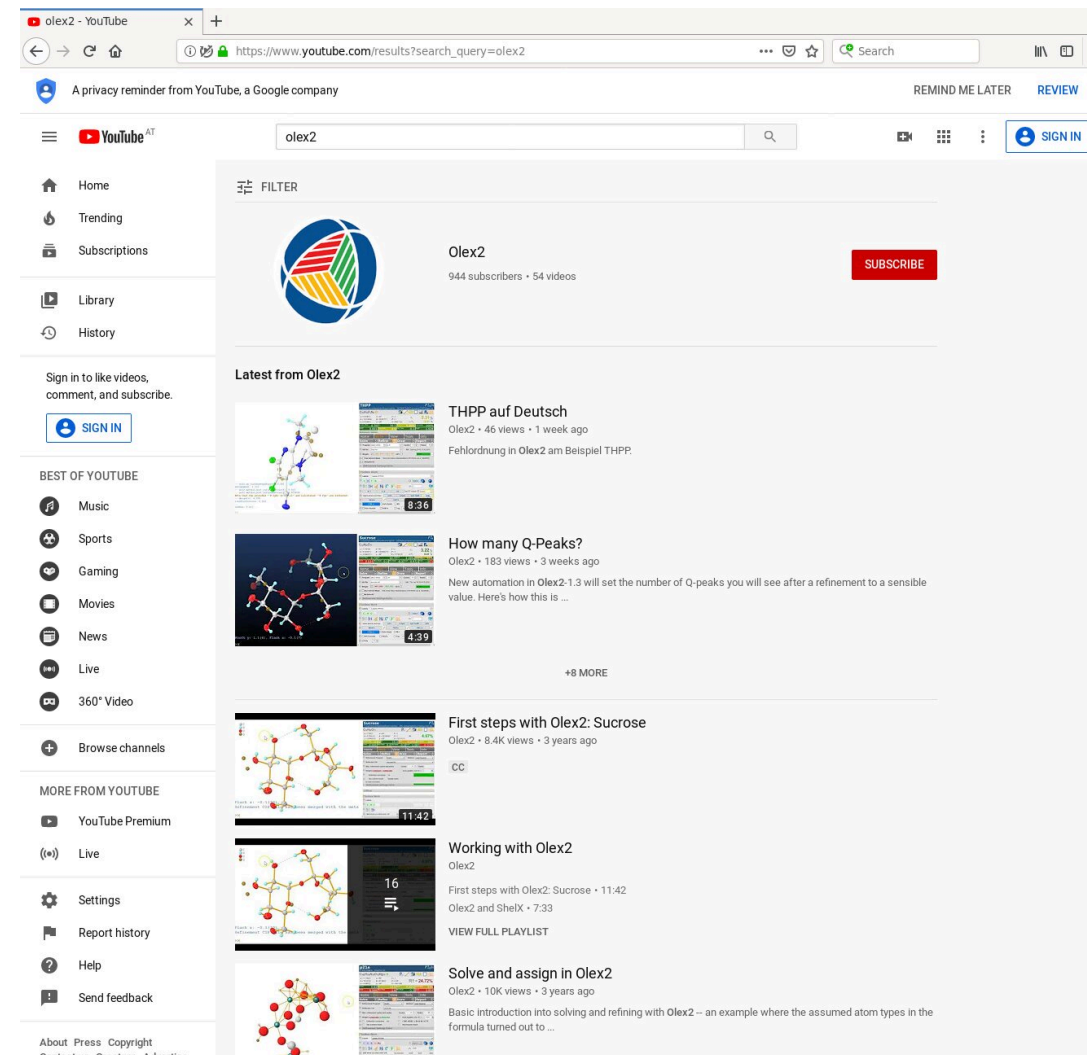
CIFTAB and **ShredCIF** - editing and processing SM CIF files from SHELXL.

SHELXC, **SHELXD** and **SHELXE** - MM phasing. SHELXD is also useful for SM direct methods.

AnoDe - preparation and analysis of MM anomalous density maps.

[George Sheldrick](#) - Last modified: February 16th, 2019

<http://shelx.uni-goettingen.de>



olex2 - YouTube

A privacy reminder from YouTube, a Google company

olex2

944 subscribers • 54 videos

THPP auf Deutsch
Olex2 • 46 views • 1 week ago
Fehlordnung in Olex2 am Beispiel THPP.

How many Q-Peaks?
Olex2 • 183 views • 3 weeks ago
New automation in Olex2-1.3 will set the number of Q-peaks you will see after a refinement to a sensible value. Here's how this is ...

First steps with Olex2: Sucrose
Olex2 • 8.4K views • 3 years ago

Working with Olex2
Olex2
First steps with Olex2: Sucrose • 11:42
Olex2 and ShelX • 7:33

Solve and assign in Olex2
Olex2 • 10K views • 3 years ago
Basic introduction into solving and refining with Olex2 – an example where the assumed atom types in the formula turned out to ...

Olex2 etc on youtube

Journals for Chemical Crystallography

JACS, Journal of the American Chemical Society

<https://pubs.acs.org/journal/jacsat>

Angewandte Chemie Int. Ed.

<https://onlinelibrary.wiley.com/doi/full/10.1002/anie.201811318>

Acta Crystallographica A-F

journals.iucr.org: International Union of Crystallography

and most other journals for chemistry

Crystallographic databases

Most journals require the deposition of structural data structures at publicly available data bases. Crystallography has long been a pioneering discipline of open access data.

Cambridge Structural Database

Crystallography Open Database

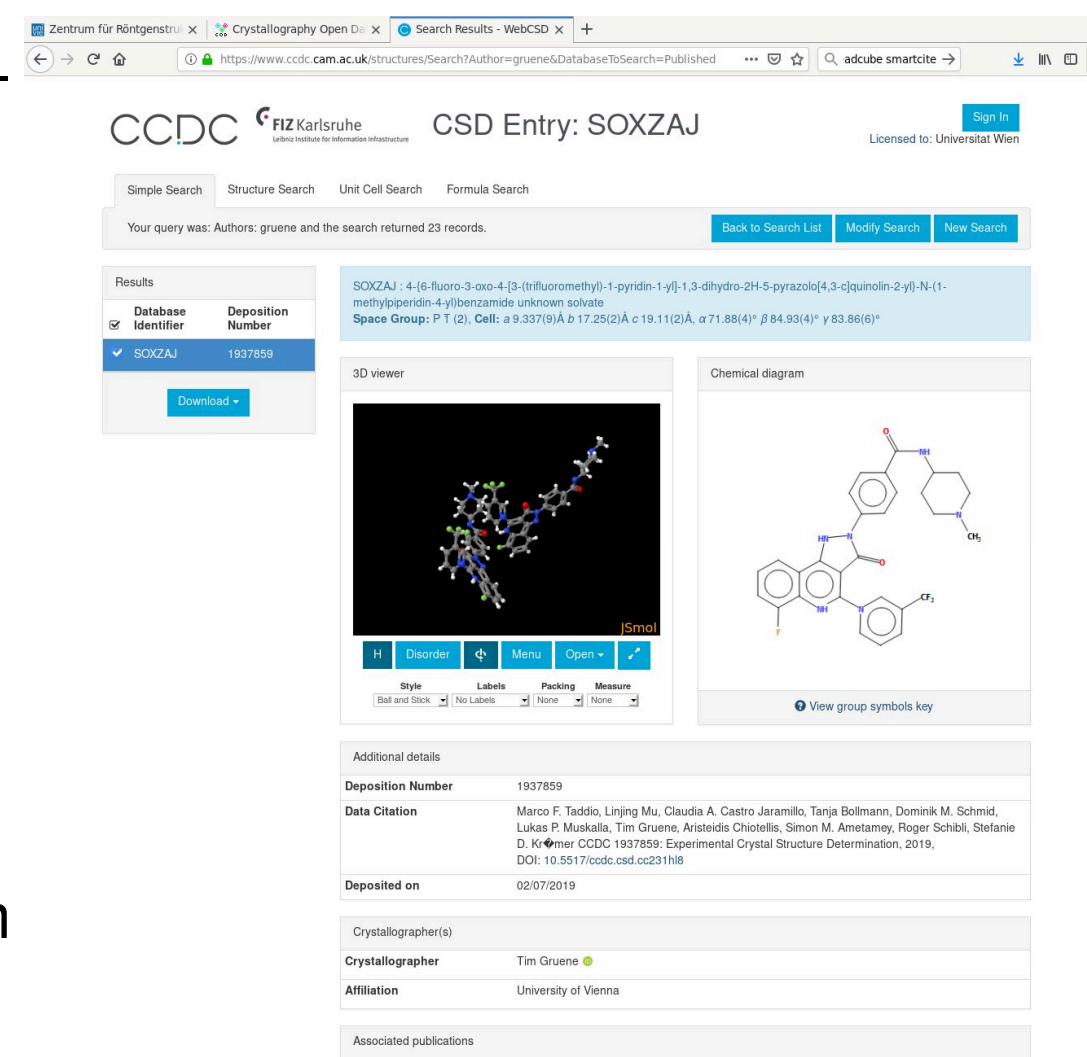
Inorganic Crystal Structure Database

Protein Data Bank

CRYSTMET®

Cambridge Structural Database (CSD)

- <http://www.ccdc.cam.ac.uk>
- “The world repository of small molecule crystal structures”
- founded 1965
- curated
- organic and metal-organic compounds
- X-ray, neutron, (and electron diffraction)
- Single crystal and powder diffraction
- publication of a synthesis usually requires deposition of the product structure at the CSD
- > 1,000,000 entries, $\approx 50,000$ /year



CCDC FIZ Karlsruhe CSD Entry: SOXZAJ

Simple Search Structure Search Unit Cell Search Formula Search

Your query was: Authors: grüne and the search returned 23 records.

Results

Database Identifier	Deposition Number
SOXZAJ	1937859

SOXZAJ : 4-(6-fluoro-3-oxo-4-[3-(trifluoromethyl)-1-pyridin-1-yl]-1,3-dihydro-2H-5-pyrazolo[4,3-c]quinolin-2-yl)-N-(1-methylpiperidin-4-yl)benzamide unknown solvate
Space Group: P T (2), Cell: a 9.337(9)Å b 17.25(2)Å c 19.11(2)Å, α 71.88(4) $^\circ$ β 84.93(4) $^\circ$ γ 83.86(6) $^\circ$

3D viewer

Chemical diagram

Additional details

Deposition Number	1937859
Data Citation	Marco F. Taddei, Linjing Mu, Claudia A. Castro Jaramillo, Tanja Bollmann, Dominik M. Schmid, Lukas P. Muskalla, Tim Grüne, Aristidis Christidis, Simon M. Ametamey, Roger Schibli, Stefanie D. K. Müller CCDC 1937859: Experimental Crystal Structure Determination, 2019, DOI: 10.5517/ccdc.csd.cc2311h8
Deposited on	02/07/2019
Crystallographer(s)	
Crystallographer	Tim Grüne
Affiliation	University of Vienna
Associated publications	

Crystallography Open Database (COD)

- <http://www.crystallography.net>
- “Open-access collection of crystal structures of organic, inorganic, metal-organics compounds and minerals, excluding biopolymers.”
- Local version available free of charge
- Organic and inorganic structures (minerals)
- Can be browsed (by journal, by year,...)
- All data from IUCr journals, and from American Mineralogist CSD
- > 450,000 entries, \approx 50,000/year

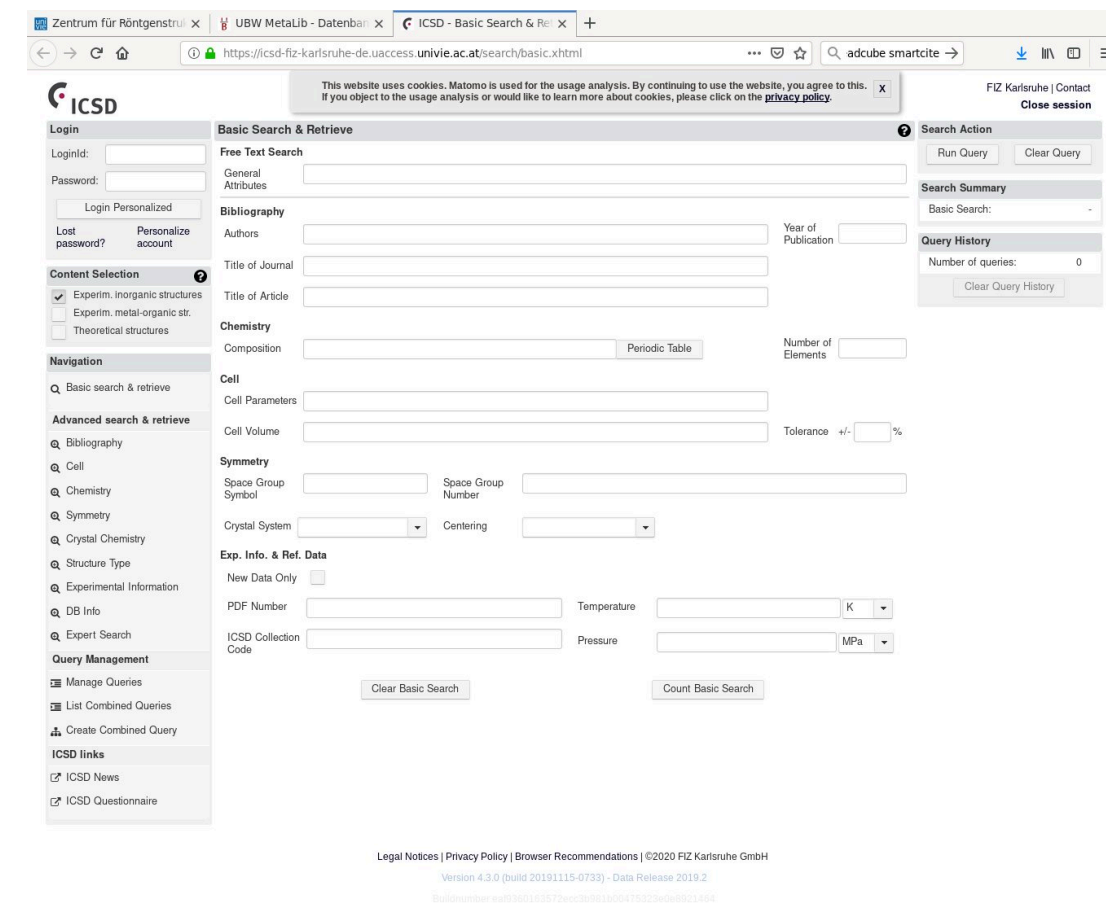


The screenshot shows the Crystallography Open Database search results page for the year 2019. The page displays a table of search results with columns for COD ID, Links, Formula, Space group, Cell parameters, Cell volume, and Bibliography. The results are filtered for the year 2019 and show 120 entries per page.

COD ID	Links	Formula	Space group	Cell parameters	Cell volume	Bibliography
4127220	CIF	C24 H36 Ag Bi 18 N4 S4	C1 2/c 1	28.951; 6.0992; 11.9821 90; 92.266; 90	2114.1	Jana, Manoj K.; Janke, Svenja M.; Dirkes, David J.; Dovietgeldi, Seyitliyev; Liu, Chi; Qin, Xixi; Gundogdu, Kenan; You, Wei; Blum, Volker; Mitzl, David B. Direct-Bandgap 2D Silver-Bismuth Iodide Double Perovskite: The Structure-Directing Influence of an Oligothiophene Spacer Cation. <i>Journal of the American Chemical Society</i> . 2019 , <i>141</i> , 7955-7964
4127221	CIF	C24 H36 Ag Bi 18 N4 S4	C1 2/c 1	29.3654; 6.1473; 12.0494 90; 92.7321; 90	2172.66	Jana, Manoj K.; Janke, Svenja M.; Dirkes, David J.; Dovietgeldi, Seyitliyev; Liu, Chi; Qin, Xixi; Gundogdu, Kenan; You, Wei; Blum, Volker; Mitzl, David B. Direct-Bandgap 2D Silver-Bismuth Iodide Double Perovskite: The Structure-Directing Influence of an Oligothiophene Spacer Cation. <i>Journal of the American Chemical Society</i> . 2019 , <i>141</i> , 7955-7964
4127222	CIF	C25 H40 O8	P 21 21 21	9.1723; 13.1708; 20.2598 90; 90; 90	2447.5	Turlik, Aneta; Chen, Yifeng; Scrusse, Anthony C.; Newhouse, Timothy R. Convergent Total Synthesis of Principinol D, a Rearranged Kaurane Diterpenoid. <i>Journal of the American Chemical Society</i> . 2019 , <i>141</i> , 8088-8092
4127223	CIF	C34 H52 N P	P 1 2/n 1	16.497; 8.9713; 20.61 90; 105.159; 90	2944.1	Liu, Liu Leo; Zhou, Jiliang; Cao, Levy L.; Kim, Youngsuk; Stephan, Douglas W. Reversible Intramolecular Cycloaddition of Phosphaalkene to an Arene Ring. <i>Journal of the American Chemical Society</i> . 2019 , <i>141</i> , 8083-8087
4127224	CIF	C28 H46 N P	P 1 21/n 1	11.104; 15.85; 14.68 90; 95.94; 90	2570	Liu, Liu Leo; Zhou, Jiliang; Cao, Levy L.; Kim, Youngsuk; Stephan, Douglas W. Reversible Intramolecular Cycloaddition of Phosphaalkene to an Arene Ring. <i>Journal of the American Chemical Society</i> . 2019 , <i>141</i> , 8083-8087
4127225	CIF	C36.5 H59 N P S	P 1 21/n 1	10.144; 16.2799; 20.1295 90; 104.252; 90	3221.9	Liu, Liu Leo; Zhou, Jiliang; Cao, Levy L.; Kim, Youngsuk; Stephan, Douglas W. Reversible Intramolecular Cycloaddition of Phosphaalkene to an Arene Ring.

Inorganic Crystal Structure Database (ICSD)

- <https://icsd.fiz-karlsruhe.de/>
- inorganic and intermetallic structures
- only licensed access
- > 215,000 entries



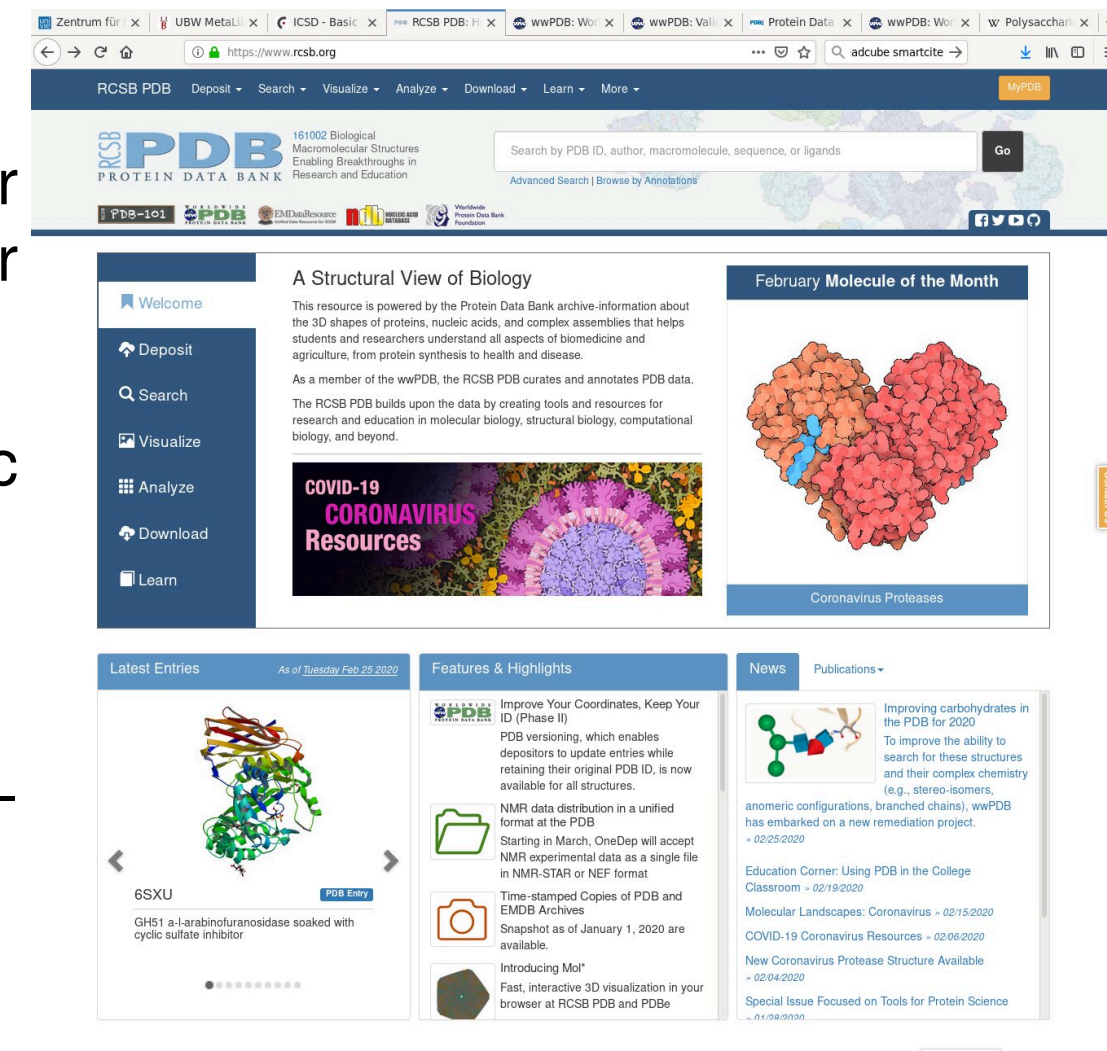
The screenshot shows the ICSD Basic Search & Retrieve interface. The page is divided into several sections:

- Login:** Fields for LoginId, Password, and a "Login Personalized" button. There are also links for "Lost password?" and "Personalize account".
- Content Selection:** A sidebar with checkboxes for "Experim. inorganic structures" (checked), "Experim. metal-organic str.", and "Theoretical structures".
- Navigation:** A list of search options including "Basic search & retrieve", "Advanced search & retrieve", "Bibliography", "Cell", "Chemistry", "Symmetry", "Crystal Chemistry", "Structure Type", "Experimental Information", "DB Info", "Expert Search", "Query Management", "ICSD links", "ICSD News", and "ICSD Questionnaire".
- Basic Search & Retrieve:** The main search area with fields for "Free Text Search", "General Attributes", "Bibliography" (Authors, Year of Publication, Title of Journal, Title of Article), "Chemistry" (Composition, Periodic Table, Number of Elements), "Cell" (Cell Parameters, Cell Volume, Tolerance), "Symmetry" (Space Group Symbol, Space Group Number, Crystal System, Centering), and "Exp. Info. & Ref. Data" (New Data Only, PDF Number, Temperature, ICSID Collection Code, Pressure).
- Search Action:** Buttons for "Run Query" and "Clear Query".
- Search Summary:** A section for "Basic Search" and "Query History" (Number of queries: 0, Clear Query History).

At the bottom of the page, there are links for "Legal Notices", "Privacy Policy", "Browser Recommendations", and "©2020 FIZ Karlsruhe GmbH". The version information is "Version 4.3.0 (build 20191115-0733) - Data Release 2019.2".

Protein Data Bank (PDB)

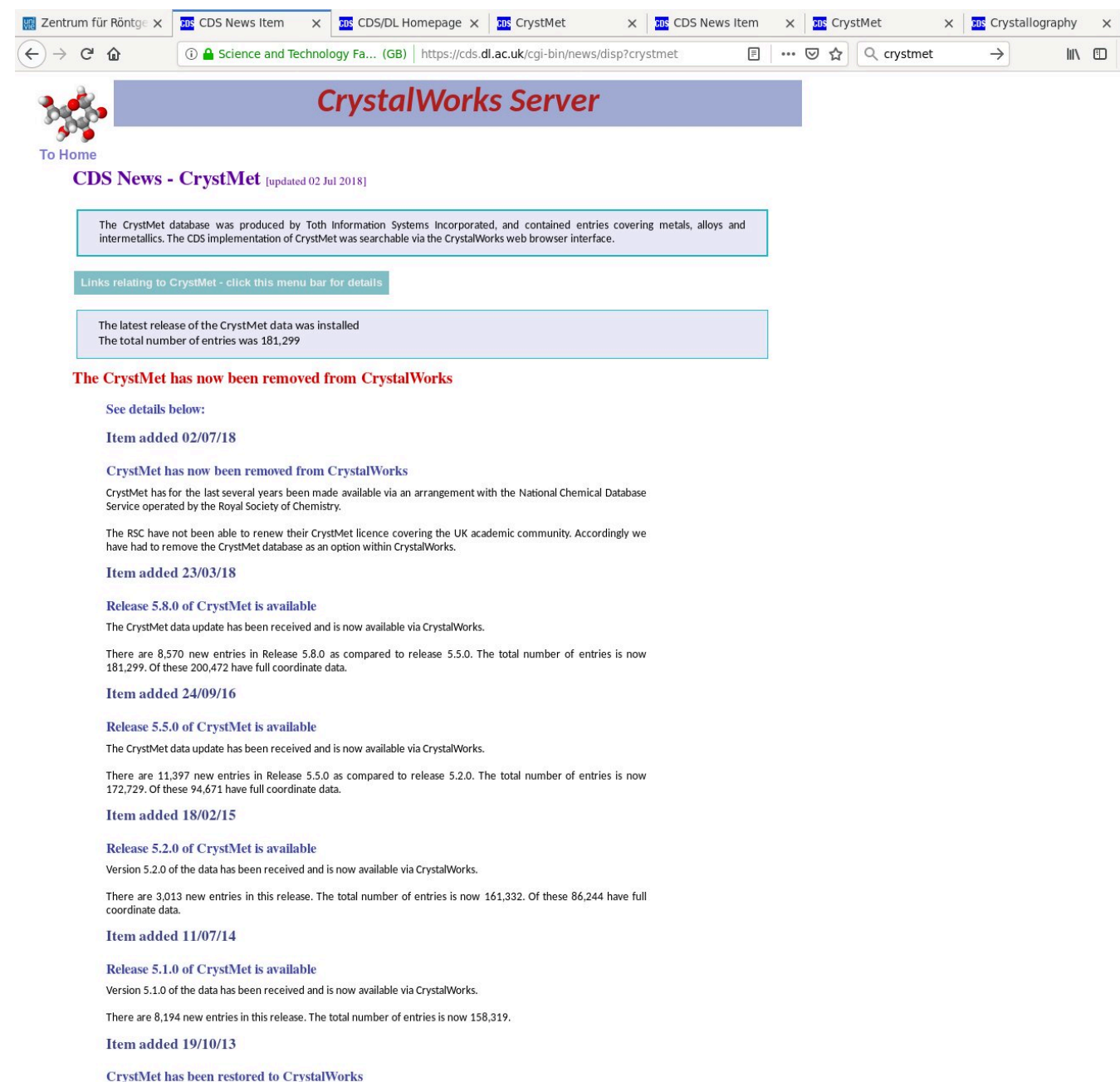
- <https://www.pdb.org>
- Search from www.rcsb.org or <https://www.ebi.ac.uk/pdbe> or <https://pdbj.org> (Japanese)
- polypeptides (proteins) and polysaccharides (nucleic acids)
- Crystal structures, NMR structures, EM structures
- Since 2007: data **must** be submitted along with coordinates
- > 160,000 structures



The screenshot shows the RSCB Protein Data Bank homepage. At the top, there is a search bar and navigation links. The main content area includes a 'Welcome' message, a 'February Molecule of the Month' section featuring 'Coronavirus Proteases', and a 'Latest Entries' section highlighting the structure 6SXU (GH51 α -L-arabinofuranosidase soaked with cyclic sulfate inhibitor). The 'Features & Highlights' section lists updates such as 'Improve Your Coordinates, Keep Your ID (Phase II)', 'NMR data distribution in a unified format at the PDB', and 'Time-stamped Copies of PDB and EMDB Archives'.

CrystMET

- <https://cds.dl.ac.uk/cds/datasets/crys/mdf/11mdf.html>
- Crystal structure data for metals and alloys
- licensed access only



The screenshot shows a web browser window with several tabs open, including 'Zentrum für Röntgen...', 'CDS News Item', 'CDS/DL Homepage', 'CrystMet', and 'Crystallography'. The address bar shows the URL <https://cds.dl.ac.uk/cgi-bin/news/disp7crystmet>. The page content includes a 'CrystalWorks Server' header, a 'To Home' link, and a 'CDS News - CrystMet' section dated 02 Jul 2018. A blue box contains the text: 'The CrystMet database was produced by Toth Information Systems Incorporated, and contained entries covering metals, alloys and intermetallics. The CDS implementation of CrystMet was searchable via the CrystalWorks web browser interface.' Below this, a link says 'Links relating to CrystMet - click this menu bar for details'. A light blue box states: 'The latest release of the CrystMet data was installed. The total number of entries was 181,299.' A red heading reads 'The CrystMet has now been removed from CrystalWorks'. The main text explains that CrystMet has been removed from CrystalWorks due to a license issue with the Royal Society of Chemistry. It lists several release dates and entry counts: 'Item added 02/07/18', 'Release 5.8.0 of CrystMet is available' (181,299 entries), 'Item added 23/03/18', 'Release 5.5.0 of CrystMet is available' (172,729 entries), 'Item added 24/09/16', 'Release 5.2.0 of CrystMet is available' (161,332 entries), 'Item added 18/02/15', 'Release 5.1.0 of CrystMet is available' (158,319 entries), 'Item added 11/07/14', 'Release 5.1.0 of CrystMet is available' (158,319 entries), 'Item added 19/10/13', and 'CrystMet has been restored to CrystalWorks'.

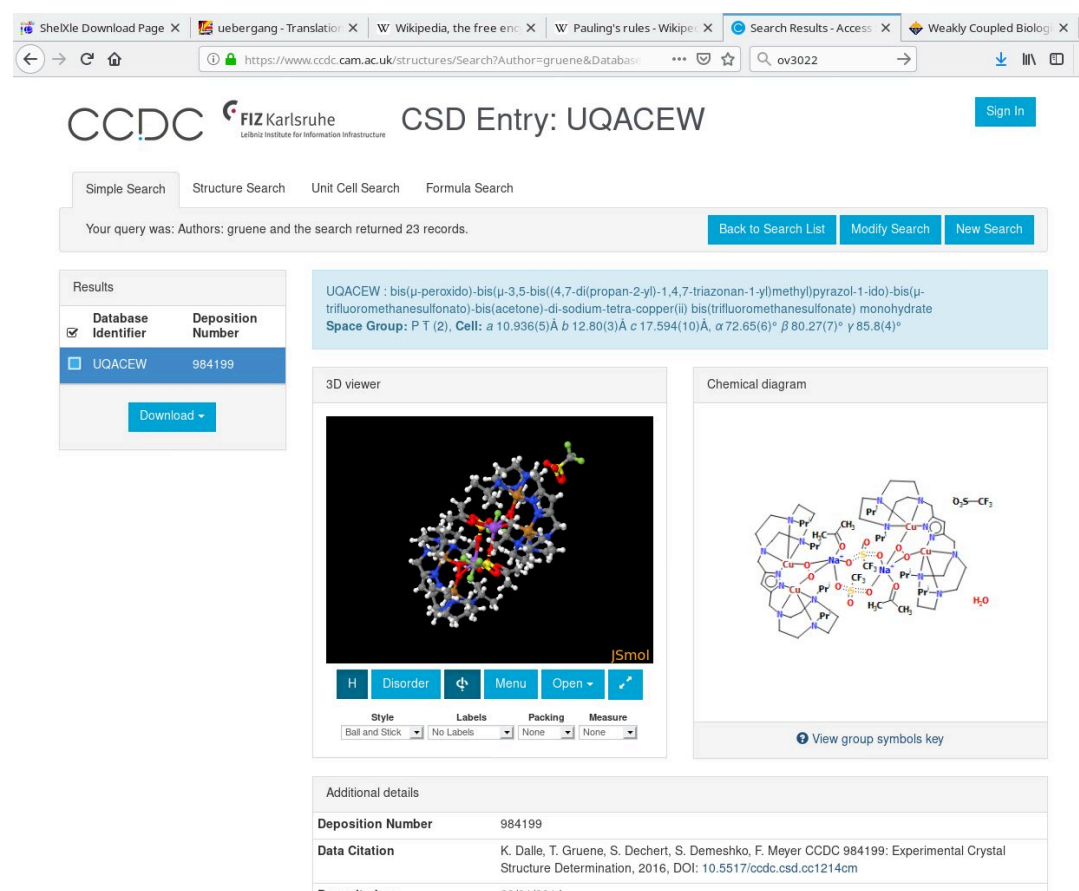
Structure, Data, Data Formats, and Visualisation Software

Structural Data: the CIF-file

- Main file format for published structures
- available from CSD, COD, ICSD, journal web-sites, etc
- pure text file
- Can contain both structure information (coordinates) and experimental data (hkl-file)

Example: CSD entry UQACEW, name of CIF-file: 984199.cif

K. Dalle *et al.*, J. Am. Chem. Soc. (2014), 136, 7428, DOI 10.1021/ja5025047: “Weakly Coupled Biologically Relevant $\text{Cu}^{\text{II}}_2(\mu\text{-}\eta^1 : \eta^1\text{-O}_2)$ *cis*-Peroxo Adduct that Binds Side-On to Additional Metal Ions”



CCDC FIZ Karlsruhe CSD Entry: UQACEW

Simple Search Structure Search Unit Cell Search Formula Search

Your query was: Authors: grüne and the search returned 23 records.

Results

Database Identifier	Deposition Number
<input checked="" type="checkbox"/> UQACEW	984199

Download

UQACEW : bis(μ -peroxido)-bis(μ -3,5-bis(4,7-di(propan-2-yl)-1,4,7-triazonan-1-yl)methylpyrazol-1-ido)-bis(μ -trifluoromethanesulfonato)-bis(acetone)-di-sodium-tetra-copper(II) bis(trifluoromethanesulfonate) monohydrate
Space Group: P T (2), Cell: a 10.936(5)Å b 12.80(3)Å c 17.594(10)Å, α 72.65(6) $^\circ$ β 80.27(7) $^\circ$ γ 85.8(4) $^\circ$

3D viewer

Chemical diagram

Additional details

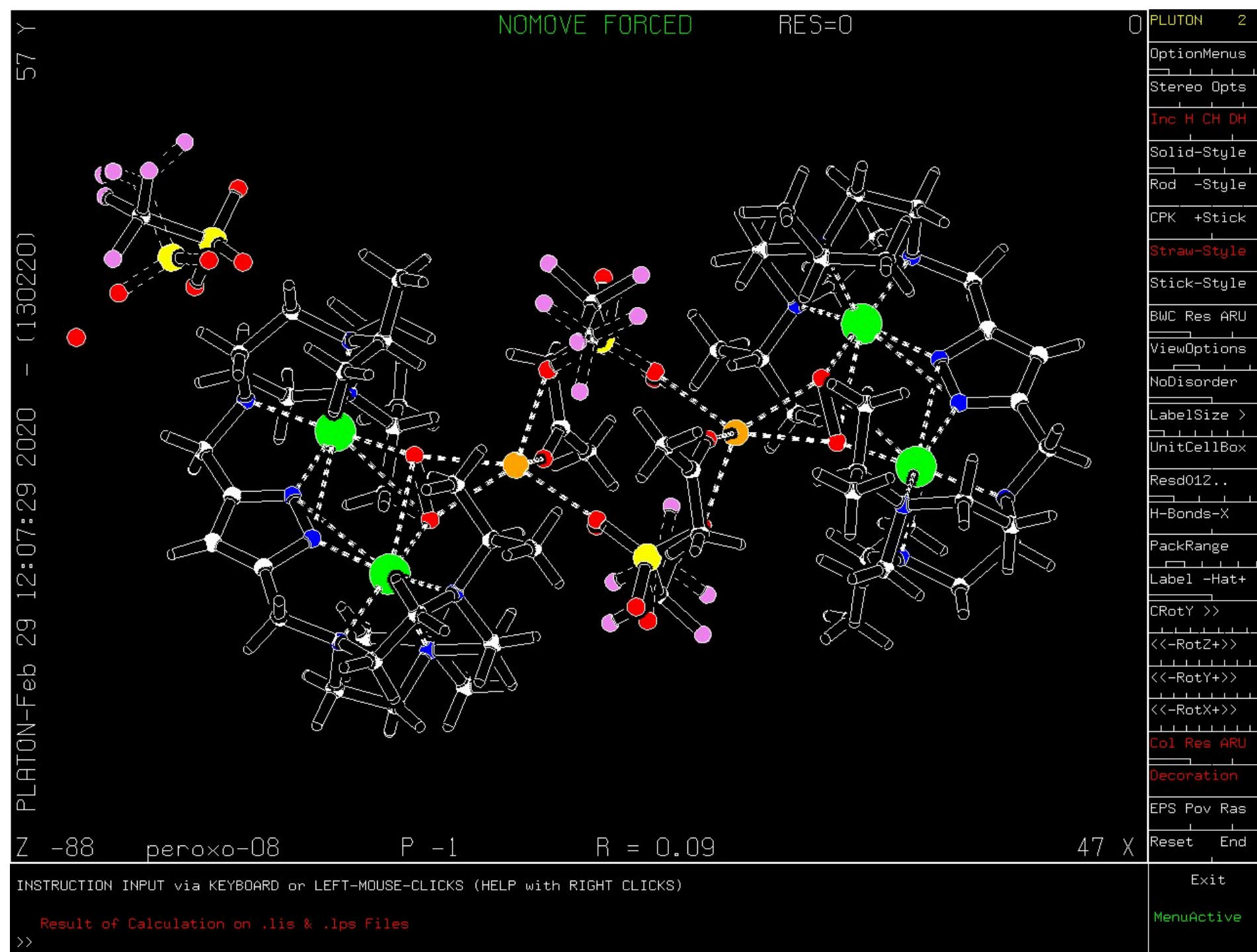
Deposition Number	984199
Data Citation	K. Dalle, T. Gruene, S. Dechert, S. Demeshko, F. Meyer CCDC 984199: Experimental Crystal Structure Determination, 2016, DOI: 10.5517/ccdc.csd.cc1214cm

Structural Data: the RES-file

- RES/INS text file: chemical structure in computer language
- developed by George Sheldrick (SHELX programs), late 1960s
- still the most sophisticated format for chemical compounds
- “work” format: refinement and model building

Platon: Validation, format conversion

<http://www.cryst.chem.uu.nl/spek/platon>

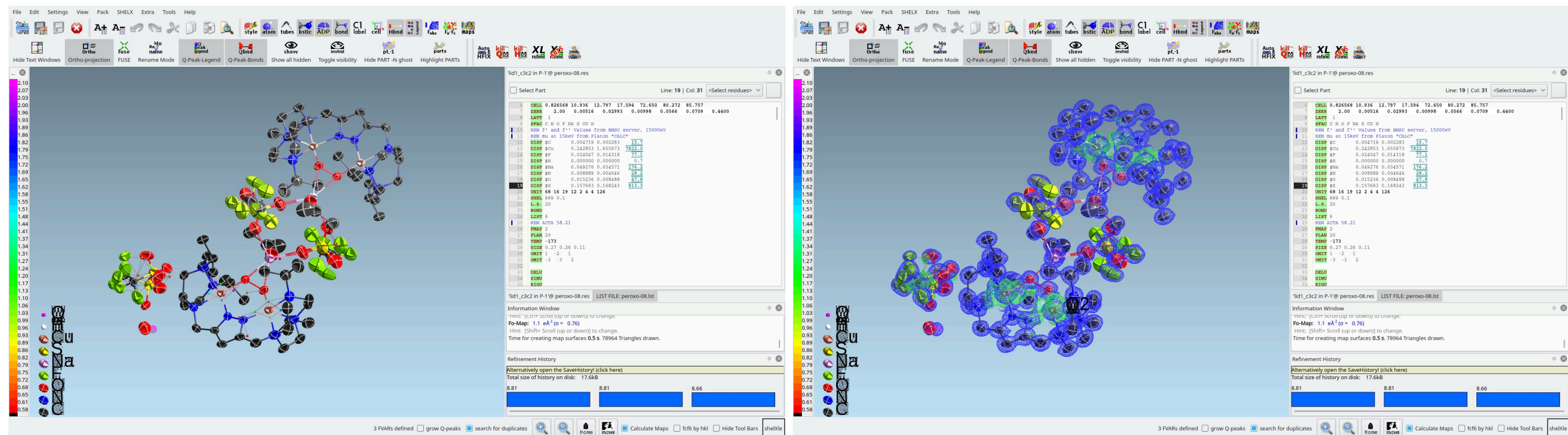


→ 984199_sx.ins and 984199_sx.hkl

ShelXle: Visualisation and Modelling

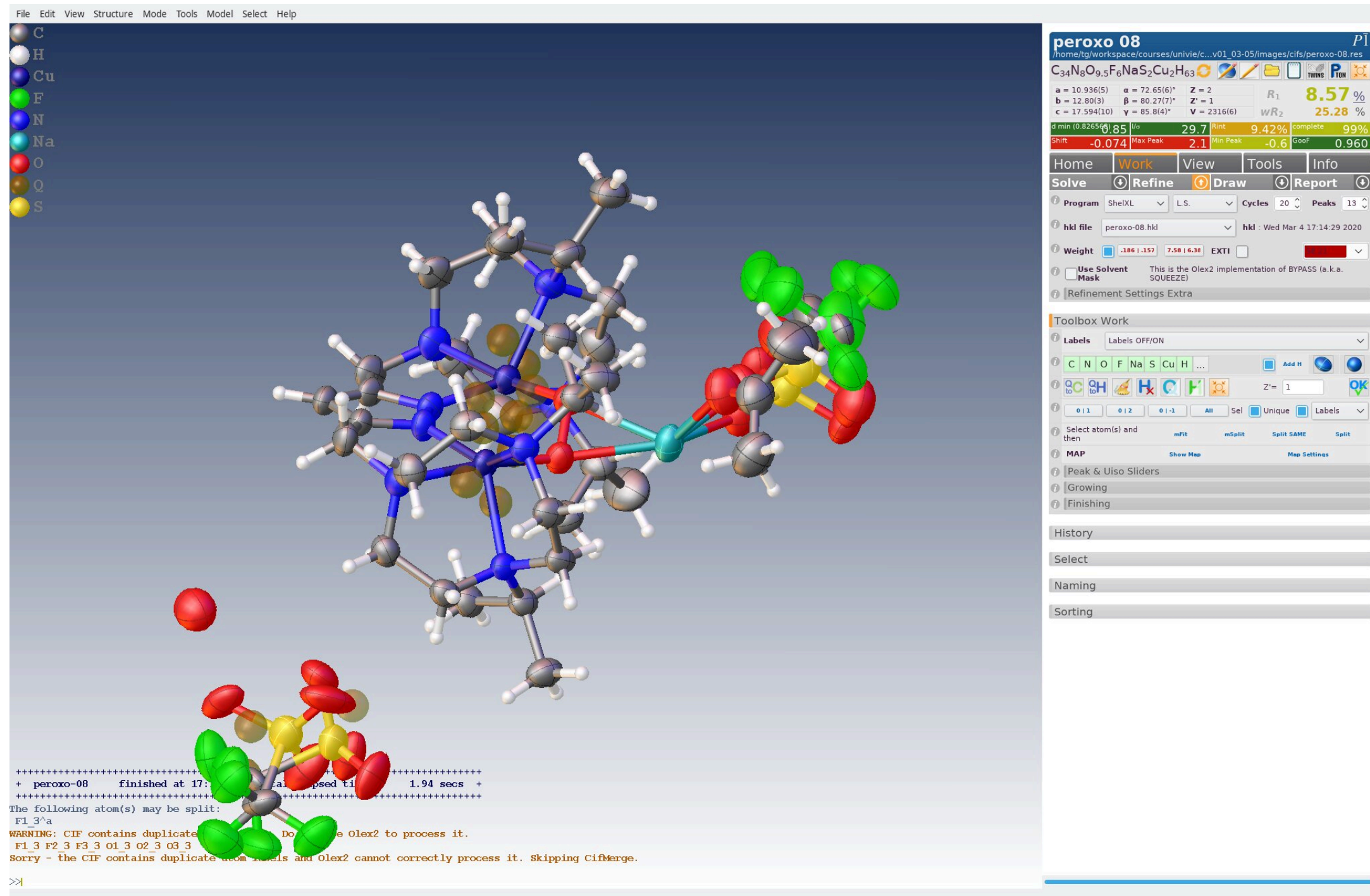
<https://www.shelxle.org/shelx>

```
#> shredcif 984199.cif
peroxo-08.res extracted, checksum O.K.
peroxo-08.hkl extracted, checksum O.K.
```



Olex2: Visualisation and Modelling

<https://www.olexsys.org/>



The screenshot displays the Olex2 software interface. The main window shows a 3D ball-and-stick model of a complex crystal structure, likely a peroxide compound, with atoms colored by element (C: grey, H: white, Cu: blue, F: green, N: cyan, Na: yellow, O: red, S: orange). A legend on the left lists the elements and their corresponding colors. The right sidebar contains the following information:

- peroxxo 08** (P1)
- Chemical formula: $C_{34}N_8O_{9.5}F_6NaS_2Cu_2H_{63}$
- Unit cell parameters: $a = 10.936(5)$, $b = 12.80(3)$, $c = 17.594(10)$; $\alpha = 72.65(6)^\circ$, $\beta = 80.27(7)^\circ$, $\gamma = 85.8(4)^\circ$; $Z = 2$, $Z' = 1$, $V = 2316(6)$
- Refinement statistics: $R_1 = 8.57\%$, $wR_2 = 25.28\%$, σ min (0.8265) = 0.85, σ max = 29.7, $R_{int} = 9.42\%$, $R_{sigma} = 99\%$, $S_{min} = -0.074$, $S_{max} = 2.1$, $S_{min} = -0.6$, $S_{max} = 0.960$
- Buttons: Home, Work, View, Tools, Info; Solve, Refine, Draw, Report
- Program: ShelXL, L.S., Cycles: 20, Peaks: 13
- hkl file: peroxxo-08.hkl, hkl: Wed Mar 4 17:14:29 2020
- Weight: .186 | .157 | 7.58 | 6.38 | EXTI
- Use Solvent Mask: This is the Olex2 implementation of BYPASS (a.k.a. SQUEEZE)
- Refinement Settings Extra
- Toolbox Work: Labels OFF/ON, Add H, Z' = 1, Select atoms and then, MAP, Peak & Uiso Sliders, Growing, Finishing
- History, Select, Naming, Sorting

At the bottom left, a terminal window shows the following output:

```
+++++  
+ peroxxo-08 finished at 17:14:29 on Wed Mar 4 2020. Elapsed time: 1.94 secs +  
+++++  
The following atom(s) may be split:  
F1_3^a  
WARNING: CIF contains duplicate atom labels. Do not use Olex2 to process it.  
F1_3 F2_3 F3_3 O1_3 O2_3 O3_3  
Sorry - the CIF contains duplicate atom labels and Olex2 cannot correctly process it. Skipping CifMerge.  
>>
```

Crystals and Crystal Growth

Crystal Types

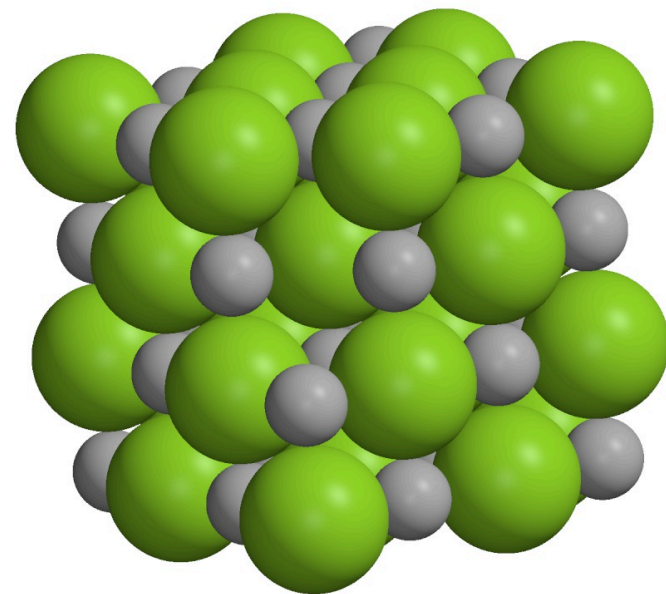
- Crystal = Solid state compound with regular composition
- interactions responsible for crystallisation
 1. ionic bond
 2. metallic bond
 3. covalent bond
 4. van-der-Waals interaction
- often not a clear cut between these types

Ionic Crystals

- Composed of anions (negative charge) and cations (positive charge)
- Geometry according to Pauling's rules

Simple example: *NaCl*:

- cubic lattice
- energy difference $Na + Cl \rightarrow Na^+ + Cl^-$: $-6.4eV$

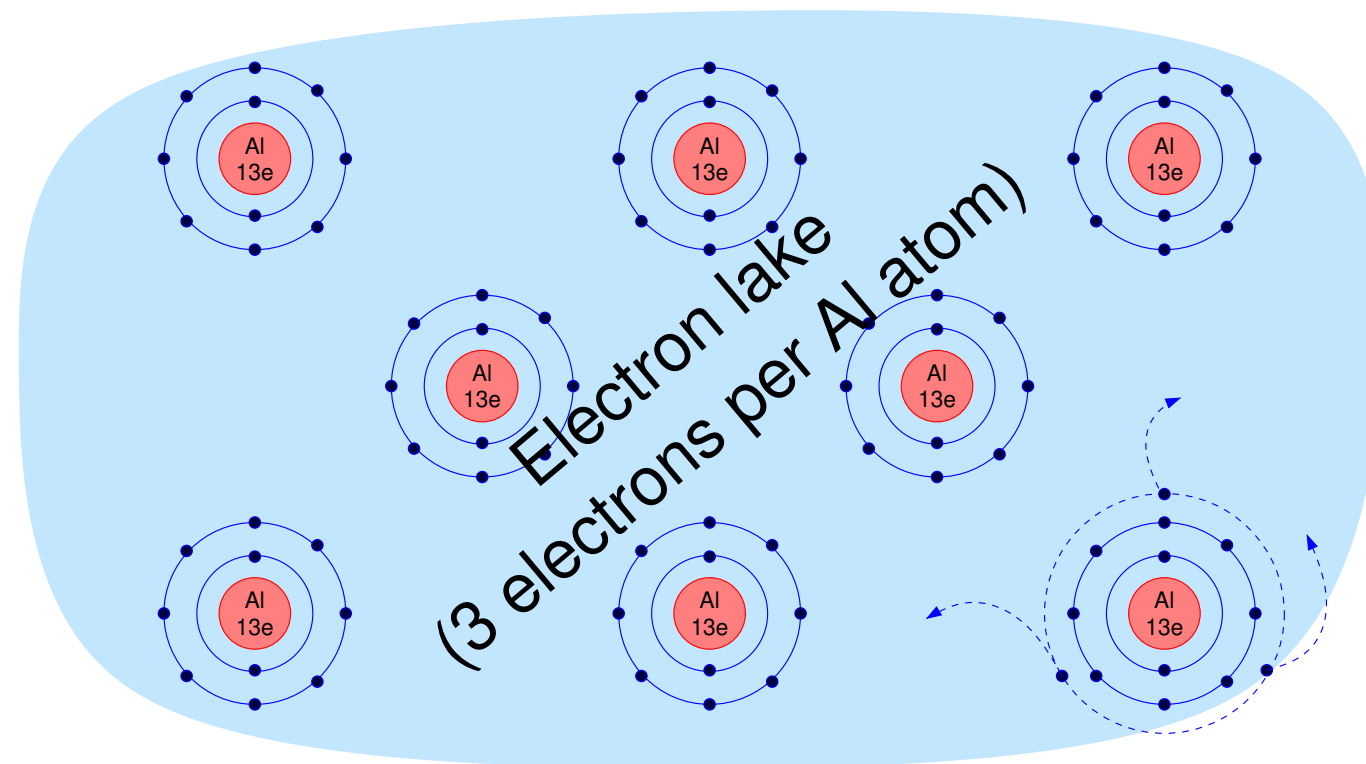


kubischer Aufbau von *NaCl*



Chrome alum,
alias Chromium(III) potassium sulfate
 $KCr(SO_4)_2$

Metallic Crystals



Valence electrons dissociate from individual atoms and form an **electron lake** (conduction band)

- electrical conductivity
- thermal conductivity (copper)
- shiny surface
- plasticity



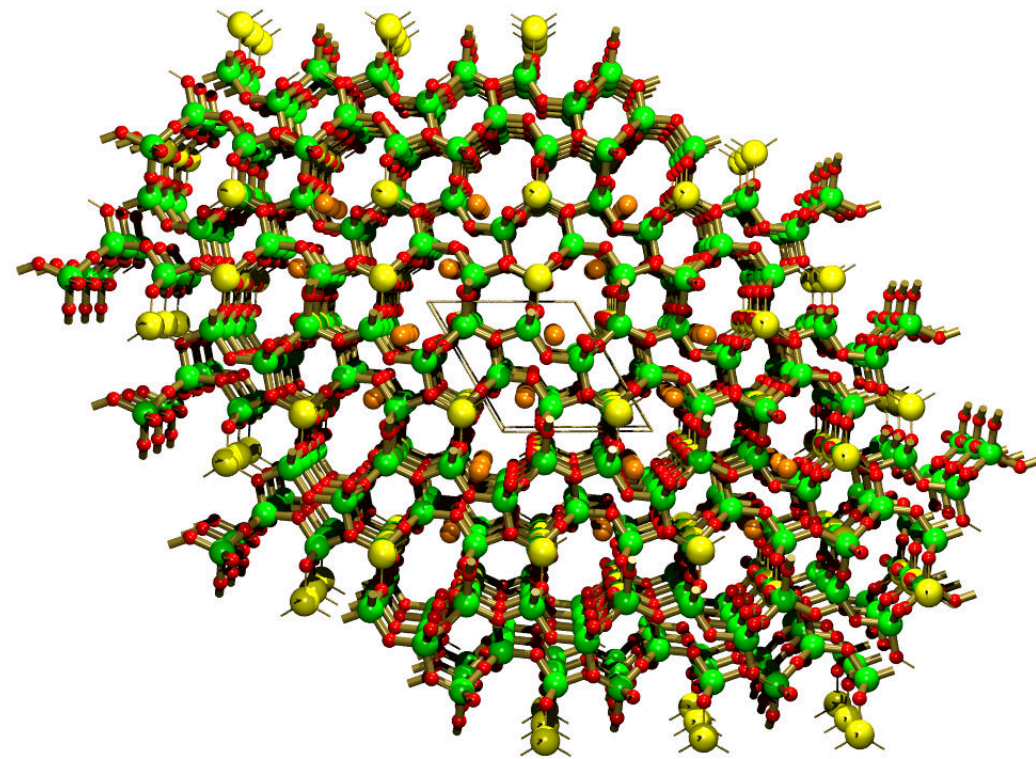
http://commons.wikimedia.org/wiki/File:Iron_electrolytic_and_1cm3_cube.jpg

Covalent bond

Two atoms share an electron to reach noble gas configuration.

Examples: zeolites, MOFs, diamond, quartz

⇒ high stability



Feldspar Albite ($NaAlSi_3O_8$)

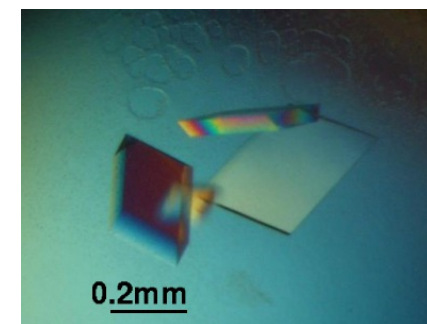
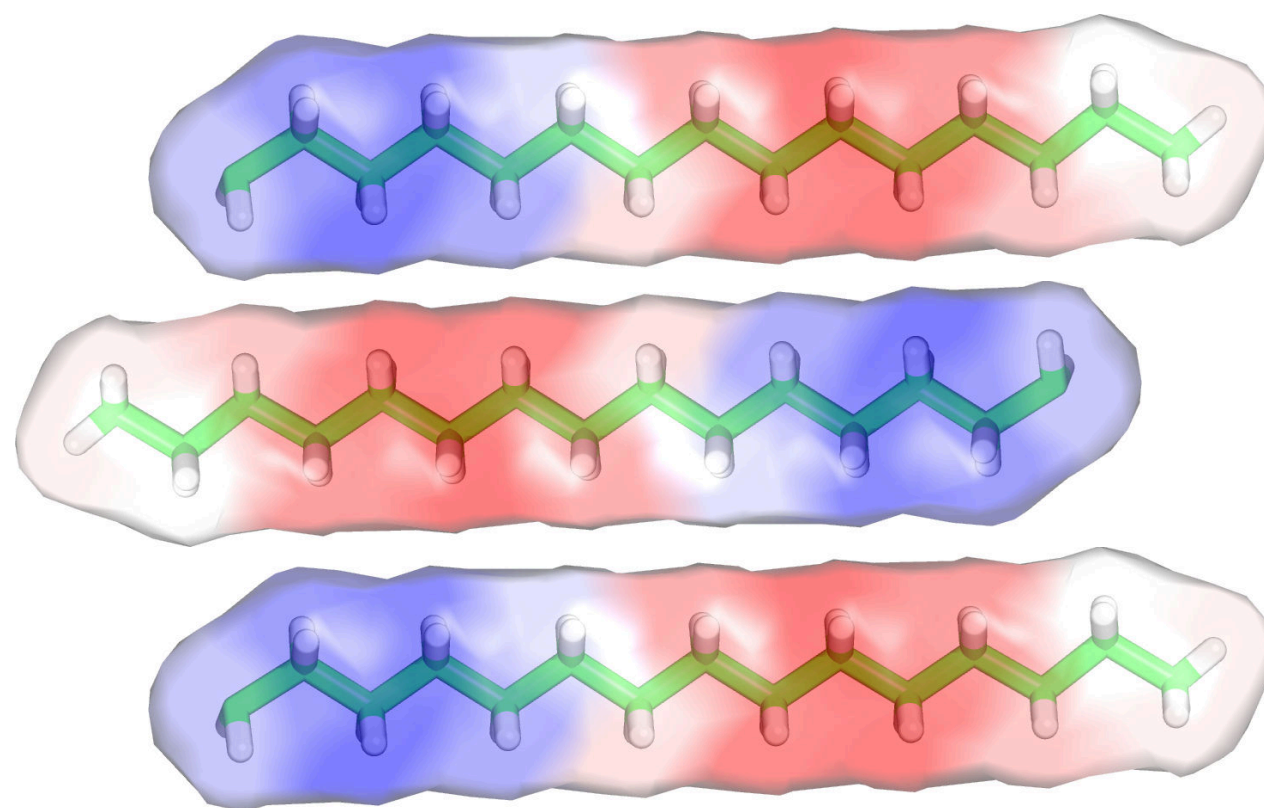


By Rob Lavinsky, iRocks.com – CC-BY-SA-3.0, CC BY-SA 3.0

<https://commons.wikimedia.org/w/index.php?curid=10137563>

van-der-Waals interaction

- mostly organic and macromolecular compounds
- stochastic charge distribution (dipole moments) causes mutual attraction between molecules
- weak interaction



protein crystals in saturated solution

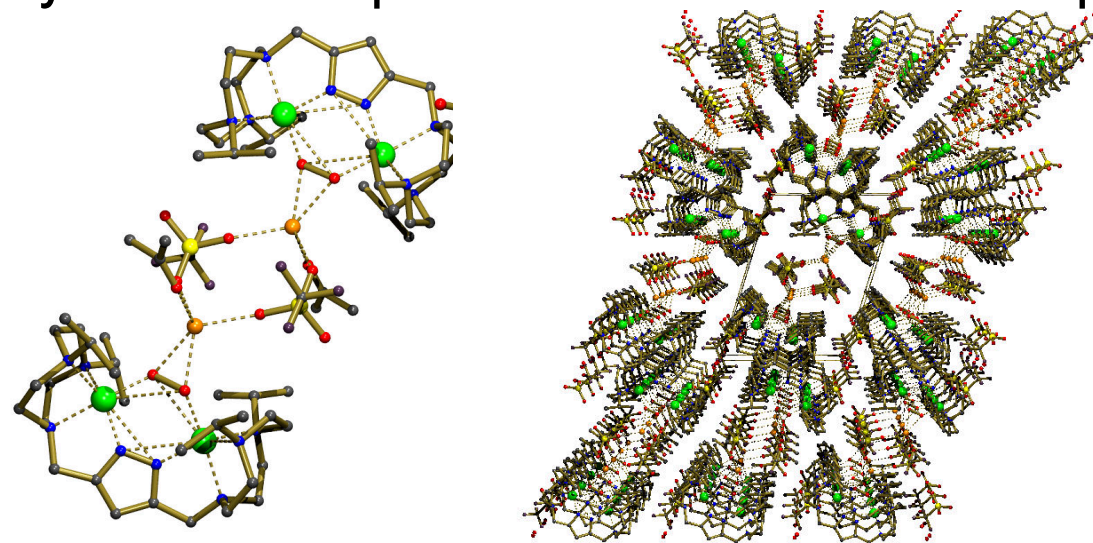
Crystals in Crystallography

Definition *International Union of Crystallography*:

“A material is a crystal if it has essentially a sharp diffraction pattern.”

Crystal in the context of this lecture:

A crystal is composed of a chemical compounds that repeats periodically in all three directions.



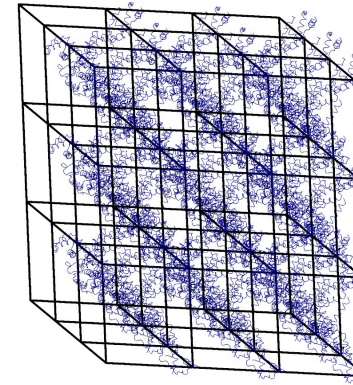
<http://de.wikipedia.org/wiki/Paralleleflach>

- The periodicity results in the diffraction pattern of the crystal
- The periodicity act like an amplifier
- The smallest unit of the periodicity is an inclined box. It is called the **unit cell of the crystal**.

Crystal Growth

Crystals are

1. solid state materials
2. highly ordered, *i.e.* their entropy is very low compared to amorphous material



Especially for large molecules: weak interaction, *i.e.* low energy gain through crystallisation \Rightarrow Crystal growth can be difficult

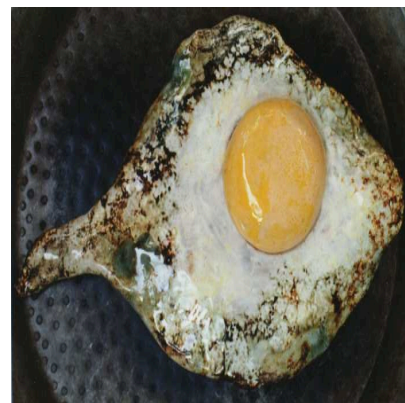
Crystal Growth

Usually: Precipitation from solution

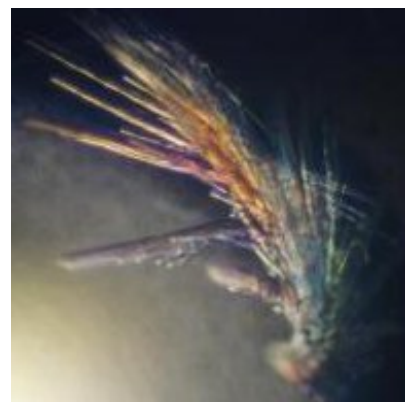
Some means for precipitation (*cf.* LeChatelier's principle)

- Changes in temperature or pressure
 - sugar: better soluble in warm water
- precipitant
 - sugar: ethanol

Requirements for **structure determination**



crystallisation (instead of amorphous precipitation)

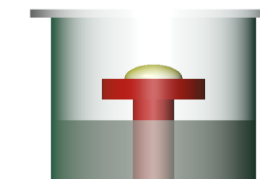


crystallise as single crystal

Examples for Crystallisation

1. Dissolve in Tetrahydrofuran (THF) in glass vial
2. Cover with parafilm: slow evaporation of THF
3. Store at -80°C

1. Dissolve in organic solvent (EtOH, Iso-propanol, ...)
2. Store sealed on water reservoir
3. Uptake of water (vapour) reduces solubility of compound



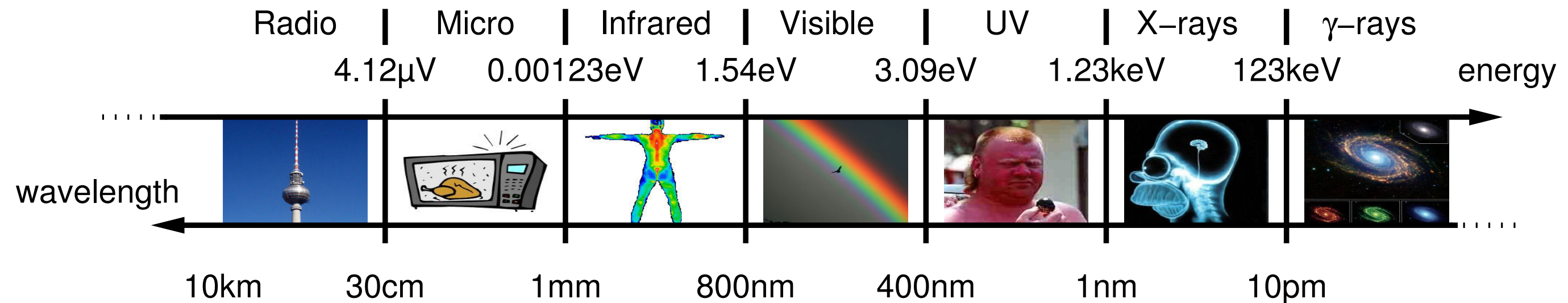
Twinned structures (cf. end of term) can often be improved with elevated temperature during crystal growth ($30-40^{\circ}\text{C}$).

(see e.g. W. Massa, *Crystal Structure Determination*, Ch. 7)

X-rays and Diffraction

X-rays as electromagnetic radiation

X-rays are one type electromagnetic radiation — like visible light, UV-radiation, or radio waves



- Energy E and wavelength λ are equivalent ($E = h\frac{c}{\lambda} = 12.4 \text{ keV \AA} / \lambda$):
- Long wavelength $\lambda \leftrightarrow$ low energy E .
- Short wavelength $\lambda \leftrightarrow$ high Energie E .
- Typical wavelength range for structure determination: 0.5-2 \AA (24.8 - 6.2 keV).
- Inhouse X-ray instruments:
 - $\text{CuK}\alpha$: 1.54 $\text{\AA} \leftrightarrow$ 8.0 keV
 - $\text{MoK}\alpha$: 0.71 $\text{\AA} \leftrightarrow$ 17.3 keV
- 1 $\text{\AA} = 10^{-10} \text{ m} = 100 \text{ pm}$

Generation of X-rays

1. **X-ray fluorescence** (mainly laboratory sources) electron beam at specific energy hits metal surface (Cu or Mo). This creates

a) Bremsstrahlung (background)

b) X-ray fluorescence

Examples: rotating anode, liquid jet anode

2. **Synchrotron radiation** Acceleration of electron bunches in a magnetic field

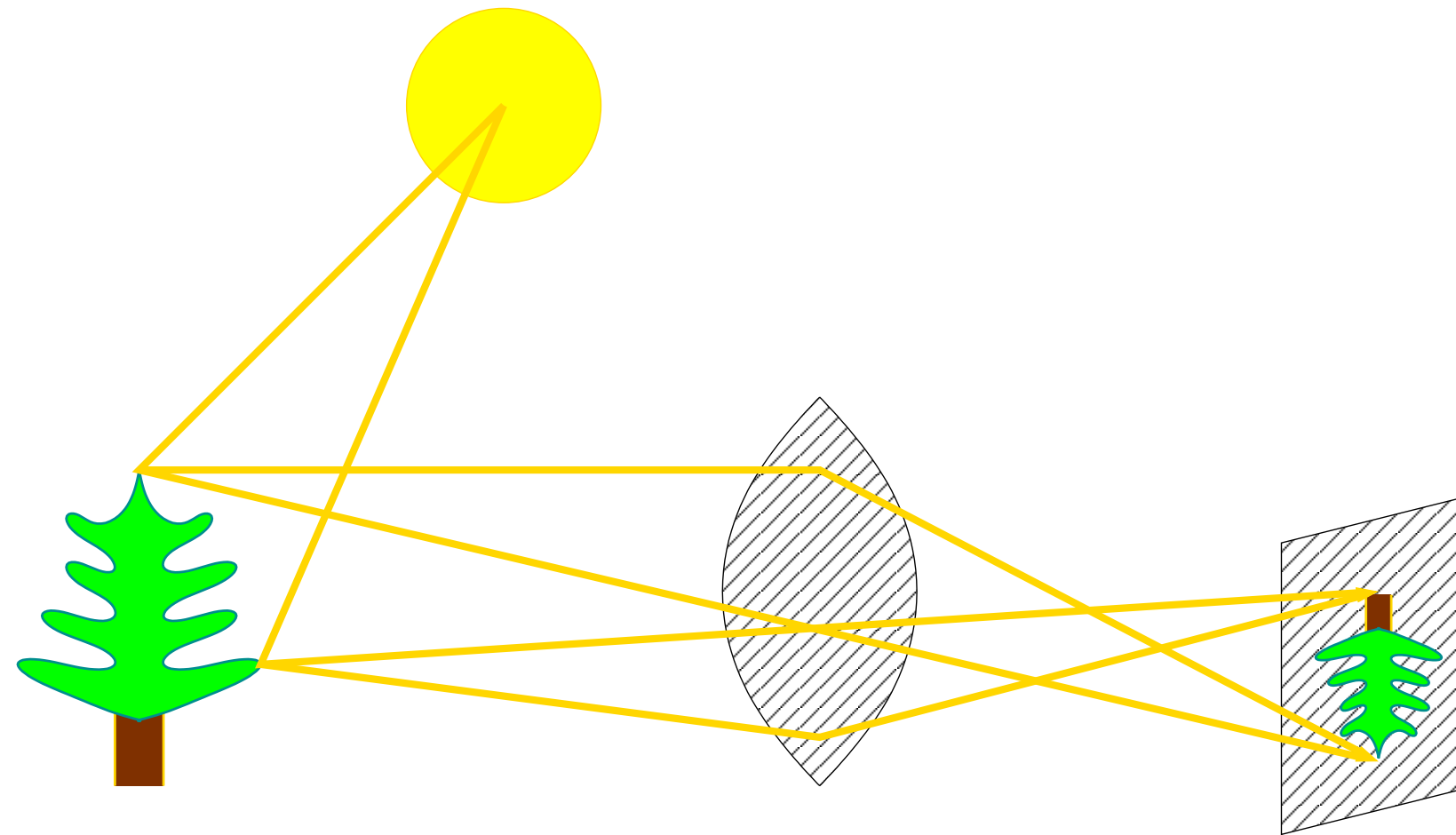
Why X-rays?

Atom distances of molecules about 1–2 Å: required resolution d

Optical instruments are limited in resolution to $d > \lambda/2$ (later: derivation *via* Bragg's law)

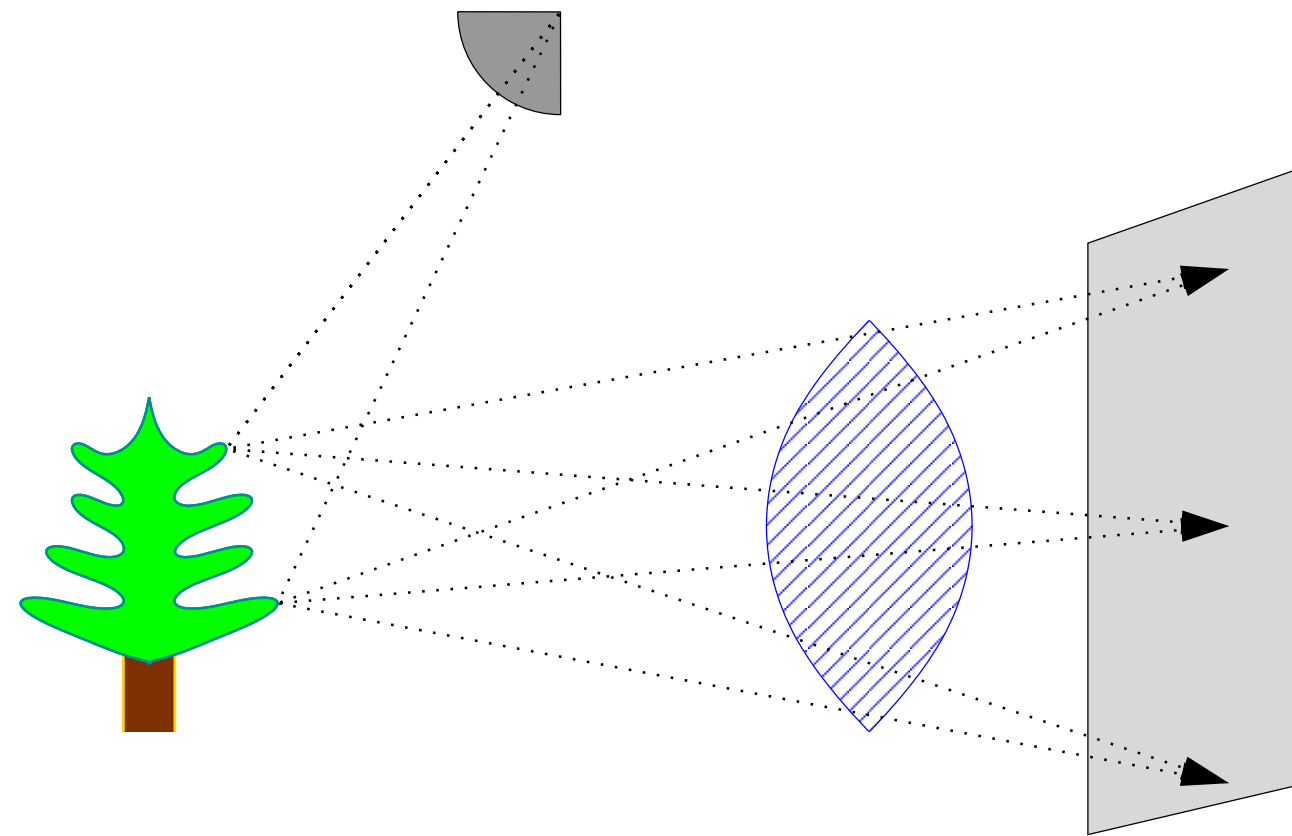
Why Crystals?

Optics and Imaging (Microscope / Telescope)



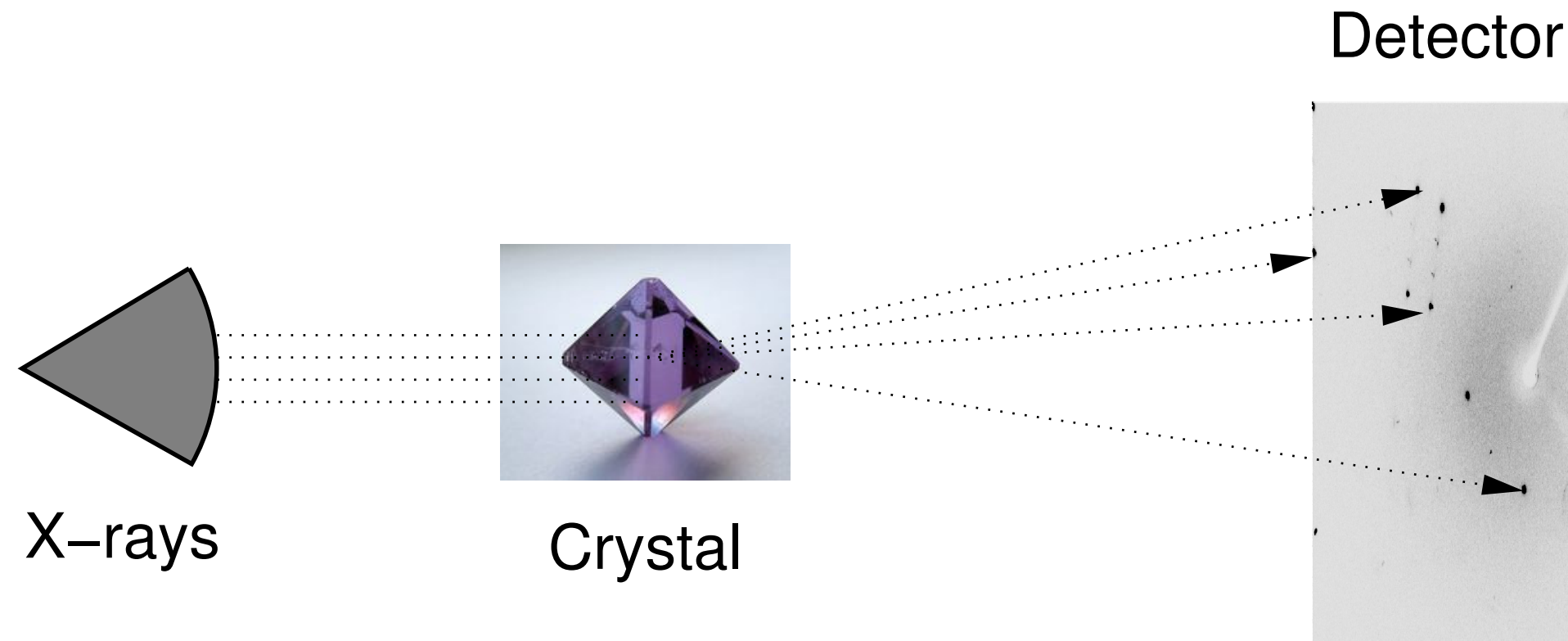
Objects scatter light. In order to see the object, the scattered light must be focused by **at least** one lens

X-ray Scattering



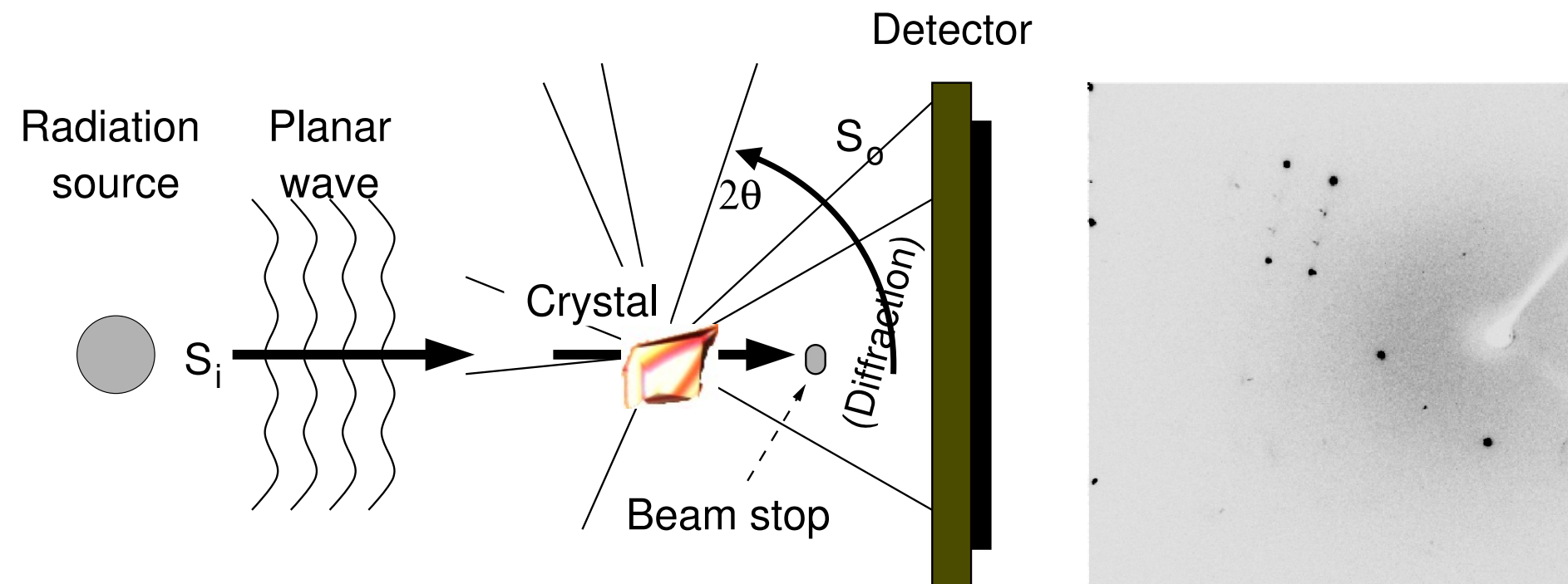
X-ray lenses do not exist: It is not possible to create a direct image of an object with X-rays.

X-ray Scattering by Crystals: Diffraction



The periodicity of the crystal results in a focussing of the scattered X-rays into **discrete spots**. The spots (reflections) can be measured without lenses. The crystal acts like a signal amplifier.

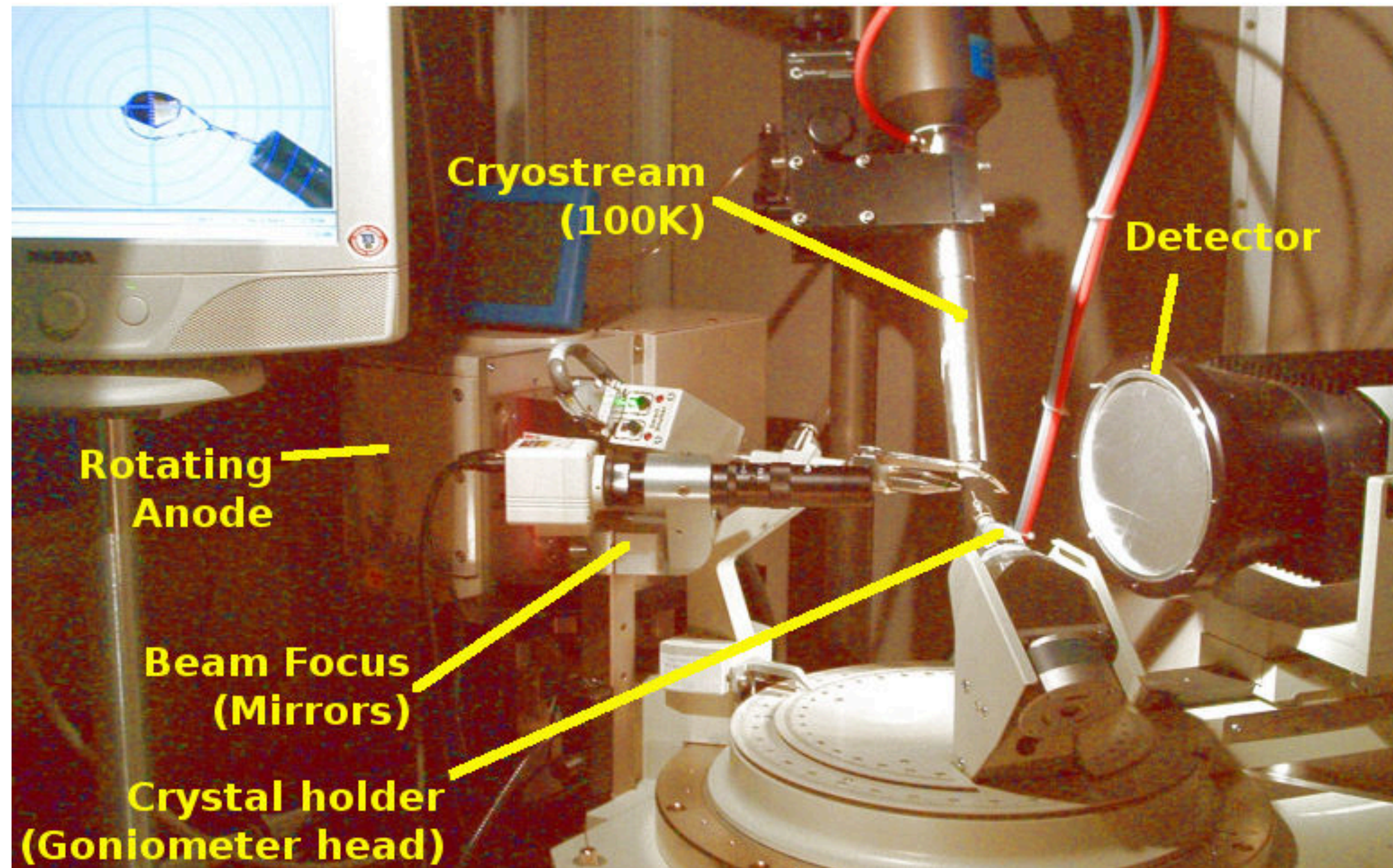
The X-ray Diffraction Experiment



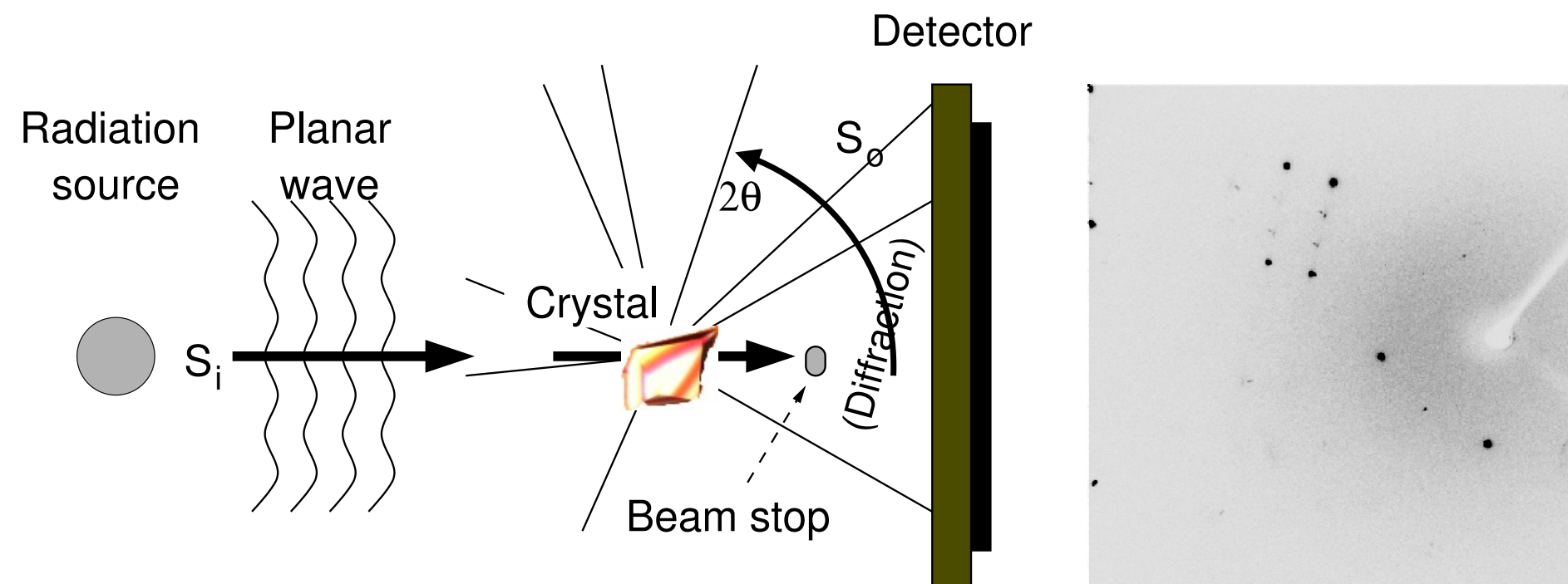
The crystal diffracts X-rays. This creates a **diffraction pattern** recorded by the detector.

The reflection spots are not images of the atoms

Typical laboratory X-ray Diffractometer



Data Collection experiment



Reflections are data point. Each one contains different information. In order to collect as many data points as possible:

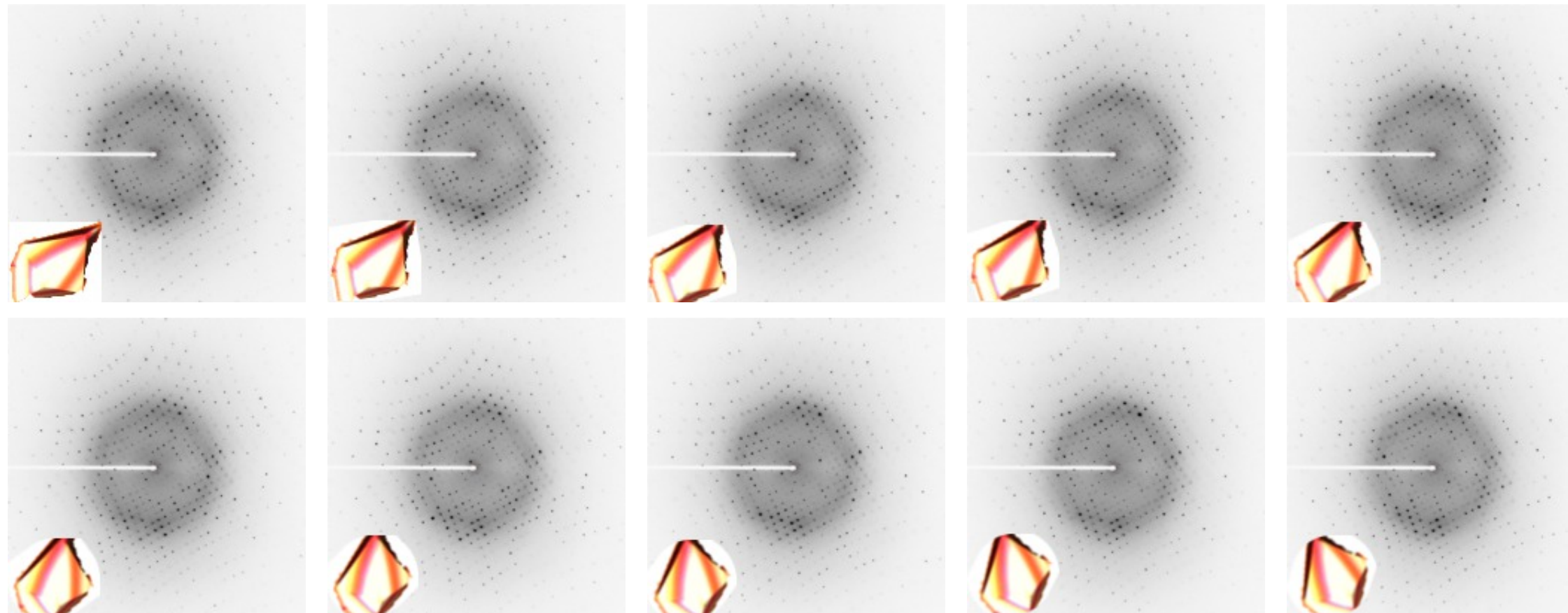
1. Rotation of the crystal (about one of three different axes, called ϕ -, ω -, and χ -circles)).
2. Rotation of the detector around the crystal, called 2θ -circle. This is parallel to the ω -circle).

The Data Set

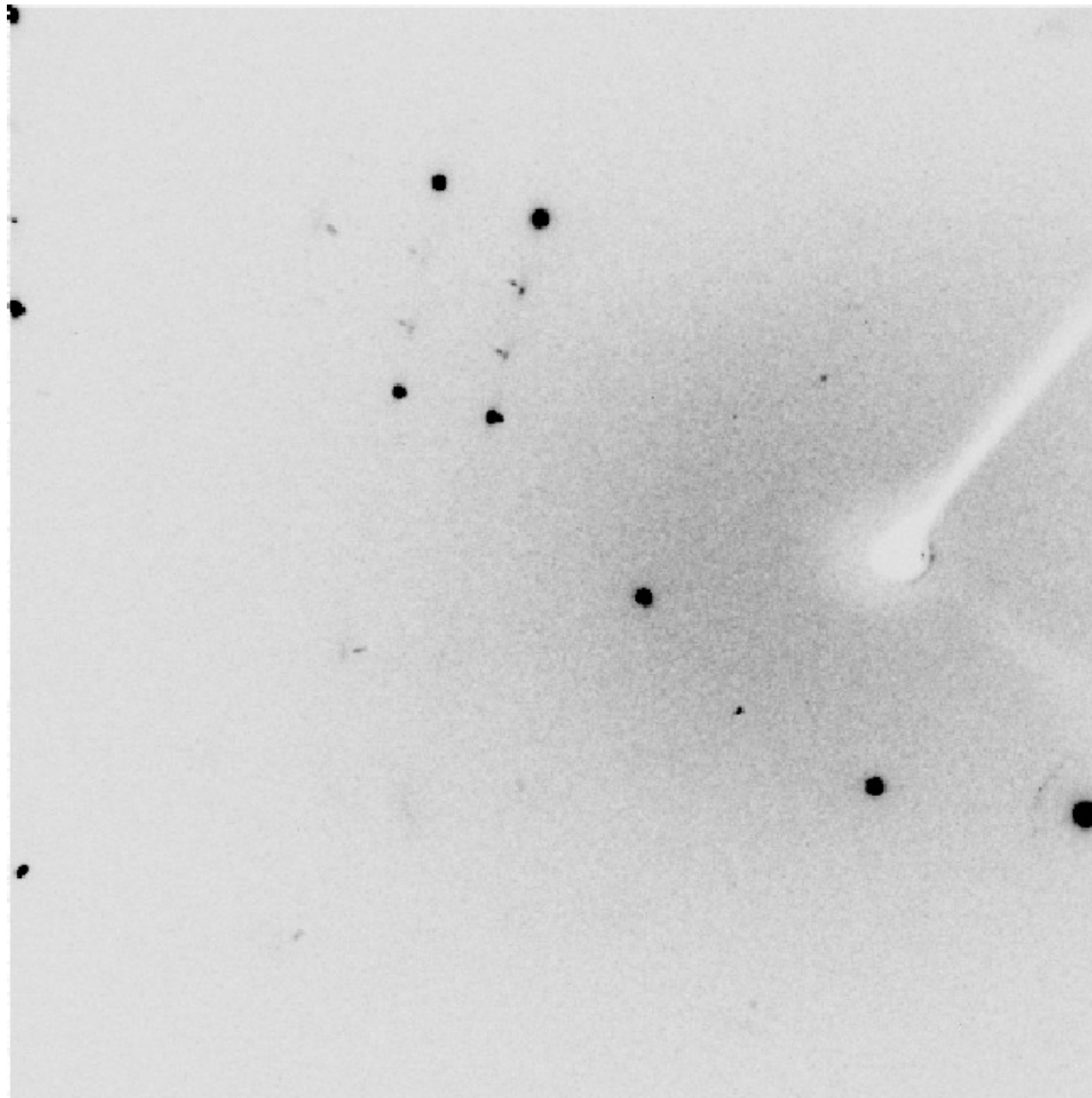
The reflections can be described as three dimensional **reciprocal lattice**. The two dimensional detector records an intersection of the three dimensional lattice.

The full experiment results in a **data set**.

One data set consists of several runs (1–20). One run is the rotation of the crystal about a single axis. Per run, 180–2,000 **frames** are recorded. One frame corresponds typically to $0.1^\circ - 1^\circ$ rotation of the crystal.

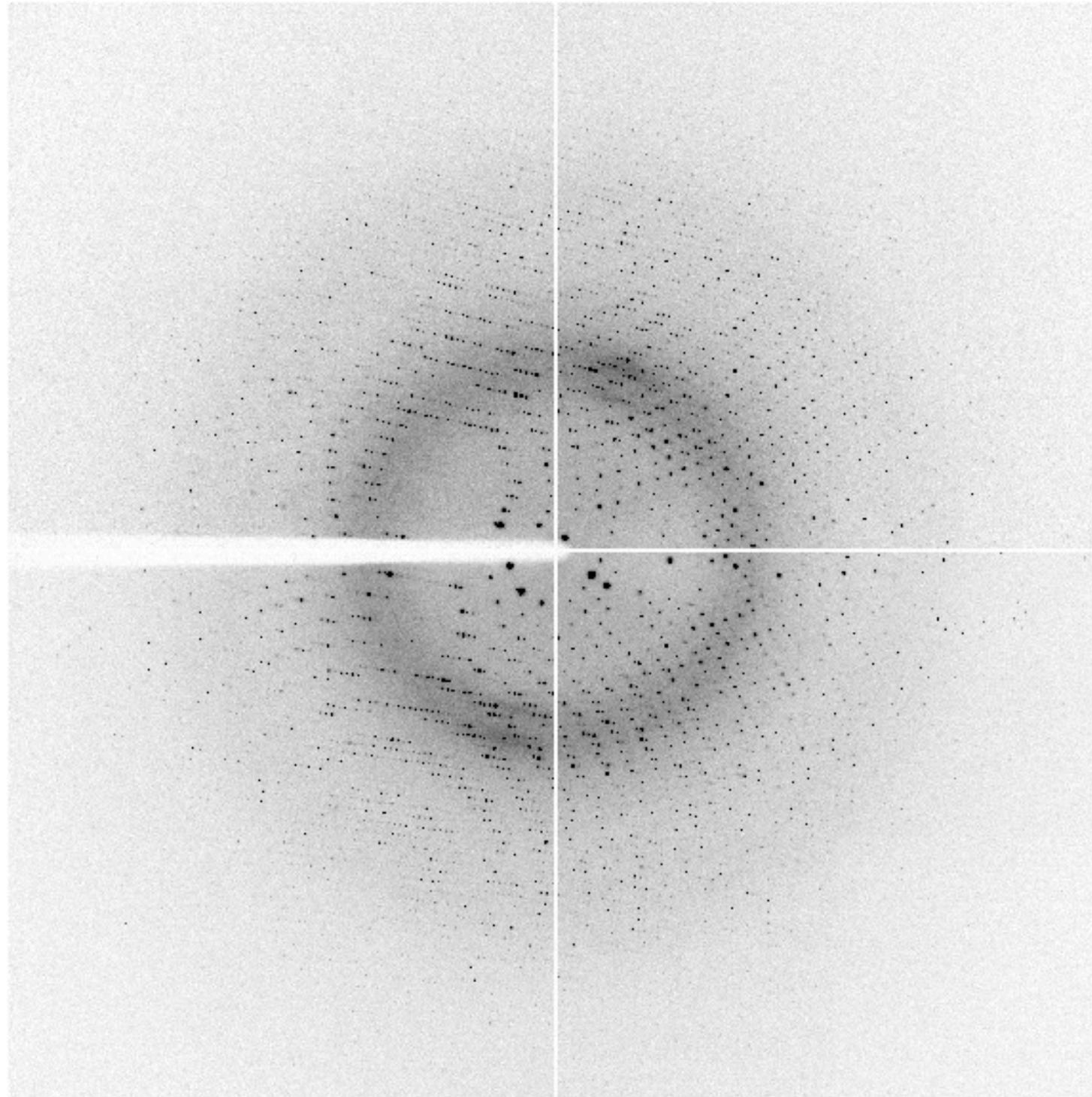


Examples of Data Frames



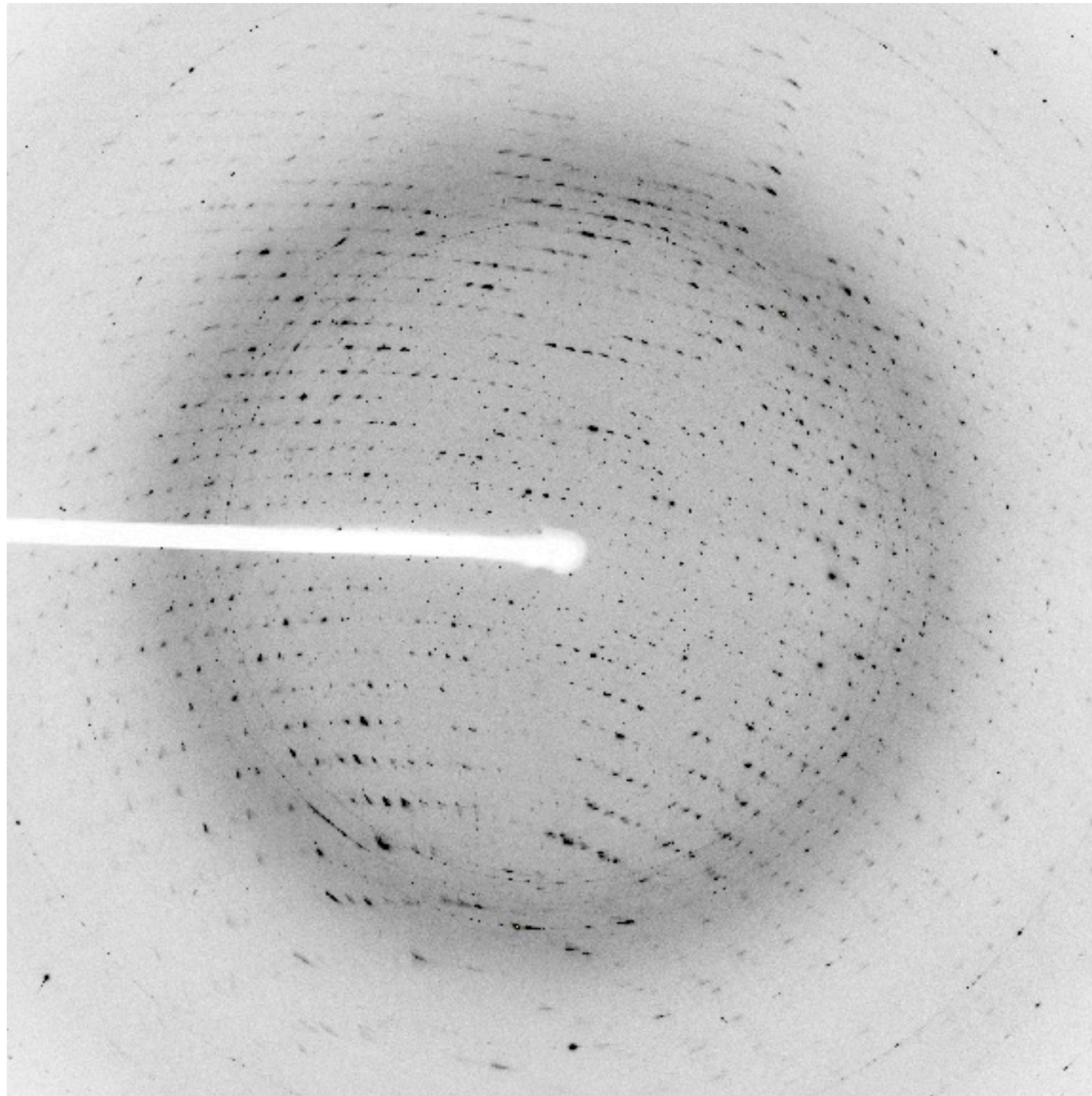
- Small molecule, unit cell dimensions: $a = 10.56\text{\AA}$, $b = 11.64\text{\AA}$, $c = 16.14\text{\AA}$, $\alpha = \beta = \gamma = 90^\circ$
- Small unit cell: \Rightarrow few reflections
- Reflections beyond edge of detector: $\rightarrow 2\theta$ offset of detector necessary
- black reflections = data; grey regions: noise, neglectable

Examples of Data Frames



- Macromolecule. unit cell dimensions: $a = 92.6\text{\AA}$, $b = 92.6\text{\AA}$, $c = 128.9\text{\AA}$, $\alpha = \beta = 90^\circ$, $\gamma = 120^\circ$
- Many more reflections
- Reflexes form patterns Muster (lunes, “Kugeldreiecke”)
- Intensity reduces towards edge of detector

Examples of Data Frames



- Macromolecule. unit cell dimensions: $a = 111.7\text{\AA}$, $b = 80.5\text{\AA}$, $c = 70.3\text{\AA}$, $\alpha = \gamma = 90^\circ$, $\beta = 94.2^\circ$
- smeared reflexes
- ice rings (formed during measurement, or due to poor shock-freezing conditions)
- Closer look: small spots between “patterns”: twinned crystal, not a single crystal.

Purpose of a Crystal Structure

Why Crystal Structure Determination?

The Structure provides atom coordinates: arrangement of elements in 3D space

Organic Chemistry:

- Purity of synthesis
- Success (or failure) of synthesis
- Determination of absolute structure

Inorganic Chemistry"

- Bonding geometry, coordination geometry (of metals . . .)

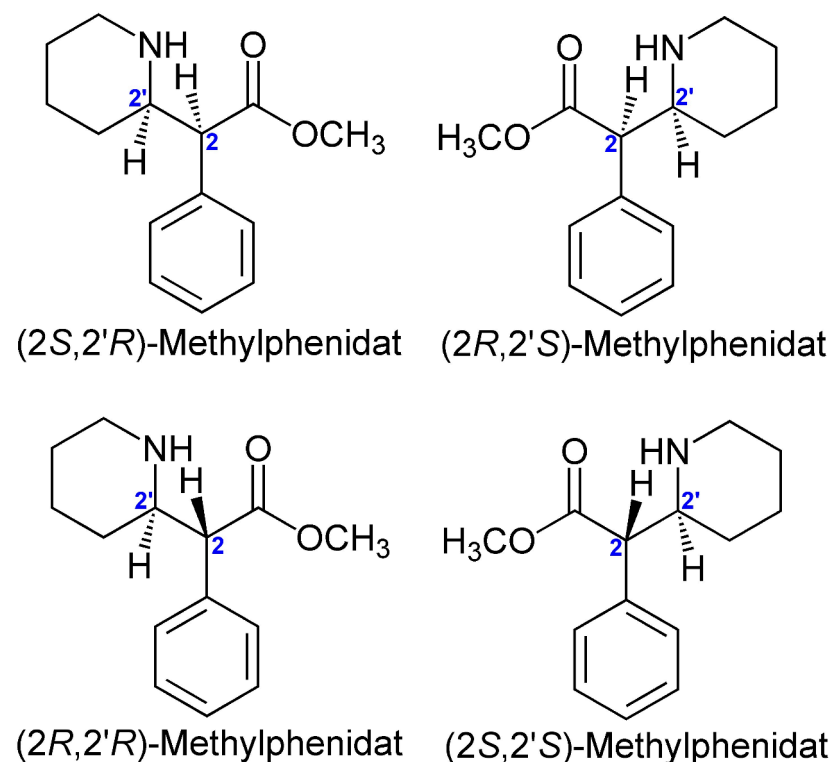
Comparison with other Structural Methods

NMR : chemical environment, sum formula. Not absolute structure

Rotational spectroscopy: (and gas phase electron diffraction): bond distances (**much more precise** than crystal structure)

Crystallography : Virtually no size limit (protein complexes > 1.5 MDa; differentiation of element types)

Examples: Absolute structure and degree of purity



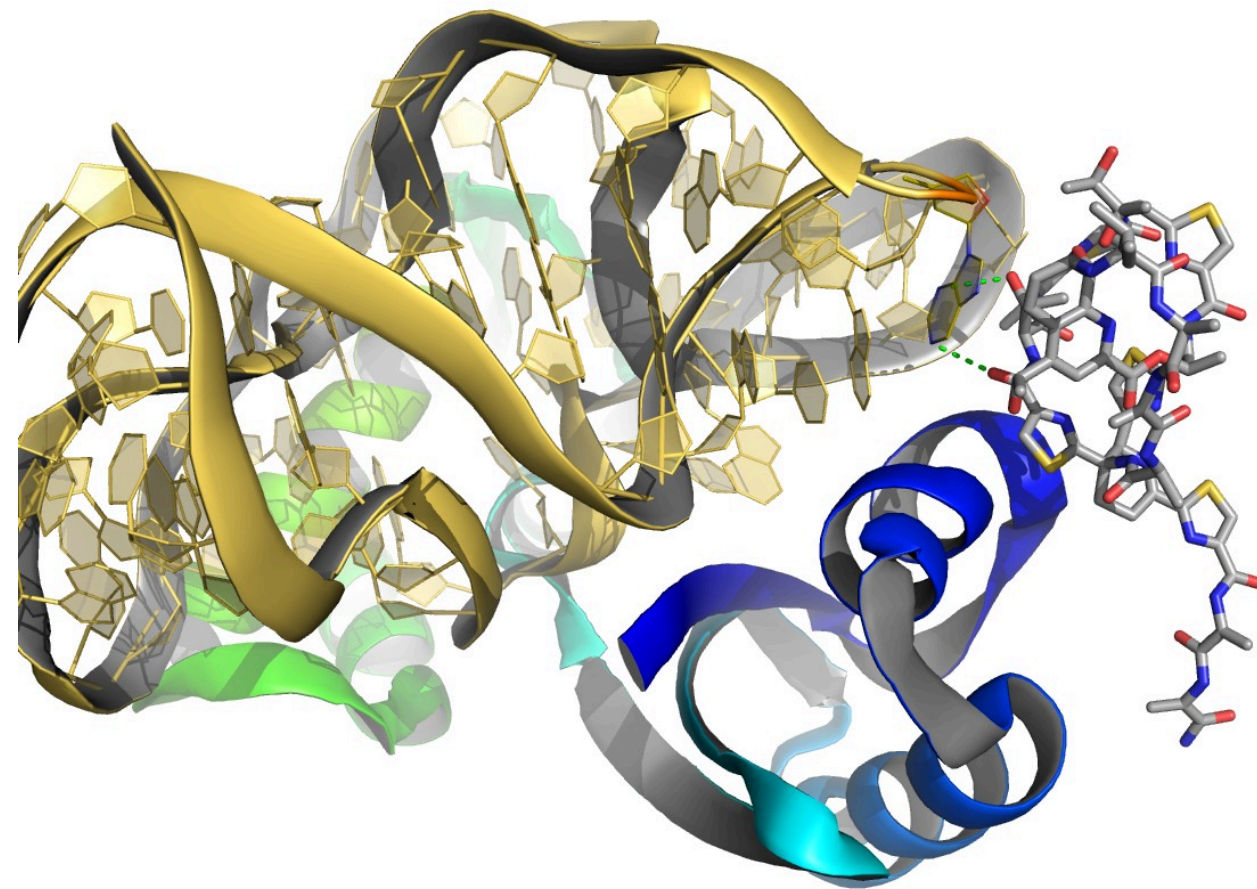
- Methylphenidate (*alias* Ritalin): medication to treat Attention Deficit Hyperactivity Disorder (ADHD).
- Two chiral centres, *four* stereoisomers
- Typical: only one stereoisomer with desired effect.
- Remaining stereoisomers: side effects

(E. J. Ariëns: *Stereochemistry, a basis for sophisticated nonsense in pharmacokinetics and clinical pharmacology*, European Journal of Clinical Pharmacology, **26** (1984), pp. 663–668).

<http://de.wikipedia.org/wiki/Methylphenidat>

The crystal structure is the only method to determine the absolute structure and the degree of purity of mixtures.

Structure based Drug Development



The antibiotic *Thiostrepton* together with its target DNA. Dr. K. Pröpper.

Knowledge of structure of ligand and target:

- Improvement of chemical interaction
- Improvement of shape / surface: Functionality and access to cell or nucleus.
- Uptake in body (cf. <http://de.wikipedia.org/wiki/Insulinpräparat>)