



Canadian National Committee
for Crystallography (CNCC)

<http://www.canadiancrystallography.ca/>



Absolute Configuration and Absolute Structure Determination

CCCW22

Calgary, AB

Presenter: Kate Marczenko



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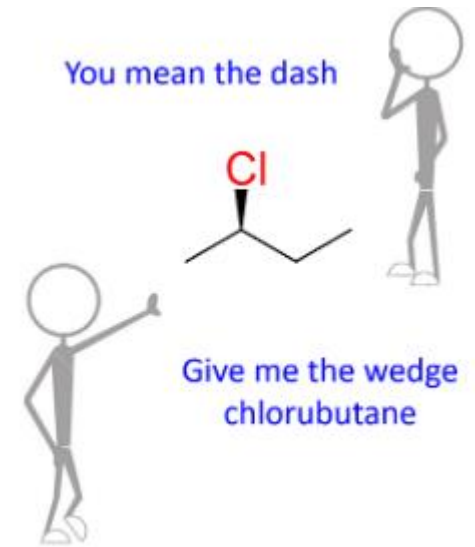
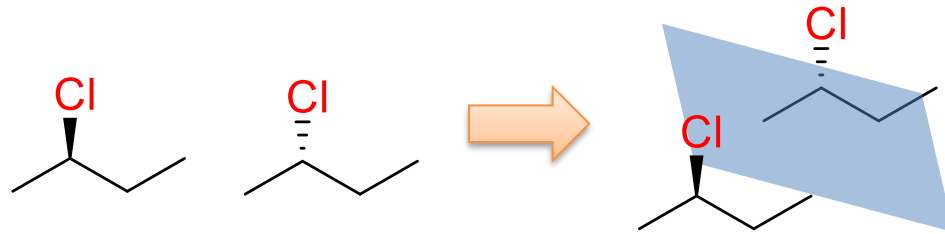


**Thank you to all that have contributed to
this presentation!**

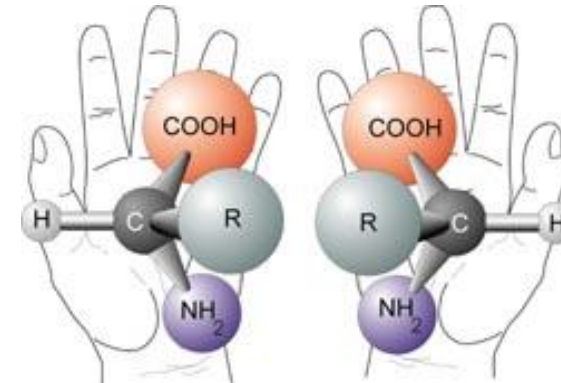
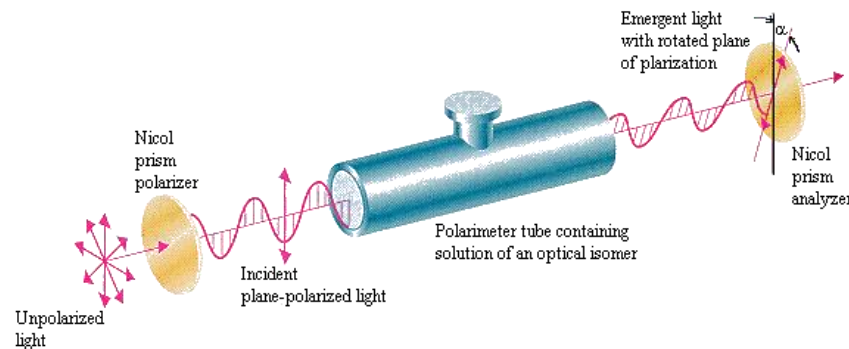
Especially: Drs. Jakub Wojciechowski
(and others from Rigaku), Frank
Schaper, Martin Martinez Ripoll, Jim
Britten, Thierry Maris

Absolute Configuration

- Absolute Configuration → spatial arrangement of the atoms for a chiral molecule (R/S, P/M or D/L assignment).



- Determination of absolute configuration → handedness of the molecule.
- Two non superimposable mirror images of a chiral molecule are called *enantiomers* – they are optical isomers.



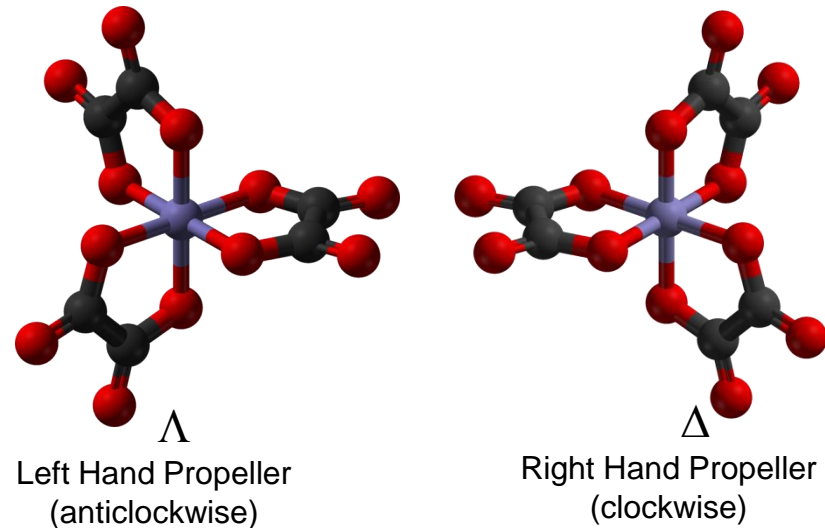
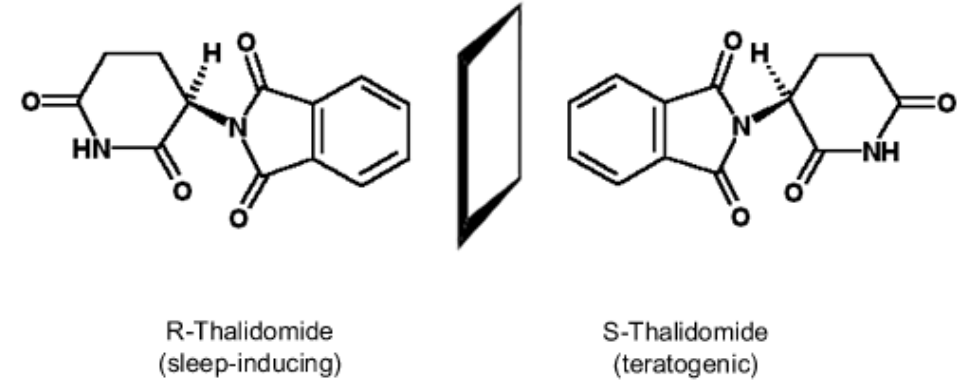
Absolute Structure

- Absolute Structure → spatial arrangement of atoms in a non-centrosymmetric crystal structure (unit-cell, space group).
- For a chiral crystal structure, absolute structure distinguishes between and specifies enantiomorphs of the crystal structure.

	Absolute Structure	Absolute Configuration
Property	Spatial Arrangement	Spatial Arrangement
Content	Atoms	Atoms
Object	Crystal	Molecule
Symmetry	Non-centrosymmetric	Chiral

Chirality

- Chirality plays an important role in the binding affinity and interactions between a drug and its target.



- Experimental techniques include optical rotation, circular dichroism spectroscopy, enantioselective chromatography, etc.
- X-ray diffraction of single crystals has the ability to distinguish between enantiomorphs of a chiral structure and enantiomers of a chiral molecule.

Crystallization

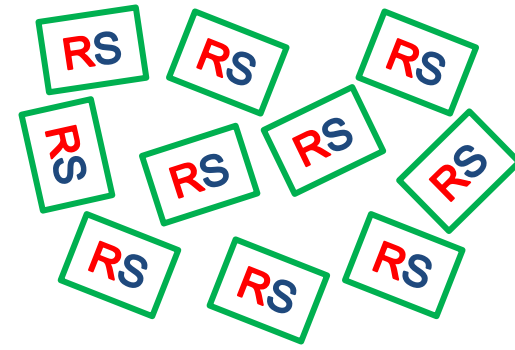
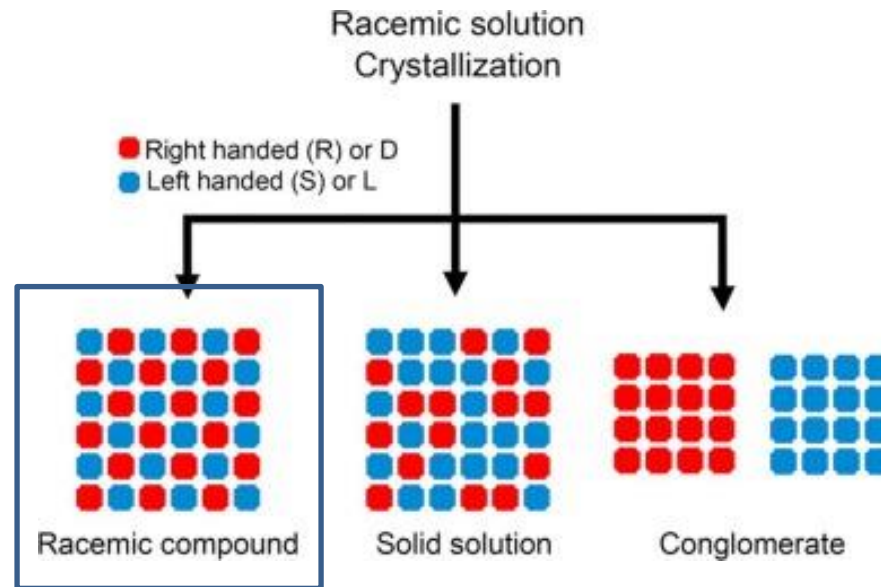
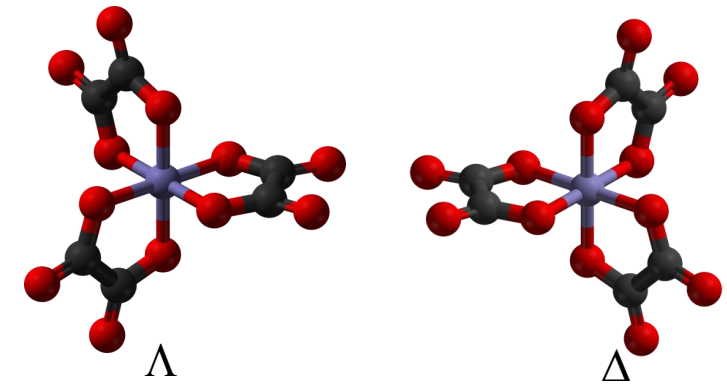
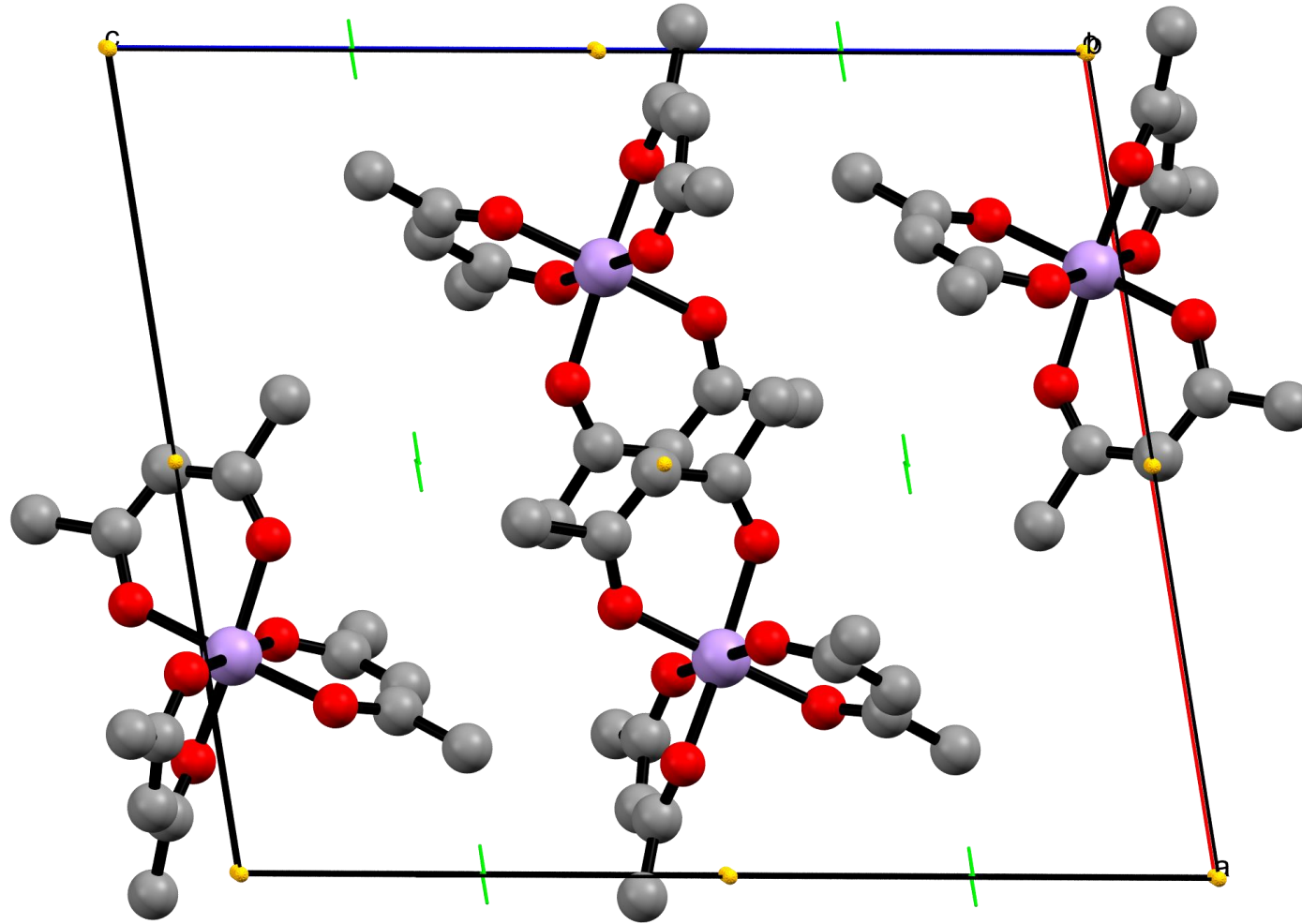




Image from: Ultrasonics Sonochemistry, 2018, 43, 184-192.

- The solid phase formed from a racemic solution can be a **racemic compound**.
 - Crystal containing an even ratio of both enantiomers in a regularly structured array.
 - No optical activity.
 - Usually centrosymmetric space group.

Racemic Compound

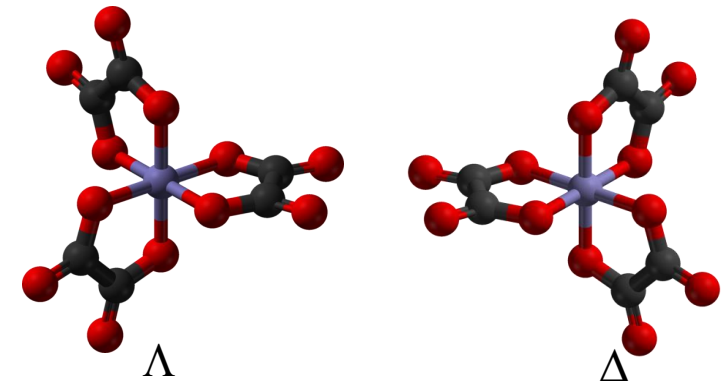
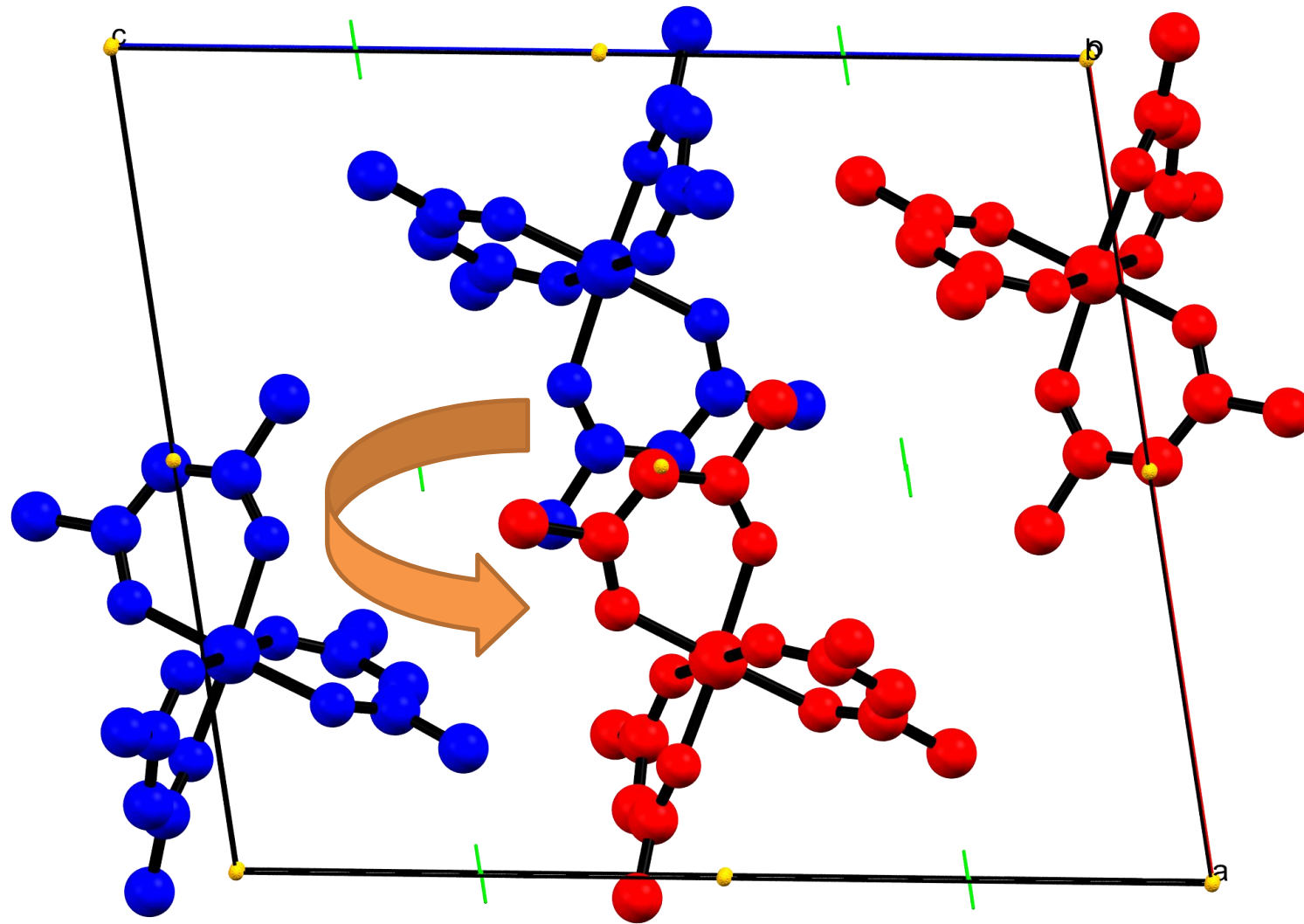


Legend

-  2-fold screw axis
-  Inversion center

ACACMN31 - $P2_1/c$

Racemic Compound



Legend

Right hand red

Left hand blue

ACACMN31 - $P2_1/c$

Crystallization

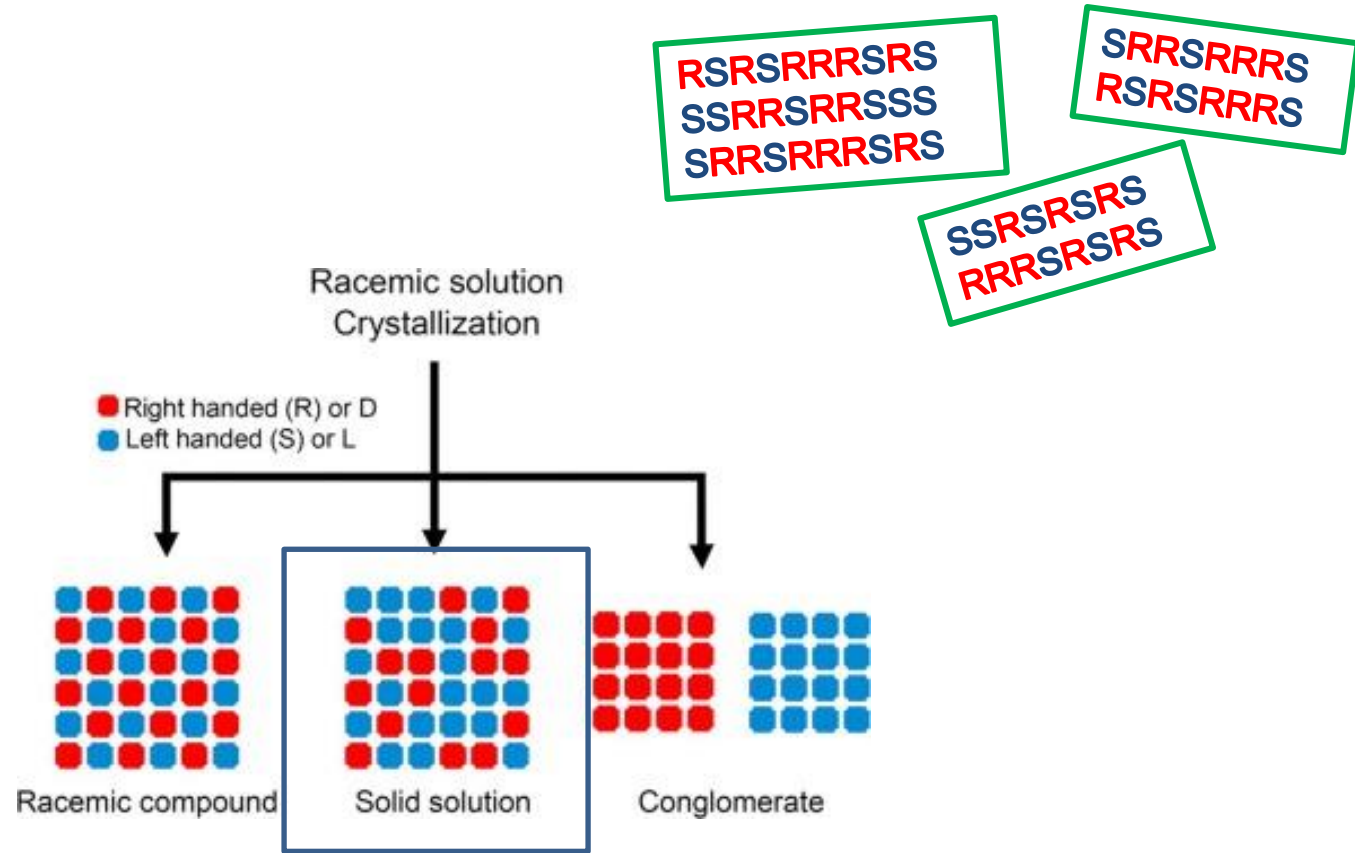


Image from: Ultrasonics Sonochemistry, 2018, 43, 184-192.

- **(Disordered) Solid Solution** is a crystal containing the two enantiomers in a disordered arrangement.
 - Usually centrosymmetric space group.

Crystallization

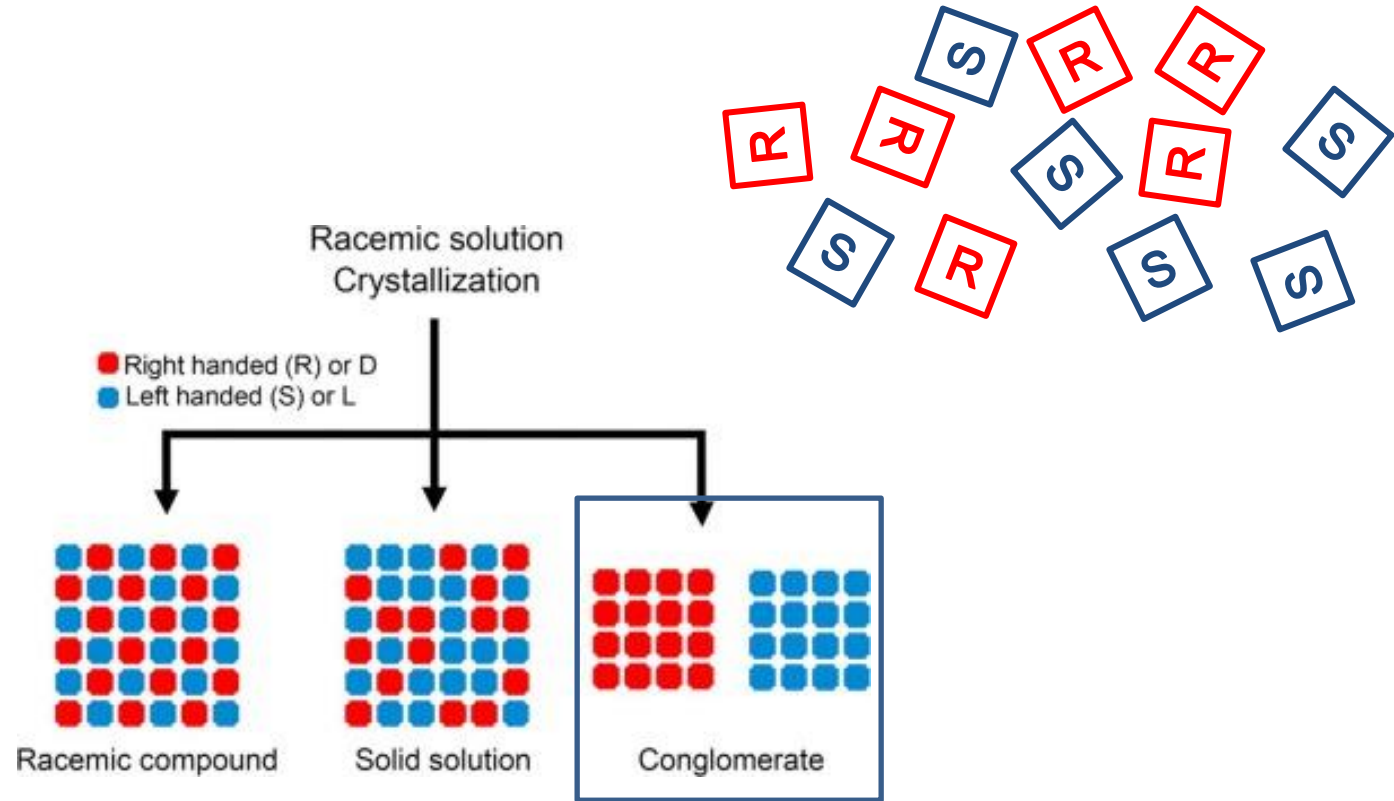


Image from: Ultrasonics Sonochemistry, 2018, 43, 184-192.

- Crystallization of a racemic solution may give a **conglomerate** with homochiral resolution of each enantiomer.
 - i.e. a mixture of well-resolved crystals of both enantiomers
 - Individual crystals have optical activity
 - Chiral space group

In the Solid-State

- Chiral molecules can crystallize as an enantiopure bulk sample or as a racemic mixture.
- For enantiopure crystals → Space group restriction:
 - Only 65 space groups allowed for enantiopure chiral molecules: No Inversion Center / No Mirror / No Glide Plane (Sohncke groups)
 - These include 11 pairs of enantiomorphic space groups (screw axes of opposite handedness)
eg: $P4_1/P4_3$ -or $P6_1/P6_5$
 - Forty-three other space groups allow for chiral crystal structures, making a complete set of sixty-five space groups known as the Sohncke groups.

Triclinic: $P1$

Monoclinic: $P2$ $P2_1$ $C2$

Orthorhombic: $P222$ $P222_1$ $P2_12_12$ $P2_12_12_1$ $C222_1$ $C222$ $F222$ $I222$ $I2_12_12_1$

Tetragonal: $P4$ $P4_1$ | $P4_3$ $P4_2$ $I4$ $I4_1$ $P422$ $P42_12$ $P4_122$ | $P4_322$ $P4_12_12$ | $P4_32_12$ $P4_222$ $P4_22_12$ $I422$ $I4_122$

Trigonal: $P3$ $P3_1$ | $P3_2$ $R3$ $P3_12$ $P321$ $P3_112$ | $P3_212$ $P3_121$ | $P3_221$ $R32$

Hexagonal: $P6$ $P6_1$ | $P6_5$ $P6_2$ | $P6_4$ $P6_3$ $P622$ $P6_122$ | $P6_522$ $P6_222$ | $P6_422$ $P6_322$

Cubic: $P23$ $F23$ $I23$ $P2_13$ $I2_13$ $P432$ $P4_232$ $F432$ $F4_132$ $I432$ $P4_132$ | $P4_332$ $I4_132$

Enantiomorphic Space Groups

$P4_1$

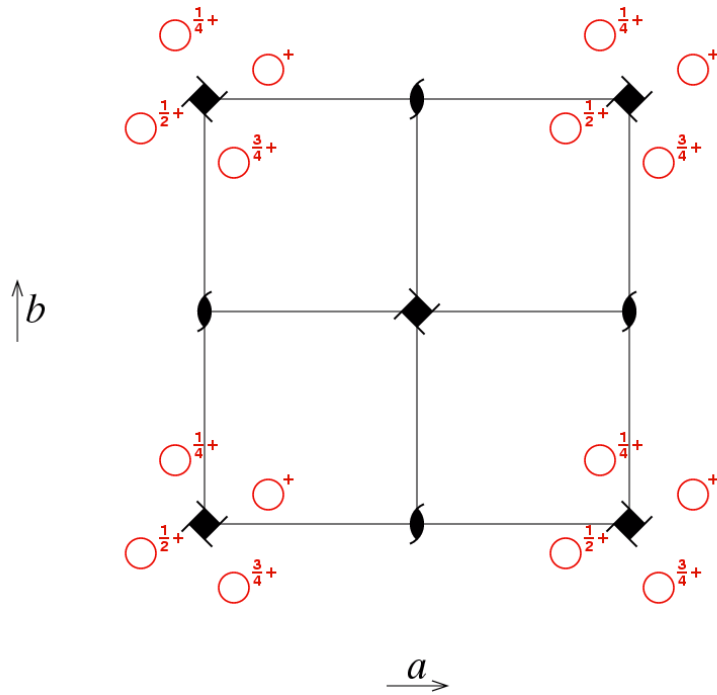
$P4_1$

4

$P4_3$

$P4_3$

4

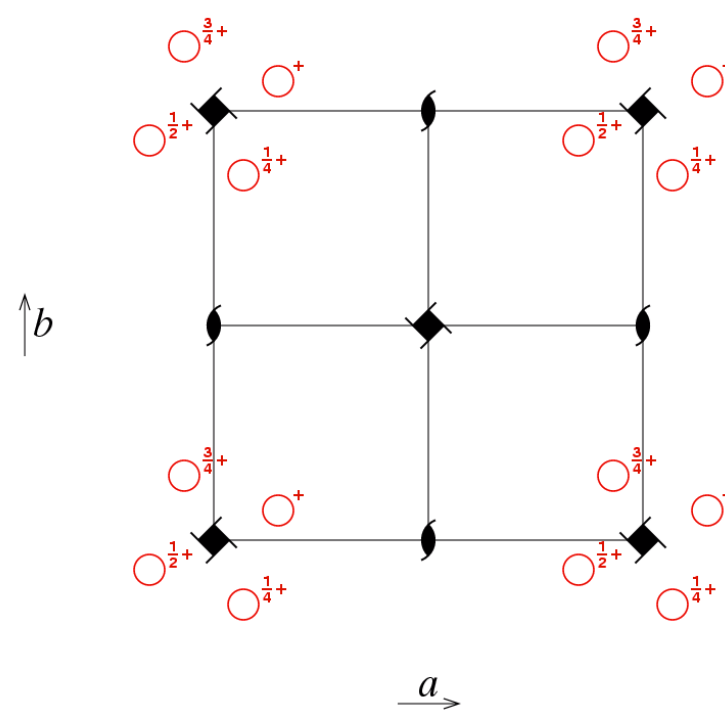


1 x, y, z

2 $\bar{x}, \bar{y}, \frac{1}{2} + z$

3 $\bar{y}, x, \frac{1}{4} + z$

4 $y, \bar{x}, \frac{3}{4} + z$



1 x, y, z

2 $\bar{x}, \bar{y}, \frac{1}{2} + z$

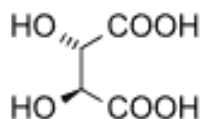
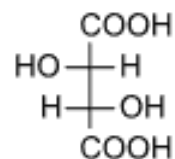
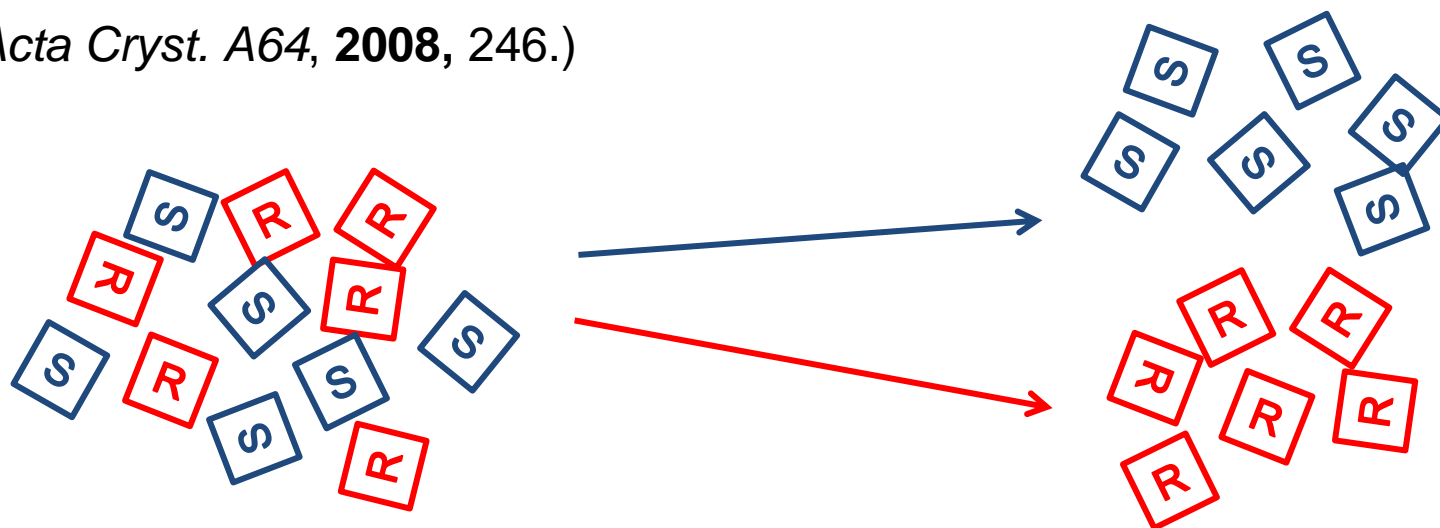
3 $\bar{y}, x, \frac{3}{4} + z$

4 $y, \bar{x}, \frac{1}{4} + z$

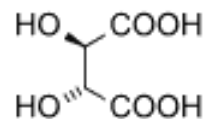
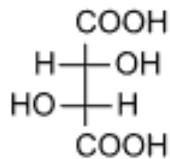
Enantiomorphous Crystals

Louis Pasteur Experiment (1848): Separation of the two enantiomers by the visual sorting of crystals of a conglomerate

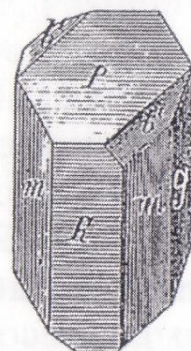
(Z. S. Derewenda, *Acta Cryst.* A64, **2008**, 246.)



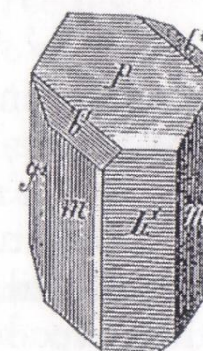
D-(-) levotartaric acid



L-(+) dextrotartaric acid



(Droit.)



(Gauche.)

Sodium ammonium tartrate crystals

feature articles

Acta Crystallographica Section A
**Foundations of
Crystallography**

ISSN 0108-7673

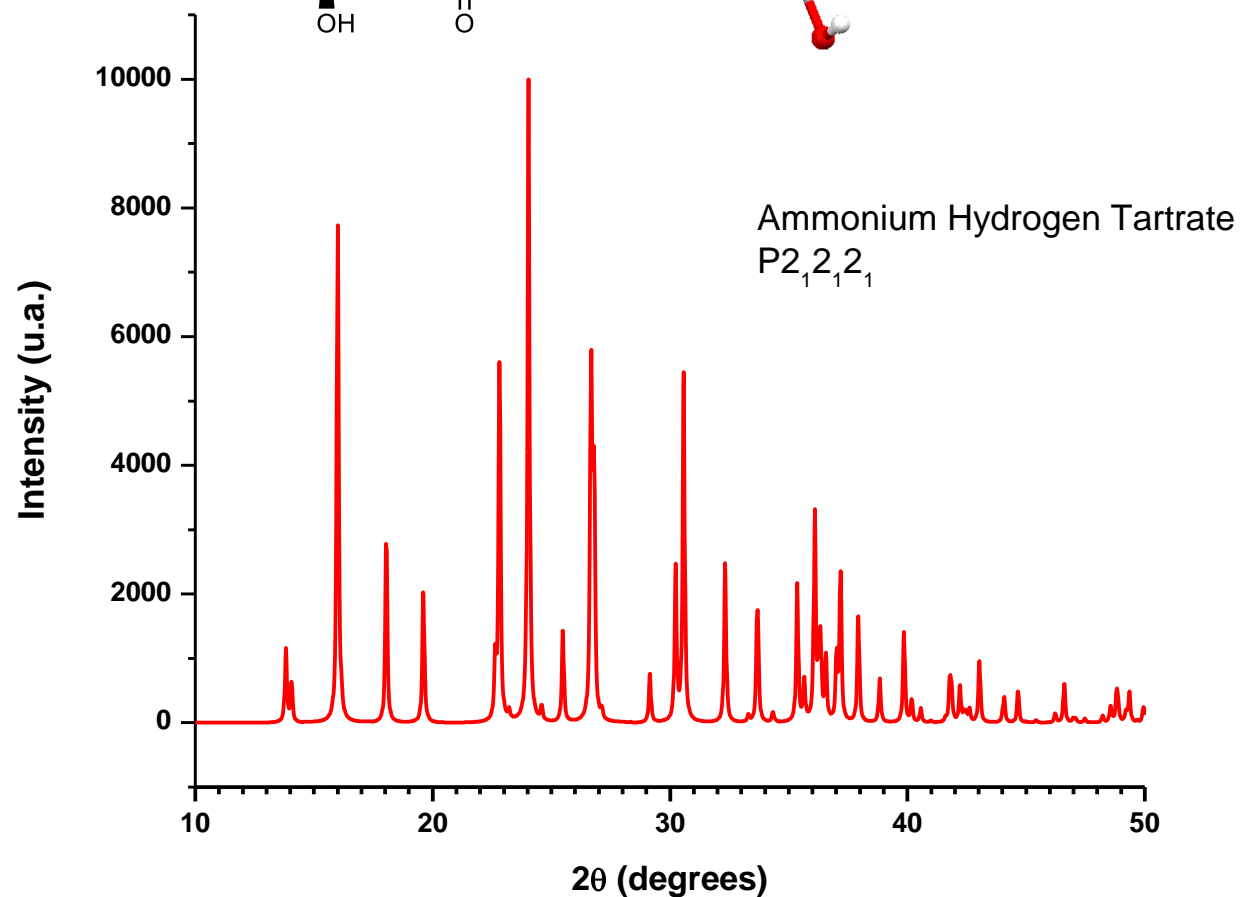
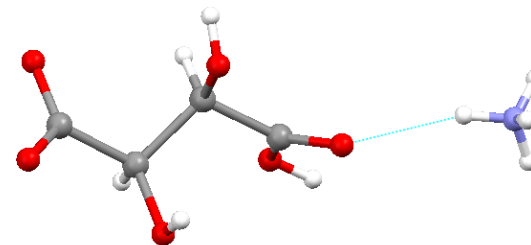
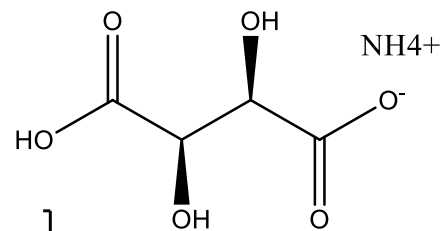
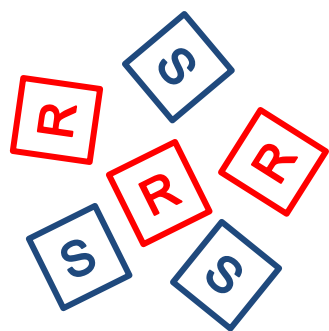
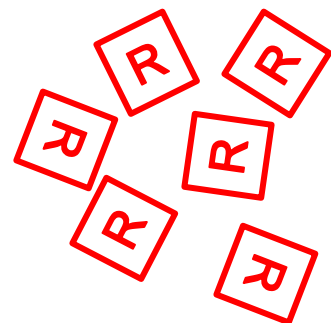
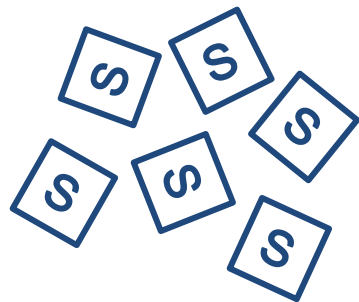
Received 2 August 2007
Accepted 30 October 2007

On wine, chirality and crystallography

Zygmunt S. Derewenda

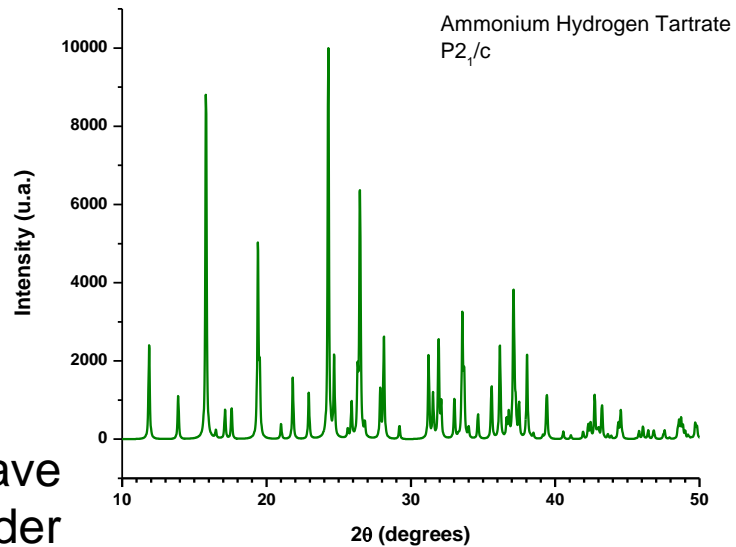
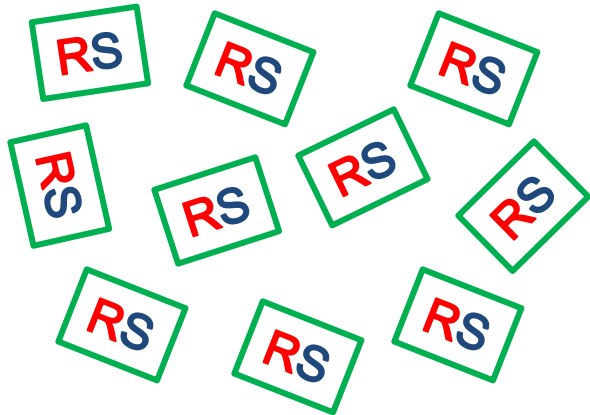
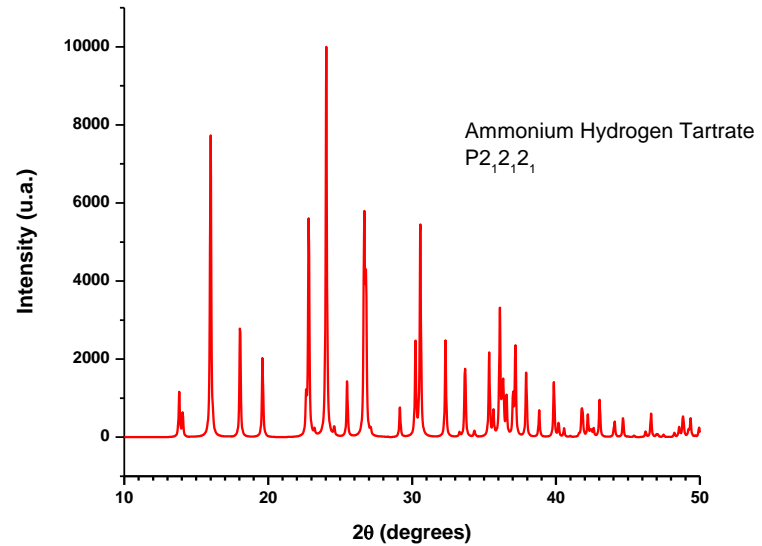
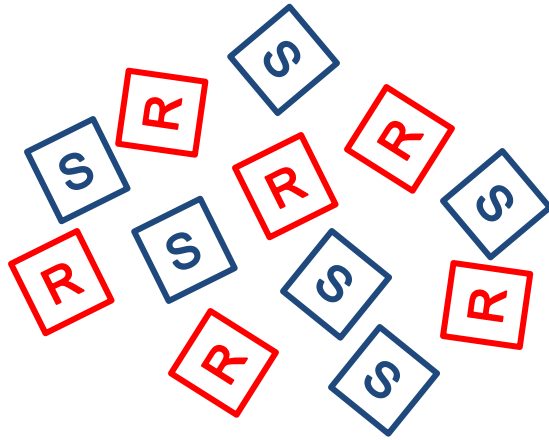
Department of Molecular Physiology and Biological Physics, University of Virginia School of
Medicine, Charlottesville, Virginia 22908-0736, USA. Correspondence e-mail: zsd4n@virginia.edu

Powder Diffraction



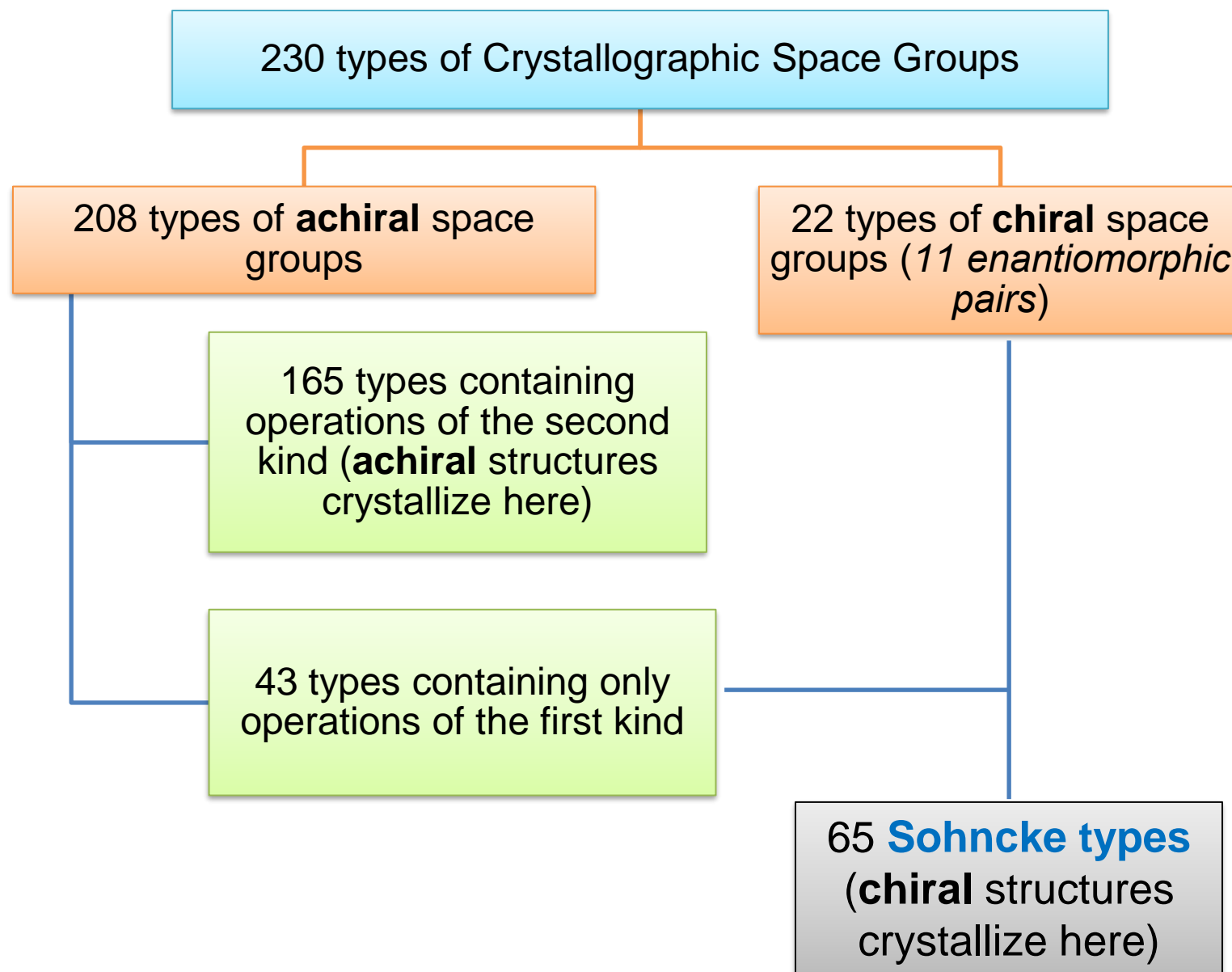
The two enantiopure samples and the conglomerate give the same powder X-ray diffraction pattern

Powder Diffraction



The conglomerate and the racemate have different space groups, so the powder diffraction pattern is different

Space Group Framework



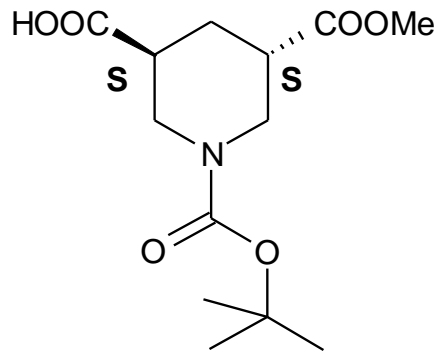
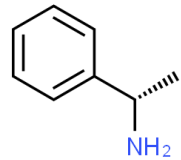
How can we determine the Absolute Configuration?

- Method 1: Internal Chiral Reference
- Method 2: Absolute configuration established by anomalous-dispersion effects in diffraction measurements on the crystal.

Method 1: Absolute configuration from an internal chiral reference

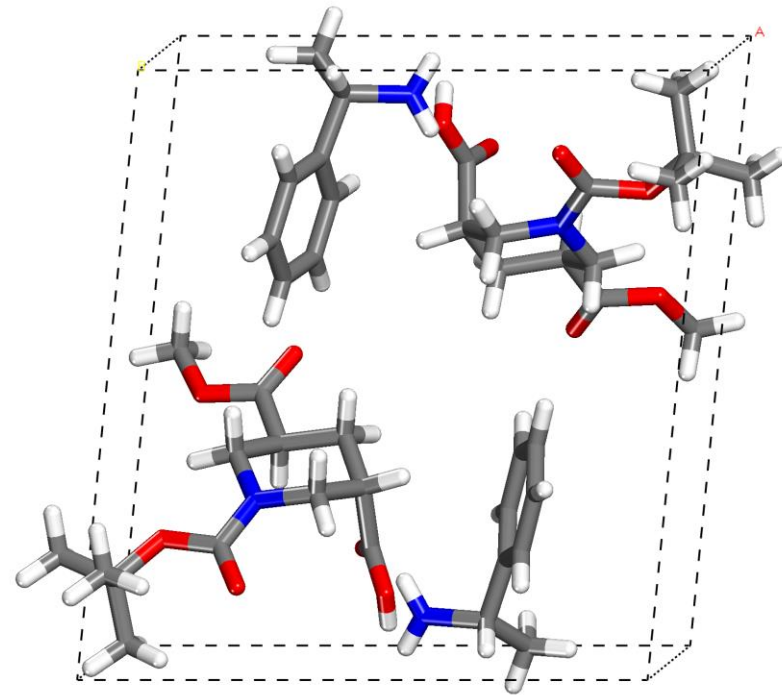
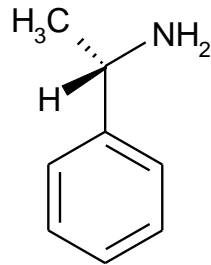
- Incorporation of a compound of known absolute configuration into the crystal structure (chemical reaction, cocrystallization).
- Using the chiral molecule as an internal reference for the absolute configuration.

(S)-(-)-1-Phenylethylamine



FOCXAX P₂₁

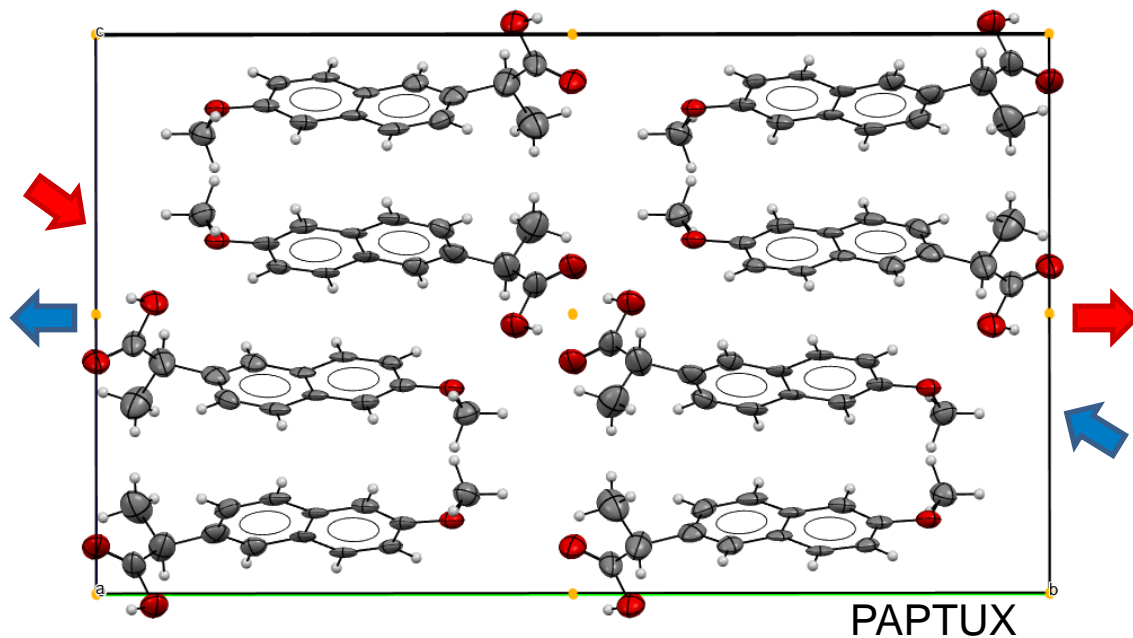
Hans Iding, Beat Wirz, Rosa-María Rodríguez Sarmiento,
Tetrahedron Asymmetry 14 (2003) 1541-1545



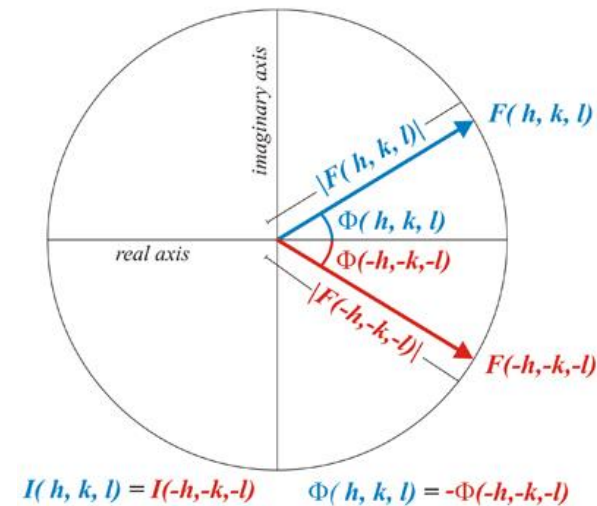
You can not always assume that chemical reaction, crystallization, or operations of mechanochemistry will conserve the chirality of the reference material.

Method 2: From the diffraction data via the absolute structure

- Method based on the *anomalous scattering (dispersion)*.
- The intensities of reflections $I(h,k,l)$ and $I(-h,-k,-l)$ are equal in either of the following situations:
 1. The crystal structure is centrosymmetric.
 2. There is no anomalous dispersion.



$$|F_{hkl}|^2 = |F_{\bar{h}\bar{k}\bar{l}}|^2$$



Friedel's Law is fulfilled in centrosymmetric crystals or in absence of anomalous dispersion.

Resonant Scattering (Anomalous Dispersion)

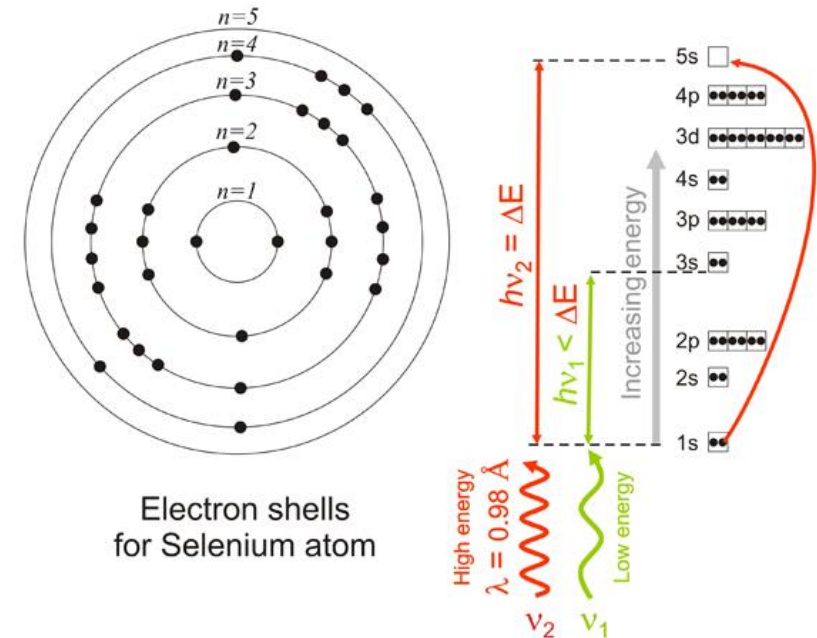
- Anomalous scattering affects the way that photons interact with electrons in an atom.
- When the incident radiation has sufficient energy to be absorbed by an atom in the structure, an electronic transition from a lower energy level to an upper one occurs.
- Some photons are absorbed and immediately re-emitted at the same energy but with a change in phase and amplitude of the diffracted wave (strong coupling to absorption edge energy).
- **Atomic scattering factor:** ratio of the amplitude of the X-rays scattered by a given atom and that scattered according to the classical theory by one single free electron.

$$f = f_o + f' + i f''$$

f_o = normal atomic scattering factor (real number)

f' and f'' = real and imaginary correction factors

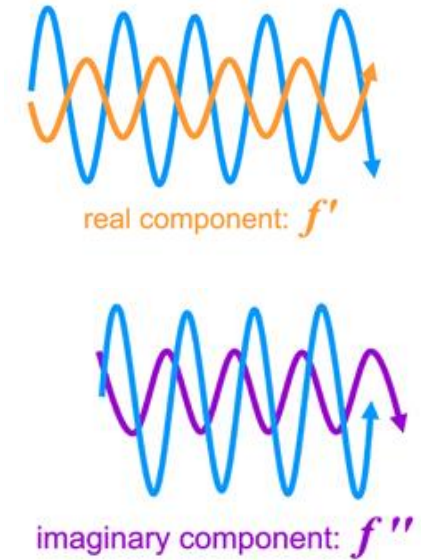
If anomalous dispersion occurs, the atomic scattering factor (f) behaves as a complex number.



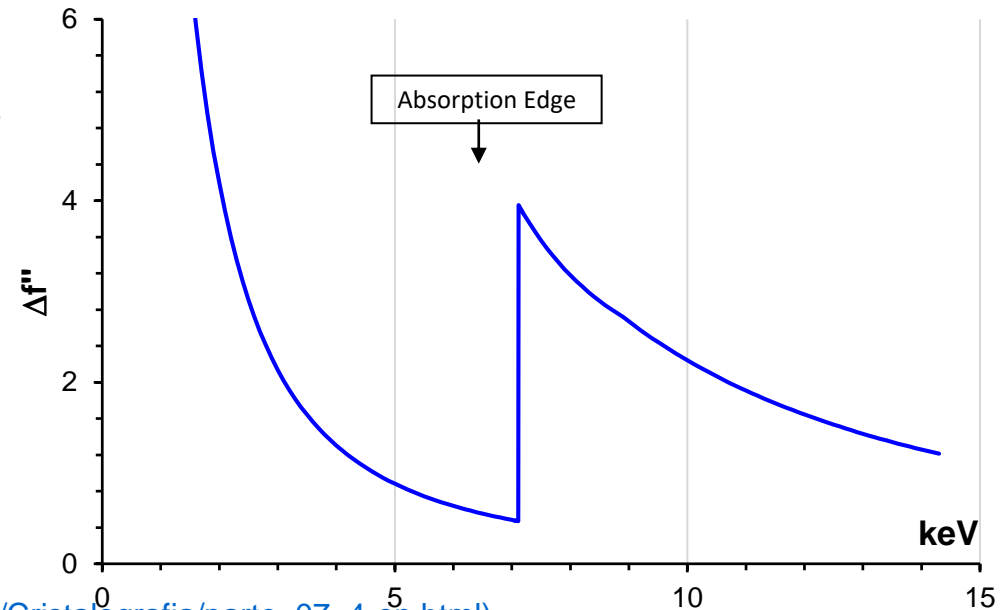
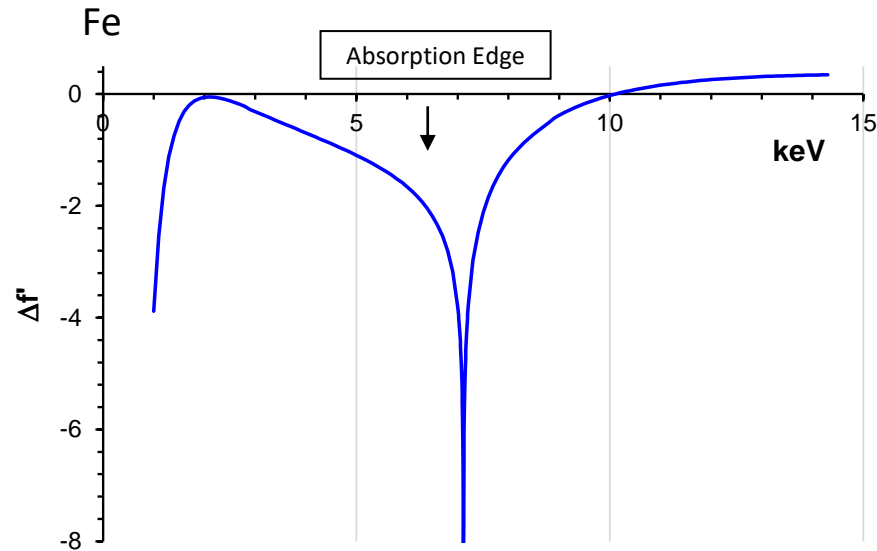
If the incident radiation has sufficient energy to be absorbed by an atom, electronic transitions can occur.

Resonant Scattering

- The values of f' and f'' are depended on the absorption edge of the element.
- The real part, $\Delta f'$, can be positive or negative. Close to the absorption edge, $\Delta f'$ is negative.
- The imaginary part, $\Delta f''$, has a 90° phase shift compared to f_{atom} . It is always positive, increases to reach a maximum close to the absorption edge then decreases close to zero after the absorption edge.

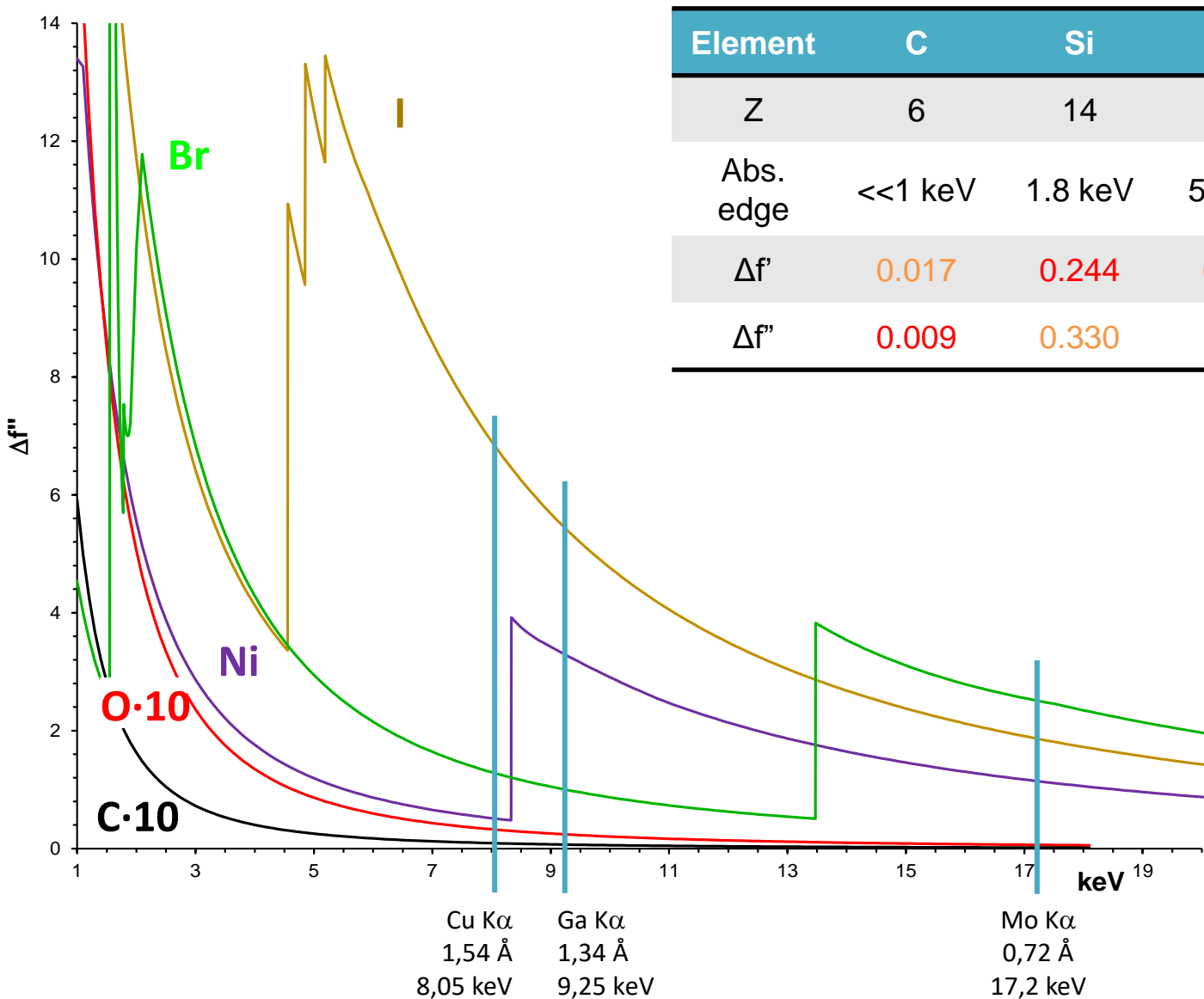


Anomalous scattering will be observed if the X-Ray energy is slightly higher than the absorption edge for the element.



Resonant Scattering

- The magnitude of the resonant scattering will be weak for light elements (C, N, O, F). Below table is for Cu K α .



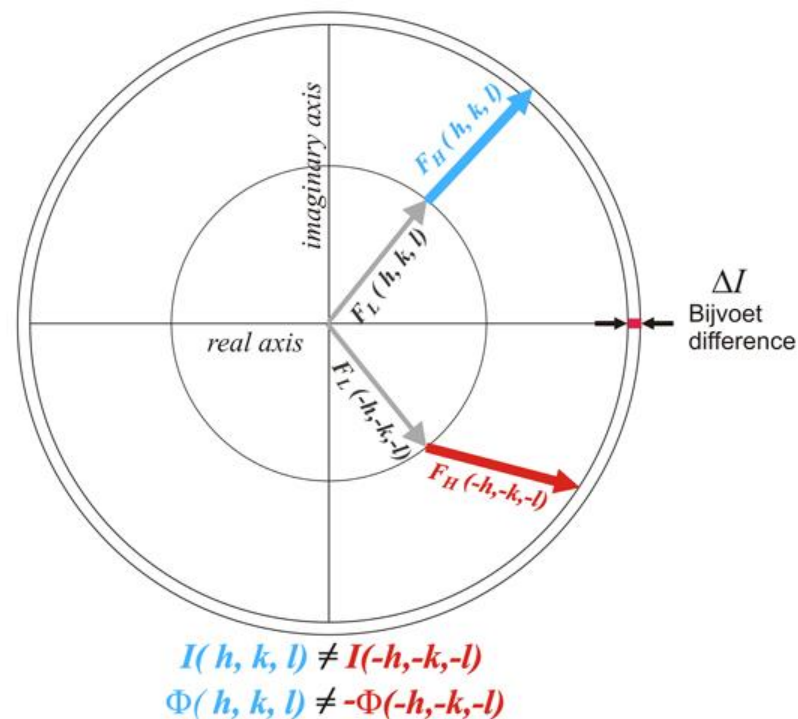
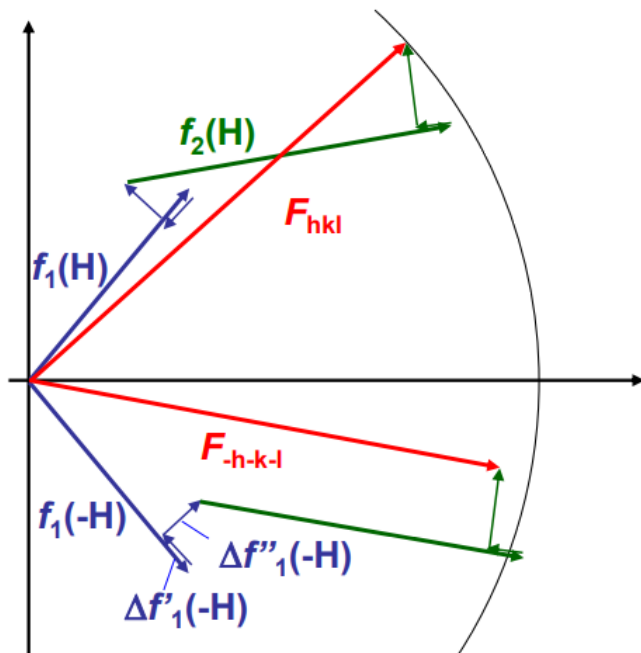
Element	C	Si	V	Fe	Co	Ni	Cu	Zn
Z	6	14	23	26	27	28	29	30
Abs. edge	<<1 keV	1.8 keV	5.5 keV	7.1 keV	7.7 keV	8.3 keV	9.0 keV	9.7 keV
$\Delta f'$	0.017	0.244	0.035	-1.179	-2.464	-2.956	-2.0255	-1.6142
$\Delta f''$	0.009	0.330	2.110	3.204	3.608	0.509	0.5885	0.6774

- As it depends on the absorption edge, it will depend on the wavelength used:

	Cu K α (1.54 Å)		Mo K α (0.72 Å)	
	$\Delta f''$	μ/ρ	$\Delta f''$	μ/ρ
C	0.01	5	0.002	1
Ni	0.51	50	1.11	71
Br	1.29	90	2.51	112
I	6.91	292	1.87	55

Resonant Scattering

- Close to an absorption edge, $\Delta f'$ becomes negative and can be related to X-ray absorption. The imaginary $\Delta f''$ is positive at a phase 90° from that of f .
- Reflections of type (h,k,l) and $(-h,-k,-l)$ are not only different in their phases. There is also an observable difference between the moduli of their structure factors $|F(h,k,l)|$ and $|F(-h,-k,-l)|$, that is between their corresponding intensities, $I(h,k,l)$ and $I(-h,-k,-l)$.



$$f = f_o + f' + i f''$$

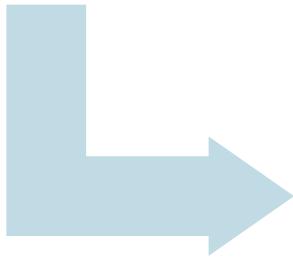
Friedel's Law is no longer valid!

Method 2: Absolute configuration established by anomalous-dispersion effects in diffraction measurements on the crystal.

Determination of the Absolute Structure

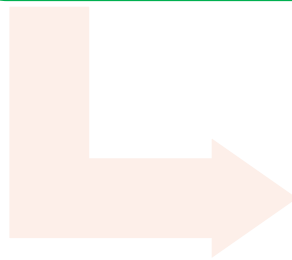
Determine the best possible crystal structure

- Screen your sample extensively.
- Mount and center properly.
- Careful with absorption correction.



Take care for Bijvoet Differences

- Collect high redundant data.
- Check the observability.
- Check amount of Friedel pairs and anomalous signal.
- Select proper X-ray source.



Assign proper absolute Configuration

- Make sure that **descriptor** values and its standard deviation make sense.

PRACTICAL CRYSTALLOGRAPHY



START/STOP

Shutter Closed

CAM **CRYO** **X-RAY** **STATUS**

CCD Ready

RED Ready

SM Screening

Screening

Mount **Screen = 60.0s**

PEAKS

UB fit with 387 obs out of 387 (100.0%)

UNIT CELL (CSD: 6.2L)

PG: 2/m (b-unique) monoclinic P

7.9251(15) 9.181(2) 18.6319(11)

90.017(17) 92.992(14) 90.008(18)

V = 1353.8(4)

QUALITY

Resolution(A)	N	I/sig	I/sig0
inf - 1.14	130	33.9	44.9
1.24- 1.14(Tast)	13	12.9	18.5

Well diffracting sample

Diff. limit: beyond 1.14 (theta res. limit) for I/sig=2.0

Mosaicity: e1=1.0, e2=1.3, e3=0.9 (deg), lso=1.09 (deg)

Experiment - Complete data for publication

Name: exp_235

User=jakub2, Detector=34.0mm, Res. = 0.837Ang, I/sig=15.0, width=0.5deg, Movie, cryo off, Strategy: Complete data (default mode), Exposure: 5.0s 20.0s

Exposure time:

What is this? **Pre-Exp. (7 m)** **Edit**

Goniometer

Omega	Theta	Kappa	Phi	Distance
12.6	-35.0	0.0	160.0	32.0

Displaying **HKL Planes**

Color table **Set runs filter** **Show base data**

☒ Show histogram preview ☐ Display above max

OpenGL version: 4.5.0 - Build 24.20.100.6286

IMAGE: scr_exp_235_1_20.rodhypix (run: 1 frame: 20)

Omega: 12.62 Theta: -35.00 Kappa: 0.00 Phi: 160.00 Distance: 32.00

GONIOMETER:

Omega: 12.62 Theta: -35.00 Kappa: 0.00 Phi: 160.00 Distance: 32.00

Olex2

Version 1.3-ac4

Rigaku

oxford diffraction

CRYALIS^{Pro} SM

STARTING EXPERIMENT WITH PRE-EXP

Pre-experiment

Path and user / Sample

Name: Experiment: exp_235 in folder C:\XcaliburData\exp_235

Path is ok! >> C:\XcaliburData

Expected chemical formula: AutoChem4 may not succeed without providing valid chemical formula!

Comment:

Experiment options

Exposure time: Detector=34.0mm, width=0.5deg, std-range, Movie, cryo off, Strategy: Complete redundant data, Exposure: 5.0s 20.0s

Total Pre-experiment Time: 0:07, No. Runs/Frames: 6/60, Pre-experiment Finish: Wed May 27 00:18:51 2020

Type of experiment: >>

I/sig Resolution Redundancy

☒ Interactive strategy after pre ☒ Attempt AutoChem ☐ External process auto-analysis (experimental)

Information

Type of experiment (1.2.1)

Absolute structure

Targets/Objectives

Resolution ☒ Theta ☐ 2Theta

Detector distance (mm):

Target I/sig:

Scan width for pre (deg):

Scan range type: ☒ Standard ☐ Extended

Strategy options

☒ Limit space groups taken into consideration ☐ All noncentrosymmetric ☒ Chiral only

Strategy: Redundancy constraint:

Completeness limit:

Experiment:

Settings

☒ Record movie during dc Step in deg:

☐ Cryo/Hot shutdown after end of experiment

Global parameters

Pre-experiment run list (multi theta)

☒ Optimal drive time ☐ Low theta first (weak diffraction) ☐ Start from high theta (strong diffraction)

☒ Time factors applied in multi theta experiments

Time factors applied in multi theta experiments: 1.0, 4.0, 4.0, 4.0,

Information

START/STOP

Shutter Open X-ray Cu Cu threshold

CAM CRYO X-RAY STATUS

CCD Collecting... (4687,5496,end:Mon Jun 01 03:48:06 2020)

RED AutoChem4 running (6, Solving structure (ShelXL_Least Squares))...

Crystal CCD

Data Collection

Data Reduction

FRAMES / RUNS

In run list: 5496/45, used: 4668/38

3D PROFILE ANALYSIS

Frames done: 4668

Reflections tested: 9420, used: 7581

Avg mosaicity (in degrees) - 38 run(s)

e1=3.05, e2=1.02, e3=1.54

Max incidence angle profile change(e2): 24%

3D INTEGRATION & FITTING

Frames done: 4668

Fitted: 9091, overf/bad: 0, hidden: 1280

Outliers rejected: 126

SCALING / NUMERICAL ABSORPTION

Empirical abs (e=2 o=1): min=0.88,max=1.15

Frame scales (5/scale): min=0.65,max=1.70

Friedel pairs treated as equivalent

RESULTS (4668 frames) - SYM: P2/m (b-unique)

Resolution(A) Redundancy F2/sig(F2) Rint

inf - 0.79 6.7 32.0 0.049

Completeness: 99.9% (0.84 ANG)

Anom compl.: 98.9% (P2 (b-unique))

SPACE GROUP DESCRIPTOR

P2(1) Group #: 4

DATA REDUCTION OPTIONS

Per-frame model refinement used

2-cycle 3D peak analysis used

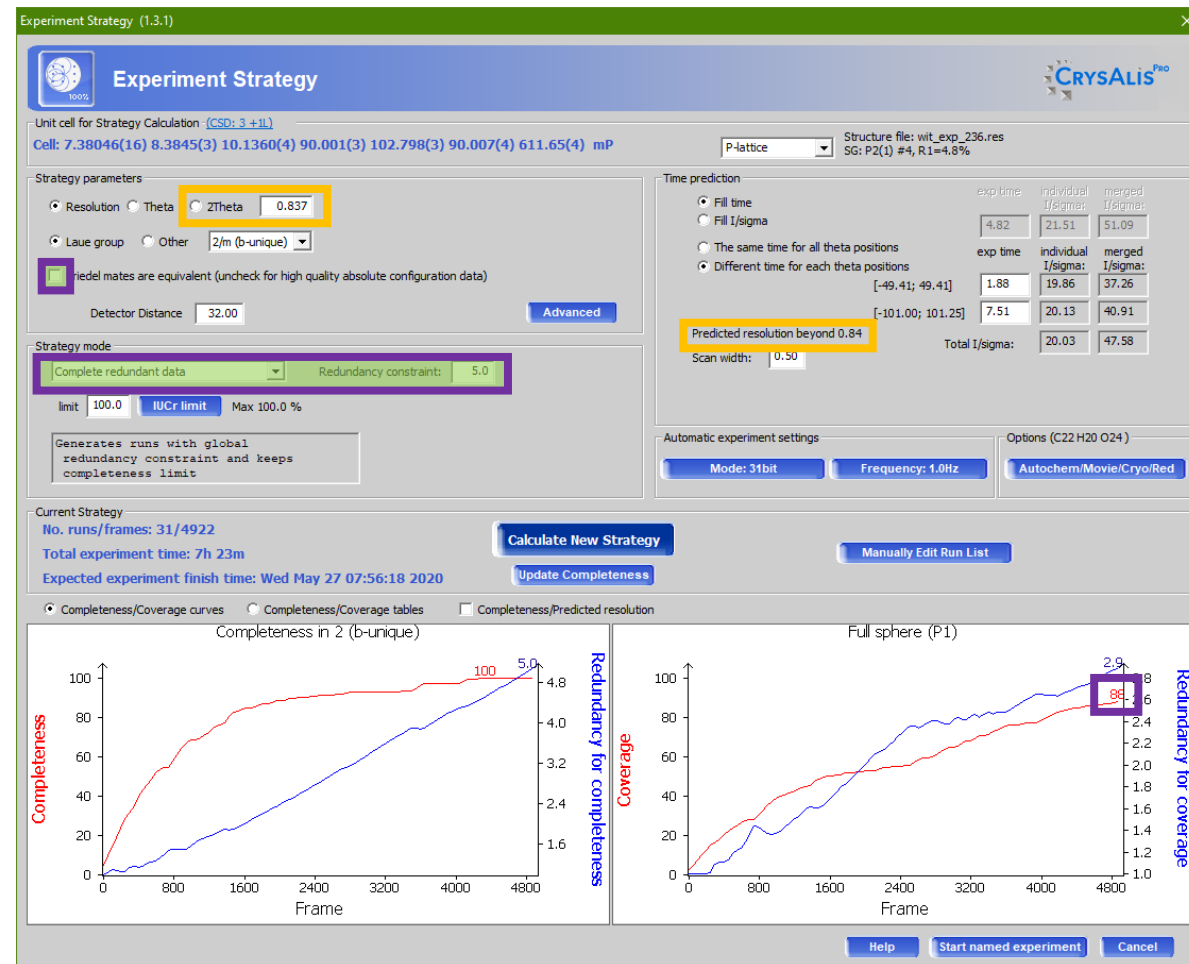
TIP: Use built-in experiment type settings.

BENEFIT: Enables chiral filter, and setup redundant data strategy calculations

STRATEGY SELECTION



TIP: if your crystal diffracts very well, collect more Friedel pairs with extra resolution.



The default strategy settings is:
Complete with recommended 5 fold redundancy

MANUAL DATA PROCESSING AND FINALIZATION OUTLINER REJECTION SETTINGS

Finalization dialog: SM experiment to hkl file (1.0.17)

Finalize: experiment to hkl file

Sample
Experiment: cho-46m-1.5H-15R Unit cell: 11.3712 10.8777 19.4880 90.0 104.2462 90.0 2336.4074 (CSD: 10 +0L)
Formula: C108 H192 Z=1.0 Lattice - mP 2/m (b-unique) **Friedel mates: non-equivalent**

Corrections
Empirical correction **Automated** **Manual**
Numerical absorption **Faces** **Sphere**

Space group and AutoChem
Search for space group **Auto** **Interactive** **Space group options**
AutoChem - attempt structure solution **AutoChem options**

Filters and limits
Automated **Manual** **Printout options**
Error model on > Model no 4 ☐ Resolution limits [Å]: inf-0.8370 (min: 0.8026) 0.8370
Filters filters not set ☒ Completeness (0.84Å) **☒ Outlier rejection (PG: 2 (b-unique))** **Advanced**

Output
X:\Application\backup\SCX DATA\HyPix-Arc\cho-46m-1.5H-15R\cho-46m-1.5H-15R
Standard set of files **Copy hkl only to cho-46m-1.5H...** **Copy hkl to ...** **Change**
Create/overwrite cho-46m-1.5H-15R files (hkl, ins, cif_od...) in X:\Application\backup\SCX DATA\HyPix-Arc\cho-46m-1.5H-15R.
Export options Exported files: cif.

Help **Defaults** **OK** **Cancel**

Finalization dialog: SM experiment to hkl file (1.0.17)

Finalize: experiment to hkl file

Sample
Experiment: cho-46m-1.5H-15R Unit cell: 11.3712 10.8777 19.4880 90.0 104.2462 90.0 2336.4074 (CSD: 10 +0L)
Formula: C108 H192 Z=1.0 Lattice - mP 2/m (b-unique) **Friedel mates: equivalent**

Corrections
Empirical correction **Automated** **Manual**
Numerical absorption **Faces** **Sphere**

Space group and AutoChem
Search for space group **Auto** **Interactive** **Space group options**
AutoChem - attempt structure solution **AutoChem options**

Filters and limits
Automated **Manual** **Printout options**
Error model on > Model no 4 ☐ Resolution limits [Å]: inf-0.8370 (min: 0.8026) 0.8370
Filters filters not set ☒ Completeness (0.84Å) **☒ Outlier rejection (PG: 2/m (b-unique))** **Advanced**

Output
X:\Application\backup\SCX DATA\HyPix-Arc\cho-46m-1.5H-15R\cho-46m-1.5H-15R
Standard set of files **Copy hkl only to cho-46m-1.5H...** **Copy hkl to ...** **Change**
Create/overwrite cho-46m-1.5H-15R files (hkl, ins, cif_od...) in X:\Application\backup\SCX DATA\HyPix-Arc\cho-46m-1.5H-15R.
Export options Exported files: cif.

Help **Defaults** **OK** **Cancel**

Profile fitting data reduction

Step 5: Outlier rejection

CCD data sets usually contain more than the unique data required for the structure determination. This redundant data can be used to check for measurement outliers. The rejection is based on R. Blessing (1997), J. Appl. Cryst., and additional CCD specific criteria.

Outlier rejection
☐ Don't use outlier rejection
☒ Use outlier rejection:
mmm
oP 6.89158 12.12423 21.29611 89.99224 89.96578 89.99409
☒ Use Friedel mates as equivalent

< Back Next > Finish Cancel Help

TIP1: CrysAlis^{Pro} outputs always unmerged hkl file. The Friedel pairs settings is used for outlier checks only.

TIP2: Processing data with Chiral filter enables correct outlier settings.

If you forgot about it, do not worry. This step is repeated with each hkl file finalization.

MANUAL DATA PROCESSING AND FINALIZATION, ENABLING CHIRAL FILTER

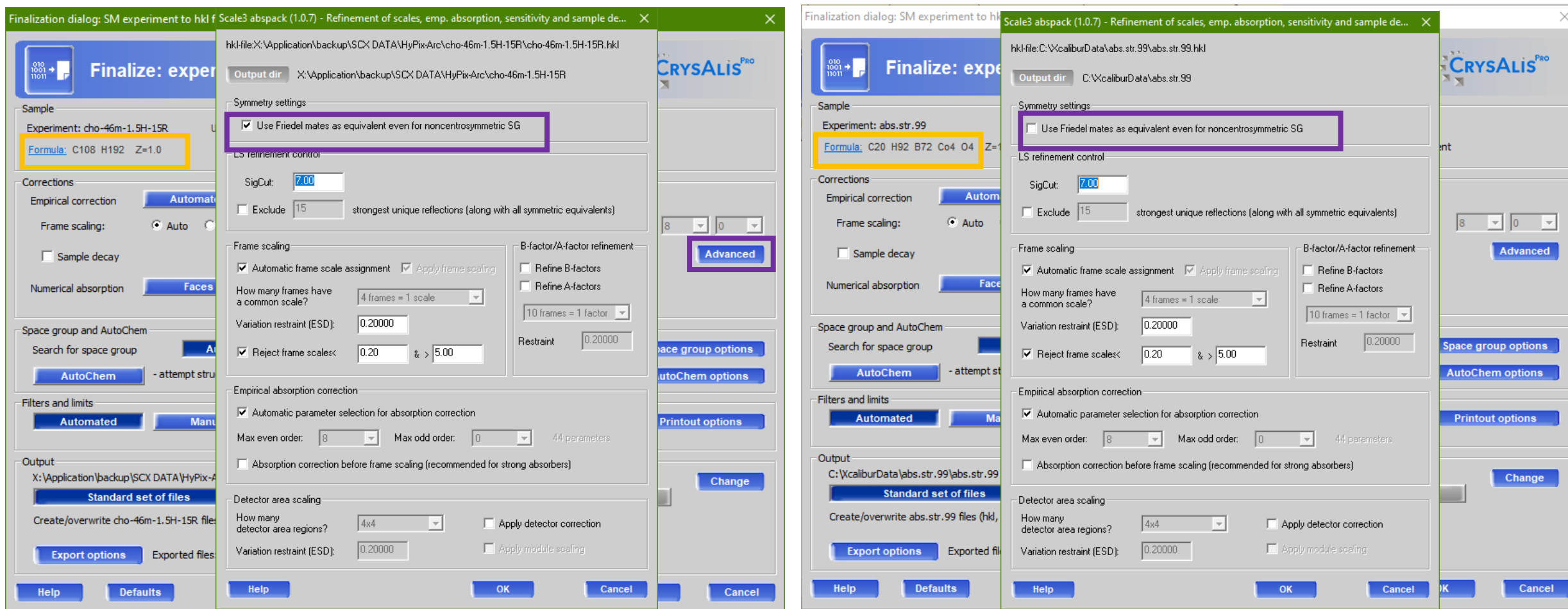
In pre-
experiment
settings

In GRAL
settings

PX mode has
as default
settings

TIP: Chiral filter in CrysAlis^{Pro} not only limit space groups but also will set up outlier rejection and anomalous signal output.

MANUAL DATA PROCESSING AND FINALIZATION SCALING OPTIONS



TIP: CrysAlis^{Pro} checks the provided formula and adjust this option automatically.

A general rule is: for weak anomalous signal: on; for extremely strong: off.

FINALIZATION AND DATA INSPECTION ANOMALOUS SIGNAL OUTPUT

Inspect data collection and reduction results

CRYALIS^{Pro}

Data reduction file contents | Data reduction output | Red graphs | Data collection output | Devices log

Statistics vs resolution (taking redundancy into account) - point group symmetry: P2 (b-unique)

resolu- tion(Å)	# kept	# theory	# unique	% complete	average redundancy	mean F2	mean F2/sig(F2)	Rint	RsigmaB	mean F2+-F2- /sig
inf-1.75	1169	234	234	100.0	5.0	54291.46	39.78	0.033	0.023	1.73
1.75-1.38	1677	234	234	100.0	7.2	14963.03	33.55	0.049	0.024	1.84
1.38-1.21	1774	234	234	100.0	7.6	11213.32	29.30	0.056	0.026	1.99
1.21-1.10	1641	234	234	100.0	7.0	13068.28	30.22	0.057	0.026	1.96
1.09-1.02	1188	234	234	100.0	5.1	9533.57	24.74	0.060	0.032	2.35
1.02-0.96	848	234	234	100.0	3.6	5118.15	21.07	0.056	0.043	1.89
0.96-0.91	757	234	234	100.0	3.2	4108.81	17.56	0.057	0.046	2.08
0.91-0.87	660	235	234	99.6	2.8	3900.30	16.46	0.058	0.048	2.35
0.87-0.84	532	238	235	98.7	2.3	2943.44	14.66	0.063	0.051	2.03
0.84-0.79	396	356	238	66.9	1.7	1659.31	11.31	0.077	0.064	1.92
inf-0.79	10642	2467	2345	95.1	4.5	14421.24	27.07	0.046	0.028	2.02
inf-0.84	10238	2107	2103	99.8	4.9	14924.69	27.68	0.046	0.027	2.03

Statistics vs resolution (taking redundancy into account) - Laue group (anomalous pairs merged): P2/m (b-unique)

resolu- tion(Å)	# kept	# theory	# unique	% complete	average redundancy	mean F2	mean F2/sig(F2)	Rint	RsigmaB
inf-1.80	1072	133	133	100.0	8.1	57298.13	52.42	0.034	0.019
1.79-1.41	1606	133	133	100.0	12.1	15603.28	44.80	0.050	0.019
1.40-1.22	1842	133	133	100.0	13.8	11456.24	41.08	0.058	0.019
1.22-1.10	1696	133	133	100.0	12.8	12854.75	40.37	0.060	0.020
1.10-1.02	1250	133	133	100.0	9.4	9632.09	34.74	0.066	0.024
1.02-0.95	883	133	133	100.0	6.6	4944.48	28.13	0.064	0.032
0.95-0.91	782	133	133	100.0	5.9	3985.38	23.03	0.069	0.036
0.91-0.86	676	133	133	100.0	5.1	3814.30	21.93	0.075	0.037
0.86-0.83	515	134	133	99.3	3.9	2876.85	19.48	0.076	0.044
0.83-0.79	320	162	133	82.1	2.4	1567.57	13.67	0.081	0.056
inf-0.79	10642	1360	1330	97.8	8.0	14421.24	36.44	0.049	0.022
inf-0.84	10238	1168	1168	100.0	8.8	14924.69	37.30	0.049	0.021

CSD: COYRUD in P2₁

Refinalize | Crystal movie | Shape optimization | Clean | OK

Inspect data collection and reduction results

CRYALIS^{Pro}

Data reduction file contents | Data reduction output | Red graphs | Data collection output | Devices log

Statistics vs resolution (taking redundancy into account) - point group symmetry: P222

resolu- tion(Å)	# kept	# theory	# unique	% complete	average redundancy	mean F2	mean F2/sig(F2)	Rint	RsigmaB	mean F2+-F2- /sig
inf-1.77	614	200	199	99.5	3.1	222805.17	110.33	0.008	0.00	13.78
1.76-1.39	669	199	199	100.0	3.4	94291.53	85.19	0.013	0.00	9.21
1.39-1.21	874	199	199	100.0	4.4	45579.59	69.39	0.021	0.01	7.70
1.21-1.10	794	204	199	97.5	4.0	40363.79	58.49	0.020	0.01	6.90
1.10-1.02	566	200	199	99.5	2.8	23259.23	37.94	0.021	0.02	5.52
1.02-0.96	514	200	200	100.0	2.6	17129.44	33.54	0.023	0.02	4.46
0.96-0.91	489	203	200	98.5	2.4	12232.77	29.20	0.026	0.02	3.64
0.91-0.87	431	208	199	95.7	2.2	8956.61	24.73	0.030	0.03	3.00
0.87-0.83	332	228	199	87.3	1.7	6477.94	21.47	0.038	0.03	3.13
0.83-0.79	272	298	202	67.8	1.3	5636.61	21.43	0.038	0.03	3.50
inf-0.79	5555	2139	1995	93.3	2.8	55313.06	55.52	0.014	0.01	5.87
inf-0.84	5226	1793	1754	97.8	3.0	58430.39	57.66	0.014	0.01	6.15

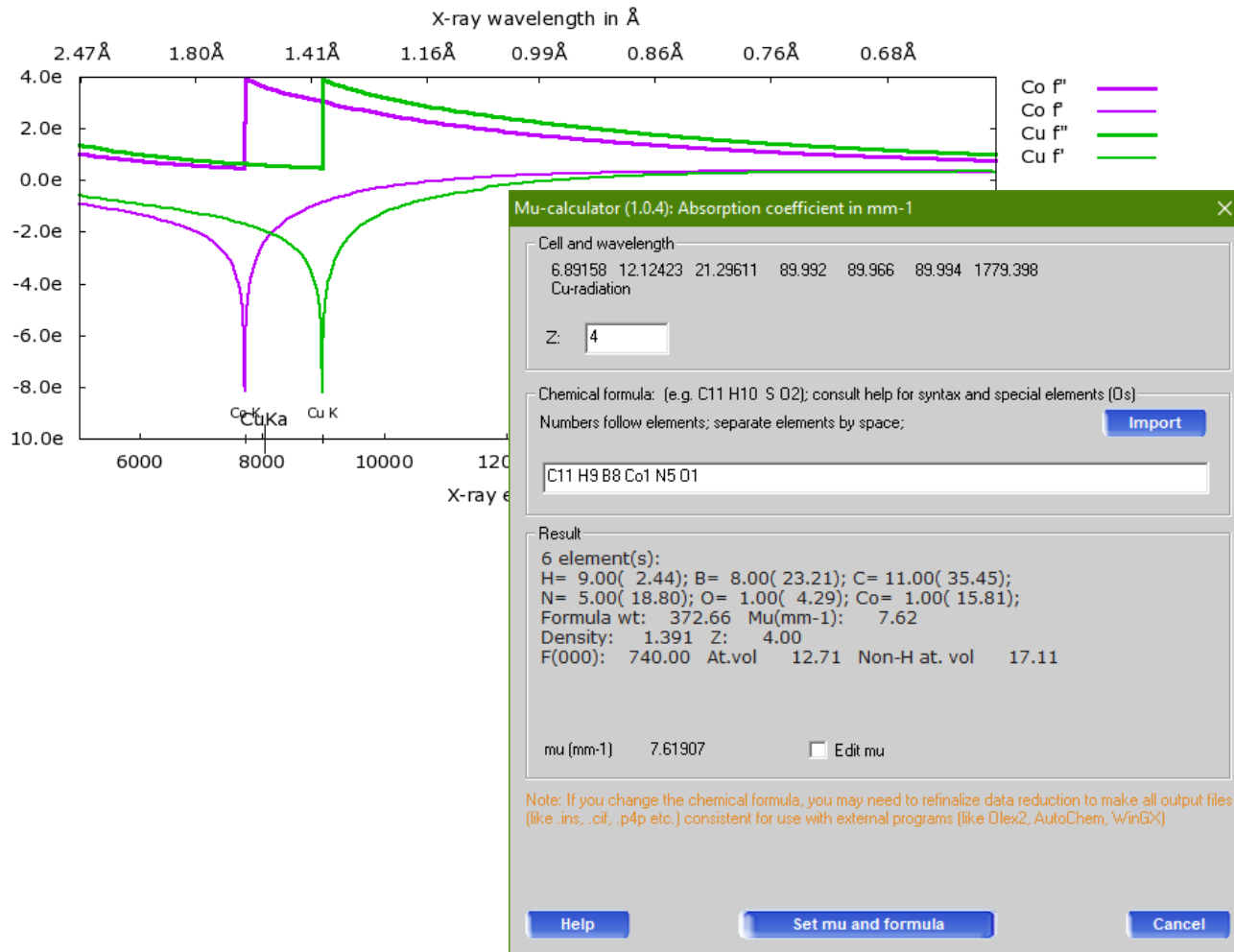
Statistics vs resolution (taking redundancy into account) - Laue group (anomalous pairs merged): Pmmn

resolu- tion(Å)	# kept	# theory	# unique	% complete	average redundancy	mean F2	mean F2/sig(F2)	Rint	RsigmaB
inf-1.84	511	123	122	99.2	4.2	261505.61	149.70	0.018	0.006
1.84-1.43	657	122	122	100.0	5.4	91001.83	109.52	0.025	0.007
1.43-1.23	834	122	122	100.0	6.8	46584.94	90.19	0.035	0.010
1.23-1.12	869	125	122	97.6	7.1	43881.70	82.94	0.034	0.010
1.12-1.02	607	124	122	98.4	5.0	22881.37	51.60	0.041	0.017
1.02-0.96	528	122	122	100.0	4.3	17533.52	44.67	0.040	0.020
0.96-0.91	514	122	122	100.0	4.2	12005.08	38.40	0.043	0.023
0.91-0.87	447	124	122	98.4	3.7	8956.52	32.81	0.043	0.025
0.87-0.83	331	132	122	92.4	2.7	6285.97	27.27	0.053	0.030
0.83-0.79	257	162	130	80.2	2.0	5680.59	26.82	0.055	0.028
inf-0.79	5555	1278	1228	96.1	4.5	55313.06	72.18	0.026	0.009
inf-0.84	5226	1081	1067	98.7	4.9	58430.39	75.04	0.026	0.009

CSD: MSULIN01 in P2₁2₁2₁

Refinalize | Crystal movie | Clean | OK

FINALIZATION AND DATA INSPECTION ANOMALOUS SIGNAL OUTPUT



Inspect data collection and reduction results

Data reduction file contents Data reduction output Red graphs Data collection output Devices log

Statistics vs resolution (taking redundancy into account) - point group symmetry: P222

resolu- tion(Å)	# kept	# theory	# unique	% complete	average redundancy	mean F2	mean F2/sig(F2)	Rint	RsigmaB	mean F2+-F2- /sig
inf-1.71	2062	379	379	100.0	5.4	88758.89	61.67	0.023	0.019	23.58
1.70-1.36	3327	379	379	100.0	8.8	60354.50	69.62	0.027	0.013	27.73
1.36-1.18	3754	379	379	100.0	9.9	37244.60	63.61	0.032	0.019	37.10
1.18-1.08	3377	379	379	100.0	8.9	22316.72	45.90	0.040	0.020	23.26
1.08-1.00	2885	379	379	100.0	7.6	19035.89	40.64	0.044	0.023	15.35
1.00-0.94	1881	379	379	100.0	5.0	18657.96	38.21	0.034	0.024	17.09
0.94-0.89	1588	379	379	100.0	4.2	15911.15	35.39	0.036	0.026	18.81
0.89-0.85	1352	379	379	100.0	3.6	14839.42	34.21	0.035	0.026	21.83
0.85-0.82	1000	380	380	100.0	2.6	11383.88	28.99	0.036	0.029	18.71
0.82-0.79	713	436	381	87.4	1.9	8951.98	25.02	0.038	0.031	18.54
inf-0.79	21939	3848	3793	98.6	5.8	34281.90	49.73	0.031	0.018	22.06
inf-0.80	21731	3662	3660	99.9	5.9	34529.47	50.00	0.031	0.018	22.26

Statistics vs resolution (taking redundancy into account) - Laue group (anomalous pairs merged): Pmmm

resolu- tion(Å)	# kept	# theory	# unique	% complete	average redundancy	mean F2	mean F2/sig(F2)	Rint	RsigmaB
inf-1.81	1764	221	221	100.0	8.0	92833.52	80.67	0.074	0.014
1.81-1.40	2938	221	221	100.0	13.3	64044.86	91.12	0.090	0.011
1.39-1.21	3763	221	221	100.0	17.0	40539.28	89.97	0.156	0.011
1.21-1.09	3449	221	221	100.0	15.6	23936.84	64.72	0.161	0.015
1.09-1.01	3131	221	221	100.0	14.2	19127.90	56.28	0.115	0.018
1.01-0.95	2013	221	221	100.0	9.1	18939.95	52.73	0.133	0.018
0.95-0.90	1670	221	221	100.0	7.6	16001.34	49.16	0.158	0.018
0.90-0.85	1423	221	221	100.0	6.4	15115.23	46.84	0.182	0.024
0.85-0.82	1064	221	221	100.0	4.8	11539.05	39.72	0.195	0.024
0.82-0.79	724	245	228	93.1	3.2	9056.24	33.34	0.208	0.027
inf-0.79	21939	2234	2217	99.2	9.9	34281.90	66.97	0.120	0.016
inf-0.80	21731	2131	2131	100.0	10.2	34529.47	67.36	0.120	0.015

CSD: OMCOBH in P2₁2₁2₁

Refinalize Crystal movie Shape optimization Clean OK

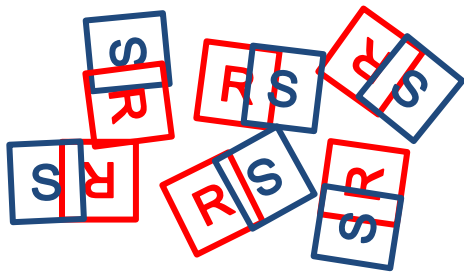
Determination of Absolute Configurations

- Old method: Compare the R-values of a structure with its inverted structure.
- Today: We use the Flack-x parameter, which refines to give the ratio of a crystal or its inversion twin which fits best the observed intensities.

$$|F(hkl, x)|^2 = (1 - x)|F(hkl)|^2 + x|F(\bar{h}\bar{k}\bar{l})|^2$$

x is the absolute structure parameter
Howard Flack, *Acta Cryst.* **1983**, A39, 876.

x = 0: correct absolute configuration
x = 1: inverted absolute configuration
0 < x < 1: racemic twin



racemic twin

- Racemic twinning is also called inversion twinning.
- Occurs in non-centrosymmetric space groups.
- Easy to identify using the Flack test.

$$|F_{hkl}|^2 \neq |F_{\bar{h}\bar{k}\bar{l}}|^2$$

Flack Parameter

$$|F(hkl, x)|^2 = (1 - x)|F(hkl)|^2 + x|F(\bar{h}\bar{k}\bar{l})|^2$$

Chiral space groups (P_1 , $P2_12_12_1$, ...):

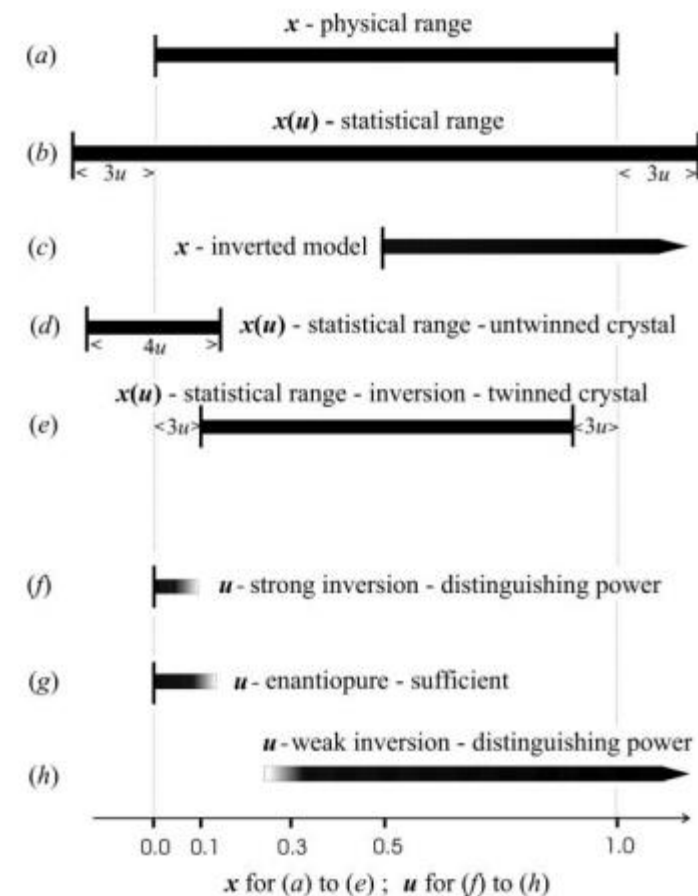
- Either no symmetry elements or only rotations
- May contain optically pure compounds
- Flack parameter has to be calculated

Polar space groups (Pm , $Pna2_1$, ...):

- Contain mirror planes, but no inversion center
- May contain only achiral molecules or racemic mixtures
- Flack parameter has to be calculated

Centrosymmetric space groups:

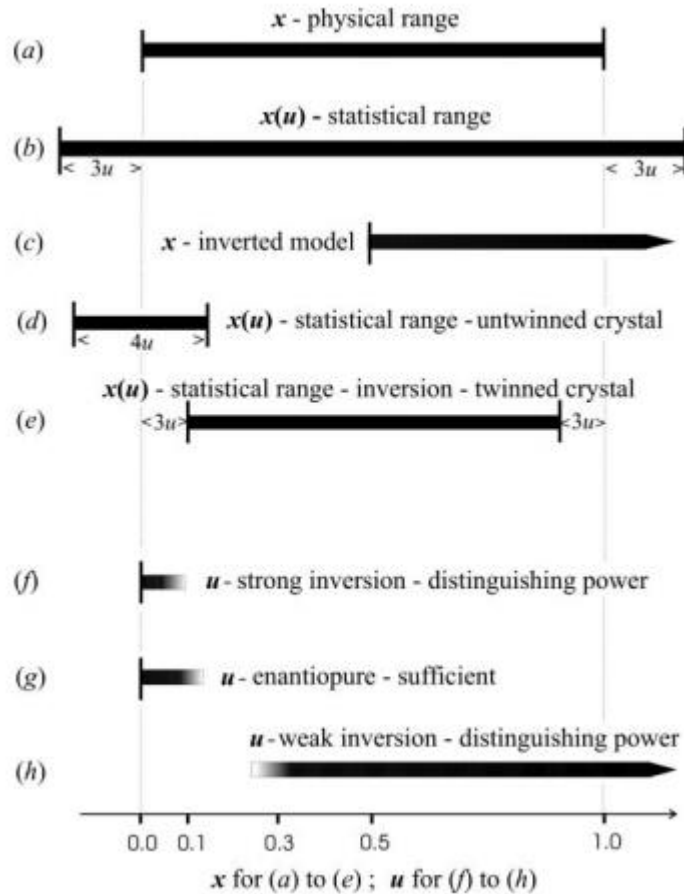
- Flack parameter is not defined, since $|F(H)|^2 = |F(-H)|^2$



Howard Flack, *Acta Cryst.* **1983**, A39, 876.

Flack Parameter

$$|F(hkl, x)|^2 = (1 - x)|F(hkl)|^2 + x|F(\bar{h}\bar{k}\bar{l})|^2$$



Domains of values of x , its u and the inversion-distinguishing power: (a) the physical domain of x ; (b) the statistical domain of x ; (c) the domain of x where the crystal and the model are inverted one with respect to the other; (d) the statistical domain of a crystal untwinned by inversion; (e) the statistical domain of a crystal twinned by inversion; (f) the domain of strong inversion-distinguishing power; (g) the domain of enantiopure sufficient inversion-distinguishing power; (h) the domain of weak inversion-distinguishing power. For (f), (g) and (h), the horizontal lines are of varying intensity. In the part of the line which is black, the inversion-distinguishing power may be deduced from the value of u alone. In the part of the line which is grey, the inversion-distinguishing power may not be deduced from the value of u alone. In (b), (d) and (e), arbitrary values of u have been drawn and in practical applications the value of u yielded by the experiment must be used.

Flack Parameter & Parsons quotients

- It was later shown that the Flack parameter can be improved using of quotients of **Friedel Pairs differences (Parsons method)**.
- Reduces the systematic errors and usually gives lower standard deviation. Flack x is still defined from:

$$|F(H, x)|^2 = (1 - x)|F(H)|^2 + x|F(-H)|^2$$
$$\Leftrightarrow I_{obs, hkl} = (1 - x)I_{hkl} + xI_{\overline{hkl}}$$

- The new method use the following **quotients of Friedel Pairs differences**

$$\frac{I_{hkl}(x) - I_{\overline{hkl}}(x)}{I_{hkl}(x) + I_{\overline{hkl}}(x)} = (1 - 2x) \frac{I_{hkl} - I_{\overline{hkl}}}{I_{hkl} + I_{\overline{hkl}}}$$

This can be measured: $I_{hkl}(x) = I_{obs}$ **This is your model:** $I_{hkl} = I_{calc}$

With $Q = \frac{I_{hkl} - I_{\overline{hkl}}}{I_{hkl} + I_{\overline{hkl}}}$, this can be written as $Q_{obs} = (2 - x)Q_{calc}$

(Parsons, S., Flack, H. D. & Wagner, T. *Acta Cryst.* **2013**, B69, 249)

The Hooft Parameter γ

- Uses Bayesian statistics i.e. it calculates the probability to have the right absolute structure.
- It uses differences between Bijvoet pairs instead of Friedel pairs.

Friedel pair: pair of reflections related by inversion symmetry: I_{hkl} and I_{-h-k-l} .

Bijvoet pair: pair of reflections that are equivalent by symmetry and are a Friedel Pair.

E.g. Space Group Pm , symmetry equivalents:

$$I_{hkl} = I_{h-k-l} \quad \& \quad I_{-h-k-l} = I_{-hk-l}$$

We therefore have the following Bijvoet pairs:

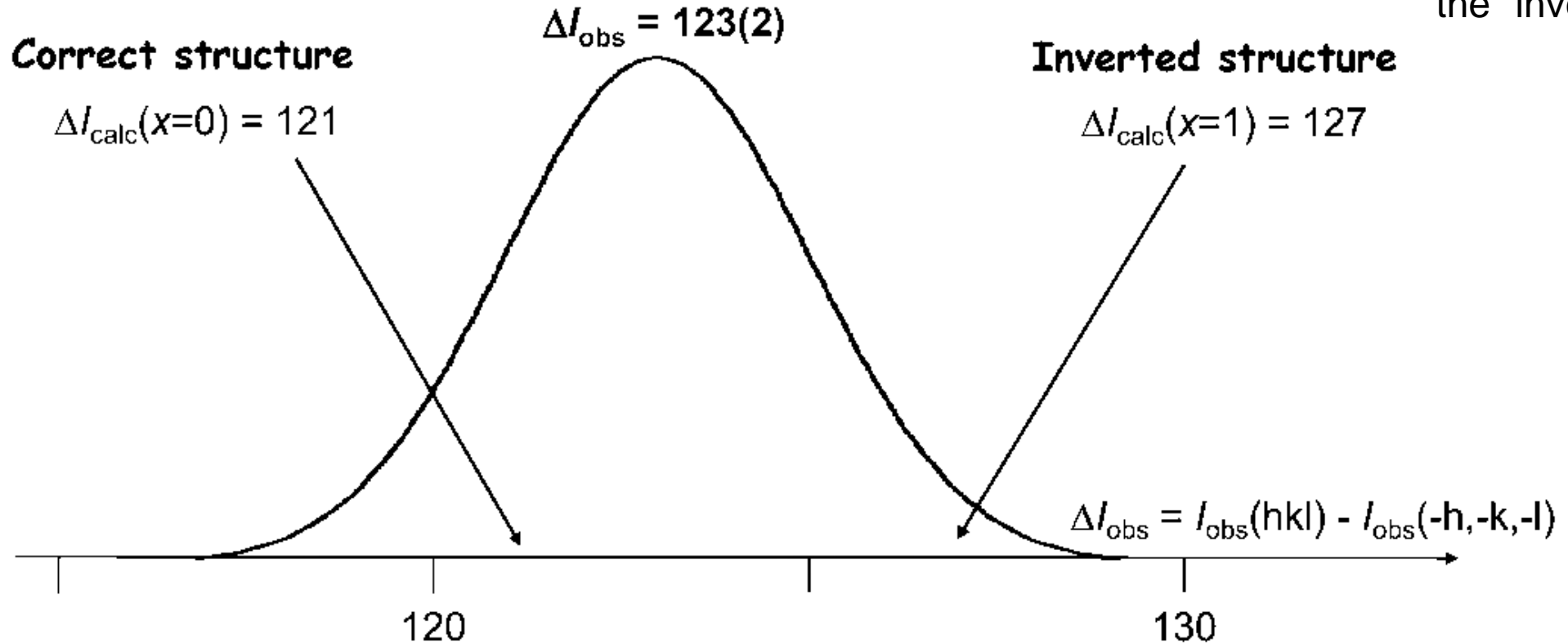
$$I_{hkl} \mid I_{-h-k-l}, \quad I_{hkl} \mid I_{-hk-l}, \quad I_{h-k-l} \mid I_{-h-k-l}, \quad I_{h-k-l} \mid I_{-hk-l}.$$
$$|F^{+}| \equiv |F_{hkl}| = |F_{\bar{h}\bar{k}\bar{l}}| \quad |F^{-}| \equiv |F_{\bar{h}k\bar{l}}| = |F_{h\bar{k}l}|$$

A Friedel pair is also a Bijvoet pair, but a Bijvoet pair is not necessarily a Friedel pair.

http://skuld.bmsc.washington.edu/scatter/AS_Bijvoet.html

The Hooft Parameter y

To be able to "weigh" all contributions from each Bijvoet pair to the decision, this method calculates how likely each observation is for each of the two model structures: the "normal" one and the "inverted" one.



Observed reflection: $\Delta I_{\text{hkl}} = 123(2)$. For the model, we calculate $\Delta I_{\text{hkl}} = 121$, for the inverted model $\Delta I_{\text{hkl}} = 127$. The probability that the model is correct for this reflection can be expressed by

$$p_0 = \frac{1}{\sqrt{2\pi}} e^{-\frac{(\frac{\Delta I_{\text{calc}} - \Delta I_{\text{obs}}}{\text{esd}(\Delta I_{\text{obs}})})^2}{2}} = \frac{1}{\sqrt{2\pi}} e^{-\frac{(\frac{2}{2})^2}{2}} = 24\%$$

The respective calculation for the inverted model yields $p_1 = 5\%$.

USEFUL OLEX2 OPTIONS FOR ABSOLUT STRUCTURE REFINEMENT

Automatic Hooft and Flack parameter calculations.

Completeness is reported for both anomalous and merge data

Useful CIF auditing options.

- Anomalous dispersion
- Reference molecule
- Reference molecule + AD
- Synthesis
- Unknown

Olex2

File Edit View Structure Mode Tools Model Select Help

an shift/esd = 0.000 Maximum = -0.001 for x H17C at 06:06:50
 shift = 0.000 A for H17C Max. du = 0.000 for H3
 = 0.0657 before cycle 4 for 2078 data and 210 / 210 parameters
 = S = 1.051; Restrained GoF = 1.050 for 1 restraints
 an shift/esd = 0.000 Maximum = 0.000 for z C1 at 06:06:50
 = S = 1.050; Restrained GoF = 1.050 for 1 restraints
 GoF = S = 1.050; Restrained GoF = 1.050 for 1 restraints
 Mean shift/esd = 0.000 Maximum = 0.000 for z O14 at 06:06:50
 Max. shift = 0.000 A for H15C Max. du = 0.000 for H14
 wr2 = 0.0657 before cycle 6 for 2078 data and 210 / 210 parameters
 GoF = S = 1.050; Restrained GoF = 1.050 for 1 restraints
 Mean shift/esd = 0.000 Maximum = 0.000 for z C12 at 06:06:50
 wr2 = 0.0657 before cycle 7 for 2078 data and 210 / 210 parameters
 GoF = S = 1.050; Restrained GoF = 1.050 for 1 restraints
 Mean shift/esd = 0.000 Maximum = 0.000 for z C12 at 06:06:50
 Max. shift = 0.000 A for H17C Max. du = 0.000 for H7
 wr2 = 0.0657 before cycle 8 for 2078 data and 210 / 210 parameters
 GoF = S = 1.051; Restrained GoF = 1.050 for 1 restraints
 Mean shift/esd = 0.000 Maximum = 0.000 for z C12 at 06:06:50
 Max. shift = 0.000 A for H5 Max. du = 0.000 for H17C
 wr2 = 0.0657 before cycle 9 for 2078 data and 210 / 210 parameters
 GoF = S = 1.051; Restrained GoF = 1.050 for 1 restraints
 Mean shift/esd = 0.000 Maximum = 0.000 for z C12 at 06:06:50
 Max. shift = 0.000 A for H2 Max. du = 0.000 for H17A
 wr2 = 0.0657 before cycle 10 for 2078 data and 210 / 210 parameters
 GoF = S = 1.050; Restrained GoF = 1.050 for 1 restraints
 Mean shift/esd = 0.000 Maximum = 0.000 for z C12 at 06:06:50
 Max. shift = 0.000 A for H15C Max. du = 0.000 for H17B
 wr2 = 0.0658 before cycle 11 for 2078 data and 210 / 210 parameters
 GoF = S = 1.051; Restrained GoF = 1.051 for 1 restraints
 wr2 = 0.0658, GoF = S = 1.051, Restrained GoF = 1.051 for all data
 R1 = 0.0233 for 1164 unique reflections after merging for Fourier
 Highest peak 0.11 at 0.6991 0.3367 0.5449 [0.71 A from C9]
 Deepest hole -0.12 at 0.7529 0.4577 0.3373 [0.79 A from C9]

Flack x = -0.008(216) by classical fit to all intensities
 Flack x = 0.002(80) from 895 selected quotients (Parsons' method)
 0 atoms may be split and 0 atoms MDN

Please cite: G.M. Sheldrick (2015) "Crystal structure refinement with SHELXL", Acta Cryst., C71, 3-8 (Open Access) if SHELXL proves useful.

+ naproxen finished at 06:06:51 Total elapsed time: 0.31 secs +
 Goof y: 0.07(6), Flack x: 0.00(8)

There is no conflicting information in the sources of metadata
 All conflicts are resolved

Naproxen
 C₁₄H₁₄O₃
 a = 7.72864(17) Å α = 90° Z = 2
 b = 5.71388(15) Å β = 93.808(2)° Z' = 1
 c = 13.3495(3) Å γ = 90° V = 588.22(2) Å³
 R₁ = 2.44%
 wR₂ = 6.58%
 S = 1.051
 Shift 0.000 Max Peak 0.1 Min Peak -0.1 Goof 1.051 Flack 0.00(8)

Refinement Finished

Home Work View Tools Info

Solve Refine Draw Report

Naproxen Image No Image Create Report

Style default.css Start default.htm End templates/footer

Table label style: As in CIF

Collection
 Crystal
 Diffraction
 Absorption Correction
 Publication
 Citations
 Reference
 Source Files

Edit CIF Info Merge CIF HKLRES Leave as is
 IUCr CheckCIF pdf CCDC Request CCDC Number

✓ Merge CIF: metaCIF Add local default CIF
 Merge metacif items even if marked for skipping

Absolute structure determination
 Flack parameter: 0.00(8)
 Hooft parameter: 0.07(6)

Anomalous dispersion
 Anomalous dispersion
 Reference molecule
 Reference molecule + AD
 Synthesis
 Unknown
 Not applicable

Toolbox Work

Labels Labels OFF/ON Add H

Select atom(s) and then mFit mSplit Split SAME Split

MAP Show Map Map Settings

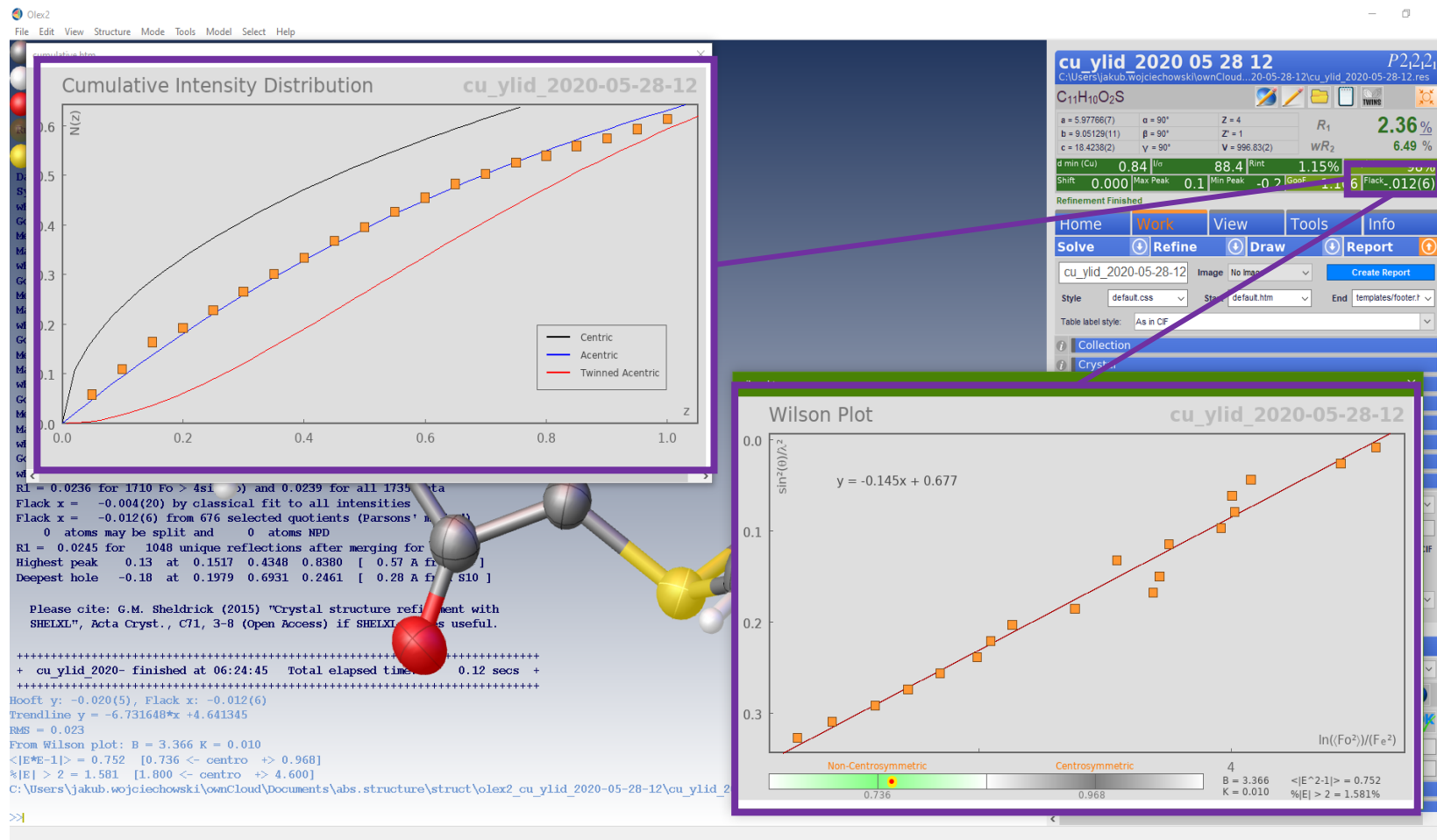
Peak & Uiso Sliders

Growing

_chemical_absolute_configuration

- **m** Absolute configuration established by the structure determination of a compound containing a chiral reference molecule of known absolute configuration.
- **ad** Absolute configuration established by anomalous-dispersion effects in diffraction measurements on the crystal.
- **rmad** Absolute configuration established by the structure determination of a compound containing a chiral reference molecule of known absolute configuration and confirmed by anomalous-dispersion effects in diffraction measurements on the crystal.
- **syn** Absolute configuration has not been established by anomalous-dispersion effects in diffraction measurements on the crystal. The enantiomer has been assigned by reference to an unchanging chiral centre in the synthetic procedure.
- **unk** Absolute configuration is unknown, there being no firm chemical evidence for its assignment to hand and it having not been established by anomalous-dispersion effects in diffraction measurements on the crystal. An arbitrary choice of enantiomer has been made.
- **.** Inapplicable.

USEFUL OLEX2 OPTIONS FOR ABSOLUT STRUCTURE REFINEMENT



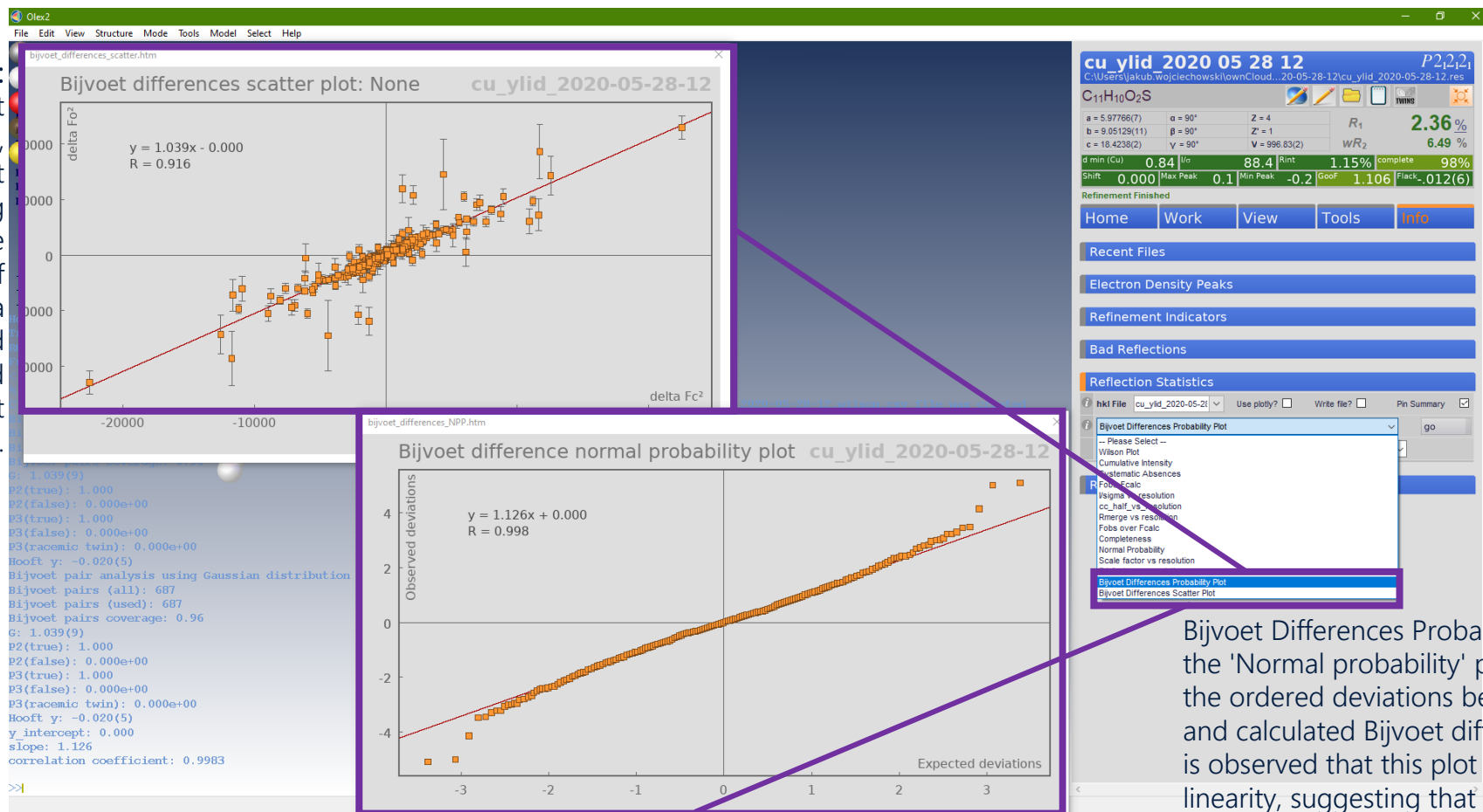
A statistical comparison of the observed intensity data with the theoretical distribution for a random atomic arrangement, since the atomic scattering decreases with increasing 2θ . Establishes an overall displacement parameter for the structure, B and scale factor for the data, K.

TIP: Right click on Flack parameter box will open useful plots (CID and Wilson).

USEFUL OLEX2 OPTIONS FOR ABSOLUTE STRUCTURE REFINEMENT

Bijvoet Differences Scatter Plot:

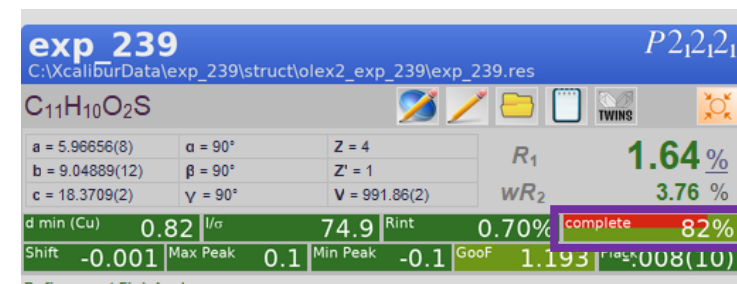
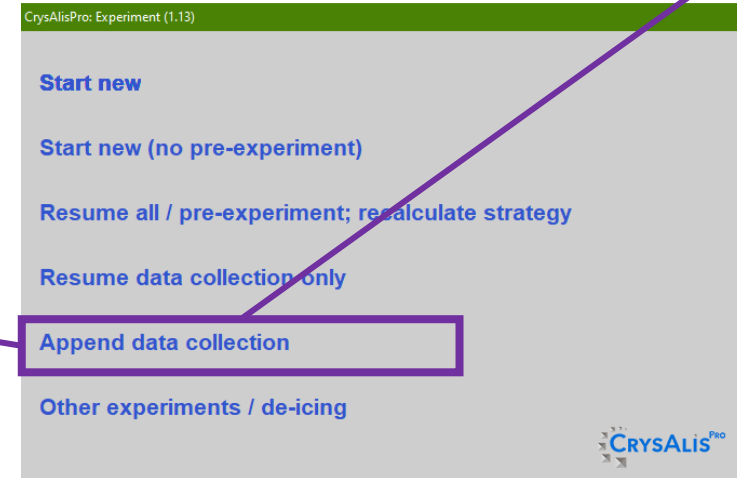
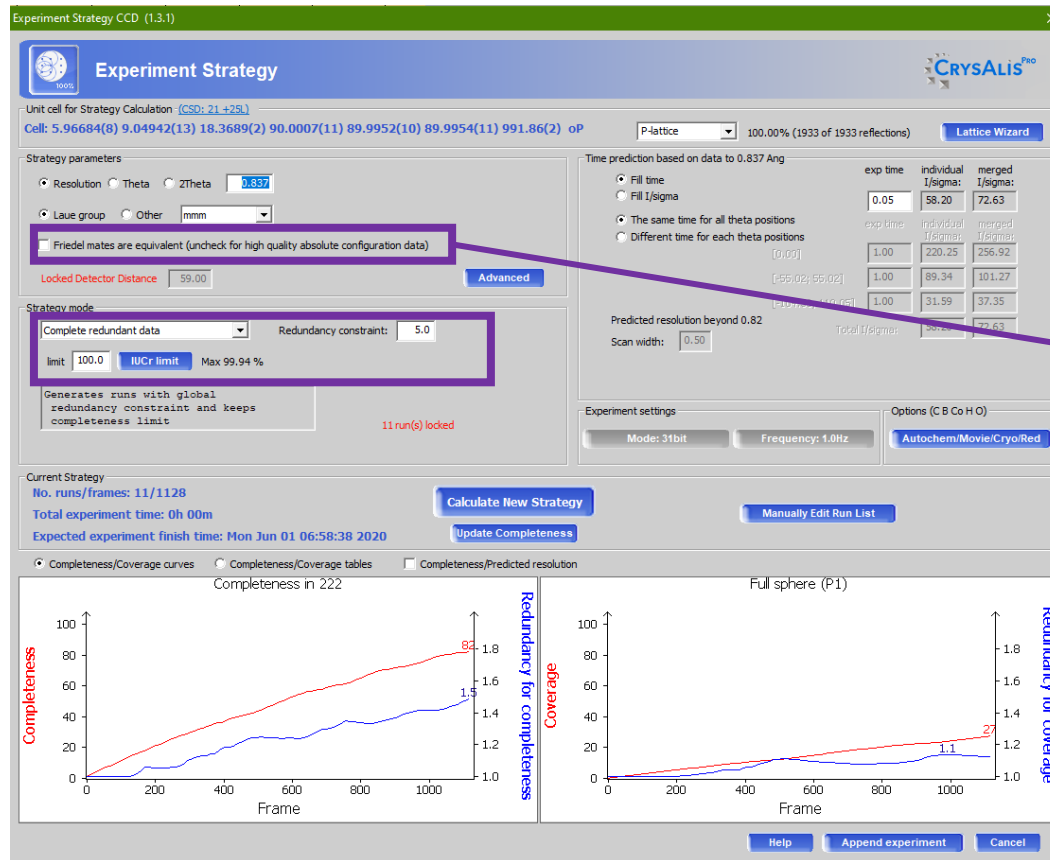
This plots the calculated Bijvoet differences, $F^2_{\text{calc}}(+)-F^2_{\text{calc}}(-)$, against the observed Bijvoet differences, $F^2_{\text{obs}}(+)-F^2_{\text{obs}}(-)$, along with error bars indicating the uncertainty in the measurement of the Bijvoet differences. For a correct, strongly determined absolute structure, this plot should form a positive slope, with gradient close to 1.



Bijvoet Differences Probability Plot: Similarly to the 'Normal probability' plot above, this plots the ordered deviations between the observed and calculated Bijvoet differences. Frequently it is observed that this plot can deviate from linearity, suggesting that the errors are not normally distributed.

TIP: Bijvoet scatter plot and normal probability plot are accessible from Info-Reflection statistics

APPENDED EXPERIMENT FOR FULL ANOMALOUS COMPLETENESS



START/STOP

Shutter Closed

CAM CRYO X-RAY STATUS

CCD Time left to turn off X-rays: 23h 50m 45s

RED Ready

Crystal ccd

Data Collection

Data Reduction

AutoChem

Olex2 Restart AutoChem

REFINEMENT STATISTICS

Chemical Formula: C₄₄ H₄₀ O₈ S₄

Space Group: P2(1)2(1)2(1) #19

Formula weight: 825.08

R₁: 1.64%

wR₂: 3.76%

GOOF: 1.19

Comp1. (0.84A): 97.1% (Pmm)

Anom compl.: 82.3% (P222)

Peak and Hole: 0.084 and -0.066

Flack (Parsons'): -0.008 (10)

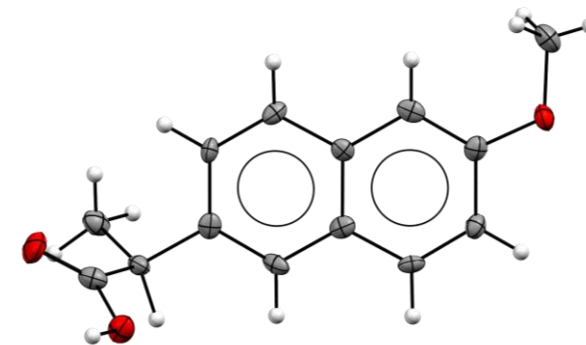
STRUCTURE FILE

Filename: exp_239

TIP: You do not need to wait till your experiment ends to append more scan to it.

PRACTICAL CRYSTALLOGRAPHY

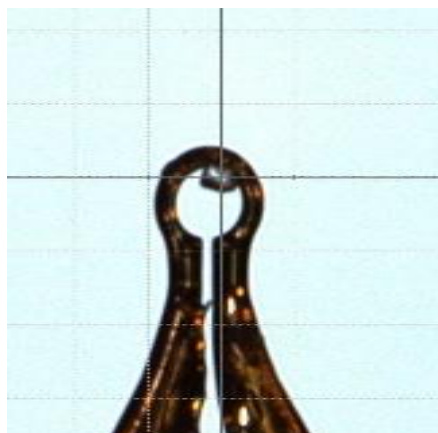
CASE 1 NAPROXEN, week anomalous signal, redundancy effect



- For statistically valid ab initio determination with help of Flack method

e.s.d. <0.04 and $|x| < 2\text{e.s.d.}$

- In case of CONFIRMED enantiopurity of the sample
e.s.d. <0.1 and $|x| < 2\text{e.s.d.}$



Data	Comp. %	Redund.	$\langle F^2/\sigma(F^2) \rangle$	R_{int}	$F2+-F2-/\text{sig}$	Flack
A	95.7	3.1	34.54	0.024	1.66	-0.04(8)
B	99.4	6.9	48.72	0.027	1.77	-0.01(5)
C	100.0	9.6	55.47	0.030	1.81	-0.04(5)
D	100.0	11.0	65.16	0.028	1.81	-0.06(5).
E	100.0	12.8	71.20	0.030	1.81	--0.01(4)
NO.ABS.STR	72%	1.8	9.02	0.061	1.5	0.00(50)

PRACTICAL CRYSTALLOGRAPHY

CASE 2 Ylid, good anomalous signal, wavelength effect

- For statistically valid ab initio determination with help of Flack method

e.s.d. <0.04 and $|x| < 2\text{e.s.d.}$

- In case of CONFIRMED enantiopurity of the sample

e.s.d. <0.1 and $|x| < 2\text{e.s.d.}$



Data	Comp. %	Redund.	$\langle F^2/\sigma(F^2) \rangle$	R_{int}	$F2+-F2-/sig$	Flack
Abs.str.11 (Mo).	81	2.7	14.45	0.054	1.60	-0.03(8)
Abs.str.13 (Mo).	99	7.3	23.07	0.062	1.64	-0.01(5)
Abs.str.10 (Cu)	94.7	2.5	27.00	0.029	3.11	-0.018(12)

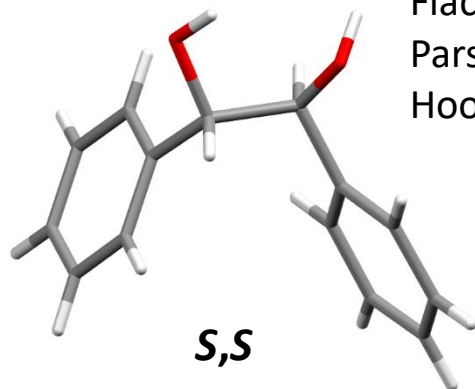
How to invert the structure?

- OLEX2: *inv -f*
- In the SHELX ins file, use the instruction :
MOVE 1 1 1 -1
- For **enantiomorphic space groups**, inversion of the structure requires changing the space group.

Special cases :

<i>Fdd2</i>	MOVE .25 .25 1 -1	<i>I4₁cd</i>	MOVE 1 .5 1 -1
<i>I4₁</i>	MOVE 1 .5 1 -1	<i>I-42d</i>	MOVE 1 .5 .25 -1
<i>I4₁22</i>	MOVE 1 .5 .25 -1	<i>F4₁32</i>	MOVE .25 .25 .25 -1
<i>I4₁md</i>	MOVE 1 .5 1 -1		

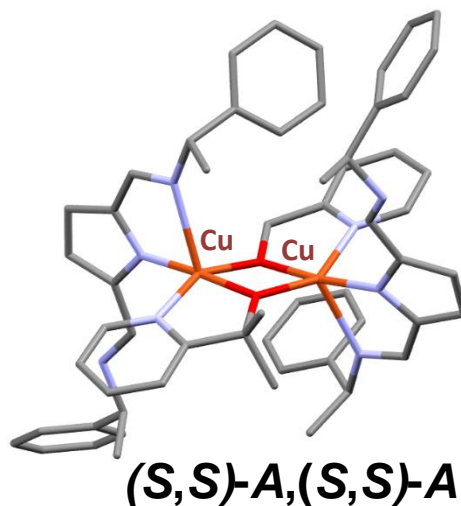
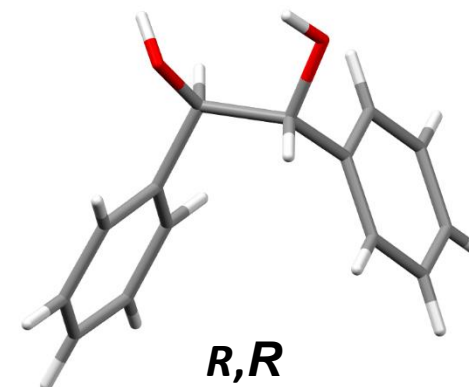
With modern diffractometers the determination of the absolute structure is quite possible with only (C, N, O, F). However, the results are typically more convincing in the presence of heavier atoms.



Flack-x : 0,1(3) = $0,1 \pm 0,9$
 Parsons : -0,02(7) = $-0,0 \pm 0,2$
 Hooft-y : 0,02(6) = $0,0 \pm 0,2$

Flack-x : 0,9(3) = $0,9 \pm 0,9$
 Parsons : 1.01(7) = $1,0 \pm 0,2$
 Hooft-y : 0,98(6) = $1,0 \pm 0,2$

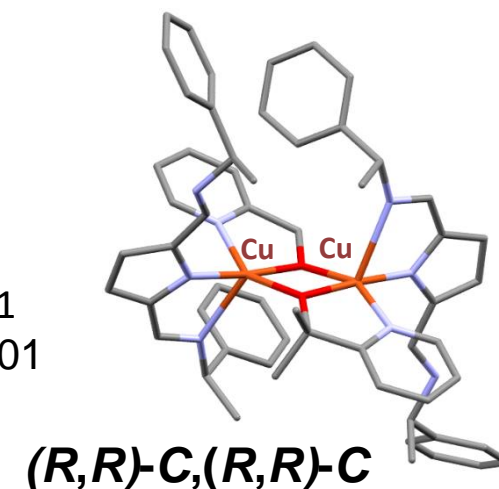
noise/signal = 2%



Flack-x : 0,045(7) = $0,04 \pm 0,02$
 Parsons : 0,098(4) = $0,10 \pm 0,01$
 Hooft-y : 0,098(3) = $0,10 \pm 0,01$

Flack-x : 0,952(6) = $0,95 \pm 0,02$
 Parsons : 0,898(4) = $0,90 \pm 0,01$
 Hooft-y : 0,915(3) = $0,93 \pm 0,01$

noise/signal = 8%



Absolute Configuration from Absolute Structure

Useful References:

H.D. Flack, G. Bernardinelli, Absolute structure and absolute configuration. *Acta Cryst*, **1999** A55, 908.

H.D. Flack, G. Bernardinelli, Reporting and evaluating absolute structure and absolute configuration determinations. *J. Applied Cryst.* **2000** 33, 1143.

Thompson A. L., Watkin D. J. X-ray crystallography and chirality: understanding the limitations. *Tetrahedron: Asymmetry* **2009** 20, 712

Parsons, S., Flack, H. D. & Wagner, T. *Acta Cryst.* **2013**, B69, 249

R. W. W. Hooft, L. H. Straver, A. L. Spek *J. Appl. Cryst.* **2008**, 41, 96

R. W. W. Hooft, L. H. Straver, A. L. Spek *J. Appl. Cryst.* **2010**, 43, 665

D.J. Watkin & R.I. Cooper, *Chemistry* **2020**, 2, 796