Canadian National Committee for Crystallography (CNCC)
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Absolute Configuration and Absolute Structure Determination

CCCW22
Calgary, AB
Presenter: Kate Marczenko

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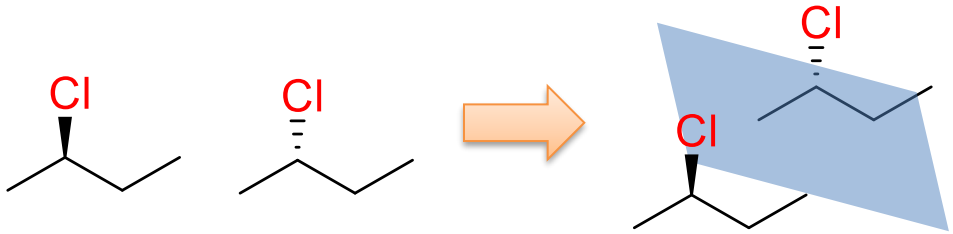
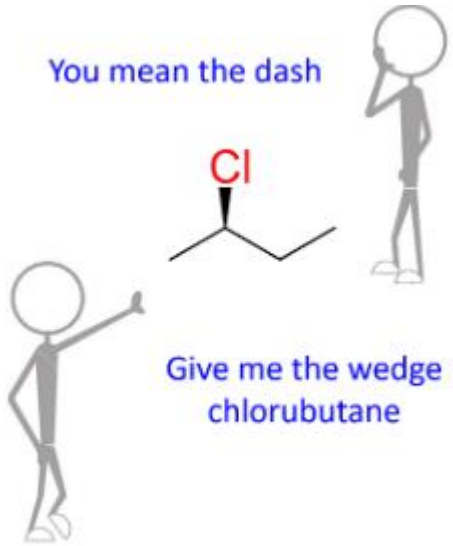
Thank you to all that have contributed to this presentation!

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

Absolute Configuration

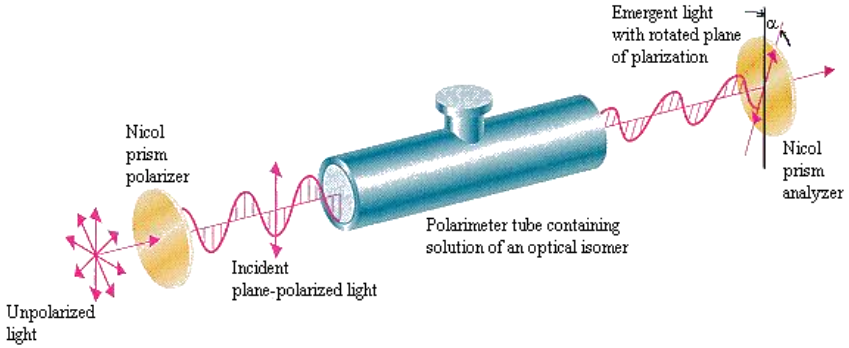
- Absolute Configuration → spatial arrangement of the atoms for a chiral molecule (R/S, P/M or D/L assignment).

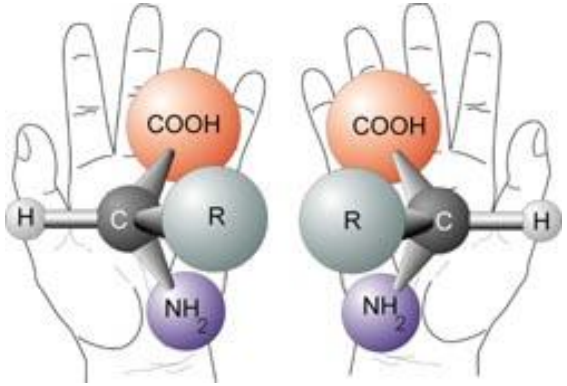




- Determination of absolute configuration → handedness of the molecule.

- 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).

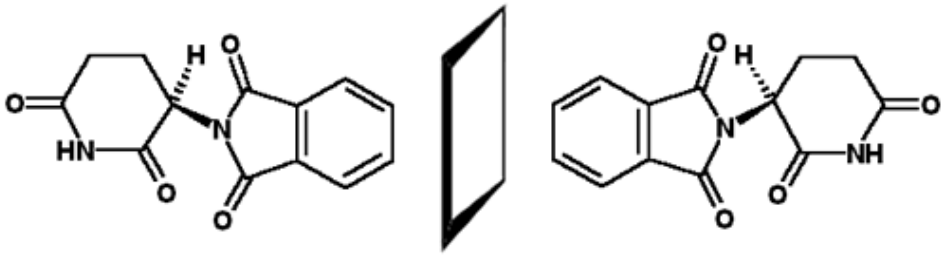
- For a chiral crystal structure, absolute structure distinguishes between and specifies enantiomorphs of the crystal structure.

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

https://dictionary.iucr.org/Absolute_structure

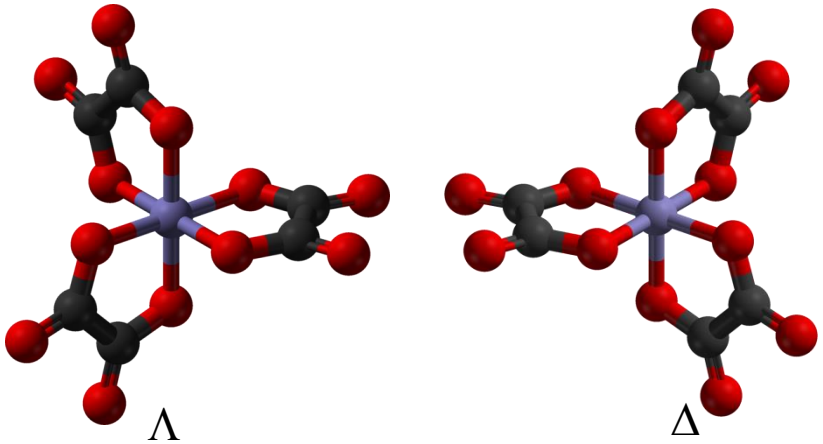
Chirality

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



R-Thalidomide
(sleep-inducing)

S-Thalidomide
(teratogenic)



Λ

Left Hand Propeller
(anticlockwise)

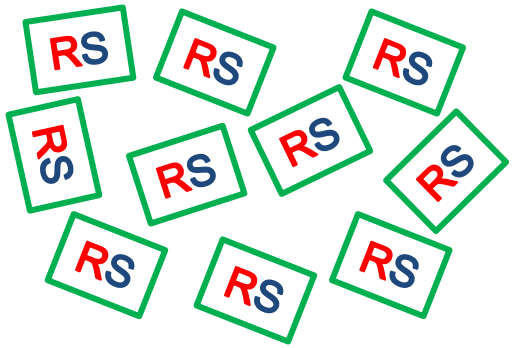
Δ

Right Hand Propeller
(clockwise)

- 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



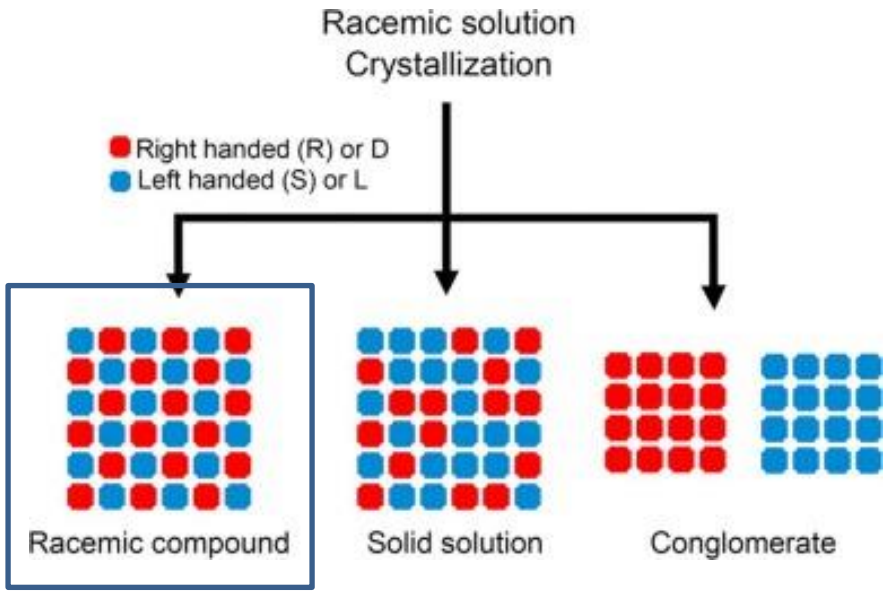
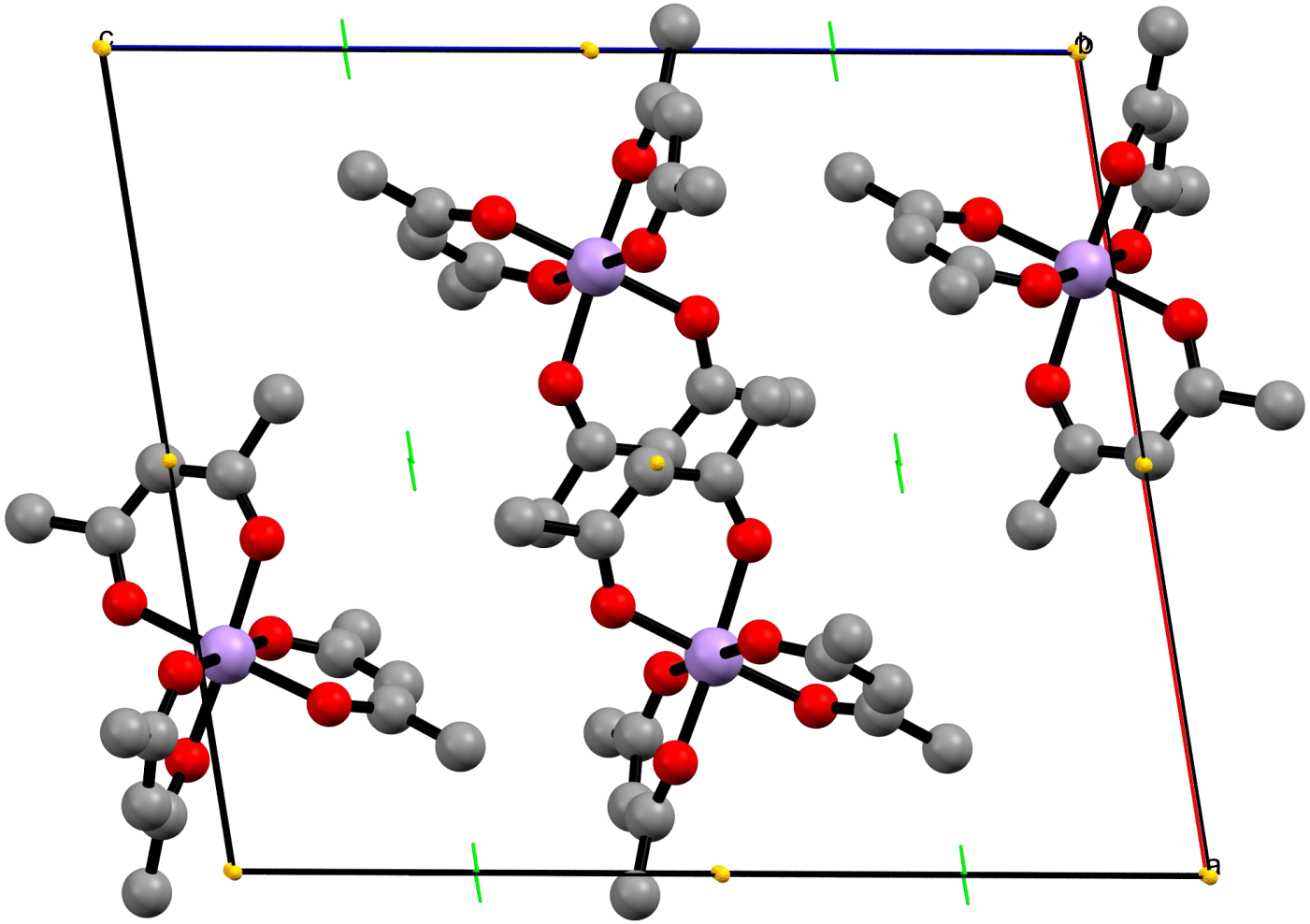


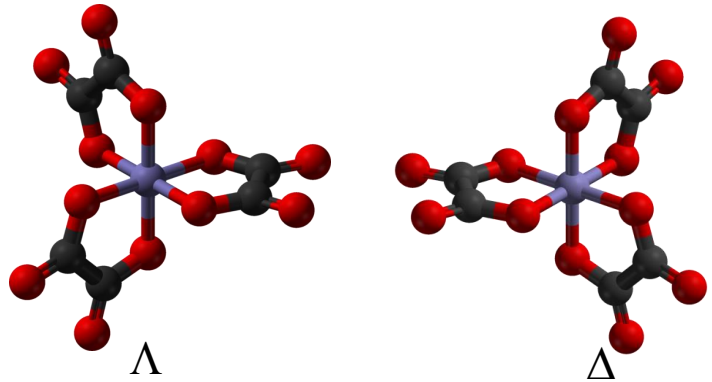
Image from: Ultrasonics Sonochemistry, 2018, 43, 184-192.

- 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.

adapted from: Frank Schaper CHM6450-H21

Racemic Compound





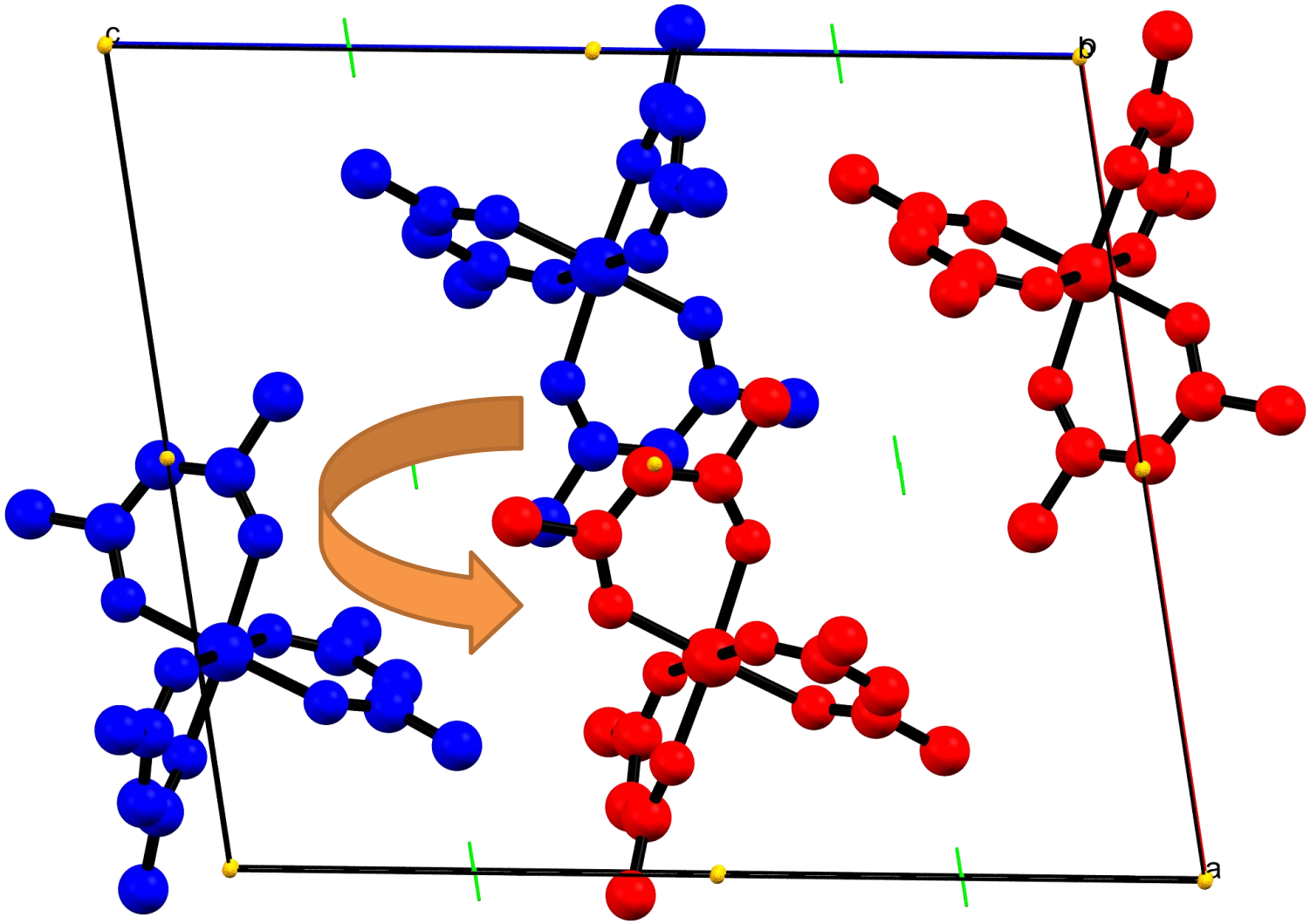
Legend

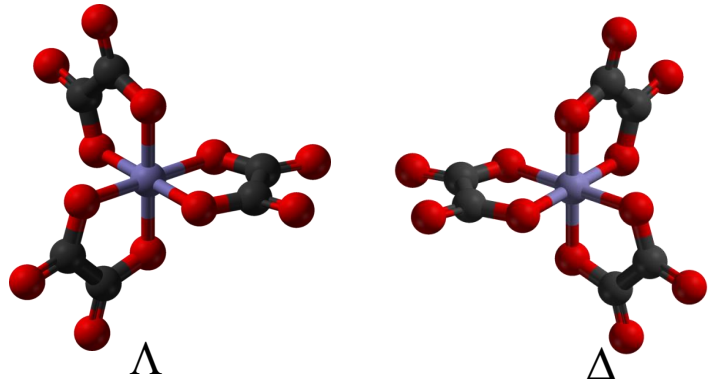
2-fold screw axis

Inversion center

ACACMN31 - $P2_1/c$

Racemic Compound





Legend

Right hand red

Left hand blue

ACACMN31 - $P2_1/c$

Crystallization

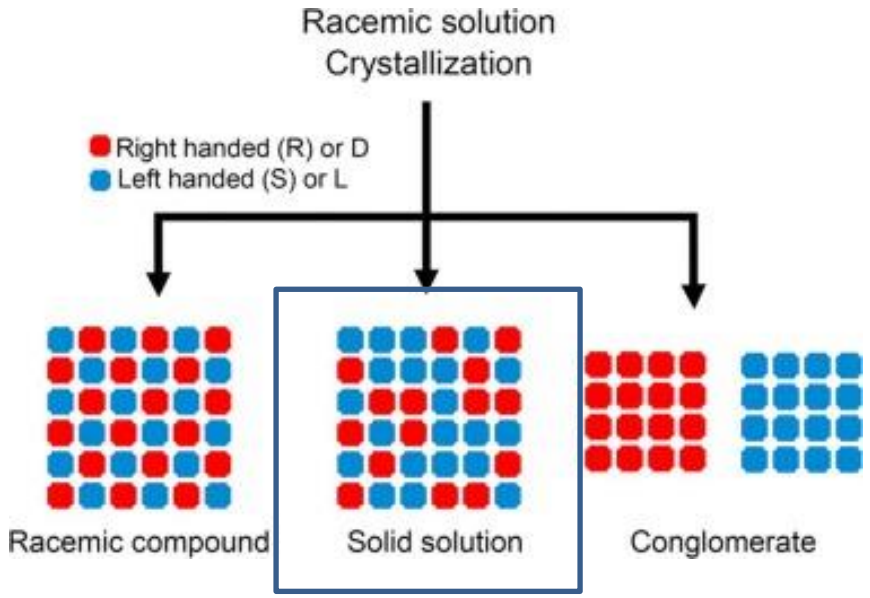
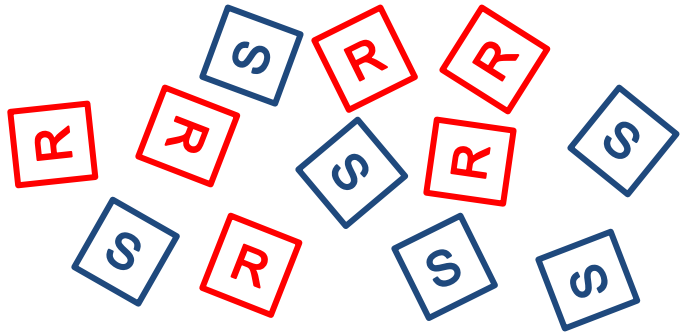


Image from: Ultrasonics Sonochemistry, 2018, 43, 184-192.

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

adapted from: Frank Schaper CHM6450-H21

Crystallization



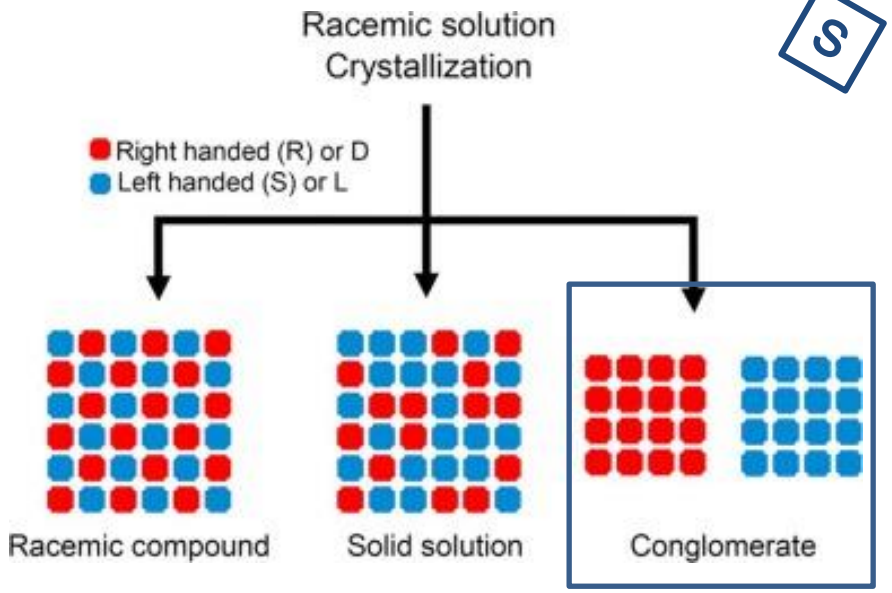


Image from: Ultrasonics Sonochemistry, 2018, 43, 184-192.

- 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

adapted from: Frank Schaper CHM6450-H21

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 eniantomorphic 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: *P*1

Monoclinic: *P*2 $P2_1$ *C*2

Orthorhombic: *P*222 $P222_1$ $P2_12_12$ $P2_12_12_1$ $C222_1$ *C*222 *F*222 *I*222 $I2_12_12_1$

Tetragonal: *P*4 **$P4_1$ | $P4_3$** $P4_2$ *I*4 $I4_1$ *P*422 $P42_12$ **$P4_122$ | $P4_322$** **$P4_12_12$ | $P4_32_12$** $P4_222$ $P4_22_12$ *I*422 $I4_122$

Trigonal: *P*3 **$P3_1$ | $P3_2$** *R*3 $P3_12$ *P*321 **$P3_112$ | $P3_212$** **$P3_121$ | $P3_221$** *R*32

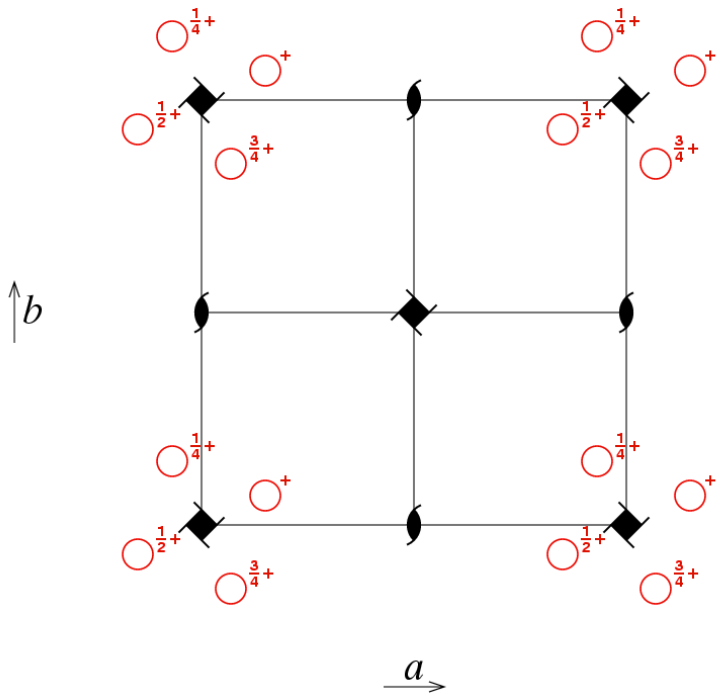
Hexagonal: *P*6 **$P6_1$ | $P6_5$** **$P6_2$ | $P6_4$** $P6_3$ *P*622 **$P6_122$ | $P6_522$** **$P6_222$ | $P6_422$** $P6_322$

Cubic: *P*23 *F*23 *I*23 $P2_13$ $I2_13$ *P*432 $P4_232$ *F*432 $F4_132$ *I*432 **$P4_132$ | $P4_332$** $I4_132$

adapted from: Frank Schaper CHM6450-H21

Enantiomorphic Space Groups

$P4_1$ $P\,4_1$ 4



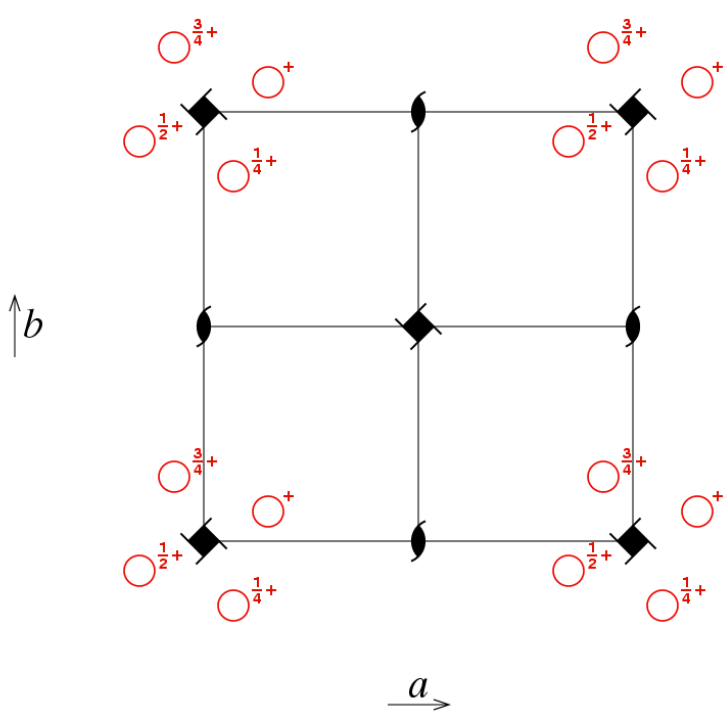
1 x, y, z

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

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

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

$P4_3$ $P\,4_3$ 4



1 x, y, z

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

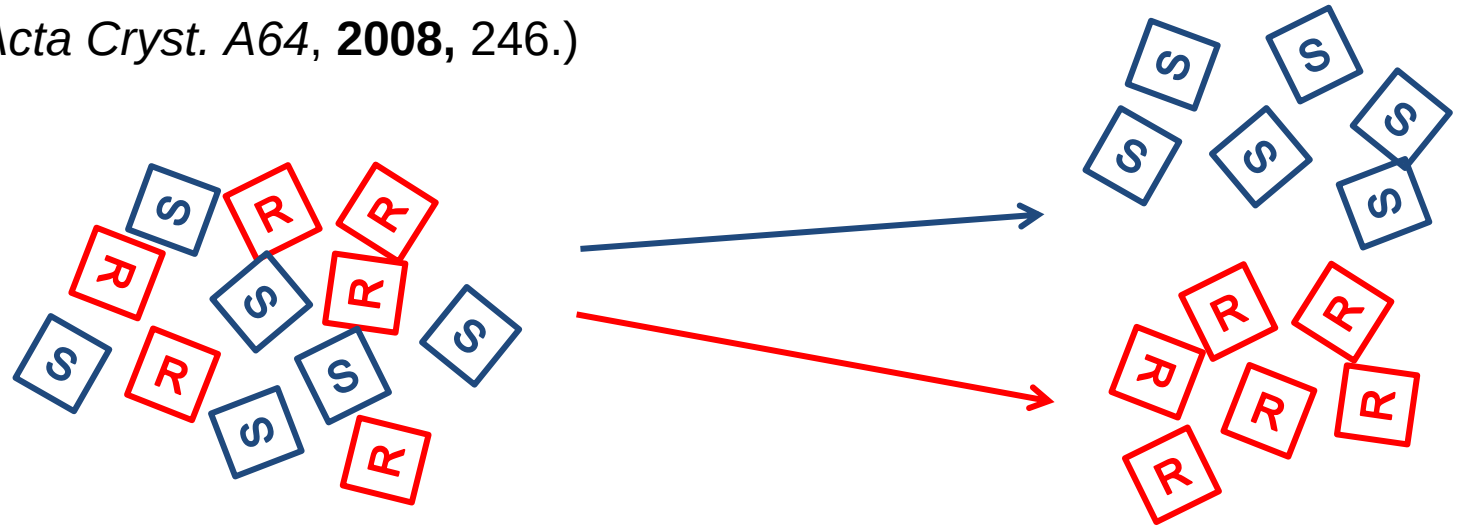
3 $\bar{y}, x, \frac{3}{4} + z$

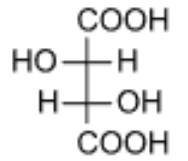
4 $y, \bar{x}, \frac{1}{4} + z$

Enantiomorphic Crystals

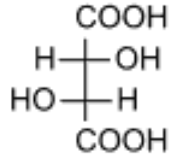
Louis Pasteur Experiment (1848): Separation of the two enantiomers by the visual sorting of crystals of a conglomerate

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

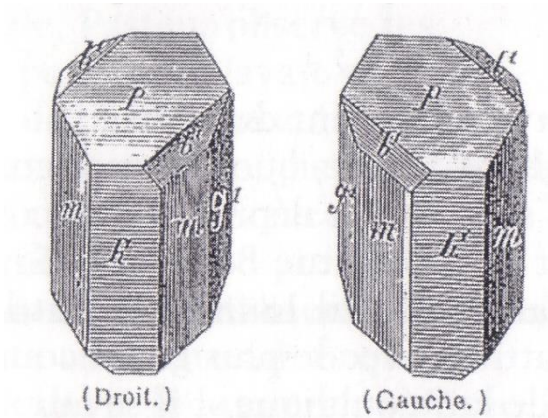




D-(-) levotartaric acid



L-(+) dextrotartaric acid



Sodium ammonium tartrate crystals

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On wine, chirality and crystallography

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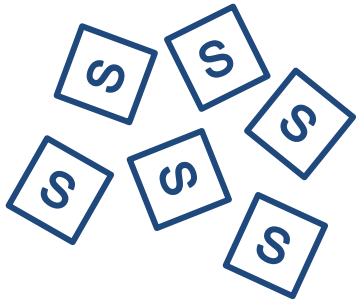
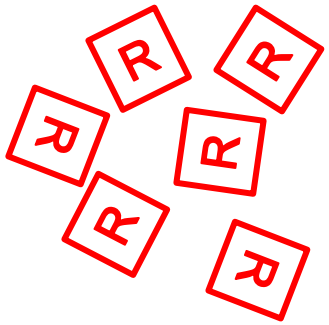
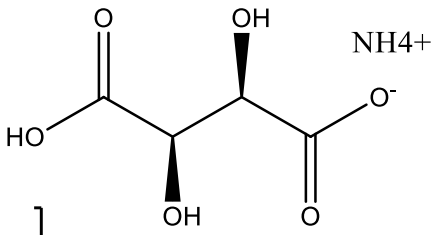
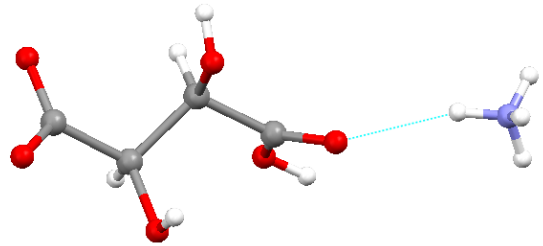
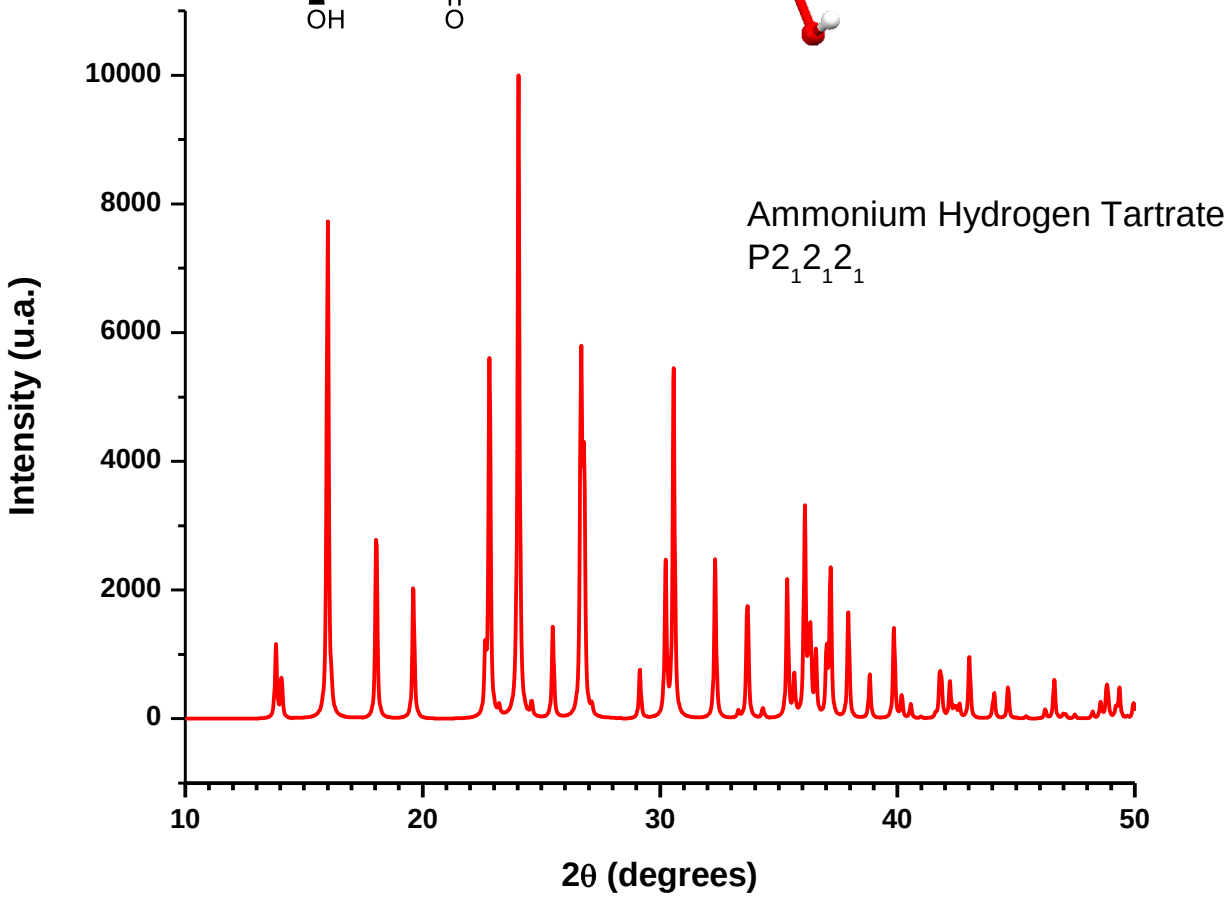
Powder Diffraction







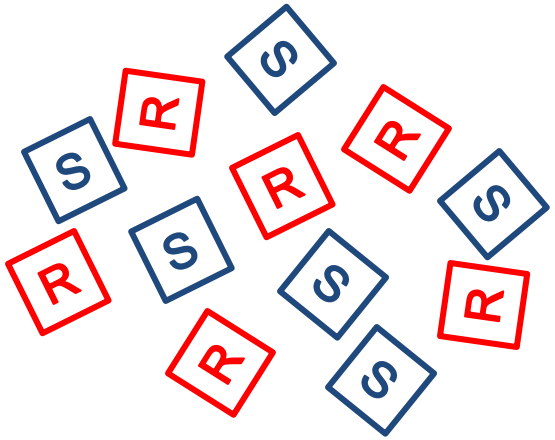


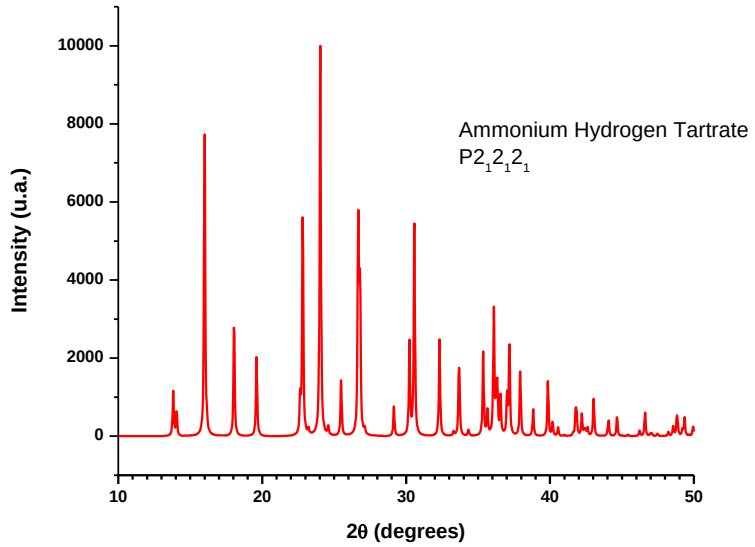


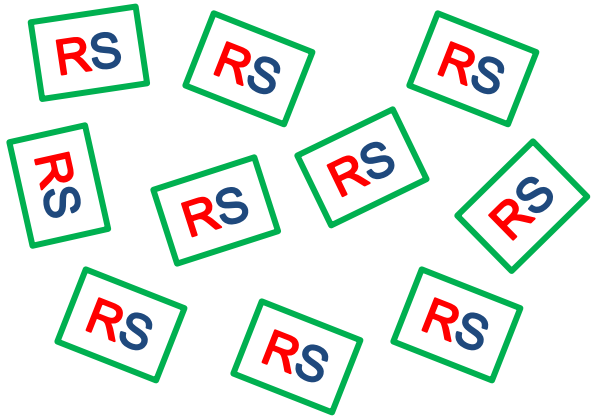
The two eniantopure samples and the conglomerate give the same powder X-ray diffraction pattern

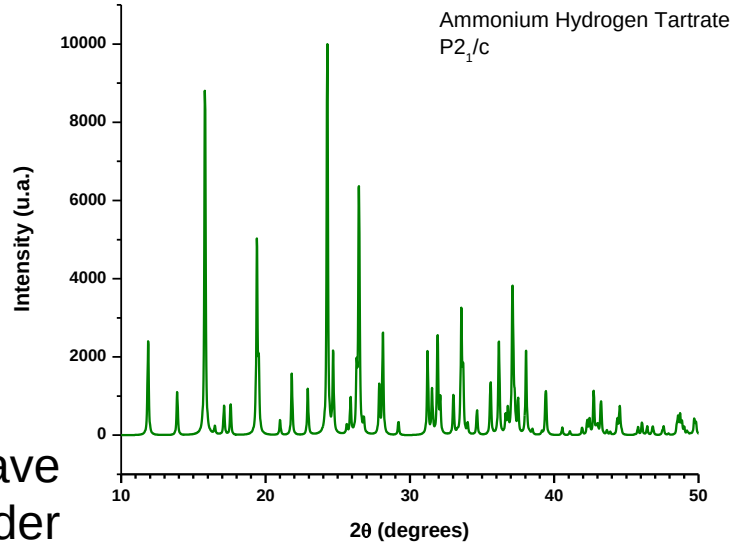
adapted from: Frank Schaper CHM6450-H21

Powder Diffraction





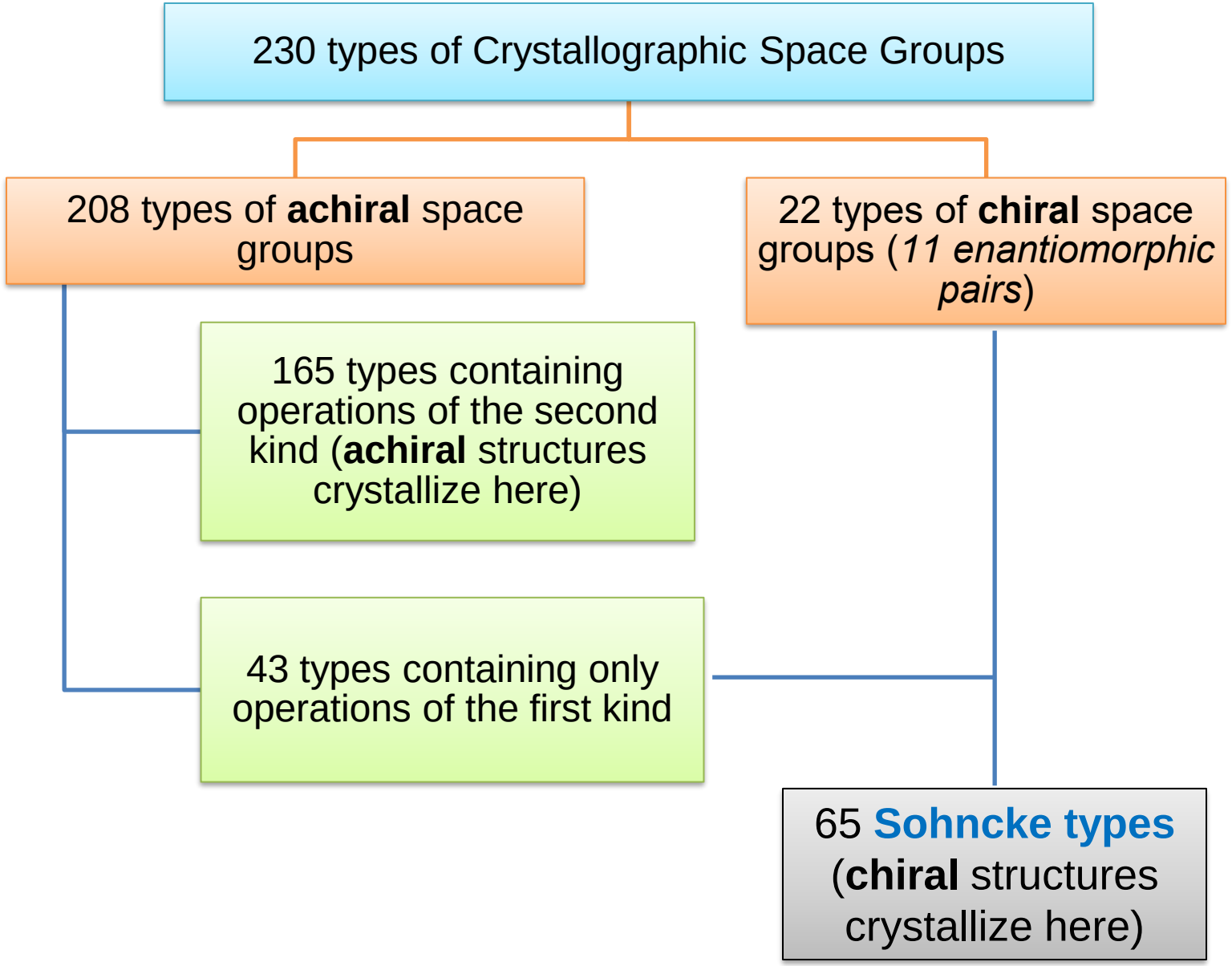




The conglomerate and the racemate have different space groups, so the powder diffraction pattern is different

adapted from: Frank Schaper CHM6450-H21

Space Group Framework



https://dictionary.iucr.org/File:Sohncke-vs-chiral-scheme.png

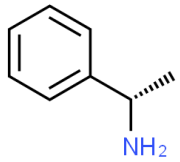
How can we determine the Absolute Configuration?

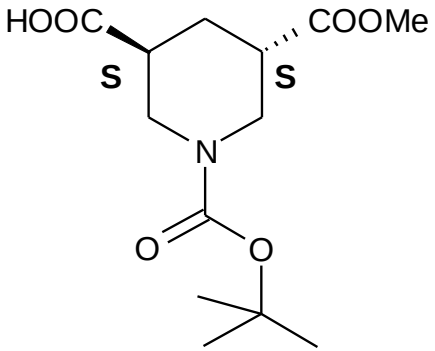
- Method 1: Internal Chiral Reference
- Method 2: Absolute configuration established by anomalous-dispersion effects in diffraction measurements on the crystal.

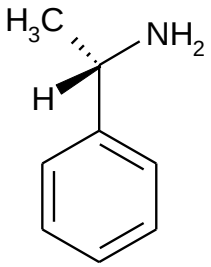
Method 1: Absolute configuration from an internal chiral reference

- 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.

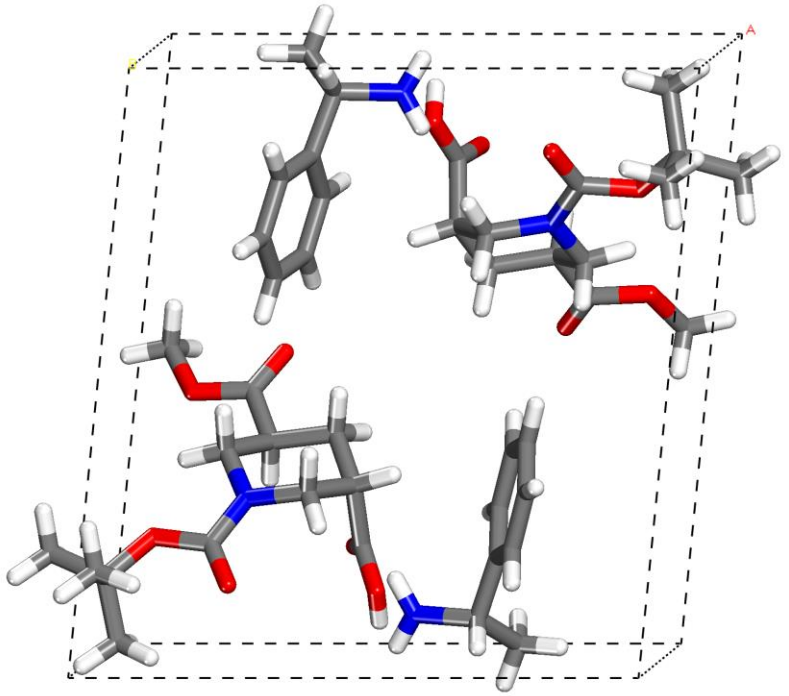
(S)-(-)-1-Phenylethylamine







FOCXAX $P2_1$
Hans Iding, Beat Wirz, Rosa-María Rodríguez Sarmiento,
Tetrahedron Asymmetry 14 (2003) 1541-1545

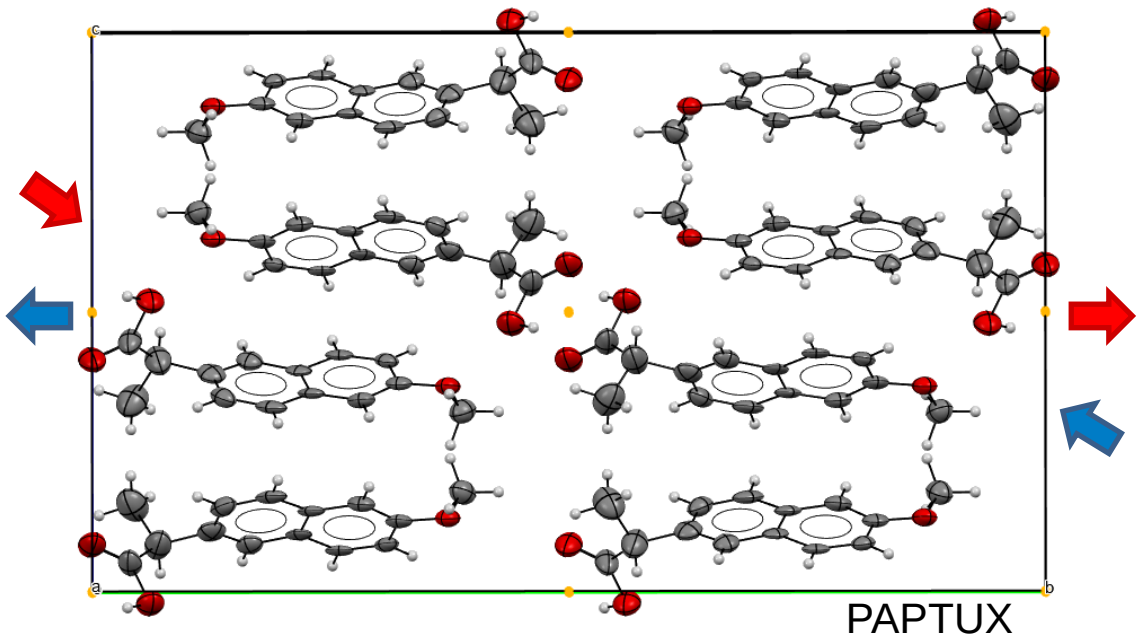


You can not always assume that chemical reaction, crystallization, or operations of mechnochemistry will conserve the chirality of the reference material.

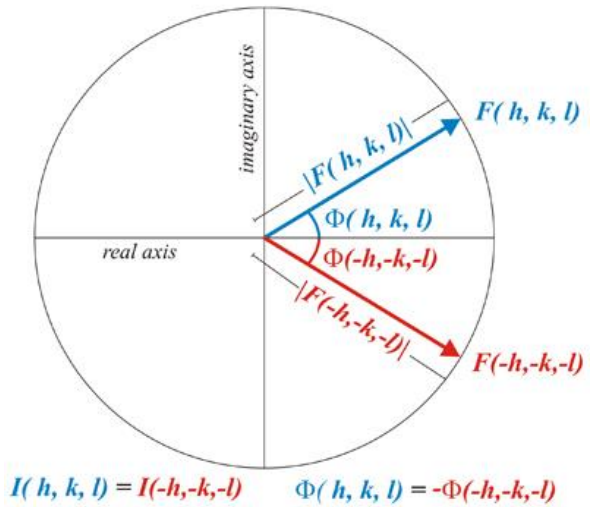
adapted from: Frank Schaper CHM6450-H21

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)

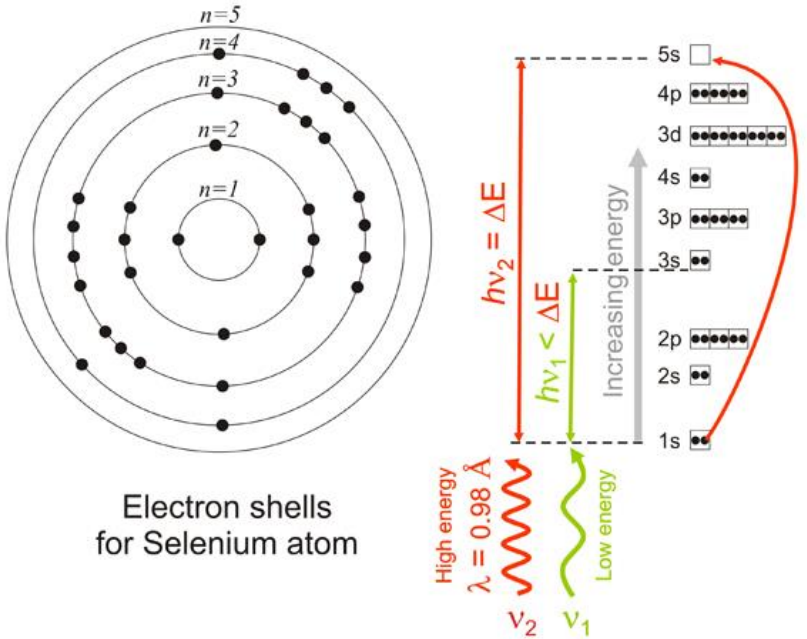
- Anomalous scattering affects the way that photons interact with electrons in an atom.
- When the incident radiation has sufficient energy to be absorbed by an atom in the structure, an electronic transition from a lower energy level to an upper one occurs.
- Some photons are absorbed and immediately 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.

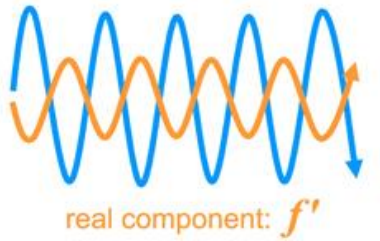


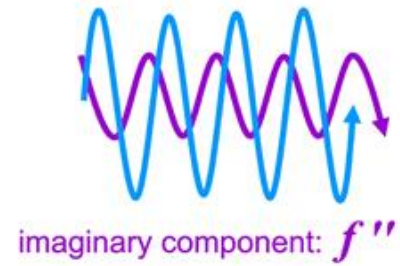
Electron shells for Selenium atom

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

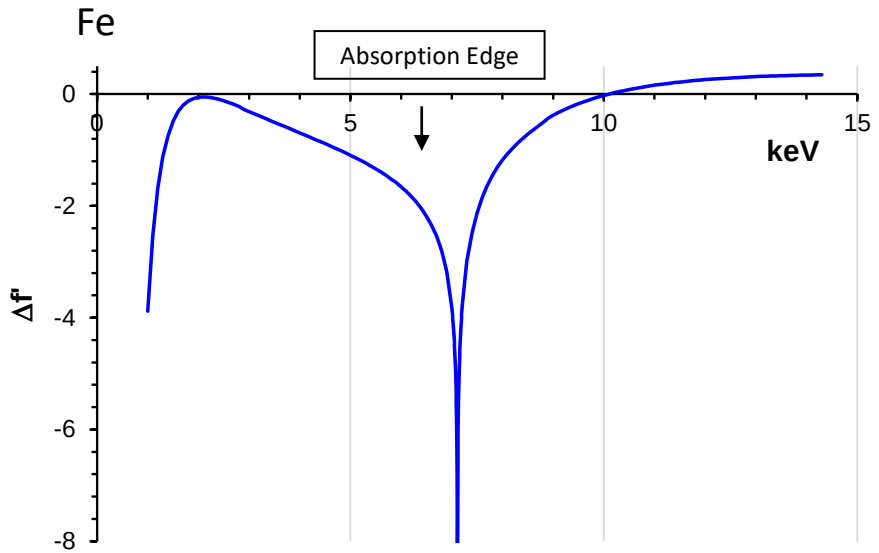
Resonant Scattering

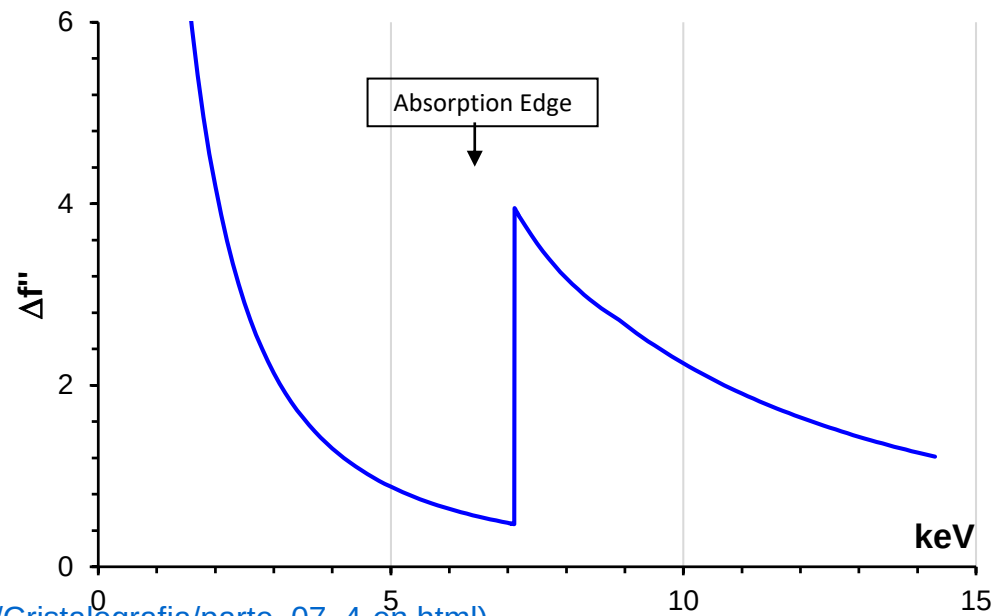
- The values of f' and f" are depended on the absorption edge of the element.
- The real part, $\Delta f'$, can be positive or negative. Close to the absorption edge, $\Delta f'$ is negative.
- The imaginary part, $\Delta f''$, has a 90° phase shift compared to f_{atom}. It is always positive, increases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





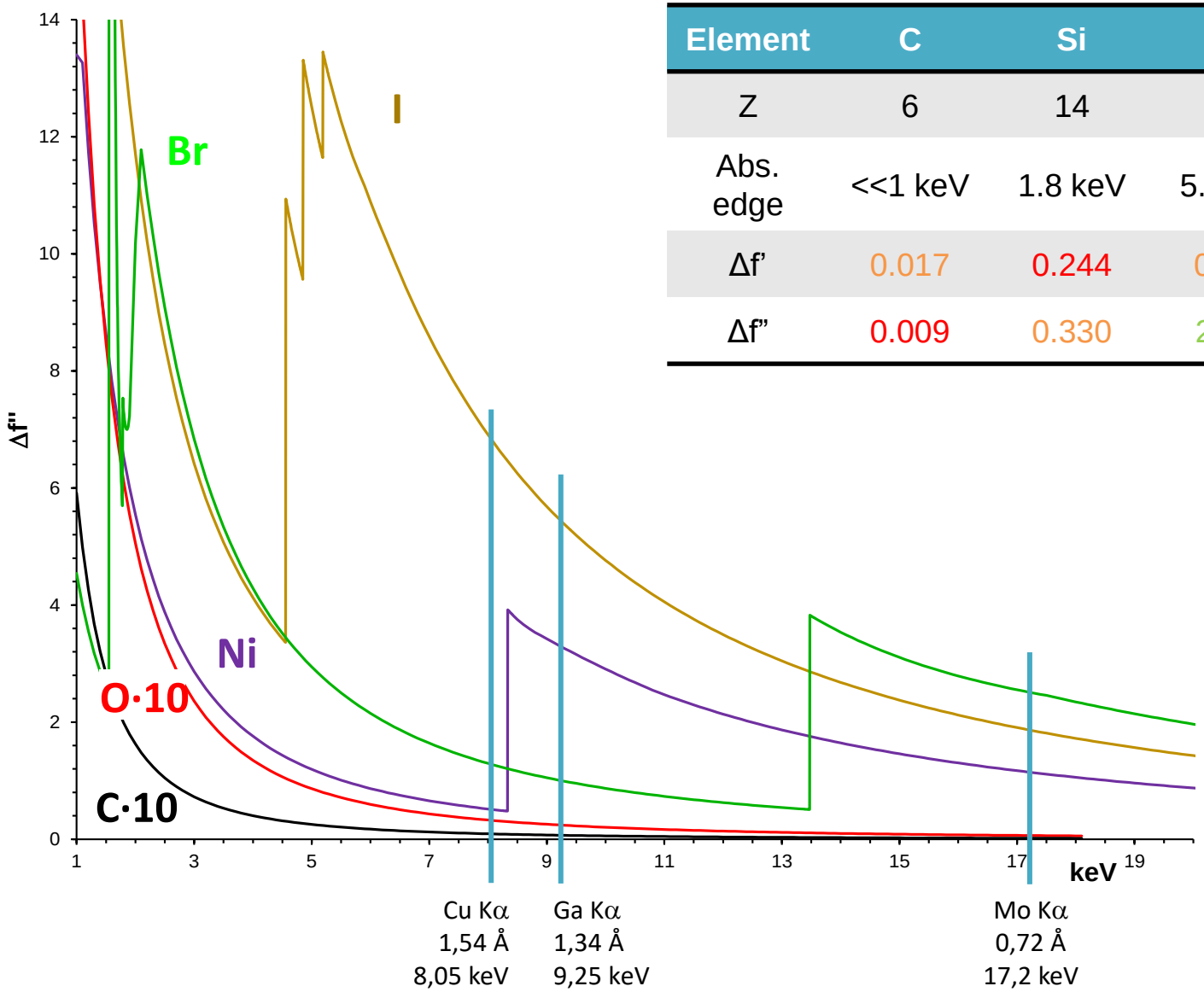
Anomalous scattering will be observed if the X-Ray energy is slightly higher than the absorption edge for the element.





Resonant Scattering

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



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
Δf'	0.017	0.244	0.035	-1.179	-2.464	-2.956	-2.0255	-1.6142
Δf"	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:

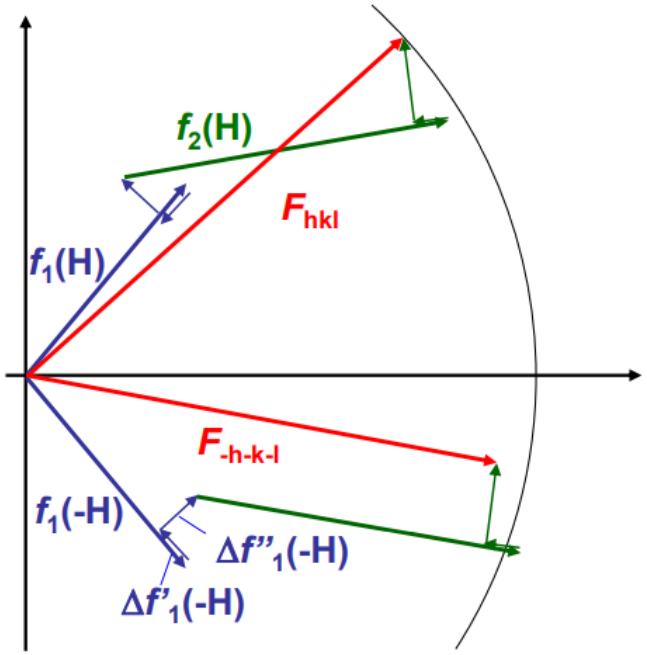
	Cu Kα (1.54 Å)		Mo Kα (0.72 Å)	
	Δf"	μ/ρ	Δf"	μ/ρ
C	0.01	5	0.002	1
Ni	0.51	50	1.11	71
Br	1.29	90	2.51	112
I	6.91	292	1.87	55

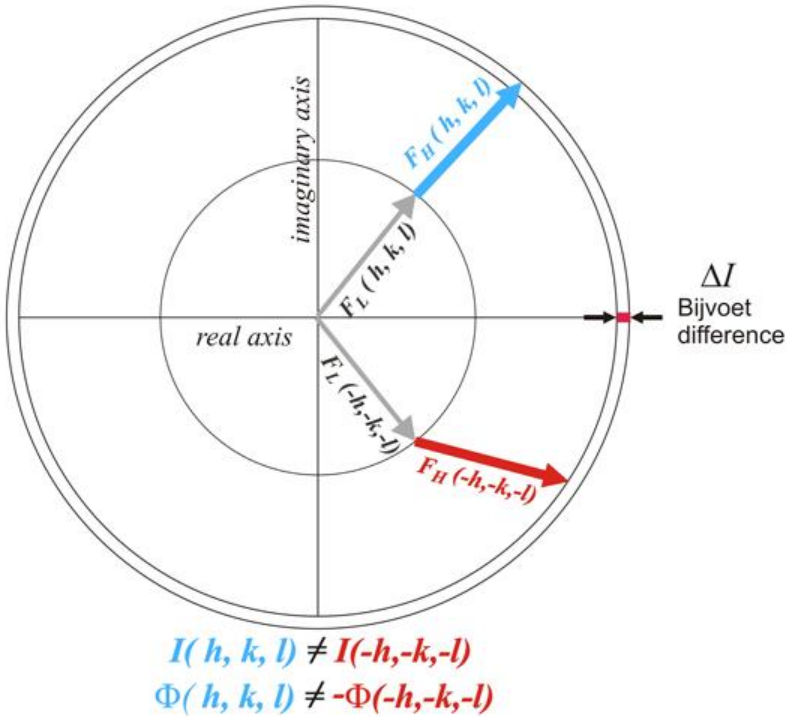
adapted from: Frank Schaper CHM6450-H21

Resonant Scattering

- Close to an absorption edge, Δf' becomes negative and can be related to X-ray absorption. The imaginary Df" 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.

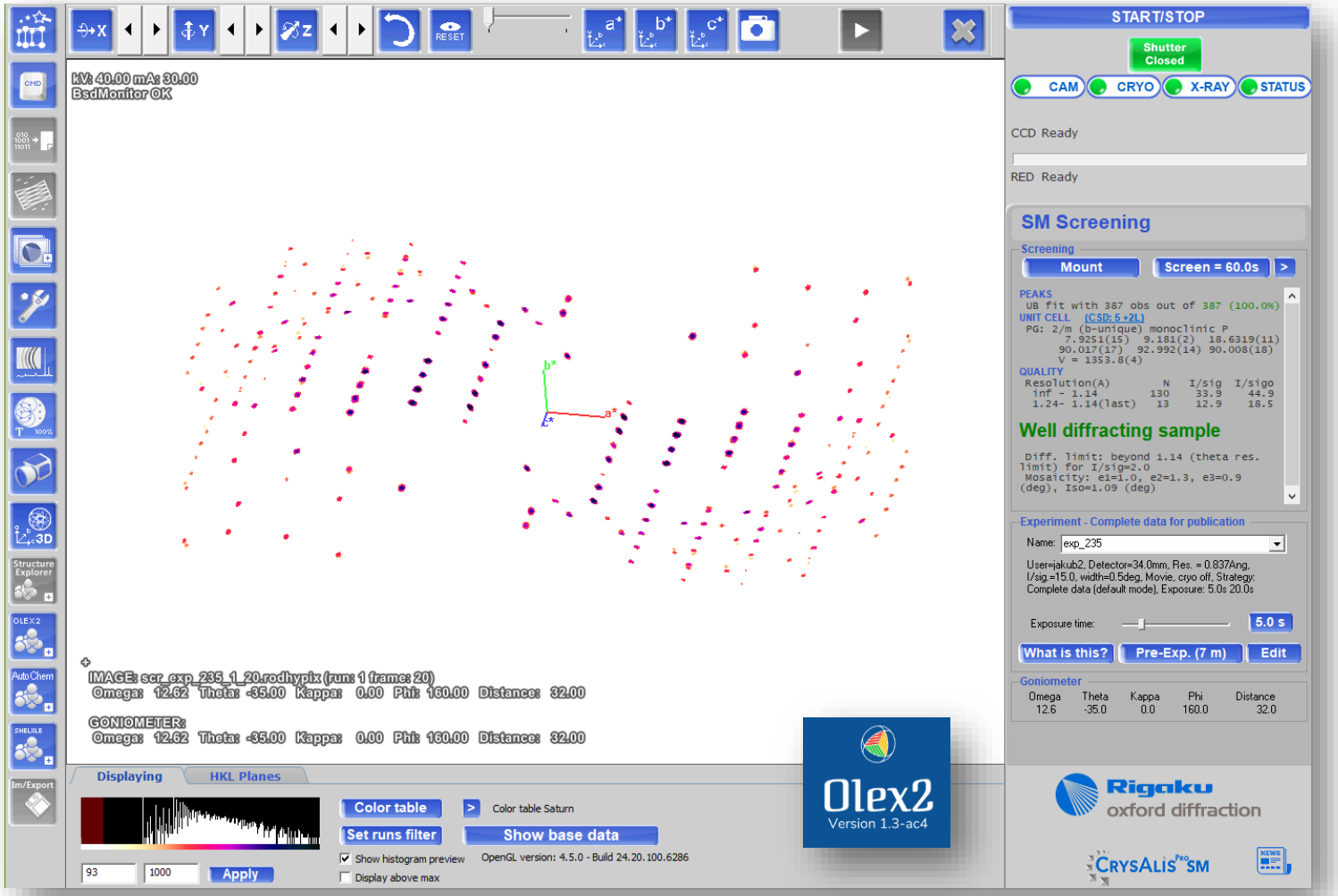
Take care for Bijvoet Differences

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

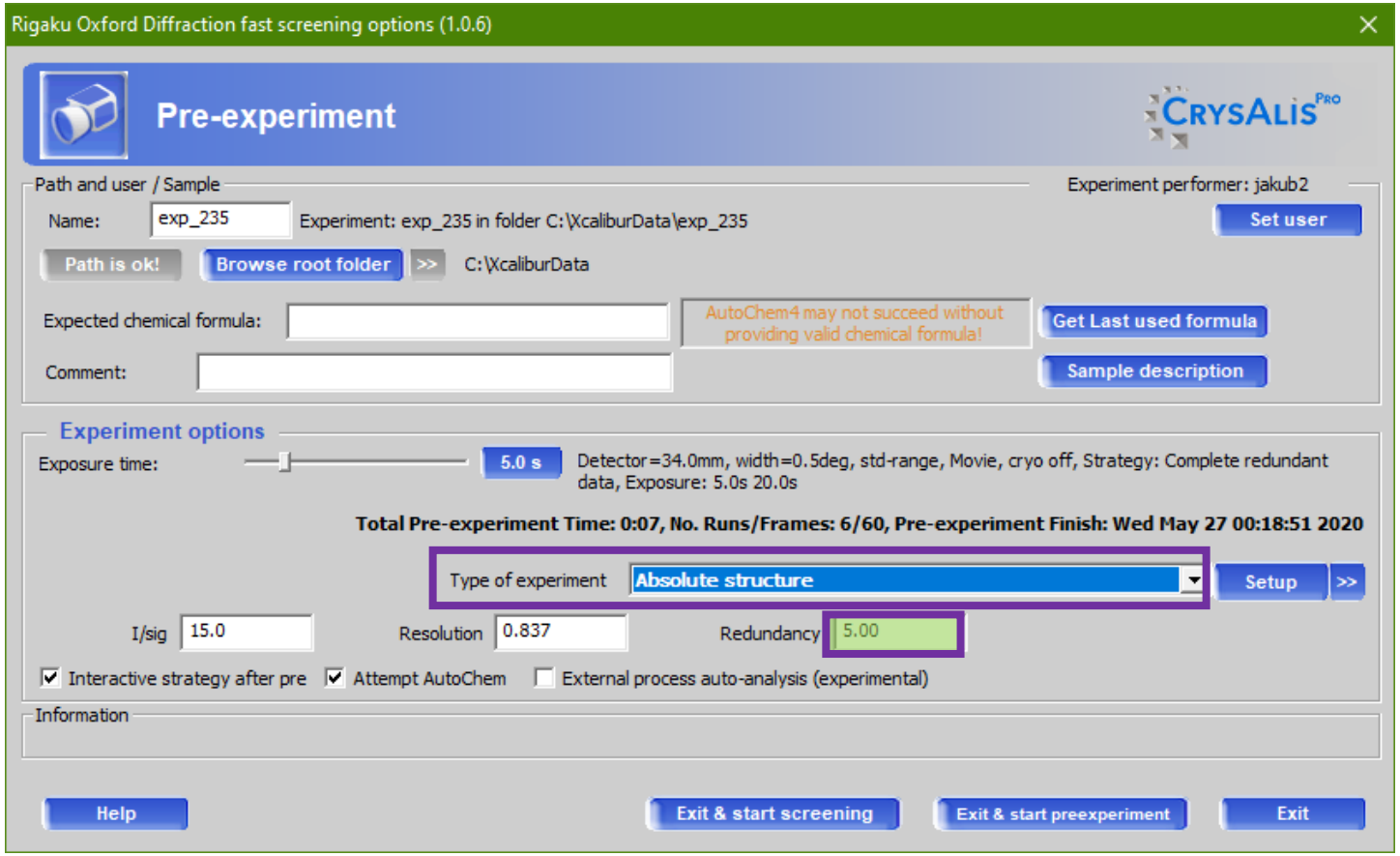
Assign proper absolute Configuration

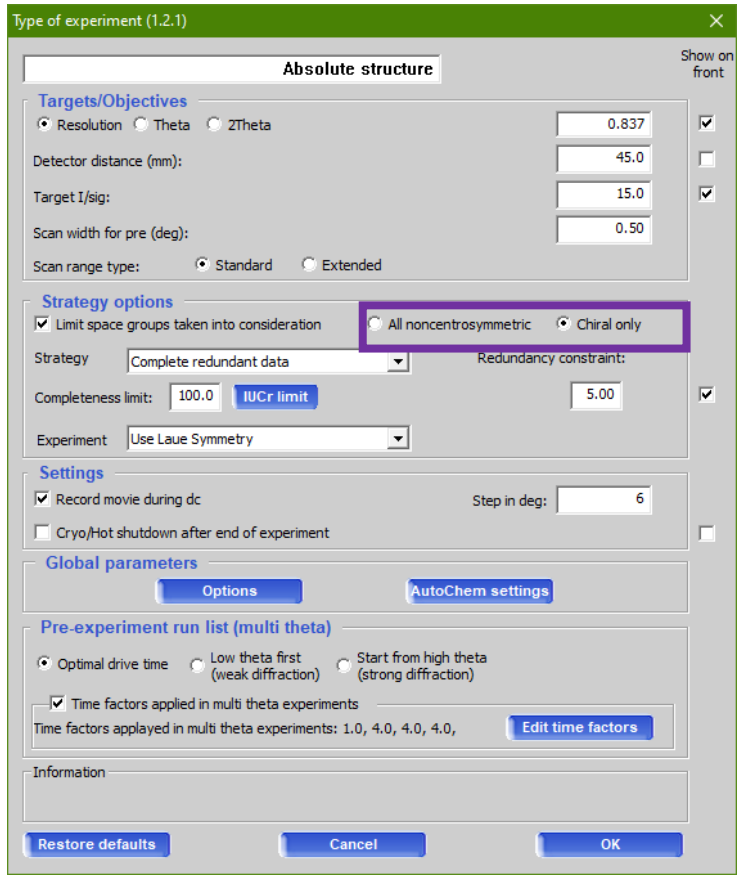
- Make sure that **descriptor** values and its standard deviation make sense.

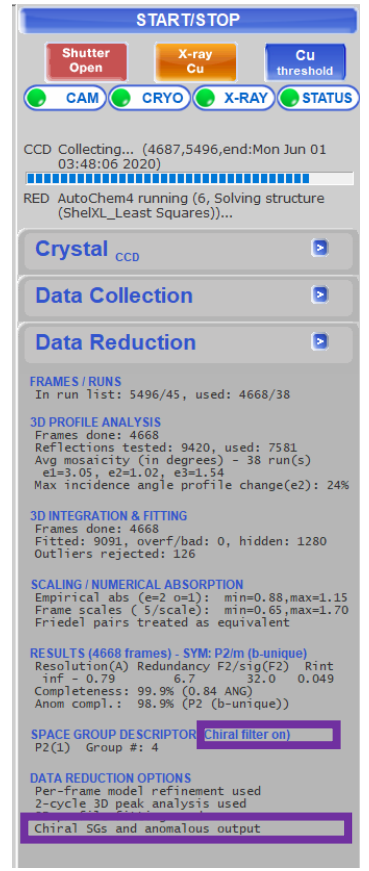
PRACTICAL CRYSTALLOGRAPHY



STARTING EXPERIMENT WITH PRE-EXP



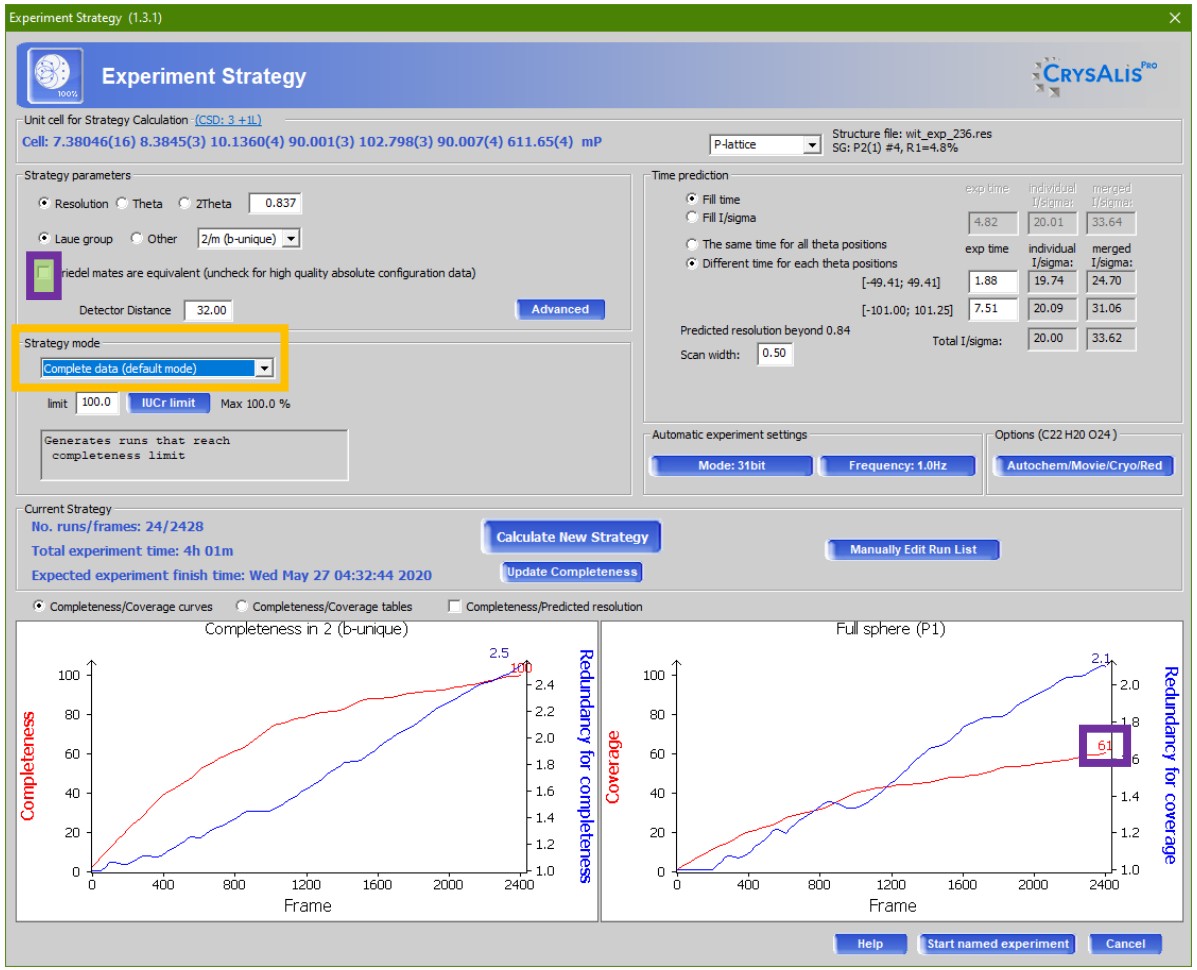




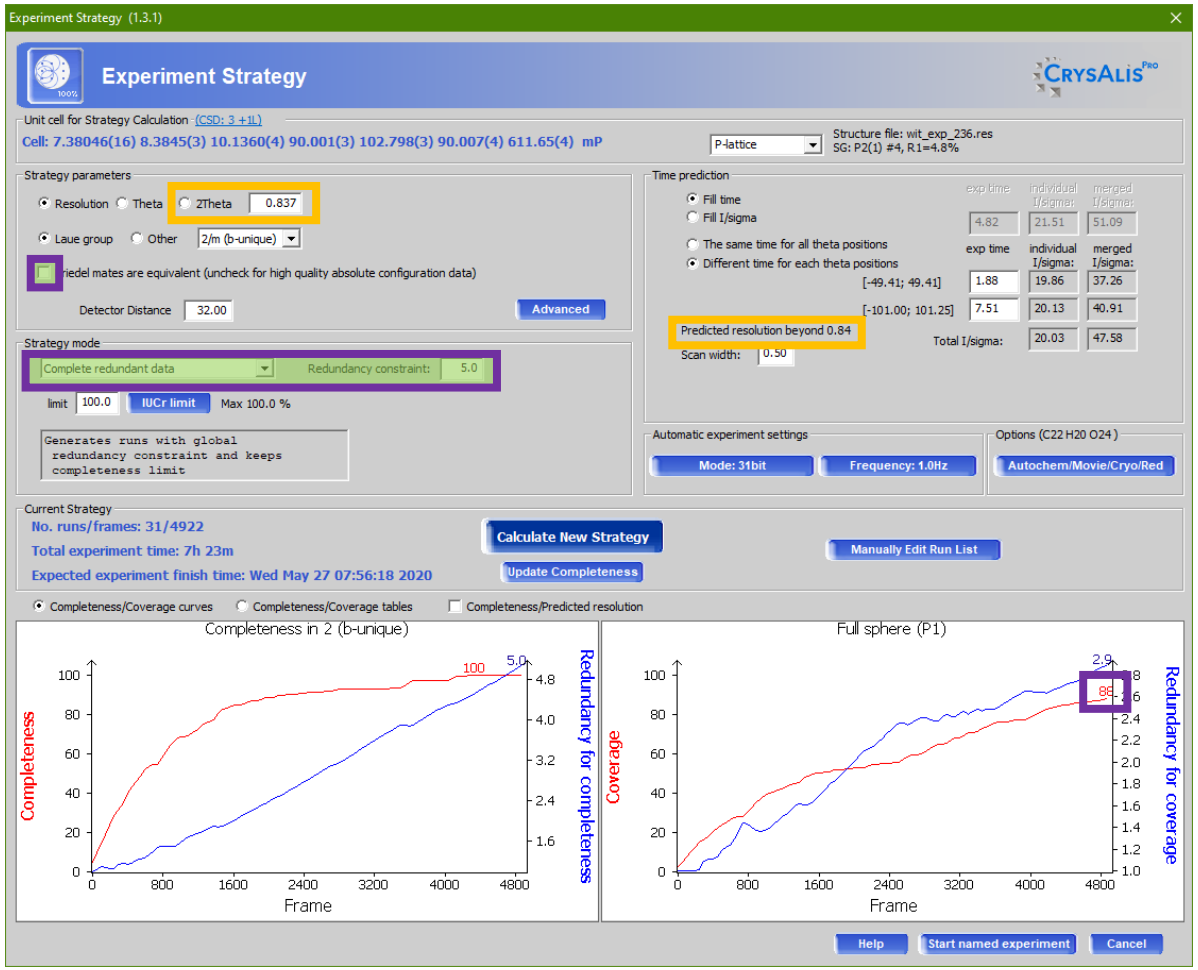
TIP: Use built-in experiment type settings.

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

STRATEGY SELECTION

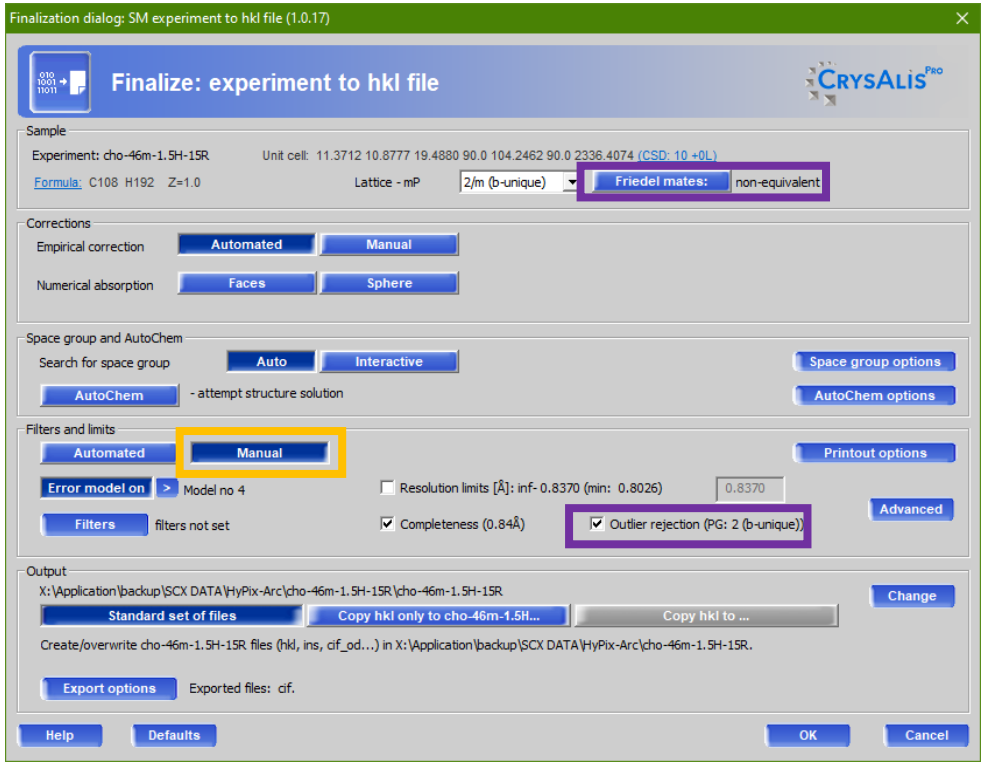


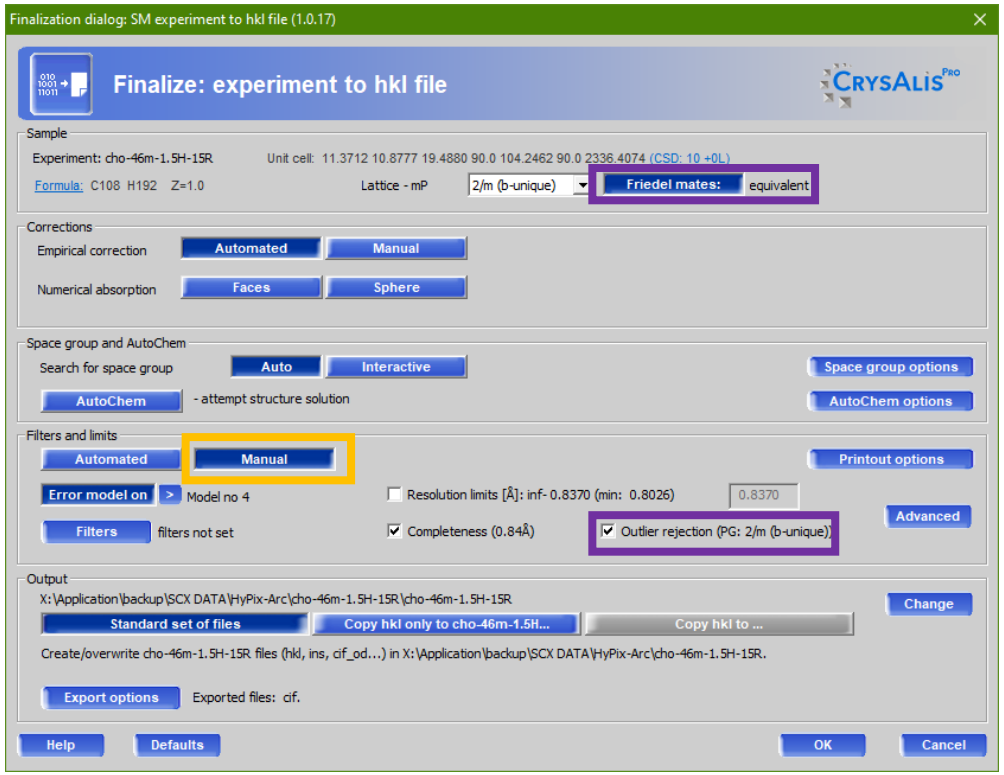
TIP: if your crystal diffracts very well, collect more Friedel pairs with extra resolution.

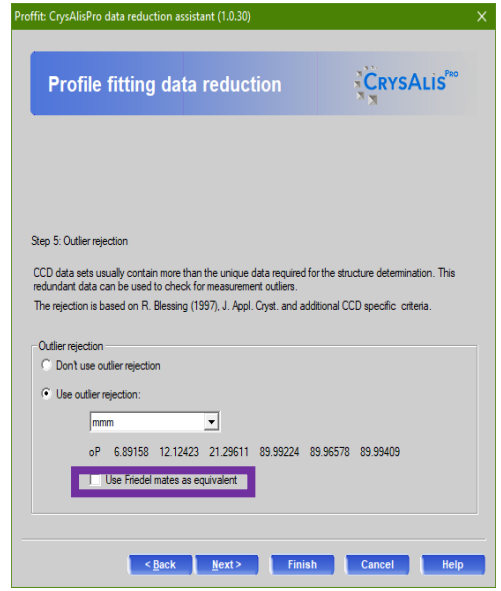


The default strategy settings is:
Complete with recommended 5 fold redundancy

MANUAL DATA PROCESSING AND FINALIZATION
OUTLINER REJECTION SETTINGS







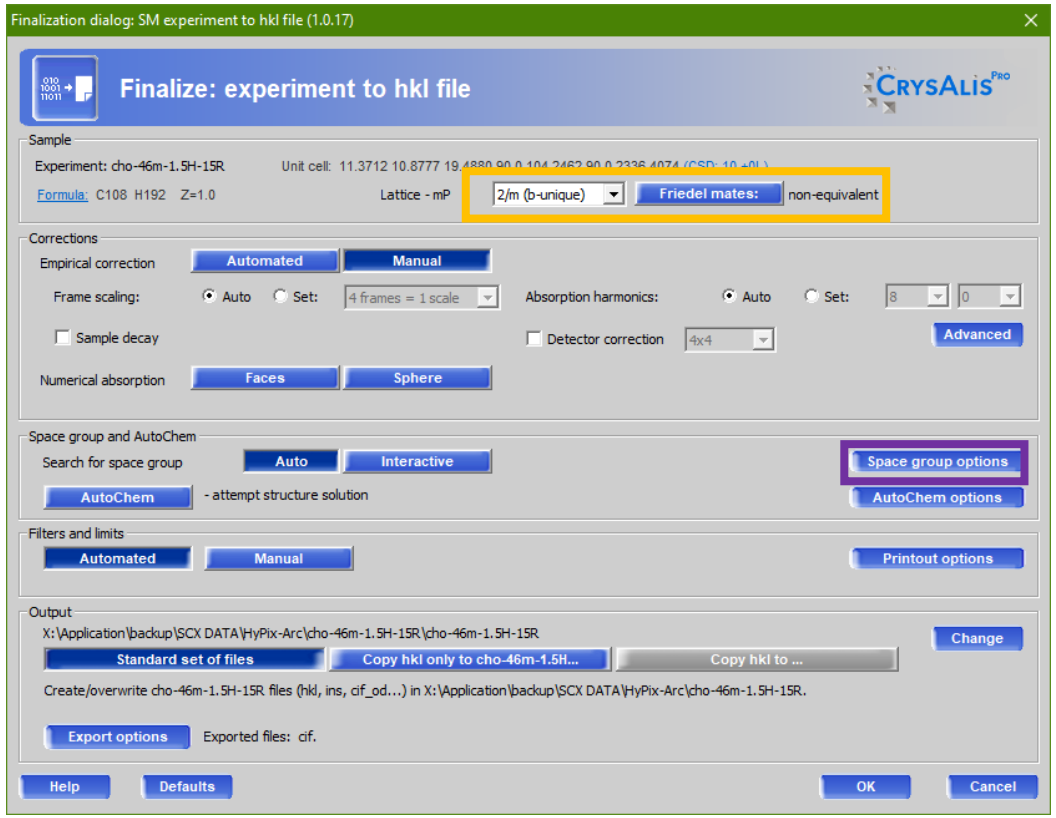
TIP1: CrysAlis^{Pro} outputs always unmerged hkl file. The Friedel pairs settings is used for outlier checks only.
TIP2: Processing data with Chiral filter enables correct outlier settings.
If you forgot about it, do not worry. This step is repeated with each hkl file finalization.

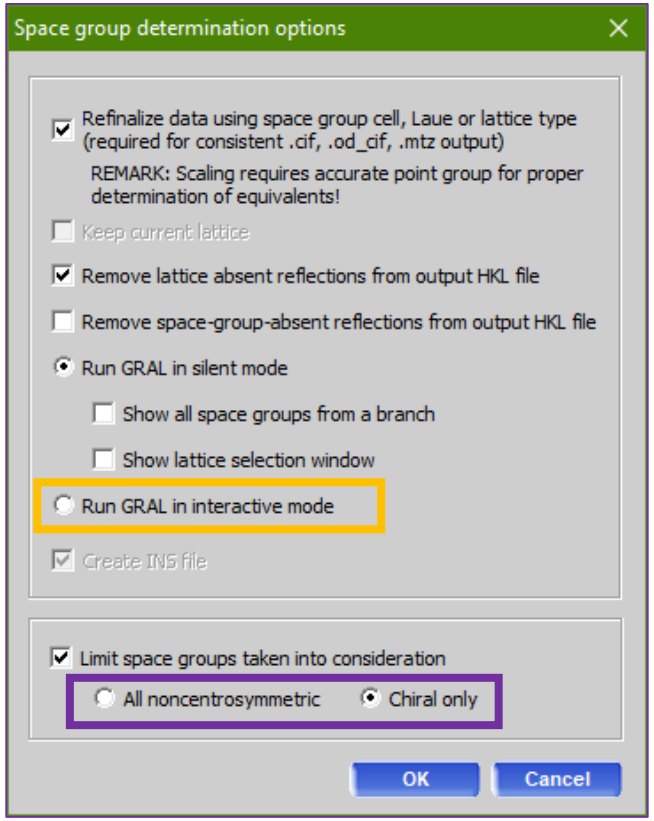
MANUAL DATA PROCESSING AND FINALIZATION, ENABLING CHIRAL FILTER

In pre-experiment settings

In GRAL settings

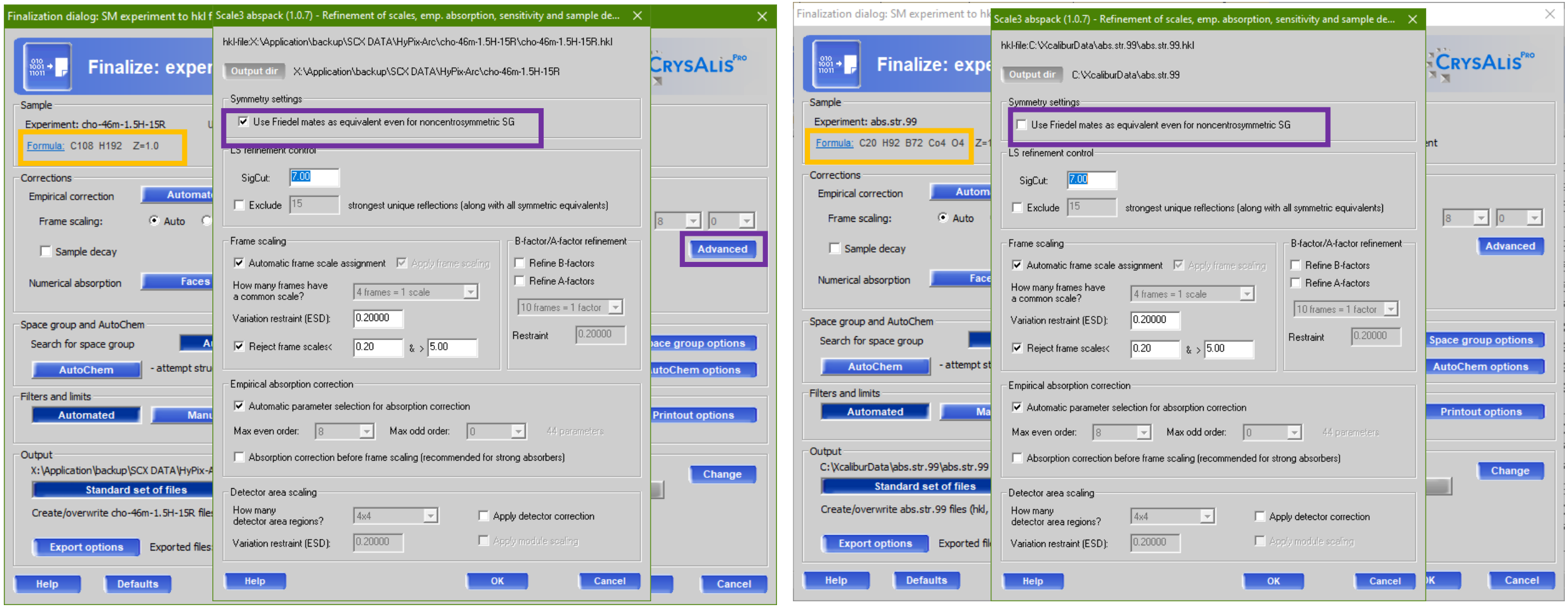
PX mode has as default settings





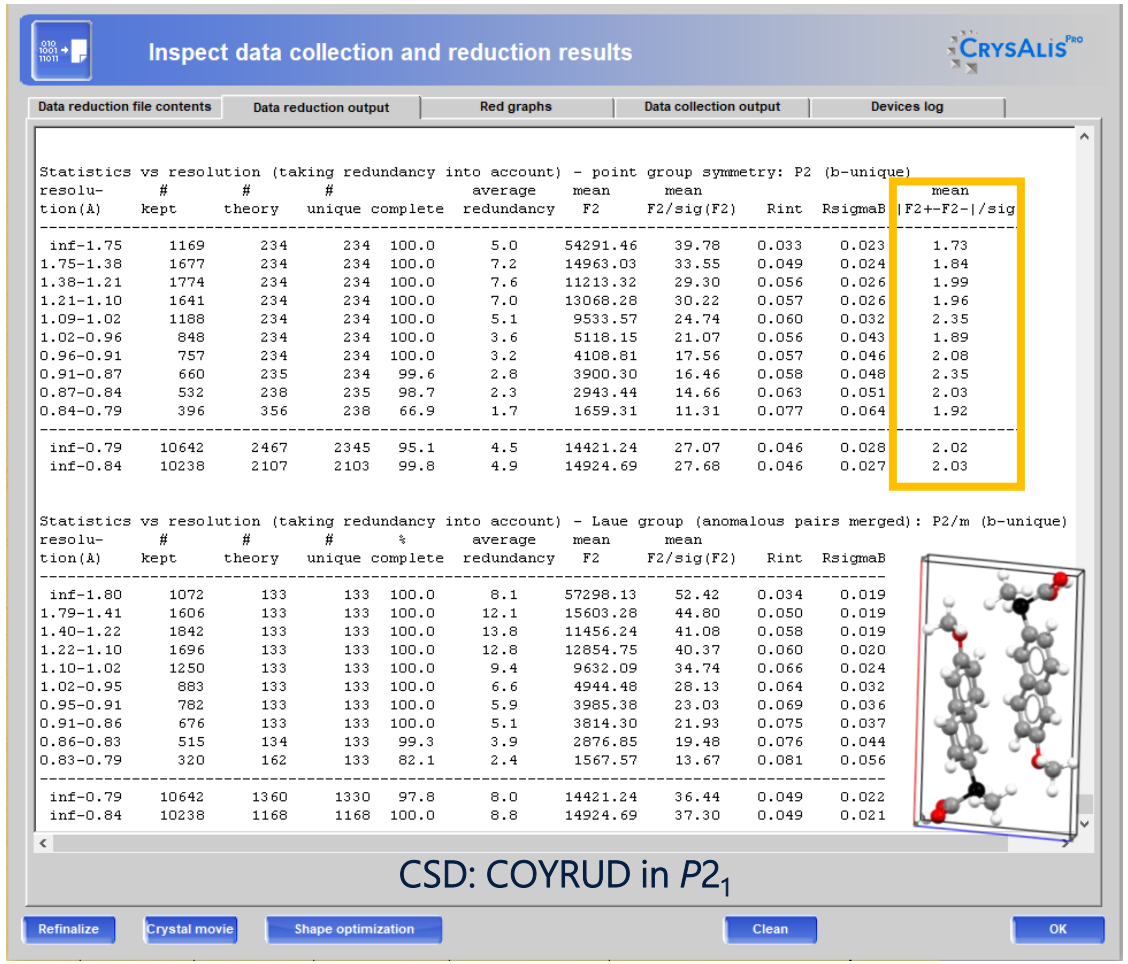
TIP: Chiral filter in CrysAlis^{Pro} not only limit space groups but also will set up outliner rejection and anomalous signal output.

MANUAL DATA PROCESSING AND FINALIZATION SCALING OPTIONS

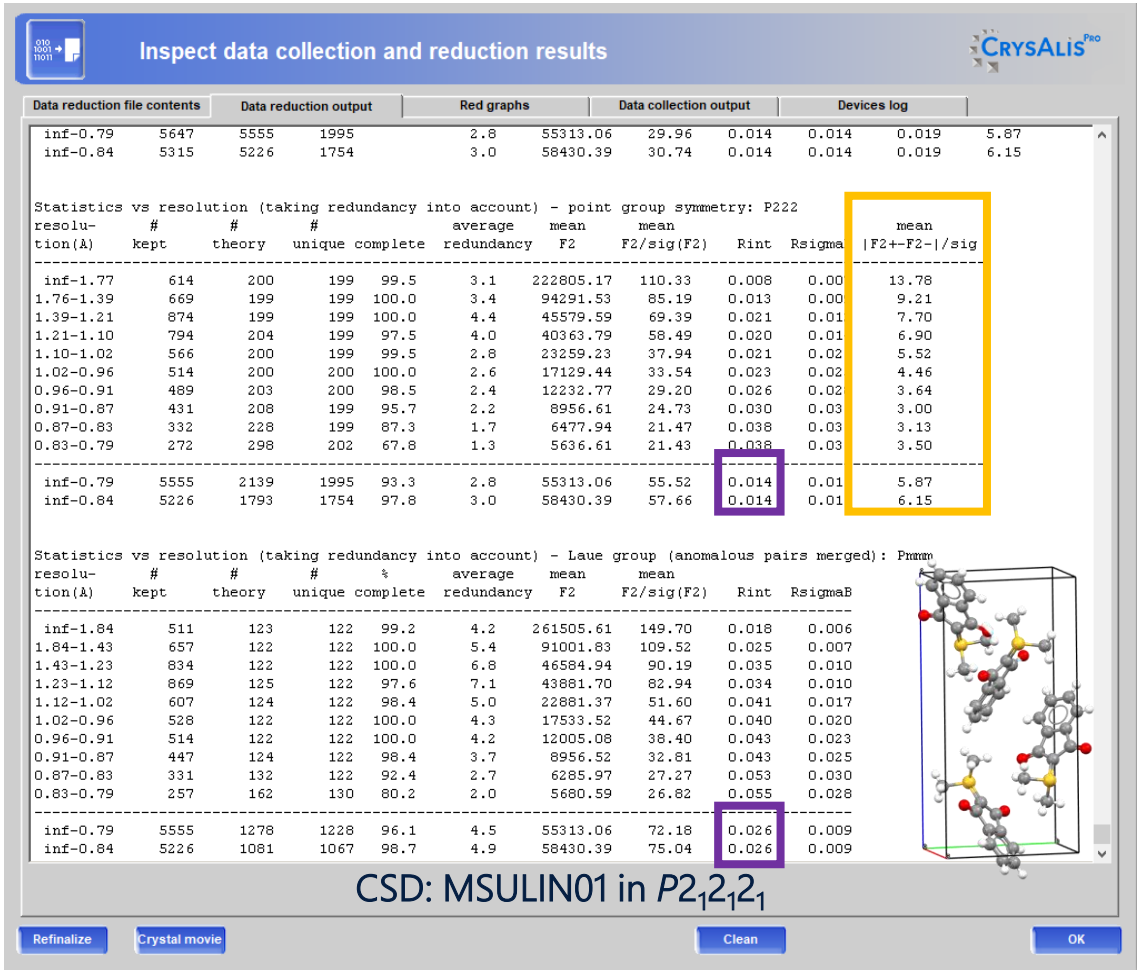


TIP: CrysAlis^{Pro} checks the provided formula and adjust this option automatically.
A general rule is: for weak anomalous signal: on; for extremely strong: off.

FINALIZATION AND DATA INSPECTION ANOMALOUS SIGNAL OUTPUT

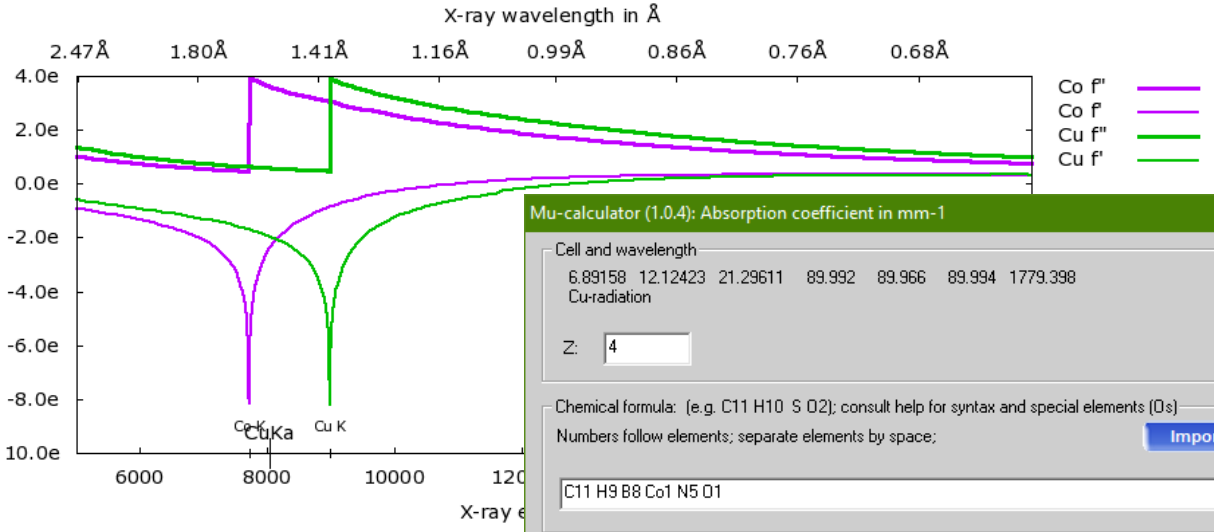


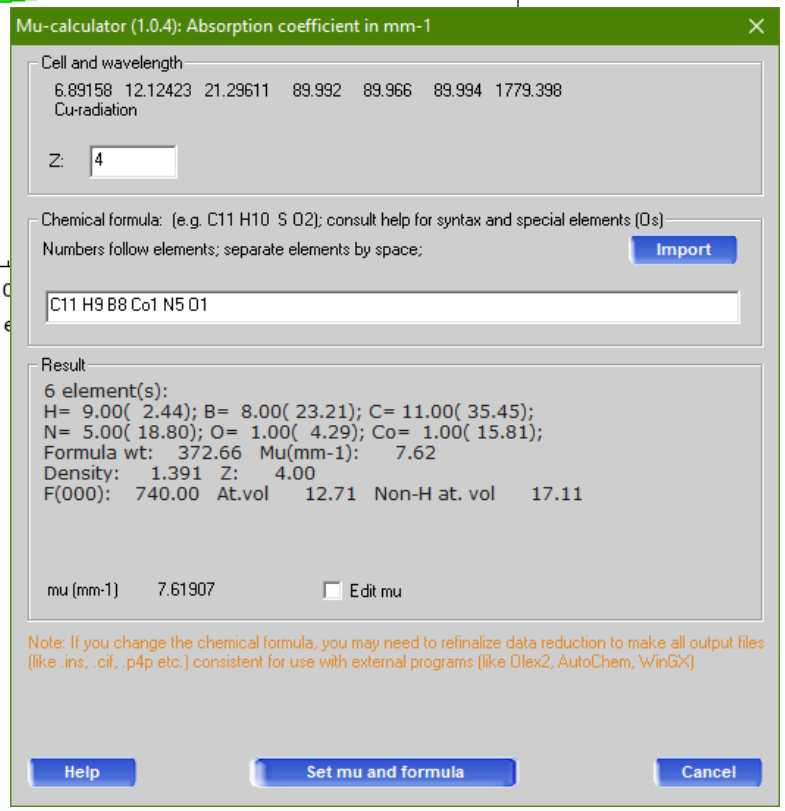
CSD: COYRUD in $P2_1$

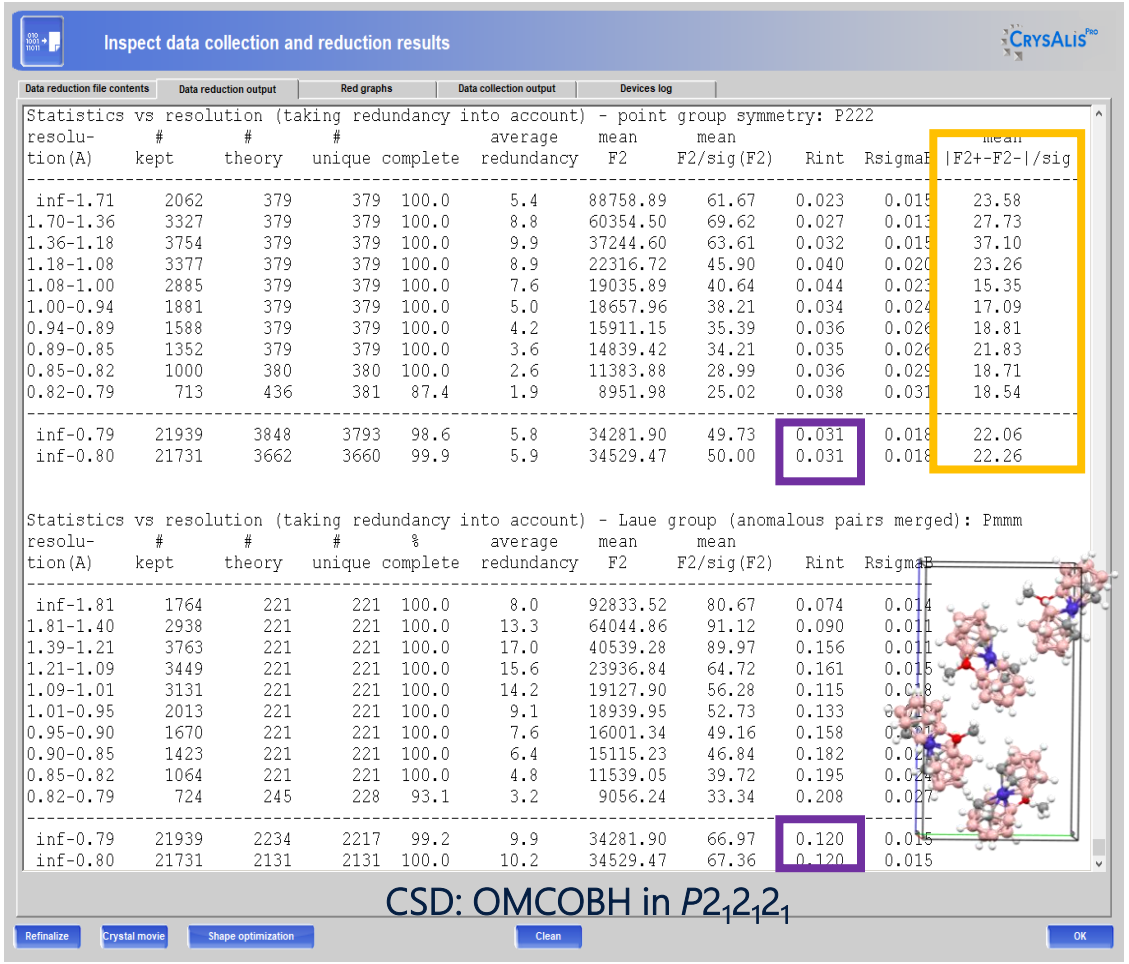


CSD: MSULIN01 in $P2_12_12_1$

FINALIZATION AND DATA INSPECTION ANOMALOUS SIGNAL OUTPUT







CSD: OMCOBH in $P2_12_12_1$

Determination of Absolute Configurations

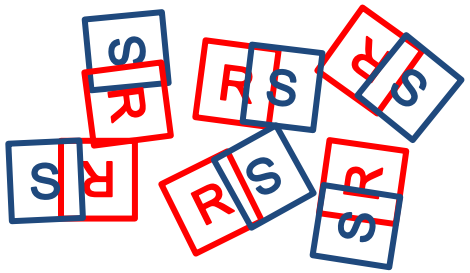
- Old method: Compare the R-values of a structure with its inverted structure.
- Today: We use the Flack-x parameter, which refines to give the ratio of a crystal or its inversion twin which fits best the observed intensities.

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

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.

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

adapted from: Frank Schaper CHM6450-H21

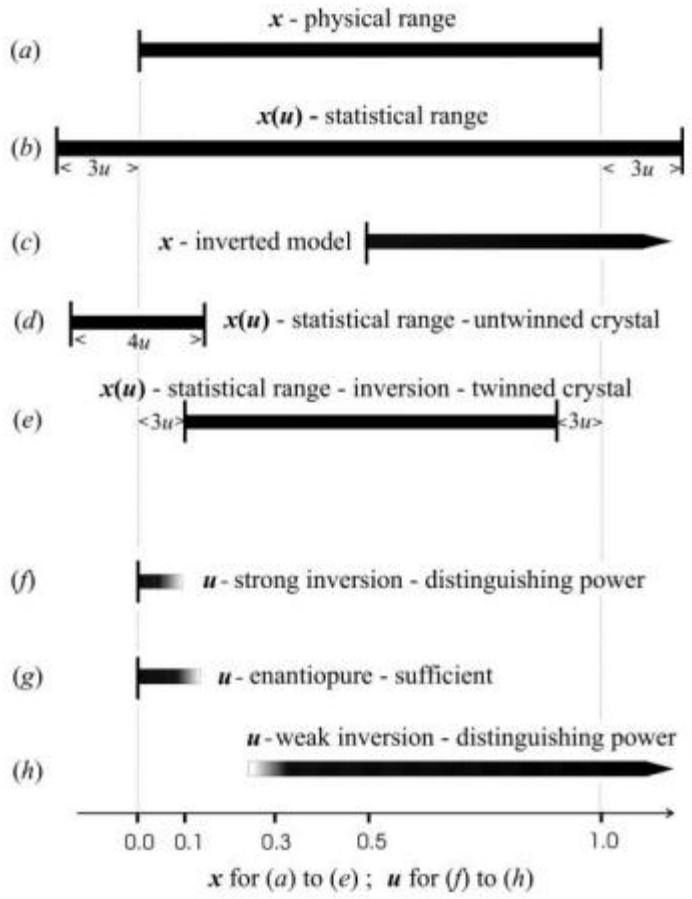
Flack Parameter

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

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, Pna21 , …) :
- Contain mirror planes, but no inversion center
- May contain only achiral molecules or racemic mixtures
- Flack parameter has to be calculated

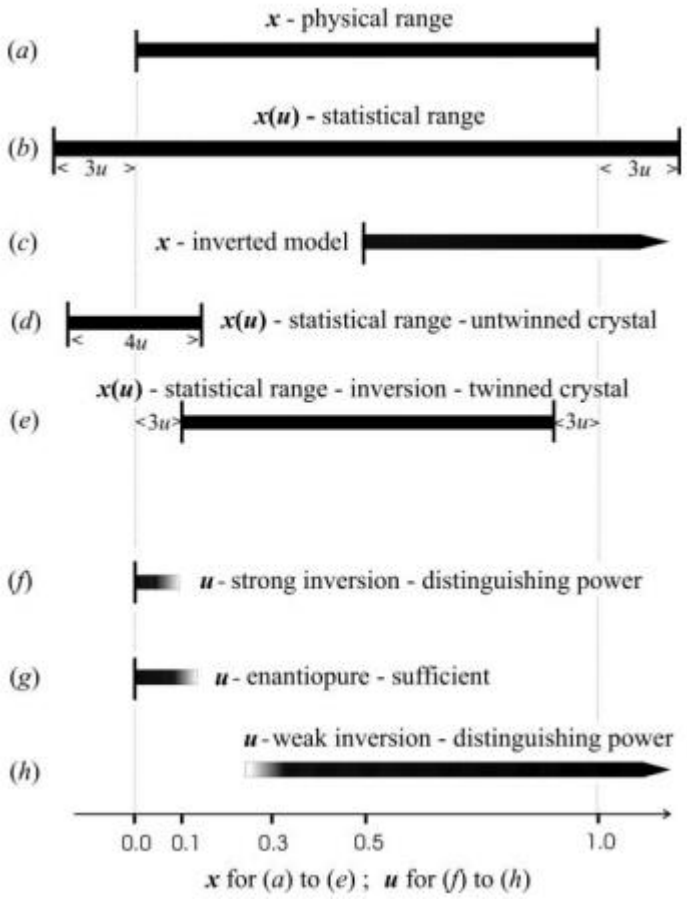
Centrosymmetric space groups:
- Flack parameter is not defined, since $|F(H)|^2 = |F(-H)|^2$



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

Flack Parameter

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



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.

F. Howard, G. Bernardinelli, *J. Appl. Cryst.,* **2000**, *33*, 1143-1148.

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)

adapted from: Frank Schaper CHM6450-H21

The Hooft Parameter y

- 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 *P*m, symmetry equivalents:

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

We therefore have the following Bijvoet pairs:

$$I_{hkl} \mid I_{-h-k-l}, \quad I_{hkl} \mid I_{-hk-l}, \quad I_{h-kl} \mid I_{-h-k-l}, \quad I_{h-kl} \mid I_{-hk-l}.$$

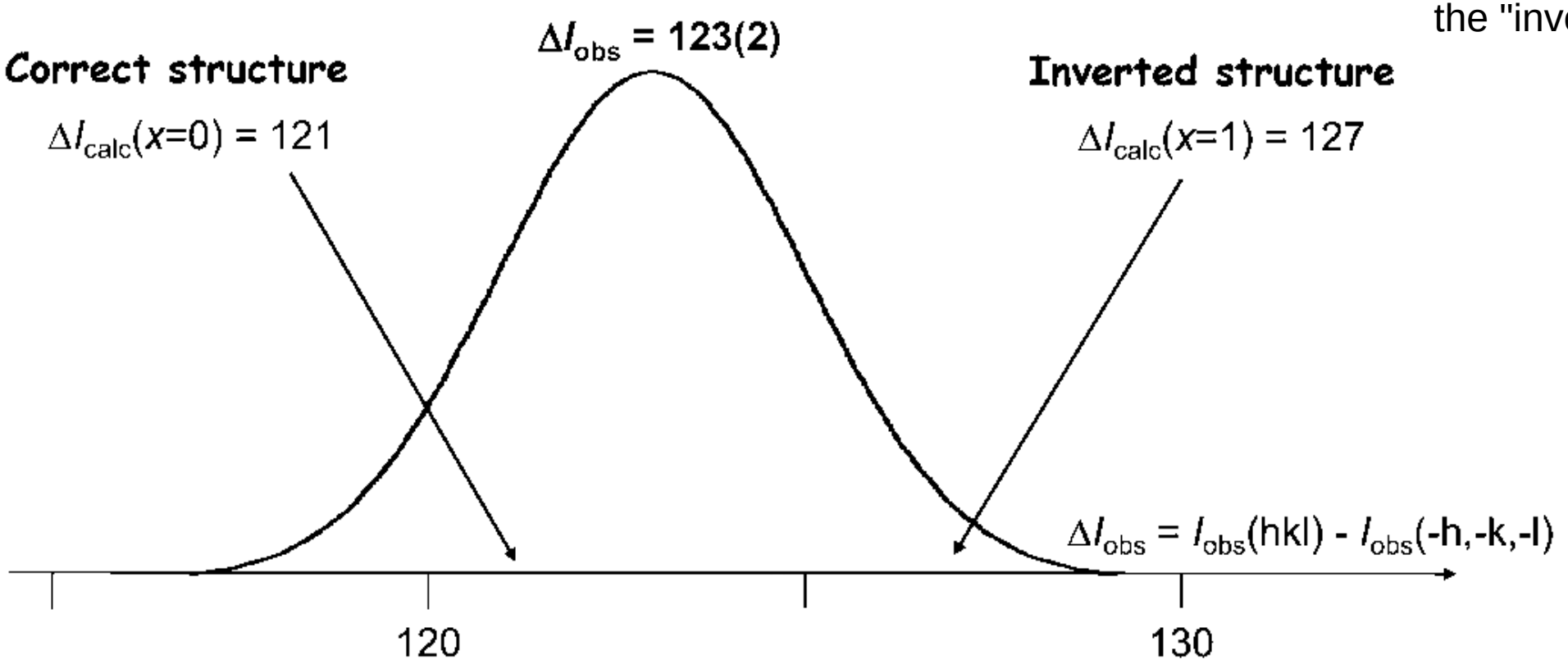
$$|F^{+}| \equiv |F_{hkl}| = |F_{\bar{h}\bar{k}\bar{l}}| \qquad |F^{-}| \equiv |F_{\overline{hkl}}| = |F_{h\bar{k}\bar{l}}|$$

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

R. W. W. Hooft, L. H. Straver, A. L. Spek J. Appl. Cryst. 2008, 41, 96 and J. Appl. Cryst. 2010, 43, 665

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

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

The respective calculation for the inverted model yields p1 = 5%.

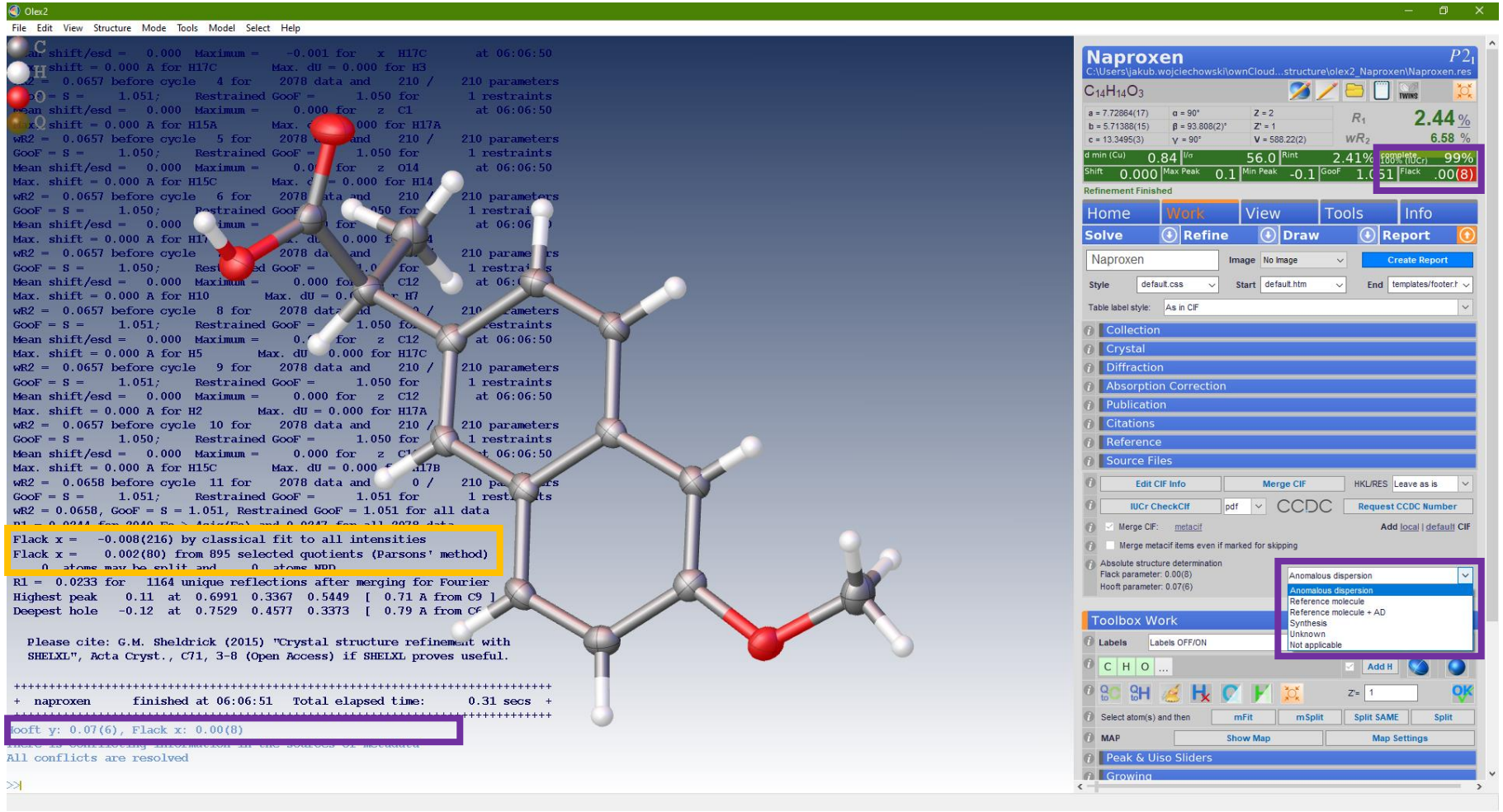
USEFUL OLEX2 OPTIONS FOR ABSOLUT STRUCTURE REFINEMENT

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

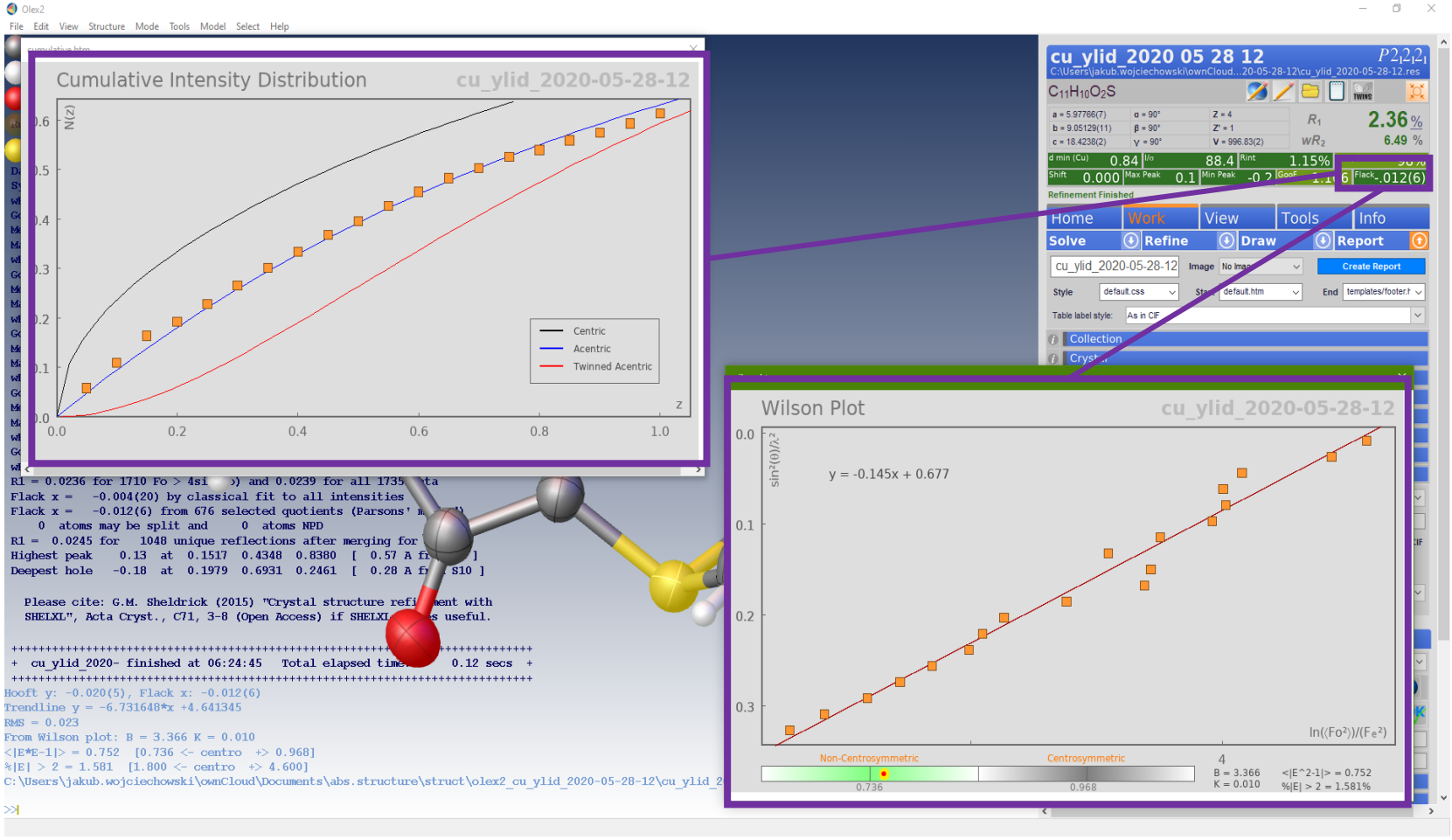


_chemical_absolute_configuration

- 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.

adapted from: Frank Schaper CHM6450-H21

USEFUL OLEX2 OPTIONS FOR ABSOLUT STRUCTURE REFINEMENT

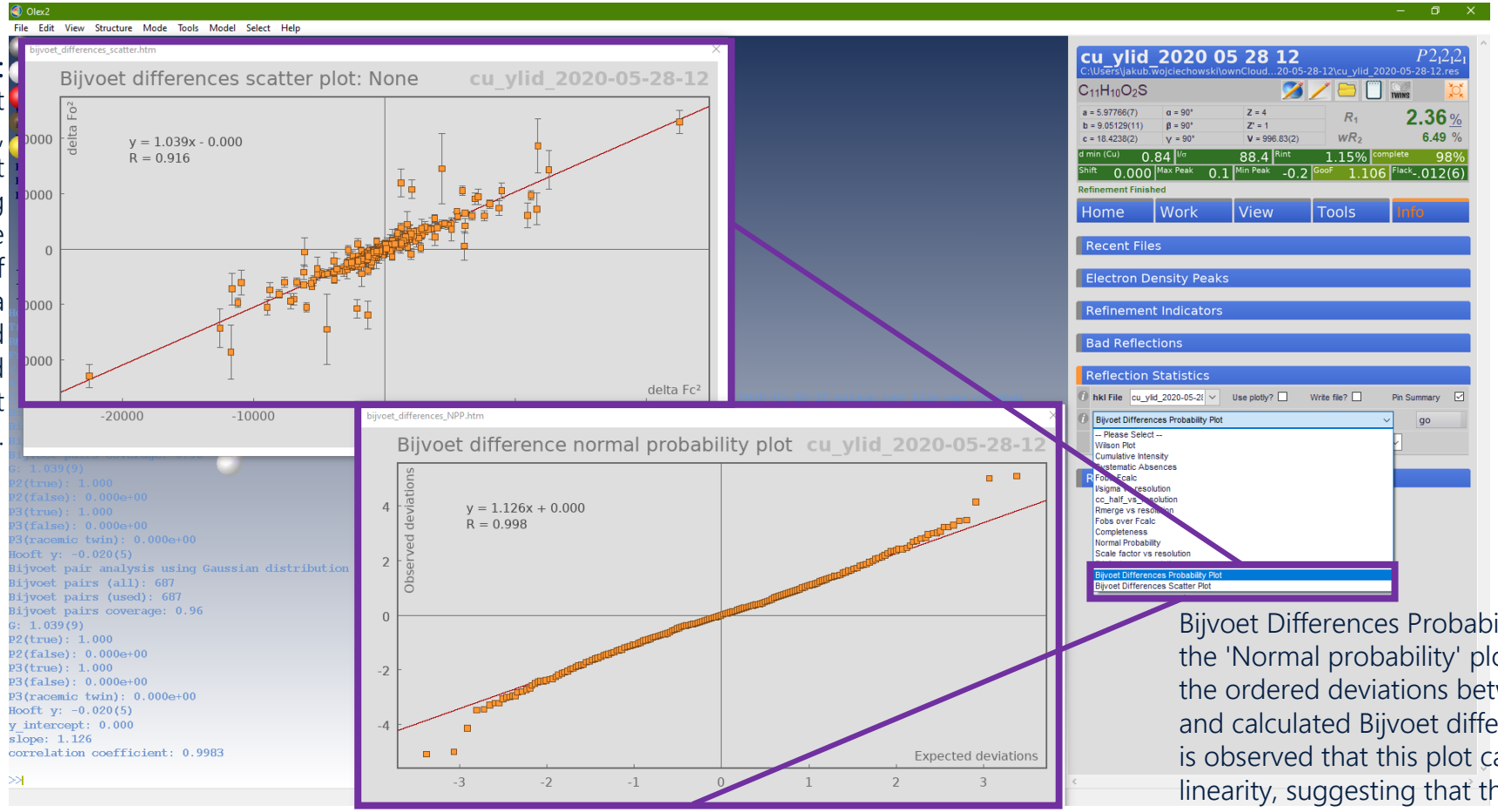


A statistical comparison of the observed intensity data with the theoretical distribution for a random atomic arrangement, since the atomic scattering decreases with increasing 2Θ. Establishes an overall displacement parameter for the structure, B and scale factor for the data, K.

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

USEFUL OLEX2 OPTIONS FOR ABSOLUT STRUCTURE REFINEMENT

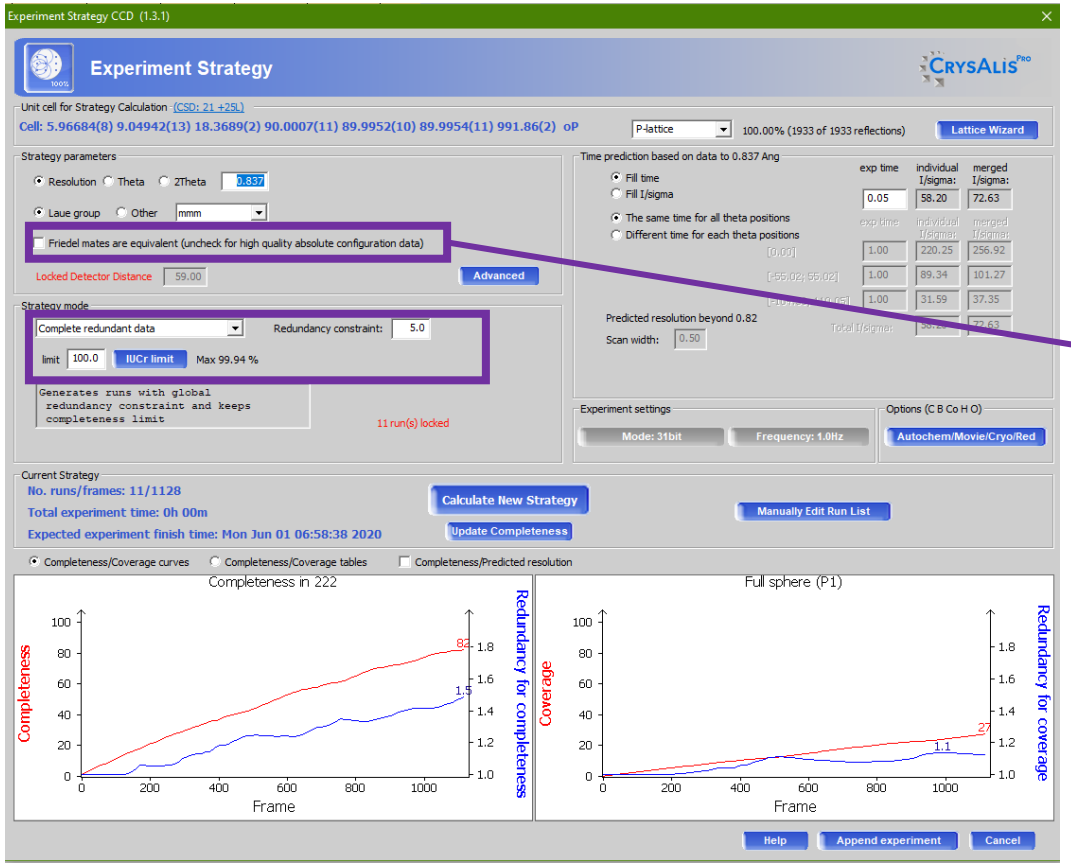
Bijvoet Differences Scatter Plot: This plots the calculated Bijvoet differences, $F^2_{calc}(+) - F^2_{calc}(-)$, against the observed Bijvoet differences, $F^2_{obs}(+) - F^2_{obs}(-)$, along with error bars indicating the uncertainty in the measurement of the Bijvoet differences. For a correct, strongly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

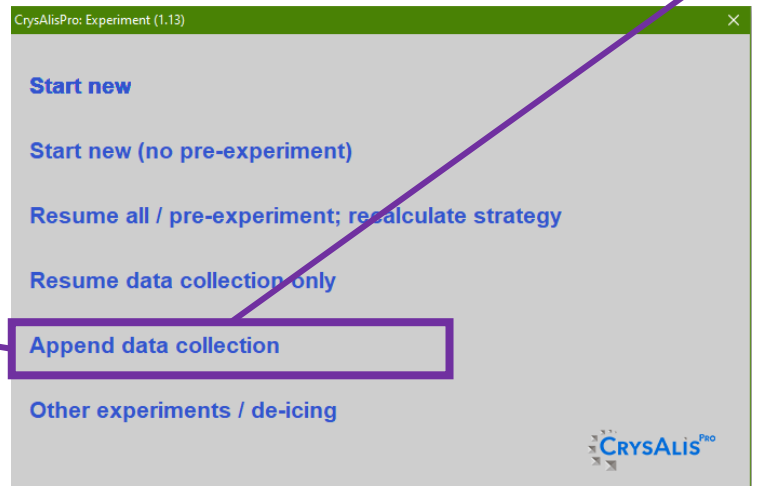


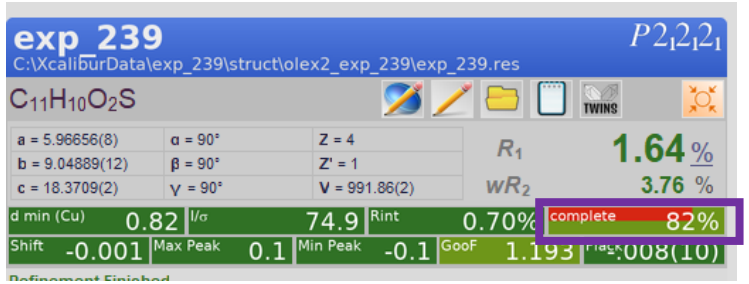
Bijvoet Differences Probability Plot: Similarly to the 'Normal probability' plot above, this plots the ordered deviations between the observed and calculated Bijvoet differences. Frequently it is observed that this plot can deviate from linearity, suggesting that the errors are not normally distributed.

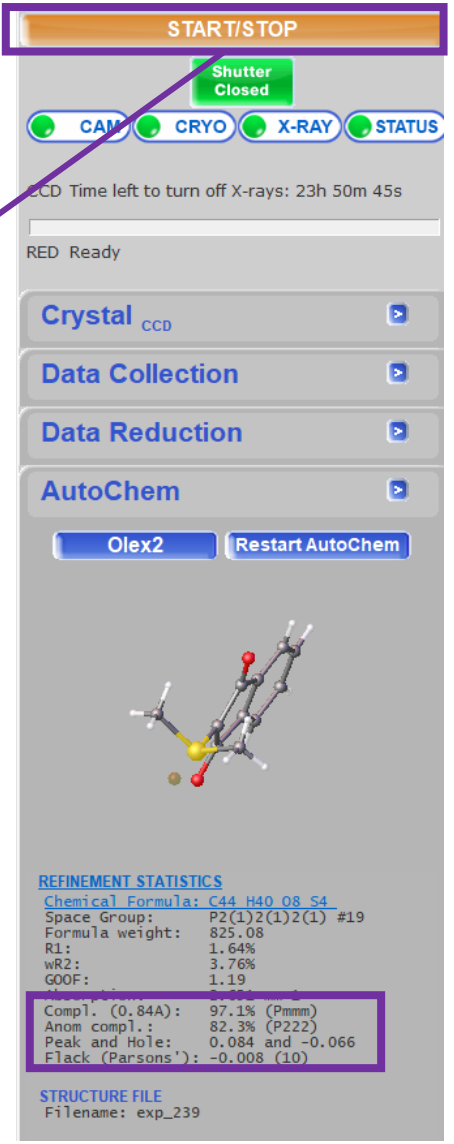
TIP: Bijvoet scatter plot and normal probability plot are accessible from Info-Reflection statistics

APPENDED EXPERIMENT FOR FULL ANOMALOUS COMPLETENESS





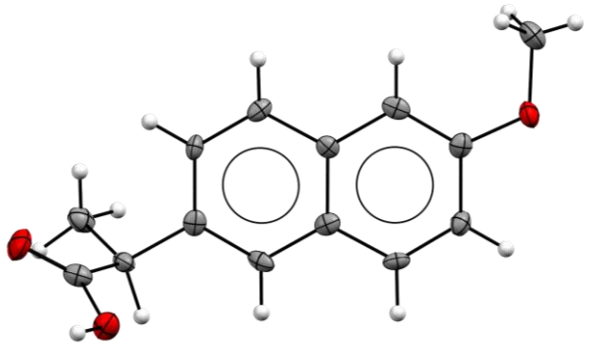




TIP: You do not need to wait till your experiment ends to append more scan to it.

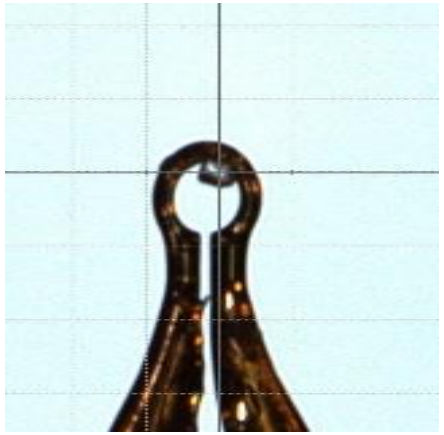
PRACTICAL CRYSTALLOGRAPHY

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| < 2e.s.d.

- In case of CONFIRMED enantiopurity of the sample
  e.s.d. <0.1 and |x| < 2e.s.d.



Data	Comp. %	Redund.	$<F^2/\sigma(F^2)>$	R_{int}	F2+-F2-/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| < 2e.s.d.

- In case of CONFIRMED enantiopurity of the sample
  e.s.d. <0.1 and |x| < 2e.s.d.

Data	Comp. %	Redund.	$<F^2/\sigma(F^2)>$	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 :

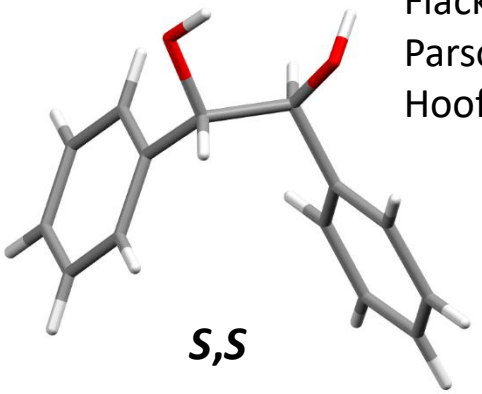
  MOVE 1 1 1 -1

- For **enantiomorphic space groups,** inversion of the structure requires changing the space group.

Special cases :

*F*dd2	MOVE .25 .25 1 -1	$I4_1$cd	MOVE 1 .5 1 -1
$I4_1$	MOVE 1 .5 1 -1	*I*-42d	MOVE 1 .5 .25 -1
$I4_122$	MOVE 1 .5 .25 -1	$F4_132$	MOVE .25 .25 .25 -1
$I4_1$md	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.

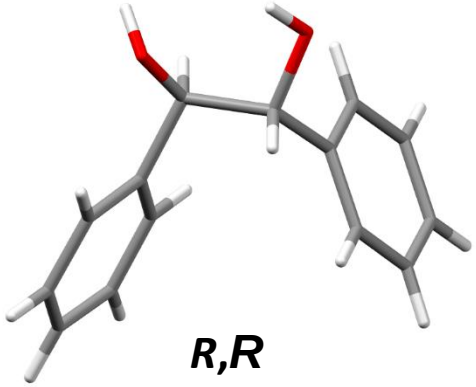


S,S

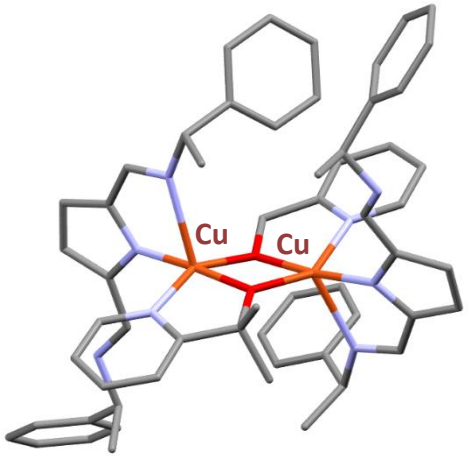
Flack-*x* : 0,1(3) = 0,1 ± 0,9
Parsons : -0,02(7) = -0,0 ± 0,2
Hooft-*y* : 0,02(6) = 0,0 ± 0,2

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

noise/signal = 2%



R,R

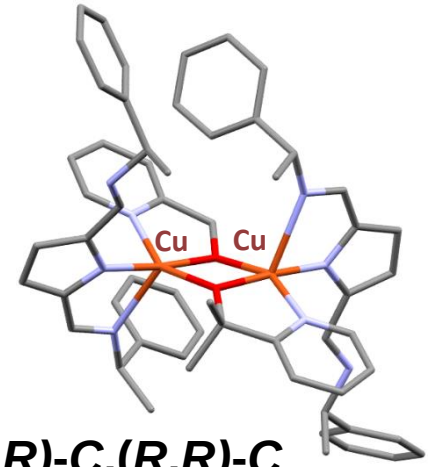


(S,S)-A,(S,S)-A

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

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

noise/signal = 8%



(R,R)-C,(R,R)-C

adapted from: Frank Schaper CHM6450-H21

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 chiralty: 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