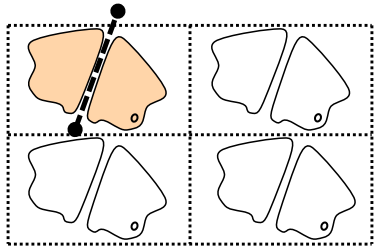
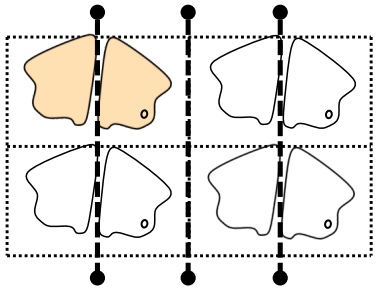
Twinning by (pseudo)merohedry

Andrey Lebedev, CCP4

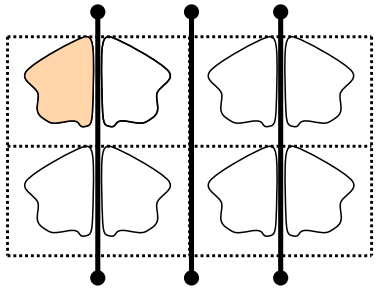
Symmetry, NCS and Pseudosymmetry



Generic Non-Crystallographic Symmetry (NCS):
- symmetry is **local** and **approximate**

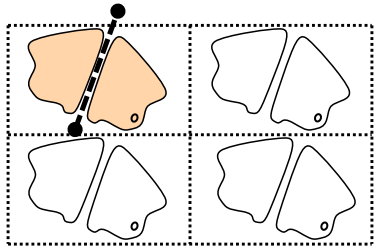


Pseudosymmetry (a limiting case of NCS)
- symmetry is **global** and **approximate**

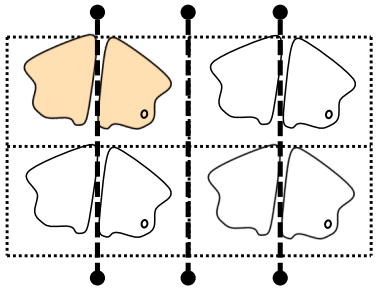


Crystallographic symmetry
- symmetry is **global** and **exact**

Symmetry, NCS and Pseudosymmetry

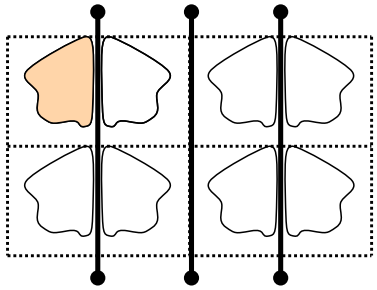


Generic Non-Crystallographic Symmetry (NCS):
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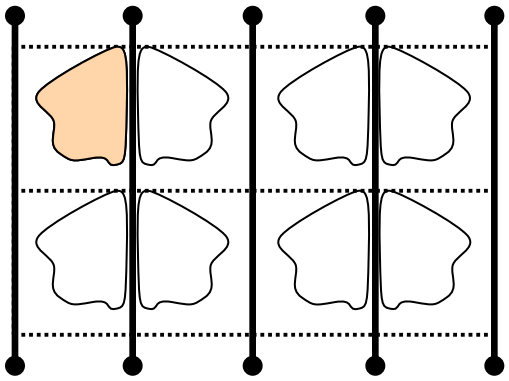
may be misinterpreted as crystallographic symmetry

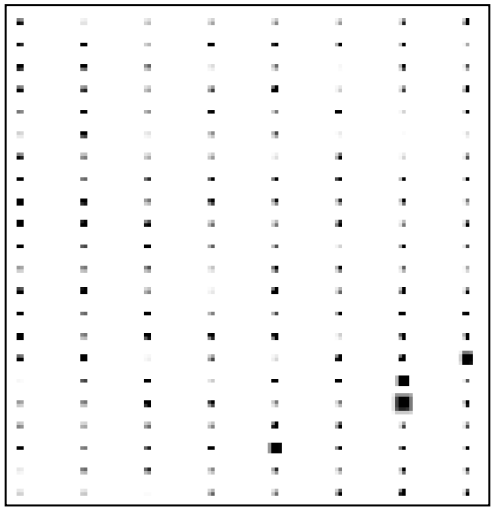


Crystallographic symmetry
- symmetry is **global** and **exact**

Pseudotranslation

Crystallographic translation





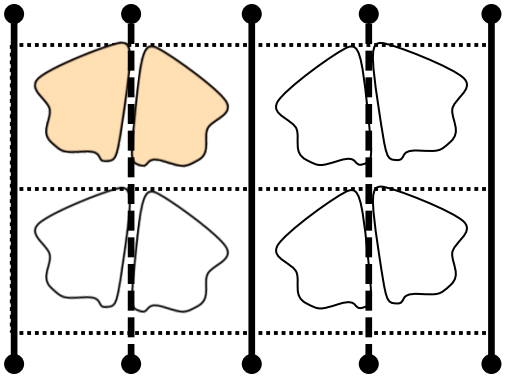
No pseudotranslation

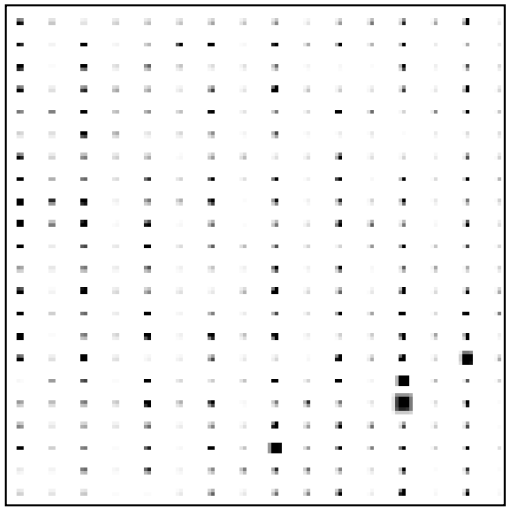
c

*c**

Crystallographic translation

Pseudo-translation





Pseudotranslation

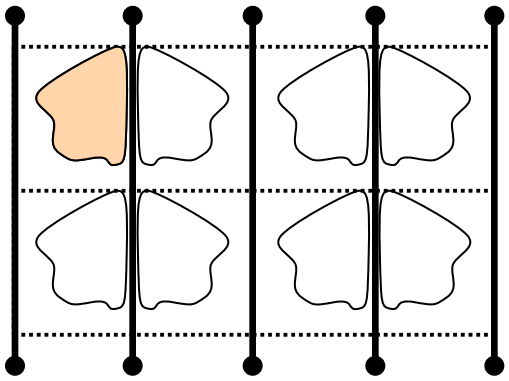
c’ = 2 *c*

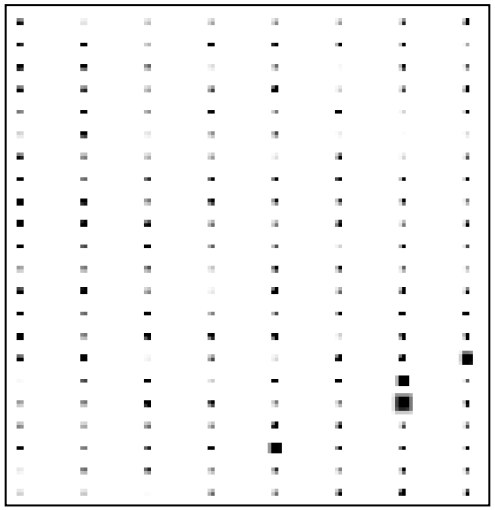
c’* = *c**/ 2

Planes 2L+1 contain weak reflections

Pseudotranslation

Crystallographic translation





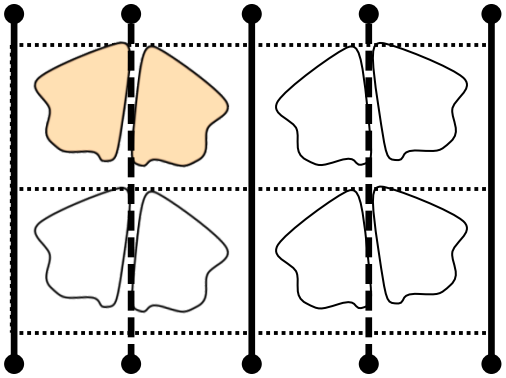
No pseudotranslation

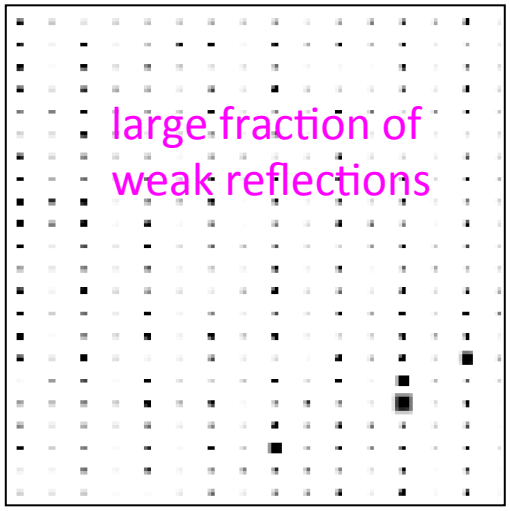
c

*c**

Crystallographic translation

Pseudo-translation





Pseudotranslation

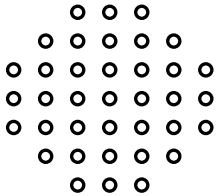
c’ = 2 *c*

c’* = *c** / 2

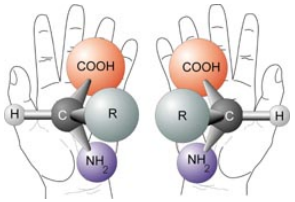
Planes 2L+1 contain weak reflections

Space group assignment (*e.g. Pointless*)

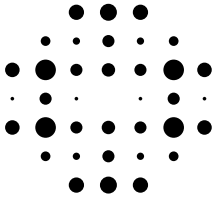
Reciprocal space lattice (positions of reflections)



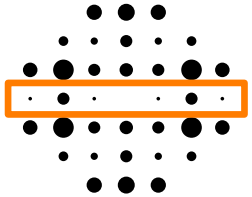
Mirror symmetry is <u>not</u> allowed in biological macromolecules

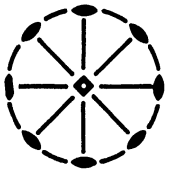


Intensities of reflections



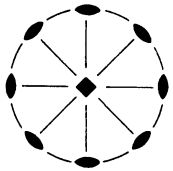
Intensities of axial reflections





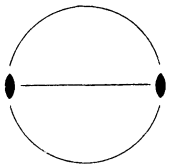
$4/mmm$

Lattice point group



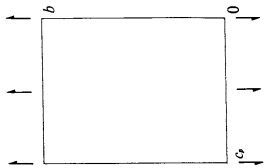
422

Highest possible crystal point group



2

Probable crystal point group



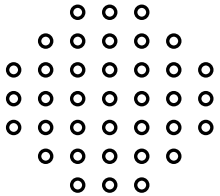
$P2_1$

Probable crystal space group(s)

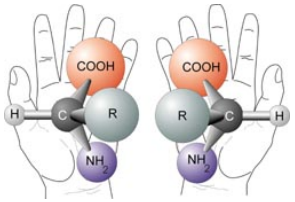
User: decision making

Space group assignment (*e.g. Pointless*)

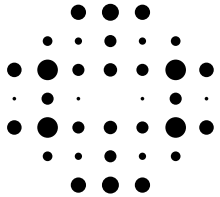
Reciprocal space lattice (positions of reflections)



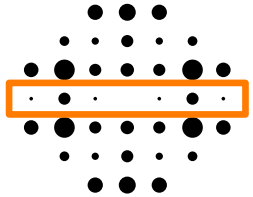
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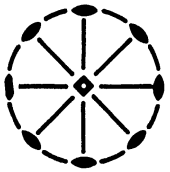
Intensities of reflections



Intensities of axial reflections

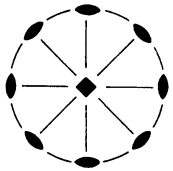


includes checks for twinning



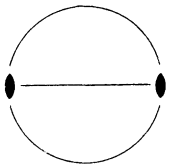
$4/mmm$

Lattice point group



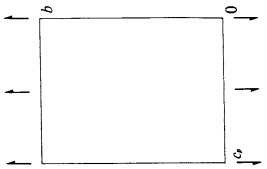
422

Highest possible crystal point group



2

Probable crystal point group



$P2_1$

Probable crystal space group(s)

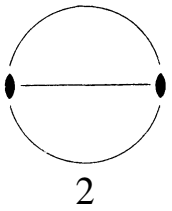
User: decision making



Lattice
point group



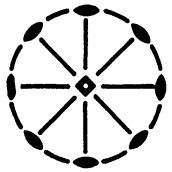




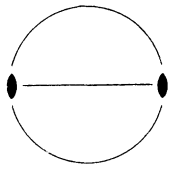
Probable
crystal point group

Online dictionary of Crystallography:
The point group of a crystal is called merohedry
if it is a subgroup of the point group of its lattice.

The word pseudomerohedry is used instead,
when the lattice has accidental high symmetry
that is not defined by crystal symmetry
(*e.g.* β=90° in P 1 2_1 1)



Lattice
point group



Probable
crystal point group

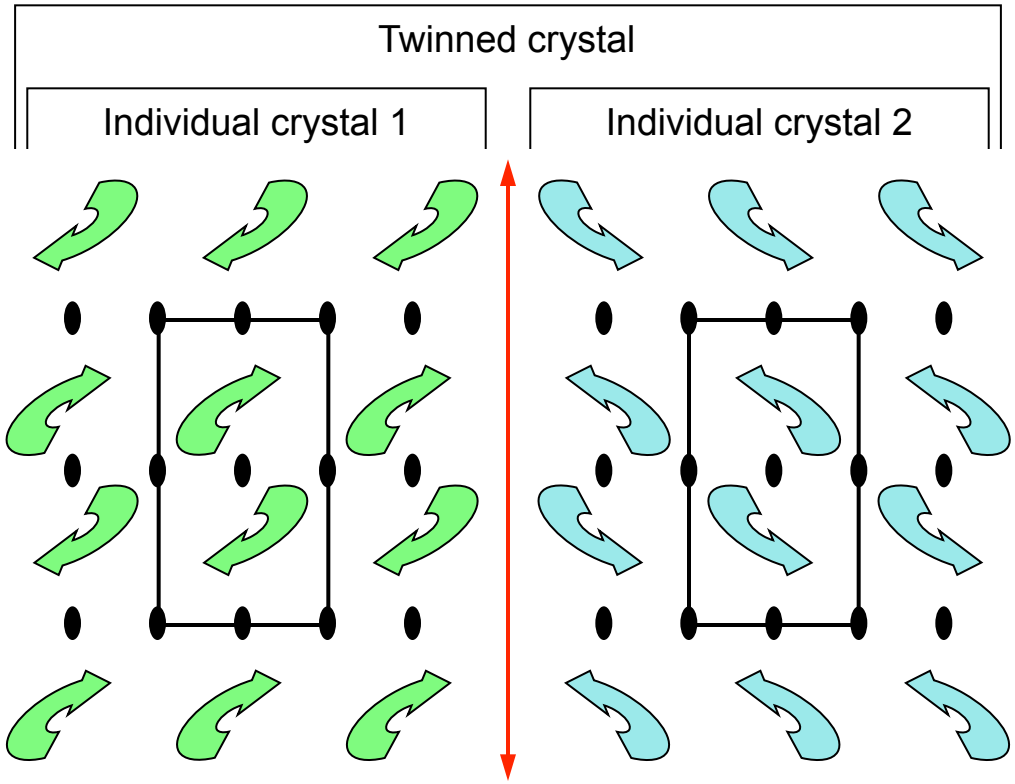
= pseudomerohedry
(here)

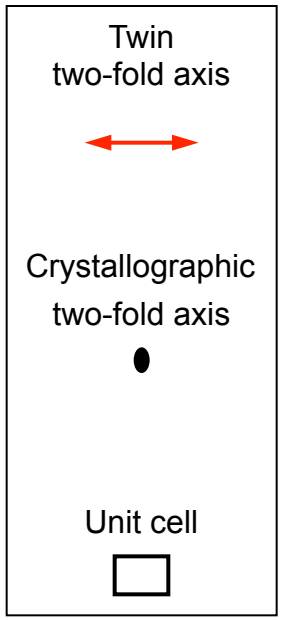
Twinning by (pseudo)merohedry

Twinning by (pseudo)merohedry

lattice in orientation 1	=	lattice in orientation 2		
crystal in orientation 1	≠	crystal in orientation 2		
crystal in orientation 1	+	crystal in orientation 2	=	Twinned crystal

Example: P2, β = 90





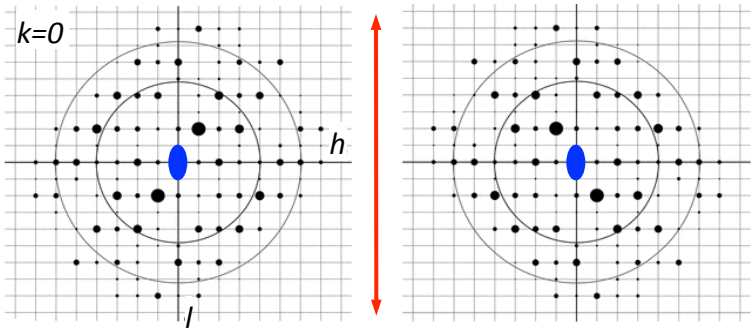
Twinning by (pseudo)merohedry

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crystal in orientation 1	≠	crystal in orientation 2		
crystal in orientation 1	+	crystal in orientation 2	=	Twinned crystal

P121, $\beta = 90$

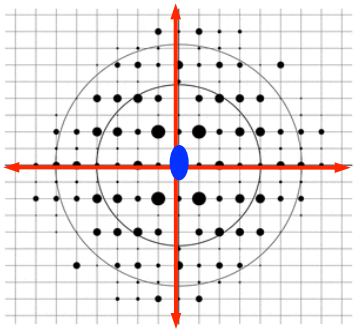
Intensities from individual crystal 1

Intensities from individual crystal 2



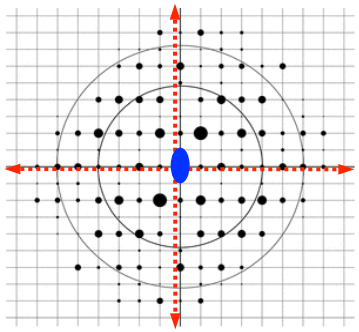
Perfect twin

(individual crystals of equal sizes)



Partial twin

(individual crystals of different sizes)



less weak reflections

Allows for twinning tests based on statistics of intensities

Twin two-fold axis

Crystallographic two-fold axis

Twinning tests

(Pseudo)merohedral twinning cannot be readily seen from diffraction images because reciprocal lattices of all the twin individuals coincide

- exactly in merohedral twins
- exactly or approximately in pseudomerohedral twins.

<u>Nevertheless:</u>

Week reflections in "twinned data" are less frequent than "in non-twinned data".

This allows for twinning tests based on statistics of normalised intensities:

- cumulative distribution of normalised intensities, Britton test, second moments tests, H-test, L-test, ...

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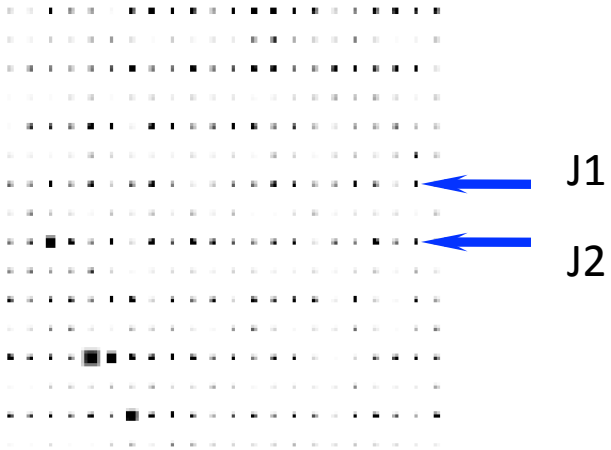
This allows for twinning tests based on statistics of normalised intensities:

- cumulative distribution of normalised intensities, Britton test, second moments tests, H-test, L-test, ...

Pseudo-translation, if present, increases relative fraction of week reflections and makes some of the twinning tests inconclusive.

L-test

$$L = | J1 - J2 | / (J1 + J2)$$

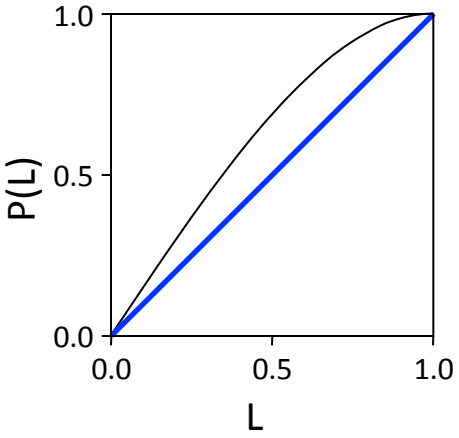


L-test is designed to be suitable for most of cases
- with and without pseudo-translation
- isotropic and anisotropic data

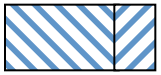
Theoretical distribution of L

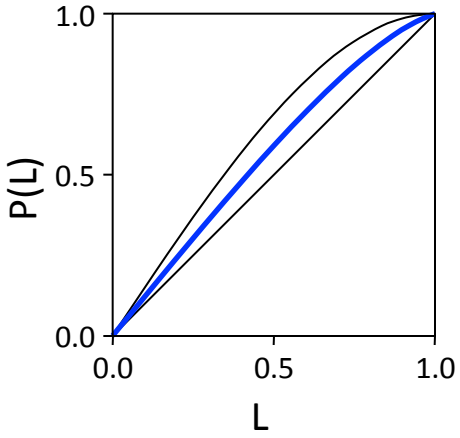
Single crystal



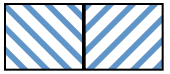


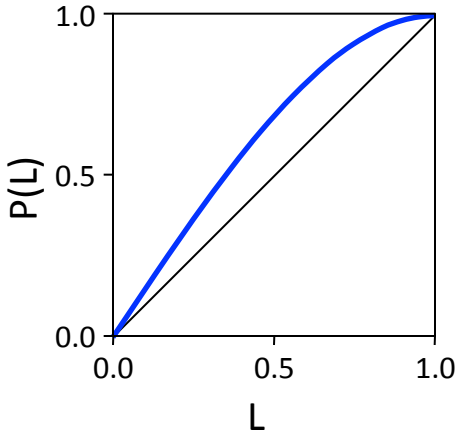
Partial twin





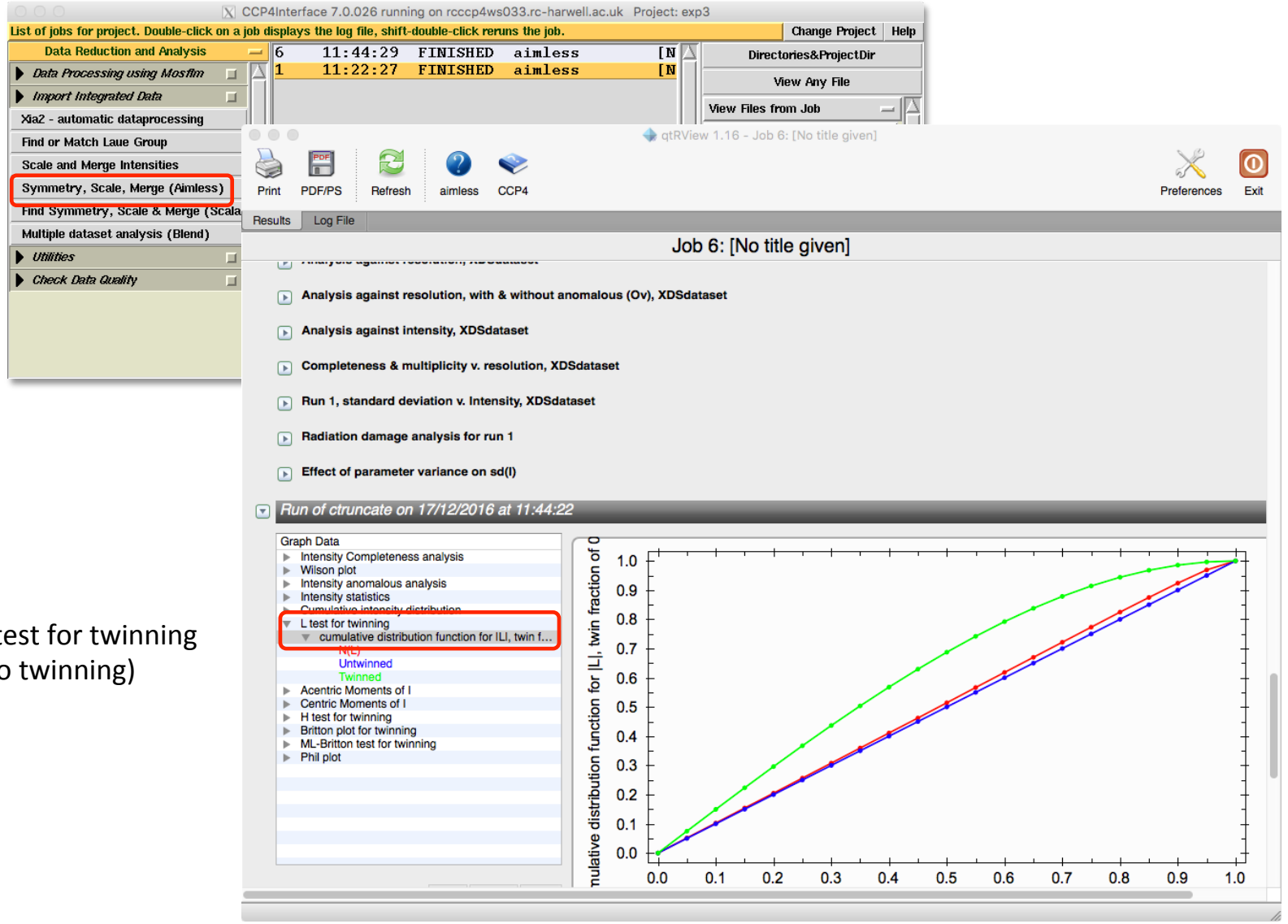
Perfect twin





CCP4i

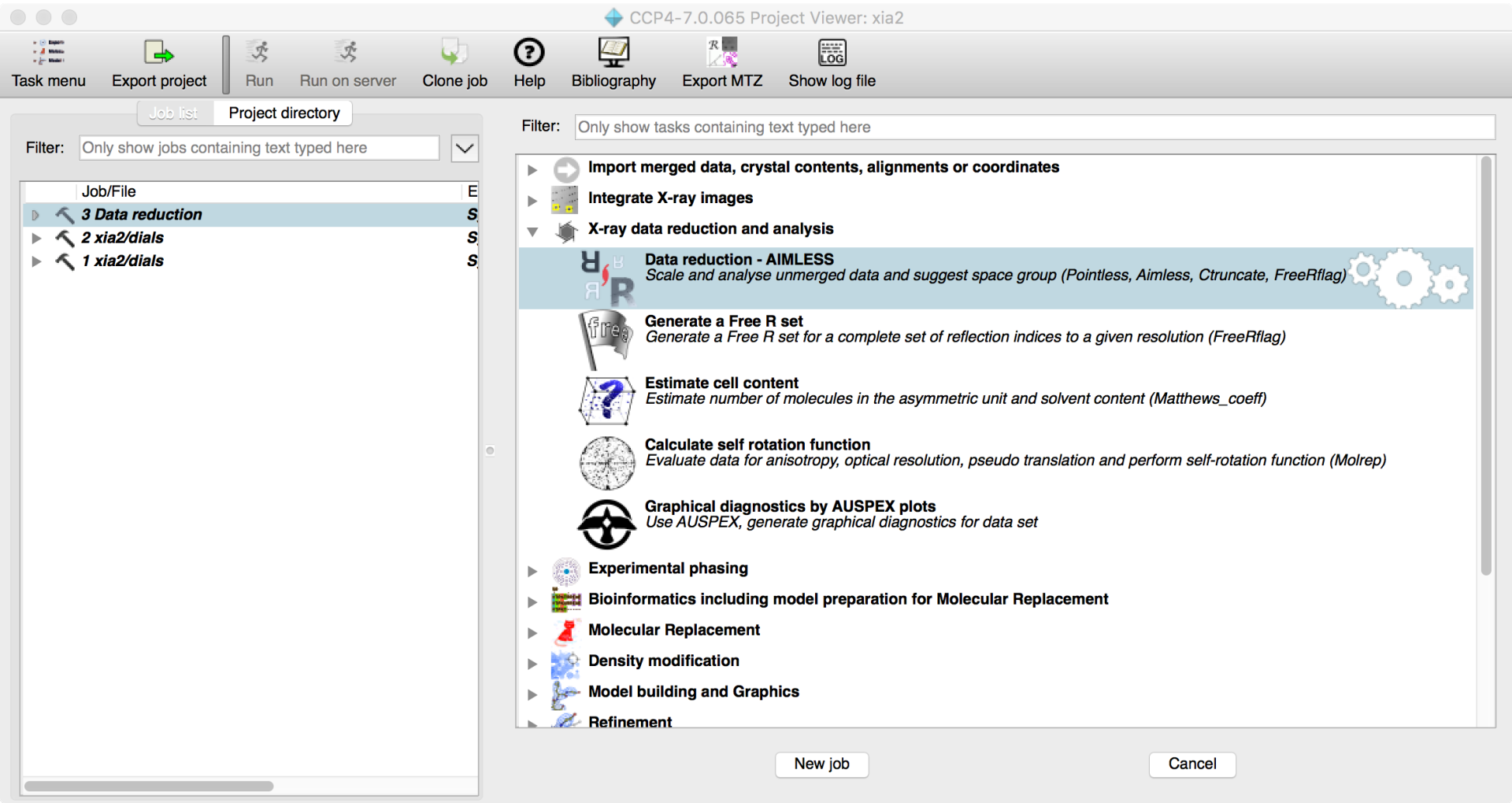
Aimless



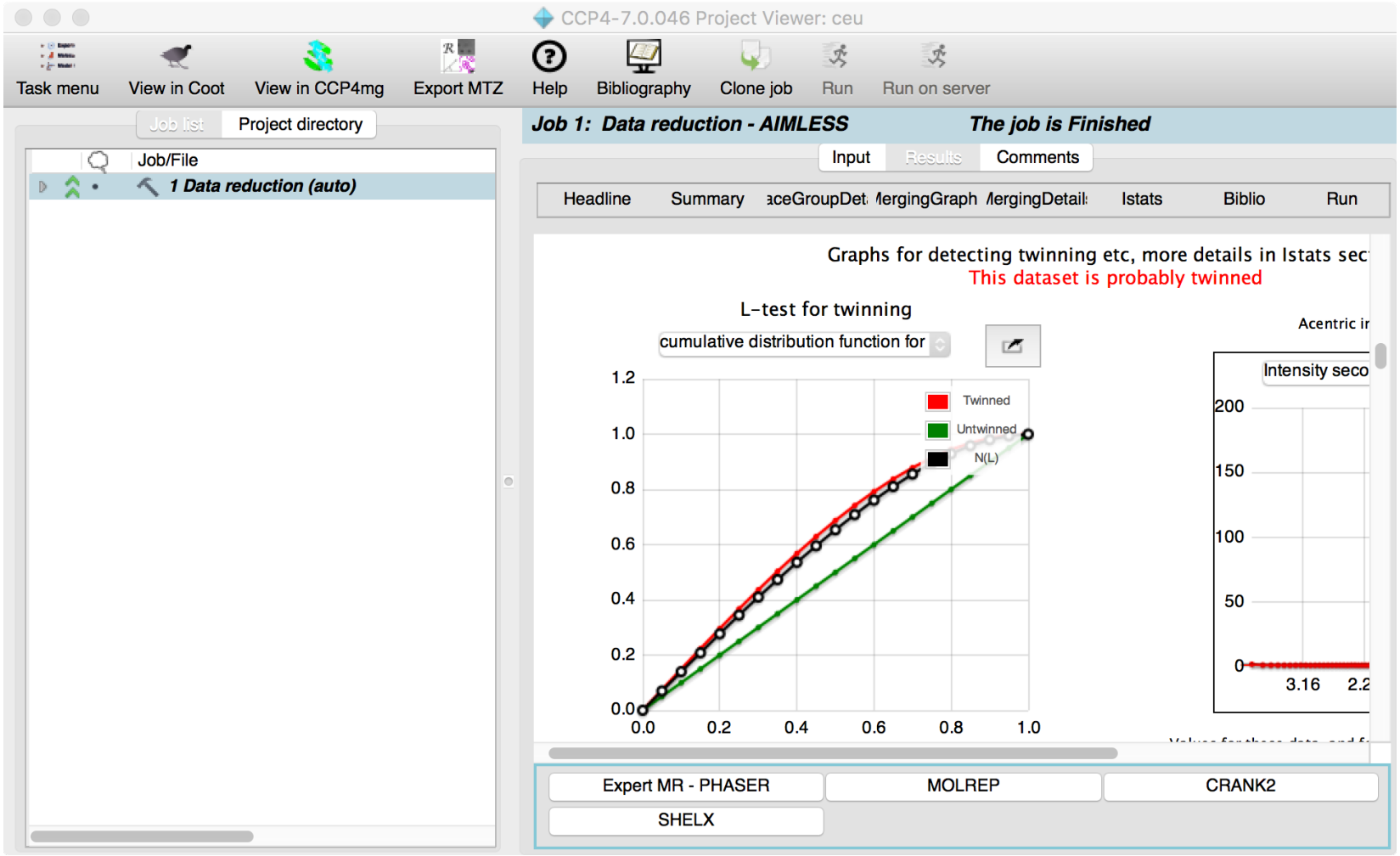
L-test for twinning
(no twinning)

CCP4i2

Data reduction - AIMLESS

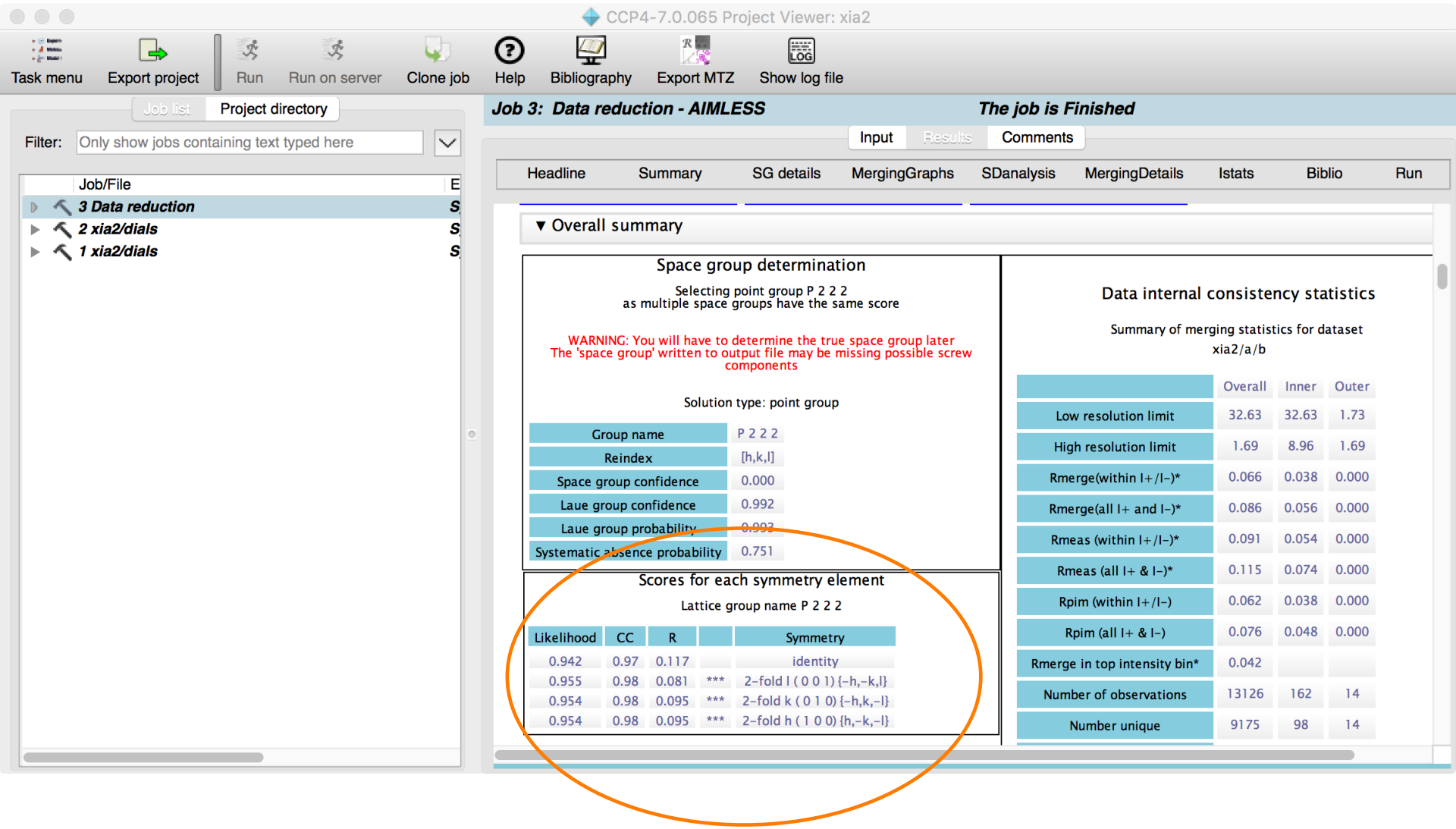


L-test plot and also a warning on possible twinning



CCP4i2

Scores for each symmetry element



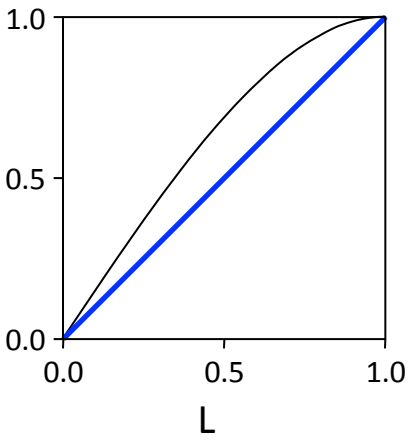
Twinning?

Scores for each symmetry element

Lattice group name P 6 2 2

Reindex operator from input to lattice: [h,k,l]

Likelihood	CC	R		Symmetry
0.952	0.97	0.146		identity
0.954	0.98	0.111	***	2-fold l (0 0 1) {-h,-k,l}
0.956	0.99	0.075	***	2-fold k (0 1 0) {-h,h+k,-l}
0.955	0.98	0.098	***	2-fold h (1 0 0) {h+k,-k,-l}
0.954	0.98	0.128	***	2-fold (1-1 0) {-k,-h,-l}
0.954	0.98	0.112	***	2-fold (2-1 0) {h,-h-k,-l}
0.956	0.99	0.100	***	2-fold (-1 2 0) {-h-k,k,-l}
0.954	0.98	0.119	***	2-fold (1 1 0) {k,h,-l}
0.953	0.97	0.105	***	3-fold l (0 0 1) {k,-h-k,l}
0.954	0.98	0.112	***	6-fold l (0 0 1) {h+k,-h,l}



Untwinned data

Scores for each symmetry element

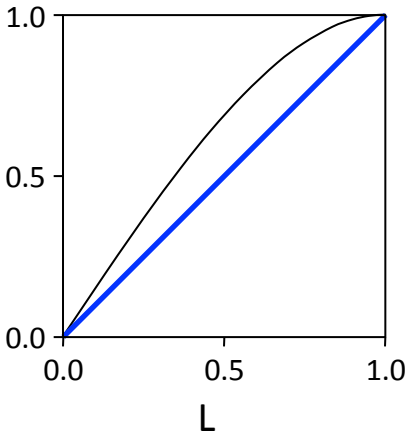
Lattice group name P 6 2 2

Reindex operator from input to lattice: [h,k,l]

Likelihood	CC	R		Symmetry
0.952	0.97	0.146		identity
0.954	0.98	0.111	***	2-fold l (0 0 1) {-h,-k,l}
0.956	0.99	0.075	***	2-fold k (0 1 0) {-h,h+k,-l}
0.955	0.98	0.098	***	2-fold h (1 0 0) {h+k,-k,-l}
0.954	0.98	0.128	***	2-fold (1-1 0) {-k,-h,-l}
0.954	0.98	0.112	***	2-fold (2-1 0) {h,-h-k,-l}
0.956	0.99	0.100	***	2-fold (-1 2 0) {-h-k,k,-l}
0.954	0.98	0.119	***	2-fold (1 1 0) {k,h,-l}
0.953	0.97	0.105	***	3-fold l (0 0 1) {k,-h-k,l}
0.954	0.98	0.112	***	6-fold l (0 0 1) {h+k,-h,l}

Single crystal





This is a **single** crystal, **P622** or **P6$_1$22** or **P6$_2$22** or ...

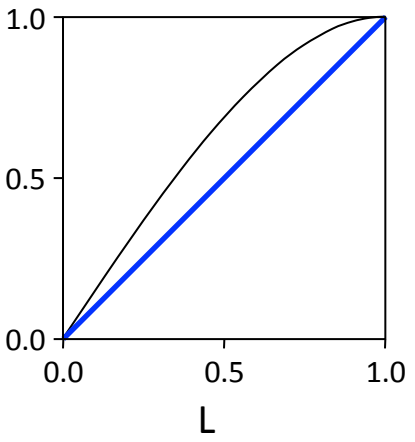
Twinning?

Scores for each symmetry element

Lattice group name P 6 2 2

Reindex operator from input to lattice: [h,k,l]

Likelihood	CC	R		Symmetry
0.898	0.90	0.060		identity
0.079	0.23	0.678		2-fold l (0 0 1) {-h,-k,l}
0.778	0.75	0.169	**	2-fold k (0 1 0) {-h,h+k,-l}
0.819	0.77	0.163	**	2-fold h (1 0 0) {h+k,-k,-l}
0.824	0.77	0.163	**	2-fold (1-1 0) {-k,-h,-l}
0.077	0.22	0.675		2-fold (2-1 0) {h,-h-k,-l}
0.079	0.22	0.674		2-fold (-1 2 0) {-h-k,k,-l}
0.080	0.23	0.675		2-fold (1 1 0) {k,h,-l}
0.903	0.88	0.089	***	3-fold l (0 0 1) {k,-h-k,l}
0.078	0.22	0.619		6-fold l (0 0 1) {h+k,-h,l}



Pseudosymmetry

Scores for each symmetry element

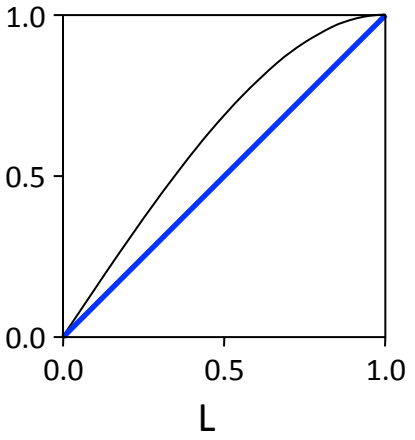
Lattice group name P 6 2 2

Reindex operator from input to lattice: [h,k,l]

Likelihood	CC	R		Symmetry
0.898	0.90	0.060		identity
0.079	0.23	0.678		2-fold l (0 0 1) {-h,-k,l}
0.778	0.75	0.169	**	2-fold k (0 1 0) {-h,h+k,-l}
0.819	0.77	0.163	**	2-fold h (1 0 0) {h+k,-k,-l}
0.824	0.77	0.163	**	2-fold (1-1 0) {-k,-h,-l}
0.077	0.22	0.675		2-fold (2-1 0) {h,-h-k,-l}
0.079	0.22	0.674		2-fold (-1 2 0) {-h-k,k,-l}
0.080	0.23	0.675		2-fold (1 1 0) {k,h,-l}
0.903	0.88	0.089	***	3-fold l (0 0 1) {k,-h-k,l}
0.078	0.22	0.619		6-fold l (0 0 1) {h+k,-h,l}

Single crystal





This is a **single** crystal, **P3** or **P3$_1$** or **P3$_2$**
There is a pseudosymmetry

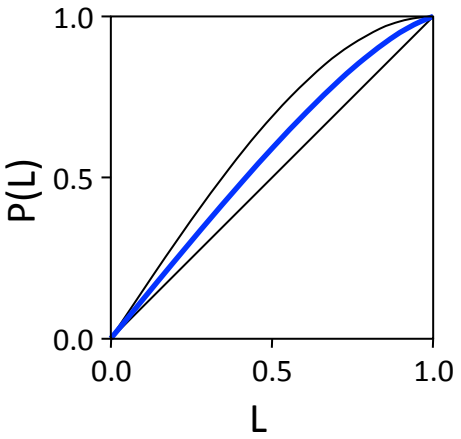
Twinning?

Scores for each symmetry element

Lattice group name P 6 2 2

Reindex operator from input to lattice: [h,k,l]

Likelihood	CC	R		Symmetry
0.898	0.90	0.060		identity
0.079	0.23	0.678		2-fold l (0 0 1) {-h,-k,l}
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0.819	0.77	0.163	**	2-fold h (1 0 0) {h+k,-k,-l}
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0.077	0.22	0.675		2-fold (2-1 0) {h,-h-k,-l}
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0.080	0.23	0.675		2-fold (1 1 0) {k,h,-l}
0.903	0.88	0.089	***	3-fold l (0 0 1) {k,-h-k,l}
0.078	0.22	0.619		6-fold l (0 0 1) {h+k,-h,l}



Partial twin

Scores for each symmetry element

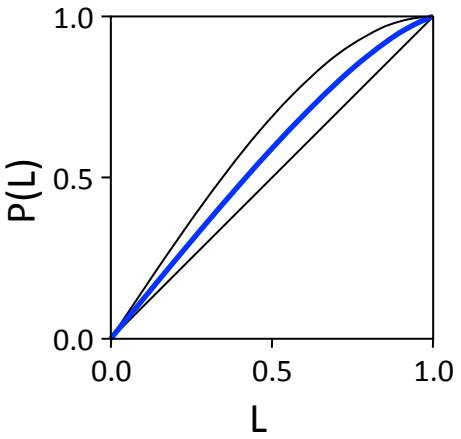
Lattice group name P 6 2 2

Reindex operator from input to lattice: [h,k,l]

Likelihood	CC	R		Symmetry
0.898	0.90	0.060		identity
0.079	0.23	0.678		2-fold l (0 0 1) {-h,-k,l}
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0.903	0.88	0.089	***	3-fold l (0 0 1) {k,-h-k,l}
0.078	0.22	0.619		6-fold l (0 0 1) {h+k,-h,l}

Partial twin





This is a partial twin, P3 or $P3_1$ or $P3_2$
There may be a pseudosymmetry

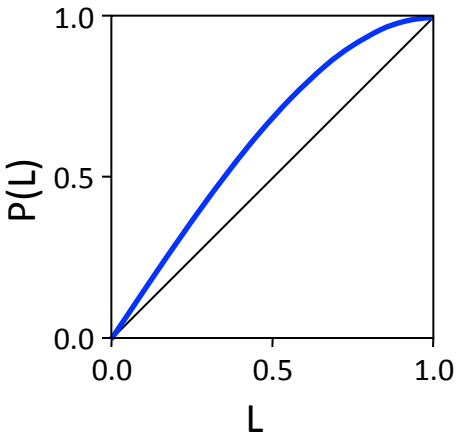
Twinning?

Scores for each symmetry element

Lattice group name P 6 2 2

Reindex operator from input to lattice: [h,k,l]

Likelihood	CC	R		Symmetry
0.952	0.97	0.146		identity
0.954	0.98	0.111	***	2-fold l (0 0 1) {-h,-k,l}
0.956	0.99	0.075	***	2-fold k (0 1 0) {-h,h+k,-l}
0.955	0.98	0.098	***	2-fold h (1 0 0) {h+k,-k,-l}
0.954	0.98	0.128	***	2-fold (1-1 0) {-k,-h,-l}
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0.954	0.98	0.119	***	2-fold (1 1 0) {k,h,-l}
0.953	0.97	0.105	***	3-fold l (0 0 1) {k,-h-k,l}
0.954	0.98	0.112	***	6-fold l (0 0 1) {h+k,-h,l}



Perfect twin

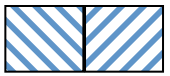
Scores for each symmetry element

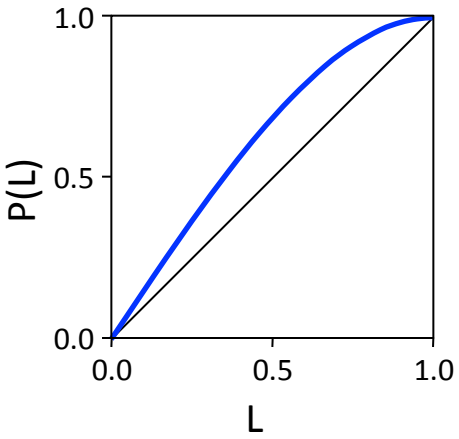
Lattice group name P 6 2 2

Reindex operator from input to lattice: [h,k,l]

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0.955	0.98	0.098	***	2-fold h (1 0 0) {h+k,-k,-l}
0.954	0.98	0.128	***	2-fold (1-1 0) {-k,-h,-l}
0.954	0.98	0.112	***	2-fold (2-1 0) {h,-h-k,-l}
0.956	0.99	0.100	***	2-fold (-1 2 0) {-h-k,k,-l}
0.954	0.98	0.119	***	2-fold (1 1 0) {k,h,-l}
0.953	0.97	0.105	***	3-fold l (0 0 1) {k,-h-k,l}
0.954	0.98	0.112	***	6-fold l (0 0 1) {h+k,-h,l}

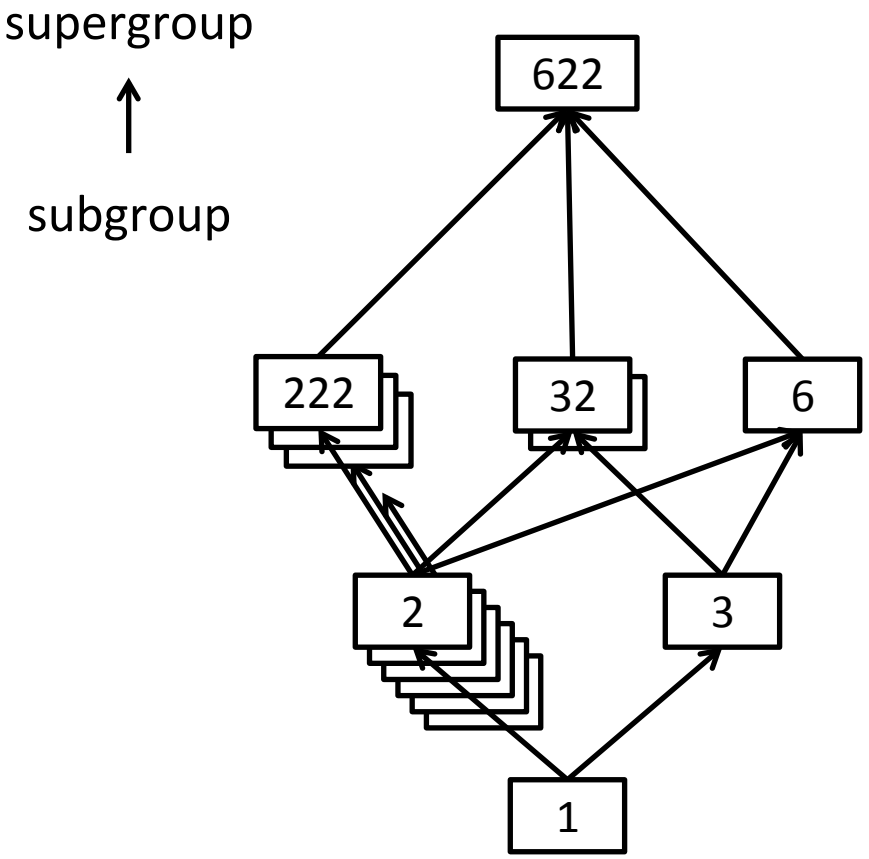
Perfect twin





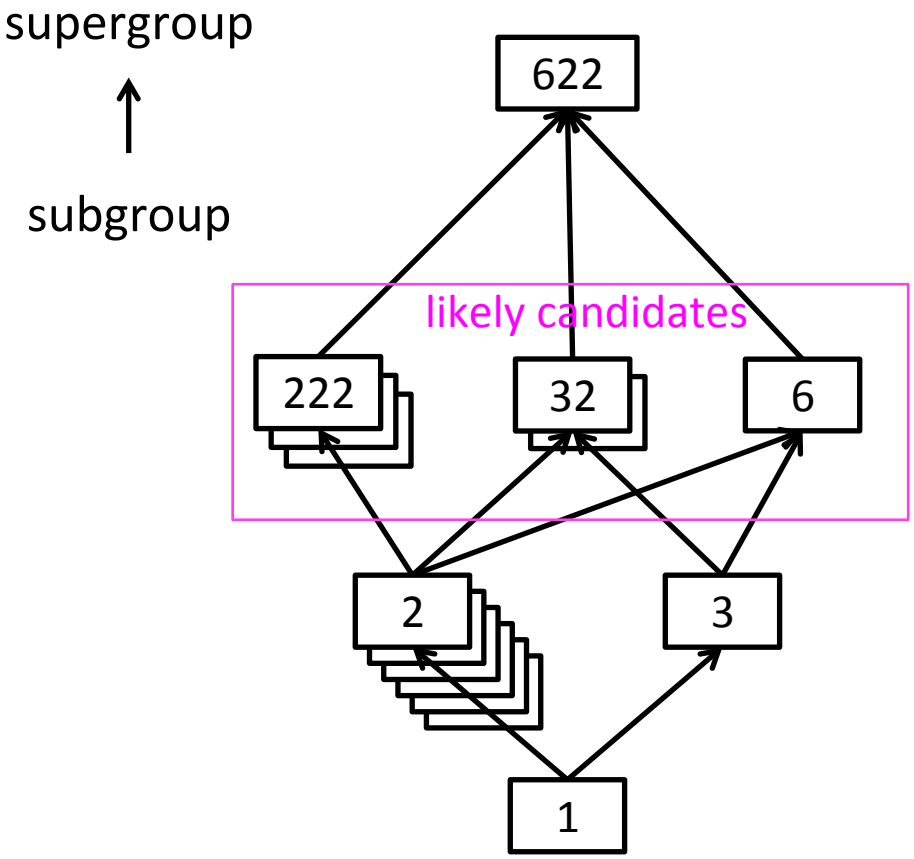
This is likely to be a perfectly twinned crystal.
Space group is quite uncertain at this point.
Most likely:
the space group is NOT $P6_X22$
but one of its subgroups:
$P6_X$, $P3_X21$, $P3_X12$, $C222_X$, or even P3 *etc.*

Subgroups of the point group 622



- To test all possibilities:
  - scale and merge data in each point group
  - run Phaser in each point group and ask to try all the corresponding space groups
  - E.g. for point group 3, Phaser will try P 3, P 3_1, P 3_2.

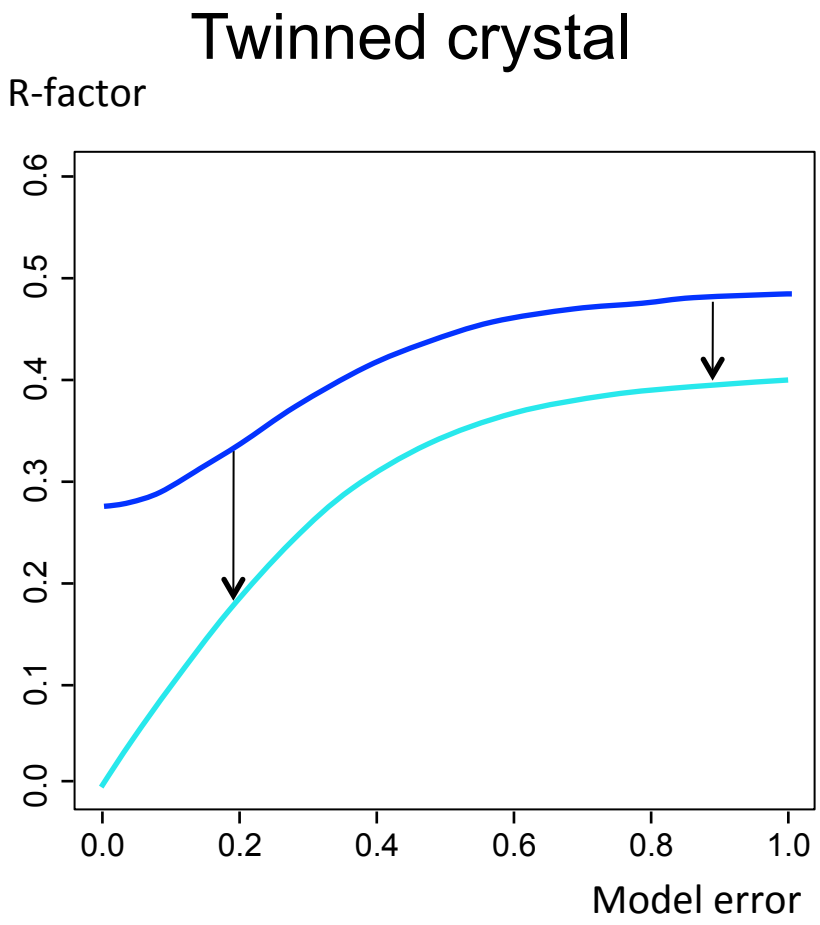
Subgroups of the point group 622

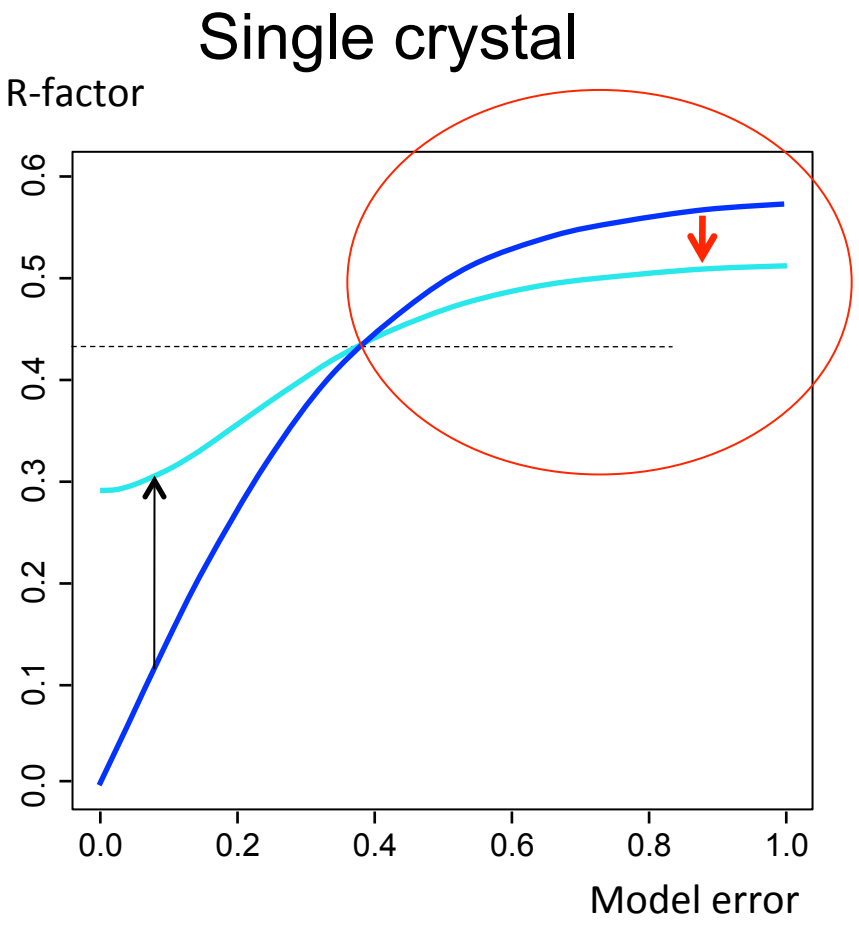


- To test all possibilities:
  - scale and merge data in each point group
  - run Phaser in each point group and ask to try all the corresponding space groups
  - E.g. for point group 3, Phaser will try P 3, P 3_1, P 3_2.

Switching to twin refinement

Twin refinement: Off On





Mini Europe

Brussels



Mini Europe



Like 2 Tweet

#BrusselsInView: No #Brexit for Brussels' Mini Europe attraction

EU Reporter Correspondent | June 20, 2017 | 0 Comments



The UK may have made known its decision to leave the EU, but there is some good news for Remainers: the British monuments at Brussels' Mini Europe family park will stay – for the time being at least.

The fear was that it would not just be the EU that will shrink in the event of Brexit, but that several British models would have to be removed from Mini Europe. It had been feared that the British landmarks would have to go if a majority of the Brits decided to leave the EU. Of course, 52% of Brits did just that in the 23 June 2016 EU Referendum.

But there is good news for those who feared a British exit at the park where landmark European buildings are created in miniature. "Mini Europe will not remove its models of British landmarks," said Thierry Meeùs, director of the popular Brussels tourist attraction. "The Brexit negotiations will take at least two years. In the meantime, (the UK) remains a member of the EU, and therefore so do our monuments."

Apart from nostalgic reasons there are good economic grounds for keeping Big Ben

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Things you don't want to see in your diffraction data

(Why we do want to see diffraction patterns in 3D)

Andrey Lebedev, CCP4

Do images indicate crystal pathologies?

If yes:

- successful structure solution is less likely
- even if structure is solved, bad refinement stats are very likely
  - explain in the manuscript (e.g. picture from dials.reciprocal_lattice_viewer)
- consider the option of finding better crystallisation conditions

A few examples are presented in this talk

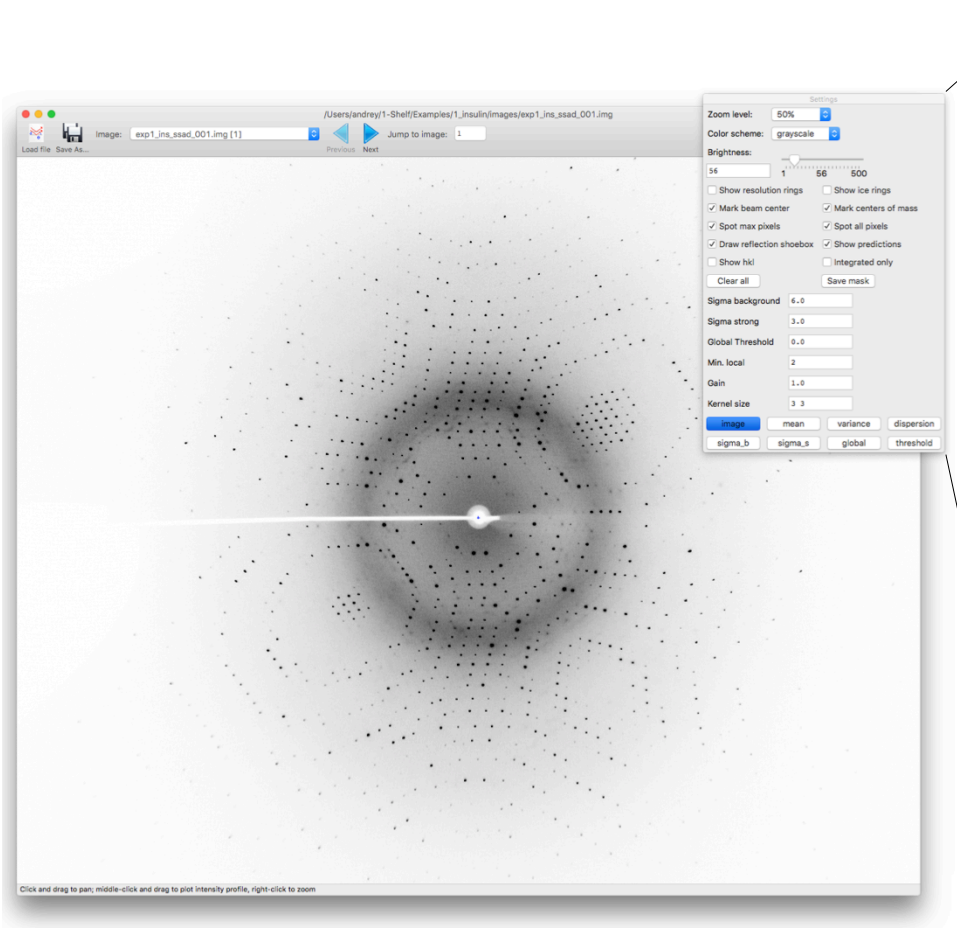
If explanation is not clear – look at pictures anyway

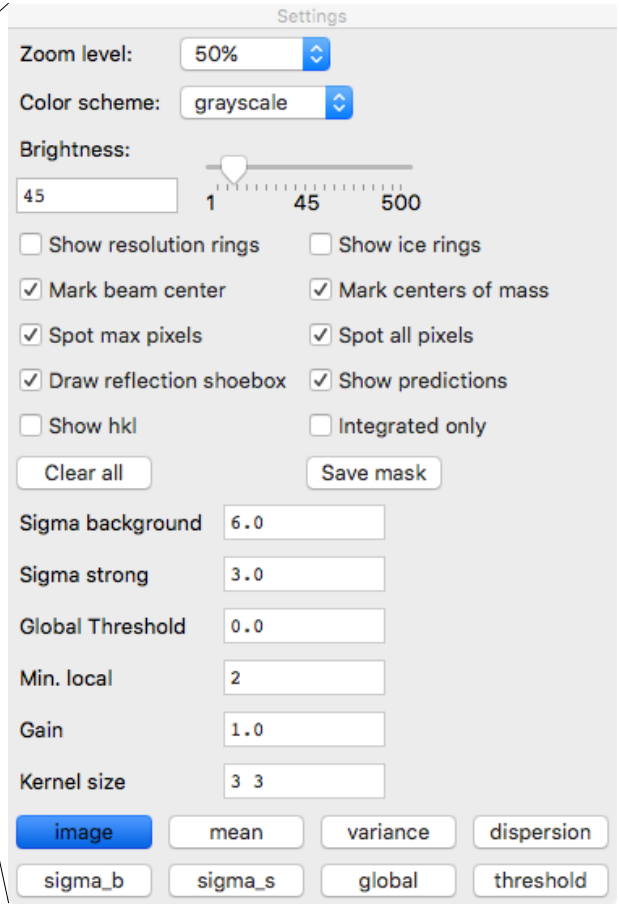
- Graphical facilities in DIALS
- Inter-grown crystals
- OD-structures
- Partially disordered OD-structures
- Pseudo-translation

Import and image viewer

Cubic insulin, the experiment 1 from HZB MX tutorial

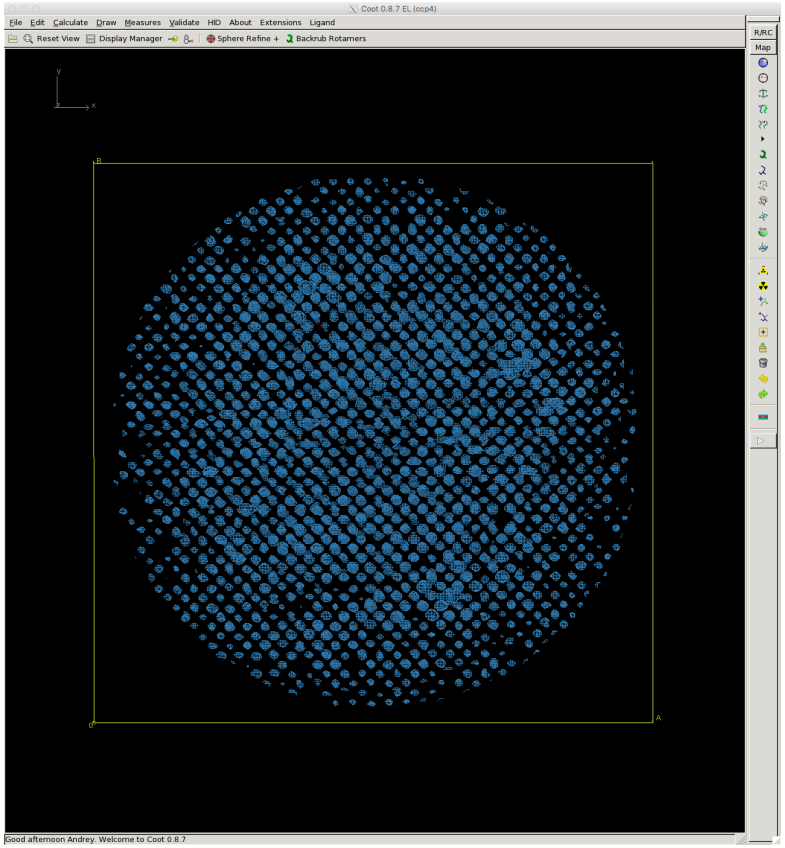
```
dials.import template=images/exp1_ins_ssad_###.img
dials.image_viewer datablock.json
```

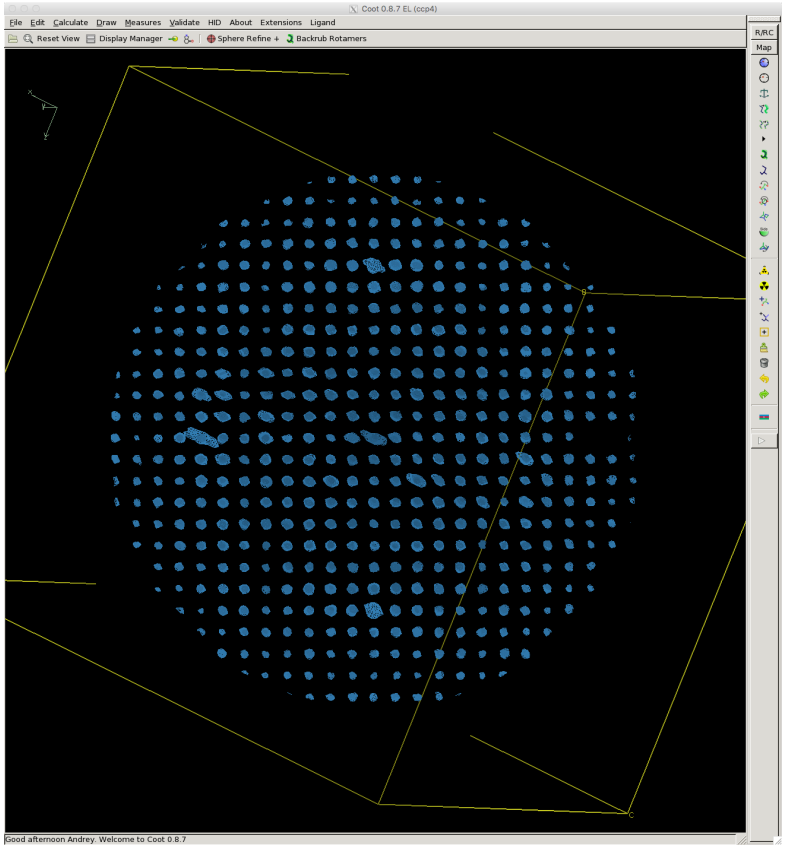




Sweep of images as 3D map

```
dials.rs_mapper map_file=output.ccp4 datablock.json
coot --map output.ccp4
```

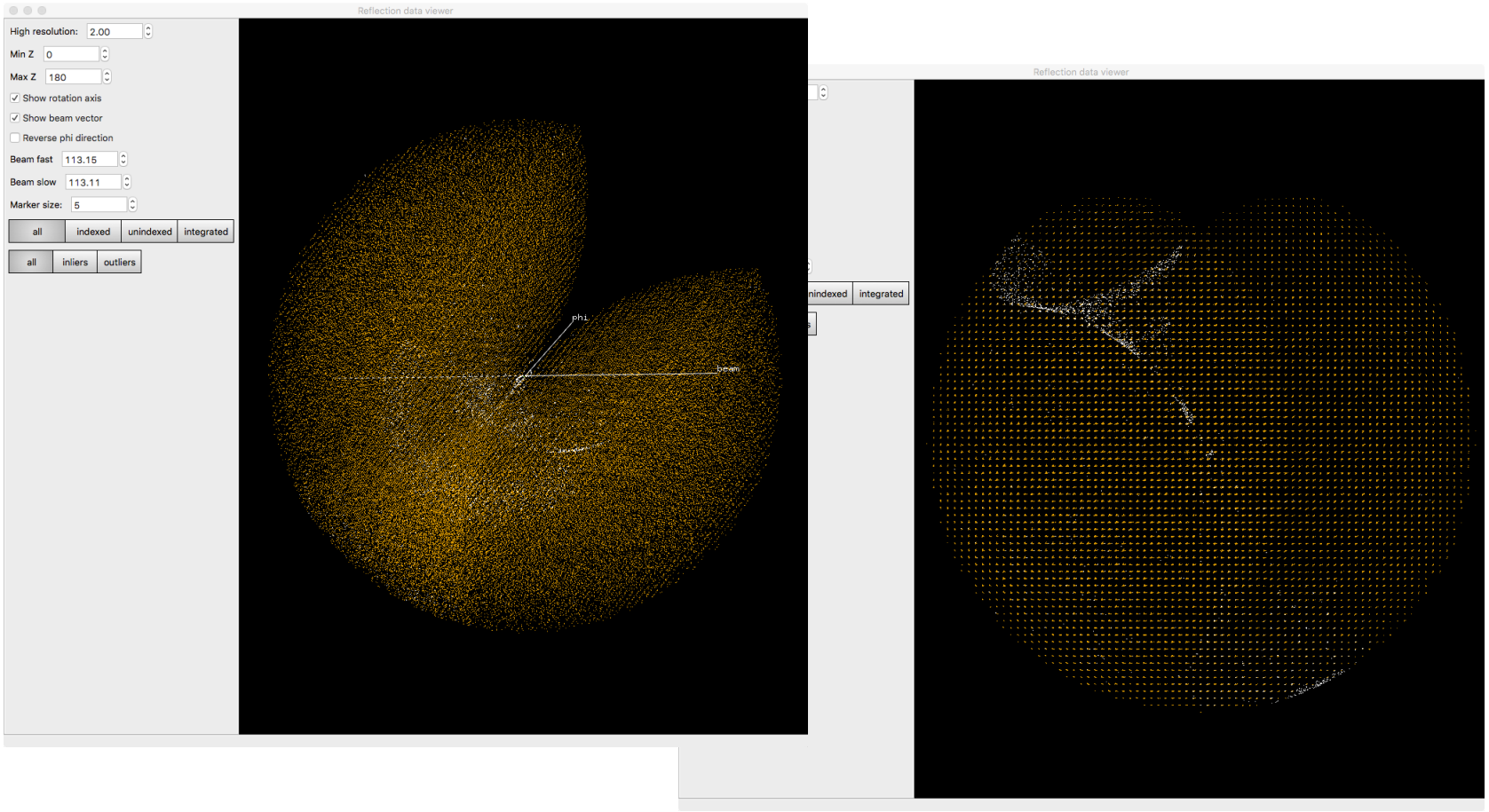




PyMol can be used as well

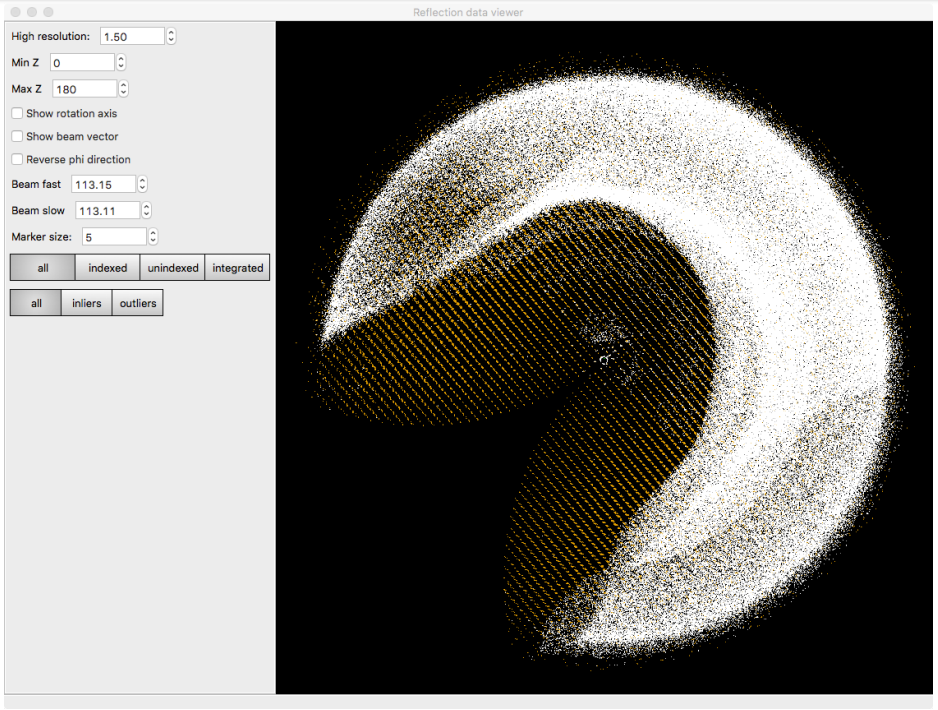
Sweep of images: spots positions in 3D

```
dials.find_spots datablock.json
dials.reciprocal_lattice_viewer datablock.json strong.pickle
```



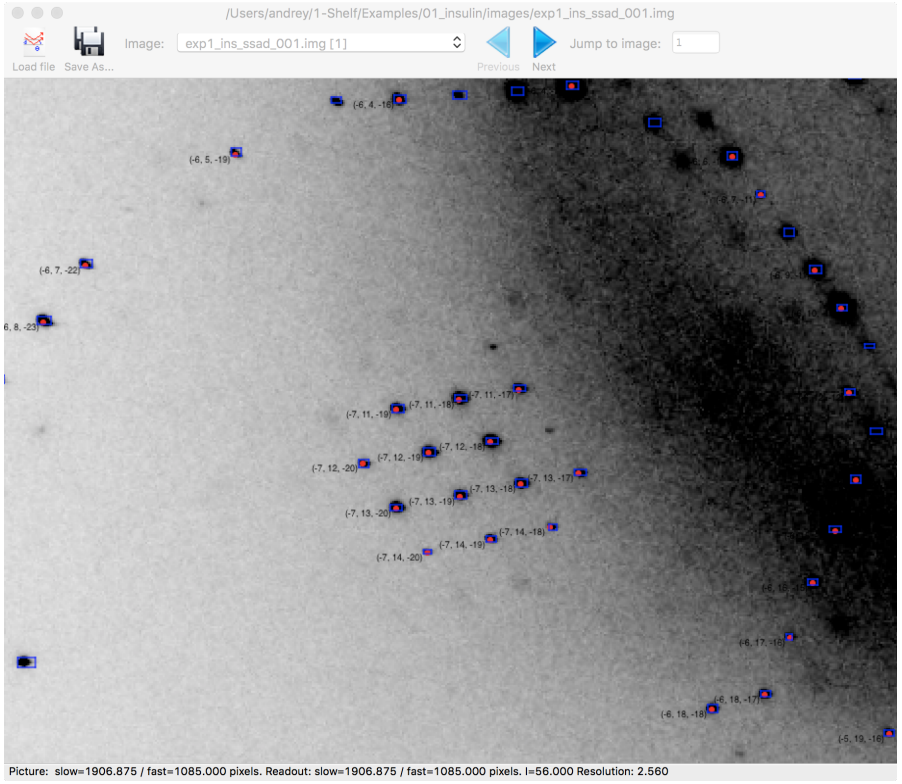
More details are available after indexing

```
dials.index datablock.json strong.pickle
dials.refine experiments.json indexed.pickle scan_varying=True
dials.reciprocal_lattice_viewer refined.pickle refined_experiments.json
dials.image_viewer datablock.json
```



orange: indexed
white: not indexed

shoeboxes, predictions



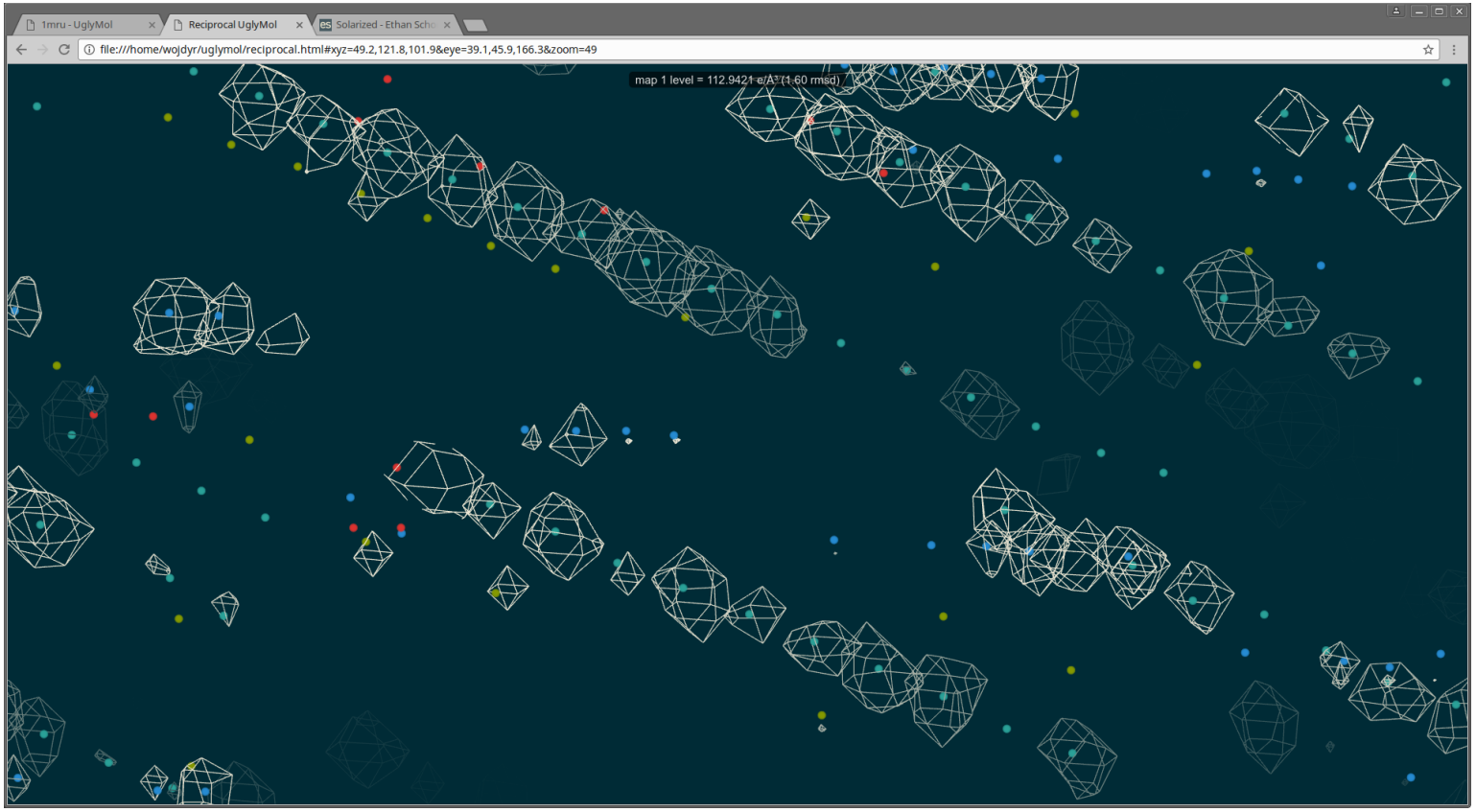
Visualising XDS results

- XDS results can be imported to DIALS and visualised in 3D

```
dials.import_xds xds/
dials.import_xds method=reflections xds/SPOT.XDS
dials.reciprocal_lattice_viewer experiments.json spot_xds.pickle
```

UglyMol

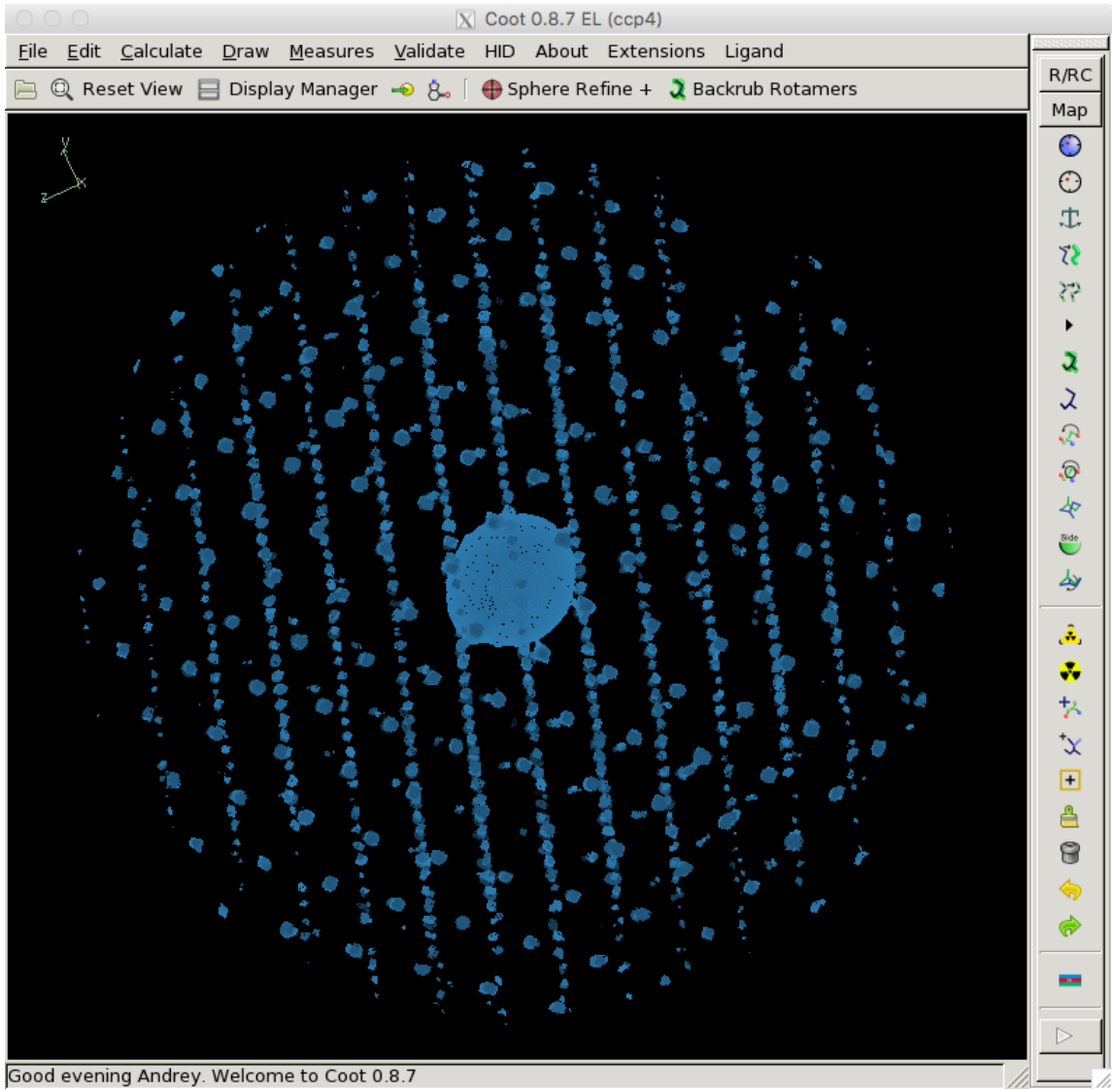
- Viewer for web-browsers combining both views, intensities as maps and spots as dots (by Marcin Wojdyr, CCP4, https://github.com/uglymol)
  - xia2 task in ccp4cloud



Inter-grown crystals (multi-lattice data)

Example of random crystal inter-growth

```
dials.rs_mapper ...
coot --map output.ccp4
```



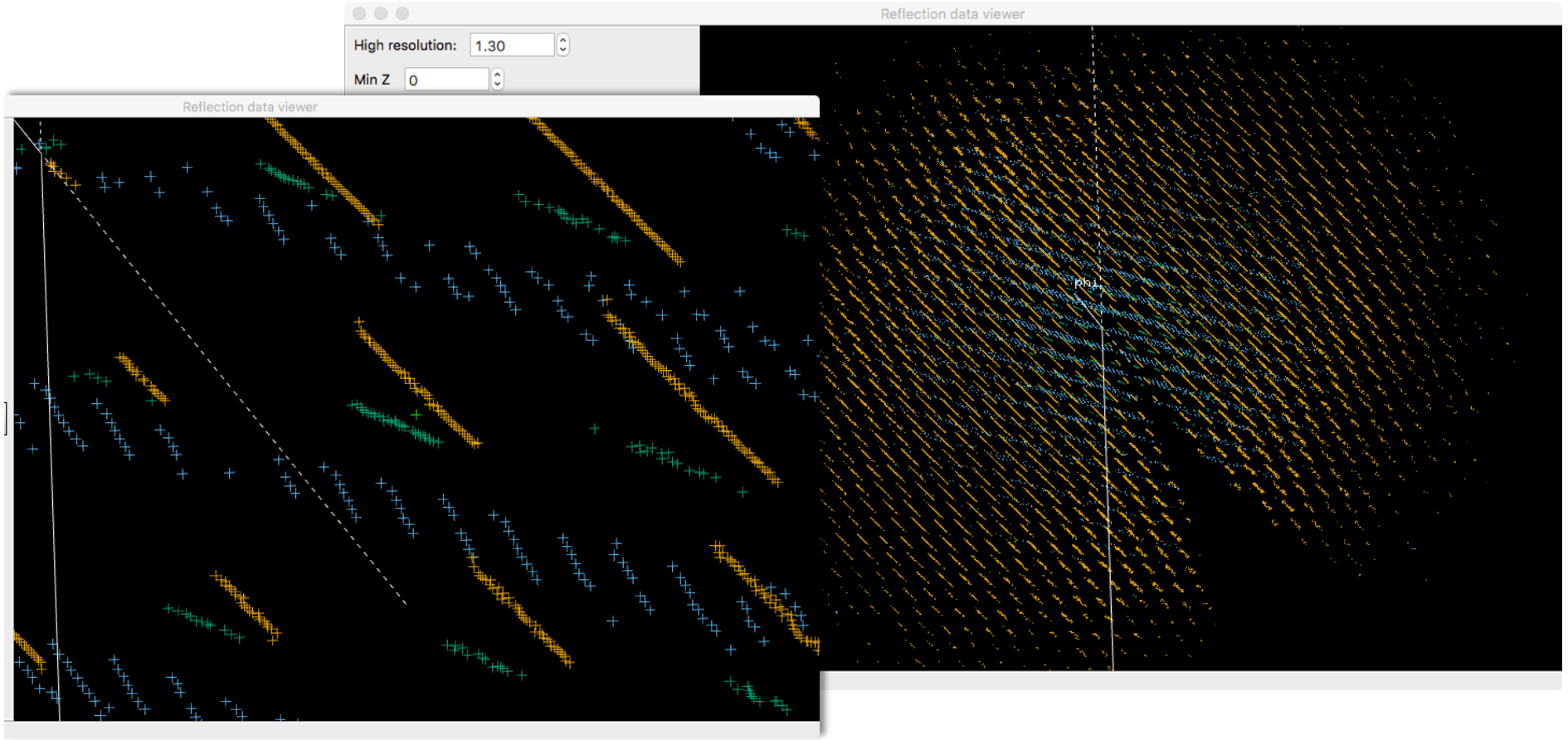
beta-lactamase OXA-163
PDB ID 4s2m

Data from Vlatko Stojanoski
Baylor College of Medicine

Example of random crystal inter-growth

```
dials.index datablock.json strong.pickle max_lattices=3 hkl_tolerance=0.1
dials.reciprocal_lattice_viewer refined.pickle refined_experiments.json
```

- different colour means different lattice
- individual lattices can be switched off and on



Example of random crystal inter-growth

Easy case:

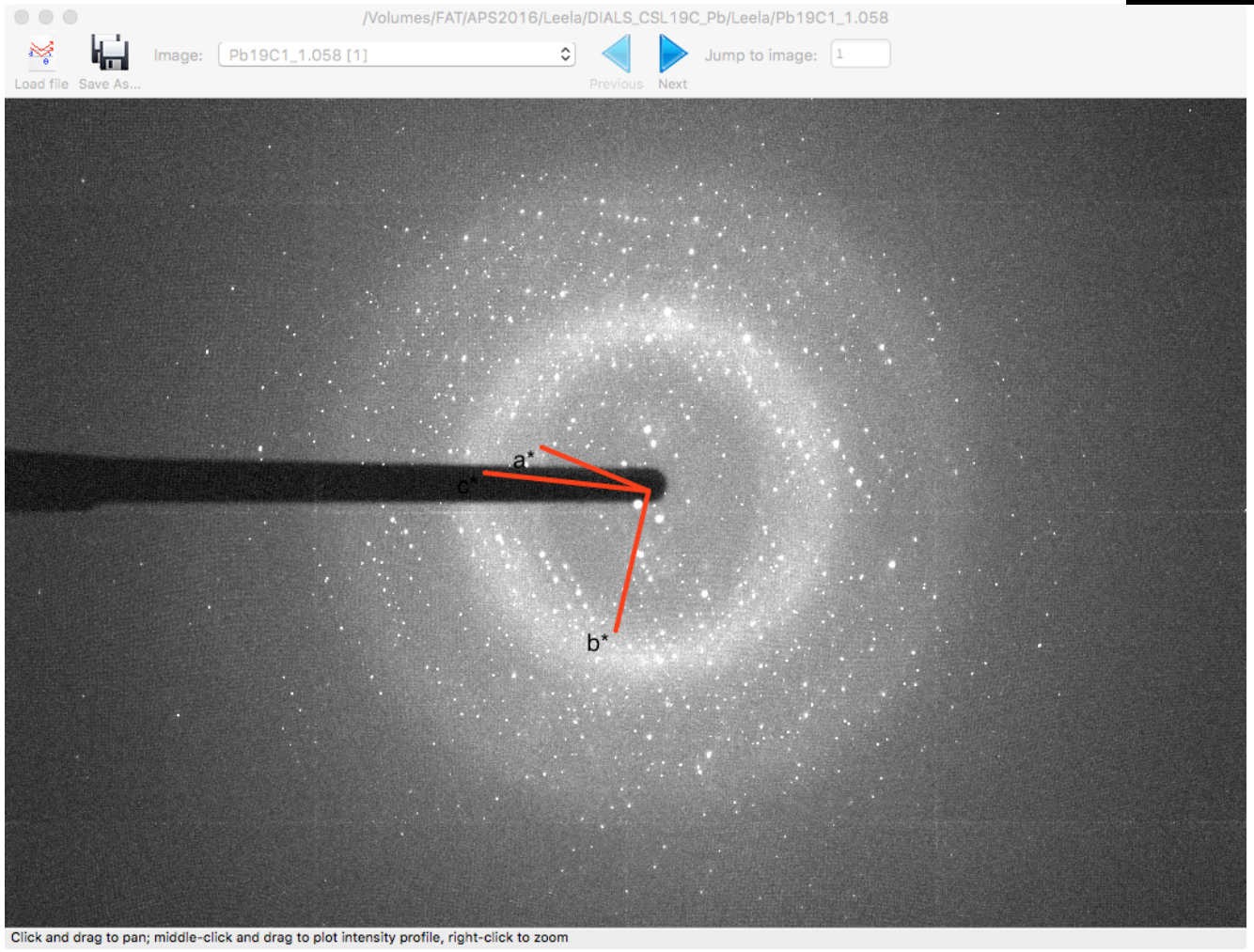
- Lattices are mainly separated, with only very few reflection overlapping
- Signal from one lattice is substantially higher than from others

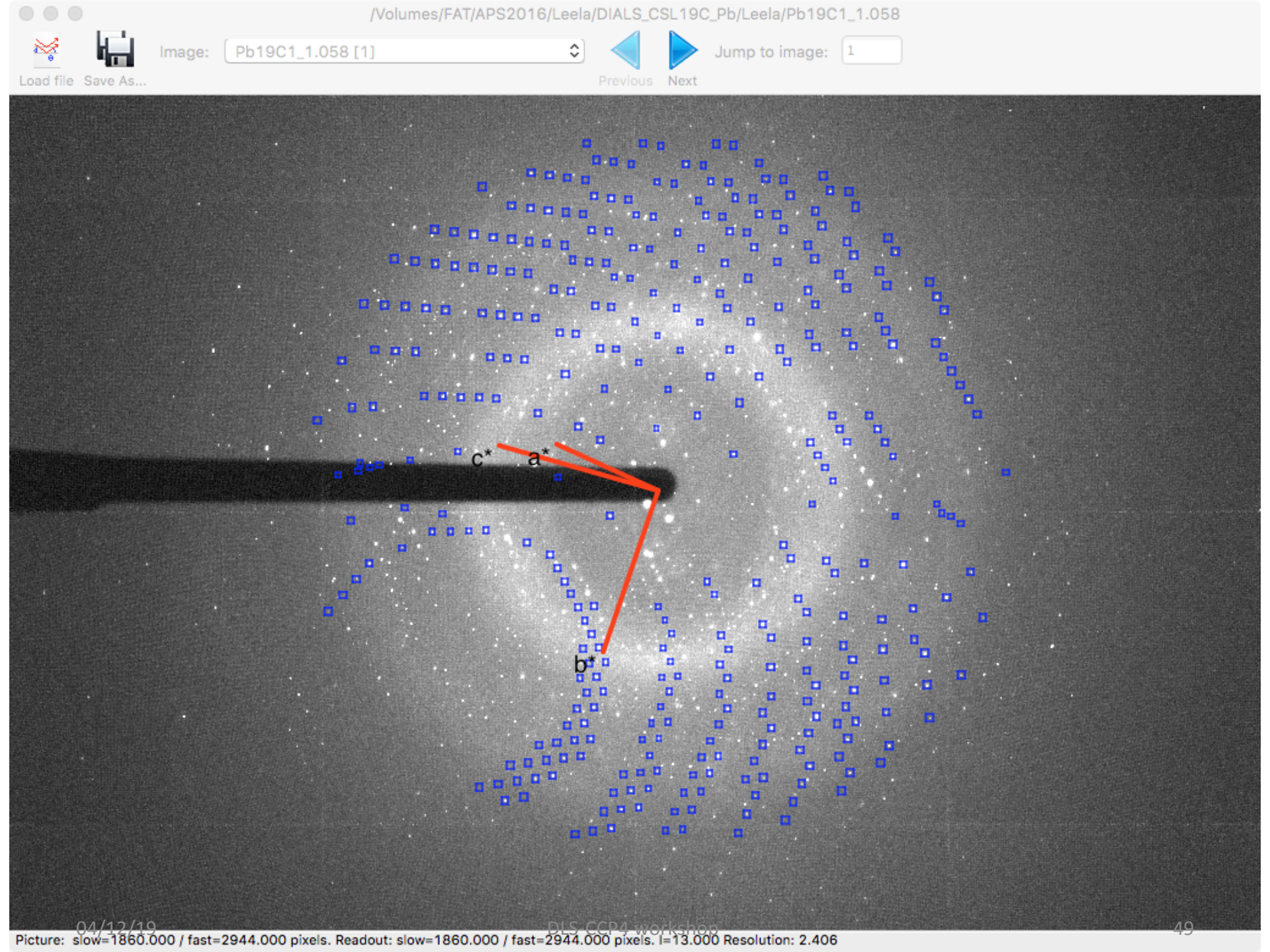
The intensities for the strongest lattice were processed,
structure solved and refined to R=0.20 R-free=0.26

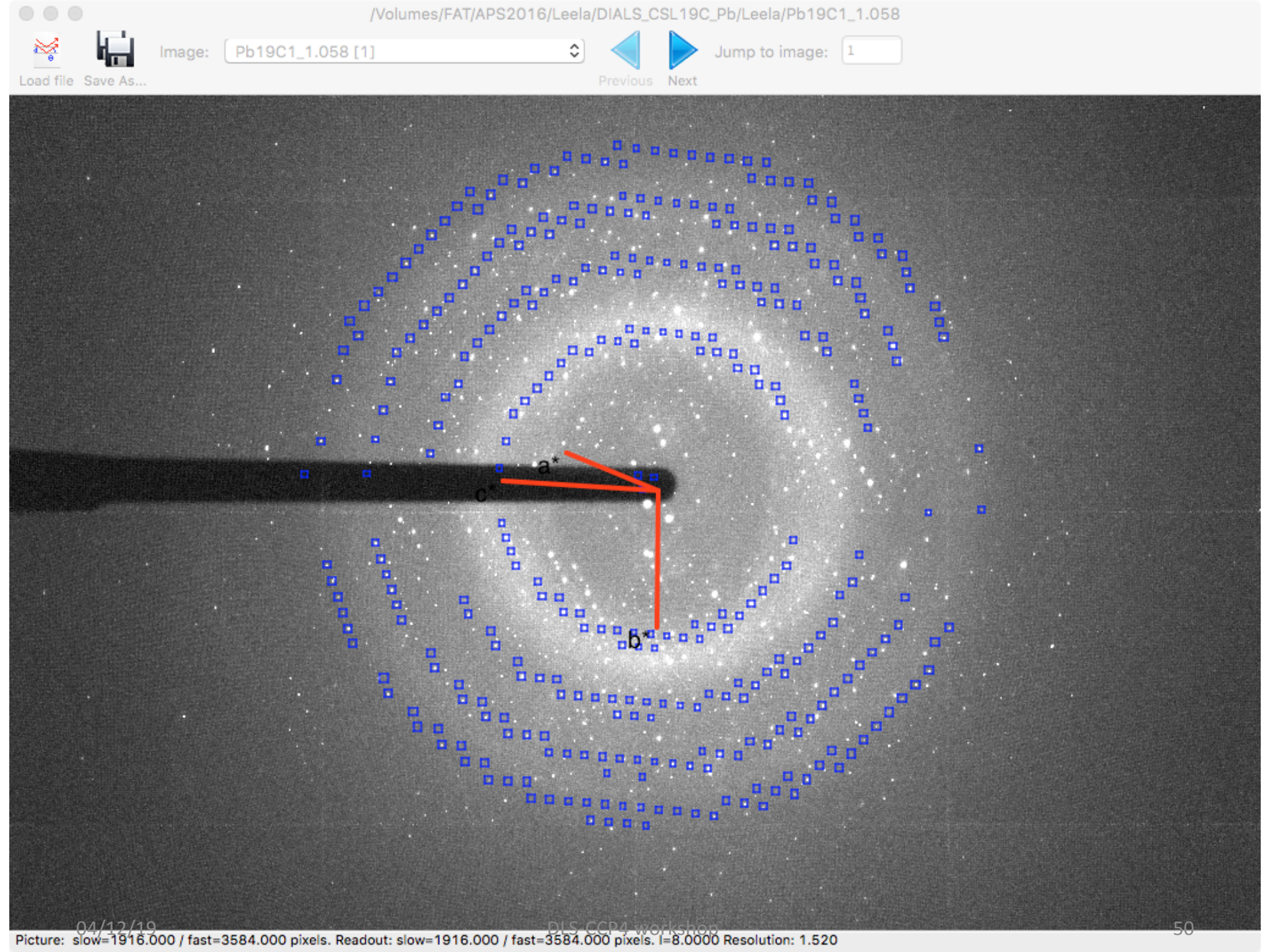
An extreme case

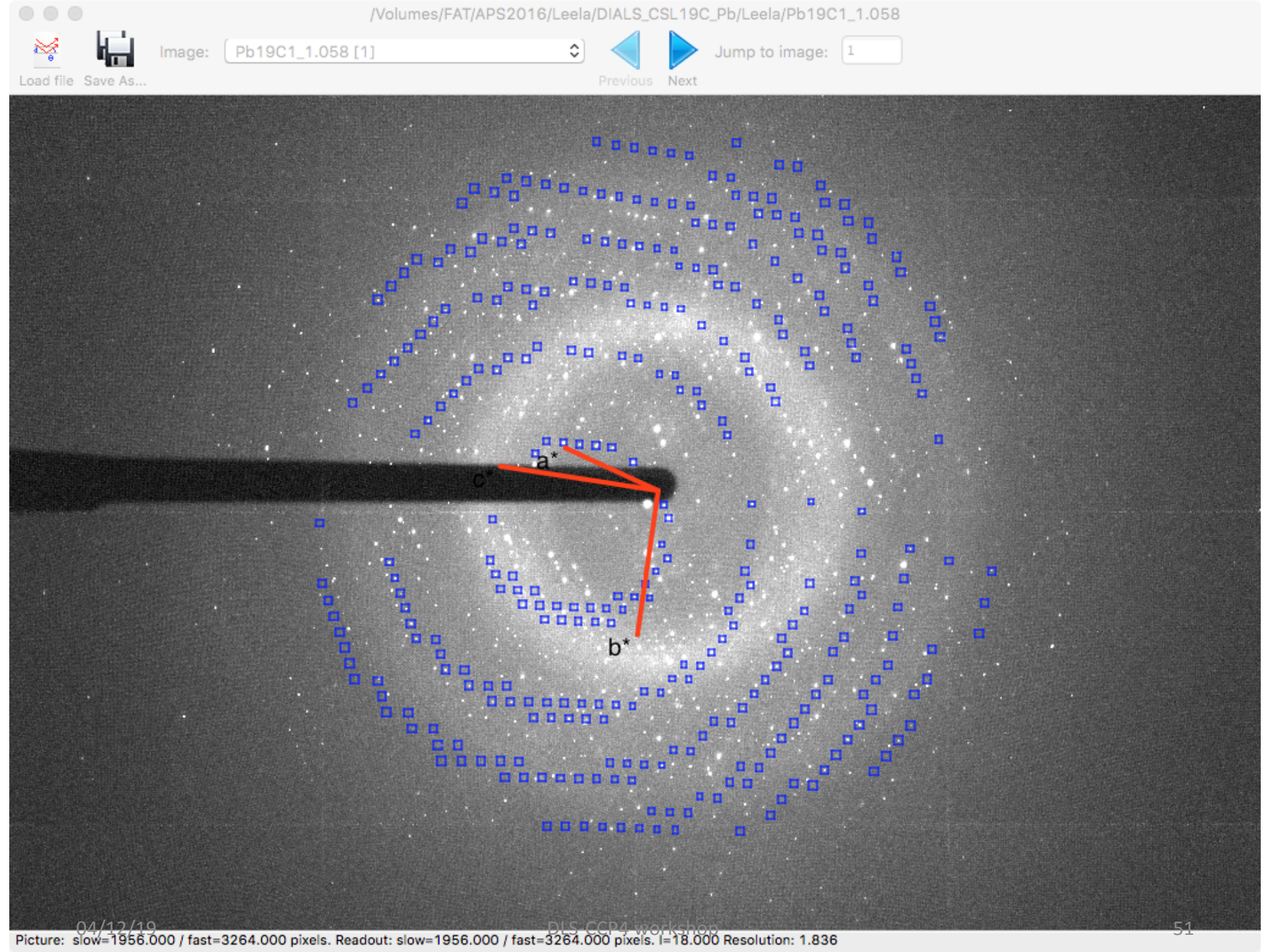
Example from Leela Ruckthong

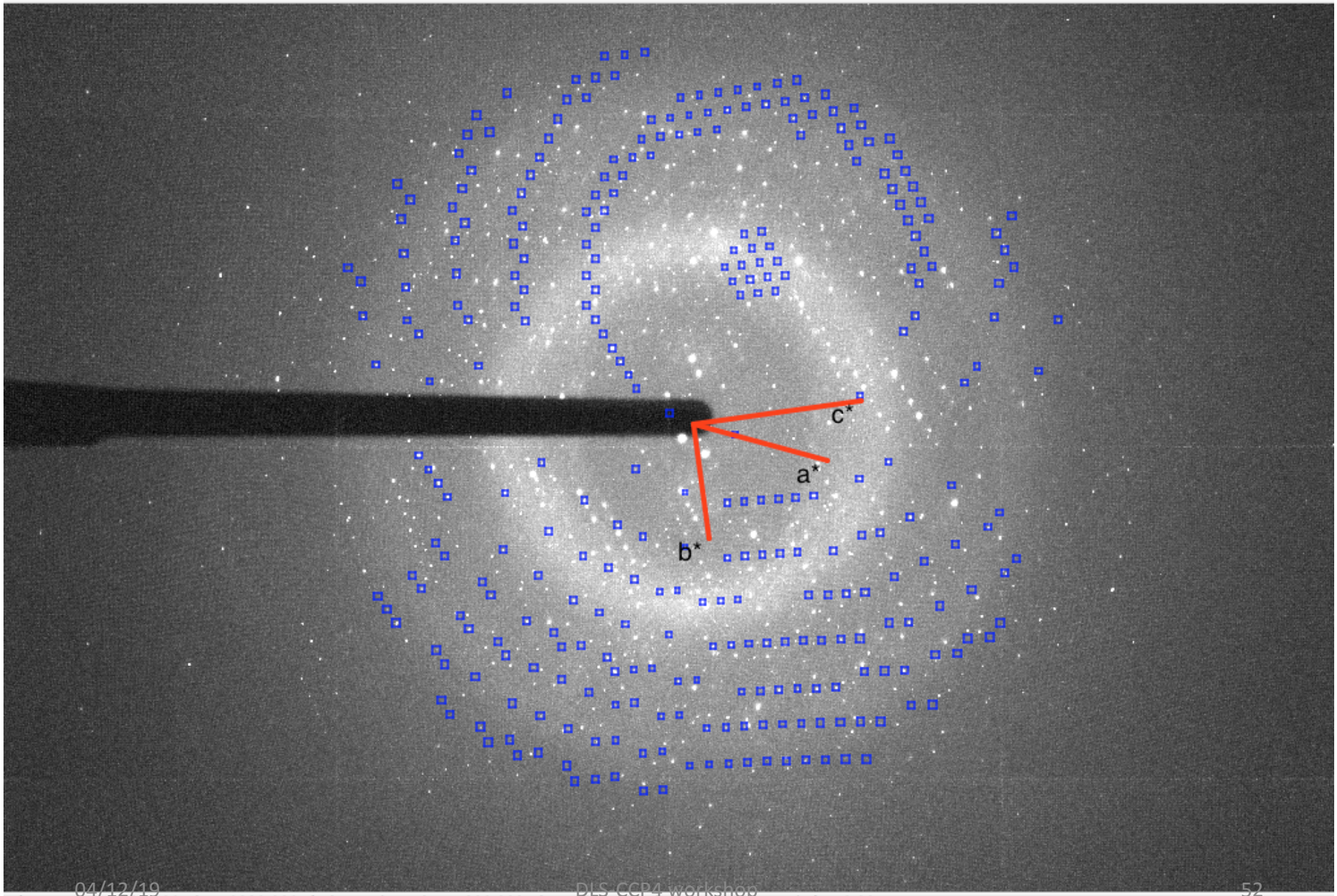
- How many lattices you can spot here?

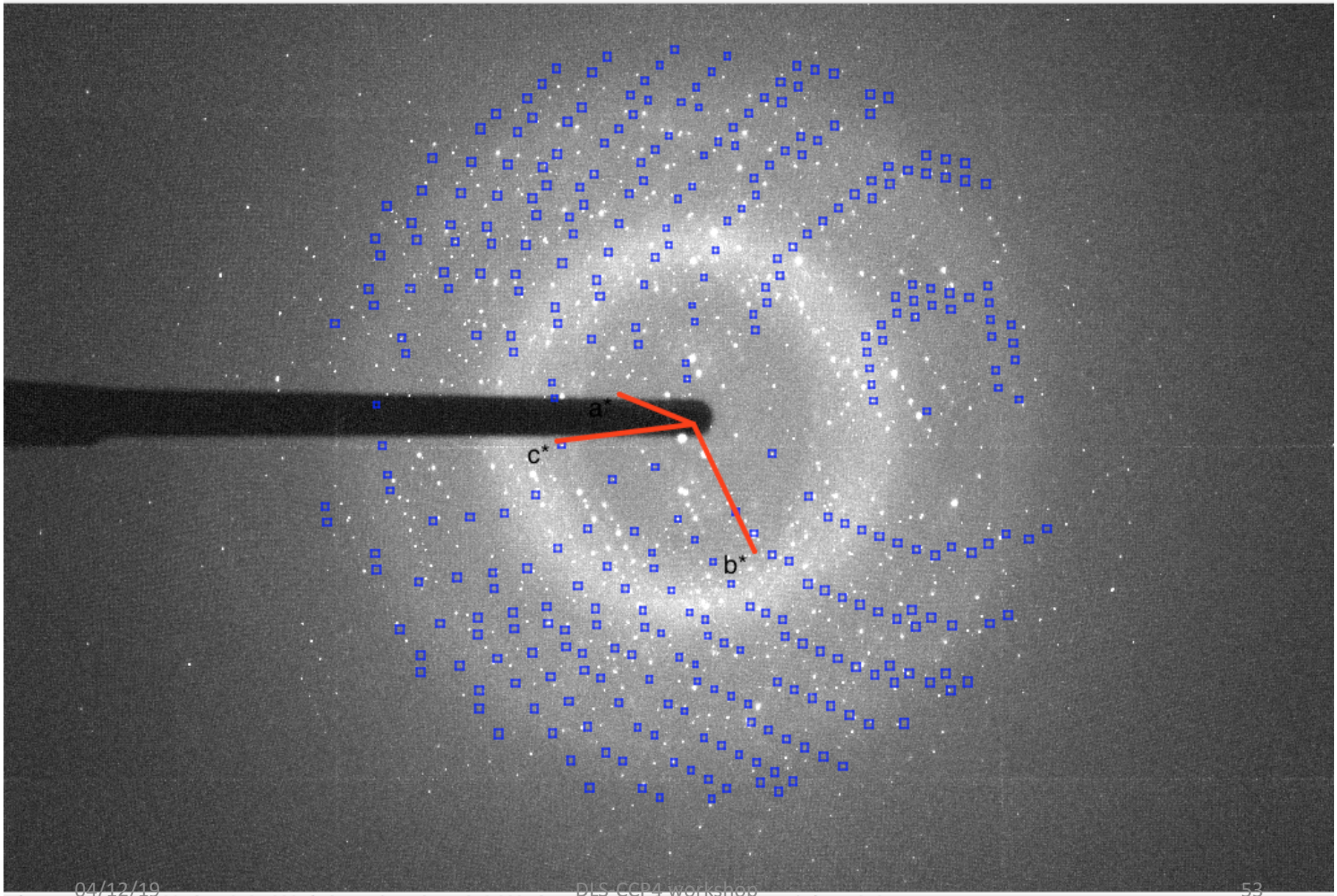


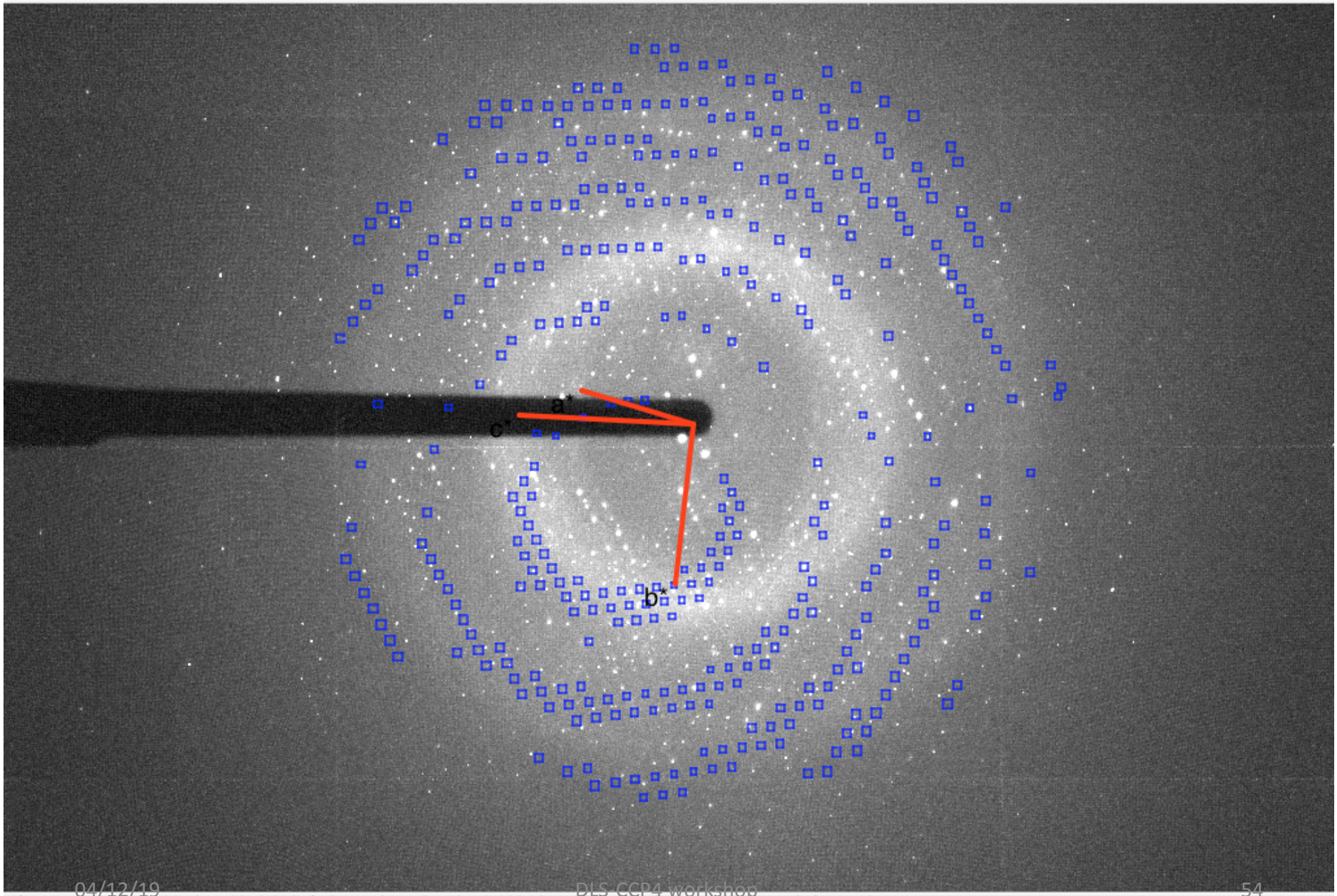

/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.058
Load file
Save As...
Image:
Pb19C1_1.058 [1]
Previous
Next
Jump to image:
1
c*
a*
b*
Picture: slow=1860.000 / fast=2944.000 pixels. Readout: slow=1860.000 / fast=2944.000 pixels. I=13.000 Resolution: 2.406

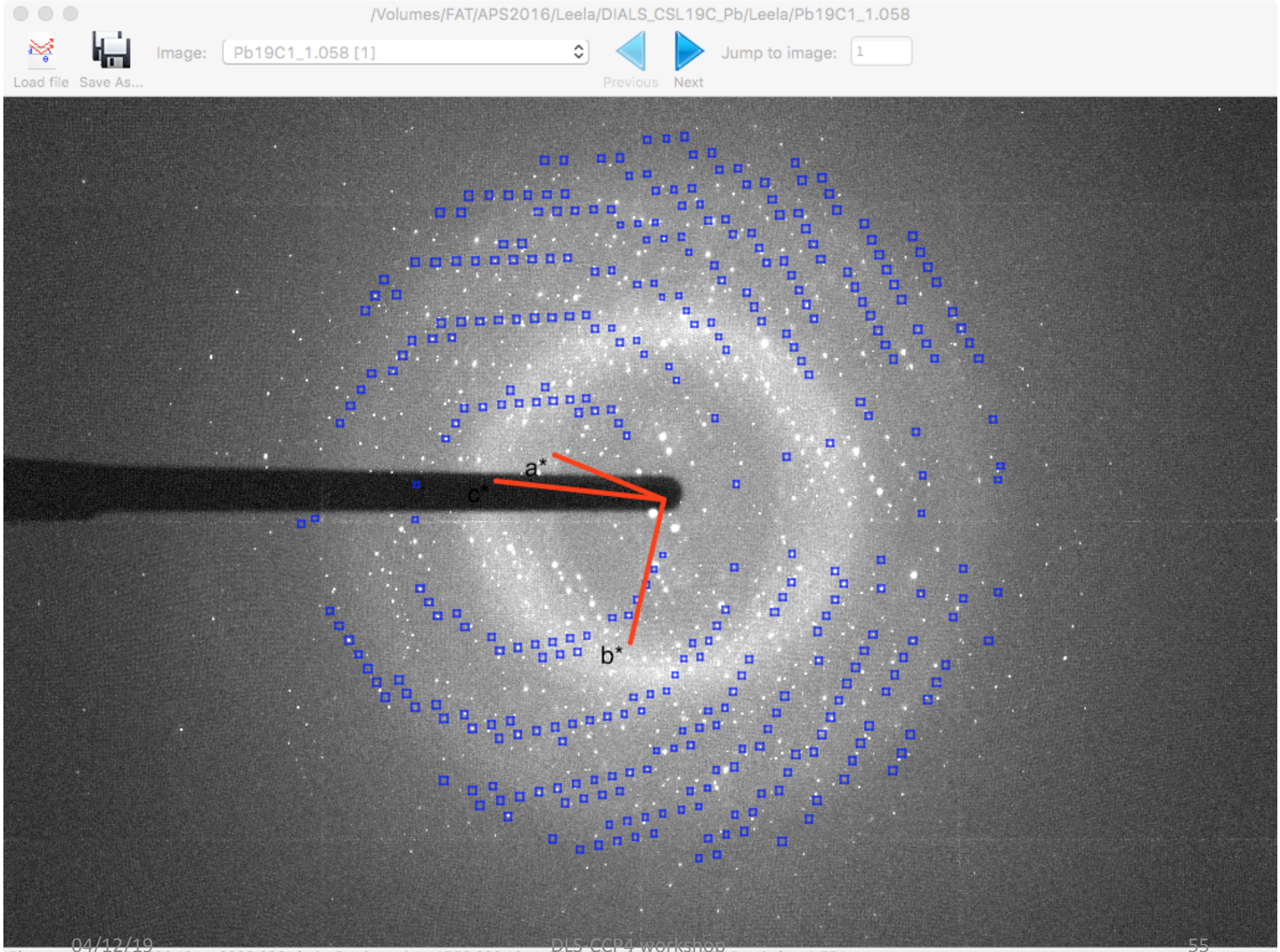

/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.058
Load file
Save As...
Image:
Pb19C1_1.058 [1]
Previous
Next
Jump to image:
1
a*
c*
b*
Picture: slow=1916.000 / fast=3584.000 pixels. Readout: slow=1916.000 / fast=3584.000 pixels. I=8.0000 Resolution: 1.520

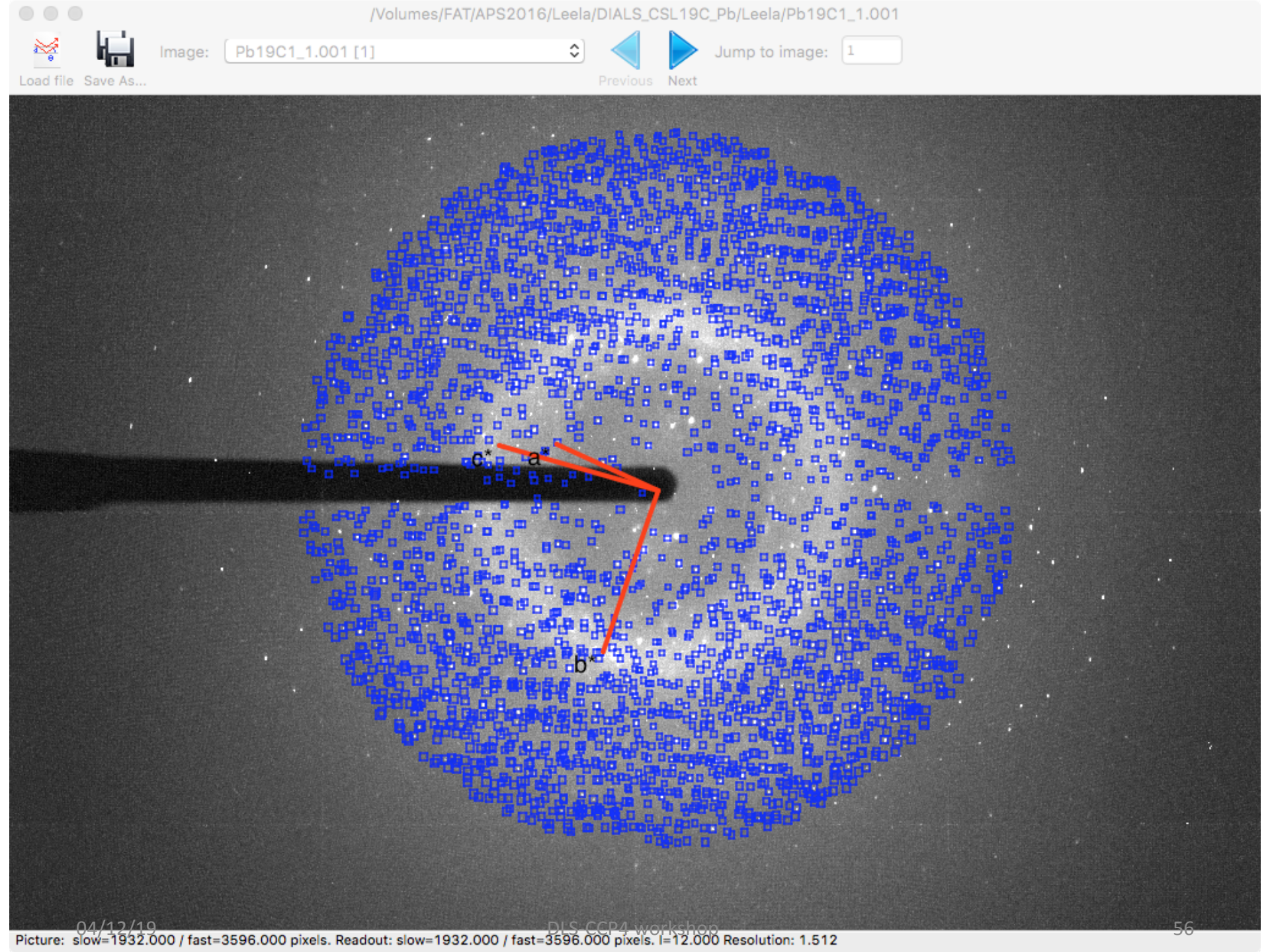

/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.058
Load file
Save As...
Image:
Pb19C1_1.058 [1]
Previous
Next
Jump to image:
1
a*
c*
b*
Picture: slow=1956.000 / fast=3264.000 pixels. Readout: slow=1956.000 / fast=3264.000 pixels. I=18.000 Resolution: 1.836

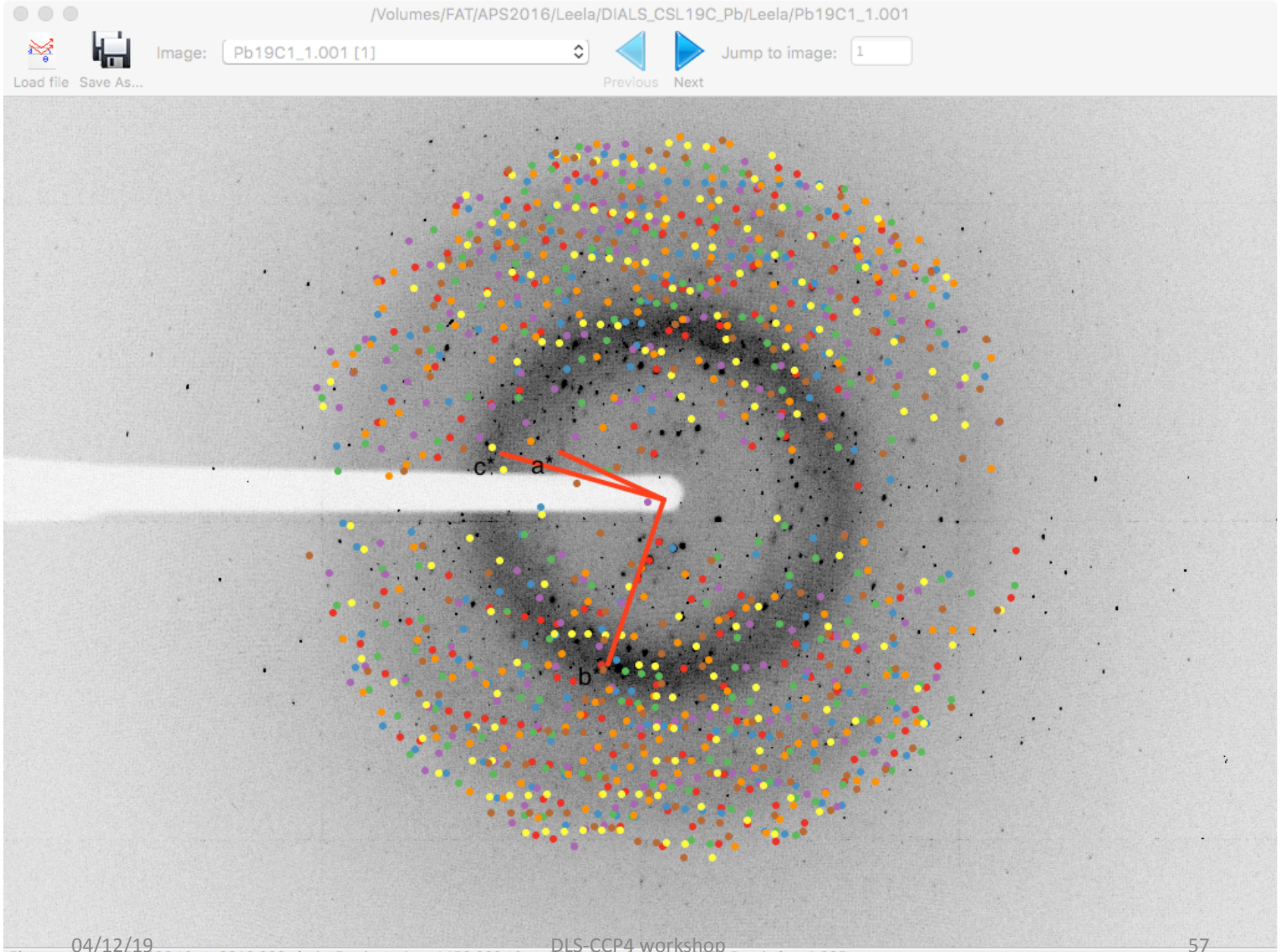

/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.058
Load file
Save As...
Image:
Pb19C1_1.058 [1]
Previous
Next
Jump to image:
1
c*
a*
b*
Picture: slow=1900.000 / fast=2992.000 pixels. Readout: slow=1900.000 / fast=2992.000 pixels. I=15.000 Resolution: 2.301


/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.058
Load file
Save As...
Image:
Pb19C1_1.058 [1]
Previous
Next
Jump to image:
1
a*
c*
b*
Picture: slow=1952.000 / fast=2484.000 pixels. Readout: slow=1952.000 / fast=2484.000 pixels. I=17.000 Resolution: 5.272


/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.058
Load file
Save As...
Image:
Pb19C1_1.058 [1]
Previous
Next
Jump to image:
1
a*
c*
b*
Picture: slow=2152.000 / fast=3312.000 pixels. Readout: slow=2152.000 / fast=3312.000 pixels. I=7.0000 Resolution: 1.761


/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.058
Load file
Save As...
Image:
Pb19C1_1.058 [1]
Previous
Next
Jump to image:
1
a*
c*
b*
Picture: slow=1752.000 / fast=3296.000 pixels. Readout: slow=1752.000 / fast=3296.000 pixels. I=13.000 Resolution: 1.771


/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.001
Load file
Save As...
Image:
Pb19C1_1.001 [1]
Previous
Next
Jump to image:
1
c*
a*
b*
Picture: slow=1932.000 / fast=3596.000 pixels. Readout: slow=1932.000 / fast=3596.000 pixels. I=12.000 Resolution: 1.512


/Volumes/FAT/APS2016/Leela/DIALS_CSL19C_Pb/Leela/Pb19C1_1.001
Load file
Save As...
Image:
Pb19C1_1.001 [1]
Previous
Next
Jump to image:
1
c*
a*
b*
Picture: slow=1456.000 / fast=3912.000 pixels. Readout: slow=1456.000 / fast=3912.000 pixels. I=9.0000 Resolution: 1.295

Seven lattices: too many overlapping spots?

- Only the strongest single lattice gave reasonable merged data
  - » all others were incomplete or had much lower I/sig(I)
  - » merging data from several lattices did not work well

- Solved and paper in preparation

Summary on multiple lattices

- Usually it is reasonable to use the data derived from one singe lattice
- Sometimes completeness can be improved by merging datasets derived from two or more lattices
- Sometimes the best lattice is not the first found by Dials
- DIALS: Indexing all the lattices together facilitates refinement of the parameters for each individual lattice

Order-Disorder structures (OD-structures)

- Definition
- Example of an OD twin
- Example of allotwin

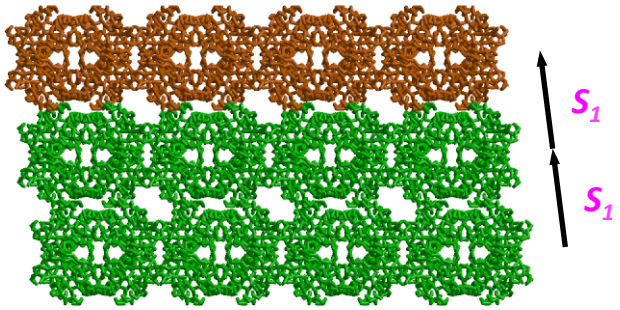
Actually disordered OD-structures:

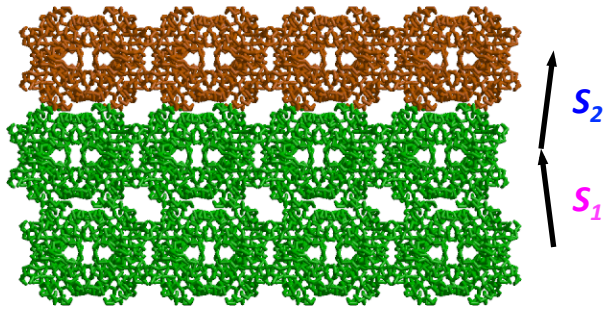
- Relatively frequent
- Data can sometimes be useful
- Good for illustration purpose

Order-disorder structures (OD-structures)

- identical layers
- identical interfaces between the layers
- but: two or more ways of packing three adjacent layers

*) MX: "identical" means Ca r.m.s.d. < 1 A



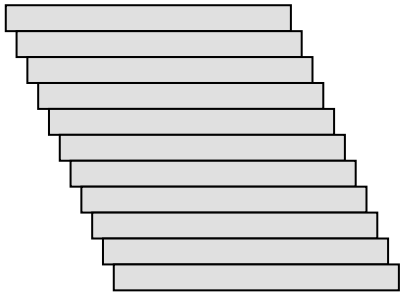


*) S_1 and S_2. are called stacking vectors

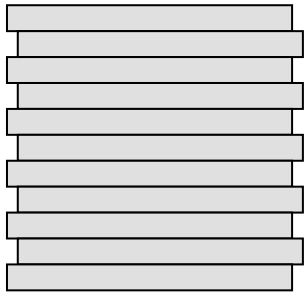
- two-dimensional periodicity
- a potential for disorder in the third dimension

OD-structures

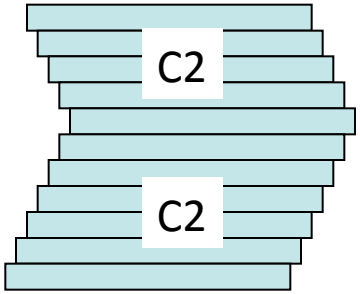
Single crystal



Single crystal

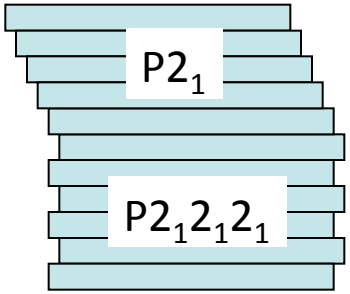


OD-twin



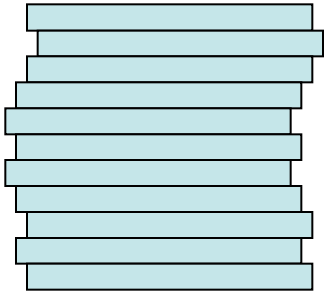
Example 1

Allotwin



Example 2

Partially disordered OD-structure



Examples in the next section

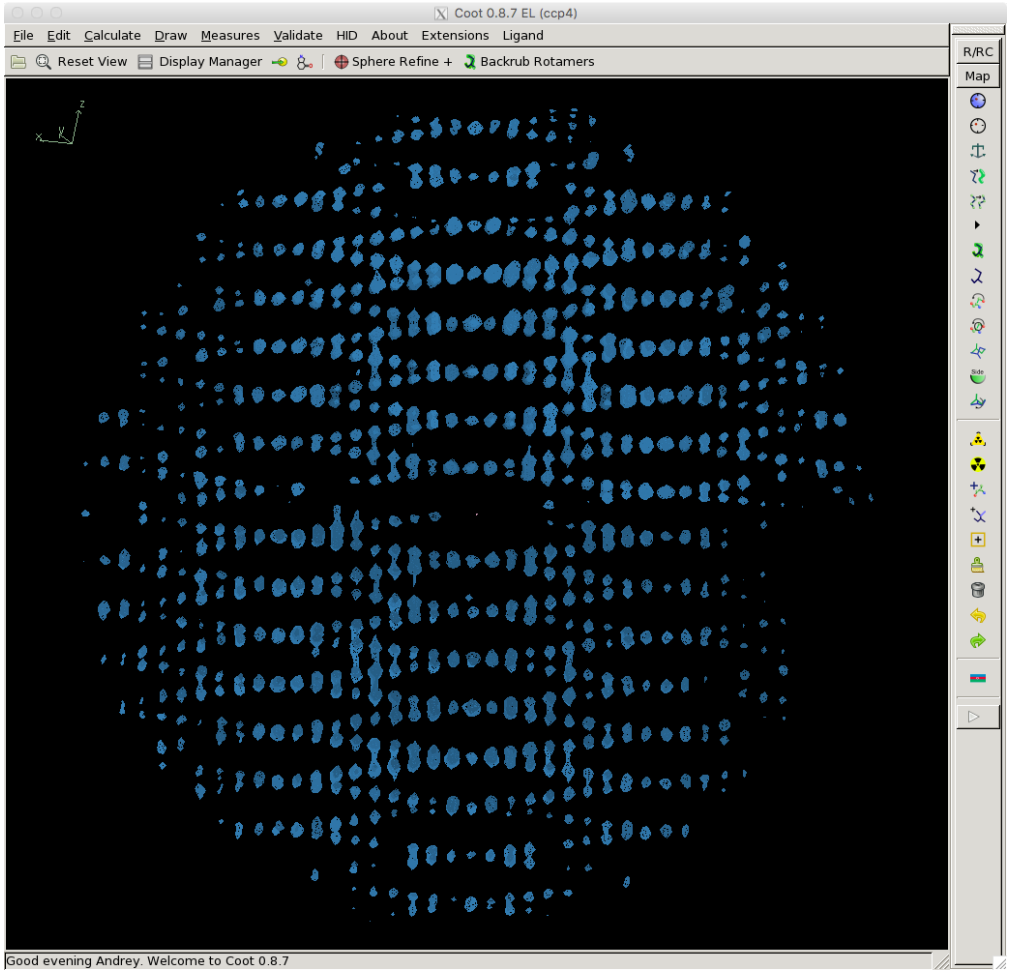
Example 1: OD-twin

Morphological classification
OD-twin

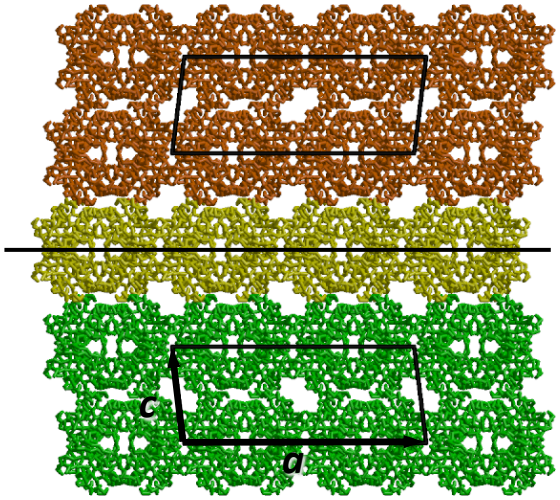
Geometrical classification
Twinning by reticular pseudo-merohedry

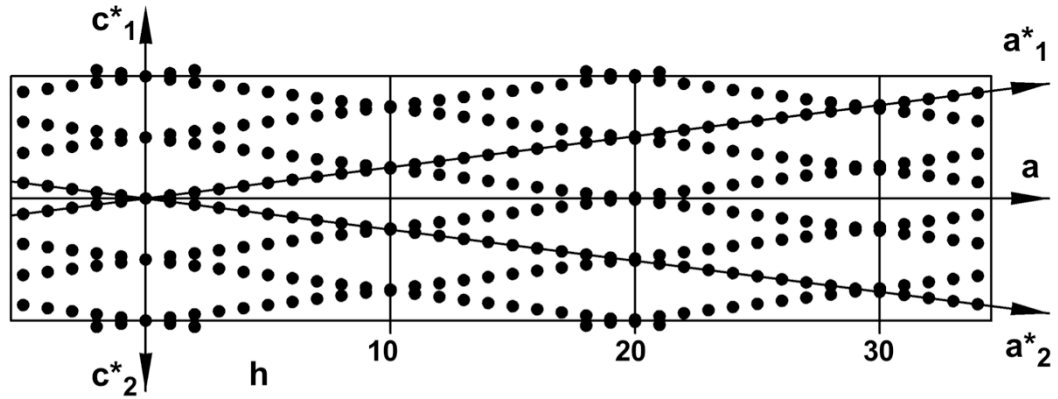
Synonym
Non-merohedral twinning

dials.rs_mapper + coot



Real and reciprocal lattices





Twinning by reticular pseudo-merohedry (Non-merohedral twinning)

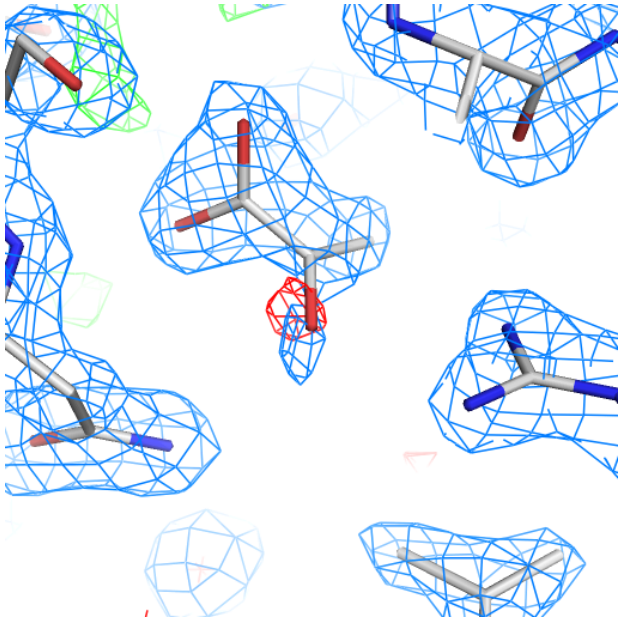
- Process data from one lattice and ignore twinning
- Process data from one lattice and demodulate the data

- Record total intensity of overlapping spots (SAINT, iMosflm) and deal with it at refinement (SHELXL)

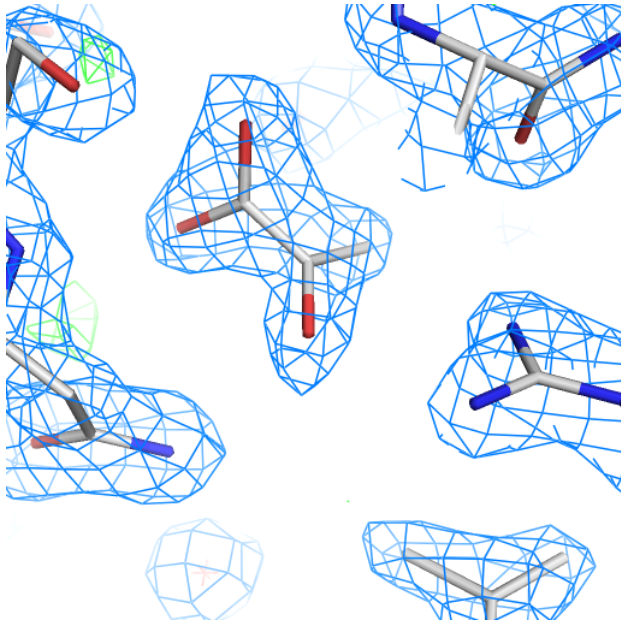
Demodulation: improvement in the electron density

Visually, improvement from demodulation occurred
only in the electron density for solvent molecules
(Poor density for solvent was the original reason for data revision)

The electron density maps (2-1 at 1.5σ and 1-1 at 3σ)
around the L-lactate molecule before and after demodulation

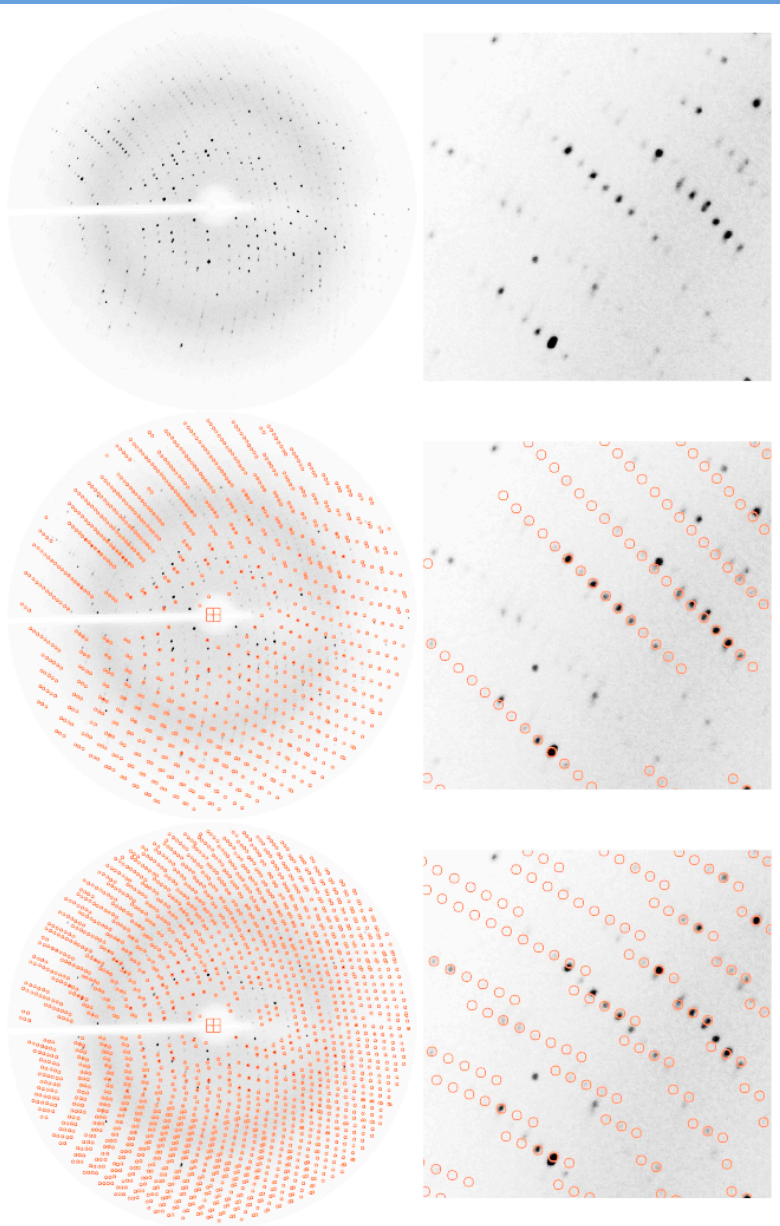


R / R-free = 0.21 / 0.27

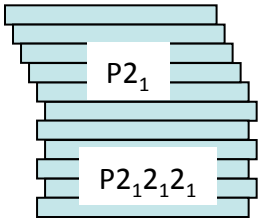


R / R-free = 0.16 / 0.23

Example 2: allotwin



Crystals of Lon protease
Resolution 3Å



Dauter *et al.* (2005).
Acta Cryst. D**61**, 967-975.

$P2_1$

a = 48.5 Å
b = 86.3 Å
c = 138.0 Å
β = 92.3°

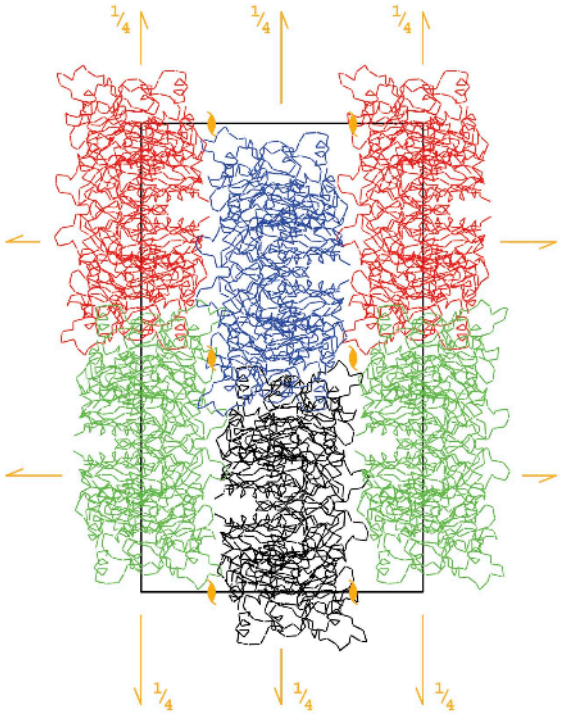
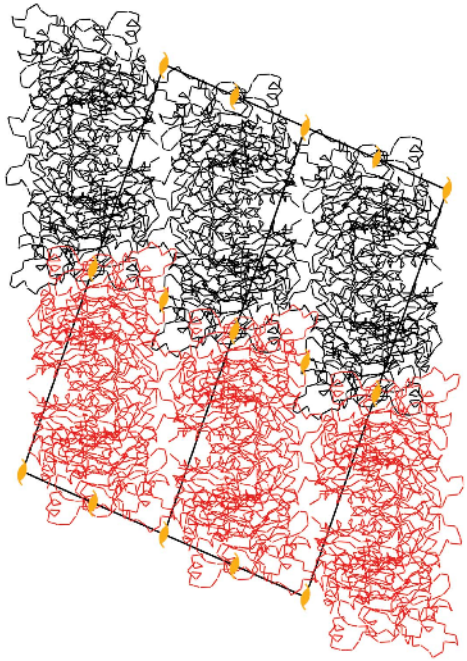
$P2_12_12_1$

a = 86.3 Å
b = 90.6 Å
c = 148.0 Å

Example 2: allotwin

Crystals of Lon protease
Resolution 3Å

Dauter *et al.* (2005).
Acta Cryst. D**61**, 967-975.

	PDB code 1z0t	PDB code 1z0v
		
Structures of both crystal forms were solved	$P2_12_12_1$	$P2_1$
R / R-free	0.19 / 0.35	0.21 / 0.31

Example 2: allotwin

- More frequently, the presence of very different indexing solutions means that the indexing program is struggling rather than domains belonging to different space groups actually exist.

- 3D viewers will help to check what is actually happening.

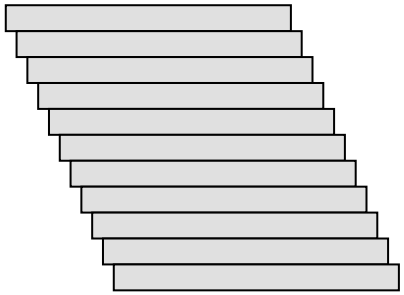
- In any case, it is a warning sign if e.g. different programs suggest different crystal point/space groups (e.g. *P* 2_1 and *P* $2_12_12_1$)

Partially disordered OD-structures

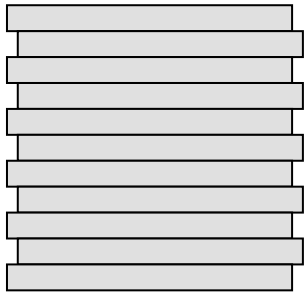
- Visualisation (detection)
- Ghost density
- Indexing
- Effect on structure solution

OD-structures

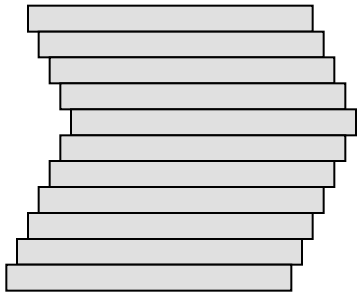
Single crystal



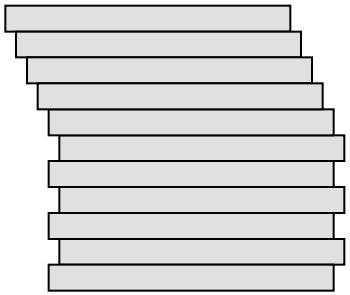
Single crystal



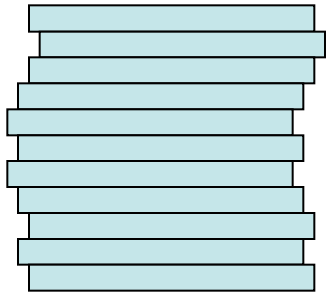
OD-twin



Allotwin

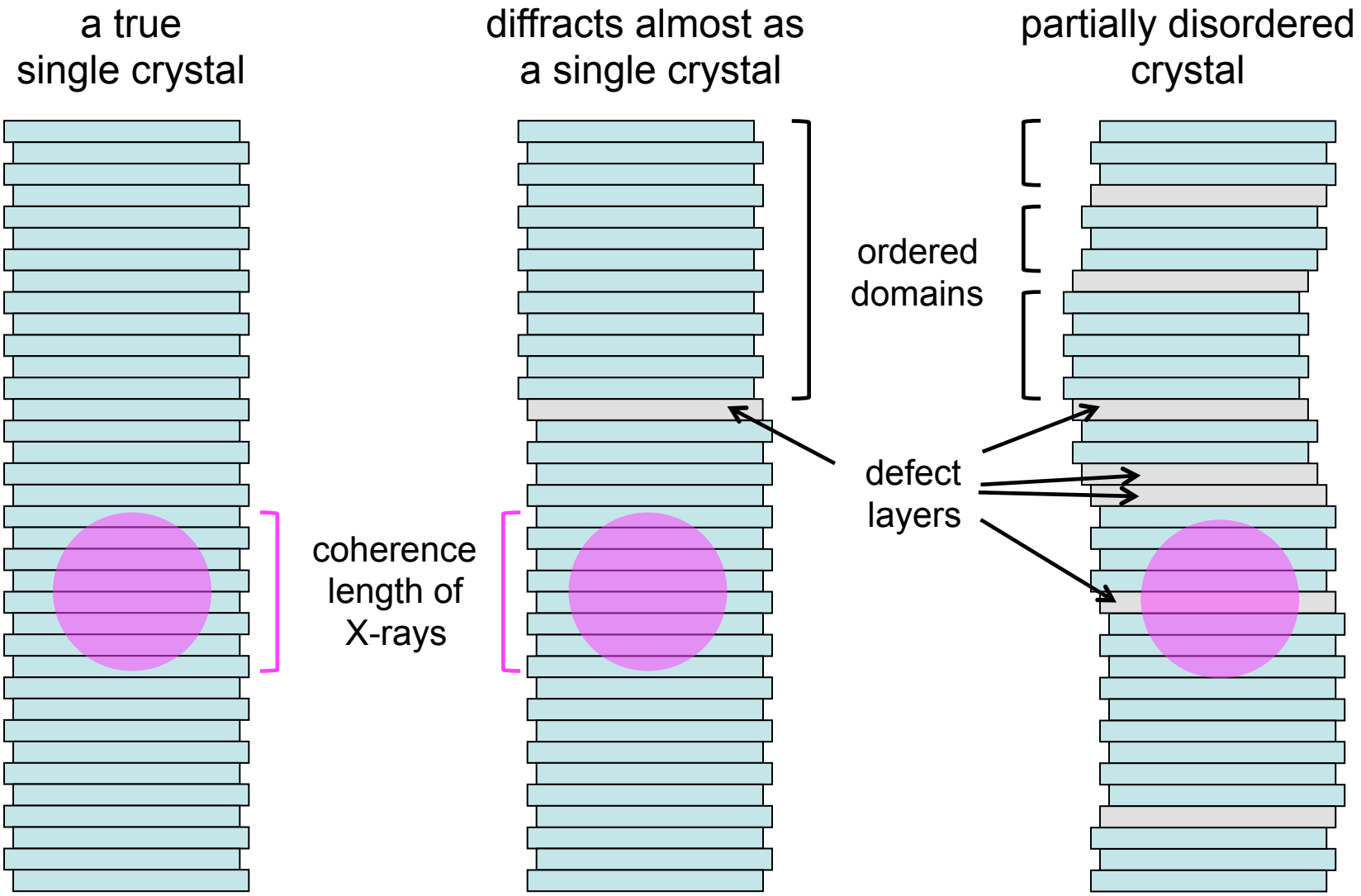


Partially disordered OD-structure



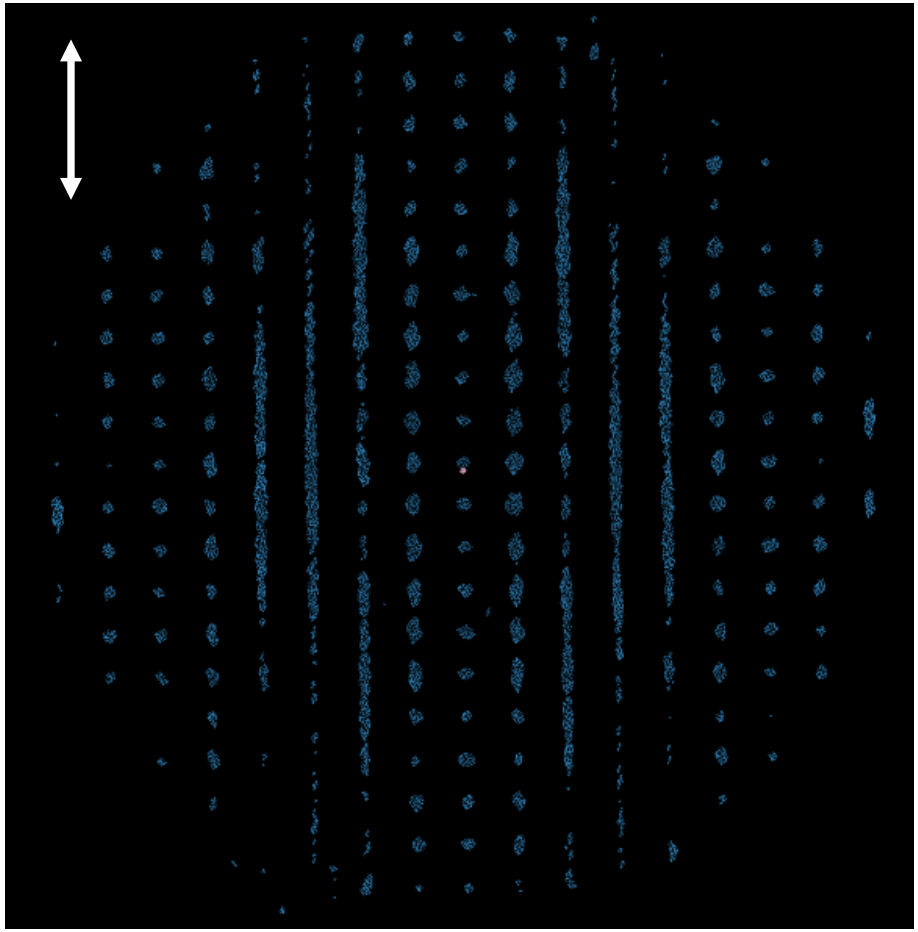
Examples 1,2 & 3

Partially disordered OD structures

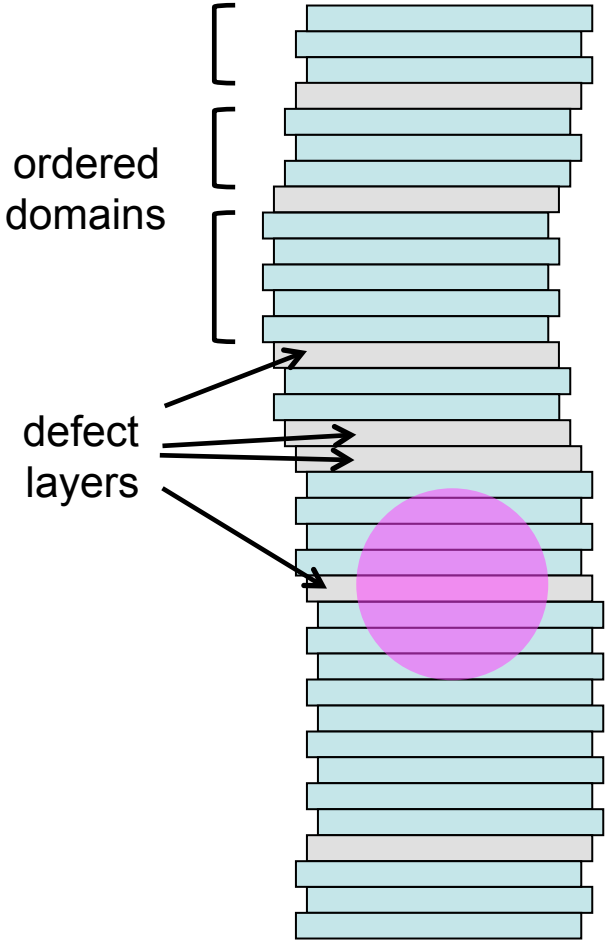


Diffraction of partially disordered structures

White arrow - direction in which global periodicity is missing

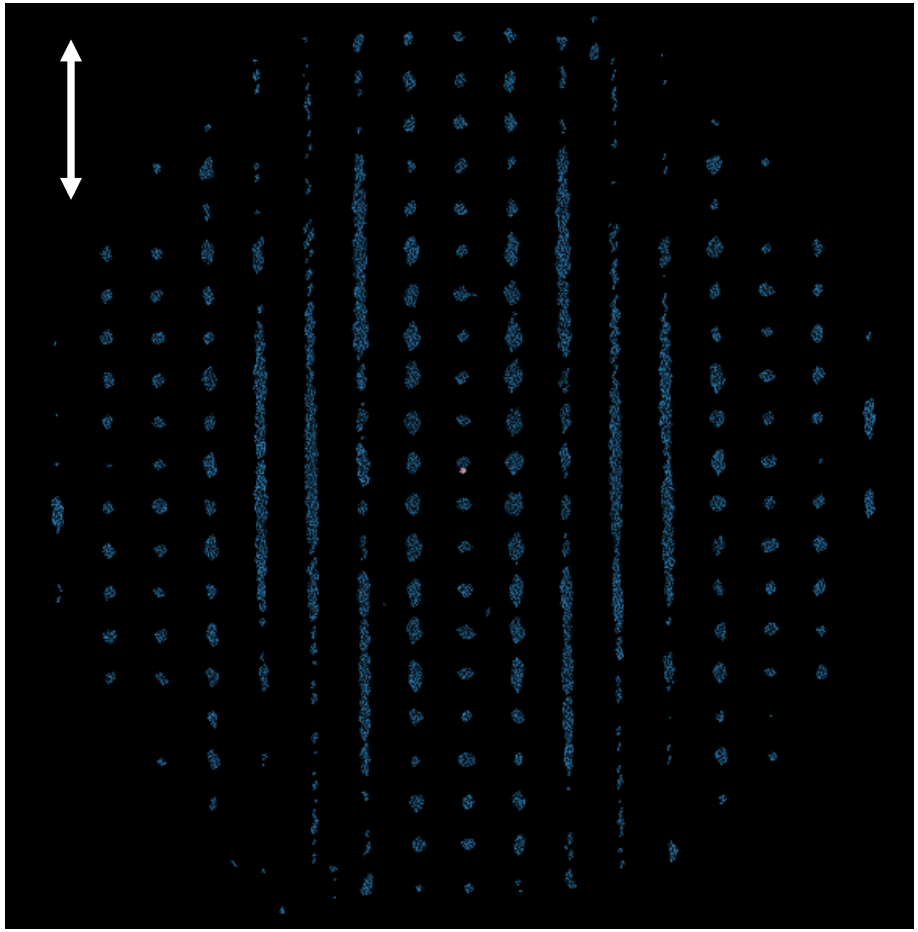


dials.rs_mapper + coot



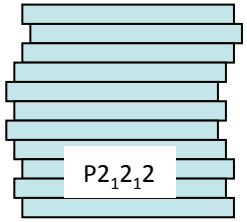
Example 1: ghost density

White arrow - direction in which global periodicity is missing



dials.rs_mapper + coot

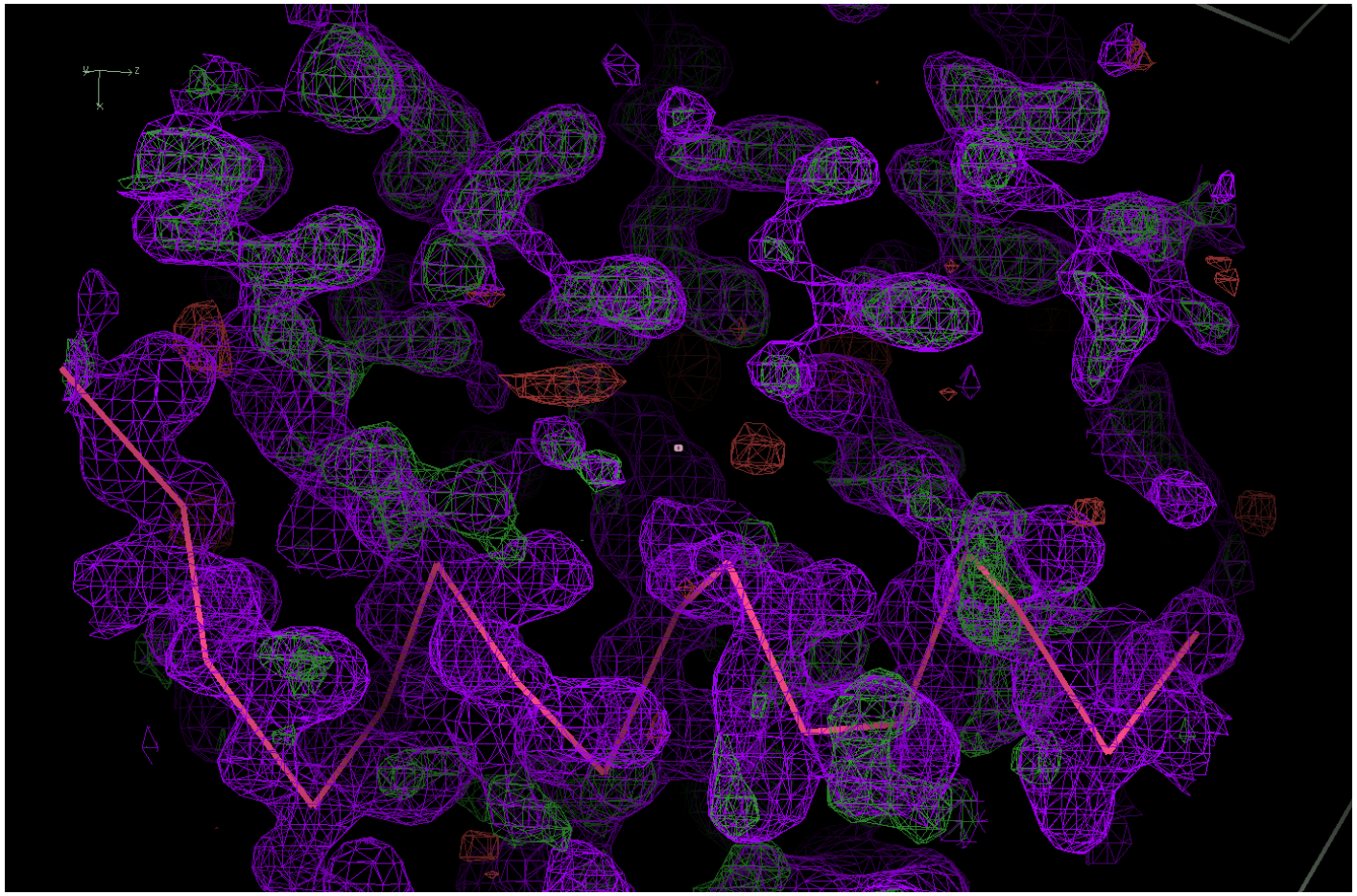
An example from **Rafael Ciges**, Biomedical Institute of Valencia



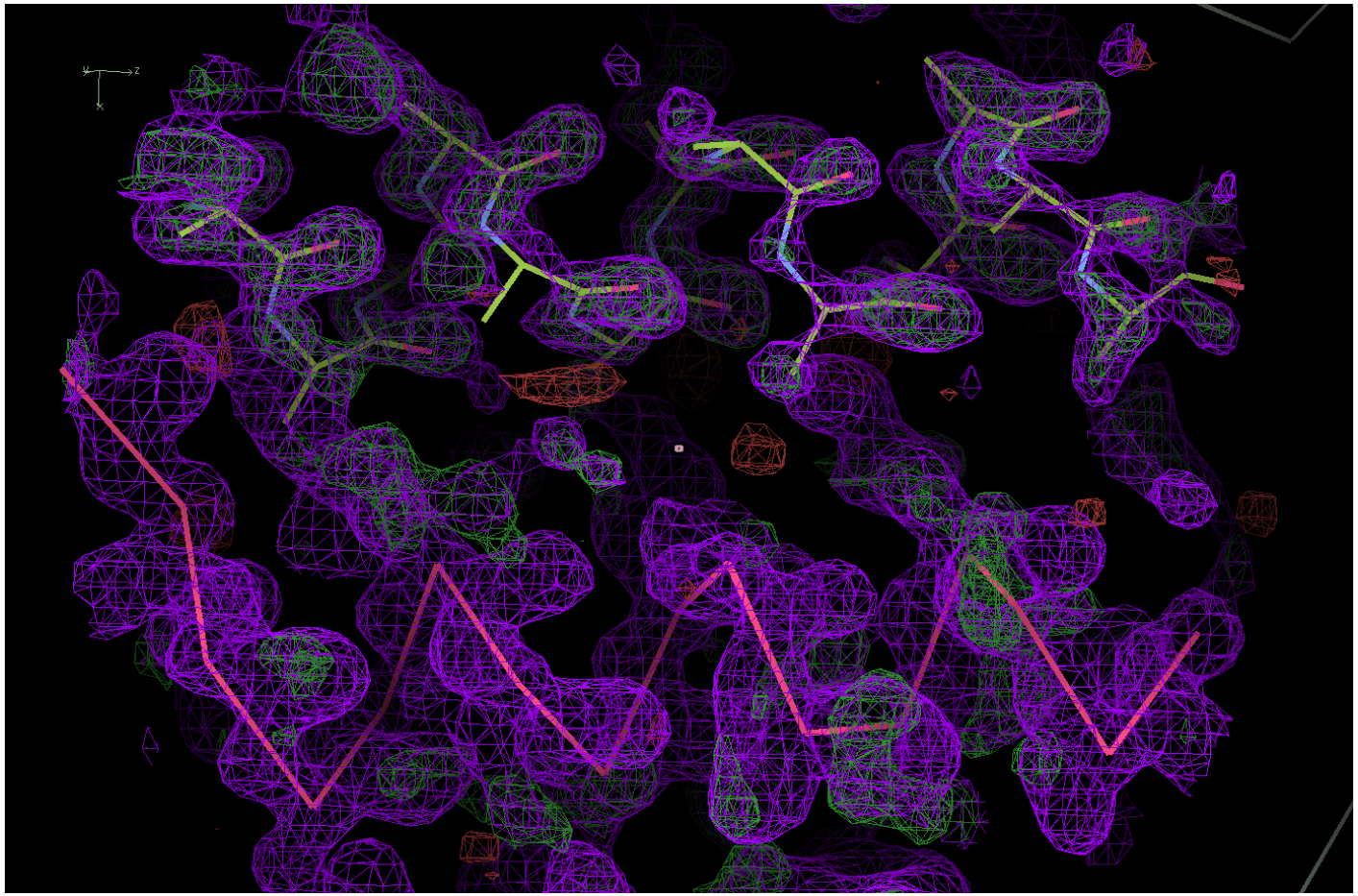
- Space group $P2_12_12$
- Resolution 1.2Å

- The diffraction images were processed with XDS
- Structure was solved with MR
- Preliminary refinement R_{free} = 0.35
- Extra residues were expected compared to MR model

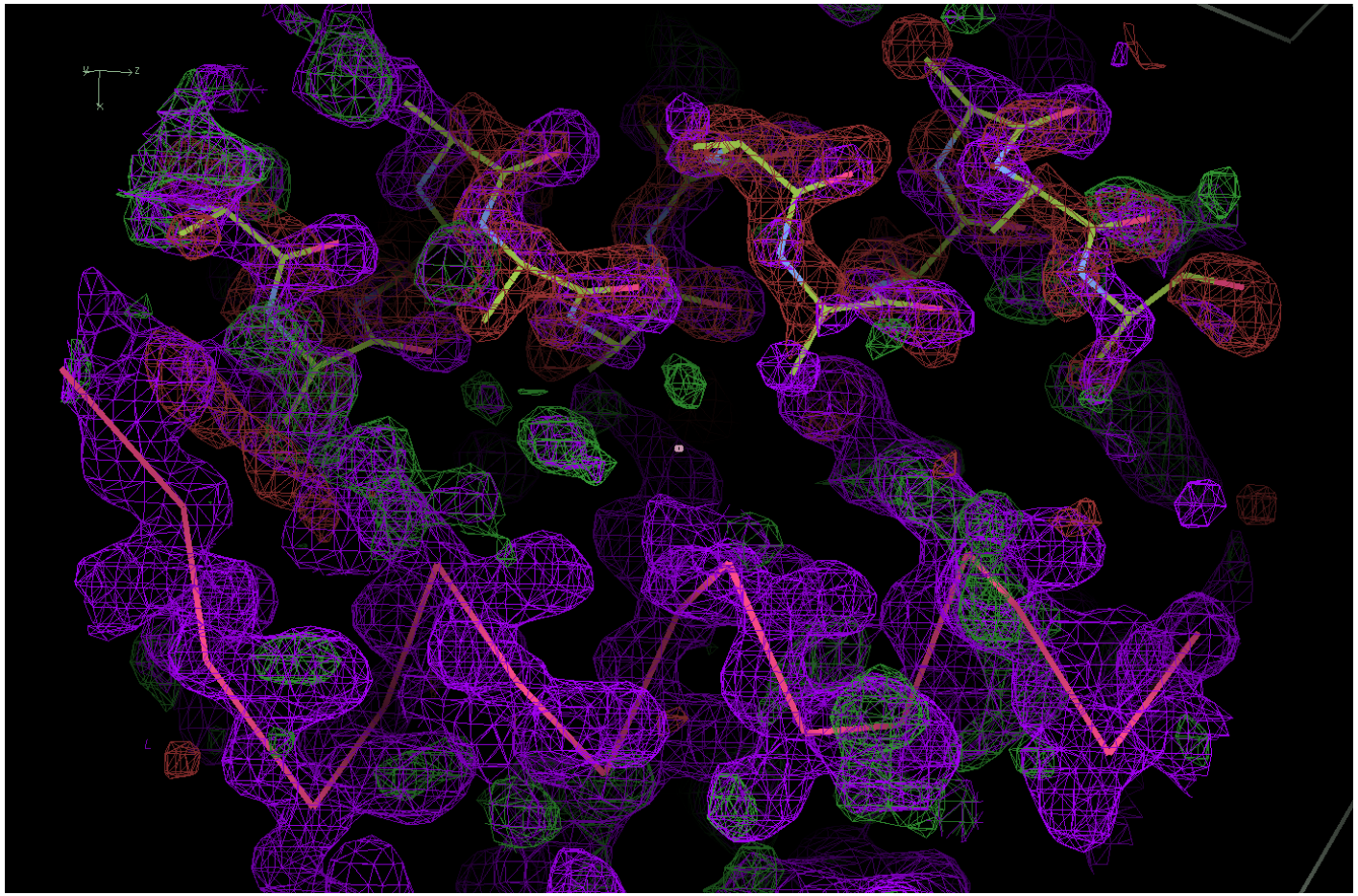
Example 1: after initial refinement



Example 1: helix added



Example 1: after refinement with extra helix

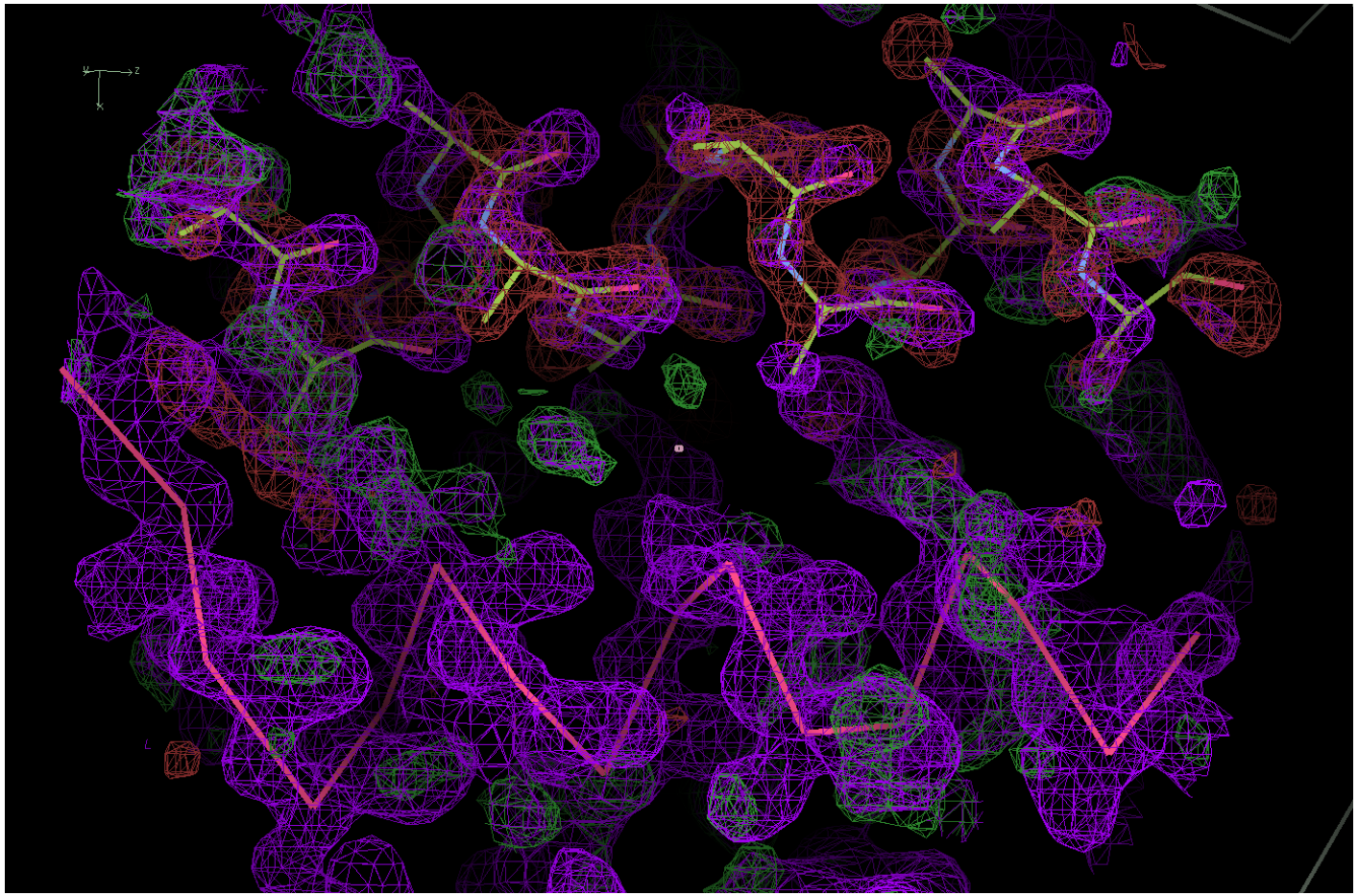


Example 1: demodulation of intensities

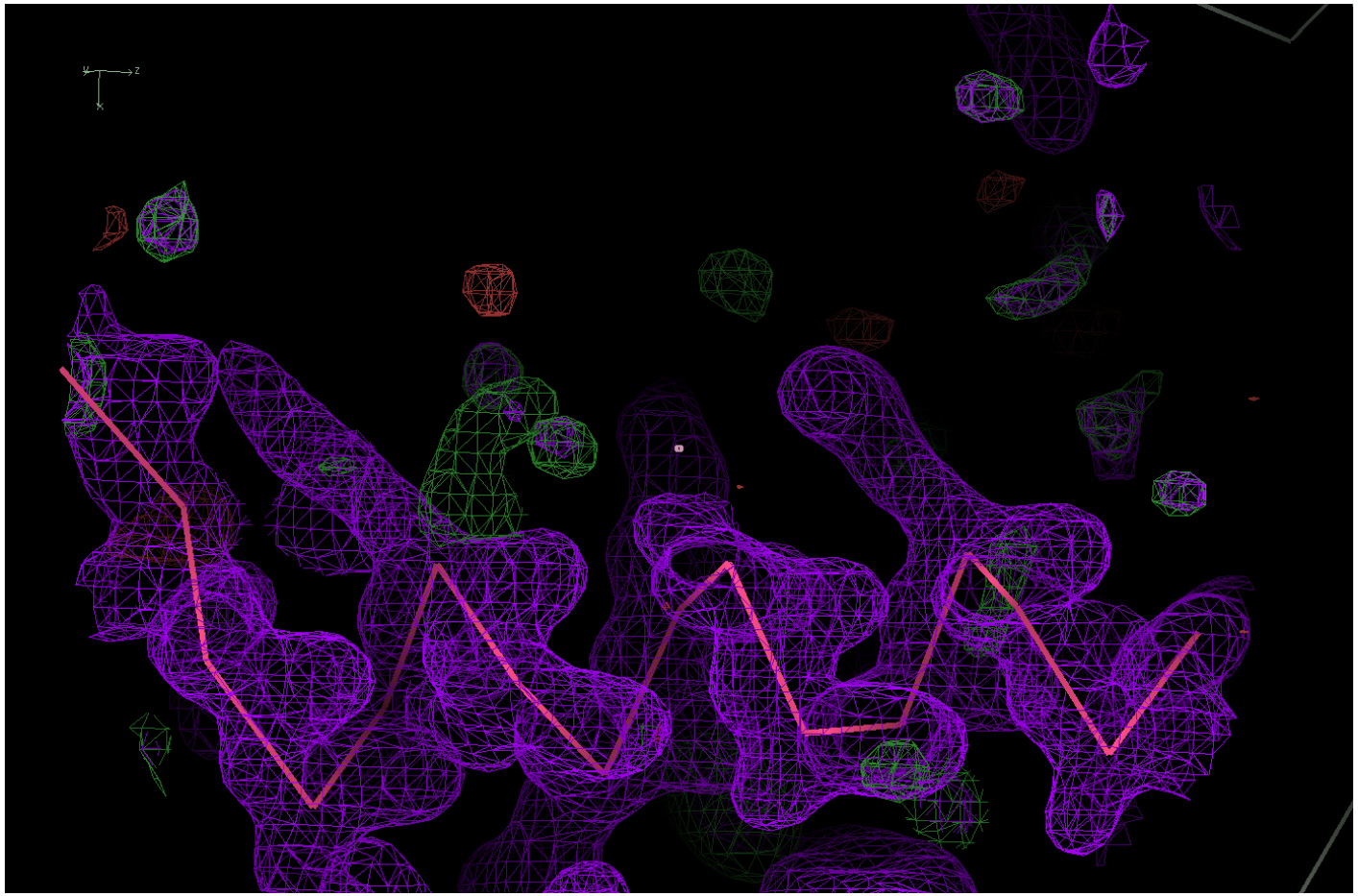
- Data were demodulated to approximately account for disorder

	R	R-free
Original data	0.33	0.34
Corrected data	0.25	0.26

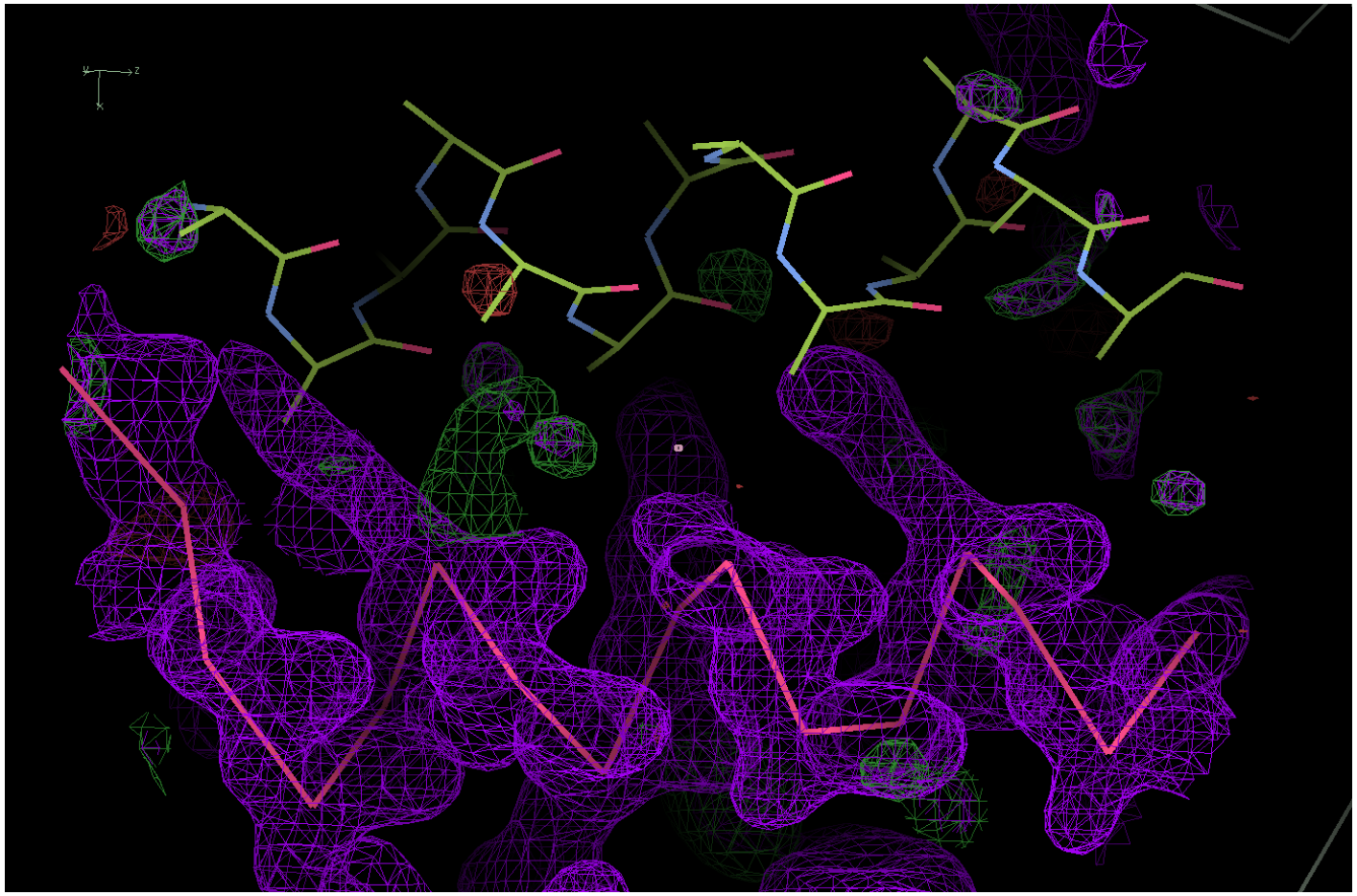
Example 1: after refinement with extra helix



Example 1: after refinement against demodulated data ...



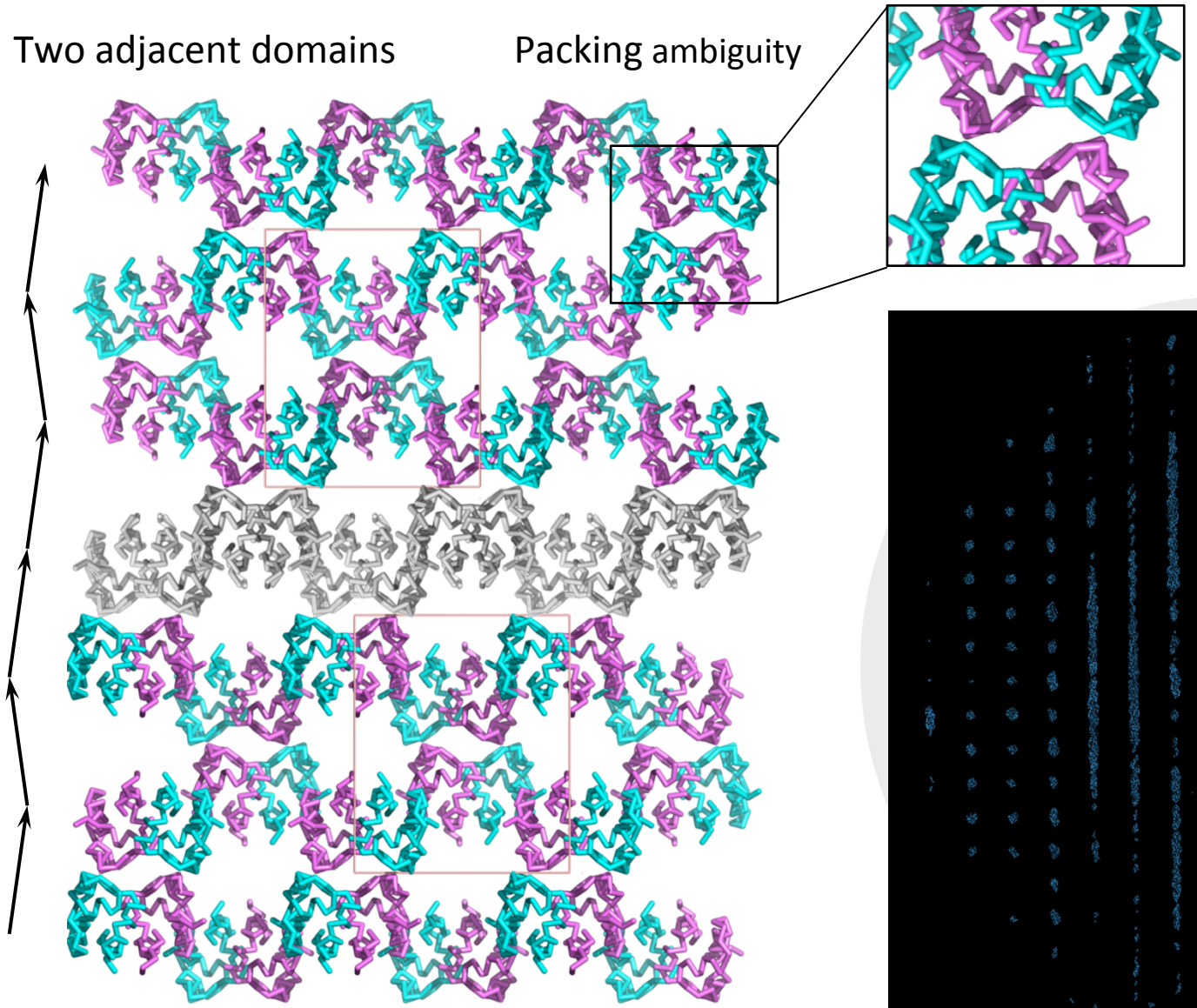
Example 1: ... there is no ED for the extra helix



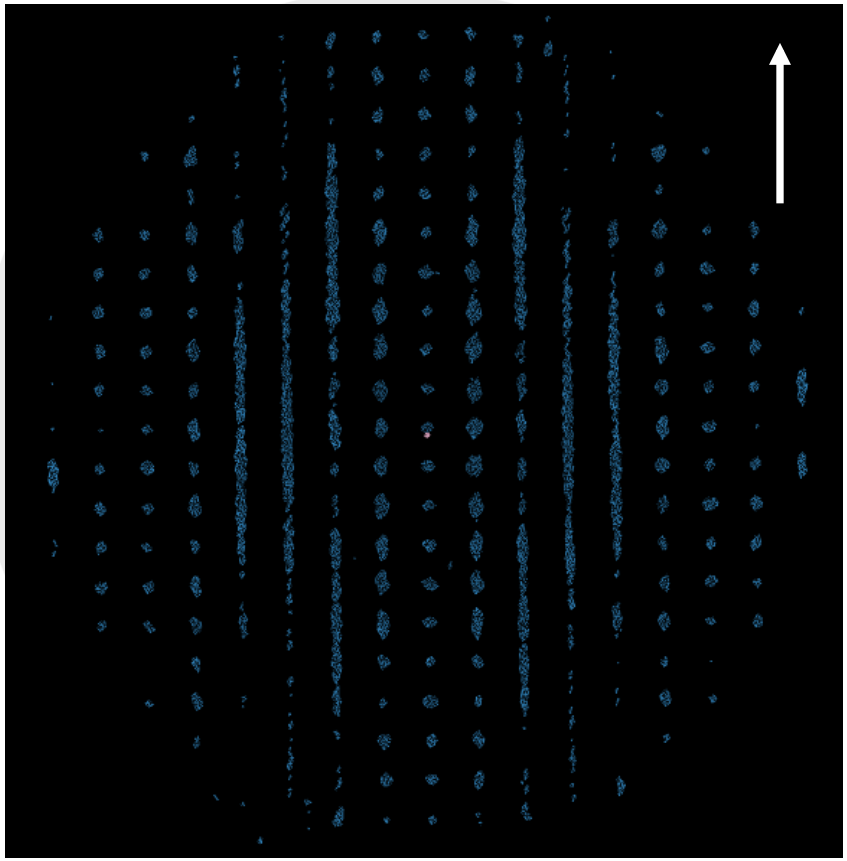
Example 1: ghost density

Two adjacent domains

Packing ambiguity



White arrow - direction in which global periodicity is missing



Example 1: Summary

- Partial disorder in OD structures results in a ghost density
- Structure can be solved and refined ignoring partial disorder
- Demodulation procedure may remove ghost density and therefore help with interpretation of the ED maps
  - » Not always badly needed
  - » Not always works
  - » There are several bespoke scripts around

Example 2: auto-indexing failure

Fast DP @ DIAMOND

R_{meas} = 0.12 ?

CC(1/2) = 0.3 at 1.56 Å

Refinement

R_{cryst} = 0.33 ?

R_{free} = 0.36

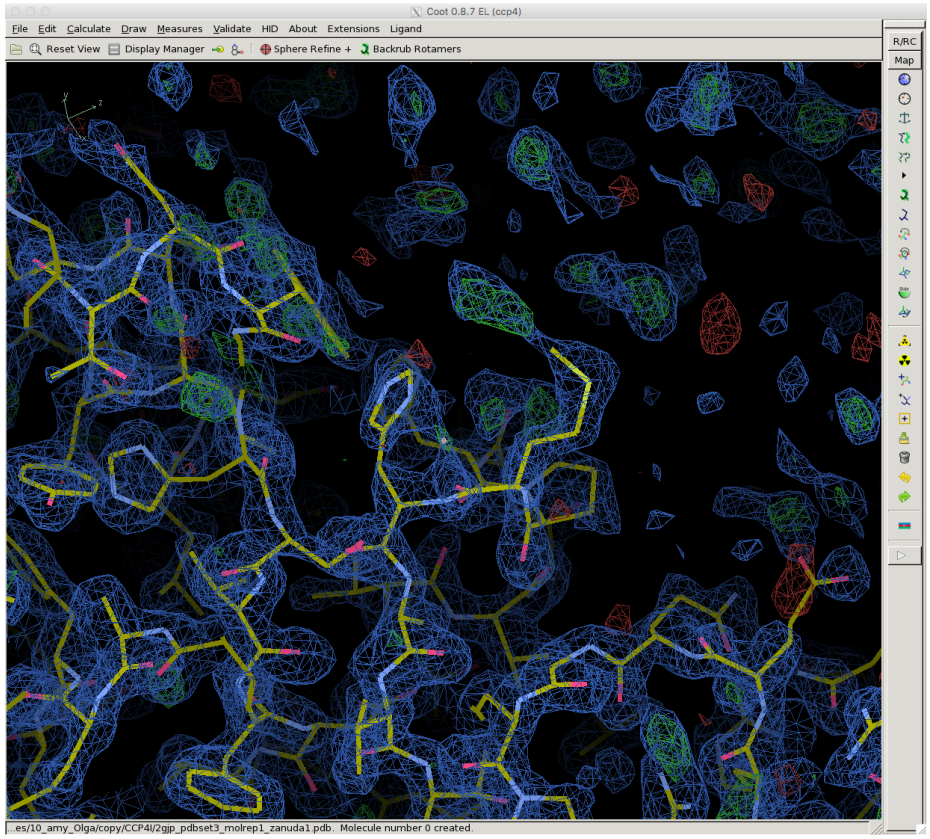
Molecular Replacement ✓

--- Peaks of Rotation Function ---

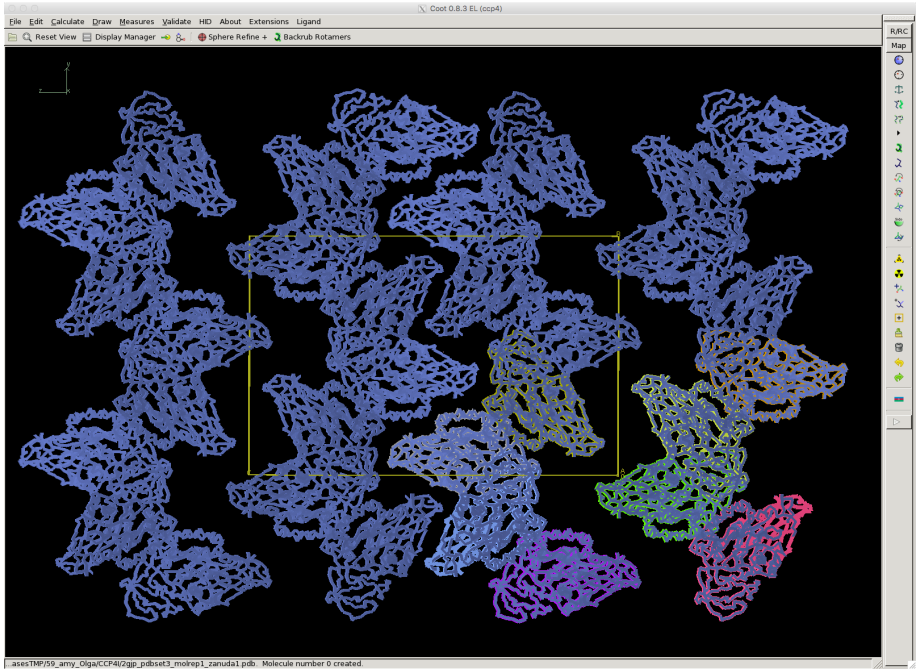
	theta	phi	chi	Rf/sigma
1	63.62	174.24	148.98	13.70
2	80.19	-58.05	61.61	13.63
3	149.48	-148.30	170.26	13.34
4	107.22	84.22	129.22	13.04
5	87.46	75.99	136.16	12.18
6	111.97	-14.20	175.28	12.10
7	157.20	173.73	153.99	11.25
8	58.77	-96.16	51.96	11.24
9	75.76	-63.11	54.46	6.21
10	102.46	82.67	133.90	5.83

Example 2: evidences of wrong indexing

Maps ?



Crystal Packing ✗

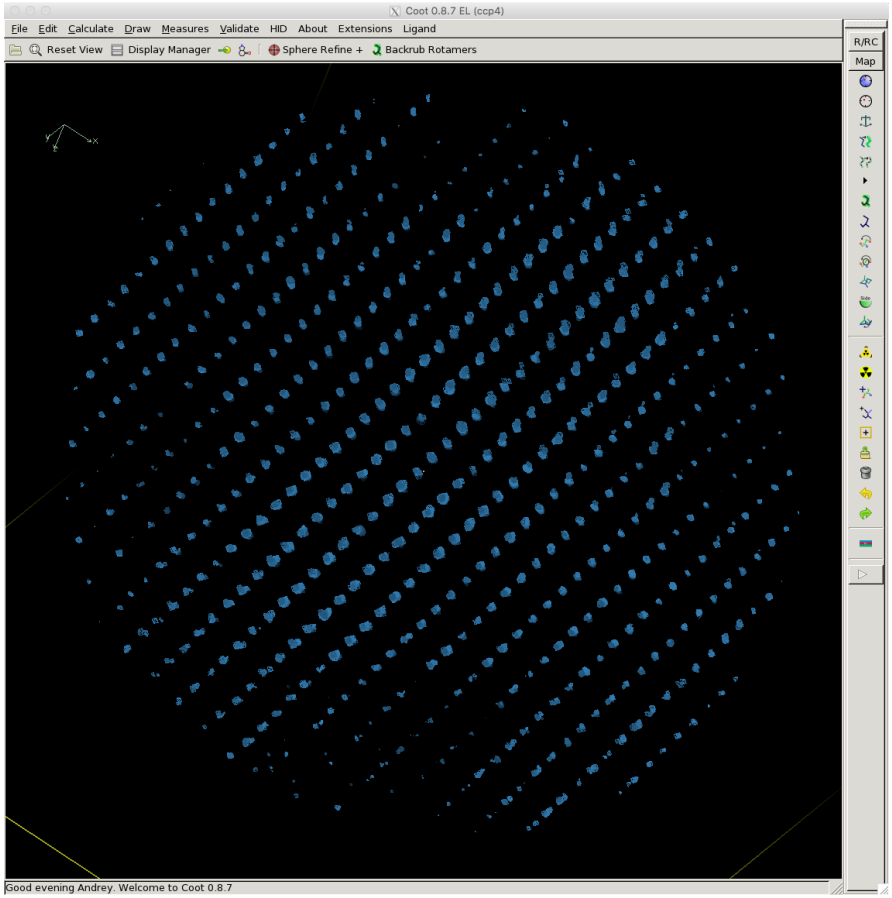


Wrong indexing?

Example 2: evidences of partial disorder

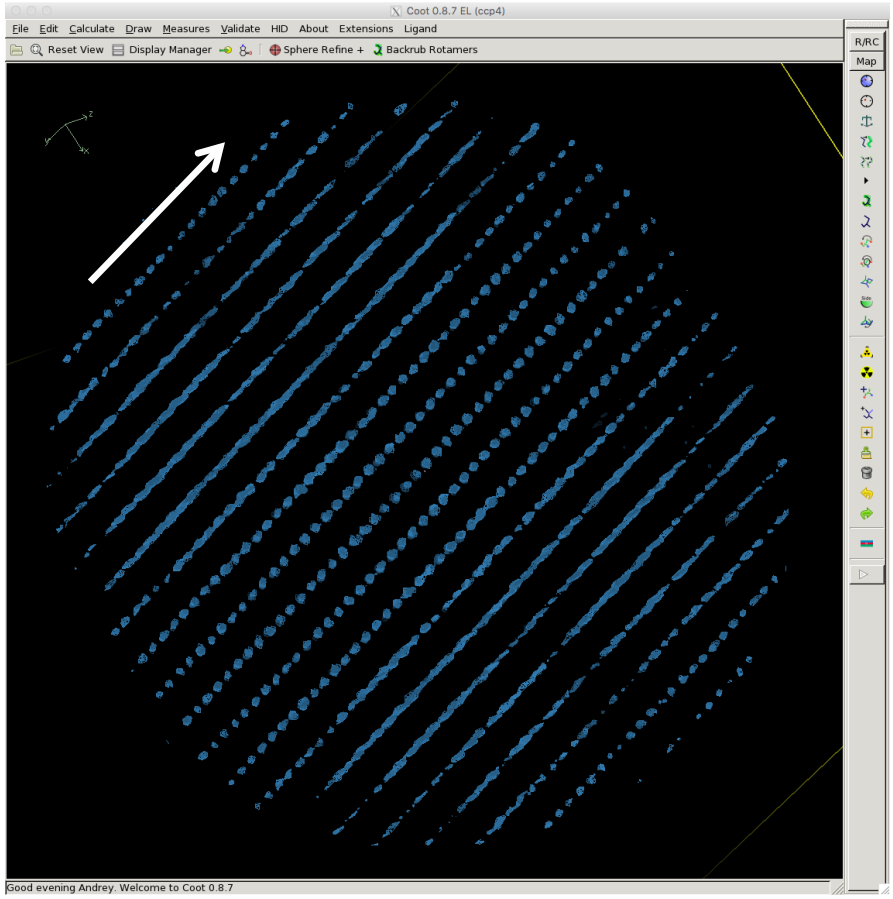
front view

There is global 2D translational symmetry in the plane of figure

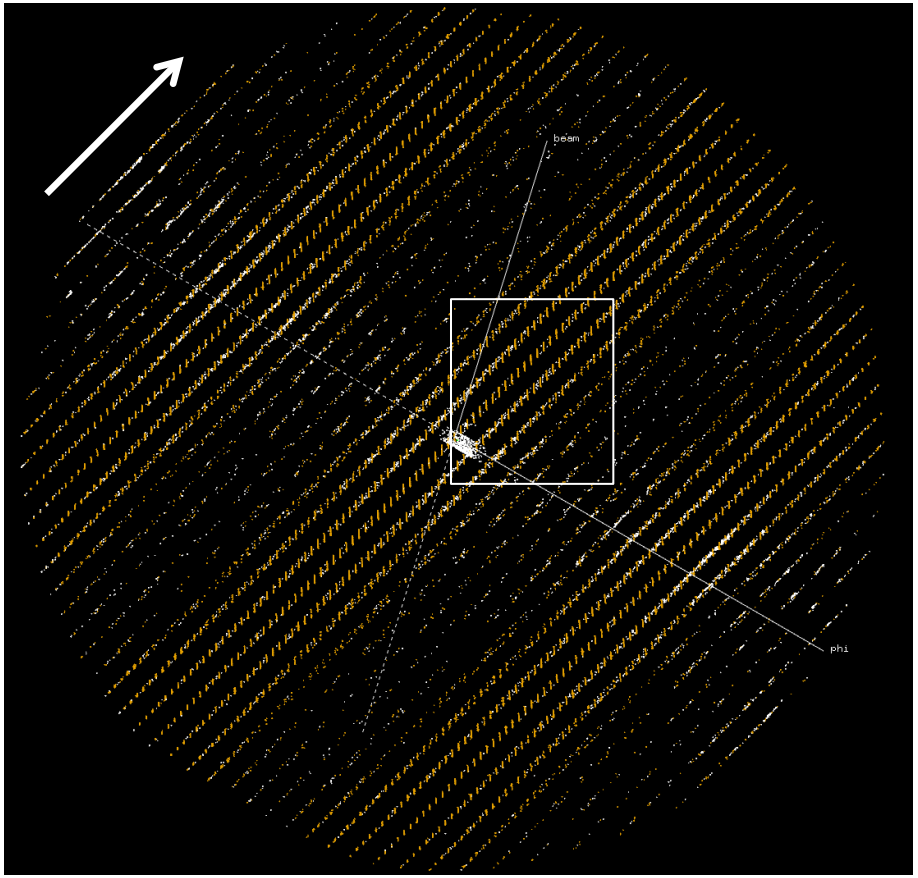


side view

White arrow indicates direction in which translational symmetry is not global (only within individual domains)



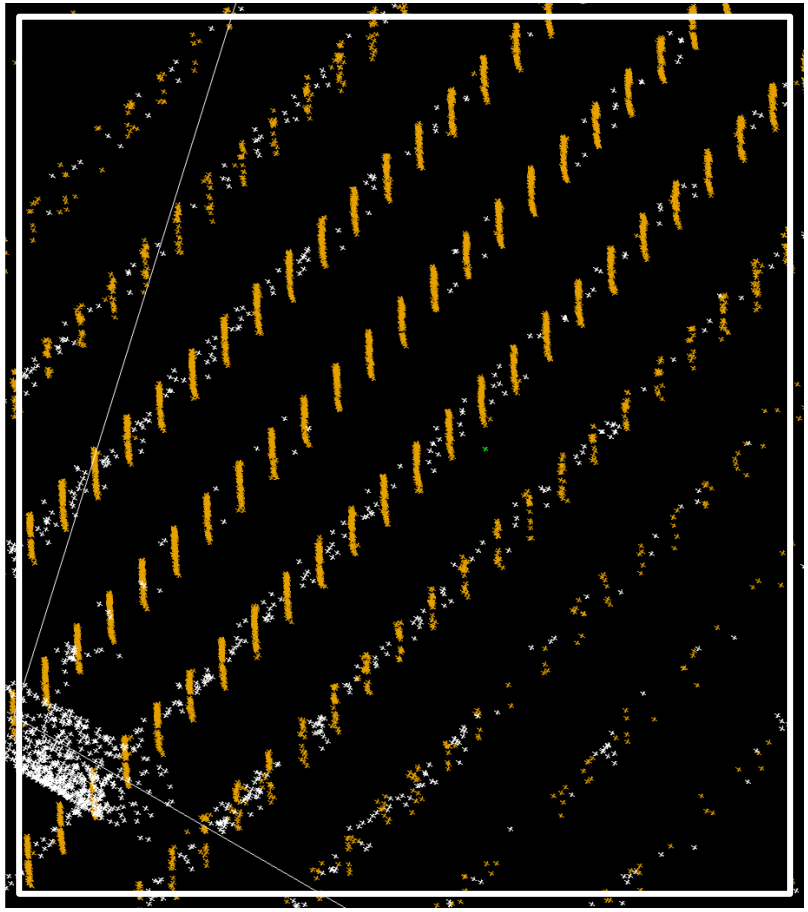
Example 2: correct indexing



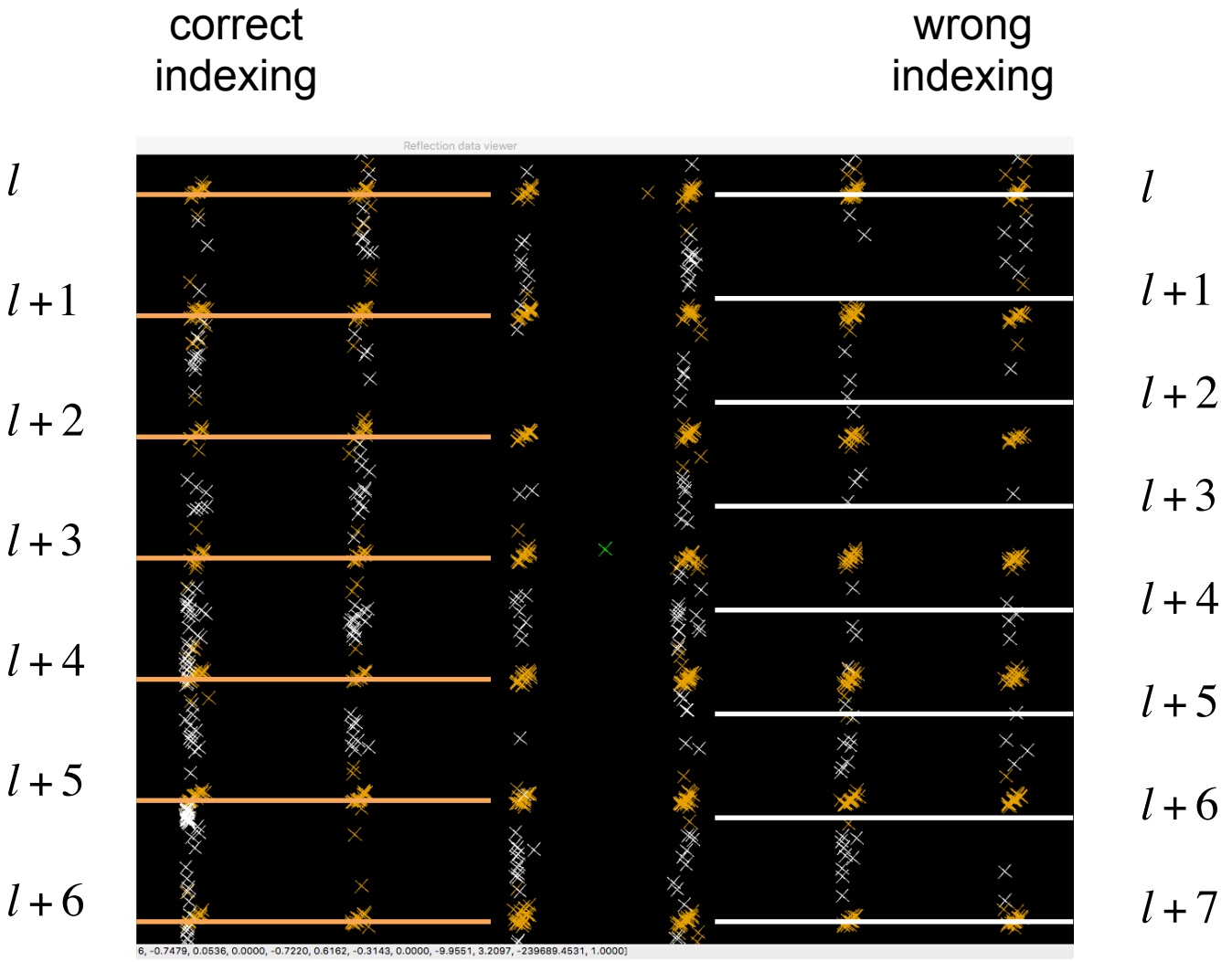
White arrow indicates direction in which translational symmetry is not global (only within individual domains)
There are also areas with less spots

White “spots” are not indexed; actually, these are tails of diffuse reflections

Indexing program may take them for real spots and produce wrong result.

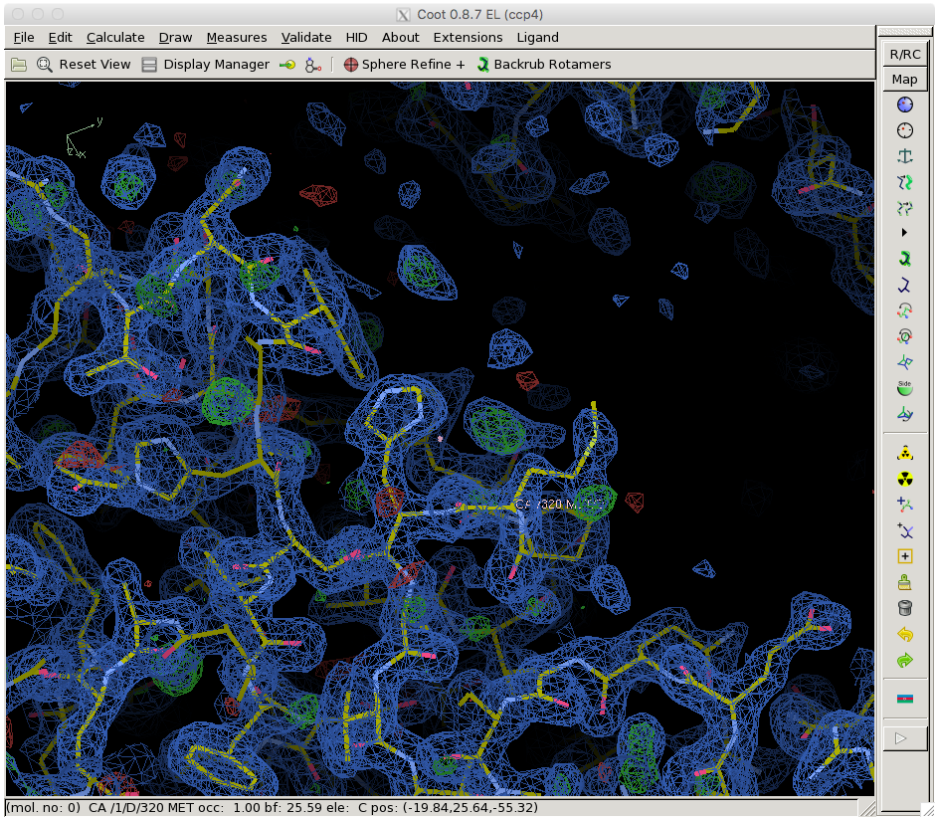


Example 2: what initially was wrong

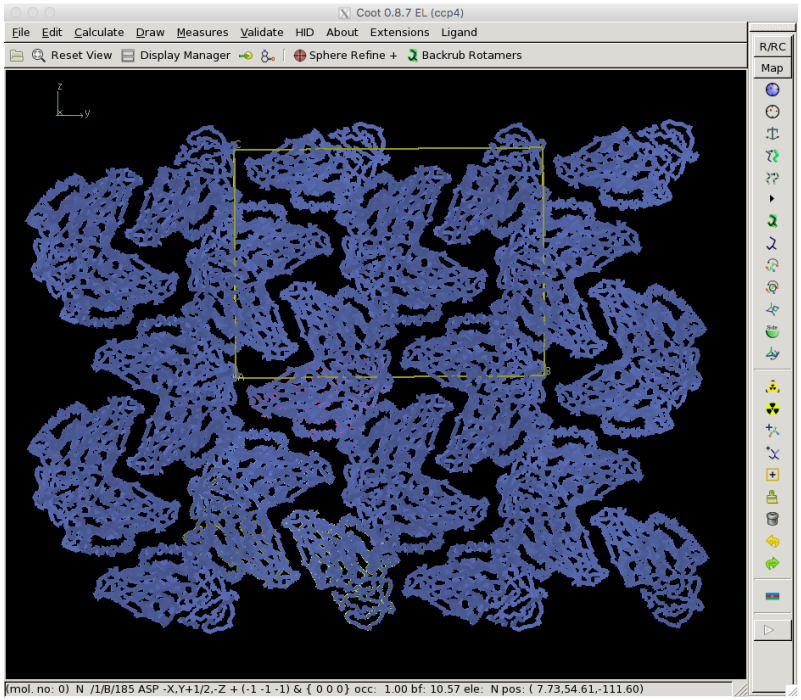


Example 2: happy end

Maps ✓



Crystal Packing ✓

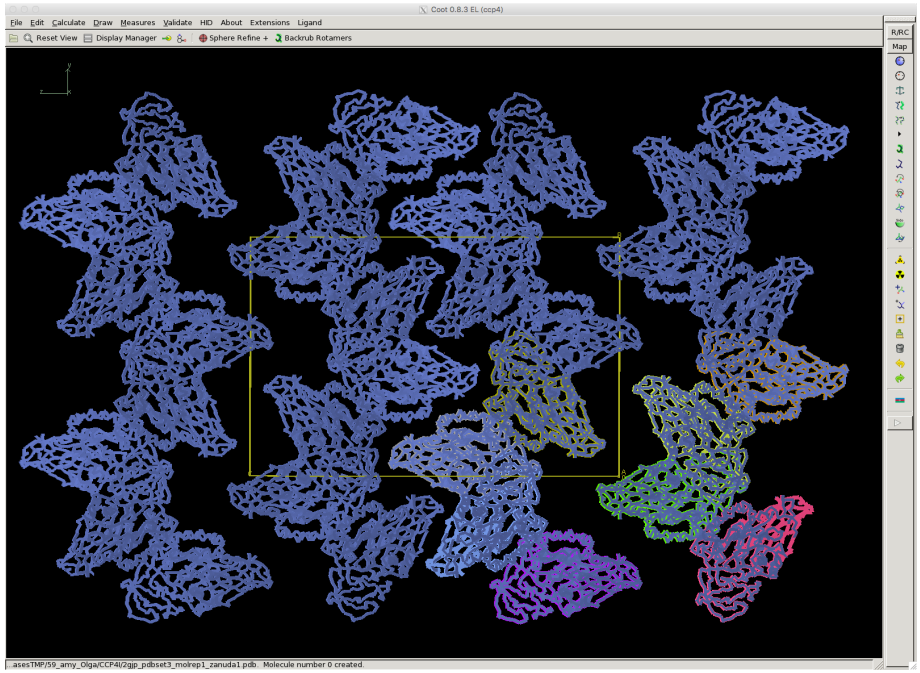


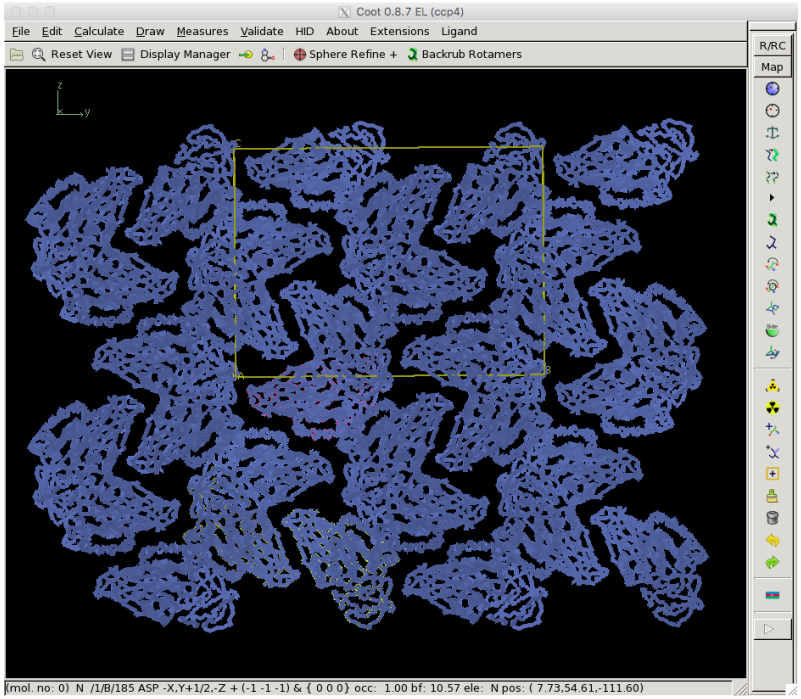
Refinement ✓

R_{cryst} = 0.23

R_{free} = 0.26

Example 2: wrong and correct





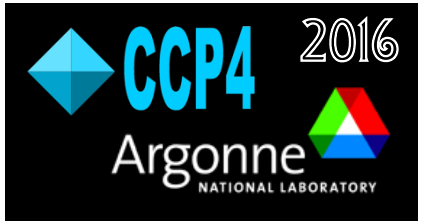
Example 2: Summary

- Partial disorder a frequent reason of indexing failure
- Use 3d viewers for diagnostics
- Warning: high contrast in MR can be obtained even for wrongly indexed data provided that the search model is highly similar to the target

Example 3: unsolvable structure

Input information:

Example from Rui Wu

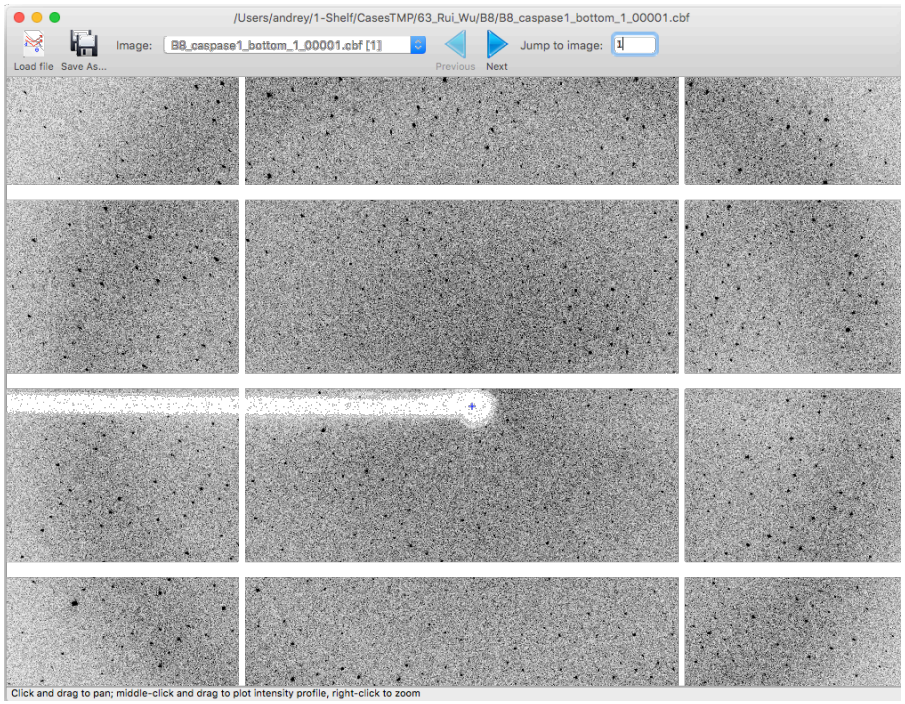


- Images are good
  - But there a several different indexing solutions
- 99% homologue for Molecular Replacement
  - But no MR solution
  - Even more, no contrast on Rotation Function
- Twinning?

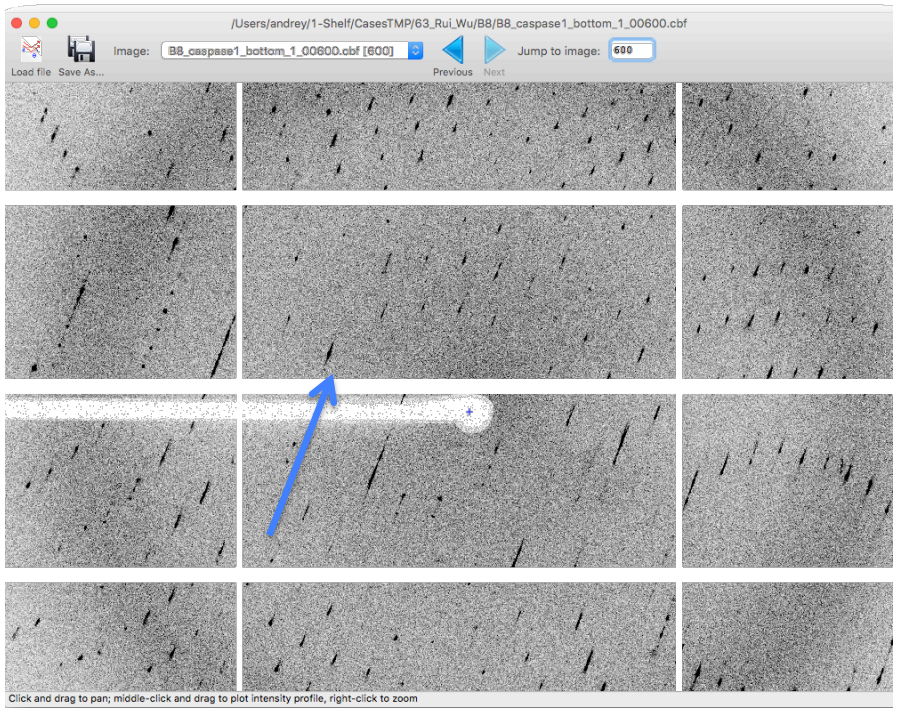
Example 3: first and last images

Partial disorder was not detected directly from images

first image



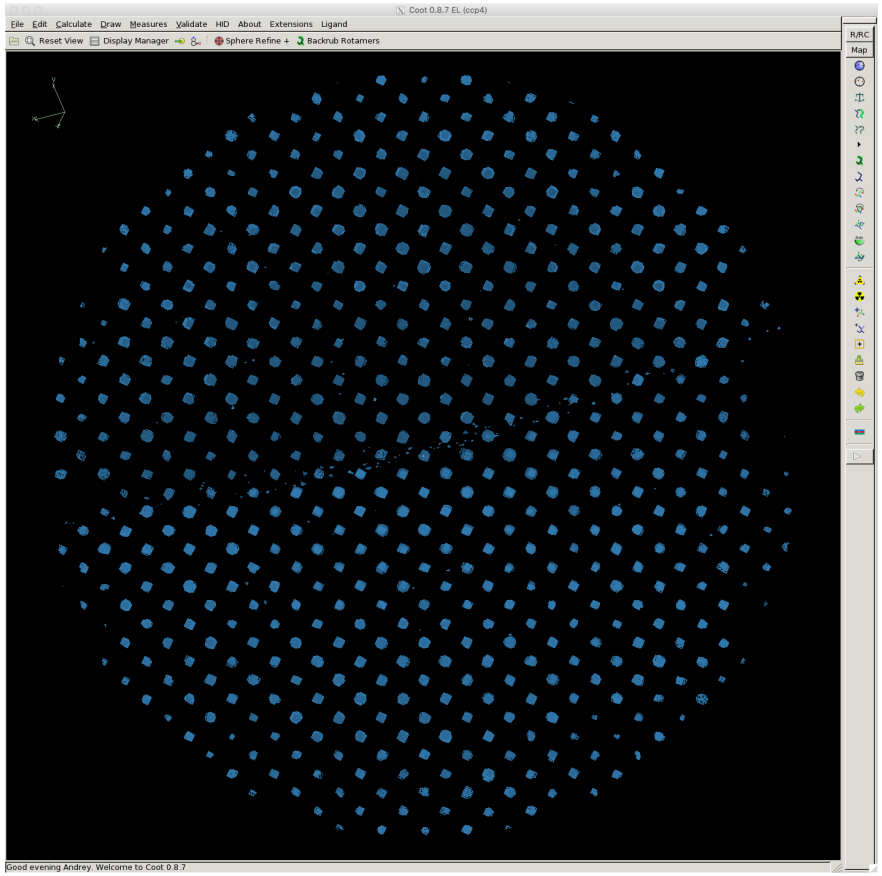
last image



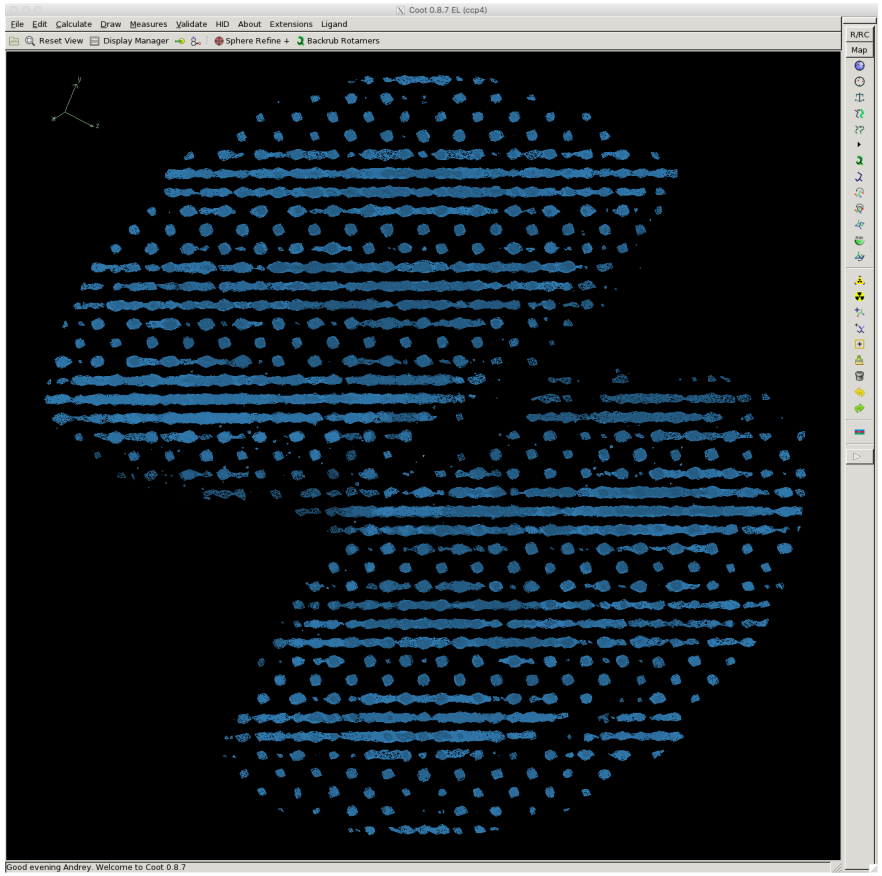
Blue arrow – direction of missing global translation

Example 3: checking diffraction in 3D

front view

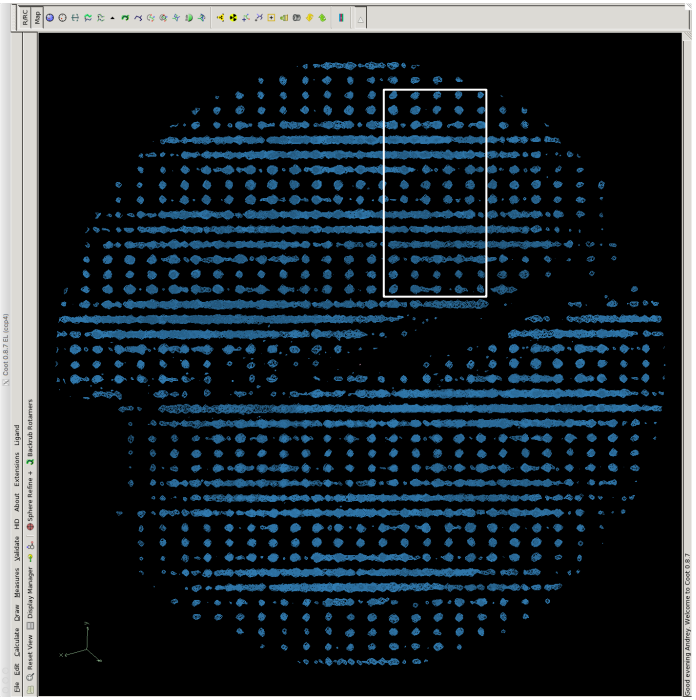


side view

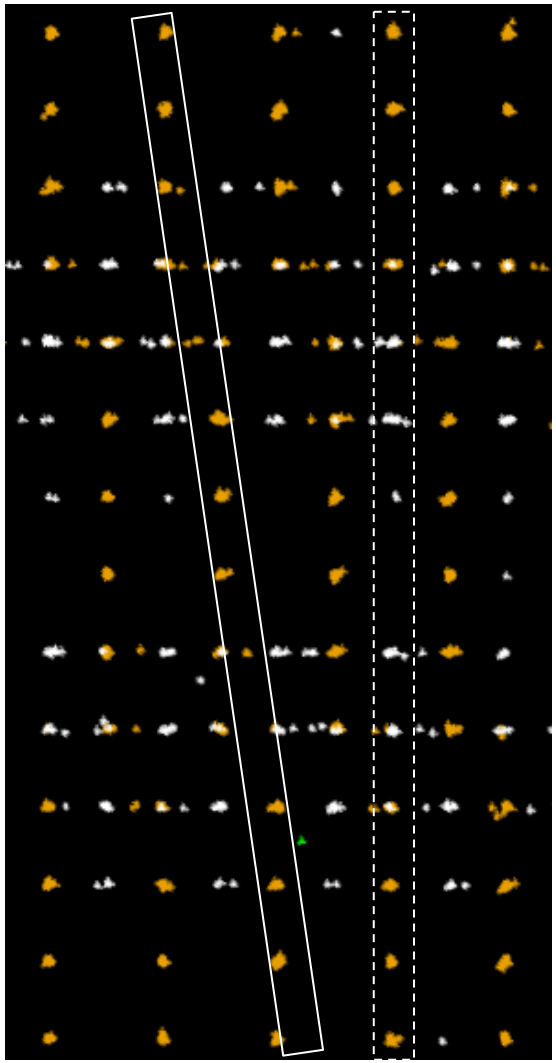


Clear partial disorder

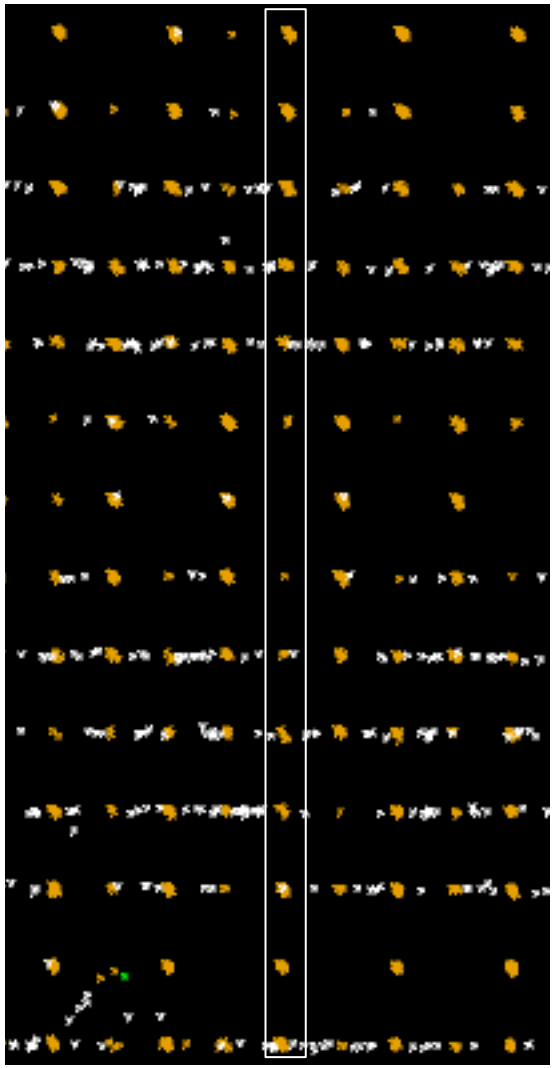
Example 3: wrong and correct indexing



2, C (wrong)



222, C (correct)



Indexed: yellow
Not indexed: white

Example 3: unsolvable structure

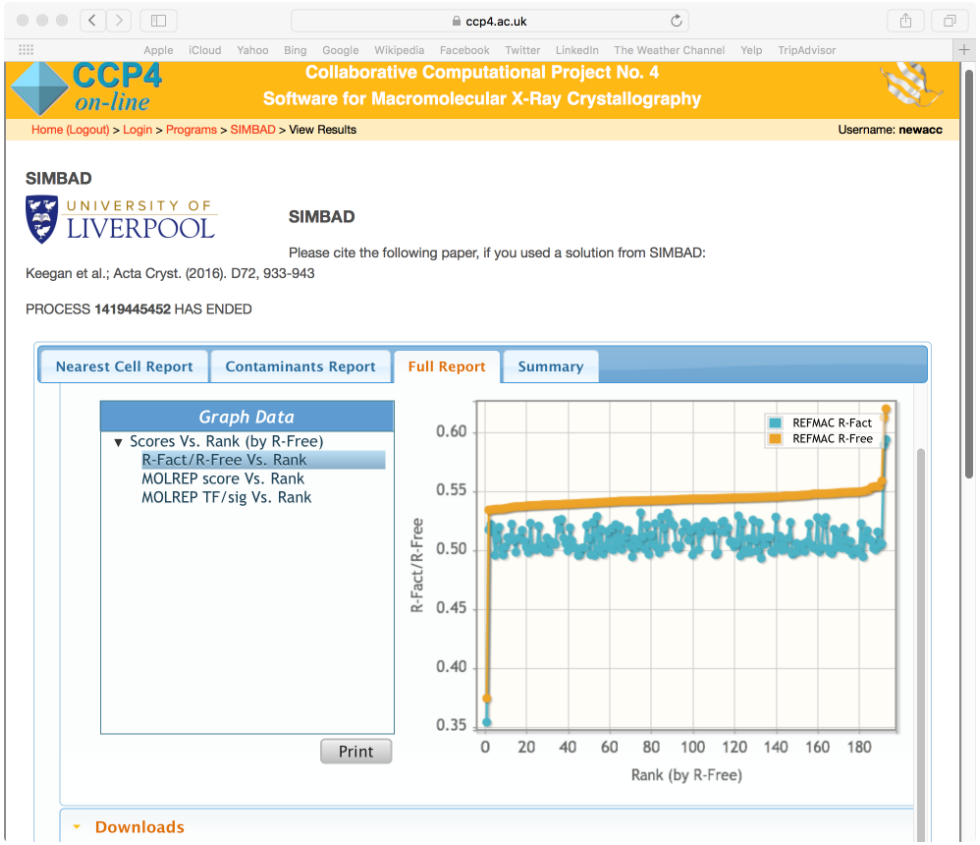
Input information:

- Images are good
  - But there a several different indexing solutions
- 99% homologue for Molecular Replacement
  - But no MR solution
  - Even more, no contrast on Rotation Function
- Twinning?

Example 3: MR against PDB (Simbad; less happy end)

Despite very clean sample
a minor contaminant has crystallised:

Crystal pathology is not necessarily a reason for failure to solve structure!



Partial disordered OD structures

- Data processing
  - Indexing can go wrong (use higher "gain" parameter, merge several adjacent images together etc. to get it right)

- Structure solution:
  - Molecular Replacement - yes
  - Experimental phasing – must be problematic

- Refinement / model building:
  - Some features of electron density may be non-interpreted (ghost density)
  - Expect higher R-factors

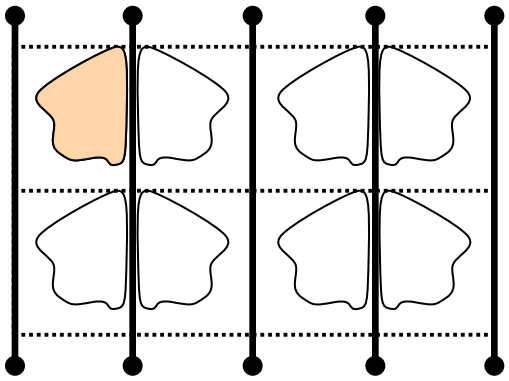
- Crystals with translocation defects
  - Term usually used in MX for partially disordered OD-structures

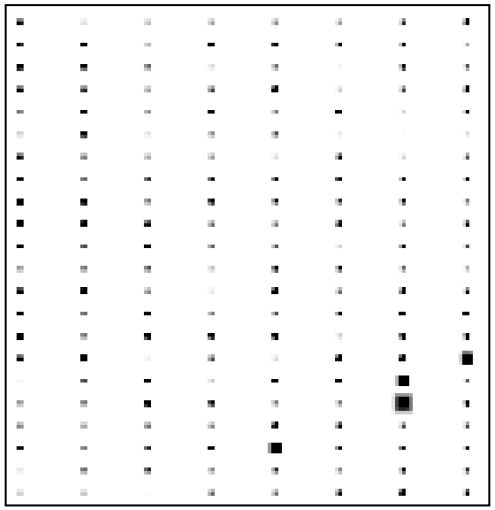
Pseudo-translation

- Visualisation
- Effect on indexing
- Pseudo-origin MR solutions

Pseudotranslation

Crystallographic translation





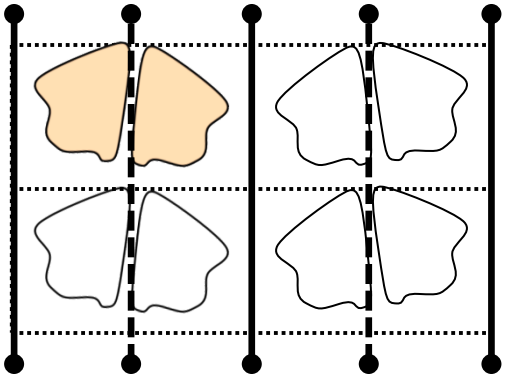
No pseudotranslation

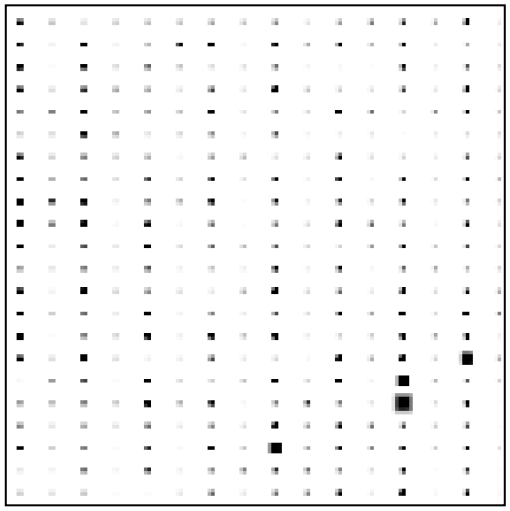
c

*c**

Crystallographic translation

Pseudo-translation





Pseudotranslation

c' = 2 *c*

c'* = *c**/ 2

Planes 2L+1 contain weak reflections

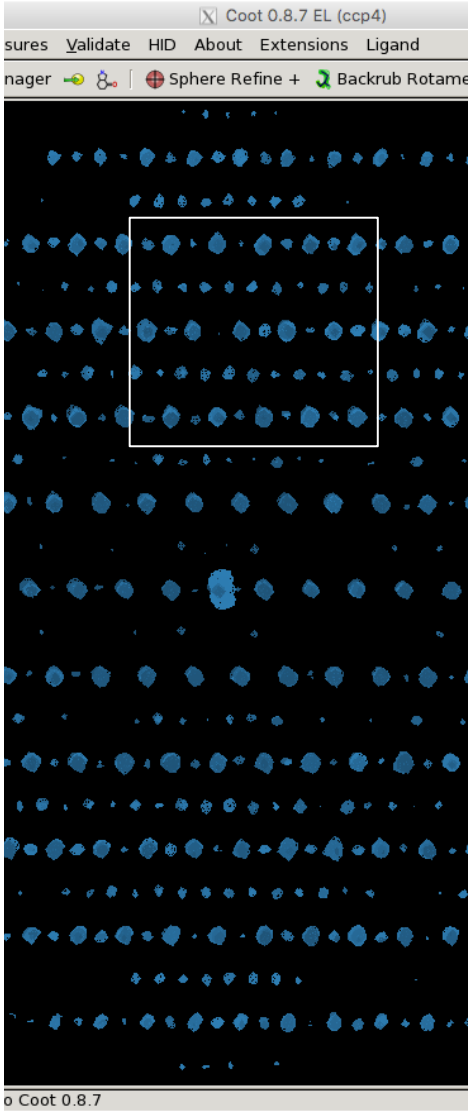
Example: two pseudo-translation vectors

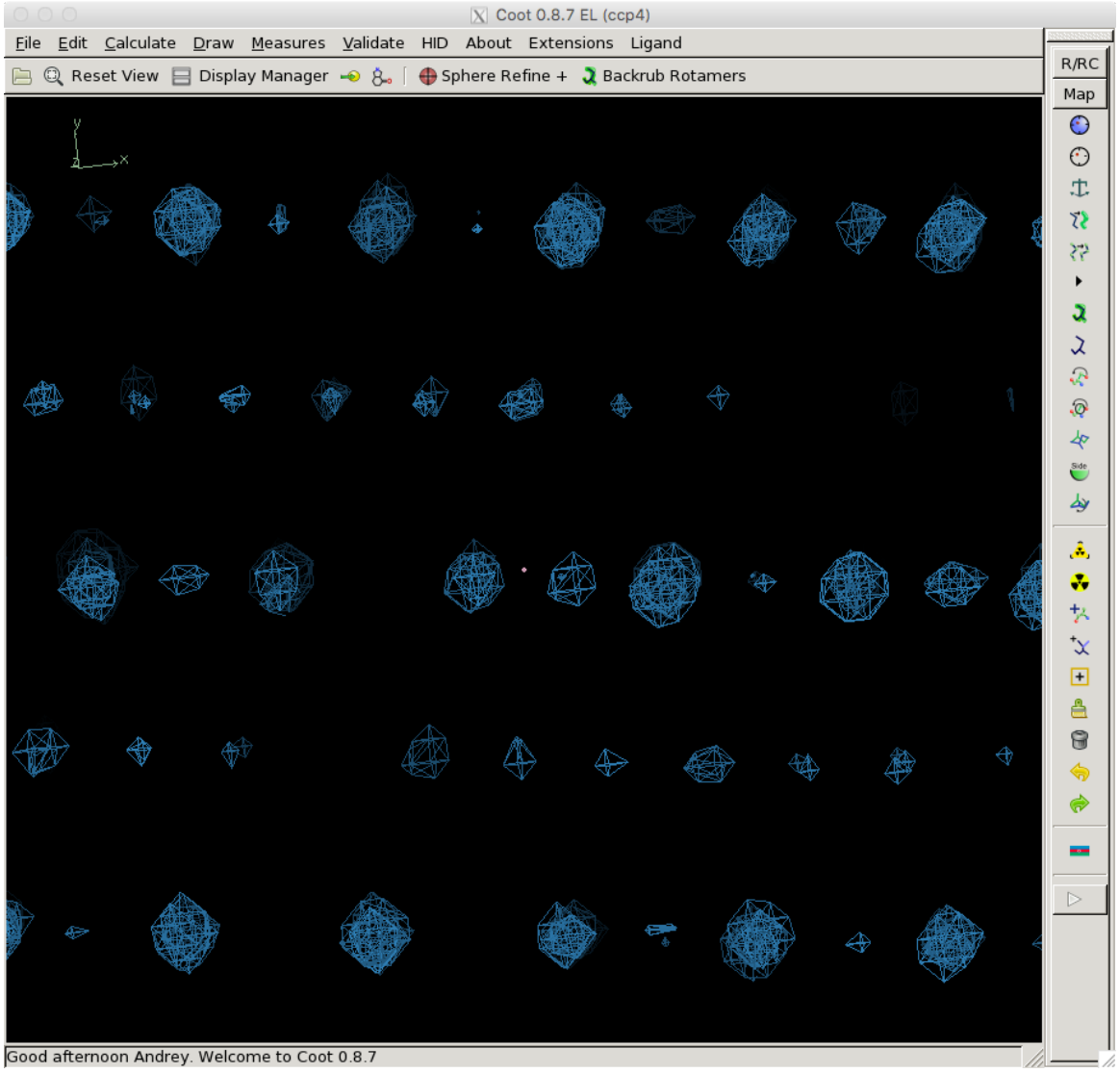
	space group	*a* (Å)	*b* (Å)	*c* (Å)
All reflections	*C* 2 2 2	74.9	122.8	125.0
Strong reflections only	*I* 2 2 2	37.5	61.4	125.0

Example from Victor Lamzin, YSBL-DESY

» structure solved using SAD

Example: two pseudo-translation vectors



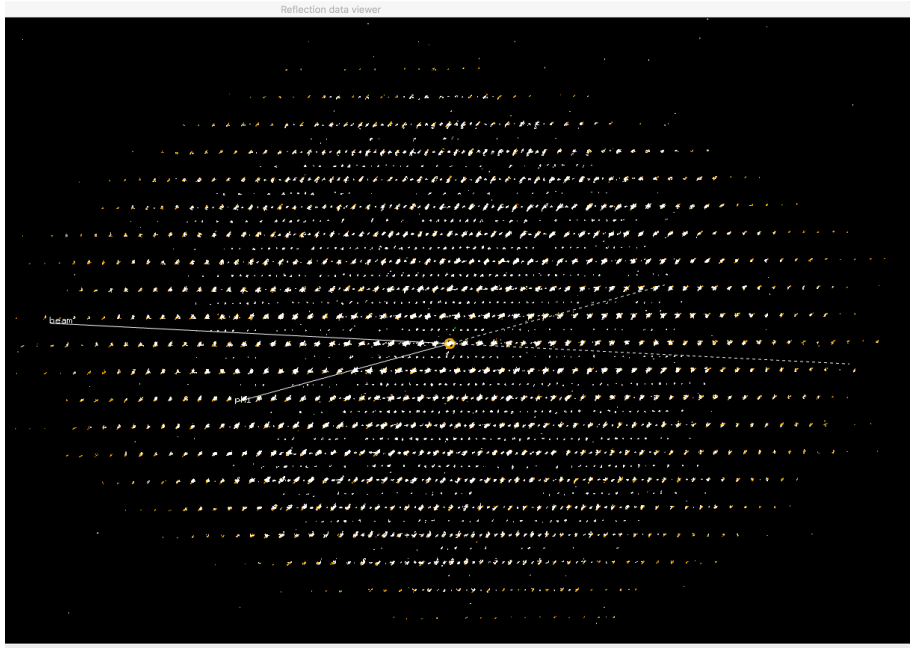


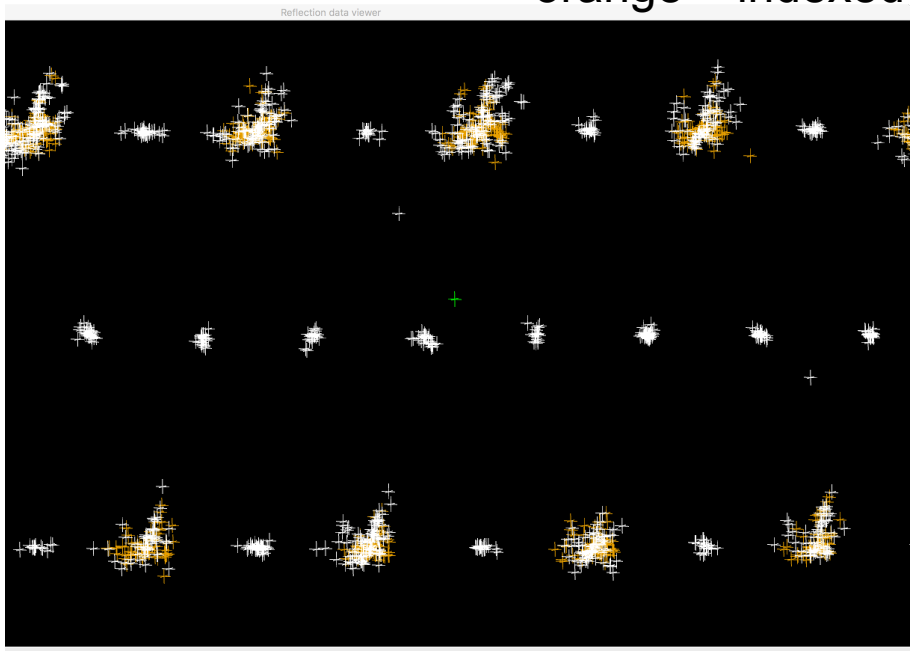
Example: two pseudo-translation vectors

Images imported as they were, oscillation 0.1°

```
dials.import template=images/SeMet_38_04_0####.cbf
dials.find_spots ...
dials.index ...
dials.refine ...
dials.reciprocal_lattice_viewer ...
```

white – not indexed
orange – indexed



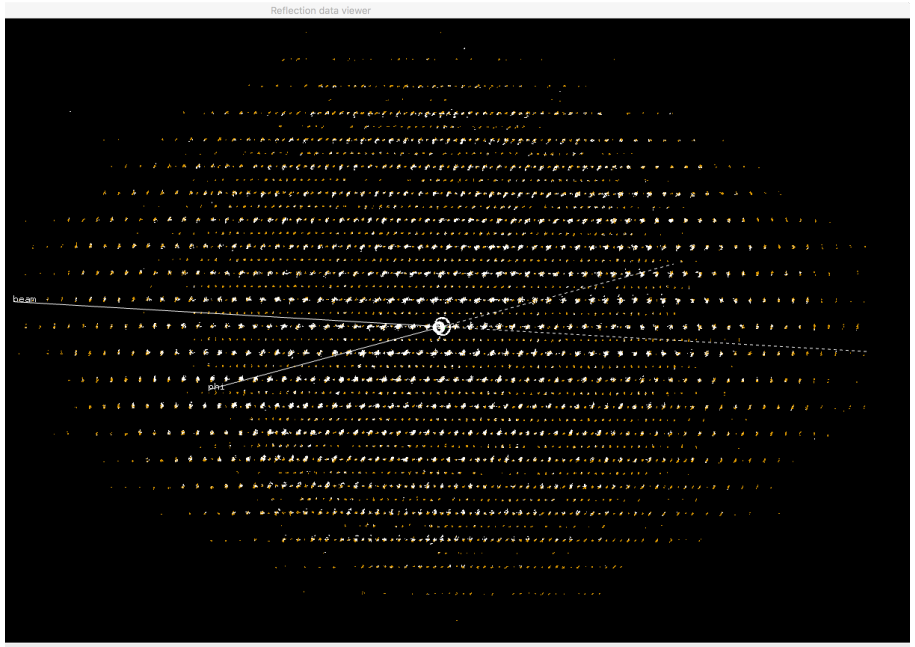


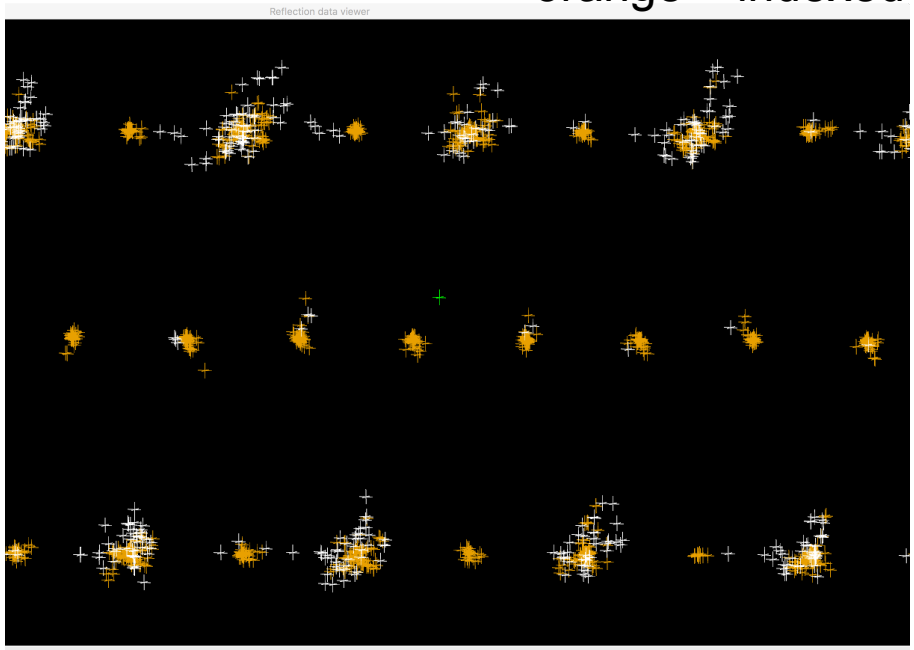
Example: two pseudo-translation vectors

Merged each 5 adjacent images to make oscillation 0.5°, then imported

```
dials.merge_cbf images/SeMet_38_04_0####.cbf merge_n_images=5
dials.import template=sum_####.cbf
dials.find_spots ...
dials.index ...
dials.refine ...
dials.reciprocal_lattice_viewer ...
```

white – not indexed
orange – indexed





Pseudo-translation and indexing

Week reflections may confuse indexing programs

Visual control using 3D viewers is useful

- check if pseudo-translation is not overlooked
- check if pseudo-translation is not an indexing artefact

How important is to use the weak reflections?

- usually improve both density and refinement stats
- there are examples when these only make refinement stats worse
- sometimes ignored to simplify the first steps of structure solution and used later

END

You are welcome to discuss your problematic data!

Non-commensurate modulated structures

- Example

» from Ivan Campeotto, Oxford and Arwen Pearson, DESY (PDB id 2wnq)

Non-commensurate modulated structure

