Progress towards connecting Global Phasing's workflow with MXCuBE

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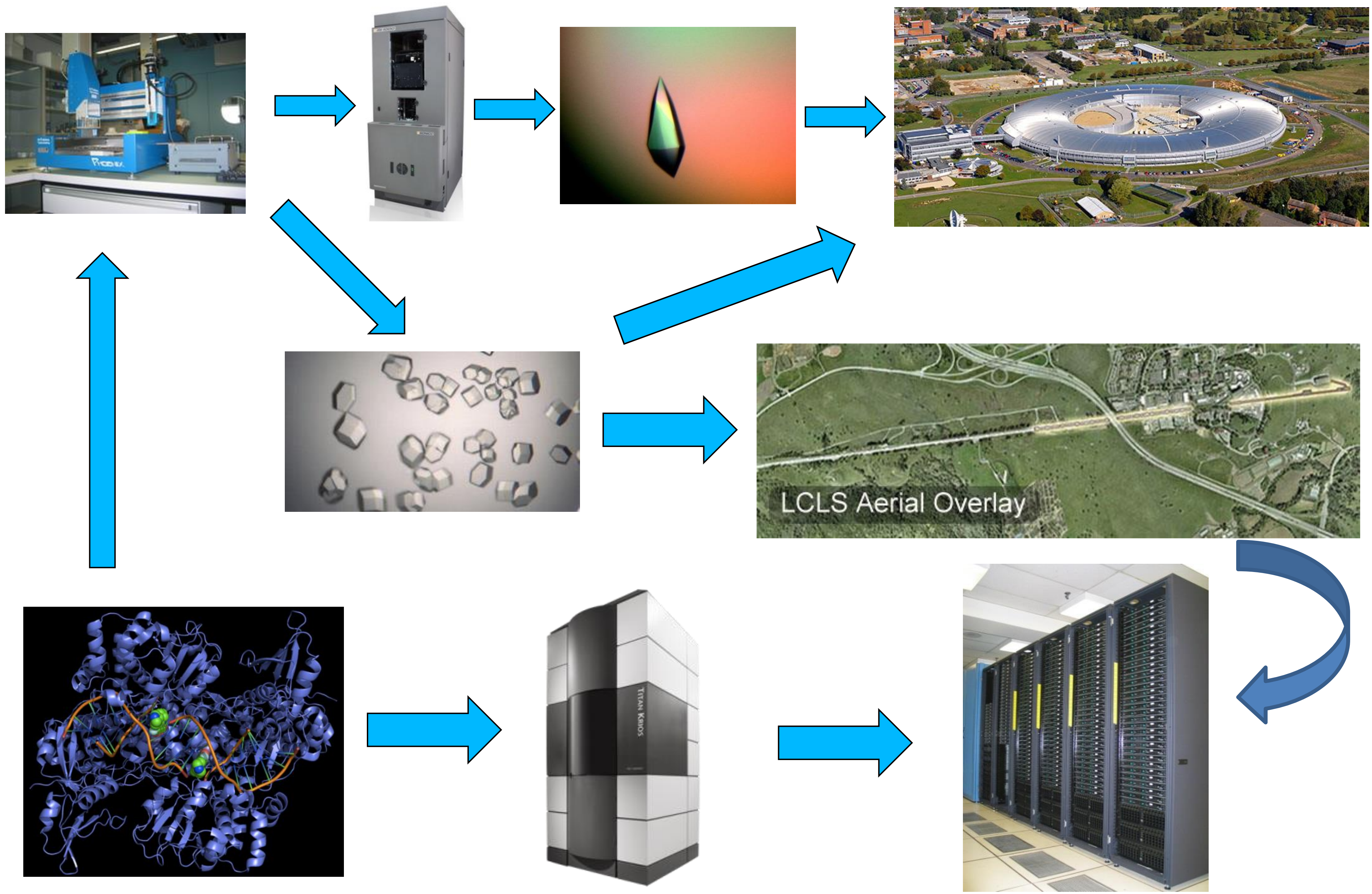
GΦL

Summary: options from molecule to structure



Humpty Dumpty

Humpty Dumpty sat on a wall,
Humpty Dumpty had a great fall.
All the king's horses and all the king's men
Couldn't put Humpty together again.

An unexplored niche: "Club Class" data collection

- The ever-increasing speed of MX beamline instrumentation is leading to ever-stronger emphasis being placed on brevity of execution as the main design goal for data collection protocols, often to the exclusion of other criteria that would aim at achieving higher data quality. This can be counter-productive.
- What about trying to make better use of Humpty Dumpty in one piece? I.e. collect better data on conventional crystals by better exploiting the available technologies?
- Global Phasing, among others, has been interested in bucking that trend by creating combined capabilities for the fast design of optimal strategies and the direct supervision of their execution on an actual beamline.

The STARANISO Server

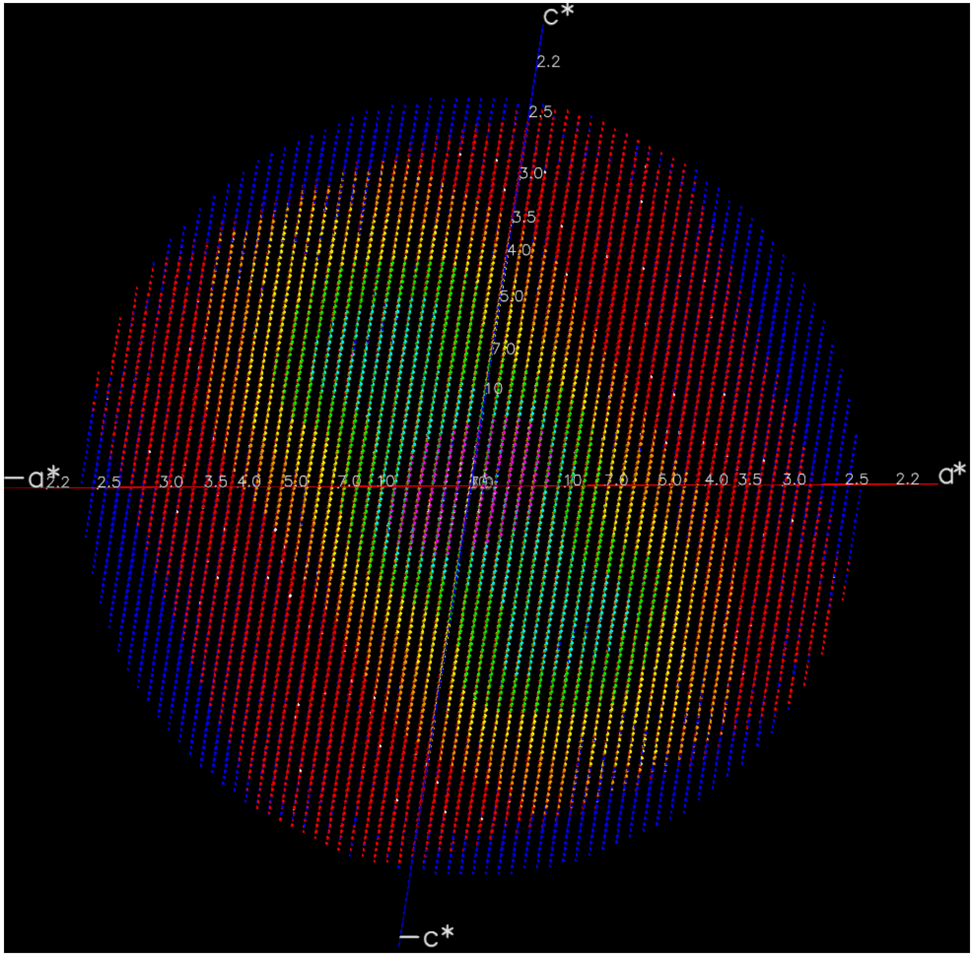
Anisotropy of Diffraction Limits
and
Bayesian Estimation of Structure Amplitudes

Global Phasing Limited

with Ian Tickle

Illicium verum

A case of anisotropy in C2
(Esther Ortega and Jose M. de Pereda)



BUSTER refinement of PDB entry XXXX from deposited data (16727 Fobs)

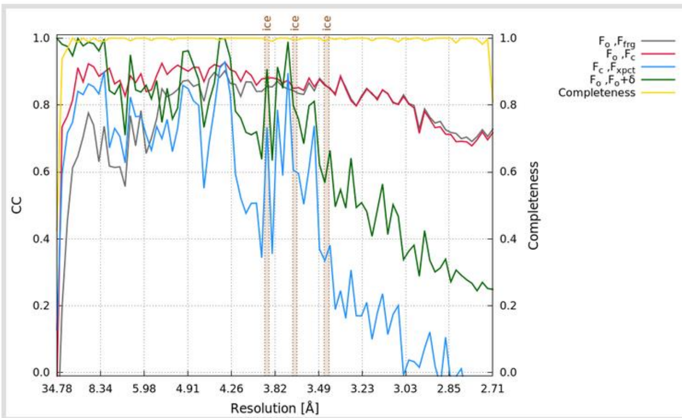


Fig 1: Start

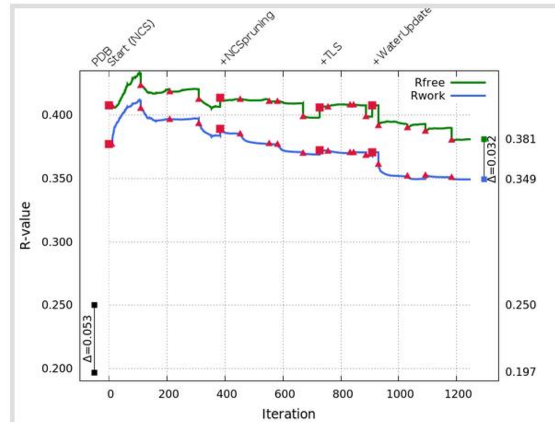


Fig 2: Refinement progress

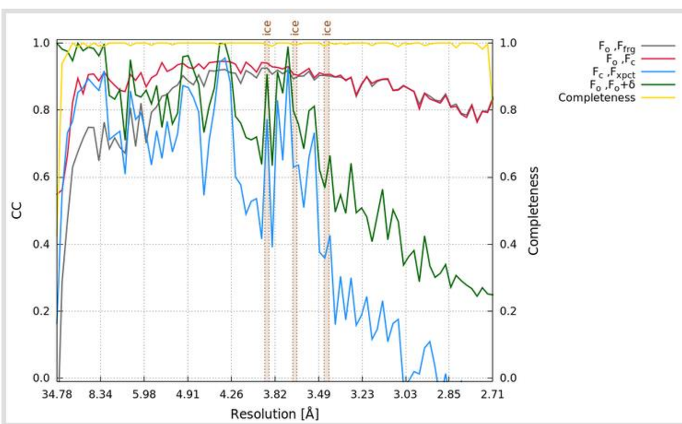


Fig 3: Final

BUSTER refinement of PDB entry XXXX amended deposited data (15947 Fobs)

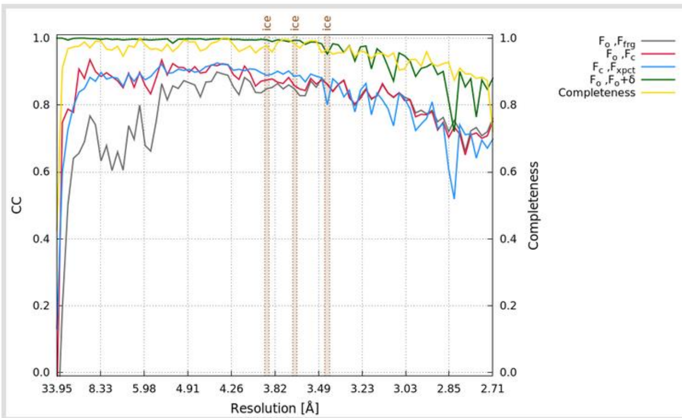


Fig 1: Start

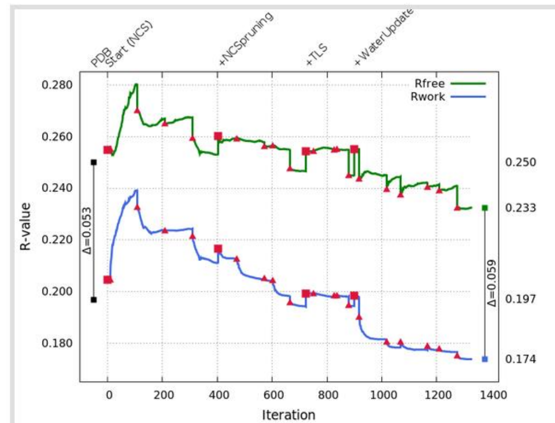


Fig 2: Refinement progress

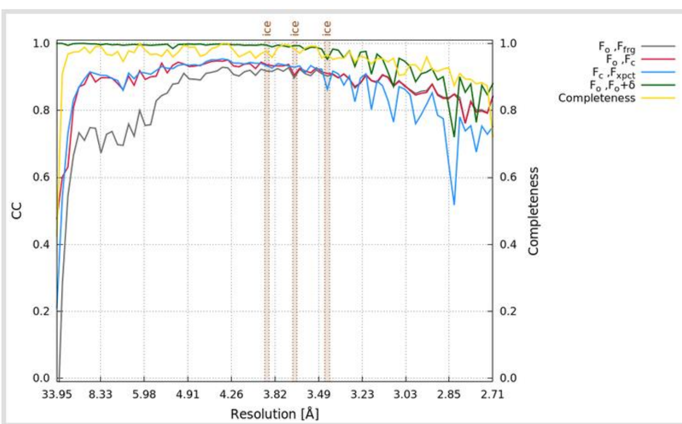
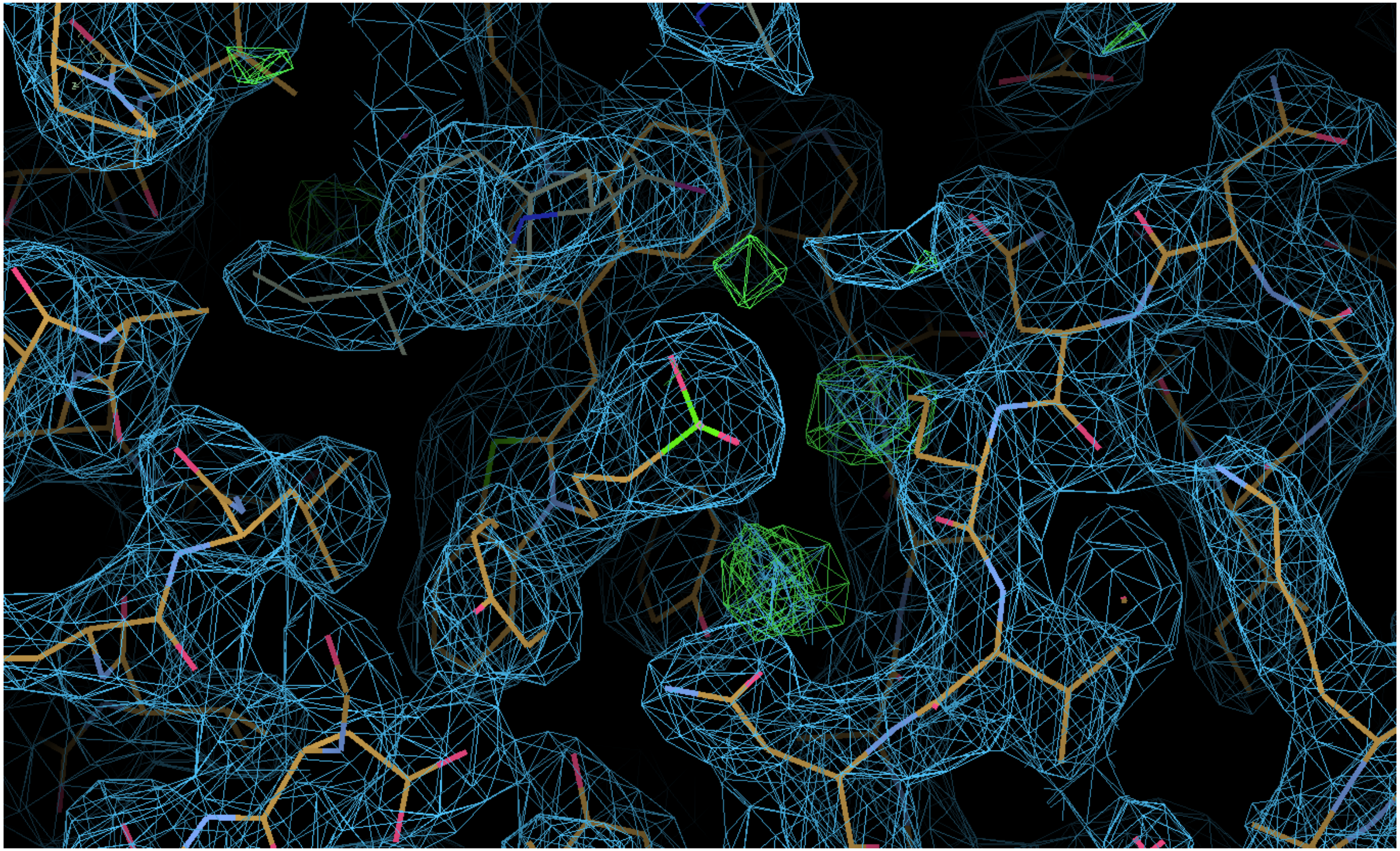
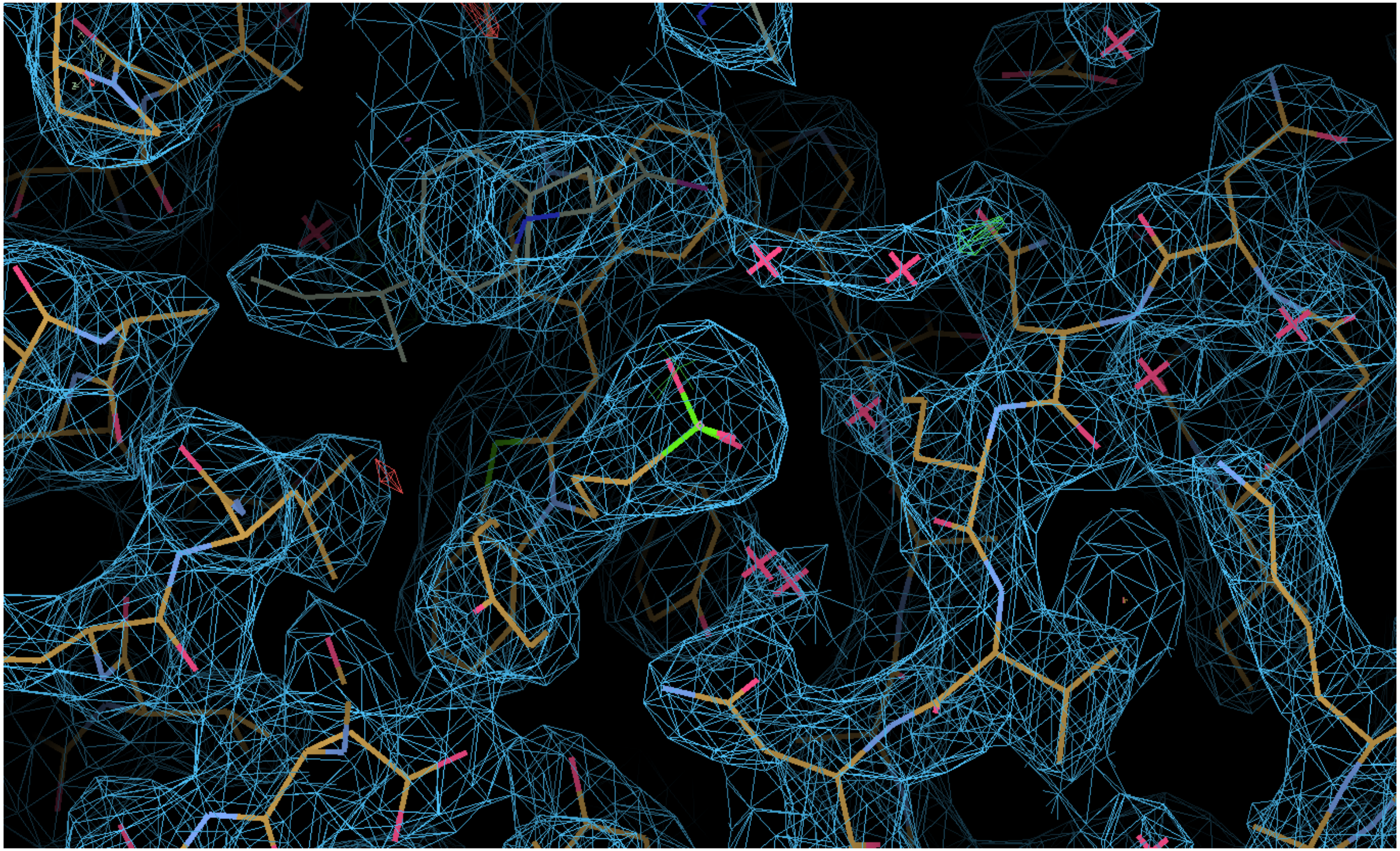


Fig 3: Final

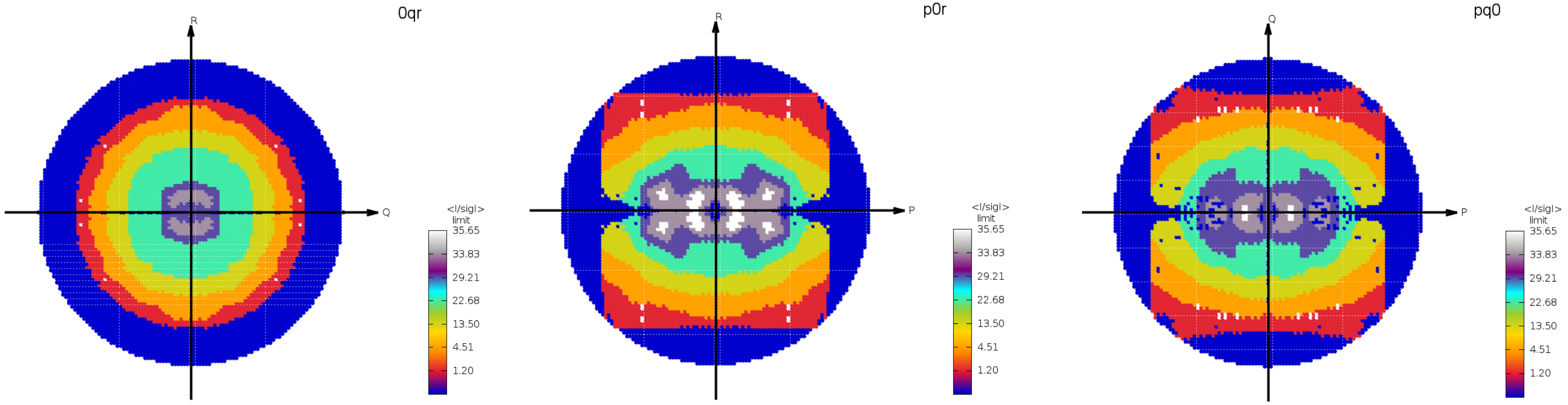
XXXX from deposited data



XXXX from deposited data after “water update” (5 -> 168)



XXXX anisotropy analysis with STARANISO (now part of autoPROC)



BUSTER refinement of XXXX STARANISO corrected data (26978 obs)

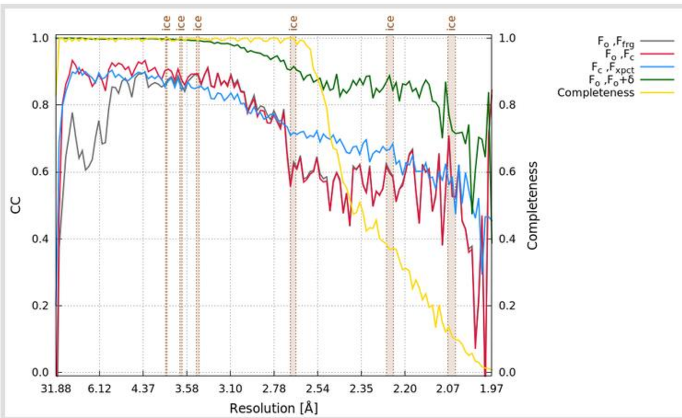


Fig 1: Start

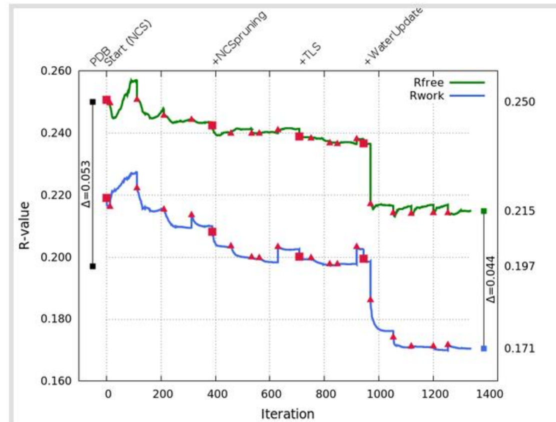


Fig 2: Refinement progress

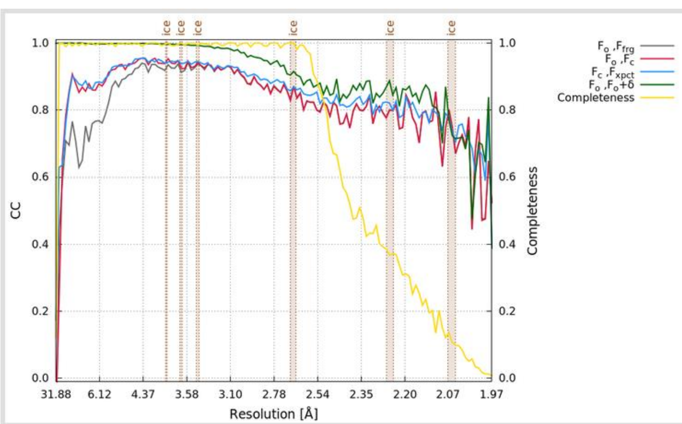
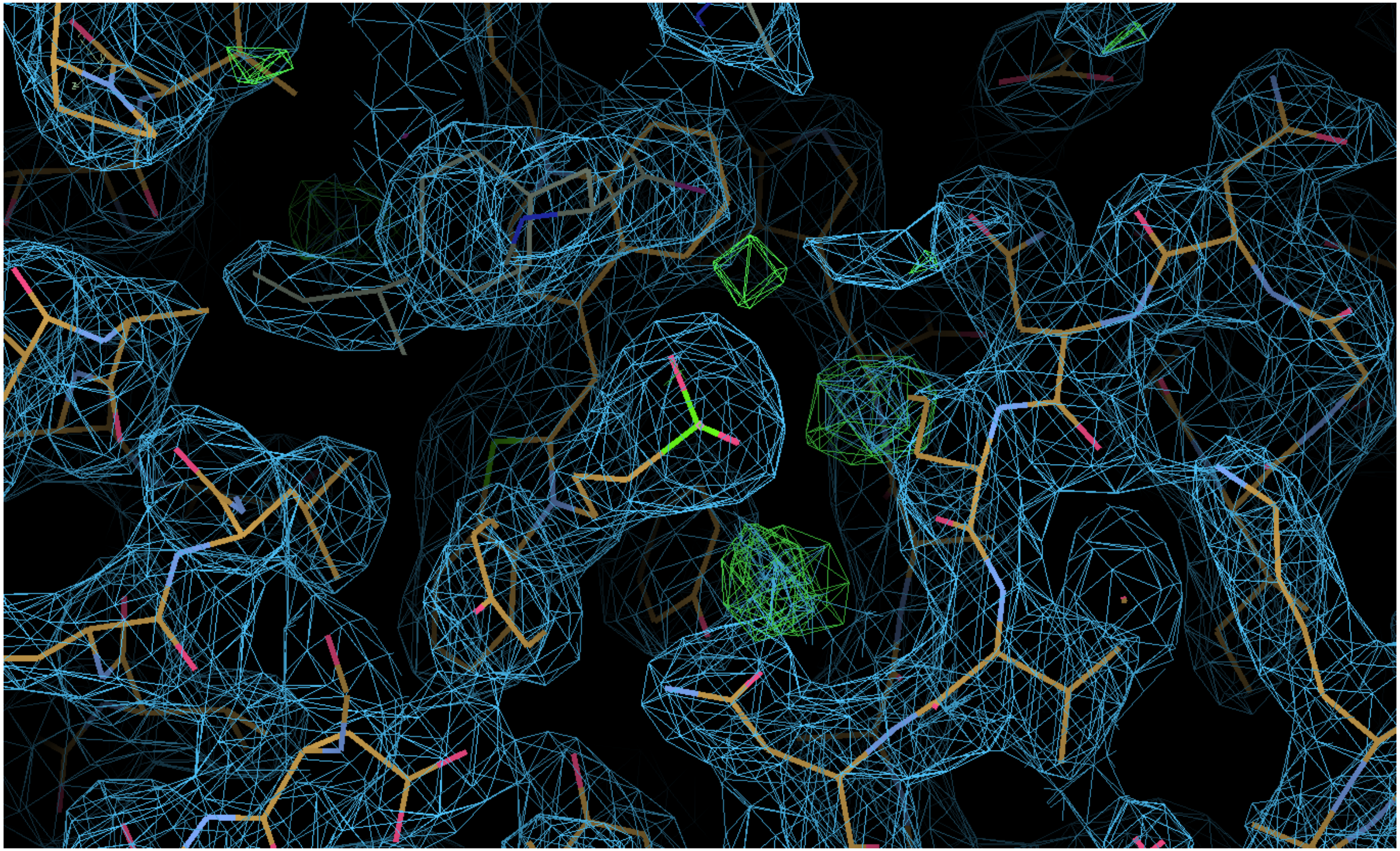
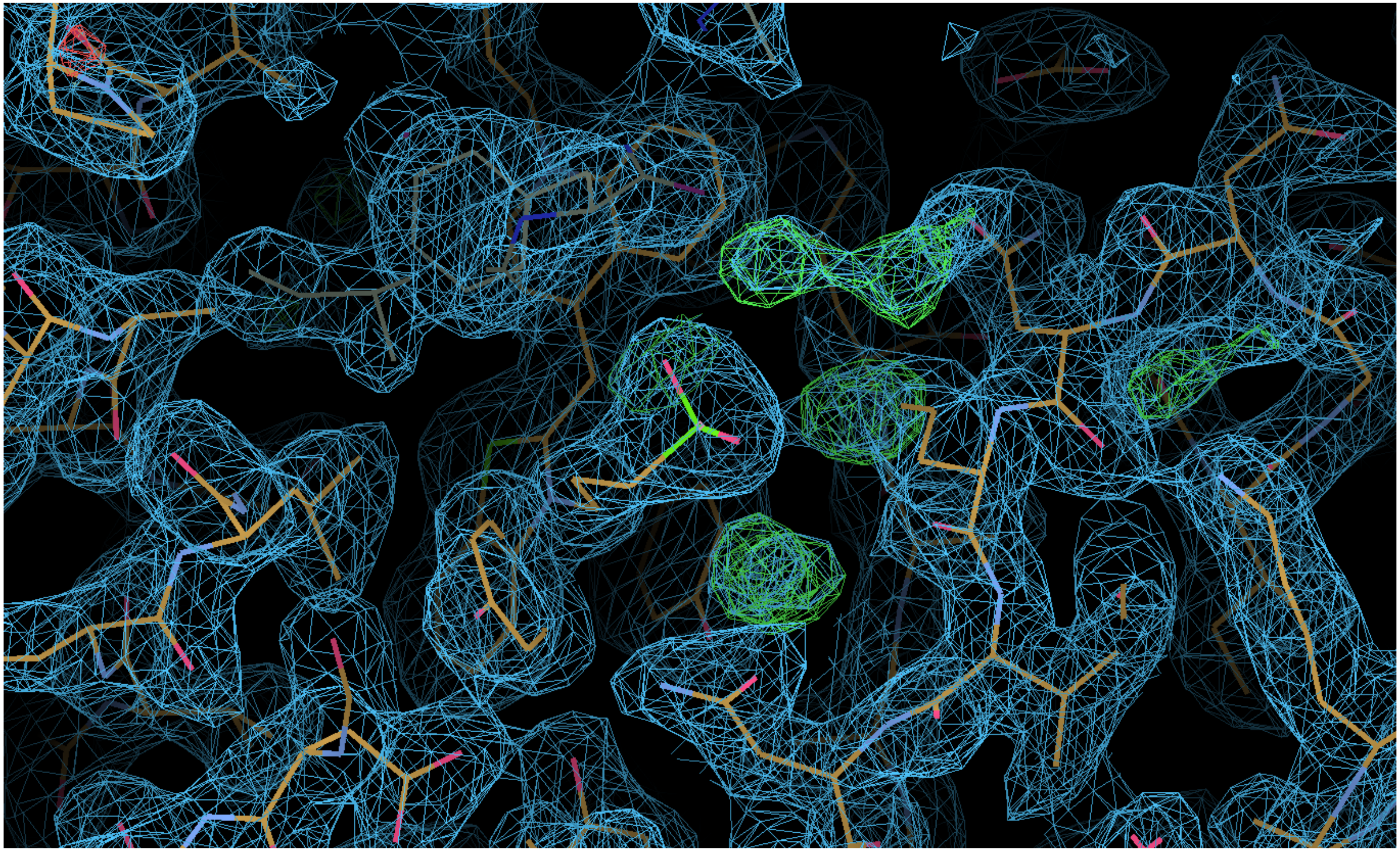


Fig 3: Final

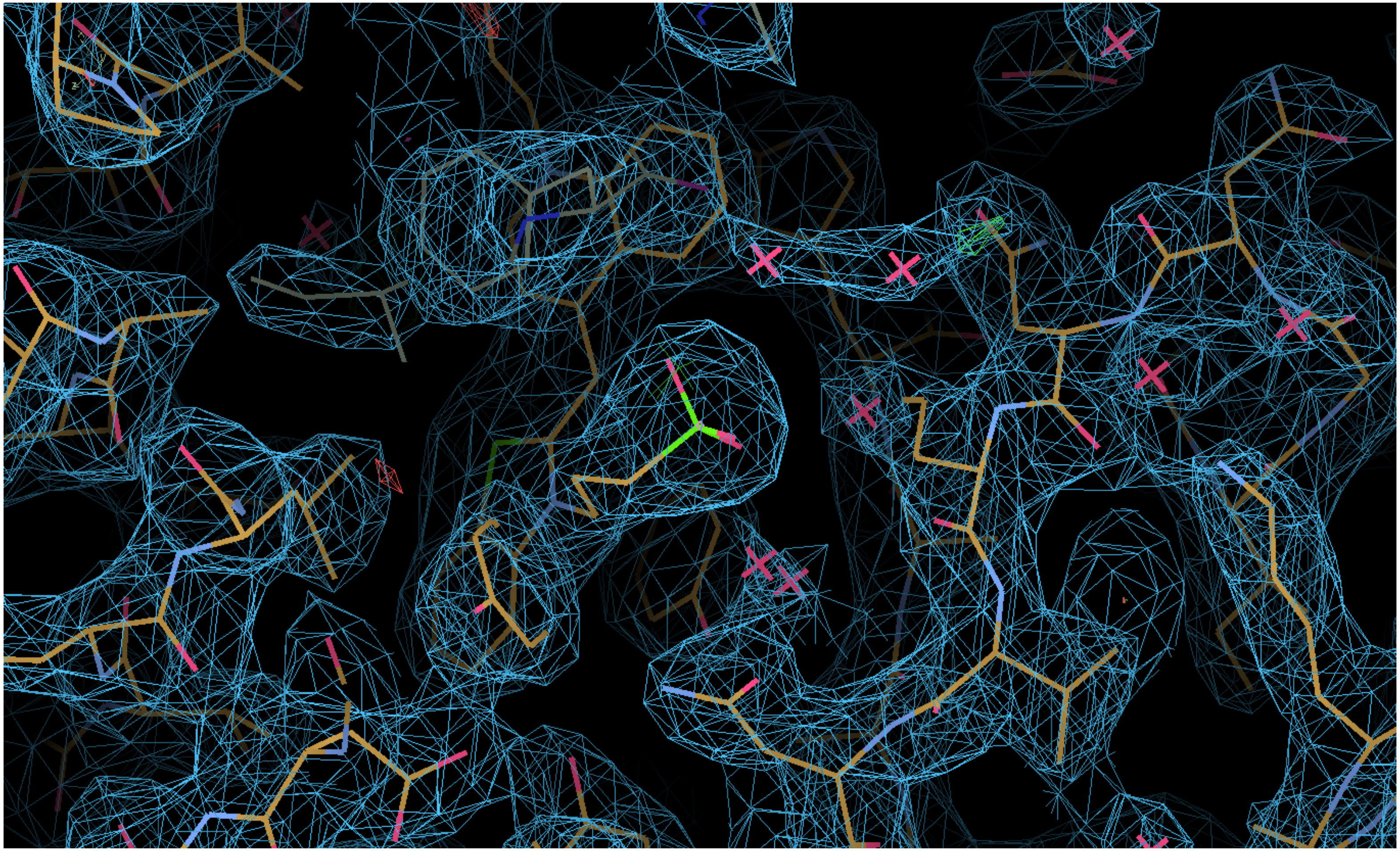
XXXX from deposited data



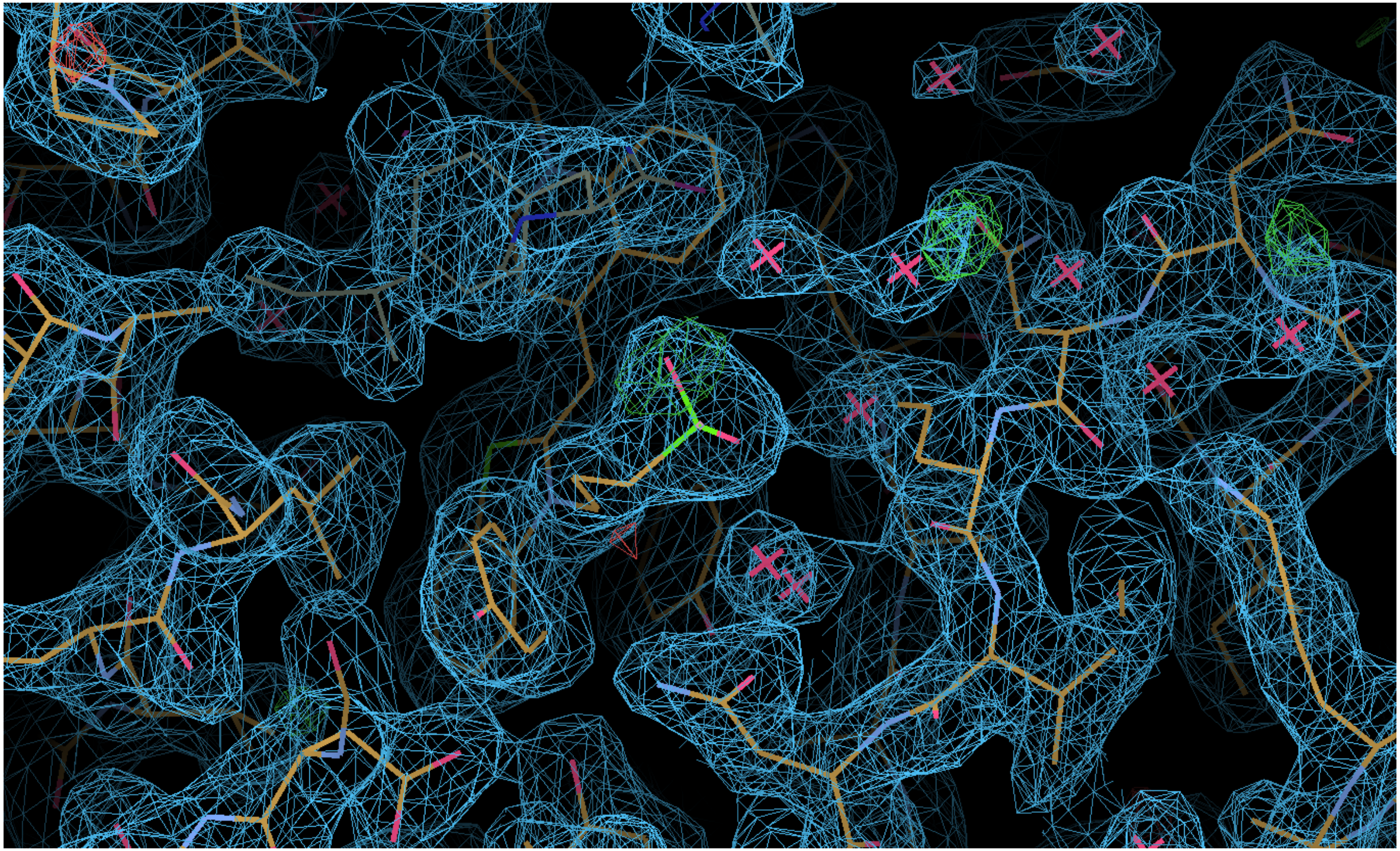
XXXX after STARANISO correction



XXXX from deposited data after “water update” (5 -> 168)



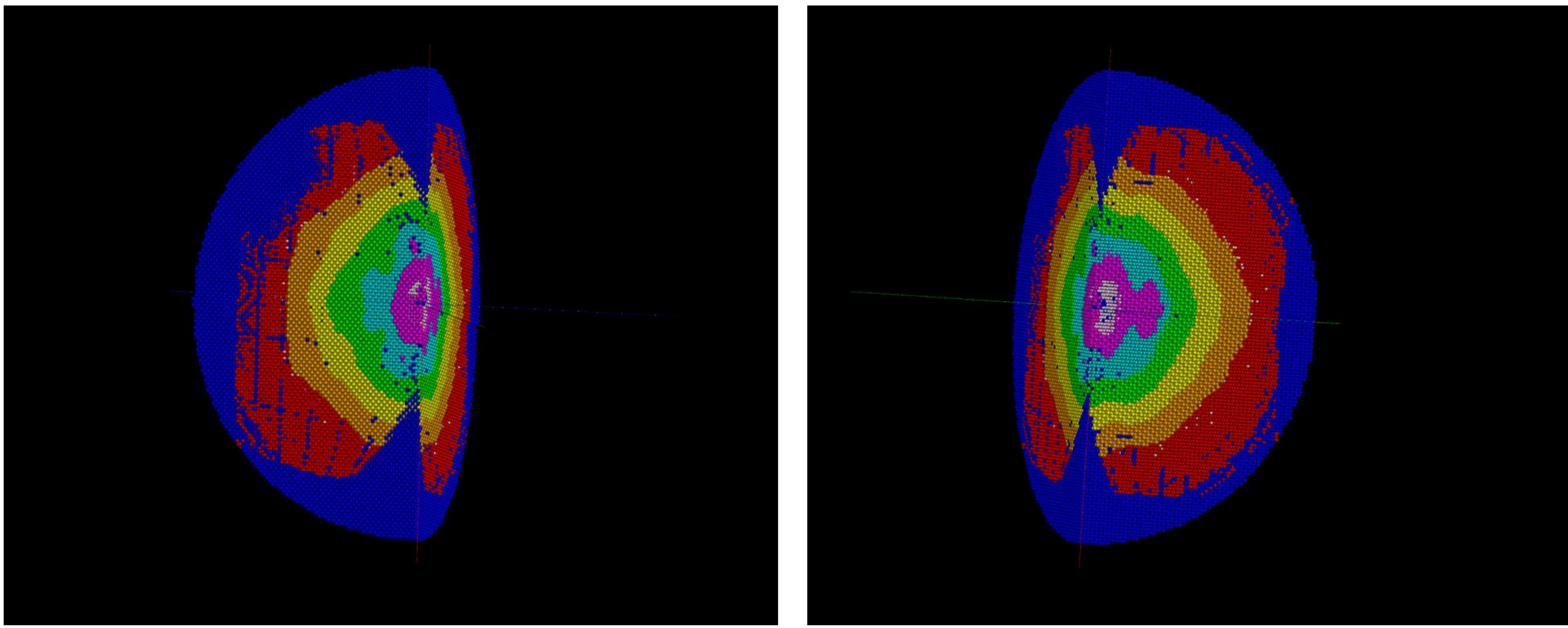
XXXX after STARANISO correction and “water update” (5 -> 322)



Outlook on anisotropy mitigation

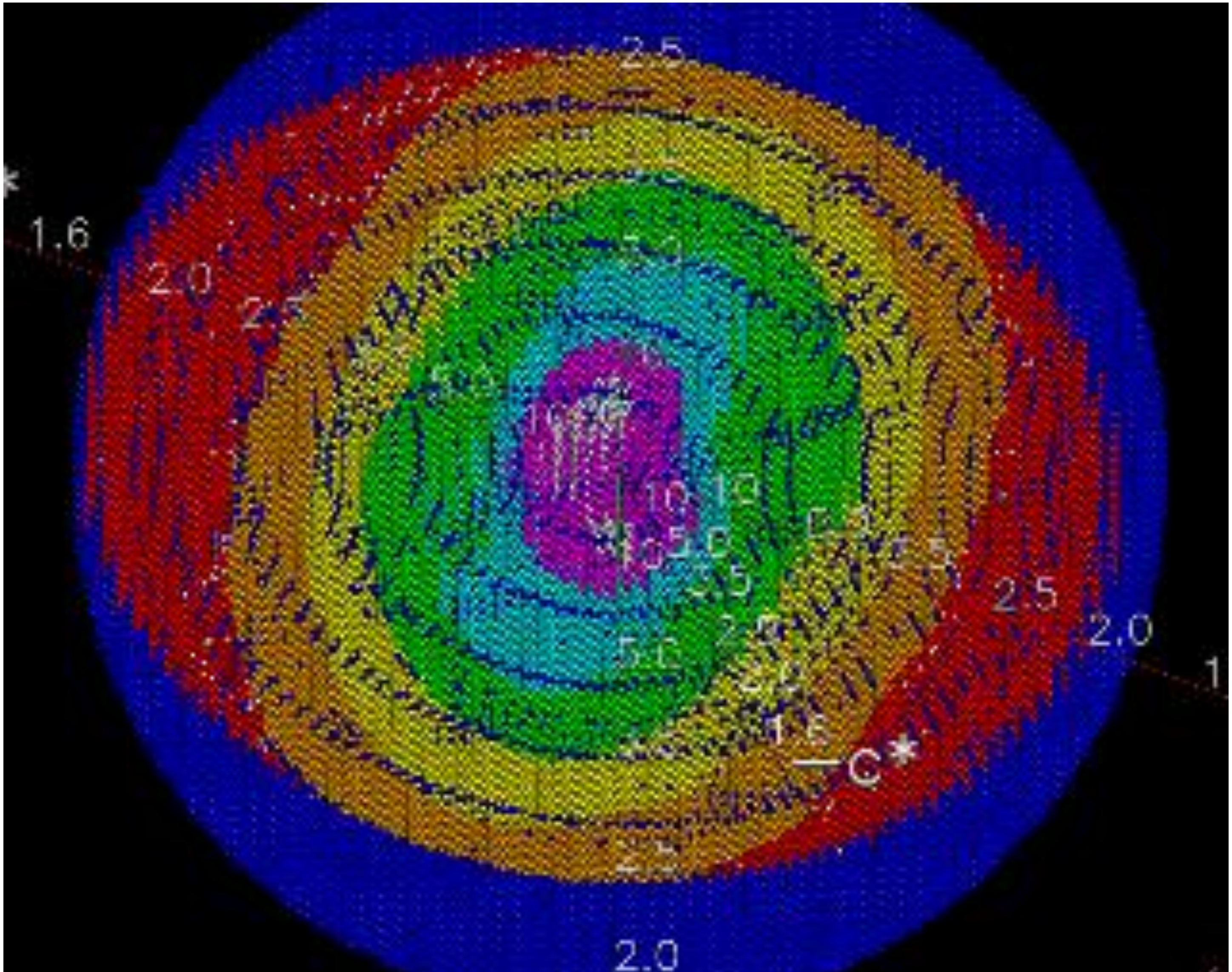
- The previous examples were of STARANISO use on deposited *merged* data or on *merged* data after reprocessing of images
- The work is being extended to *unmerged* data
- Shortcomings of experimental protocols were clearly visible, e.g. *cusp and truncation by detector's edges*
- STARANISO can detect anisotropy from sparse characterisation images: use this diagnostic at data collection time to design a better strategy!

Some poorly collected data are called upon to adjudicate on serious matters

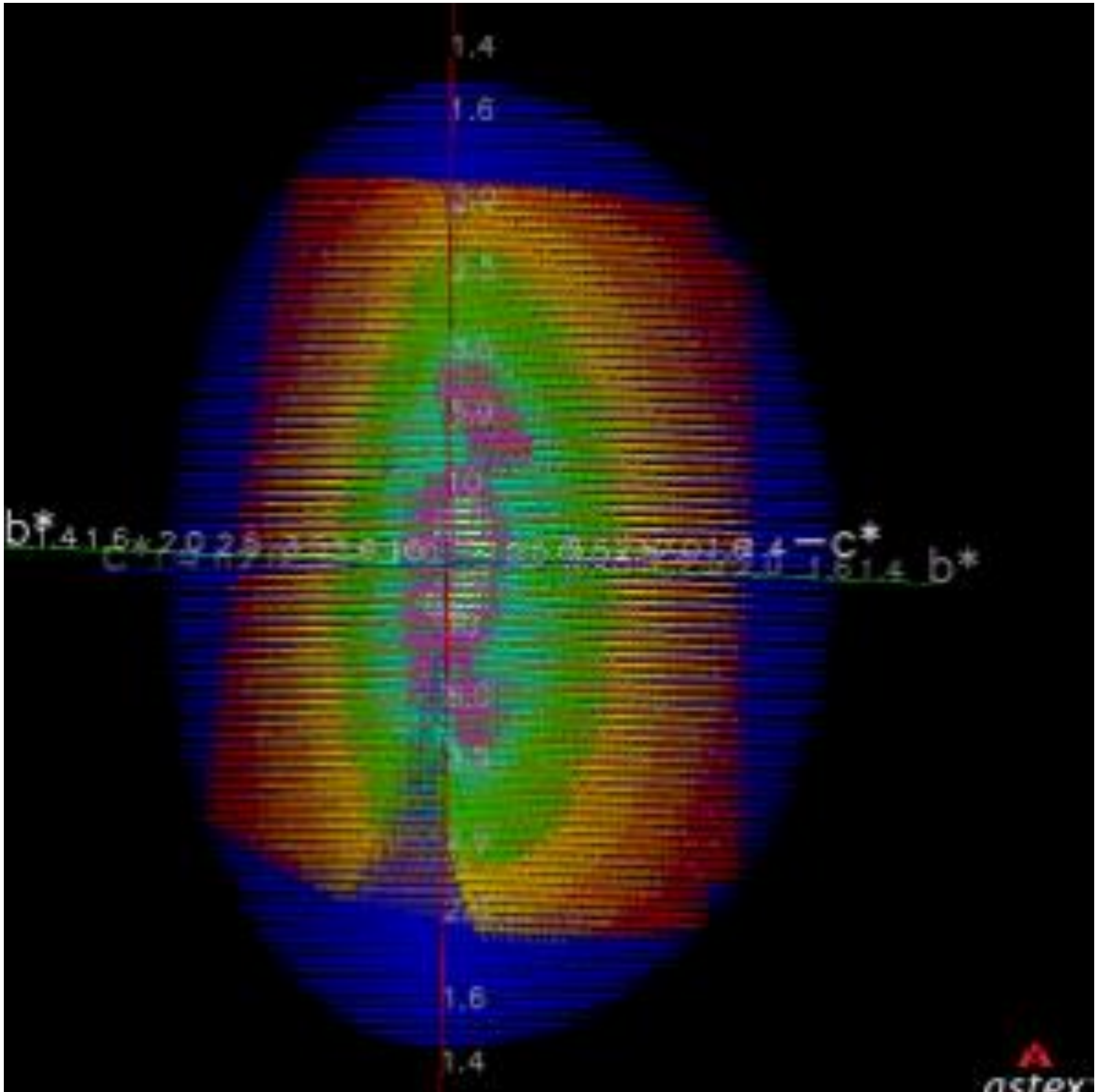


This dataset was meant to help assess the power of crystallography to characterise local disorder

STARANISO analysis of 4HPE



STARANISO analysis of 4IS3



Introducing Transferable Expertise into Automated Data Collection

- The ever-increasing speed of MX beamline instrumentation is leading to ever-stronger emphasis being placed on **brevity of execution** as the main design goal for data collection protocols, **often to the exclusion of** other criteria that would aim at **achieving higher data quality**. This can be counter-productive, especially, but not only, for phasing experiments.
- Global Phasing, among others, has been interested in bucking that trend by creating combined capabilities for the **fast design of optimal strategies and the direct supervision of their execution** on an actual beamline.
- Our approach has been to aim for a full "**third-party design and control**" capability rather than for separate add-on programs that would need to be invoked by local software on each specific beamline or group of beamlines running under the BCS.
- To **make this capability as transferable as possible** across the huge diversity of beamline instruments and BCSs, **finding the correct level of abstraction** for all the components and processes involved is of paramount importance.

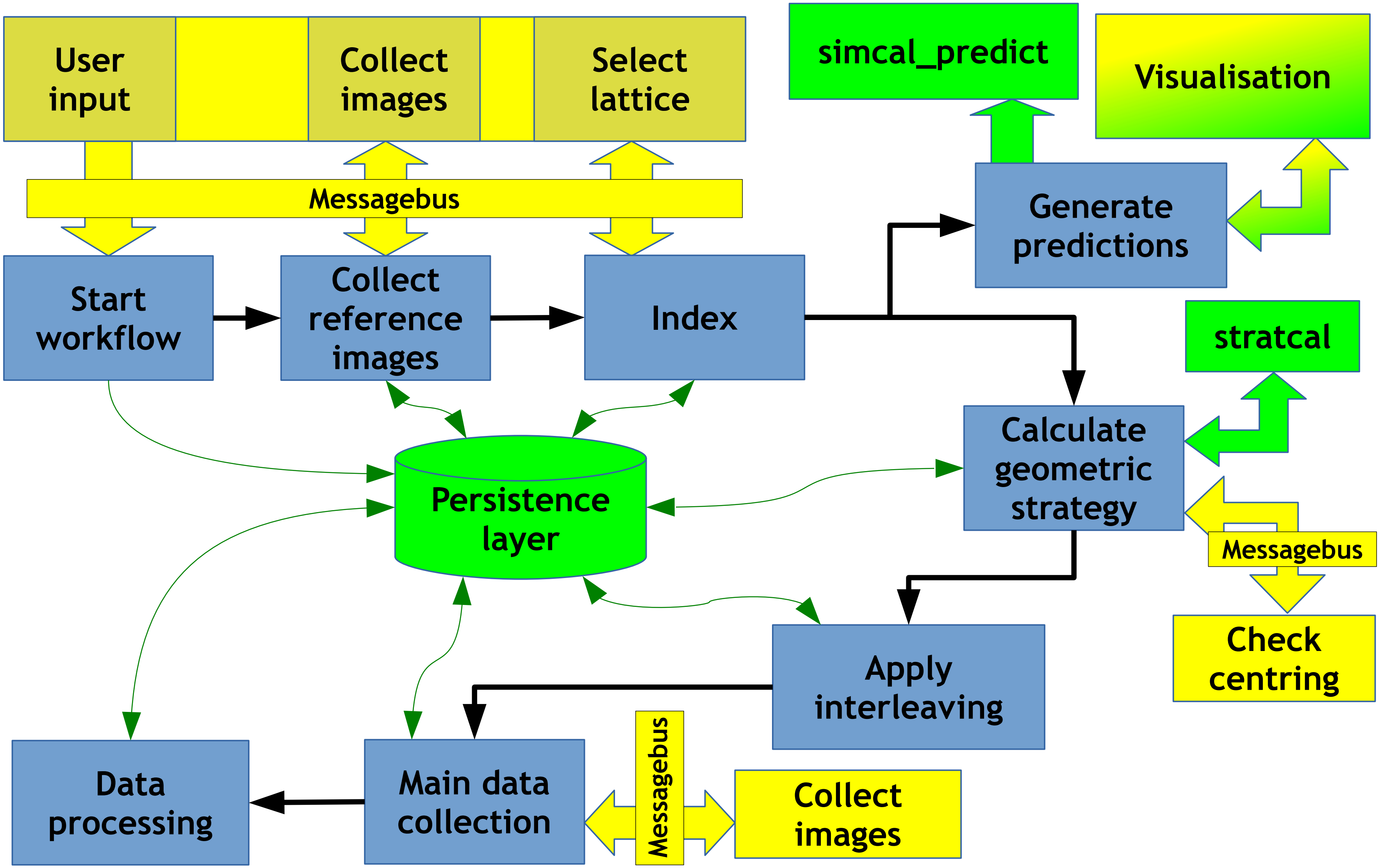
What expertise do we need to capture?

- Achieving completeness in spite of all impediments
  - e.g “filling the cusp” for low-symmetry samples
- Achieving maximum resolution and uniform data quality
  - e.g. making fullest use of each available sample
  - using a multi-axis goniometer to collect data in multiple orientations
- Eliminating systematic errors
  - e.g. taking advantage of partial cancellation of RD effects by using interleaved strategies and multi-axis goniometry

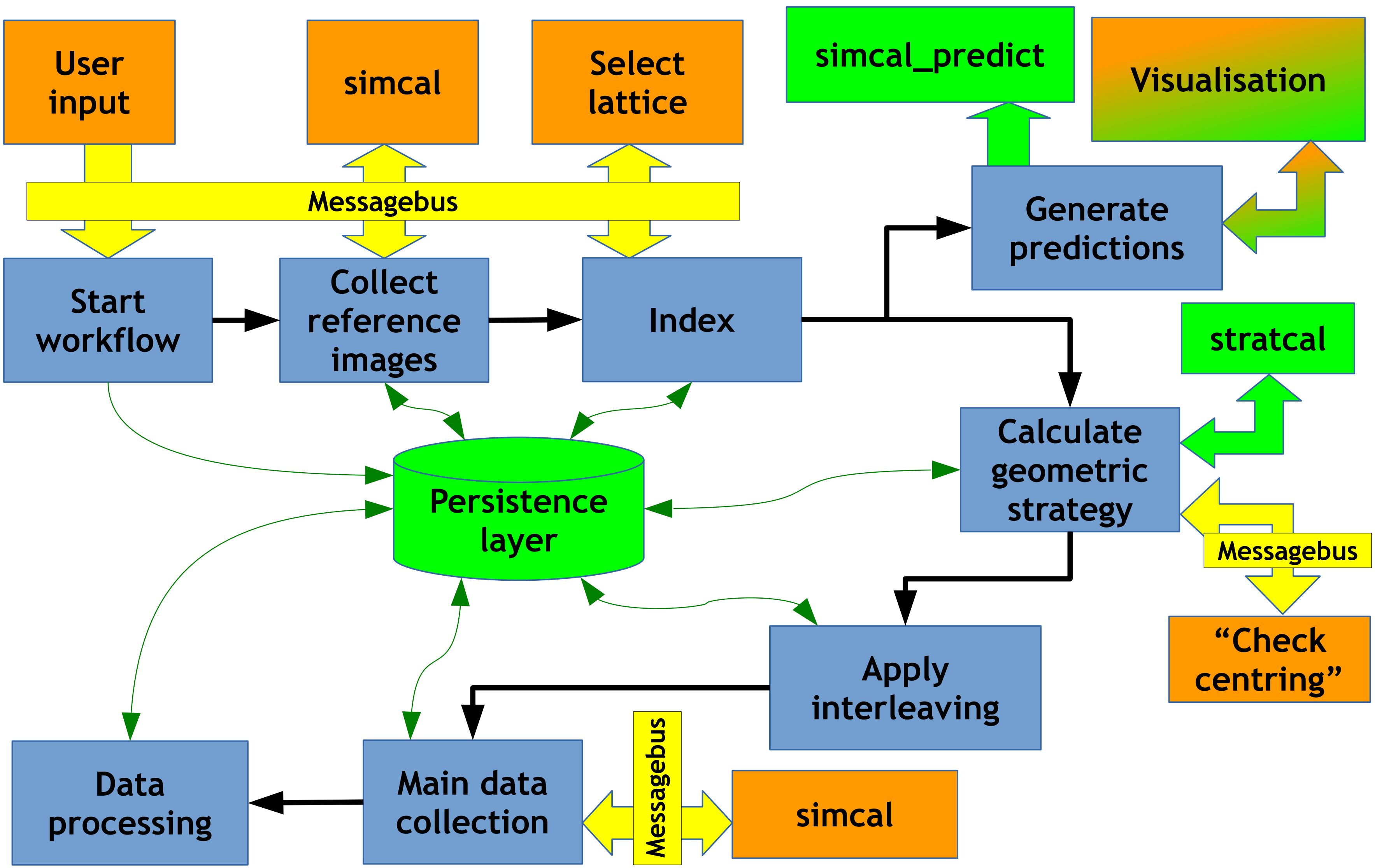
Classical (and other) examples of expertise

- "Interleaved" protocols for MAD Phasing
  - Optimal anomalous S/N was achieved
    - by the **re-orientation** of crystals on a **multi-axis goniometer** to record Bijvoet pairs on the same image, **or**
    - by the **interleaving** of thin wedges (typically, 5 to 10 degrees) of data collected 180 degrees apart in rotation angle ("inverse-beam" method).
  - High-S/N dispersive differences were obtained by similarly interleaving inflection point and remote wavelengths.
  - The special accuracy of these phasing differences was then exploited via the MADSYS software suite.
- Exploiting the anisotropy of anomalous scattering, especially now that vertical Omega axes are available
- Collecting "Club Class" native datasets (e.g. for SBDD)

Workflow: beamline mode



Workflow: emulation mode



STOP PRESS

- Our workflow was successfully run live on the Diamond I04 beamline on 30 Sep 2016
  - steered a 3-wavelength MAD experiment on a mini-kappa-aligned crystal
- See Rasmus's presentation for more detail.