Linking X-Ray Diffraction Data to Our Publications Allows Objectivity in Our Science

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And IUCr Representative to CODATA

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Talk Contents

• Trust in science
• Opportunities linking raw diffraction data to our publications
• Consulting the IUCr Commissions
• Unpublished data
• Modern data rates
• Some topical questions on raw diffraction data preservation/release
• Can traditional peer review of article with data used by IUCr Journals be applied to databases or facility data archives?
  • Collaboration with PDBj and its XRDa raw diffraction data archive (ongoing)
  • Synchrotron, XFEL and Neutron facilities’ data catalogues
• Conclusions
Trust in Science

• “FAIR” is a very widely used acronym in science meaning data need to be **Findable, Accessible, Interoperable and Reusable** [M. D. Wilkinson et al (2016) Comment: The FAIR Guiding Principles for scientific data management and stewardship Scientific Data | 3:160018 | DOI: 10.1038/sdata.2016.18]


For a scientist, trust is not blind or uncritical, and the availability of underpinning data is essential in revisiting a study (and so forming a judgement on the level of reliability).
The Crystallographic Information Framework facilitates trust in crystal structures

Trust is needed in:

• Data transmission/exchange
  • Crystallographic Information File (1991)

• Data consistency
  • checkCIF for derived (coordinate) data (1998)
  • checkCIF including structure factors (2007)

# IUCr COMMITTEE FOR THE MAINTENANCE OF THE CIF STANDARD (COMCIFS)

In 2003 wwPDB Validation started, which IUCr keenly supported; “Validation Report” as a term was 2010 onwards
Data can mean any or all of:

1. raw measurements from an experiment

2. processed numerical observations

3. derived structural information

Our modern data zoo

Each includes metadata i.e. also are data.

A raw diffraction image; Thousands or more of these make a complete experimental raw diffraction dataset.
Today we can start to include our raw data as part of our preserved workflow.

\[ \text{Science Article "Narrative"} \]

- Subjective
- Derived Data
- Processed Data
- Raw Experimental Data (Ground Truth)

\[ \text{\(\£\) Nb an instrument must be calibrated by a person and this leaves some degree of subjectivity} \]

Digital data storage capability

[Image: The Evolution of Data Storage]

- 1940s
- 1950s
- 1960s
- 1970s
- 1980s
- 1990s
- 2000s
- 2010s
Coherent approach of crystallography:
Crystallographic Information Framework (CIF) ontologies at each stage
A recent development (mid-2022) https://journals.iucr.org/services/datasharingpolicy.html

IUCr journals mandate data sharing and peer review of crystal structure data

The IUCr has adopted a data-sharing policy that requires the crystal structure data supporting the results in an article to be peer reviewed and archived either with the IUCr or in an appropriate public repository. Full details of the requirements are given in the Notes for authors. For articles describing scripts or program code, whenever possible these and any other documentation necessary for reproduction of the published results should also be publicly archived. This policy applies to all IUCr journals. (In rare cases exceptions may be granted by the editors, for example when the sharing of data may compromise ethical standards or legal requirements.)

Published articles contain links to the data either on the IUCr site or in the repository together with links to other supporting information. All relevant accession, reference or identification codes, or other persistent identifiers such as DOIs are included in articles.

It is the practice of IUCr journals to provide free access to all supplementary materials and supporting data files deposited with a published article. When the data are reused, we ask that proper attribution is given to the associated source article.

DATA REPOSITORIES

The IUCr recommends that authors deposit data sets in standard, subject-specific public repositories. A list of repositories relevant to crystallographic data is available at https://www.iucr.org/resources/data/databases. Additional repositories may be found by visiting https://www.re3data.org or https://fairsharing.org, which list registered and certified data repositories.

DATA REFERENCES

Identification of individual structures in an article by use of database codes should be accompanied by a full citation of the original literature in the reference list.

Where authors have used a publicly available data set from a repository this should be cited in the published article according to the following style:

Authors (Year). Data set title. Persistent Identifier.

An example citation is:

New opportunities and initiatives stemming from being able to store large quantities of raw data

- Better understanding of what we do experimentally
- Harnessing new methods and software
- Enabling new science
- Understand the subjective choices made in data processing

The above are in addition to the decades long benefits of:-
  - archived coordinates (structure and bonding trends and snapshots of conformational dynamics)
  - then processed diffraction data (re-use/re-refinement of a structure based on authors’ SFs)
IUCr Journals has launched IUCrData’s Raw Data Letters

IUCrData launches Raw Data Letters

L. M. J. Kroon-Batenburg, J. R. Hellwell and J. R. Hester

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Keywords: Raw Data Letters; imgCIF.
checkImgCIF report
[CheckCif for Raw Data]

ImgCIF checker version 2022-07-16

Checking block 5888687 in he4557/m.png.cif

Running checks (no image download)

Testing: Required items: PASS
Testing: Data source: PASS
Testing: Axes defined: PASS
Testing: Our limitations: PASS
Testing: Detector translation: PASS
Testing: Scan range: PASS
Testing: All frames present: PASS
    All frames present and correct for SCANI
Testing: Detector surface axes used properly: PASS
Testing: Pixel size and origin described correctly: PASS
Testing: Check calculated beam centre: PASS
Testing: Check principal axis is aligned with X: PASS
Testing: All archives are accessible: PASS

Running checks with downloaded images

Testing image 4: Image type and dimensions: PASS
Testing image 4: Overloaded values present: PASS

****End of Check****
Accurate intensity integration in the twinned c-form of o-nitroaniline

Martin Lutz and Loes Kroon-Batenburg

Figure 4
Left: simulated precession photograph in the h0l plane of (1) up to a resolution of 0.9 Å. The reconstruction is based on seven scans with a total of 3324 raw images. Right: zoomed image, is from the yellow square in the left image. White circles are the predicted impacts for the first twin component, blue circles for the second.
Are all areas of crystallography & diffraction the same in their raw data archiving needs?

• IUCr Commission on Biological Macromolecules has effected changes in IUCr Journals Notes for Authors that data processing methods and new structures papers must have their underpinning raw diffraction data doi cited.

• Chemical crystallographers organised a Workshop linked to IUCr Prague https://www.iucr.org/resources/data/commdat/prague-workshop-cx to examine the question When should small molecule crystallographers publish their raw diffraction data? Answer: in special cases

• X-ray powder diffraction has a “policy discussion paper” in J Appl Cryst in 2018 by Miguel Aranda (ALBA Science Director until recently) Sharing powder diffraction raw data: challenges and benefits
Open Science: publications and data

• Link all the underpinning data to the publication, raw, processed and derived. Exemplars are for eg:

proteindiffraction.org
Examples from Europe’s facilities

• Diamond Light Source, ESRF and Soleil save all measured data and have a policy committed to release of all raw data after 3 years.

• Pioneering from 2018, for 2 years ESRF have generated one DOI per proposal using DataCite (examples: https://search.datacite.org/works?query=10.15151%2F*), users can also create additional DOI per dataset using the ESRF data portal. ESRF asks their users to provide their DOI of the data in their scientific articles.

• In Germany there is the National Forschungsdateninfrastruktur (https://www.nfdi.de/) bringing proper data management tools and metadata harvesting to many science areas including the photon and neutron sciences (DAPHNE4NFDI, DAten aus PHotonen und Neutronen Experimenten).

• A coordinated European Open Science Cloud is imminent, to which PANOSC is affiliated (Photon and Neutron Open Science Cloud).
Open Science as a Grand Principle?

• Grand Principle: *All measured data, including even unpublished raw data with no derived molecular structure model, should be made open*

• Certainly useful would be such as:
  • *ESRF Paleontology initiative; Researchers agree that they cannot analyse all the data unless they make it open*
  • *Diamond Light Source covid research initiative; raw data are copied to Zenodo by the researcher*

• *Unuseful experimental data are empty data frames such as when the beam fails to hit a crystal; so, delete.*

• *Grey area for me: automatic release after 3 years even when no publication*
Future challenges

Presented here with the permission of Filip Leonarski, PSI
[from the High Data Rates in Macromolecular Crystallography Workshop April 2022, Organised by Herbert Bernstein]
What about tape storage capacities?

Roadmap for tape storage capacity. GEN8 is the current standard in 2021 (source: https://www.lto.org/roadmap/)

From: The vital role of primary experimental data for ensuring trust in (Photon & Neutron) science
With such data rates, facilities are providing at-facility-raw-data-processing. This also provides clarity about the workflow that was used for a particular project. If a doi is provided then a publication can reference those raw and processed data files.

Examples:-

CCP4: Software for Macromolecular X-Ray Crystallography

ExPaNDS=European Open Science Cloud Photon and Neutron Data Services
As explained at the recent PANOSC training day for VISA by Jean-Francois Perrin of ESRF EBS:

High level objectives for Data Analysis Services

- Keep the high level of RI users’ scientific articles production despite the growing complexity of experiments (volume of datasets, ...)

- Contain the necessary time for RI users to publish their work after experiments

- Try to get data processing as FAIR as possible (especially Findable and Reproducible)

- Keep the RI computing infrastructure a safe place for research activities

- Running cost for RIs as low as possible

Presented here with the permission of Jean-Francois Perrin, ESRF EBS.
Actually, we need to understand better:

Q1. What fraction of measured raw data leads to publication? *i.e.* if every measured data frame leads to publication, we have a ‘permanent’ storage, and costs, challenge.

Q2. If a publication doesn’t work out **who** should decide those data can be deleted? and after how many years? [Presumably the entity bearing the costs decides.]

Q3. Maybe, in due course different areas of science could/would reach maturity in the same way as chemical crystallography, *i.e.* where raw data are not vital to be preserved in every experiment?
How to approach Question 2?

• The IUCrData Raw Data Letters, amongst various possibilities, can allow a PI to explain why an analysis is taking longer than (say) 3 years. The PI might be under such a (legitimate) pressure from their Facility.

• Alternatively it could be agreed between the PI and their Facility to delete a data set, even where a DOI had been previously assigned. If so then:-
  • Might it be fruitful to start thinking about standard ways of annotating a DOI on deletion of the data set to declare why it was deleted?
Open Discussion: There is the IUCr CommDat Forum for Public Inputs on Data

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<td>Just who does own research data?</td>
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Can traditional peer review of article with data used by IUCr Journals be applied to databases?

The Diffraction Data Case Study for CODATA’s GOSC of PDBj+XRDa
We focus on medically important proteins

John R Helliwell (UK) and Genji Kurisu (Japan)
with
Loes Kroon-Batenburg (The Netherlands)
Deliverables
Reproducibility of data sets is paramount.

We aim for a single point of contact for definitive molecular models, namely at the PDBj and its XRDa, the X-ray Diffraction Data Archive based at the Institute of Research in Japan.

We aim to avoid dispersed multiple versions of a protein model derived from a single raw diffraction data set. Controlled versioning procedure of PDB entries should be tightly linked.

A critical deliverable is to realise metrics of ‘definitive reusability’ which would then be applicable to the individual diffraction data sets held in the XRDa. These metrics and the definitive diffraction data files are a bedrock of interoperability.
Achievements and progress

We have provided assessments of *medically relevant protein crystal structure* deposits into PDBj which have XRDa raw diffraction data equivalent data files.

We have presented our work thus far at the:-

British Crystallographic Association Annual Conference held at the University of Leeds just before Easter 2022 and the ECM33 in Versailles:-

We have given clear guidelines for the ‘proper’ diffraction resolution limit, linked to the best protein model, based on the method of Diederichs and Karplus implemented as described here IUCrJ (2020) 7, 681-692.

We have emphasised the importance of the elimination, or if necessary description, of residual difference Fourier peaks which show up mismatches between the protein model and the diffraction data.
A glimpse of the variation of X-ray diffraction resolution limit choice involving the commonly used metrics in macromolecular crystallography:

Via the Diederichs and Karplus method, using the XRDa entry the resolution limit should be 2.29Å. The depositor, Sato et al (Biochem. J. 478, 1023–1042) used 2.40 Å.

Resolution cut off estimates:

- Resolution of all data: 1.913 Å
- Based on CC(1/2) >= 0.33: 1.946 Å
- Based on mean(I/sigma) >= 2.0: 3.037 Å
- Based on R-merge < 0.5: 2.411 Å
- Based on R-meas < 0.5: 2.497 Å
- Based on completeness >=90%: 2.335 Å
- Based on completeness >=50%: 2.155 Å

PDBj: 7ccy
In several overview reviews of medically important protein crystal structure studies we have extensively tabulated the currently available protein models and diffraction data with comments on any areas of the possible improvements of their PDB files.


Helliwell, J R (2021) The crystal structures of the enzyme hydroxymethylbilane synthase, also known as porphobilinogen deaminase *Acta Cryst F77*, 388-398.

A common feature of all these crystal structures are difference Fourier map peaks which have not been dealt with; 66 protein crystal structures altogether were scrutinised.
Can traditional peer review of article with data used by IUCr Journals also be applied to Facility data catalogues?

[This idea is as yet untested but CheckCif for raw data will surely help]
Conclusions

• Crystallographers have again seized opportunities to link their publications to raw diffraction data, especially Macromolecular Crystallographers

• The journal IUCrData has launched a new category of article: *IUCr Raw Data Letters*

• New raw data sharing types of research modes have started eg *the ESRF Paleontologists, the covid-19 Macromolecular Crystallographers*....

• All researchers can better understand the subjective choices made in their processing of raw data through to structure factors

• The collaboration with PDBj and its provision of its XRDa we see as an important development for *definitive reusability of our MX results by biologists and medical scientists ie who are not MXers*
Acknowledgements

• Members of the IUCr DDDWG 2011-2017 and to the current Members of the IUCr Committee on Data (2017 onwards)
  https://www.iucr.org/iucr/governance/advisory-committees/committee-on-data

• The CODATA Data Policy Committee
  • https://codata.org/initiatives/data-policy/international-data-policy-committee/

• The checkcif for raw data Project Team, which underpins the IUCrData Raw Data Letters initiative:
  • Loes Kroon-Batenburg (Main Editor of IUCrData’s Raw Data Letters), James Hester (ANSTO and Chair of ComCIFS), Fabio Dall’Antonia, Julian Hörsch (EuroXFEL) and Andy Gotz (ESRF and PANOSC) and the staff at the IUCr Editorial Office.
Thankyou