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IUCr Diffraction Data Deposition Working Group

IUCr

Access to raw diffraction data: A revolution in the making

John R Helliwell

School of Chemistry, University of Manchester, M13 9PL, UK

Polish Crystallographic conference

john.helliwell@manchester.ac.uk

Overview

Towards a future structural science based on raw data archiving: the IUCr's Diffraction Data Deposition Working Group (DDDWG)

- ***IUCr Commissions*** are actively working on

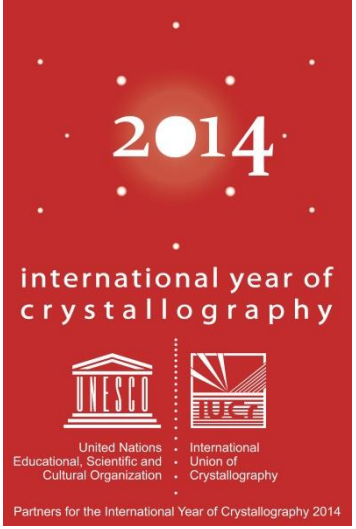
  "defining their commission's metadata for raw diffraction data"

  namely:-

  Commission on EXAFS;
  Commission on Small angle scattering;
  Commission on High pressure;
  Commission on Biological Macromolecules.

- ***The ICDD has been active on the harnessing of raw powder diffraction data sets*** for some time and reported to us at ECM30 in Rovinj that they now have incorporated 10,000 raw powder diffraction data sets into their powder diffraction file. ***The Commission on Powder Diffraction*** is planning further work on neutron powder diffraction raw data and will liaise with the Commission on Neutron Scattering as appropriate.

- The ***Commission on Structural Chemistry*** had enthusiastic participants in Madrid, Bergen and Rovinj DDDWG events.



Crystallography in modern life

2014 is proclaimed International Year of Crystallography

United Nations

"Crystallography has an important place as we work for inclusive sustainable development – policies that are good for people and the planet"

Ban Ki-Moon, UN Secretary-General • IYCr 2014 Opening Ceremony

Some history; let's go back to the first crystal structures…..

William Lawrence Bragg

Raw data 1913

Bragg, W. L. (1913). The Structure of Some Crystals as Indicated by their Diffraction of X-rays. Proc. R. Soc. London Ser. A, 89, 248-277; contained a lot of raw data (Laue patterns)

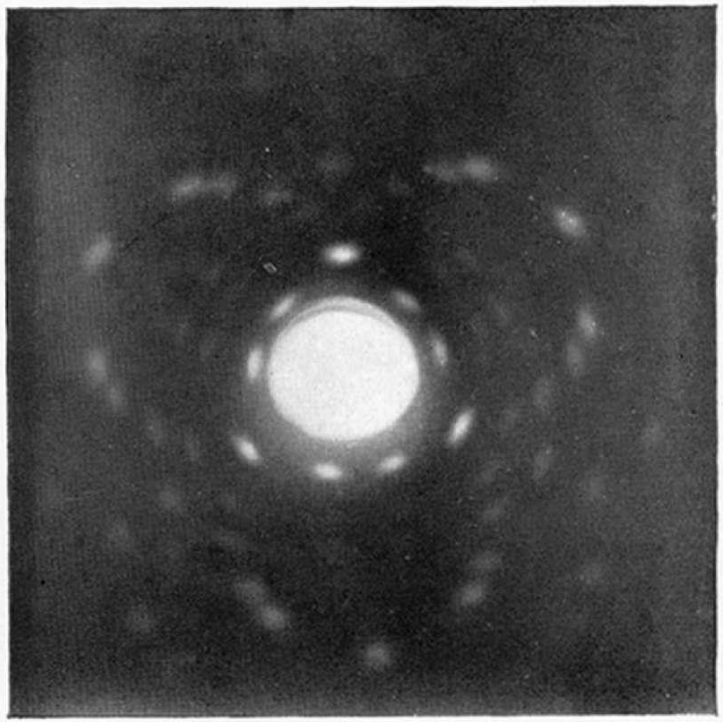


FIG. 11.—Fluorspar.

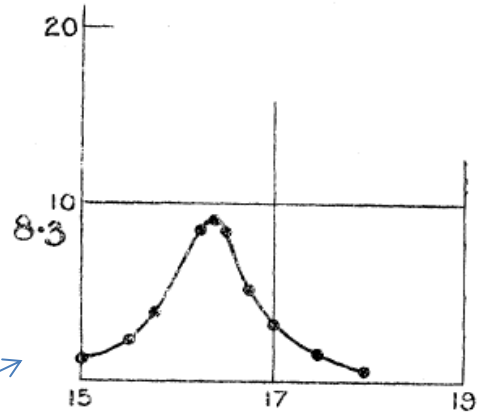
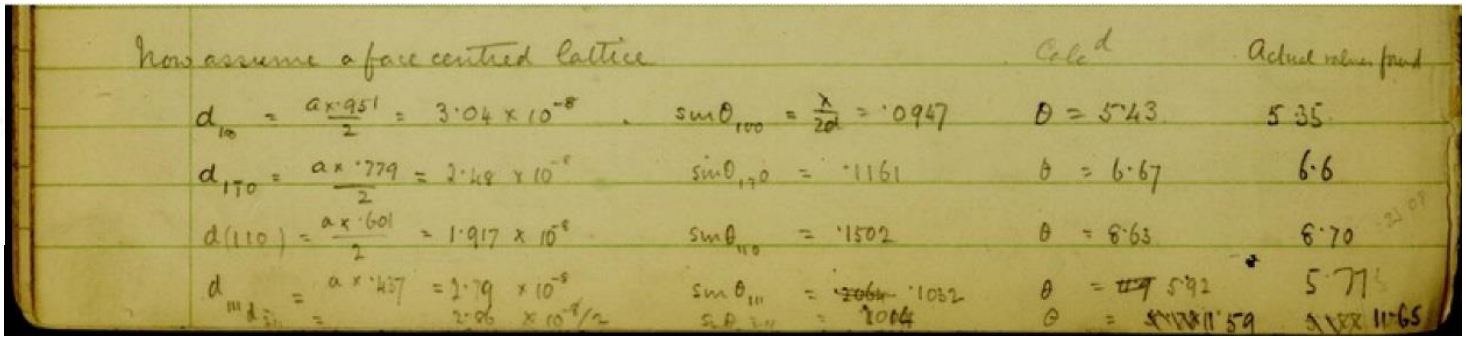


FIG. 1.—Regular reflection from cleavage face of rock-salt, glancing angle 8·3°.

W. H. Bragg and W. L. Bragg *The Reflection of X-rays by Crystals*
Proc. R. Soc. Lond. A **1913 88, 428-438** *using the WHB X-ray spectrometer*

Sir William Henry Bragg

Processed diffraction data 1913



Plane.	Calculated Spacing.	Calculated Angle.	Observed Angle.
100	$d_{(100)} = 3.04.$	5° 26′	5° 21′
$1\bar{1}0$	$d_{(1\bar{1}0)} = 2.48.$	6° 40′	6° 36′
110	$d_{(110)} = 1.92.$	8° 38′	8° 42′
111	$d_{(111)} = 2.79.$	5° 55′	5° 46′
$2\bar{1}\bar{1}$	$d_{(2\bar{1}\bar{1})} = 1.43.$	11° 35′	11° 39′

The upper figure is from the Braggs' notebook, showing observed angular locations of diffracted beams from different crystal planes, and their calculated values. The lower figure is a similar published tabulation from the 1915 book X-rays and Crystal Structure.

The Nobel Prize in Chemistry 1964
Dorothy Crowfoot Hodgkin

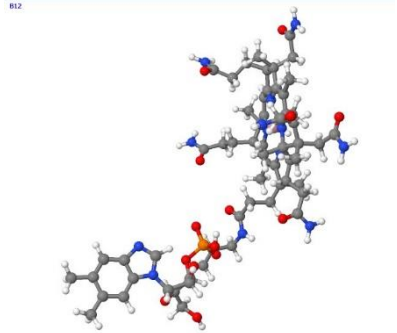
The Nobel Prize in Chemistry 1964

Dorothy Crowfoot Hodgkin

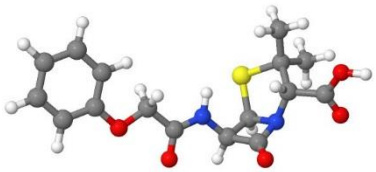
Prize share: 1/1

Dorothy Hodgkin (1910-1994): still a major inspiration today

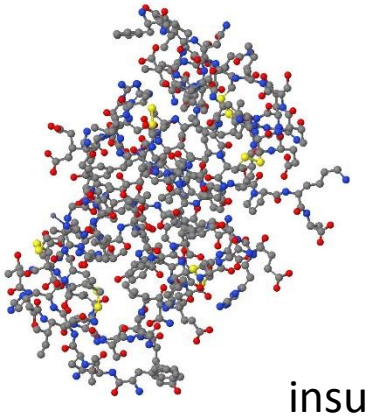
The Nobel Prize in Chemistry 1964 was awarded to Dorothy Crowfoot Hodgkin *"for her determinations by X-ray techniques of the structures of important biochemical substances"*.

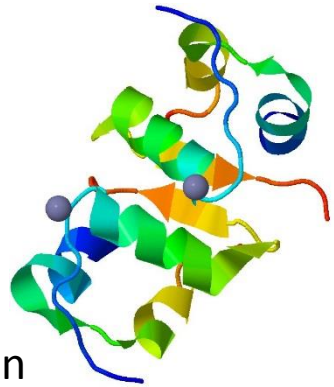


vitamin B12 (cobalamin)



penicillin

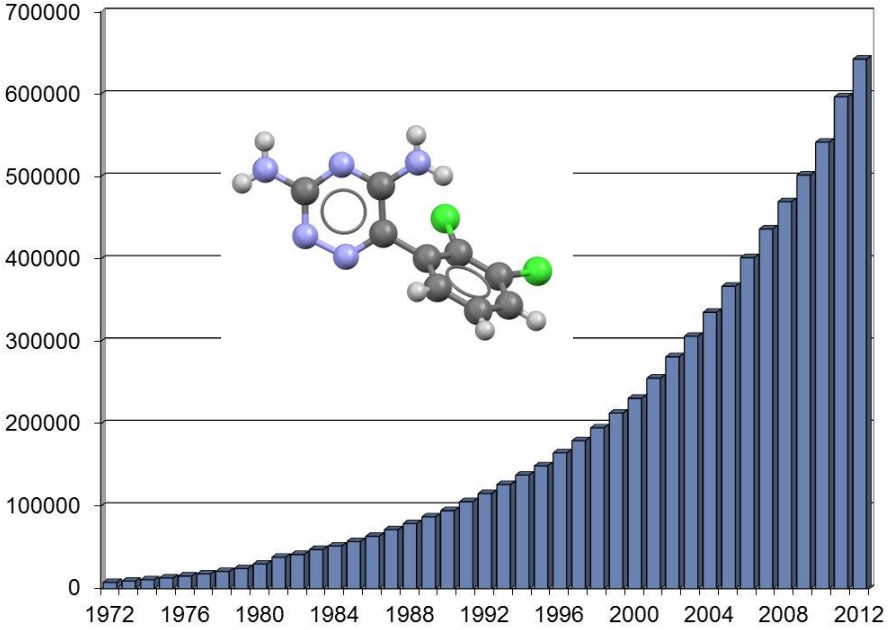




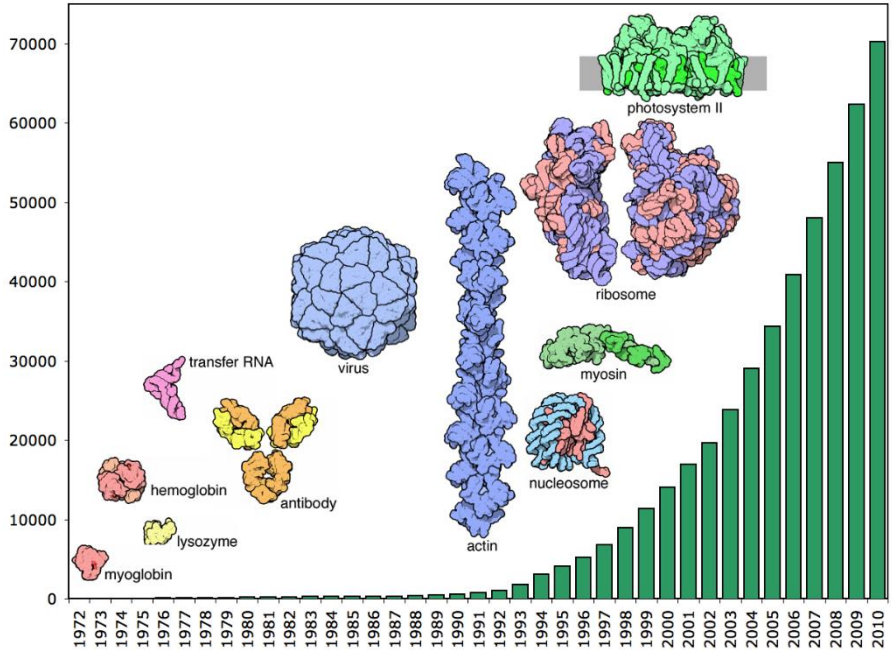
insulin

"The Nobel Prize in Chemistry 1964". *Nobelprize.org.* Nobel Media AB 2014. Web. 22 Oct 2014. <http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1964/>

Structures large and small

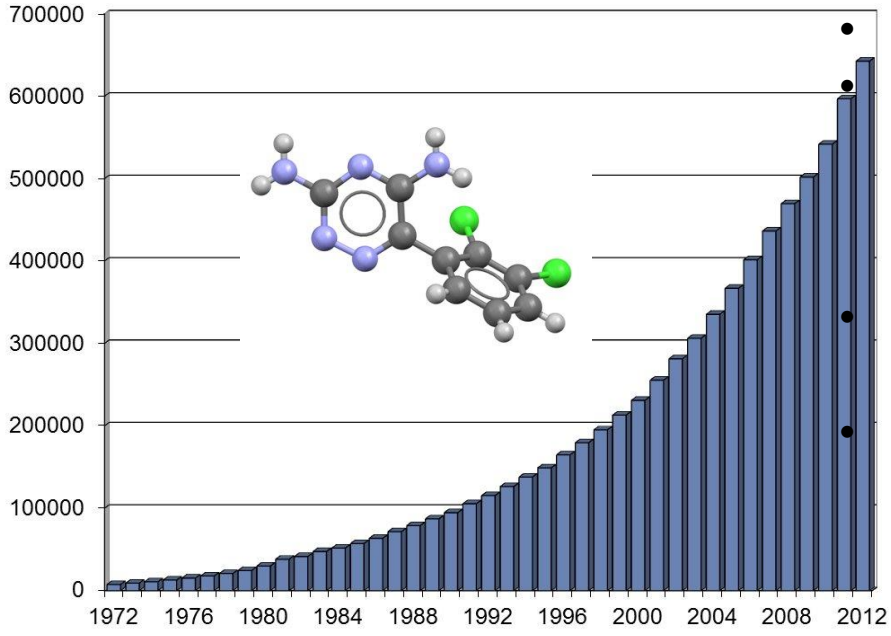


Cambridge Structural Database



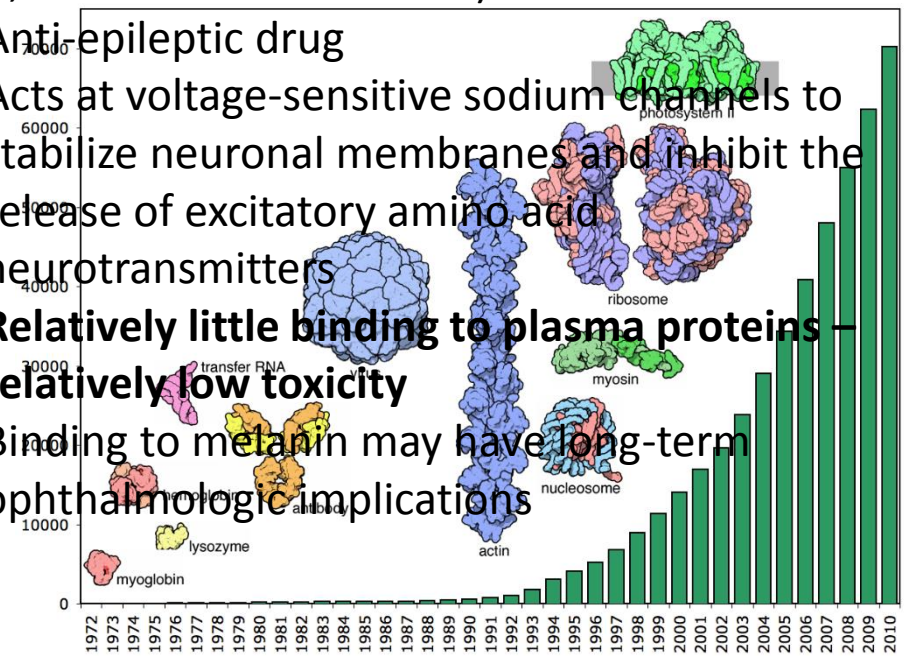
Protein Data Bank

Interactions between large and small



Lamotrigine
(500,000th structure in CCDC)

- Anti-epileptic drug
- Acts at voltage-sensitive sodium channels to stabilize neuronal membranes and inhibit the release of excitatory amino acid neurotransmitters
- **Relatively little binding to plasma proteins – relatively low toxicity**
- Binding to melanin may have long-term ophthalmologic implications



Cambridge Structural Database

Protein Data Bank

What has this all to do with "data"?

- *Structural models, stored in curated databases, have immense value for comparative studies, new compound discovery etc.*
- *Experimental data, stored as reduced and processed data sets, are invaluable for validating models and re-refinement of structures*
- *Raw experimental data has the potential for unleashing new methods and new science*

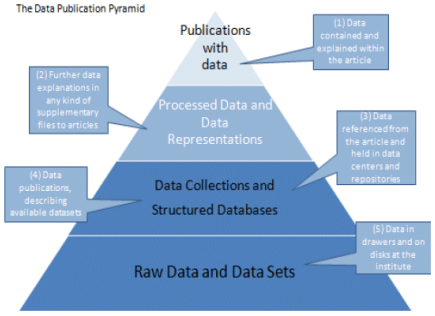
"Ideally, the full scientific record should provide access to the raw data……the IUCr is beginning to consider longer-term approaches to archiving the raw data"

P. Strickland, B. McMahon and J. R. Helliwell, Learned Publishing 21 (2008) 63.

Raw diffraction images offer the opportunity of

- *analysing data at higher resolution than used in the original work*
- *serving as benchmarks in developing improved methods of analysis*
- *checking the interpretation of the symmetries of the crystals*
- *analysing diffraction from multiple lattices present in the crystals*
- *analysing the diffuse scattering that reflects correlated motions or disorder of atoms in the crystals*

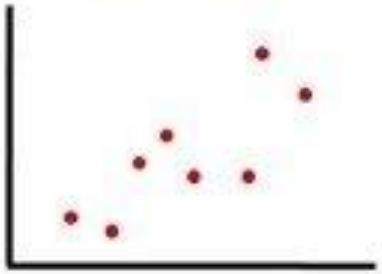
- ***Nb the philosophical view of the importance of access to raw diffraction data; namely analysis through one's own eyes not the lens of someone else***



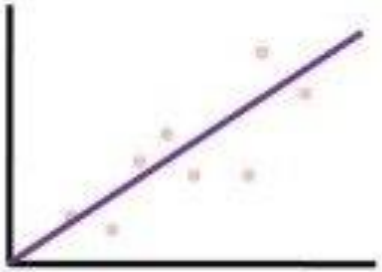
Data seen through the lens of others!

PhD tips # 22

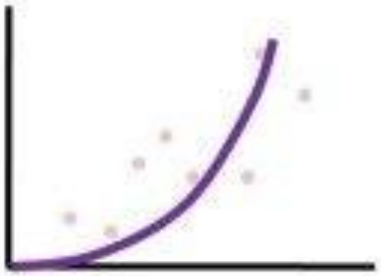
Actual data



How you saw it:
Perfectly linear, as expected



How your supervisor saw it:
Perfectly exponential, amazing new stuff



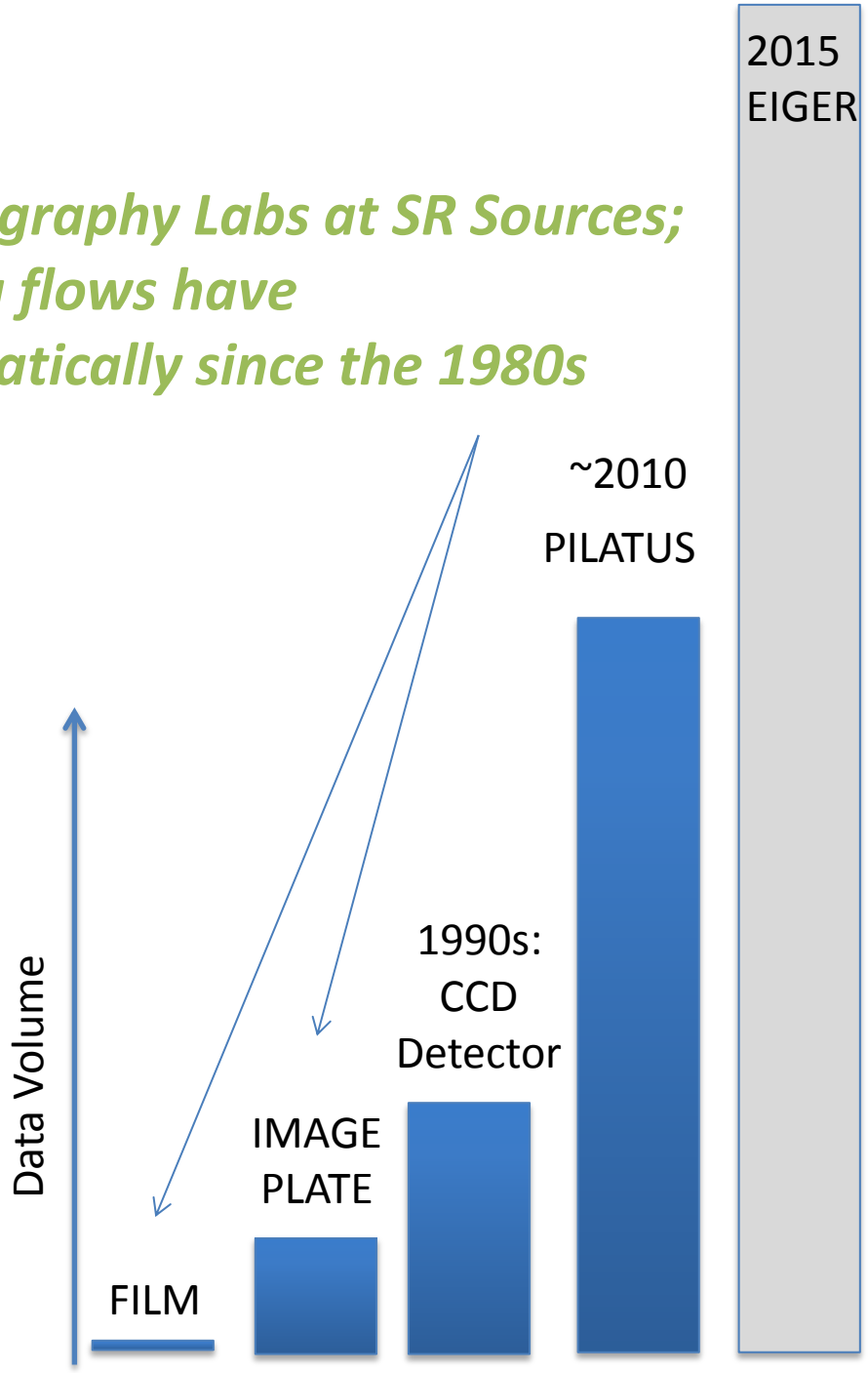
How the referee saw it:
Pure noise

Modern data flows in biologcal crystallography are extreme>>>>

Would keeping all these raw data be "worth the pain"?

*A group of 4 articles in Acta Cryst D October 2014 Biological Crystallography led by **Tom Terwilliger** explained why keeping raw data is a natural next step for crystallography ....*

Biological crystallography Labs at SR Sources; data flows have increased dramatically since the 1980s



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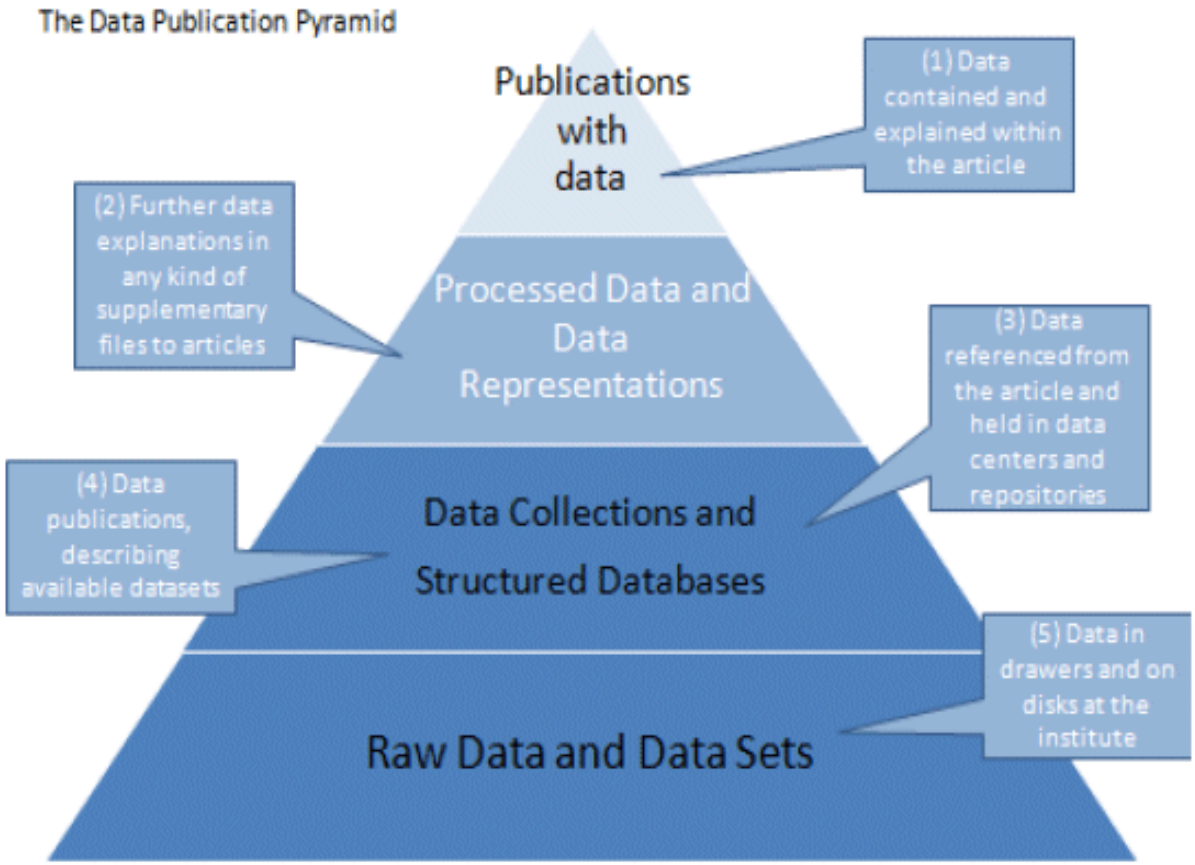
The University of Manchester
Manchester Institute of Biotechnology

The data publication pyramid

- the publishers' view

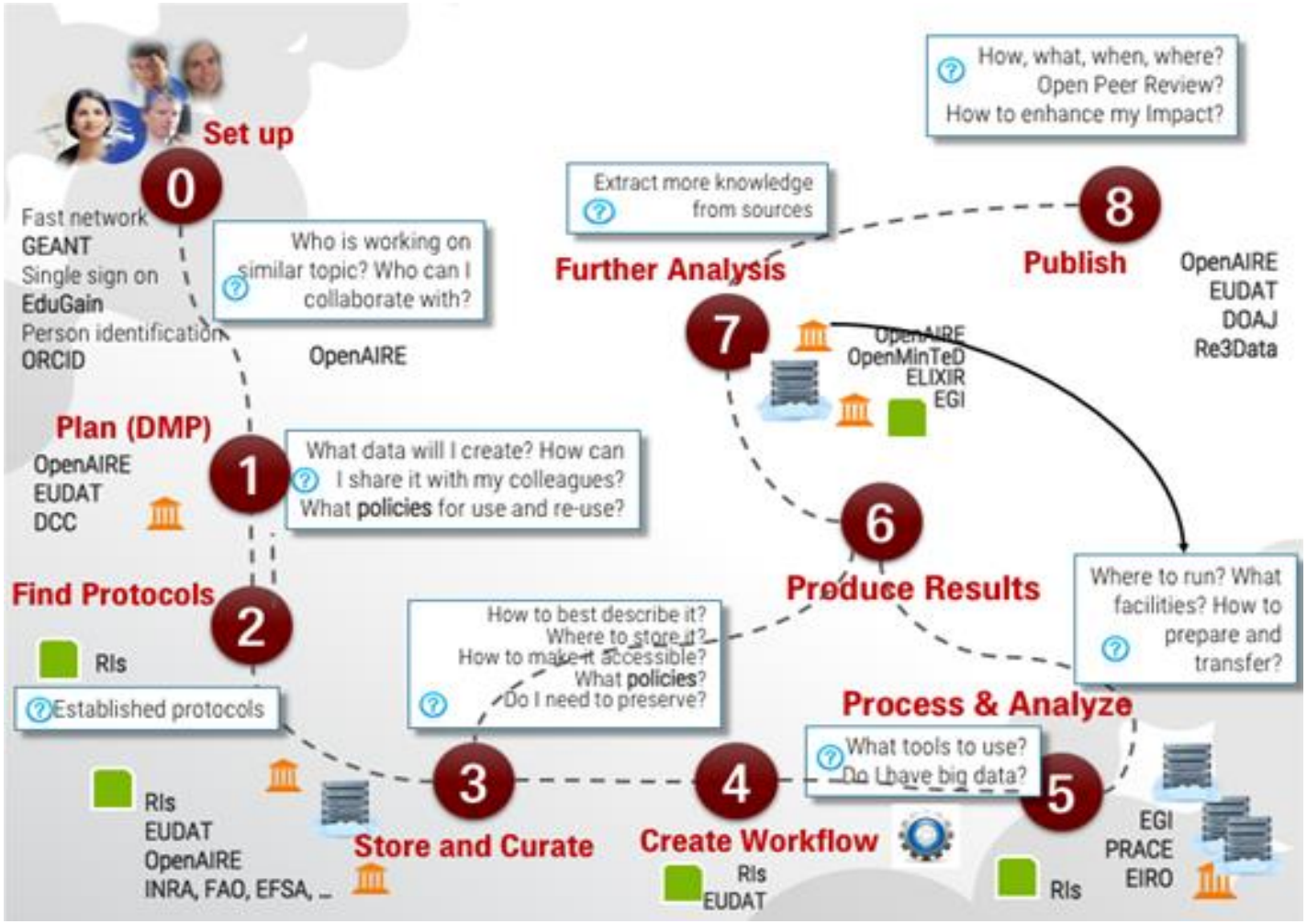


Reilly, S., Schallier, W., Schrimpf, S., Smit, E. & Wilkinson, W. (2011). Report on Integration of Data and Publications.

Available from http://www.stm-assoc.org/integration-of-data-and-publications/

Context

A call for legal interoperability of data and for (a more) open science



Concept for a European Open Science Cloud for Research

Context

‘FAIR Data’ (Findable, Accessible, Interoperable and Reusable)

www.nature.com/scientificdata

SCIENTIFIC DATA

OPEN

SUBJECT CATEGORIES

» Research data

» Publication characteristics

Comment: The FAIR Guiding Principles for scientific data management and stewardship

Mark D. Wilkinson *et al.*#

Box 2 | The FAIR Guiding Principles

To be Findable:
F1. (meta)data are assigned a globally unique and persistent identifier
F2. data are described with rich metadata (defined by R1 below)
F3. metadata clearly and explicitly include the identifier of the data it describes
F4. (meta)data are registered or indexed in a searchable resource

To be Accessible:
A1. (meta)data are retrievable by their identifier using a standardized communications protocol
A1.1 the protocol is open, free, and universally implementable
A1.2 the protocol allows for an authentication and authorization procedure, where necessary
A2. metadata are accessible, even when the data are no longer available

To be Interoperable:
I1. (meta)data use a formal, accessible, shared, and broadly applicable language for knowledge representation.
I2. (meta)data use vocabularies that follow FAIR principles
I3. (meta)data include qualified references to other (meta)data

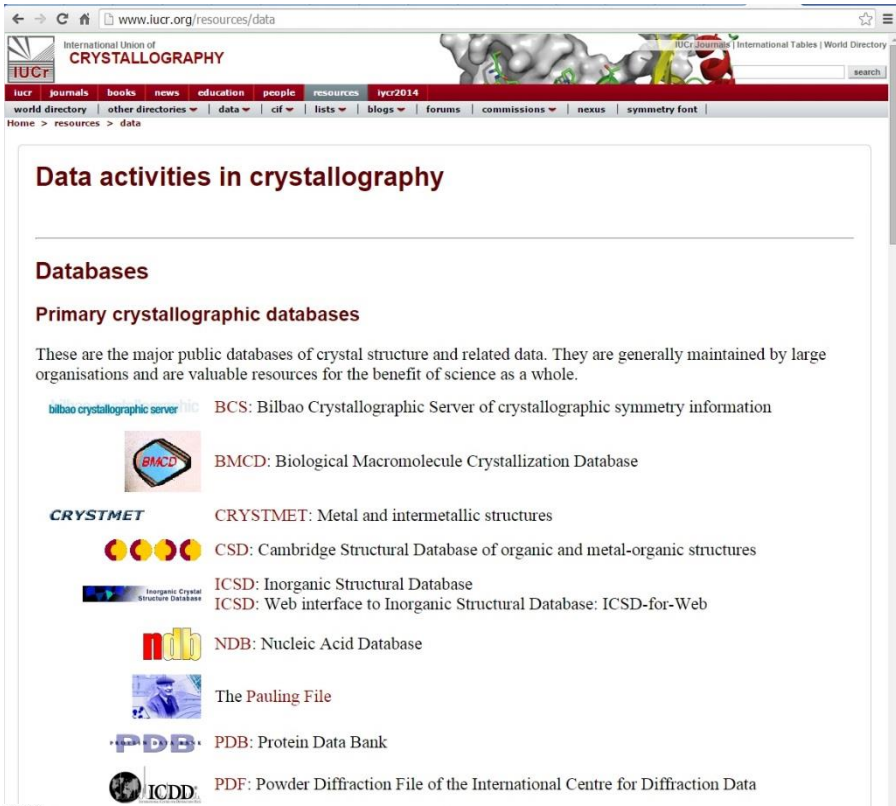
To be Reusable:
R1. meta(data) are richly described with a plurality of accurate and relevant attributes
R1.1. (meta)data are released with a clear and accessible data usage license
R1.2. (meta)data are associated with detailed provenance
R1.3. (meta)data meet domain-relevant community standards

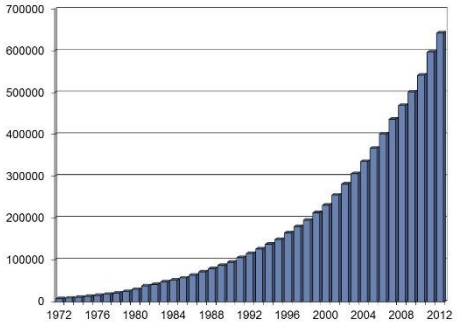
Examples of crystallography in the life sciences and urgent societal problems demand an open science approach

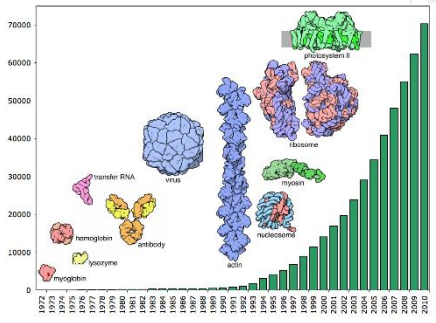
Based on IUCr website 11 September 2014

Benefits of retaining derived data

- *Scientific record*
- *Database-driven discovery*
- *Protein-ligand interactions*
- *New pathways to synthesis, manufacturing, energetics…*
- *Identification/indexing (e.g. forensic science)*







Benefits of retaining processed data

- *Structure validation*
- *Re-refinement*
- *Systematic bias, methods development*
- *Guard against structures associated with incorrect data sets*
- *Help guard against 'bad apples' in the databases (Minor et al. 2016)*

journals.iucr.org/b/issues/2002/01/00/bm0047/

Acta Crystallographica Section B
STRUCTURAL SCIENCE, CRYSTAL ENGINEERING AND MATERIALS

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research papers

STRUCTURAL SCIENCE CRYSTAL ENGINEERING MATERIALS

Volume 58 | Part 1 | February 2002 | Pages 62-77
doi:10.1107/S0108768101017128

ISSN: 2052-5206

Some 60 new space-group corrections

ICSTI Insights

Article 2

Continuous improvement of macromolecular crystal structures

Thomas C. Terwilliger

Summary

Accurate crystal structures of macromolecules are of high importance in biological and biomedical fields. Models of crystal structures in the Protein Data Bank (PDB) are in general of very high quality, but methods for modeling protein structures and for determination of structures are still improving. We suggest that it is both desirable and feasible to carry out small and large-scale efforts to continuously further improve the models deposited in the PDB. Small-scale efforts could focus on optimizing structures that are of interest to specific investigators. Large-scale efforts could focus on systematic optimization of all structures in the PDB, on redetermination of groups of related structures, or on redetermination of groups of structures focusing on specific questions. All the resulting structures could be made generally available, with various views of the structures available depending on the types of questions that users are interested in answering.

1. Introduction

1.1 Crystal structures of macromolecules

The three-dimensional structures of biological macromolecules such as proteins, DNA and RNA are of high importance in many areas of biology and biotechnology. Structures of proteins and of complexes between proteins, between proteins and small molecules, and between proteins and nucleic acids are all crucial for understanding how these molecules function to catalyze chemical reactions and to control metabolism, growth and development. Structures of proteins bound to candidate drug molecules are highly useful in the development of new pharmaceuticals. Structures of natural and engineered proteins are crucial for rational engineering of these molecules to give them new functions or altered properties.

CONGRÈS ET ASSEMBLÉE GÉNÉRALE
DE L'UNION INTERNATIONALE DE CRISTALLOGRAPHIE

IUCr Diffraction Data Deposition Working Group (DDDWG) report to the IUCr General Assembly Montreal

John R Helliwell on behalf of the DDDWG

CONGRESS AND GENERAL ASSEMBLY
OF THE INTERNATIONAL UNION OF CRYSTALLOGRAPHY

Members of the DDDWG 2011 to 2017

- *John R Helliwell and Brian McMahon (UK)*, Chair and Co-Chair;
- *Steve Androulakis (Australia)*
- *Sol Gruner (USA)/Dolothea Szebenyi (USA)*
- *Loes Kroon-Batenburg (Netherlands)*
- *Tom Terwilliger (USA)*
- *John Westbrook (USA)*
- *Heinz-Josef Weyer (Switzerland)* †

Recommendations from the DDDWG for the upcoming Triennium

- IUCr Commissions to define their metadata;
- *J. Appl. Cryst.* to introduce a 'Difficult Raw Data' Section (Loes Kroon-Batenburg);
- A centralised crystallographic repository of raw data set metadata should be scoped, inc a search interface, leading to a pilot service;
- With a viable pilot metadata registry ***authors should*** provide a permanent and prominent link from an article to their raw data sets underpinning a journal publication.

Issues for the IUCr

- The IUCr's science involves 'Big data' up towards the level of the data-deluge of the Square Kilometre Array radio telescope; we may have to consider subsets of data retention or limited time periods for retention;

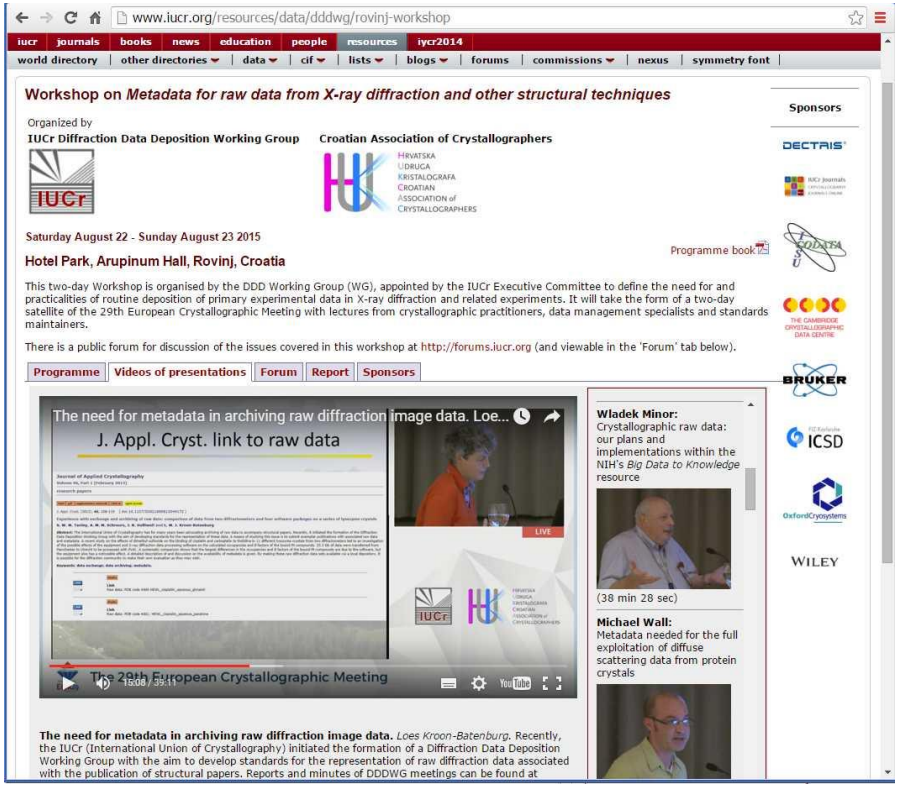
- Rights of access to publicly funded, but unpublished, crystallographic research data after *e.g.* 3 to 5 years.

Charge to the ECM29 Rovinj IUCr Workshop Participants

- *Define your Metadata or at the least Define the Challenges you face*
- *We have provided a template form for you to supply information about metadata for your specific research field / IUCr Commission*
- *We consider the challenge of aligning scientific metadata with generic standards like the 'Dublin Core of Metadata descriptors'*
- *We have to understand each other's fields; this will assist the philosophical challenge of 'seeing a data set through a new-user's eyes'*

Complete video record of Rovinj Workshop: http://tinyurl.com/diffraction-metadata

Session I: Introduction
Session II: Diffraction images - what can we get out?
Session III: Metadata for diffraction images and other experimental methods
Session IV: Data in the Wider World - From Laboratory to Database
Session V: What new metadata items are needed?
Session VI: Metadata schemas

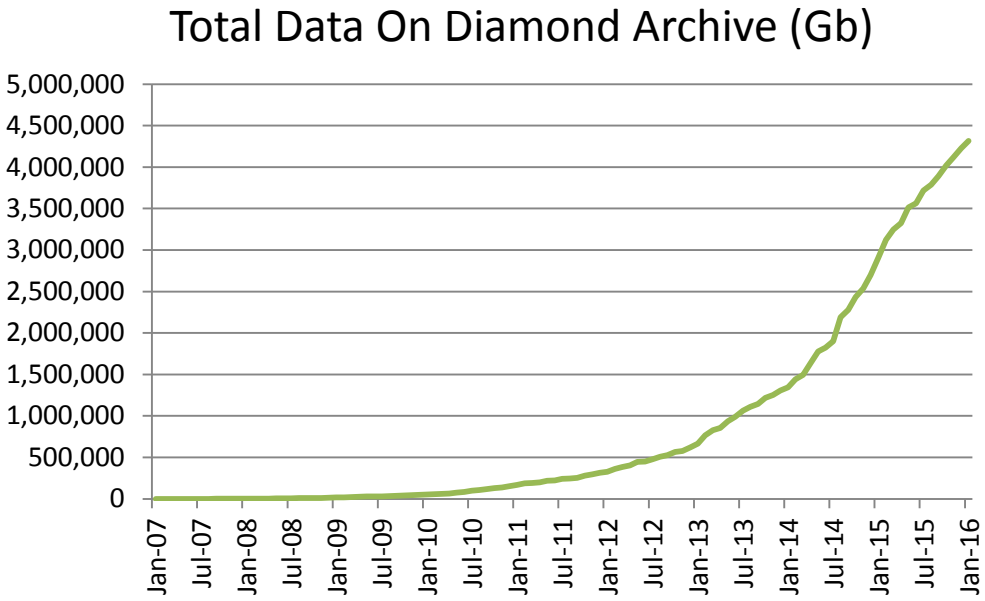


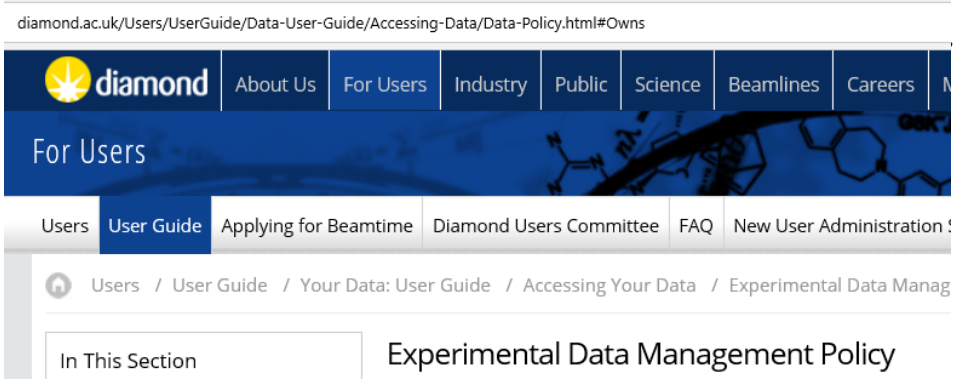
Significant pioneering developments

- Australian synchrotron MX raw data archive https://store.synchrotron.org.au/public_data/
- The USA NIH funded various structural genomics projects with raw data archives
- The Institut Laue Langevin and ISIS are exemplar at preserving all data and with dois eg

Current Data Archive Status at Diamond

A pioneer SR facility retaining all data since start up





Users conducting Peer Reviewed Research will own the Experimental Data that they produce."

"…Following the initial 30 day storage period, Diamond will create a single archive copy of the Experimental Data on tape."

"…Users of Diamond Facilities are responsible for meeting any third-party data management obligations that may be applicable."

Recent developments

- University data repositories with doi registrations.
- EC's Zenodo science data archive (free of charge!)
- The University of Virginia BD2K for MX, led by Wladek Minor http://www.proteindiffraction.org/ (USA)
- The PDB now requests the information on raw data and metadata for raw data during a deposition ie their dois
- ESRF Data Archive ("every raw data set measured with a registered doi")
- IUCrData (initially, *derived* data sets)
- The Structural Biology Data Grid has been launched (Nature Comms Meyer et al 2016)

4XAN_Carboplatin_NaBr_Diamond_I04

Tanley, Simon

[Experimental data]. 2014. The University of Manchester.

Access to files

carboplatin_NaBr_diamond_1_1-180.ZIP (x-zip-compressed)
carboplatin_NaBr_diamond_1_181-360.ZIP (x-zip-compressed)

Abstract

Carboplatin is a second-generation platinum anticancer agent used for the treatment of a variety of cancers. Previous X-ray crystallographic studies of carboplatin binding to histidine (in hen egg-white lysozyme; HEWL) showed the partial conversion of carboplatin to cisplatin owing to the high NaCl concentration used in the crystallization conditions. HEWL co-crystallizations with carboplatin in NaBr conditions have now been carried out to confirm whether carboplatin converts to the bromine form and whether this takes place in a similar way to the partial conversion of carboplatin to cisplatin observed previously in NaCl conditions. Here, it is reported that a partial chemical transformation takes place but to a transplatin form. Thus, to attempt to resolve purely carboplatin binding at histidine, this study utilized co-crystallization of HEWL with carboplatin without NaCl to eliminate the partial chemical conversion of carboplatin. Tetragonal HEWL crystals co-crystallized with carboplatin were successfully obtained in four different conditions, each at a different pH value. The structural results obtained show carboplatin bound to either one or both of the N atoms of His15 of HEWL, and this particular variation was dependent on the concentration of anions in the crystallization mixture and the elapsed time, as well as the pH used. The structural details of the bound carboplatin molecule also differed between them. Overall, the most detailed crystal structure showed the majority of the carboplatin atoms bound to the platinum centre; however, the four-carbon

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FEEDBACK AND ENQUIRIES

HEWL_cisplatin_5percentDMSO_RT: 4g4a

Tanley, Simon

[Experimental data] version online. 2012. The University of Manchester.

Access to files

HEWL_cisplatin_5percentDMSO_RT_01_0001to01_0347.zip (zip)
HEWL_cisplatin_5percentDMSO_RT_02_0001to02_0200.zip (zip)
HEWL_cisplatin_5percentDMSO_RT_03_0001to03_0235.zip (zip)
HEWL_cisplatin_5percentDMSO_RT_04_0001to04_0303.zip (zip)
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HEWL_cisplatin_5percentDMSO_RT_09_0001to09_0310.zip (zip)
HEWL_cisplatin_5percentDMSO_RT_09_0311to09_0658.zip (zip)

Abstract

Abstract: The anticancer complexes cisplatin and carboplatin are known to bind to both the N and the N atoms of His15 of hen egg-white lysozyme (HEWL) in the presence of dimethyl sulfoxide (DMSO). However, neither binds in aqueous media after 4 d of crystallization and crystal growth, suggesting that DMSO facilitates cisplatin/carboplatin binding to the N atoms of His15 by an unknown mechanism. Crystals of HEWL cocrystallized with cisplatin in both aqueous and DMSO media, of HEWL cocrystallized with carboplatin in DMSO medium and of HEWL cocrystallized with cisplatin and N-acetylglucosamine (NAG) in DMSO medium were stored for between seven and 15 months. X-ray diffraction studies of these crystals were carried out on a Bruker APEX II home-source diffractometer at room temperature. Room-temperature X-ray diffraction data

Related resources

Full-text held externally
DOI: 10.15127/1.215887
DOI: doi:10.1107/S1744309112042005
DOI: doi:10.1107/S1744309112042005

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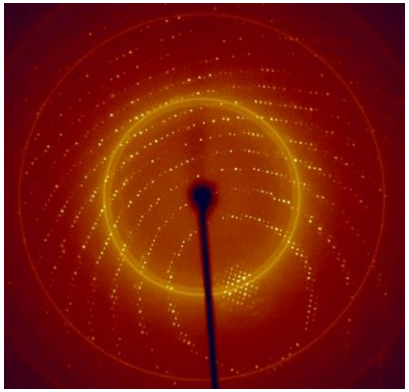
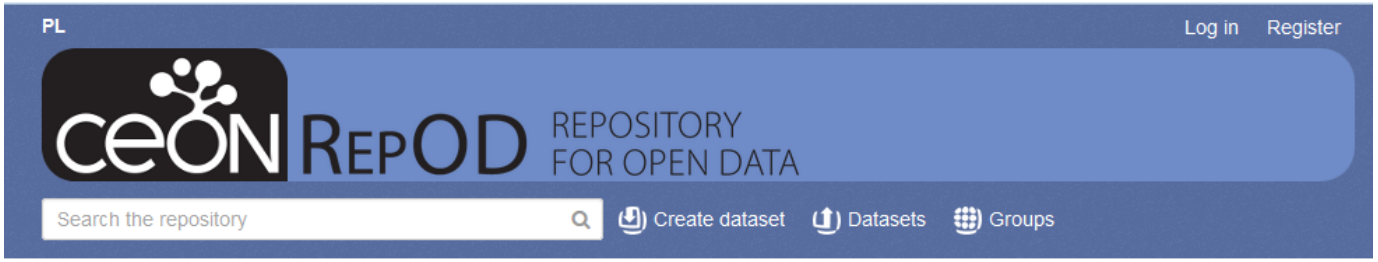
Academic department(s)
Faculty of Engineering and Physical Sciences' website
Faculty of Life Sciences' website
School of Chemistry 's website



Each entry also includes a variety of metadata

The Interdisciplinary Centre for Mathematical and Computational Modelling (ICM) University of Warsaw

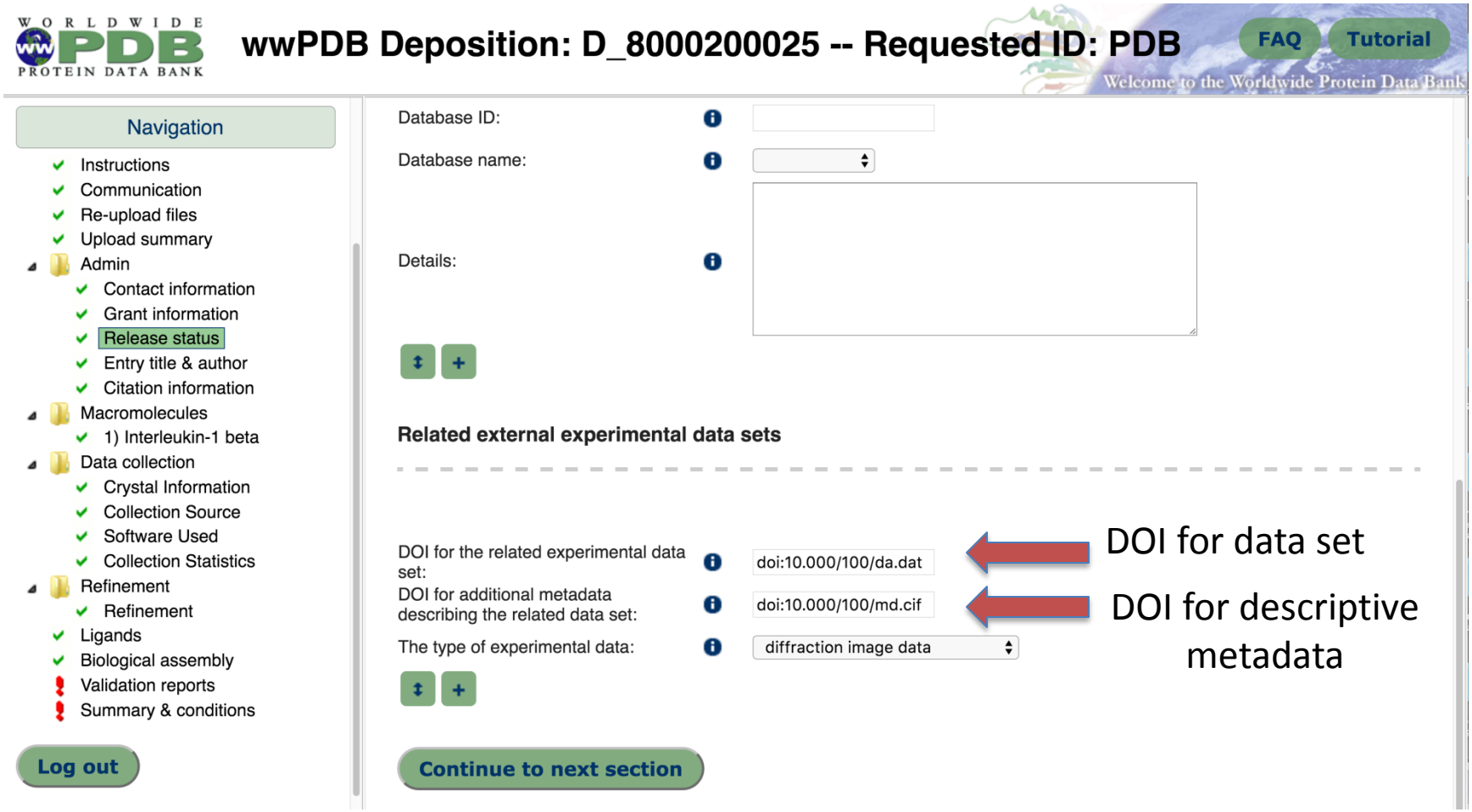
- *In 2015 initiated archiving of raw diffraction images with assigned DOI numbers in their RepOD (https://repod.pon.edu.pl/) open science repository;*
- *At present there are just a few deposits, but macromolecular crystallographers in Poland are encouraged to archive their raw data there.*



Mariusz Jaskolski personal communication

wwPDB Deposition & Annotation System

Identifying Primary Data



Big Research needs Big Machines leads to Big Data

World leading

ESRF premiere X-ray source

Institut Laue Langevin Neutron source

The European Synchrotron Radiation Facility (ESRF) in Grenoble, in which the UK has a 14% share, and the Institut Laue Langevin nuclear reactor is to the right (UK share 25-33%)

ESRF DATA POLICY SINCE LAST PROPOSAL ROUND

- ESRF Council officially adopted a Data Policy (1/12/2015)
- ESRF is custodian of data and metadata
- ESRF to collect high quality metadata to facilitate reuse of data
- ESRF will keep raw (or reduced) data for 10 years + metadata for ever

- Data will be registered in a data catalogue (icat) + published with a Digital Object Indentifier (DOI)
- Principal investigators have exclusive access to data during the embargo period (3 years but can be extended)
- Data will be made public after the embargo period under CC-BY
- Data Policy will be implemented on all beamlines by 2020

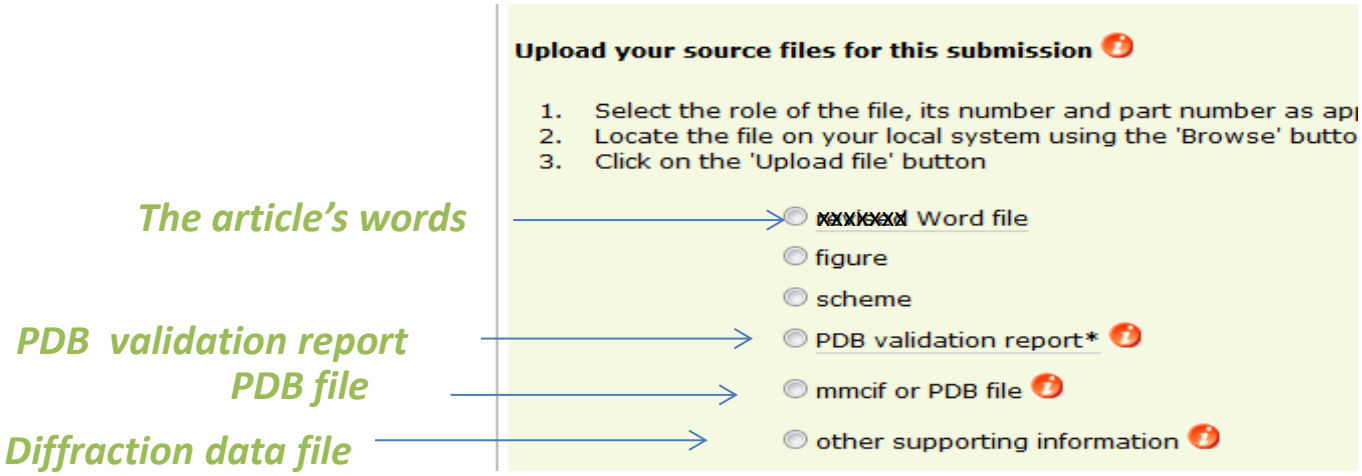
http://www.esrf.eu/home/UsersAndScience/UserGuide/esrf-data-policy-implementation.html

Editor, referee and reader/user

- In the early 1990s *Acta Cryst. C* pioneered refereeing of articles as well as their structure factors and coordinates; any one or all of these could be revised!
- Databases can then harvest the fruits of that peer review thoroughness;
- In 2002 JRH as IUCr EinC proposed at IUCr Geneva that the *Acta Cryst. C* method should be harnessed for *Acta Cryst. D* submissions (sadly, was rejected);
- Today I still commend the *Acta Cryst. C* method to the benefit of journals, databases, authors and readers;
- ***Now we also have the technology and organisation to have access to the raw diffraction data as well.***

IUCr Journals

Provides file upload options that include:- the .doc word file, the PDB validation reports, the PDB files and e.g. mtz processed diffraction data files



The article text can also obviously provide the dois for the raw diffraction images if the authors wish to

IUCrData

- *Data publishing platform launched 2016*
- *Addresses immediate need for concise reporting of peer-reviewed structural model data sets*
- *Intends to develop new synergies between journal publications and data sets*

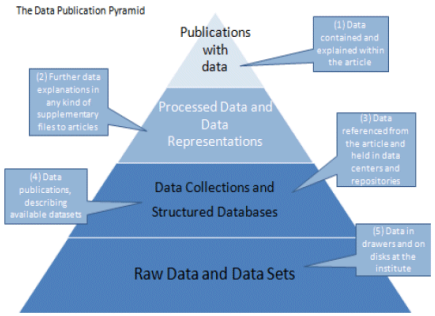
In conclusion

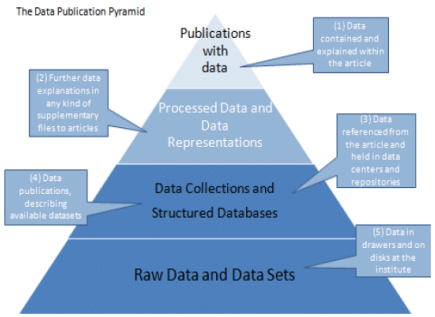
- New modus operandi for ***published funded research***; access to all data and should be open access.
- A ***limited time for funded researchers to analyse their data and publish***; typically 3 years. Then the raw data are put on open access.
- Policy makers are now discussing new ways to '***speed up science and discovery for tax payers to reap quicker benefits***'; ***Open Science***. New rules of conduct for funded research would be essential!

- Next actions of the IUCr DDDWG; articles are in preparation from ECM29 Rovinj Workshop; with IUCr COMCIFS a checkcif for raw data; planned workshop on ***metadata for raw data at*** ACA New Orleans; sessions at IUCr Hyderabad…..

- Current actions of JRH as a researcher; inviting other ***platins with proteins*** and nucleic acids researchers to contribute to the ***fully open access raw data, SFs, coordinates and publications***…….

Join in with the raw diffraction data revolution


The Data Publication Pyramid
Publications with data
(1) Data contained and explained within the article
(2) Further data explanations in any kind of supplementary files to articles
Processed Data and Data Representations
(3) Data referenced from the article and held in data centers and repositories
(4) Data publications, describing available datasets
Data Collections and Structured Databases
(5) Data in drawers and on disks at the institute
Raw Data and Data Sets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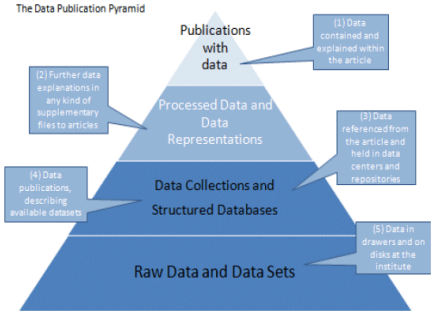
Thank you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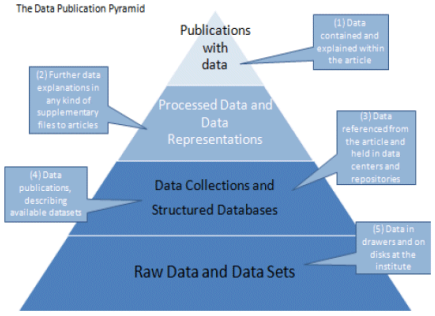
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