



Roadmap for Crystal Structure Determination with CCP4

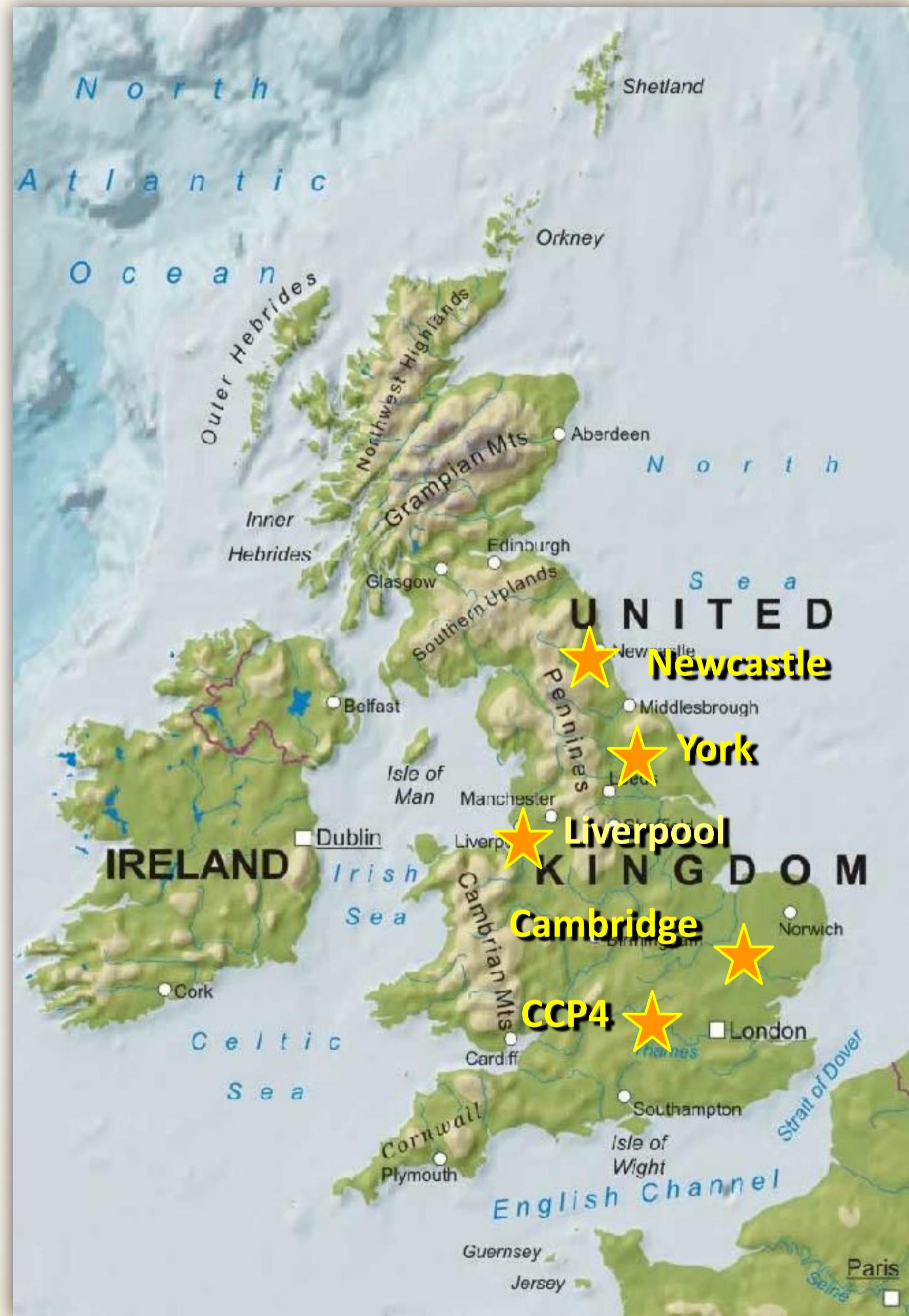
Eugene Krissinel
eugene.krissinel@stfc.ac.uk

CCP4-DLS workshop
Nov. 3 2025

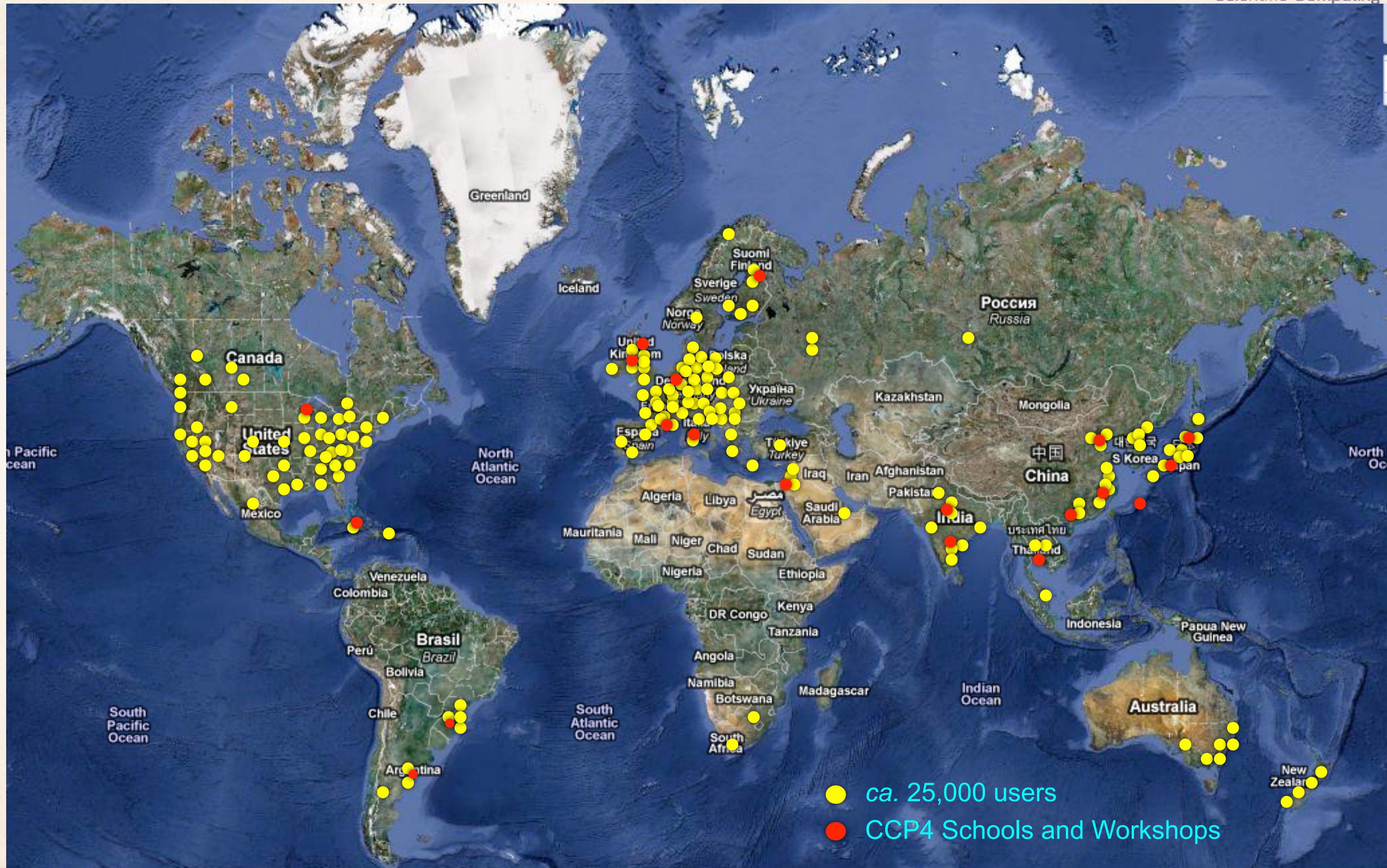
Harwell, UK

- CCP4 stands for "**Collaborative Computational Project No. 4 in Protein Crystallography**"
- One of several CCPs set up in the UK to advance and support scientific software developments
- CCP4 is not a single group in RCaH-Rutherford but a world-wide collaboration of developers and users
- CCP4 was formally set up in **1979** to support collaboration between researchers working on MX software in the UK, and to assemble a comprehensive collection of software to satisfy the computational requirements of the relevant UK groups
- CCP4 was originally supported by the UK Science and Engineering Research Council (SERC), and is now supported by the Biotechnology and Biological Sciences Research Council (BBSRC).
- The project is coordinated at the **Scientific Computing Department of STFC UK**

- Core Group @ RAL/Harwell (Oxford)
 - ~ maintain and support software suite
 - ~ application and infrastructural software developments
 - ~ collaborate with Diamond synchrotron on beam line deployment of CCP4 software and joint developments
 - ~ educational outreach
 - ~ maintain CCP4 resources such as the CCP4 bulletin board and CCP4 Cloud
- MRC/LMB (Cambridge)
 - ~ data processing software (Mosflm, Aimless)
 - ~ refinement software (Refmac)
 - ~ model building (Coot)
- Phaser group (University of Cambridge)
- University of York, Newcastle University
 - ~ Software developments (Moorhen, CCP4mg, Modelcraft, Privateer)
 - ~ CCP4 GUI-2 developments
- Associated projects
 - ~ Experimental Phasing from Leiden (Crank-2)
 - ~ Arcimboldo MR Software (Barcelona)
 - ~ MR-related and bioinformatics tools, University of Liverpool (SIMBAD)
 - ~ Arp/wArp (EMBL-Hamburg)
 - ~ SHELX (Goettingen and Barcelona)
 - ~ PDB-Redo (NKI, the Netherlands)



CCP4 on the Map



CCP4 Study Weekend

- ~ <https://studyweekend ccp4.ac.uk/>
- ~ January every year
- ~ Focuses on software developments.
- ~ Streamed live
- ~ Youtube <https://www.youtube.com/@ccp4579>



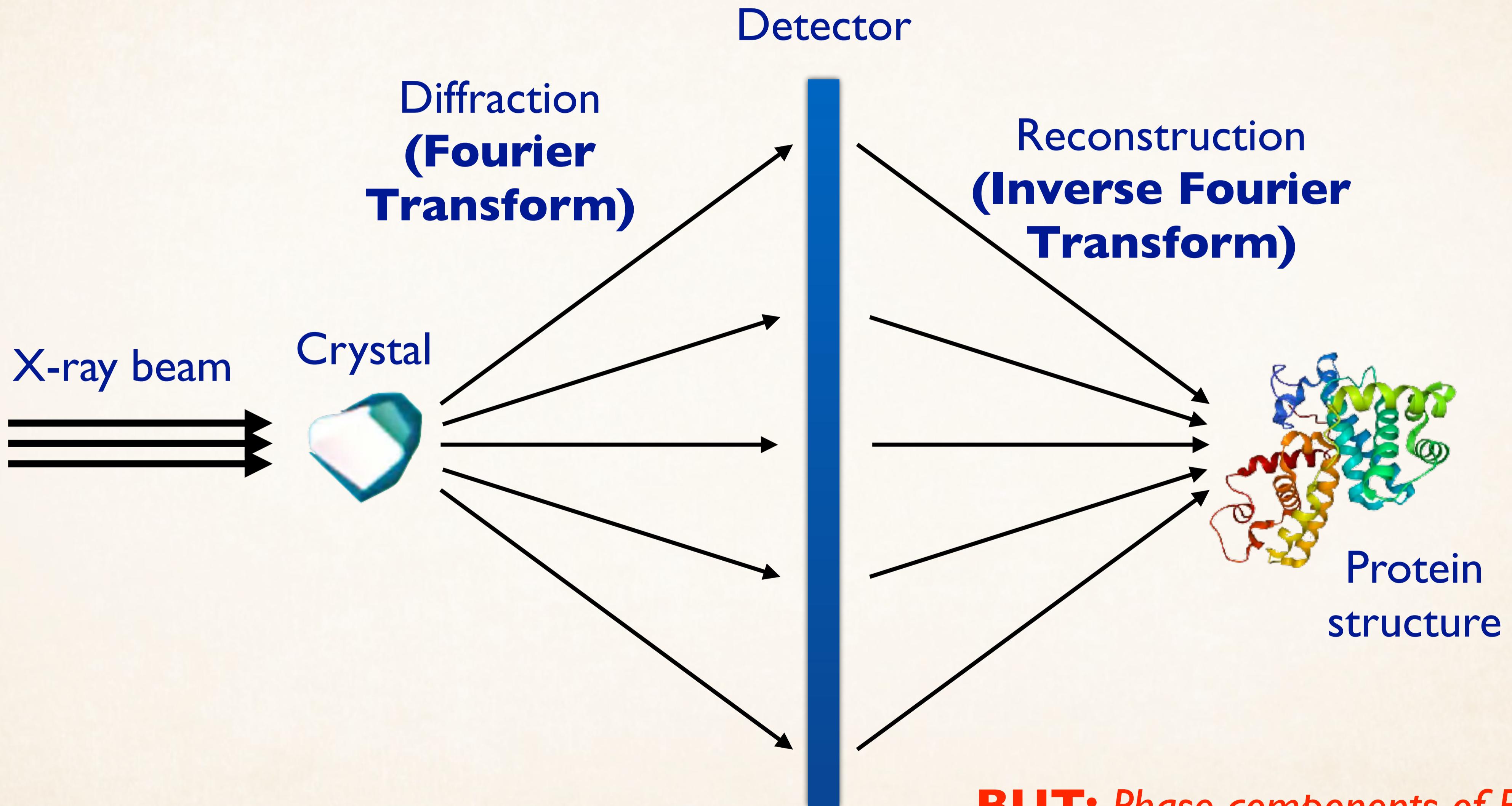
Acta D

- 2023 [Data – subtle details to big insights](#)
- 2022 [Current trends in macromolecular model refinement and validation](#)
- 2021 [Integrating Structural Biology](#)
- 2020 [Model building, validation and representation in MX and cryoEM](#) Acta Crys. D Volume 78, Part 10 (October 2022)
- 2019 [Molecular Replacement](#) Acta Crys. D Volume 77, Part 2 (February 2021)
- 2018 [Multi and Serial Crystal Data Collection and Processing](#) Acta Crys. D Volume 75, Part 2 (February 2019)
- 2017 [From Crystal to Structure \(Part 2\)](#) Acta Crys. D Volume 74, Part 3 (March 2018)
- 2017 [From Crystal to Structure \(Part 1\)](#) Acta Crys. D Volume 74, Part 2 (February 2018)
- 2016 [Protein-ligand complexes: understanding biological chemistry \(Part 2\)](#) Acta Crys. D Volume 73, Part 2 (February 2017)
- 2016 [Protein-ligand complexes: understanding biological chemistry \(Part 1\)](#) Acta Crys. D Volume 73, Part 1 (January 2017)
- 2015 [Advances in Experimental Phasing](#) Acta Crys. D Volume 72, Part 3 (March 2016)
- 2014 [Crystallography and complementary methods](#) Acta Crys. D Volume 71, Part 1 (January 2015)
- 2013 [Molecular replacements](#) Acta Crys. D Volume 69, Part 11 (November 2013)
- 2012 [Data collection and processing](#) Acta Crys. D Volume 69, Part 7 (July 2013)
- 2011 [Model building, refinement and validation](#) Acta Crys. D Volume 68, Part 4 (April 2012)
- 2010 [From Crystal to Structure with CCP4](#) Acta Crys. D Volume 67, Part 4 (April 2011) Some [talks](#) available.
- 2009 [Experimental Phasing and Radiation Damage](#) Acta Crys. D Volume 66, Part 4 (April 2010)
- 2008 [Low-resolution structure determination and validation](#) Acta Crys. D Volume 65, Part 2 (February 2009) ([photos](#))
- 2007 [Molecular Replacement](#) Acta Crys. D Volume 64, Part 1 (January 2008) ([photos](#))
- 2006 [Crystallography of complexes](#) Acta Crys. D Volume 63, Part 1 (January 2007) ([photos](#))
- 2005 [Data collection and analysis](#) Acta Crys. D Volume 62, Part 1 (January 2006) ([photos](#))
- 2004 [Model Building and Refinement](#) Acta Crys. D Volume 60, Part 12 Number 1 (December 2004) ([photos](#))
- 2003 [Experimental Phasing](#) Acta Crys. D Volume 59, Part 11 (November 2003) ([photos](#))
- 2002 [High-throughput structure determination](#) Acta Crys. D Volume 58, Part 11 (November 2002) ([photos](#))
- 2001 [Molecular Replacement and its Relatives](#) Acta Crys. D Volume 57, Part 10 (October 2001) ([photos](#))
- 2000 [Low Resolution Phasing](#) Acta Crys. D Volume 56, Part 10 (October 2000) ([photos](#))
- 1999 [Data Collection and Processing](#) Acta Crys. D Volume 55, Part 10 (October 1999) ([photos](#))
- 1998 [Databases for Macromolecular Crystallographers](#) Acta Crys. D Volume 54, Part 6 Number 1 (November 1998)s



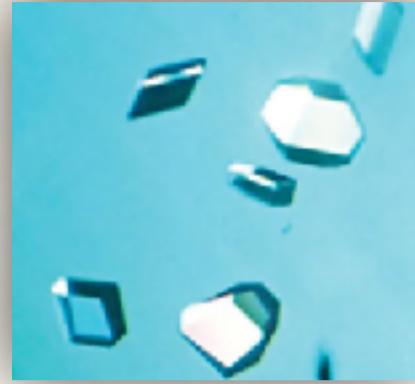


Structure Determination in a Nutshell

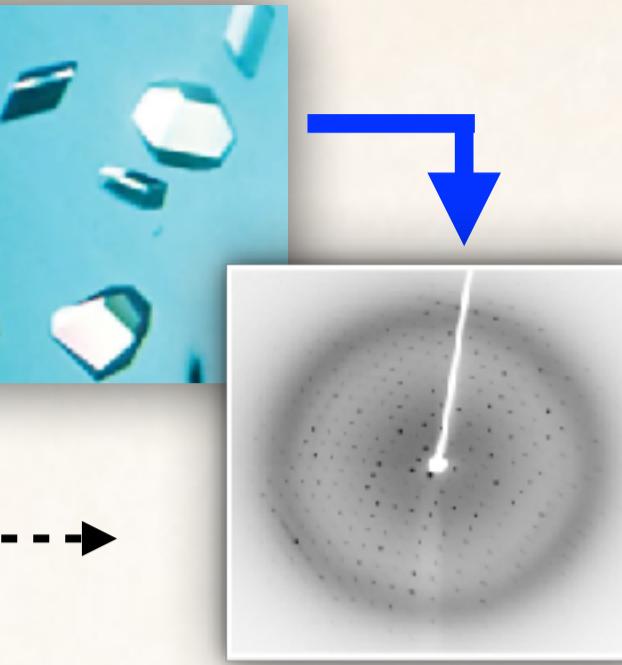
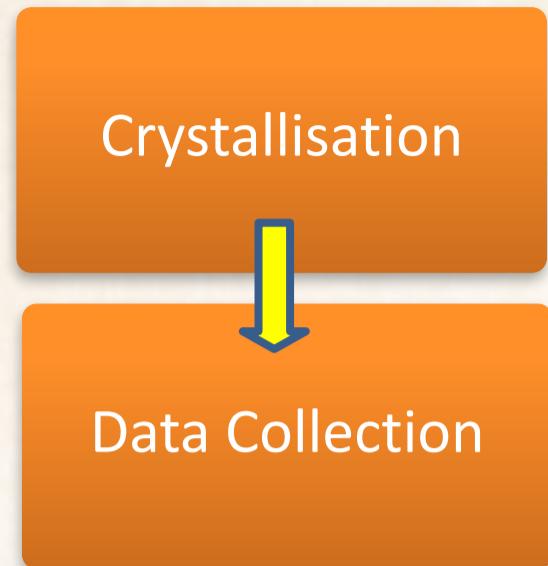


BUT: *Phase components of Fourier Transform cannot be measured*

Crystallisation

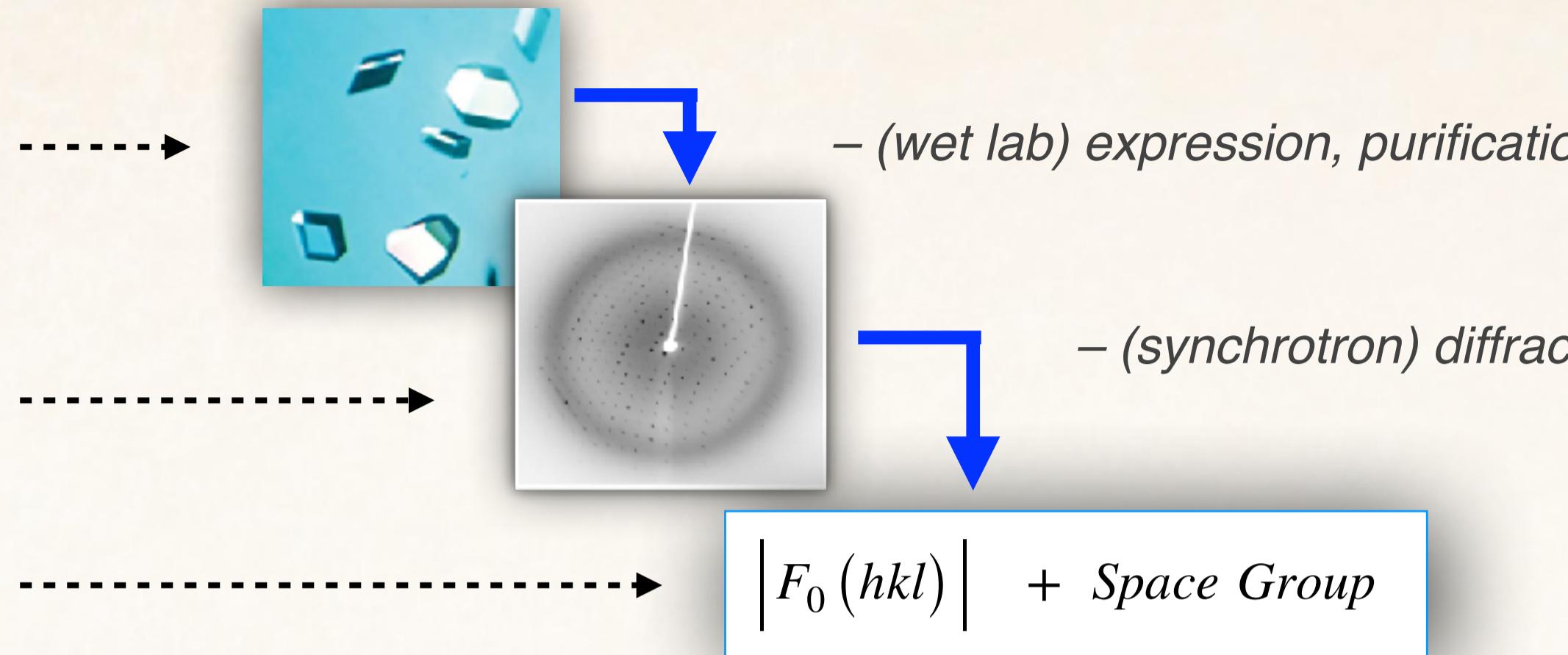
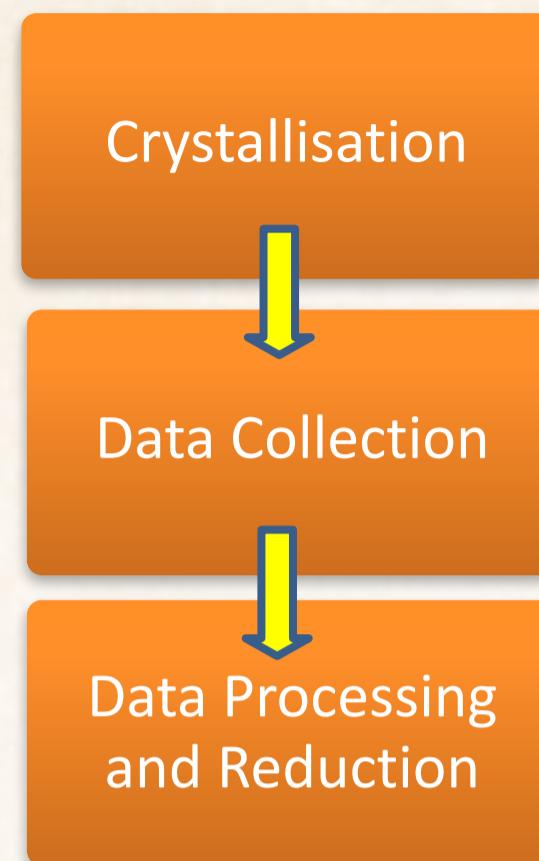


– *(wet lab) expression, purification, crystallisation*



– *(wet lab) expression, purification, crystallisation*

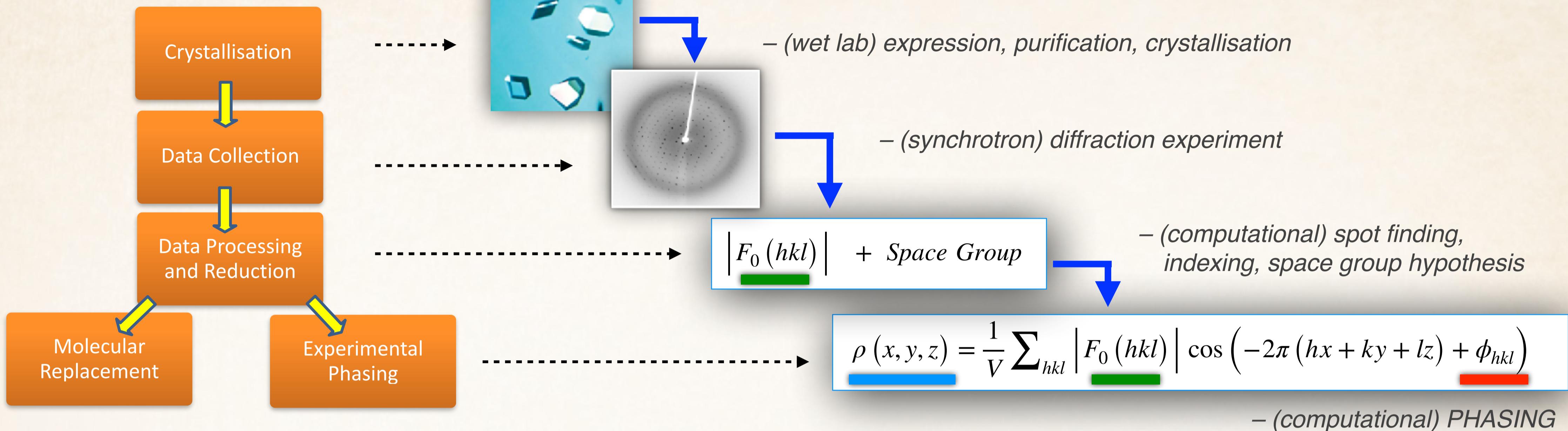
– *(synchrotron) diffraction experiment*



– (wet lab) expression, purification, crystallisation

– (synchrotron) diffraction experiment

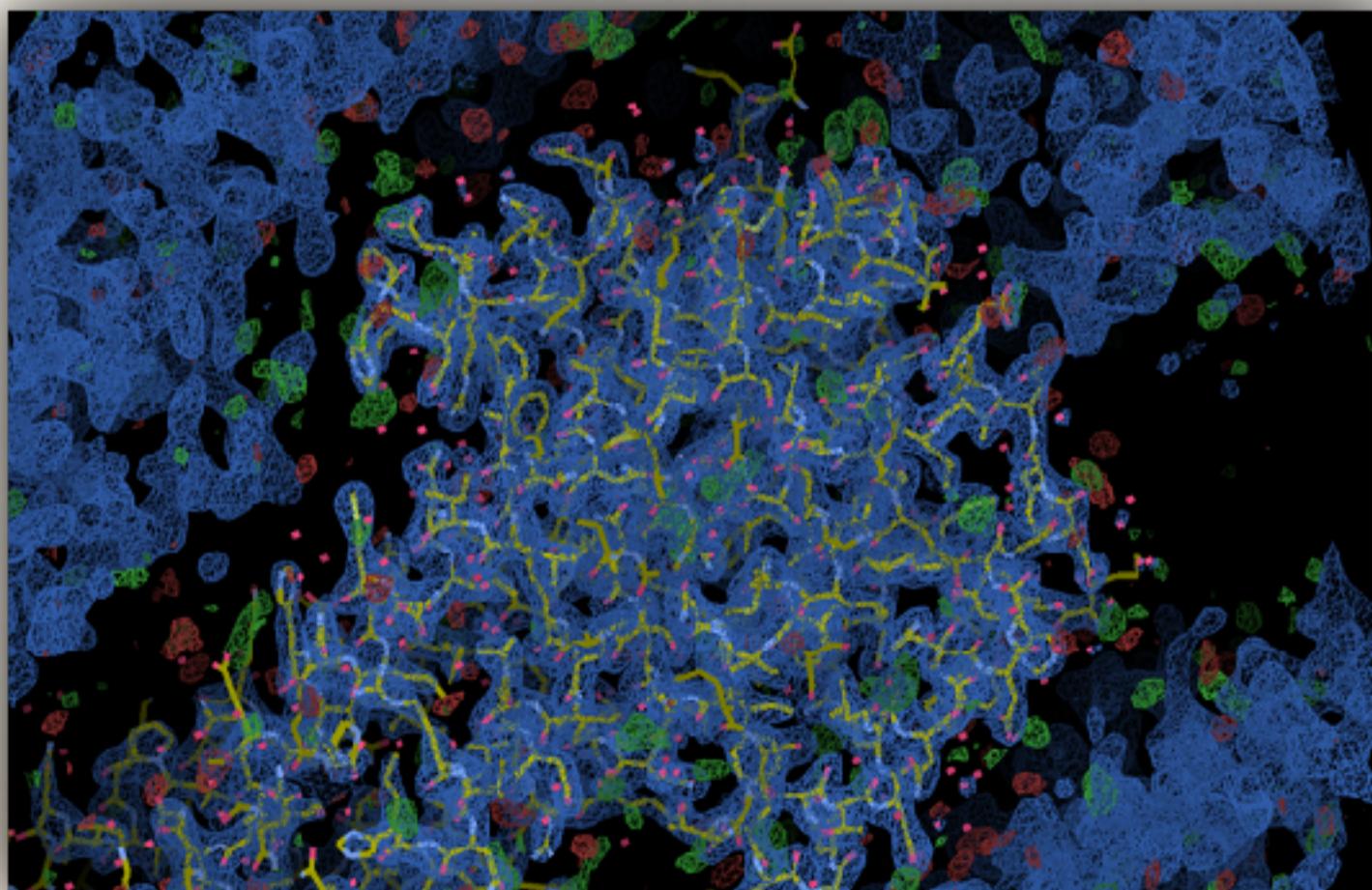
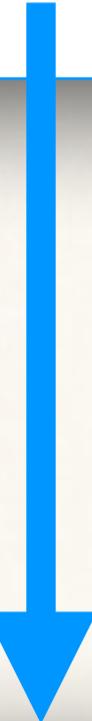
– (computational) spot finding,
indexing, space group hypothesis



*electron density
at (x,y,z)*

Amplitudes

$$\rho(x, y, z) = \frac{1}{V} \sum_{hkl} |F_0(hkl)| \cos(-2\pi(hx + ky + lz) + \phi_{hkl})$$



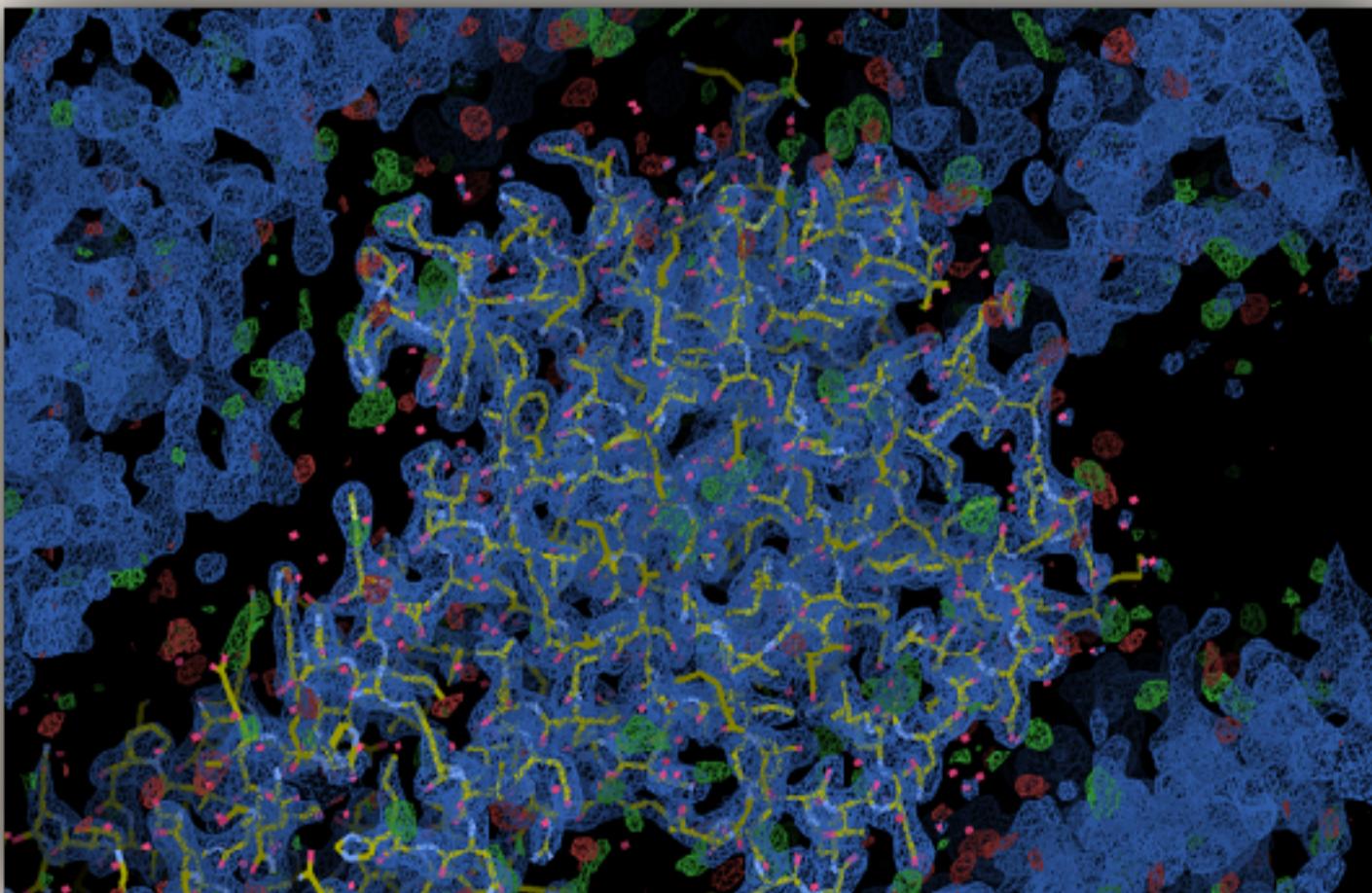
electron density & model

electron density
at (x, y, z)

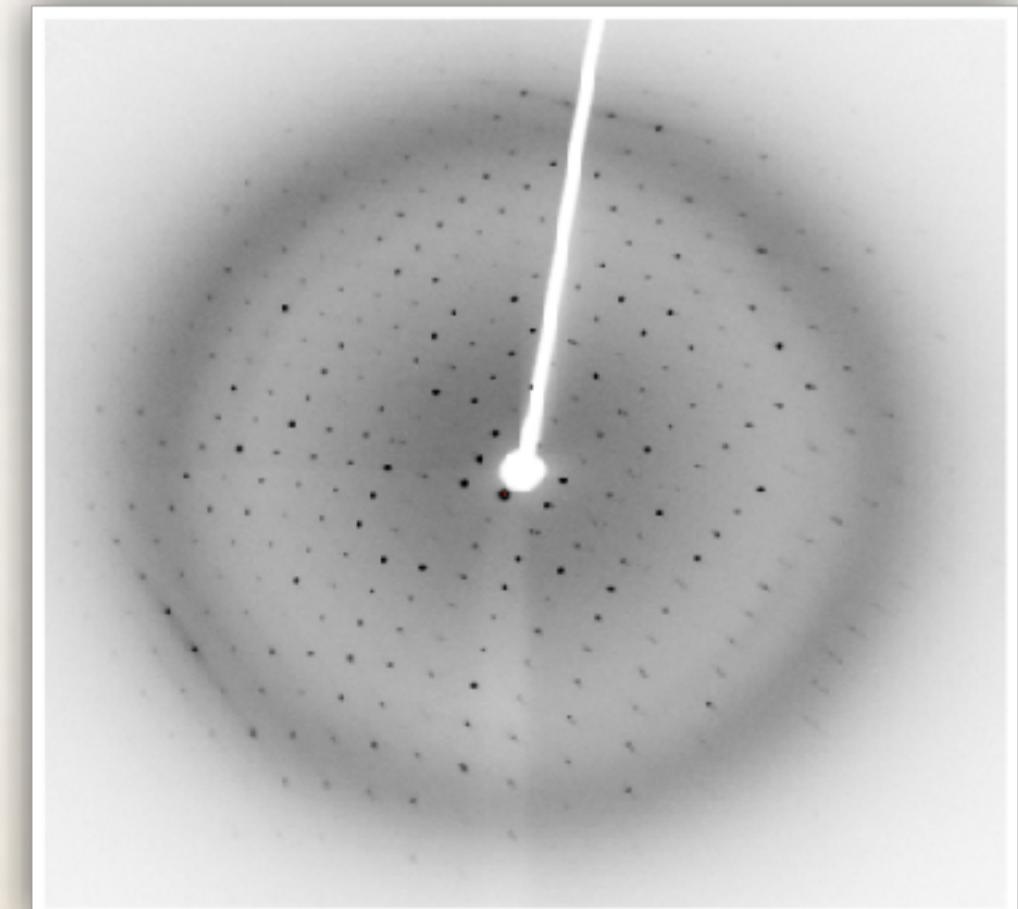
Amplitudes
(known)

Phases
(unknown)

$$\rho(x, y, z) = \frac{1}{V} \sum_{hkl} |F_0(hkl)| \cos(-2\pi(hx + ky + lz) + \phi_{hkl})$$



electron density & model

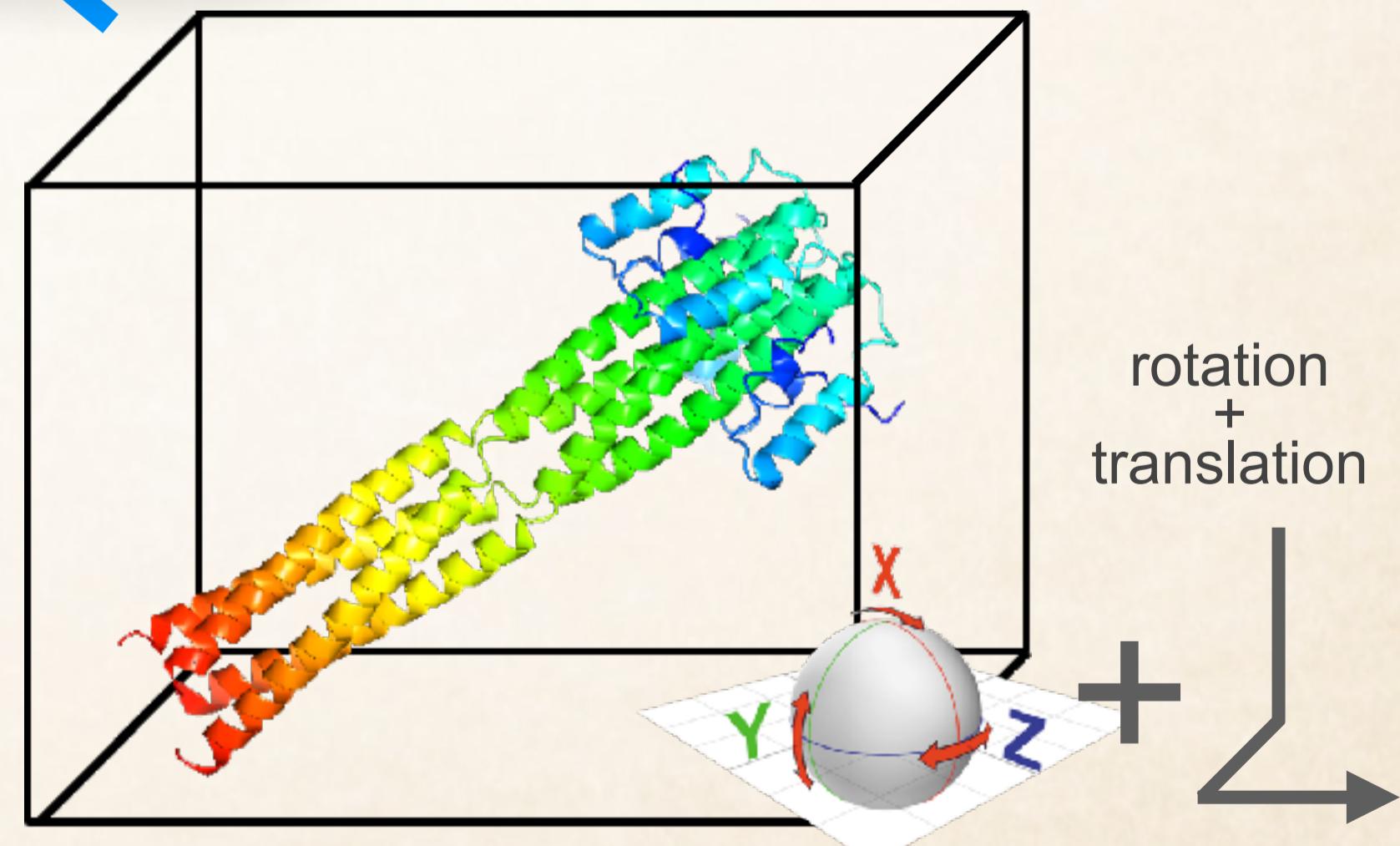
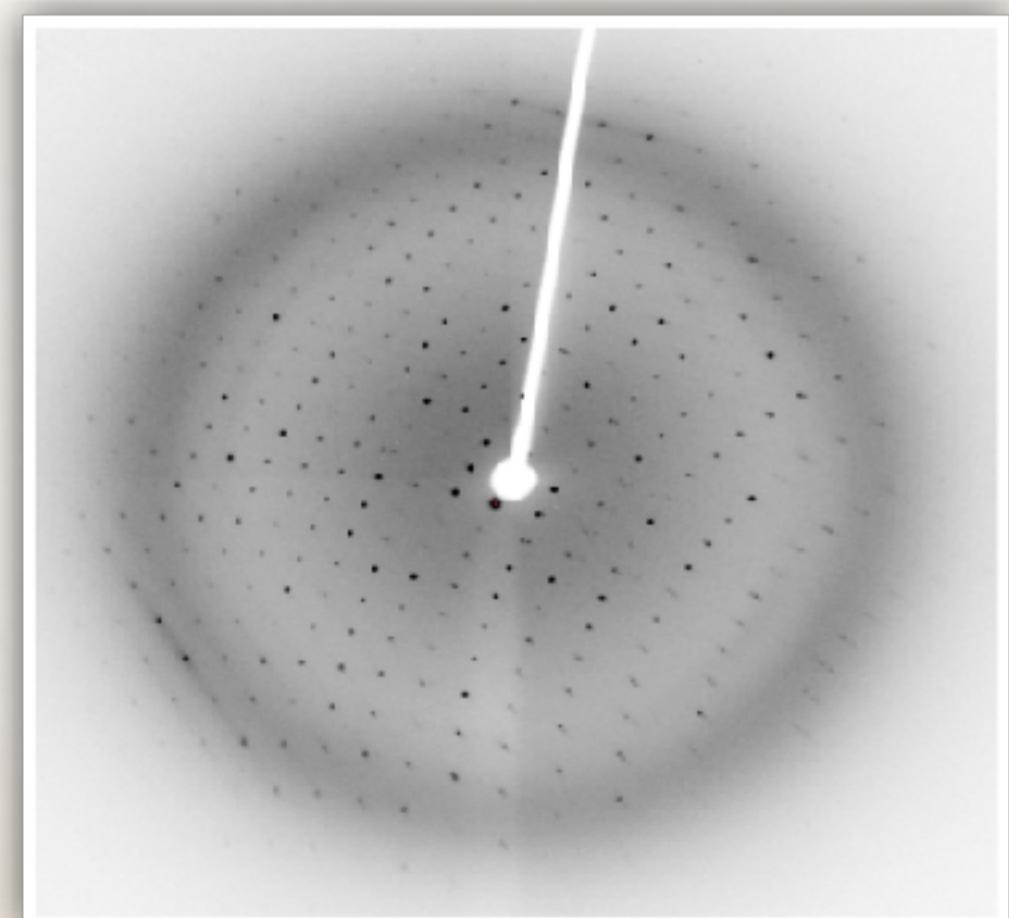
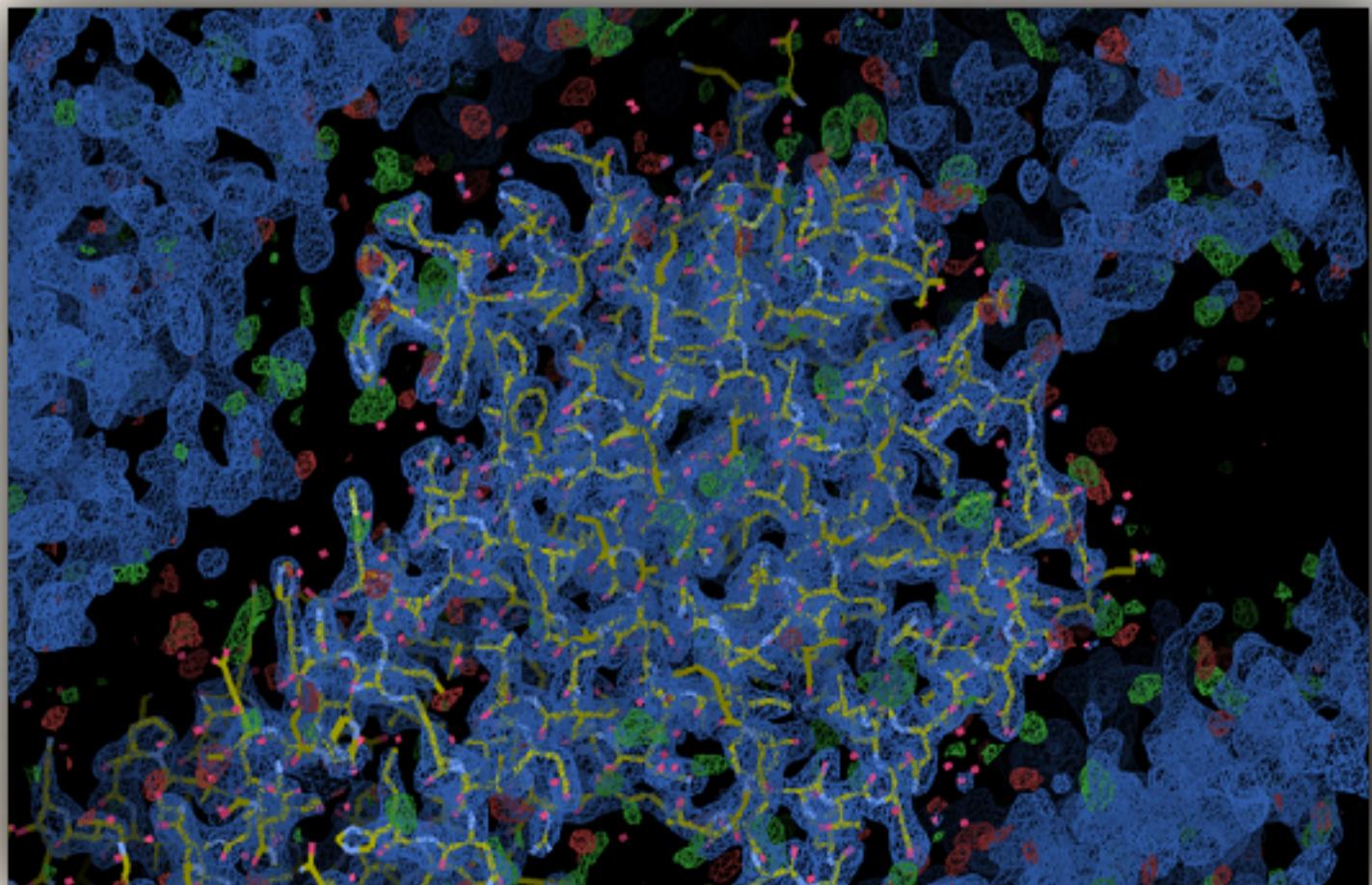


diffraction intensities

electron density
at (x, y, z)

Amplitudes
(known)

$$\rho(x, y, z) = \frac{1}{V} \sum_{hkl} |F_0(hkl)| \cos(-2\pi(hx + ky + lz) + \phi_{hkl})$$



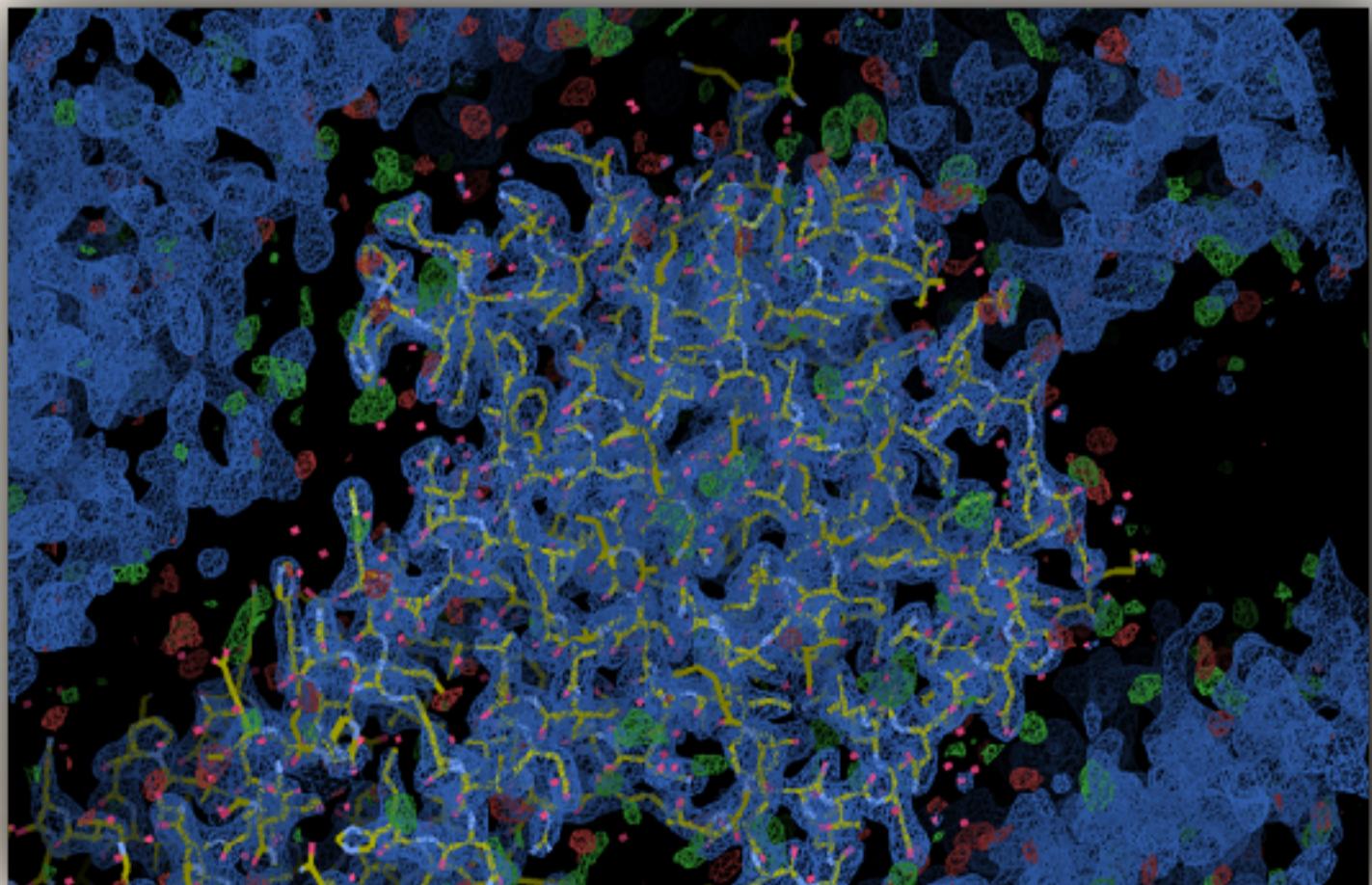
$$|F_{calc}(hkl)| \approx |F_0(hkl)|$$

electron density
at (x, y, z)

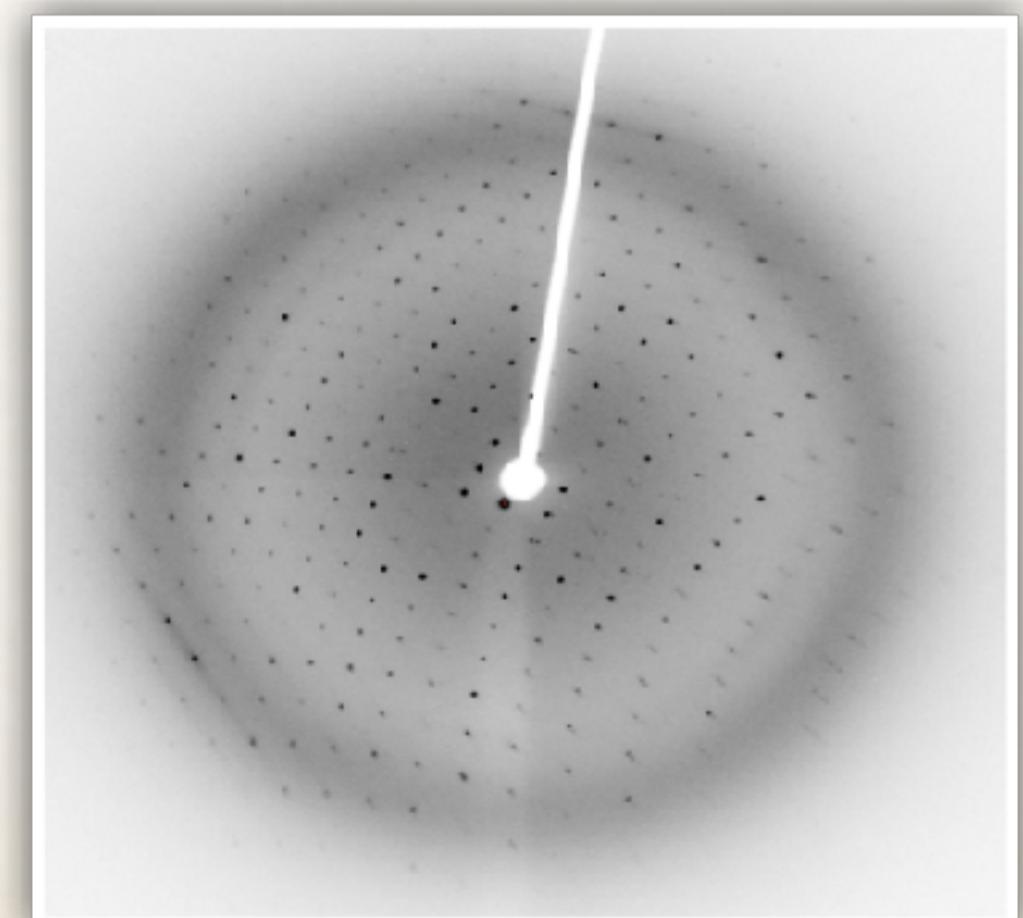
Amplitudes
(known)

Phases
(approximated)

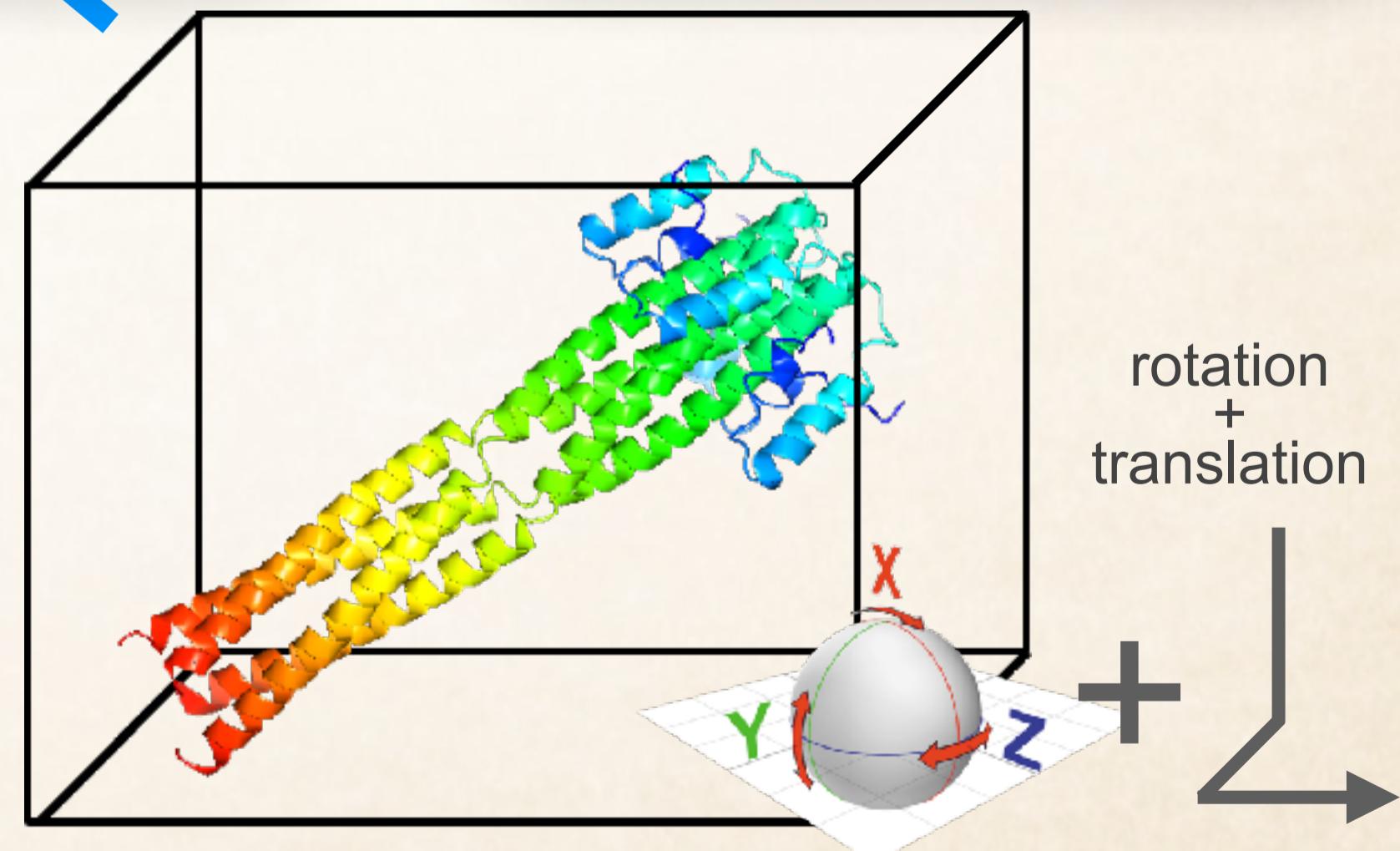
$$\rho(x, y, z) = \frac{1}{V} \sum_{hkl} |F_0(hkl)| \cos(-2\pi(hx + ky + lz) + \phi_{hkl})$$



electron density & model



diffraction intensities



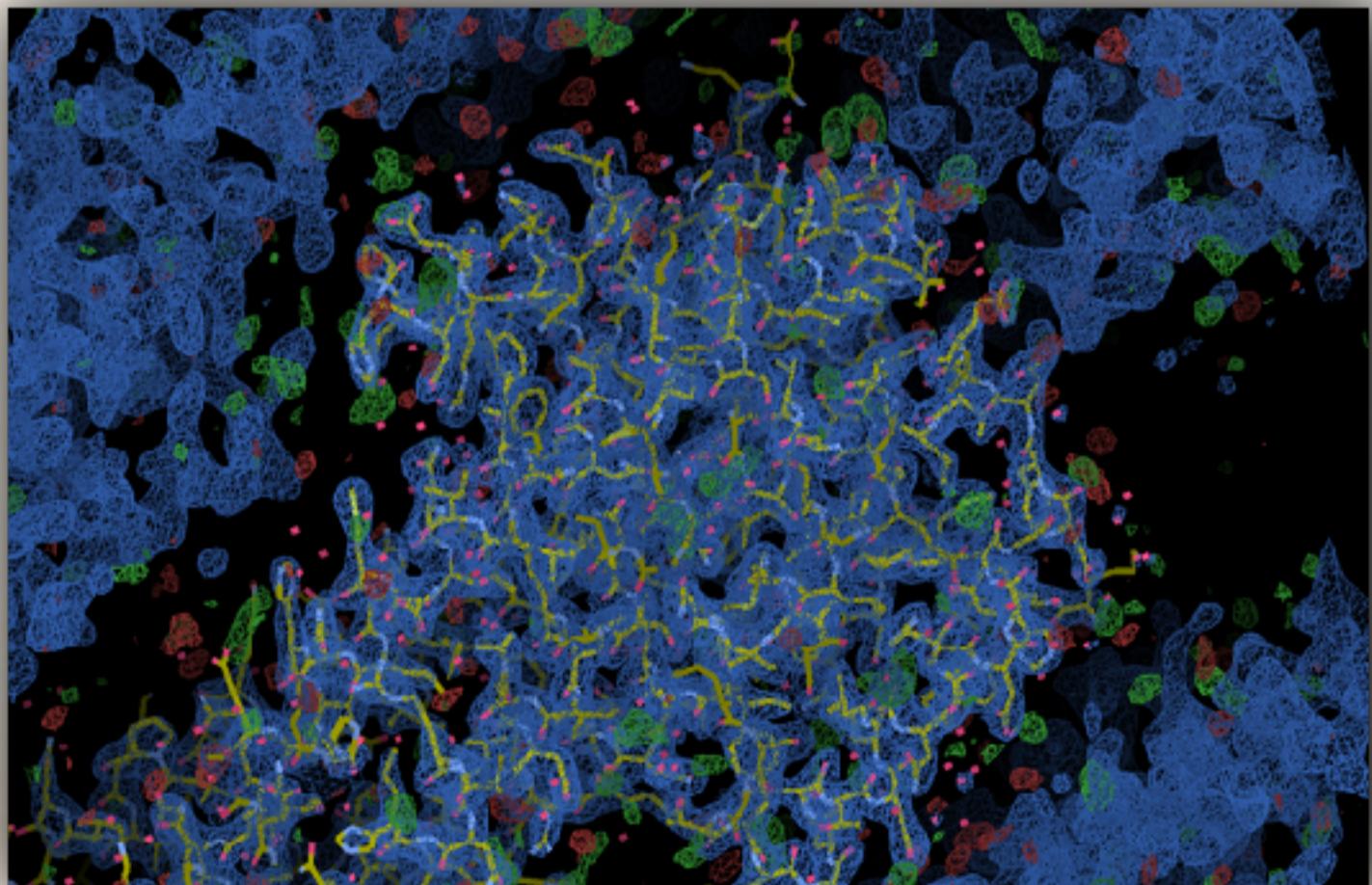
homologous model

electron density
at (x, y, z)

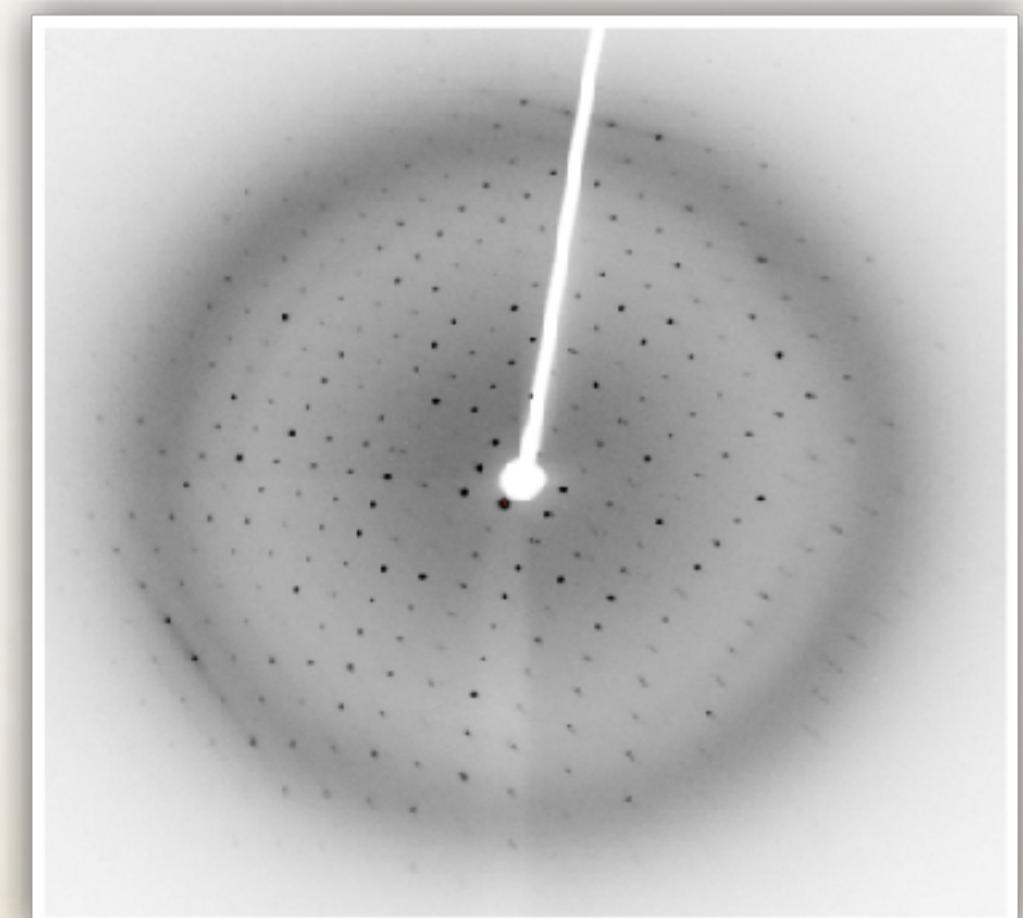
Amplitudes
(known)

Phases
(approximated)

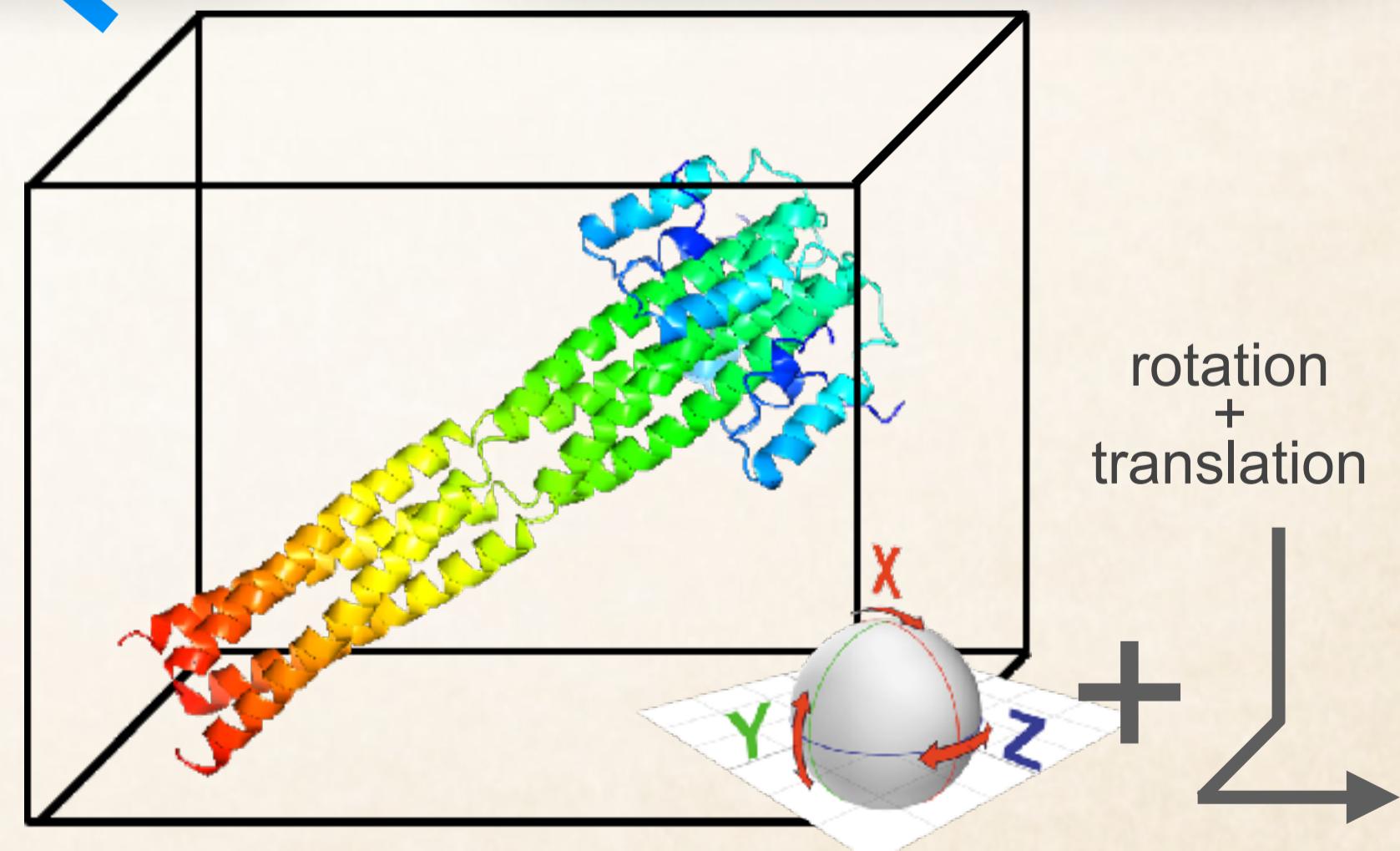
$$\rho(x, y, z) = \frac{1}{V} \sum_{hkl} |F_0(hkl)| \cos(-2\pi(hx + ky + lz) + \phi_{hkl})$$



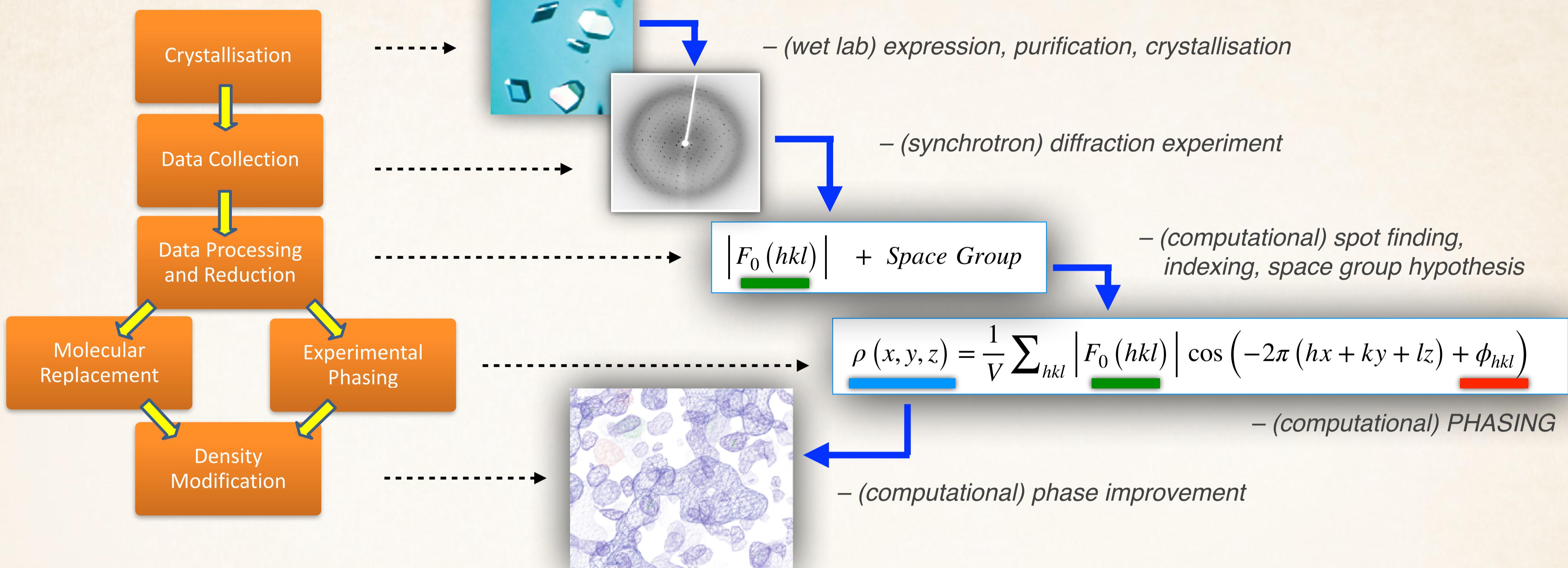
electron density & model

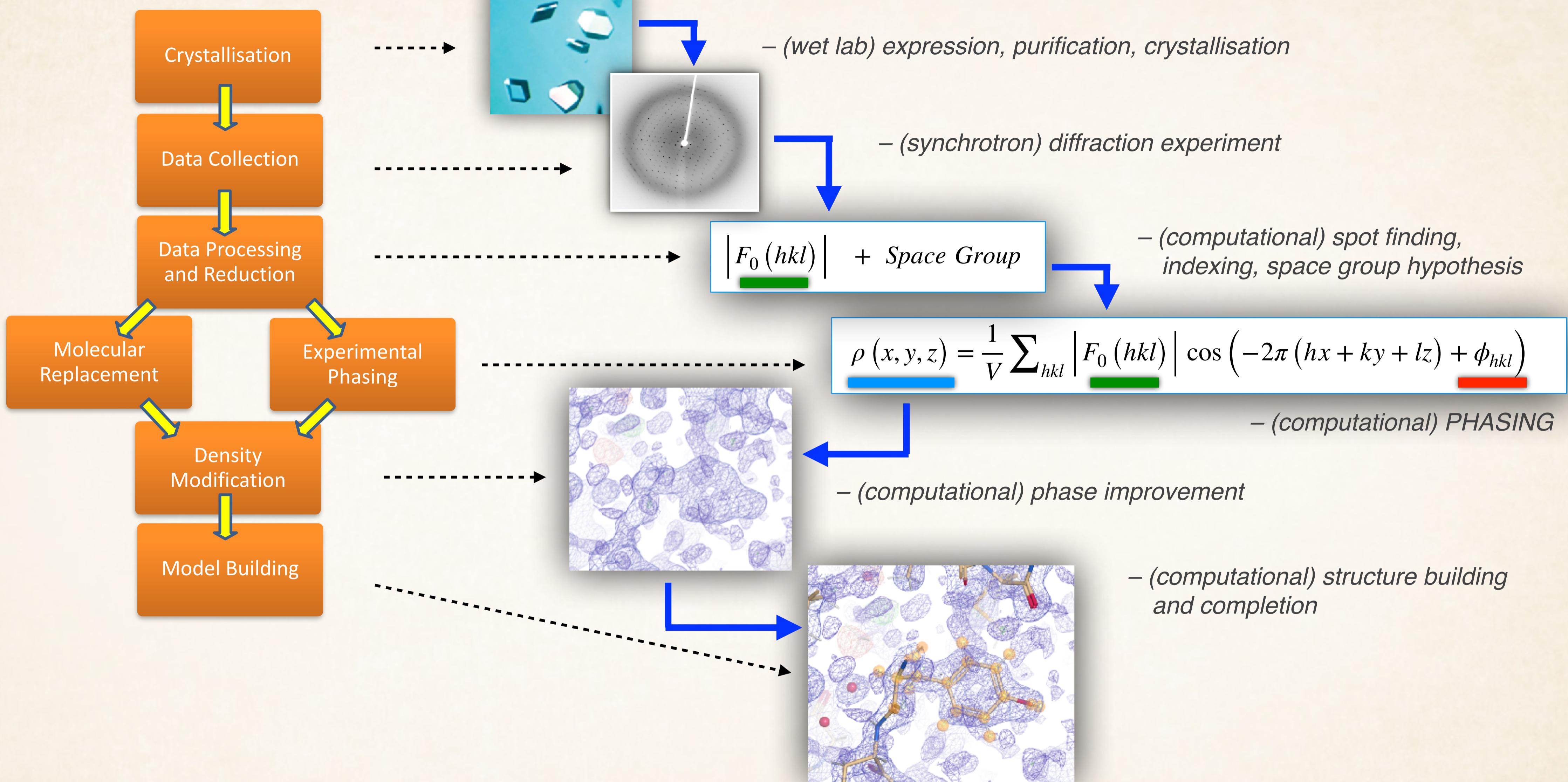


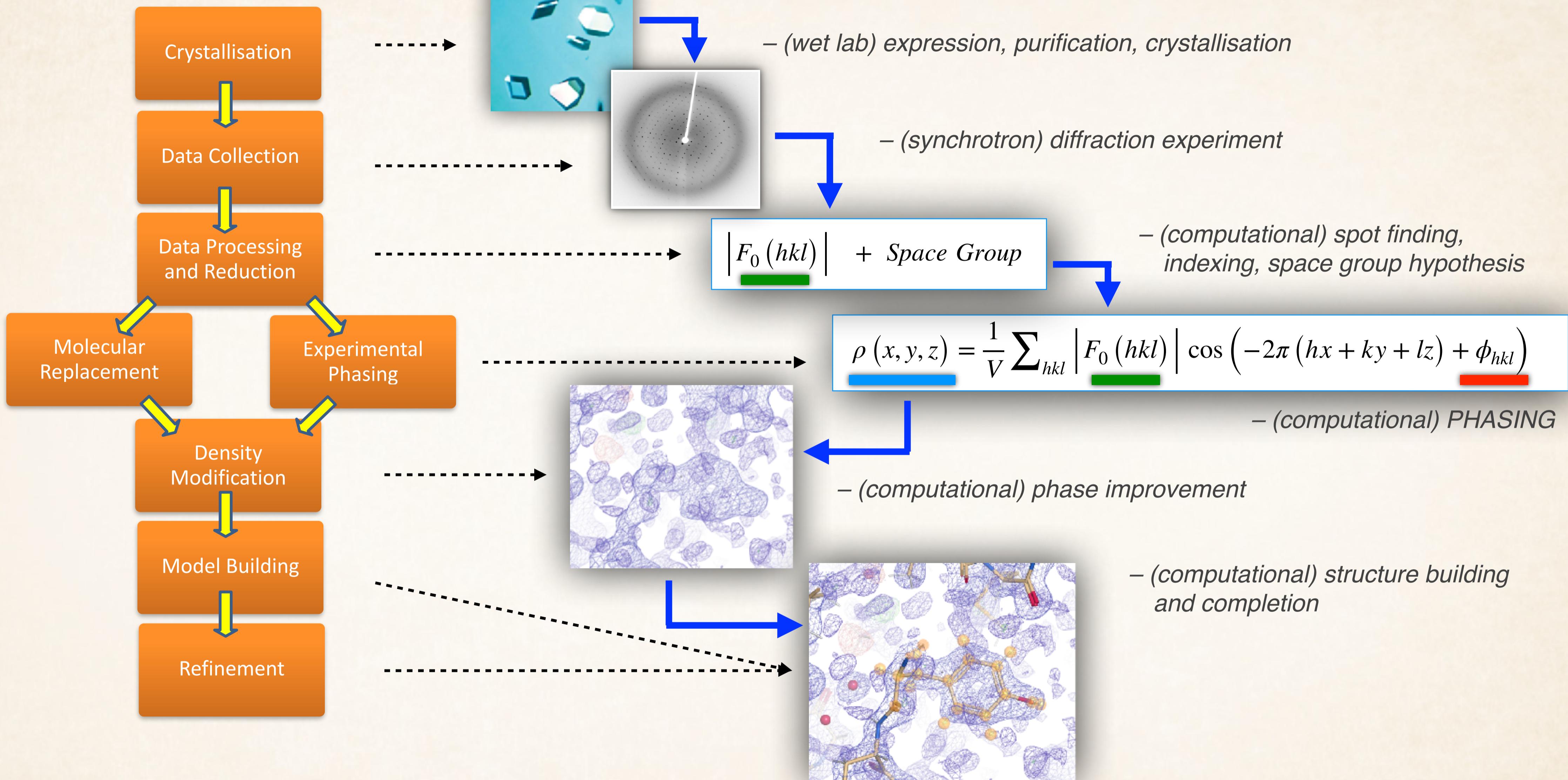
diffraction intensities

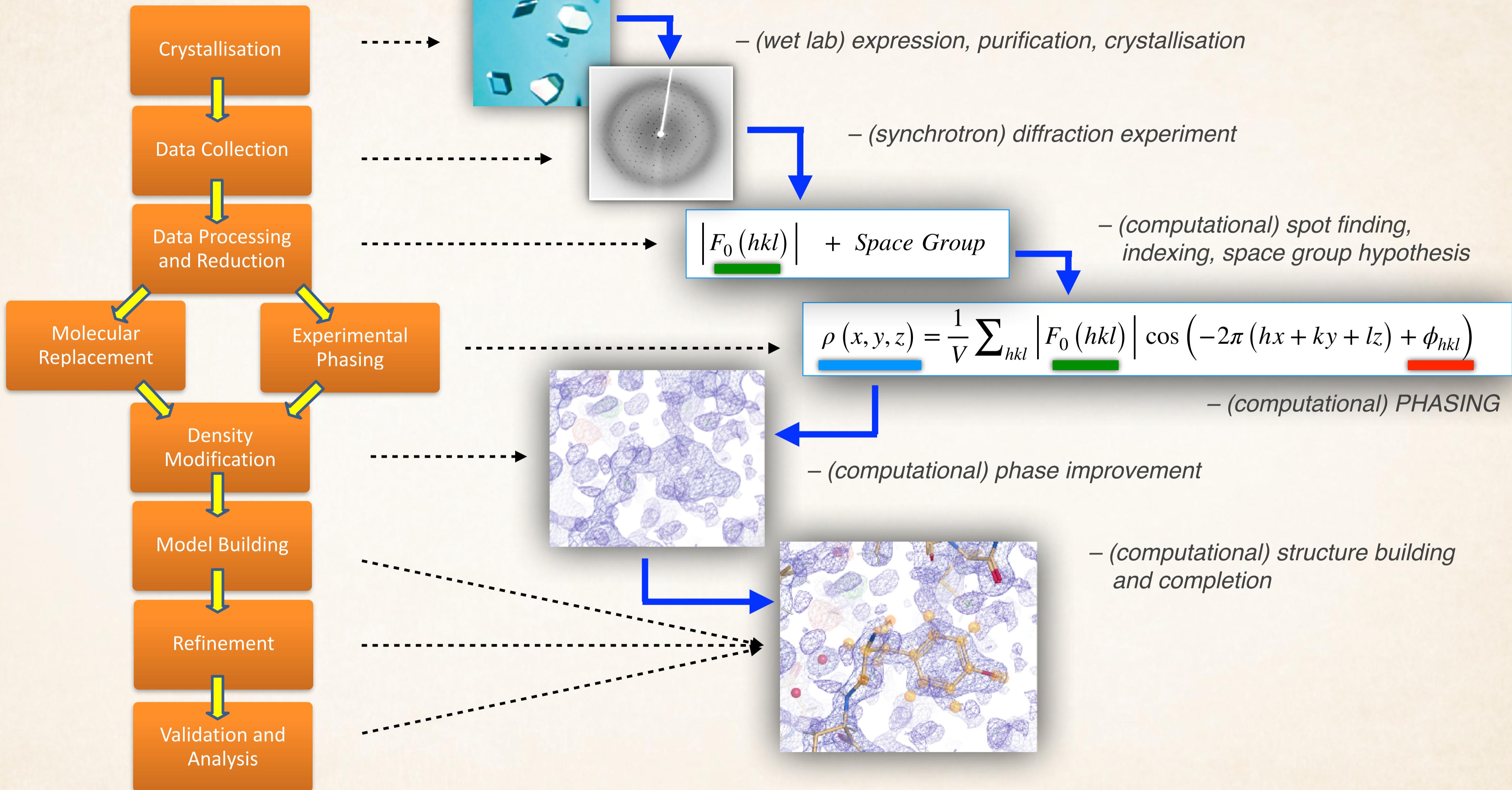


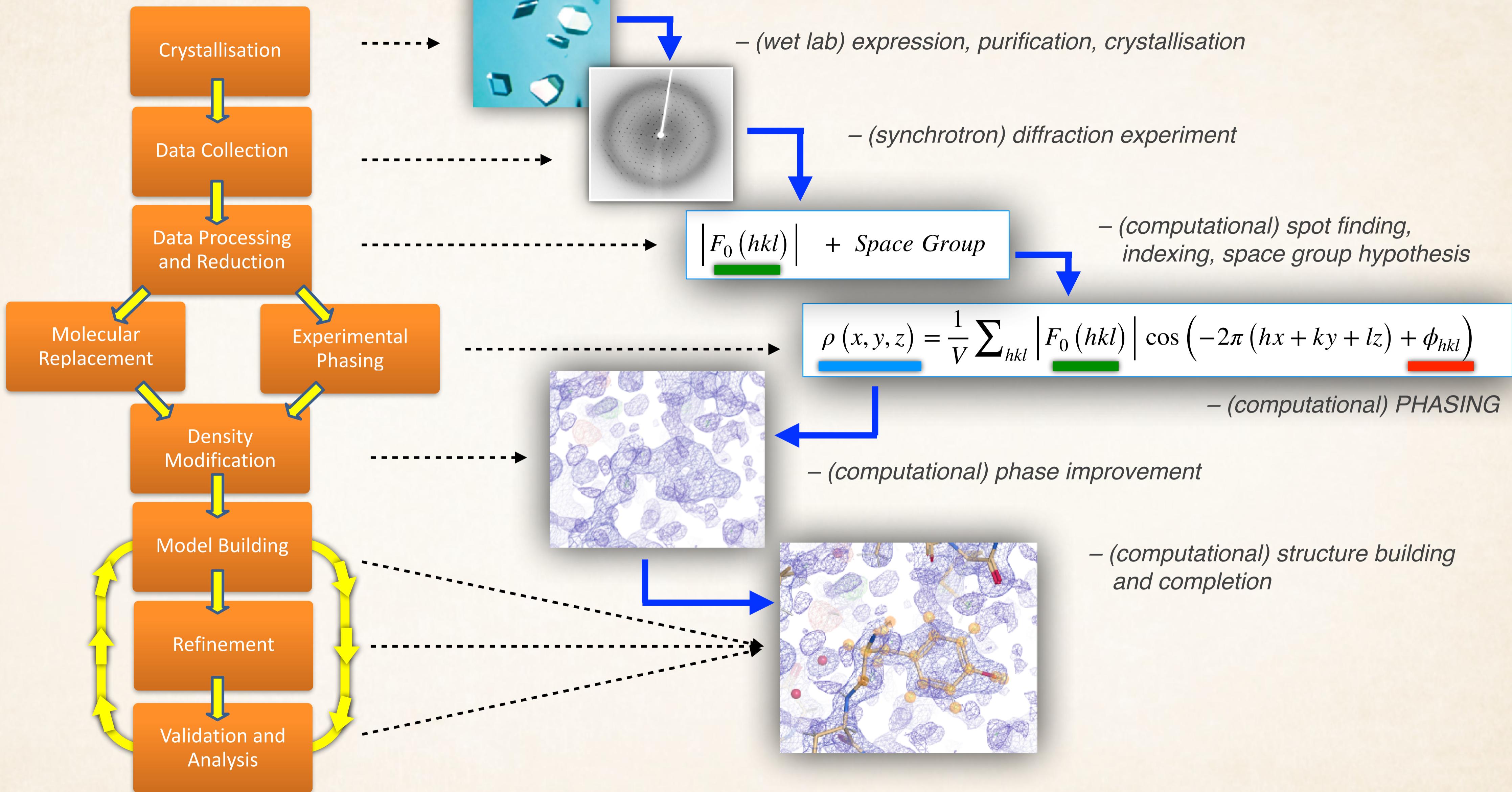
homologous model

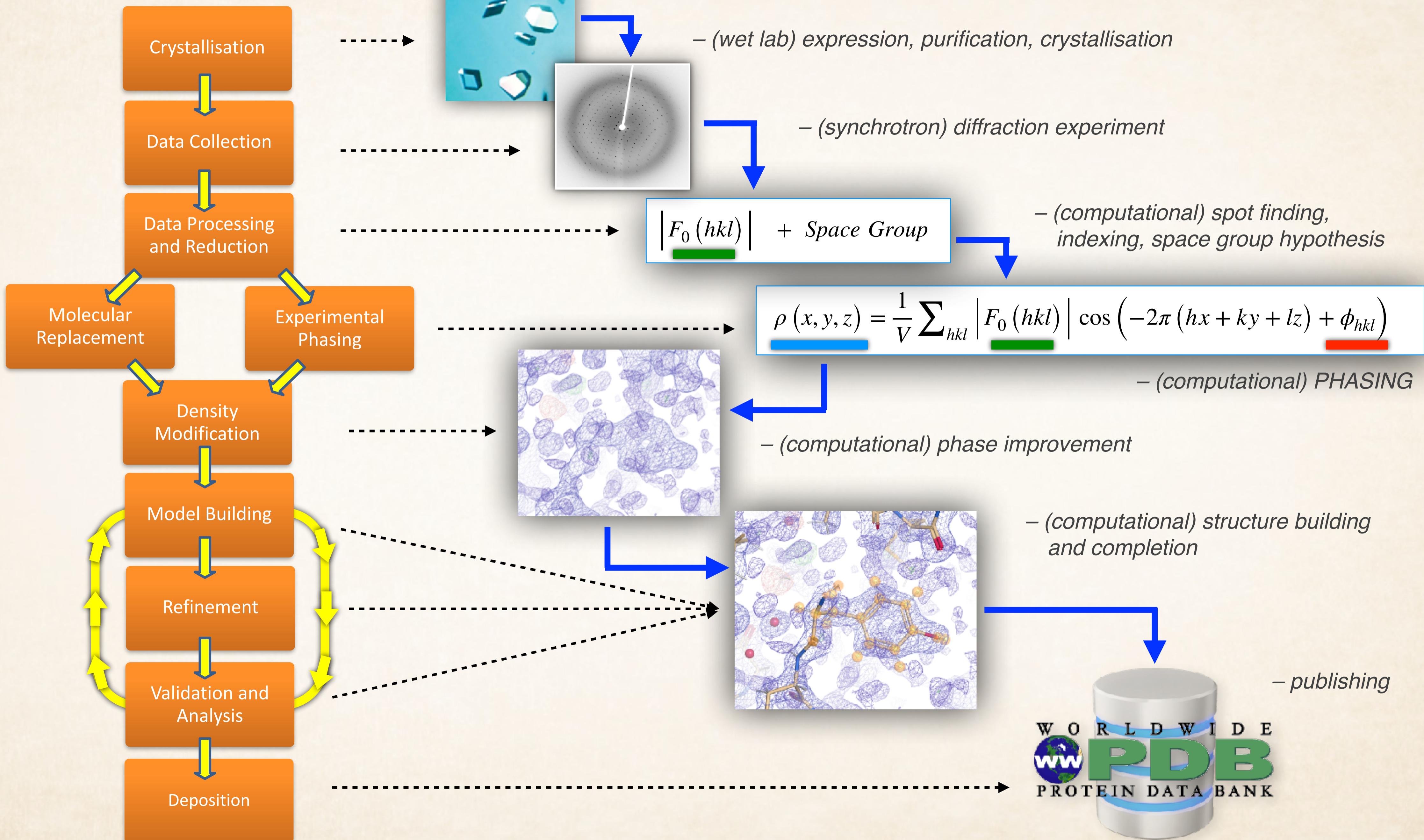


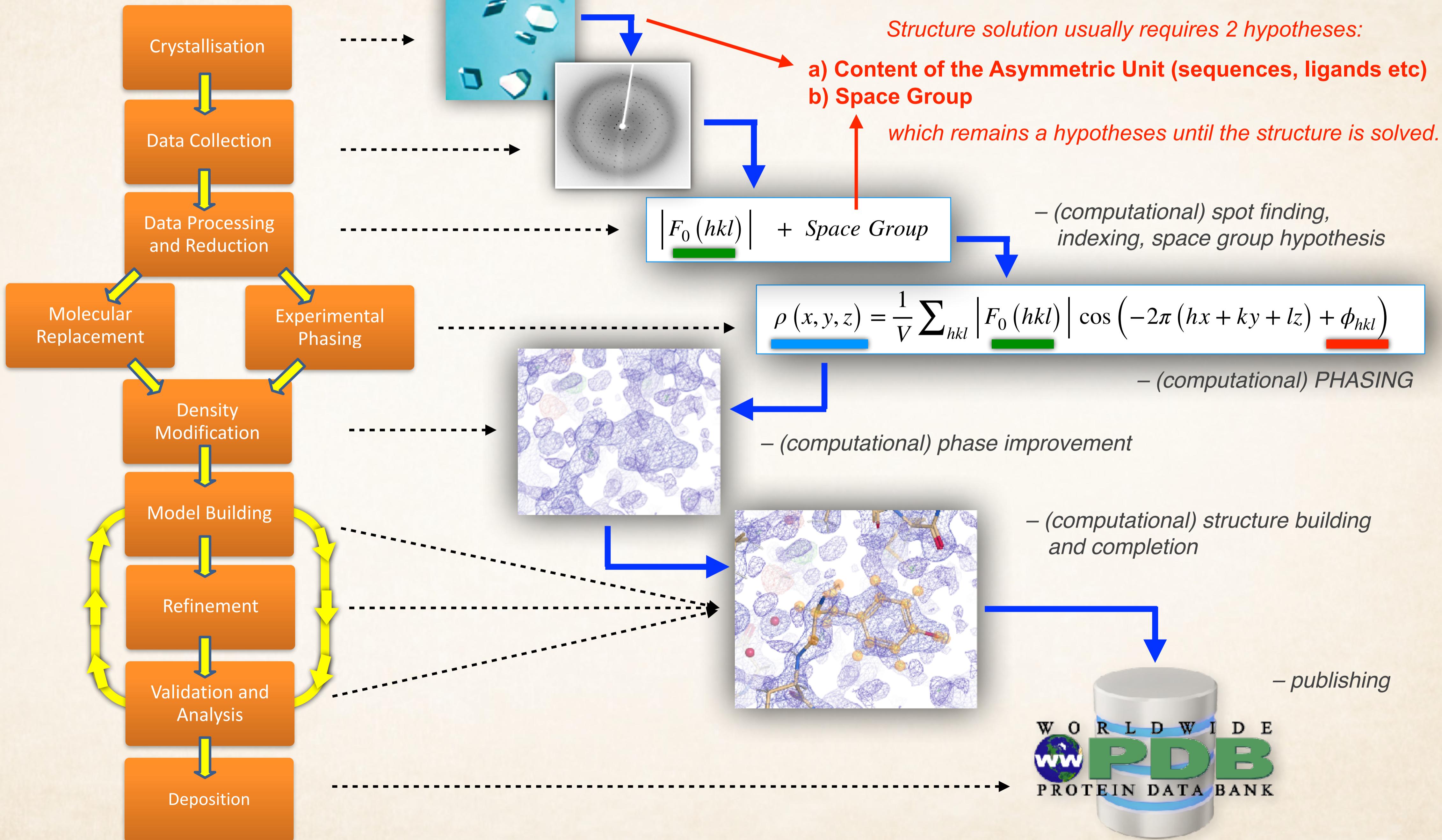


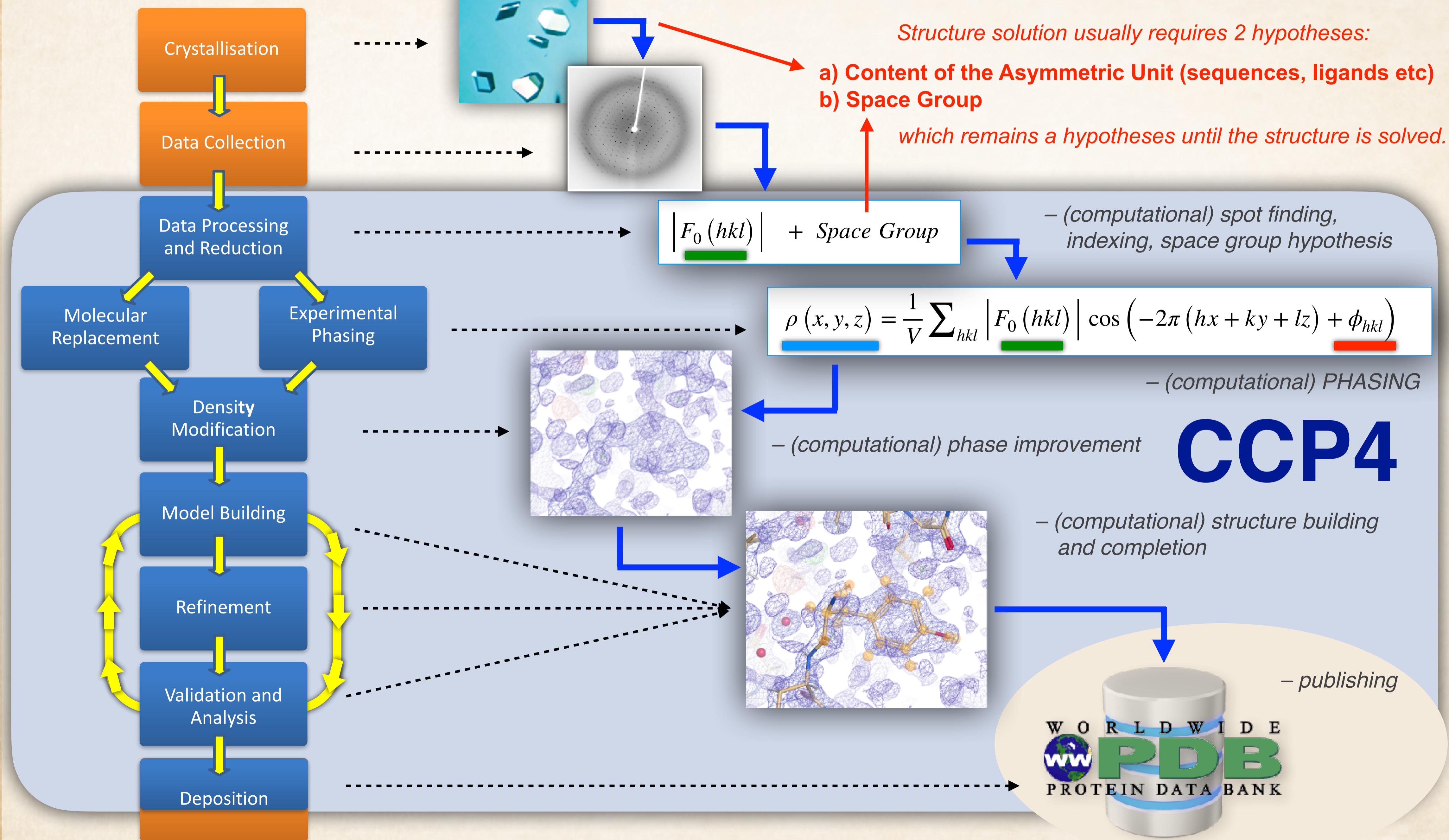












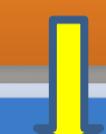


CCP4 Software Suite for Macromolecular Structure Determination

Crystallisation



Data Collection

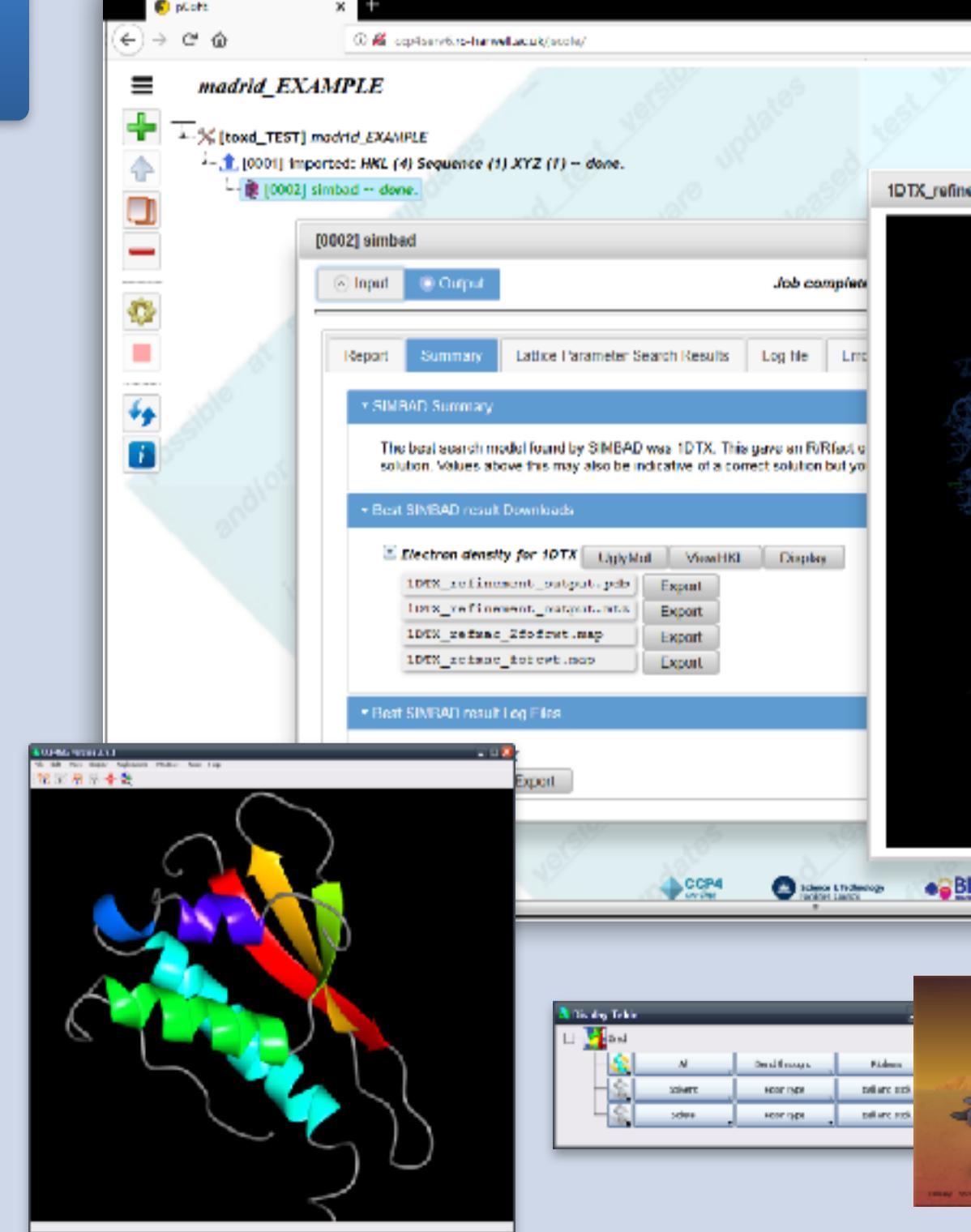
Data Processing
and ReductionDIALS
Diffraction Imaging for Advanced Light SourcesMolecular
ReplacementDensity
Modification

Model Building

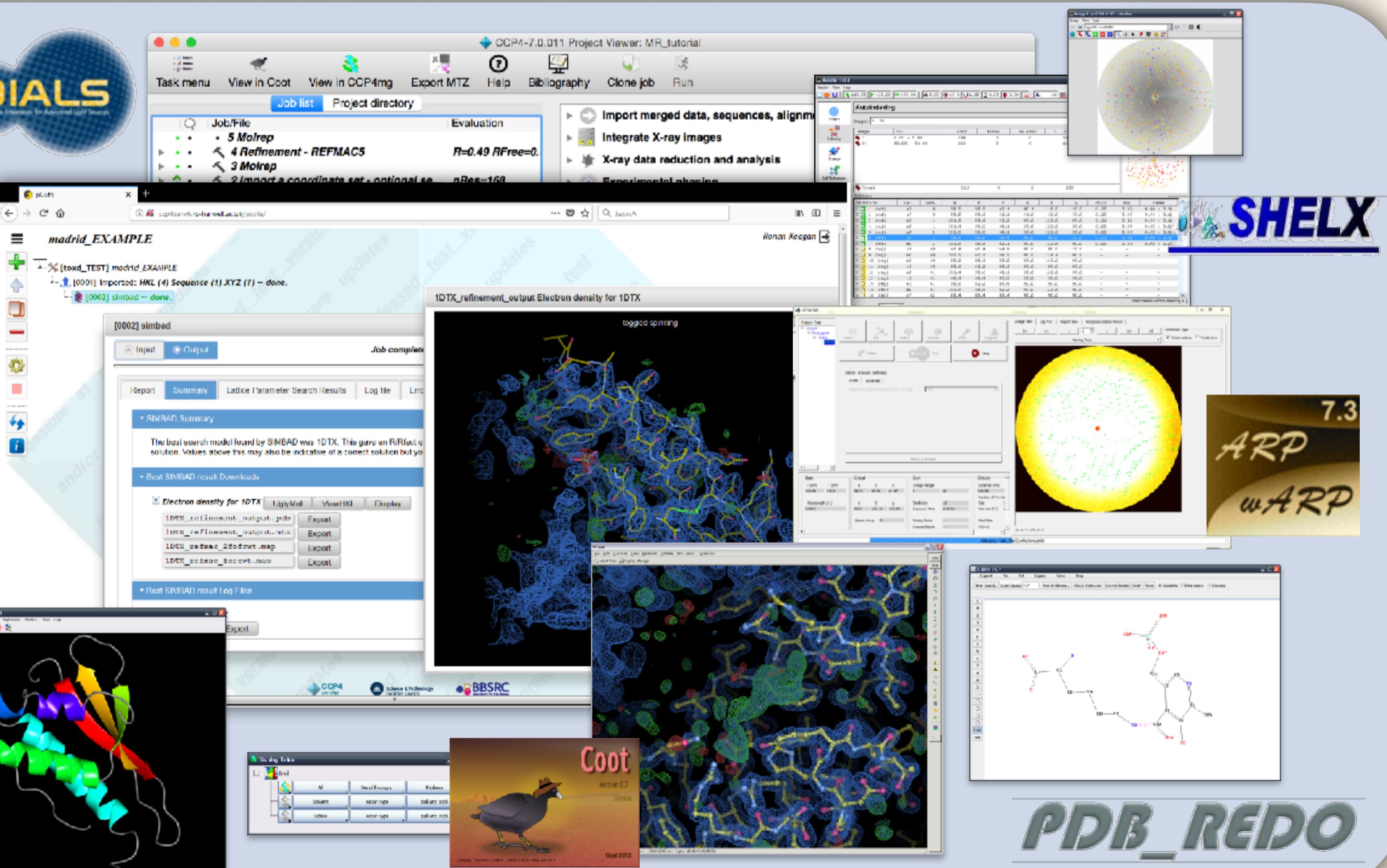
Refinement

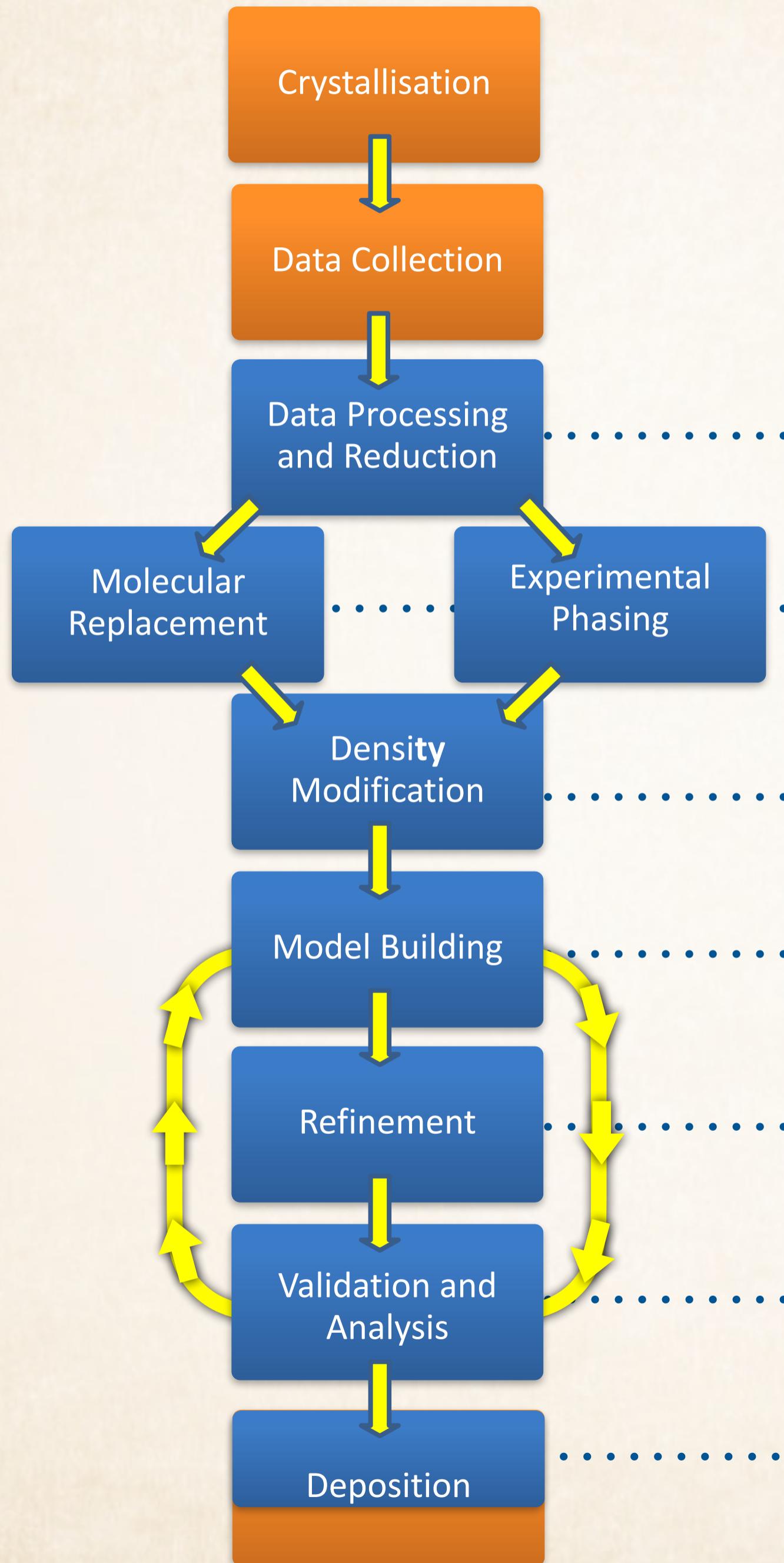
Validation and
Analysis

Deposition

Experimental
Phasing

CCP4 Functionality Scope

an MX eco-system with about 680 program components**PDB_REDO**



Structure Solution Stages

Automated*

Xia-2

MrBump, Slicendice,
Balbes, MorDA, Crank-2,
Simbad, Ample, Arcimboldo

Modelcraft,
Arp/wArp, CCP4Build

Lorestr, Dimple

Zanuda

PDB Deposition module

Fundamental*

XDS, DIALS, Aimless, DUI,
XDSGui, iMosflm

Phaser, Molrep, MrParse,
ShelxCd, Sculptor, Chainsaw

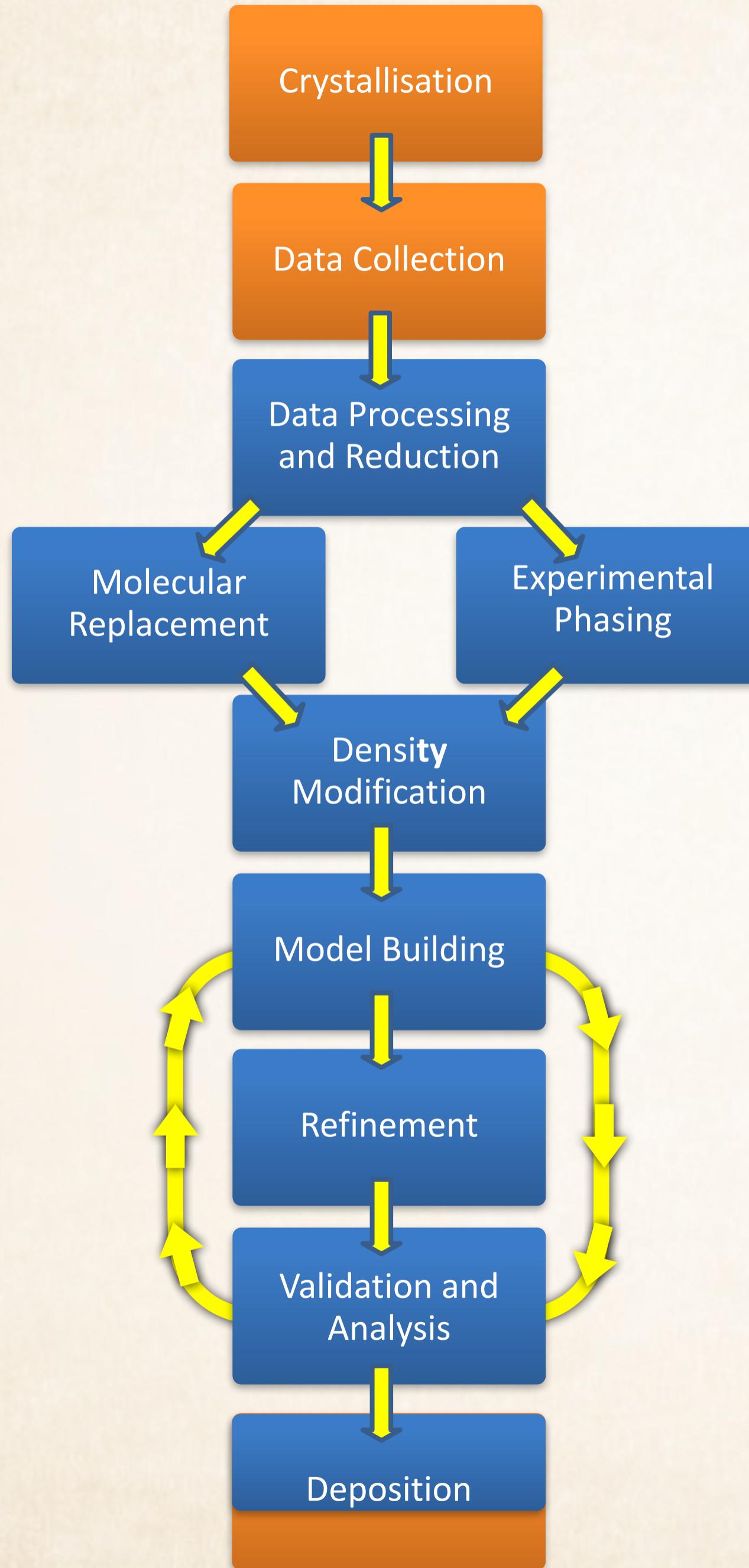
Parrot, Acorn, ShelxE

Coot, Moorhen, AceDrg,
jLigand

Refmac, Prosmart

Molprobity, EDStats,
BAverage, PISA, Gesamt, ...

* only selected programs are shown



A more comprehensive summary*†‡ §#+ :

<https://cloud ccp4.ac.uk/html/roadmap.html>

* still not complete!

† links to in-depth CCP4 documentation

‡ links to CCP4 Cloud documentation

§ links to CCP4 Cloud Project Atlas

links to CCP4 Cloud tutorials and demo projects

+ links to recorded CCP4 Cloud webinars

CCP4 v8.0 Program Documentation

CCP4Docs documentation

Other Versions Not Found

Reference:

Collaborative Computational Project, Number 4. 1994.
"The CCP4 Suite: Programs for Protein Crystallography". Acta Cryst. D50, 760-763

There is a partial list of [program references](#) extracted from the individual program documentation.

Changes:

List of the [major program changes](#) since the previous release.

This list can also be seen in [function grouping](#).

BASIC

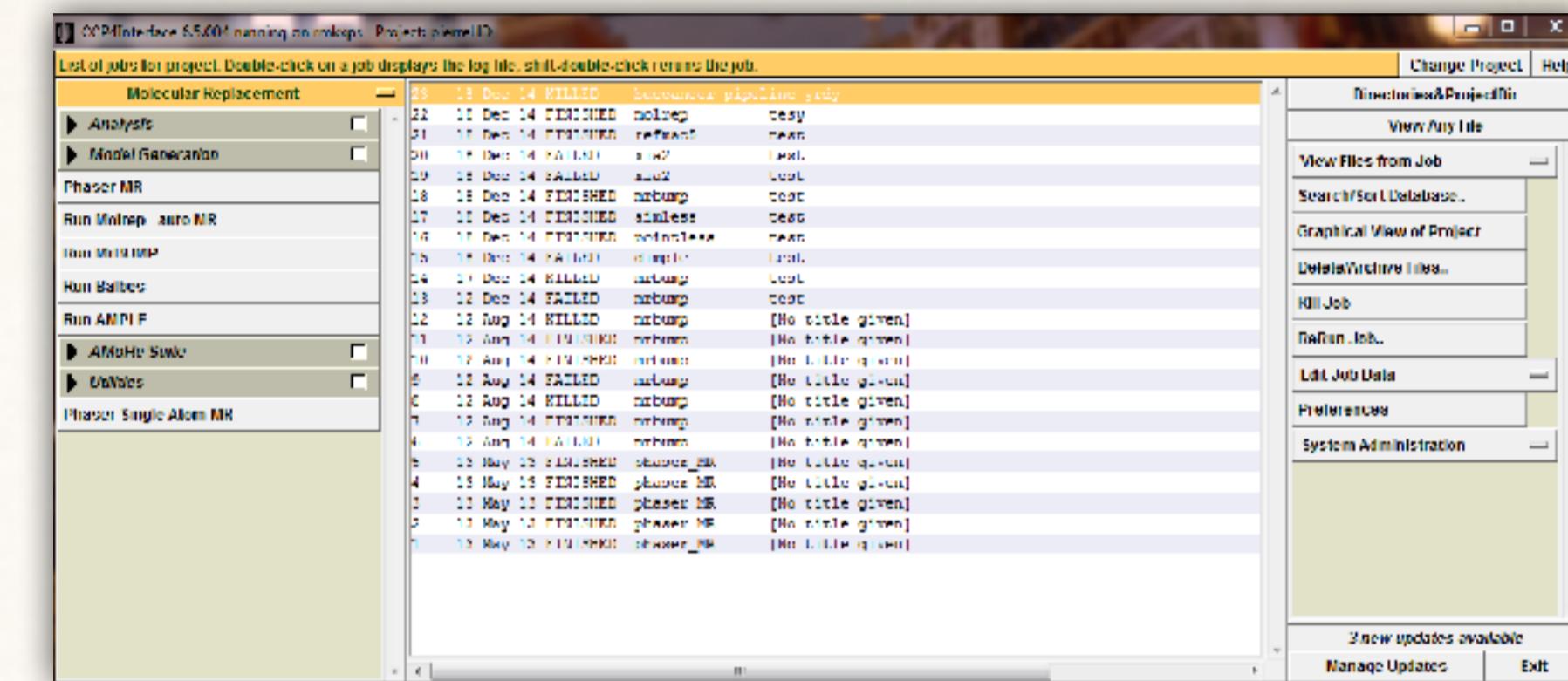
- [ccp4](#) - introduction to the CCP4 Program Suite
- [ccp4_interface_installation](#) - Installation of CCP4 Interface
- [ccp4i](#) - interface to the CCP4 programs & file display
- [ccp4i2](#) - the new modernised interface to the CCP4 program suite
- [ccp4 Cloud](#) - the system for remote computation in macromolecular crystallography based on the CCP4 program suite.

"Contents"

- CCP4 v8.0 Program Documentation
- BASIC
- GENERAL
- SUPPORTED
- UNSUPPORTED
- DEPRECATED
- LIBRARY
- FILE FORMATS

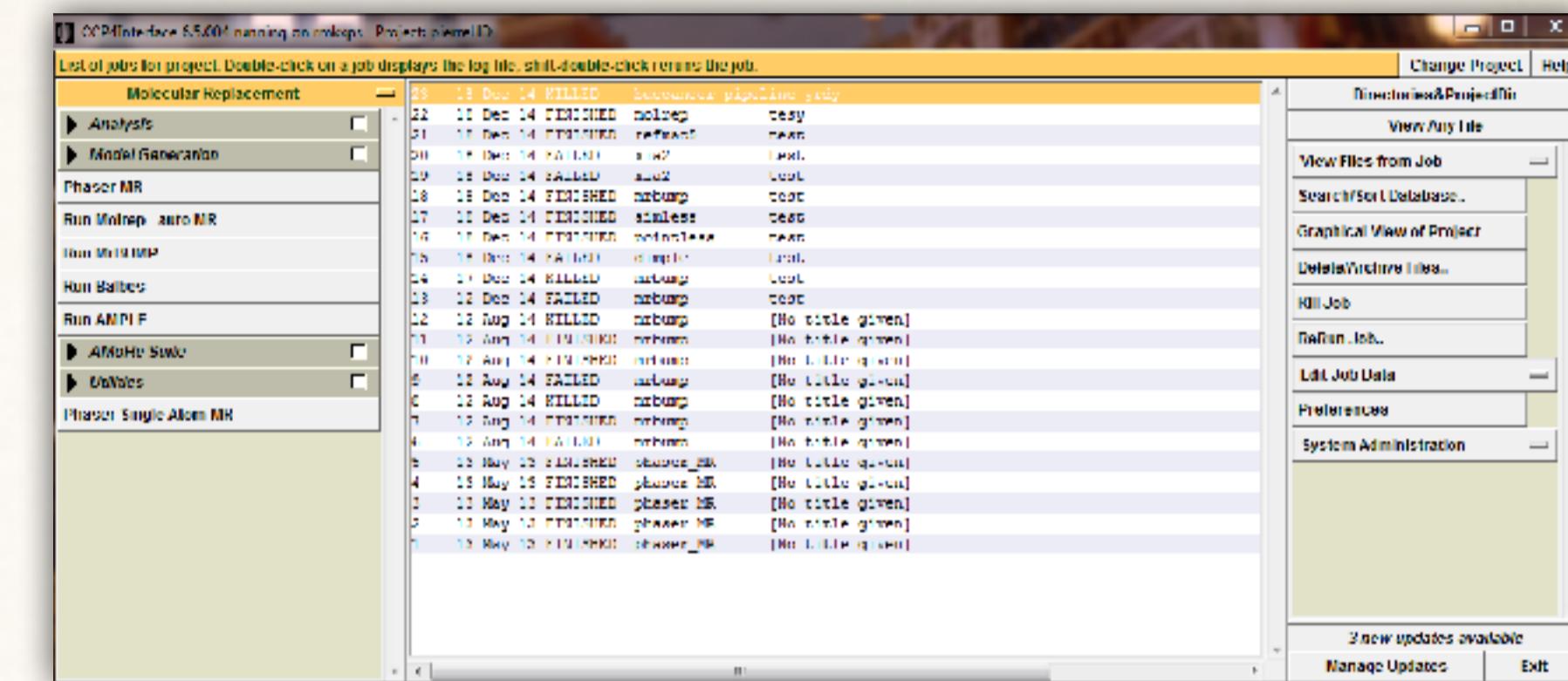
- Three main interfaces to the CCP4 suite

1. CCP4i – original interface developed around 2000

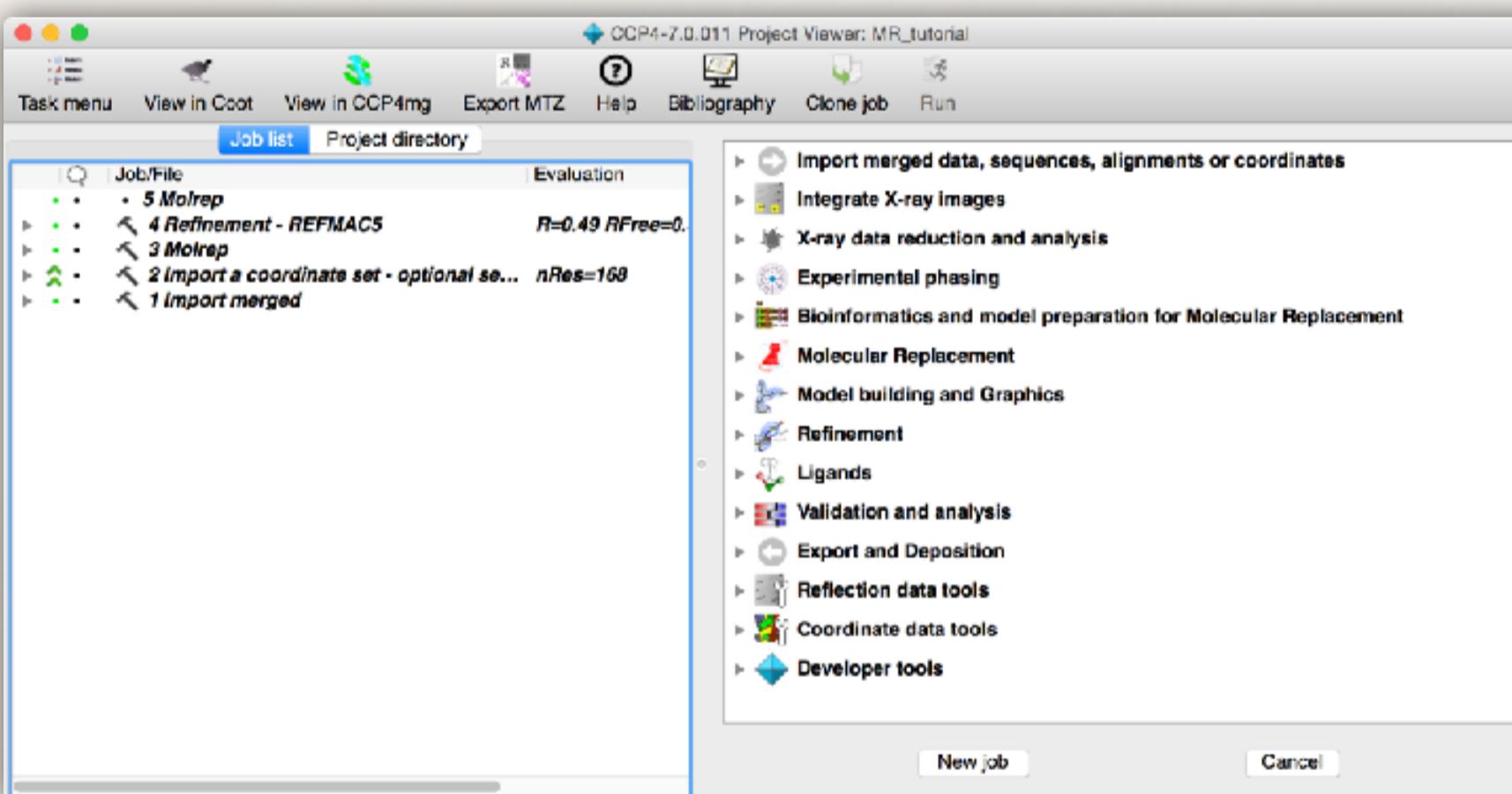


- Three main interfaces to the CCP4 suite

1. CCP4i – original interface developed around 2000

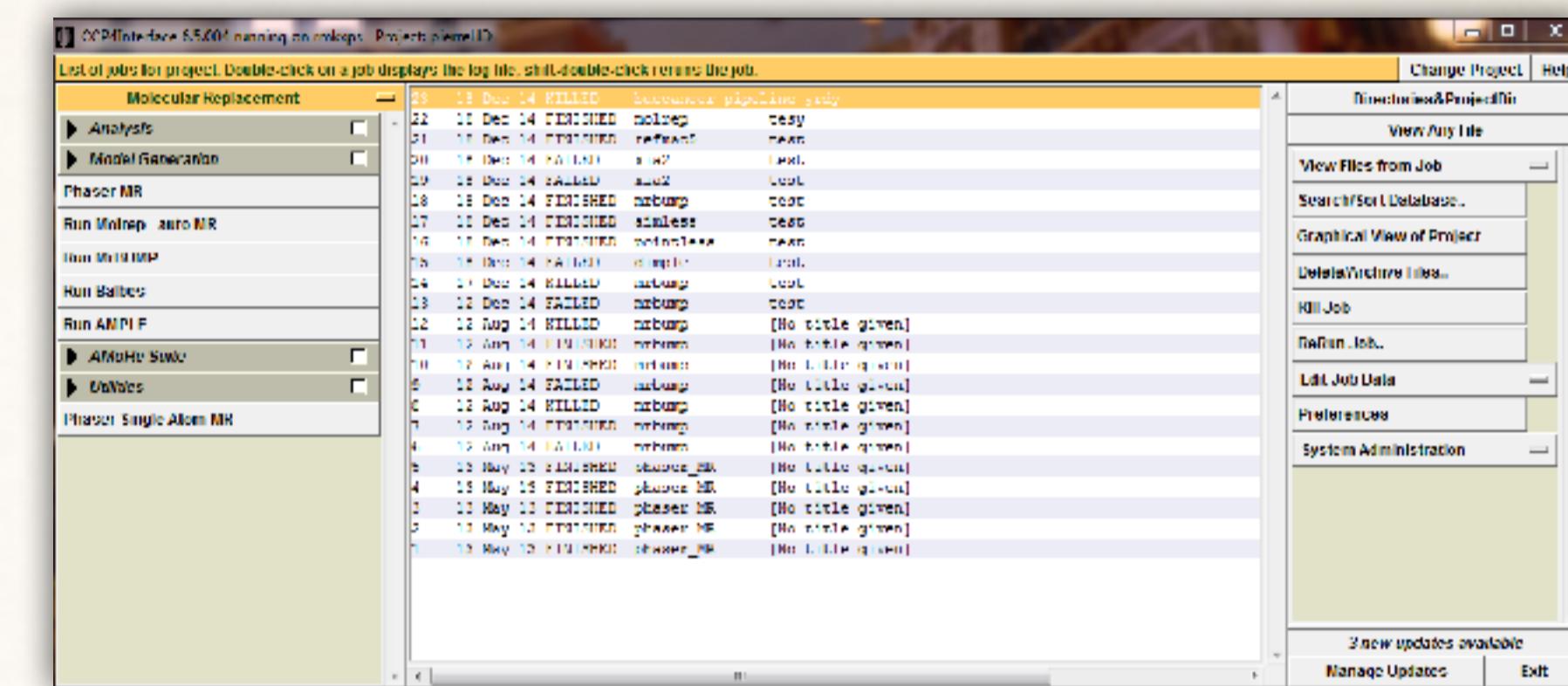


2. CCP4i2 – new graphical desktop interface (2016)

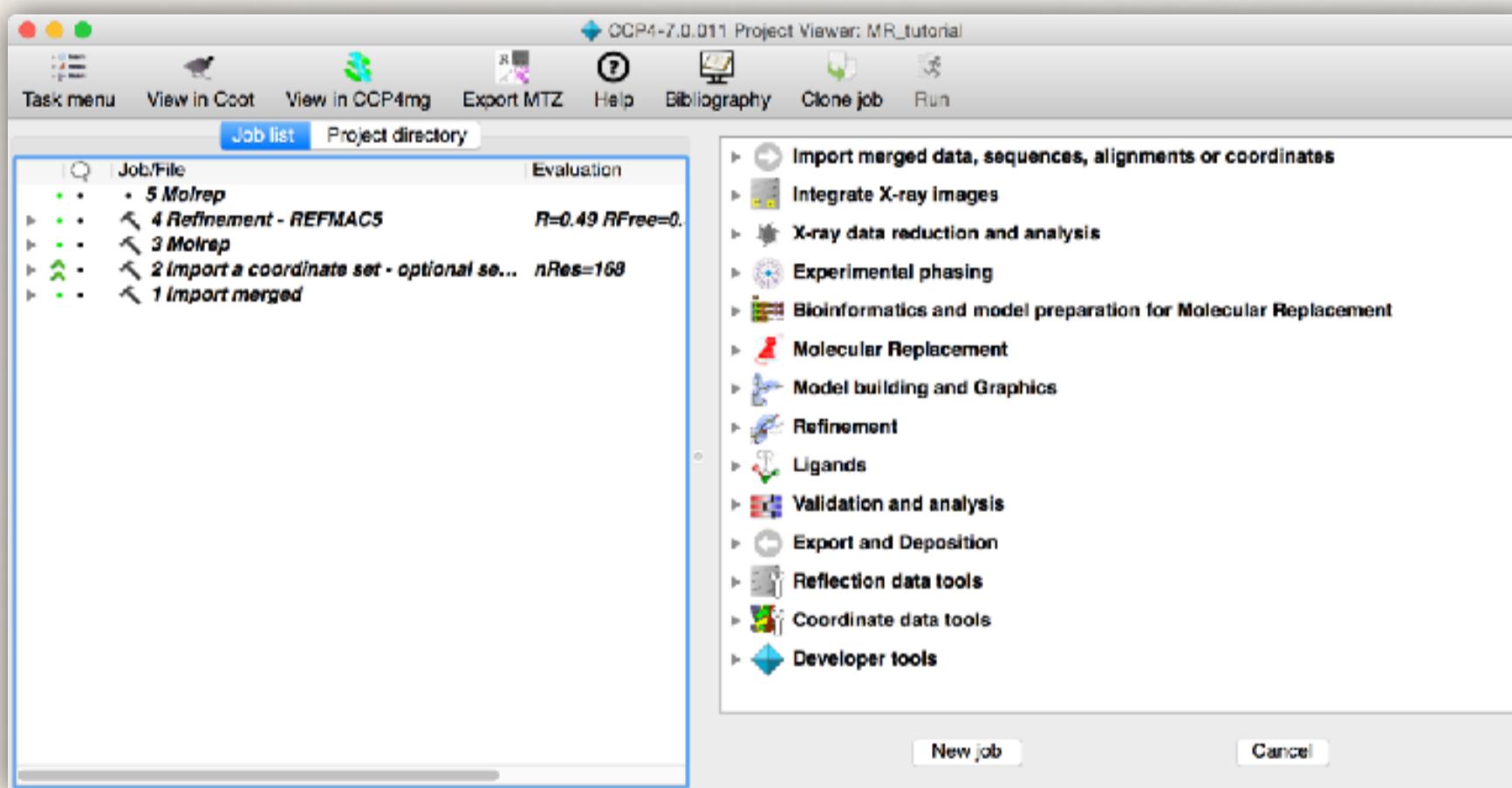


- Three main interfaces to the CCP4 suite

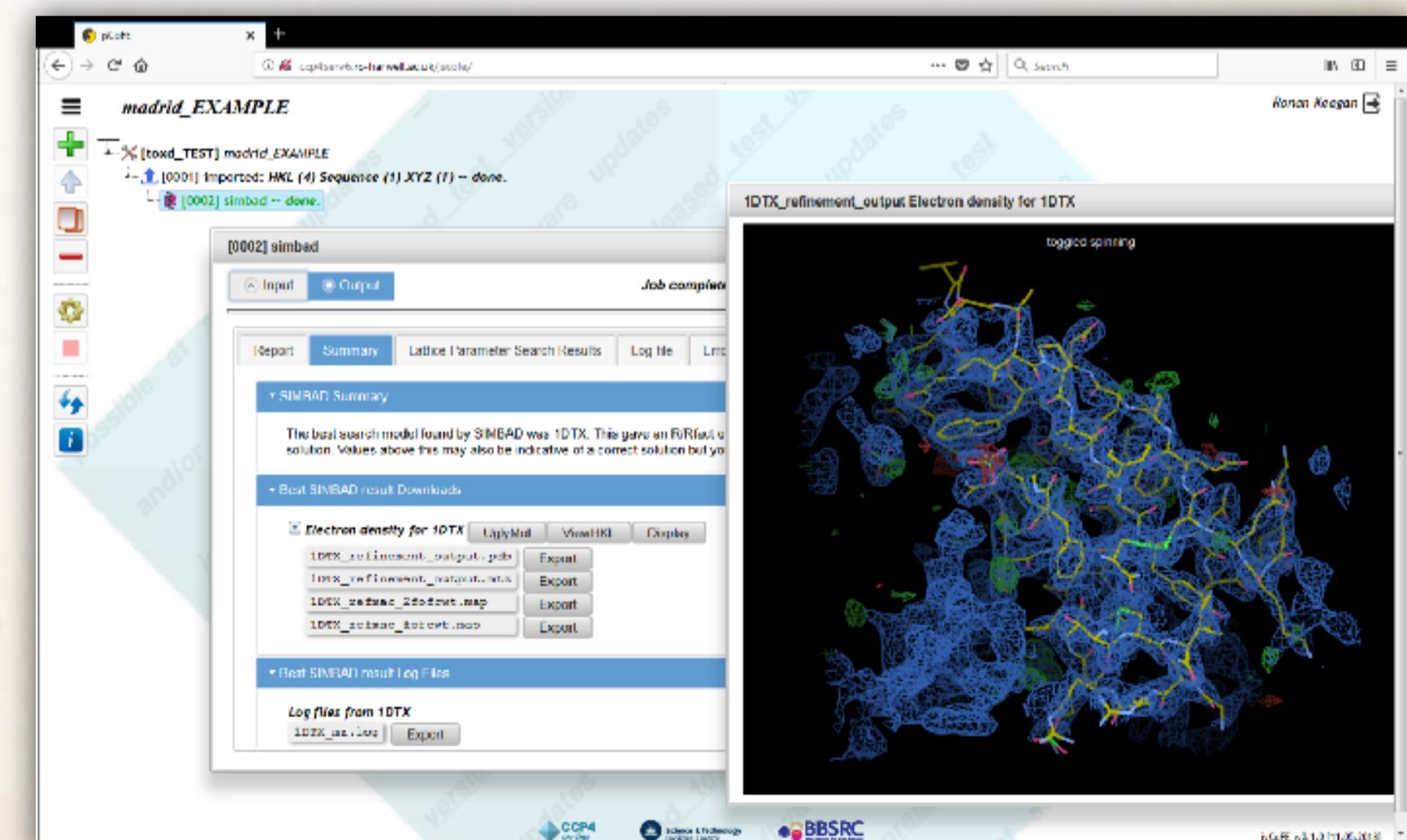
1. CCP4i – original interface developed around 2000



2. CCP4i2 – new graphical desktop interface (2016)

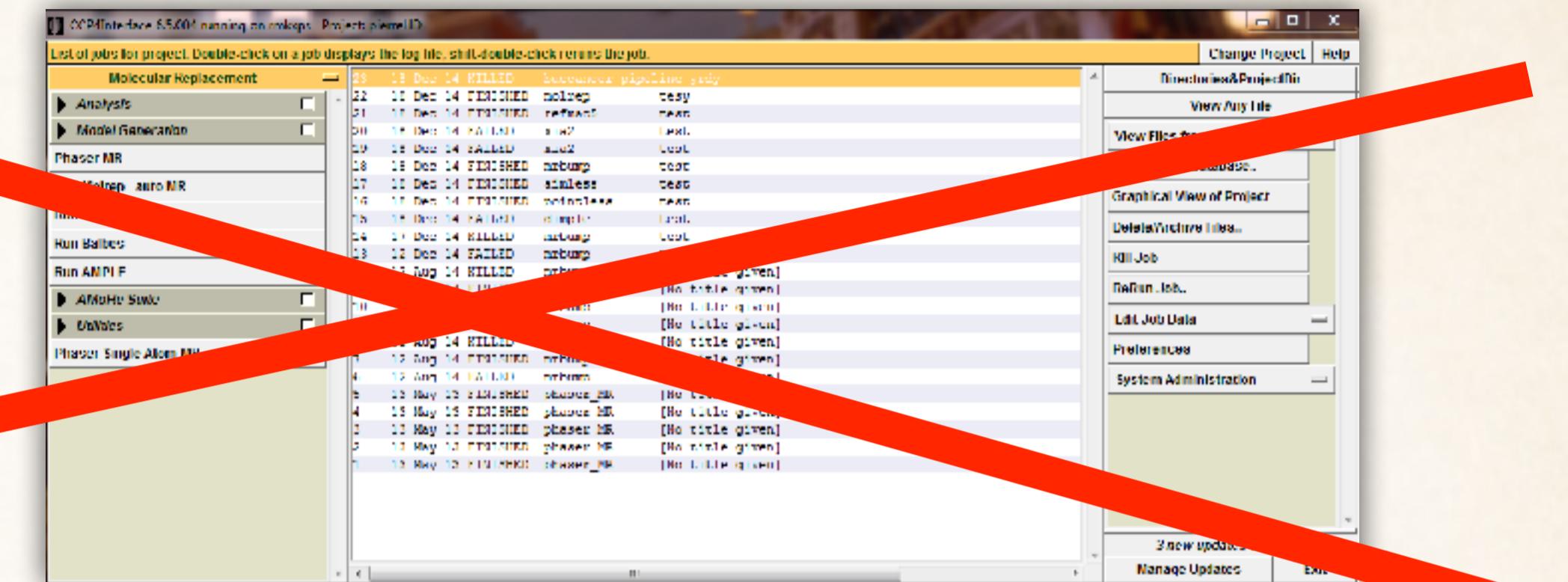


3. CCP4 Cloud, browser based (2019)

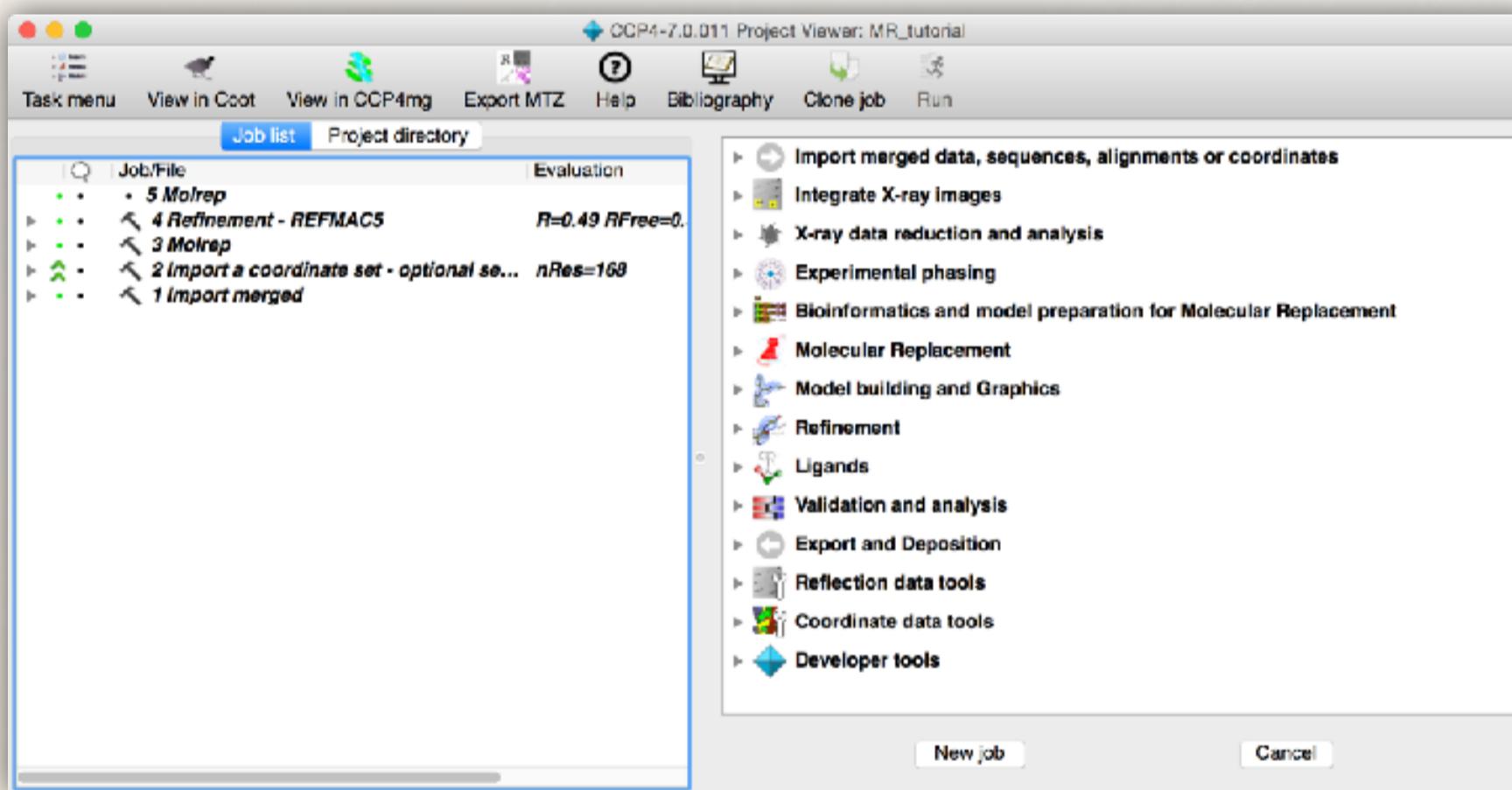


- Three main interfaces to the CCP4 suite

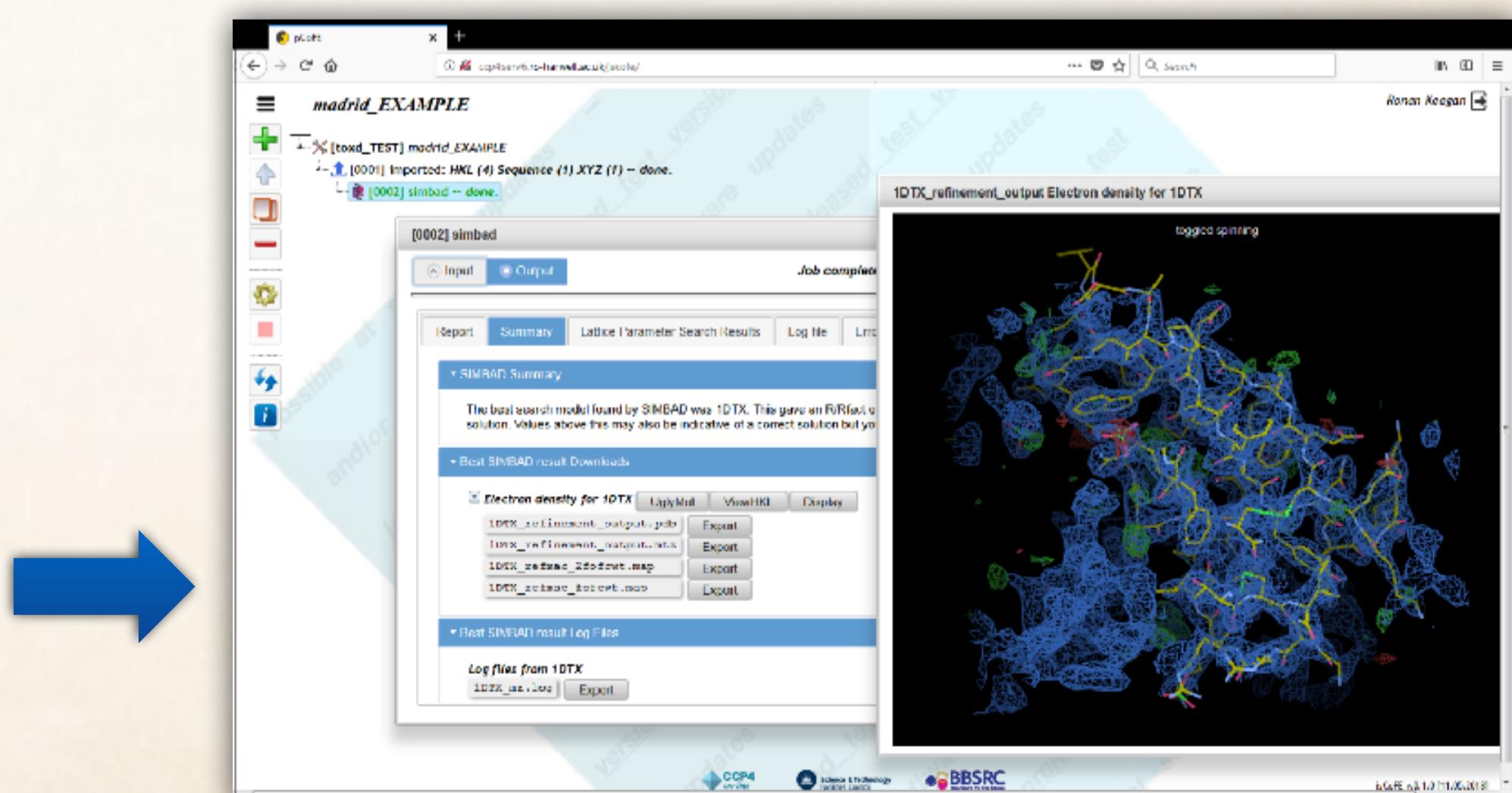
1. CCP4i – original interface
developed around 2000
deprecated



2. CCP4i2 – new graphical desktop interface (2016)

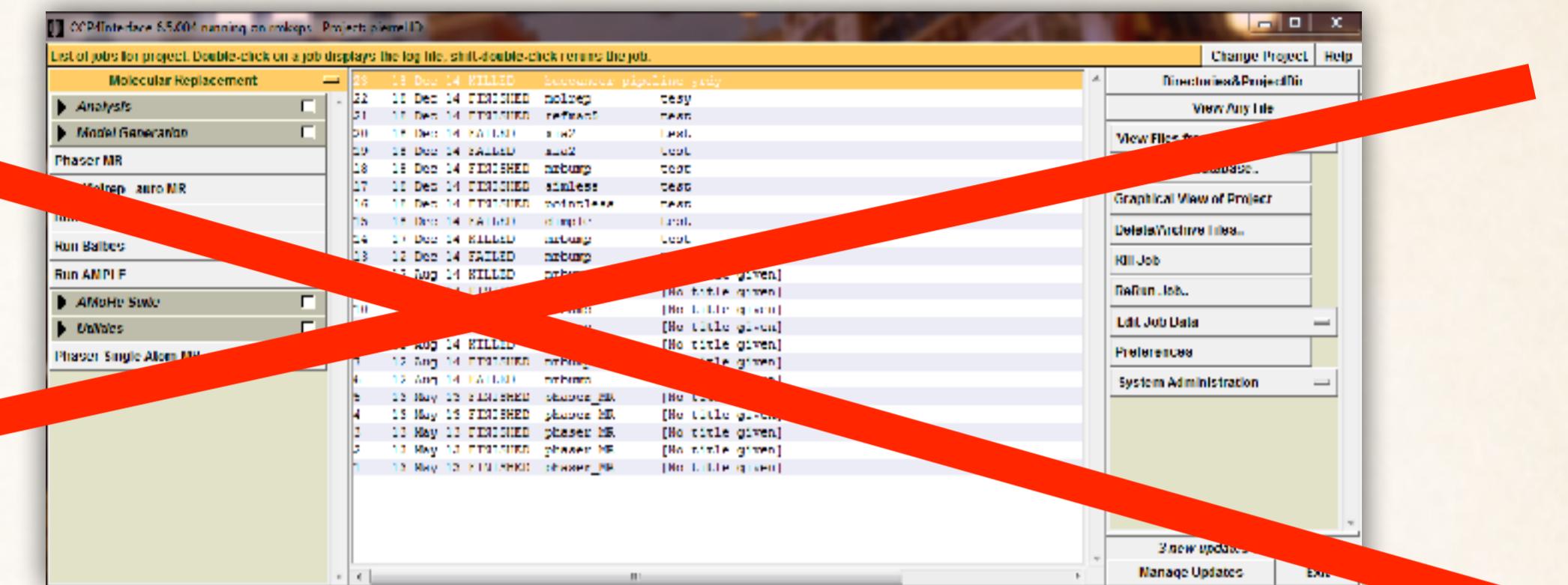


3. CCP4 Cloud, browser based (2019)

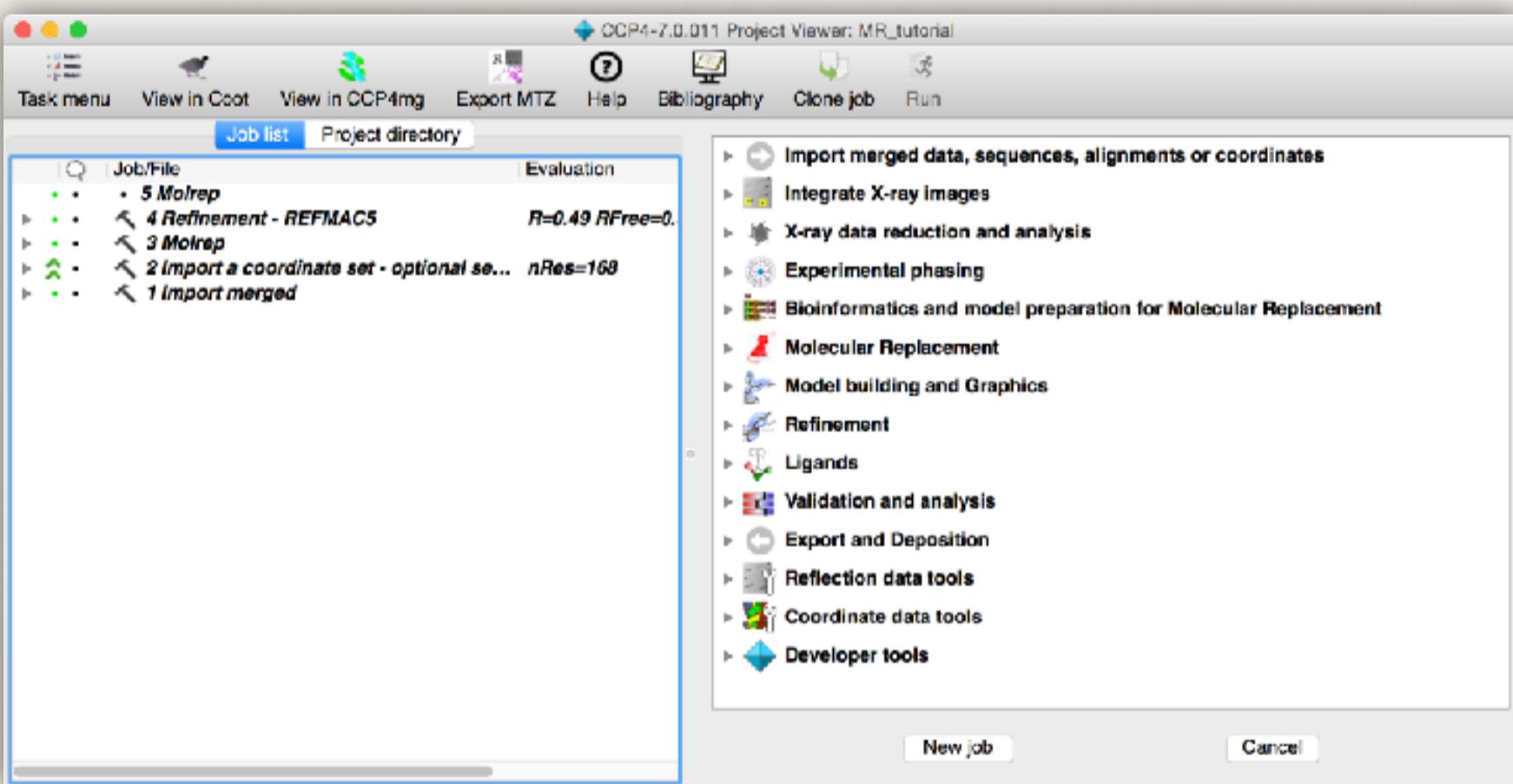


- Three main interfaces to the CCP4 suite

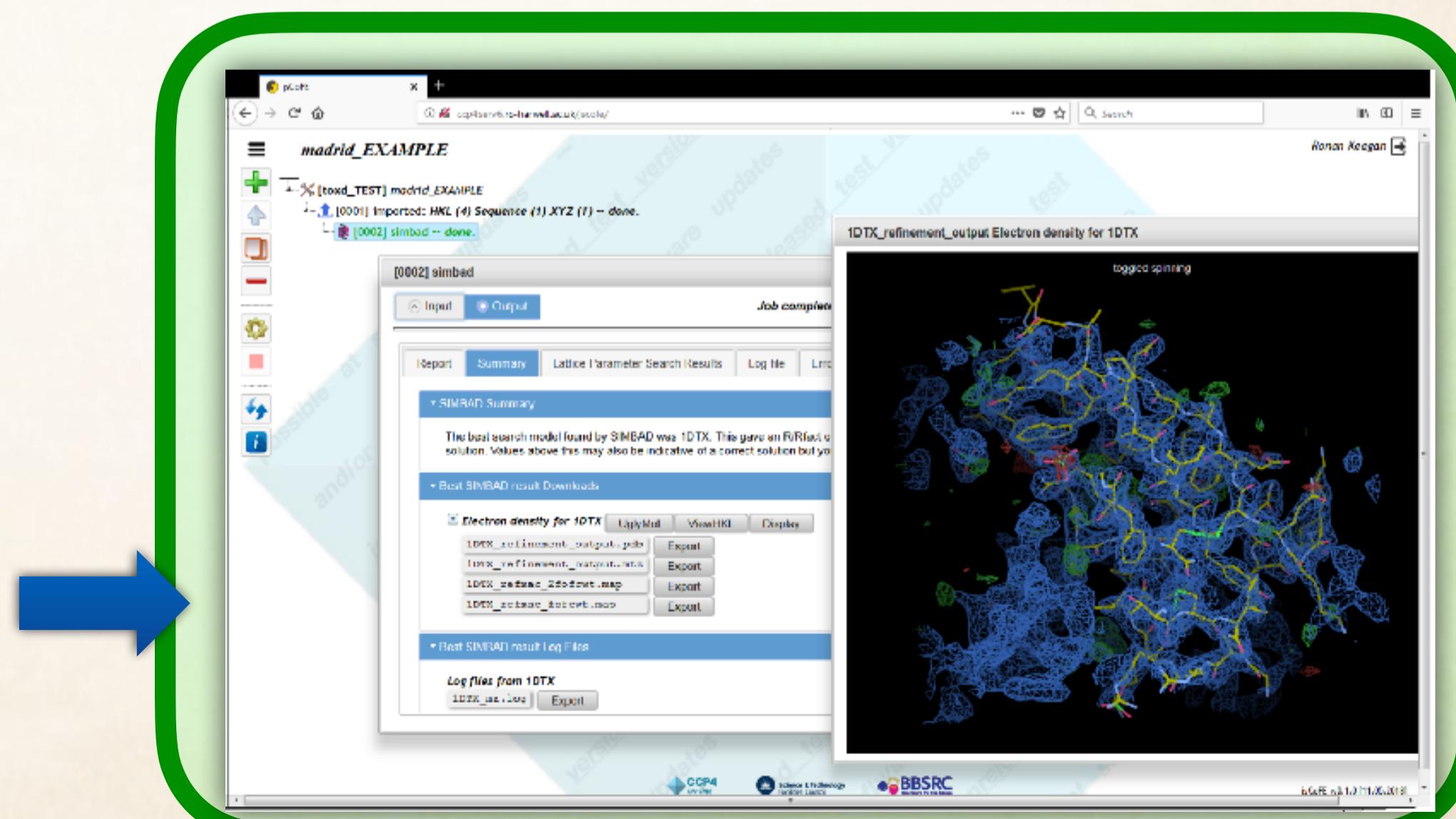
1. CCP4i – original interface
developed around 2000
deprecated



2. CCP4i2 – new graphical desktop interface (2016)



3. CCP4 Cloud, browser based (2019)



Growing software complexity

- ~ Supporting wide variety of computing platforms is difficult
- ~ Full installation with 3rd party databases and software is difficult

Growing software demands

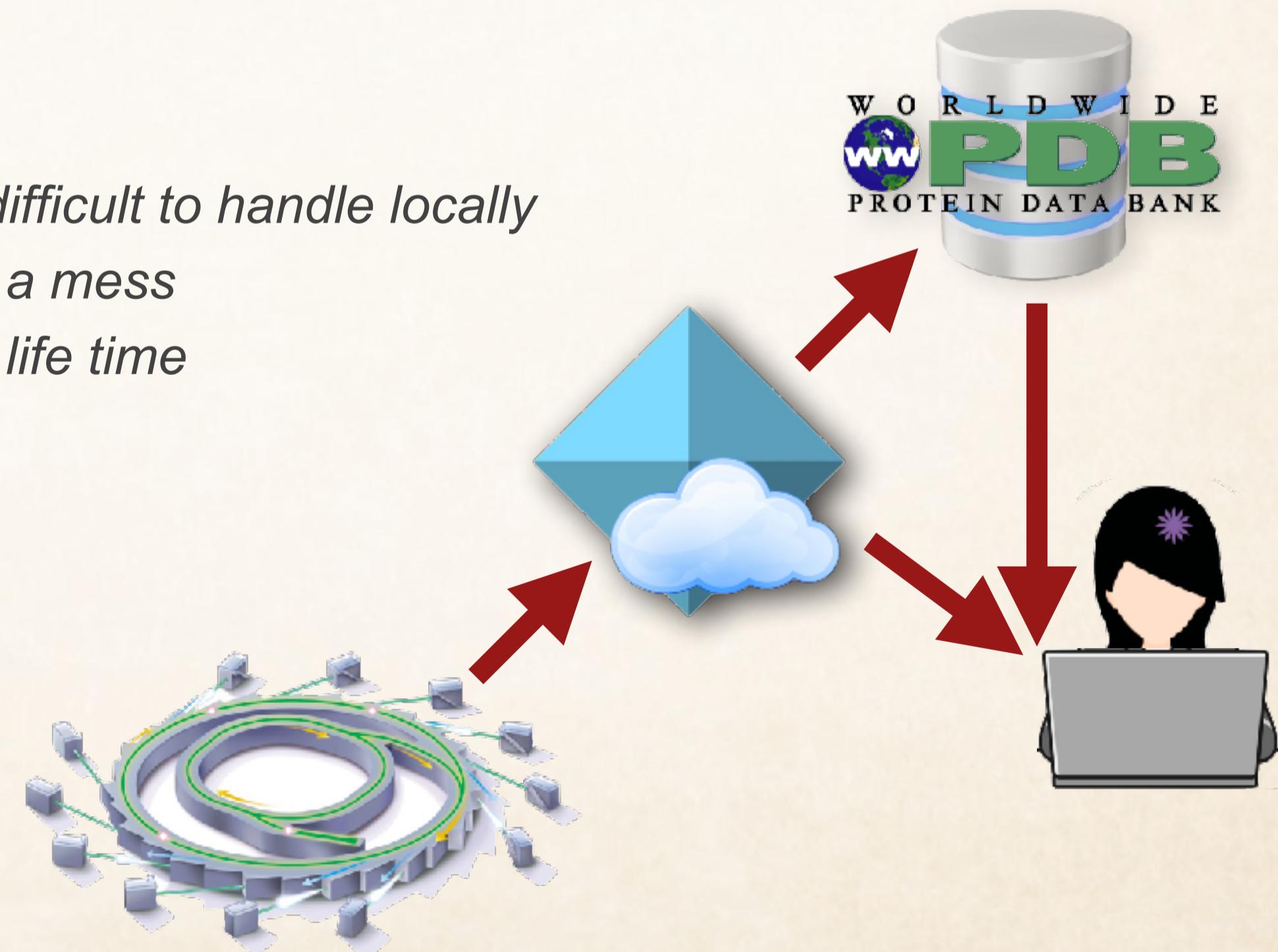
- ~ Modern automatic methods require more CPU and memory than most local setups can afford

Data logistics and team working

- ~ Growing volumes of data from modern sources are difficult to handle locally
- ~ File exchange in distributed collaborations is usually a mess
- ~ Local data and project archives have usually a short life time

Security

- ~ Increasingly more difficult to distribute for modern systems and corporate environments
- ~ Cloud solutions are safer, getting preferential in industry



- ✓ Image Processing
- ✓ Data Scaling and Merging
- ✓ Molecular Replacement
- ✓ Experimental Phasing
- ✓ Density Modification
- ✓ Model Building
- ✓ Ligand fitting
- ✓ Refinement
- ✓ Validation
- ✓ PDB Deposition

The screenshot shows the CCP4 Cloud interface. On the left, there's a project tree for 'Insulin' with various tasks listed under it, such as 'dui (image processing)', 'xia2 datasets', 'HKL import', 'asymmetric unit', 'EP with Coot', 'shelx subs', 'change asymmetric unit', 'EP with Coot', 'shelx subs', 'phaser', 'Coot', 'Ligands', 'Validation, Analysis and Deposition', and 'Toolbox'. On the right, a 'Task List' window is open, showing a list of tasks categorized by type: Data Import (5), Data Processing (4), Asymmetric Unit and Structure Revision (0), Automated Molecular Replacement (1), Molecular Replacement (0), Fragment-Based Molecular Replacement (0), Experimental Phasing (0), Density Modification (0), Refinement and Model Building (0), Coot (0), Ligands (1), Validation, Analysis and Deposition (0), and Toolbox (1). The total number of tasks is highlighted as 'Total 94 tasks and counting'.

Task List

Suggested tasks All tasks Workflows

▶ Data Import (5)

▶ Data Processing (4)

▶ Asymmetric Unit and Structure Revision (0)

▶ Automated Molecular Replacement (1)

▶ Molecular Replacement (0)

▶ Fragment-Based Molecular Replacement (0)

▶ Experimental Phasing (0)

▶ Density Modification (0)

▶ Refinement and Model Building (0)

▶ Coot (0)

▶ Ligands (1)

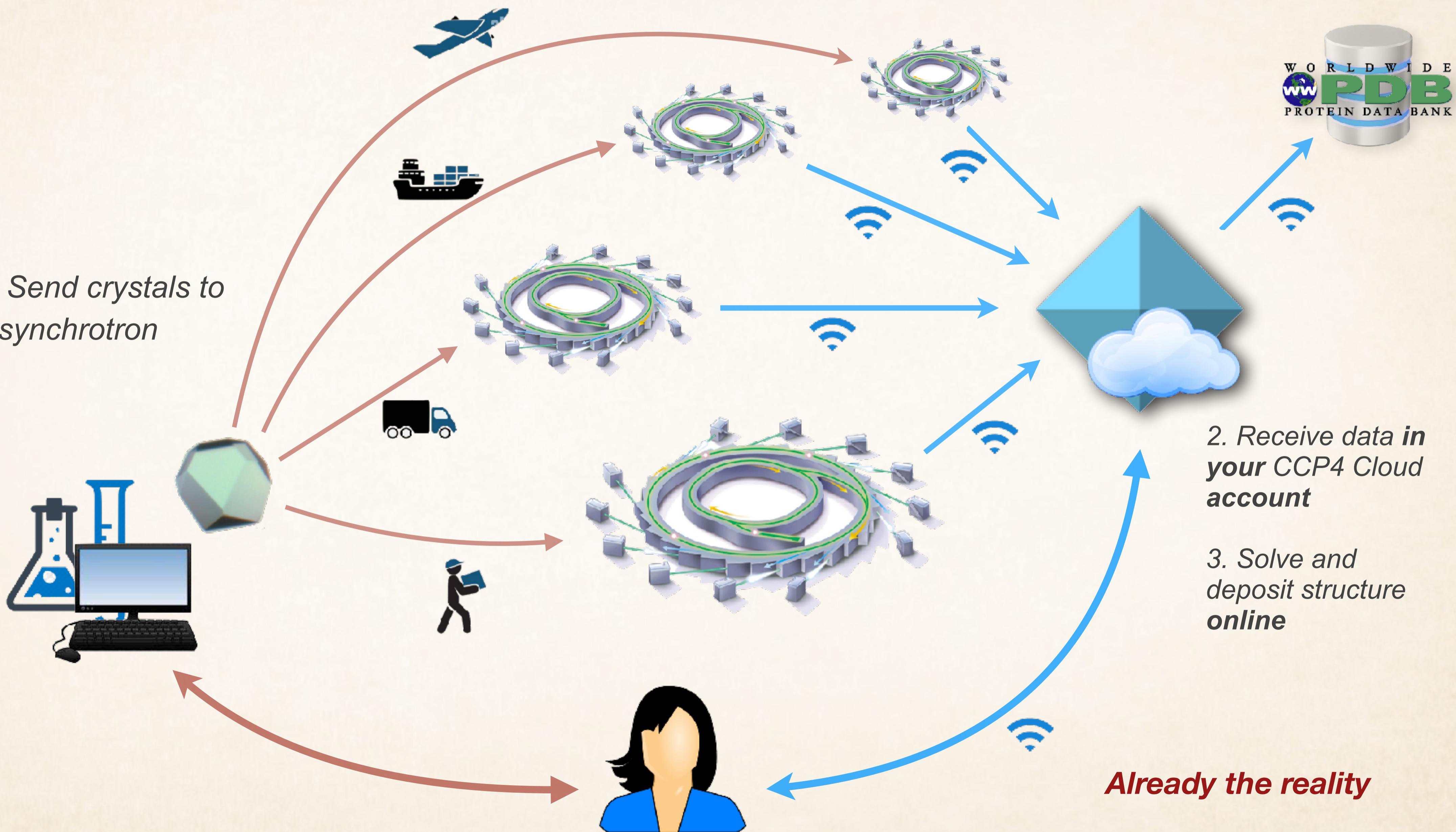
▶ Validation, Analysis and Deposition (0)

▶ Toolbox (1)

Total 94 tasks and counting

Powered by CCP4 v.7.1.018

Help Cancel



CCP4 Cloud x +

cloud.ccp4.ac.uk

All projects

Eugene Krissinel

Change project folder

My Account

Admin Page

Failed Tasks Safe

Developer's Documentation

Start Globus

Toggle fullscreen

Toggle dark mode

Tune dark mode

Log out

15 A sw2025-demo

16 Aaa Solving MDM2 Protein

First Previous 1 2 3 4 5

Name Clone Delist Delete Export Import Join Tutorials Help

Name	R _{free}	Disk (MBytes)	CPU (hours)	Date Created	Last Opened
gamma protein	0.2629	168.7	0.2642	2024-10-20	2025-04-01
DM-v10					
bonuclease					
molecular replacement					
v nz4 - twinned - pro					
NA solved by exper					
ESY workshop					
david Waterman's da					
ata collected at DIA					
v NZ4 twinned					
yC4test					
EEEEEE					
determining the Stru					
.GOS Demo					

File Manager | Globus

app.globus.org/file-manager?destination_id=1e35e2c6-03ad-4dd9-a3ce-1ae597c72943&destination_path...

File Manager

Panels

Collection Diamond Light Source Data

Path /

Start Transfer & Timer Options Start

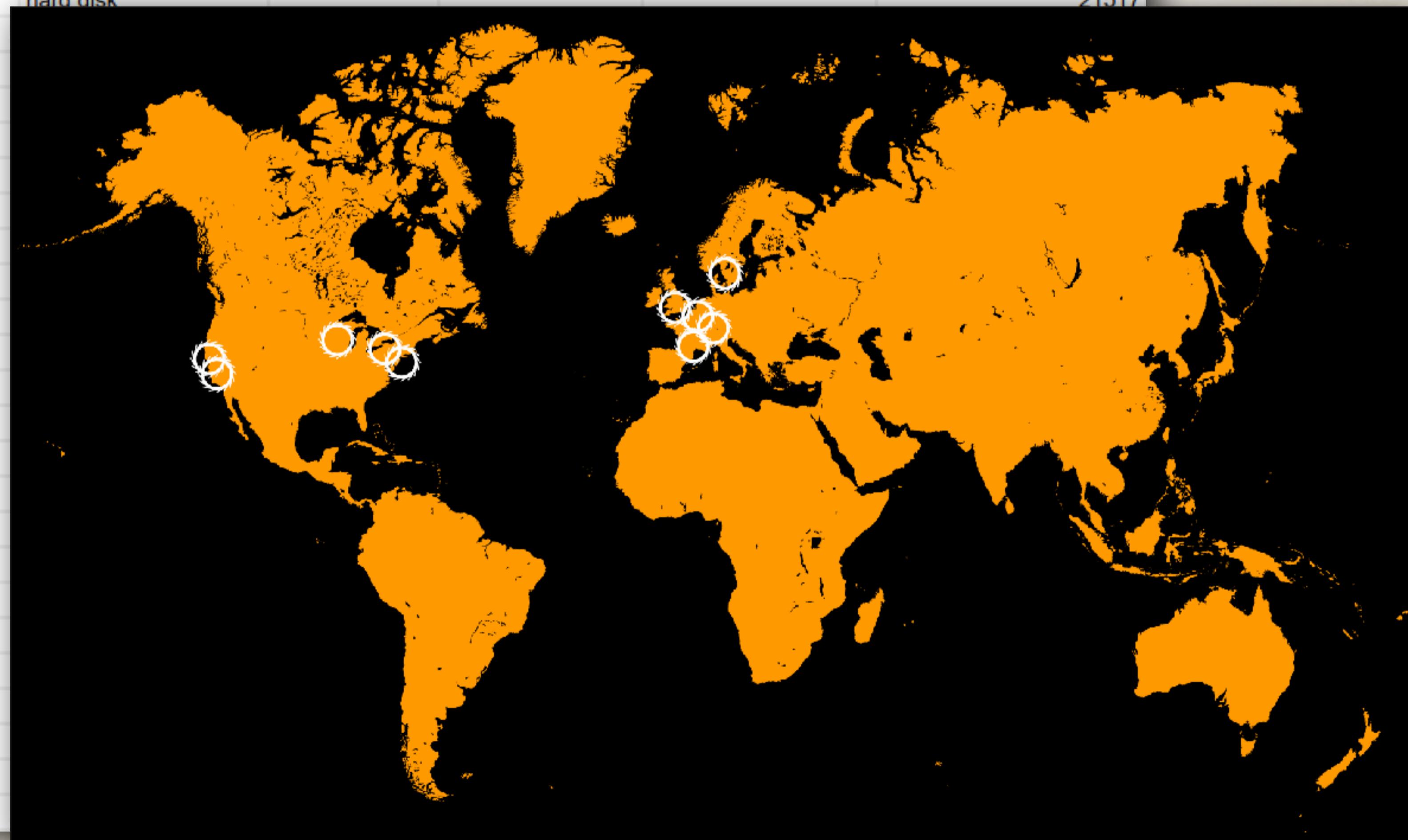
First Previous 1 2 3 4 5

CCP4 Cloud v.1.8.006 [08.03.2025]

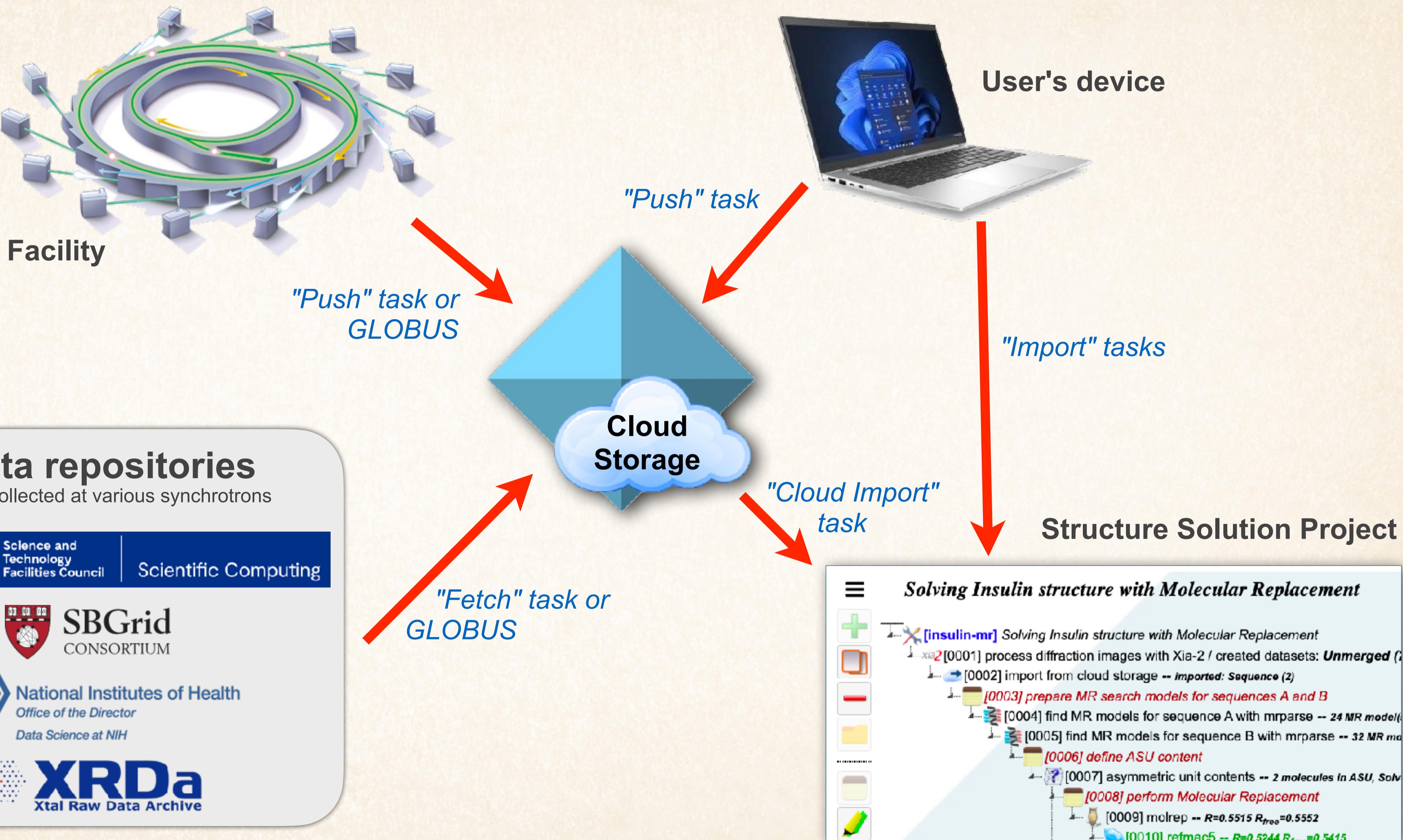
Powered by CCP4 v.9.0.007

CCP4 Research Complex at Harwell iris alc

	A	B	C	D	E	F	G
1	synchrotron	location	data transfer	syncweb?	remote access	automated processing	marcin stats (depositions)
2	aps-gmca	Chicago	globus		no machine	yes	21517
3	aps-lscat	Chicago	globus		web portal		21517
4	aps-biocars	Chicago	globus, hard disk				21517
5	aps-sercat	Chicago	globus, hard disk		no machine, x2go		21517
6	aps-sbc-cat	Chicago	globus, rsync, hard disk				21517
7	aps-necat	Chicago	globus, sftp		ssh, web portal		21517
8	aps-imca-cat	Chicago	hard disk				21517
9	aps-irl-cat	Chicago					
10	home source						
11	esrf	France/Europe					
12	diamond	UK					
13	sls	Switzerland					
14	als	Berkeley					
15	ssrf	Shanghai					
16	ssrl	San Francisco					
17	nsls-ii	Brookhaven					
18	photon factory	Japan					
19	spring8	Japan					
20	bessy	Berlin					
21	australian	Melbourne					
22	desy	Hamburg					
23	soleil	France					
24	pli-ii	Korea					
25	nsrrc	Taiwan					
26	cls	Canada					
27	chess	Cornell					
28	max4	Sweden					
29	alba	Spain					
30	sirius	Brazil					
31	elettra	Italy					



Getting Data into Cloud

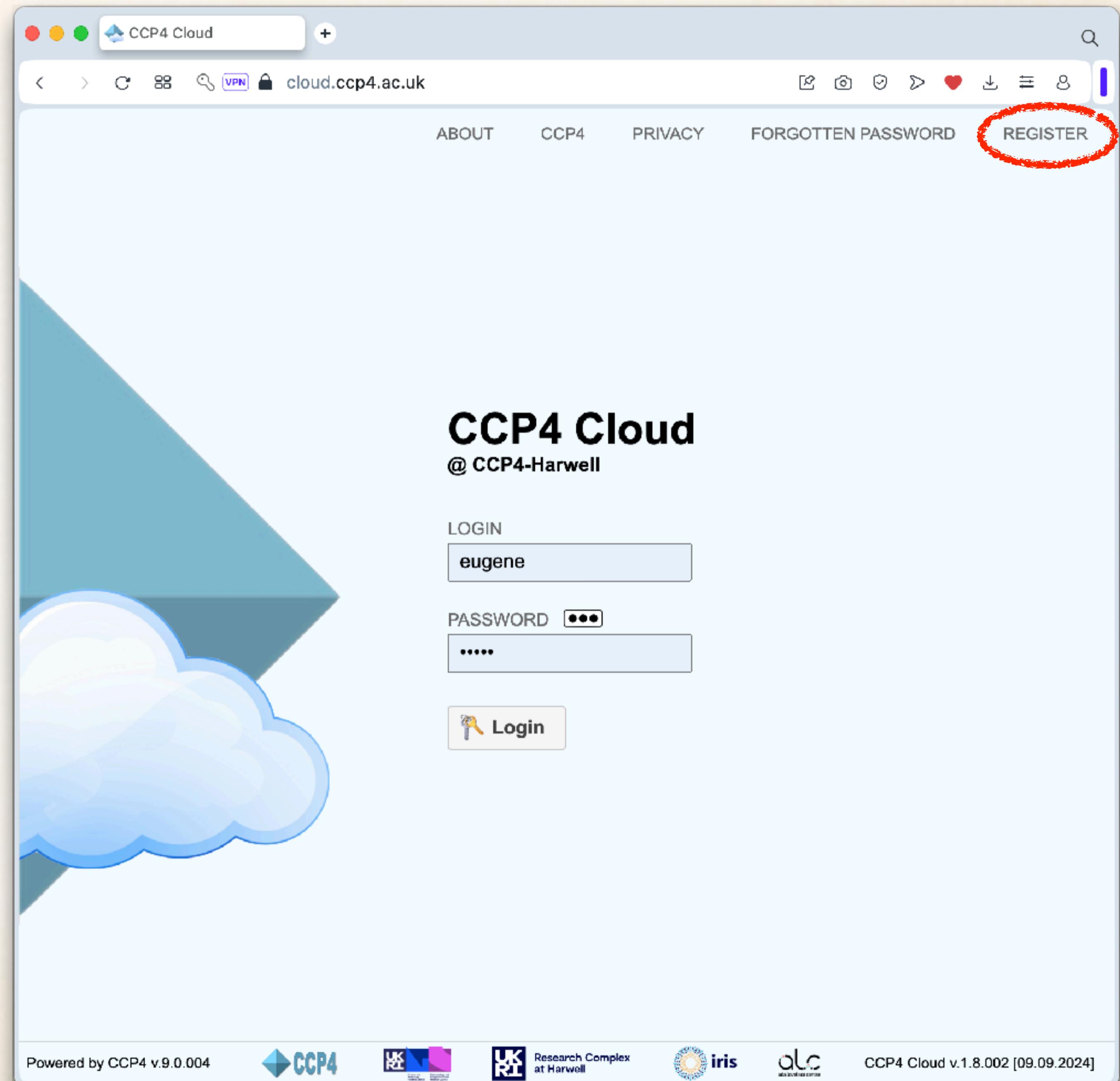




Principal Stages of Structure Solution with CCP4 (Cloud)

<https://cloud ccp4.ac.uk>

*Detail introduction in CCP4 Cloud will
be given later on today at tutorials*



CCP4 Cloud
@ CCP4-Harwell

LOGIN

eugene

PASSWORD

 Login

Powered by CCP4 v.9.0.004   Research Complex
at Harwell   CCP4 Cloud v.1.8.002 [09.09.2024]

Starting with CCP4 Cloud

You **could** go to <https://cloud ccp4.ac.uk> in any browser

Recommended: use CCP4 Cloud icons in CCP4 9+ setup



CCP4 Cloud Local
runs on your machine
(no internet)



CCP4 Cloud
runs on remote
servers



CCP4 Cloud
configurator/
maintainer

If started in browser from <https://cloud ccp4.ac.uk>:



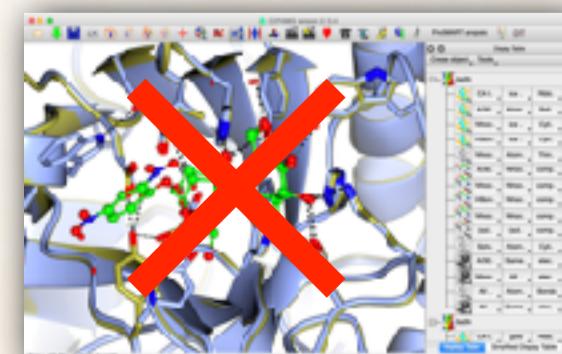
No Coot



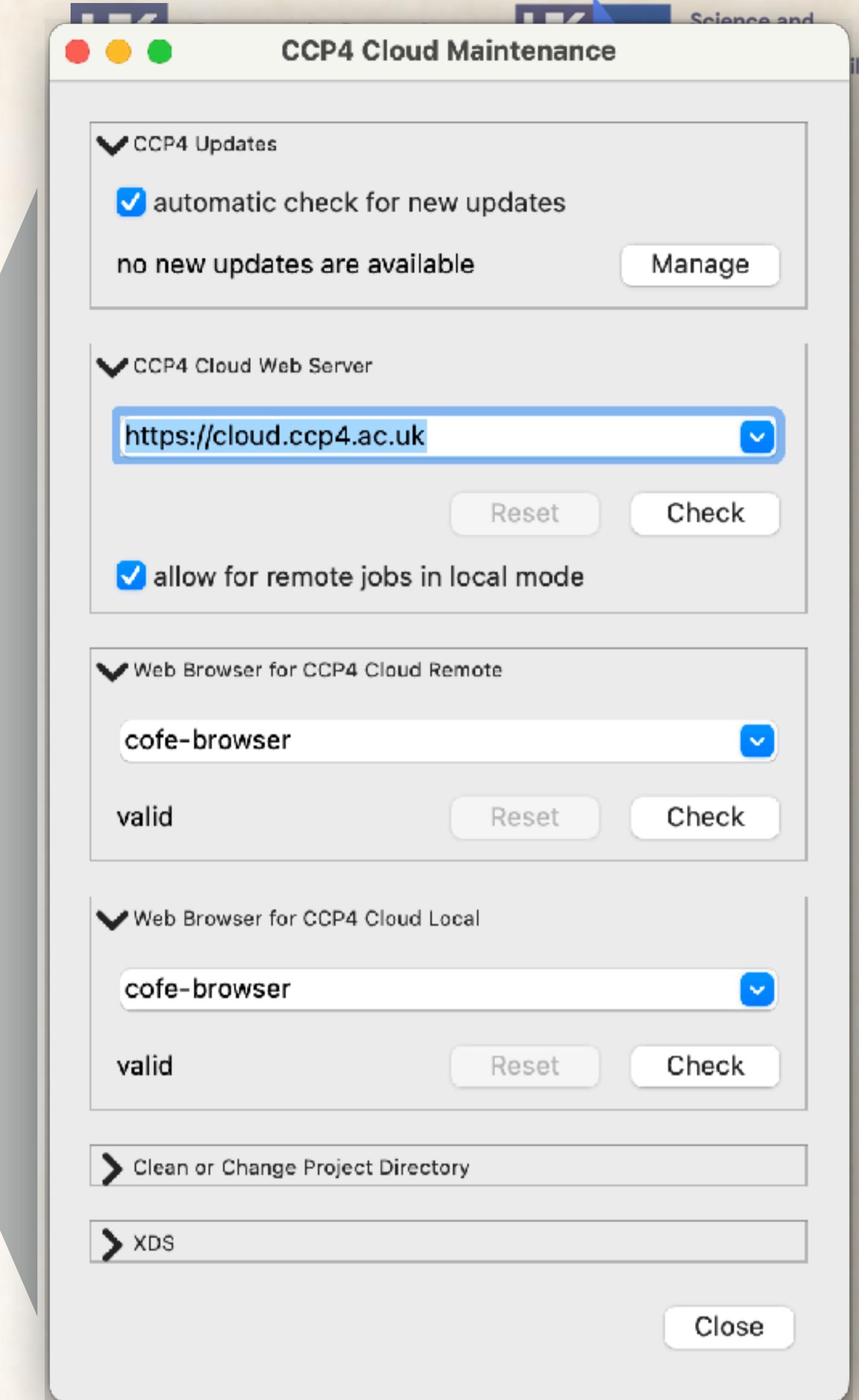
Moorhen



No DUI



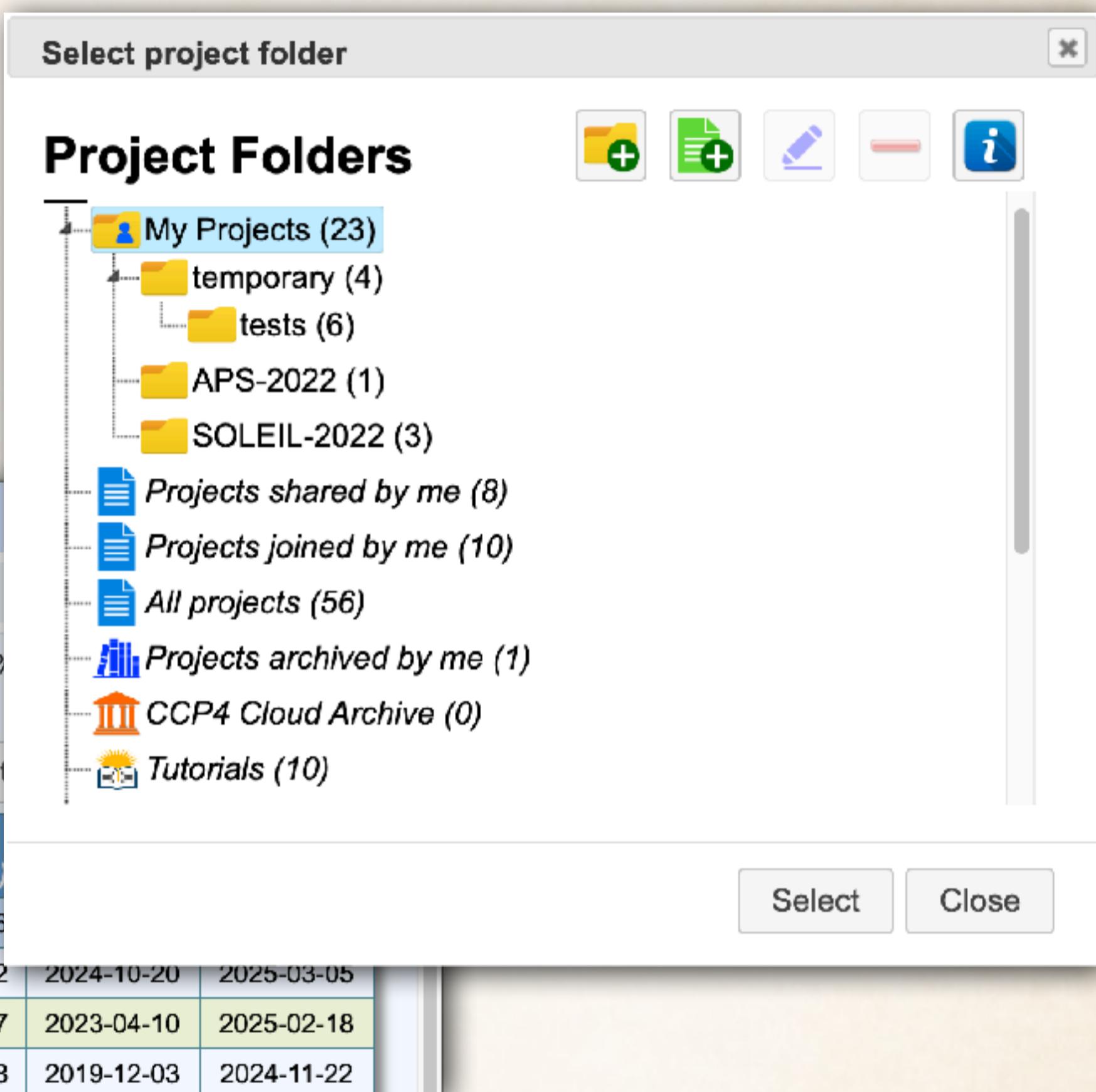
No CCP4mg



Available only
through a browser

- Designed for organising a large number of projects
 - organising in folders, subfolders and lists
 - renaming and cloning
 - supporting project authorship attributes
 - archiving

#	ID	Name	R _{free}	Disk (MBytes)	CPU (hours)	Start Date	End Date
1	mdm2	MDM2 protein bound to Nutlin molecule		38.6	0.0976	2024-10-20	2025-03-05
2	gamma	Gamma protein	0.2703	168.7	0.2642	2023-04-10	2025-02-18
3	crambin	Crambin	0.1108	372.4	4.2677	2019-12-03	2024-11-22
4	dna	DNA complex	0.2258	51.9	1.3758		



- Project export, import and sharing

- exchange between users and collaborators
- exchange between Cloud instances
- local backup copies
- simultaneous work of many users on same project in real time



CCP4 Cloud

cloud ccp4.ac.uk

All projects

Add New Project

ID: e.g., project-1 Name: Put a descriptive title here

Project plan: Manual mode

- Manual mode
- Plan 1. Molecular Replacement using AlphaFold model
- Plan 2. Molecular Replacement using structure databases
- Plan 3. Molecular Replacement using a known model
- Plan 4. Automatic Experimental Phasing
- Plan 5. Import already solved structure for completion

Add Project Cancel

Last ↑ Opened

CCP4 Cloud

cloud ccp4.ac.uk

All projects

Add New Project

#	ID	Name
	project.one	My First CCP4 Cloud Project

Project plan: Plan 2. Molecular Replacement using structure databases

Data needed:

- reflection data (merged or unmerged; .mtz, .hkl, .sca)
- sequence (.fasta, .pir, .seq)
- (optional) ligand description (.cif, .lib)

Plan description: Finding structure template in the PDB, AFDB and ESM data banks; ASU estimate; Molecular Replacement; ligand fitting (if provided); refinement and water modelling

Add Project Cancel

CCP4 Cloud x +

← → C ⌂ cloud ccp4.ac.uk ⌂ 0% 0%:0% Eugene.Krissinel E :

My First CCP4 Cloud Project

(eugene.krissinel):[project.one]
aMR auto-MR:[0001] MR automatic workflow

[0001] MR automatic workflow (new)

Input Output Run

Workflow: Molecular Replacement with MrBump or MoRDa

job description: MR automatic workflow
output id: ccp4go_automr

Import data from local file system

Reflection Data Browse mdm2_unmerged.mtz

Sequence(s) Browse 4hg7.seq

Ligand to fit SMILES COc1ccc(C2=N[C@H]([C@H](N2C(=O)N2CCNC(=O)C2)c2ccc(Cl)cc2)Cl)

Codes XXX, LIG, DRG, INH, LG0, LG1, LG2, LG3, LG4, LG5, LG6, LG7, LG8, LG9 are reserved by Coot and cannot be used here. If no code is given (recommended), a suitable new one will be autogenerated

The screenshot shows the CCP4 Cloud web interface with the title "My First CCP4 Cloud Project". The main content area displays a workflow log for project "eugene.krissinel:[project.one]". The log entries are as follows:

- auto-MR:[0001] MR automatic workflow -- imported Unmerged, Sequences (1), Ligands (1); workflow started
- auto-MR:[0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- auto-MR:[0003] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- auto-MR:[0004] simbad -- best model: 4hg7, LLG=132.0 TFZ=13.7 R=0.3301 R_{free}=0.3193 SpG=P 65 2 2, 1 molecule in ASU, Solv=66.3%
- auto-MR:[0005] modelcraft -- Compl=100.0%, R=0.303 R_{free}=0.312
- XYZ auto-MR:[0006] xyz utils -- waters removed
- auto-MR:[0007] make ligand -- ligand "00Z" prepared
- auto-MR:[0008] fit ligand -- N_{fitted}=1
- auto-MR:[0009] refmacat -- R=0.2834 R_{free}=0.2790 MolProbity=1.11
- auto-MR:[0010] fit waters -- N_{waters}=57 R=0.2579 R_{free}=0.2603 MolProbity=1.42
- auto-MR:[0011] refmacat -- R=0.2613 R_{free}=0.2661 MolProbity=1.71
- auto-MR:[0014] refmacat -- R=0.2337 R_{free}=0.2490 MolProbity=1.23
- auto-MR:[0015] PDB validation report -- pdb report obtained
- auto-MR:[0016] Automated Workflow has finished successfully (look inside for comments)

The sidebar on the left contains icons for various CCP4 tools: +, Import, Export, Sequence, Model, Refinement, XYZ, Modelcraft, Ligand, Waters, Refmacat, Validation, and Help.

CCP4 Cloud

cloud ccp4.ac.uk

My First CCP4 Cloud Project

(eugene.krissinel):[project.one]

- auto-MR:[0001] MR automatic workflow -- import
- auto-MR:[0002] aimless -- Compl=75.8% CCR=2
- auto-MR:[0003] define asymmetric unit co
- auto-MR:[0004] simbad -- best model: 4
- auto-MR:[0005] modelcraft -- Compl=100% CCR=2
- XYZ auto-MR:[0006] xyz utils -- water
- auto-MR:[0007] make ligand
- auto-MR:[0008] fit ligand
- auto-MR:[0009] refmac5
- auto-MR:[0010] fit waters
- auto-MR:[0011] fit ligand
- auto-MR:[0012] fit waters
- auto-MR:[0013] fit ligand
- auto-MR:[0014] fit waters
- auto-MR:[0015] fit ligand
- auto-MR:[0016] fit waters
- [0017] mrbump -- R=0.3499 R_{free}=0.3374 S=0.999
- [0018] modelcraft -- Compl=103.1%, R=0.2675 R_{free}=0.2801 MolProbity=1.05
- [0019] +(0007) fit ligand -- N_{fitted}=1000
- [0020] refmacat -- R=0.2675 R_{free}=0.2801 MolProbity=1.05
- [0021] fit waters -- N_{waters}=53 R=0.2330 R_{free}=0.2481 MolProbity=1.29

Task List

- Suggested tasks
- All tasks
- Workflows
- A-Z

- ▶ Data Import (6)
- ▶ Structure Prediction (1)
- ▶ Data Processing (2)
- ▶ Asymmetric Unit and Structure Revision (3)
- ▶ Molecular Replacement (8)
- ▶ Experimental Phasing (4)
- ▶ Density Modification (0)

Help Close

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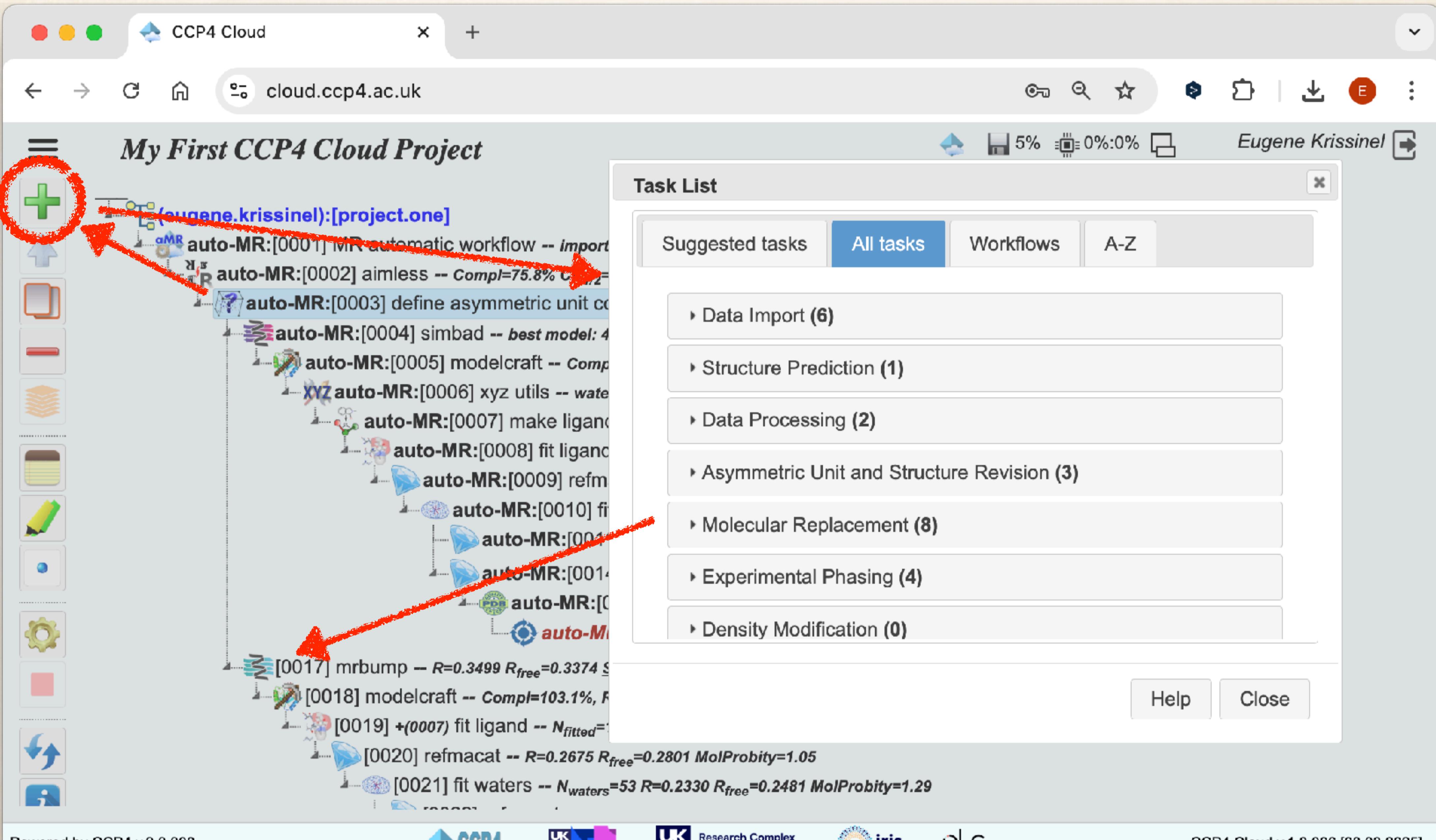
CCP4

UKRI Research Complex at Harwell

iris

alC

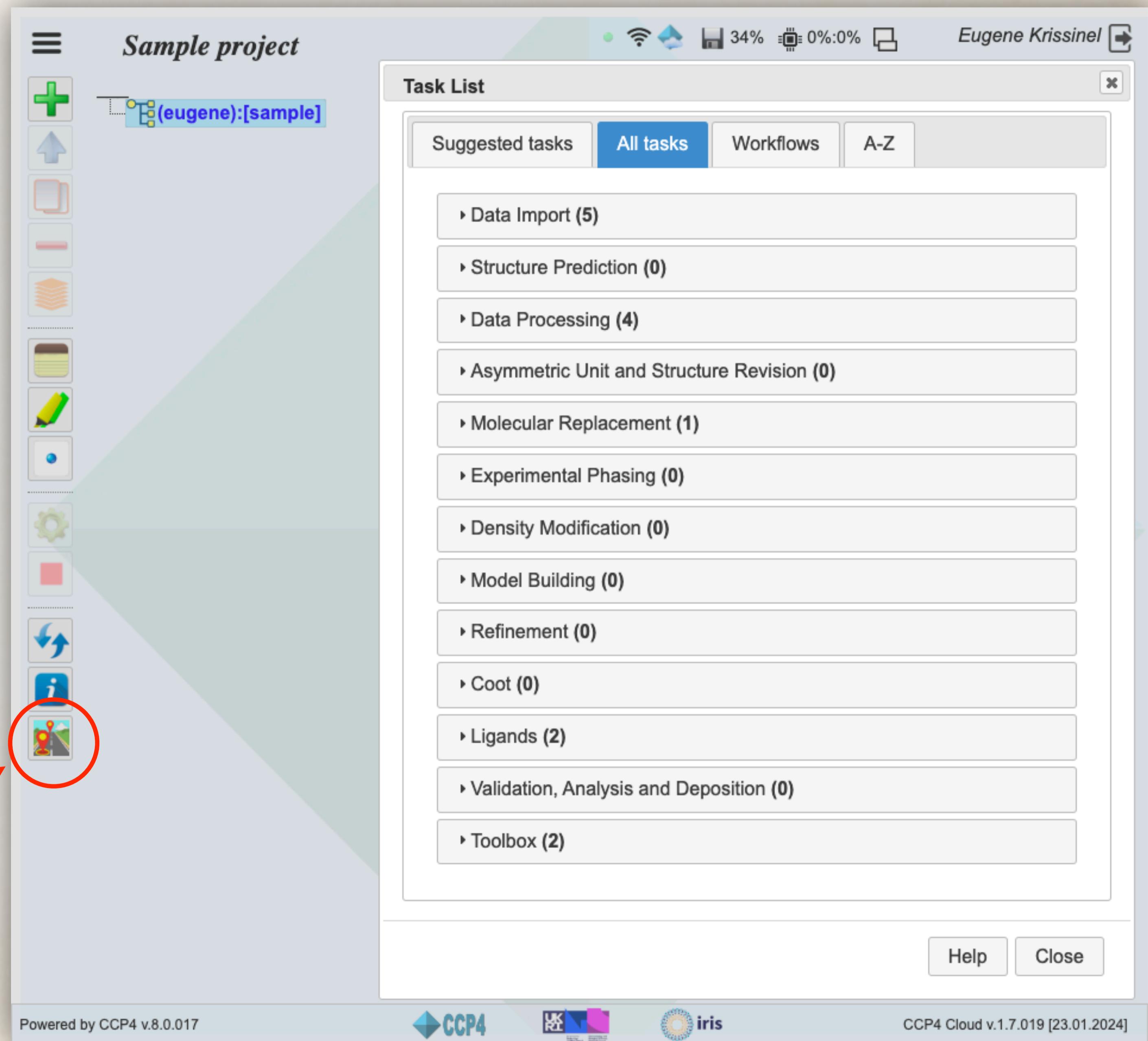
CCP4 Cloud v.1.8.006 [08.03.2025]



Work the Task List from top down

- ~ tasks are arranged into unfolding sections, following the Road Map logics
- ~ section titles show the total number of tasks available at current point of the Project
- ~ you don't need to use every task - they are selected based on specific project scenarios, which you'll explore during the workshop

Road Map page



Start your project from Data Import

- ~ you can import all data in a single import task, or run several of them in sequence
- ~ having all your data on top of the Project will help to keep it well organised and avoid repeat data imports in parallel project branches.
- ~ data may be imported at any point in the Project
- ~ relevant tasks include:

 generic file upload

 copy-paste sequences

 import from PDB or AFDB

 import from Cloud storage



The screenshot shows the CCP4 Project interface. On the left is a vertical toolbar with icons for adding data, generic file upload, copy-paste sequences, PDB/AFDB import, and Cloud storage. The main area is titled "Sample project" and shows a recent task: "(eugene):[sample]" with the message "[0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)". The top right shows connectivity, battery level (34%), and a user profile for "Eugene Krissinel". The bottom navigation bar includes CCP4, UKRI, and iris logos, along with the text "Powered by CCP4 v.8.0.017" and "CCP4 Cloud v.1.7.019 [23.01.2024]".

After import, prepare your data

- ~ merge reflections
- ~ prepare MR search templates
- ~ prepare ligand descriptions
- ~ relevant tasks include:

xia2 Image processing with Xia-2

DIALS Image processing with DUI

Aimless

MrParse

Prepare model from XYZ

Slice'n'Dice

Prepare MR Ensemble

Prepare MR with CCP4mg

Make ligand

The screenshot shows the CCP4 graphical user interface. On the left is a vertical toolbar with icons for various tasks. The main area is titled "Sample project" and shows a tree view of tasks. A task labeled "[0002] aimless" is highlighted with a red border. The status bar at the bottom indicates the project is powered by CCP4 v.8.0.017, and there are logos for CCP4, UKRI, and iris.

Powered by CCP4 v.8.0.017 CCP4 UKRI iris CCP4 Cloud v.1.7.019 [23.01.2024]

You have to make a hypothesis about the content of ASU before phasing

- ~ estimate solvent content
- ~ estimate the number of monomeric chains of each type to look for
- ~ relevant tasks include:



ASU Definition

Sample project

(eugene):[sample]

[0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)

[0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2

[0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)

[0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%

Eugene Krissinel

Powered by CCP4 v.8.0.017

CCP4

UKRI

iris

CCP4 Cloud v.1.7.019 [23.01.2024]

Estimate structure factors phases

- ~ consider automatic solvers first
- ~ can use Molecular Replacement (MR), Experimental Phasing (EP) or their combination (MR-SAD)
- ~ relevant tasks include:

 MrBump (Auto-MR)

 MorDA (Auto-MR)

 Crank-2 (Auto-EP)

 Simbad (No-sequence MR)

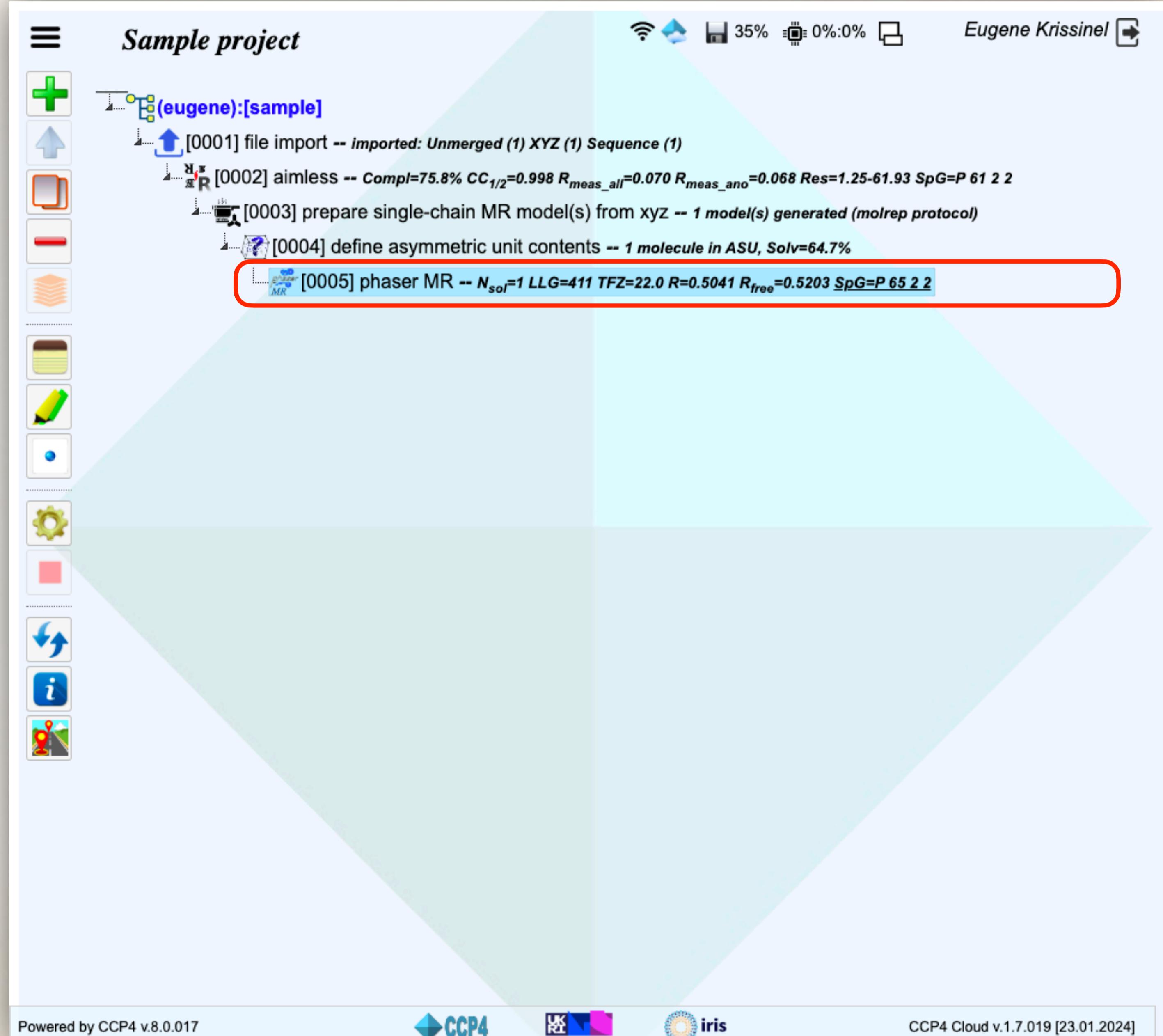
 Arcimboldo (No-sequence MR)

 Phaser (Fundamental MR&EP)

 Molrep (Fundamental MR)

 Shelx C/D/E (EP)

 Dimple (High-homology MR)



The screenshot shows the CCP4 Cloud interface with a project titled "Sample project". The project tree on the left lists the following steps:

- [0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)
- [0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- [0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)
- [0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- [0005] phaser MR -- N_{sol}=1 LLG=411 TFZ=22.0 R=0.5041 R_{free}=0.5203 SpG=P 65 2 2

The fifth step, "phaser MR", is highlighted with a red border.

At the bottom of the interface, it says "Powered by CCP4 v.8.0.017" and shows logos for CCP4, UKRI, and iris.

Decrease phase error with density modification

- ~ optional for MR, a must for EP
- ~ included in auto solvers, do not use after them
- ~ included in some model builders, do not use before them
- ~ relevant tasks include:

- Parrot
- Acorn
- Shelx

The screenshot shows the CCP4 Cloud interface with a project titled "Sample project". The project tree on the left lists the following tasks:

- [0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)
- [0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- [0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)
- [0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- [0005] phaser MR -- N_{sol}=1 LLG=411 TFZ=22.0 R=0.5041 R_{free}=0.5203 SpG=P 65 2 2
- [0006] parrot DM -- FOM=0.691 F_{corr}=0.943

The task [0006] parrot DM is highlighted with a red box.

At the bottom of the interface, there are logos for CCP4, UKRI, and iris, along with the text "Powered by CCP4 v.8.0.017" and "CCP4 Cloud v.1.7.019 [23.01.2024]".

Build or re-build your structure using improved phases

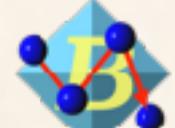
- ~ recover trimmed parts (MR)
- ~ initial interpretation of electron density (EP)
- ~ use automatic builder
- ~ try several builders if completeness is low (70%)
- ~ relevant tasks include:



Modelcraft (AA & NA chains)



Arp/wArp (AA chains)



CCP4Build (AA chains)



Nautilus (NA chains)



AWNuce (NA chains)

The screenshot shows the CCP4 Cloud interface with a project titled "Sample project". The project tree includes:

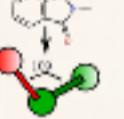
- [0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)
- [0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- [0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)
- [0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- [0005] phaser MR -- N_{sol}=1 LLG=411 TFZ=22.0 R=0.5041 R_{free}=0.5203 SpG=P 65 2 2
- [0006] parrot DM -- FOM=0.691 F_{corr}=0.943
- [0007] modelcraft -- Compl=94.8%, R=0.352 R_{free}=0.372

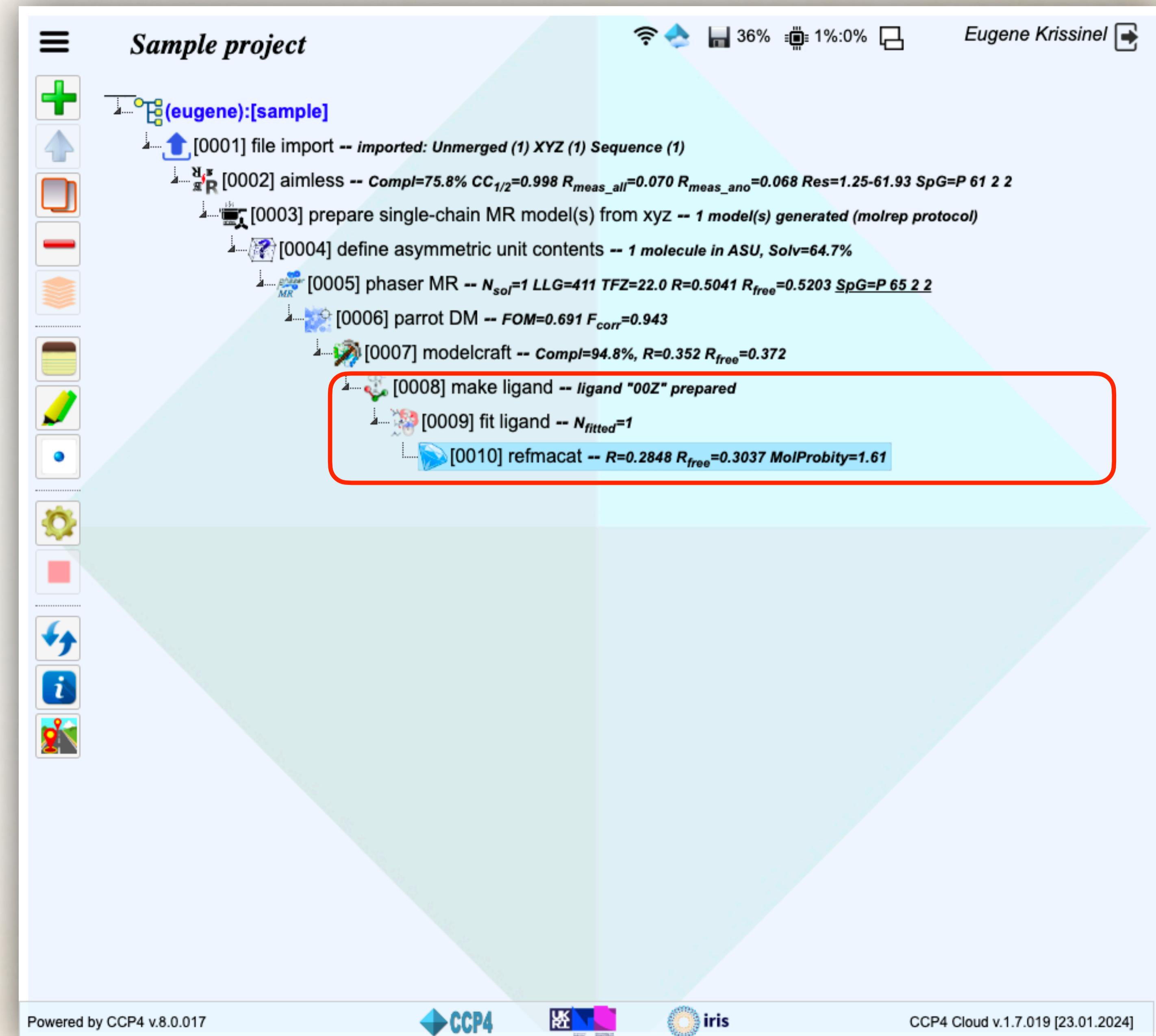
The step [0007] "modelcraft" is highlighted with a red border.

At the bottom of the interface, it says "Powered by CCP4 v.8.0.017" and shows logos for CCP4, UKRI, and iris.

Interpret as much of the green (vacant) electron density as possible

- ~ R_{free} should be 33% or below
- ~ may require structure trimming
- ~ correct results with Coot
- ~ improve phases by refinement
- ~ relevant tasks include:

-  MakeLigand
-  FitLigand
-  Coot
-  Moorhen (Web-Coot)
-  Refmacat (Refinement)



The screenshot shows the CCP4 Cloud interface with a project titled "Sample project". The timeline lists the following steps:

- [0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)
- [0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- [0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)
- [0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- [0005] phaser MR -- N_{sol}=1 LLG=411 TFZ=22.0 R=0.5041 R_{free}=0.5203 SpG=P 65 2 2
- [0006] parrot DM -- FOM=0.691 F_{corr}=0.943
- [0007] modelcraft -- Compl=94.8%, R=0.352 R_{free}=0.372
- [0008] make ligand -- ligand "00Z" prepared
- [0009] fit ligand -- N_{fitted}=1
- [0010] refmacat -- R=0.2848 R_{free}=0.3037 MolProbity=1.61

A red box highlights the [0008] make ligand and [0009] fit ligand steps.

At the bottom, it says "Powered by CCP4 v.8.0.017" and shows logos for CCP4, UKRI, and iris.

Fix all remaining structure issues and improve phases

- ~ based on iterative model correction and refinement
- ~ iterations stop when structure and phases can no longer be improved
- ~ consult validation metrics
- ~ relevant tasks include:

Coot

Moorhen (Web-Coot)

Refmacat (Refinement)

G ϕ L Buster (refinement)

LoRestr (low-resolution refinement)

PDB-REDO (validation)

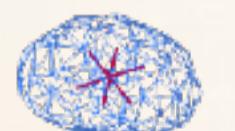
The screenshot shows the CCP4 Pipeline interface with a project titled "Sample project". The pipeline log on the right lists the following steps:

- [0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)
- [0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- [0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)
- [0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- [0005] phaser MR -- N_{sol}=1 LLG=411 TFZ=22.0 R=0.5041 R_{free}=0.5203 SpG=P 65 2 2
- [0006] parrot DM -- FOM=0.691 F_{corr}=0.943
- [0007] modelcraft -- Compl=94.8%, R=0.352 R_{free}=0.372
- [0008] make ligand -- ligand "00Z" prepared
- [0009] fit ligand -- N_{fitted}=1
- [0010] refmacat -- R=0.2848 R_{free}=0.3037 MolProbity=1.61
- [0011] coot (model building) -- model saved
- [0012] refmacat -- R=0.2817 R_{free}=0.3041 MolProbity=1.38

The last two steps, [0011] and [0012], are highlighted with a red box.

Complete your structure with placing water molecules in suitable positions

- ~ use a combination of automatic placement and manual inspection and editing
- ~ improve phases
- ~ assign to suitable chains
- ~ relevant tasks include:



Fit waters



Coot



Moorhen (Web-Coot)



Refmacat (Refinement)



GφL Buster (refinement)



Optimise ASU

Sample project

- [0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)
- [0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- [0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)
- [0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- [0005] phaser MR -- N_{sol}=1 LLG=411 TFZ=22.0 R=0.5041 R_{free}=0.5203 SpG=P 65 2 2
- [0006] parrot DM -- FOM=0.691 F_{corr}=0.943
- [0007] modelcraft -- Compl=94.8%, R=0.352 R_{free}=0.372
- [0008] make ligand -- ligand "00Z" prepared
- [0009] fit ligand -- N_{fitted}=1
- [0010] refmacat -- R=0.2848 R_{free}=0.3037 MolProbity=1.61
- [0011] coot (model building) -- model saved
- [0012] refmacat -- R=0.2817 R_{free}=0.3041 MolProbity=1.38
- [0013] fit waters -- N_{waters}=119 R=0.2479 R_{free}=0.2778 MolProbity=2.21**
- [0014] refmacat -- R=0.2477 R_{free}=0.2747 MolProbity=2.31

Powered by CCP4 v.8.0.017 CCP4 UKRI iris CCP4 Cloud v.1.7.019 [23.01.2024]

Check quality indicators to make sure that results are compliant to reflection data and chemical sense

- ~ check validation section in last refinement task
- ~ run validation tools in Coot or Moorhen
- ~ run dedicated validation tasks
- ~ relevant tasks include:



Zanuda



PDB-REDO



Coot



Moorhen (Web-Coot)



PISA



Privateer (Sugar validation)



PaiRef (Resolution validation)

Sample project

(eugene):[sample]

- [0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)
- [0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- [0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)
- [0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- [0005] phaser MR -- N_{sol}=1 LLG=411 TFZ=22.0 R=0.5041 R_{free}=0.5203 SpG=P 65 2 2
- [0006] parrot DM -- FOM=0.691 F_{corr}=0.943
- [0007] modelcraft -- Compl=94.8%, R=0.352 R_{free}=0.372
- [0008] make ligand -- ligand "00Z" prepared
- [0009] fit ligand -- N_{fitted}=1
- [0010] refmacat -- R=0.2848 R_{free}=0.3037 MolProbity=1.61
- [0011] coot (model building) -- model saved
- [0012] refmacat -- R=0.2817 R_{free}=0.3041 MolProbity=1.38
- [0013] fit waters -- N_{waters}=119 R=0.2479 R_{free}=0.2778 MolProbity=2.21
- [0014] refmacat -- R=0.2477 R_{free}=0.2747 MolProbity=2.31
- [0015] PDB-REDO -- R=0.2141 R_{free}=0.2393 MolProbity=1.67

Eugene Krissinel

Powered by CCP4 v.8.0.017

CCP4 UKRI iris CCP4 Cloud v.1.7.019 [23.01.2024]

Acquire the PDB validation report and make your results public by depositing in the PDB

- ~ prepare mmCIF deposition files
- ~ obtain and check PDB Validation report
- ~ archive your Project in CCP4 Cloud (optional)
- ~ proceed to PDB deposition site
- ~ relevant tasks include:



PDB Validation Report



Prepare Deposition Files



CCP4 Cloud Archive

Sample project

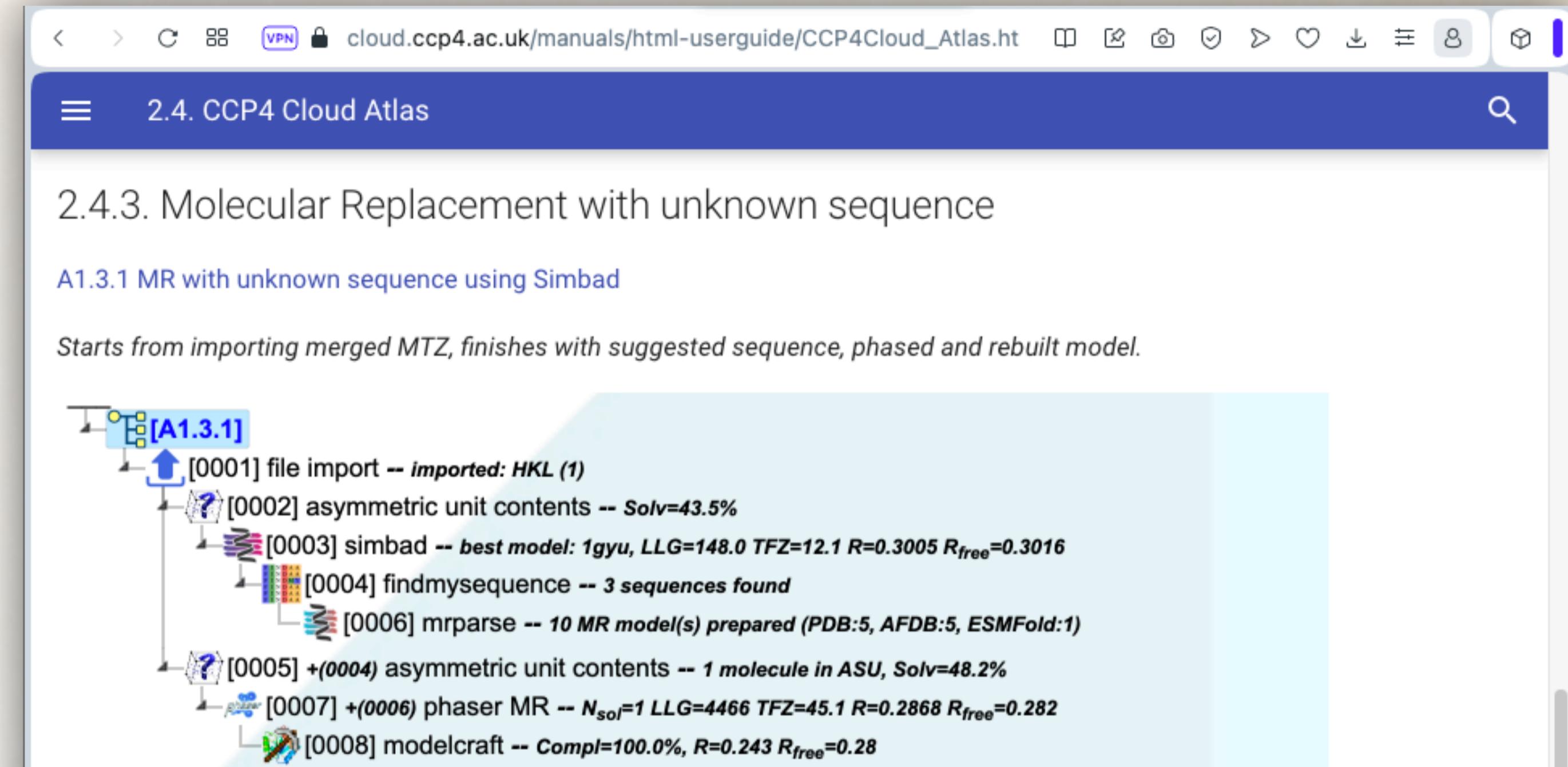
- [0001] file import -- imported: Unmerged (1) XYZ (1) Sequence (1)
- [0002] aimless -- Compl=75.8% CC_{1/2}=0.998 R_{meas_all}=0.070 R_{meas_ano}=0.068 Res=1.25-61.93 SpG=P 61 2 2
- [0003] prepare single-chain MR model(s) from xyz -- 1 model(s) generated (molrep protocol)
- [0004] define asymmetric unit contents -- 1 molecule in ASU, Solv=64.7%
- [0005] phaser MR -- N_{sol}=1 LLG=411 TFZ=22.0 R=0.5041 R_{free}=0.5203 SpG=P 65 2 2
- [0006] parrot DM -- FOM=0.691 F_{corr}=0.943
- [0007] modelcraft -- Compl=94.8%, R=0.352 R_{free}=0.372
- [0008] make ligand -- ligand "00Z" prepared
- [0009] fit ligand -- N_{fitted}=1
- [0010] refmacat -- R=0.2848 R_{free}=0.3037 MolProbity=1.61
- [0011] coot (model building) -- model saved
- [0012] refmacat -- R=0.2817 R_{free}=0.3041 MolProbity=1.38
- [0013] fit waters -- N_{waters}=119 R=0.2479 R_{free}=0.2778 MolProbity=2.21
- [0014] refmacat -- R=0.2477 R_{free}=0.2747 MolProbity=2.31
- [0015] PDB-REDO -- R=0.2141 R_{free}=0.2393 MolProbity=1.67
- [0016] PDB validation report -- pdb report obtained
- [0017] PDB deposition files -- finished.

Powered by CCP4 v.8.0.017 CCP4 UKRI iris CCP4 Cloud v.1.7.019 [23.01.2024]

The Road Map is merely a schematic

- ~ (almost) every Project is special
- ~ with AlphaFold, MR scenarios became even more dominating than before
- ~ MR scenarios also differ in many details
- ~ CCP4 Cloud Atlas contains schematics of many useful Project scenarios – use it
- ~ look up for link to CCP4 Cloud Atlas on top of the Road Map page
- ~ direct link is as follows:

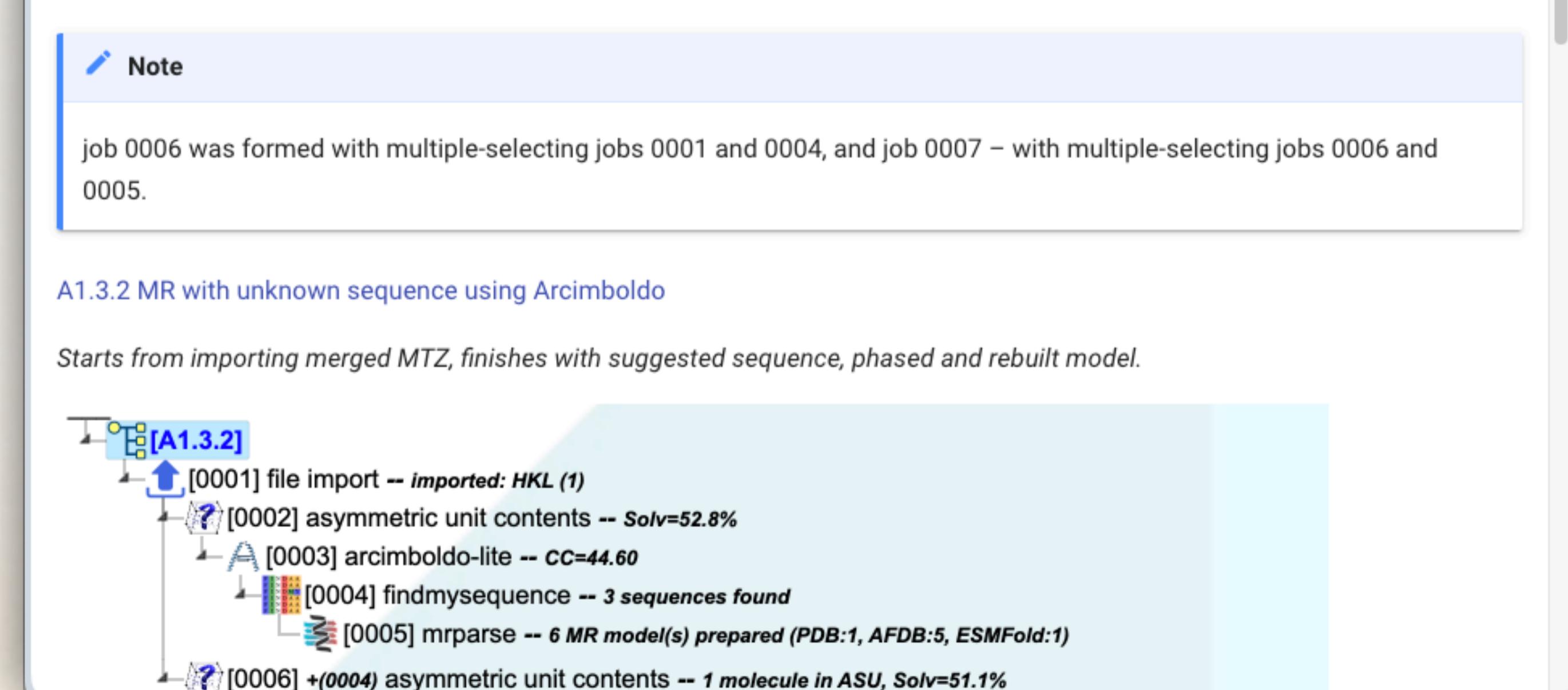
**[https://cloud ccp4.ac.uk/
manuals/html-userguide/
CCP4Cloud_Atlas.html](https://cloud ccp4.ac.uk/manuals/html-userguide/CCP4Cloud_Atlas.html)**



The screenshot shows a web browser displaying the CCP4 Cloud Atlas user guide. The title "2.4. CCP4 Cloud Atlas" is at the top, followed by "2.4.3. Molecular Replacement with unknown sequence". Below this, a section titled "A1.3.1 MR with unknown sequence using Simbad" is shown. It includes a note: "Starts from importing merged MTZ, finishes with suggested sequence, phased and rebuilt model." A detailed workflow diagram is provided, starting with a file import job (0001) which imports HKL (1). This leads to an asymmetric unit contents job (0002) with Solv=43.5%. Job 0003 uses simbad to find a best model: 1gyu, LLG=148.0, TFZ=12.1, R=0.3005, R_{free}=0.3016. Job 0004 uses findmysequence to find 3 sequences. Job 0006 uses mrparse to prepare 10 MR models (PDB:5, AFDB:5, ESMFold:1). Job 0005 uses +0004 to find asymmetric unit contents for 1 molecule in ASU, Solv=48.2%. Job 0007 uses phaser MR to produce N_{sol}=1, LLG=4466, TFZ=45.1, R=0.2868, R_{free}=0.282. Job 0008 uses modelcraft to complete the model with Compl=100.0%, R=0.243, R_{free}=0.28.

Note

job 0006 was formed with multiple-selecting jobs 0001 and 0004, and job 0007 – with multiple-selecting jobs 0006 and 0005.



The screenshot continues to show the CCP4 Cloud Atlas user guide. Below the first workflow, another one is shown for "A1.3.2 MR with unknown sequence using Arcimboldo". It follows a similar structure: file import (0001), asymmetric unit contents (0002, Solv=52.8%), arcimboldo-lite (0003, CC=44.60), findmysequence (0004, 3 sequences found), mrparse (0005, 6 MR models prepared, PDB:1, AFDB:5, ESMFold:1), and finally asymmetric unit contents (0006, Solv=51.1%).

- Running CCP4 Cloud projects from command prompt (CloudRun)
- Scripting CCP4 Cloud projects for repetitive experiments
- 3rd party software authorisation
- Integrated tutorials
- Using Task dock
- Crashed Coot recovery
- Project Folders
- Using project remarks
- Project archiving

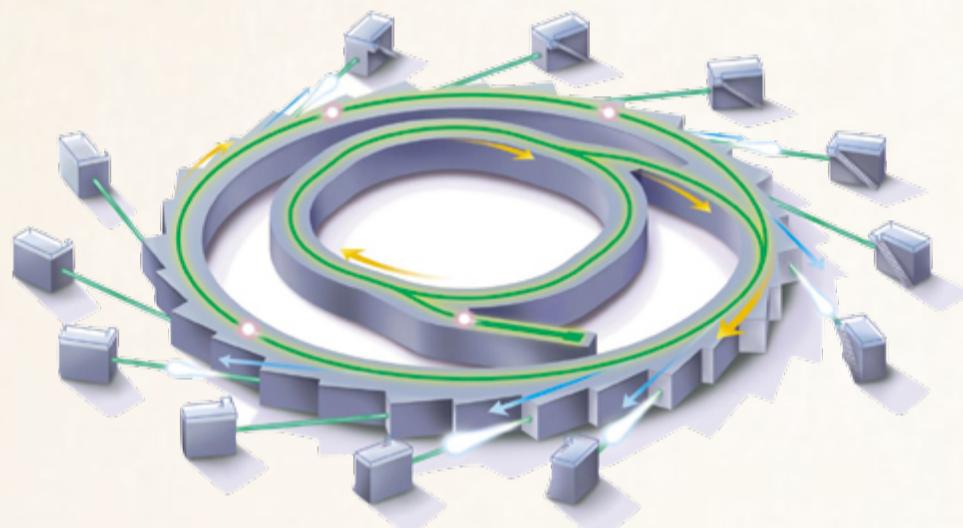
<https://cloud ccp4.ac.uk/manuals/html-userguide/index.html>



When the Road ends ...

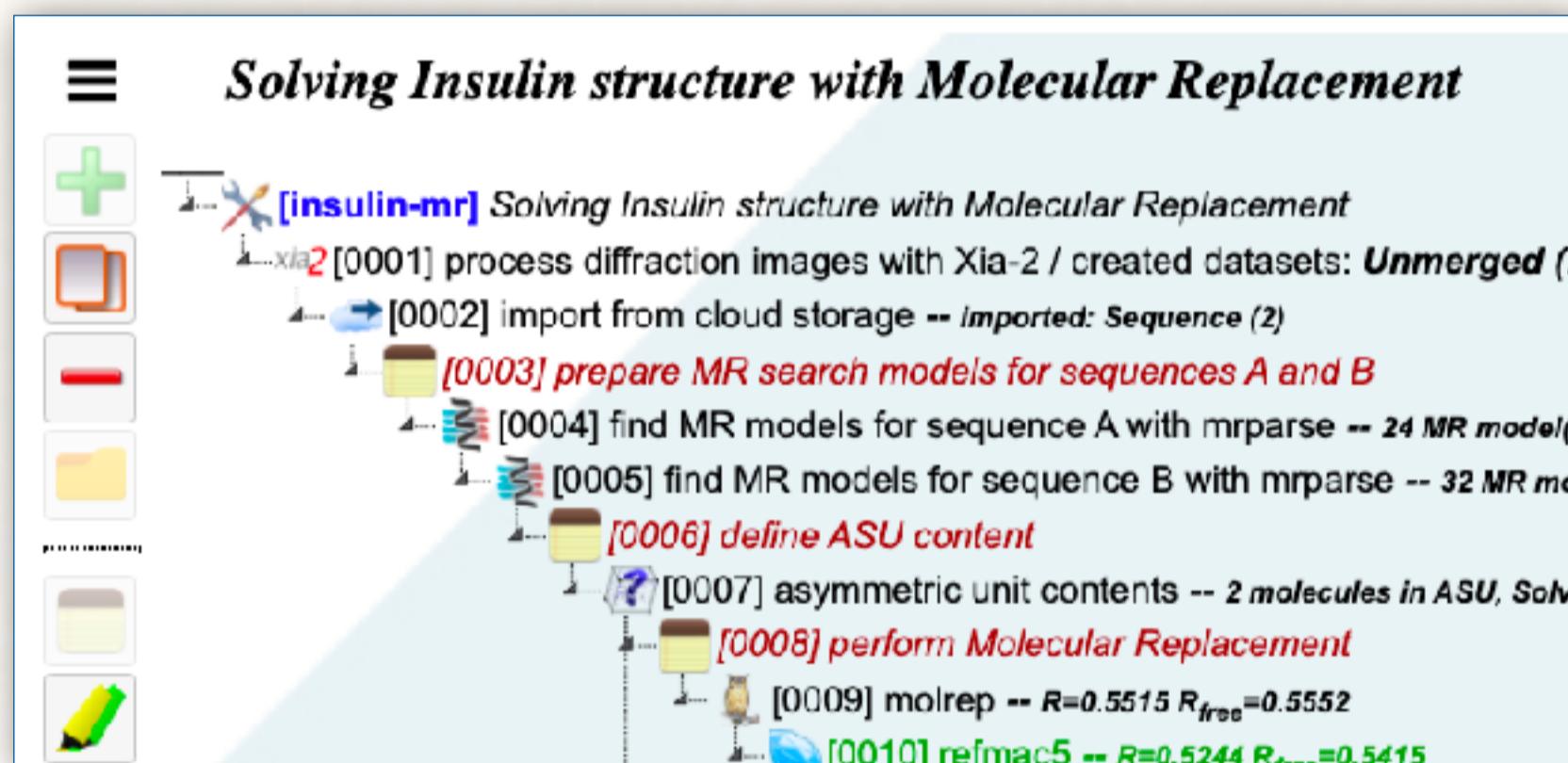
Structure solution project is integral part of your Data

Experiment



evidence

Structure Solution Project

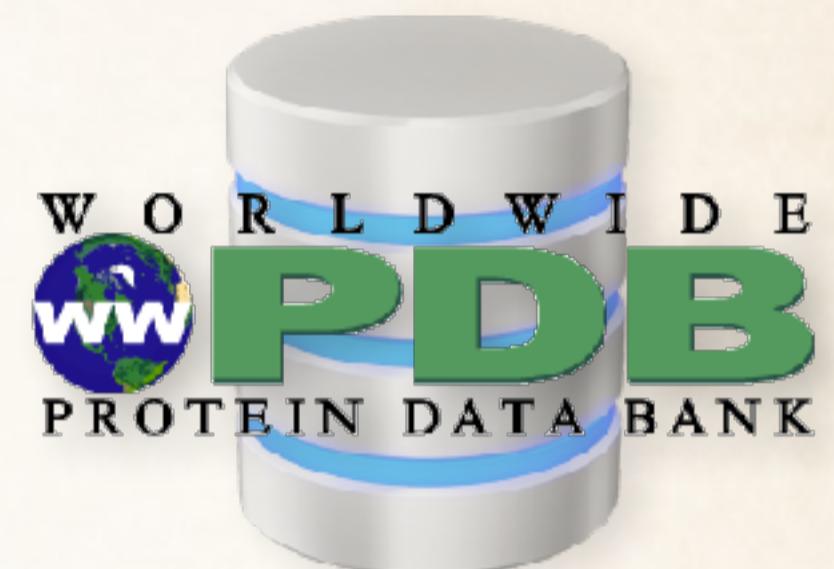


interpretation

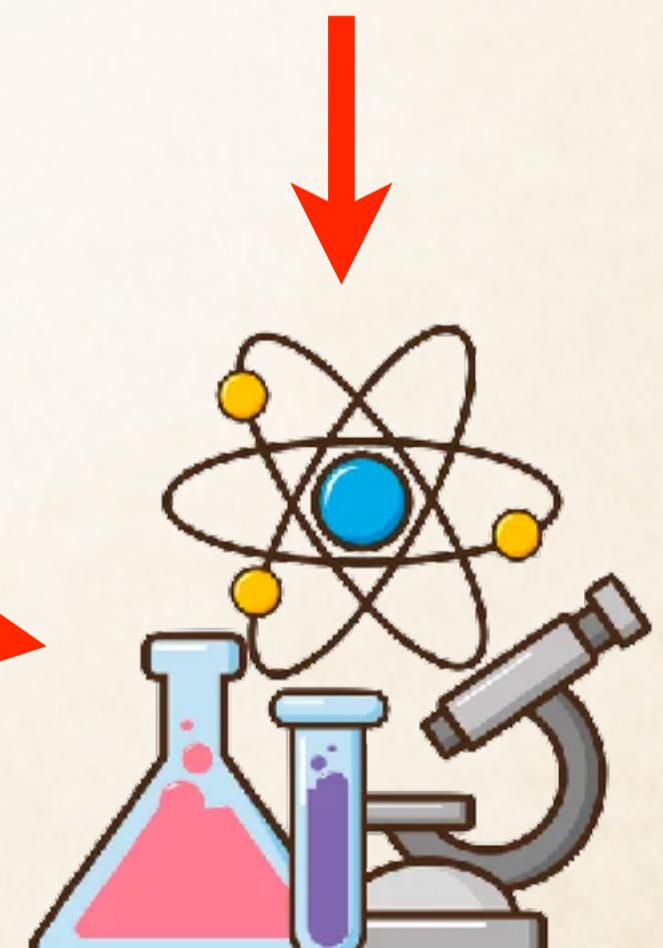
Currently only
described in
papers

- methods
- decisions
- assumptions
- doubts resolution
- validation
- alternatives

Repository



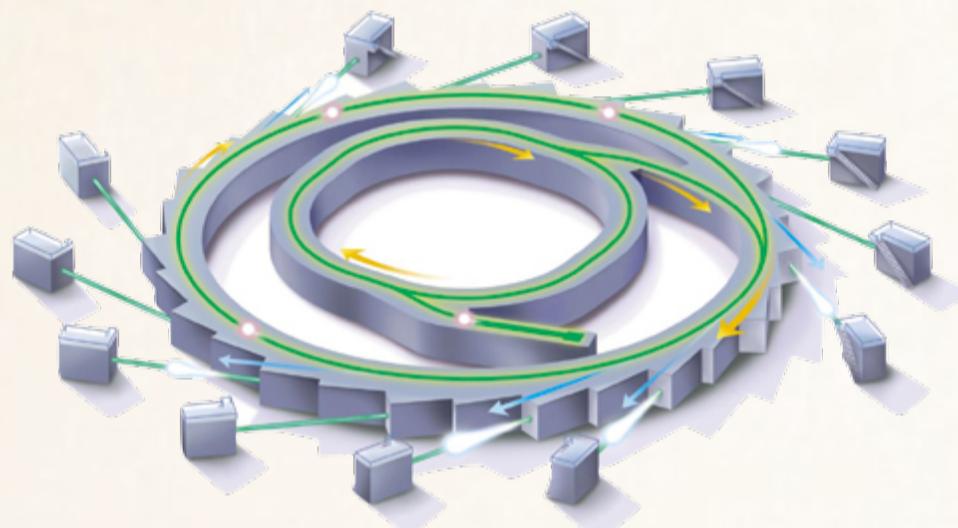
structures



Research

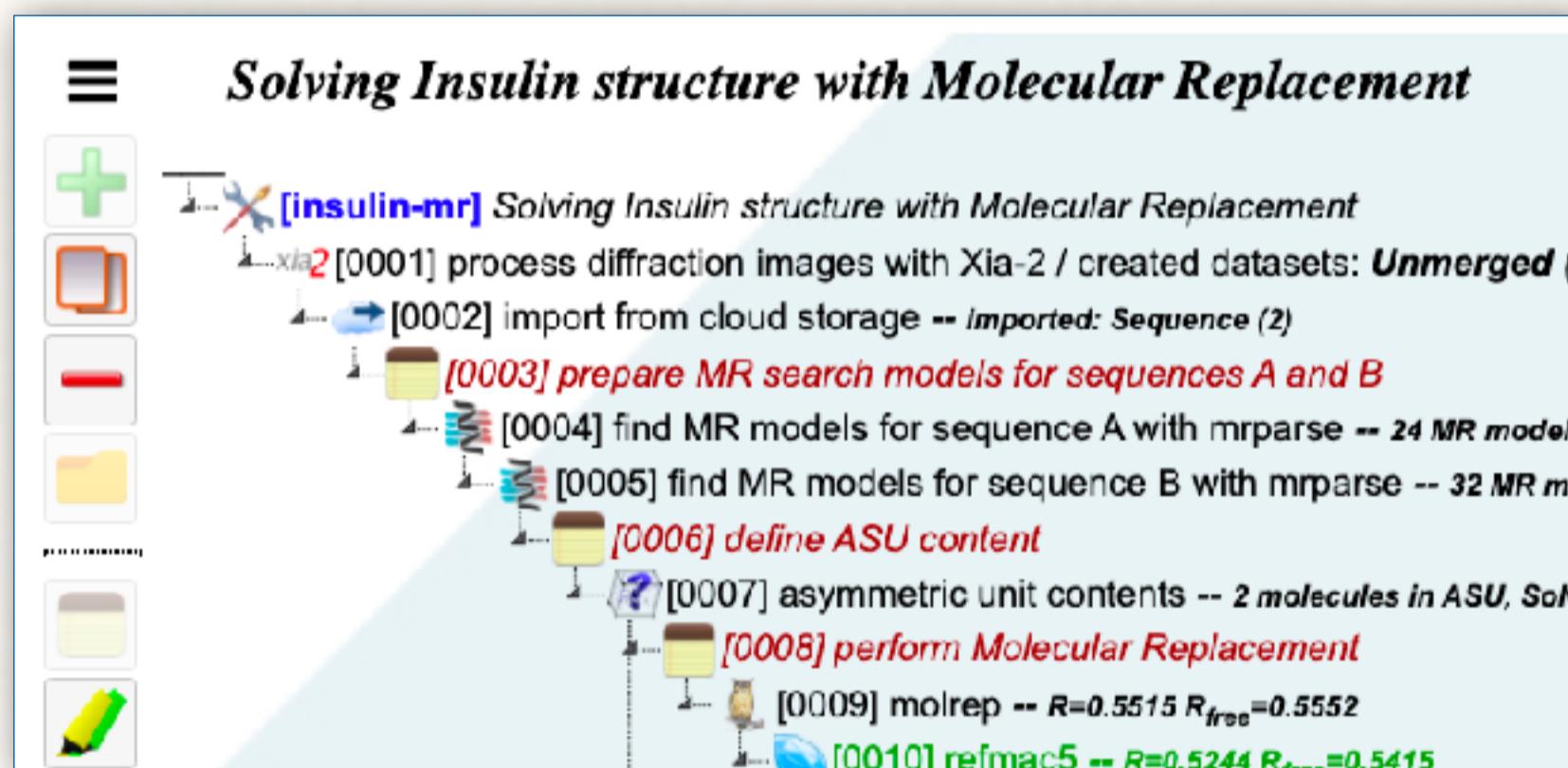
Archiving structure solution projects in CCP4 Cloud

Experiment



evidence

Structure Solution Project

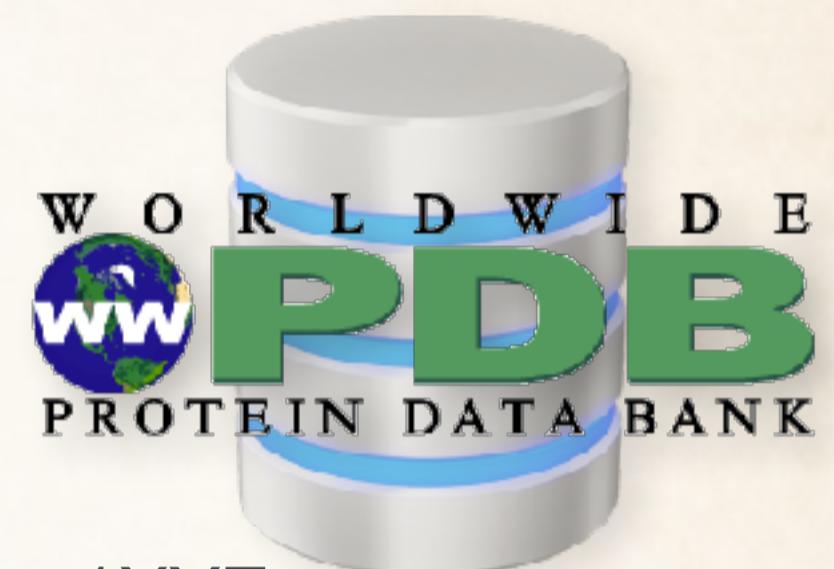


interpretation



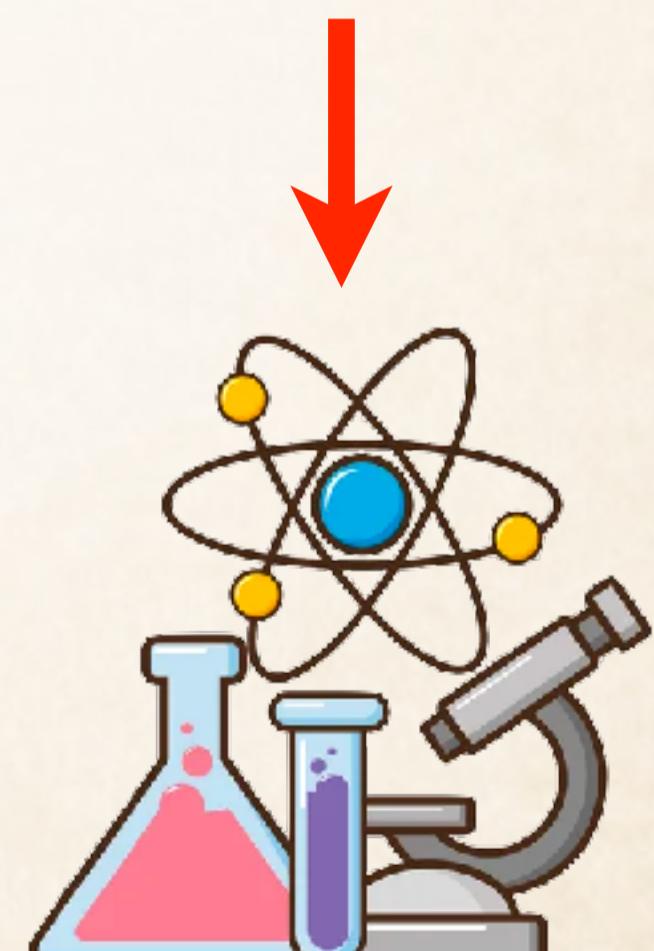
Project Archive

Repository



PDB Code: 1XYZ

structures



Archive ID: CCP4-1XYZ



Research

Example

CCP4 Cloud Archive ID: CCP4-RNASE (could be published in a paper on web-site etc.)

Access URL:

<https://cloud ccp4.ac.uk/archive/access.html?id=CCP4-RNASE>

Consider archiving completed projects in CCP4 Cloud when publishing your work

Many thanks to:

CCP4, STFC & RCaH

Fantastic work environment, support and dissemination

**CCP4 Collaboration,
CCP4 School hosts and
CCP4 developers**

**~300 test users
Worldwide**

Contribution of task reports, tutorials, general support and valuable feedback

Trial use and feedback on development versions of CCP4 Cloud

Andy Purkiss
Francis Crick Institute, London

Grzegorz Chojnowski
EMBL-Hamburg

Arnaud Basle
Newcastle University

Michael Isupov
University of Exeter

Adam Lee, Marc Deller
Incyte Inc.

Setup and maintenance of CCP4 Cloud instances in their home labs



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