

CCP4 Workshop at DLS, Harwell, UK, Dec 13–20, 2016

# CCP4 Roadmap

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# CCP4 History and Background

- 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 Computational Science and Engineering Department of STFC

## Main CCP4 Groups

- Core Group (Oxford)
  - ~ maintain and support software suite
  - ~ application and infrastructural software developments
  - ~ collaborate with Diamond on beam line deployment of CCP4 software and joint developments
  - ~ educational outreach
  - ~ maintain CCP4 resources such as the CCP4 bulletin board
- MRC/LMB (Cambridge)
  - ~ data processing software (Mosflm, Aimless)
  - ~ refinement software (Refmac)
  - ~ model building (Coot)
- Phaser group (University of Cambridge)
- University of York
  - ~ Software developments (CCP4mg, Buccaneer, Privateer)
  - ~ CCP4 GUI-2 developments
- Others
  - ~ Experimental Phasing from Leiden (Crank-2)
  - ~ Ab-initio MR, University of Liverpool (AMPLE)
- Associated projects
  - ~ Arp/wArp (EMBL-Hamburg)
  - ~ PDB Redo (NKI, the Netherlands)



# CCP4 Users Geography



# CCP4 Study Weekend

- Annual CCP4 users meeting taking place in January in the UK
- Each year tackles a different topic:
  - ~ Data processing
  - ~ Experimental phasing
  - ~ Molecular replacement
  - ~ Model building and refinement
  - ~ Related topics: Complementary methods (EM, NMR, SAX etc.), Structure analysis, Complexes, Ligands, Databases
- Proceedings published in special edition of Acta Cryst. D
- 2016: *“Protein-Ligand Complexes: Understanding Biological Chemistry”*
- 2017: *“From crystals to structure with CCP4”*
- 2018: *“Serial crystallography”*

# CCP4 Schools and Workshops

- Main aim is to give education and expert help to researchers working with collected crystal data
- Some schools also provide expert help with collecting crystal data (APS, Hamburg, Diamond)
- Applicants with challenging crystals and/or data are given strong consideration but this is not mandatory
- Software developers from CCP4, Phenix (APS Workshop), SHELX, Arp/wArp, XDS and HKL as well as others give lectures, tutorials and are also available to help with data processing and data solution throughout the meetings

<http://www.ccp4.ac.uk> – Courses & Events

## Public CCP4 Resources

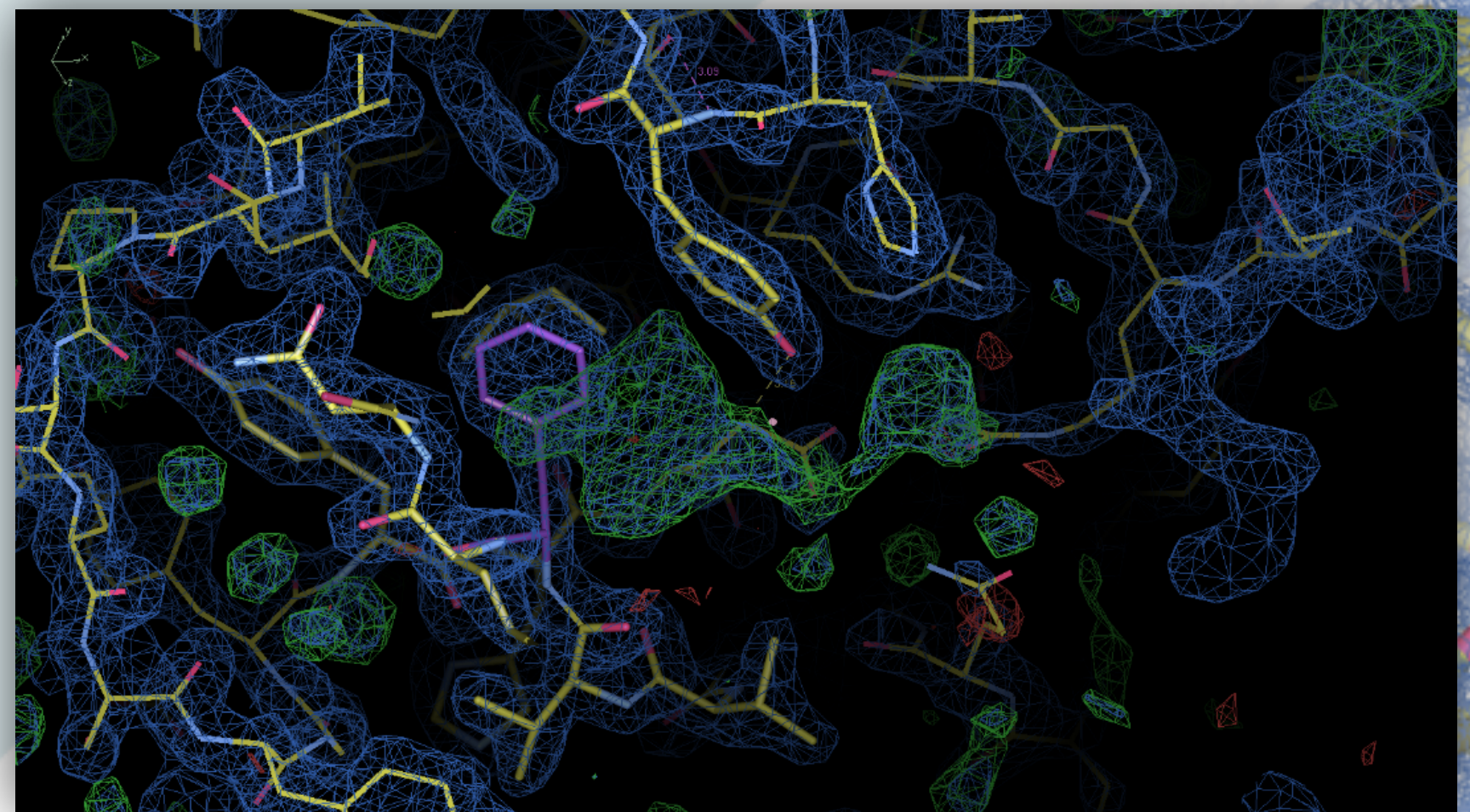
- CCP4BB mailing list — <http://www.jiscmail.ac.uk/lists/ccp4bb.html> — bulletin board, news, expert help and advice
- CCP4 help desk — [ccp4@ccp4.ac.uk](mailto:ccp4@ccp4.ac.uk) — bug reports, problems with software
- CCP4 wiki — <http://ccp4wiki.org> — program documentation and tutorials
- CCP4 web site — <http://www.ccp4.ac.uk> — documentation, developers info, news, links to the above resources and CCP4-online services for structure solution.

# The CCP4 Software Suite

- The CCP4 Suite is a comprehensive suite of software for macromolecular crystallography and it contains about 250 program components
- New versions of the suite are released about every 12 months
  - ~ New programs
  - ~ Major updates to existing programs
  - ~ Other new features such as changes to CCP4i interface
- Revisions to the current release (CCP4 7.0) are made available through the CCP4 updates manager

# Structure Solution in Essence

- X-ray diffraction as such produces a reciprocal image of a target structure, or Fourier transform of its atomic coordinates. As an ultimate goal, one would like to find an atomic model for their target from X-ray diffraction images and other information available (such as sequence)
- This could be achieved by applying the inverse Fourier transform to experimental structure factors (which are Fourier transform of the structure's atomic coordinates) if they were known or could be indeed recorded in an experiment
- In reality, the X-ray diffraction experiment produces only moduli, **but not phases**, of structure factors
- Therefore, phases need to be elicited by other means



# Structure Solution Pathway

- As a first step, one need to derive structure factor amplitudes from the intensities of spots in X-ray images
- Next, phases need to be approximated by using methods such as
  - ~ Experimental Phasing: SAD, MAD, SIRAS etc.
  - ~ Molecular Replacement
  - ~ Combination of the above
- Then, structure factors can be converted into electron density via inverse *Fourier transform*
- The obtained electron density map need to be interpreted via model building and refinement to produce a model for target structure
- The model need to be analysed to answer biochemical questions and deposited in the PDB

*sounds like we know what to do ...*

## CCP4 Scope

**PiMS**

Crystallisation

Data Collection

Data Processing  
and Reduction

**DIALS**  
Collection, Integration, for Advanced Light Sources

Experimental  
Phasing

Molecular  
Replacement

Density  
Modification

Model Building

Refinement

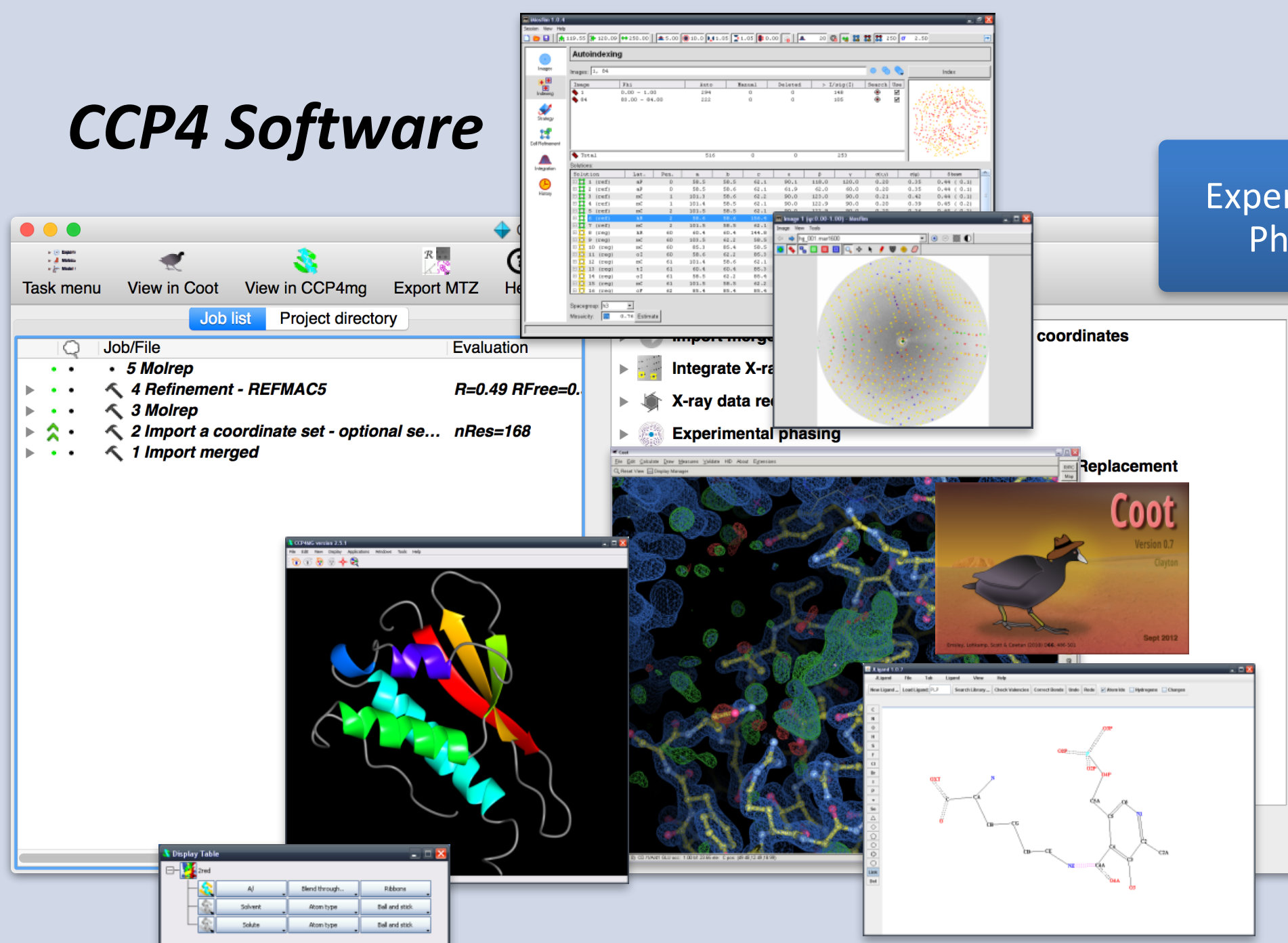
Structure Analysis

Deposition

**SHELX**

7.3  
*ARP*  
*wARP*

## CCP4 Software



**PDB\_REDO**

## External components

*SHARP/  
autoSHARP*

*PiMS*

*XDS &  
autoPROC*

Crystallisation

Data Collection

Data Processing  
and Reduction

**DIALS**  
Collection Integration for Advanced Light Sources

Experimental  
Phasing

Molecular  
Replacement

Density  
Modification

Model Building

Refinement

Structure Analysis

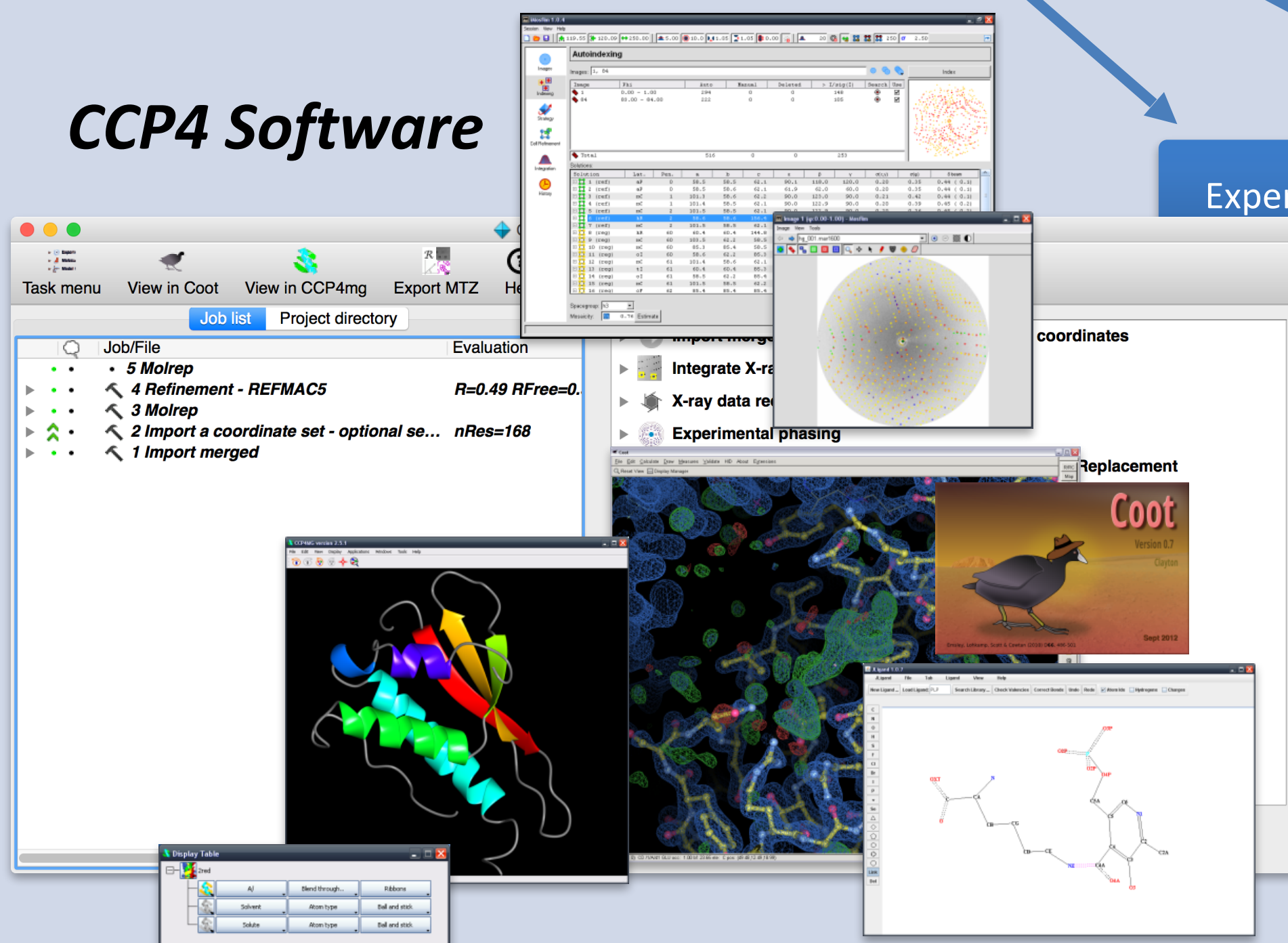
Deposition

**SHELX**

7.3  
*ARP*  
*wARP*

**BUSTER**

**CCP4 Software**



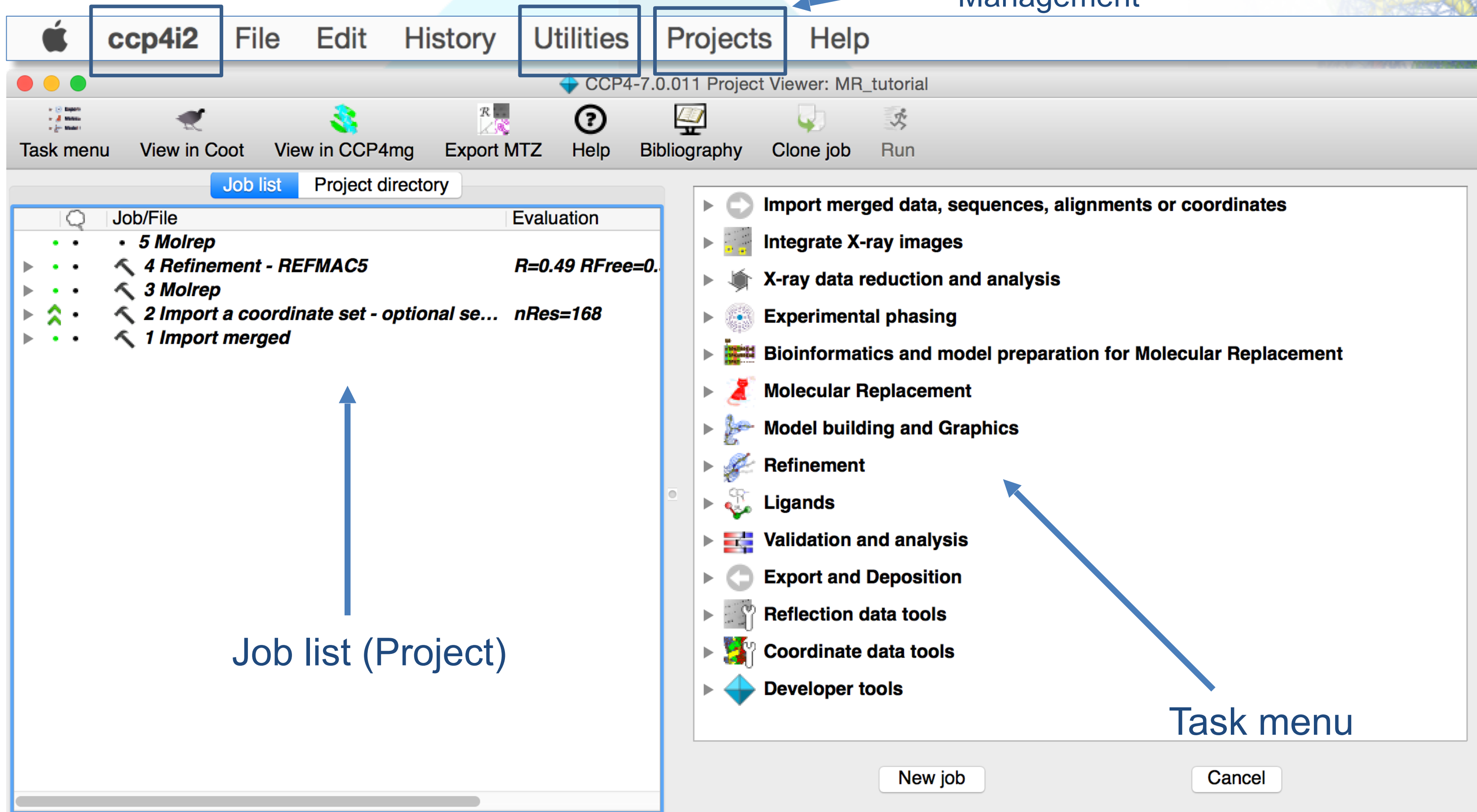
**PDB\_REDO**

# The CCP4i2 Interface

Preferences  
and Settings

Managing Software Updates

Project  
Management



The screenshot displays the CCP4i2 interface with the following components:

- Menu Bar:** Apple logo, **ccp4i2**, File, Edit, History, Utilities, Projects, Help.
- Task menu:** Task menu, View in Coot, View in CCP4mg, Export MTZ, Help, Bibliography, Clone job, Run.
- Job list (Project):** A table with columns Job/File and Evaluation.

| Job/File                                     | Evaluation      |
|----------------------------------------------|-----------------|
| • 5 Molrep                                   |                 |
| ▶ 4 Refinement - REFMAC5                     | R=0.49 RFree=0. |
| ▶ 3 Molrep                                   |                 |
| ▶ 2 Import a coordinate set - optional se... | nRes=168        |
| ▶ 1 Import merged                            |                 |
- Task menu:** A list of tasks with icons:
  - Import merged data, sequences, alignments or coordinates
  - Integrate X-ray images
  - X-ray data reduction and analysis
  - Experimental phasing
  - Bioinformatics and model preparation for Molecular Replacement
  - Molecular Replacement
  - Model building and Graphics
  - Refinement
  - Ligands
  - Validation and analysis
  - Export and Deposition
  - Reflection data tools
  - Coordinate data tools
  - Developer tools
- Buttons:** New job, Cancel.

## The CCP4i2 Interface

CCP4-7.0.011 Project Viewer: MR\_tutorial

Task menu View in Coot View in CCP4mg Export MTZ Help Bibliography Clone job Run

Job list Project directory

Job/File Evaluation

- 6 Autobuild - BUCCANEER
- 5 Molrep
- 4 Refinement - REFMAC5 *R=0.49 RFree*
- 3 Molrep
- 2 Import a cool
- 1 Import merge

se... nRes=168

Delete  
Clone  
Edit label  
Open  
View  
Export  
Next task..

Input  
Output  
Comments

Job actions (right-click)

Job 4: Refinement - REFMAC5 The job is Finished

Input Results Comments

Default weight Per cycle Picture Outliers Other Biblio Run

|                          |              |
|--------------------------|--------------|
| No. reflections all/free | 21135 / 106  |
| R-factor/R-free          | 0.492 / 0.53 |
| RMS Deviations           |              |
| Bonds                    | 0.0135       |
| Angles                   | 1.782        |
| Chain mean B (No. atoms) |              |
| AA                       | 17.7914 ( 1  |
| Aa                       | 42.3363 ( 6  |

Download

Running refmac R-factors

R-factor

Cycle

R\_Factor  
R\_Free  
rmsBonds

Refinement - REFMAC5 Manual model building - COOT Autobuild - BUCCANEER

## The CCP4i2 Interface

CCP4-7.0.011 Project Viewer: MR\_tutorial

Task menu View in Coot View in CCP4mg Export MTZ Help Bibliography Clone job Run

Job list Project directory

**Job 4: Refinement - REFMAC5** *The job is Finished*

Input Results Comments

Default weight Per cycle Picture Outliers Other Biblio Run

**Input Data**

Atomic model 2 Molecular Replacement and refinement - MOLREP

View Annotate Copy Export Help

Quick view View as text View in CCP4mg View in Coot

**Output Data**

Atomic model Model refined by Prosmart/Refmac

Map coefficients Weighted difference map from refinement

Map coefficients Weighted map from refinement

Phases Calculated phases from refinement

Coot history Coot script written from refinement

Bibliographic references

Job run details

Refinement - REFMAC5 Manual model building - COOT Autobuild - BUCCANEER

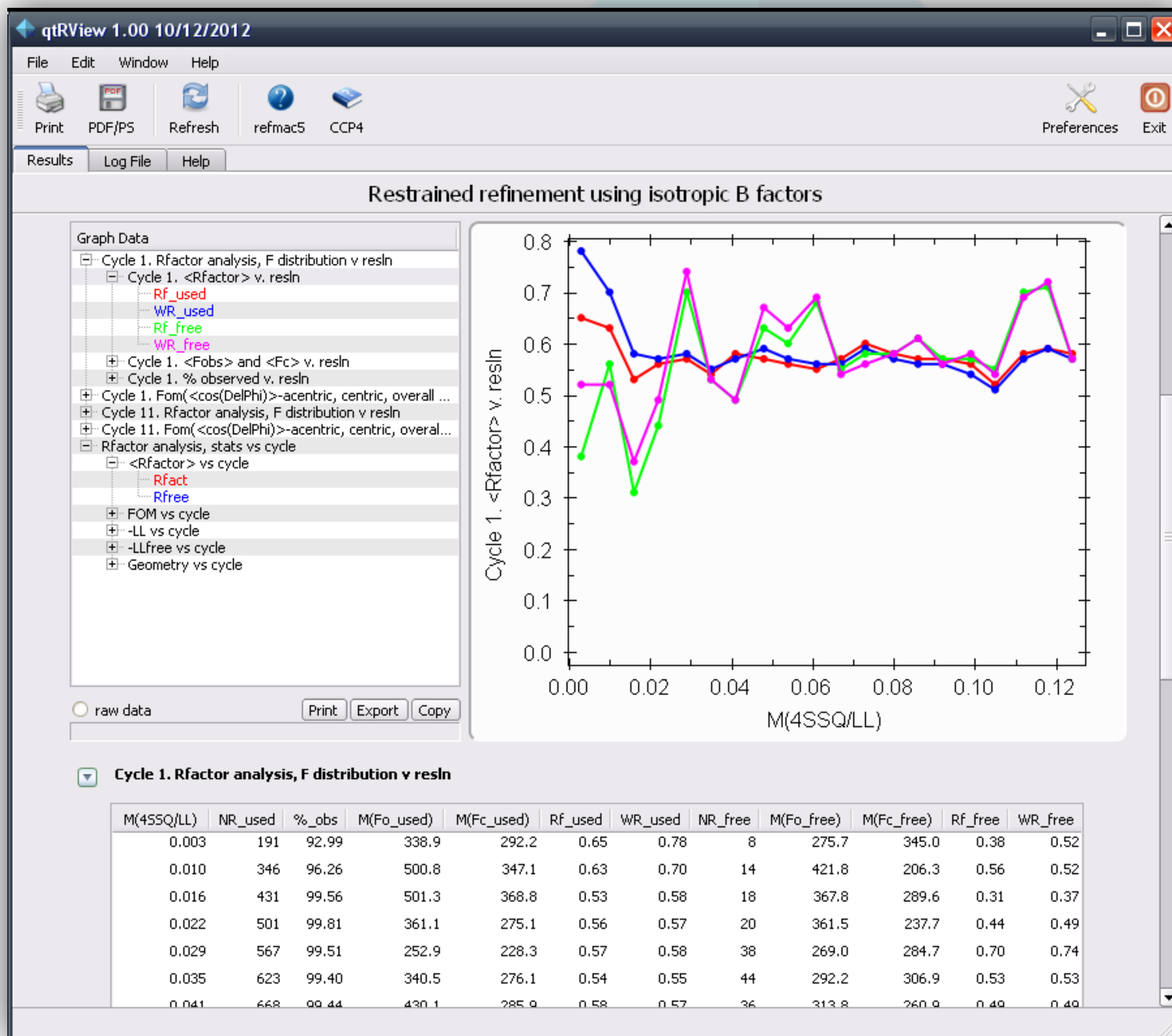
*Data actions (right-click)*

*Job input*

*Job output*

*Next job suggestions*

# Report and Log File Viewer QtRView



- Graphical log file viewer
- View graphs, tables and job summary information
- Launch Coot, CCP4mg and ViewHKL to work with the content of data files
- Export result files
- Can still view the original (plain text) log file

## The CCP4i(1) Interface

Project  
Management

CCP4Interface 6.5.004 running on rmxps Project: pierreHD

List of jobs for project. Double-click on a job displays the log file, shift-double-click reruns the job.

| Molecular Replacement |           | Automatic structure solution |                    | Data Reduction and Analysis |  | Experimental Phasing |  | Molecular Replacement |  | Density Improvement |  | Model Building |  | Refinement |  | Structure Analysis |  | Validation & Deposition |  |
|-----------------------|-----------|------------------------------|--------------------|-----------------------------|--|----------------------|--|-----------------------|--|---------------------|--|----------------|--|------------|--|--------------------|--|-------------------------|--|
| 25                    | 18 Dec 14 | KILLED                       | buccaneer_pipeline | yray                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 22                    | 18 Dec 14 | FINISHED                     | molrep             | tesy                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 21                    | 18 Dec 14 | FINISHED                     | refmac5            | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 20                    | 18 Dec 14 | FAILED                       | xia2               | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 19                    | 18 Dec 14 | FAILED                       | xia2               | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 18                    | 18 Dec 14 | FINISHED                     | mr bump            | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 17                    | 18 Dec 14 | FINISHED                     | aimless            | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 16                    | 18 Dec 14 | FINISHED                     | pointless          | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 15                    | 18 Dec 14 | FAILED                       | dimple             | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 14                    | 17 Dec 14 | KILLED                       | mr bump            | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 13                    | 12 Dec 14 | FAILED                       | mr bump            | test                        |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 12                    | 12 Aug 14 | KILLED                       | mr bump            | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 11                    | 12 Aug 14 | FINISHED                     | mr bump            | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 10                    | 12 Aug 14 | FINISHED                     | mr bump            | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 9                     | 12 Aug 14 | FAILED                       | mr bump            | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 8                     | 12 Aug 14 | KILLED                       | mr bump            | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 7                     | 12 Aug 14 | FINISHED                     | mr bump            | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 6                     | 12 Aug 14 | FAILED                       | mr bump            | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 5                     | 13 May 13 | FINISHED                     | phaser_MR          | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 4                     | 13 May 13 | FINISHED                     | phaser_MR          | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 3                     | 13 May 13 | FINISHED                     | phaser_MR          | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 2                     | 13 May 13 | FINISHED                     | phaser_MR          | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |
| 1                     | 13 May 13 | FINISHED                     | phaser_MR          | [No title given]            |  |                      |  |                       |  |                     |  |                |  |            |  |                    |  |                         |  |

Directories&ProjectDir

View Any File

View Files from Job

Search/Sort Database..

Graphical View of Project

Delete/Archive Files..

Kill Job

ReRun Job..

Edit Job Data

Preferences

System Administration

3 new updates available

Manage Updates

Exit

Task/program  
menu

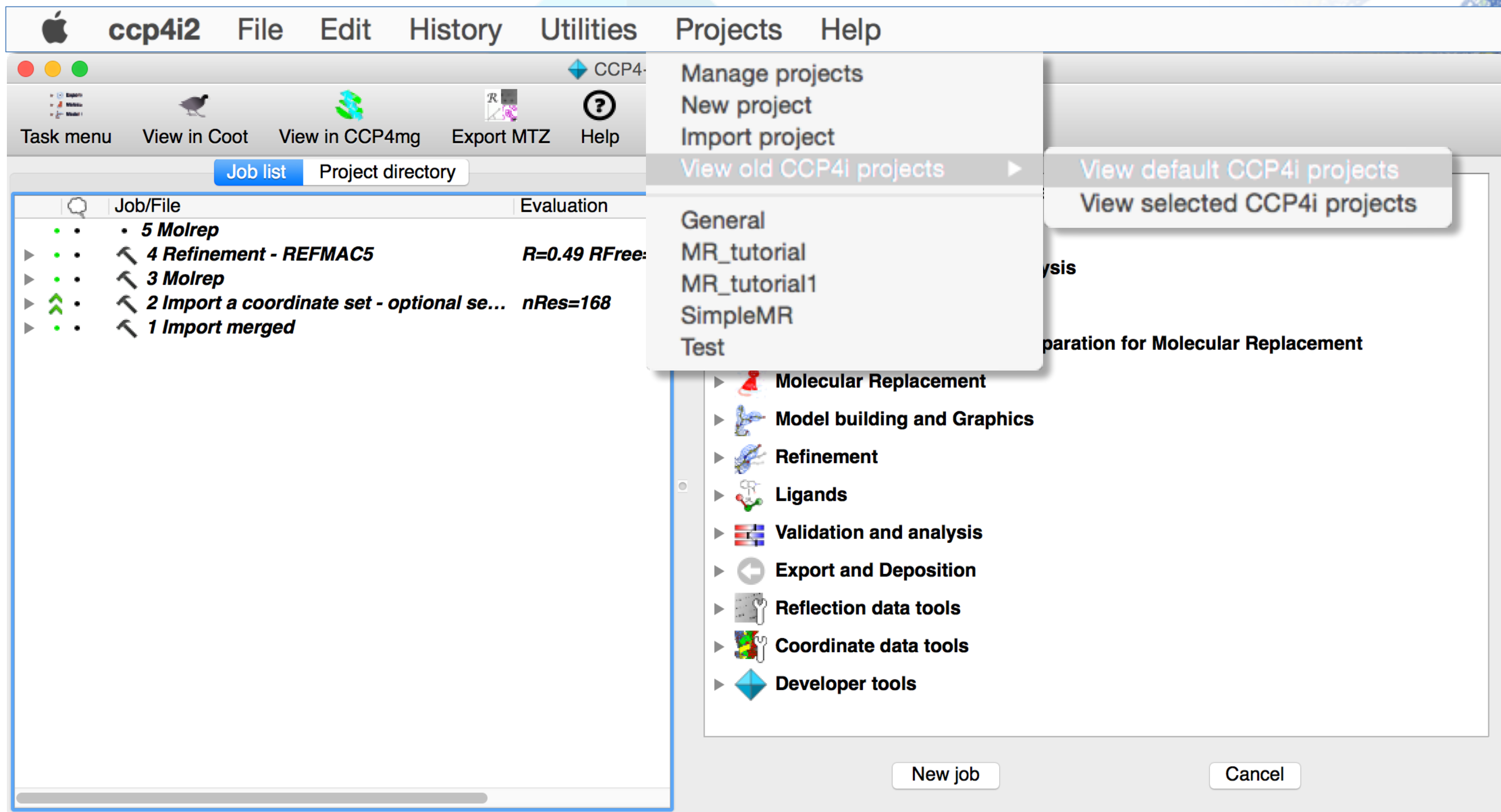
Job list

Job actions:  
clone, kill, delete,  
view files, etc.

Preferences  
and Settings

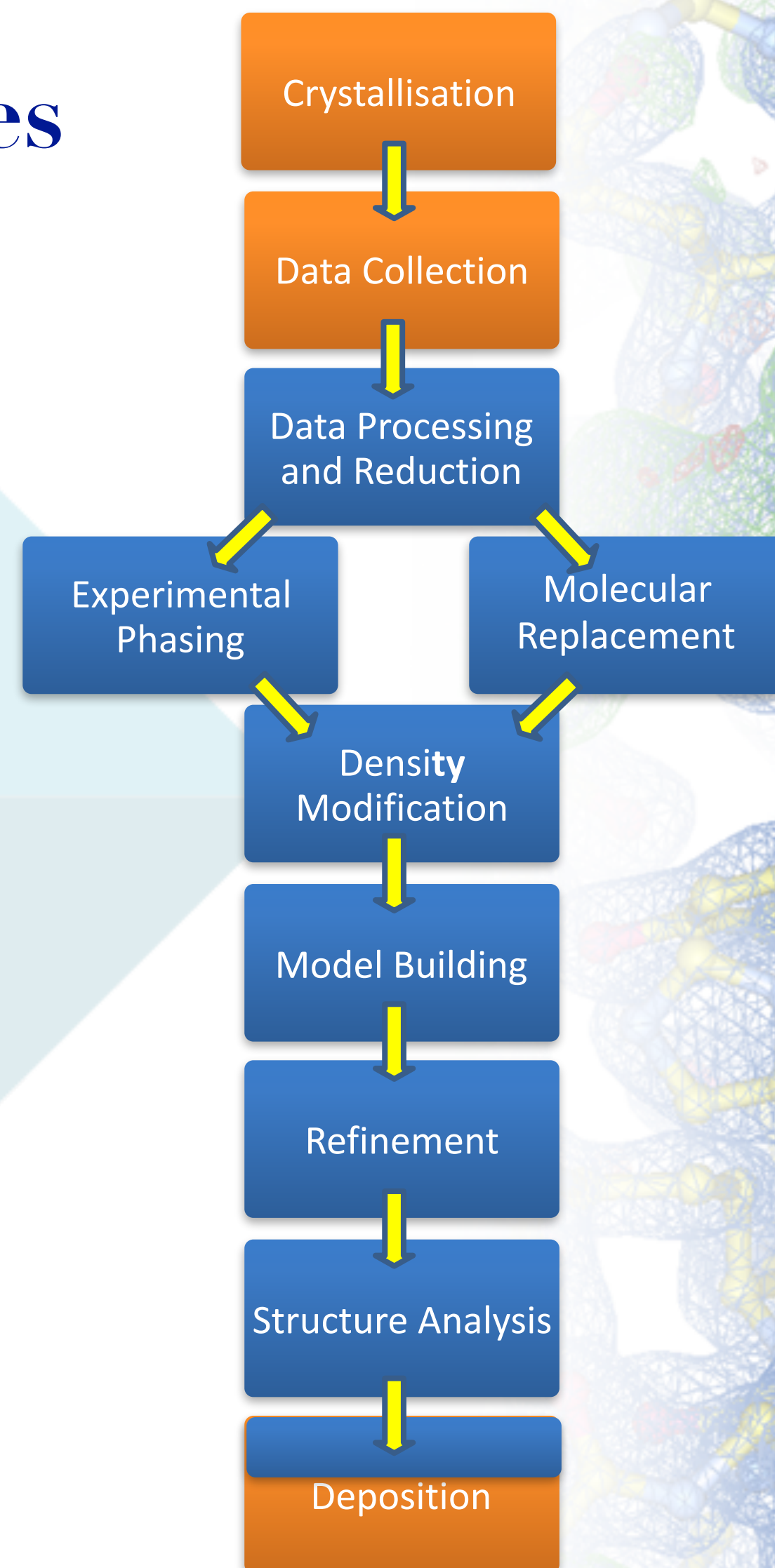
CCP4  
Updates

# From CCP4i(1) to CCP4i2



... one-way road

# The Structure Solution Stages



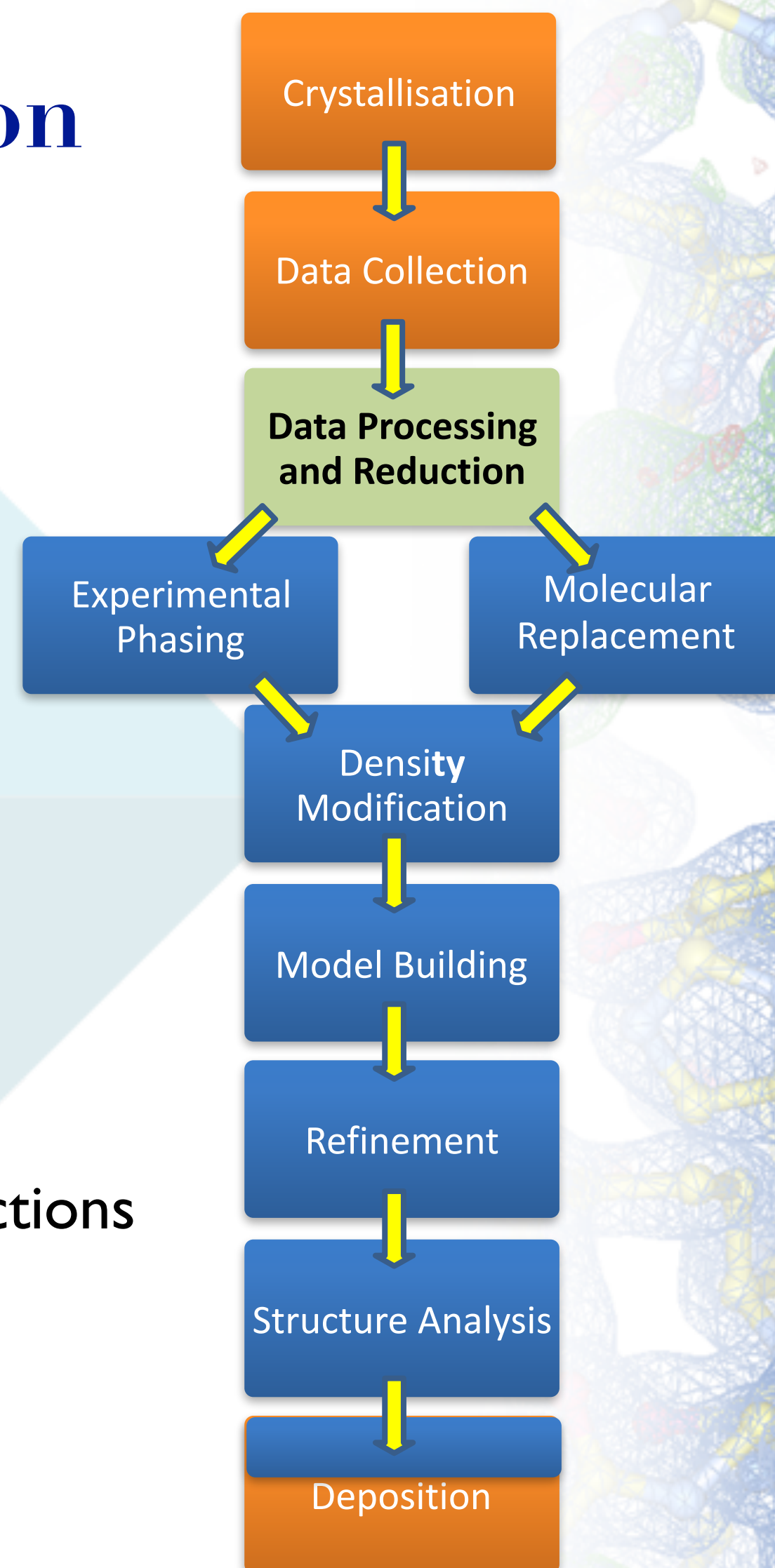
# Data Processing and Reduction

## • Data Processing:

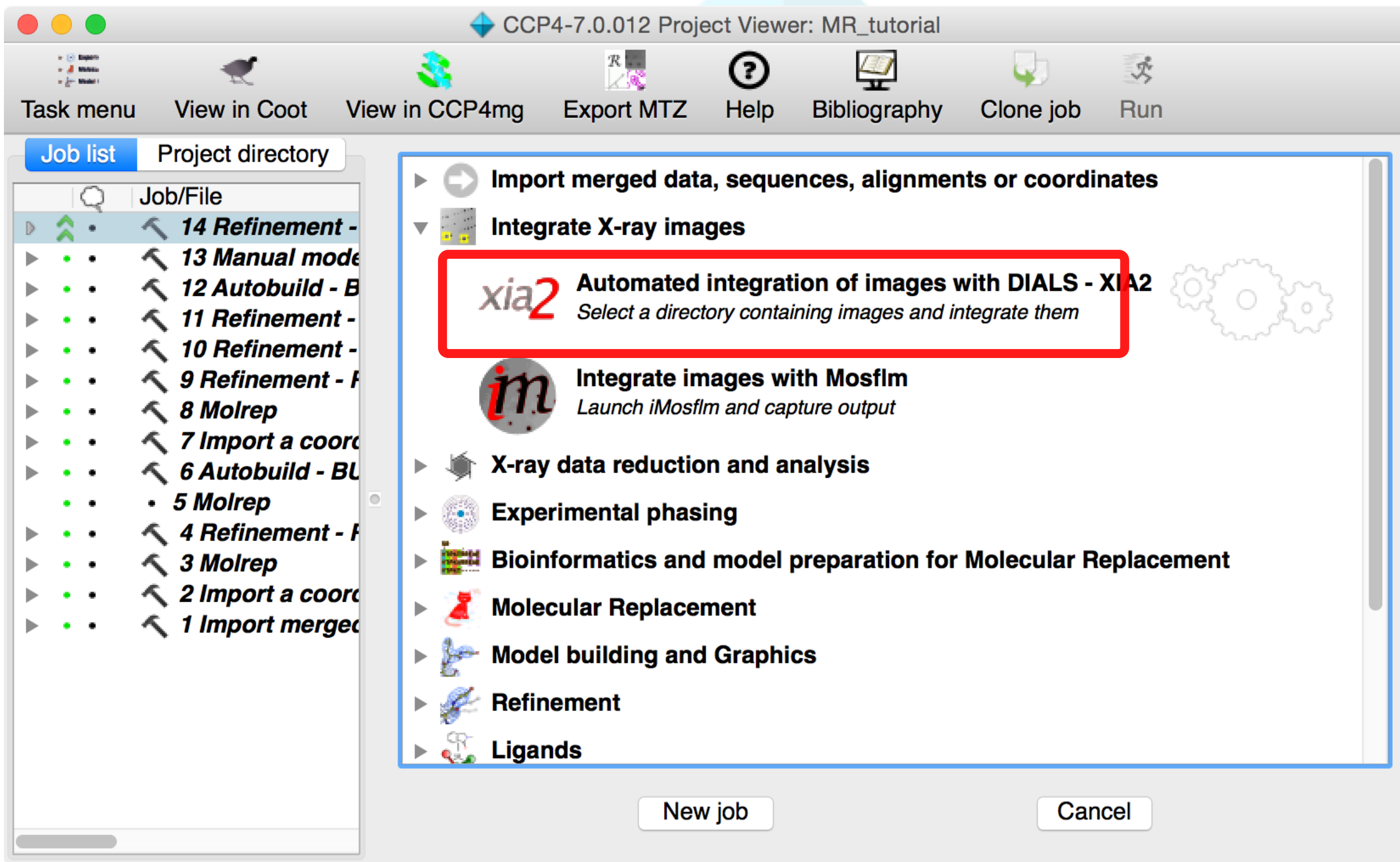
- ~ Calculate intensities from images
- ~ Initial estimation of space group and cell parameters (indexing)
- ~ Look for problems in images
  - ◆ multiple lattices,
  - ◆ weak reflections
  - ◆ mosaicity
  - ◆ anisotropy

## • Data Reduction: Scaling and merging

- ~ Scale and merge multiple observations of reflections
- ~ Assignment of point group/space group
- ~ Look for problems in images
- ~ Calculate structure factor amplitudes



# Data Processing and Reduction



**DIALS:** New data processing and data reduction tool, available through Xia-2 pipeline

**Xia-2:** Expert knowledge-based, decision-making system for automated data processing from images to merged MTZ file. Uses DIALS and XDS.

# Data Processing and Reduction

## Pointless

- Determines point-group (and space group)

## Aimless

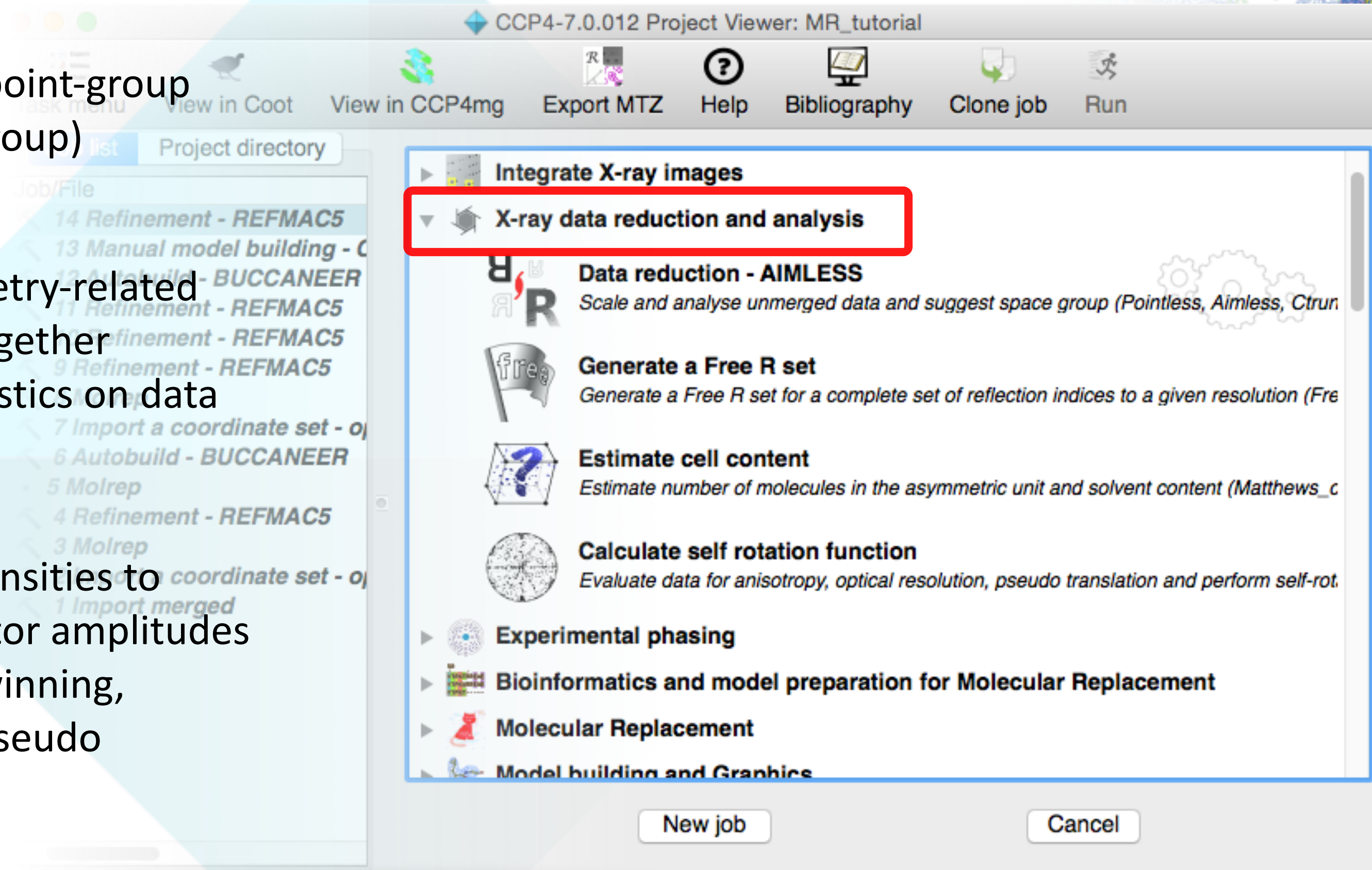
- Scales symmetry-related intensities together
- Produce statistics on data quality

## Ctruncate

- Converts intensities to structure factor amplitudes
- Checks for twinning, anisotropy, pseudo symmetry

## SFcheck

- Analyses data and check for problems – postscript report



# Phasing

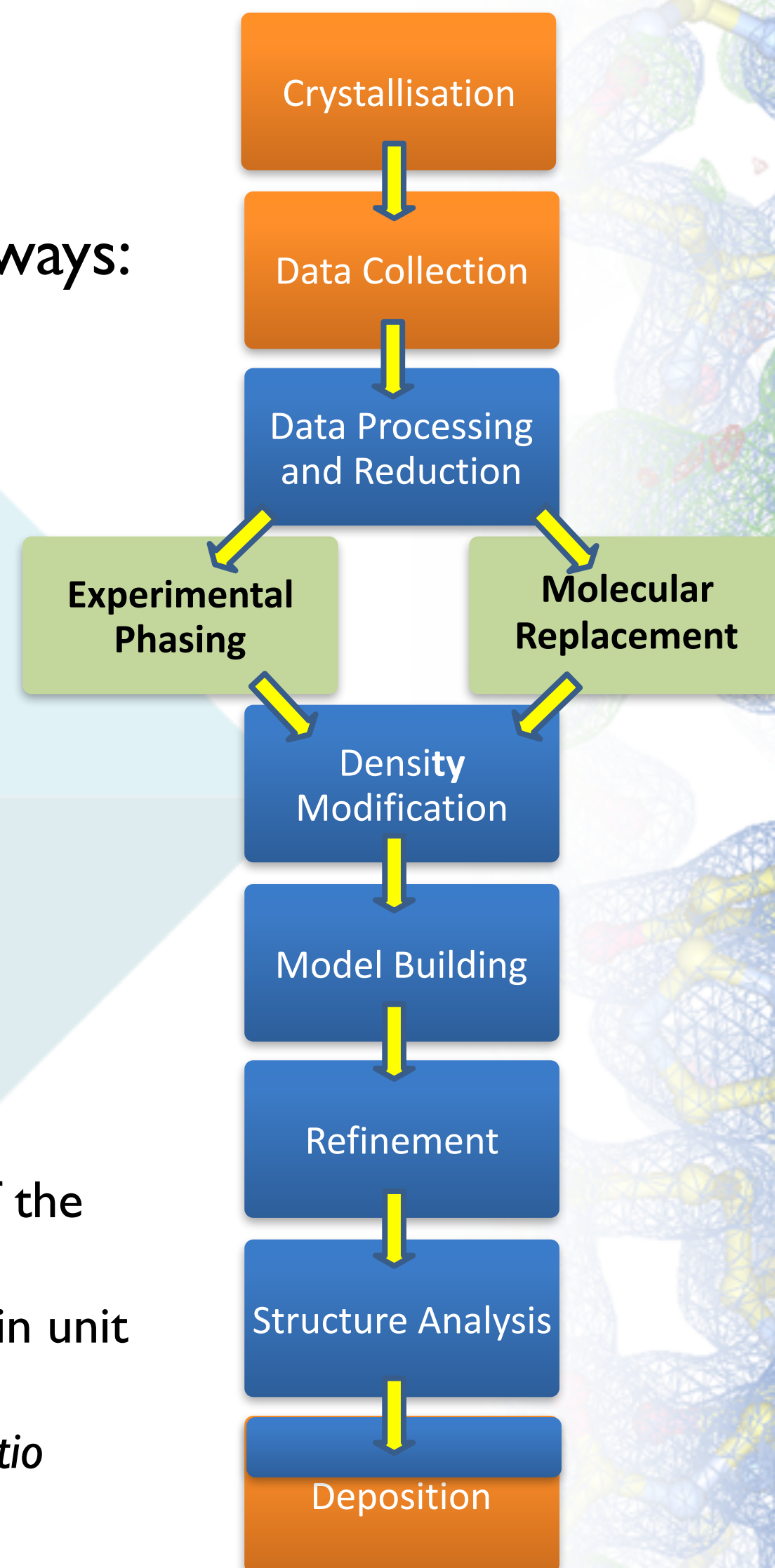
- Phase information may be derived in two main ways:

- *Experimental phasing:*

- ~ collect multiple data sets with anomalous or isomorphous differences or differences produced by radiation damage
- ~ Determine the differences in atomic structure which lead to the differences in observations — usually a heavy atom substructure
- ~ Refine the parameters of the substructure and use the observations and the substructure to estimate phases

- *Molecular Replacement:*

- ~ Use the structure of an already solved, homologous macromolecule as a first approximation for the phases of the target
- ~ Requires correct repositioning of homologous structure in unit cell of target
- ~ Can also generate homologue from sequence using *ab initio* modelling



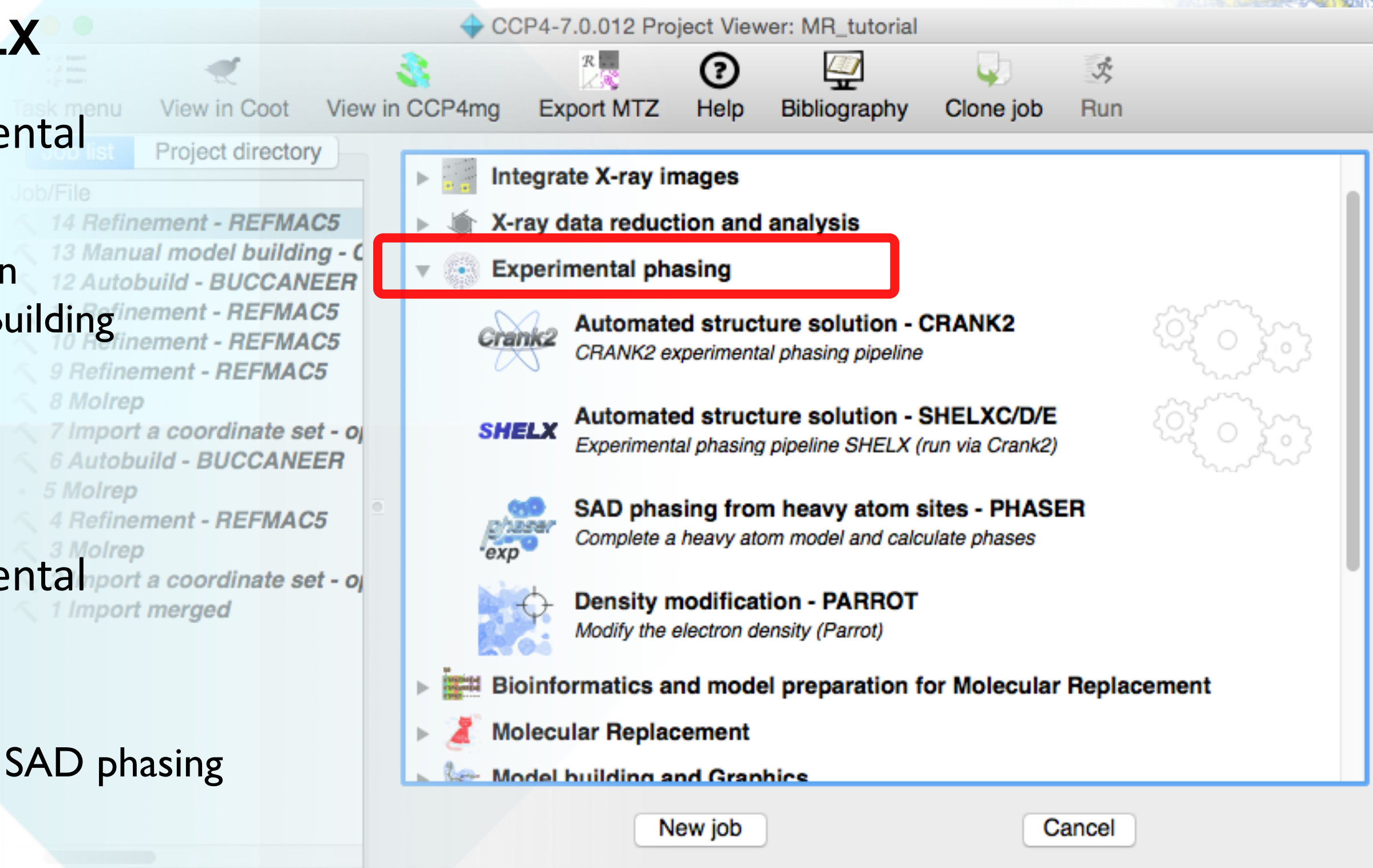
# Experimental Phasing

## Crank, Crank2 & SHELX

- Automated experimental phasing pipelines
  - ~ Heavy atom location through to Model Building
  - ~ SAD, MAD, SIRAS

## Phaser EP

- Automated experimental phasing
  - ~ SAD phasing
  - ~ Combined MR and SAD phasing



# Molecular Replacement

## Phaser MR

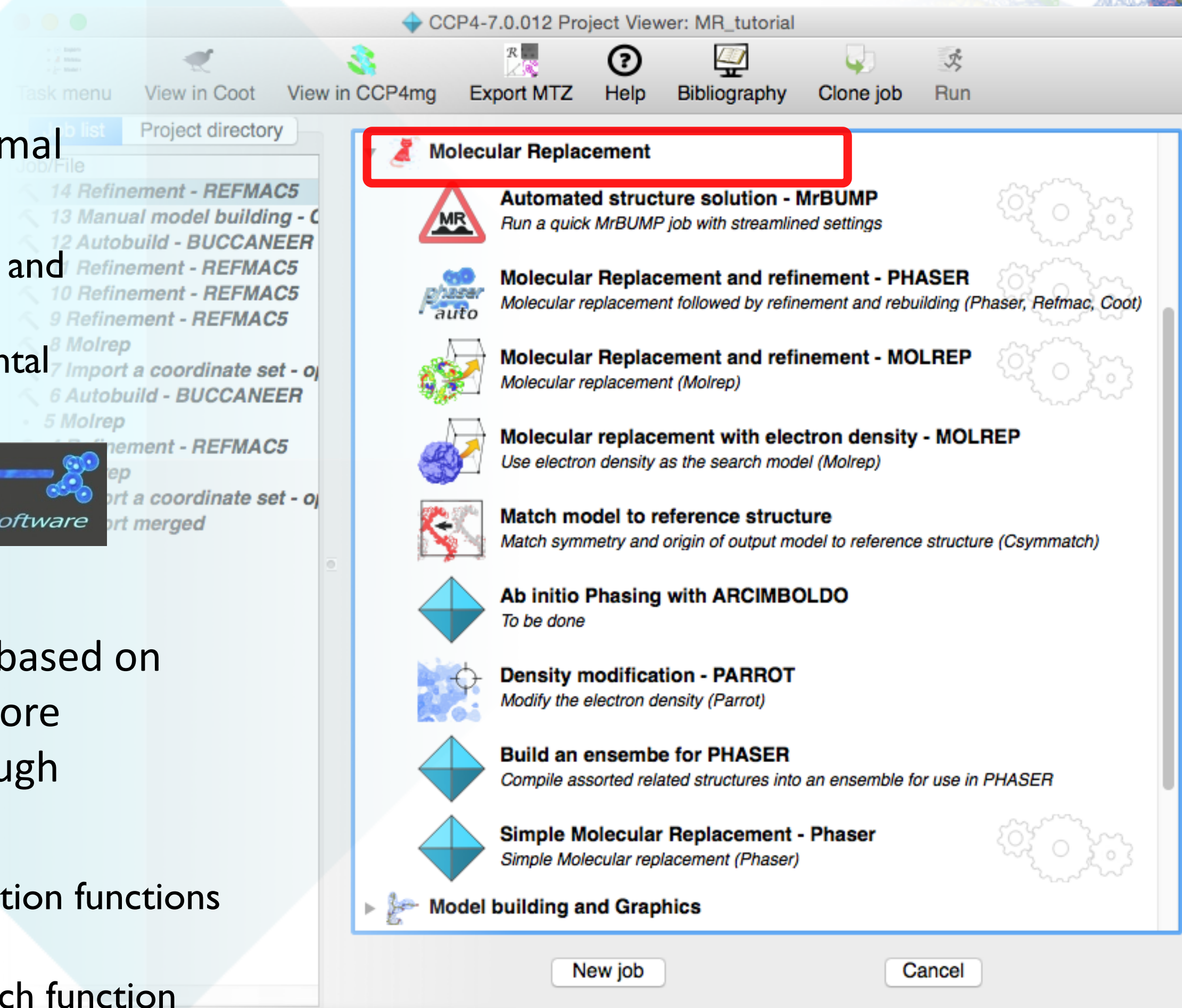
- Automated molecular replacement using Maximal Likelihood method

- ~ Sophisticated workflow and decision making
- ~ Accounts for experimental and model errors



## Molrep

- Molecular replacement based on Patterson search with more manual interaction through specialised functions
- ~ Phased Translation/Rotation functions
- ~ Multi-copy search
- ~ Spherical averaging search function



# Automatic Molecular Replacement

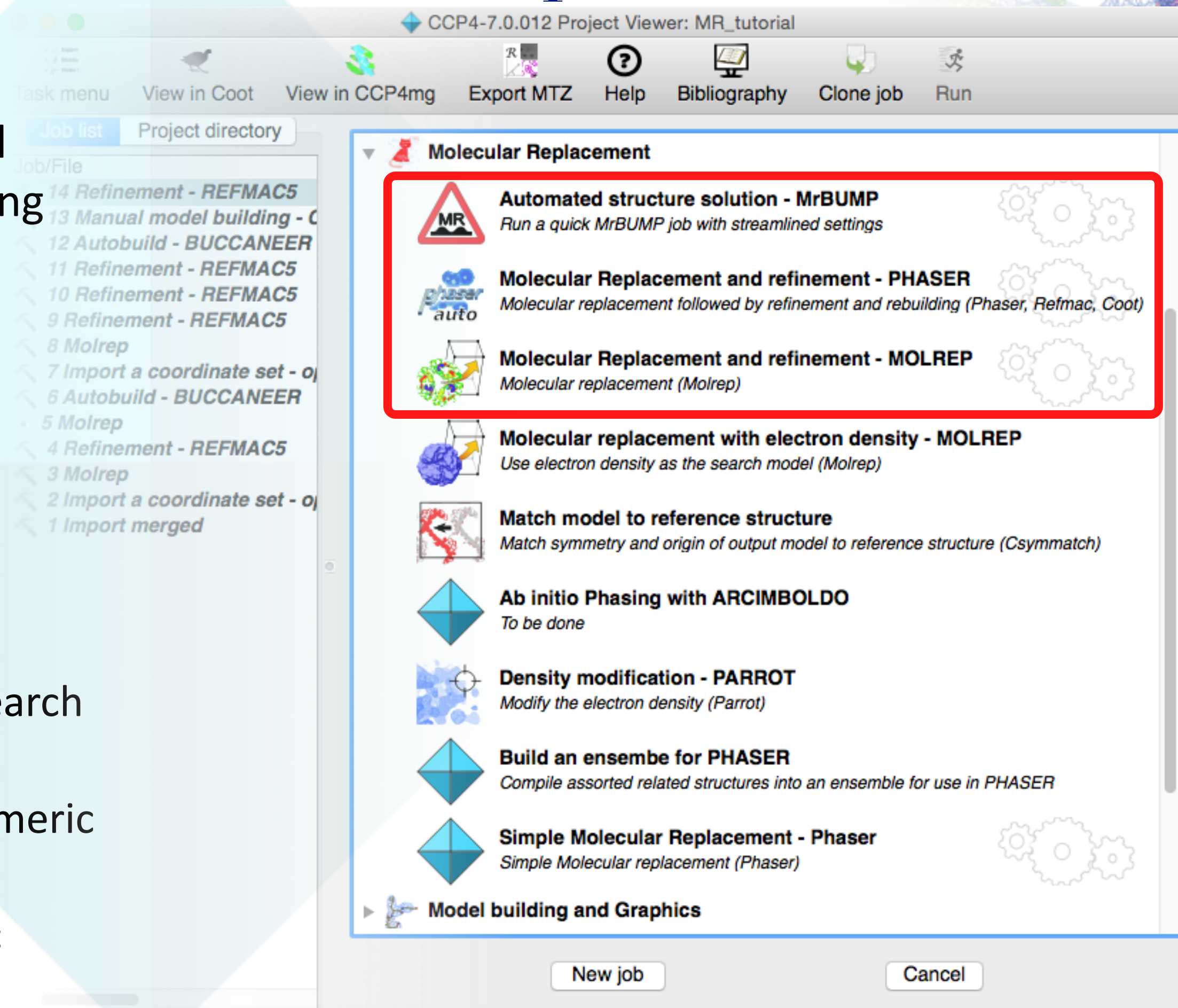
From model search and preparation through to initial refinement and model building

## MrBUMP

- Online model search
- Uses Phaser and Molrep

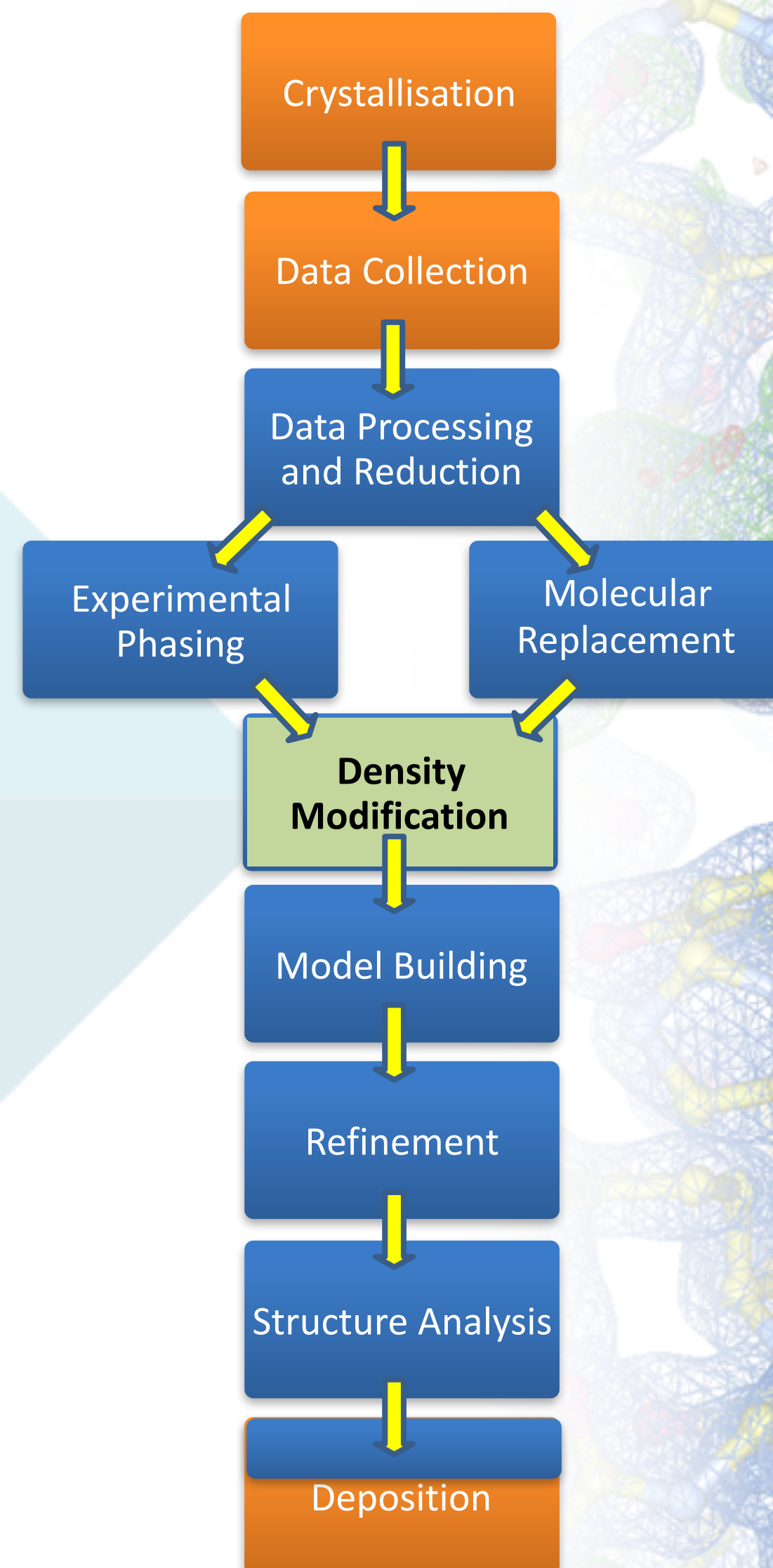
## BALBES

- Custom database with search models
- Capable of making multimeric models (uses PISA)
- Uses Molrep and Refmac



# Density Modification

- A tool for phases improvement
- *Traditional approaches:*
  - ~ NCS averaging
  - ~ Histogram matching
  - ~ Solvent flattening
  - ~ Phase combination
    - ◆ Experimental phases
    - ◆ Phases from modified map
  - ~ Iterative procedure
- *Statistical approaches:*
  - ~ Improved phase probability distributions
  - ~ Removes bias
  - ~ Slower than traditional approaches



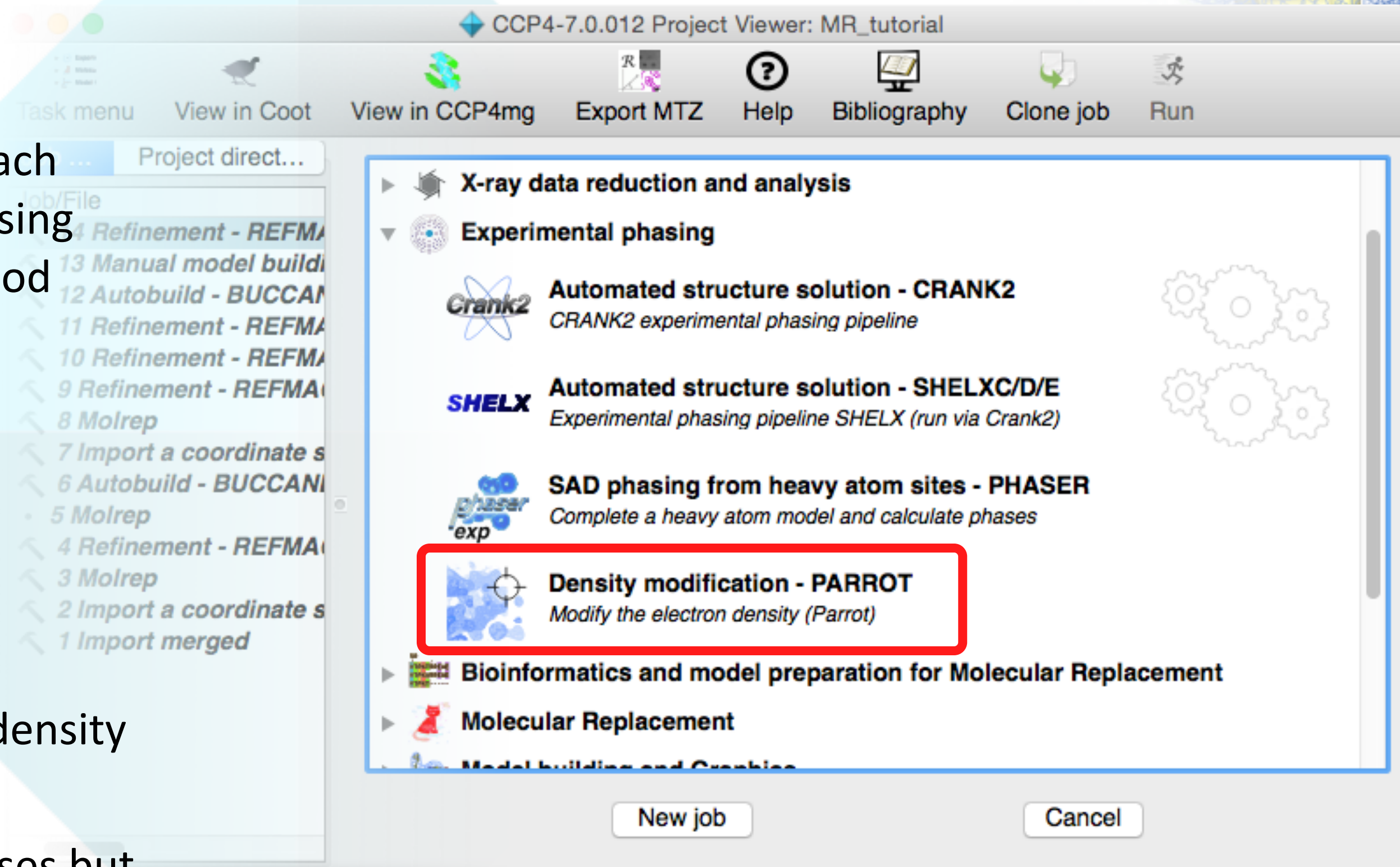
# Density Modification Tools

## Parrot

- Traditional approach benefiting from using maximum likelihood methods
- Fast and fully automated

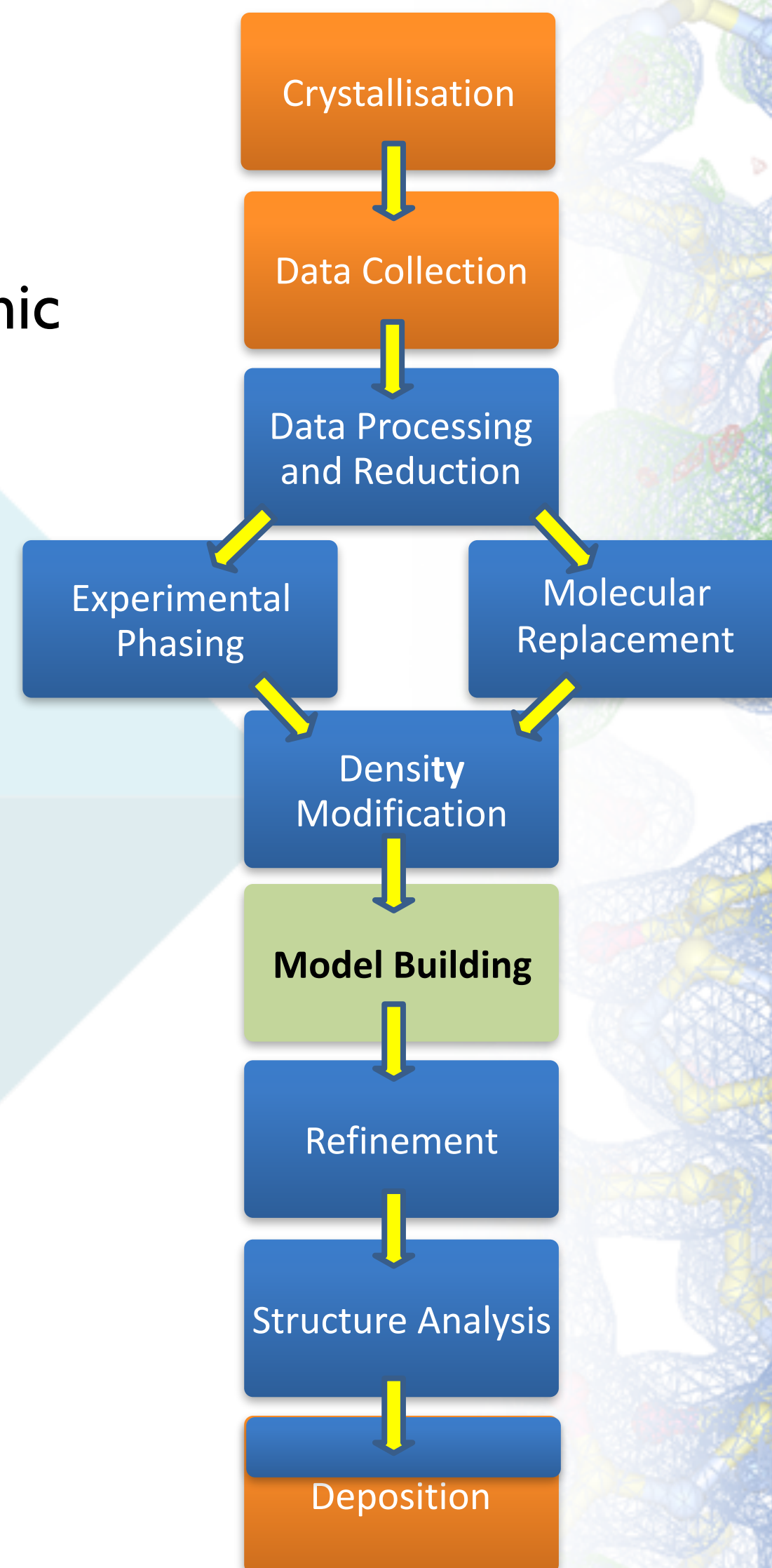
## Pirate

- Statistical-based density modification
- Better in some cases but slower than Parrot



# Model Building

- Interpret electron density map in terms of atomic coordinates
  - ~ X-ray experiment and phasing yield the electron density map
  - ~ Model's atom need to be put in the correct locations of the map
  - ~ The process is aided by the chemical knowledge of residue structure, as well as secondary structure assignments
  - ~ Validation tools are essential for choosing the right electron density interpretation:
    - ◆ Quality of density fit
    - ◆ Ramachandran restraints
    - ◆ Geometry analysis
- Try to account for as much of the density as possible including solvent molecules



# Model Building Tools

## Buccaneer

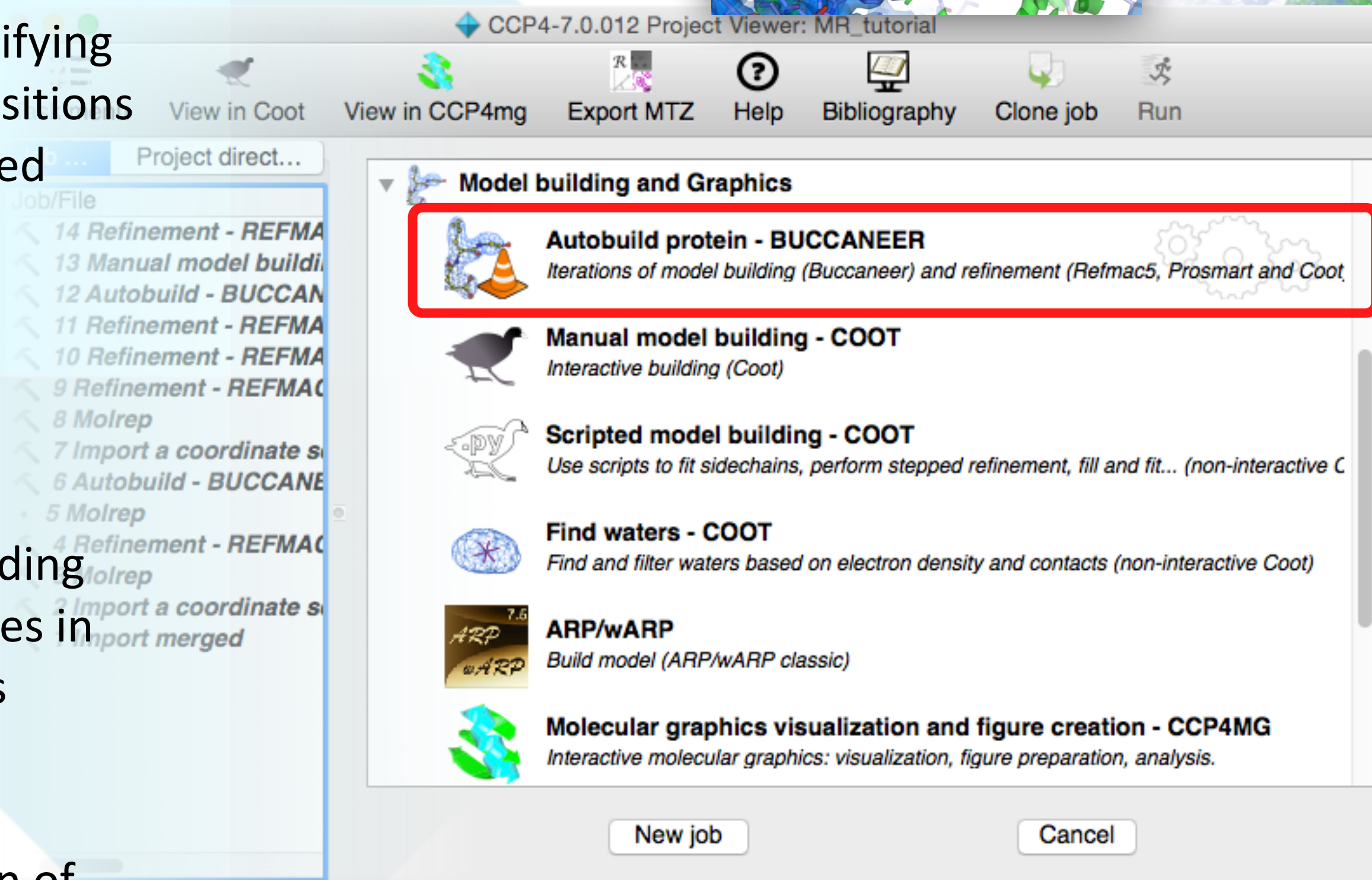
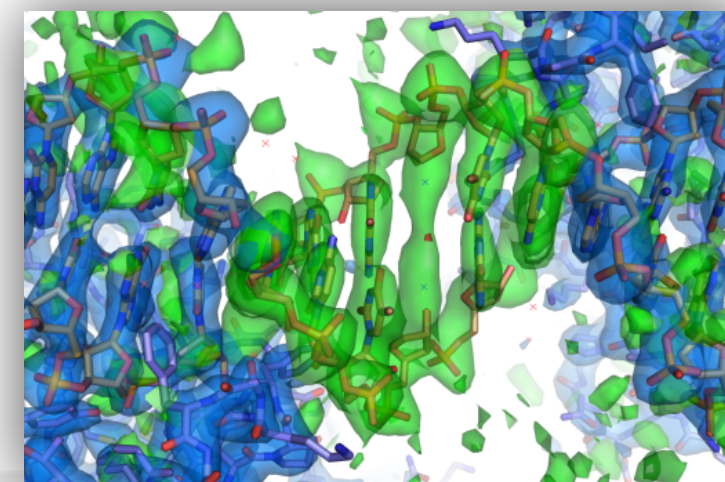
- Chain tracing by identifying connected C-alpha positions using a likelihood-based density target
- Low-resolution model building

## Nautilus

- Automatic model building of nucleotide structures in electron density maps

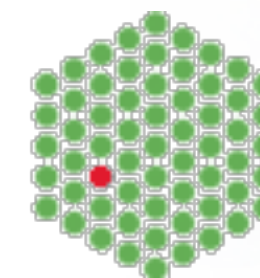
## Privateer

- Building and validation of carbohydrates



# Model Building Tools

EMBL

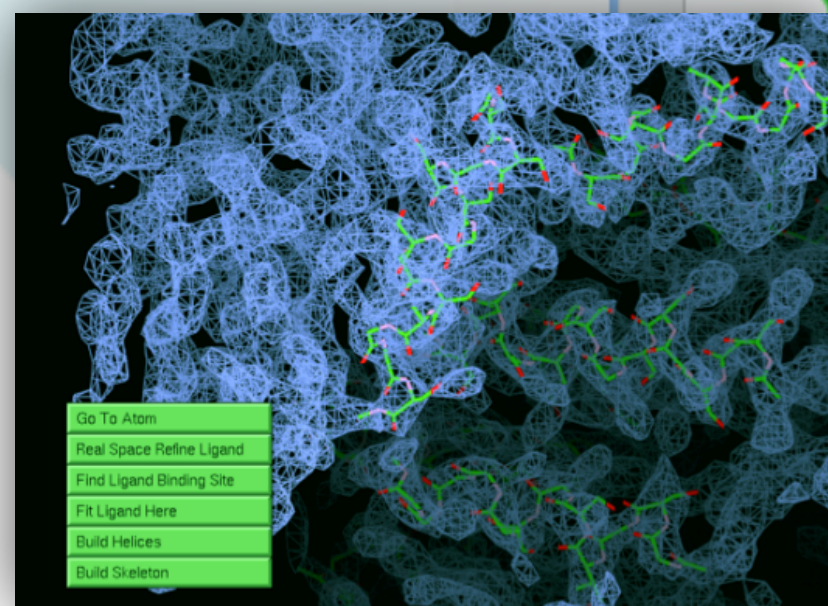
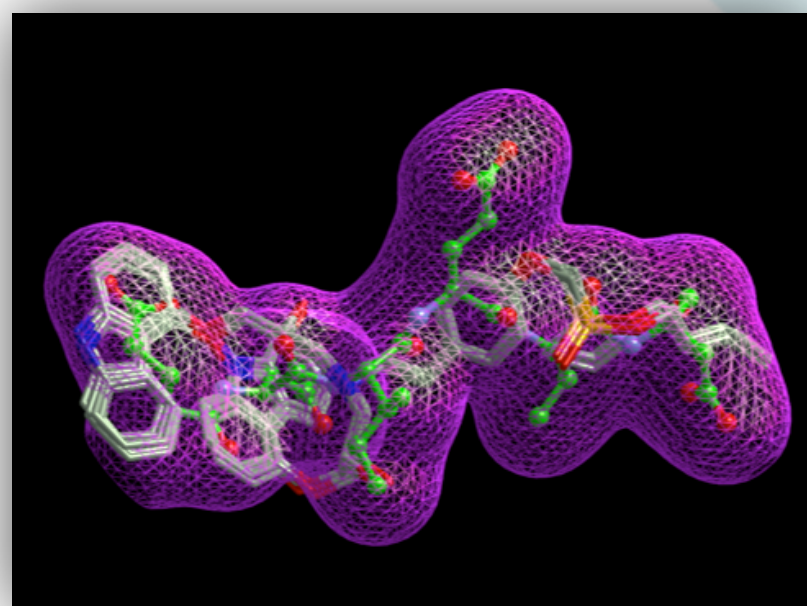
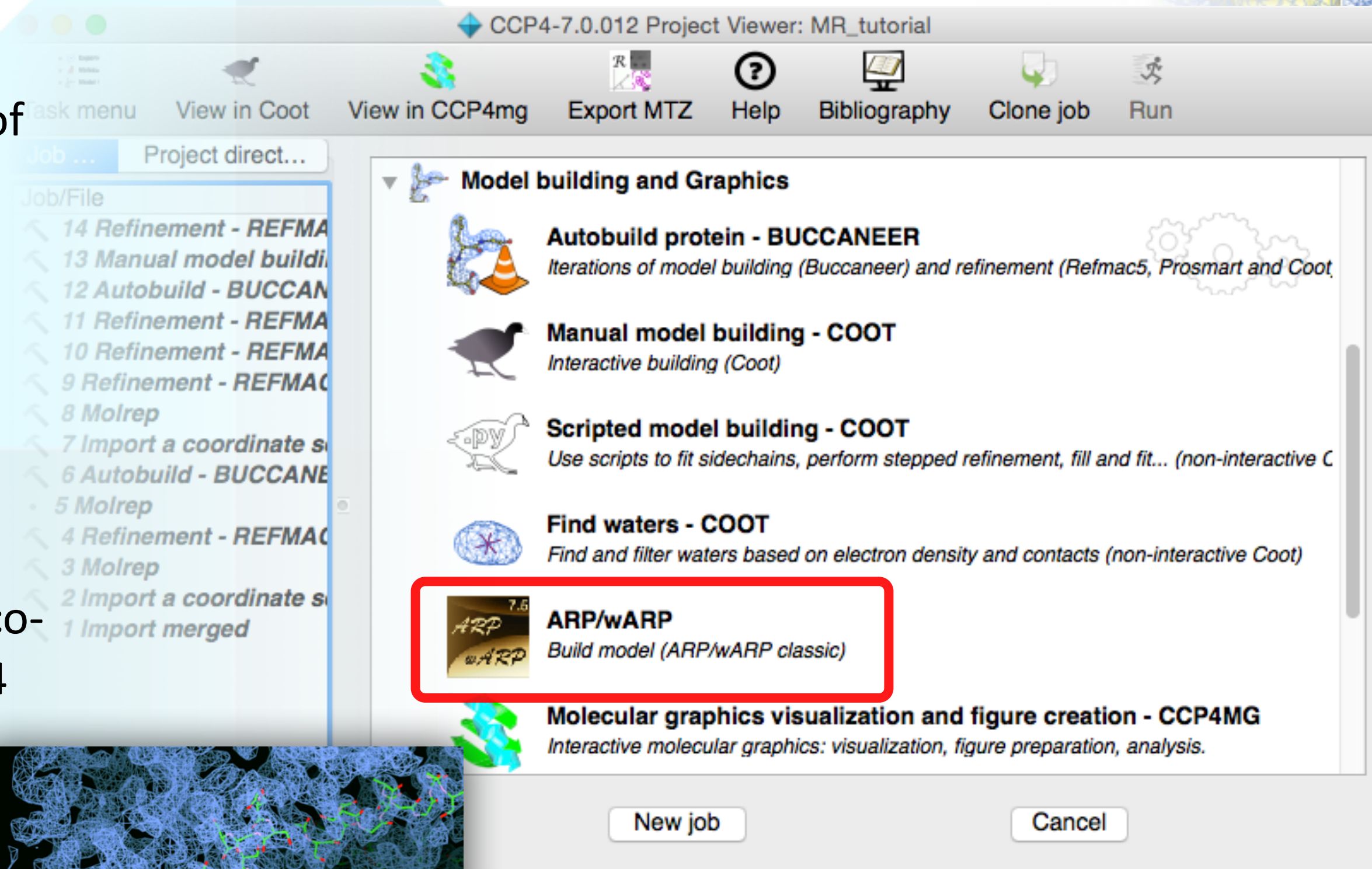


## Arp/wArp 7.6

- Automated building of

- ~ proteins
- ~ RNA/DNA
- ~ secondary structure
- ~ side chains
- ~ loops
- ~ solvent
- ~ ligands

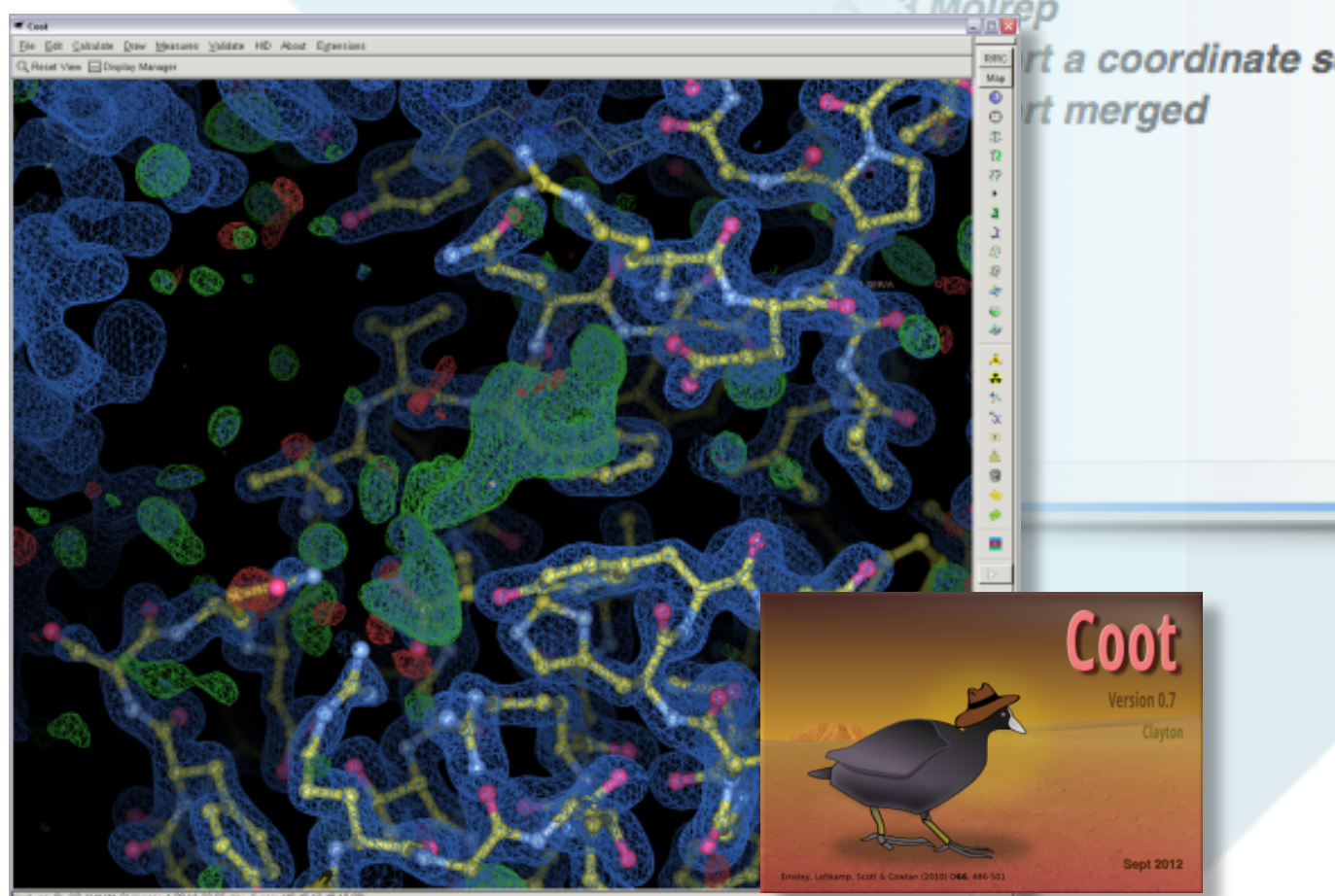
- Now integrated and co-distributed with CCP4



# Model Building Tools

## Coot 0.8.3

- Manual and semiautomatic model building
- Interactive graphics
- Ligand building and fitting
- Real-space refinement
- Paired with Refmac and jLigand
- Wealth of validation tools
- Integrated with CCP4



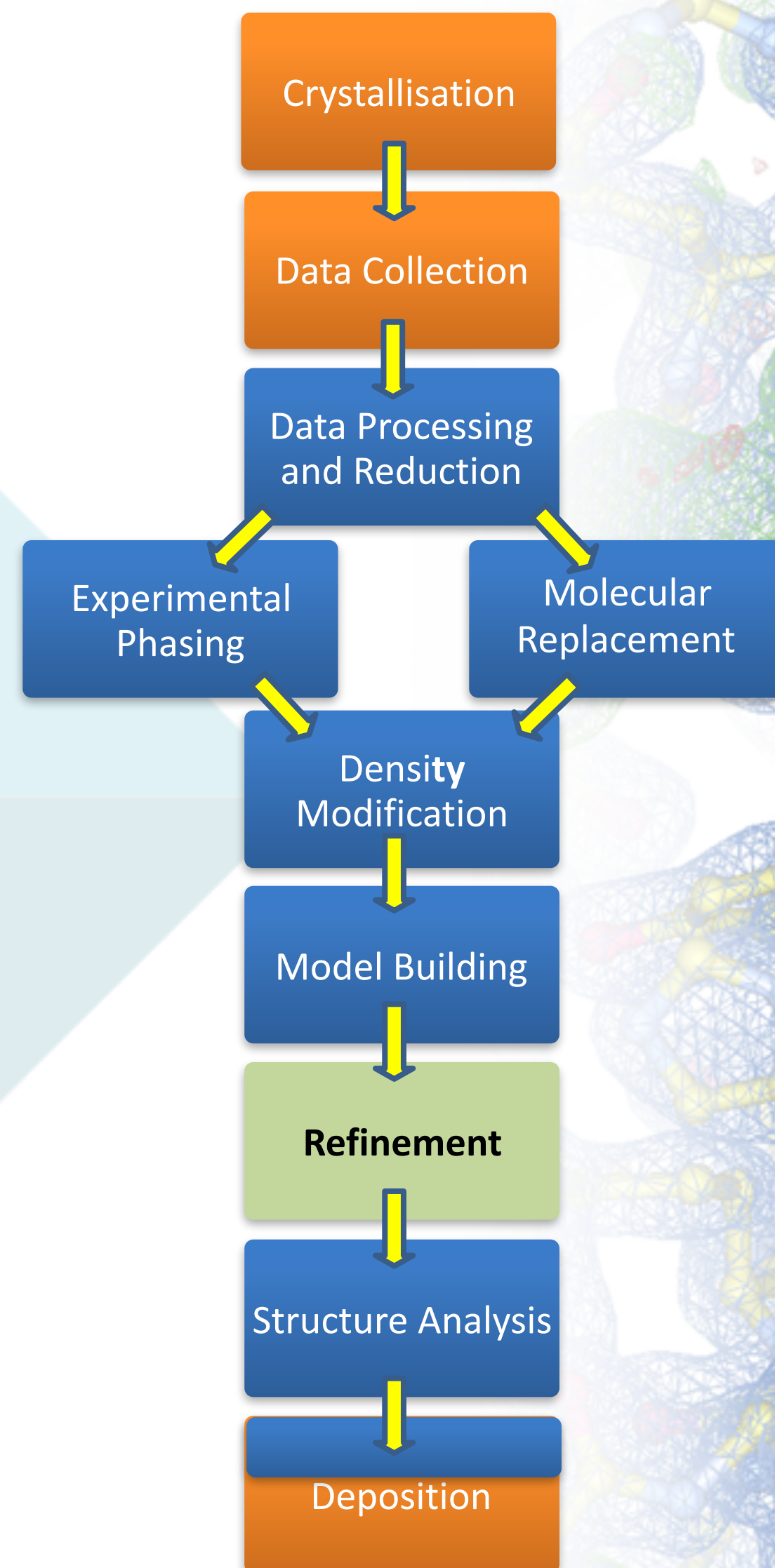
Model building and Graphics

- Autobuild protein - BUCCANEER**  
*Iterations of model building (Buccaneer) and refinement (Refmac5, ProSMART and Coot).*
- Manual model building - COOT**  
*Interactive building (Coot)*
- Scripted model building - COOT**  
*Use scripts to fit sidechains, perform stepped refinement, fill and fit... (non-interactive Coot)*
- Find waters - COOT**  
*Find and filter waters based on electron density and contacts (non-interactive Coot)*
- ARP/wARP**  
*Build model (ARP/wARP classic)*
- Molecular graphics visualization and figure creation - CCP4MG**  
*Interactive molecular graphics: visualization, figure preparation, analysis.*

New job Cancel

# Refinement

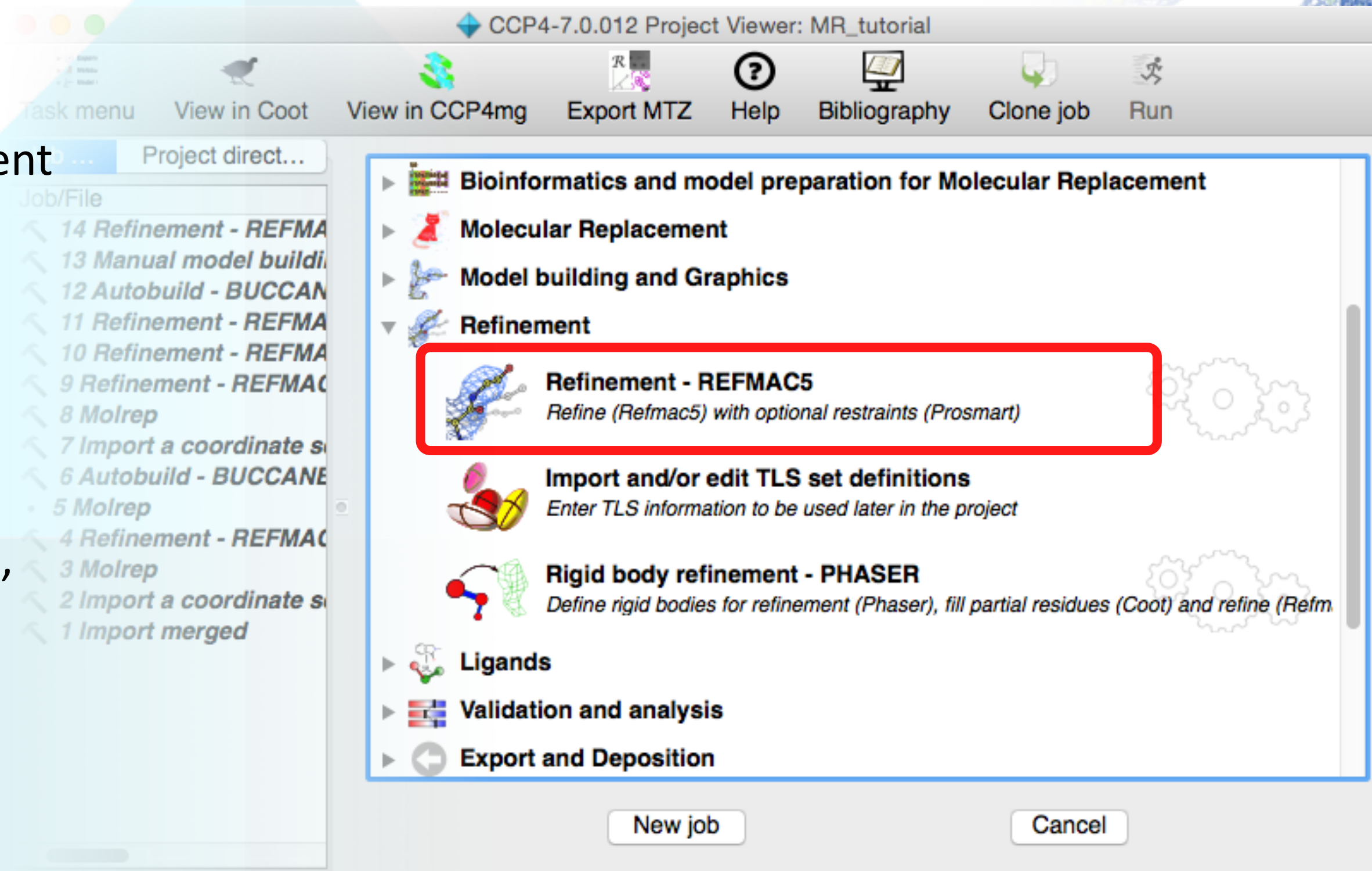
- Refinement is one of most important procedures in structure solution process
- Refinement is used mainly to
  - ~ produce a structure which is properly balanced between chemistry restraints and experimental observations
  - ~ improve density maps for further cycle of model building
- Refinement often uses additional information from various sources
  - ~ Phases
  - ~ Twinning (if detected)
  - ~ External restraints
  - ~ NCS restraints
  - ~ TLS groups



# Refinement

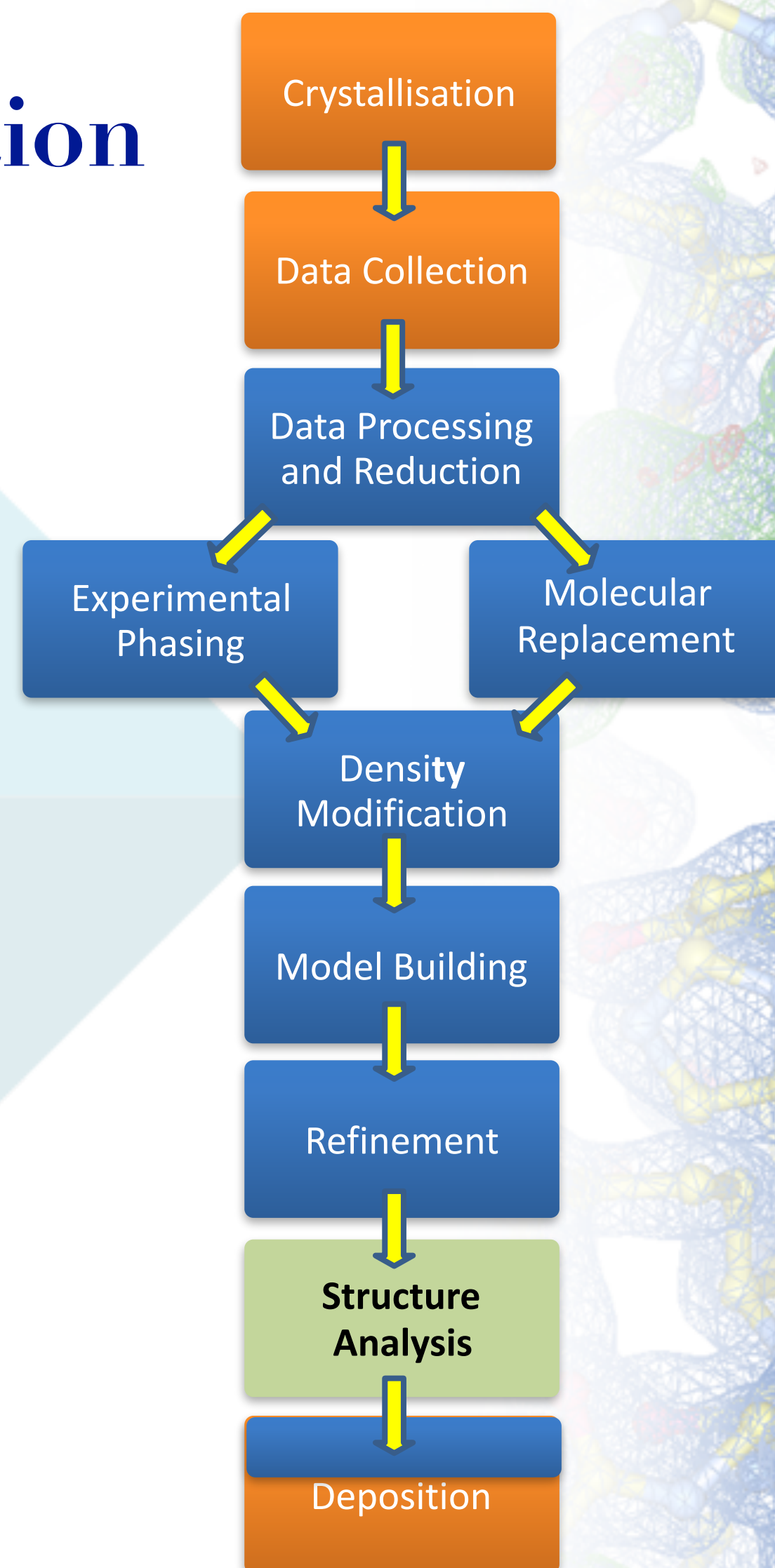
## Refmac 5.8

- CCP4's main refinement program
- Implements several likelihood target functions for experimental data (amplitudes, twinned data, external phases, Lattman coefficients)
- Restraints
  - ~ CCP4 monomer library
  - ~ Custom library
  - ~ External restraints
- Several refinement protocols
  - ~ Rigid body
  - ~ Restrained
  - ~ Jelly-body
- NCS refinement
  - ~ local
  - ~ global



# Structure Analysis & Visualisation

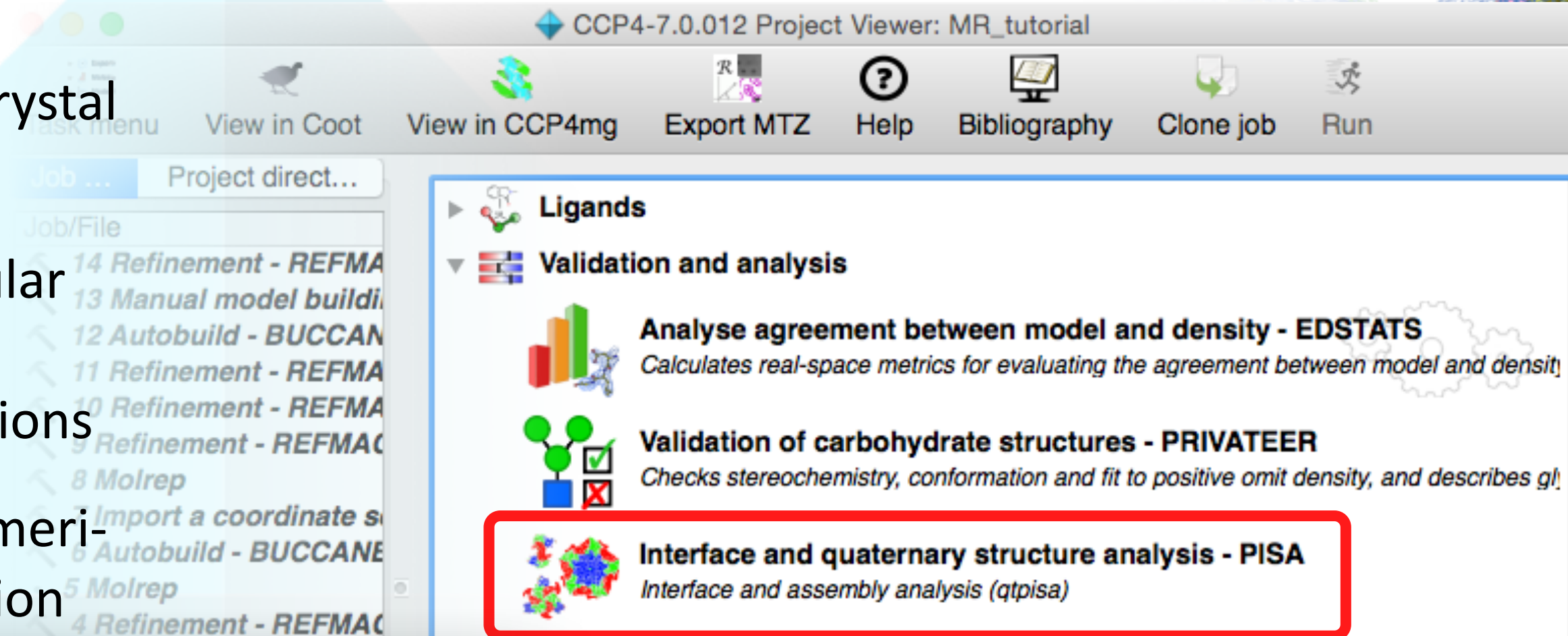
- To find out structural features which may shed light on chemical activity or structure function
- Identification of complexes (quaternary structures)
- Finding and comparing homologues
- Visualise and inspect the target structure
- Can also be used earlier on in structure solution process
- ~ Provide information on complexes, domains, mobility of structure for use in molecular replacement or for construct design



## PISA

## Structure Analysis

- Automatic inference on multimeric states from crystal packing
- Analysis of macromolecular interfaces and macromolecular interactions
- Analysis of protein oligomerisation versus concentration



QtPISA 1.12 25/06/2012 [PDB => 1nio]

File View Help

Contents

- Data
- Monomers
- Interfaces
- Assemblies
  - Stable
    - 1. A(2)
    - 2. a
    - 3. a
    - 4. a
    - 5. A(2)
    - 6. a
    - 7. a
    - 8. a
  - Grey area
  - Unstable
  - As given

**Assembly summary**

|                      |      |                     |           |                                       |        |
|----------------------|------|---------------------|-----------|---------------------------------------|--------|
| Multimeric state     | 2    | Surface area, sq. A | 6561404.6 | Free energy of dissociation, kcal/mol | 8910.2 |
| Copies in Unit Cell  | 2    | Buried area, sq. A  | 561296.4  | Entropy of dissociation, kcal/mol     | 71.5   |
| Symmetry number      | 2    |                     |           |                                       |        |
| Formula              | A(2) |                     |           |                                       |        |
| Composition          | A(2) |                     |           |                                       |        |
| Dissociation pattern | 2{A} |                     |           |                                       |        |

**Engaged interfaces**

|   | Monomer 1 | Monomer 2 | Spec. | Sym. op-n   | Sym. ID | Area     | Delta G | P-value | Nhb | Nsb | Nds |
|---|-----------|-----------|-------|-------------|---------|----------|---------|---------|-----|-----|-----|
| 4 | A         | A         | 1*    | -X-1,Y,-Z+1 | 2_456   | 280648.2 | -8980.7 | 0.339   | 2   | 0   | 0   |

**Assembled monomers**

|   | Monomer | Class   | Type | Sym. op-n   | Sym. ID | Area      | BSA      | Delta G | Nhb | Nsb | Nds |
|---|---------|---------|------|-------------|---------|-----------|----------|---------|-----|-----|-----|
| 1 | A       | Protein | 1    | X,Y,Z       | 1_555   | 3561350.5 | 280648.2 | -4490.4 | 2   | 0   | 0   |
| 2 | A       | Protein | 1    | -X-1,Y,-Z+1 | 2_456   | 3561350.5 | 280648.2 | -4490.4 | 2   | 0   | 0   |

- QtPisa – QT based interface

# Validation and Deposition

## Coot

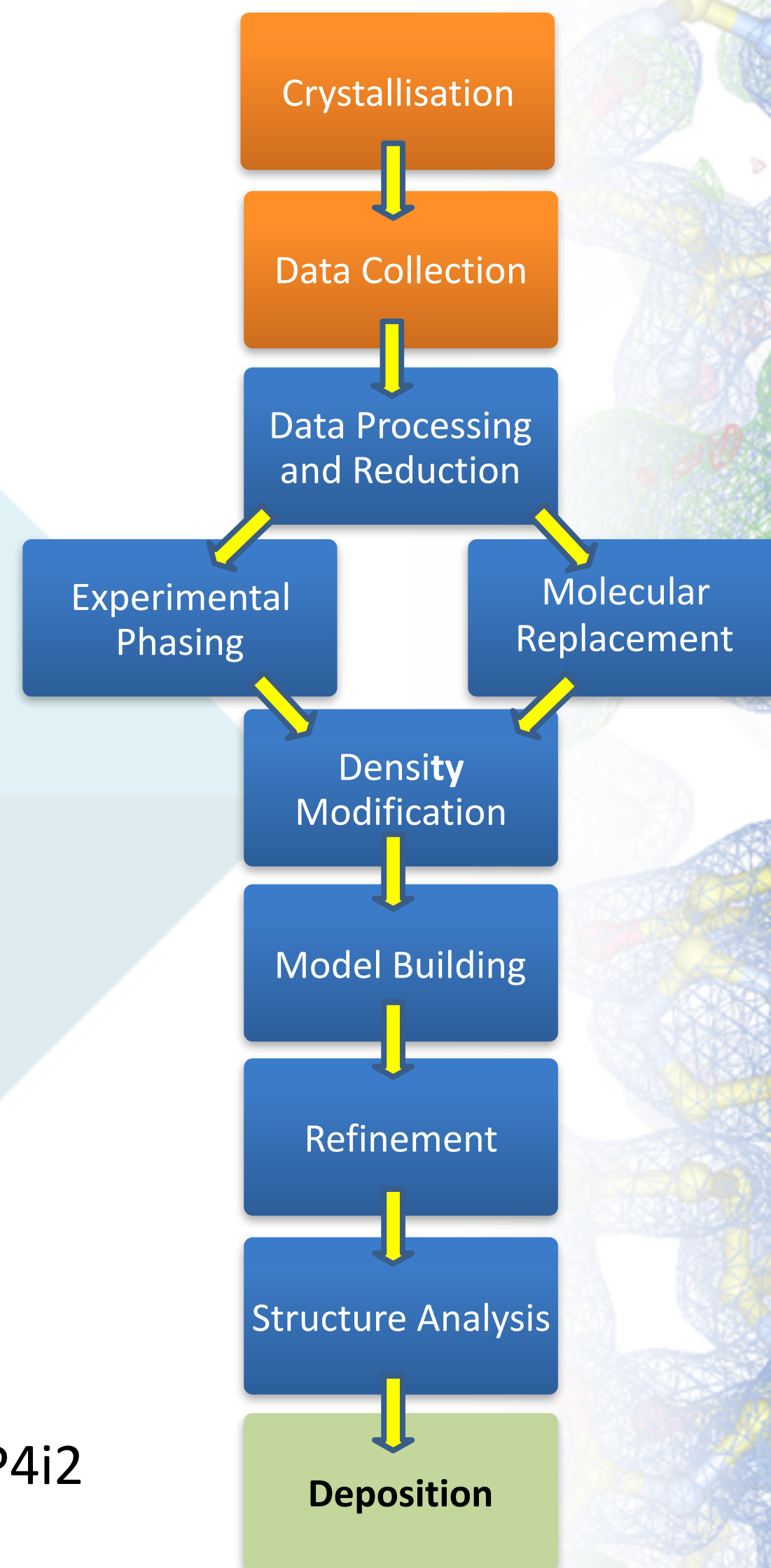
- Comprehensive set of validation tools: Ramachandran plots, density fit analysis, geometry analysis, unmodelled blobs etc.

## PDB\_REDO

- Optimisation of refinement parameters: weighting of X-ray terms, B-factors
- Checking rotomers
- Comparison of refinement with rest of PDB statistics

## Deposition

- Dedicated deposition preparation module in CCP4i2



# Command Line Operation

## Example:

*refmac5 HKLIN my.mtz HKLOUT output.mtz XYZIN my.pdb XYZOUT output.pdb*

## Keywords:

- Most CCP4 programs take “keywords” as command options through standard input to the program
- Gives access to all options of the program and the most fine-grained control
- Can be provided through ccp4i using “**Run & view com file**”

## Scripting:

- Repetitive tasks can be scripted
- Pipelines of programs can be created in a script

**Command  
line**

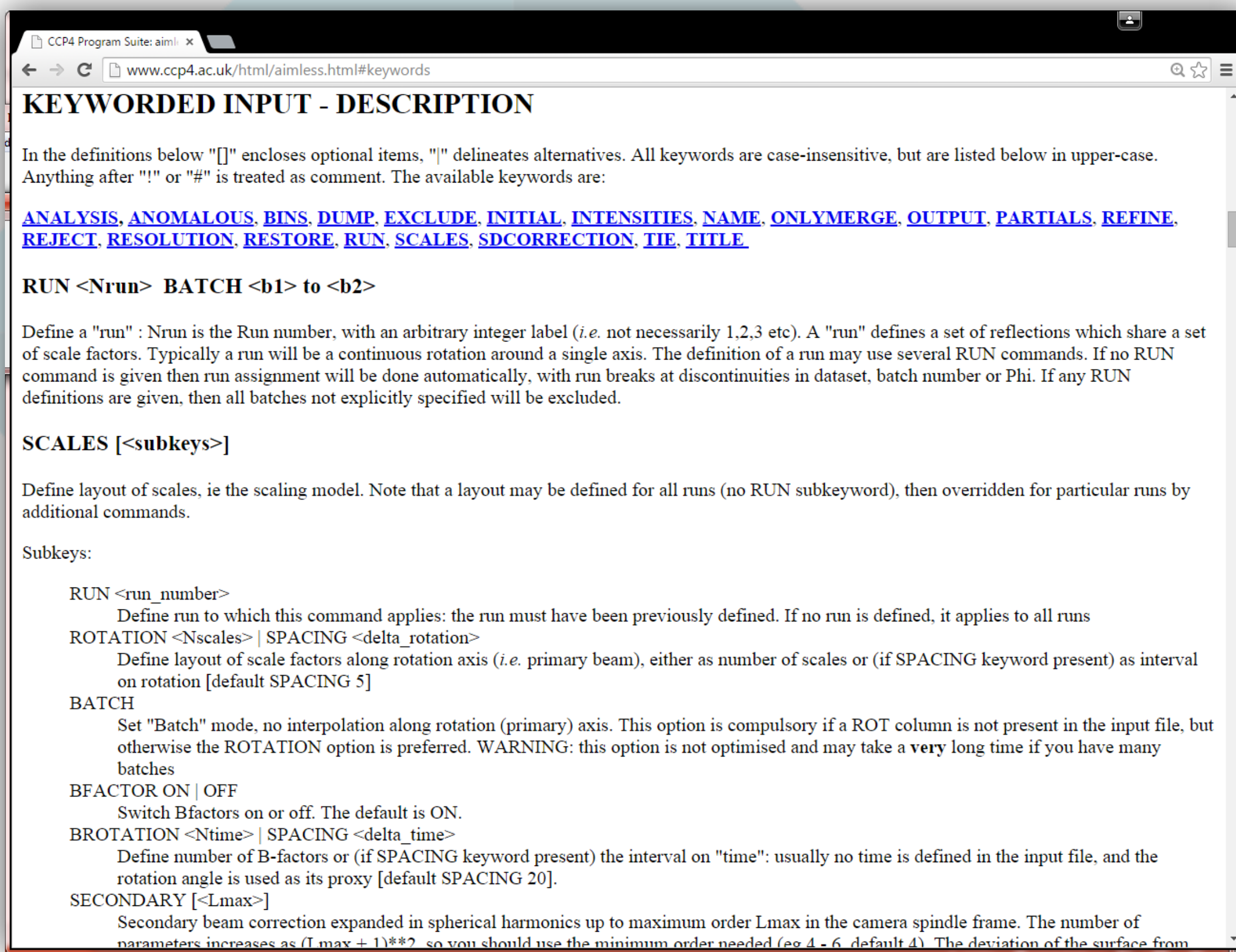
```
f2mtz hklin ${1} hklout shelxe-output.mtz << eof
```

```
TITLE ample  
cell      ${cell}  
symm      ${symm}  
labout    H K L F FOM PHI SIGF  
CTYPOUT   H H H F W P Q  
pname     ample  
dname     ample  
END
```

**Keywords**

# Command Line Operation

- Documentation for CCP4 program keywords provided by documentation pages online or in the suite (`$CCP4/html/INDEX.html`):



CCP4 Program Suite: aiml

www.ccp4.ac.uk/html/aimless.html#keywords

## KEYWORDED INPUT - DESCRIPTION

In the definitions below "[]" encloses optional items, "|" delineates alternatives. All keywords are case-insensitive, but are listed below in upper-case. Anything after "!" or "#" is treated as comment. The available keywords are:

[ANALYSIS](#), [ANOMALOUS](#), [BINS](#), [DUMP](#), [EXCLUDE](#), [INITIAL](#), [INTENSITIES](#), [NAME](#), [ONLYMERGE](#), [OUTPUT](#), [PARTIALS](#), [REFINE](#), [REJECT](#), [RESOLUTION](#), [RESTORE](#), [RUN](#), [SCALES](#), [SDCORRECTION](#), [TIE](#), [TITLE](#)

### RUN <Nrun> BATCH <b1> to <b2>

Define a "run" : Nrun is the Run number, with an arbitrary integer label (*i.e.* not necessarily 1,2,3 etc). A "run" defines a set of reflections which share a set of scale factors. Typically a run will be a continuous rotation around a single axis. The definition of a run may use several RUN commands. If no RUN command is given then run assignment will be done automatically, with run breaks at discontinuities in dataset, batch number or Phi. If any RUN definitions are given, then all batches not explicitly specified will be excluded.

### SCALES [<subkeys>]

Define layout of scales, i.e. the scaling model. Note that a layout may be defined for all runs (no RUN subkeyword), then overridden for particular runs by additional commands.

Subkeys:

**RUN <run\_number>**  
Define run to which this command applies: the run must have been previously defined. If no run is defined, it applies to all runs

**ROTATION <Nscale> | SPACING <delta\_rotation>**  
Define layout of scale factors along rotation axis (*i.e.* primary beam), either as number of scales or (if SPACING keyword present) as interval on rotation [default SPACING 5]

**BATCH**  
Set "Batch" mode, no interpolation along rotation (primary) axis. This option is compulsory if a ROT column is not present in the input file, but otherwise the ROTATION option is preferred. WARNING: this option is not optimised and may take a very long time if you have many batches

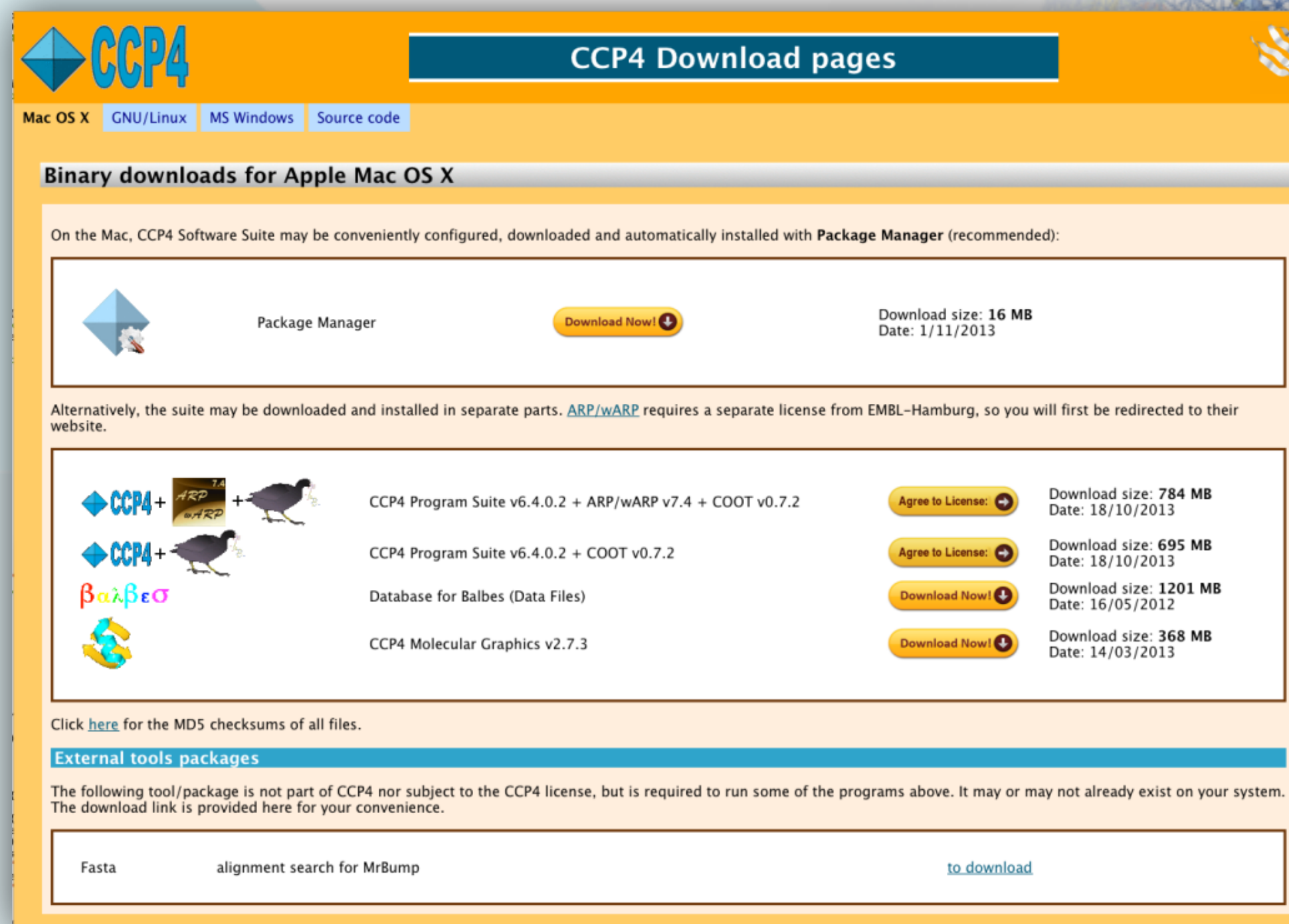
**BFACTOR ON | OFF**  
Switch Bfactors on or off. The default is ON.

**BROTATION <Ntime> | SPACING <delta\_time>**  
Define number of B-factors or (if SPACING keyword present) the interval on "time": usually no time is defined in the input file, and the rotation angle is used as its proxy [default SPACING 20].

**SECONDARY [<Lmax>]**  
Secondary beam correction expanded in spherical harmonics up to maximum order Lmax in the camera spindle frame. The number of parameters increases as  $(L_{max} + 1) * 2$ , so you should use the minimum order needed (e.g. 4 - 6, default 4). The deviation of the surface from

# Downloading the Suite

- Download CCP4 for Windows, Mac or Linux
- Co-distribution of ARP/wARP
- Package Manager – easy installation
- Only 64-bit version for Mac OSX, both 32-bit and 64-bit versions for other systems
- Additional software dependencies also available
- Download page accessible from <http://www.ccp4.ac.uk>



The screenshot shows the CCP4 Download pages website. The header includes the CCP4 logo and navigation tabs for Mac OS X, GNU/Linux, MS Windows, and Source code. The main content area is titled "Binary downloads for Apple Mac OS X" and provides instructions for downloading the CCP4 Software Suite. It offers two options: downloading the entire suite via Package Manager (recommended) or downloading individual components. The Package Manager option includes a "Download Now!" button and details: Download size: 16 MB, Date: 1/11/2013. The individual components section lists four options with their respective download sizes and dates:

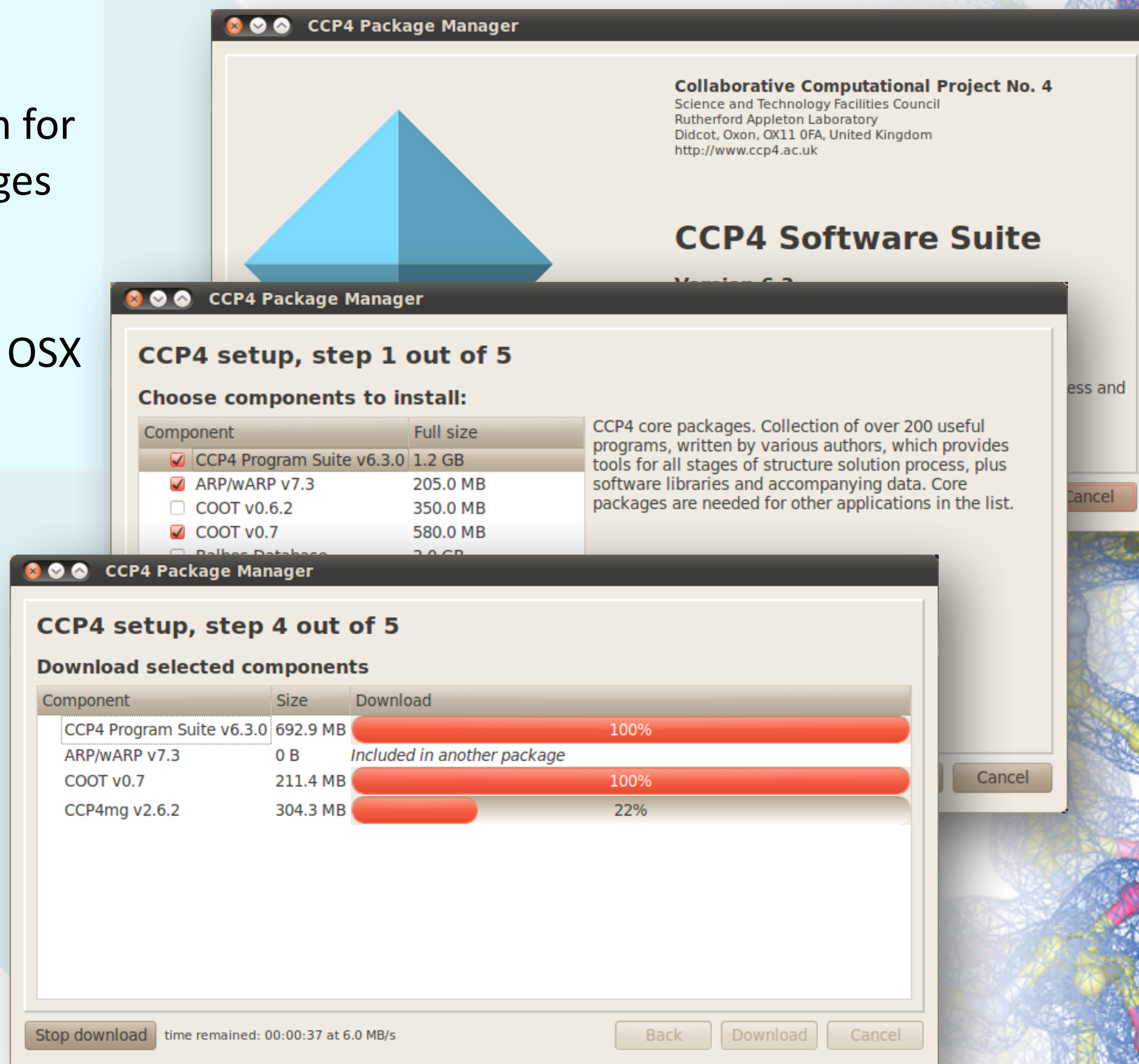
| Component                                                 | Download size | Date       |
|-----------------------------------------------------------|---------------|------------|
| CCP4 Program Suite v6.4.0.2 + ARP/wARP v7.4 + COOT v0.7.2 | 784 MB        | 18/10/2013 |
| CCP4 Program Suite v6.4.0.2 + COOT v0.7.2                 | 695 MB        | 18/10/2013 |
| Database for Balbes (Data Files)                          | 1201 MB       | 16/05/2012 |
| CCP4 Molecular Graphics v2.7.3                            | 368 MB        | 14/03/2013 |

Below the download links, there is a section for "External tools packages" which includes a link to download Fasta alignment search for MrBump.



# CCP4 Setup Manager

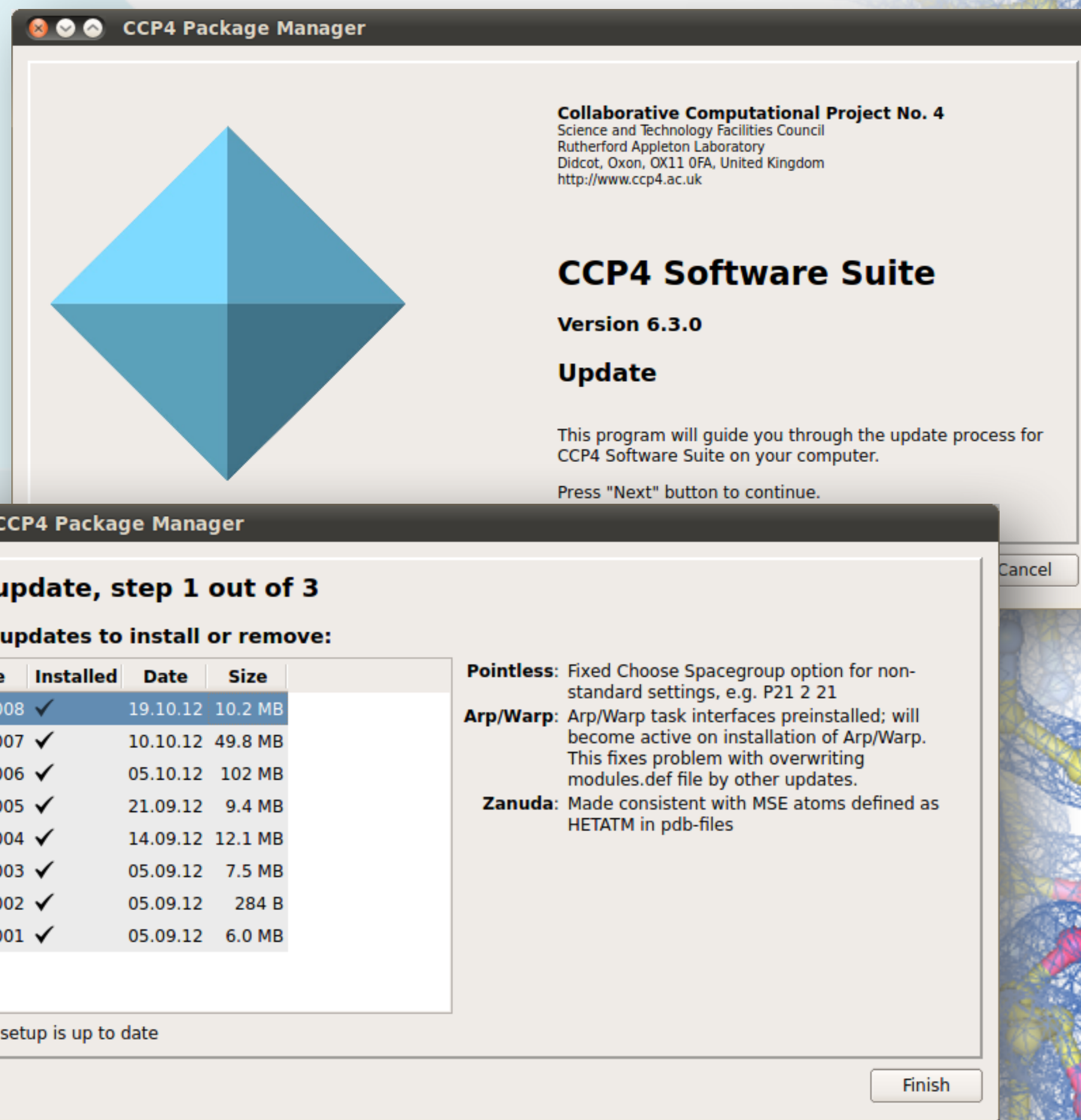
- Easy installation mechanism for CCP4 and associated packages (Coot, ARP/wARP, CCP4mg)
- Available on Linux and Mac OSX platforms
- Sets up system variables automatically if you wish





# Update Manager

- Automatically install latest fixes and new features
- Allows for rolling back to previous versions
- Updates made available once every two weeks or as and when they are needed
- Available on Linux, Mac OSX and Windows



## CCP4 on-line services

<http://www.ccp4.ac.uk/ccp4online>

### Welcome to CCP4 online

Login

Other Options - [Register](#), [Forgot](#)

#### Runnable programs

The following programs and pipelines are available:

##### Balbes

An automated Molecular Replacement pipeline that searches for the components necessary for a successful search.

##### MrBUMP

An automated Molecular Replacement pipeline that searches for the structure factors, it will search for the template structure and restrained refinement.

##### Zanuda

Space group and crystallographic data analysis.

##### jsPISA

Calculation and analysis of protein-protein interfaces.

##### AMPLE

Automated ab initio search for a protein structure.

##### SHELX

Automated SHELXC/D/E steps for data in XDS, Scalepack, SHARPE, etc. protein sequence is provided.

##### CRANK2

Automated structure solution using CRANK2.

**BETA**



Collaborative Computational Project No. 4  
Software for Macromolecular X-Ray Crystallography

Home (Logout) > Login > Programs > MrBUMP > New MrBUMP Run

### New MrBUMP Run

The file formats accepted for input are **mtz** and **cif** (structure factors).

Structure Factors:  No file

Sequence Target:  No file

Instead of entering a file name, you can enter a PDB ID (Note that a comment is required for the PDB ID).

I have the SHELX licence (optional): ☐ (You can get the licence from the SHELX website)

(after clicking submit, **PLEASE WAIT** for your files to be processed)



jsPISA 2.0.3 [PDB 1e94]

Print Refresh Help

Input Monomers Interfaces Stock Crystal Splits Log file

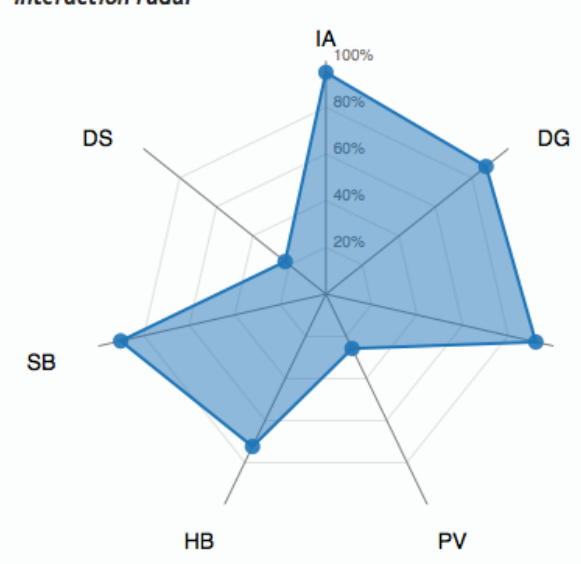
### Interface F || E

Summary

|                            | Monomer 1 |        | Monomer 2 |        |
|----------------------------|-----------|--------|-----------|--------|
| Monomer ID                 | F         |        | E         |        |
| Class                      | Protein   |        | Protein   |        |
| Symmetry operation         | X, Y, Z   |        | X, Y, Z   |        |
| Symmetry ID                | 1_555     |        | 1_555     |        |
| Interface atoms            | 232       | 7.3%   | 221       | 6.9%   |
| Surface atoms              | 1925      | 60.5%  | 1921      | 60.4%  |
| Total atoms                | 3184      | 100.0% | 3183      | 100.0% |
| Interface residues         | 66        | 16.1%  | 65        | 15.9%  |
| Surface residues           | 380       | 92.9%  | 385       | 94.4%  |
| Total residues             | 409       | 100.0% | 408       | 100.0% |
| BSA, Å <sup>2</sup>        | 2146.6    | 9.6%   | 2345.5    | 10.6%  |
| ASA, Å <sup>2</sup>        | 22253.4   | 100.0% | 22072.6   | 100.0% |
| Solvation energy, kcal/mol | -331.9    |        | -334.3    |        |
| SE gain, kcal/mol          | -7.5      |        | -5.0      |        |

Download PDB Download PDBx View in JSMol

Interaction radar



Interface parameters

| Parameter                           | Value  |
|-------------------------------------|--------|
| IA : Interface area, Å <sup>2</sup> | 2246   |
| DG : Solvation Energy, kcal/mol     | -12.46 |
| BE : Total Binding Energy, kcal/mol | -26.65 |
| PV : Hydrophobic P-value            | 0.3542 |
| HB : Number of Hydrogen Bonds       | 11     |
| SB : Number of Salt Bridges         | 25     |
| DS : Number of Disulphide Bonds     | 0      |

# Acknowledgements

**CCP4 Core group:** Andrey Lebedev, Ronan Keegan, Charles Ballard, David Waterman, Marcin Wojdyr, Ville Uski, Karen McIntyre, Kyle Stevenson, Martyn Winn

**LMB/MRC:** Andrew Leslie, Phil Evans, Garib Murshudov, Rob Nicholls, Oleg Kovalevskyi, Harry Powell, Owen Johnson, Fei Long, Paul Emsley, Andrea Thorn

**Phaser Group:** Airlie McCoy, Randy Read, Rob Oeffner, Gabor Bunkoczi

**YSBL York:** Keith Wilson, Kevin Cowtan, Liz Potterton, Stuart McNicholas, Jon Agirre, Eleanor Dodson

**Diamond:** Gwyndaf Evans, Graeme Winter

**Leiden:** Raj Pannu, Pavol Skubak

**Others:** Bernhard Lohkamp, Clemens Vornrhein, Frank Von Delft, Martin Noble, Jaclyn Bibby, Daniel Rigden, Jens Thomas, Alun Ashton, David Brown, Arwen Pearson, Tim Gruene, George Sheldrick and many more..