XChem Data Processing
XCE & PanDDA

2024

Working directory

You will have a proposal number starting with lb, e.g.:

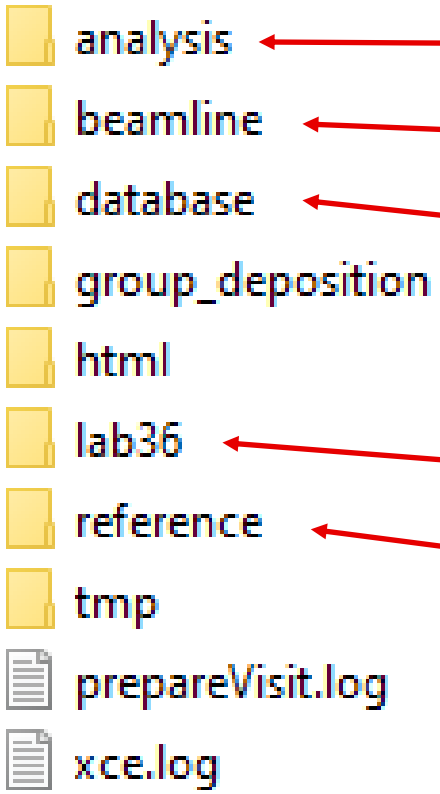
- lb13385

- **For each target/screen you will have a visit number, e.g.:**
  - lb13385**-1**

- **You will end up with visits assigned to both:**
  - Lab34: labxchem
  - The beamline: I04-1

- **For data analysis you should be working in the processing subdirectory of your labxchem visit**

Working directory structure

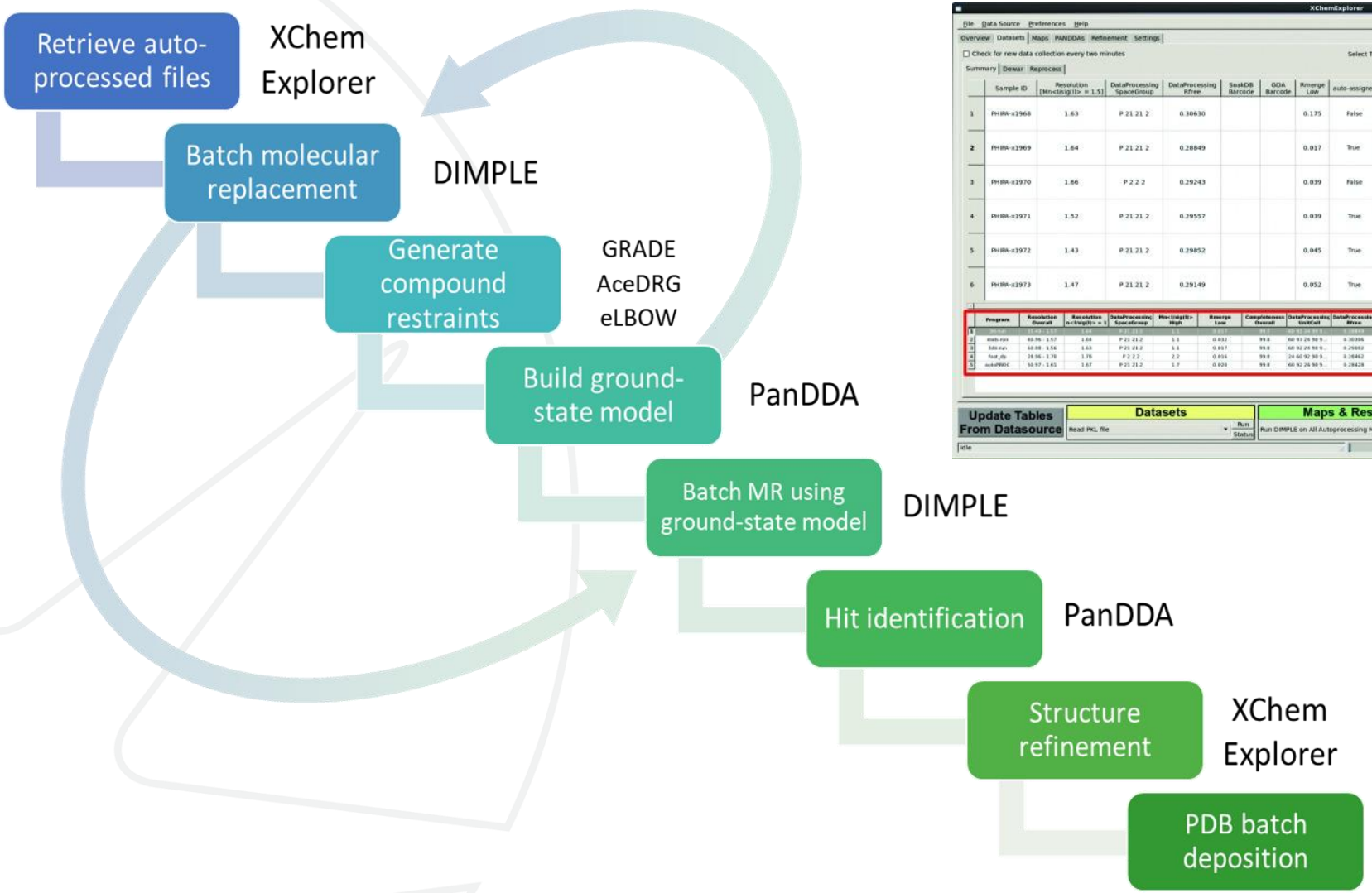


- **Data collection results and pandda analysis**
- Links to beamline visit directories ***(obsolete – do not use)***
- **SQlite datafile (and backups)**
- **Files for PDB deposition**
- **Directory for lab work (soakDB, echo, shifter)**
- **pdb of a good reference model**

Useful linux commands

- Setup useful commands **(do this first)**:
  - cd /dls/labxchem/data/proposal/visit/processing/
  - source /dls/science/groups/i04-1/software/XChem/xchempaths.sh
- xchempaths.sh will set paths for these commands:
  - preparevisit - to create the subfolders needed for XChem
  - tserver - to launch a windows remote desktop from linux
  - xce - to launch XChemExplorer
    - **Needs to be run under the 'processing' folder**
  - csv2ispyb - to automatically load the data collection information in iSPyB
- Checking the status of jobs on the cluster (type into terminal):
  - *"ssh wilson"* – connect to the Wilson Cluster
  - *"sacct"* – display jobs
  - *"scancel **<jobid>**"* – cancel a job
  - "*watch sq.sh -u **<yourfedid>*** -nf" – watch jobs

Data Analysis Workflow



10.1107/S2059798316020234

XChem jargon and experimental philosophies

- Reference model = Dimple/MR model = PanDDA input model = **ground-state model**
- PanDDA model = ligand model = **bound-state model**
- Ensemble model = ground-state model + bound-state model

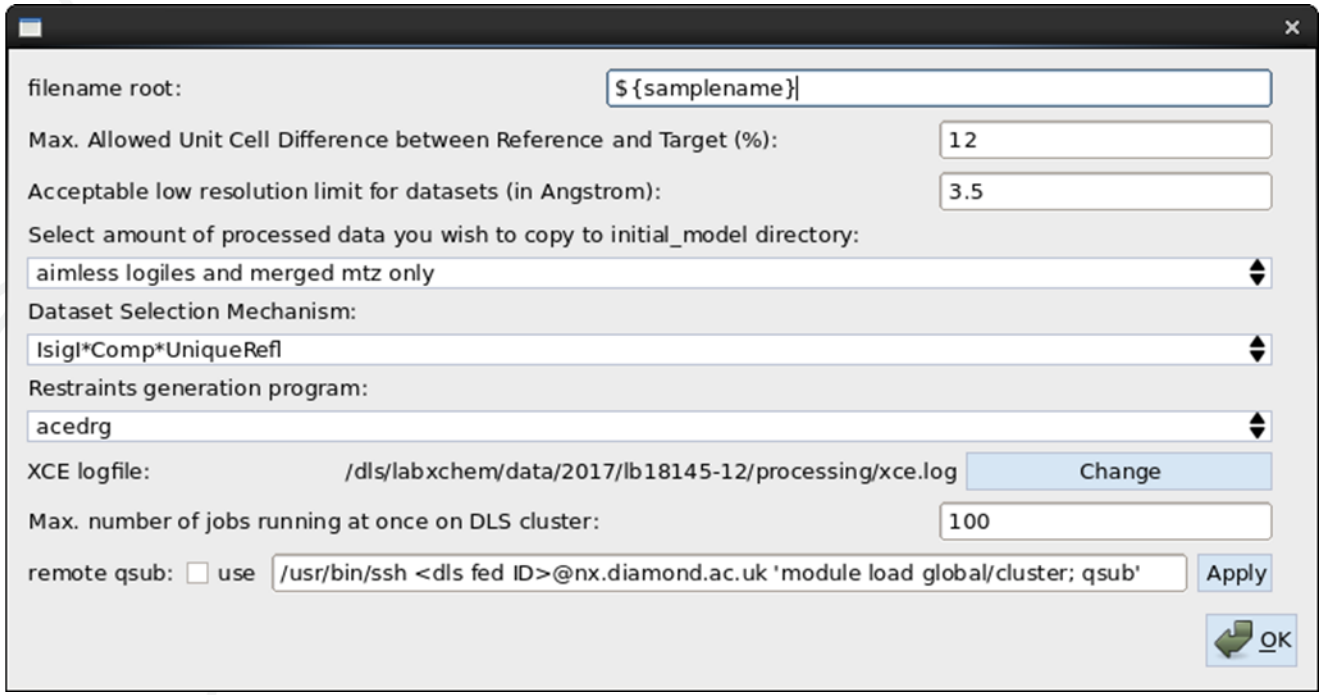
- The ensemble model is usually the one refined, particularly with low occupancy fragments
- The bound-state model will be the one you will update in the XCE refinement Coot window and the one which will be deposited on the PDB

XCE Preferences

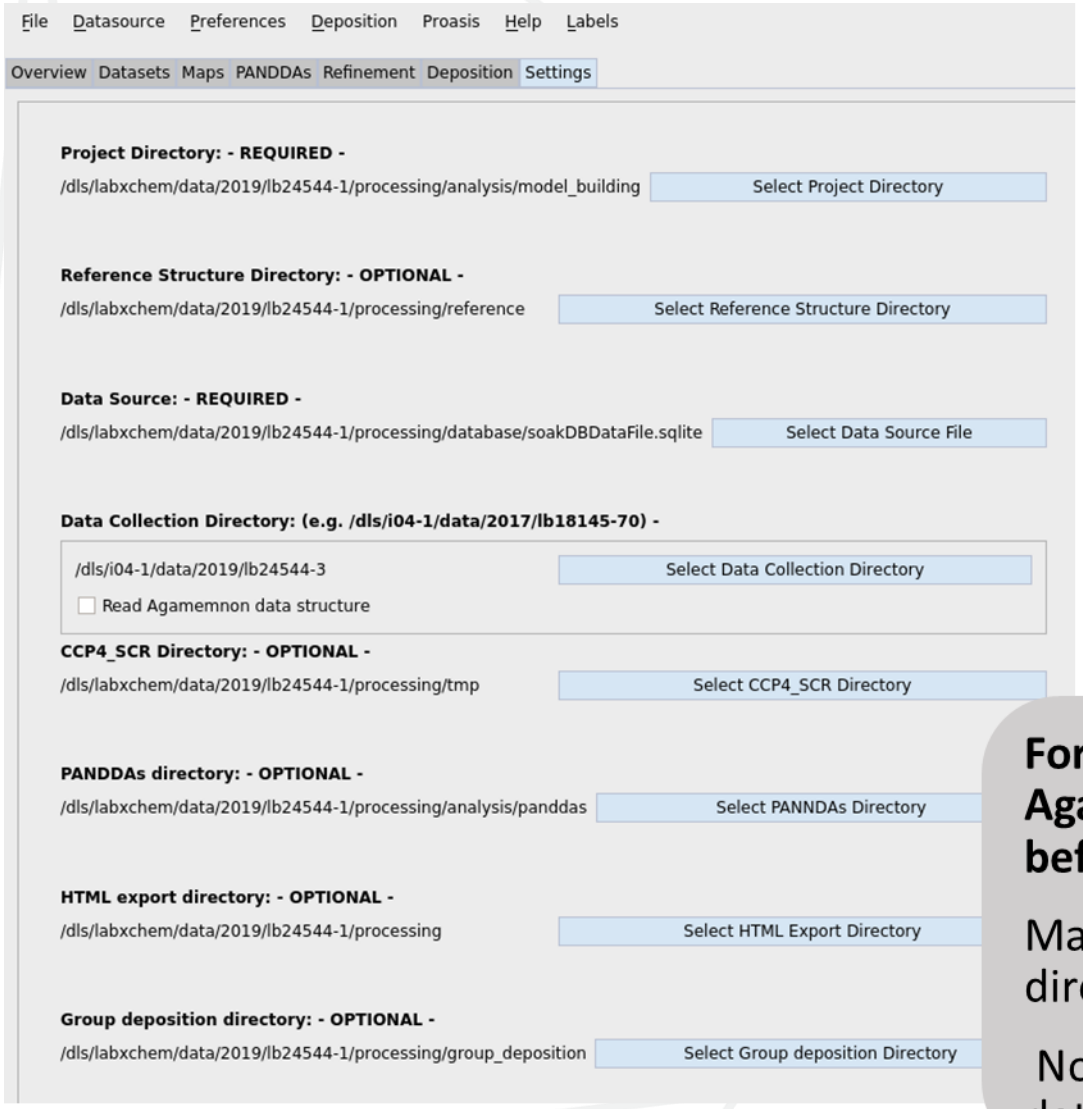
Dimple reference model selection criteria ⇨

Datasets tab options

Restraints generation program options ⇨



XCE Settings



Paths should look like this.

If not, this is because you haven't opened XCE in your processing directory!

Project directory is: **/analysis/model_building**

For UDC visits, select "Read Agamemnon data structure" before setting directory

Manually set the data collection directory (/dls/i04-1/…)

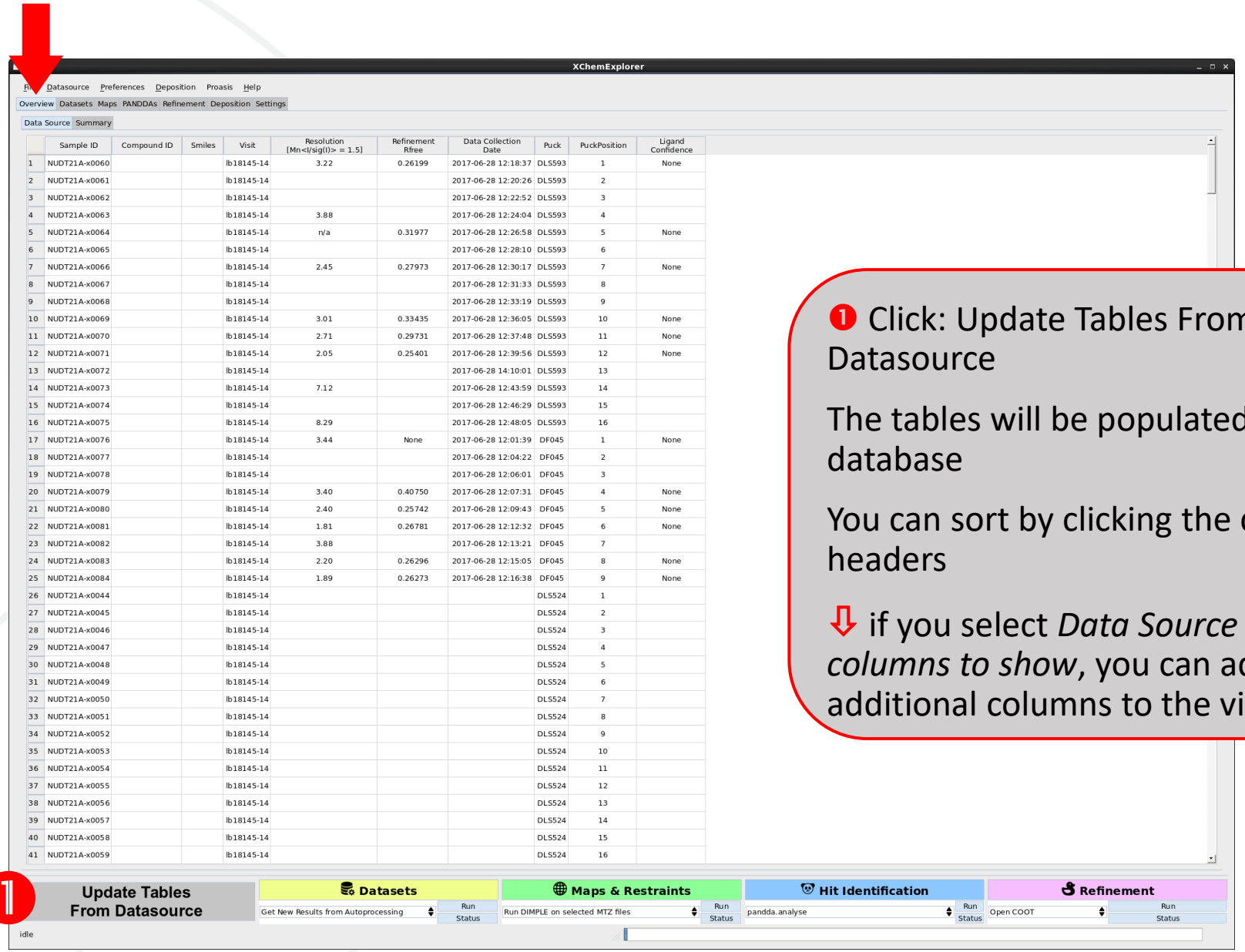
Now, XCE can link your SoakDB data to the x-ray diffraction data

Running jobs on Wilson cluster with SLURM

Whenever you launch a group of jobs on the Wilson cluster, you will need to provide your FedID password for authentication.

Default token time 1 hour – may need to re-enter password or restart XCE to launch jobs.

Data source tab: Overview of your experiments



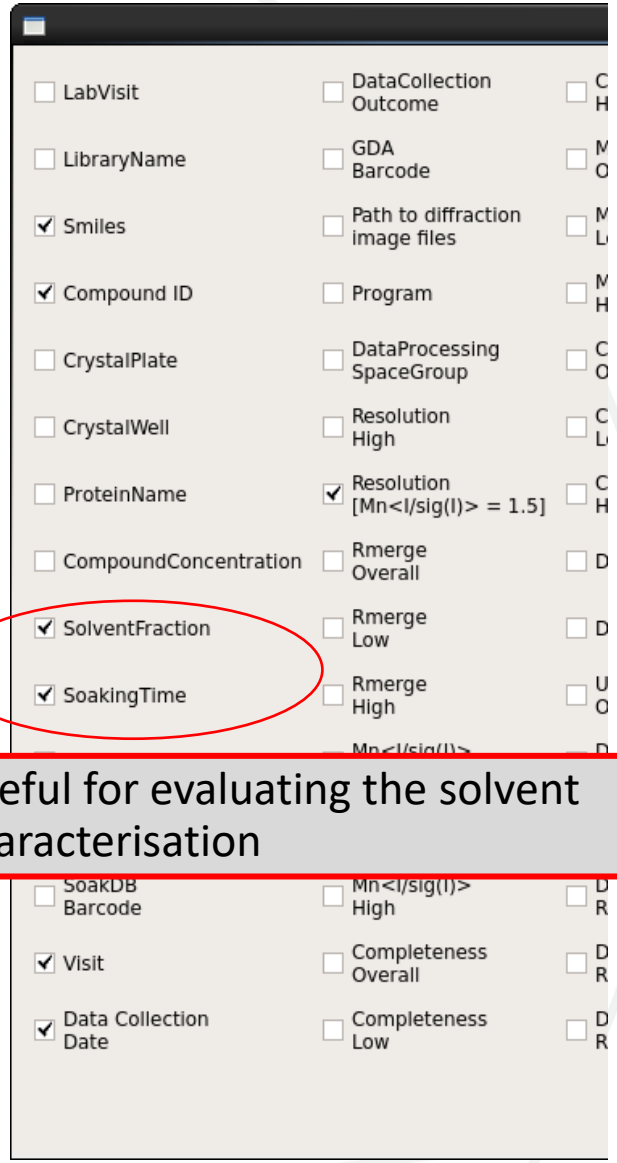
	Sample ID	Compound ID	Smiles	Visit	Resolution [Mn<I/sig(I)> = 1.5]	Refinement Rfree	Data Collection Date	Puck	PuckPosition	Ligand Confidence
1	NUDT21A-x0060			lb18145-14	3.22	0.26199	2017-06-28 12:18:37	DLS593	1	None
2	NUDT21A-x0061			lb18145-14			2017-06-28 12:20:26	DLS593	2	
3	NUDT21A-x0062			lb18145-14			2017-06-28 12:22:52	DLS593	3	
4	NUDT21A-x0063			lb18145-14	3.88		2017-06-28 12:24:04	DLS593	4	
5	NUDT21A-x0064			lb18145-14	n/a	0.31977	2017-06-28 12:26:58	DLS593	5	None
6	NUDT21A-x0065			lb18145-14			2017-06-28 12:28:10	DLS593	6	
7	NUDT21A-x0066			lb18145-14	2.45	0.27973	2017-06-28 12:30:17	DLS593	7	None
8	NUDT21A-x0067			lb18145-14			2017-06-28 12:31:33	DLS593	8	
9	NUDT21A-x0068			lb18145-14			2017-06-28 12:33:19	DLS593	9	
10	NUDT21A-x0069			lb18145-14	3.01	0.33435	2017-06-28 12:36:05	DLS593	10	None
11	NUDT21A-x0070			lb18145-14	2.71	0.29731	2017-06-28 12:37:48	DLS593	11	None
12	NUDT21A-x0071			lb18145-14	2.05	0.25401	2017-06-28 12:39:56	DLS593	12	None
13	NUDT21A-x0072			lb18145-14			2017-06-28 14:10:01	DLS593	13	
14	NUDT21A-x0073			lb18145-14	7.12		2017-06-28 12:43:59	DLS593	14	
15	NUDT21A-x0074			lb18145-14			2017-06-28 12:46:29	DLS593	15	
16	NUDT21A-x0075			lb18145-14	8.29		2017-06-28 12:48:05	DLS593	16	
17	NUDT21A-x0076			lb18145-14	3.44	None	2017-06-28 12:01:39	DF045	1	None
18	NUDT21A-x0077			lb18145-14			2017-06-28 12:04:22	DF045	2	
19	NUDT21A-x0078			lb18145-14			2017-06-28 12:06:01	DF045	3	
20	NUDT21A-x0079			lb18145-14	3.40	0.40750	2017-06-28 12:07:31	DF045	4	None
21	NUDT21A-x0080			lb18145-14	2.40	0.25742	2017-06-28 12:09:43	DF045	5	None
22	NUDT21A-x0081			lb18145-14	1.81	0.26781	2017-06-28 12:12:32	DF045	6	None
23	NUDT21A-x0082			lb18145-14	3.88		2017-06-28 12:13:21	DF045	7	
24	NUDT21A-x0083			lb18145-14	2.20	0.26296	2017-06-28 12:15:05	DF045	8	None
25	NUDT21A-x0084			lb18145-14	1.89	0.26273	2017-06-28 12:16:38	DF045	9	None
26	NUDT21A-x0044			lb18145-14				DLS524	1	
27	NUDT21A-x0045			lb18145-14				DLS524	2	
28	NUDT21A-x0046			lb18145-14				DLS524	3	
29	NUDT21A-x0047			lb18145-14				DLS524	4	
30	NUDT21A-x0048			lb18145-14				DLS524	5	
31	NUDT21A-x0049			lb18145-14				DLS524	6	
32	NUDT21A-x0050			lb18145-14				DLS524	7	
33	NUDT21A-x0051			lb18145-14				DLS524	8	
34	NUDT21A-x0052			lb18145-14				DLS524	9	
35	NUDT21A-x0053			lb18145-14				DLS524	10	
36	NUDT21A-x0054			lb18145-14				DLS524	11	
37	NUDT21A-x0055			lb18145-14				DLS524	12	
38	NUDT21A-x0056			lb18145-14				DLS524	13	
39	NUDT21A-x0057			lb18145-14				DLS524	14	
40	NUDT21A-x0058			lb18145-14				DLS524	15	
41	NUDT21A-x0059			lb18145-14				DLS524	16	

❶ Click: Update Tables From Datasource

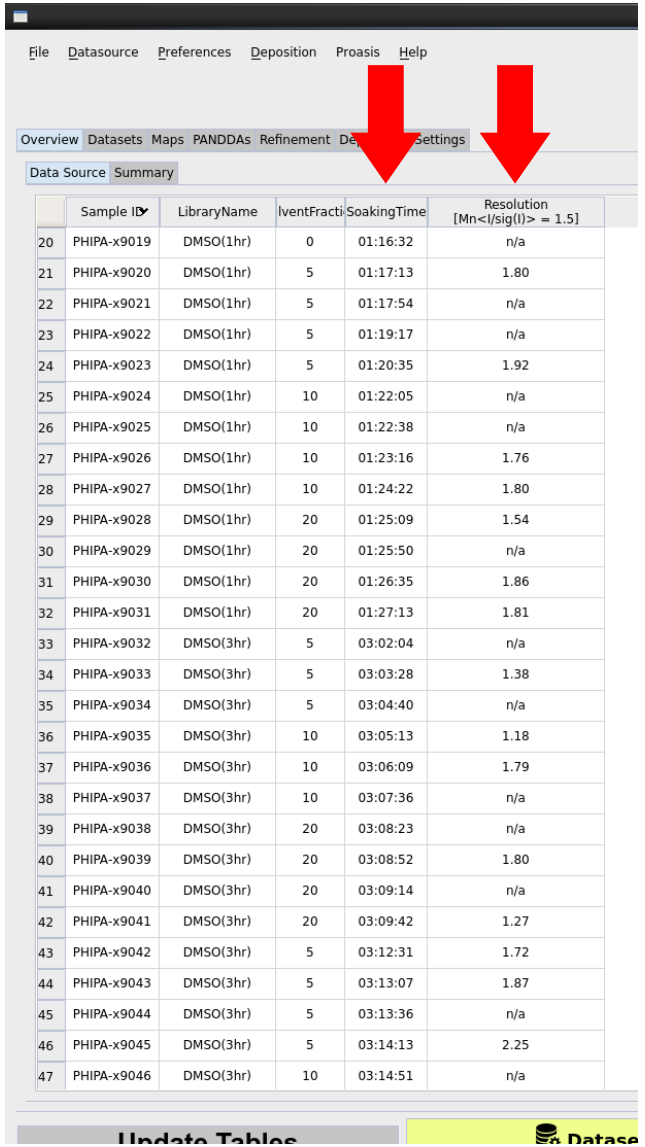
The tables will be populated from the database

You can sort by clicking the column headers

⇩ if you select *Data Source* → *Select columns to show*, you can add some additional columns to the view.

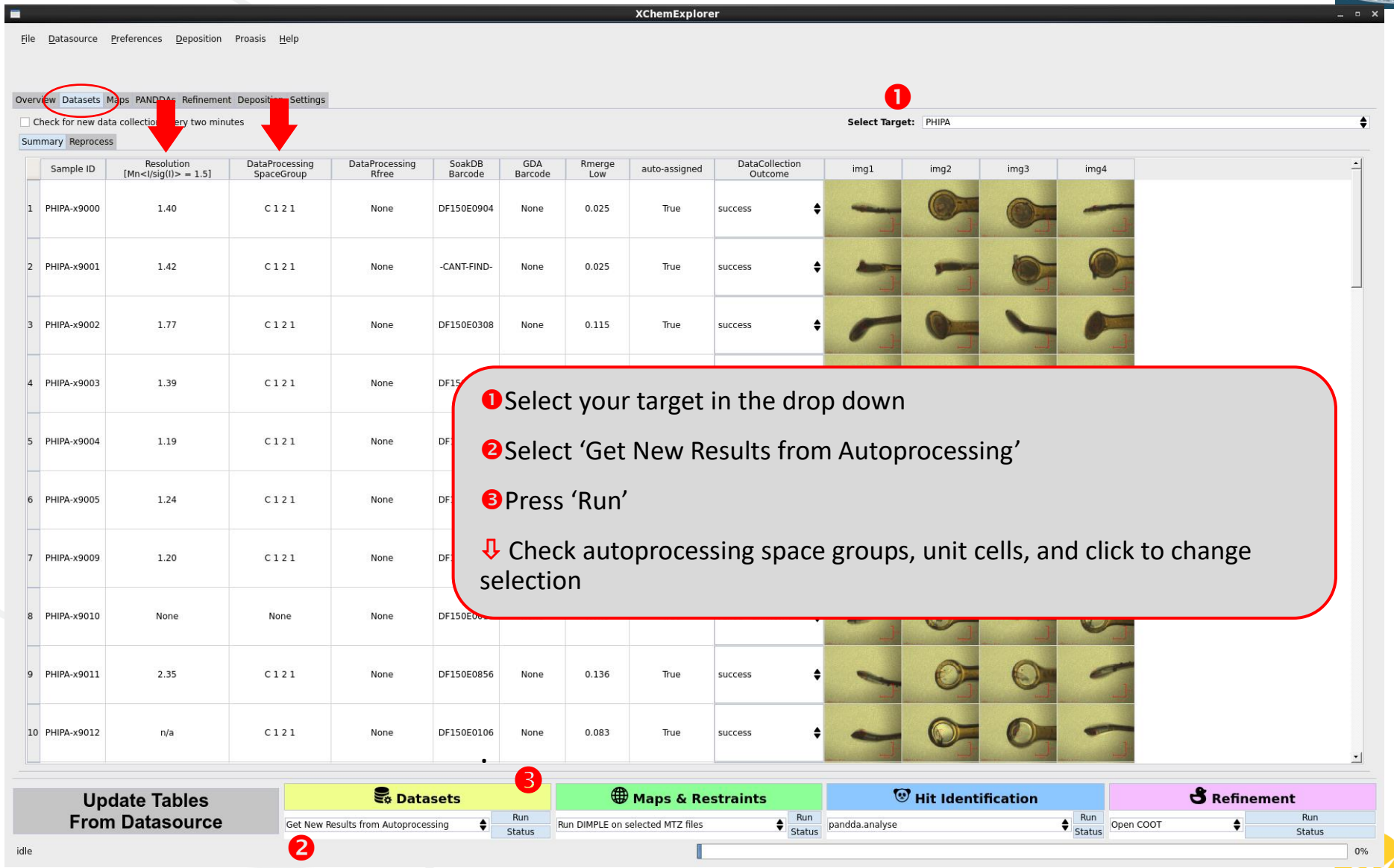


Useful for evaluating the solvent characterisation

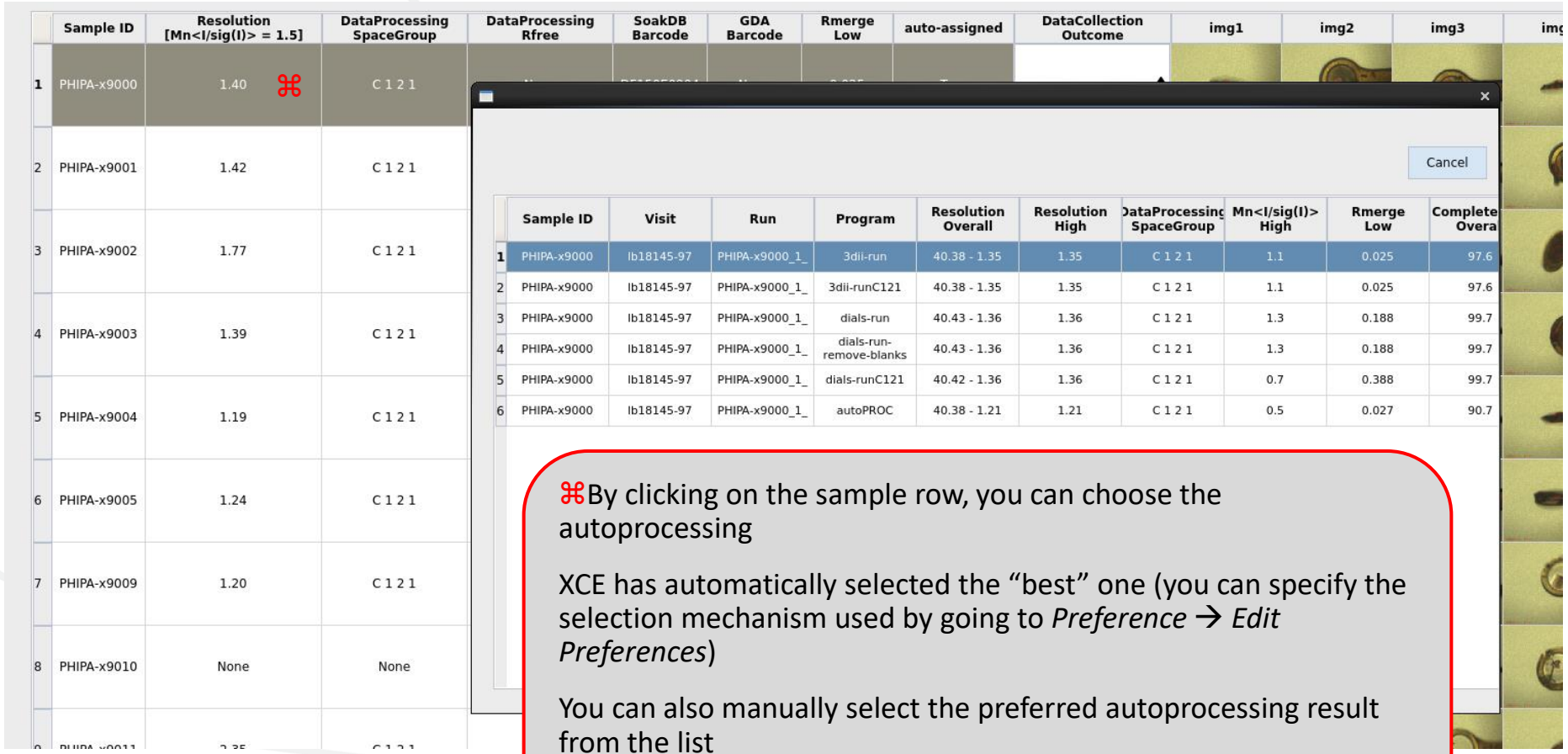


	Sample ID	LibraryName	SoakingTime	Resolution [Mn<I/sig(I)> = 1.5]
20	PHIPA-x9019	DMSO(1hr)	01:16:32	n/a
21	PHIPA-x9020	DMSO(1hr)	01:17:13	1.80
22	PHIPA-x9021	DMSO(1hr)	01:17:54	n/a
23	PHIPA-x9022	DMSO(1hr)	01:19:17	n/a
24	PHIPA-x9023	DMSO(1hr)	01:20:35	1.92
25	PHIPA-x9024	DMSO(1hr)	01:22:05	n/a
26	PHIPA-x9025	DMSO(1hr)	01:22:38	n/a
27	PHIPA-x9026	DMSO(1hr)	01:23:16	1.76
28	PHIPA-x9027	DMSO(1hr)	01:24:22	1.80
29	PHIPA-x9028	DMSO(1hr)	01:25:09	1.54
30	PHIPA-x9029	DMSO(1hr)	01:25:50	n/a
31	PHIPA-x9030	DMSO(1hr)	01:26:35	1.86
32	PHIPA-x9031	DMSO(1hr)	01:27:13	1.81
33	PHIPA-x9032	DMSO(3hr)	03:02:04	n/a
34	PHIPA-x9033	DMSO(3hr)	03:03:28	1.38
35	PHIPA-x9034	DMSO(3hr)	03:04:40	n/a
36	PHIPA-x9035	DMSO(3hr)	03:05:13	1.18
37	PHIPA-x9036	DMSO(3hr)	03:06:09	1.79
38	PHIPA-x9037	DMSO(3hr)	03:07:36	n/a
39	PHIPA-x9038	DMSO(3hr)	03:08:23	n/a
40	PHIPA-x9039	DMSO(3hr)	03:08:52	1.80
41	PHIPA-x9040	DMSO(3hr)	03:09:14	n/a
42	PHIPA-x9041	DMSO(3hr)	03:09:42	1.27
43	PHIPA-x9042	DMSO(3hr)	03:12:31	1.72
44	PHIPA-x9043	DMSO(3hr)	03:13:07	1.87
45	PHIPA-x9044	DMSO(3hr)	03:13:36	n/a
46	PHIPA-x9045	DMSO(3hr)	03:14:13	2.25
47	PHIPA-x9046	DMSO(3hr)	03:14:51	n/a

Datasets tab: Load datasets



Datasets tab: Load datasets



⌘By clicking on the sample row, you can choose the autoprocessing

XCE has automatically selected the “best” one (you can specify the selection mechanism used by going to *Preference* → *Edit Preferences*)

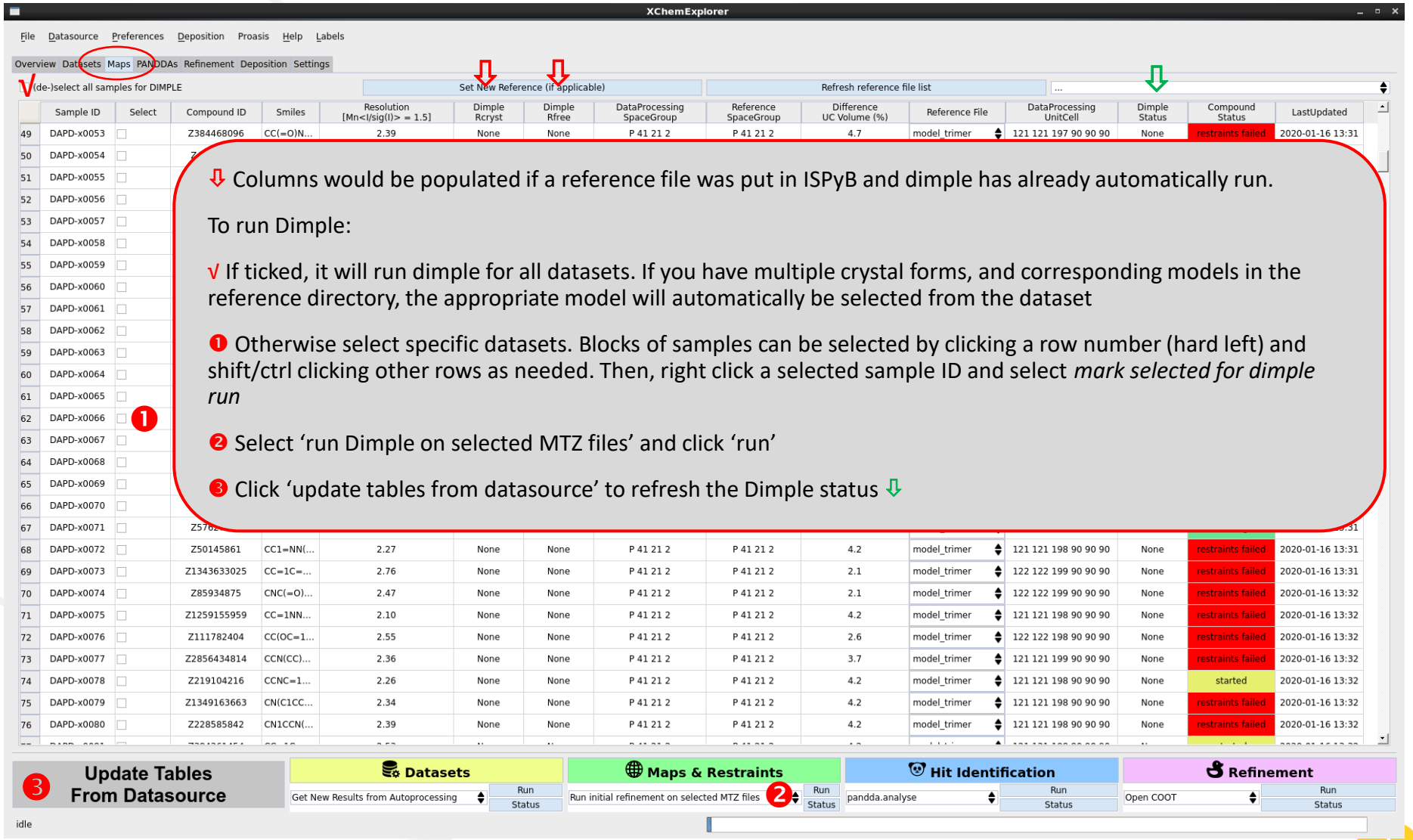
You can also manually select the preferred autoprocessing result from the list

Click on Update Datasource to push the changes in the database

Reference Model

- Use a model that you are confident best represents your crystal system as used in the XChem experiment:
  - Used previously for solving by molecular replacement
  - Containing all waters, cofactors, ligands
  - Intrinsic ligands and cofactors need PDB official three letter codes, or codes that are **not** ‘LIG’ or ‘DRG’

Maps tab: Running Dimple for MR ("Run initial refinement")

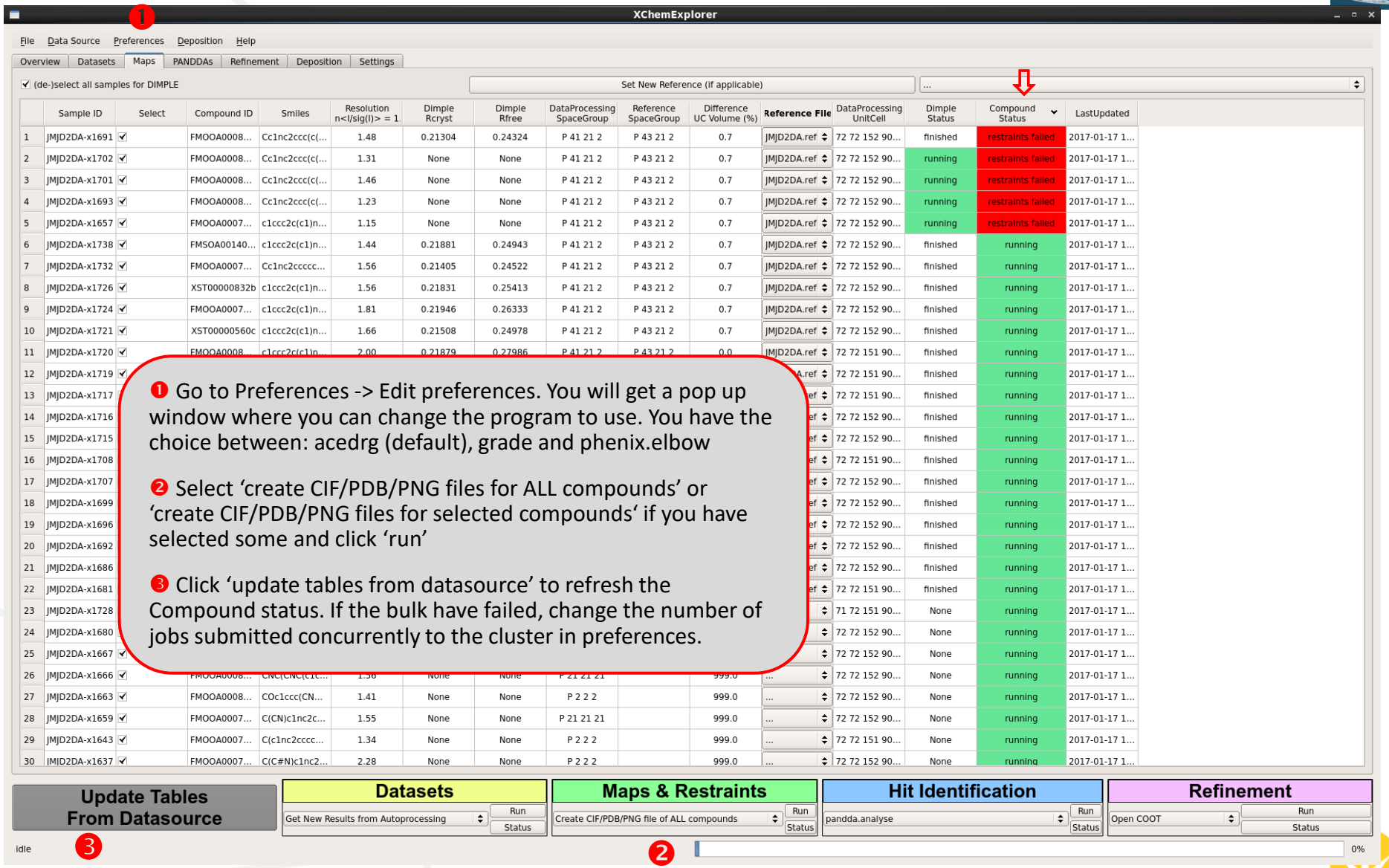


Check jobs are running

- To check the status of jobs on the cluster, type into terminal:
  - *"ssh wilson"* – connect to the Wilson Cluster
  - *"sacct"* – display jobs
  - *"scancel **<jobid>**"* – cancel a job
  - "*watch sq.sh -u **<yourfedid>*** -nf" – watch jobs
  - "*sbatch **<script>***" – submit batch job

```
Every 2.0s: sq.sh -u ill13029 -nf

ill13029's queue

No jobs running.

No jobs pending.

Previous 10 jobs (last fortnight):

JobID    'Job Name'    #N #C  Start Time     Run Time  Status
9363997  'xce_buster'  1 1c   Jul 1st 08:38  40m 20s   Completed
9368556  'xce_buster'  1 1c   Jul 1st 12:58  36m 21s   Completed
9370433  'xce_buster'  1 1c   Jul 1st 13:50  33m 4s    Completed
9372944  'xce_buster'  1 1c   Jul 1st 14:55  24m 30s   Completed
```

Maps tab: Creating the ligands restraints



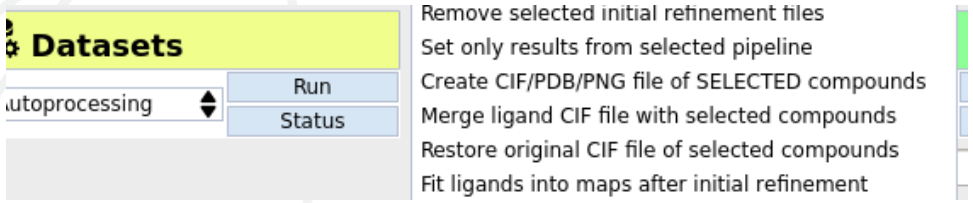
❶ Go to Preferences -> Edit preferences. You will get a pop up window where you can change the program to use. You have the choice between: acedrg (default), grade and phenix.elbow

❷ Select ‘create CIF/PDB/PNG files for ALL compounds’ or ‘create CIF/PDB/PNG files for selected compounds‘ if you have selected some and click ‘run’

❸ Click ‘update tables from datasource’ to refresh the Compound status. If the bulk have failed, change the number of jobs submitted concurrently to the cluster in preferences.

Merge ligand restrains from non-standard ligand

1. Open ‘Preferences’ menu (Edit preferences) and select the CIF file of your non-standard ligand in ‘Additional CIF file for non-standard ligand’.
2. Select the samples which you want to merge in the Maps tab
3. Choose ‘Merge ligand CIF file with selected compounds’ and press Run.



XCE will now prepare a merged version of the file in the sample directory with the same name. It does not touch the original files in the compound subfolder.

Before you start merging: **the ligand code of the additional ligand cannot be LIG or DRG!** Both codes are reserved for ligands generated by XCE.

Merge ligand restrains from non-standard ligand

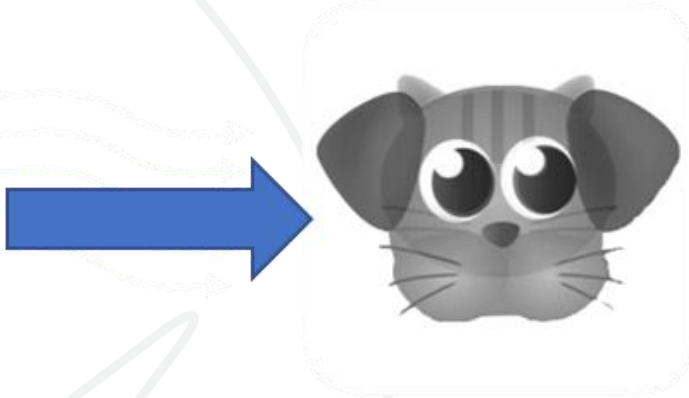
Restore original CIF file

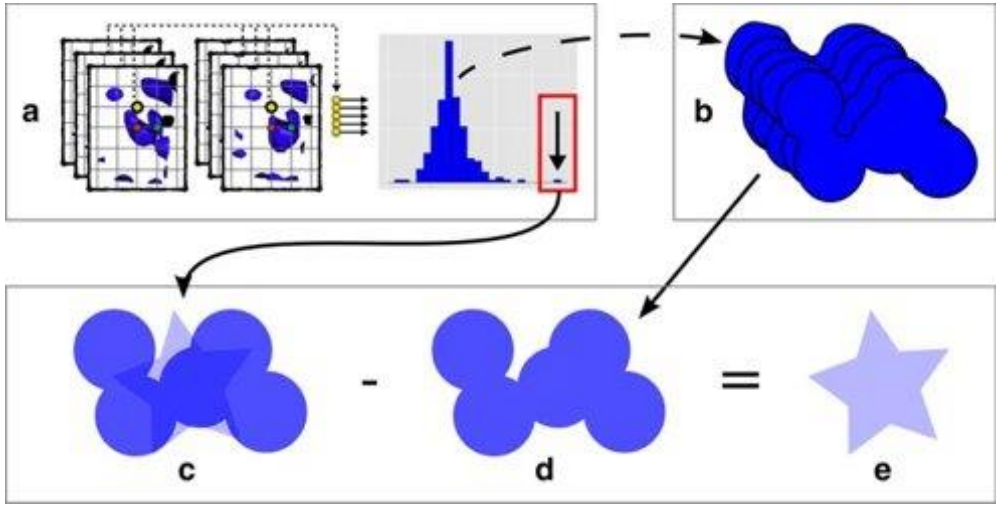
In case you need/ want to restore the original CIF file:

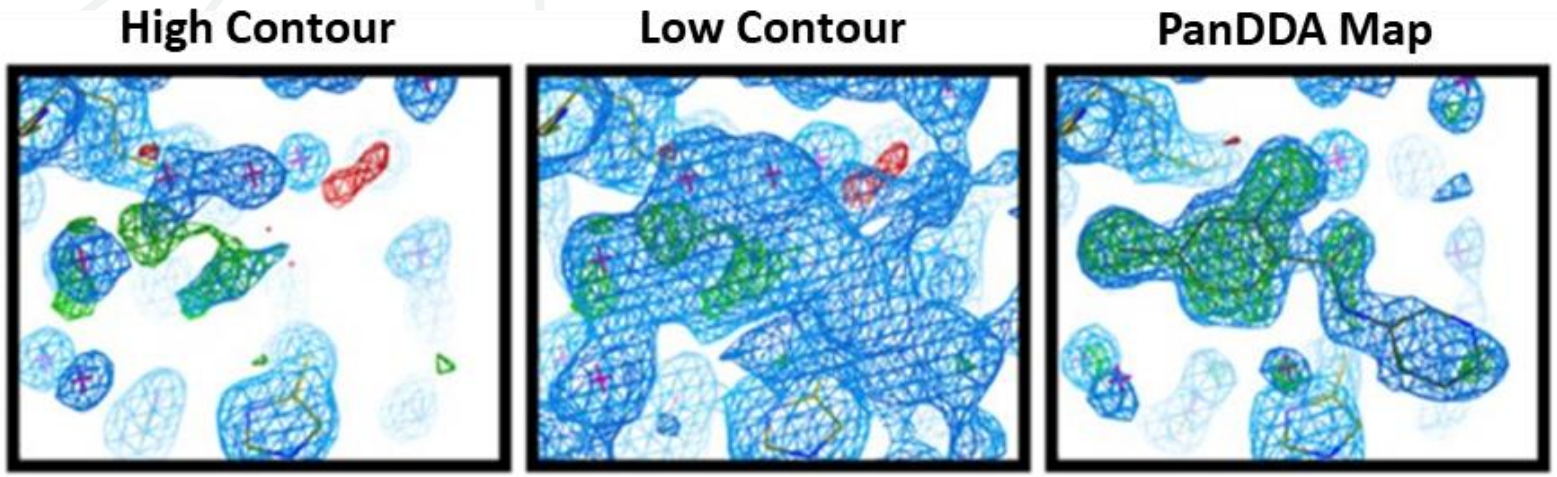
1. select the samples in the Maps tab which you want to restore (see above).
2. choose '*Merge ligand CIF file with selected compounds*' from the green action box and press *Run*.

Please note that this is not a requirement in case you want to merge another ligand. XCE will in this case first remove the old, merged CIF file, before doing the merging as described before.

Finding hits - Pan Density Dataset Analysis (PanDDA)



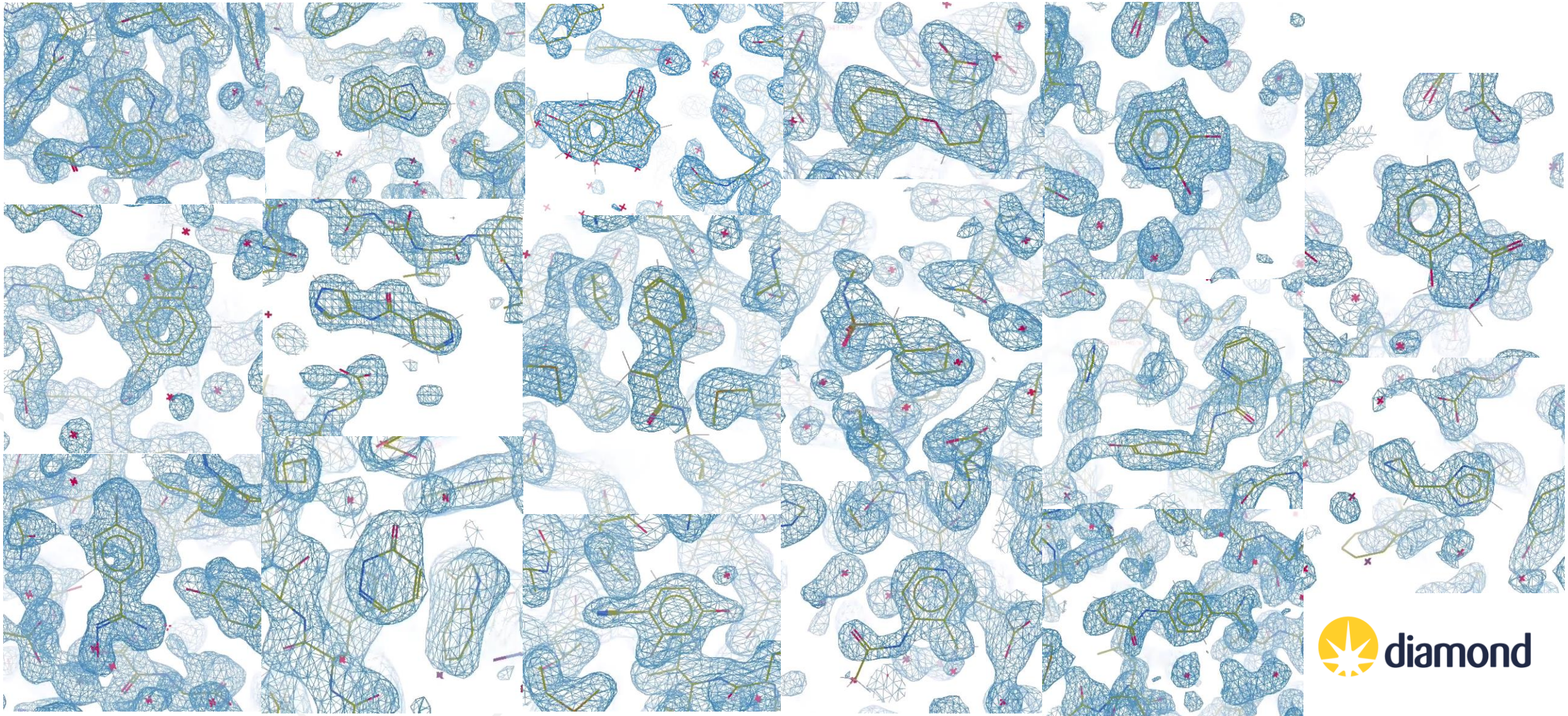




https://doi.org/10.1038/ncomms15123
https://doi.org/10.1063/1.4974176

PanDDA 2 discovers new hits

Convincing models in every studied system with over 15 systems studied in detail



Ground-state model building

A PanDDA pre-run allows you to build the best possible reference model: the ground-state model.

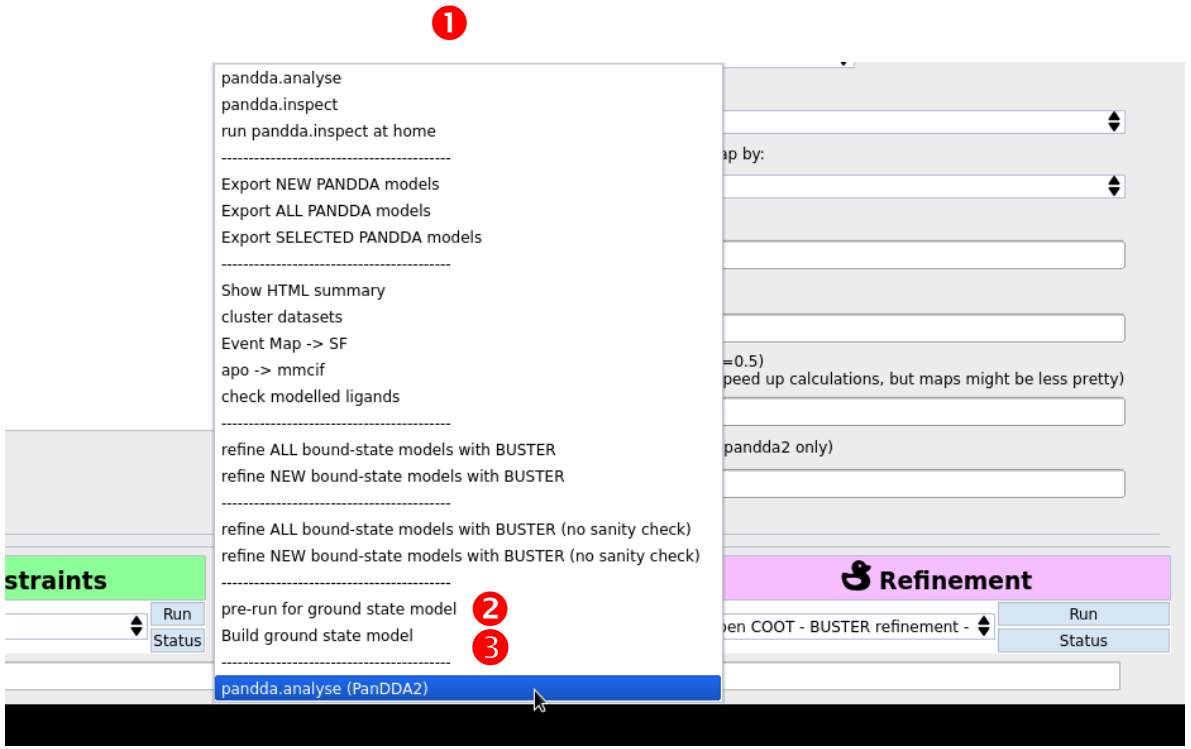
❶ Click on the drop-down menu in the “Hit identification” action box

❷ Select “pre-run for ground state model”.

Wait for the job to finish. This creates a subdirectory in the reference directory with all the required files.

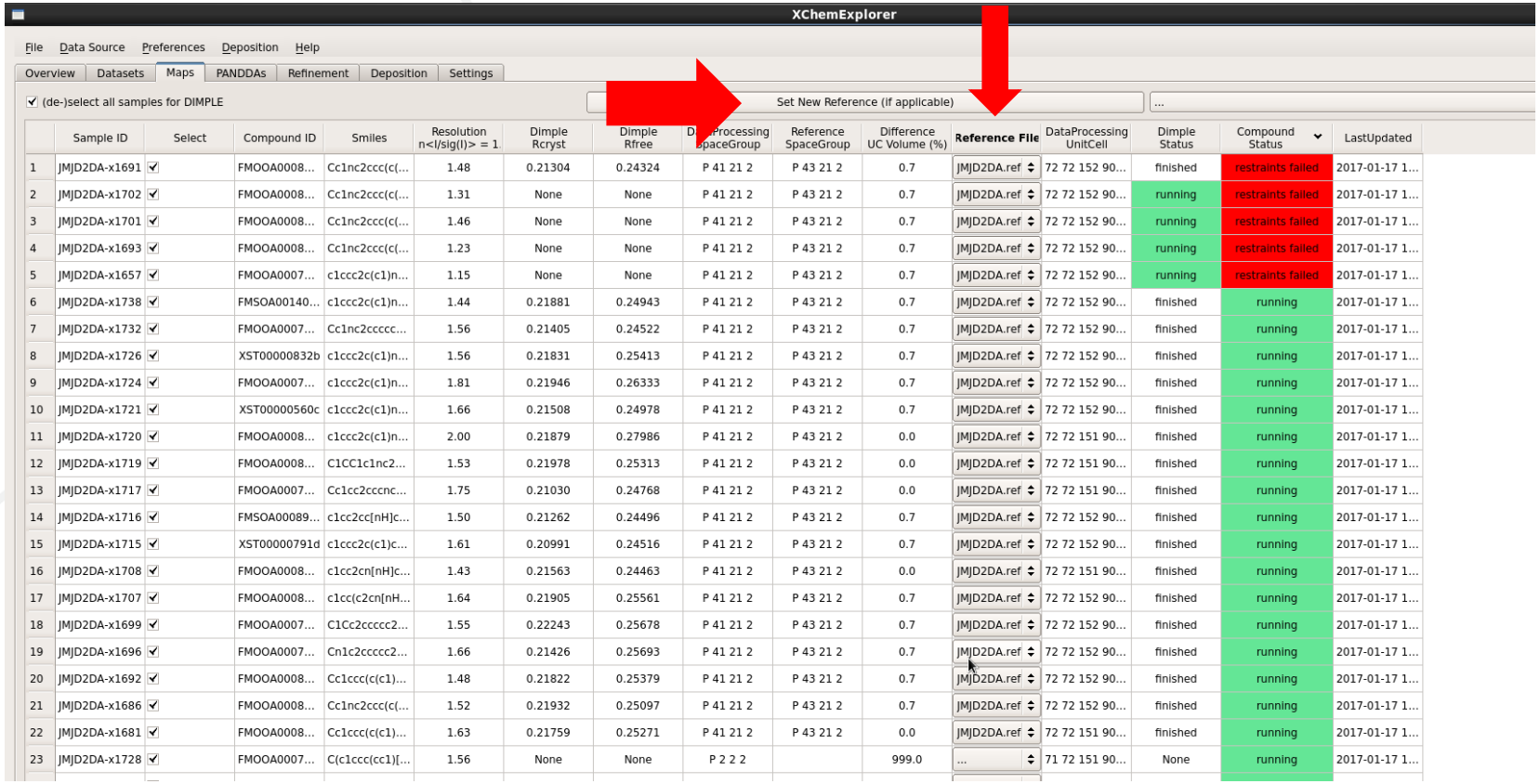
❸ Once the PanDDA pre-run is done, select “build ground state model”.

Coot will open the PanDDA mean-map and the 2Fo-Fc/Fo-Fc maps loaded from the new reference/subdirectory



Ground-state model building

- Remodel and refine the reference model as you wish using the PanDDA mean map in Coot.
- Re-run Dimple (XCE – Maps table) by using this ground-state model as new reference

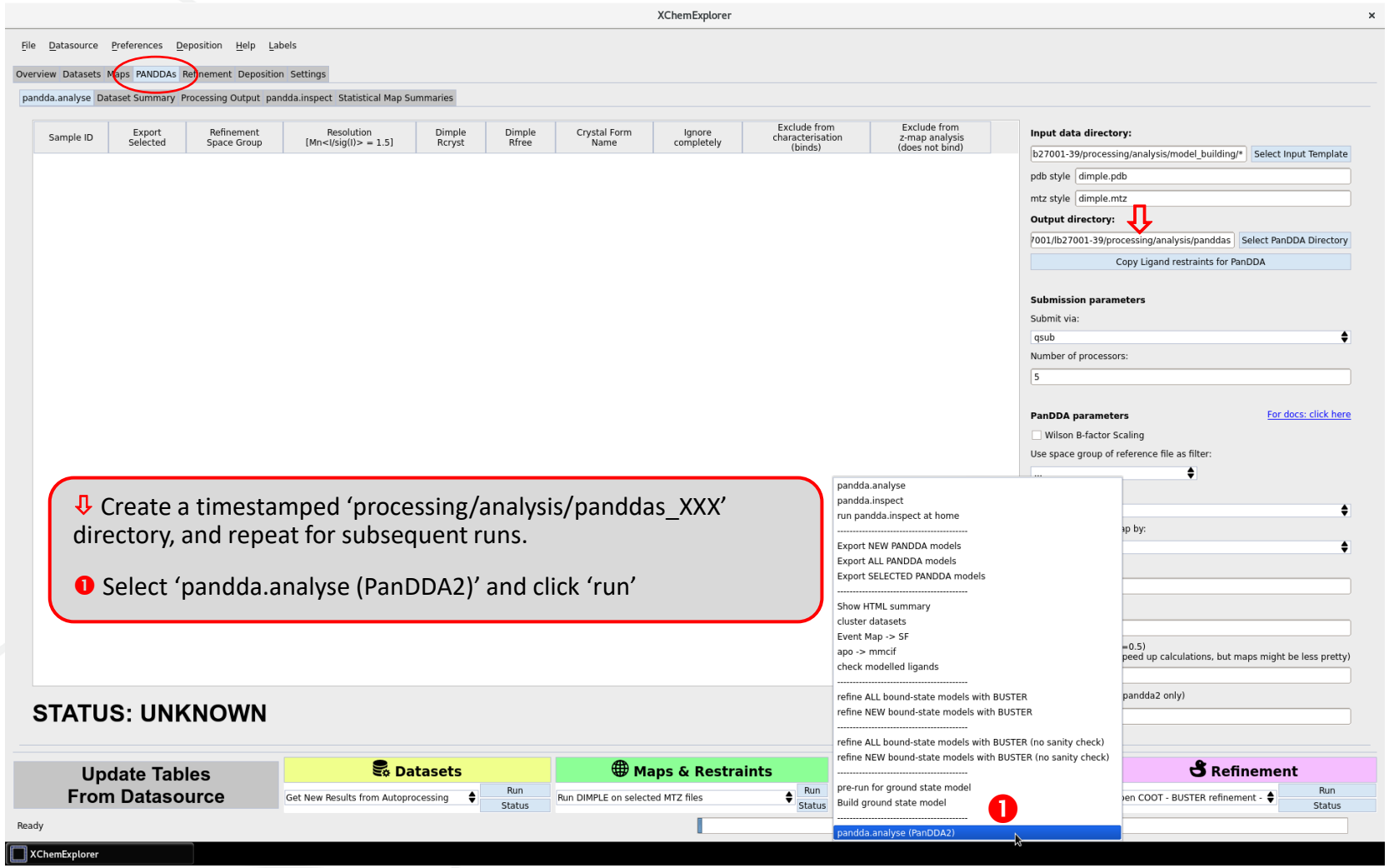


	Sample ID	Select	Compound ID	Smiles	Resolution n<I/sig(I)> = 1	Dimple Rcryst	Dimple Rfree	D... Processing SpaceGroup	Reference SpaceGroup	Difference UC Volume (%)	Reference File	DataProcessing UnitCell	Dimple Status	Compound Status	LastUpdated
1	JMJD2DA-x1691	☑	FMOOA0008...	Cc1nc2ccc(c(...	1.48	0.21304	0.24324	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	restraints failed	2017-01-17 1...
2	JMJD2DA-x1702	☑	FMOOA0008...	Cc1nc2ccc(c(...	1.31	None	None	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	running	restraints failed	2017-01-17 1...
3	JMJD2DA-x1701	☑	FMOOA0008...	Cc1nc2ccc(c(...	1.46	None	None	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	running	restraints failed	2017-01-17 1...
4	JMJD2DA-x1693	☑	FMOOA0008...	Cc1nc2ccc(c(...	1.23	None	None	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	running	restraints failed	2017-01-17 1...
5	JMJD2DA-x1657	☑	FMOOA0007...	c1ccc2c(c1)n...	1.15	None	None	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	running	restraints failed	2017-01-17 1...
6	JMJD2DA-x1738	☑	FMSOA00140...	c1ccc2c(c1)n...	1.44	0.21881	0.24943	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
7	JMJD2DA-x1732	☑	FMOOA0007...	Cc1nc2ccccc...	1.56	0.21405	0.24522	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
8	JMJD2DA-x1726	☑	XST00000832b	c1ccc2c(c1)n...	1.56	0.21831	0.25413	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
9	JMJD2DA-x1724	☑	FMOOA0007...	c1ccc2c(c1)n...	1.81	0.21946	0.26333	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
10	JMJD2DA-x1721	☑	XST00000560c	c1ccc2c(c1)n...	1.66	0.21508	0.24978	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
11	JMJD2DA-x1720	☑	FMOOA0008...	c1ccc2c(c1)n...	2.00	0.21879	0.27986	P 41 21 2	P 43 21 2	0.0	JMJD2DA.ref	72 72 151 90...	finished	running	2017-01-17 1...
12	JMJD2DA-x1719	☑	FMOOA0008...	C1CC1c1nc2...	1.53	0.21978	0.25313	P 41 21 2	P 43 21 2	0.0	JMJD2DA.ref	72 72 151 90...	finished	running	2017-01-17 1...
13	JMJD2DA-x1717	☑	FMOOA0007...	Cc1cc2cccnc...	1.75	0.21030	0.24768	P 41 21 2	P 43 21 2	0.0	JMJD2DA.ref	72 72 151 90...	finished	running	2017-01-17 1...
14	JMJD2DA-x1716	☑	FMSOA00089...	c1cc2cc[nH]c...	1.50	0.21262	0.24496	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
15	JMJD2DA-x1715	☑	XST00000791d	c1ccc2c(c1)c...	1.61	0.20991	0.24516	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
16	JMJD2DA-x1708	☑	FMOOA0008...	c1cc2cn[nH]c...	1.43	0.21563	0.24463	P 41 21 2	P 43 21 2	0.0	JMJD2DA.ref	72 72 151 90...	finished	running	2017-01-17 1...
17	JMJD2DA-x1707	☑	FMOOA0008...	c1cc(c2cn[nH...	1.64	0.21905	0.25561	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
18	JMJD2DA-x1699	☑	FMOOA0007...	C1Cc2ccccc2...	1.55	0.22243	0.25678	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
19	JMJD2DA-x1696	☑	FMOOA0007...	Cn1c2ccccc2...	1.66	0.21426	0.25693	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
20	JMJD2DA-x1692	☑	FMOOA0008...	Cc1ccc(c(c1)...	1.48	0.21822	0.25379	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
21	JMJD2DA-x1686	☑	FMOOA0008...	Cc1nc2ccc(c(...	1.52	0.21932	0.25097	P 41 21 2	P 43 21 2	0.7	JMJD2DA.ref	72 72 152 90...	finished	running	2017-01-17 1...
22	JMJD2DA-x1681	☑	FMOOA0008...	Cc1ccc(c(c1)...	1.63	0.21759	0.25271	P 41 21 2	P 43 21 2	0.0	JMJD2DA.ref	72 72 151 90...	finished	running	2017-01-17 1...
23	JMJD2DA-x1728	☑	FMOOA0007...	C(c1ccc(cc1)[...	1.56	None	None	P 2 2 2		999.0	...	71 72 151 90...	None	running	2017-01-17 1...

PanDDA Workflow

- “pandda.analyse” – uses PanDDA to generate event maps
- “pandda.analyse (PanDDA2)” – uses PanDDA 2 to calculate statistical models, generate event maps, and autofit ligands
  - Many datasets, larger unit cells, and multimers can all increase run time
  - Even though ligands are autofit, you **must:**“mark events as interesting”; select “Ligand placed”; and assign a confidence level in pandda.inspect for relevant datasets
- pandda.inspect: COOT plugin to inspect, annotate and place the fragments
  - Not traditional model refinement – do not use to refine model at large
- Export models for refinement
- Refine models
- Deposit/disseminate data

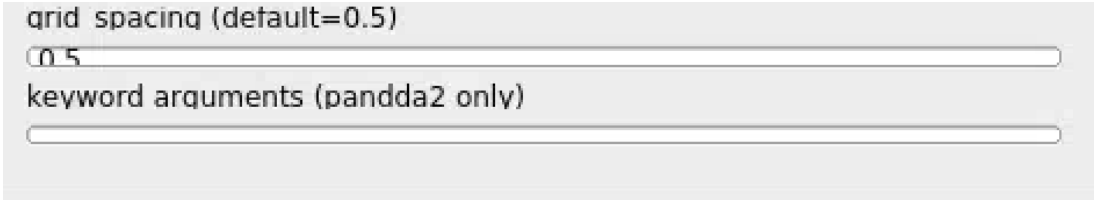
PanDDAs Tab: pandda.analyse



Check if jobs are running on the cluster as described previously

pandda.analyse PanDDA2 - Useful tricks

PanDDA 2 accepts several keyword arguments that may be useful:



To Run Subsets Of Data

```
--dataset_range="100-200"
```

```
--only_datasets="BAZ2BA-x102,BAZ2BA-x097“
```

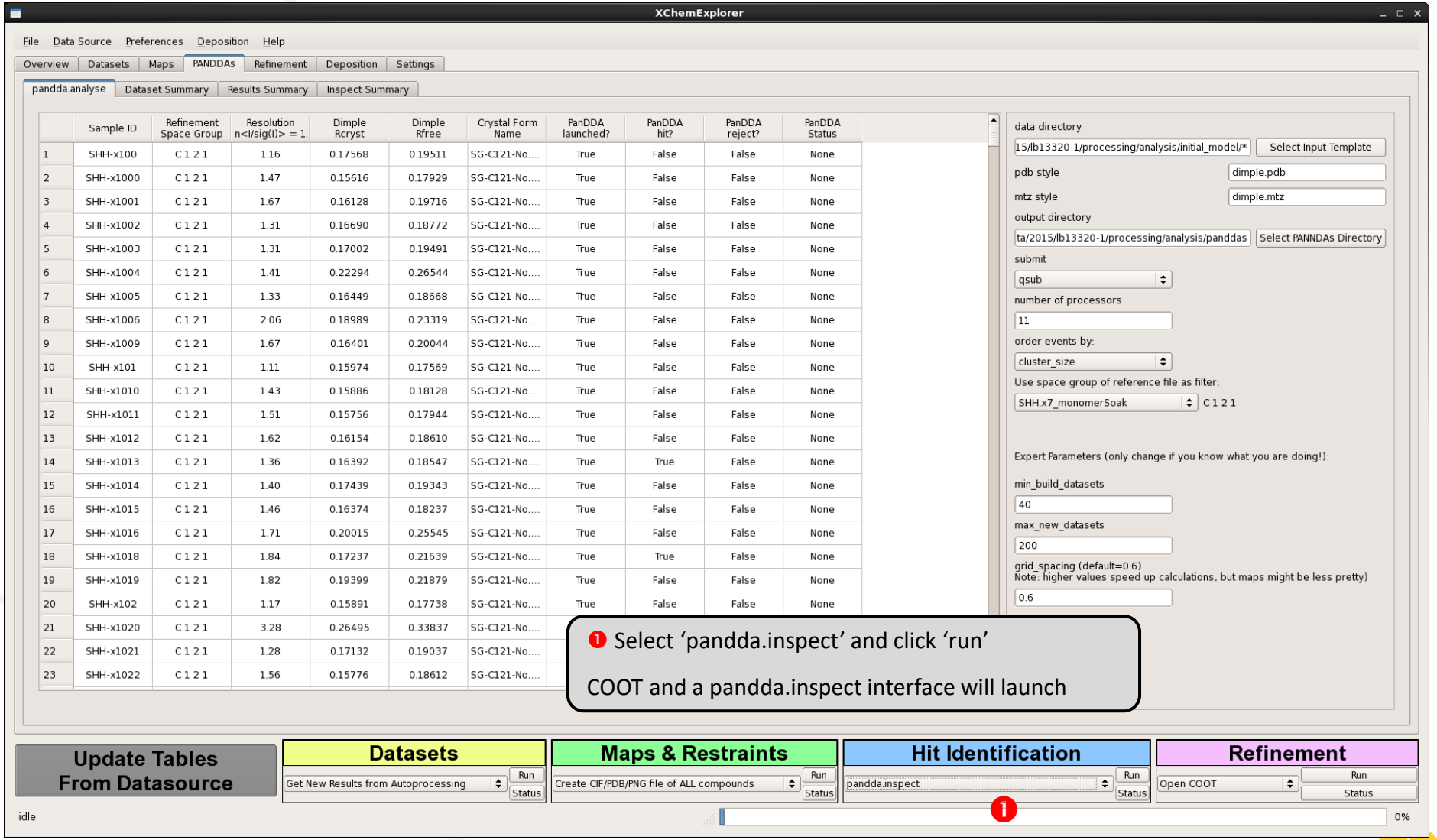
To Filter Poor Quality Data

```
--high_res_lower_limit=3.0
```

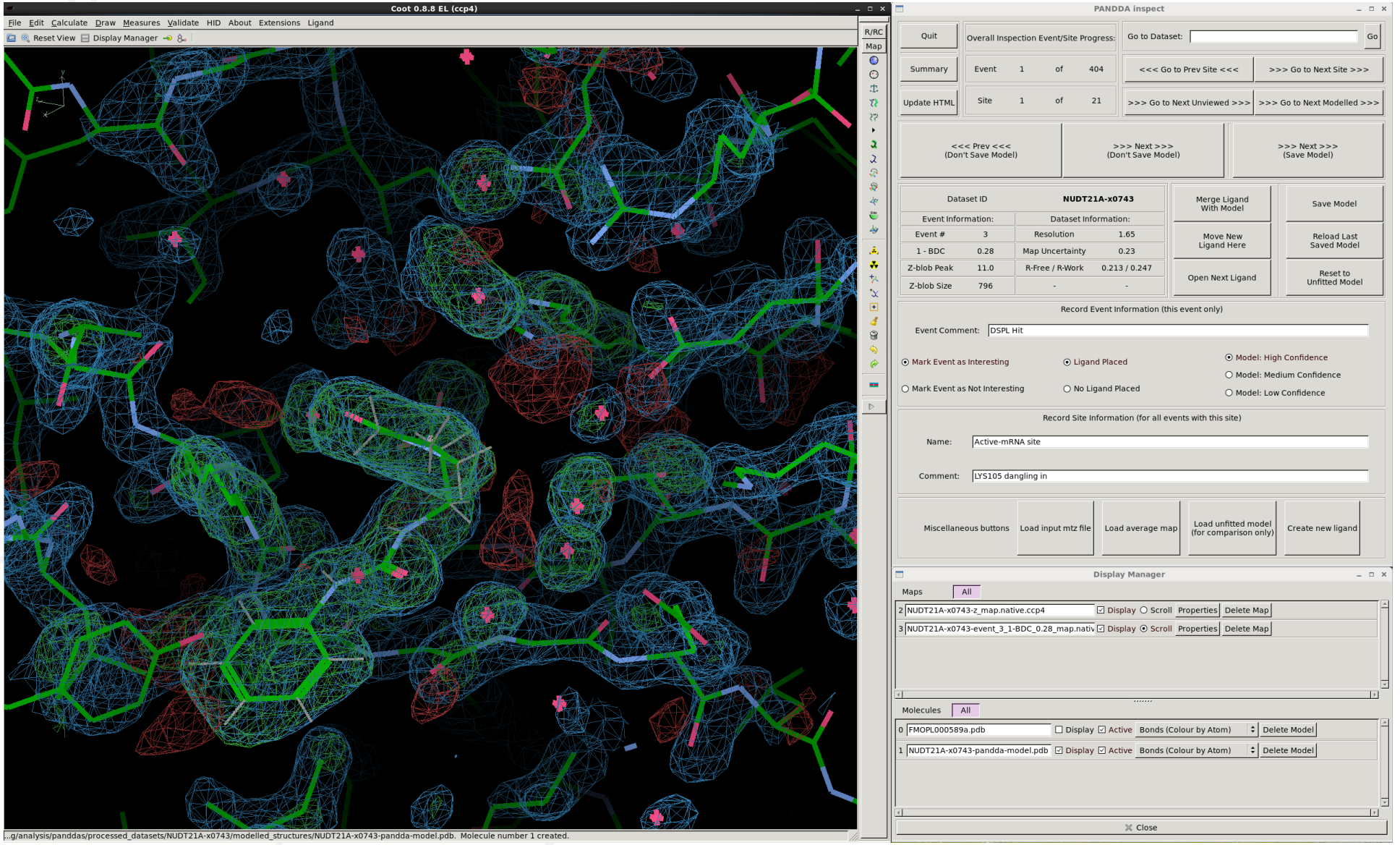
```
--max_rfree=0.3
```

PanDDA2 Documentation

PanDDAs Tab: pandda.inspect

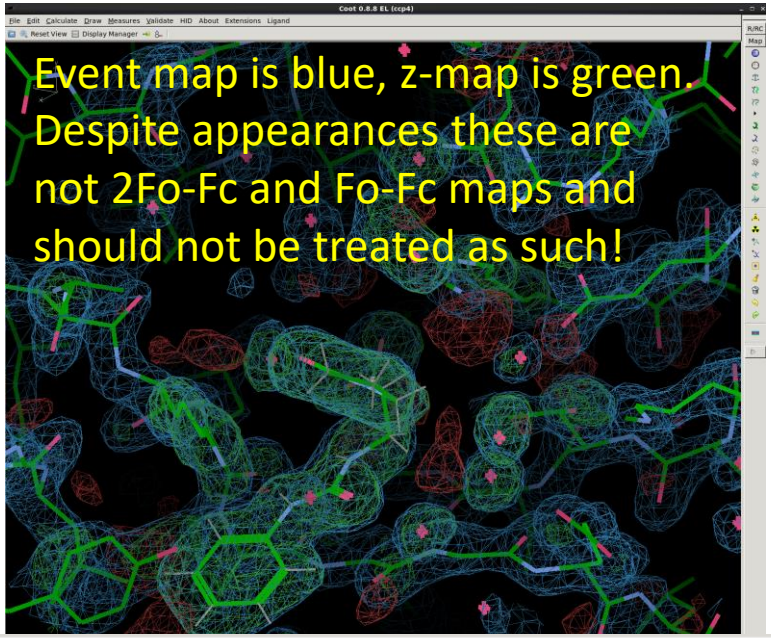


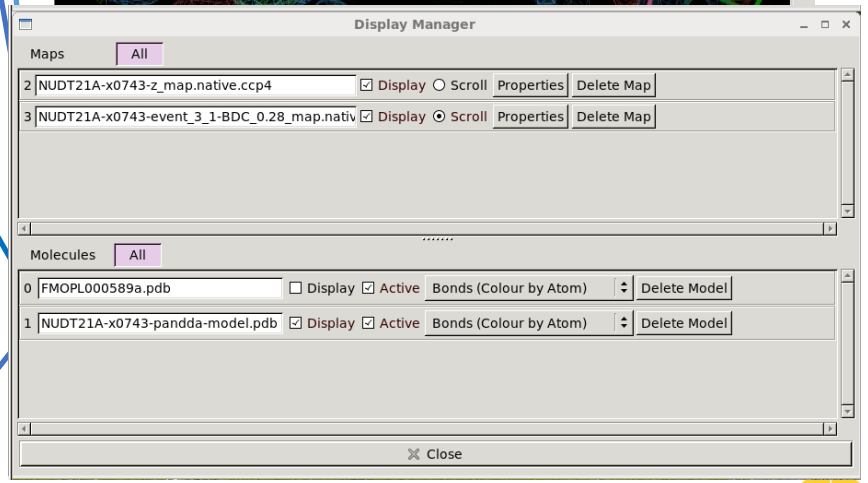
pandda.inspect COOT interface



pandda.inspect COOT interface

z_map.native.ccp4 (set to appear like a difference map, on by default)	Shows the extent of deviations from the ensemble of crystallographic datasets. Large positive or negative Z-scores (±3) indicate significant deviations from the ensemble, and may represent interesting features.
event_X_1-BDC_Y_map.ccp4 (the important one! On by default)	Partial-difference density obtained by subtracting a fraction of the mean map from the dataset map. This reveals the density for low-occupancy binding events. X indicates which event in this dataset is being inspected, and Y indicates the amount of mean map that has been subtracted (amount subtracted = 1-Y).
ligand files	Loaded automatically. PanDDA 2 will have attempted ligand fitting, but this file is present/hidden in case of multiple sites, re-fitting.
-pandda-model.pdb	The output of pandda2-analyse, with auto-fitted ligand in position (if an autobuild occurred)





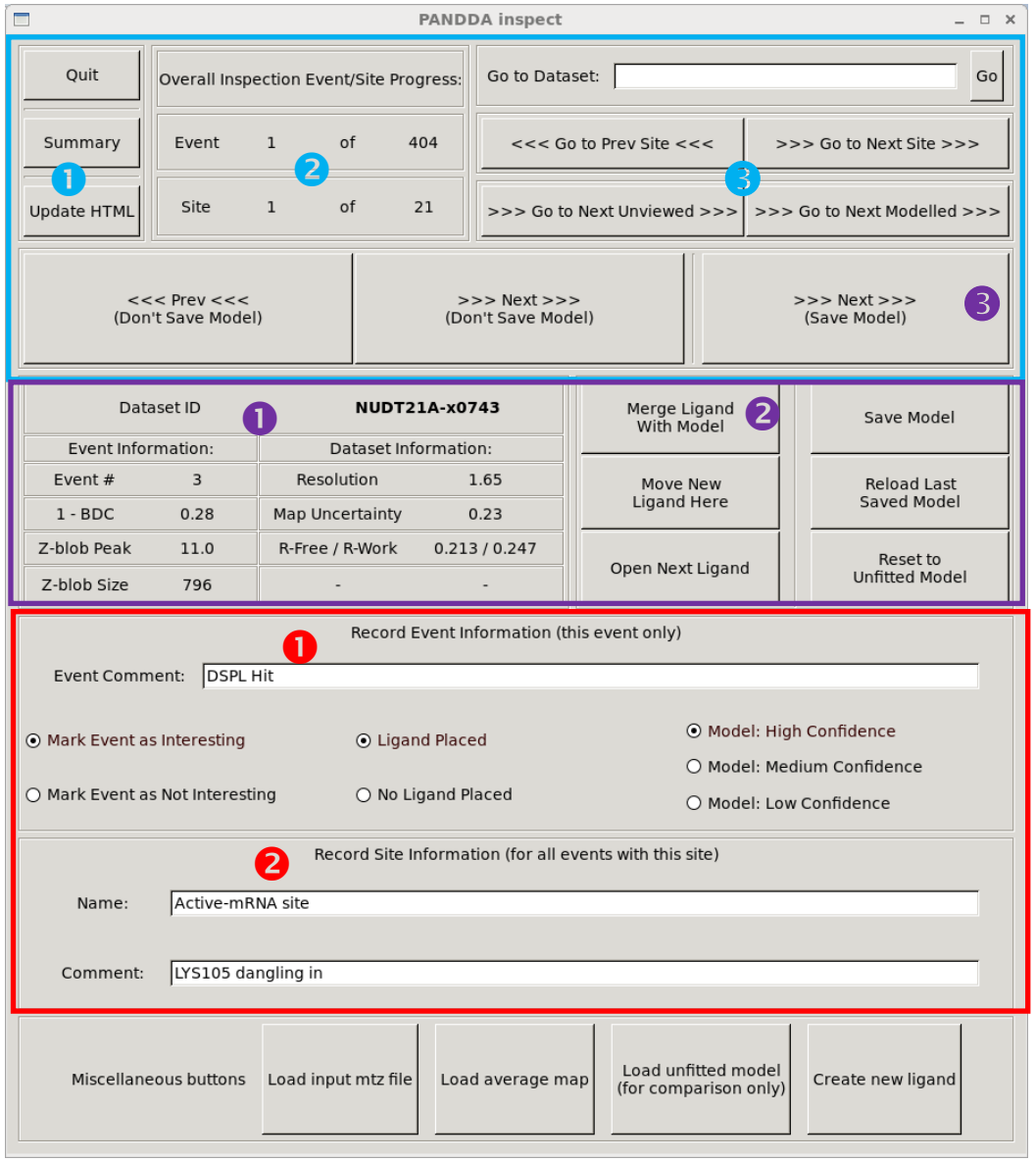
pandda.inspect COOT interface

❶ Open html summary page of the data analysis
❷ Indicates number of sites and events to review
❸ Navigate through the events and sites, or go straight to a dataset of interest
❶ Summary of PanDDA statistics
❷ **Merge or add ligands to the model**
❸ **Save your model or roll back to previous models.**

❶ To **annotate the event**.
❷ To **annotate the sites**. It will be used by XCE to categorise models in refinement.

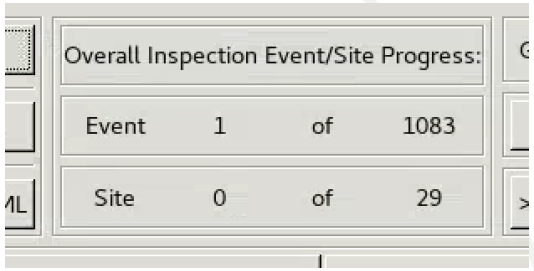
For your hits to be taken to the next step (If you do not follow these steps you will not be able to export your models!):

- 'Mark Event as Interesting' and 'Ligand Placed' **must** be selected
- Save model (or 'Next' (Save model)). A pandda-model.pdb will be saved in processed_datasets/*/modelled_structures/
- Update the event information as necessary
- Do not save useless/empty/dubious model

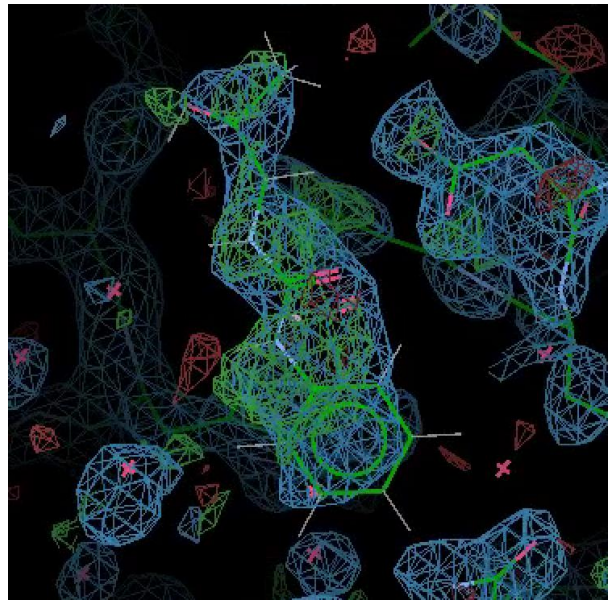


Using pandda.inspect with PanDDA2

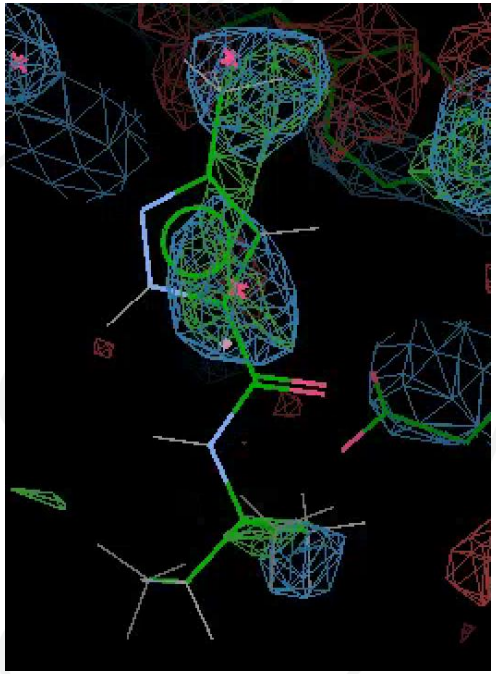
Expect more events but they are better ranked within sites



Autobuilt models will be present in some events



Autobuilt models may be spurious and should be deleted if so



Z-blob peak now contains a score from 0.0 to 1.0, with higher being more ligand-binding-event-like

1 - BDC	0.18
Z-blob Peak	0.9
Z-blob Size	247

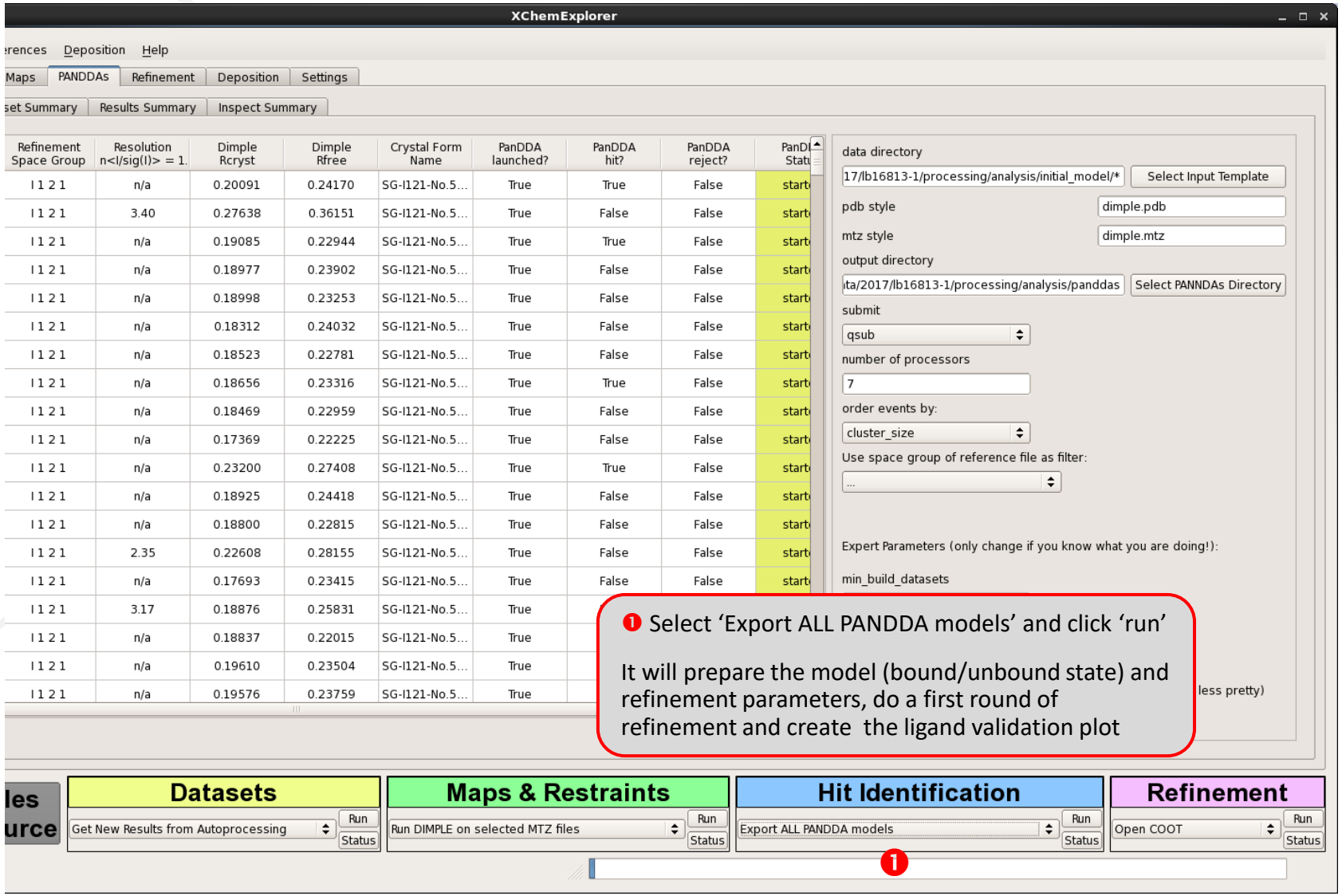
Modelling in pandda.inspect

With PanDDA, you are not trying to build the entire model – just a model of the protein when something is bound to it: **i.e. the bound-state model**.

- Focus on the centred event map - **do not navigate away** from the initial view or search for blobs using Coot
- If you cannot clearly see the ligand pose in the PanDDA event map move on, there will be plenty more events to check!
- **Only change/delete atoms that are "important"** - with large peaks in the Z-map, clear shifts in location - other smaller changes can be built in refinement
- Think **'would I give this model to a chemist for follow-up compound design?'** 'Would I spend 3 months and £10K on follow-up chemistry'??

1.	**Prune solvent molecules and alternate sidechain conformations**	Delete those atoms and alternate conformations that are not present in the event map.
2.	**Fix conformations and rotamers that have changed**	For residues where a sidechain or water has changed, simply correct the model as normal. Every residue that is moved in the model will lead to an alternate conformation when the ensemble model is constructed, so it is normally only necessary to model large changes from the reference model.
3.	**Model the ligand (if present) and add new solvent molecules.**	Add new solvent molecules to the protein model where required. The ligand should be modelled in a preliminary location of it was supplied to PanDDA2. You can move it using standard COOT tools, and use 'Mark Event as Interesting' and 'Ligand Placed' to add the structure to the list for export.
4.	**Save the changes to the model.**	use the "Save Model" or "Next Event >>> (Save Model)" button to have the model before progressing

PanDDAs Tab: pandda.export



❶ Select 'Export ALL PANDDA models' and click 'run'

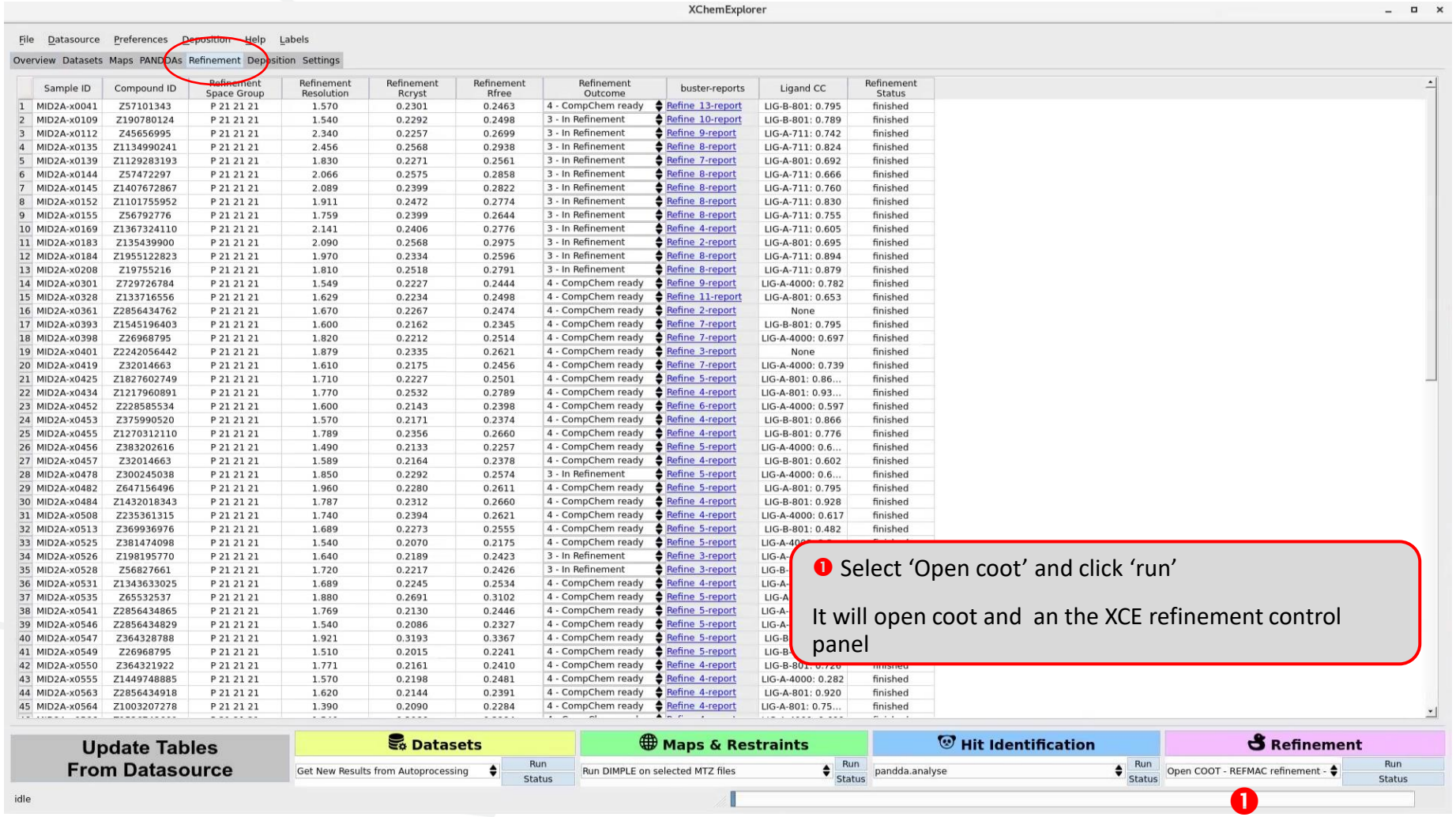
It will prepare the model (bound/unbound state) and refinement parameters, do a first round of refinement and create the ligand validation plot

PanDDAs Tab: pandda.export

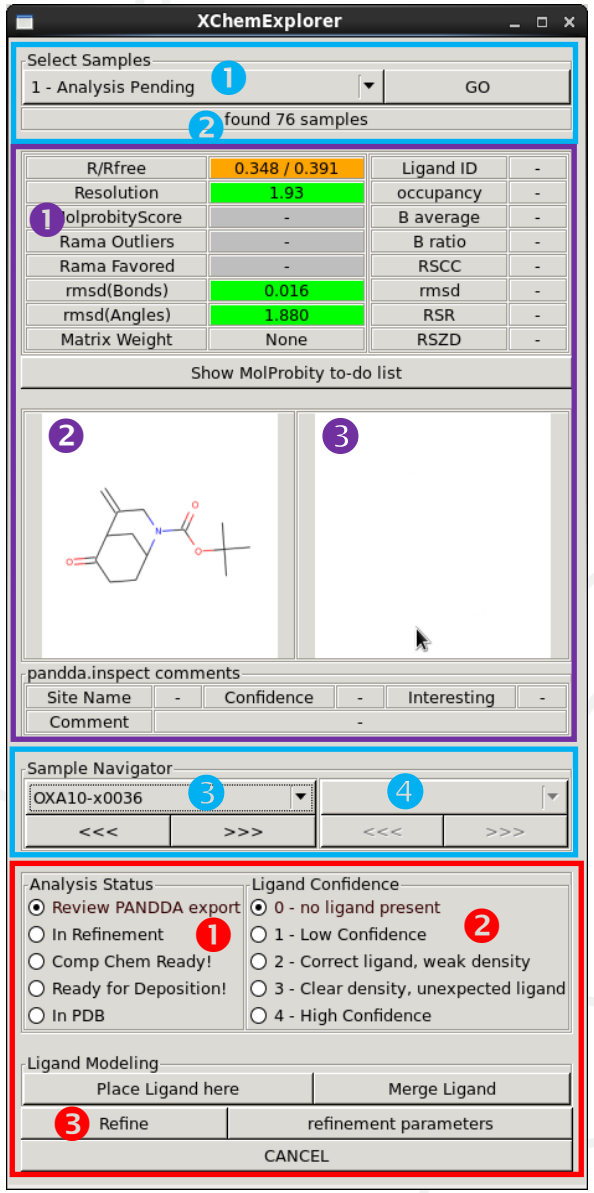
pandda.export

- "Export ***NEW/ALL/SELECTED*** PanDDA models":
  - Generates an ensemble model of bound and ground states and launches refinement
  - Uses REFMAC for refinement
  - Generates occupancy and restraints parameters for refmac and phenix
  - Ligand stats are calculated
- "Refine ***ALL/NEW*** bound-state models with BUSTER":
  - Launches refinement of **bound-state only**
  - Useful for high occupancy ligands with single protein conformations
  - Can launch without sanity checks ("no sanity check") but not recommended
    - If refinement job fails then check the buster log files to see why and fix

Refinement Tab



Refinement Tab



❶ Select the category/status of samples you want to refine (at the beginning: **3 – in refinement**) and click 'GO'
❷ It will tell you how many samples were found for that category
❸ To navigate through the samples in the selected category
❹ To select the event of interest

N.B - XCE has already run on cycle of refinement straight after pandda.export

❶ Summary of refinement statistics
❷ & ❸ are currently unavailable

❶ Manually change the status of a model:
"**In Refinement**" – currently being refined
"**Comp Chem Ready**!" - Ligand and binding site refined, ready for interpretation, some atoms to refine elsewhere may remain.
"**Ready for Deposition!**" – drawn into any deposition actions
❷ Maually select the ligand confidence for ***this event***
❸ Launch a refinement of the current model (plus other options)

'Comp chem ready' structure can be shared with your chemist to start follow-up work.

PDB Group Deposition

- We can deposit XChem fragment structures to the RCSB in a single group
- Models and integrated data are deposited as .mmcif files
- Instructions are contained within the XCE interface – the process is still clunky so some manual file edits may be necessary, but your local contact should be able to help

References

XChem Explorer

Krojer, T., *et al.* **The *XChem Explorer* graphical workflow tool for routine or large-scale protein-ligand structure determination.** *Acta Cryst D*, **73**, 267-278 (2017). https://doi.org/10.1107/S2059798316020234

PanDDA

Pearce, N., *et al.* **Partial-occupancy binders identified by the Pan-Dataset Density Analysis method offer new chemical opportunities and reveal cryptic binding sites.** *Structural Dynamics,* **4**, 032104 (2017). https://doi.org/10.1063/1.4974176

Pearce, N., *et al.* **A multi-crystal method for extracting obscured crystallographic states from conventionally uninterpretable electron density**. *Nat. Commun.,* **8**, 15123 (2017). https://doi.org/10.1038/ncomms15123

https://github.com/ConorFWild/pandda_2_gemmi

XChem pipeline overview

Douangamath, A., *et al*. **Achieving Efficient Fragment Screening at XChem Facility at Diamond Light Source.** *JoVE journal (2021). https://www.jove.com/t/62414/achieving-efficient-fragment-screening-at-xchem-facility-at-diamond*

XChem Bulletin Board

https://www.jiscmail.ac.uk/cgi-bin/webadmin?A0=XCHEMBB