XChem training

Rev May 2022

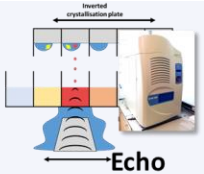
XCE v1.8.2

XChemExplorer

PanDDA

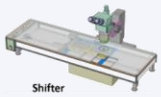
PDB Batch deposition

XChem at Diamond
Complete screening experiment: crystal-to-model

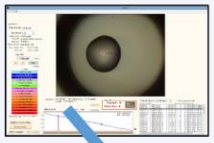


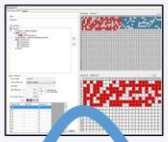
TeXRank
Crystal targeting

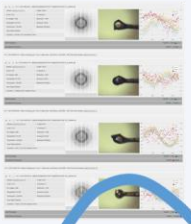
Echo
Crystal soaking



Shifter
Crystal mounting





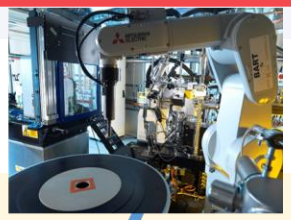


ISPyB
Sample registration

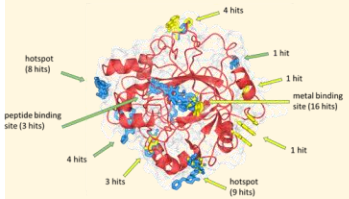
Prepare 1000+ crystals

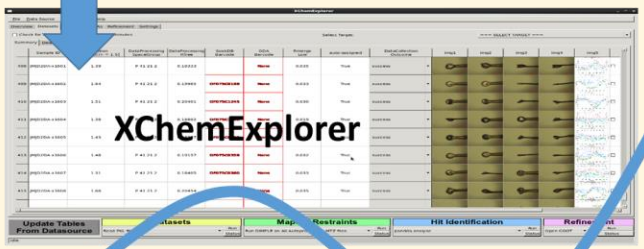
I04-1
Data collection

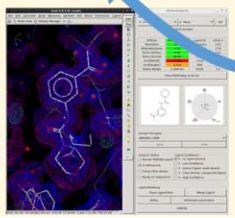
Fragment Library



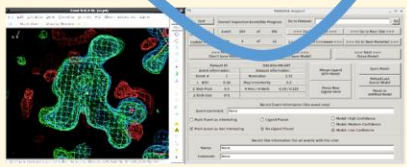
Measure 1000+ crystals







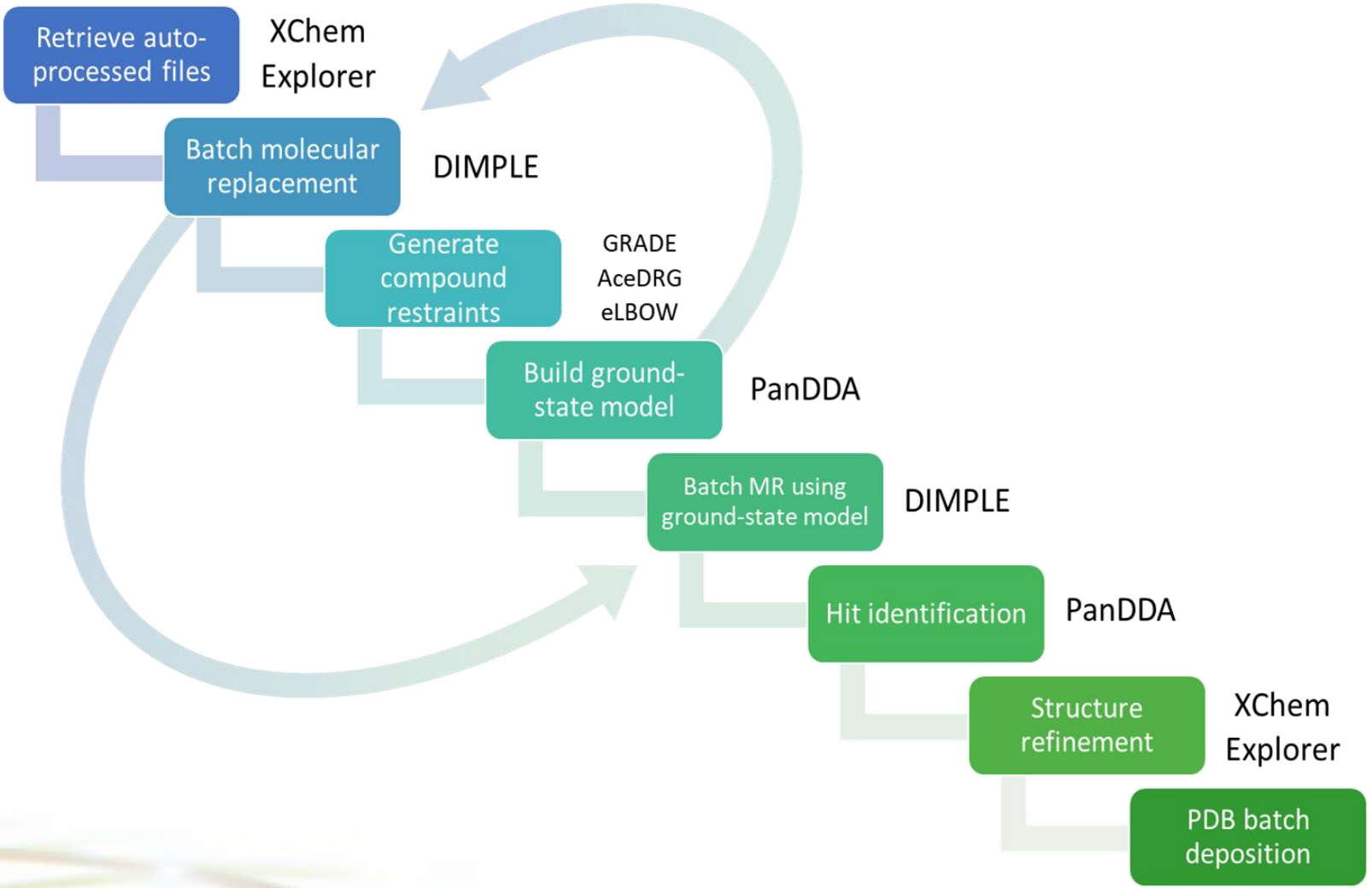
XCE-Coot
Model refinement



PanDDA
Hit detection

Analyse 1000+ datasets

XChem data processing overview



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

XChemBB

Register and email your questions to XChem Bulletin Board:

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

XChemExplorer
How to get started

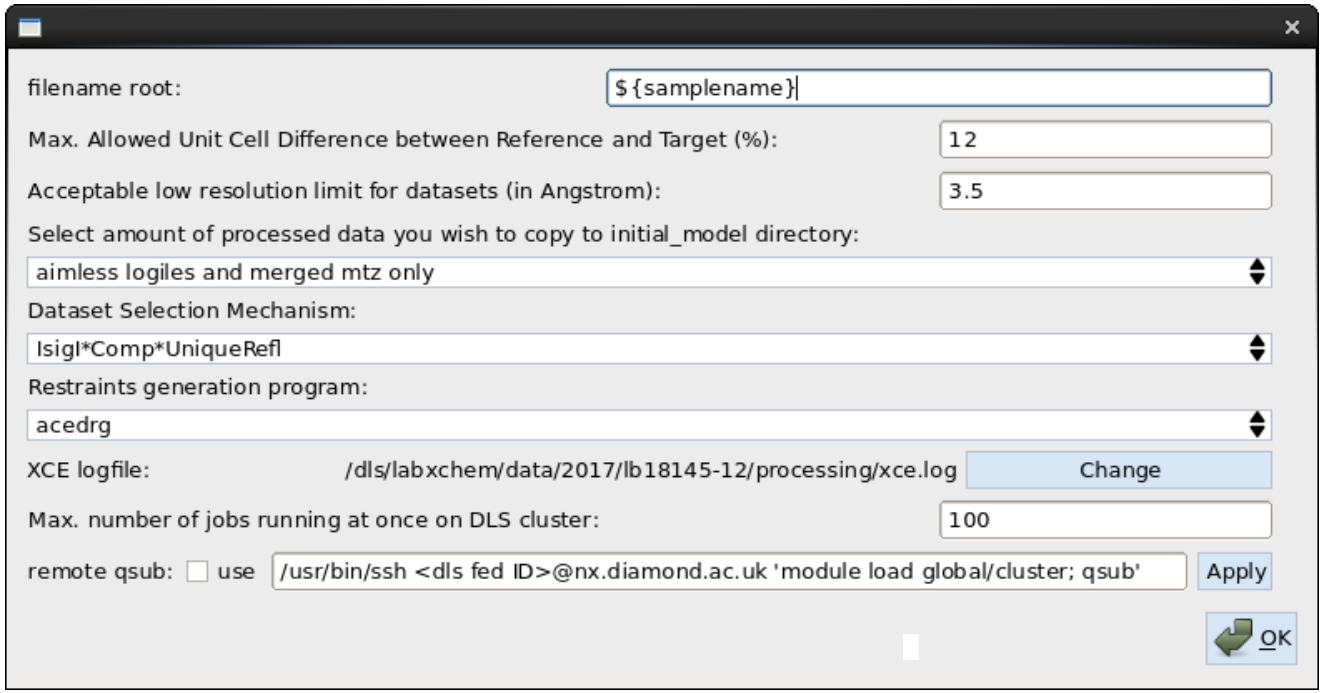
- Go to the processing directory of your visit:
  - `cd /dls/labxchem/data/`**`proposal`**`/`**`visit`**`/processing/`
- Put your initial reference pdb (waters included, non-conserved ligand excluded) in the directory:
  - `/ dls/labxchem/data/`**`proposal`**`/`**`visit`**`/processing/reference`
- Start XCE **in your visit processing directory**
  - `go in / dls/labxchem/data/`**`proposal`**`/`**`visit`**`/processing/`
  - `xce`

XCE preferences

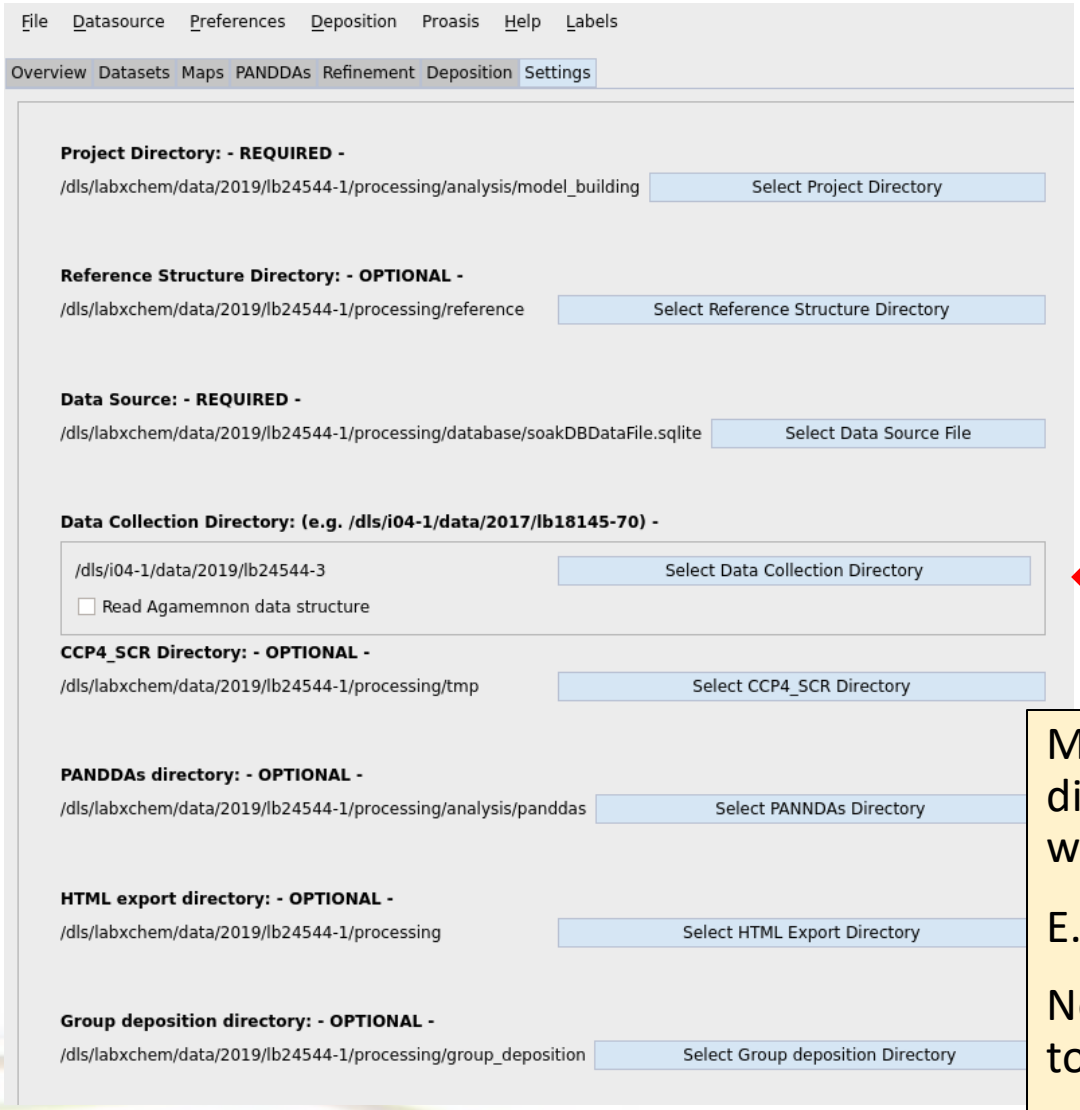
Dimple reference model selection criteria ⇨

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

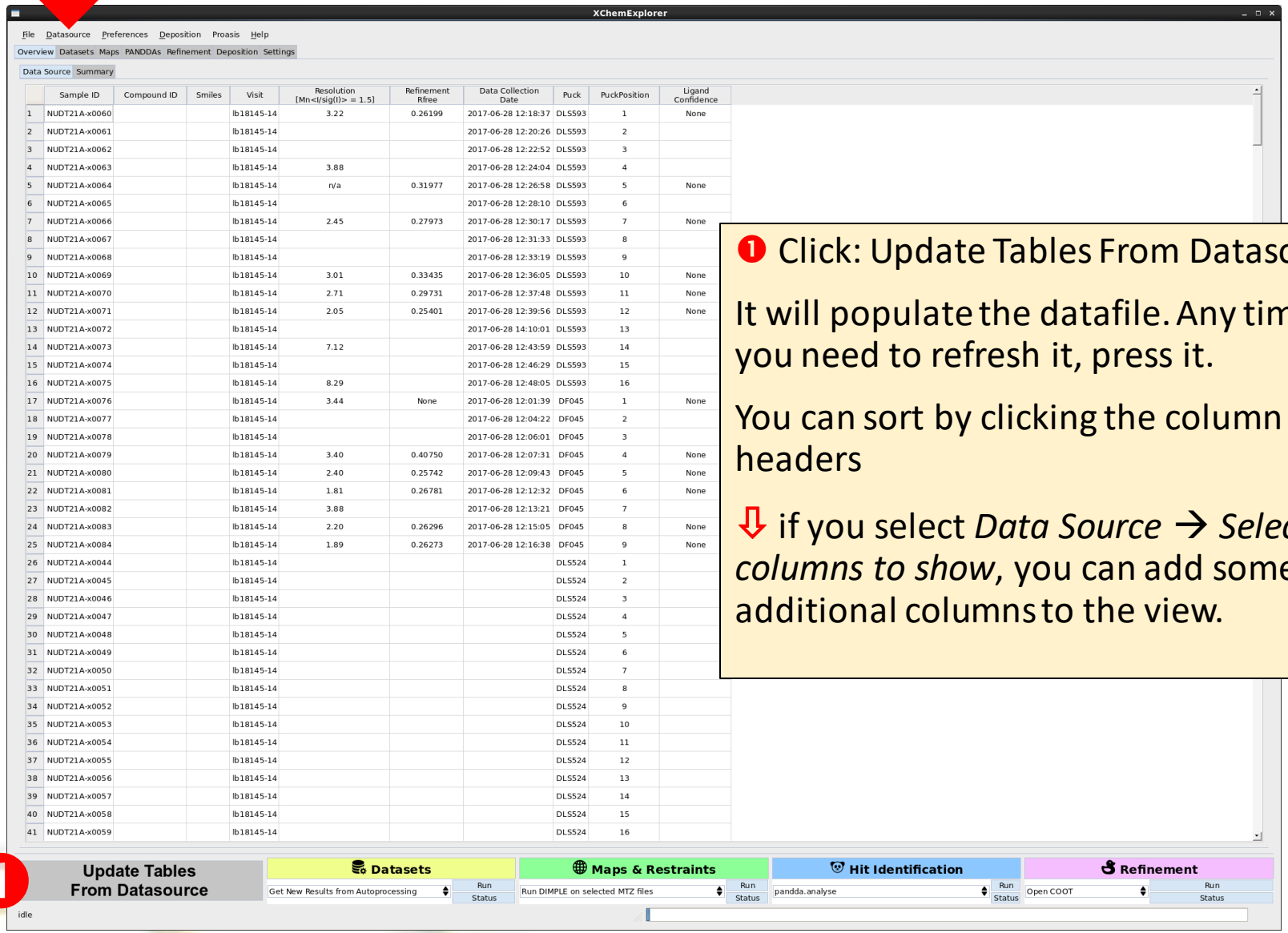
Manually change the data collection directory to the i04-1 directory where you have collected your data.

E.g. /dls/i04-1/data/year/proposal-2

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

If data collected with UDC, select "Read Agamemnon data structure" before setting directory

Data source tab: Overview of your experiments



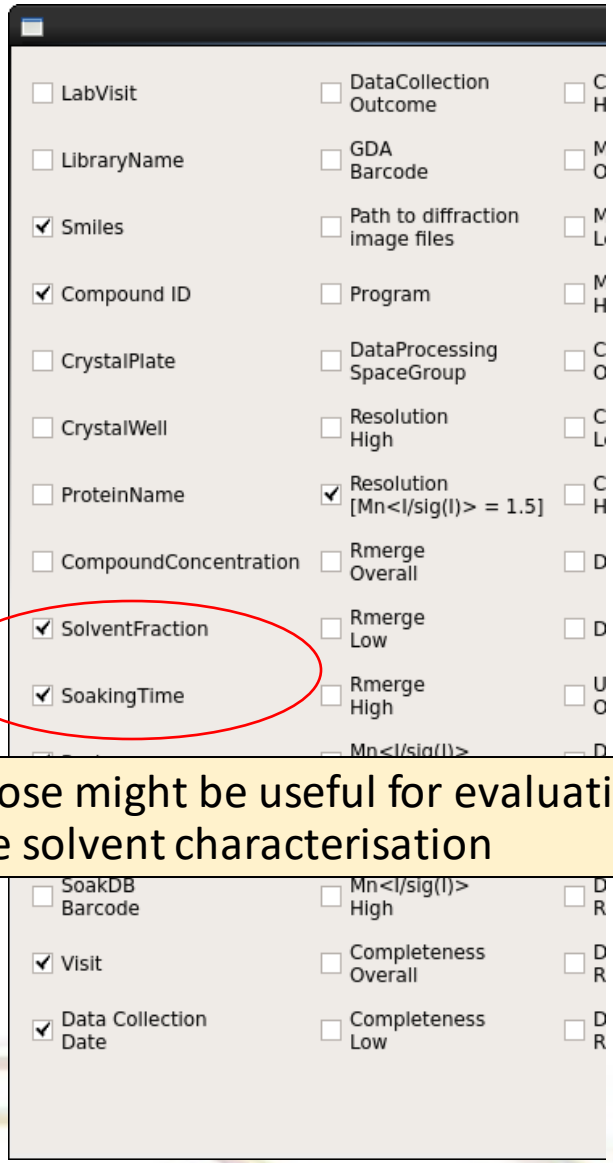
	Sample ID	Compound ID	Smiles	Visit	Resolution [Mn<I/sig(I)> = 1.5]	Refinement Rfree	Data Collection Date	Puck	PuckPosition	Ligand Confidence
1	NUDT21A-x0060			lb18145-14	3.22	0.26199	2017-06-28 12:18:37	DLS593	1	None
2	NUDT21A-x0061			lb18145-14			2017-06-28 12:20:26	DLS593	2	
3	NUDT21A-x0062			lb18145-14			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

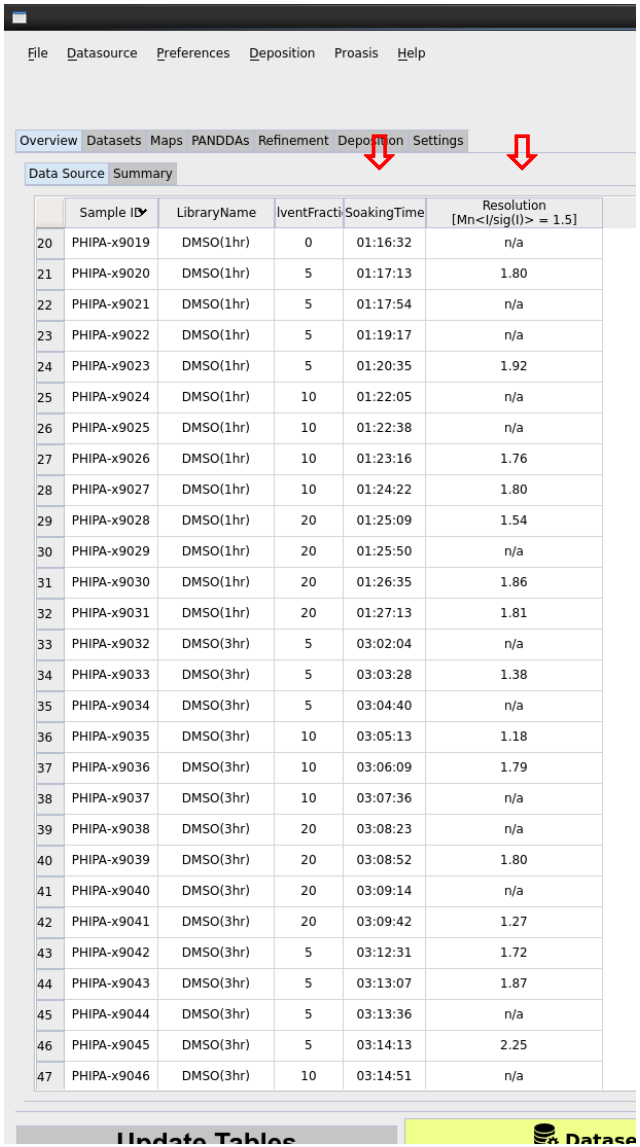
It will populate the datafile. Any time you need to refresh it, press it.

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.

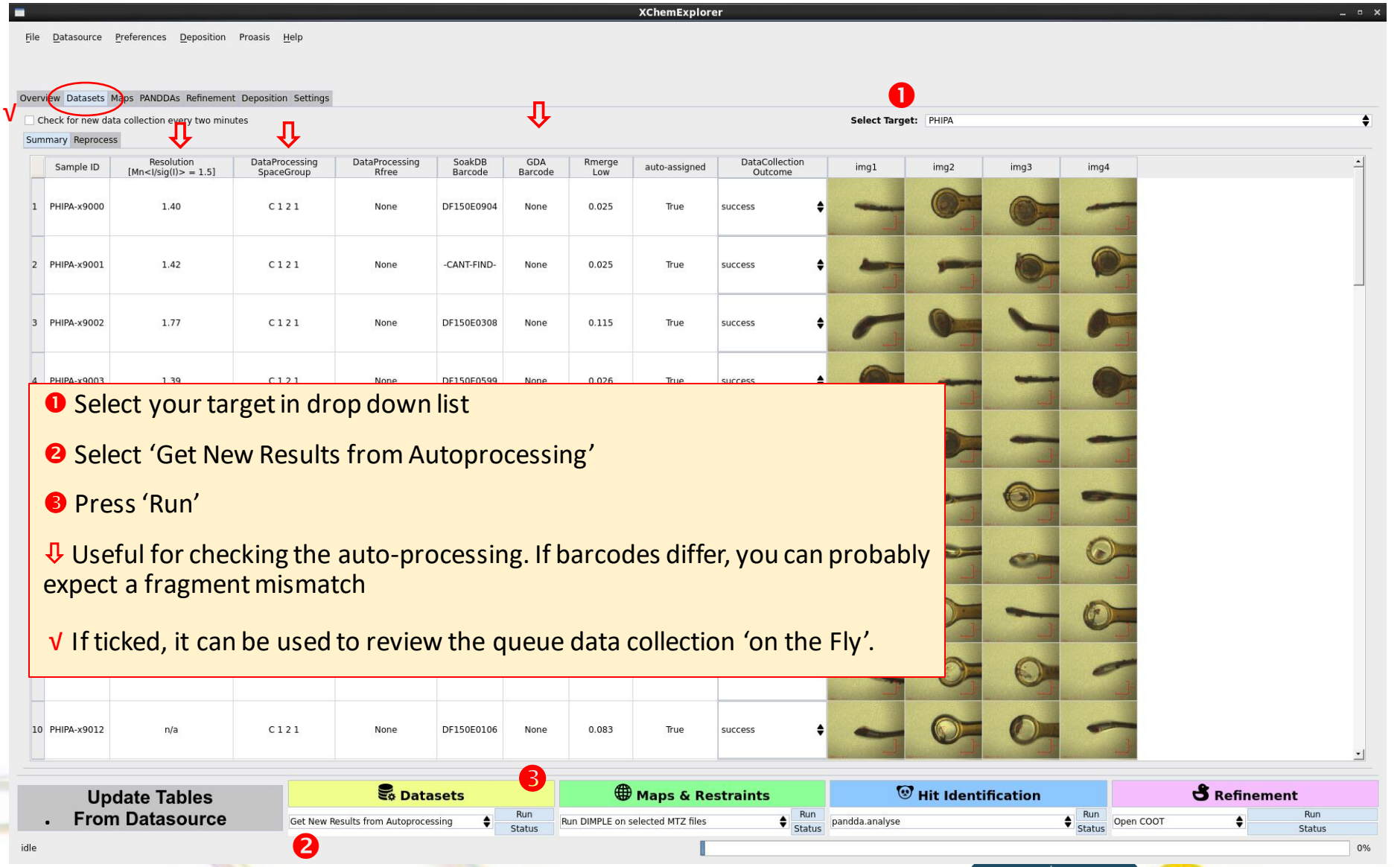


Those might be useful for evaluating the solvent characterisation



	Sample ID	LibraryName	IventFracti	SoakingTime	Resolution [Mn<I/sig(I)> = 1.5]
20	PHIPA-x9019	DMSO(1hr)	0	01:16:32	n/a
21	PHIPA-x9020	DMSO(1hr)	5	01:17:13	1.80
22	PHIPA-x9021	DMSO(1hr)	5	01:17:54	n/a
23	PHIPA-x9022	DMSO(1hr)	5	01:19:17	n/a
24	PHIPA-x9023	DMSO(1hr)	5	01:20:35	1.92
25	PHIPA-x9024	DMSO(1hr)	10	01:22:05	n/a
26	PHIPA-x9025	DMSO(1hr)	10	01:22:38	n/a
27	PHIPA-x9026	DMSO(1hr)	10	01:23:16	1.76
28	PHIPA-x9027	DMSO(1hr)	10	01:24:22	1.80
29	PHIPA-x9028	DMSO(1hr)	20	01:25:09	1.54
30	PHIPA-x9029	DMSO(1hr)	20	01:25:50	n/a
31	PHIPA-x9030	DMSO(1hr)	20	01:26:35	1.86
32	PHIPA-x9031	DMSO(1hr)	20	01:27:13	1.81
33	PHIPA-x9032	DMSO(3hr)	5	03:02:04	n/a
34	PHIPA-x9033	DMSO(3hr)	5	03:03:28	1.38
35	PHIPA-x9034	DMSO(3hr)	5	03:04:40	n/a
36	PHIPA-x9035	DMSO(3hr)	10	03:05:13	1.18
37	PHIPA-x9036	DMSO(3hr)	10	03:06:09	1.79
38	PHIPA-x9037	DMSO(3hr)	10	03:07:36	n/a
39	PHIPA-x9038	DMSO(3hr)	20	03:08:23	n/a
40	PHIPA-x9039	DMSO(3hr)	20	03:08:52	1.80
41	PHIPA-x9040	DMSO(3hr)	20	03:09:14	n/a
42	PHIPA-x9041	DMSO(3hr)	20	03:09:42	1.27
43	PHIPA-x9042	DMSO(3hr)	5	03:12:31	1.72
44	PHIPA-x9043	DMSO(3hr)	5	03:13:07	1.87
45	PHIPA-x9044	DMSO(3hr)	5	03:13:36	n/a
46	PHIPA-x9045	DMSO(3hr)	5	03:14:13	2.25
47	PHIPA-x9046	DMSO(3hr)	10	03:14:51	n/a

Datasets tab: Load datasets



❶ Select your target in drop down list

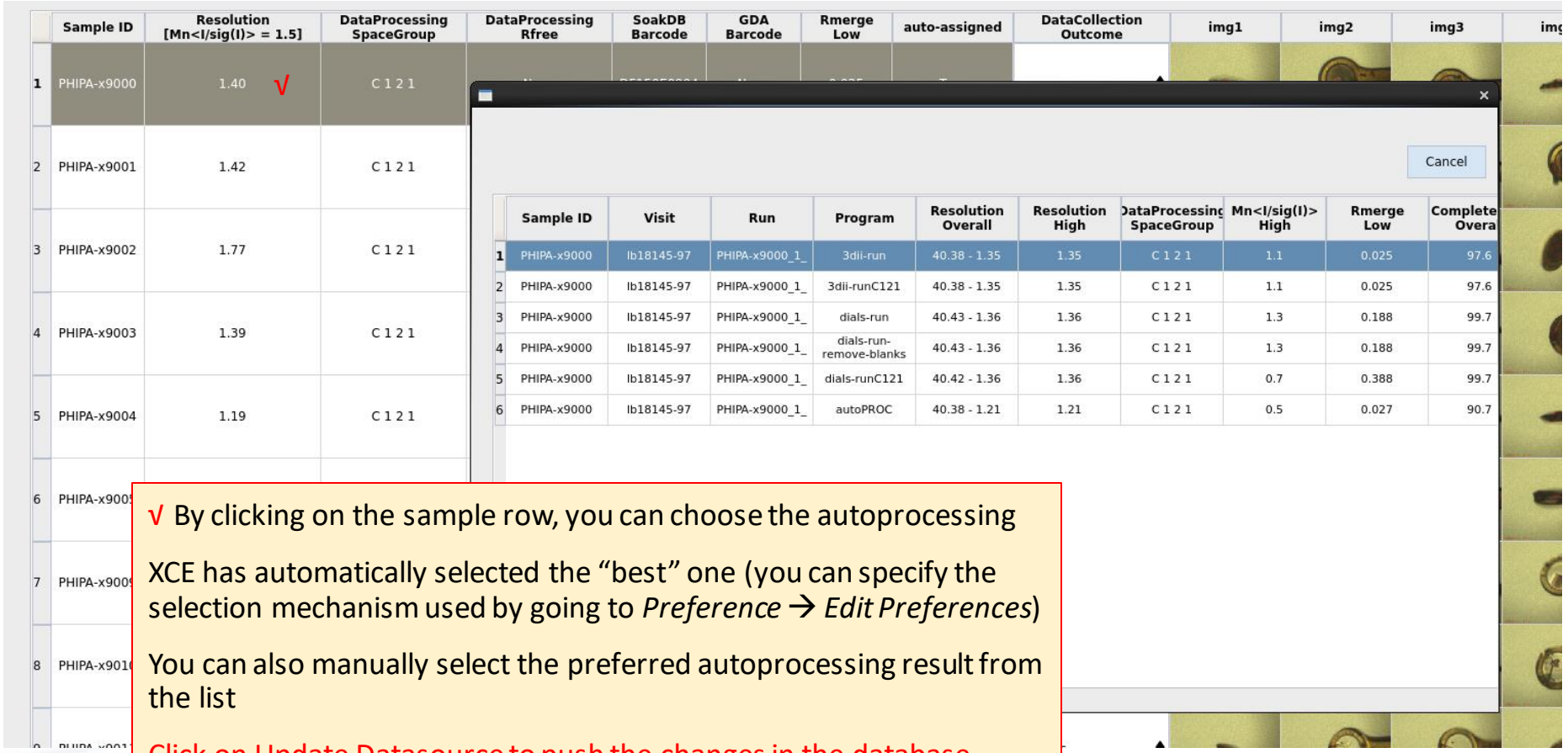
❷ Select ‘Get New Results from Autoprocessing’

❸ Press ‘Run’

⇩ Useful for checking the auto-processing. If barcodes differ, you can probably expect a fragment mismatch

√ If ticked, it can be used to review the queue data collection ‘on the Fly’.

Datasets tab: Load datasets



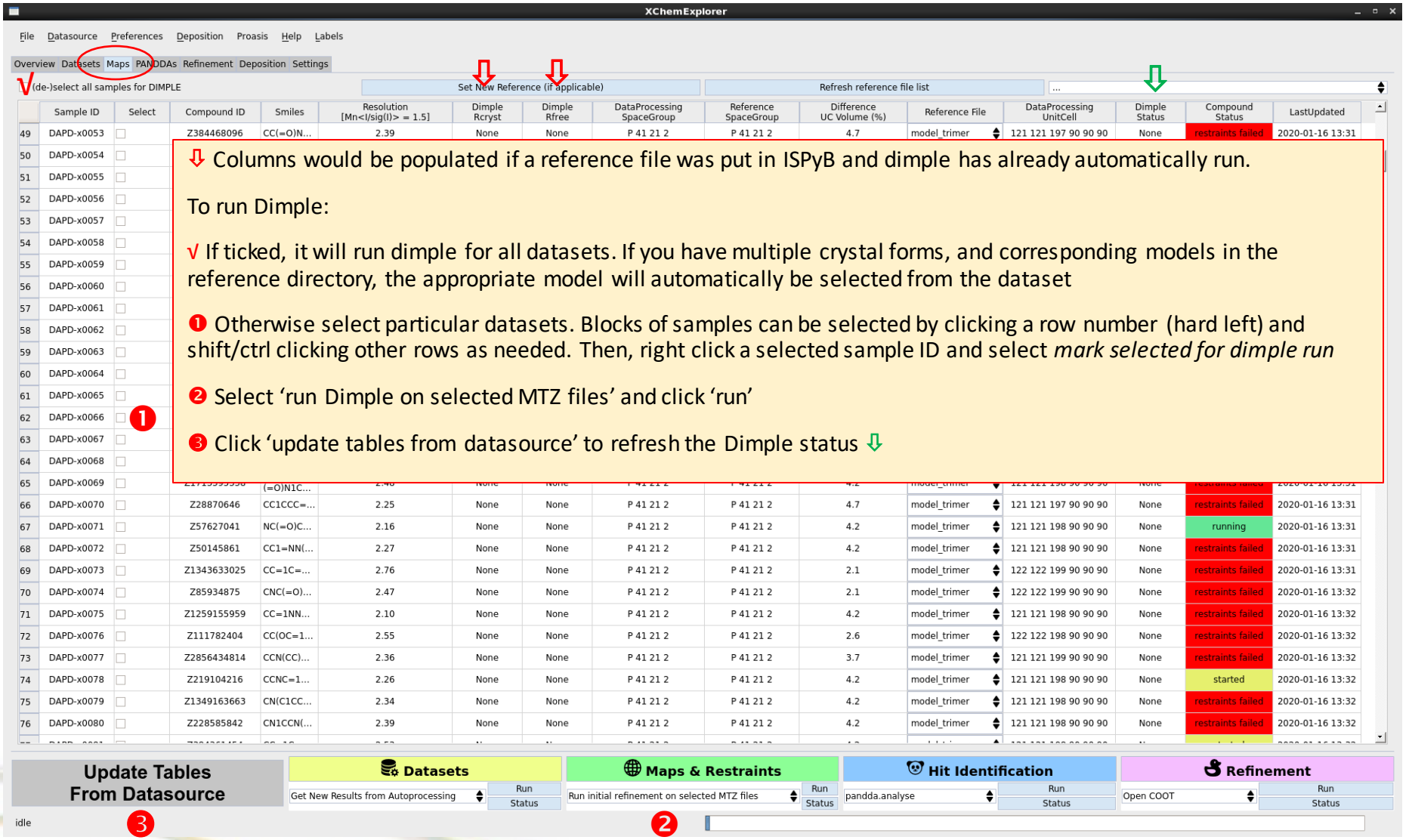
√ By clicking on the sample row, you can choose the autoprocessing

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

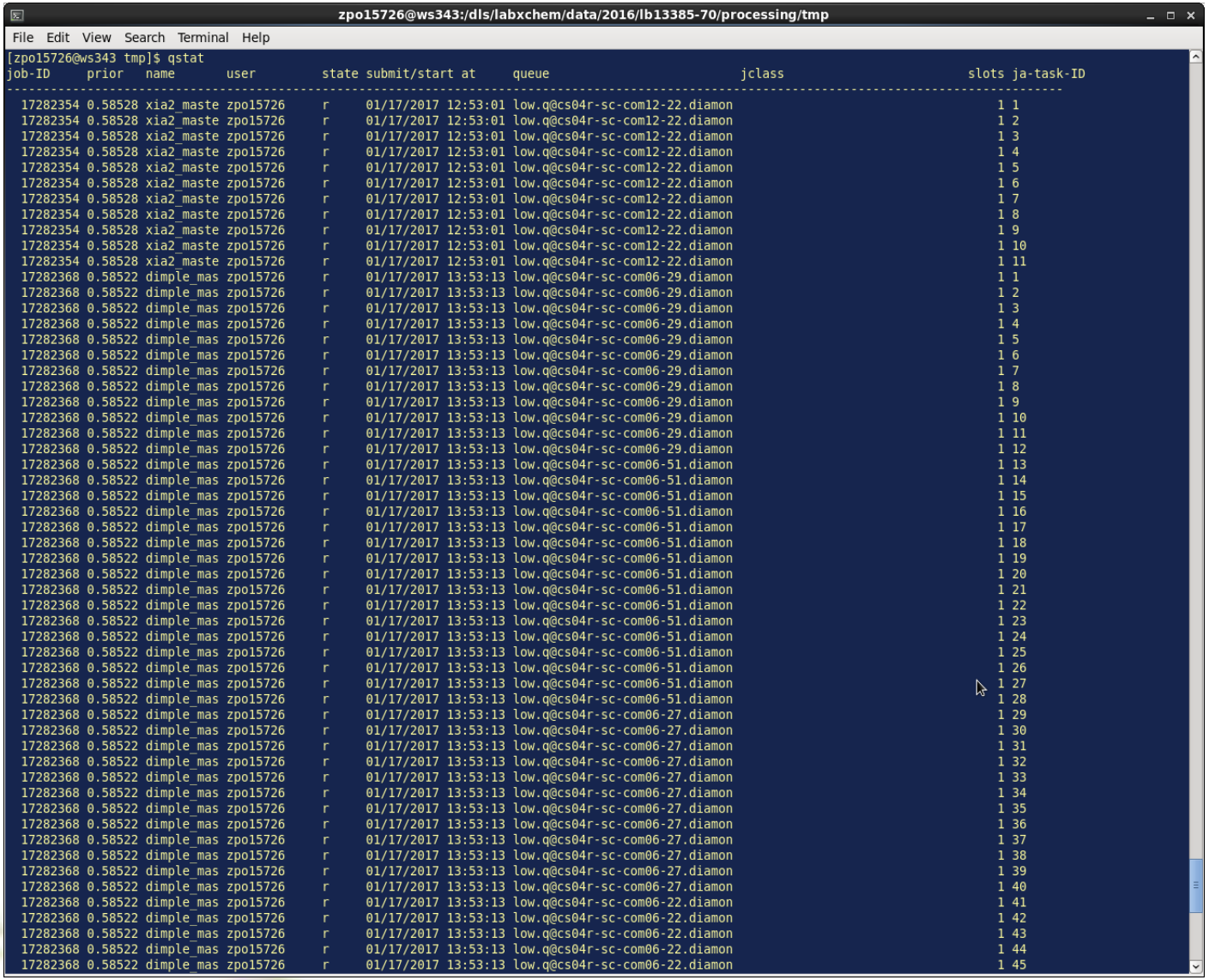
You can also manually select the preferred autoprocessing result from the list

Click on Update Datasource to push the changes in the database

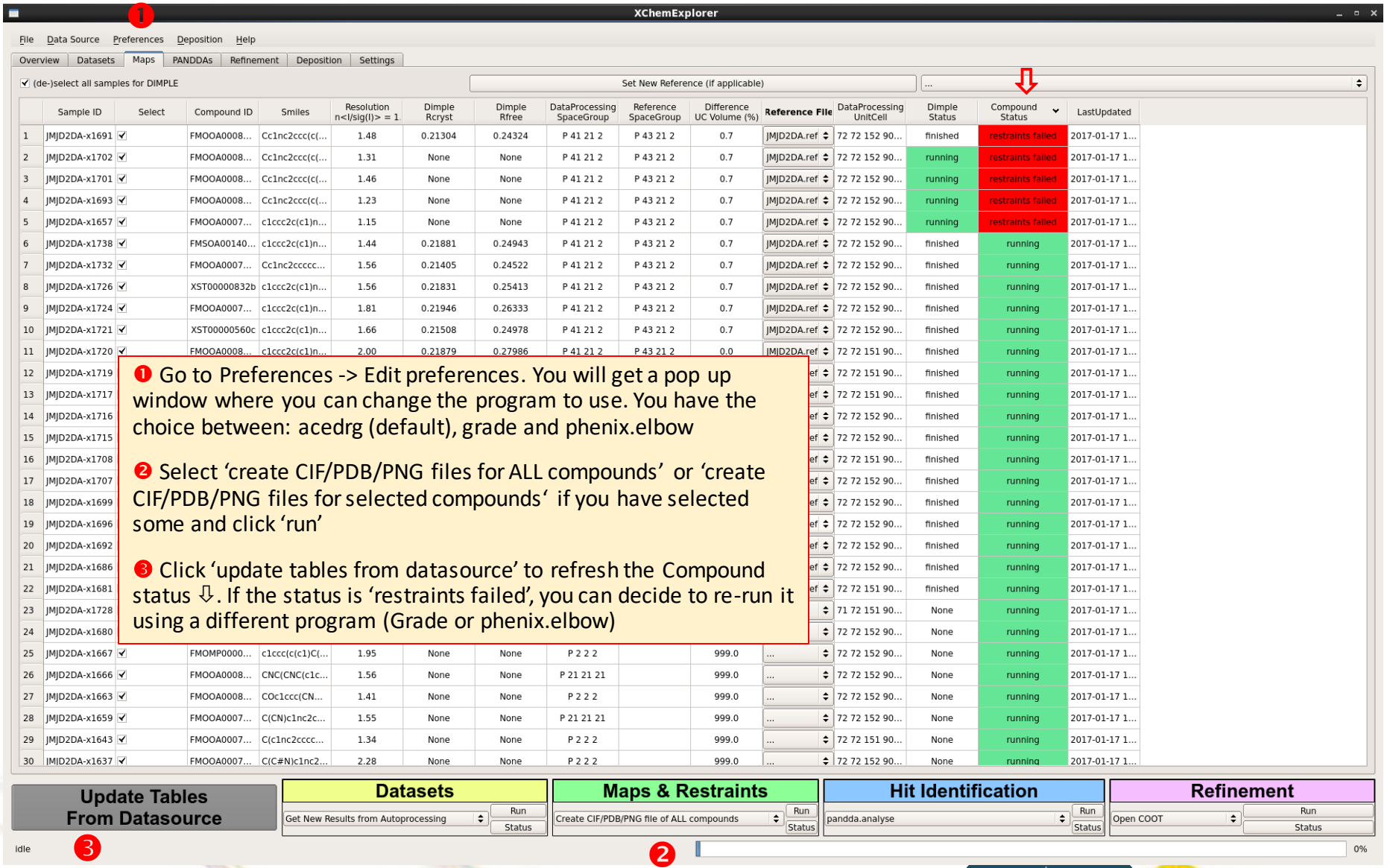
Maps tab: Running Dimple for MR ("Run initial refinement")



Check that dimple jobs are running: qstat (or watch qstat)



Maps tab: Creating the ligands restraints



Ground-state model building

- Pre-screen data are used to build the best possible reference model: the ground-state model.
  - A PanDDA pre-run is required to calculate the mean map you will use to build the ground-state model

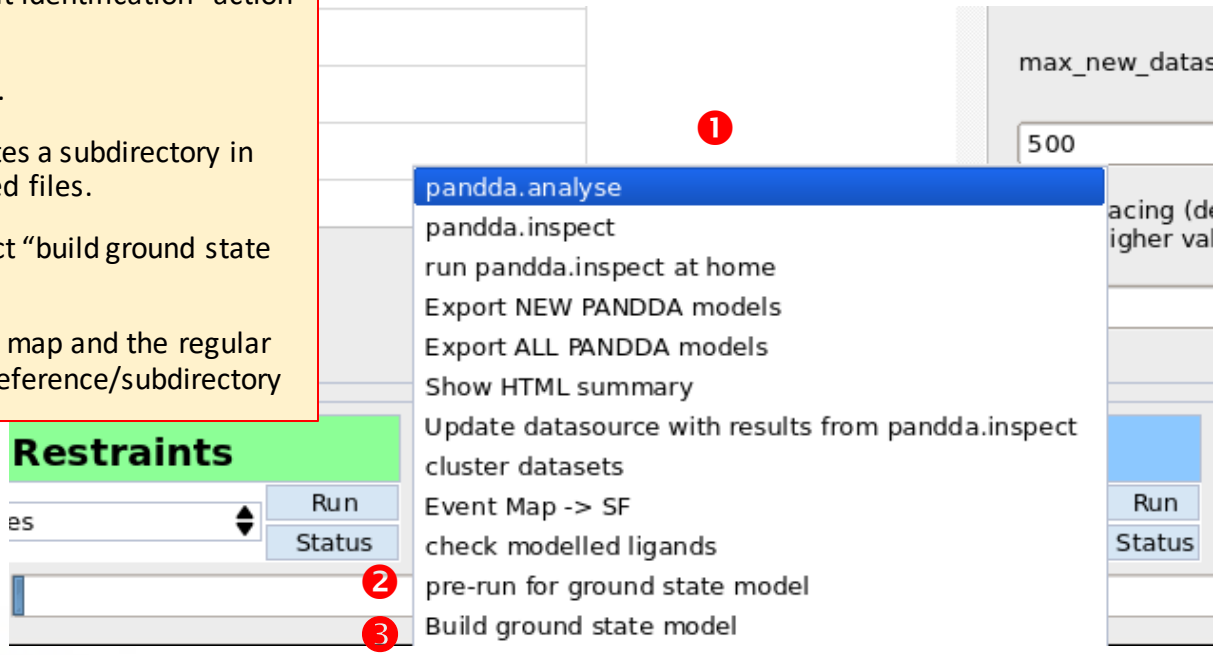
❶ Click on the drop-down menu in the "Hit identification" action box

❷ Select "pre-run for ground state model".

Wait for the job to finish (qstat). 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".

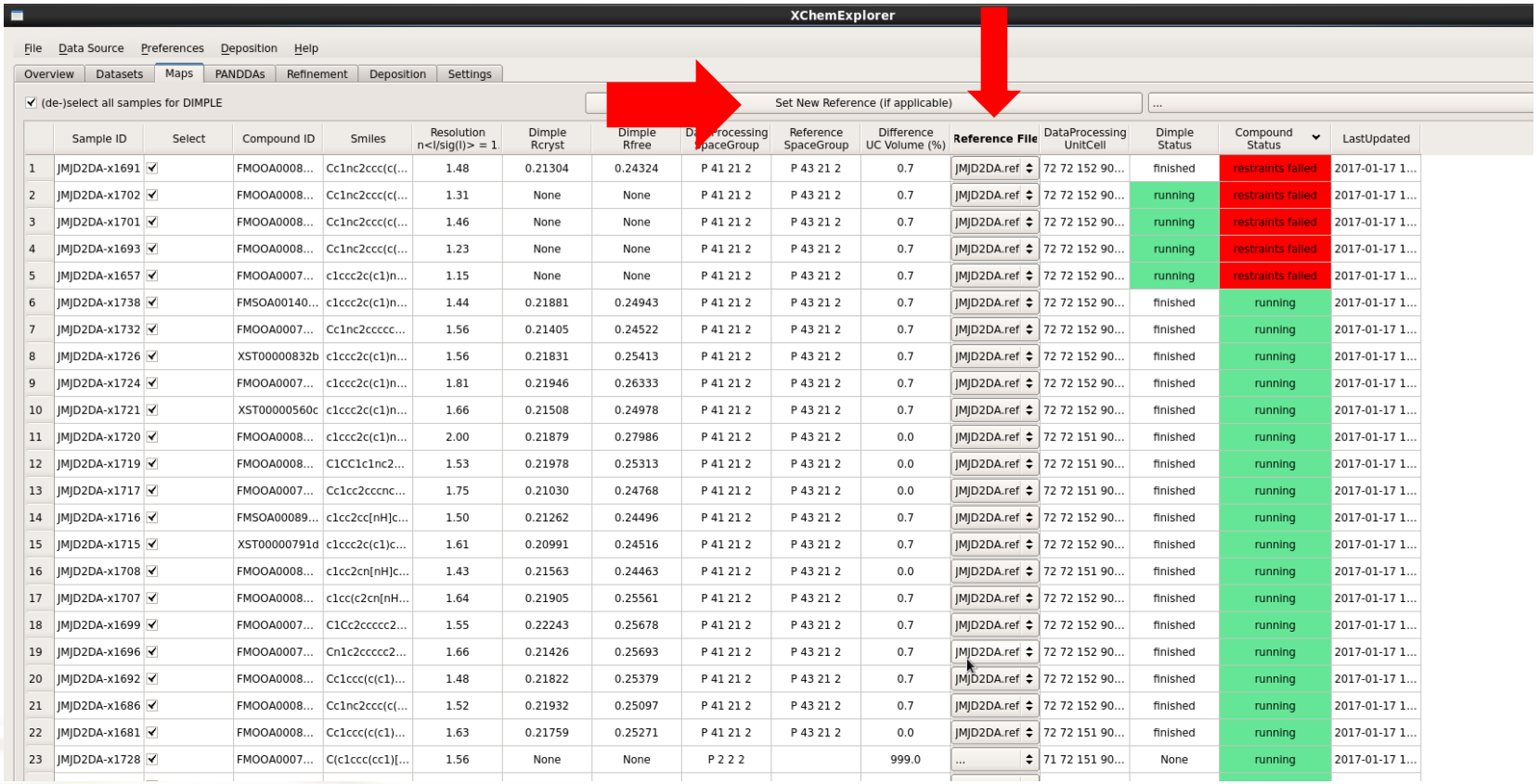
This will open Coot with the pandda mean map and the regular 2Fo-Fc, Fo-Fc maps loaded from the new reference/subdirectory



Ground-state model building

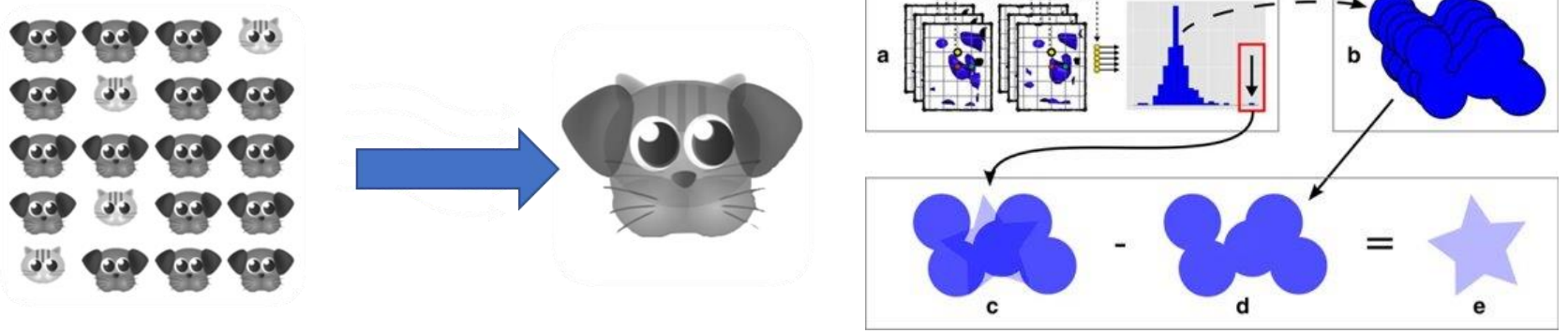
4) Remodel and refine the reference model as you wish using the PanDDA mean map in Coot.

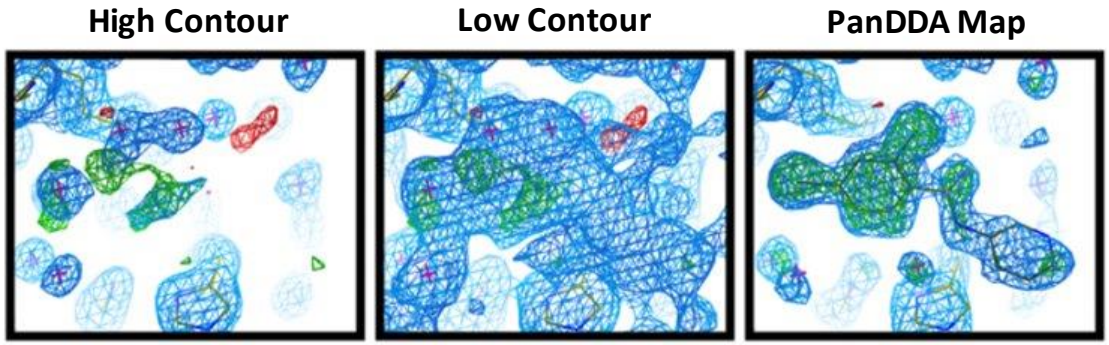
5) Re-run Dimple (XCE – Maps table) by using this ground-state model as new reference



	Sample ID	Select	Compound ID	Smiles	Resolution n<I/sig(I)> = 1.	Dimple Rcryst	Dimple Rfree	DataProcessing 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...

Finding hits - Pan Density Dataset Analysis (PanDDA)



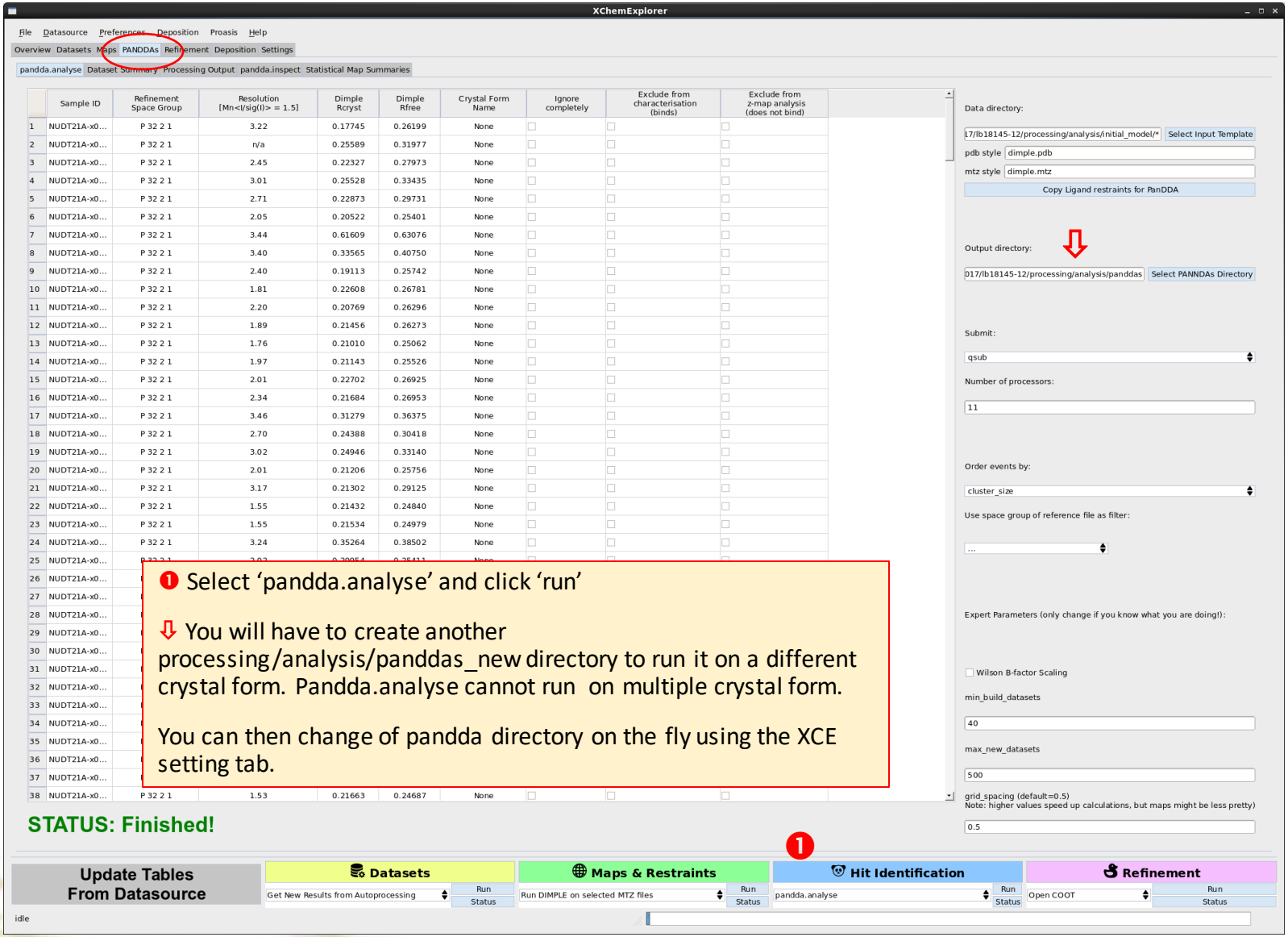


https://doi.org/10.1038/ncomms15123
https://doi.org/10.1063/1.4974176

PanDDA workflow

- pandda.analyse: Largest component of the program. Does all the heavy lifting
  - It analyses all the data, aligns structures to a reference structure, calculates the statistical maps, identifies events, calculates event maps
  - It can take some time to run on the cluster if there are lots of datasets and the unit cell is large
- pandda.inspect: Allows the user to inspect, annotate and place the fragment in Coot - Not a refinement tool despite appearances.
- pandda.export: Generates bound+unbound ensemble models for refinement
  - Occupancy and restraints parameters for refmac and phenix are generated
  - XCE will launch a first cycle of refinements on the cluster
  - Ligand stats are calculated
- Refine bound-state model with BUSTER
  - Useful for high occupancy ligands and follow-up compounds

PANDDAs Tab: pandda.analyse



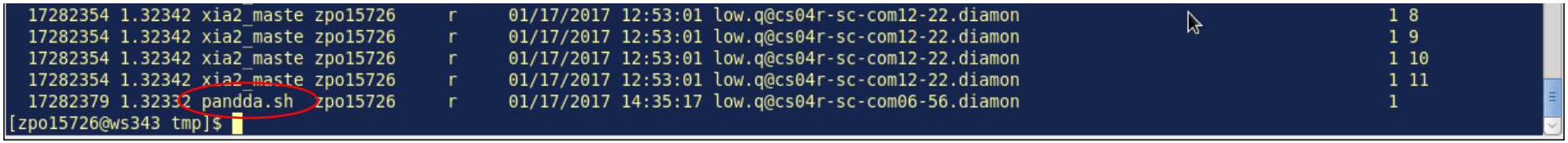
❶ Select 'pandda.analyse' and click 'run'

⇩ You will have to create another processing/analysis/panddas_new directory to run it on a different crystal form. Pandda.analyse cannot run on multiple crystal form.

You can then change of pandda directory on the fly using the XCE setting tab.

How to check pandda.analyse is running?

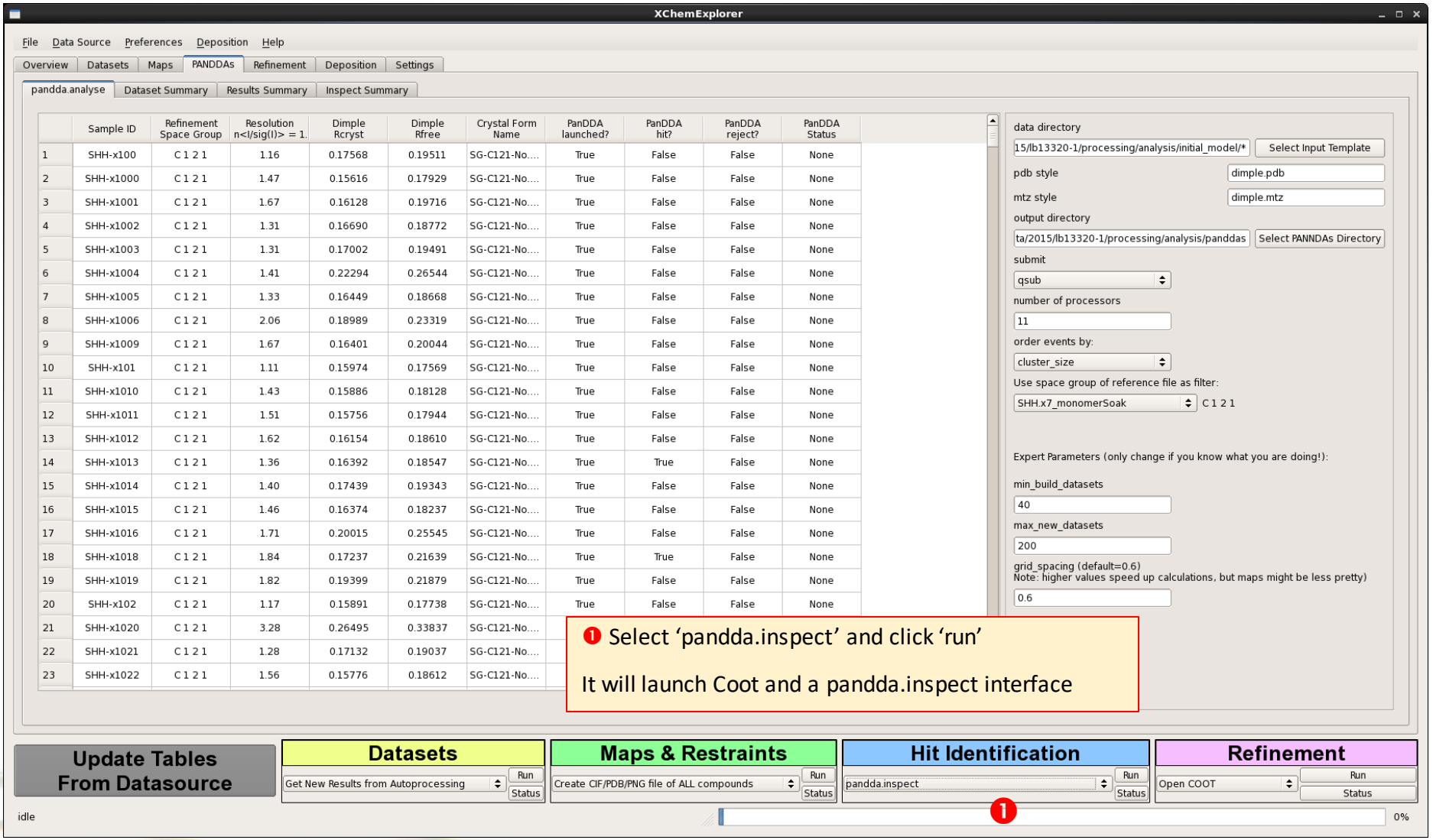
In a terminal, type ‘qstat’, PANDDA job should be listed



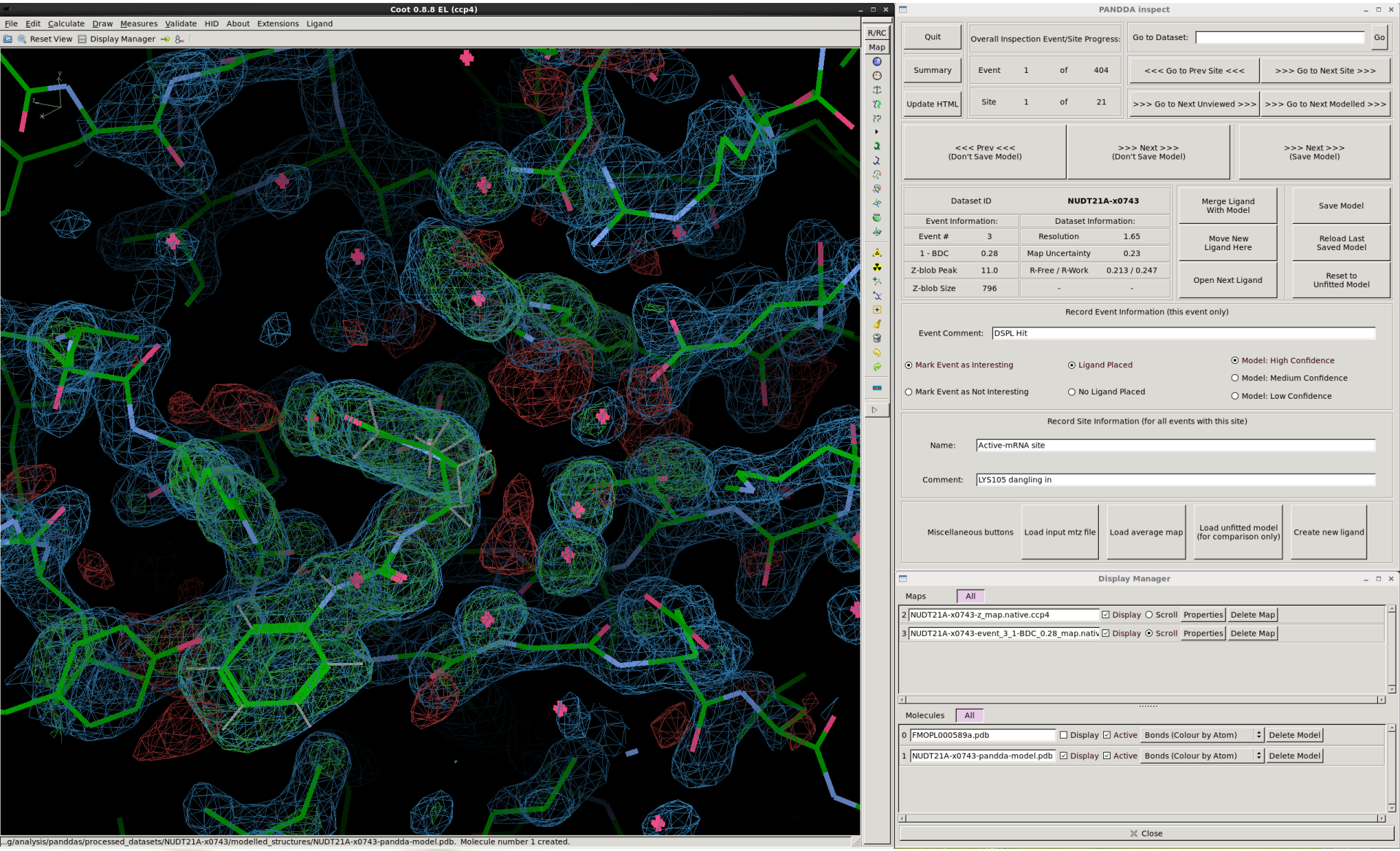
In /dls/labxchem/data/proposal/visit/processing/analysis/panddas

- Current status of pandda job is also given by typing “tail logs/pandda-timestamp.log”
- pandda.sh is the script to edit if you want to customise your pandda.analyse job (see manual in : http://pandda.bitbucket.org)

PanDDAs Tab: pandda.inspect

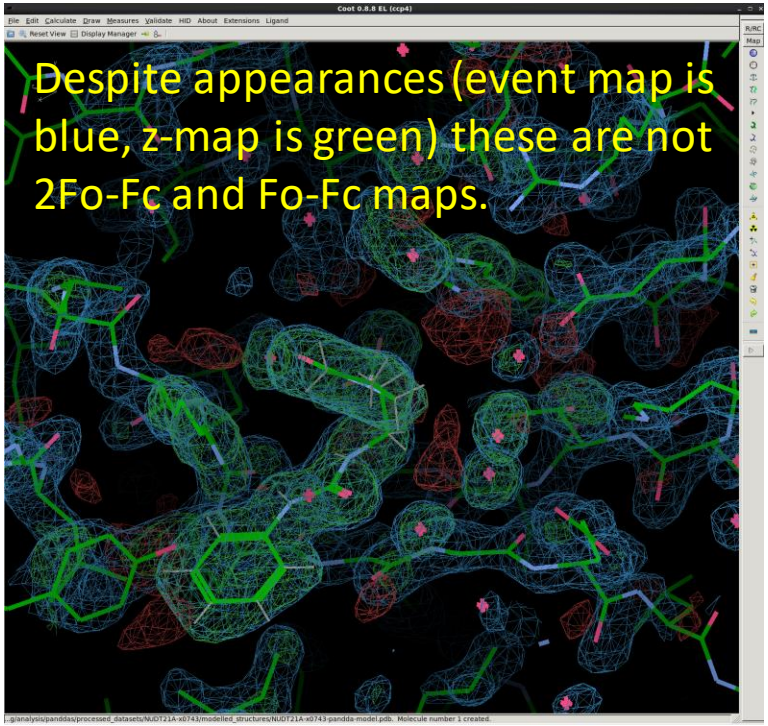


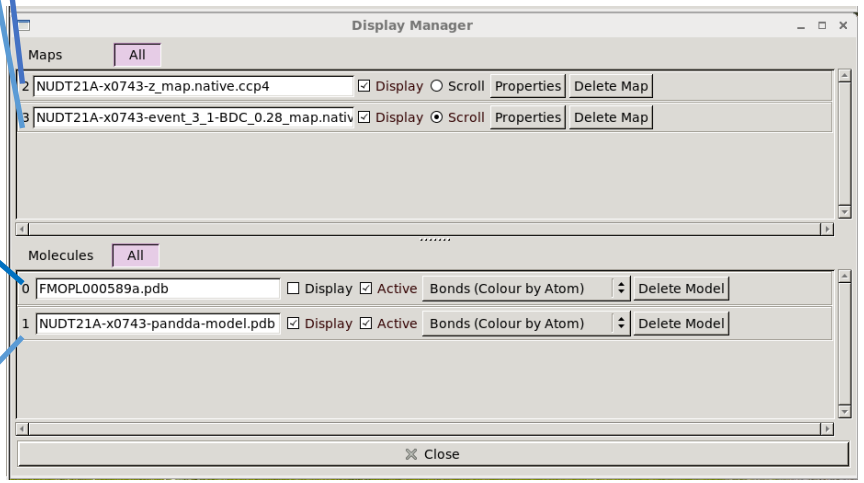
pandda.inspect



pandda.inspect

<label>-z_map.native.ccp4 (looks 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.
<label>-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	These will be automatically loaded. The ligand will be placed in the centre of the screen. Non-displayed but remains loaded if already merged
<label>-pandda-model.pdb	The input structure to pandda.analyse = dimple model = ground state model





pandda.inspect control panel

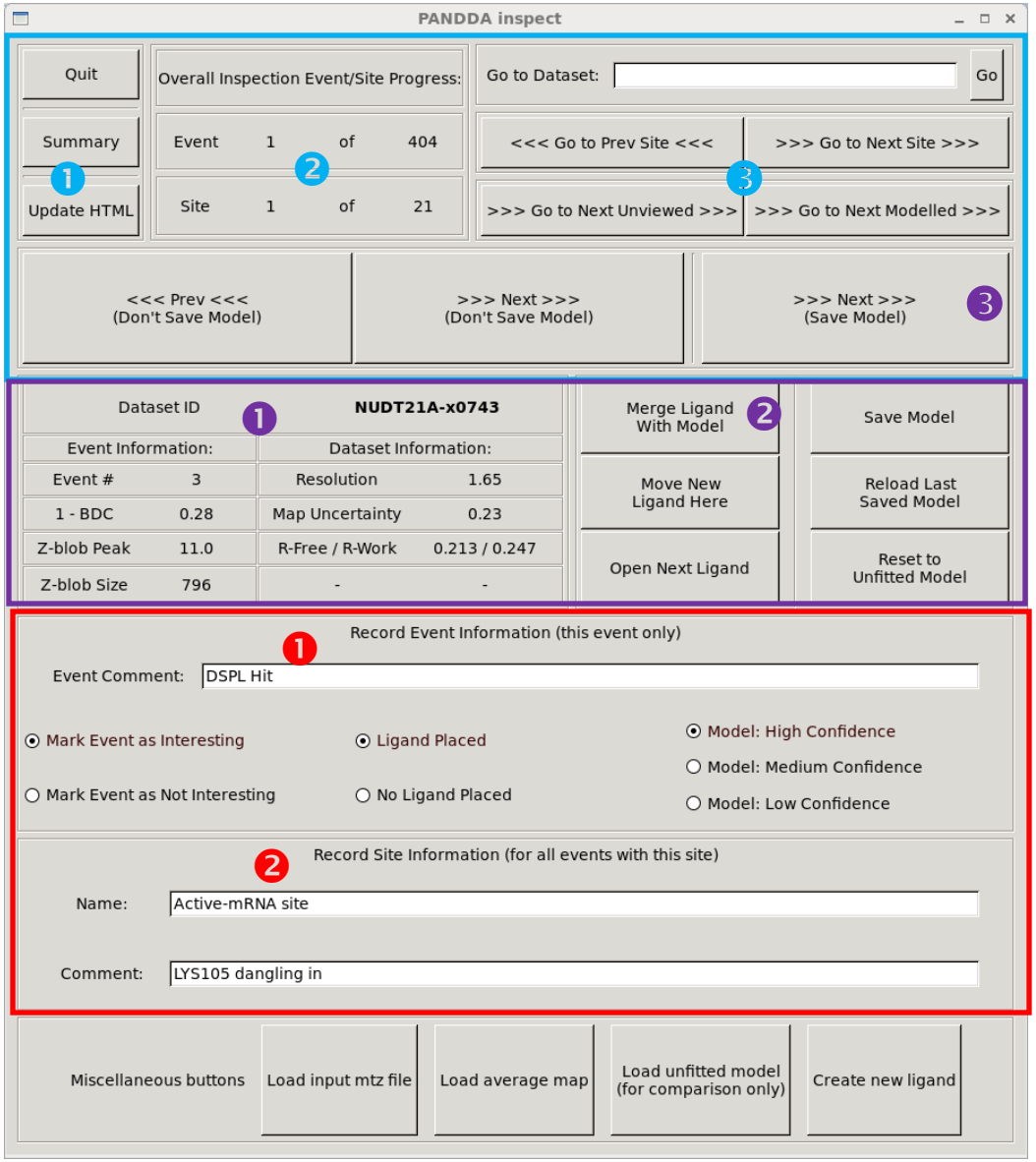
❶ Provide an html summary page that can be updated through the data analysis
❷ Indicate number of sites and events to review and its progress
❸ To navigate through the events and sites, with the option to go straight to a dataset of interest

❶ Summary of PANDDA statistics
❷ To merge the ligand to the model or add another one
❸ To save your work or roll back.

❶ To annotate the event.
❷ To annotate the sites. It will be used in xce in the refinement step to navigate between the sites.

For your real hits to be taken to the next step, you need to have done:

- **Merge ligand with Model**
- 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**



Modelling in pandda (at least read this one slide!)

In the PanDDA paradigm, you are not trying to build the full crystallographic model. You are building a view of the protein when something is bound to it: **the bound-state model**.

- Focus on the event map of the fragment binding pocket (centred view). Do not navigate too far from the initial view, do not search for blobs using Coot tools.
- Only change/delete atoms that are “worth a change”, “which mean something”: which exhibit large Z-peaks in the Z-map. No action on small atom shift or very small conformation change. Every time you validate a change, pandda.inspect save it as an intermediate model which will
- Flick through your events/blobs! There is no need to linger over dubious blobs. If you cannot clearly see the ligand pose in the PanDDa fragment event map, no current tech can. You can still annotate.
- Put yourself in your chemist shoes. Would you give this model to your chemist for follow-up compound design? Would you spend 3 months and 10K of follow-up chemistry based on this blob?

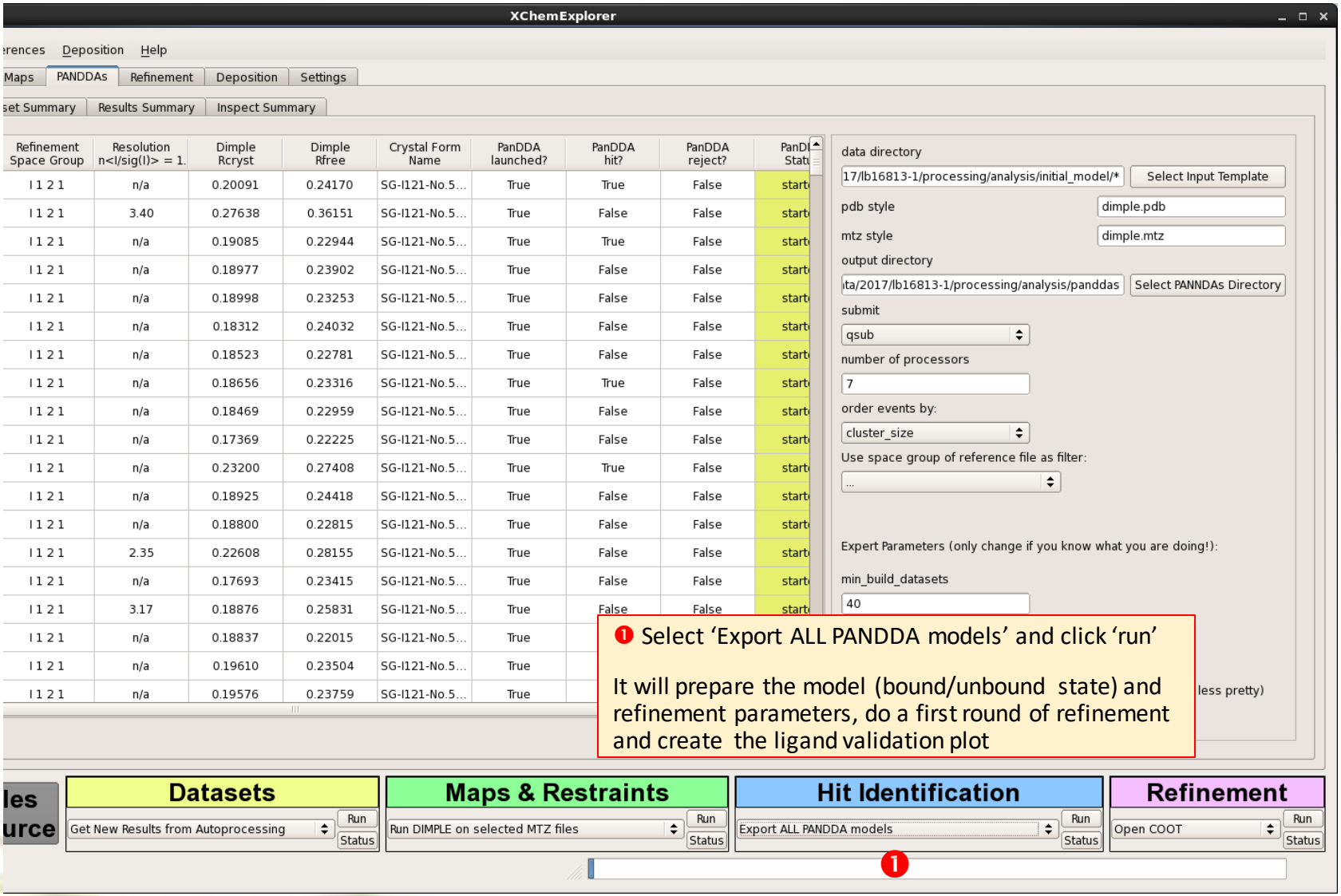
1)	**Prune solvent molecules and alternate sidechain conformations**	**Delete those atoms and alternate conformations that are not present in the event map.**
2)	Fix conformations and rotamers that have changed	For those residues where the sidechain conformation or water molecule position has changed, simply correct the model as would be normal practice. 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 already be loaded if it was supplied to pandda.analyse. You can move it to the centre of the screen using the Move new ligand here button, and you can merge it with the model using the Merge new ligand button.
4)	Save the changes to the model.	If you want to save the changes to the model you can use the Save Model button. Or, if you use the >>> Next Event >>> (Save Model) button, the model will be saved and the next dataset will be loaded.

Oh! And did we already tell you this?

YOU DO NOT REFINE IN PanDDA!

- Don't forget to "merge ligand with Model"
- 'Next' (Save model) interesting models only
- Do not save useless/empty/dubious models
- Annotate as you go

PanDDAs Tab: pandda.export



pandda.export

pandda.export

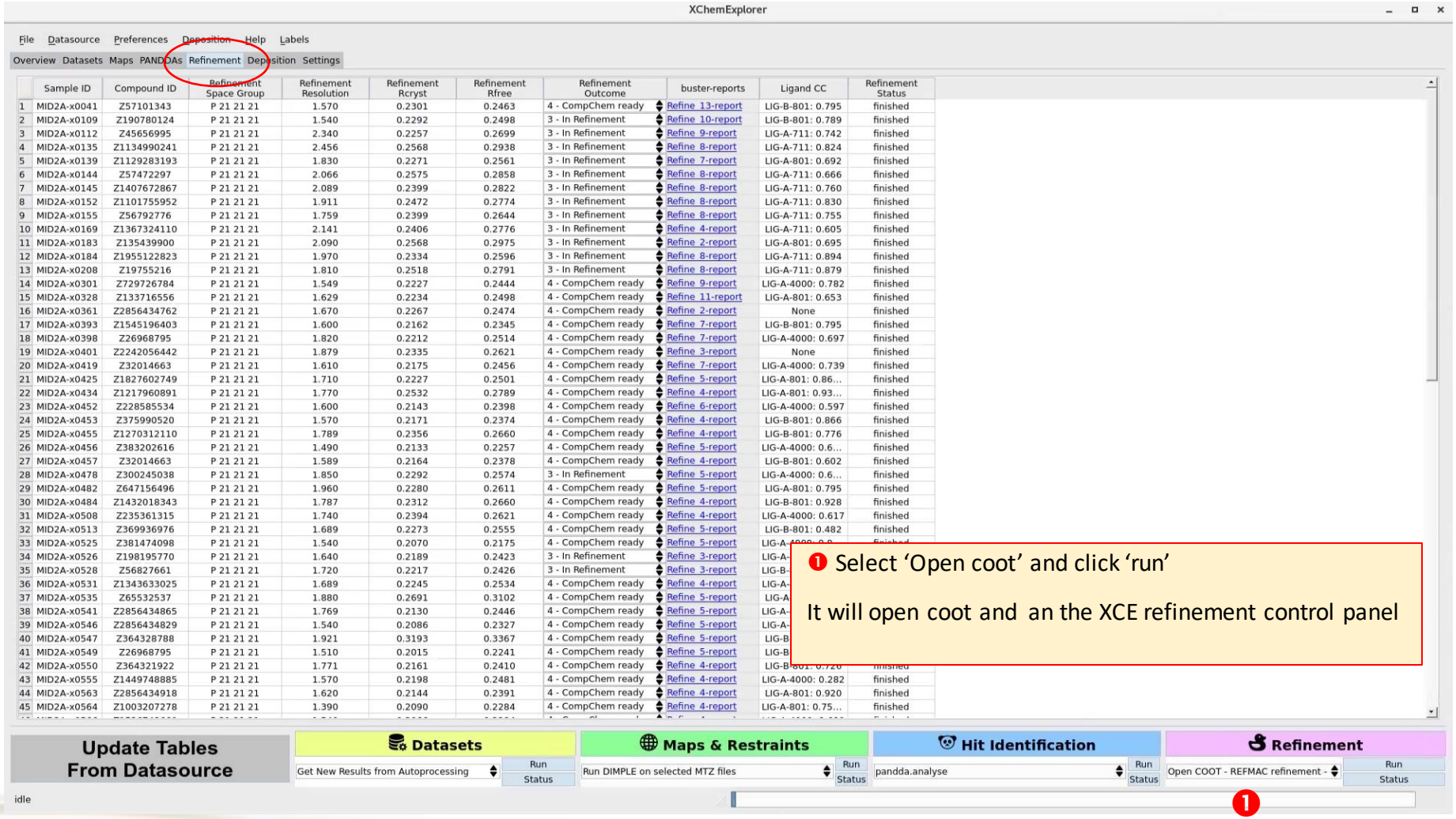
- Generates bound+unbound ensemble models for refinement
- Generates occupancy and restraints parameters for refmac and phenix
- XCE will launch a first cycle of refinements on the cluster
- Ligand stats are calculated

XChem jargon

- Reference model = Dimple model = no-ligand model = pandda input model = ground-state model
- Pandda model = ligand model = bound-state model
- Ground-state model + bound-state model = Ensemble model

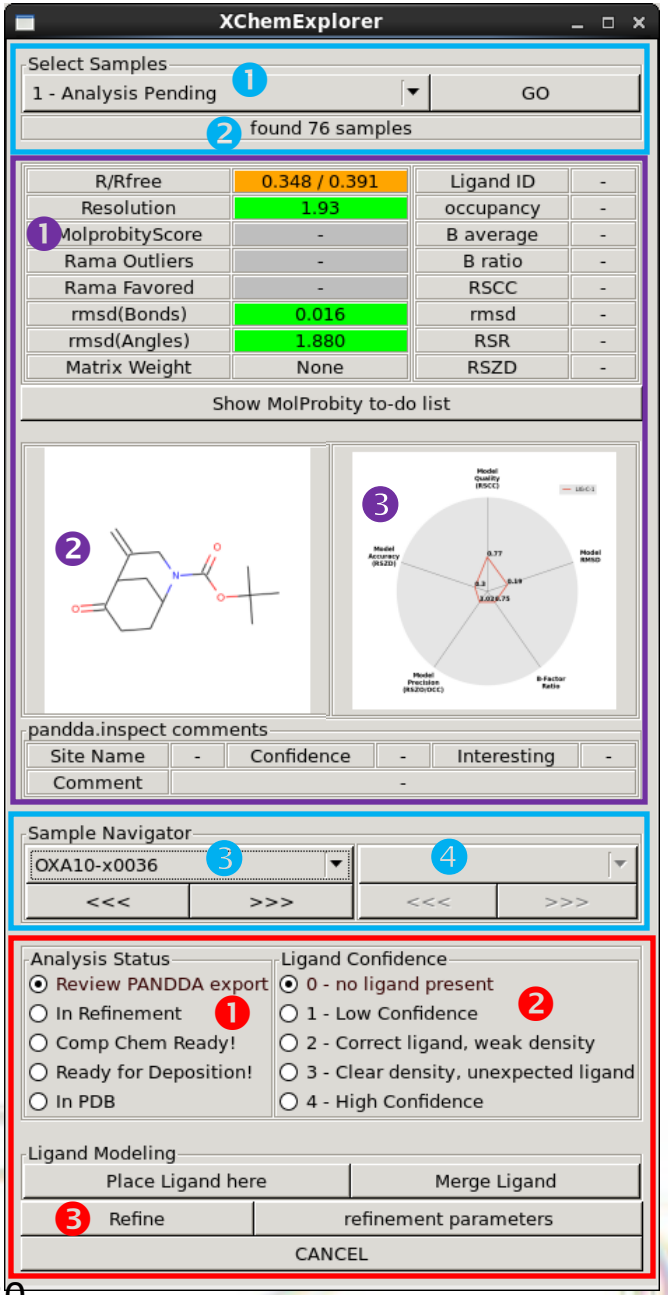
- The ensemble model is the one refined
- The bound-state model will be the one you will update in the XCE refinement Coot window and the one which will be deposited on the PDB

Back to XCE: Refinement tab



	Sample ID	Compound ID	Refinement Space Group	Refinement Resolution	Refinement Rcryst	Refinement Rfree	Refinement Outcome	buster-reports	Ligand CC	Refinement Status
1	MID2A-x0041	Z57101343	P 21 21 21	1.570	0.2301	0.2463	4 - CompChem ready	Refine_13-report	LIG-B-801: 0.795	finished
2	MID2A-x0109	Z190780124	P 21 21 21	1.540	0.2292	0.2498	3 - In Refinement	Refine_10-report	LIG-B-801: 0.789	finished
3	MID2A-x0112	Z45656995	P 21 21 21	2.340	0.2257	0.2699	3 - In Refinement	Refine_9-report	LIG-A-711: 0.742	finished
4	MID2A-x0135	Z1134990241	P 21 21 21	2.456	0.2568	0.2938	3 - In Refinement	Refine_8-report	LIG-A-711: 0.824	finished
5	MID2A-x0139	Z1129283193	P 21 21 21	1.830	0.2271	0.2561	3 - In Refinement	Refine_7-report	LIG-A-801: 0.692	finished
6	MID2A-x0144	Z57472297	P 21 21 21	2.066	0.2575	0.2858	3 - In Refinement	Refine_8-report	LIG-A-711: 0.666	finished
7	MID2A-x0145	Z1407672867	P 21 21 21	2.089	0.2399	0.2822	3 - In Refinement	Refine_8-report	LIG-A-711: 0.760	finished
8	MID2A-x0152	Z1101755952	P 21 21 21	1.911	0.2472	0.2774	3 - In Refinement	Refine_8-report	LIG-A-711: 0.830	finished
9	MID2A-x0155	Z56792776	P 21 21 21	1.759	0.2399	0.2644	3 - In Refinement	Refine_8-report	LIG-A-711: 0.755	finished
10	MID2A-x0169	Z1367324110	P 21 21 21	2.141	0.2406	0.2776	3 - In Refinement	Refine_4-report	LIG-A-711: 0.605	finished
11	MID2A-x0183	Z135439900	P 21 21 21	2.090	0.2568	0.2975	3 - In Refinement	Refine_2-report	LIG-A-801: 0.695	finished
12	MID2A-x0184	Z1955122823	P 21 21 21	1.970	0.2334	0.2596	3 - In Refinement	Refine_8-report	LIG-A-711: 0.894	finished
13	MID2A-x0208	Z19755216	P 21 21 21	1.810	0.2518	0.2791	3 - In Refinement	Refine_8-report	LIG-A-711: 0.879	finished
14	MID2A-x0301	Z729726784	P 21 21 21	1.549	0.2227	0.2444	4 - CompChem ready	Refine_9-report	LIG-A-4000: 0.782	finished
15	MID2A-x0328	Z133716556	P 21 21 21	1.629	0.2234	0.2498	4 - CompChem ready	Refine_11-report	LIG-A-801: 0.653	finished
16	MID2A-x0361	Z2856434762	P 21 21 21	1.670	0.2267	0.2474	4 - CompChem ready	Refine_2-report	None	finished
17	MID2A-x0393	Z1545196403	P 21 21 21	1.600	0.2162	0.2345	4 - CompChem ready	Refine_7-report	LIG-B-801: 0.795	finished
18	MID2A-x0398	Z26968795	P 21 21 21	1.820	0.2212	0.2514	4 - CompChem ready	Refine_7-report	LIG-A-4000: 0.697	finished
19	MID2A-x0401	Z2242056442	P 21 21 21	1.879	0.2335	0.2621	4 - CompChem ready	Refine_3-report	None	finished
20	MID2A-x0419	Z32014663	P 21 21 21	1.610	0.2175	0.2456	4 - CompChem ready	Refine_7-report	LIG-A-4000: 0.739	finished
21	MID2A-x0425	Z1827602749	P 21 21 21	1.710	0.2227	0.2501	4 - CompChem ready	Refine_5-report	LIG-A-801: 0.86...	finished
22	MID2A-x0434	Z1217960891	P 21 21 21	1.770	0.2532	0.2789	4 - CompChem ready	Refine_4-report	LIG-A-801: 0.93...	finished
23	MID2A-x0452	Z228585534	P 21 21 21	1.600	0.2143	0.2398	4 - CompChem ready	Refine_6-report	LIG-A-4000: 0.597	finished
24	MID2A-x0453	Z375990520	P 21 21 21	1.570	0.2171	0.2374	4 - CompChem ready	Refine_4-report	LIG-B-801: 0.866	finished
25	MID2A-x0455	Z1270312110	P 21 21 21	1.789	0.2356	0.2660	4 - CompChem ready	Refine_4-report	LIG-B-801: 0.776	finished
26	MID2A-x0456	Z383202616	P 21 21 21	1.490	0.2133	0.2257	4 - CompChem ready	Refine_5-report	LIG-A-4000: 0.6...	finished
27	MID2A-x0457	Z32014663	P 21 21 21	1.589	0.2164	0.2378	4 - CompChem ready	Refine_4-report	LIG-B-801: 0.602	finished
28	MID2A-x0478	Z300245038	P 21 21 21	1.850	0.2292	0.2574	3 - In Refinement	Refine_5-report	LIG-A-4000: 0.6...	finished
29	MID2A-x0482	Z647156496	P 21 21 21	1.960	0.2280	0.2611	4 - CompChem ready	Refine_5-report	LIG-A-801: 0.795	finished
30	MID2A-x0484	Z1432018343	P 21 21 21	1.787	0.2312	0.2660	4 - CompChem ready	Refine_4-report	LIG-B-801: 0.928	finished
31	MID2A-x0508	Z235361315	P 21 21 21	1.740	0.2394	0.2621	4 - CompChem ready	Refine_4-report	LIG-A-4000: 0.617	finished
32	MID2A-x0513	Z369936976	P 21 21 21	1.689	0.2273	0.2555	4 - CompChem ready	Refine_5-report	LIG-B-801: 0.482	finished
33	MID2A-x0525	Z381474098	P 21 21 21	1.540	0.2070	0.2175	4 - CompChem ready	Refine_5-report	LIG-A-	
34	MID2A-x0526	Z198195770	P 21 21 21	1.640	0.2189	0.2423	3 - In Refinement	Refine_3-report	LIG-A-	
35	MID2A-x0528	Z56827661	P 21 21 21	1.720	0.2217	0.2426	3 - In Refinement	Refine_3-report	LIG-B-	
36	MID2A-x0531	Z1343633025	P 21 21 21	1.689	0.2245	0.2534	4 - CompChem ready	Refine_4-report	LIG-A-	
37	MID2A-x0535	Z65532537	P 21 21 21	1.880	0.2691	0.3102	4 - CompChem ready	Refine_5-report	LIG-A	
38	MID2A-x0541	Z2856434865	P 21 21 21	1.769	0.2130	0.2446	4 - CompChem ready	Refine_5-report	LIG-A-	
39	MID2A-x0546	Z2856434829	P 21 21 21	1.540	0.2086	0.2327	4 - CompChem ready	Refine_5-report	LIG-A-	
40	MID2A-x0547	Z364328788	P 21 21 21	1.921	0.3193	0.3367	4 - CompChem ready	Refine_5-report	LIG-B	
41	MID2A-x0549	Z26968795	P 21 21 21	1.510	0.2015	0.2241	4 - CompChem ready	Refine_5-report	LIG-B	
42	MID2A-x0550	Z364321922	P 21 21 21	1.771	0.2161	0.2410	4 - CompChem ready	Refine_4-report	LIG-B	
43	MID2A-x0555	Z1449748885	P 21 21 21	1.570	0.2198	0.2481	4 - CompChem ready	Refine_4-report	LIG-A-4000: 0.282	finished
44	MID2A-x0563	Z2856434918	P 21 21 21	1.620	0.2144	0.2391	4 - CompChem ready	Refine_4-report	LIG-A-801: 0.920	finished
45	MID2A-x0564	Z1003207278	P 21 21 21	1.390	0.2090	0.2284	4 - CompChem ready	Refine_4-report	LIG-A-801: 0.75...	finished

XCE: Refinement control panel



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
-> pandda maps and spider plot will only be loaded after selecting the event

*XCE has already run on cycle of refinement straight after pandda.export

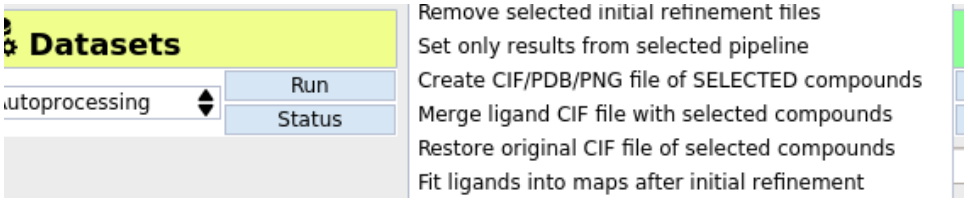
❶ Summary of refinement statistics
❷ Ligand 2D plot
❸ Ligand validation plot. The closer the values are to the center, the higher your confidence (See Nick Pearce's paper for the details)

❶ Manually change the status of a model:
"**In Refinement**", Leave it as this if you still need to refine
"**Comp Chem Ready**!". Ligand and binding site refined. Ok to be sent to chemist. Some atoms to refine elsewhere may remain.
"**Ready for Deposition!**". Means…
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 works.

Merging ligand restrains with CIF file from non-standard ligand

1. Open the Preferences menu (Edit preferences) and at the very bottom of the page, select the CIF file of your non-standard ligand in the 'Additional CIF file for non-standard ligand' section (see Figure 18).
2. Select the samples which you want to merge in the Maps tab (exactly the same way as described before).
3. Choose 'Merge ligand CIF file with selected compounds' and press Run.



XCE will now remove the symbolic link to the compound CIF file in the sample directory and prepare a merged version of the file in the sample directory with the same name. It does however not touch the original files in the compound subfolder!

There is only one important thing to consider 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.

Merging ligand restrains with CIF file 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.

PDB Batch deposition

- We can now deposit on the RCSB PDB our XChem fragment structures by batch
- Models and integrated data are deposited on the PDB
- PanDDA files and compound files are uploaded on the Zenodo repository
- Email the XChem team when you are ready for the batch deposition