

XChem training

Rev May 2022

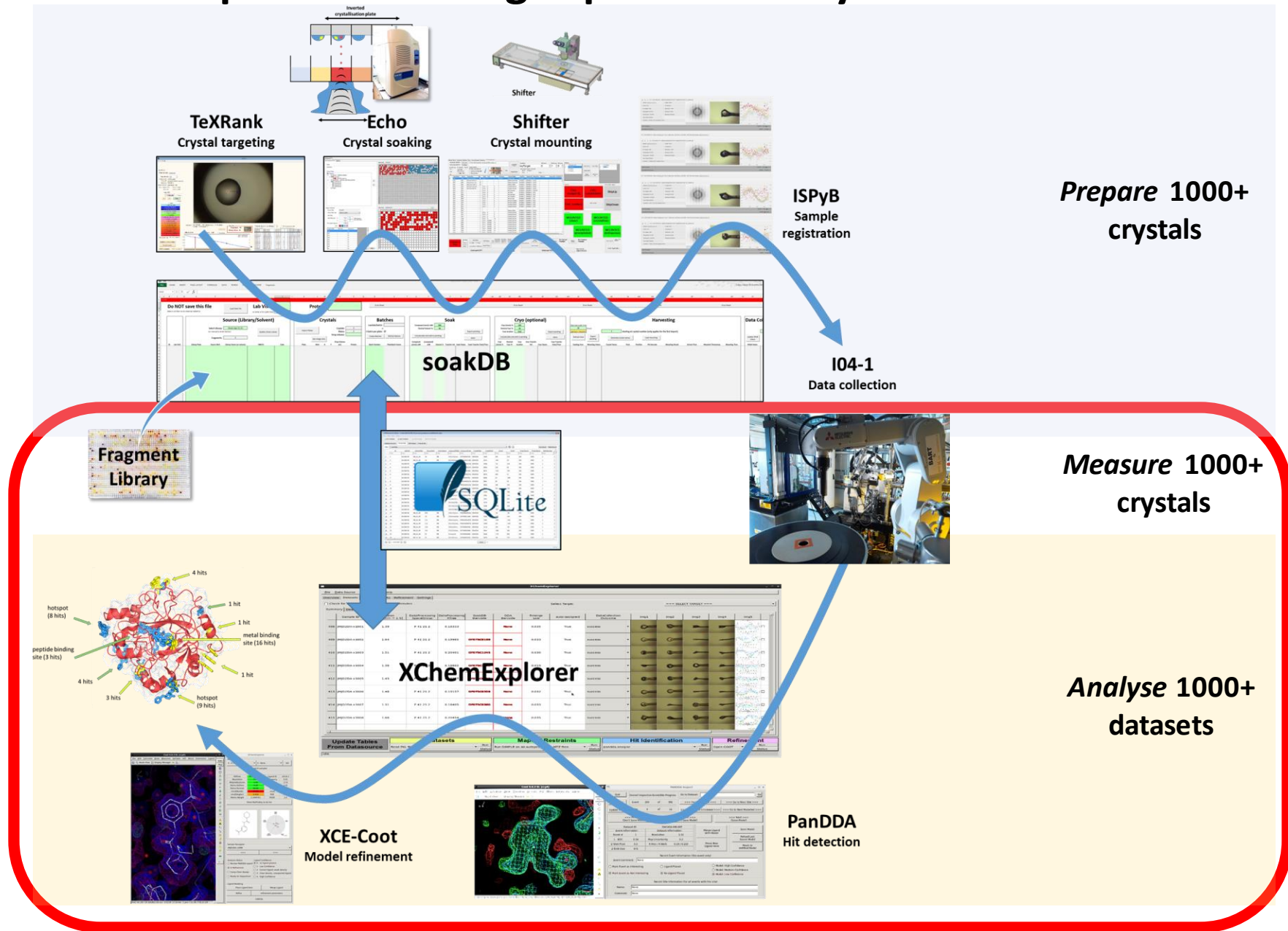
XCE v1.8.2

XChemExplorer
PanDDA
PDB Batch deposition

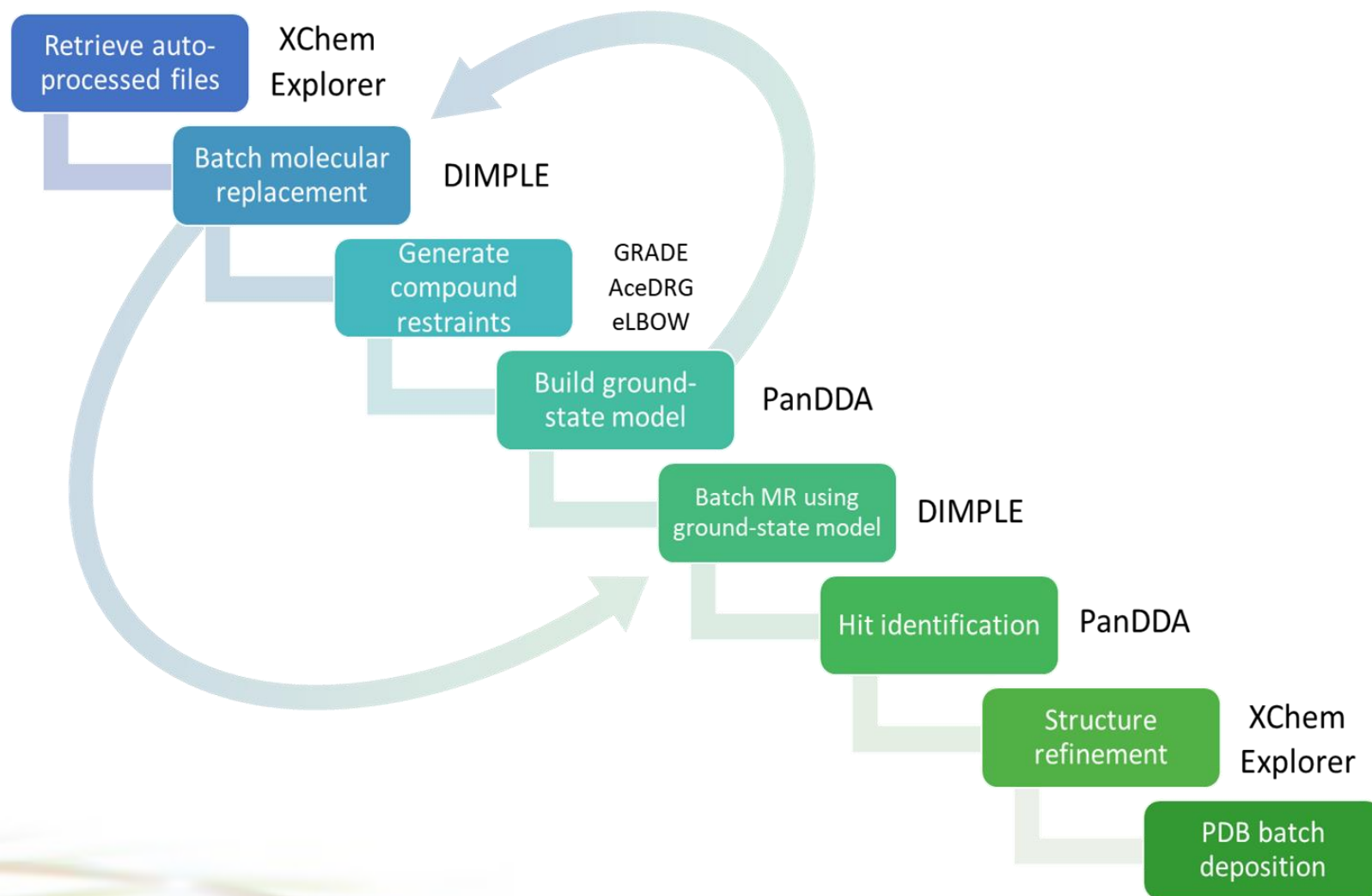


XChem at Diamond

Complete screening experiment: crystal-to-model



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



Restrains generation
program options



The screenshot shows the XCE preferences dialog box with the following settings:

- filename root:
- Max. Allowed Unit Cell Difference between Reference and Target (%):
- Acceptable low resolution limit for datasets (in Angstrom):
- Select amount of processed data you wish to copy to initial_model directory:
- Dataset Selection Mechanism:
- Restrains generation program:
- XCE logfile:
- Max. number of jobs running at once on DLS cluster:
- remote qsub: use
-

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

File Datasource Preferences Deposition Proasis Help Labels

Overview Datasets Maps PANDDAs Refinement Deposition Settings

Project Directory: - REQUIRED -
/dls/labxchem/data/2019/lb24544-1/processing/analysis/model_building

Reference Structure Directory: - OPTIONAL -
/dls/labxchem/data/2019/lb24544-1/processing/reference

Data Source: - REQUIRED -
/dls/labxchem/data/2019/lb24544-1/processing/database/soakDBDataFile.sqlite

Data Collection Directory: (e.g. /dls/i04-1/data/2017/lb18145-70) -

/dls/i04-1/data/2019/lb24544-3
 Read Agamemnon data structure

CCP4_SCR Directory: - OPTIONAL -
/dls/labxchem/data/2019/lb24544-1/processing/tmp

PANDDAs directory: - OPTIONAL -
/dls/labxchem/data/2019/lb24544-1/processing/analysis/panddas

HTML export directory: - OPTIONAL -
/dls/labxchem/data/2019/lb24544-1/processing

Group deposition directory: - OPTIONAL -
/dls/labxchem/data/2019/lb24544-1/processing/group_deposition

Data source tab: Overview of your experiments

The screenshot shows the XChemExplorer interface. The 'Data Source' tab is active, displaying a table with columns: Sample ID, Compound ID, Smiles, Visit, Resolution [Mn</math>/sig(I)> = 1.5], Refinement Rfree, Data Collection Date, Puck, PuckPosition, and Ligand Confidence. The table lists 41 experiments. At the bottom, there is a toolbar with buttons for 'Update Tables From Datasource', 'Datasets', 'Maps & Restraints', 'Hit Identification', and 'Refinement'. The 'Update Tables From Datasource' button is highlighted with a red circle containing the number 1.

	Sample ID	Compound ID	Smiles	Visit	Resolution [Mn</math>/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	DL5593	1	None
2	NUDT21A-x0061			lb18145-14			2017-06-28 12:20:26	DL5593	2	
3	NUDT21A-x0062			lb18145-14			2017-06-28 12:22:52	DL5593	3	
4	NUDT21A-x0063			lb18145-14	3.88		2017-06-28 12:24:04	DL5593	4	
5	NUDT21A-x0064			lb18145-14	r/a	0.31977	2017-06-28 12:26:58	DL5593	5	None
6	NUDT21A-x0065			lb18145-14			2017-06-28 12:28:10	DL5593	6	
7	NUDT21A-x0066			lb18145-14	2.45	0.27973	2017-06-28 12:30:17	DL5593	7	None
8	NUDT21A-x0067			lb18145-14			2017-06-28 12:31:33	DL5593	8	
9	NUDT21A-x0068			lb18145-14			2017-06-28 12:33:19	DL5593	9	
10	NUDT21A-x0069			lb18145-14	3.01	0.33435	2017-06-28 12:36:05	DL5593	10	None
11	NUDT21A-x0070			lb18145-14	2.71	0.29731	2017-06-28 12:37:48	DL5593	11	None
12	NUDT21A-x0071			lb18145-14	2.05	0.25401	2017-06-28 12:39:56	DL5593	12	None
13	NUDT21A-x0072			lb18145-14			2017-06-28 14:10:01	DL5593	13	
14	NUDT21A-x0073			lb18145-14	7.12		2017-06-28 12:43:59	DL5593	14	
15	NUDT21A-x0074			lb18145-14			2017-06-28 12:46:29	DL5593	15	
16	NUDT21A-x0075			lb18145-14	8.29		2017-06-28 12:48:05	DL5593	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				DL5524	1	
27	NUDT21A-x0045			lb18145-14				DL5524	2	
28	NUDT21A-x0046			lb18145-14				DL5524	3	
29	NUDT21A-x0047			lb18145-14				DL5524	4	
30	NUDT21A-x0048			lb18145-14				DL5524	5	
31	NUDT21A-x0049			lb18145-14				DL5524	6	
32	NUDT21A-x0050			lb18145-14				DL5524	7	
33	NUDT21A-x0051			lb18145-14				DL5524	8	
34	NUDT21A-x0052			lb18145-14				DL5524	9	
35	NUDT21A-x0053			lb18145-14				DL5524	10	
36	NUDT21A-x0054			lb18145-14				DL5524	11	
37	NUDT21A-x0055			lb18145-14				DL5524	12	
38	NUDT21A-x0056			lb18145-14				DL5524	13	
39	NUDT21A-x0057			lb18145-14				DL5524	14	
40	NUDT21A-x0058			lb18145-14				DL5524	15	
41	NUDT21A-x0059			lb18145-14				DL5524	16	

1 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.

1

Update Tables From Datasource

Datasets

Get New Results from Autoprocessing

Run Status

Maps & Restraints

Run DIMPLE on selected MTZ files

Run Status

Hit Identification

panda.analyse

Run Status

Refinement

Open COOT

Run Status

LabVisit DataCollection Outcome C H
 LibraryName GDA Barcode M O
 Smiles Path to diffraction image files M L
 Compound ID Program M H
 CrystalPlate DataProcessing SpaceGroup C O
 CrystalWell Resolution High C L
 ProteinName Resolution [Mn<I/sig(I)> = 1.5] C H
 CompoundConcentration Rmerge Overall D
 SolventFraction Rmerge Low D
 SoakingTime Rmerge High U O
 Mn<I/sig(I)> D

SoakDB Barcode Mn<I/sig(I)> High D R
 Visit Completeness Overall D R
 Data Collection Date Completeness Low D R

Those might be useful for evaluating the solvent characterisation

File Datasource Preferences Deposition Proasis Help

Overview Datasets Maps PANDDAs Refinement Deposition Settings

Data Source Summary

	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

Update Tables



Datasets tab: Load datasets

XChemExplorer

File Datasource Preferences Deposition Proasis Help

Overview **Datasets** Maps PANDDAs Refinement Deposition Settings

Check for new data collection every two minutes

Select Target: PHIPA

Sample ID	Resolution [Mn</sig!> = 1.5]	DataProcessing SpaceGroup	DataProcessing Rfree	SoakDB Barcode	GDA Barcode	Rmerge Low	auto-assigned	DataCollection Outcome	img1	img2	img3	img4
1 PHIPA-x9000	1.40	C 1 2 1	None	DF150E0904	None	0.025	True	success				
2 PHIPA-x9001	1.42	C 1 2 1	None	-CANT-FIND-	None	0.025	True	success				
3 PHIPA-x9002	1.77	C 1 2 1	None	DF150E0308	None	0.115	True	success				
4 PHIPA-x9003	1.39	C 1 2 1	None	DF150E0599	None	0.026	True	success				
10 PHIPA-x9012	n/a	C 1 2 1	None	DF150E0106	None	0.083	True	success				

- Select your target in drop down list
- Select 'Get New Results from Autoprocessing'
- 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'.

Update Tables From Datasource

Datasets **Maps & Restraints** **Hit Identification** **Refinement**

Get New Results from Autoprocessing Run DIMPLE on selected MTZ files pandda.analyse Open COOT

idle 0%

Datasets tab: Load datasets

Sample ID	Resolution [Mn$\langle I/\sigma(I) \rangle = 1.5]$	DataProcessing SpaceGroup	DataProcessing Rfree	SoakDB Barcode	GDA Barcode	Rmerge Low	auto-assigned	DataCollection Outcome	img1	img2	img3	img4
1 PHIPA-x9000	1.40 ✓	C 1 2 1										
2 PHIPA-x9001	1.42	C 1 2 1										
3 PHIPA-x9002	1.77	C 1 2 1										
4 PHIPA-x9003	1.39	C 1 2 1										
5 PHIPA-x9004	1.19	C 1 2 1										
6 PHIPA-x9005												
7 PHIPA-x9006												
8 PHIPA-x9007												
9 PHIPA-x9008												

Sample ID	Visit	Run	Program	Resolution Overall	Resolution High	DataProcessing SpaceGroup	Mn$\langle I/\sigma(I) \rangle$ High	Rmerge Low	Complete Overa
1 PHIPA-x9000	lb18145-97	PHIPA-x9000_1_	3dii-run	40.38 - 1.35	1.35	C 1 2 1	1.1	0.025	97.6
2 PHIPA-x9000	lb18145-97	PHIPA-x9000_1_	3dii-runC121	40.38 - 1.35	1.35	C 1 2 1	1.1	0.025	97.6
3 PHIPA-x9000	lb18145-97	PHIPA-x9000_1_	dials-run	40.43 - 1.36	1.36	C 1 2 1	1.3	0.188	99.7
4 PHIPA-x9000	lb18145-97	PHIPA-x9000_1_	dials-run-remove-blanks	40.43 - 1.36	1.36	C 1 2 1	1.3	0.188	99.7
5 PHIPA-x9000	lb18145-97	PHIPA-x9000_1_	dials-runC121	40.42 - 1.36	1.36	C 1 2 1	0.7	0.388	99.7
6 PHIPA-x9000	lb18145-97	PHIPA-x9000_1_	autoPROC	40.38 - 1.21	1.21	C 1 2 1	0.5	0.027	90.7

✓ 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”)

File Datasource Preferences Deposition Proasis Help Labels

Overview **Maps** PANDAs Refinement Deposition Settings

(de-)select all samples for DIMPLE

Set New Reference (if applicable) Refresh reference file list

Sample ID	Select	Compound ID	Smiles	Resolution [Mn</sig(I)> = 1.5]	Dimple Rcryst	Dimple Rfree	DataProcessing SpaceGroup	Reference SpaceGroup	Difference UC Volume (%)	Reference File	DataProcessing UnitCell	Dimple Status	Compound Status	LastUpdated
49	<input type="checkbox"/>	Z384468096	CC(=O)N...	2.39	None	None	P 41 21 2	P 41 21 2	4.7	model_trimer	121 121 197 90 90 90	None	restraints failed	2020-01-16 13:31
50	<input type="checkbox"/>													
51	<input type="checkbox"/>													
52	<input type="checkbox"/>													
53	<input type="checkbox"/>													
54	<input type="checkbox"/>													
55	<input type="checkbox"/>													
56	<input type="checkbox"/>													
57	<input type="checkbox"/>													
58	<input type="checkbox"/>													
59	<input type="checkbox"/>													
60	<input type="checkbox"/>													
61	<input type="checkbox"/>													
62	<input type="checkbox"/>													
63	<input type="checkbox"/>													
64	<input type="checkbox"/>													
65	<input type="checkbox"/>													
66	<input type="checkbox"/>	Z28870646	CC1CCC...	2.25	None	None	P 41 21 2	P 41 21 2	4.7	model_trimer	121 121 197 90 90 90	None	restraints failed	2020-01-16 13:31
67	<input type="checkbox"/>	Z57627041	NC(=O)C...	2.16	None	None	P 41 21 2	P 41 21 2	4.2	model_trimer	121 121 198 90 90 90	None	running	2020-01-16 13:31
68	<input type="checkbox"/>	Z50145861	CC1=NN(...	2.27	None	None	P 41 21 2	P 41 21 2	4.2	model_trimer	121 121 198 90 90 90	None	restraints failed	2020-01-16 13:31
69	<input type="checkbox"/>	Z1343633025	CC=1C=...	2.76	None	None	P 41 21 2	P 41 21 2	2.1	model_trimer	122 122 199 90 90 90	None	restraints failed	2020-01-16 13:31
70	<input type="checkbox"/>	Z85934875	CNC(=O)...	2.47	None	None	P 41 21 2	P 41 21 2	2.1	model_trimer	122 122 199 90 90 90	None	restraints failed	2020-01-16 13:32
71	<input type="checkbox"/>	Z1259155959	CC=1NN...	2.10	None	None	P 41 21 2	P 41 21 2	4.2	model_trimer	121 121 198 90 90 90	None	restraints failed	2020-01-16 13:32
72	<input type="checkbox"/>	Z111782404	CC(OC=1...	2.55	None	None	P 41 21 2	P 41 21 2	2.6	model_trimer	122 122 198 90 90 90	None	restraints failed	2020-01-16 13:32
73	<input type="checkbox"/>	Z2856434814	CCN(CC)...	2.36	None	None	P 41 21 2	P 41 21 2	3.7	model_trimer	121 121 199 90 90 90	None	restraints failed	2020-01-16 13:32
74	<input type="checkbox"/>	Z219104216	CCNC=1...	2.26	None	None	P 41 21 2	P 41 21 2	4.2	model_trimer	121 121 198 90 90 90	None	started	2020-01-16 13:32
75	<input type="checkbox"/>	Z1349163663	CN(C1CC...	2.34	None	None	P 41 21 2	P 41 21 2	4.2	model_trimer	121 121 198 90 90 90	None	restraints failed	2020-01-16 13:32
76	<input type="checkbox"/>	Z228585842	CN1CCN(...	2.39	None	None	P 41 21 2	P 41 21 2	4.2	model_trimer	121 121 198 90 90 90	None	restraints failed	2020-01-16 13:32

↓ Columns would be populated if a reference file was put in ISPyB and dimple has already automatically run.

To run Dimple:

✓ If ticked, it will run dimple for all datasets. If you have multiple crystal forms, and corresponding models in the reference directory, the appropriate model will automatically be selected from the dataset

- 1 Otherwise select particular datasets. Blocks of samples can be selected by clicking a row number (hard left) and shift/ctrl clicking other rows as needed. Then, right click a selected sample ID and select *mark selected for dimple run*
- 2 Select 'run Dimple on selected MTZ files' and click 'run'
- 3 Click 'update tables from datasource' to refresh the Dimple status ↓

Update Tables From Datasource **Datasets** **Maps & Restraints** **Hit Identification** **Refinement**

Get New Results from Autoprocessing Run Status Run initial refinement on selected MTZ files Run Status pandda.analyse Run Status Open COOT Run Status

idle 3 2

Maps tab: Creating the ligands restraints

1

XChemExplorer

File Data Source Preferences Deposition Help

Overview Datasets Maps PANDDAs Refinement Deposition Settings

✓ (de-)select all samples for DIMPLE

Set New Reference (if applicable)

Sample ID	Select	Compound ID	Smiles	Resolution n<math>\leq 1/\text{sig}(I)> = 1	Dimple Rcryst	Dimple Rfree	DataProcessing SpaceGroup	Reference SpaceGroup	Difference UC Volume (%)	Reference File	DataProcessing UnitCell	Dimple Status	Compound Status	LastUpdated
1	✓	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	✓	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	✓	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	✓	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	✓	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	✓	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	✓	FMOOA0007...	Cc1nc2cccc...	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	✓	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	✓	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	✓	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	✓	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	✓	FMOOA0008...	c1ccc2c(c1)n...	1.95	None	None	P 2 2 2	P 2 2 2	999.0	...	72 72 152 90...	None	running	2017-01-17 1...
13	✓	FMOOA0008...	CNC(CNC)(c1C...	1.56	None	None	P 21 21 21	P 21 21 21	999.0	...	72 72 152 90...	None	running	2017-01-17 1...
14	✓	FMOOA0008...	COc1ccc(CN...	1.41	None	None	P 2 2 2	P 2 2 2	999.0	...	72 72 152 90...	None	running	2017-01-17 1...
15	✓	FMOOA0007...	C(CN)c1nc2c...	1.55	None	None	P 21 21 21	P 21 21 21	999.0	...	72 72 152 90...	None	running	2017-01-17 1...
16	✓	FMOOA0007...	Cc1nc2cccc...	1.34	None	None	P 2 2 2	P 2 2 2	999.0	...	72 72 151 90...	None	running	2017-01-17 1...
17	✓	FMOOA0007...	C(C#N)c1nc2...	2.28	None	None	P 2 2 2	P 2 2 2	999.0	...	72 72 152 90...	None	running	2017-01-17 1...

1 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

2 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'

3 Click 'update tables from datasource' to refresh the Compound status ↓. If the status is 'restraints failed', you can decide to re-run it using a different program (Grade or phenix.elbow)

3

Update Tables From Datasource

Datasets

Get New Results from Autoprocessing Run Status

Maps & Restraints

Create CIF/PDB/PNG file of ALL compounds Run Status

Hit Identification

pandda.analyse Run Status

Refinement

Open COOT Run Status

0%

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

Restrains

es	Run	Status

- pandda.analyse
- pandda.inspect
- run pandda.inspect at home
- Export NEW PANDDA models
- Export ALL PANDDA models
- Show HTML summary
- Update datasource with results from pandda.inspect cluster datasets
- Event Map -> SF
- check modelled ligands
- pre-run for ground state model
- Build ground state model

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

XChemExplorer

File Data Source Preferences Deposition Help

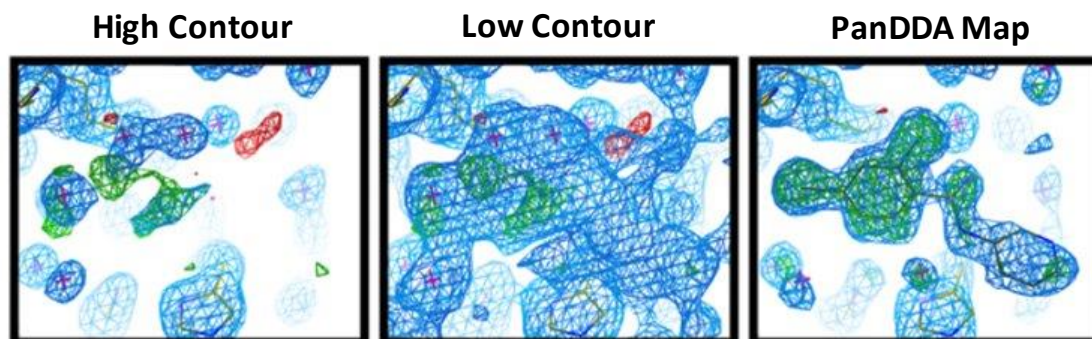
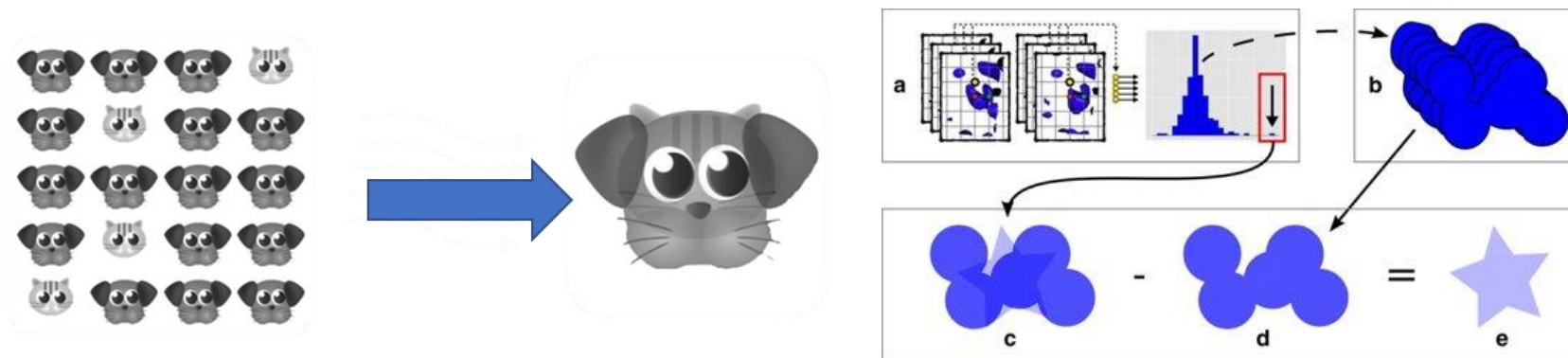
Overview Datasets Maps PANDDAs Refinement Deposition Settings

✓ (de-)select all samples for DIMPLE

Set New Reference (if applicable)

	Sample ID	Select	Compound ID	Smiles	Resolution n<1/sig(l)> = 1.	Dimple Rcryst	Dimple Rfree	Data 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...	Cc1nc2cccc...	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...	Cc1cc2cccc...	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...	c1cc2c[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...	c1cc2c[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(c2c[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...	C1Cc2cccc2...	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...	Cn1c2cccc2...	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...	Cc1ccc(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)



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

XChemExplorer

File Datasource Preferences Deposition Proasis Help

Overview Datasets Maps PANDDAs Refinement Deposition Settings

pandda.analyse Dataset Summary Processing Output pandda.inspect Statistical Map Summaries

Sample ID	Refinement Space Group	Resolution [Mn<math>\langle I \rangle / \sigma(I)> = 1.5]	Dimple Rcrystr	Dimple Rfree	Crystal Form Name	Ignore completely	Exclude from characterisation (binds)	Exclude from z-map analysis (does not bind)
1	NUDT21A-x0...	P 32 2 1	3.22	0.17745	0.26199	None	<input type="checkbox"/>	<input type="checkbox"/>
2	NUDT21A-x0...	P 32 2 1	n/a	0.25589	0.31977	None	<input type="checkbox"/>	<input type="checkbox"/>
3	NUDT21A-x0...	P 32 2 1	2.45	0.22327	0.27973	None	<input type="checkbox"/>	<input type="checkbox"/>
4	NUDT21A-x0...	P 32 2 1	3.01	0.25528	0.33435	None	<input type="checkbox"/>	<input type="checkbox"/>
5	NUDT21A-x0...	P 32 2 1	2.71	0.22873	0.29731	None	<input type="checkbox"/>	<input type="checkbox"/>
6	NUDT21A-x0...	P 32 2 1	2.05	0.20522	0.25401	None	<input type="checkbox"/>	<input type="checkbox"/>
7	NUDT21A-x0...	P 32 2 1	3.44	0.61609	0.63076	None	<input type="checkbox"/>	<input type="checkbox"/>
8	NUDT21A-x0...	P 32 2 1	3.40	0.33565	0.40750	None	<input type="checkbox"/>	<input type="checkbox"/>
9	NUDT21A-x0...	P 32 2 1	2.40	0.19113	0.25742	None	<input type="checkbox"/>	<input type="checkbox"/>
10	NUDT21A-x0...	P 32 2 1	1.81	0.22608	0.26781	None	<input type="checkbox"/>	<input type="checkbox"/>
11	NUDT21A-x0...	P 32 2 1	2.20	0.20769	0.26296	None	<input type="checkbox"/>	<input type="checkbox"/>
12	NUDT21A-x0...	P 32 2 1	1.89	0.21456	0.26273	None	<input type="checkbox"/>	<input type="checkbox"/>
13	NUDT21A-x0...	P 32 2 1	1.76	0.21010	0.25062	None	<input type="checkbox"/>	<input type="checkbox"/>
14	NUDT21A-x0...	P 32 2 1	1.97	0.21143	0.25526	None	<input type="checkbox"/>	<input type="checkbox"/>
15	NUDT21A-x0...	P 32 2 1	2.01	0.22702	0.26925	None	<input type="checkbox"/>	<input type="checkbox"/>
16	NUDT21A-x0...	P 32 2 1	2.34	0.21684	0.26953	None	<input type="checkbox"/>	<input type="checkbox"/>
17	NUDT21A-x0...	P 32 2 1	3.46	0.31279	0.36375	None	<input type="checkbox"/>	<input type="checkbox"/>
18	NUDT21A-x0...	P 32 2 1	2.70	0.24388	0.30418	None	<input type="checkbox"/>	<input type="checkbox"/>
19	NUDT21A-x0...	P 32 2 1	3.02	0.24946	0.33140	None	<input type="checkbox"/>	<input type="checkbox"/>
20	NUDT21A-x0...	P 32 2 1	2.01	0.21206	0.25756	None	<input type="checkbox"/>	<input type="checkbox"/>
21	NUDT21A-x0...	P 32 2 1	3.17	0.21302	0.29125	None	<input type="checkbox"/>	<input type="checkbox"/>
22	NUDT21A-x0...	P 32 2 1	1.55	0.21432	0.24840	None	<input type="checkbox"/>	<input type="checkbox"/>
23	NUDT21A-x0...	P 32 2 1	1.55	0.21534	0.24979	None	<input type="checkbox"/>	<input type="checkbox"/>
24	NUDT21A-x0...	P 32 2 1	3.24	0.35264	0.38502	None	<input type="checkbox"/>	<input type="checkbox"/>
25	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
26	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
27	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
28	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
29	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
30	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
31	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
32	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
33	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
34	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
35	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
36	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
37	NUDT21A-x0...	P 32 2 1	3.03	0.30064	0.36411	None	<input type="checkbox"/>	<input type="checkbox"/>
38	NUDT21A-x0...	P 32 2 1	1.53	0.21663	0.24687	None	<input type="checkbox"/>	<input type="checkbox"/>

1 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.

STATUS: Finished!

Update Tables From Datasource

Datasets

Get New Results from Autoprocessing

Maps & Restraints

Run DIMPLE on selected MTZ files

Hit Identification

pandda.analyse

Refinement

Open COOT

Data directory: 17/lb18145-12/processing/analysis/initial_model/*

pdb style dimple.pdb

mtz style dimple.mtz

Output directory: 017/lb18145-12/processing/analysis/panddas

Submit: qsub

Number of processors: 11

Order events by: cluster size

Use space group of reference file as filter: ...

Expert Parameters (only change if you know what you are doing!):

Wilson B-factor Scaling

min_build_datasets: 40

max_new_datasets: 500

grid_spacing (default=0.5) Note: higher values speed up calculations, but maps might be less pretty) 0.5

How to check pandda.analyse is running?

In a terminal, type 'qstat', PANDDA job should be listed

```
17282354 1.32342 xia2_maste zpo15726 r 01/17/2017 12:53:01 low.q@cs04r-sc-com12-22.diamon 1 8
17282354 1.32342 xia2_maste zpo15726 r 01/17/2017 12:53:01 low.q@cs04r-sc-com12-22.diamon 1 9
17282354 1.32342 xia2_maste zpo15726 r 01/17/2017 12:53:01 low.q@cs04r-sc-com12-22.diamon 1 10
17282354 1.32342 xia2_maste zpo15726 r 01/17/2017 12:53:01 low.q@cs04r-sc-com12-22.diamon 1 11
17282379 1.32332 pandda.sh zpo15726 r 01/17/2017 14:35:17 low.q@cs04r-sc-com06-56.diamon 1
[zpo15726@ws343 tmp]$
```

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

XChemExplorer

File Data Source Preferences Deposition Help

Overview Datasets Maps **PANDDAs** Refinement Deposition Settings

pandda.analyse Dataset Summary Results Summary **Inspect Summary**

	Sample ID	Refinement Space Group	Resolution n$\langle I \rangle \ge 1$	Dimple Rcryst	Dimple Rfree	Crystal Form Name	PanDDA launched?	PanDDA hit?	PanDDA reject?	PanDDA Status
1	SHH-x100	C 1 2 1	1.16	0.17568	0.19511	SG-C121-No....	True	False	False	None
2	SHH-x1000	C 1 2 1	1.47	0.15616	0.17929	SG-C121-No....	True	False	False	None
3	SHH-x1001	C 1 2 1	1.67	0.16128	0.19716	SG-C121-No....	True	False	False	None
4	SHH-x1002	C 1 2 1	1.31	0.16690	0.18772	SG-C121-No....	True	False	False	None
5	SHH-x1003	C 1 2 1	1.31	0.17002	0.19491	SG-C121-No....	True	False	False	None
6	SHH-x1004	C 1 2 1	1.41	0.22294	0.26544	SG-C121-No....	True	False	False	None
7	SHH-x1005	C 1 2 1	1.33	0.16449	0.18668	SG-C121-No....	True	False	False	None
8	SHH-x1006	C 1 2 1	2.06	0.18989	0.23319	SG-C121-No....	True	False	False	None
9	SHH-x1009	C 1 2 1	1.67	0.16401	0.20044	SG-C121-No....	True	False	False	None
10	SHH-x101	C 1 2 1	1.11	0.15974	0.17569	SG-C121-No....	True	False	False	None
11	SHH-x1010	C 1 2 1	1.43	0.15886	0.18128	SG-C121-No....	True	False	False	None
12	SHH-x1011	C 1 2 1	1.51	0.15756	0.17944	SG-C121-No....	True	False	False	None
13	SHH-x1012	C 1 2 1	1.62	0.16154	0.18610	SG-C121-No....	True	False	False	None
14	SHH-x1013	C 1 2 1	1.36	0.16392	0.18547	SG-C121-No....	True	True	False	None
15	SHH-x1014	C 1 2 1	1.40	0.17439	0.19343	SG-C121-No....	True	False	False	None
16	SHH-x1015	C 1 2 1	1.46	0.16374	0.18237	SG-C121-No....	True	False	False	None
17	SHH-x1016	C 1 2 1	1.71	0.20015	0.25545	SG-C121-No....	True	False	False	None
18	SHH-x1018	C 1 2 1	1.84	0.17237	0.21639	SG-C121-No....	True	True	False	None
19	SHH-x1019	C 1 2 1	1.82	0.19399	0.21879	SG-C121-No....	True	False	False	None
20	SHH-x102	C 1 2 1	1.17	0.15891	0.17738	SG-C121-No....	True	False	False	None
21	SHH-x1020	C 1 2 1	3.28	0.26495	0.33837	SG-C121-No....	True	False	False	None
22	SHH-x1021	C 1 2 1	1.28	0.17132	0.19037	SG-C121-No....	True	False	False	None
23	SHH-x1022	C 1 2 1	1.56	0.15776	0.18612	SG-C121-No....	True	False	False	None

data directory
[15/lb13320-1/processing/analysis/initial_model/*] Select Input Template

pdb style [dimple.pdb]

mtz style [dimple.mtz]

output directory
[ta/2015/lb13320-1/processing/analysis/panddas] Select PANDDAs Directory

submit [qsub]

number of processors [11]

order events by:
[cluster_size]

Use space group of reference file as filter:
[SHH.x7_monomerSoak] C 1 2 1

Expert Parameters (only change if you know what you are doing!):

min_build_datasets [40]

max_new_datasets [200]

grid_spacing (default=0.6)
Note: higher values speed up calculations, but maps might be less pretty!
[0.6]

1 Select 'pandda.inspect' and click 'run'
It will launch Coot and a pandda.inspect interface

Update Tables From Datasource

Datasets Get New Results from Autoprocessing [Run Status]

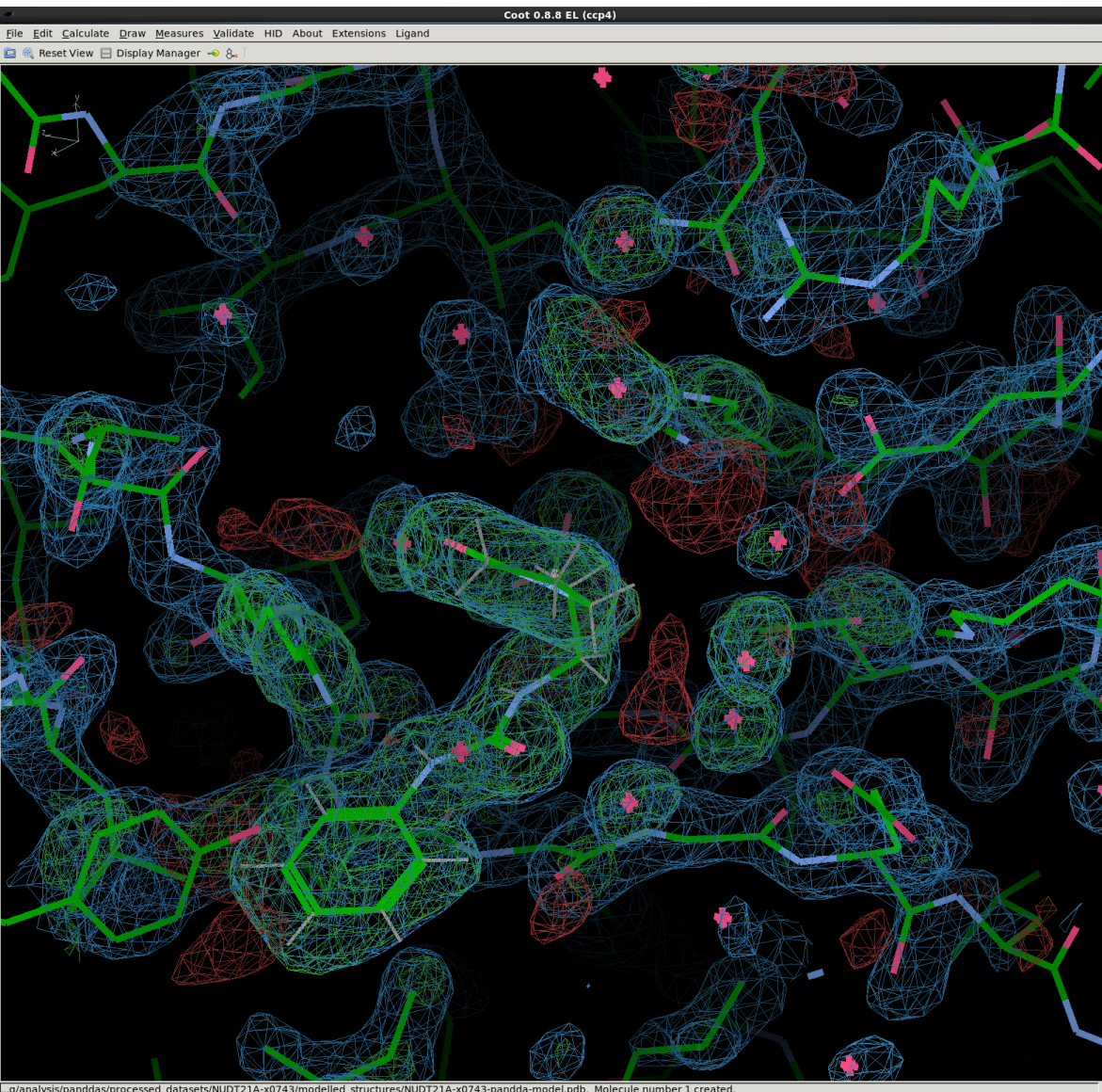
Maps & Restraints Create CIF/PDB/PNG file of ALL compounds [Run Status]

Hit Identification pandda.inspect [Run Status]

Refinement Open COOT [Run Status]

idle 0%

pandda.inspect



PANDDA inspect

Quit Overall Inspection Event/Site Progress: Go to Dataset: Go

Summary Event 1 of 404 <<< Go to Prev Site <<< >>> Go to Next Site >>>

Update HTML Site 1 of 21 >>> Go to Next Unviewed >>> >>> Go to Next Modelled >>>

<<< Prev <<< (Don't Save Model) >>> Next >>> (Don't Save Model) >>> Next >>> (Save Model)

Dataset ID		NUDT21A-x0743		Merge Ligand With Model	Save Model
Event Information:		Dataset Information:		Move New Ligand Here	Reload Last Saved Model
Event #	3	Resolution	1.65	Open Next Ligand	Reset to Unfitted Model
1 - BDC	0.28	Map Uncertainty	0.23		
Z-blob Peak	11.0	R-Free / R-Work	0.213 / 0.247		
Z-blob Size	796				

Record Event Information (this event only)

Event Comment:

Mark Event as Interesting Ligand Placed Model: High Confidence

Mark Event as Not Interesting No Ligand Placed Model: Medium Confidence

Model: Low Confidence

Record Site Information (for all events with this site)

Name:

Comment:

Miscellaneous buttons Load input mtz file Load average map Load unfitted model (for comparison only) Create new ligand

Display Manager

Maps All

2	NUDT21A-x0743-z_map.native.ccp4	<input checked="" type="checkbox"/> Display	<input type="checkbox"/> Scroll	Properties	Delete Map
3	NUDT21A-x0743-event_3_1-BDC_0.28_map.nativ	<input checked="" type="checkbox"/> Display	<input type="checkbox"/> Scroll	Properties	Delete Map

Molecules All

0	FMOPL00589a.pdb	<input type="checkbox"/> Display	<input checked="" type="checkbox"/> Active	Bonds (Colour by Atom)	Delete Model
1	NUDT21A-x0743-pandda-model.pdb	<input checked="" type="checkbox"/> Display	<input checked="" type="checkbox"/> Active	Bonds (Colour by Atom)	Delete Model

Close

.../analysis/panddas/processed_datasets/NUDT21A-x0743/modelled_structures/NUDT21A-x0743-pandda-model.pdb. Molecule number 1 created.

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)

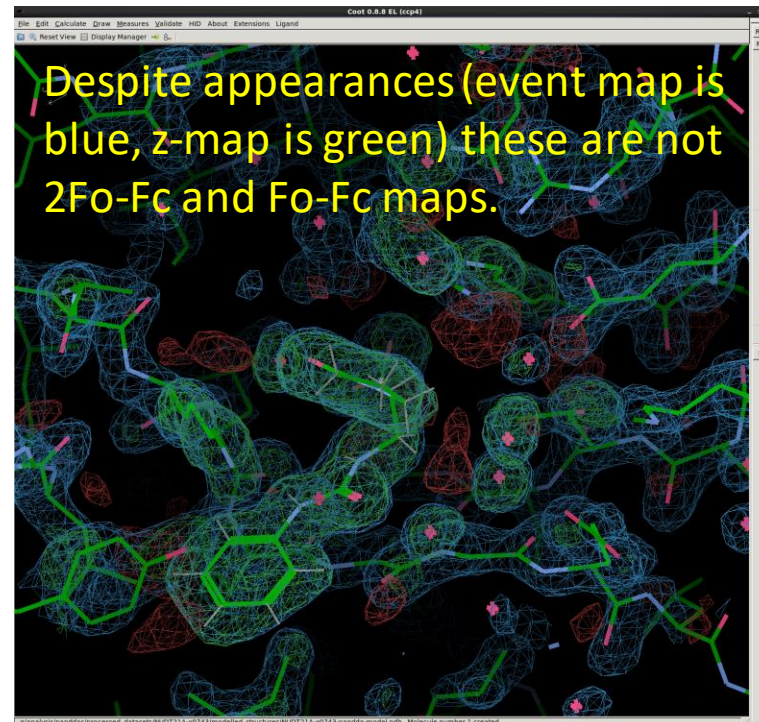
Partial-difference density obtained by subtracting a fraction of the mean map from the dataset map. This reveals the density for low-occupancy binding events. X indicates which event in this dataset is being inspected, and Y indicates the amount of mean map that has been subtracted (amount subtracted = 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

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

- 1 Summary of PANDDA statistics
- 2 To merge the ligand to the model or add another one
- 3 To save your work or roll back.

- 1 To annotate the event.
- 2 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**

PANDDA inspect

Quit

Overall Inspection Event/Site Progress: Go to Dataset: Go

Summary

Event 1 of 404

Site 1 of 21

<<< Go to Prev Site <<< >>> Go to Next Site >>>

>>> Go to Next Unviewed >>> >>> Go to Next Modelled >>>

<<< Prev <<< (Don't Save Model) >>> Next >>> (Don't Save Model) >>> Next >>> (Save Model)

Dataset ID	NUDT21A-x0743		
Event Information:	Dataset Information:		
Event #	3	Resolution	1.65
1 - BDC	0.28	Map Uncertainty	0.23
Z-blob Peak	11.0	R-Free / R-Work	0.213 / 0.247
Z-blob Size	796		

Merge Ligand With Model

Save Model

Move New Ligand Here

Reload Last Saved Model

Open Next Ligand

Reset to Unfitted Model

Record Event Information (this event only)

Event Comment:

Mark Event as Interesting Mark Event as Not Interesting Ligand Placed No Ligand Placed Model: High Confidence Model: Medium Confidence Model: Low Confidence

Record Site Information (for all events with this site)

Name:

Comment:

Miscellaneous buttons

Load input mtz file

Load average map

Load unfitted model (for comparison only)

Create new ligand

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 <small>Move new ligand here</small> button, and you can merge it with the model using the <small>Merge new ligand</small> button.
4)	Save the changes to the model.	If you want to save the changes to the model you can use the <small>Save Model</small> button. Or, if you use the <small>>>> Next Event >>> (Save Model)</small> 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

XChemExplorer

References Deposition Help

Maps PANDDAs Refinement Deposition Settings

Dataset Summary Results Summary Inspect Summary

Refinement Space Group	Resolution n$\langle I \rangle / \sigma(I) > = 1$	Dimple Rcryst	Dimple Rfree	Crystal Form Name	PanDDA launched?	PanDDA hit?	PanDDA reject?	PanDDA Status
I 1 2 1	n/a	0.20091	0.24170	SG-I121-No.5...	True	True	False	start
I 1 2 1	3.40	0.27638	0.36151	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.19085	0.22944	SG-I121-No.5...	True	True	False	start
I 1 2 1	n/a	0.18977	0.23902	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.18998	0.23253	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.18312	0.24032	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.18523	0.22781	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.18656	0.23316	SG-I121-No.5...	True	True	False	start
I 1 2 1	n/a	0.18469	0.22959	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.17369	0.22225	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.23200	0.27408	SG-I121-No.5...	True	True	False	start
I 1 2 1	n/a	0.18925	0.24418	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.18800	0.22815	SG-I121-No.5...	True	False	False	start
I 1 2 1	2.35	0.22608	0.28155	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.17693	0.23415	SG-I121-No.5...	True	False	False	start
I 1 2 1	3.17	0.18876	0.25831	SG-I121-No.5...	True	False	False	start
I 1 2 1	n/a	0.18837	0.22015	SG-I121-No.5...	True			
I 1 2 1	n/a	0.19610	0.23504	SG-I121-No.5...	True			
I 1 2 1	n/a	0.19576	0.23759	SG-I121-No.5...	True			

data directory
17/lb16813-1/processing/analysis/initial_model/*

pdb style

mtz style

output directory
/ta/2017/lb16813-1/processing/analysis/panddas

submit
qsub

number of processors

order events by:
cluster_size

Use space group of reference file as filter:

Expert Parameters (only change if you know what you are doing!):

min_build_datasets

less pretty

1 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

less
source

Datasets
Get New Results from Autoprocessing

Maps & Restraints
Run DIMPLE on selected MTZ files

Hit Identification
Export ALL PANDDA models

Refinement
Open COOT

1

pandda.export

pandda.export

- Generates bound+unbound ensemble models for refinement
- Generates occupancy and restraints parameters for reftmac 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

XChemExplorer

File Datasource Preferences Deposition Help Labels

Overview Datasets Maps PANDAs **Refinement** Deposition Settings

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-4000: 0.8...	finished
34	MID2A-x0526	Z198195770	P 21 21 21	1.640	0.2189	0.2423	3 - In Refinement	Refine 3-report	LIG-A...	finished
35	MID2A-x0528	Z56827661	P 21 21 21	1.720	0.2217	0.2426	3 - In Refinement	Refine 3-report	LIG-B...	finished
36	MID2A-x0531	Z1343633025	P 21 21 21	1.689	0.2245	0.2534	4 - CompChem ready	Refine 4-report	LIG-A...	finished
37	MID2A-x0535	Z65532537	P 21 21 21	1.880	0.2691	0.3102	4 - CompChem ready	Refine 5-report	LIG-A...	finished
38	MID2A-x0541	Z2856434865	P 21 21 21	1.769	0.2130	0.2446	4 - CompChem ready	Refine 5-report	LIG-A...	finished
39	MID2A-x0546	Z2856434829	P 21 21 21	1.540	0.2086	0.2327	4 - CompChem ready	Refine 5-report	LIG-A...	finished
40	MID2A-x0547	Z364328788	P 21 21 21	1.921	0.3193	0.3367	4 - CompChem ready	Refine 5-report	LIG-B...	finished
41	MID2A-x0549	Z26968795	P 21 21 21	1.510	0.2015	0.2241	4 - CompChem ready	Refine 5-report	LIG-B...	finished
42	MID2A-x0550	Z364321922	P 21 21 21	1.771	0.2161	0.2410	4 - CompChem ready	Refine 4-report	LIG-B-801: 0.720	finished
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

Update Tables From Datasource

Datasets Run Status Get New Results from Autoprocessing

Maps & Restraints Run Status Run DIMPLE on selected MTZ files

Hit Identification Run Status pandda.analyse

Refinement Run Status Open COOT - REFMAC refinement -

1 Select 'Open coot' and click 'run'
It will open coot and an the XCE refinement control panel

1

XCE: Refinement control panel

Select Samples

1 - Analysis Pending **1** GO

2 found 76 samples

R/Rfree	0.348 / 0.391	Ligand ID	-
Resolution	1.93	occupancy	-
1 MolprobityScore	-	B average	-
Rama Outliers	-	B ratio	-
Rama Favored	-	RSCC	-
rmsd(Bonds)	0.016	rmsd	-
rmsd(Angles)	1.880	RSR	-
Matrix Weight	None	RSZD	-

Show MolProbity to-do list

2 CC(C)C(=O)N1C=CC2C1CC2

3

Model Accuracy (R2SD)	0.37	Model Mean	-
Model Precision (R2SD)	0.3	B Factor Ratio	-

pandda.inspect comments

Site Name	-	Confidence	-	Interesting	-
Comment	-				

Sample Navigator

OXA10-x0036 **3** **4**

<<< >>> <<< >>>

Analysis Status

Review PANDDA export

In Refinement **1**

Comp Chem Ready!

Ready for Deposition!

In PDB

Ligand Confidence

0 - no ligand present

1 - Low Confidence **2**

2 - Correct ligand, weak density

3 - Clear density, unexpected ligand

4 - High Confidence

Ligand Modeling

Place Ligand here Merge Ligand

3 Refine refinement parameters

CANCEL

1 Select the category/status of samples you want to refine (at the beginning: **3 – in refinement***) and click ‘GO’

2 It will tell you how many samples were found for that category

3 To navigate through the samples in the selected category

4 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

1 Summary of refinement statistics

2 Ligand 2D plot

3 Ligand validation plot. The closer the values are to the center, the higher your confidence (See Nick Pearce’s paper for the details)

1 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...

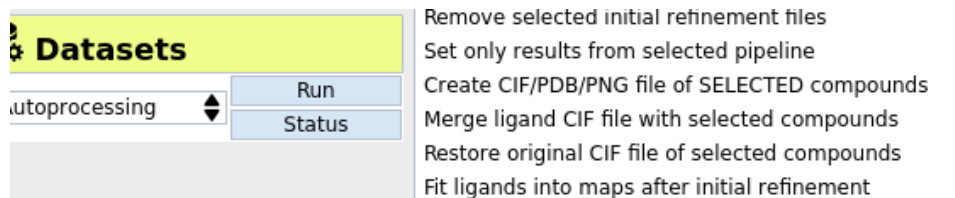
2 Manually select the ligand confidence for *this event*

3 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