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Using the Gold Standard for data archival at kilohertz speeds

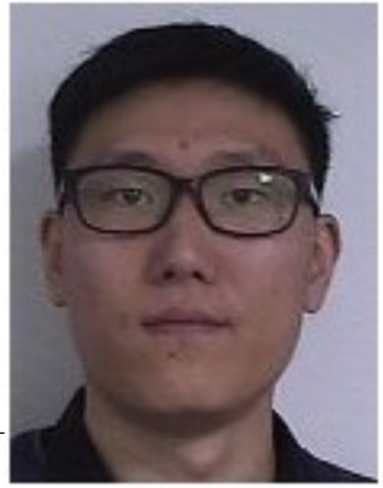
Aaron S. Brewster

August 14th, 2021

Acknowledgements: NERSC, DLS and EuXFEL

Johannes Blaschke, NERSC

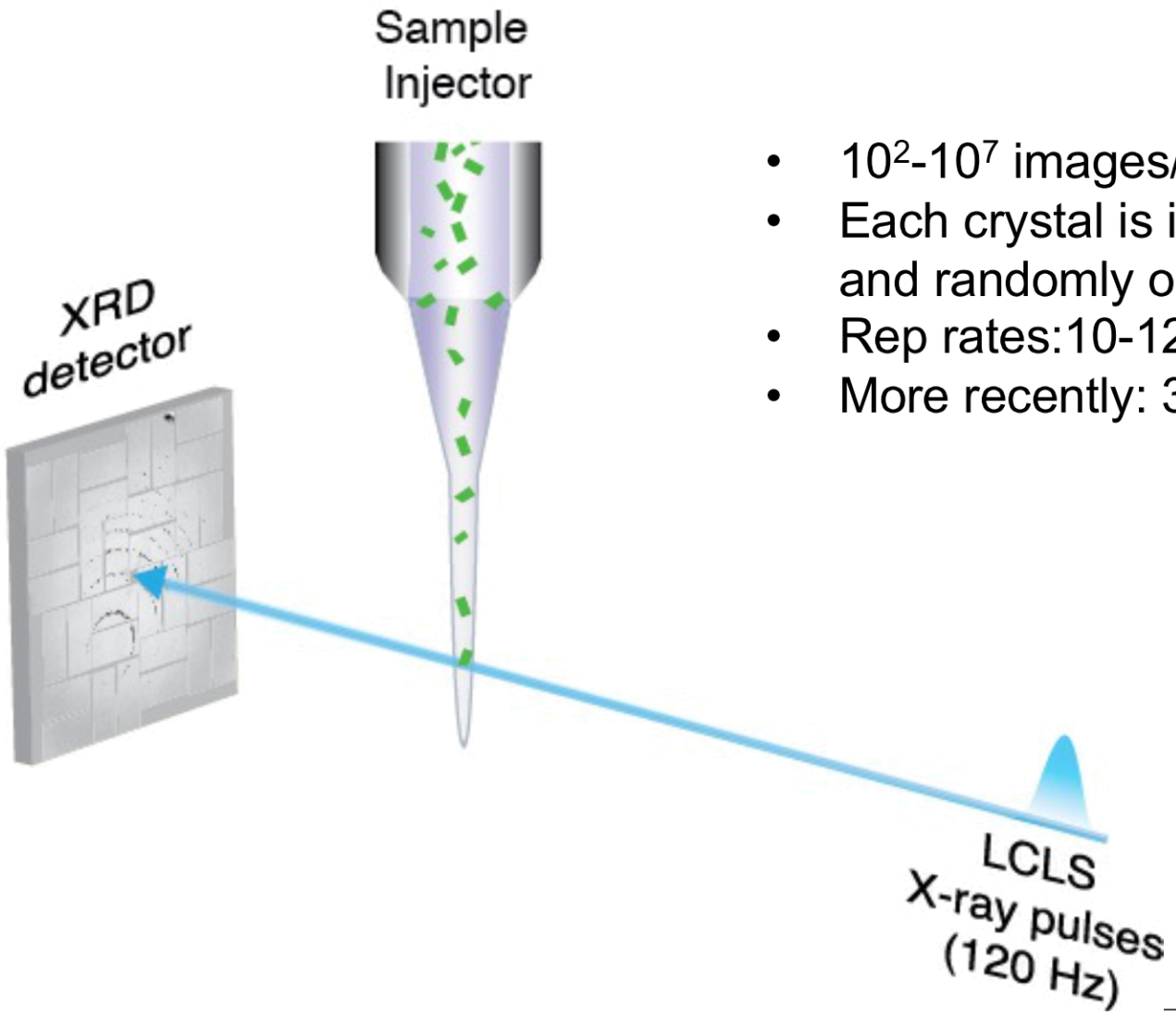
Robert Bosman, DLS



Tiankun Zhou, DLS

Fabio Dall'Antonia, EuXFEL

Serial crystallography



- 10^2-10^7 images/dataset
- Each crystal is independent and randomly oriented
- Rep rates:10-120 Hz
- More recently: 3 kHz

SFX: The Experiment

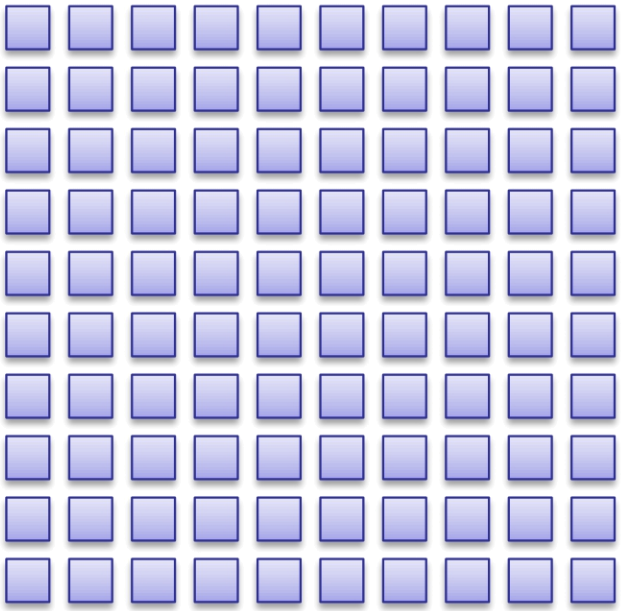
- Pump/probe (many datasets)
  - Laser excitation
  - Mixing (gas, ligand)
  - Temperature
  - Femtosecond dynamics
- Not usually *ab initio* structure determination
- Beam time is...
  - Scarce
  - Concentrated
  - Fast
- What are the data processing goals?

Goal: scale up

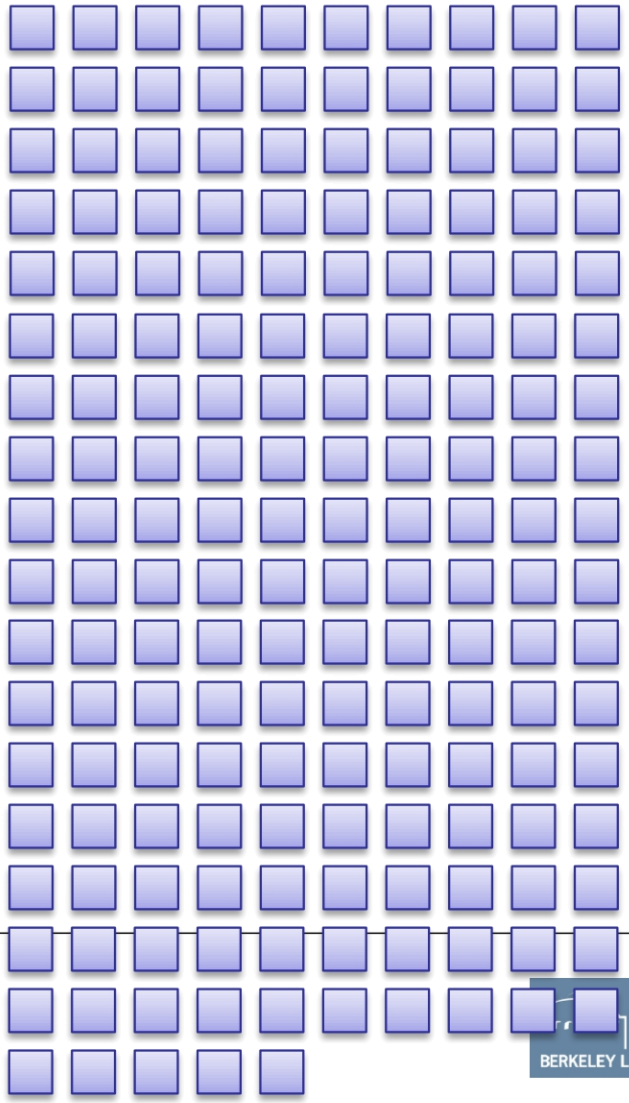
LCLS: 20 Hz Rayonix
6K images in 5 min

LCLS: 120 Hz CSPAD
36K images in 5 min

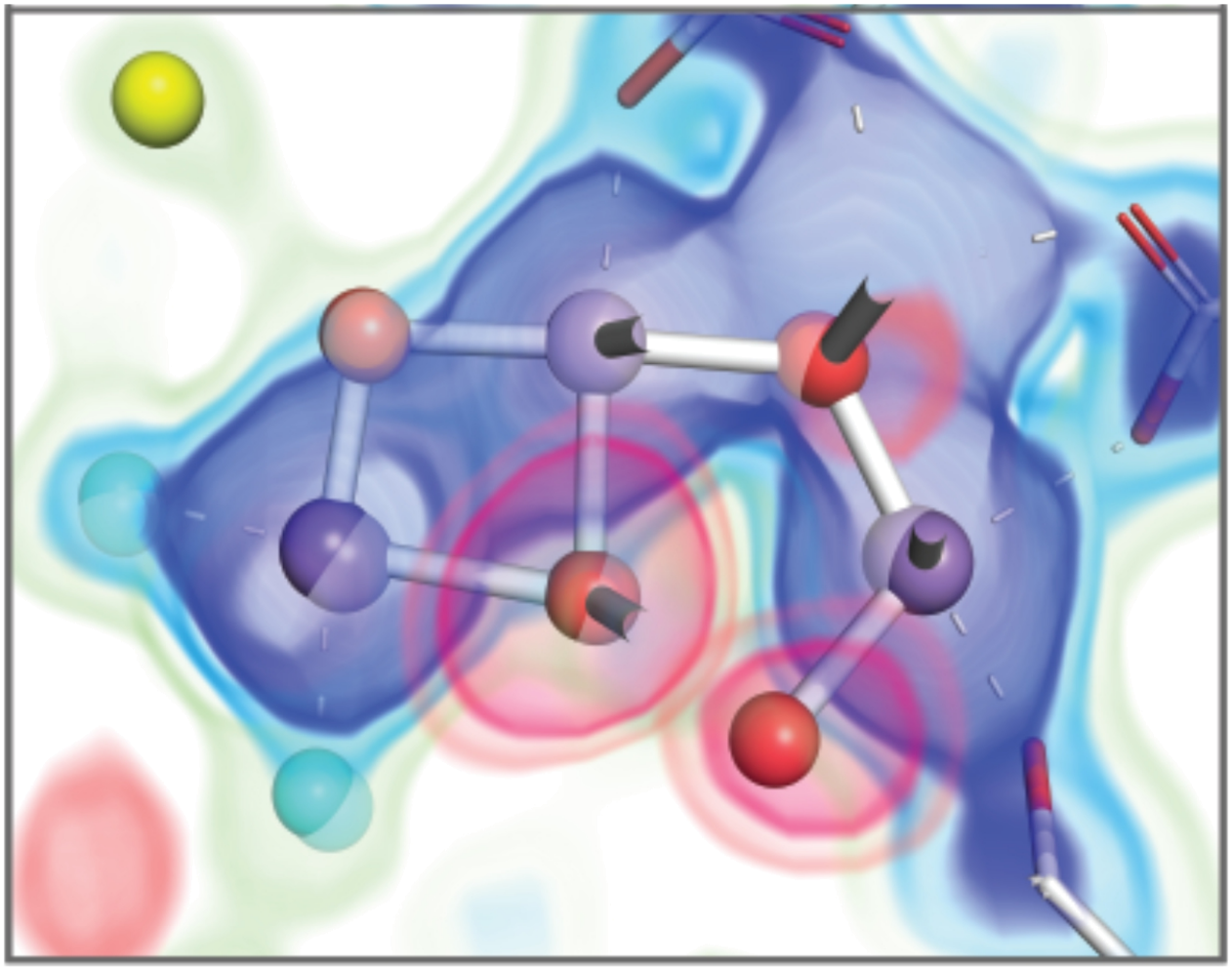
EuXFEL: 2000 Hz AGIPD
600K images in 5 min



EuXFEL: 3500 Hz AGIPD
900K images in 5 min



Goal: answer biological questions



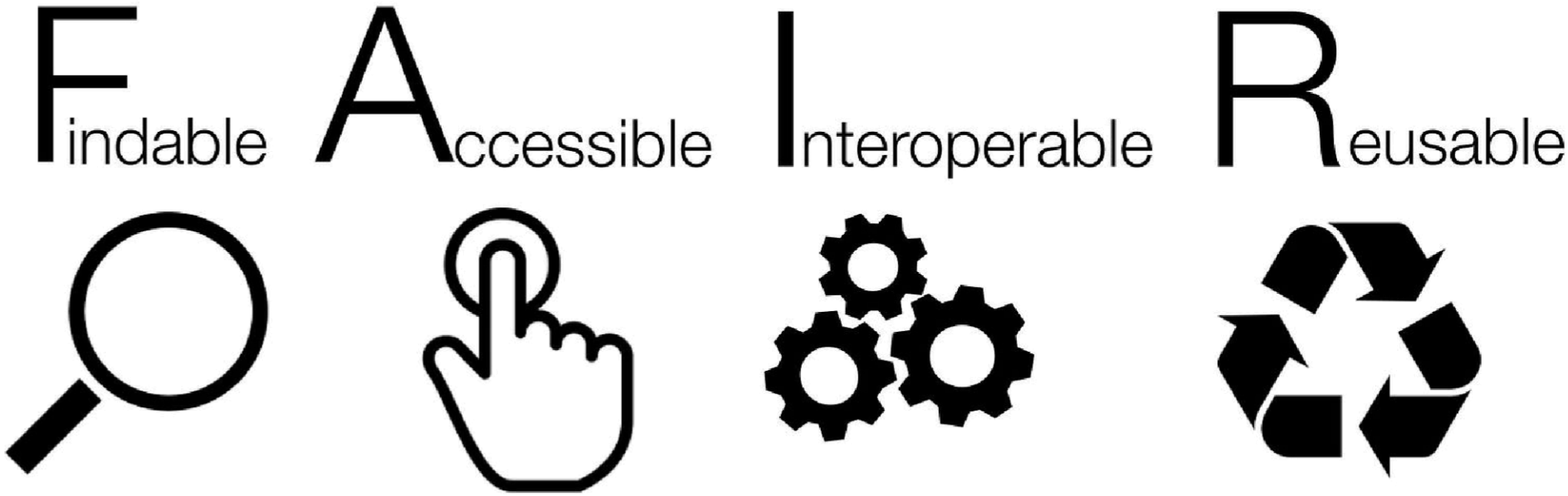
PSII 2Fo-Fc and Fo-Fc at 2.07 Å, S3 state

Kern et al., 2018 Nature 563:421

Goal: Fast Feedback

- Per-image metrics
  - Solvent hits
  - Crystal hits
  - Indexing rates
  - Crystal quality
- Global metrics
  - Unit cell isomorphism
  - Merged completeness/resolution

Goal: FAIR



Wilkinson, M., Dumontier, M., Aalbersberg, I. *et al.* The FAIR Guiding Principles for scientific data management and stewardship. *Sci Data* **3**, 160018 (2016). https://doi.org/10.1038/sdata.2016.18

NeXus

SwissFEL: JF16M
EuXFEL: AGIPD
PAL: JF4M

Bernstein, H. J., Forster, A., *et. al.* Gold Standard for macromolecular crystallography diffraction data (2020). IUCrJ 7, 784-792.

Goal: organize datasets
Example: LCLS / MFX December 2018

- Four 12-hour shifts at MFX (LU50 / P143)
- 20 – 30 Hz overall collection rate (Rayonix 340)
- 594,230 total indexed images
- > 8.4 indexed images s^{-1} (31% of all shots)
- Overall 48% collection duty cycle
- ~ 54 tr-SFX + tr-XES data sets
- ~ 12 types of enzymes
- Typically ~ 1 mg protein per dataset
- Some data beyond 1.3 Å resolution

dataset						x 340 r rate
1						z
2						z
3						z
4						z
5						z
6						z
7						z
8						z
9						z
10						z
11						z
12						
13						z
14						z
15	Enz 01 oxidized (no run 20, no data in run	1.6	1.76	16851	45	30 Hz

Goals

- Real-time statistics
- Real-time electron density maps
- Dataset/metadata organization
- FAIR
- At kHz speeds

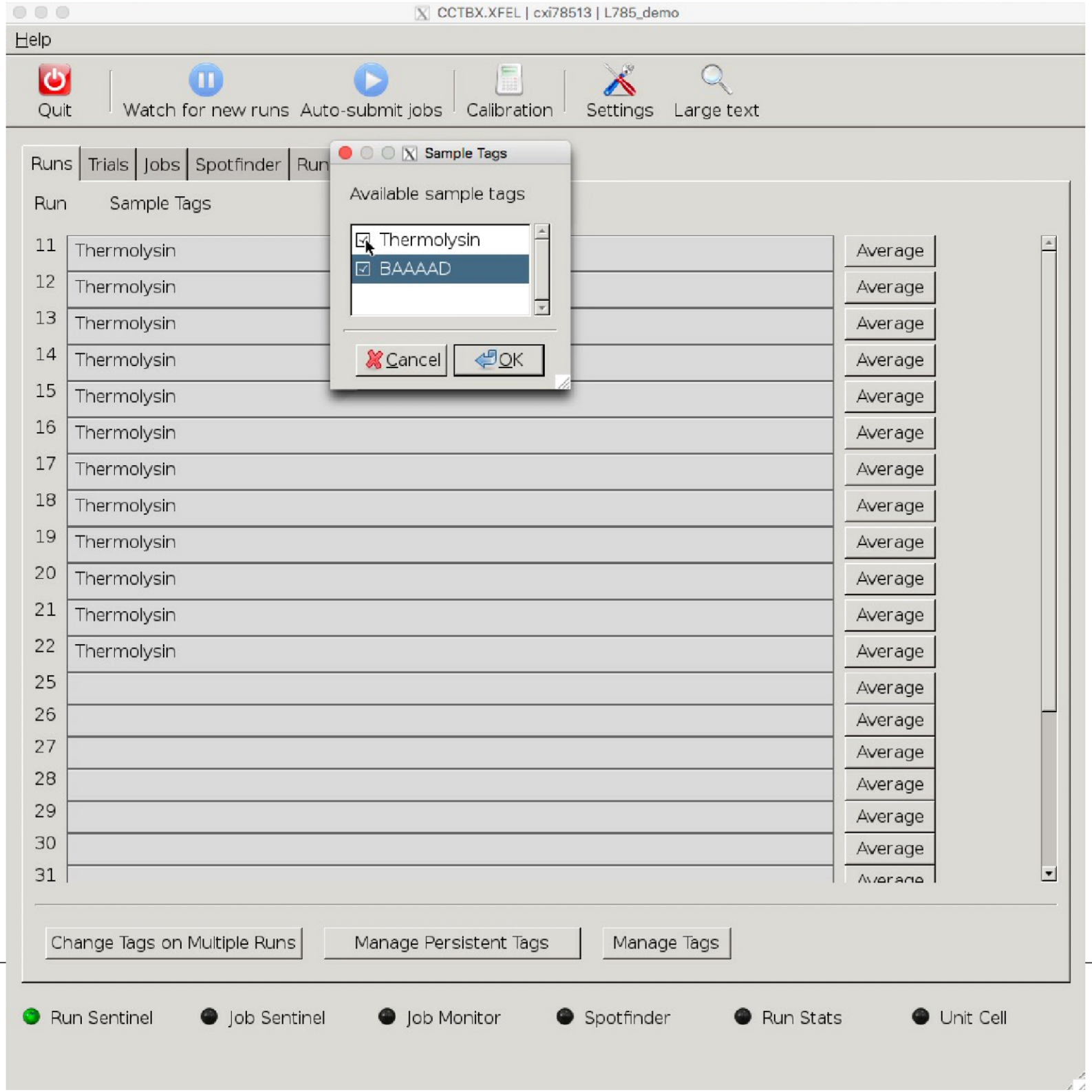
cctbx.xfel GUI

- Built on *cctbx* and DIALS

Winter G. (2018). DIALS: implementation and evaluation of a new integration package. *Acta Crystallogr D Struct Biol* **74**, 85-97

Brewster AS, et. al (2019): Processing serial crystallographic data from XFELs or synchrotrons using the *cctbx.xfel* GUI. *Computational Crystallography Newsletter* **10**, 22-39.

- Full SX workflow
  - Each image: import, spot-find, index, integrate, scale, post-refine
  - Dataset: merge, phenix.refine, upload
  - Monitor for new data and submit jobs
  - Organize processing many datasets
  - Massively parallel multiprocessing on the biggest computing clusters
  - MySQL backend allows scaling to the kHz regime


CCTBX.XFEL | cxi78513 | L785_demo
Help
Quit
Watch for new runs
Auto-submit jobs
Calibration
Settings
Large text
Runs
Trials
Jobs
Spotfinder
Run
Run
Sample Tags
11 Thermolysin
12 Thermolysin
13 Thermolysin
14 Thermolysin
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Sample Tags
Available sample tags
Thermolysin
BAAAAD
Cancel
OK
Change Tags on Multiple Runs
Manage Persistent Tags
Manage Tags
Run Sentinel
Job Sentinel
Job Monitor
Spotfinder
Run Stats
Unit Cell

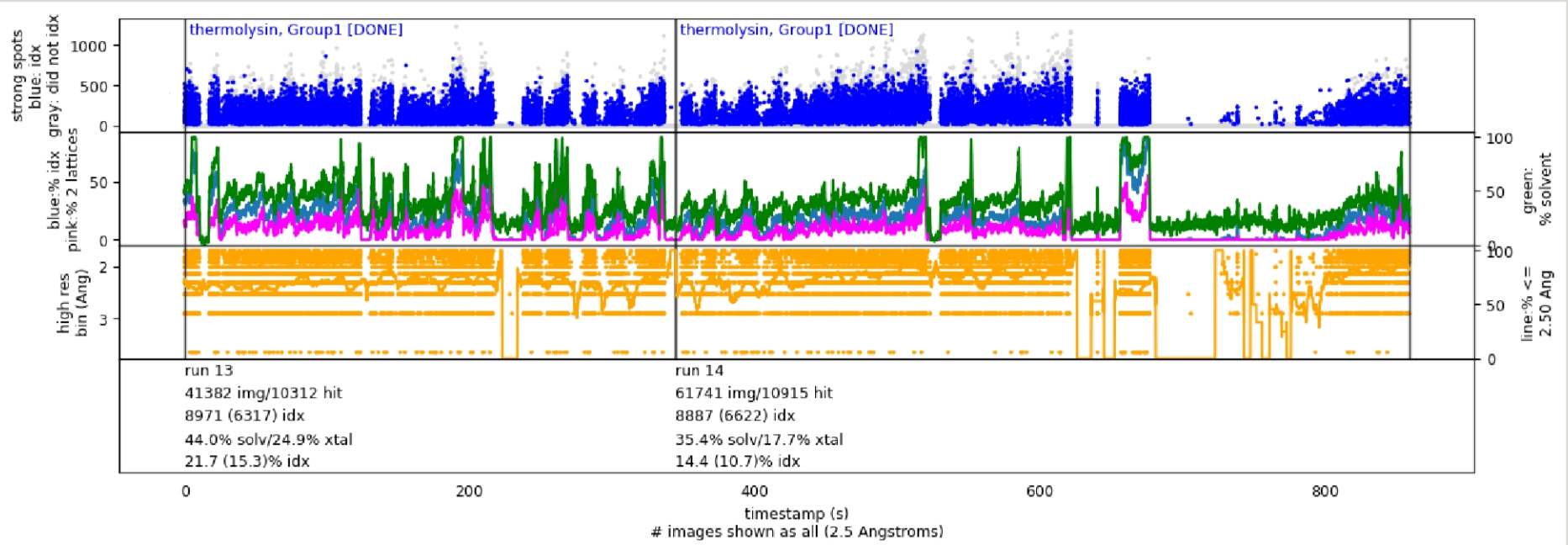
CCTBX.XFEL | cxi78513 | L785

Help

Quit | Watch for new runs | Auto-submit jobs | Calibration | Settings | Large text

Runs | Trials | Jobs | Spotfinder | Run Stats | Unit Cell | Merge

Run Statistics - Trial 17



Statistics Options

Trial: 17 Selected runs:

Auto plot last five runs

Auto plot entire experimer

high resolution limit: 2.5

multiples 2

two theta ratio 1.5

I/sig(I) cutoff: 1

strong spots 40

images to dump: 10

- [ ] 11
- [ ] 12
- [x] 13
- [x] 14
- [ ] 15
- [ ] 16
- [ ] 17
- [ ] 18

Strongest Indexed Images

/reg/d/psdm/cxi/cxi78513/scratch/brewster/paper_2017/
results/r0013/017_rg013/out/
idx-20130301060250689.cbf
/reg/d/psdm/cxi/cxi78513/scratch/brewster/paper_2017/

Open Images

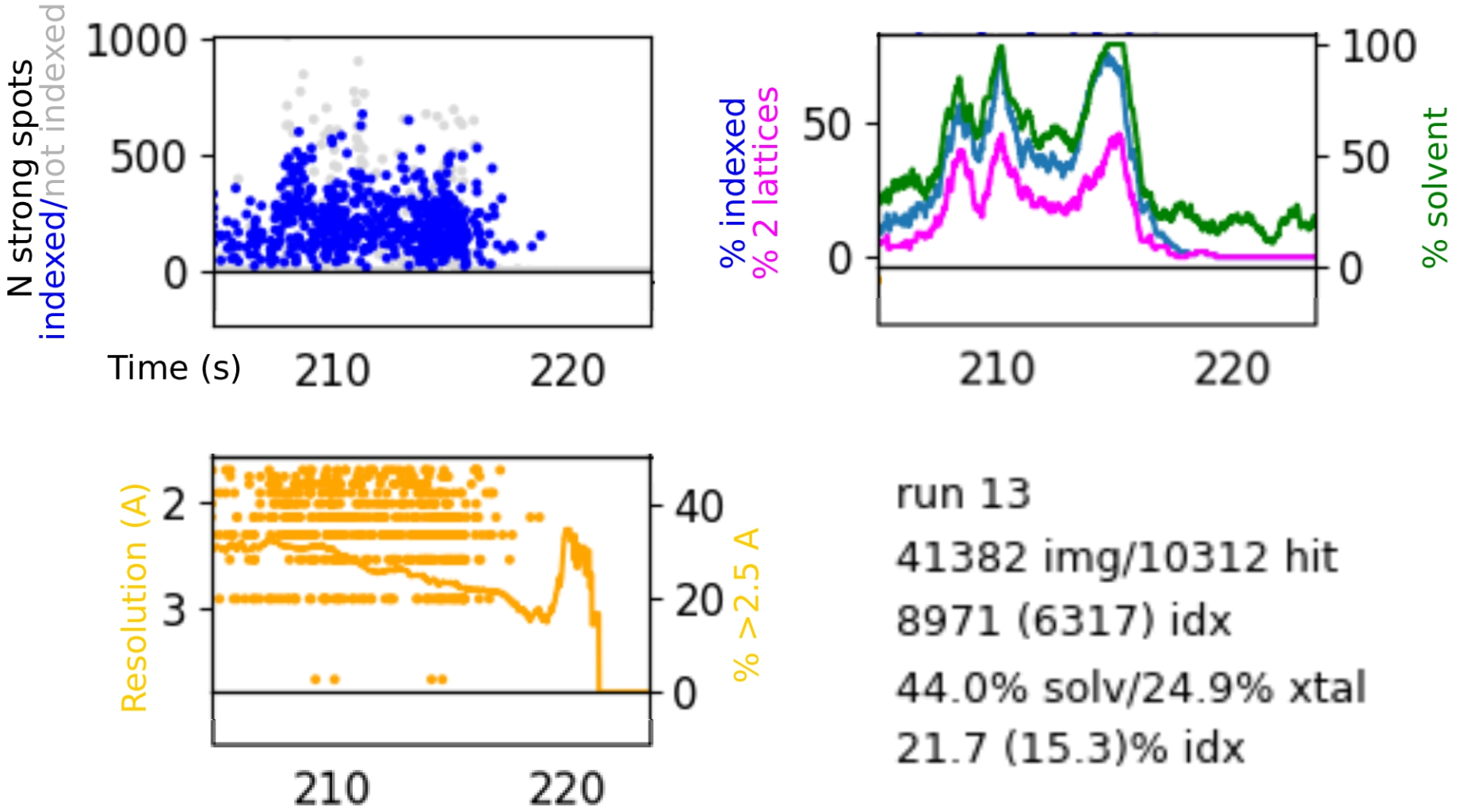
Strong Images that Didn't Index

/reg/d/psdm/cxi/cxi78513/scratch/brewster/paper_2017/
results/r0013/017_rg013/all/
shot-20130301060251056.cbf
/reg/d/psdm/cxi/cxi78513/scratch/brewster/paper_2017/

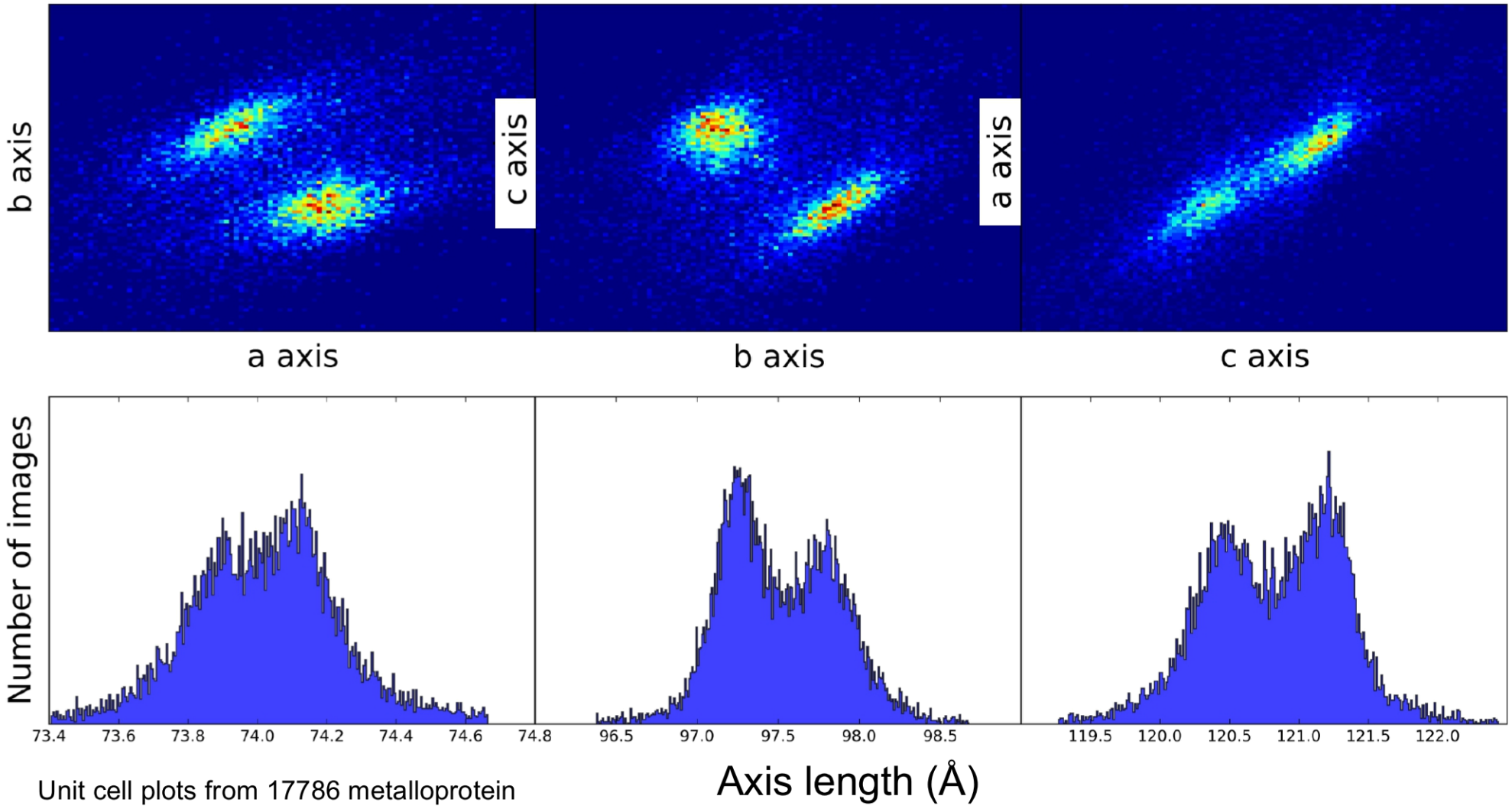
Dump Images

Run Sentinel | Job Sentinel | Job Monitor | Spotfinder | Run Stats | Unit Cell

Rate tracking

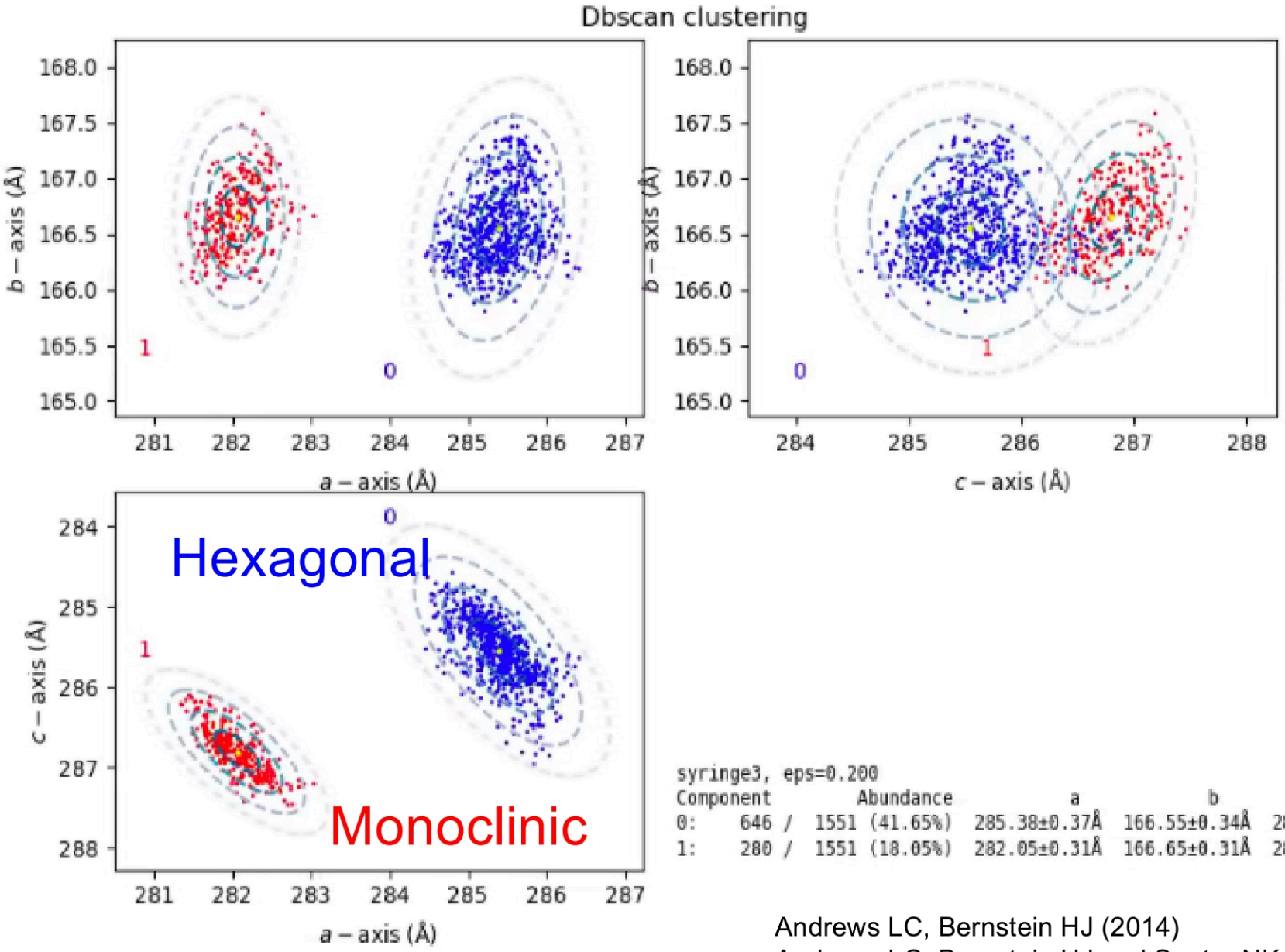


Non-isomorphism: two clusters



Unit cell plots from 17786 metalloprotein crystals (space group $P2_12_12_1$) collected at LCLS beamline MFX.

Resolve clustering on the fly



syringe3, eps=0.200

Component	Abundance	a	b	c
0:	646 / 1551 (41.65%)	285.38±0.37Å	166.55±0.34Å	285.55±0.39Å
1:	280 / 1551 (18.05%)	282.05±0.31Å	166.65±0.31Å	286.81±0.29Å

Andrews LC, Bernstein HJ (2014)
Andrews LC, Bernstein HJ and Sauter NK (2019)

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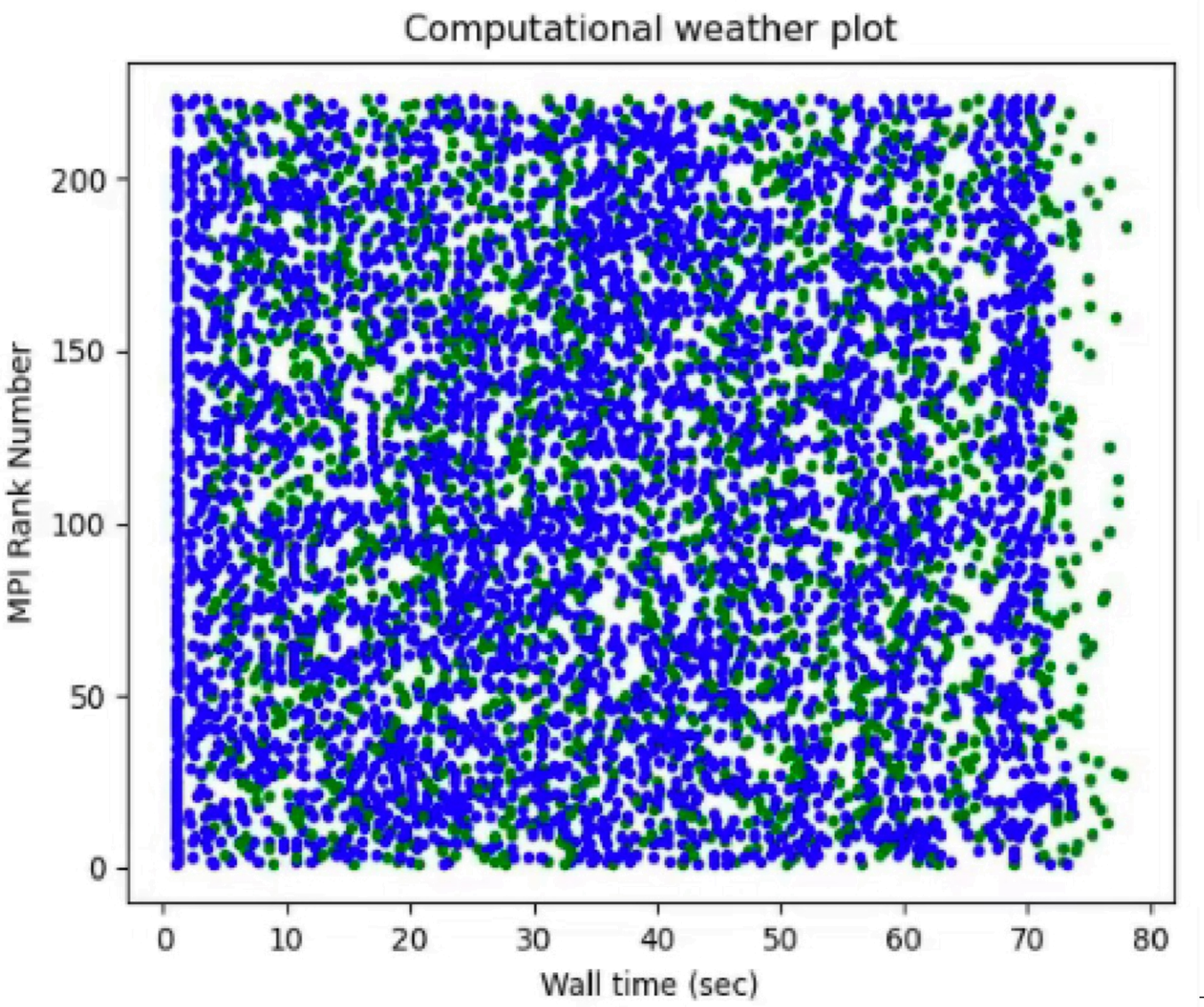
How many computing cores do we need?



- Most recent experiment: 20 Hz Rayonix, processed at NERSC
- How's the weather today?
- Median times:
  - Hits: 5.4s
  - Misses: 1.4s
- 256 cores

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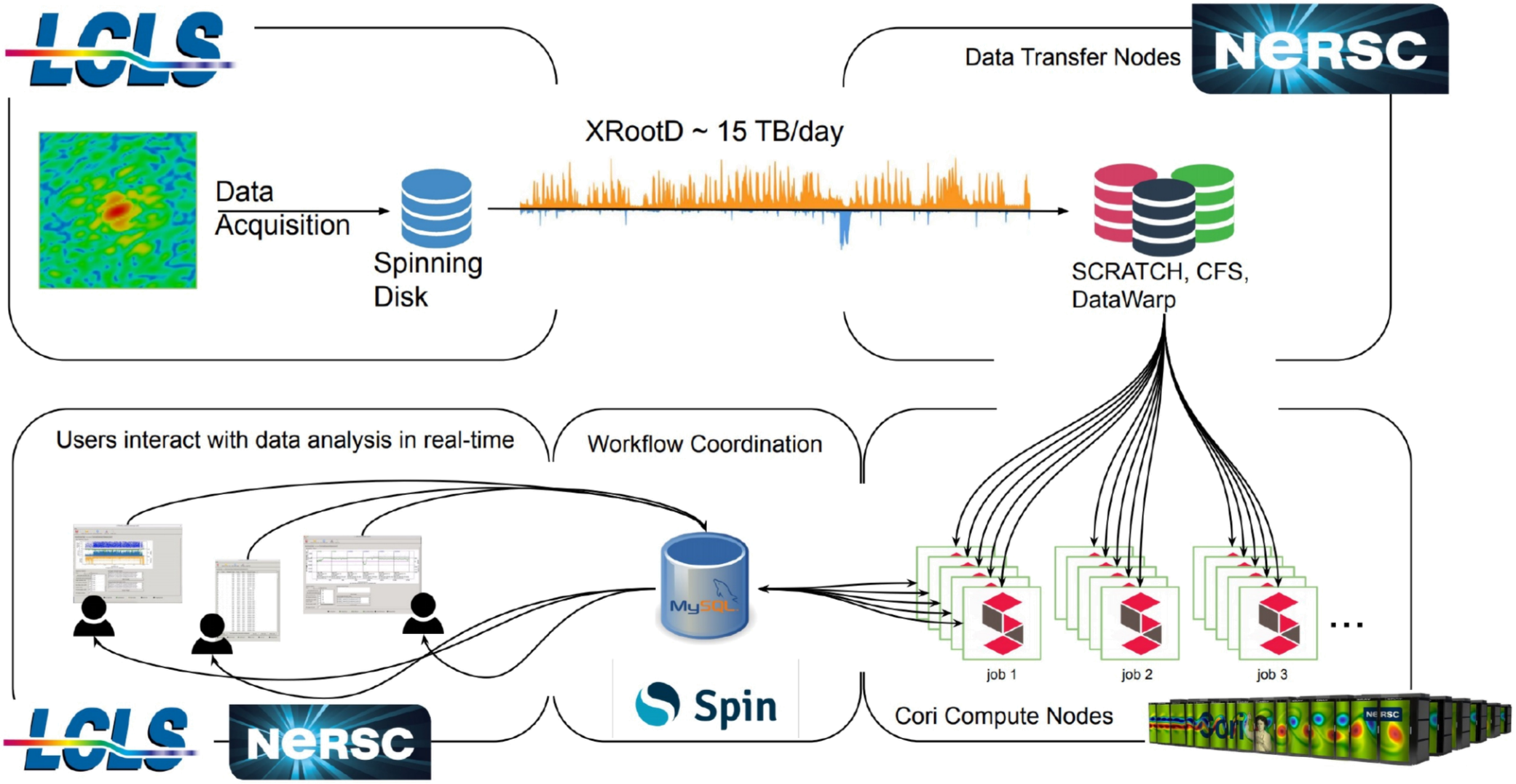
DOE ExaFEL project



Blaschke JP, *et al.* Real-Time XFEL Data Analysis at SLAC and NERSC: a Trial Run of Nascent Exascale Experimental Data Analysis. Preprint. ArXiv. 2021;arXiv:2106.11469v1. Published 2021 Jun 22.

EuXFEL: Spring 2021

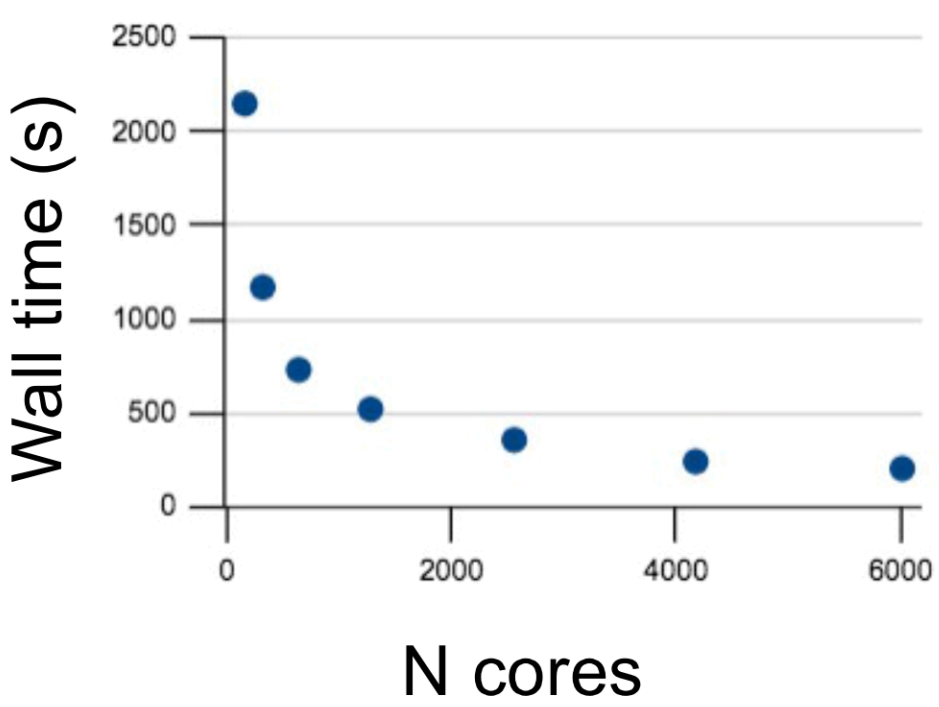
- Two 5-day experiments, separated by a month
- 593TB with a total of 354 runs, 256 with protein
- 2 kHz data collection, 600K images per run
- Maxwell HPC cluster at DESY: 96 nodes, 80-144 cores per node
- Week 1: focus on cctbx.xfel command line programs
- Week 2: focus on GUI integration

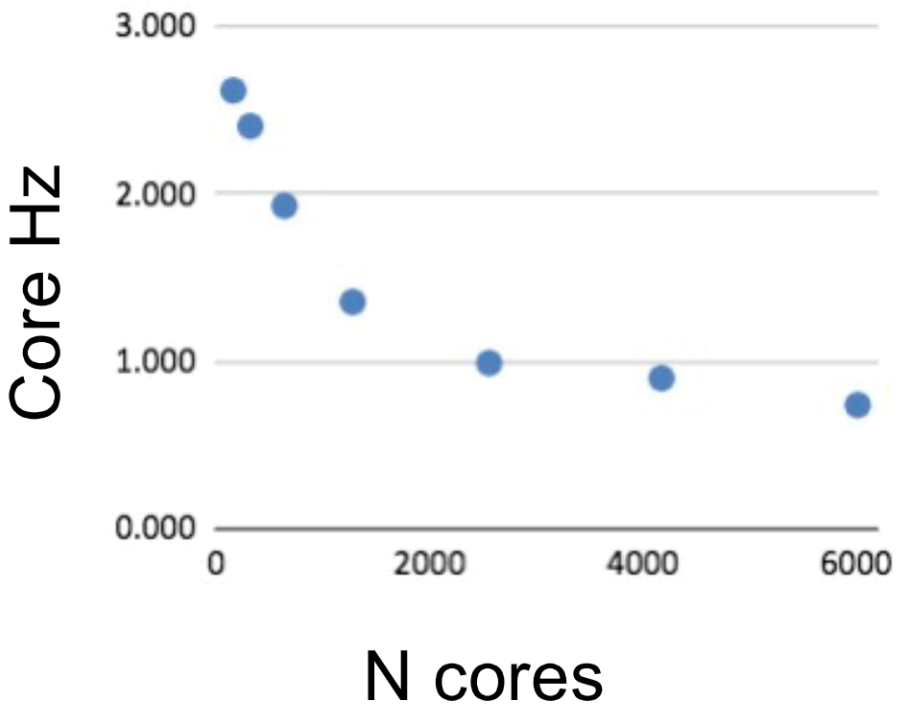
cctbx.xfel build on the Maxwell cluster

- ✗ Conda build (openmpi + HDF5)
- ✗ Attempt to use other pre-built Maxwell MPI's
- ✗ Build own MPI
- ✓ Get help! Local Maxwell MPI/networking expert, Frank Schluenzen.
  - Specific gcc9.3 build of python3 + openmpi 3.1.6 + an mpi-enabled hdf5 library (1.10.6)
  - Use virtual environment + pip to install cctbx dependencies
  - Build cctbx (some linking adjustments needed)
  - Use communication protocol named UCX to take advantage of Infiniband. Frank's openmpi build had this enabled using a custom flag.

Early profiling: 3.5 kHz run, 5 min (900K images)

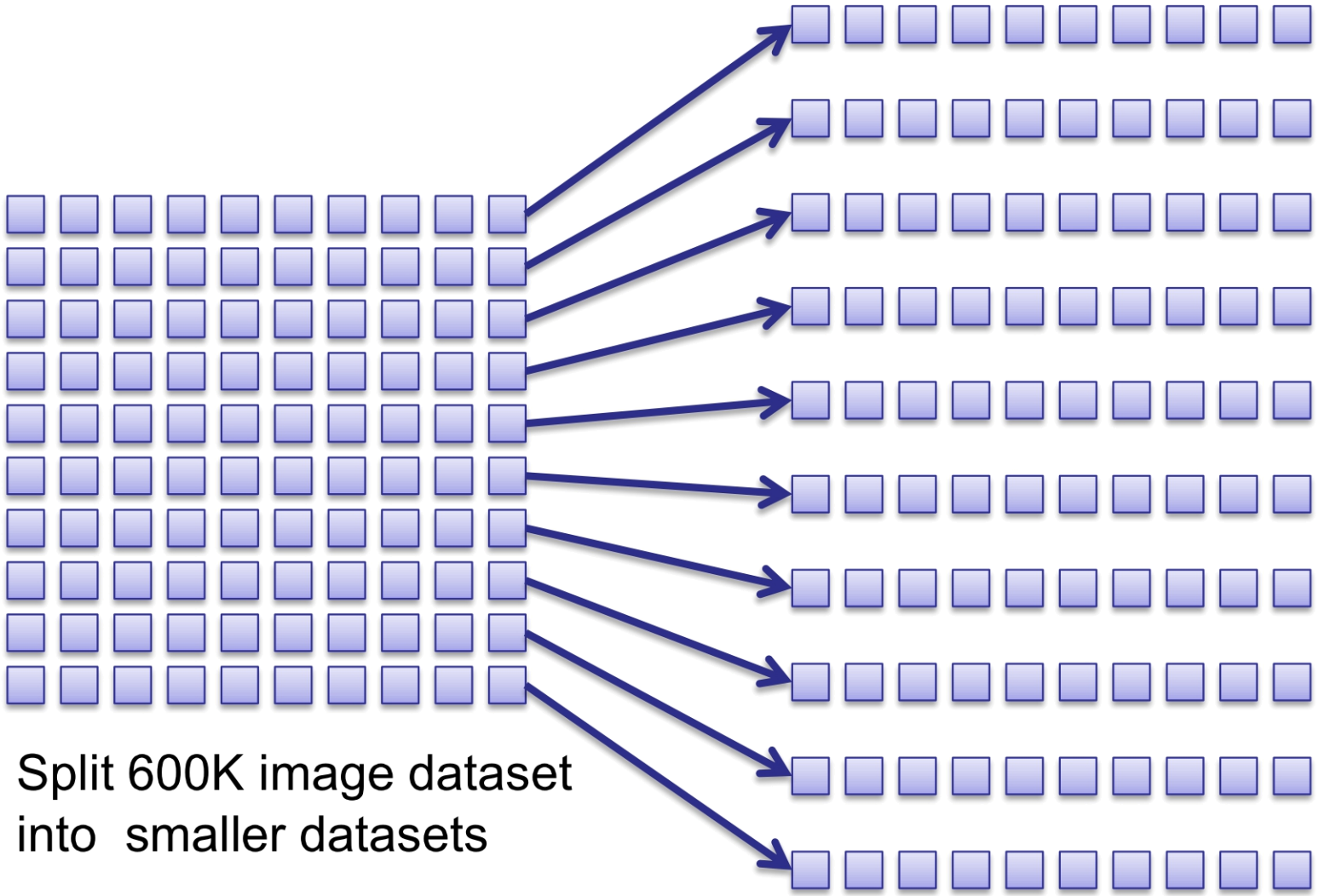
- Simple test: only read and sum the images: non linear scaling





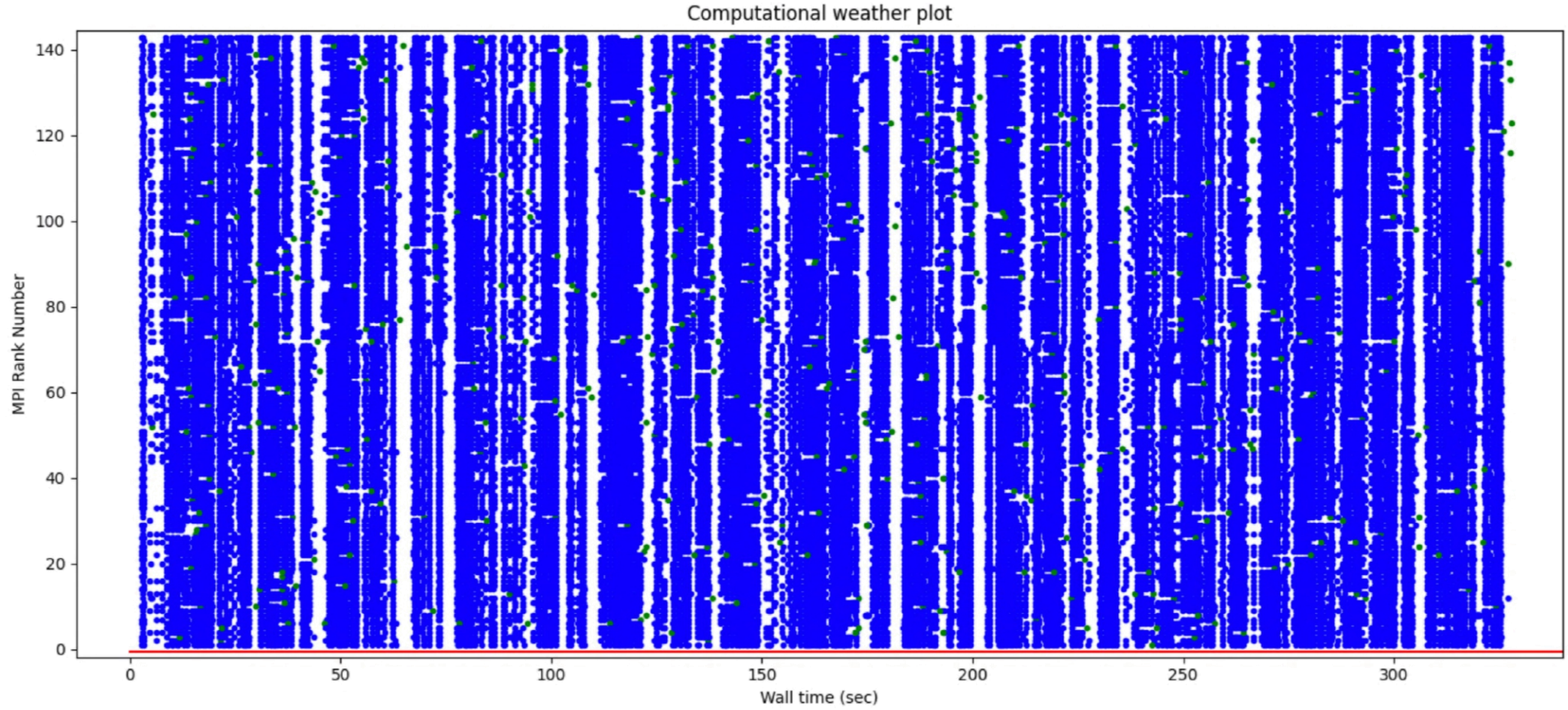
- cctbx.xfel also did not scale linearly

Solution: subfiling



Separate jobs,
8 nodes each

Split 600K image dataset
into smaller datasets



Median timings:

- Hits: 3.3s
- Misses: 0.6s

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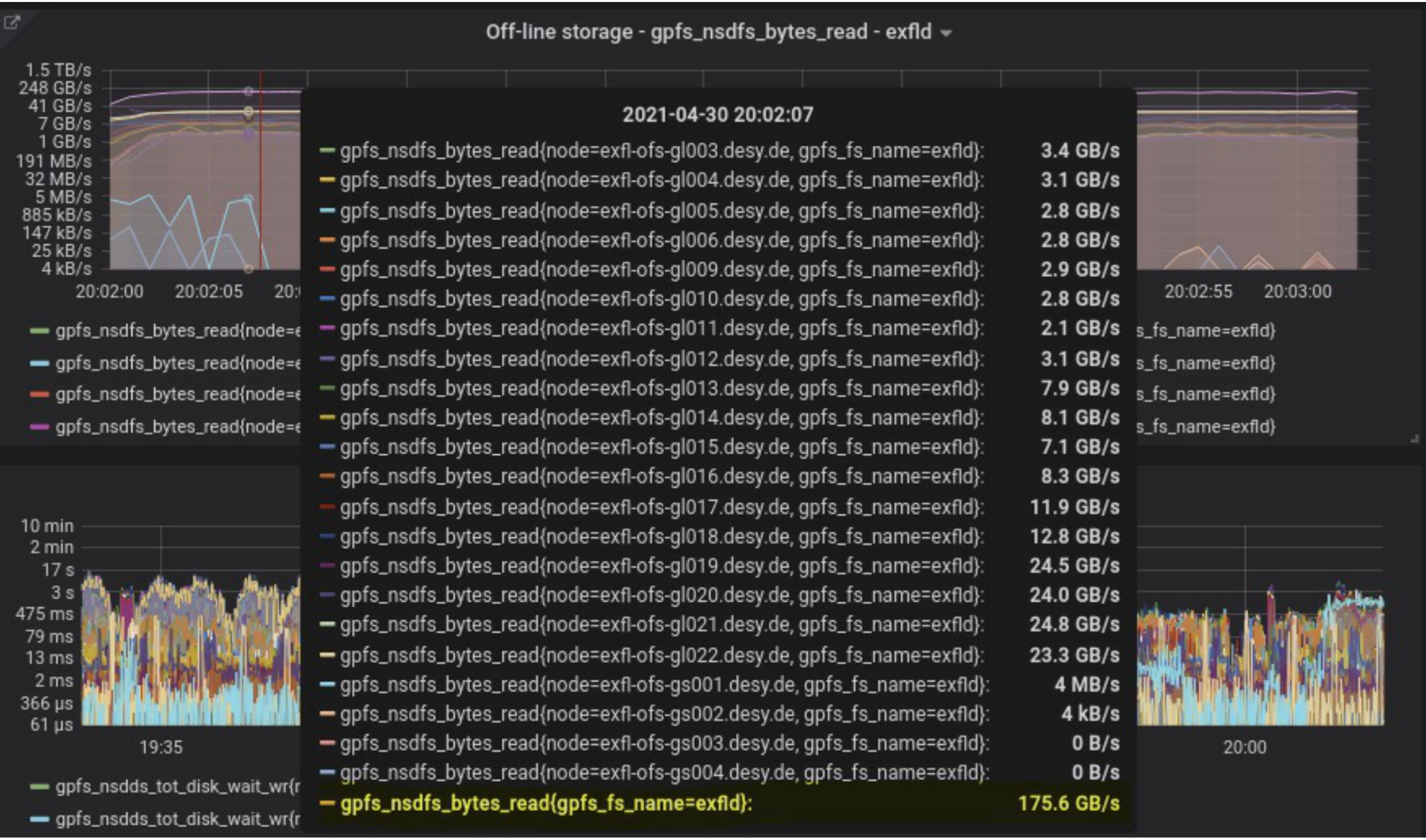

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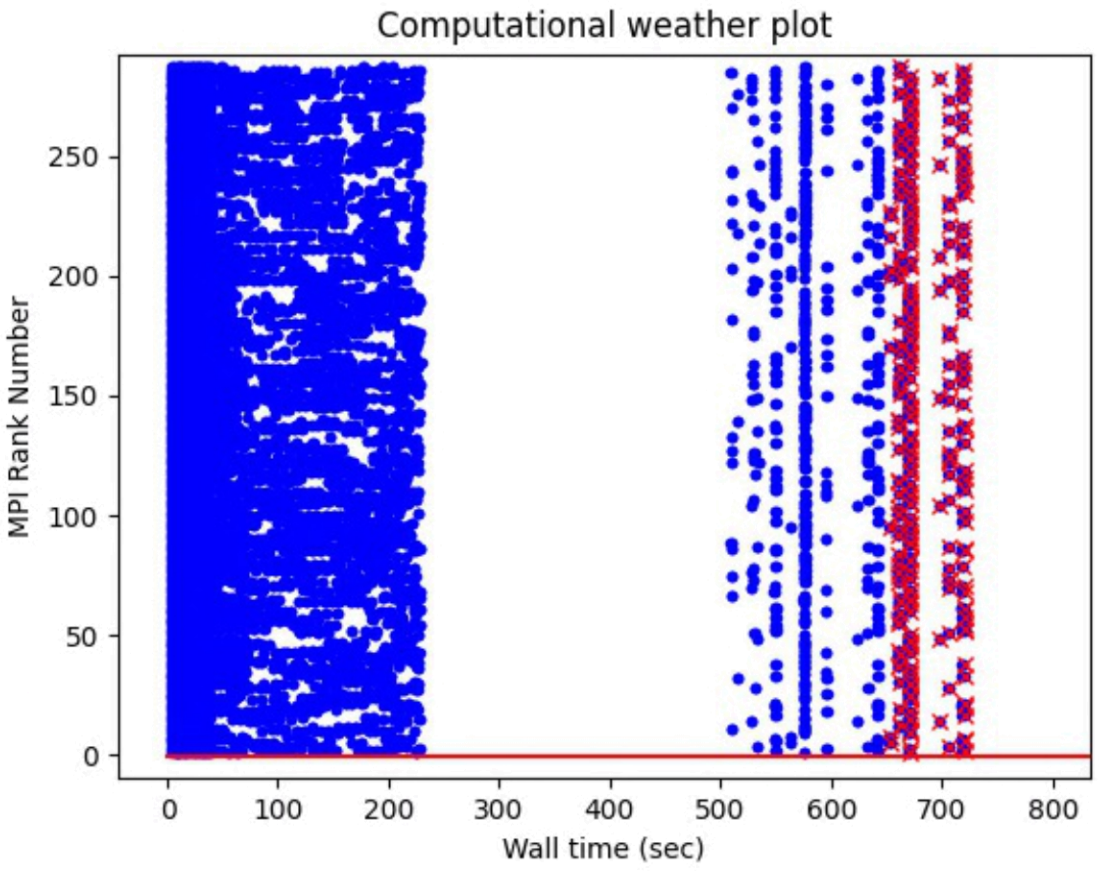
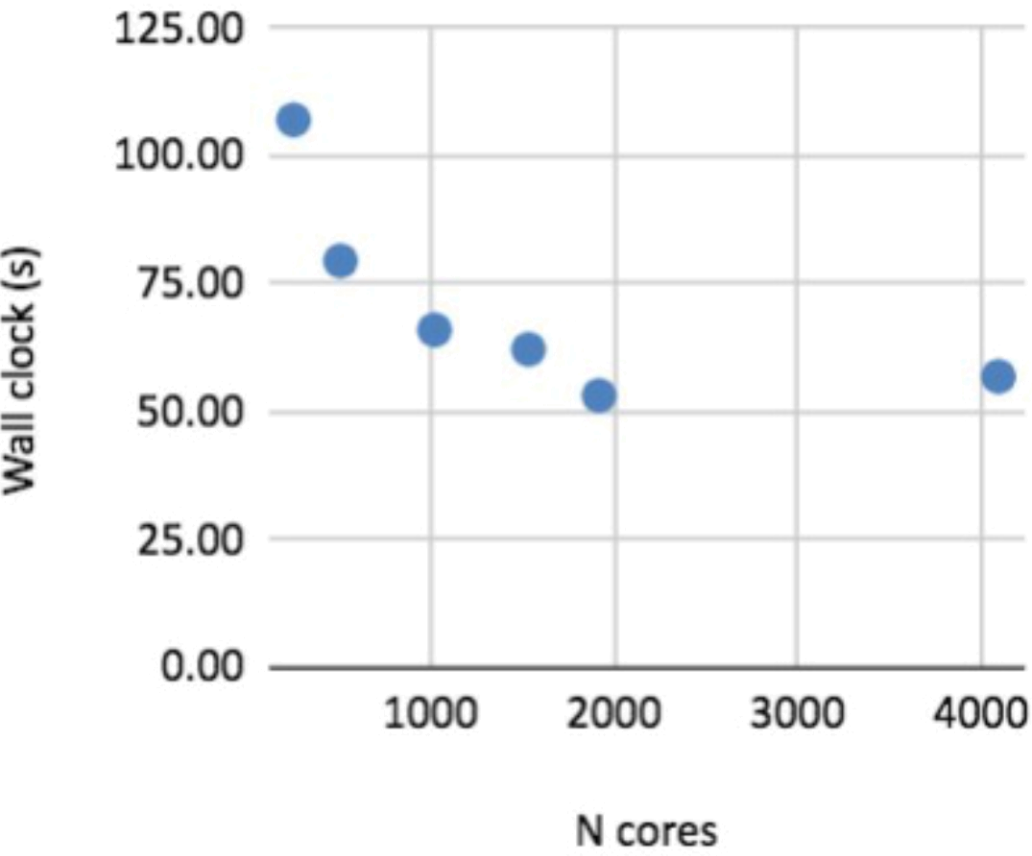
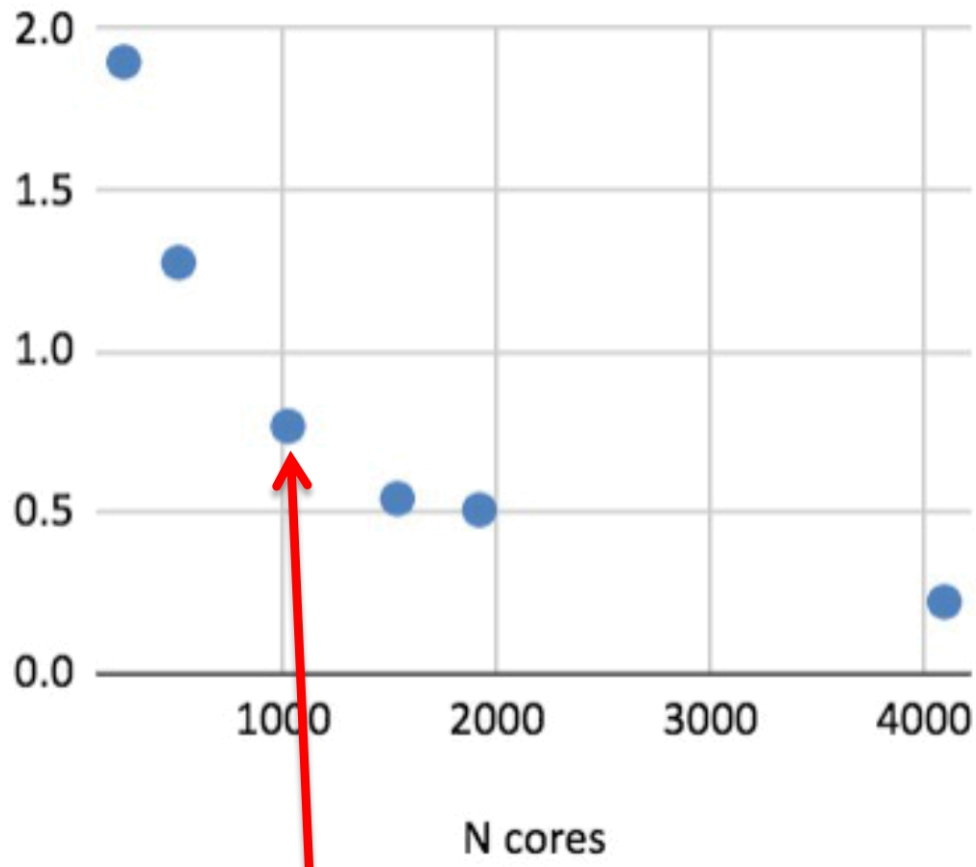
Scale up: GUI



- Queue full: huge delays from MySQL
- >1hr to log 50K images
- Solution: restructure MySQL commits using transactions
- 50K images: log in 0.07s using single MySQL query comprising 130K lines

Future work: still need better scaling





Scaling test on 50K image subfile

Overall: on 8x12 nodes, 9.4 kHz!

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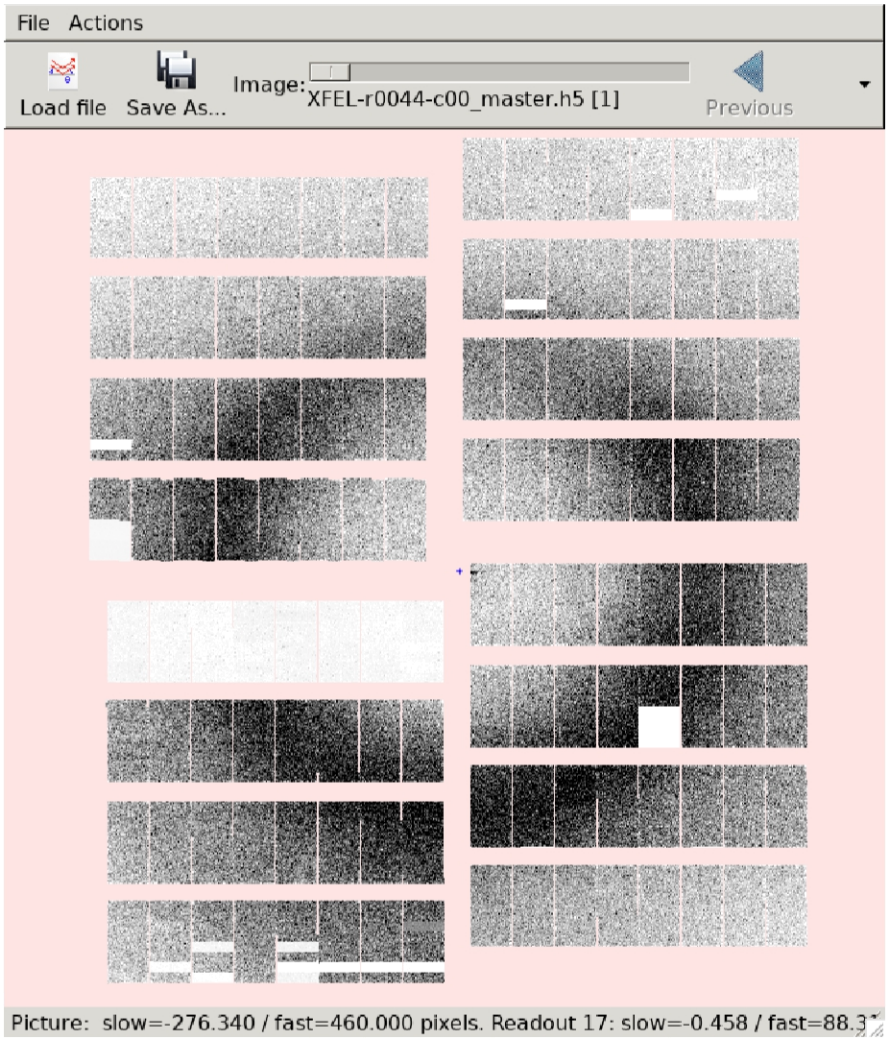
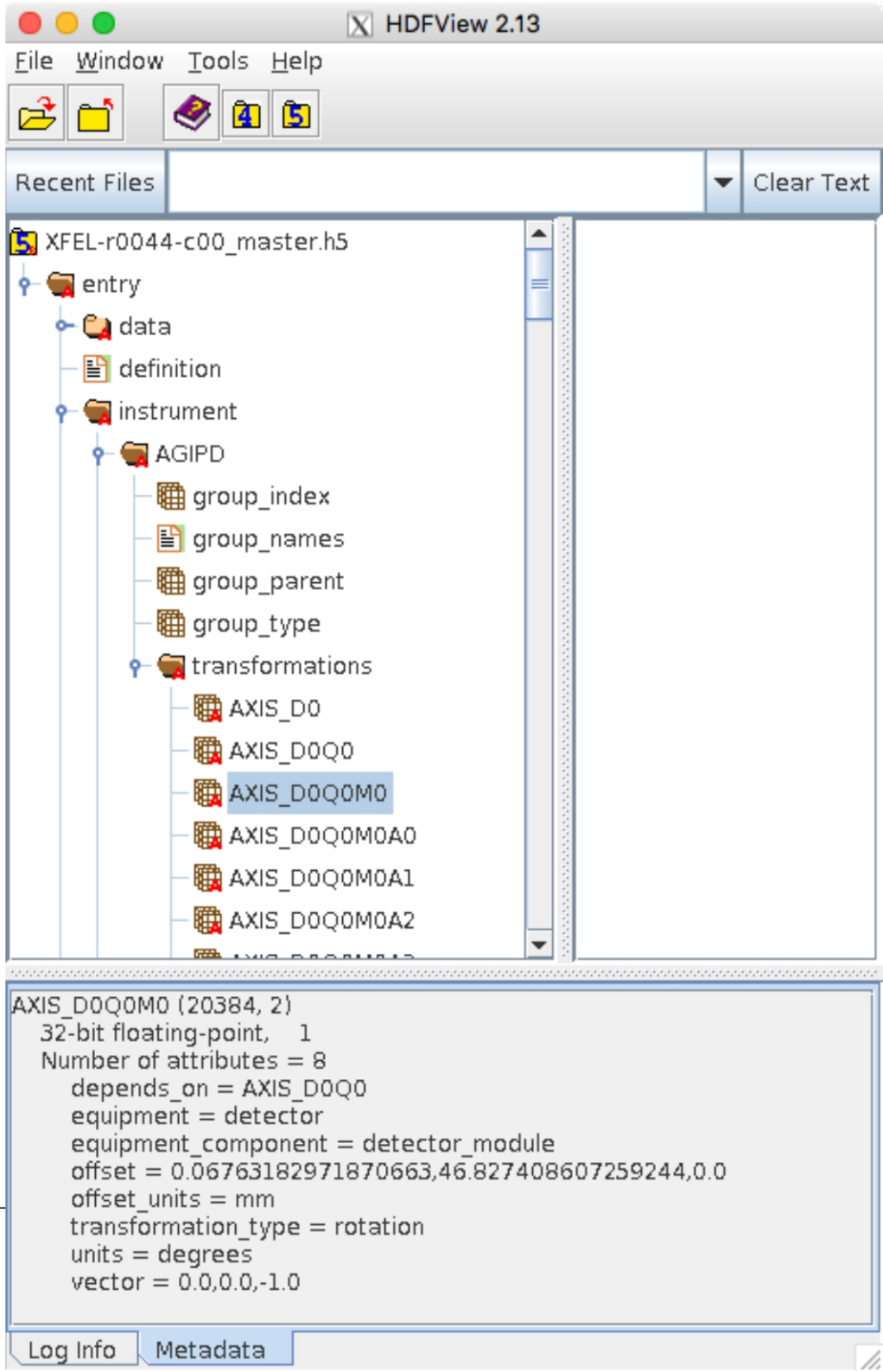
FAIR using NeXus





Bernstein, H. J., Forster, A., *et. al.* Gold Standard for macromolecular crystallography diffraction data (2020). IUCrJ 7, 784-792.

Full automated pipeline

- Spotfind/Index
- Joint refinement/integrate
- Scale/postrefine
- Merge
- Phenix.refine
- Upload to google drive

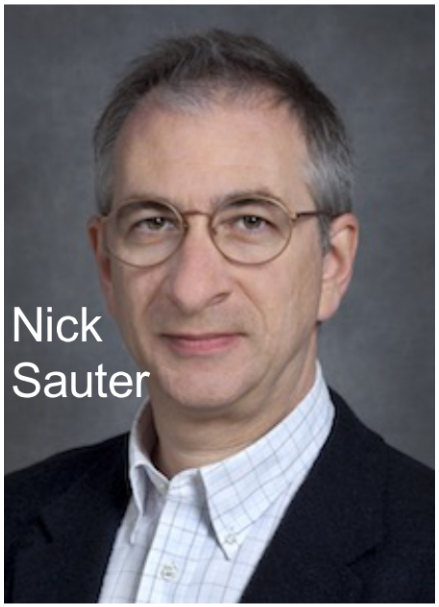
Ready to scale up to even higher rep-rate XFELs coming online

Deployment: every XFEL

	LCLS	SACLA	PAL-XFEL	SwissFEL	EuXFEL
Location	Stanford, CA USA	Harima, Japan	Pohang, South Korea	Aargau, Switzerland	Schenefeld, Germany
Computing	NERSC or SDF	Local	KISTI	PSI	Maxwell
Detectors	CSPAD, ePix, Jungfrau, Rayonix	Octal-8 MPCCD, Rayonix	Rayonix	Jungfrau 16M	AGIPD

Supports LSF, SGE, Slurm, HTCondor, Docker/Shifter
New use of GUI: DLS beamline I24 (Pilatus3 6M)
Example of a current result: LCLS + NERSC, 5 minute turnaround for fully merged dataset

XFEL @ LBL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Andrea Schmidt
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Patrick Scheerer

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Nat Echols
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Oliver Zeldin
Sheraz Gul
Robert Bolotovsky
Kyle D. Sutherlin

IBS
Jacques-Philippe Colletier

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Zoom background: "Black Lotus" from Magic the Gathering

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References

Brewster AS, et. al (2019): Processing serial crystallographic data from XFELs or synchrotrons using the *cctbx.xfel* GUI. *Computational Crystallography Newsletter* **10**, 22-39.

http://www.phenix-online.org/newsletter

Bernstein, H. J., *et. al*. (2020). Gold Standard for macromolecular crystallography diffraction data. IUCrJ **7**, 784-792.

Blaschke JP, *et al.* (2021) Real-Time XFEL Data Analysis at SLAC and NERSC: a Trial Run of Nascent Exascale Experimental Data Analysis. Preprint. ArXiv. 2021;arXiv:2106.11469v1.

http://cci.lbl.gov/xfel

http://dials.github.io