Real-time pre-processing for serial crystallography

Jérôme Kieffer [1], Nicolas Coquelle [1], Gianluca Santoni [1], Shibom Basu [2], Samuel Debionne [1], Alejandro Homs [1], Andy Götz [1], Daniele De Sanctis [1].

[1]ESRF - Grenoble (France), [2]EMBL - Grenoble (France)

STREAMLINE has received funding from the European Union’s Horizon 2020 research and innovation prog. under grant agreement No. 870313.

Outline

- Serial crystallography at the ESRF ID29 beamline
- Image analysis for single crystal frames
- Lossy data compression
- Peak-finding
- Conclusions

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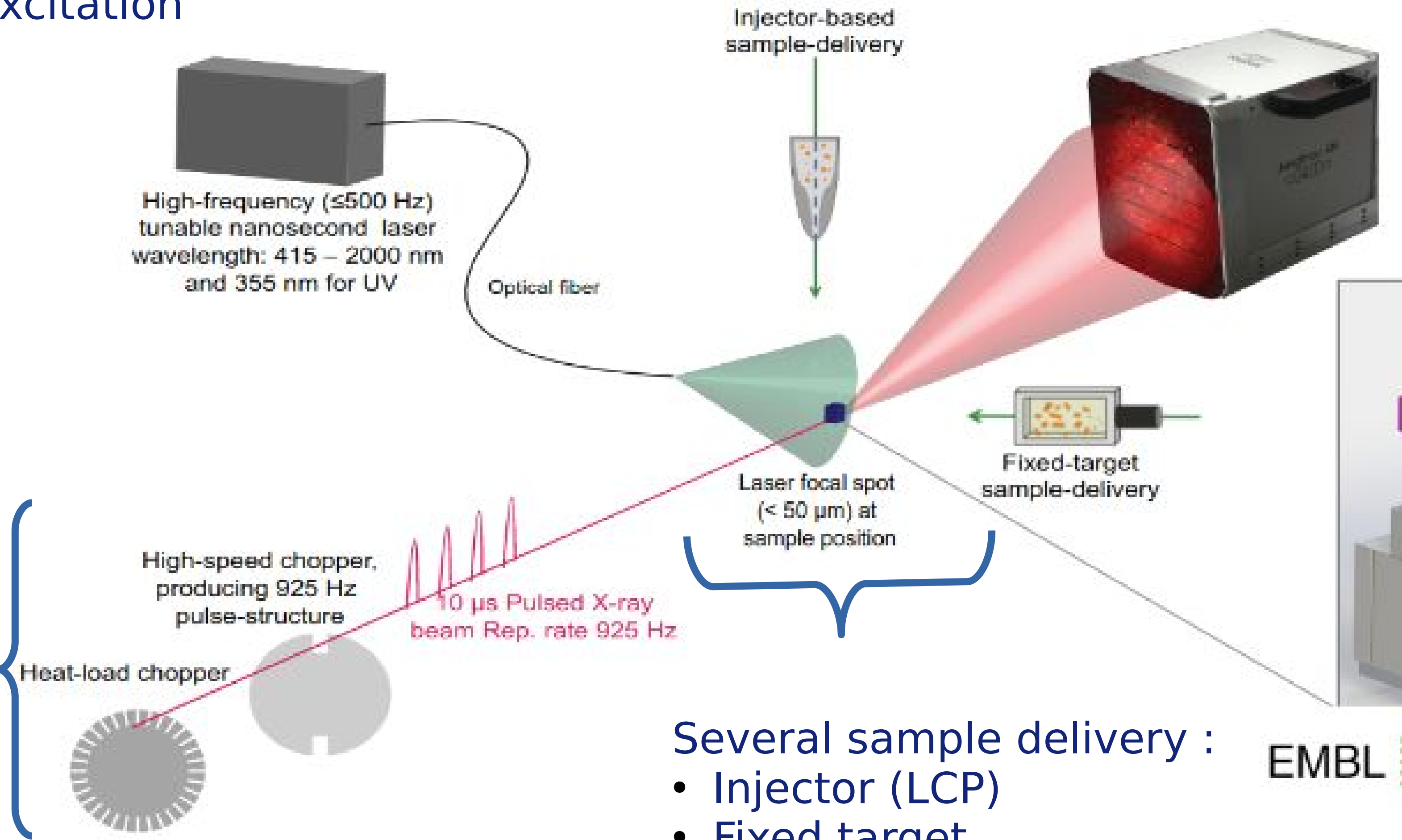
Synchrotron serial crystallography

Synchronous laser excitation

Fast detector



Choppers produce a train of pulses at 1 kHz synchronized with synchrotron pulses

Several sample delivery :

- Injector (LCP)
- Fixed target
- Micro-fluidic
- …

Credit: Julien Orlans

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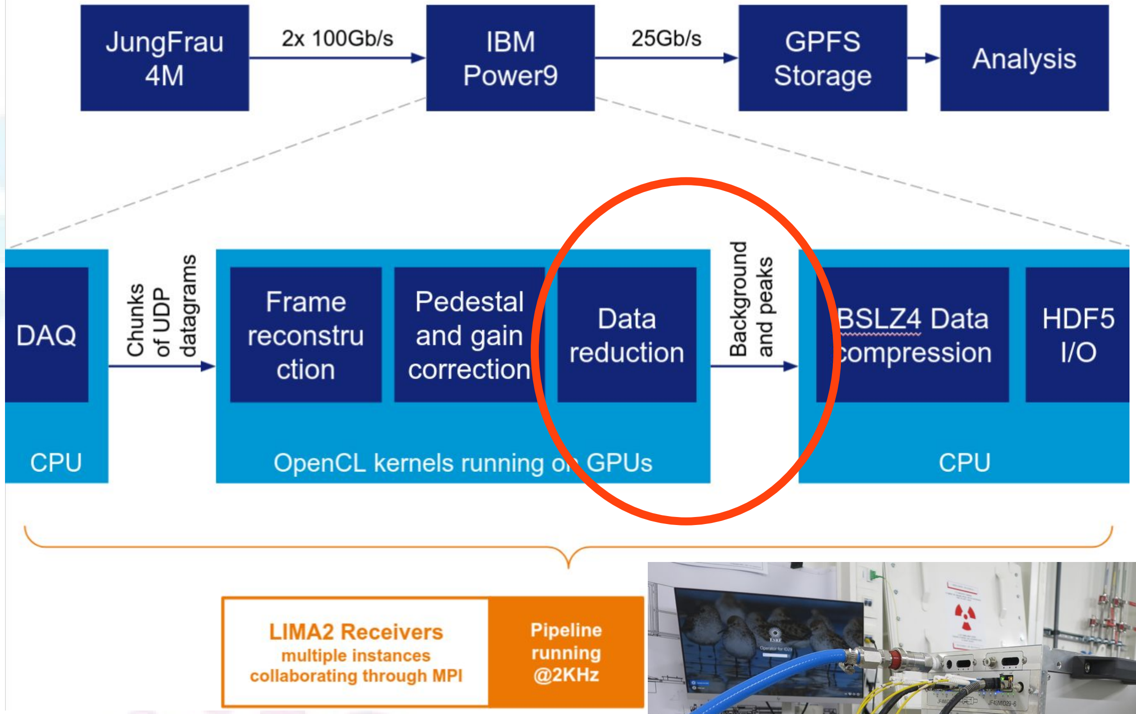
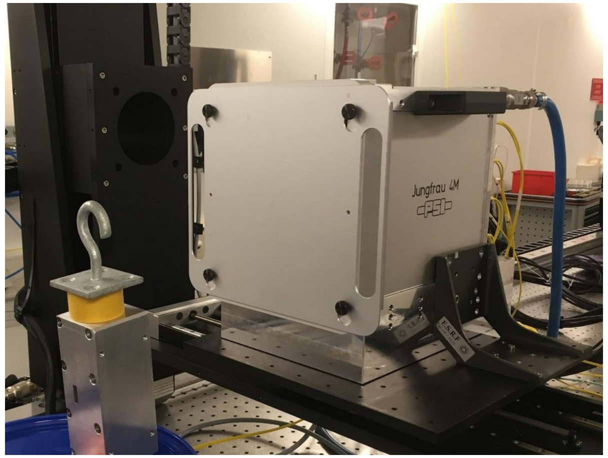
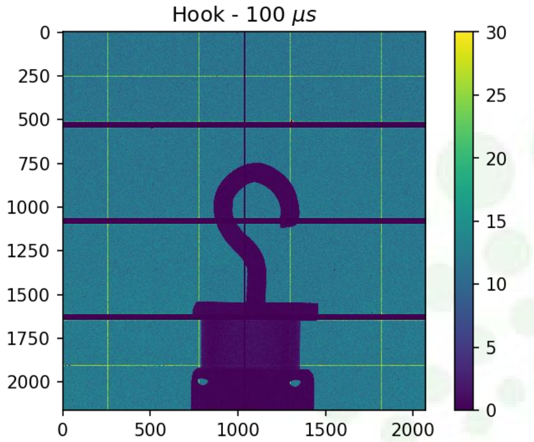
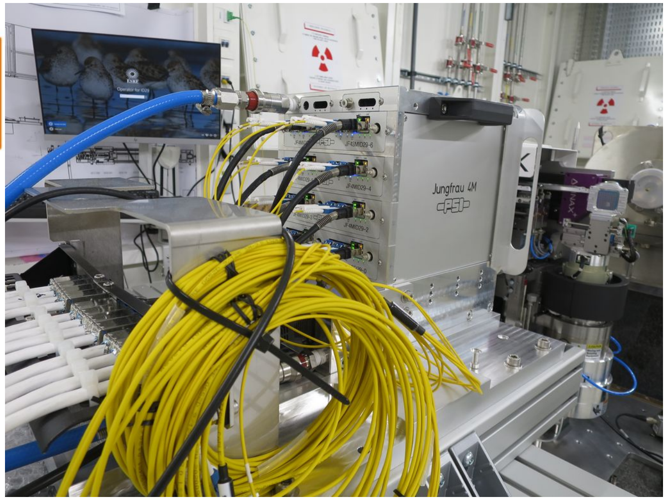
Lima2 controls the Jungfrau 4M detector

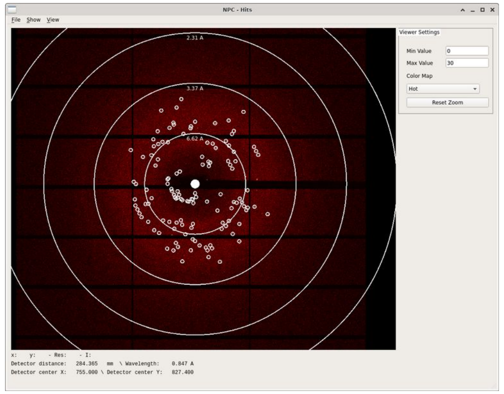


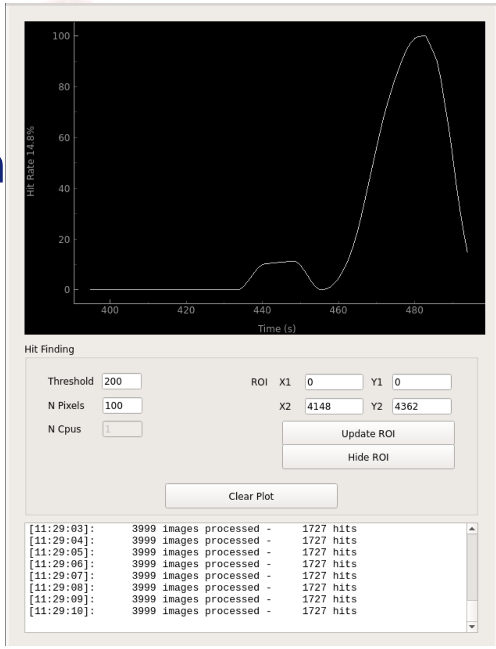






NanoPeakCell:
Live feedback of peak position during acquisition





Debionne, S., Homs, A., Claustre, L., Kieffer, J., De Sanctis, D., Santoni, G., Goetz, A. & Meyer, J. (2022). In Proceedings of the 14 th international conference on Synchrotron Radiation Instrumentation (SRI2021). https://indico.desy.de/event/27430/abstracts/

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Online processing for serial crystallography

- Integration
- Indexing ← Most difficult
- Peak-finding
- Intense pixel saving

  } This contribution
- Veto algorithm
  - Leonarsky & al. Struct.Dyn. 7, 014305 (2020)
- Image reconstruction
  - Debionne & al., SRI2021
- Dump data to disk

Holton J. M., see https://bl831.als.lbl.gov/~jamesh/lossy_compression/

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Separation of background from peaks

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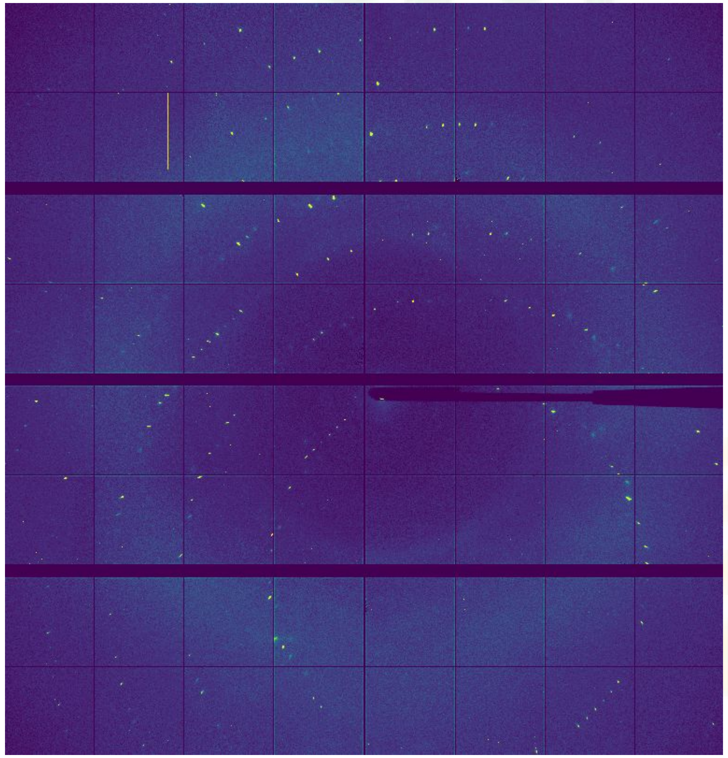

First diffraction image obtained at the ID29

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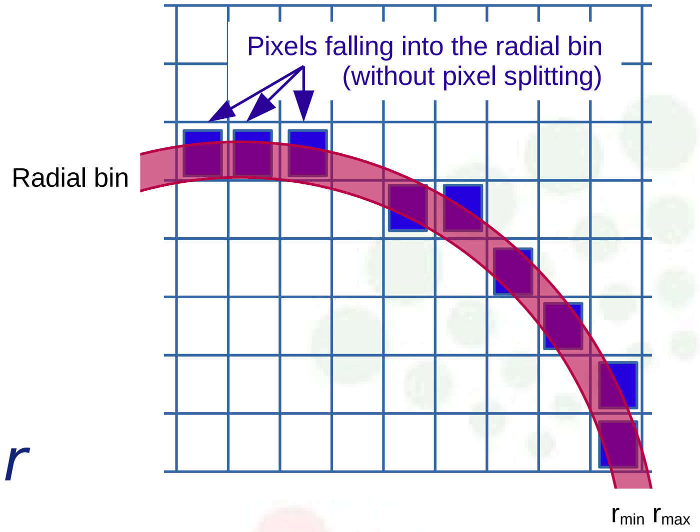
Average pixels along Debye-Scherrer rings

- Pixel intensity needs to be corrected:

$$I_{cor} = \frac{I_{raw} - I_{dark}}{F \cdot \Omega \cdot P \cdot A \cdot I_0} = \frac{signal}{normalization}$$



- Intensity average per ring:
  - Pixel splitting: $c_{i,r}$ is the fraction of pixel *i* in the ring *r*
  - Normalization issue due to polarization, …

→ this is a weighted average: implemented in pyFAI

$$\overline{I_r} = \frac{\sum_{i \in bin_r} c_{i,r} \cdot signal_i}{\sum_{i \in bin_r} c_{i,r} \cdot normalization_i} = \frac{V_{bin_r}}{\Omega_{bin_r}}$$

- Use of accumulators:
  - Simplifies notation
  - Suitable for parallel reduction

$$V = \sum \omega \cdot v = \sum c \cdot signal$$

$$\Omega = \sum \omega = \sum c \cdot normalization$$

$$\Omega\Omega = \sum \omega^2 = \sum c^2 \cdot normalization^2$$

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Uncertainties in azimuthal integration (1)

- Uncertainties on the average value
  - Called *sem* and reported by pyFAI
  - Not of interest for background evaluation

$$\sigma(\overline{I}_r)=\frac{\sqrt{\sum_{i\in bin_r} c_i^2\cdot variance_i}}{\sum_{i\in bin_r} c_i\cdot normalization_i}=\frac{\sqrt{VV_r}}{\Omega_r}$$

- Uncertainties on pixel value
  - Called *std* and larger than *sem by a factor √N*

$$\sigma(I_r)=\sqrt{\frac{\sum_{i\in bin_r} c_i^2\cdot variance_i}{\sum_{i\in bin_r} c_i^2\cdot normalization_i^2}}=\sqrt{\frac{VV_r}{\Omega\Omega_r}}$$

- Poisson error model:
  - For all pixels belonging to a common distribution:

    variance = <signal>
  - Usually simplified in:

$$\begin{cases} variance_i=signal_i \\ VV=\sum c^2\cdot signal \end{cases}$$

$$V=\sum \omega\cdot v=\sum c\cdot signal$$

$$\Omega=\sum \omega=\sum c\cdot normalization$$

$$\Omega\Omega=\sum \omega^2=\sum c^2\cdot normalization^2$$

Erich Schubert and Michael Gertz. 2018.
Numerically Stable Parallel Computation of (Co-)Variance.
SSDBM ’18: 30th Intl. Conf. on Sci, & Statistical DB Mangt.

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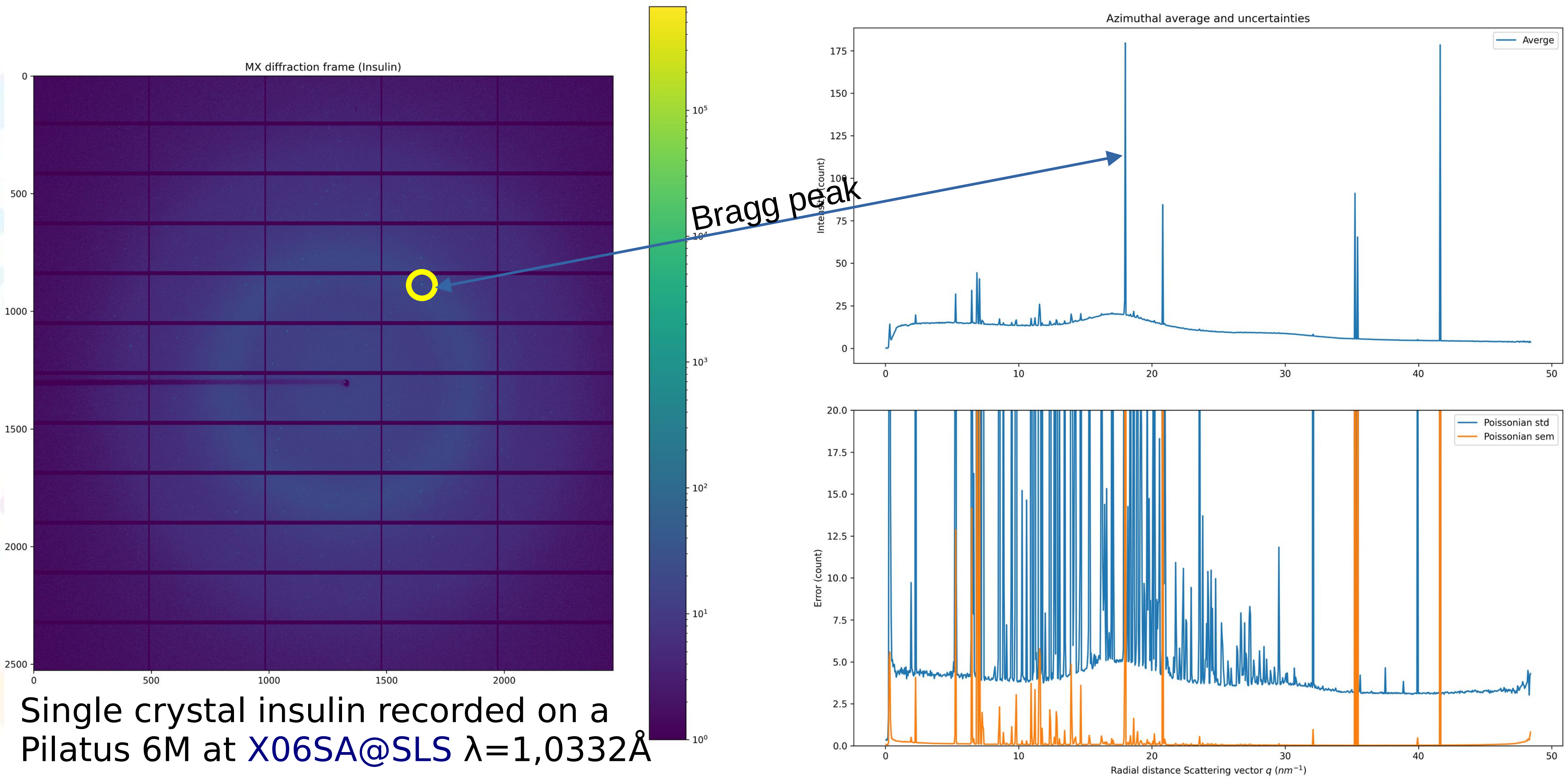
Example on an insulin diffraction frame:



Single crystal insulin recorded on a Pilatus 6M at X06SA@SLS λ=1,0332Å

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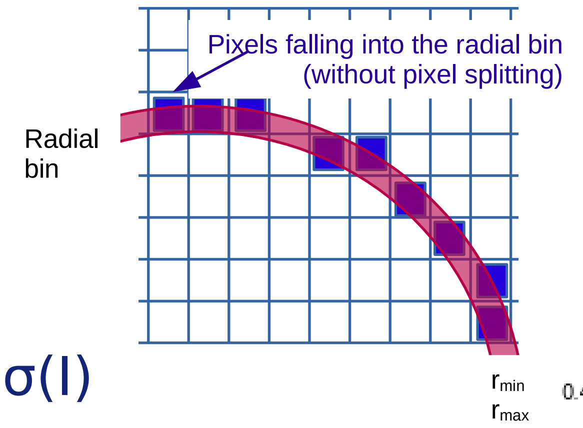
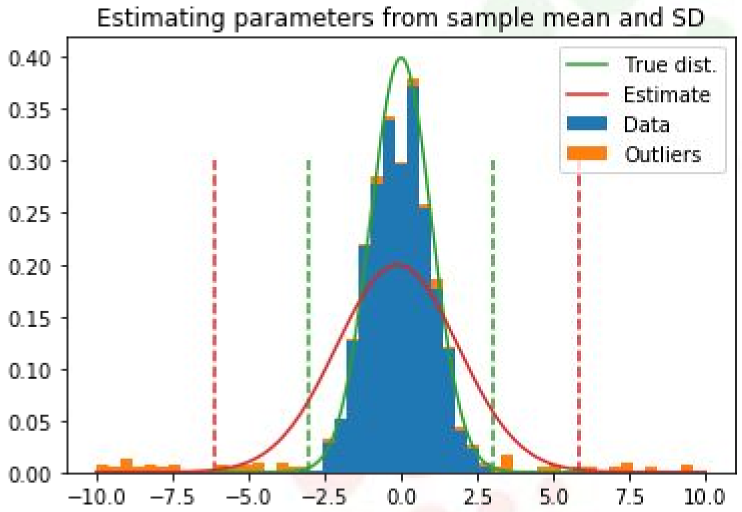
Sigma-clipping



- Iterative algorithm:
  - Integrate to calculate $\bar{I}$ and σ(I)
  - Mask out any pixel with: $|I - \bar{I}| > n \cdot \sigma(I)$
- Removes both tails from the distribution:
- Good approximation of the background
- Number of iterations:
  - 3 to 5 are common
- Cut-off parameter (SNR)
  - Default value provided by Chauvenet:
  - Discard at worse 1 pixel per ring per cycle on a normal distribution
  - Depends on the size, thus on the number of bins: SNR_{clip}=2.7~3.5



$$SNR_{chauvenet} = \sqrt{2\log\left(\frac{N}{\sqrt{2\pi}}\right)}$$

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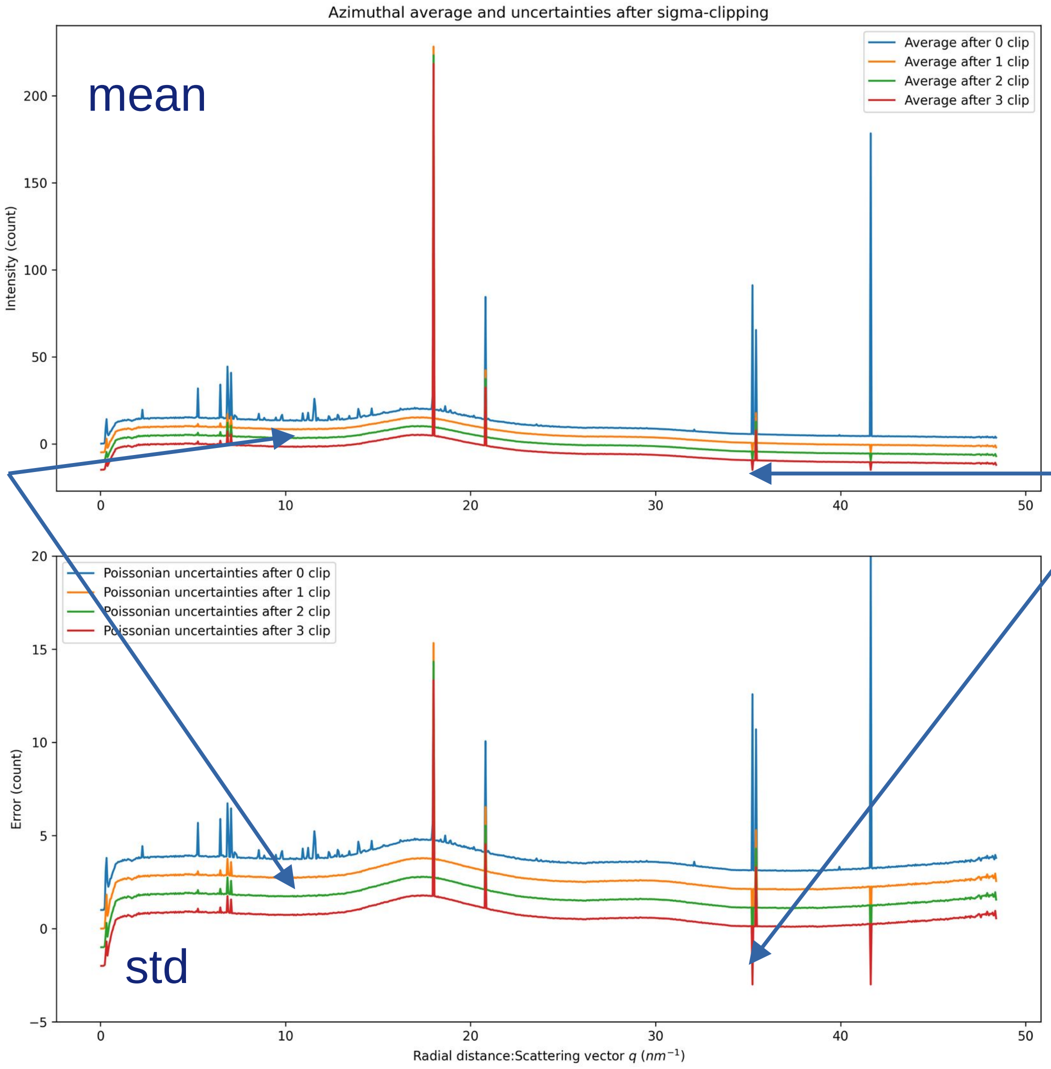
Sigma-clipping with Poisson error-model



Remove most peaks with few cycles

Empty bins results with mean=0 & std=0

Jeopardizes subsequent analysis

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Uncertainties in azimuthal integration (2)

- Limits of the Poisson error model:
  - Requires all pixels in a ring to be from the **same** distribution
  - Thus incompatible with Bragg-peaks!
  - Consider for example a distribution of 2 pixels of value 1 and 99:
    - Mean: 50, std: 10, both pixels are at 5σ –> empty ensemble

- Azimuthal error model:

$$\begin{cases} variance_i = \omega_i^2 \cdot \left(v_i - \overline{v_r}\right)^2 \\ VV = \sum \omega^2 \cdot \left(\frac{signal}{normalization} - \frac{V}{\Omega}\right)^2 \end{cases}$$

  - Single-pass implemented with:

$$VV_{A\cup b} = VV_A + \omega_b^2 \left(v_b - \frac{V_A}{\Omega_A}\right)\left(v_b - \frac{V_{A\cup b}}{\Omega_{A\cup b}}\right)$$

$$V_{A\cup b} = \sum \omega \cdot v = V_A + \omega_b \cdot v_b$$

$$\Omega_{A\cup b} = \sum \omega = \Omega_A + \omega_B$$

$$\Omega\Omega_{A\cup b} = \sum \omega^2 = \Omega\Omega_A + \omega_B^2$$

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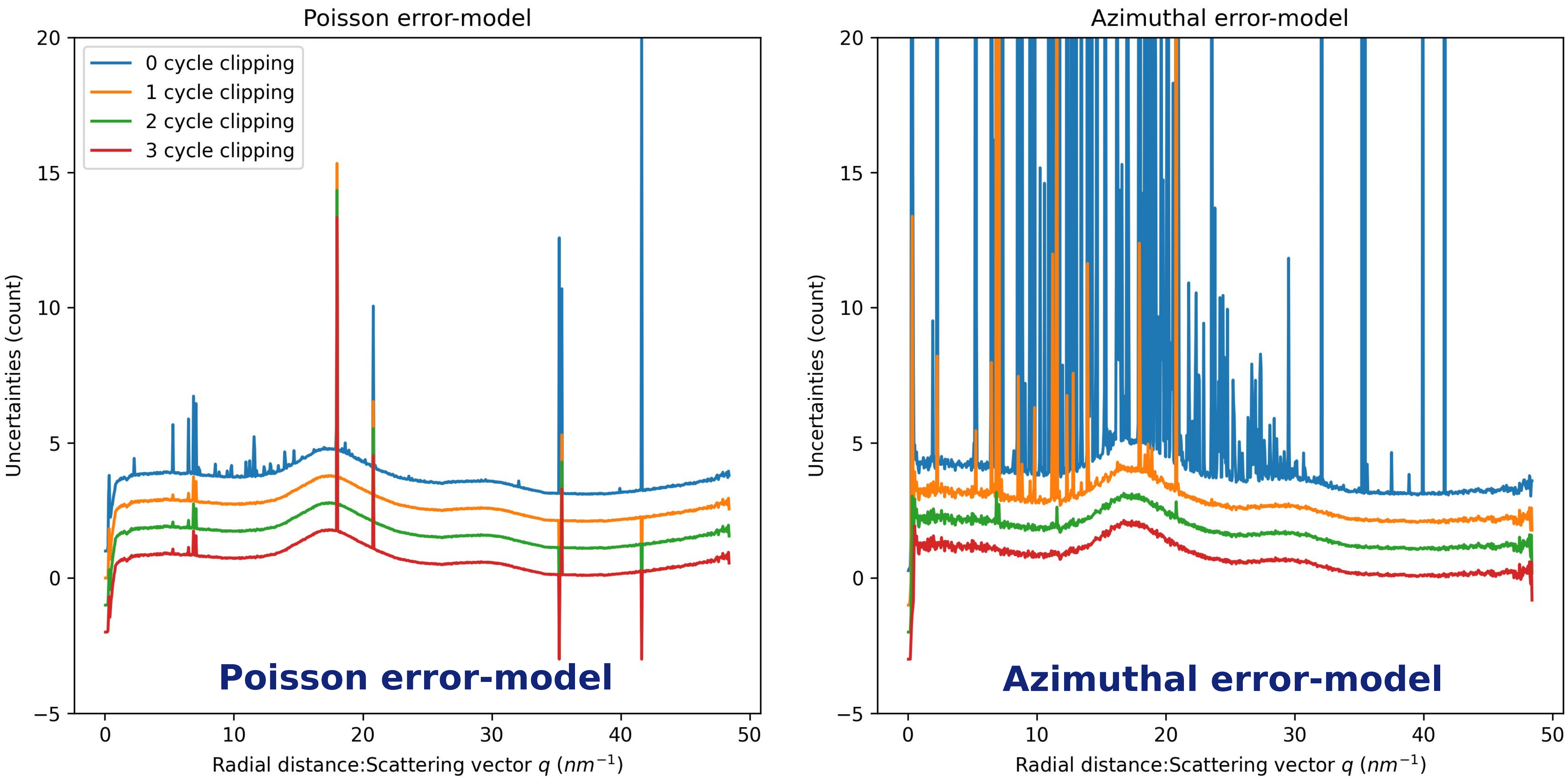
Comparison of error-models for σ-clipping



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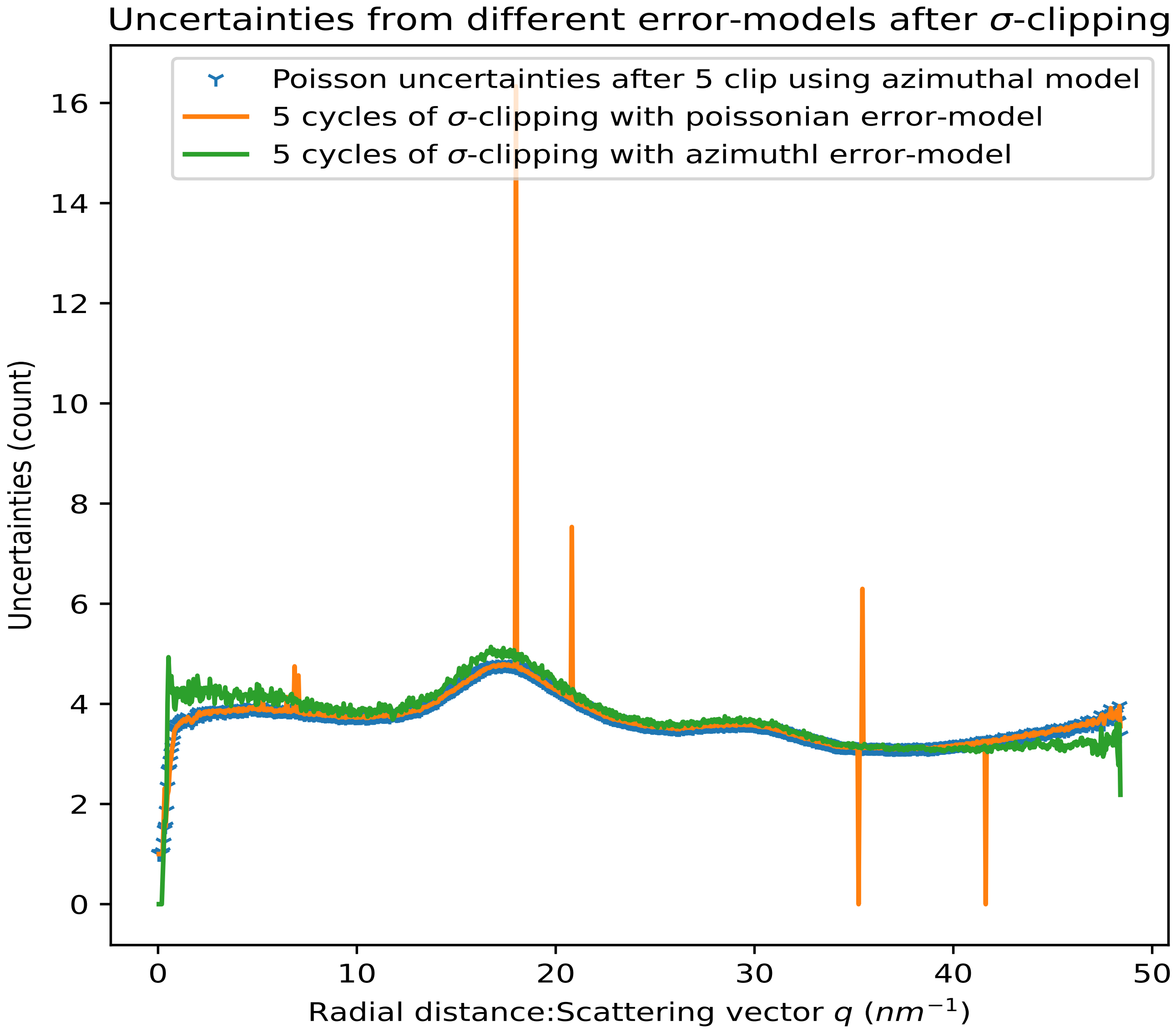
Hybrid error-model:

- Use azimuthal model for σ-clipping
  - Robust to Bragg-peaks
- Use Poisson model for subsequent analysis
  - Less noisy
  - Limits of Poisson when count → 0



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Save only intensity of pixel of interest

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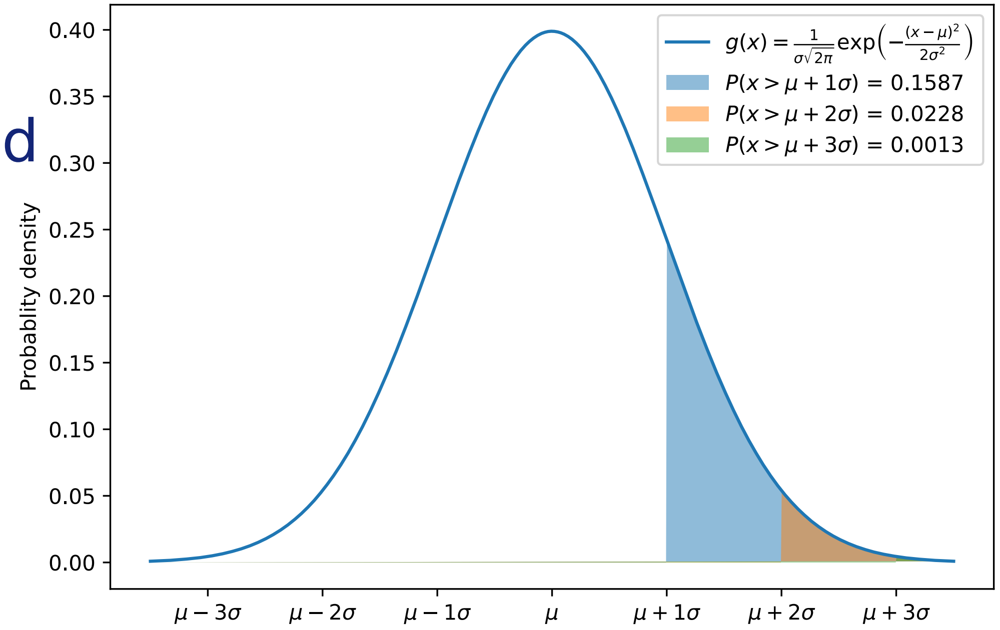
Sparsification: lossy compression

- Sparsification:
  - Store positive outlier with SNR > threshold
  - Record also its position
  - Record background avg (μ) & std (σ)
  - Compression-rate can be estimated assuming a normal distribution
  - Implemented using OpenCL in pyFAI



- Densification:
  - Available as part of FabIO
  - Restores frames with (or without) background noise
  - Implemented in C (GIL-free) + multi-threading

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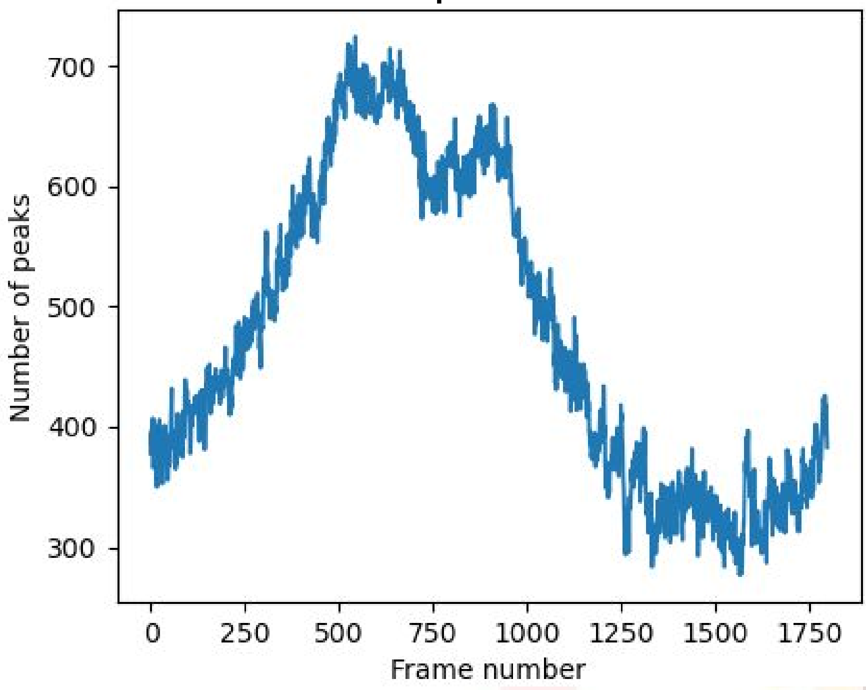
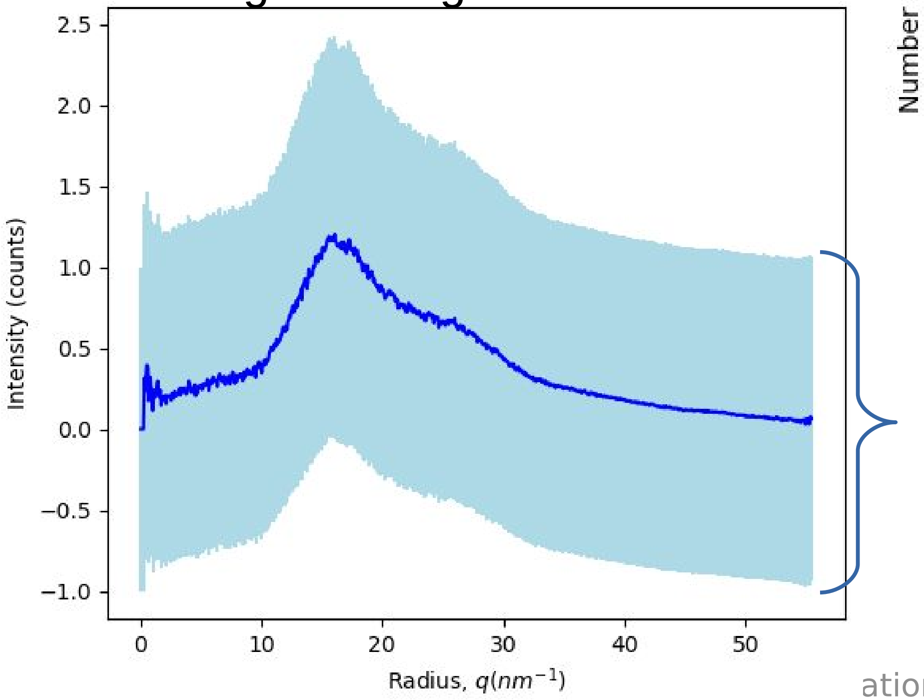
Validation of sparsified dataset:

- Raw dataset: Insulin acquired at SLS with an Eiger4M
- Comparison of quality indicator from XDS
- Sparse data compressed with:
  - Poissonian error-model
  - SNR_{clip}: automatic
  - SNR_{pick}: 1σ
  - SNR_{peak}: 5σ
  - Cycles: 5
  - Bins: 800

Peaks per frame



Background signal/uncertainties



Signal null at large q
→ std tend to 1
→ pixels ≥ 2 get recorded

Performances & quality:

- Compression of a factor: **5x** when cut-of at 1σ
- Compression speed: **250 fps** (GPU)
- Decompression speed: **200 fps** (CPU)
- Limits of the Poisson model at low count rate :μ=0→ σ=1

Indicator	Raw data			Spasified (1σ, poisson) + densified (noise)		
Size	2357 MB			439 MB		
Shell	2.91 Å	2.06 Å	total	2.91 Å	2.06 Å	total
Completeness	99.8 %	93.7 %	92.9%	99.8 %	94.1 %	93.2 %
R_{obs}	9.8 %	56.9 %	12.4%	8.9 %	67.8 %	11.0 %
R_{exp}	8.7 %	73.7 %	14.7%	8.0 %	85.6 %	12.0 %
R_{meas}	10.3 %	60.8 %	13.1%	9.3 %	72.6 %	11.6 %
$CC_{1/2}$	99.7	94.6	99.7	99.7	94.4	99.8
I/σ	25.86	5.38	10.54	26.85	3.70	10.14

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Peak finding algorithm on a diffraction frame

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Layout of the peak-picking algorithm:

- Subtract background intensity (from σ-clipping)
  - Clip to 0 negative values. Those are all discarded.
- Pixel is a peak if:
  - Maximum within the local neighborhood (3x3 or 5x5)
  - Subtracted signal is greater than a picking threshold (SNR_{pick})
  - At least 2 or 3 other pixels in the neighborhood meet the SNR_{pick} criteria
- Then:
  - Sum subtracted intensities on the neighborhood (+ uncertainties propagation)
  - Calculate the center of mass of the peak
- Implemented on GPU using OpenCL
  - Same execution time as sparsification

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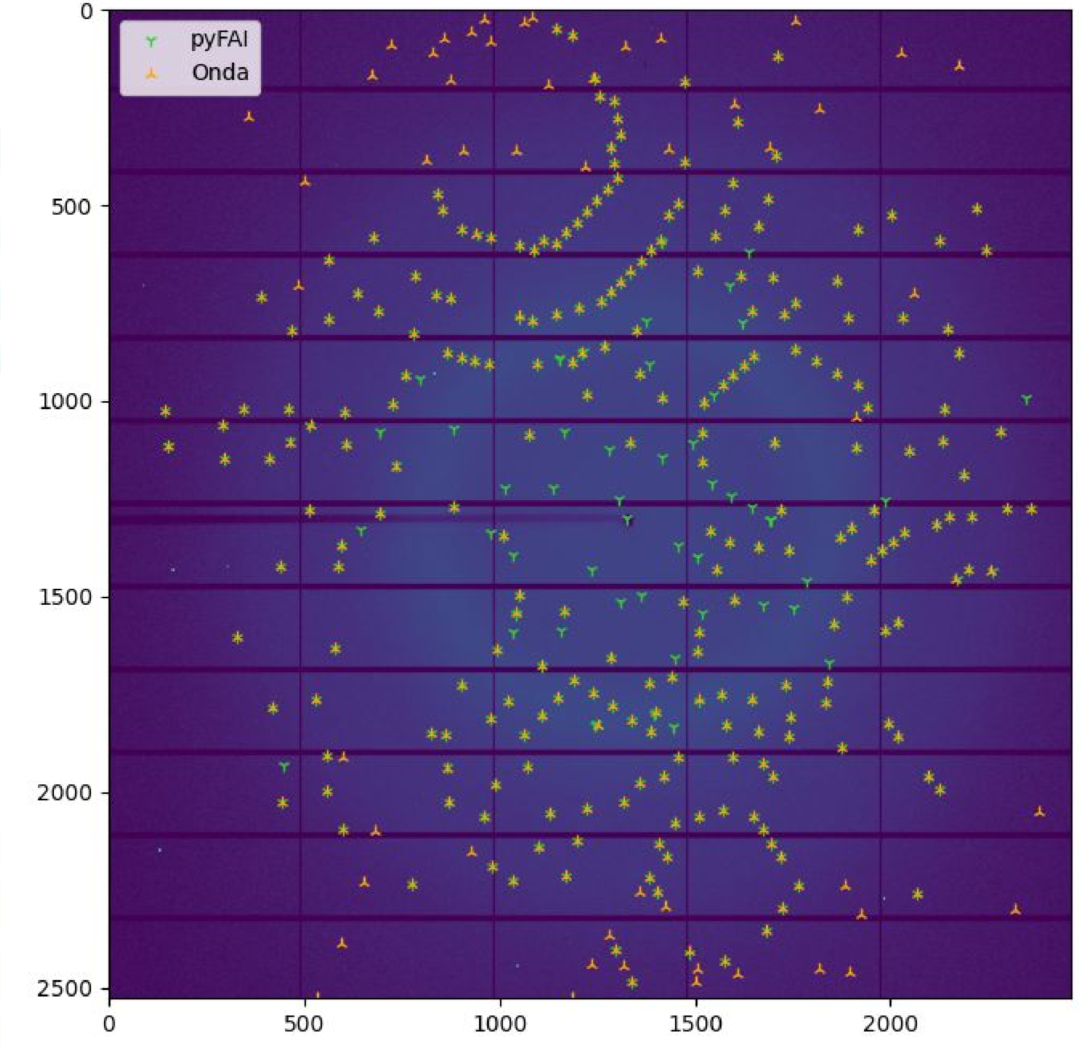
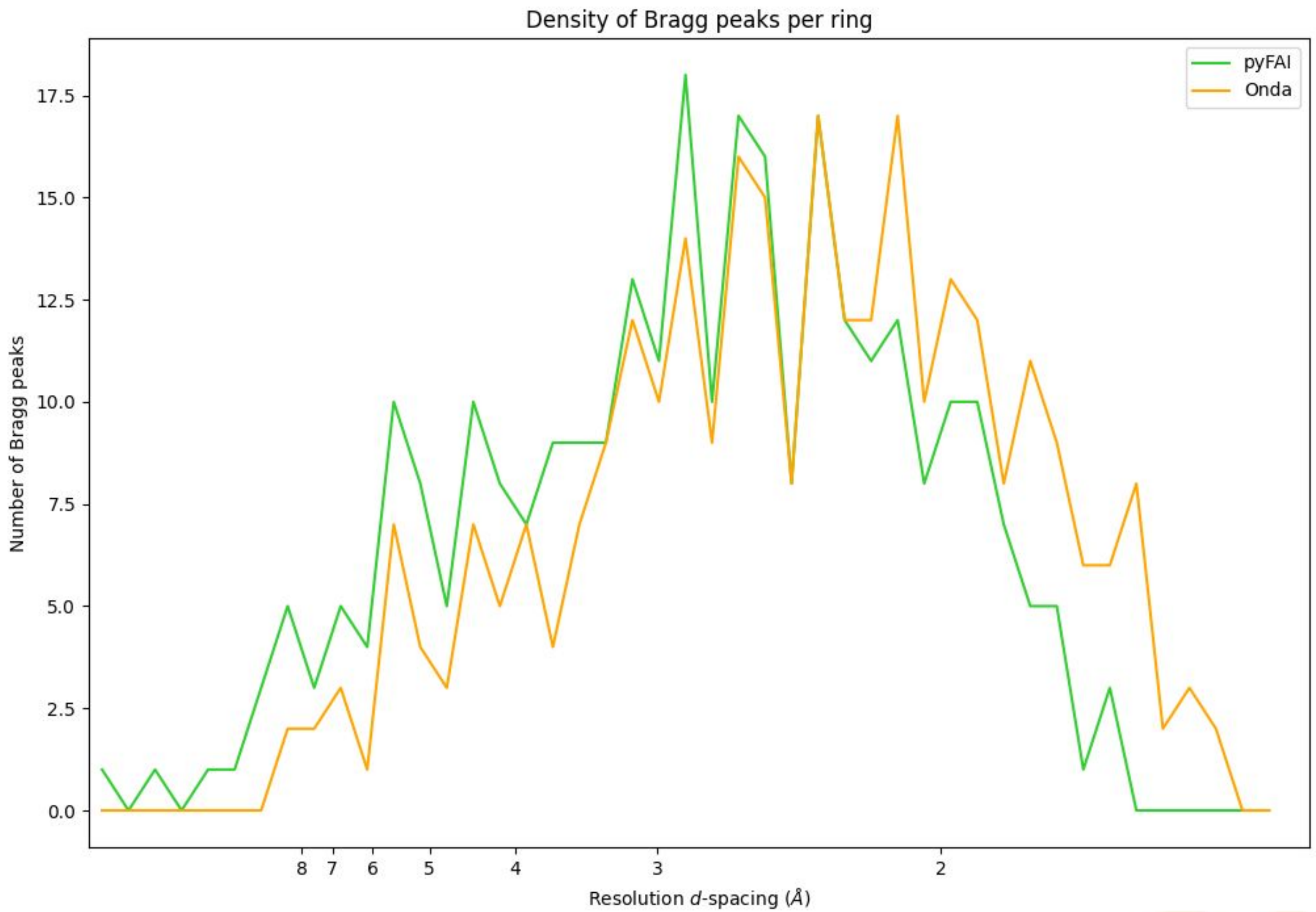
Comparison with PeakFinder8





OnDA : Mariani, V et al. J. Appl. Cryst. 49, 1073-1080 (2016).

Cheetah: Barty, A. et al., J. Appl. Crystallogr. 47, 1118–1131 (2014).

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Indexation with CrystFEL / XGANDALF

Indexer :	XGANDALF		XGANDALF-Fast	
Peak-picker	Indexation rate	Run-time	Indexation rate	Run-time
Zaef	10 %	2178 s	10 %	430 s
PeakFinder8	49.5 %	10397 s	48.5 %	1757 s
PeakFinder9	44.2 %	8328 s	43.5 %	1436 s
Robust PeakFinder	22.4 %	6314 s	21.2 %	1628 s
PyFAI peakfinder	50.2 %	9325 s	50.0 %	1595 s

1000 micro-crystal from HEWL Lysozyme collected on an Eiger 4M at ESRF-ID30a3

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Conclusion

- Separation of Bragg-peaks from amorphous background using σ-clipping
  - Several error-models: Poisson, azimuthal and hybrid
  - Performance critical section for all algorithms (~3-4 ms for 4 Mpix)
- Sparse & lossy data compression for single crystal diffraction
  - Compression rate 5-100x (tuneable thanks to SNR_{pick})
  - Compression speed: 250 fps, single GPU stream
  - Decompression on CPU with background reconstruction
  - Data quality validated with XDS reduction software
- Peak-finder
  - Similar in many point to the PeakFiner8 from Cheetah (Barty, 2014)
  - Implemented on GPU @ 250 fps
  - Peak-position validated by indexing with CrystFEL

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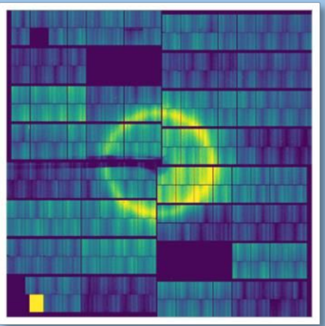
Outlook

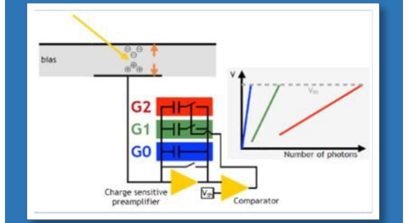
- Modify CrystFEL to be able to read sparse-frames
- Implement it online at 1kHz within LImA2 (needs 4 GPUs in //)

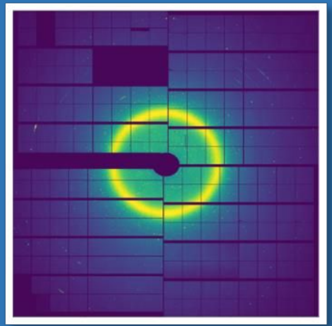
Image Reconstruction



UDP packets data from detector are geometrically assembled (CPU)

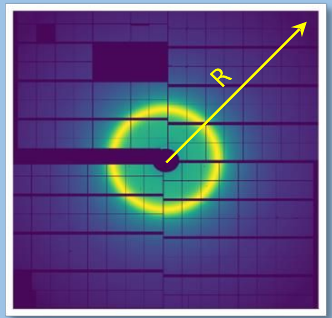
Background and Gain Corrections

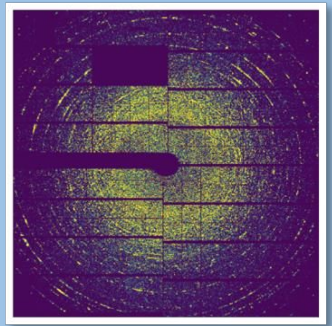




Per pixel & per frame gain selection: 3 pedestal + 3 gain maps

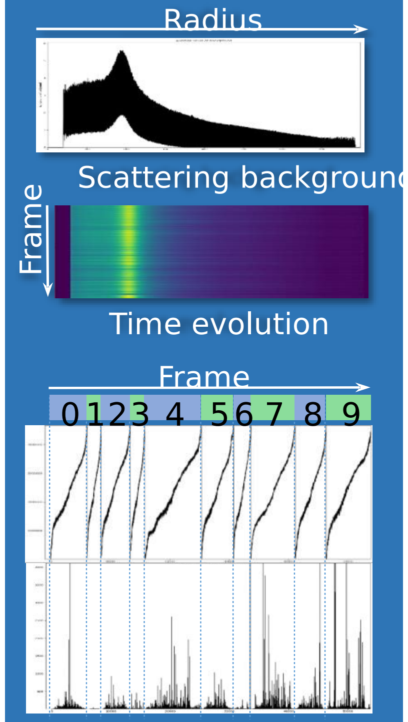
pyFAI-based Data Reduction





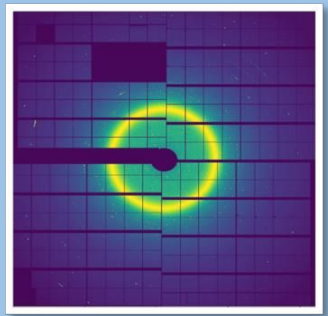
Peak finding and background extraction using Sigma Clipping

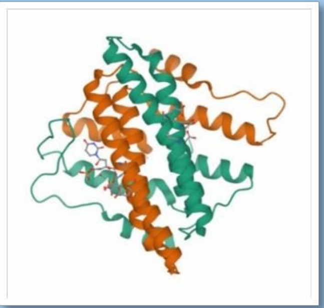
Sparse Data Saving



Peak pixel position & intensity per frame (CSR)

Offline re-densification





Performed to feed SMX data processing software

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