DECTRIS®

detecting the future

Optimizing data quality with Hybrid Photon Counting detectors

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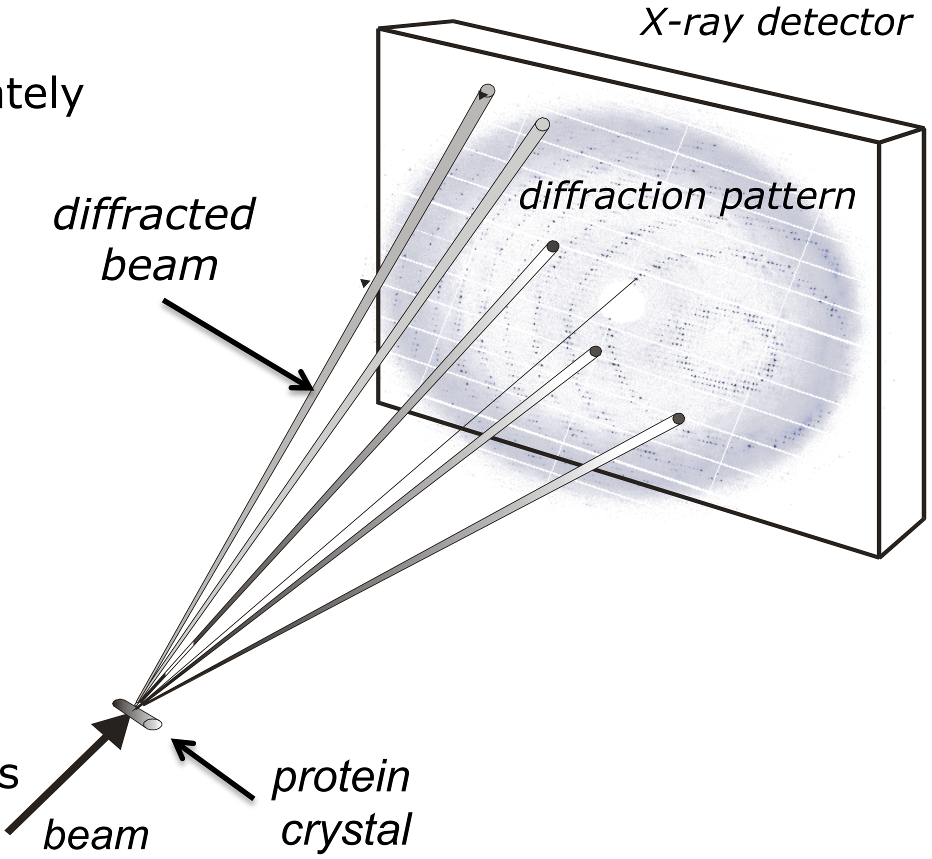
Outline

- ***Characteristics of HPC detectors***
- ***Data collection – best practice***
  - *Accurate data*
  - *Fine φ-slicing*
  - *Anomalous data*
  - *Think about your experiment*

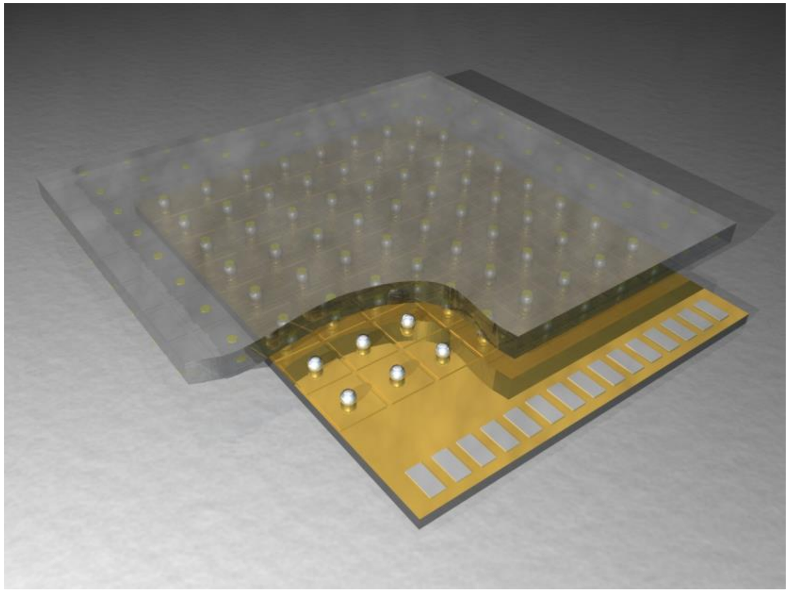
The perfect detector should have

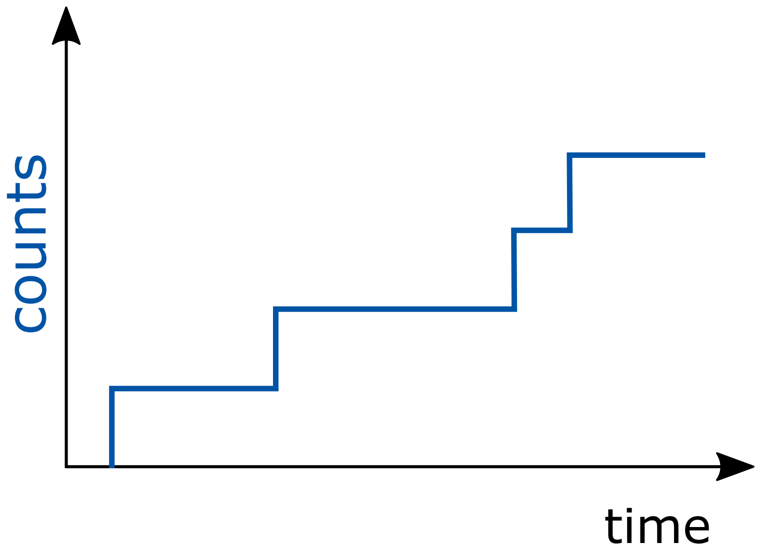
- **High dynamic range**
  Measure weak and strong reflections simultaneously
- **No readout noise**
  Measure weak reflections accurately
- **Uniformity**
  Measure differences accurately
- **High quantum efficiency**
  Minimize dose
- **High spatial resolution**
  Resolve large unit cells
- **High frame rate**
  Continuous rotation collection
- **High count rate**
  Take advantage of bright sources



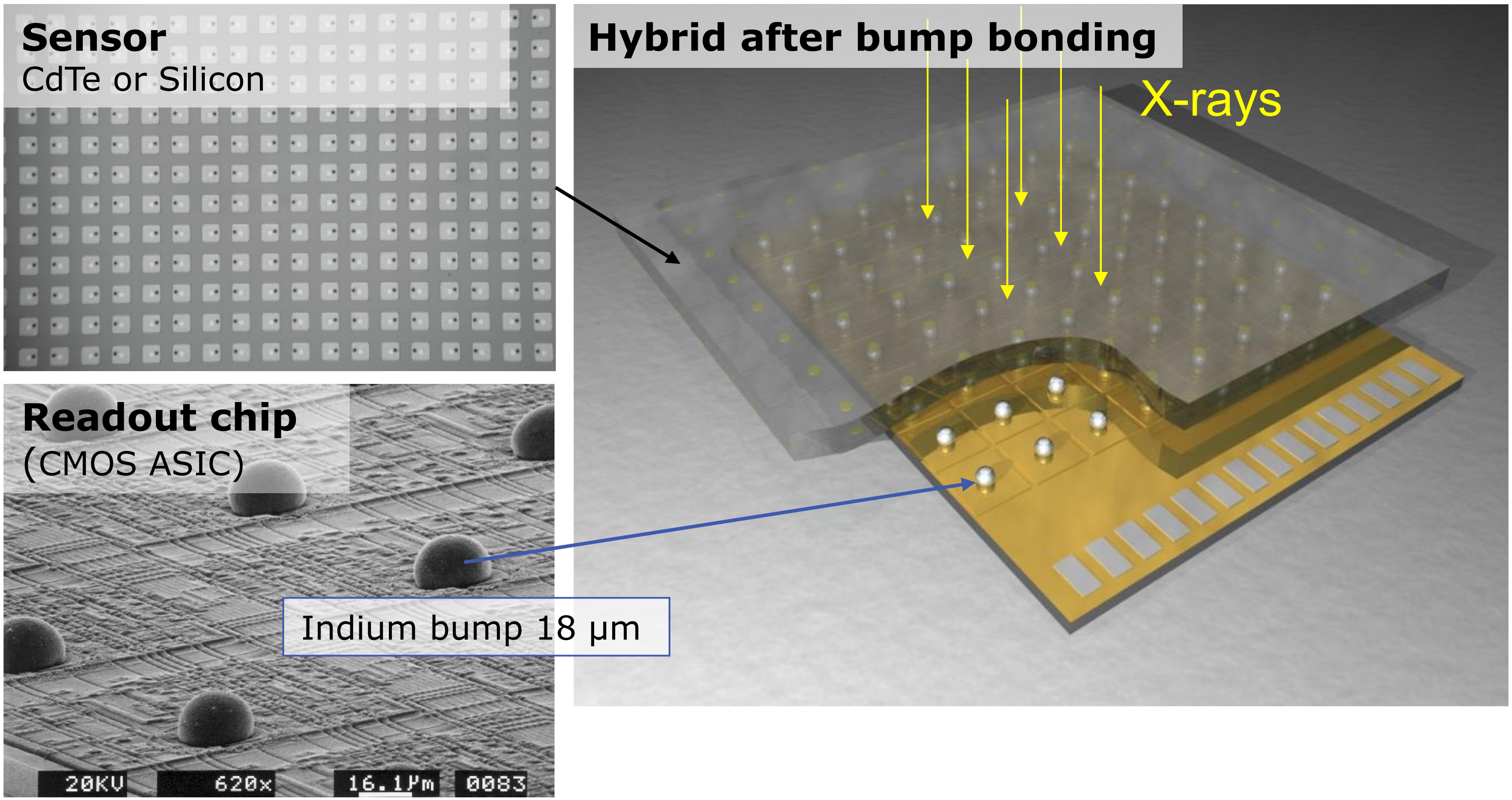
The meaning of HPC counting

Hybrid pixels + single Photon Counting

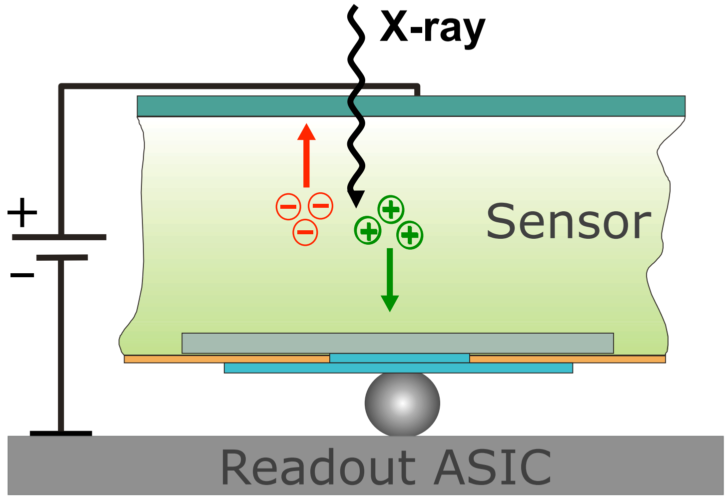




Hybrid pixel = sensor + readout



Direct detection in hybrid pixels



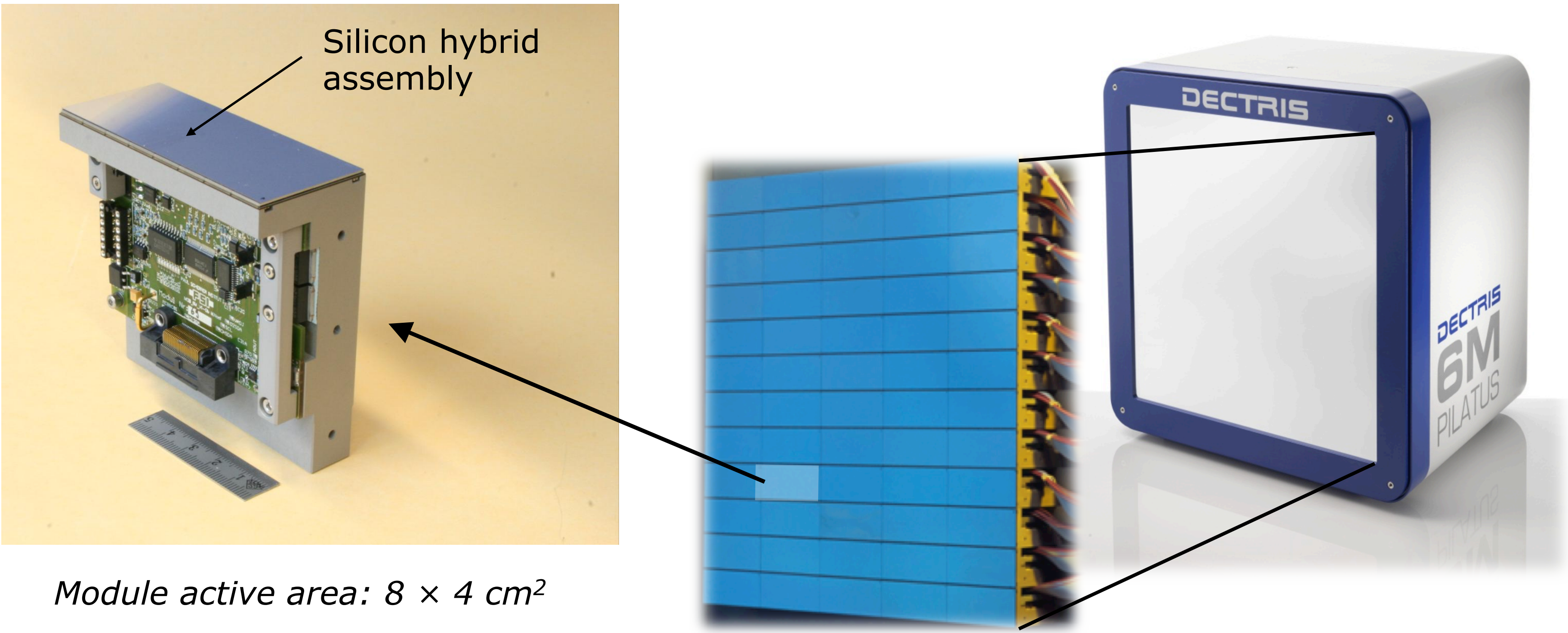
Sensor pixel

– *Direct detection of X-ray photons*
-> one e^-/hole pair per 3.6 eV

Pixel electronics

– *Counting of charge pulses*

Modular assembly of HPC detectors



Module active area: 8 × 4 cm²

100k pixels on PILATUS (172 µm)

500k pixels on EIGER (75 µm)

Superiority of direct detection

Direct detection

X-ray

↓

Electrical signal

Indirect detection

X-ray

↓

Light (Scintillator)

↓

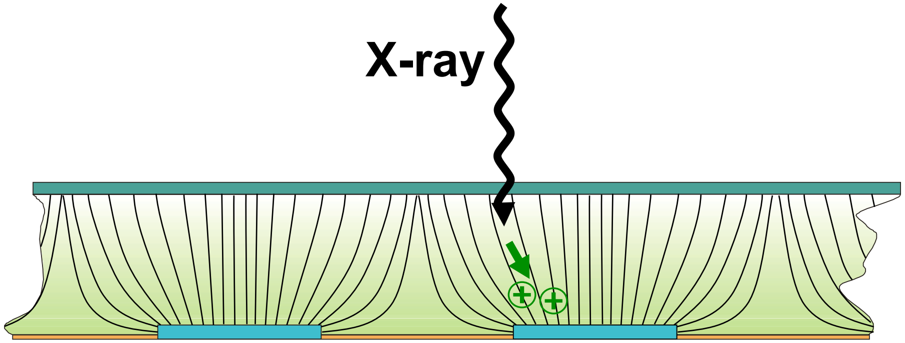
Electron (Photodiode)

↓

Electrical signal

Superiority of direct detection

Direct detection

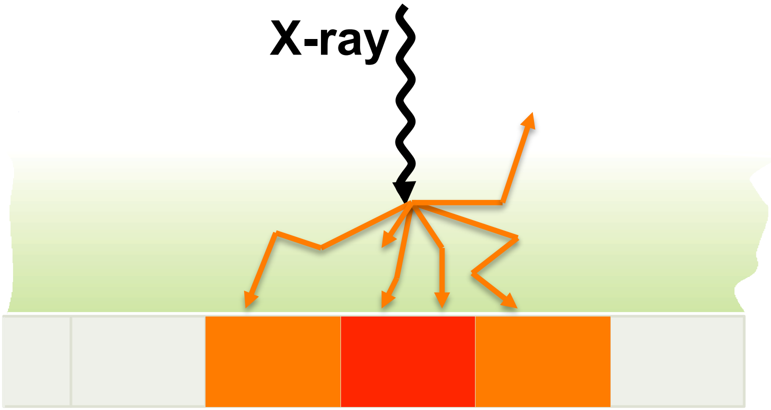


– *Charge captured in electric field*

=> **All photons counted**

=> **Signal remains in pixel**

Indirect detection



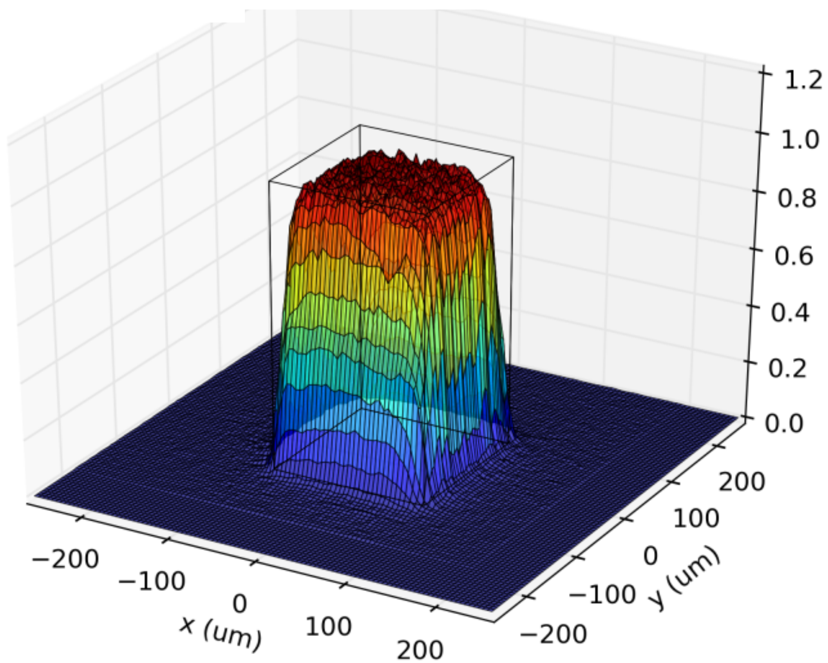
– *Secondary radiation scattered in scintillator*

=> **Signal spread across pixels**

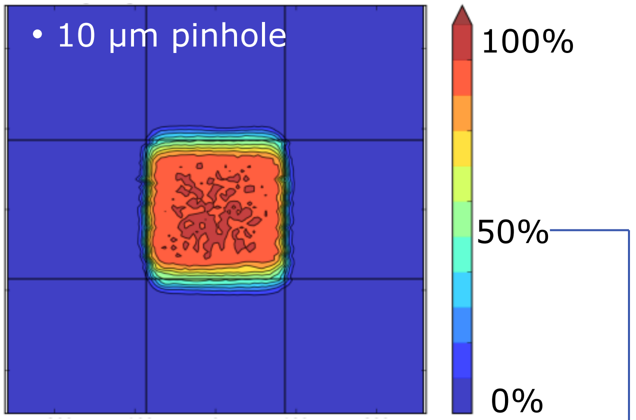
=> **Light partially lost**

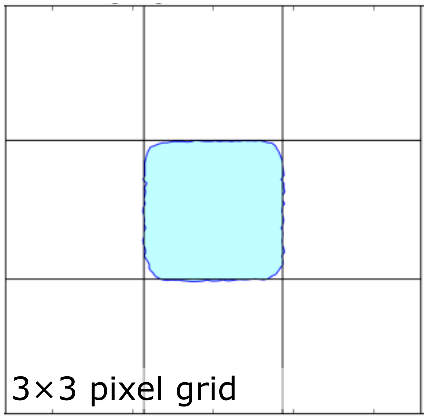
Spatial resolution PILATUS3 CdTe

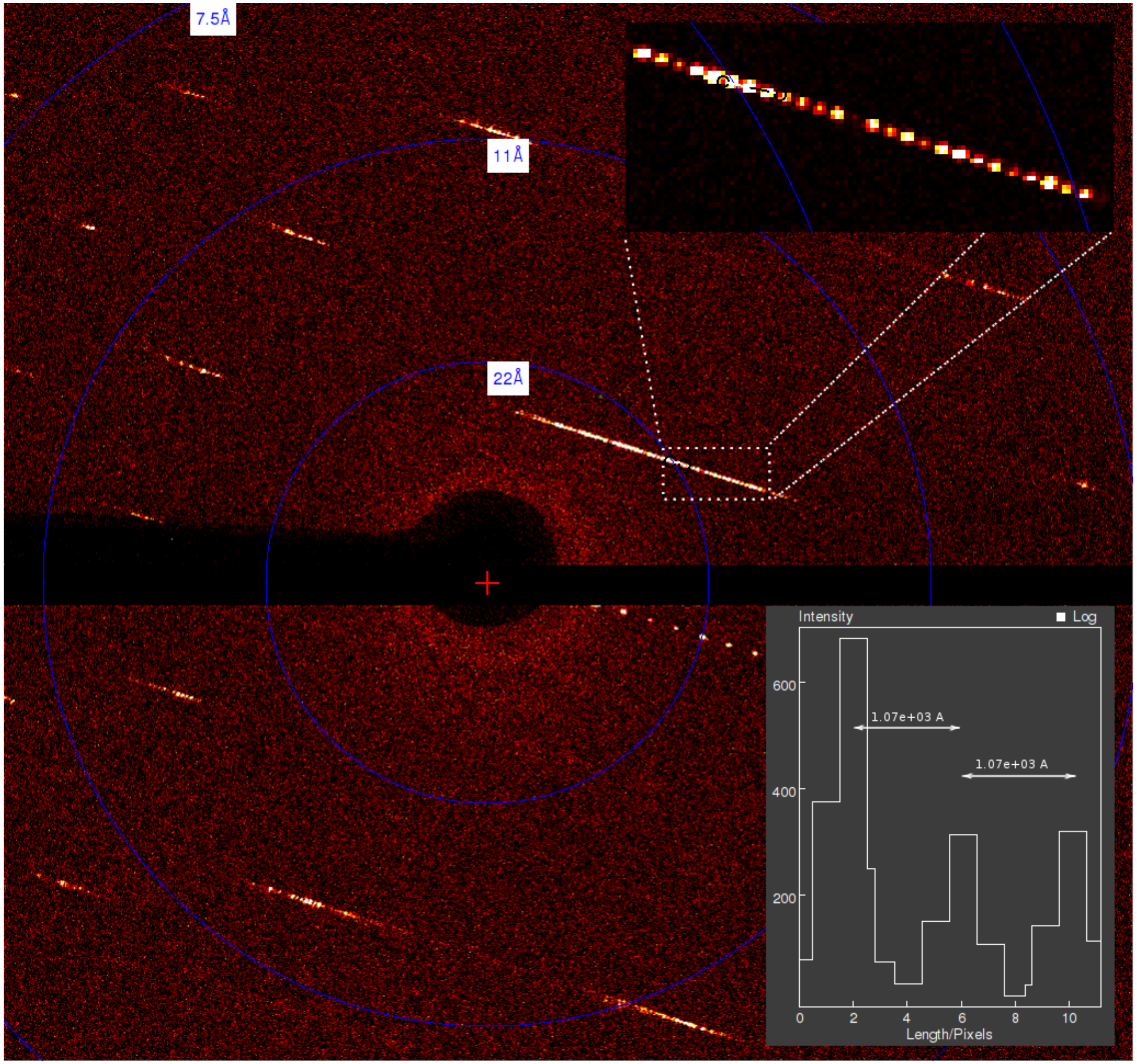
For CdTe as for silicon



10 µm pinhole at Ag Kα wavelength





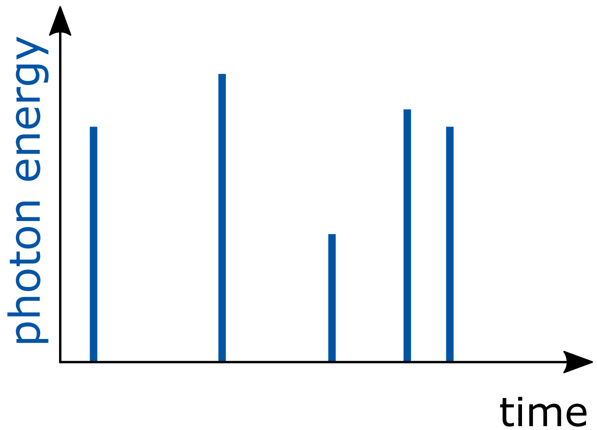


EIGER

Resolution of spots from a 1000 Å unit cell with diffraction to 2.3 Å

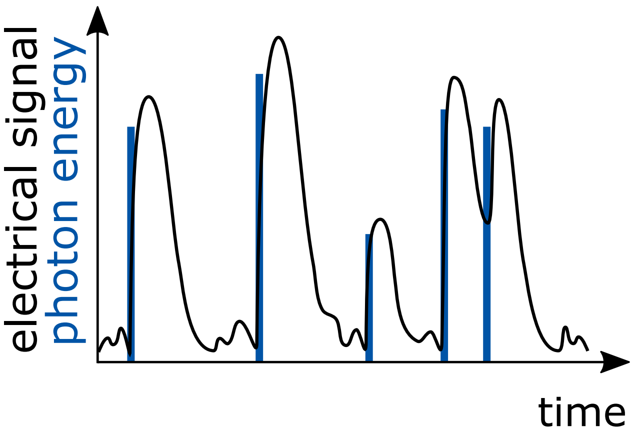
Casanas et al. (2016)

Photon counting – one by one



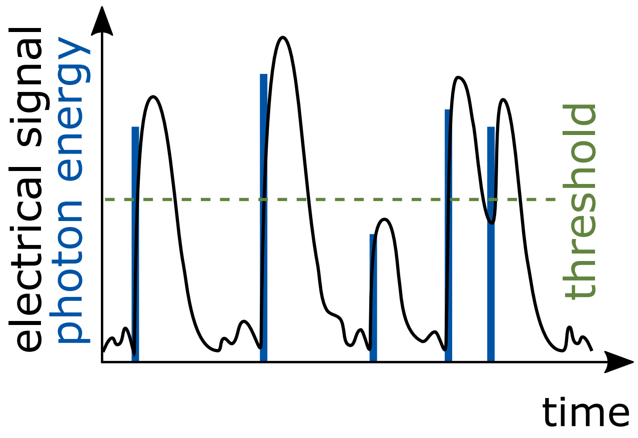
– *Photons absorbed in sensor pixel*

Photon counting – one by one



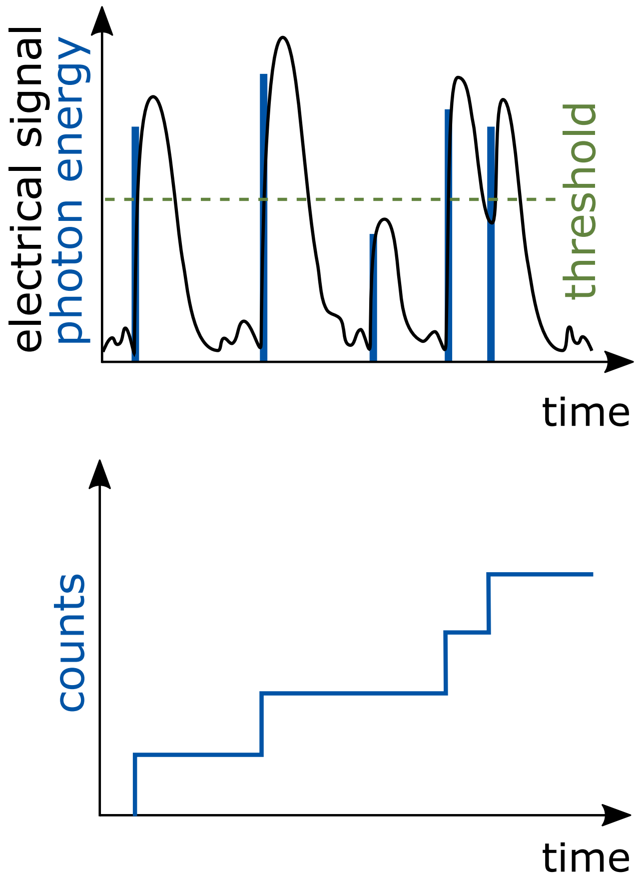
- *Photons absorbed in sensor pixel*
- *Charge pulse proportional to energy*

Photon counting – one by one



- *Photons absorbed in sensor pixel*
- *Charge pulse proportional to energy*
- *Threshold to discard noise*

Photon counting – one by one



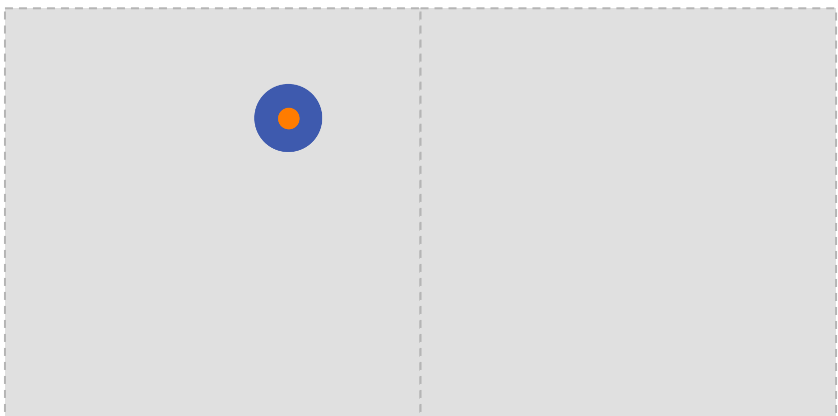
- *Photons absorbed in sensor pixel*
- *Charge pulse proportional to energy*
- *Threshold to discard noise*

- *Signals above threshold are counted*
  - ***Suppression of dark signal***
  - *Suppression of fluorescence*
  - *Suppression of electronic noise*

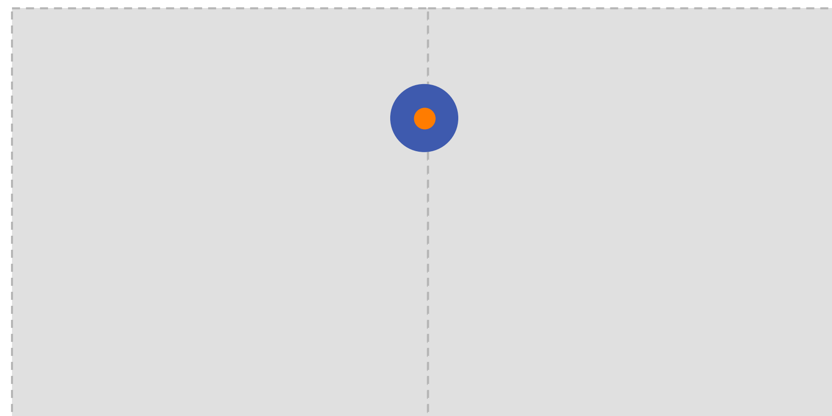
- *On-the-fly digitization in digital counter*
  - ***No readout noise***
  - *Fast readout*
  - *High dynamic range*

Threshold at half photon energy

All signal counted within one pixel



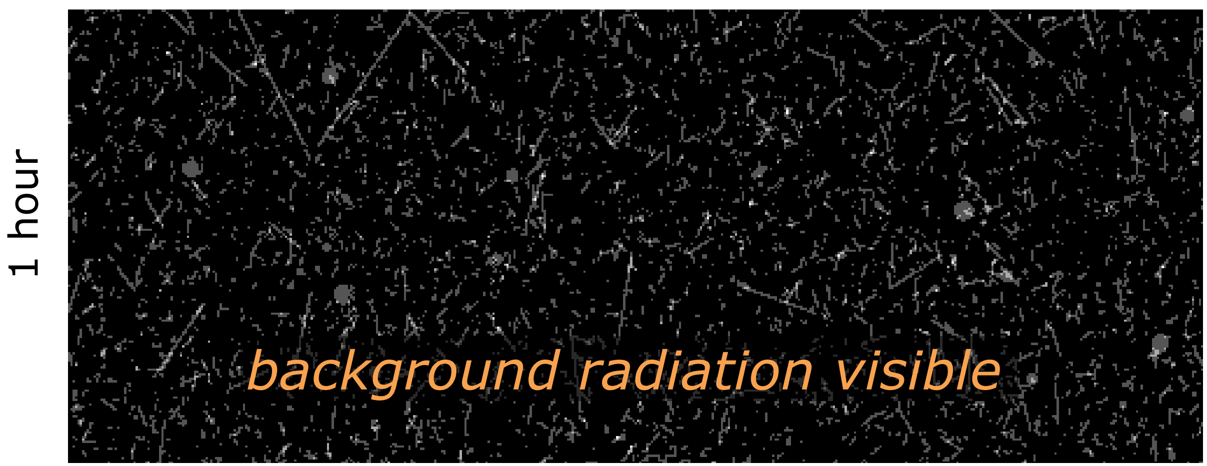
1 photon
100% charge
1 count



1 photon

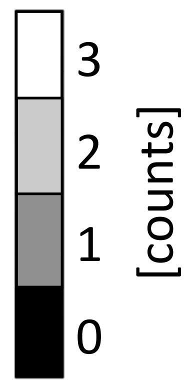
60% charge	40% charge
1 count	-

Noise-free detection



100K detector

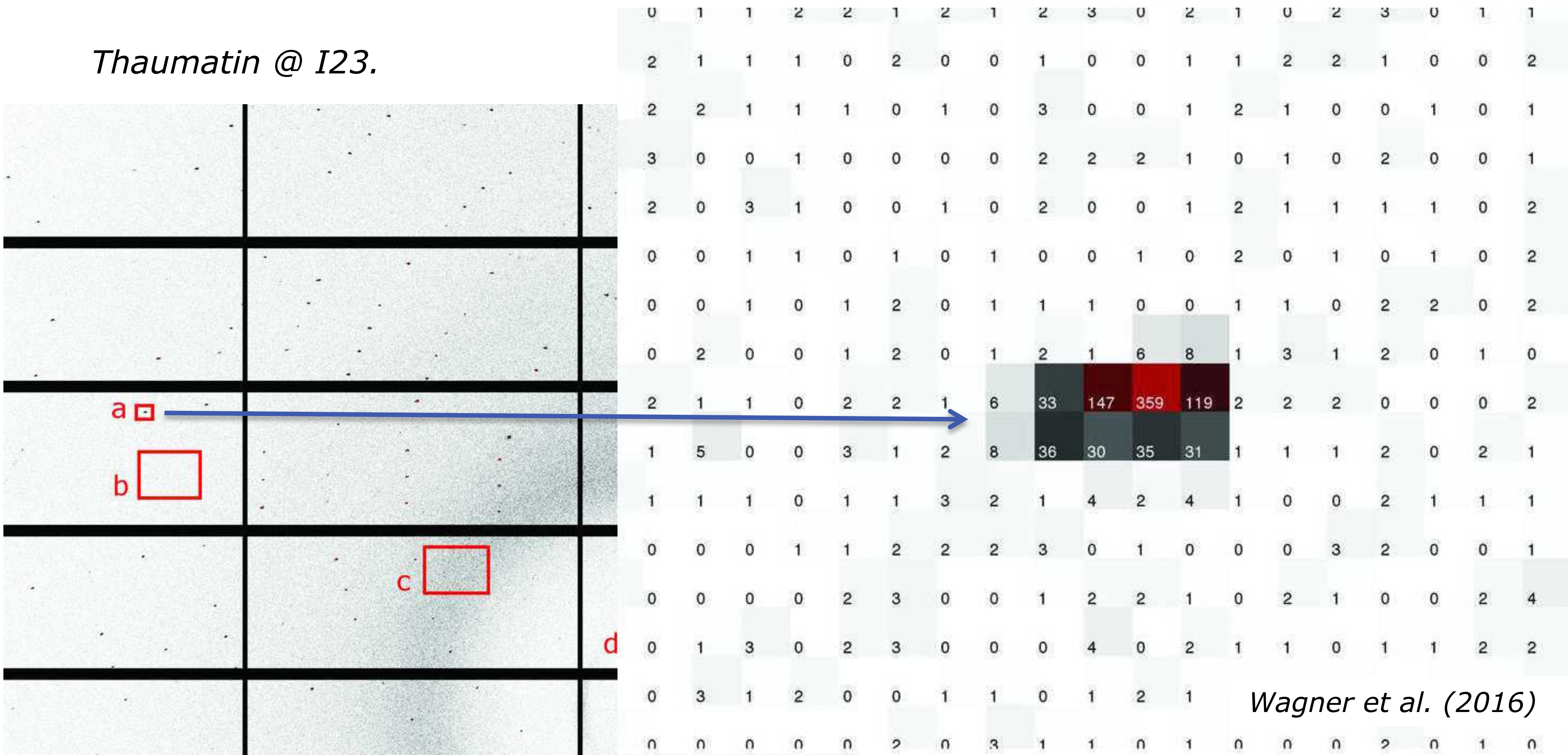
No readout noise
No dark signal



Negligible background for max. I/σ(I)

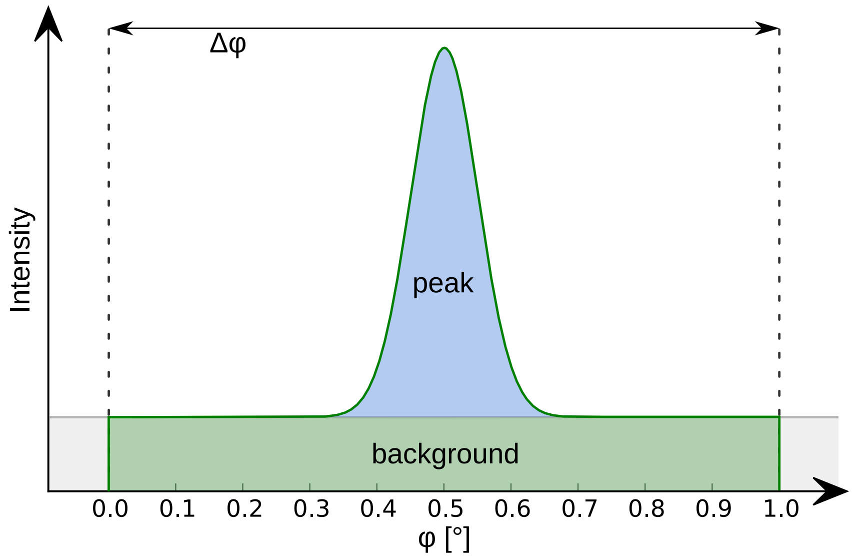
Protein crystallography in vacuum

Thaumatin @ I23.



Wagner et al. (2016)

Accuracy of intensity estimates



Q : Quantity of photons
$var(Q) = Q$
$\sigma(Q) = [var(Q)]^{1/2} = Q^{1/2}$

I : Observed intensity
$I = \Sigma(Peak_i - Bkg_i)$
$var(I) = \Sigma[var(Peak_i) + var(Bkg_i)]$
$R_{err} = \sigma(I)/I$

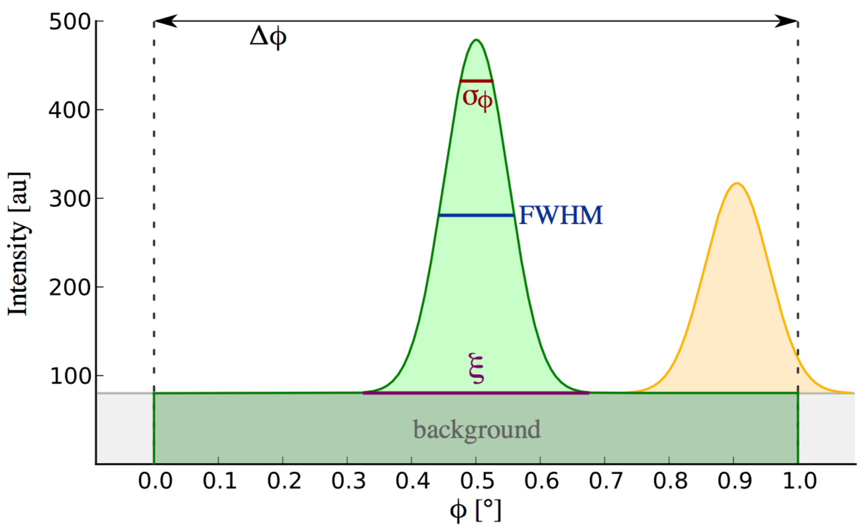
Relative error [%]	Background [photons]		
Integrated intensity [photons]	0	500	1000
100	10.0	33.2	45.8
500	4.5	7.7	10.0
1000	3.2	4.5	5.5
10000	1.0	1.0	1.1

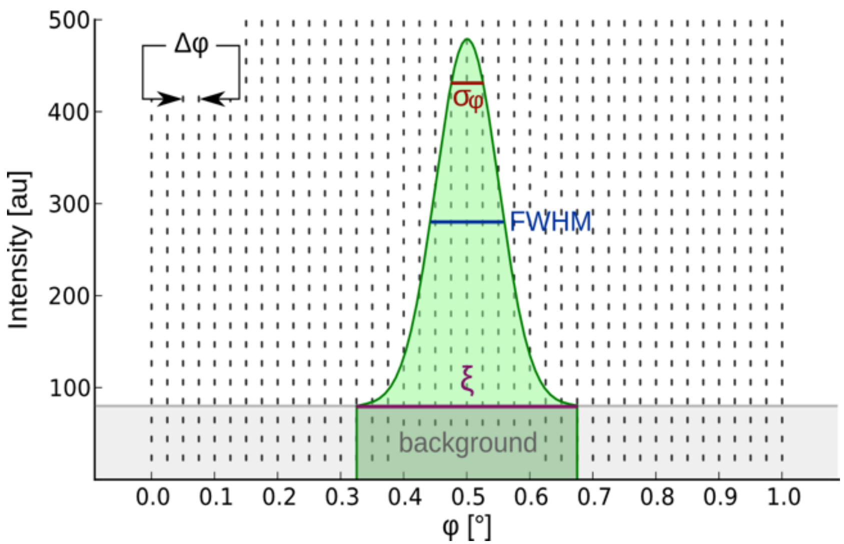
Less background

=> better data

Pflugrath (1999)

Fine φ-slicing minimizes background





Wide φ-slicing

- $\Delta\varphi > \xi$
- Lots of background
- Few images

Fine φ-slicing

- $\Delta\varphi \ll \xi$
- Minimal background
- Many images

Mueller et al. (2012)

Fine φ-slicing without readout noise

Detector with readout noise (CCD)

minimize readout noise ← compromise → minimize background

more images and smaller Δφ

Hybrid pixel detector without readout noise

take full advantage of fine φ-slicing

minimize background

more images and smaller Δφ

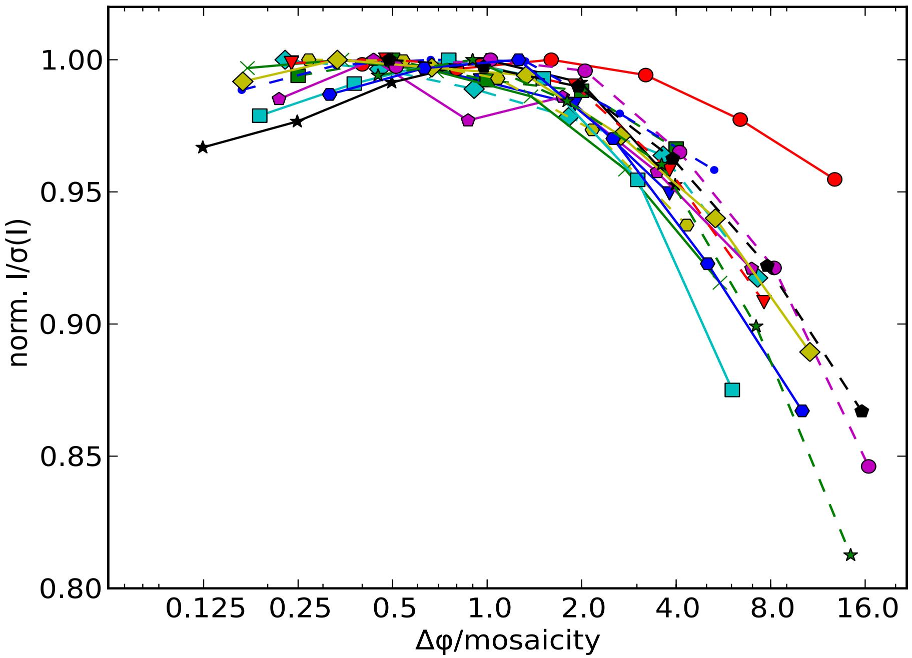
Fine φ-slicing improves data quality

Δφ < mosaicity improves:

- ***overall statistics***
- ***anomalous signal***
- ***highest-shell statistics***
- ***number of overlaps***

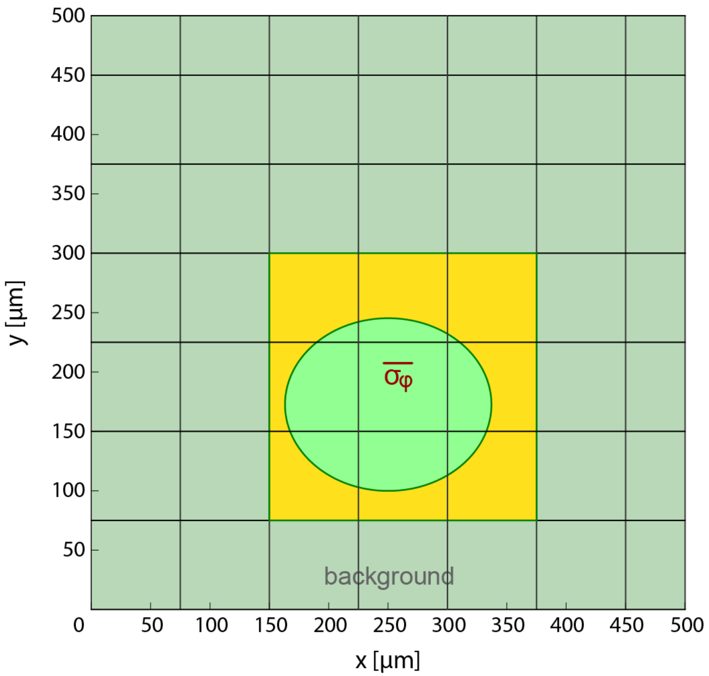
on PILATUS.

higher I/sig(I)

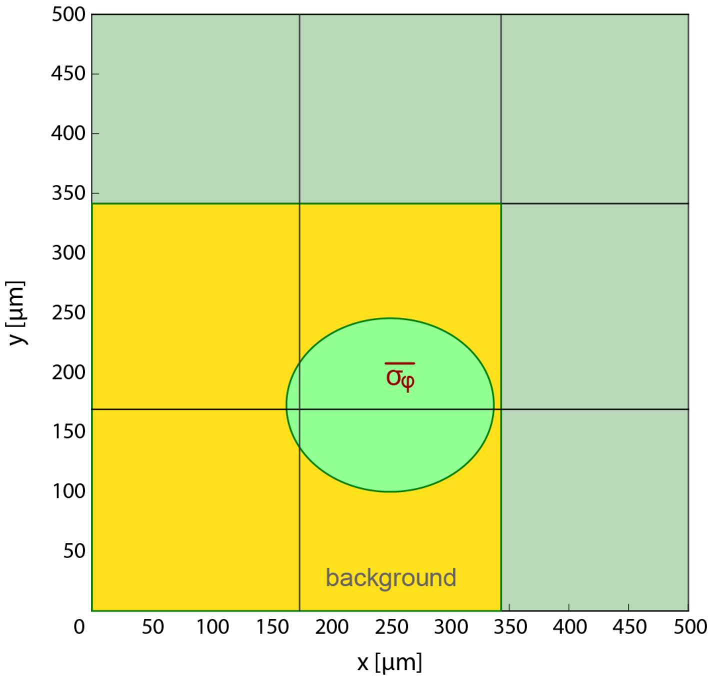


Mueller et al. (2012)

Smaller pixels improve data quality

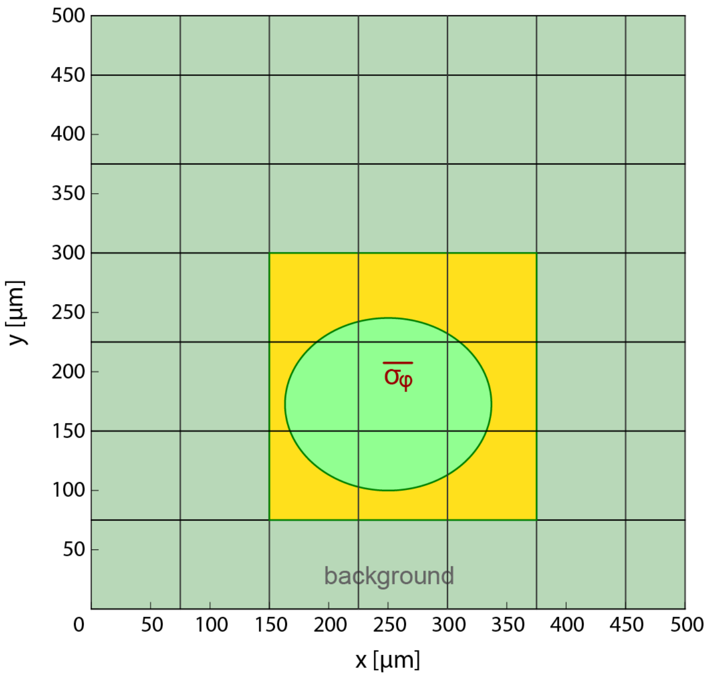


Reflection on EIGER

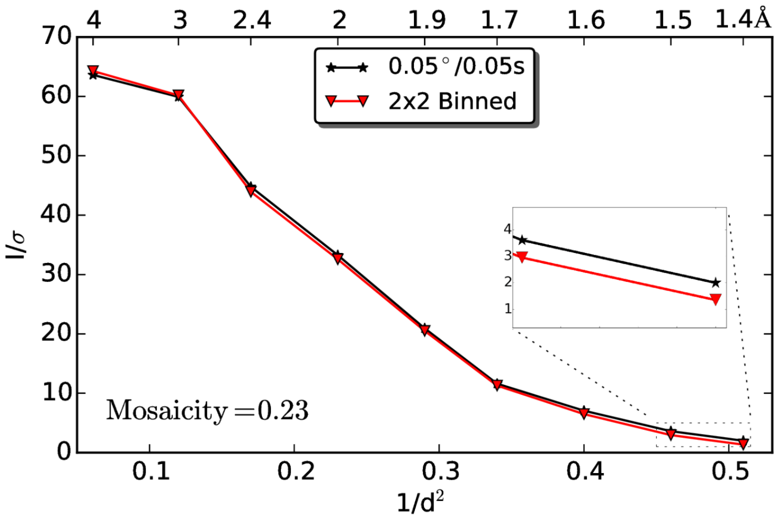


Reflection on PILATUS

Smaller pixels improve data quality



Reflection on EIGER



Better high-resolution data

Casañas et al. (2016)

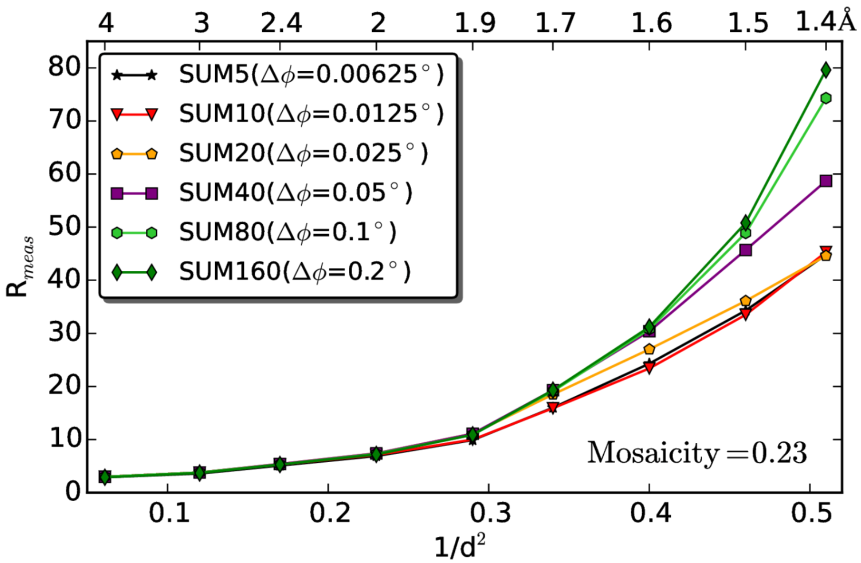
Smaller pixels allow for finer φ-slicing

Δφ ≈ 1/10 mosaicity improves:

- ***overall statistics***
- ***highest-shell statistics***
- ***anomalous signal***
- ***number of overlaps***

on EIGER.

lower R_{meas}

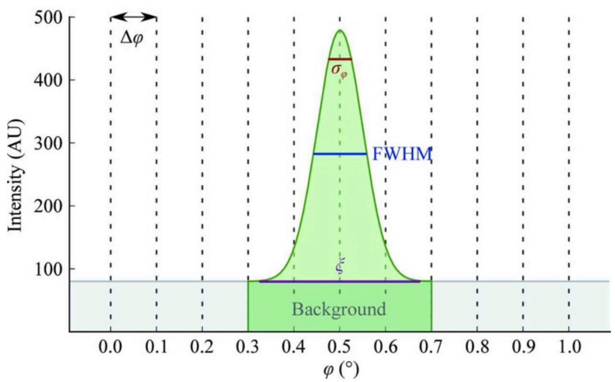


Casañas et al. (2016)

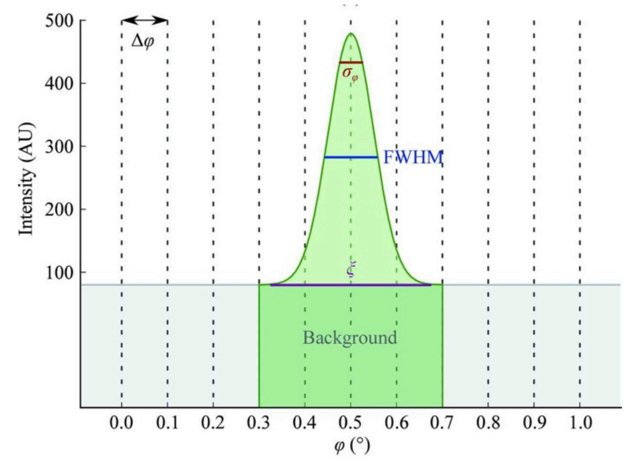
Improve your data by

- ***Using EIGER and PILATUS detectors***
- ***Using fine φ-slicing***
- ***Moving the detector as far back as possible***

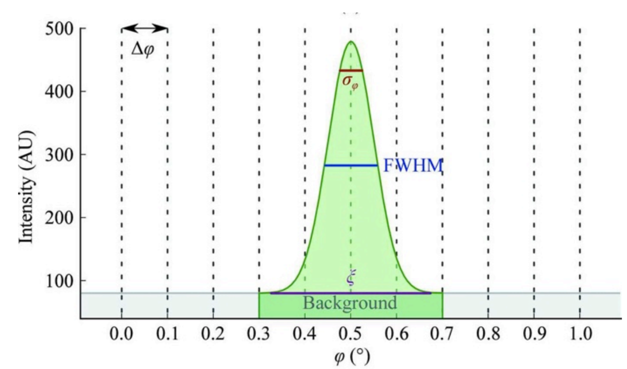
Decrease absolute background

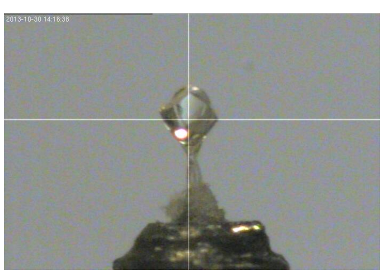


rubbish!



good!





Improve your data by

- ***Using EIGER and PILATUS detectors***
- ***Using fine φ-slicing***
- ***Moving the detector as far back as possible***
- ***Minimizing solvent around crystal***
- ***Matching beam size to crystal***

There is no native data

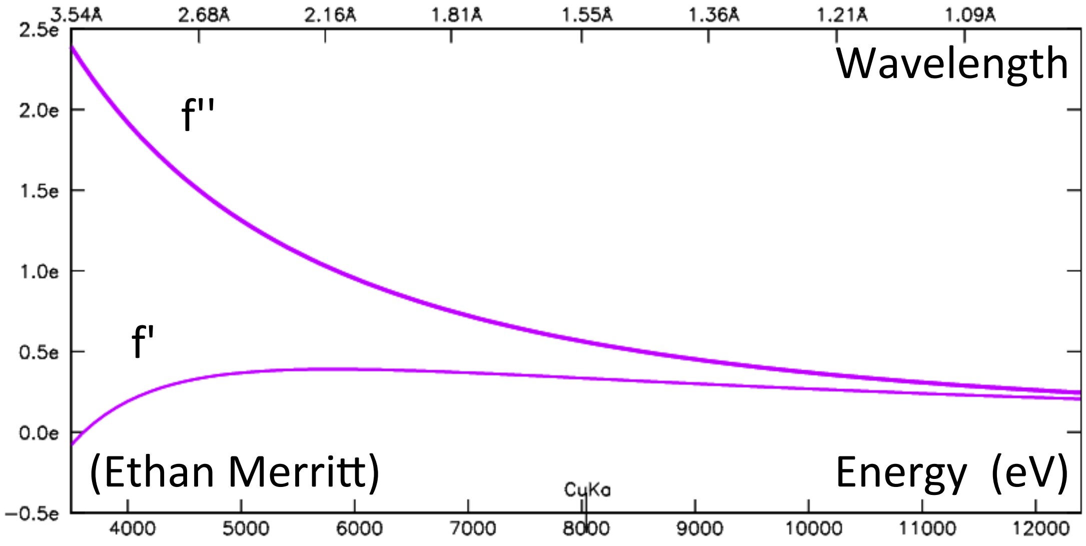
Current paradigm

- ***Molecular replacement***
- ***In case of failure***
  - *Se-Met substitution*
  - *Heavy atom soaking*

Always measure anomalous differences

- *Experimental phasing*
- *Improved MR phases*
- *Identify metal ions*
- *Without extra work*

Native SAD phasing



Anomalous signal for sulfur

Some strategy considerations

- ***Inverse beam?***
- ***Which wavelength?***
- ***How to distribute dose?***
- ***How to achieve multiplicity?***
  => kappa, chi, 2-theta

Never measure less than 360° of data.

Maximize anomalous signal

- ***Multiplicity amplifies anomalous signal***
  - Change crystal orientation for true multiplicity
- ***Radiation damage must be avoided***
  - Low-intensity data collection
  - Collect more images at lower dose
- ***Combine data from multiple crystals***

Detector must be free of readout noise.

Improve your data by

- ***Using Hybrid Photon Counting detectors***
- ***Moving the detector as far back as possible***
- ***Minimizing solvent around crystal***
- ***Matching beam size to crystal***
- ***Lowering intensity and collecting more images***
- ***Thinking about your experiment***

Use beam time efficiently

- ***Mount crystal – 1 min***
- ***Center crystal – 1 min***
- ***Collect a dataset – 1 min***
- ***Five-hour shift – 300 min***

- ***Person A :***
  - Collects 82 datasets
  - Takes 1 TB of data home
- ***Person B :***
  - Thinks about experiment
  - Talks to beamline scientist about hardware/best strategy
  - Has a tea to focus
  - Collects a dataset
  - Has a chat
  - Collects two more datasets
  - Solves structure

Conclusions

– ***Collect accurate data***

– ***Δφ ≈ ½ XDS mosaicity for best***
  - overall statistics
  - highest-shell statistics
  - anomalous signal

– ***There is no native data***
  - especially at high multiplicity

– ***Ask your beamline scientist / think !***

detecting the future

Thank you for your attention!

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