2013 ALS User Meeting
October 9, 2013, Bldg. 15, Room 300
Can Diffuse X-Ray Scattering Reveal Protein Dynamics?

Next generation detectors and software to measure diffuse scatter

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Workshop: http://cci.lbl.gov/dials/oct_2013_diffuse.htm

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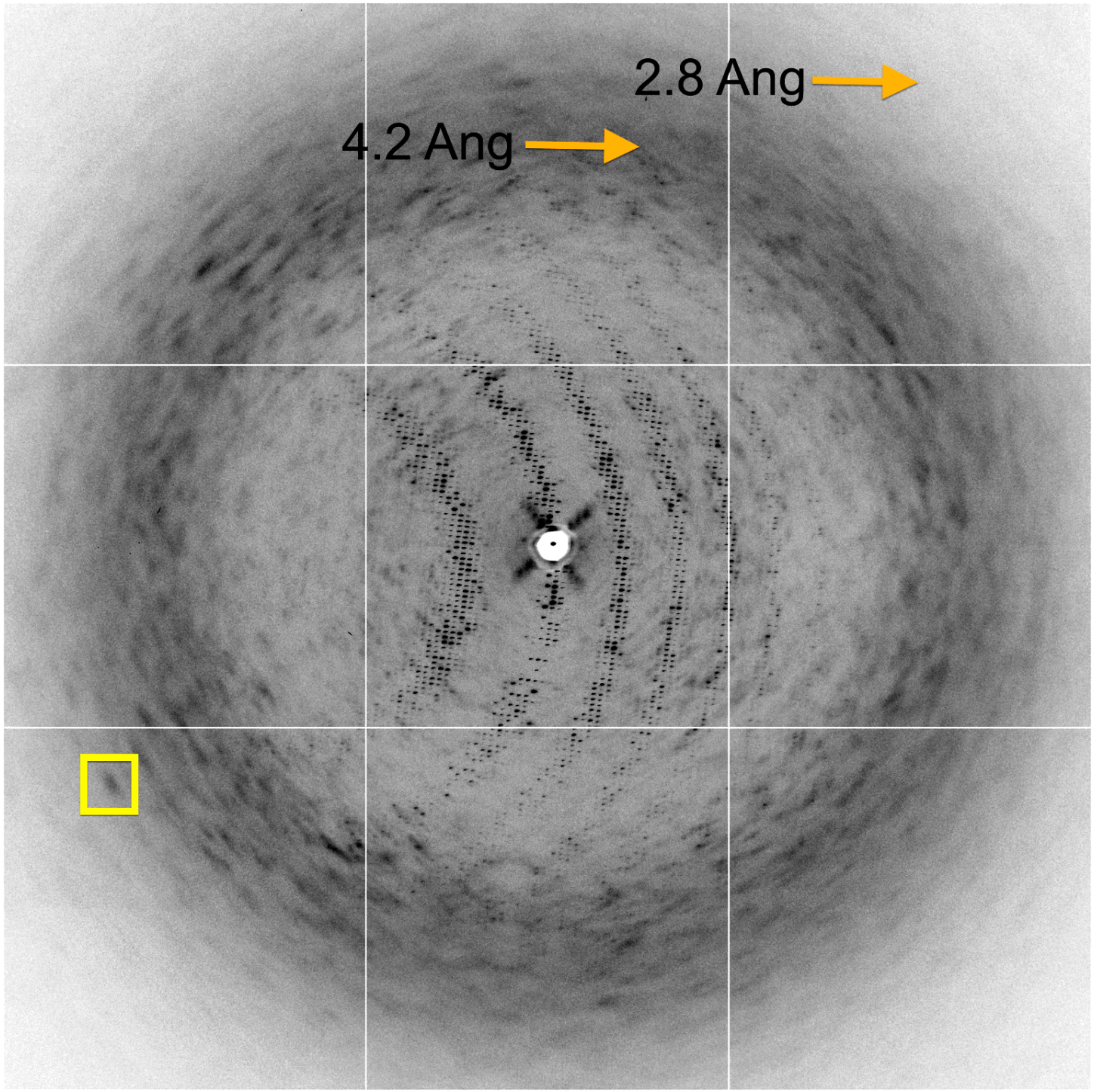
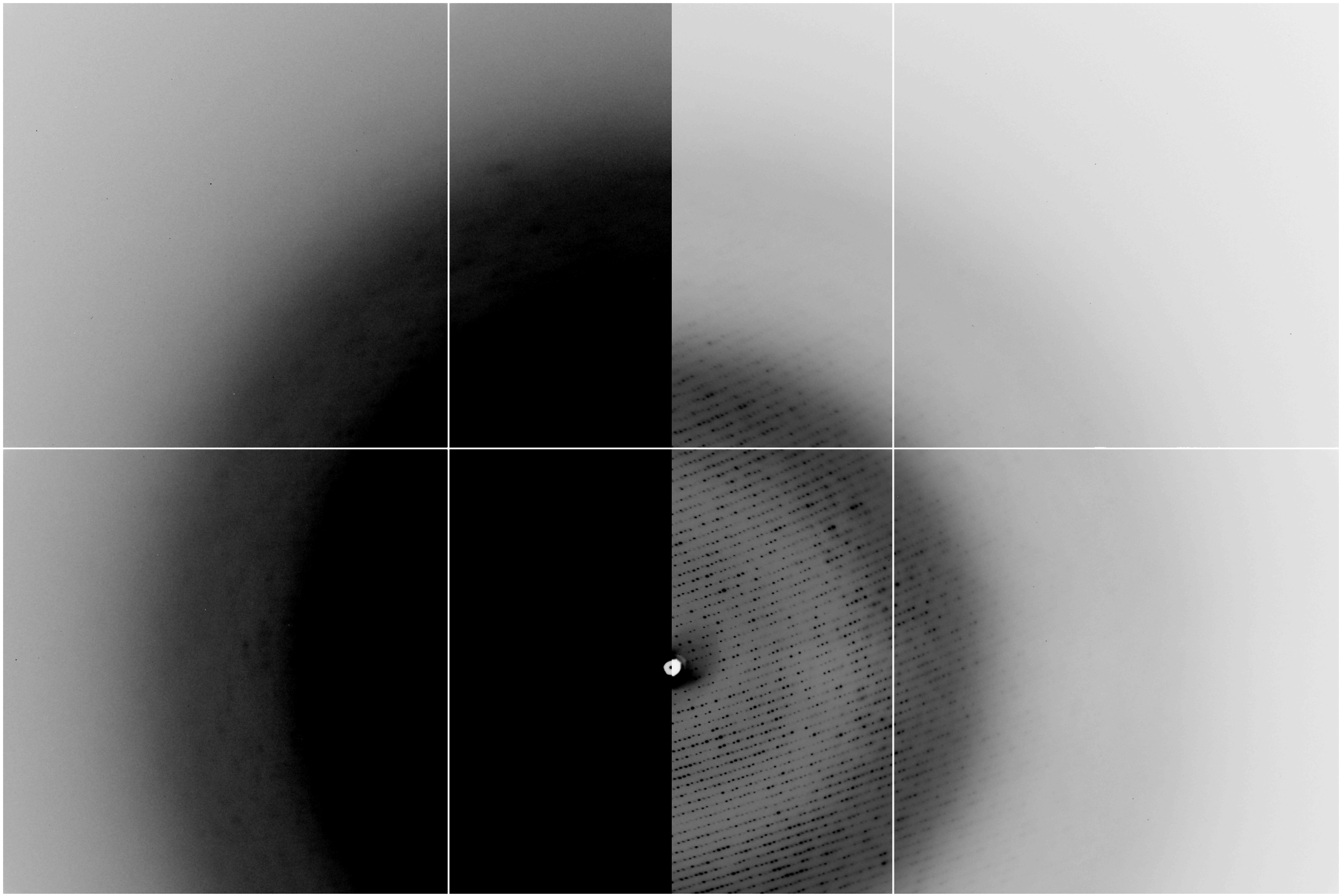


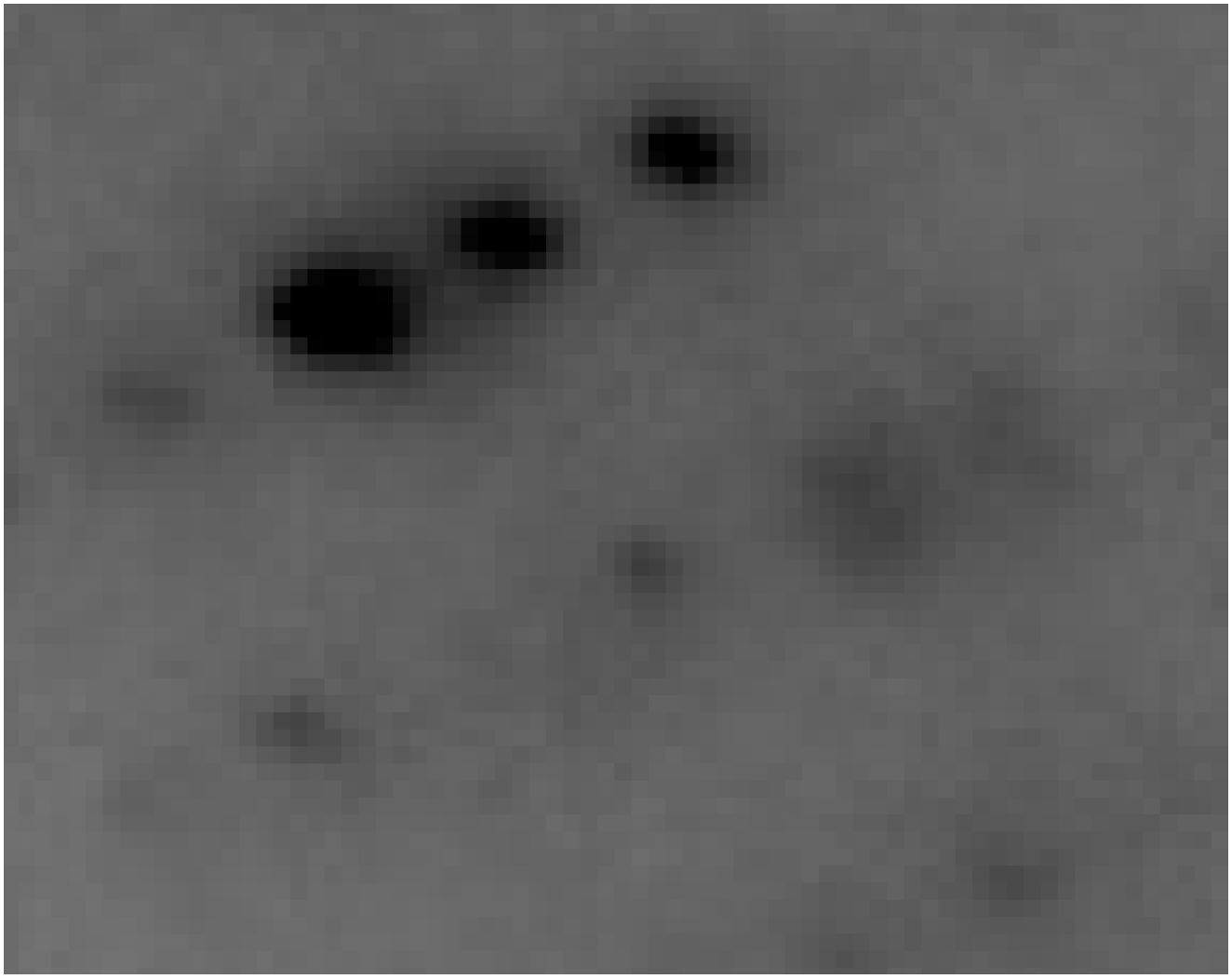
Thermal Diffuse Scatter from Photosystem II

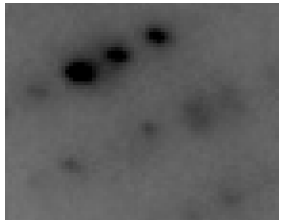
ALS 5.0.2
Dec 2012

Thermal Diffuse Scatter from Photosystem II

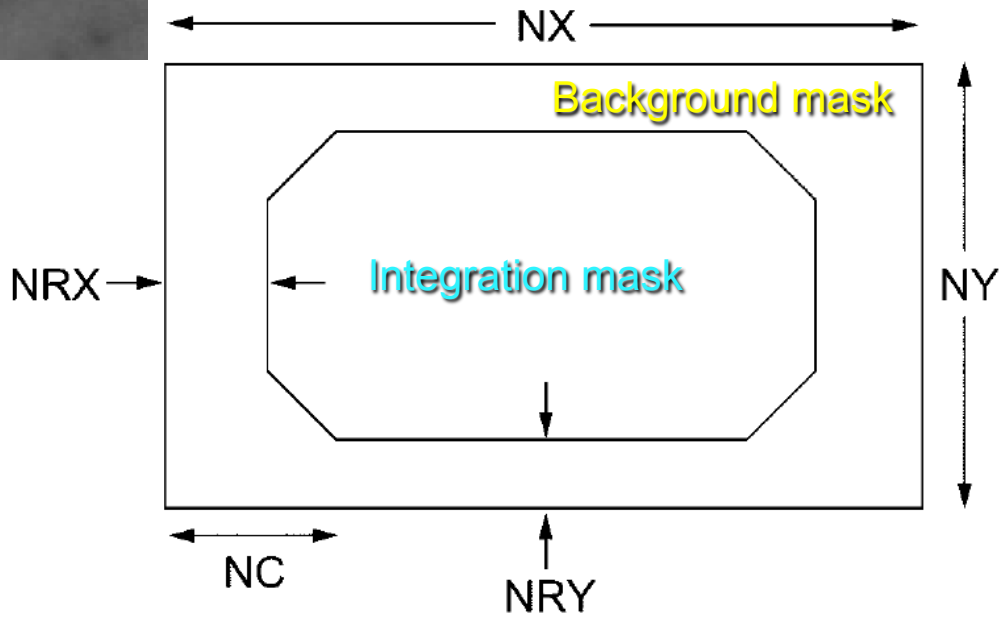


Challenges for the extraction of diffuse scattering





Summation integration over 2D masks or profiles



Mosflm
Leslie (1999) *Acta D* **55**, 1696

2D empirical mask:

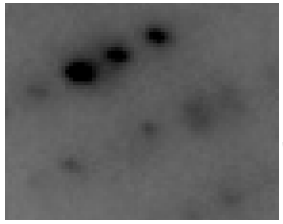
$$I_s = \sum_{i=1}^{m}(\rho_i - ap_i - bq_i - c)$$

$$\sigma_{I_s}^2 = \sum_{i=1}^{m} G\rho_i + (m/n)^2 \sum_{j=1}^{n} G\rho_j$$

$$= G\left[I_s + I_{\text{bg}} + (m/n)(m/n) \sum_{j=1}^{n} \rho_j \right]$$

Fit to a 2D empirical profile:

$$R_3 = \sum w_i(KP_i + ap_i + bq_i + c - \rho_i)^2,$$



3D empirical profile offers better accuracy

AVERAGE PROFILE OF 379 STRONG REFLECTIONS

γ=-0.4°

0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	1	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0

γ=-0.3°

0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	1	1	0	0	0	0
0	0	1	1	0	0	0	0	0
0	0	0	1	1	1	0	0	0
0	0	0	1	0	0	0	0	0
0	0	0	1	1	1	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0

γ=-0.2°

0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	1	1	1	0	0	0	0
0	0	1	2	1	1	0	0	0
0	0	1	2	2	1	1	0	0
0	0	1	1	2	1	1	1	0
0	0	0	1	1	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0

γ=-0.1°

0	0	0	0	0	0	0	0	0
0	0	0	1	2	1	1	0	0
0	0	2	5	8	6	3	1	0
0	1	4	12	23	14	4	1	0
0	1	4	20	38	20	4	1	0
0	1	4	16	25	12	3	1	0
0	1	3	6	9	4	1	0	0
0	0	1	2	1	1	0	0	0
0	0	0	0	0	0	0	0	0

γ= 0.0°

0	0	0	0	0	0	0	0	0
0	0	1	2	4	3	1	0	0
0	0	4	12	20	14	5	1	0
0	1	8	31	61	38	9	2	0
0	1	9	49	100	53	10	1	0
0	1	8	35	64	32	7	2	0
0	1	4	13	19	10	3	1	0
0	0	2	3	4	2	0	0	0
0	0	0	0	0	0	0	0	0

γ= 0.1°

0	0	0	0	0	0	0	0	0
0	0	1	2	3	2	1	0	0
0	1	2	7	11	7	2	0	0
0	1	5	17	29	16	4	1	0
0	1	5	24	46	23	4	1	0
0	1	3	15	29	15	4	1	0
0	0	1	6	9	5	2	0	0
0	0	1	2	2	1	0	0	0
0	0	0	0	0	0	0	0	0

γ= 0.2°

0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	1	1	1	1	1	0	0
0	0	1	1	2	1	0	0	0
0	0	1	2	3	2	1	0	0
0	0	1	2	2	1	1	0	0
0	0	0	1	1	1	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0

γ= 0.3°

0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	1	0	1	0	0	0	0
0	0	0	1	1	0	0	0	0
0	0	0	1	1	0	0	0	0
0	0	1	1	1	1	1	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0

γ= 0.4°

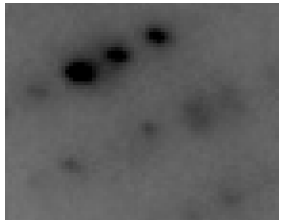
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	1	0	0	0	0	0
0	0	1	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0

β

α

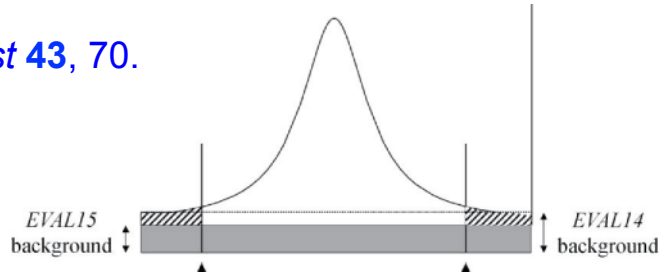
- Profile is constructed in reciprocal space, not image space

Kabsch[1988] *J Appl Cryst* **21**, 916

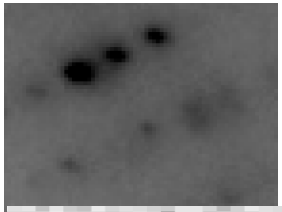


EVAL15 approach holds promise for MX data

Eval15: Schreurs [2010] *J Appl Cryst* **43**, 70.

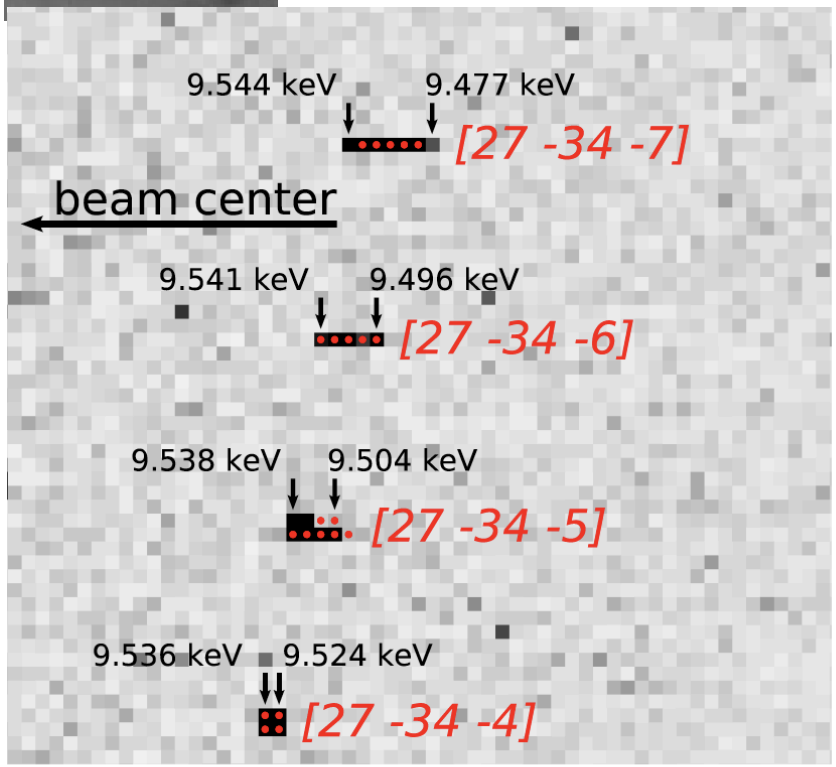


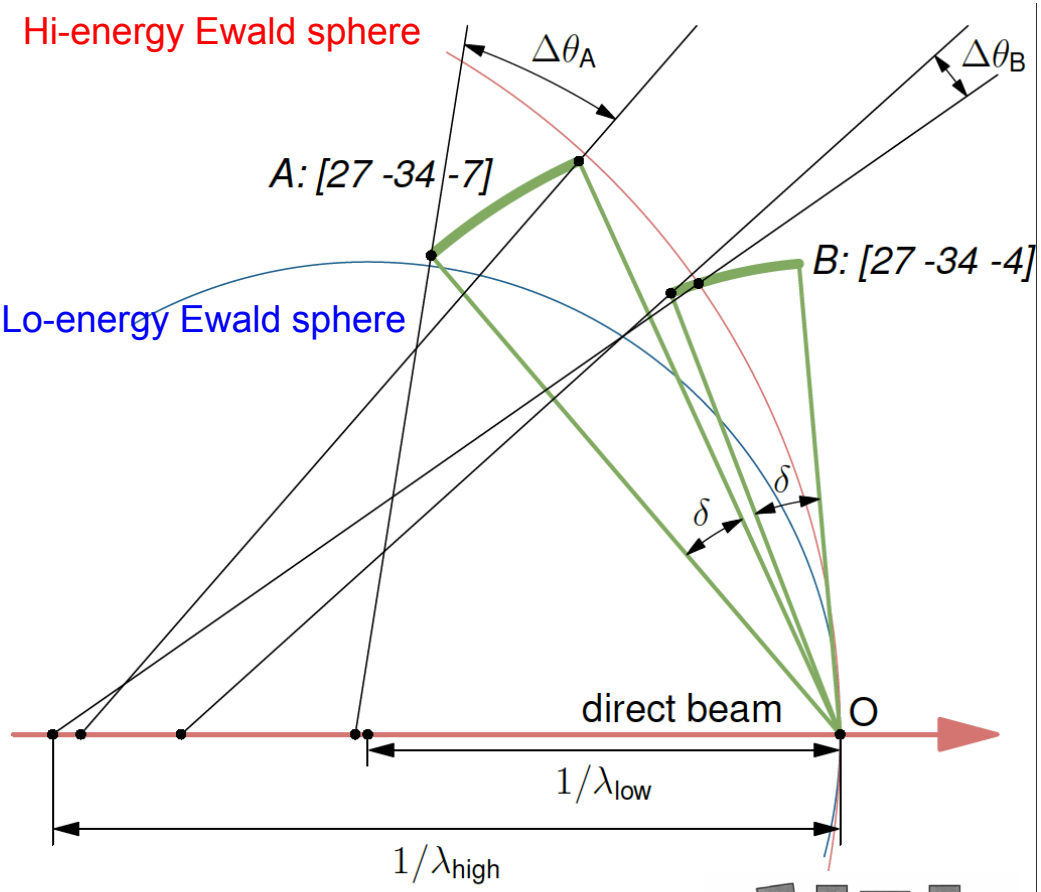
- Bragg spot shapes are modeled explicitly based on underlying parameter model; thus they vary continuously throughout reciprocal space. Input parameters are:
  - Beam profile, divergence, and wavelength
  - Crystal size, shape, and mosaicity
  - Point spread function
- Structure factor intensities are fit by solving a normal matrix.
- The model explicitly treats the pixel intensity as having contributions from [potentially] many nearby Bragg spots.
  - Helps get the background right
  - Framework for deconvoluting overlapping spots
- Could potentially reveal diffuse scattering by subtracting off the profile-fit Bragg spots.
- Use refined structure to bootstrap the structure factor intensities?



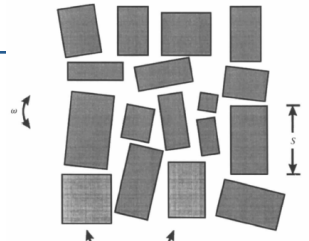
Parametric profile also used for XFEL Bragg spots

Model: Dispersion + mosaicity accounts for neighboring-spot variation

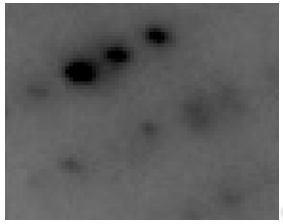




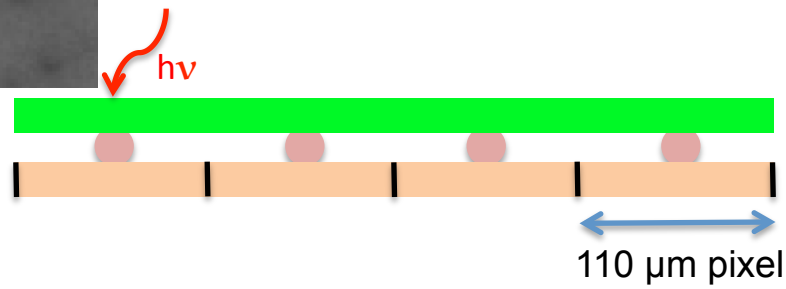
- Wide spots: reciprocal lattice point completely inside energy limits
- Three-parameter model predicts the [near] exact pixels with signal
- λ_{high} = 9.556 keV; λ_{low} = 9.443 keV; FW mosaic spread = 0.174°

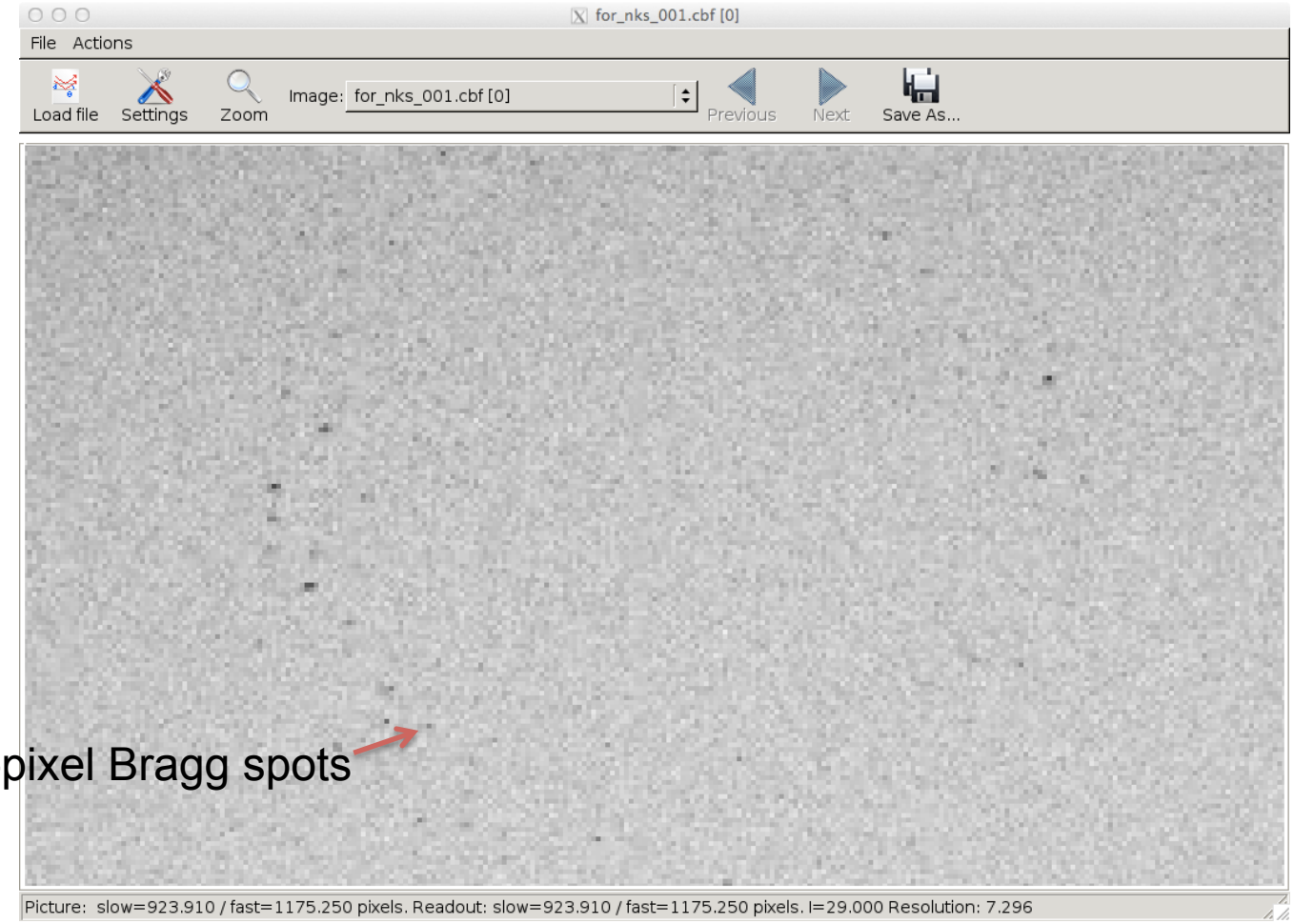


Colin Nave, 1998



Pixel array detectors would have better spatial resolution





Advantages of latest (Pilatus3) detectors

Spatial resolution

- Zero point spread: Bragg spots can be 1 px^2
- Pixel size 172 µm

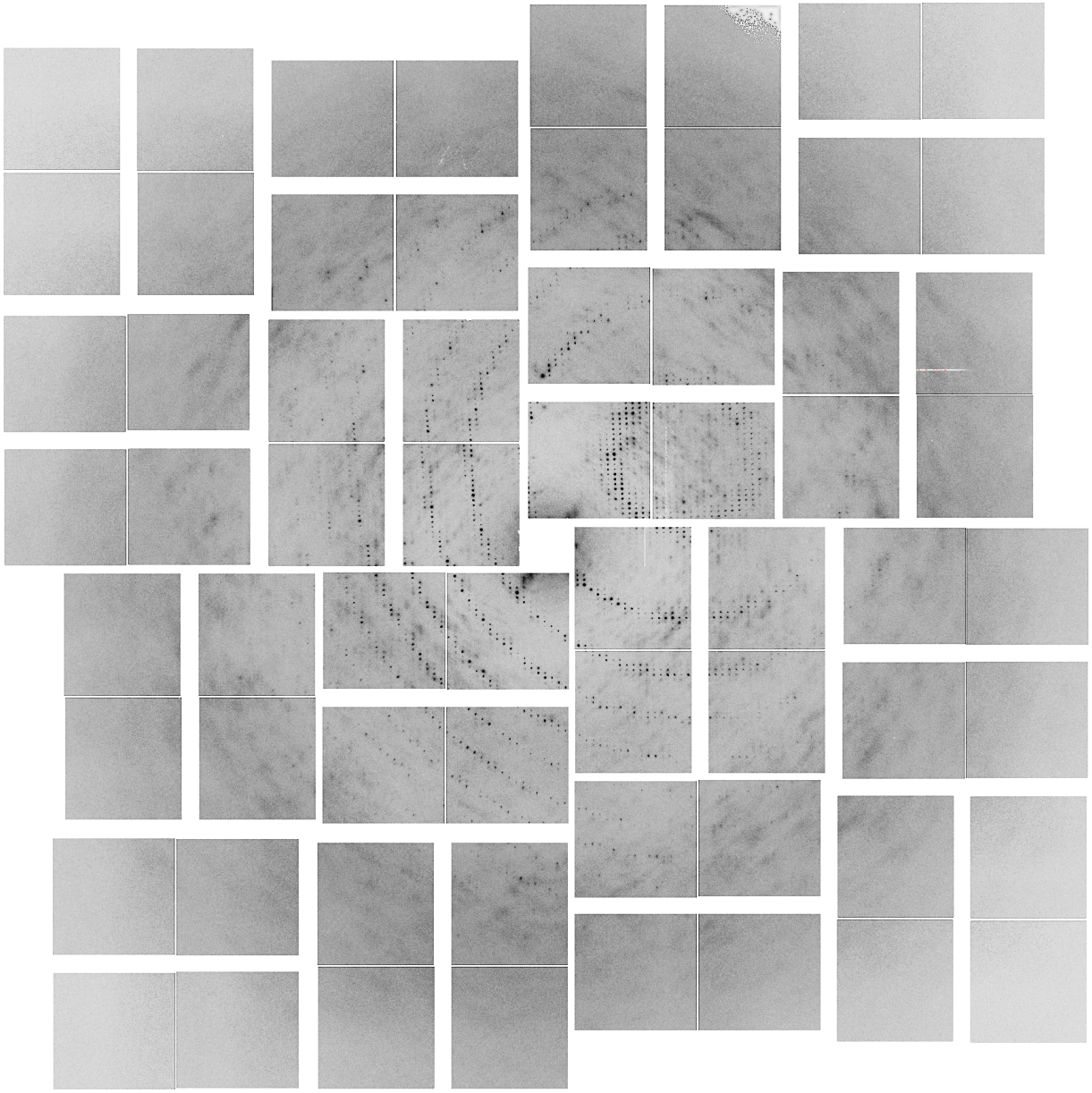
Adequate signal depth

- Linear response up to 10^7 s^{-1}, deep enough for Bragg + diffuse
- Sensitivity at photon-counting level (≈ zero instrument noise)
- 20-bit counter depth, overflow controlled
- No dark current

Angular resolution

- Framing rates of 100 Hz allow extremely fine phi-slicing
- 0.95 ms readout allows shutterless aquisition

Diffuse pattern: room temperature / XFEL source / PAD detector

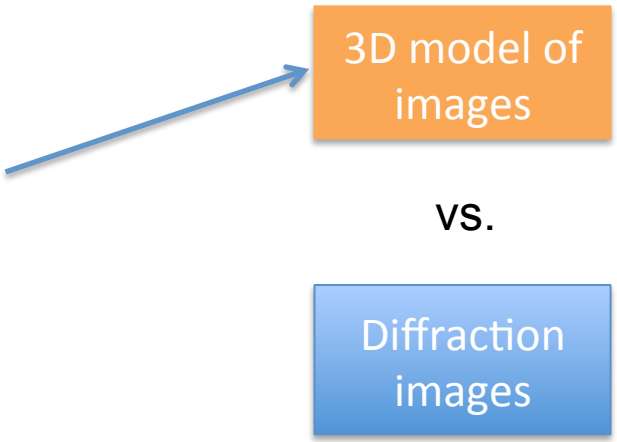


Data processing: Modeling the diffraction pattern

MOSFLM / XDS
Bragg spots: forward problem

EVAL15--Bragg spots
Diffuse scattering: inverse problem

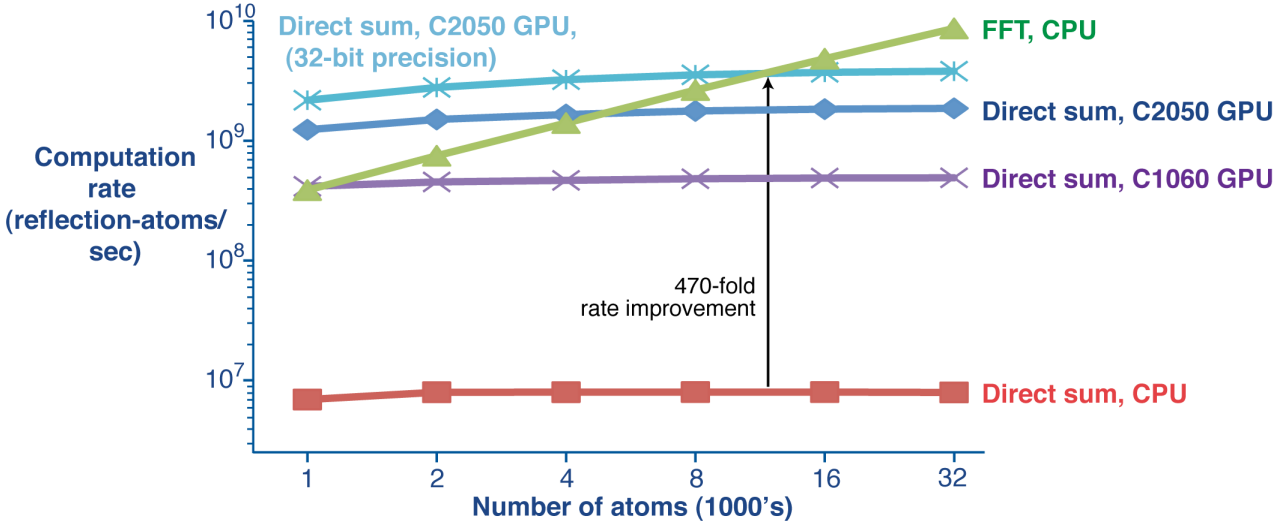
<u>Parameters</u>
Beam properties
Detector properties & defects
Structure factor intensities
3D model of diffuse scattering

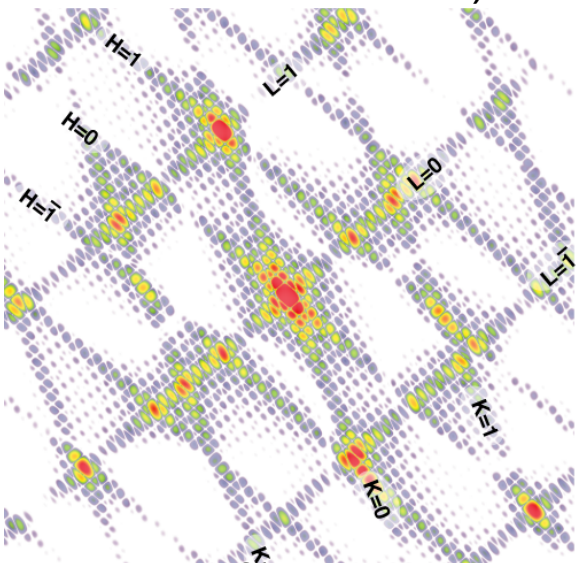


…role for parallel or GPU computing?

Stress/strain diffraction becomes tractable with GPUs

- Nvidia Tesla C2050 (448 hardware threads,inexpensive)
- Algorithm must be organized in such a way that the same input data is used numerous times by independent output channels.
- Computation of structure factors by direct summation (fractional Miller indices):

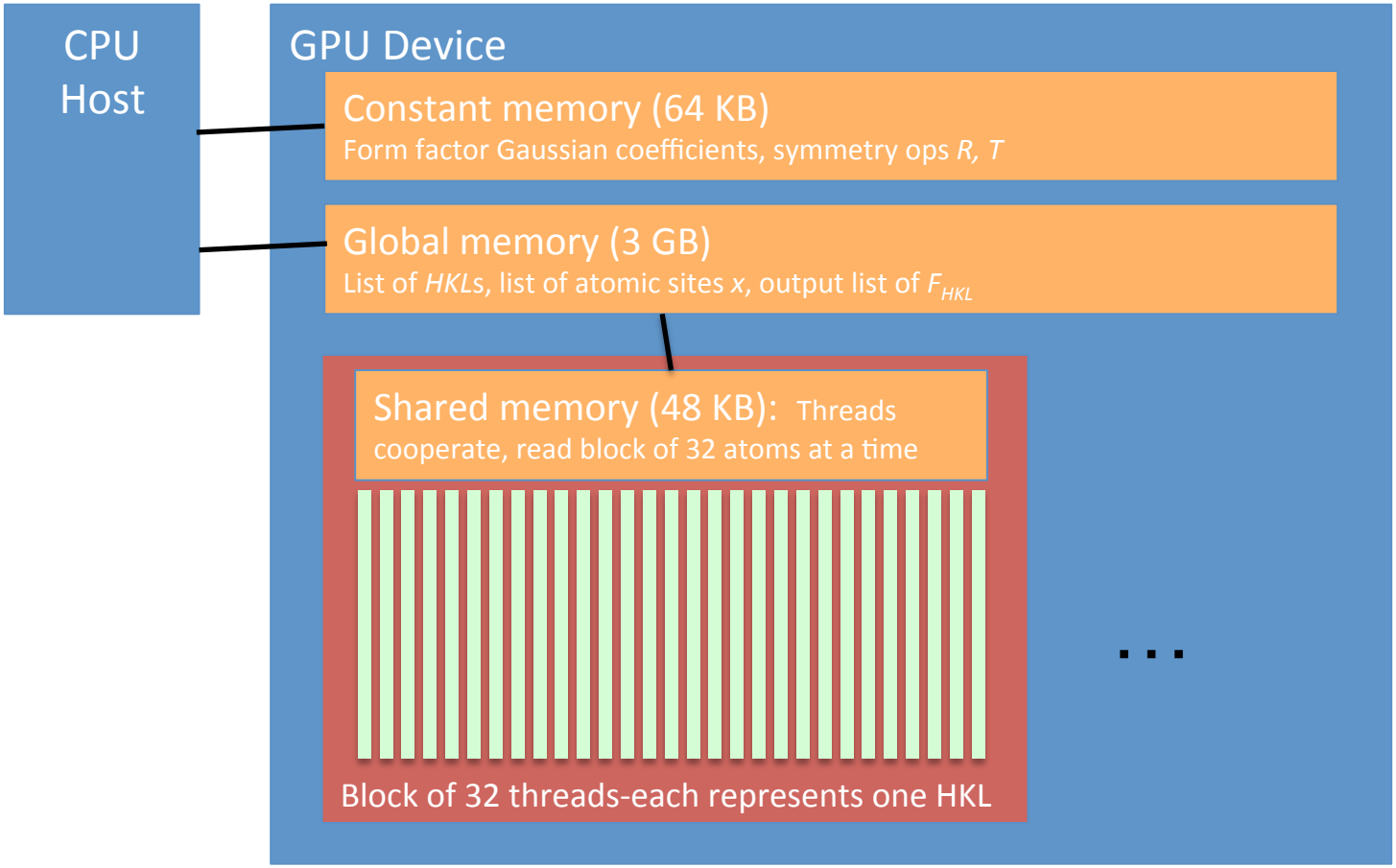




Detailed fringe-pattern on the low-order spots (Photosystem I, all atoms) simulated in < 2 minutes

$$F_{HKL} = \sum_{\substack{\text{unit cells} \\ \Delta U}} \sum_{\substack{\text{rotational} \\ \text{symmetries} \\ R}} \sum_{\substack{\text{translational} \\ \text{symmetries} \\ T}} \sum_{\substack{\text{atomic} \\ \text{sites} \\ x}} f_x \cdot w \cdot e^{2\pi i H \cdot (Rx + T + \Delta U)} \cdot e^{-2\pi^2 u_{iso} d^{*2}}$$

GPU efficiency: reorganize the algorithm to manage memory



$$F_{HKL} = \sum_{\substack{\text{unit cells} \\ \Delta U}} \sum_{\substack{\text{rotational} \\ \text{symmetries} \\ R}} \sum_{\substack{\text{translational} \\ \text{symmetries} \\ T}} \sum_{\substack{\text{atomic} \\ \text{sites} \\ x}} f_x \cdot w \cdot e^{2\pi i H \cdot (Rx + T + \Delta U)} \cdot e^{-2\pi^2 u_{iso} d^{*2}}$$

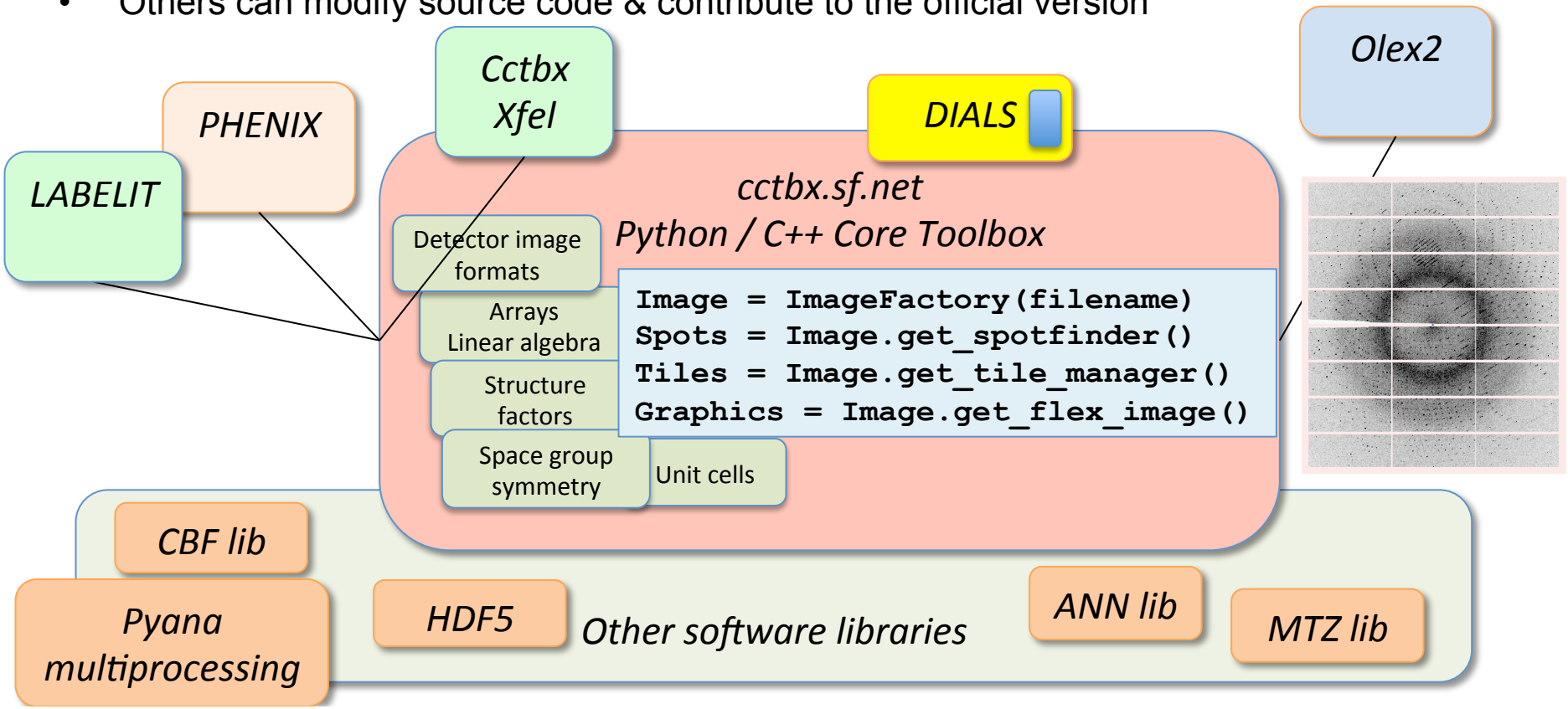
DIALS: Diffraction Integration for Advanced Light Sources

Software collaboration with common goals but separate funding sources:

- Berkeley Labs, Nick Sauter, NIH funding
- BioStruct-X consortium, Gwyndaf Evans, European Union funding

Approach to software management:

- Open source; BSD-style license to allow distribution of derivative works
- Others can modify source code & contribute to the official version



DIALS Goals

http://www.ccp4.ac.uk/newsletters/newsletter49/content.html

- Standard methods for treating all types of detectors
  - Unusual geometry: cylindrical Pilatus detector
  - Subpixel detector corrections (for XFEL)
- Toolbox for unusual experimental configurations
  - Two-color experiments
  - Reticular twinning
  - Multiple lattices
  - Diffuse scattering!
- Parallelization & Speed
- Timeline
  - Twice-yearly workshops: DIALS developers + detector manufacturers + beamline groups
  - XDS + MOSFLM algorithms being tested now

Diffuse Scattering Goals

- Discussion…

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