Large Area CMOS Detectors for High Speed Crystallography

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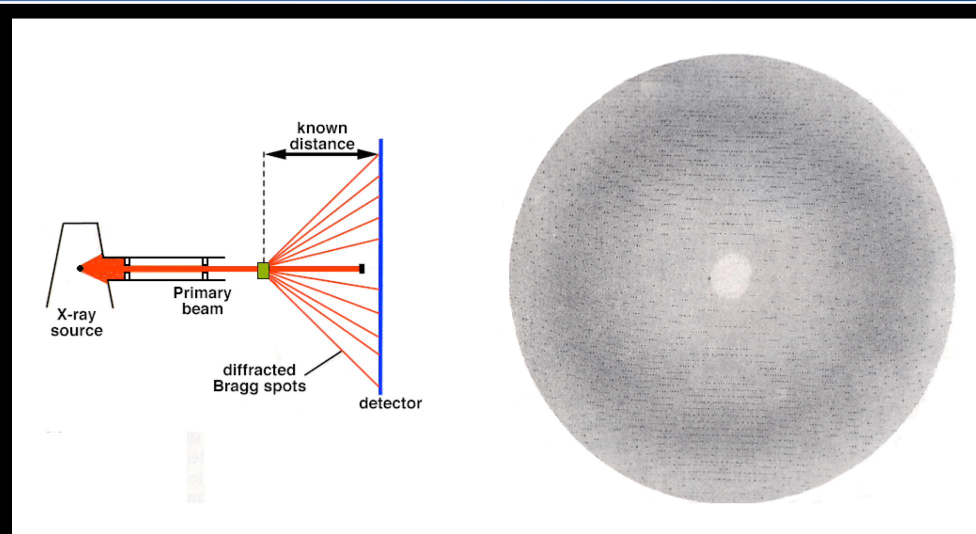
Talk Outline

- Detector needs at X-ray synchrotrons
- What are the advantages of CMOS detectors
- How do CMOS X-ray detectors work?
- Technical specifications of our CMOS detector
- Description of imaging system for crystallography

Recent results

- Future Plans

Improving Protein Crystallography Experiments



Typical Experiment:
- Mount crystal
- Center crystal on rotation axis (2-5 minutes)
- Take a series of rotation images, each of 0.5° – 1.0°, for 180°
- After every frame stop, close shutter and readout camera
  (every frame takes several seconds; experiment lasts 15-45 min)

Optimum experiment:
- Automatic centering of crystal (<30 sec)
- Take complete set of images continuously over 180° while the crystal is rapidly rotated without shuttering the X-ray beam. There is less radiation damage and potentially better results
- Analysis in less than 10 min

New Requirements of Crystallography Detectors at Synchrotrons

- Improvements in intensity, energy resolution and collimation allow experiments that were impossible a few years ago.
- The count rate limitation and energy resolution of many detectors are now the limiting factor in many experiments.
- Area detectors using CCD's provide excellent performance but their readout style and speed limit next generation experiments.
- Si Pixel detectors like a Pilatus system are useful but they are very expensive and have some limitations.

Why a CMOS Detector?

-*Phone cameras, high end cameras, microscopes, synchroton-based microtomography*

- CMOS is a new technology that is rapidly replacing CCDs in most imaging applications, due to reduced cost, higher speed, and larger size. It has equivalent image quality.
- Fast, continuous readout at video rates.
- Large area sensors are readily available. No need for image photo-reduction, so gain is high.
- No spatial distortion, and high fill-factor.
- Low noise and high signal/noise ratio.

How Do CMOS Imagers Work?

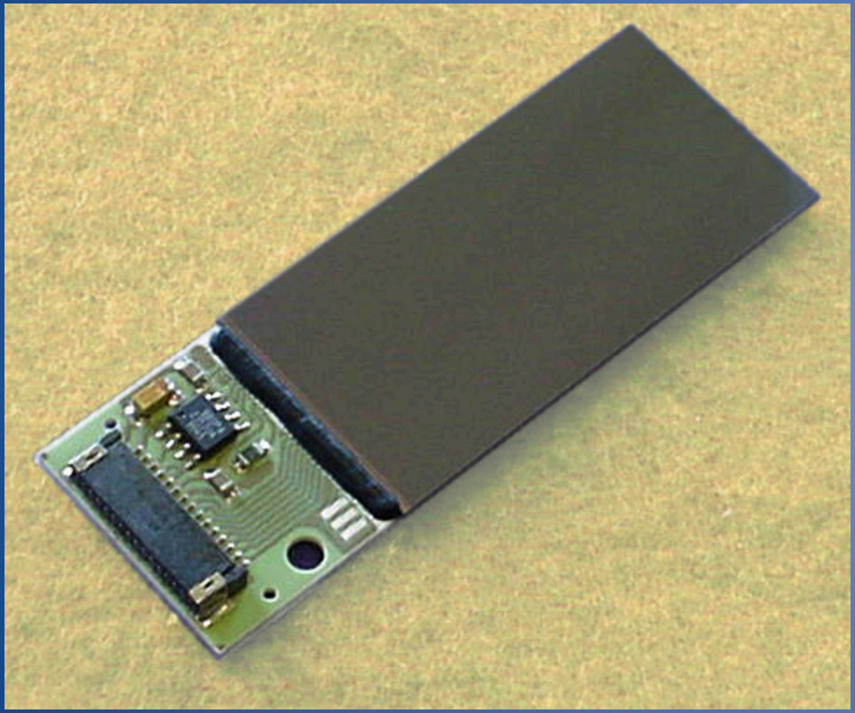
CMOS and CCD technologies are similar in some ways:

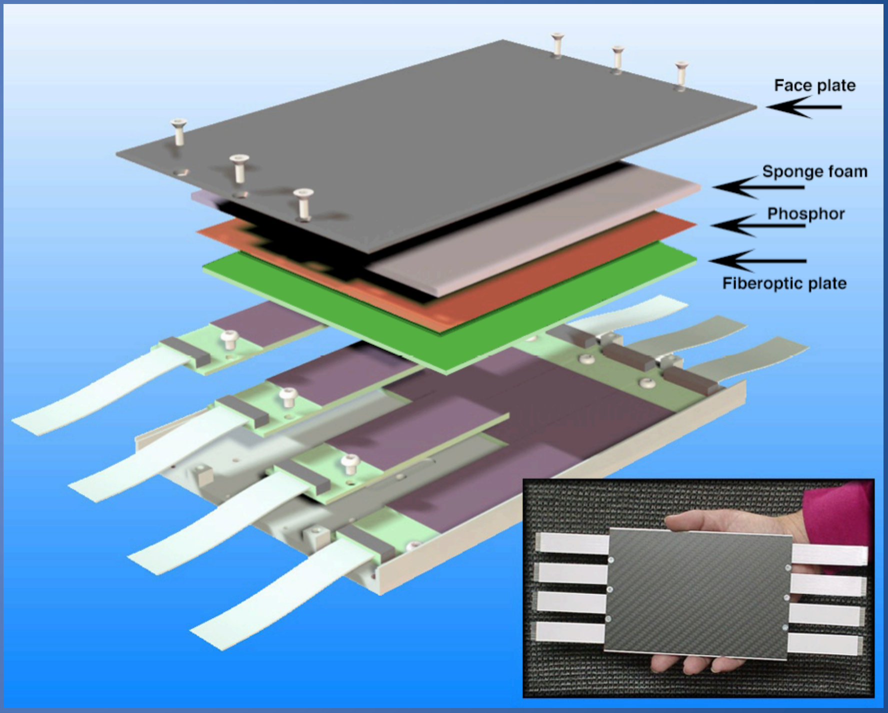
- Fabricated as arrays of square pixels; made of silicon.
- Visible-light sensors, so X-ray field intensity is first converted to light in a phosphor sheet
- Sensor then converts light into an electric charge.

CMOS differs from CCD in two important ways:

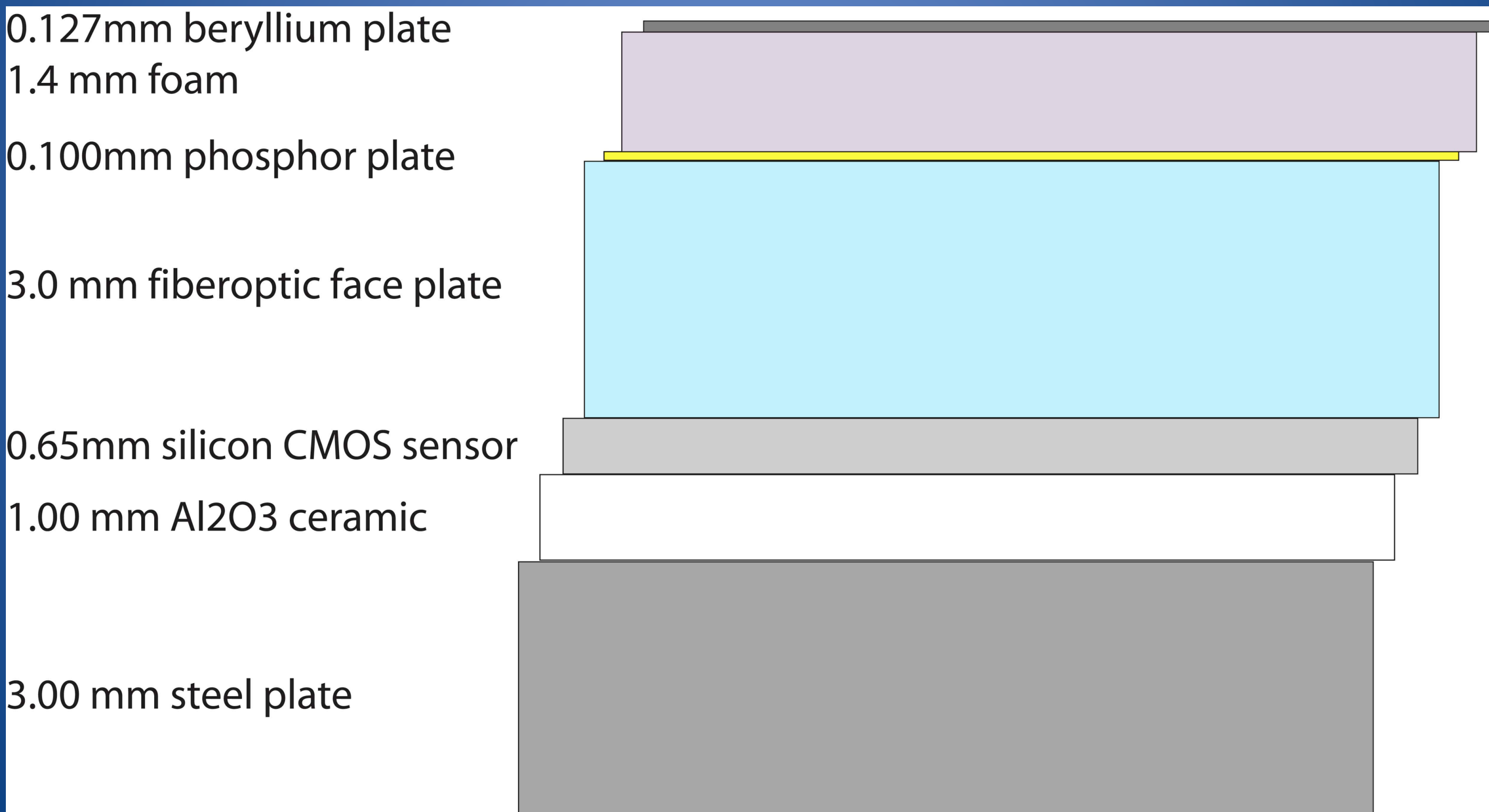
- CCD readout requires an X-ray shutter, because image passes across entire sensor in a charge-transfer process. In contrast, each CMOS pixel readout is an individual process. The entire CMOS sensor can remain active during readout. No shutter is needed.
- CMOS imagers can be made BIG.

CMOS is fabricated with 3 sides buttable, thus allowing assembly of large tiled arrays.

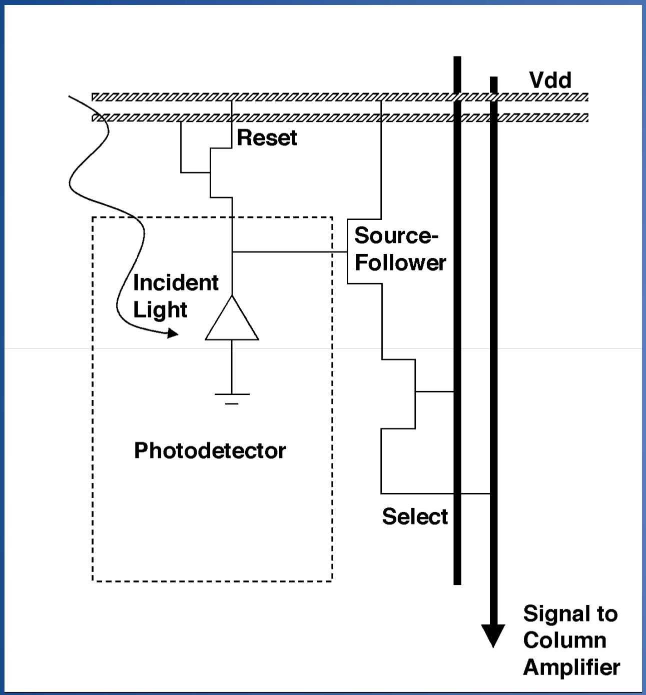




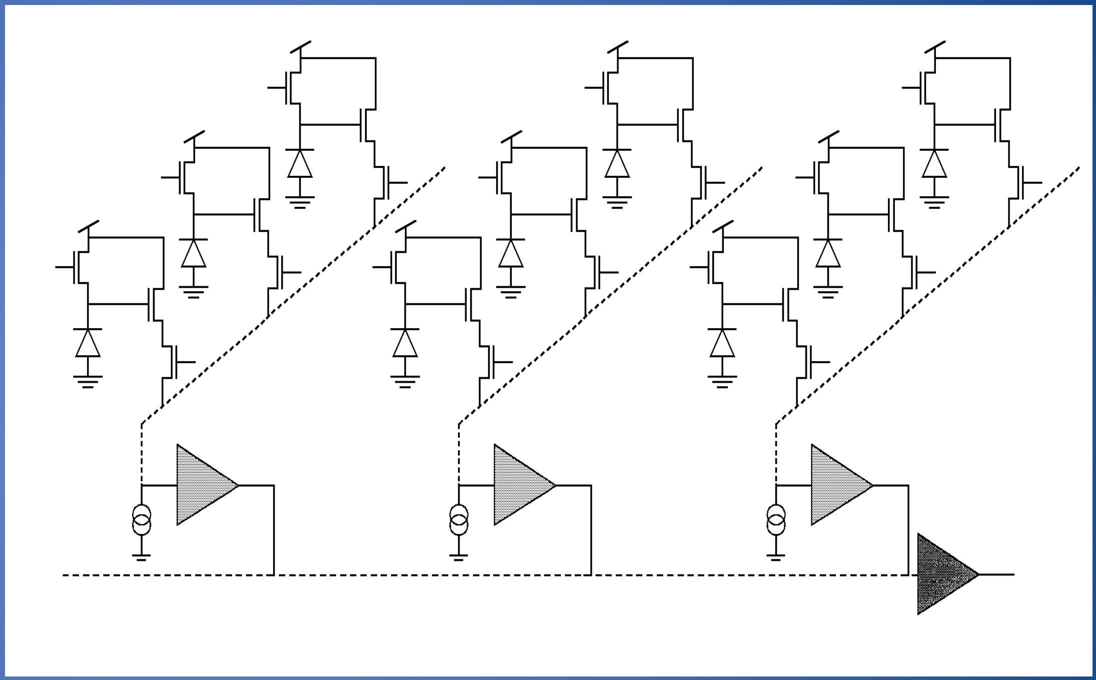
Layers of CMOS sandwich:



Very simple electronics; each pixel only contains 3 transistors so fabrication yield is high



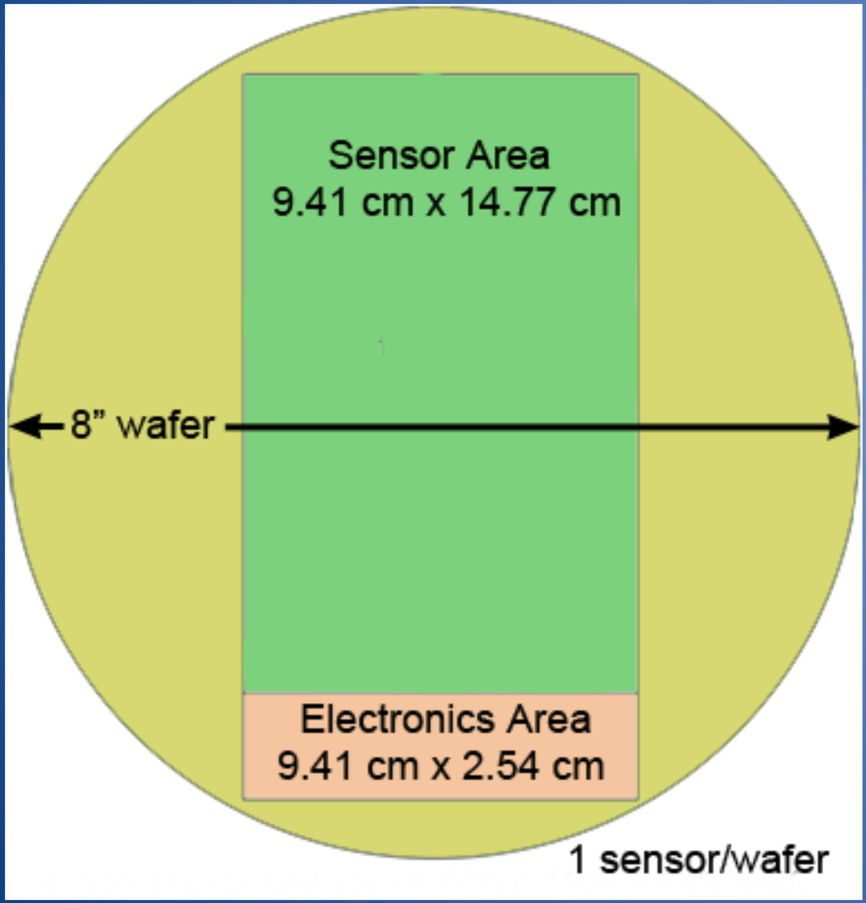
Single pixel Schematic. Photodetector covers ~85% of surface area.



Readout in row-sequential ‘rolling-shutter” mode

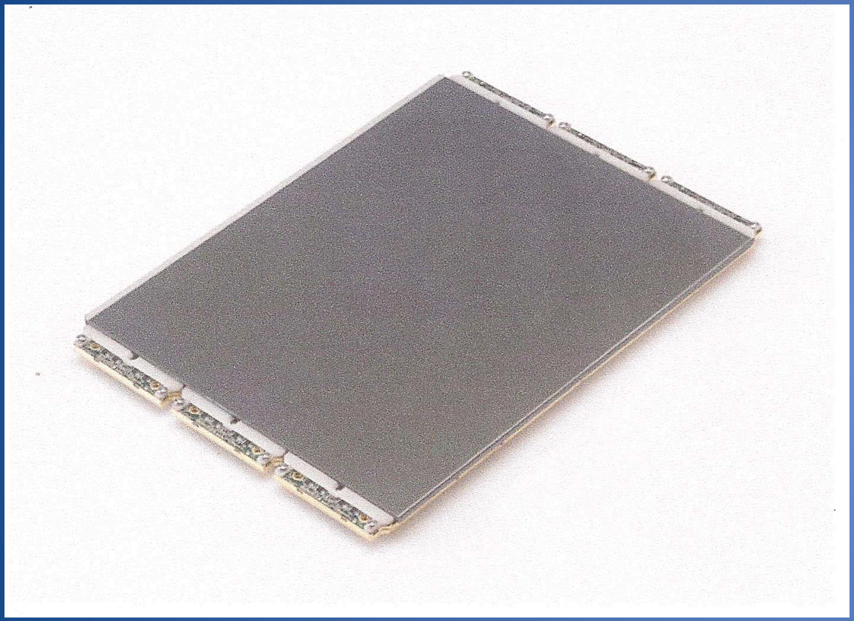
New Sensors Are Improved

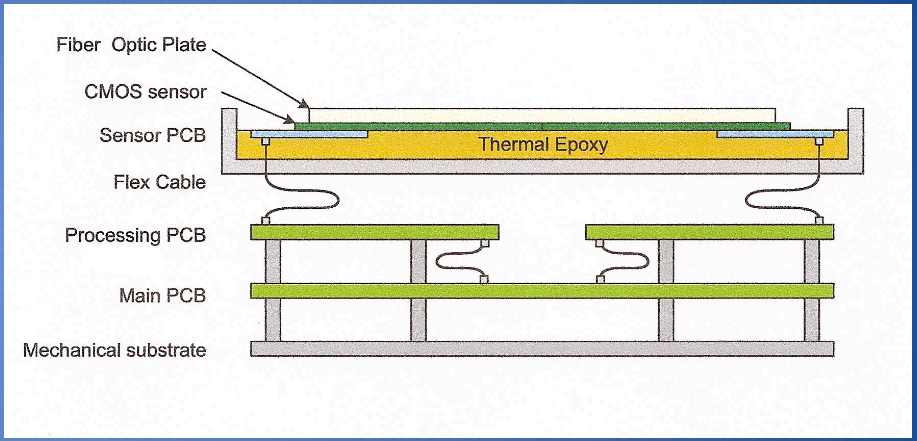
Produced by Teledyne/Dalsa/Rad-icon Imaging in 2011 to our specifications



- Based on a design for mammography and angiography detectors
- 10 cm x15 cm sensors come from an 8" silicon wafer (1 sensor/wafer!)
- Improved readout speed (up to 30 Hz) and better dynamic range
- Improved radiation hardness and linearity
- Still 3 side buttable.

New Generation of CMOS Imaging Systems



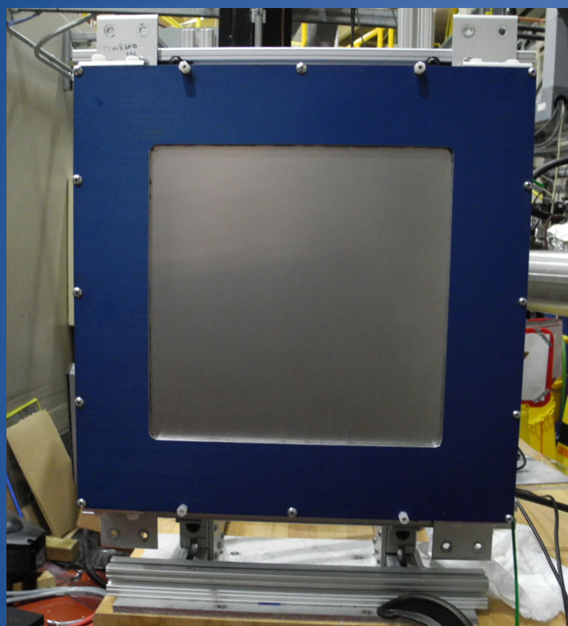


3x2 array of 10 x 15 cm sensors gives a

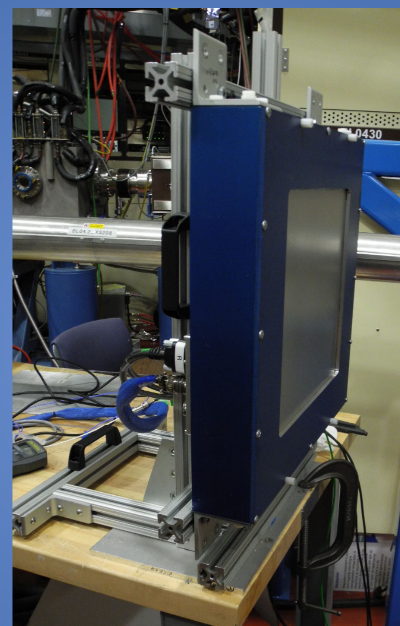
28.2 x 29.5 cm imaging area

Teledyne/Rad-icon separated the sensor and electronics, so we have access to the back side of the sensor, for cooling.

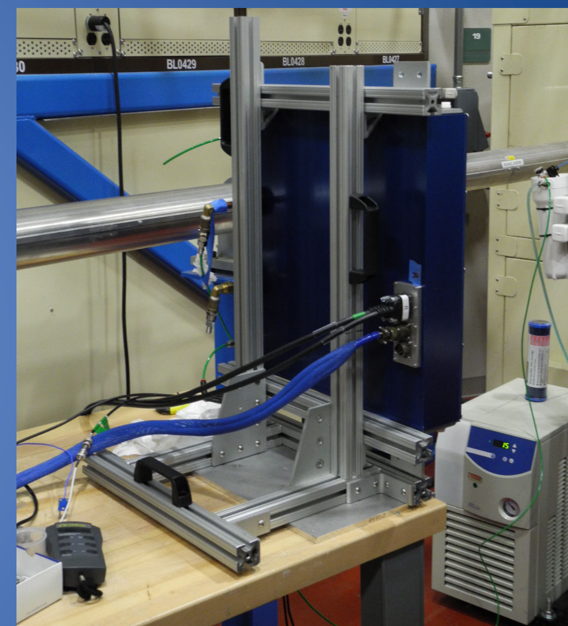
Pictures of the CMOS Detector



Front View

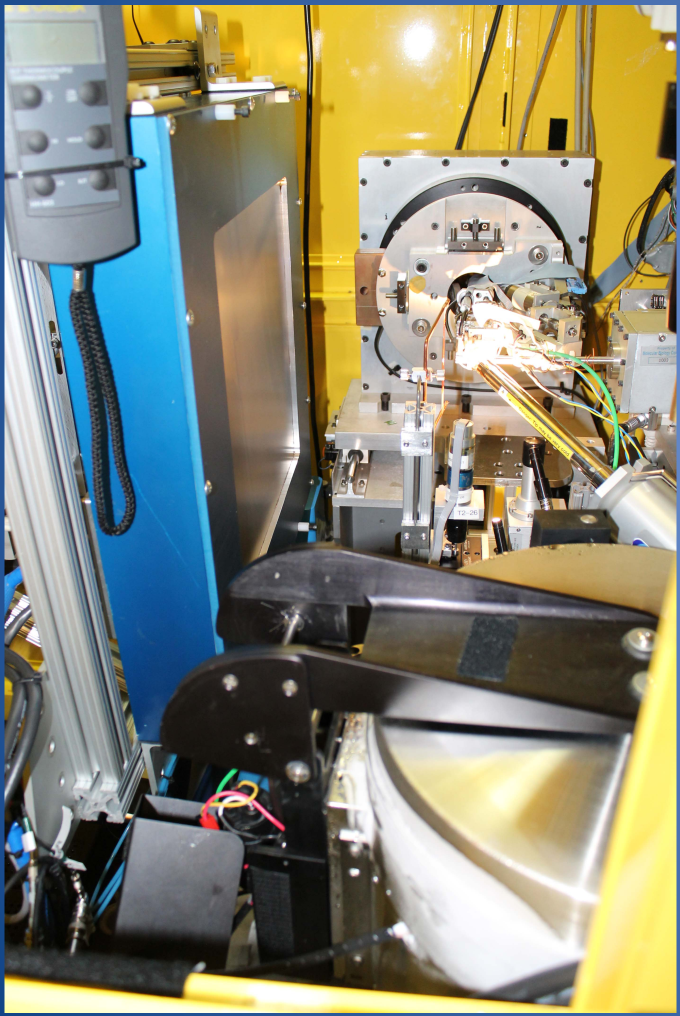


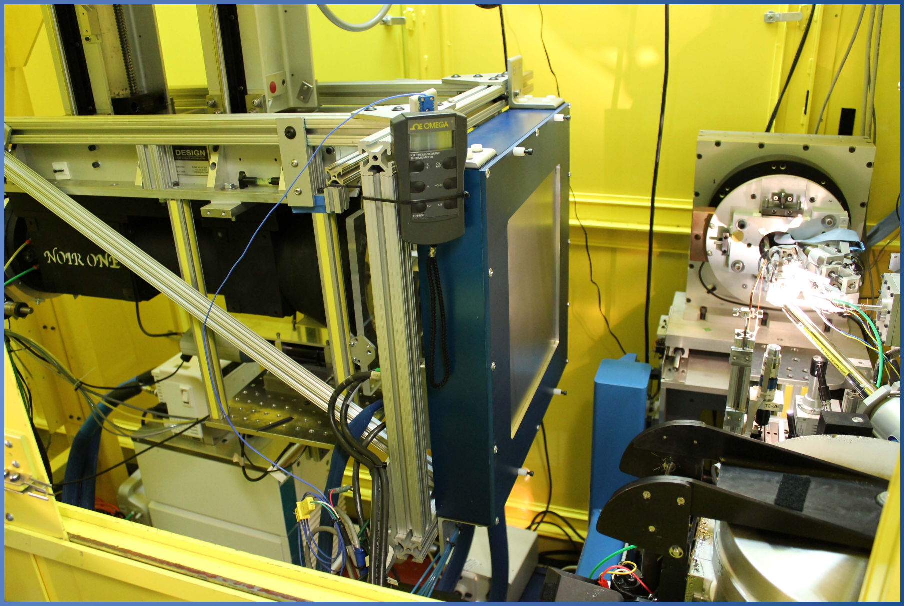
Side View



Rear View

Detector in ALS Crystallography Hutch





Blue Box is 50cm x 50cm, and is 10cm deep.

Specifications of CMOS Detector

- Size: 28.2 cm x 29.5 cm; 2820 x 2952 pixels, each 100.1 x 100.1 microns.
- Speed: readout in 0.033 sec; sustained data rate up to 30 frames per second, with **no** shutter.
- High gain: signal from one 12keV X-ray photon is ~ 400 electrons stored in the pixel.
- Read noise ~ 175 electrons.
- Dark signal < 25 electrons/sec/pixel, @ -20°C. Dark noise in a 0.1second image: ~1 electron.
- Dynamic range ~14,000.
- Detective Quantum Efficiency ~ 60%.
- Light weight: 32 kg

CMOS Detector Allows Shutterless Acquisition

(It can't be done with a CCD instrument)

We now routinely collect at ALS in completely shutterless mode.

Our standard procedure is to collect 1,800 images, each 0.1˚ and 0.1 second long (3 minutes total run time, 180˚ total angular coverage).

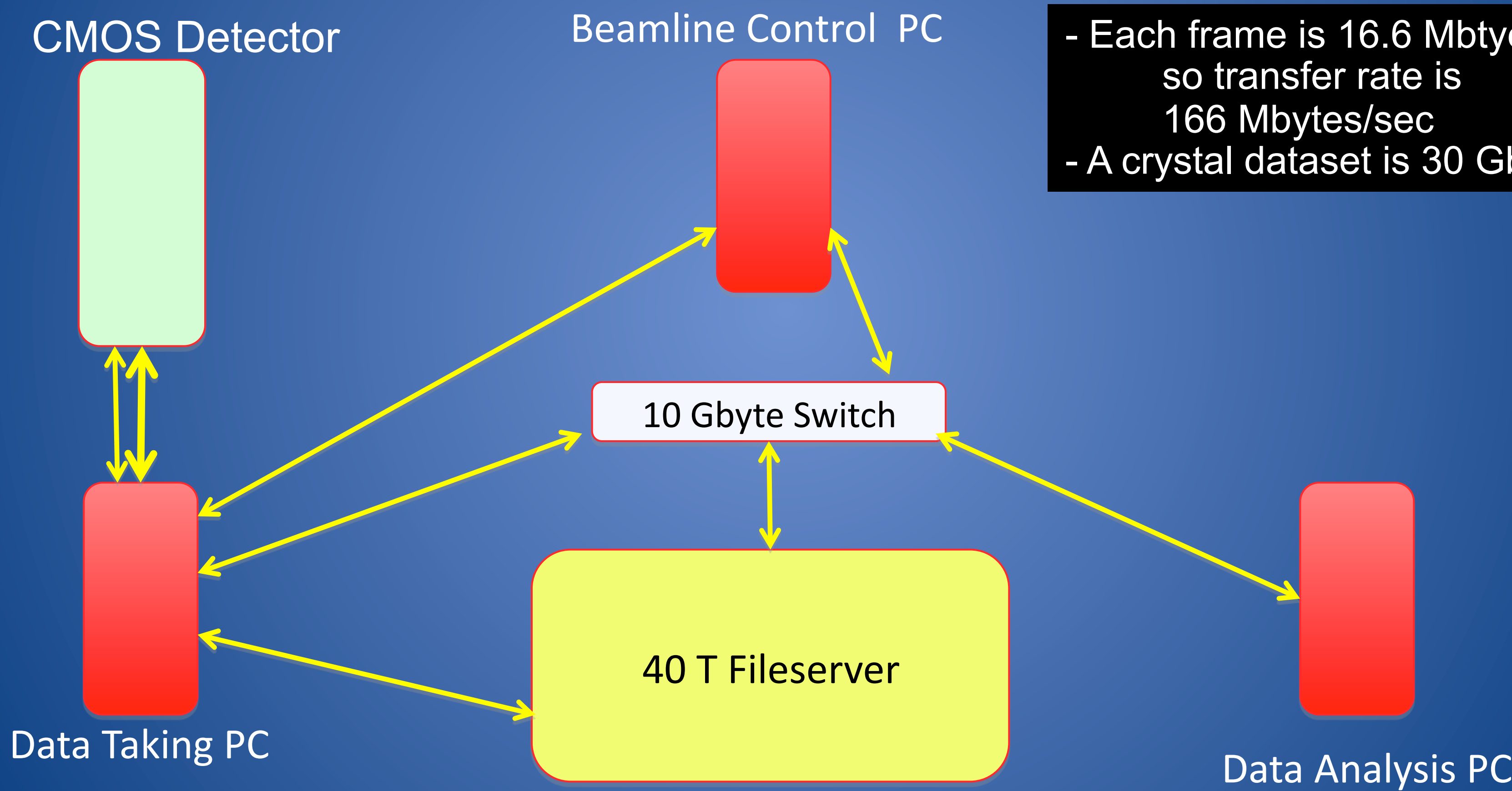
These data are processed (dark subtracted and nonuniformity corrected) as separate images – typically 1,800 images with 0.1˚/image.

Sets of 5 contiguous images can be grouped together, processed and available as a dataset of 360 images, 0.5˚ per image for rapid analysis at user request.

Hardware Configuration

(similar to an existing system on the ALS microtomography beamline)

- Each frame is 16.6 Mbtyes so transfer rate is 166 Mbytes/sec
- A crystal dataset is 30 Gbytes



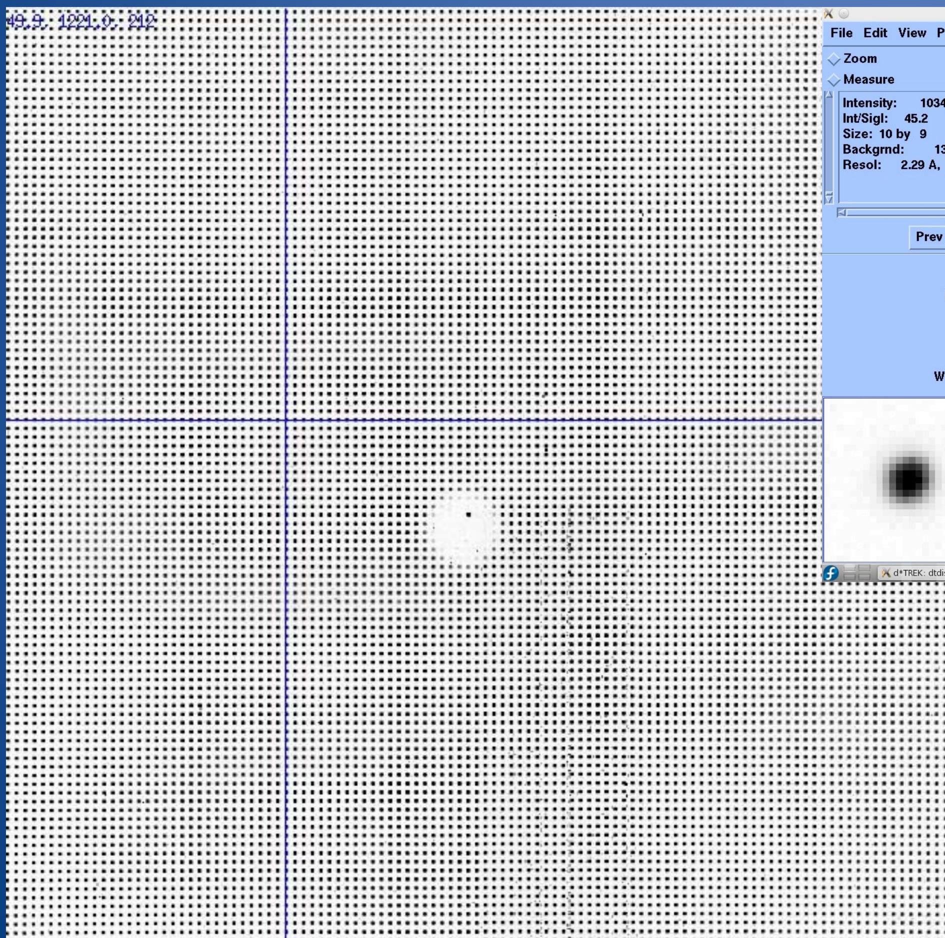
Features of Hardware

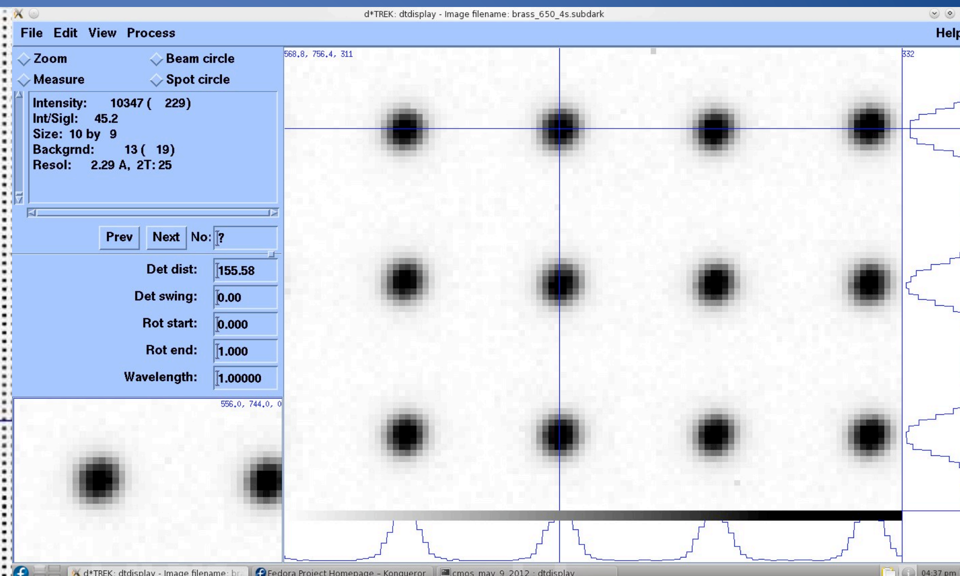
- Detector linked to PC through a commercial Cameralink interface (492 Mb/sec).
- Data-collection PC: 6-processor Intel running Windows 7; 64 Gbyte memory, SSD disk.
- File server: 40Tb, 12-disk configuration with high speed (10Gb) link to data PC.
- Data analysis PC: 64 Gb memory with 6Tb local disk drives, running Linux.
- Fast Link to Beamline Control Computer

Software Features

- Data Acquisition Computer
  - Windows 7;
  - Takes data from Detector and stores RAW data locally on SSD drive;
  - Corrects data for pixel variations and stores corrected images;
  - Calculates and stores summed images;
  - Transfers data to file server with high speed 10 Gbyte link;
  - Real time display of images available on monitor;
  - Provides snapshots, image statistics to beamline control computer, for on-line data display and analysis (overflows, beam centering, etc).
- Data Analysis Computer
  - Linux;
  - Rapid crystallographic analysis of data during and after crystal exposure;
  - Analysis using standard processing software (XDS, D*Trek, Mosflm, and/or HKL3000).

The "brass plate" image shows there is no distortion or gaps between the 6 sensors

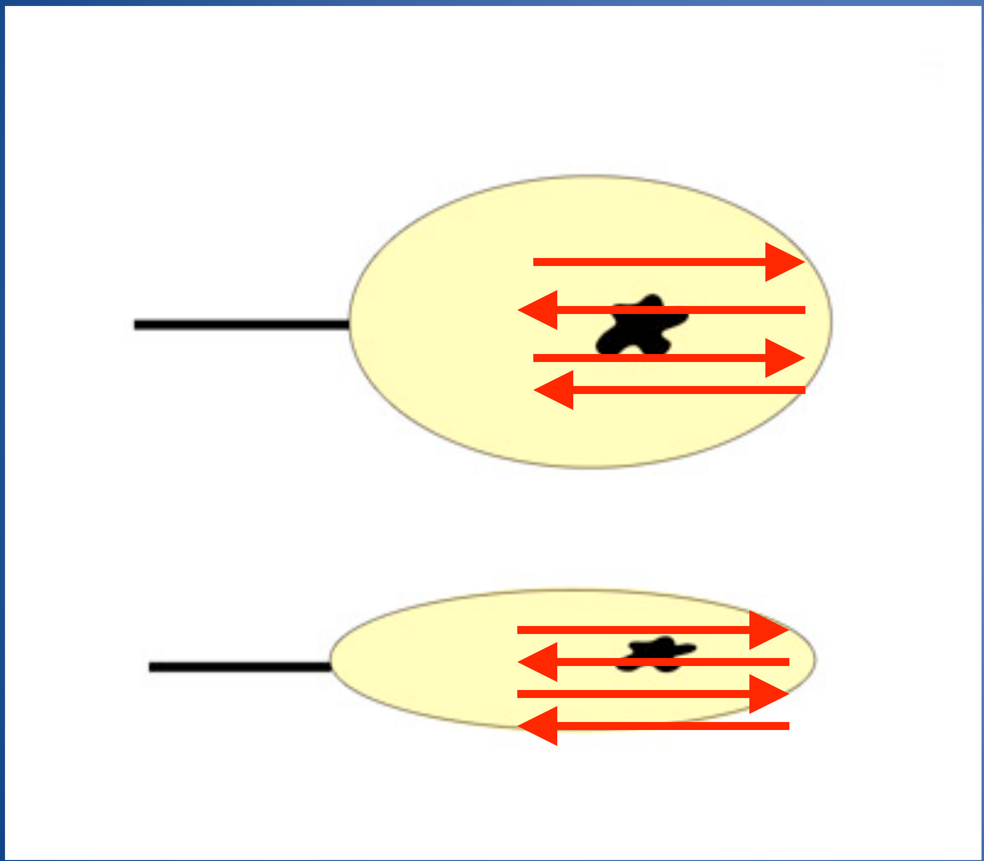




Close-up image

Point response same as CCD system (same phosphor used).

CMOS System Allows Automated Centering



Use fast collimator to scan beam across the loop while taking diffraction data continuously

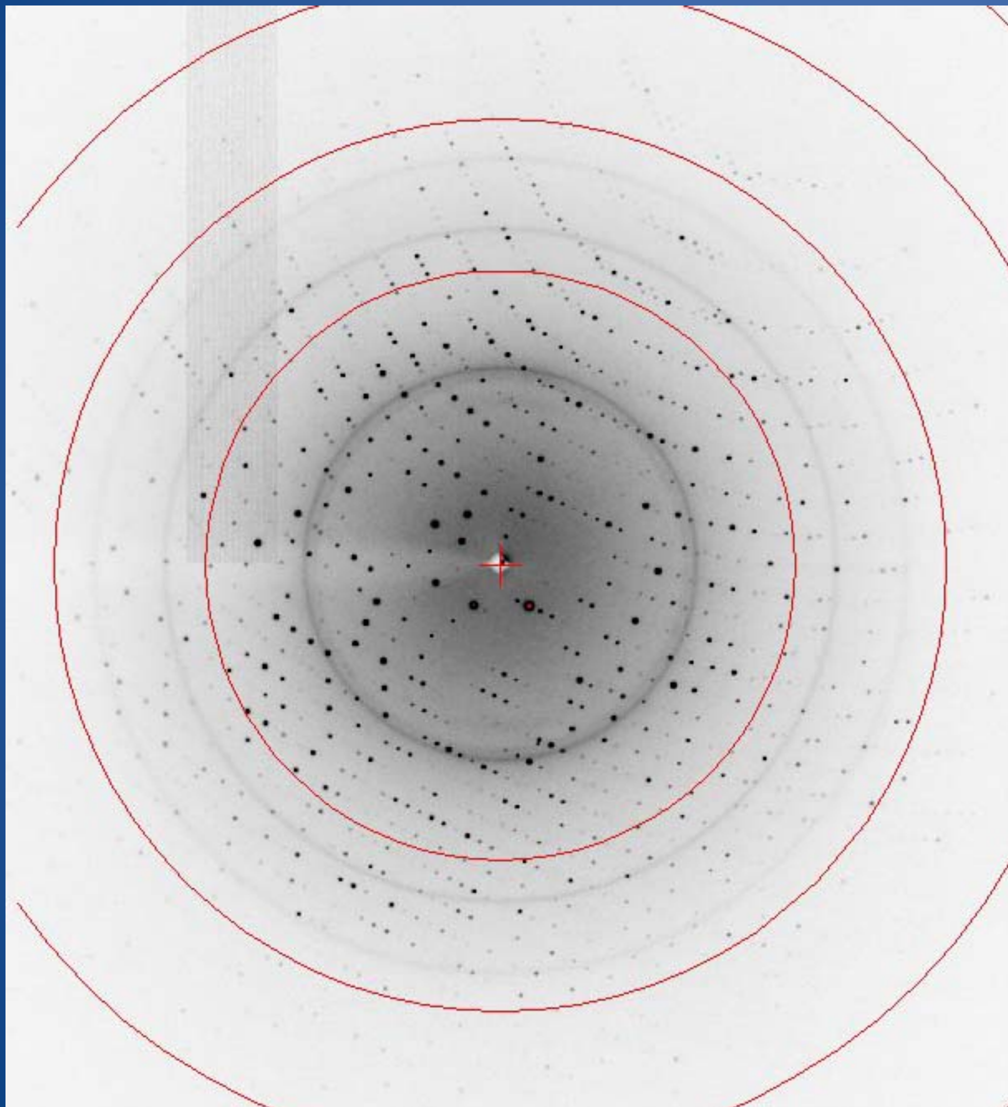
Rotate goniometer 90 deg and repeat measurement

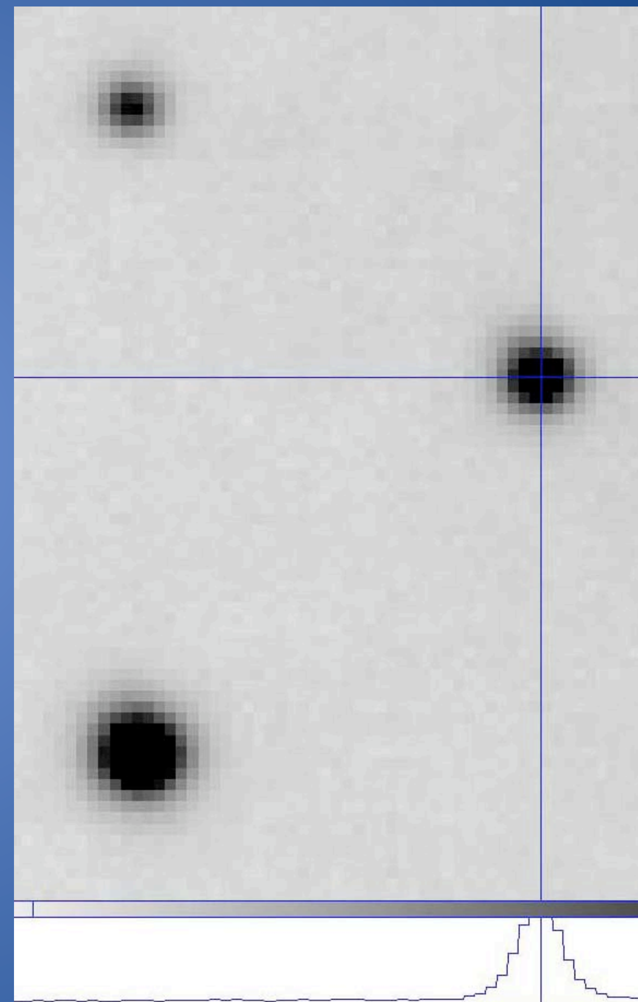
Calculate the **integrated diffraction data** at each point to find the best spot to take complete dataset

Move crystal to spot and take dataset

With Simon Morton collimator it could be done in < 30 sec

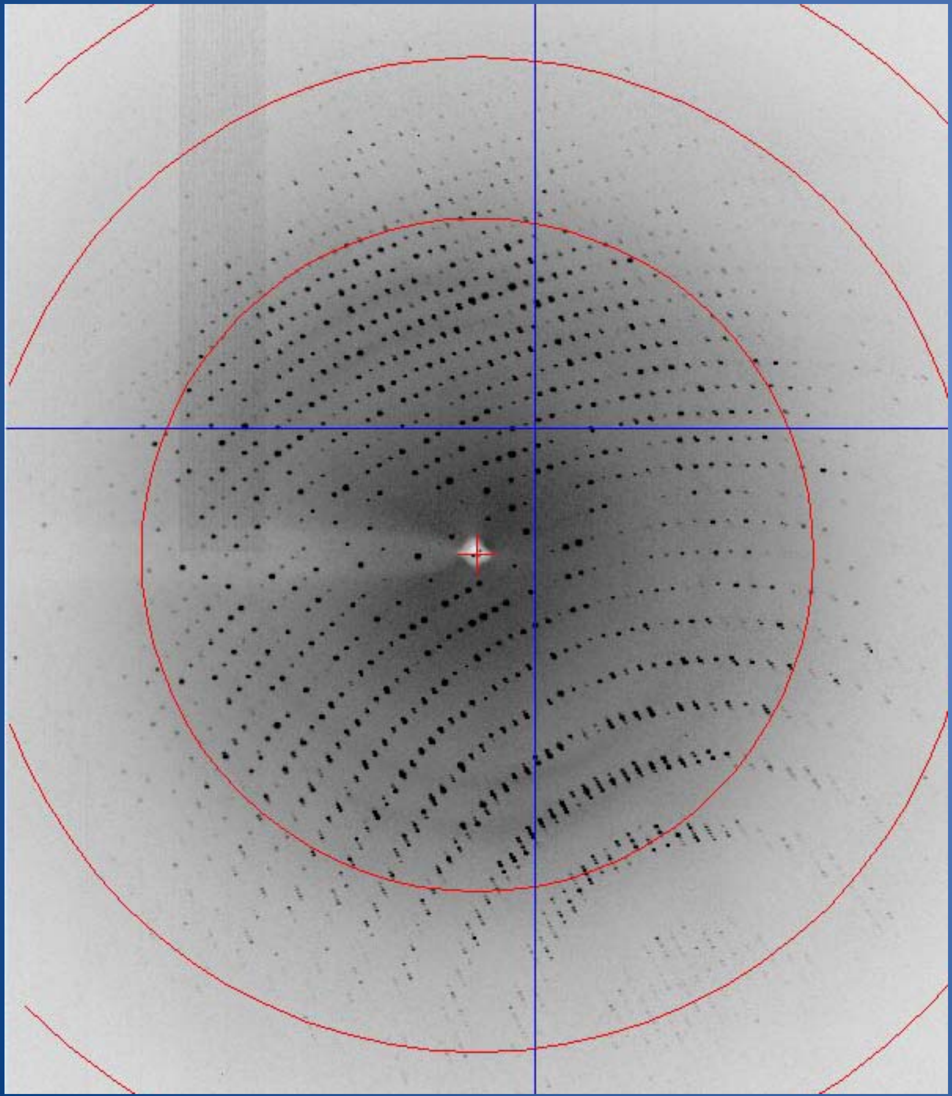
Diffraction Image of Lysozyme

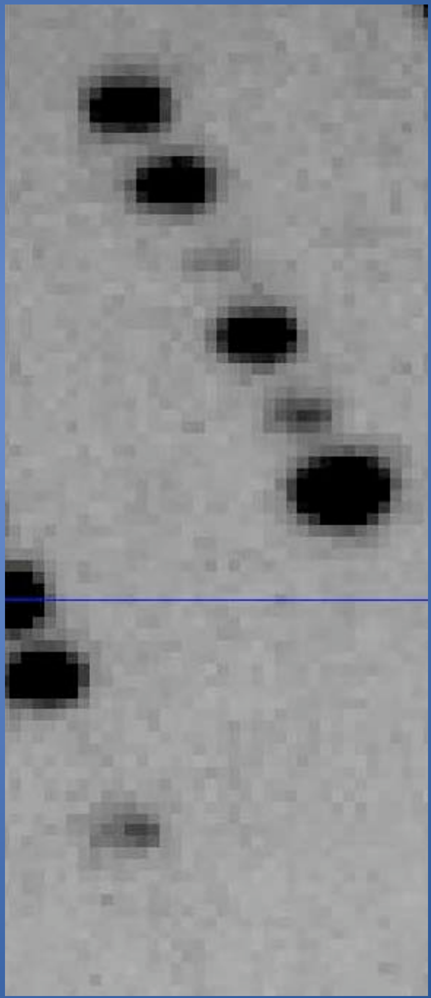




Lysozyme 1.5Å datasets typically have ~3% Rmerge

Diffraction Image of Crystal gc202: a "big cell"





214.4mm Distance,

0.3sec per 0.1degree Frame.

1,800 frames record in 9 minutes.

5% Rmerge to 1.8Å

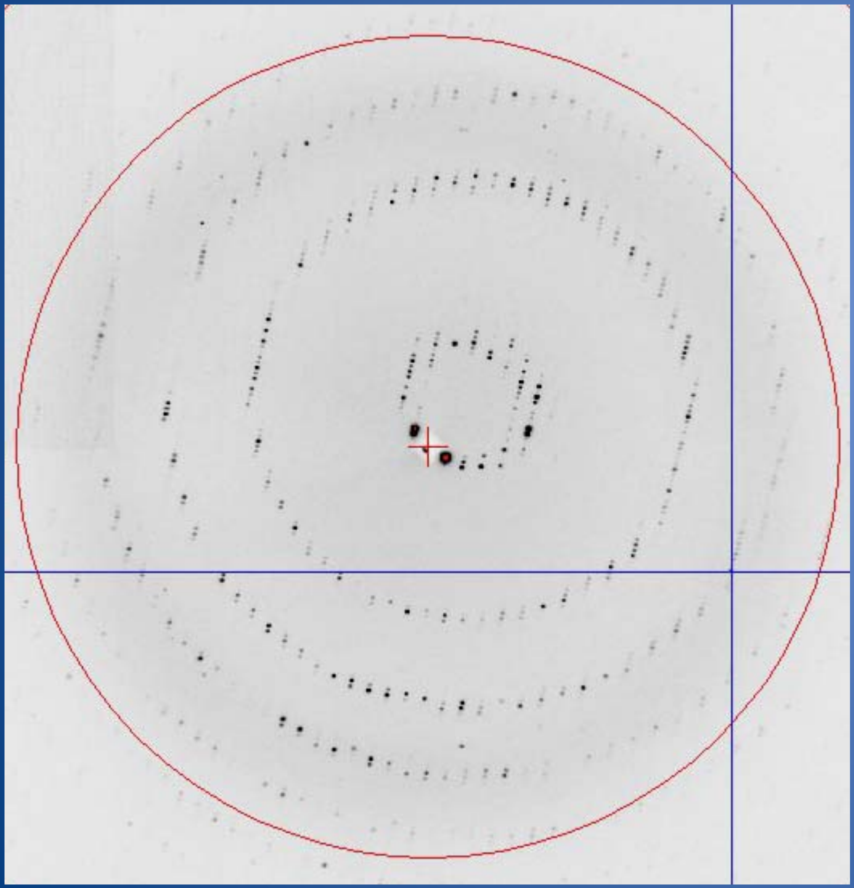
Processing of Datasets

- Good processing results with D*Trek, XDS, Mosflm; HKL will be available soon.

- Best results from XDS.

- Consensus of independent review committee: CMOS data are much better than CCD data: higher resolution, better statistics.

Histidine Acid Phosphatase
(courtesy Jack Tanner, U. Missouri)
data collected Jan 2013



Diffraction Image #1

Structure cartoon.
Solved by SAD phasing
With 3 minutes of data.

Analysis of Histidine Acid Phosphatase

Unit cell: 62 x 62 x 211 Å, $P4_12_12$

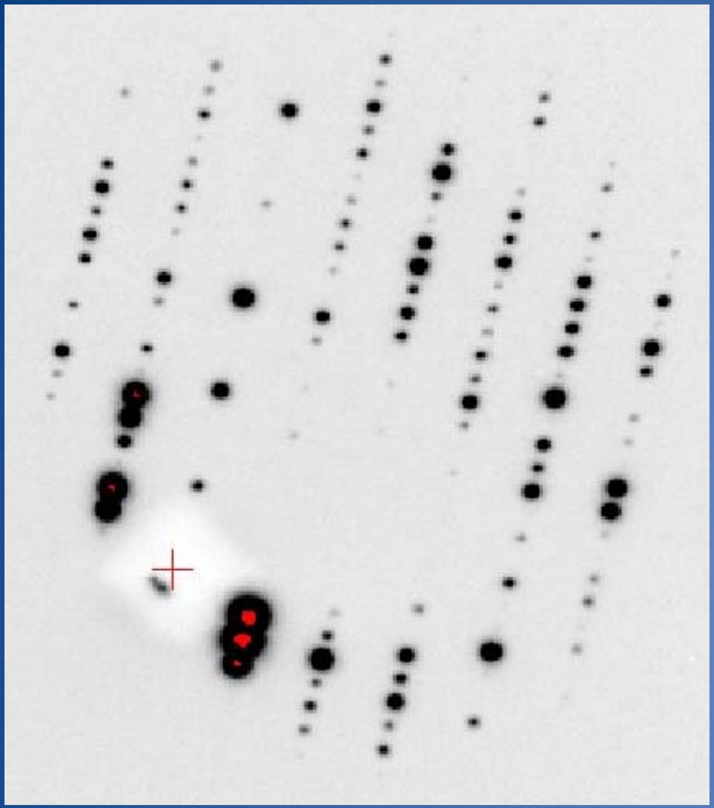
1,800 data frames, each of 0.1sec, 0.1degree (180 degree total rotation range). 3 minutes. Max resolution 1.80Å. Equivalent CCD data required 6x slower angular rotation speed (6 sec/degree).

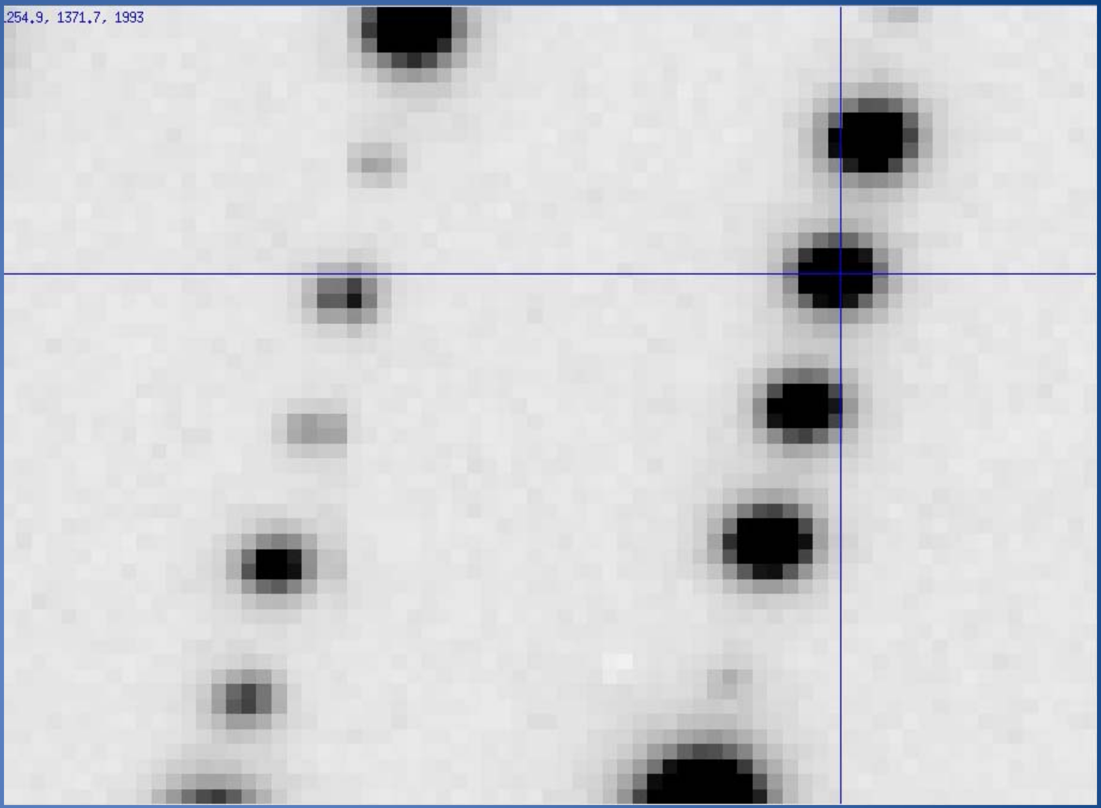
541,002 total Bragg peaks, 39,295 unique (13.8 redundancy). 99.8% completeness.

Rmerge: 2.9% overall (1.0% in inner shell).
Mean I/σ: 26.8 overall (67.7 in inner shell).

Solved immediately by Selenium SAD.

Histidine Acid Phosphatase

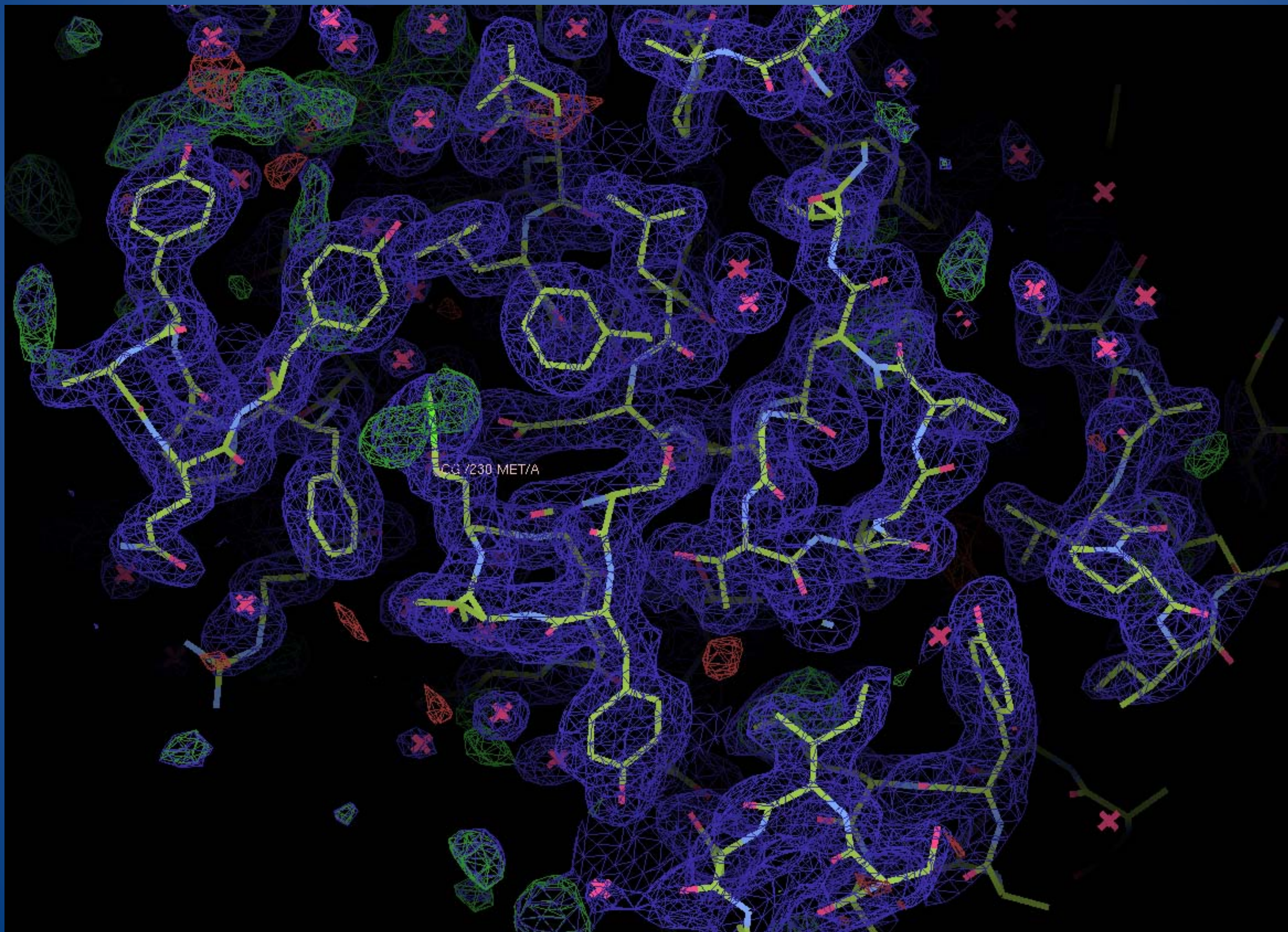




Overlay of 20 images (2°), Showing 4/1 screw axis

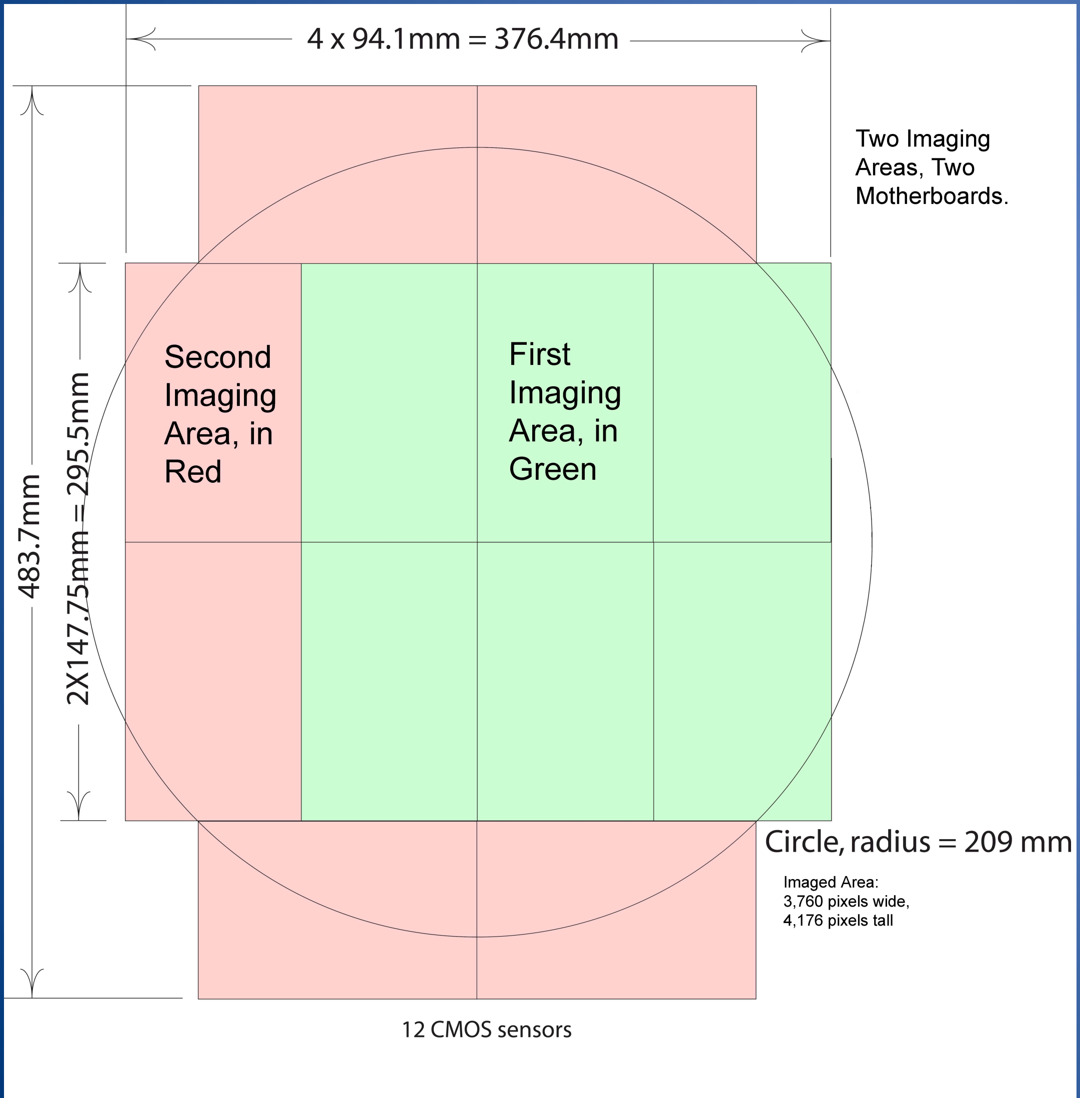
Closeup, showing complete resolution of Bragg spots separated by 0.8mm

Electron Density Map of Histidine Acid Phosphatase; crystallographic Rfactor: 18%



CMOS systems can be scaled in size, while cost remains modest

There is little added complexity from adding more modules



-12 module system, 38cm x 48cm, 3760x4176 pixel array (Pilatus 6M is only 2463x2527 pixels).

-Pilatus cannot be easily scaled, and remains costly.

- More pixels, and more angular resolution, yield greater information density.

-30 Hz max (at least 10 Hz easily realizable) readout cycle.

-No image gaps: image remains simply connected.

Conclusions

- CMOS detectors provide a way to dramatically improve synchrotron based experiments:
  - large area at reasonable cost
  - high frame rates (30 Hz today)
  - readout while acquiring: shutterless collection
  - good dynamic range

- CMOS system provides equivalent data quality as that recorded on a CCD system, with ¼ - ⅙ the total X-ray dose: greater sensitivity, greater I/σ. Therefore reduced X-ray damage = better data.

- Fine (0.1°) angular resolution increases information density through 3-D data processing, relative to coarse (1°) angle resolution, typical of CCD data sets.

- Modest cost relative to Silicon pixel array detectors (SPAD). CMOS system has no image gaps, finer pixel raster, so better spatial resolving power than SPAD. It can also easily be scaled in size.

Acknowledgments

- Software by Bill Lavendar
- Detector developed in collaboration with Teledyne/Rad-icon Imaging Corp.
- Experiments at ALS beamline 4.2.2
  - Beamline scientist Jay Nix
  - Beamline technician Chuck Lindquist
- Scientists at MBC and BCSB contributed their crystals and crystallographic expertise