A large area CMOS detector for shutterless collection of x-ray diffraction data

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Abstract. Recent developments in CMOS devices have improved their radiation hardness, response linearity, readout noise and thermal noise, making them suitable for x-ray crystallography detectors. Large (14.8 x 9.4 cm) CMOS sensors with a pixel size of 100 x 100 microns are now available that can be butted together on three sides. We have fabricated a 6-tile system in a 2x3 array with a 28.2 x 29.5 cm continuous imaging area. To make an x-ray detector the CMOS sensor is covered with a 3 mm flat fibre-optic plate (for radiation protection) and a Gd₂O₂S:Tb scintillator screen. A special feature of these systems is that they can be read out continuously at 10 frames/sec with excellent dynamic range without interrupting data collection.

We have installed this system at beamline 4.4.2 of the Advanced Light Source synchrotron. Anomalous diffraction data were recorded without an x-ray shutter, rotating the crystal sample continuously with an exposure time of 0.1 sec/frame and a rotation speed of 1°/sec for 180 degrees. The 1,800 frame datasets were processed in D*TREK and XDS data analysis programs and experimental phases were determined in PHENIX. The crystallographic results are typically significantly better than equivalent data recorded on a conventional CCD system, due to the 10X finer angular resolution of the recorded data. Very large systems can now be made that would have an active area of 56 x 59 cm² with 33 x 10⁶ pixels.

1. Introduction

Large area Complementary Metal Oxide Semiconductors (CMOS) detectors are now available with sufficient radiation tolerance and response linearity that they are now suitable for demanding scientific applications such as x-ray crystallography. The readout noise and readout speed have also been significantly improved in the last five years. Hasegawa et al¹ in 2009 used a single large CMOS device to demonstrate the advantages of these detectors for x-ray crystallography experiments. We have now developed a CMOS sensor with an active area of 9.4 x 14.8 cm² with 100 x 100 µm² pixels. The sensors are buttable on three sides so systems can be built with a large active area with no gaps between sensors. A special feature of these chips is that they can be read out continuously; while one pixel is being read, all the other pixels remain active. This feature allows x-ray diffraction data to be acquired in a shutterless mode, in which the crystal is rotated smoothly through 180° while 1800 image frames are recorded.
2. Description of Detector

We have developed a detector system suitable for use at synchrotron facilities. It is a 2x3 sensor array with an active area of 28.2 x 29.5 cm. As shown in Figure 1 the system has no gaps between sensors. The top of the sensor is covered with a 3 mm thick fiber-optic plate (to protect it from radiation damage), on top of which is placed a thin Gd₂O₂S:Tb phosphor plate that converts the incoming x-rays to optical photons, which are detected by the sensors. The sensors are cooled to below -5° C to reduce thermal leakage noise. Figure 2 shows how the system is packaged with the electronic processing cards below the detector with room to insert a cooled copper plate to cool the sensors. The direct coupling between the phosphor plate and the CMOS sensor gives high conversion efficiency to the system so that one 12 keV photon produces about 400 electrons in the chip. The dark accumulation rate is about 25 electrons/pixel/sec and the readout noise is about 180 electrons. The sensors are readout with 6 analog readout cards that each have five analog channels that use 14-bit digital to analog convertors that can be readout as fast as 30 Hz to a PC using a CameraLink interface. The complete system is mounted inside a 50 x 50 x 10 cm aluminum box weighing 32 kg with the analog processing cards mounted below the sensor and the digital interface card below the analog cards. The box has a 250 µm Be entrance window as shown in Figures 3. The detector is coupled to a fast PC with 64 Gbyte of memory and a 40 Tbyte fileserver. Another PC is coupled to the fileserver to enable rapid data analysis immediately after a data sequence is acquired. This allows data analysis of one data set to be done while another data set is acquired.

Figure 1. 2x3 array of six large-format CMOS sensors to cover a large imaging area.  
Figure 2. Arrangement of detector and electronic cards that permit cooling of the sensors.

3. Detector Performance

The commercial version of this detector was installed at the Molecular Biology Consortium beamline (4.2.2) of the Advanced Light Source. A brass plate with 1 mm holes spaced uniformly in a 5 mm grid was used to verify the minimal spatial distortion and a thin gold foil sample was used to calibrate the dose response and linearity of all pixels. All pixels are corrected for their individual background count rate and gain before the images are written to disk.

The detector performance was measured by collecting diffraction data on a series of crystals from Olve Peerson of Colorado State University and Jack Tanner of the University of Missouri. Data were typically collected in shutterless mode over 180° with rotation speed of 0.2 - 1° per second and an image frame rate of 0.1 – 0.5 seconds per frame. Thus, 1800 images with an angular resolution of 0.1° per image can be collected in 3-15 minutes. Figure 4a is a single frame taken of a lysozyme crystal with an exposure time of 0.1 second and an angular range of 0.1°. Figure 4b is an enlarged part of a data frame taken of a crystal of histidine acid phosphatase (HAP), courtesy of Dr. Tanner, in which the spots, separated by only 0.8 mm, are clearly resolved.
3. Data analysis
Dr. Tanner had substituted selenium for sulfur in the methionine residues of his HAP protein. Therefore diffraction from these crystals, stimulated by 12,700 eV x-ray radiation, exhibit an anomalous dispersion component to their Bragg reflections (the absorption edge of selenium is 12,658 eV). We collected 900 images, each of 0.2° and 0.2 sec/frame, for a total rotation range of 180°. The dataset was taken in 6 minutes at 12,700 eV with a detector-to-crystal distance of 150 mm. Data were processed both by Jim Pflugrath’s dtprocess\textsuperscript{3} and by Wolfgang Kabsch’s XDS programs\textsuperscript{4}.

The structure of histidine acid phosphatase (HAP) was solved with a single crystal. The HAP unit cell is 62 x 62 x 211 Å, P4\textsubscript{2}12\textsubscript{2}. The dataset refined to a crystallographic R-factor of 18%, which is
excellent for protein structures. The data processed with XDS to a resolution of 2.0 Å, as shown in the following table.

| RES  | Rmerge | I/sig | completeness | redundancy | Anom R |
|------|--------|-------|--------------|------------|--------|
| 5.95Å| 3.2%   | 60.0  | 92.0%        | 6.95       | 5.87   |
| 4.23Å| 2.9%   | 61.5  | 98.8%        | 7.66       | 4.14   |
| 3.00Å| 3.7%   | 47.0  | 99.9%        | 7.76       | 3.04   |
| 2.68Å| 5.2%   | 34.2  | 99.9%        | 7.78       | 2.40   |
| 2.27Å| 9.1%   | 20.3  | 99.8%        | 7.76       | 1.57   |
| 2.12Å| 12.2%  | 15.9  | 99.7%        | 7.73       | 1.36   |
| 2.00Å| 18.3%  | 11.0  | 99.1%        | 7.68       | 1.15   |
| Average | 5.0% | 30.8  | 99.3%        | 7.71       | 2.22   |

4. Summary
The new generation of large CMOS sensors with excellent sensitivity, linearity, radiation hardness and fast readout speed allow the fabrication of detector systems with improved performance compared to CCD systems. The ability to readout the detector while acquiring data reduces the time to take a complete dataset since the goniometer does not need to be oscillated as it does for CCD systems. In addition, taking more frames in a fine-phi slice mode produces higher quality data that can be refined to higher resolution than the standard 0.5° datasets used in standard CCD systems.

The CMOS technology we have developed now permits the fabrication of very large imaging x-ray detectors for macromolecular crystallography. We have recently developed a technique by which we can butt together our CMOS sensors on all four edges, with minimal restrictions. We can now make 12-tile, 18-tile, and 24-tile systems that can cover contiguous circle diameters respectively of 37.6 cm, 48.3 cm, and 56.4 cm as shown in figure 5. The 42.5 cm circular coverage of the Dectris Pilatus 6M silicon pixel array detector is also shown for comparison. Single sensor systems are also available.

![Diagram of three possible large CMOS detector configurations and the Pilatus 6M detector.](image)

Figure 5. Diagram of three possible large CMOS detector configurations and the Pilatus 6M detector. The CMOS systems would have 100x100 μm² pixels and the Pilatus has 172x172 μm² pixels.

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