

The intensifier-coupled CCD has a higher DQE compared with the fiber-coupled CCD and the imaging plate. The measured DQEs of the above three types of the detectors will be compared quantitatively and the physics of noise propagation underlying the DQEs of these detectors will be discussed. Other performance characteristics such as dynamic range, linearity of response, and image distortion will be also compared among the three types of the detectors. Finally, advantage and disadvantage of the three types of x-ray detectors ("imaging plate", "intensifier-coupled CCD", and "fiber-coupled CCD") will be discussed from the viewpoint of application for macromolecular crystallography.

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**MS01.04.03 IMAGING PLATE DATA PROCESSING FOCUSED ON CHEMICAL CRYSTALLOGRAPHY.** T. Higashi, Rigaku Corporation, 3-9-12 Matsubara-chi, Akishima-shi, Japan 196

Rapid data collection using an area detector developed for protein crystallography is now successfully applied to small molecule crystallography, especially when crystals are unstable. As far as imaging plate data processing is concerned, however, software strategy suited to chemical crystallography is not yet completed.

In a physical sense, diffraction phenomena do not discriminate small molecule or macromolecule crystals, difference is just size of cell dimensions, i.e. a protein data acquisition method can be straightforwardly applicable to small molecules, except a few points.

- 1) Alpha-1 alpha-2 splitting of spots, resulting in re-consideration of a measurement box. One solution could be superposition of two separated spot boxes. Local profile fitting of DENZO may compensate it to some extent, or a dynamic box based on the seed-skewness method would be another possibility.
- 2) Less dense reciprocal lattice points, causing sometimes difficulty in indexing. Real space indexing would be a solution. On the other hand, an area detector loses benefits of four-circle diffractometry in the points.
  - 1) Less accurate cell constants, arising from rough estimation of diffraction geometry. Direct two-theta measurement of reflections, calibrated with a standard powder sample, may be required.
  - 2) No experimental absorption correction, such as a psi-scan method, available. Since easy DIFABS correction is banned in Acta Crystallographica, an alternative method is highly required. Discussed will be some solutions to those problems.

**MS01.04.04 AN EXTREMELY FAST DIRECT PHOTON COUNTING DETECTOR FOR PROTEIN CRYSTALLOGRAPHY.** Ng.H. Xuong<sup>1</sup>, P. Datte<sup>1</sup>, E. Beuville<sup>2</sup>, T. Earnest<sup>2</sup>, H. Padmore<sup>2</sup>, J. Millaud<sup>2</sup>, D. Nygren<sup>2</sup>, Department of Physics, UCSD, La Jolla, CA 92093-0359<sup>1</sup>. Lawrence Berkeley Laboratory, Berkeley, CA 94720<sup>2</sup>.

A Smart Pixel Array Detector (SPAD) is being designed which will collect a complete set of monochromatic data for protein crystals in 1.5 minutes and a good Laue picture in less than 10 ms. The readout will also allow framing of up to 16 successive Laue pictures with a switching time of less than 100  $\mu$ s between pictures. The SPAD will consist of 1000 x 1000 pixels of 150  $\mu$ m x 150  $\mu$ m in size<sup>1</sup>. The system is being designed around the Column Readout Architecture presently being developed at LBNL<sup>2</sup>. The column readout will allow a photon count rate of 1 million (photons/second) at the pixel and a photon count rate of 8 million

(counts/sec/column) total output (i.e. up to 8 billion counts per second for the complete detector). Each pixel has its own preamplifier, shaper, discriminator, and a 3 bit prescaler. The material used for the detector will be Si, however we are investigating the use of CdZnTe for measurements that require a larger photon dynamic range or a higher monochromatic photon energy. The data will be stored in real time, in a large histogram memory capable of gathering data for 16 successive pictures. The preliminary results of an 8 x 8 prototype of both Si and CdZnTe will be presented.

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**MS01.04.05 THE DEVELOPMENT OF MAD PROTEIN CRYSTALLOGRAPHY AT THE ESRF.** A. Thompson, V. Biou ESRF, Grenoble and IBS, Grenoble, L. Claustre, F. Felisaz and A. Thompson EMBL, Grenoble Outstation, A. Gonzalez ESRF Grenoble, current address EMBL Grenoble Outstation, J. Helliwell University of Manchester, J.L. Smith Purdue University and EMBL, Grenoble Outstation, A. Hammersley and P. Thorander ESRF, Grenoble

BL19, has been built on a bending magnet at the ESRF as a collaboration with EMBL Grenoble, and is a dedicated beamline for the measurement of Multi-Wavelength Anomalous Diffraction (MAD) data. The beamline has been operational in commissioning mode since June 1995, and in user mode since September 1995.

The power of the MAD technique for rapidly solving structures using a dedicated beamline with very stable beam is illustrated by the fact that 6 new structures (phased solely using MAD) are already in an advanced state of refinement, with good electron density maps available from other samples. The size of problems successfully tackled has varied from 12 kDa to 39 kDa, with various anomalous scatterers (Se-Met, Fe, Sm, Hg). In favourable cases it has even been possible to solve the anomalous Patterson and examine the initial MAD map during the data collection time. It would be true to say that MAD is now a routine technique at the ESRF for reasonable sized proteins (up to 20 kDa) with several anomalous scatterers (Se-met or good derivatives) and reasonable (a few percent) anomalous signal. With a fast readout detector, powerful local computing permitting online integration and scaling of data, and a combination of direct methods or Patterson search routines, an initial map could be arrived at in 48 hours permitting users to leave the synchrotron with HKL I|F| and phi.

Further development at the ESRF includes the use of a CCD based detector for rapid measurement (3.4 s per image to 16 bits, and 0.4 s per image to 12 bits), investigation of the impact of phislicing and dynamic range extension on the quality of MAD data (particularly at high resolution), the development of data collection and strategy software to ensure correct coverage of Bijvoet mates, and the development of an undulator beamline for MAD measurements (to be operational by the end of the decade).

The advantages of a high intensity, collimated, stable beam for MAD will be discussed and illustrated with examples of data collected on the beamline using both image plate and CCD detector. Data collection strategy will be discussed for both cryo-protected and unprotected crystals, and future possibilities indicated.