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A xenon-filled multiwire area detector for X-ray diffraction.

By CARL CORK, RON HAMLIN, WAYNE VERNON and NGUYEN HUU XUONG, *Departments of Physics, Chemistry and Biology University of California, San Diego, La Jolla, CA* 92037, *U.S.A.*, and VICTOR PEREZ-MENDEZ, *Lawrence Berkeley Laboratory and Department of Radiology, University of California, San Francisco, CA* 94112, *U.S.A.*

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A xenon-filled multiwire proportional chamber with high and uniform photon-detection efficiency has been built and incorporated into a high-speed data-collection system for protein crystallography. This system has been used to collect more than 200 000 reflection intensities from one parent and four heavy-atom derivative crystals of a complex of dihydrofolate reductase and metho-trexate (a cancer drug). Its data collection rate is about 30 times faster than the rate of a standard diffractometer (1400 reflection intensities per hour *versus* 50 reflection intensities per hour). The precision of the chamber data is also better with an intensity reliability R of 5% as compared with 6·7% from the diffractometer data. The difference Patterson maps between parent and heavy-atom derivative data show very clearly the positions of the heavy atoms.

We have reported previously the use of an argon-filled multiwire proportional chamber as an area X-ray detector for protein crystallography (Cork, Fehr, Hamlin, Vernon, Xuong & Perez-Mendez, 1973, 1974). Since then we have successfully built a xenon-filled chamber with much higher photon-detection efficiency, better spatial resolution and more uniform quantum-detection efficiency. This chamber is now incorporated into a high-speed data-collection system for protein crystallography. The system collects reflection intensities at a rate about 30 times faster than a standard diffractometer. The precision of the new data is better than that obtained with the diffractometer.

The advantage of a xenon chamber over an argon-filled chamber is higher photon-detection efficiency. Xenon is, however, much more expensive than argon so the chamber enclosure must be carefully built to reduce gas leakage. The new chamber has three electrodes: one beryllium window and two wire detection planes. The window, made of a flat beryllium plate (1 mm thick), is mounted in electrical contact with the aluminum enclosure. The two detection planes are similar to those in the previously described argon chamber. The center electrode consists of 150 horizontal wires (20 μm stainless steel with 2 mm spacing). The back electrode consists of 300 vertical wires (50 μm of stainless steel with 1 mm spacing). The two wire planes are mounted on 4 mm thick fiber-glass frames and stacked behind the beryllium window. The aluminum enclosure is composed of three parts: a picture frame holding the front window, another picture frame containing the detection planes and a back plate. The three parts are mounted together with O-rings to eliminate gas leakage. There is enough extra room inside the container for the two delay lines used in the read-out process (Cork *et al.*, 1974). All electrical feed-through connections are standard B.N.C. seated in a leak-tight adhesive sealant. The chamber is filled with a gas mixture of 90% xenon and 10% CO_2 at a pressure of about 1 atm. The center electrode is maintained at 2·8 kV, the front window and the aluminum container are grounded. The back electrode is held at -80 V. The front window has to be kept flat to within 0·2 mm to avoid severe pulse-height variation. To avoid further deformation of the front window caused by differential pressure variation we installed a low-pressure input regulator to add more gas mixture when the differential pressure drops below zero. When the differential pressure rises above 0·5 cm of water, the excess gas mixture bubbles out of the chamber through a simple oil plug manometer. It takes about seven liters to fill the chamber and an additional ten to fifteen liters to keep it running for about three months.

The electronic readout and storage system has been described elsewhere (Cork *et al.*, 1973, 1974). When a photon is detected, its position on the chamber is decoded giving a binary coded X and Y address (8 bits × 8 bits); the contents of a corresponding location in the mass core are then incremented by one. After an exposure, the diffraction pattern stored in the mass core can be displayed on a TV monitor. The mass core is also connected to an IBM 1800 computer which is used to extract the integrated intensities of the reflections from the protein crystal.

This multiwire area detector is used together with an ultrastable X-ray generator, a standard copper X-ray tube and a three-circle G. E. goniostat to form a high-speed data-collection system. The chamber is mounted on a moving stage and can be positioned at any distance from the crystal. A helium box is placed between the crystal and the detector to reduce air scattering. The chamber can also be placed at high 2θ (up to 90°) to collect data at high resolution. The crystal orientation is controlled by the IBM 1800 computer with the help of three stepping motors mounted on the goniostat.

With a useful thickness of 0·8 cm the xenon chamber has a theoretical quantum detection efficiency of about 60% for Cu $K\alpha$ X-ray photons. This is about four times higher than with the argon chamber. Because of the absorption of the beryllium window (about 20%), the overall quantum detection efficiency of the new chamber is about 48% or about three times the efficiency of the argon chamber. This ratio is verified by experimental observations. The method used to measure the spatial linearity, resolution and uniformity of the detector has been described elsewhere (Cork *et al.*, 1974). The linearity of the new chamber is similar to that of the argon chamber. The measured position of a reflection on the chamber never deviated by more than two address partitions from the predicted values. Most of the time it falls within one address partition (1·25 mm). The spatial resolution of the new chamber is slightly better than that of the argon chamber. A 1 mm X-ray beam gives rise to a spot with a full width at half intensity of 2·0 mm.

The quantum detection efficiency is uniform enough for us to collect intensity data *without* any correction for non-uniformity. Since, as shown later, our symmetry-related reflection intensities agree with each other to within 5% on the average and since some reflection intensity deviation can be attributed to quantum statistics, we can conclude that

the average nonuniformity of the chamber is less than 5%.

The new multiwire area detector is used routinely to collect data from crystals of a complex of dihydrofolate reductase and metho-trexate (a cancer drug) (Poe, Greenfield, Hirshfield, Williams & Hoogsteen, 1972). This work is done in collaboration with Drs D. Matthews, R. Alden, S. Freer and J. Kraut of the UCSD Chemistry Department. The data-collection method using a series of 'stationary pictures' has been described elsewhere (Cork *et al.*, 1974; Xuong, Vernon, Hamlin, Freer, Cork & Anh, 1974). With one DHFR crystal (space symmetry $P6_1$ with $a=b=93$ Å and $c=74$ Å), a standard diffractometer can measure about 6000 reflection intensities (in 120 h) before the intensities have decreased by 15% in average. The new high-speed data collection system can measure about 168 000 reflection intensities in the same time. However, we usually make only 40 000 intensity measurements (out to 2·5 Å resolution) per crystal, after which the crystal reflection intensities have decreased only about 7%. The precision of the chamber data is also better with an intensity reliability R of 5% as compared with 6·7% from the diffractometer data. The two sets of data also agree with each other ($R=5{\cdot}7$%). We have measured more than 200 000 reflection intensities for one parent and four heavy-atom derivative crystals. The difference Patterson maps between parent and heavy-atom derivative data show very clearly the positions of the heavy atoms. Difference Patterson maps between parent data collected by the diffractometer and the heavy-atom derivative data collected with the multiwire area detector show exactly the same heavy-atom peaks. These maps prove then that the chamber data are of at least the same quality as the data collected with the standard diffractometer.

Our experience shows therefore that a flat xenon-filled multiwire area detector is relatively simple to build and that it can collect protein intensity data quite efficiently and with higher precision than has so far been achieved with an area detector composed of phosphorescent screen, image intensifier and TV camera (Minor, Milch & Reynolds, 1974; Arndt & Ambrose, 1968).

Charpak, Hajduk, Jeavons, Stubbs & Khan (1974) have suggested the building of a spherical drift multiwire chamber as an area detector for protein crystallography. This chamber is more difficult to build than a flat chamber and requires a fixed crystal-to-detector distance that would impose an upper limit on the crystal parameters. A flat chamber can always be positioned at an optimum crystal-to-detector distance depending on the parameters and the size of the reflection spots on the chamber. To reduce the elongation effect of the reflection spots at high incident angles due to the thickness of the chamber, and to improve the data collection rate further, one can use a system of two or more flat chambers.

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The measurement of anomalous scattering factors near the Ga *K* absorption edge in GaP: erratum.

BY T. FUKAMACHI and S. HOSOYA, *Institute for Solid State Physics, University of Tokyo, Roppongi, Minato-ku, Tokyo, Japan*

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A correction is given to Fukamachi & Hosoya [*Acta Cryst.* (1975). A**31**, 215–220]. On p. 216 special position $(\frac{3}{4},\frac{3}{4},\frac{3}{4})$ should read $(\frac{1}{4},\frac{1}{4},\frac{1}{4})$.

In Fukamachi & Hosoya (1975) the following correction should be made. Page 216, line 7 of §3: $(\frac{3}{4},\frac{3}{4},\frac{3}{4})$ should read $(\frac{1}{4},\frac{1}{4},\frac{1}{4})$.

Reference

FUKAMACHI, T. & HOSOYA, S. (1975). *Acta Cryst.* A**31**, 215–220.