Position-Sensitive Detectors: An "Electronic Film" for X-rays

X-rays are commonly used for finding the locations of the atoms in crystals (x-ray diffraction) and for studying the shapes of microscopic objects that need not have a well-defined crystal structure (small-angle x-ray scattering). For many applications, the time-tested means of recording diffraction or scattering patterns (photographic emulsions and single electronic detectors) are more than adequate. But both methods are of limited usefulness for experiments in which the specimen examined changes with time, gives rise to only a weak x-ray pattern, or produces tens of thousands of diffracted beams. Researchers have, in the last 2 years, solved this problem by constructing two-dimensional position-sensitive detectors, which combine the sensitivity to weak signals of electronic detectors with the ability of film to record several diffracted or scattered x-ray beams at once. Although the most obvious advantage of the new devices is speed, a far-reaching consequence is that experiments once considered impossible can now be done with comparative ease.

Photographic emulsions, which provided the first means of recording x-rays, have the advantage that the entire pattern for each orientation of a specimen can be collected on a single sheet of film. Films are comparatively insensitive, however, and need a considerable exposure time (up to a week for small crystals of large proteins or viruses), if the intensity of the diffracted or scattered x-rays is low. Moreover, in this day of digital data processing, films are cumbersome and inconvenient because steps such as developing the image and digitizing it with a densitometer stand between data collection and analysis.

Electronic detectors are much more sensitive than film and can respond to a wider range of intensities. And they are directly compatible with digital data systems. Unfortunately, most electronic detectors, unless several are arranged together in an array, can record data at only one position at a time. To accumulate a full x-ray pattern requires moving the detector and rotating the specimen to collect data at numerous points around the sample, a necessarily time-consuming procedure.

Sometimes researchers like to follow changes in structure with time, as when a crystal grows from the melt or a living biological tissue responds to a stimulus. On other occasions, specimens may be unstable and decompose with time, a common problem in protein crystallography. In these cases, an experiment is not possible if complete x-ray patterns (or sets of patterns) cannot be obtained in shorter times than the conventional way of recording them permits. In a few cases, the sheer tedium involved in collecting and readying data for computerized structural determinations can be enough to discourage experimenters.

A solution that is beginning to appear in a few laboratories in the United States and in Europe takes the form of an electronic detector that not only can record the intensity and energy of x-rays, but also can determine the position of the beam as it strikes the detector surface. Such devices, which may have active areas of 20 or 30 centimeters on a side, are called two-dimensional position-sensitive detectors and might well be called "electronic film" because they combine the advantages of each. Although there are several types of position-sensitive detectors, the ones currently generating enthusiasm among x-ray researchers are of the type known as multiwire proportional counters.

Multiwire proportional counters can legitimately be described as a spin-off of intense effort on the part of high energy and nuclear physicists to find ways to record the trajectories of electrically charged particles created during the collisions between elementary particles in accelerators. The basic single wire counter consists of a cylindrical chamber filled with an inert gas at a pressure of 1 atmosphere or more. Through the center of the chamber runs a wire (anode) that is at a positive potential with respect to the chamber walls. An incoming x-ray photon ionizes a gas atom when it is absorbed, and the freed electron is accelerated toward the anode wire. As it approaches the anode, the increasingly energetic electron causes more ionization of the gas atoms by way of collisions. The resulting current pulse is a measure of the energy of the x-ray photon that initiated the avalanche. And, provided that the intensity is not so high that the pulses due to successive photons overlap, the number of pulses per unit time determines the intensity of incident x-rays.

The problem in diffraction or scattering experiments is to count the number of x-ray photons with position on a surface perpendicular to the path of the x-ray beam striking the specimen. As described, the basic one-wire proportional counter does not give information about position. Beginning in the mid-1960's, physicists discovered that the current pulse is localized along the length of the wire and therefore can be used to determine the position of the incoming photon. Two methods of position encoding were developed. In both methods, use is made of the difference in some property of the pulse, such as its height or shape, at each end of the wire. Such one-dimensional position-sensitive detectors—that is, detectors that record the number of photons as a function of one coordinate—are now available commercially and these have had a substantial impact on x-ray research in their own right.

The next step was two-dimensional position-sensitive detectors; these have not yet reached the commercial stage in the United States and may not for several years. At present, a few such devices have been built and integrated into x-ray diffraction or scattering facilities, but these are home-made detectors that are still very expensive.

The first two-dimensional position-sensitive detector to be used in research involving x-ray diffraction or scattering (but not the first to be constructed) was installed in a protein crystallography facility at the University of California at San Diego 20 months ago under the guidance of Nguyen-huu Xuong. Broadly speaking, protein crystallography involves three steps: obtaining x-ray diffraction patterns, computing so-called three-dimensional electron density maps from the patterns, and constructing a model of the crystal structure from the densities. So far, researchers at San Diego have used the two-dimensional detector to gather data from four different proteins. And crystallographers there working under Joseph Kraut have in two cases (dihydrofolate reductase from *Escherichia coli* and *Lactobacillus casei*) completed models, and in another (cytochrome c peroxidase) they have calculated a density map and are now working on a model.

The multiwire proportional counter was a joint project of Xuong, Wayne Vernon, and their associates at San Diego and Victor Perez-Mendez of the Lawrence Berkeley Laboratory, who has also designed similar detectors for

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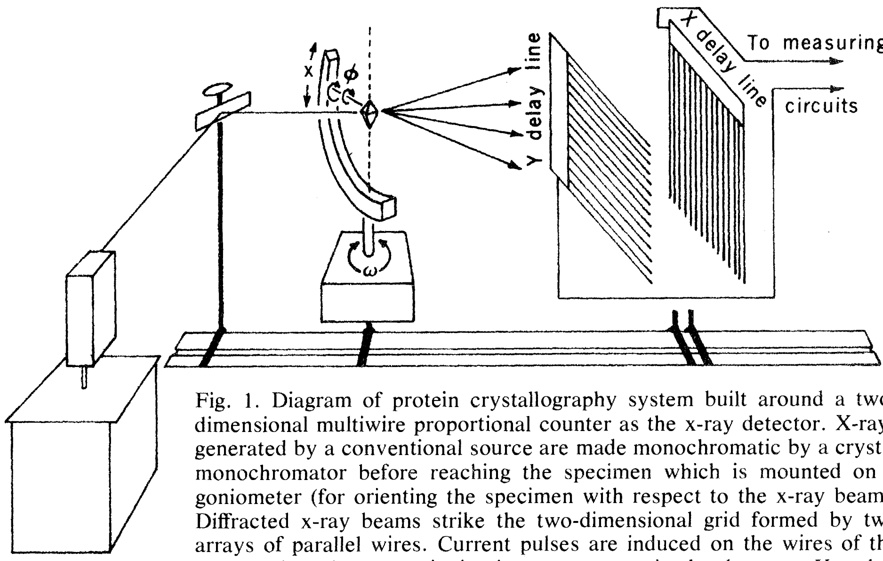

Fig. 1. Diagram of protein crystallography system built around a two-dimensional multiwire proportional counter as the x-ray detector. X-rays generated by a conventional source are made monochromatic by a crystal monochromator before reaching the specimen which is mounted on a goniometer (for orienting the specimen with respect to the x-ray beam). Diffracted x-ray beams strike the two-dimensional grid formed by two arrays of parallel wires. Current pulses are induced on the wires of the arrays when the x-rays ionize inert gas atoms in the detector. X and Y coordinates of each photon are determined from the time it takes current pulses from each array to reach the measuring circuit through the delay lines. [Drawing by Eleanor Warner]

medical imaging applications. Coordinates in two dimensions are obtained by generalizing the basic proportional counter design. The single anode wire becomes a planar array of 150 parallel wires spaced 2 millimeters apart. A second array of 300 parallel wires spaced 1 millimeter apart serves as a cathode. The two arrays are 4 millimeters apart and parallel, but the wires are perpendicular, forming a grid when viewed in projection.

The basic idea behind the position sensitivity involves devices called delay lines. One delay line is coupled to the anode wires and one delay line is coupled to the cathode wires. Current pulses from the affected wires of each array pass through these delay lines and reach the ends of the delay lines in times proportional to the X and Y coordinates of the detected x-ray photon (Fig. 1). Electronic circuits convert the two delay times into X and Y coordinates. A computer core memory is used to store the two-dimensional histogram required to keep track of the number of detected photons that strike each location on the detector surface during a given interval. The data gathering is under the control of a minicomputer. Diffraction patterns are taken at several orientations of the specimen at angular increments of 0.05°. Depending on the symmetry of the crystal structure, enough patterns are taken to cover a total angle of about 35° to 180°. The resulting data, consisting of hundreds of thousands of intensity measurements, are put on magnetic tape for transport to a large computer which is needed for calculating the electron density maps.

Speed is the primary advantage of a two-dimensional detector, according to Xuong. Diffraction patterns can be taken in about one-tenth the time required by a conventional diffractometer, which is used with an electronic detector to record data at only one position at a time. A related benefit is that fewer protein crystals, which are notoriously hard to grow and which tend to degrade with time under an x-ray beam, are needed. The dihydrofolate reductase experiment, for example, required only three crystals (one "parent" and two heavy atom derivatives needed to obtain "phase" information). Finally, because the system is so automated, crystallographers can easily learn to take diffraction data. Xuong says the system has been so successful that an enlarged data collection system with a higher power x-ray source and four two-dimensional multiwire proportional counters is being assembled in his laboratory by Ronald Hamlin. Scheduled to be completed in 6 months, the new system will be 100 times faster than a conventional diffractometer.

Other researchers are getting into the act. A group headed by Robert Kretsinger and Stanley Sobottka at the University of Virginia is proposing a national protein crystallography center which will be based on a diffraction system with a two-dimensional multiwire proportional counter similar to the one at San Diego. The chamber will contain xenon—which is more highly absorbing than argon, the most commonly used gas—at a pressure of 10 atmospheres in order to increase detection efficiency. Kretsinger notes that the data collection capability of such a system is so great that a single group could not keep it running full time, hence the idea for a national facility. Moreover, he adds, new classes of structure problems will be addressable that once were not, including rapidly degrading crystals, crystals that diffract weakly, and proteins with large unit cells. For example, structures with large unit cells tend to have large numbers of diffracted x-ray beams very closely spaced, an ideal situation for a two-dimensional detector but an exceedingly tedious task for the standard diffractometer that must measure the diffracted beams one by one. And, according to Larry Faller of the National Science Foundation (NSF), the increased rate of data collection may make it possible to obtain structures of intermediate species in enzymatic reactions at low temperatures, which would be a major advance.

For similar reasons, a group at the Massachusetts Institute of Technology headed by Martin Deutsch and Alexander Rich is also proposing a regional protein crystallography center which will have as a major ingredient a related gaseous detector known as a drift chamber. This device was first conceived in the 1940's by Otto Frisch of the University of Cambridge and has been recently developed for high energy and nuclear physics applications by Georges Charpak of the European Organization for Nuclear Research (CERN) and others. In the application to crystallography, it overcomes a resolution-limiting effect known as parallax, which is due to the finite thickness of the proportional chamber. In a drift chamber, ionization occurs in an extended gaseous volume in front of a proportional counter to which electrons are transferred by an electric field. In the chamber to be used at MIT, this field is radial and diverges from the crystal position. Thus, all x-rays following the same path will be registered at the same position regardless of the depth of the ionization event, resulting in an unsmeared diffraction spot. The drift chamber also has advantages when used with the high-intensity pulsed radiation from synchrotron radiation sources. In fact, many synchrotron radiation centers that have the capability for x-ray research are in various stages of developing multiwire proportional counters or drift chambers for their own laboratories.

A second operating facility that has a two-dimensional position-sensitive detector for x-rays is in Robert Hendricks' laboratory at the Oak Ridge National Laboratory (Fig. 2). Hendricks and his associates use a technique called small-angle x-ray scattering. The technique has certain similarities to light scattering when it is used to find the size and shape of particles. In small-angle x-ray scattering, investigators measure the intensity and the angular distribution of x-rays scattered at angles less then 5° from the incident beam. Objects that can be studied have dimensions of 10 to 2000 angstroms or larger, but need not have the periodic structure of a crystal. Examples of such objects include macromolecules and other particulates in solution, defects such as voids in neutron-irradiated metals, precipitate particles in alloys, and the angular distribution of x-rays mers. In addition, structures with long periodicities, such as collagen and muscle, can also be studied.

The detector at Oak Ridge was developed by Casimir Borkowski and Manfred Kopp and consists of three parallel planes of wires. The central plane is an array of fine anode wires spaced 2 mm apart. It is on these wires that the electrons created by the ionizing radiation are collected. The anode array is sandwiched between two cathode arrays, each 6 millimeters away. Each cathode array is made from a single wire. The wires in the two cathode arrays are orthogonal to each other. Borkowski and Kopp compare the shape of current pulses generated (induced) on each cathode. A measurement of the differences in the slopes of the pulses emerging from the ends of each cathode decodes the X and Y coordinates of the photon. This technique was actually the first one to be made practical and is the basis for the numerous commercially available one-dimensional position-sensitive detectors.

Another feature is the inclusion of a drift space in front of the active area of the multiwire proportional counter to increase detector efficiency. The argon or xenon gas used in the counter absorbs only a fraction of the x-rays, a fraction that depends on the energy of the photons. The drift space is six times as thick as the detector and is also filled with an absorbing gas (now argon, soon to be xenon). It effectively increases the thickness of the detector and hence its efficiency, but there is no loss of spatial resolution as would have occurred if the detector thickness were simply increased. Since parallax is less a problem in small-angle scattering, the field in the drift space can be linear rather than radial.

As with the San Diego facility, operation at Oak Ridge is under the control of a large minicomputer. But because the protracted computation needed to transform diffraction patterns into electron density maps is absent in small-angle scattering, all the data analyses can be done "on line." The memory is large enough for several scattering patterns to be retained at once, as, for example, a sequence of patterns taken at successive times. In this way, changes in structure can be followed as they occur.

The vastly enhanced speed of data taking permitted by the two-dimensional multiwire proportional counter permits such sequential structure changes to be observed. In one experimental collaboration between Jerold Schultz of the University of Delaware and Hendricks and J. S. Lin of Oak Ridge, it was possible to obtain a scattering pattern for polyethylene in as little as 30 seconds. The experimenters were therefore able to observe the kinetics of crystallization of the polymer as molten polyethylene was cooled to below the melting temperature.

Fig. 2. Small-angle x-ray scattering facility at the Oak Ridge National Laboratory. A rotating anode x-ray source is at the right end of a 10-meter long evacuated tube. The length of the tube depends on the requirement that angles less than 0.1° be resolvable by the detector, whose spatial resolution is better than but still limited by the spacing between the wires in the anode and cathode arrays. Specimens are mounted in the box near the center of the tube. The position-sensitive detector is at the far left end of the tube. In the right rear corner are the minicomputer and other electronics devices for controlling and monitoring operation of the experiment. [Source: R. W. Hendricks, Oak Ridge National Laboratory]

The high rate of data collection also makes it possible to use so-called pinhole collimation. In the past, in order to obtain a high enough flux of scattered x-rays to record a complete pattern in a reasonable time (several hours), it was necessary to use long slits to collimate the x-rays. But this method introduces certain complications in interpreting the data; in particular, it makes analysis of anisotropic structures almost impossible. A position-sensitive detector is sufficiently sensitive that data can be obtained simultaneously at all angles in short times, even with the lower flux from the pinhole.

This capability is illustrated by another polymer experiment by Stanley Baczek and Richard Stein of the University of Massachusetts and R. Douglas Carlson and Hendricks at Oak Ridge. They were able to use pinhole collimation and position-sensitive detection to follow the change in the structure of polyethylene which became increasingly anisotropic as it was deformed by elongation. Significant differences were found when the investigators compared scattering data taken in this way with that taken in the conventional long slit geometry.

Other two-dimensional multiwire proportional counters for x-rays are in operation at Cornell University, at the Institute for Nuclear Physics in Novosibirsk, and at the Centre National de la Recherche Scientifique in Orsay, France.

Hendricks says that about 20 groups from outside Oak Ridge have used the new facility since it became fully operational a year and a half ago. Currently in the works is a proposal to formalize what is already a de facto arrangement for a national facility. The NSF is considering proposals to establish a national facility for small-angle neutron scattering, a technique analogous to small-angle x-ray scattering but for which there are limited facilities in the United States at present. Oak Ridge is one of the bidders, and part of the proposal is to include the small-angle x-ray facility for about 30 percent of its running time.

The obvious trend toward large facilities of a regional or national character is a direct result of the cost of computerized data collection, which is required when two-dimensional detectors are used. Oak Ridge has already spent a half-million dollars on its facility, including time spent in developing the computer programs. Upgrading the facility to the level outlined in the proposal to NSF would take another quarter-million dollars. Xuong estimates that during the 6 years from conception to operation of the protein crystallography system at San Diego, he has spent \$450,000, although he adds that it would be considerably cheaper to duplicate. For this reason, it is unlikely that x-ray equipment with two-dimensional detectors will be available in every laboratory. But experiments such as protein crystallography are already very expensive, and an optimistic assessment by Kretsinger at Virginia is that, in 10 years, manufacturers may be able to sell diffractometers equipped with two-dimensional multiwire proportional counters for less than the price of conventional diffractometers now, allowing for inflation.

—ARTHUR L. ROBINSON

Information Theory: A Surprising Proof

When a long-standing mathematical problem is solved, the proof is usually complicated and technical, if not voluminous. Many of these proofs can be understood only by researchers in narrow subspecialties of mathematics. Mathematicians are taken aback, then, by a recent solution to a well-known problem in information theory. The problem was first posed by Claude Shannon, the founder of information theory, more than 20 years ago. The solution, devised by Lászlo Lovász of the József Attila University at Szeged, Hungary, is short (only a few typed pages), simple enough to be easily understood by most mathematicians, and ingenious.

Many who have seen Lovász's solution to Shannon's problem agree with Ronald Graham of Bell Laboratories in Murray Hill, New Jersey, who says the proof is "remarkable" but that he is not surprised that Lovász is the one who came up with it. Although only 28, Lovász has already made quite a name for himself by solving, within a short period, several notable problems. According to Bruce Rothschild of the University of California at Los Angeles (UCLA), Lovász seems to work only on the hard problems.

The information theory problem Lovász solved is that of measuring the rate at which information can be sent, with no possibility of error, over noisy channels. These are channels in which one signal may be confused with another when the signals are received. Information theorists sometimes assume that not all signals transmitted over noisy channels can be confused with each other. In these idealized situations, two signals may be confused but a third may be so different from either of them that it is never confused with them.

When some of the signals sent over a noisy channel cannot be mutually confounded, Shannon noted a way to transmit error-free messages at a maximum rate. The trick is to send blocks of signals, rather than individual ones, and use nonconfoundable signals in the design of the blocks. In that way, no block can be confused with another. It turns out that, in each case, there is an upper limit to the amount of information that can be sent in this way. This maximum—known as the Shannon capacity—has, except in a few simple cases, proved impossible to determine exactly.

When studying sets of confoundable signals, mathematicians often represent the systems as graphs. Each point on such a graph denotes a signal, and two points are connected by a line if the signals they represent can be confused. The problem of determining the Shannon capacity of a system whose graph is a pentagon (Fig. 1) has been described by David Cantor of UCLA as "the first nontrivial case of the problem of finding Shannon capacities." He says that the problem has proved a continuing challenge to mathematicians, and some of the brightest people he knows have worked on it. This is the problem that Lovász solved.

In order to find the Shannon capacity of the pentagon, Lovász transformed the problem from one in information theory into one in geometry. Other investigators had previously used methods of linear programming to estimate upper bounds for the problem. Lovász's method not only provides upper bounds at least as accurate as those given by linear programming, but also, in the case of the pentagon, provides an upper bound that is the same as a lower bound known previously. Thus Lovász's method gives the exact value of the Shannon capacity. Moreover, Lovász's proof is so simple, Cantor says, that if someone had devised it 20 years ago, mathematicians would have dismissed the problem as a trivial one. Nonetheless, Edgar Gilbert, also of Bell Laboratories, points out that Lovász's inspiration for his proof seems unprecedented. "What he did took me by surprise," Gilbert says.

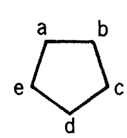

Fig. 1. A graph of the problem Lovász solved. Points a, b, c, d, and e refer to distinct signals. Points connected by a line can be confused with each other. Thus a and b can be confused, but a and d cannot. If one-letter messages are sent, only two signals, such as a and d, can be sent in one time period with no danger of confusion. Thus, in two time periods, four different messages can be sent with no errors. If two-letter messages are sent (constituting blocks of two signals), there are five distinct nonconfoundable messages that can be sent in two time periods. These messages are aa, bc, ce, db, and ed.

Although Lovász's proof is just beginning to circulate among mathematicians, some are already applying his method to other information theory problems. For example, Lawrence Shepp and Andrew Odlyzko of Bell Laboratories in Murray Hill and, independently, Howard Rumsey, Eugene Rodemich, and Robert McEliece at the Jet Propulsion Laboratory in Pasadena, California, have applied it to a problem centering on error-correcting codes. These are codes in which a certain amount of redundancy is introduced, thereby allowing those receiving a message to detect errors. Odlyzko says that "it is possible that Lovász's method can be pushed still further" in applications to information theory problems. Lovász himself says that he is applying his method to other problems similar to the one he solved.

Most investigators familiar with Lovász's solution say it has no immediate practical import because, in practice, there is no such thing as two signals that can never be confused with each other. Thus, most codes are designed so that the probability of errors is small, but not zero. Even Shannon describes the problem of finding Shannon capacities as a "conceptual problem." However, he says that many important scientific problems were first posed as conceptual problems, and he hopes that Lovász's method will lead to solutions for a whole class of problems. In any event, he says, "I am interested and happy to see this whole problem of the pentagon finally laid to rest."—GINA BARI KOLATA

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