X-ray Crystallography: 3-D Structures by Optical Computing

What many scientists believe to be a major breakthrough in the processing of x-ray crystallography data has been achieved by a group of investigators at the State University of New York at Stony Brook. George W. Stroke and his colleagues have partially replaced digital techniques on a computer with optical techniques to develop a process that substantially reduces the time and effort required to produce a three-dimensional model of the structure under analysis. The technique shows great promise for converting x-ray data almost directly to a three-dimensional image of the structure that shows the spatial position of individual atoms precisely.

The production of three-dimensional models of biological macromolecules from x-ray data by conventional techniques requires a great deal of computation and manual labor. After the data are collected by a computer-controlled x-ray diffractometer, they are subjected to phase determination and three-dimensional Fourier transformation, a complicated series of integrations whose results are then printed out in large sheets corresponding to cross sections of the molecule; numbers on the sheet represent the electron density at each point.

Electron density contours are then drawn manually on the printed sheets and, manually again, transferred to sheets of clear plastic. This process is repeated until there are enough cross sections to give a complete picture of the molecule. The plastic sheets are then combined in a device known as a Richard's Box, in which visual techniques are used to locate the centers of highest electron density, and thereby the centers of individual atoms. From this information, a model of the structure can be built. This process is, however, being improved by the use of computer graphics.

Stroke's technique bypasses much of the calculation and most of the manual labor. The diffractometer data are subjected to a digital phase determination that is similar to that employed in conventional techniques. The data are then subjected to a digital one-dimensional Fourier transformation, which is substantially simpler than the three-dimensional transformation required by conventional techniques. The results from the transformation are transferred onto a photographic transparency with an optical writer. The optical writer takes each piece of digital information and puts it on the film as a dot whose darkness corresponds to its numerical value. Similar devices are used in the space program to convert digital information into photographs.

The transparency thus produced is known as a Fourier-domain projection hologram. By shining coherent laser light through the transparency and then through a noiseless lens, a two-dimensional Fourier transformation is accomplished and one obtains a three-dimensional image of a section of the molecule which directly displays the individual atoms. The images can then be magnified so that the precise positions of atoms within the molecule can be readily viewed and measured. The final three-dimensional structure can be recorded either in the form of a fanlike set of photographic plates, such as the one in Fig. 1, or displayed from a single hologram.

(When a crystal scatters x-rays, it performs, in effect, a Fourier transformation in which the spatial coordinates of individual atoms are converted into a series of interference patterns. Holography performs much the same operation with larger objects, but the interference patterns are generated somewhat differently. The encoded information in the x-ray diffraction patterns can be retrieved by reversing the Fourier transformation, a process that is performed by a lengthy series of mathematical calculations in each dimension. In holography, the same function is achieved by shining coherent light through the hologram. What Stroke has done, in effect, is to devise a way to convert x-ray diffraction patterns into holographic interference patterns.)

Stroke's optical technique has the additional advantage that it cuts down on the noise or error associated with locating the centers of atoms. This results, in part, from the fact that digital integrations in the Fourier transformation must necessarily be truncated to make the calculation manageable. When the transformation is performed optically, the integration is complete and there is less noise. It is still possible, though, that other errors may be introduced by the technique. Stroke and his colleagues are now studying the system carefully to see if such errors are present and, if they are, how they can be prevented.

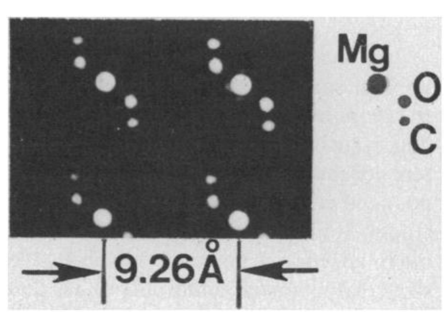

Fig. 1. A cross section of a triclinic crystal of $MgBr_2{\cdot}4(C_4H_8O){\cdot}2H_2O$ obtained by Stroke and his colleagues using the new optodigital computing method.

Stroke's work is a direct outgrowth of optical techniques that have been used to enhance the resolution and three-dimensionality of electron micrographs; it is a good example of the benefits that can be obtained from an interdisciplinary approach to problems. Stroke is director of the Electro-Optical Sciences Laboratory at Stony Brook and a pioneer in the uses of holography. He recognized the manner in which laser optics could be applied to the problems of crystallography and, about a year ago, described the fundamental mathematics of the process, including a new "Fourier-domain projection theorem." He expected crystallographers to take over from there, but they did not, probably because most of them have no experience with the optical systems required. He then collaborated with Maurice Halioua, V. Srinivasan, and R. Sarma of Stony Brook to show how the system can work. The simple crystal illustrated in Fig. 1 represents their first attempt.

The technique has not yet been demonstrated to many crystallographers in this country, but the few scientists who are familiar with it seem enthusiastic. Jack Kinsinger of Michigan State University, who until recently was director of the Chemistry Division of the National Science Foundation, which funds Stroke's work, says the achievement may be a major technological breakthrough in the processing of x-ray diffraction data. At the very least, Kinsinger says, the new method will be a valuable auxiliary technique that will improve the science of crystallography; at best, it should compete effectively with the new graphics approach and could be better. Other investigators are less effusive, but they agree that the method could be quite useful for the investigation of large molecules. Many seem to agree, though, that the method will not truly capture the imagination of crystallographers until Stroke and his colleagues produce a "flashier" demonstration, such as a three-dimensional hologram showing a complete crystal. That, they agree, would make even the doubters sit up and take notice.—THOMAS H. MAUGH II