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ally). The results have recently been confirmed by electron microscopic analysis of polyoma mutants that form tubes instead of spherical coats. The tubes also appear to be composed exclusively of pentamers.

It is well known that, theoretically, it is impossible to tile the plane with regular pentagons. In general, the same is true for the sphere. In practice, as shown by polyoma, one can use any shape tile if the gaps are filled with grout. The nature of the grout in polyoma remains to be determined.

E. E. Lattman, Johns Hopkins University School of Medicine


Influenza Virus

Influenza virus is a larger and more complex agent than polyoma. Its outermost layer is a membrane coat pinched off from the host cell surface during maturation. This viral membrane contains two glycoproteins, a neuraminidase (NA) and a hemagglutinin (HA) that define most interactions of the virus with cells or molecules.

The structure of both of these molecules has now been determined by x-ray diffraction analysis. They represent two of the first membrane-bound proteins to be successfully crystallized and studied in this way. NA catalyzes the removal of a terminal sugar residue from cell polysaccharides and, thereby, probably facilitates the mobility of the virus to and from the site of infection. HA, in contrast, has no known catalytic activity, but rather serves to bind the virus to host cells.

Both of these molecules are anchored in the membrane through strongly hydrophobic regions that were cleaved during the solubilization process required for crystallization. The soluble portions of the molecules, which extend out from the viral membrane in vivo, display complex and almost bizarre architecture by the standards of the usual globular protein. HA is a trimer comprising a stalk-like region extending some 76 Å from the membrane and crowned by a globular region containing the sites that bind to specific molecules on cell surfaces and that stimulate the host immune response. The stalk is a triple-stranded coiled coil of alphahelices unique among globular proteins.

NA is tetrameric and also has a flower-like aspect, consisting of a fourfold symmetric, propeller-shaped head attached to the viral membrane by a slender stalk that was removed prior to crystallization. The catalytic site of NA has been located by synthesizing images with and without the reaction product sialic acid bound. In addition, many of the antigenic sites in NA and HA have been located. Changes in the amino acid sequence of these proteins in different strains of influenza virus alter the antigenic specificity of the virus, and allow it to escape the immune response directed against previous strains. Thus, we can be reinfected with influenza every few years as new viral strains emerge. These changes have been localized exactly on the protein molecules.

Although no simple strategy for disease control is obvious from these observations, important experiments involving viral peptides that define potential antigenic determinants common to all virus strains have become possible.

These, in turn, may lead to much more broad-spectrum vaccines. All this results from the exact description of the viral surface that makes it possible to understand in atomic detail the interaction of influenza virus with its surroundings.

E. E. Lattman, Johns Hopkins University School of Medicine


Basic New Techniques in Crystallography

The first crystal structure analyses were done by W. L. Bragg almost 70 years ago, and the application of his technique, diffraction x rays from crystals, shows no signs of slowing down. The size of atomic assemblies that can be imaged by the technique has gradually grown from 1 or 2 atoms in 1913 to 10^6 atoms, sometimes cases, today. Development now in the research stage may in time push the technique still further. We will briefly consider four of these.

Crystallographic structure analysis proceeds first by measuring the diffraction pattern of a crystal specimen produced by x rays or neutrons, then by associating the correct phase for each point of the diffraction pattern, and finally by Fourier inverting the correctly phased pattern to produce an image of the specimen. The second step, that of phasing, is generally the hardest. The amplitude of the diffracted x-ray radiation is a complex number. While it has always been possible to measure x-ray intensity (given the square of the amplitude), measuring the phase of the amplitude is difficult.

Over the years a number of methods for phasing have been developed, but it has generally been assumed that the task of simultaneously measuring both the phase and the intensity at each point in the pattern could not be done. Now, however, some techniques resembling this has been done, at least in simple cases, by Benjamin Post of the Polytechnic Institute of New York and some of his colleagues.

Post's method consists in setting the crystal in such an orientation that x rays are diffracted into two Bragg reflections simultaneously, and then observing the behavior of the two diffraction intensities as the crystal orientation is varied slightly about this setting. In 1977 Post pointed out that the dynamical theory of crystal diffraction, first developed by Paul Ewald in 1917, predicts that the detailed behavior of the diffraction intensities in this situation depends on the sum of the phases at three points in the diffraction pattern, namely the two diffraction patterns, namely the two diffraction points and the point which is the negative of their vector sum. The sum of the phases for such a triplet of points is an important quantity in the phasing process, and is called the amplitude structure invariant. Post's observation, therefore, amounted to the suggestion that the three-phase structure invariants can be measured by observing the behavior of the diffraction intensities in the neighborhood of the positions in which the crystal is doubly diffracting. This suggestion has since been experimentally demonstrated on a number of rather simple crystals.

For many years crystallographers have been using mathematical techniques to estimate the three-phase structure invariants from the diffraction intensities, and deducing phases from these estimates. The technique as a whole is called the direct phasing method, and is an extremely convenient technique for phasing, requiring only what is nothing more than the measured diffraction intensities. Both steps, the estimation of the invariants and the deducing of the phases, present difficulties, but the method usually succeeds for assemblies of up to about 100 atoms. What Post's technique promises is to measure the invariants to be measured, at the cost only of a more detailed exploration of the diffraction intensities in the regions where double diffraction is taking place.

A second development is due to Gerard Brion of the College of Physicians and Surgeons at Columbia. His work is aimed at improving both steps in the direct phasing method, with the intention of allowing the method to succeed with structures much larger than 100 atoms. Brion's methods are highly mathematical and will not be explained here, but preliminary tests now taking place at several centers, using diffraction data from structures much larger than could previously have been attempted by direct phasing, are encouraging.

The third development can be ascribed to the group headed by Herbert Hauptman, centered at the Medical Foundation of Buffalo. For years the structure of proteins involving really large assemblies of atoms have been solved by a phasing technique based on the comparison of two or more diffraction patterns obtained by varying the number and position of atoms not properly belonging to the structure, but intentionally added to produce small changes in the dif-
fraction intensities; when properly interpreted these changes can be used to determine the diffraction phases of the original structure. (In a related technique, the changes are induced not by adding atoms but by exciting resonances in specific atoms by tuning the x rays close to the appropriate atomic absorption edges.) Hauptman, who was one of the developers of the direct phasing methods, has now generalized the concept of structure invariant to apply to the case of several diffraction patterns, and has developed methods of estimating the invariants in this case. The result could be a major improvement in the strength and convenience of the phasing techniques for very large structures.

The previous developments all considered the problem of phasing the diffraction patterns of crystals of increasingly complex atomic assemblies. The last development, however, assumes that at a certain level of complexity crystallization of the assemblies may not be feasible. An example is the giant assembly known as a single biological cell, which nature does not make to a pattern sufficiently precise to permit a crystal formed of such cells to exist. With this in mind, a team composed of D. Sayre and R. P. Haelbuch at IBM Research, and J. Kirz and W. B. Yun at the State University of New York at Stony Brook, has embarked on an attempt to see whether diffraction patterns from single giant assemblies can be obtained. Calculations suggest that by using x rays of wavelength roughly 30 Å, the diffraction patterns from such minute specimens, although still extremely weak, should be measurable at intense synchrotron x-ray sources. Current sources are still marginal for this purpose and no pattern has as yet definitely been observed, but an improved source due to be installed at the Brookhaven Synchrotron Radiation Source in 1984 should be able to provide observable patterns. Should this be true, the way may be open for the first time for the three-dimensional imaging of such assemblies at 15-Å resolution.

David Sayre, IBM


FORTHCOMING MEETINGS

Aug 27–31, 1984: Sixth National Congress, Australian Institute of Physics, Griffith University, Brisbane. Contact: Dr. B.W. Thomas, Dept. of Physics, Q.I.T., GPO Box 2434, Brisbane 4001.

Sep 11–13, 1984: Cruickshank Symposium: Modern Experimental and Theoretical Studies of Crystal and Molecular Structure, University of Manchester Inst. of Sci. and Tech. Contact: Dr. B. Beagley, Dept. of Chemistry, UMIST, PO Box 88, Manchester, M60 1QD, U.K.


Dec 9–12, 1984: 9th Annual Meeting Australian Society for Biophysics, University of Wollongong. Contact: Dr. B.A. Cornell, CSIRO Division of Food Research, PO Box 52, North Ryde, NSW 2113.
Jan 7-11, 1985: Arizona State University Centennial Conference on High Resolution Electron Microscopy, Scottsdale, Arizona, USA. Contact: Dr P.R. Buseck, Centre for Solid State Sciences, ASU, Tempe, AZ 85287, USA.

Feb 11-14, 1985: Polymer 85 (Characterization and Analysis of Polymers), Melbourne. Contact: Polymer 85, RACI, 191 Royal Parade, Parkville, Vic 3052.

May 12-16, 1985: Crystal 15 and Computing School, Flinders University/Haven Motel, Adelaide. Contact: Dr M.R. Taylor, School of Physical Sciences, Flinders University, Bedford Park, South Australia 5042.

May 26 - June 6, 1985: Static and Dynamic Implications of Precise Structural Information, 11th Course of the International School of Crystallography, Erice, Italy. Contact: Dr P. Murray-Rust, Glaxo Group Research, Greenfors, Middlesex UB6 0HE, U.K.

Aug 12-20, 1987: 14th General Assembly and Congress of the International Union of Crystallography, Perth, Western Australia. Contact: Dr E.N. Maslen, Crystallography Centre, Univ. of Western Australia, Nedlands 6009, Western Australia.

EDITOR'S NOTES

An astute reader has pointed out several errors relating to the photograph included on page 8 of the last Newsletter. The correct information is as follows:

(i) The photograph was taken in the Staff Club at Monash University in 1977 and marks the occasion of the retirement of Janis Fridrichsons from the CSIRO Division of Chemical Physics.

(ii) Barry Dawson's date of death was the 20th of February, 1974.

(iii) Dave Wadsley's initials are A.D.

The same astute reader also pointed out that it was W.L Bragg, and not his father W.H., who discovered the law describing diffraction from a crystal plane (page 5).

Finally (I hope), for those of you wondering how a certain J. Stonehouse got on to the National Committee for Crystallography (page 9) when nobody appears to have heard of her/him, the new member should in fact be B.M.K. Gatehouse.

If Moses was the son of Pharoah's daughter
Then Moses was the daughter of Pharoah's son.