This model works well when applied to the satellites of the major planets of the outer solar system, but it does not explain the size of the present moon or—since accretion over a period of 10^8 years is too gradual to melt the outer layers of the moon—how it came to be heated. To overcome these limitations, Ruskol proposes that one or more large bodies were captured from heliocentric orbits, supplying the additional mass. Melting of the moon might have occurred, Ruskol points out, if several submoons formed first and then ultimately collided.

In contrast to this view, several American theorists propose that the terrestrial planets—and hence the moon—accreted much more rapidly from a larger nebula. Formation on a short enough time scale (1000 years for the moon) would cause extensive heating and melting from the rapid release of the kinetic energy of the incoming particles, not only for the moon but for many other planetary bodies as well. This emerging view of lunar origin (few explicit binary accretion models have appeared in the U.S. literature) is thus dynamically similar to the Russian version, except that the process occurs much more quickly. Kaula and A. W. Harris, also of the University of California, Los Angeles, do not favor rapid accretion but do propose that the embryo moon must have started early in the accretional process to have grown as large as it is.

Explaining the seemingly unique composition of the moon with binary accretion models is still the major difficulty, reflecting the complexity of the accretional process itself, although a number of possible explanations have been advanced. Among Russian investigators, the emphasis is on differences in the physical properties and history of the materials that formed the earth and moon. Ruskol, for example, proposes that high-energy collisions in the swarm of particles in orbit around the earth would have released volatile elements, which were then swept away by the solar wind. Similarly, silicate minerals are more susceptible to fracturing in collisions than metallic particles, and the resulting silica-rich small planetesimals and dust are more easily captured into earth orbit, she believes, than the large, metal-rich particles. These processes might well serve to make the moon rich in silicates and depleted in iron and volatiles, but some investigators believe they do not adequately explain the detailed chemical makeup of the moon.

In addition to these processes, proponents of the rapid-accretion scenario can also explain the moon's compositional differences from the earth by assuming that some chemical fractionation occurred within the solar nebula, which—in this view—may not have completely cooled before accretion began. Wood, however, points out that metallic iron and magnesium silicate, the two most abundant components, respectively, on the earth and the moon, condense at about the same temperatures, so it is difficult to attribute even gross differences to this process.

A further question about the binary accretion model concerns the consistency of its application to all the planets and satellites of the solar system. If the moon's formation is a natural consequence of the accretionary process, why don't other planets have moons of comparable size? Some parties to the debate argue that it is more plausible to assume a special circumstance for the moon than to invent reasons why several other planets do not have major satellites. Others argue that the collisional nature of the accretionary process inherently involves the statistics of small numbers—that the variety in satellite systems might in some cases simply reflect the differences between a violent collision with a large body, late in the accretionary process, and a near miss. In addition, several investigators have concluded that even large satellites of Mercury and Venus would probably have been destroyed by tidal forces from the sun. According to this point of view it is the tiny martian satellites that pose the real exception to the accretional model, and not the moon.

Even strong advocates of the binary accretion mechanism admit that the model, like fission and capture models, falls considerably short of a satisfactory explanation for how (and where) the moon came into existence. Certainly the accretional process is not yet well understood in detail. As a measure of the changing opinions on this matter, it is perhaps noteworthy that two recent reviews of lunar origins, one focusing on dynamics and the other on chemistry, both conclude that binary accretion currently looks to be the most promising mechanism. Thus the issue of the moon's origin now seems to be closely tied to the larger question of how the solar system was formed. At present, however, moonwatchers may gain a measure of satisfaction that the uniqueness of the earth's nearest neighbor remains intact.—ALLEN L. HAMMOND

Additional Reading

1. J. A. Wood, *Icarus*, in press.
2. W M. Kaula and A. W. Harris, *Rev Geophys. Space Phys.*, in press.

X-ray Crystallography: A Refinement of Technique

Many scientists believe that a complete knowledge of the mechanism of action of enzymes and other proteins will not be possible without a detailed knowledge of the protein's three-dimensional structure. But the x-ray crystallographic determination of these structures at high resolution is a laborious, time-consuming, expensive process that does not always necessarily succeed. Within the last year, however, at least two new methods of handling x-ray data have appeared, and these promise not only to improve the facility with which high-resolution protein structures can be determined, but also to reduce the time and expense involved. These methods, which are in a sense similar to the data-processing techniques used to improve fuzzy television pictures from space vehicles, may not be a revolution in x-ray crystallography, but they are the next best thing to one.

The structure of a molecule can be uniquely specified by a set of x-ray diffraction intensities (structure factors) and phase angles that, in effect, define the spatial relation of the structural elements. A representation of the structure can be obtained by combining the structure factors and phase angles in a three-dimensional Fourier series to produce an electron density map. This mathematical process is analogous to the electronic process in which an FM radio receiver decodes a multiplexed monaural signal to produce a stereophonic program.

The phase angles, unfortunately, cannot be obtained directly from the experimental data, so some other way must be found to get at them. For

small molecules, they can usually be calculated ab initio, but this calculation is exceptionally difficult for molecules the size of proteins. A major breakthrough was thus achieved in the 1950's when John C. Kendrew and Max F. Perutz of Cambridge University and David Harker of the Roswell Park Memorial Institute, Buffalo, New York, developed the heavy atom isomorphous replacement technique for proteins. In this process, x-ray diffraction data are obtained from a series of protein crystals in which different heavy atoms have been substituted. From the differences in the diffraction patterns between these crystals and the native (unsubstituted) crystal, it is possible to calculate phase angles. But insertion of the heavy atom often distorts the structure of the protein; and the magnitude of the distortion, which may be in the range of 2.0 to 2.5 Å, places a limit on the resolution of the structure. This resolution is sufficient to show major features of the protein, but individual atoms can be discerned only at a resolution of about 1.5 Å or better. A way must thus be found to refine the data.

If the x-ray data are very good, the investigator can guess about the location of individual atoms, construct a model of the protein, and calculate theoretical electron densities. Refinement may then sometimes be achieved by least-squares techniques, in which parameters of the model are varied to minimize differences between calculated and experimental electron densities or between calculated and experimental structure factors. Variations of this technique have been the only way to refine x-ray data, but it is only rarely that the data are good enough for such a process. The procedure itself, moreover, is arduous and can be prohibitively expensive for macromolecules.

The new methods of refinement eliminate many of the distortions that result from the heavy atoms and reduce the time and cost of the refinement. These new methods were developed by David Sayre of the IBM Thomas J. Watson Research Center, Yorktown Heights, New York, and Douglas M. Collins of Texas A & M University, College Station. Somewhat similar techniques have subsequently been developed by Georges Tsoucaris of the University of Paris and Alberto Podjarny of the Weizmann Institute in Israel.

The new methods are actually extensions of the direct, equation-solving techniques that are normally applied to small molecules. Since the equations cannot be solved ab initio for proteins, however, both Sayre and Collins began with experimentally derived phase angles obtained by the isomorphous replacement technique. Each chose to work with rubredoxin, a small (6100 daltons) protein that had previously been refined with conventional techniques by Lyle H. Jensen and his associates at the University of Washington, Seattle. Using Jensen's rough phase angles at 2.5-Å resolution as a starting point, Sayre and Collins were able to refine the diffraction data from the native protein crystal, thereby avoiding the distortions produced by heavy atoms. Their techniques were similar, but they approached the problem from opposite sides of the Fourier transform: Sayre worked with structure factors, while Collins worked with electron density maps.

A Physical Constraint

In making his calculations Sayre employed the "squaring method system of equations," which he developed more than 20 years ago. Implicit in these equations is a physical constraint that is generally not applied in protein structure calculations—that the molecule is composed of nonoverlapping atoms which are all of the same size and shape. Although this assumption is fine in the case of carbon, nitrogen, and oxygen, it does introduce local distortions in the areas of heavier atoms in the molecule. The equation system was then solved numerically by varying the phases until a measure of the degree to which the equation system is satisfied had been minimized.

After making the computations, which required about 550 minutes on a very large computer, Sayre obtained an electron density map that compared favorably with that obtained earlier by Jensen using the model-building and least-squares technique. Sayre's map even correctly identified five amino acids that were obscure in Jensen's map. Jensen's map, moreover, was obtained by starting with phase angles at a resolution of 2 Å, and could not have been obtained using 2.5-Å phase angles.

Collins applied the constraint that there should be no areas of negative electron density in the final map, a condition that makes physical sense since there is no antimatter in the molecule. (Experimental electron density maps generally contain many such areas.) Furthermore, he devised a unique function to provide a subtle shaping of the electron density map so that the Fourier series converges to the ultimate value more rapidly. Finally, use of this function made it possible to use only one-eighth as many data points as are normally used in performing the calculations—an advantage that decreases the complexity of the calculations by an order of magnitude. The net effect of these constraints was that Collins obtained an electron density map of rubredoxin which was substantially the same as that produced by Sayre. But his calculations required only about 40 minutes of time on a smaller computer at a cost of about $100 compared to the minimum of $7500 required by Sayre. Sayre says, though, that further refinements in his technique should lower the required time substantially.

Both approaches are currently being further tested by applying them to larger and more representative proteins. Collins' technique is being applied to staphylococcal nuclease, a bacterial enzyme whose structure had previously been determined at a resolution of 2.2 Å by F. Albert Cotton, Edward E. Hazen, Jr., and their associates at Texas A & M. Refinement of the data to 1.5 Å has resulted in a sharper and more detailed electron density map which should yield a vastly improved structure model. Dorothy Hodgkin and her associates at the University of Oxford are using Sayre's technique to determine the high-resolution structure of insulin. And Demetrius Tsernoglou and Greg Petsko of Wayne State University, Detroit, Michigan, are using Sayre's technique to determine the structure of a neurotoxin from snake venom. Neither of the last two projects is far enough along, however, to have produced definitive results.

The constraints and assumptions used in both methods are relatively simple and straightforward, but they result in increases of several orders of magnitude in efficiency. Why, then, has no one used them before? In Collins' case, the individual assumptions have been used before, but it is apparently the interaction of all three that makes the technique successful. And in the case of Sayre's technique, it appears that no one has attempted it before at the level of proteins simply because the calculations looked far too forbidding.

—THOMAS H. MAUGH II