Nobels

Chemistry: Math for molecular structure

The Royal Swedish Academy of Sciences has awarded a Nobel Prize for the tenth time for work using X-ray crystallography to determine the structure of molecules. This year's winners in chemistry were honored not for working out a particular structure but for constructing a system of mathematical equations, about 35 years ago, that has greatly facilitated analysis of the position of atoms in crystals of a wide variety of organic and inorganic materials.

The originators of this "direct method" for structure determination are Jerome Karle of the U.S. Naval Research Laboratory in Washington, D.C., and Herbert A. Hauptman, formerly of the Naval Research Laboratory and now at the Medical Foundation of Buffalo (N.Y.)

X-ray crystallography "revolutionized" inorganic chemistry and supported "important progress" in natural product chemistry, the Nobel award states. It explains, "In order to understand the nature of chemical bonds, the function of molecules in biological contexts and the mechanism and dynamics of reactions, knowledge of the exact molecular structure is absolutely essential."

The structures of thousands of compounds have been described using this technique, Karle told reporters at a press conference at the Pentagon. Whereas a single structure formerly took years to determine, now the direct method and modern computers routinely allow chemists to work out a structure in a day or two.

Structures that have been analyzed by the Hauptman-Karle method include hormones, vitamins, antibiotics, potential anticancer drugs and plant-growth promoters. Among compounds of particular interest to the Department of Defense are new propellants, which may be used for rockets, and potential antimalarial drugs.

The analytical method of Hauptman and Karle was controversial for more than 10 years after it was first published in 1949, and came into wide use only in the middle 1960s. "Initially it was hard for people to believe that the mathematics would, even in principle, do what it does," Karle says.

When an X-ray beam strikes a crystal, the rays are deflected, primarily by the electrons in the material, in a manner that produces spots of different intensities on a photographic film. Hauptman and Karle devised mathematical equations to describe these spots and to deduce from their intensities the location of atoms in the crystal.

This analysis rests primarily on two conditions, the Nobel award states. First, in a crystal, the electron density is never less than zero. Second, the number of measurements possible is much greater than the number of unknown values in the

Hauptman

Karle

Photos: Wide World

equations to be solved. Solving many equations, each "only statistically probable," makes the determinations more reliable.

The Swedish Academy cites several scientists instrumental in the practical application of the method, including Karle's wife, Isabel Karle, also of the Naval Research Laboratory. "We work together separately," Isabel Karle says. "He does the theory. I do the experiments."

The current method is applicable only to relatively small molecules. According to Isabel Karle, the largest molecule so far analyzed by the direct method is the nervous system peptide, enkephalin, which consists of five amino acids and contains 230 carbon, nitrogen and oxygen atoms.

Both Hauptman and Karle are working on new mathematical methods to determine more easily with X-ray crystallography the structures of large molecules, such as proteins, and even such complex entities as viruses. —*J.A. Miller*

Nobels

Physics: Honor to von Klitzing

For the discovery of the quantized Hall effect, Klaus von Klitzing of the Max Planck Institute for Solid State Research in Stuttgart, West Germany, is the sole recipient of the 1985 Nobel Prize in physics. Von Klitzing's discovery, made in 1980, is a variation of the ordinary Hall effect.

von Klitzing

Wide World

The American physicist E.H. Hall had discovered that if a metal conducting an electric current is subjected to a magnetic field, the electrons that make up the current are deflected, and there appears a Hall conductivity in the direction transverse to the original current direction. Von Klitzing found that if the metal is made very thin and bonded to a semiconductor and the assembly is chilled to near absolute zero, the Hall conductivity is quantized: It appears in integral multiples of the fundamental constant e^2/h, the square of the electron charge divided by Planck's constant. The quantized Hall effect facilitates precise measurement of fundamental constants and makes possible precise standards of electrical resistance. It has many applications in electronics.

Born in 1943 to a Germany family in territory that is now part of Poland, von Klitzing studied in West Germany at the Technical University in Brunswick and at the University of Würzburg. Before joining the Max Planck Institute, he taught at the Technical University in Munich and Marburg University. □

Toward safer scoliosis screening

Due in part to increased school screening programs for scoliosis, an estimated 120,000 U.S. adolescents now are being monitored with X-rays for a lateral curvature of the spine — creating concern among health experts over the long-lasting effects of radiation exposure.

For several years, cancer researchers have suspected a link between early use of X-rays and later development of breast cancer (SN: 12/5/81, p. 359). Because scoliosis assessment may depend on repeated X-rays of the spine, and because two-thirds of the patients are young females, the Food and Drug Administration (FDA) is urging physicians to carefully evaluate their X-ray methods.

According to Charles Showalter, a director in FDA's Center for Devices and Radiological Health, at each scoliosis exam the average patient receives radiation exposure eight times that of a chest X-ray, and individual exposures may greatly exceed that. In addition, some patients may be X-rayed every three to six months for several years, from adolescence to skeletal maturity.

Speaking at an FDA seminar last week, Showalter and health physicist Alvin Thomas agreed that the actual increased risk of breast cancer due to scoliosis monitoring may be small, but they emphasized that it is an "avoidable risk." Thomas said breast tissue is "bearing full force of the X-ray beams" in commonly used techniques, but a recent FDA study at the Bethesda (Md.) Naval Hospital proved exposure could be reduced 10- to 360-fold. Citing that study, Showalter said that, for no more than $1,000, radiologists could "virtually decrease exposure to zero," depending on how many of the FDA's recommended methods are used:

- Turn the patient around so the chest faces away from the X-ray beam (gives a fuzzier but adequate image).
- Use faster rare-earth film/screen systems to shorten exposure time.
- Add gradient filters or shadow shields onto X-ray equipment to decrease or stop radiation to areas of the upper chest.
- Give patients specially designed vests with attenuating materials sewn over the breast area. —*D. D. Edwards*