utions to biological problems and the relative simplicity of the fusion mechanism in influenza virus suggest that other systems may employ different tactics. On the other, the strategy of using proteolytic cleavage to set a molecular trap seems to have found more general application. Thus many viruses produce precursor polyproteins which are cleaved to form the mature polypeptides, often with substantial separation of the freed ends. An example of this is found in the Picornaviridae which, in spite of possessing no lipid and hence having no need of membrane fusion to get their genetic material into the cell, appear to drive infection in an analogous way. In this case, cleavage of the polypeptide chains during maturation of the capsid seems to prime the virus for pH- or receptor-mediated extrusion of a hydrophobic structure into the host cell membrane, initiating release of the viral RNA[10]. Indeed, like many really useful biological engines, this one pops up in disparate contexts, for instance in what is perhaps the most dramatic irreversible structural rearrangement yet seen among eukaryotic protein molecules, the serpin family of protease inhibitors[11]. □

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OBITUARY

Dorothy Hodgkin (1910–94)

DOROTHY Hodgkin died on 29 July, thirty years after her receipt of the Nobel Prize for Chemistry "for her determination by X-ray techniques of the structures of biologically important molecules". Each of her structures extended X-ray crystallography to molecules of greater complexity than any previously analysed. She established it as one of the fastest methods of finding the chemical constitution of natural products; nuclear magnetic resonance has since become the other.

In 1943, Dorothy solved her first structure, that of cholesterol iodide. She assumed that the scattering contributions of the heavy iodine atoms outweighed the combined ones of all the light atoms and hence determined the phases; but because the two iodines in the unit cell are related by a centre of symmetry, and the molecule contains chiral centres, this gave the right structure superimposed on its mirror image. Undeterred, she devised an ingenious way of distinguishing the correct from the spurious peaks in the electron density map, and the structure fell out. She was disappointed when it added merely a few stereochemical details to the formula of cholesterol already elucidated by the chemists.

Penicillin, first isolated in 1942 by Ernst Chain a stone's throw away from Dorothy's Oxford laboratory, presented a greater challenge because its chemical constitution was then still unknown. Initially the crystals proved useless, and she had to wait until February 1944 when the first good ones arrived from the United States. Fourier projections of the sodium salt phased by the heavy atom method, and of the rubidium and potassium salts phased by isomorphous replacement, gave only the vaguest outlines of the molecule. Again, Dorothy refused to be discouraged. By a remarkable piece of chemical intuition, she inferred the right answer and proved it by an elegant three-dimensional Fourier synthesis which revealed the complete stereochemistry, including the very unusual β-lactam ring proposed a few weeks earlier by E. P. Abraham.

The next challenge was vitamin B_{12}, which contains more than four times as many atoms as penicillin. But in 1948, when Dorothy took the first X-ray pictures, even its molecular weight was unknown. She records that "the discovery of the cobalt atom... first stimulated us to attempt a detailed investigation". Dorothy solved its structure and discovered its remarkable chemical constitution by her imaginative, bold interpretation of three-dimensional Patterson functions and of blurred electron-density maps phased on the cobalt atom alone, ingeniously picking out the significant peaks from a jungle of spurious ones. To succeed, she had to shed the obvious assumption that the groups surrounding the cobalt were pyrrole rings as in porphyrins and discovered the quite novel ring structure which she named corrin.

In 1935, at the very start of her career, Dorothy had prepared her first crystals of insulin and discovered their rich X-ray diffraction pattern which made her determined to solve its structure. She persevered with her attempts in parallel with all her other work. To her disappointment, however, insulin did not yield until 1969, mainly because it crystallized in the rhombohedral space group R3 which lacks centrosymmetric projections and rendered the determination of heavy atom positions needed for isomorphous replacement extremely difficult. Dorothy was delighted when, in 1988, a genetically modified human insulin promised an improved treatment for diabetes. This could not have been designed without the structure on which she had laboured for most of her active life.

AP

Dorothy Hodgkin — a brilliant mind and an iron will to succeed.

Dorothy Hodgkin radiated love: for science, her family, her friends, her students and her crystals. That love was combined with a brilliant mind and an iron will to succeed. Her uncanny knack of solving structures owed much to her wide knowledge of stereochemistry (she used to write the chapters on crystal structures for the Annual Reports of the Chemical Society and kept all their stereochemistry in her head). She and her students had to solve their structures laboriously by taking series of Weissenberg photographs with weak X-rays from sealed tubes, by estimating the intensities of hundreds or even thousands of spots visually, and by calculating structure factors and initially even Fouriers on manually operated calculators. Any of these structures could now be solved in a few days by feeding X-ray data collected on computer-controlled diffractometers into other computers programmed to find atomic positions automatically by direct methods. Even Dorothy's favourite molecule, insulin, with a molecular weight of 5,778, is now beginning to yield to direct methods, and may also soon be solved automatically. She would have rejoiced at that phenomenal progress of X-ray analysis.

Science apart, Dorothy's life was devoted to many good causes. But I thought that in this memoir I should concentrate on her research rather than her work for peace, for the Third World, or the students of Somerville College and of Bristol University of which she was Chancellor. In *Nature* she would have wanted to be remembered above all as the superb scientist she was. Max Perutz

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