OBITUARY

Linus Pauling (1901–1994)

LINUS Pauling died on 19 August at his home in California at the age of 93. He was widely regarded as the greatest chemist of the twentieth century — such was the depth of his intuitive understanding of the subject that his co-workers felt he sometimes knew the answer to a question before developing a theory to explain it.

Pauling's scientific work had a special style. There was frequently a boldness in his proposal of new ideas, often at first thought outrageous for the simplicity with which they explained complicated phenomena. The essence of his approach to chemistry lay in the way in which he related quantitative physical chemical measurements, especially molecular structure parameters, to theoretical interpretations. Pauling was aided by his enormous knowledge of chemical properties, his phenomenal memory, and a theoretical understanding that allowed him to make often unexpected correlations between physical measurements and chemical properties. An example is his early work in the late 1920s in formulating a simple set of rules governing the structure of ionic minerals, especially silicates.

Likewise, in his work on the nature of the chemical bond, Pauling started with such facts as bond distances, bond angles and molecular dipole moments — the elementary data of structural chemistry — and, applying quantum mechanics, developed a theoretical structure based on the hybridization of orbitals that predicted the directed valence of atoms. This work was an aid in predicting the chemical properties of molecules and also established an outlook that has influenced nearly everyone who subsequently entered this field of science. This is simply the attitude that one can explain and correlate by theory the many diverse physical and chemical properties of atoms and molecules.

In 1939 Pauling published *The Nature of the Chemical Bond*. More than any other, this book revolutionized the study of chemistry. It presented a way of understanding chemistry based on rational physical principles and drove home the importance of thinking in three dimensions. The 1954 Nobel Prize for Chemistry was awarded to him largely in recognition of these contributions.

In the 1930s Pauling's interest began to spread beyond small molecules to haemoglobin and antibodies. The nature of proteins was not understood at that time. He recognized the central role of hydrogen bonding and other weak interactions in determining and maintaining macromolecular structure. In 1940 he and Max Delbrück developed the idea of the importance of molecular complementarity in macromolecular interactions. They suggested that such interactions were, very probably, an essential part of the molecular basis of genetics.

Perhaps one of the best examples of Pauling's audacious thinking was in his proposals enumerating the possible structures of polypeptides, including the α-helix and pleated sheet. These discoveries were made through intuition and model building — all this being done, as Pauling said, "with one's feet higher than one's head, for convenience" (he often did his best thinking with his long legs propped up on his desk). The rules for determining possible configurations were simple, and, in essence, they minimized the total energy of the structures. His approach to structure solving has served as a model for many workers in the field, including those who have solved the structure of a variety of polymeric molecules ranging from DNA and collagen to polypropylene.

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Pauling — "a real genius".

In 1945, Pauling attended a lecture in which William Castle described sickle-cell anaemia, a disease characterized by intracellular aggregation of haemoglobin molecules in non-aerated blood. While listening to the lecture, he imagined that this phenomenon might be explained by a hereditary alteration of the surface of a haemoglobin molecule that would make it complementary to another part of the surface, so that in the absence of oxygen these altered haemoglobin molecules might combine together. This idea was the beginning of our understanding of molecular disease.

A frequent characteristic of Pauling's work was that, after his interpretation of a phenomenon, its acceptance became widespread and it began to appear obvious. One example was his description, in 1946, of the importance of the surface of proteins in determining specificity through complementarity of shape. He also realized that enzyme action could go in both directions, and thus it seemed apparent to him that what the enzyme had to do was lower the activation energy for the transition. Another example was his work with Zuckerkandl in 1962. By looking at changes in the amino-acid sequence of haemoglobin in different animals, they could correlate the changes with the evolutionary period at which the animals diverged from each other. This suggested that mutations accumulate in a fairly regular manner with time in a particular protein and therefore that they could be used to measure evolutionary time. This principle was the beginning of the field of molecular evolution. It was a startling idea when it was presented. It is now so widely accepted that it seems almost self-evident.

In 1948, Pauling described the gene as two complementary units held together by weak forces such as hydrogen bonding. Although he failed to solve the structure of DNA, Watson and Crick's achievement in doing so owes much to Pauling's methodology.

Pauling was a warm, compassionate man, who cared deeply for people who were oppressed for their political beliefs. With the development of huge nuclear arsenals after the Second World War, he became an active campaigner for peace, stimulated by his wife Ava Helen. Here, too, his intuition played a key role. He became convinced that radiation was harmful to the genome, even in small amounts, and crusaded tirelessly for a cessation of nuclear testing. Today, it is generally understood that radiation from radioactive fallout or X-rays is harmful. But when Pauling started his campaign, the idea was regarded as outrageous, and even subversive. In 1962 Pauling won the Nobel Peace Prize for his efforts in helping to bring about a Test Ban Treaty.

By the 1970s Pauling's attention turned to antioxidants — vitamin E and especially vitamin C. His analysis and his intuition led him to the conclusion that we would be healthier if we took supplements of these vitamins. The debate on the role of antioxidants in general and vitamin C in particular continues; however, many analyses are emerging which support Pauling's views on the importance of these compounds.

Linus Pauling was widely honoured. In addition to two Nobel Prizes he received over 50 medals and awards from a great variety of organizations, and almost as many honorary degrees from universities. The esteem with which he was regarded was vividly illustrated to me in 1951 when, as a postdoctoral fellow of Pauling's, I visited Albert Einstein in Princeton. Einstein's comment to me was "Ah, that man is a real genius!"

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