ISSN:2249-5347
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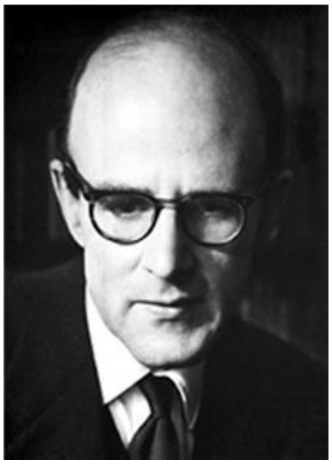
International Journal of Science Innovations and Discoveries
An International peer Review Journal for Science

Nobel Prize in Chemistry 1962




Max Ferdinand Perutz **John Cowdery Kendrew**

The Nobel Prize in Chemistry 1962 was awarded jointly to Max Ferdinand Perutz and John Cowdery Kendrew *"for their studies of the structures of globular proteins"*

RESEARCH INFORMATION:

In the year 1869 the Swedish chemist Christian Wilhelm Blomstrand wrote, in his at that time remarkable book *Die Chemie der Jetztzeit* (Chemistry of Today):

"It is the important task of the chemist to reproduce faithfully in his own way the elaborate constructions which we call chemical compounds, in the erection of which the atoms serve as building stones, and to determine the number and relative positions of the points of attack at which any atom attaches itself to any other; in short, to determine the distribution of the atoms in space.

In other words, Blomstrand gives here as his goal the knowledge of how compounds are up from atoms, i.e. knowledge of what is nowadays often called their "structure". Moreover, structure determination has been one of the biggest tasks of chemical research, and has been approached using many different techniques. For several reasons, the structure determination of carbon compounds, the so-called organic compounds, experienced an initial rapid development. At this stage the techniques were generally those

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of pure chemistry. One drew conclusions from the reactions of a compound, one studied its degradation products, and tried to synthesize it by combining simpler compounds. The structure thus arrived at, however, was in general rather schematic in character; it showed which atoms were bonded to a given atom, but gave no precise values for interatomic distances or interbond angles. However, for an up-to-date treatment of the chemical bond and in order to derive a correlation between structure and properties, these values are needed, and they can only be obtained using the techniques of physics.

The physical method which, more than any other, has contributed to our present-day knowledge of these mutual dispositions of the atoms is founded on the phenomenon which occurs when an X-ray beam meets a crystal. This phenomenon, called diffraction, results in the crystal sending out beams of X-rays in certain directions. These beams are described as reflections. The directions and intensities of such reflections depend on the type and distribution of the atoms within the crystal, and can therefore be used for structure determination. It is 50 years ago this year since Max von Laue discovered the diffraction of X-rays by crystals, a discovery for which he was awarded the 1914 Nobel Prize for Physics. This work opened up a whole new range of possibilities for studying both the nature of X-rays and the structure of compounds in the solid state. The initial application of structure determination was developed first and foremost by the two English scientists, Bragg father and son, and as early as 1915 they were rewarded with the Nobel Prize for Physics. The techniques have since been considerably refined, and it has been possible to solve more and more complicated structures. However, considerable difficulties were encountered as soon as any other than very simple structures were considered. There is no simple general way of progressing from experimental data to the structure of the compound under investigation. Moreover, the mathematical calculations are exceedingly time-consuming. However, by about the middle of the 1940's a point had been reached where it was becoming possible to carry out X-ray determinations of the structures of organic compounds which were so complicated that they defied all attempts using classical chemical methods.

In 1937 Max Perutz performed some experiments in Cambridge to find out whether it might be possible to determine the structure of haemoglobin by X-ray diffraction, since no other method could be imagined for this purpose. Sir Lawrence Bragg, who tirelessly continued the work begun jointly with his father, in 1938 became the head of the Cavendish Laboratory in Cambridge. When he saw the results obtained by Perutz, he encouraged him to continue and has ever since lent a very efficient support. Haemoglobin belongs to the proteins which play such an enormous part in life processes, and which are a basic material in living organisms. Haemoglobin is a component of the red blood corpuscles. It contains iron which can take up oxygen in the lungs and later give it up to the body's other tissues. Haemoglobin is counted among the globular proteins, whose molecules are nearly spherical. It was chosen for the initial attempt, partly because it could develop good crystals, and partly because the haemoglobin molecule is quite small for a protein molecule. About ten years later, John Kendrew joined Perutz' research group, and the task allotted to him was to try to determine the structure of myoglobin. Myoglobin is another globular protein, closely related to haemoglobin, but with a molecule only a quarter as large. It is found in the muscles, and enables oxygen to be stored there. Particularly large amounts of myoglobin are found in the muscular tissues of whales and seals, which need to be able to store large quantities of oxygen when diving.

However, Perutz and Kendrew encountered considerable difficulties. In spite of exceptionally comprehensive work, the result was not forthcoming until 1953, when Perutz succeeded in incorporating heavy atoms, namely those of mercury, into definite positions in the haemoglobin molecule. By this means the diffraction pattern is altered to some extent, and the changes can be utilized in a more direct structure determination. The method was already known in principle, but Perutz applied it in a new way, and with great skill. Kendrew also succeeded, by an alternative method, in incorporating heavy atoms, generally mercury or gold, into the myoglobin molecule, and could subsequently proceed in an analogous manner.

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A necessary condition for this technique is that the addition of the heavy atoms should not alter the positions of the other atoms of the molecule within the crystal. In this connection it is simply because of its enormous dimensions that the molecule remains practically unaltered. Bragg has rather aptly said that "the molecule takes no more notice of such an insignificant attachment than a maharaja's elephant would of the gold star painted on its forehead".

But even if the path was now open for a direct structure determination of haemoglobin and myoglobin, there was still an enormous amount of data to be processed. Myoglobin, the smaller of the two molecules, contains about 2,600 atoms, and the positions of most of these are now known. But for this purpose, Kendrew had to examine 110 crystals and measure the intensities of about 250,000 X-ray reflections. The calculations would not have been practicable if he had not had access to a very large electronic computer. The haemoglobin molecule is four times as large, and its structure is known less thoroughly. In both cases, however, Kendrew and Perutz are currently collecting and processing an even greater number of reflections in order to obtain a more detailed picture.

As a result of Kendrew's and Perutz' contributions it is thus becoming possible to see the principles behind the construction of globular proteins. The goal has been reached after twenty-five years' labour, and initially with only modest results. We therefore admire the two scientists not only for the ingenuity and skill with which they have carried out their work, but also for their patience and perseverance, which have overcome the difficulties which initially seemed insuperable. We now know that the structure of proteins can be determined, and it is certain that a number of new determinations will soon be carried out, perhaps chicfly following the lines which Perutz and Kendrew have indicated. It is fairly certain that the knowledge which will thus be gained of these substances which are so essential to living organisms will mean a big step forward in the understanding of life processes. It is thus abundantly clear that this year's prize-winners in chemistry have fulfilled the condition which Alfred Nobel laid down in his will, they have conferred the greatest benefit on mankind.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1962/press.html