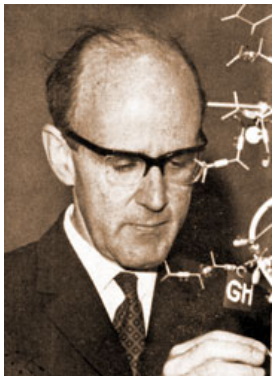
Max F. Perutz



Vienna, Austria, 19 May 1914 – Cambridge, UK, 6 Feb. 2002

Title Professor of Cellular and Molecular Biology, Medical Research Council Laboratory of Molecular Biology, Cambridge, UK. Nobel Prize for Chemistry, 1962.

Field Cellular and Molecular Biology

Nomination 12 May 1981

Most important awards, prizes and academies

Nobel Prize for Chemistry (1962); Royal Medal of the Royal Society (1971); Copley Medal of the Royal Society (1979); Fellow of the Royal Society (1954); Corresponding Member of the Austrian Academy of Sciences; Associé étranger de l'Académie des Sciences, Paris; Socio straniero Accademia Nazionale delle Scienze, Rome; Socio straniero Accademia dei Lincei, Rome; Corresponding Member of the Bavarian Academy of Sciences; Member of the Akademie Leopoldina; Foreign Member of the Royal Netherlands Academy of Sciences; Foreign Associate of the National Academy of Sciences of the USA; Honorary Fellow of the Royal Society of Edinburgh.

Summary of scientific research

Perutz was an X-ray crystallographer and molecular biologist. He began his work on the structure of haemoglobin crystals in 1937, but it took him until 1953 before he found the way to interpret their X-ray diffraction patterns. In that year he showed that comparison of the diffraction pattern from a crystal of pure haemoglobins and from a crystal of haemoglobin to which two atoms of mercury were attached allowed the phase angels of the X-ray reflexions to be measured. This discovery opened the field of protein crystallography. Its first successful application was to the structures of myoglobin and haemoglobin, but by now more than a hundred protein structures have been solved this way.

Haemoglobin is in equilibrium between two structures, the deoxy and the oxy structure. Determination of these structures in atomic detail by Perutz and his collaborators allowed him to interpret the physiological properties of haemoglobin, and, together with H. Lehmann, to account for the symptoms of carriers of abnormal haemoglobins in stereochemical terms.

In his final years Perutz published papers on electrostatic effects in proteins, on species adaptation in the haemoglobin molecule, on haemoglobin as a model of a drug receptor, on the search for possible drugs against sickle cell anaemia and on the molecular mechanism of Huntington's Disease. All his work was concerned with the application of stereochemistry to biological function.

Main publications

Perutz M.F., *Proteins and nucleic acids: Structure and Function* (8th Weizmann Memorial Lecture). Elsevier Publishing Company, 1962; Fermi G. and Perutz M.F., *Haemoglobin and myoglobin*. In: *Atlas of Molecular Structures in Biology*. Eds. D.C. Philips & F.M. Richards. Clarendon Press, Oxford, 1981; Perutz M.F., *Stereochemical mechanism of oxygen transport by haemoglobin*. «Proc. R. Soc. Lond.», B *208*, 135-62 (1980); Perutz M.F., *Stereochemistry of cooperative effects in haemoglobin*. «Nature», *228*, 726-39 (1970); Perutz M.F. *et al.*, *Interactions between the quaternary structure of the globin and the spin state of the heme in ferric mixed spin derivatives of haemoglobin*. «Biochemistry», *17*, 3640-52 (1978); Perutz M.F., *Regulation of oxygen affinity of haemoglobin. Influence of structure of the globin on the heme iron*. «Ann. Rev. Biochem.», *48*, 327-86 (1979); Perutz M.F., *Species adaptation in a protein molecule*. «Mol. Biol. Evol.», *1*, 1-28 (1983); Fermi G., Perutz M.F., Shaanan B. and Fourme R., *The Crystal Structure of Human Deoxyhaemoglobin at* 1.74Å *Resolution*. «J. Mol. Biol.», *175*, 159-74 (1984); Nagai K., Perutz M.F. and Poyart C., *Ozygen binding*

properties of human mutant hemoglobins synthesized in Escherichia coli. «Proc. Nat. Acad. Sci. USA», *82*, 7252-5 (1985); Perutz M.F., Fermi G., Abraham D.J., Poyart C. and Bursaux E., *Hemoglobin as a receptor of drugs and peptides: X-ray studies of the stereochemistry of binding*. «J. Amer. Chem. Soc.», *108*, 1064-78 (1986); Perutz M.F., *Protein Structure: New Approaches to Disease and Therapy*. Freeman, New York 1992; Perutz M.F., *Glutaminu repeats as polar zippers: their role in inherited neurodegenerative disease*. «Molecular Medicine», *1*, 718 (1995); Perutz M.F., *Haemoglobin, the Breathing Molecule and the Flow of Gluciers*. Word Scientific Publishing Company, Singapore 1996.

Commemoration – I feel honoured to speak in memory of Max Perutz. I appreciated him extremely, both as a very competent scientist and as a lovely person. What also linked me to him was that twenty years ago, in 1981, we became members of this Academy at the same time. Looking back to these twenty years of having had meetings here, I still see him sitting for a short while in the – at that time – very hard seats, and then standing up and remaining standing because he had obvious back pains, but his face was with us and looked very happy. I think that he overcame his pain just by loving to talk about Science with us. Max Ferdinand Perutz was born in 1914 in Vienna, where he grew up and studied chemistry. Doing his chemical studies, he started to pick up interest in applying his knowledge to investigating the structure and functions of proteins. This was at a very early time, in 1936, when he decided to go for his Ph.D. degree to Cambridge, England, where there was a well established X-ray crystallography group. At that moment very little work was done with bio-molecules, but that was his aim. Max Perutz chose a very particular protein which is relevant for all of us and for many other living organisms, namely haemoglobin. Haemoglobin is a rather complex molecule, and Max Perutz devoted enormous efforts and time to find access to its structure. This was not easy, because he had first to develop methodology which was not yet available; he had first to elaborate it, and I think that it is his merit together with some colleagues, to have found a way to introduce heavy metal atoms into the proteins under study and then to compare responses to X-ray irradiation of crystals with and without metal inclusions. Mathematical treatment of the obtained data allowed them to draw a picture of the three-dimensional structure of the protein. You can imagine that this gave a very big impulse to comprehend protein function. This development can be seen as a forerunner of what we now call proteomics. On the way to his scientific breakthrough, Max Perutz spent some time in the Swiss mountains to study the formation and structure of ice crystals in glaciers. This best illustrates his efforts as a scientific investigator to find novel approaches to overcome difficulties of methodology in order to gain insight into the structure of complex biomolecules. It was shortly after the war in 1947 that the Medical Research Council of England decided on the proposition of Max Perutz and his colleagues to create in Cambridge the MRC unit for studies of molecular structures. This institution later became the Laboratory of Molecular Biology. Max Perutz was its first Director until 1979. During those 32 years of scientific activities a remarkable amount of novel knowledge was acquired in this laboratory. I shall just remind you of a few names of investigators like Francis Crick and Jim Watson, describing the DNA structure, Fred Sanger exploring protein and later DNA sequence analysis, Sydney Brenner unravelling elements of gene expression and so on, and a big number of young investigators who received their doctoral and postdoctoral education. The scientific success of research done in the laboratory of Molecular Biology may, in part, be due to its attraction of highly qualified investigators, but it might also be linked with the readiness of these scientists to develop new methodologies and research strategies, as exemplified by Max Perutz. From 1945, he closely collaborated with John Kendrew, joining at that time the laboratory with the aim of unravelling the structure of myoglobin, a protein related to haemoglobin. Both projects led to successful results. This found its highest recognition in 1962 when Max Perutz and John Kendrew were awarded the Nobel Prize in Chemistry for their studies of the structures of globular proteins. Max Perutz's interests were not limited to structure, he wanted to find out the functional mechanisms of proteins. He thus investigated the binding of oxygen to haemoglobin. He was able to show that in this complex molecule the binding of different atoms of oxygen is cooperative. This important finding led him to look at differences between oxyhaemoglobin and desoxyhaemoglobin. In the same context he also studied abnormal forms of haemoglobin, such as those of some haemoglobin mutants. Following the same line, he also started to compare haemoglobins of different animals, and this gave him some insight on how these molecules must have evolved in the course of long-term history. The resulting knowledge offered explanations on how some particular adaptations to very specific life conditions, life styles, must have occurred. For example, he compared the haemoglobin of migratory birds that fly very long distances at very high altitudes requiring much energy, with that of sedentary land animals. This led Max Perutz to a deep understanding of protein functions and how living organisms can evolve to carry out their required functions. The career of Max Perutz as a scientist, starting as a young doctoral student in Cambridge, lasted sixty-five years, until his death, which occurred last winter at the age of eighty-eight years. We still remember his reports in recent years on novel aspects of his research concerning studies of the electrostatic effects of proteins and their medical implementations as for example seen for Huntington's disease. Thereby, he pointed to relations between stereochemistry and biological functions, such as those in aggregates of polyglutamine fibres. These are questions at the forefront of today's research. So Max Perutz kept up with scientific progress as a passionate

researcher until the end of his days. His personality was impregnated by that passion, and his influence on his colleagues and certainly on all his students is enormous and long lasting.

Lastly, in order to show the high regard and affection that he had for our Academy I would like to read out the letter that Max Perutz sent to the Chancellor shortly before his death:

Dear Monsignor Sorondo,
It seems that my days are numbered and I feel like expressing to you and the President my deep appreciation of having been a Member. I received the Pope's telegram appointing me to the Academy at the same moment as the news of the attempt to assassinate him. It roused a terrible conflict of emotion in me, on the one hand my great pleasure about this Honour, and on the other hand my deep sorrow at that tragic crime. I first attended a study-week in 1961, in fact organized it myself, which you could almost call 'The Birth of Molecular Biology'. People presented an extraordinary series of exciting new discoveries, and I first met some of the protagonists from other countries. Since then I have attended and organized other study-weeks and much enjoyed that privilege, but the greatest privilege was being a Member of that unique body, a truly international Academy, covering all the natural sciences. I came across there many more people whom I would never otherwise have met, such as the Indian physicist Menon, and then there was the wonderful setting, that Renaissance court, looking over the back of St. Peter's like the view of the Matterhorn from Zermatt. I think that the Pontifical Academy is a unique institution and I very much hope that the Holy Father and his successors will continue to give it their support. I should be delighted if you were able to communicate any of this letter to the Holy Father and assure him again how much I appreciated my Membership.
With kindest regards to you and the President.
Yours, Max Perutz

Werner Arber