implication of the Earth system's deep nonlinearities is that estimates of climatic parameters based on observations from the recent past are unreliable for making forecasts about the state of the world at CO_2 concentrations of 560 p.p.m. or higher. Moreover, the nonlinearities mean that doing more of a bad deal (Kyoto) may well be very good.

These truths seem to escape Lomborg. His cost–benefit analysis involves only point estimates of variables (interpreted variously as 'most likely', 'expected', and so forth), implying that he believes we shouldn't buy insurance against potentially enormous losses resulting from climate change. His concerns over the prevalence of malaria, undernutrition and HIV in today's world show that he is an egalitarian. There is, then, an internal contradiction in his value system, because if you are averse to inequality you should also be averse to uncertainty.

The integrated assessment models of Earth's system on which Lomborg builds his case are arbitrarily bounded on either side of his point estimates. It can be shown that if those bounds are removed (as they ought to be), even a small amount of uncertainty — when allied to only a moderate aversion to uncertainty — would imply that humanity should spend substantial amounts on insurance, even more than the 1–2% of world output that has been advocated. If the uncertainties are not small, standard cost–benefit analysis as applied to the economics of climate change becomes incoherent, even if those uncertainties are judged to be thin-tailed (gaussian, for example); this is because the analysis would say that no matter how much humanity chooses to invest in protecting Earth from passing through those later tipping points, we should invest still more.

Economics helps us to realize what we are able to say about matters that will reveal themselves only in the distant future. Simultaneously, it helps us to realize the limits of what we are able to say. That, too, is worth knowing, for limits on what we are able to say are not a reason for inaction. Lomborg's seemingly persuasive economic calculations are a case of muddled concreteness. ■

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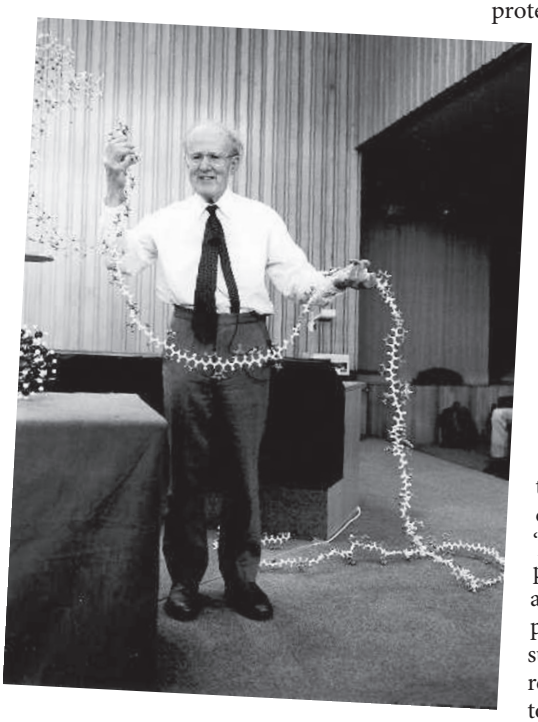
Max in three dimensions

Max Perutz and the Secret of Life
by Georgina Ferry
Chatto & Windus/Cold Spring Harbor Laboratory Press: 2007. 304 pp. £25/$39

Gregory A. Petsko

I have a problem with the title of this book, but it's almost my only quibble with this marvelous biography of one of the least known of the twentieth century's great scientists. By no measure could Max Perutz be said to have discovered the secret of life — a claim that might be defended for Gregor Mendel, or Charles Darwin and Alfred Russel Wallace, or James Watson and Francis Crick. The mechanism of oxygen's reversible binding to haemoglobin, which Perutz elucidated in 1970 after more than 25 years of work, doesn't even apply to most living organisms (and oxygen is deadly to most anaerobes). That said, Perutz did many extraordinary things, including winning the Nobel Prize in Chemistry in 1962 for solving haemoglobin's three-dimensional structure.

It is hard to write a biography of someone only recently deceased (Perutz died in 2002). The biographer must accurately portray someone who was known personally to many readers, yet at the same time expose previously hidden aspects of his or her character. Georgina Ferry achieved both in her biography of Dorothy Crowfoot Hodgkin, and now she has done it again in her engrossing account of the life and work of Max Perutz.



PERUTZ FAMILY

Perutz the showman: Max continued to captivate audiences well into his eighties.

Perutz, whom I knew well for 30 years, can't have been an ideal subject. No scandal colours his career; his personal life was stable and happy; his accomplishments were clear in terms of priority; he made a number of significant mistakes; his major discoveries are not easily understood by the layperson; and he lacked the forceful manner of a Crick or Bernal. But as the father of protein crystallography — arguably one of the greatest scientific advances of the last century — and the founder of the Medical Research Council (MRC) Laboratory of Molecular Biology in Cambridge, UK, his influence was enormous.

Ferry succeeds in bringing what could, in lesser hands, be considered a somewhat drab character sharply to life. As an Austrian Jew born during the First World War, Perutz left for Cambridge in 1936, where he joined the laboratory of one of the larger-than-life figures of modern science, John Desmond Bernal. Together with Dorothy Hodgkin, Bernal had, just two years earlier, taken the first X-ray diffraction photograph of a single crystal of a protein molecule, the digestive enzyme pepsin. This showed that, in principle, the extraordinary power of crystallography could reveal the atomic details of even large biological molecules. Undeterred by the scale of his task, Perutz ventured to use crystallography to unravel how haemoglobin could bind oxygen tightly enough to transport it around the bloodstream, yet release it when and where it was needed.

I doubt whether most people, even today, understand how pioneering this was. Determining the three-dimensional structure of proteins was a goal of Nobel-prize potential for several powerful research groups of that time, but none particularly cared what the protein was. Only Perutz had a greater aim. He wanted to understand the function of haemoglobin, which meant solving all the problems presented by this large, flexible protein. What would he have made of the recent International Structural Genomics Initiative, I wonder, which aims to turn out massive numbers of protein crystal structures without regard to biological or biochemical function?

Perutz's greatest achievement was demonstrating that the method of 'isomorphous replacement', previously used to solve the structures of small organic compounds, could be used to crack the 'phase problem' in protein crystallography. This is the problem of how to deduce a wave's phase component in diffraction patterns. This method made it possible to sum up the scattered X-ray waves in proper registration with each other and therefore to reconstruct the molecule's structure. It opened the way to solving the structure of any large crystalline molecule. Ferry explains the many false starts, and embarrassing errors, that led up to that moment, while allowing the reader to feel the frustrations and joys along the way. It's as good an account of a scientific breakthrough as you will find.

Haemoglobin's structure followed. More

than a decade later, Perutz showed that it was the minute movement of the iron atom into the plane of the haem group upon binding oxygen that triggered the shape change from the deoxygenated form of the protein. He once spent an hour explaining the new mechanism to me when I was a graduate student (even though he had just published it and must have talked about it many times before), as enthusiastically as a child with a new toy.

Perutz's sometimes child-like character is the surprise in Ferry's biography. Apparently, he had a desire to be praised for his discoveries, which sometimes manifested as petulance and led to ruthlessness towards competitors. But he was equally ready to confess his blunders, which endeared him to many younger scientists. Fragile health, combined with an acute sense of his failures, may have explained his reserve, particularly around the boisterous young molecular biologists at Cambridge. Ferry avoids the pop-psychology that permeates so many modern biographies, while offering insight into Perutz's temperament and behaviour.

For Ferry, one of Perutz's finest achievements was the creation in 1962 of the MRC Laboratory for Molecular Biology, which has produced an astounding number of Nobel laureates and Fellows of the Royal Society. She devotes an entire chapter to its history and to Perutz's unique, hands-off style of managing it. His skill in identifying and nurturing talent at a time when molecular biology was just starting out is one of the things that makes Perutz a central figure in modern scientific history.

Ferry doesn't end the book with Perutz's death from Merkel cell carcinoma, just days after submitting his manuscripts on the structure of the protein aggregates in Huntington's disease. Instead, she follows it with a chapter about his avocation as a writer of popular essays about science and society. This is a masterstroke, because his wise and witty writings present Perutz to us at his most candid, and so the chapter sums up the book, and the man, very nicely.

Ferry has mined gold in the lives of two of the founders of structural biology; I can't wait to see whom she tackles next. Frederick Sanger, one of only four people to win two Nobel prizes? Or how about William H. Bragg or Max von Laue? ■

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One man and his molecule

Piccole Visioni: La Grande Storia di una Molecola
by Marta Paterlini
Codice Edizioni: 2006. 263 pp. €19

Ermanno Gherardi

Max Perutz and his 1959 model of oxygenated haemoglobin is one of the iconic images of twentieth-century biology. It encapsulates a journey that began in 1936 when, armed with a degree in chemistry from the University of Vienna, Perutz moved to Cambridge to work as John Desmond Bernal's research student on the task of solving protein structures at atomic resolution using X-ray crystallography. At the time, Bernal and his former research student, Dorothy Crowfoot Hodgkin, were probably the only two people to believe that the atomic structure of a protein was within reach — having themselves obtained promising diffraction patterns from hydrated crystals of pepsin just two years earlier. Perutz was thus charged with the responsibility of realizing Bernal's dream. A year later, he opted to work on haemoglobin, the oxygen-transporting protein in red blood cells, a study that lasted for the next 60 years.

Piccole Visioni ('Small Visions'), written in Italian by Marta Paterlini, narrates the story of how Perutz arrived at the atomic structure of haemoglobin and, from there, at the finely tuned mechanism that regulates oxygen binding, transport and off-loading at its destination. The book also provides a vivid account of Perutz's life and his role in founding the Medical Research Council (MRC) Laboratory of Molecular Biology, the main institution responsible for the birth of 'new biology' in the second half of the twentieth century.

Perutz's early years in Cambridge saw him concentrating on the crystallographic analysis of haemoglobin. He was under considerable personal strain at the time, because his parents had lost their home and property following Hitler's invasion of Austria; they arrived as refugees in Cambridge in 1939. Perutz himself, a potential 'enemy alien', was initially interned and deported to Canada until January 1941, when — in a dramatic change of heart — the British government involved him in a secret war project to produce reinforced ice to act as floating airfields (but which were never built).

SVENSKT PRESSFOTO/PHOTOSHOT

A glowing Perutz at the 1962 Nobel ball, with his wife Gisela.

Throughout the war years, funding from the Rockefeller Foundation in the United States and later from Imperial Chemical Industries in the United Kingdom — obtained with the help of William Lawrence Bragg, Cavendish professor from 1938 — enabled Perutz to carry on with his work. In 1947, Bragg persuaded the MRC to set up a "unit for the study of molecular structure of biological systems" involving himself, Perutz, John Kendrew and two assistants. This unit later became the present MRC Laboratory of Molecular Biology in Cambridge.

The early chapters of *Piccole Visioni* cover these events and introduce the basic concepts of crystallography and the problems that were faced in analysing protein crystals at the time. The rest of the book is taken up with Perutz's discovery of the basic features of protein structure through his studies on haemoglobin. A breakthrough came in 1951, when he experimentally confirmed the structure of the α-helix shortly after Linus Pauling had proposed its existence on theoretical grounds. Two years later, Perutz developed the technique of isomorphous replacement for protein crystallography (see 'Max in three dimensions', opposite).

Perutz's method enabled him to determine a low-resolution structure of haemoglobin and helped Kendrew to solve the structure