Max Perutz: chemist, molecular biologist, human rights activist

John Meurig Thomas

DOI: 10.1039/b507503n

Tribute paid to Max Perutz prior to the Max Perutz Memorial Lecture given by Professor Sari Nusseibeh at The International Human Rights Network of Academics and Scholarly Societies, Royal Society, London, 19 May 2005.

In tracing the trajectory of Max Perutz's life, future historians of science will doubtless highlight several great scientific adventures and achievements:

(i) He founded, with Sir Lawrence Bragg and John Kendrew, the Medical Research Council (MRC) Unit of Molecular Biology in the Cavendish Laboratory, Cambridge in 1947, and then he was the principal scientific architect of the Laboratory of Molecular Biology (LMB) which he founded in Cambridge in 1962.

Dept. of Materials Science, University of Cambridge, Cambridge, CB2 3QZ, UK and Davy Faraday Research Laboratory, Royal Institution, London W1S 4BS

(ii) Along with his associate, John Kendrew, he solved the first protein structures[2] (haemoglobin and myoglobin), and this earned them the Nobel Prize in Chemistry in 1962.

(iii) Again, with John Kendrew, he founded the European Molecular Biology Organisation (EMBO), and became its founding chairman in 1963.

(iv) By focusing on numerous mutants of haemoglobin, from a large range of living creatures and numerous humans, he gained a deep understanding of several inherited diseases enabling him to open up the new field of molecular pathology and adding to our knowledge of molecular evolution. He elucidated the nature of such tragic diseases as thalassemia and sickle-cell anaemia.

(v) In 1970, he finally worked out the mode of action of haemoglobin[3] and, in 1986, nearly a quarter of a century after his Nobel Prize-winning work, he discovered how haemoglobin acts as a drug receptor.

(vi) As Francis Crick wrote in 2002,[4] Max Perutz was the still centre of the revolution in molecular biology that occupied the second half of the twentieth century.

And the careful historian of science will also record that, in 1948, the 34 year-old Perutz solved the problem of how a glacier flows. (It moves, not like treacle, but more like a ductile metal when it is extended, with planes of atoms gliding over one another.)

All these, and many other scientific achievements, are associated with Max Perutz's name. But to those who knew him, to those who worked or lived alongside him, to those who observed his quiet, effective negotiating skills, and to those who had the pleasure of talking to or corresponding with him, or attending his lectures, or of reading his evocative book reviews, essays and letters, there was far more to Max Perutz. He combined, in a singular fashion, all the noblest instincts of mankind.

Max Perutz was a man of warm humanity and of great human decency and compassion. He had immense moral courage. He was morally incorruptible. And he possessed huge reserves of intellectual energy, as well as a youthful

John Meurig Thomas

John Meurig Thomas, a pioneer of modern solid-state and materials chemistry, has long been active in the design and in situ characterization of heterogeneous catalysts and the development of novel techniques in chemistry. After establishing leading solid-state and surface chemistry laboratories in Wales (Bangor and Aberystwyth), he initiated, on his appointment as Head of the Department of Physical Chemistry, Cambridge (1978–86), the study of solid-state chemistry there. He introduced the techniques of solid-state NMR (magic-angle-spinning NMR was invented in Bangor), high-resolution (real-space) electron microscopy and computer graphics to the Cambridge Department. On becoming Director of the Royal Institution, London (1986) he set up a (still) active solid-state and computational chemistry unit at the Davy Faraday Laboratory. More than 10 percent of his 950 or so research papers were published in Chemical Communications, his first being in 1967, on the role of defects in the photoactivity of organic solids. Subsequently, his work on crystal engineering, sheet-silicate and pillared clay catalysts, geochemistry, Si, Al ordering and recurrent-intergrowths in zeolitic and other solid catalysts as well as his discovery and synthesis of new zeolites were initially reported in this journal.

The twenty or so articles of his that have appeared in Chem. Commun. in the last decade deal with nanoparticle bimetallic and single-site, open-structure catalysts which exhibit regio-, shape- and enantio-selectivities. He has also developed (with P. A. Midgley[1]) scanning electron tomography as a tool in solid state and catalytic research.

His work has earned him numerous national and international awards; and he was knighted in 1991 for his services to chemistry and the popularization of science.

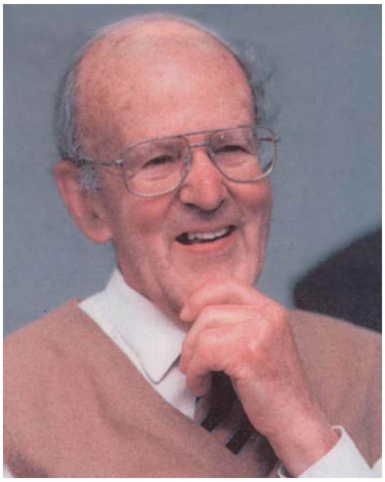


Fig. 1 Max Perutz

voracity for new knowledge. He was a stylish and incisive author of popular scientific articles and reviewer of books – books that he meticulously researched and fastidiously, though eloquently, analysed. He wrote charming and sensitive personal letters. Above all, he was an indefatigable warrior, passionately committed to social and political justice. Intellectual honesty and freedom, and especially human rights mattered to him profoundly.

Max Perutz often exhibited the temperament of the artist and the imaginative sensibility of the poet. It pleased his many admirers, and Max himself, when Rockefeller University accorded him their first Lewis Thomas Prize, recognising the Scientist as Poet.

Max delighted in the beauty of the natural world. He was the kind of man who, before starting his laboratory work at the LMB on a Spring morning, would occasionally take a walk on the Gog-Magog hills (outside Cambridge) filling his heart and soul, in so doing, with pantheistic pleasure.

But Max was resolute in his opposition to what he perceived to be wrong-headed and erroneous arguments or decisions. Long before his work at Cambridge came to fruition – long before he made his monumental scientific breakthroughs – he felt impelled to resign from his post as lecturer in the University of Cambridge, as a protest against the decisions of the central authorities.

Another example of how forthright he could be is seen in his attack on certain philosophers and historians of science whose theses he disputed. Max rejected as nonsense the view, popular among modern sociologically oriented philosophers of science, that scientific truth is relative and shaped by a scientist's personal concerns, including his or her political, philosophical, even religious instincts. When he attacked such opinions, he once quoted Max Planck's memorable assertion:

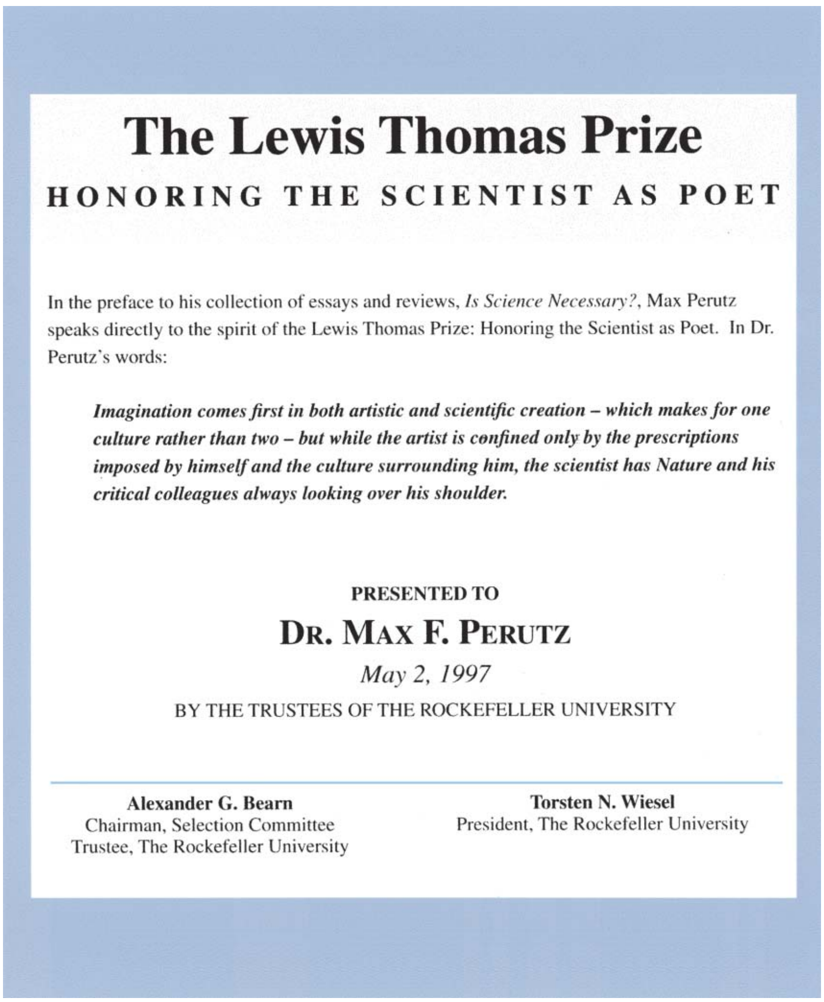
"There is a real world independent of our senses: the laws of nature were not invented by man, but forced upon him by that natural world. They are the expression of a rational order."

Max would probably have agreed with Richard Feynman's flippant remark:

"Philosophers of science are about as helpful to scientists as ornithologists are to birds."

Max's long, labyrinthine path as a research scientist began when he studied chemistry at the University of Vienna, his home city. He acquired a special interest in organic biochemistry and heard about the work of Sir Gowland Hopkins, the discoverer of vitamins. Max decided that he wanted to solve a great problem in biochemistry. His teacher, Hermann Mark, visited Cambridge and had planned to pave the way for Max to join Hopkins' group there. But Mark met J. D. Bernal, a pyrotechnically brilliant conversationalist, who said he would take Max as his student. (Mark forgot to approach Hopkins!) So, in 1936, Max became a researcher in the Cavendish Laboratory where Bernal taught and researched in physics, and a graduate student at Peterhouse.

On Bernal's advice, he learned X-ray crystal structure analysis in the Department of Mineralogy. A year or so later, he visited his cousin Felix Horauwiz (in Prague) who convinced him that an appropriate target for his ambitions was the structure of haemoglobin, first, because it was the protein that was most abundant and easiest to crystallise; second, because oxyhaemoglobin and



The Lewis Thomas Prize

HONORING THE SCIENTIST AS POET

In the preface to his collection of essays and reviews, *Is Science Necessary?*, Max Perutz speaks directly to the spirit of the Lewis Thomas Prize: Honoring the Scientist as Poet. In Dr. Perutz's words:

Imagination comes first in both artistic and scientific creation – which makes for one culture rather than two – but while the artist is confined only by the prescriptions imposed by himself and the culture surrounding him, the scientist has Nature and his critical colleagues always looking over his shoulder.

PRESENTED TO

DR. MAX F. PERUTZ

May 2, 1997

BY THE TRUSTEES OF THE ROCKEFELLER UNIVERSITY

Alexander G. Bearn
Chairman, Selection Committee
Trustee, The Rockefeller University

Torsten N. Wiesel
President, The Rockefeller University

deoxyhaemoglobin had different crystal structures – but no one knew what these structures were. Gradually, it emerged that each unit repeat volume in a crystal of haemoglobin has about 12,000 atoms. In 1937, when Max made his decision, X-analysis had solved structures containing no more that about 100 atoms. *That* was the magnitude of the problem Max set himself.

He had been encouraged, however, by the success J. D. Bernal and Dorothy Crowfoot (later Hodgkin) had achieved in obtaining in 1934 beautiful X-ray diffraction patterns of the protein crystal, pepsin, in its mother liquor. Soon, he, Bernal and Fankuchen obtained[5] similarly encouraging diffraction patterns from haemoglobin and chymotrypsin. But it was not until the late 1950s, under the aegis of Sir Lawrence Bragg, that he finally reached his target of elucidating the structure of haemoglobin. And when he did, it made him famous. From 1936 to the late 1950s, however, he suffered a succession of setbacks: there were many scientific, personal and political obstacles to surmount. In 1940, his studies at the Cavendish Laboratory were rudely interrupted by his internment (along with hundreds of German-speaking people then living in the UK) first in the Isle of Man, then in Quebec, Canada. He returned to work of national importance during the war. In 1942, after a whirlwind romance, he married Gisela Peiser, a Berlin-born lady then working in Cambridge; and in 1943 he became a British citizen. In 1944, he was back again at the bench in the 'Cavendish', where, in 1945, he was joined by John Kendrew. Francis Crick, a physicist, joined the group as Max's PhD student in 1948. Jim Watson, a geneticist, came in 1951 and was soon working with Crick on DNA.

In early 1951, after some six years extracting what X-ray crystallographers call Patterson maps (which, in the case of haemoglobin crystal, consisted of some 25 million lines between the thousands of atoms in the haemoglobin molecule), Max Perutz felt elated when they seemed to tell him that haemoglobin consists simply of bundles of parallel chains of atoms spaced apart at equal intervals. I quote his words:

"Shortly after my results appeared in print, a new graduate student joined me. As his first job, he performed a calculation which proved that no more than a small fraction of the haemoglobin molecule was made up of the bundles of parallel chains that I had persuaded myself to see, and that my results, the fruits of years of tedious labour, provided no other clue to its structure. It was a heartbreaking instance of patience wasted, an ever-present risk in scientific research."

That graduate student made himself unpopular in the MRC unit of the Cavendish at the time. But he was very clever. In fact, years later, Max Perutz told me that that student turned out to be one of the cleverest men he ever met. His name was Francis Crick – a man who won the Nobel Prize, with Watson and Wilkins, before he completed his PhD!

After a period of deep depression, which disturbed Max emotionally and physically, a ray of brilliant light appeared in 1953. Max, remembering an earlier suggestion by Bernal, realised that he could benefit by tagging molecules of haemoglobin with heavy ions such as silver or mercury. Being the expert crystallographer that he was, he knew immediately that such heavy-atom-tagging should enable him to solve the structure of haemoglobin in a manner quite different from his early approach, which Francis Crick had so comprehensively and unceremoniously demolished. Both Perutz and Kendrew redoubled their efforts. Max it was who first demonstrated the validity of the method, by computing the X-ray diffraction patterns of haemoglobin with and without a mercury tag. (Sir Lawrence Bragg was so thrilled that, to quote Max, he *"went around telling everyone that I had discovered a goldmine"*.)

But John Kendrew, in 1958, working both at the Cavendish and with David Phillips at the Royal Institution, solved the three-dimensional structure of myoglobin, an achievement greeted worldwide as sensational. Max was both pleased and somewhat depressed with this breakthrough. Pleased because his method and his laboratory and his partner, John Kendrew, had triumphed. But he said later that he was also depressed, partly because he had not "got" to haemoglobin first, but partly also because he had a nagging uncertainty that the solution of the haemoglobin problem might prove bewilderingly and interminably elusive. In September 1959, however, Max Perutz and his colleagues, using 40,000 measurements from crystals of haemoglobin and six heavy-atom derivatives, calculated the three-dimensional structure of the molecule. At last, he had reached the longed-for shore.

Max officially retired from the LMB in 1979, but he worked there almost every day up until the time of his death in 2002. And only a few days before he entered hospital during his terminal illness, he completed the text of a research article that followed on from his important work on the fundamental causes and molecular aspects of neurodegenerative diseases.

It is universally acknowledged that the LMB is one of the most famous and successful research laboratories now in existence. Max had set up a simple structure for running the LMB from its inception in 1962. "I persuaded the MRC" he said "to appoint me as Chairman of the Governing Board rather than Director, a Board to be made up of Kendrew, Crick, Sanger and me" (four wise men, five Nobel Prizes!). "This arrangement reserved major decisions of scientific policy to the Board and left their execution to me. The Board met only rarely!

Shortly after he passed away in 2002, I discussed elsewhere[6] the scientific and humane legacy of Max Perutz. In particular, I sought to divine the secret of the extraordinary success of the LMB, and to contrast his methods of running a research laboratory with the advice nowadays given to scientists by the Paladins of accountability in various Funding and Research Councils, and increasingly by university administrators. The principles he used were:

choose outstanding people and give them intellectual freedom; show genuine interest in everyone's work, and give younger colleagues public credit; enlist skilled support staff who can design and build sophisticated and advanced new apparatus and instruments; facilitate the interchange of ideas, in the canteen as much as in seminars; have no secrecy; be in the laboratory most of the time and accessible to everybody where possible; and engender a happy environment where people's morale is kept high.

These are lofty principles, obviously and compellingly correct, but difficult to live up to. A crystallographer friend of mine, who visited me recently, said of them that they reminded him of the "Sermon on the Mount" or the "Declaration of Independence". Max, however, complied with these principles, and he was ably assisted for many years by his devoted wife, Gisela, who made the canteen of the LMB a focal point of intellectual stimulus.

My friendship with Max extended over the last 24 years of his life: we lived a few doors from one another; we were members of the same Cambridge college, Peterhouse; and for part of that time I had responsibilities for running the Royal Institution and the Davy Faraday Research Laboratory, places where he and John Kendrew had been Readers for 13 years from the time of the appointment of my predecessor-but-one, Sir Lawrence Bragg, as Director. Through my friendship with Max, I benefited enormously from his wisdom, guidance and humour, which I grew to appreciate during our numerous walks around the playing fields adjacent to our homes, while strolling in the Botanical Garden, or sitting for tea in the intimacy of our homes. During those discussions, I recall particularly two anecdotes worthy of reciting here. The first relates to an incident that occurred while he attended a "Human Rights" gathering. A Soviet scientist had said that one should cease to use the term "freedom of speech" and replace it with "freedom after speech". The second involves his retort when I asked him how he had become such a skilled negotiator. He replied by quoting what a former Fellow of Trinity College, Cambridge had once said:

"In Cambridge, to reach your goal, you must learn to combine the linear persistence of the tortoise with the circuitous locomotion of the hare."

Max was utterly repulsed by the thought of the use of torture on political or other prisoners. He could be seen to cringe while talking about it. His revulsion of such practices was partly what animated him as a human rights activist. But he detested injustice of any kind, and was dedicated to the eradication of ignorance. He did something about it. Members of this audience will know that, ten years ago, in Amsterdam at the Dutch Academy, he read a paper on "By What Right Do We Invoke Human Rights?" This widely published lecture[7] is a closely reasoned history of the concept of human rights from the days of Aeschylus (458 BC) to the present day. His response to the terrorist attack in New York on 9/11 was to organise a petition intended for world leaders. Amongst other things it said, "Avoid military actions against innocent people. Military retaliation does not solve the problem of fanaticism, but instead fuels the anger by demanding 'counter' revenge."

In closing this tribute, having heard repeated mention today of liberty, freedom, the pursuit of truth and the elimination of injustice, I can think of no better way to remember Max, and to remind us of the things that he stood for, than to quote some of the words of the Hindu mystic and poet, Rabindranath Tagore (Gisela, Max's wife, had met Tagore in Berlin). Tagore and Einstein had an interesting correspondence some 90 years ago. Tagore held that scientific truth was realised through man, whereas Einstein maintained (as did Max Planck, whom I quoted earlier) that scientific truth must be conceived as a valid truth that is independent of humanity.

Knowing that the premier academics and scholarly bodies of the world are committed to the restless pursuit of truth and knowledge (as Max was), it is appropriate that I should recite, to end, Song 35 of Tagore's "Gitanjali":

Where the mind is without fear and the head is held high;

Where knowledge is free;

Where the world has not been broken up into fragments by narrow domestic walls;

Where words come out from the depth of truth;

Where tireless striving stretches its arms towards perfection;

Where the clear stream of reason has not lost its way into the dreary desert sand of dead habit;

Where the mind is led forward by thee into ever-widening thought and action –

Into that heaven of freedom, my Father, let my country awake.

Notes and references

1 J. M. Thomas and P. A. Midgley, *Chem. Commun.*, 2004, 1253–1267.

2 The protein structure data base in the USA now contains over thirty thousand structures, essentially all derived using the crystallographic method pioneered by Perutz and Kendrew.

3 The words used by him were: *Haemoglobin is not just an oxygen tank: it is a molecular lung. It changes its structure every time it takes up and releases oxygen. You can hear your heart going 'thump, thump, thump'; but in your blood the haemoglobin molecules go 'click, click, click' – but you can't hear that."*.

4 Francis Crick, *Phys. Today*, 2002, Aug. issue.

5 J. D. Bernal, I. Fankuchen and M. F. Perutz, *Nature*, 1938, **141**, 523.

6 J. M. Thomas, *Angew Chem. Int. Ed.*, 2002, **41**, 3155.

7 M. F. Perutz, *Proc. Am. Philos. Soc.*, 1996, **140**, 135.