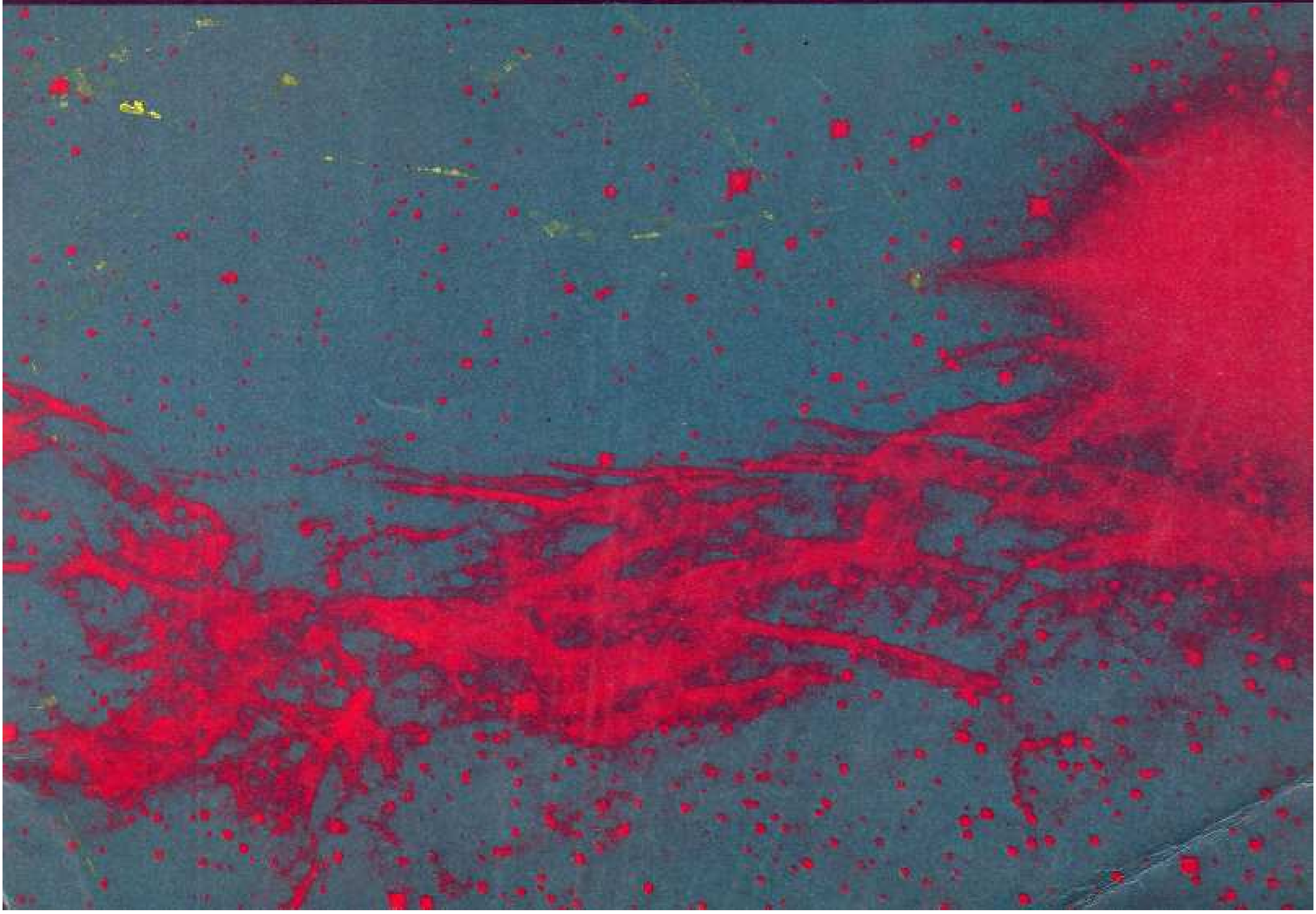
Chemistry Background Book

The Way of Discovery



facts and theories

This book is composed of articles based on personal interviews with fourteen famous scientists. All of them have been awarded the Nobel Prize. The interviewer sought to find answers to various questions, such as how the interest of each scientist was first awakened in his particular field and how the realization of a particular discovery flashed upon him. Certain qualities these scientists share: a devotion to their work and the ability to spend hours of unremitting attention on it. Another quality is that they had to find out the answers for themselves: they had to *desire* to find the truth.

Frequently, however, in these passages, one comes across the recognition that the scientist makes use of the unexpected. He has to learn to trust, as Linus Pauling describes, the mysterious ways of the creative imagination. Science in fact depends utterly upon what science knows least about: how the human brain works; how man knows that he knows; how he can make contact within himself with the still consciousness that finds order in the moving universe.

This dependence upon faculties which are known only by their results and not by their means of working is shared by scientists with poets and composers. But let us take one example.

In 1865, the German chemist Kekulé was trying to work out the structure of benzene which, in many of its reactions, behaves quite differently from most other simple organic compounds. He tells the story of how he was sitting in front of the fire and fell into a half sleep: 'The atoms flitted before my eyes. Long rows, variously, more closely, united; all in movement wriggling and turning like snakes. And see, what was that? One of the snakes seized its own tail and the image whirled scornfully before my eyes. As though from a flash of lightning I awoke; I occupied the rest of the night working out the consequences of the hypothesis.' So emerged the picture of benzene as a hexagonal ring – previously the structures of all organic compounds had been thought to be chains. The benzene ring brought many changes to organic chemistry and small wonder that Kekulé was to offer this famous advice to scientists: 'Let us learn to dream, gentlemen, and we may perhaps find the truth.' However, he was then careful to add: 'But let us beware of publishing our dreams before they have been tested by a discerning mind that is wide awake.'

Many scientific discoveries are, like that of the benzene structure, of a theoretical kind. They are *explanations* of the experimental facts but are not themselves facts. Kekulé had no way of demonstrating the physical existence of a benzene ring; if it existed at all, it was far too small to be seen, even under the highest-powered microscope; but it did explain satisfactorily the known experimental facts about benzene. If facts emerged that it failed to explain, the scientists would have to think again – to date, all the facts have tended to confirm Kekulé's picture although his explanation of the bonding structure has been improved by Pauling.

Then there are scientific discoveries of new experimental facts, for example, of a new substance or property of a substance. Such a discovery was that of Becquerel when he found that uranium fogged a photographic plate. Unlike a theory, which can be superseded by another theory, an experimental fact is permanent: if it is measurable (say the specific gravity of a substance) it may be measured more accurately, but it cannot be replaced. Often, a new experimental fact leads to a new theoretical explanation: for example, Rutherford's explanation of how uranium fogs a photographic plate in terms of radioactive decay. Similarly, a new theory often leads to the discovery of new experimental fact; for example, Einstein's General Theory of Relativity led to the discovery that light is influenced by gravity. In this way fact leads to theory, and theory to fact.

How a scientist comes to make a discovery may arise in a number of ways. It may be a chance observation that starts the scientist's mind thinking, such as Newton seeing the apple fall from the tree. It may be something unexpected that happens in an experiment, such as Priestley heating mercuric oxide and finding that a gas (oxygen) is given off. It may be something the scientist reads or hears that places something he knows in an entirely new perspective, such as the three bits of knowledge that clicked together in the mind of Lawrence Bragg and led to his new understanding of the X-ray patterns from a crystal (see the Background Book, *The Start of X-ray Analysis*). A planned piece of research may follow on from a previous discovery, as Faraday's experiments to produce electricity from magnetism followed from Oersted's discovery that magnetism could be produced by

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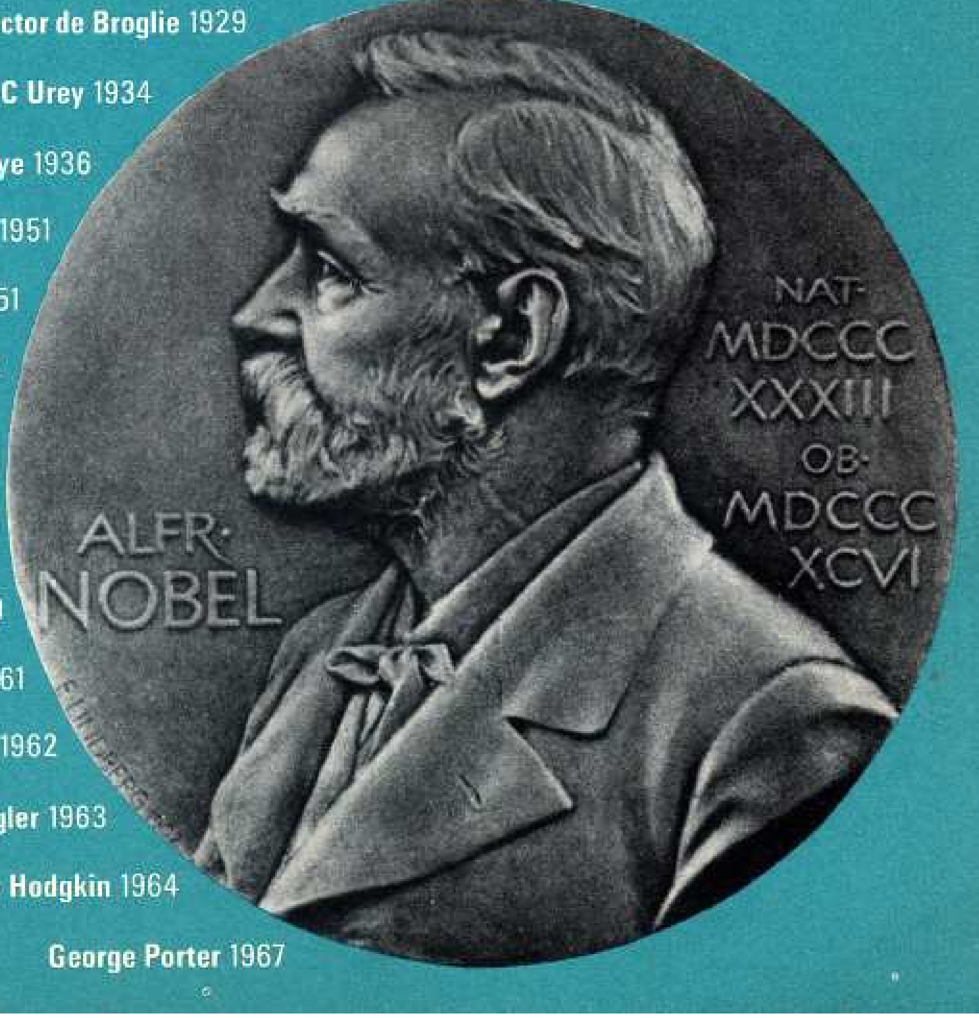
electricity. Or something may happen quite by chance, as Fleming discovered the antibiotic properties of penicillin from the mould that spoilt his culture of bacteria. Chance plays a part in many discoveries but, as Pasteur said, 'Chance favours the prepared mind'.

In this book, we learn of the discoveries of some famous scientists of this century and how they came to make them. Some of the discoveries are experimental fact – for example, de Broglie's wave theory of the electron. Some combine experiment with theory – for example, Seaborg's synthesis of new elements and their placing in the Periodic Table. Some of the discoveries have direct practical value – Ziegler's discovery of high-density polyethylene or Martin's of partition chromatography. Others have, as yet, no practical applications – for example Calvin's research into the chemistry of photosynthesis. However, to quote Madame Curie: '. . . scientific work must not be considered for the direct usefulness of it. It must be done for itself, for the beauty of science, and then there is always the chance that a scientific discovery may become, like radium, a benefit for all humanity.'

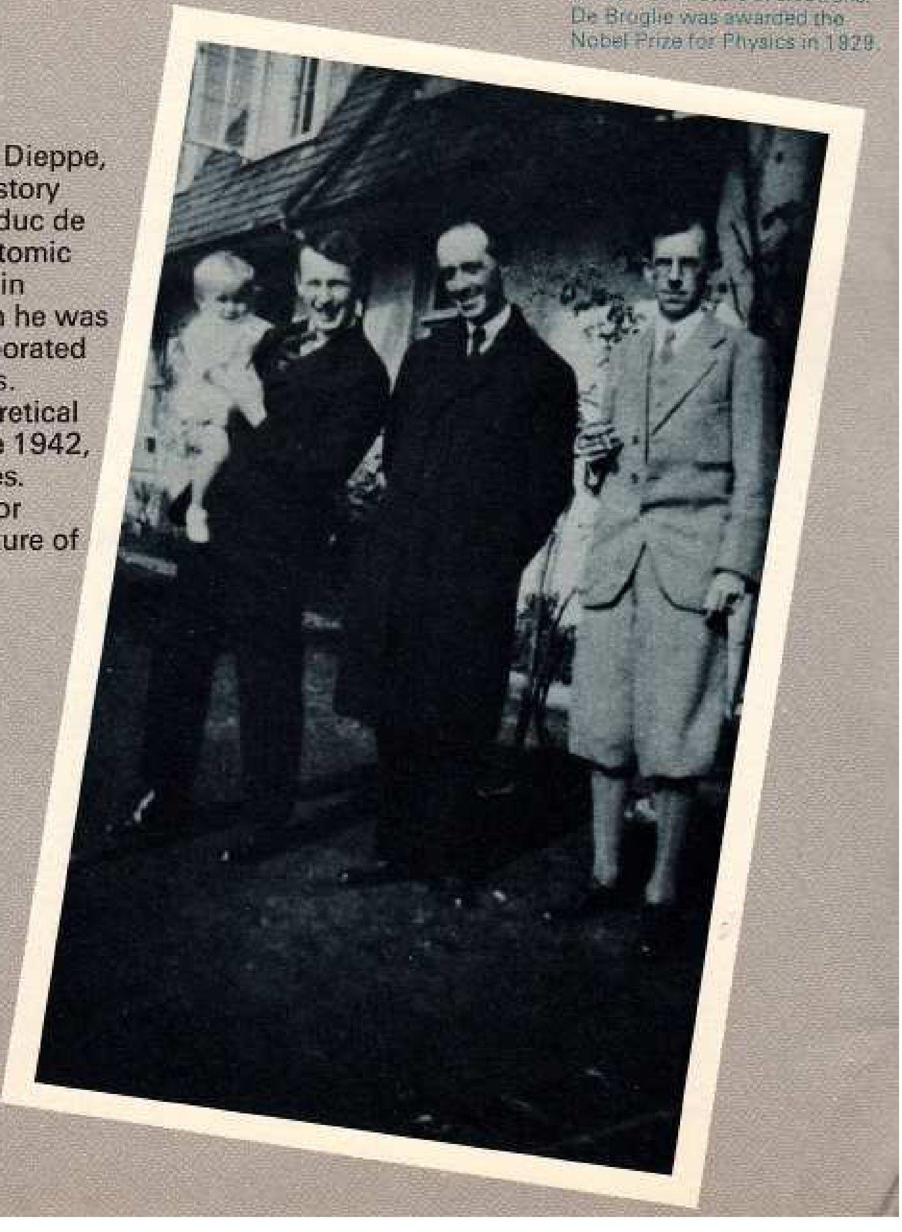
We consider these scientists and their discoveries in the order in which they received the Nobel Prize

Louis Victor de Broglie 1929
Harold C Urey 1934
Peter J W Debye 1936
Glenn T Seaborg 1951
Sir John Cockroft 1951
Archer J P Martin 1952
Linus Pauling 1954
Peace Prize 1962
Lord Todd 1957
Willard F Libby 1960
Melvin Calvin 1961
James D Watson 1962
Karl Ziegler 1963
Dorothy Hodgkin 1964
George Porter 1967



Louis Victor de Broglie
the wave properties of the electron

Prince Louis-Victor de Broglie (centre), shown here with G. P. Thomson (left), son of Sir J. J. Thomson, the discoverer of the electron, and C. F. Davisson (right). Davisson and G. P. Thomson gave experimental confirmation of de Broglie's theory of the wave nature of electrons. De Broglie was awarded the Nobel Prize for Physics in 1929.



Prince Louis-Victor de Broglie was born in Dieppe, France, in 1892. His first studies were in history but under the influence of his brother (the duc de Broglie, a physicist noted for his work on atomic physics and X-rays), he became interested in science. After the First World War, in which he was concerned with radio-telegraphy, he collaborated with his brother in various research projects.
Since 1928, he has been Professor of Theoretical Physics at the University of Paris and, since 1942, Life Secretary of the Académie des Sciences.
In 1929, he was awarded the Nobel Prize for Physics – 'for his discovery of the wave nature of electrons'.

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In the early years of this century, there was no doubt among scientists that electrons were particles. Even the mass of an electron was accurately known – $\frac{1}{1860}$ that of the hydrogen atom. In the model of the atom devised by Niels Bohr in 1913, electrons orbited round an atomic nucleus like planets round the sun. However, shortly after the First World War, Louis-Victor de Broglie, put forward the idea that electrons had the properties of waves as well as those of particles.

This connected with an old argument among scientists about the nature of light. Isaac Newton had said in 1704 that light consisted of tiny particles. About a hundred years later, however, Thomas Young discovered that light produced interference patterns and diffraction effects which can be accounted for only if light is regarded as waves. Consequently Newton's particle theory was replaced by a wave theory. At the turn of this century it was found that if a metal is irradiated with ultraviolet light, electrons are expelled from the metal. Einstein pointed out that this could be explained satisfactorily only if light were regarded as consisting of particles. Scientists were forced to accept that light had the properties both of waves and of particles.

Why, de Broglie wondered, should this apply to light and not to matter? Why was it that the mathematics used to describe the motion of electrons in an atom involved whole numbers when the only other phenomena in physics involving whole numbers known at that time were those of interference and vibration – properties of waves? 'A consideration of such problems led me, in 1923, to the conviction that matter, like light, should be thought of in terms of waves as well as particles. Only in this way would it be possible to arrive at a single theory that allowed the simultaneous interpretation of the properties of light and those of matter.'

Whereas the wave particle theory of light had resulted from experiment, de Broglie had conceived his theory through the 'spirit of intuition'. Because there was no experimental evidence to support it, all the leading scientists except Einstein dismissed it. If de Broglie could show that electrons produced diffraction effects this would be sufficient. At that time, an experiment of this nature was difficult to attempt. De Broglie was not a good experimentalist; working with pencil and paper, he followed up some of the mathematical implications of his theory.

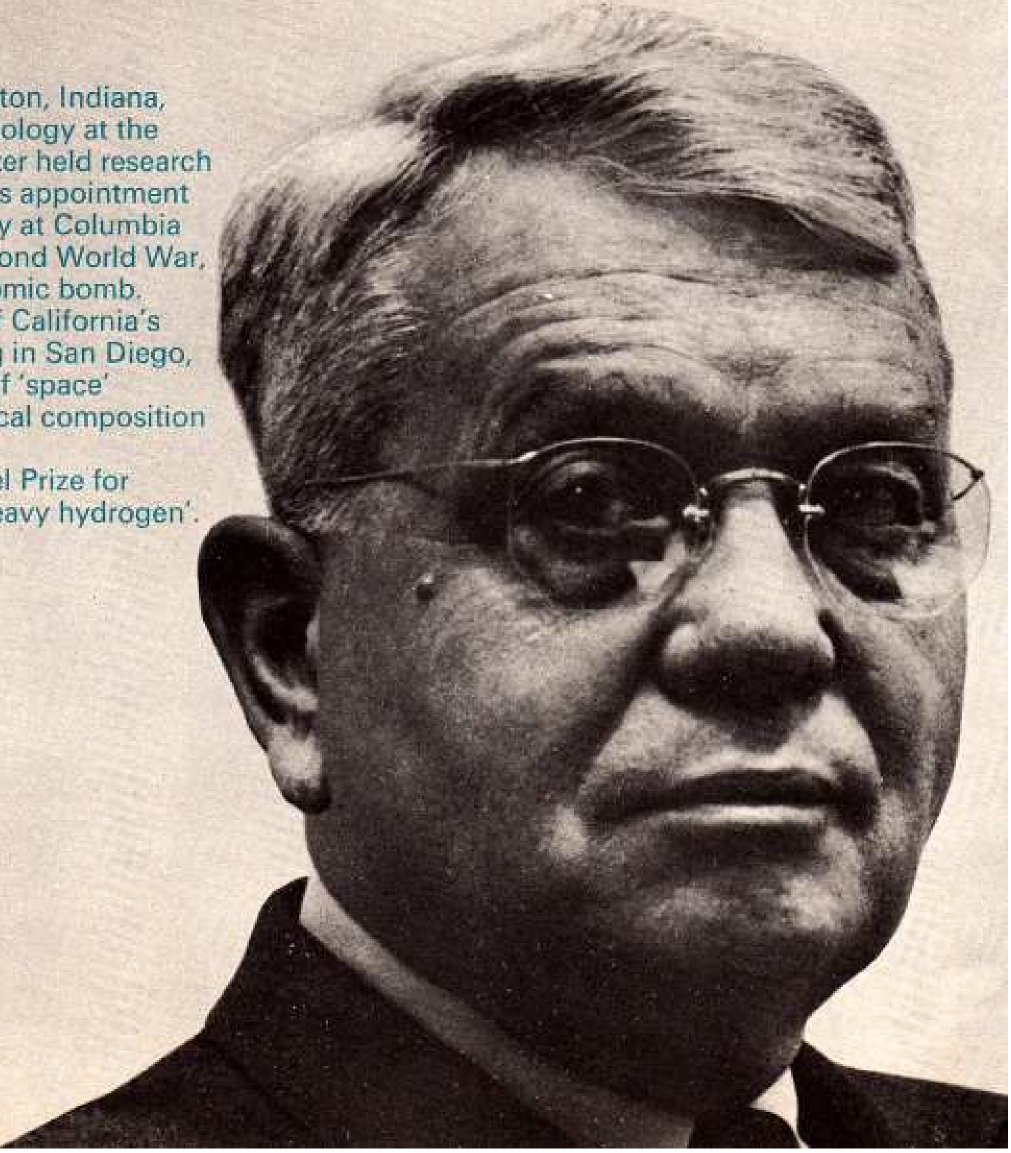
In 1927, Davisson and Germer in the United States and G. P. Thomson in Britain passed beams of electrons through crystals and obtained diffraction effects. 'Thereafter,' said de Broglie, 'it was no longer possible to imagine an electron simply as a minute particle of electricity: a wave had to be associated with it. And this wave was not just a fiction: its length could be measured and its interference effects calculated in advance.' As a result, the simple picture of the atom with electron particles orbiting round the nucleus had to be radically altered.

Elaborating on de Broglie's mathematical work, the Austrian scientist Schrödinger developed a system of equations known as wave mechanics. These equations could be applied to electrons irrespective of whether they were regarded as waves or particles. At a mathematical level, the wave/particle contradiction was solved. 'At a physical level,' says de Broglie, 'the reason why these two aspects exist and the manner in which it might be possible to merge them in one superior unity, remain a mystery.' Nevertheless, he believes that one day the mystery will be solved although, as he says, 'it will need fresh young minds to do it.'

Harold C Urey
the discovery of heavy hydrogen

Harold C. Urey, awarded the Nobel Prize in 1934 for his discovery of heavy hydrogen.

Harold C. Urey was born in Walkerton, Indiana, U.S.A. in 1893. He graduated in zoology at the University of Montana and thereafter held research posts at several universities until his appointment as Associate Professor of Chemistry at Columbia University in 1929. During the Second World War, he was involved in work on the atomic bomb.
He is at present at the University of California's School of Science and Engineering in San Diego, where he is engaged in problems of 'space' chemistry, such as what the chemical composition of the moon's surface might be.
In 1934, he was awarded the Nobel Prize for Chemistry – 'for his discovery of heavy hydrogen'.



At the age of fourteen, Harold Urey took the Indiana state examination to go to high school. He got 76 marks; the pass mark was 75. 'Had my marks been one the other way, I should probably have spent my life as a farmer in Indiana.'

When he went to university Urey studied biology and chemistry. During the early 1920s, he began to do research on isotopes. Little was known about them at this time although at Cambridge F. W. Aston was then investigating isotopes in his mass spectrometer. Although Aston had discovered many others, he had found no isotopes of either hydrogen or oxygen. In 1929 two isotopes of oxygen (O_{17} and O_{18}) were identified. This had interesting implications: according to measurements made by Aston in the mass spectrometer, the atomic weight of hydrogen relative to that of oxygen was always in the precise ratio of 1 to 16; if some of the oxygen had an atomic weight of 18, it followed that there must be an isotope of hydrogen heavier than 1 to maintain the ratio. 'I determined,' said Urey, 'to try and discover this heavier isotope of hydrogen.'

It had been estimated that, assuming the hydrogen isotope had a mass of 2, 1 part should be present in about 4,500 parts of hydrogen of mass 1. Up to then it had been impossible to detect an isotope which was present in such a small quantity. Urey's chief problem was to concentrate it. He and his research assistant worked day and night to find a way of doing this. 'The only way to solve a problem of this kind is to saturate yourself in it.' After doing pages of theoretical calculations, Urey came to the conclusion that it should be possible to concentrate the isotope by distilling hydrogen near the triple point where it exists in all three states – solid, liquid, and gas. Urey hoped that the lighter hydrogen with a lower vapour pressure would distil over first and leave a residue in which the heavier hydrogen was concentrated. Samples were prepared; 4,000 cm^3 of liquid hydrogen were distilled near the triple point until only about 1 cm^3 of residue was left. In the autumn of 1931, Urey examined the atomic spectra of these residues under a large diffraction grating. Lines indicating heavy hydrogen were plain to see. Some of these lines, Urey subsequently discovered, were fairly visible in natural hydrogen, but it needed the concentrated samples to establish their presence.

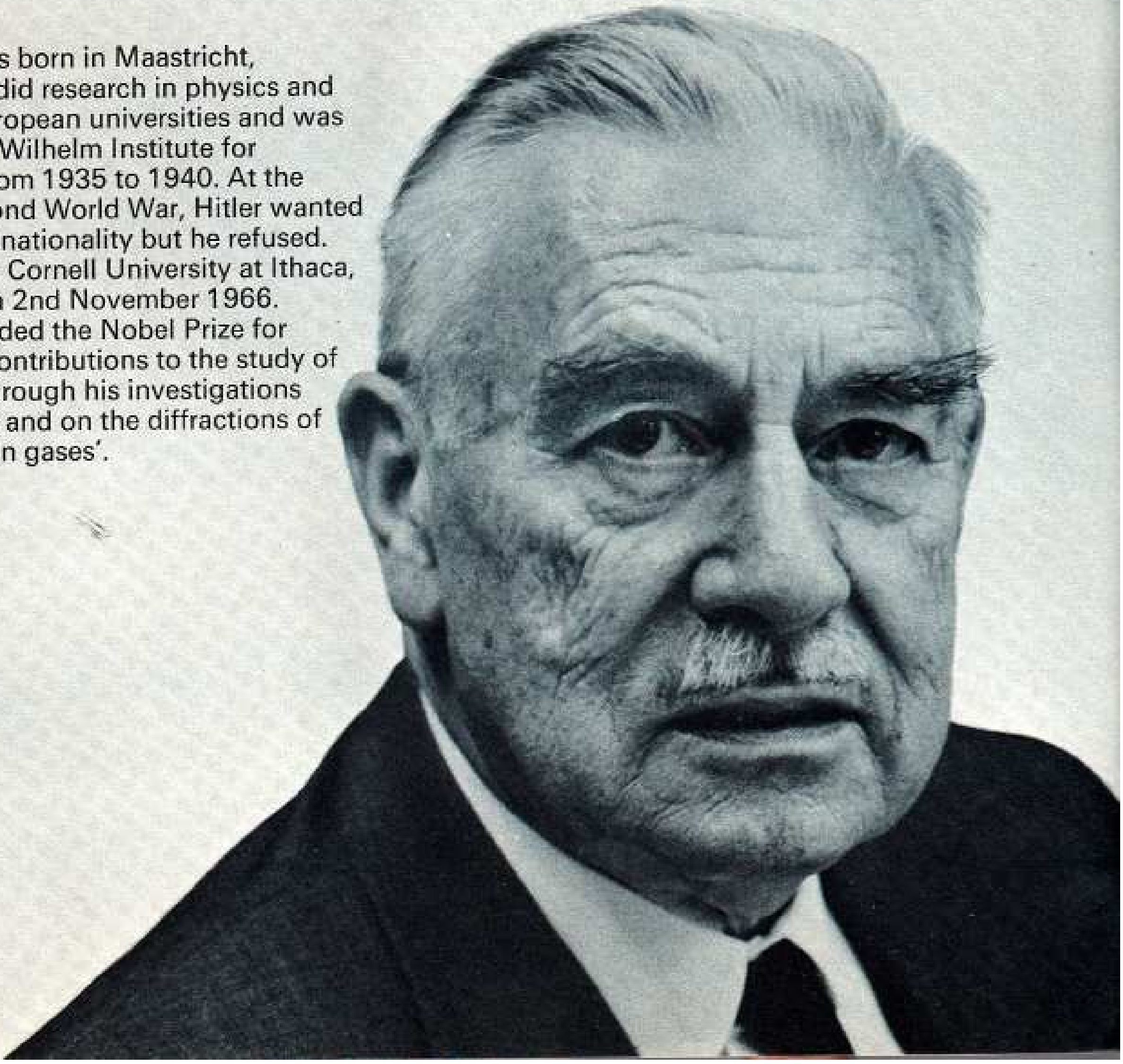
Urey then set about investigating the properties of heavy hydrogen – or 'deuterium' as it came to be called (from the Greek *deuteros* meaning second). As suspected, it had an atomic mass of 2. Another hydrogen isotope, tritium, with a mass of 3, was discovered in 1935. Deuterium has proved a useful tracer element in biological experiments. Its nuclei (deuterons) have been extensively used in transmutation experiments (see Seaborg, page 8). However, its main applications have been to atomic energy; it is the chief element used in fusion reactions, at present confined to the hydrogen bomb. Its oxide, heavy water, is used in large quantities to slow down neutrons in atomic reactors.

Behind Urey's discovery of heavy hydrogen there lay a piece of irony which presently came to light. Aston's measurements of the atomic weights of hydrogen and oxygen, from which the existence of heavy hydrogen had been predicted, were found to be in error. 'It was one of the few errors that Aston ever made, but, as he later jokingly remarked, he could hardly advocate that scientists should make mistakes on purpose so that other scientists might possibly benefit from them. It was a lucky break for me. Having started to look for heavy hydrogen, my future could have been very different if I hadn't found it.'

Peter J W Debye

properties of atoms and molecules

Peter J. W. Debye was born in Maastricht, Holland, in 1884. He did research in physics and chemistry at many European universities and was Director of the Kaiser Wilhelm Institute for Theoretical Physics from 1935 to 1940. At the beginning of the Second World War, Hitler wanted him to adopt German nationality but he refused. From 1940, he was at Cornell University at Ithaca, New York. He died on 2nd November 1966.
In 1936, he was awarded the Nobel Prize for Chemistry – 'for his contributions to the study of molecular structure through his investigations on dipole movements and on the diffractions of X-rays and electrons in gases'.



Peter J. W. Debye, who discovered an X-ray method for studying the structure of substances. For his contributions to the study of molecular structure, he received the Nobel Prize for Chemistry in 1936.

This account of Peter Debye is based on an interview granted shortly before his death. For most of his working life he was concerned with the behaviour of atoms and molecules and the various ways in which they interact with each other. Usually he observed what happened to atoms or molecules when they are irradiated with either long-wave vibrations such as heat or short-wave vibrations such as light. He could then deduce something about the properties of the substance he studied. 'I enjoy work that combines experiment with theory. When, in 1912, I was appointed Professor of Theoretical Physics at the University of Utrecht, I stayed for only a year because theoretical physicists were supposed to work with pencil and paper and not to need a laboratory.'

At that time, Debye was curious about the electron structure of molecules. He had in mind an experimental technique for irradiating a simple compound with X-rays and seeing how the X-rays were scattered: 'just doing some experiments and photographing what happened.' He chose to examine lithium fluoride because it is a compound with few electrons. Scherrer, a young man who was working in the laboratory next to Debye's at Göttingen, where Debye had gone from Utrecht, became very interested in Debye's experiments. He took away some of the films to develop. Next morning, a Sunday, he came hurrying round to Debye's house. 'Look!' he said excitedly, handing Debye the film. 'There are a lot of lines on this thing. What do they mean?' Debye examined the film carefully. The lines, he realized, were due to diffraction of the X-rays by the lithium fluoride powder. They failed to provide any information about the electrons, but they did indicate the positions of atoms. This was the beginning of an X-ray method for studying the structure of substances. Instead of using single crystals, as in the method initiated by the Braggs, this X-ray method used a powder or a mixture of crystals.

One of the theories for which Debye is best known concerns the attraction and repulsion of the ions in a concentrated solution. In the ionic theory Arrhenius put forward in 1887, he took no account of the interaction of the ions; this was generally regarded as a defect in the theory. Debye was prompted to think about this in 1920, when he attended a conference at Zurich. One of the speakers suggested that the ions in concentrated solution were arranged in a fixed lattice like the ions in a sodium chloride crystal. To Debye, this idea was preposterous, and he got up and said so. 'Look here,' he argued, 'the ions cannot be stationary; they must have motions.' 'If you know so much better,' the speaker replied, 'then suggest something else.' Debye asked his assistant Hückel to look up all the literature on the subject. Between them they built up a picture of how ions really behave in solution. Debye worked out the mathematical implications of this picture; and he and Hückel tested the theory by measuring electrical conductivity. The experimental results confirmed that their theoretical picture was right.

'It is the urge to understand that makes me study things. Perhaps in an experiment something happens that astonishes me. I think about what it could mean – try this, try that in my mind. Discontent pushes me. It is discontent that is the driving force. Soon I become impatient, and then I get nowhere. So I forget about it and then, months later, the answer suddenly comes to me. Once I have it and have tested that it is the right answer, I lose interest. I want to explore something new.'

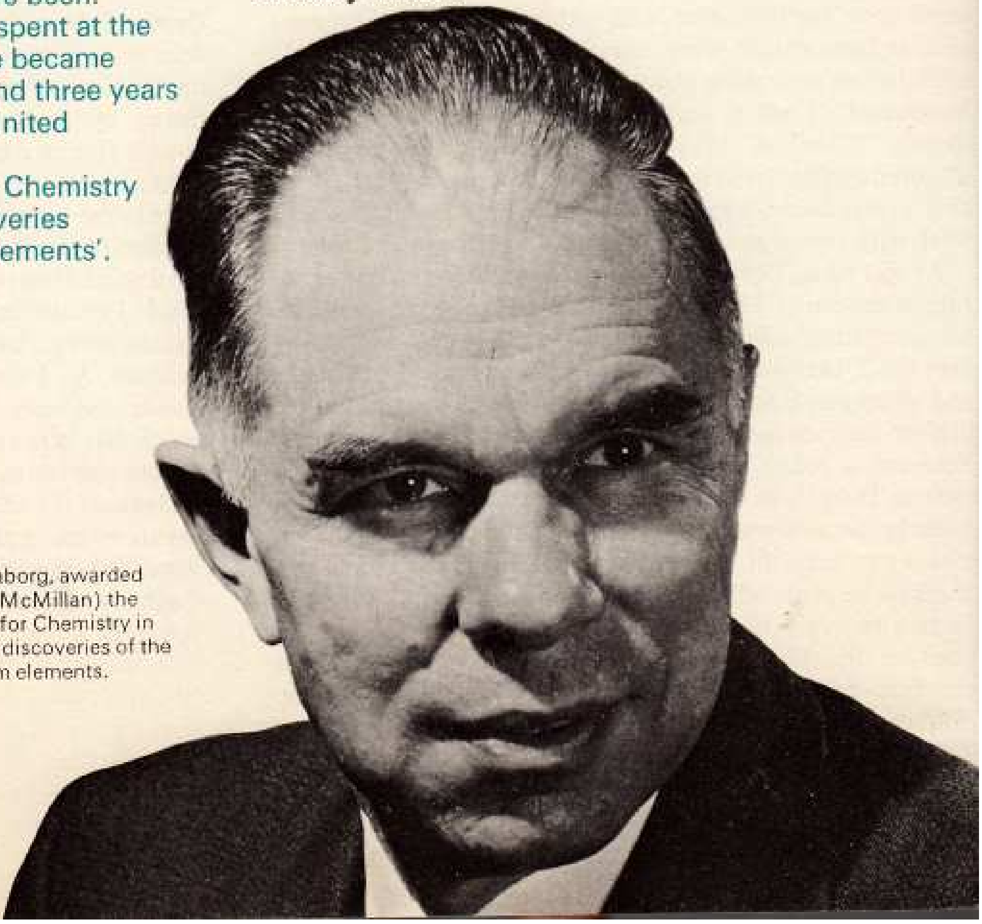
Towards the end of his life Debye was studying the interactions of molecules in liquids by passing light and X-rays through them and measuring the scattering. At eighty years of age his urge to understand was undiminished.

Glenn T Seaborg

the making of new elements

Glenn T. Seaborg was born in Ishpeming, Michigan, U.S.A. in 1912. His father, grandfather, and great-grandfather had been metal-workers, and he says, 'Had I shown greater aptitude for it, that is very probably what I should have been.' Most of his academic career has been spent at the University of California in Berkeley. He became Chancellor of the University in 1958 and three years later was appointed Chairman of the United States Atomic Energy Commission.
In 1951, he shared the Nobel Prize for Chemistry with E. M. McMillan – 'for their discoveries in the chemistry of the transuranium elements'.

For as far back in time as we can trace, radioactive elements have been decaying to form other elements. But the first experiment in which one element was converted into another was carried out by Lord Rutherford at the Cavendish Laboratory in Cambridge in 1919. Rutherford bombarded nitrogen gas with α particles from radium, and converted some of the nitrogen atoms into oxygen. During the next twenty years, many other transmutation experiments were carried out, but always from one known element into another known element. Ways were also found of accelerating particles in different kinds of apparatus and using them to bring about transmutations instead of particles from radioactive substances (see Cockcroft, page 10). One of the most successful of these particle accelerators was the cyclotron, invented by Dr E. O. Lawrence at Berkeley in California in the early thirties.



Glenn T. Seaborg, awarded (with E. M. McMillan) the Nobel Prize for Chemistry in 1951 for his discoveries of the transuranium elements.

After graduating in chemistry at the University of California in Los Angeles in 1924, Glenn Seaborg went to Berkeley to do research – 'largely,' he says, 'because I was interested in nuclear science and Lawrence's Radiation Laboratory was there.' Seaborg's early research was very varied; it included physics and organic chemistry. It was not until 1940 that he began experiments on the transmutation of elements. E. M. McMillan was working at this time in the Radiation Laboratory at Berkeley. He was following up earlier experiments of the German chemist Otto Hahn. Hahn and his co-workers had been the first to consider the possibility of building up heavier elements from the heaviest known element uranium (atomic number 92), but their experiments in bombarding uranium with neutrons produced fission of uranium, which, if it resulted in a huge release of energy, did not, as far as they could judge, lead to the formation of any heavier elements. However, on careful examination of the fission products, McMillan identified a radioactive element with a half-life of $2\frac{3}{10}$ days – this was an isotope of element 93 (neptunium). McMillan was then transferred elsewhere to do research on radar. Seaborg took up the research where McMillan left off, to produce and identify element 94.

Using the large cyclotron in the Radiation Laboratory, Seaborg and his co-workers accelerated deuterons (heavy hydrogen nuclei) to bombard a beryllium target which, in turn, produced fast neutrons. These neutrons were slowed down by paraffin which surrounded about 7 lb of uranium nitrate. Although the bombardment procedure may be complex, the chief difficulty in this kind of work is to separate and identify the very small quantity of the new radioactive element that is produced. Seaborg separated element 94 from the residual uranium by solvent extraction in water and ether; the uranium dissolved in the ether, leaving element 94 ('plutonium', as he called it, after the planet Pluto) in the water. 'We had suspected that one of the isotopes of plutonium might be a fissionable material like uranium 235 and we produced half a microgram specially to test this. The test proved our suspicion correct.' Nowadays, plutonium produced in reactors has become an important atomic energy fuel. Subsequently Seaborg detected minute traces of natural plutonium (less than one part per million million) in mineral ores such as pitchblende and carnotite.

The next step in the research programme – making elements 95 and 96 – proved to be very much more difficult. After two years' work, Seaborg was still unable to identify elements 95 and 96 among the reaction products. His lack of success merely served to make him work harder and think more deeply about the problem. Then he had a brainwave: 'It occurred to me that these heavy elements, starting with actinium (element 89), formed a separate series in the Periodic Table analogous to the rare-earth series (elements 57–71). Consequently, the isolation of elements 95 and 96 would need separation techniques different from those that had been used for neptunium and plutonium.' Using different separation techniques, element 96 (curium) was isolated almost overnight and element 95 (americium) a few months later.

Despite this success, many people remained sceptical about Seaborg's idea that these elements formed a separate series and it was some years before the idea was generally accepted. As he says, 'Most ideas go through two stages: at first people think you're crazy; then a long time afterwards, they think you were slow not to have thought of it before.'

Following the analogy between the heavy elements and their rare-earth counterparts, elements 97 to 103 have been made and identified. The quantities produced have tended to become smaller and smaller, sometimes only a few atoms, and their half-lives have tended to be shorter and shorter, sometimes less than an hour. It has become progressively more difficult to identify them. With the synthesis of element 103 (called 'Lawrencium', after the inventor of the cyclotron) in 1961, this series in the Periodic Table is now complete.

Recently Seaborg has been able to devote much less of his time to scientific research. His work has been carried on by his colleagues Ghiorso, Thompson, and others. The next stage in the research programme is to make a new series of elements starting with 104. 'It is impossible to tell where there is a limit. When the half-lives were getting shorter, we imagined that we were approaching a limit. But now it is predicted that the half-lives in this new series of heavier elements will be much larger than we originally supposed, and there is even talk of making elements as heavy as 126.'

'I hope,' he says, 'shortly to return to research and to work on these undiscovered elements.'

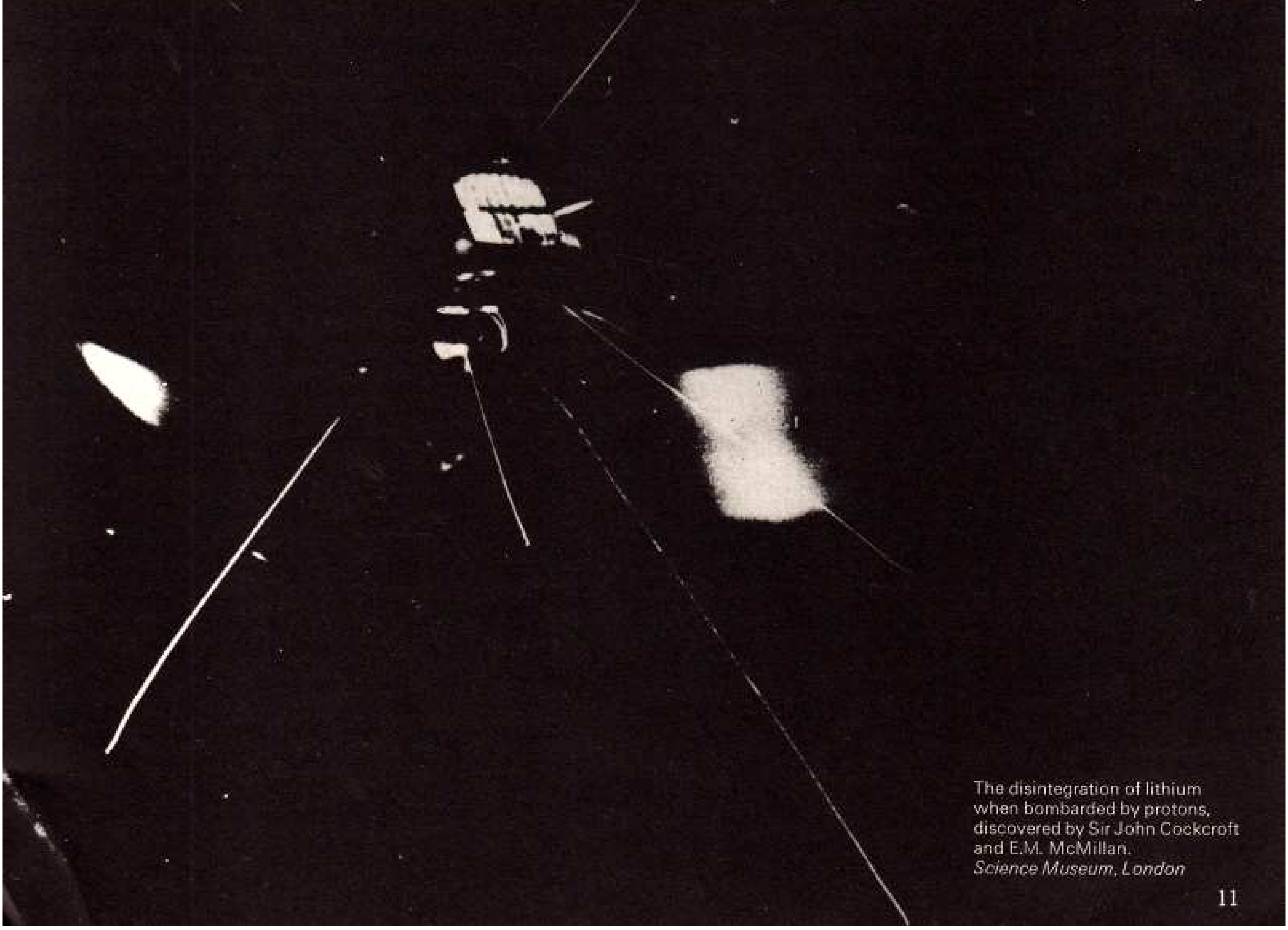
Sir John Cockcroft
splitting the atom

Sir John Cockcroft, at the time (1932) of his famous experiment in bombarding lithium with protons. He was awarded the Nobel Prize for Physics in 1951.

Sir John Cockcroft was born in Todmorden, Yorkshire, in 1897. He graduated in electrical engineering from Manchester University where he first encountered Rutherford. In 1924, he went to the Cavendish Laboratory at Cambridge where he carried out research in nuclear physics. During the Second World War, he worked on radar development and afterwards became Director of the United Kingdom Atomic Energy Research Establishment at Harwell. He was knighted in 1948. From 1960 till his death in 1967 he was Master of Churchill College, Cambridge.
In 1951, he shared the Nobel Prize for Physics with E. T. S Walton – 'for their pioneer work in carrying out nuclear changes with artificially accelerated particles'.

In 1924, a research student in his middle twenties joined the famous Cavendish Laboratory in Cambridge. His name was John Cockcroft. At that time, nuclear physics was in an exciting state of development: Rutherford, not long before, had transmuted atoms of one element into those of another; Aston had experimentally demonstrated the existence of isotopes; and de Broglie was soon to put forward his wave theory of the electron. The hub of much of this development was the Cavendish Laboratory where Rutherford himself was in charge. Cockcroft remembers him as 'a strict but humane father looking after the needs of his Cavendish family'. Working under Rutherford were such well-known pioneers of nuclear physics as C. T. R. Wilson, James Chadwick, F. W. Aston, P. M. S. Blackett, and later, M. L. E. Oliphant.

Cockcroft's first months at the Cavendish were spent learning to make and use laboratory equipment, investigating how to produce what then passed for high vacuums, and practising alpha particle counting on a scintillation screen. In those days, the 'instrument' for counting the particles was the human eye. Rutherford was successfully continuing his



The disintegration of lithium when bombarded by protons, discovered by Sir John Cockcroft and E.M. McMillan.
Science Museum, London

transmutation experiments by bombarding elements with alpha particles from a natural radioactive source. However he was not getting as many transmutations as he would have liked and was restricted to work on the light elements. In his Presidential Address to the Royal Society on 30th November 1927 he urged 'the development of sources of atoms and electrons with an energy far transcending that of alpha particles and beta particles from radioactive matter'.

The higher the energy of a particle, the more likely that when it collides with an atom it will penetrate the potential barrier of positive charge surrounding the nucleus and bring about a nuclear transmutation. An alpha particle from a natural radioactive source already has a very high energy. 'Fortunately,' Cockcroft said, 'I was saved from trying to take up Rutherford's challenge as it stood by the timely arrival at the Laboratory of George Gamow.' Gamow, a young physicist from Leningrad, introduced a theory according to which the energy needed by a nuclear particle to break out of an atomic nucleus was less than what was generally believed at that time. Cockcroft immediately saw the consequences of this theory. 'It occurred to me,' he said, 'looking at Gamow's theory the other way about, that the energy a particle would need to penetrate a nucleus might also be less than was believed. I did some calculations which showed that it might be possible to bring about transmutations using light projectiles such as protons.' Unlike naturally-generated alpha particles, protons (which are merely hydrogen ions) could be produced in very large numbers. It was open to question whether or not it would be possible to accelerate them to the energies that Cockcroft's calculations showed necessary. Work in America on accelerating electrons with an electrical source of 300 kilo-volts suggested that it might be. 'And this I believe is often the key to scientific discovery: keeping a very close watch on unusual developments in your own line of work, studying their implications, and following them up.'

Cockcroft sent a memorandum to Rutherford showing that transmutations with protons were theoretically possible. Rutherford told him to go ahead and try. In this work, Cockcroft was joined by E. T. S. Walton, an Irish research student whom Cockcroft described as a 'very brilliant experimentalist'. Their problem was to build a sufficiently powerful proton accelerator. Cockcroft, who had come to the Cavendish with a degree in electrical engineering, was fortunate in combining nimble fingers with a nimble mind. The apparatus that they built consisted of a vacuum tube producing beams of hydrogen ions (protons) which were discharged into a stack of glass cylinders forming the accelerator tube. By producing a high vacuum in this tube and by putting a high voltage of over 300 kV across it, they hoped to be able to accelerate protons to sufficiently high energies to penetrate the nuclei of some of the lighter elements: the lighter the element, the lower the electrical charge on the nuclei and therefore the lower the potential barrier. Their idea was to put a target of lithium, the lightest metal, in the path of the beam of protons and to observe transmutations, if any, on a scintillation screen. They worked patiently for two years to build up and test the equipment. Their chief difficulty was getting a sufficiently good vacuum. Much of their time was spent sealing up the joints which were made with Plasticine. Despite these makeshift methods, their apparatus, which cost over £500, was by far the most expensive in the Laboratory. Not unnaturally Rutherford became impatient that they should get some results from it. On the morning of 13th April 1932 they decided to try it out on the lithium target. Flashes on the screen revealed the presence of alpha particles as well as protons. Alpha particles were a certain sign that protons were penetrating some of the lithium nuclei and transmuting them into alpha particles (helium nuclei). For the first time, one element was being changed into another by projectiles of man's own making.

In this transmutation of lithium with protons, there is considerable energy release. 'At that time our work represented about the best experimental proof of Einstein's relationship between mass and energy ($E=mc^2$) put forward some twenty-five years before. Rutherford, on being questioned about the possibility of harnessing the energy of the atomic nucleus, dismissed it as moonshine – which, of course, at the time of our experiment, it still was. But within a few years, with the fission of the uranium nucleus, the harnessing of atomic energy was to become a reality.' Making it a reality was a project with which Cockcroft himself became closely involved. He was responsible for the building of the first atomic pile outside the United States and for the postwar development of atomic energy in Britain.

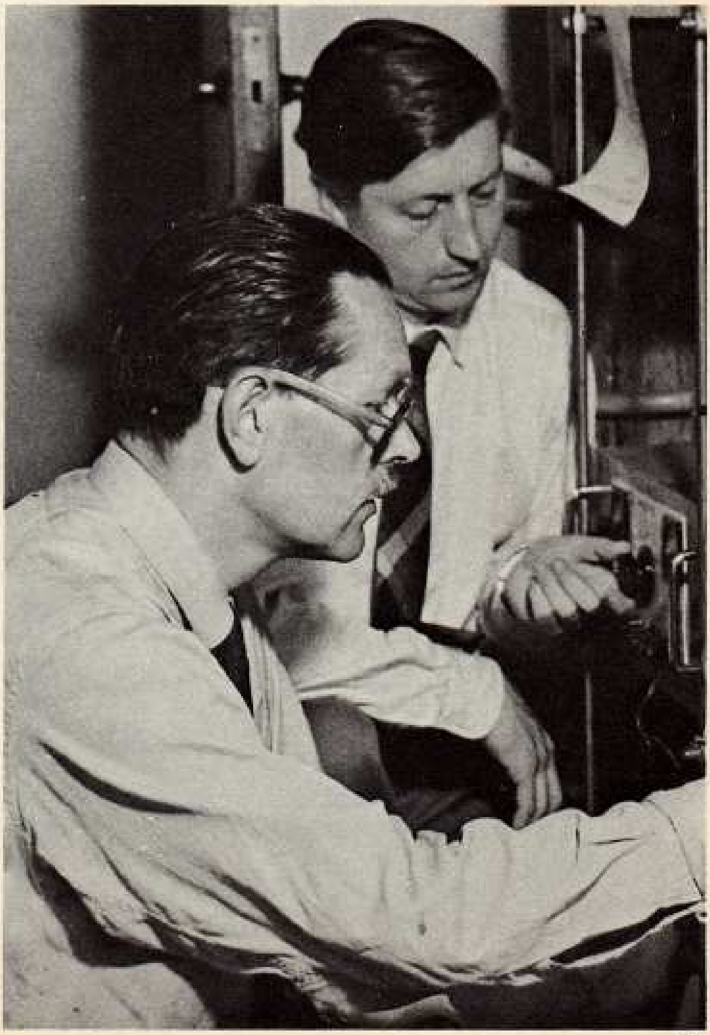
Archer J P Martin

the invention of partition chromatography

Archer J. P. Martin was born in London in 1910. After graduating from Cambridge in biochemistry in 1932, he worked at the Dunn Nutritional Laboratory in Cambridge, at the Wool Industries Research Association in Leeds, and in the Research Department of Boots Pure Drug Co. in Nottingham.
He joined the Medical Research Council in 1948 but, for the past few years, has been working independently at a research project at his home in Elstree outside London.
In 1952, he shared the Nobel Prize for Chemistry with R. L. M. Synge – 'for their discovery of partition chromatography'.

'While still a schoolboy,' says A. J. P. Martin, 'I was fascinated by fractional distillation. I built distillation columns in the cellar of my home; some of them were five feet high. They were packed with coke of graded size. I made them from coffee tins. I removed the bottoms and soldered the tins together. Experience with these columns served me in good stead. By the time I graduated, I had a useful understanding of the problems of distillation.'

For the man who was to contribute so much to separation techniques, it was an auspicious beginning.



Archer J. P. Martin (left), awarded the Nobel Prize in 1952 for the discovery of partition chromatography.

At Cambridge, Martin became interested in biochemistry. Shortly after he had taken his degree in 1932, he began work on isolating Vitamin E from wheat-germ oil. He first used a conventional solvent extraction method. He converted the oil into a soap, dissolved the soap in water, and then shook up the soap solution with ether in a separating funnel. The Vitamin E dissolved in the ether and the soap remained in the water. Then the water, which does not mix with ether, was run off, and the ether was distilled to leave the Vitamin E. But Martin found shaking large funnels very irksome; he had the bright idea of putting a bottle of soap solution on the flat roof of his laboratory and a bottle of ether on the ground, and connecting the two with glass tubing. The ether was less dense than the water and passed up the tube, thereby displacing the water. He set up this apparatus in the afternoon and the two liquids had changed places by the next morning. Unknown to Martin, this process, called counter-current solvent extraction, had previously been used in industry, but the idea was new for the laboratory.

Martin then began to ponder how he could improve on this roof-to-ground apparatus. He constructed a counter-current machine consisting of 45 tubes, ½ inch wide and 5 inches high, connected to each other by a system of small-bore tubes with ball valves. This was equivalent to a column 200 feet high. With this new apparatus Martin obtained the first evidence that Vitamin E was made up of several substances. At that time, R. L. M. Synge, with whom Martin later shared the Nobel award for chemistry, was working on the separation of amino-acid derivatives by solvent extraction with chloroform and water. Obviously, Martin, with his machine, could be helpful; they were put in touch with each other.

Martin's original machine would not function properly with chloroform and water. He built a second machine which did the job satisfactorily, but was difficult to operate. He tried to make something still better: 'I made dozens of new designs, which I put up in turn to Synge who became very tired of listening to me. But none of them seemed easy to make, and no construction was undertaken. I then had an idea of a radically different kind. This was to pack a tube with a mixture of cotton and wool fibres parallel to the axis of the tube. Now cotton is wet preferentially by water, and wool by chloroform. By putting chloroform above and water below, I hoped that I should obtain a large number of parallel streams of the two solvents with a large area of contact. When I tried it out, I was very disappointed to find that a large domain went over to one solvent or the other and the arrangement was actually less efficient than an unpacked tube.

'Up to this time, my thinking had been dominated by the idea of moving the two solvent phases in opposite directions simultaneously. But, in considering the failure of the cotton and wool experiment, I realized that it should be comparatively simple to hold one phase stationary and move the other one. The arrangement would be essentially a chromatogram. I put this idea to Synge. He was full of enthusiasm, and we decided to work on it at once.

'We decided to use silica gel to hold the water. A tube was packed with this, and chloroform was run down the column. We first tried to separate amino-acid derivatives, acetyl alanine and acetyl leucine. We at once faced the task of determining what was happening and how to decide whether separation had occurred or not. We quailed at the thought of evaporating down and titrating a large number of cuts (a method used extensively later). The idea occurred to us of using an indicator to show the presence of the acetyl amino-acid. The indicator would be held stationary with the water in the silica gel. We chose methyl orange. The first column we made showed the separation we looked for as bright red bands on an orange column.'

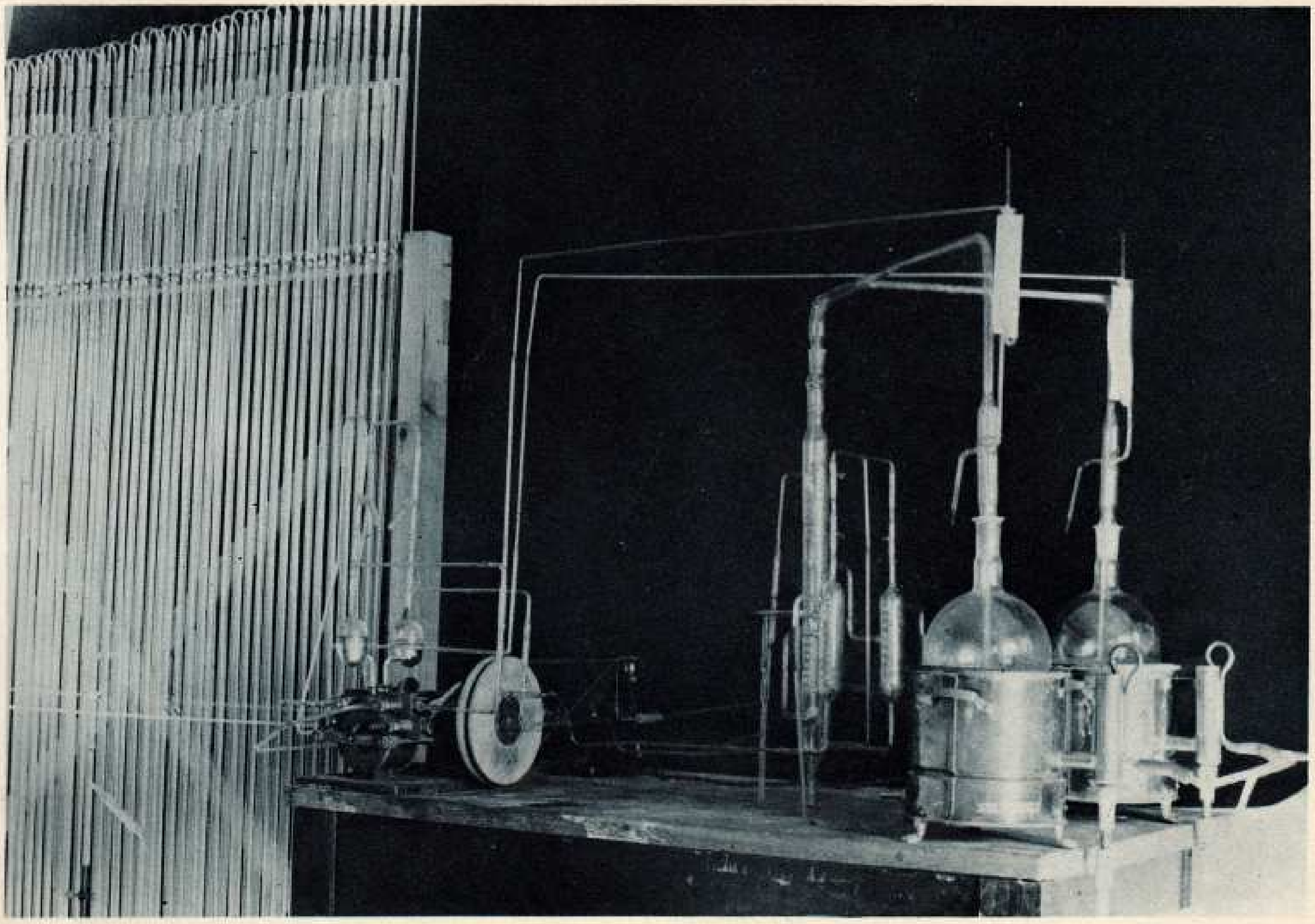
This first experiment was a rough one, but, Martin advocates, 'One should take a minimum of care and preparation over first experiments. If they are unsuccessful one is not then discouraged, since many possible reasons for failure can be thought of and improvements can be made.'

From this marriage of chromatography and counter-current solvent extraction, the new technique of partition chromatography came into being. Using this technique, Synge quickly separated amino-acid derivatives. He and Martin together extended the technique to the separation of many other substances and, equally important, established the technique on a quantitative basis. Many of the spectacular advances in present-day protein chemistry have stemmed from this technique.

Another extension of the technique was foreshadowed in the first paper published by Martin and Synge in 1941: 'The mobile phase need not be a liquid but may be a vapour. . . . Very refined separation of volatile substances should therefore be possible in a column in which a permanent gas is made to flow over gel impregnated with a non-volatile substance . . . .' Martin himself followed up this idea ten years later. As a result of his work, gas chromatography has now become one of the most important of all analytical methods. It is extensively used in industry when quick and accurate separation of volatile substances is required.

Martin is interested in analytical techniques for their own sake. He has left their exploitation to others: 'I am somebody who likes to think of ways of *doing* things.' At present, he is working on the manufacture of small pairs of hands, as identical as possible in construction to the human hand, with which to carry out micro-manipulation. If his work comes to fruition, it may well have an even bigger impact on scientific analysis than his work on partition chromatography.

Part of the apparatus for counter-current solvent extraction.



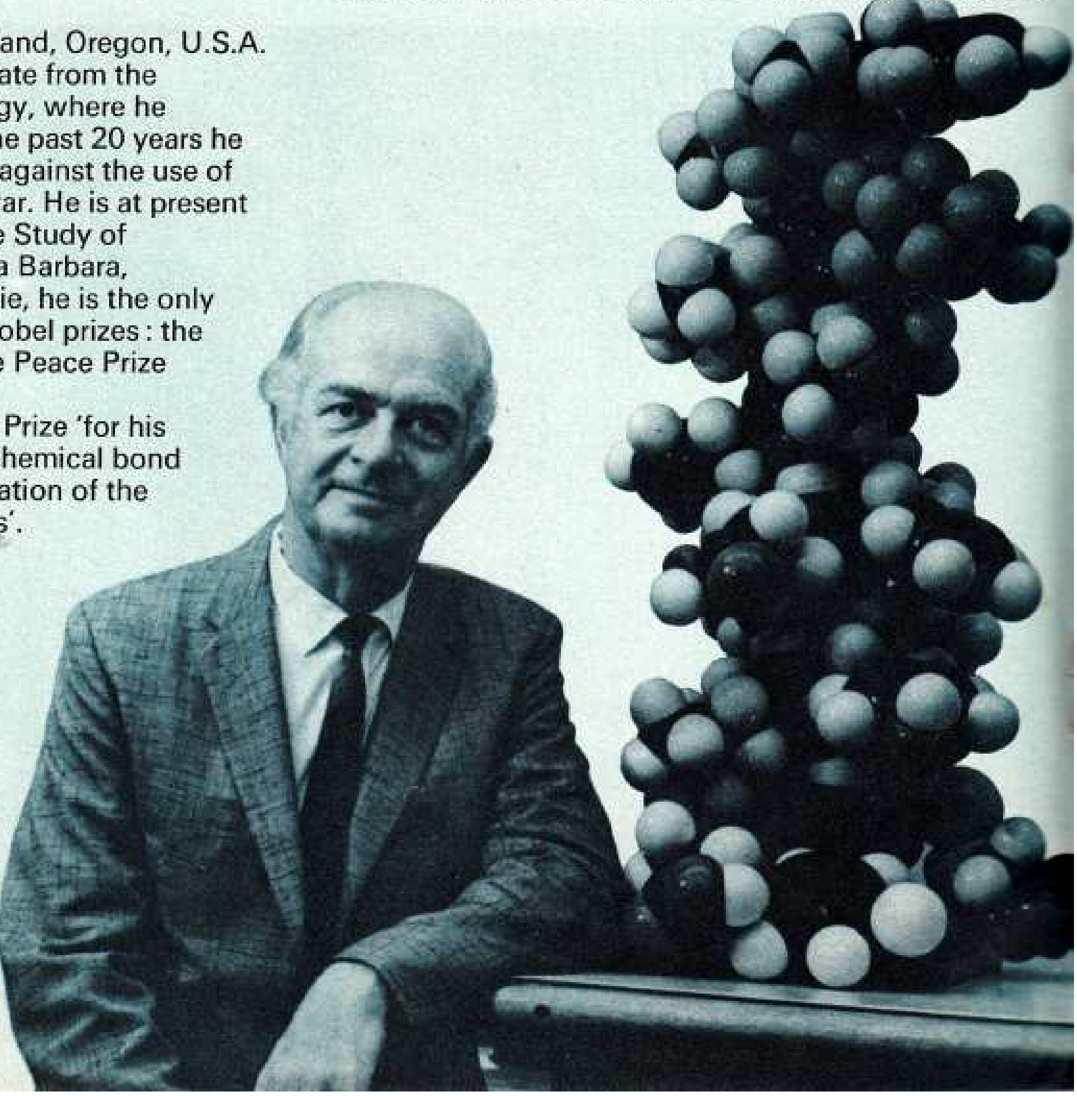
Linus Pauling

bonding and structure

When Linus Pauling was eighteen, he worked as a paving-plant inspector in Oregon during an interlude in his student career. His job was merely to test the temperature and composition of the mixes about once an hour. To pass the time he tried working out a theory that related the structure of substances to their magnetic properties. Chemical structure, the arrangement of atoms in substances and the ways in which they are linked together, has remained his predominant interest ever since. But his contributions to scientific knowledge have been many and varied – from proposing

Linus Pauling was born in Portland, Oregon, U.S.A. in 1901. He received his doctorate from the California Institute of Technology, where he worked for over 40 years. For the past 20 years he has been an active campaigner against the use of nuclear weapons and against war. He is at present on the staff of the Center for the Study of Democratic Institutions in Santa Barbara, California. Apart from Mme Curie, he is the only person ever to have won two Nobel prizes: the Chemistry Prize in 1954 and the Peace Prize in 1962.

He was awarded the Chemistry Prize 'for his research into the nature of the chemical bond and its application to the elucidation of the structure of complex substances'.



Linus Pauling, beside the α-helix, a configuration of the polypeptide chain of proteins.

the electronegativity scale in 1931 to his chemical explanation of anaesthesia in 1961.

When Pauling began research at the California Institute of Technology in 1922, he made X-ray diffraction studies of many substances, measuring such things as the bond angles, interatomic distances, and ionic radii. 'I enjoy experimental work but I tend to be rather impatient. I prefer simple experiments and try to find an experimental technique that, once the apparatus is built, can be applied to a large number of substances.' He was the first in America to build electron-diffraction apparatus. This, in contrast to apparatus for X-ray diffraction, can be used to study gases. With this apparatus he and his research students determined the structures of over 200 gases. 'Its great merit was that it enabled us to find out the structure of molecules without having to take into account the influence of other surrounding molecules, as in a crystal.'

On the theoretical side, Pauling showed how the geometry of molecules is influenced by bonds between atoms that share electrons. He also proposed the resonance theory, which explains the structure of substances such as benzene in which there is more than one possible valence-bond structure. These far-reaching theories were published in the early thirties and established Pauling's reputation.

At this time X-ray techniques were very much less advanced than they are now. Pauling determined the geometrical structure of many complex substances using a method which, in his usual way, he worked out very largely for himself. He calls the method 'stochastic' – guessing the truth. 'Here, for example, I have a crystal of pseudobrookite (Fe_2TiO_5). I can obtain sure information by X-ray diffraction – size of the unit, space symmetry – so that there are some simple restrictions on the possible structure. Keeping within these restrictions, what would be the most reasonable way for two atoms of iron, one of titanium, and five atoms of oxygen, to link together ? Often, after working with pencil and paper and simple ball and stick models, I end up with only one possible structure. I make some calculations based on this structure and test them experimentally. If the calculations and experimental results agree, then I accept the structure. If not, that's too bad; I usually drop it.' Using this method, which requires extraordinary understanding of how atoms behave, Pauling determined the structure of topaz, mica, chlorite, and many other minerals, with all the atoms located in their correct places. One of his failures was sodium dicadmide ($NaCd_2$). One of his students eventually used the stochastic method to work this out. It proved to be the most complex inorganic structure known, with 1192 atoms in the unit cell.

In 1937, Pauling began to explore the geometrical structure of proteins. He was unsuccessful at first, because he had too few data to go on. During the next ten years, his research team made X-ray diffraction studies of amino acids and peptides, of which proteins are composed; they measured bond distances and bond angles. In 1948, using these new data, Pauling conceived the idea that the fibrous protein molecule of α-keratin was folded into a helical structure. This idea of a helix was to prove fundamental in understanding the structure of a number of complex biological substances.

'For solving problems that initially defeat me I deliberately make use of my unconscious mind. I think about the problem for about half an hour in bed and then go to sleep still thinking about it. I do this, perhaps, for several nights, and then forget about it all together. Months or sometimes years later, as with the structure of α-keratin, the answer pops into my head.' He chooses, of course, problems to work on that he thinks he will be ultimately able to solve. This is a matter of judgment – the ability to sort through a mass of ideas quickly and fix on the interesting ones. 'One of the most important things is to be willing to accept new ideas and to be able to look at problems from a fresh perspective.' The rapidity with which Pauling's mind adjusts to a new perspective is exemplified by an idea he had at a dinner in 1945 when a doctor began talking about sickle cell anaemia. The doctor mentioned that the red blood cells were sickle shaped only in the venous blood, and it immediately occurred to Pauling that this must be something to do with the difference between haemoglobin in the venous blood and oxyhaemoglobin in the arterial blood. 'Do you suppose,' he asked the doctor, almost before the doctor had finished his sentence, 'that the sickling could be due to linking together of haemoglobin molecules to form long needle-like crystals which distort the red blood cells ?' After three years research, one of Pauling's students proved this off-the-cuff suggestion to be substantially correct.

Lord Todd
the structure of life

Lord Todd, receiving the Nobel Prize from King Gustav of Sweden in 1957 for his work on nucleotides and nucleotidic co-enzymes.

Alexander R. Todd was born in Glasgow in 1907. He graduated from Glasgow University in 1928, and following research at the Universities of Frankfurt, Oxford, and London, he became Professor of Chemistry at Manchester in 1938. Since 1944, he has been Professor of Organic Chemistry at Cambridge. He has served on many committees connected with science and, in 1962, was created a life peer. In 1957, he was awarded the Nobel Prize for Chemistry.

'Two things attracted me to organic chemistry: it is such a logical and systematic subject – you can see where you are going, yet at the the same time it has limitless possibilities; and it is closely associated with living matter and the nature of life.'

In 1928, when Alexander Todd began doing research, little was known about the chemistry of such complex substances as vitamins, enzymes, and nucleic acids. These substances, which are vital to living organisms, were to be the focal points of his later research. His first major achievement (at Edinburgh between 1934 and 1936) was his work on the structure of Vitamin B_1, the anti-beriberi vitamin, and his discovery of a method for synthesizing it.

Todd's methods of discovery in this, and in his subsequent work, have been the traditional ones of the organic chemist – analysis and synthesis: 'This is the only way you can be absolutely sure where you are. You subject the substance you want to know about to a routine analysis to find out the reactive groups in its molecule. Using this knowledge, you then break the substance up into smaller bits, examine the bits, and so build up a complete picture of what you think the molecular structure might be – rather like fitting together a jigsaw. But, having done this, there's only one way to make certain – to synthesize a substance with your structure from smaller substances whose structure is already well known – and to do it by a route which permits no ambiguity. Here you can spend a long time working out the best way to do it. You could perhaps get at your structure by one route, but it would involve a lot of reactions. Another route might be quicker; but you doubt whether one of the steps would work, so you try it out first on simpler compounds. Eventually, but not always, you end up with the substance you are after. You can then compare it with the natural material and, if the two are identical in every respect, then you really know that your deductions were correct.'

This kind of work is very difficult to do, especially with the extremely complex substances which Todd has studied. It needs imagination to predict whether discovering the structure of a natural substance will lead to something worthwhile – new light on its biological role or a step towards unravelling the structure of even more complex substances. Then to tackle the structural problem itself, which is of course different for every substance, needs patience, disciplined experiment, and a fund of practical wit.

His work on Vitamin B_1 led Todd to take an interest in the way in which vitamins act in the body. This brought him to the coenzymes. Many coenzymes are derived from vitamins. They are associated with certain enzymes and are responsible for the chemical reactions in living matter which these enzymes catalyse. Some of them contain, in addition to vitamins, substances called nucleotides, which are the phosphate esters of heterocyclic glycosides. These nucleotides are best known as the breakdown products of the nucleic acids – macromolecular substances which are vital constituents of the nuclei in all living cells.

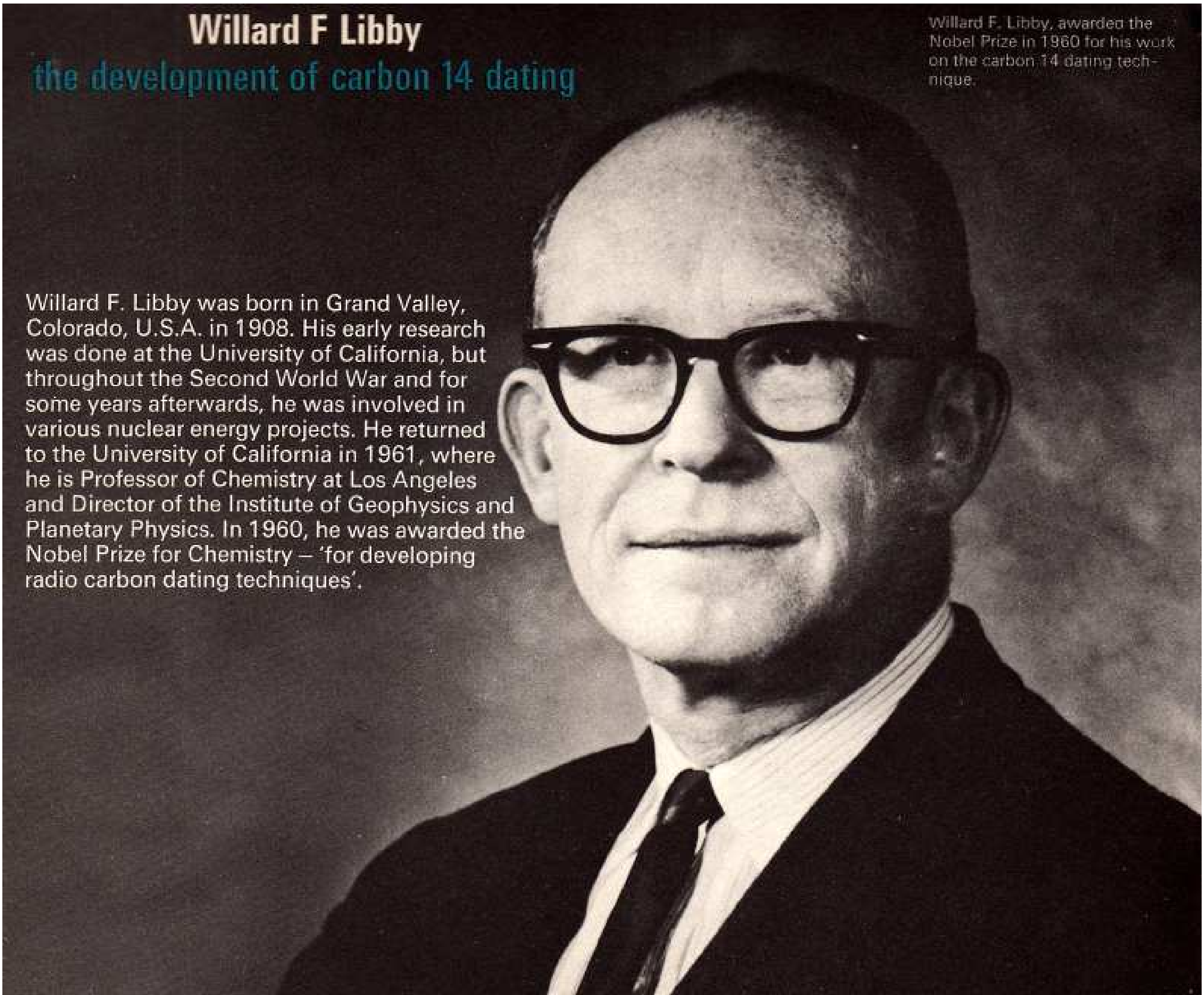
The chemical structures of both the coenzymes and nucleic acids were virtually unknown. After preliminary investigations at Manchester, and later at Cambridge, Todd and his co-workers started a large-scale research programme to study these substances in 1940. By 1948, he had synthesized adenosine triphosphate (ATP), the coenzyme responsible for the supply of energy used in muscular contraction and, by 1956, all the major coenzyme types had been synthesized in the Cambridge laboratory. Despite the enormous complexity of nucleic acids, Todd and his co-workers were able, by 1951, to work out the general chemical structure of these huge molecules. The structures they established could be fitted perfectly into the X-ray diffraction pictures of nucleic acids. They provided the basis for the three-dimensional pattern of DNA as a double helix made up of two nucleic acid chains, as postulated by Crick and Watson (see page 24). From this picture of the nucleic acid molecule has come much of the exciting biological work on the chemical basis of heredity.

The unravelling of the structure of the nucleic acids is an interesting example of cooperation between the organic chemist, the X-ray crystallographer, and the biologist. Here the organic chemist has had less of the limelight than is, perhaps, his due: 'In a field like this, the organic chemist's contribution is fundamental. X-ray analysis of a macromolecule can give a picture of its geometrical configuration, but it cannot give the detailed chemical information which is needed if you are to understand the molecule's function.'

As well as the coenzymes and nucleic acids, Todd has been responsible for finding out the structures of numerous other organic substances. 'There is a peculiar satisfaction in this kind of work. Unlike, say, the theories of the physicist, which can be refuted in a moment, the structure of a substance is permanent, and the organic chemist can prove that he has it right – by synthesis. At the same time, each new structure is no more than a link in a chain of exploration. There is no finality.'

Willard F Libby

the development of carbon 14 dating



Willard F. Libby, awarded the Nobel Prize in 1960 for his work on the carbon 14 dating technique.

Willard F. Libby was born in Grand Valley, Colorado, U.S.A. in 1908. His early research was done at the University of California, but throughout the Second World War and for some years afterwards, he was involved in various nuclear energy projects. He returned to the University of California in 1961, where he is Professor of Chemistry at Los Angeles and Director of the Institute of Geophysics and Planetary Physics. In 1960, he was awarded the Nobel Prize for Chemistry – 'for developing radio carbon dating techniques'.

At school, Willard Libby was interested chiefly in history and English literature. But when he entered the University of California at Berkeley in 1927, he decided to take up science.

After graduation, he remained at Berkeley to do research in atomic chemistry. As he says, 'the time was ripe for it'. He was particularly interested in radioactivity. In 1930, he constructed the first Geiger counter in the United States. Shortly afterwards Lawrence built the first cyclotron at Berkeley. The bombardment of elements with accelerated particles resulted in numerous radioactive isotopes which Libby helped to study. At first there seemed nothing particularly useful to be gained from these isotopes. Dr G. N. Lewis, the Professor of Chemistry at Berkeley and perhaps the greatest American chemist of all, said one day to Libby, 'I am all for fun, especially in science, but do you think this work you are doing has any practicality whatsoever?' 'No, I don't think so, Professor Lewis,' said Libby, 'but it is good training.' Lewis agreed that it was. But in fact, like many scientific curiosities which at first seem to have no practical value, radioactive isotopes were later found to be very useful. Libby himself was to discover one of these uses.

Just before the Second World War, some experiments were done in which balloons were used to carry neutron counters high up into the atmosphere. It was found that the number of neutrons increased to a maximum at about fifty thousand feet: evidently neutrons were formed when cosmic rays from space collided with gas molecules in the outer atmosphere. After the war, Libby became interested in this disintegrating effect of cosmic rays: 'I knew from my research at Berkeley that neutrons combine with the carbon nuclei to form the radioactive isotope carbon 14 (with 6 protons and 8 neutrons), and I began to wonder what the consequences of this might be.

'Many discoveries are made from asking the right question. Here my own discovery came from asking myself what is it that cosmic rays do to the Earth? The answer I arrived at was that they wrote down human history.'

The reasoning behind his answer was that atoms of radioactive carbon 14 in the atmosphere produce radioactive carbon dioxide; this is mixed with the carbon dioxide which is taken up by plants and some of the plants are eaten by animals. Thus radiocarbon enters all living beings. However, when a plant or animal dies, it stops assimilating carbon 14; carbon 14 decays with a half-life of 5,760 years and so dead organic matter loses its radioactivity at the rate of half every 5,760 years; therefore, from measuring the radioactivity of dead organic matter, its age (defined as the time since death occurred) can be established.

Using a radioactive substance for dating was not new. The age of rocks millions of years old had been determined from uranium decay by measuring the amount of lead formed by disintegration of uranium, which has a half-life of $4{\cdot}5 \times 10^9$ years. But until this time there was no precise way of dating historical human materials from measurement of their radioactivity.

Logical as his argument seemed, however, Libby had no experimental evidence for any of his assumptions. He had first to establish that organic matter really did contain this radioactive isotope of carbon, and that it came from the atmosphere.

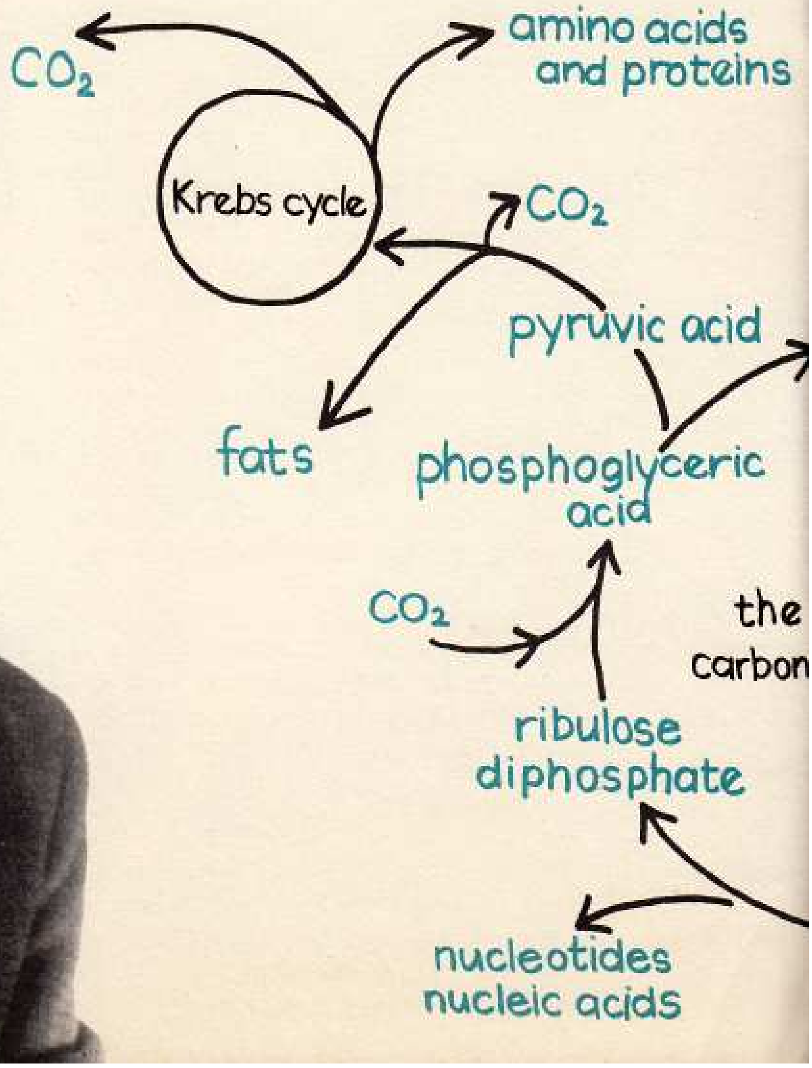
Since radioactivity at such a very low level had never before been measured, he had to try to concentrate carbon 14 from organic samples. He compared the radioactivity of methane from a local sewer (which, if he was right, should be at a maximum), with that of methane from an oil well (which, since it was formed millions of years ago, should have lost all its radioactivity). The results confirmed Libby's deductions: the radioactivity of the fresh methane was about the figure he had predicted; the methane from the oil well was not radioactive.

Subsequently, Libby built apparatus sufficiently sensitive to measure the radioactivity directly. He then checked the radioactivity of organic material which was already known to be 5,000 years old. He found that the age given by the radioactivity agreed with the known age. So came into being a technique for determining accurately the age of organic matter for as far back as fifty thousand years. Carbon 14 has since been used to date many archaeological findings. In retrospect, Lewis's doubts about the practical value of Libby's early research seem rather ironic.

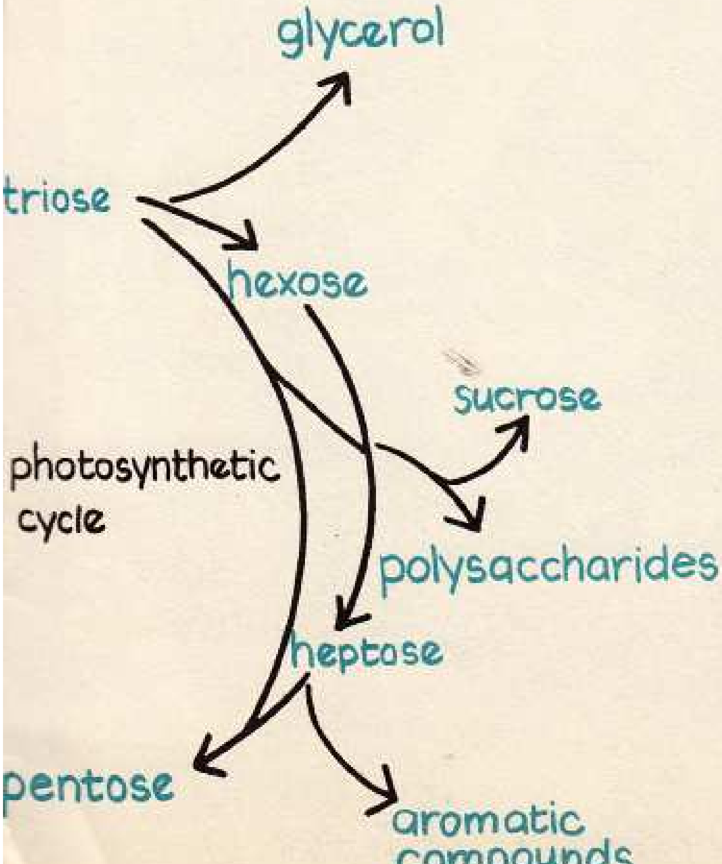
Melvin Calvin
the chemistry of photosynthesis

Melvin Calvin, awarded the Nobel Prize in 1961 for his work on photosynthesis.
Photo, Lawrence Radiation Laboratory, University of California, Berkeley, California.

Melvin Calvin was born in St. Paul, Minnesota, U.S.A. in 1911. After receiving his doctorate, he spent two years doing research in Manchester. On his return to the United States, he joined the University of California and, since 1946, has been Director of the Bio-organic Division, Lawrence Radiation Laboratory, at Berkeley.
In 1961, he was awarded the Nobel Prize for Chemistry – 'for his work in photosynthesis'.



The photosynthetic carbon cycle according to Calvin.



Although the way in which plants convert carbon dioxide and water into sugar, a reaction on which life depends, remains something of a mystery, a great deal of our understanding of the reaction has followed from the work of Melvin Calvin at the University of California, Berkeley.

'My first interest was catalysis: I remember as a young student learning about these mysterious substances called catalysts which could influence the rates of reactions without themselves being in any way changed. This seemed to me to be completely incongruous, and led me into research on the catalytic properties of various substances, including some synthetic substances related to chlorophyll and haem.'

His first photosynthesis experiments began in 1945. He fed the carbon dioxide to single cell algae, then killed the algae and analysed the compounds containing radioactive carbon dioxide. He separated these compounds in an ion-exchange column. Because of the difficulty he had in getting the principal radioactive material to pass through the column, he concluded that it must be a carboxylic acid, one that was strongly acidic. What that substance might be came to Calvin while he was sitting in his car waiting for his wife. 'It occurred to me quite suddenly that it was phosphoglyceric acid, and that another substance might act as an acceptor for the carbon dioxide coming into the plant, combining with it to form the phosphoglyceric acid. I had been turning over the problem in my mind for several weeks, but why the answer should have popped into my head just then, I don't know. Possibly because I had nothing else to do but sit and wait.'

Tests confirmed that Calvin was right about the acid. The search for a substance that would act as an acceptor for the carbon dioxide proved much more difficult than he had originally supposed. During the course of the search, which extended over several years, a number of compounds in the photosynthesis reaction were identified. The picture emerged of a cycle of reactions, some of them driven by high energy compounds produced in the light. The accompanying diagram shows just how complicated it turned out to be. But the big breakthrough came with that moment of inspiration when Calvin was sitting in his car.

James D Watson
the structure of D.N.A.

James D. Watson was born in Chicago, Illinois, U.S.A. in 1928. He studied biology at the Universities of Chicago and Indiana and, after a year's research in Copenhagen, came to the Cavendish Laboratory in Cambridge in 1951.
He is at present Professor of Biology at Harvard University where he is continuing his research on genetics. His vivid description of the events leading to the discovery of the structure of DNA can be found in *The Double Helix.*
In 1962, he shared the Nobel Prize in Medicine and Biology with F. H. Crick and M. F. H. Wilkins – 'for their discoveries concerning the structure of nucleic acids and its significance for information transfer in living material'.

In the nucleus of each living cell are millions of long thread-like molecules of a substance called deoxyribonucleic acid (DNA). For many years it had been thought that these molecules were in some way responsible for transferring hereditary information from parent organisms to the next generations. It was not understood how. In the early fifties, Todd and his co-workers at Cambridge worked out the chemical composition of DNA (see page 19), but nothing was known about the geometrical arrangement of the atoms. And it is often the geometrical structure of biological

James D. Watson was awarded the Nobel Prize in 1962, with Maurice Wilkins and Francis Crick, for his work on the structure of DNA. Shown here from left to right are Maurice Wilkins, Max Perutz, Francis Crick, John Steinbeck, James D. Watson, and John Kendrew.

substances that provides the clue to how they function.

In 1951 a young American biologist called James Watson came to the Department of Molecular Biology in the Cavendish Laboratory at Cambridge. He was interested in genetics and wanted to discover the structure of DNA. At the time, most people thought the problem was too difficult. Sharing a room with Watson at the Cavendish was Francis Crick who was working on a thesis. Crick wasn't particularly interested in the subject of his thesis. He was fascinated by the structural problem confronting Watson.

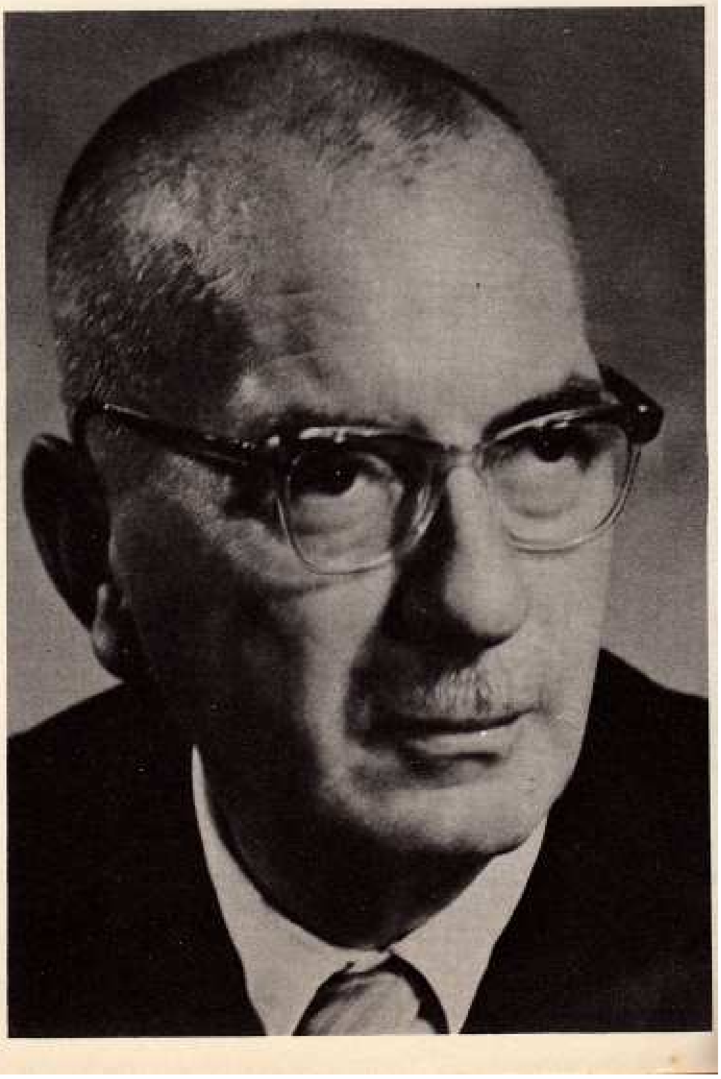
The backbone of the DNA molecular chain consists of an alternating sequence of phosphate groups and sugar groups. A side group of atoms called a base projects from each sugar group. There are four different types of base. 'For hours every day Crick and I talked about how these groups and bases could fit together in a sensible geometrical shape. We built simple ball-and-stick models, using the same kind of conjectural approach devised by Pauling (see page 16), but for a long time we seemed to be getting nowhere.' Pauling, who had previously shown that many proteins have a helical structure, tried briefly to work out the structure of DNA himself, but he had no success. Another person studying the same problem was Maurice Wilkins at London University. He was trying to do it experimentally from X-ray diffraction pictures; these pictures suggested that the DNA molecule had a symmetrical structure.

After two years of discussion, of trial-and-error rearrangement of models, of grappling with a base whose structure had been wrongly represented in the textbooks, it occurred to Watson and Crick that the framework of the DNA structure might be that of a double helix. 'After that we had the structure of the whole molecule virtually worked out in less than a week.' It consisted of two chains of alternating phosphate and sugar groups spiralling round each other to form a double helix with the two bases filling in the centre.

This structure provides a simple explanation of how characteristics are transferred in cell division: the two chains in the double helix separate and can then form a pattern for the synthesis of another chain. Division of the helix has been experimentally demonstrated using an isotope of nitrogen (N_{15}) as a tracer element. Watson and Crick then showed how the sequence of the four different bases constitutes a kind of four-letter code which controls such reactions as the order in which amino acids link together to form the different protein molecules that constitute the bulk of the cell. Various people have contributed towards the cracking of this code. Although much has still to be understood, the discovery of the structure of DNA was a great step forward towards explaining the biology of cells in fundamental molecular terms. 'It is impossible,' says Watson, 'to distinguish between the separate contributions of Crick and myself to solving this problem; but if either of us hadn't been there, then it wouldn't have happened.'

Karl Ziegler
from free radicals to plastics

Karl Ziegler, awarded the Nobel Prize in 1963 for his work on polymers.



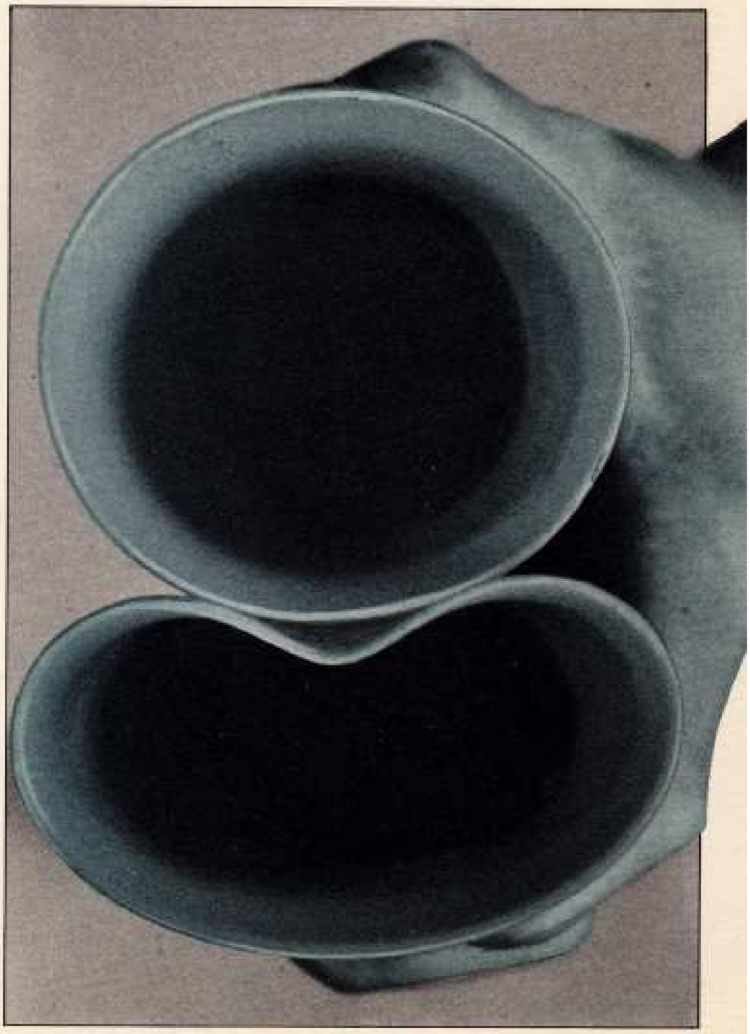
Karl Ziegler was born in Helsa, Germany, in 1898. He studied organic chemistry at the University of Marburg, and was then for some years Professor of Chemistry, first at Heidelberg and then at Halle. In 1943, he became Director of the Max Planck Institute at Mülheim-Ruhr where he has been ever since.
In 1963, he shared the Nobel Prize for Chemistry with G. Natta – 'for their discoveries in the field of the chemistry and technology of high polymers'.

In 1923, when Karl Ziegler became a research assistant at Marburg University in Germany, he was chiefly interested in organic chemistry and decided to investigate free radicals. These radicals are hydrocarbon groups with an unpaired electron: for example, methyl CH_3, and ethyl C_2H_5. Most of them combine so rapidly with each other that it is extremely difficult even to detect their existence. In 1900 a fairly stable free radical (triphenylmethyl) had been discovered, and chemists were searching for others.

Ziegler's earliest success was to synthesize the first stable unsaturated free radical – a free radical containing a double bond, between two of the carbon atoms. He tried to saturate the double bond, but the reaction did not go as predicted; when he added potassium to an ether corresponding to that radical, the double bond did not react but the ether-group unexpectedly split, and two organic compounds each containing a potassium atom were formed. Such compounds are known as organo-metallics. They had previously been known, but Ziegler's experiment led to a new way of making them. It also stimulated Ziegler's interest in them. Subsequently, he discovered that organo-metallic compounds would cause short-chain molecules of an unsaturated hydrocarbon such as butadiene to link together to form long-chain molecules. In this growth or polymerization reaction, the organo-metallic compound acts as a catalyst although, unlike a catalyst, it is not regenerated at the end of the reaction.

In 1943, Ziegler became Director of the Max Planck Institute at Mulheim in the Ruhr. The Institute was originally founded for research into uses of coal, but Ziegler was allowed to investigate anything that interested him, and he continued his studies into the reactions of organo-metallics. Using an organo-lithium compound, he and his research

Two plastic beakers: the bottom one is of low-pressure polyethylene developed by Ziegler, the top one of high-pressure polyethylene.
Photo, The Plastics Institute.



team tried to make ethylene combine by a similar growth reaction. They succeeded but the reaction was very slow and troubled by side reactions: it was useful for extending short molecular chains but was impracticable for building up molecules with very long chains such as are found in the plastic polyethylene.

In his next attempt to bring about a growth reaction with ethylene, Ziegler tried a new organo-metallic compound in which the metal was aluminium instead of one of the alkali metals (lithium, sodium, or potassium). The ethylene molecules combined to form organo-aluminium compounds with medium sized molecular chains. But one day it happened that the reaction went a quite different way giving nothing but butane from two molecules of ethylene. 'When an experiment works out differently from what you expect,' says Ziegler, 'then you may be at the start of a discovery. You begin searching around for reasons that will account for the difference and sometimes something interesting emerges.' So it was with this experiment.

First, after weeks of careful analysis, a trace of nickel was discovered in the steel of the reaction vessel. In the growth reaction beyond aluminiumbutyl, this trace of nickel catalysed the splitting-off of butane with the recovery of aluminium methyl, preventing the molecular chains from building up further. Ziegler concluded that it should be possible to extend the growth reaction by ensuring that no nickel was present. Before trying this, he investigated the effect of other metals on such reactions. Again the result was unexpected: some metals, far from inhibiting the so-called growth reaction as nickel had done, vigorously promoted it. In his next experiments to polymerize ethylene, Ziegler used an organo-metallic catalyst mixed with traces of the metal zirconium. Previously it had only been possible to make the plastic polyethylene by polymerizing ethylene at a pressure of over 1000 atmospheres. 'We succeeded in producing polyethylene,' said Ziegler, 'first at a pressure of 100 atmospheres, then at 10 atmospheres, and finally at normal pressure. Of great interest was the fact that the polyethylene made in this way had a greater density than conventional high-pressure polyethylene.' Ziegler performed this famous experiment in 1953. His high-density polyethylene is now being manufactured in chemical plants throughout the world.

Unlike ethylene, propylene had never before been polymerized. Ziegler managed to do this using an organometallic catalyst mixed with titanium only to find that it had been done some weeks earlier by G. Natta, in Italy, who knew of Ziegler's work in ethylene and used one of his catalysts. Polypropylene was also to become a very important plastic.

'I was very pleased that Natta followed up my work,' said Ziegler, 'because, with his wide experience of X-ray crystallography, he was better able to investigate the structural effects produced by the catalysts.' Natta showed that 'Ziegler's catalysts' (as they are commonly called) influence the geometrical orientation of side groups on a chain. Interesting uses have been made of this discovery, such as a synthesis of rubber that is identical with natural rubber.

From free radicals to plastics and rubbers was a circuitous route. 'Yet had I set out in the beginning to discover a method for polymerizing ethylene at normal pressure,' says Ziegler, 'I should never have found one. The whole secret of our success at Mulheim has been that we did nothing else but follow with open eyes and receptive minds through a not yet explored area of organic chemistry: chemistry itself was our guide.'

Dorothy Hodgkin
X-ray analysis of organic molecules

'Crystals are the most obvious thing to like when you're starting chemistry and I've kept with them ever since.' Dorothy Hodgkin realized, during the lectures she attended at Oxford at the beginning of the thirties, that evidence for the chemical formulae of such organic compounds as the sterols and strychnine was very sketchy and that the geometrical arrangement of the atoms was virtually unknown. Here it seemed were problems that X-ray analysis might be able to solve. She had been interested in the technique of X-ray analysis even before going to Oxford. When it came to

Dorothy Hodgkin (née Crowfoot) was born in Egypt on 12th May 1910. After graduating in chemistry from Oxford in 1932, she spent two years doing research at Cambridge, and then returned to Oxford where she has been ever since. She married in 1937 and, along with her research studies, has brought up a family of three. 'Looking after children,' she says, 'is the main difficulty that faces a woman who wants to do research.' She is only the third woman ever to win a Nobel Prize in Chemistry – Mme Curie and her daughter Irene Joliot-Curie were the others. She was awarded the Chemistry Prize in 1964 'for her determination by X-ray techniques of the structure of important biochemical substances'.

X-ray photograph of Vitamin B_{12}.

research, it was the X-ray study of organic substances that attracted her.

Of the many complex structures that Dorothy Hodgkin has examined, two in particular have established her reputation: that of penicillin, which she determined during the Second World War; and that of Vitamin B_{12} which she determined during the early fifties. Her general approach was to discover the geometrical arrangement of the atoms in space, and from this, the precise way in which the atoms were linked together which established the actual chemical structures of the compounds. In the case of penicillin, parts of the structure were found by chemical methods before the compound was crystallized; it was, however, the X-ray measurements which showed clearly how these parts were joined together. In the case of Vitamin B_{12} even the number and the precise chemical nature of the atoms present were found through the X-ray crystal structure determination. Dorothy Hodgkin's success, combined with that of many others, did much to establish X-ray crystallography as a method for determining the chemical structure of complex molecules as well as reaffirming its use for establishing molecular geometry when the chemical structure is known. Nowadays analyses of this kind have been made much easier by greater use of computers. Mrs Hodgkin dismisses much of her achievement as 'pig-headedness' which led her to pursue difficult structure analysis before the techniques had been developed that were to make them easy.

'The kind of skill needed in X-ray analysis is a feeling for the way in which atoms are arranged in a molecule, being able to look at a series of X-ray photographs to see how the atoms might fit together. It needs imagination, too, to visualize the various possible arrangements, and it needs judgment born of experience to select those possibilities which might lead to an answer. Sometimes the answer comes out very quickly: but with complex molecules such as Vitamin B_{12}, it may take years – working out the arrangement of atoms piece by piece and then seeing how the pieces fit together in the whole molecule. In each analysis there may be several interesting stages – getting an awkward substance to crystallize; seeing just what one is up against from the first X-ray photographs; and a point, often long before the end, when one knows that the answer is in sight. Of course, X-ray work has its limitations: one cannot necessarily predict from the arrangement of the atoms how a substance will behave in a chemical reaction. But it is a useful tool and can give one the position of the atoms in space more quickly and with greater certainty than any other method.'

Dorothy Hodgkin is at present studying the geometrical arrangement of the atoms in insulin. Here, in a sense, the wheel has come full circle; for she took an X-ray photograph of insulin as long ago as 1935, the second protein crystal ever to be X-ray photographed. She remembers this as the most exciting moment in her career: 'I developed the photographs late at night and walked elated round the streets of Oxford before going to bed. Then I woke up early, worried that the crystals might not be insulin after all. I slipped round to the laboratory before breakfast to test that I really had protein crystals.' At the time, too little was known about proteins for her to be able to make much out of the photograph but, thanks to Dorothy Hodgkin and others, our chemical understanding of complex biological substances has since come a long way.

George Porter
the invention of flash photolysis

George Porter, who invented the technique of flash photolysis for recording the lifetimes of short-lived substances. For work in the field of fast reactions, he was jointly awarded the Nobel Prize in 1967.

George Porter was born on 6 December 1920. He was educated at Thorne Grammar School and Leeds University. From 1941 to 1945 he served as an R.N.V.R. radar officer. After the war he went to Cambridge where he began his research in the field of fast reactions and photochemistry.
On the retirement of Sir Lawrence Bragg in 1966 he became Director of the Royal Institution and Fullerian Professor of Chemistry. Since then he has been directing a research group in the Davy-Faraday Research Laboratory of the Royal Institution.
In 1967 he was awarded the Nobel Prize for Chemistry together with Professor R. G. W. Norrish and Professor Manfred Eigen.
Professor Porter's particular contribution was the introduction of the technique known as flash photolysis, which makes use of intense flashes of light to produce excited states and other transient intermediates in chemical systems.

George Porter had just spent four and a half years in the Royal Navy as a radar officer when he went up to Cambridge in 1945 to do research. 'It seemed a good idea,' he says, 'to apply to chemistry the electronic and pulse techniques that I had learned in the Navy.' At Cambridge Professor Norrish gave him the task of looking at free radicals and other short-lived substances. There is a great problem here: how do you study a substance that exists for only a fraction of a second? 'From indirect methods we knew that free radicals and many other chemical substances lived only for thousandths or even millionths of a second. But in those days "millisecond" and "microsecond" were words almost unheard of in a chemistry department and the chance of doing chemical experiments in such short times seemed remote.'

Professor Porter's development of the technique of flash photolysis was therefore a direct result of the interactions of a problem in chemistry with the ideas of radar. 'My technique is to use a pulse of electromagnetic irradiation and to observe what happens a short time afterwards. That's precisely what you do in radar but for a different purpose.'

At this point the connection between the two was still only an idea. 'I needed another thing to be fed in and that occurred by another fortunate coincidence. In the spring of 1947 I went up to Siemens' lamp works at Preston to collect a lamp. While I was there I was shown some extremely powerful electronic flash lamps they had made. In Cambridge I was using a reaction vessel a metre long and it happened that the flash lamps they were making were a metre long. The flash lasted about a millisecond and this was the lifetime of some of the radicals I was studying. Everything clicked.

'I went back to my hotel bedroom in Preston. You cannot imagine anything with less distractions than that hotel bedroom. I had had an interesting day, I had absolutely nothing else to do, and so this didn't all slip. I wrote the whole thing out in detail on a couple of sheets of paper. I did a few calculations on energies. It was clear that a single flash lasting a millisecond would have enough energy to decompose pretty well all the stuff in the tube and turn it into free radicals, and my electronics experience told me that there should be no real problem of recording such high concentrations in a time of a few milliseconds. I was quite confident that here was the answer.

'This isn't always the case; you have an idea and gradually you see snags, it's not so good as you first thought. There were a few alterations and additions which came later but the basic idea remained. Also it struck me that since I was going to be using intensities a million times higher than had been used in chemistry and photochemistry before, there were probably quite new phenomena to be encountered.'

The most important addition to the basic idea was the use of a second flash, timed to go off a thousandth of a second later, by which the spectrum of the substance is photographed. It was a year or so before Porter thought of this. At first he tried to record the free radicals by the use of a scanning spectrometer which took him six months to build. 'It was a very poor instrument indeed. As I realized later, it went counter to information theory. If you are going to do something in a short time, you mustn't ask for too much information.' However, the use of the second flash solved the problem and substances which, because of their instability, had never been observed before were now brought under the scrutiny of the chemist. 'I still remember the appearance of beautiful time-resolved sequences of free radical absorption spectra under the safe-light of a developing dish as one of the most rewarding experiences of my life.'

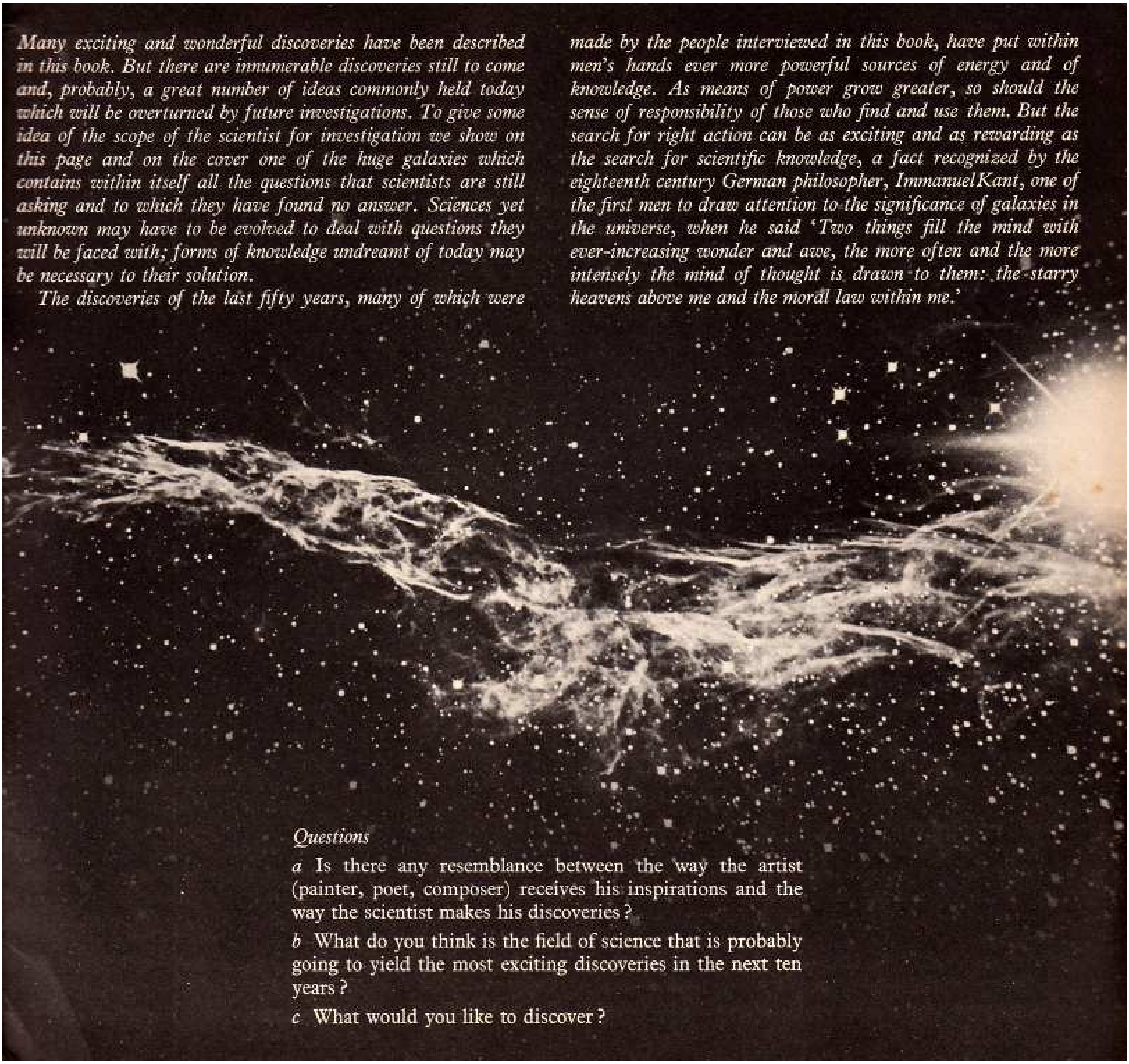
The significance of the technique is brought out by the fact that there are more chemical substances which exist for less than a second than exist for more than a second. 'Chemical substances cover an enormous range of lifetimes. Very few of them are stable; even the ones in the bottle on a laboratory shelf are not really stable and are decomposing slowly. But the only ones a chemist can study in the normal way are those which exist at least for a few minutes and these cover a very small part of the time range of chemistry. The short-lived chemical substances are just as interesting and, in fact, it is essential to know about them because they determine the course of chemical change. In almost every reaction there are, as intermediates, chemical substances of very short life, atoms, free radicals, excited states, and so forth.' The implications of this discovery in extending the chemist's range of investigation are of course very exciting. The method was rapidly improved so that microsecond lifetimes could be studied, and recently lasers and other new devices have made it possible to study substances which exist for only a few nanoseconds – a few thousandths of a millionth of a second.

Professor Porter believes that the field of science which is today producing the most original and valuable work is molecular biology. His main work at present, apart from extending his techniques of flash photolysis to shorter and shorter times, is on photosynthesis. 'What we should all like to do is to make a leaf. It's going to take years and we may never do it but anything we learn from nature on the way will be interesting and may have applications in quite different fields. We are laying down monomolecular layers of chlorophyll plus quinones and carotenes and other things which are in the leaf using a well-known technique called the Langmuir trough. We use our flash technique, and other methods, to study what happens a fraction of a second after the chlorophyll absorbs light. It is terribly complicated compared with the simple molecules which I studied in the early days. But the *problem* is clear and that's half the battle – somebody, sometime, will almost certainly solve it.'

The photograph, reproduced opposite and on the cover, shows the western loop of the Veil Nebula in Cygnus. *Photograph from the Mount Wilson and Palomar Observatories.*

Many exciting and wonderful discoveries have been described in this book. But there are innumerable discoveries still to come and, probably, a great number of ideas commonly held today which will be overturned by future investigations. To give some idea of the scope of the scientist for investigation we show on this page and on the cover one of the huge galaxies which contains within itself all the questions that scientists are still asking and to which they have found no answer. Sciences yet unknown may have to be evolved to deal with questions they will be faced with; forms of knowledge undreamt of today may be necessary to their solution.

The discoveries of the last fifty years, many of which were made by the people interviewed in this book, have put within men's hands ever more powerful sources of energy and of knowledge. As means of power grow greater, so should the sense of responsibility of those who find and use them. But the search for right action can be as exciting and as rewarding as the search for scientific knowledge, a fact recognized by the eighteenth century German philosopher, Immanuel Kant, one of the first men to draw attention to the significance of galaxies in the universe, when he said 'Two things fill the mind with ever-increasing wonder and awe, the more often and the more intensely the mind of thought is drawn to them: the starry heavens above me and the moral law within me.'



Questions

a Is there any resemblance between the way the artist (painter, poet, composer) receives his inspirations and the way the scientist makes his discoveries?

b What do you think is the field of science that is probably going to yield the most exciting discoveries in the next ten years?

c What would you like to discover?

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