Massimi, Michela. *Pauli's Exclusion Principle: The Origin and Validation of a Scientific Principle.* Cambridge, U.K.: Cambridge University Press, 2005. Includes citations to earlier historical literature.

Cathryn Carson

PAULING, LINUS CARL

(*b.* Portland, Oregon, 28 February 1901; *d.* Big Sur, California, 19 August 1994), *chemistry, quantum chemistry, nature of the chemical bond, x-ray crystallography and molecular structure, biochemistry and molecular biology, molecular medicine.*

Often called the Einstein of chemistry, Pauling is widely regarded as the most important chemist of the twentieth century. Best known for his foundational work in theoretical chemistry, and in biochemistry and molecular biology, he played a formative role in at least five major developments in twentieth-century science: the application of quantum physics to chemistry; the use of theories of chemical structure in biology; the construction of molecular models that became a characteristic tool of modern chemistry; the study of diseases as a product of molecular processes; and the role of scientist as public citizen and political activist. Pauling received the Nobel Prize in Chemistry for 1954 and the Nobel Peace Prize for 1962. He is the only individual to receive two unshared Nobel awards.

Early Life and Education. Pauling was born in Portland, Oregon. His father, Herman Henry William Pauling, was a pharmacist who moved to Condon in eastern Oregon, and young Linus watched his father make extracts and salves, measure and mix powders, and test solutions with litmus papers. Among the boy's early reading were his father's pharmacopoeia and dispensatory, along with the Bible and Charles Darwin's *Origin of Species*. His father died suddenly of a perforated stomach ulcer in June 1910, and Pauling's mother Lucy Isabelle moved Linus and his two younger sisters back to Portland, where Belle took boarders into their house. Linus attended Washington High School, where his coursework included general sciences, chemistry, and physics. He failed to complete the American history requirement because of a scheduling conflict, and he entered Oregon Agricultural College (later Oregon State University) in Corvallis without a diploma in 1917.

At that time the college in Corvallis was one of the nation's largest land-grant institutions, with four thousand students and two hundred instructors. Pauling quickly attracted the attention of his teachers in his chemical engineering major, and they enlisted him to teach freshman- and sophomore-level chemistry courses while he was still a student. As he prepared his chemistry lectures in 1920, Pauling ran across Irving Langmuir's articles in the 1919 *Journal of American Chemistry* on the structure of atoms and the electron theory of the valence bond. Langmuir's publications led Pauling back to the 1916 paper of Gilbert Newton Lewis, whom he revered for the rest of his life. In this paper Lewis proposed the electron pair as the fundamental chemical bond, with the loss or capture of electrons accounting for chemical reactivity when an atom tends to achieve the two-electron or eight-electron structure of an inert gas. From 1920 on, Pauling rarely had the chemical bond far from his mind. Nor did he relinquish the fascination with molecular form and structure that first engaged him in a course in Corvallis with Samuel Graf on the crystallography of metals. The chemical bond and molecular structure became permanent leitmotifs for Pauling's chemical career.

Pauling was ambitious early on. He applied unsuccessfully for a Rhodes Scholarship and, like others of his twelve classmates in chemical engineering, he applied to graduate school. Six of the twelve completed their PhDs, including Paul Emmett, who married Pauling's sister Pauline. In the fall of 1922 Pauling and Emmett both entered the California Institute of Technology (Caltech), where Arthur Amos Noyes headed the chemistry department.

During the summer before graduate school, Pauling worked for the Oregon Highway Department near Astoria. By then, he had proposed marriage to Ava Helen Miller (1903–1981), a student in Chemistry for Home Economics Majors, a class he had taught the previous spring. Pauling's summer letters to Ava Helen give insights into his aims and ambitions, which, he wrote, included not only a PhD but also a Nobel Prize. Ava Helen and Linus were the closest of companions following their marriage in June 1923, and she played an important role in his later political activism. It was her influence that led him to change his registration in 1934 from the Republican to the Democratic Party, and they worked closely together in the campaign of the 1950s for a ban on nuclear testing. The first of their four children, Linus Carl Pauling Jr., was born in 1925, followed by Peter Jeffress Pauling (b. 1931), Linda Helen Pauling (b. 1932), and Edward Crellin Pauling (1937–1997).

After arriving at Caltech in fall 1922, Pauling's coursework included thermodynamic chemistry with Noyes, statistical mechanics and atomic structure with Richard Chace Tolman, kinetic theory with Robert Millikan, advanced dynamics with Arnold Sommerfeld's student Paul Epstein, and statistical mechanics and quantum theory with the visiting Austrian theoretical physicist Paul Ehrenfest. Pauling's first paper, on the structure of the

mineral molybdenite (MoS_2), appeared in 1923. It was coauthored with Roscoe G. Dickinson, his research supervisor in x-ray crystallography. In the next three years, Pauling authored or coauthored a dozen crystal-structure publications, completing his PhD in 1925 with the dissertation "The Determination with X-Rays of the Structure of Crystals." In 1928 Pauling developed systematic rules governing the geometry of the coordination polyhedron of negative ions around a positive ion in an ionic crystal, enabling him to solve the structures of silicates such as mica, talc, and topaz. The work on silicates gained him his first international recognition.

Pauling's 1926 application for a Guggenheim Foundation Fellowship focused on something different, however. Pauling expressed the aim to take up the programmatic goal expressed by Sommerfeld for working out a topology of the interior of the atom and a system of mathematical chemistry that would detail the exact position of electrons and explain the formation of molecules and chemical compounds. Embarking on a physicist-inspired reductionist program for chemistry during his first trip to Europe, Pauling spent a year with Sommerfeld in Munich, a month in Copenhagen with Niels Bohr, and six months in Zürich with Erwin Schrödinger, whose electron wave theory and equation had just appeared in 1926.

While in Zürich, Pauling met Fritz London and Walter Heitler, who were working out a valence bond (atomic orbital or AO) treatment of the electron bond in the hydrogen molecule, which they published in 1927 using Werner Heisenberg's new notion of exchange or resonance energy arising from the interchange of two electrons with opposite spin. About the same time, in Göttingen, Friedrich Hund was developing a molecular orbital approach (MO), generalizing recent work by the Danish physicist Oyvind Burrau. The AO approach treats the hydrogen molecule as two hydrogen nuclei with the wave function of each electron centered on one of the nuclei and electrons tending to aggregate in the region between the two protons. In contrast, the MO theory assumes that any one electron moves in a potential field that results from all the nuclei and other electrons together. The AO method exaggerates the covalent character of chemical bonds, and the MO method the ionic character. In the long run, Pauling was to become a champion of the AO theory, and Robert S. Mulliken, who met Hund in Göttingen, became an outspoken advocate in the United States of the MO theory.

Pauling became an assistant professor of theoretical chemistry when he returned to Caltech in late 1927. He corresponded and collaborated with Samuel Goudsmit, whom he had met in Copenhagen, on an expansion and English translation of Goudsmit's Leiden doctoral thesis under Ehrenfest, into a book *The Structure of Line Spectra,* which appeared in 1930. While working on the structure of silicates, Pauling also published an explanation in *Chemical Reviews* of the AO and MO theories that he had learned in Germany, and he began to sketch out his own ideas for a theoretical treatment of the chemical bonds in methane, which, as a chemist, he considered the most crucial molecule after hydrogen.

The Chemical Bond and Quantum Chemistry. Methane is composed of one atom of carbon and four atoms of hydrogen. The carbon atom has six electrons, which should be distributed on the basis of quantum principles into energy states of $1s^2$, $2s^2$, $2p^2$. Carbon has four valence electrons, however, and they are identical in their energy states. Pauling's notion was to do away with a distinction between 2s and 2p energy sublevels in favor of four mixed levels or orbitals of the same energy value. From 1929 to 1934 Pauling presented these ideas to advanced students and faculty in Lewis's chemistry department at Berkeley, where he shared his time in teaching with Caltech. In these lectures Pauling presented his notion of mixed or "changed quantization" (later called hybridization) of electron energy levels, setting up quantum wave functions to represent valence, or electron-pair, bonds, in carbon compounds. In 1931 Pauling (and, independently, John Slater at Harvard University) demonstrated that wave functions project out in characteristic directions: p-level energy waves, for example, are represented by three dumbbell-shaped distributions or contour-lines at right angles to one another, whereas the s-level wave is a spherically shaped distribution. Pauling extended this treatment to other kinds of bonds, for example, double and triple bonds using trigonal and digonal mixed orbitals. Energy data from thermochemistry and from spectroscopy provided solutions to calculations of the bond energies, while information from x-ray crystallography about bond angles and interatomic distances further grounded the theory in chemical and physical facts. Pauling also developed a scale or table of atomic electronegativities for the chemical elements that predicted the energy and electric dipole moment, or ionic character, of any type of bond.

Among the most puzzling molecular structures that had been studied since the nineteenth century were conjugated molecules of alternating single and double bonds, including aromatic compounds such as benzene. Benzene resisted representation by any one structural formula, and its conflicting structures came to be identified with the names of August Kekulé and James Dewar in the late nineteenth century. In the 1920s and 1930s Pauling's Caltech colleague Howard J. Lucas, along with the British chemist Christopher Ingold and the German chemist Fritz Arndt, were among those who proposed that the real structure for a conjugated molecule such as benzene may

be one single structure that is different from any of the familiar valence-bond structures that had been used simultaneously and interchangeably. Arndt used the term *Zwischenstufe* for this nonvisualizable real structure and Ingold coined the word *mesomer.*

Collaborating with George Willard Wheland, Pauling explained aromatic structure as another instance of resonance or the behavior of wave functions in quantum mechanical exchange phenomena. Their paper was one of a series of seven papers written or coauthored by Pauling (with Wheland or Albert Sherman) that appeared from 1931 to 1933 under the title "The Nature of the Chemical Bond" in the *Journal of the American Chemical Society* and the *Journal of Chemical Physics.* Pauling followed up these papers by enlisting Edgar Bright Wilson Jr. to help write the rigorously mathematical *Introduction to Quantum Mechanics, with Applications to Chemistry.* The 1935 book's claims are modest but profound: All the chemical properties of atoms and molecules are explicable in terms of the laws and equations governing the motions of the electrons and nuclei composing them.

In 1939 Pauling revised the earlier papers on the chemical bond into a series of lectures at Cornell University. The manuscript became his classic textbook, *The Nature of the Chemical Bond and the Structure of Molecules and Crystals.* It was a textbook that changed the way scientists thought about chemistry, presenting chemistry as a discipline unified by an underlying theory. By demonstrating how the characteristics of the chemical bond determine the structure of molecules and how the structure of molecules determine their properties, Pauling showed for the first time, as the Austrian-born British biochemist Max Perutz later said, that chemistry could be understood rather than simply memorized. Fifty years later, in 1989, *The Nature of the Chemical Bond* still ranked among the top five most-cited books in the Institute for Scientific Information database.

The valence-bond atomic-orbital theory shared theoretical territory with an increasingly powerful MO theory in the long run. Pauling's AO approach, well-grounded in traditional chemical theory of the nineteenth century and in Lewis's hypothesis of the electron-valence bond, earned most chemists' allegiance until the 1950s and 1960s, when MO methods became more widespread, partly as the result of developments in molecular spectroscopy and in electronic computers, and partly through the influence of English theoretical chemist Charles Alfred Coulson, whose book championing MO theory, *Valence,* first appeared in 1952. Pauling himself always preferred the valence-bond AO approach, but quantitatively-minded quantum chemists came to prefer the convenience of calculation of the MO approach, especially for large molecules.

Pauling

Molecular Structure, Biology, and Medicine. Pauling became professor at Caltech in 1931, the year that he received the American Chemical Society's first Langmuir Prize for the most promising young chemist in the country. In 1933 Pauling became the youngest member ever elected to the National Academy of Sciences. He was appointed director of the Gates Laboratory and chairman of the Division of Chemistry and Chemical Engineering at Caltech in 1937, following the death of Noyes. Like many chemists in the 1930s, Pauling found himself in a university-level institution in which biology and medicine increasingly were gaining prominence in teaching and research. After Thomas Hunt Morgan organized a biology division at Caltech in 1928, Pauling began to participate in biology seminars on campus, and in 1931 some of the Caltech biologists invited Pauling to give a seminar on a German article about a mathematical theory of crossing over in chromosomes. His reading in biology began to affect his thinking about chemistry, including his adoption of the term *hybridization* to describe the "changed quantization" of the chemical bond.

Biologically significant compounds such as urea, oxamide, and oxamic acid were among the compounds that Pauling and his associates investigated in the 1930s from the standpoint of thermodynamics, bond configurations, and resonance structure in the amide group. The nucleic acid bases guanine and purine were among the compounds for which Sherman and Pauling calculated resonance energy in 1933. Pauling's visit to Hermann Mark's Berlin laboratory in 1930 familiarized Pauling with Mark's use of x-ray diffraction data in the study of proteins and with Mark's and Kurt Meyer's ideas on the structure of proteins whereby long and flexible polypeptide chains are attracted to one another by forces between the C=O groups and the NH groups on adjunct chains. Pauling himself turned in 1932 to the structures of proteins, including hemoglobin and other molecules of medical interest.

A shift in emphasis toward a biological program at the Rockefeller Foundation, which had been funding Pauling's work in chemistry, offered support for his investigations in biochemistry. This biologically oriented research included a 1935 paper on the shape of the oxygen equilibrium curve for the protein hemoglobin and an investigation in 1936 with Charles Coryell of the magnetic properties of a hemoglobin molecule. In another paper, written with Alfred Mirsky from the Rockefeller Institute, Pauling proposed a coiled, or folded, structure for the protein keratin, arguing, like Mark and Meyer, for the molecular structure of proteins at a time when the colloidal theory of proteins was not yet dead. In 1939 Pauling wrote a controversial paper with Carl Niemann discrediting Dorothy Wrinch's cyclol theory of a symmetrical geometry in protein structure.

Correlating his interest in molecular structure or shape with an emerging focus on biological function, Pauling tried to answer a question posed to him by Karl Landsteiner at the Rockefeller Institute in 1936: could the properties of antibodies and antigens be a result of molecular structure? In 1940 Pauling proposed that polypeptide chains might fold and wind around the exterior of an antigen structure, creating an antibody that is complementary in structure to the invading antigen, similar to a lock-and-key (a metaphor used by the German protein chemist Emil Fischer in 1894 for an enzyme and its substrate). After discussing with his Caltech colleague Max Delbrück the need to explain the duplication of the antibody form, they collaborated in a note to *Science* on a speculation that biological replication likely is a matter of complementary shapes.

Another example of the usefulness of the hypothesis of complementary molecular shapes came in Pauling's work with Harvey Itano on sickle-cell anemia in the late 1940s. Using electrophoresis, Itano discovered in 1949 that a sickle-cell individual's hemoglobin has more positive charge on its surface than normal hemoglobin. Pauling proposed that this alteration in surface charge created an area complementary in shape to neighboring hemoglobin, like antigen and antibody. The molecules stick together, twisting the red blood cells out of shape into sickles rather than flat disks and clogging small blood vessels in the body. Pauling coined the term *molecular disease.*

During the early 1940s, Pauling's systematic research program was interrupted by two events: illness and war. In 1941 he fell ill with a serious form of Bright's disease, an often fatal kidney disease. His grandfather Linus Darling had died of kidney disease. For the next fifteen years Pauling followed a diet advocated by Dr. Thomas Addis of Stanford University, which stressed a low protein, salt-free diet with lots of water, and he improved remarkably after only six months.

At this time he already was at work at Caltech on military-related projects following a meeting in Washington, D.C., in October 1940, at which military officers presented chemical researchers with a list of needed breakthroughs in medicines, explosives, and monitoring and detection devices. Pauling immediately went to work on an oxygen meter for monitoring the air in submarines, and he arranged its production with Arnold Beckman, who had left teaching chemistry at Caltech to establish a scientific instruments business. Money flowed to Caltech during the war, and Pauling traveled once per month to Washington for meetings, making a three-day train trip each way. Pauling directed research projects at Caltech on rocket propellants and explosives powders. He headed a team for the synthesis of artificial plasmas that enlisted the expertise of Addis and the immunology expert Dan Campbell. Pauling also continued work, which had begun before the war with Campbell, on the synthesis of artificial antibodies. When J. Robert Oppenheimer asked Pauling in early 1943 to join the Manhattan Project at Los Alamos as head of the chemistry division, Pauling declined, preferring to remain at Caltech. In 1948 he received the Presidential Medal for Merit for his war-related work.

Pauling's government and Rockefeller Foundation–sponsored research during the war years kept him focused on hemoglobin, immunology, and proteins along with other projects. Protein research was one of the major areas of study in x-ray crystallography and biochemistry, with British x-ray crystallographers such as John Desmond Bernal, Dorothy Hodgkin, and William Astbury among the pioneers in the field. While visiting Oxford in 1948 and confined with the flu, Pauling started building protein models, constructing a three-dimensional model of keratin as a spiral molecular structure using paper, ruler, and pencil to sketch out a chain of amino acids, and drawing the atomic-bond lengths and angles from memory. He realized, however, that an x-ray pattern produced from his model would not match the x-ray patterns that Astbury had published. After his return to Caltech, Pauling set to work with Herman Branson and Robert Corey to come up with an accurate model. In 1950 he and Corey published two structures for keratin, using hydrogen bonding for a coiled peptide chain. Their alpha-helix model had 3.7 amino acid residues per turn and called for a diffraction pattern showing about 5.4 angstroms between each turn, not quite on target with Astbury's value of 5.1 angstroms. The fiber manufacturing firm of Courtaulds in London soon confirmed the alpha-helix in its commercial synthesis of artificial fiber similar to natural keratin, as did Perutz in later studies of natural keratin in the form of horsehair. In May 1951 Pauling and his coworkers published seven papers on protein structures in one issue of the *Proceedings of the National Academy of Sciences* (*PNAS*), including the alpha helix, parallel and antiparallel pleated sheets, and a winding three-helix model for the protein collagen.

Pauling's method of modeling structures employed not only paper and pencil but wooden and plastic models constructed in Caltech's chemistry shop. In the fall of 1938 Pauling had initiated correspondence with Joseph Hirschfelder at the University of Wisconsin about the usefulness of three-dimensional molecular models for teaching and research. The German chemist Herbert Arthur Stuart had designed "space-filling" models in 1934. In this type of model, spherical atom units are brought into contact with each other in diameters roughly proportional to van der Waals radii (the estimated atomic radius for a hard atom sphere). By 1939 the Fisher Scientific Company was selling kits of the space-filling models, while technicians at Caltech continued making models locally that were

designed by Pauling, Verner Schomaker, and James Holmes Sturdivant. In the late 1940s the design and combination of atoms in these molecules used data about atomic sizes and interatomic distances and bond angles from x-ray spectrography, electron diffraction, and an electrical Fourier synthesizer.

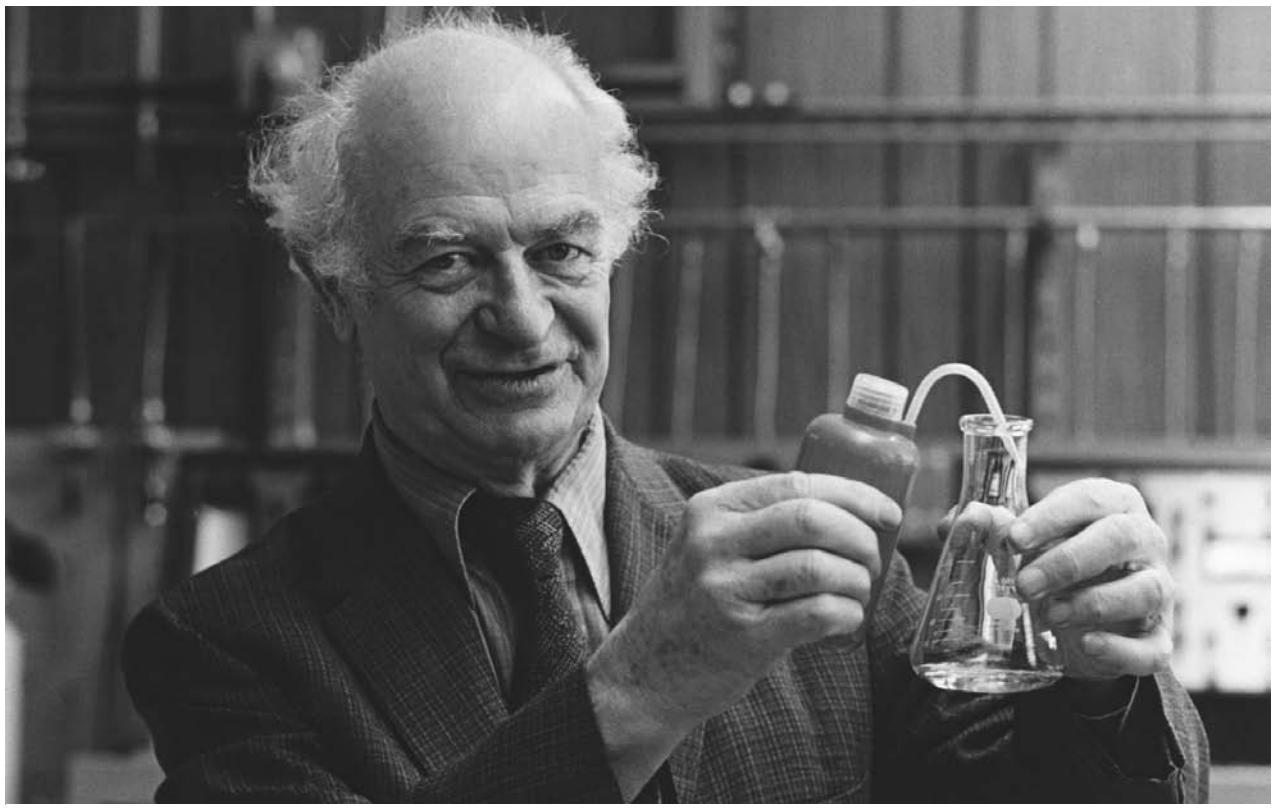
Following his success with protein, Pauling began to apply his methods for uncovering molecular architecture to deoxyribonucleic acid (DNA), the molecule that the Rockefeller Institute bacteriologist Oswald Avery identified in 1944 as the transforming principle or material that transferred genetic traits between *Pneumococcus* bacteria. Most biochemists and biologists had assumed that protein is the principal material of the gene, but because DNA is the most common form of nucleic acid in chromosomes, Avery's findings directed attention to the possible significance of DNA. A protein is a more complex molecule than DNA, and protein seemed the most likely candidate for the complexity of a genetic carrier. Protein consists of polypeptide chains of amino acids, of which twenty different ones are available for combinations within protein. In contrast, DNA contains only four nucleotides, each consisting of a sugar attached to a phosphate group and to one of four organic nitrogenous bases.

In February 1953 Pauling and Corey published a paper modeling DNA with three polynucleotide intertwined chains and with negatively charged phosphates at the core and nitrogenous bases on the outside. They based their structure on what turned out to be a misleading photograph made by Astbury in 1947 of what in fact was a mixture of two forms of DNA. The Astbury photograph resulted in calculation of an inaccurate figure for the density of the DNA molecule. Pauling did not try to make x-ray photographs himself, nor did he build a three-dimensional model before publishing his three-chain structure in 1953, nor did he focus on DNA as the possible genetic material. At the time, Pauling knew that Maurice Wilkins was working on DNA at King's College and that Wilkins had some unpublished DNA photographs, but Wilkins had declined to share them when Pauling wrote him in the summer of 1951. Pauling did not contact Wilkins again when Pauling was in England in the summer of 1952.

In April 1953, Wilkins's laboratory had new photographs of the dry and hydrated forms of DNA that had been made by Rosalind Franklin. Wilkins showed Franklin's picture of the pure beta (extended and hydrated) DNA to James Watson and Francis Crick, who were working in the Cavendish Laboratory of William Lawrence Bragg, one of the founders and masters of x-ray crystallography. Watson and Crick immediately published a structure for DNA: two helical chains, each coiled round the same axis, with bases on the inside of the helix and phosphates on the outside. Franklin herself earlier had told them, when they were toying with a three-strand model, that the phosphates must be on the outside. All this was detailed by Watson himself in his popular but controversial book *The Double Helix,* published in 1968.

Watson, a young microbiologist, had worked with Delbrück for a few months in 1949 in Pasadena and stayed in touch with him. More significantly, Pauling's son Peter, who was sharing an office at the Cavendish Laboratory with Watson and Crick in 1953, showed them a copy of his father and Corey's prepublication paper with the three-strand model of DNA, precipitating what Watson and Crick later described as their mad pursuit to beat Pauling to the prize. In their work Watson and Crick self-consciously and successfully used Pauling's method of model building. Their paper in *Nature* explicitly contrasted their double helix model with Pauling's triple helix model and noted the implications of the two-strand model for genetic replication. Pauling was gracious about his missed discovery, later expressing puzzlement that he had ignored his earlier idea published with Delbrück in 1940 that genetic material might consist of two complementary molecules.

Nuclear Weapons and Political Activism. In 1954 Pauling received the Nobel Prize in Chemistry for his research into the nature of the chemical bond and its application to the elucidation of the structure of complex substances. The award came at a time when his work on proteins and DNA was getting much welcome attention, in contrast to the unwelcome attention paid his political activities. Following the war, Pauling joined several organizations concerned with atomic-science issues, including the Emergency Committee of Atomic Scientists, chaired by Albert Einstein, whom Pauling had first met in Pasadena in 1932. Pauling's criticism of U.S. nuclear policy included worries about the Truman administration's talk of a first nuclear strike against the Soviet Union. Pauling and Ava Helen joined the Independent Citizens' Committee for the Arts, Sciences, and Professions (ICCASP), a left-wing organization of Los Angeles–area artists and intellectuals, which came under scrutiny from the House Un-American Activities Committee in 1947. In 1948 Federal Bureau of Investigation agents investigated Pauling for Communist sympathies, and in November 1950 he was called to testify before the California Senate Investigating Committee on Education, where he defended his objection to loyalty oaths. Under criticism for his political views from Caltech trustees, he began losing consulting contracts, committee appointments, and speaking engagements, and he was denied a passport in early 1952, preventing him from attending a spring Royal Society discussion on proteins. Ironically, Pauling was an object of denunciation by the Chemists' Division in the Soviet



Linus Carl Pauling. **OMIKRON/PHOTO RESEARCHERS, INC.**

Academy of Sciences in the summer of 1951 on the grounds that his chemical resonance theory was an idealistic, antimaterialistic, and bourgeois invention.

Following his trip to Stockholm to receive the Nobel chemistry prize in December 1954, Linus and Ava Helen Pauling visited Israel, India, Thailand, and Japan, arriving in Japan in February 1955, when the crew of the *Lucky Dragon* still was under observation following the U.S. explosion of thermonuclear devices over Bikini Atoll the previous spring. In July 1955 he joined more than fifty other Nobel laureates in issuing the Mainau Declaration, which called for an end to all war, especially nuclear war. Pauling also entered a long-running scientific debate over the biological effects of chronic, low-level radiation from atmospheric nuclear tests, connecting the problem of possible genetic damage to his knowledge of DNA and nucleic acids as carriers of inherited characteristics.

In 1958 and 1959 Pauling wrote papers, one of them with his future son-in-law Barclay Kamb, on the probabilities of genetic mutations from radionuclides in atmospheric fallout, concentrating on ^{90}Sr, which the U.S. Atomic Energy Commission (AEC) had previously been studying, and ^{14}C, which had not been considered to pose a possible hazard. In opposition to optimistic reports from the AEC and scientists such as Willard Frank Libby, Edward Teller, and Miriam Finkel that radioactive isotopes in fallout were unlikely to cause genetic or somatic effects, Pauling adopted the linear hypothesis of Edward B. Lewis, his Caltech colleague in genetics, that even minimum levels of radiation are cumulative in effect and can cause cell damage. A live debate between Teller and Pauling aired on public television in San Francisco in February 1958.

In May 1957, following a visit to Washington University in St. Louis, Pauling joined with the biologist Barry Commoner and the physicist Edward Condon in writing an appeal for a ban on the testing of nuclear weapons. By late 1957 he and Ava Helen had circulated letters that garnered more than nine thousand signatures from scientists in forty-nine countries on a petition that they presented to United Nations (UN) Secretary-General Dag Hammarskjöld at the UN in January 1958, supplemented by an additional two thousand signatures received shortly afterward. In the same year Pauling's book *No More War!* appeared. At this time President Dwight D. Eisenhower and Secretary of State John Foster Dulles tended to support a test ban, while the Department of Defense and the AEC opposed it. At the end of 1958 the United States, United Kingdom, and Soviet Union agreed to a moratorium on nuclear weapons testing, but the

Pauling

Soviet leader Nikita Khrushchev announced the end of the moratorium after the French government tested their first atomic bomb in the Sahara Desert in 1960. By this time Pauling had been subpoenaed by the U.S. Senate Internal Security Subcommittee to explain possible Communist involvement in the nuclear-test ban movement and refused, under threat of being held in contempt, to reveal the names of those who helped circulate the UN petition. The Cuban missile crisis of 1962 moved the United States and Soviet Union to a focused effort on achieving in August 1963 a Limited Test Ban Treaty, which allowed only underground nuclear testing.

In December 1963 Pauling received the deferred 1962 Nobel Peace Prize. The reaction from his colleagues and the public was a divided one because many people had come to identify Pauling with radical or suspect political actions considered unfitting for a responsible scientist. Caltech's president Lee DuBridge had asked Pauling in 1958 to resign as chairman of the chemistry and chemical engineering division on the grounds that Pauling's attention was insufficiently focused on his laboratory and his department. When DuBridge made a public statement acknowledging the difference of opinion among Pauling's colleagues about Pauling's campaign against nuclear war, Pauling announced in October 1963 that he was leaving the institution with which he had been associated since 1922. After the *Journal of the American Chemical Society* mentioned the peace prize only in a single paragraph in the back pages of an issue, Pauling resigned from the American Chemical Society, whose presidency he had held in 1949.

Vitamin C and Molecular Medicine. Pauling's next years were spent in several institutions: 1963 to 1967 as a research professor at the Center for the Study of Democratic Institutions in Santa Barbara; 1967 to 1969 as professor of chemistry at the University of California at San Diego; 1969 to 1972 as professor of chemistry at Stanford University; and 1973 to 1992 as chairman of the board of trustees for the Laboratory of Orthomolecular Medicine, which he founded and which in 1974 became the Linus Pauling Institute of Science and Medicine in Palo Alto. Two new research interests emerged in the 1960s from some of his earlier work: the use of the hemoglobin protein molecule as an evolutionary clock and the application of vitamin therapy in molecular medicine.

Pauling proposed investigation of the idea of an evolutionary clock to Emile Zuckerkandl, who arrived as a postdoctoral fellow at Caltech in 1959. The project began as one to track the evolution, or mutations, of the molecule hemoglobin by comparing its size and structure in different animals. A study of horse hemoglobin, for example, showed that it differs from human hemoglobin by approximately eighteen amino-acid substitutions in each of its four chains. When this information was compared with paleontologists' estimates of the divergence of horse and human lines, Pauling and Zuckerkandl arrived at a value of one evolutionary mutation every 14.5 million years in hemoglobin. They found that there was a closer relationship between the hemoglobin of humans and apes than between humans and orangutans, and they estimated that human and apes diverged more than 11 million years ago after their hemoglobin had stabilized. Pauling and Zuckerkandl's work was pathbreaking in founding a new research specialty, with DNA soon replacing hemoglobin in the role of evolutionary clock. Zuckerkandl served as director of the Linus Pauling Institute from 1980 to 1991.

Pauling continued to think about sickle-cell anemia as a molecular disease and to consider how abnormal hemoglobin might have evolved as a mutagenic mistake that turned out to be helpful in preventing malaria. Pauling's long bout with Bright's disease, which is a disease linked to protein metabolism, likely contributed to his preoccupation with how diseases are caused and cured by molecules. In 1962 it occurred to Pauling that the human need for vitamins might be the result of molecular diseases contracted millions of years earlier. Not surprisingly he found attractive the hypothesis of the biochemist Irwin Stone that vitamin C in large doses is effective in treating viral diseases, heart disease, and cancer, and that humans' inability to synthesize their own vitamin C is an evolutionary condition shared with other primates and only a few other mammals. Pauling also was intrigued with psychiatrists' use of niacin in the treatment of schizophrenia as another instance of vitamin therapy, and he enlisted Arthur Robinson, who had completed a PhD with the chemist Martin Kamen at the University of California at San Diego, to head studies of mental diseases and therapies at Pauling's institute.

In 1970 Pauling published a paper in *PNAS* on evolution and the need for ascorbic acid. The same year he published the best seller *Vitamin C and the Common Cold,* in which he surveyed the results of scientific trials on the preventive and therapeutic effects of doses of vitamin C ranging from 0.25 to 4.0 grams per day. In 1971 Dr. Ewan Cameron informed Pauling of his work near Glasgow in treating cancer patients with large doses daily of 10 grams of vitamin C. *PNAS* rejected a paper they coauthored, presaging the controversies that would follow in the next decade with members of the Mayo Clinic and the broader medical community over the merits of vitamins in the treatment of cancer. Pauling's personal commitment to vitamin C became only more pronounced with the diagnosis in 1976 of Ava Helen Pauling's stomach cancer, which led to her death in December 1981 after five years of good health following surgery and vitamin C therapy. In 1991, at the age of ninety, Pauling was diagnosed with

rectal and prostate cancer, which was treated with surgeries and megadoses of vitamin C. He died at his ranch in Big Sur in August 1994.

Before his death, Pauling had the pleasure of seeing a change in attitude toward vitamin C therapies. In the fall of 1990 the National Cancer Institute (NCI) sponsored an international conference on "Ascorbic Acid: Biological Functions in Relation to Cancer," to which he was invited as a speaker. In early 1992 the New York Academy of Sciences held a meeting that emphasized, like the NCI conference, the importance of vitamin C in enzymatic and nonenzymatic reactions, its effect in delaying tumor growth and prolonging survival times, and its action as an antioxidant that quenches free radicals implicated in the onset of cancer. After his death, the Linus Pauling Institute moved in 1996 to Oregon State University, where Pauling and Ava Helen had graduated. The institute continues to focus on the role of vitamins and essential minerals and plant chemicals in human health and disease.

Although Pauling's public crusades in politics and medicine discredited him in some professional and public circles in the 1970s and early 1980s, the rancor had abated by the time of his death. On his eighty-fifth birthday, in 1986, Caltech declared an academic holiday and hosted a banquet where Pauling received praise as the greatest chemist of the twentieth century, a man deserving of a third Nobel Prize for his work on sickle-cell hemoglobin, and the true father of molecular biology. Pauling's scientific work ranged broadly across physics, chemistry, biology, and medicine. His textbook *General Chemistry,* first published in 1947, defined a new chemistry just as *The Chemical Bond* had done in 1939. The 1947 textbook and its later editions emphasized both the dissimilarity and the similarity of chemistry and physics, and it taught chemistry on a firm theoretical foundation of electrons, atoms, and molecules with dimensions and images captured by three-dimensional models and by data from both physical instruments and chemical reactions. The high school chemistry curriculum in the United States in the 1960s was based in Pauling's chemical bond approach, and Corey-Pauling Space Filling Models with Improved Koltun Connectors became as common in chemistry classrooms as the periodic table of the elements.

Pauling's role as brilliant scientist and charismatic personality was not unlike Einstein's in the twentieth century. Pauling was a legendary speaker and performer in lectures and public appearances, as well as a media star. Like Einstein, Pauling took delight in crossing boundaries and frontiers, and in confounding and even scandalizing his peers and colleagues. Neither Einstein nor Pauling lived tranquil lives, but they chose to become and remain public figures. Pauling was one of the great revolutionary scientists of the twentieth century, and few chemists doubt his place as the greatest of twentieth-century chemists.

BIBLIOGRAPHY

For a listing of all of Pauling's publications, manuscripts, correspondence, and other materials, with commentary and illustrations, see The Pauling Catalogue: Ava Helen and Linus Pauling Papers at Oregon State University. *6 vols. Edited by Chris Petersen and Cliff Mead. Corvallis: Valley Library Special Collections, Corvallis, Oregon State University Libraries, 2006. The most detailed and comprehensive source for references to Pauling's published and unpublished papers, details of his life, honors and degrees that he received, and essays and articles on his life and work with accompanying photographs, illustrations, and documents is the Web site at Oregon State University for the Ava Helen and Linus Pauling Papers in Special Collections at the Valley Library: http://osulibrary.oregonstate.edu/specialcollections/.*

WORKS BY PAULING

With Samuel Goudsmit. *The Structure of Line Spectra.* New York: McGraw-Hill, 1930.

"The Nature of the Chemical Bond." Parts I and II. *Journal of the American Chemical Society* 53 (1931): 1367–1400, 3225–3237.

"The Nature of the Chemical Bond." Parts III and IV. *Journal of the American Chemical Society* 54 (1932): 988–1003, 3570–3582.

With George W. Wheland. "The Nature of the Chemical Bond." Part V. *Journal of Chemical Physics* 1 (1933a): 362–374.

With Jack Albert Sherman. "The Nature of the Chemical Bond." Parts VI and VII. *Journal of Chemical Physics* 1 (1933b): 606–617, 679–686.

With E. Bright Wilson. *Introduction to Quantum Mechanics, with Applications to Chemistry.* New York: McGraw-Hill, 1935.

The Nature of the Chemical Bond and the Structure of Molecules and Crystals: An Introduction to Modern Structural Chemistry. Ithaca, NY: Cornell University Press; London: Oxford University Press, 1939.

General Chemistry: An Introduction to Descriptive Chemistry and Modern Chemical Theory. San Francisco: W.H. Freeman, 1947.

With Robert B. Corey and Herman R. Branson. "The Structure of Proteins: Two Hydrogen-Bonded Helical Configurations of the Polypeptide Chain." *Proceedings of the National Academy of Sciences of the United States of America* 37 (1951): 205–210.

With Robert B. Corey. "A Proposed Structure for the Nucleic Acids." *Proceedings of the National Academy of Sciences of the United States of America* 39 (1953): 84–97.

No More War! New York: Dodd, Mead, 1958.

Vitamin C and the Common Cold. San Francisco: W.H. Freeman, 1970.

How to Live Longer and Feel Better. New York: W.H. Freeman, 1986. A reprint in paperback, with an introduction by

Melinda Gormley, was published by Oregon State University Press in 2006.

Linus Pauling on Peace: A Scientist Speaks Out on Humanism and World Survival; Writings and Talks by Linus Pauling. Selected and edited by Barbara Marinacci and Ramesh Krishnamurthy. Los Altos, CA: Rising Star, 1998.

Linus Pauling: Selected Scientific Papers. 2 vols. Edited by Barclay Kamb et al. River Edge, NJ: World Scientific, 2001.

OTHER SOURCES

Dunitz, Jack D. "Linus Carl Pauling: February 28, 1901–August 19, 1994." *Biographical Memoirs of the National Academy of Sciences* 71 (1997): 220–261. Available from http://www.nap.edu/readingroom/books/biomems/lpauling.html.

Francoeur, Eric. "Molecular Models and the Articulation of Structural Constraints in Chemistry." In *Communicating Chemistry: Textbooks and Their Audiences, 1789–1939,* edited by Anders Lundgren and Bernadette Bensaude-Vincent. Canton, MA: Science History Publications, 2000.

Gavroglu, Kostas, and Ana I. Simões. "The Americans, the Germans, and the Beginnings of Quantum Chemistry." *Historical Studies in the Physical and Biological Sciences* 25 (1994): 47–110.

Goertzel, Ted, and Ben Goertzel. *Linus Pauling: A Life in Science and Politics.* New York: Basic, 1995.

Hager, Thomas. *Force of Nature: The Life of Linus Pauling.* New York: Simon and Schuster, 1995.

Jolly, J. Christopher. "Linus Pauling and the Scientific Debate over Fallout Hazards." *Endeavour* 26 (2002): 149–153.

Krishnamurthy, Ramesh, et al., eds. *The Pauling Symposium: A Discourse on the Art of Biography.* Corvallis: Oregon State University Libraries, 1996.

Mason, Stephen F. "The Science and Humanism of Linus Pauling (1901–1994)." *Chemical Society Reviews* 26 (1997): 29–39.

Nye, Mary Jo. "What Price Politics? Scientists and Political Controversy." *Endeavour* 23 (1999): 148–154.

———. "Physical and Biological Modes of Thought in the Chemistry of Linus Pauling." *Studies in the History and Philosophy of Modern Physics* 31B (2000): 475–492.

Richards, Evelleen. *Vitamin C and Cancer: Medicine or Politics?* New York: St. Martin's Press, 1991.

Mary Jo Nye

PAULZE-LAVOISIER, MARIE-ANNE-PIERETTE (*b.* Montbrison, France, 20 January 1758; *d.* Paris, France, 10 February 1836), *chemistry, botany, economics, social reform.*

Marie-Anne Paulze-Lavoisier was the wife of Antoine-Laurent Lavoisier (1743–1794), the figure known as the father of the chemical revolution. She was an active collaborator across the full range of her husband's encyclopedic activities as chemist, financial administrator, and social reformer, but she especially exerted herself to help bring about the success and widespread diffusion of the chemical revolution.

Paulze-Lavoisier was born into the wealthy bourgeois class in 1758. As was customary at that time, she received her elementary education at a boarding school attached to a convent and was not given any education in science. Her father was a colleague of Lavoisier in the Ferme Général. Paulze-Lavoisier's apprenticeship in science began in December 1771, after she had married Lavoisier. The occasion that first led her to embark on this goal is not known, but it is apparent that this young woman wanted to become a suitable wife for her husband, the great scholar, and it is also apparent that this is what her husband wanted. She learned the basics of chemistry from Lavoisier's colleagues, particularly Jean-Baptiste Michel Bucquet (1746–1780). She learned Latin from a private tutor and her older brother and studied drawing with Jacques-Louis David (1748–1825). She also learned Italian and English (which Lavoisier found difficult) and even mastered the technique of print engraving. Paulze-Lavoisier was present at scientific experiments as well, and many volumes of laboratory notes that she took are in the archives of the French Academy of Sciences in Paris. The thirteen copperplate illustrations included in Lavoisier's *Traité élémentaire de chimie,* in particular, and the drawings of the laboratory in their residence in the Paris Arsenal were works by Paulze-Lavoisier. These provide precious concrete documentation of her role in Lavoisier's chemical experiments as well as illustrations of the advanced nature of Lavoisier's experimental techniques.

Paulze-Lavoisier also contributed to the Chemical Revolution through her translations. She translated into French *An Essay on Phlogiston* (1787) and *Of the Strength of Acids* (1791), both written by Richard Kirwan, who opposed Lavoisier's theory of oxygen. Her translations of these works were published in 1788 and 1792, respectively, the former with her preface and both with her translator's notes containing brief refutations of Kirwan's arguments. In the manuscript of the later work, however, the notes are written in Lavoisier's hand. The manuscript of the earlier work has not been found. The identity of the true author of these notes remains a mystery. What is certain is that the Republic of Letters treated Paulze-Lavoisier as an intellectual who was worthy of having authored the notes. The savants received by Paulze-Lavoisier in her own salon were dazzled by the brilliance of this woman's clear exposition of the theories of her husband.

After Lavoisier and her father were executed as farmers-general in 1794 during the Terror, Paulze-Lavoisier edited and published his posthumous writings as the *Mémoires de physique et de chimie* (1805), with a preface praising her late husband. That same year, Paulze-Lavoisier