KEYNOTE LECTURE

A Career at the Center: Linus Pauling and the Transformation of Chemical Science in the Twentieth Century

Mary Jo Nye

Oregon State University, Corvallis Oregon, USA

In my talk today, I want to focus on Linus Pauling in order to analyze some of the principal transformations in chemical science during the twentieth century. Pauling lived throughout most of that century, from 1901 to 1994, and chemistry was the center of his life. His career was spent mostly at an American institution that was an outpost when Pauling first went there in 1922, but the California Institute of Technology became a major player in chemical science by the height of Pauling's career at mid-twentieth century. Pauling moved from one cutting edge in chemistry to another, always on the lookout for something new, but never abandoning his earlier areas of research, whether X-ray crystallography, statistical mechanics and quantum mechanics, electron diffraction, thermodynamic studies of molecules, the chemistry of life and molecular biology, immunology, structural studies of metals and of intermetallic compounds, or studies of disease in relation to genetic abnormalities and diet.

At the meeting of the International Conference in the History of Chemistry in Uppsala in August 2013, I included Pauling as one of three case studies for an analysis of patterns of collaboration and co-authorship in 20th century chemistry. One of my points in that paper was not only to highlight differences in styles of scientific leadership, by personality and institution, but also to focus attention on the increase in collaborative chemical work during the course of the twentieth century. In 1800 only about 2% of all published scientific papers were co-authored, a figure that increased to 7% in 1900.[1] In chemical science, co-authorship was more frequent than in other fields. Around 20% of chemistry papers were co-authored in 1900, increasing to 80% in the early 1960s and into the high 90s percentile by the end of the twentieth century.[2] This exponential increase in collaboration and co-authorship is one of the striking transformations in twentieth-century science.

The increase in co-authorship occurred partly because of the introduction of a broad range of increasingly specialized instruments that required expertise that a laboratory director might not personally possess even if wanting to make use of a new technique. University laboratory facilities became larger, with a greater division of labor, in order to support a steadily increasing clientele in undergraduate, graduate, and postgraduate education and research. In addition, more rapid means of transportation made possible an expansion in international exchange and collaboration across the Atlantic and Pacific thoroughfares. Yet, the main driver

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[1] Donald de B. Beaver and Richard Rosen, "Studies in Scientific Collaboration: Part II. Scientific Co-Authorship, Research Productivity and Visibility in the French Scientific Elite, 1799-1830," *Scientometrics*, 1, #2 (1979): 133-149, on 134.

[2] Derek J. deSolla Price, *Little Science, Big Science* (New York: Columbia University Press, 1963), 86-91; and Beverly L. Clarke, "Multiple Authorship Trends in Scientific Papers," *Science*, new series, 143, #3608 (21 February 1964): 822-824.

for change was innovation in physical instrumentation, a point persuasively argued in his 2006 book on post-1950 chemistry by Carsten Reinhardt.[3]

In an article on very recent laboratory science, the sociologist Edward J. Hackett emphasizes two kinds of skills required of the successful laboratory director. One is the craft skill of bench manipulation, working with one's hands and achieving knowledge that is "experiential, embodied, or etched in the senses." The laboratory leader's main skill, however, according to Hackett, is design of research strategy and tactics, requiring the "articulation work" of "managing people, ordering supplies, remaining in touch with collaborators, competitors, and funding agencies."[4] Hackett finds that the laboratory director often gradually withdraws personally from craftwork, and this withdrawal may be essential for a group to "progress" by adopting new techniques and instrumentation that the laboratory head may never have mastered in practice.[5]

In this paper I focus on the instruments and techniques that Pauling gradually introduced for his researches and his researchers at Caltech from 1922 to 1963, in the period when co-authorship increased from around 30% to 80% of all published chemistry papers. The expansive range of Pauling's research agenda and the growth at Caltech required new strategies for organizing workers into collaborative research groups, a theme that Jeremiah James has explored in his study of what he calls Pauling's program for "naturalizing the chemical bond" from 1927 to 1942.[6] In keeping with Hackett's generalizations, we will see in what follows that Pauling did not himself master all the craft skills of instruments that were necessary to solve problems, but he did master knowledge of how new techniques could be useful and how to interpret their results. That was his genius. Let us turn now to some of the transformations in Pauling's research agenda and in twentieth century chemistry, more generally.

The 1920s and 1930s: The Craftsmanship of X-Ray Crystallography and Quantum Chemistry

When Linus Pauling first came to Pasadena in 1922, he had majored in chemical engineering at Oregon Agricultural College. He was inspired as an undergraduate by his reading of Irving Langmuir's and G. N. Lewis's recently published articles on the electron theory of the valence bond. At Caltech Pauling studied classical thermodynamics, statistical mechanics, kinetic theory, and elements of the new quantum theory as taught by Richard Chace Tolman, Arthur Noyes, Robert Millikan, and visiting European scientists. He scoured the CRC Chemical Handbook for details and values of physical properties in molecules, such as diamagnetism and paramagnetism, and he tabulated and compared interatomic distances in crystals published by William and Lawrence Bragg.[7] Part of Pauling's later success was the result of his astonishing memory for data and his relentless search for order and meaning in numbers, much like Dmitri Mendeleev in the nineteenth century.

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[3] Carsten Reinhardt, *Shifting and Rearranging: Physical Methods and the Transformation of Modern Chemistry* (Sagamore Beach, MA: Science History Publications, 2006).

[4] Edward J. Hackett, "Essential Tensions: Identity, Control, and Risk in Research," *Social Studies of Science*, 35, #5 (October 2005): 787-826, on 796.

[5] Hackett (note 4), 797-799.

[6] Jeremiah Lewis James, "Naturalizing the Chemical Bond: Discipline and Creativity in the Pauling Program, 1927-1942" (Harvard University Ph.D. dissertation, 2007).

[7] Sources for the History of Quantum Physics, Interview with Dr. Linus Pauling by John L. Heilbron, Pasadena, 27 March 1964. Online at: http://www.aip.org/history/ohilist/3448.html (accessed 23 January 2015).

At Caltech in 1922, Arthur Noyes assigned Pauling to work in the new field of X-ray crystallography. Pauling learned the craft under young Roscoe Dickinson who about that time made the first crystal structure determination of an organic compound with his student Albert Raymond.[8] Dickinson had begun using photographic plates, rather than the Bragg technique of ionization effects, to register X-ray reflections, and Pauling learned Dickinson's methods.

One procedure in the photographic method (the rotational "spectral" method) directed X-rays onto the crystal under investigation and also onto a reference crystal, with the two crystals mounted one above the other on a holder that oscillated or rotated about an axis in the plane of the crystal faces. The rays that were reflected from both crystals hit a photographic plate placed perpendicularly to the incident beam. This technique gave the size of the smallest possible size of the crystal's unit cube. Then, a second process (the Laue method) was used, as developed originally at Cornell by Ralph W. Wyckoff and the Japanese scientist Shoji Nishikawa.[9] A thin section of a crystal was ground into powder and fixed on a rod, or, alternatively, a thin crystal was mounted in a holder, and photographs were made with an X-ray beam traversing the crystal.[10]

Calculations to determine the crystal and molecular structure used the wavelength of incident radiation, the spacing of planes in the atomic lattice, and the angle between the incident ray and the scattering planes. The hundreds or thousands of spots appearing on a photographic plate, after an exposure time of four to twenty-four hours, had to be assigned to particular planes in the crystal. Calculations were made of angles of reflection of the X-rays from the crystal planes, using data from the rotation photographs which specified the smallest possible size of the unit cell and its multiples. Measurements of density and molecular weight also had to be made, along with the initial growing or purification of the crystal. Finally, the nineteenth-century theory of 230 possible space groups was applied to find arrangements of atoms compatible with observed crystal symmetry and with the other data, resulting in a decision on the best fit. In the early years, Pauling learned to do all these tasks himself.[11]

It is hardly surprising, given the many steps in a crystal structure analysis, that most of Pauling's crystal structure papers were co-authored. His earliest student research notebooks include data and calculated results in the handwriting of his wife Ava Helen, who spent time with him at the laboratory when he was a student. By the late 1920s detailed entries for X-ray data calculations and, then, quantum mechanical calculations can be found in the handwriting of Pauling's student and later assistant Sidney Weinbaum. Pauling's notebooks indicate that Pauling persisted in doing hands-on work in X-ray diffraction into the mid-1930s (now with film rather than plates).[12]

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[8] See James (note 6), 261-262.

[9] Linus Pauling, "Fifty Years of Physical Chemistry in the California Institute of Technology," *Annual Reviews of Physical Chemistry*, 16 (1965): 1-15, on 27.

[10] Linus Pauling, "Early Work on X-Ray Diffraction in the California Institute of Technology," in *Fifty Years of X-Ray Diffraction*, ed. P.P. Ewald (Utrecht: Oosthoek's Uitgeversmaatschappij, 1962): 623-628; and Pauling, "X-ray Crystallography in the California Institute of Technology," in *Crystallography in North America,* eds. Dan McLachlan, Jr. and Jenny P. Glusker (New York: American Crystallographic Association, 1983): 27-30.

[11] Pauling, "Early Work" (note 10), 625-626; Roscoe G. Dickinson and Linus Pauling, "The Crystal Structure of Molybdenite," *Journal of the American Chemical Society*, 45 (1923): 1466-1471, on 1466.

[12] Pauling Research Notebook #3 (1923-1925), OSU Special Collections Box 3R, pp. 37-38; Notebook #6 (begins August 9, 1929), no numbered pages, Special Collections Pauling RNB6; Notebook #8 (1931-1936), Box 8R, letter tucked in between pp. 138-139, dated 27 September 1935 from LP to Lynn (Hoard). Weinbaum co-authored two crystal structure papers with Pauling.

Pauling had completed his Ph.D. on crystal structure work in 1925. He then embarked for eighteen months in Europe, where he thoroughly learned quantum mechanics in Munich, Copenhagen, and Zurich just at the time that the quantum wave interpretation of the stability of the hydrogen bond was first developed. After returning to a new faculty position at Caltech in 1927, Pauling began to sketch out a theoretical treatment of the chemical bonds in methane, which, as a chemist, he considered to be the most crucial molecule after hydrogen. By developing the notion of mixed or "changed quantization" (later called hybridization) of electron energy levels, Pauling (and independently, John Slater at Harvard University) demonstrated that electron wave functions project out in characteristic directions, thus explaining mathematically the distribution in space of atoms in molecules such as methane. Pauling next explained the aromatic structure of benzene and other conjugated molecules as an effect of the quantum mechanical exchange phenomenon.

Nineteenth-century chemists had pioneered the notion of chemical valence, with lines representing bonds, but they had not been able to explain how the bond works. They also had proposed three-dimensional geometries of molecules on the basis of chemical isomerism and substitution patterns, but without a firm explanatory basis. The atomic orbital theory of chemical bonding, developed by Walther Heitler, Fritz London, Slater and Pauling, complemented by the rival molecular orbital theory developed by Friedrich Hund, Robert Mulliken and Erich Hückel, transformed and motivated researches in theoretical chemical science for the rest of the twentieth century.

1930s and 1940s: Expanding Strategies and Technologies

In 1930 Pauling visited Munich, where he met Herman Mark in his laboratory in Ludwigshafen and discovered Mark's electron diffraction apparatus for studying the structure of gas molecules.[13] With Mark's encouragement, Pauling took sketches of Mark's apparatus back to Pasadena and asked his graduate student Lawrence O. Brockway to build the apparatus with help from Pauling's faculty colleague Richard Badger, whose research field was molecular spectroscopy.[14]

Brockway and Pauling's first co-authored paper on electron diffraction in 1932 reported on the atomic configuration and interatomic distances in three inorganic molecules using photographic results calculated according to equations based in the work of Peter Debye and Nevil Mott. In this technique, a well-defined beam of electrons traveling with uniform velocity intersects a jet of gas, and the scattered electrons are recorded on photographic film set at right angles to the direction of the initial beam. Comparison is made of measured curves (rings) on a photograph with theoretical intensity curves that have been calculated for different models corresponding to different relative positions of the atoms.[15]

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[13] "I was overwhelmed by the possibilities of this new technique," Pauling later wrote, because "for some time I had been looking for a diffraction method of determining the structure of molecules without having at the same time to determine the sometimes very complicated way in which the molecules are arranged relative to one another in a crystal." Pauling, "Fifty Years" (note 9), 10-11.

[14] Pauling, "Fifty Years" (note 9), 7, 11. On electron diffraction, see Mari Yamaguchi, "Pursuit of Accurate Measurements: Gas Electron Diffraction from the 1930s to the 1960s," paper delived at the 2015 International Workshop on the History of Chemistry, Tokyo, 2-4 March 2015.

[15] L. O. Brockway and Linus Pauling, "The Determination of the Structures of the Hexafluorides of Sulfur, Selenium and Tellurium by the Electron Diffraction Method," *Proceedings of the National Academy of Sciences*, 19, #1 (January 1933): 68-73, quotation on 69.

Brockway became head of Pauling's group assigned to electron diffraction studies. For the next seven years after completing his Ph.D., Brockway continued in this role, until another new Caltech Ph.D., Verner Schomaker, took it over when Brockway left for England and the University of Michigan.[16] From about 1917 to the mid-1960s the Gates and Crellin Labs at Caltech published about 400 papers on the structure of some 400 crystals, complemented after 1930 by electron diffraction determinations of the structure of some 225 molecules.[17] Jeremiah James writes that Pauling never sought personally to master the craftsmanship of the electron diffraction apparatus, unlike X-ray diffraction. Thus Pauling's role became an example of what Hackett calls articulation, rather than craftsmanship, in laboratory leadership.[18]

By the mid-1930s, Pauling was head of Caltech's Division of Chemistry and Chemical Engineering. He supervised twice as many graduate students and postdocs as other faculty colleagues in two large, multi-story and adjoining laboratory buildings.[19] As Jeremiah James discusses in his 2007 dissertation, Pauling introduced divisions of labor and forms of collaboration previously foreign to Caltech.[20] His broad interests and program of chemical researches required collaborators who were experts in different areas and who came and went from far and wide, as Pnina Abir-Am has discussed in a study of what she calls "Pauling's Boys."[21]

James Holmes Sturdivant became one of Caltech's paid Research Fellows after he took his Caltech Ph.D. He helped, and then took over, what previously had been Pauling's craft work of making X-ray diffraction photos, indexing diffraction patterns, and analyzing simple structures. Eventually Sturdivant ran the X-ray laboratory and expanding instrument shop.[22] For mathematical assistance, Pauling turned to graduate students such as the postdoctoral fellow George Willard Wheland (who has been studied by Buhm Soon Park), and the graduate students Jacob (Jack) Sherman and E. Bright Wilson, Jr.[23] Each became co-author as well as assistant. Wilson, for example, later a star at MIT, co-authored with Pauling the

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[16] James, (note 6), 281, 283. On Badger, see "Richard M. Badger, 1896-1974," *Engineering and Science*, 38 (December 1974-January 1975): 24. At http://calteches.library.caltech.edu/357/1/badger.pdf (accessed 23 January 2015); and Oliver R. Wulf, "Richard Mclean Badger 1896-1974," *National Academy of Sciences Biographical Memoir* (Washington DC: NAS, 1987): 1-20. [Mclean is the correct spelling.]

[17] Pauling, "Fifty Years" (note 9), 7, 11.

[18] James (note 6), 250.

[19] James, (note 6), 71-78; and Thomas Hager, *Force of Nature: The Life of Linus Pauling* (New York: Simon and Schuster, 1995), 170, 203. Pauling recruited personnel from his undergraduates, graduate students, postdocs, and other institutions, with the advantage of being able to appoint short-term, but renewable, experienced researchers as Research Fellows, some of whom eventually became Caltech faculty members or, mostly, took positions elsewhere. For the numbers, see *Bulletin of the California Institute of Technology. Catalogue for 1934* (Pasadena: The Institute, December 1933), 45.

[20] James (note 6), 249.

[21] See: Pnina G. Abir-Am at https://paulingblog.wordpress.com/2012/11/21/dr-pnina-abir-am-resident-scholar/ (accessed 23 January 2015) and Pnina G. Abir-Am, "Pauling's 'Boys' and the Mystery of DNA Structure: On Mentorship in Structural Chemistry and Molecular Biology," paper delived at the 2015 International Workshop on the History of Chemistry, Tokyo, 2-4 March 2015.

[22] James (note 6), 66, 279; and Pauling, "Fifty Years" (note 9), 7. Sturdivant became Assistant Professor at Caltech in 1938 and studied crystal structures until well after the Second World War, although his focus on inorganic structures was increasingly distant from Pauling's interests. See James (note 6), 280.

[23] Buhm Soon Park, "Chemical Translators: Pauling, Wheland and Their Strategies for Teaching the Theory of Resonance," *British Journal for the History of Science*, 32 (1999): 21-46.

1935 textbook *Introduction to Quantum Mechanics with Applications to Chemistry*. [24] Pauling's longest-term mathematical collaborator was Sidney Weinbaum, who worked regularly with Pauling from the late 1920s until 1943, spending months at a time with desktop electric calculators carrying out calculations in X-ray and electron-diffraction analysis, as well as quantum mechanics.[25] Weinbaum later assisted with calculations for the work that became Pauling's papers of 1950 and 1951 with Robert Corey and Herman Branson on the spiral or helix structure of polypeptide chains.[26]

Transformations in instrumentation soon changed mathematical calculation. When Weinbaum and Pauling first were working together, they were using pencil and paper, slide rules, published trigonometric tables, and adding machines. For X-ray studies of molecular structure it was necessary to evaluate one, two, or three-dimensional Fourier series. In the 1930s the series were evaluated by use of an adding machine and the Beever-Lipson cardboard strips in which each strip represents a sine or cosine function for one value of wavelength and one value of frequency. A strip corresponding to each term of the series was taken from a file, and the strips were then arranged to permit the convenient addition of terms for constant x coordinate. For electron diffraction, similarly designed strips were the Sherman-Cross strips.[27]

As Pauling later described in *The Journal of Chemical Physics*, the process of calculation was slow and required the constant attention of the operator putting numbers into the adding machine and recording the results. The wrong strips might be drawn or errors made in summing them. Tabulated functions were not sufficiently precise. By the early 1940s, however, there was a breakthrough that transformed twentieth century chemical science everywhere. It was the appearance of the punched card automated computer.

Wartime computer development hastened the access to such machines in the sciences. In using this new technique, Pauling again was an articulator and strategist, not a craftsman, for the work at Caltech. In the early 1940s, Verner Schomaker had started putting data from the Beevers-Lipson strips onto cards using sixteen 4-place fields on one card each and wiring a tabulating machine to get the sixteen different totals.[28] In doing this, Schomaker worked with Edward W. Hughes, who arrived at Caltech from Cornell in 1938 and had introduced the

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[24] James, (note 6), 261, 278-279; Pauling, "Fifty Years" (note 9), 11. The textbook is Linus Pauling and E. Bright Wilson, Jr., *Introduction to Quantum Mechanics, with Applications to Chemistry* (New York: McGraw-Hill, 1935).

[25] Weinbaum later described his thesis as the first application of quantum mechanics to molecular problems. From oral history interview of Sidney Weinbaum by Mary Terrall, 15, 20, and 25 August 1985, Pasadena, in Mary Terrall, "Sidney Weinbaum: Politics at Mid-Century," *Engineering and Science,* Fall 1991: 30-38, on 33.

[26] See Ted Goertzel and Ben Goertzel, *Linus Pauling: A Life in Science and Politics* (New York: Basic Books, 1995), 95-98, quoting from Pauling's letter to Branson.

[27] For one dimension,

$$f(x) = \sum_{h=0}^{\infty} (A_h \cos 2\pi hx + B_h \sin 2\pi hx)$$

where x = distance of a point in the x direction along a lattice and h = a component of the Miller index h,k,l for the position of a lattice plane. In the 1930s the series were evaluated by use of an adding machine and the Beever-Lipson Strips, which were cardboard strips on which are printed values of $\boldsymbol{A \cos 2\pi hx}$ and $\boldsymbol{B \sin 2\pi hx}$, with $\boldsymbol{A = +/- 1, 2, 3, 4 \ldots 100}$, $\boldsymbol{h = 0, 1, 2, 3, \ldots, 20}$, and $\boldsymbol{x = 0}$ **to** $\boldsymbol{1/4}$, $\boldsymbol{\Delta x = 1/60}$. Each strip represents a sine or cosine function for one value of the wavelength and one value of frequency.

[28] California Institute of Technology Oral History Project. Interview with Verner Schomaker by Shirley K. Cohen. Pasadena, Caltech Archives, 1998. 4 session, 2 Feb, 4 Feb, 8 Feb, 10 Feb 1993: 79 pages, on pp. 33-34.

technique of the method of least squares for handling data in crystallography.[29] Around 1945 International Business Machines Corporation made one of their new automated punched-card machines available to Pauling.[30]

In a 1946 article in the *Journal of Chemical Physics*, co-authored with Schomaker and P. A. Shaffer, Pauling and his collaborators could hardly contain enthusiasm in the article's description of the cards, brushes, roller, synchronized card feed, plugboard, electrical circuit, etc. of the IBM machine. They reported that a structure problem could be solved in "only a few hours, as compared to one or two days with use of an adding machine, and . . . the accuracy of the work is assured."[31]

Hughes remarked later in 1979 on the differences that new machines made for X-ray crystallography in research centers across the globe, first computers and then the automated diffractometer that was invented in 1963. Instead of estimating visually perhaps 5,000 spots on photographic film, a diffractometer could automatically work away night and day measuring and counting photons from crystals. One round of refinement of a structure based in over a hundred observations and eighteen unknowns used to take 24 hours, but after computers it took one minute.[32]

1930 to 1950s: Larger Molecules and Instruments of Biological Chemistry

As is well known, Pauling's interests turned to larger and larger molecules as research funds from the Rockefeller Foundation and other agencies were redirected in the mid-1930s away from physical chemistry toward medically relevant studies of biological molecules. Pauling continued studies of inorganic structures, ionic crystals, minerals, metals, and alloys, with funding from industry and other sources, but his priorities shifted, his collaborations broadened into new fields, and his level of funding increased.[33] In 1946 Pauling submitted a 74-page proposal to the Rockefeller Foundation and to the National Foundation for Infantile Paralysis, co-authored with the Caltech geneticists George W. Beadle and Alfred H. Sturtevant, requesting $6 million to be expended over 15-20 years. The focus of the cooperative research aimed at what they called the great fundamental problems of biology and medicine: the structure and nature of proteins, nucleic acids and other constituents of living matter, the structure of the gene and mechanisms of inheritance, cell division and growth, the molecular and structural basis of the physiological activity of chemical substances, and the structure and properties of antibodies, enzymes, viruses, and bacteria.[34] All this was to be

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[29] In the method of least squares, the best fit to data that overdetermines the system is obtained by minimizing the sum of residuals, where a residual is the difference between an observed value and the fitted value provided by a model.

[30] P.A. Shaffer, Jr., Verner Schomaker, and Linus Pauling, "The Use of Punched Cards in Molecular Structure Determinations. I. Crystal Structure Calculations," *Journal of Chemical Physics*, 14, #11 (November 1946): 648-658, on 647-649. P.A. Shaffer, Jr., Verner Schomaker, and Linus Pauling, "The Use of Punched Cards in Molecular Structure Determinations. II. Electron Diffraction Calculations," *Journal of Chemical Physics*, 14, #1 (November 1946): 659-664.

[31] Schaffer, Schomaker, and Pauling, "Use of Punched Cards. I" (note 30), 658.

[32] Caltech Oral History. Edward W. Hughes. Caltech Archives, 1984. Interview by Graham Berry, Pasadena, 20 November 1979: 35 pp. on pp. 16-17. For the diffractometer, "H. Cole, Y. Okaya, and F. W. Chambers, "Computer-Controlled Diffractometer," *Review of Scientific Instruments*, 34, #8 (August 1963): 872-876.

[33] Caltech Archives, 1.020.4 Meetings, Correspondence, etc. C&CE, 1945-1949. 2-page typescript of meeting of professorial staff of the Division of C&CE, 13 December 1945.

[34] Caltech Archives. 1.020.1. CIT Materials re Div. C&CE 1946-1956. G. W. Beadle, Linus Pauling, and A. H. Sturtevant, "A Proposed Program of Research on the Fundamental Problems of Biology and Medicine by the

accomplished by collaboration of chemical, physical, and biological methodologies in what they called chemical biology.[35]

Biologically significant compounds like urea, oxamide, and oxamic acid were among the compounds that Pauling and his associates investigated in the 1930s from the standpoints 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 Herman Mark's Ludwigshafen laboratory, near Mannheim, in 1930 had familiarized Pauling with Mark's ideas on the structure of proteins, which Mark and Kurt Meyer described in 1932 as large molecules composed of long and flexible polypeptide chains, a history described by Yasu Furukawa in his book on macromolecular science.[36] Pauling himself turned to the structures of proteins in 1932, including hemoglobin and other molecules of medical interest.

In 1934 Pauling borrowed a large water-cooled magnet from the astronomer George Ellery Hale's private laboratory, so that E. Bright Wilson might do an experimental part in his doctoral thesis by investigating the magnetic properties of nitroso-compounds, a problem corresponding to Pauling's interest in the three-electron-bond theory of the triplet normal state of the oxygen molecule.[37] Wanting to better understand the interaction between oxygen molecules and hemoglobin, Pauling directed his postdoctoral fellow Charles Coryell to study the difference in magnetic properties of different hemoglobin derivatives, thus beginning Pauling's laboratory collaborations on proteins and biological chemistry.[38]

Pauling was encouraged by Rockefeller Institute immunologist Karl Landsteiner to think about possible structural relationships between molecules of antibodies and antigens in serological reactions, since antibodies and most antigens are proteins. Pauling arranged for Landsteiner's young colleague Alfred Mirsky to come to Caltech from the Rockefeller Institute. They published a paper in 1936 on the structure and shape of the polypeptide chain in protein, suggesting that the chain is coiled in a specific shape stabilized largely by hydrogen bonds. The next year Robert B. Corey came to Caltech from the Rockefeller Institute and joined Pauling's project.

In 1940 Pauling proposed that polypeptide chains might fold and wind around the exterior of a foreign 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). As Bruno Strasser puts it, Pauling's was an "instructive" theory in which the antigen directs the folding of a peptide chain into a complementary structure.[39] In the long run, this template theory turned out to be wrong, but it inspired a great deal of work by other scientists as they followed up on Pauling's research.

Division of Biology and the Division of Chemistry and Chemical Engineering of the California Institute of Technology. 1946. 74-page typescript, 1-3.

[35] California Institute of Technology Archives, Division of Chemistry. Box 1.Letter, dated October 28, 1945 from G. W. Beadle at Stanford to LP.

[36] Yasu Furukawa, *Inventing Polymer Science: Staudinger, Carothers, and the Emergence of Macromolecular Chemistry* (Philadelphia: University of Pennsylvania Press, 1998).

[37] Pauling, "Fifty Years" (note 9), 11.

[38] Pauling, "Fifty Years" (note 9), 12; Pauling, "Fifty Years of Progress in Structural Chemistry and Molecular Biology," in *Daedalus*, Vol. 99, #4, *The Making of Modern Science: Biographical Studies*, Fall, 1970: 988-1014, p. 1002.

[39] Bruno Strasser, "A World in One Dimension: Linus Pauling, Francis Crick, and the Central Dogma of Molecular Biology," *History and Philosophy of the Life Sciences*, 28 (2006): 491-512, on 497.

The early template theory was given initial experimental support in the work of Harvey Itano, a second-generation Japanese-American who received his medical degree in 1945 from the St. Louis School of Medicine after having been briefly interred along with thousands of other West-Coast Japanese American families in the winter of 1942. After Itano entered Caltech as a graduate student in the fall of 1946 to study for a Ph.D. in chemistry and physics, Pauling directed him to study molecular differences between normal hemoglobin and hemoglobin in the blood of individuals afflicted with sickle-cell anemia. After failing to get results using absorption spectra or magnetic techniques, Itano began studying the hemoglobins using moving boundary electrophoresis, which makes use of the movement of particles through fluid in an electric field.[40]

Electrophoresis was another new technique and kind of instrumentation. The machine had been invented in 1937 by Arne Tiselius in Uppsala and was available in the 1940s only if constructed in a laboratory. Pauling's Rockefeller Foundation money included funds for such construction. Stanley M. Swingle, a general chemistry instructor at Caltech, had an idea for an improved design using mirrors rather than lenses in the optical system (as well as a kinematic mechanical design and a current regulating power supply). He relied on Sturdivant for advice on the mechanical design and on George G. Wright, who was working in the group on antibodies, for cooperation in the initial installation and operation of the apparatus. The instrument makers Alex Logatcheff and William Schuelke made sure that the design worked, and A. L. Wahrhaftig designed the power supply. Swingle and Wahrhaftig were part of the team that worked on punched cards for automated computer diffraction calculations.[41]

Itano and another postdoctoral fellow, Seymour Jonathan Singer, later like Itano an eminent cell biologist at the University of California at San Diego, used the Caltech machine to find that sickle-cell hemoglobin has more positive charge on its surface than does normal hemoglobin. Pauling proposed that this extra charge on the surface led to hemoglobin molecules sticking together, twisting the red blood cells out of shape from flat discs into sickles and clogging small blood vessels in the body. Pauling coined the term "molecular disease" in their co-authored paper, which became Pauling's third most cited paper.[42]

During the war years, Pauling worked at Caltech on military-related projects, and at war's end he continued wartime research on the synthesis of artificial antibodies, working with immunologists Dan Campbell and David Pressmann.[43] Among the members of this research

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[40] Tiselius received the 1948 Nobel Prize in chemistry for his work on the separation of colloids through electrophoresis.

[41] Stanley M. Swingle, "An Electrophoresis Apparatus Using Parabolic Mirrors," *Review of Scientific Instruments*, 18, #2 (1947): 128-132; and Stanley M. Swingle, "Improved Electrophoresis Cell and Cell Holder," *Science*, new series, 105, #2732 (9 May 1947): 501-502.

[42] Russell F. Doolittle, "Harvey A. Itano. 1920-2010," *Biographical Memoirs of the National Academy of Sciences*, 2014: 1-25; Letter from Linus Pauling to Stanley Swingle, 2 March 1948, Correspondence ID corr378.2-lp-swingle-19480302; and Letter from Linus Pauling to Robert B. Corey, 3 March 1948, Correspondence 67.5 LP to Corey, OSU Special Collections.

[43] These included the invention with colleagues of an oxygen meter for monitoring the air in submarines. This instrument made use of the magnetic susceptibility of oxygen and consisted of a small glass dumbbell with attached mirror suspended on a stretched fused-silica fiber in an inhomogeneous magnetic field produced by a small permanent magnet. He arranged its production with Arnold Beckman, who had left teaching chemistry at Caltech to establish a scientific instruments business. Linus Pauling, Reuben E. Wood, and J. H. Sturdivant, "An Instrument for Determining the Partial Pressure of Oxygen in a Gas,"*Journal of the American Chemical Society*, 68 (May 1946): 795-798. Pauling also directed wartime research projects at Caltech on rocket propellants and

group were two undergraduate students, Miyoshi or "Mike" Ikawa and Carol Kazuo Ikeda, who prepared compounds used in the experiments. Pauling was determined to help the two Nisei students avoid internment in 1942, following their Caltech graduation in 1941. In this, Pauling succeeded. Ikawa, known by his undergraduate classmates for his phenomenal grades, early bedtime hours, and membership in the Fleming House wrestling team, entered the University of Wisconsin graduate program, where he became a co-discoverer with his mentor Karl Paul Link of warfarin, or Coumadin, before eventually joining the biochemistry department at the University of New Hampshire.[44] Ikeda became one of 104 Nisei students enrolled at the University of Nebraska between 1942 and 1945, where he finished his doctorate and became a research chemist for Dupont Chemicals.[45]

1950s: Proteins, DNA, and Technologies of Molecular Models

Pauling's government and Rockefeller Foundation-sponsored research during the war years kept him focused on hemoglobin, immunology, and proteins along with other projects. A striking characteristic in Pauling's work in these years was his straddling two different communities of molecular researchers, one relying on immunological and biochemical techniques and another applying physical methods to the study of large molecules of biological interest.[46] Protein research had become an expanding research area by the 1930s, with British X-ray crystallographers such as J. D. Bernal, Dorothy Hodgkin, and William Astbury among its pioneers.

While visiting Oxford in 1948, where he cemented a friendship with Hodgkin, Pauling started building protein models by using paper, ruler, and pencil. After his return to Caltech, his collaboration with Corey and visiting physicist Herman Branson resulted in the single-coiled alpha-helix model, which broke with the usual assumption that the helix should have an integral number of residues per turn. Pauling also demonstrated the triple helix structure of collagen, in which two identical chains entwine with an additional chain that differs slightly in its chemical composition. As has often been recounted, the triple helix made an unfortunate reappearance in Pauling and Corey's proposed structure for deoxyribonucleic acid (DNA), the molecule that some biologists were beginning to think played a major role in genetics. James Watson and Francis Crick's double helix structure, published in spring 1953, from Lawrence Bragg's Cavendish Laboratory, instead won the day, relying on Rosalind Franklin's photographs of hydrated DNA and on chemical insights and model-building techniques gleaned from Pauling's own work.

This DNA research brings to the fore one of Pauling's most powerful instruments in chemical research: the material model of the chemical molecule. Pauling's method of modeling

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explosives powders, and he headed a team for the synthesis of artificial plasmas that enlisted the expertise of the immunology expert Dan Campbell.

[44] See "The 'T'", California Institute of Technology Yearbook, 1941, pp. 33 and 34. Online: http://caltechcampuspubs.library.caltech.edu/2260/1/1941.pdf (accessed 23 January 2015); and "Ikawa, One of Inventors of Warfarin, Dies at 87," *The Capital Times* (Madison, Wisconsin), 27 May 2006, Metro Section, p. B3.

[45] Obituaries, *Caltech News*, 30, #1 (Winter 1996), p. 18. Online: http://caltechcampuspubs.library.caltech.edu/2120/1/1996_30_1.pdf (accessed 23 January 2015).

Also, "Nisei Collection at the University of Nebraska." Online: http://unlhistory.unl.edu/exhibits/show/nisei/nisei-experience-at-unl/list-of-nisei-students (accessed 23 January 2015).

[46] On the two communities, see Angela N. H. Creager and Gregory J. Morgan, "After the Double Helix: Rosalind Franklin's Research on Tobacco Mosaic Virus," *Isis*, 99, #2 (June 2008): 239-272, on 262-262.

structures employed not only paper and pencil, but also wooden and then plastic models including new and precise “space-filling” models. These models transformed chemical research and education in the late twentieth century.

Space-filling models first were designed in Germany by H. A. Stuart in 1934, and they began to be marketed in 1939 by the Fisher Scientific Company using a redesign by University of Wisconsin chemist Joseph Hirschfelder. Pauling found these commercial models inexact for his purposes. Instead, he directed the Caltech instrument shop, managed by Sturdivant, to make two types of model kits that Corey and Pauling described in an article in 1953 in *The Review of Scientific Instruments*.

One set was made of hard wood to the scale 1 inch = 1 Angstrom, with dimensions tied to experimental Van der Waals radii, bond radii, and bond angles. Atoms, such as carbon, hydrogen, oxygen, and nitrogen, were joined together by means of short pieces of 5/16 inch steel rod, which fit into steel bushings imbedded in the atoms. The bushings were locked on the rod in any desired position for fixing the relative orientation of atoms around a bond. Different valences for a single atom were modeled into different atom spheres, and the dimensions for the bonding of N-H with O for amino acids and peptides were incorporated into a model of the hydrogen-bonding atom. Data from X-ray crystallography, electron diffraction, and quantum mechanical mathematical modeling refined measurements and structures. This kind of model was intended to study probable molecular configuration, including steric hindrance, and intermolecular packing, and the models could be substituted for mathematical calculation.[47] In contrast, the second kind of model had parts cast on a smaller scale from colored, rubber-like vinyl plastic with easy alteration of molecular configuration. Hydrogen bonds were simulated by embedding magnets in the hydrogen and oxygen atoms. Corey and Pauling cautioned that these smaller-scale models were useful for qualitative studies only and could not be substituted for large-scale models in quantitatively precise work.[48]

Technicians at Caltech continued to make space-filling models in the laboratory shop through the 1950s. Caltech provided selected scientists elsewhere with blueprints, conforming to designs from visual drawings by Roger Hayward and data provided by Pauling, Verner Schomaker and Sturdivant.[49] Barbara Low, a former student of Dorothy Hodgkin’s and visitor at Caltech who joined the physical chemistry laboratory at Harvard, bought a kit in 1951 for $880. In the spring of 1959, Alexander Rich, a former Pauling protégé now at MIT, learned that his order would likely be the last one to be supplied to outside institutions.[50] By

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[47] Robert B. Corey and Linus Pauling, “Molecular Models of Amino Acids, Peptides, and Proteins,” *The Review of Scientific Instruments*, 24, #8 (August 1953): 621-627.

[48] Ina Heuman, “Linus Pauling, Roger Hayward und der Wert von Sichtbarmachungen,” *Berichte zur Wissenschaftsgeschichte*, 32 (2013): 313-333, on Hayward. Richard Marsh, “Robert Brainard Corey. 1897-1971. A Biographical Memoir,” *Biographical Memoirs. National Academy of Sciences* (Washington DC: National Academies Press, 1997): 49-68, on 62.

[49] Eric Francoeur, “The Forgotten Tool: The Design and Use of Molecular Models,” *Social Studies of Science*, 27, No. 1 (Feb., 1997): 7-40, on 23-24; and Jeremiah James, “Modeling the Scale of Atoms and Bonds: The Origins of Space-Filling Parameters,” in *Objects of Chemical Inquiry*, eds. Ursula Klein and Carsten Reinhardt (Sagamore Beach, MA: Science History Publications, 2014): 281-320, esp. 308-310. See Ewart Thomas, “Molecules Tailored to Order,” *Popular Mechanics*, Aparil 1952: 149-153, 250, 254.

[50] The kit included 100 carbon (tetrahedral), 25 carbon (ethylene double bond), 25 carbon (carboxyl), 200 hydrogen, 30 hydrogen (H-bond), 70 oxygen (single bond), 30 oxygen (double bond), 30 nitrogen (trigonal), 12 nitrogen (tetrahedral), 12 phosphorus (tetrahedral), 8 purine nucleus, 6 pyrimidine nucleus, 10 benzene rings, 30 peptide amide group (planar OCN), 12 sulfur, 20 nitrogen radius adapters, 500 stud connectors, 50 orienting pins. Labor $510, Material (150), Overhead (220). Cal Tech Archives. The Papers of Robert Brainard Corey.

the 1960s, commercially available kits made their way into laboratories and classrooms following a five-year development program that involved Caltech and other scientists, federal agencies, and scientific societies.[51]

Conclusion

Pauling received the Nobel Prize in Chemistry in 1954. Following his trip to Stockholm, he and Ava Helen Pauling visited Israel, India, Thailand, and Japan, arriving in Japan in February 1955. They were appalled to learn that the crew of the *Lucky Dragon* still was under observation following the US explosion of thermonuclear devices over Bikini Atoll the previous spring. Pauling entered a long-running scientific debate over the biological effects of chronic, low-level radiation from atmospheric nuclear tests, and he organized scientists worldwide to press for a ban on atmospheric nuclear testing. After criticism by colleagues of his (1962) Nobel Peace Award in 1963, he resigned from Caltech and founded his own research institution in 1974 after appointments at the University of California at Santa Barbara and at San Diego, and then at Stanford University. His collaborations continued, although with fewer numbers of publications and fewer coworkers, in researches on the evolutionary molecular clock and on the health effects of Vitamin C.[52]

During his Caltech period from 1922 to 1963, Pauling published a total of 370 scientific publications. He had 106 different co-authors on 175 co-authored papers, and 23 individuals

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1.11. Carbon copies of Letter from Corey to Dr. Barbara Low at Laboratory of Physical Chemistry, Harvard, 19 November 1951; carbon copy of Letter from G. A. Green, Caltech Vice-President for Business Affairs to Professor Herbert Jehle, Physics Department, University of Nebraska, 10 January 1958 , with cc to Corey; carbon copy of letter from Corey to Dr. Alexander Rich, Dept. Biology, MIT, 1 May 1959. Jack Dunitz, a former collaborator of both Pauling's and Hodgkin's, wrote Corey in late 1958 from the ETH in Zurich that none of the commercially-available atomic models were as good as the ones from Caltech. Letter to Corey from Jack Dunitz at Laboratorium für organische Chemie, Eidg. Technische Hochschule, Zurich, 17 November 1958.

[51] Caltech Archives. The Papers of Robert Brainard Corey. 1.11. Correspondence between Walter L. Koltun, Program Director, Molecular Biology Section, NSF and Robert Corey at Caltech, 11 March 1965, 16 March 1965, for the naming of the Koltun-Corey-Pauling models in a recommendation by Koltun, 9 March 1965, to Robert A. Harte at the American Society of Biological Chemists, etc., chair of the Atomic Models Committee meeting in San Francisco. Also see Francoeur (note 49), and Mary Jo Nye, "Paper Tools and Molecular Architecture in the Chemistry of Linus Pauling,"in *Tools and Modes of Representation in the Laboratory Sciences*, ed. Ursula Klein, *Boston Studies in the Philosophy of Science* (Dordrecht: Kluwer, 2001): 117-132.

[52] One of Pauling's collaborators at the Linus Pauling Institute was Roy Teranishi, a Japanese-American researcher, who was already well known in the field of food and flavor chemistry and worked with the USDA in the Bay area. The Japanese-American researcher, Koichi Miyashita, later assisted with metabolic and Vitamin C studies in the 1970s. For example, Linus Pauling, Arthur B. Robinson, Roy Teranishi, and Paul Cary, "Quantitative Analysis of Urine Vapor and Breath by Gas-Liquid Partition Chromatography," *Proceedings of the National Academy of Sciences*, 68, #10 (October 1971): s2374-2376; "Dedication to Dr. Roy Teranishi, 1922-2000," *Journal of Agricultural and Food Chemistry*, 49, #2 (February 2001): 535. On Miyashita, letter from Stephen Lawson to Mary Jo Nye, 13 October 2014. The Vitamin C research received a great deal of public and professional attention, including interest in Pauling's research from several Japanese researchers with whom Pauling talked or corresponded. One coauthored paper appeared in 1983 with Fukumi Morishige: "Eiji Kimoto, Hidehiko Tanaka, Junichiro Gyotoku, Fukumi Morishige, and Linus Pauling, "Enhancement of Antitumor Activity of Ascorbate against Ehrlich Ascites Tmuor Cells by the Copper:Glycylglycylhistidine Complex," *Cancer Research*, 43 (February 1983): 828-828. Akira Murata of Saga University visited the Pauling Institute during 1977-1978 while collaborating on vitamin C and immunology with George Feigen at Stanford. Morishige did clinical trials at Fukuoka Torikai Hospital. Naoyuki Ohtsu, one of their colleagues, spent time briefly at the Pauling Institute in the early 1980s, according to Stephen Lawson, in letter to Mary Jo Nye, 13 October 2014.

co-authored three or more publications with Pauling.[53] Many hundreds of chemists in diverse specialties, and especially in physical techniques and modeling applied to structural chemistry, learned or extended their expertise under his leadership at Caltech. Pauling's success, like that of so many eminent leaders of large laboratories in twentieth-century chemical sciences, was based in skills of consummate "craftsmanship" achieved at an early age and in skills at a later stage in his career that Hackett calls "articulation." Pauling's research precipitated and reflected achievements and transformations in chemical sciences of the twentieth century. To this work, Pauling consistently applied the vocabulary of "discovery" and "progress" as well as "puzzle" and "surprise" when he described transformations in twentieth-century chemistry. He did not use the more radical language of "revolution."[54]

Pauling had his faults, to be sure. His open-mindedness did not always extend to chemical theories that he viewed as contrary to his own way of seeing things. His resistance to molecular orbital theory is one case in point. He was highly competitive, protective of his personal claims to discovery, and sometimes ungenerous in giving credit to coworkers. In conclusion, however, I want to emphasize that it was not possible for one person, no matter how intelligent and creative, no matter how hard-working and disciplined, to achieve the range of results associated with Pauling's name. His discoveries and innovations may appear at first glance to be the achievement of a single individual, relying of course on other chemists' work with which he became familiar, but his accomplishments were collaborative and collective. This fact is the result of a very real transformation in laboratory organization and allocation of expertise. Pauling is exemplary of the eminent chemist whose career made use of the skills both of craftsmanship and articulation, while demonstrating ingenious creativity, mastery of current chemical knowledge, and a passion for leadership in the vanguard of chemical practices.

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[53] Pauling's most frequent co-authors were Robert B. Corey (33 papers on the structure of proteins and nucleic acids in the 1950s), David Pressmann and Dan H. Campbell (18 and 10 papers mostly on serology and antibodies in the 1940s), Lawrence O. Brockway (10 papers on electron-diffraction studies of structure in the 1930s), Jacob (Jack) Henry Sherman (7 papers on quantum mechanics and chemical structure in the 1930s) and Richard (Dick) Marsh (7 papers on chemical structure). For a complete list of Linus Pauling's papers, see Chris Petersen and Cliff Mead, eds. *The Pauling Catalogue*, 6 volumes (Corvallis: Oregon State University Valley Library Special Collections, 2006), Volume 1, 106-152.

[54] For example, see Pauling, "Fifty Years of Progress" (note 38); Linus Pauling, "Chemical Achievement and Hope for the Future," *American Scientist*, 36, #1 (1948): 50-58; or Pauling and Wilson, *Introduction to Quantum Mechanics* (note 24), where "discovery" appears (n35, n44, n59, n217, n323, n399), but where there are no claims of radical transformation or revolution.