Walter Kauzmann

1916–2009

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by
D. S. McClure

NATIONAL ACADEMY OF SCIENCES

WALTER **KAUZMANN**

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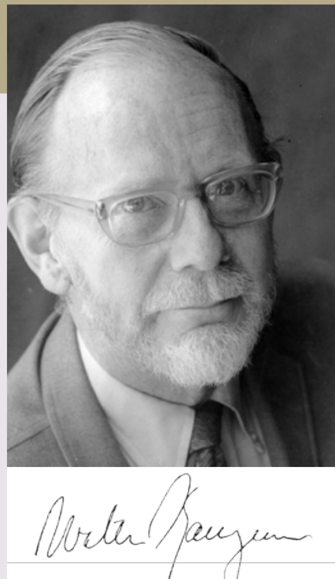

Photo Courtesy of Princeton University Office of Communications.

By D. S. McClure

Walter Kauzmann was a modest person of significant and enduring accomplishments as a teacher, scientist, administrator, and family man. He was born in Mt. Vernon, NY, and raised in New Rochelle, NY, two towns near enough to New York City that his father could on weekends show him the wonders of that major metropolis. There he learned to appreciate symphonic music and opera, which sparked a lifelong interest in music. He was given a chemistry set and a microscope in his early teens and was favored with an outstanding physics teacher in high school—circumstances that turned his interests toward science. His outstanding high-school record brought him a full scholarship to Cornell University which he entered in the fall of 1933.

Fateful encounters

In his autobiographical memoir [Reminiscences from a life in protein physical chemistry. *Protein Science* (1993), 2:671-691], Walter used up four pages out of 21 on the unfortunate influence of Wilder Bancroft on physical chemistry. Walter pointed out that while organic and inorganic chemistry were well taught at Cornell, physical chemistry was a disaster. Bancroft was editor of the *Journal of Physical Chemistry* but tried to keep out papers using mathematics, physics, and quantum theory. Cornell's physical chemistry course was similarly weakened. Still, there was a great course in thermodynamics at Cornell, given by John Kirkwood at the beginning of his career, but it was too advanced for Walter. Out of this confusion came Walter's decision to major in organic chemistry.

While browsing through current journals in the library, Walter came across the *Journal of Chemical Physics*; and the name of Henry Eyring, from Princeton, kept showing up with intriguing titles. Thinking that even if he were to be an organic chemist it would be good to be in a place where such a lively intellect resided, Walter applied to Princeton for graduate work.

He was accepted, and entered Princeton in 1937, but after a few months of trying to be an organic chemist in Eugene Pacsu's lab, he realized that he didn't belong there. Department head Hugh Taylor talked with Walter and convinced him to instead be a physical chemist and, further, to work with Henry Eyring, who was interested in optical rotation at this time (among many other things). Walter was surprised and delighted; maybe this is what he had hoped for all along.

Meanwhile, Edward U. Condon had finished the *Theory of Atomic Spectra*[1] and was also interested in optical rotation. By 1937, Condon had published a review of the theory of circular dichroism (CD) and, with William Altar and Eyring, a paper on fitting the theory to an actual molecule. Thus Walter met Condon as well as Eyring, two people who he elevated to the status of his local "gods."

The hard part of using CD was interpreting the measurements in terms of molecular conformation. This was a part of Walter's thesis project, and a big job, as each asymmetric molecule had to be examined to see what its parts may contribute to quenching or enhancing the CD signal. His thesis work was published in the *Journal of Chemical Physics* in January 1941. But he continued to keep the problem in mind and, with graduate students F. B. Clough and I. Tobias, published a long and detailed paper (1961) on an empirical method for finding the molecular conformation. This story may now be ending with the increasingly accurate density functional theory for molecular structures.[2]

Returning to the source

Walter received his PhD from Princeton University in June 1940. At about the same time, Condon left Princeton to set up a basic research unit at the Westinghouse Corp. in Pittsburgh. To attract good people, he established 10 two-year postdoctoral fellowships whose recipients were promised that they could do whatever research most interested them. Walter could not resist a promise like that from Condon, and he spent two productive years at Westinghouse. Ideas derived from work at Westinghouse led to one of his most influential papers, "The nature of the glassy state and the behavior of liquids at low temperatures," published in 1948. More on this later.

After his fellowship's two years were over (in August 1942), Walter moved to a war research laboratory in Bruceton, PA, a few miles south of Pittsburgh, where he was assigned to work on explosives. George Kistiakowsky headed this lab and Louis Hammett, Frank Long, and Rufus Lumry were there as well. Walter enjoyed having these brilliant scientists as colleagues, but he was adversely affected by Pittsburgh's air and longed to get away. So after a year and a half (in February 1944), he left for Los Alamos, NM, and the Manhattan Project. There he used his recently acquired knowledge of explosives on the design of triggers for atomic bombs. His health also improved in the clean Los Alamos air, and he found the intellectual climate stimulating as well.

> At the end of January 1946, Walter left Los Alamos and drove to Colorado to a cabin in the mountains about 50 miles from Boulder. There he could study and play his flute and once a week drive to Boulder to buy groceries and borrow books from the library of the University of Colorado. His goal was to understand the molecular basis of muscular contraction.

Three atomic bombs were detonated in the summer of 1945 (the Trinity test in New Mexico and the two dropped on Hiroshima and Nagasaki), bringing the Japanese surrender and the knowledge that the ultimate weapon could be made. Walter received a commendation for his efforts on "military explosives."

About his work at Los Alamos, Walter was generally close-mouthed, but he did later relate two experiences to his students. One involved his being reprimanded by J. Robert Oppenheimer—for possibly delaying progress on the bomb—when he organized a cross-country skiing expedition during which someone broke a leg. The other regarded Walter and others, having not been invited to the Trinity test in July 1945, taking a camping trip to the mountains some 20 miles away from the test site. Walter rose predawn on the morning of the test, hoping he might see the result from that distance. But after a while he tired of staring in the direction of the test site; he stood up and was walking in the opposite direction when suddenly a tremendous flash illuminated the sky.

At the end of January 1946, Walter left Los Alamos and drove to Colorado to a cabin in the mountains about 35 miles from Boulder. There he could study and play his flute and once a week drive to Boulder to buy groceries and borrow books from the library of the University of Colorado. His goal was to understand the molecular basis of muscular contraction.

This idyllic period ended one day in June when Hugh Taylor managed, with some difficulty, to locate Walter in his cabin and offered him a job on the Princeton faculty. A vacancy had been created when Henry Eyring decided to leave the university and return to Utah and his Mormon roots. Of course, Walter accepted. It was a lucky day for him and for Princeton.

Walter Kauzmann as a Princeton professor

Walter was well prepared for this position both by nature and his educational background. He had a reputation for "knowing everything." He read widely on many subjects, often at times when most people were asleep. He enjoyed teaching in the classroom or informally at the blackboard. Students in his freshman chemistry class one year were treated to a lecture on paper making because he was curious about it and had made a trip to a paper mill in Georgia to educate himself.

Throughout his career to this point, there had been discussions about proteins: What is their molecular structure? How do they interact with the solvent water? How do they change shape with shifts in temperature? How do they function in living matter? During Walter's graduate-school days, Taylor made sure that people in this field were invited to give seminars at Princeton. Now, as an assistant professor, Walter had a chance to apply physical chemistry to proteins in his own way. Graduate students were attracted to his research group, which amounted to 10 to 12 students or postdocs, who he kept busy.

> As a triumph in abstract thinking, Kauzmann's inferences outshone even those of Pauling, whose ideas were based on X-ray-derived structures of small segments of proteins. Walter's ideas emerged not from structures but from his analysis of the thermodynamics of solutions.

Protein molecules are at once simple and extraordinarily complex. They are strings of alpha amino acids. But only 20 of them (out of hundreds) are used in living matter. Thus the first member of the polymer chain could be any one of the 20 amino acids, and so could the second, third, and so on, so that a chain of medium length—say, 300 units—could have 20^{300} possibilities, a figure far greater than the number of atoms in the sun. Actually there are only thousands of known protein molecules, a simplification that results from evolution by natural selection. Still, enormous complexity remains, and Walter and his students took on the task of finding order there.

The remainder of this section was contributed by David Eisenberg.

The two great thinkers about protein science in the 20th century were Linus Pauling and Walter Kauzmann. Pauling in the early1950s pointed out the importance of hydrogen bonds in stabilizing the structural elements of proteins. However great, his work told little about the overall organization of these complex protein structures. A larger-scale understanding rested on the ideas of Kauzmann in the late 1950s. With phenomenal insight and brilliant reasoning, Walter argued that charged and polar amino acids would tend to decorate the surfaces of proteins, with their apolar residues clustered in the interior. He called this effect “the hydrophobic bond.”

As a triumph in abstract thinking, Kauzmann’s inferences outshone even those of Pauling, whose ideas were based on X-ray-derived structures of small segments of proteins. Walter’s ideas emerged not from structures but from his analysis of the thermodynamics of solutions. His understanding of thermodynamics was profound, as was his ability to reason on the right track. His general predictions about the structures of proteins were outlined in a long *Advances in Protein Chemistry* review article in 1959—a year before the first protein structures were known.

After the first protein structures were revealed by John Kendrew and Max Perutz in Cambridge, England, they praised Walter’s insights. In 1965 these Nobelists wrote: “The most striking feature common to all globin chains is the almost complete exclusion of polar residues from interior sites. This is a remarkable vindication of the predictions of Kauzmann in 1959.”

Perhaps even more remarkable than Walter’s talent for research was his apparent first priority of teaching. He was invariably modest about his discovery of the hydrophobic bond, claiming that the “idea was in the air.” He showed no trace of some scientists’ tendency to concern themselves with credit and rank. Instead, his pleasure seemed to come in large part from passing on the tools of physical chemistry to new generations of scientists. Lucky were the students in Walter’s classroom and laboratory. From their exposure to him, they came away with a sense of the joy of making discoveries, and also with the confidence that they themselves could make discoveries.

Walter Kauzmann’s research program

There are three areas of chemistry to which Walter made major contributions: protein folding and the hydrophobic factor; the theory and applications of circular dichroism; and the nature of the glassy state and the behavior of liquids at low temperatures.

In the first, he introduced the idea of the hydrophobic effect. His 1959 article on the subject—“Some factors in the interpretation of protein denaturation” (in *Advances in Protein Chemistry*)—was among the most cited papers from 1961 to 1975, according to the Science Citation Index.

The second area, the uses of circular dichroism, was a part of Walter's doctoral thesis, and it was revived in a 1961 paper with F. B. Clough and I. Tobias, "The principle of pairwise interaction as a basis for an empirical theory of optical rotatory power," in *Tetrahedron*.

The last of these areas arose from his work at Westinghouse and led to a paper "The nature of the glassy state and the behavior of liquids at low temperatures," published by *Chemical Reviews* in 1948. In this encyclopedic but also profound paper, Walter showed that the data for the entropy of a supercooled liquid, when extrapolated to a temperature of absolute zero, indicate a conversion to glass with an entropy substantially lower than that of the stable crystal phase. This putative violation of the third law of thermodynamics came to be called the "Kauzmann paradox."

The paper also received special notice. E. U. Condon, having gone to Corning Glass, corresponded with Walter and asked for a reprint. In 1992, R. W. Cahn wrote: "It is rare indeed for a scientific paper to remain central to current concerns several decades after publication." And in 1997 a related symposium "Glasses: Paradoxes, Properties, and Applications" honored Walter.

The ideas expressed or implied in these three monumental works were correct, and they stimulated further studies. In addition, many publications resulted from collaborations with students. And Walter found the time to write three textbooks and a book on the properties of water with coauthor David Eisenberg.

Walter's time off

In late 1950, Walter met Elizabeth Flagler, who was assisting in the laboratory of Frank Johnson in Princeton's biology department. Sixteen days later they were engaged, and they married on April 1, 1951. Their three children were Peter (1953), Eric (1955), and Lise (1957).

Walter had wonderful "time off" periods during which he hiked in the Rocky Mountains or the Swiss Alps, but with wife and children a scaled-down vacation was necessary. During an automobile camping trip in New England and maritime Canada in 1959, they came upon some abandoned property on the northern tip of Cape Breton Island. It had a beautiful beach, many acres of land, and a decaying old house. They bought the property and fixed the old house, which was their summer home from then on. Later they built another house to accomodate the increasing number of grandchildren. Much of Walter's book writing was done in a small shack near the main house. He would wake up at 5 a.m.

and, while watching the sunrise and noting the number of herons feeding in the shallows of the harbor just outside the window, would write until the family began breakfast.

The surroundings at Cape Breton also inspired other creative activities. There was an abundant bed of clay, which brought on pottery making; there were cattails, which could be converted into papyrus; the availability of boulders of the right size, and the large acreage of land, suggested the building of a medieval trebuchet (a machine for hurling large stones); and there were forests and hills for hiking. One memorable hike is described here in the sidebar, "An unplanned overnight on a Cape Breton cliff."

Walter made good use of sabbatical leaves. Because the work of the Carlsberg Laboratory in Copenhagen on proteins was outstanding, he made two visits there (in 1949 and 1957). In 1974 to 1975 he made a trip around the world, stopping in Japan, India, Nigeria, and Europe, accompanied by his wife and daughter.

Well known and respected in the world of science, Walter carried on correspondence with leading scientists, usually replying to letters within two weeks. (This was not the e-mail age.) When Bruce Alberts moved from Princeton to the University of California, San Francisco, he told Walter in a letter: "I learned more from you than in all my graduate courses."

Further evidence of the high regard and affection his colleagues had for Walter was a festschrift: a special issue of Biophysical Chemistry (later published as a book.) The issue opens with an excellent short biography of Walter written by his last graduate student, Arthur Henn, and contains numerous writings in his honor.[3]

Another excellent biographical memoir was written by John Schellman, one of Walter's first graduate students.[4]

Walter's was a life well lived. He used his 92 years productively and happily to the great benefit of his family, friends, students, and colleagues.

ACKNOWLEDGEMENTS

Walter Kauzmann's daughter and sons—Lise, Peter, and Eric—made important corrections and additions. David Eisenberg gave us a wonderful assessment of Walter's intellect and modesty. Members of the Princeton faculty also helped: Kurt Mislow, E. C.Taylor, Michael Hecht, Zoltan Soos, Herschel Rabitz, Jeffrey Schwartz, C. E. Schutt, Jannette Carey, and Salvatore Torquato of the chemistry department; and some members of the geology and biochemistry departments.

An unplanned overnight on a Cape Breton cliff

By Ted McClure

In late August of 1970, the five McClures drove to Cape Breton Island to visit the Kauzmann family at their summer home. During our visit, Walter proposed a day hike for both families along the coast, northward from Neil's Harbor to White Point.

Walter had already spoken to some local residents about the route and he had been told very definitely that the way was impassible. I am sure the possibility of achieving a "first" only fired Walter's interest, and it did not deter the rest of us. The McClure family had just come from several days of camping and hiking at Mt. Katahdin in Maine. Another year, the whole family had been camping and hiking in the High Sierras in California. A hike along the shore seemed mild by comparison.

Lunchtime found us still on the rocks, having made good progress toward our goal. After our lunch break, we came upon vertical cliffs plunging directly to the water. We turned uphill into dense woods to find our way along the tops of the cliffs. Walter, in the lead, began hacking his way through the branches with his machete. Don McClure remembered that the machete was a birthday present from Walter's wife Liz. The rest of us would stop and wait until we could move forward a few steps, then stop again while Walter chopped some more. I marveled at how he could do so much work.

The daylight gradually faded into twilight with no sign of an end to the dense woods. There were no flashlights among us. The two men, Walter and Don, agreed that it would be best to choose a place to spend the night while we could still see. The women, Laura Lee and Liz, were horrified at the thought of an unplanned bivouac, and they insisted that we press on in hopes of getting out of the woods. We shared one orange and a little chocolate—the only remains of lunch—and the women prevailed for a time. As twilight faded into pitch black, we formed a human chain and felt our way forward with our feet.

After some more slow progress, we heard waves crashing against rocks quite close below us. We had seen in the daylight that there were occasional inlets in the cliff. We had had to turn away from the ocean to go around at least one of these. It was apparent that, in the dark, we risked walking over the edge of one of these inlets and plunging down the cliff. It was time to stop where we were. Walter found a small clearing, just a few steps away from us, with a large flat rock that was perfect for building a large bonfire, and there was space on two sides of the rock where we could lie down. Also, Walter had brought matches.

The first light of dawn found us damp and tired from too little sleep. Walter resumed his work with the machete, and in about half an hour we were out of the woods. In the grassy margin on top of the cliff, we found wild blueberries and we all ate them eagerly. A little more walking and we were back to the car. We went to a local shop where they served us a pancake brunch.

Some of us gathered all of the downed wood we could lay our hands on and piled it near the rock. A large fire was lit and everyone huddled close to it for warmth, while remaining wary of a possible burning log rolling off the rock. My brother Kevin, the youngest of the party, was given a place close to the fire. He remembers having "the annoying/amusing experience of roasting on one side of your body and feeling bone cold on the opposite side!" My sister Kathy remembers that the Kauzmanns' dog helped keep some people warm.

Walter, Don, and I stayed awake all night feeding the fire. At one point, a burning log did roll off the fire and landed right next to Kevin as he slept on the ground. Those closest to him acted quickly to kick it away and he was unharmed.

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I recall Walter remarking on our adventure to the effect that "It's good to have such an experience at least once. You find out it's possible to live through something you didn't know you could live through." I wish I could recall his exact words. But I agree with his viewpoint—as long as someone remembers to bring matches!

HONORS AND AWARDS

Guggenheim Fellow (1957, 1974-1975)

American Academy of Arts & Sciences (1963)

National Academy of Sciences (1964)

Linderstrom-Lang Gold Medal (1966)

Ph.D. (honorary), University of Stockholm (1992)

Stein-Moore Award, Protein Society (1993)

William Pyle Philips Lecturer, Haverford College (1998)

ADDITIONAL NOTE

(in Walter's Words, March 1998):

Ph.D thesis at Princeton with Henry Eyring, who had a strong influence on my entire career. During the six years (1940-1946) when away from Princeton I had valuable interactions with E. U. Condon (at Westinghouse), Louis P. Hammett (at Bruceton) and George Kistiakowsky (at Los Alamos). Later Kai Linderstrøm-Lang (at the Carlsberg Laboratory in Copenhagen) made important impressions in many ways. I should also like to acknowledge an intellectual debt to the late Dr. Charles Masson (National Research Council of Canada, Halifax), who introduced me to the field of molten oxides.

NOTES

1. Condon, E. U., and G. H. Shortly. 1935. *Theory of Atomic Spectra*. New York: Macmillan.
2. See, for example, McCann, D. M., and P. J. Stephens. 2006. *J. Org. Chem.* 71:6074-6098.
3. Henn, A. R. (ed.). 2003. Special Issue in Honour of Walter J. Kauzmann. *Biophysical Chemistry* 105:153-755. Amsterdam: Elsevier.
4. Schellman, John. In memoriam: Walter Kauzmann. 2010. *Protein Science* 19(3): 363-371.

SELECTED BIBLIOGRAPHY

1941 With H. Eyring. The effect of rotation of groups about bonds on optical rotatory power. *J. Chem. Phys.* 9:41-53.

1948 The nature of the glassy state and the behavior of liquids at low temperatures. *Chem. Rev.* 43:219-256.

1952 With R. B. Simpson. The kinetics of protein denaturation I. The behavior of the optical rotation of ovalbumin in urea solutions. *J. Am. Chem. Soc.* 75:5139-5152.

With R. B. Simpson. The kinetics of protein denaturation ll. The optical rotation of ovalbumin in solutions of guanidinium salts. *J. Am. Chem. Soc.* 75:5152-5154.

With R. B. Simpson. The kinetics of protein denaturation Ill. The optical rotations of serum albumin, b-lactoglobulin, and pepsin in urea solutions. *J. Am. Chem. Soc.* 75: 5154-5157.

With H. K. Frensdorff and M. T. Watson. The kinetics of protein denaturation IV. The viscosity and gelation of urea solutions of ovalbumin. *J. Am. Chem. Soc.* 75:5157-5166.

With H. K. Frensdorff and M. T. Watson. The kinetics of protein denaturation V. The viscosity of urea solutions of serum albumin. *J. Am. Chem. Soc.* 75:5167-5172.

1957 *Quantum Chemistry*. New York: Academic Press.

1959 Some factors in the interpretation of protein denaturation. *Adv. Protein Chem.* 14:1-63.

1961 With O. Sovers. *d*-hybridization of the pi bond in the $2\rho\pi_u$ state of H^+_2. *J. Chem. Phys.* 35:652-655.

With F. B. Clough and I. Tobias. The principle of pairwise interactions as a basis for an empirical theory of optical rotatory power. *Tetrahedron* 13:57-105.

1962 With J. Rasper. Volume changes in protein reactions I. Ionization reactions of proteins. *J. Am. Chem. Soc.* 84:1771-1777.

With A. Bodanszky and J. Rasper. Volume changes in protein reactions. II. Comparison of ionization reactions in proteins and small molecules. *J. Am. Chem. Soc.* 84:1777-1788.

With J. P. Simko. The kinetics of the urea denaturation of hemoglobin I. Beef oxyhemoglobin. *Biochem.* 1:1005-1017.

1966 *Thermal Properties Of Matter I. Kinetic Theory Of Gases.* New York: W. A. Benjamin, Inc.

1967 *Thermal Properties Of Matter II.. Thermodynamics and Statistics With Applications To Gases*. New York: W. A. Benjamin, Inc.

1968 With J. J. Kozak and W. S. Knight. Solute-solute interactions in aqueous solutions. *J. Chem. Phys.* 48:675-690.

1969 With David Eisenberg. *The Structure and Properties of Water*. Oxford, UK: Oxford University Press.

1973 With A. Zipp. Pressure denaturation of metmyoglobin. *Biochem.* 12:4217-4228.

With A. Zipp. Anomalous effect of pressure on spectral solvent shifts in water and perfluoro n-hexane. *J. Chem. Phys.* 59:4215-4224.

1974 With I. D. Kuntz, Jr. Hydration of proteins and polypeptides. *Adv. Protein Chem.* 28:239-345.

With K. Moore and D. Schultz. Protein densities from x-ray crystallographic coordinates. *Nature* 248:447-449.

1976 Pressure effects on water and the validity of theories of water behavior. *Colloq. Int. C.N.R.S.* 246:63-71.

1980 With K. Kim. Concentration dependence of the specific volumes of human oxyhemoglobin, bovine serum albumin, and ovalbumin solutions. *J. Phys. Chem.* 84:163-165.

1989 With A. Henn. Equation of state of a random network, continuum model of liquid water. *J. Phys. Chem.* 93:3770-3783.

1993 The Kauzmann paradox: A thermodynamic quandary. *Current Contents* 44:8.
Reminiscences from a life in protein physical chemistry. *Protein Sci.* 2:671-691.