BIOGRAPHICAL MEMOIRS

Paul Delos Boyer

July 31, 1918–June 2, 2018
Elected to the NAS, 1970

A Biographical Memoir by Steven G. Clarke and David S. Eisenberg

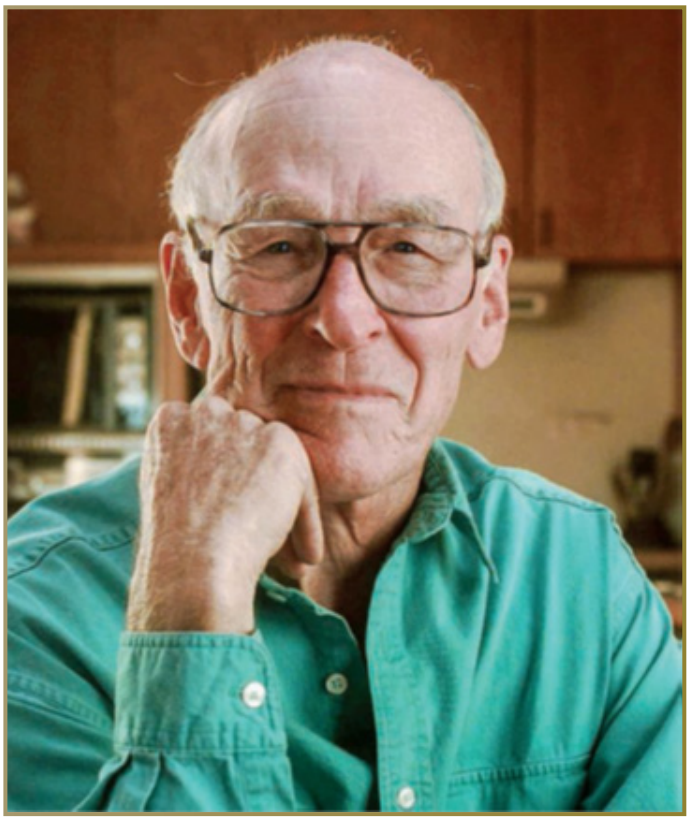

Figure 1 Paul D. Boyer. *Photo courtesy of UCLA.*

Paul Boyer was a biochemist extraordinaire, a promulgator and spokesperson for the field of enzymology, a powerful voice for molecular biology, and a master academic administrator. His career was punctuated by sharing the 1997 Nobel Prize in Chemistry, his editorship of eighteen volumes of the third edition of *The Enzymes* from 1971 to 1990, the 1976 opening of the Molecular Biology Building at the University of California, Los Angeles (UCLA), and his founding directorship of the UCLA Molecular Biology Institute from 1965 to 1983.

A Love of Enzymes

"I never met an enzyme I couldn't love" was a catchphrase of Boyer. His discoveries of the activation of the glycolytic enzyme pyruvate kinase by potassium ion as a graduate student, of the role of sulfhydryl groups in the ATP-generating potential of glyceraldehyde 3-phosphate dehydrogenase and of the crucial phosphorylated histidine intermediate in succinate thiokinase in the citric acid cycle, each demonstrated Boyer's uncanny skill in unlocking the pathways and chemical mechanisms of ATP formation in cells. But Boyer's most ardent enzymatic love was reserved for ATP synthase. Present in nearly all cells, ATP synthase uses the proton-motive force generated by electron transport chains to convert ADP and inorganic phosphate to ATP, the major energy currency of the cell used to drive biosynthesis and biological motion.

Boyer's success was based on his superb understanding and creative applications of chemistry. The problem of how energy from electron transport is conserved in ATP formation by the ATP synthase had eluded the best chemists and biochemists, even after Peter D. Mitchell showed that a gradient of protons across the membrane was the coupling force. Boyer's genius was knowing how to apply mass spectrometry to monitor the O^{18} and P^{32} exchange kinetics of ATP synthase in cells and in the test tube. His experiments showed that the energy of oxidation is coupled to the release of ATP from the enzyme, rather than to ATP synthesis (his so-called "binding change mechanism"), and that the enzymatic reaction of ATP synthesis must involve more than one catalytic site. From these insights, he correctly proposed a rotary

Figure 2 Lyda and Paul Boyer (foreground) facing news photographers after notice of Paul's receipt of the 1997 Nobel Prize in Chemistry. *Photo courtesy of S.G. Clarke.*

molecular engine, later confirmed and gloriously illuminated by the crystal structure of ATP synthase by John E. Walker. For their work on ATP synthase, Boyer and Walker shared half of the 1997 Nobel Prize in Chemistry [Figure 2]. It is still remarkable to the present authors.

Boyer had the curiosity and confidence to grapple with big questions and big projects. Though he studied some twenty different enzymes during the course of his career, he kept returning to ATP synthase. As he said in a biographical memoir, "Although the larger questions [about oxidative phosphorylation] were not likely to be answered, at least I wanted to try." He knew that "Effort is difficult without optimism, and accomplishment is rare without effort." In 2002, Boyer summed up his 325 published scientific contributions in an article in the Centennial Series of the *Journal of Biological Chemistry*.

In addition to the Nobel Prize, Boyer's work was recognized by other awards, including the 1955 American Chemical Society Award in Enzyme Chemistry, election to the American Academy of Arts and Sciences in 1968 and to the National Academy of Sciences in 1970, the William C. Rose Award of the American Society for Biochemistry and Molecular Biology (ASBMB) in 1989 and the Seaborg Medal from UCLA in 1998. Boyer was also recognized by honorary degrees from the University of Stockholm in 1974, the University of Minnesota in 1996, and the University of Wisconsin in 1998.

Scientists across the world remember Paul Boyer for his foresight, bordering on the visionary, about ATP synthase, but those of us who knew and worked with Paul remember him also for his combination of character, leadership, capacity for friendship, love of competitive tennis, golf, and bridge, and practical skills rarely found in one person. Paul died peacefully two months before his 100th birthday, surrounded by family, including Lyda, his mate of nearly seventy-nine years. They were in their home in Los Angeles, which Paul had built, serving as the general contractor. Recalling Paul's mechanical skills, his daughter Gail said, "We never had a repairman in this house." While at the University of Minnesota, where he held his first independent academic appointment, Paul and Lyda had designed their first home, for which Paul was the plumber, electrician, and cabinet maker. Paul was teaching his class at the university when the municipal building inspector arrived at their home site to evaluate the plumbing. The inspector lingered intently over each fitting and junction and then confronted Lyda with the question, "Who did this work?" Her heart sank, and she replied, "My husband." "He must have been trained in the old country," said the inspector, "They don't do fine work like this anymore." It is interesting to speculate that Boyer's intuitive understanding of the mechanics of submicroscopic enzymes was related to his understanding of macroscopic plumbing and electricity.

Early Life and Education

Boyer was raised in Provo, Utah, the fourth of seven children, a descendant of what he called "hardy Mormon pioneer stock." Although he rejected the religious tenets of his church, he attributed his scientific career to parental and community devotion to education. He attended Brigham Young University, a few blocks from his home, graduating with a B.S. in chemistry in 1939. That autumn, he left for graduate school at the University of Wisconsin-Madison, armed with $150 in cash, a $400 per year scholarship, and his new bride, Eliza Mae ("Lyda") née Whicker. When his new department realized he was married, they revoked his scholarship. "Not a problem," said Lyda, who promptly took a job in a book shop. Her father had died when she was two, and she had supported herself through college. With Lyda now the source of family income, Paul developed a new love—for biochemistry.

For his doctoral research, Boyer worked in the laboratory of Paul Phillips in the Department of Biochemistry at Wisconsin. This work resulted in ten publications, ranging from the effects of phenylalanine and tyrosine derivatives on basal metabolic rates in rats to nutritional studies on vitamin A, vitamin C, manganese, and carotenes, to the role of potassium in muscle phosphorylation. Boyer received his Ph.D. in 1943 and then spent two years as an instructor and research associate in the Department of Chemistry at Stanford University. There he published nine papers on the chemistry and biochemistry of serum albumin, a crucial component of plasma preparations for wounded soldiers. Boyer then served in the United States Navy from 1945–46 in the Naval Medical Research Institute in Bethesda developing an assay to determine citric acid in blood and plasma.

In 1946, Boyer joined the faculty of the Department of Biochemistry in the School of Agriculture at the University

of Minnesota in St. Paul as an assistant professor. There he initially focused his work on vitamin E but soon turned to studies on how ATP was synthesized in glycolysis and oxidative phosphorylation. In a classic 1956 paper in the *Journal of Biological Chemistry,* he showed how O^{18} and P^{32} exchange reactions could be used to probe oxidative phosphorylation—techniques that his laboratory then used successfully over the ensuing years, culminating in the 1997 Nobel Prize. In 1955, Boyer moved across the Mississippi River to become the Hill Professor of Enzymology at the University of Minnesota Medical School in Minneapolis. There his discovery of a phosphorylated histidine residue in succinyl coenzyme A synthetase (succinate thiokinase) provided an additional clue about the mechanism for substrate-level formation of ATP in cells.

Coming to UCLA

In August 1961 at the Fifth International Congress of Biochemistry in Moscow, U.S.S.R., Boyer met Professor Charles A. West of UCLA, who initiated the process of his recruitment there. These negotiations cumulated with the move in 1963 of the Boyer lab to the Department of Chemistry, later renamed the Department of Chemistry and Biochemistry, at UCLA. The Boyer laboratory was a continuous beehive of activity from that time to his retirement, resulting in the publication of some 220 research papers. Boyer closed his laboratory in 1990, forced into retirement by the age limit of 70 then mandated by the University of California system, but he stayed active in campus life until his death on June 2, 2018.

A National and International Legacy

Boyer had the passion, energy, and dedication to work outside of his own laboratory to ensure the development not only of enzymology but the larger field of biochemistry as well. He was the editor of eighteen volumes of the third edition of the definitive series *The Enzymes* from 1971 to 1990. From 1963–90, he served as an associate editor and then editor of the prestigious *Annual Review of Biochemistry,* the premier review series of the field. Increasingly aware of Boyer's integrity, fairness, and unassuming but effective management style, his biochemical colleagues repeatedly turned to him for leadership at the national level, where he worked assiduously for biochemistry and biomedical sciences. He joined the American Society of Biological Chemists (ASBC) in January 1944 and was in his seventy-fifth "diamond anniversary" year of membership when he died. He became an effective spokesperson for the closely allied discipline of molecular biology and strongly supported the name change of the ASBC to the American Society for Biochemistry and Molecular Biology (ASBMB) in 1987. His commitment to the ASBC/ASBMB included elected membership on the council from 1965 to 1971, president from 1969 to 1970, and chair of the Public Affairs Advisory Committee from 1982 to 1987. He also served as chair of the Division of Biological Chemistry of the American Chemical Society from 1959 to 1960. Boyer was always the instigator of policies that brought together chemistry and biology to foster the new field of molecular biology.

Strengthening Molecular Biology at UCLA and Elsewhere

In the early 1960s at UCLA and elsewhere, there were active efforts to take advantage of the synergy between chemistry and biology, and even physics, in the emerging field of molecular biology. The UCLA administration supported the establishment of an institute where faculty from a variety of departments could work together. Paul Boyer became the clear choice to lead this new venture and, in 1965, was appointed the inaugural director the UCLA Molecular Biology Institute (MBI). Boyer took this responsibility to heart, not only bringing existing faculty together and recruiting new faculty, but making the push for a new building to house this new enterprise.

Boyer's vision was one in which faculty from different departments but with mutual and complementary scientific interests could collaborate "horizontally" on floors with appropriate research infrastructure. The funding climate in the late 1960s and early 1970s was lean, and only Boyer's matchless resilience could cobble together a mosaic of funds that enabled the construction of the UCLA Molecular Biology Building, which opened in 1976. Boyer was instrumental in the design of the building, which housed thirty laboratories, many directed by faculty new to UCLA, as well as common facilities and seminar rooms. Boyer provided his faculty the intellectual and physical resources as well as a culture that allowed them to take full advantage of collaborative opportunities. Faculty meetings were brief and uncontentious because Paul had made the effort to discuss the issues beforehand with each of us and thus had forged a consensus before such meetings. As a fitting testament to Paul, in 1999 the building was renamed in his honor as "Paul D. Boyer Hall" in an era when UCLA buildings were generally named for the donors of the money used to construct them. In Boyer's case, the naming was to recognize him as the donor of the vision, leadership, inspiration, and collegial glue that made the building a reality! Richard Dickerson's book *The Making of an Institute: The MBI at UCLA 1960-1978* describes well Boyer's achievement in the success of the unit.

Postdoctoral Fellows Are "Unsung" Heroes

After receiving the Nobel Prize in 1997, Boyer devoted a good part the award to establishing a fund to recognize postdoctoral fellows—scientists whom he felt deserved more acknowledgment and appreciation for their contributions

to science. His initial gift to set up the UCLA Postdoctoral Awards in Molecular Biology was matched by former Ph.D. student and postdoctoral fellow James B. Peter, founder of Specialty Laboratories, Inc., who was one of laboratory medicine's most successful scientist-entrepreneurs. In recent years, these awards have been sponsored by Phyllis Parvin, wife of the late Beverly Hills philanthropist Albert Parvin and president of the Albert Parvin Foundation, whose keystone contribution allowed construction of the Molecular Biology Building (now Boyer Hall) to begin**.** After the death of her husband, Phyllis Parvin maintained a close friendship with Paul and Lyda and always wanted to support his vision for the betterment of molecular biology.

Remembering and Learning from Paul Boyer

What traits enabled Paul Boyer's many achievements? Of course there was the ambition, the optimism, the relentless effort, and the know-how, but there was something more: character. In our every encounter with Paul over a span of fifty years, we sensed and appreciated his drive to get at the truth, his generous judgments of others and their work, and his modesty. At the same time, he was direct in his criticisms, yet positive and constructive. University administrators, scientific colleagues, postdocs, and students all respected him and trusted him. Together, these traits made him the most effective leader that either of us has ever personally known.

A generous author, Boyer in his several scientific autobiographies carefully noted the advances made by each of his graduate students and postdoctoral fellows. Also, he invariably took care to credit the results from the labs of other scientists. Even when he disagreed, the tone was one of respect, sometimes noting where in hindsight his own interpretation had been wrong.

Upon Boyer's death, we heard from many of his former lab members. One frequent statement was, "When I face a tough situation, I ask myself, what would Paul Boyer do here?" Paul Boyer's life continues to stand a model of the proper path for all of us who had the privilege of knowing him.

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