



Biographical Memoirs V.80

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Biographical Memoirs

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PREFACE

On March 3, 1863, Abraham Lincoln signed the Act of Incorporation that brought the National Academy of Sciences into being. In accordance with that original charter, the Academy is a private, honorary organization of scientists, elected for outstanding contributions to knowledge, who can be called upon to advise the federal government. As an institution the Academy's goal is to work toward increasing scientific knowledge and to further the use of that knowledge for the general good.

The *Biographical Memoirs*, begun in 1877, are a series of volumes containing the life histories and selected bibliographies of deceased members of the Academy. Colleagues familiar with the discipline and the subject's work prepare the essays. These volumes, then, contain a record of the life and work of our most distinguished leaders in the sciences, as witnessed and interpreted by their colleagues and peers. They form a biographical history of science in America—an important part of our nation's contribution to the intellectual heritage of the world.

R. STEPHEN BERRY
Home Secretary

Biographical Memoirs

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Photograph by Reinhard Bachofen, University of California at Berkeley, Summer 1988

San Amos

DANIEL I. ARNON

November 14, 1910–December 20, 1994

BY BOB B. BUCHANAN

THE ELDEST OF FOUR children, Daniel Arnon was born in Warsaw, Poland, on November 14, 1910. The family lived in Warsaw, but spent summers on a farm where young Daniel first became intrigued by plants and agriculture. He was something of a child prodigy, being by far the youngest in his class. When he joined a private library, the young man amazed the librarian by often devouring four books a day. He also developed a lifelong love of sports and physical fitness. Soccer he especially enjoyed. He learned to swim so as to be able to scull on the Vistula River and tutored classmates in swimming, gymnastics, and mathematics to supplement the family income. His father was a food wholesaler who, in the aftermath of World War I, lost his business and became a purchasing agent.

As a result of witnessing the great famines following World War I, Arnon was attracted to the cause of scientific farming, which he had read about in the California novels of his hero Jack London. Convinced that there was no future for him in Poland, he saved his earnings and by age 18 secured his passage to New York. He worked there for a summer until he had money to buy a Greyhound bus ticket to California. As a student in Poland he had earlier applied

by mail and been admitted to the University of California at Berkeley, but owing to a mix-up in the admissions office his matriculation was delayed. He thus attended a local college in Ontario (Chaffey Junior College of Agriculture, now Chaffey College), where he also worked in the orange orchards of southern California. After a year he transferred to Berkeley. Although the Great Depression was at its worst, he supported himself by taking odd jobs like gardening and in the summer by working on farms. At an early age Arnon became accustomed to hard work and maintained demanding work habits throughout his career. When the United States entered World War II, Arnon volunteered for the Army. He became a major in the Army Air Corps, where as we will see later he continued his work on plant nutrient culture. His military service later resulted in many picturesque anecdotes, and he maintained it had reinforced his inherent self-discipline—habits he faithfully maintained.

Except for military service during World War II Arnon spent his entire professional career at the University of California at Berkeley. He earned a bachelor's degree in 1932 and went on to obtain a Ph.D. in 1936 under Professor Dennis R. Hoagland, a member of the Berkeley faculty who did pioneering work on the mineral nutrition of plants (Hoagland was elected to the National Academy of Sciences in 1934). Their research provided the basic formula for a nutrient solution (known as Hoagland's solution) that continues to be used worldwide for the cultivation of plants.

ARNON THE PERSON AND THE SCIENTIST

Throughout his long career of groundbreaking research, Arnon held fast to simple principles that guided his research efforts. Repeating experiments was first on his agenda. Repetition is the mother of learning, he would remind those who tended to become weary of duplicating results. Design

of simple experiments that yielded important new results was another important goal. New ideas and scientific advances were usually first presented at the weekly group meeting (the “kitchen seminar”), where dishes were prepared and tested before being served to the public. These sessions generated spirited discussions and served as an excellent forum for developing ideas and future experiments. Selected works from the current literature were also addressed. When a scientific paper was presented, the only rule was that the tenor of the discussion had to be on a level appropriate to the author’s being present in the room. Otherwise, participants were encouraged to air their views and argue any position.

As in other endeavors, Arnon’s energy and patience were boundless throughout these meetings, which often lasted for two hours or more. During this time, laboratory members had an opportunity to observe his dedication to ethics and scholarship in science. One could not leave these meetings without being impressed by the depth of Arnon’s knowledge of the photosynthesis field—especially in the history of its development—and his conviction to upholding the highest scientific principles. In these sessions one also learned that Arnon was a debater at heart. He would play the devil’s advocate with zest, not only to extend his own knowledge but also to air all possible objections in advance. In this way he was seldom unprepared when later challenges arose. But he never lost sight of the fact that truth was at stake. Once convinced of something he stalwartly defended it, whatever the cost to his reputation. Perhaps as a result of his rhetorical skills Arnon was lucid both as a speaker and a writer. These talents were undoubtedly an asset in enabling him to convey his research findings to the scientific community and the general public. In a little known contribution Arnon at mid-career served on a post-*Sputnik* national committee

that developed the “Blue Series” high-school biology textbook for which he wrote four chapters on the evolution of life processes. Widely translated, it enjoyed national acclaim and use.

Arnon was recognized widely for his accomplishments. In addition to the National Academy of Sciences he was a member of the Royal Swedish Academy of Sciences, the Académie d’Agriculture de France, the Deutsche Akademie der Naturforscher Leopoldina, the Scandinavian Society of Plant Physiologists, and an honorary member of the Spanish Biochemical Society. Arnon was a fellow of the American Academy of Arts and Sciences and the American Association for the Advancement of Science. He served his profession as president and vice-president of the American Society of Plant Physiologists and was the leading force in establishing the *Annual Review of Plant Physiology and Plant Molecular Biology*. In the early 1950s he also led successful efforts to broaden the scope of the journal *Plant Physiology* to include emerging topics in plant biochemistry.

Arnon gave extensive service to the university, both as a faculty member and long-term department chair. He received the Berkeley Citation, the highest honor of the campus, “for distinguished achievement and for notable service to the University.” In addition to honorary lectureships his awards included the Newcomb Cleveland Prize (American Association for the Advancement of Science); a Charles F. Kettering research award (Kettering Foundation/National Academy of Sciences); the Finsen Medal (International Association of Photobiology); the Stephen Hales Prize, the Charles Reid Barnes Life Membership Award, and the Kettering Award in Photosynthesis (American Society of Plant Physiologists); Docteur honoris causa (Université de Bordeaux and Universidad de Sevilla); and the U.S. National Medal of Science “for fundamental research into the mechanisms

of green plant utilization of light to produce chemical energy and oxygen and for contributions to our understanding of plant nutrition.”

Arnon spent sabbatical periods in Europe with legendary figures, first as a Guggenheim fellow (with David Keilin in Cambridge and Hugo Theorell in Stockholm) and then as a Fulbright research scholar (with Otto Warburg in Berlin-Dahlem). These visits provided Arnon an opportunity to establish lifelong friendships with a number of other notable individuals, including Britton Chance, Robin Hill, Helmut Holzer, Henrik Lundegårdh, Roy Markham, and E. C. (“Bill”) Slater. Later in his career Arnon spent a third sabbatical year in California with Cornelius B. Van Niel in Pacific Grove.

While his early work was done on limited budgets, much of Arnon’s later research was accomplished in the post-*Sputnik* era, when funding was generous. He was particularly grateful for the excellent support he received from the National Institutes of Health (his first extramural grant), the U. S. Navy (funds for large equipment), and the Charles F. Kettering Foundation (post-retirement research support). During his prime Arnon thus had to spend relatively little time in raising support for the laboratory and was able to devote most of his attention to science. Arnon was shrewd when it came to money and without fail used time and circumstances to budgetary advantage. Until his retirement his laboratory was well financed: He took pride in stating that an experiment had never been postponed because of lack of funds.

Following his death Arnon’s unspent funds formed the nucleus of an endowment that Berkeley’s Department of Plant and Microbial Biology established to support a graduate fellowship and an annual lecture in his memory. As a part of this effort his papers have been placed in a permanent collection at the Bancroft Library on the Berkeley

campus. It includes laboratory notebooks, slides, transparencies, and other research materials; manuscripts, preprints and publications; and grant applications and reprints. The archive is rich in resources that tell the story of photosynthesis at Berkeley, including the controversies surrounding Arnon's discoveries. The collection includes letters exchanged with many colleagues, including such well-known members of the Berkeley faculty as Melvin Calvin and Glenn Seaborg. In addition, members of the Arnon family have contributed a wealth of personal photographs, documents and other memorabilia that provide a fuller picture of the life of the man behind the scientist. (The website for the Arnon Papers is being constructed at the time of this writing. The material can be access using the Bancroft Library Finding Aids, <http://www.oac.cdlib.org/dynaweb/ead/ead/berkeley>.)

It is perhaps not surprising that Arnon's style of laboratory management was European, modeled to some extent after that of Warburg. Arnon believed in maintaining a core staff whose job was not only to carry out their own projects but also to instruct and guide incoming postdoctoral fellows and graduate students. In part because of this style and his high international visibility he tended to attract more postdoctoral scholars from Europe and Japan than from the United States. Another factor that discouraged American postdoctoral biochemists was Arnon's affiliation with the College of Agriculture, which at the time created a relative stigma that persisted until his election to the National Academy of Sciences in 1961.

Arnon had relatively few graduate students. While he encouraged them to join his laboratory, he was not presented with a steady supply of students because of the small size of his department. Arnon thought the ideal mix was one graduate student to perhaps three or four postdoctoral fellows. At its peak his laboratory consisted of no more

than 20 members. Numerous students and postdoctoral scholars trained in the laboratory rose to positions of national and international leadership. Most kept in close contact with Arnon, as he remained fully active until his death. Arnon remained particularly close to Joseph-Marie (Jose) Bové (Bordeaux), Manuel Losada (Sevilla), Kunio Tagawa (Osaka), Achim Trebst (Bochum), and Robert Whatley (Oxford). Arnon also remained in contact with his long-time collaborator Harry Tsujimoto, who continued to live in San Francisco following his retirement from the university.

Arnon believed that small was virtuous. In 1961 he established the Department of Cell Physiology, where for many years the focus was restricted to his own interests—photosynthesis and nitrogen fixation—and he was the only Academic Senate faculty member. With time, new principal investigators joined the staff and the program broadened. In 1989 cell physiology became a part of the newly formed Department of Plant and Microbial Biology, which remained Arnon's academic home for the remainder of his life.

Typical of his European contemporaries, Arnon retained a certain formality and encouraged a quiet, professional atmosphere in the laboratory. He took science seriously. Nonetheless, the daily discussions he held with members of the laboratory were made engaging by his sagacious jokes and analogies. As a consequence, the vein was lighter than one would have suspected from Arnon's public demeanor. His attitude toward the laboratory began to change somewhat as his group became smaller and as he passed the official university retirement age of 68 (at which time he became a recalled professor, as he disliked the emeritus title). While his presence on campus did not noticeably change, he became more informal and relaxed in his daily routine and in his last decade he increasingly enjoyed vigorous discussions with colleagues and young academics alike.

His lifelong fondness for classical music also became more evident in later years, and he listened nightly to selected works, often of Beethoven.

Arnon died suddenly on December 20, 1994, at age 84. His five children survive him: Anne Arnon Hodge, Ruth Arnon Hanham, Stephen Arnon, Nancy Arnon Agnew, and Dennis Arnon. His wife, the former Lucile Soulé, preceded him in death by eight years. I was especially pleased that Arnon was able to work closely with fellow faculty member Anastasios Melis and me on a special volume of articles submitted by former students, postdoctoral scholars, and colleagues (*Photosynthesis Research*, November 1995, 46, no. 1-2). The volume was originally planned to commemorate Arnon's eighty-fifth birthday, but turned out to be a memorial as he died while the articles were in press. Much of the information contained in this write-up is taken from the articles published in that volume (see especially B. B. Buchanan, pp. 3-6 and B. B. Buchanan and K. Tagawa, pp. 27-35). The 1995 memorial volume was preceded by a special collection of invited articles published ten years earlier to honor Arnon on the occasion of his seventy-fifth birthday (*Physiologie Végétale* 73:707-875). The collection was presented to him at a gala celebration held on his birthday at the UC Berkeley Faculty Club when he received the Berkeley Citation.

OUR RELATIONSHIP

I first saw Daniel Arnon and learned of his work in two lectures he presented at Duke University in the spring of 1960. The lectures were part of a memorable series, "Recent Advances in Photosynthesis," organized by Aubrey Naylor of the Botany Department. As a second-year microbiology graduate student in the Duke Medical School, I had not known earlier of either Arnon or his research. What I remember is how impressed I was with his knowledge and

contributions to photosynthesis. I also recall his effective and witty response to penetrating questions from the audience, including skeptical queries from James Franck, who by then had retired from the University of Chicago and was spending half of his time at Duke, where his wife, Herta Sponer, was a professor of physics. At the time I had no idea that I would meet much less become associated with Arnon, as I had every intention of continuing my microbiology career with heterotrophic bacteria.

The situation was, however, soon to change. After completing my Ph.D. at Duke in early 1962 I went to Berkeley for postdoctoral work on the biochemistry of anaerobic bacteria (clostridia) with Jesse C. Rabinowitz (Rabinowitz was elected to the National Academy of Sciences in 1981). Following the early work on *Clostridium pasteurianum* ferredoxin, Walter Lovenberg (also a new postdoctoral fellow in the laboratory) and I started a project on the chemistry of bacterial ferredoxin. In a relatively short period we obtained sufficient new information to contribute an abstract to the 1963 federation meeting in Atlantic City. Being without a job, I was chosen to make the oral presentation, my first at a national meeting, and was introduced by Robert Burris (Burris was elected to the National Academy of Sciences in 1961). Arnon was present at the same session in connection with Masateru Shin's contribution on the crystallization and characterization of chloroplast ferredoxin-NADP reductase. Arnon heard my presentation and afterward made several unsuccessful attempts to contact me at the meeting.

Back in Berkeley, Arnon tracked me down. We met in his office and, after introductory remarks, he offered me a tenure-track job as an assistant microbiologist in the California Agricultural Experiment Station. Having no plans at that point, I accepted his offer and joined the Department of Cell Physiology in September 1963. While both the name

of the department and the title of my position have undergone change, I continue to hold this appointment.

Since our initial meeting in 1963 I remained associated with Arnon and spoke and visited with him almost daily—the last time at a laboratory Christmas party at our Berkeley home three days before his death. Arnon was in extraordinary spirits that evening and, in addition to telling an assortment of entertaining stories in his distinctive style, he participated in lively discussions of contemporary events, including the political changes underway in Washington. After the guests had left and Arnon had driven away, I commented to my wife, Melinda, on his seemingly excellent mental and physical condition and how much he reminded me of the man I had met for the first time more than 30 years earlier. I have since thought how fortunate it was to have arranged that party, as it provides a benchmark, however modest, for culminating our long-term association, in which he was first a mentor and then a colleague and friend.

THE PLANT NUTRITION YEARS (1936-50)

His graduate work with Hoagland brought Arnon international recognition and set the stage for his later becoming a major in the U.S. Army Air Corps in the course of his wartime military service. In that capacity, during 1943-46, he was commanding officer of a project designed to use nutrient culture for the production of food plants on Ascension Island—a 34-square-mile area of volcanic origin that served as a key refueling station in the South Atlantic theater for aircraft transporting war material into North Africa. The techniques developed on Ascension Island later served as a model for the extensive nutrient culture farms used to feed General Douglas MacArthur's occupation forces in Japan.

In the first part of his professional career Arnon (and

collaborators) discovered the essentiality of molybdenum for the growth of all plants and of vanadium for the growth of green algae. These findings led to far-reaching developments in the study of nitrogen metabolism, in which both elements were shown to play critical roles. The molybdenum research later found agronomic application: The addition of a small amount of molybdenum to deficient soils restored fertility and dramatically increased crop yields in many regions of the world, especially Australia. In later life, well into his photosynthesis career, he jokingly referred to his nutrition years as “my first incarnation.”

THE PHOTOSYNTHESIS PERIOD (1951-78)

Arnon's plant micronutrient work led him to photosynthesis, where in 1954 he discovered (and named) photosynthetic phosphorylation (photophosphorylation)—a finding that ranks in importance with the discovery of respiration in animals. He demonstrated that chloroplasts use the energy of sunlight to generate adenosine triphosphate (ATP), the universal energy carrier of living cells. Arnon discovered the cyclic type of photophosphorylation in which ATP is the sole product of energy conversion and the noncyclic type in which the formation of ATP is accompanied by the liberation of oxygen and the generation of reductant (reduced pyridine nucleotide, or NADPH). As a part of this research Arnon was the first to obtain complete photosynthesis outside the living cell—a feat comparable to that of Büchner's cell-free fermentation. This discovery opened the door to a new epoch in photosynthesis and made possible the elucidation of the systems that regulate the assimilation of carbon dioxide and the paths of biosynthesis of major cellular products. As has occurred with other major advances, Arnon's discoveries were for years either unaccepted or unappreciated by influential workers in the field.

When it became apparent that neither the photolysis of water nor the reduction of carbon dioxide was involved in cyclic photophosphorylation, Arnon developed the electron flow theory. Here, electrons emitted from photoexcited chlorophyll are transferred via a series of intermediate carriers back to chlorophyll in a stepwise cyclic transport linked to phosphorylation. This concept provided a framework for much of the later work in the field, including studies on nitrogen fixation and hydrogen evolution. Arnon's path-breaking work on photosynthesis was accomplished with chloroplasts isolated from spinach leaves. Following his lead, laboratories around the world adopted spinach as the experimental plant for research on photosynthesis.

A far-reaching discovery came in the year 1962, when Arnon showed that a red iron-sulfur protein, now known as ferredoxin, is a universal part of the photosynthetic apparatus. He found that ferredoxin, reduced by light, provides the electrons for generating the NADPH required for carbon dioxide assimilation. Arnon demonstrated that, in the presence of ferredoxin-NADP reductase, photoreduced ferredoxin provided the electrons for the reduction of NADP—a process itself found to be independent of light. He showed that ferredoxin is linked to the formation of ATP as a catalyst of both cyclic and noncyclic photophosphorylation. Moreover, in the presence of a bacterial hydrogenase (an enzyme missing in higher plants) ferredoxin photoreduced by chloroplasts provided the electrons for the production of hydrogen gas. This work laid the foundation for recently renewed efforts to use hydrogenase-containing green algae for the generation of hydrogen gas as an energy supply.

An extension of the noncyclic photophosphorylation experiments revealed that ferredoxin could also catalyze pseudocyclic photophosphorylation, a light-driven process in which oxygen rather than NADP serves as the acceptor

in the transport of electrons from water. The use of monochromatic light to separate the cyclic, noncyclic, and pseudocyclic pathways proved to be a major asset in unraveling these processes. Agents that disrupted photophosphorylation were also useful.

During this period crystallization efforts were successfully extended to ferredoxins from a number of oxygenic and anoxygenic photosynthetic organisms. This research led to the discovery of novel ferredoxins and functionally related proteins from heterotrophic aerobic bacteria. In research stemming from the ferredoxin work Arnon and his colleagues discovered a new path of photosynthetic carbon dioxide assimilation in bacteria, the reductive carboxylic acid cycle (reverse citric acid cycle). This work uncovered the ferredoxin-linked mechanism of carbon dioxide fixation and gave insight into the evolution of photosynthesis. The finding of other novel autotrophic paths of carbon dioxide assimilation of carbon dioxide followed. Ferredoxin thus emerged as a central electron carrier that functioned broadly in plants and bacteria.

During the 1970s Arnon did extensive work with cytochromes of chloroplasts and cyanobacteria. This effort led to the discovery of an absorbance change at 550 nm that was later shown to be due to an acceptor of the oxygen-evolving photosystem (photosystem II). Cytochrome b-559 was examined in considerable detail during the decade. Three redox forms of cytochrome b-559 were identified, first in the chloroplasts and then in cyanobacteria—a system Arnon believed would be easy to dissect biochemically. Work in the laboratory during this period also extended our knowledge of cytochromes in photosynthetic bacteria. There is little doubt that the cytochrome efforts provided the stimulus for others to pursue subsequent work on these components and their role in electron transport.

The 1970s brought forth new evidence for the requirement for cyclic photophosphorylation in carbon dioxide assimilation by chloroplasts and an increase in our understanding of ferredoxin as a catalyst of photophosphorylation—a topic of continuing investigation in a number of laboratories. The identification of chloroplast membrane-bound iron-sulfur proteins at Berkeley and elsewhere soon followed and opened a new field of research that has increased greatly our understanding of electron transport in oxygenic photosynthesis.

SUMMING UP, MOVING FORWARD (1978-94)

Following his retirement in 1978 up to the time of his death Arnon continued to conduct research and write daily. During this time he spent considerable effort refining his unfashionable concept of three light reactions in photosynthesis. Arnon formulated this concept in the late 1960s, when he analyzed the effectiveness of photosystem II in promoting absorption changes in cytochrome b-559 and the C-550 component. The results led Arnon to abandon the Z-scheme, the widely accepted mechanism of photosynthetic electron transport that he himself had originally helped formulate. Arnon then proposed an alternative electron transport mechanism that involved not two but three light reactions. While eliciting spirited debate, his hypothesis still awaits wide acceptance. His last article, written shortly before his death, described these ideas in detail (1995).

In his last decade Arnon wrote four short articles chronicling his major discoveries, in his own words, “to set the historical research record straight for posterity.” The first article traced the history of the discovery of photophosphorylation, the second complete photosynthesis by isolated chloroplasts, and the third chloroplast ferredoxin. The fourth described the beginnings of the reductive carboxylic acid cycle and

the long struggle before its acceptance by the scientific community. The popular highlight of the period was, however, Arnon's short 1982 article, reminiscent of his classic 1960 *Scientific American* contribution, in which in his inimitable style he extolled the wonders of photosynthesis (1982).

Arnon mentioned on several occasions that he hoped his program of jogging and swimming, together with a salubrious diet, would enable him to remain active well into his tenth decade. Had that happened he undoubtedly would have continued to add important knowledge to the field of photosynthesis. Nonetheless, his contributions remain monumental, reflecting the fact that he was able to work full-time until his death at 84. He improved the scientific basis of agriculture, and in the long term his work will increasingly find application in the production of food, and thus in the prevention of famine. In short, his boyhood dreams have been fulfilled.

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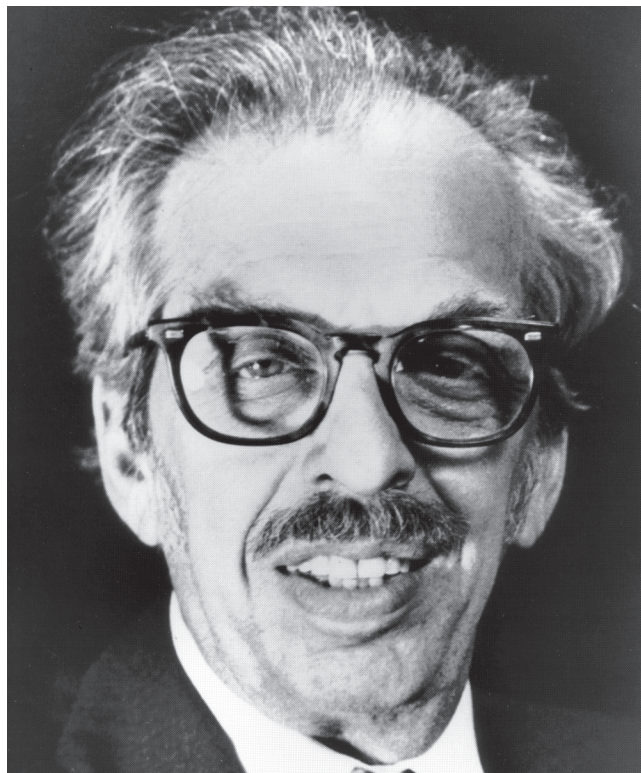
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Courtesy of Victor Bers

Cipriani

LIPMAN BERS

May 22, 1914–October 29, 1993

BY IRWIN KRA AND HYMAN BASS

INTRODUCTION

LIPMAN BERS WAS BORN in Riga, Latvia, on 22 May 1914 into a secular intellectual Jewish family. At the time of his death, in New Rochelle, New York on 29 October 1993, he was the focal point of a large extended group of scientists—mostly mathematicians, many former doctoral students with whom he maintained close and continuous ties for decades. His friends and colleagues knew him as “Lipa.” His life was a twentieth-century Jewish and intellectual odyssey. He had close encounters with fascism and Stalinism. In an irrational world he approached all issues through his intellect. He was born in Europe on the brink of revolutionary changes. He died in America after several tyrannies had come and gone. He started as a Bundist with strong anti-nationalist leanings, but over the years he grew increasingly fond of Israel.

He opposed nuclear armaments as if there were no cold war; he fought tyranny as if this struggle had no arms control implications. He played an important role in American

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scientific politics. He made important and lasting contributions to both mathematics and the protection of human rights. He was never afraid to take strong moral positions, even from platforms of official leadership, yet he was pragmatic and effective. His optimism and good humor remained unflagging. Above all, he was a mathematician, and in whatever subfields of the subject he worked, he did complex analysis. All that he did, he did with style.

THE EARLY YEARS

The simmering Russian Revolution failed to cloud Lipa's happy memories of his earliest years in Petrograd. He began school in Riga, where his mother was principal of the secular Yiddish-language elementary school, and his father principal of the gymnasium. In the elementary school he met Mary Kagan. He subsequently lived in Berlin, where his mother trained at the Berlin Psychoanalytic Institute. His love for learning and for mathematics, his faith in rationalism, and his worldly awareness were largely molded during the early years in Riga. His entire intellectual outlook was strongly influenced by a school environment that included the classics such as Shakespeare in Yiddish.

After a brief period in Zurich, Lipa returned to the university in Riga, as a politically involved social democrat in an atmosphere of growing political turmoil and violence. He wrote for an underground newspaper that mocked the prevailing dictatorship. With an unerring instinct for survival that, happily, was never compromised by his political courage and boldness, Lipa fled Riga for Prague when an arrest warrant was issued for him. Mary later joined him there, where they married.

At Charles University Lipa worked under the effective, but not overly nurturing, mentorship of Karl Löwner. That this thesis supervision style agreed with Lipa is obvious from

his strong affection for Karl and the life-long friendship between the Bers and Löwner families. The deadline for Lipa's dissertation, on potential theory, was dictated less by scientific considerations than by the imminent fall of Czechoslovakia to the Nazis. Stateless, leftist, and Jewish, the Berses were vulnerable, on several accounts, in Nazi-dominated Europe. They fled to Paris, where their application for an American visa resulted in not uncommon frustration.

The brief interlude in Paris produced two short mathematical papers: one on Green's functions, another on integral representations of biharmonic functions; these were partly inspired by Stefan Bergman's then-influential work on kernel functions. It also produced their daughter, Ruth, now a psychoanalyst, and a professor of psychology at John Jay College of the City University of New York.

Ten days before the Nazis arrived in Paris, the Bers family moved south to unoccupied France, at Mary's insistence. There they benefited from the ten thousand American visas for political refugees issued after the personal intervention of Eleanor Roosevelt. Lipa's mother and stepfather, Beno Tumarin—an actor, director, and in the last years of his life a teacher at the Julliard School—were already in New York. Finding no available professional positions, Lipa at first received aid from YIVO, the Institute for Jewish Research, for which he produced a paper in Yiddish about Yiddish mathematics textbooks.

WARTIME MATHEMATICS AND THE SYRACUSE YEARS

In 1942 Bers accepted a position in the program for advanced research and instruction in applied mathematics at Brown University. His was a low-paying entry-level job in the academic sector of the war effort. In Providence he began his investigations of two-dimensional subsonic flows. He initiated a collaboration with Abe Gelbart, which later

developed into the theory of pseudoanalytic functions. He also supervised the work of the first three of his forty-eight doctoral students, an impressive list that includes sixteen women. A few of his papers and technical reports on differential equations, subsonic flows, and pseudoanalytic functions appeared during this period; some of his publications in this area appeared as late as 1953, long after he started to work on different problems. These laid the foundation for the work that led to the 1958 monograph *Mathematical Aspects of Subsonic and Transonic Gas Dynamics*, published by John Wiley and Sons (for whom he would later become a consultant), and the 1964 book *Partial Differential Equations*, written jointly with his New York City colleagues F. John and M. Schechter.¹ The Bers's son, Victor, now a professor of classics at Yale University, was born in Providence.

Bers spent the four academic years 1945-49 at Syracuse University, where mathematics then flourished. Its faculty included for a brief period Paul Erdős, Dan Mostow, and Atle Selberg, among others. Bers's interests shifted further toward partial differential equations and Riemann surfaces. A beautiful theorem, which he discussed at the 1950 International Congress of Mathematicians (ICM) and published in the *Annals of Mathematics* the next year, on removable singularities of minimal surfaces, was the result of work initiated during this time. Although the result belongs to the field of partial differential equations, the methods are from complex analysis, hinting at the direction of his most important future work.

QUASICONFORMAL MAPPINGS, TEICHMÜLLER THEORY, AND
KLEINIAN GROUPS

Bers's 1948 paper in the *Bulletin of the American Mathematical Society*, "On rings of analytic functions," created a small industry that contributed to an algebraization of ques-

tions in analysis, subsequent contributions by S. Kakutani, W. Rudin, and I. Richards, and a dissertation by one of the authors of this article. The two years at the Institute for Advanced Study (1949-51) transformed Bers into a full-fledged member of the “quasi world”—the world of quasiconformal mappings and their diverse applications. His subsequent work on moduli of Riemann surfaces and Kleinian groups would include some of the most important contributions to complex analysis in the second half of the twentieth century. He attributed his entry into the field to its beauty and wide applicability,² and to the fact that it was practiced by gifted individuals of unusual generosity of spirit. Most notable among these, for Bers, was Lars Ahlfors, a distinguished mathematician of very different temperament and personality, with whom Bers maintained a close mathematical and social connection for the rest of his life.

Lipman Bers's most productive mathematical years followed, at New York University (NYU) (1951-64) and at Columbia (1964-82).³ His research would henceforth lie in the broad field that can be described as Riemann surfaces, Kleinian groups and Teichmüller theory. Investigators of these subjects are interested in understanding the different ways one can do complex analysis on a fixed topological surface. One of the important open problems, the moduli problem, left to us from the nineteenth century, was to make rigorous and precise Bernhard Riemann's claim that the complex analytic structure on a closed surface with $p \geq 2$ handles depends on $3p-3$ complex parameters. What turned out to be the most fundamental result of this period was announced by Bers⁴ at the 1958 ICM as a new proof⁵ of what is now called the *measurable Riemann mapping theorem*.⁶ The new proof yielded much more than the previous methods.⁷ It showed that properly normalized homeomorphic solutions of the fundamental Beltrami equation⁸ depend

holomorphically on parameters. Among the consequences, Bers obtained a solution of Riemann's problem of moduli that significantly extends Ahlfors's earlier solution.⁹ Bers continued to work on moduli problems for the rest of his life. He marveled at being paid for doing something that gave him so much joy and pleasure. Teichmüller theory, the brilliant mathematical work, and even more brilliant mathematical insights of O. Teichmüller¹⁰ established the connection between quasiconformal mappings and the metric/topological theory of moduli of Riemann surfaces. Bers's contributions had two surprising consequences. Quasiconformal mappings can also be used to study complex analytic aspects of moduli theory.¹¹ There is a deep connection between the theory of moduli and univalent functions since a very important class of such functions can be obtained as solutions of Beltrami equations. This last fact led Bers to a number of important conjectures, some of them still open, that influenced complex analysis for more than twenty-five years.

During the first half of this century much progress was made in our understanding of discrete subgroups of $\text{PSL}(2, \mathbb{R})$, *Fuchsian* group, in part because of their deep connections to Riemann surfaces and two-dimensional hyperbolic geometry. Poincaré suggested that the study of discrete subgroups of $\text{PSL}(2, \mathbb{C})$ *Kleinian* groups, should exploit and be based on their connections to three-dimensional hyperbolic geometry. The passage from the real to the complex universe proved surprisingly difficult. Significant progress had to wait more than fifty years. Little was known about three-dimensional topology/geometry throughout the sixties. The progress in the theory of Kleinian groups during three decades illustrates both Lipa's influence on the field and his strong interactions with Ahlfors. In 1965, Bers published, in the *American Journal of Mathematics*, a new proof of a

finiteness theorem for Fuchsian groups. The new ingredient was the use of Eichler cohomology, which had proved important in the solution of a number of problems in number theory. Bers used meromorphic functions to construct cohomology classes. Ahlfors saw that this idea could be greatly expanded. He made a conceptual and a technical advance that were extremely surprising and far-reaching. He used smooth functions to construct cohomology classes from a class of holomorphic functions known as *cusp forms*. He then needed a delicate *approximate identity* to establish that a natural map is injective. The result was the “Ahlfors Finiteness Theorem” (AFT) for Kleinian groups:¹² A finitely generated Kleinian group represents a finite number of surfaces each of which can be compactified by the addition of finitely many points. Bers noticed that Ahlfors’s proof had a small gap. He, among others, filled in the gap in 1967.¹³ In the same year, he also noticed that Ahlfors’s method can be generalized to produce quantitative versions of AFT, now known as the *Bers Area Theorems*. These in turn led Ahlfors and Kra to a study of the structure of the Eichler cohomology groups in 1969. The same ideas were further developed in the eighties to translate questions in the “transcendental” theory of convergence of series of rational functions, *Poincaré series*, to an algorithmic linear algebra theory.

In the seventies a new force appeared in mathematics: William Thurston. Thurston revolutionized practically every field he touched. He brought new insights to old and new problems. His studies in topology/geometry revealed new structures in what we thought were well-understood areas (for example, the structure of self maps of [two-dimensional] surfaces) and led to remarkably rapid and dramatic progress in not so well understood topics (for example, the classification of three-dimensional manifolds). Bers’s attempt to understand and translate Thurston’s work

on topological automorphisms of surfaces to the language of Teichmüller theory, led him to the formulation and solution of an elegant new extremal problem. This extremal problem is both natural and simple. The question should have been asked over thirty years before. It waited for Thurston's vision and Bers's inspired efforts to understand his young colleague's insights to be posed. Its solution, published in *Acta Mathematica* in 1978, provided an alternate classification of self-maps of surfaces, showed the intimate connections of this set of problems to moduli problems, and involved Riemann surfaces with simple singularities, a topic already of interest to Bers for other reasons (to construct analytically the compactification of moduli spaces of nonsingular curves).¹⁴

Bers claimed that he was very lucky to be surrounded by first-rate colleagues. After retiring from Columbia in 1984, Bers accepted an invitation to join the Graduate Center of the City University of New York. His colleagues there included not only a number of his former students, but also the Einstein Professor, Dennis Sullivan, a mathematician Bers greatly admired, and who admired him as well. Sullivan's interaction with Bers resulted in a broadening of his research interests to include complex dynamics (the "no wandering domains" theorem), to alternate proofs of the AFT, as well as studies of holomorphic motions. His research on this last subject resulted in an important paper, among his final scientific manuscripts, with Halsey L. Royden, published in 1986 by *Acta Mathematica*.

At the time of his death, Lipa had a partially completed manuscript on compactification of moduli spaces. It was a topic he knew well and needed only time to complete. He announced results on this topic as early as 1974. His fertile imagination found so many distractions that, twenty years later, detailed Bers proofs regarding compactified moduli

spaces were still missing. The distractions were fortunate for mathematics. Many probably know how to finish this project on moduli. Few, if any, could have produced the new extremal problem or contributed as he has to the programs of Thurston and Sullivan. There were other unfinished projects at the time of his death. Lipa was interested in presenting a first-person account of his life and times. The first chapters of an autobiography are in the hands of the Bers family.

MENTOR AND EXPOSITOR

Lipman Bers's students were immediately admitted to the extended "Ahlfors-Bers family"—a mutually supportive group of mathematicians with common research interests consisting mostly, but not exclusively, of colleagues and former doctoral students of Ahlfors and Bers. Bers treated each of his students with respect, as a future friend and current colleague.¹⁵ His love for his students was, in part, independent of the level of their mathematical achievements and successes. His students returned this love and quite naturally extended it to embrace Mary Bers, whose warmth and genuine interest in them made most of Lipa's students feel that they were part of a wonderful family. Lipa was successful both at NYU and Columbia in attracting large numbers of talented students. For a long period, he and Ahlfors engaged in a gentle and "gentlemanly" competition to determine who had more students at various family gatherings. These occurred roughly every four years beginning with the 1965 Tulane conference. In the eighties this competition was extended to include grandstudents. At NYU Lipa's weekly lunch with "his children" was an event which attracted more than his students. Here and later, more noticeably, at Columbia he partially reverted to his advisor's style (in his unique "deformation" of it), supervising each

student's work *only* to the extent necessary. He designed an individual research program (thesis problem) for each student, suited to his or her abilities. At times, the original problem took years to solve—a dissertation resulted from an interesting special case or a related, but probably less central, set of questions. For example, Maskit received his Ph.D. in 1964. His task of extending Klein's work on combination theorems and describing how to construct an arbitrary function group from simpler groups was not completed before 1975. His success can be measured by the fact that the series of results previously known as the "Klein combination theorems" have become the "Klein-Maskit combination theorems."

Mathematics has been regrettably slow to change from its historically male-dominated status. An extraordinarily high proportion—sixteen of forty-eight—of Lipa's doctoral students were female. He was comfortable with women, as with men, and encouraged the inquiring minds of his students and colleagues without reference to gender. He practiced, in a most real and effective way, a policy of "equal opportunity/affirmative action," long before it became a part of public policy. He offered the same care and nurturing to all students who showed an interest or a talent for mathematics, working diligently to bring out the best in each. He was equally proud of the student who, in his opinion, would make first-rate contributions to research, to teaching, or to administration. He even admired would-be deans.

Lipa was a model expositor. His papers are clear and well written; he identified the key elements of the problem and the solution. He believed that before one left a subject, one ought to write a book. His books on gas dynamics and partial differential equations are such examples. His graduate teaching at NYU produced influential sets of lecture notes on pseudoanalytic functions (1952), on topology (1955),

on Riemann surfaces (1957), and on several complex variables (1963). He did not need to leave the field to produce the latter, nor the 1964 notes on moduli of Riemann surfaces based on his Zurich ETH lectures. He never wrote a book on moduli of Riemann surfaces since he never left the field. Partly in recognition of his 1972 article on moduli of Riemann surfaces and Kleinian groups in the *Bulletin of the London Mathematical Society*,¹⁶ which reported on his Hardy Lectures,¹⁷ the American Mathematical Society (AMS) awarded him the Steele Prize for exposition in 1974.

POLITICS AND SOCIAL ACTIVISM

When graduate study in Prague initiated his mathematical career, Bers was already a seasoned political and social activist and veteran. His concern for human rights was never diminished by his love for mathematics and his scientific and administrative efforts and achievements. He sought to broaden the social consciousness and elevate the conscience of the institutions that he could influence. A rare combination of personal qualities made his efforts extraordinarily effective. He was broadly cultured, with a rich and insightful knowledge of history; he was eloquent, witty, civil, and always good humored. His deep and passionate moral concerns found a tempered and effective, rather than righteous and polarizing, expression. His convictions were rendered in what he called “the international language of science: heavily accented English.”

Lipa’s experiences during his flight from Nazi-dominated Europe educated him about the excesses of some governments and people, and the generosity and courage of others. In America, the experience and wisdom that he brought to social issues played itself out mainly on three stages: at Columbia during the anti-Vietnam War protests; at the American Mathematical Society, as vice president 1963-65 and presi-

dent 1975-77; and at the National Academy of Sciences (NAS), as founder and chair of the Committee on Human Rights. In the fifties, before his prominence in the American scientific community extended beyond mathematics, he helped victims of McCarthyism and cold-war politics obtain academic positions.

In opposing the Vietnam War, Lipa felt a strong moral sympathy with the protest movement, but often tried to temper its destructive excesses. Echoes of these same political tensions reverberated during his leadership of the AMS, a historically conservative scholarly society narrowly focused on research-related issues. Bers helped orchestrate a substantial, but not destabilizing, broadening of its focus to include both general professional matters and issues of political and moral concern, but only insofar as they specifically affected professional mathematicians. In particular, he was instrumental in founding the AMS Committee on the Human Rights of Mathematicians, whose initial charge he drafted.

Lipa was poignantly aware of the importance of providing support for oppressed people, in particular scientists, throughout the world. The Human Rights Committee he helped found and lead at the NAS has had a distinguished record of interventions on behalf of persecuted scientists, engineers, and health professionals. Its continuing work is a living tribute to Bers's inspiration and example.

There is no better way to convey Bers's convictions, eloquence, and style than to quote his own words. Appealing to the Council of the NAS to speak out publicly on behalf of Andrei Sakharov, Lipa said, "When Sakharov began speaking out about victims of injustice, he risked everything, and he never knew whether his intervention might help. Should we, living in a free country, do less?" The Council was persuaded.

In a 1984 commencement address at the State University of New York at Stony Brook, on the occasion of receiving an honorary degree, Lipa articulated his moral credo for human rights activism:

. . . By becoming a human rights activist, as I urge you to do, you do take upon yourself certain difficult obligations. . . I believe that only a truly even-handed approach can lead to an honest, morally convincing, and effective human rights policy. A human rights activist who hates and fears communism must also care about the human rights of Latin American leftists. A human rights activist who sympathizes with the revolutionary movement in Latin America must also be concerned about human rights abuses in Cuba and Nicaragua. A devout Moslem must also care about the human rights of the Bahai in Iran and of the small Jewish community in Syria, while a Jew devoted to Israel must also worry about the human rights of Palestinian Arabs. And we American citizens must be particularly sensitive to human rights violations for which our government is directly or indirectly responsible, as well as to the human rights violations that occur in our own country, as they do.

Lipa's humane pragmatism was eloquently expressed during a symposium on human rights at the 1987 annual meeting of the NAS. He explained his belief that the Committee on Human Rights should focus on political and civil rights, which he called "negative rights," rather than on a "positive" economic, social, and cultural agenda. Negative rights prohibit government restraint of certain individual actions; for example, associating freely with colleagues from abroad. Positive rights instead require a government action, such as providing food, shelter, medical care, education, employment, and so forth. Lipa spoke thus:

As an old social democrat—I would say an old Marxist, if the word had not been vulgarized—I certainly recognize the importance of positive rights. Yet, I think there is a good reason why the international human rights movement, of which our committee is a small part, concentrates on negative rights. It makes sense to tell a government, "Stop torturing people." An order by the prime minister or the president to whomever is in charge

could make it happen. It makes sense to tell a foreign ambassador that, "The American scientific community is outraged that you keep Dr. X in jail. Let him out and let him do his work." It requires no planning, no political philosophy, and it can unite people with very different opinions.

Lipa, who was never accused of mincing words, added: ". . . the idea that people of the Third World are somehow less appalled by torture or by government-sponsored murder than citizens of developed nations [is, to me] rank racism." He then added: "It is quite a different matter to tell a foreign government of a developing country, 'You really should give this or that positive right to your people.' If we make such a demand in good faith, it must be accompanied by some plan for implementing this right and by some indication of the cost and of who will pay it and how it will be paid. . . . I think that the basic emphasis on negative rights by the international human rights movement is a reasonable thing." Lipman, ever the politician, continued: "Now, if we want to do things beyond this and participate in organizing a social democratic party in America, I will gladly discuss this later."

In his personal life and in advancing his social agenda, especially on human rights, Lipa was remarkably accurate in foreseeing the future. But he was not as able a prophet on all fronts. During 1966-68, Bers chaired the NAS/National Research Council Committee on Support of Research in the Mathematical Sciences. Its report boasted of the health and promise for mathematical research, and projected that there would be an expanding need for production of Ph.D.'s continuing into the next century. This was a great tribute to his optimism, if not to his appreciation of population dynamics.

COLLEAGUE AND FRIEND

Lipa and Mary were the co-founders of the extended Ahlfors-Bers family that provided a nurturing environment

for friends and colleagues. Many, probably most, complex analysts, quasiconformal mappers, and Russian dissidents who passed through the New York City area made at least one trip to the Bers home in New Rochelle. There they were welcomed; their good causes were given moral and, at times, financial support. Lipa's lifelong friendship and respect for Lars Ahlfors¹⁸ helped create a community and a mathematical dynasty. It helped shape the way a whole generation thinks about and does mathematics. Many of his professional colleagues, especially those from NYU and Columbia, were an important part of his social/political entourage. Perhaps most lasting and permanent were his ties to most of his former students. These students did not leave the family upon receiving "the union card." They stayed in touch and relied on his advice on professional, social, and family matters. No one could show more excitement about even the most trivial advance than Lipa. No one can forget his supreme compliment, "you sly dog," when he encountered a clever proof or surprising result by a student.

CONCLUDING REMARKS

Lipa joked that the president of the AMS had one statutory obligation and one traditional privilege. The obligation was to deliver a retiring presidential address. His was published in 1978, in the *Bulletin of the AMS*. The privilege, which disappeared by 1993, was to have an obituary published in the *Bulletin*. It was however quite fitting that the first issue of the new revised¹⁹ *Notices of the AMS* (January 1995) featured a number of articles "Remembering Lipman Bers." In the words of his friend Aryeh Dvoretzky "Like the sun in our sky, he cast a giant light."

NOTES

1. Published by Interscience.
2. He was looking for an inequality that would establish an existence theorem in partial differential equations and suspected that quasiconformal mappings might provide the needed a priori estimate.
3. He served for a period as chairman of the graduate program at NYU and for three years (1972-75) as department chair at Columbia.
4. Lipa's style in scholarship paralleled his teaching method. The low key and modest declaration that it was "merely" a new proof was followed by the dramatic listing of consequences of the result.
5. The paper containing the result, the only joint publication with L. V. Ahlfors, was published in the *Annals of Mathematics* in 1960.
6. Lipa objected to this name—the theorem is not measurable, the data that appear in the hypothesis are measurable, he explained.
7. Due to Lavrentiev in special cases and Morrey in the general case.
8. A generalization of the classical Cauchy-Riemann equations.
9. One of the most important aspects of this problem was reduced to showing that a cover of Riemann's moduli space, called the *Teichmüller space*, has a natural complex structure.
10. That Lipa, a fighter for social justice and against nazism, built his work on that of Teichmüller, an active opponent of racial justice and a proponent of nazism, was an oft-cited irony of his career. One of Lipa's early papers in this area quotes Plutarch (*Pericles* 2.1): ". . . It does not of necessity follow that, if the work delights you with its grace, the one who wrought it is worthy of your esteem."
11. This circle of ideas was completed in 1966 when H. Royden proved that the metric structure of Teichmüller space can be recovered from its complex structure.
12. Although Ahlfors describes Bers's finiteness proof as a model for his finiteness theorem, Ahlfors's paper, also published in the *American Journal of Mathematics*, appeared a year before Bers's.
13. All dates concerning mathematics research results refer to publication dates—the relevant theorem may have "circulated" for two to three years before publication. The "gentlemanly" manner in which mathematics was done in this field is illustrated by Ahlfors's frequent reference to his finiteness theorem as the "theorem finally

established by Bers” because he filled in the above-mentioned gap. Needless to say, Bers always thought of AFT as one of Ahlfors’s greatest accomplishments.

14. Carried out earlier, by others, in the setting of algebraic geometry.

15. As a result of his socialist background or European traditions, a student would be introduced to a visitor as Mr. or Ms. X; the visitor would in turn be introduced as Mr. or Ms. Y no matter what her or his titles might have been.

16. Another first-rate expository article appeared in the *Bulletin of the AMS* in 1981.

17. Bers was the first Hardy Lecturer, an honor bestowed by the London Mathematical Society.

18. Completely reciprocated.

19. And improved.

MOST SIGNIFICANT PUBLICATIONS OF
LIPMAN BERS

Bers worked in several areas of mathematics including partial differential equations (he coauthored an important book on the subject), minimal surfaces and complex analysis. It was to the latter field that he devoted his last and best productive scientific years (a span of over 40 years) and to which he made the most significant contributions; in some sense all of his work was in (certainly, preparation for) complex analysis. All the papers referenced here deal with this subject and appear in his selected works, [26]. His paper on minimal surfaces [3] is a perfect example of the role of complex analytic methods in related fields. His only paper on spaces of analytic functions [2] started a whole industry. The most productive period in Bers's scientific life saw fundamental contributions to Teichmüller theory. No papers perhaps have been more influential in this field than [1] and [9]. What appeared to him an oddity, [5], proved to be a key tool for understanding what is today called the *Bers embedding* [7]; other Teichmüller theory papers include [21], [12], [14], [19], [23] and [24]. Results about compactified moduli spaces are announced in [16]. The close relation between quasiconformal mappings and Teichmüller theory are explored in [4], [11] and [18]. Fundamental contributions to the theory of Fuchsian and Kleinian groups are contained in [6], [8], [10] and [15]. The expository papers [13] and [20] introduced a whole generation to subfields of complex analysis. In [22], Teichmüller theoretic methods are used to prove results about iteration of rational maps; [25] is a contribution to the study of holomorphic motions; [17] opens up areas for future contributions by others.

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Photo by Bachrach

George D. Buhfuff

GEORGE DAVID BIRKHOFF

March 21, 1884–November 12, 1944

BY OSWALD VEBLEN

GEORGE DAVID BIRKHOFF was born at Overisel, Michigan, on the twenty-first of March, 1884. His ancestry was Dutch on both sides. His father, David Birkhoff, came from Holland in 1870, and during George David's growing years was a physician in Chicago. Birkhoff studied at the Lewis Institute, Chicago, from 1896 to 1902, and at the University of Chicago for a year. After this he went to Harvard, where he received the Bachelor's degree in 1905.

Beginning in the year 1900 there appeared in the problem department of the *American Mathematical Monthly*, edited by B. F. Finkel, a series of notes, solutions, and problems by H. S. Vandiver, of Bala, Pennsylvania. In 1901 Birkhoff, who had doubtless found the monthly in the old John Crerar Library, began exchanging letters about various questions in the theory of numbers with Vandiver, who was then nineteen years old. This correspondence resulted in the publication in 1904 of their joint paper in the *Annals of Mathematics* "On the integral divisors of $a^n - b^n$." So far as I know this was Birkhoff's only publication in the theory of numbers,

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but Vandiver has told me that Birkhoff was in possession in those days of at least one number-theoretical theorem which is now counted among the notable contributions of a distinguished mathematician in another part of the world. In later life Birkhoff often showed an interest in number theory, but seems never to have taken the deep plunge which would have been necessary in order to bring up new results of the sort that would have satisfied him. It was not until his Princeton period that he met Vandiver personally.

During his undergraduate years he also made a definite beginning in analysis, as is proved by the fact that he read a paper entitled "A general remainder theorem" before the American Mathematical Society in New York in February 1904 (*Amer. Math. Soc. Bulletin* 10: 280). This was the basis of a paper entitled "General mean value and remainder theorems with applications to mechanical differentiation and quadrature," published in the *Transactions of the American Mathematical Society*, volume 7 (1906).

Birkhoff returned to the University of Chicago in the fall of 1905 and received his Ph.D. *summa cum laude* in 1907 at the age of twenty-three. This is not an unusual age for a European doctorate but, unfortunately for the New World, it is an exceptionally early one in the United States. Birkhoff's student period had been divided between the only two great mathematical centers which existed in America at that time. From Osgood and Bôcher he obtained a thorough introduction to the classical methods of analysis, and from E. H. Moore who was then at the outset of his adventure in "General Analysis," a grasp of the abstract modernistic ideas which have characterized so much of mathematics during the last four decades. Birkhoff reacted rather strongly against the latter and in favor of the former. His view was that while one should understand the analogies between the linear problems of analysis and those of classical geometry and

algebra, his attention should be concentrated on strategically important specific problems of the classical type.

His doctoral dissertation on asymptotic problems of ordinary linear differential equations does in fact continue the tradition to which Bôcher belonged. But it also uses the powerful methods of the Fredholm theory of integral equations and the broad general ideas which E. H. Moore was trying to exploit. It initiated a series of studies by which he left his mark on most of the principal branches of the theory of linear differential equations: regular and irregular singular points, expansion and boundary value problems, separation theorems, and his generalization of the Riemann problem. With these researches it seems reasonable to group his work on matrices of analytic functions and his remarkable contributions to the theory of linear difference equations, as constituting one of the three principal periods of Birkhoff's scientific activity. In time, this period overlaps his whole career, but his most intense effort in these fields belongs to his earlier years.

After receiving his doctorate in 1907, Birkhoff spent two years in Madison as an instructor in the University of Wisconsin. Here he learned more analysis from E. B. Van Vleck, and in particular had his attention directed toward linear difference equations. This period also includes his marriage in 1908 to Miss Margaret Elizabeth Graftus, a union of mutual devotion and helpfulness which lasted throughout the rest of his life. There were three children, Barbara (Mrs. Robert Treat Paine, Jr.), Garrett, and Rodney. Garret has already gained distinction as a mathematician of quite different tendencies from those of his father.

In 1909 he came to Princeton University as a preceptor and was promoted to a professorship on the occasion of a call to Harvard in 1911. At Princeton during this period a third significant current of American mathematical thought,

a geometrical one, was gathering force. Birkhoff shared in the exploratory studies then being made of analysis situs, as it was called before being formalized into "topology," and saw their close relation to the class of dynamical problems which were at this time taking definite form in his mind. Incidentally, he had more than one try at the four-color map problem, to solve which remained throughout life one of his dearest aspirations.

In 1912 Birkhoff reconsidered the question of returning to Harvard, and accepted an assistant professorship in that university, in which rank he remained for another seven years. He thus returned to the most stable academic environment then available in the country, and settled into a long period of creative work undisturbed by necessity, common in American universities of this epoch, to build an environment in which scientific work can bear fruit. The final transition to Harvard was recognized by Birkhoff himself and his most intimate friends as marking the end of the formative period of his career. I remember in particular a delightful letter which he received from E. H. Moore, ending with the words written out in bold characters: AVE ATQUE VALE.

As remarked by Marston Morse, however, "Poincaré was Birkhoff's true teacher." I remember well how frequently, in the walks we used to take together during his sojourn in Princeton, Birkhoff used to refer to his reading in Poincaré's *Les Méthodes Nouvelles de la Mécanique Céleste*, and I know that he was intensively studying all of Poincaré's work on dynamics. In a very literal sense Birkhoff took up the leadership in this field at the point where Poincaré laid it down.

Poincaré died in 1912 and his last paper reached Princeton in the summer of that year. In it Poincaré showed that the existence of periodic solutions of the restricted problem of three bodies can be deduced from a very simple-

sounding geometric theorem. But he had not been able to prove the theorem except in special cases, and he felt that at his age (he was only fifty-eight when he died) he could not be sure of being able to return to it again, as he should have liked to do, after letting his ideas lie fallow for a while. Before the year was over Birkhoff had given a simple but profound proof of "Poincaré's Geometric Theorem." The publication of this proof in the *Transactions of the American Mathematical Society* for January 1913 brought immediate and worldwide fame to its author, an acclaim which, for once, was justified by subsequent events.

His researches in dynamics constitute the middle period of Birkhoff's scientific career, that of maturity and greatest power. Their chief characteristics can be seen already in his first publication, "Quelques théorèmes sur le mouvement des systèmes dynamiques," which appeared in the *Bulletin de la Société Mathématique de France* in 1912. In this paper after a careful examination of the properties of stable motion, Birkhoff introduced his concept of "recurrent motion" which has played a role alongside the classical concept of periodic motion in all further discussions of the descriptive properties of dynamical trajectories. It is, for example, the starting point of the "symbolic dynamics" of Morse and Hedlund. While Poincaré had made good use of topology in the theory of dynamical systems, it was Birkhoff's merit to have powerfully supplemented this by the use of the Lebesgue measure theory. In the unfolding of the geometric picture of the general case in dynamics, one of the significant stages was the introduction of the concept of "metric transitivity" which appeared for the first time in his joint paper with Paul Smith on "Structure analysis of surface transformations" in *Liouville's Journal* (1928) where it was applied to two-dimensional problems of a class more general than those of dynamics. This line of thought reached its climax in the

winter of 1931-32 when under the stimulus of closely related discoveries by Koopman and von Neumann he succeeded in proving his justly famous “ergodic theorem.” Birkhoff’s ergodic theorem, though it does not completely solve the basic problem of statistical mechanics at which it is aimed, has reduced that problem to a definite question about metric transitivity, and is also a milestone in the progress of measure theory. Birkhoff’s proof, which, characteristically, used the rough and ready tools picked up along the path which led him to it, has been replaced by simpler and more sophisticated methods, and there has grown up a rather extensive literature of “ergodic theory.”

Most of Birkhoff’s publications in dynamics are devoted to dynamical systems of two or three degrees of freedom. Here he enjoyed Poincaré’s concept of a “surface of section” and the transformations in it determined by a family of dynamical trajectories. Poincaré’s geometric theorem is a case in point. He also carried the use of the representation of trajectories by means of geodesics on surfaces considerably beyond the stage reached by Poincaré and Hadamard. His “minimax principle” was the starting point of Morse’s “Analysis in the Large” which has done so much to make topology effective in analysis.

Although Birkhoff’s most notable successes were in the geometrical aspect of dynamics, he did not neglect, nor was he deficient in power over the analytic formalism. He achieved as good a view of the whole field of theoretical dynamics as did anyone in his time. For more authoritative accounts and evaluations of Birkhoff’s work both in this field and in what I have called his first period, I should like to refer the reader to the notices by E. T. Whittaker in the *Journal of the London Mathematical Society*, volume 20 (1945), and by Marston Morse in the *Bulletin of the American Mathematical Society*, volume 52 (1946). In addition, there are many interesting

comments on his own work and revelations of his point of view toward that of his contemporaries, in Birkhoff's address on "Fifty years of American mathematics" which was published in 1938 in a volume celebrating the semicentennial of the American Mathematical Society.

The third phase of Birkhoff's scientific career was that in which he sought to extend mathematical methods into other fields of thought,—physics, aesthetics, and even ethics. He was already speculating on the possibility of a mathematical theory of music, and indeed of art in general, while he was in Princeton. But he did not give these ideas to the world until 1928 when he delivered one of the principal addresses of an international mathematical congress under the title, "Quelques éléments mathématiques de l'art," in the Salon del Cinquecento of the Palazzo Vecchio at Florence. Later on, after much reflection and a trip around the world, he published his book *Aesthetic Measure*, in 1933. In 1942, "A mathematical approach to ethics" appeared in the *Rice Institute Pamphlets* (vol. 28). These studies, though Birkhoff took them quite seriously, seem to me to be definitely less likely than his purely mathematical work to survive.

Something similar, I think, must be said about his efforts in physics. Like Goethe and Hilbert, he always remained an outsider. It may have been that the very strength of his faith in mathematical insight prevented him from properly appreciating the insight of the physicists. His active interest in physics seems to have begun with a course in relativity which he gave in the winter of 1921-1922 and it continued increasingly up to the time of his death when he was engaged in exploiting a gravitational theory of his own. As his contribution to physics there remain some unquestionable improvements in mathematical technique, some criticisms of present tendencies, and a physical theory which can sur-

vive only if it passes the tests both of experiment and assimilability into the growing body of science.

Among the unconscious revelations of the address on "Fifty years of American mathematics," one of the most vivid is that of the depth and sincerity of Birkhoff's devotion to the cause of mathematics, and particularly of "American mathematics." This, along with his devotion to Harvard, was always a primary motive. It may be added that a sort of religious devotion to American mathematics as a "cause" was a characteristic of a good many of his predecessors and contemporaries. It undoubtedly helped the growth of the science during this period. By now, mathematics is perhaps strong enough in the United States to be less nationalistic. The American mathematical community has at least been healthy enough to absorb a pretty substantial number of European mathematicians without serious indigestion.

Birkhoff was always on the lookout for talent among the young mathematical aspirants who came to Harvard. I recently looked over some of his letters and found them full of comments on the young men for whom he had hopes. Some of the names I had forgotten, but many of the comments are still enjoyable. His capacity for intelligent study of the qualifications and needs of younger mathematicians was used for the benefit of science on a much wider stage during the years (1925 to 1937) that Birkhoff, Bliss, and I were the mathematical members of the National Research Fellowship Board. I am sure that Bliss will agree with me about Birkhoff's remarkable capacity for picking "the good ones" and guessing what they needed. While Birkhoff was subject to as many prejudices as most of us, he kept always what most of us lose as we grow older, the power to see people and events simply and naively rather than with reference to current opinion.

Birkhoff unhesitatingly accepted the public responsibilities that came his way. He served as Dean of the Faculty of Arts and Sciences at Harvard from 1937 to 1939. He carried his share of military research work during both World Wars. He traveled extensively and accepted a large number of invitations to lecture, both those of an honorific sort and those that simply afforded an opportunity to extend mathematical culture into new areas. He did much of the unrewarded administrative work of the American Mathematical Society. For example, he served on the committee which, after a lively debate, decided to undertake the publication of *Mathematical Reviews*. After the main issues had been decided against his judgment, he cooperated loyally and actively in the working out of details.

It is pleasant to record that Birkhoff received nearly all the distinctions, such as honorary degrees and elections to societies and academies, that can come to a mathematician, and received many of them at an unusually early age. He became a member of the American Philosophical Society in 1921 and was a frequent attendant at its meetings.

During the last few years of his life Birkhoff knew that his heart was no longer as strong as it had been, but he never slackened up his scientific and other work. He died in his sleep on November 12, 1944.

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KARL WOLFGANG DEUTSCH

July 21, 1912–November 1, 1992

BY RICHARD L. MERRITT, BRUCE M. RUSSETT, AND
ROBERT A. DAHL

KARL WOLFGANG DEUTSCH was born in 1912 in Prague, Czechoslovakia. His father was an optician. His mother, active in various political causes both at home and internationally, eventually became one of Czechoslovakia's first female parliamentarians. After graduating with high honors in 1931 at the German Staatsrealgymnasium in Prague, Deutsch went on to take his first degree in 1934 at the Deutsche Universität in Prague. His advanced studies at that university were interrupted because of his outspoken leadership of anti-Nazi groups. After a clash with the faculty of the Deutsche Universität, which by then had fallen under the control of a pro-Nazi majority, he left for a period to study optics in England. Fortunately for the social sciences, his study of optics, together with his study of mathematics there and earlier, helped prepare him for his later pioneering work in quantitative political science. On returning to Czechoslovakia he was granted admission to the Czech national Charles University, a signal honor for a German-ethnic Czech, where he attained high honors in seven fields and received his doctorate in law (JUDr) in 1938. Shortly thereafter, Deutsch and his new bride, Ruth, went to the United States for what was intended to be a brief stay. But with the capitulation of Britain and France to Hitler at Munich

and the Nazi takeover of the Sudetenland, Karl and Ruth decided it would be unsafe to return.

In 1939 Karl and Ruth began a new life in the United States. The recipient of a student-funded scholarship for refugees from Nazism, Deutsch entered Harvard University for further graduate training. During his first years in America, he toured the country extensively, speaking on behalf of the Free Czechoslovak movement. America's entry into the war led Deutsch into the service of the United States government, where among other things he was a major contributor to the famous "Blue Book" on Juan Peron's efforts to extinguish democracy in Argentina. Later he was a member of the International Secretariat of the San Francisco Conference of 1945, which created the United Nations.

The war over, Deutsch resumed his doctoral studies at Harvard while teaching at the Massachusetts Institute of Technology. Simultaneously he began publishing articles that showed both his mature scholarship and, more significantly, perspicacity in his view of society and politics. His dissertation, "Nationalism and Social Communication," was awarded Harvard's Sumner Prize in 1951. The following year Deutsch was promoted to the rank of professor of history and political science at MIT, and a year later his dissertation appeared as a book.¹

Almost immediately Deutsch was in great demand in the scholarly community. In 1953-54 he was at the Center for Research on World Political Institutions at Princeton University, where he integrated the findings of an interdisciplinary group with his own thinking and turned the result into a highly significant theoretical analysis of large-scale political integration, *Political Community and the North Atlantic Area*.² During the year 1956-57 he was a fellow at the Center for Advanced Study in the Behavioral Sciences at Palo Alto, California, where he laid the basis for the

book that would prove to be one of his most significant contributions, *The Nerves of Government*.³ During the same period he held a visiting appointment at the University of Chicago (in 1954) and received his first Guggenheim Fellowship (in 1955).

In 1957 Deutsch went to Yale University as visiting professor and a year later accepted a permanent appointment as professor of political science. His first substantive accomplishment there was the completion of a book (with Lewis J. Edinger), *Germany Rejoins the Powers*,⁴ that used data on public opinion, the background of elites, and economics to analyze the federal republic's postwar progress, and was a highly original study of politics and society in West Germany. During his 10 years at Yale he completed the intellectual framework and set up an organization—the Yale Political Data Program—to develop quantitative indicators for testing significant theories and propositions in social science; organized a multi-university research team, sometimes called the Yale Arms Control Project, to investigate the prospects for arms control, disarmament, and steps toward unification in the Western European environment; and took on an increasingly important role in the development of international social science. In 1960 he also held a visiting appointment at Heidelberg University and in 1962 he was a visiting fellow at Nuffield College of Oxford University.

Deutsch moved to Harvard University in 1967, and in 1971 was appointed Stanfield Professor of International Peace. Despite the rapidly growing demand for his appearance as a guest lecturer and his dramatically expanding role in international social science, he continued his steady record of initiating and completing new projects. He held guest professorships at the Goethe University in Frankfurt-am-Main, the University of Geneva, Heidelberg University, the University of Mannheim, the University of Paris, and the

University of Zurich. He also lectured at major universities throughout the world, and served as consultant to various government agencies. And he received such further honors as a second Guggenheim Fellowship (in 1971) and appointment as resident scholar at the Aspen Institute of Humanistic Studies (1973-74).

His colleagues gave testimony to their esteem for his work by electing him to offices in numerous scholarly organizations. Deutsch was elected president of the New England Political Science Association in 1964-65; president of the American Political Science Association in 1969-70, after having served as program chairman of its 1963 annual meeting; and president of the Peace Science Society (International) in 1973. He served the International Political Science Association as a member of the program committee (1970-76), coordinator of the triennial International Political Science Association world congress (Montreal, 1973), vice-president, and finally as president for 1976-79. He received six honorary degrees from American and European universities.

Deutsch made his impact on scholarship not only by his numerous publications but also equally from the force and manner of his personal presentations. His commitment to teaching was manifested in both lectures and seminars. His undergraduate lectures, although often extemporaneous, almost always combined profundity with wit. At Yale he gave uncounted lectures to packed lecture halls, and virtually without exception each lecture was followed by an ovation. Yale undergraduates honored him in 1965 by awarding him the William Benton Prize of the Yale Political Union for having done most to stimulate and maintain political interest on campus—an award, incidentally, that alone was featured prominently in the Deutsch home.

During a period when many graduate students in political science were seeking a greater degree of analytical rigor

and concern for quantitative evidence than had characterized the field, they found Deutsch's combination of intellect, range, and verve enormously stimulating. His teaching skills were also revealed in his two influential textbooks, *The Analysis of International Relations*⁵ and *Politics and Government*,⁶ which not only made basic material accessible to students but also stimulated their involvement in serious analysis of political phenomena. His influence on students was so great that some of the most productive scholars who followed him in the fields of international and comparative politics had been students in his seminars.

Deutsch believed that an important part of his task as educator was to present guest lectures at universities and elsewhere in the United States. He was invariably generous with his time and his thoughts and seemed happiest when he engaged an individual or audience in an intellectual dialogue where the give and take of discussion, with both challenges and stimulation, provided an opportunity for him, as well as his audience, to learn something new. He was noted for his ability to generate enormous numbers of ideas in rapid-fire fashion, typically in what appeared to be, and probably was, a spontaneous association of ideas, when he would briefly consider a bit of data or an idea and immediately ask for more information or come forth with a new hypothesis or even a full-blown theory. Although he ran the risk of propounding ideas that were not well thought out and on further consideration might prove to be mistaken, the sheer volume of his intellectual sparks generated a fire that stimulated his audiences to think more deeply about his remarks.

In his relations with students Deutsch was interactive, nurturant, generative. He truly cared about his students and former students. Above and beyond normal expectations, he helped them with the challenges of getting a job,

writing assignments, conference invitations, and other opportunities. He wrote many articles and books with students and junior colleagues, during which he shared work and authorship equitably. Perhaps the most unkind comment any of his former students could recall him making concerned a senior colleague who, he said, was the sort who never sends the elevator back down.

Although his work contributed directly or indirectly to many different aspects of political science, in several areas his work revolutionized scholarly thought and research: large-scale political community formation at the national and international levels; cybernetic approaches to politics and society; and the development and use of quantitative data to test and reformulate political theories.

Deutsch's youth was spent in a multinational state destined to endure a series of tragedies. Doubtless in response to his observation of the horrors brought to Europe by narrow-minded nationalism before and during the Second World War, Deutsch early in his career focused his emotional and intellectual energies on issues involving nationalism and the formation of large-scale political communities. Indeed, he wrote his doctoral dissertation on nationalism—a brave decision given both the flood of past writing on the topic and the strong emotions it engendered among even the most intellectual of scholars. *Nationalism and Social Communication*¹ recast the traditional literature into a more rigorous form, enriched not only by concepts drawn from anthropology, social psychology, and other social sciences but also by Deutsch's own insights. What was perhaps even more innovative at the time, he tested his conjectures against quantitative data from the real world. The book presented a new model of nationalism based upon the idea of a "people" bound together by habits of and facilities for communication. New data derived from four case studies of national

growth and decay demonstrated the validity of the model and set the stage for further data gathering and tests of the basic model. For many years the paradigm offered by Deutsch in these books and elsewhere⁷ dominated the scholarly study of nation building and international integration.

Many of the theoretical perspectives that animated Deutsch's analysis of nationalism and social mobilization also apply to his work on large-scale political integration and unification. He used these perspectives to focus the sometimes-divergent research performed by members of the research group at Princeton University's Center for Research on World Political Institutions. Each individual member had worked on a case study of national integration or disintegration but the various pieces were essentially an accumulation of case studies. Deutsch was invited to join the project with the specific hope that, by applying his historical knowledge of nationalism and his concepts derived from the study of communication in societies, he could integrate these disparate pieces.⁸ The result was the pioneering study *Political Community and the North Atlantic Area*.² In this view, the formation of large-scale community rested less on factors like common language or high levels of mutual responsiveness and, as with the development of nationalism, more on the existence of two-way channels of communications between elites and mass and among non-elites.

Although one manifestation of political integration may be the creation of a new state by amalgamating two or more previously separate units, Deutsch emphasized the creation of "expectations of peaceful change," that is, "security communities" among peoples who may or may not be unified under a single government. This focus on community formation, rather than on amalgamation per se, was central not only to Deutsch's work but also to that of the integration theorists who worked with him or otherwise attempted

to apply his insights. While much work remains to be done, Deutsch's highly original formulations lend themselves well to cumulative research.⁹ His attention to domestic politics and transnational actors as powerful influences on relations between nation-states was taken up in the transformation of theory and research on international politics at the end of the twentieth century.¹⁰

One of Deutsch's key insights in his treatments of integration at the national and supranational levels was that unified government is neither a necessary nor a sufficient condition for peace among the various parties. Indeed, in some cases unified government may even damage the prospects for peace. Deutsch focused attention on two possible sources of failure. First, if unification is undertaken before certain necessary or desirable background conditions exist the outcome may be conflict and a breakdown of the association. Second, if unification occurs among unequal partners, their association may lend a degree of rigidity and legitimacy to the exploitation of the weak by the strong.

Central to Deutsch's new paradigm was his view of anarchy, war, and amalgamation. Picking up an earlier strand of political thought from Hugo Grotius, Deutsch argued that no axiomatic relationship exists between anarchy and war. Indeed, historical evidence suggests that ineffective or premature efforts to mitigate anarchy may even cause war. Using the language of communications theory, Deutsch showed that amalgamation engenders transactions that increase loads on a governmental system. If the system does not have or is unable to develop capabilities commensurate with these added loads, the consequence may be mutual frustration and hostility. Accordingly, the search for world government can become self-defeating.

This concern, derived from his theoretic study of communications and his empirical examination of nationalism

and political community in the North Atlantic area, informed the investigation undertaken in the mid-1960s by Deutsch and others of arms control and unification in Western Europe. The project rested on systematic interviews with French and West German political and economic leaders, studies of public opinion, and quantitative analyses of the press in four countries. It sought to determine existing trends and then to project these trends into the short-range future.¹¹ In general, the study found an imbalance between what was commonly expected from a united Europe and the infrastructural support needed to create whatever institutions were necessary to satisfy these expectations. On the basis of this research Deutsch cautioned against further immediate steps toward unification.

Strong ties among unequal partners, Deutsch argued, also carried dangers. Although a structure that enforces a rigorous division of labor between the masters and the enslaved may indeed enhance the overall production in a society, the appearance of stability may be deceptive. Deutsch's studies of nationalism and national integration revealed that an imbalanced scheme for organizing society, in which some pay an extraordinary price while others enjoy extraordinary benefits, is inherently unstable and hides the development of patterns of social communication, which can lead to unrest and even revolution. In the global system, too, members of some nation-states, especially those with poorly developed economic systems, fear that their involvement in the world economy and the political system produces an extremely disproportionate distribution of benefits both globally and within their own states. This leads them to question the legitimacy of the prevailing structures. At the same time, however, the costs of dissociating themselves from those structures can be immense. These conflicting demands, anticipated by Deutsch and manifested under the pressures

of globalization, pose one of the great dilemmas of our times.

Throughout much of Deutsch's scholarly life this dilemma, spawned by economic and political interdependence, led to furious debate and some scientific analysis. Analyses directed against the industrialized states, which were perceived as benefiting most in the long run from the status quo, became commonplace, as did strident exhortations to the less developed world to dissociate itself from the prevailing system, whatever the immediate cost might be. Deutsch insisted on scientific analysis directed to the central questions: How accurately did conflicting interpretations of this great dilemma reflect the real world? How could we devise means to ascertain the direction and speed of current developments? In addition to his cool analysis of the assumptions and logic of theories about dependency and structural imperialism,¹² Deutsch forced scholars to search for objective, reproducible, and when possible, quantitative data with which to test assertions and the theories themselves.

Although the field of cybernetics was first developed by Norbert Wiener of the Massachusetts Institute of Technology, Deutsch spelled out the political implications of cybernetics in a series of impressive articles that formed the basis for *The Nerves of Government*.³ His subsequent research examined a number of questions stimulated by his interest in cybernetics: the ratio between internal and external communications and transactions of a country as an indicator of the degree of its self-preoccupation or self-closure over time; governments' share of facilities for controlling the flow of information and the effect of this variable on governmental performance; the ways decision-making systems deal with communications overload; and the forms and consequences of decentralization in governmental decision making.

Applying cybernetics to politics made crystal clear the need for data—impersonal, replicable, quantitative—to test significant propositions derived from major theories. Deutsch assembled data on population movements, language assimilation, and the flow of such international transactions as trade and mail. In a seminal article of 1960 “Toward an Inventory of Basic Trends and Patterns in Comparative and International Politics,”¹³ Deutsch generalized this research experience and assessment of needs to suggest how large-scale data banks could aid in the development and testing of theory on such topics as political development and the probabilities of war and peace.

Deutsch’s ideas on the development of cross-national data banks contained four elements. First, it was necessary to use data that, however insufficient they might be, could be obtained fairly readily to show that the entire notion had intellectual merit and theoretic promise. Second, efforts would have to be undertaken, always within a theoretic frame of reference that informed the researcher’s criteria of relevance and reliability, to gather systematically sets of better data. Third, since no single scholar could accomplish the task of assembling adequate data relevant to political theories, data programs should comprise multidisciplinary and, Deutsch hoped, multinational research teams. Even if this was not always possible, it was imperative to create a multidisciplinary and cross-national network of conferences and other means of communication to exchange scientific information, evaluate each other’s efforts, and search out new directions for future research and analysis. Fourth, new techniques must be developed to analyze the data in a theoretically meaningful way.

Deutsch was in the forefront of all these developments, which he viewed as simultaneous, mutually reinforcing, and requiring prodigious organizational and intellectual work.

With the intellectual collaboration of Harold D. Lasswell and the practical support of two younger political scientists, Richard L. Merritt and Bruce M. Russett,¹⁴ Deutsch set up the Yale Political Data Program. Its first major publication, *World Handbook of Political and Social Indicators*,¹⁵ provided a massive body of data that was drawn on in numerous scholarly articles by Deutsch, Russett, and others in contributions to the development of empirical theory.¹⁶ Deutsch's insistence on the speedy publication of these volumes and on the widespread dissemination of the machine-readable data sets epitomized his commitment to the sharing of scientific information.

Deutsch's influence and the importance of quantitative data were felt in other ways as well. For one thing, Deutsch together with Stein Rokkan and others helped to create a series of conferences to discuss questions of quantitative data, data banks, and social science theory. Many of these resulted in substantial volumes that contributed to what some have called the data movement.¹⁷ This work stimulated other collections of political and social indicators by scholars across the world.¹⁸ In short, the increasing use of aggregate data and the increasing sophistication of modes of mathematical analysis have revolutionized the study of politics.

Returning to the concept of steersmanship: Nation-states can act in ways to enhance or diminish the chances of war. Steersmanship is even more possible when we have data and models for projecting nation-state behavior into the future. Only in recent years have scholars developed data-based econometric and sociometric models sufficiently sophisticated to permit reasonably accurate forecasting and hypothetical adjustments of variables to stimulate contingent futures. The possibility of creating comprehensive models

for world politics nonetheless once seemed remote to most scholars.

The possibility of global modeling intrigued Deutsch not only because of the challenge it posed but no doubt also because it brought together all his interests and skills: a concern with preventing the outbreak of violence, the need of nation-states for strategic roadmaps to help them steer their way in the global system, and a focus on generating hypotheses about human behavior, testable by data from the real world, that can be used to model social processes. Early efforts at global modeling he found disappointing because of their questionable assumptions and lack of attention to key social and especially political variables.¹⁹

The next logical step, then, was to create the organizational framework to make global modeling more useful for political decision makers. The opportunity came in 1976 when Deutsch was asked to help found and co-direct the International Institute for Comparative Social Research of the Science Center Berlin. There he created a research team on global modeling with the aim of producing a functioning, computerized model of global society based not only on an integrated set of mathematical equations but also on hard data about political and social processes.

Advances in global modeling with the stress on data and the use of increasingly sophisticated modes of mathematical analysis have revolutionized the study of politics. Deutsch was at the forefront of this movement. His own research broke new paths, and his teaching inspired others to push out even farther the frontiers of knowledge. His organizational efforts at the international level helped to create a worldwide network of scholars and data-based research programs that have provided a firm basis for still further developments.²⁰

Here again, as in all his teaching, lectures, and writing, Karl Deutsch displayed his deep commitment to the development and use of knowledge for the betterment of humankind.

NOTES

1. K. W. Deutsch. *Nationalism and Social Communication: An Inquiry into the Foundations of Nationality*. Cambridge, Mass.: Technology Press of the Massachusetts Institute of Technology, and New York: Wiley, 1953; 2nd ed., Cambridge, Mass.: MIT Press, 1966.

2. K. W. Deutsch, S. A. Burrell, R. A. Kann, M. Lee, Jr., M. Lichterman, R. E. Lindgren, F. L. Loewenheim, and R. W. van Wagenen. *Political Community and the North Atlantic Area: International Organization in the Light of Historical Experience*. Princeton, N.J.: Princeton University Press, 1957.

3. K. W. Deutsch. *The Nerves of Government: Models of Political Communication and Control*. New York: Free Press, 1963; 2nd ed., 1966).

4. K. W. Deutsch and L. J. Edinger. *Germany Rejoins the Powers: Mass Opinion, Interest Groups, and Elites in Contemporary German Foreign Policy*. Stanford, Calif.: Stanford University Press, 1959.

5. K. W. Deutsch. *The Analysis of International Relations*. Englewood Cliffs, N.J.: Prentice-Hall, 1968; 2nd ed., 1978.

6. K. W. Deutsch. *Politics and Government: How People Decide Their Fate*. Boston: Houghton Mifflin, 1970; 3rd ed., 1980.

7. See, for example, K. W. Deutsch and W. J. Foltz, eds. *Nation Building*. New York: Atherton Press, 1963; K. W. Deutsch. *Nationalism and Its Alternatives*. New York: Knopf, 1969; K. W. Deutsch. *Nationenbildung-Nationalstaat-Integration*, ed. A. Ashkenasi and P. Schulze. Düsseldorf: Bertelsmann Universitätsverlag, 1973; and numerous articles.

8. Deutsch spelled out his own ideas in *Political Community at the International Level*. Garden City, N.Y.: Doubleday, 1954.

9. Deutsch's basic ideas on nationalism and integration stimulated numerous monographs exploring their implications, leading to independent contributions. A few of those were B. M. Russett. *Community and Contention: Britain and America in the Twentieth Century*. Cambridge, Mass.: MIT Press, 1963; W. J. Foltz. *From French West Africa to the Mali Federation*. New Haven, Conn.: Yale University Press, 1965; A. Lijphart. *The Trauma of Decolonization: The Dutch and*

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10. A recent example is B. Russett and J. R. Oneal. *Triangulating Peace: Democracy, Interdependence, and International Organization*. New York: Norton, 2001.

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12. K. W. Deutsch. Imperialism and neocolonialism. In Peace Science Society (International) *Papers: The Fifth International Conference, November 1973*, ed. W. Isard and T. M. Fogarty 23 (1974):1-26.

13. K. W. Deutsch. Toward an inventory of basic trends and patterns in comparative and international politics. *Am. Polit. Sci. Rev.* 54(1)(1960):34-57.

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15. B. M. Russett, H. R. Alker, Jr., K. W. Deutsch, and H. D. Lasswell. *World Handbook of Political and Social Indicators*. New Haven, Conn.: Yale University Press, 1964. Subsequent editions are C. L. Taylor and M. C. Hudson. *World Handbook of Political and Social Indicators*, 2nd ed., New Haven, Conn.: Yale University Press, 1972, and C. L. Taylor and D. A. Jodice. *World Handbook of Political and Social Indicators*, 3rd ed., New Haven, Conn.: Yale University Press, 1983.

16. See D. H. Jodice, C. L. Taylor, and K. W. Deutsch, *Cumulation in Social Science Data Archiving: A Study of the Impact of the Two World Handbooks of Political and Social Indicators* (Konigstein/Ts.: Anton Hain, 1980). An earlier review is B. M. Russett. The *World Handbook* as a tool in current research. In *Aggregate Data Analysis: Political and Social Indicators in Cross-National Research*, ed. C. Lewis Taylor, pp. 143-63. Paris: Mouton, 1968.

17. See, for example, S. Rokkan, ed. *Data Archives for the Social Sciences*. Paris: Mouton, 1966; M. Dogan and S. Rokkan, eds. *Quantitative Ecological Analysis in the Social Sciences*. Cambridge, Mass.: MIT Press, 1969; H. R. Alker, Jr., K. W. Deutsch, and A. H. Stoetzel, eds. *Mathematical Approaches to Politics*. San Francisco: Jossey-Bass, 1973; and K. W. Deutsch and R. Wildenmann, eds. *Mathematical Political Analysis: From Methods to Substance*. In *Sozialwissenschaftliches Jahrbuch für Politik*, vol. 5, ed. R. Wildenmann. München: Günter Olzog Verlag, 1976.

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19. See K. W. Deutsch. Toward drift models and steering models. In *Problems of World Modeling: Political and Social Implications*, ed. K. W. Deutsch, B. Fritsch, H. Jaguaribe, and A. S. Markovits, pp. 5-10. Cambridge, Mass.: Ballinger, 1977.

20. A festschrift *From National Development to Global Community: Essays in Honor of Karl W. Deutsch*, eds. R. L. Merritt and B. M. Russett.

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London: George Allen and Unwin, contains, in addition to many essays on topics central to Deutsch's work, a complete bibliography of his publications through 1980. This essay is adapted from the introduction to that volume.

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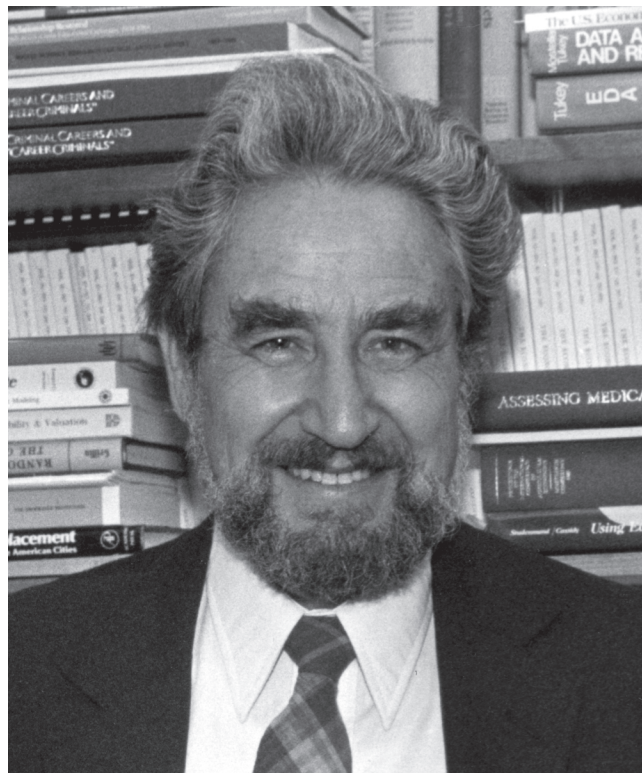
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Jane Reed photo/Harvard University

John Lubery

ZVI GRILICHES

September 12, 1930–November 4, 1999

BY MARC NERLOVE

I. PROLOGUE

ZVI GRILICHES was born in Kaunas, Lithuania, on September 12, 1930, and died on November 4, 1999, in Cambridge, Massachusetts. The story of how he got from there to here is a long one with a harrowing beginning. It has been told by Griliches himself in a talk presented on the eve of Yom Hashoah at the Harvard-Radcliffe Hillel Foundation (1992) and in an interview given to Alan Krueger and Timothy Taylor about four months before his death (Krueger and Taylor, 2000). The beginning was harsh: In 1940 the Soviet Union annexed Lithuania and the other Baltic republics. The Nazis occupied the country in 1941. Griliches and his family were confined to the ghetto in Kaunas in August of that year. He managed to evade the periodic roundups for transport to the concentration camps until sometime during the summer of 1944. After that he was moved, often by foot, from one camp to another until he was liberated from Dachau by the American advance in May 1945. Except for a sister, he lost all his immediate family in the Holocaust. Eventually Griliches made his way via a British internment camp on Cyprus to what was then Palestine. After working on a kibbutz and participating in

the War of Independence Griliches managed to pass what we would call a high-school equivalency exam despite his lack of formal education. He spent a year studying history and languages at the Hebrew University, 1950-51. He then matriculated in the College of Agriculture at the University of California, Berkeley, where he obtained a bachelor's degree, 1953, and a master's degree, 1954, both in agricultural economics.

While most people's subsequent intellectual development, ideas, and perspective in a social science such as economics would be expected to have been affected profoundly by the horrific experiences through which Griliches lived in the decade before he emigrated to the United States, I find remarkably little evidence that his subsequent work and contributions were affected at all. As he himself once remarked, "After we came out of the Holocaust, we did not look back. We had too much trouble re-establishing some kind of life and getting going. Besides, there was no point in dwelling. People like me were a dime a dozen. Lots of people, everyone had a story. No one out there was interested in our stories" (quoted in Weinstein, 1999). He was surely not one of a "dime a dozen," but the story of his life and work I want to tell here begins in the fall of 1954 at the University of Chicago, where he received his Ph.D. degree in 1957. He joined the faculty there in 1956 and remained until 1969, when he moved to Harvard University.

The intellectual atmosphere and ferment at Chicago in the 15 years Griliches was there, first as a graduate student, 1954-56, and subsequently on the faculty, 1957-69, were heady. I have described the milieu and cast of characters in some detail in a previous paper (Nerlove, 1999) and need not repeat it here. Perhaps the greatest influence on his subsequent work was T. W. Schultz, but also important to his intellectual development were Gregg Lewis, D. Gale Johnson,

Al Harberger, and Carl Christ. Hans Theil visited, 1954-55, and his lectures provided a neat framework that Griliches adapted in his paper on specification bias in the estimation of production functions (1957). Trygve Haavelmo visited during the academic year 1957-58, and his work on the theory of investment (Haavelmo, 1960) completed that year played a pivotal role in Griliches's development of his ideas on capital heterogeneity and, more importantly, in accounting for economic growth and productivity change. I think though that it was Schultz's influence that was really formative, and a strong interaction between the two continued until Schultz's death in 1998, only a year and a half before Griliches's.

Over the years Griliches garnered many honors and awards for his work: the prestigious John Bates Clark Medal of the American Economic Association in 1965; presidencies of the Econometric Society and American Economic Association in 1975 and 1993, respectively; and an honorary degree from the Hebrew University, Jerusalem, in 1991. He was elected to fellowships in the Econometric Society, 1964; the American Academy of Arts and Sciences and the American Statistical Association, 1965; the American Association for the Advancement of Science, 1966; the American Agricultural Economics Association, 1991; and the American Economic Association, 1994. In 1975 he was elected to the National Academy of Sciences. He served on many Academy and national committees, the most notable being the so-called Boskin Commission to Study the Consumer Price Index, 1995-97, and had an important and far-ranging influence on economic statistics in the United States, a part of which I deal with in Section 3 below. Much of his contribution was through his interaction with students and research associates, particularly over the 30 years he spent at Harvard University and the National Bureau of Economic Research, and not merely through his published work. I will try to

deal with these influences *ad passim*. (One of Griliches's former students, Iain Cockburn, has put together two formidable lists of Griliches's former students, postdocs, and research associates, listing also their students and students' students in the manner of a genealogical tree. These can be accessed at <http://people.bu.edu/cockburn/tree_of_zvi.html>.) At the time of his death Griliches was Paul M. Warberg Professor at Harvard University and director of the program of Research on Productivity at the National Bureau of Economic Research. Many in the profession thought he should have been awarded a Nobel Prize in economics for his work. But, although the selection committee for the prize was aware that he was terminally ill, they did not choose to grant him that distinction before his death in 1999.

I knew Griliches since we were together at the University of Chicago in the years 1954-56. I followed his work closely over the years. I will share with you in this biographical memoir my appreciation and assessment, not uncritical however, of his contribution to the science of economics. Much of his work was of profound and far-reaching significance for economics. But his contributions were many and diverse and some of his work was of lesser importance and long-run significance than the more central core. In his obituary Michael Weinstein (1999) characterized Griliches as one of "the world's leading authorities on the statistical analysis of economic data" and states that he "develop[ed] techniques of statistical estimation, including methods for analyzing 'panel' data that trace the behavior of many individuals or companies over time." Indeed, much of our profession regarded Griliches as pre-eminently an econometrician. Griliches's own assessment of his contributions to econometric methodology, however, was somewhat different. He later said (Krueger and Taylor, 2000), "Much of the stuff I did was empirical. I did some econometric theory, but the

econometric theory was by and large theory I needed to develop for the problems I was working on, not because it was out there. By today's standard, I was woefully under-prepared to be an econometrician." I would say however that, although statistical and econometric methodologies were not at the central core of his contribution, he was an empirical economist in the best sense, perhaps the best his generation of economists produced. Many of the areas in econometrics that he opened up because they were relevant to the substantive work he was doing later proved to be methodologically seminal, perhaps in part because they were relevant to real economic problems. I hope that what follows provides a guide and assessment of what he accomplished, albeit a personal one, and a delineation of the central core of his contribution, which was, in my view, principally a fuller and more quantitative understanding of the process of economic growth.

Economics is an empirical science and thus is concerned with the real economic world and with understanding economic behavior and the implications of such behavior for economic policy. However, economic research, in common with research in other academic disciplines, is largely driven by its own internal logic and structure in the sense that most work is on problems that flow from previous work, rather than from any attempt to understand reality. The subdiscipline of econometrics is no exception in this respect. Griliches's contributions invariably had their origin in a serious attempt to resolve some real economic problem and to understand some real economic phenomenon, rather than to solve some outstanding methodological issue. Griliches was pre-eminently an empirical scientist and was from the beginning virtually consumed with the desire to understand and modify the real world. Such methodological conclusions of more general applicability that he may have

made draw their inspiration and strength from the substantive issues with which he was concerned. If his ideas have been held aloft, away from contact with economic reality, it is by others who have followed in his footsteps but not in his lead. It has not been his methodological contributions divorced from their substantive context that constitute Griliches's principal contribution to economic knowledge but rather his answers to the substantive questions themselves. More importantly, raising the questions themselves in the right way is his lasting legacy to our discipline.

In his presidential address to the American Economic Association (1994) Griliches wrote:

The major message that I will be trying to convey is that we often misinterpret the available data because of inadequate attention to how they are produced and that the same inattention by us to the sources of our data helps to explain why progress is so slow [in this instance in understanding the process of economic growth]. It is not just the measurement of productivity that is affected. Other fields of empirical economics are also struggling against limitations imposed by the available data. Great advances have been made in theory and in econometric techniques, but these will be wasted unless they are applied to the right data.

For most of his professional life and in the great bulk of his papers, Griliches attempted to deal with such data problems and with issues related to the appropriate ways to measure the relevant variables of economic theory. Framing the issues in this way was the key to his contribution.

Much of Griliches's substantive work dealt with the process of technological change and its interpretation as an economic phenomenon. In the introduction to a collection of early papers (1988) covering the period of his work through 1971, he wrote:

[M]easurement frameworks can be expanded to bring more aspects of technological change into the domain of "standard" economics, removing thereby some of the mystery from this range of topics. This kind of work,

however, takes much effort, is heavily data dependent, and is rarely definitive. At best it opens up new subjects rather than providing closure. It shows by example, what can be done and what it might be interesting to do more of; and often the question is as interesting as the possible answers.

The tentative and incomplete nature of much of Griliches's work is indicated by the many papers that he titled "Notes on . . .," but this hesitancy should not blind us to the importance or significance of the contributions made. If one broadly construes econometrics as dealing with problems of appropriate measurement in addition to problems of inference, Griliches's contributions have been of immense and far-reaching significance. But, if one more narrowly interprets econometrics as concerned primarily with inference, his contributions to econometric methodology per se, derive largely from his more substantive work and his concern with measurement.

Griliches's bibliography is very large; my review of his work must, at best, be highly selective. His opera can be roughly sorted into five main categories, although some work falls in more than one category and almost all are related to the theme of appropriate measurement to a greater or lesser degree: (1) technological innovation and diffusion, R&D, and patents; (2) hedonics, including proper measurement and adjustment of input and output measures in the analysis of economic growth and productivity measurement; (3) production functions, growth accounting, and supply and derived demand; and (4) unobserved or latent variables and specification errors, including substantial substantive research on the relation among income, education or schooling, and ability, and with important implications for panel data econometrics (summarized in Nerlove, 2000). Of the four, the second and third are most central to the theme of measurement. I provide a selective bibliography at the end of this biographical memoir. Griliches, himself,

collected his most important papers in two volumes published in 1998, as well as in the earlier 1988 collection.

2. TECHNOLOGICAL INNOVATION AND DIFFUSION, R&D,
AND PATENTS

Griliches's paper (1957), arguably his best known, is essentially a summary of his Ph.D. dissertation, "Hybrid Corn: An Exploration in the Economics of Technological Change." The ideas presented in this paper foreshadow much of Griliches's subsequent work in this area. "A unifying thread that runs through . . . is the view that technological change is itself an economic phenomenon and hence also an appropriate topic for economic analysis" (1988, p. 1). But appropriate measurement of inputs and outputs is essential to this goal. Looking at the differential geographical spread of hybrid corn in the United States, Griliches (1957) sought to interpret it in terms of both the supply of the new technology in the form of specific hybrids adaptable to specific areas and the speed of adoption by farmers (i.e., their demand for the new technology). Using a logistic growth curve to summarize the spread of hybrid corn in the various states of the United States, Griliches is able to parameterize the process by three parameters: origin, slope, and ceiling. Origins are interpreted in terms of the supply of hybrid varieties by the various state experiment stations. Slopes and ceilings are interpreted in terms of farmers' incentives to adopt. But differences in ceilings are inadequately explained. The model that Griliches used is as follows:

$$P = \frac{K}{1 + e^{-(a+bt)}}$$

where P is the percentage of total corn acreage planted

with hybrid seed, K is the ceiling or equilibrium value, t is time, and b is the rate of growth coefficient; a is a location parameter. The proportional rate of growth is

$$\frac{1}{P} \frac{dP}{dt} = b \frac{P}{K}.$$

The framework Griliches developed has been the basis for many studies of technological diffusion.

Less directly, but more importantly, Griliches's interest in hybrid corn led to a concern with the other major changes that were occurring in U. S. agriculture, principally mechanization (1959) and the spectacular growth in fertilizer use (1960, collected in a 1998 volume) and thus to his concern, which I regard as central to his work, with appropriate measurement of inputs and output and thus to his pioneering resurrection of hedonic analysis. These early studies of agricultural inputs employed econometric tools sophisticated for their time and led to Griliches's papers on distributed lags and aggregation, discussion of which I omit here. I will take up hedonics in the next section and Griliches's work on production function estimation in Section 3. His concern with appropriate measurement of inputs and estimation of production functions is also reflected in his work on measurement of labor inputs and thus to that on the relation among education or schooling, ability and income as a way of adjusting labor input in studies of productivity and total factor productivity.

Much of Griliches's more recent work dealt with productivity growth in the United States, Israel, Japan, and France. To a great extent this work is related to production function estimation, but there is one very large group of papers more directly related to the source of technical change

and its explanation by economic factors, namely, those papers on R & D and patents (collected in the 1998 volume). Central to this work is the idea that technical change, and more generally knowledge, is produced. The late Jacob Schmookler pioneered in the study of patents as an indicator of inventive activity and technical change (Schmookler, 1954), but the link has proved elusive (see especially Griliches, 1990). In his presidential address to the American Economic Association (1994), Griliches characterizes patents as “a shrinking yardstick” but nonetheless valuable. Moreover, the relationship between patents and R & D is also problematic (1994). More recent work on the quality of patents rather than a simple count has demonstrated a closer relationship between inventive activity and growth at the firm level. A more rewarding direction of research has been the study of the relation between productivity growth and R & D expenditures, particularly at the level of the individual firm.

Griliches (1979) lays out the production function approach to the estimation of returns to R & D, the issues associated with output measurement in R & D intensive industries, and the problem of defining the stock of R & D capital as a factor of production. In this work he continues a leitmotiv from the part of his work on hybrid corn dealing with the supply of hybrids. One of Griliches’s most important contributions in this area was to link Census of Manufactures data on firms and industries with National Science Foundation data on R & D expenditures, no mean accomplishment in a country obsessed with privacy and maintaining confidentiality, and which required considerable managerial and administrative skill. A collaborator, Bronwyn Hall, was instrumental in these studies, as she was in the collection and collation of the patent data. In this connection mention should also be made of Griliches’s collaborators in France, Israel, and Norway: Jacques Mairesse (Institut National de

la Statistique et des Études Économiques), Tor Jakob Klette (Central Bureau of Statistics, Norway), and Haim Regev (Central Bureau of Statistics, Israel). Griliches's first collaboration, using Norwegian microdata at the firm level, was with Vidar Ringstad on production function estimation (see Section 5). Work on these data was certainly facilitated by a more open tradition of academic research in France, Israel, and Norway as contrasted to the United States. Many of Griliches's subsequent papers and those of numerous co-investigators at the National Bureau of Economic Research rest on these data. Several appear in the 1984 volume edited by Griliches. The papers in this volume deal, inter alia, with the following questions: "What is the relationship of R & D investments at the firm and industry level to subsequent performance indicators such as patents, productivity, and market value? How does one formulate and estimate such relationships? What makes them vary across different contexts and time periods? To what extent can one use patent counts as indicators of R & D output? Can one detect the output of R & D in the market valuation of the firm as a whole? What determines how much R & D is done and how many patents received?" (1984) In a paper published posthumously Klette and Griliches (2000) developed a sophisticated model of the growth of heterogeneous firms in which R & D and stochastic innovation are the engines of firm growth and applied this model to a panel of Norwegian firms. There are many innovations (nonstochastic!) in application of panel data methods in this work on micro firm data more generally. I have more to say about Griliches's contribution to panel data econometrics below in Section 5.

An important paper of Griliches is joint with D. W. Jorgenson, "The Explanation of Productivity Change" (1967). This paper has, in my view, provided a sound basis for the field of growth accounting and has been of major influence

in the study of economic development in general and of great significance in recent debates over the supposed slowdown in U. S. productivity growth. This work is foreshadowed in (1963) in some detail (indeed, the basic structure is already in place there) and earlier by Abramovitz (1950, 1956, 1962) and Denison (1962); it is more properly treated as an aspect of production function analysis in Section 4 below. For his own view of the history of this subject see Griliches (1996).

3. HEDONICS: PROPER MEASUREMENT OF PRICES AND ADJUSTMENT
OF INPUT AND OUTPUT MEASURES

In 1964 (p. 382) Griliches wrote:

Economists use price series for two main purposes: (1) to deflate expenditures and receipts for the purpose of arriving at some conclusions about either changes in welfare (in the case of consumption expenditures and earning receipts) or productivity (in the case of sales receipts, wage bills, and investment expenditures); and (2) to explain and predict changes in quantities used or purchased. In either case we are likely to have a broader concept of "price" in mind than just one of the particular numbers recorded during a transaction.

Thus stated, the problem of constructing an appropriate price index for a multitude of different transactions involving different commodities of differing qualities or efficacies is basically an aggregation problem (Frisch, 1936). On the consumer side, appropriate aggregation weighting is by marginal utilities or marginal rates of substitution; on the producer side, weighting is by marginal productivities, marginal rates of transformation, or marginal rates of substitution. Under certain circumstances these marginal rates of substitution or transformation can be treated as given prices, actual or implicit. (For consumer theory Muellbauer [1974] presents several models of utility-maximizing behavior that justify such an interpretation in terms of underlying con-

sumer preferences, but he is quick to admit that his analysis neglects the other, producer, side of the market. A central problem for both consumer and producer prices is how to treat new commodities and quality changes. (Griliches's collaborations with Ernst R. Berndt on personal computers and with Iain Cockburn on pharmaceuticals should be mentioned in this connection.)

The traditional method of adjusting for quality changes over time in the measurement of prices is to "match models," that is, to use only prices for varieties of a commodity that are unchanged in specification between two adjacent periods, chaining pairs of periods over time. Difficulties arise for commodities, the varieties of which are changing rapidly over time or for totally new commodities. The hedonic technique (Waugh, 1929; Court, 1939) involves regressing unit prices for different varieties on measures of quality characteristics or attributes; if the varieties are distinguished by time periods, a simple technique for obtaining a quality-adjusted price index is to introduce dummy variables for periods in a multiple regression framework (Court, 1939). Griliches's contribution to hedonics was largely to resurrect and to promote with great vigor and effect Court's formulation. He used the technique very effectively in work on productivity growth and its sources, as described in the next section.

Although hedonic analysis for all its practical importance was not central to Griliches's work, the idea that commodities are bundles of attributes has important implications for the appropriate measurement of inputs and outputs in the analysis of changes in total factor productivity, for if the growth in quality-adjusted inputs is misestimated and/or if the growth in quality-adjusted output is likewise, total factor productivity growth will be biased. The need to adjust both inputs and outputs to measure them appropriately in this context was

recognized very early by Griliches and exploited very fully in his subsequent work, especially in his paper with Jorgenson (1967) discussed in the next section. Indeed, it set his research agenda throughout his professional career.

4. PRODUCTION FUNCTIONS, TOTAL FACTOR PRODUCTIVITY
MEASUREMENT, SUPPLY AND DERIVED DEMAND

The basic framework for growth accounting, equivalently, measurement of total factor productivity, was laid out many years ago by Abramovitz (1950, 1956, 1962); Griliches elaborated and extended this basic framework in important ways, beginning with his early paper on U. S. agriculture (1960). In 1988 (pp. 6-7) he laid the problem and the method out as follows:

A conventional measure of residual technical change (TFP) in an industry can be written as

$$\hat{t} = y - sk - (1-s)n$$

where y , k , and n are percentage rates of growth in output, capital, and labor respectively; s is the share of capital in total factor payments, and the relevant notion of capital corresponds to an aggregate of actual machine hours weighted by their respective base period (equilibrium) rentals. This procedure assumes that all the variables are measured correctly, that all the relevant variables are included, and that factor prices represent adequately the marginal productivity of the respective inputs. The last assumption is equivalent to the assumption of competitive equilibrium and constant returns to scale.

Griliches then proceeded to break $TFP = \hat{t}$, or total factor productivity, up into six components:

1. the effect of the rate of growth in the measurement error of conventional capital measures on the estimated “residual”;
2. errors in the measurement and definition of labor input;
3. errors in assessing the relative contribution of labor and capital to output growth (it would be zero if factor shares were in fact proportional to their respective production function elasticities or if all inputs were growing at the same rate; then the relative weights do not matter);
4. economies of scale, which would be zero if there were no underlying economies of scale in production or if the rate growth in the number of new firms (plants) just equaled the growth in total (weighted) input;
5. the contribution of left-out inputs (private or public);
6. various remaining errors in the measurement of output.

This decomposition is revealing in terms of Griliches’s research agenda and his progression through it: Griliches’s work on hybrid corn led him to consider two other major changes in U. S. agriculture, increasing use of chemical fertilizer (1960) and mechanization (1959), and in turn to a more general formulation of the total factor productivity problem (1960). Along the way he encountered difficulties in the measurement of fertilizer and machinery and other capital inputs. Because these measures are obtained by dividing expenditures by an index of prices, it is possible to interpret the “errors” in terms of mismeasurement of prices, and this in turn led straight to hedonics, discussed in Section 3. Much of the work on patents and R & D discussed in

Section 2 is related to the fifth component. Proper measurement of capital input requires not only attention to quality changes and prices but, in addition, to the determination of new investment, additions to the stock, and as to how such investments are translated into the relevant input variable and more recently the computer “revolution.” Measurement of the “correct” labor input requires attention to the quality of the labor force, or the stock of “human capital” embodied in it; and this in turn leads to the attempt to measure the effects of education on the productivity of labor. These studies are all closely related to Griliches’s work on the analysis of unobserved or latent variables; consequently, I will deal with them in detail in the next section. Griliches dealt relatively little with the mismeasurement of output per se in the context of total factor productivity and not at all, as far as I can discover, with cyclical effects on productivity, except insofar as these affect capital utilization. Finally, the fourth component, returns to scale, or more generally increasing returns, is related to Griliches’s attempts to estimate production functions in a variety of contexts in order to ascertain the significance and extent of such increasing returns.

Although measurement of total factor productivity and estimation (possibly inefficiently from an econometric point of view) of a production function, not necessarily parametrically specified, are equivalent, most of Griliches’s work on productivity measurement does not explicitly introduce such a function. This is also the case with his paper with Jorgenson (1967, p. 249), hereinafter G & J:

The purpose of this paper is to examine a hypothesis concerning the explanation of changes in total factor productivity. This hypothesis may be stated in two alternative and equivalent ways. In the terminology of the theory of production, if quantities of output and input are measured accurately, the growth in total output is largely explained by growth in total input, “properly

measured." Associated with the theory of production is a system of social accounts for the real product of real factor input. The rate of growth of total factor productivity is the difference between the rate of growth of real product and the rate of growth of real factor input. Within the framework of social accounting the hypothesis is that if real product and real factor input are accurately accounted for, the observed growth in total factor productivity is negligible.

G & J assume that the underlying production technology is constant returns to scale, that factors are paid their marginal products, and that the economy is in competitive equilibrium. They proceed by a series of adjustments to eliminate what they consider to be "errors" in the measurement of real output and real factor input, in order to compute average total factor productivity growth (TFP) for the period 1945-65:

1. Output = U. S. private domestic product in constant prices; input = sum of labor and capital services in constant prices, labor and capital services assumed proportional to stocks; TFP = 1.60 percent.

2. Correction for aggregation errors by weighting labor and capital services in various categories by shares in total factor payments and output by weighting by shares of consumption and investment goods in total expenditures; TFP = 1.49 percent.

3. Correction of investment goods prices using output prices on both the output and input sides, correcting the implicit deflator for producers' durables to be the same as for consumers' durables, and correcting the implicit deflator for changes in business inventories; TFP = 1.41 percent.

4. Adjustment of labor and capital for relative utilization separately, assuming the relative utilization of capital in manufacturing and nonmanufacturing is the same and adjusting by relative utilization of electric motors, correc-

tion of data on manhours for variations in labor intensity, TFP = 0.96 percent.

5. Correct aggregation of capital services by the before tax prices of various categories of investment goods (land, residential and nonresidential structures, equipment and inventories), TFP% = 0.58 percent.

6. Correct aggregation of labor services, males only by relative earnings for categories broken down by years of schooling, TFP = 0.10 percent.

There is thus remarkably little left over for the “residual,” that is the unexplained growth in output per unit of total input—too little. One suspects “overkill.” Perhaps for this reason, much of the subsequent work of both Griliches and Jorgenson was devoted to refining these adjustments. Of course, this is not an *explanation* of total factor productivity growth but rather an accounting of the sources of it.

Beginning with his early paper (1957), applying Theil’s analysis of the effects of left-out variable in OLS regression to the problem of differential managerial ability in production function estimation, Griliches published a number of papers dealing explicitly with the estimation of agricultural, manufacturing, or aggregate production functions, or the associated systems of derived demand and supply functions. In a somewhat neglected book (1971), Griliches and Ringstad estimate a number of production functions from data on a large number of individual manufacturing establishments from the 1963 Norwegian Census of Manufactures. Their particular concern is to separate economies of plant size from market size. Since their pioneering study, more such studies using individual establishment data have been attempted by others. The main contribution of (1971) was to demonstrate the feasibility of using census of manufactures data on individual establishments, an approach Griliches

was later to put to good use in his work on R & D, using the Census-National Science Foundation matched sample (1982).

5. UNOBSERVED OR LATENT VARIABLES: THE RELATION AMONG
EARNINGS, EDUCATION OR SCHOOLING, AND ABILITY

As indicated in the previous section, Griliches's interest in the proper measurement of labor input led him to a series of studies relating earnings to schooling and, perforce, the unobservable variable, ability. Although, from the standpoint of Griliches's core contribution, this work may have been incidental in that it was largely related to a desire to adjust the quality of the labor input over time, I regard it as fundamental to the development of panel data econometrics (Nerlove, 2000). Disturbances in the structural equations are the best-known example of latent or unobserved variables in econometrics: "An unobservable variable is one that is measured with error. Sometimes, the error is due to inaccurate measurement in the narrow sense. More broadly, it arises whenever measurable quantities differ from their theoretical counterparts." (Goldberger, 1974, p. 193; see also 1971, 1972.) Here is a typical example from Griliches and Mason (1972): Let y_{kij} be the k th indicator of success (earnings, occupational status, etc.) of an individual j belonging to a family i ; X_{kij} are some exogenous observed factors affecting the individual or the family into which he was born; S_{ij} is schooling received; A_{ij} is an unobserved variable reflecting "ability"; u_{kij} is the usual econometric disturbance reflecting everything else (see Haavelmo, 1944) and is assumed to be independent of the disturbance for any other indicator of success and of X_{kij} , S_{ij} , and A_{ij} . A and X are also assumed to be independent. The relations we want to estimate are

$$y_{kij} = X_{kij}\alpha_k + S_{ij}\beta_k + A_{ij}\gamma_k + u_{kij},$$

one for each k . The parameter of interest is b , the effect of schooling on earnings in particular, for the adjustment of labor input in the measurement of total factor productivity. The problem is, of course, that we don't observe A_{ij} . We can assume that it is highly correlated with schooling so that just leaving it out would bias the measured effects of schooling upwards. Assume

$$s_{ij} = Z_{ij}\delta + A_{ij}\theta + w_{ij},$$

where Z_{ij} are some exogenous variables, possibly among those included in X , and w_{ij} is a disturbance independent of u_{kij} . Although we cannot observe A_{ij} , we have what Goldberger refers to as multiple indicators of it, namely schooling *and* all the success measures, which however also depend on schooling. We might have other indicators of ability not depending also on the amount of schooling received, such as IQ test scores or scores on the Armed Services Qualification test. Such "multiple indicators," as Goldberger (1974) refers to them, help to identify the coefficients in the earnings schooling relationship despite the unobservability of the latent ability variable.

In subsequent papers published in the decade Griliches (1972, 1976, 1977) and Chamberlain and Griliches (1975) further refined these methods relating them to the notion of individual-specific unobserved effects due to left-out variables. The contribution of Chamberlain and Griliches (1975) is specifically to take into account the information afforded by more than one relationship involving the *same latent variable*, that is, to confront the problem of simultaneous-equations bias head on. They write (pp. 422-423):

The usual response to the availability of data with a group structure, e.g., families and family members, firms and time, is to estimate the relationships of interest from the within-group data. In the context of estimating income and schooling relationships such calculations would “take care” of parental background differences, even though inefficiently (they ignore the between families information in the sample), but would not correct for possible bias from the individual (within family) genetic differences which may be correlated with achieved schooling levels later on. To take this explicitly into account would require the availability of direct measures of such ability, which were not available in the particular data set we were interested in analyzing. But even in their absence, if the missing variable (such as ability) affects more than one *dependent* variable, a bootstrap operation [not in the sense used today] may be possible. The basic idea for the new approach comes from the realization that such a left out variable must cause similar biases (proportional to each other) in different equations and that taking advantage of that fact may allow one to achieve identification of most of the coefficients of interest.

6. THE CENTRAL CORE

Over the years Griliches made a number of other important contributions to econometric methodology, with which I will not deal here. The central core of Griliches’s contribution to economic science consists of his contributions to our understanding of productivity growth in the context of general economic growth. His central insight was to see that “technical change,” which Abramovitz (1956) and Solow (1957) pinpointed as the principal engine of growth, is not a purely exogenous phenomenon but rather largely the result of economic activity, the main purpose of which is to generate such change. T. W. Schultz (1953), who was Griliches’s teacher at the University of Chicago, held that most of technical change in U. S. agriculture had been due to public investments in agricultural research, perhaps too extreme a view. That the rate and direction of technical change ought to be subject to the same rules as other purposeful economic activity was not particularly new or novel at the time

Griliches began his pioneering work on the spread of hybrid corn in the United States, but there was little or no quantitative evidence. Beginning with his 1957 paper Griliches systematically provided such evidence and measured its impact on growth.

Because technical change is typically measured by changes in total factor productivity, be it at the firm, industry, or economy-wide level, measurement of these factor inputs becomes crucial. But more significantly, changes in the quality of factors of production are much more than mere errors of measurement. They “embody” the sources of growth: New knowledge spreads through training and investment in new capital, which “embodies” this knowledge. Changes in education and health and other forms of human capital affect the quality of the labor input and thus its productivity. Investment in R & D is “embodied” in new equipment or in new products or in new organizational forms. Again, Griliches systematically measured these effects, and by so doing identified the sources of economic growth. I regard Griliches as the founder of modern growth accounting.

At his death Griliches was editing his Kuznets lectures, which he intended to be a definitive statement on growth and its sources. I suspect that, as he usually did, Griliches will raise a great many unanswered questions. It is sad that those of us who remain to find the answers will no longer have his wise counsel and the benefit of his extraordinary intuition and insight.

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spondence with several of Griliches's former students, Pascal Mazodier, Tor Jakob Klette, Vidar Ringstad, and Clint Cummins. A longer and more detailed version is available at <<http://www.arec.umd.edu/mnerlove/Griliches.pdf>>.

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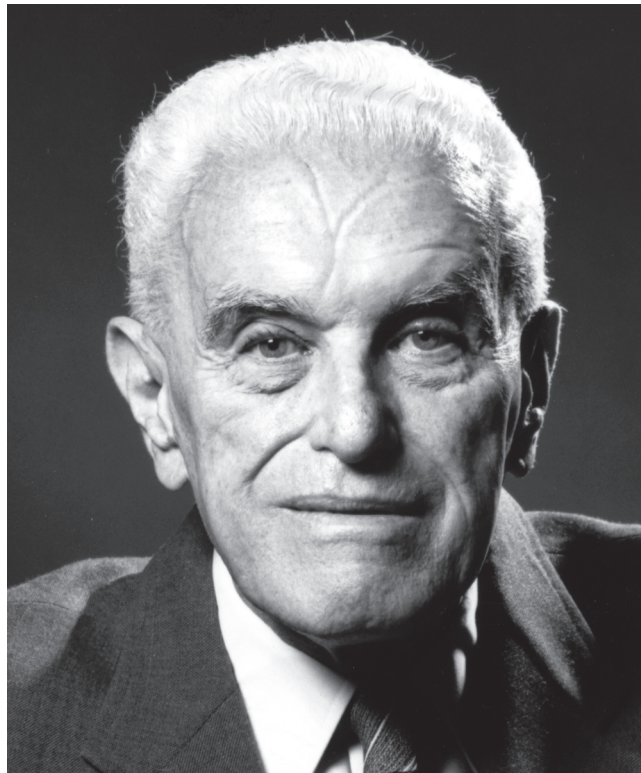


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John C. Hansbury

JOHN C. HARSANYI

May 29, 1920–August 9, 2000

BY KENNETH J. ARROW

JOHN CHARLES HARSANYI was born on May 29, 1920, in Budapest, Hungary, an only child. His father owned a pharmacy from which he derived a comfortable income. Both parents were Jewish but had converted to Catholicism. His parents were, according to his account, well educated and cultured. He was tutored at home for the first few grades. After elementary school he went to the famous Lutheran Gymnasium in Budapest, graduates of which included John von Neumann, Eugene Wigner (the physicist), and Nicholas Kaldor.

After two years of studying leather chemistry at Grenoble, France, he returned to Hungary with the imminence of World War II to study pharmacy so that he could continue his father's business. He then started (though with little real interest) a doctoral program in botany, mainly to avoid conscription into the army; however, the Germans entered Hungary in March 1944, and in May he was conscripted into forced labor. Fortunately, his work was done in or near Budapest. He was required to wear a white armband, identifying Christians of Jewish origin. His unit was under some form of protection from the Vatican, but when the Russians

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came close to Budapest, the Nazis decided to deport the Jewish forced laborers to Austria. Harsanyi managed to escape from the railway station and hide in the monastery of a Jesuit friend. He was finally freed when the Soviet troops arrived in January 1945.

Harsanyi then enrolled in the University of Budapest. At first he studied mathematics but then shifted to the study of philosophy, psychology, and sociology. Although clearly anti-Marxist, he was allowed to be a university assistant and do some teaching, at which time he met his future wife, Anne. The repression gradually increased, and they decided in 1950 to escape across the border to Austria with Anne's parents. Their guide took three days to take them across because he took a circuitous route to avoid capture (the guide was in fact captured on his next journey and sent to prison).

In Austria they waited seven months for a permit to go to Australia (the Hungarian quota for immigration to the United States was filled for years ahead). The two were married almost immediately on arrival in Australia. He then entered the University of Sydney for an M.A. degree, which was awarded in 1953. Although he intended to continue in sociology, he found the interests of the sociologists there remote from his and enrolled in economics. He then became a lecturer at the University of Queensland, with primary responsibility for external studies (correspondence courses).

He started publishing with great rapidity. By 1955 he had published four papers on economic theory, two of them classics in welfare economics. The others (1953, 1954) were highly competent studies of the economics of research and of the meaning of optimality theorems when tastes are varying over time (a subject then in the literature). The two papers on the foundations of welfare judgments (1953, 1955) were startlingly original. They stemmed from two then cur-

rent developments in economic analysis, the expected-utility hypothesis for behavior under risk, revived and supplied with an axiomatic foundation by John von Neumann and Oskar Morgenstern (1947, Appendix) and Abram Bergson's formulation of the social welfare function (1938).

Bergson sought to ground welfare economics in individual welfare judgments by assuming that ethical evaluations of alternative resource allocations should be represented by a function of individual utilities for them. Let $U_i(x)$ be individual i 's utility for alternative x . Then, postulated Bergson, there is a social welfare function of individual utilities, $W(u_1, \dots, u_n)$, increasing in each argument, where n is the number of individuals in the society, which represents society's ethical choices in the sense that alternative x is socially preferred to alternative y if and only if $W(U_1(x), \dots, U_n(x)) > W(U_1(y), \dots, U_n(y))$. Though this representation seems to involve cardinal utilities, Bergson held that it could be interpreted to be valid even for ordinal utilities with no interpersonal comparison.

Harsanyi's contribution was to observe that choices could be made over probability distributions as well as over sure outcomes. Then, he argued, both individuals and society should be assumed rational in their choices under uncertainty in the sense of obeying the von Neumann-Morgenstern axioms. It followed, by a clever argument, that the range of possible welfare functions is very limited. Specifically, if U_i is interpreted to be individual i 's von Neumann-Morgenstern utility function, then W must be a positive linear combination of individual utilities,

$$W(u_1, \dots, u_n) = \sum a_i u_i, \text{ with } a_i > 0, \text{ all } i.$$

The individual utility functions, U_i , are defined up to individual positive-linear transformations; they are cardinal

but not interpersonally comparable. However, argued Harsanyi, variations in the scaling of any individual's utility function can be offset by a corresponding variation in the coefficient, a_i .

It will be seen that Harsanyi's approach leads to a justification of classical utilitarianism from a remarkably new point of view. (The same basic idea, expressed much more informally, had already appeared as almost a side remark in Vickrey (1945, p. 329), but, as I can testify on my own account, it was easy to overlook.)

At this point, evidently, Harsanyi's interests turned more definitely to game theory, in the first instance, to cooperative game theory. The first fruits were his comparison of alternative approaches to the theory of bargaining (1956), comparing the developments of Frederik Zeuthen, John R. Hicks, and John F. Nash, Jr. As long ago as 1930 the Danish economist Zeuthen had written a study of monopoly and what he called "economic warfare" (i.e., oligopolistic competition). He included an analysis of bargaining, which, as Harsanyi showed, was essentially the same as that developed by Nash (1950). (In my view, Zeuthen's contributions to economic theory have never received the recognition they deserve.)

Harsanyi went much farther in seeking to found the theory of cooperative games in general. The publication of this work was bound up with the next stage in his career. At that time, the Rockefeller Foundation offered fellowships to Australians for study in the United States (the Rockefeller Foundation had a major program for bringing senior foreign scholars on visits to the United States even before World War II, and that program had many major consequences). Harsanyi was accepted, with the aim of coming to Stanford University to study for the Ph. D. and work with me.

Harsanyi had written me, and with his publications, some of which I had already known, there was no question of my

willingness to work with him. I more or less assumed that he was probably someone with a strong mathematical background who needed to develop his knowledge of economic theory. On his arrival I found out quickly enough that his knowledge of economics (or at least of economic theory) was such that there was little we could teach him. It was also clear that he had already worked out the ideas for founding cooperative game theory on bargaining analysis, which were to form his dissertation. I finally asked him why he was bothering to take a Ph.D., since neither the Stanford department nor I could provide much added value. He was candid; the Ph.D. was a necessary step in his academic career.

Because I was on leave for the two years Harsanyi was in residence, I was, strictly speaking, not his official thesis supervisor, but we did have many discussions on his work, from which I learned more than he did. In this thesis and the publication (1959) derived from it, the possible outcomes from games involving a coalition and its complement provide the disagreement points for other games, leading ultimately to the allocation by the coalition of the whole. A distinctive feature is that each coalition is considered as playing a zero-sum game with its complement, the payoff being the difference in the values of the two coalitions. While cooperative game theory has still to find a universally accepted solution concept, the Harsanyi analysis is still one of the major tools.

Harsanyi's fellowship was for only one year. He continued as a visitor for one semester at the Cowles Foundation for Research in Economics at Yale University and as visiting assistant professor at Stanford. He returned to Australia in 1958, as required by his visa, and after a short continuation in Queensland, became a senior fellow at the Australian National University until 1961. At this point he was free to

return to the United States, where he took a position as a full professor of economics at Wayne State University in Detroit. In 1964 he was offered a professorship at the School of Business (now the Haas School of Business) at the University of California, Berkeley, where he remained for the rest of his life. His breadth of interests was shown in several papers interpreting bargaining theory in such areas of application as ethics, the measurement of social power, and social status, but these have not had much impact.

At this point Harsanyi began his studies on games with incomplete information, where one player has some information that the other has not (of course, each player may have some private information). An early version (1962) was followed by a fully worked-out analysis (1968). This analysis provided a Magna Carta for an entirely new approach to problems of industrial organization while operating at a very high level of abstraction in which the formal difficulties of mutual knowledge and lack of knowledge were resolved.

The deep problem is that of what might be called interactive knowledge. Suppose there are just two players in the game. Player 1 knows something, say, his or her own payoff function. Player 2 does not know Player 1's information but does know several alternative possibilities (with their probabilities). Player 2 may argue that if Player 1 had payoff function π_1 , Player 1 would take action a_1 , but if Player 1 had payoff function π_2 , Player 1 would take action a_2 . If these are different, then Player 2 can infer what Player 1's payoff function is. Player 1, knowing that his or her actions could reveal his or her type, may prevent this revelation by taking the same action for either payoff function. (This concealment may or may not be profitable to Player 1, depending on the actual game.)

The question is how to formulate the question so as to arrive at a clear application of standard Nash equilibrium

theory. Harsanyi proposed a way of thinking about the matter that got to its heart. Assume each player can be one of a finite number of types; the types of the different players have a known joint distribution. Each player knows his or her own type and therefore has a conditional distribution of the types of the other players. A strategy for an individual is a choice of action for each of his or her possible types. So stated, the game of incomplete information is now a game in the ordinary sense with a larger strategy space for each player. Each player can now make inferences by Bayesian updating conditional on the actions chosen by others.

This approach gave a very general formalism, into which all specific cases could be fitted. Thus, if sellers have more knowledge about the quality of their output than the buyers, we have a game of incomplete information analyzable along Harsanyi lines. Similar examples occur if borrowers know more about the prospects of their firms than the lenders do, and even more complex situations can easily be described. The result was a profound effect, particularly in the field of industrial organization but also with strong application to labor negotiations (with the possibility of strikes) and to finance (e.g., bank runs). Research driven by considerations of abstract theory found rapid application to practical problems probably undreamed of by its creator.

This work was probably Harsanyi's most influential contribution, certainly with regard to applied economics. From the viewpoint of game theory there was one further paper of great importance, a new interpretation of mixed strategies (1973). The concept of mixed strategies was troublesome to many interested in applications of game theory. They did not perceive individuals deliberately randomizing, and somehow these scholars felt that a definite decision had to be made. Suppose, argued Harsanyi, that we think

of the payoff to any one player as being randomly perturbed, though the other players do not observe the perturbation. This is a game of incomplete information. Each individual then has a strategy, which may be regarded as pure, for each possible perturbation. However, because the other players do not observe the perturbation, the strategy of any one player will be a random variable from the viewpoints of other players. Harsanyi showed that as the magnitude of the perturbations tended to zero, the resulting distributions converged to the mixed strategies of ordinary game theory. This understanding is a great clarification of the concept and shows that mixed strategies need not be regarded as the result of deliberate randomization.

There are three more themes that run through much of Harsanyi's work. Two were applications of his work to philosophical considerations: the founding of ethics on utilitarian principles and the implications of the Bayesian approach for epistemology. Though his writings on these subjects were fairly extensive, philosophers were not very responsive. A third, mostly in collaboration with Reinhard Selten, tried to find a general method for selecting among multiple equilibrium points in games, a subject that others have also worked on under the heading of "refinements."

His work was well received from its beginning. The culminating honor was the award of the Nobel Prize in economic science in 1994 jointly to Harsanyi, John F. Nash, Jr., and Reinhard Selten, the first (and thus far only) recognition of game theory by that august body.

Let me conclude by quoting (with slight alteration) two paragraphs from an introduction I wrote to Harsanyi's oral history.

Just a few weeks before his death in August 2000, the newly formed Game Theory Society had held its first International Congress in Bilbao, Spain, and all regretted his absence. In his, the generation that first established game theory as a viable discipline, there were five universally agreed-on outstanding leaders, and unfortunately John alone was absent. But his actual death came as a shock.

John Harsanyi was devoted to matters of the intellect. His physical appearance and demeanor, tall, grave, courteous, cautious in his speech, yet not to be dissuaded from a point or a position he felt strongly about, all fitted a man to whom the intellect and the life of science and rigorous inquiry were the most important things in life. On the subjects he found important, he thought deeply and spoke and wrote only after long reflection.

THE BIOGRAPHICAL STATEMENTS in this memoir are derived from an oral history taken by the Regional Oral History Office, University of California, Berkeley, and from his vita supplied by the Haas School of Business, University of California, Berkeley.

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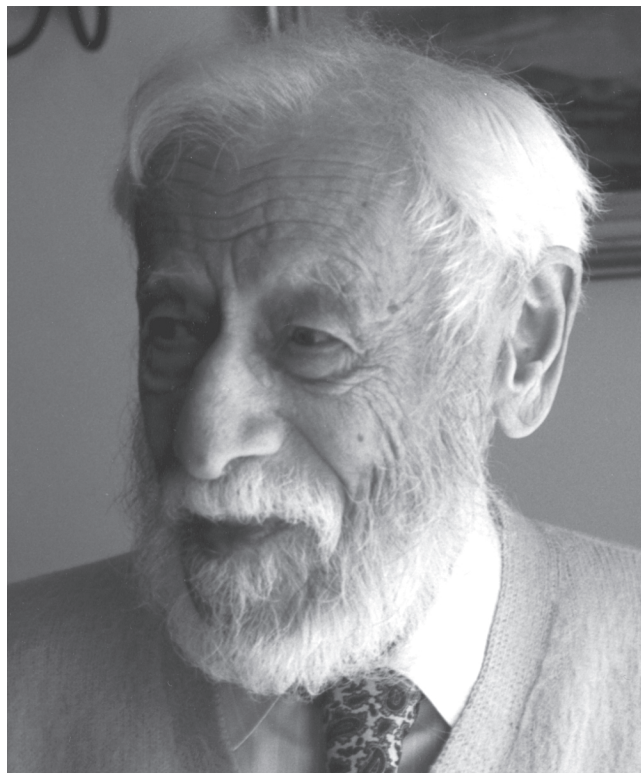


Photo by Otto Westphal

Michael Heidelberger

MICHAEL HEIDELBERGER

April 29, 1888–June 25, 1991

BY HERMAN N. EISEN

WHEN I FIRST MET Michael Heidelberg he was a professor in the Department of Medicine of Columbia University's medical school, the College of Physicians and Surgeons. He seemed as old as Methuselah, though only 57 as I later realized. It was in 1944, and he seemed ancient not just because I was then so young, in my mid-twenties, a resident and instructor in the medical school's Pathology Department, but rather, I think, because of his appearance and demeanor. Slender and short, his hair was snow white, his skin a remarkable almond-like color, and he moved and spoke slowly and deliberately, as though in complete sentences.

If scientists are classified according to Isaiah Berlin's well-known taxonomic scheme for scholars into foxes with diverse accomplishments and hedgehogs having one great accomplishment, Heidelberg seemed the quintessential hedgehog. Though he was highly productive for much of his long life—he lived to be 103—nearly all of his many important contributions stemmed from a steadfast and innovative pursuit of his discovery, with Oswald Avery, that powerful antigens of the highly pathogenic pneumococcus are polysaccharides. This discovery ultimately enabled him and a small group of colleagues to show decisively that antibodies

are proteins (until then a debated issue), to establish from careful quantitative analyses of immune precipitates the multivalency of antibodies and antigens, and to develop a simple vaccine that in modified form is still useful almost 60 years after its effectiveness was first demonstrated in U.S. Army troops during World War II.

Michael Heidelberger was born in New York City in 1888. His grandparents were German Jews who had immigrated to the United States around 1850. Because he attended a fine private secondary school, the Ethical Culture High School, it is likely that his parents were in relatively comfortable circumstances. His undergraduate and graduate education were all received at Columbia University, where he earned a Ph.D. degree in organic chemistry in 1911. After a postdoctoral year in Zurich in the laboratory of the renowned Richard Willstater, he returned to New York to work at the Rockefeller Institute on a series of projects in association with more senior investigators.

Initially, with Walter Jacobs, he synthesized many drugs, especially aromatic arsenicals designed to treat various infectious diseases, including poliomyelitis and syphilis. One of their notable successes was a variant of Paul Ehrlich's "magic bullet" for syphilis (606 or Salvarsan). Called Tryparsemide, it proved to be more effective against the trypanosomes that cause African sleeping sickness than against the treponemes responsible for syphilis. In recognition of its value in treating sleeping sickness, a serious problem in the Belgian Congo, he shared with Jacobs and others the Belgian Order of Leopold II award.

Subsequently, Heidelberger joined van Slyke and Baird Hastings in their studies on the reversible binding of oxygen to hemoglobin. Van Slyke and Hastings were experiencing difficulties in obtaining sufficient supplies of oxyhemoglobin, and Heidelberger was asked to help them. Though the

production of purified hemoglobin was hardly a task for an organic chemist, Heidelberg had no qualms about attacking the problem, and he succeeded in “soon making many grams at a time of crystalline equine oxyhemoglobin with virtually 100% oxygen-carrying power.”

The production of large amounts of hemoglobin required repeated centrifugation steps in a cold room at about 4 degrees. The taxing effect on his technician in having to repeatedly go in and out of the cold led Heidelberg to suggest that the company making the centrifuges incorporate cold-brine-carrying coils in the outer shield. Low temperature centrifugation could then be carried out with the instrument at ordinary room temperatures. The result was the first model of the International Equipment Company's refrigerated no. 2 centrifuge, a white instrument that subsequently became an indispensable “workhorse” in most laboratories engaged in biochemistry or microbiology or immunology. Instead of reaping some of the financial benefits that must have flowed from this inventive idea, Heidelberg noted wryly, with his typically quiet humor, that he received \$50 from the company for writing a descriptive manual for the new instrument.

Later, when Karl Landsteiner, the noted immunologist who had discovered human blood groups, moved from the Netherlands to become a member of the Rockefeller Institute, he asked Heidelberg to join him in studying the antigenic properties of oxy- and reduced hemoglobin. The resulting collaboration led to Heidelberg's acquiring first-hand familiarity with immunological methods from the most accomplished immunologist of the era, an experience he put to great use several years later. But before that could happen he was asked by the director of the Rockefeller Institute, Simon Flexner, to serve as the chemist for the group then studying the pneumococcus, a major pathogen in man.

Before the introduction of sulfonamides in the late 1930s, and especially penicillin in the late 1940s, annual outbreaks of pneumonia, the principal disease caused by pneumococcal infection, kept city hospitals periodically jammed with the sick each winter. Antisera to pneumococci isolated from blood and sputum of infected patients led to the identification of several serologically distinguishable types, called I, II, and III (others, then lumped as type IV, were later divided into a great many other serologically distinguishable types). Death rates varied and in some outbreaks were as high as 25 percent from the type II pneumococcus. Those alive at the time remember how families dreaded the diagnosis in a family member. The only effective treatment throughout most of the 1920s and 1930s involved the injection of type-specific antisera, produced by pharmaceutical companies from horses and rabbits injected with killed pneumococci. The treatment required accurate typing of the organism responsible for the individual patient's disease, and medical students at the time learned how to type pneumococci simply by adding a drop of type-specific antiserum to sputum from infected patients. A match between antiserum and microbe was revealed within minutes by an easily observed swelling of the bacteria's outermost capsule (the Quelling reaction).

Avery and Raymond Dochez at the Rockefeller Institute then made the important finding that a patient's serum or urine could specifically inhibit the Quelling reaction elicited with the pneumococci that were isolated from that patient or from others infected by the same type. They inferred that the specific soluble substance they had discovered was type-specific capsular material shed from the live, virulent pneumococci. Besides being present in serum and urine of patients, it was relatively abundant in supernatants of pneumococcal cultures. Avery, the microbiologist on the pneumonia

team, was bent on isolating and characterizing the capsular material, in part because recovery seemed to be tied to the appearance in the patient's serum of antibodies specific for the capsule of the infecting pneumococcus. He sought to interest Heidelberg in its chemical nature, and Flexner finally persuaded Heidelberg to join the institute's pneumococcus group.

When Heidelberg and Avery started their effort to purify the capsular material, they were faced with a choice of what pneumococcal type to begin with. They rejected type I because its capsules are small and type III because of some ambiguities in its serological reactivity. The choice of type II proved to be fortunate not only because of its abundance but also because of the structural simplicity of its capsule. In the course of carrying out purification steps the nitrogen content of each fraction was measured, because the capsular antigen was expected to be a protein, as was then thought to be the case with all antigens. As material of increasing purity was isolated, however, Heidelberg found that the nitrogen content surprisingly decreased progressively. As he tells the story with characteristic simplicity and honesty, "when it [the purified capsular material] was virtually nitrogen free, Fess [as Avery was called] said, 'Could it be carbohydrate?'" To answer the question at the time, before the development of modern analytical tools, was a major undertaking. To begin with, it meant starting with large amounts of bacterial culture fluid, hydrolyzing the purified material, and analyzing various derivatives of the resulting sugars. Finally, the identity of the purified carbohydrate as the long sought specific soluble substance was accomplished by precipitating it with antiserum specific for pneumococcus type II, and then recovering the carbohydrate from the precipitate. Subsequently, the capsular material from many other pneumococcal types was isolated. The long and arduous

task of determining their diverse carbohydrate structures engaged the attention of Heidelberger and associates off and on for decades to come.

Despite his accomplishments at the Rockefeller Institute, Heidelberger was not offered a permanent position there and was urged by Flexner, the director, to move on. Why? Flexner said, perhaps correctly, that because Heidelberger's accomplishments were made in association with outstanding senior investigators (Jacobs, Landsteiner, van Slyke, and Baird Hastings, then Avery), his work there "would be known as someone else's."

Accordingly, he accepted an offer to become "chemist" to the Mt. Sinai Hospital in New York, heading up their busy analytical chemistry lab, a job that left little time for research. Within a year, however, he was recruited by William Palmer, then the new head of the Department of Medicine at the College of Physicians and Surgeons and its prestigious teaching hospital (Presbyterian Hospital) to become chemist to the department. Palmer was highly respected as a physician and educator. He was also evidently an effective administrator and accumulated around him a group of accomplished clinician-scientists, building that department into one of best academic centers for internal medicine in the United States. Palmer had spent some time at the Rockefeller Institute in the van Slyke laboratory and had there become acquainted with Heidelberger during a short stay with the pneumonia group. He must have seen what a skillful and collegial chemist could contribute to those engaged in clinical research, and when he assumed the chairmanship of the new department he offered Heidelberger an appointment as chemist to the Presbyterian Hospital with an academic position as associate professor of medicine. One assumes that, because he did not have an M.D. degree, Heidelberger was more comfortable with the subsequent

changes in title to Professor of Biochemistry and finally to Professor of Immunochemistry. To support Heidelberg's lab Palmer obtained a substantial gift from Edward Harkness, establishing a Harkness Research Fund. This would essentially free Heidelberg of the need to devote energy and time to raising funds, a situation that later generations of investigators could only regard with great wonder and envy.

Since the pneumococcal capsular antigen was a polysaccharide, and antibodies were thought to be proteins, Heidelberg realized that by measuring the amount of protein in specific precipitates made with the capsular antigen he could determine their antibody content. Together with Forrest Kendall, who had joined the Heidelberg lab, the protein content of immune precipitates was determined by measuring total nitrogen, using the Kjeldahl procedure that came to be the hallmark of laboratories carrying out Heidelberg-type quantitative immunochemistry.

Quantitative analyses of immune precipitates established that the proportions of antigen and antibody molecules in diverse antigen-antibody complexes varied systematically with the amounts of reactants introduced. The findings went a long way toward establishing the multivalency of antibodies and antigens and the lattice nature of the complexes they formed. More importantly perhaps, Heidelberg found out how to isolate pure, native antibody from immune precipitates. To measure the amount of protein (antibody) in polysaccharide antigen-antibody precipitates, the precipitates were routinely digested with sulfuric acid to yield ammonium sulfate for Kjeldahl determination. However, it was noted that the amount of material initially precipitated on mixing antiserum with polysaccharide antigens was reduced when precipitation reactions were carried out in high-salt concentration. Thus, by forming precipitates in the presence of "physiological" salt concentration, 0.15 M NaCl, then

washing them to remove trapped serum proteins, the precipitates could be dissolved in 0.5-1.0 M NaCl to eventually yield highly purified antibodies. These were subsequently analyzed by the then new methods of free electrophoresis and ultracentrifugation in collaboration with A. Tiselius and K. O. Pedersen, who had developed the required instrumentation and procedures. The studies revealed that antibodies came in two principal forms, distinguished by their mass and sedimentation rate: high molecular weight molecules designated 19S and low molecular weight ones termed 7S (now called IgM and IgG, respectively).

The isolation of purified antibodies from specific precipitates also helped solve another problem. It had long been known that antisera produced against bacteria, say staphylococci, exhibit diverse specific activities. An antiserum could, for example, protect animals against infection with those bacteria, agglutinate the bacteria, precipitate soluble components from culture medium in which they had been cultivated, and enhance their phagocytosis by white blood cells. These diverse manifestations were ascribed by some immunologists to different types of antibody molecules, called agglutinins (if they agglutinated the bacteria) or precipitins (if they precipitated soluble components) or opsonins (if they specifically enhanced leukocyte phagocytosis of the bacteria). In opposition to this pluralistic view, other immunologists (unitarians) maintained that a given antibody could, on associating with its antigen, give rise to any of these diverse responses, depending upon the state of the antigen (e.g., whether in solution or part of an intact microbe or taking place in a mouse).

The debate between the pluralists and unitarians was largely settled by Heidelberger and Elvin Kabat. Kabat was Heidelberger and Kendall's first graduate student, and was described by Heidelberger as a whirlwind. Using purified antibody to

the pneumococcal polysaccharide that had been isolated from a precipitation reaction, they showed it could specifically precipitate the antigen from solution and agglutinate pneumococci of the appropriate type, demonstrating the identity of agglutinins and precipitins. The clincher followed from Heidelberg's having previously shown that the capsular polysaccharide of type III pneumococcus was a polymer of cellobiuronic acid. By immunizing animals with an antigen made by linking cellobiuronic acid covalently to a carrier protein, Avery and W. F. Goebel showed that the resulting antiserum (anticellobiuronic acid) could specifically precipitate the type III polysaccharide, agglutinate type III pneumococci, and most notably, protect mice against a lethal infection with these bacteria.

Because of his appointment in a department of medicine, Heidelberg apparently felt obligated to work on some problems more obviously related to clinical issues than those centered on antigen-antibody precipitin reactions. He became involved, for example, in the purification and characterization of thyroglobulin. But the bacterial capsular polysaccharides he had discovered with Avery proved again to be the basis for his major contribution to clinical medicine, for the polysaccharides turned out to be critical virulence factors for the pathogenicity of pneumococci.

A study at the Rockefeller Institute suggested that antipolysaccharide antibodies in rabbit antipneumococcal sera were helpful in treating patients with pneumonia. The antibodies were of the 7S form (now called IgG). Having found out how to produce purified antibodies to particular types of pneumococci, Heidelberg's lab was then able to provide antibodies to treat patients hospitalized with pneumonia. Once the type of pneumococcus responsible for a particular patient's disease was identified (by testing sputum or blood or urine with type-specific antisera), the corre-

sponding antibodies in partially purified form were given to that patient by intravenous injection. Precipitin tests carried out on the patient's serum obtained about half an hour later indicated whether a sufficient amount of antibody had been given. If the test showed free antibody (antibody excess), no more was needed. But, if the free antigen (i.e., soluble polysaccharide shed by the bacteria *in vivo*) was detected rather than excess antibody, additional antibody was administered. Usually 400-600 mg of antibody was sufficient to establish antibody excess. The therapeutic effectiveness of this procedure was evident from the great decline in the number of deaths from pneumonia due to types of pneumococci for which purified antibodies could be provided (types I, II, and III).

With the entry of the United States into World War II, Heidelberger engaged in several war-related studies. One involved protection (presumably by antisera) against anthrax and the highly toxic castor bean protein called ricin, both of which the Germans were thought to be preparing to use against allied troops. Another project, carried out with Manfred Mayer (then a graduate student and later a leading figure in the study of complement) was aimed at developing the use of lysed red blood cells from malaria-infected individuals as a therapeutic vaccine in malaria-infected troops returning to the United States from the South Pacific.

But Heidelberger's most significant war-related research effort stemmed again from the pneumococcal polysaccharides. In an effort to reduce the large number of cases of pneumonia in some Army camps, where recruits lived under crowded conditions, studies were carried out to determine whether injections of purified polysaccharide would elicit protective antibody responses. Volunteer medical students at the College of Physicians and Surgeons were first injected with around 50 μg of purified polysaccharide types I, II,

and V, and found to produce measurable amounts in serum of antipolysaccharide antibodies. Because the students could obviously not be deliberately challenged with virulent pneumococci to determine whether the antibodies were protective, a large-scale clinical trial was organized by Colin MacLeod. MacLeod had worked with Avery and Maclyn McCarty in the classic study that first showed genetic information to be carried in DNA (the DNA, in fact, that specified a pneumococcus's type of capsular polysaccharide), and he later become a charismatic and brilliant head of the Microbiology Department at the New York University School of Medicine. In the trial he organized at an Army Camp in South Dakota, 8,500 individuals in one group were each injected with 1 ml containing 50-70 μg of polysaccharide types I, II, V, and VII, types that together accounted for about 60 percent of the cases at that camp. A similar number of individuals comprising a control group were injected with 1 ml saline. Over the ensuing 16 weeks there were 26 cases of pneumonia of types I, II, V, and VII in the control group and only 4 cases in the injected group, whereas control and injected groups experienced essentially the same number of cases of pneumonia due to other types of pneumococci. The clear and striking results of that wartime trial led to the continued use of the vaccine (or a variant of it, see below): It is now generally recommended that people who are at particular risk of coming down with pneumococcal pneumonia, especially the elderly, receive each autumn an injection of a mixture of pneumococcal polysaccharides.

The antipolysaccharide antibodies must be remarkably effective, as it appears that at extremely low levels they can prevent infection. Once formed, they persist for many months in serum with little decrease, perhaps because mammalian tissues lack enzymes that degrade polysaccharide antigens. It is now known that polysaccharides generally are T-

independent antigens (i.e., they are not recognized by the T cells that normally enhance antibody production by B cells). Currently, therefore, pneumococcal and other bacterial polysaccharide antigens are linked in vaccines to carrier proteins, the protein moiety providing the antigenic peptides that stimulate the T cells needed for optimal antibody responses. That essentially protein-free pneumococcal polysaccharide injected alone was so effective in protecting against pneumococcal infection in the World War II trial testifies to the remarkable potency of the antibodies they elicited. Because antibodies produced by memory B cells are more reactive (i.e., have higher affinity for their antigen) and are longer-lived than those made by naïve B cells, it is possible that the great success of the wartime trial organized by MacLeod came about because the protein-free polysaccharides selectively stimulated memory B cells.

Faced with mandatory retirement at age 65, Heidelberger was pleased to accept a position at the Institute of Microbiology connected with Rutgers University in New Jersey. The institute had been established by his friend Selman Waksman with royalties emanating from Waksman's discovery of streptomycin. There Heidelberger continued to carry on with research and to participate in a course in immunology. During his 27 highly productive years at the College of Physicians and Surgeons, his laboratory group had never numbered more than perhaps 4 or 5 associates, in contrast to many modern academic laboratories with their 20 to 30 postdoctoral associates. Hence the downsizing associated with the move from Physicians and Surgeons to the microbiology institute was not much of a change for Heidelberger, particularly as he enjoyed a steady flow of foreign visitors to work with him for various periods. Though conditions at the institute in New Jersey were highly congenial, the commuting arrangements were arduous, because he continued

to maintain his residence in New York. And so he was happy after nine years there to retire again, this time to an adjunct professorship in the Department of Pathology at the New York University School of Medicine. There he continued to work on polysaccharides, and was writing a paper a week before his death at the age of 103.

Any effort to describe Michael Heidelberg would be wanting if it ignored his lifelong interest in music. By all accounts he was an accomplished clarinetist and an active performer alone and with small groups. These included the chamber music sessions organized by Waldo Cohen at annual meetings of the Federation of American Societies for Experimental Biology. One notable musical came about at a small conference in Bermuda (organized to consider the validity of heterologous organ transplantation practiced by a notorious physician in Switzerland, involving among other things transplants of sheep testicles to elderly gentlemen). Afternoons at the meeting were left free for enjoyment of Bermuda's wonderful beaches. But one afternoon it rained, and Heidelberg and his wife, an accomplished violinist, and Felix Haurowitz, a fine pianist (and the originator of the antigen template hypothesis to explain the diversity and specificity of antibodies), entertained the gathering with an impromptu performance of wonderful chamber music.

As expected, Heidelberg's personal life had joys and sorrows. He was married twice, both times happily, but lived to mourn the passing of each wife, and he suffered the loss of his only child, Charles Heidelberg, a distinguished professor of biochemistry at the University of Wisconsin, who discovered 5-fluorouracil, a powerful agent still used for cancer chemotherapy.

Heidelberg's published papers appeared in every decade of the twentieth century; he was twice president of the

American Association of Immunologists; he received a great number of awards and medals, including two Lasker awards, and an astonishing number (15!) of honorary degrees from American and European universities.

At his one-hundredth birthday he happened to be visiting a friend in Boston, and a party was arranged in his honor in a departmental library at the Harvard Medical School. Not surprisingly, to those who had not seen him for several years, he had grown even smaller and more frail, but they were not prepared to see that he had grown a long beard, white of course. It was, he explained, due to his hands having become too unsteady to continue shaving. But his intellectual powers were not noticeably diminished. Some in the gathering tried to guess how many papers he had written during his lifetime. When the question was put directly to him, he looked up and replied slowly, "three hundred and four." Then pausing, his eyes twinkling, he added, "So far." Given his consistency over a long lifetime as the epitome of rational and thoughtful behavior, one had to wonder if he had anticipated the question and with his quiet humor had enjoyed planning the answer.

For those prone to draw sharp distinctions between basic and applied research, it may be useful to ponder the accomplishments of the pneumonia group at the Rockefeller Institute with which Heidelberger was closely associated for a critical period. From that intensive study of the pneumococcus, and the infectious disease it causes in humans, there emerged the Heidelberger-Avery discovery that the potent capsular antigen of the pneumococcus was a polysaccharide and Avery, McCarty, and MacLeod's demonstration that DNA is the carrier of genetic information for the polysaccharide's production. Heidelberger's continued pursuit of the immune response to those polysaccharides had a profound impact on immunology: It changed the concept of the antibody

from an essentially ill-defined set of serum activities to a protein molecule, measurable in conventional chemical units and isolable as a pure protein whose recognition of antigens could be analyzed in molecular terms. And his work led directly to the development of a simple vaccine that continues to this day to help reduce morbidity and mortality from what was once one of the most feared infectious diseases.

IN PREPARING this memoir I have drawn extensively on Heidelberg's detailed autobiographical accounts that appeared in *Annual Review of Biochemistry* (48[1979]:1-21), *Immunological Reviews* (83[1985]:6-22), and the *Annual Reviews of Microbiology* (31[1977]:1-12), an obituary prepared by Elvin Kabat (*Journal of Immunology* 148[1992]:301-307), and on my own recollections.

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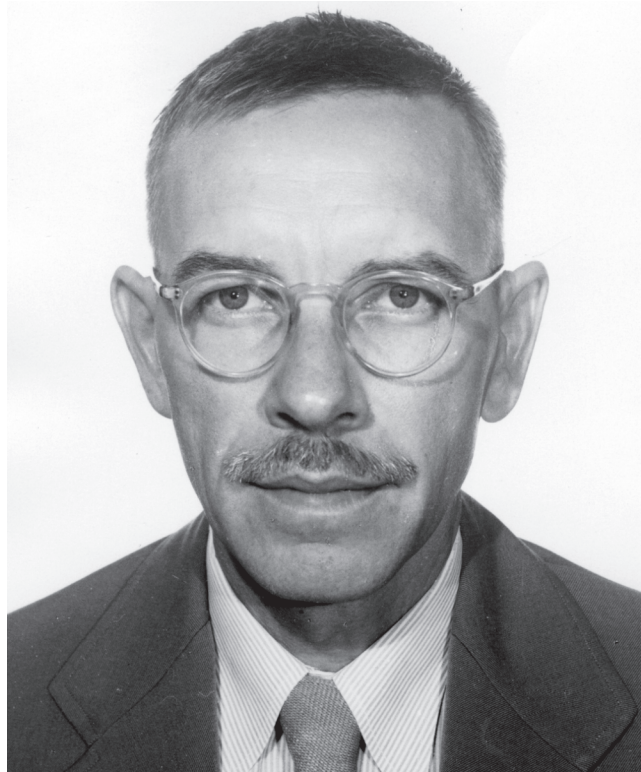


Photo by Henry Jones

Carl L. Jones

ALFRED DAY HERSHEY

December 4, 1908–May 22, 1997

BY FRANKLIN W. STAHL

MOST STUDENTS OF BIOLOGY know of Hershey—his best known experiment is described in texts of both biology and genetics. This work (1952,1) provided cogent support for the hypothesis that DNA is the conveyor of genetic information. The Hershey-Chase experiment used DNA-specific and protein-specific radioactive labels to show that the DNA of an infecting T2 bacteriophage entered the bacterium while most of the protein could be stripped from the surface of the cell by agitation in a Waring blender. Such abused cells produced a normal crop of new phage particles. Previous evidence implicating DNA in heredity had shown that a property of the surface coat of the pneumococcus bacterium could be passed from one strain to another via chemically isolated DNA. The Hershey-Chase observation justified the view that the entire set of hereditary information of a creature was so encoded. This work counted heavily in making Hershey a shareholder, with Max Delbrück (1906-81) and Salvadore E. Luria (1912-91), of the 1969 Nobel Prize in physiology or medicine.

Al Hershey was born on December 4, 1908, in Owosso, Michigan. He obtained a B.S. in 1930 and a Ph.D. in 1934 from Michigan State College. From 1934 until 1950 he was

employed in teaching and research in the Department of Bacteriology at Washington University School of Medicine. He married Harriet Davidson in 1945; they had one son, Peter. In 1950 Al became a staff member at the Department of Genetics, Carnegie Institution of Washington, Cold Spring Harbor, New York; in 1962 he was appointed director of the Genetics Research Unit of that institution. Al was elected to the National Academy of Sciences in 1958 and was awarded its Kimber Genetics Award in 1965.

Al's Ph.D. thesis, prepared in the departments of chemistry and bacteriology at Michigan State College, described separations of bacterial constituents identified by the quaint definitions of the times. Except for its evident care and industry the work was unremarkable, merely part of an ongoing study "to arrive ultimately at some correlation between the chemical constitution of [*Brucella* species], and the various phenomena of specificity by them" (1934).

Al then assumed an instructorship in bacteriology and immunology at Washington University in St. Louis, where he collaborated with Professor J. Bronfenbrenner. From 1936 to 1939 their papers reported studies on the growth of bacterial cultures. From 1940 to 1944 Al's experiments dealt with the phage-antiphage immunologic reaction and with other factors that influenced phage infectivity. During both those periods about half of the 28 papers bearing Al's name were authored solely by him. (It was apparently here that Al learned how to handle phage. It may also have been here that Al acquired the idea that authorship belongs to those who do the experiments and should not reflect patronization, rank, title, or even redaction of the manuscript.) Some of these papers may have been important contributions to the understanding of antigen-antibody reactions. To me they appear original, thoughtful, and quantitative, especially those on the use of phage inactivation to

permit the study of the antigen-antibody reaction at “infinite” dilution of antigen (e.g., 1941). But, they interested an audience that did not include many geneticists or others interested in biological replication (except, perhaps, for Linus Pauling).

While at St. Louis Al (1951) showed that phage particles were “killed” by the decay of the unstable isotope ^{32}P incorporated within their DNA. After the central importance of DNA to the phage life cycle (and to genetics) had been demonstrated this “suicide” technique was exploited in other labs in efforts to analyze the phage genetic structure and its mode of replication. Like most early experiments in “radiobiology” these analyses were fun, but not much more.

As recounted by Judson (1996, p. 35), Max Delbrück was attracted by Al’s papers. Perhaps he liked their mathematical, nonbiochemical nature. He must have liked their originality, logical precision, and economy of presentation. Max invited Al to Nashville in 1943 and recorded the following impression: “Drinks whiskey but not tea. Simple and to the point . . . Likes independence.” Al’s first “interesting” phage papers appeared soon thereafter (1946, 1947).

The ease with which large numbers of phage particles can be handled facilitated the discovery and characterization of mutants that were easily scored. Al recognized that the high infectivity of phage and the proportionality of plaque count to volume of suspension assayed allowed for quantification of mutation far exceeding that possible in most other viral systems. Al measured mutation rates, both forward and back, and demonstrated the mutational independence of r (rapid lysis) and h (host range). He succeeded also in showing (in parallel with Delbrück) that these mutationally independent factors could recombine when two genotypes were grown together in the same host cells (1946, 1947). Thus phage genetics was born as a field of study, and it became

conceivable that not only could the basic question of biological replication be addressed with phage but so also could phenomena embraced by the term "Morgan-Mendelism."

Al continued the formal genetic analyses of T2 with investigations of linkage. Hershey and Rotman (1948) demonstrated that linkage analysis would have to take into account the production of recombinant particles containing markers from three different infecting phage genotypes. The same authors (1949) used mixed indicators to enumerate all four genotypes from two-factor crosses involving *h* and *r* mutants. That trick made it feasible to analyze fully the yields from individual mixedly infected bacterial cells. The signal finding was that all four genotypes of phage could be produced by an individual cell but that the numbers of complementary recombinants, which were equal on the average, showed little correlation from cell to cell. This demonstration of apparent nonreciprocity in the exchange process leading to recombination raised the specter that crossing over in phages would prove to be fundamentally different from that occurring in meiosis. The desire to unify this and other apparently disparate properties of phage and eukaryotic recombination into a single theoretical framework motivated a populational analysis of phage recombination by Visconti and Delbrück (1953).

By most criteria individual T2 particles are haploid (i.e., they contain but one set of genetic material), however heterozygous particles, which contain two different alleles at a single locus, were described by Hershey and Chase (1952,2) at the 1951 Cold Spring Harbor Symposium. Following the elucidation of DNA as a duplex molecule (Watson and Crick, 1953), it was possible to propose heteroduplex models for those heterozygotes. Such models played a central role in all subsequent thinking about recombination,

especially that involving relationships between meiotic crossing over and gene conversion.

Al, like Levinthal (1954) before him, expanded on the Visconti-Delbrück analysis in an effort to connect observations on heterozygotes, which had molecular implications, with the formal concepts proposed to deal with the populational aspects of phage crosses. The paper (1958) convinced many, including Al, that this approach to understanding biological replication was unlikely to be productive.

From this time on, Al's studies became more down-to-earth (and successful) as he turned from mathematically based genetic analyses to serious studies of phage structure and the biochemistry of phage development. There is no doubt, however, that these studies were informed by Al's acute awareness of the genetical and radiobiological facts that had to be explained. These new studies were jump started by the blender experiment described above.

Several subsequent papers refined the conclusions of the blender experiment by showing, for instance, that some protein is injected along with the phage DNA (1955). With Watson-Crickery well established by this time these studies were interesting but not threatening to the view that the genetic substance was DNA. During this period Al's lab published works that described DNA and protein production, and relations between them, in infected cells. They provided the biochemical counterpart of the genetically defined notion of a pool of noninfective, vegetative phage (Visconti and Delbrück, 1953; Doermann, 1953). This change of emphasis allowed Al to write (1956),

I have proposed the ideas that the nucleic acid of T2 is its hereditary substance and that all its nucleic acid is genetically potent. The evidence supporting these ideas is straightforward but inconclusive. Their principal value is pragmatic. They have given rise to the unprecedented circumstance that chemical hypotheses and the results of chemical experiments

are dictating the conditions of genetic experiments. This development I regard as more important than the bare facts I have presented, which may yet prove to be of little or no genetic interest.

Biochemical studies on phage development were clouded by the lack of understanding of phage genome structure. It was not even clear how many chromosomes (DNA molecules) a phage particle contained. Furthermore, although Watson and Crick had specified what any short stretch of DNA should look like (plectonemically coiled, complementary polynucleotide chains), they had been understandably proud of their model, which was structurally coherent in the absence of any specification of longitudinal differentiation. For them it was enough to say that therein lay genetic specificity. For Al that was not enough, and his lab pursued studies dedicated to the physical description of phage DNA. The results of these studies were succinctly reviewed by Al (1970,1) in his Nobel lecture. I'll briefly summarize my view of them, dividing the studies by phage type.

Al developed and applied chromatographic and centrifugal methods to the analysis of T2 chromosome structure (e.g., 1960,1,2). This work systematized our understanding of the breakage of DNA during laboratory manipulation and had its denouement in the demonstration that a T2 particle contains just one piece of DNA (1961) with the length expected of a linear double helix (Cairns, 1961). That conclusion was in apparent contradiction to genetical demonstrations that T4 chromosomes contained more or less randomly located physical discontinuities (Doermann and Boehner, 1963). A major insight into the structure of T-even phage chromosomes resulted from attempts to reconcile the apparently contradictory physical and genetical descriptions of T-even chromosomes. The basic idea, elaborated and confirmed in a series of papers orchestrated by George Streisinger, was that the nucleotide sequences in

any clone of phage particles were circularly permuted and that the sequence at one end of a given chromosome was duplicated at the other end (the chromosomes were terminally redundant). The predicted circular linkage map provided an elegant frame for displaying the functional organization of the T4 chromosome, as revealed by the pioneering studies of Epstein et al. (1963).

The terminal redundancies of the T-even phage chromosomes provided an additional physical basis for Al's heterozygotes. (See Streisinger [1966] for references and a more detailed recounting.) These insights were exploited and elaborated by Gisela Mosig, who spent the years 1962-65 in Al's lab. There she combined her genetical savvy of T4 with studies on the structure of the truncated, circularly permuted DNA molecules that she discovered in certain defective T4 particles. Those studies formed the basis for an elegant demonstration of the quantitative relations between the linkage map of T4 (as constructed from recombination frequencies) and the underlying chromosome (Mosig, 1966). Fred Frankel (1963) and Rudy Werner (1968) in Al's lab examined the intracellular state of T-even phage DNA. Their discovery that it was a network undermined the Visconti-Delbrück analyses of phage recombination as a series of tidy, pairwise, meiosis-like matings, and well-aimed triparental crosses by Jan Drake (1967) killed the pairwise-mating idea once and for all.

Meselson and Weigle (1961) demonstrated that phage λ DNA, like that of *E. coli* (Meselson and Stahl, 1958), is replicated semiconservatively in agreement with Watson and Crick's proposal that the replication of DNA involves separation of the two complementary strands; however, uncertainties about the structure of the semiconserved entities identified by Meselson prevented those experiments from being taken as proof of the Watson-Crick scheme. Careful

measurements of the molecular weight of λ 's DNA (1961) demonstrated that there was just one molecule per particle. That conclusion, combined with autoradiographic measurement of the length of λ DNA (Cairns, 1962), established that λ 's semiconservatively replicating structure is indeed a DNA duplex, putting the issue to rest.

The chromosome of λ also provided a surprise (1963, 1965). Though the chromosomes in a λ clone are all identical (i.e., not permuted), each chromosome carries a terminal 12-nucleotide-long segment that is single stranded and is complementary to a segment of the same length carried on the other end. The complementary nature of the segments gives λ "sticky ends." These ends anneal at the time of infection, circularizing the chromosome, which can then replicate in both theta and sigma modes. The demonstration of a route by which the λ chromosome can circularize provided physical substance to Alan Campbell's (1962) proposal that the attachment of λ prophage to the host chromosome involves crossing over between the host chromosome and a (hypothesized) circular form of λ . And, of course, the understanding of λ 's sticky ends, whose annealing creates *cos*, is exploited by today's gene cloners whenever they work with a cosmid.

The nonpermuted character of λ 's chromosome made it susceptible to analyses prohibited in T-even phage. For instance, Hershey et al. (1968) demonstrated the mosaic nature of the chromosome: Major segments differed conspicuously from each other in their nucleotide composition. (That conclusion foreshadowed our current understanding of the role of horizontal transmission in prokaryotic evolution.) Al's lab demonstrated that these differing segments had distinguishable annealing (hybridization) behavior. They exploited those differences to identify the approximate location of the origin of replication (Makover, 1968) and to

identify regions of the chromosome that were transcribed when λ was in the prophage state (Bear and Skalka, 1969).

Al appreciated that progress in science depends on the development of new methods. Among those to which Al's lab made important contributions were fixed-angle Cs gradients, methylated albumin columns for fractionating DNA, methods of handling DNA that avoid breakage and denaturation as well as methods that would break phage chromosomes into halves and quarters, and the calibration of methods for measuring molecular weights of DNA. Al confessed that the development of a method was painful: His view of heaven was a place where a new method, finally mastered, could be applied over and over. Bill Dove quoted Al as saying, "There is nothing more satisfying to me than developing a method. Ideas come and go, but a method lasts."

Al occasionally blessed us with his thoughts about the deeper significance of things. His papers "Bacteriophage T2: Parasite or Organelle" (1957), "Idiosyncrasies of DNA Structure" (1970,1), and "Genes and Hereditary Characteristics" (1970,2) delighted his contemporaries and can still be read with pleasure and profit.

But how many people really knew Al Hershey? From his works we can say he was interested in this or that, but such a contention might leave the impression that we have adequately summarized his interests. That is hardly likely. Each of Al's contributions was truly original: He never copied even himself! Consequently, each paper was a surprise to us. We can surmise, therefore, that his published works do not begin to saturate the library of ideas available to him. His papers must be but a small sampling of his scientific thoughts.

And the rest of his mind? Who knows? Al exemplified reticence. His economy of speech was greater even than his

economy of writing. If we asked him a question in a social gathering, we could usually get an answer like “yes” or “no.” However, at a scientific meeting one might get no answer at all, which was probably Al’s way of saying, in the fewest possible words, that he had no thoughts on that subject suitable for communication at this time.

Encounters with Al were rare, considering that he worked at Cold Spring Harbor, which hosted hundreds of visitors every summer. That’s because Al spent his summers sailing in Michigan, and except at occasional symposia or the annual phage meetings, which came early and late in the season, he was not to be seen.

Thus, most of us who valued Al as a colleague and acquaintance, didn’t really know him. I am one of those, and I suppose that status qualifies me for this assignment: The Al about whom I write is the same Al that most other people did not really know, either. (Some who worked with Al say that his lab functioned well because Laura Ingraham, Al’s long-time associate, really did know his mind.)

The Phage Church, as we were sometimes called, was led by the Trinity of Delbrück, Luria, and Hershey. Delbrück’s status as founder and his *ex cathedra* manner made him the pope, of course, and Luria was the hard-working, socially sensitive priest-confessor. And Al was the saint. Why? How could we canonize Al when we hardly knew him?

Maybe some of the following considerations apply: The logic of Al’s analyses was impeccable. He was original, but the relevance of his work to the interests of the rest of us was always apparent; he contributed to and borrowed from the communal storehouse of understanding, casual about labeling his own contributions but scrupulous about attributing the ones he borrowed. He was industrious (compulsively so—each day he worked two shifts). He was a superb editor (e.g., 1971) and critic, devastatingly accurate but never

too harsh; he deplored that gratuitous proliferation of words that both reflects and contributes to sloppiness of thought. And his suggestions were always helpful.

Does that qualify him for sainthood? It would if he were in all other respects perfect. And he may have been. Who could tell? Who among us knew this quiet man well enough to know if there was a dark side? Perhaps canonization was a mark of our deep respect for this quintessential scientist. Maybe by canonizing Al we could accept the relative insignificance of our own contributions. Maybe we were just having fun.

But, in his papers Saint Al was *there*. He talked to the reader, explaining things as he saw them, but never letting us forget that he was transmitting provisional understanding. We got no free rides, no revealed truths, no invitation to surrender our own judgment. And we could never skim, since *every* word was important. I think this style reflected his verbal reticence, which in turn mirrored his modesty. Examples: "Some clarification, at least in the mind of the author, of the concepts 'reversible' and 'irreversible' has been achieved" (1943). "On this question we have had more opportunity in this paper to discover than to attack difficulties" (1944). Al's modesty was dramatically documented by Jim Ebert (at Al's memorial service, Cold Spring Harbor, summer 1997), who recalled that Al, whose research support was guaranteed by the Carnegie Institution, argued with Carnegie directors for the right to apply for NIH support so that he might benefit from the critiques of his peers.

In science Al appeared to be fearless. Fearlessness and modesty might seem an unlikely combination. Not so. Modesty is kin to a lack of pretense. In the absence of pretense there is nothing to fear.

Tastes of the many flavors of Hershey's mind and the accomplishments of his laboratory can be best gained from

the annual reports of the director of the Genetics Research Unit, Carnegie Institution of Washington Yearbook (reprinted in Stahl [2000]). The principal investigators of this unit were he and Barbara McClintock. In 1963 Al wrote,

Our justification for existence as a Unit, however, resides in the value of our research. We like to think that much of that value is as unstorable and as durable as other human produce that cannot be sold. Some can be put on paper, however. That we offer with the usual human mixture of pride and diffidence.

Those who worked with Hershey at Cold Spring Harbor include Phyllis Bear, Elizabeth Burgi, John Cairns, Connie Chadwick, Martha Chase, Carlo Cocito, Rick Davern, Gus Doermann, Ruth Ehring, Stanley Forman, Fred Frankel, Dorothy Fraser, Alan Garen, Eddie Goldberg, June Dixon Hudis, Laura Ingraham, Gebhard Koch, André Kozinsky, Nada Ledinko, Cy Levinthal, Shraga Makover, Joe Mandell, Norman Melechen, Teichi Minagawa, Gisela Mosig, David Parma, Catherine Roesel, Irwin Rubenstein, Ed Simon, Ann Skalka, Mervyn Smith, George Streisinger, Neville Symonds, René Thomas, Jun-ichi Tomizawa, Nick Visconti, Bob Weisberg, Rudy Werner, Frances Womack, and Hideo Yamagishi.

Al Hershey is remembered for his contributions to the understanding of the chemical basis of heredity. He is respected for the style in which those contributions were presented. He is revered for his unwavering respect of the scientific method and of his scientist colleagues. A more complete review of Al's work, including testimonials from colleagues, can be found in Stahl (2000).

THIS BIOGRAPHICAL memoir is modified from Stahl (1998) with permission of *Genetics*. Copies of Carnegie yearbook reports and other documents were kindly supplied by the Archives of the Cold Spring Harbor Laboratory.

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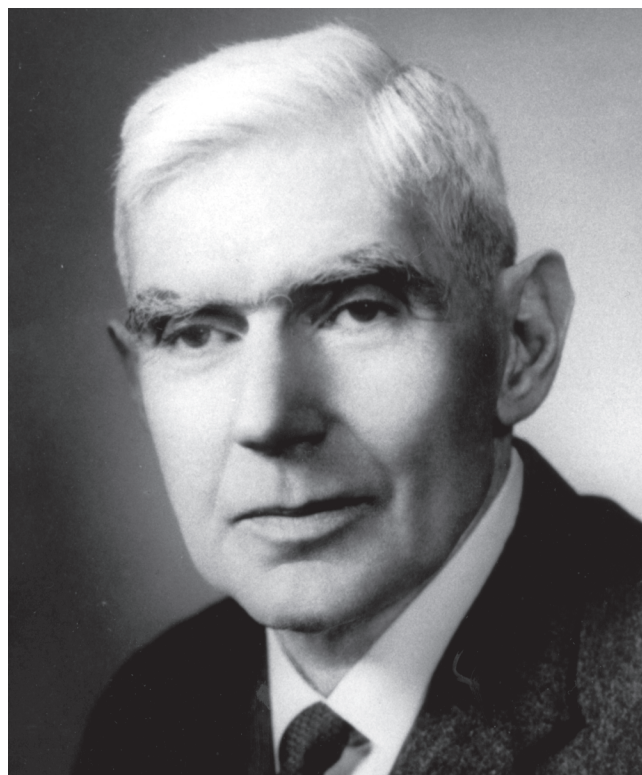
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Karl F. Herzfeld

KARL FERDINAND HERZFELD

February 24, 1892–June 3, 1978

BY JOSEPH F. MULLIGAN

KARL F. HERZFELD, BORN in Vienna, Austria, studied at the university there and at the universities in Zurich and Göttingen and took courses at the ETH (Technical Institute) in Zurich before receiving his Ph.D. from the University of Vienna in 1914. In 1925, after four years in the Austro-Hungarian Army during World War I and five years as *Privatdozent* in Munich with Professors Arnold Sommerfeld and Kasimir Fajans, he was named extraordinary professor of theoretical physics at Munich University. A year later he accepted a visiting professorship in the United States at Johns Hopkins University in Baltimore, Maryland. This visiting position developed into a regular faculty appointment at Johns Hopkins, which he held until 1936. Herzfeld then moved to Catholic University of America in Washington, D.C., where he remained until his death in 1978.

As physics chairman at Catholic University until 1961, Herzfeld built a small teaching-oriented department into a strong research department that achieved national renown for its programs in statistical mechanics, ultrasonics, and theoretical research on the structure of molecules, gases, liquids, and solids. During his career Herzfeld published about 140 research papers on physics and chemistry, wrote

two important books: *Kinetische Theorie der Wärme* (1925), and (with T. Litovitz) *Absorption and Dispersion of Ultrasonic Waves* (1959), and made major contributions to Felix Klein's *Encyklopädie der Mathematischen Wissenschaften*, to the *Handbuch der Physik*, and to the *Handbuch der Experimental Physik* on a variety of topics relating to physicochemical properties of matter.

John A. Wheeler, whose doctoral dissertation Herzfeld had directed at Johns Hopkins, summed up Herzfeld's career as follows: "No one who came so early [1926] from Europe to America continued longer to give so richly to this country out of the great European tradition of theoretical physics."¹

Karl Ferdinand Herzfeld was born in 1892 in the Vienna of the Hapsburgs and the Austro-Hungarian Empire. He came from a prominent, recently assimilated Jewish family. His father was a physician with an extensive practice and an associate professor of obstetrics and gynecology at the University of Vienna; his mother, nee Camilla Herzog, was the daughter of a newspaper publisher and sister of a well-known organic chemist, R. O. Herzog. Karl's grandfather had begun the assimilation of his family into the predominantly Christian culture in Vienna. Karl's parents were both baptized, as was Karl himself soon after birth; he remained a dedicated Catholic for the rest of his life.

The Herzfeld family had a strong sense of duty to members of the family and to the larger Viennese society of which they were part. His parents also had a strong commitment to serving that society as true professionals. This parental commitment throws much light on Karl's extraordinary dedication to duty throughout his entire life. These were the values of the Herzfeld family—values that were constantly in evidence in Karl's later career.

When he was 10, his parents enrolled Karl in a private *Gymnasium* run by the Benedictine Order of the Roman

Catholic Church. It was called the *Schottengymnasium*, since the Benedictines who had founded the school came from Scotland. Karl continued his education there until he was 18. He always retained fond memories of the rigorous classical education, the thorough training in science and mathematics, and the great appreciation for intellectual activity he acquired during these formative years.

In 1910 Herzfeld enrolled in the University of Vienna to study physics and chemistry. His mentor in physics was Friedrich Hasenöhr (1874-1915), who had taken the place of Ludwig Boltzmann as head of the Theoretical Physics Institute in Vienna following Boltzmann's lamentable suicide in 1906. Hasenöhr was well known in Vienna for having proved in 1904 the validity of the equation $E=mc^2$ for cavity radiation, just a year before Einstein established its general validity.

Due to the tradition established by Boltzmann, Vienna was considered the outstanding university in statistical physics in all of Europe. Although Herzfeld did take a course from Hasenöhr that included thermodynamics and statistics, he always said that he had learned little statistical physics in Vienna, and had mastered the subject only during the year he spent in Zurich, where he met Otto Stern (1888-1969). (Stern is better known today as an experimentalist, who received the 1943 Nobel Prize in physics for his work on molecular beams.) In 1912 Stern was Einstein's assistant at the Technische Hochschule in Zurich. Einstein was lecturing there on thermodynamics and statistical mechanics, but all his research time was devoted to general relativity. Herzfeld was not interested in this subject, and his interactions with Einstein were infrequent and disappointing. But he did find a kindred soul in Stern, as indicated in his statement: "I profited enormously from contact with him [Stern] and

acquired from his conversations whatever deeper understanding of thermodynamics I have.”²

In 1914 Herzfeld returned to Vienna. He successfully defended his doctoral dissertation, which applied statistical mechanics to a gas of free electrons as a model for a theory of metals (1913). By the time he completed his physics degree in 1914 he already had six research papers to his credit. One of these was an attempt to derive a model for the hydrogen atom (1912), published just before Bohr’s famous 1913 paper. Herzfeld used a technique similar to that of Bohr to quantize the allowed energy levels for a modified Thomson atom, leading to the quantization of the radii of the electron orbits. He had failed to grasp the essential point, however, that it was the energy differences between the quantized energy levels that were required to find agreement with the experimental Balmer spectrum. Though he had missed this crucial feature of Bohr’s theory, Herzfeld had clearly demonstrated his ability to do high-level research in a new field.

Herzfeld received his Ph.D. in July 1914, and he immediately signed up for one year of service in the Austro-Hungarian Army. When the First World War broke out a few months later, however, he served with distinction for three more years as an officer in a heavy-artillery battery on the Russian, Serbian, and Italian fronts. Later Herzfeld looked back on his military service without regret: “I had the luck that I could do some work even during the war, being a theoretical physicist. . . . I was an observer in the mountains, sitting in a hut. You could go out six or eight times a day for twenty minutes. And either you play cards or you are luckier and write a paper.”³

Herzfeld wrote six papers while in military service from 1914 to 1918. All involved the application of statistical methods to problems in physics and chemistry. By the end of the

war he had established a solid reputation as a competent, well-trained physicist, with particular strength in statistical mechanics. He had also displayed in his papers a strong interest in the structure of matter and the ways molecules arranged themselves to form gases, liquids, and solids—problems at that time of more interest to chemists than to physicists.

When Herzfeld returned to Vienna late in 1918, he found the economic situation so bad that the university was in danger of closing. Conditions in Munich, only a four-hour train ride from Vienna, were somewhat better, and so Herzfeld decided to move there to study analytical chemistry, hoping eventually to land a job in the highly respected German chemical industry. But he found none of the challenge and thrill of discovery in the quantitative analysis laboratory that he had enjoyed in his more speculative and, for him, intellectually more exciting work in theoretical physics.

He therefore shifted back to physics and at the Ludwig-Maximilians-Universität in Munich attended the lectures of Arnold Sommerfeld, professor of theoretical physics, and of Kasimir Fajans, professor of physical chemistry. He impressed both professors so favorably that he was offered a position as *Privatdozent* in theoretical physics and physical chemistry, combined with an assistantship under Fajans for research in the latter field. Such an interdisciplinary appointment was a good predictor of the road Herzfeld's subsequent career would follow.

Physics in Munich was thriving because of Sommerfeld's ability and personality, and physicists well known to us today—such as Werner Heisenberg, Wolfgang Pauli, Otto Laporte, Fritz London, Gregor Wentzel, and Alfred Landé—all profited from spending time at Sommerfeld's institute. Herzfeld usually taught an advanced course in theoretical physics and one in physical chemistry. When Sommerfeld was away,

which happened quite frequently, Herzfeld took over his lectures. It appears that Herzfeld had a considerable impact on some of Sommerfeld's own research students, among whom were Walter Heitler⁴ and Linus Pauling. Herzfeld's lectures were highly praised and well attended by chemists, for whom he kept the mathematics as simple as possible. At the same time he held special lectures on problems of greater difficulty for the physics and mathematics students.⁵

During his years in Munich (1919-26)—five years of which were spent as a *Privatdozent*—Herzfeld's research was dedicated to problems that straddled the fields of physics and chemistry. He made a major contribution to the theory of chemical reaction rates by showing that a third particle was always needed to supply the extra energy to produce a chemical reaction between two atoms or molecules (1919). The ensuing debate between defenders of Herzfeld's collision theory and the chemists' proposal that the extra energy required was provided by radiation from the walls of the reaction vessel was finally settled in Herzfeld's favor.

An important problem in physical chemistry was the relationship between statistical mechanics and thermodynamics. In an important paper in the *Zeitschrift für physikalische Chemie* (1920), Herzfeld investigated this relationship both from the standpoint of classical mechanics and of quantum theory. The next year (1921) Herzfeld published a long article in Felix Klein's *Encyklopädie der Mathematischen Wissenschaften* on Physikalische und Electrochemie, which indicated his main fields of interest at this early point in his career as a physical scientist.

Herzfeld's scientific productivity during his years in Munich was truly remarkable. He published the first modern book in any language on kinetic theory and statistical mechanics (1925), which soon became a very popular graduate-level textbook in German-speaking universities. In

the second edition of Hugh S. Taylor's *Treatise on Physical Chemistry*, Herzfeld and H. M. Smallwood wrote the sections on the kinetic theory of gases and liquids and on imperfect gases and the liquid state (1931). During his Munich years Herzfeld also contributed a number of important articles to the *Handbuch der Physik*, including one on Grösse und Bau der Moleküle (1924), another on Klassische Thermodynamik (1926), and a third with K. L. Wolf on Absorption und Dispersion (1928).

In addition to the above monograph on the kinetic theory of heat, his *Handbuch* articles, and two articles in the *Handbuch der Experimental Physik*, one of which was a long article on the lattice theory of solids (1928), Herzfeld published over 30 shorter research papers in German journals during the years 1919-26. One secret of his productivity was his ability to write most of his shorter papers without having to consult previously-read journal articles by other scientists on the same topic. He seems to have had an encyclopedic memory for the literature in both physics and chemistry, perhaps a result of the papers he wrote during World War I, when no scientific periodicals were available to him.

Herzfeld's research output has often been underestimated by physicists and chemists mainly for two reasons: (1) His published research was a rich mixture of articles on physics, articles on chemistry, and articles embracing aspects of both disciplines and (2) his interest in physics extended over a very wide range of topics, which made it difficult for him to become a leading authority in any one field. His name was well known and highly respected by all theoretical physicists in Germany in the 1920s, however, especially for his long, authoritative articles in the handbooks so popular with German physicists at that time.

Because he had been successful in both teaching and research, Herzfeld was finally named extraordinary professor

of theoretical physics in Munich for the academic year 1925-26. During that year he took over full responsibility for a number of courses previously taught by Sommerfeld. Then in 1926 Herzfeld left Germany quite unexpectedly. He had received an offer to become the first Speyer visiting professor at Johns Hopkins University in Baltimore. Because there were no attractive academic jobs available in Europe at the time, Herzfeld accepted this position with gratitude and enthusiasm.

Herzfeld's life in Baltimore was characteristically modest. For the ten years (1926-36) that he was on the faculty at Johns Hopkins, he lived in a dormitory room on Hopkins's attractive Charles Street campus. As a bachelor, he had no need for more space and he liked being close to his office and the university library. He learned English by going to the movies, especially to westerns, which he enjoyed immensely. In 1927 Princeton University offered Herzfeld a full professorship, but he turned it down, probably because he thought it unfair to leave Hopkins so soon after arriving there. The second physicist on Princeton's list, Eugene Wigner (Nobel Prize, 1963) took the position. This offer by Princeton strengthened Herzfeld's bargaining power with the Hopkins administration, and he succeeded in persuading President J. S. Ames to hire two additional young faculty members and to fund improved research laboratories for the physics department.

Herzfeld did considerable research at Johns Hopkins in collaboration with his colleague Francis O. Rice, a chemist born in Liverpool in 1890, who received his D.Sc. degree from Liverpool University in 1919 and spent the rest of his life in the United States. Rice joined the chemistry department at Hopkins as an associate professor in 1926, the same year Herzfeld arrived from Munich. Rice was interested in the same kind of physicochemical problems as Herzfeld,

and they soon began to work together. They published an important joint article in the *Physical Review*, under the title "Dispersion and Absorption of High-Frequency Sound Waves" (1928), which considered the role of molecular vibrations in the transfer of energy between ultrasonic waves and gas molecules. Herzfeld and Rice postulated that the velocity of sound propagating through a gas should depend not only on viscosity and heat conduction (as in classical theory) but also on the rate at which energy in the translational degrees of freedom of the molecules is exchanged with the internal degrees of freedom. They then sought to derive equations for the absorption and dispersion of sound waves in a gas that would lead to a characteristic relaxation time for this energy conversion process. This paper was extremely influential in proposing a novel way to use measurements of sound propagation to determine the rate at which molecules transfer energy from translational to vibrational modes of motion.

During his 10 years at Johns Hopkins, Herzfeld had the pleasure of seeing other European colleagues added to its physics faculty. These included two Nobel Prize winners in physics: James Franck (Nobel Prize, 1925) and Maria Goeppert-Mayer, who received her Nobel Prize only in 1963 after she and her husband, the physical chemist Joseph Mayer, had left Hopkins, first for the University of Chicago and in 1960 for the new campus of the University of California in San Diego. There Maria finally received her first regular appointment as professor of physics (at Hopkins she had only the title "research associate in physics"). When Maria Mayer was at Hopkins, Herzfeld published articles with her on the states of aggregation (1934), on the behavior of hydrogen dissolved in palladium and on the theory of nuclear fusion reactions (1935). He joined James Franck in publishing articles on a tentative theory of photosynthesis (1937),

on the photochemistry of polyatomic molecules, and (after they had both left Johns Hopkins) another article on a more complete theory of photosynthesis (1941).

The reasons for Herzfeld's move from Hopkins to Catholic University in Washington, D.C., at the end of the 1935-36 academic year are well set forth in a letter of May 19, 1936, from Herzfeld to Professor Arnold Sommerfeld in Munich.⁶

Herzfeld began this letter by discussing the unfortunate financial situation at Johns Hopkins. The university's deficit for the academic year 1935-36 was \$270,000, and a drive for additional funds did not come close to raising this sum of money. The Hopkins physics department was very upset by the financial situation, and Herzfeld wrote that "I have the feeling of sitting on a volcano." Two other factors, moreover, aggravated the problem: first, his relations with R. W. Wood, professor of experimental physics at Hopkins from 1901 to 1938 and for many years its chairman, had deteriorated. Second, J. A. Bearden, another experimentalist on the Hopkins faculty, suspected that Herzfeld had ambitions to be chairman, and had brought Franck to Hopkins to foster that goal. Bearden also disliked what he considered the excessive emphasis on theoretical physics in the department, and the presence of so many German physicists in a rather small department. (In addition to Herzfeld, Franck, and Maria Mayer the Dutch spectroscopist G. H. Dieke was also a physics faculty member.) Bearden blamed Herzfeld for causing dissension in the physics department by his strong support of Maria Mayer for a regular faculty appointment.⁷

Herzfeld's unhappiness soon became common knowledge, and he received offers of professorships in the physics departments of both Fordham University in New York City and Catholic University. Neither of these was a strong research department, a situation that Herzfeld did not like, but he decided to talk over these two offers with Isaiah

Bowman, then president of Johns Hopkins. After listening to Herzfeld for a few minutes, the Hopkins president immediately suggested that Herzfeld would be wise to accept one of these firm offers, since there was no guarantee that Hopkins would not in the near future have to reduce the size of its physics faculty.

Herzfeld therefore decided to accept Catholic University's offer. The news of his leaving Johns Hopkins to go to Catholic University as professor and chairman of the physics department shocked many of the scientists at Hopkins, which had a reputation for a strong physics department from its very beginning in 1876, when Henry Rowland (1848-1901) had been its first chairman. Catholic University, on the other hand, had only five faculty members in its physics department, and none of them did much research. Herzfeld's teaching load and salary at Catholic University were to be about the same as at Johns Hopkins, but he would as chairman of the physics department have many more administrative duties to consume his time.

The members of the Johns Hopkins University chemistry department on March 12, 1936, felt so strongly about the departure of Herzfeld that they wrote a letter of protest to President Bowman containing the following sentiments:⁸

We know of no theoretical physicist who enjoys nearly the reputation of Professor Herzfeld and who has at the same time the thorough knowledge of the science of chemistry and the acquaintance with chemical problems which he possesses. We regret particularly that the absence of Professor Herzfeld will necessarily mean the loss of a very efficient and fruitful connecting link between physics and chemistry.

Nothing ever came of this loyal protest by the chemists at Johns Hopkins. Two years later, however, F. O. Rice also left Hopkins and joined Herzfeld at Catholic University as chairman of its chemistry department.

Another, perhaps less important, factor in Herzfeld's decision to leave Johns Hopkins was related to his strong religious faith, which made him welcome the opportunity to become associated with a university that had a religious orientation. Herzfeld also saw in Catholic University's unique location in the nation's capital the opportunity to build a strong physics department by gradually adding a few outstanding part-time teachers, who in their full-time positions in government laboratories had already established impressive research reputations. This would allow him time to recruit a full-time research-oriented physics faculty. He also saw the need in Washington for substantial Ph.D. programs tailored to the needs of part-time students. These were often bright students with excellent M.S. degrees, who wanted to find an institution that would offer them the possibility of earning a solid doctoral degree. Herzfeld received encouragement for these ideas from the National Bureau of Standards administration and staff. These factors increased Herzfeld's confidence in the feasibility of what he planned to do. He probably would have been somewhat less confident had he realized the time and effort he would personally have to invest to convert his dream into a reality, but convert it he did.

In the late 1940s Herzfeld gave increased attention at Catholic University to quantum-mechanical calculations on the electronic structure of polyatomic molecules (1947, 1949), a field in which he and colleagues like C. C. J. Roothaan in the physics department and Virginia Griffing in the chemistry department trained many doctoral students (including this writer). Catholic University soon established a respected position in this field.

John C. Hubbard (1879-1954) had been one of the leaders in experimental ultrasonic research in the years 1927-46 at Johns Hopkins. After Hubbard's retirement from Hopkins

in 1947, Herzfeld invited him to Catholic University as research professor of physics. Beginning in the early 1950s Herzfeld devoted much time to theoretical work in ultrasonics to complement the experimental work of Hubbard and Theodore Litovitz, a gifted experimentalist on the Catholic University faculty. In 1959 Herzfeld and Litovitz collaborated on a book *Absorption and Dispersion of Ultrasonic Waves* (1959), a title almost exactly that of a theoretical contribution by Herzfeld 30 years earlier (1928). This book contains a summary of most of Herzfeld's thinking between the years 1928 and 1959 on many of the issues that most interested physical chemists at that time. Another very important theoretical paper, written about the same time, was the one by Schwartz, Slawsky, and Herzfeld (1952) on the calculation of vibrational relaxation times for gases.

The last 40 years of Herzfeld's life were warmed by his marriage in June 1938 to Regina Flannery of Washington, D.C., who was then an instructor in anthropology at Catholic University. By the time she retired in 1970, she had risen to be professor and head of that department. The Herzfelds had no children of their own, but a nephew, Charles Herzfeld, the son of Karl's only brother, August, was very close to them and, like his uncle, had a great interest in physical chemistry, in which field he obtained his Ph.D. from the University of Chicago in 1951. Charles Herzfeld became a well-known physical chemist and held many important leadership positions in government and private industry after World War II.

Karl Herzfeld retained ties with his family and with the German physics community by occasional visits to Germany. In 1948 he accepted an invitation from Arnold Sommerfeld to lecture on both theoretical physics and physical chemistry in Munich during the spring semester, and enjoyed this wonderful opportunity to spend some time with his old

colleague. In 1951 Sommerfeld was killed in an automobile accident while out walking with his grandchildren. Though this tragedy was enormously sad for Herzfeld, in 1958 he again accepted an invitation to lecture on physical chemistry during the spring semester in Munich.

Herzfeld was a wonderfully caring man: He cared about his students, his colleagues, his relatives, his friends, and even the maintenance workers in the physics building. He was also concerned about the future of physics, about philosophy and theology, about the role of religion and the problems of the world. On first meeting him in the summer of 1947, I was immediately struck by his stiff, almost military bearing. (He had, after all, reached the rank of first lieutenant in the Austro-Hungarian Army by the end of World War I.) However, I soon realized that beneath this protective cloak were a deep humanity, a surprising humility, and a penetrating understanding of people. (For example, he immediately saw through any attempt by a student to bluff his way through an oral examination or the answer to a question from a professor.)

He was a man of brilliant intellect who had an unusual breadth of knowledge in both physics and chemistry and a remarkable depth of interest in the most fundamental problems of physics. Still, he was willing to sacrifice his own success and future fame as a physicist to help a cause he thought more pressing: the improvement of physics instruction and research in his adopted country.

Although Herzfeld pushed his colleagues and students to produce, he drove himself to work harder than anyone else in the physics department (as a graduate student I was tempted at times to think that he might have been even more productive as a scholar if he had not been overly tired from teaching evening graduate courses to accommodate part-time students). His work ethic was astonishing.

His door was always open to both faculty colleagues and to students. (There were even recurrent rumors around the Catholic University campus that he had assisted physics students with his own money when they were in dire financial need.)

Of the 85 Ph.D. degrees awarded by Catholic University in the years 1936 to 1962, when Herzfeld chaired the department, almost half were directed by Herzfeld himself. Every Saturday he set aside the whole day for meetings with a number of theoretical students who were working on Ph.D. dissertations under his direction. (In one case he even agreed to be available in his office at the university on Sunday to meet with an orthodox Jewish student who could not come on Saturday.) Herzfeld was also generous with his ideas, many of which appear in the published literature under the names of the students he mentored.

He was extremely scrupulous in using university funds. On one occasion he was found wandering through the physics building looking for a pay phone to call the automotive shop where his car was being repaired, since he thought it improper to use his own office phone for anything but business calls. He found time, however, for an occasional joke. One he especially enjoyed ran as follows: "There was a teacher who was dreaming that he was teaching a class and when he woke up, he found that he was!"

In encouraging women and blacks to pursue careers in physics Herzfeld was far ahead of his time. At Johns Hopkins he published research papers jointly with Maria Mayer and invited her to join him in conducting a seminar on the quantum mechanics of molecules. He published three papers with Virginia Griffing of the Catholic University chemistry department (1955) and another with Hertha Sponer, James Franck's wife. Then, after World War II he brought Lise Meitner to Catholic University as a visiting professor for the

spring 1954 semester. Finally, of the 85 Ph.D. degrees awarded in the years 1936-62, about 10 percent went to women, which was an unusually high percentage for those years.

Herzfeld also entered into an informal arrangement with Howard University in which the physics chairman there agreed to steer his best and brightest black students in physics to Catholic University for their advanced degrees, because they had Herzfeld's assurance that he would do everything in his power to make the Howard students feel at home on the campus and provide any assistance needed on their road to a Ph.D. This arrangement worked well at first, but later fell victim to the increased efforts of the biggest and best physics departments in the country to recruit graduate students from black colleges with offers that Catholic University could not match.

After enjoying excellent health throughout most of his life, just a year before his death Herzfeld began to fail. He suffered a severe stroke at his home in Washington in late May 1978, and an ambulance took him to George Washington University Hospital, where he died peacefully a few days later on June 3.

Those of us who profited so greatly from the teaching and advice of this kindly, dedicated, and uniquely skilled mentor will always be grateful for the opportunity Karl Herzfeld gave us to share in the great European tradition of theoretical physics that he represented and that he communicated so generously to his students and colleagues.

Herzfeld was elected to the American Academy of Arts and Sciences in 1958 and to the National Academy of Sciences in 1960. He was a fellow of the American Physical Society and of the Acoustical Society of America. During World War II he served on a number of Navy advisory committees and in 1964 he received the Navy's Meritorious Service Citation for his research and service as an advisor to the

Navy during the war. Some words of Elliott Montroll in 1984 are worth repeating here:⁹

At Catholic University, he [Herzfeld] developed a program to respond to the needs of young staff members of the many government laboratories, especially the National Bureau of Standards and the Navy laboratories. Many part-time students from these organizations received their Ph.D.'s under his sympathetic direction. . . . The Catholic University acoustics program initiated by Herzfeld had a profound influence on the Navy underwater sound program. . . .

Herzfeld received many honorary degrees and other tributes. Among these were honorary doctorate of science degrees from Marquette University, Milwaukee (1933); University of Maryland, College Park (1956); Fordham University, New York (1960); Technische Hochschule, Stuttgart (1962); Providence College, Rhode Island (1965); and an LL.D degree from the University of Notre Dame, Indiana (1965). He received the Mendel Medal from Villanova University in 1931, the Secchi Medal from Georgetown University in 1938, and the Cardinal Gibbons Medal from Catholic University in 1960. In 1964 he received the Bene Merenti medal from the Vatican for his 28 years of distinguished service to the Catholic University of America.

THE CONTENTS OF THIS BIOGRAPHICAL memoir are based in great part on materials provided by the National Academy of Sciences and on the Archival Collections at the American Institute of Physics Niels Bohr Library in College Park, Maryland. The most relevant Herzfeld documents in the American Institute of Physics collection are designated as OH 213 and OH 214 (oral history interviews), AR 85 (archives) and MB 246 (a manuscript biography of Herzfeld).

I have also profited from two long interviews with Regina Herzfeld, whose insights into her husband's career and contributions to science have made this memoir both more accurate and more interesting; from meetings, telephone conversations, and correspondence with faculty members who had been contemporaries of Karl Herzfeld on the Catholic University of America physics faculty—including, in

particular, James Brennan, Theodore Litovitz, and Paul Meijer. In addition, other colleagues of mine—including Fernand Bedard, Russell McCormach, Donald Osterbrock, and Alfons Weber—have read this paper at various stages of its development and have by their perceptive comments greatly improved its final form. I am especially grateful to Charles Herzfeld, Karl's nephew, for suggesting some significant changes that improved the final form of this memoir.

The article by Karen E. Johnson referred to in Note 8 was of great assistance in my understanding of Herzfeld's early contributions to science and especially to statistical mechanics. I found the 1936 letter of Herzfeld to Sommerfeld referred to in Note 6 at the Deutsches Museum in Munich when I was in Germany in 1988. I am grateful to the Deutsches Museum for making a copy of this important document available to me.

Finally, I would like to express my thanks to Heather Lindsay of the Niels Bohr Library and to Jenny S. Mun, biographical memoirs coordinator of the National Academy of Sciences, who generously provided me with the helpful assistance I needed to complete this project.

NOTES

1. J. A. Wheeler. Karl Herzfeld. *Phys. Today* (Jan. 1979):99. This is a short but beautiful and moving obituary of Karl Herzfeld by his best-known and now most renowned doctoral student. In this one-page obituary Wheeler writes, "Physics for Herzfeld was not a secular, but a religious calling; it aimed, in his view, to make clear the structure and beauty of God's creation."

2. Quote from a brief typewritten (nine double-spaced pages), unpublished autobiography by K. F. Herzfeld, p. 4. This short autobiography was probably prepared by Herzfeld for the American Institute of Physics in 1963, at which time he also sent a copy to the National Academy of Sciences. This copy still remains in the Academy's archives.

3. Oral History OH 213, p. 11.

4. Heitler chose Herzfeld as his mentor for his Ph.D. dissertation because his research was "sort of border line between physics and chemistry." Interview of Heitler by John Heilbron on March 18, 1963. OH 205, p. 5.

5. In OH 204, p. 7, Werner Heisenberg makes the terse statement: "Herzfeld was a good teacher, so I liked his lectures."

6. Letter of May 19, 1936, from Herzfeld to Arnold Sommerfeld in Munich, Germany. This letter is in the Sommerfeld Archive at the Deutsches Museum in Munich.

7. In OH 214, p. 21, Herzfeld confesses that he turned down R. W. Wood's position as chairman of physics and then acted as if he really were the chairman. He also admits that, in retrospect, he probably did try too hard to bring European physicists to the Johns Hopkins University physics department, despite the fact that a number of his colleagues there were not enthusiastic about his initiative in this regard.

8. Members of the Johns Hopkins chemistry department to President Isaiah Bowman, March 12, 1936; in Joseph Mayer Papers, University of California, San Diego; in Special Collections Department, University Library, UCSD. This useful document is referred to by K. E. Johnson in "Bringing Statistical Mechanics into Chemistry: The Early Scientific Work of Karl F. Herzfeld," *J. Stat. Phys.* 59 (1990):1547-72, on p. 1549.

9. E. W. Montroll. On the Vienna school of statistical thought. *Am. Inst. Phys. Conf. Proc.* 109(1984):1-10, on p. 7.

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1912

Über ein Atommodell, das die Balmer'sche Wasserstoffserie aussendet. *Sitzungsberichte der Koniglichen Akademie der Wissenschaften Wien* 121 (2a):593-601.

1913

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1919

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1920

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1921

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1924

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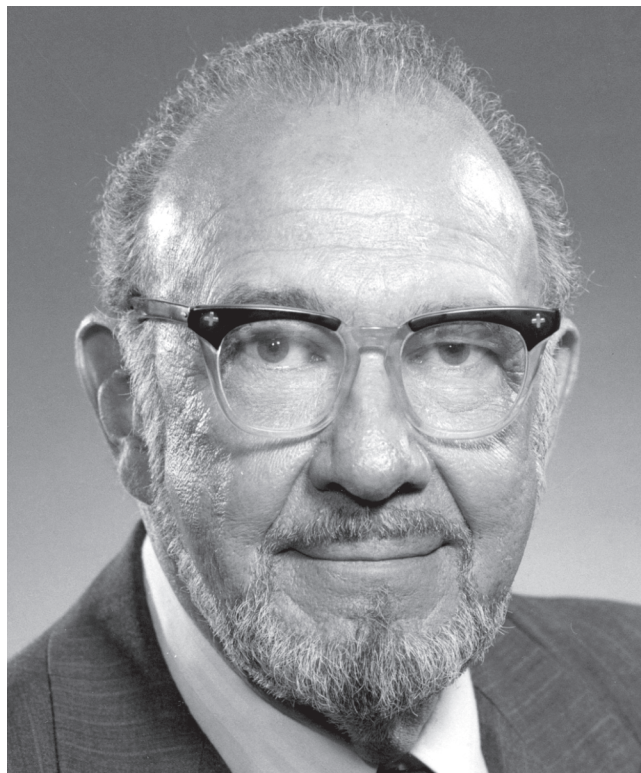
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Courtesy of Stanford University

William S. Johnson

WILLIAM SUMMER JOHNSON

February 24, 1913–August 19, 1995

BY GILBERT STORK

WILLIAM SUMMER JOHNSON, one of the major figures in the development of the art and science of organic synthesis in the second half of the twentieth century, was born in New Rochelle, New York, on February 24, 1913, the second child of Roy Wilder Johnson and Josephine Summer. He received his early education in New Rochelle and finished high school in Massachusetts at the Governor Dummer Academy, which his father had also attended. Bill Johnson showed himself to be a young man of many talents who spent much of his spare time in serious hobbies—from constructing radios, an activity that he mastered when barely a teenager, to developing his considerable musical ability with enough enthusiasm to provide serious competition for his school work. This did not prevent him, however, from getting very interested in chemistry at Dummer and doing well enough to receive a scholarship to be admitted to Amherst.

At Amherst, Johnson's interest in chemistry became specifically focused on organic chemistry. Because this was the Depression, Johnson had to be totally self-supporting. He managed to survive by a combination of scholarships, menial jobs, and playing the saxophone in dance bands in the Catskills, even arranging to pay his way for a round trip to

Europe on a transatlantic liner by playing in one of the ship orchestras. In spite of all these demands on his time, he did well enough as a chemistry major at Amherst to be elected to Phi Beta Kappa in his junior year and to graduate magna cum laude. The chemistry department was obviously quite impressed with Bill Johnson, and he was asked to remain at Amherst an additional year after graduation to teach organic chemistry.

Not surprisingly, Johnson was admitted to the Ph.D. program at Harvard, where he did his research in Professor Louis Fieser's group and began a lifelong fascination with steroids and related polycyclic systems. At Harvard, Johnson who was supporting himself in part by working during the summers as a chemist at Eastman Kodak in Rochester, New York, accomplished the remarkable feat of completing his research work for the Ph.D. in January 1940, after less than two years of residence!

After a few months as a postdoctoral assistant at Harvard with Professor R. P. Linstead, Johnson was appointed instructor in the chemistry department of the University of Wisconsin in Madison, starting in September 1940. Shortly afterwards, on December 27, Johnson married Barbara Allen, whom he had met in Cambridge. This was the beginning of a remarkably successful partnership that lasted some 55 years until Johnson's death. Barbara's extraordinary ability to empathize with people, from small children to the elderly, contributed much to the Johnsons' gift for making every visitor to their home feel welcome and for building long-lasting friendships with most of those who had the good fortune to know them.

After some 20 years as one of the best known members of the chemistry department at Wisconsin, becoming Homer Adkins Professor in 1944, Johnson was known as a great organic chemist, and some of the more perceptive members

of chemical academia had also become aware of his administrative skills and of his ability to recognize creative talent in chemists, whether organic chemists or not.

Johnson liked the chemistry department in Madison. When efforts were made to entice him to join Stanford University to build up its chemistry department, he was asked to make a list of requests Stanford would have to meet. I think he hoped subconsciously that Stanford would find them unacceptable. They did not, and Johnson moved to Stanford as professor and executive head of its chemistry department in 1960. As the saying goes, the rest is history. Under Johnson's leadership, helped by the decisive support of Stanford's president, Wallace Sterling, and its provost, Fred Terman, the chemistry department at Stanford succeeded in attracting within just four years individuals like (chronologically) Carl Djerassi, Paul Flory, Henry Taube, Eugene Van Tamelen, and Harden McConnell, so that, even before Johnson relinquished his executive head responsibilities in 1969, the Stanford chemistry department had become one of the top chemistry departments in the world.

Johnson made many contributions to his profession, in addition to the scientific achievements that will be addressed in the following section. Some of these contributions were made in his capacity as chemical consultant with a number of chemical and pharmaceutical companies. Two of the longer lasting of these associations were with the Winthrop Chemical Company, which later became the Sterling-Winthrop Research Institute, and with DuPont. Johnson also contributed much to the American Chemical Society, which he served as chairman of its Wisconsin Section in 1949; as chairman of the Organic Division in 1951; and as a member of the important Committee on Professional Training (1952-56). He also served on editorial or executive boards of numerous Journals: *Journal of Organic Chemistry* (1954-56); *Journal of the American*

Chemical Society (1956-65); *Tetrahedron* (1957-95); *Bioorganic Chemistry* (1971-82); and *Synthesis* (1975-95). He also served on panels of the National Academy of Sciences: the Subcommittee on Synthesis of the Committee for the Survey of Chemistry (in 1964) and the U.S.-Brazil Science Cooperation Program, Office of the Foreign Secretary (1968-72). He, of course, also served both on the Chemistry Advisory Panel of the National Science Foundation (1952-56) and on one of the medicinal chemistry study sections of the National Institutes of Health (1970-74).

SCIENTIFIC CONTRIBUTIONS

In the fall of 1940, when Johnson started his independent career, the concept of controlling the stereochemical course of the reactions envisaged for a particular synthesis belonged to science fiction. The few syntheses of natural products that had been recorded, such as those of camphor, cocaine, glucose, and hydroquinine, were tributes to the brilliant experimental work and courage of the organic chemists who engaged in these difficult journeys, knowing that they would face complex and tedious separations of the various isomers to be expected from their efforts. The extraordinary difficulties they surmounted served to emphasize the improbability of success in attempting to put together the complex structures that were being suggested for a host of natural products. Some brilliant and original chemists of the time handled the problem by concentrating on devising methods to achieve chemical *connectivity*, simply ignoring stereochemistry. They seemed to consider it an unreasonable handicap to the free exercise of their imagination. While they did design important new methods, most of their efforts at total synthesis were doomed to failure. Quite aside from stereochemical control, knowledge had not yet advanced to the point that even *regioselectivity* could be planned.

Johnson, from the very start of his stay at Wisconsin, found himself fascinated by these problems of regio- and stereochemistry. Steroids had become the object of considerable interest by 1940 because of their involvement in many important biological processes, but one of the numerous hurdles to their attempted laboratory syntheses was the presence of methyl groups in the so-called angular positions between certain of their rings. The available methods of methylation had failed to introduce methyl groups selectively at the proper locations: They produced the wrong *regiochemistry*.

Johnson solved the problem by devising an angular methylation sequence, in which an easily introduced temporary controlling group prevented the unwanted regiochemistry. The scheme was successful, but removing the temporary group, after its controlling function had been served, proved difficult. Johnson used his command of mechanistic concepts, some just emerging, to devise a very imaginative sequence of reactions that resolved the difficulty, thus producing the first solution of some generality to an extremely common problem in regioselective carbon-carbon bond formation. Johnson went one step further: He had given a solution to the regiochemical problem, but there remained a stereochemical one. The stereochemistry of the bicyclic system resulting from his regiochemically controlled methylation turned out to be quite cleanly *cis*. How could the angular methylation process be changed to give the *trans* system encountered in natural steroid frameworks? Johnson later concluded, again on the basis of mechanistic considerations, that the desirable *trans* bicyclic system should become the major product if he carried out his angular methylation scheme on a bicyclic system bearing a double bond parallel to the ring junction. This proved to be correct.

I have dwelled on this particular methodology, now mostly

of historical interest, because it illustrates that, at the very beginning of his career, Johnson was acutely aware of the important problems that had to be solved to make complex synthesis into a rational endeavor. This early work also illustrates his conviction that attention to reaction mechanism principles is crucial to the design of new synthetic methodology. This work also illustrates his commitment to stay with a problem until a solution is reached.

These qualities served Johnson well in the work for which he is best known, the introduction of carbocation-based chemistry as a powerful tool for the construction of polycyclic systems. At the time Johnson began to contemplate the possibility that cationic polyene cyclization might go beyond the realm of intriguing theoretical speculation, attempts at constructing complex organic structures relied almost entirely on *base-catalyzed* formation of enolate ions derived from carbonyl compounds, followed by their reaction with electrophilic carbon entities. The importance of Johnson's contribution to changing this state of affairs cannot be overemphasized. When he started his work on the cationic cyclization of polyenes, the scattered efforts in this area had convinced everyone but himself that there was no serious possibility that the core of a complex structure like that of a natural steroid, with all the problems, regio- and stereochemical, implied by the existence of six, seven, or more asymmetric centers, could some day be assembled in just one or two steps. And that the process would eventually be able to create a single predictable structure, rather than the several dozen isomers that would result from a random process.

Johnson's extraordinary success in this area was not the result of lucky accidents. It followed a number of many fundamental contributions that benefited the entire field of synthesis. Central to the eventual success was Johnson's

recognition that the initiation of the cyclization process was crucially related to the possibility of achieving concertedness in interaction with the multiple olefinic centers in the polyene chain. His brilliant perception was that the high-energy carbocations used to start a polycyclization process by earlier workers were too reactive and unstable to result in stereospecificity or, for that matter, even chemoselectivity, but that less energy-rich and longer-lived α -alkoxy or allylic tertiary carbonium ions might well be much more effective. And, indeed, they were.

The design of effective and useful nucleophilic terminators for the polycyclization process also proved important. There again, Johnson's solutions to the problem were firmly based on mechanistic concepts. They have had an impact well beyond the steroid targets for which they were originally devised: The propargylsilane terminator, which led as he expected to an allene, is a case in point. It was designed not only as an efficient terminator, but the resulting allene, when generated at what would become the steroid 17-position, could be easily transformed to the characteristic dihydroxyacetone side-chain of such adrenal hormones as cortisone.

Johnson's desire to induce not only *stereospecificity* but *enantiospecificity* as well led to further important contributions. One of them was the demonstration that the cyclization conditions he eventually devised were sufficiently mild that a single secondary allylic alcohol enantiomer, at the position which would eventually become the 11-oxygen center of a corticosteroid, was able to survive the cyclization process and to induce the correct enantioselectivity *at all the relevant centers produced by the cyclization*.

An even more general contribution to synthesis methodology followed Johnson's study of the α -alkoxy cations he sometimes used to initiate certain polyene cyclizations. This was the demonstration that the alkoxylation derived by

cleavage of an acetal made from a homochiral, C₂ symmetric, 1,3-glycol can lead to efficient transfer of chirality in its electrophilic attack on an olefin. This resulted in a very useful new method for the formation of enantiocontrolled centers adjacent to a carbon-oxygen bond, such as in the synthesis of optically active α -hydroxyacids.

I now refer to three more contributions that originated from problems Johnson encountered in the polyene cyclization work, but which have left their mark much beyond it.

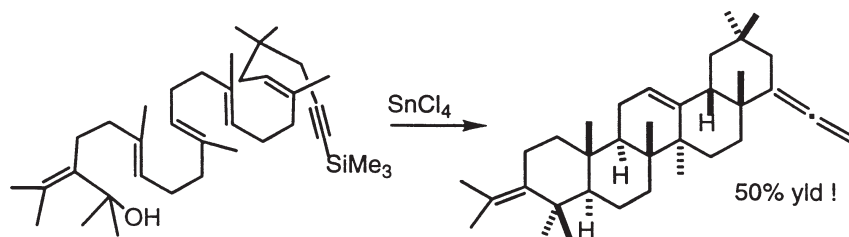
Johnson showed that careful analysis of the E-selectivity resulting from the Julia olefin synthesis of disubstituted olefins strongly suggested that it might also lead to selectivity in the construction of *trisubstituted* olefins, an even more demanding problem. This proved correct, and the resulting process is now called the Julia-Johnson reaction. It was that same insistence on understanding the mechanistic basis of a synthetic operation that led Johnson to invent a process, now known as the Johnson-Claisen orthoester rearrangement, that has led to a great simplification of the venerable reaction known as the Claisen rearrangement. It has achieved great importance because of its experimental simplicity, as well as its ability to control regio- and stereochemistry. It has become a major tool in complex synthesis.

Among the many other contributions of Johnson and his research group, one that has not yet been appreciated as much as it eventually will be, is the realization that a fluorine atom, in spite of its high electronegativity, is very effective in stabilizing an adjacent carbonium ion. So far as I know, this rationalizable but somewhat counter-intuitive fact was first used to major advantage in Johnson's polyene cyclization work. Johnson took advantage of this remarkable property in his use of the vinyl fluoride terminator (which, in a steroid context, led to the desirable 20-keto-steroid system). Johnson also made highly effective use of a

fluorine atom as a controlling substituent to favor a particular cationic center in a desired polycyclization intermediate.

It is not often that a field is created and developed by the work of one individual. There is little doubt, however, that the entire field of controlled synthesis based on cationic polyene cyclization would have lain fallow for a very long time without Johnson's vision, and his absolute dedication to achieving his goal.

Perhaps the most demanding test of someone's contribution to their chosen field is the question, "What can be done or understood now that was not feasible or understood previously?" In the case of William S. Johnson, the answer is, "a lot," as is illustrated, *inter alia*, in the striking transformation, reported in one of his last papers (1994).



WILLIAM S. JOHNSON—THE MAN

It is, of course, not possible to derive Bill Johnson's human qualities from the important contributions he made to organic chemistry. I have alluded to his love of music. It would lead him to spend the large part of a trip to Paris to search for a rare and highly prized saxophone; to leave a chemical meeting surreptitiously for a visit to a session of a jazz congress where Jerry Mulligan was performing; to engage in friendly and enthusiastic cross-country telephone com-

petition to see who could be the first to identify the artist on a particular jazz recording; or to join a few other talented musicians like Harry Wasserman and Richard Turner to produce memorable spur-of-the-moment performances. Johnson took great pride in the extremely high quality of the electronic equipment, especially the loudspeakers, that he had carefully positioned in the living room of the beautiful home he shared with Barbara in Portola Valley.

Johnson was an outstanding teacher. Not only because of his command of the material but also because of the passionate enthusiasm he had for his subject and the deep interest he had in his students. This was especially evident in his interaction with his graduate students and postdoctoral associates who became in effect part of his family. Many, like David Gutsche, Ralph Hirschmann, Hans Wynberg, Robert Ireland, Richard Franck, James Marshall, John Keana, Kathlyn Parker, Martin Semmelhack, Paul Bartlett, Bruce Ganem, and Glenn Prestwich, became themselves leaders in their field in academia, while many others, such as Barry Bloom, Raphael Pappo, Jacob Szmuszkovicz, John Pike, and J. W. Scott, made their marks in industry.

Bill Johnson's love of chemistry, and his empathy for kindred spirits, had happy consequences, as on the occasion of the visit of Professor John D. Roberts of Caltech to Madison, as Folkers Lecturer. The interaction resulted not only in the lifelong friendship of Bill and Barbara with Jack and Edith Roberts, but also in the joint authorship of a communication on the acid-catalyzed methylation of alcohols with diazomethane (M. C. Caserio, J. D. Roberts, M. Neeman, and W. S. Johnson, "Methylation of Alcohols with Diazomethane," *J. Am. Chem. Soc.* 80:2584-85, 1958).

My wife, Winifred, and I enjoyed deep friendship with the Johnsons. The word friendship in fact seems inadequate. It certainly survived some unusual stress. One such instance

I remember well was on the occasion of the celebration in New York of the centennial of the American Chemical Society. Johnson, the last of the distinguished speakers, was just starting to address the large crowd in the darkened hotel ballroom, when word came to the organizers that the hotel needed to have the room vacated within five minutes to prepare for a scheduled wedding. The frantic organizers, who knew of my friendship with Johnson, begged for my help, and I climbed on the darkened stage to tell the startled Johnson that his just-begun lecture was over. Our friendship survived, and by the time Bill Johnson died, it had lasted over half a century.

AWARDS AND RECOGNITION

Many prestigious honors came to Johnson in acknowledgment of his scientific stature. Among the most notable was his election to the National Academy of Sciences as early as 1952. He was also a member of the American Academy of Arts and Sciences; received both the Roger Adams and the Arthur C. Cope awards; the Award for Creative Research in Organic Chemistry; the Tetrahedron Prize for Creativity in Organic Chemistry; and the Nichols Medal. A particularly significant recognition came when he was selected by an international jury in France to be the first recipient, in 1970, of the Roussel Prize for Steroid Chemistry. Another award that he must have particularly prized was this country's highest award in science, the National Medal of Science, which he received in 1987. This list is not exhaustive, but it should include the annual, highly successful Johnson Symposium, which Johnson's colleagues at Stanford started in his honor in 1986. It was a gesture that touched him deeply.

The title Johnson chose for his autobiographical memoir was "A Fifty Year Love Affair with Chemistry." The love was obviously reciprocated.

SOME OF THE introductory biographical material has been gathered from W. S. Johnson's fascinating autobiographical account of his life in chemistry: *A Fifty Year Love Affair with Chemistry*. Washington, D.C.: American Chemical Society, 1998.

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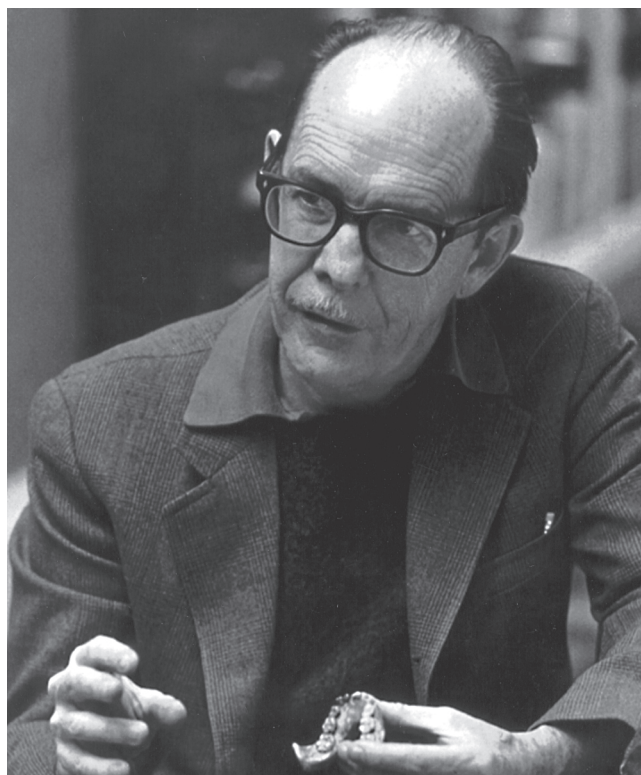
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Richard A. Near West

RICHARD STOCKTON MACNEISH

April 29, 1918–January 16, 2001

BY KENT V. FLANNERY AND JOYCE MARCUS

IN THE 1940s, BEFORE the extensive surveys and excavations of archaeologist Richard S. (“Scotty”) MacNeish, little was known about the origins of agriculture and the transition from hunting and gathering to sedentary life in the New World. Over a period of six decades, MacNeish supplied us with enormous quantities of data and developed new ways of thinking about how Native Americans lived during thousands of years of nomadic foraging. He eventually extended his work to places as diverse as the Yukon, New Mexico, Mexico, Belize, Peru, and China.

Richard Stockton MacNeish was born in New York City and grew up in Eastchester and White Plains. His father, Harris Franklin MacNeish, was a professor of mathematics who received his Ph.D. from the University of Chicago in 1912; his dissertation was on “Linear Polars of the k -hedron in n -space.” He also wrote a book entitled *Algebraic Technique of Integration*, which was reprinted in 1950. MacNeish’s mother, Elizabeth Stockton, was descended from a founder of Princeton University; she hoped her son would attend that institution, but he ended up at his father’s alma mater.

MacNeish developed an early interest in Maya archaeology. In the spring of 1930 his teacher in eighth-grade art history

gave him a prize for a picture album on Maya archaeology. A year later he wrote to Alfred Vincent Kidder, one of the leading archaeologists working for the Carnegie Institution of Washington, asking if he could be a water boy on a Maya dig. Although unable to add the 13-year-old to his project, Kidder did encourage the young MacNeish to study archaeology, thereby initiating a longstanding friendship. Forty years later, in 1971, Scotty would win the medal named for Kidder.

In 1936 MacNeish entered Colgate. His first excavation was at the Nichols Pond Iroquois site in central New York. By 1937 he had managed to join the Rainbow Bridge-Monument Valley Expedition in northeast Arizona, helping to excavate a Tsegi Canyon Pueblo I pithouse under the direction of Ralph Beals. Scotty returned in the summer of 1938 to work with Beals at Cobra Head Canyon, with Watson Smith at Black Mesa, and with George Brainerd at two sites: a Basketmaker III pithouse and Swallow Nest Cave. MacNeish was imprinted in several ways by this early fieldwork. First, Brainerd showed him how to excavate a cave by carefully stripping off one living floor at a time, a technique he would later use in Mexico. Second, MacNeish never stopped suspecting that Basketmaker-style pithouses had preceded the wattle-and-daub residences of Formative Mexico—a view later reinforced by his discovery of a possible pithouse site in the Tehuacán Valley of Puebla.

By his sophomore year, MacNeish was being urged by several Southwestern archaeologists to transfer to the University of Chicago to study with Fay-Cooper Cole. There was unfinished business, however, before he could enroll at Chicago. MacNeish was by this time an accomplished amateur boxer, desirous of a Golden Gloves championship. In 1938 he won the Golden Gloves in Binghamton, New York, an achievement in which he took great pride.

At the time MacNeish enrolled at the University of Chicago, it was an archaeological paradise. The Midwest United States was filled with excavation crews supported by the Depression-era Works Progress Administration. His professor, Fay-Cooper Cole, had staked out the Kincaid Mounds in southern Illinois as the location for Chicago's field school. At Kincaid MacNeish would hear endless discussions of method and theory from James A. Ford, William Haag, Jesse D. Jennings, John Cotter, Glen Black, Tom Lewis, Madeline Kneberg, and of course, Cole himself.

MacNeish would learn the WPA method of digging in 6" levels with special shovels and plasterers' trowels, removing the dirt with a dustpan and screening everything. MacNeish also learned the University of Chicago method of vertical slicing with mattocks, recording everything on square description forms, feature forms, and photo forms. The horizontal scraping techniques by which he found postmolds and earthen floors were to be adapted 10 years later at Pánuco, Veracruz, where he became the first to find postmolds from a Formative Mesoamerican house.

MacNeish received his B.A. from Chicago in 1940. By 1941 he was a graduate student supervisor at Kincaid, receiving \$150 a month. In 1944 he wrote his M.A. thesis on the Lewis Focus, a prehistoric culture of Illinois. It would be hard to overestimate the effect of those years at Chicago. First, MacNeish learned how to direct a crew of 80, including surveyors, draftsmen, diggers, screeners, and the "scribes" who filled out the forms; one could still see this organization during his projects in Tehuacán and Ayacucho. Second, he wrote a class term paper for Robert Redfield on Julian Steward's recently published *Basin-Plateau Aboriginal Socio-political Groups* (1938). Steward's monograph so impressed Scotty that, for the rest of his career, his syntheses made virtually every region he investigated sound like the Great

Basin. He often used a model, inspired by Steward's description of the Paiute, in which foragers broke up into microbands in lean seasons and came together to form macrobands during times of plenty.

HIS CAREER IN ARCHAEOLOGY

In 1946 James B. Griffin invited MacNeish to spend a year at the University of Michigan to "settle the problem of Iroquois origins." In what is still considered a tour de force, MacNeish used the direct historical approach to solve the problem, beginning with the pottery of the historic Iroquois and working back to the ceramics of the prehistoric Owasco and Point Peninsula complexes. In a 1976 article on the Iroquois, MacNeish reminisced on this collaboration: "He [Griffin] wanted to explode this poorly documented speculation and felt that Scotty MacNeish was just the sort of little troublemaker to do the job. What is more, I agreed with him. So, in the fall of 1946, I folded up my tent and migrated to the Museum of Anthropology in Ann Arbor, fired with enthusiasm, to become, I hoped, a dynamite dynamiter." After analyzing half a million pottery sherds, Scotty did confirm Griffin's view that the Iroquois had developed in situ rather than being Mississippian immigrants. It was MacNeish's work on the Iroquois that led to his being honored with the Cornplanter Medal in New York in 1977.

A similar investigation of immigration and culture contact led to MacNeish's greatest discoveries. The decade of the 1940s was an era when diffusionists sought to explain the Mound Builders of the Southeast United States in terms of migrations from Mesoamerica. Fay-Cooper Cole decided that MacNeish should investigate this explanation for his Ph.D. thesis, so in 1945 he sent Scotty to survey in southern Texas and northern Tamaulipas. MacNeish found no evidence of migration by Mexican groups into Texas, but he

did find five intriguing rockshelters in the Cañon Diablo of the Sierra de Tamaulipas. Protected from rain by the cliffs above and desiccated by high evapotranspiration, the caves were chock full of prehistoric plant remains, twine, basketry, and other normally perishable artifacts.

In retrospect it seems surprising that it took MacNeish two years to raise enough funds to dig these caves, which were destined to change the course of New World prehistory. Finally, in 1948 a grant from the Viking Fund of the Wenner-Gren Foundation got him back to Tamaulipas for an eight-month season. In January of 1949 his crew chief found three tiny, early prehistoric maize cobs at La Perra Cave. Overnight, the period of incipient agriculture in Mexico—a theoretical construct that had been discussed in classrooms but never actually seen—had come to light.

The three most important caves MacNeish found in Tamaulipas were Nogales, Diablo, and La Perra. MacNeish began his excavation at Nogales Cave using the arbitrary 6" levels and WPA/Chicago methods learned at Kincaid, but soon saw that these would be inappropriate for dry caves. Recalling the way Brainerd had stripped off living floors with a trowel at Swallow Nest Cave in 1938, MacNeish switched to this method at Diablo Cave. By the time he reached La Perra Cave, he had begun to develop his own personal style of cave excavation. First, he divided the cave floor into a grid of squares; then he excavated a small number of alternate squares. This left the natural or cultural stratigraphy of the intervening squares exposed on several sides, making it easier to follow a specific living floor from square to square with a trowel. Gradually, the old inches and feet of the WPA era gave way to the more universally accepted metric system. MacNeish would later refer to this system of excavating by natural or cultural levels, using alternate one-meter grid squares, as the La Perra method.

At the urging of Gordon Ekholm of the American Museum of Natural History, MacNeish took a brief detour in 1948 from his Tamaulipas excavations to the Gulf coastal plain of northern Mexico. At Pánuco, Veracruz, Ekholm had exposed a sequence of six cultural phases in a deep stratigraphic cut in the bank of a river. MacNeish dug a step trench 26 feet down to water level, adding three earlier periods to Ekholm's sequence.

In Pánuco a local collector of artifacts showed MacNeish the clay model of a house made in prehistoric times. The building was shown as having an oval or apsidal plan, a door in one of the long sides, and a thatched roof like those still used by the Huastec Indians of northeast Mexico. While excavating at Pánuco in deposits of the Middle Formative period (ca. 400 B.C.), MacNeish found a curving line of four postmolds from a similar house crossing his excavation. Not only was this the first archaeologically recovered Middle Formative house from Mexico, it was our first evidence that Gulf Coast houses of that period had been apsidal rather than rectangular.

MacNeish realized that only the introduction of Kincaid-style horizontal scraping into Mexico had allowed him to recover the floor and post pattern of a wattle-and-daub house, something that had eluded George Vaillant of the American Museum of Natural History at El Arbolillo and Zacatenco (near Mexico City) in the 1930s. Vaillant had been trained on the great midden at Pecos Pueblo, and he understandably treated Zacatenco as a midden rather than a village. MacNeish concluded that Midwest techniques were more appropriate than Southwest techniques for finding houses in Formative villages.

In 1949 MacNeish completed a Ph.D. thesis on his Tamaulipas survey and left Chicago for a job with the National Museum of Canada. He was temperamentally suited for

museum work, which allowed him time for field trips and research and provided no distractions (such as teaching). His position did, however, require him to do a reasonable amount of archaeology in Canada. That was no problem. Immediately in 1949 Scotty was off for three months to survey the barrenlands of the Northwest Territories. By 1952 he had surveyed the upper Mackenzie River and excavated sites at Pointed Mountain, Fort Liard, and Great Bear Lake on the Arctic Circle. Taking advantage of the fact that the Northwest Territories were frozen all winter—exactly the season when Mexico was dry and balmy—MacNeish worked out an appropriately ambitious schedule: summer fieldwork in the Arctic, winter fieldwork in Mexico.

MacNeish's excavations in the Sierra de Tamaulipas had pushed maize agriculture back to 2500 B.C., but he sensed that earlier corncocks were out there somewhere. Encouraged by botanist Paul Mangelsdorf of Harvard, MacNeish turned to the Sierra Madre near Ocampo in southwest Tamaulipas. Javier Romero and Juan Valenzuela of the Mexican National Institute of Anthropology and History had told him that, in 1937, a man named Guerra had led them to mummy-filled dry caves in the Cañon del Infiernillo. MacNeish relocated Guerra, who took him on a harrowing three-day horseback ride through the wilderness. The trip ended at "two magnificent caves with preservation," sites that Scotty named for Romero and Valenzuela.

In 1953 MacNeish returned with three assistants to excavate. Romero's Cave had 17 cultural layers, superb activity areas, baskets, mats, string, wild plants, coprolites, and early domestic plants; Valenzuela's Cave was not as deep, but had equivalent preservation. Bruce Smith of the Smithsonian Institution later reanalyzed and obtained accelerator mass spectrometric (AMS) dates on many of the cultivars from MacNeish's Ocampo caves. The earliest dates (calibrated to

“real” time) were 4360 B.C. for *Cucurbita pepo* squash, 4200 B.C. for bottle gourd, and 2455 B.C. for maize.

The caves of Tamaulipas yielded prodigious numbers of projectile points, and MacNeish based his typology on the pioneering efforts of his Texas colleagues. MacNeish did not want to create a new name for every point that looked exactly like one found on the other side of the Río Grande, so he continued to use Texas point names even when he was working hundreds of kilometers from the Río Grande. In response to his Texas critics (who did not like MacNeish’s use of Texas names for Mexican point types), he sometimes displayed his distinctive brand of humor. For example, when MacNeish encountered what looked like a miniature version of the Gary point from Texas, he simply gave it a Mexican diminutive, calling it the Garyito point. This was only one of many legendary MacNeishisms. Others include his naming a serrated point type Pelona, because it reminded him of a woman with disheveled hair.

MacNeish’s career was filled with impressive monographs, which reflected his capacity for monumental amounts of work. During the 1940s and 1950s when he was in the Yukon and Northwest Territories, he was working in regions so remote as to make his three-day trip to Romero’s Cave seem like a picnic. To survive while on survey in some areas of northern Canada, MacNeish had to have bush pilots drop 50-gallon drums of food at critical landmarks along his route. He and his Inuit assistants would then hike from food drop to food drop.

In 1954 he surveyed the coast of the Beaufort Sea to either side of the Mackenzie River delta by whaleboat and canoe, discovering the important Engigstciak site; for the next two summers, he returned to excavate it. Although beset with the problems of solifluction and frost cracks common to many Arctic sites, Engigstciak produced a tentative

sequence of nine cultural complexes. The oldest, the British Mountain complex, contained extinct *Bison priscus* hunted by early Native Americans; the youngest complexes contained tools recent enough to be considered “Eskimo.” As he often did, MacNeish had found a site that contained virtually the entire archaeological sequence for its region.

Inspired by Engigstciak, MacNeish decided in 1959 to survey on foot a 600-mile stretch of the Firth River, accompanied by a few Inuit assistants. This trip produced only 24 archaeological sites, but twice that many good anecdotes. At one point the hikers found that one of the food drums dropped by their bush pilot had split open on impact, with the odor inspiring a bear to devour most of the contents. “The worst part,” said MacNeish, “was that the bear ate all the cigarettes, so for the rest of the trip two Inuit and I had to share the three remaining smokes.” One hundred miles from the finish line, MacNeish broke his ankle. He was able to hobble the rest of the way only because his boot froze to his foot, “becoming the equivalent of a plaster cast.”

Despite all kinds of hardships, MacNeish emerged from the Canadian barrenlands with a working hypothesis. The campsites of the earliest hunting peoples, he predicted, would tend to occur on eskers—serpentine ridges of gravelly and sandy drift believed to have been formed by streams below glacial ice—which wound across the northern swamps like railroad trestles. From here the hunters could take caribou when they forded the wetlands between eskers. This was one more example of MacNeish’s ability to “think like a prehistoric man,” a skill which later led to his discovery of many of his most important sites.

The final stage of MacNeish’s Yukon work began in 1959, when he moved to Kluane Lake in the southwestern part of the territory. There he would be able to arrive via the Al-Can Highway and buy his supplies in Whitehorse, a consider-

able improvement in logistics. Moreover, he could build on the work of Frederick Johnson of the R. S. Peabody Foundation in Andover, Massachusetts, since Johnson had excavated there in the 1940s. Johnson and MacNeish became good friends and published their Yukon work jointly in 1964.

What intrigued MacNeish about the region was that its Northwest Microblade Tradition had been compared by the likes of Nels Nelson to material from Lake Baikal in Siberia. This might be evidence for at least one of the waves of immigrants crossing the Bering Straits into North America. MacNeish spent 1957-61 excavating at the Gladstone site, the Little Arm site, the Taye Lake site, and other localities in the Kluane River valley. With grizzly bears wandering past his excavation trenches, MacNeish put together a tentative sequence from 8000 B.C. to the first century A.D.

At the stratified Gladstone site, MacNeish found the Northwest Microblade Tradition associated with hunter-gatherers who fished Kluane Lake in the summer and hunted and trapped mammals in the winter. Their favorite game included moose, black bear, caribou, and bison, and their tool tradition might have begun as early as 5500 B.C. MacNeish separated the stone tools into those of local origin, those with possible Siberian influence and into those showing ties with groups to the south.

By 1958 MacNeish had reached 40 years of age, and while 600-mile hikes down the Firth River were not beyond his ability, he was drawn back to Mexico's balmy winters and the intellectual challenge of early agriculture. His botanist friends were convinced that Tamaulipas lay too far north to be the place where Mexican agriculture had begun. MacNeish therefore began to look for early sites farther to the south.

The region of Copán in Honduras had caves, but none were sufficiently dry. The same was true of Tegucigalpa,

Comayagua, and the Valley of Zacapa in Guatemala. MacNeish then crossed the border into Chiapas and surveyed the valleys of Comitán and San Cristóbal las Casas; neither had dry caves. In 1959, at the suggestion of Frederick A. Peterson of the New World Archaeological Foundation, he tested the Santa Marta Rockshelter near Ocozocoautla, in the Grijalva River depression of Chiapas. This was a huge shelter with five preceramic levels covering the period from 7000 to 3500 B.C. The animal bones give us a rare glimpse of Archaic hunting in tropical riverine forest, but MacNeish and Peterson found that the shelter had no desiccated plants and only poor preservation of pollen.

Moving north in 1960, MacNeish briefly toured the Valley of Oaxaca and the Río Balsas depression of Guerrero, but found nothing of interest. Huajuapán de León in northern Oaxaca had caves but none were dry, so he continued east through Tequixtepec into Puebla's Tehuacán Valley. Discouraged after a fruitless three-year search, MacNeish had no inkling that he was about to find just what he was looking for.

The Tehuacán Valley lies in a deep rain shadow between two mountain ranges; it is an area of permanent drought, where evapotranspiration exceeds precipitation for most of the year. MacNeish began surveying at the northwest end of the valley in December 1960 and soon found a series of dry caves near the mineral springs of El Riego. Near Altepexi and Ajalpan in the central valley, the caves were lower in elevation and drier. By January 1961 he was near the southeast end of the valley, where the caves were lower and drier still. The fiftieth site of his Tehuacán survey was a large rockshelter in a cliff called Cerro Agujereado ("Pierced Hill") near Coxcatlán. During the six-day excavation of a 2-m-by-2-m test pit, MacNeish reached deposits with corncobs the size of a cigarette filter.

MacNeish realized that he might be on the threshold of a great project, yet as an employee of the Canadian government he could not apply to the National Science Foundation for funds. Then he remembered his Yukon collaboration with Frederick Johnson of the R. S. Peabody Foundation in Massachusetts. Douglas S. Byers, director of the Peabody Foundation, agreed that that institution would apply for grants from the NSF and Rockefeller Foundation to fund a Tehuacán Archaeological-Botanical Project with MacNeish as field director.

For the next four years MacNeish used all the managerial skills he had learned at Kincaid to direct a large interdisciplinary project in the Tehuacán Valley. He brought Peterson up from Chiapas to run his field headquarters. He invited Melvin L. Fowler (whose work at the Modoc Rock Shelter in Illinois had impressed him) to dig at Coxcatlán Cave. José Luis Lorenzo sent two of his best students, Angel García Cook and Antoinette Nelken, down from Mexico City to participate. A team of botanists including Mangelsdorf, Walton Galinat, C. Earle Smith, Lawrence Kaplan, Hugh Cutler, and Thomas Whitaker analyzed the plant remains. Richard Woodbury and James Neely studied prehistoric irrigation systems, and Kent Flannery, then a graduate student, was hired to identify animal bones from the excavations. MacNeish and his team tested 15 caves, then concentrated on 6 named El Riego, Tecorral, San Marcos, Purrón, Abejas, and Coxcatlán. All were important, but the greatest was surely Coxcatlán Cave; it belongs in the world-class category of archaeological caves like Tabun and Kebara in Israel, Ksar Akil in Lebanon, and Combe Grenal and Abri Pataud in France.

The Tehuacán Project made MacNeish a household name. He recovered what were (at that time) the oldest maize, the oldest squash and bottle gourds, the oldest chile peppers

and beans, the oldest tomatoes and avocados, the oldest New World cotton, the oldest domestic dogs and turkeys, and the oldest Mexican honey bees. While AMS dates obtained in the 1990s made some of those domesticates younger than originally thought, MacNeish had definitely pushed agriculture back before 7000 B.P. (calibrated).

These finds were important both as agricultural discoveries and as new insights into the origins of sedentary life in Mexico. MacNeish found that a Late Archaic complex of stone bowls was followed by Mexico's first pottery. Named for Purrón Cave, where they first appeared, these monochrome ceramics resembled (and briefly coexisted with) the stone bowls.

One of the most often reprinted essays to emerge from the Tehuacán Project was MacNeish's 1964 *Science* article, "Ancient Mesoamerican Civilization." That paper featured seven drawings of the Tehuacán Valley, depicting different stages of sociopolitical evolution from 10,000 B.C. to A.D. 1500. Each drawing showed the mountainous valley in three dimensions, a low-level aerial oblique view, with all relevant archaeological sites indicated. How those drawings were created demonstrates the intuitive side of MacNeish's work.

In 1962 his project had taken over a large house on one of Tehuacán's main streets. MacNeish shared a bedroom next to the laboratory with his dig foreman and a graduate student. One night Scotty sat bolt upright, got out of his bed, and went to the lab. Others followed, thinking they might be needed. MacNeish seized a felt-tipped Marks-a-Lot and approached a lab table covered with protective brown wrapping paper. On the paper he first sketched the seven three-dimensional maps of the valley, then went back and filled in the archaeological sites for each moment in time. His staff watched in amazement as he located every mountain range, canyon, river, and site from memory.

Although an artist drafted the published version, essentially what you see in MacNeish's article is what he produced in an hour with a large marking pen. This "eureka" moment typifies the way his syntheses came together on a subconscious level once he had absorbed enough data.

MacNeish always said that the Tehuacán years were the happiest of his life. The intellectual high it produced left him eager to return to the field as soon as his five-volume report was in press. Next he wanted to take on the origins of agriculture and animal domestication in the Andes; the key would be to find a highland valley arid enough to have dry caves.

In 1966 MacNeish sought advice from Andeanists Frédéric Engel, Edward Lanning, Thomas Patterson, and Rogger Ravines, and reconnoitered the Peruvian valleys of Huancayo, Huancavelica, the Río Mantaro, the Río Pampas, and Ayacucho. This was rugged country; on one occasion, Ravines had to pull MacNeish from the water when he slipped and was swept away by a swift mountain stream they were fording. Many prospective caves had preceramic deposits, but their altitude made them too cool and moist for plant preservation. The Huanta-Ayacucho area seemed the most promising, and MacNeish and Ravines eventually came upon Pikimachay ("Flea Cave") not far from the famous ruins of Wari.

This Andean survey took place during one of MacNeish's brief forays into teaching. He had moved from the museum in Ottawa to a professorship at Calgary, only to discover that teaching "drove him nuts" and his position in Canada still would not let him apply to the National Science Foundation. The job of his dreams—pure research—finally opened up when Byers and Johnson began to retire from the Peabody Foundation in Andover, paving the way for MacNeish to become director in 1969.

From 1969 through 1975, with National Science Foun-

dation support, MacNeish directed the large interdisciplinary Ayacucho-Huanta Archaeological-Botanical Project. He reunited many of his former collaborators from the Tehuacán Project and made Ayacucho one of the most intensively studied highland valleys in Peru, with more than 600 sites located and a stratigraphic sequence from Late Pleistocene to the Spanish Conquest.

The range of environmental zones covered was impressive, and the major caves reflected this. The Puente Rockshelter lay at 2582 m in thorny scrub and contributed hundreds of guinea pig remains, dating the domestication of this rodent to the preceramic. Pikimachay Cave, at 2850 m, produced a spectacular complex of Pleistocene animals, including extinct horse and giant sloth. Jaywamachay Cave, at 3350 m in humid woodland, was a hunting camp at which large numbers of guanaco and huemal deer had been taken. Tukumachay Cave, at 4350 m in the treeless *puna* or Alpine tundra, looked out on vicuña territory. Thanks to a large set of measurements taken and a discriminant analysis done by Elizabeth S. Wing, the project was able to document the appearance of domestic llama (and perhaps alpaca) in the preceramic era. Plant preservation was not as good as in Tehuacán, but the excavations shed light on the early history of squash and quinoa and suggested that maize had arrived in Ayacucho by 3000 B.C.

While the archaeological community waited to see what he would do next, MacNeish looked for new worlds to conquer. He had long talked about investigating the origins of rice cultivation, but U.S.-China relations were not yet good enough to make such a project feasible. In 1975, however, the National Science Foundation sponsored an exchange program with China, and MacNeish found himself enroute to Beijing. Then came the unexpected: During a layover in Seattle, MacNeish suffered his first heart attack and under-

went double bypass surgery. As if that were not bad enough, an overdose of anaesthetic left him unconscious for 21 days. He recovered, but with instructions to scrap his travel plans and get some rest. Everyone who knew MacNeish predicted that he would not rest for long; he would simply look for an archaeological region closer to home. That region turned out to be Belize.

In the spring of 1980 MacNeish, S. Jeffrey K. Wilkerson, and Antoinette Nelken began a reconnaissance of coastal Belize. During a survey that sounds like the tropical equivalent of MacNeish's Arctic barrenlands work, they roamed over 14,000 km² by boat and truck, locating 230 sites and creating five tentative preceramic phases. Although MacNeish found evidence of a long preceramic sequence, his Belizean sites were shallow open-air localities, unlike the dry caves where he had desiccated plants plus deep stratigraphy. The shallowness of the Belizean sites forced him to rely on seriating the artifact types. MacNeish's proposed sequence began with a Paleoindian complex called Lowe-ha, which had dart or spear points like those of Loltún Cave, Yucatán, and Madden Lake, Panama (9000-7500 B.C.). It ended with a complex of tools called Progreso; sites of this period (3000-1800 B.C.?) had grinding stones and were large enough to be incipient agricultural hamlets. Although the tool types assigned to each phase in MacNeish's Belizean sequence are still being debated, it is impressive how many preceramic sites he found in tropical vegetation in a short period of time.

By 1983, at age 65, MacNeish had retired from the Peabody Foundation. A second period of teaching, this time at Boston University, ended even sooner than the first, providing further proof that only research (and especially fieldwork) could hold his attention. On October 1, 1984,

MacNeish, Frederick Johnson, and physicist Bruno Marino created the Andover Foundation for Archaeological Research.

It had been 46 years since MacNeish assisted Brainerd at Swallow Nest Cave, and he was now ready to go back to the Southwest. He consulted with Linda Cordell, Steadman Upham, and others who might know of dry caves with evidence of early agriculture. Several tests in New Mexico rockshelters produced maize dating to 1225 B.C., but even more intriguing to MacNeish were hints of material that might antedate Clovis, one of North America's earliest hunting-gathering societies. Not all of his colleagues had been convinced that the Pleistocene fauna in Pikimachay Cave was associated with human occupation. As a result, nothing was likely to please MacNeish more than a cave with indisputable pre-Clovis deposits.

In 1989 the staff of the Environmental Office at the Fort Bliss military base, about 48 km south of Alamogordo, led MacNeish to two caves on the MacGregor Firing Range. One of them, Pendejo Cave, was in a limestone cliff overlooking the dry beds of glacial lakes. The fact that the cave's name was an obscenity in Spanish delighted MacNeish. Accompanied by project administrator Jane G. Libby and a team from the Andover Foundation, MacNeish dug at Pendejo Cave from 1990 to 1992.

Pendejo Cave was amazing indeed. It had 22 "extremely well defined" strata and produced 72 radiocarbon dates, 60 of which were pre-Clovis. Levels G and H were at least 25,000-31,000 years old; there were no dates available for Level O (the oldest), but Level N had a date in excess of 36,240 B.P. Two levels produced hair diagnosed as human, the younger sample giving an AMS date of 12,300 B.P. The older hair sample, dating to 19,180 B.P., was initially identified as Mongoloid rather than Native American, suggesting a very early stage in the peopling of the New World. What appear

to be human finger and palm prints were found on clay in Level I and could be older than 30,000 B.P. The two lowest levels had extinct Pleistocene animals.

MacNeish relished the inevitable controversy stirred up by Pendejo Cave. He knew that at least one group of Paleoindian specialists—widely known as the Clovis Police—would be skeptical of any attempt to push human occupation of the New World back to 30,000 B.C. They would question whether the “artifacts” found with extinct fauna were really of human manufacture. A few would suggest that the alleged hearths from which some radiocarbon dates had come were simply burned pack-rat middens. None of this bothered MacNeish; as a former boxer, he was prepared to spar with his opponents until he won on points.

Besides, as exciting as his Fort Bliss work had been, MacNeish was already becoming involved in a new project. In 1991, sixteen years after bypass surgery had thwarted his first attempt to visit China, he was invited to a conference on early agriculture in Jiangxi Province. During a tour of the region, MacNeish was shown many promising caves and rockshelters; in 1992 he applied for permission to test them. After considerable negotiation it was agreed that a joint Sino-American effort—the Jiangxi Origin of Rice Project—would be codirected by MacNeish and Prof. Yan Wenming of Beijing University.

In 1993 MacNeish, Jane Libby, Geoffrey Cunnar, and a team of Chinese and American students began the excavation of Xian Ren Dong (“Benevolent Spirit Cave”) and Wang Dong (“Bucket Handle Cave”). In need of an Old World zooarchaeologist, they added Richard Redding to the team in 1995. By then MacNeish had been given a Chinese name, Mah Nish, which he freely translated “nobleman of the Horse lineage.” Appropriately, it reinforced Scotty’s preferred pro-

nunciation of his family name: MacNish, rather than McNeesh.

MacNeish dug the Jiangxi caves by the La Perra method, establishing a stratified sequence from Upper Paleolithic (24,540 B.P.) to Final Neolithic (4000 B.P.). These caves did not resemble those in Tehuacán, of course; like European or Near Eastern caves, they had good preservation of flint, pottery, and bones but no desiccated plant remains. Fortunately, MacNeish was able to get Deborah Pearsall to train a gifted Chinese student, Zhao Zhijun, in phytolith analysis at the University of Missouri. It was mainly through phytoliths (and flotation of carbonized plant remains) that the origins of agriculture in Jiangxi could be documented.

Preliminary results suggested that phytoliths of wild rice, *Oryza nivara*, were present at Wang Dong by 17,040 B.P. The first rare phytoliths of domestic rice, *Oryza sativa*, appeared in both caves between 14,000 and 11,200 B.P. in a period MacNeish named Xian Ren. Domestic rice did not become dominant, however, until 9600-8000 B.P., a time coeval with the advent of cereal agriculture in the Near East. Regarding early animal domestication, Redding's preliminary results suggested that the chicken may have been present in Neolithic levels dated to 7500 B.P. Thus MacNeish could add to his résumé another world region where he had contributed important data on the origins of agriculture.

By the year 2000 MacNeish was 81, an age by which most archaeologists have long since retired; Scotty, however, was planning his next project in Turkey. He had barely worked out the itinerary when he suffered a mild heart attack, and his "Origins of Agriculture in Turkey" project was put on hold. MacNeish was of course told to rest, but his idea of rest was to visit archaeological sites. On January 16, 2001, during a tour of Maya ruins in Belize, one of

archaeology's most prolific and colorful practitioners was fatally injured in the crash of his rental car. Having endured for 82 years despite cancer, heart attacks, a near drowning in the Andes, and double bypass surgery, the seemingly indestructible Scotty MacNeish was taken from us by accident. Had he lasted 102 years, we would still consider his death premature.

HIS LEGACY

MacNeish has to be considered one of the greatest American archaeologists of the twentieth century. Almost everything we know about the origins of agriculture and sedentary life in Mexico is directly or indirectly the result of his work; his La Perra method of cave excavation is still being used there. By adding Peru, China, Belize, the Iroquois region, and the Midwest and Southwest United States to the list of regions to which he made contributions, he achieved almost legendary status on an international scale.

MacNeish will also be remembered as an inexhaustible source of amusing anecdotes and first-hand stories of excavations past and present. He was loved by everyone who worked with him in the field, and even won the begrudging respect of his occasional critics, who found him to be pugnacious but entertaining in defense of his work. It may be a long time before archaeology sees a researcher possessed of so superhuman a capacity for hard work. It will be even longer before we see someone so adept at "thinking like a prehistoric man" and, hence, so skilled at finding the best archaeological sites in every region.

CHRONOLOGY

- 1918 Born April 29 in New York City to Harris and Elizabeth Stockton MacNeish
- 1936 Entered Colgate University
- 1938 Transferred to the University of Chicago
- 1940 B.A., University of Chicago (major: anthropology; minor: vertebrate paleontology)
- 1944 M.A., University of Chicago
- 1945 Married to June Helm (divorced 1958)
- 1947 Research Fellow, University of Michigan
- 1949 Ph.D., University of Chicago
- 1963 Married Diana Walter (two sons, Richard Roderick and Alexander Stockton)
- 2001 Died in Belize January 16

HONORARY DOCTORATES

- 1970 Universidad de San Cristóbal de Huamanga, Ayacucho, Peru
- 1980 Simon Fraser University, British Columbia, Canada

PROFESSIONAL RECORD

- 1941-42 Graduate Supervisor, Kincaid Site, Southern Illinois
- 1944 Archaeological Supervisor, Havana Mounds, Illinois
- 1947 Archaeological Supervisor, Eastern Pennsylvania
- 1948 Director, Summer Field School, Wolf Creek Dam, Kentucky
- 1949-62 Senior Archaeologist, National Museum of Canada
- 1964-68 Head, Department of Archaeology, University of Calgary, Canada
- 1969-83 Director, Robert S. Peabody Foundation for Archaeology, Andover, Massachusetts
- 1982-86 Professor, Department of Archaeology, Boston University
- 1984-2001 Director, Andover Foundation for Archaeological Research, Andover, Massachusetts

AWARDS AND HONORS

- 1944 Sigma Psi, University of Chicago
- 1963 Húesped Distinguido y Amigo Predilecto de Tehuacán,
Mexico
- 1964 Spinden Medal for Archaeology, Smithsonian Institution
- 1965 Lucy Wharton Drexel Medal for Archaeological Research,
University of Pennsylvania Museum
- 1966 Addison Emery Verrill Medal, Peabody Museum, Yale
University
- 1967 Elected to the American Academy of Arts and Sciences
- 1970 Alfred Vincent Kidder Medal, American Anthropological
Association
- 1971 President, Society for American Archaeology
- 1973 Elected to the British Academy
- 1974 Elected to the National Academy of Sciences
- 1977 Cornplanter Medal for Iroquois Research, Auburn, New
York
- 1985 Fiftieth Anniversary Award for Outstanding Contributions to
American Archaeology, Society for American Archaeology
- 1996 Award of Recognition, Chinese Historical Society of
Southern California, Los Angeles
- 2000 Fryxell Medal for Interdisciplinary Archaeology, Society for
American Archaeology

MEMBERSHIPS

- American Association for the Advancement of Science
- American Anthropological Association
- Society for American Archaeology
- Society of Professional Archaeologists

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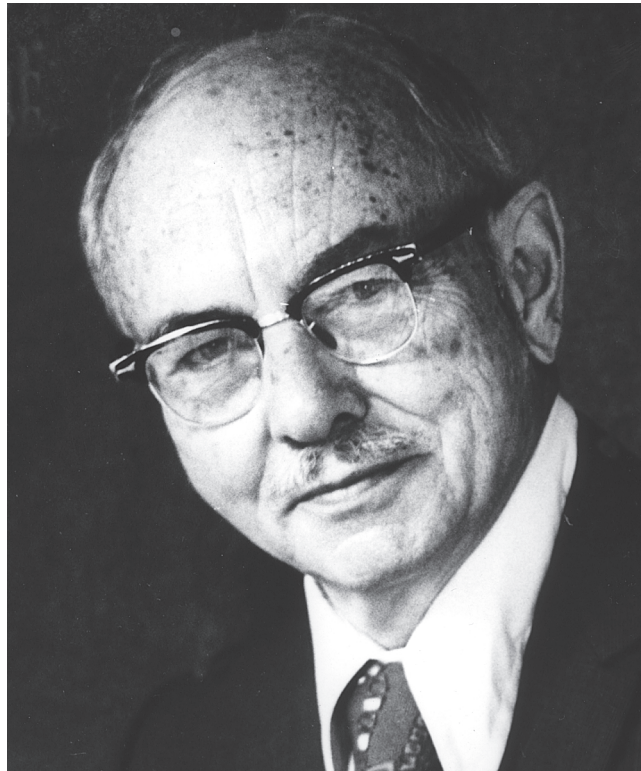
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E. Y. McShare

EDWARD JAMES McSHANE

May 10, 1904–June 1, 1989

BY LEONARD D. BERKOVITZ AND
WENDELL H. FLEMING

DURING HIS LONG CAREER Edward James McShane made significant contributions to the calculus of variations, integration theory, stochastic calculus, and exterior ballistics. In addition, he served as a national leader in mathematical and science policy matters and in efforts to improve the undergraduate mathematical curriculum.

McShane was born in New Orleans on May 10, 1904, and grew up there. His father, Augustus, was a medical doctor and his mother, Harriet, a former schoolteacher. He graduated from Tulane University in 1925, receiving simultaneously bachelor of engineering and bachelor of science degrees, as well as election to Phi Beta Kappa. He turned down an offer from General Electric and instead continued as a student instructor of mathematics at Tulane, receiving a master's degree in 1927.

In the summer of 1927 McShane entered graduate school at the University of Chicago, from which he received his Ph.D. in 1930 under the supervision of Gilbert Ames Bliss. He interrupted his studies during 1928-29 for financial reasons to teach at the University of Wichita. It was at Chicago that McShane's long-standing interest in the calculus of variations began. From 1930 to 1932 he held a National Research Council Fellowship, spent at Princeton, Ohio State,

Harvard, and Chicago. In 1931 he married Virginia Haun. The McShanes had three children, Neill (deceased), Jennifer, and Virginia.

Because of the Great Depression, openings in mathematics departments were virtually nonexistent in 1932. The McShanes spent 1932-33 at Gottingen, where he translated into English the two volumes of Courant's *Differential and Integral Calculus*. They also saw firsthand some frightening aspects of the onset of Nazi power in Germany.

After two years (1933-35) on the Princeton faculty McShane joined the Department of Mathematics at the University of Virginia as a full professor in the fall of 1935. He remained there for the rest of his career, except for leaves of absence spent at other institutions. With the onset of World War II McShane agreed to head a mathematics group at the Ballistics Research Laboratory in Aberdeen, Maryland. During this time he wrote a book with John L. Kelley and Frank V. Reno entitled *Exterior Ballistics*, which is regarded as the definitive work on the subject. In 1947 Tulane University awarded him an honorary D.Sc. degree.

McShane served as president of the Mathematical Association of America during 1953-54. He took an active interest in efforts just then getting underway to revitalize undergraduate mathematics in the United States. As president, McShane appointed a committee to prepare texts and other material to improve the quality of undergraduate mathematical instruction. For several years after his term as president he chaired and served on this committee, which evolved into the Committee on the Undergraduate Program in Mathematics, a leader in these endeavors. McShane was elected to the National Academy of Sciences in 1948 and served on the National Science Board from 1956 to 1968. During 1958 and 1959 he was president of the American Mathematical Society. In 1964 he received the Mathematical Association

of America's Annual Award for Distinguished Service to Mathematics.

McShane had a lifelong interest in music. His early interest in opera led him to learn to read Italian libretti. In addition to Italian he was fluent in Dutch, French, German, and Spanish. His knowledge of Italian, in turn, led Gilbert Ames Bliss to suggest to McShane that he read the then new book *Fondamenti di Calcolo delle Variazione* by Leonida Tonelli, which started McShane on his study of multiple integral problems in the calculus of variations. Later, in the 1950s, McShane learned to play the cello and became an amateur chamber music performer.

The injustices suffered by some of his colleagues during the post-World War II anti-Communist hysteria deeply offended McShane. He himself, in response to the question on the Aberdeen Proving Ground security form that asked whether he had ever been involved with organizations that at any time advocated the overthrow of the U.S. government by force and violence, replied that, yes, he was an employee of the Commonwealth of Virginia. During the McCarthy era, the House Un-American Activities Committee (HUAC) "invited" him to express his views, but he was not subpoenaed. He did not cooperate with HUAC but wrote a letter in which he stated his views and backed them up with quotations from various sources.

Victor Klee, recalling his experience as a graduate student at Virginia from 1945 to 1949, wrote: "He [McShane] was very popular with the graduate students because of his clear lectures, his amusing anecdotes, and unusual kindness." Klee went on to tell how McShane turned his office over to the graduate students, who had no offices of their own: "His generosity contributed a lot to the quality of the graduate program by providing a place for the graduate students to meet with each other and talk about mathematics. . . . It is

simply impossible, in a few words, to convey the extent of the graciousness, kindness, and hospitality that have been [and are] exhibited by Virginia and Jimmy McShane in their relations with those lucky enough to know them. These go far beyond professional matters.”

E. J. McShane died of congestive heart failure on June 1, 1989, in Charlottesville, Virginia.

Most of McShane’s work in the 1930s was in the calculus of variations. The late 1920s and 1930s saw many changes in the calculus of variations. Leonida Tonelli’s book had introduced the “direct method,” which was advantageous for proving semicontinuity and the existence of absolute minima. The solution to Plateau’s problem by Jesse Douglas and Tibor Rado stimulated the rapid development of the calculus of variations for multiple integral problems and the theory of Lebesgue area of surfaces. (The Plateau problem is to find a surface of minimum area with given boundary.) McShane was at the forefront of these developments. While still a graduate student McShane obtained the necessary condition of Weierstrass for quasiconvex variational problems with an arbitrary number of functions of several variables. Soon afterward he turned to questions of semicontinuity and existence of a minimum for multiple integral geometric calculus of variations, of which the Plateau problem was a prototype. Hidden in these problems were notorious analytical and topological difficulties, which were later overcome by other mathematicians as part of Lebesgue surface area theory. McShane provided an elegant solution for geometric variational integrands that do not vary spatially. The key idea was that it suffices to find the minimum in the smaller class of “saddle surfaces,” which are representable parametrically by a vector function monotone in Lebesgue’s sense.

In 1939 McShane published a paper in the *American Journal of Mathematics* entitled “On Multipliers for Lagrange

Problems," which was important in itself and some 20 years later had a profound, but not generally recognized, influence on optimal control theory and nonlinear programming. A solution of the problem of Lagrange satisfies two first-order necessary conditions, the Euler equations and the Weierstrass condition. Prior to the appearance of this paper the Weierstrass condition could only be established under the assumption that the Euler equations satisfied a condition called normality. This condition is not verifiable a priori. In this paper McShane established the Weierstrass condition without assuming normality. The proof was novel and consisted of first constructing a convex cone generated by first-order approximations to the end points of perturbations of the optimal trajectory and, second, showing that optimality implies that this cone and a certain ray can be separated by a hyperplane. Twenty years later, this idea was used by Lev S. Pontryagin and his coworkers in their proof of the necessary condition for optimal control now known as the Pontryagin maximum principle. The classic book by Pontryagin, Boltyanskii, Gamkrelidze, and Mischchenko entitled *The Mathematical Theory of Optimal Processes*, which collected their previous work and for which they received the Lenin Prize, popularized the convex cone and separation constructions. These constructions were subsequently used by most authors in deriving necessary conditions not only for control problems but also for nonlinear programming problems and abstract optimization problems.

Another body of work, which was definitive for problems in the calculus of variations in one independent variable, was the series of three papers that appeared in 1940 in volumes six and seven of the *Duke Mathematics Journal*. These papers concerned a broad class of problems (called of Bolza type) without convexity assumptions needed to ensure that there exists an ordinary curve that is minimizing. McShane

showed that if the problem of Bolza is phrased in terms of generalized curves (which were introduced in 1937 for simple problems in the plane by L. C. Young) then the problem of Bolza has a solution. He then derived the generalizations of the standard necessary conditions that must hold along a minimizing generalized curve. Finally, he gave conditions under which the minimizing generalized curve is an ordinary curve. Definitive as this work was, it did not seem to attract attention outside the circle of cognoscenti in the calculus of variations until 20 years later, in the 1960s, when generalized curves were rediscovered by control theorists as relaxed controls, or sliding states. In a 1967 *SIAM Journal on Control* paper McShane adapted his 1940 work to the control theory setting. This paper is more elementary and self-contained than most treatments of relaxed controls and reflects McShane's dedication to teaching as well as research.

After the war McShane developed a serious interest in providing completely rigorous mathematical foundations for quantum field theory. Although the ambitious program that he undertook in this direction did not reach fruition, the attempt profoundly influenced his subsequent work on integration processes and stochastic calculus. This is seen, for example, in his excellent *Bulletin of the American Mathematical Society* survey article "Integrals Designed for Special Purposes" (1963) and his book *Stochastic Calculus and Stochastic Models* (1974), which is the definitive treatment of his approach to that subject.

In *Proceedings of the American Mathematical Society* (1967) and corrigenda and addenda (1969) McShane and R. B. Warfield proved a general version of Filippov's implicit function theorem. This lemma gives conditions that guarantee the existence of a measurable solution to an equation whenever a point-wise solution exists and is one of the basic tools in optimal control theory.

His 1973 paper in the *American Mathematical Monthly* entitled “The Lagrange Multiplier Rule” is another example of McShane’s interest in instruction. Here he gave a penalty function proof of the Fritz John and Kuhn-Tucker necessary conditions for nonlinear programming problems that is short and accessible to anyone who knows standard undergraduate real analysis. Later other authors applied the arguments used here to obtain necessary conditions for a variety of control and optimization problems.

Over the years McShane achieved an extraordinarily deep understanding of integration processes as they arise in various guises. He wrote three books on integration, in addition to a number of research articles and the 1963 *Bulletin of the American Mathematical Society* survey already mentioned. His 1944 volume *Integration* gave a readable introduction to the Lebesgue theory at a time when few such books existed in English. The 1953 monograph, *Order Preserving Maps and Integration Processes*, was an outgrowth of his search for a mathematically correct setting in which to treat divergent integrals in quantum physics. In 1957 J. Kurzweil defined a modification of the Riemann integral, which turned out to be more general than the Lebesgue integral. McShane’s 1983 volume *Unified Integration* develops in a similar vein a complete theory of integrals, together with a wealth of applications to physics, differential equations, and probability. An appealing feature of this approach from a pedagogical standpoint is that point-set topology and measurability issues can be deferred.

During the 1960s and 1970s McShane’s interests turned toward developing a stochastic differential and integral calculus. The Ito stochastic calculus was by then already in existence. It provided a convenient way to represent an important class of stochastic processes, called Markov diffusions, as the solutions to stochastic differential equations.

The random inputs to an Ito-sense stochastic differential equation are Brownian motion processes whose formal time derivatives are “white noises.” At that time, however, there was considerable confusion in the engineering literature about the correct interpretation if an idealized white noise is replaced either by a physical “wide band” noise or by some discrete process introduced for numerical approximation to the solution of the stochastic differential equation. This issue was clarified by the work of McShane, Stratonovich, and Wong-Zakai.

McShane’s approach provided a particularly satisfying resolution of this issue. His stochastic integral has an important consistency property that ensures that solutions of differential equations representing physical systems driven by wide-band noises tend in the white noise limit to the solution of the corresponding McShane-sense stochastic differential equation. McShane’s *Stochastic Calculus and Stochastic Models* (1974) gave a definitive account of this work. Even today the consistency question is often not addressed in the applied literature in such areas as chemical physics, financial economics, and biology. Consistency becomes a more delicate matter for systems on a time interval of length T that is large (or infinite), as happens in questions of large deviations or ergodicity. It is perhaps ironic that it has been left to probabilists to sort out these practical consistency questions.

Edward James McShane will be remembered for his many important and often definitive contributions to mathematics, for his service to and leadership in the mathematical community and for his warmth and kindness to his students and colleagues.

THIS BIOGRAPHICAL MEMOIR is a revision of a tribute to E. J. McShane, written by us for the September 1989 issue of the *SIAM Journal on Control and Optimization*, which was a collection of research papers

contributed in his honor. Our preparation of that tribute was greatly facilitated by unpublished biographical material that McShane provided a few months before his death the same year. We also wish to thank McShane's family and Victor Klee for many helpful suggestions and for their warm encouragement.

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Robert L. Metcalf

ROBERT LEE METCALF

November 13, 1916–November 11, 1998

BY MAY BERENBAUM AND RICHARD LAMPMAN

ON WEDNESDAY, NOVEMBER 11, 1998, two days before what would have been his eighty-second birthday, Robert Lee Metcalf died in his home in Urbana, Illinois. Thus ended one of the most influential lives of twentieth-century entomology. More than any other single individual, Metcalf made the goal of environmentally compatible pest management achievable. Over the course of five decades, he worked tirelessly toward implementing scientifically rational and environmentally sustainable pest control, and for many of those years he was a passionate, courageous, and articulate spokesperson for a viewpoint that was distinctly unpopular among some of his peers.

Metcalf was born on November 13, 1916, at Columbus, Ohio, son of Clell Lee and Cleo Esther Fouch Metcalf. At the time, his father was an assistant professor of entomology at Ohio State University. Metcalf's entomological heritage was deep, indeed; Clell's brother, Zeno P. Metcalf, also became a well-known entomologist. When Robert was five, he moved with his family to Urbana, Illinois, where his father had been appointed as head of the Department of Entomology; Clell would serve in this capacity for 26 years. Robert attended the University of Illinois and received his bachelor's degree in 1939; a year later, in his father's department and under

the tutelage of Clyde Kearns, he received his master's degree, based on a study of the toxicity and repellency of derivatives of toluanesulfonyl chloride and picramic acid (1944). He left home to pursue his doctoral studies at Cornell University, obtaining a Ph.D. degree in 1942. Although his thesis focused on fluorescence-microscopic studies of the physiology and biochemistry of the Malpighian system of *Periplaneta americana* (L.), his far-ranging work extended the use of fluorescence techniques in entomology in a number of other contexts, including fluorescence-based detection of malarial parasites in vertebrate hosts (1943). While he was at Cornell, on June 22, 1940, Metcalf married Esther Jemima Rutherford, a biochemist by training. Esther would be both marriage partner and intellectual partner for her husband for over 50 years; together they had two sons, Robert Alan and Michael Rutherford, and a daughter, Esther Lee.

Although Metcalf eventually won acclaim for alerting the scientific community and the public to the environmental consequences of pesticide abuse, he began his career as a traditional chemical toxicologist. In 1943 he obtained his first job, as an assistant entomologist for the Tennessee Valley Authority. There he spent six years developing methods for improving chemical control of mosquitoes in impounded waters. In 1949 he left TVA to become a member of the faculty at the University of California, Riverside. He rose rapidly through the ranks, advancing to full professorship in 1953 and serving as department chair from 1953 to 1965 and as vice-chancellor for research from 1965 to 1968. It was during this period that Metcalf began to recognize some of the environmental and toxicological limitations of insect chemical control, this despite the fact that he entered his professional career at the same time that synthetic organic insecticides were being heralded as the ultimate insect control agents.

In retrospect, the level of enthusiasm that permeated the entomological community and society at large is mind-boggling in its naivety. *Reader's Digest* stories trumpeted the ability of "entire towns" to "abolish flies" and *Time* magazine proclaimed in 1947 that "the flies in Iowa can now be counted on the fingers of one hand" as a result of using the new pesticides (1952, 1980). Metcalf was among a handful of prescient entomologists who recognized the dangers of excessive zeal. He observed first-hand the now familiar problems with synthetic organic insecticides, including insecticide resistance, secondary pests, bioaccumulation in non-target organisms (including humans), and accidental poisonings. Metcalf realized that the overuse of insecticides selected efficiently and rapidly for resistance, thus rendering them useless. He and his Riverside colleagues were among the first to document carefully and incontrovertibly the acquisition of DDT and lindane resistance in houseflies in southern California (1949). Moreover, he described one of the first known examples of cross-resistance; these flies, which had never before been exposed to dieldrin, a new cyclodiene insecticide, displayed resistance upon their first encounter with the toxin.

Because quantitative approaches to measuring resistance were sorely needed, Metcalf developed a laboratory bioassay using a microliter applicator to estimate precisely the LD_{50} , or dose lethal to 50 percent of a sample population; this technique rapidly became the standard in the field. Less than a decade after the first recorded example of resistance to synthetic organic insecticides was described in the scientific literature, Metcalf wrote an article in the popular journal *Scientific American* explaining to the general public the phenomenon of resistance and its implications for human and environmental health (1952). The phenomenon of cross-resistance led to widespread recognition of the importance

of characterizing mode of action; chemicals with a shared mode of action were particularly prone to the development of cross-resistance. Soon, Metcalf became one of the world's authorities on mode of action of chemical insecticides (1955). In addition to developing quantitative measures of resistance, Metcalf also used his finely honed chemical skills to develop sensitive quantitative methods for determining both metabolic and environmental fates of pesticides.

Beginning in the 1950s and continuing through the 1960s, Metcalf pioneered the use of insecticide synergists, compounds that lack inherent toxicity but that by various means potentiate the toxicity of co-occurring toxins as a means of reducing insecticide inputs into the environment. He investigated the biological properties of synergists, such as their effects on non-target arthropods and biocontrol agents, as well as their chemical properties, thereby insuring that these compounds provided people with a safe alternative to applying increasingly larger amounts of insecticides to counteract resistant strains (1963, 1967). Metcalf was thus an early advocate and successful practitioner of the approach of reducing pesticide inputs without compromising efficacy—an approach that is environmentally more compatible yet acceptable to users. Metcalf and coworkers developed synthetic insecticides, such as the carbamates, that were biodegradable and more toxic to target organisms than to mammals.

Metcalf left Riverside in 1968 to return to his childhood home, Urbana, Illinois, recruited to the faculty of the Department of Entomology by the head at the time, Clyde Kearns, his former mentor and lifelong friend. A year later Metcalf began a three-year stint as head of the Department of Zoology; in 1971 he was designated a Distinguished Professor of Biology. During this period, Metcalf extended his interest in environmental fates of pesticide to the ecosystem level

and in doing so developed what may well have been the most effective tool for demonstrating the impact of pesticides on the environment in a quantitative and repeatable fashion. Up to that point, information about the environmental behavior of pesticides was gleaned from decades of widespread use, which often resulted in massive environmental catastrophes. In Metcalf's view this was unacceptable. Thus, he developed a realistic laboratory model for determining the environmental fate of proposed new pesticides. Metcalf's brilliant solution was to create a miniature model ecosystem—a microcosm—in the laboratory. Metcalf designed self-contained functioning ecosystems in a series of tanks, "an Illinois farm pond in a box," as he described them (1971). Over the years Metcalf and his coworkers evaluated more than 200 chemicals, generating invaluable information on the environmental compatibility not only of insecticides and herbicides but also of animal supplements and industrial chemicals, such as polychlorinated biphenyls. Model ecosystem analyses provided data consistent with information garnered laboriously from decades of field studies, validating the method as an inexpensive, rapid, and reliable index of environmental fate. In large part because of these studies and others inspired by Metcalf's pioneering efforts, biodegradability is a prerequisite for approval of any new pesticide (1971).

In pursuit of alternative approaches to pest management Metcalf eventually turned his attention to chemical modification of insect behavior, a move perhaps facilitated by collaborations with his son Robert A. Metcalf, who had also become an insect biologist (e.g., 1970). In 1975 he highlighted a promising new approach to reduce the amount of synthetic organic insecticide applied in the environment: the use of chemicals, particularly naturally occurring plant compounds, to manipulate insect behavior rather than destroy

metabolic function (1975). With his wife, Esther, and colleague Wally Mitchell in Hawaii, he commenced a long-standing collaboration to elucidate the attractants facilitating host finding and mate finding in tephritid fruit flies, economic scourges of fruit crops worldwide (1975, 1979). His work with fruit fly attractants allowed him to take his experience with the chemistry of insecticides and their mode of action and apply it to insect behavior. He felt that structure-activity studies had a dual function: the discovery of new attractants and the elucidation of the mode of action (harking back to his studies of the anticholinesterase “biochemical lesion”). He was involved in one of the first tests of the efficacy of kairomones (or attractants), a term he helped to popularize, as control agents; a single gram of methyl eugenol resulted in the mass trapping of over 7000 male Oriental fruit flies in a single day. Metcalf and Esther traveled almost annually to Hawaii to work with Wally Mitchell and his wife on *Dacus* attractants. For Metcalf, this was the perfect concept of a vacation.

Subsequent work on kairomones focused on developing attractant baits for corn rootworms, the most important pests of corn in the United States. His work had both practical significance for rootworm management and theoretical importance for understanding the evolution of host-plant specialization in insects. Metcalf and his students and colleagues documented compulsive feeding behavior by corn rootworms and cucumber beetles in response to cucurbitacins, tetracyclic triterpenoid compounds characteristic of the cucurbit host plants. In the early 1970s, Metcalf and A. M. (“Dusty”) Rhodes cut open a bitter cucurbit fruit and dusted it with carbaryl. The next day, the fruits were covered with thousands of dead beetles. To say this result impressed him would be an understatement.

He immediately saw the utility of cucurbitacins for con-

trolling one of the most important crop pests in the Midwest. From 1978 to 1990 numerous field tests were conducted with collaborators in several states to show the efficacy of cucurbitacin baits to reduce the pounds per acre of insecticide to grams per acre without loss of efficacy. Metcalf often said that the early breakthrough with *Diabrotica* was the development of beetle prints, a technique that allows the beetles to analyze the complex chemistry of the triterpenoids for the investigator. The beetles were sensitive to nanogram quantities of cucurbitacins and would eat the silica off the thin-layer chromatography plates wherever they were present. Metcalf's group produced an abundance of research articles on the cucurbitacin chemistry of the Cucurbitaceae, sensitivity of beetle species to different cucurbitacins, sequestration of cucurbitacins by beetles, and the allomonal properties of cucurbitacins (e.g., 1985; 1986). Metcalf poured his energy into elucidating the basic chemical ecology of plant and insect co-evolution, a subject of intense interest to him and one on which he lectured enthusiastically and elegantly in the chemical ecology course he started in 1983 with one of us (M.B.) in the Department of Entomology and colleague David Seigler from the Department of Plant Biology. This work led to what may be the best example in entomology of an Old World-New World co-adaptation of insects and plants (Aulacophorites and Diabroticites with the Cucurbitaceae) (1986).

In the 1980s Metcalf and his students conducted a range of studies that provided even greater insight into the chemical basis of host-plant utilization by Diabroticites. It soon became evident that corn rootworms exhibited a compulsive flight response to volatile attractants. Once again Metcalf used his biochemical lesion experience with insecticides to study the chemistry of olfaction. By 1988 structure-activity studies resulted in attractants for all of the native Diabroticites in

Illinois, both pest and non-pest species (five species in two genera). This investigation generated over 20 papers and added a new chapter to the chemical ecology of corn rootworms and cucumber beetles (1991). It is inspiring to note that the majority of these papers came after his mandatory retirement at the age of 70 in 1987.

The early 1990s also marked a period in Metcalf's life when all of his scientific prowess could not help him; he discovered he had prostate cancer, and on May 13, 1991, his wife and best friend, Esther, died, a loss that left him rudderless. He concentrated all of his efforts on writing "Plant Kairomones in Insect Ecology and Control" (1992) as a tribute to his wife, with whom he had collaborated for so many years. To his friends and colleagues he hinted he was giving up his research after the completion of the book, but he had underestimated his own resiliency. With his marriage to Elaine Reynolds, the widow of his late friend Hal Reynolds, on January 1, 1992, Metcalf displayed a sudden revitalization. He re-focused his research on the attractants of corn rootworms and continued to make cutting-edge advances in both chemical ecology and insect pest management. Metcalf split his time for the next six years about equally between Paradise, California (his second wife's home) and Urbana, Illinois. In Paradise he was known as the outstanding clarinetist with an interest in insects, and every summer he returned to Urbana to continue working with corn rootworms. From 1992 to 1998 his publication record burgeoned with descriptions of the role of indole as a synergist in corn and cucurbit blossoms, the chemical basis for attraction of *Diabrotica* to native thistle blossoms, and with reviews on trends in entomology and insecticide research.

In the summer 1998 Metcalf concentrated on a new approach for manipulating corn rootworm behavior. In collaboration with Hans Hummel from the University of Giessen

and Robert Novak from the Center of Economic Entomology at the Illinois Natural History Survey, once again he discovered an unexpected phenomenon: the inhibition of pheromone responses in beetles exposed to sources of kairomones. This novel concept reminded him of the mating disruption technology used for several important insect pests. In addition, he found that large numbers of gravid western and northern corn rootworm adults were attracted to baited traps in alfalfa and soybean fields, presaging the subsequent discovery of rotation-resistant rootworms in the Midwest. Metcalf seemed so revitalized that Hans Hummel returned to Germany and told colleagues of Metcalf's good health and stamina. In retrospect it is remarkable how he willed himself to go out to the field almost every day, analyze data, complete two publications, and leave manuscripts for at least three additional papers while coping with terminal metastatic cancer. In the last conversation one of us (R.L.) had with him he talked about the summer research, the exhilarating joy of discovery of the attractants, and the fun of walking the prairie, cornfields, and soybean fields of Illinois.

Metcalf was dramatically affected by Rachel Carson's *Silent Spring*. He was aware of the controversy about the accuracy of some of the examples she used in her book, but he was nonetheless deeply moved by her spirit. It was one of the few books he always had out in his living room and was fond of picking up and repeatedly reading. After his funeral, friends and colleagues paying their respects to his family could have spotted a well-worn copy of *Silent Spring* sitting on a table by a lamp. Although scientifically rewarded and praised for his research, Metcalf was often criticized as being anti-insecticide. It perplexed him that anyone would hold that opinion considering the fact that his publications stressed the importance of selective insecticides and the need to

preserve them by taking an ecological approach to insect management. His integrated pest management text, edited with his friend and collaborator William Luckmann, brought together all of the developing concepts of environmental toxicology, insecticide resistance, and chemical ecology for the integrated management of insect pests.

More than most of his peers, he was deeply committed to public service; he never shirked his responsibility to serve as an advocate of responsible pest control, within and beyond academic circles. At Riverside his laboratory functioned as the International Insecticide Reference Center for the World Health Organization. He served on the Environmental Protection Agency's Pesticide Advisory Panel from 1976 to 1982 (a crucial period in the creation of that agency). During his service on the panel he played a critical role in the banning of at least 10 highly toxic pesticides in wide use. As a member of the National Academy of Sciences, elected in 1967, he served on committees considering the impact of polychlorinated biphenyls on the environment (1977-79), the role of pesticides in urban pest management (1978-80), pesticides and water quality (1976-78), and cotton insect control (1980-81). With respect to control of insects in cotton, he testified before Congress in a charged atmosphere about the ill-advised nature of ongoing insect control efforts aimed at eradication (such as those that eventually led to \$55 million failure to stop the spread of fire ants). Years later, his view—that eradication is neither a desirable nor achievable goal for all insect introductions—is the prevailing one; his testimony may well have spared the southeastern United States from massive pesticide contamination. In 1976 Metcalf traveled to China in one of the first scientific exchanges with that nation with an aim of learning more about alternative low-impact control methods (1977).

Metcalf was proud of his accomplishments. He used to say that he had an affinity for using simple tools (topical application, colorimetric assay, model ecosystem, beetle prints, sticky traps, and the like) for answering complex questions. Although he was undeniably brilliant, by his own admission, the well from which he drew most deeply was the intellectual interaction he had with his students and collaborators; many of his discoveries were either because of the challenges he presented to his students or challenges his students presented to him. Robert Metcalf was entomology's Thomas Edison. Both believed in the practical application of scientific principles and both believed that a research laboratory should consist of a team of workers systematically investigating a topic. To put it simply, Metcalf was driven to excel, whether at science (he authored or coauthored over 450 scientific papers and advised over 80 students and postdoctoral associates), sports (he played professional-level golf, tennis, and ping-pong), or music (he owned every type of clarinet known). Among the many honors he received were election as a member of the National Academy of Sciences, a fellow of the American Academy of Arts and Sciences, and a fellow of the American Association for the Advancement of Science. He was also honored with the Order of Cherubini, Pisa, Italy. Past president of the Entomological Society of America, he received its Founder's Award in 1978. In 1991 he received an honorary doctorate from Ohio State University, and in 1997 the University of Illinois, his intellectual home for over 30 years, recognized him with an honorary degree of doctor of science. Metcalf's contributions, although limited by the untimely death of a still productive scientist to the twentieth century, will continue to have impact throughout the twenty-first century in the form of a cleaner environment and a more rational approach to pest management.

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Courtesy of Dr. Ronald Bentley

David Rittenberg

DAVID RITTENBERG

November 11, 1906–January 24, 1970

BY DAVID SHEMIN AND RONALD BENTLEY

DAVID RITTENBERG WAS a leader in the development of the isotopic tracer technique for the study of biochemical reactions in intermediary metabolism. In a brief but historic paper published in *Science* in 1935, Rittenberg and Rudolph Schoenheimer described work at the Department of Biochemistry at Columbia University's College of Physicians and Surgeons. Their pioneering experiments used deuterium, ^2H , the heavy, stable isotope of hydrogen, to trace the fate of various compounds in the animal body. The metabolites containing ^2H had properties essentially indistinguishable from their natural analogs by the methods commonly used. Nevertheless, the presence of the isotope made it possible to trace their metabolic fate. Thus, if a ^2H -containing compound, *B*, was isolated after feeding the ^2H -labeled compound, *A*, to an animal, the metabolic conversion $A \rightarrow B$ was established. Prophetically, these authors noted that "the number of possible applications of this method appears to be almost unlimited." Subsequent developments have shown that they were true prophets.

In the mid-1930s little was known about the chemical reactions used by living systems to synthesize and degrade cellular components. One difficulty was that methods for the isolation and purification of carbohydrates, lipids, and

proteins were primitive and methods for the detailed study of enzymes were lacking. Moreover, the important role played by comparatively simple molecules with low relative molecular mass in the biosynthesis of more complex molecules was not yet appreciated. In the first of 15 papers published in the *Journal of Biological Chemistry* with the general title "Deuterium as an Indicator in the Study of Intermediary Metabolism" ("the deuterium series"), Schoenheimer and Rittenberg elaborated as follows on other problems inherent in metabolic studies (1935).

The study of the metabolism of substances which occur in nature in large amounts and are continually synthesized and destroyed in the animal body presents almost insuperable difficulties. If substances such as natural fatty acids, amino acids, etc., are administered to an animal, we lose track of them the moment they enter the body, since they are mixed with the same substances already present. Furthermore, if a substance *A* is given to an animal and an excess of a substance *B* is afterwards discovered in the body or in the excretions, we can never be sure that the substance *A* has been converted into *B*, for a stimulation of the formation of *B* from some other source may equally well have occurred. The difficulty in following physiological substances in the course of their transportation in the body, and their conversion into other substances, accounts for our ignorance with respect to many of the most fundamental questions concerning intermediate metabolism. The solution of these problems will be possible only when direct methods for tracing such substances are available.

The isotope work at the College of Physicians and Surgeons (P&S) provided a realistic experimental method that overcame many of the difficulties and did provide for direct tracing of metabolites.

While there had been previous uses of tracers in biology, both chemical and isotopic, the P&S results reported initially in 1935 were the first in which an isotope was systematically introduced into an organic compound so that a defined reaction could be studied. For example, cholest-4-en-3-one was reduced with ^2H to provide $[4,5\text{-}^2\text{H}_2]\text{-}5\beta\text{-}$

cholestan-3-one. The latter metabolite was converted to ^2H -containing coprosterol (5β -cholestan- 3β -ol) in both a dog and a human subject, thus indicating that the biological reduction of the ketone function in cholestan-3-one was possible.

Although humans had ingested $^2\text{H}_2\text{O}$ previously, this historic experiment was the first in which a substrate, specifically labeled with ^2H , was ingested by a human. The experimental detail deserves to be noted, if only for the ingenious use of another biological indicator system.

A healthy man, 24 years of age, took 1 g of the ketone at 5 o'clock in the afternoon on two successive days. The substance was dissolved in butter and taken with bread. 5 Hours before the first, and five hours after the last coprostanone meal he ate grapes, the seeds of which served as an indicator in the stools. . . . The isolation of the sterols was performed on the portion of stool excreted between the two grape seed markers, in which the greatest concentration of the newly formed coprosterol was to be expected.

The brave volunteer, not identified in 1935, was actually Hans Hirschmann; the conversion was presumably accomplished by his intestinal bacterial flora. In any case, he survived the experiment and later obtained a Ph. D. degree with O. Wintersteiner at P&S. Hirschmann had a distinguished subsequent career at Case Western Reserve University, retiring as emeritus professor in 1978.

Rittenberg had found himself at P&S through the convergence of several unusual circumstances. At Columbia University's main campus Harold Urey had identified and isolated deuterium in 1932. Rittenberg, one of Urey's graduate students, obtained a Ph.D. degree in 1934 for his 30-page thesis, "Some Equilibria Involving Isotopes of Hydrogen." Urey was anxious to promote the study of both chemical and biological properties of deuterium, and received funding from the Rockefeller Foundation. In 1934 Rittenberg had no prospects of a position as a physical chemist. He

was instead assigned to H. T. Clarke, chair of the Department of Biochemistry at P&S to promote biological uses of ^2H . At that time one interest of Clarke's was the possibility of demonstrating optical activity for a compound, $\text{Cab}^1\text{H}^2\text{H}$. Clarke also suggested to Rittenberg a "roving commission" to talk with other members of the department about possible uses of ^2H . These developments have been reviewed comprehensively by the historian Robert E. Kohler (*Historical Studies in Physical Sciences*, vol. 8, pp. 257-98, R. McCormach and L. Pyerson, eds., Johns Hopkins University Press, Baltimore, London, 1977).

A second circumstance was that Schoenheimer, forced from his position as head of the Institute of Pathology at the University of Freiburg by the policies of the Third Reich, had accepted a position in Clarke's department in 1933. There he continued a long-standing interest in sterol metabolism. When Rittenberg presented to him the prospect of the use of ^2H Schoenheimer quickly appreciated the possibilities. Schoenheimer had, in fact, some prior experience, having worked with Hevesy on the partition of radioactive lead between normal and tumor tissue. Clearly, the meeting of these two individuals was propitious. While Schoenheimer could formulate problems in metabolism, Rittenberg was perhaps the only individual at that time with the necessary background and training to tackle the difficult experimental details required for biochemical work with ^2H . This was still the era of "string and sealing wax," when experimenters used glass blowing and workshop skills to make a necessary apparatus. To appreciate Rittenberg's skill in that art one has only to consult the methods articles that he wrote with elegant figures of complex glassware. In particular, the second part of the deuterium series contains methods for the generation of ^2H as gas; the combustion of samples to water, followed by purification by distillation; and the use of the

submerged-float technique to determine density and hence ^2H content. In 1937 measurement of the refractive index of water samples and the falling-drop technique were added to the methods.

Significant results with the new technique were obtained very quickly after Rittenberg's approach to Schoenheimer sometime in 1934. Before the brief announcement of the use of deuterium as an indicator in the August 16, 1935, issue of *Science*, the first four papers of the deuterium series had already been submitted to the *Journal of Biological Chemistry* (June 26, 1935) and they appeared in volume 111 (1935) of that journal. The deuterium series continued until 1938. Over that period, results obtained in connection with fatty acid metabolism were more interesting than those concerned with sterol metabolism. The degradation and synthesis of saturated fatty acids was shown to proceed two carbon atoms at a time, and saturated fatty acids could be converted to monounsaturated fatty acids and vice versa. A particularly significant observation was that when mice were fed ^2H -labeled fatty acids, most of the ^2H was recovered in the fat tissues rather than being immediately utilized. Of the 15 papers in the deuterium series only the last was not coauthored by Rittenberg, and 8 of them were authored only by Rittenberg and Schoenheimer.

By 1937, again thanks to Urey, the stable, heavy isotope of nitrogen, ^{15}N , became available and opened up the investigation of nitrogen metabolism. Rittenberg was now confronted with a new challenge. At that time the only practicable method for ^{15}N assay required a mass spectrometer, an instrument not then commercially available. Rittenberg, with the help of I. Sucher, A. Keston, and F. Rosebury, constructed at P&S a 180° mass spectrometer of the Bleakney type similar to that used by Urey. For assay a sample of dinitrogen gas was bled into the high-vacuum system of the

mass spectrometer through a glass capillary leak. The size of the leak was important. The international standard was eventually defined as the diameter of a hair from Rittenberg's head. Inside the spectrometer the intensities of ions due to $^{14}\text{N}^{14}\text{N}$ (m/z ratio = 28) and $^{14}\text{N}^{15}\text{N}$ (m/z ratio = 29) were determined.

It was necessary to devise means whereby nitrogen of a metabolite (e.g., an amino acid) could be converted to dinitrogen. A two-step process was used. Ammonia from a Kjeldahl digestion was trapped in a dilute solution of H_2SO_4 . The ammonium salt was then oxidized by sodium hypobromite:



The reaction had to be carried out in a vacuum system. To mix the reagents a rather cumbersome rotating flask was used initially. Finally, Rittenberg devised a two-legged, Y-shaped tube (see Figure 1). After freezing the contents of each leg and evacuation on a separate vacuum line the two solutions were thawed and mixed; following a further freezing the tube was attached to the mass-spectrometer vacuum system. While the tubes were generally known as Rittenberg tubes, their characteristic shape gave rise to the name "Rittenberg trousers" in Israel. With his excellent glass-blowing capabilities Rittenberg could always locate and repair any pinhole leaks in a vacuum system with the aid of a Tesla coil. Drawings of the Kjeldahl apparatus and of the rotating flask set up were provided by Rittenberg in 1946.

The first ^{15}N work at P&S was a study of hippuric acid metabolism in 1937. By this time the isotope group had expanded and there were five authors on the paper (Schoenheimer, Rittenberg, M. Fox, A. S. Keston, S. Ratner). Ammonia was found to be converted to both glycine and

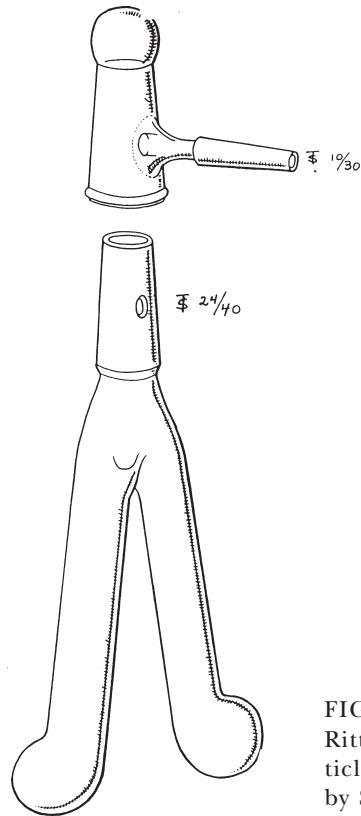


FIGURE 1 This elegant drawing of a Rittenberg tube was provided in the article on gas sample preparation published by Sprinson and Rittenberg (1948).

hippuric acid in animals. The hippuric acid was absorbed from the intestinal tract without hydrolysis and glycine was used directly for hippurate formation. In a final sentence it was confidently asserted that “the nitrogen isotope should prove to be as useful in the study of the intermediary metabolism of nitrogen compounds as deuterium is in the study of fat and sterols.” Descriptions of the use of isotopes in metabolic studies and specifically of the use of ^{15}N were provided for a general scientific audience in *Science* in 1938 and 1939. A series of papers with the general title

“Studies in Protein Metabolism” was published between 1937 and 1941 and, like the deuterium studies, also ran to 15 papers.

In September 1941 Schoenheimer took his own life. By that time the ^2H work on lipids and the ^{15}N experiments on proteins had led to a new biochemical generalization: the dynamic state of body constituents. The large, complex macromolecules were constantly involved in rapid chemical reactions with their smaller component units, a continuing and constant process of degradation and resynthesis. The generalization overthrew the prevailing opinion that the dietary constituents were used only for repair and for energetic purposes. Schoenheimer was to have delivered three Edward K. Dunham lectures on this topic at Harvard in October 1941. His lecture drafts were revised by Clarke, Ratner, and Rittenberg and the lectures were presented by Clarke. The book form of these lectures ran to two editions and is a classic in biochemical history.

In 1941 Rittenberg was appointed director of the isotope laboratory. The research group included many individuals who later became well known, such as K. Bloch, S. Ratner, D. Shemin, and D. Sprinson. The areas of investigation widened and other stable isotopes, ^{13}C and ^{18}O , became available. Rittenberg and H. Waelsch did the first ^{13}C experiment at P&S in 1940: a study of the conversion of $\text{NaH}^{13}\text{CO}_3$ to urea. Not until 1949 was work with ^{18}O reported by Bentley (but carried out with the constant support and enthusiasm of Rittenberg): a study of the mechanism of hydrolysis of acetyl phosphate. There was a decline in the use of stable isotopes beginning about 1950 as radioactive isotopes also became readily available following the end of World War II.

In 1937 during the early exciting days of work with ^2H , Rittenberg and Schoenheimer made an observation that

had bountiful repercussions. When $^2\text{H}_2\text{O}$ was administered to mice, it was found that 50 percent of the hydrogen atoms of cholesterol derived from the hydrogen atoms of the water. This high level of ^2H incorporation eliminated large molecules (e.g., sterols) as cholesterol precursors. With considerable foresight Rittenberg and Schoenheimer stated that cholesterol "is formed by the coupling of smaller molecules, possibly those which have been postulated to be intermediates in the fat and carbohydrate metabolism." In another laboratory, yeast grown in the presence of $[2\text{-}^2\text{H}]$ acetate contained a high ^2H level in unidentified sterols. Following this observation, Bloch (a Ph. D. student with Schoenheimer) and Rittenberg proved in 1942 that $[2\text{-}^2\text{H}]$ acetate was actually a cholesterol precursor in mice and rats. A little later cholesterol biosynthesis was demonstrated by Bloch, Borek, and Rittenberg in surviving liver slices from both $[2\text{-}^2\text{H}]$ acetate and $[2\text{-}^2\text{H}, 1\text{-}^{13}\text{C}]$ acetate. In subsequent work at the University of Chicago and at Harvard, Bloch uncovered many details of the biosynthetic pathway from acetate to cholesterol and received a Nobel Prize in 1964 (jointly with F. Lynen) for his work. The beginnings of this work clearly owed much to Rittenberg. Moreover, Rittenberg and Bloch demonstrated for the first time a role for acetate in the biosynthesis of fatty acids (1944).

Work reported by Shemin and Rittenberg in 1945 on the utilization of glycine also led to important findings. Shemin himself, with much courage, ingested over a three-day period 66 g of $[^{15}\text{N}]$ glycine. At stated intervals blood was withdrawn and the ^{15}N concentration of blood proteins was determined. The data were consistent with the concept of the dynamic state of body constituents. However, when the ^{15}N content of the heme component of hemoglobin was examined, it appeared to reach a maximum value about 20 days after the start of the experiment. Thereafter, it

remained approximately constant for 80 days and then declined. It was clear that hemoglobin was not in a dynamic state. From the data the life span of the human red blood cell could be calculated; it was found to be 127 days, much higher than the then quoted figure of 30 days. There was also an important bonus; it could be concluded that glycine was the nitrogenous precursor of heme and other porphyrins.

There were two elaborations as a result of this work. With an accurate and physiological method for determining the life span of the red blood cell, Shemin and Rittenberg organized a collaborative program with I. M. London and R. West (Department of Medicine, P&S) to study the life span of red blood cells in patients with blood abnormalities. The dynamics of red cell survival in patients with polycythemia vera, sickle cell anemia, and pernicious anemia were described in several papers. Rittenberg was also an author on a paper dealing with porphyrin formation and hemoglobin metabolism in congenital porphyria.

The second elaboration was that Rittenberg, Shemin, and London began to study the synthesis of protoporphyrin *in vitro* using immature non-nucleated mammalian erythrocytes and the red blood cells of the duck. Particularly with the latter system, Shemin and his colleagues elucidated the pathway for porphyrin biosynthesis in the red cell. N. Radin and Shemin, in collaboration with Rittenberg, studied the roles of both glycine and acetate in heme biosynthesis.

A further achievement of the isotope work was a method for assay of amino acids in protein hydrolysates with a very low error. Since the usual laboratory methods do not result in isotope separation, a measurement of the dilution of a labeled compound added to an unlabeled mixture provided the amount of substance originally present. The method depended only on the isotope content of added and iso-

lated material, and the weight of added isotopic material. Hence the amount of isolated substance did not need to be determined and large losses during isolation could be tolerated. The method was first described by Rittenberg and G. L. Foster in 1940. Although originally used for amino acid and fatty acid analysis, the method has general application.

After 1950 Rittenberg's research was scaled back on account of administrative responsibilities (see below). Even so, he used glucose labeled with ^{18}O and ^{13}C to determine the contribution of the oxidative and nonoxidative pathways for pentose formation. His analysis of the enzyme hydrogenase in *Proteus vulgaris* and other microorganisms no doubt was influenced by his work as a graduate student. It was demonstrated in work with A. Krasna that the enzymatic cleavage of hydrogen is a heterolytic process, whereas the same cleavage catalyzed by platinum is homolytic.

This brief and incomplete account of the isotope work at P&S has focused on the many key contributions made by Rittenberg and on published papers that he coauthored. Many other workers in the Department of Biochemistry benefited from his advice. For instance, in several papers DeWitt Stetten acknowledged help and cooperation from Rittenberg. David Sprinson worked with Rittenberg on ammonia utilization for protein synthesis and the rate of reaction of dietary amino acids with tissue proteins before going on to the major, independent study of the pathway for shikimic acid biosynthesis, for which he received much recognition.

Historian Robert Kohler has pointed out that the isotope work at P&S "entailed a special social organization: the interdisciplinary group. An organic chemist was needed to synthesize labeled compounds; a physical chemist to build and operate the complex instruments for measuring isotope ratios; a physicist to provide concentrated heavy isotopes

(or radioactive isotopes from a cyclotron); and a biochemist to work with metabolism in animals.” In fact the group at P&S set the trend to interdisciplinary research efforts. There was a definite progression from the early experiments by Schoenheimer and Rittenberg working by themselves, and then to the large, interdisciplinary group. In all of this Rittenberg can be fairly described as the keystone. Eventually, with the development of commercial instruments and supply sources, a biochemist alone could hope to perform these specialized tasks.

The man who became the leader of the isotope group at P&S and made many contributions to biochemical knowledge was born in New York City on November 11, 1906. He was educated in public schools and received a B. S. degree from the College of the City of New York in 1929. That year marked the beginning of the Great Depression, and he must have encountered financial difficulties. He once claimed that he had made money as a consultant to a bootlegger making bathtub gin. He worked as a refractories chemist for two years at the Nonmetallic Minerals Experiment Station, U.S. Bureau of Mines, at Rutgers University. This work led to his first scientific publication with P. S. Roller: a method for the production of refractory crucibles of magnesium oxide that were recrystallized to translucence and were impervious to air under pressure at room temperature. Following this experience, he became a graduate student with Harold Urey as already noted.

Rittenberg’s contributions to the isotope tracer technique were recognized in 1941 by the Eli Lilly Award in Biological Chemistry from the American Chemical Society, Division of Biological Chemistry. A further recognition was his election to the National Academy of Sciences in 1953. Rittenberg survived Schoenheimer by almost three decades and he served as a faculty member at P&S for 36 years. He was appointed

chair of the Department of Biochemistry in 1956. He had met Chaim Weizmann, founder of the Weizmann Institute of Science in Rehovoth, Israel, in 1944 and was invited to become a member of the Planning Board of that institute. Later he became a member of the Board of Governors and was made an honorary fellow of the institute in 1967. His interest in the development of science in Israel led him to accept an invitation to join the Advisory Board of the Hadassah Medical School. He made important contributions especially in the early development of their science and in ferreting out very capable young scientists.

David Rittenberg had a well-developed sense of humor and a fund of stories. At a 1948 Cold Spring Harbor symposium "Biological Applications of Tracer Elements" he noted that modesty on the part of George Hevesy had prevented him from evaluating his own contributions. He said that "Hevesy, to employ terms suitable to a biological science, was not only one of the fathers of the isotope technique but also the attending gynecologist." Modesty on Rittenberg's part did not allow him to describe himself as one of the founding fathers. It has been recorded, however, that he liked to be introduced as "the most refractory chemist remaining in the field of biochemistry."

No doubt as a young member of the Department of Biochemistry he may have overplayed his hand by being overconfident, thus creating some tension with other department members. To some the introduction of techniques by a brash physical chemist was seen as a threat and several biochemists were suspicious of the isotope technique, especially when it began to require what were for those days large sums of money. It was even hinted that ^2H -labeled compounds might be toxic although Hans Hirschmann's survival should have put that idea to rest. Moreover, there was a feeling that, at least initially, Rittenberg did not know

any biochemistry. In the late 1930s it is said that many believed the papers titled "Studies of Intermediary Metabolism with the Aid of Isotopes" should have been titled "Studies of Isotopes with the Aid of Intermediary Metabolism." Perhaps it was inevitable that as his responsibilities increased, more tensions were created. Many may have felt that Rittenberg's success owed much to Schoenheimer's imagination, without realizing that Schoenheimer owed equally much to Rittenberg. Sarah Ratner has noted that toward the end of the relationship, some unpleasantness developed between Rittenberg and Schoenheimer.

David Rittenberg—born, raised, and educated in New York City—was a quintessential New Yorker. Almost all of his working life was spent in that city and once at P&S he never moved to a different institution. An anecdote illustrates his love-hate relationship with New York. When a visitor from the U.K. twice failed a New York driving test, Rittenberg offered the following advice for attempt number three: "Arrive late for the test and apologize that you were detained at Mass. Hand the examiner a cigar wrapped in a ten dollar bill. You will have no further trouble." Needless to say, the visitor did not feel able to accept the advice. David Rittenberg and his wife, Sara, were unfailingly generous in extending hospitality to visitors to the department. Many individuals remember superb meals prepared by Sara. As a youth Rittenberg had contracted rheumatic fever and his death on January 24, 1970, was from heart disease. In his personal life, David Rittenberg was a very proud father. His son, Stephen, a 1963 graduate of P&S, is now in practice as a psychoanalyst. Moreover, two grandchildren have also become physicians.

David Rittenberg was uniquely qualified for a challenging task at a particular time and place. He fulfilled his role with skill and honor. In 1935 isotopes were strange entities,

exciting considerable interest and even generating suspicion. Almost seven decades later they are widely accepted and require no special comment. They are defined in non-specialist dictionaries and are often referred to in the press. Isotopes find extensive applications not only in biological sciences but also in such fields as chemistry, environmental studies, medicine (both in diagnosis and treatment), and physics. The darker side is that some radioactive isotopes have very adverse effects in humans. Rittenberg had unbounded optimism and enthusiasm and clearly anticipated great future developments for his isotopes. He could probably not have foreseen how extensive and important the developments would be. For example, when he went to P&S in 1934, one possible research project was to determine if the $^1\text{H} \rightarrow ^2\text{H}$ substitution would give rise to measurable optical activity in the chiral substance, $\text{Cab}^1\text{H}^2\text{H}$. While this possibility has now been long established, it has also become possible to investigate stereochemical problems in compounds containing all three hydrogen isotopes, $\text{Ca}^1\text{H}^2\text{H}^3\text{H}$. Work with “chiral methyl groups” is now well known and similar work with the three oxygen isotopes has concerned “chiral phosphate groups” in compounds such as $\text{RO-P}^{16}\text{O}^{17}\text{O}^{18}\text{O}$. David Rittenberg would have been pleased and excited by such possibilities and by the ever expanding role of isotopes in the modern world.

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Ruth Sager

RUTH SAGER

February 7, 1918–March 29, 1997

BY ARTHUR B. PARDEE

RUTH SAGER HAD TWO distinguished careers. In the first she was a leading exponent of organelle, non-nuclear genetics; in the second she was a major innovator in cancer genetics, proposing, discovering, and investigating roles of tumor suppressor genes. At the pinnacle of research on the problem of non-nuclear or cytoplasmic genetics for many years, she almost single-handedly developed this subject of non-Mendelian, cytoplasmic genetics (“A vast, unexplored region of genetics was opened here today” [1963]). The very existence of hereditary determinants other than nuclear genes was doubted by a large part of the scientific community, although it was proposed in 1908 from observations on higher plants. Sager gathered data and argued in support of a second genetic system in the face of great skepticism and finally made this a respectable and exciting major area of genetics.

During her final 25 years she transferred her efforts to the genetics of cancer. Among her outstanding contributions, she devised the first cell lines and culture medium capable of culturing and comparing normal and cancer cells. She emphasized the major role of chromosome rearrangements and the accelerated evolution of cancer cells and the

requirement in a cancer of more than one mutated gene, importantly of tumor suppressor genes in addition to oncogenes. She proposed as early as 1974 that individual genetic defects could be corrected by transferring DNA into cells. "One need not be doomed by one's genes."¹ She was a pioneer in the novel subject she named "expression genetics," the identification by their mRNAs of genes that are functionally modified in cancers. She successfully identified numerous genes that are not mutated but whose expressions are altered in breast cancers, such as the mammary serpin maspin. She worked to the end, publishing innovative articles and obtaining a National Institute of Health grant in the month before her death. During her career she published two books (1961, 1972) and more than 200 research articles.

Ruth Sager was born in Chicago on February 7, 1918, daughter of Leon Sager, a businessman with strong intellectual interests, and Deborah Borovik Sager, who died in the 1918 influenza epidemic. She and her sisters, Esther and Naomi, were bought up by her stepmother, Hannah, in an atmosphere honoring learning. She graduated at 16 from New Trier High School. She received an S.B. in mammalian physiology in 1938 at the University of Chicago: "the best thing that ever happened to me." Her interest in science was sparked by Anton J. Carlson's lectures: "He was just a fantastic teacher."² In 1944 she received an M.S. in plant physiology at Rutgers University. Her World War II years were spent as a secretary and an apple farmer. Her 1948 Ph.D. in maize genetics was under Marcus M. Rhoades at Columbia University. From 1949 to 1951 she was a Merck postdoctoral fellow with Sam Granick at the Rockefeller Institute, working on the chloroplast. From 1951 to 1955 she was a staff member at Rockefeller, where she chose the alga *Chlamydomonas reinhardi* as a model organism. She was

a research scientist from 1955 to 1965 at Columbia University and worked for a year in Edinburgh during that period.

For 20 years, until the age of 48, she could not obtain a faculty position. "I guess I knew I was right, and I wasn't terribly upset."² Beginning in 1966 and until 1975 she was a professor at Hunter College. Finally, in 1995, she was appointed professor of cellular genetics at Harvard Medical School—among the first women to gain a full professorship at Harvard—and chief of the Division of Cancer Genetics at the Dana-Farber Cancer Institute. She was also a Guggenheim fellow at the Imperial Cancer Research Fund, London, during 1972-73, and was elected to membership of the National Academy of Sciences in 1977.

Sager was first married to Seymour Melman in 1944 and then to the author of this memoir in 1973. She had no children. She died March 29, 1997, of bladder cancer in her home in Brookline, Massachusetts, at the age of 79. She is survived by her sisters, Esther Altschul and Naomi Sager, and her husband, Arthur Pardee.

Ruth Sager was innovative, highly intelligent, enthusiastic, very dedicated to her science, and hard-working; she had high standards and expected equal dedication from her coworkers. She did not suffer fools gladly. Her views of science as a career were:³

The first thing is to be sure of your own abilities. Science is very demanding, you have to be able to think very well and also have a very good memory. You have to really love it. Science is a way of life. I think it all comes from the inside. It really gets to the very core of your existence. It is much like being an artist or a dancer. It's something that demands everything from you that you are capable of.

I have always been intrigued by the physicists' approach to scientific inquiry, particularly in the fact that the way to find out something really new is to question the basic tenet of existing theory.

Very early Sager believed that genetics was the core of biology; she knew she was right and she set out to prove it. She never ceased introducing new techniques and concepts into her field, but she found her work ignored until her discoveries proved the majority wrong. But she never really paid a lot of attention to what other people think.

She was described in her fifties as “a calmly articulate and attractive woman (who looks younger by about 15 years) . . . a tall, striking brunette with a ready smile and a voice that carries a merry lilt.”^{4,5} She early described herself as “probably the happiest person I know.”⁵

Not at all narrowly devoted to her science, Sager had numerous outside interests: modern art, travel, music and theater, a rich social life, and she was a fine cook. She took up tennis late in life and played it with great enthusiasm—in spite of limited ability. She was especially fond of relaxing at Woods Hole, where she had a cherished second home, and where she is buried.

Among her honors and distinctions were Phi Beta Kappa in 1938, Sigma Xi in 1947, Guggenheim Fellowship in 1972, Schneider Memorial Lecture Award in 1973, National Academy of Sciences membership in 1977, American Academy of Arts and Sciences membership in 1978, Harvey Society Lecture in 1984, outstanding investigator at the National Cancer Institute in 1985, Gilbert Morgan Smith Medal from the National Academy of Sciences in 1988, membership in the Institute of Medicine in 1992, Princess Takamatsu Award (Japan) in 1992, alumni medallist of the University of Chicago in 1994, and membership on the Advisory Council of the National Institute on Aging.

At the beginning of her career Sager saw the advantages of studying genetics with a model microorganism that had a chloroplast, a sexual life cycle, grew rapidly, and could readily be manipulated for controlling growth and mating.

She chose the single cell alga "*Chlamydomonas*, a peerless group of organisms . . . nutritious, esthetically pleasing, and amenable to laboratory experimentation."²

With talented coworkers, especially her long-time collaborator Zenta Ramanis, she:

- Developed a mating system for the organism.
- Early investigated the genetics of the organism—both Mendelian and non-Mendelian—with clear demonstration of the maternal inheritance pattern of the latter.
- Discovered with Y. Tsubo the first specific “cytoplasmic” gene mutagen, streptomycin, and identified mutants by their resistance to this drug.
- Discovered ribosomes in the chloroplast of *Chlamydomonas*, different from those in the cytoplasm, thus providing evidence that expression of genetic information as proteins is carried out by a different system.
- Discovered with M. R. Ishida that unique DNA is located in isolated chloroplasts. This was the evidence that convinced most scientists that there is indeed a separate non-nuclear organelle genetic system.
- Performed biochemical studies of the mechanism of exclusion of paternal genes.
- Developed a system that makes genetic mapping possible by permitting expression of paternal genes.
- Developed several mapping methods and first published cytoplasmic linkage groups and extensive mapping of an organelle. She showed that the chloroplast DNA is circular.
- Demonstrated with an in vitro system the basis of maternally inherited drug resistance.
- Discovered a eukaryotic restriction enzyme.
- Discovered that there is communication between nucleus and organelles—they send molecular signals back and forth.

- Showed that maternal DNA is methylated and paternal DNA is not and proposed this difference as the basis of selective destructive elimination of the paternal DNA.

Of her second career, cancer research, she said, “I had really wanted to work on cancer, but it seemed like a very difficult thing to do. . . . We think that the first change in cancer is a genetic change—something acts to transform an individual cell—whether that something be a viral infection or a chemical or radiation.”² Entry into the subject was during her sabbatical at the Imperial Cancer Research Fund in 1972-73. From that time her career and her husband’s were independent but highly mutually supportive.

The question was: Which genes cause normal cells to become cancer cells? Oncogenes, recently discovered at that time, were proposed as the basis, but Sager championed inactivations of tumor suppressor genes. “Nature’s own approaches to cancer protection” are in addition deeply involved and are “a vast untapped resource for anticancer therapy.”² Sager suggested a yin-yang balance of these for cellular homeostasis. Among her cancer research accomplishments were the following:

- She developed a model system that allows detailed comparisons in the same culture medium between well-matched normal and tumor Chinese hamster embryo fibroblasts (CHEF cells).
- She emphasized the multigenic basis of tumorigenicity. As with her earlier work she was among the first to champion this then unpopular view at a time when all attention was on single oncogenes. In the late 1970s she initiated investigations into tumor suppressor genes. As with her researches on chloroplast genetics, “there was really no interest in tumor suppressor genes at all until about maybe . . . 1990.”²

She demonstrated tumor suppression with cell hybrids and cybrids. Remarkable examples are suppressor genes that promote programmed cell death of defective cells, and these are inactivated in tumors.

- She showed an initial example of increased genetic instability in cancer cells. A genetic change, amplification of the methotrexate resistance gene, developed much faster in tumor cells than in normal cells.

- She decided that gene expression would best be investigated in human cells. For this purpose she created a workable human breast cancer cell culture system in which normal and tumor epithelial cells could grow and at similar rates.

- She introduced the concept of expression genetics, the study of changed gene expressions. Using subtractive hybridization, she discovered the IL-8-related *gro* gene and others whose mRNA level is modified in tumor cells. She then shifted to the new, simpler differential display technique to discover numerous additional potential tumor suppressor genes, ones whose expression is lost in breast cancers. And she began an investigation of the means to reactivate their expression. Her favorite example was maspin, the gene for a serine protease inhibitor, which is lost in advanced breast cancers and inhibits tumor invasion and metastasis. Vigorous research on this gene continues in numerous laboratories, including those of several of her past students and fellows.

- She found that these under-expressed genes were not mutated, unlike classical tumor-related genes. Her plan was to use these under-expressed genes as markers for detection and diagnosis, and she hoped for therapies based on restoring their functions.

Her later interests included methylation of DNA and its specific enzymatic cutting and chromosome rearrangements in tumor cells.

Her legacy is expressed in the quotation:⁵ “For more than half a century Ruth Sager has been a role model for women in health-related scientific research. . . . She demonstrated vision, insight and determination to develop novel scientific concepts in the face of established dogmas. . . . Her pioneering researches and original ideas continue to make contributions to biology.”

When asked near the end of her life what she considered to be her most important contribution, she answered, “Well, I don’t think I’ve made it yet.” Many colleagues have carried on her researches, and papers based upon these researches continue to appear. She was a major constructive force in the scientific and personal lives of her many friends and students. She was a role model for many women, being among the earliest successful woman scientists in spite of major career obstacles, but she was never highly active in the women’s liberation movement. When faced with the built-in prejudice of the male scientific community against women, she responded by saying there was nothing she could do, except to be as good a scientist as possible.

She had great concerns in 1994 about politics and the future of science. “The strong influence of fashions in scientific thought continues to play an inhibitory role in scientific progress. I think science is in a rut right now. The way grants are given out just makes matters worse, because the experiment has to be so obvious and practically done already before they’ll fund it.”²

Her career twice demonstrated that some of the best science needs faith and support of novel ideas from the most creative minds.

NOTES

1. The unattributed quoted material in this memoir is derived from personal conversations with Ruth Sager.
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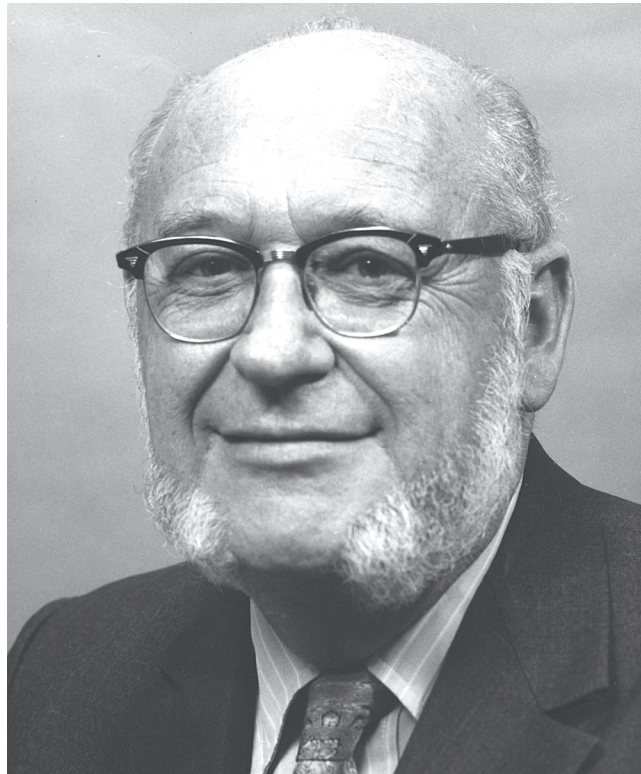
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Ray F. Smith

RAY FRED SMITH

January 20, 1919–August 23, 1999

BY PERRY ADKISSON, WILLIAM ALLEN,
JOHN CASIDA, AND EDWARD SYLVESTER

RAY F. SMITH, emeritus professor of entomology at the University of California at Berkeley, died August 23, 1999, at his home in Lafayette, California. He was 80 years old. Ray was born on January 20, 1919, in Los Angeles, California. He grew up in Monterey, where his father was a pharmacist, and after graduating from high school, Ray entered the University of California at Berkeley; he completed his B.S., M.S., and Ph.D. degrees there.

Ray joined the Berkeley faculty in 1941 and became not only a significant builder of its entomology program but also an internationally recognized champion of ecological pest control. From each of his distinguished Berkeley faculty mentors he garnered a lifetime appreciation of history, books, and collecting (E. O. Essig); field ecology and service to agricultural entomology (A. E. Michelbacher), and a deep respect for and interest in systematic entomology and evolution (E. G. Linsley). From the beginning of his academic and experiment station career it was apparent that the hallmark of his teaching, research, and advocacy was to be centered on an ecological approach to analysis and management of the economic ravages of arthropod pests. He enthusiastically adopted the strong Berkeley tradition in agricultural and medical entomology and fully appreciated the

university's historical accomplishment in biological pest control.

Ray accepted the dictum that pesticides must be considered in the context of existing natural factors of population regulation and, if pesticides are to be used, such use should be minimal and precise in time and target. Shortly after the end of World War II he began a period during which he attracted, stimulated, and trained a formidable group of future leaders in ecological pest management. Building on his early collaborative work with Michelbacher, he pushed the concept of supervised control and for a period of 10 years put it into practice for the management of key pests of alfalfa. The demonstrated success of his approach, one that was solidly based upon pest population assessment and an impressive array of ecological and biological data, gradually evolved into the concept of integrated pest management.

His administrative potential was soon recognized, and in 1959 he was appointed chair of the Department of Entomology and Parasitology, a position he held until 1973. During his tenure the combined leadership of Ray and his dean, E. G. Linsley, saw the department grow, diversify, and consolidate its place on the Berkeley campus. The 1960-1975 Master Plan for Higher Education in California and the policy of the university's president, Clark Kerr, to decentralize administrative authority and establish campus autonomy provided additional organization opportunities. The department was reformed into one of entomological sciences, with an academic instructional unit of the Department of Entomology and Parasitology and four autonomous research divisions, viz., agricultural entomology, biological control, invertebrate pathology, and parasitology and medical entomology. With a faculty of 46 and a vigorous broad-based program in research and teaching, its academic ranking became first in the United States.

On a more personal level, Ray's tolerance, encouragement, and willingness to discuss diverse problems and ideas characterized his stewardship as department chair. No matter the hour or how pressing the work, his door was open to colleagues and students alike—to anyone in need of advice or merely an ear to bend. His energy, patience, and eagerness to be of help were amazing.

After resigning as chair Ray felt there was much more to be done with the concept of integrated pest management. Although Rachel Carson's *Silent Spring* had exposed the ecological hazards associated with wide and indiscriminate use of persistent broad-spectrum pesticides, agriculture, forestry, and public health remained beset with serious pest problems that needed resolution. Professor Smith increasingly began to apply his knowledge and administrative talent to build what was to become a second career at national and international levels.

Before stepping down as chair, he was an associate project director (1970-77) of the International Biological Program, a National Science Foundation project entitled "Principles, Strategies and Tactics of Pest Population Regulation and Control in Major Crop Ecosystems," directed by Carl B. Huffaker, later known as the Huffaker project. Ray also was director for the University of California for Pest Management and Related Environmental Protection Project with the U. S. Agency for International Development (UC/AID), and from 1979 until his retirement in 1982 executive director of the Consortium for International Crop Protection (CICP), which assumed supervision of the UC/AID project.

Professor Smith took a lead in forming the Panel of Experts on Integrated Pest Control of the United Nations Food and Agricultural Organizations (UN/FAO) and the Environmental Program (UN/EP), organized to advise both agencies on the scientific, technical, and education issues

involved in integrated pest management. He headed this panel from 1967 to 1982 and during his tenure both as chair of the FAO panel and as director of CACP he became more deeply involved in promoting integrated pest management globally. Under his leadership the two groups jointly worked to publish materials on the philosophy, principles, strategies, and tactics of integrated pest control, guidelines for implementing integrated pest management systems on major food crops and agromedical approaches to pesticide management, and also established several technical assistance programs in many developing countries.

An enlightened policy of the University of California allows distinguished faculty to accept, with a reduction in programmatic time commitment, leadership positions in affiliated undertakings. Thus, it was within the framework of a multi-university Intersociety Consortium for International Plant Protection (CACP) (Entomological Society of America, Weed Science Society of America, Society of Nematologists, American Phytopathological Society) that Professor Smith put his major effort in the final years of his career as executive director of CACP. He did not use that position simply for administration but for a personal effort, continuous and exhausting, to take the concept, philosophy, and practice of integrated pest management to those responsible for policy in agriculture production and agromedical practices around the world. In particular, he focused on needs of underdeveloped areas of the Americas (Mexico, El Salvador, Guatemala, Nicaragua, Brazil, Colombia, and Peru), Asia (Ceylon, Korea, Thailand, Philippines, and Pakistan) and Africa (Egypt, Kenya, and Senegal). His bibliography, in which some citations were translated and published in German, French, Italian, and Spanish, became filled with references to invitations to speak and participate in symposia, conferences,

seminars, workshops, panels, advisory committees, and consultations.

Professor Smith's tireless effort and relentless travel through the world's time zones took their physical toll and eventually led in 1982 to a decision to retire from leadership of the consortium and from the university. This was early for the latter. We are certain that he fully intended to remain active in the international field of integrated pest management, but a debilitating health event, while on a consulting trip in South America, necessitated a professional hiatus. Unfortunately, subsequent health problems continued to restrict his potential for further professional activity. His final illness with throat cancer, prolonged and painful, was spent in the security of home and family. We lost an academic colleague, teacher, friend, and champion of more rationality in the management of arthropod pests, and we are not alone.

He is survived by his wife of 59 years, Elizabeth J. Smith; two children, Kathrine Stark of Lafayette and Donald Smith of McKinleyville, California; a sister, Betty Webler, in Alaska; and seven grandchildren.

ACCOLADES FOR RAY SMITH'S
PROFESSIONAL ACHIEVEMENTS INCLUDE:

Member of the National Academy of Sciences
Honorary degree of doctor of agricultural sciences, College van
Dekanen, Wageningen, Netherlands
The C. M. Woolworth Award for Outstanding Achievements,
Entomological Society of America
Guggenheim fellow
Fellow, American Academy of Arts and Sciences
Fellow, American Association for the Advancement of Science
Fellow, California Academy of Sciences
Fellow, Honorary member, and president, Entomological Society
of America
Fellow, Entomological Society of Canada
Honorary member, Korean Society of Plant Protection
Co-recipient, 1997 World Food Prize
Berkeley Citation
Congress Medal, 1983, X International Congress for Plant
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Courtesy of Ames Lab

F H Murray

FRANK HAROLD SPEDDING

October 22, 1902–December 15, 1984

BY JOHN D. CORBETT

FRANK HAROLD SPEDDING is recognized and honored for the impact he had on understanding of spectra of the rare-earth elements; for the major leadership and scientific role he played in important process development and production of pure metals during the war, especially uranium and thorium; for the separation of the rare-earth elements and provision of them as high-quality salts and metals; for major scientific studies of many aspects of the chemistry and physics of rare-earth compounds; for the establishment of a national Ames Laboratory for the U. S. Atomic Energy Commission (now Department of Energy).

Frank Harold Spedding was born on October 22, 1902, in Hamilton, Ontario, to Howard Leslie Spedding and Mary Ann Elizabeth (Marshall) Spedding. Soon after his birth the family moved to southeastern Michigan and then to Chicago. In 1918 they moved to Ann Arbor, Michigan, where his father set up shop as a photographer. Spedding matriculated at the University of Michigan in the fall of 1920, from which he subsequently received a B.S. degree in chemical engineering in 1925 and an M.S. degree in analytical chemistry in 1926. From there he went to the University of California, Berkeley, from which he obtained a Ph.D. in physical chemistry in 1929 under Professor Gilbert N. Lewis.

As an undergraduate at Michigan, Frank Spedding displayed the curiosity and creativity that was to be the hallmark of his life as a first-class researcher. He found the then current explanation for how the six carbon atoms in benzene were held together unconvincing and came up with a different scheme of his own. This was prior to the application of quantum mechanics to chemical problems, and the prevailing bonding theory was mainly that of E. A. Kekulé. Spedding took his model to Professor Moses Gomberg, from whom he had taken a class, and Gomberg immediately recognized his model as that proposed by Professor A. Landenburg in 1869 during the much heralded debate between Victor Meyer, Kekulé, and Landenburg. Spedding switched to analytical chemistry for his M. S. after he had worked as an undergraduate co-op student at a local industry. It was the foregoing association with Gomberg that led Spedding to the University of California at Berkeley. Gomberg not only recommended that he go to Berkeley but he also put in a good word with G. N. Lewis so that he was accepted and given a teaching fellowship in physical chemistry. Lewis became his major professor, and Spedding felt he had arrived in a young chemist's heaven.

Spedding's research during graduate school years was spent learning about electronic spectroscopy, especially absorption spectra. Spedding's first publication with Simon Freed (1929) had to do with line absorption of solids at low temperature in the visible and ultraviolet regions. This was also a time when his interest in the rare-earth elements was whetted. Later publications with Freed made comparisons of the spectral properties of crystalline halogen compounds of samarium and gadolinium. Spedding was also put to work testing some of Lewis's theories and found that the first three or four turned out to be "wild goose chases." However, the experiments gave valuable experience, leading

Spedding to the conviction that, although a genius may have 10 ideas but only one success, a large part of the success ordinarily attributed to genius was the result of sheer hard work and an ability to overcome frustrations.

Spedding finished his research for his Ph.D. in 1929 and was greeted by the Great Depression. Jobs for chemists were virtually nonexistent, and so for the next seven years he lived on promises and a series of temporary fellowships. Although these carried prestige and honor, they were financially meager and offered at best only a hand-to-mouth existence. The stress of the period probably produced the ulcer that plagued him much of his life. For the years 1930-32 Spedding was awarded a National Research Fellowship, which enabled him to stay on at Berkeley doing full-time research. After that, Lewis hired him as a temporary chemistry instructor for 1932-34 with his main duties being continued research on the absorption spectra of solids.

It was during this time that Spedding started to integrate ideas from the newly developing quantum mechanics into his chemical thinking and his spectroscopic studies of atomic and molecular structure. It was already well established that gaseous elements gave sharp-line spectra, whereas liquids and solids generally did not. However, it was already known that the rare-earth-containing mineral xenotime did exhibit sharp lines when cooled to $\sim 80\text{K}$, which Spedding reasoned was because of the unusual electronic structure of the rare-earth constituents. But *pure* rare-earth compounds were scarce and almost impossible to obtain even in small amounts. Professor B. Smith Hopkins of the University of Illinois had a small supply of some rare-earth salts in relatively pure form, so Spedding appealed to him for a loan of a few tenths of a gram with the promise that it would not be consumed in any way. "I practically went down on my knees to Dr. Hopkins," is the way Spedding told the story,

and he did get the loan. The samples gave sharp lines, and Spedding went on to show that their fine structure depended upon the symmetry of neighboring atoms or molecules in their crystals, and this enabled him to determine the symmetry of various crystals (1931). It was for this work that he was presented with the Langmuir Award in 1933, then given to outstanding young chemists who had not yet reached 31 years of age. Only Oscar K. Rice and Linus Pauling preceded him in this achievement. The award was thereafter changed to the Award in Pure Chemistry of the American Chemical Society and the age limit was raised to 35.

Frank Harold Spedding and Ethel Annie MacFarlane were married on June 21, 1931. She had been born in Winnipeg, Manitoba, graduated from the University of Saskatchewan in 1919 with distinction, and received a further master's degree in history from the University of Toronto. She was teaching at Victoria High School, Victoria, British Columbia, when she and Frank Spedding met while hiking in northern California. They took up housekeeping during his tenure of the National Research Fellowship and under rather Spartan conditions. He related that their greatest source of pleasure and recreation was in the great outdoors, camping, hiking, and mountain climbing, because it was what they could afford. They later had a daughter, Elizabeth.

The Langmuir Award in 1933 was bestowed at the Chicago World's Fair. This exposition dramatized the progress in technology during the first 100 years of the city's existence, and his award was an appropriate showpiece for the exposition. Spedding was to give a talk describing his work and so he borrowed money in order to travel to Chicago. After he was introduced, he related, "I froze and could not remember how to get started." He went on to say that he was struck dumb for an interminable time, actually perhaps only ~10 seconds, and then he called for the first slide. The talk

went off without a hitch thereafter and was greeted by a pleasant round of applause.

At the end, after answering a question or two and the award presentation, an elderly gentleman made his way up to the platform. Spedding relates that the man's appearance reminded him of a then current comic strip character called "Foxy Grandpa," short, bald, and with a long white beard. Getting Spedding's attention, the man blurted out, "How would you like to have a pound of europium and two or three pounds of samarium?" (These were among the scarcer of the rare earths and were ordinarily obtainable only in milligram quantities.) Spedding said, "I thought this guy was crazy," but "I was polite to him and agreed that it would be fine and would help to further my work." Not long after his return to California a box arrived containing fruit jars of europium and samarium oxides. It was then that he found out that his benefactor was Herbert M. McCoy, a retired professor of chemistry at the University of Chicago. McCoy had earlier succeeded in separating some of the rare earths by fractional crystallization, as had Hopkins. When he further learned that Lindsey Light and Chemical Company had a supply of residues containing these elements left over after thorium extraction, that europium could be reduced to the divalent state and as such easily separated from the other elements, and that a related process had been developed for the neighboring samarium, he arranged to work up some of these rare-earth-metal residues. He was very generous according to Spedding and gave deserving people such quantities of europium compounds. (Spedding's life was to be influenced again by H. M. McCoy about nine years later in his career.)

The Langmuir Award included not only a gold medal but also an honorarium of \$1,000, a lot of money in 1933. This augmented his University of California stipend, so he

and Ethel looked forward to an easing of their lives in Berkeley. However, the depression was becoming more severe, universities were hardly able to pay their faculty, and G. N. Lewis was likewise hard pressed to support other promising potential staff members. Spedding recounts being called into Lewis's office during the 1933-34 academic year to be greeted by, "Now that you won your \$1,000, you won't need all the money we're paying you, so your salary for the year will be cut by \$500." Still no jobs were to be had, so he applied for and received a then rare Guggenheim travel grant for the year 1934-35. He planned to spend part of the time abroad, working in Germany with James Franck, a Nobel Prize winner, who had made a brief visit to Berkeley, and also part-time with Professor Francis Simon, a leading low-temperature physicist. Germany had by then come under Hitler, and Franck and Simon, both Jews, had fled to Denmark and England. Frank and Ethel went instead to England. He was warmly received at the Cavendish Laboratory in Cambridge by Ralph Fowler, professor of theoretical physics, and while there had the chance to work with John E. Lennard-Jones in quantum mechanics, meet Max Born who had also left Germany, and attend Born's seminars.

Travel expenses were to be paid by the Guggenheim Foundation, but the first quarterly payment would have had Frank and Ethel arriving in Europe with little left on which to live. Frank found that they could travel on a Japanese liner across the Pacific and then on other ships to England for less than half the quoted fares across the United States and the Atlantic Ocean. Spedding relates that their tourist-class tickets restricted their shipboard quarters only until they were beyond land; at that point they were allowed free access to all parts of the ship. "The captain was all too happy to have paying customers aboard," so the story went. There were leisurely stopovers in Japan, China, Malaya, and

Ceylon; they sailed up through the Red Sea and the Mediterranean and finally landed in Southampton about four months after leaving. The young couple profited immensely by their roundabout route to England: no charges for food or lodging all the way and immeasurable experiences to boot.

Abraham F. Joffe, a Soviet physicist whom Spedding had met in Berkeley and knew was in England, invited him to lecture in Leningrad, Moscow, and Kharkov at the expense of the Russian government. With some reservations, the Speddings accepted. Frank lectured at Leningrad but for unknown reasons never went to the other cities. Being in Europe had other advantages for the young scientist. There were side trips to the Netherlands to visit Kamerlingh Onnes's low-temperature laboratory, to research laboratories in France, Germany, and Latvia, and to Copenhagen to visit Niels Bohr. Bohr was a kindly man and greeted the then unknown young scientist warmly. Spedding liked Bohr not only because he treated Spedding as a friend but also because of his "brilliant mind." Bohr's English was difficult to understand, and "one really had to listen to him twice," according to Spedding, "but there was no doubt about his grasp of a subject." He spent a month in Bohr's institute, and although he did some theoretical work, he was determined to be an experimentalist and so he left. After the Guggenheim Fellowship ended, the Speddings felt they had to get back to the United States to look for a position that would pay a regular stipend. They returned to his parent's home in Michigan full of grand experiences but in dire need of a permanent job.

Canvassing the job market for a permanent position proved fruitless, but the George Fisher Baker assistant professor position at Cornell University was open, so Spedding took yet another temporary position, this time from 1935-37. Spectroscopic studies of other crystalline compounds of

samarium continued there and were expanded to compounds of thulium, gadolinium, neodymium, erbium, and praseodymium. During this time, working with Hans Bethe, Spedding showed conclusively that the sharp lines observed in the absorption spectra of rare-earth compounds arose from their inner shells and originated with 4f transitions (1937).

The entire period between 1930 and 1937 had been an enriching one for Spedding. He had also studied the effect of magnetic fields on the sharp lines in crystals and how they affected energy levels, and had done some spectroscopy in assisting G. N. Lewis in his efforts to concentrate deuterium. This work was described in his only publication bearing G. N. Lewis's name.¹ Spedding also used spectroscopic techniques to add another significant figure or two to the value of e/m , the charge-to-mass ratio of the electron, and to determine a better value for a , the fine structure constant. The broad scope of Spedding's spectroscopic studies at the time made him one of the premier electronic spectroscopists in the country and also one of the country's experts in the chemistry of rarer elements. Thus the next period in his life was set.

As the position at Cornell was winding down, he was again on the job market. After following several unproductive leads, he heard about a chance for a tenure-track position at Ohio State University, so he and Ethel got into their old Chevrolet and drove to Columbus. There an interview with Professor W. L. Evans, then head of chemistry, proved to be another frustration because Evans had just hired a new physical chemist. However, Evans knew that his friend Winfred F. (Buck) Coover at Iowa State College had lost much of his physical chemistry staff from resignations stimulated by greener pastures and was looking for a replacement. (Frank is quoted as saying, "I wouldn't normally have chosen the place, but I was desperate. I thought: I can go

there and build up physical chemistry and when jobs really open up I can go to another school.”) Again the Speddings trekked west.

An interview with Coover was encouraging in that Spedding was offered an assistant professorship on the spot. Although this was one step above the instructor rank at which young staff members were hired at Iowa State, it still was no assurance of anything more than a three-year appointment, subject to review before possible promotion to associate professor with tenure. Spedding already had seven years of uncertain positions behind him, so he asked for an associate professorship from the onset. Coover could not offer him this without consultation with college administrative officers and the regents. The situation was left that way, with the Speddings continuing to head west. They hoped to stop at Yellowstone National Park for several days on their way, and Coover was to wire him in care of general delivery at the Yellowstone Lodge. Several days followed and no wire. On the day Frank and Ethel were to leave the park, a last-minute check produced the wire from Coover. Spedding's name had been garbled in the address, but the associate professorship with tenure had come through. So in the fall of 1937, the Speddings checked into Ames, Iowa, where he became the head of the physical chemistry section of the Chemistry Department at Iowa State College.

There was meager modern equipment at Iowa State when Spedding got there. Funds were very tight, but some money was made available for a good ruled grating to be mounted on a Rowland circle in the basement of the chemistry building to enable him to continue his spectroscopic studies. Meanwhile, he changed the rest of his research program to a type of chemistry possible with equipment available at the college. Since he earlier had great trouble getting even small amounts of pure rare-earth compounds, Spedding started a

program to separate adjacent rare earths from one another, looking for a process that would automatically repeat the enrichment interaction thousands of times and do this rapidly. He thus had his students work on problems involving chromatographic columns with various forms of aluminum oxide or silica gel absorbers, but they had very little success with the separations. They also explored paper chromatographic methods that were being developed at that time, but these too were not very successful. This work was interrupted by the onset of World War II and was never reported in the literature.

By this time World War II had already started in Europe and select scientific circles recognized the possibility of a nuclear fission bomb with ^{235}U if the chain reaction problem could be solved. Accordingly, in what is a well-known story, the U.S. government decided to become active in this research program, and scientists who knew something about the subject were gathered at three research centers at the University of California, Berkeley; Columbia University; and the University of Chicago. Professor A. H. Compton of the University of Chicago was put in charge of the last, with the object of seeing whether a nuclear chain reaction could be achieved with natural uranium. In December 1941, the month of Pearl Harbor, Compton decided that the physicists needed chemists to help them in this program, and he asked his chemist friends to suggest outstanding inorganic chemists in the country who also knew something about the rarer elements, particularly uranium and the rare-earth elements. He learned of Spedding from H. M. McCoy, and from the list of names suggested, invited Spedding in February 1942 to head the chemistry program in the Chicago program. G. Seaborg (Berkeley), C. Coryell (MIT), M. Burton (Notre Dame), and G. Boyd (Oak Ridge) became involved in various chemistry sections.

After Spedding acquainted himself with the chemical problems, he informed Professor Compton that he had some space available at Iowa State College in Ames, and that he could enlist a number of his associates to help. It was then decided that Spedding would spend half of each week in Ames, working with his group there to solve some of the immediate chemical problems, and the other half of the week in Chicago organizing the chemistry division. (A recollection of a new student who entered Iowa State in the fall of 1941: "I took physical chemistry from Dr. Spedding. During the fall quarter he was a well-prepared and effective teacher. After the Christmas break, he was less organized and often came into the lecture hall opening his copy of the text and asking what page we had stopped on in the last class period. It was much later that I discovered that his lack of preparation was due to his spending most of his time on a special research project in Chicago.")

One of the most pressing problems was to get materials that were pure enough to build a nuclear reactor at Stagg Field, Chicago, in which the chain reaction would have a chance of going critical. Because of the small amount of ^{235}U in ordinary uranium, the reactor would have to be built to very exacting specifications, and the materials (uranium and graphite in particular) would have to be of exceptional purity, since many expected impurities were known to absorb neutrons. Therefore, one of the great needs of the program was to find a process that could produce ultra pure uranium metal in large quantity. Very little uranium metal had been produced prior to that time. Westinghouse and Metal Hydrides agreed to step up their processes and to supply Chicago with uranium metal. However, the metal from these sources was very slow in coming to Chicago and was cast or compacted into very small blocks—1-inch cubes or smaller—that were not very pure at the beginning. All

handbooks published prior to 1942 reported the melting point of what must have been quite impure uranium to be $\sim 1800^{\circ}\text{C}$, whereas it was later shown that the pure metal melted at 1132°C .

One immediate need was a source of a pure uranium compound as input to any process of metal production. While it had been known for a long time that uranium could be purified by an ether extraction from an aqueous solution of uranyl salts, the course of various impurities in the process was not well known. One of the first problems for Boyd's group at Chicago was to determine whether uranium so extracted would be satisfactory with regard to purity, and they reported that the method looked very promising. Spedding reported to Compton that they ought to arrange for the ether separation instead of other alternatives. As a result Compton and Spedding visited the Mallinckrodt Chemical plant in St. Louis, the chief manufacturer of ether, to contract for the solvent extraction work. At that time not many people were anxious to scale up this process since it was inherently *very* dangerous. Unless the plant was carefully designed, it would very likely burn down before much pure uranium was produced. While Compton spent his time at St. Louis discussing contract terms with Mr. Mallinckrodt, Spedding discussed with Dr. Ruhoff, superintendent of the plant, a flow sheet for the chemical engineering operations that would provide the necessary purity of uranium. Mallinckrodt accepted the contract, and Ruhoff with his staff designed the type of plant needed in detail. They did a remarkable job in building a plant that turned out large quantities of highly purified uranium oxide with minimal hazard in an exceptionally short time.

The groups at Chicago were very crowded for space at first; only a few rooms were available in the chemistry laboratories because other University of Chicago professors also

had important programs connected with the war effort. At that time the so-called "Compton's folly" of trying to get energy from the atomic nucleus did not have too high a local priority. To get some of the chemical work underway immediately, the Office of Scientific Research and Development gave Iowa State College a letter of intent for a three-month contract in February 1942, with the understanding that, as soon as suitable space became available at the University of Chicago, Spedding would move his group to Chicago. Professors Harley Wilhelm and I. B. Johns of the Iowa State Chemistry Department joined him at Ames as associate directors. They immediately enlisted their graduate students, and this was the nucleus of a group that started the work, soon to be joined by other graduate students and professors in the department as the group grew very rapidly. Spedding later remarked that he was "very lucky" to have had Wilhelm on the team. The latter had completed a Ph.D. in physical chemistry 10 years before, was then head of the graduate program in metallurgical science in the department and also had extensive experience in analytical spectroscopy.

One of the first problems was material that would contain molten uranium. Although graphite was known to react with uranium metal, the Ames team soon found that most of the carbide formed remained at the interface between the metal and the graphite if the graphite container was kept at a temperature slightly lower than the molten uranium and not for too long. This made it possible to make large castings of uranium in which the carbon and oxygen content in the bulk was less than 0.02 percent or 0.03 percent by weight, and this was improved with time.

The Ames team initially tried to reduce uranium oxide to the pure metal using H_2 but did not have much success. But by August 1942 the Spedding-Wilhelm team had also worked out a process for the production of high-quality

metal by a thermite-like reaction. A UF_4 sample had been circulated at a board meeting in Chicago (from the Y-12 isotope separation process at Oak Ridge), and it occurred to Spedding that this might be better than the troublesome oxide. This was successfully bomb reduced by calcium in a capped steel pipe lined with calcium oxide to prevent the ready U-Fe alloying reaction. In the month of November 1942 the process was scaled up, and two tons of high-purity uranium metal as machined cylinders, 2 inches in diameter and 2 inches long, were sent to Chicago, one-third of the six tons needed for the Stagg Field reactor. As a result, the Chicago group succeeded in achieving history with the attainment of criticality on December 2, 1942. Spedding was present on this occasion as director of the Chemistry Division of the Chicago Manhattan Project, as it was then called. By March 1943 the process had been improved so that magnesium could serve as a cheaper and purer reductant.

The ingots of uranium furnished from Ames were so much purer and less expensive than the uranium metal being produced by others that the Manhattan District asked three companies, Mallinckrodt, the Electrometallurgical Division of Union Carbide Co., and DuPont to produce large amounts of metal by this process for other reactors. Their company scientists and technicians studied the Ames process and went back and started building facilities to produce the metal. In the meantime, the government asked Spedding and his coworkers to produce all the uranium metal they could. During the ensuing several months, more than 2 million pounds of uranium metal were produced at Iowa State College in a scaled-up pilot plant set up in a temporary wooden building the college inherited after World War I. A large amount of this metal was used in Oak Ridge to build the prototype plutonium production reactor. Other large amounts went to various sites around the Manhattan

Project for research and development work. The remainder went to Hanford to help build the first plutonium production reactor. This Iowa State work was all carried out on two floors in one quadrant of the chemistry building, partly in the former physical chemistry laboratory. Security was very tight, although remarkable sights were sometimes visible through the windows, particularly at night during casting operations.

In July 1943 these companies started producing metal, and Ames reduced its uranium production and then discontinued it by the start of 1945. It was the success of this effort that led to the decision not to move the Spedding-directed effort to Chicago. Even today, general commercial uranium production uses the Ames thermoreduction process as modified during scale-up.

Stories about this secret and rushed production abound. The effort involved around-the-clock shifts seven days a week and, with these reactive materials and a wooden building, fires were always a problem, but never seriously so. One "mysterious" explosion (or innovation) on the graveyard shift moved one wall of the building out a foot, although no record of the exact cause could be found. A former shift worker said that Spedding "often reminded us that we were being deferred from army service to work here, and therefore we were expected to put in many extra hours." Shipping the uranium ingots to Chicago involved some novel circumstances because of the metal's high density, 19.05 g/cm^3 (1187 lb/ft^3). An American Express driver needed help from two guards to lift a small (120-pound) crate containing the first two ingots. The driver first thought that someone had screwed the container to the desk. In addition, the locals wondered about "loaded" freight cars that seemed to go out nearly empty. Because of the intensive schedule, information meetings or "Speddinars" were held on Sunday morn-

ings and later on Saturdays. Waste CaF_2 and uranium turnings were to be shipped off site for recovery. The need for watertight containers led a former Kentuckian to suggest white-oak barrels that had been used for aging bourbon, which were ordinarily destroyed after one use. Even though the central administration had been told to rush and not to question any purchases that Spedding requested, he was called to the university president's office to explain the order to Hiram Walker for "50 Barrels Bourbon" (with a missing comma, it turned out).

The demonstrated capabilities and expertise of the pure metals program were called on for other wartime production needs. A total of 437 pounds of very pure cerium was supplied in 1944-45 for the production of CeS crucibles used at that time in the plutonium program. Other concerns over whether there were sufficient uranium supplies led to the development of reactors to convert ^{232}Th to fissionable ^{233}U . A route to high-purity thorium metal was therefore developed on request, a more difficult problem because of both the melting point of the thorium, which is 500°C higher than that of uranium, and the greater stability of ThF_4 , etc. Over 1944-46 a calcium reduction process "boosted" by added ZnF_2 together with the use of beryllia crucibles for vacuum casting at $1850\text{-}1900^\circ\text{C}$ was developed. By December 1946 over 4,500 pounds of thorium had been cast and shipped to other sites.

After peace was declared in 1945 an Institute for Atomic Research was set up by Iowa State College with modest support from state funds, and Spedding became its director. The building constructed afforded space for the director, for administration, and a seminar room; a second floor Physical Sciences Reading Room; and in the basement Spedding's spectroscopy laboratories. However, the national need was recognized to reorganize the laboratories all over the coun-

try that had accomplished so much during Manhattan Project days under federal auspices. This was accomplished by the creation of the Atomic Energy Commission (AEC), whose objective was to fill in the gaps in research developed during the war years and to promote peaceful uses of atomic energy. In 1947 the Ames Laboratory of the AEC was set up on the campus of Iowa State, and Spedding became its director. Research at the Ames Laboratory at that time was considered by the AEC to be related to the development of nuclear power, and materials research along these lines was particularly encouraged. A strong emphasis on pure metals and their properties became a lasting feature. Spedding spoke on many occasions about his role in the Manhattan Project and the overall effort that led to the end of World War II. Although some other scientists later regretted their participation in such work, Spedding never expressed any misgiving or regret about his role. He evidently believed it was the "right thing to do," given the war in Europe and Asia.

The first permanent government building for the Ames Laboratory was completed in 1948 and a second in 1950. These are now named Wilhelm Hall and Spedding Hall, respectively. The first enabled the research housed in part of the chemistry building and in two temporary buildings elsewhere on campus to be consolidated into modern quarters, and the chemistry space was turned back to the college. An interesting remnant came with the reversion of space. As noted earlier, Spedding idolized his mentor, G. N. Lewis. The latter had a modest seminar room, a long table with seating for about 6 around it, plus a raised level around three sides with seats for 16 and a blackboard at the open end. Lewis and his senior grad students—and sometimes visitors—sat around the table with the junior grad students on the raised sides. Spedding had a very close copy of the

seminar room constructed at Iowa State, but with a double row of seats on the elevated level. This was the faculty conference room in chemistry when I arrived in the early 1950s. Another similarity was that G. N. Lewis was a cigar lover and had a lighted one at hand all the time, and so too did Spedding. The latter would become very attentive during meetings with his students and senior scientists, and these onlookers would sometimes fear for Spedding's safety when he inattentively attempted to relight cigars, and put the used matches and ashes in his coat pocket. It was not unusual to find several partially smoked cigars around his office, some still lit! He was also reported to take the cigar out of his mouth and hold it behind his back when he took visitors into the calorimetry laboratory where they were making heat capacity measurements and venting gaseous hydrogen (with warning signs everywhere). Fortunately, the ventilation in the building was quite good!

Historically, separation of the rare-earth elements from one another had been difficult, owing to their very similar chemical properties. Chemists had succeeded in separating all of them in modest purity but in very small amounts by fractional crystallization, some cases requiring hundreds, even thousands, of separations. Among the major fission products of ^{235}U are the rare earths, namely the elements La-Lu and Y, and the very high neutron-capture cross-sections of some of these would inhibit any chain reaction after some U^{235} had been consumed. Samples of the individual members were needed so that both the nuclear properties related to the fission reactor as well as chemical processes that could separate them from unfissioned uranium and plutonium could be studied. Spedding's separation efforts were resumed in late 1944 by Jack Powell, Adolf Voigt, Elroy M. Gladrow, Norman R. Sleight, and others, who used citrate elution at high pH on ion exchange columns to separate

adjacent rare earths in moderate quantities (1947, 1951). The separation with citrate as the complexant was really only effective for the lighter half of the rare earths where the inter-element differences are somewhat larger.

A major improvement in these separations was achieved later with a switch to EDTA as the complexing agent, leading to a pilot-plant-scale operation by 1953. This advancement resulted from a cooperative effort with Gerard Schwarzenbach (ETH, Zurich) who aided the measurement of the EDTA-rare-earth ion complex formation constants, and the recognition by Powell and Spedding that displacement ion exchange chromatography gave by far the best separations (1954). In some cases oxides were produced that contained only a few parts per million of all other metals. This was scaled up by request to produce kilogram quantities of all the rare-earths salts for general research purposes throughout the AEC laboratories and elsewhere. More than 80 commercial companies sent their scientists to Iowa State to study this process, and several set up plants to make these elements generally available. Once the rare-earth compounds became generally available to the general scientific community, many practical applications were found, and a considerable industry developed that involved the use of rare earths.

Parallel with this work, Spedding, Wilhelm, Adrian Daane, Wayne Keller, and others developed processes for producing very pure rare-earth metals in quantity (1952, 1953, 1958). During the early 1950s much interest in yttrium developed because it was a light, high-melting metal that formed a particularly stable hydride. Development of a nuclear reactor that could be used in airplanes was conceived in which the deuteride might serve as an ideal neutron moderator. Thus in 1954 and early 1955 the group produced tons of yttrium metal and further scaled up the

methods already developed for producing kilogram quantities of the other metals. A process similar to one used for thorium was developed, namely co-reduction of the trifluoride with calcium and magnesium to form a low-melting Y/Mg alloy. The magnesium was sublimed from this alloy under high vacuum, and the resulting yttrium sponge then formed into acceptable billets by vacuum arc melting. By 1957, 20,000 pounds of cast Y metal had been produced at Iowa State along with 65,000 pounds of YF_3 that was supplied to commercial metal producers all over the country. Again the research group under the direction of Spedding was able to take a process developed on a laboratory scale and produce gross amounts of a needed commodity.

In this period Spedding also established extensive joint programs in fundamental solid-state physics and in metallurgy. The novel properties of many of the metals, salts, and their alloy systems were determined in these programs (1953, 1962). After about 1950 Spedding set up a program to study the thermodynamic, conductance, transference, etc., properties of electrolytic solutions of rare-earth salts, in part to enable fundamental considerations of a series of electrolytes that differed principally only in the radii of the cations. An extensive literature accumulated as a result (1952, 1954, 1959).

Graduate students' recollections of these busy and productive times are most illuminating and give real insights into the director as a person and as a scientist. His interests and abilities were very wide in scope, and he actively participated in the joint programs with physics and metallurgy. A major attitude that he passed onto students (and faculty) was his insistence on getting the physical picture behind any phenomenon or theoretical treatment. The power of critical thinking and the need (because of Spedding's busy schedule) to work independently came with these as well.

Spedding generated intense loyalty from his students, in part because they knew he generally spent more time at work than they did, and that was already at least 60 hours per week. One student commented on this when he found Spedding at work on a Sunday afternoon, to which his rejoinder was, "I would rather wear out than rust out." Another student comment was that he had never heard of or seen Spedding lose his temper with or jump on anyone. But he could also be very firm, which included dealing with young outside visitors who thought the older administrator must be out of touch with science. Because of his bleeding ulcer, he had to go to the hospital for a blood transfusion every once in a while, but this was generally not known. One of his graduate students learned of this circumstance and commented that he would be glad to donate blood any time he needed it. "Oh God, no," Spedding replied, "can you imagine how it would look if people knew I was taking blood from my students?"

Over the years Spedding published 260 scientific articles, a select 25 of which are listed at the end of this memoir. The nature of the Ames Laboratory research and development also led to 22 patents in his name and others, all of which were assigned to the U. S. government. A good measure of his educational efforts and contributions as well is the fact that 88 students received Ph.D. degrees under his guidance and tutelage.

Professor Spedding was elected to the National Academy of Sciences in 1952, before the main impact of the very effective ion-exchange separation of the rare-earth elements was felt. He also became the first to bear the title Distinguished Professor of Sciences and Humanities at Iowa State, in 1957. Among his 50-plus honors and awards was the William H. Nichols Award of the New York section of the American Chemical Society in 1952; the James Douglas Gold Medal

from the American Institute of Mining, Metallurgical, and Petroleum Engineers in 1961 for achievements in nonferrous metallurgy; and the Francis J. Clamer Award from the Franklin Institute in 1969 for achievements in metallurgy. He was awarded an honorary LL.D. by Drake University in 1946, D.Sc degrees from the University of Michigan in 1949 and Case Institute of Technology in 1956, and an honorary membership in Verein Osterreichischer Chemiker in 1958.

Frank Spedding's major scientific and leadership roles have been many, the most noteworthy being the process development and production of large amounts of high-purity uranium and thorium during and after World War II, the discovery and development of the first workable separations of the rare-earth elements, and their reduction to high-purity metals. This was accompanied by a deep lifelong involvement in research that led to 260 publications. His crowning accomplishment in many eyes was the establishment of the Ames Laboratory, a national laboratory now supported by the U. S. Department of Energy, at a present level of \$25 million per year for relevant research in chemistry, physics, metallurgy, materials sciences, environmental sciences, engineering, and mathematics. The breadth of Spedding's work was large; although his coworkers were many, the inspiration and drive to do the work originated largely with Spedding's perception of what needed to be done, how it should be done, and when it should be accomplished.

Frank Spedding retired as an active academician in 1972 at the age of 70 as emeritus professor of chemistry, physics, and metallurgy. For several years he carried on research with postdoctoral students and full-time scientists. He co-authored an additional 60 or so publications during this time. In the beginning he was in his office almost every day, but finally his energies began to fail. His last scientific

publications came out in 1982. Early in the fall of 1984 he suffered a stroke that was to end his life on December 15, 1984. His remains are interred in the Iowa State University cemetery, along with those of his wife Ethel, who died in October 1996.

I HAVE DEPENDED A great deal on other sources for the information in this memoir. First are two public documents^{2,3} and, most especially, an earlier summary of Spedding's career written by Professor Harry J. Svec and published in 1988 in the leading serial series on the rare earths.⁴ Second are the former graduate students and colleagues of Spedding, who furnished many of the more personal experiences with and insights into the man: Adrian Daane, Jim Dye, Jack Powell, Bernie Gerstein, Earl Wheelwright, Joe Rard, John Croat, and Karl Gschneidner.

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Courtesy of Robert P. Matthews

Sam Treiman

SAM BARD TREIMAN

May 27, 1925–November 30, 1999

BY STEPHEN L. ADLER

SAM BARD TREIMAN WAS a major force in particle physics during the formative period of the current Standard Model, both through his own research and through the training of graduate students. Starting initially in cosmic ray physics, Treiman soon shifted his interests to the new particles being discovered in cosmic ray experiments. He evolved a research style of working closely with experimentalists, and many of his papers are exemplars of particle phenomenology. By the mid-1950s Treiman had acquired a lifelong interest in the weak interactions. He would preach to his students that “the place to learn about the strong interactions is through the weak and electromagnetic interactions; the problem is half as complicated.” The history of the subsequent development of the Standard Model showed this philosophy to be prophetic.

After the discovery of parity violation in weak interactions, Treiman in collaboration with J. David Jackson and Henry Wyld (1957) worked out the definitive formula for allowed beta decays, taking into account the possible violation of time reversal symmetry, as well as parity. Shortly afterwards Treiman embarked with Marvin Goldberger on a dispersion relations analysis (1958) of pion and nucleon beta decay, a

major outcome of which was the famed Goldberger-Treiman relation for the charged pion decay amplitude. Subsequent reformulations of their derivation led to the hypothesis of the partially conserved axial vector current (PCAC) and at a deeper level to our understanding of the spontaneously broken chiral symmetry of the strong interactions. A subsequent important PCAC application was made by Treiman and Curtis Callan (1966) in deriving the Callan-Treiman relations for K meson decay. Another widely quoted Treiman paper was his analysis with David Gross (1971) of scaling in vector gluon exchange theories, which anticipated the quantum chromodynamics treatment of this phenomenon and coined the now standard term “twist” for the difference between the dimension and spin of an operator. An important facet of Treiman’s research was his ability to devise simple, incisive experimental tests for important theoretical hypotheses. Prime examples are what became known as the Treiman-Yang angle test for single pion exchange dominance (the result of a 1962 collaboration with Chen-Ning Yang) and his paper (1972) with Abraham Pais giving the implications of weak neutral currents for inclusive neutrino reactions (which is how the existence of neutral currents was first established).

Equally important for Treiman’s impact on physics was his outstanding ability as a teacher and mentor to two dozen graduate students over three decades. Three of his students (Steven Weinberg, Callan, and myself) are members of the National Academy of Sciences and Weinberg is a Nobel laureate for his contributions to electroweak unification. Treiman’s students, building on his basic philosophy, contributed much to the current edifice of the Standard Model. Treiman’s teaching style has been termed Socratic. He was always willing to engage in a dialogue on any serious topic in physics, and one always came away from such discussions

with valuable insights. For his contributions as an educator Treiman was honored in 1995 with the Oersted Medal of the American Association of Physics Teachers. Other honors included election to membership in the American Academy of Arts and Sciences and the American Philosophical Society.

PERSONAL HISTORY

Sam Treiman was born in Chicago to a first-generation immigrant family. His father, Abraham, had come to the United States from Lithuania and his mother, Sarah, from Russia, both before World War I. Sam had one sibling, a six-year-older brother, Oscar, who became an accountant. It is hard to improve on the vivacity of his own description of his youth, given in the autobiographical notes that he submitted when he was elected to the Academy in 1972.

The family lived in Jewish ghetto areas in Chicago, within a larger network of maternal relatives. Although my parents had little formal education, they attached high value to learning and provided an encouraging, if impoverished, environment. I attended local public schools. They were pretty awful, in retrospect, but I didn't know that at the time. In any case I did very well in school and did have several stimulating teachers. In high school I read a fair amount of mathematics and popular science, on my own, and traded insights with a few other bright students in a small circle. I edited the high school newspaper, played clarinet in the band, and otherwise spent my time aimless but content. Intellectual stimuli came chiefly from my brother, an uncle, and books.

After high school, in 1942, I went into chemical engineering at Northwestern University, on a scholarship. This going to college was a first for the wider family and, to a considerable extent, for the neighborhood. I can't now reconstruct why I chose chemical engineering, but it seemed "scientific" and important in war time. The freshman physics course was taught by Hartland Snyder, a very colorful and talented fellow; and it occurred to me that physics was what I wanted. After two years at Northwestern I joined the Navy, received training in radar repair, and spent the last year of the war as a petty officer in the Philippines, where I fixed radars and did a prodigious amount of reading in the peaceful jungles—novels and science.

As is evident from these passages, Treiman was at ease with his background even though his natural talents propelled him far beyond it, and he had an unusual ability to cut through to the essence in all matters he dealt with, an ability that figured in his later great success as a mentor to a generation of young physicists. And as the passages also show, Treiman viewed himself and the events through which he lived with a charming and often understated wit that, in the words of Princeton University's memorial resolution, "lay at the heart of his persona and was an important factor in his effectiveness in debate and counsel: Sam's ability to see wry humor in the face of serious issues lightened many a difficult moment, gave warmth to all of us, and was something he took great pleasure in sharing."

In a second autobiographical piece, a beautiful, detailed account of his career in particle physics written for *Annual Review of Nuclear and Particle Science* (1996) Treiman attributed his choice of both Northwestern and a chemical engineering major to his teachers, who were motivated by wartime concerns. Although Treiman did not then know of Snyder's past or future accomplishments, the man who stimulated him to choose physics as a career had written with Oppenheimer the seminal paper on gravitational collapse to what are now called black holes and would later discover with M. Stanley Livingston and Ernest Courant (and independently, Nicholas Christofilos) the strong focusing principle on which all modern particle accelerators are based.

At the end of the war, with GI Bill support, Treiman moved on from the Navy to the University of Chicago as a physics major, completing his undergraduate education with a B.S. in 1949 and earning an M.S. degree in 1950. Chicago at that time was a remarkable place, with a physics faculty that included Enrico Fermi, Maria Goeppert-Mayer, Edward Teller, and Gregor Wentzel. Treiman's immediate predecessors

were the stellar group of graduate students who gravitated to Chicago after the war, among them Owen Chamberlain, Geoffrey Chew, Richard Garwin, Goldberger, Tsung-Dao Lee, Marshall Rosenbluth, Jack Steinberger, Lincoln Wolfenstein, and Yang. They set a seemingly impossible expectation level for the students, including Treiman, who followed, who were themselves an exceptional bunch. When Treiman taught an introductory physics section, his students included Fred Zachariasen and Jerry Friedman. Treiman did "well enough" on the notoriously difficult Chicago exams, and supported by an Atomic Energy Commission predoctoral fellowship, wrote his doctoral thesis on cosmic ray physics under the supervision of John Simpson, receiving his Ph.D. in 1952.

Sam Treiman met his wife, Joan Little, during their student days at the University of Chicago, where she majored in educational psychology and worked with disturbed children at the Orthogenic School, under the supervision of Bruno Bettelheim. They married in December 1952, and had three children, Rebecca, Katherine, and Thomas. Sam was always very proud that all three of his children earned Ph.D. degrees, Rebecca in psychology (specializing in psycholinguistics) from the University of Pennsylvania, Katherine in health education from the University of Maryland (following up on a masters in public health from Johns Hopkins), and Thomas in economics from the University of Wisconsin at Madison.

The Treiman home at McCosh Circle was the scene of frequent dinner parties for students and colleagues, with wide-ranging conversation in which Sam's humorous streak had free rein; for a graduate student or junior colleague, being invited to one of these was a memorable point in the progression of one's career. Sam prided himself on being up-to-date on all the latest experimental developments in particle physics, and he was also an avid reader, particularly of history. He was a passionate tennis player, with a savvy kit

of skills that defeated many players who thought they excelled him in strength or form.

Only a few years after his retirement, following more than 46 years of service to Princeton University and to the national and international physics community, Sam was diagnosed with leukemia. After a valiant, brave, and characteristically graceful and good-humored struggle, he died in Memorial Hospital in New York on November 30, 1999, at the age of 74. Scarcely six weeks before, during a period of remission from his illness, I had the honor to have Sam as an after-dinner speaker at my sixtieth birthday conference, which was held at the Institute for Advanced Study on October 16, 1999. This was to be his last public occasion; it was hard to imagine then, and to accept later, that he would be gone so soon afterwards.

PROFESSIONAL HISTORY

After completing his doctorate, Treiman moved in the fall of 1952 to Princeton University as an instructor. Apart from periods when he was on leave, he spent his entire academic career at Princeton, rising through the ranks to associate professor (1958-63), professor (1963-77), and Eugene V. Higgins Professor of Physics (1977 to his retirement in 1998). He also served Princeton as chair of the Physics Department (1981-87), and as chair of the University Research Board (1988-95). In both capacities he was a major voice in shaping the future of the university and its science policy.

Following naturally on his thesis in cosmic ray physics, Treiman associated himself with the cosmic ray group in Princeton, which had been set up a number of years previously by John Wheeler and then was under the leadership of George Reynolds. Their activities focused on the new particles (e.g., K mesons, Lambda hyperons) that were being

found in cosmic radiation. Treiman worked as house theorist for the group, writing papers on how to extract such information as particle spins and parities from the observed production and decay distributions.

This work led over a few years to a shift in Treiman's focus from cosmic rays to the new particles and their properties and in particular to the weak interactions responsible for their decays. Among his significant early particle physics papers were an analysis with Wyld (1955) of K meson decay accompanied by radiation of a gamma ray and an analysis with Robert Sachs (1956) of the K meson decay channel into pion, lepton, and neutrino. He also began a lifelong friendship and collaboration with Abraham Pais, who was then at the Institute for Advanced Study, studying such topics as the spectral structure of K meson decays (1957). After the parity revolution of 1957, in which it was discovered that the weak interactions do not respect left-right reflection symmetry, Treiman with Jackson and Wyld re-analyzed nucleon beta decay (1957), allowing for the presence of all of the four Fermi coupling types and for time reversal violation as well. Testing for time reversal violation in nuclear decays became an important topic, and the results of their paper were widely quoted. Treiman's interest in tests for symmetry violations in weak processes continued throughout his career and surfaced later on, for example, in papers with Callan (1967) on signatures of time reversal violating vector triple product correlations and with Barry Holstein (1976) on tests for so-called "second class" or abnormal G-parity currents (which, in agreement with subsequent experiments, are absent in the current Standard Model).

Treiman's first two graduate students, Steven Weinberg and Nicola Khuri, completed their dissertations in 1957. Weinberg's thesis topic dealt with strong interaction effects in weak decays and Khuri's with the derivation of disper-

sion relations for nonrelativistic potential scattering by a wide class of potentials. In the course of his career Treiman had two dozen students; the complete list with dates of completion is: Nicola Khuri and Steven Weinberg (1957); Carl Albright (1960); Kenneth Edwards and Young Suh Kim (1961); John Bronzan, Binayak Dutta-Roy, and Paul Kantor (1963); Stephen Adler, Curtis Callan, and Alfred Goldhaber (1964); Jonathan Rosner (1965); Porter Johnson and Rein Uritam (1967); Herbert Chen (1968); Stephen Schutz, Kazuo Fujikawa, and Glennys Farrar (1970); William Shanahan (1972); Bennie Ward (1973); Robert Schrock (1975); Evelyn Monsay (1977); Cornell Chun (1978); Dean Preston (1980); and Michael Musolf (1989, joint supervision with Barry Holstein and Robert Naumann). A majority on this list are now prominent faculty members at universities in the United States and overseas, and their research has played an important role in establishing the current Standard Model of particle physics.

Treiman makes an illuminating comment on his philosophy of teaching in his memoir (1996).

A word here about graduate student research “supervision.” Khuri and Weinberg needed no technical support or supervision from me. It was in fact the other way round as they patiently guided me along in the intricacies of their investigations. That largely continued to be the case with a long string of subsequent graduate students. The great trick is to get good students in the first place, then ask them to teach you.

As part of Treiman’s self-education a student could count on a succession of penetrating questions by Sam whenever they met, which either exposed fallacies (leading to a research track being abandoned) or developed a good but only half-understood idea into one with a firm conceptual base on which a project could be built.

Khuri’s thesis topic was part of a larger Princeton effort in dispersion relations, which was spurred by the presence

there of Goldberger, who had achieved a great theoretical and phenomenological success by his derivation of forward pion nucleon scattering dispersion relations (the particle physics analog of the optical Kramers-Kronig relations). Treiman participated in a number of aspects of the dispersion relations program. With Paul Federbush and Goldberger he carried out (1958) an extensive dispersion relations analysis of the nucleon electromagnetic form factors, and in a tour de force with Richard Blankenbecler, Khuri, and Goldberger (1960) he was able to prove the Mandelstam double dispersion relation representation for nonrelativistic potential scattering in the case of potentials that can be expressed as a superposition of Yukawa potentials (the same class used by Khuri earlier in his thesis).

The most significant dispersion relations paper by Treiman, which had far-ranging implications, was his dispersion relations analysis with Goldberger (1958) of charged pion decay into a muon or electron plus a neutrino. Using the pion off-shell mass as the variable to be analytically continued into the complex plane and making some astute approximations, they deduced a simple formula relating the charged pion decay amplitude f_π to the nucleon mass m , the pion-nucleon coupling constant g , and the weak axial vector coupling parameter measured in beta decay g_A ,

$$gf_\pi = mg_A.$$

This relation, the famed Goldberger-Treiman relation, fit the data at the time and remains good to about 10 percent accuracy. In a subsequent paper (1958) Treiman and Goldberger used their approach to calculate the so-called induced pseudoscalar coupling constant relevant for mu meson capture by a proton, again with good agreement with experiment.

These unexpected connections between the strong and weak interactions attracted much attention, and were soon found by Yoichiro Nambu, by Murray Gell-Mann and Maurice Lévy, and by Kuang-Chao Chou to be derivable from simpler assumptions concerning the near conservation of the axial-vector current and its relation to the pion field, for which the acronym PCAC (partially conserved axial vector current) was later coined. In modern terms an exactly conserved axial vector current, together with the fact that the nucleon is massive and has no opposite parity partner, implies that chiral symmetry is spontaneously broken by the strong interactions, with the appearance of massless pions as the corresponding Goldstone bosons. There are then low-energy theorems relating pion emission or absorption amplitudes to amplitudes with one less pion, of which the Goldberger-Treiman relation for pion decay is the simplest. In actual fact there are also explicit chiral symmetry-breaking terms in the Standard Model (coming from the quark masses), and so the axial current is only approximately or partially conserved, but the various low-energy theorems implied by axial current conservation are still useful approximations.

The PCAC hypothesis coming out of the Goldberger-Treiman relation served as the axial-vector current counterpart of the CVC (conserved vector current) hypothesis for the weak vector current proposed in 1958 by Richard Feynman and Murray Gell-Mann. Together with the current commutator algebra abstracted from the quark model in 1964 by Gell-Mann, they formed the basis for the “current algebra” program, which led to many phenomenological successes in the period 1964-66. My thesis project with Treiman, and subsequent work deriving from it, played a pivotal role in these developments. Entitled “High Energy Neutrino Reactions and Conservation Hypotheses,” my thesis had the original aim of exploring the simplest quasi-

elastic and inelastic accelerator neutrino reactions. However, Treiman had educated me about the CVC and PCAC hypotheses, which at that point had few tests—as Sam would often point out, PCAC was supported by “only one number,” the success of the Goldberger-Treiman relation. With this stimulus the topic of my thesis broadened into finding further tests and applications of CVC and PCAC, suggested by the context of neutrino weak pion production. Before long, Sam was able to say “now there is a second number,” and after my derivation of a sum rule relating the axial vector coupling constant to pion nucleon scattering cross sections (also derived independently by William Weisberger), which Sam was one of the first to learn about, this number blossomed into a multitude. An important addition to the current algebra program was contributed by Callan and Treiman (1966), who applied the general methods to K meson decays, achieving a number of striking, experimentally successful predictions.

Beyond its immediate phenomenological successes the larger significance of PCAC and CVC, together with Gell-Mann’s current algebra, was that they refocused attention on quantum field theory methods, which had been in eclipse during the heyday of the dispersion relations program. More specifically, the non-Abelian structure of the Gell-Mann algebra, together with the near conservation of the currents implied by CVC and PCAC, was suggestive (to an astute few) of a gauge theory structure for the weak interactions as well as electromagnetism. This led rapidly to the work of Sheldon Glashow, Abdus Salam, and Steven Weinberg, and of Martinus Veltman and Gerard ‘t Hooft on non-Abelian electroweak unification using the group $SU(2) \times U(1)$, thus providing one of the two pillars of the current Standard Model.

One of the hallmarks of Treiman’s style in physics was his ability to find incisive experimental tests of the various

hypotheses and theories currently under discussion within the high-energy physics community. The most famous example is his paper with Pais (1972) on signals for the neutral currents predicted by the $SU(2) \times U(1)$ electroweak theory, in which they focused attention on the neutral current inclusive process in which a neutrino incident on a nucleon produces a final neutrino and a spray of strongly interacting particles. They showed that this cross section is at least 0.24 times the corresponding charged current inclusive cross section, in which, instead of an outgoing neutrino, there is an outgoing muon. This result was the basis for the first experimental confirmation of the existence of neutral currents. Other equally incisive papers were another paper with Pais (1975) giving inequalities that soon ruled out heavy leptons as a source for recently observed dimuon events, a paper with Kenneth Johnson (1965) using a proposed approximate $SU(6)$ symmetry of the strong interactions to give successful predictions for the forward elastic scattering and total cross sections of pseudoscalar mesons on protons, and a paper with Yang (1962) giving a characteristic signal for single pion exchange dominance, expressed as the prediction that the differential cross section should have a specific axis of rotational invariance.

Treiman was also active on more theoretical issues as well. Following the theoretical work of James Bjorken on scaling and its experimental discovery at the Stanford Linear Accelerator Center, Gell-Mann proposed the dictum that “nature reads the free-field theory books.” Using the connection between the Bjorken scaling limit for the electroproduction inclusive cross section and the commutator of electromagnetic currents near the light cone, Treiman and Gross analyzed the extent to which this dictum was true in quantum field theory and found that in a formal sense it is satisfied for strong interaction theories with a vector gluon

exchange dynamics. In the course of this work they laid the groundwork for the later analysis by Gross and Frank Wilczek and others of deep inelastic processes within the framework of quantum chromodynamics (or, as now abbreviated, QCD, the second pillar of the Standard Model), which is a vector exchange theory and leads to scaling as a first approximation, with calculable logarithmic corrections. In a quite different direction, I collaborated with Treiman, Benjamin Lee, and Anthony Zee on a paper (1971), using effective Lagrangian methods to turn the axial anomaly prediction for neutral pion to two gamma ray decay into a prediction for the reaction in which two incident gamma rays produce three pions, anticipating a more general relation between different anomaly-induced processes found not long afterwards by Julius Wess and Bruno Zumino.

One of the great events in physics in the mid-sixties was the 1964 discovery by Treiman's Princeton colleagues Val Fitch, James Cronin, James Christenson, and René Turlay of the failure of CP (charge conjugation times parity) symmetry in K meson decays. Sam was fascinated by this development, and in its aftermath wrote a number of influential papers on implications of CP violation. With Doug Toussaint, Wilczek, and Zee (1979) Treiman wrote one of the first papers on implications of CP violation for the production of the observed baryon asymmetry of the universe, within the context of grand unified models linking the electroweak and strong interactions. This work gave a concrete realization of earlier, prescient ideas of Sakharov. In yet another collaboration with his longtime friend Pais, Treiman wrote a phenomenological paper (1975) on CP violation in charmed meson decays, which was a forerunner of the current searches for CP violation in B meson factories.

In addition to his research articles Treiman co-authored several books of lectures on topics in high-energy physics.

After his retirement he wrote an insightful book on quantum mechanics for a mathematically literate but non-specialist audience, entitled *The Odd Quantum* (1999). This book was published by Princeton University Press during the month he died, and he had a copy with him on his last trip to the hospital.

Beyond his research and mentoring of students Treiman served the physics community and influenced unfolding events in other capacities. To quote again from his memoir (1996):

But I do claim some credit for Bram (Pais)'s literary successes. During my incarnation as an associate editor of *Reviews of Modern Physics*, I invited him to write a historical piece on particle physics. Instead he produced an article on Einstein and the quantum theory. It was later vastly enlarged and transmuted into his highly acclaimed scientific biography of Einstein, *Subtle is the Lord*. Subsequently, he published *Inward Bound*, the originally conceived though greatly broadened history of particle physics in the twentieth century.

When Fermilab was set up by Robert Wilson in 1970, Treiman was invited by Wilson to direct the laboratory's theory group. Rather than leaving Princeton permanently, Treiman went to Fermilab on several extended leaves to get the theory group successfully launched. Treiman was also active on various accelerator program committees and served extensively on the Department of Energy's HEPAP (High Energy Physics Advisory Panel) and a number of its subpanels. In addition, he was an active participant in the JASON group, which consulted on national defense issues from its inception in 1960. He left Jason in the late 1960s, but rejoined again in 1979, and the regular trips to the JASON summer study in San Diego were an important part of his and Joan's annual calendar. Finally, Treiman and Joan were early participants in the CUSPEA (Chinese/U.S. Physics Examination and Application Program) conceived by Tsung-Dao Lee in

1980 to help facilitate the admission of mainland Chinese students to physics graduate education in the United States. He and Joan went to China in 1981, 1982, and again in 1988 to examine and interview prospective candidates for the program. In his memoir (1996) Sam noted:

The experiences were memorable. In our first visit we encountered many older applicants whose education had been interrupted by the cultural revolution . . . By 1988 most of the students were young and on track . . . Altogether, over the period of a decade, the CUSPEA program brought close to a thousand mainland Chinese students to America and fostered Chinese-US physics contacts on a broader front.

In opening his memoir (1996) Treiman remarked: “Looking back now, I am convinced that my own trajectory in fact spans another Golden Age and that I have been luckily situated within it.” The first Golden Age of twentieth-century physics saw the development of relativity, quantum mechanics, and quantum field theory and their early applications to atomic and nuclear structure. A second Golden Age saw the wartime development of nuclear energy and radar and the subsequent use of the new technologies that emerged in postwar basic research. The third Golden Age, in which Treiman participated as a theorist, phenomenologist, and mentor, saw the application of quantum field theory to organize masses of experimental data on subnuclear physics into today’s Standard Model. Sam Treiman, both through his own keen research insights and through his extraordinary ability to communicate his love of physics and to catalyze the work of his students and associates, was a major figure in particle physics during this exciting period of synthesis.

THE INTRODUCTORY SECTION of this narrative is taken with minor changes from an obituary that I wrote for *Physics Today* (August 2000, p. 63.) Both in passages directly quoted above and in many other places I have used the biographical account supplied by Sam Treiman to

the National Academy of Sciences and his beautiful memoir (1996) published in *Annual Review of Nuclear and Particle Science*. I have also benefited in preparing this narrative from my personal association with Sam and with many of his collaborators, first as his graduate student at Princeton from 1961 to 1964 and later as a colleague at the nearby Institute for Advanced Study from 1966 onwards. I wish to thank Joan Treiman for supplying family information and to thank Sarah Brett-Smith, Curtis Callan, Val Fitch, and Joan Treiman for reading a draft of this memoir.

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Fermilab Photo

Robert R. Weir

ROBERT RATHBUN WILSON

March 4, 1915–January 16, 2000

BY BOYCE D. McDANIEL AND ALBERT SILVERMAN

ROBERT RATHBUN WILSON was one of the most important figures in accelerator development and research since Ernest Lawrence. He was the driving force for the creation of two of the four world-class high-energy physics laboratories in the United States: the Cornell Laboratory of Nuclear Studies and Fermilab, which houses the world's highest-energy accelerator—initially the 500-GeV proton synchrotron and since 1990 the *tevatron*, the world's first high-energy superconducting magnet synchrotron.

A brief review of his career cannot begin to describe his central role in high-energy experimental physics. His insistence on bolder, more compact, and economical design, seen clearly in the accelerators he built at Cornell, influenced the design of most modern accelerators, and his development of the first superconducting magnet accelerator at Fermilab made possible both technically and economically the very-high-energy accelerators now under construction.

Wilson was an inspiring leader. Each new project was the beginning of an adventure, a cause for celebration. The more challenging the project, the more exuberantly he embraced it. His attitude was contagious, and his colleagues responded with their very best efforts.

Wilson was born on March 4, 1914, in frontier Wyoming, the son of Platt and Edith Rathbun Wilson. His mother's family were pioneer ranchers, and Wilson spent much of his early youth on the cattle ranches of his relatives in the vicinity. When he was eight years old, his parents separated and Robert attended the Todd school in Woodstock, Illinois, for several years. It was here that his interest in mechanics became pronounced enough for him to be dubbed "The Inventor." During his primary and secondary education he changed schools almost every year. In spite of this frequently interrupted educational career he set up a rudimentary laboratory where he experimented with vacuum phenomena using high vacuum pumps of his own design and construction.

Wilson was admitted to the University of California in Berkeley in 1932 and received his A.B. degree cum laude in 1936. During his junior year he began research under the direction of E. O. Lawrence. His first work was in the field of gaseous discharge, where he developed a new method of studying the time lag of spark discharges, a work of considerable importance that was published in *Physical Review* during his senior year.

Wilson continued his studies under Lawrence as a graduate student. Among the four papers he published as a graduate student were the first theoretical analysis of the stability of cyclotron orbits, which he verified experimentally, and a paper on the theory of the cyclotron. During his graduate career he made important contributions to the development of the cyclotron as a useful tool in the study of the atomic nucleus; for example, a vacuum sliding seal so that material, such as targets, could be inserted into the vacuum chamber without losing the vacuum. In 1940 he received his doctor's degree.

THE WAR YEARS

In 1940 Wilson married Jane Inez Scheyer of San Francisco, accepted an appointment at Princeton as instructor, and very soon found himself involved in the scientific war effort that was then developing. He collaborated with Fermi and Anderson in some experiments preliminary to the production of a chain reaction. In the fall of 1941 he invented an electromagnetic method for separating the isotopes of uranium and led a group of about 50 scientists and technicians at Princeton in developing this technique.

Early in 1943 the work on the separation of uranium isotopes was limited to those methods that were ready for production. The work at Princeton was terminated, and Wilson was asked to set up a cyclotron laboratory at the new Los Alamos laboratory. He and some of his Princeton staff moved the Harvard cyclotron to the new site and began to study the properties of the fission process. At Los Alamos he was the leader of the Cyclotron Group, and in the summer of 1944 Oppenheimer appointed him to head the Physics Research Division, which was responsible for experimental nuclear research and later for nuclear measurements that were made during the test of the first atomic bomb.

Toward the end of the war Wilson worked effectively for civilian control of atomic energy. He played a leading role in the formation of the Federation of Atomic Scientists, became its chairman in 1946, and later served a term as a member of its council and a second term as chairman.

In the fall of 1946 Wilson accepted an associate professorship at Harvard. He spent the first eight months of 1946 at Berkeley, where he designed a 150-MeV cyclotron for Harvard. His stay at Harvard was short, for in the winter of 1947 he went to Ithaca to become the director of the new Laboratory of Nuclear Studies and professor of physics at

Cornell University. He remained in that position until 1967, when he left Cornell to assume the directorship of the National Accelerator Laboratory, now Fermilab, in Batavia, Illinois.

THE CORNELL YEARS

During Wilson's tenure at Cornell he and his colleagues built four electron synchrotrons, each with unique physics capability. In 1948, shortly before the first synchrotron began to operate, he described in his yearly report to the Office of Naval Research what he thought the research program would be:

The most important problems of nuclear physics, to our minds are: What are the elementary particles of which nuclei are made and what is the nature of the forces that hold these particles together? A more general but connected problem concerns the general expression of electrical laws at such high energies as will be produced by our synchrotron. Our experiments are planned to attack all three problems. Thus we hope to produce artificial mesons which are supposedly elementary particles and to study the interactions of these mesons with nuclei. Further, we shall explore the electrical interactions of high energy electrons with electrons and protons in search of evidence pointing to a correct theory of electricity at high energy.

Wilson's vision about future research was right on target. One would be hard put to improve on it today. It is the statement of a physicist with a very clear notion of why he was building the accelerator and where he was going. He built accelerators because they were the best instruments for doing the physics he wanted to do. No one was more aware of the technical subtlety of accelerators, no one more ingenious in practical design, no one paid more attention to their aesthetic qualities (he thought of accelerator builders as the contemporary equivalent of the builders of the great cathedrals in France and Italy), but it was the physics potential

that came first. And the clear ideas he had about the physics he hoped to do is amply demonstrated in the almost prophetic statement quoted above.

For some 20 years as director of the Laboratory of Nuclear Studies Bob remained deeply embedded in the physics program, both as mentor and experimenter. He did important experiments in pi-meson photo production, including the first observation of the second nucleon excited state and published an analysis of its properties; he did the first measurements of the photo-production of strange particles; he pioneered a class of experiments using the circulating synchrotron beam and with this technique did fundamental work on the structure of neutrons and protons, extending the pioneering work of Hofstadter at Stanford.

The first synchrotron, at 300 MeV, was designed and partly constructed before Wilson arrived at Cornell. It was a very productive machine, but by 1952 it was clear that the physics was urgently calling for higher energy and Bob initiated the construction of a 1-GeV synchrotron. Here is how Bob described his proposal in his 1953 annual report to the Office of Naval Research.

The Laboratory has indulged itself in some high adventure. A new synchrotron has been designed which is to give over a billion electron volts of energy. The design is highly controversial in that the new machine is exceedingly small and cheap for what it will do, hence there is considerable risk that it may not work at all. On the other hand, if we are successful, we shall have the largest electron accelerator in the world and new areas of research will be opened to us. . . .

This annual report tells us much about Bob as an accelerator builder. It really was a great adventure for the reasons enumerated, made even more adventurous by switching in midstream to the just-published strong-focusing design of Courant, Snyder, and Livingston. What is also revealing is the candor of the proposal. There was no guarantee of

success, only the guarantee of a scientifically exciting project worth the risk. Despite Bob's warning, the 1.4-GeV machine was very successful. Among the physics contributions were sensitive tests of quantum electrodynamics (QED) at short distances; discovery of the second nucleon resonance; first measurements of K-meson and rho-meson photo production; and precise measurements of nucleon structure. It was the first operating strong-focusing synchrotron and its design paved the way to more compact, less expensive accelerators. It should be noted that, characteristically, Bob had a fallback position for the riskiest aspect. The magnet was designed so that the pole pieces could be changed rather easily between strong-focusing and a conventional weak-focusing design. Bob was prepared to "climb out on a limb" if the reward was worth the risk, but he provided a safety net where he could.

The last machine that Bob built at Cornell was the 12-GeV synchrotron. This was the first accelerator to have the entire magnet evacuated so that it was not necessary to insert a separate vacuum chamber inside the magnet aperture. This made it possible to reduce the vertical magnet aperture to 1 inch, simplifying the magnet construction and reducing the power demands. This idea was subsequently adopted for the Fermilab booster accelerator. After about seven years of fruitful physics, devoted largely to QED studies at small distances, properties of the vector mesons, various tests of quark theory, and a big emphasis on the inelastic scattering of electrons, the 12-GeV synchrotron retired to a useful future as the injector for the Cornell electron storage ring, the electron-positron collider built between 1977 and 1999, and still serves that purpose.

In the 1940s and 1950s most of the accelerators were built at universities. There were perhaps 15 universities that had front-line accelerators. The only university for which

this is true today is Cornell, which has endured as an important center of experimental high-energy research in this age of giant national and international laboratories, because it has always had an accelerator with unique physics capability built for a modest price. Wilson insisted on this during his tenure as director, and the two subsequent directors, B. D. McDaniel and K. Berkelman, continued in this “Cornell style.”

FERMILAB

In 1967, after completing the 12-GeV synchrotron, Bob left Cornell to become the director of the new National Accelerator Laboratory (now Fermilab) in Batavia, Illinois. Wilson’s performance at Fermilab was remarkable. Starting on a “green field” site with no staff, he began the job of building the most ambitious accelerator project ever undertaken up to that time. In addition to the challenge of building a cascade of large accelerators at a virgin site in less than five years Wilson promised to double the energy of the accelerator over the original proposal without an increase in cost. In fact this was accomplished at a 30 percent lower cost than the first proposal for the facility. He was able to do that primarily by redesigning the magnetic structures and lattice. This meant he could build the magnets with smaller aperture and higher magnetic fields, thereby doubling the energy of the protons circulating in the same size tunnel. This approach was later adopted by the European Organization for Nuclear Research (CERN) for the super proton synchrotron. Despite a serious setback, which required repairing a large fraction of the magnets because of insulation failure, the accelerator was completed on time and under budget. The achievement of higher energy and more physics reach at the same cost are hallmarks of Wilson’s career, appearing bold and imaginative when proposed and often

considered risky and unrealistic. The fact that most of these principles were adopted in subsequent accelerators is further tribute to Wilson's vision and courage.

Wilson had a number of very positive principles having to do with construction projects. One was that there are certain design parameters that control the major costs. For example, in accelerator construction the magnetic aperture is likely to be the most sensitive cost-controlling factor. The amount of steel, copper, power, power handling equipment, and building costs all depend sensitively on this factor. He also believed that to build cheaply it was necessary to build rapidly. Rapid construction maintains excitement and esprit de corps, while slow construction runs up costs. He believed that it was essential to complete all those parts that could be made functional at the earliest possible time, in order that performance tests could be performed to confirm the validity of design and construction. He also felt that a highly engineered design was likely to end as being an over-design and in the end might be a faulty design requiring further modification anyhow. He preferred to make a design without a lot of safety factors, taking the risk that modification might be required later. He believed that, with the appropriate consideration for back-up provisions, this saved time and, in the long run, money.

Wilson followed these principles in designing the Fermilab accelerator. In his first design study he reduced the estimated time to seven years, but as construction proceeded rapidly he reduced the official schedule to six years. He had also set an internal target for the accelerator staff of completion in only five years. This made it possible to complete the facility within the official schedule in spite of major problems with the guide field magnets. The project was finished under budget and fully operating within six years of its start.

In addition to the technical success of the original accelerator Fermilab was also designed with a grace and beauty that makes it unique among high-energy physics laboratories. This fact, attested to by a number of prizes awarded for its architecture, shows the other side of Wilson: The artist who believed art and science should blend to form a harmonious whole that not only benefits scientific research and society but also extends its culture. This concern of Wilson is eloquently expressed in his colloquy with Senator John Pastore in testimony before the Congressional Joint Committee on Atomic Energy on April 17, 1969.

Senator Pastore: "Is there anything connected with the hopes of this accelerator that in any way involves the security of the country?"

Robert Wilson: "No sir, I don't believe so."

Pastore: "Nothing at all?"

Wilson: "Nothing at all."

Pastore: "It has no value in that respect?"

Wilson: "It has only to do with the respect with which we regard one another, the dignity of men, our love of culture. It has to do with are we good painters, good sculptures, great poets? I mean all the things we really venerate in our country and are patriotic about. It has nothing to do directly with defending our country except to make it worth defending."

Fortunately, during the construction of the Fermilab accelerator tunnel adequate space had been provided for flexibility. This foresight was rewarded some years later with

the construction in the same tunnel of the world's first superconducting collider at an energy of 2 TeV. At this writing that is still about twice the energy of any other operating accelerator.

The tevatron undertaking was vintage Wilson. The accelerator required approximately 1,000 very accurate and reliable superconducting magnets to guide the circulating beams. It required an enormous leap in superconducting technology. Wilson provided the vision and leadership and devoted personal involvement during the several years of difficult R&D required to establish the mass-production technology and to make it possible for a remarkably low cost. The tevatron demonstrated the feasibility of large accelerators built with superconducting magnets and paved the way for HERA in Hamburg, Germany, the relativistic heavy ion collider at Brookhaven, the ill-fated Superconducting Super Collider in the United States, and the large hadron collider now under construction at CERN. Without the superconducting technology the capital and operating costs for multi-TeV storage rings would be prohibitive. Construction of the tevatron led to a large expansion in commercial production of superconducting cable, now used extensively in magnetic resonance imaging.

It must be noted that Wilson was unable to lead personally the tevatron construction to completion. Near the end of the R&D period Wilson asked the Department of Energy for a higher level of funding in order that the development could proceed at a fast pace and at the same time support the heavy financial burden of fully utilizing the existing 400-GeV accelerator for research. It was typical of Bob's driving determination that he handed in his resignation as a matter of principle to protest against what he considered to be under-funding of the laboratory. Somewhat later the support level was increased, but unfortunately by that time

it was too late. Subsequently Leon Lederman was named director; then he, together with the Wilson-trained staff, brought the Wilson-inspired tevatron into operation. After his resignation from Fermilab Wilson held professorships at the University of Chicago and Columbia University and retired in 1983.

Wilson's influence was enormously important to the physics program and to the results achieved at Fermilab, the two most important being the discovery of the b-quark and the top quark. This third and heaviest family of quarks "belongs" to Fermilab. Running at the highest possible machine energy was crucial to these discoveries. It was Wilson's insistence on operating the main ring at the highest possible energy (in the face of considerable opposition from some experimenters who wanted to reduce the energy to improve the momentary reliability of the accelerator) that made possible the discovery of the b-quark. For Wilson, energy was the key to new discovery. This was, of course, also the case for the much heavier top quark, for which the full energy of the tevatron was required.

HADRON CANCER THERAPY

A paper of Wilson's published in the journal *Radiology* in 1946 and entitled "Radiological Use of Fast Protons" has assumed great importance. In 1941 Wilson had made accurate measurements of the range and energy deposition of fast protons as they traversed matter. He observed that protons deposit most of their energy near the end of their path in what is called the Bragg peak. There was nothing unexpected about this measurement, but it led him to a happy and far-reaching idea—to use protons for cancer therapy. Wilson noted that, because of the Bragg peak and by carefully controlling the energy of a proton beam, most of its energy could be deposited in a cancerous tumor inside the body.

This is in stark contrast with radiation treatment by electron or photon beams obtained from radioisotopes like cobalt, which attack healthy and cancerous tissues indiscriminately. The first facility for this therapy was at the Harvard cyclotron. Subsequently a similar facility was installed at Fermilab. Proton beams have now been used successfully for cancer therapy at a number of accelerators. With the advent of magnetic resonance imaging and positron emission tomography, which can determine the positions of cancerous tumors with high precision, there has been a large increase in interest in this therapy, and single-purpose hospital-based proton accelerators have been built for hadron therapy in many different countries. Wilson was honored for his pioneering work in this area at an international conference held at CERN in 1996.

AWARDS AND HONORS

Wilson was awarded honorary degrees from Notre Dame University, Harvard University, University of Bonn, and Wesleyan University. Among the many other honors he received were the Elliot Cresson Medal from the Franklin Institute, the National Medal of Science, the Enrico Fermi award, the Wright prize, the del Regato Medal, and the Gemant award. He was a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society. In 1985 he was elected to the presidency of the American Physical Society.

Throughout the course of his life, in everything he did, Wilson's effervescent personality came through. He was a man filled with exciting ideas; inventions; interest in art, humanities, and nature; and high ideals and moral principles. Some examples of these interests include the restoration of the grasses of the Great Plains and the buffalo herds on the Fermilab site; his artistic stamp on the archi-

tecture at Fermilab; his personal sculptures at the laboratory and in his own home; his role in promoting international cooperation as one of the organizers of the International Committee on Future Accelerators; his very effective affirmative action program at Fermilab; his commitment to the Federation of Atomic Scientists and the American Physical Society and his long-time work toward proton therapy; his determination never to give up a difficult recovery attempt in a squash game; and dozens of other examples. Wilson was truly a man who enjoyed living life to the fullest.

Wilson's legacy to high-energy physics and the laboratories he built survives his death. This feeling was eloquently expressed by Judy Jackson, director of public affairs at Fermilab, in a letter to Bob's son, Jonathon. She wrote,

It is probably impossible to overstate his [Bob's] influence on Fermilab. I think most of the time institutional memories are rather short; even people who play important roles are forgotten surprisingly quickly. This is emphatically not the case for Fermilab and your father. One cannot spend a day, or an hour, without feeling his presence in the architecture, the prairie, the accelerators, and the attitude. For once it is no cliché to say he lives on; he really does.

WE WISH TO THANK Jane S. Wilson for much helpful information about Bob's work and life.

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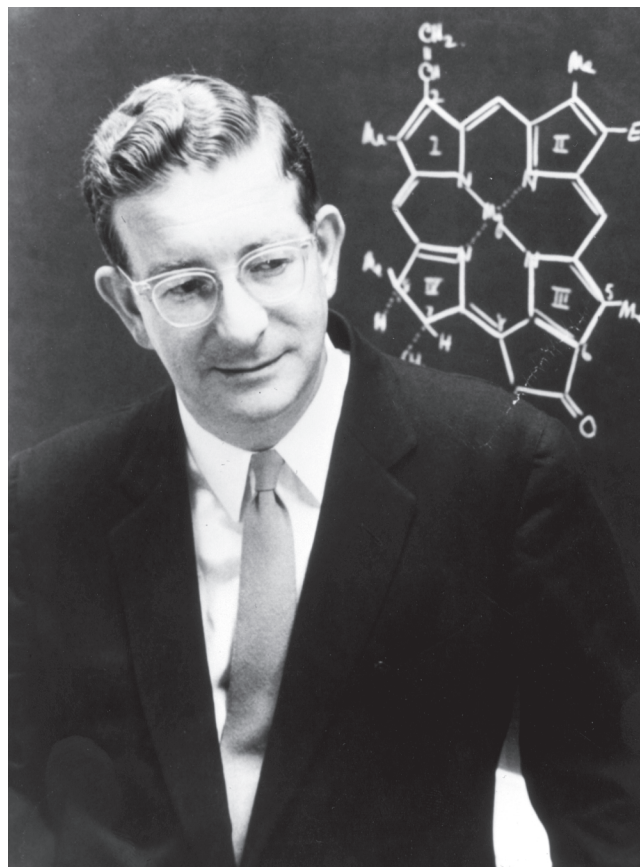
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ROBERT BURNS WOODWARD

April 10, 1917–July 8, 1979

BY ELKAN BLOUT

ROBERT BURNS WOODWARD was the preeminent organic chemist of the twentieth century. This opinion is shared by his colleagues, students, and by other distinguished chemists. Bob Woodward was born in Boston, Massachusetts, and was an only child. His father died when Bob was less than two years old, and his mother had to work hard to support her son. His early education was in the Quincy, Massachusetts, public schools. During this period he was allowed to skip three years, thus enabling him to finish grammar and high schools in nine years. In 1933 at the age of 16, Bob Woodward enrolled in the Massachusetts Institute of Technology to study chemistry, although he also had interests at that time in mathematics, literature, and architecture. His unusual talents were soon apparent to the MIT faculty, and his needs for individual study and intensive effort were met and encouraged.

Bob did not disappoint his MIT teachers. He received his B.S. degree in 1936 and completed his doctorate in the spring of 1937, at which time he was only 20 years of age. Immediately following his graduation Bob taught summer school at the University of Illinois, but then returned to Harvard's Department of Chemistry to start a productive period with an assistantship under Professor E. P. Kohler.

He remained at Harvard until his death in 1979. Although Bob remained formally at Harvard for his entire professional life, he traveled extensively in order to lecture, receive awards, and sometimes to relax for a day or two with friends.

During the period 1945 through 1978 he received 24 honorary degrees. He was also the recipient of 26 medals and awards, which included the most prestigious in the world of chemistry. He was elected to the National Academy of Sciences in 1953 at the notably young age of 36. In addition, Bob was elected to membership in numerous academies and learned societies. A more complete and personal biographical summary, including a listing of his honors and awards, can be found in the Royal Society memoir by Lord Todd and Sir John Cornforth.¹

What kind of a person was Bob, and how do we remember him? He was a genius and a very sensitive individual with a prodigious memory. He also had a drive to solve difficult problems and liked teaching in the broadest sense of the word. His lectures were models of clarity, originality, and insight. He enjoyed starting at the upper left-hand corner of a very large blackboard and finishing at the lower right-hand corner with precise formulation of his ideas and thoughts and a total package that was characteristically Woodwardian. He really relished lecturing to students and to colleagues, but he did not enjoy formal courses. Fortunately, in the middle of his Harvard career, Bob was given an endowed professorship in 1962 that eliminated the need for him to teach regular courses. However, he maintained, "I teach all the time so that I don't have to teach formal courses." He taught in the laboratory, in seminars, and via lectures, so here was no question that he was an expert in this kind of teaching.

He accomplished much in several diverse areas (e.g., the correlation of various physical methods with organic

structures, determination of the structures of complex compounds, the syntheses of many naturally occurring biological compounds, and devising beautiful and concise synthetic pathways for complicated molecules). Last but not least, he had a deep appreciation of the wonders of nature and often attempted to understand many of the relations between the biological world, the chemical world, and the synthetic chemistry world in which he practiced so adroitly. Among the achievements of Woodward in the field of organic synthesis are the total syntheses of quinine, steroids, strychnine, reserpine, chlorophyll, and, finally, one of the most important and complicated naturally occurring molecules, vitamin B₁₂.

During his lifetime he authored or coauthored 196 publications, of which 85 are full papers, the remainder comprising preliminary communications, the text of lectures, and reviews. The pace of his scientific activity soon outstripped his capacity to publish all experimental details, and much of the work he participated in is even now being published by his colleagues and coworkers.

In preparing this review I was assisted by written communications relating to Bob's work by Derek Barton, Albert Eschenmoser, and Roald Hoffmann. Many of his students and postdoctoral fellows wrote to describe their feelings, attitudes, and assessments of Bob Woodward as a mentor, as a teacher, and as a friend. We regret that space does not allow us to include many of these statements, but we will do our best to present the feelings of some of them in the next sections.

EARLY SCIENCE

(WITH INPUT FROM DEREK BARTON)

In 1948, when he was 31, Woodward gave a brilliant lecture at Imperial College, London, on the structure of santonic acid. He spoke without notes or slides and covered

the blackboard with beautifully drawn formulae. He argued that santonic acid, a compound obtained from santonin and hitherto without a structure, was formed by the base-catalyzed opening of the lactone ring with alpha-beta double bond shift to give a keto-acid, the anion of which cyclized to give santonic acid. He showed that the latter must be a derivative of cis-decalin.

Every scientist must be judged by the standards of his time. In 1948 we had never heard anyone pose, and then resolve, a problem in such a clear and logical manner. Woodward was the first to show that problems in chemistry could be solved by thinking about them. The scientific world first heard of Woodward between 1940 and 1942 because of his publications on the correlation of ultraviolet spectra with structure (1941,1942). He next became famous for the formal synthesis of quinine (1944), in association with W. von E. Doering.² This was Woodward's first multistep synthesis. For this synthesis he immediately gained the respect of the older generations of organic chemists.

Woodward was exceptionally gifted in deducing structures. At a time when physical methods were not yet perfected he could integrate an enormous number of facts, both clear and misleading, into a coherent whole better than any chemist who had ever lived. During World War II he started with a reasoned argument (1944) for the beta-lactam formula for penicillin, in contrast to the incorrect oxazoline formula advocated by Sir Robert Robinson and others.

The problem of the structure of strychnine had been a challenge to organic chemists for more than a century. Robinson had worked hard and well on this subject for many years, and immediately after the war he made it his major project. It was a perfect challenge for Woodward. There was an enormous body of fact that, with the aid of a

minimum of concise experimentation, led him to deduce the correct formula (1954).

In 1949 Barton was invited to spend a year at Harvard to replace Woodward, who was on sabbatical leave. It was no surprise to anyone also that Woodward stayed exactly where he was. At that time his evening seminars were marvelous, with Gilbert Stork also participating in a stimulating way. In theory a speaker would be recruited to talk about his work starting at 8:00 p.m., but in fact at approximately 8:30 p.m. The speaker would be closely questioned by all. At about 10:00 p.m. Woodward would pose a problem from the literature. Guests and students would then spend up to an hour trying to solve this problem. When they had all failed Woodward would give his solution, which was always correct. He would then call for anyone else to pose a problem. This being done, it was usually Woodward who proposed the correct answer first. However, this was somewhat unfair, because as midnight approached Woodward got better and better; at least it seemed like that, while others tired.

The most brilliant analysis ever done on a structural puzzle was surely the solution (1953) of the terramycin problem. It was a problem of great industrial importance, and hence many able chemists had performed an enormous amount of work trying to determine the structure. There seemed to be too many data to resolve the problem, because a significant number of observations, although experimentally correct, were very misleading. Woodward took a large piece of cardboard, wrote on it all the facts and, by thought alone, deduced the correct structure for terramycin. Nobody else could have done that at the time.

The first major synthesis by Woodward after quinine was that of the steroid nucleus, including cholesterol (1951) and cortisone (1951). Woodward went to the United Kingdom in 1951 to deliver a Centenary Lecture. He spoke about

his total synthesis of steroids, which was brilliant, and all in the audience were impressed when he showed the formula and said that this was known as chrimasterol because it was first synthesized on Christmas day in 1950.

The next important target chosen was strychnine (1954). Strychnine had five asymmetric centers, and therefore would seem to be a difficult objective. However, Woodward realized that the constitution of the molecule was such that it defined its own configurations and that a total synthesis should be relatively easy. An elegant synthesis was planned and executed with highly talented collaborators, again in a short time.

During the same *époque* Woodward and Barton collaborated on another total synthesis (by relay). The determination of the structure (1954) of lanosterol suggested to Woodward that this biosynthetically important compound should be synthesizable by the addition of three methyl groups to cholesterol, whose total synthesis he had just accomplished more easily than expected.

Woodward now began what may be the most beautiful synthesis of his life, the synthesis (1956) of the medicinally important alkaloid reserpine. This synthesis was meticulously planned and executed in less than two years by a highly gifted group of coworkers. It was a challenging stereochemical problem, and it was a pleasure to see how skillfully he used the now mature theory of conformational analysis.

Now we come to the funding of the Woodward Institute in Basel by the Ciba Company. Ciba research was reorganized with Dr. Heusler, who had participated in the Woodward steroid synthesis, joining the new Woodward Institute, directed by Woodward. Their first project was the synthesis of cephalosporin C starting with L-cysteine, and he produced an elegant and sophisticated synthesis that was completed just in time (1966) for the Nobel Prize ceremony in

1965. The Woodward Institute continued to do good work until his death.

This account of Woodward's earlier scientific life reflects his unique intellectual superiority in his own generation. In the 1940s he was already a mature and apparently self-assured young man who knew more organic chemistry than anyone else did, and who could instantly integrate the remembered facts to face a new challenge. He pretended to be lazy and to be without ambition; he was just the opposite. In the 1950s his work in several areas reached a level of brilliance that may never be equaled.

INTERMEDIATE SCIENCE
(WITH INPUT FROM ROALD HOFFMANN)

In 1983 Woodward gave a lecture at an American Chemical Society meeting in which he described his pleasure at seeing the original publication by Diels and Alder describing the discovery of the reaction that bears their name and his lifetime preoccupation with that reaction. He made use of the Diels-Alder reaction in a marginally commendable (in his own words) approach to the synthesis of oestrone during the middle 1930s in the course of his work for his Ph.D. degree. Much later he used the Diels-Alder reaction with greater effect in the syntheses of cholesterol, cortisone, and reserpine. And beginning in 1939 he remembered that he pursued a number of investigations explicitly concerned with the detailed course and mechanism of Diels-Alder reactions.

Theoretically, interesting molecules always intrigued Woodward. The paper that marks the beginning of modern organometallic chemistry, the assignment of the correct sandwich structure of ferrocene, bears not only the name of one of the future leaders of the field, Geoffrey Wilkinson, but also of Woodward and two of his coworkers, M. Rosenblum and M. C. Whiting.

It is likely that it was his colleague William Moffitt who sharpened Woodward's perception of modern theoretical chemistry and introduced him to molecular orbital theory. Though the remarkable generalization that is the octant rule was initially empirically formulated by Woodward, Klyne, and Djerassi, the theoretical support it received from Moffitt and Moscovitz was essential (1961).

Woodward then began to think in orbital ways. One interesting piece of evidence of this was a comment he made after a lecture by Rolf Huisgen at a Welch conference in 1961, where he drew quite explicitly the orbitals of a vinyl carbene and asked, "Do we have specific orbital requirements for this reaction and would they in this case preclude the operation of the mechanism, which is so general in many of the cases?"

It is clear that Woodward was exceedingly well prepared for what ensued. In the course of the synthesis of vitamin B₁₂ he raised and considered many theoretical points in trying out some reactions that would create several asymmetric compounds in one step. He concluded that electronic effects had to be at work to explain the observed results. The reaction was the cyclization of a hexatriene to a cyclohexadiene. It is clear that one of Woodward's main interests in his latter years was the rationalization of organic synthesis through the use of orbital symmetry in predictions of conformations. In 1964, after a brief discussion with E. J. Corey and others of his thoughts and his chemical results, Woodward was able to formulate his important ideas in this area. Some of them were published in the book *The Conservation of Orbital Symmetry* (1970) with his collaborator, Roald Hoffmann. Woodward turned for theoretical support to a promising young theoretician, then a junior fellow at Harvard (as Woodward had been 20 years earlier). This was Roald Hoffmann, then 26 years old. Hoffmann began by corroborating

Woodward's simple orbital idea. Quickly a true collaboration developed that led to five communications (1965) that changed the nature of the interaction theory with experimental organic chemistry.

Woodward and Hoffmann in a remarkable blue-green paper in *Angewandte Chemie* (1969) and book showed that frontier orbital arguments, the simple nodal structure of orbitals, enforced by their symmetry could explain the concertedness or lack thereof and many important stereochemical selectivities in every reaction. They extended their consideration from electrocyclic reactions to cycloaddition and other concerted reactions. Here recall Woodward's nearly 40-year-long interest in the Diels-Alder reaction and to sigmatropic reactions, which included the Cope rearrangement and various bond shift reactions. The predictions made by Woodward and Hoffmann were easily accessible to modern organic chemists already introduced to orbitals by important books on this subject. The predictions were readily verifiable, and there was a large community of physical organic chemists ready and able to test them. Within two years, in a flood of beautiful experimental work, the fantastic insight into the workings of nature achieved by the orbital symmetry rules lay clear. Quantum mechanics and organic chemistry were drawn much closer to each other.³

SCIENCE IN THE LAST YEARS

(WITH INPUT FROM ALBERT ESCHENMOSER)

It is clear that two of the major synthetic achievements of Woodward are those that occurred in the 20 years prior to his death, namely, the synthesis of chlorophyll and the synthesis of vitamin B₁₂. Woodward's analysis of the complex structure of chlorophyll and the transformational aspects of what he called "a chemical fairyland" rests securely among the great chapters of interpretative natural products

chemistry. The result of this analysis was a visionary plan for the synthesis of chlorophyll. The essence of his approach and his synthetic plan derived from his stereochemical analysis that a porphyrin substituted in the γ position can be expected to be convertible into a chlorin with the correct structure.

Woodward's conclusion that he would be able to use the porphyrin to chlorin transformation was the key to his synthesis but was not supported on the basis of any known change from a suitably constructed porphyrin molecule. He had the faith of "an impassioned mountaineer" who would negotiate the critical phase of an ascent on the basis of analysis, experience, and strength. This synthesis bears witness to Woodward's extraordinary ability to explore and also to deal with discoveries made in the course of the synthesis.

It was a source of some satisfaction to Woodward that a photochemical reaction was incorporated into his chlorophyll synthesis as an important step. It has been stated that perhaps the most important element in his synthesis was when he could pit his intellect against the puzzles provided by unforeseen observations, and perhaps his greatest strength in synthesis was his capacity of overcoming the experimental difficulties that could interfere with his original plan. He had a deeply rooted conviction, nurtured by the history of natural products chemistry, that the chemist is offered an opportunity to explore new phenomena as a consequence of the elucidation of unanticipated findings in synthesis.

With the completion of this synthesis, Woodward stood at the summit of recognition: He had mastered chlorophyll, the material that gives the continents their primary color and the heart of photosynthesis in all green plants on Earth. It is a substance deeply anchored in the consciousness of humanity as a material upon which ultimately our entire existence depends. Finally, it could be argued that natural

product synthesis had been invoked at an important time in the exercise of one of its original functions, namely, to provide chemical proof of the constitutional formula of a natural product.

As Woodward began to tackle the synthesis of more and more complicated biologically important natural products, he ultimately chose to attack vitamin B₁₂.⁴ At Harvard this work started in 1961 and gradually evolved into a unique collaboration between Woodward's group and the group of Eschenmoser at ETH. This work culminated in the announcement by Woodward of the total synthesis of cobyrinic acid (1973).

The two major challenges posed by the vitamin B₁₂ structure were the novelty of the ligand chromophore and the stereochemical complexity of the ligand's periphery. Woodward's main focus was the latter. This led him to create a great synthesis of the so-called "Harvard component"—the part of the B₁₂ molecule that is the most complex and contains rings A and D. This synthesis, both in design and execution, appears today as the apotheosis of all that constituted the Woodwardian art and science in natural products total synthesis. Forever in the history of chemistry it will also remain connected with that creative insight of Woodward that eventually grew into the message of the Woodward-Hoffmann rules, changing the way organic chemists think about the reactivity of organic molecules.

REMINISCENCES ABOUT A SPECIAL MAN

I first met Bob Woodward a week or so after I arrived at the Chemistry Department of Harvard as a National Research Council fellow. In this initial meeting he was as advertised by his senior colleagues—intense, committed, and brilliant. As a result of this meeting he and I worked together experimentally for well over a month, and this resulted in the

publication of a paper in the *Journal of the American Chemical Society*. Perhaps this was the last time that I knew he did experiments in the laboratory.

As a result of this initial experience he invited me to join an embryonic poker game that met in the basement of Harvard's Converse Laboratory on some late evenings each month. This poker game still exists now, in a slightly altered form, some 50 years later. The following are some not-so-random thoughts about Bob and many of his qualities. His intensity as a scientist is well known (*vida supra*), but he was just as intense in the nonscientific areas of his life. When he wanted to be, he was quite a social person. I remember some of the parties at his Belmont, Massachusetts, home, where puzzles and games were played at his behest and with his participation. He loved such challenges, and as an example, I should tell that he loved doing *The New York Times* crossword puzzle every day, but of course, only in ink. It wasn't necessary for him to erase. He loved and appreciated good food and also good drink. In fact, there was a period in his life where he was drinking a lot and enjoyed having contests with a select few visiting scientists whom he liked socially. He loved to be able to drink more than his colleagues, and he loved trying to prove it (successfully) on many occasions.

Was he into sports? I would say not really, but although on occasion his competitive instincts got the better of him, and he played baseball with some of his younger colleagues. Did Bob have any strong likes except for research and science? Well, as we know, he was married to his first wife Irja Pullman at a very early age, and with Irja he fathered two daughters, Siiri and Jean. Following his separation from Irja, he tried to play the field with women he knew, but he was too straightforward a person to do it with abandon. After this period, he did undertake a second marriage with Eudoxia Muller,

and this marriage had very good times as well as many rough spots. As a result of this marriage he fathered two additional children: a daughter who Bob and Doxie named Crystal and a son named Eric. When this marriage broke apart in 1966, he became a not-so-willing bachelor. He still enjoyed female companionship and several, including his secretary, were close to him during this period.

One relationship (not female) that was important to him was with Edwin ("Din") Land, the founder and chief executive officer of Polaroid Corporation. He became a consultant to Din in 1940, and it was a relationship that was maintained despite varying interests by each party through a long period of years. As a result of Bob's input, when I left Harvard temporarily to join Polaroid as its chief chemist in 1960, Bob and I spent a lot of time together while he was a consultant to the company during the critical phases of the development of the Polaroid instant photographic color process. He was a wonderful consultant; he was able to be as intense and thoughtful in his criticism and imagination in fields relating to color chemistry as he was in his own active fields of chemistry (i.e., natural products). During this period he gave us at Polaroid many suggestions and much criticism that helped in the final development of the color photographic process. It was also during this period that Polaroid issued options to its most important personnel (e.g., the vice-presidents of the company). Knowing Bob's contribution to Polaroid, I talked to Din Land about doing an unusual thing: Give this unusual scientist, who was not a Polaroid employee, an option on Polaroid stock. Land agreed after some discussion, and Bob received this option; it played a very positive part in the financial aspects of his later life. In some ways it allowed him to be as independent financially as he was scientifically.

He loved to smoke and smoked two or three packs a day

from 1942 until his death in 1979. Many of us tried to get him to give up this habit, but we were not successful.

As we know from some of his scientific activities, symmetry played a large part in his thinking and, in fact, it played a part in his personal life. He had a very symmetrical license plate, and he tried to have symmetrical relations with his children, although that was not always successful. He had very strong likes as a person. Some of these were his love of the color blue, which he showed by only using blue neckties and only wearing dark blue suits. His parking place at Harvard was painted blue (by a couple of students) so that no one would use it inadvertently. In addition, in his later years he had a well-loved blue Mercedes sedan that occupied this parking space during the days and nights when he was doing science in Converse.

I can testify that he also liked adventure in areas other than science. I remember well when I bought a new twin-engine fishing boat in 1960, and we tried it out one day by going from Cuttyhunk to Doxie's homeport of Bridgehampton on Long Island. The day was very foggy, and we didn't have any instruments aboard except a compass and a depth meter. Did Bob want to try running the boat? "Of course," he said. He loved it, and actually very much enjoyed piloting the boat for several hours without incident.

In his later years, although he was most interested in science, I observed that he was much more aware of the importance of one-to-one relationships; some he had with his children and some he had professionally. I can testify that when he had a personal relationship he spared no effort. It was as intense as the way he did science. He came through for me in many critical times in my life, and I hope I did the same for him. In personal relationships he knew what was important; he tried to further them with thoughtfulness and intense understanding. I, along with many

of his friends, students, and colleagues, can testify how he came through for us in critical areas and times in our lives. He was an emotional man, although he didn't show it often. This emotion led him to be very supportive in close relationships like we had. After the breakup of his second marriage, Bob showed many interests in addition to science. For example, it was clear that he had become a strong Anglophile, and he spent a lot of time in London in its multiple galleries and hotels. In addition, an interest in antiques was awakened, and he began to collect English furniture as intensively as he did science. I regret that many of the beautiful pieces he collected and had in his apartment have now been sold.

In his last years he became much more social, not in a global sense, but in his relationships. When he was in Cambridge we had dinner at least once a week. Even though he loved having a home-cooked meal practically every week with my wife, Gail, and me, we varied the routine by occasionally going to local restaurants. The night before he died we had a wonderful dinner together at the Stockyard and left him in a very good mood when we separated at about 11:00 p.m. During the next hours he suffered a fatal heart attack, and I never saw him again. Although in this period he had many symptoms of a cardiac condition, he ignored them as if they weren't important, and maybe such symptoms were not important to him.

SOME PERSONAL RELATIONSHIPS

In addition to the personal relationships indicated above, Bob had at least two corporate relationships that he specially valued. The first was to a small company called CHON Corporation and the second one was to a very large company Ciba-Geigy. CHON Corporation was set up in 1974 by a group of scientists with the idea of encouraging academic

research that might have practical value. One project undertaken by CHON was the development of a high-temperature superconducting polymer. Bob spent several days and weeks trying to think of suitable approaches of what would be new substances. The writings on his ideas are still in the CHON files.

The second corporate relationship that was important to Bob Woodward was his involvement in a research institute in Basel, Switzerland. It started in 1963 and was appropriately named the Woodward Research Institute. This institute, which was his own domain, allowed him to do original research with a practical flavor. J. Gostelli was his senior colleague there. It was well supported originally by Ciba Company and eventually by Ciba-Geigy. His involvement with Ciba-Geigy increased over time, especially after he was elected to its Board of Directors in 1970. In spite of his other interests I am told that his directorship at Ciba-Geigy allowed him to be involved in the real world of the chemical industry in practice, and he found this exciting. Perhaps it appealed to another aspect of Bob Woodward's character.

When it became clear that we were going to write a memoir for the National Academy of Sciences, many of his former colleagues and students wrote to give us some of their thoughts on this remarkable man. A selection of some of these personal feelings follows.

Obviously, a life like Woodward's is not lived without working long hours. Much of his peace and quiet used to come in the night hours after everybody else had left the laboratory. As his noon-to-three-a.m. hours became proverbial, and his eager disciples acquired the habit in increasing droves, so the midnight solitude was no more.

He had the courage to work on a series of more and more complex and difficult natural products during his career, and the intelligence, imagination, energy, and skill to succeed. He inspired the revolution in synthetic

organic chemistry, which continues until this day. His synthetic routes are often described as elegant. They incorporate features, which are surprising and would not be expected to occur to other chemists. Often some aspects of the synthesis were inspired by Woodward's ideas concerning the biogenesis of these molecules.

We arrived at the night club and Armstrong was already playing. I introduced Bob to my friend saying, "This is Bob Woodward." My friend turned around impatiently, shook his hand, and returned his attention to the music. I said, "Look, Bill, Bob Woodward is to organic chemistry what Louis is to the trumpet!" At that my friend turned around slowly, looked Bob in the eye, and said, "Man, you must be one hell of a chemist!" Bob said he thought that was the most sincere compliment he ever got.

Bob was very interested in architecture, and at least on one occasion said that he might have liked to become an architect. . . . His habit to start a new pack of cigarettes when the former one was half-empty and to order two daiquiris, which might in both cases have been a sign of continuity of keeping a chain uninterrupted.

I know that he was very interested in mathematical problems. I exchanged problems with him for a while. I once heard him say that, when he was young, he thought of becoming a mathematician. The reason that he did not do so was that in mathematics any new original idea you had was okay. He contrasted this with chemistry where one always had to test any new idea against experimental results in the real world. He considered that this challenge made chemistry a much more demanding and therefore more attractive field to work in.

I owe a lot to R. B. Woodward. He showed me that one could attack difficult problems without a clear idea of their outcome, but with confidence that intelligence and effort would solve them. He showed me the beauty of modern organic chemistry, and the relevance to the field of detailed careful reasoning. He showed me that one does not need to specialize. Woodward made great contributions to the strategy of synthesis, to the deduction of difficult structures, to the invention of new chemistry, and to theoretical aspects as well. He taught his students by example the satisfaction that comes from total immersion in our science. I treasure the memory of my

association with this remarkable chemist, and deeply regret his premature death.⁵

Originally, this manuscript was to be the responsibility of Konrad Bloch, Frank Westheimer, and Elkan Blout. Unfortunately, Konrad Bloch became ill before he could contribute to the writing. I am indebted to Derek Barton, Roald Hoffmann, and Albert Eschenmoser for comprehensive pieces about Bob's scientific work. I am also indebted to the several former students, postdoctoral fellows, and colleagues who contributed anecdotes and quotations about Bob's life and scientific achievements. Finally, I want to acknowledge the continuing and thoughtful advice on this memoir by a wonderful colleague who should have been a coauthor, Frank Westheimer.

NOTES

1. Lord Todd and Sir John Cornforth. *Robert Burns Woodward Biographical Memoir*, pp. 629-95. London: The Royal Society, 1982.

2. It should be recorded that at least part of the stimulus for Bob Woodward to do a quinine synthesis in the 1940s was due to the need of quinine by the Polaroid Corporation for a synthetic polarizer invented by Edwin H. Land. Although the synthesis was accomplished by Woodward and Doering, it was never used industrially, because new polarizers with superb qualities had been invented by that time. Gilbert Stork has pointed out recently that Woodward and Doering's synthesis was not a complete synthesis of quinine and raises questions about the stereospecificity of the synthesis, while not detracting from its originality (J. Am. Chem. Soc., 123, 3239 (2001)).

3. In 1981 Roald Hoffmann and Kenichi Fukui received the Nobel Prize in chemistry for discovering the rules governing the course of chemical reaction. Many scientists feel that, if Bob had lived, he would surely have shared in this award.

4. A. Eschenmoser. RBW, vitamin B₁₂, and the Harvard-ETH collaboration. In *Robert Burns Woodward: Architect and Artist in the World of Molecules*. American Chemical Society-Chemical Heritage Foundation, in press.

5. When Konrad Bloch and I were raising money for a Woodward professorship at Harvard, many of the organizations cited above indicated their strong and positive feelings about Bob by contributing generously to this professorship.

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