Associations with outstanding scientists during a research career in microbiology and biochemistry

by Howard Gest

Distinguished Professor Emeritus of Microbiology
Adjunct Professor, History and Philosophy of Science
Indiana University, Bloomington

Associations with distinguished scientists during an academic career of over 60 years. Memorabilia include various research papers, books, correspondence, photographs and obituaries.

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Barber, James (FRS)                              Levi-Montalchini, Rita (Nobel L)
Berg, Paul (Nobel L)                               Lipmann, Fritz (Nobel L)
Calvin, Melvin (Nobel L)                           Luria, Salvador (Nobel L)
Coryell, Charles (AAAS)                           Mandelstam, Joel (FRS)
Delbrück, Max (Nobel L)                            Mitchell, Peter (Nobel L)
Hershey, Alfred (Nobel L)                         Szilard, Leo (NAS)
Hill, Robert (FRS)                                van Niel, Cornelis (NMS)
Horowitz, Norman (NAS)                            Wood, Harland (NMS)
Kamen, Martin (NAS)                               Yanofsky, Charles (NMS)
Krebs, Hans (Nobel L)

AAAS: American Academy of Arts and Science
FRS: Fellow, Royal Society of London
NAS: Member, U.S. National Academy of Sciences
NMS: National Medal of Science
Nobel L: Nobel Prize Laureate.

*It can be assumed that Americans awarded Nobel prizes (or NMS) were or became members of NAS. This is also true for many foreign Nobel Laureates.*
Introduction

There is little doubt that future historians will designate the 1930’s to 1980’s as the “Enlightenment” decades of cell biology and biochemistry. During this period, pioneering scientists explored biological phenomena with great ingenuity and erected a basic framework of understanding for coming generations of investigators.

After World War II ended, an expanding explosion of research began in the biological sciences. The use of radioactive and stable isotopes as tracers became powerful tools for exploring the complexities of cell growth and metabolism. Major metabolic cycles were delineated, and when the basic structure of DNA was determined in 1953, our understanding of genetics took a giant leap forward. It was not long before genetics became a molecular science. These developments were paralleled by important insights into the mechanisms of virus replication. Meanwhile, minute details of cellular structures and their functions were discovered and our understanding of enzymes—the cell’s catalysts—became very sophisticated. The basic principles of bioenergetics were solved. The foregoing is only a sketchy account of the great advances during the “Biological Enlightenment.” With new automated and other research techniques introduced during the past fifteen years, further details of biochemical processes are being actively pursued, yielding an avalanche of data that will take decades to decipher.

My research career happened to coincide with the extraordinary period 1940-1990. Fortunately, along the way, I interacted with a considerable number of outstanding scientists. In this narrative, I review the nature of my associations with about twenty of them, and focus on their
important contributions to our present state of knowledge. In a 1994 publication (1), I touched on some of these aspects of my career, but primarily in the context of technical details of microbiological and biochemical researches in my laboratory.

**Associations during formative years: 1940’s – 1960’s:**

- Charles D. Coryell 1912-1971
- Max Delbrück 1906-1981
- Alfred D. Hershey 1908-1997
- Norman H. Horowitz 1915-2005
- Martin D. Kamen 1913-2002
- Hans A. Krebs 1900-1981
- Salvador Luria 1912-1991
- Joel Mandelstam 1919 –
- Leo Szilard 1898-1964
- Cornelis B. van Niel 1897-1985

See photographs after References.
Formative years

During my high school years in Los Angeles, I became firmly committed to a career in science. I vividly recall journeys to the California Institute of Technology in Pasadena on Friday nights to observe dramatic lecture demonstrations by famous scientists, mostly physicists. The popular novel *Arrowsmith* by Sinclair Lewis influenced me to become a bacteriologist (2), and after two years at Los Angeles City College I became a junior majoring in bacteriology at the University of California at Los Angeles (UCLA).

In the novel, Dr. Martin Arrowsmith discovers bacteriophages (bacterial viruses) and intends to use them for fighting infectious diseases such as the plague. So, I became particularly interested in bacteriophages and somehow learned that such viruses might be research subjects at the Cold Spring Harbor Laboratory in New York. I wrote to the director Milislav Demerec, asking if this was so. He responded that a physicist named Max Delbrück did summer research on bacteriophages at the laboratory. In response to my letter of inquiry, Delbrück (a member of the physics department faculty at Vanderbilt University) agreed that I could come to his laboratory at Cold Spring Harbor for the summer of 1941 (at my own expense) and assist in his collaborative research with Salvador Luria. My fondest dreams were about to be realized. The only way I could afford to get to Cold spring Harbor was a lengthy and arduous bus trip – the fare was $39, pillow and all meals included! The summer was inspiring and very busy for me – working in the lab at all hours except at meal times, when I waited on tables in the dining hall to earn free board and room.

During the preceding academic year 1940-41, I had become acquainted with Charles D. Coryell, a physical chemist on the Chemistry Department faculty at UCLA, and it came to pass that he had a great effect on my later
activities. Coryell was a brilliant chemist with a passionate personality. He had special interests in thermodynamics and energetics in both chemistry and biology, and he invited me to join a small group of faculty and students that met informally to discuss bioenergetics. I soon learned that Coryell had recently introduced the important terms *exergonic* and *endergonic*. Coryell was a quick-thinking and fast-talking “dynamo,” and was responsible for organizing a number of special lectures at UCLA, including one by Leonor Michaelis (1875-1949), a pioneer in the study of oxidation/reduction reactions. Michaelis’s lecture made a deep impression on me, and his research findings on the low redox potential viologen dyes played a significant role in my later investigations on the biological production and utilization of molecular hydrogen (e.g., see refs. 3 and 4).

After graduation from UCLA in 1942, I spent the summer again assisting Delbrück and Luria at Cold Spring Harbor. At the end of the summer, we moved to Nashville (Tenn.), where I continued to assist Delbrück in research, and also began thesis research as a graduate student in biology under his supervision. One of my most enduring impressions of this period was the great care with which Delbrück planned the details of all experimental protocols. My research was concerned with the effects of inorganic salts on the multiplication of *E. coli* bacteriophages, and resulted in my first publications (5, 6).

As the fall term progressed, the rapidly increasing intensity of World War II caused research in universities to grind to a halt. One evening I received a phone call from Coryell, informing me that he was head of a research unit on a secret project important to the war effort at the University of Chicago. He asked me to join his group. Although I had no idea of the research subject, I decided to accept. In large measure, this decision was a product of anxiety generated by the desperate war situation. Historians have described 1942 as “the year of dismay”
noting: “Despite Allied naval victories, the late summer and autumn of 1942 was the blackest period of the war.” The U.S. Chief of Staff General George C. Marshall wrote some years later, “Few realized how close to complete domination of the world” were Germany and Japan and “how thin the thread of Allied survival had been stretched.”

The Manhattan Project

The day I arrived at the Chicago laboratory, Coryell informed me that our group was part of the Manhattan Atomic Bomb project. Our urgent central function was characterization of the radioactive isotopes formed during uranium fission. In the late summer of 1943, our group was divided into two contingents; the major part remained in Chicago and the rest proceeded with Coryell to “Site X.” Coryell had made a preliminary scouting trip to the new site and described it to us as a “scientific utopia.” I chose to go with Coryell, who was a mesmerizing character. Site X turned out to be the newly constructed Clinton Laboratories at Oak Ridge (Tenn.), a major scientific installation within a large army reservation under tight military security. When my wife (Janet Gest, deceased 1994) and I arrived in Oak Ridge, it looked much like a frontier town in a western movie; the sidewalks were wooden and on a rainy day, the roads were morasses of mud. We were soon referring to Oak Ridge as “Dogpatch,” after the backward village in Al Capp’s cartoon strip Li’l Abner. On the other hand, it was an extraordinary scientific community, composed of leading physicists and chemists (and a small contingent of biologists) from all over the U.S. Among them were a number of accomplished musicians, and this led biochemist Waldo Cohn to organize the Oak Ridge Symphony. This provided the opportunity for me to continue playing the string bass, and our small
orchestra gave numerous concerts in this unusual and isolated locale.

Coryell had great scientific intuition and imagination, and he was particularly keen to squeeze out the last bit of information from any experimental data. So, we were encouraged to acquire this valuable trait. Our frequent research conferences were exciting events. Typically, Coryell would either lie on the floor on his back with his feet on the lower drawer of his desk or sit on a metal wastebasket, with the rest of us sitting around in whatever convenient places we could find.

Clinton Laboratories was the site of the uranium chain reaction “pile” (reactor) used for early physics and chemistry research on atomic bombs. Associated with the pile, there was a pilot plant for the production of plutonium. Our responsibilities in the chemistry division, under Coryell’s leadership, focused primarily on characterization of more than 250 radioactive isotopes that are created by the fission of uranium, and the development of a process for chemical isolation of plutonium. We also investigated chemical processes associated with the spontaneous disintegration of radioactive atoms. After declassification of some of our secret research, I became the co-author of 12 papers on the properties of radioactive isotopes (7-18). One of these papers, of which I was the senior author, dealt with the element barium.

As a special assignment, our group prepared gigantic quantities of a radioactive isotope of barium (produced in uranium fission) that was needed by Los Alamos physicists for testing atomic bomb detonation characteristics. Preparation of the radioactive barium (mass 140) required chemical processing by remote control, at a time when there was almost no equipment available for such work. Nevertheless, we managed somehow. Late on the night of September 18, 1944, from a considerable distance away, our group witnessed a dramatic transfer, by crane, of 280 curies of the isotope – a huge, glowing
radioactive source – from a thick-walled preparation laboratory to a large lead
vault in an unmarked army truck. This truck was part of a convoy that left
immediately for Los Alamos. Subsequently, we made shipments of as much as
1000 curies! About ten days after our first shipment, the Germans began
destructive attacks on southern England with more than 1500 V-2 rockets.

On May 19, 1970, in an impressive ceremony at M.I.T. in the presence of
about 300 of Coryell’s friends from around the country, Chairman Glen Seaborg
of the Atomic Energy Commission presented him with an A.E.C. Citation:
“For his distinguished contributions to the Nation’s atomic energy
program in the field of fission products research and radiation chemistry
while serving as section chief in the chemistry division of the
Metallurgical Laboratory and the Clinton Laboratories from 1942 to 1946;
for his outstanding research, in cooperation with L.E. Glendinin and J.A.
Marinsky, which led to the identification in 1945 of promethium, the rare
earth element with atomic number 61; for his sound judgment and
guidance as a consultant to the Oak Ridge and Brookhaven National
Laboratories and the Los Alamos Scientific Laboratory; and for his
continuing service to research and education as professor of chemistry at
the Massachusetts Institute of Technology.”

Coryell was also honored as a Fellow of the American Academy of Arts
and Sciences, the American Physical Society, the American Association for the
Advancement of Science and the American Nuclear Society. This remarkable
scientist and “moving spirit” died at the age of 59 on January 7, 1971.
The Szilard Petition

Physicist Leo Szilard was primarily responsible for initiating the Manhattan Atomic Bomb Project in that he persuaded Albert Einstein to write President Roosevelt in 1939 about the urgency of developing atomic power for domestic and military purposes. This influential letter was in fact drafted by Szilard, who became a leading scientist on the Manhattan Project.

In 1944 or early 1945, scientists at the Clinton Laboratories formed an organization called “The Association of Oak Ridge Scientists at Clinton Laboratories” for discussion of issues relating to atomic bombs and peaceful uses of atomic energy. When telephone calls from the Chicago site and Oak Ridge to Los Alamos were suddenly prohibited, Szilard realized that the bomb would soon be tested: “I knew by this time that it would not be possible to dissuade the government from using the bomb against the cities of Japan. . . . I thought the time had come for the scientists to go on record against the use of the bomb against the cities of Japan on moral grounds. Therefore I drafted a petition which was circulated in the project.”

During the early days of July 1945, Szilard’s petition was discussed, and various criticisms led to revised versions. The Clinton Laboratories version that I signed included the following statements.

“We the undersigned scientific personnel of the Clinton Laboratories, believe that the world-wide social and political consequences of the power of the weapon being developed on this project impose a special moral obligation on the government and people of the United States in introducing the weapon in warfare.

“It is further believed that the power of this weapon should be made known by demonstration to the peoples of the world, irrespective of the course
of the present conflict, for in this way the body of world opinion may be made the determining factor in the absolute preservation of peace.

“Therefore we recommend that before this weapon be used without restriction in the present conflict, its powers should be adequately described and demonstrated, and the Japanese nation should be given the opportunity to consider the consequences of further refusal to surrender. We feel that this course of action will heighten the effectiveness of the weapon in this war and will be of tremendous effect in the prevention of future wars.”

Use of the atomic bombs that destroyed Hiroshima and Nagasaki during the first two weeks of August 1945 was soon followed by the surrender of Japan, and the Atomic Age had begun. Immediately after the bombs were dropped, Szilard felt it was important to “tell people what this was about and what we were facing in this century.” The petition had been declared to be a “classified” document, but Szilard notified the responsible officer of the Manhattan Project that he (Szilard) intended to declassify the petition on his own accord and make the contents public. His attempt did not succeed: “Shortly thereafter I received a call from the Manhattan District, saying that General [Leslie] Groves wanted the petition to be reclassified “Secret.” I said that I would not do this on the basis of a telephone conversation, but I would want to have a letter explaining for what reason the petition, which contained nothing secret, should be reclassified. Soon after I received a three-page letter, stamped “Secret,” in which I was advised that while the officer writing the letter could not possibly know what was in General Groves’ mind when he asked that the petition be reclassified Secret, he assumed that the reason for this request was that people reading the petition might conclude there must have been some dissension in the project prior to the termination of the war, which might have slowed down the work of the project
which was conducted under the Army.” General Groves managed to prevent the petition from reaching President Truman, and it was not declassified until 1958.

July 17, 1995, was the 50th anniversary of the Szilard Petition. To mark the event, a special program was held at the National Archives in Washington, D.C. The Archives contains the vast files of the Manhattan Project. The program was organized by William Lanouette, author of the Szilard biography *Genius in the Shadows*. Three signers of the Szilard Petition were the main speakers — physicists Ralph Lapp and John Simpson, Jr., and myself. In 2001, a recollection of my experiences on the Manhattan Project and an analysis of the background and fate of the petition was posted on the Internet under the title: “The July 1945 Szilard Petition on the Atomic Bomb: Memoir of a signer in Oak Ridge” (19).

During the summer of 2005, a 60th anniversary reunion of Manhattan Project scientists and engineers was convened in Oak Ridge, and I attended this remarkable event. During the course of the reunion, I was interviewed by representatives of two Japanese TV networks, for documentaries to be broadcast in Japan on August 7, the anniversary of the Hiroshima bomb. On special tours, we were able to see facilities that were used from 1943-1945. These included the nuclear reactor where I did research on uranium fission, and huge installations used for production of the U$^{235}$, the fuel of the Hiroshima bomb. In 1980, I visited the Peace Museum in Hiroshima and was overwhelmed by large photographs of the destruction and devastation.
Szilard, after 1945

After the end of World War II, Szilard decided to stop further research in physics, and became Professor of Biophysics at the University of Chicago. After a short learning period, he made notable contributions to our knowledge of the dynamics of bacterial growth and mutation rates in populations of bacteria. At the same time, he continued his political activities and was one of the leaders in establishing civilian control over peaceful development of nuclear energy in the United States and international control of nuclear weapons. In 1959, he received the Atoms for Peace Award.

As a prelude to beginning research in biology, Szilard audited an outstanding summer course in microbiology given by Professor C.B. van Niel at the Hopkins Marine Station in Pacific Grove (CA). Van Niel was a great authority in microbiology and was a fascinating lecturer. The reputation of his summer course led many outstanding scientists in other fields to attend as auditors, and Szilard did this in 1947 or 1948 (probably 1948). This provided the occasion for me to meet Szilard personally. During the completion of my graduate work at Washington University after the end of World War II, I was a student in van Niel’s course in 1947, and returned as a “research student” in the summer of 1948. The great experience of attending van Niel’s course was aptly described in a recent book about “Seymour Benzer’s Adventures in Phage Genetics” (20).

“In June and July 1950 Benzer took time out from his work at Caltech to take the course in general microbiology taught by C.B. van Niel at Pacific Grove that he had hoped to attend the previous year. Van Niel’s lectures were famous, and Benzer found them as enjoyable as their reputation had led him to expect. The students also did experiments every day, often on bacteria fished from the ocean. Van Niel set up the experiments to
illustrate the problems he discussed in lectures, often providing trick problems for them to solve. In one they were given a bacterial colony to purify. When they attempted to do so, they always found two very different types of bacteria under their microscopes. No matter how often they repeated the purification, the same thing happened. It turned out that the two bacterial types were symbiotic. Some of their observations, such as the growth of luminescent bacteria on a dead fish, were spectacular. Altogether Benzer greatly broadened his knowledge of the practical problems of culturing and performing experiments with bacteria; . . .there were many pleasant diversions accompanying the serious work. The Pacific Grove Laboratory was situated next to the Monterey Bay Aquarium, right on the rocky southern California coast. The students regularly ate lunch sitting on the rocks while watching the surf and the cavorting sea lions. At the end of the course there was a lively party, including skits. Benzer impersonated, with appropriate exaggerations, van Niel’s demonstration of the way to sterilize an agar tube containing a bacterial culture. The technique required one to push a cotton plug into the tube while rotating the tube in a Bunsen flame, wait until the protruding end of the plug caught fire, and then quickly blow it out.”

Return to academia: Kamen, viruses and photosynthesis

Several months after World War II ended (in the summer of 1945), Coryell accepted a professorship in the chemistry department of the Massachusetts Institute of Technology, and a number of the young members of our group accompanied him to complete their Ph.D. work. Although I had this option, I decided to return to biology. In view of my experience with radiochemistry, Coryell suggested that I resume graduate study with Martin
Kamen at Washington University (St. Louis). In addition to being the co-discoverer of $^{14}$C, Kamen was a well-known pioneer in the use of radioactive isotopes as tracers for biochemical research. At the time, Kamen was using $^{14}$C for studying photosynthetic CO$_2$ reduction by unicellular green algae. With Coryell’s recommendation, Kamen accepted me promptly. Kamen was an excellent musician (viola) and I suspected that his knowledge that I played the classical string bass helped clinch the arrangement.

My situation at Washington University was somewhat jumbled in the sense that Kamen’s appointment was in the Chemistry Department, his laboratory was in the Mallinkrodt Institute of Radiology at the School of Medicine, and I was formally registered as a graduate student in the Department of Bacteriology and Immunology. I soon felt that the requirements for the Ph.D. degree in bacteriology were too restrictive, and I prevailed on Kamen to arrange a special interdepartmental “microbiology” graduate committee; Alfred Hershey (who shared the 1969 Nobel Prize in Physiology or Medicine with Delbrück and Luria) served on the committee as a representative of the bacteriology department.

**Discovery of $^{32}$P suicide of bacteriophage**

During 1947-48, several reports appeared in the literature on the origin of the phosphorus found in the DNA of bacteriophages. Because of my previous work with Delbrück and my then current work on P metabolism in photosynthesis using radioactive P, I became interested in exploring phosphorus metabolism during phage infection of *E. coli*. This led to discussions with Alfred Hershey, who was then an associate professor in the Washington University Department of Bacteriology and Immunology. Since we had $^{32}$P
available, I convinced Hershey and Kamen that we should start collaborative research. At the time Hershey was not biochemically inclined but did express an interest in determining the P content of phage.

Eventually we decided on a novel experiment in which we would infect the bacterial host cells with viruses that contained extremely radioactive P, and follow the fate of the phosphorus in the virus progeny. Joseph Kennedy, chairman of the Washington University Chemistry Department, was enlisted in the research because of his wide expertise in radioactivity measurements. (He had been head of the Chemistry Division at the Los Alamos Laboratory of the Manhattan Project).

We never did the intended experiment because of unexpected events. Hershey and I had gone so far as to make the radioactive phage preparation, which was stored in a refrigerator. The $^{32}\text{P}$ preparation used was so “hot” that the only feasible way I could assay it was with an electroscope! But it turned out that Hershey was then occupied for about a month with teaching duties, and I was busy with course work and other matters. When we were ready to set up the actual experiment we first checked the virus titer again, and were surprised to find that it had decreased significantly. This was quite bothersome, and had the effect of causing another delay in doing the “big” experiment. Several weeks later we found that the virus titer was still declining rapidly. Finally it dawned on us that the virus titer was declining at the same rate that the $^{32}\text{P}$ was undergoing radioactive decay. We had accidentally discovered the phenomenon of “$^{32}\text{P}$ suicide” (21). Thus, as $^{32}\text{P}$ in the phage DNA disintegrated spontaneously, the transmutation of P to sulfur sheared the DNA chains causing inactivation of the virus. In retrospect, I regard this as a curious episode of serendipity since one of the main problems I had worked on at Oak Ridge was the chemical effects that occur when radioactive elements in inorganic compounds undergo
transmutation by beta decay to other elements. For further details of the “$^{32}$P suicide” experiments and their implications for the famous 1952 Hershey-Chase experiment, see ref. 22.

**Energy metabolism in photosynthetic microorganisms**

As noted earlier, during the summer of 1947, I was privileged to be one of the 10 or so students in the famed microbiology course given by C.B. van Niel. He was well known for his research on purple photosynthetic bacteria. During the course we isolated a number of such organisms in pure culture from natural sources. I fell in love with the “purples” at first sight; the beautiful red and purplish cultures fascinated me.

When I was a research student with van Niel during 1948, I made some unusual observations on the production of gases by purple photosynthetic bacteria. After return to St. Louis, these led me to the discovery that these organisms can use atmospheric nitrogen ($N_2$) as a nitrogen source for growth. In 1949, we published two papers in *Science* describing photosynthetic “$N_2$ fixation” which were featured in a *New York Times* news article (June 25) under the headline “New Clue Is Found to Photosynthesis.” (Details are given in ref. 23.)

My experiences with Kamen had a major influence on my career as a scientist and on my political and cultural development; we continued a lively correspondence for decades; I published an appreciation of Martin in the 2005 *magnum opus, Discoveries in Photosynthesis*, part of which follows:
Martin D. Kamen traveled brilliantly in many worlds: radiochemistry, nuclear physics, biochemistry, academia, music and culture. I was very privileged to share in some of these travels when I became Kamen’s first graduate student at Washington University (St. Louis, Missouri) in 1946. My thesis research, during 1946 to 1949, happened to coincide with the beginning of a period of great stress in Martin’s life. He was an innocent victim of Communist witch-hunts during the 1940’s and 1950’s. There were false rumors and accusations that he had leaked atomic bomb secrets. As a consequence, in 1944 he lost his position managing cyclotron production of radioactive isotopes at the University of California, Berkeley. With no other recourse, he worked for a while as an inspector at a shipyard. In 1945 Arthur Compton, who was then chancellor of Washington University, recruited Kamen to run the cyclotron program of the university medical school. It took many years of effort and anguish for Kamen to finally clear his name. The details are given in Kamen’s autobiography Radiant Science, Dark Politics (University of California Press, Berkeley, 1986 [revised paperback edition]).

Despite distraction in fighting the serious accusations, Kamen confidently forged ahead in research, and we had exciting adventures. When I returned to St. Louis after the summer of 1947 in van Niel’s laboratory, I brought a culture of the photosynthetic bacterium Rhodospirillum rubrum. Greatly attracted to the colorful purple bacteria, I convinced Martin that we should adopt them as prime experimental systems. This decision dominated the future course of both our careers. After unexpectedly observing photoproduction of molecular hydrogen by R. rubrum (Gest and Kamen Science 109: 558-559, 1949), we were
especially challenged in unraveling the clues that led to our discovery of N₂ fixation by photosynthetic bacteria (see Kamen and Gest, *Science* 109:560, 1949; Gest, Kamen and H.M. Bregoff, *J.Biol. Chem.* 182: 153-170, 1950). We also developed a project to study the fate of phosphorus during the bacteriophage replication of *Escherichia coli*, which unexpectedly revealed the phenomenon of $^{32}$P-decay “suicide” of the virus (see Gest, *Photosynthesis Research* 74: 331-339, 2002).

In 1957, Kamen moved to Brandeis University, and four years later he joined the Chemistry Department of the University of California, San Diego (UCSD). He became one of the founding fathers of the new campus, and was important in academic leadership of the developing university. At the same time, he and his research group undertook a systematic and comprehensive study of the cytochromes and heme proteins of various kinds of photosynthetic bacteria. Kamen’s outstanding contributions were recognized by many awards, including the prestigious Enrico Fermi Prize (1996) given by the US Department of Energy. UCSD honored Kamen at the time of his retirement (1978) with a gala symposium, accompanied by outstanding musical events. The papers presented at the symposium were published in the book *From Cyclotrons to Cytochromes*, edited by N.O. Kaplan and R. Robinson (Academic Press, New York, 1982); it had a remarkable scope, reflecting Kamen’s many talents.

The discovery of $^{14}$C by Samuel Ruben and Martin Kamen in 1940 had a profound effect on research in biochemistry. During the decade 1945-1955, the use of $^{14}$C as a metabolic tracer resolved many basic questions that had been debated for a half-century. This should have been recognized by a Nobel Prize, but Ruben’s untimely death apparently precluded this well deserved award.

Kamen was a talented writer who had excellent style. Even while he was under great political pressure, he managed to write his seminal book on
Radioactive Tracers in Biology (Academic Press, New York, 1947), which went through a number of editions. His book on Primary Processes in Photosynthesis (Academic Press, New York, 1963) was an important modern assessment of the state of photosynthesis knowledge, particularly in respect to physical and biochemical aspects. Throughout his scientific career, Kamen managed to indulge in another passion, music. He was an excellent viola player and wherever he went, musical events were arranged. Kamen was a close friend of the famous violinist Isaac Stern and when they happened to be in the same vicinity, they met to play chamber music.

Hugo Theorell (Nobel Laureate, 1955) was unable to attend Kamen’s retirement festivities, but he sent the following letter (reproduced here, From Cyclotrons to Cytochromes):

My dear old friend Martin Kamen,

I happen to know that you will reach a matured age on August 27 this year and therefore grasp the occasion to send you my very best wishes and heartiest congratulations. Margit of course joins me.

Among the hundreds of biochemists I have met and collaborated with in my life you belong to a separate, higher class than most of the others, because you are a master not only in science – biochemistry – but also in art – music, and as you well know I do the little I can in the same directions in music promoted by Margit. You and I also had the opportunity of collaborating in this field. Let me take this occasion to tell you that I am greatly thankful to the fate that brought us together. All the best for the future.

Yours ever, Hugo Theorell
During Kamen’s political troubles, the State Department abruptly revoked his passport in 1947. In this connection, a suit was filed against the Secretary of State Foster Dulles. Several years later, one half-hour before the case was to be argued in court, the passport was suddenly issued. Kamen was now able to make music again with Theorell in Stockholm and attend international meetings. In his autobiography, Martin recounts his pleasure at his retirement festivities, and ends with the sentence: “The evil specters of the past had been exorcised.”

Origins of life on Earth, microbial evolution, and the possible existence of extraterrestrial life

An early lecture in van Niel’s microbiology course dealt with historical highlights, including A.O. Oparin’s 1938 classic *The Origin of Life*. This book had a great impact on concepts of early biochemical evolution. Oparin developed the argument that the first organisms must have been heterotrophs, rather than autotrophs. Evidently the latter had more highly evolved biosynthetic mechanisms than heterotrophs. Van Niel also discussed an extension of Oparin’s thesis developed in 1945 by Norman Horowitz at Cal Tech. Horowitz proposed a sensible theory of how autotrophs could have evolved from heterotrophs living in a “prebiotic soup” that presumably contained organic compounds produced by nonbiological processes. As an example, he considered the contemporary pathway for arginine biosynthesis in heterotrophic microorganisms and explained how this could have emerged in autotrophs as the prebiotic supply of arginine became exhausted.

The foregoing led me to spend my first sabbatical leave in 1956 working with Horowitz. Daily coffee sessions with Horowitz, Ed Lewis (Nobel Laureate,
1995), and the *Drosophila* pioneer A.H. Sturdevant opened my eyes to genetics and biochemical evolution. In 1957, I took part in the International Symposium on Enzyme Chemistry in Tokyo/Kyoto, and was fascinated when Oparin arrived. He was lionized by the news media and was headlined in all the Japanese newspapers. Later (1979-1980), my continuing interests in microbial evolution led to my participation in the Precambrian Paleobiology Research Group (PPRG), organized by J.W. Schopf at the University of California Los Angeles. The group consisted of 24 scientists from various universities and research organizations. This extraordinary group held discussion meetings and made field trips to collect microfossils and other samples for study from diverse locations around the world, including desolate Shark Bay on the west coast of Australia (to examine modern stromatolites). The efforts of the PPRG led to publication in 1983 of *Earth’s Earliest Biosphere/Its Origin and Evolution*, an outstanding source of information for future researches (this book is included in the collection).

In 1996, NASA scientists published a paper in *Science*, claiming the observation of fossil microbes in a Martian meteorite designated as ALH84001. It had been collected in Antarctica and had a complex history. Various kinds of analyses showed that after wandering in interplanetary space for about 16 million years, ALH84001 blazed through the Earth’s atmosphere and crashed onto the Antarctic ice cap some 13,000 years ago. According to the NASA scientists, this meteorite contained “wormlike” microscopic fossils that resembled, in general appearance, certain kinds of terrestrial microfossils. However, the Mars “fossils” were very much smaller than cells of typical bacteria on Earth. So, it was immediately questionable that structures of such small dimensions could have contained even the minimum essentials of life.
The NASA report listed several other kinds of indirect evidence to support their claim of “evidence for primitive life on early Mars.”

I was invited to attend a meeting in March 1997 of the “Martian Meteorite Working Group,” organized by the Lunar and Planetary Institute, to evaluate applications from independent scientists who requested small samples of ALH84001 for further study. The invitation was probably based on recognition of my membership (1967-1969) in a National Academy of Sciences-National Research Council committee on “Microbiological problems of man in extended space flight” and my long-term interests in the origin of life, biochemical evolution, and Precambrian paleobiology.

Within two years, it became clear that the claims of the NASA scientists could not be substantiated. The general consensus was that the so-called “Martian microfossils” were simply bits of inorganic debris. As the Mars microbe story deflated, NASA developed a virtual “Astrobiology Institute,” which described astrobiology as “study of the origin, evolution, distribution and destiny of life in the universe. Astrobiology represents a synthesis of disciplines from astronomy to zoology, from ecology to molecular biology, and from geology to genomics.” This description, which has boundless dimensions, is obviously not the definition of a science. Words beginning with “astro” define subjects dealing with stars and celestial bodies (e.g., astronomy, astrology). Since there is no biology of any kind known other than that on earth, the word astrobiology is an oxymoron. The word is now exploited to generate media interest and excitement, but it conveys the false idea that life has actually been discovered in places other than Earth.

In my opinion, the promotion of “astrobiology” by NASA’s massive “public relations” division (350 people!) is unique in modern scientific endeavors, and I have criticized this development in a number of publications
There is a large background of serious scientific literature dealing with the origin of life on Earth in the form of microbes, subsequent evolution of microbes to more complex forms (i.e., plants and animals), and possible scenarios for extraterrestrial life forms. For over 50 years, I have collected relevant literature and this is included in this Special Collection.

Many interactions with outstanding scientists

I was very fortunate in this respect throughout my career, even while I as an undergraduate at UCLA (see Coryell, Delbrück, Luria). This continued in the course of my academic life. My first university appointment was in the Department of Microbiology of Western Reserve University School of Medicine (WRU, 1949-1959). During the 1950’s, WRU was renowned as a Mecca of research in microbiology and biochemistry. Harland Wood, chairman of the Biochemistry Department, was a top-rank biochemist; he and his outstanding faculty attracted important visitors, including Sir Hans Krebs and Fritz Lipmann who shared a Nobel Prize in 1953. There were many other visitors in the forefront of microbiology and biochemistry. My research at WRU focused on bioenergetics and intermediary metabolism, especially in photosynthetic bacteria.

From 1959 to 1966, I was Professor of Microbiology at Washington University in the Henry Shaw School of Botany and the Zoology Department. Washington University had, and still has, world-wide recognition as one of the most distinguished centers of life science research. For some years I was chairman of the Graduate Program in Molecular Biology. Again, I was in a milieu that attracted world-class visitors such as Nobel Laureates James Watson and Albert Szent-Gyorgyi. My research at Washington University radiated into various aspects of bacterial metabolism, e.g., biosynthesis of amino acids in
photosynthetic bacteria and study of their membrane systems that convert light into chemical energy.

In 1966, I came to Indiana University as Chairman of the Department of Microbiology (Bloomington). My research in photosynthesis branched into new areas: mechanism of light-dependent production of molecular hydrogen by purple bacteria; isolation and characterization of new species of phototrophic bacteria. In addition, I pursued investigation of microbial evolution (paleomicrobiology) and accelerated my studies on the history of research in microbiology and biochemistry. Details of my experimental research are discussed in ref. 1: *A microbiologist’s odyssey: Bacterial viruses to photosynthetic bacteria*, and in ref. 29. An almost complete collection of reprints of my research publications is included in this Special Collection.

My interactions with about 20 remarkable scientists are documented in the Files of this collection (augmented with their books, monographs, reprints, photographs, obituaries, etc.) There is no doubt that my career spanned a Golden Age, which included the “Age of Atomic Power,” and discovery of the fundamental fabric of cell biochemistry and genetics, the ultimate basis for the molecular biology of today.
James Barber  (Fellow, Royal Society)

Barber has been on the academic staff of Imperial College (London) since 1968. He was head of the Biochemistry Department from 1989 to 1999, and has been Dean of the Royal College of Science at Imperial College. Barber and I have had common interests in the mechanisms of photosynthesis for decades, and I have been a “research visitor” in his laboratory a number of times. And he has visited me in Bloomington. His outstanding research has focused on the detailed structure of the photosystems of green plants. A recent summary of his research contributions is presented in his 2004 paper “Engine of life and big bang of evolution: A personal perspective” (see below).

Photosystem II; A brief summary of Barber’s career (from Google)
J. Barber and B. Andersson: Revealing the blueprint of photosynthesis. 
J. Barber: Engine of life and big bang of evolution: A personal perspective.
J. Barber: A new type of photosynthetic reaction centre. 
This editorial describes the discovery in Gest’s laboratory of a new genus and species of photosynthetic bacteria that contains a previously unknown kind of photosynthetic pigment system (30).

Paul Berg  (Nobel Laureate)
Paul Berg received the Ph.D. degree in biochemistry from Western Reserve University School of Medicine in 1952. At that time, I was on the faculty (1949-1959) and participated in team-taught graduate courses. Paul was a student in these courses, and we have maintained contact over the years. Since 1959, Paul has been on the faculty of Stanford University School of Medicine. I have made many academic visits to Stanford University and this has provided occasions for interactions. Paul is a pioneer in genetic engineering. His Nobel lecture was entitled: “Dissections and reconstructions of genes and chromosomes.” His remarkable career is detailed in a recent book: *The Discoveries*, by Alan Lightman (see below). In addition to the Nobel Prize, Paul has received a very impressive number of other honors. In October 2005, Berg, Charles Yanofsky, Howard Gest (and their wives) met in San Francisco to attend a performance of the new opera, *Dr. Atomic*, by John Adams. The opera relates to the Manhattan Project, in which I did basic research on uranium fission (1943-1946).

Paul Berg, curriculum vitae


Melvin Calvin (Nobel Laureate), Peter Mitchell (Nobel Laureate) and Robert Hill (Fellow, Royal Society)

Photosynthesis has been a major theme of my research since 1946. This process is probably the most complex biological system since it involves radiation physics, photochemistry, as well as biochemistry. I group Calvin, Hill and Mitchell together because of relationships between their research fields — photosynthesis and bioenergetics. A major aspect of photosynthesis involves the conversion of light energy to chemical energy in the form of adenosine triphosphate (ATP), which is the direct energy source for biosynthesis in all kinds of cells.

Calvin, Hill and I shared a strong interest in unraveling the history of early (18th century) investigations of photosynthesis, which we pursued by correspondence and in personal encounters. Calvin’s experimental research focused on the chemical path of carbon as it is transformed from carbon dioxide to sugar in photosynthesis. His group at Berkeley was able to do this using radioactive carbon, $^{14}$C, as a tracer. In recognition of elucidation of this complex problem, Calvin was awarded a Nobel Prize in Chemistry in 1961. It should be noted that $^{14}$C was discovered by Martin Kamen (my Ph.D. mentor) and Samuel Rubin in 1940 (also in Berkeley).

I have been a friend of Andrew Benson for many years. This is relevant because Benson was Calvin’s chief collaborator in defining the path of carbon in photosynthesis, which is often referred to as the “Calvin-Benson Cycle.” The details of this great research accomplishment are discussed in two articles in Discoveries in Photosynthesis (2005, edited by Govindjee, Beatty, Gest and Allen); one article by Benson (pp. 793-813) and the other by James Bassham (pp. 815-832).
Robert (Robin) Hill was one of the great pioneers of photosynthesis research. I visited him often at the University of Cambridge, and he had a strong influence on my scientific development. A tribute to Hill, by David Walker, is in *Discoveries in Photosynthesis* (pp. 109-112). Hill’s research made it clear that the source of molecular oxygen produced in green plans photosynthesis is water. He also developed the rationale for explaining why oxygenic photosynthesis requires two sequential light reactions to generate chemical energy (ATP).

In 1966, I published a paper on the comparative biochemistry of photosynthetic processes (*Nature* **209**: 879-882). I asked Hill (in 1965) to comment on an early draft, and he suggested that, in connection with the conversion of light energy to chemical energy, I should note the revolutionary ideas of Peter Mitchell. I did so, even though the prominent researchers in bioenergetics considered Mitchell a “crank.” Despite extensive studies over many years by numerous investigators, the mechanisms of ATP generation in oxidative and photosynthetic metabolism remained obscure until Mitchell developed a novel theory that proved to be correct.

I contacted Mitchell in 1970, and he invited me for discussions at his remote home-laboratory (in a very old manor house) in the village of Bodmin, Cornwall. At the time, he gave me two small books, printed at his own expense, which explained his theories of bioenergetics in detail (see below). After several more years of controversy, Mitchell was awarded the 1973 Ciba Medal, and the 1978 Nobel Prize in Chemistry. In 2001, I was invited to speak at the 125th meeting of the American Chemical Society on “Landmark discoveries in the trail from chemistry to cellular biochemistry, with particular reference to mileposts in research on bioenergetics.” The published text of my talk included a cartoon in which Mitchell discards erroneous ideas into a wastebasket.
Calvin
Nobel Prize biography (Google)
Subtitle: Molecular evolution towards the origin of living systems on the earth and elsewhere.

Mitchell
This article discusses how "Mitchell, Moyle, a few able technicians and the occasional visiting research fellow have profoundly influenced thinking on one of the most important problems in biochemistry in a manner out of all proportion to their number and relatively small budget."
Peter Mitchell biography; Nobel Prize.org (Google)
Robert (Robin) Hill

R. Hill: The Biochemists’ Green Mansions: The photosynthetic electron-transport chain in plants. From: Essays in Biochemistry (Campbell and Greville, eds.) (1965) pp. 121-151. This is one of Hill’s most important papers.


An Eightieth Birthday Tribute to Robert Hill. A tribute from friends and colleagues. The bound volume (44 pages) includes reprints of three of Hill’s research papers. 120 copies were printed by Will Carter at the Rampant Lions Press, Cambridge in 1979.

12 letters between Gest and Hill over the period 1965-1989
2 obituaries; March 21, 1991. London Times, and Independent

M.C. Anderson: Robin Hill, FRS: A Cambridge neighbor’s appreciation of a great man and his hemispherical camera.


Charles D. Coryell (American Academy of Arts and Sciences)

Mimeographed, 71 pages. An internal Manhattan Project document.

Coryell obituary, by Glen E. Gordon, in *Journal of Inorganic and Nuclear Chemistry* 34: 1-11 (1972). Coryell published 98 research papers; I was a co-author on two of them.

Photo of Coryell group; Oak Ridge, October 1945


Charles Coryell: a Google search. This 18 page document is an excellent condensed account of the Manhattan Project.

Pages 12 and 13 show a photo of Coryell ("one of many brilliant chemists who served at Clinton Laboratories during the war."). Page 14 shows a photo of construction of the "hot cells" used by our group for the first production of a radioisotope on a large scale. Page 18 shows the graphite reactor at Clinton Laboratories; our group used the reactor for investigating uranium fission products.

Letter (3/29/76) from Dr. Nathan Sugarman to Dr. Laurence E. Glendenin, with a draft manuscript of a talk to be given at the American Chemical Society Nuclear Chemistry Division on April 6, 1976. The talk is dedicated to the memory of Coryell. This rare document gives a fascinating account of the contributions made by the uranium fission product chemists (including the Coryell group). Dr. Sugarman also gave his account of the first test of an atomic bomb at the Alamagordo test site. Among the numerous activities of the Coryell group, [17 scientists (see photo)] was the successful first
isolation of Element 61 by Glendenin, Jacob ("Jack") Marinsky and Coryell.
Element 61 is a radioactive “rare earth” metal, produced in uranium fission. Glendenin at al. named it promethium, after the Greek god Prometheus (see Google description).

Google cache of “Chemical element: promethium”


Max Delbrück, Salvador Luria, Alfred Hershey
(Nobel Laureates 1969)
My associations with Delbrück, Luria and Hershey are described in the narrative of this collection. I note in addition that during my sabbatical leave at Cal Tech in 1956-1957, I had many academic and social interactions with Delbrück. During subsequent visits to Cal Tech, I always visited with Delbrück, E.B. Lewis and N. Horowitz.

Historical note: Max Delbrück’s brother, Justus Delbrück (a lawyer), his sister Emmi Bonhoeffer, and his brother-in-law Klaus Bonhoeffer (brother of theologian Dietrich Bonhoeffer) were in the German Resistance against the Nazi regime. Klaus and Dietrich were executed in the last days of Hitler’s Germany.

M. Delbrück: Problems of Modern Biology in Relation to Atomic Physics (A series of lectures given at Vanderbilt University School of Medicine in 1944. Mimeographed.
M. Delbrück: A Renaissance Physician. Tape of a lecture given at Indiana University, October 7 or 8, 1969.

Science News, April 25, 1981. An issue featuring “Max Delbrück, Missionary of
Molecular Genetics.” The article by J.A. Miller includes a photo of Delbrück and Luria at the lab bench during the summer of 1941, when I worked with them as a laboratory assistant.

Three letters from Delbrück, 1941-1942. The letter of April 1, 1942 is particularly interesting. A typed copy follows:

April 1st, 1942

Dear H.G.

It is correct that you would have to pay tuition ($300) from the stipend. Living expenses here are fairly low, $300 are supposed to be enough for a single student. I am afraid I cannot offer you more now.

I am glad to hear that you would like to come here. We will also have Luria and Spizizen here next year. But I must warn you that this is a very poor place to come to when you have your chances for the future in mind. You will do here very specialized work – phages – which may have a future, but not a very immediate one. And the Southerners are very conservative and narrowminded when it comes to appointments. Also they are self satisfied, you will not meet here people from the north or make the contacts that might help you on. I believe all this would be better in Wisconsin. I, of course, would be very glad to have you, but don’t think because you like phages and like me it is the best thing to come here. You cannot afford to follow your liking. It may well be that in another year or two I will be in a stronger position, so that I can take the responsibility of advising you to come here.

With best regards,
P.S. There is a lurking possibility of trouble here because I am technically an enemy alien.

Article from *Science*, 24 October 1969: The 1969 Nobel Prize for Physiology or Medicine. This article gives a good review of the research accomplishments of Delbrück, Luria, and Hershey, the “three prime movers of molecular genetics.”

M. Delbrück – biography (from Google).

My narrative describes the discovery of "³²P suicide of bacteriophage" by Hershey, Kamen, J. Kennedy and H. Gest. ["The mortality of bacteriophage containing assimilated radioactive phosphorus," *Journal of General Physiology* 34: 305-319 (1951)]. A copy of this paper is included, as well as reprints of two articles that explain the events leading to discovery of "³²P suicide" and the significance of this research in later work by Hershey.

H. Gest: Photosynthesis and phage: Early studies on phosphorus metabolism in photosynthetic microorganisms with ³²P, and how they led to the serendipic discovery of "³²P-decay suicide" of bacteriophage. *Photosynthesis Research* 74: 331-339 (2002). This paper includes a photo of "Bacteriophage researchers at Cold Spring Harbor Laboratory, summer 1942" [Delbrück, Luria, John Spizizen, and graduate students Howard Gest and Edna Cordts].


Norman H. Horowitz  (National Academy of Science)

Obituaries:

Norman H. Horowitz, 90, Explorer of Mars.  New York Times,  
June 4, 2005
Norman Horowitz Dies; Conducted Experiment with Viking  
Lander to Search for Life on Mars.  Cal Tech Media  
Relations; June 1, 2005.
In Memoriam: Norman Horowitz (1915-2005). Planetary News:  
Space People (2005).

N.H. Horowitz: The evolution of biochemical syntheses –  
Retrospect and Prospect.  In: Evolving Genes and Proteins, V.  
York, 1965.

Engineering and Science; Published by the California Institute of  
Technology.

November 1956.  The cover shows a photo of  
Horowitz in his laboratory.  This issue features an article  
by Horowitz on “The Origin of Life” (pages 21-25).  The  
article was adapted from a Friday Evening Demonstration  
Lecture given by Horowitz on March 16, 1956.

H. Gest and N. H. Horowitz: Activation and thermostability of  
Neurospora crassa  
tyrosinase.  Journal of General Microbiology 18: 64-70  
(1958).

N.H. Horowitz: To Utopia and Back/ The Search for Life in the  

Martin D. Kamen  (National Academy of Science)

Gest-Kamen correspondence, copies of ca.155 letters covering the  
period 1945-1971. The letters detail many aspects of the personal  
and academic lives of Kamen and Gest, their interactions  
throughout the years, relations with many other scientists. Also,
details of travel and discussion of numerous research projects (of Kamen and Gest and others). In numerous letters, Kamen gives details of his "political" problems (loss of passport, etc.).


Patten Lecture announcement: Martin D. Kamen, Visiting Patten Professor of Biochemistry for 1974-75. (at Indiana University)


H. Gest: Samuel Ruben's contributions to research on photosynthesis and bacterial metabolism with radioactive carbon. Photosynthesis Research 80: 77-83 (2004). This paper describes discovery of the important isotope $^{14}C$ by Ruben and Kamen.


Martin D. Kamen, 89, a Discoverer of Radioactive Carbon-14.


Sir Hans Krebs (Nobel Laureate)

Sir Hans Krebs and Fritz Lipmann were “giants” of biochemical research in the 20th century. They shared the 1953 Nobel Prize for Physiology or Medicine in recognition of their numerous contributions, especially in explaining the mechanisms used by animals and most microbes for providing the chemical energy for growth from foodstuffs. While I was a graduate student at Washington University, I heard Krebs present a seminar on his research to the Biochemistry Department (probably in 1947). I first met Krebs in 1954 when he and Lipmann visited Western Reserve University School of Medicine, where I was an Assistant Professor of Microbiology. The research programs of Krebs and Lipmann overlapped strongly with research in our Microbiology and Biochemistry Departments. Krebs and I shared many scientific interests and I visited him in Oxford numerous times to discuss the evolution of bioenergetics systems and many other topics. He was very generous with his time and often reviewed drafts of technical manuscripts I was writing.

E. Willcocks, A Lucky Man, Chemistry in Britain, vol. 39, No. 6, June 2003.

This issue contains an article (p. 34) about Krebs. Ms. Willcocks consulted me for information on Krebs and cited my paper listed below (“Landmark discoveries. . .”)

Copy of letter to Ms. Willcocks about Krebs (April 14, 2003).

H. Gest: Landmark discoveries in the trail from chemistry to cellular biochemistry,

with particular reference to mileposts in research on bioenergetics.

Audiotape and slides. Based on an interview (1973) with Krebs discussed in my
letter to Ms Willcocks noted above. Title: “The citric acid cycle / An
historical analysis, and a further analysis of metabolism and its
complications.” In this educational lecture, Krebs discusses his education,
discoveries, and personal views on life.
Copy of letter (6/14/37) to Krebs from Nature rejecting his paper on discovery of
the citric acid cycle, also known as “the Krebs cycle.”
This discovery was the major basis for his Nobel Prize. Krebs gave me the copy.
Program of the Dunham Lectures at Harvard University, 1980-1981, given by Krebs. I attended several and had lunch with Krebs on May 21, 1981.
H.A. Krebs: The discovery of the ornithine cycle of urea synthesis.

*Biochemical Education* **1**: 19-23 (1973).

Hans Krebs biography. Nobelprize.org (Google)


Inscribed: For Howard, from Hans Krebs.


Krebs’ Citric Acid Cycle—Half a Century and Still Turning.

Symposium 54 of the Biochemical Society, ed. by J. Kay and P.D.J.


Contains a paper by H. Gest: Evolutionary roots of the citric acid cycle in prokaryotes, pp. 3-16.

Hans Krebs: *Otto Warburg / Cell physiologist, biochemist and eccentric*.


**Rita Levi-Montalcini** (Nobel Laureate)

Rita Levi-Montalcini was born in Turin, Italy, in 1909 and graduated from medical school in 1936. Because of the anti-Jewish edicts of Mussolini, she was unable to advance an academic career. She built a small research unit in her bedroom at home, and pursued research under difficult circumstances. Her inspiration was a 1934 research article by Viktor Hamburger, a distinguished embryologist who later became chairman of the Zoology Department at Washington University. In 1947,
Hamburger invited Rita to join him in research on the development of the chick embryo. She joined the faculty in the early 1950’s and remained a member until her retirement in the 1980’s. Her research with biochemist Stanley Cohen led to discovery of “nerve growth factor” and “epidermal growth factor,” and was recognized by a Nobel Prize to Rita and Cohen in 1986. Many neuroscientists believe that omission of Hamburger from this award was a serious omission on the part of the Nobel Committee [see Washington University Magazine articles on Hamburger (Spring 1987) and Levi-Montalcini (Midsummer 1992)]. A short history of bioscience at Washington University, from a 2003 publication is included in this collection.

The great scientific success story of Levi-Montalcini at Washington University was not an easy road, and I became involved in struggles along the way. During my last few years at Washington University, I was chairman of the Graduate Committee on Molecular Biology, and was involved in administrative affairs relating to future development of the biological sciences. During this time, Hamburger was attempting to increase research space for Zoology, especially in connection with Rita’s program. Hamburger’s plans were thwarted by Professor Barry Commoner, who was determined to dominate all activities in biology at the university. Vigorous confrontations with Commoner, in support of Hamburger, led me to propose combination of the Department of Zoology and the Henry Shaw School of Botany to form a single Department of Biology.

At one point, we almost achieved this goal, but Commoner again undermined our efforts. During the winter of 1965, while I was on sabbatical leave in Mandelstam’s laboratory in London, I was invited by Rita for a social visit in her home in Rome. About the same time, I was approached by Indiana University to become chairman of the Microbiology Department (in Bloomington). In view of the problems at Washington University, I decided that my future was in Indiana,
and I came to I.U. in 1966. Some years later, I suggested that Joel Mandelstam would be an excellent candidate for chairmanship of the Biology Department at Washington University (finally established in 1969). My suggestion received considerable support, and Mandelstam was offered the position in 1975. He was prepared to accept and visited St. Louis to discuss final details. During this visit, Mandelstam became acutely aware of Commoner’s maneuvering to undermine any arrangement in which he (Commoner) would not be “top dog.” It became clear to Mandelstam that the situation would be intolerable and he declined the offer to become chairman. The details of this dismal saga are clear from the news articles noted below.

The final outcome, in brief

1. Commoner eventually left Washington University to become Director of the Center for the Biology of Natural Systems at Queen’s College in New York.
2. A single Biology Department was established in 1969.
3. Hamburger obtained funds for constructing a new research wing from the Monsanto Chemical Company.
4. Levi-Montalcini and Cohen were awarded a Nobel Prize in 1986.
5. More than 350 scientists celebrated Hamburger’s 100th birthday at a day-long symposium at Washington University. He died on June 12, 2001, one month shy of his 101st birthday.

Rita Levi-Montalcini – Autobiography, Nobelpize.org
Washington University Magazine, Spring 1987; featuring Viktor Hamburger.

St. Louis Post Dispatch news article on celebration of Hamburger’s 100th birthday,
Fritz Lipmann  (Nobel Laureate)

In 1941, Lipmann published a review in *Advances in Enzymology* that led to a revolution in theories of bioenergetic mechanisms. Lipmann introduced the concept of “phosphate bond energy,” also referred to as “high energy phosphate bonds.” As of 1947, my Ph.D. research with Kamen was primarily concerned with testing the possibility that in photosynthesis, light energy is converted to chemical energy in the form of “high energy phosphate bonds.” In 1947 (or 1948), Lipmann visited us in St. Louis to discuss bioenergetic problems. He had discovered acetyl phosphate as a metabolic intermediate, but its role was puzzling.

My research at the time of Lipmann’s visit strongly indicated that in photosynthetic bacteria, light energy was converted to “high energy phosphate bonds.” The experimental results were described in ref. 31. Sometime later, A.W. Frenkel investigated this problem in Lipmann’s laboratory; Lipmann instructed him to first study our 1948 paper. Frenkel was able to demonstrate conclusively that light energy was, in fact, converted to “high energy phosphate bonds” (in the form of ATP by preparations made from photosynthetic bacteria). This advance led to reformulation of key aspects of energy conversion in photosynthetic processes.
Studies on acetyl phosphate in Lipmann’s laboratory eventually led to discovery of Coenzyme A, the coenzyme of acetylation. Acetyl-coenzyme A turned out to be a crucial substance in initiation of the Krebs cycle, which is responsible for energy conversion in the respiration of animals and microbes. The 1953 Nobel Prize Award to Krebs and Lipmann recognized their great contributions in explaining major metabolic cycles in living organisms.

As noted in the Krebs file, Krebs and Lipmann visited the Departments of Microbiology and Biochemistry at Western Reserve University in 1954. These occasions were marked by memorable celebrations. My first Ph.D. graduate student, Harry Peck, was still with me and we arranged for him to do postdoctoral research with Lipmann at the Massachusetts General Hospital (1956) and then at Rockefeller University (1957), where Lipmann spent the rest of his outstanding career. In 1994 I delivered the first Harry D. Peck, Jr. Lecture at the University of Georgia, where Peck established and developed a highly regarded Department of Biochemistry.

*Current Aspects of Biochemical Energetics*, Fritz Lipmann


Remarkable testimony to a great scientist.


A fascinating account that shows the extraordinary range of Lipmann’s insights of biological mechanisms.

A. W. Frenkel: Fritz Lipmann’s contributions to photosynthesis.

Fritz Lipmann biography. Nobelprize.org

Joel Mandelstam  (Fellow, Royal Society)

Joel Mandelstam was educated in South Africa, and emigrated to London, England, in 1947. After four years as a Lecturer at Queen Elizabeth College, he joined the staff of the National Institute for Medical Research (Mill Hill, London). During a sabbatical leave from Washington University (1965-66), I did collaborative research with Mandelstam at the National Institute, and this was the beginning of a close friendship.

In 1966, Sir Hans Krebs invited Mandelstam to become head of the Microbiology Unit of the Department of Biochemistry of Oxford University. At Oxford, Mandelstam developed an extensive research program on the mechanism of spore formation by the bacterium Bacillus subtilis. With numerous graduate and post-doctoral students, and technicians, Mandelstam successfully explored the biochemistry and genetics of spore formation and this became a “model system” of developmental microbiology and biochemistry.

I have visited Mandelstam in Oxford many times for scientific discussions, and we became close friends. When he retired in 1987, a special symposium was held in his honor, which I attended. A list of the large number of scientists who attended, from many countries, is attached to the “Seating Plan for High Table, Joel Mandelstam Dinner” (at Wadham College). Professor Keynan from Israel
was a keynote speaker at the symposium. Sir Hans Kornberg (a protégé of Sir Hans Krebs) was an old friend. A special note on Sir Edward Abraham: He was a young member of the extraordinary team of Oxford scientists that first isolated penicillin in the late 1930’s. He later designed modifications of penicillin of great therapeutic value. It is especially noteworthy that Abraham donated all of his royalties to Oxford University to fund an Abraham Fellowship for distinguished visitors, and for construction of Abraham House, a modern house for use by the current Abraham Fellow. In 1987, Professor Frank Gibson (from Australia) was the Abraham Fellow. My first wife, Janet (deceased 1994) and I were invited with the Mandelstams to an intimate dinner with the Abrahams and Gibsons at Abraham House soon after it was completed.

During the 1970’s, I was involved in an unsuccessful attempt to persuade Mandelstam to accept the chairmanship of the Biology Department at Washington University. The complicated events in this connection are summarized in the Levi-Montalcini file.

A very brief biography of Joel Mandelstam, from Wikipedia.
H. Gest and J. Mandelstam: Heat denaturation of Beta-galactosidase:
Joel Mandelstam Dinner – 28 September 1987; Seating Plan for High Table;
List of attendees, Mandelstam Symposium.
Selected Gest-Mandelstam correspondence (1966-1983); 21 letters from a large file.

Leo Szilard (National Academy of Science)
The file includes:
W. Lanouette: *Genius in the Shadows / A Biography of Leo Szilard, the Man*  
Inscription to 
H. Gest.
Leo Szilard – A Biographical Chronology. From Google.
Leo Szilard: Humanist of the Year. *The Humanist* (magazine) May-June 1960, 
pp. 130-132. This announces an annual award to people of distinguished 
achievement in the cause of humanism, and includes a brief but informative biography. (It notes that Szilard will receive a 1959 Atoms for Peace Award.)
H. Gest: *The July 1945 Szilard Petition on the Atomic Bomb / Memoir by a signer in* 
Copy of the 1945 Szilard Petition signed in Oak Ridge.
Declassified in 1958.

Copy of photograph: July 17, 1995; at the National Archives, Washington, D.C. 
shows William Lanouette and three signers of the Szilard Petition: Ralph 
Lapp, Howard Gest, and John Simpson, Jr. In the foreground, petitions 
with their signatures.
Article from the Sunday *Herald-Times*, Bloomington, July 16, 1995. “Scientists to
recall atom-bomb dilemma. Retired IU Professor among those to speak in Washington on Monday.”

Article from Hoosier Times, Bloomington, July 17, 2005.

“Scientist had hand in nuclear discovery.” Interview with Howard Gest regarding the Szilard Petition, and the 60th anniversary gathering of Manhattan Project scientists in Oak Ridge (June 2005).


DVD, Interview of Howard Gest, by E Noguchi. NHK Japan Broadcasting Corp.; June 18, 2005. Oak Ridge, Tenn. Subject: The Szilard Petition

Reprints of scientific papers by Aaron Novick and Leo Szilard. (I was a friend of Novick’s at the University of Chicago during the early days of the Manhattan Project.):


**Cornelis van Niel** (National Medal of Science)

Obituary (from Google). A comprehensive survey of van Niel’s career (research contributions, teaching excellence, and influence on development of microbiology in the United States).


C.B. van Niel: The culture, general physiology, morphology, and classification of the non-sulfur purple and brown bacteria. *Bacteriological Reviews* 8:
1-118 (1944). This is a classic in the field. The bound reprint is inscribed: Howard Gest with best wishes, C. B. van Niel

*Journal of Bacteriology* **42**: 437-466 (1941).

**Harland G. Wood** (National Medal of Science)

When I assumed my first academic position in the Department of Microbiology at (Case) Western Reserve University School of Medicine in 1949, I was fortunate in having colleagues in our department and the Department of Biochemistry who were very knowledgeable in the metabolism of bacteria and animal cells. Harland Wood, Chairman of the Biochemistry Department had made the important discovery in 1937 that bacteria and animal cells used carbon dioxide for synthesis of certain essential metabolites. Before 1937, it was believed that only plants could use carbon dioxide in biosynthetic processes. Wood’s discovery proved to have important significance for later research in a number of areas of biochemistry.

Wood came to Western Reserve in 1946, and quickly assembled a top-flight faculty, who became world-renowned researchers in biochemistry. In addition, he led a curricular reform of teaching for the first two years of medical school that became a model for many other schools of medicine. Despite his many administrative and other obligations, Wood continued productive research that was recognized by many awards and honors, including the National Medal of Science.
He also contributed to public service in many ways, including service on the
President’s Scientific Advisory Committee under Presidents Johnson and Nixon.

Wood was a man of high moral standards, and this was an outstanding
feature of his persona. His obituary in the Biographical Memoirs of the National
Academy of Sciences ends with the following tribute:

“Over the sixty years that Harland Wood spent in science, he made countless
friends in many countries who revered him not just for his accomplishments but for
his intellectual honesty. Here was a man without pretensions whose opinions and
decisions were based on principles and not on personal factors, a man whose mind
was open to new ideas and concepts, a man who by his example and
encouragement got the best out of his associates, and a man who, once he made up
his mind, would drive straight toward his goal. In him one felt the warmth,
strength, and integrity that made him unique and irreplaceable.”

Wood had a strong interest in my own research program with photosynthetic
bacteria, and we collaborated in developing an analytical method for a biochemical
metabolite. (H. G. Wood and H. Gest: Determination of formate. In Methods in
Academic Press, 1957.)

On Wood’s 80th birthday, a symposium was held in his honor (October
22-23, 1987), which included many luminaries of biochemistry and micro-biology.
I was unable to attend, but Harland sent me a unique memento of the symposium
with a warm personal message (see list below). In 1985, Wood published a
detailed review, describing his life and scientific career, in the Annual Review of
Biochemistry (this is also included in the collection). Harland Wood was my ideal
of a truly great scientist and humanist, and I was lucky to become a good friend.

D.A. Goldthwait: Harland Wood – active at 80. It is not clear in which journal this was published. The copyright is that of the Federation of American Societies of Experimental Biology; possibly the Journal of Biological Chemistry. The date is 1987.

A Memento of the Symposium on Harland G. Wood’s 80th Birthday; including a cartoon of Wood and his wife Millie. I sent him a quotation in which Cicero describes how in old age, one can still command the ship, without having to climb the rigging. His written message on the memento was:

Dear Howard, what a pleasant surprise to receive that glowing quote from Cicero. It hangs in a prominent place in my office. Wish I could have had you here in person but the frame in my office will remind of the days you were here at Reserve and we had good times and good science together. My best to you and yours. Harn.

P.S. I’m still climbing the rigging in Lab. Merry Christmas.


Charles Yanofsky (National Medal of Science)

In addition to the National Medal of Science, Yanofsky has received numerous prestigious awards including the Albert Lasker Award in Basic Medical
Research. His research on the mechanism of gene expression has been described as one of the “most significant events during the past 125 years.” He remains at the frontiers of basic research in biochemistry, microbiology, and molecular biology.

I have been a close colleague of Yanofsky’s for more than 50 years, and have been a visiting investigator in his laboratory at Stanford University a number of times. We have frequently exchanged views on each other’s manuscripts. In the year 2000, Yanofsky asked me to edit a comprehensive account of his research during the previous 50 years. This was published in the *Annual Reviews of Biochemistry*, vol. 70, 2001. A copy is enclosed in this collection.

a review of his career.
Photo: Yanofsky receiving the award from President Bush.
C. Yanofsky: Advancing our knowledge in biochemistry, genetics, and microbiology through studies on tryptophan metabolism. *Annual Review*
of Biochemistry 70: 1-37 (2001). [There is an acknowledgement of my “excellent comments and helpful suggestions.”]

Three letters from H.G. to Yanofsky. The first two (July 21, 2000 and August 10, 2000) apparently are related to the manuscript of the Annual Review of Biochemistry article (2001).
References


6. H. GEST: The effects of inorganic salts on the multiplication of bacterial viruses, *Journal of Infectious Diseases*
73: 158-166 (1943).


8. H. GEST, N.E. BALLOU, B.M. ABRAHAM, and C.D. CORYELL:

9. H. GEST, W.H. BURGUS, and T.H. DAVIES:


16. R.R. EDWARDS and H. GEST: Note on reactions of tracer
bromine exchange with silver bromide and lack of exchange with bromate ion, ibid. Publication 8, paper 234, pp. 1454-1455 (1951).


29. GOVINDJEE, J.T. BEATTY, H. GEST, and J.F. ALLEN, eds.  


P. 1. Bacteriophage researchers at Cold Spring Harbor Laboratory (Long Island), Summer 1942. Bottom row, left to right: Howard Gest, Salvador Luria, John Spizizen, Max Delbrück. Top row, left to right: Edna Cordts (graduate student from Vanderbilt University), and wives: Manny Delbrück, Evelyn Spizizen, Janet Gest (deceased 1994).

Coryell, Kamen, Wood, de Hevesy. From *Radiant Science, Dark Politics*, University of California Press, Paperback Edition 1986. de Hevesy (in lower photo) was a Nobel Laureate (1943), who originated the technique of using radioactive isotopes as tracers in studying biological systems. Kamen supplied de Hevesy (in Copenhagen) with radioactive phosphorus in 1939 when de Hevesy was unable to make the isotope in quantities adequate for research. (For more on this topic, see H. Gest: The early history of $^{32}$P as a radioactive tracer in biochemical research. *Biochemistry and Molecular Biology Education, 33*, 159-164 (2005).

H. Gest is circled. At bottom right, Lawrence Glendenin (left) and Jacob Marinsky (right) who, with Coryell first isolated element 61, promethium. The radioactive element was isolated from fission products of uranium.
Martin D. Kamen (left) and Howard Gest in Montecito (California); February 13, 2002. Kamen died during August 2002.

P. 8. [A copy of this photo is available in the original booklet housed in the Indiana University Lilly Library]

P. 9. [A copy of this photo is available in the original booklet housed in the Indiana University Lilly Library]
P. 10. Harland Wood on his 70th birthday. He had studied an enzyme which, under some conditions, appeared in the electron microscope like the head of Mickey Mouse with two ears.
P. 11. [A copy of this photo is available in the original booklet housed in the Indiana University Lilly Library]
Norman Horowitz, on the cover of *Cal Tech* magazine (Nov. 1956) featuring his research on the origin of life.

P. 12. [A copy of this photo is available in the original booklet housed in the Indiana University Lilly Library]


P. 16. [A copy of this photo is available in the original booklet housed in the Indiana University Lilly Library]

Drs. Gerty and Carl Cori, as I knew them at Washington University in 1947 (from Science, 20 October 2006). They were awarded the 1947 Nobel Prize in Psychology or Medicine. Carl was chairman of the Biochemistry Department at the School of Medicine. The Friday afternoon research seminar of the department was always an outstanding event. Aside from faculty, postdoctorals, and a few graduate students, attendance was by invitation only. I delivered my first research seminar to this sophisticated audience and survived!
P. 17. [A copy of this photo is available in the original booklet housed in the Indiana University Lilly Library]


P. 18. Charles Yanofsky (early 1960’s).
P. 22. Charles Coryell (in dark glasses) at a reception at M.I. T. on May 19, 1970, following presentation of an award for his notable contributions to nuclear chemistry. Left to right: Jerome B. Wiesner, President of M.I.T., Barbara Buchman Coryell (sister), Charles D. Coryell, Evelyn Padway Brady, Edward L. Brady, Glen T. Seaborg (Nobel Laureate, 1951). Ed Brady and I were members of Coryell’s research group at the University of Chicago and Oak Ridge.