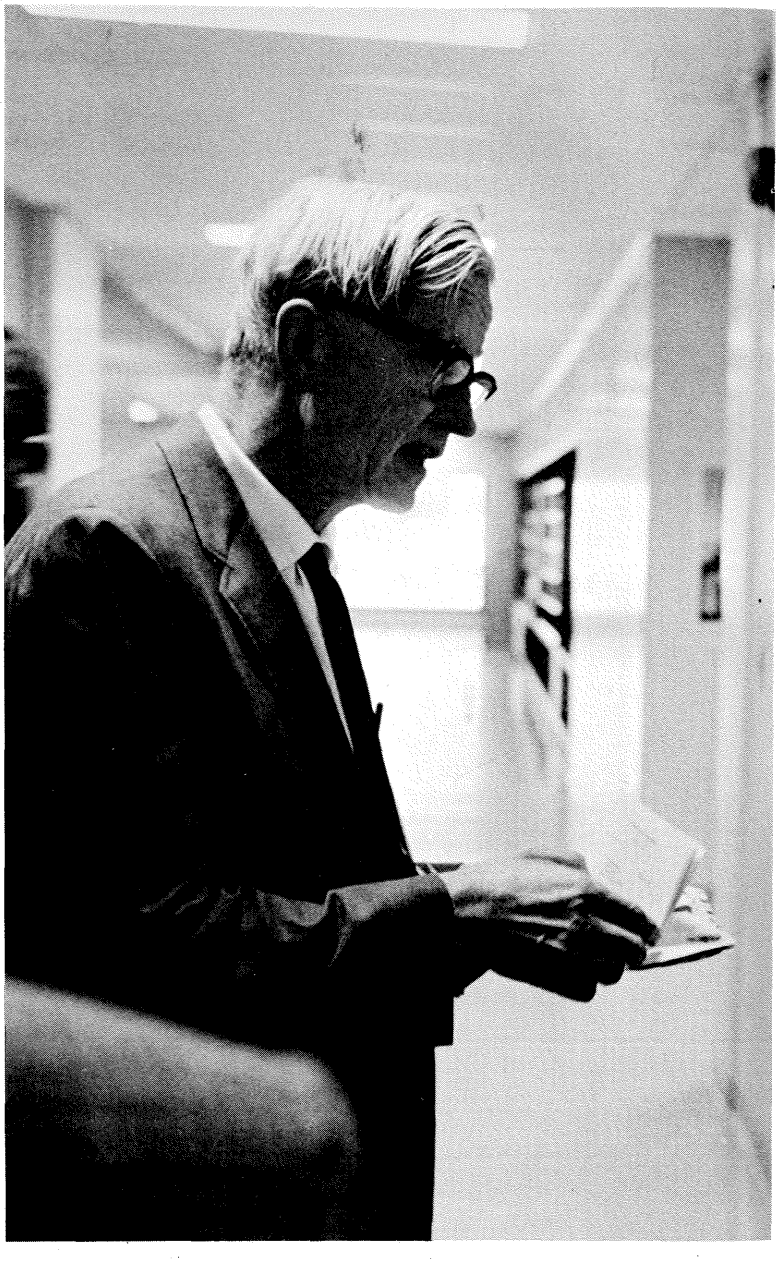
Delbrück: Conscience, Goad, and Sage

While looking for a paradox he never discovered, he helped found molecular biology and inspired hundreds of colleagues to emulate his own high standards of scholarship



For 30 years the question "What will Max think of it?" has guided biologists as they home in on the secrets in the DNA molecule. Max Delbrück's presence at Caltech for most of that time has been instrumental in maintaining the Institute's prominence in biology, which began when Thomas Hunt Morgan came to Pasadena in 1928. Now Delbrück, like Morgan, has won the Nobel Prize in medicine and physiology, along with his long-time friends and collaborators Alfred Hershey of the Carnegie Institution and Salvador Luria of MIT.

The award recognizes Delbrück's research in the years 1937 to about 1952. There is a fairly direct line from his and Emory Ellis's early work on the growth of viruses, through his and Luria's early work on viral genetics, to Hershey's prime evidence that DNA carries genetic instructions, to Watson's and Crick's climactic discovery of the double helix structure of DNA in 1953. But perhaps even more, the prize honors Delbrück's unifying influence on the developments in the new field of molecular biology in that period.

Delbrück was leader of the informal Phage Group of scientists, a group born one summer at the Carnegie Institution's genetics research laboratory at Cold Spring Harbor, New York, and meeting at Caltech during each

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In 1969–Two Nobel Prizes

academic year to evaluate progress. These two institutions were described as the "Mecca and Medina of the Phage Group to which the faithful made their periodic hadj" in the introduction to a collection of essays written in honor of Delbrück's 60th birthday in 1966. Although the Group didn't begin to assume much importance until after the war, its origins were earlier—a meeting of Delbrück and Luria in 1940. In 1945 Delbrück taught the first of his famous summer courses in phage at Cold Spring Harbor; after that, taking the course became the *sine qua non* for a person to be considered a phage biologist.

Phage—or bacteriophage—is a kind of virus that attacks relatively simple, single-celled bacteria. Although the existence of bacteriophages had been known about for years, it was not until the mid-thirties that their applicability for the study of biological reproduction was recognized. Delbrück's and Luria's early work was really a fresh start for phage. They set aside other people's results for the preceding 25 years, began again, and produced an exciting new area of research characterized by simplicity, elegance, and precision.

The group concentrated on seven strains of virus, all of which infected the bacterium *E. coli.* They were identified as T1 through T7, and most of the work was done with T2 and T4. The mechanism they studied was the way the phage infects the host cell, which later bursts and releases mutiple progeny of the infecting phage.

In the early thirties Delbrück was well launched on a brilliant career in physics. He had taken his PhD in 1930 under Born and Heitler at Göttingen with a thesis on the "theory of homoplanar bonding of the lithium molecule." He had written a paper earlier with Eugene Wigner on group theory and quantum mechanics, and identified a kind of elastic scattering of photons in the coulomb field known as the Delbrück Effect. Following his graduate work, he studied physics in Bristol, Copenhagen, Zurich, and Berlin. In a period of about four years he worked with or under seven men who ultimately won the Nobel Prize in physics.

Delbrück, youngest of seven children in a large and distinguished family of German statesmen and scholars, developed an early interest in astronomy—largely, he says, "as a means of finding my own identity in an environment of many strong personalities, all of them senior to me, many of them with high accomplishment, but none in science." During his graduate study he shifted to theoretical physics, a natural move in light of the revolution in physics occurring then and centered at Göttingen.

While in Copenhagen, Delbrück became interested in biology as a result of Niels Bohr's speculation that aspects of quantum mechanics might have applications to other fields, particularly biology. In 1932, with his interest turning to biology, Delbrück moved home to Berlin, largely

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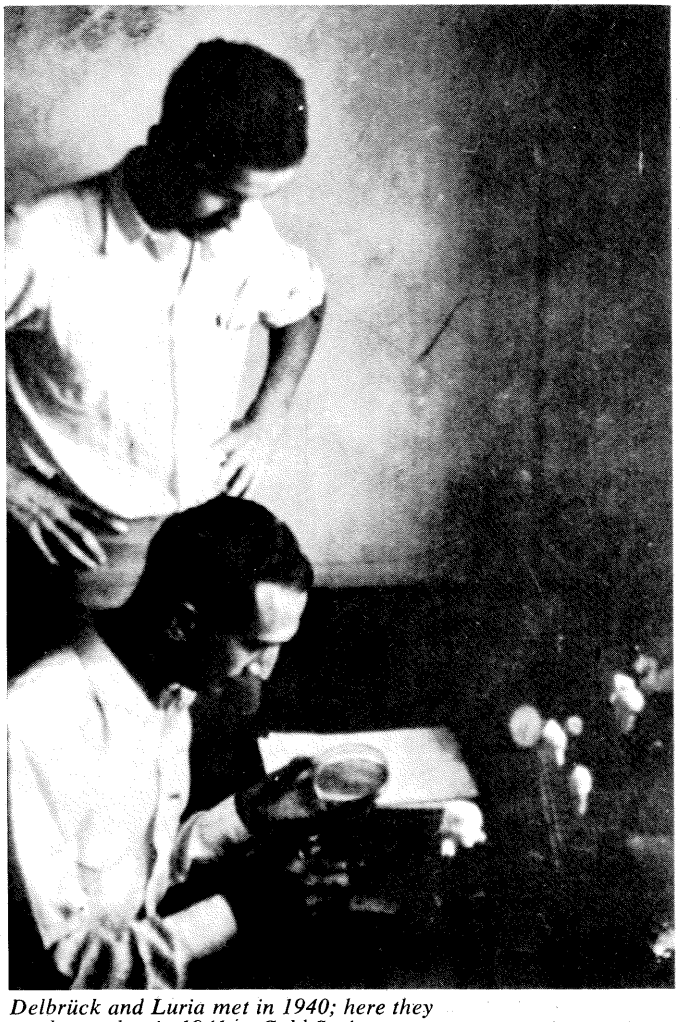


Delbrück and Luria met in 1940; here they work together in 1941 at Cold Spring Harbor, which later became the summer home of the Phage Group.

Phage Group members at Caltech lunching with Delbrück in 1949 are Jean Weigle, Ole Aaloe, Elie Wolman, Gunther Stent, and G. Soli.

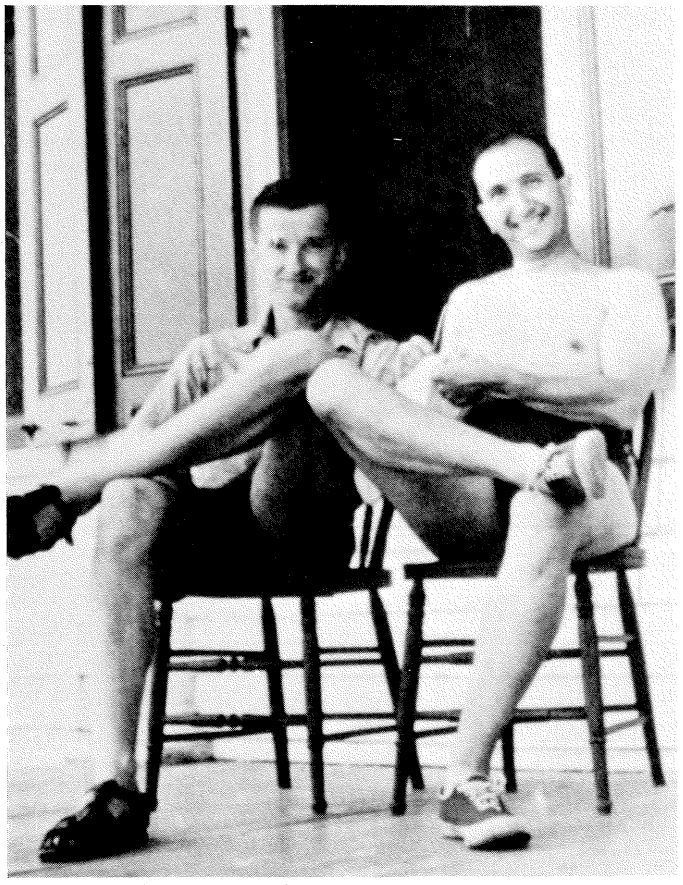
in hope that the proximity of the various Kaiser Wilhelm Institutes would help him learn the new field. Starting in 1934 a small group of physicists and biologists met privately, mostly in Delbrück's mother's house. Several papers resulted from the meetings; part of one of those papers (by Timofeeff, Zimmer, and Delbrück on mutagenesis) was restated ten years later in a little book called *What is Life?* by Nobel physicist Erwin Schrödinger. Most biologists took little notice, but several excellent physicists in that immediate postwar period read Schrödinger's account of the "Delbrück Model" and subsequently found their way into phage biology.

Delbrück, with the support of the Rockefeller Foundation, left Germany in 1937 and came to study biology at Caltech. He was attracted, as were many others,

to Thomas Hunt Morgan and Alfred Sturtevant, the *Drosophila* geneticists. In his two years at Caltech his interest in viruses solidified, and he and Emory Ellis did their early work on the growth of bacteriophage. When the war broke out in Europe, Delbrück chose to remain in the United States. Many members of his family in Germany became leaders in the anti-Nazi resistance, and many (including his brother, brother-in-law, and several cousins) were killed. After two years at Caltech he took a job in the physics department at Vanderbilt University in Nashville, Tennessee. He remained there until 1947, when he was brought back to Caltech by its new biology division chairman, George Beadle, another of Caltech's Nobel Laureates.

Delbrück met Luria at a dinner with two German physicists in Philadelphia in late 1940. Luria says, "The talk was mostly in German, mostly about theoretical physics, and mostly above my head." But afterwards he and Delbrück spent two days experimenting in phage plating methods in Luria's laboratory at Columbia University. At that time the two men were probably the only ones interested in molecular biology aspects of phage. They agreed to meet for further collaboration in the summer of 1941 at Cold Spring Harbor where Delbrück was to attend a symposium. They worked together again in the fall of 1942 in Nashville—Delbrück the German alien, Luria the Italian, almost alone in the field while other scientists concentrated on wartime research projects.

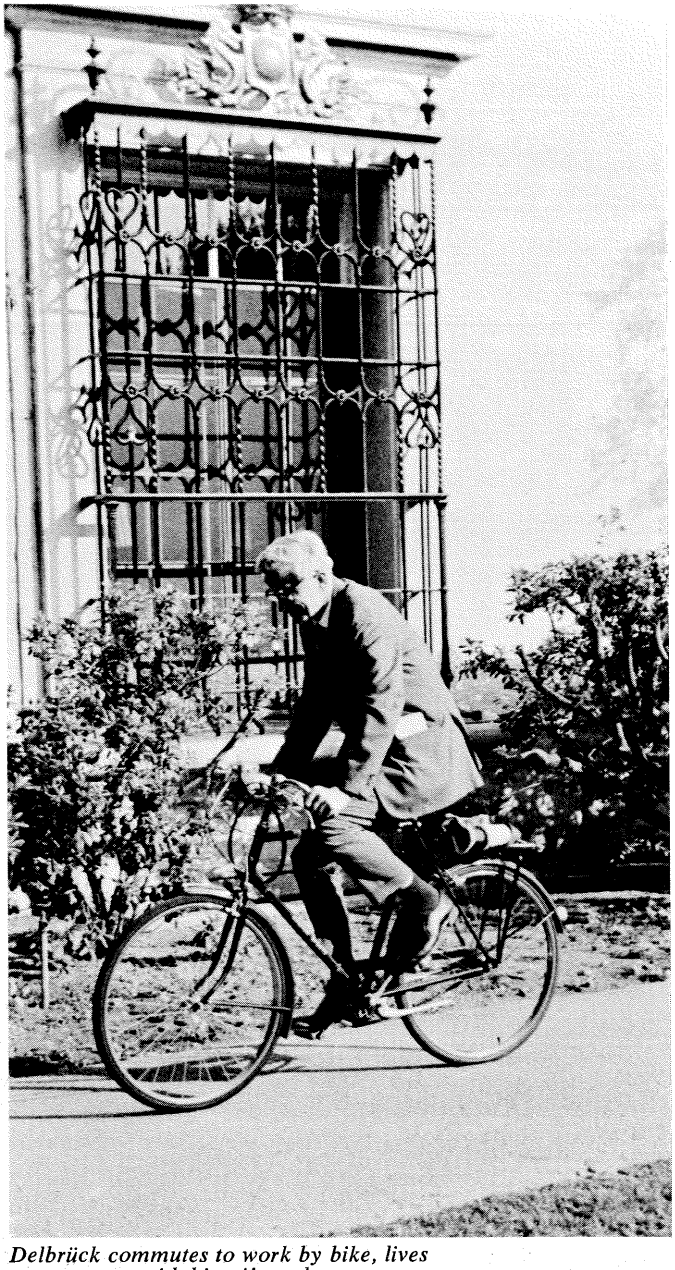
From 1942 to 1944 they published five papers (one with Thomas Anderson). Delbrück and Luria sensed the potential importance of what they were doing and worked to attract others to the field. Eight people, including the three 1969 Nobel Laureates, showed up for a meeting of the Phage Group in Nashville in 1947. Today hundreds attend the annual phage meetings in Cold Spring Harbor.



Delbrück and Luria at Cold Spring Harbor, 1953.

The late forties and early fifties, with the Phage Group growing and secrets of genetics being revealed little by little, were exciting times at Caltech. Thomas Anderson, who did early electron microscopy of phage, says that "at each phase in our groping toward discovery, Max Delbrück seemed to be present not so much as a guide, perhaps, but as a critic . . . an enquiring, and sometimes merciless, logician. If one persevered, he would be fortunate to have Max as conscience, goad, and sage."

With experiments being done almost nonstop, Delbrück, always anxious to keep workers elsewhere in the world up to date, sometimes used forceful techniques to get results



Delbrück commutes to work by bike, lives near campus with his wife and two younger children. Two older ones are in college.

into print. He would take his colleagues to Caltech's marine biology laboratory at Corona del Mar, lock them up with paper and pencils, and order them to write. Delbrück's wife, Manny, typed up the reports as rapidly as they were written. Participants criticized each other's drafts, and at the end of three days each would have a completed paper.

On other occasions Delbrück would stop all work in the lab to take everyone available to the desert for a few days of talk and fellowship. Caltech biologist Seymour Benzer recalls that sometimes Delbrück would declare Wednesday and Thursday to be the weekend. Then they would drive off into the sand until the car stuck; that determined the campsite. The next day was spent digging the car out. Desert trips are still a favorite means of entertaining visitors—at least for Delbrück. Luria long ago refused to visit Caltech unless he was granted immunity from camping.

Delbrück had taken up biology expecting that perhaps radical new principles, comparable to quantum mechanics in physics, would be revealed in the course of its development. But biologists encountered no "wave/particle" kind of paradox as physicists had 25 years before; molecular genetics was explained by conventional processes.

In the early fifties, with phage "in good hands," Delbrück turned to studies of the nervous system, which have since turned out to be the "hot" area of biology. And, just as he began his study of biological reproduction with the lowly phage, he has taken up a simple fungus called *Phycomyces*—whose growth is affected by light—as a way of understanding sensory processes. There is now a small *Phycomyces* Group, and Delbrück gives a course on *that* topic each summer at Cold Spring Harbor.

Luria, in reflecting on the Phage Group a few years ago, said, "Seldom has a group of men been so richly rewarded as have we, the molecular biologists, whom the physicist Max Delbrück, more than anyone else, guided to the exploration of the deep mysteries of life."

But Delbrück's influence has been broader, even, than molecular biology. He is a lively member of Caltech's—and the world's—community of scholars, endowed with a warm humanitarianism all his own. Generations of students and colleagues have been stimulated to insight through their associations with him. According to Caltech colleague and former division chairman, Ray Owen, "There has never been a Nobel Prize more deeply deserved than his."