MAX DELBRÜCK
1906-1981

BY JULIE ANN MILLER

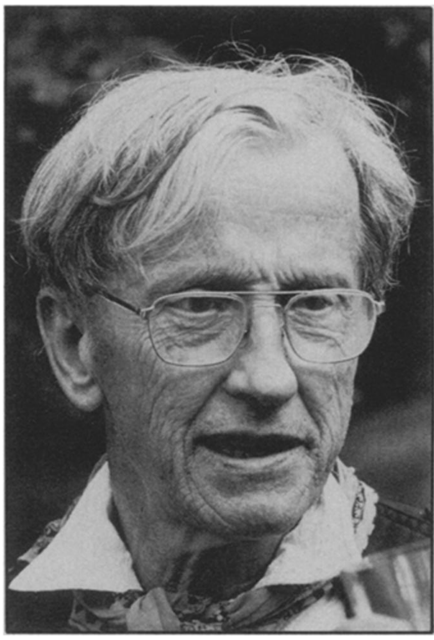
"Molecular genetics, our latest wonder, has taught us to spell out the connectivity of the tree of life in such palpable detail that we may say in plain words, 'This riddle of life has been solved.'"

—Max Delbrück, 1969 Nobel Lecture

When Max Delbrück received a Nobel Prize in 1969, the reaction of his colleagues was "What took so long?" Although little known outside the scientific community, Delbrück, a physicist-turned-biologist who died this March, was a major driving force behind the research that changed genetics from algebraic abstraction into biochemical reality.

"We owe it all to Max," was the refrain in a skit Delbrück's Caltech colleagues put on at the party celebrating his Nobel prize. They portrayed the Nobel committee giving awards, with group after group of winners saying, "We owe it all to Max." In 1958 it's George Beadle, Edward Tatum and Joshua Lederberg, in 1959 it's Severo Ochoa and Arthur Kornberg, in 1962 it's James D. Watson, Maurice Wilkins and Francis Crick, in 1965 it's Andre Lwoff, Francois Jacob and Jacques Monod (they say, "Nous devons tout à Max") and in 1968 it's Robert Holley, Gobind Khorana and Marshall Nirenberg. Again and again the committee members say, "Who's Max? Max who? Never heard of him." Finally, in 1969, the committee can't think of anyone to receive the prize. They say the time has come to scrape the bottom of the barrel, and a committee member scrapes inside the barrel with a rake and pulls out the book *Phage and the Origins of Molecular Biology,* a series of essays dedicated to Delbrück on his 60th birthday. After a song in which "Professors of biology, virology, astrology, state without apology they owe it all to Max," the committee begins to get the idea: "What time do you think it is in Pasadena?" they ask.

The Nobel prize committee cited Delbrück, Salvadore Luria and Alfred Day Hershey for "their discoveries concerning the replication mechanism and genetic structure of viruses," work done in the 1940s. But it is not specific scientific discoveries that are considered Delbrück's greatest contribution to science. Rather, it is his success in attracting people to a very productive field of research and in setting rigorous standards for it. Delbrück was such an effective missionary to the cause of research on simple organisms, especially the viruses (or phage) that infect



Joan James/Cold Spring Harbor Lab

bacteria, that a colleague once described early molecular genetics as the "phage church" in which Max Delbrück was pope "because he defined the doctrine."

As a student in Germany, Delbrück's earliest scientific interest was in astronomy, and he did graduate and postgraduate work in physics with such luminaries as

Roger M. Cole, NIAID, Magnification 270,000

Delbrück preached the value of studying simple viruses, such as these T4 phage.

Max Born and Niels Bohr. But he was not content in these fields. "I had not felt that I had been doing well in astronomy, and I did not feel that I was doing well in physics; and I was just hoping that something would happen that I *was* doing well and was willing to carry on with," Delbrück later recalled.

Eventually he found it. While working in physics, Delbrück began to think about genetics, especially about the possibility of genes being relatively stable macromolecules. As he said in 1969: "Genes at that time [the mid-1930s] were algebraic units of the combinatorial science of genetics and it was anything but clear that these units were molecules analyzable in terms of structural chemistry."

Delbrück felt that biology was not using the most productive tactics. In 1949 he lectured, "Biology is a very interesting field to enter for anyone ... but to the physicist it is also a depressing subject, because, insofar as physical explanations of physical phenomena go, like excitation, or chromosome movement, or replication, the analysis seems to have stalled around in a semidescriptive manner without noticeably progressing toward a radical physical explanation."

Gunther Stent, a biologist who worked with Delbrück, saw more to the lure of the life sciences. In *Phage and the Origins of Molecular Biology,* Stent recalled, "... it was the romantic idea that 'other laws of physics' might be discovered by studying the gene that really fascinated the physicists." Others who followed Delbrück's shift from theoretical physics into biology include Francis Crick, Maurice Wilkins and Leo Szilard.

In 1937 Delbrück received a Rockefeller Foundation fellowship to pursue biology at the California Institute of Technology. By then the Nazis were in power in Germany and had prevented Delbrück from becoming a university lecturer. "It must have been transparent that I wasn't in love with the new regime," Delbrück said last spring in an interview for the Caltech Archives.

At Caltech Delbrück began studying classical fruitfly genetics, but he became discouraged. "I didn't make such progress reading those forbidding-looking papers; every genotype [description of the fly's genetic constitution] was about a mile long, terrible, and I just didn't get any grasp of it."

A colleague at Caltech, Emory L. Ellis, was working with viruses, isolated from Los Angeles sewage, that infect a bacterium "that nobody had heard of before, called *E. coli,* which is now the thing you hear about in grade school," Delbruck recounted. "You could put them [the viruses] on a lawn of bacteria, and the next morning every virus particle would have eaten a macroscopic one-millimeter hole in the lawn. ... This seemed to me just beyond my wildest dreams of doing simple experiments on something like atoms in biology. ..." So Delbrück teamed up with Ellis and then continued working on the viruses, also called bacteriophage or phage, when Ellis returned to research with mouse tumors.

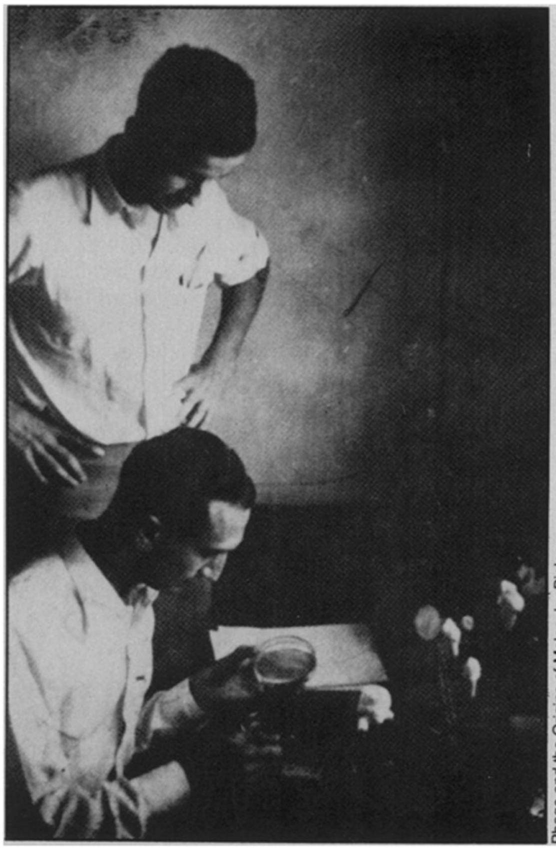
For many years Delbrück's dominant, some say single-minded, interest was phage replication. He was fascinated that just 30 minutes after a single virus invades a bacterium, some hundred progeny phage suddenly burst out of the cell. The group of scientists centered around Delbrück became known as the "Phage School." Their rapid progress was in a large part due to an agreement to concentrate on seven strains of bacteriophage (numbered T1 to T7), an agreement Delbrück negotiated in 1944 at Cold Spring Harbor and that has been called the "Phage Treaty."

In 1945, to drum up further interest in bacterial viruses, Delbrück and another pioneer in the work, Salvadore Luria, gave the first phage course at Cold Spring Harbor. It attracted a "marvelously motley crew," only a few of whom shifted their work to phage, but most of whom subsequently followed the phage literature.

One scientist, Aaron Novick, who took the annually offered course in 1947, called it "a biology that had been made comfortable for people with backgrounds in the physical sciences. ... It seemed to us that Delbrück had created, almost single-handedly, an area in which we could work."

Delbrück described the study of phage as "a fine playground for serious children who ask ambitious questions." Luria tried to explain Delbrück's influence: "It's not so much that he's good at picking people as he is attracting to people. Because he is terribly intelligent. Because it is so exciting to work with him. His ideas, the way he thinks, the order..." (from *The Eighth Day of Creation* by Horace Freeland Judson, Simon and Schuster, 1979).

Similarly, a Caltech colleague, Roy Owens, says, "Max was a model of 'focus' in his attention to research; he identified important problems, thought about them deeply and intensely in terms of what experiments might best be done to solve them, with what material, most economically; he evaluated his results and conclusions, and those of others, mercilessly, and pressed for publication to promote scrutiny and advancement by others. He had a faculty for gathering groups of the most able people around himself, often attracting them from other fields, particularly physics, teaching them by example and catechism, willing to learn himself from almost everything."



Delbrück and Luria infected bacteria with viruses in experiments at Cold Spring Harbor Laboratory, 1941.

Delbrück's interest in phage lasted until about 1950, when he sensed that the question of replication would be answered without any major paradoxes. Saying that he could leave the phage problems "in good hands," he turned his attention to the nervous system. There he began looking for a simple organism to be the "phage" of neurobiology. For the work that would consume the remainder of his career, he chose light-stimulated growth of a fungus called *Phycomyces*.

According to Stent, Delbrück's shift again reflected hope of finding "other laws of physics." At that time biologists were unable to imagine "any reasonable molecular explanation for such manifestations of life as consciousness and memory," Stent has said.

Although Delbrück moved on to another field, his influence continued to be felt in molecular genetics, both as a critic and as a communicator. A whole generation of researchers held themselves to rigorous standards by the threat of "What will Max think?"

Delbrück's criticism could be devastating; he routinely told speakers, "That was the worst seminar I ever heard." Owens says, "Sometimes his behavior seemed inhumane, because he valued an impersonal search for truth, and held a standard that permitted no sham or sloppiness to go unmasked. But he had an extraordinarily warm and humane and perceptive heart. A sense of humor pervaded all of his relationships."

Delbrück's insistence on impartial truth is seen clearly in Horace Judson's description of Delbruck as the messenger of the discovery of the double helix. In 1953 when Watson and Crick in Cambridge, England, first figured out the structure of DNA, Delbrück at Caltech was the first person to whom Watson wrote about it. And in his characteristic abhorrence of secrecy, Delbrück immediately showed the letter to Linus Pauling, who was also trying to work out DNA's structure. Delbrück hesitated only momentarily in respect to the final sentence of the letter: "We would prefer your not mentioning this letter to Pauling."

The same year that Delbrück received the Nobel prize in physiology or medicine, playwright Samuel Beckett was the winner in literature. Delbrück, who greatly admired Beckett, was led to muse on the similarities and differences between science and art. In his Nobel address, Delbrück said, "The scientist has in common with the artist only this: that he can find no better retreat from the world than his work and also no stronger link with the world than his work."

"[A scientist's] message is not devoid of universality but its universality is disembodied and anonymous. While the artist's communication is linked forever with its original form, that of the scientist is modified, amplified, fused with the ideas and results of others and melts into the stream of knowledge and ideas which forms our culture," he said.

Delbrück's long scientific career stands to exemplify that view of research. His work, his communication, melded with the work of many others, has shaped our present understanding of life. □