The virus from the basement

The theoretical physicist **Max Delbrück** is considered to be one of the co-founders of molecular genetics. He began his career in biology in the 1930s when he was an assistant at the **Kaiser Wilhelm Institute for Chemistry**. He was awarded the Nobel Prize for Medicine 50 years ago, for his work on the genetic structure of viruses and how they reproduce.

TEXT **ELKE MAIER**

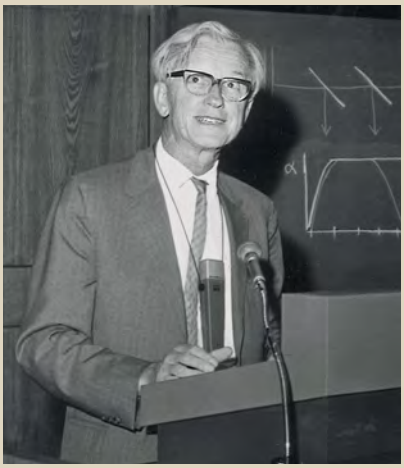
Pasadena, October 13th, 1969. The phone in the Delbrück residence at 1510 Oakdale Street rings in the early hours of the morning. It's a call from Sweden: the Nobel Committee of the Karolinska Institute congratulates Delbrück on winning the Nobel Prize for Physiology or Medicine, which they awarded him along with Salvador E. Luria and Alfred D. Hershey.

When a journalist asks him about his initial thoughts after this call, he answers: "These folks in Stockholm should bear in mind the 9-hour time difference between Sweden and California. It's a terrible thing to call a guy before breakfast."

Max Delbrück, the youngest of seven siblings, was born into an educated family in Berlin on September 4th, 1906. His father was the historian Hans Delbrück and his great-grandfather was Justus von Liebig, a chemist who founded the field of organic chemistry. Delbrück began studying astronomy in 1924. After working in Tuebingen, Berlin and Bonn, he relocated to Goettingen, which at that time was the center of an exciting new scientific discipline – quantum mechanics.

He therefore shifted his focus from the vastness of space to the world of atoms. He obtained his doctorate in theoretical physics under the supervision of Max Born and received a scholarship from the Rockefeller Foundation, which enabled him to work with Niels Bohr in Copenhagen and Wolfgang Pauli in Zurich.

His research career took a radical turn on August 15th, 1932, when Niels Bohr gave a lecture on "Light and Life" at an international conference about light therapy (heliotherapy) in Copenhagen. According to Bohr, just as in atomic physics, where an electron can be thought of either as a wave or a particle, but never as both simultaneously, a complementarity of observational viewpoints also exists in biology. The young Max Delbrück was sitting among the audience. Fascinated by Bohr's ideas, he decided to set off in search of the "elementary fact of life."



At home in two worlds: Max Delbrück considers questions of biology from the perspective of a physicist.

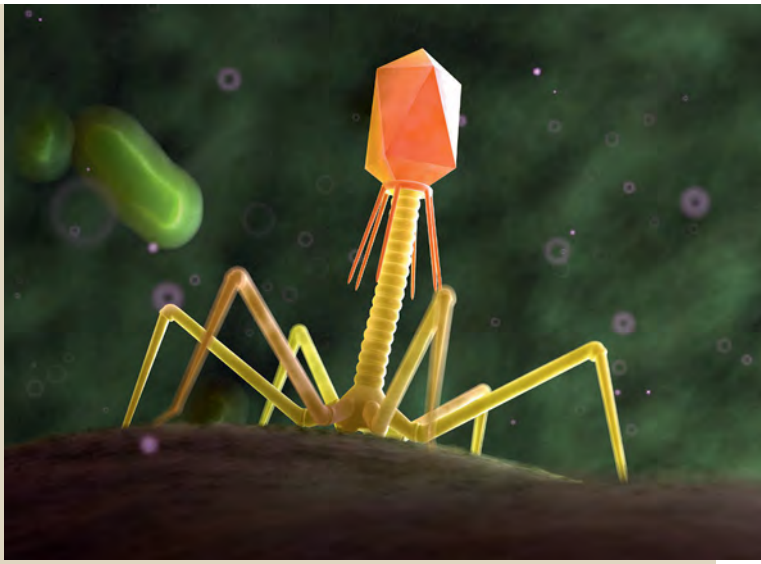
In the same year he began working as an assistant to Lise Meitner at the Kaiser Wilhelm Institute for Chemistry in Berlin-Dahlem, where he attended to his duties as an "in-house mathematician and theorist." Later, he admitted to having misinterpreted experimental results, thereby delaying the discovery of nuclear fission by years. He devoted his spare time to his new passion, biology, organizing private meetings with like-minded people at his parents' home in Kunz-Buntschuh-Strasse in Grunewald. Each of these four-hour sessions, he said, "took place in Papa's large study, into which I had already moved by then. We had painted an old cutting board black and hung it on two coat racks to make a blackboard. We would sit around in very comfortable chairs and sofas and would meet at around four in the afternoon. [...] someone would usually hang around and have dinner with my mother after most of the others had left at around half past seven or eight [...]."

Nikolaj V. Timoféeff-Ressovsky, a Russian geneticist who worked at the Kaiser Wilhelm Institute for Brain Research in Berlin-Buch, where he was experimenting with X-rays to produce mutations in the genome of the fruit fly Drosophila, was also a member of the group. Delbrück published a paper in 1935 entitled "On the nature of gene mutation and gene structure", which he co-authored with Timoféeff-Ressovsky and the physicist Karl Günther Zimmer.

In it, the three scientists were the first to describe the gene – until then an abstract unit – as an atomic structure within which mutations can occur as a result of the rearrangement of atoms or bond dissociation. This famous "three-man book" – also known as the "green pamphlet" – paved the way to modern genetics.

Its success helped Delbrück to obtain a second Rockefeller scholarship, with the aid of which he traveled to California, where he worked with Thomas H. Morgan, a drosophila geneticist and winner of the Nobel Prize for Medicine, at the California Institute

Photo: Archive of the Max Planck Society, Berlin-Dahlem



Lunar Module in miniature format: a phage touches down on a bacterium to smuggle its genome in.

of Technology (Caltech) in Pasadena. However, he soon realized that working with the fruit fly would get him nowhere: he wanted to discover how genes multiply, and for that he needed a simpler system. He was also running out of time, as his scholarship was limited to just a year.

That was when, having almost given up any hope of success, he came across the viruses. He had just returned from a camping trip in early 1938 when he noticed that he had missed an interesting seminar at the Institute, in which biochemist Emory Ellis had presented his experiments with bacterial viruses – the so-called bacteriophages. So Delbrück paid a visit to his colleague, who was of the same age, in his basement laboratory.

The bacteriophages – or phages for short – are viruses that infect bacteria. The so-called T-phages specialize in the intestinal bacterium *Escherichia coli*, and consist of a head, which contains their genetic material, and a tail, which serves as grappling hook. Whenever a phage encounters a bacterium with an appropriate cell surface, it attaches itself and introduces its genetic material into the bacterial cell.

The phage genes then reprogram the cell in such a way that it starts producing new viruses as if on an assembly line until it finally bursts. The new phages are released and immediately enter any other "suitable" bacteria in the immediate vicinity. After just a few hours, holes become visible on a bacterial lawn cultivated by researchers in the laboratory and inoculated with phages. Ultimately, each of these holes is created by a single virus.

Ellis showed Delbrück his equipment: all the phage researcher needs for his work are a few petri dishes, pipettes and an autoclave. Delbrück can't believe it: "I was absolutely overwhelmed that such simple procedures could be used to make viruses visible [...] You could conduct the simplest experiments with something akin to the atoms of biology."

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» Delbrück was one of the founders of the new biology. His research into bacteria and bacteriophages in the 1940s laid the foundations for modern genetics.

With that, Delbrück had found the perfect model system, and without hesitation, he asked his colleague if he could collaborate with him. Whilst Ellis had to give up the phages a year later because his sponsors were no longer prepared to cooperate, Delbrück won the Nobel Prize three decades later.

After his scholarship expired, he took up a position as a physics lecturer at Vanderbilt University in Nashville, Tennessee and continued his research into phages on the side. Having become an American citizen, Delbrück then accepted a professorship at Caltech in 1947. He transformed phage research into a predictable and reproducible science that soon attracted more and more enthusiasts. In the 1940s he founded the legendary "Phage Group" – a loose association of scientists all conducting research into the T-phages.

The phage courses he presented each summer at Cold Spring Harbor near New York also became widely known, and attracted researchers from all over the world. During the early 1960s, the courses were also offered in Germany. The Institute of Genetics was founded at the University of Cologne and Delbrück was appointed as its Director. He continued his research and teaching activities on the banks of the Rhine from 1961 to 1963,

during which time Fritz Melchers, now Senior Research Group Leader at the Max Planck Institute for Infection Biology in Berlin, was a PhD student at the Institute. He remembers Max Delbrück, his "second doctoral supervisor" very well: "His working environment was characterized by a cheerful kind of anarchy, which he had inherited from Niels Bohr's laboratory," he remembers: "His colleagues didn't always have an easy time with him. His first reaction when someone presented important new research results would be: 'I don't believe a word of it!' And he liked to interrupt seminars with statements like: 'I haven't understood a single word yet. Start from the beginning please! And would you please use three short sentences instead of one long one'." His phage courses also achieved cult status in Cologne: "Everyone in Germany who had helped to advance the field of molecular biology had taken part," says Melchers.

One of Delbrück's most important works was published in the journal Genetics in 1943. It describes the so-called Luria-Delbrück experiment, in which he and the physician Salvador E. Luria demonstrate that mutations, which make bacteria resistant to phage attacks, are random and do not occur as an adaptation to the viruses.

Max Delbrück, Salvador E. Luria and the biologist Alfred D. Hershey won a Nobel Prize in 1969 "for their discoveries on the mechanism of replication and genetic structure of viruses." By that time, Delbrück had long since moved on to other fields of research. Phages had become too fashionable for his liking, and the versatile scientist was currently working on questions of perception, such as the reaction of fungal cells to light.

The field of molecular genetics that Delbrück and his colleagues set in motion is still developing at a rapid pace today. Reminiscing towards the end of his life, he once said: "What I discovered for myself at a very early stage is that as a scientist, you could potentially change the world to a far greater extent than Caesar or any of the great military or political figures ever did. And you can sit in a corner and relax while you're about it." Max Delbrück passed away in Pasadena on March 9th, 1981.

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