A Virologist between Two Worlds

Almost no other research field generated insights as exciting as those produced by molecular biology in the decade from 1950 to 1960. Some of these results were attained at the **Max Planck Institute for Virus Research** in Tübingen, where **Alfred Gierer** investigated what it is that makes viruses infectious.

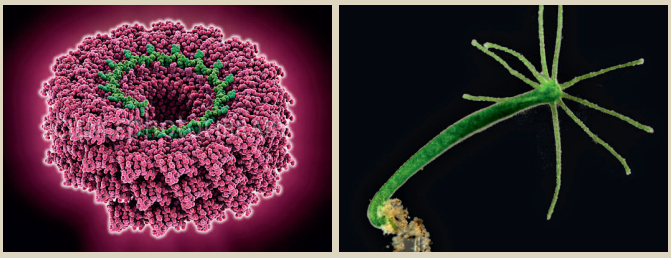
TEXT **MAREN EMMERICH**

Niels Bohr, Werner Heisenberg, Erwin Schrödinger – many of the most renowned physicists from the first half of the 20th century were also great philosophers. From the end of the Second World War, however, if they wanted to be successful in their chosen fields, researchers were increasingly forced to specialize. As a result, it has now become impossible for them to excel in more than one scientific discipline – or so one might think.

Nonetheless, there still exist today some individual high-fliers who manage to do just that. These include Alfred Gierer, born in 1929, who studied physics and went on to publish numerous philosophical works. But it was in a third scientific field – that of virus research – that he attained particular renown.

Alfred Gierer was born in Berlin. From 1934 to 1937, he lived in Shanghai, as his father was working there. A physics teacher who was a great admirer of Werner Heisenberg inspired the young Gierer's interest in science. "When I heard that Heisenberg was coming to Göttingen, I did everything in my power to study there and work at the newly established Max Planck Institute for Physics," says the now 84-year-old scientist. He wasn't disappointed – he still recalls the stimulating atmosphere at the institute with great fondness today.

Alfred Gierer completed his doctorate on the subject of hydrogen bonds, which also play an important role in biological molecules, under the supervision of Karl Wirtz in 1953. He then became one of the first post-war German postdoctoral students to be awarded a Fulbright Fellowship. This enabled him to carry out research for one year at the Massachusetts Institute of Technology in the USA. At MIT, the young scientist focused on enzyme kinetics and investigated how the ambient temperature influences the speed at which the body's detoxification mechanism breaks down alcohol.



In the eye of research: Based on the tobacco mosaic virus (left), in the 1950s, Alfred Gierer proved that the virus's ability to infect plants originates in the nucleic acid. Gierer later focused on biological structure formation and worked on freshwater polyps (right).

When Gierer returned to Germany in 1954, he obtained a new post at the Max Planck Institute for Virus Research in Tübingen. The institute had been established that year from a research group of the same name at the Max Planck Institute of Biochemistry. A new era was gradually dawning in the life sciences: it was the golden age of molecular biology, and the discipline was producing one astounding finding after another.

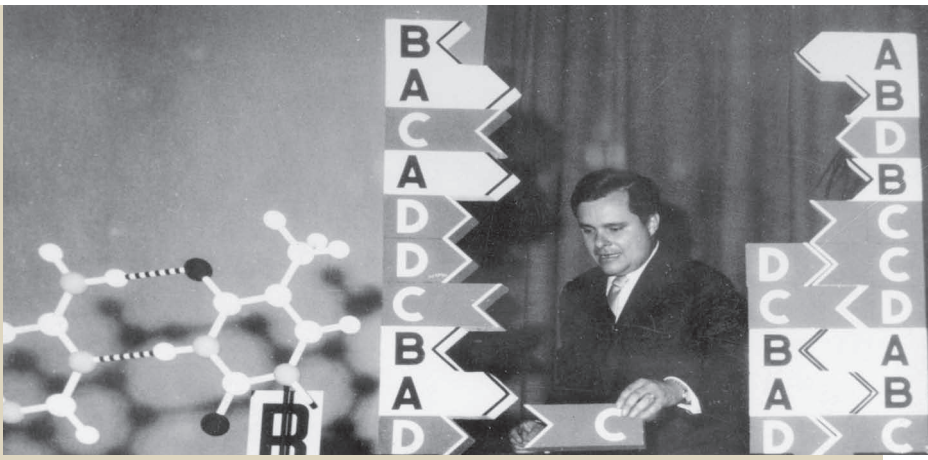
James Watson and Francis Crick had recently brought their investigation of the mysteries surrounding the structure of the genetic substance DNA to a dazzling conclusion with their legendary article in NATURE: the article, which the renowned scientific journal published on April 25, 1953, was entitled *Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid*.

"The Max Planck Institute for Virus Research was an ideal home for a physicist who had changed fields to work in biology. My boss, Hans Friedrich-Freksa, was a very inspiring and open-minded mentor, and Gerhard Schramm and his department established the tobacco mosaic virus as one of the model systems of the new molecular biology," says Alfred Gierer. "It was a wonderful experience for me to do science in this early, romantic phase in the life of molecular biology."

Why viruses, of all things? Exactly one year before the structure of DNA was explained, Alfred Hershey and Martha Chase had used viruses that infect bacteria – known as bacteriophages – to show that nucleic acid is the bearer of genetic information and not proteins, for example, as many scientists had assumed. The nucleic acid is contained in a protein shell in the nucleus of the virus, which doesn't have many other components. In the case of the bacteriophages, the virus injects the nucleic acid alone into the host cell. This showed how viruses infect bacteria. However, at the time, the researchers were still unable to assess the extent to which this mechanism could be applied to animal or plant victims of viruses.

The actual existence of viruses unfolds within animal, plant or bacterial cells. When viruses infect cells, they reprogram them so that they produce the virus nucleic acid, the virus shell and the other virus proteins. When sufficient components have been pro-

Photos: SPL – Agentur Focus (left); Frank Fox – www.mikro-foto.de (right)



Dialog with the public: Alfred Gierer giving his lecture "*Die Geheimschrift des Lebens – Vererbung und molekulare Biologie*" ("The Secret Code of Life – Heredity and Molecular Biology") at the General Meeting of the Max Planck Society on June 20, 1966 in Frankfurt.

duced to equip a complete team of viral offspring, they make a bid for freedom, bursting the cell that has provided them with such vital services. This causes lesions in the organs whose cells are involved – and gives rise to the typical symptoms of the viral disease in question.

The experiments begun by Alfred Gierer and Gerhard Schramm around 60 years ago at the institute in Tübingen made a crucial contribution to elucidating this cycle. "We wanted to find out which components of the virus trigger the infections," explains Alfred Gierer. The researchers worked with the very first virus to be described, the tobacco mosaic virus. Apart from tobacco plants, this virus also infects pepper and tomato plants with tobacco mosaic disease, a pest that once decimated entire harvests.

Die Zeit October 11, 1985
from the review of Alfred Gierer's book *Physics, Life and the Mind*

» The scientist from Tübingen puts his cards on the table. He reclaims the debate surrounding the impenetrable complexity of reality from the philosophers, theologists and mystics. And he officially abandons scientific reductionism, also a product of the excessively narrow, mechanistic world view.«

Gierer and Schramm delicately separated the virus's protein components from its nucleic acid ones and swabbed some tobacco leaves with a solution containing intact viruses, and others with a solution containing its nucleic acid. The result: 10 micrograms of viral nucleic acid caused as much damage to the leaves as 0.2 micrograms of intact viruses. The nucleic acid solution didn't contain any proteins that could be involved in the biological activity. With these experiments, the scientists demonstrated that the ability to infect plants is due to the nucleic acid and that this is therefore the virus's genetic substance. This finding was published in NATURE on April 14, 1956.

Why 50 times more free nucleic acid was needed to trigger the same effect as the intact viruses was, initially, something Gierer and Schramm could only speculate on. Just one year later, however, Alfred Gierer explained the reason for this in a follow-up study: the nucleic acid in the tobacco mosaic virus forms a single, large molecule that is extremely prone to decomposition without the protective virus shell.

Another important discovery followed in 1958: Working with Wolfgang Mundry from the Max Planck Institute for Biology, Gierer found that mutations of the virus can be generated by chemically altering the nucleic acid. The chemical conversion of just one of the 6,000 building blocks of the viral genetic material is sufficient to cause a mutation with a strong biological effect on the infection of tobacco plants: the mutated nucleic acid gave rise to a different kind of lesion on the leaves of the target plant than the original solution.

Following these results, at the invitation of the renowned microbiologist Max Delbrück, Alfred Gierer went to the USA for the second time, this time to the California Institute of Technology in Pasadena. At Caltech, he moved away from virus research and began to study how animal cells produce proteins.

Gierer initially stayed with this topic when, one year after his return to the institute in Tübingen in 1960, he became a Scientific Member of the Max Planck Society and head of a new Department of Molecular Biology. Rapid progress had since been made in this field, and an important intermediate goal had been reached with the unraveling of the genetic code. "The discipline underwent a huge wave of expansion, but the romantic phase was over," says Gierer today. "So why not try something new?"

The scientist was plagued by the question of whether the laws of physics are also fully applicable to biology, and how they can be used to explain the formation of biological structures. Developmental biology was the field that would provide him with the answers he sought. Based on the example of freshwater polyps *Hydra*, he went on to research the factors that control how organisms assume their structural form and the physical principles that underlie this process.

Alfred Gierer's shift in focus from the biology of viruses to the biology of development influenced the orientation of the entire institute at which he worked. Accordingly, in 1984, the Max Planck Institute for Virus Research became the Max Planck Institute for Developmental Biology. Over time, Gierer increasingly linked his areas of research with questions concerning the philosophy of science. In 1985, he published his first book, *Die Physik, das Leben und die Seele* (Physics, Life and the Mind), a work that attracted a very broad media response.

Gierer constantly sought contact with the public. By claiming that "scientists must make science understandable" in an article in the Neu-Ulmer Zeitung newspaper in 1992, he clearly distanced himself from the image of the academic who withdraws to the ivory tower of the university to focus exclusively on his research.

Today, Alfred Gierer remains active as an emeritus member at the Max Planck Institute in Tübingen. He recently summarized the processes for which the development of freshwater polyps can provide a model of structural formation in a philosophy and history of science study published in 2012. It could, perhaps, be said that Alfred Gierer himself provides an interesting model – of the type of researcher who constantly focuses his attention far beyond the boundaries of his own discipline while doing excellent work within them.

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