RETROSPECTIVE

Dieter Oesterhelt (1940–2022)

Pioneer of membrane protein research

By **Peter Hegemann**[1] *and* **Hartmut Michel**[2]

Dieter Oesterhelt, the biochemist who identified the first known microbial rhodopsin, died on 28 November 2022 at age 82. Dieter's discovery of the color and function of the so-called purple membrane of the halophilic bacterium *Halobacterium salinarum*—and the availability, simplicity, and stability of its single protein, bacteriorhodopsin—laid the foundations for the membrane protein research field that he launched in 1971. Microbial rhodopsins act as light-driven pumps, channels, and enzymes, making the field of optogenetics, in which light controls the activity of targets such as neurons, possible.

Born in 1940 in Munich, Dieter spent much of his career close to home. After receiving his diploma in chemistry in 1965 from the University of Munich, he remained there to work with biochemist and Nobel laureate Feodor Lynen on the structure of fatty acid synthetase, earning his PhD in biochemistry in 1967. Disappointingly, the crystals he obtained were disordered, so he joined the laboratory of Walther Stoeckenius, a biophysicist at the University of California, San Francisco, in 1969 to use electron microscopy. In 1979, after brief stints at the Friedrich Miescher Laboratory in Tübingen and the University of Würzburg, Dieter was appointed as a director at the Max Planck Institute of Biochemistry in Martinsried, near Munich, where he worked until his retirement in 2008.

While in San Francisco, Dieter met biophysicist Allen Blaurock, who was working on purple-colored membrane patches from *H. salinarum*. Dieter started the biochemical characterization of this strange membrane as a side project. He discovered that it contains only one protein and showed that its color is caused by the cofactor retinal, just as in animal rhodopsins. For that reason, he named the chromoprotein "bacteriorhodopsin" (BR).

Back in Munich, Dieter found that illumination bleached the purple color reversibly, similar to the color change of rhodopsin in animal eyes upon illumination. But the color of BR regenerated rapidly and did not require enzymatic reactions. In 1972, Dieter proposed that BR functions as a light-driven proton pump, constituting the second most abundant type of photosynthesis in the oceans. BR energizes halobacteria by creating an electrochemical proton gradient across the cytoplasmic membrane, which is used to drive the synthesis of adenosine triphosphate. This relation was the essence of Peter Mitchell's chemiosmotic theory, which BR experiments finally confirmed.

As a Max Planck director, Dieter carefully characterized the bioenergetic functionality of BR, studied its reconstitution from apoproteins, and analyzed the dynamics of the light-triggered proton-pumping reaction cycle. At a time when no membrane protein sequence, gene sequence, or structural information about membrane proteins was available, Dieter and his collaborators used x-ray crystallography, ultrafast spectroscopy, Fourier transform infrared spectroscopy, Raman spectroscopy, and nuclear magnetic resonance to conduct pioneering work on the structure and function of BR.

In 1978, Dieter's new field leapt forward when Har Gobind Khorana and Yuri Ovchinnikov each independently published the amino acid sequence of BR—the first known sequence of a membrane protein. Khorana sequenced the BR gene 2 years later. These two findings triggered a long process of molecular characterization of BR, led by a fruitful and friendly competition between Dieter and Khorana, who shared a deep mutual respect. Both labs, with their many collaborators, elucidated the molecular properties and constraints that determine BR's color, photodynamics, and constituent amino acids. The technology and molecular approaches that were developed for and with BR laid the groundwork for Dieter's and others' rapid characterization of myriad related microbial rhodopsins.

Dieter contributed to other fields as well. He discovered a plant ferredoxin in halobacteria, representing one of the earliest known cases of horizontal gene transfer. He and colleagues showed that the accessory chlorophyll of the photosynthetic reaction center is the first transient electron acceptor of the electron released by the chlorophyll special pair after photoexcitation. With great enthusiasm, Dieter supported diverse technical BR applications, including in biocomputing, holography, and pattern recognition.

Dieter's passion for science came through in his support for fellow scientists. He encouraged many former students and co-workers to launch independent research in his department; we were both grateful beneficiaries of this generosity. The success of Dieter's department arose from its creative atmosphere, where science came first but every individual was appreciated, respected, and supported. Dieter enjoyed lab parties and welcomed everyone to join him on excursions. An avid runner, tennis player, downhill skier, and mountaineer, he enjoyed being challenged athletically by his group members.

In addition to being an enthusiastic experimentalist, Dieter was an active science administrator and science policy adviser, always seeking to identify the best science that could be supported by the available funds. With geneticist Ernst-Ludwig Winnacker, Dieter established the Gene Center Munich, which served as a model for collaboration between the University of Munich and the Max Planck Society. Above all, he generously supported young colleagues as they made their transitions to independence.

For his groundbreaking science and scientific leadership, Dieter received many honors and awards. Already in 1982, he received the Feldberg Prize for Anglo-German Scientific Exchange. His pioneering achievements in biochemistry and molecular biology earned him the Otto Warburg Medal of the German Society for Biochemistry and Molecular Biology in 1991. In 2021, he shared the Albert Lasker Basic Medical Research Award for the development of optogenetics.

Dieter's collaborators and trainees around the world have lost a deeply respected and trusted adviser, supervisor, and friend, who appreciated both strengths and weaknesses but always pushed his colleagues forward into unexplored territories. The global scientific community has lost an exceptional scientist and visionary leader. We owe him a great deal and will continue to honor his memory in our work. ■

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