

served as crucibles for the origin of life itself. Perhaps the deepest root in the evolutionary tree of life was an ancestral, thermophilic, prokaryotic member of the Archaea that derived from precursor, monomolecular organic layers bound to positively charged mineral surfaces of pyrite (FeS₂) in contact with hot vent waters. This pyrite theory, postulated by Wächterhäuser and reviewed by Van Dover, provides an energy-yielding, cationic surface system that can combine with organic compounds to get life off and running. It also accounts for the importance of sulfide in the biochemical pathways of diverse bacteria.

Van Dover has nearly two decades of experience probing deep-sea vents and has made more than 100 dives to depths below 2000 m. Her comprehensive account of these extraordinary ecosystems will prepare readers for the future surprises that await those who delve into the recesses of Earth and space seeking signatures of life in the most unexpected places.

BOOKS: VIROLOGY

From Infectious Filtrate

Hans-Jörg Rheinberger

Few objects have had such a long-lasting and multifaceted impact on the history of 20th-century life sciences as tobacco mosaic virus (TMV). In 1898, Martinus Beijerinck from the Polytechnical Institute of Delft, Holland, published a remarkable paper entitled "Concerning a *contagium vivum fluidum* as cause of the spot disease of tobacco leaves." On the basis of his innovative experiments, Beijerinck judged the causative agent to be non-particulate, thus a contagious live fluid. This remarkable work opened a new field of research and began the scientific career of an infective entity distinctly different from bacteria. Early viral phenomenology became based on three characteristics that contrasted with bacteria. Viral agents proved to be filterable, to be invisible under the light microscope, and to require a host for multiplication.

Prepared to commemorate the centennial of virology, *Tobacco Mosaic Virus* provides a collection of classic research papers on TMV accompanied by brief commentaries on their significance. The editors, Karen-Beth Scholthof, John Shaw, and Milton Zaitlin, have assembled a distinctive

contribution to the history of virology. They have not presented the history of a discipline, but their concentration on one particular object of changing epistemic interest reveals surprising insights into the trajectories and vagaries of scientific research.

On examination of the chronology of the papers collected in this volume, separate periods of TMV research can be distinguished, each with fairly different scope and orientation. Until the beginning of the 1930s, TMV remained the agent of a particular plant disease; it was mainly of interest, for its phytopathological effects, at agricultural research stations. The year 1935, when Wendell Stanley (at the Rockefeller Institute in Princeton) published "Isolation of a crystalline protein possessing the properties of tobacco-mosaic virus," marked

a turning point. TMV was redefined as a huge macromolecule that was crystallizable and susceptible to physico-chemical characterization through the use of the techniques of a rising molecular biology (including ultracentrifugation, electrophoresis, x-ray crystallography, and electron microscopy).

In the few years between 1935 and 1940, the composition, size, and structure of what had turned from a "fluid" into a macromolecular particle was assessed. Frederick Bawden (at the Rothamsted Experimental Station) and William Pirie (at Cambridge) showed that Stanley's "protein" contained a small but significant amount of ribonucleic acid. J. D. Bernal and I. Fankuchen (also at Cambridge) took a series of x-ray pictures revealing the contours of an internal structure to the particle. Gustav Kausche, Edgar Pfankuch, and Helmut Ruska (at Berlin) presented the first electron micrographs of a TMV preparation. Within a short time, TMV advanced from a fairly restricted instance of plant disease to the general model of a macromolecule located at the boundary between life and inert matter. In addition, it became a privileged test object for sophisticated new instrumentation. There were also indications that the particles were able to undergo lasting changes comparable to mutations. Thus, they might be taken as a model of the units of heredity found in higher organisms, that is, the genes. Around 1940, however, TMV research got stuck. Although the virus had come to be seen as a nucleoprotein, its nucleic acid part remained marginal in the hands and minds of those who worked with it.

It was not until 1955 that TMV resurfaced as a hot spot in the golden decade of molecular biology. In the mid-1950s, Rosalind Franklin at Birkbeck College in London developed the x-ray crystallography of

TMV to the extent that she could determine the location of the RNA within the particle. Researchers at the Max Planck Institutes of Biology and Virus Research in Tübingen, among them Gerhard Schramm, Alfred Gierer, and Karl-Wolfgang Mundry, showed that TMV's ribonucleic acid is the infective part responsible for replication. Heinz

Fraenkel-Conrat and Robley Williams (from Stanley's lab in Berkeley) made TMV into a model of molecular self-assembly by demonstrating that it could be taken apart and reconstituted to a functional whole in the test tube. For a while, Heinz-Günter Wittmann in Tübingen and Fraenkel-Conrat in Berkeley had high hopes of making TMV into a tool with which to decipher the genetic code. Separately, they set out to systematically characterize mutations in the nucleic acid of the particle with the corresponding amino acid replacements in its coat protein, whose amino acid sequence had become available in 1960. Their hopes ended in 1961 when Marshall Nirenberg and Heinrich Matthaei identified the first code word through an elegant assay based on a completely different, *in vitro* prokaryotic protein synthesis system. Again TMV research receded into a lag phase.

Phages, not TMV, became the tool of choice for dissecting the machinery of replication and gene expression in bacteria. It was not until the period between 1975 and 1985 that the genes of TMV, the molecular dynamics of the particle's assembly, its RNA-protein interaction, the details of its RNA as a messenger, and its nucleotide sequence were characterized. This renewed burst of activity had to await the era of reverse transcription and the availability of complementary DNA, the most important of the technical developments that allowed recombinant DNA work with RNA viruses.

TMV has experienced highs and lows as a model organism through the history of molecular biology. In the current era of genetic engineering, the field appears to be returning to where it came from: agriculture and phytopathology. (It is perhaps not by chance that the book was issued by the American Phytopathological Society.) The most recent papers in *Tobacco Mosaic Virus* show that transgenic plants, which carry parts of the viral genome and so are rendered resistant to infection, have become the targets of an intensified collaboration between academic researchers and agribusiness. The anthology thus conveys a vivid impression of the changing status of and interest in TMV as a research object, from the late 19th century to the present.

Tobacco Mosaic Virus One Hundred Years of Contributions to Virology

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American Phytopathological Society Press, St. Paul,
MN, 1999. 264 pp. \$49.
ISBN 0-89054-236-8.

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