

Marvin D A & Hohn B. Filamentous bacterial viruses.

*Bacteriol. Rev.* 33:172-209, 1969.

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The genetics, structure, and physiology of filamentous bacteriophages are reviewed. Individual virus functions are described at the molecular level and interactions between these functions are discussed. [The *SCI*® indicates that this paper has been cited in over 420 publications.]

## Life with Filamentous Bacteriophages

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In 1960 I completed my doctorate with Maurice Wilkins in London and moved to Alfred Gierer's lab in Tübingen, Federal Republic of Germany, to join his work on reticulocyte ribosomes and to set up X-ray diffraction facilities. There in 1961 I met Hartmut Hoffmann-Berling, a biologist visiting from Heidelberg, who had recently isolated some small male-specific bacteriophages. Crystallizing ribosomes was proving difficult, so to try something new I offered to apply to these phages some of the solution physical chemistry that I had learned from Alfred. According to received wisdom, all small phages were spherical, like  $\phi$ X174. But one of these new phages, fd, resisted our efforts to purify it from filamentous "contaminants" until we realized that the filaments were the phage.<sup>1</sup>

The project that was intended as a short break has now lasted over a quarter of a century. I became interested in using this simple system to study the principles of macromolecular assembly and also the mechanics and regulation of DNA replication. To study phage assembly at the molecular level, it is essential to know the structure of the phage, and I had experience with the X-ray fiber diffraction techniques appropriate to study a filamentous structure. With the optimism of youth, I thought that I could solve the phage structure "with the left hand," as the German

expression goes, while putting most of my effort into experiments on functioning rather than static biological assemblies. I spent several pleasant and educational years in Tübingen working on aspects of fd physiology, genetics, and structure and continued the work with a small research group after I moved to Yale University as an assistant professor. When in May 1967, Ed Adelberg, editor of *Bacteriological Reviews* (as *Microbiological Reviews* then was), invited me to write a review on filamentous bacteriophage, my interests and experience therefore already covered most of the phage life cycle. Barbara Hohn, a friend from Tübingen who had done her doctorate on genetic studies of fd, joined my group for a post-doctoral year that fall and agreed to help with the review. During the year she produced a baby, and this event gave her a break from the lab, which she employed to search through kilograms of *Current Contents*®. Her sharp, thorough intelligence and biochemical background were essential ingredients in the review.

We tried to be comprehensive, and this led to some areas new to us, notably phage classification and nomenclature. Here we had fun inventing names. We proposed that the closely related phages fd, f1, and M13 should be called Ff phages, which stands for "F-specific filamentous phage," but is also the way my wife (who helped with the phage work from the earliest days) abbreviates her nickname. Trying to meld disparate facts led to some proposals that later proved to be substantially correct. For instance, we suggested that filamentous phage DNA could recombine with unrelated plasmid DNA, and progeny DNA molecules from this union could be incorporated into new phage particles and thereby transfer genetic information to a new host. This presaged the widespread use of Ff (especially M13) as a cloning vector. On the other hand, my attempt to decipher Ff structure was premature, although Barbara saved us from my worst excesses. Our literature search turned up some filamentous phages that differed somewhat from Ff, and X-ray diffraction studies of these gave the key to understanding the structure of all filamentous phages.<sup>2</sup>

As with most early maps, our map of the phage life cycle had gaps and mistakes, and areas marked "here be dragons," but the fact that it has become a *Citation Classic* suggests that it did help later explorers. This territory has now been thoroughly remapped<sup>3,4</sup> and remains interesting.

1. Marvin D A & Hoffmann-Berling H. Physical and chemical properties of two new small bacteriophages. *Nature* 197:517-8, 1963. (Cited 125 times.)
2. Marvin D A, Wiseman R L & Wachtel E J. Filamentous bacterial viruses XI. Molecular architecture of the class II (Pfl, Xf) virion. *J. Mol. Biol.* 82:121-38, 1974. (Cited 80 times.)
3. Rasched I & Oberer E. Ff coliphages: structural and functional relationships. *Microbiol. Rev.* 50:401-27, 1986. (Cited 10 times.)
4. Model P & Russel M. Filamentous bacteriophage. (Calendar R, ed.) *The bacteriophages*. Volume 2. New York: Plenum, 1988. p. 375-456.