

Mercedes Berlanga

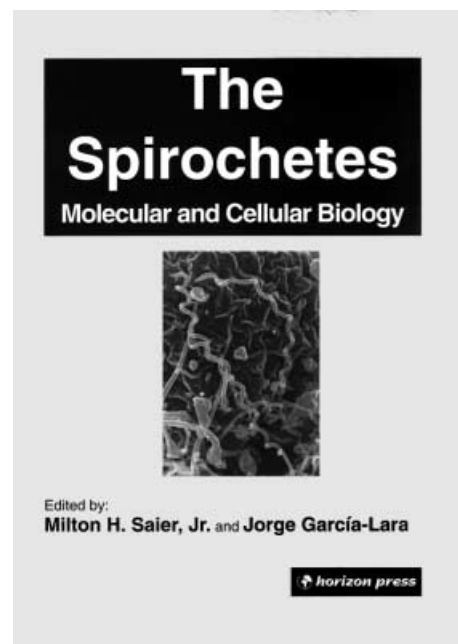
Milton H. Saier, Jorge García-Lara (eds): *The spirochetes. Molecular and cellular biology*

Horizon Scientific, Norfolk, UK, 2001. 222 pp, 28 × 21 cm (ISBN: 1-898486-27-1) £ 84.99

Published online: 18 April 2002
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Although invisible to the naked eye, prokaryotes are an essential component of the Earth's biota, including plants and animals. Spirochetes form a cohesive phylogenetic group in Bacteria, and they are cosmopolitan in distribution, in aquatic environments and in animals. Spirochetes are also of significant medical interest as they cause a variety of diseases in humans, some quite prevalent: Syphilis is a major health problem in several parts of the world; leptospirosis is the most common worldwide waterborne zoonosis; Lyme disease is the most prevalent arthropod-borne disease in the United States; and periodontal disease, which is the major cause of tooth loss, is among the most frequent human infections. Spirochetes have occasionally been confused with spirilla and also with protozoan infection. Fritz Schaudinn (1871–1906) discovered that a spirochete caused syphilis and thought that it might be related to the trypanosome. The 606 compound (Salvarsan) that Paul Ehrlich (1854–1915) synthesized proved to be effective in curing the trypanosome (protozoan) infection, so he proceeded to test 606 as a cure for syphilis. It was remarkably successful and thus the “magic bullet” against the dreaded syphilis had been found. Spirochetes had already been observed by direct microscopy by Antonie van Leeuwenhoek (1632–1723), the discoverer of both protists and bacteria. Van Leeuwenhoek's “animalcules” drawings of his own mouth presumably corresponded to many oral treponemes. Hideo Noguchi (1876–1928) recognized that the chancres manifested early in the course of syphilis were replete with tiny spirochetes. He named them *Treponema pallidum* (“pale turning threads”) because of their appearance and failure to take up stain.

The book edited by Saier and García-Lara contains 18 chapters that summarize important overall aspects of spirochetes, such as motility and chemotaxis



(2 chapters); genetics (10 chapters); spirochete-specific bacteriophage (1 chapter) and host-parasite interactions (5 chapters). Each chapter is written in a scientific-journal-like review format by specialists in this field. For more information, there is an updated bibliography. Figures, schemes and tables contribute additional information to the text.

The phylogenetic foundation of spirochetes based on comparative analysis of 16S rRNA sequences is discussed in Chap. 1. Spirochetes are presently classified as belonging to the Class *Spirochaetes* in the order *Spirochaetales* and are divided into three major phylogenetic groupings. The first family, *Spirochaetaceae*, contains species of the genera *Borrelia*, *Brevinema*, *Cristispira*, *Spirochaeta*, *Spiroplasma* and *Treponema*. The second named “*Serpulinaceae*” contains the genus *Brachyspira* (*Serpulina*). The third, *Leptospiraceae*, contains species of the genera *Leptonema* and *Leptospira*. Novel spiro-

chetal species have been identified from the human oral cavity, the termite gut, and other host-associated or free-living sources. Spirochetes have received much attention not only because of their infectious potential, but also because of their interesting morphological and motility features. Spirochetes have a unique structure and, as a result, their motility differs from that of other bacteria. Chapter 2 explains spirochete gyrations, rotations and their periplasmic flagella; to understand spirochete motility at a molecular level, the proteins and genes involved in motility are being analyzed. Motile bacteria are generally chemotactic, which allows the organism to perform directed movements in response to various environmental signals. Enteric bacteria such as *Escherichia coli* or *Salmonella* respond with movement towards nutrients. Chapter 3 reveals the role of chemotaxis in the pathogenesis of spirochetes. Note that the size of the chromosome of both *Borrelia burgdorferi* and *Treponema pallidum* barely exceeds 1 Mb and lacks genes for many metabolic functions. However, motility and chemotaxis genes take up more than 6% of the chromosome in *T. pallidum* and about 5% in *B. burgdorferi*. Chapter 4 describes the characterization of bacteriophage Φ BB-1 of Lyme disease agent *B. burgdorferi*. Spirochete-specific bacteriophages have coevolved with their hosts over evolutionary time. For this reason, the study of phages can provide clues to the ecology and molecular biology of their host organisms. Chapter 5 focuses on the genetics of lipopolysaccharide (LPS) in *Leptospira*. LPS is the dominant antigen on the surface of *Leptospira* and *Brachyspira*, in complete contrast to *T. pallidum* and *B. burgdorferi* which have no LPS. Chapter 6 discusses the triangle of parasitic interactions between the spirochete and its vertebrate host, and the spirochete and its tick vector using *Borrelia* spirochete as a model. Understanding the key events at the tick vector-host interface will provide a better understanding of the epidemiology and ecology of these important human pathogens.

In the last few years, the genomes of many bacteria, including *B. burgdorferi* (1997) and *T. pallidum* (1998), have been sequenced, Chapters 7, 8 and 9 provide a comprehensive genomic analysis of these two spirochetes. With the availability of genomic data, it is possible to draw their metabolic maps (Chap. 7). Chapter 8 analyzes membrane transporters, and finally, Chap. 9 describes the housekeeping genes of *Borrelia*. All examined *Borrelia* species contain numerous, small circular and linear extrachromosomal DNA molecules that may exceed half the size of the linear chromosome. Why are these bacteria driven toward a minimalist (\approx 1 Mb) chromosome, while at the same time they maintain large numbers of extrachromosomal elements? Chapter 10

focuses on the most obvious example of sequence repetition found in *Borrelia* species, the cp32 plasmid family. Chapter 11 discusses the current repertoire of antibiotic markers that are useful for spirochetal genetic manipulation. Chapter 12 reviews the methods that have been used in spirochetes for gene inactivation and DNA exchange, with a primary focus on *B. burgdorferi*. Chapter 13 offers strategies for constructing shuttle vectors in *Treponema pallidum*. Genome analysis renders a prediction of gene function, and it may also be used to identify DNA elements involved in transcription, replication, recombination and other cellular processes. Chapter 14 describes the role of genomics in approaching the study of *Borrelia* DNA replication.

Characterization of mechanisms governing the expression of the outer membrane protein (OMP) genes in *Leptospira* are described in Chap. 15; these genes should provide insight into host-parasite interactions. Furthermore, recent advances in heterologous expression of leptospiral OMP genes are opening new avenues of vaccine development. Chapter 16 discusses several genetic regulatory mechanisms adopted by *B. burgdorferi* to sense and adapt to different host and environmental conditions either in vitro or in vivo. Chapter 17 focuses on the environmental transitions that spirochetes undergo during their life cycles and the mechanisms of transcriptional regulation that might possibly mediate spirochetal adaptations to such changes. Chapter 18 analyzes the aspects of the biology of *T. pallidum* in the context of a century of experimental studies and the recently determined genome sequence. *T. pallidum* and a group of closely related pathogenic spirochetes have evolved to become highly invasive, persistent pathogens with little toxigenic activity and an inability to survive outside the mammalian host. The genome sequence will provide useful raw data for additional functional studies on the structure, metabolism and pathogenesis of these organisms.

Compared to what we know about other pathogenic bacteria, our information concerning spirochetes is quite minimal. This book is devoted to the structural, molecular, physiological and evolutionary aspects of spirochetes. The chapters contain summaries of recent accomplishments and exciting new genetic tools for studying several spirochete species. It is truly an interesting time in the discipline of spirochetology! This book is especially recommended for advanced students, senior researchers, physicians and dentists; but all microbiologists have the exceptional opportunity for extending their understanding of unusual prokaryotic characteristics, such as linear chromosomes, a cytoskeleton and the periplasmic flagella that confer rapid motility and uncommon chemotactic capabilities.