Preface

This book may seem like three or four books even though the main focus is on a specialized topic—the bacterial cell wall. Its job is to formulate the innovations that caused life to initiate on earth, those that caused cell physiology to develop without diversity developing, those that allowed the murein walls of the cells to arise, those that led to the separation of the domain of Bacteria from other organisms, those that allowed the Archaea and the Eukarya to develop independently, and those that then led to the development of a very diverse biosphere. It must have taken a long time after the origin of the first cell; evolution had to proceed to produce very effective organisms. At some point a collection of very similar organisms arose that were first called collectively the Last Universal Ancestor (LUA), and stable divergence developed from there. The first bacterium had a protective cell wall and its descendants developed in many diverse evolutionary directions, gave rise to many species of bacteria with various life strategies, and expanded to fill the many niches in the collection.

As the kingdoms or domains of Archaea and Eukarya evolved, many of these organisms (and even some bacteria) acted against bacteria. The development of antibiotics acting on the wall of bacteria and lytic enzymes, called lysozymes, produced by protozoa, plants and animals, led to destruction of many bacteria. These antagonistic challenges to bacteria resulted from its own cell wall structure. This structure was both bacteria's most prominent advantage and its greatest liability. It led to growth success of bacteria and to development of a widespread domain—and to their destruction by other organisms. Man subsequently extended and elaborated these destructive tricks against bacteria, which led to the antibiotic era of medicine. Sometimes however, medical progress has turned out to be retrograde to long term medical advances. The attempt here is present the physics, chemistry and the evolution of life forms that created targets for antibiotics and the bacterial response to antibiotics. Logically all aspects must be considered together in order that new treatments for infection will not only work but will be effective for a long time.

Most of today's bacteria maintain a peptidoglycan or murein wall (called a sacculus or exoskeleton) that surrounds them completely. This strong wall protects them against osmotic differences between the inside and the outside

that otherwise might lead to the influx of water and the resultant rupture of the cell, but it also has many roles in the biology of bacteria. This book focuses first on the chemistry and mechanics of the cell's wall formation and function and how evolutionary forces probably led to its development. The makeup and structure of the wall permit bacteria to occupy diverse habitats and niches. It allows bacteria to do the same things that larger, multicellular organisms do, but in different ways. The book questions and tries to answer: (1) How does the bacterial envelope enlarge safely with the maintenance of cell shape? (2) How does the wall function as a critical cell organelle for other vital bacterial needs? (3) How does division of the sacculus and the bacterial cell occur? (4) How do other living organisms (the Archaea, Eukarya, and particularly, *Homo sapiens*) combat bacteria? (5) How have bacteria evolved in the recent past to overcome human production and distribution of wall-directed antibiotics? The ideas presented are logical conclusions from what we do know, but only tentative answers can be given because ideas about early evolution and more recent evolution have been deduced largely from properties of modern organisms and the current knowledge of molecular genomics.

Arguments throughout the book are mustered to illustrate that prokaryotic life is more directly and simply dependent on physical and chemical principles than are the life forms of multicellular organisms. Of course, either directly or indirectly, the exploitation of physical laws and chemical reactions is dependent on Darwin's three principles. In modern translation these are (1) replication of informational biomolecules must be accurate most of the time; (2) only occasionally do mutations take place, and (3) the translation into functional working forms takes place from the information propagated in molecular form. The role of antibiosis in evolution and man's attempt to use it is for his own advantage include the successes and the failures. In the future, the concepts presented in this book, I am certain, will be critical for medical advances in treatment of infectious diseases.