Antonio van Leeuwenhoek, a draper from Delft, using a tiny homemade microscope, first described microbes or 'animalcules' in a number of letters to the Royal Society. The letters specifically describe 'animalcules' in pepper water in 1676 (published 1677). The famous drawing of a swimming animalcule from a scraping of his teeth was in a letter of 1684 (reference [1] is the original letter while reference [2] uses replica microscopes to interpret the letters and reference [3] is a recent article concisely putting this early work in context). These 'animalcules' were identified as living because they moved, and some were almost certainly bacteria because of their calculated size and swimming pattern ‘...whereas an eel always swims head first, these animalcules swam as well backwards as forwards’. Notwithstanding the Royal Society’s initial scepticism, including wondering whether van Leeuwenhoek was inebriated at the time of his observations, subsequent verification by Robert Hooke unambiguously proved the existence of living, microscopic organisms invisible to the naked eye. van Leeuwenhoek was ingenious in his use of everyday objects (grains of sand, hair of a flea) to guesstimate the size of his animalcules (approx. 3 \( \mu m \)), although his fear at not being believed made him underestimate the number of such organisms in a drop of water in his correspondence with the Royal Society.

van Leeuwenhoek’s use of his single lens microscope changed perceptions about our world. In the intervening 350 years, our knowledge of these animalcules (bacteria) has similarly been transformed. In particular, major technical advances in microscopy, and the advent of genetic, biophysical, biochemical and structural approaches have brought us unparalleled insights into these microscopic organisms. We now also have a far greater understanding of their central importance to human health and disease and to the global environment. In this edition, we focus on a region of bacteria, the cell envelope, that in most bacteria accounts for only 10% of the cell volume but to which the organism typically devotes a quarter of its genome.

The cell envelope gives bacteria their shape, provides the means by which they generate usable forms of energy for growth and division, protects the organism from host immune responses, promotes pathogenesis, is integral to the horizontal transfer of plasmids and other mobile elements and forms the conduit through which bacteria interface with their surroundings. The essential nature of the cell envelope makes it vulnerable to small molecules that bacteria deploy when competing for resources, which is the foundation of antibiotic therapy today. Moreover, the cell envelope remains a popular target in the search for novel antibiotics to combat the rise in multidrug resistance. All the complex functions carried out by bacteria require a high degree of organization, and much of the recent excitement regarding envelope biology stems from our newly formed appreciation of this organization. The reviews published in this collection reflect some of the major advances in the field in the past few years from leaders in their respective fields. While we have endeavoured to capture all that is novel and innovative in bacterial cell envelope biology, inevitably some areas are absent for which the editors apologize. There is only so much you can do (or indeed beg for).

In general, the bacterial cell envelope comes in two types: that of Gram-negative bacteria which have two membranes, a cytoplasmic and outer membrane separated by the periplasm in which is a thin cell wall made up of peptidoglycan, and that of Gram-positive bacteria which have only a cytoplasmic membrane surrounded by a much thicker peptidoglycan layer. The structures and processes described in this theme issue emanate from the cytoplasmic membrane and cover the entirety of the cell envelope, and include studies in both Gram-positive and Gram-negative microorganisms.
The edition begins with the key problem unicellular organisms face, that of identifying their middle at the right time to ensure the even segregation of genetic and cellular material at cell division [4]. The following article covers how proteins move across the cytoplasmic membrane, so that the cell envelope can be built [5]. Peptidoglycan cell wall composition and assembly are then dealt with in the two following reviews [6,7]. The next five articles deal with the problems associated with building the outer membrane. In contrast to the cytoplasmic membrane, the outer membrane is asymmetric, composed of an inner leaflet of phospholipids and an outer leaflet of lipopolysaccharide (LPS). Another key difference is the fact that the outer membrane is devoid of an energy source. All these features mean that building and maintaining the outer membrane has been until recently a puzzle. The five reviews within the theme issue reflect the huge advances that have made and tackle complementary aspects of this problem; these include building LPS at the cytoplasmic membrane, and transporting it across the periplasm and then inserting it into the outer membrane [8,9]; the following two articles deal with the folding and insertion of the major proteins in the outer membrane, which are almost all β-barrels [10,11]. The other major protein component in the outer membrane is lipoprotein, which is dealt with in the next review [12]. The authors highlight how lipoproteins can be displayed on the surface of bacteria. Finally, we deal with structures that span the cell envelope, including the rotary motor of the bacterial flagellum and the related injectisome of the type III secretion system [13], and the type VI secretion system used by bacteria to kill each other during inter- and intraspecies competition [14].

Given the rate of progress in understanding the bacterial cell envelope since van Leeuwenhoek’s time, we can only imagine what the next 350 years will bring. Already, single ribosomes can be resolved almost at atomic resolution in bacteria! The forthcoming decades will undoubtedly furnish us with ever more detailed knowledge of how the structures of the cell envelope are built, maintained and regulated, which will ultimately allow their exploitation as much needed new targets for antibiotic therapy and biomaterials.

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