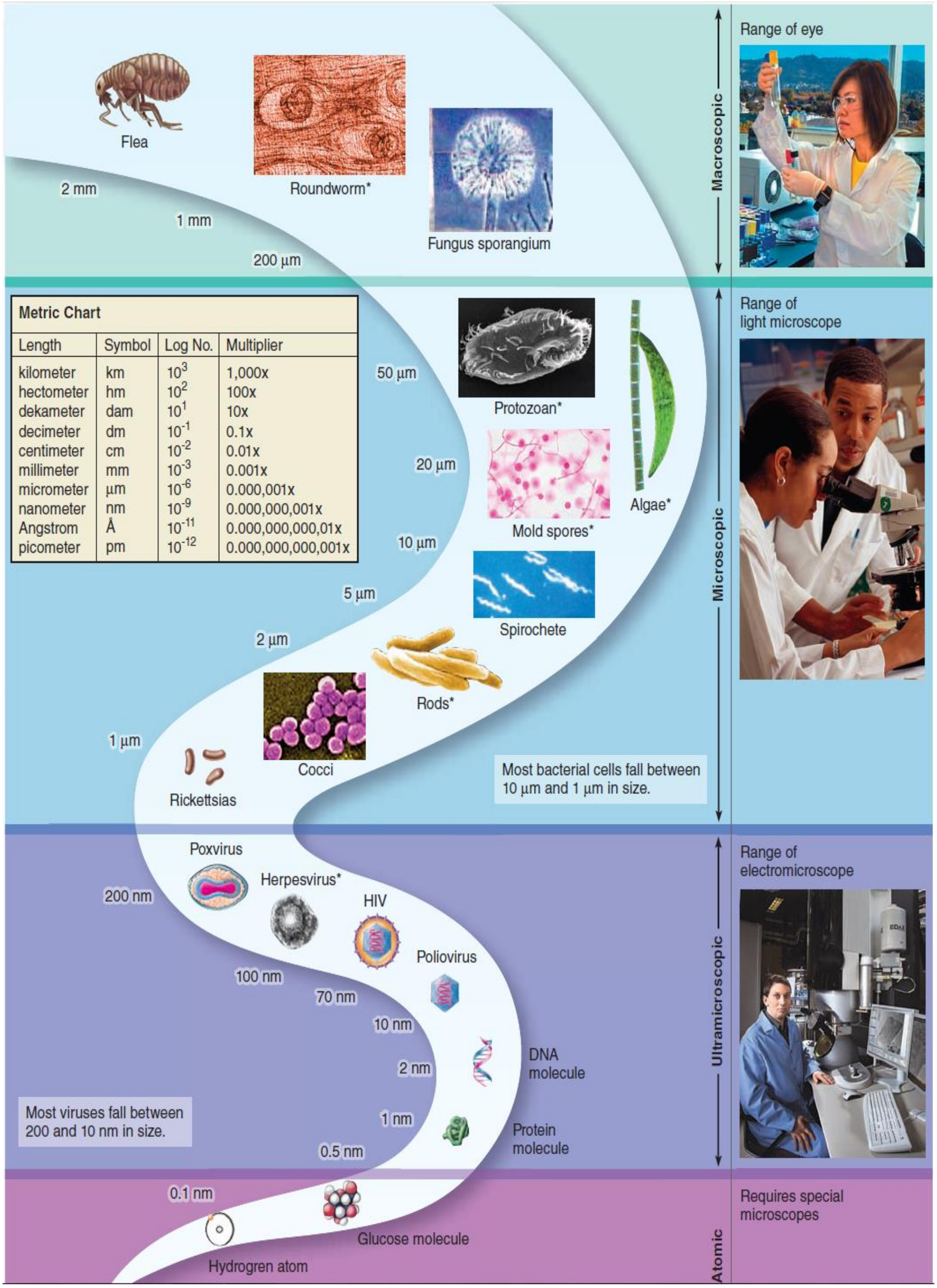
Medical microbiology

Is a branch of medicine concerned with the prevention, diagnosis and treatment of infectious diseases. In addition, this field of science studies various clinical applications of microbes for the improvement of health. There are four kinds of microorganisms that cause infectious disease: bacteria, fungi, parasites and viruses.

Bacteria, along with blue-green algae, are prokaryotic cells. That is, in contrast to eukaryotic cells, they have no nucleus; rather the genetic material is restricted to an area of the cytoplasm called the nucleoid. Prokaryotic cells also do not have cytoplasmic compartment such as mitochondria and lysosomes that are found in eukaryotes. However, a structure that is found in prokaryotes but not in eukaryotic animal cells is the cell wall which allows bacteria to resist osmotic stress. These cell walls differ in complexity and bacteria are usually divided into two major groups, the *gram-positive* and *gram-negative* organisms, which reflect their cell wall structure. The possession of this cell wall, which is not a constituent of animal cells, gives rise to the different antibiotic sensitivities of prokaryotic and eukaryotic cells. Prokaryotes and eukaryotes also differ in some important metabolic pathways, particularly in their energy metabolism and many bacterial species can adopt an anaerobic existence.

In this section, we shall look at the structure of typical bacterial cells and the ways in which they liberate energy from complex organic molecules. Various aspects of bacterial structure and metabolism are the basis of bacterial identification and taxonomy. Bacteria are constantly accumulating mutational changes and their environment imposes a strong selective pressure on them. Thus, they constantly and rapidly evolve. In addition, they exchange genetic information, usually between members of the same species but occasionally between members of different species.

Bacteria have its parasites, called bacteriophages (a type of viruses) which are obligate intracellular parasites that multiply inside bacteria by making use of some or all of the host biosynthetic machinery. Eventually, these lyze the infected bacterial cell liberating new infection phage particles. The interrelationships of bacteria and the phages will be investigated.



Length	Symbol	Log No.	Multiplier
kilometer	km	10^{3}	1,000x
hectometer	hm	10^{2}	100x
dekameter	dam	10^{1}	10x
decimeter	dm	10^{-1}	0.1x
centimeter	cm	10^{-2}	0.01x
millimeter	mm	10^{-3}	0.001x
micrometer	µm	10^{-6}	0.000,001x
nanometer	nm	10^{-9}	0.000,000,001x
Angstrom	Å	10^{-11}	0.000,000,000,01x
picometer	pm	10^{-12}	0.000,000,000,001x

Figure 1.4 The sizes of the smallest organisms and objects. Even though they are all very small, they still display extensive variation in size. This illustration organizes the common measurements used in microbiology along with examples of organisms or items that fall into these measurement ranges. The scale includes macroscopic, microscopic, ultramicroscopic, and atomic dimensions. Most microbes we study measure somewhere between 100 micrometers (mm) and 10 nanometers (nm) overall. The examples are more or less to scale within a size zone but not between size zones.

THE BACTERIAL CELL

PROKARYOTES AND EUKARYOTES

"True" bacteria (which include all bacteria that infect man) are members of one kingdom (the eubacteria, bacteria). In addition, a group of organisms often found in extreme environments form a second kingdom (archaebacteria, *Archaea*). Morphologically, the two kingdoms of organisms appear similar, especially in the absence of a nucleus, and thus are classified together as prokaryotes. However, they have major biochemical differences. Most archaea live in environments such as hot sulfur springs where they experience temperatures as high as 80 degrees C and a pH of 2. These are called thermoacidophiles. Others live in methane-containing (methanogens) or high salt (extreme halophiles) environments.

Archaea

Based on DNA sequence similarities, it appears that the archaea and eukaryotes diverged from the eubacteria before they diverged from each other and in some ways, archaea are biochemically more like eukaryotes than they are the eubacteria. For example, the RNA polymerase of archaea is as complex, in terms of number of subunits, as the eukaryote nuclear polymerases and there is considerable amino acid homology with some of the eukaryotic subunits. Gene promoter structure in archaea is also more similar to that of eukaryotes than eubacteria, although, like the eubacteria, archaea have operons and transcribe these to polycistronic mRNA. Similarity also exists between the protein synthesis factors of archaea and eukaryotes suggesting that the overall protein synthesis mechanisms of eukaryotes and archaea may be similar. The 16S rRNAs of the eubacteria and the archaea are quite distinct in sequence.

Eubacteria (with the exception of the genera *Mycoplasma* and *Chlamydia*) possess peptidoglycan (synonyms: murein, mucopeptide, cell wall skeleton). Peptidoglycan, contains a unique sugar, muramic acid, not found elsewhere in nature. Archaebacteria contain a pseudomurein that is different in structure from eubacterial murein.

In view of the increasing number of similarities between the archaea and the eukaryotes, the term archaebacteria is no longer used. All other cellular forms of life (including plants, animals, and fungi) are referred to as eukaryotes.

Members of the *Archaea* are not human pathogens and will not be discussed further.

Similarities between Archaea and Eukaryotes

	Eubacteria	Archaea	Eukaryotes
Nucleus	No	No	Yes: membrane-bound
Nucleosomes/histones	No	**Yes**	**Yes**
Operons/polycistronic mRNAs	Yes	Yes	No
Introns	No	No	Yes
TATA Box binding	No	**Yes**	**Yes**

protein			
Organelles	No	No	Yes: mitochondria, lysosomes, endoplasmic reticulum etc.
Chromosomes	One Circular	One Circular	More than one
RNA polymerase	One (simple)	**More than one (complex)**	**More than one (complex)**
Protein initiator amino acid	N-formyl methionine	**Methionine**	**Methionine**
Protein synthesis sensitivity to diphtheria toxin	Insensitive	**Sensitive**	**Sensitive**
Peptidoglycan	Yes	**No**	**No**
Protein synthesis	• initiation factors • ribosomal proteins • elongation factors of Archaea are more similar to those of eukaryotes than eubacteria		

DIFFERENCES BETWEEN PROKARYOTES/EUKARYOTES

The prokaryotic cell, in contrast to the eukaryotic cell, is not compartmentalized. Nuclear membranes, mitochondria, endoplasmic reticulum, Golgi body, phagosomes and lysosomes are not present. Prokaryotes generally possess only a single circular chromosome. Since there is no nuclear membrane, the chromosome is bound to a specific site on the cell membrane - the mesosome. Prokaryotic ribosomes are 70S (S stands for Svedberg unit, a measure of size), whereas eukaryotic ribosomes are larger (80S). Prokaryotic ribosomal subunits are 30S and 50S (eukaryotic are larger). The 30S ribosome has 16S RNA, whilst the 50S ribosome contains 23S and 5S RNA. Ribosomal RNA is larger in eukaryotes (e.g. 18S versus 16S rRNA). Bacterial membranes generally do not contain sterols (e.g. cholesterol).

BACTERIAL STRUCTURES

Despite their lack of complexity compared to eukaryotes, a number of eubacterial structures may be defined. Not all bacteria possess all of these components.

Plasmids

These are extra-chromosomal DNA, usually present in multiple copies, that often code for pathogenesis factors and antibiotic resistance factors. Some forms are also involved in bacterial replication.

The cell envelope

Bacteria can be divided into two groups on the basis of staining with the Gram stain; Gram positive bacteria remain stained by crystal violet on washing, Gram negative do not. All bacteria have a cell membrane where oxidative phosphorylation occurs (since there are no mitochondria). Outside the cell membrane is the cell wall which is rigid and protects the cell from osmotic lysis. In Gram positive bacteria, the cell wall peptidoglycan layer is a much thicker layer than in Gram negative bacteria. Gram negative bacteria have an additional outer membrane. The outer membrane is the major permeability barrier in Gram negative bacteria. The space between the inner and outer membranes is known as the periplasmic space. Gram negative bacteria store degradative enzymes in the periplasmic space. Gram positive bacteria lack a periplasmic space; instead they secrete exoenzymes and perform extracellular digestion. Digestion is needed since large molecules can not readily pass across the outer membrane (if present) or cell membrane.

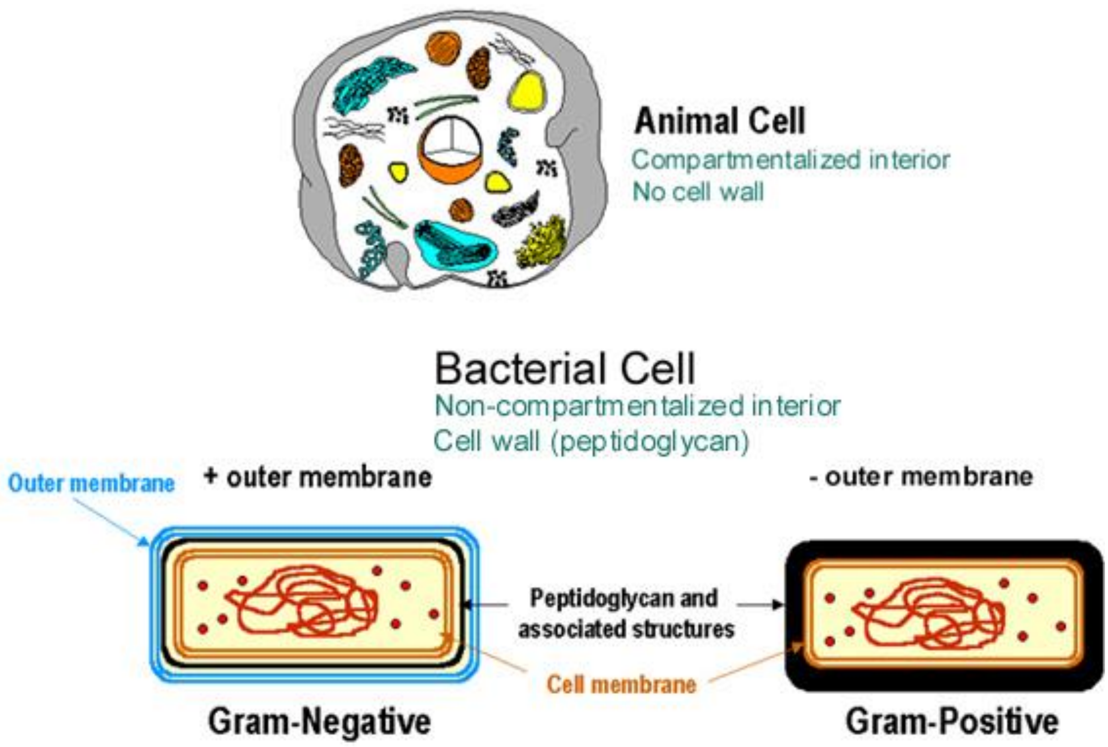


Figure: Comparison of eukaryotes and "eubacterial" prokaryotes

Wall-less forms of Bacteria

When bacteria are treated with 1) enzymes that are lytic for the cell wall e.g. lysozyme or 2) antibiotics that interfere with biosynthesis of peptidoglycan, wall-less bacteria are often produced. Usually these treatments generate non-viable organisms. Wall-less bacteria that can not replicate are referred to as spheroplasts (when an outer membrane is present) or protoplasts (if an outer membrane is not present). Occasionally wall-less bacteria that can replicate are generated by these treatments (L forms).

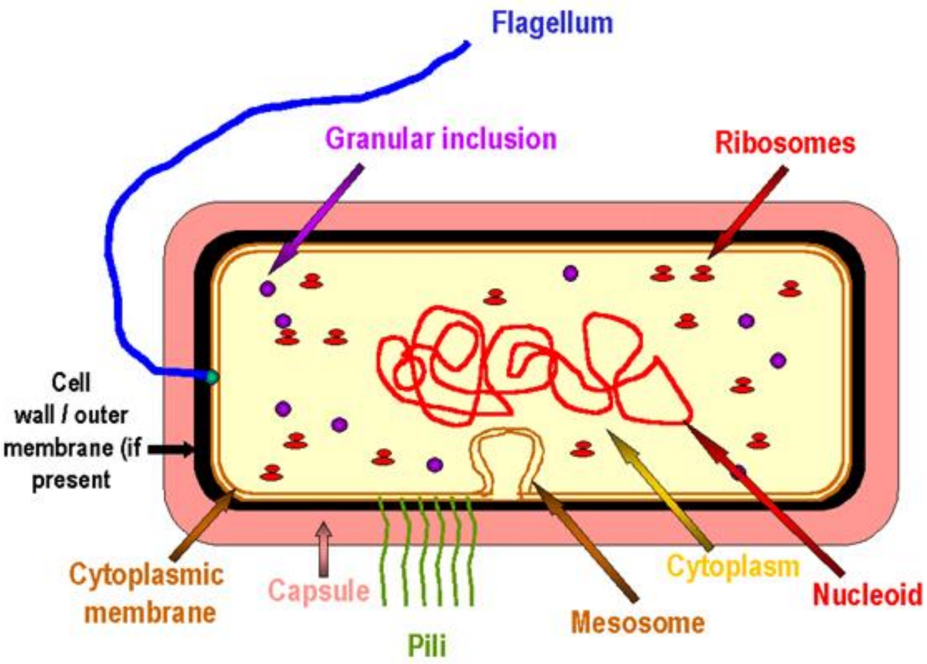


Figure : The prototype bacterial cell

Flagella

Some bacterial species are mobile and possess locomotory organelles - flagella. Those that do are able to taste their environment and respond to specific chemical foodstuffs or toxic materials and move towards or away from them (chemotaxis). Flagella are embedded in the cell membrane, extend through the cell envelope and project as a long strand. Flagella consist of a number of proteins including flagellin. They move the cell by rotating with a propeller like action. Axial filaments in spirochetes have a similar function to flagella. Binding proteins in the periplasmic space or cell membrane bind food sources (such as sugars and amino acids) causing methylation of other cell membrane proteins which in turn affect the movement of the cell by flagella. Permeases are proteins that then transport these foodstuffs through the cell membrane. Energy and carbon sources can then be stored when necessary in cytoplasmic "storage granules" which consist of glycogen, polyhydroxybutyrate or polyphosphate.

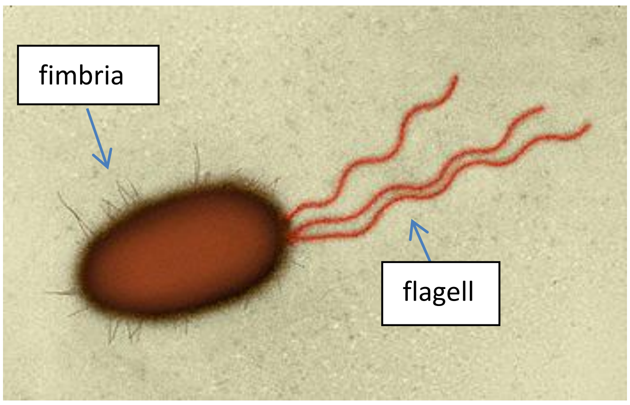


Figure 4. E. coli - rod prokaryote with multiple flagella

Pili (synonym: fimbriae)

The types of pili (or whether they are produced at all) varies both among and between species. Pili are hair-like projections of the cell. Some are involved in sexual conjugation and others allow adhesion to host epithelial surfaces in infection.

Capsules and slime layers

These are structures surrounding the outside of the cell envelope. When more defined, they are referred to as a capsule when less defined as a slime layer or glycocalyx. They usually consist of polysaccharide; however, in certain bacilli they are composed of a polypeptide (polyglutamic acid). They are not essential to cell viability and some strains within a species will produce a capsule, whilst others do not. Capsules of pathogenic bacteria inhibit ingestion and killing by phagocytes. Capsules are often lost during *in vitro* culture.

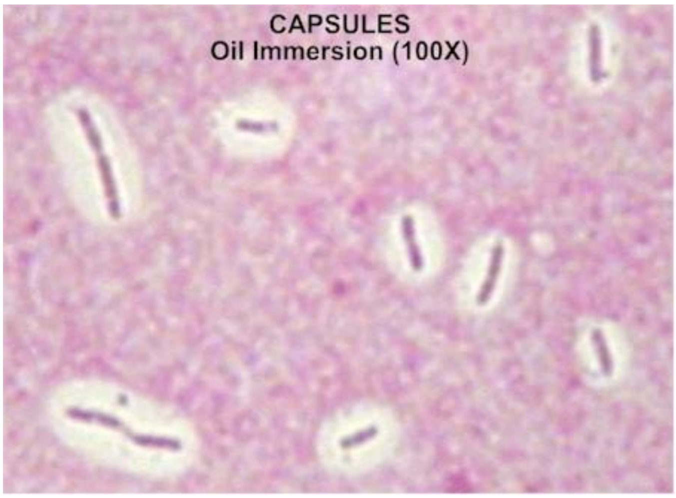


Figure : bacterial capsule structure.

Endospores (spores)

These are a dormant form of a bacterial cell produced by certain bacteria when starved; the actively growing form of the cell is referred to as vegetative. The spore is resistant to adverse conditions (including high temperatures and organic solvents). The spore cytoplasm is dehydrated and contains calcium dipicolinate which is involved in the heat resistance of the spore. Spores are commonly found in the genera *Bacillus* and *Clostridium*.

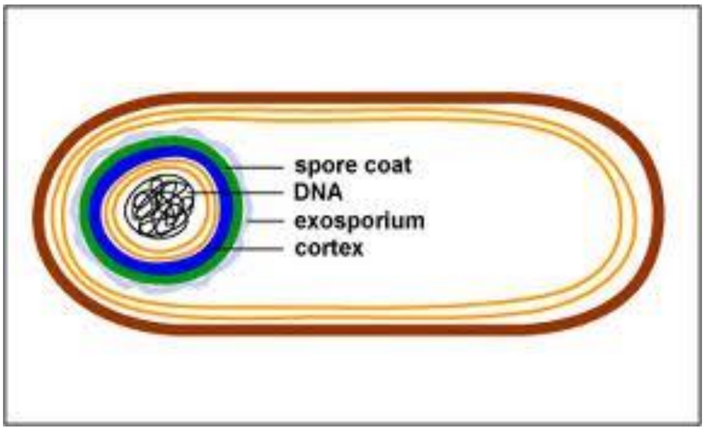


Figure: bacterial endospore structure.