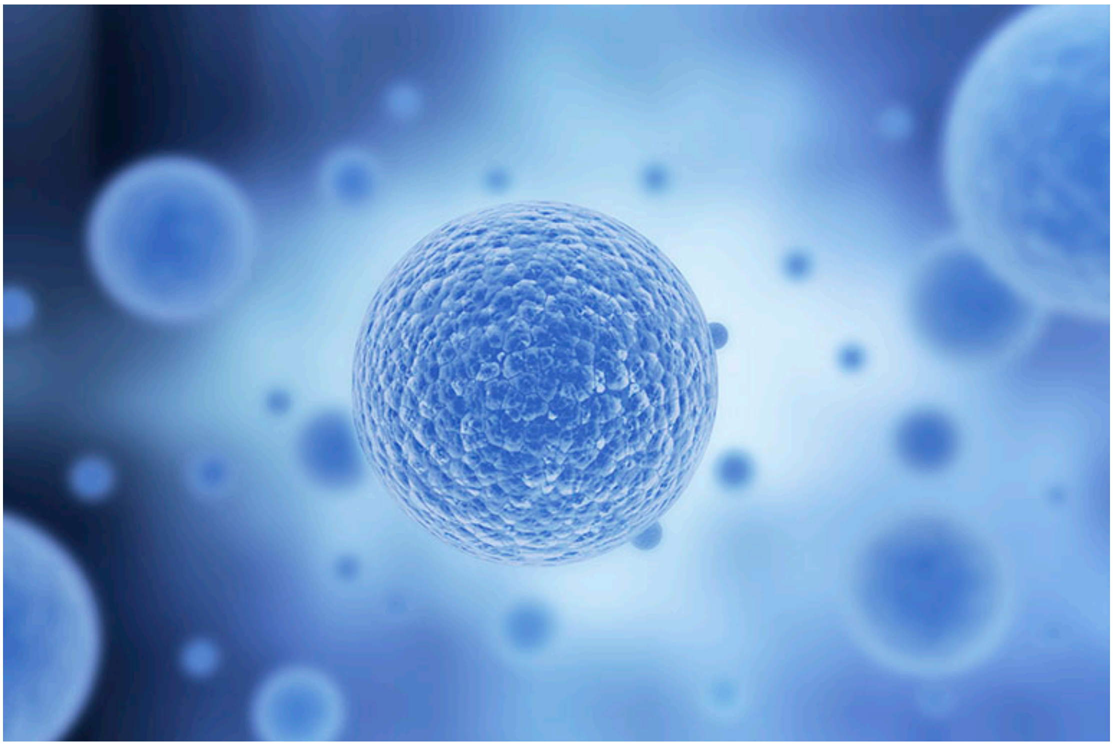
Cells



All living beings are cellular (most biologists do not regard viruses as being “alive’). The broadest definition of the structure of a cell is that it is a bag made of lipid enclosing a thick water based soup of lifes chemicals and processes. This is an absurdly inadequate definition though, which fails to impress on you how extremely complex and dynamic a cell is. The cell is bounded by a plasma membrane which is made of special phospholipids and is studded with many complex protein pores, channels, gates, receptors, recognition proteins etc. Within is the cytoplasm which contains water, and many chemicals and special structures, as well as the genome, the sum total of the cells genetic information - in the form of genes - linear DNA sequences, or in the case of bacteria – a single circular DNA macromolecule. Cells are exceedingly complex - they possess thousands of different chemicals undertaking thousands of different but interrelated reactions, simultaneously, at enormous speed and under exquisite control.

All cell membranes are based on what is known as the lipid bilayer structure, and are “studded’ with very large numbers and many types of proteins, some of these span the membrane and are transport proteins, some are receptor or recognition proteins. There is a high capacity for

these protein molecules to move around in the cell membrane, as can the actual lipid molecules of the membrane to some extent, so that the modern understanding of the general properties and structure of the cell membrane is referred to as the fluid-mosaic model.

The prokaryotic and eukaryotic cell membranes perform similar functions but differ in the chemical nature of their lipids, carbohydrate, and protein components. Cell membranes function in protection, transport, cell to cell recognition, and especially in bacterial cells they also participate in the biochemical reactions of metabolism.

Surface area to volume ratio (SA/V). The ratio of a cells surface area to its volume places critical limits on its lifestyle - its activities, and its size. As a cell increases in size (let us assume that the cell is a sphere), its volume increases far more than its surface area (in other words, as the radius of the cell increases by an amount X, its surface area increases by an amount proportional to X2, but its volume increases by an amount proportional to X3). This places a limit on how large a cell can grow, because the huge increase in volume relative to the increase in surface area means that there is now too little membrane surface area to cope with the increased import and export processes across the cell membrane required by the hugely increased cell volume. Eukaryotic cells have evolved some means to cope with this, principally by means of membrane bound organelles, but particularly by means of an extensive proliferation of internal membrane surface area called the endoplasmic reticulum, but the SA/V ratio does place fundamental limits on how large a cell can become. Bacteria do not ‘solve” this SA/V problem, they remain small – this has it’s advantages, a high surface area to volume area allows rapid growth for instance, and when this is coupled with the fact that their DNA is much more subject to mutation than is the case for eukaryotic cells– the result is rapidly proliferating growth and many mutation derived variants in the bacterial population that can quickly adapt to changing ecological circumstances.

There are two basic types of cell: prokaryotic and eukaryotic.

(Viruses are not cellular and most biologists consider them to be biological entities of course, but as not being alive in the generally accepted sense of the word. Do not make the common mistake of thinking of viruses as being cells, they are not!)

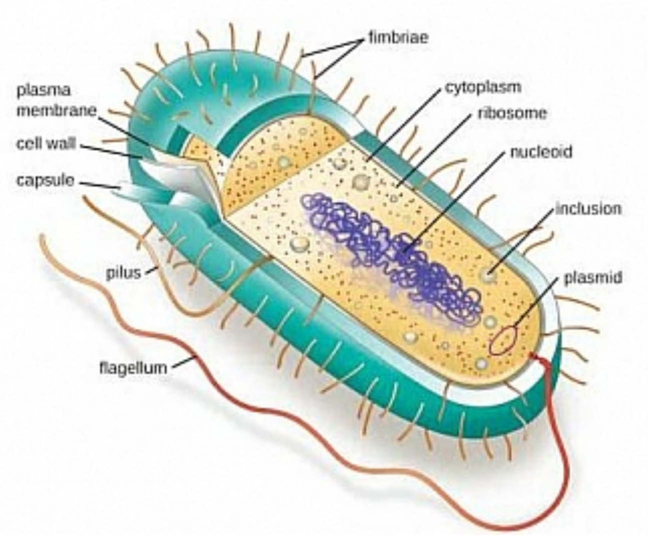
Prokaryotic cells do NOT have a discrete membrane bound nucleus that contains chromosomes, this is the defining feature of a prokaryotic cell. Prokaryotic cells have a none membrane bound single circular DNA chromosome (properly speaking it should not be referred to as a chromosome, but it in practice is often called a chromosome). ONLY the Archaea, Cyanobacteria and the Eubacteria are prokaryotic, ALL other cellular life forms are eukaryotic. Prokaryotes are absolutely and fundamentally defined on the basis of NOT having a nucleus, the region where their circular DNA macromolecule exists is called the nucleoid. Unlike eukaryotic DNA, bacterial DNA is not associated with special cationic proteins called histones.

Eukaryotic cells DO have a membrane bound genome - consisting of more than one LINEAR chromosome, bounded by a double layered nuclear membrane.Fungal, protist, plant and animal cells are eukaryotic.

Prokaryotic cells are much smaller than eukaryotic cells and though they can assemble together to form masses or chains, prokaryotic organisms are NOT multicellular in the accepted sense, which is that multicellularity involves association of different cell types in a discrete organism, and that the cells undertake division of labour, they have differing functions, this is seen only in a very simple way in some bacteria, which are fundamentally UNI-cellular. A typical size for a bacterium is that of a cell of Escherichia coli, about 1 um (one micron or one micrometer) diameter. A typical yeast cell (a fungus) might have a diameter of 6-8 um or more, and contains much more cytoplasm.

In terms of “internal architecture” prokaryotic cells are far simpler than eukaryotic cells, as we discuss below, they lack all of the complex internal membrane based structure of eukaryotic cells. Actually, there are some recent reports that do indicate the presence of some simple membrane bound vesicles in some bacteria, so it is no longer an absolute axiom to state that bacteria do not have membrane bound organelles (MBO’s), but nonetheless, bacteria are still much less structurally complex, internally, than eukaryotic cells. The lack of complex internal

structure in bacteria should not lead you into believing that they are also biochemically simple, bacteria have complex biochemical systems - metabolism in other words, they just do not operate their biochemical events within specialized "walled off" membrane bound organelle structures.



A typical prokaryotic cell, no nucleus, but a region where the DNA exists called a nucleoid, a cell wall, and a cytoplasm with no membrane bound organelles

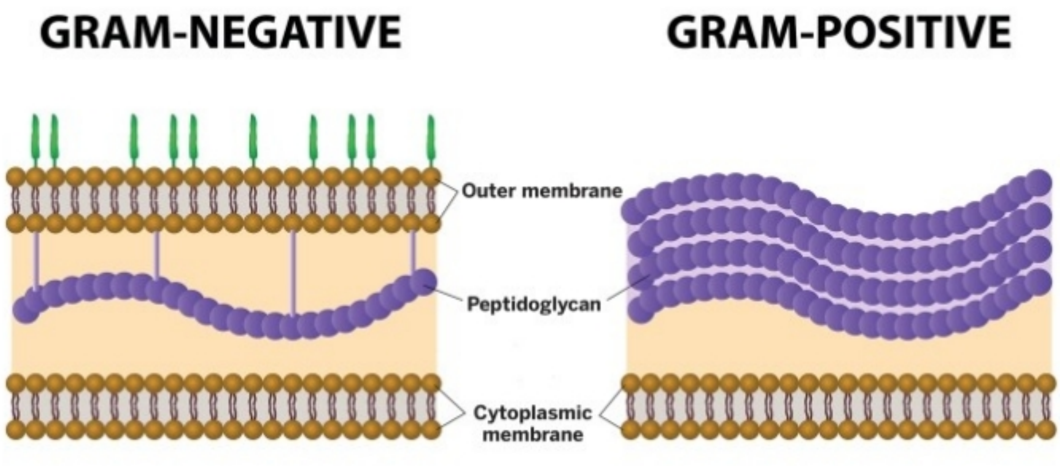
Nearly all prokaryotes have a rigid cell wall, which determines the shape of the cell, and in most cases the wall contains peptidoglycan, a unique and complex acidic polysaccharide that lends rigidity to the wall. The bacterial cell wall serves to resist the very high internal osmotic pressure that would burst (lyse) the cell unless the wall was present. The cell wall is metabolically inert, it does not participate actively in transport processes in and out of cells, it is there as a structural strengthening agent – to provide rigidity and shape. Penicillins kill bacteria by interfering with the synthesis of peptidoglycan in cell walls as it is being formed during bacterial reproduction, this weakens the cell wall structure and the bacterial cell bursts. There are a few bacterial genera that do not have cell walls, Mycoplasma is a classic example, they are parasites of animals such as cattle and are able to exist at the same osmotic pressure as the animal cells that they live in and among. Archaebacteria DO have cell walls, but peptidoglycan is not a part of their cell wall structure.

Most Gram negative bacteria have a tiny but definite space between their cell walls and the cell membrane, this is called the periplasmic space. This space is of significance in pathological behaviour, it is metabolically active in many bacteria, it contains enzymes and transport proteins and other factors that mediate the ability of the bacterium either to cause disease in hosts or to evade destruction, enzymes in this space can, for instance, destroy antibiotics before they can enter the bacterium. A periplasmic space is present in some Gram positive bacteria, but it is much rarer.

From now on, unless I say differently, ALL of my discussion about prokaryotic structure and function should be taken as referring specifically to eubacteria – these are the types of bacteria that cause human disease problems although the vast majority of the eubacteria are not pathogenic to man and in fact, many eubacteria are beneficial to man, either as symbiotic components of the digestive tract, as bacteria involved in food manufacture, or as components of our ecosystem that synthesize new biomass by photosynthesis or that fix nitrogen into soils for use by plants.

There are two major categories of bacteria on the basis of cell wall structure: Gram positive bacteria have thick walls with a dense homogeneous layer of peptidoglycan (a complex polysaccharide polymer composed of two types of sugar subunit, - we look at this later)

Gram negative bacteria have thin cell walls with much less peptidoglycan and an EXTRA outer lipid membrane (not a cell membrane) that contains a toxic compound called lipopolysaccharide (LPS).



A Gram positive bacterium with a thick exposed layer of peptidoglycan. Gram positive walls also contain a unique substance called teichoic acid

A Gram negative bacterium with an extra outer lipid membrane covering a thin layer of peptidoglycan. The outer membrane contains lipopolysaccharide (LPS) also known as endotoxin

The term "Gram stain" refers to a dye staining procedure involving sequential treatment of bacteria on a slide with crystal violet dye, iodine, alcohol and safranin dye. We will look at this in detail in a later tutorial. The completed Gram stain has one of two results, the dyed cell is red when viewed under the microscope and is termed as Gram negative, or it is purple when viewed under the microscope and is termed as Gram positive. The particular Gram result is correlated with a particular cell wall structure, and it is the iodine treatment step that distinguishes between Gram positive and Gram negative, but the alcohol is the point where Gram positive and Gram negative are

differentiated. The nature of the cell wall, Gram negative or Gram positive, has a high relevance to the general type of human disease the bacterium might cause and what kind of antibiotic might be used to treat it, and thus the Gram stain is the FIRST bit of knowledge one needs when analyzing a bacterial infection. For instance, many skin and wound infections are caused by gram positive bacteria, whereas many gut dwelling bacteria are gram negative.

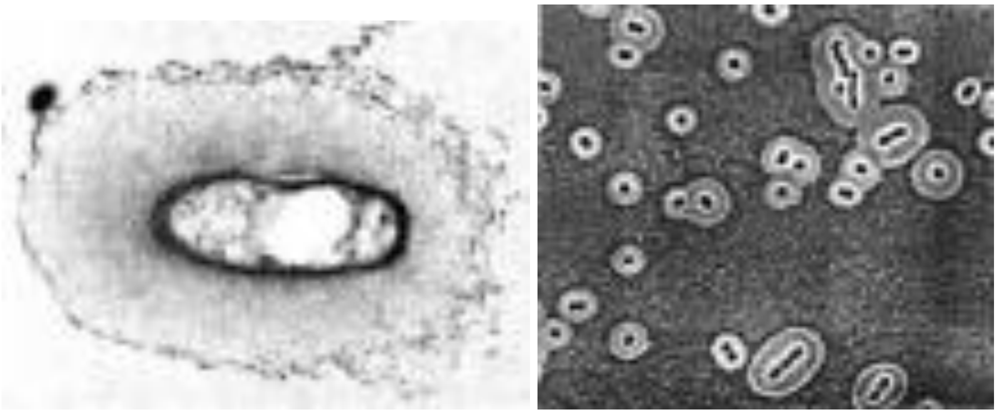
There are also a few bacteria which do not stain well by the Gram stain, such as the acid-fast bacteria, they have a lot of waxy lipid in their cell walls and capsules that interferes with the Gram stain. The tuberculosis and leprosy causing genus Mycobacterium which we will look at later, is an example of an acid fast bacterium which is initially identified in sputum or other body fluids by means of an acid-fast dye staining procedure. As mentioned, very few bacterial species lack a cell wall, Mycoplasma species are the best example, these commonly infect meat and are nuisance contaminants of cell cultures in research laboratories, Mycoplasma cannot be identified with a gram stain, they will accept the dyes involved, but the result is meaningless in the absence of a cell wall.

All cells, prokaryotic and eukaryotic, contain ribosomes (non-membrane bound organelles) which synthesize proteins, but those of the prokaryotes are smaller, this is an important consideration in treating bacterial infections, some antibiotics such as tetracycline attack and inactivate the smaller bacterial ribosome but not our larger eukaryotic ribosome. Ribosomes are complex macro (very large) molecules composed of a smaller and a larger subunit, they consist of a special nucleic acid (ribosomal nucleic acid) and protein and their function is to synthesize proteins by reading the mRNA copy of sections of DNA (more detail later on this topic). Ribosomes are organelles but they are NOT membrane bound. There are two sizes of ribosomes, 80S in eukaryotic cells and 70S in bacteria and

mitochondria (don't worry about what is meant by 80S and 70S, just understand 80S is heavier than 70S). It is no accident that mitochondria have bacterial sized ribosomes - mitochondria evolved from bacteria.

Bacteria may have flagella, which are whip like structures that extend through the cell wall from the cell membrane, they allow movement, and some bacteria have much smaller flexible rod like extensions which are called pili (not found in eukaryotic cells) and function in reproduction and adherence to surfaces. When bacteria can move, either by means of flagella or a process called gliding which does not involve flagella, they are referred to as being motile.

Many bacteria have a thick layer called a capsule, which can help the bacteria to evade immune detection and make them more virulent (able to cause disease more aggressively).



The photo on the left shows a single bacterium surrounded by a thick capsule, the photo on the right shows a nigrosin negative stain which outlines unstained bacteria and their capsules which appear like surrounding halo's. The capsule may be composed of modified amino acids, small peptides, waxy lipids, or carbohydrate substances.