BME 1532-CELL BIOLOGY

Fundamentals of Life

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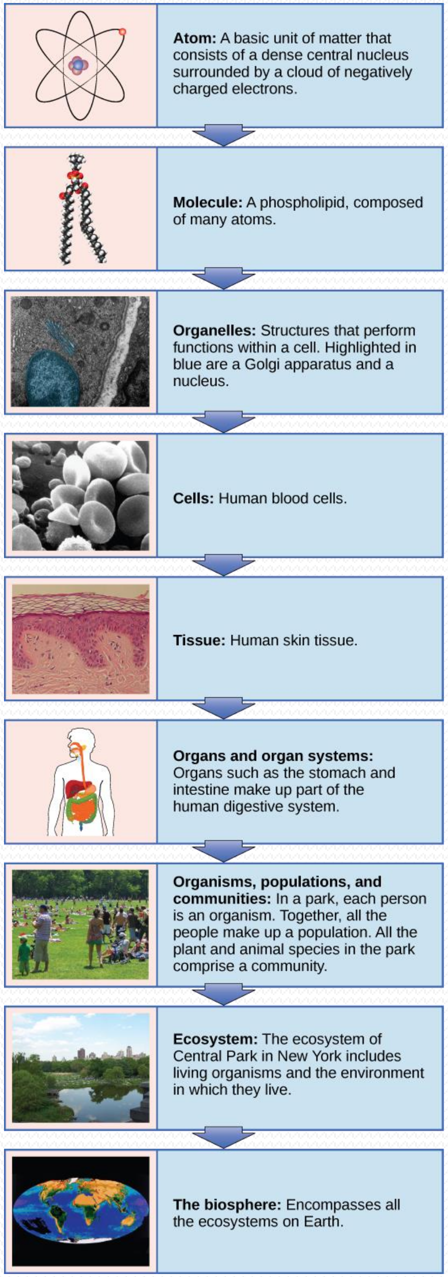
Cell

- Cells are the structural and functional units of all living organisms.
- They are the building blocks of life.
- They are the smallest living unit which can exist on their own.
- Cells can live on their own, in case of unicellular organisms, or can organize into multicellular organisms.
- A human being is known to have more than 10 trillion of cells mathematically it is 10^{13} cells and seen mostly by a microscope, meaning that you cannot see them by a naked eye.
- Antoni van Leeuwenhoek (1632-1723) was probably the first human to ever observe a living cell. He built his own microscope.



Cell Theory

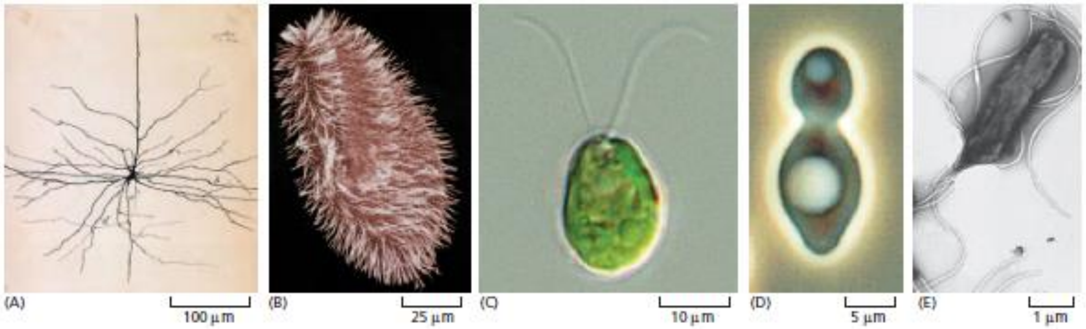
- The cell theory states that
  - Cells are the basic units of structure and function in organisms.
  - All organisms are composed of cells.
  - Cells come only from preexisting cells because cells are self-reproducing.
  - Groups of cells can be organized and function as multicellular organisms.
  - Cells of multicellular organisms can become specialized in form and function to carry out subprocesses of the multicellular organism.

A structure that can do all of the below is considered living:

- **Organization:** They are highly organized, meaning they contain specialized, coordinated parts.
- **Metabolism:** They must use energy and consume nutrients to carry out the biochemical reactions that sustain life.
- **Homeostasis:** They regulate their internal environment to maintain the conditions needed for cell function.
- **Growth:** Cells become larger in size, and multicellular organisms accumulate many cells through cell division.
- **Response:** They respond to stimuli or changes in their environment
- **Reproduction:** They reproduce themselves to create new organisms.
- **Evolution:** They evolve to be better suited to their environment.

Living Cells All Have a Similar Basic Chemistry

- Although the cells of all living things are infinitely varied when viewed from the outside, they are fundamentally similar inside.
- Cells resemble one another in the details of their chemistry. They are composed of the same sorts of molecules, which participate in the same types of chemical reactions.

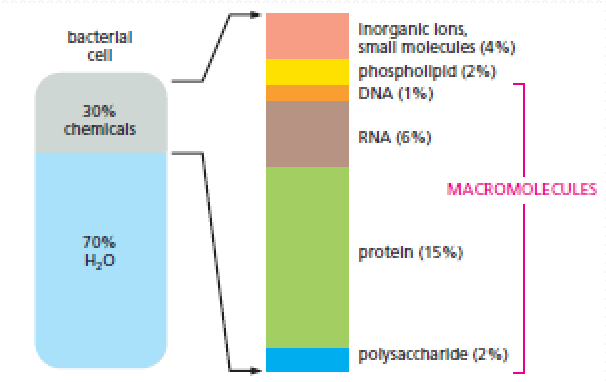


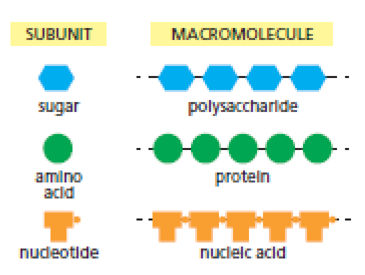
Cells Contain a Universal Set of Small Molecules

- This collection of molecules includes the common amino acids, nucleotides, sugars and fats.
- The molecules are polar or charged, water soluble, and present in micromolar to millimolar concentrations.
- They are trapped within the cell because the plasma membrane is impermeable to them—although specific membrane transporters can catalyze the movement of some molecules into and out of the cell or between compartments in eukaryotic cells.
- The universal occurrence of the same set of compounds in living cells is a manifestation of the universality of metabolic design, reflecting the evolutionary conservation of metabolic pathways that developed in the earliest cells.
- Macromolecules are the major constituents of the cells.

Cells Contain Four Major Families of Macromolecules

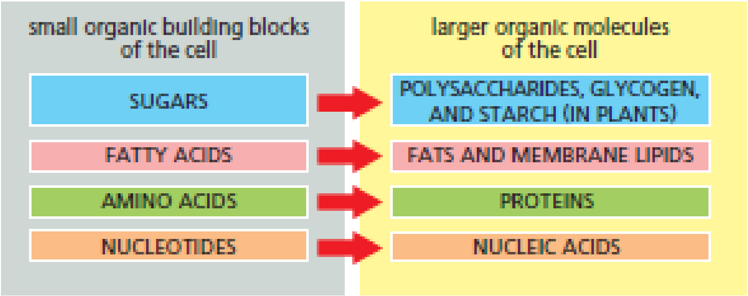
- Macromolecules are the principal building blocks from which a cell is constructed and also the components that confer the most distinctive properties on living things.
- Macromolecules are constructed simply by covalently linking small organic monomers, or *subunits*, into long chains, or polymers.
- **There are 4 macromolecules in cells: Proteins**, **Nucleic acids**, **Carbohydrates**, **Lipids.**
- All organic molecules are synthesized from—and are broken down into—the same set of simple compounds.





Macromolecules

- **Proteins,** long polymers of amino acids, constitute the largest fraction (besides water) of cells. Some proteins have catalytic activity and function as enzymes; others serve as structural elements, signal receptors, or transporters that carry specific substances into or out of cells. Proteins are perhaps the most versatile of all biomolecules.
- The **nucleic acids**, DNA and RNA, are polymers of nucleotides. They store and transmit genetic information, and some RNA molecules have structural and catalytic roles in supramolecular complexes.
- The **polysaccharides,** polymers of simple sugars such as glucose, have two major functions: as energy-yielding fuel stores and as extracellular structural elements with specific binding sites for particular proteins. Shorter polymers of sugars (oligosaccharides) attached to proteins or lipids at the cell surface serve as specific cellular signals.
- The **lipids,** greasy or oily hydrocarbon derivatives, serve as structural components of membranes, energy-rich fuel stores, pigments, and intracellular signals.



Sequence of the subunits is the key

- The biological functions of proteins, nucleic acids, and many polysaccharides are absolutely dependent on the particular ***sequence of subunits*** in the linear chains.
- By varying the sequence of subunits, the cell can make an enormous diversity of the polymeric molecules.
- Thus, for a protein chain 200 amino acids long, there are 20^{200} possible combinations, while for a DNA molecule 10,000 nucleotides long, with its four different nucleotides, there are $4^{10,000}$ different possibilities.
- Thus the machinery of polymerization must be subject to a sensitive control that allows it to specify exactly which subunit should be added next to the growing polymer end.

- Many biological molecules are **macromolecules**, polymers of high molecular weight assembled from relatively simple precursors (**monomeric units** or **subunits**).
- Proteins, nucleic acids, and polysaccharides are produced by the polymerization of relatively small compounds.
- Synthesis of macromolecules is a major energy-consuming activity of cells. Macromolecules themselves may be further assembled into **supramolecular complexes** which then form the cell and its compartments.

Structural hierarchy in the molecular organization of cells

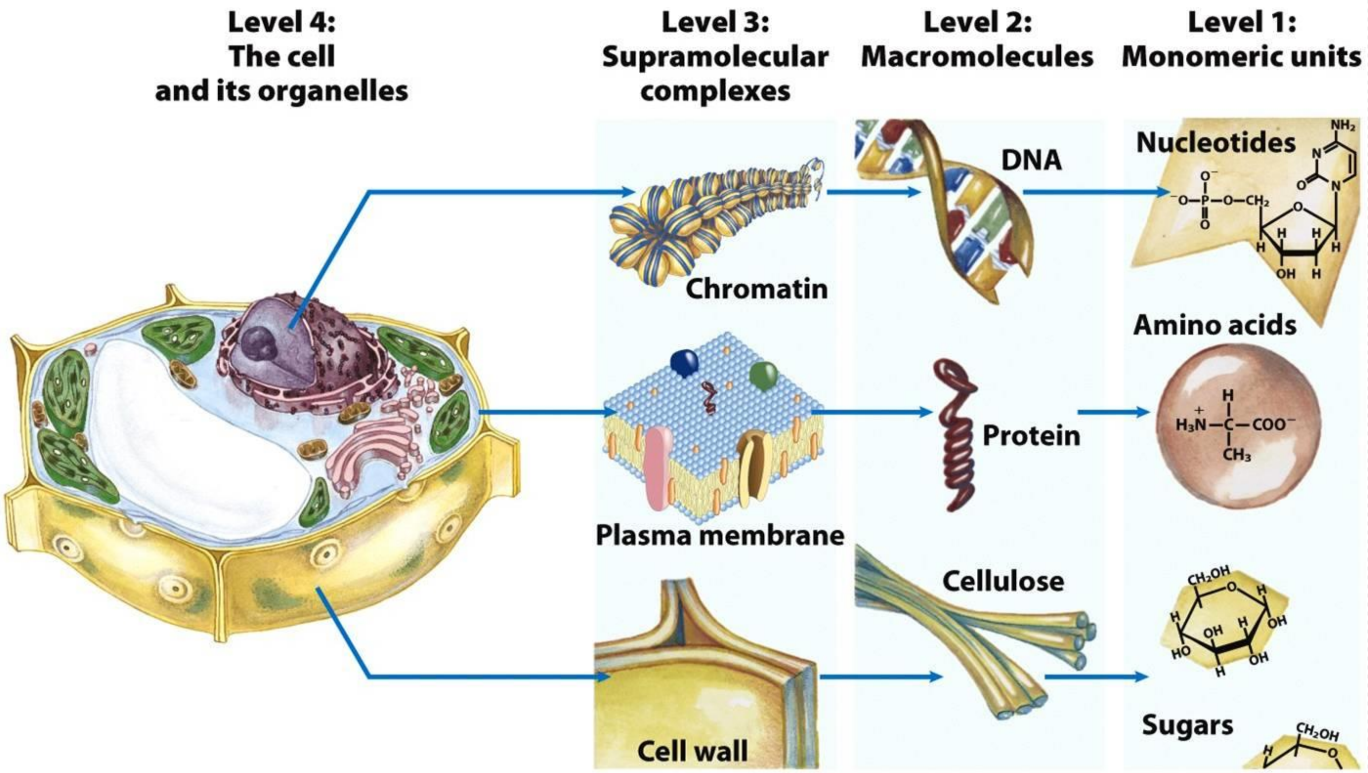
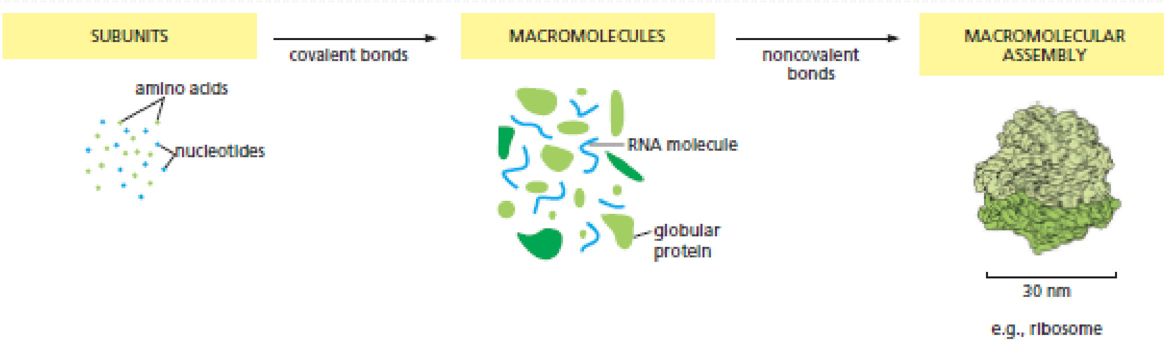


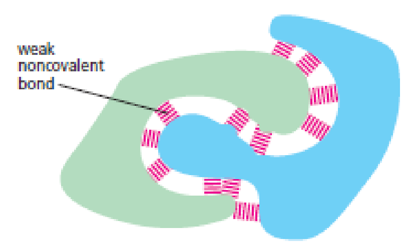
Figure 1-11
Lehninger Principles of Biochemistry, Fifth Edition

- The monomeric subunits in proteins, nucleic acids, and polysaccharides are joined by covalent bonds.
- However, the shapes of most biological macromolecules are highly constrained because of weaker, noncovalent bonds that form between different parts of the molecule.
- Noncovalent bonds thereby allow macromolecules to be used as building blocks for the formation of much larger structures.
- Noncovalent interactions are weaker than covalent bonds, however, weak interactions between macromolecules can promote strong and specific binding and stabilize macro- and supramolecular complexes, producing their unique structures.
- Non-covalent interactions include hydrogen bonding, electrostatic interactions and hydrophobic interactions.



WEAK NONCOVALENT CHEMICAL BONDS

Organic molecules can interact with other molecules through three types of short-range attractive forces known as *noncovalent bonds*: van der Waals attractions, electrostatic attractions, and hydrogen bonds. The repulsion of hydrophobic groups from water is also important for these interactions and for the folding of biological macromolecules.



Weak noncovalent bonds have less than 1/20 the strength of a strong covalent bond. They are strong enough to provide tight binding only when many of them are formed simultaneously.

The Universal Features of Cells

- Living organisms reproduce themselves by transmitting genetic information to their progeny.
- The individual cell is the minimal self-reproducing unit, and is the vehicle for transmission of the genetic information in all living species.
- Every cell on our planet stores its genetic information in the same chemical form as double-stranded DNA. The cell replicates its information by separating the paired DNA strands and using each as a template for polymerization to make a new DNA strand with a complementary sequence of nucleotides.
- The same strategy of templated polymerization is used to transcribe portions of the information from DNA into molecules of the closely related polymer, RNA.
- These in turn guide the synthesis of protein molecules by the more complex machinery of translation, involving a large multimolecular machine, the ribosome, which is itself composed of RNA and protein.

The Universal Features of Cells

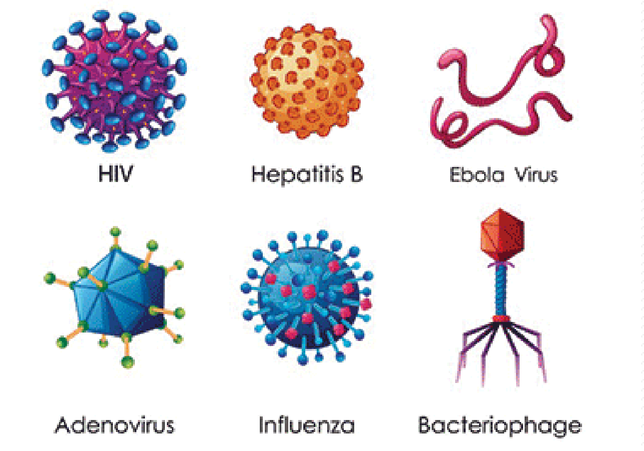
- Proteins are the principal catalysts for almost all the chemical reactions in the cell; their other functions include the selective import and export of small molecules across the plasma membrane that forms the cell's boundary.
- The specific function of each protein depends on its amino acid sequence, which is specified by the nucleotide sequence of a corresponding segment of the DNA the gene that codes for that protein.
- In this way, the genome of the cell determines its chemistry; and the chemistry of every living cell is fundamentally similar, because it must provide for the synthesis of DNA, RNA, and protein.

The Universal Features of Cells

- All cells store their hereditary information in the same linear chemical code (DNA).
- All cells replicate their hereditary information by templated polymerization.
- All cells transcribe portions of their hereditary information into the same intermediary form (RNA).
- All cells use proteins as catalysts.
- All cells translate RNA into protein in the same way.
- All cells function as biochemical factories dealing with the same basic molecular building blocks.
- Life requires free energy.
- All cells are enclosed in a plasma membrane across which nutrients and waste materials must pass.

Viruses

- If cells are the fundamental unit of living matter, then nothing less than a cell can truly be called living.
- Viruses are compact packages of genetic information—in the form of DNA or RNA—encased in protein but they have no ability to reproduce themselves on their own.
- Instead, they hijack the reproductive machinery of the cells that they invade to get themselves copied.
- Thus, viruses are chemical zombies: they are inert and inactive outside their host cells, but they can exert a malign control over a cell once they gain entry.



All Present-Day Cells Have Evolved from the Same Ancestral Cell: EVOLUTION

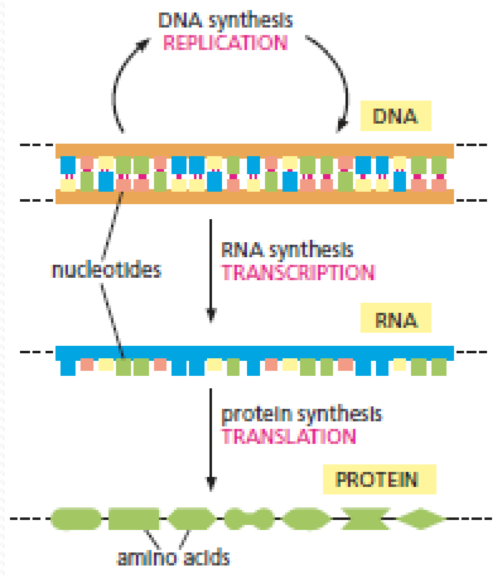
- A cell reproduces by replicating its DNA and then dividing in two, passing a copy of the genetic instructions encoded in its DNA to each of its daughter cells.
- That is why daughter cells resemble the parent cell. However, the copying is not always perfect, and the instructions are occasionally corrupted by ***mutations*** that change the DNA. For this reason, daughter cells do not always match the parent cell exactly.
- Mutations can create offspring that are changed for the worse (in that they are less able to survive and reproduce), changed for the better (in that they are better able to survive and reproduce), or changed in a neutral way (in that they are genetically different but equally viable). The struggle for survival eliminates the first, favors the second, and tolerates the third.
- The genes of the next generation will be the genes of the survivors.

- On occasion, the pattern of descent may be complicated by sexual reproduction, in which two cells of the same species fuse, pooling their DNA. The genetic cards are then shuffled, re-dealt, and distributed in new combinations to the next generation, to be tested again for their ability to promote survival and reproduction.
- These simple principles of genetic change and selection, applied repeatedly over billions of cell generations, are the basis of evolution—the process by which living species become gradually modified and adapted to their environment in more and more sophisticated ways.
- Evolution offers a startling but compelling explanation of why present-day cells are so similar in their fundamentals: they have all inherited their genetic instructions from the same common ancestor. It is estimated that this ancestral cell existed between 3.5 and 3.8 billion years ago, and it contained a prototype of the universal machinery of all life on Earth today.
- Through a very long process of mutation and natural selection, the descendants of this ancestral cell have gradually diverged to fill every habitat on Earth with organisms that exploit the potential of the machinery in an endless variety of ways.

Nothing in Biology Makes Sense Except in the Light of Evolution

Code of Life

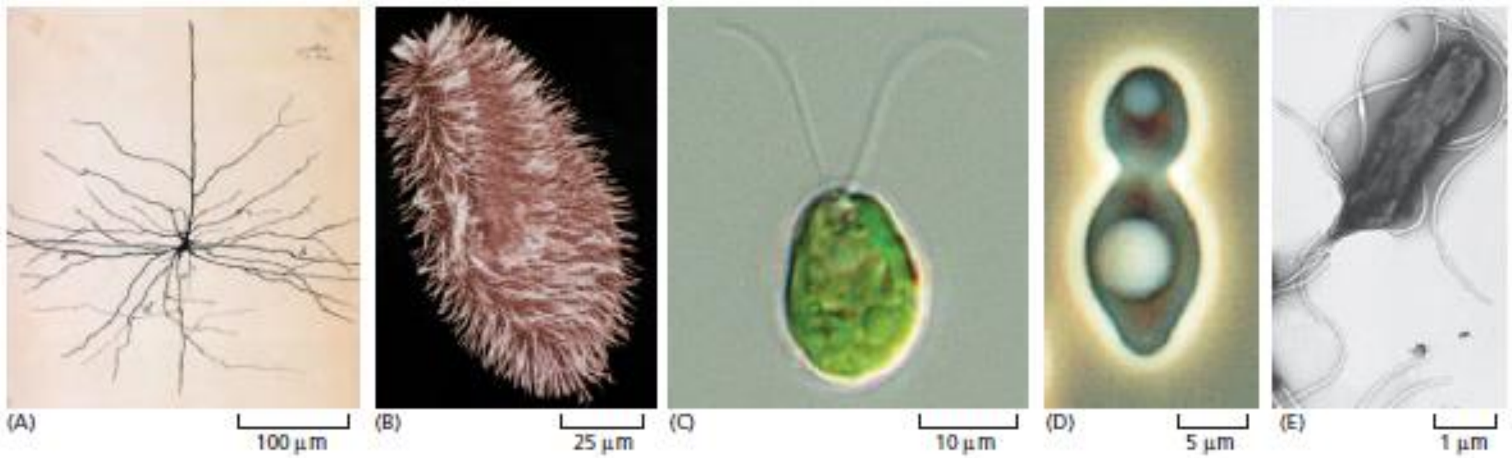
- In all organisms, genetic information—in the form of *genes*—is carried in DNA molecules.
- This information is written in the same chemical code, constructed out of the same chemical building blocks, interpreted by essentially the same chemical machinery, and replicated in the same way when an organism reproduces.
- Thus, in every cell, the long DNA polymer chains are made from the same set of four monomers, called *nucleotides*, strung together in different sequences like the letters of an alphabet to convey information.
- In every cell, the information encoded in the DNA is read out, or *transcribed*, into a chemically related set of polymers called RNA.
- A subset of these RNA molecules is in turn *translated* into yet another type of polymer called a protein. This flow of information—from DNA to RNA to protein—is so fundamental to life that it is referred to as the ***central dogma.***



Gene Expression

- A cell's genome—that is, the entire sequence of nucleotides in an organism's DNA—provides a genetic program that instructs the cell how to behave.
- Fat cells, skin cells, bone cells, and nerve cells seem as dissimilar as any cells could be. Yet all these *differentiated cell types* are generated during embryonic development from a single fertilized egg cell, and all contain identical copies of the DNA of the species.
- Their varied characters stem from the way that individual cells use their genetic instructions differently.
- Different cells *express* different genes: that is, they use their genes to produce some proteins and not others, depending on their internal state and on cues that they and their ancestor cells have received from their surroundings—mainly signals from other cells in the organism.
- Thus, the appearance and behavior of a cell are dictated largely by its protein molecules.

Cells come in a variety of shapes and sizes



(A) A single nerve cell from a mammalian brain. (B) *Paramecium.* (C) *Chlamydomonas*. single-celled green algea. (D) *Saccharomyces cerevisiae*. (E) *Helicobacter pylori*.

Limitations of Cell Dimensions

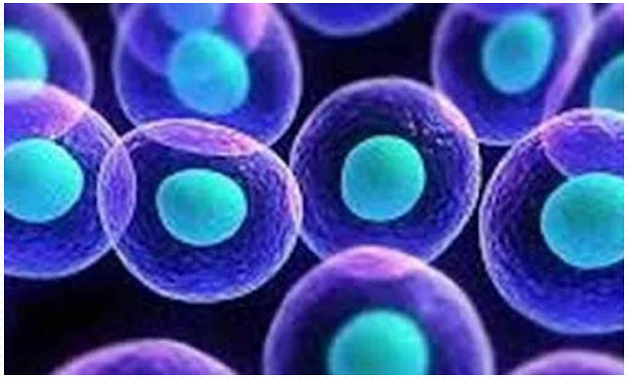
- Cells obtain nutrients, gain information and rid waste through their plasma membrane. As cell size increases, a cell's ability to exchange with its environment becomes limited by the amount of membrane area that is available for exchange, placing a theoretical upper limit on the size of the cell.
- The lower limit is probably set by the minimum number of each type of biomolecule required by the cell.
- As cell size increases the volume increases much faster than the surface area.
- Thus, the upper limit of cell size is probably set by the rate of diffusion of molecules, especially O2 across the cell membrane.

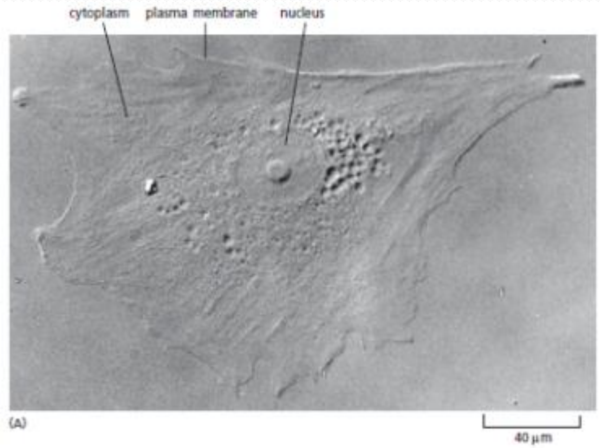
Cell Size

- Most cells are microscopic, invisible to the unaided eye. **Animal and plant cells** are typically 5 to 100 μm in diameter, and many **bacteria** are only 1 to 2 μm long.
- A **frog egg**—which is also a single cell—has a diameter of about 1 millimeter.
- The largest cell of the body is **female ovum (egg)**, with a diameter of 100 μm.
- The longest cell of the body is **sciatic nerve** which arises from spine, runs through the legs down to toes and can be 1 m in length .

Building Blocks of Living Organisms: Cells

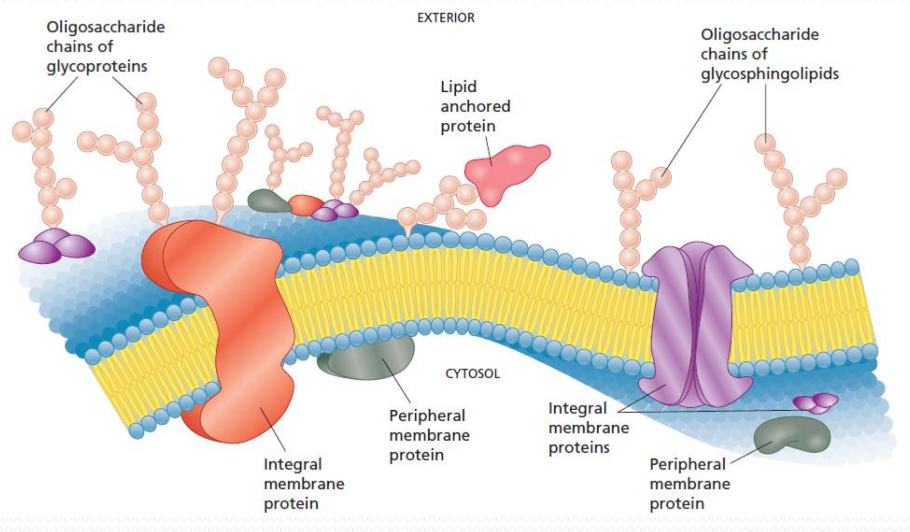
- All cells have a **nucleus or nucleoid**, a **plasma membrane**, and **cytoplasm**.





Plasma Membrane

- The **plasma membrane** defines the periphery of the cell, separating its contents from the surroundings. It is composed of lipid and protein molecules that form a thin, tough, pliable, hydrophobic barrier around the cell.
- The membrane is a barrier to the free passage of inorganic ions and most other charged or polar compounds.
- Transport proteins in the plasma membrane allow the passage of certain ions and molecules; receptor proteins transmit signals into the cell; and membrane enzymes participate in some reaction pathways.
- Because the individual lipids and proteins of the plasma membrane are not covalently linked, the entire structure is remarkably flexible, allowing changes in the shape and size of the cell.



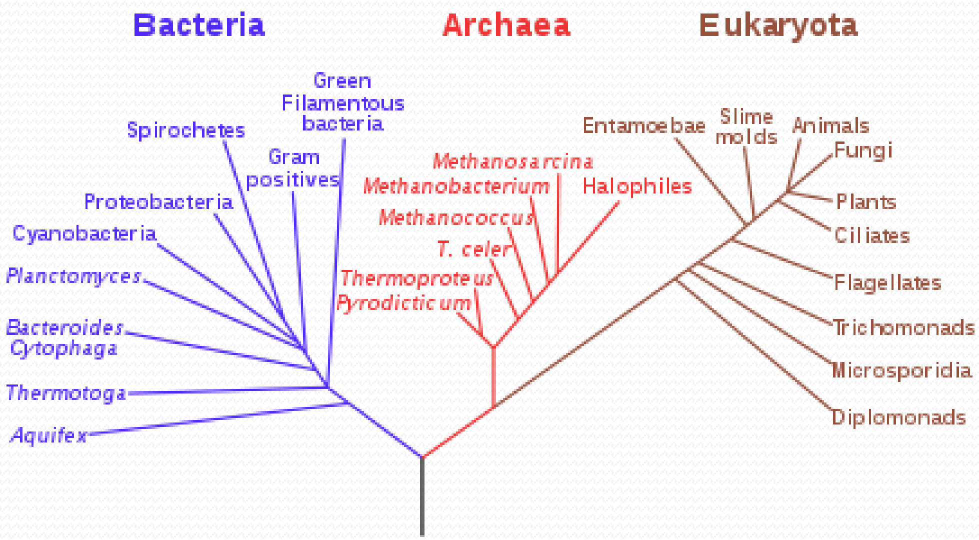
Cytoplasm

- The internal volume bounded by the plasma membrane, the **cytoplasm** is composed of an aqueous solution, the **cytosol,** and a variety of suspended particles with specific functions.
- The cytosol is a highly concentrated solution containing **enzymes** and the **RNA molecules** that encode them; the components (**amino acids and nucleotides**) from which these macromolecules are assembled; hundreds of small organic molecules called **metabolites, intermediates** in biosynthetic and degradative pathways; **coenzymes,** compounds essential to many enzyme-catalyzed reactions; **inorganic ions**; and **ribosomes,** small particles (composed of protein and RNA molecules) that are the sites of protein synthesis.

Nucleus or Nucleoid

- All cells have, for at least some part of their life, either a **nucleus** or a **nucleoid**, in which the **genome**—the complete set of genes, composed of DNA—is stored and replicated.
- The nucleoid, in bacteria, is not separated from the cytoplasm by a membrane; the nucleus, in higher organisms, consists of nuclear material enclosed within a double membrane, the nuclear envelope.
- Cells with nuclear envelopes are called **eukaryotes** (Greek *eu*, "true," and *karyon*, "nucleus"); those without nuclear envelopes—bacterial cells—are **prokaryotes** (Greek *pro*, "before").

Domains of Life



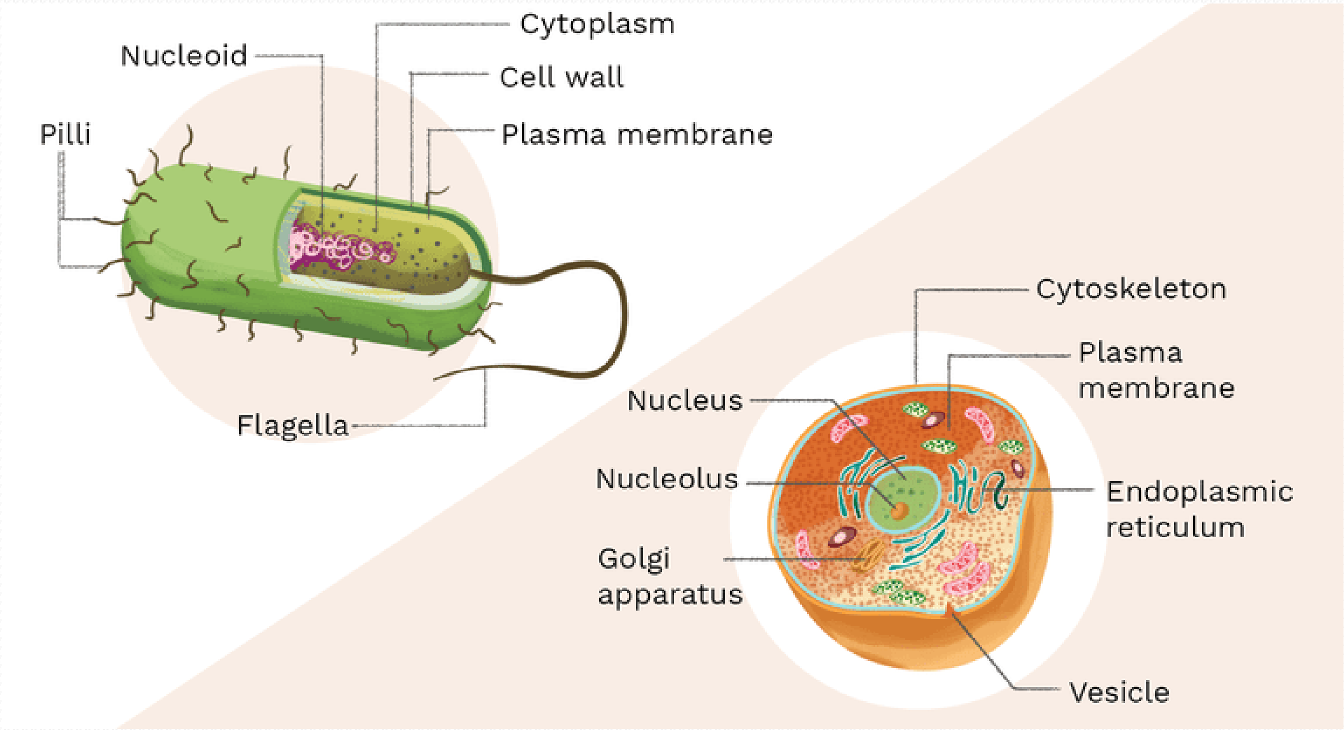
Eubacteria: inhabit soils, surface waters, and the tissues of other living or decaying organisms

Archeabacteria: inhabit extreme environments such as salty, hot, acidic or high pressure.

Eukaryotes

Prokaryotes

Prokaryotes vs. Eukaryotes



Prokaryotes

- Most prokaryotes live as single-celled organisms, although some join together to form chains, clusters, or other organized multicellular structures.
- In shape and structure, prokaryotes may seem simple and limited, but in terms of chemistry, they are the most diverse and inventive class of cells.
- Members of this class exploit an enormous range of habitats, from hot puddles of volcanic mud to the interiors of other living cells, and they vastly outnumber all eukaryotic organisms on Earth.
- Some are aerobic, using oxygen to oxidize food molecules; some are strictly anaerobic and are killed by the slightest exposure to oxygen.




Prokaryotes

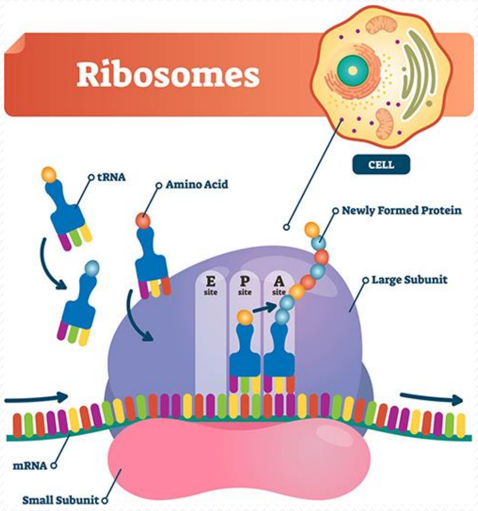
- Prokaryotes often have a tough protective coat, or cell wall, surrounding the plasma membrane, which encloses a single compartment containing the cytoplasm and the DNA.
- DNA is contained in a nucloid region other than a true membrane enclosed nucleus.
- Cell interior typically appears as a matrix of varying texture, without any obvious organized internal structure.
- The cells reproduce quickly by dividing in two. Under optimum conditions, when food is plentiful, many prokaryotic cells can duplicate themselves in as little as 20 minutes. In 11 hours, by repeated divisions, a single prokaryote can give rise to more than 8 billion progeny (which exceeds the total number of humans presently on Earth).
- Thanks to their large numbers, rapid growth rates, and ability to exchange bits of genetic material by a process akin to sex, populations of prokaryotic cells can evolve fast, rapidly acquiring the ability to use a new food source or to resist being killed by a new antibiotic.

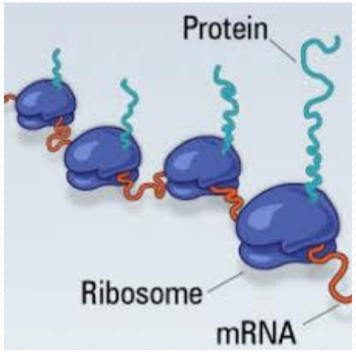
Prokaryotes

- Any organic, carbon-containing can be used as food by one sort of bacterium or another.
- Even more remarkably, some prokaryotes can live entirely on inorganic substances: they can get their carbon from CO_2 in the atmosphere, their nitrogen from atmospheric N_2, and their oxygen, hydrogen, sulfur, and phosphorus from air, water, and inorganic minerals.
- Some of these prokaryotic cells, like plant cells, perform *photosynthesis*, using energy from sunlight to produce organic molecules from CO_2; others derive energy from the chemical reactivity of inorganic substances in the environment.
- In either case, such prokaryotes play a unique and fundamental part in the economy of life on Earth: other living things depend on the organic compounds that these cells generate from inorganic materials.

Ribosomes

- Ribosomes are the organelles made of RNA and protein that carry out protein synthesis.
- Ribosomes synthesize proteins by linking aminoacids together reading the mRNA transcribed from protein coding genes.
- They consist of two subunits that fit togeher: the small subunit which reads the mRNA, and the large subunit which join amino acids to form proteins.
- In cell they can exist as free or bound forms. *Free ribosomes* are suspended in the cytosol, while *bound ribosomes* are attached to the outside of the endoplasmic reticulum or nuclear envelope.





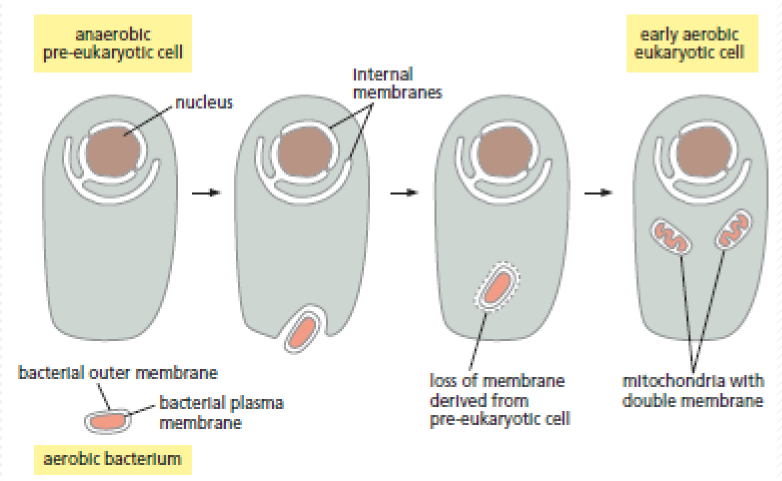
Prokaryotic Ribosomes vs. Eukaryotic Ribosomes

- Prokaryotes have 70S ribosomes, each consisting of a small (30S) and a large (50S) subunit. They have 16S RNA in their small subunit.
- Eukaryotes have 80S ribosomes located in their cytosol, each consisting of a small (40S) and large (60S) subunit.
- They have 18S RNA in their small subunit.
- Mitochondria and chloroplasts have ribosomes similar to the prokaryotic ribosomes.
- The differences between the bacterial and eukaryotic ribosomes are exploited by pharmaceutical industry to create antibiotics that can destroy a bacterial infection without harming the cells of the infected person.
- Due to the differences in their structures, the bacterial 70S ribosomes are vulnerable to these antibiotics while the eukaryotic 80S ribosomes are not.
- Even though mitochondria possess ribosomes similar to the bacterial ones, mitochondria are not affected by these antibiotics because they are surrounded by a double membrane that does not easily admit these antibiotics into the organelle.

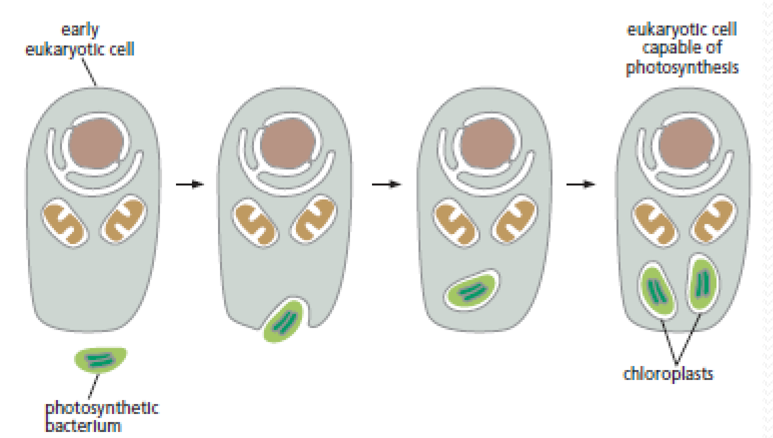
Endosymbiotic Theory

- According to endosymbiotic theory, the ancestral eukaryotic cell was a predator that fed by capturing other cells.
- It proposes that mitochondria and chloroplasts were formerly small prokaryotes that are engulfed by an ancestral eukaryotic cells living within larger cells.
- Such a way of life requires a large size, a flexible membrane, and a cytoskeleton to help the cell move and eat.
- The nuclear compartment may have evolved to keep the DNA segregated from this physical and chemical chaos, so as to allow more delicate and complex control of the way the cell reads out its genetic information.
- The symbiosis eventually became mutually beneficial for both parties.
- In the process of becoming more interdependent in time, the host and endosymbionts became a single organism.

- Such a primitive cell, with a nucleus and cytoskeleton, was most likely the sort of cell that engulfed the free-living, oxygen-consuming bacteria that were the likely ancestors of the mitochondria.



- A subset of these cells later acquired chloroplasts by engulfing photosynthetic bacteria.



The evidence supporting an endosymbiotic origin

- The inner membranes of both organelles have enzymes and transport systems that are homologous to those found in the plasma membranes of living prokaryotes.
- Both mitochondria and chloroplasts contain a single, circular DNA molecule that, like the chromosomes of bacteria, is not associated with histones or other proteins.
- These organelles contain the transfer RNAs, ribosomes, and other molecules needed to transcribe and translate their DNA into proteins.
- Mitochondria and plastids replicate by a splitting process very similar to binary fission in certain prokaryotes.
- In terms of size, nucleotide sequence, and sensitivity to certain antibiotics, the ribosomes of mitochondria and plastids are more similar to prokaryotic ribosomes than they are to the cytoplasmic ribosomes of eukaryotic cells.

Eukaryotes

- Eukaryotic cells, in general, are bigger and more complex than bacteria and archaea.
- Some live independent lives as single-celled organisms such as amoebae and yeasts; others live in multicellular assemblies.
- All of the more complex multicellular organisms—including plants, animals, and fungi—are formed from eukaryotic cells.
- By definition, all eukaryotic cells have a nucleus. But also a variety of other organelles, most of which are membrane-enclosed are common to all eukaryotic organisms.

Next Week on BME 1532

- Organelles and Microscopy Techniques