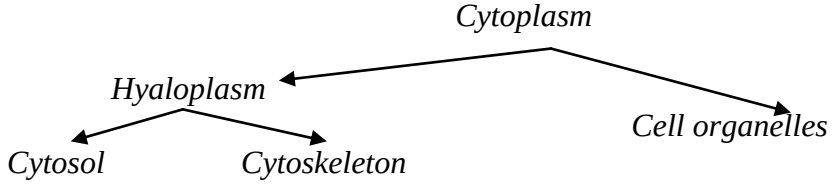
COMPARTMENTALIZATION OF EUKARYOTIC CELL

In eukaryotes (which are approximately a thousand times the volume of bacteria) the rates of chemical reactions would be limited by the diffusion of small molecules if a cell were not partitioned into smaller compartments termed **organelles.** Each organelle is surrounded by one or more **biomembranes,** and each type of organelle contains a unique complement of proteins – some embedded in its membrane(s), others in its aqueous interior space, or **lumen.** These proteins enable each organelle to carry out its characteristic cellular functions.

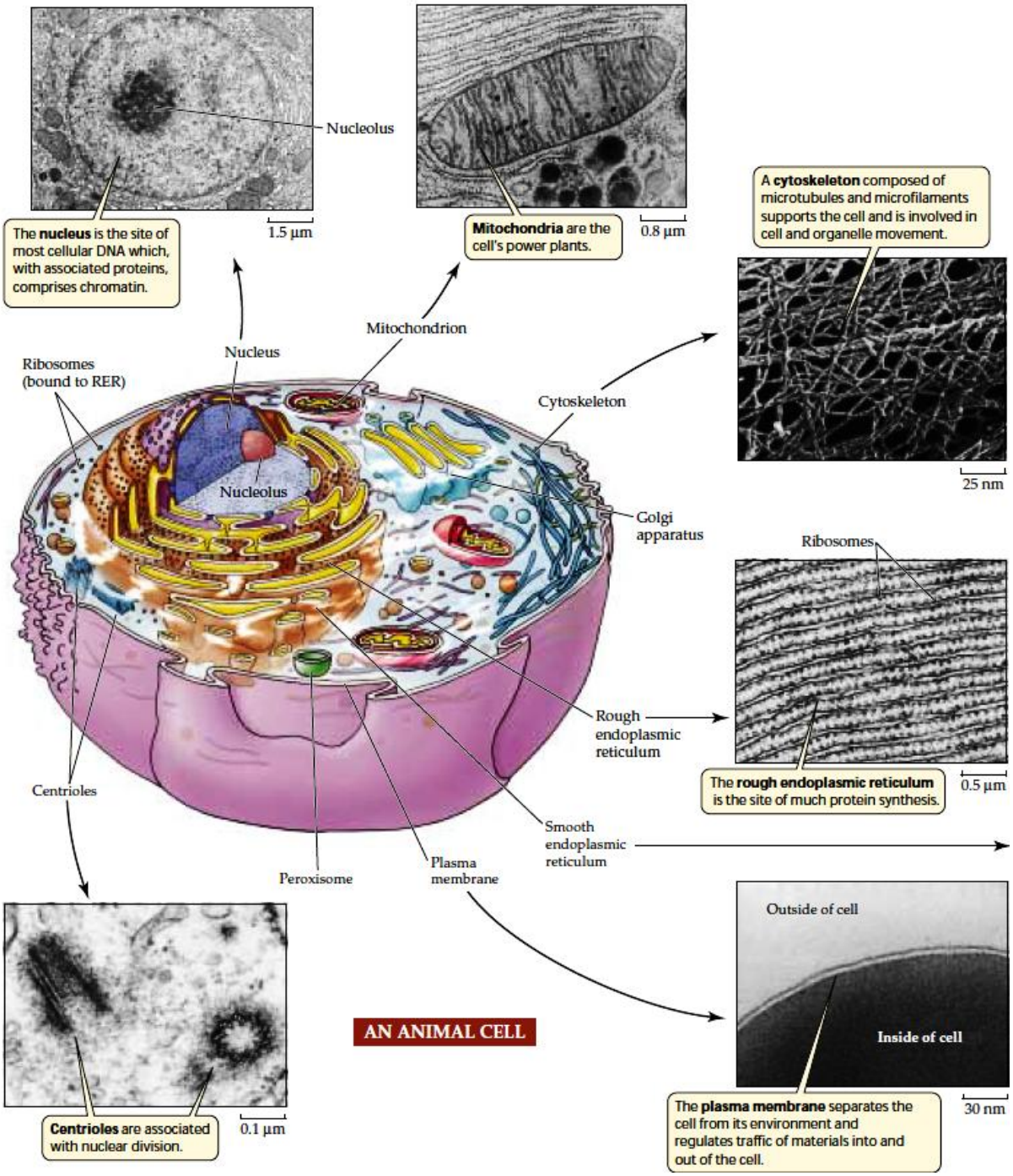
The table below provides a short description of the main organelles of an animal cell:

STRUCTURE	DESCRIPTION	BIOLOGICAL ROLE
STRUCTURAL ELEMENTS		
Cytosketeton	Network of protein filaments	Structural support; cell movement
Flagella(cilia, microvilli)	Cellular extensions	Motility or moving fluids over surfaces
Centrioles	Hollow microtubules	Moving chromosomes during cell division
ENDOMEMBRANE SYSTEM		
Plasma membrane	Lipid bilayer in which proteins are embedded	Regulates what passes into and out of cell; cell-to-cell communication
Endoplasmic reticulum	Network of internal membranes; forms compartments and vesicles	Rough type processes proteins for secretion and synthesizes phospholipids; smooth type synthesize fats and steroids
Nucleus	Structure bounded by double membrane; contains chromosomes	Control center of cell; directs protein synthesis and cell reproduction
Golgi apparatus	Stacks of flattened vesicles	Modifies and packages proteins for export from cell; forms secretory vesicles
Lysosomes	Vesicles derived from Golgi complex that contain hydrolytic digestive enzymes	Digest worn-out mitochondria and cell debris; play role in cell death
ENERGY-PRODUCTING ORGANELLES		
Mitochondria	Bacteria-like elements with double membrane	Power plant of the cell; site of oxidative metabolism; synthesis of ATP
ORGANELLES OF GENE EXPRESSION		
Chromosomes	Long threads of DNA that form a complex with protein	Contain hereditary information
Nucleolus	Site of rRNA synthesis	Assembles ribosomes
Ribosomes	Small, complex assemblies of protein, often bound to ER	Site of protein synthesis

The **cytoplasm** is the part of the cell outside the largest organelle, the nucleus. It is composed of hyaloplasm and cell organelles dispersed in it. The **cytosol,** the aqueous part of the hyaloplasm also contains its own distinctive proteins.



The cytoplasm is a colloidal solution. It is viscous, semifluid and precipitates if placed into water. It is constantly active (rotation and streaming), allowing the cell to be in a continuous dynamic flux.



ER - ENDOPLASMIC RETICULUM

Generally, the largest membrane in a eukaryotic cell encloses the endoplasmic reticulum (ER) – an extensive network of closed, flattened membrane-bounded sacs called **cisternae**. The endoplasmic reticulum has a number of functions in the cell but is particularly important in the synthesis of lipids, membrane proteins, and secreted proteins.

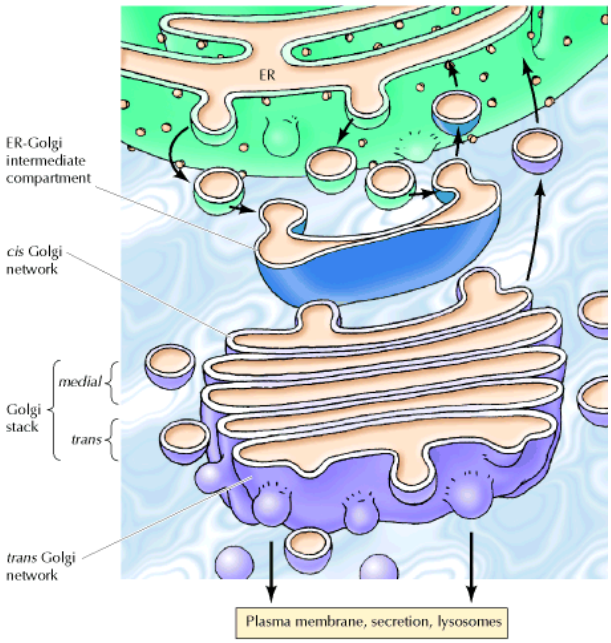
The Smooth Endoplasmic Reticulum - it lacks ribosomes and is the place for synthesis of fatty acids and phospholipids. Although many cells have very little smooth ER, this organelle is abundant in hepatocytes. Enzymes in the smooth ER of the liver also modify or detoxify

hydrophobic chemicals such as pesticides and carcinogens by chemically converting them into more water-soluble, conjugated products that can be excreted from the body. High doses of such compounds result in a large proliferation of the smooth ER in liver cells.

The Rough Endoplasmic Reticulum – its cytosolic face is studded with ribosomes**. Ribosomes** bound to the rough ER synthesize certain membrane and organelle proteins and virtually all proteins to be secreted from the cell. A ribosome that fabricates such a protein is bound to the rough ER by the nascent polypeptide chain of the protein. As the growing polypeptide emerges from the ribosome, it passes through the rough ER membrane, with the help of specific proteins in the membrane. Newly made membrane proteins remain associated with the rough ER membrane, and proteins to be secreted accumulate in the lumen of the organelle. All eukaryotic cells contain a noticeable amount of rough ER because it is needed for the synthesis of plasma membrane proteins and proteins of the extracellular matrix. Rough ER is particularly abundant in specialized cells that produce an abundance of specific proteins to be secreted. For example, plasma cells produce antibodies, pancreatic acinar cells synthesize digestive enzymes, and cells in the pancreatic islets of Langerhans produce the polypeptide hormones insulin and glucagon. In secretory cells a large part of the cytosol is filled with rough ER and secretory vesicles.

Several minutes after proteins are synthesized in the rough ER, most of them leave the organelle within small membrane-bounded transport vesicles. These vesicles, which bud from regions of the rough ER not coated with ribosomes, carry the proteins to another membrane-limited organelle, the **Golgi complex**.

GOLGI COMPLEX (GOLGI APPARATUS)



This organelle is a series of flattened membrane vesicles or sacs (***cisternae***), surrounded by a number of more or less spherical membrane-limited vesicles. The stack of Golgi cisternae has three defined regions—the *cis*, the *medial*, and the *trans.* Transport vesicles from the rough ER fuse with the *cis* region of the Golgi complex, where they deposit their protein contents. These proteins then progress from the *cis* to the *medial* and to the *trans* region. Within each region are different enzymes that modify proteins to be secreted and membrane proteins differently, depending on their structures and their final destinations.

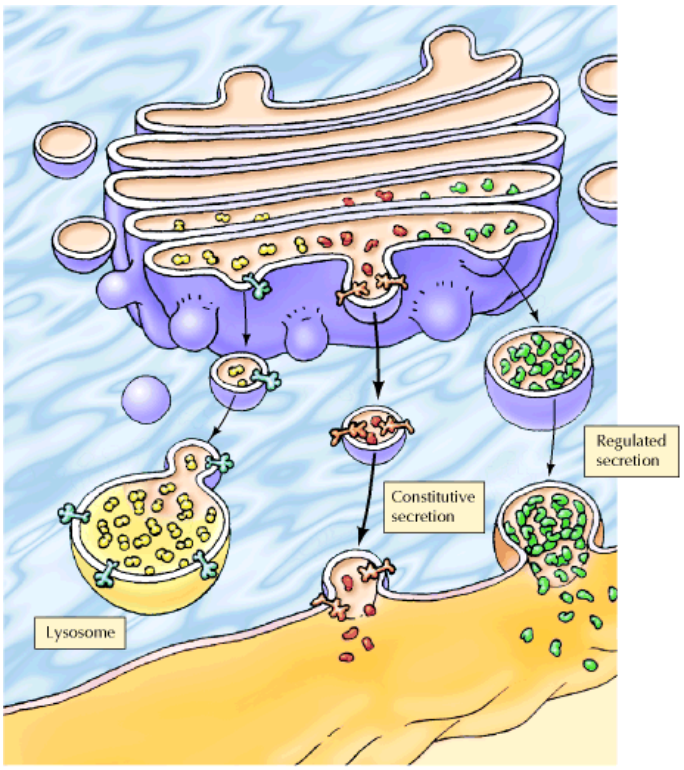
After proteins to be secreted and membrane proteins are modified in the Golgi complex, they are transported out of the complex by a second set of vesicles, which seem to bud from the *trans* side of the Golgi complex. Some vesicles carry membrane proteins destined for the plasma membrane or soluble proteins to be released from the cell surface; others carry soluble or membrane proteins to lysosomes or other organelles.

So, Golgi complex functions as a factory in which proteins received from the ER are further processed and sorted for transport to their eventual destinations: lysosomes, the plasma membrane, or secretion. In addition, glycolipids and sphingomyelin are synthesized within the Golgi. Proteins, as well as lipids and polysaccharides, are transported from the Golgi apparatus to their final destinations through the secretory pathway. This involves the sorting of proteins into different kinds of transport vesicles, which bud from the *trans* Golgi network and deliver their contents to the appropriate cellular locations. Proteins that function within the Golgi apparatus must be retained within that organelle, rather than being transported along the secretory pathway. In contrast to the ER, all of the proteins retained within the Golgi complex are associated with the Golgi membrane

rather than being soluble proteins within the lumen. The signals responsible for retention of some proteins within the Golgi have been localized to their transmembrane domains, which retain proteins within the Golgi apparatus by preventing them from being packaged in the transport vesicles that leave the *trans* Golgi network.

Functions of Golgi apparatus:

1) the formation of the plasma membrane;
2) the synthesis of polysaccharides, glycoproteins, glycolipids and sphingomyelin (the only nonglycerol phospholipid in cell membranes);
3) the modification of products through the addition of fatty acids, sulfation and glycosylation;
4) the concentration and packaging of synthesized material into secretory versicles;
5) the biogenesis of lysosomes.

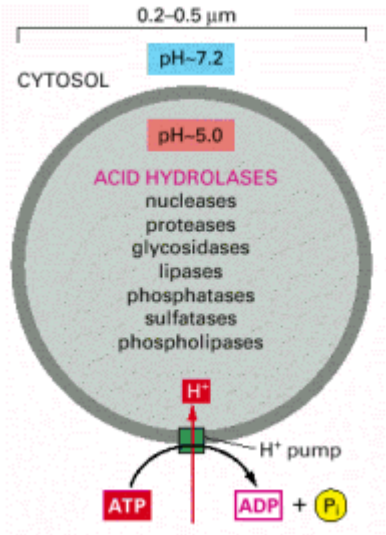


Transport from the Golgi apparatus Proteins are sorted in the *trans* Golgi network and transported in vesicles to their final destinations. In the absence of specific targeting signals, proteins are carried to the plasma membrane by constitutive secretion. Alternatively, proteins can be diverted from the constitutive secretion pathway and targeted to other destinations, such as lysosomes or regulated secretion from the cells.

Biogenesis: Large membrane-bounded organelles, such as the Golgi apparatus and the endoplasmic reticulum, break up into many smaller fragments during M phase, which ensures their even distribution into daughter cells during cytokinesis. In such a way these organelles are developed from the preexisting organelles (ER or GA).

LYSOSOMES

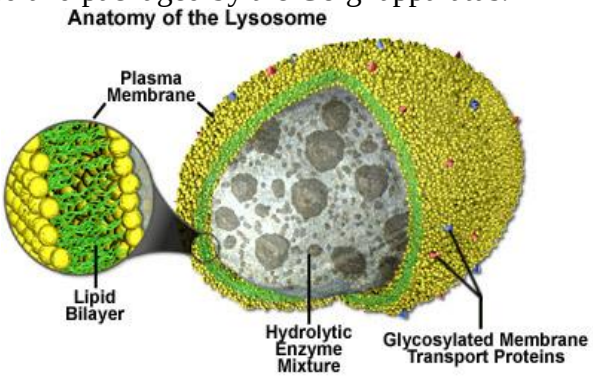
Lysosomes provide an excellent example of the ability of intracellular membranes to form closed compartments in which the composition of the lumen differs substantially from that of the surrounding cytosol. Found exclusively in animal cells, lysosomes are responsible for degrading certain components that have become obsolete for the cell or organism. The process by which an aged organelle is degraded in a lysosome is called ***autophagy*** ("eating oneself"). A process in which excessive amounts of secreted material (ex.: proteins, hormones, etc.) are fused with lysosomes for hydrolysis is called ***crinophagy***. Materials taken into a cell by endocytosis or phagocytosis also may be degraded in lysosomes. In phagocytosis, large, insoluble particles (e.g., bacteria) are enveloped by the plasma membrane and internalized.



Content of a Lysosome

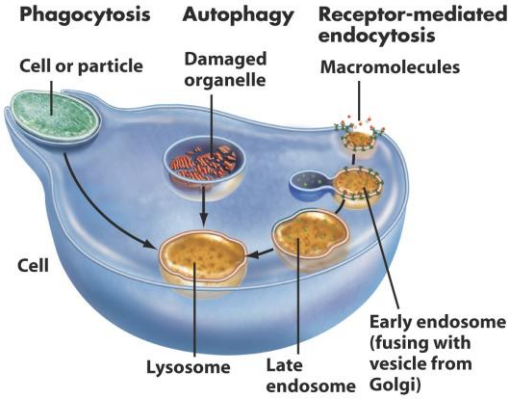
Lysosomes contain a group of enzymes that degrade polymers into their monomeric subunits. For example, **nucleases** degrade RNA and DNA into nucleotides; **proteases** degrade a variety of proteins and peptides; **phosphatases** remove phosphate groups from nucleotides, phospholipids, and other compounds, etc. All the lysosomal enzymes work most efficiently at acid pH values and collectively are termed ***acid hydrolases.*** The enzymes are

synthesized by ribosomes on the ER and are processed and packaged by the Golgi apparatus.



Like all other intracellular organelles, the lysosome not only contains a unique collection of enzymes, but also has a unique surrounding membrane. Two types of transport proteins in the lysosomal membrane work together to pump H^+ (*H^+-ATPase*) and Cl^- ions from the cytosol across the membrane, thereby acidifying the lumen. The acid pH helps to denature proteins, making them accessible to the action of the lysosomal hydrolases. Most of the lysosomal membrane proteins are unusually highly glycosylated, which helps to protect them from the lysosomal proteases in the lumen (making the lysosomal membrane resistant to acid denaturation). Lysosomal enzymes are poorly active at the neutral pH of cells and most extracellular fluids. Thus, if a lysosome releases its enzymes into the cytosol, where the pH is between 7.0 and 7.3, they cause little degradation of cytosolic components.

Lysosomes vary in size and shape, and several hundred may be present in a typical animal cell. Several types of lysosomes can be distinguished: ***Primary lysosomes*** are roughly spherical and do not contain obvious particulate or membrane debris. ***Secondary lysosomes***, which are larger and irregularly shaped, appear to result from the fusion of primary lysosomes with other membrane-bounded organelles and vesicles. They contain particles or membranes in the process of being digested.



The functions of lysosomes include:

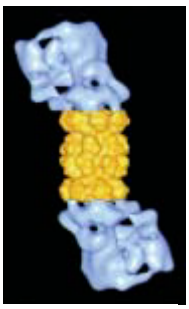
- The digestion of intracellular and extracellular materials;
- The autolysis (the self destruction if a cell is deformed or aged);
- The function of defense of a cell against invasion by bacteria, viruses and toxic substances;
- They play an important role in the fertilization of an ovum by a sperm cell. The *acrosome* at the tip of the head of the sperm contains lysosomes which hydrolyze the membrane of the ovum.

Lysosomal storage diseases result in the accumulation of the undigested substrates in lysosomes, with severe pathological consequences, most often in the nervous system. This occurs in ***Hurler's disease,*** for example, in which the enzyme required for the breakdown of glycosaminoglycans is defective or missing. ***Tay-Sachs disease*** is caused by a defect in one enzyme catalyzing a step in the lysosomal breakdown of gangliosides. The resulting accumulation of these glycolipids, especially in nerve cells, has devastating consequences. The symptoms of this inherited disease are usually evident before the age of 1. Affected children commonly become demented and blind by age 2 and die before their third birthday. Nerve cells from such children are greatly enlarged with swollen lipid-filled lysosomes. The most severe form of lysosomal storage disease, however, is a very rare disorder called ***inclusion-cell disease*** (***I-cell disease***). In this disease almost all of the hydrolytic enzymes are missing from the lysosomes of fibroblasts, and their undigested substrates accumulate in lysosomes, which consequently form large "inclusions" in the patients' cells.

PROTEASOMES

Cytosolic and nuclear proteins generally are not degraded in lysosomes but rather in **proteasomes**, large multiprotein complexes located mainly in the cytosol. The numerous proteasomes dispersed throughout the cell proteolytically cleave ubiquitin-tagged proteins in an

ATP-dependent process that yields short (7- to 8-residue) peptides and intact ubiquitin (Ub - a special polypeptide) molecules.



proteasome

Proteasomes functions:

1. They remove abnormal and misfolded proteins from the cell.
2. They are involved in the cell's stress response.
3. As part of the Ub system, they are involved in regulating the cell cycle.
4. They are involved in cellular differentiation (where they degrade transcription factors and metabolic enzymes).
5. They play an important role in the immune system.

Proteasomes are cylindrical structures very similar to **chaperons** (a large group of protein families whose role is to stabilize unfolded proteins, unfold them for translocation across membranes or for degradation, and/or to assist in their correct folding and assembly).

PEROXISOMES

All animal cells (except erythrocytes) contain **peroxisomes,** a class of single-membrane bound, roughly spherical organelles that contain several ***oxidases*** – enzymes that use molecular oxygen to oxidize organic substances, in the process forming hydrogen peroxide (H_2O_2), a corrosive substance.

$$RH_2 + O_2 \rightarrow R + H_2O_2$$

Peroxisomes also contain abundant amounts of the enzyme ***catalase***, which utilizes the H_2O_2 generated by other enzymes in the organelle to oxidize a variety of other substrates, such as *phenols*, *formic acid*, *formaldehyde*, and *alcohol*, by the "peroxidative" reaction:

$$H_2O_2 + R'H_2 \rightarrow R' + 2H_2O$$

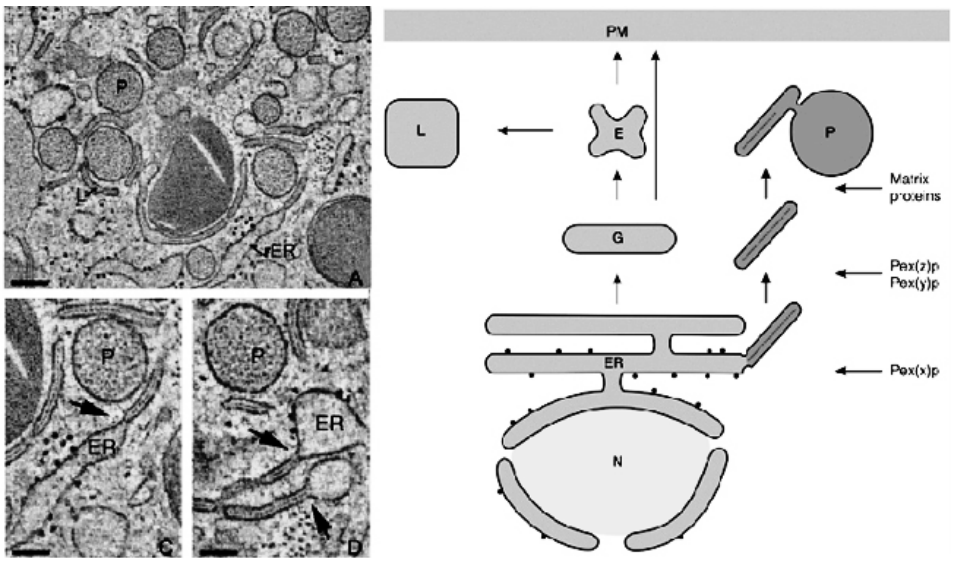
This type of oxidative reaction is particularly important in liver and kidney cells, where the peroxisomes detoxify various toxic molecules that enter the bloodstream. About 25% of the ethanol we drink is oxidized to acetaldehyde in this way. Catalase also degrades hydrogen peroxide to yield water and oxygen:

$$2\ H_2O_2 \xrightarrow{\text{Catalase}} 2\ H_2O + O_2$$

In contrast with the oxidation of fatty acids in mitochondria, which produces CO_2 and is coupled to the generation of ATP, peroxisomal oxidation of fatty acids yields acetyl groups and is not linked to ATP formation. The energy released during peroxisomal oxidation is converted into heat, and the acetyl groups are transported into the cytosol, where they are used in the synthesis of cholesterol and other metabolites. In most eukaryotic cells, the peroxisome is the principal organelle in which fatty acids are oxidized, thereby generating precursors for important biosynthetic pathways. Particularly in liver and kidney cells, various toxic molecules that enter the bloodstream also are degraded in peroxisomes, producing harmless products.

In the human genetic disease ***X-linked adrenoleukodystrophy (ADL)***, peroxisomal oxidation of very long chain fatty acids is defective. The *ADL* gene encodes the peroxisomal membrane protein that transports into peroxisomes an enzyme required for the oxidation of these fatty acids. Persons with the severe form of ADL are unaffected until midchildhood, when severe neurological disorders appear, followed by death within a few years. Another example of peroxisomal misfunction is the inherited human disease ***Zellweger syndrome***, in which a defect in importing proteins into peroxisomes leads to a severe peroxisomal deficiency. These individuals, whose cells contain "empty" peroxisomes, have severe abnormalities in their brain, liver, and kidneys, and they die soon after birth. One form of this disease has been shown to be due to a mutation in the gene encoding a peroxisomal integral membrane protein, the **peroxin** Pex2, involved in protein import.

Biogenesis: Since 1985 it has been thought that peroxisomes are autonomous organelles multiplying by growth and division (like mitochondrion). Lately though support for an ER-peroxisome connection came. Recent studies show that peroxisomes are at most semi-autonomous organelles because the ER supplies the membrane of peroxisomes. This process is guided by a few pioneering peroxisomal membrane proteins that start their life in the ER and contribute to the formation of a specialized extension from the rough ER. After reaching a considerable size, this specialized ER is detached from the rough ER. Additional integral membrane and peripheral proteins are recruited until the protein import machinery has been assembled and the import of matrix proteins can start as the last step in the peroxisome maturation pathway.



ER-Peroxisome Connection
PM - plasma membrane; L - lysosome; E - endosome, P - peroxisome; G - Golgi; ER - endoplasmic reticulum; N - nucleus.

Peroxisomal proteins are synthesized on free polyribosomes. The folding starts in the cytosol before they are taken en route to their final destination within the cell. Peroxisomal targeting signals (PTSs) are recognized by cytosolic proteins (receptors) that guide their cargo to the peroxisomal membrane.

NUCLEUS

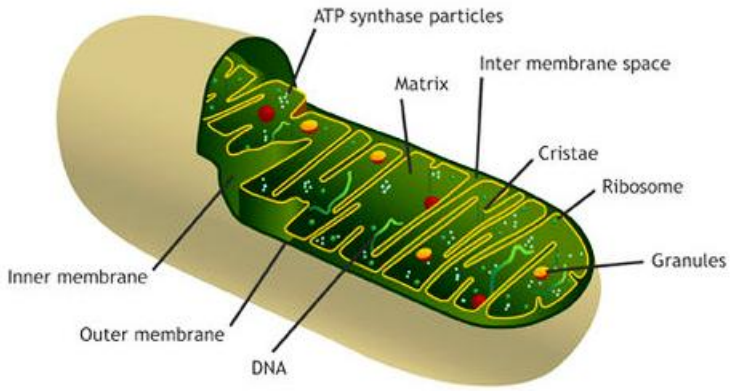
The nucleus**,** the largest organelle in animal cells, is surrounded by two membranes, each one a phospholipid bilayer containing many different types of proteins. The inner nuclear membrane defines the nucleus itself. In most cells, the outer nuclear membrane is continuous with the rough endoplasmic reticulum, and the space between the inner and outer nuclear membranes is continuous with the lumen of the rough endoplasmic reticulum. The two nuclear membranes appear to fuse at ***nuclear pores,*** the ringlike complexes composed of specific membrane proteins through which material moves between the nucleus and the cytosol. In a growing or differentiating cell, the nucleus is metabolically active, replicating DNA and synthesizing rRNA, tRNA, and mRNA. Within the nucleus mRNA binds to specific proteins, forming ribonucleoproteid particles. Most of the cell's ribosomal RNA is synthesized in the **nucleolus,** a subcompartment of the nucleus that is not bounded by a phospholipid membrane. Some ribosomal proteins are added to ribosomal RNAs within the nucleolus as well. The finished or partly finished ribosomal subunits, as well as tRNAs and mRNA-containing particles, pass through a nuclear pore into the cytosol for use in protein synthesis. In mature erythrocytes from nonmammalian vertebrates and other types of "resting" cells, the nucleus is inactive or dormant and minimal synthesis of DNA and RNA takes place.

In a nucleus that is not dividing, the chromosomes are dispersed and not dense enough to be observed in the light microscope. Only during cell division individual chromosomes are visible by light microscopy. In the electron microscope, the nonnucleolar regions of the nucleus, called the ***nucleoplasm***, can be seen to have dark- and lightstaining areas. The dark areas, which are often closely associated with the nuclear membrane, contain condensed concentrated DNA, called ***heterochromatin***. Fibrous proteins called **lamins** form a two-dimensional network along the inner

surface of the inner membrane, giving it shape and apparently binding DNA to it. The breakdown of this network occurs early in cell division. The lightstaining areas form the ***euchromatin*** – transcriptionally active part.

MITOCHONDRION

Most eukaryotic cells contain many mitochondria**,** which occupy up to 25 percent of the volume of the cytoplasm. The two membranes that bound a mitochondrion differ in composition and function. The outer membrane, composed of about half lipid and half protein, contains **porins** that make the membrane permeable to certain molecules. The inner membrane, which is much less permeable, is about 20 – 25% lipid and 75 - 80% protein - a higher proportion of protein than exists in other cellular membranes. The surface area of the inner membrane is greatly increased by a large number of infoldings, or ***cristae***, that protrude into the ***matrix***, or central space.



In nonphotosynthetic cells, the principal fuels for ATP synthesis are fatty acids and glucose. The complete aerobic degradation of glucose to CO_2 and H_2O is coupled to the synthesis of as many as 30 molecules of ATP. In eukaryotic cells, the initial stages of glucose degradation take place in the cytosol, where 2 ATP molecules per glucose molecule are generated. The terminal stages of oxidation and the coupled synthesis of ATP are carried out by enzymes in the mitochondrial matrix and inner membrane. As many as 28 ATP molecules per glucose molecule are generated in mitochondria. Similarly, virtually all the ATP formed in the oxidation of fatty acids to CO_2 is generated in mitochondria. Thus mitochondria can be regarded as the "power plants" of the cell.

Mitochondrial genome: Mitochondria contain also their own genetic apparatus composed of DNA (circular), mRNA, tRNA, rRNA, which is situated in matrix. The mt genome contains 37 genes, all of which are involved in the production of energy and its storage in ATP. Thirteen of these genes encode proteins; 22 genes encode tRNAs and 2 genes - ribosomal RNAs that translate the proteins' genes within the mitochrondrion. Mammalian mt genes use a slightly different genetic code than nuclear genes.

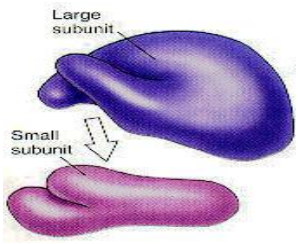
Biogenesis: Mitochondria are self-replicative, which means that one mitochondrion can form a second one, a third one, whenever the cell needs increased amounts of ATP.

RIBOSOMES

Ribosomes are essential for almost all prokaryotic and eukaryotic cells. Prokaryotic ribosomes have a sedimentation value of 70S when centrifuged and are found in bacteria, mitocondria and chloroplasts. Eukaryotic ribosomes have a value of 80S and are found in the cytoplasm of eukaryotic cells.

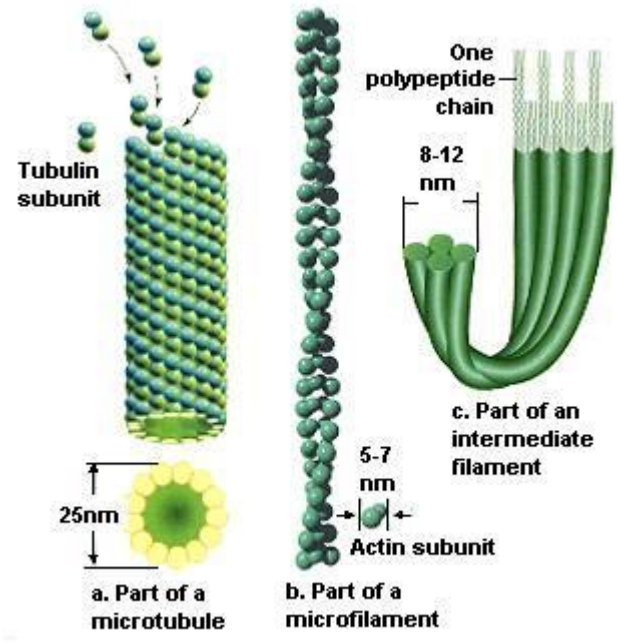
The ribosome complex may be attached to both the endoplasmic reticulum and the nuclear membrane. They are also as free floating structures in the cytoplasm. They often cluster together in groups along a strand of mRNA to form polyribosomes (polysomes).

	Free ribosomes	*Attached ribosomes*
Location:	Cytosol	Attached to ER
Proteins are synthesized for:	Mitochondria Nucleus Peroxisomes	Golgi complex Lysosomes Secretor vesicles Cell membrane



Biogenesis: Ribosomes are approximately 150-200 A^o in size and consist of 1 large and 1 small subunit. Normally these subunits exist independently in different regions of the cell, but associate to perform protein synthesis. The subunits consist of rRNA and ribosomal proteins, which associate together in the nucleolus (place of ribosomal biogenesis).

CYTOSKELETON



Structural Organization of Microtubule, Microfilament and Intermediate Filament

The cytosol is a major site of cellular metabolism and contains a large number of different enzymes. Proteins constitute about 20–30% of the cytosol by weight, and from a quarter to half of the total protein within cells is in the cytosol. The cytosol of a eukaryotic cell contains three types of filaments that can be distinguished on the bases of their diameter, type of subunit, and subunit arrangement.

Microfilaments, also called **actin filaments** (because they are made mainly of a globular protein - actin)**,** are 8–9 nm in diameter and have a twisted two-stranded structure. They play an important role in the movement of substances within the cell, form an elastic support for the cell membrane, in muscle cells they are organized into a special contractile machine that is the basis of muscle contraction.

Microtubules are hollow tube-like structures, 25 nm in diameter, that radiate from the centrioles towards the periphery of a cell. Their walls are formed by 13 parallel filaments called protofilaments. Microtubules are made of **tubulin** subunits. They are presented in cytoplasm, in flagellum of a sperm, in cilium, in centrioles and the mitotic spindle.

Intermediate filaments (IFs) have the structure of a 10-nm-diameter rope. Unlike microfilaments and microtubules, which are assembled from one or two proteins, intermediate filaments are assembled from a large diverse family of proteins. The most common intermediate filaments, found in the nucleus, are composed of ***lamins***. Intermediate filaments constructed from other proteins are expressed preferentially in certain tissues: for example, ***keratin***-containing filaments in epithelial cells, ***desmin***-containing filaments in muscle cells, and ***vimentin***-containing filaments in mesenchymal cells.

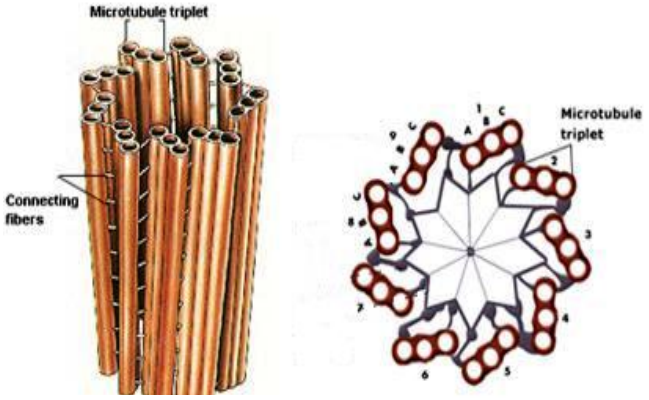
Most eukaryotic cells contain all three types of cytoskeletal filaments, often concentrated in distinct locations. For example, in the absorptive epithelial cells that line the lumen of the intestine, actin microfilaments are abundant in the apical region, where they are associated with cell–cell junctions and support a dense carpet of microvilli. Actin filaments are also present in a narrow zone adjacent to the plasma membrane in the lateral regions of these cells. Keratin intermediate filaments, forming a meshwork, connect microvilli and are tethered to junctions between cells. Lamin intermediate filaments support the inner nuclear membrane. Finally, microtubules, aligned with the long axis of the cell, are in close proximity to major cell organelles such as the endoplasmic reticulum, Golgi complex, and vesicles.

The cytoskeleton has been highly conserved in evolution. A comparison of gene sequences shows only a small percentage of differences in sequence between yeast actin and tubulin and

human actin and tubulin. This structural conservation is explained by the variety of critical functions that depend on the cytoskeleton. A mutation in a cytoskeleton protein subunit could disrupt the assembly of filaments and their binding to other proteins. Analyses of gene sequences and protein structures have identified bacterial homologs of actin and tubulin. The absence of IF-like proteins in bacteria and unicellular eukaryotes is evidence that intermediate filaments appeared later in the evolution of the cytoskeletal system. The first IF protein to arise was most likely a nuclear lamin from which cytosolic IF proteins later evolved.

CENTRIOLES

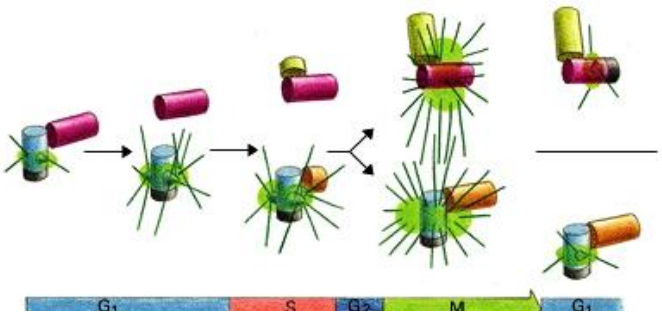
Centrioles both assemble and organize long, hollow cylinders of microtubules. Under the electron microscope the centrioles appear as two short, hollow, cylinders usually lying at right angles to each other. Each centriole is made up of nine microtubule triplets, which lie evenly spaced in a ring. There are no microtubules in the center (9+0 arrangement).



Centriole Structure

The centrioles appear as two, darkly staining granules, usually above the nucleus in animal cells. They are generally absent in plant cells, except in motile cells. The centrioles lie in a small mass of specialized cytoplasm called **centrospheres** (or **pericentriolar material**). The centrioles and the centrosphere are together described as **centrosome** that serves as microtubule organizing centers (**MTOC**s). Microtubules help determine the cell shape, move chromosomes during cell division, and provide the internal structure of cilia and flagella.

Biogenesis: During interphase of each cell cycle, the centrioles and other components of the centrosome are duplicated but remain together as a single complex on one side of the nucleus. As mitosis begins, this complex splits in two and each centriole pair becomes part of a separate MTOC that nucleates a radial array of microtubules called an aster. The two asters move to opposite sides of the nucleus to form the two poles of the mitotic spindle. As mitosis ends and the nuclear envelope re-forms around the separated chromosomes, each daughter cell receives a centrosome (the former spindle pole) in association with its chromosomes.



Centriole Replication. At a certain point in G_1 phase the two centrioles separate by a few micrometers. During S phase a daughter centriole begins to grow near the base of each old centriole and at a right angle to it, the elongation being completed by G_2 phase. The two centriole pairs remain close together in a single centrosomal complex until the beginning of M phase, when the centrosome splits in two and the two halves begin to separate.