Section One: Chapter 4: The Organelles in our Cells

In terms of the levels of organization, the next level after atoms and molecules is **organelles**. From the very name organelle, it tells us useful information; *-elle* as a suffix (at the end) of a word is diminutive, meaning 'little', 'teeny tiny', such that *organelle* can read as 'tiny organ'. Organelles are small structures within the cytoplasm of cells that carry out specific functions necessary for cells to maintain homeostasis.

Most of what biologist know regarding the structure of many organelles is from electron microscopy. Interestingly, the way the cell is examined will have an impact on what we 'see' and what we can deduce. Although tissues in the body obviously do extraordinary things, few organelles have actually been visualized in living cells, so we must keep in mind that knowledge in this filed is still growing.

In this section we will give an overview of what it is postulated that major organelles do, in order to provide context for when we encounter them in future sections. In the conventional sense, there are many organelles (see **Fig. 4.1**). Most often people remember the mitochondria, the nucleus and the Golgi something. A basic way to classify organelles is structurally. That is, whether they are surrounded by their own membrane (membranous organelles) or not (non-membranous organelles).

- Examples of **membranous organelles** are the *plasma membrane*, *nucleus, mitochondria, endoplasmic reticulum, Golgi apparatus, lysosomes,* and *peroxisomes.*

- Examples of **non-membranous organelles** are *ribosomes*, *cytoskeleton*, and *centrosomes*.

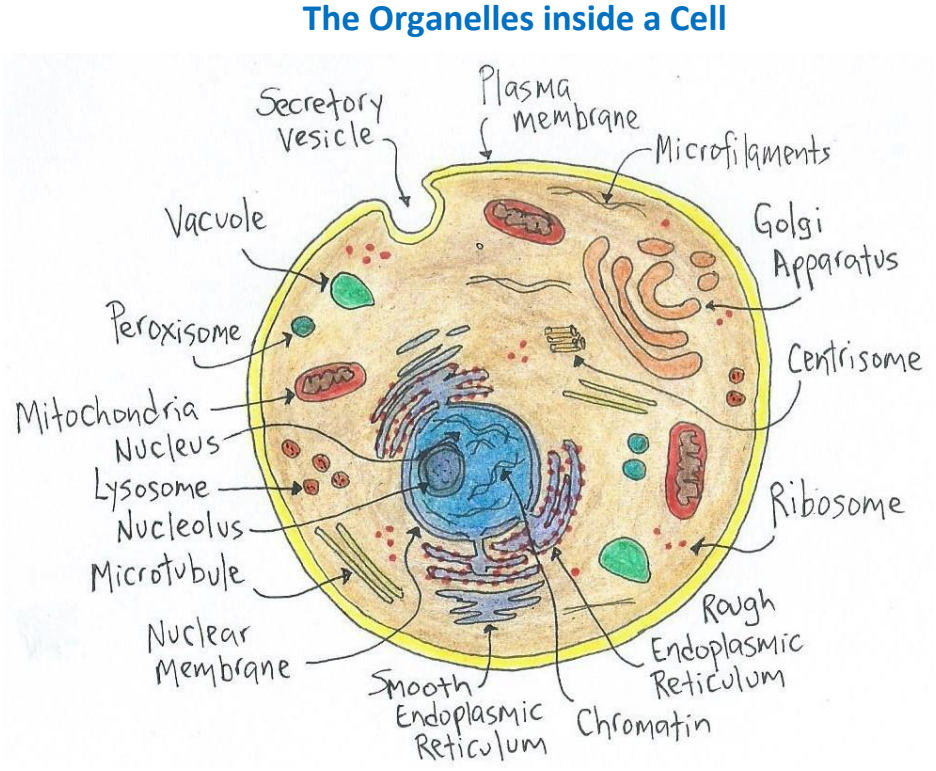


Figure 4.1 The drawing above shows a typical hypothetical cell containing most of the important the organelles that are discussed in this chapter. The diagrammatic drawing is useful in showing the various organelles, their relative size, typical arrangements and locations within a cell.

Membrane Organelles

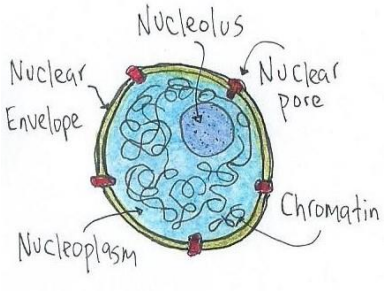
The Plasma Membrane

Since the plasma (cell) membrane is the physical boundary of the cell, we will include it here briefly in our discussion of organelles, even though all of the other organelles discussed will be contained within this structure. There are many theories about the cell membrane, but the most predominant one promoted about the plasma (cell) membrane is that it's a structure made up of a **phospholipid bilayer** with embedded proteins in it, and functions to separate the interior of the cell from the outside environment. It protects the cell from its environment and also regulates passage, communication, and cell shape.

The Nucleus

The nucleus is usually the largest organelle which contains information in the form of deoxyribonucleic acid (**DNA**), which carries genetic instructions for the development, functioning, growth and reproduction of our cells. Surrounding it is the nuclear membrane (envelope), it is like a mini double plasma membrane which separates the genome from the cytoplasm in order to protect it and ensure efficiency with gene transcription (making copies of genes).

The nuclear envelope contains proteins channels called "nuclear pores" (see image at right) which allows for molecules like ribonucleic acid (RNA) and ribosomes to move in and out of the nucleus. Inside is the **nucleoplasm**, filled with liquid where chromosomes (tightly packed strands of DNA) are located. The **nucleolus** is a subspace within the nucleus that is concerned with producing and assembling the cell's ribosomes and ribosomal RNA (**rRNA**). Following assembly, ribosomes are transported to the cell cytoplasm where they serve as the sites for protein synthesis.



Endoplasmic Reticulum – the Rough and the Smooth

The endoplasmic part of this term means 'inside the cell', and reticulum means network, so this is alike a crazy intracellular network. It is membrane attached to the nuclear envelope that folds around itself. There is the rough endoplasmic reticulum (rough ER) and the smooth endoplasmic reticulum (smooth ER).

Figure 4.2 The drawings show **a)** rough endoplasmic reticulum, and **b)** smooth endoplasmic reticulum (ER). As their names imply, rough ER appears rough in the electron microscope from being studded with ribosomes that make proteins, whereas smooth ER has a very smooth, buttery appearance as it has no ribosomes and is mostly concerned with making smooth and buttery lipids!

Most often in the cytoplasm, the **rough ER** comes directly **from the nuclear envelope** and radiates outward (see **Figure 4.1**). The **smooth ER** is often a continuation of that rough ER membrane outward away from the nucleus, but the **ribosomes are absent** and packages of lipid molecules start being created.

Rough Endoplasmic Reticulum

The rough endoplasmic reticulum (ER) has a bumpy appearance of ribosomes, as the term 'rough' implies. This structure is for the production proteins. **Translation**, the making of a protein from RNA instructions, may take place here, or on free ribosomes in the cytoplasm. Proteins made here will fold and be tagged with a marker, usually carbohydrate (glycosylation) to initiate transport to the Golgi apparatus for further modification. Proteins from here are often destined for **exocytosis** (release from cell) or deployment into **lysosomes** (see below).

Smooth Endoplasmic Reticulum

The smooth ER is involved in **lipids** and **steroids** (fats) synthesis and **cell detoxification**. The lack of ribosomes gives it a 'smooth' appearance. The lipid-based molecules are important in energy storage, membrane structure, and communication (such as steroids hormones). As an interesting note, the body's liver cells (hepatocytes), which are vital for most of the body's detoxification, have a much larger amount of smooth ER that most other cells because of the significant level of detoxification occurring there.

Golgi Apparatus (Complex or Body)

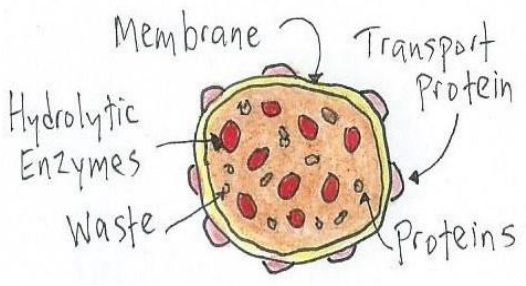
The Golgi part of the name is an *eponym* (named after a person), for the physician Camillo Golgi in 1898. This structure functions to **process and package proteins and lipids** that are received from the ER, to be further processed and sorted for transport to their eventual destinations: Either to lysosomes, the plasma membrane, or for secretion (release) from cell. A helpful analogy is to think of the Golgi apparatus (or complex, or body) as a post office. It is responsible for packing proteins from the rough ER into membrane-bound vesicles, which can fuse with the plasma membrane bilayer and either become part of the plasma membrane or be released to the exterior by the cell.

Within the Golgi complex, tagging proteins with sugar molecules act as shipping directions, identifying which route it will take. The molecules are usually sent to one of four (4) places: **a)** the plasma membrane, **b)** the cytoplasm, **c)** lysosomes, or **d)** peroxisomes.

Lysosome

These are spherical membrane-enclosed organelles replete with **powerful enzymes** requiring a pH of 5internally to hydrolyze (breakdown) macromolecules (large molecules), recycle cellular waste, and play a role in cellular signaling and energy metabolism. As the cell's recycling center, it can re-use any valuable raw materials it degrades.

There are at least 50 **hydrolytic** ('breaking with water') enzymes that have been identified, including ***proteases, nucleases, glycosidases, lipases, phospholipases, and phosphatases***. These organelles provide a good example of the value of compartmentalization, since the necessary pH for reactions to occur is 5, whereas that of the cytosol (cytoplasm) is about 7, that's two orders of magnitude, or 100 times more acidic. However, this can safely occur within the lysosome when the membrane of the lysosome is intact.



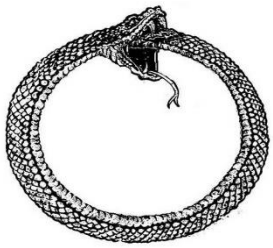
There are several types of cells that are required for a specific function or task, and then they die. After completing their task, quick changes occurs such as the membrane becomes bubbled, the nucleus condenses and the cells shrink up and disintegrate, this is called **apoptosis** (*apo* means away, and *ptosis* falling or dropping), which is referred to as programmed cell death. In these instances, the contents of the

lysosomes becomes an important factor, since when their membranes leak out their contents into the cytoplasm, the cell is digested! **Leukocytes** (white blood cells) are good examples of cells that undergo apoptosis and they are filled with lysosomes. It's ultimately a great type of recycling.

In **hepatocytes** of the liver, lysosomes break down glycogen, (the storage molecule for glucose), and liberate glucose for release into the blood stream if **hypoglycemia** (low blood sugar) is detected in order to elevate blood glucose to maintain homeostasis.

The Body Cleansing itself of Toxins

It is worth noting here that lysosomes also play an important role in **cleansing and detoxing cells**, they do this by digesting other older or worn out organelles in a natural process call **autophagy** (*auto* means self and *phagy* means to eat). Autophagy is the method by which your body cleans out damaged cells and toxins, helping us regenerate newer, healthier cells. Any cell will accumulate a variety of dead organelles, damaged proteins and oxidized particles over time, and this hampers function and accelerates aging and age-related diseases as cells aren't able to divide and function normally.



The image of the snake devouring itself (at right) is the "**Ouroboros**", a symbol of death and rebirth. Since many of our cells need to sustain us for a lifetime, the body has an amazing system of ridding itself of broken-down parts and defending itself naturally against disease, in a way, by eating itself!

This process is vital for good health, as the dysfunction of autophagy has been linked to neurodegenerative disorders, including Alzheimer's disease. This practice is occurring regularly **all the time**, but fasting (willful refrainment from eating and sometimes drinking), and other forms of practices (e.g., exercise, cold water showers) appear to accelerate autophagy and in this way provide increased cleansing of the body. In terms of the number of hours of fasting required to really have an impact, it is likely that in the later stages of at least a 1 day fast (over 24 hours) is where this effect will be most pronounced.

Peroxisome

Like the lysosome, the peroxisome is a spherical organelle responsible for destroying its contents, but they have different enzymes. Peroxisomes are the site of **fatty acid breakdown**, unlike lysosomes which predominantly degrades proteins. They are especially abundant in the **liver** and **kidney** cells where they help detoxify alcohol and other drugs and to **neutralize** damaging free radicals.

Peroxisomal enzymes are responsible for several crucial metabolic processes such as β-oxidation of specific fatty acids and biosynthesis of ether phospholipids. The enzymes within peroxisomes act to transfer H atoms from various molecules to oxygen, producing hydrogen peroxide (H_2O_2). Then, the peroxisomal enzyme **catalase**, for example, degrades the toxic H_2O_2 into water (H_2O) and oxygen (O_2). In this way, **peroxisomes neutralize poisons,** such as alcohol, that enter the body.

Free Radicals

Free radicals are also called **reactive oxygen species** (ROS), or **oxygen radicals**. They are a type of unstable molecule that contains oxygen or peroxides and can easily react with other molecules in a cell. They are created as a byproduct of normal cellular metabolism (**Fig. 4.3),** but also generated by refined carbs, refined sugar drugs, radiation, air pollutants, and industrial chemicals. They cause what is known as **oxidative stress** in the cell by reacting with and **damaging DNA** and lipid-based molecules like **cell membranes**. These ROSs are one reason that we may benefit from antioxidants in our diet, to reduce the

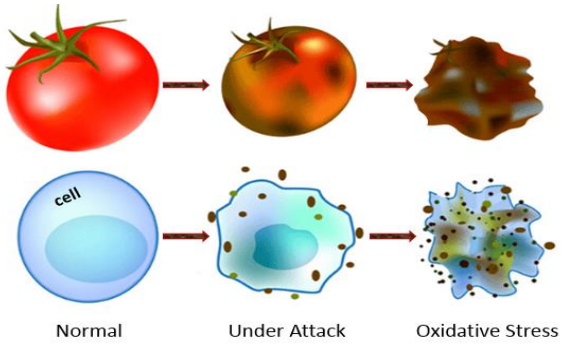


Figure 4.3 The top row shows how a tomato can be degraded as it is exposed to oxidative stress. The bottom row shows how a cell may be similarly degraded as a consequence oxidative stress.

damage they can cause. There are also many other powerful substances in fresh, organic food that provide protection to our cells and tissues. One example is a substance called **salvestrols**, which are found in leafy greens and red fruits like strawberries. Salvestrols belong to a group of phytochemicals called **phytoalexins**, most often produced by plants as a direct challenge from pathogenic organisms. Salvestrols have been used as anticancer agents.

Vacuoles

Vacuoles are membrane-bound organelles that handle waste products by degrading and removing them from the cell. They help sequester waste products, or store useful substances the cell may need at a later time. They are somewhat like specialized lysosomes, except vacuoles can store materials like water, salts, proteins, and carbohydrates, whereas lysosomes break down proteins, lipids, carbohydrates, etc., for re-use by the rest by the cell. They are also involved in breaking down organelles that have outlived their usefulness.

Vesicles are tiny compartments created by a lipid bilayer that store molecules for secretion to other parts of the body. As we will see in later sections, **neurotransmitters** are stored and released via **exocytosis** by vesicles. Before vesicles can fuse with the plasma membrane and release their contents, they must accumulate enough material inside them, since vesicles are for releasing either large macromolecules or large quantities of a molecule. They require a special chemical signal to be released which will be explored in future sections.

Mitochondria

Mitochondria are semi-spheroid rod-shaped structures that are encompassed in a double membrane (the inner and outer mitochondrial membranes) and are the site for the generating most of the chemical energy needed to power the cell's biochemical reactions. To be pedantic and accurate, energy is not really made here, but is extracted (in the presence of oxygen, O_2) from organic compounds here, and this energy is stored in the high energy phosphate bonds of **adenosine triphosphate** (**ATP**).

The **ATP** is produced in a process known as **cellular respiration,** so named because it requires O_2. This process starts in the cytoplasm, however, the vast majority of the energy harnessed comes from the steps that follow in the mitochondria and require O_2 as the final electron acceptor! The ATP produced here can then be used to power activities in the cell.

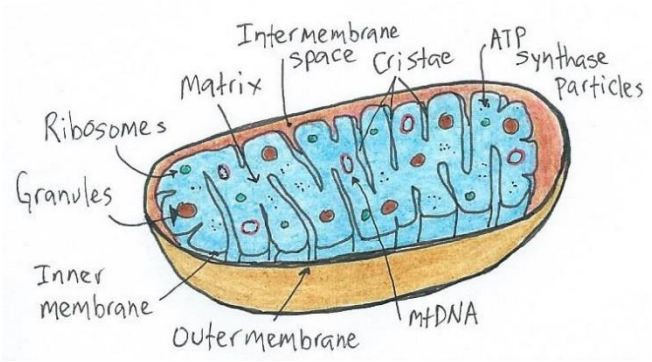


Figure 4.4 This drawing shows a longitudinal section of a mitochondrion (singular), with the inner and outer membrane, the cristae and other critical structures where ATP is generated. Within the mitochondria, the biochemical pathways require oxygen (O_2) in order to complete the process of producing ATP.

The inner mitochondrial membrane is highly folded into structures called **cristae** (crests), and the space between the cristae is called the **mitochondrial matrix** (see **Fig. 4.4** above). The space between the two membranes is called the **intermembrane space** and the **electron transport chain** (ETC) is embedded in the inner membrane and pumps protons (H^+) into it, therefore creating an acidic low pH area here. Energy comes from the protons moving back into the matrix down their gradient from the intermembrane space. Mitochondria also have their own ribosome in the matrix.

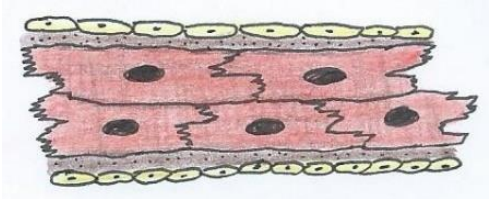
Mitochondrial DNA

In the mitochondrial matrix there is also circular DNA called **mitochondrial DNA** (mtDNA), which is genetically different from the DNA in the nucleus. As a consequence, mitochondria are self-replicating. The **endosymbiotic theory** regarding mitochondria is that larger cells may have engulfed smaller cells (like mitochondria) but because they were so useful, a symbiotic relationship formed and the mitochondria became part of the cell as an organelle. Mitochondrial DNA, unlike nuclear DNA, is inherited only from the mother, while nuclear DNA is inherited from both parents. This is because the mitochondria in sperm cells are lost during fertilization, therefore the zygote (fertilized egg cell) only inherits the mitochondria from the egg, and so the only donor will be the mother.

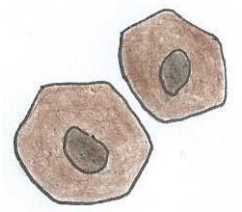
Note: Not all cells will have the same types of organelles or even similar numbers of organelles in them. These differences in composition and quantity of organelles will be determined by the function of the cells, within their tissue and the organ.

Which cells have a lot of Mitochondria? Which cells don't? And why?

In our body, it is our heart muscle cells, or **myocardiocytes**, that have the most mitochondria. They have about **5,000 mitochondria per cell**. Whoa. This incredible number is needed because on average our heart beats about **100,000 times in one day**, amazing right! That is about **35 million times in a year**. Keep in mind that the healthy myocardiocytes and the heart as an organ, never stop contracting, so these myocardiocytes never stop working. This means these cells (the tissue and organ) **require a lot of energy** to keep working, therefore it makes perfect sense to have a lot of mitochondria because as long as there is **O_2** present, they can make a lot of **ATP** for busy cells.



Another example of cells with high mitochondrial content are **hepatocytes** of the liver, and many **kidney** cells because of all the detoxing that both organs do for the body. **Slow twitch skeletal muscle fibers** (cells) used for endurance also require plenty of mitochondria. All of these cells are dependent on the energy (ATP) that their mitochondria produce. Note: The female reproductive **egg cell** has many thousands of mitochondria in preparation for the developing embryo, while **sperm cells** contain from 50 to 75 mitochondria in its mid-piece to produce the energy needed for the whipping flagellum to provide movement for the sperm cell.



In humans, our erythrocytes, or **red blood cells** (RBCs), **contain no mitochondria**! None. The reason for this is because the main function of RBCs in the body is to transport O_2 to the tissues, and as we will see, the mitochondria need to use O_2 in order to make their vast amounts of ATP. Therefore, in order to ensure the RBCs does not use the O_2 they are carrying and delivering, they use **glycolysis** to make their ATP **anaerobically** (without O_2), and therefore do not need any mitochondria to make any of the ATP they require.

Non-Membrane Organelles

Now for a look at the specialized structures and functions of the non-membrane bound organelles that are found within cells.

Ribosomes

Ribosomes are composed of proteins and ribonucleic acid (RNA), in about equivalent amounts. There are two sections, or subunits and each subunit is made of one or more **ribosomal RNAs** (rRNAs) and many ribosomal proteins (r-proteins). The relationship between these two subunits kind of resembles a bread bun, with the larger subunit on top (see **Fig. 4.5** below), this is the place the **amino acids** are assembled, and the smaller subunit below, this is where the **messenger RNA** (mRNA) binds and is read (translated) into a sequence of amino acids to create proteins.

Ribosomes can be considered "**protein factories**" of the cell as apparently they can very rapidly make proteins as long as the mRNA is being delivered to it. Ribosomes can be free in the cytoplasm floating around making proteins, or they can be bound to the **endoplasmic reticulum** (ER), and the entire complex is then called rough ER (see section above). Wherever they are located, the two main functions of ribosomes are:

1) Decoding the message from the mRNA; and
2) Generating the peptide bonds.

These two activities occur in the two ribosomal subunits or ribonucleoprotein particles (**RNPs**) show below in **Fig. 4.5**, where the mRNA is read like a ticker tape as the protein is assembled.

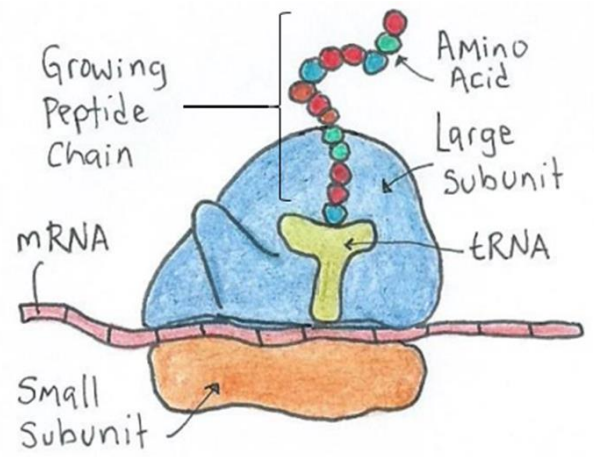


Figure 4.5 Here is a ribosome, with the large and small ribosomal subunits assembled like a bread bun for an mRNA sandwich! The tRNA brings out the mRNA (a code for a gene) from the nucleus so it can be read and translated into a protein, which are assembled one amino acid at a time to create the final peptide chain.

The "Central Dogma" Theory has never been Shown to be Correct

The "Central Dogma" is the belief that genetic information flows only in one direction, from DNA, to RNA, to proteins. That each protein made in the body is from a specific gene (sequence of DNA) that coded for it, with the mRNA as a disposable copy of those instructions. However, this has been shown to be incorrect! It is still in most textbooks to this day, even though much better explanations can be entertained, like the great suggestions from the field of epigenetics in studies with the **Agouti mice**!

The **Human Genome Project** (2003), which purportedly mapped out all the genes in humans, discovered something very different to what they believed. Though the numbers reported vary, the theme is consistent. It is clearly not 1 gene = 1 protein. For example, it was determined that a human cell can make **75,000** different proteins, but there are only about **20,000** human genes. There appears to be at least 3 times as many proteins as there are genes. Some rationales suggest that alternative splicing of these genes can make many mRNA's, thus different types of proteins. The important element to keep in mind is that experts and genius are routinely wrong. It is OK to be wrong, we probably all know this by now. The critical point is acknowledging an idea was incorrect and continuing to look for more accurate explanations.

One more point. The term 'dogma' means "the doctrine of belief in a religion or a political system". Therefore, the term 'the central dogma' seems like an odd choice of terms to apply if the nature of science and pursuing knowledge and the truth is then described in terms of religious or political beliefs. Of all things, a religious connotation gets associated with the Darwinian theory of random genetic mutations being responsible for all of our traits. It seems beyond odd :)

Not all cells will have the same organelles or even similar numbers of organelles. These differences are determined by the functions of the cells, their tissue and organ. For example, ribosomes are particularly abundant in the pancreas because the cells in specific structures called **pancreatic acini** (acinar meaning 'round') synthesize large amounts of digestive enzymes for the breakdown of food. Not only that, the pancreas has structures called **pancreatic islets** (meaning 'islands') which synthesizes several protein hormones, such as **insulin** and **glucagon** that regulate glucose levels in the blood.

Centrosome

A centrosome is a cellular structure involved in the process of **cell division**. It consists of two **centrioles** oriented at right angles to each other. The centrosome is the primary microtubule-organizing center (MTOC) and regulates cell motility, adhesion and polarity in interphase, and facilitates the organization of the spindle poles during mitosis (cell division). Also, proteins called **microtubules** assemble into a spindle between the two centrosomes and help separate the replicated chromosomes into the daughter cells.

Cytoskeleton

Within the cytoplasm and tethered to the plasma membrane, is network of protein fibers known as the **cytoskeleton**. This structure helps cells maintain their shape and internal organization, and it also provides mechanical support for cells to carry out their essential functions, like cell division and movement. The major components of the cytoskeleton are **microtubules**, **intermediate filaments**, and **microfilaments**. All three of these structures are **polymers of protein subunits** that vary greatly in diameter (as seen in **Fig. 4.6** below) These different components work together to generate contraction, cell motility, cell stability, movement of organelles and vesicles through the cytoplasm, cytokinesis (cell division), establishment of the intracellular organization of the cytoplasm, establishment of cell polarity (sidedness), and many other functions that are essential for cellular homeostasis and survival.

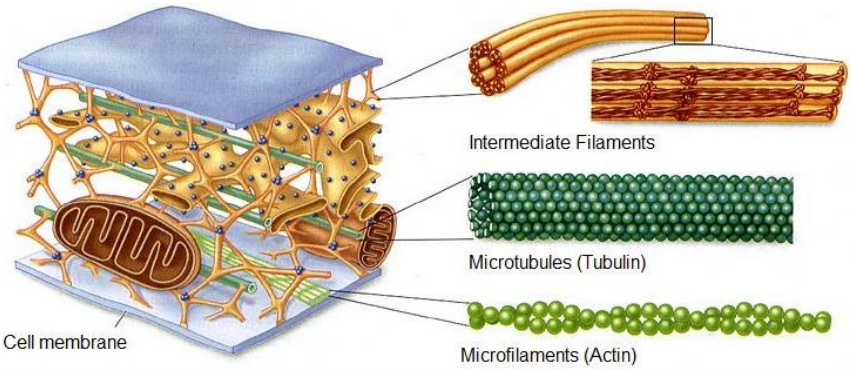


Figure 4.6 Shows the arrangement of the cytoskeleton within a cell (right), and a zoom in of the major separate components of the cytoskeleton (right); the microtubules, intermediate filaments, and microfilaments.

The three main elements of the cytoskeleton shown in **Fig. 4.6** above are described below.

Microtubules

Microtubules are small tubes made from the protein **tubulin** and they are the largest structure of the cytoskeleton, with a diameter of about **25 nm**. These tubules are found in cilia (meaning hair) and flagella (meaning whip or scourge), and both of the structures are involved in cell movement: Cilia moves substances across a cell surface, and flagella propel cells to move through substances. Microtubules can

create a type of track system, almost **like railroad tracks**, to help provide pathways for **secretory vesicles** to move through the cell. They are also involved in cell division as they are a part of the mitotic spindle, which pulls homologous chromosomes apart.

Intermediate filaments

These are fibers that are smaller than the microtubules, but larger than the microfilaments, thus are intermediate (as their name implies) with a diameter of about **10 nm**. The intermediate filaments are made of a variety of proteins such as **keratin** and **neurofilaments** (found in the cytoplasm of neurons). They are very stable, and help provide structure to the nuclear envelope and anchor organelles.

Microfilaments

The thinnest part of all the elements of the cytoskeleton are the microfilaments. These are created by intertwined double-stranded protein structures of about **5 to 7 nm** in diameter. They are made of the protein **actin** (which along with **myosin**, is one of the two main proteins in muscle cells). Actin is both flexible and strong, making it a very useful protein for cell contraction and movement. As we will see in the muscle sections, contractions of the heart, skeletal and smooth muscle are mediated through the overlapping structural arrangement of the two contractile proteins actin and myosin. Interestingly, muscles cells are not the only cells that can contract, plenty of epithelia and other cells are contractile, thanks to actin within their cytoskeleton.

Review Questions for Chapter 4: Organelles

1. For the **nucleus**, which of these statements are true?

- **a)** it has a nuclear envelope
- **b)** it contains DNA
- **c)** ribosomes make proteins inside the nucleus
- **d)** a and b

2. The **rough ER** has its name due to what structures associated with it?

- **a)** Golgi apparatus
- **b)** ribosomes
- **c)** lysosomes
- **d)** proteins

3. Which of these organelles makes large amounts of ATP if the cell has both glucose and O_2?

- **a)** mitochondria
- **b)** peroxisomes
- **c)** lysosomes
- **d)** endoplasmic reticulum

4. Which of the following is a feature common to all three components of the **cytoskeleton**?

- **a)** They all serve to protect the organelles within the cell.
- **b)** They are all characterized by roughly the same diameter.
- **c)** They are all polymers of protein subunits.
- **d)** They all help the cell resist compression and tension.

5. Which of the following is a function of **lysosomes**?

a) regulation of intracellular calcium concentration
b) production of proteins
c) synthesis of steroid hormones
d) breaks down and recycles cellar waste with digestive enzymes

6. What type of cell in the human body has the highest number of **mitochondria**?

a) hepatocytes
b) osteocytes
c) myocardiocytes
d) erythrocytes
e) skeletal muscle

7. Are there any human cells that have **no mitochondria**?

a) all cells have mitochondria
b) hepatocytes
c) myocardiocytes
d) egg cells and sperm cells
e) erythrocytes

8. Peroxisomes have many _____ enzymes to detoxify _____.

a) hydrolytic; proteins
b) neutralizing; free radicals
c) mitochondrial: lipids
d) hydrolytic; lipids
e) microbial; vesicles

9. The **non-membrane** organelles include which of the following?

1. free ribosomes **2.** mitochondria **3.** cytoskeleton **4.** centrosome **5.** vesicles

a) 1 only
b) 2 and 5
c) 3, 4 and 1
d) 3 and 4
e) 3 only

10. The **cytoskeleton** includes which of these structures?

1. microtubules **2.** ribosomes **3.** intermediate filaments **4.** peroxisome **5.** microfilaments

a) 1 and 5
b) 2 and 4
c) 1, 2, 3, and 5
d) 1, 3, and 5
e) 3, 4 and 5

Answers in Appendix B