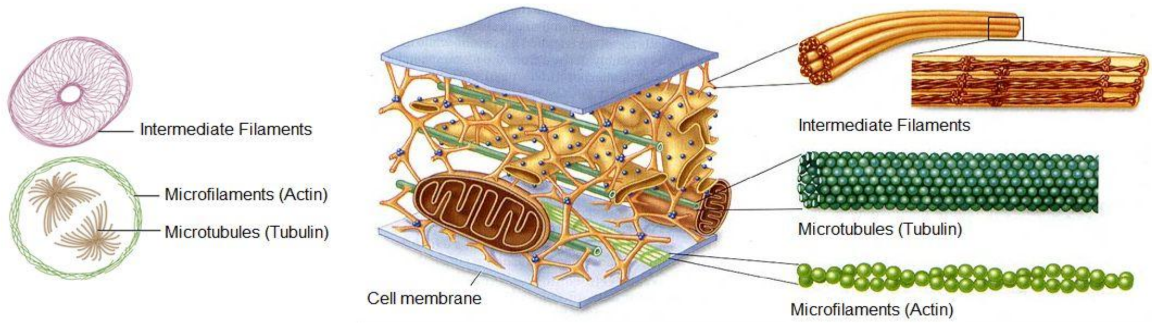
The Cytoskeleton is a complex array of protein polymers of **filaments** and **tubules** that extend throughout the cytoplasm. It Provides structural support to cell and stabilizes junctions between cells (structural functions); anchors the organelles or assists in the movements of organelles and cytoplasmic vesicles; allows the movement of entire cells and also helps move chromosomes during cell division (movement functions)



Types of cytoskeletons

1. Microtubules (MTs)

- Microtubules are found in almost all eukaryotic cell types except red blood cells.
- They are the largest elements of the cytoskeleton.
- Microtubules are none branching and rigid hollow tubes of protein that can rapidly disassemble in one location and reassemble in another.
- Microtubules are elongated polymeric structures composed of heterodimer of α tubulin and β tubulin.
- Polymerization of tubulins is directed by microtubule organizing centers (MTOCs), which contain tubulin assemblies that act as nucleating sites for polymerization
- All microtubules originate from the microtubule-organizing center (MTOC), the dominant MTOC in most somatic cells is the centrosome, has gamma tubulin (γ).
- The centrosome is the microtubule-organizing center for the mitotic spindle and consists of paired centrioles.
- Microtubules grow from γ tubulin rings within the MTOC that serve as nucleation sites for each microtubule.
- The length of microtubules changes dynamically as tubulin heterodimers are added or removed in a process of dynamic instability.
- In the centrosome, the tubulin subunits polymerize and from two types of microtubules**:**
  1. **Dynamic microtubules** are continuous assembly and disassembly (reshaping of cell) determine cell shape and function in intracellular movement of organelles and secretory granules and form spindles that guide the movement of chromosomes during cell division or mitosis.
  2. **Stable microtubules** form walls of centrioles, cilia and flagella.

Transport along microtubules is under the control of proteins called motor proteins, which use ATP in moving the larger structures. Kinesins carry material away from the MTOC near the nucleus toward the plus end of microtubules; cytoplasmic dyneins carry material along microtubules in the opposite direction generally toward the nucleus. Important roles for this system include extending the ER from the nuclear envelope to the plasmalemma and moving vesicles to and through the Golgi apparatus.

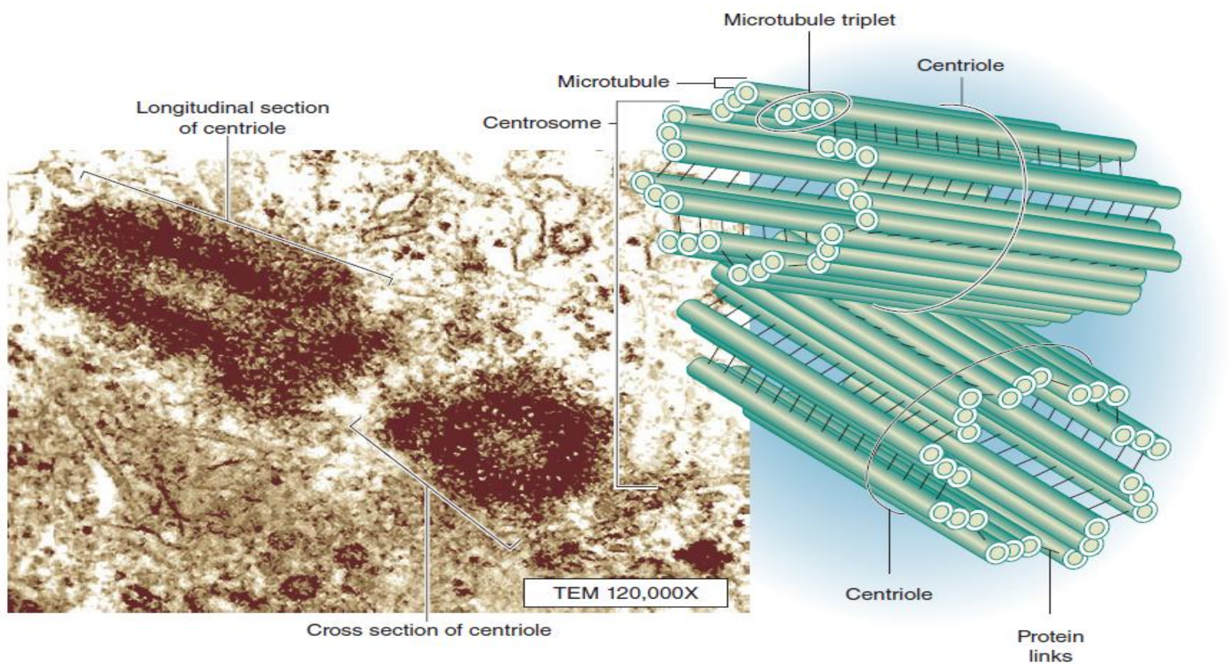
Microtubules are involved in numerous essential cellular **functions**:

- Intracellular vesicular transport (e.g., movement of secretory vesicles, endosomes, and lysosomes).
- Structure of centrioles, cilia and flagella.
- Attachment of chromosomes to the mitotic spindle and their movement during mitosis and meiosis.
- Cell elongation and movement (migration).
- Maintenance of cell shape, particularly its asymmetry.

Medical application

Several inhibitory compounds used by cell biologists to study details of microtubule dynamics are also widely used in cancer chemotherapy to block activity of the mitotic spindle in rapidly growing neoplastic cells. Such drugs include vinblastine, vincristine, and paclitaxel, all of which were originally discovered as plant derivatives.

Centrioles: are non membranous organelles. Small cylindrical structures composed of highly organized microtubules located within centrosome, perpendicular to each other. Each centriole consists of nine evenly spaced clusters of three microtubules arranged in a circle. The microtubules have longitudinal orientation and are parallel to each other. Before mitosis, the centrioles in the centrosome replicate and form two pairs. During mitosis, each pair moves to the opposite poles of the cell, where they become microtubule organizing centers for **mitotic spindles** that control the distribution of chromosomes to the daughter cells.



EM of centrioles and centrosome.

Cilia

- Cilia (sing., cilium) are involved in movement. Motile structure use to move something like the ciliated cells that line respiratory tract sweep debris trapped within mucus back up the throat. This helps keep the lungs clean by rhythmic beating. Similarly, ciliated cells move an egg along the oviduct, where it will be fertilized by a flagellated sperm cell.

- Origin of cilia from centrioles, each centrioles give only one cilium, so ciliated cells have many centioles embedded in cytoplasm under cell membrane called basal body. Basal bodies associated structures firmly anchor cilia in the apical cell cytoplasm.
- Cilia have another function; act as receptor in special cells (rods and cones cells of the eyes retina).

Flagella

Flagella (sing. Flagellum) is motile projection use to move cell itself**,** like tail of sperm. Have an inner core of microtubules within a covering of plasma membrane. Flagellum is the same structure of cilium but always single and extremely longer.

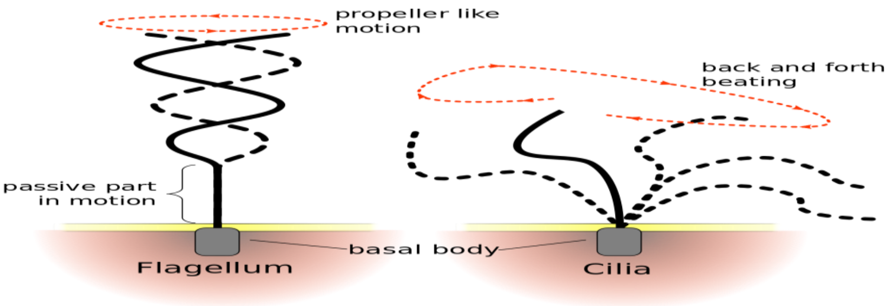


Figure shows the different between cilia and flagellum motion

Medical application

The importance of normal cilia and flagella is illustrated by the occurrence of a **genetic disorder**. Some individuals have an inherited genetic defect that leads to malformed microtubules in cilia and flagella. Called **immotile cilia syndrome**

1. These individuals suffer from recurrent and severe respiratory infections. The ciliated cells lining respiratory passages fail to keep their lungs clean. (chronic respiratory infections)
2. They are also unable to reproduce naturally due to the lack of ciliary action to move the egg in a female or the lack of flagella action by sperm in a male. (Immotile sperm).

2.Filaments

Each cytoskeletal filament type is formed by polymerization of a distinct type of minute protein subunit and has its own characteristic shape and intracellular distribution.

There are three types of filaments:

Microfilaments, intermediated filaments and thick filaments

1. **Microfilament** (thin filament or known as actin filaments):

- Microfilaments are the thinnest structures of the cytoskeleton.
- They are composed of helical two-stranded polymers assembled from **globular actin subunits.** Actin filaments are also highly dynamic, Assembly of actin filaments (F-actin) is polarized, with

- G-actin subunits added to the plus (+) end and removed at the minus (–) end. Balancing G-actin assembly and disassembly at the opposite ends, with a net movement or flow along the polymer known as **treadmilling.**
- Actin is very abundant in all cells, usually concentrated as networks of actin filaments and abundant free globular G-actin subunits concentrated near the cell membrane (a region sometimes called the **cell cortex**) and in cellular extensions. Microvilli are extensions that increase a cell's surface area for improved cellular absorption, while other protrusions are used in cell motility. In cells attached to firm substrates, actin filaments may be concentrated into parallel bundles called **stress fibers.**
- various **myosin** motors (motor protein) use ATP to transport along F-actin. Movement is usually toward (+) end of actin filaments; myosin VI is the only known myosin that moves in the other direction. Interactions between F-actin and myosins form the basis for various cell movements:

    1. Transport of various organelles, vesicles, and granules through the cell (*cytoplasmic streaming*)
    2. Contractile rings of microfilaments and with myosin II that constrict to produce two cells at the end of mitosis (*cytokinesis*)
    3. Membrane-associated molecules of myosin I whose movements along microfilaments are important in the cell surface changes that underlie phagocytosis and pinocytosis
    4. Contraction of cytoplasm that shortens cells or rapidly retracts cellular extensions

2. Intermediate filaments

- Cytoskeleton includes class of filaments intermediate in size between microtubules and actin filaments. **Intermediate filaments** are much more stable than microtubules and actin filaments. These filaments are composed of different protein subunits in different cell types.
- It has important function in anchoring of cells with extracellular matrix and connects cells to each others also anchor the organelles inside the cell at specific location**.**

Intermediate filament proteins with particular biological, histological, or pathological importance include the following:

1. **Keratin** filaments (cytokeratins) form large bundles (tonofibrils) that attach to certain junctions. In epidermal cells, cytokeratins accumulate in the differentiation process termed keratinization, which results in an outer layer of nonliving skin cells that reduces dehydration. Keratinization also provides some protection from minor abrasions and produces various hard protective structures of skin, such as nails
2. **Vimentin** filaments are found in many mesenchymal cells.
3. **Desmin** filaments are found in both smooth and striated muscles.
4. **Glial fibrillar acidic protein (GFAP)** found especially in astrocytes, supporting cells of central nervous system tissue.
5. **Neurofilament** proteins are found in the nerve cells and their processes.
6. **Glial** filaments are found in astrocytic glial cells of the nervous system.
7. **Lamin** intermediate filaments are found on the inner layer of the nuclear membrane.

Medical application

The presence of a specific type of intermediate filament in tumors can often reveal the cellular origin of the tumor, information important for diagnosis and treatment of the cancer. Identification of intermediate filament proteins by means of **immunocytochemical methods** is a routine procedure. One example is the use of Glial Fibrillary Acidic Proteins (GFAP) to identify astrocytomas, the most common type of brain tumor.

3. **Thick filaments** consist primarily of the protein myosin so that called myofilaments. Each thick filament is approximately 15 nm in diameter, and each is made of several hundred molecules of myosin.

In muscle tissues are the **actin** filaments (microfilaments) fill the cells and associated with **myofilaments** to induce muscle contractions.

Inclusions

The cytoplasmic inclusions are cytoplasmic structures or deposits filled with stored macromolecules and are not present in all cells that accumulate in the cytoplasm of certain cells not able to carry out any metabolic activity and are not bound by membranes. Inclusions are stored nutrients, secretory products, and pigment granules. Examples of inclusions are:

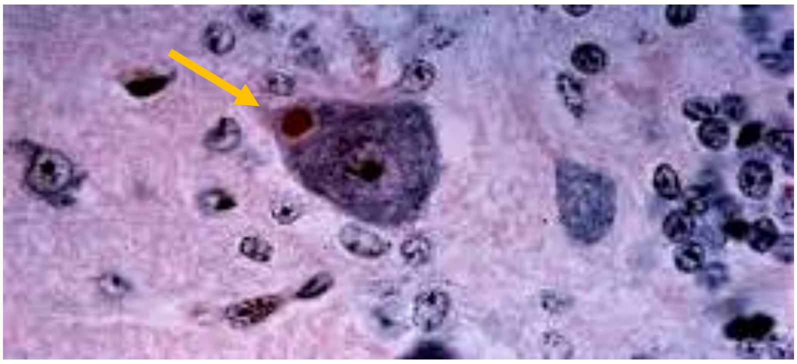
Glycogen: Glycogen granules are the most common form of glucose in animals and especially abundant in cells of muscles and liver.

Lipids: Lipids are triglycerides in storage form the common form of inclusions not only are stored in specialized cells (adipocytes) but also are located as individual's droplets in various cell type especially hepatocytes. These are fluid at body temperature and appear in living cells as refractile spherical droplets.

Crystals: Crystalline inclusions have long been recognized as normal constituents of certain cell types such as Sertoli cells and Leydig cells of the human testis, and occasionally in macrophages. It is believed that these structures are crystalline forms of certain proteins which is located everywhere in the cell such as in nucleus, mitochondria, endoplasmic reticulum, Golgi body, and free in cytoplasmic matrix.

Pigments: The most common pigment in the body, besides hemoglobin of red blood cells is melanin, manufactured by melanocytes of the skin and hair, pigments cells of the retina and specialized nerve cells in the substantia nigra of the brain. These pigments have protective functions in skin and aid in the sense of sight in the retina but their functions in neurons is not understood completely. Furthermore, cardiac tissue and central nervous system neurons shows yellow to brown pigment called lipofuscin, some believed that they have lysosomal activity.

This type of inclusion called **endogenous pigment** because is formed by the cells, while other type of inclusion come from outside called **exogenous pigment** like tattoo marks, carotene and dust
the epithelial surface of lung alveoli where it inhaled particulate matter known as dust cells.



The inclusion body (<u>lipofuscin</u>) in neuron

<u>Hemosiderin</u> is a dense brown aggregate of denatured ferritin proteins with many atoms of bound iron. It occurs in phagocytic cells, especially macrophages of the liver and spleen, where it results from phagocytosis of red blood cells.

Medical application

A condition termed hemosiderosis, in which the iron containing inclusion hemosiderin occurs in cells of organs throughout the body, may be seen with increased uptake of dietary iron, impaired iron utilization, or with excessive lysis of red blood cells. Hemosiderosis itself does not damage cell or organ function. However, extreme accumulations of iron in cellular hemosiderin can lead to disorders such as **hemochromatosis and iron overload syndrome**, in which tissues of the liver and other organs are damaged.