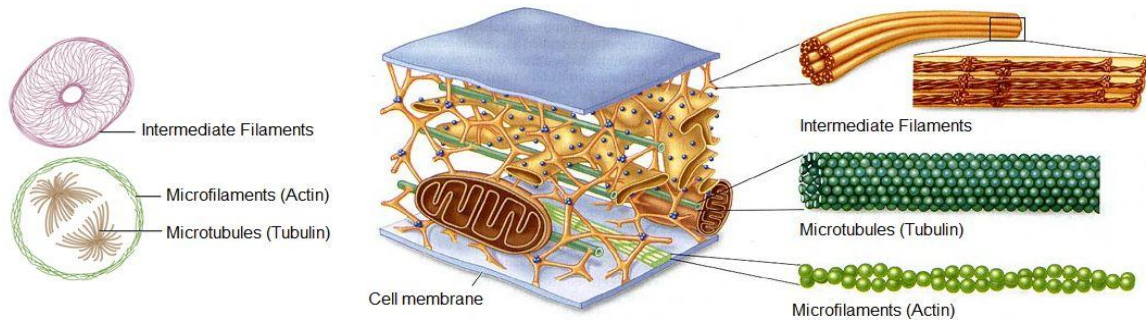


The **Cytoskeleton** is a complex array of protein polymers of **filaments** and **tubules** that extend throughout the cytoplasm. It Provides structural support to cell and stabilizes junctions between cells (structural functions); anchors the organelles or assists in the movements of organelles and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



Types of cytoskeletons

- **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 non-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 form 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.

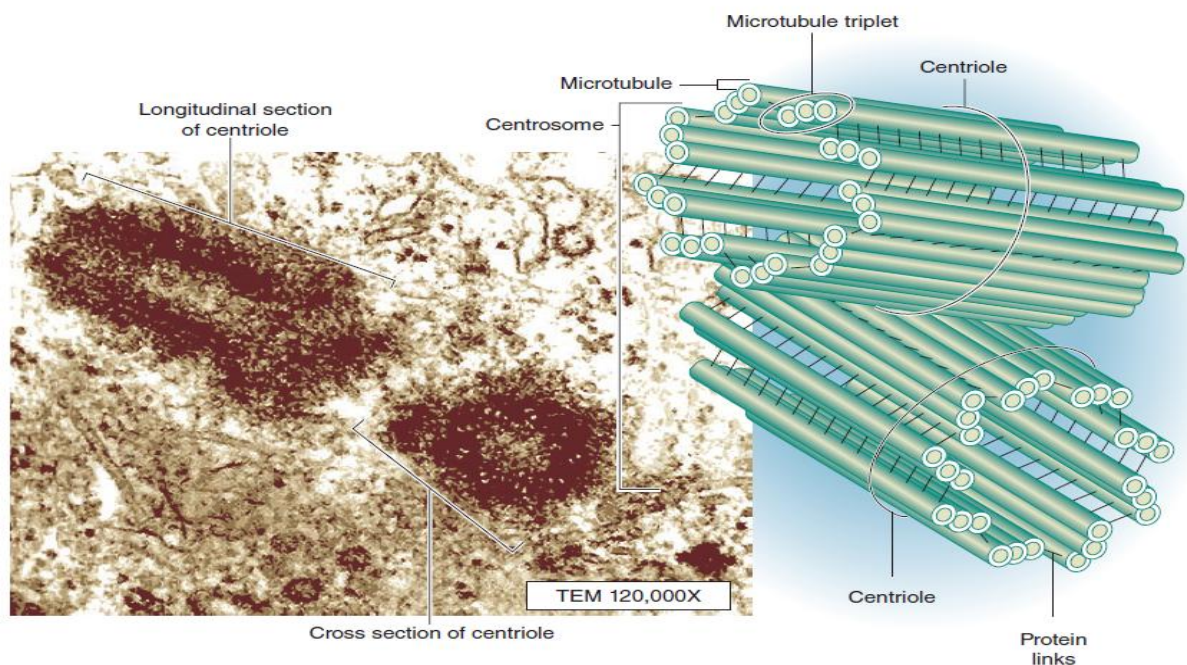
Microtubules are involved in numerous essential cellular **functions**:

- 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.



TEM 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 centrioles 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.

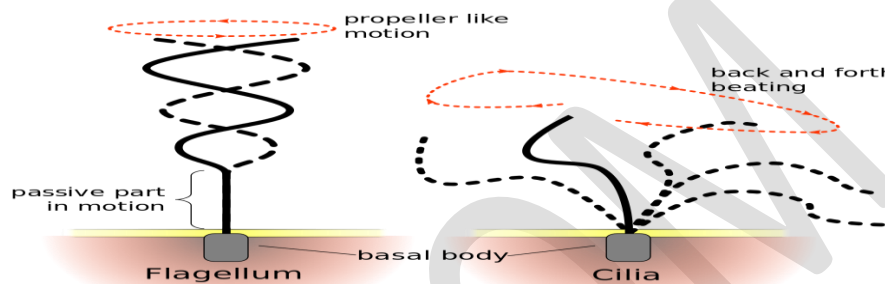


Figure shows the different between cilia and flagellum motion

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).

• 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 (+) ends 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:

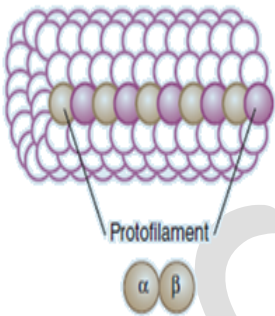
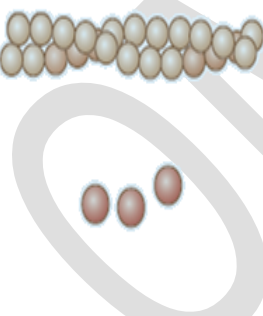
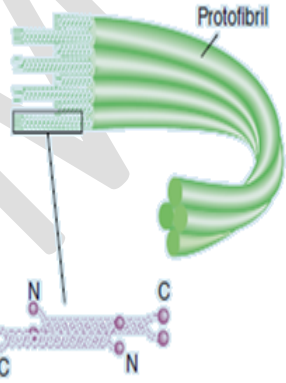
1. **Keratin** filaments (cytokeratins) form large bundles (tonofibrils) that attach to certain junctions. In epidermal cells, cytokeratins accumulate in the differentiation process termed **keratinization**, which results in an outer layer of nonliving skin cells that reduces dehydration. Keratinization 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.

- 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.

	Microtubules	Microfilaments	Intermediate filaments
Polymer			
Subunit	Heterodimers of $\alpha\beta$ -tubulin	G-actin monomers	Antiparallel tetramers of 2 rod-like dimers
Overall structure	Hollow tube with a wall of 13 parallel protofilaments	2 intertwined filaments of F-actin	Cable of 4 intertwined protofibrils, each consisting of bundled tetramers associated end to end
Diameter	25 nm	5-7 nm	8-10 nm
Monomeric proteins	α and β tubulin (54 kDa)	Globular G-actin (42 kDa)	Various α -helical rod-like proteins (~55 kDa, Table 2-5)
Polarity	+ and - ends	+ and - ends	No apparent polarity
Relative stability	Dynamic in cytoplasm; stable in axonemes	Dynamic	Stable
General locations	Radiating through cytoplasm from concentration at centrosomes; axonemes	Concentrated beneath cell membrane; in cell extensions like microvilli	Arrayed throughout cytoplasm; at desmosomes; inside nuclear envelop
Key functions	Maintain cell's shape and polarity; provide tracks for organelle and chromosome movement; move cilia and flagella	Contract and move cells; change cell shape; cytokinesis; cytoplasmic transport and streaming	Strengthen cell and tissue structure; maintain cell shape; maintain nuclear shape (lamins)