B. The cytoskeleton

The cytoskeleton generally ensures the shape and internal architecture of the cell. A characteristic component of eukaryotic cells, the cytoskeleton is a complex network of protein filaments and tubules that extends throughout the cytoplasm and gives the cell its shape and mechanical strength. The cytoskeleton is a highly dynamic structure that continuously reorganizes itself during various cellular events (migration, division, etc.). All elements of the cytoskeleton are elongated protein structures resulting from the polymerization of monomeric elements. It comprises three distinct protein networks: microtubules, intermediate filaments, and the actin network.

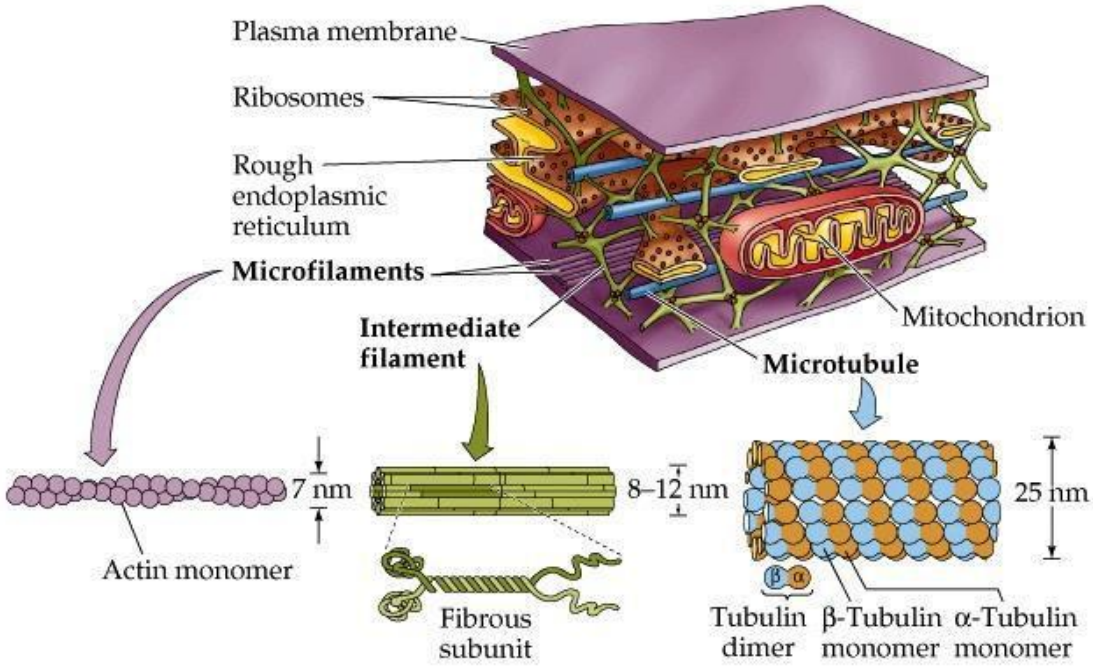

Figure III.6. Cytoskeletal structure **[24].**

I. Microtubules

I.1. Definition

Tubulin is a major component of the eukaryotic cytoskeleton and forms microtubules (MT). Eukaryotic MT determine the position of organelles and direct intracellular transport. They play a central role in chromosome segregation by forming the mitotic spindle, which allows chromosomes to be positioned and the two chromatids to be separated during cell division.

α- and β-tubulin dimers bond to each other via non-covalent bonds to form a heterodimer called a protofilament. Thirteen protofilaments assemble laterally in the form of a hollow cylinder to form a MT with a diameter of 25 nm. MTs are unstable elements because they are highly dynamic. They constantly polymerize and depolymerize due to the GTPase activity of tubulin. The two ends of a protofilament polymerize at different rates. One end, known as the "plus" end, polymerizes rapidly and forms the base of the MT. In contrast, the "minus" ends depolymerize more rapidly.

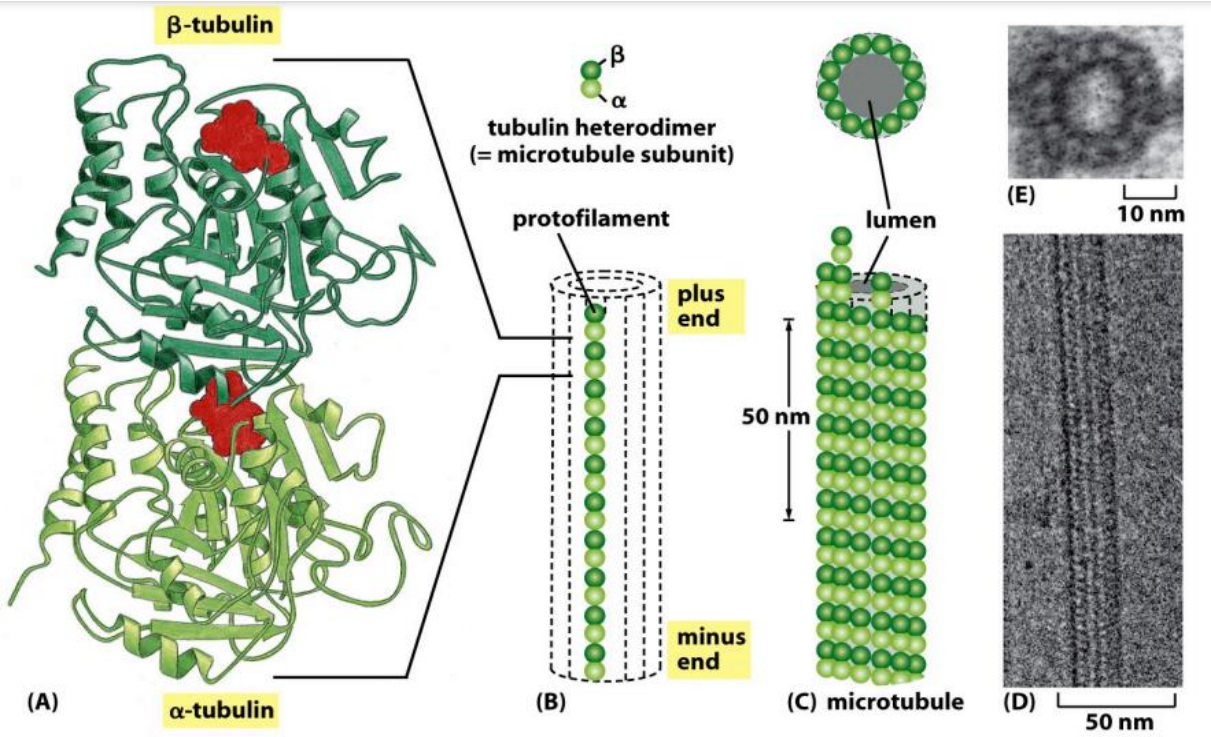

Figure III. 7. The structure of microtubule and its subunit **[25].**

(A) The subunit of each protofilament is a tubulin heterodimer formed from a pair of α- and β-tubulin monomers. The two GTP nucleotides are shown in red. (B) A tubulin subunit (α−β heterodimer) and a protofilament. (C) The microtubule is a hollow tube formed by a parallel alignment of 13 protofilaments. (D) Electron microscope view of a short segment of microtubule. (E) Cross-sectional view of a microtubule showing the ring formed by 13 distinct protofilaments.

I.2. Microtubule-associated proteins

MTs are associated with MAPs (Microtubule Associated Proteins), some of which play a role in stabilizing MTs, while others specialize in the movement of vesicles and organelles along MTs. These associated proteins are ATPases: kinesins enable transport from the negative pole to the positive pole of the microtubule (anterograde transport: from the center of the cell to the periphery), while dynein enables transport from the positive pole to the negative pole (retrograde transport: from the periphery to the cell center).

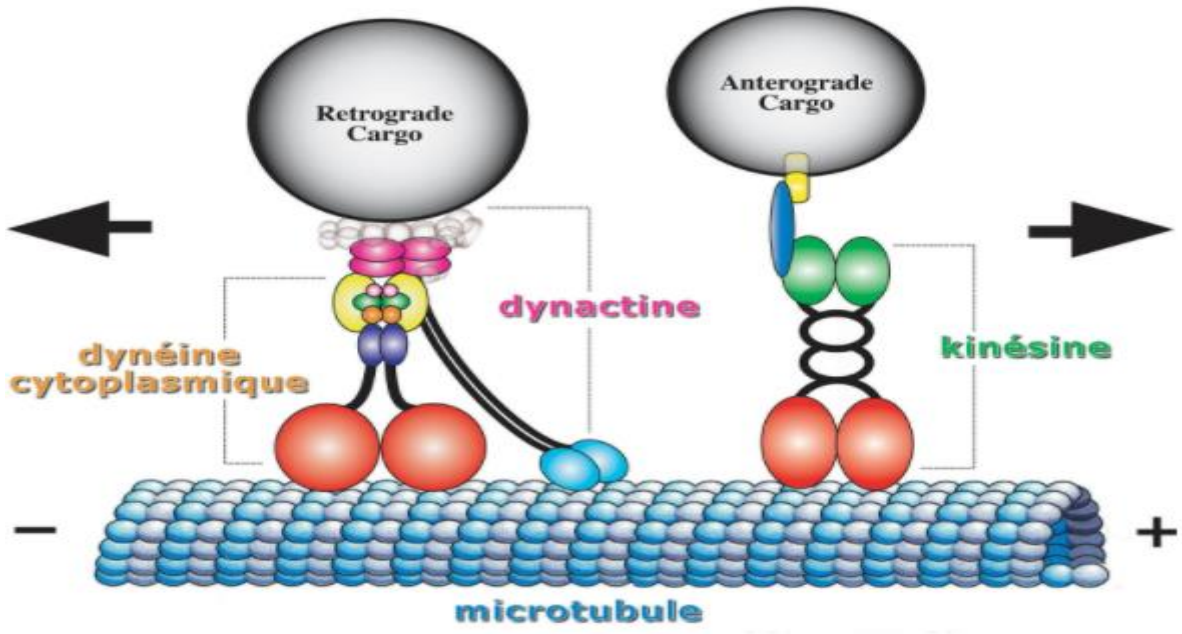

Figure III. 8. Movement of kinesin and dynein along a microtubule **[26].**

I.3. Roles of microtubules

Microtubules help maintain cell shape. They are also involved in motor phenomena:

- Movement of cells equipped with flagella;
- Transport of exocytosis, endocytosis, phagocytosis, and pinocytosis vesicles;
- Movement of intracellular organelles;
- Migration of chromosomes during mitosis.

II. Intermediate filaments

Intermediate filaments (IFs) were named for their size (8 to 12 nm), which is intermediate between that of actin filaments (5-9 nm) and microtubules (~25 nm). In eukaryotes, IFs constitute a family of proteins that are highly diverse in terms of their sequence and functions. IFs consist of three parts: the head at the amino-terminal end, a central coiled-coil region, and the carboxy-terminal tail. Both ends can vary in size and sequence. IFs are flexible but very resistant structures. They are formed by the assembly of filamentous protein monomers; the monomers assemble to form parallel dimers. The dimers then assemble into antiparallel tetramers. The tetramers assemble end-to-end with the C-terminal end facing the N-terminal end to form a protofilament. Eight protofilaments then assemble to form an intermediate filament 10 nm thick. Their main function is to form a scaffold that helps maintain

the shape and integrity of the cell, as well as anchor cellular organelles. It has also been suggested that they play a role in cell migration and signal induction.

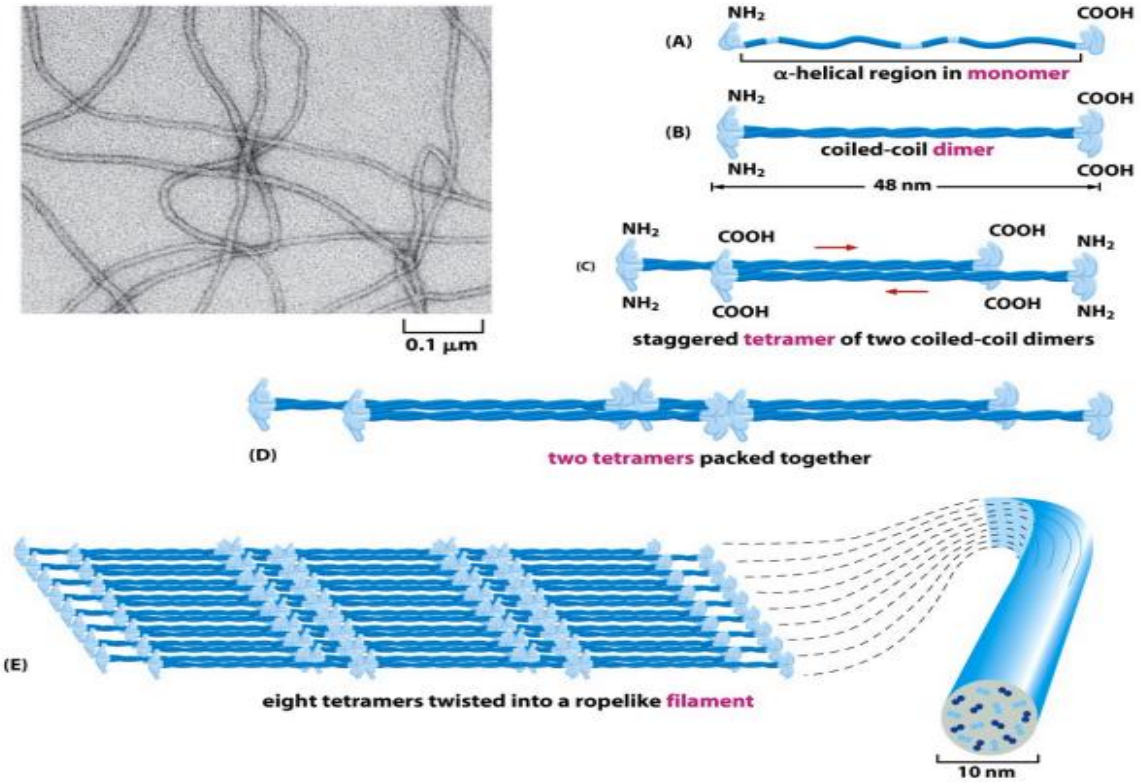

Figure III.9. A model for constructing an intermediate filament **[25].**

(A) Schematic representation of a monomer that pairs with another identical monomer to form a dimer (B) with an identical central domain aligned in parallel in a coiled-coil structure. (C) Two dimers align side by side and form an antiparallel tetramer consisting of four polypeptide chains. (D) Within each tetramer, the two dimers are offset from each other in order to establish associations with other tetramers. (E) The tetramers are packed together into a helix containing 16 dimers (32 coiled-coils). In total, this results in 10 nm rope-like filaments. Half of these dimers are oriented in one direction, while the other half point in the opposite direction.

The proteins that make up the IF belong to four main families :

- **Lamins:** forming the peripheral network of the cell nucleus.
- **Vimentin and related proteins: vimentin is characteristic of mesoblastic epithelial and non-epithelial cells (mesothelium and fibroblasts). Related proteins include:**

-Desmin: characteristic of muscle cells. It connects myofilaments to each other and to the plasma membrane.

-Glial fibrillary acidic proteins (GFAP): characteristic of astrocytes and Schwann cells.

- **Cytokeratins**: present in all epithelial cells.
- **Neurofilaments:** specific to neurons. They form the skeleton of axons and dendrites.

III. Actin filaments

The actin matrix is located just below the plasma membrane, where it forms a mesh associated with the membrane, and within the cell, where it forms a network that gives the cytosol a gelatinous appearance. Numerous proteins that interact with actin have been identified: they are involved in functions as diverse as filament consolidation (tropomyosin), filament bundle formation (fimbrin), filament fragmentation (gelsolin), the movement of vesicles on filaments (myosin II), and the anchoring of filaments to the plasma membrane (spectrin). All of these sets of actin-binding proteins can act cooperatively to generate cell surface movements, phagocytosis, and cell locomotion.

- **The cell cortex**

This is a network of actin microfilaments located under the plasma membrane, to which it is attached by numerous anchor points. This cortex is responsible for cell expansion and retraction movements and for cell movement on their substrate. It is also involved in plasma membrane movements during exocytosis and endocytosis and during pseudopod formation in macrophages.

- **Contractile apparatus**

Sarcomeres, which represent the units of muscle contraction. The sarcomere results from the highly organized assembly of actin, myosin, and associated proteins.

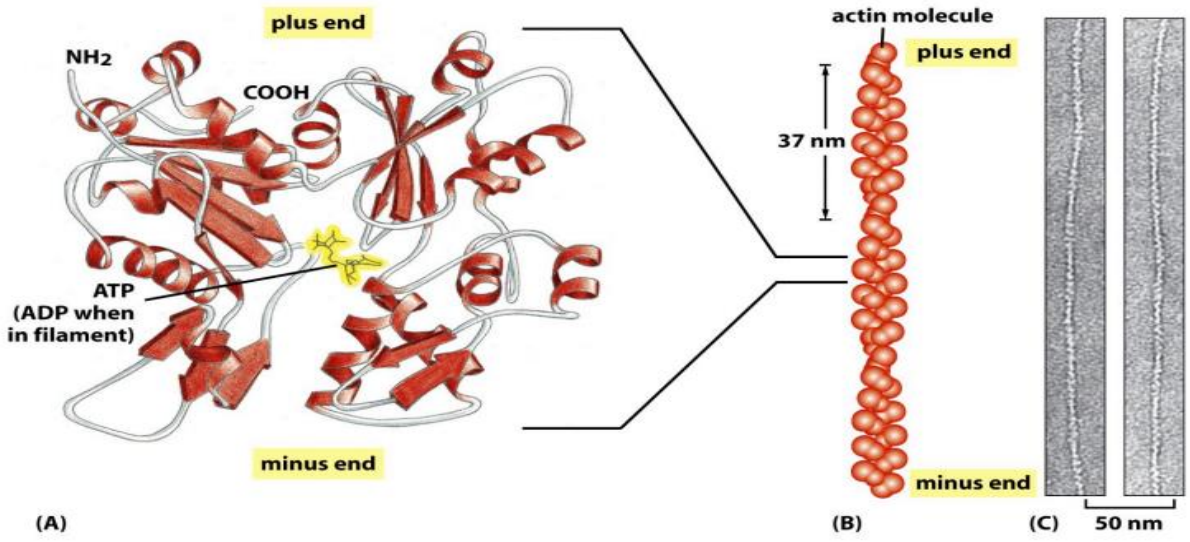

Figure III.10. The structures of an actin monomer and an actin filament **[25].**

(A) The actin monomer has a nucleotide bound in a deep pocket located at the center of the molecule. (B) Schematic representation of the arrangement of monomers in the filament. Two protofilaments held together by lateral contacts and winding around each other like two parallel strands of a helix. (C) Electron microscope image of actin filaments.