CYTOSKELETON

1. Cytoskeleton is a collective structure that helps cells maintain their shape and internal organization, and it also provides mechanical support that enables cells to carry out essential functions like division and movement.
2. No single sub-cellular component forms a cytoskeleton rather, several different components work together to form the cytoskeleton.
3. The cytoskeleton of eukaryotic cells is made of filamentous proteins, and it provides mechanical support to the cell and its cytoplasmic constituents.
4. All cytoskeletons consist of ***3 major classes of elements that differ in size and in protein composition.***

   A. MICROTUBULES

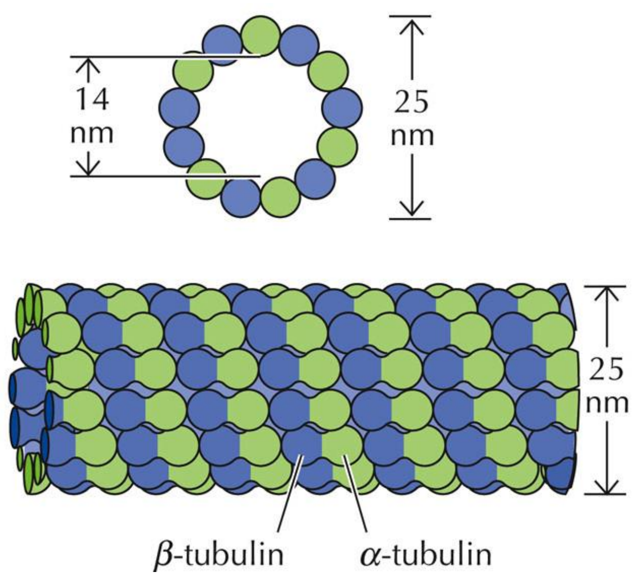
   B. ACTIN FILAMENTS

   C. INTERMEDIATE FILAMENTS

MICROTUBULES

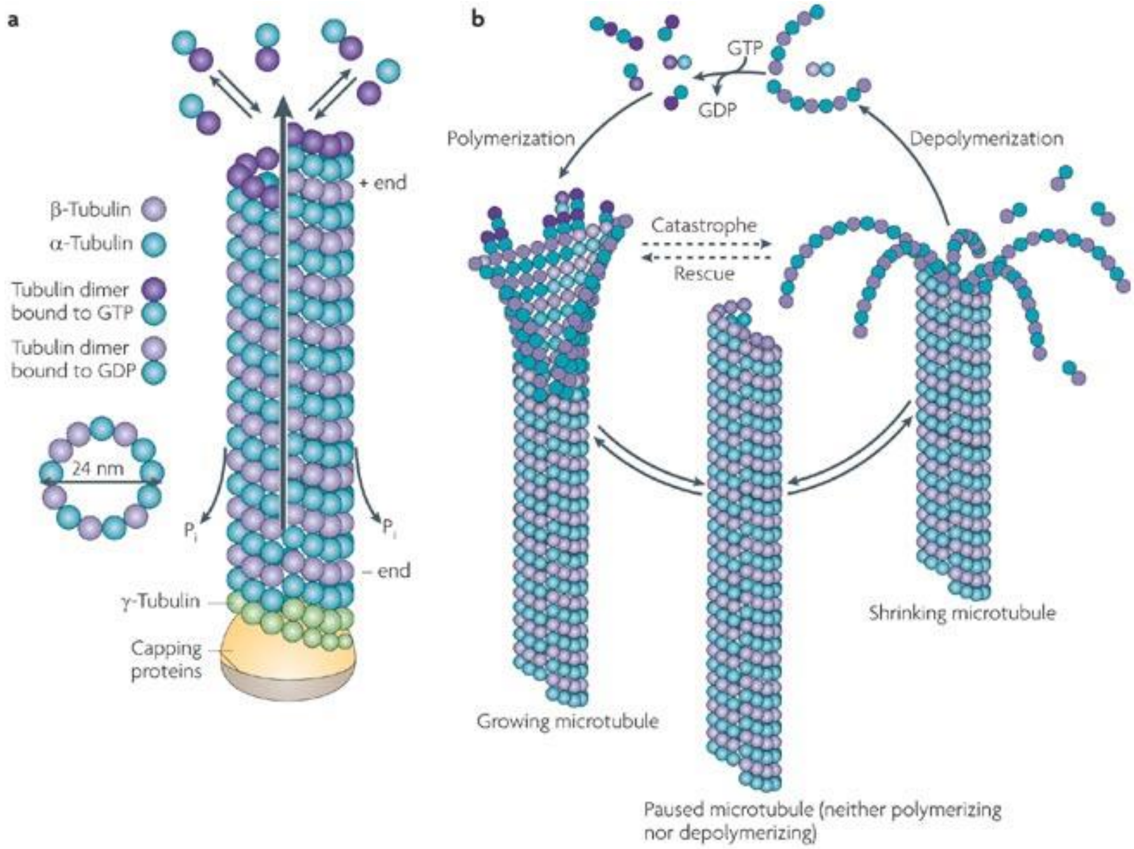
a. Microtubules are the largest type of filament, with a diameter of about 25 nanometers (nm), and they are composed of a protein called tubulin.

b. Tubulin contains two polypeptide subunits, and dimers of these subunits string together to make long strands called **protofilaments**. Thirteen protofilaments then come together to form the hollow, straw-shaped filaments of microtubules.



c. Microtubules are ever-changing, with reactions constantly adding and subtracting tubulin dimers at both ends of the filament. The rates of change at either end are not balanced — one end grows more rapidly and is called the **plus end**, whereas the other end is known as the **minus end**. In cells, the minus ends of microtubules are anchored in structures called **microtubule organizing centers** (MTOCs).

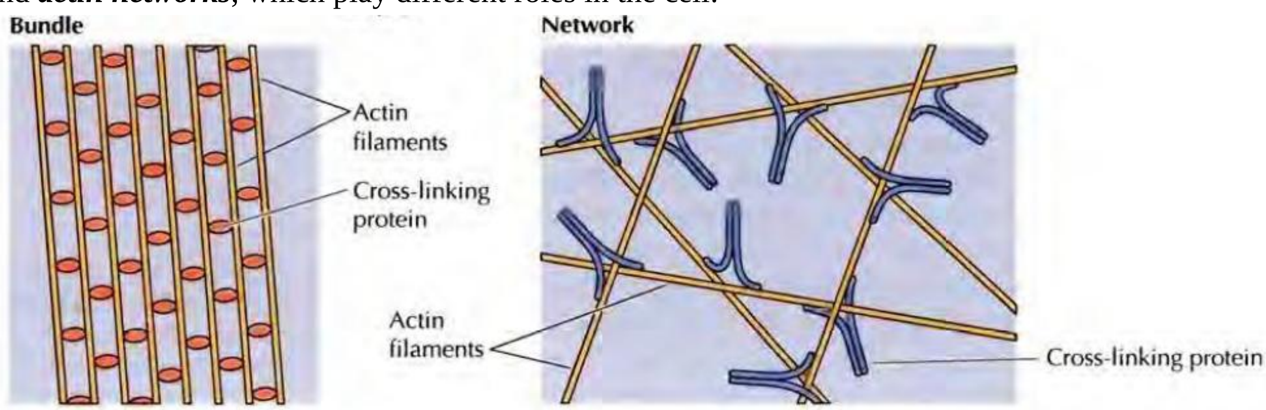
d. The primary MTOC in a cell is called the **Centrosome**, and it is usually located adjacent to the nucleus. Microtubules tend to grow out from the Centrosome to the plasma membrane. In non-dividing cells, microtubule networks radiate out from the Centrosome to provide the basic organization of the cytoplasm, including the positioning of organelles.



ACTIN FILAMENTS

a. Actin filaments are most abundant in all eukaryotic cells, smallest type, with a diameter of only about 6 nm and are polymer of G-**actin**.

b. Individual actin filaments are assembled into two general types of structures called ***actin bundles*** and ***actin networks***, which play different roles in the cell.



c. It was first discovered in skeletal muscle, where actin filaments slide along filaments of another protein called **myosin** to make the cells contract. In non-muscle cells, actin filaments are less organized and myosin is much less prominent.

d. Actin filaments are made up of identical actin proteins arranged in a long spiral chain. Like microtubules, actin filaments have plus and minus ends, Actin filaments are highly concentrated at the periphery of the cell where they form a three-dimensional network beneath the plasma membrane.

e. This network of actin filaments and associated **actin-binding proteins (ABP)** determines cell shape and is involved in a variety of cell surface activities, including movement. The association of the actin cytoskeleton with the plasma membrane is thus central to cell structure and function.

WHY RBC IS USEFUL FOR CYTOSKELETON STUDY?

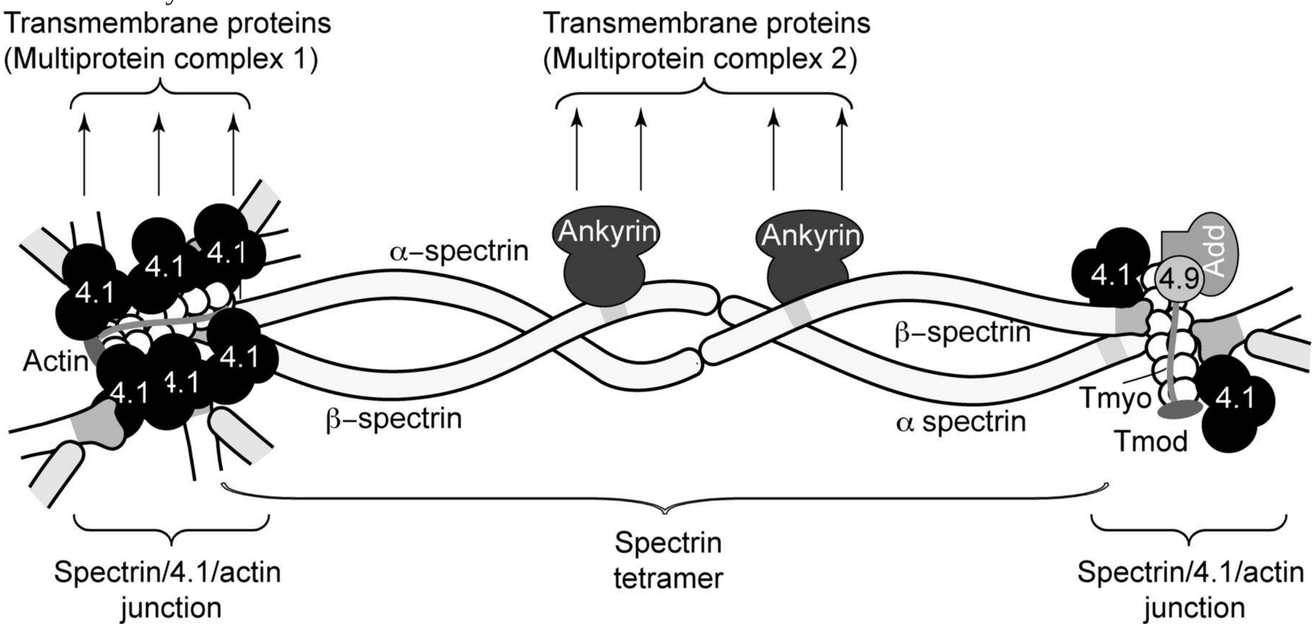
Red blood cells or erythrocytes have proven particularly useful for studies of both the plasma membrane and the cortical cytoskeleton. The principal advantage of red blood cells for these studies is that they contain no nucleus or internal organelles, so their plasma membrane and associated proteins can be easily isolated without contamination by the various internal membranes that are abundant in other cell types. In addition, human erythrocytes lack other cytoskeletal components (microtubules and intermediate filaments), so the cortical actin cytoskeleton is the principal determinant of their distinctive shape as biconcave discs.

SPECTRIN

The major protein that provides the structural basis for the cortical cytoskeleton in erythrocytes is the actin-binding protein **SPECTRIN**. Spectrin is a member of the large calponin family of actin-binding proteins, which includes a-actinin, filamin, and fimbrin.

Erythrocyte spectrin is a tetramer consisting of two distinct polypeptide chains called α and β, with molecular weights of 240 and 220 kd, respectively. The β chain has a single actin-binding domain at its amino terminus.

The α and β chains associate laterally to form dimers, which then join head-to-head to form tetramers with two actin-binding domains separated by approximately 200 run. The ends of the spectrin tetramers then associate with short actin filaments, resulting in the spectrin-actin network that forms the cortical cytoskeleton of red blood cells.



ANKYRIN, BAND 3, PROTEIN 4.1, FILAMIN, DYSTROPHIN

The major link between the spectrin-actin network and the plasma membrane is provided by a protein called **ANKYRIN**, which binds both to spectrin and to the cytoplasmic domain of an abundant transmembrane protein called **BAND 3**.

An additional link between the spectrin-actin network and the plasma membrane is provided by **PROTEIN 4.1**, which binds to spectrin-actin junctions as well as recognizing the cytoplasmic domain of glycophorin (another abundant transmembrane protein).
For example, a family of proteins related to protein 4.1 link actin filaments to the plasma membranes of many different kinds of cells, and another member of the calponin family - **FILAMIN and DYSTROPHIN**.

INTERMEDIATE FILAMENTS

a. Intermediate filaments come in several types, but they are generally strong and ropelike. Their functions are primarily mechanical and, as a class, intermediate filaments are less dynamic than actin filaments or microtubules. Intermediate filaments commonly work in tandem with microtubules, providing strength and support for the fragile tubulin structures. All cells have intermediate filaments, but the protein subunits of these structures vary.
b. Some cells have multiple types of intermediate filaments, and some intermediate filaments are associated with specific cell types. For example, neurofilaments are found specifically in neurons (most prominently in the long axons of these cells), ***desmin filaments*** are found specifically in muscle cells, and keratins are found specifically in epithelial cells. Other intermediate filaments are distributed more widely.
c. For example, ***vimentin filaments*** are found in a broad range of cell types and frequently colocalize with microtubules.
d. Similarly, ***lamins*** are found in all cell types, where they form a meshwork that reinforces the inside of the nuclear membrane.