Cytoskeleton, Motility

Cytoskeleton:

- It helps to maintain the shape and internal organization of a cell
- It also provides mechanical support to divisions and movements.
- Motor proteins can associate to cytoskeletal filaments and drive organelle trnasport and movements
- All type is made of protein filaments.

3 different components work together to form the cytoskeleton

Microfilaments:

smallest type (diameter: 7-9 nm), they are composed of actin, one of the most abundant protein of the cells

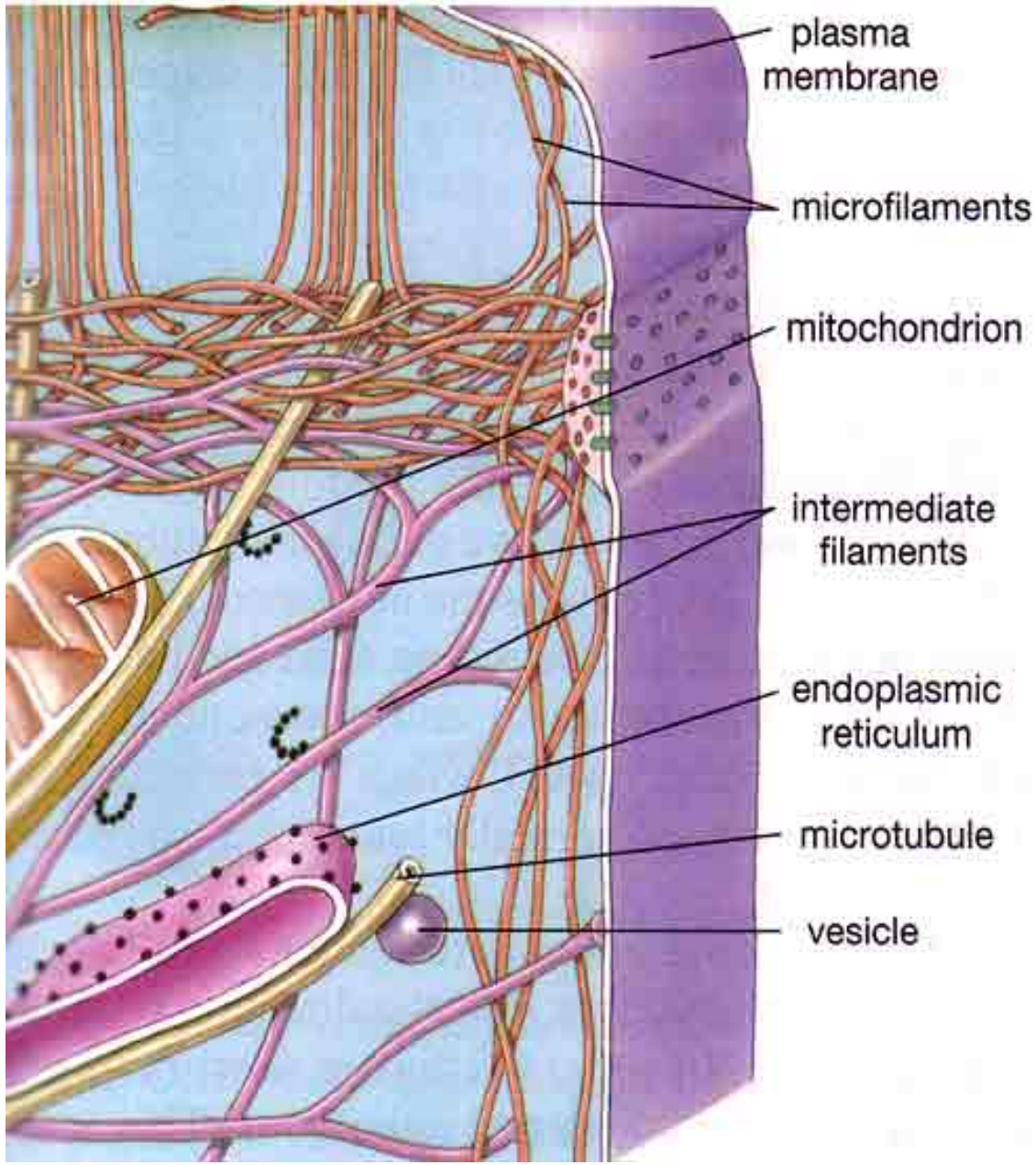
Intermedier filaments:

mid-sized (diameter 10 nm) they are constructed from a number of different subunit proteins, their chemical nature is cell specific

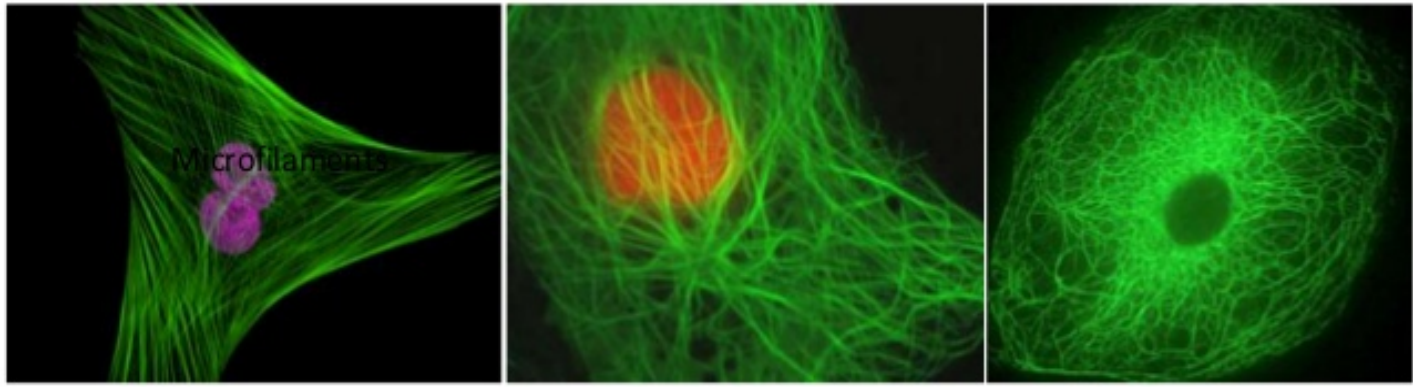
Mikrotubules:

largest type (diameter 25 nm), they are composed of tubulin

Elements of the cytoskeleton:



Three major cytoskeleton components



Microfilaments
(Actin)

Microtubule
(Tubulin)

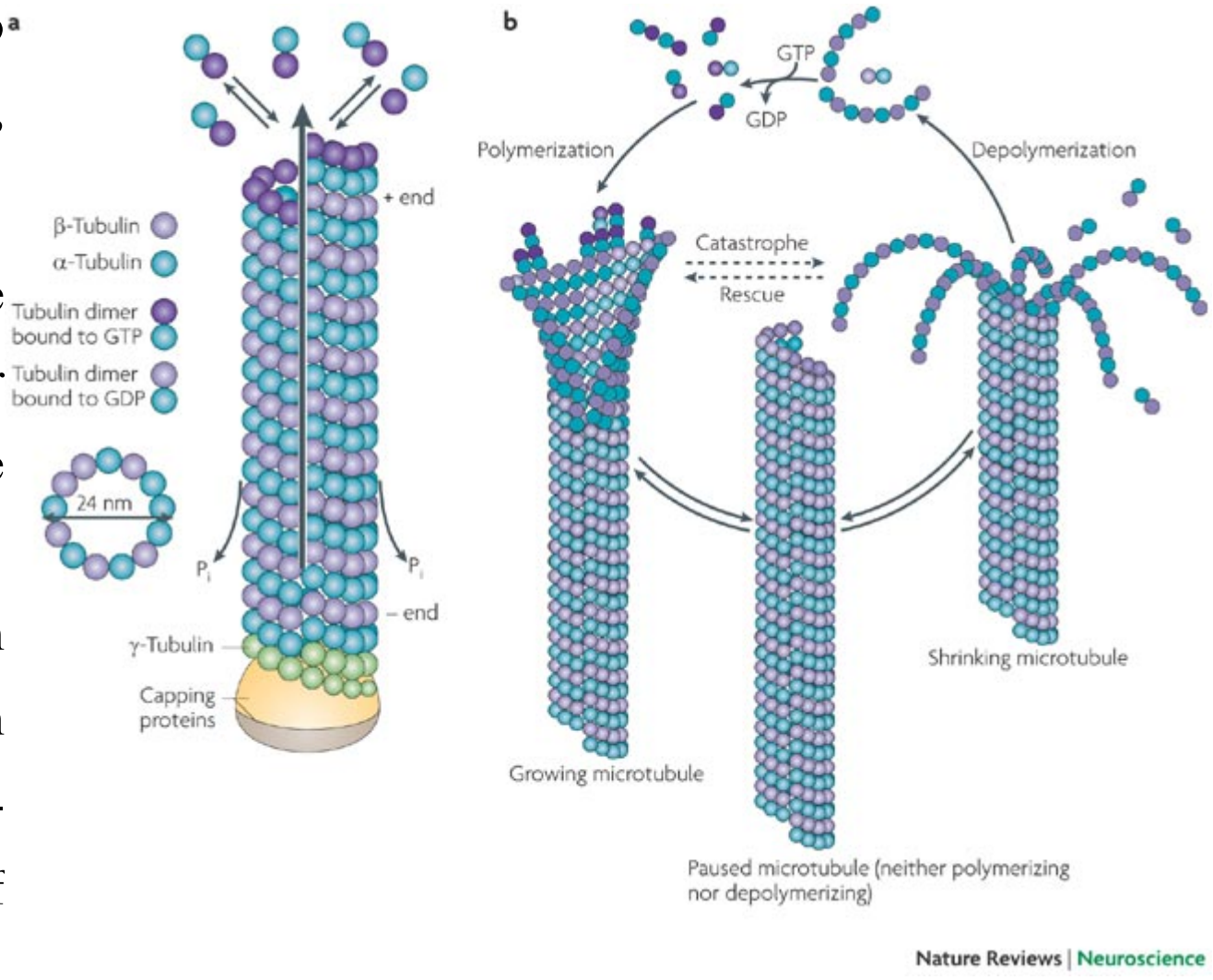
Intermediate filaments
(Keratin, vimentin..)

Microtubules

Tubulin contains two polypeptide subunits, (α and β tubulin)

Dimers of these tubulins string together to make the protofilaments.

13 protofilaments then come together to form the hollow, straw-shaped filaments of microtubules.



Microtubules reorganization:

Microtubules are ever-changing, with reactions constantly adding and subtracting tubulin dimers at both ends.

The rates of change at either end are not balanced:

the plus end grows more rapidly than the other end, the minus end.

The minus ends of microtubules are anchored in microtubule organizing centers (MTOCs).

The primary MTOC is the centrosome, located adjacent to the nucleus.

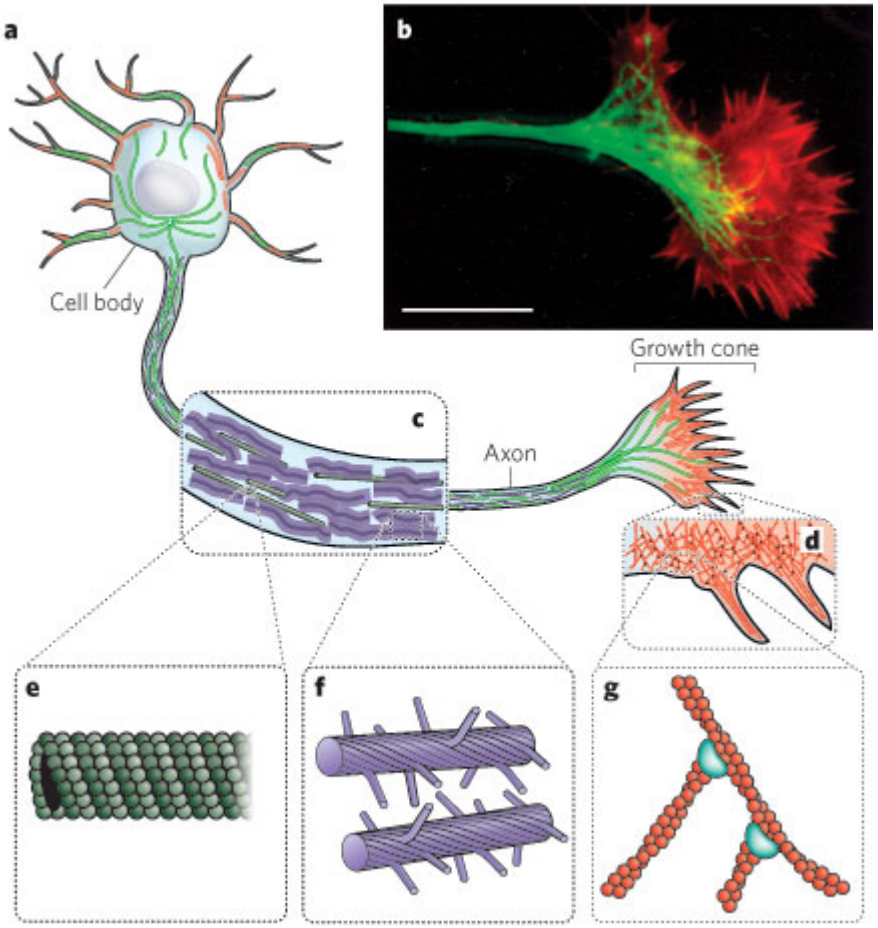
In nondividing cells, microtubule networks radiate out from the centrosome to provide the basic organization of the cytoplasm, including the positioning of organelles.

Actin Filaments

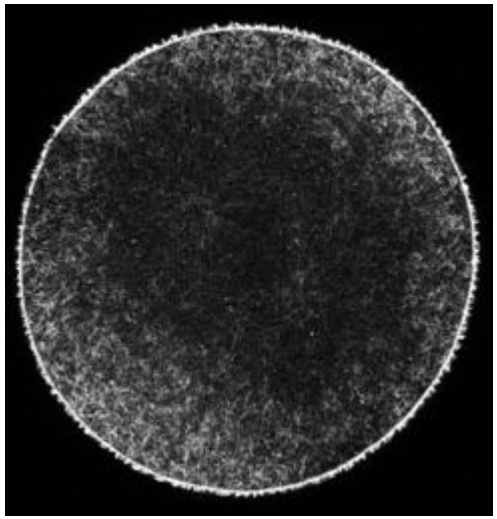
Actin filaments are made up of identical actin proteins arranged in a long spiral chain.

Actin filaments also have plus and minus ends, with more ATP-powered growth occurring at a filament's plus end.

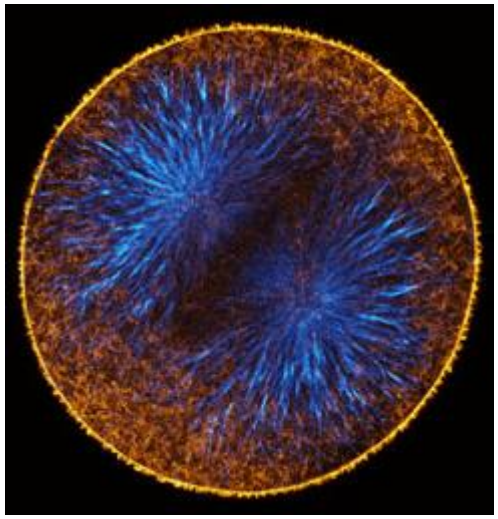
Networks of actin filaments are found beneath the cell cortex, which is the meshwork of membrane-associated proteins that supports and strengthens the plasma membrane.



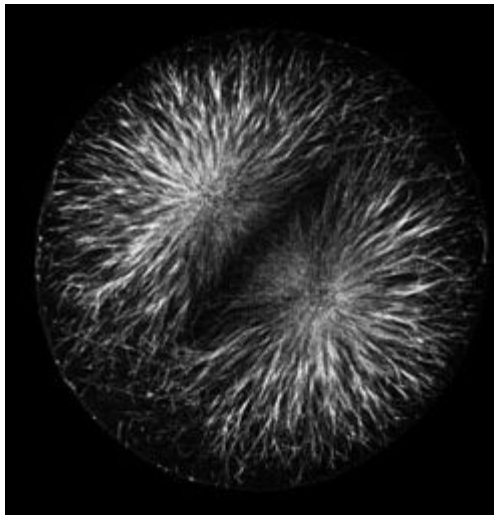
Actin filaments are also involved in cytokinesis and cell movement.



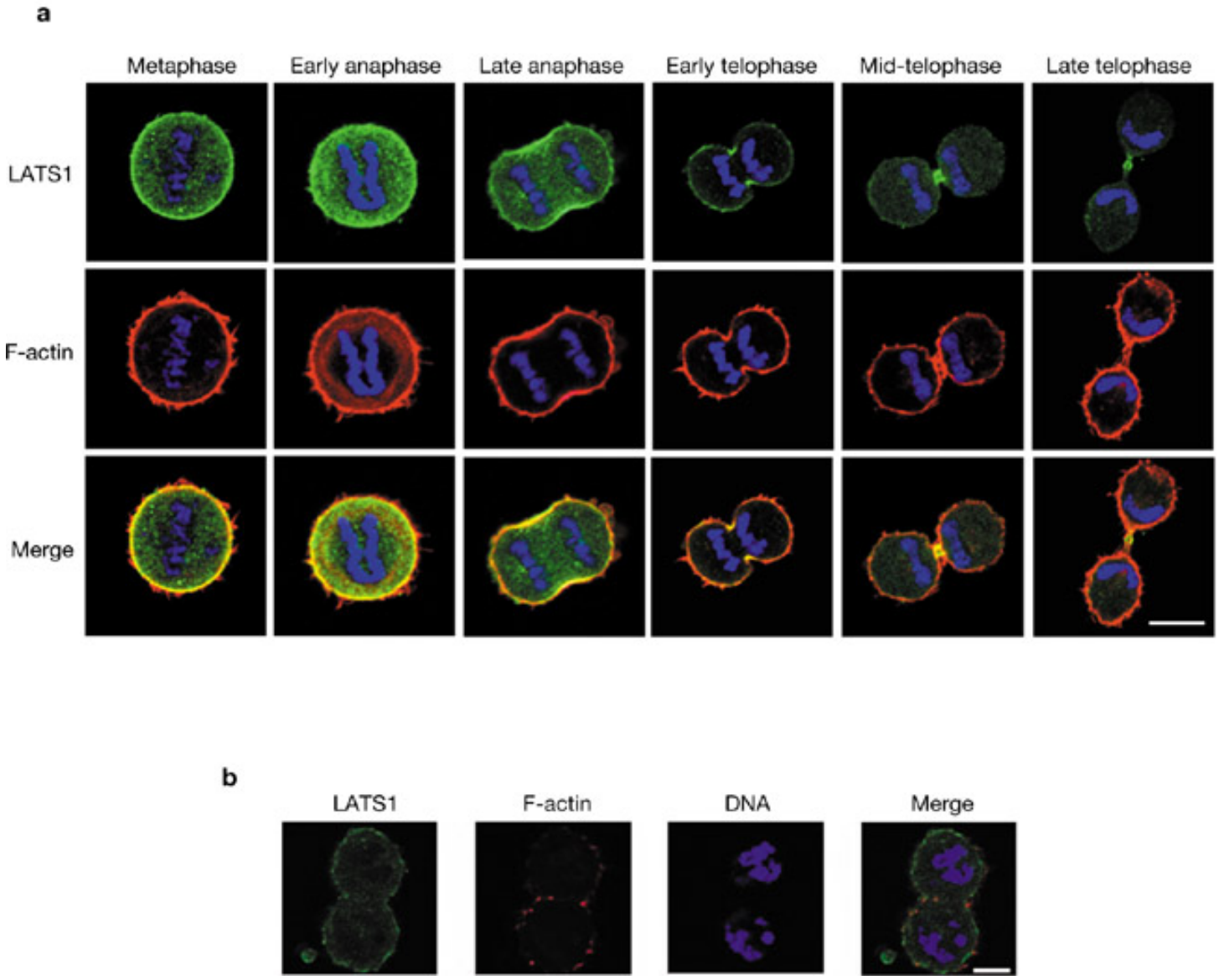
Actin



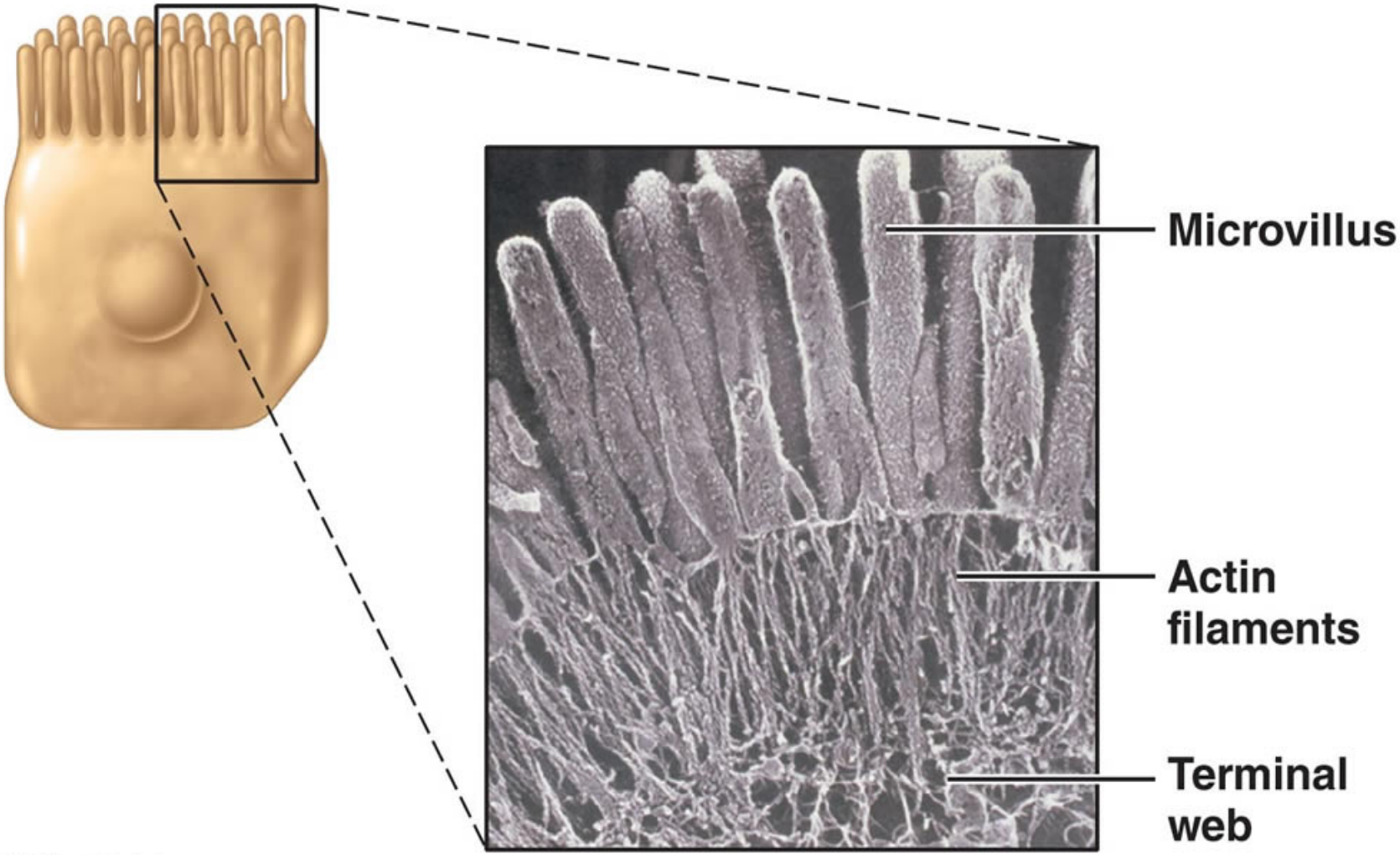
Actin+microtubules



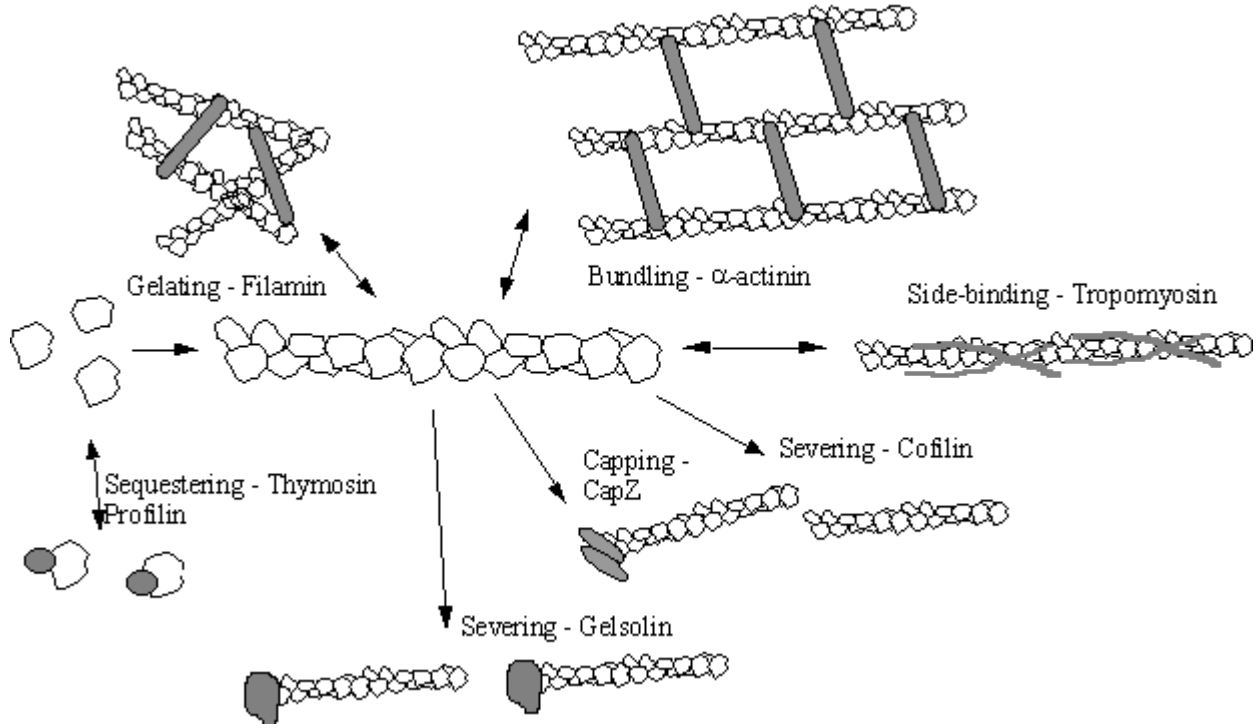
Microtubules


a
Metaphase
Early anaphase
Late anaphase
Early telophase
Mid-telophase
Late telophase
LATS1
F-actin
Merge
b
LATS1
F-actin
DNA
Merge

Actin networks allow cells to hold — and move — specialised shapes, such as the brush border of microvilli.



Actin binding proteins:



About 48 different types, many have complex function.

Main types are the bundling and cross linking ABPs:

Bundling proteins hold actin filaments prallel (microvilli)

cross linking proteins produce a gel-like meshwork (cell cortex)

Intermedier filaments

Intermediate filaments come in several types, but they are generally strong and ropelike.

Their functions are primarily mechanical, provide mechanical and stress-coping resilience to cells,

They also contribute to subcellular and tissue-specific biological functions,

They are less dynamic than actin filaments or microtubules.

Some cells have multiple types of intermediate filaments, and some intermediate filaments are associated with specific cell types.

Intermediate filaments are not polar in the way that actin or tubulin are.

Neurofilaments: neurons

desmin filaments: muscle cells

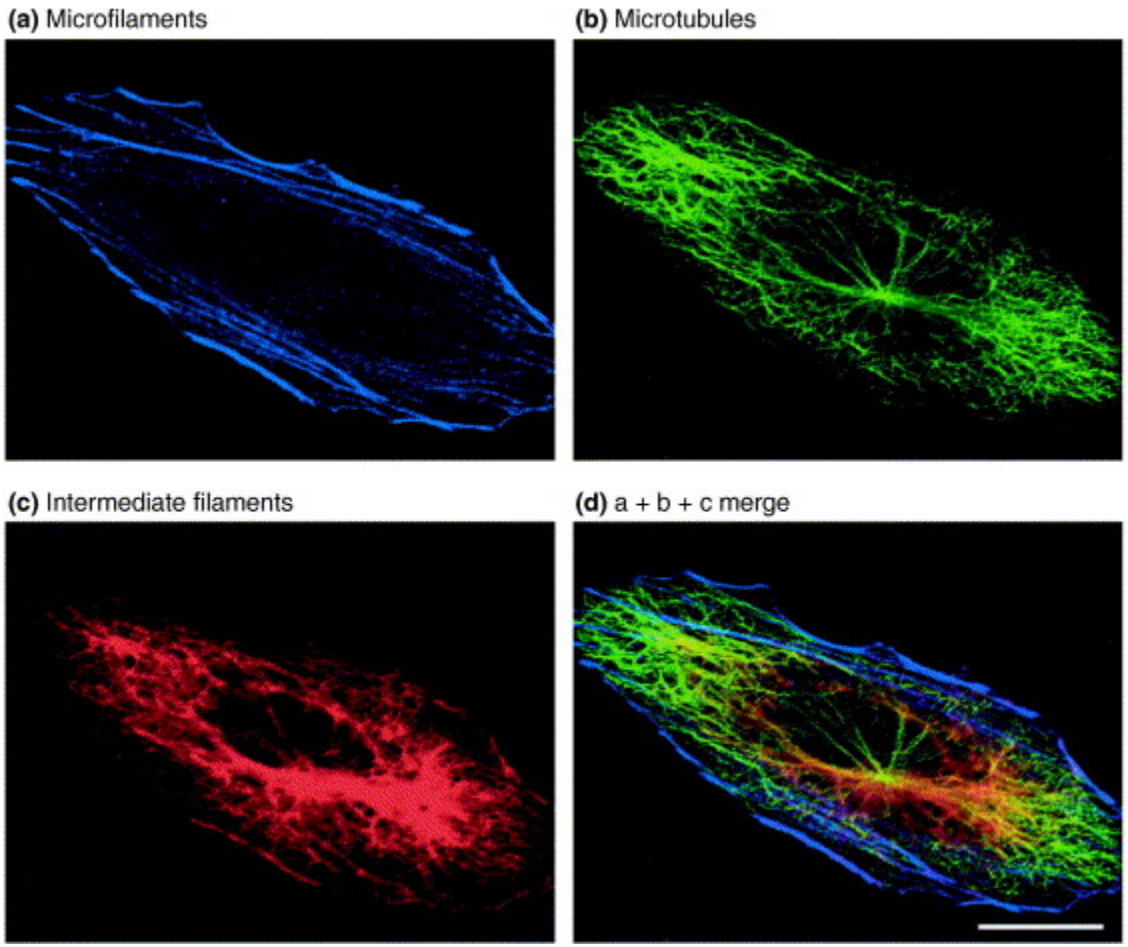
keratins: epiuthelial cells

Laminin: nucleuar membrane of every cell

Vimentin: several mesenchymal cell types

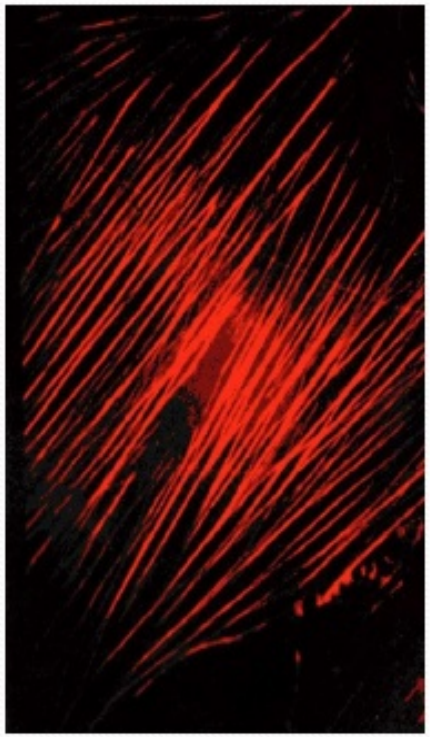
Astrocytes: GFAP

Hepatocytes: keratins

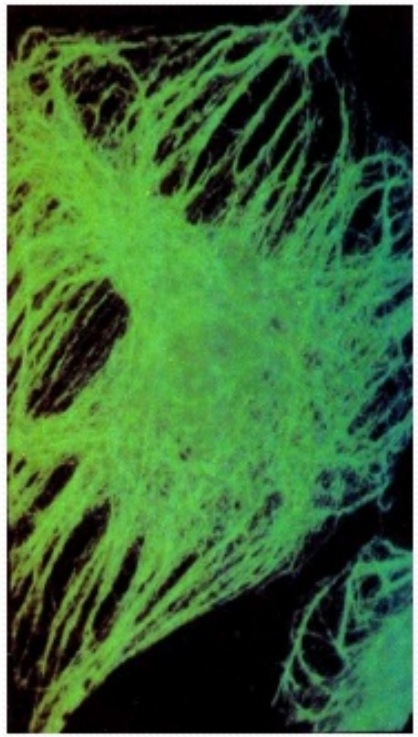


Huh7 cultured human hepatocytes

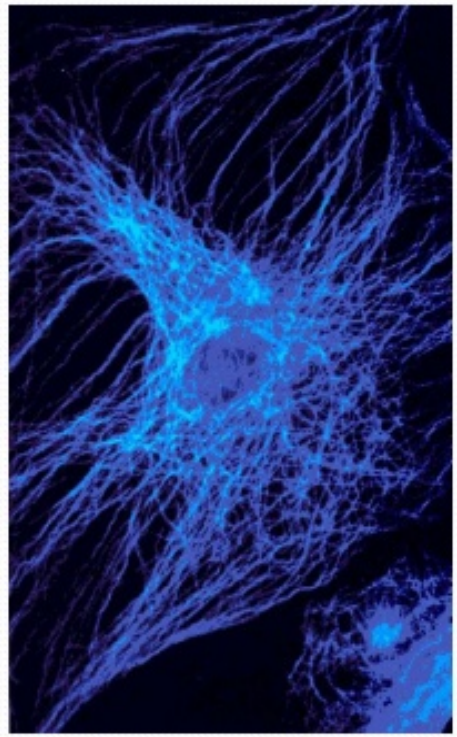
Distribution of different cytoskeletal elements in the same cell



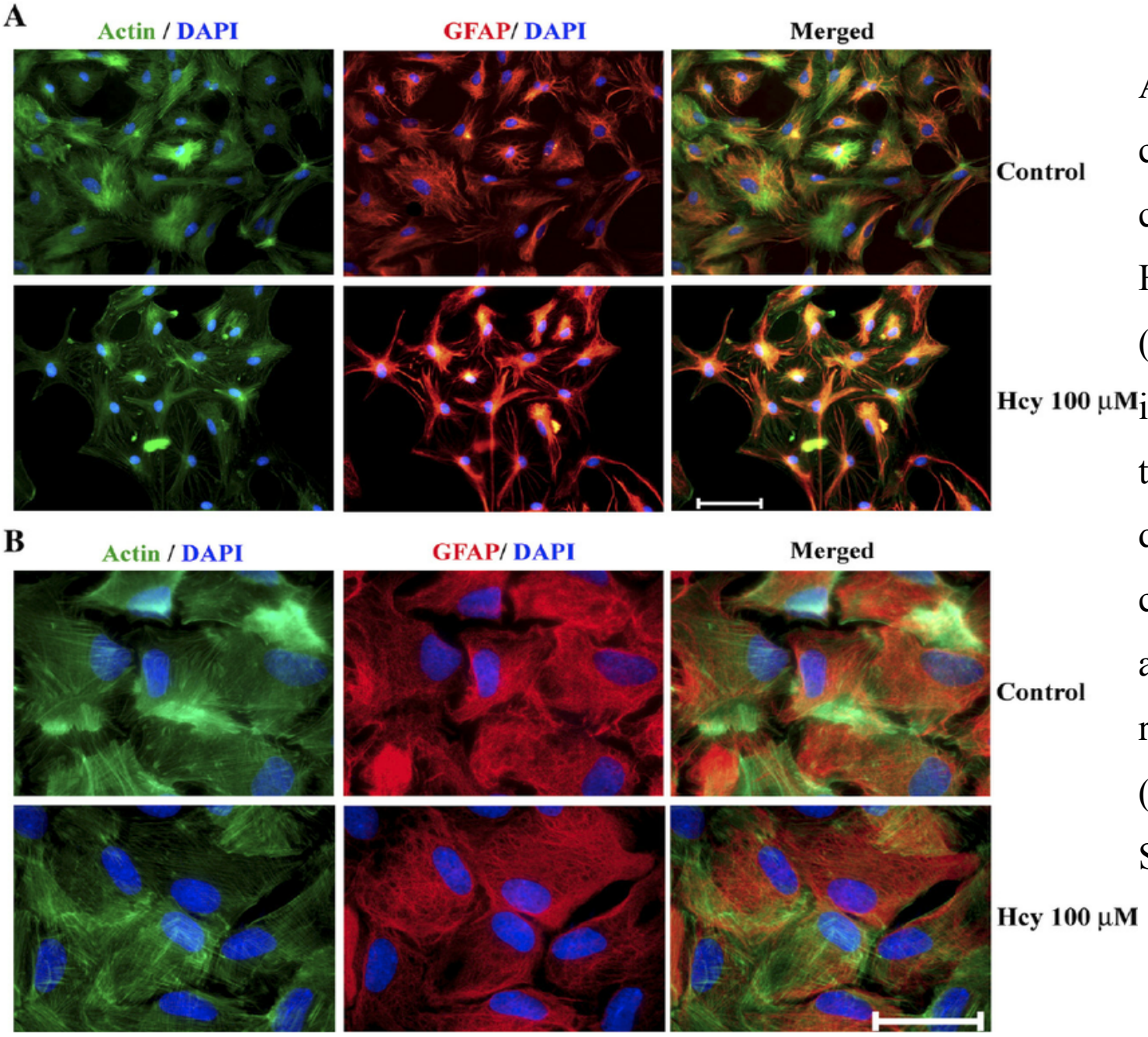
actin filaments (F-actin)
(rhodoamin-phaloidin)



intermediate filaments (IF)
(anti-vimentin)



microtubules MT)
(anti-tubulin)



Actin and GFAP co-staining of cortical astrocytes Hcy:

(A) Representative images of Hcy treated cells. GFAP disruption concomitant with actin reorganization

(B) Recovery

Scale bar = 50 µm.

Homocystinuria, in inborn errors of metabolism. Homocysteine (Hcy) levels are normally kept low by remethylation to methionine in a reaction that requires folate and vitamin B12. In addition, Hcy can be converted to cystathionine by the activity of the enzyme cystathionine beta-synthase, a vitamin B6-dependent enzyme, to form cysteine. Patients with severe hyperhomocysteinemia exhibit a wide range of clinical manifestations including neurological abnormalities such as mental retardation, cerebral atrophy, and seizures. Hcy can induce neuronal apoptosis, and Hcy, at a concentration found in hyperhomocysteinemia, acted on the endogenous IF- associated phosphorylating system.

How Do Cells Move?

Cytoskeletal filaments provide the basis for cell movement.

For instance, cilia and flagella move as a result of microtubules sliding along each other.

Other cell movements, such as the pinching off of the cell membrane in the final step of cell division are produced by the contractile capacity of actin filament networks.

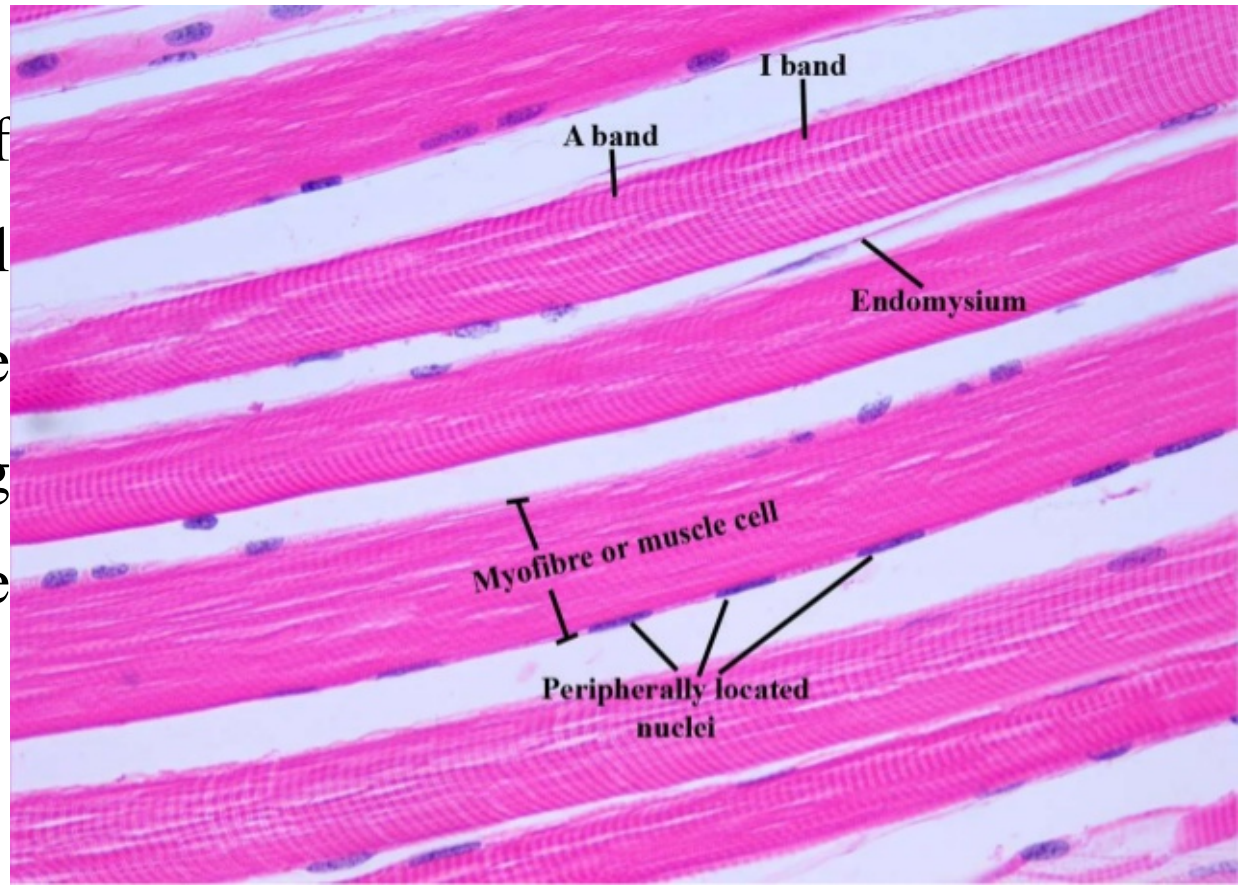
Actin filaments are extremely dynamic and can rapidly form and disassemble. This dynamic action underlies the crawling behavior of cells such as amoebae.

Muscle:

Muscle is a specialized contractile tissue that is a distinguishing characteristic of animals.

Changes in muscle length support an exquisite array of animal movements.

The process of contraction has several key steps, which have been conserved during evolution across the majority of animals



Muscle cell basic units are sarcomeres.

There can be thousands of highly stereotyped sarcomeres within a single muscle cell.

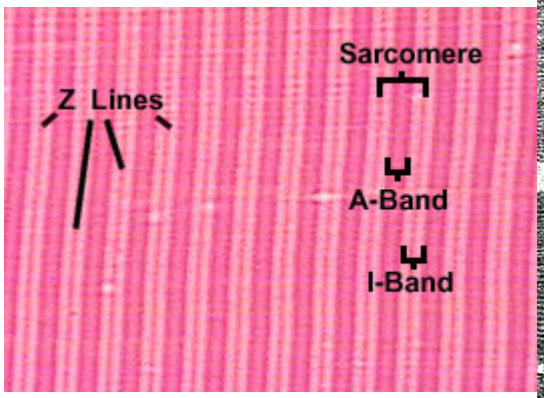
An individual sarcomere contains many parallel actin (thin) and myosin (thick) filaments.

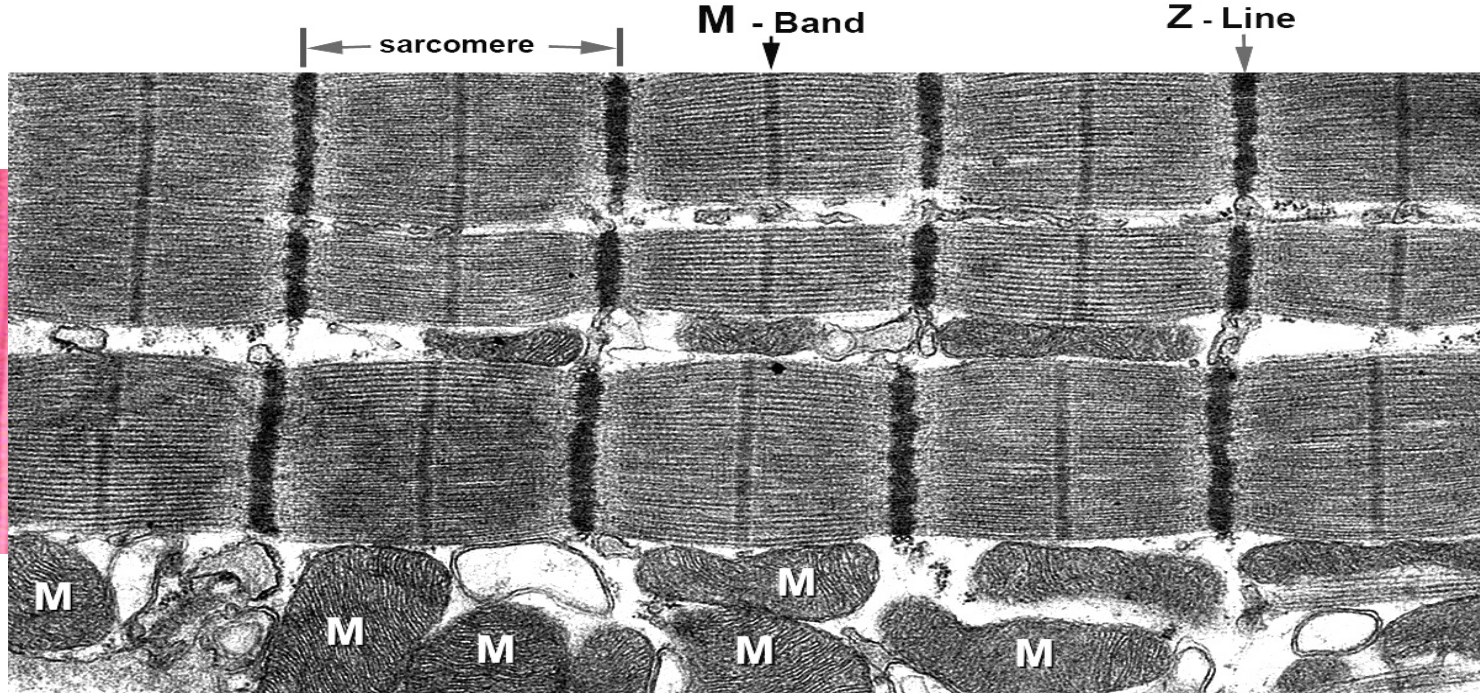
The proteins within them can change in length, which causes the overall length of a muscle to change. The interaction of myosin and actin proteins is at the core of our current understanding of sarcomere shortening.

How does this shortening happen? It has something to do with a sliding interaction between actin and myosin.

In 1954, scientists published the molecular basis of muscle contraction. They described the position of myosin and actin filaments at various stages of contraction in muscle fibers.

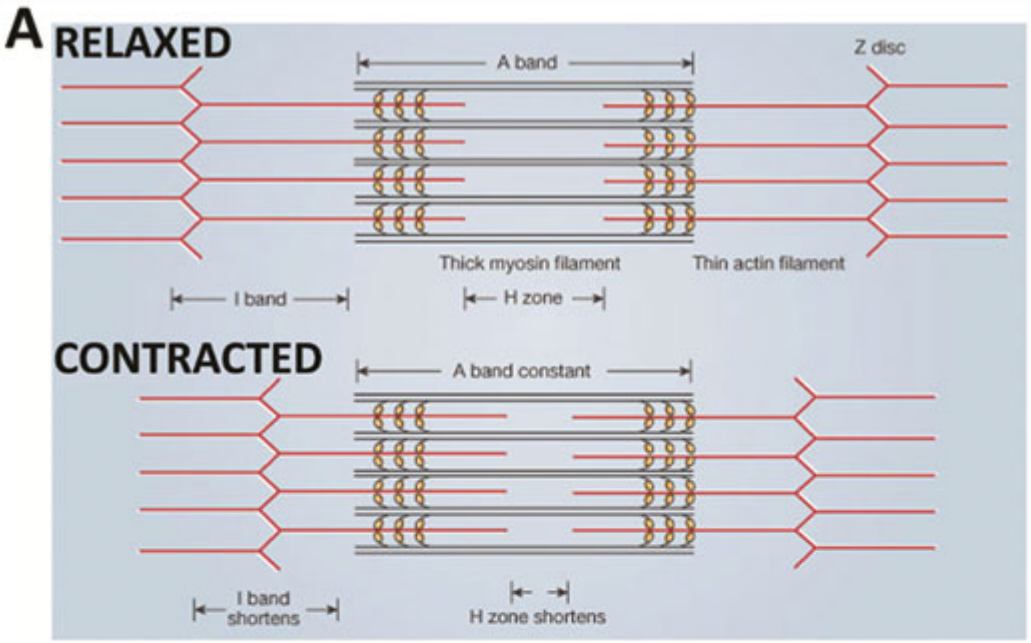
They observed that the "A band," of the sarcomere cointaining the myosin (thick filament) remained relatively constant in length during contraction. The "I band," rich in actin (thinner filaments), changed its length along with the sarcomere. These observations led them to propose the sliding filament theory, which states that the sliding of actin past myosin generates muscle tension.

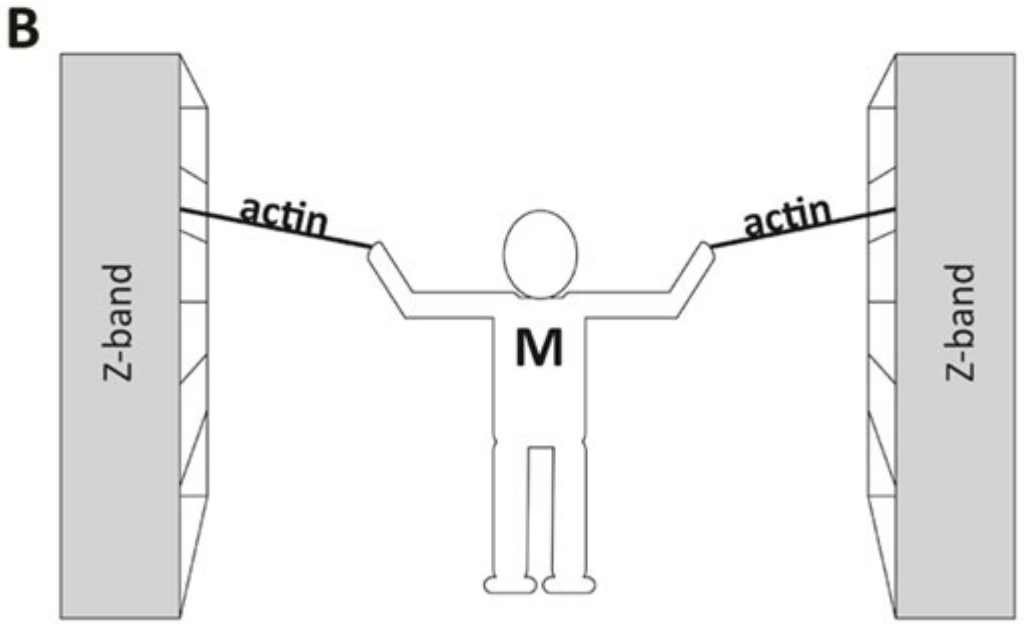




(A) The basic organization of a sarcomere subregion, showing the centralized location of myosin (A band). Actin and the z discs are shown in red.

(B) A conceptual diagram representing the connectivity of molecules within a sarcomere. A person standing between two bookcases (z bands) pulls them in via ropes (actin). Myosin (M) is analogous to the person and the pulling arms. (z bands are also called z discs.)

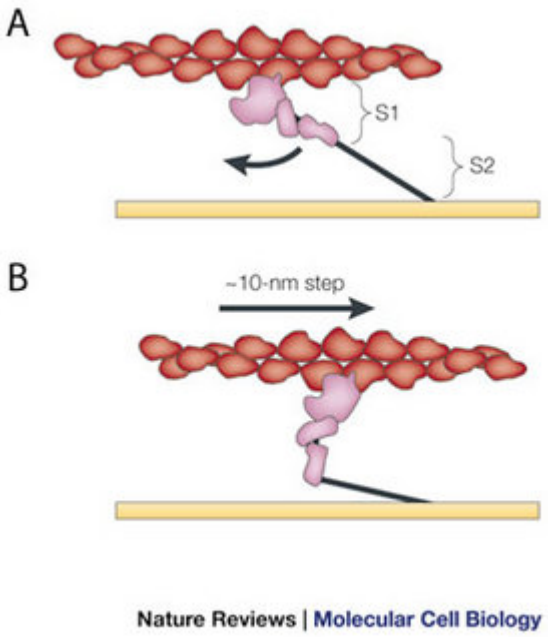




The movements of myosin appear to be a kind of molecular dance.

The myosin reaches forward, binds to actin, contracts, releases actin, and then reaches forward again to bind actin in a new cycle.

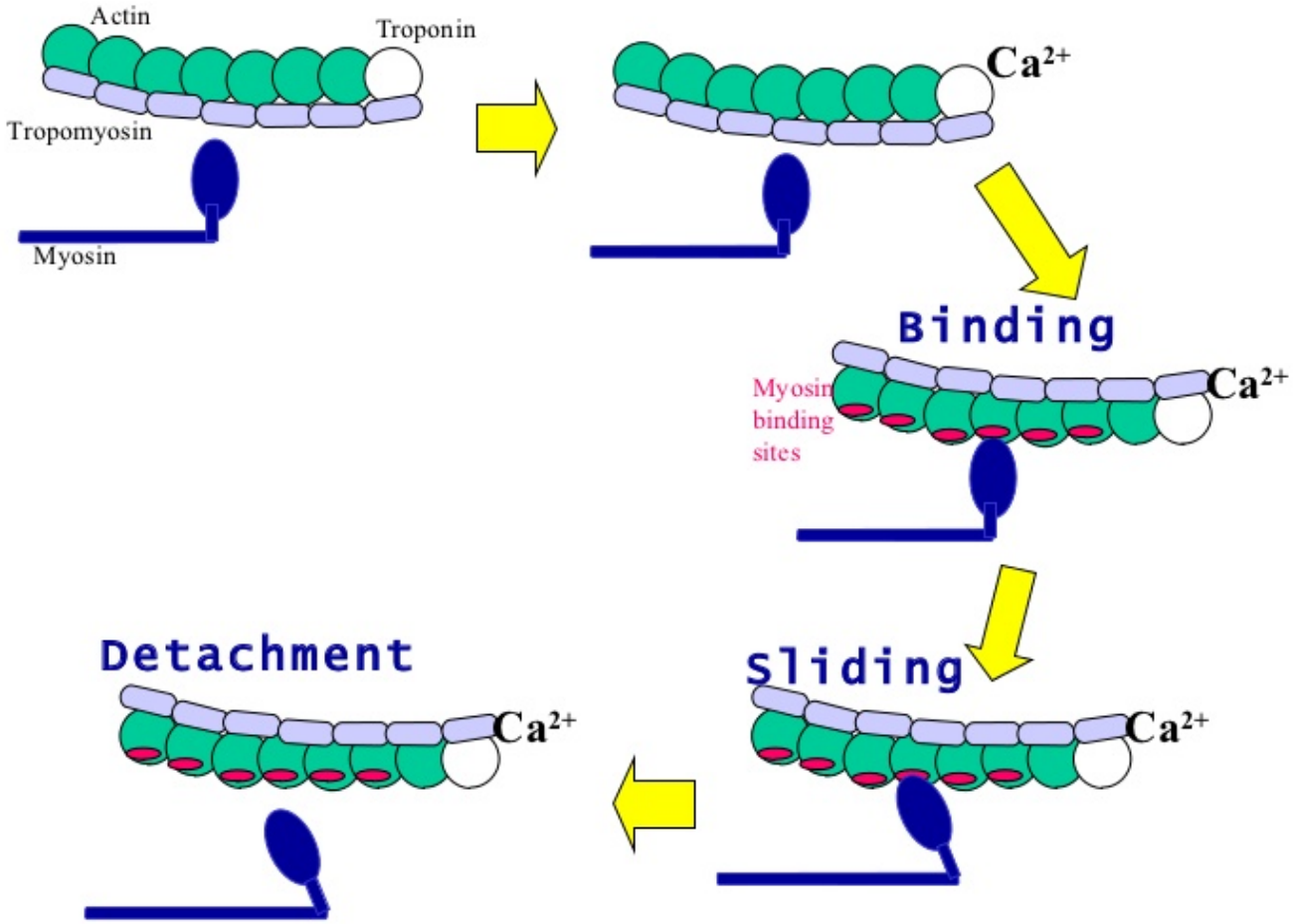
This process is known as myosin-actin cycling.



Actin (red) interacts with myosin, shown in globular form (pink) and a filament form (black line). The model shown is that of H. E. Huxley, modified to indicate bending (curved arrow) near the middle of the elongated cross bridge (subfragment 1, or S1) which provides the working stroke. This bending propels actin to the right approximately 10 nanometers (10 nm step). S2 tethers globular myosin to the thick filament (horizontal yellow line), which stays in place while the actin filament moves.

Modified from Spudich (2001).

llustration of the cycle of changes in myosin shape during cross-bridge cycling



Calcium and ATP are cofactors required for the contraction of muscle cells.

ATP supplies the energy, calcium is required by troponin and tropomyosin, two proteins that regulate muscle contraction by blocking the binding of myosin to actin.

In a resting sarcomere, tropomyosin blocks the binding of myosin to actin. For myosin to bind actin, tropomyosin must rotate around the actin filaments to expose the myosin-binding sites. The presence of Ca^{2+} is essential for the contraction. Troponin shifts the position of tropomyosin and moves it away from the myosin-binding sites on actin, effectively unblocking the binding site. Once the myosin-binding sites are exposed, and if sufficient ATP is present, myosin binds to actin to begin cross-bridge cycling. Then the sarcomere shortens and the muscle contracts. In the absence of calcium, this binding does not occur.

By studying sarcomeres, the basic unit controlling changes in muscle length, scientists proposed the sliding filament theory to explain the molecular mechanisms behind muscle contraction. Within the sarcomere, myosin slides along actin to contract the muscle fiber in a process that requires ATP. Scientists have also identified many of the molecules involved in regulating muscle contractions and motor behaviors, including calcium, troponin, and tropomyosin. This research helped us learn how muscles can change their shapes to produce movements.