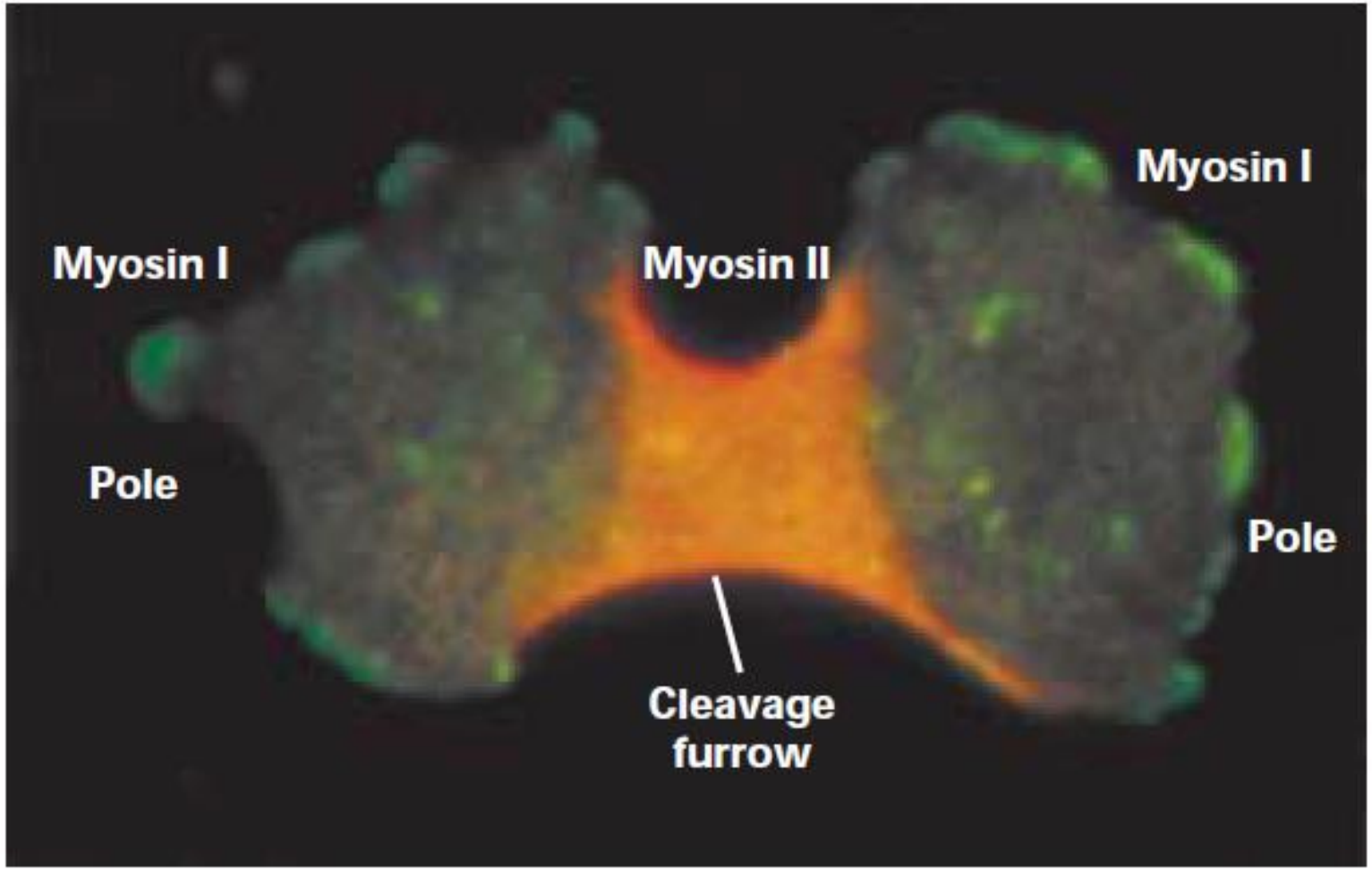
# Lecture 6

# Myosin II is required for cell division

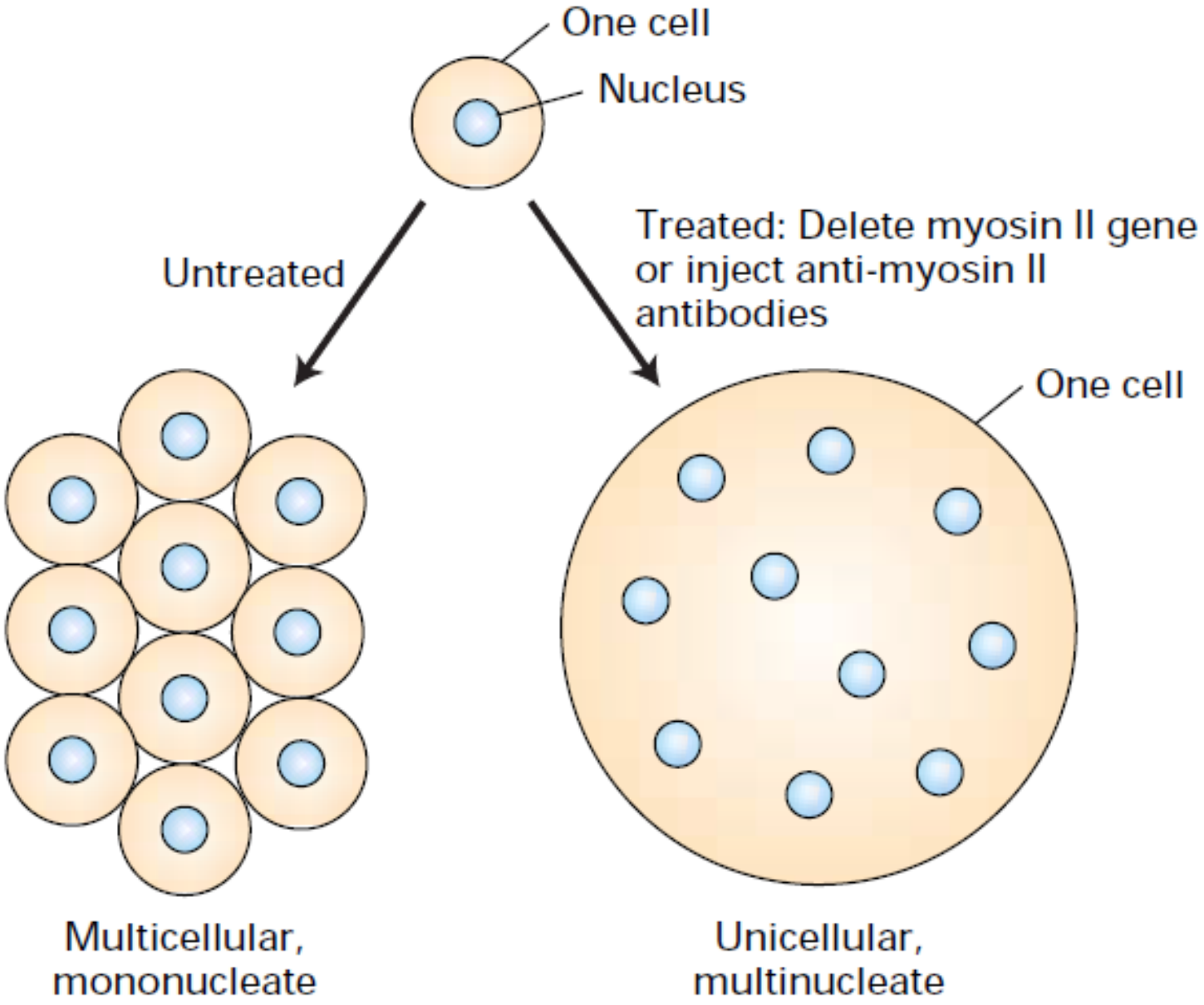



Dictyostelium

The contractile ring, a transient bundle of actin and myosin II, forms in a dividing cell and pinches the cell into two halves in cytokinesis.

Myosin II (red) is concentrated in the cleavage furrow, whereas myosin I (green) is localized at the poles of the cell.

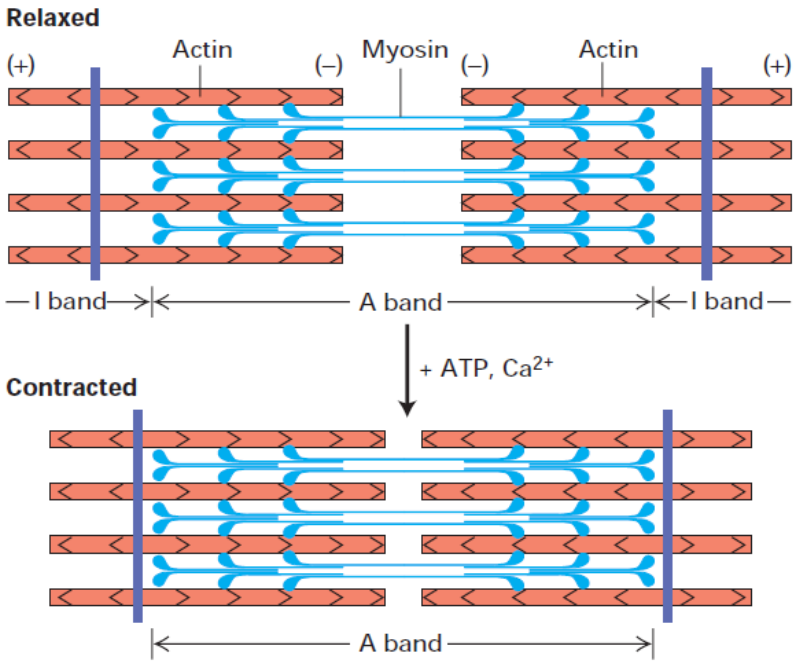
# Myosin II is required for cell division




A cell that lacks myosin II is able to replicate its DNA and nucleus but fails to divide; as a result, the cell forms a large, multinucleate syncytium over a period of time.

In comparison, an untreated cell during the same period continues to divide, forming a multicellular ball of cells in which each cell contains a single nucleus.

# The sliding-filament model of contraction in striated muscle.




Muscle cells have evolved to carry out one highly specialized function—contraction.

A typical skeletal muscle cell, called a myofiber, is cylindrical, large (1– 40 mm in length and 10–50 m in width), and multinucleated (containing as many as 100 nuclei)

The cytoplasm is packed with a regular repeating array of filament bundles organized into a specialized structure called a **sarcomere. (structural and functional unit of skeletal muscle)**

In skeletal muscle cells, actin thin filaments and myosin thick filaments are organized into highly ordered structures, called sarcomeres. The (+) end of the thin filaments is attached to the Z disk, the demarcation between adjacent sarcomeres.

During skeletal muscle contraction, myosin heads at each end of a thick filament walk along thin filaments toward the Z disks bounding a sarcomere.

The force generated by myosin movement pulls the thin filaments toward the center of the sarcomere, shortening its length

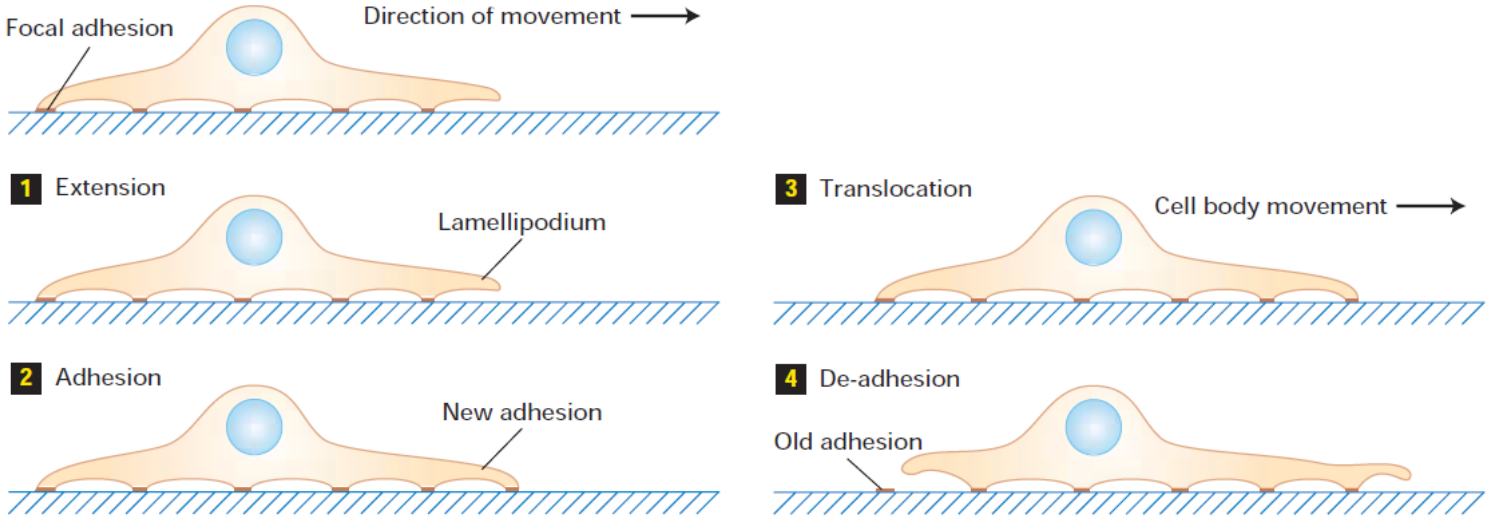
# A property exhibited by all moving cells is polarity

Cell migration is initiated by the formation of a large, broad membrane protrusion at the leading edge of a cell.

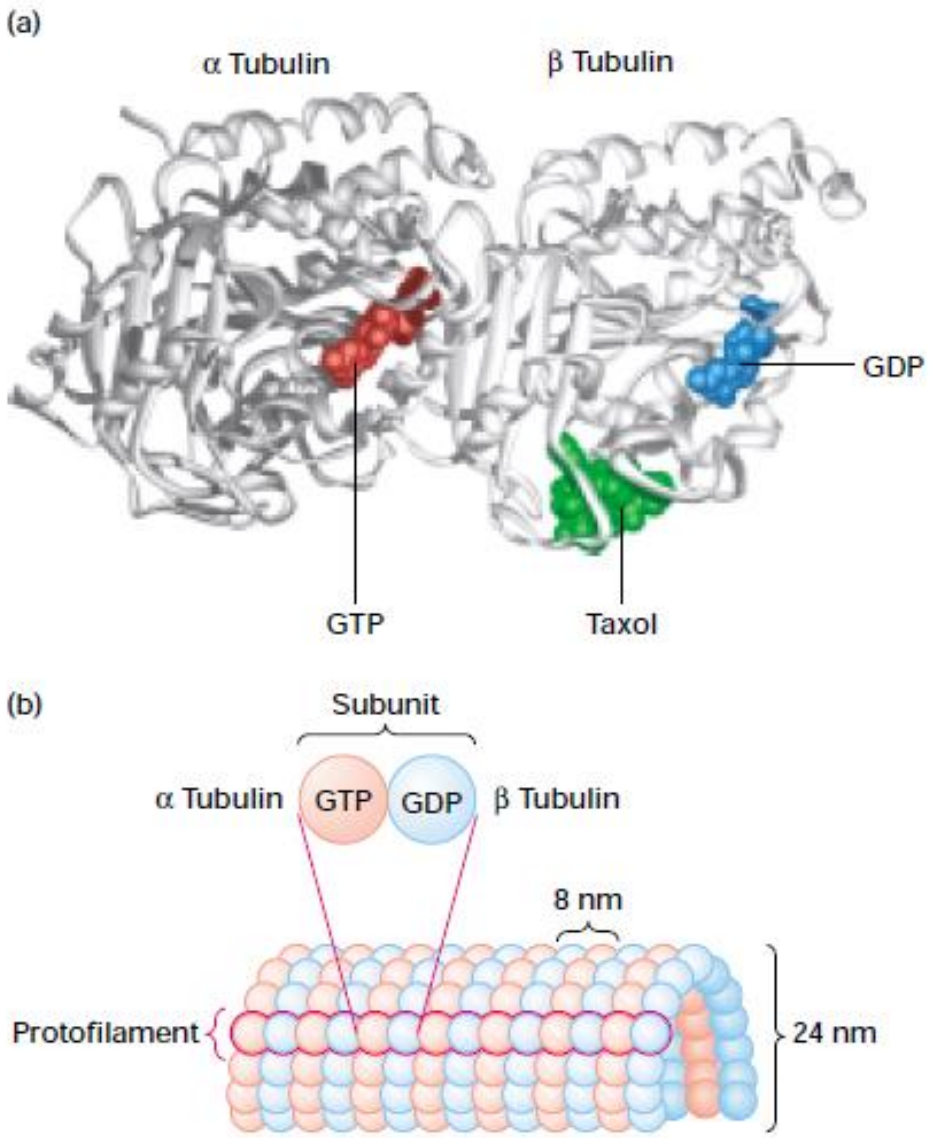
A major feature of this movement is the polymerization of actin at the membrane.

In addition, actin filaments at the leading edge are rapidly cross-linked into bundles and networks in a protruding region, called a *lamellipodium* in vertebrate cells.

In some cases, slender, fingerlike membrane projections, called *filopodia,* also are extended from the leading edge.



# Heterodimeric Tubulin Subunits Compose the Wall of a Microtubule




A microtubule is a polymer of globular **tubulin** subunits, which are arranged in a cylindrical tube measuring 25 nm in diameter

Varying in length from a fraction of a micrometer to hundreds of micrometers, microtubules are much **stiffer than either microfilaments or intermediate filaments** because of their tubelike construction

The building block of a microtubule is the tubulin subunit, a **heterodimer of α and β tubulin.**
Both of these 55,000-MW monomers are found in all eukaryotes, and their sequences are highly conserved.

Although a third tubulin, **γtubulin,** is not part of the tubulin subunit, it probably nucleates the polymerization of subunits to form microtubules.

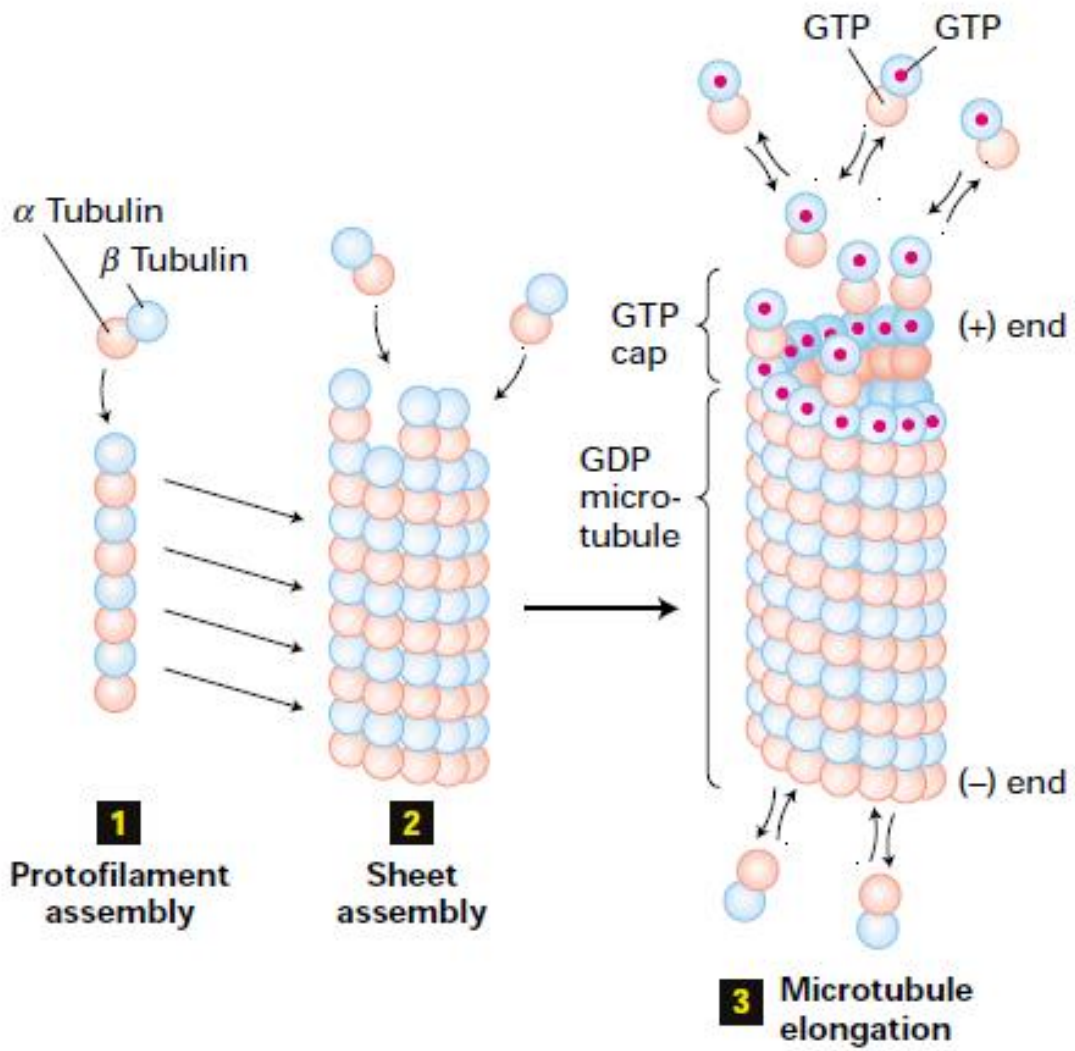
Encoded by separate genes, the three tubulins exhibit homology with a 40,000-MW bacterial GTPase, called FtsZ

**Each tubulin subunit binds two molecules of GTP.**
One GTP-binding site, located in α tubulin, binds GTP irreversibly and does not hydrolyze it.

The second site, located on β tubulin, binds GTP reversibly and hydrolyzes it to GDP

The head-to-tail arrangement of the α and β tubulin dimers in a protofilament confers an overall polarity on a microtubule. Because all protofilaments in a microtubule have the same orientation, one end of a microtubule is ringed by α -tubulin, whereas the opposite end is ringed by β -tubulin.

As in actin microfilaments, the two ends of a microtubule, designated the (+) and (-) ends, differ in their rates of assembly and critical concentrations ($C_c$).




1) protofilaments
assemble from –tubulin subunits,
(2) Protofilaments associate to form the wall of the microtubule, and
(3) the addition of more subunits to the ends of the protofilaments elongates the microtubule

Cells contain two populations of microtubules: **stable, long-lived microtubules and unstable, short-lived microtubules**.

Stable microtubules are generally found in nonreplicating cells.

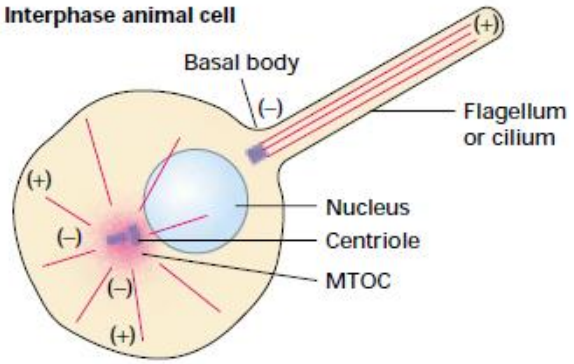
They include a central bundle of microtubules in **cilia** and **flagella,** extensions of the plasma membrane that beat rhythmically to propel materials across epithelial surfaces, to enable sperm to swim, or to push an egg through the oviduct

In contrast with these permanent, stable structures, unstable microtubules are found in cells that need to assemble and disassemble microtubule-based structures quickly.

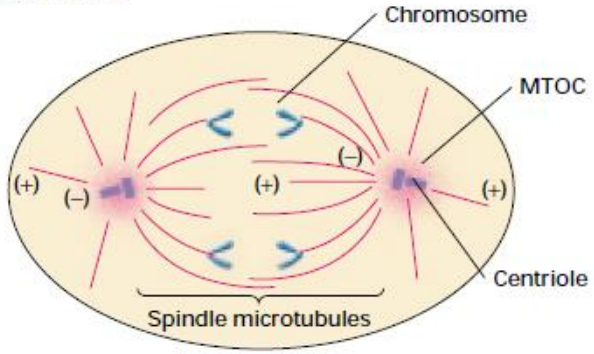
For example, in mitosis, the cytosolic microtubule network characteristic of interphase cells disassembles, and the tubulin from it is used to form the spindle-shaped apparatus that partitions chromosomes equally to the daughter cells

When mitosis is complete, the spindle disassembles and the interphase microtubule network re-forms.

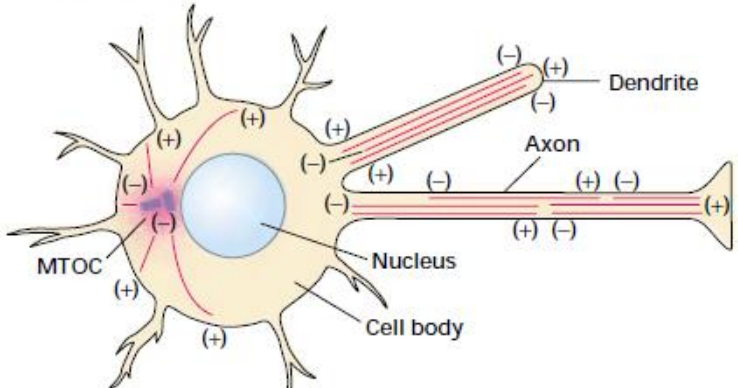
(a) **Interphase animal cell**



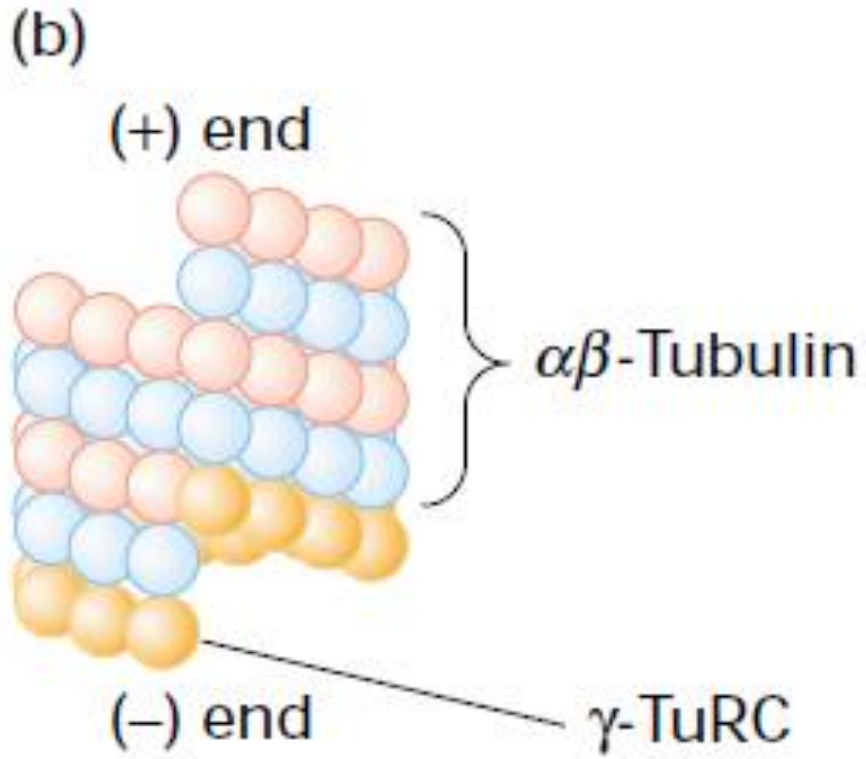

(b) **Mitotic animal cell**

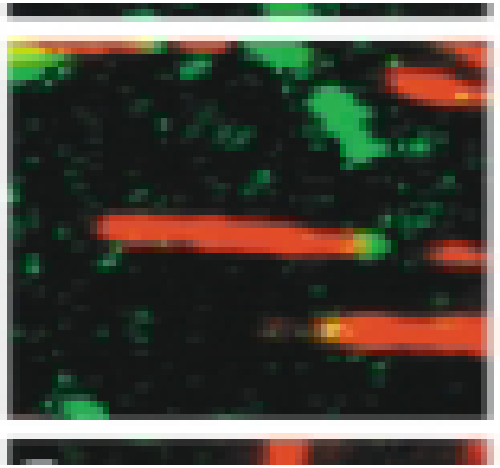



(c) **Nerve cell**



# The γ tubulin ring complex (-TuRC) is localized to one end of the microtubule.

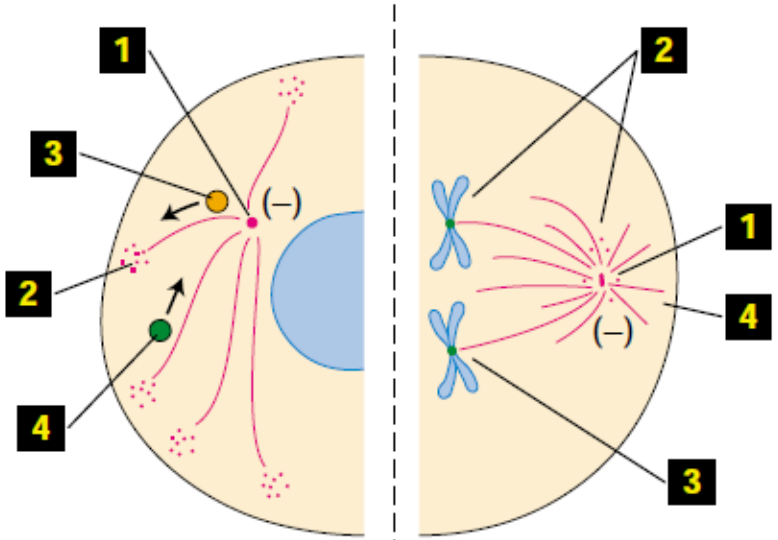


Microtubules assemble by the polymerization of dimeric tubulin.
Assembly and stability of microtubules are temperature dependent.

The parameters that determine the stability of a microtubule are

- the growth rate,
- the shrinkage rate,
- the catastrophe frequency, and
- the rescue frequency.




Interphase cell

Mitotic cell

| CYTOSKELETAL COMPONENT | CELL FUNCTION |
|---|---|
| 1 MTOC, spindle pole | Organizing cell polarity |
| 2 Microtubule dynamics | Chromosome movements<br>MT assembly |
| 3 Kinesin motors | (+) end–directed vesicle and chromosome transport |
| 4 Dynein motors | (–) end–directed vesicle transport spindle assembly |

# Microtubule-associated proteins (MAPs)

Microtubules function as tracks in the intracellular transport of various types of “cargo.”

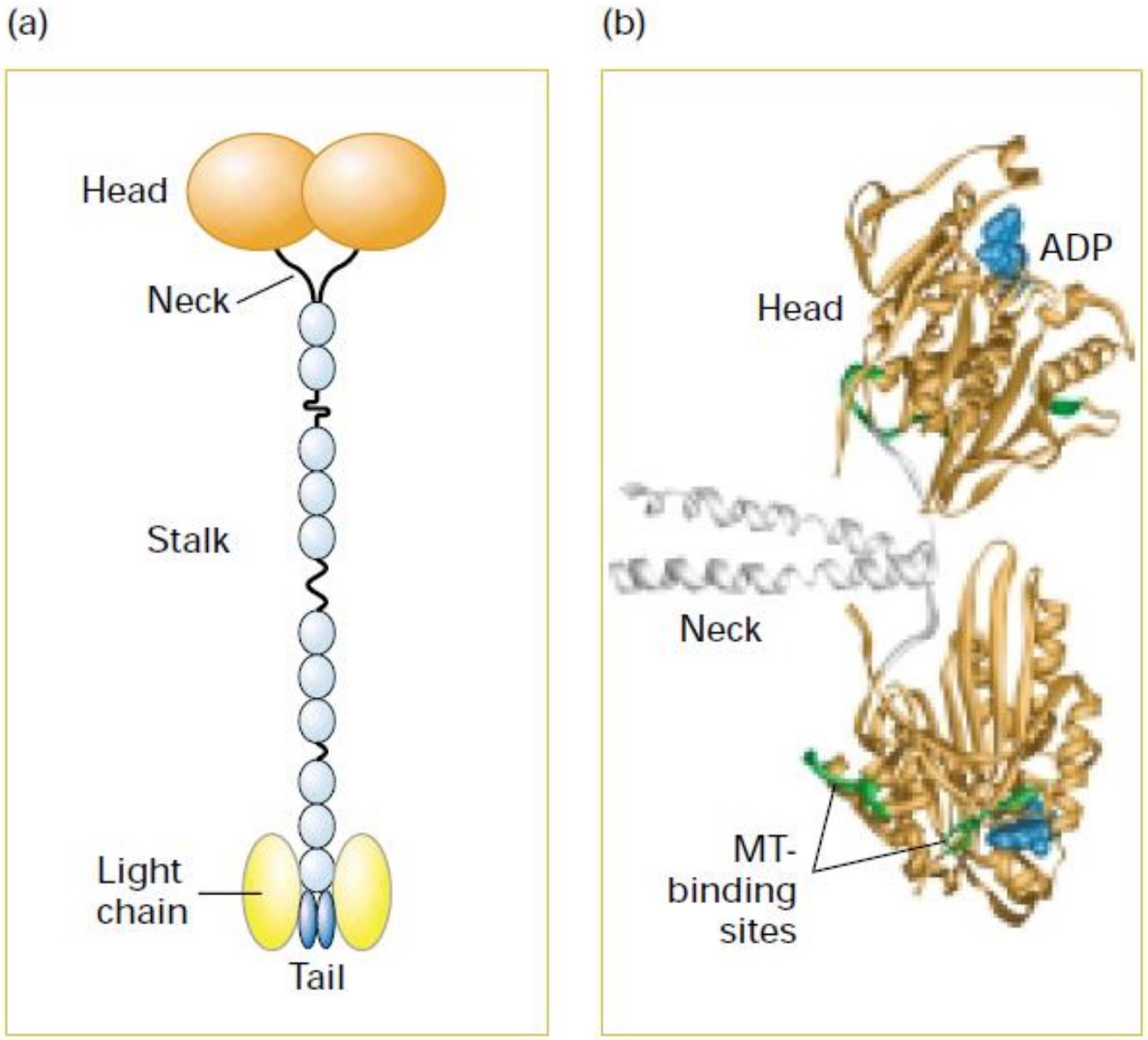
Two families of motor proteins—**kinesins** and **dyneins**— were found to mediate transport along microtubules

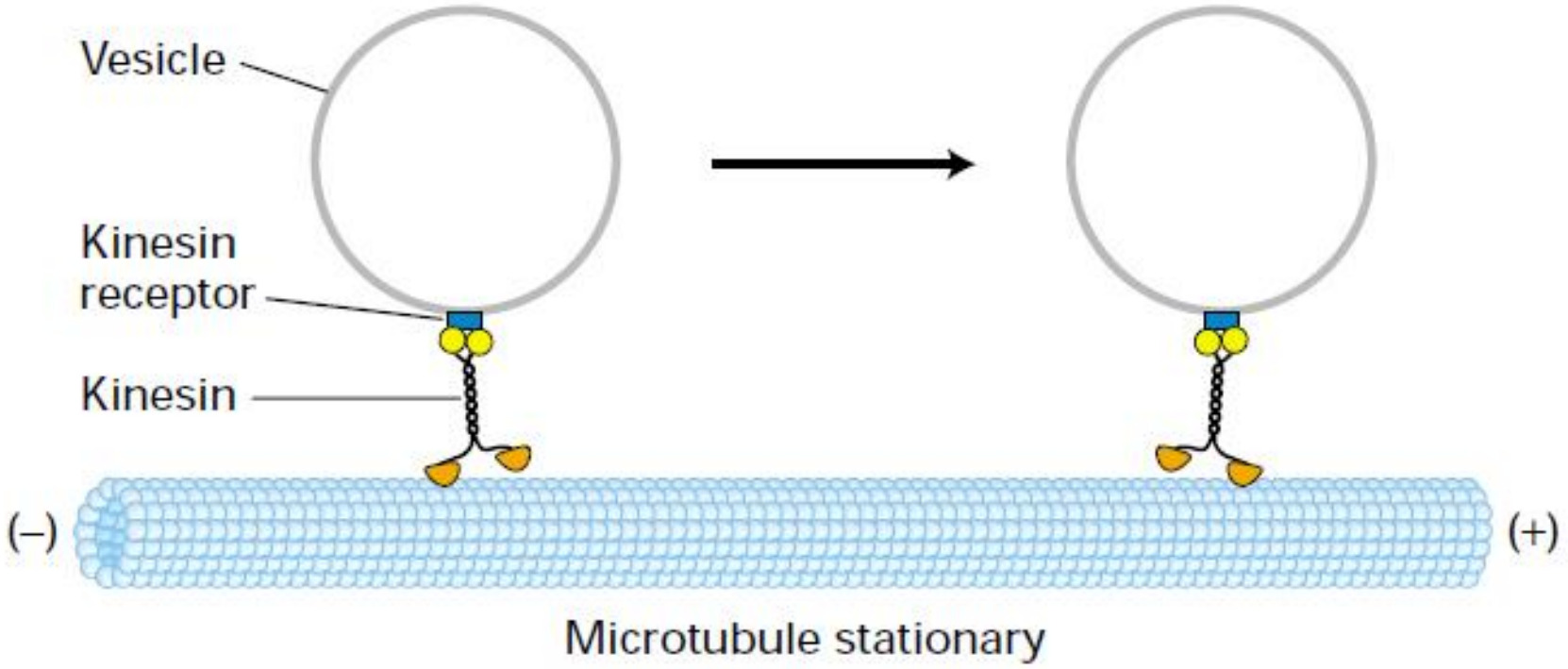
MAPs are classified into two groups on the basis of their function.

One group stabilizes microtubules.

A second group of MAPs directly destabilizes microtubules in many cell types.

# Kinesin I Powers Anterograde Transport of Vesicles in Axons

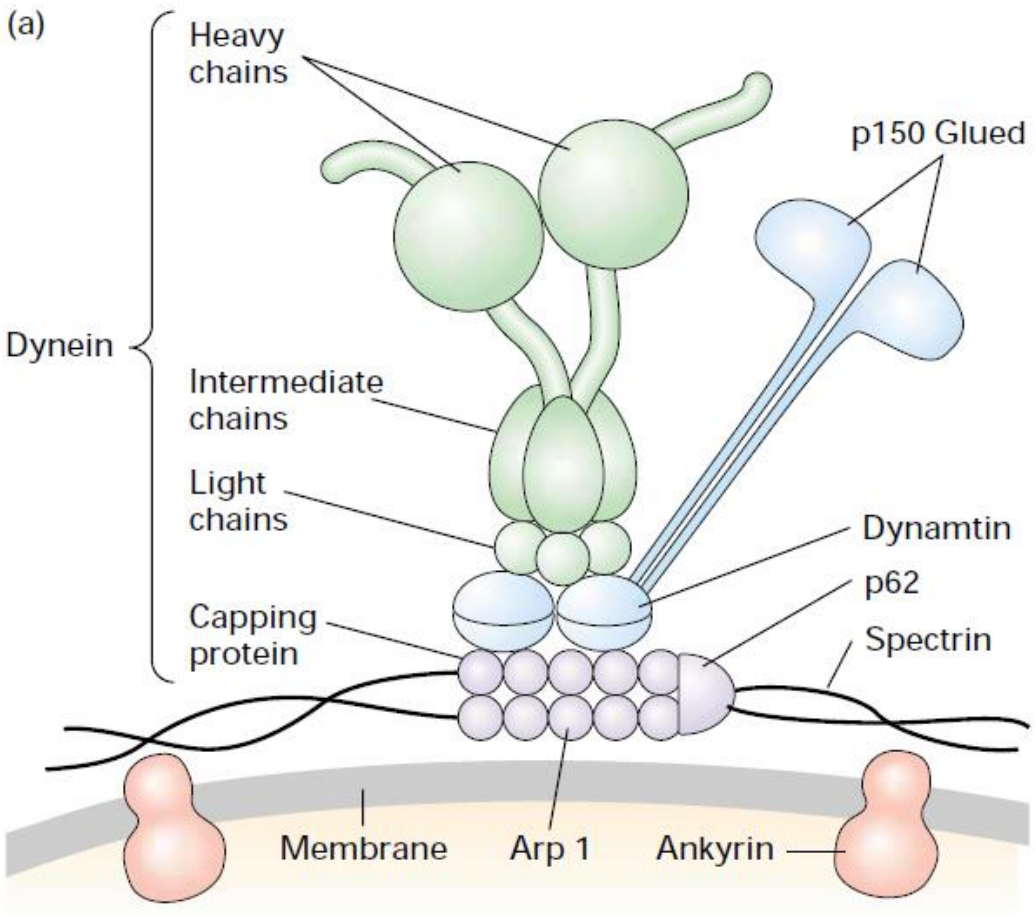





A kinesin molecule can move along a microtubule for a long distance without detaching from it, a property referred to as *processivity.*

Because of their high processivity, dimeric kinesins are very efficient in transporting cargo from one part of a cell to another.

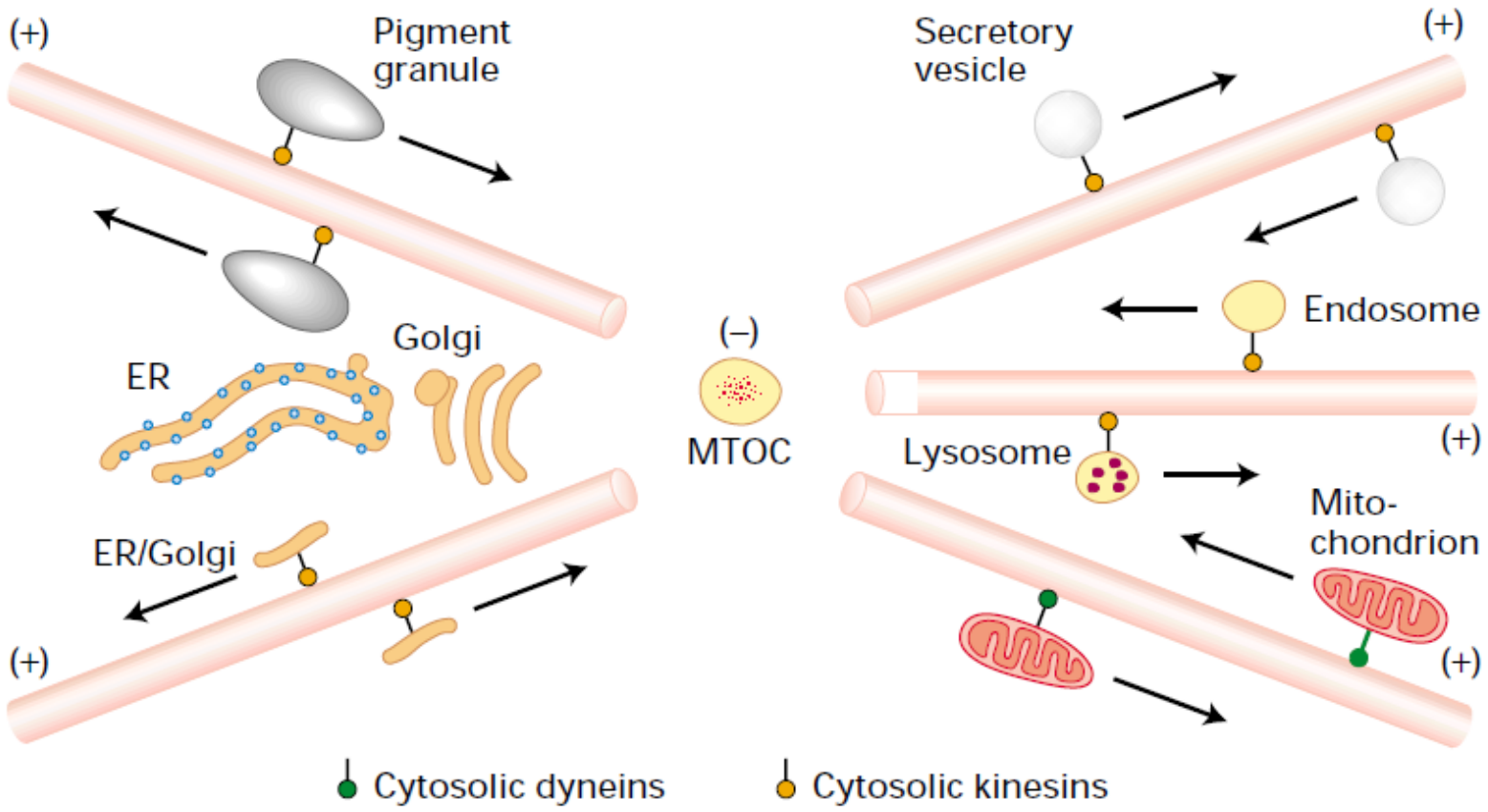
# Cytosolic Dyneins Are () End–Directed Motor Proteins That Bind Cargo Through Dynactin




However, unlike kinesin, dynein cannot mediate cargo transport by itself.

Rather, dynein-related transport requires *dynactin,* a large protein complex that links vesicles and chromosomes to the dynein light chains

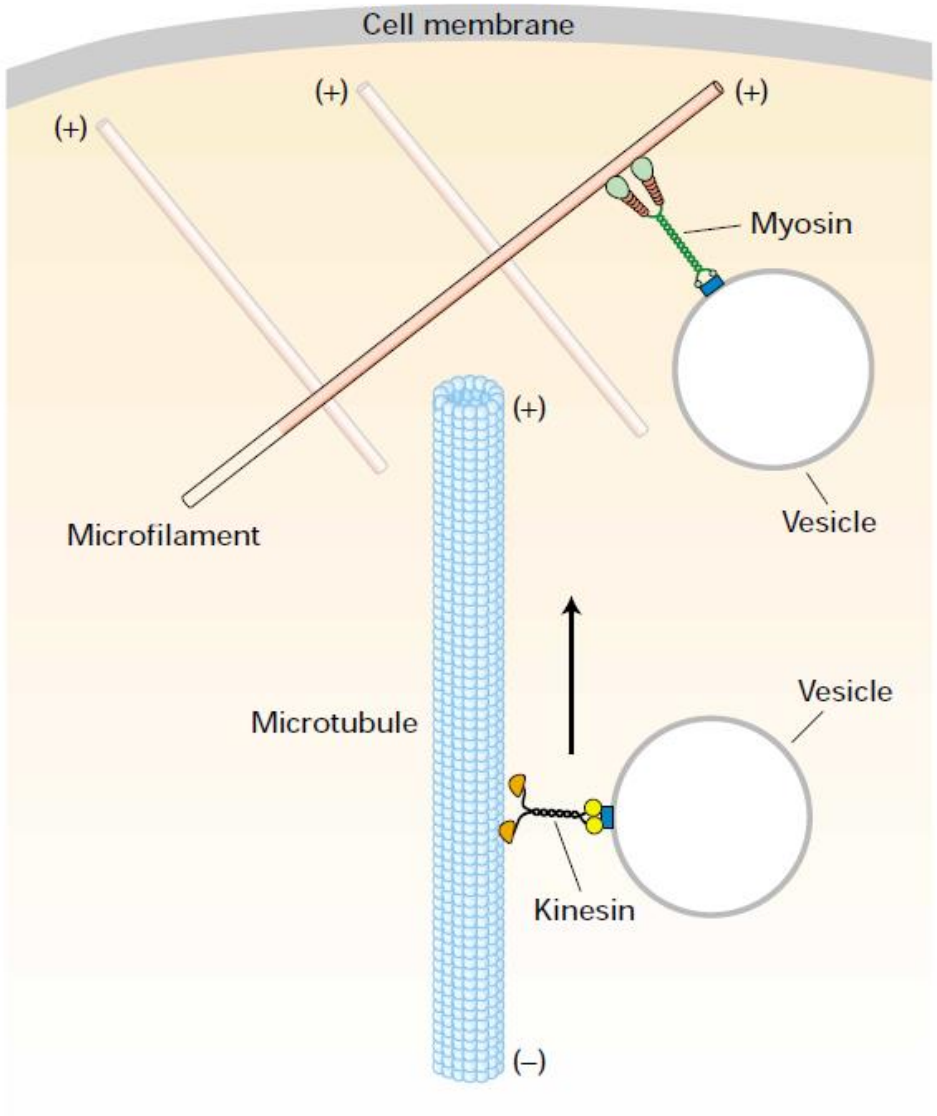
# General model of kinesin- and dynein-mediated transport in a typical cell.




The array of microtubules, with their (+) ends pointing toward the cell periphery, radiates from an MTOC in the Golgi region.
Kinesin-dependent anterograde transport (red)

conveys mitochondria, lysosomes, and an assortment of vesicles
to the endoplasmic reticulum (ER) or cell periphery.

Cytosolic dynein–dependent retrograde transport (green) conveys mitochondria, elements of the ER, and late endosomes to the cell center.




**Cooperation of myosin and kinesin at the cell cortex.** Microtubules approach the actin-rich cell membrane.
Consequently, some cargoes are transported to the cell periphery by kinesin motor proteins on microtubules but complete the journey on microfilaments under the power of myosin motor proteins.

Unlike microfilaments and microtubules, however, intermediate filaments do not contribute to cell motility.

There are no known examples of IF-dependent cell movements or of motor proteins that move along intermediate filaments.