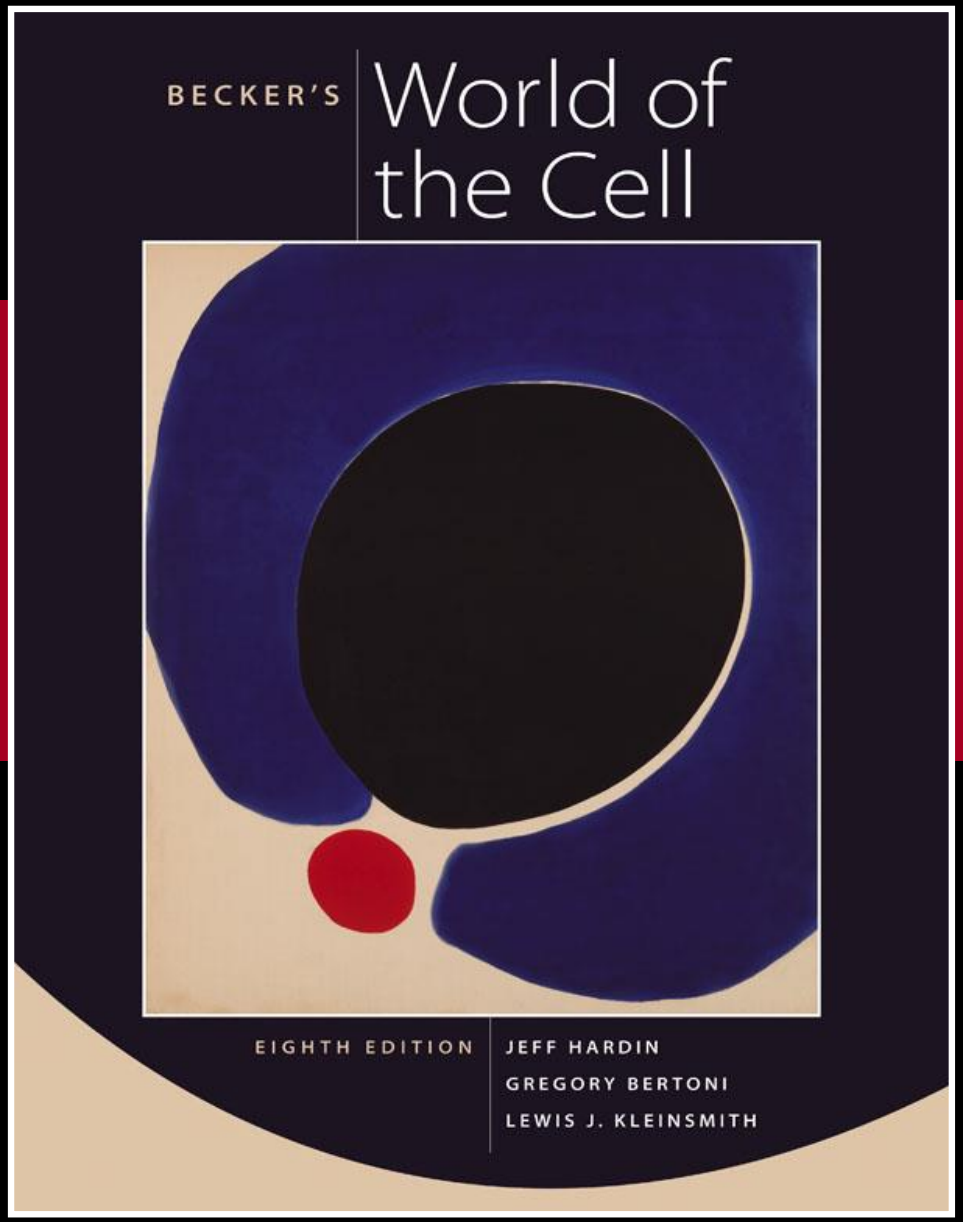


Chapter 13

Cytoskeletal Systems

Lectures by
Kathleen Fitzpatrick
Simon Fraser University

Cytoskeletal Systems

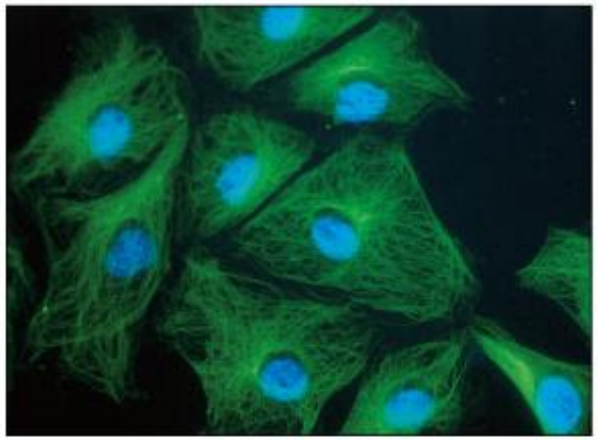
- The interior of a cell is highly structured
- The cytoskeleton is a network of interconnected filaments and tubules extending through the cytosol
- It plays roles in cell movement and division
- It is dynamic and changeable

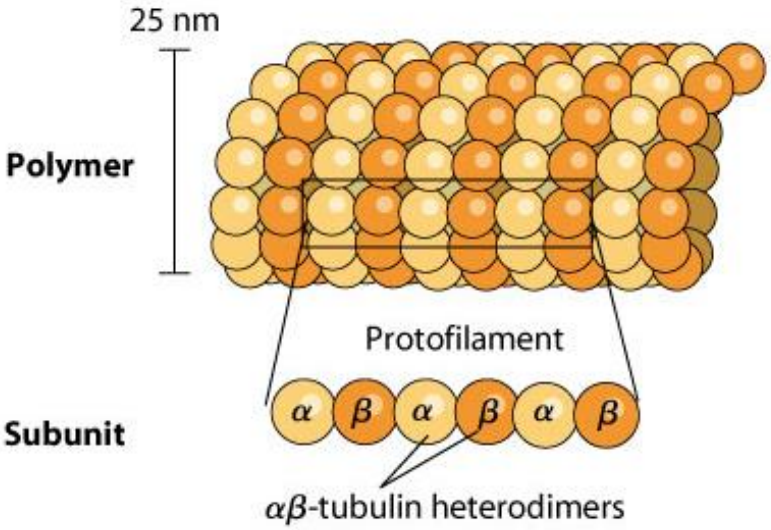
Major Structural Elements of the Cytoskeleton

- The major structural elements of the cytoskeleton are
  - Microtubules
  - Microfilaments
  - Intermediate filaments

Table 13-1 - Microtubules

Microtubules





Structure	Hollow tube with a wall consisting of 13 protofilaments
Diameter	Outer: 25 nm
	Inner: 15 nm
Monomers	α-tubulin
	β-tubulin
Polarity	(+), (−) ends
Functions	Cytoplasmic:
	Organization and maintenance of animal cell shape and polarity
	Chromosome movements
	Intracellular transport/ trafficking, and movement of organelles
	Axonemal: Cell motility

Table 13-1 - Microfilaments

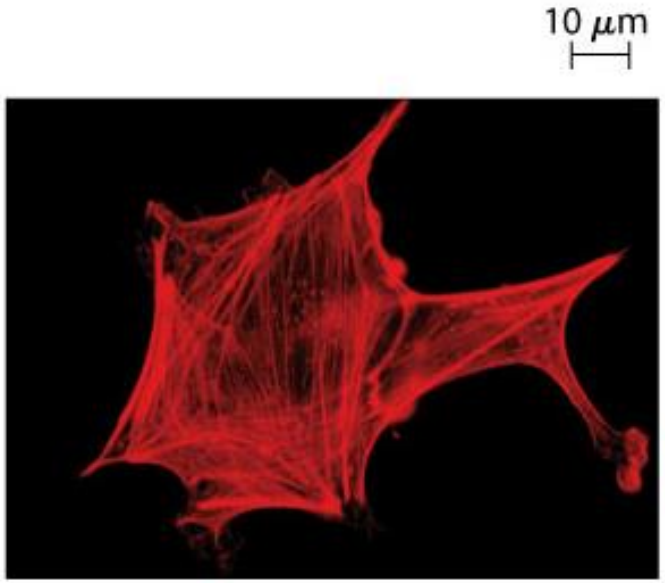
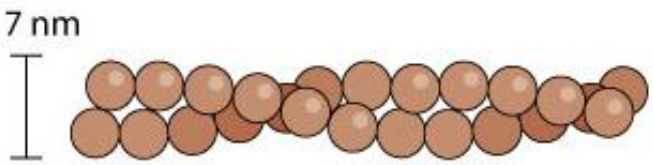
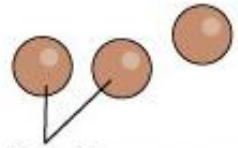
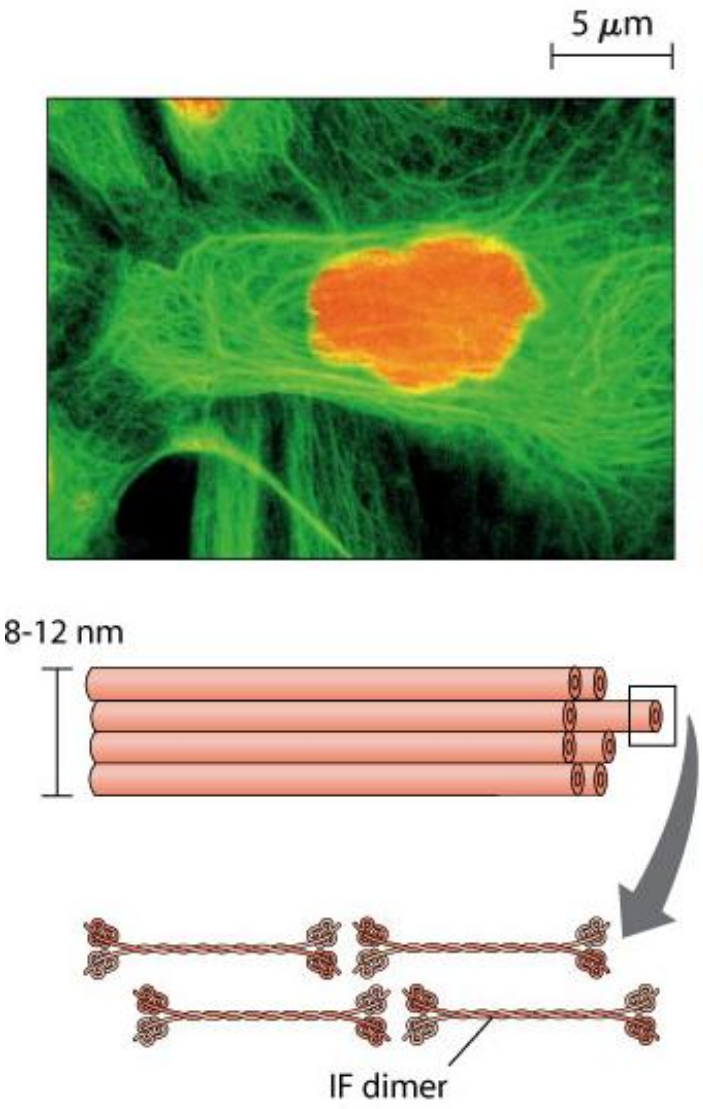
Microfilaments	
	Two intertwined chains of F-actin
	7 nm
	G-actin
	(+), (−) ends
	Muscle contraction
	Cell locomotion
	Cytoplasmic streaming
	Cytokinesis
	Maintenance of animal cell shape
	Intracellular transport/trafficking

Table 13-1 – Intermediate Filaments

Intermediate Filaments



Eight protofilaments joined end to end with staggered overlaps

8–12 nm

Several proteins; see Table 15-4

No known polarity

Structural support

Maintenance of animal cell shape

Formation of nuclear lamina and scaffolding

Strengthening of nerve cell axons (neurofilament protein)

Keeping muscle fibers in register (desmin)

The Cytoskeleton Is Dynamically Assembled and Disassembled

- Microfilaments are essential components of *muscle fibrils* and microtubules are structural elements of *cilia* and *flagella*
- These structures are large enough to view by a variety of microscopic techniques
- Also, certain drugs can be used to perturb cytoskeletal function

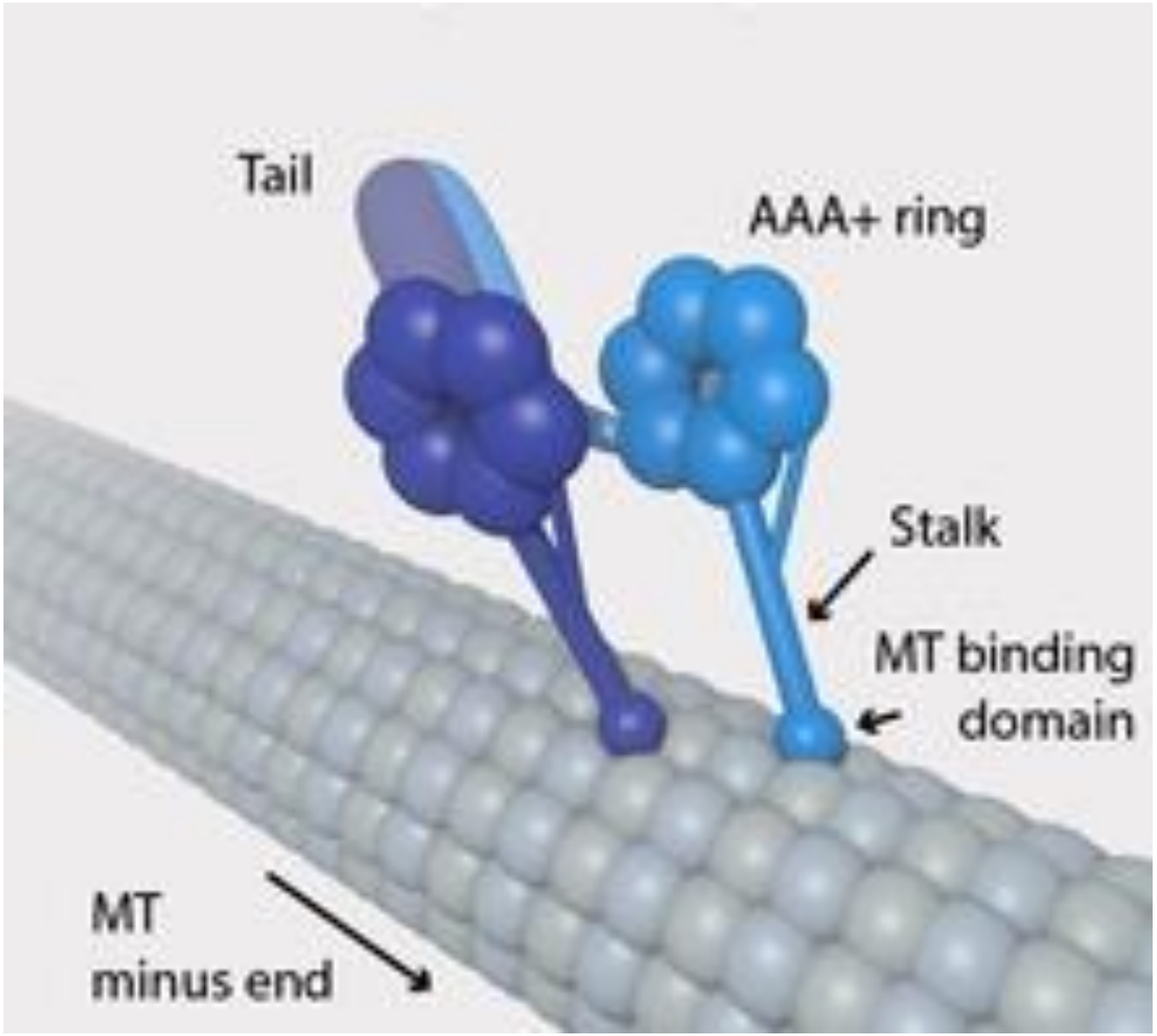
Microtubules

- Microtubules are the largest of the cytoskeletal components of a cell
- There are two types of microtubules
- They are involved in a variety of functions in the cell

Two Types of Microtubules Are Responsible for Many Functions in the Cell

- **Cytosolic microtubules** pervade the cytosol and are responsible for a variety of functions

  - Maintaining axons
  - Formation of mitotic and meiotic spindles
  - Maintaining or altering cell shape
  - Placement and movement of vesicles

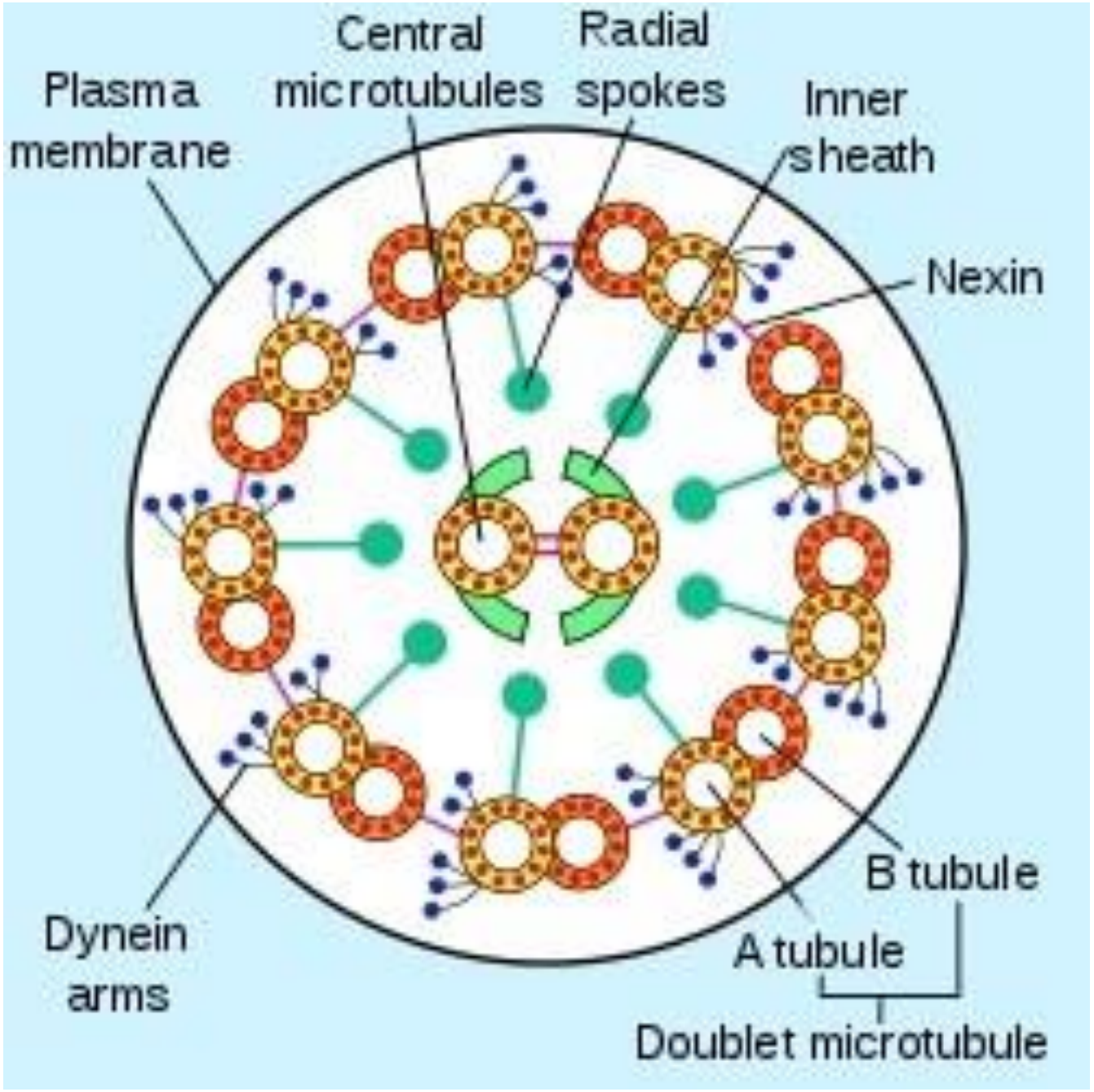


Two types of microtubules (MTs)

- **Axonemal microtubules** include the organized and stable microtubules found in structures such as

  - Cilia
  - Flagella
  - Basal bodies to which cilia and flagella attach

- The *axoneme*, the central shaft of a cilium or flagellum, is a highly ordered bundle of MTs



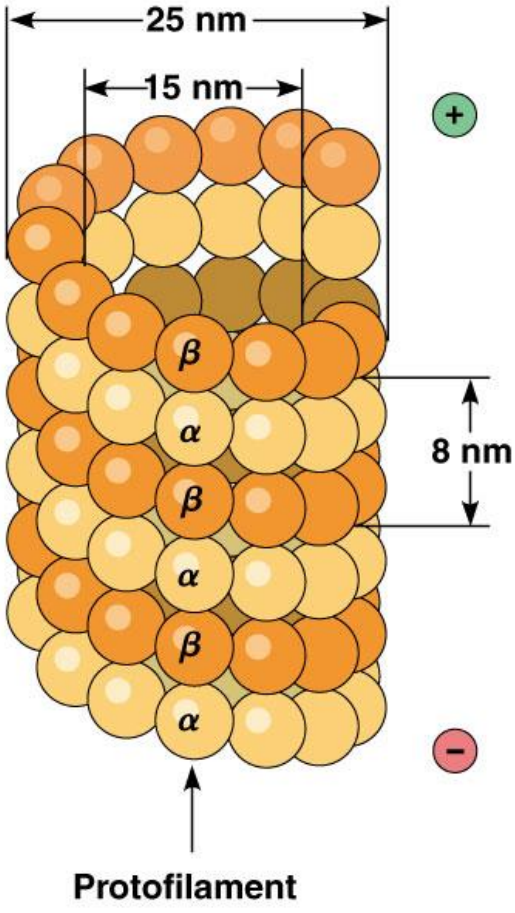
Tubulin Heterodimers Are the Protein Building Blocks of Microtubules

- MTs are straight, hollow cylinders of varied length that consist of (usually 13) longitudinal arrays of polymers called **protofilaments**

- The basic subunit of a protofilament

is a **heterodimer** of **tubulin**, one **α-tubulin** and one **β-tubulin**

- These bind **noncovalently** to form an **αβ-heterodimer**, which does not normally dissociate

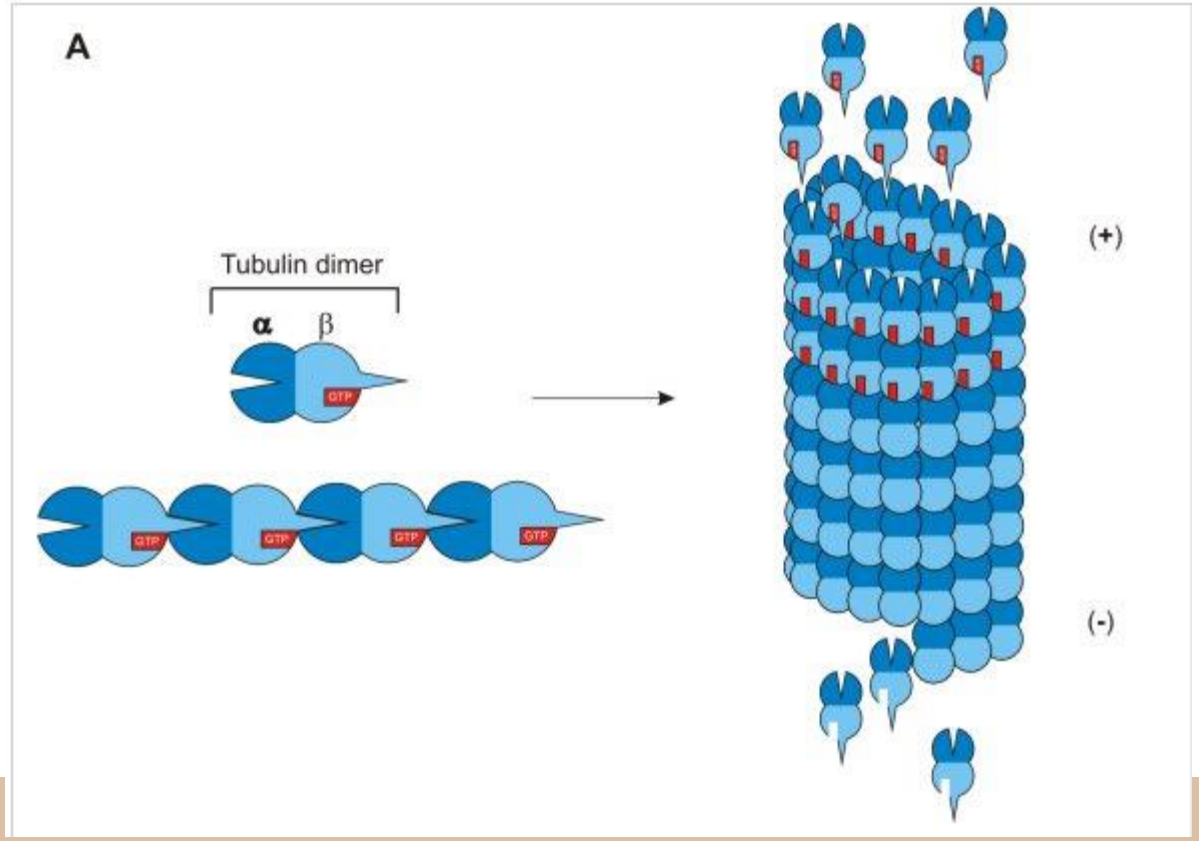


Subunit structure and polarity

- α and β subunits have very similar 3-D structure, but only 40% amino acid identity

- Each has an
- 1. N-terminal GTP binding domain,
- 2. a central domain to which colchicine can bind
- 3. a C-terminal domain that interacts with MAPs (microtubule-associated proteins)
- All the dimers in the MT are oriented the same way

- **Because of dimer orientation, protofilaments have an inherent polarity (*the two ends differ both chemically and structurally*)**

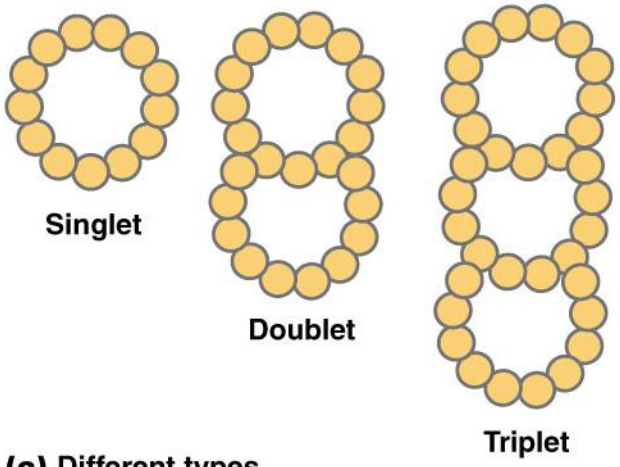


Microtubules Can Form as Singlets, Doublets, or Triplets

- Cytoplasmic MTs are simple tubes, or *singlet* MTs, with 13 protofilaments

- Some axonemal MTs form *doublet* or *triplet* MTs

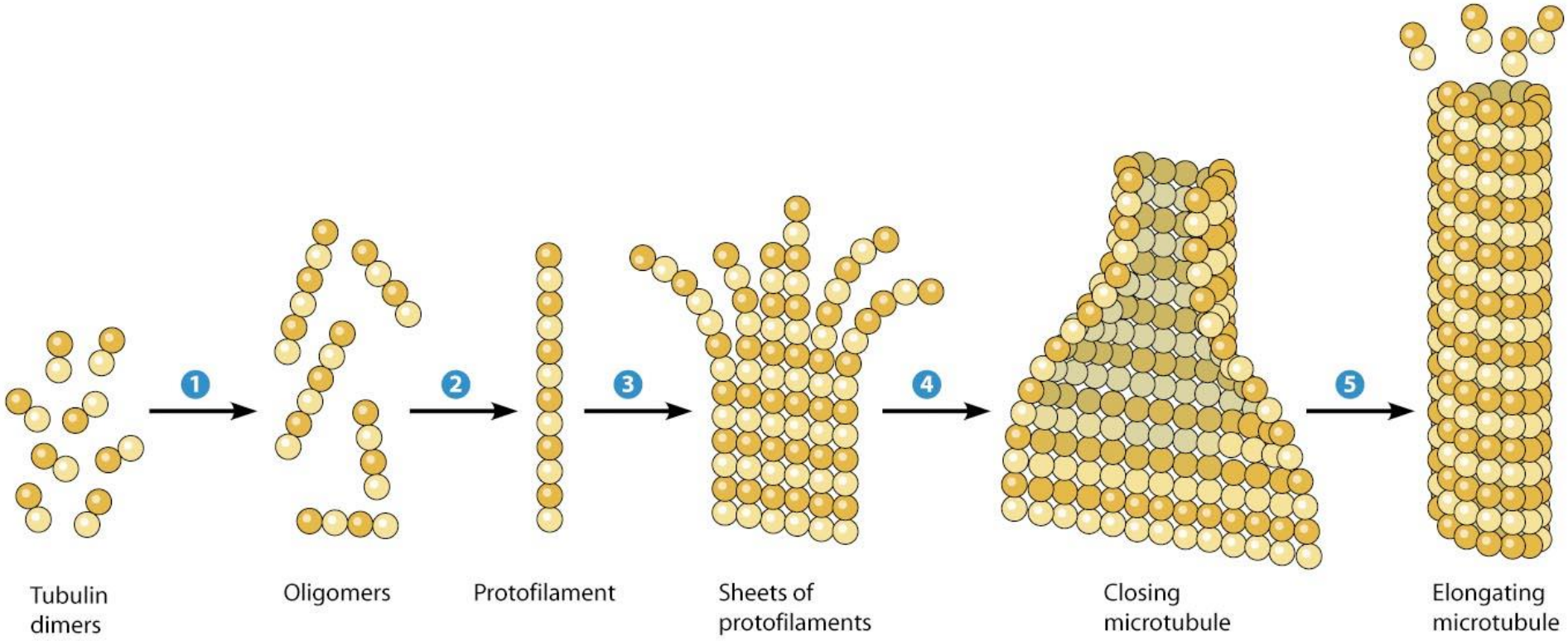
- Doublets and triplets contain one 13-protofilament tubule (the *A tubule*) and one or two additional incomplete rings (*B* and *C tubules*) protofilaments

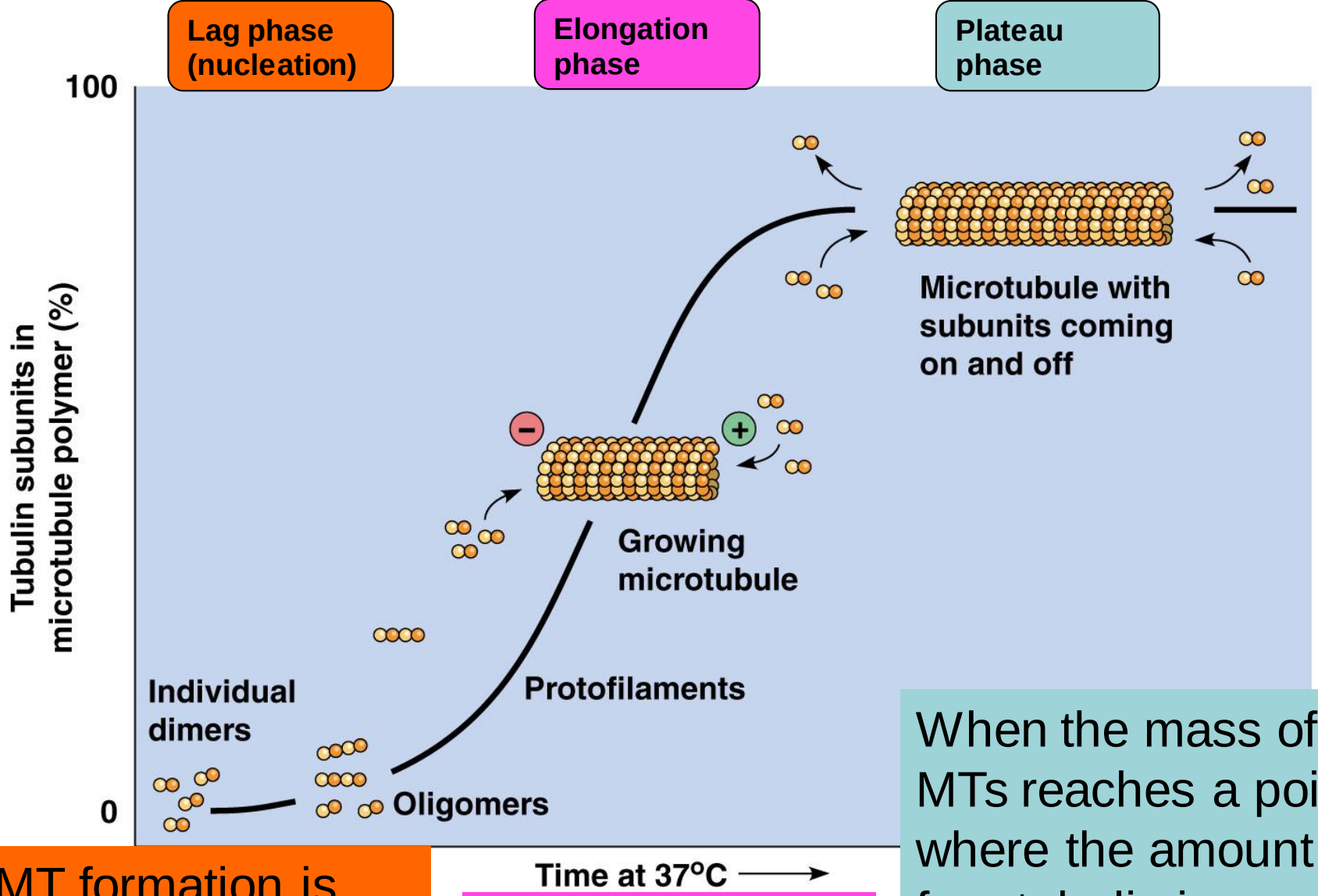


(c) Different types of microtubules

Microtubules Form by the Addition of Tubulin Dimers at Their Ends

MTs form by the reversible polymerization of





MT formation is slow at first due to the slow process of nucleation

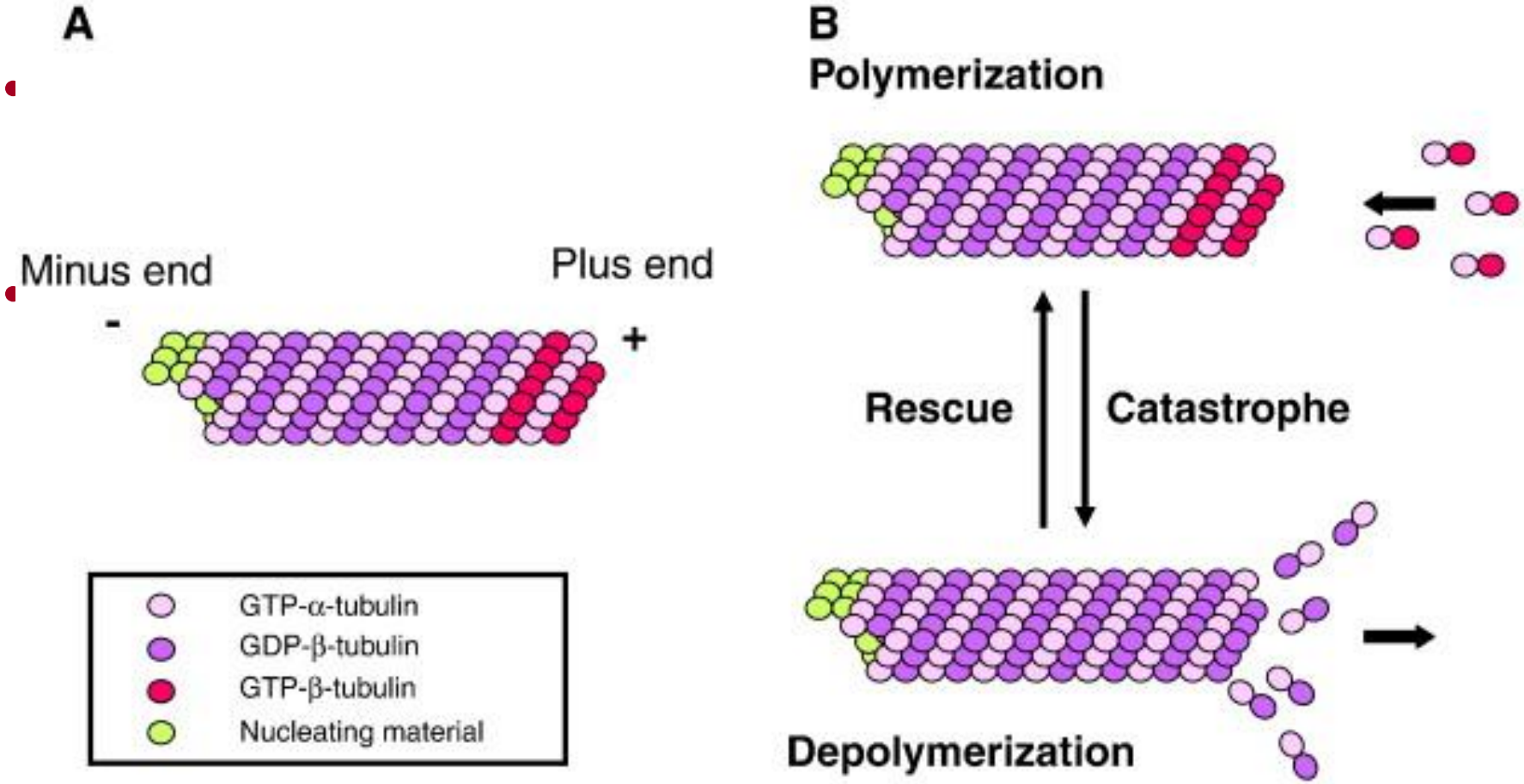
Elongation is much faster

When the mass of MTs reaches a point where the amount of free tubulin is diminished, the assembly is balanced by disassembly

Critical concentration

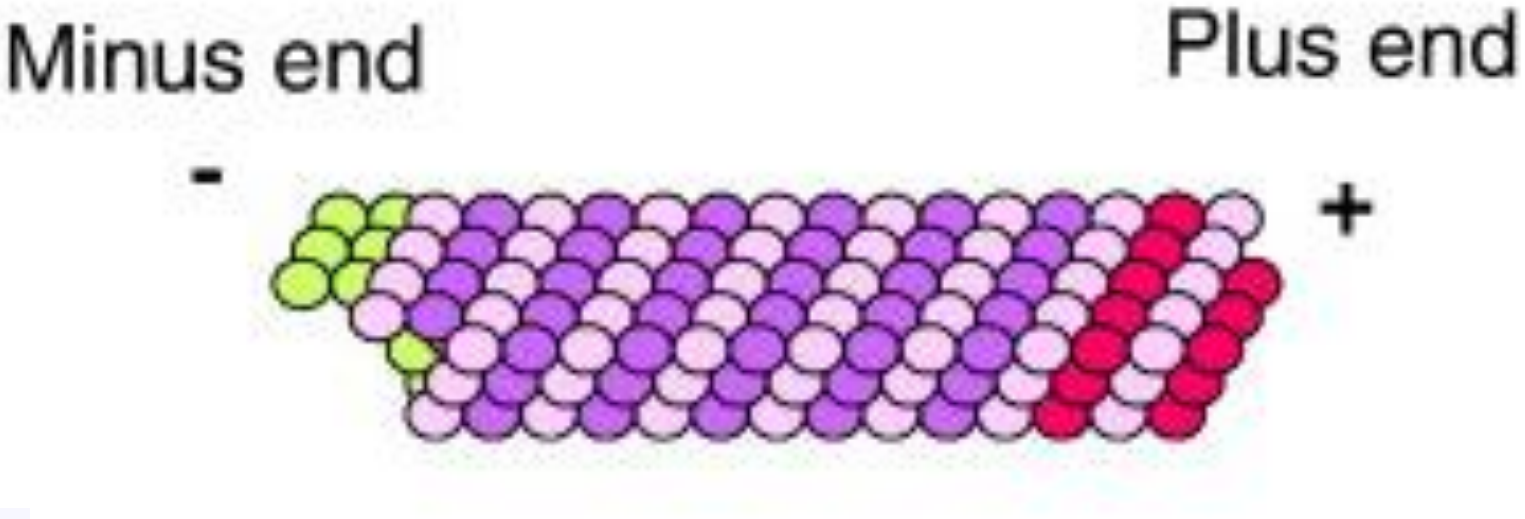
- Microtubule assembly in vitro depends on concentration of tubulin dimers
- The tubulin concentration at which MT assembly is exactly balanced by disassembly is called the **critical concentration**
- MTs **grow** when the tubulin concentration *exceeds* the critical concentration and vice versa

Addition of Tubulin Dimers Occurs More Quickly at the Plus Ends of Microtubules



Microtubule treadmilling

- The plus and minus ends of microtubules have **different critical concentrations**: The CC for the + end is **LOWER** than that for the – end



Critical concentration (CC)

CC < [tubulin] ➔ assembly of MT

CC > [tubulin] ➔ disassembly of MT

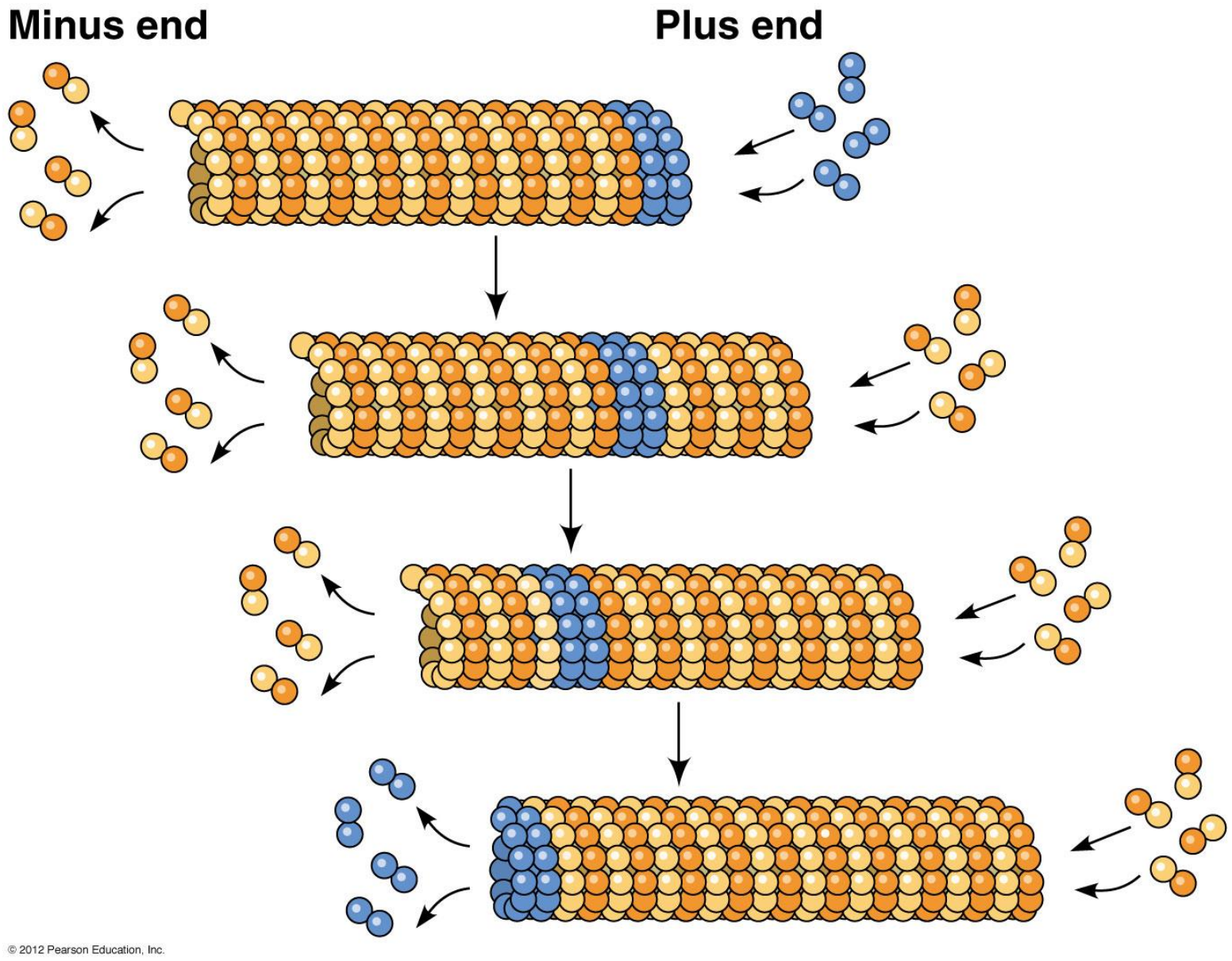
Microtubule treadmilling

If $CC_{plus\ end}$ < [free tubulin] < $CC_{minus\ end}$
→ assembly will occur at the plus end and disassembly will occur at the minus end

➔*treadmilling* will occur

Treadmilling: addition of subunits at the plus end, and removal from the minus end

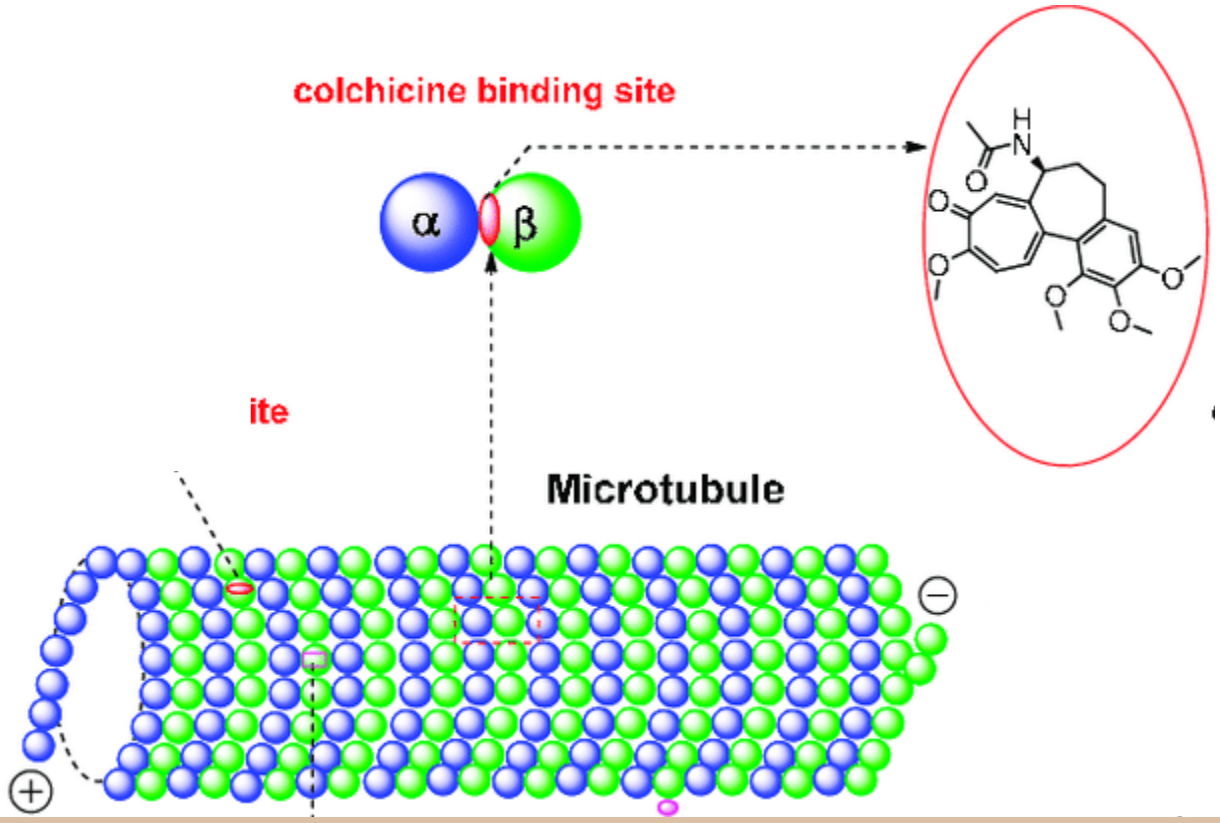
Figure 13-5



Drugs Can Affect the Assembly of Microtubules

Colchicine binds to tubulin monomers, inhibiting their assembly into MTs and promoting MT disassembly

Nocodazole inhibits MT assembly, and its effects are more easily reversed than those of colchicine

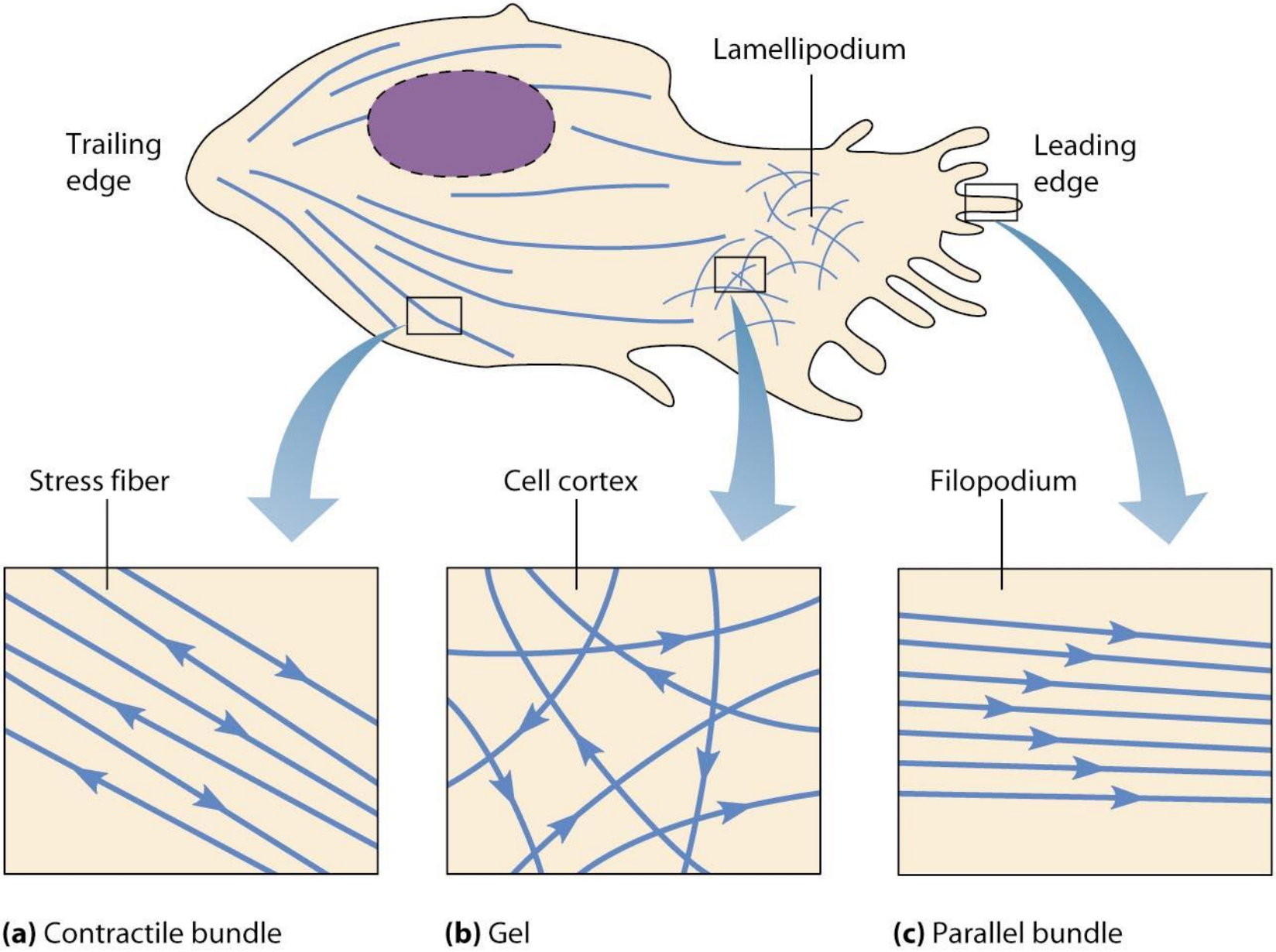


Polarity of microfilaments

- The polarity of MFs is reflected in more rapid addition or loss of G-actin at the plus end than the minus end
- After the G-actin monomers assemble onto a microfilament, the ATP bound to them is slowly hydrolysed
- So, the growing MF ends have ATP-actin, whereas most of the MF is composed of ADP-actin

Specific Drugs Affect Polymerization of Microfilaments

- **Cytochalasins** are fungal metabolites that prevent the addition of new monomers to existing MFs
- **Latrunculin A** is a toxin that sequesters actin monomers and prevents their addition to MFs
- **Phalloidin** stabilizes MFs and prevents their depolymerization



Actin-Binding Proteins Regulate the Polymerization, Length, and Organization of Actin

- Cells can precisely control where actin assembles and the structure of the resulting network
- They use a variety of **actin-binding proteins** to do so
- Control occurs at the nucleation, elongation, and severing of MFs, and the association of MFs into networks

Figure 13-16

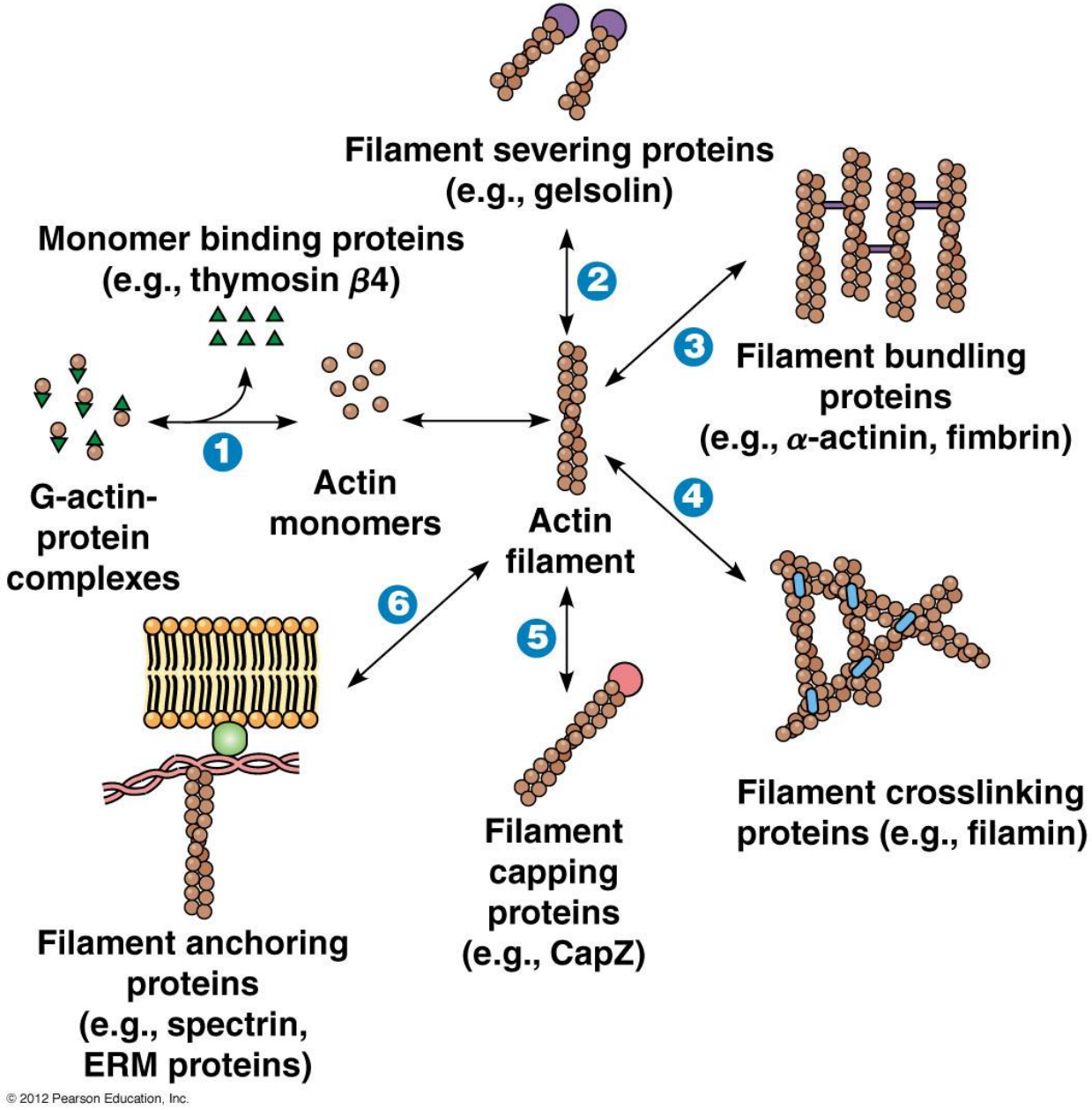
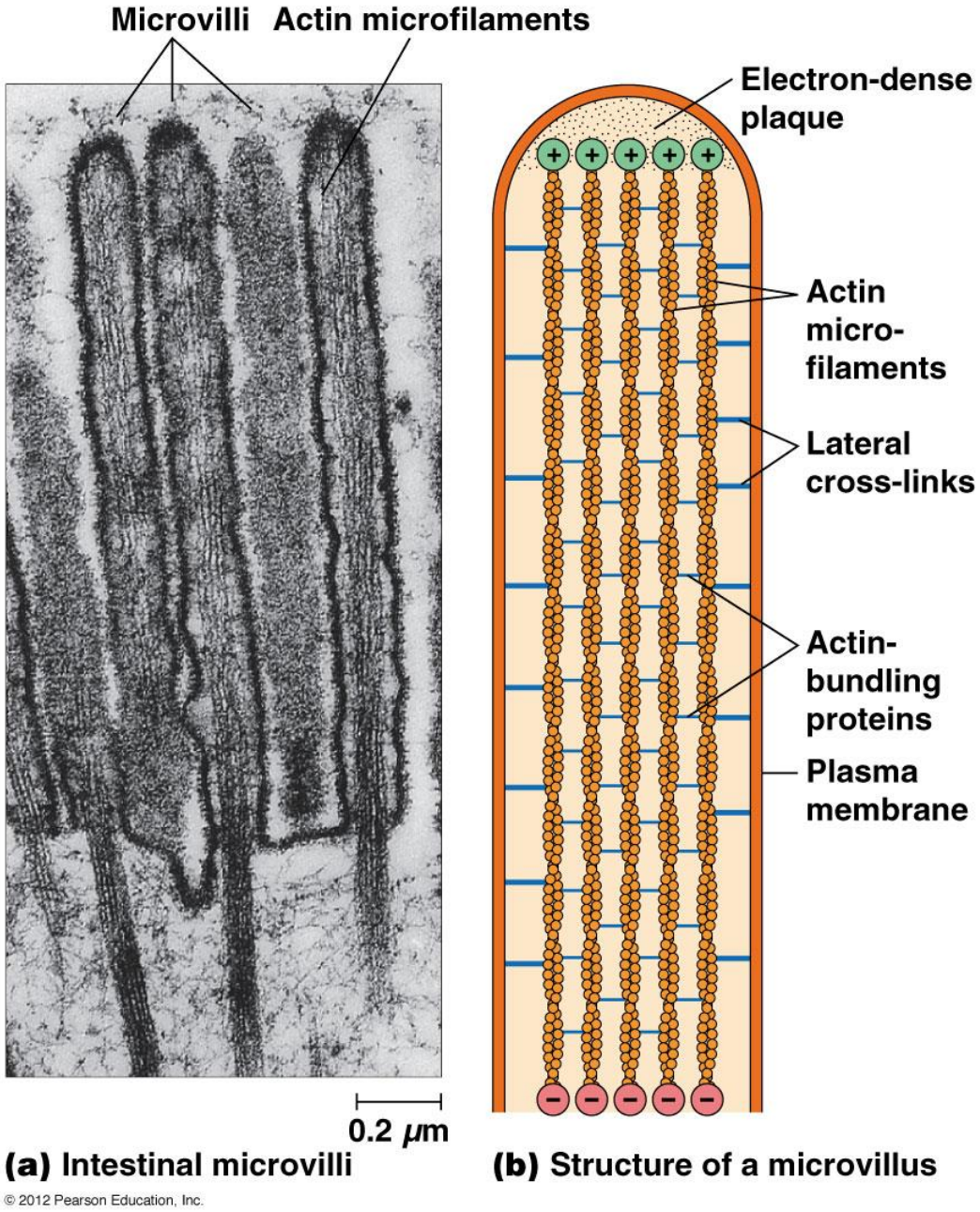


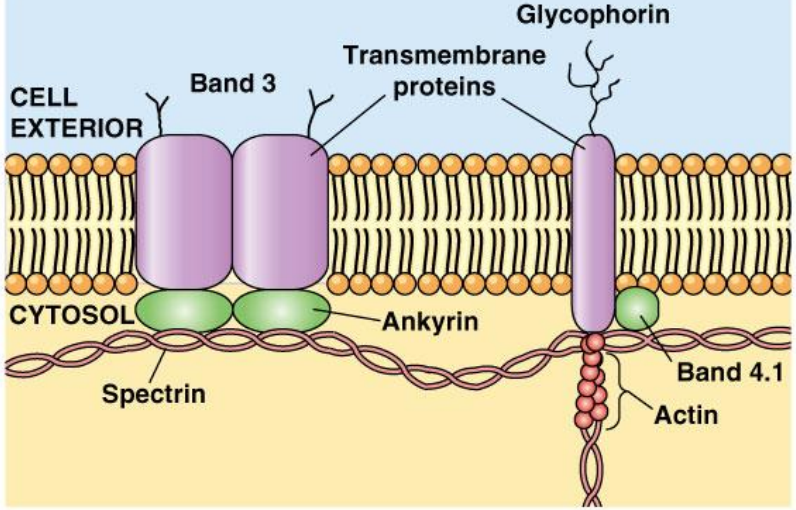
Figure 13-17

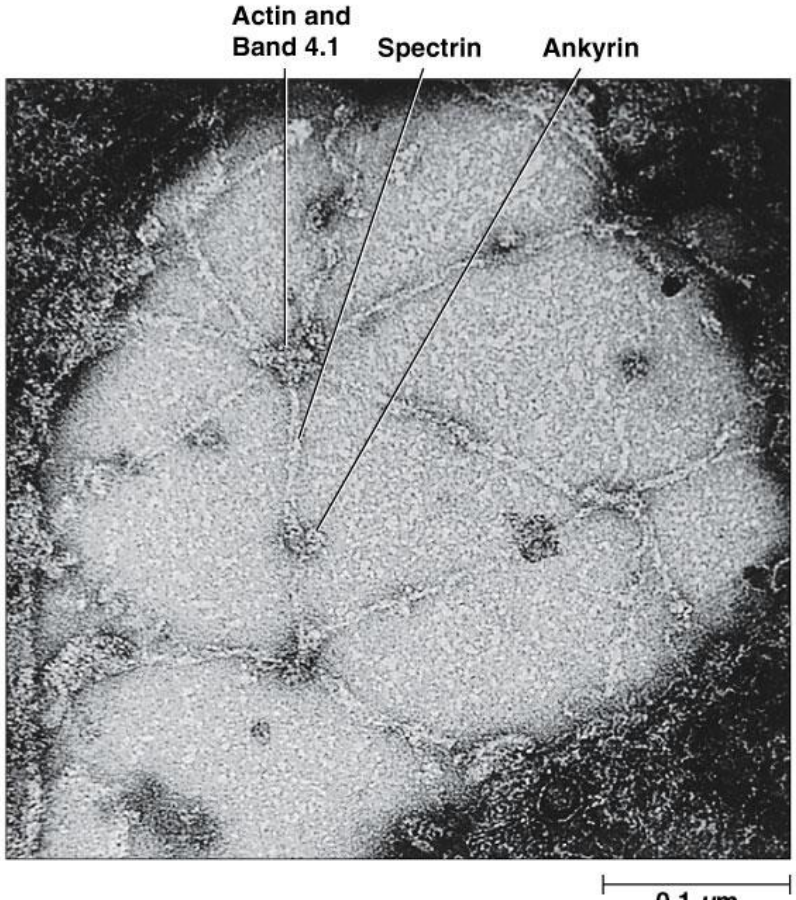


Proteins That Link Actin to Membranes

- MFs are connected to the plasma membrane and exert force on it during cell movement or cytokinesis
- This (indirect) connection to the membrane requires one or more linking proteins
- One group of such proteins is the *band 4.1*, *ezrin*, *radixin,* and *moesin* family; another is *spectrin* and *ankyrin*

Figure 13-19





Intermediate Filaments

- Intermediate filaments are the most stable and least soluble cytoskeletal components and are not polarized
- An abundant intermediate filament (IF) is *keratin*, an important component of structures that grow from skin in animals
- IFs may support the entire cytoskeleton

Figure 13-22