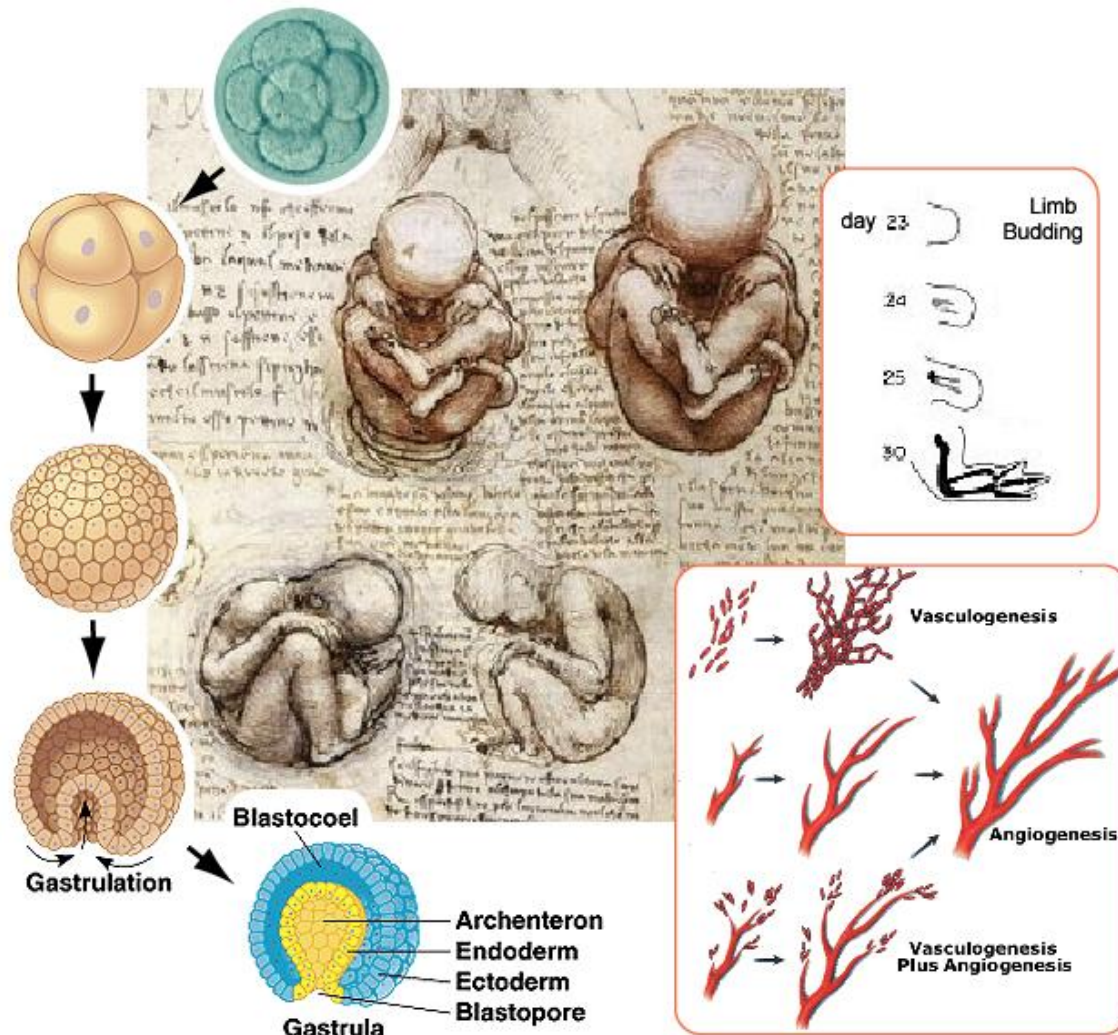ME 411 / ME 511

Biological Frameworks for Engineers

ME 411 / ME 511

Cell Movement
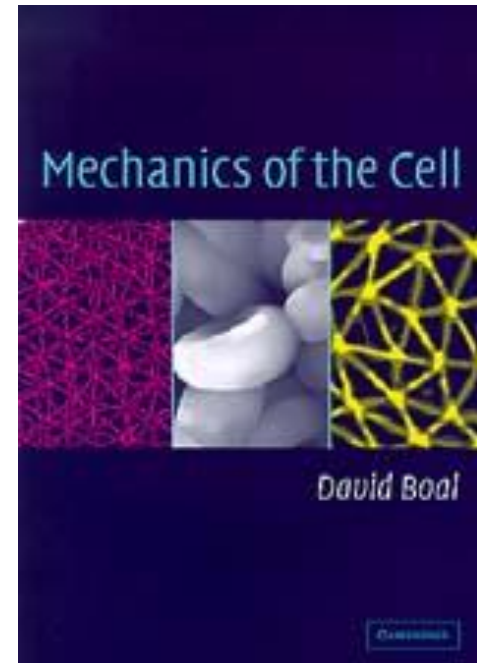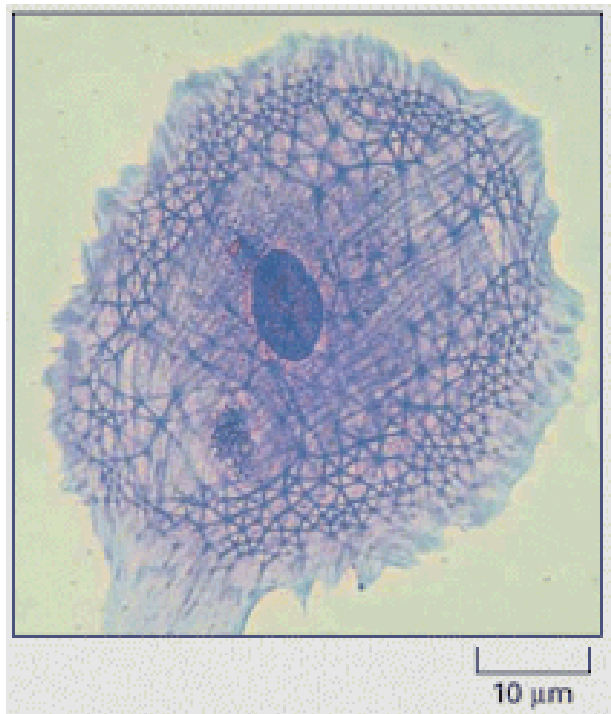
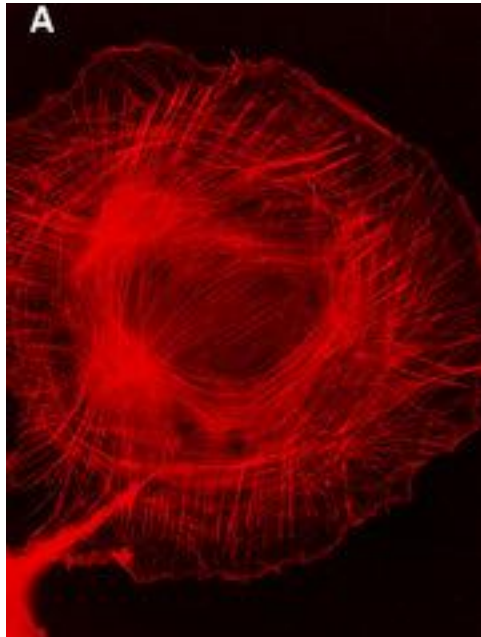# First Movements…

Important Movements

- Development
- Contraction of Cells
- Elongation of Neurons
- Migration of cells
- Flagella and cilia
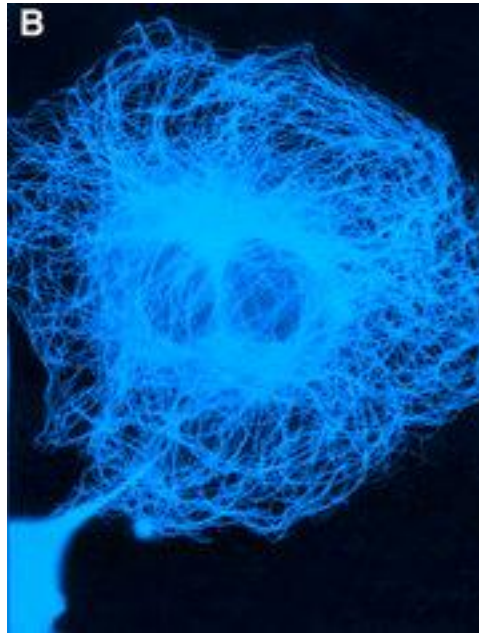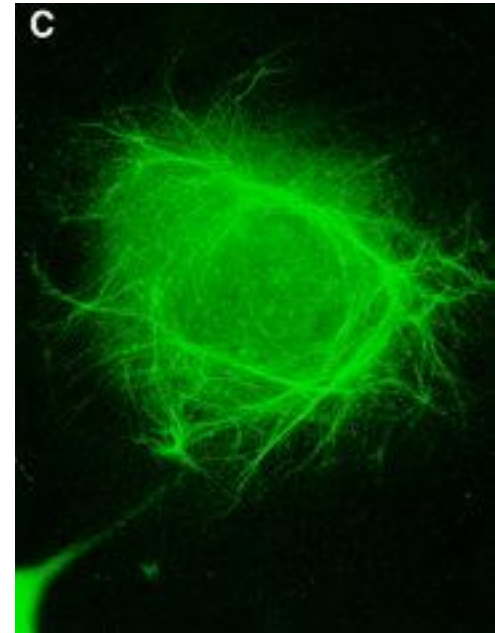- Cytokinesis
- Active Intracellular Transport
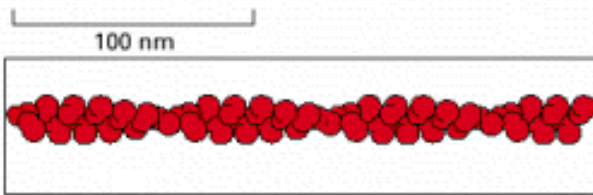
Cytoskeleton

CSK players

Actin   Microtubules (MT)   Intermediate Filaments (IF)

Actin

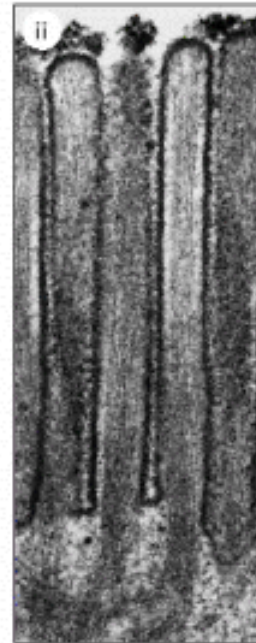Stress Fibers & Focal Adhesions

ACTIN FILAMENTS

100 nm

25 nm

Actin filaments (also known as *microfilaments*) are two-stranded helical polymers of the protein actin. They appear as flexible structures, with a diameter of 5–9 nm, and they are organized into a variety of linear bundles, two-dimensional networks, and three-dimensional gels. Although actin filaments are dispersed throughout the cell, they are most highly concentrated in the *cortex*, just beneath the plasma membrane.

Micrographs courtesy of Roger Craig (i and iv); P.T. Matsudaira and D.R. Burgess (ii); Keith Burridge (iii).
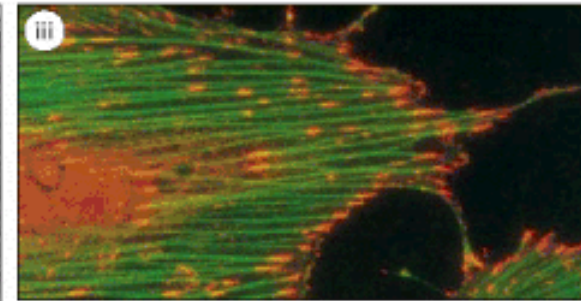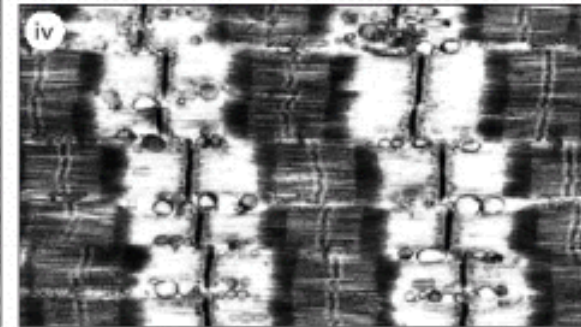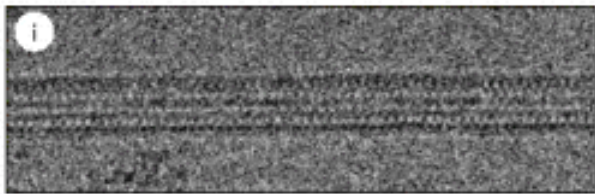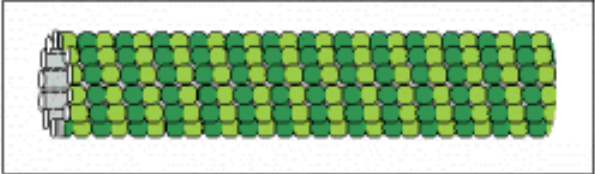
Lamellipodia
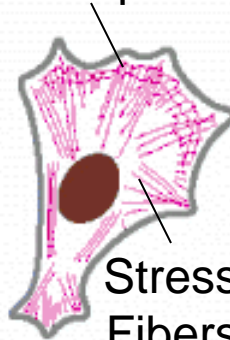
Stress Fibers

Microvilli   Myofibrils

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Microtubules

MICROTUBULES

100 nm

25 nm

Microtubules are long, hollow cylinders made of the protein tubulin. With an outer diameter of 25 nm, they are much more rigid than actin filaments. Microtubules are long and straight and typically have one end attached to a single microtubule-organizing center (MTOC) called a *centrosome*, as shown here.

Micrographs courtesy of Richard Wade (i); D.T. Woodrow and B.W. Linck (ii); David Shima (iii); A. Desai (iv)
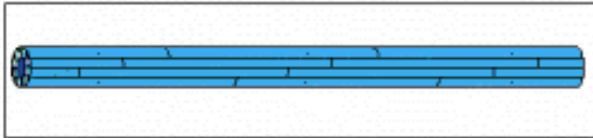
MTOC
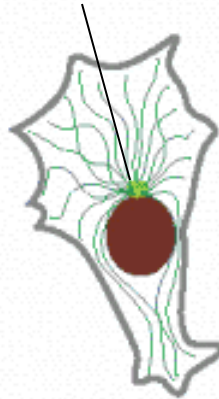
Cilia
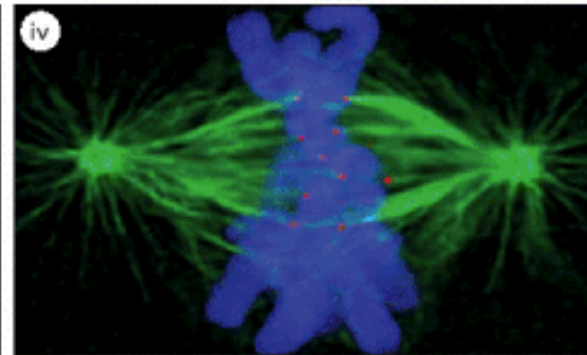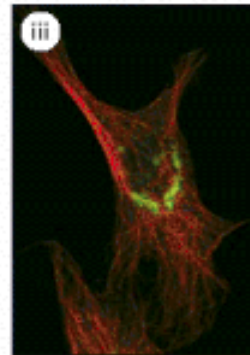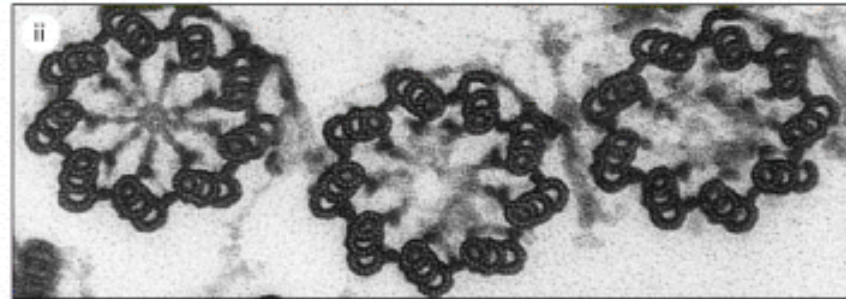
Star-Like   Mitotic Spindle

Intermediate Filaments
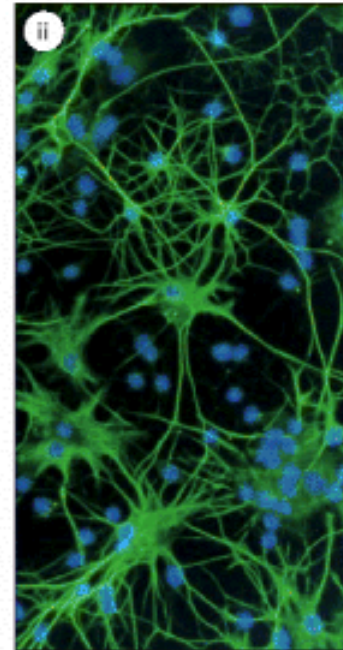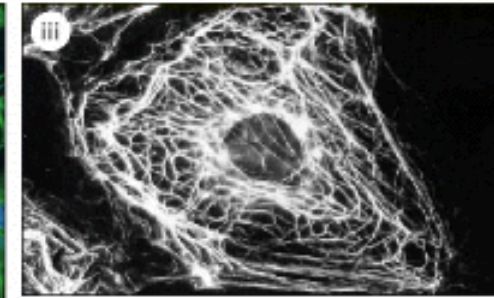

INTERMEDIATE FILAMENTS

100 nm

25 nm

Intermediate filaments are ropelike fibers with a diameter of around 10 nm; they are made of intermediate filament proteins, which constitute a large and heterogeneous family. One type of intermediate filament forms a meshwork called the nuclear lamina just beneath the inner nuclear membrane. Other types extend across the cytoplasm, giving cells mechanical strength. In an epithelial tissue, they span the cytoplasm from one cell-cell junction to another, thereby strengthening the entire epithelium.
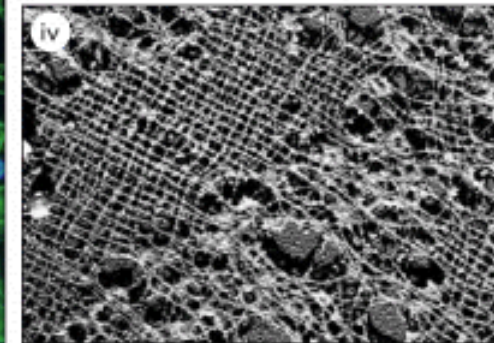
Micrographs courtesy of Roy Quinlan (i); Nancy L. Kedersha (ii); Mary Osborn (iii); Ueli Aebi (iv).

Strength

Axons   Nuclear Lamina

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Mechanism of Movement

Extend… Stick…
Slide … Unstick…

Focal adhesion

Direction of movement ⟶

1 Extension

Lamellipodium

2 Adhesion

New adhesion

3 Translocation

Cell body movement ⟶

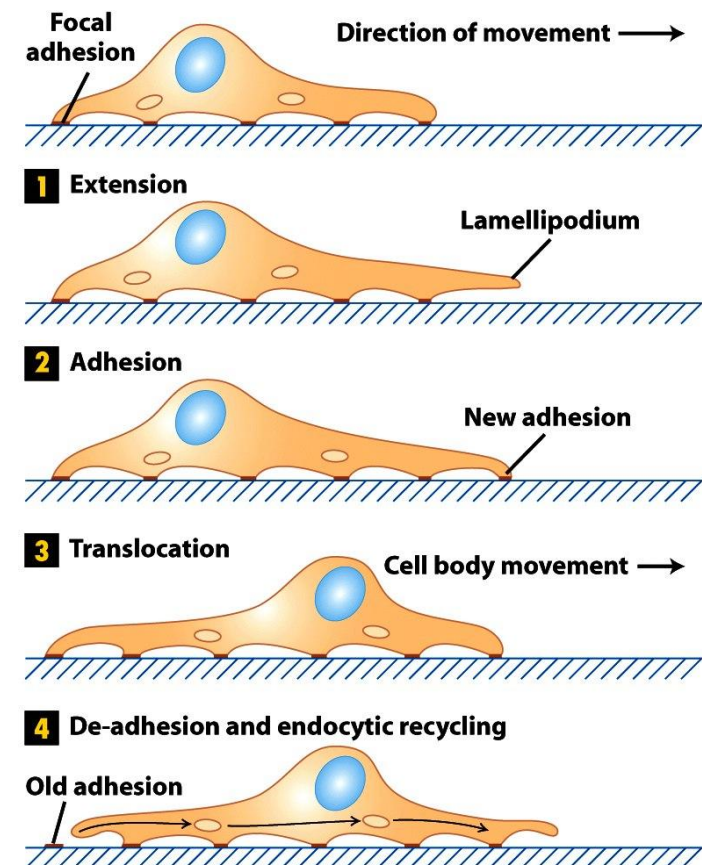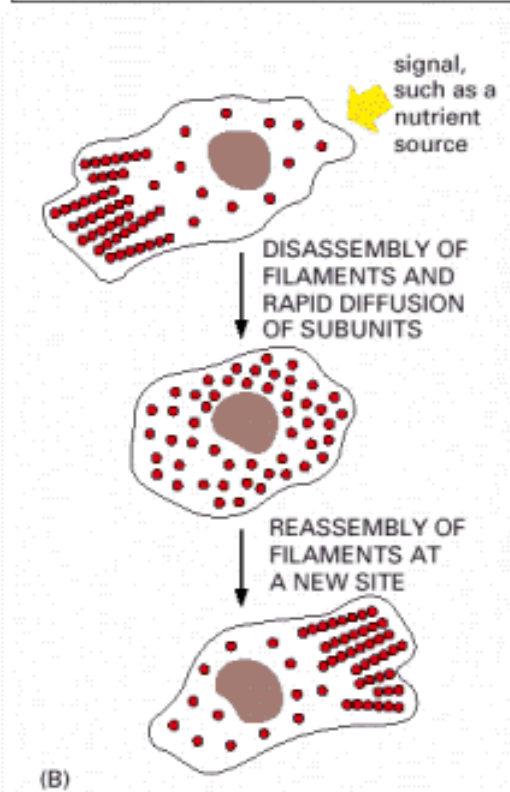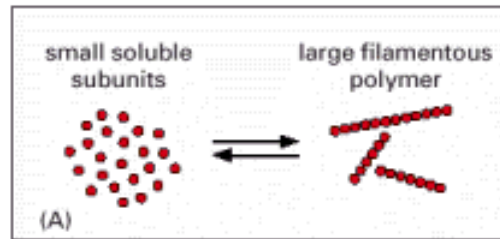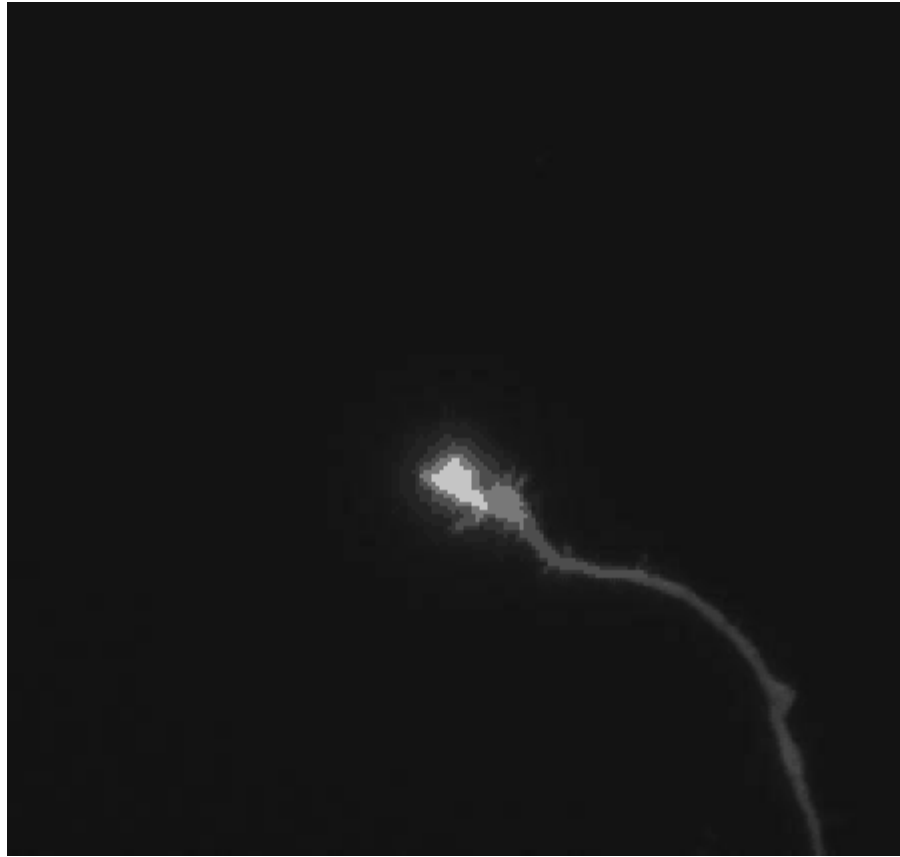**4** De-adhesion and endocytic recycling

Old adhesion

Figure 17-38
Molecular Cell Biology, Sixth Edition
© 2008 W. H. Freeman and Company

Polarization

small soluble subunits ⇌ large filamentous polymer

(A)

signal, such as a nutrient source

DISASSEMBLY OF FILAMENTS AND RAPID DIFFUSION OF SUBUNITS
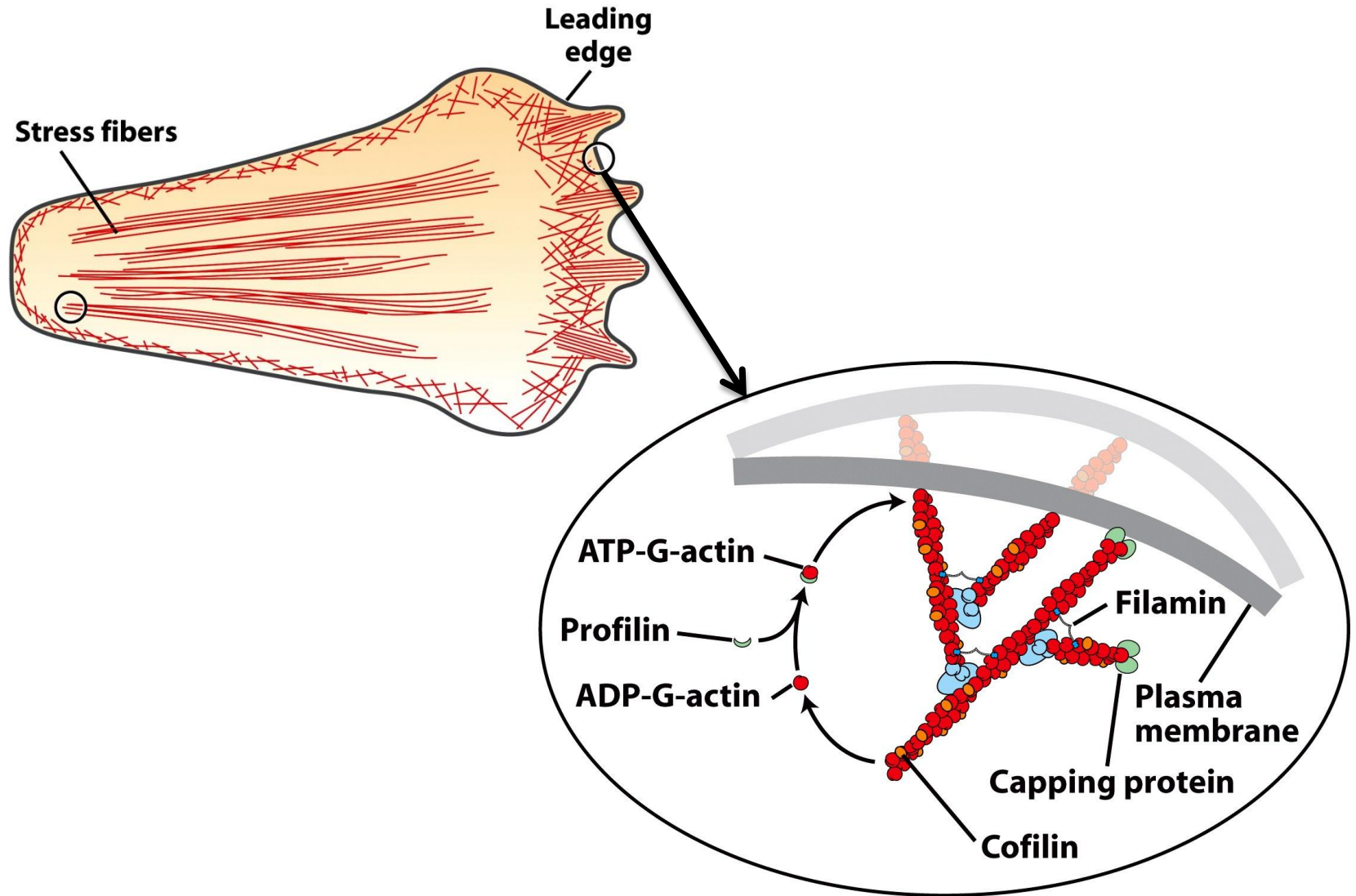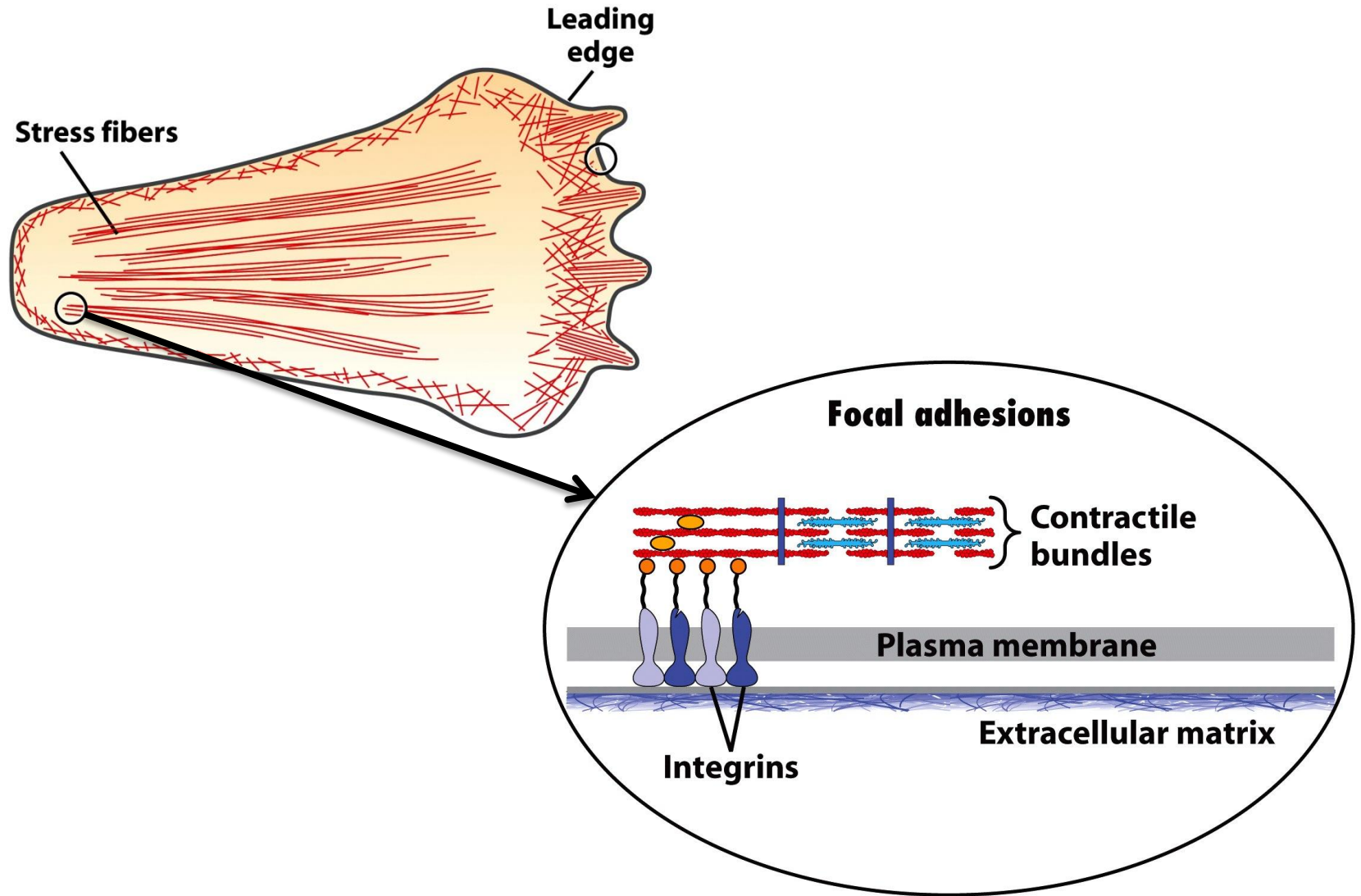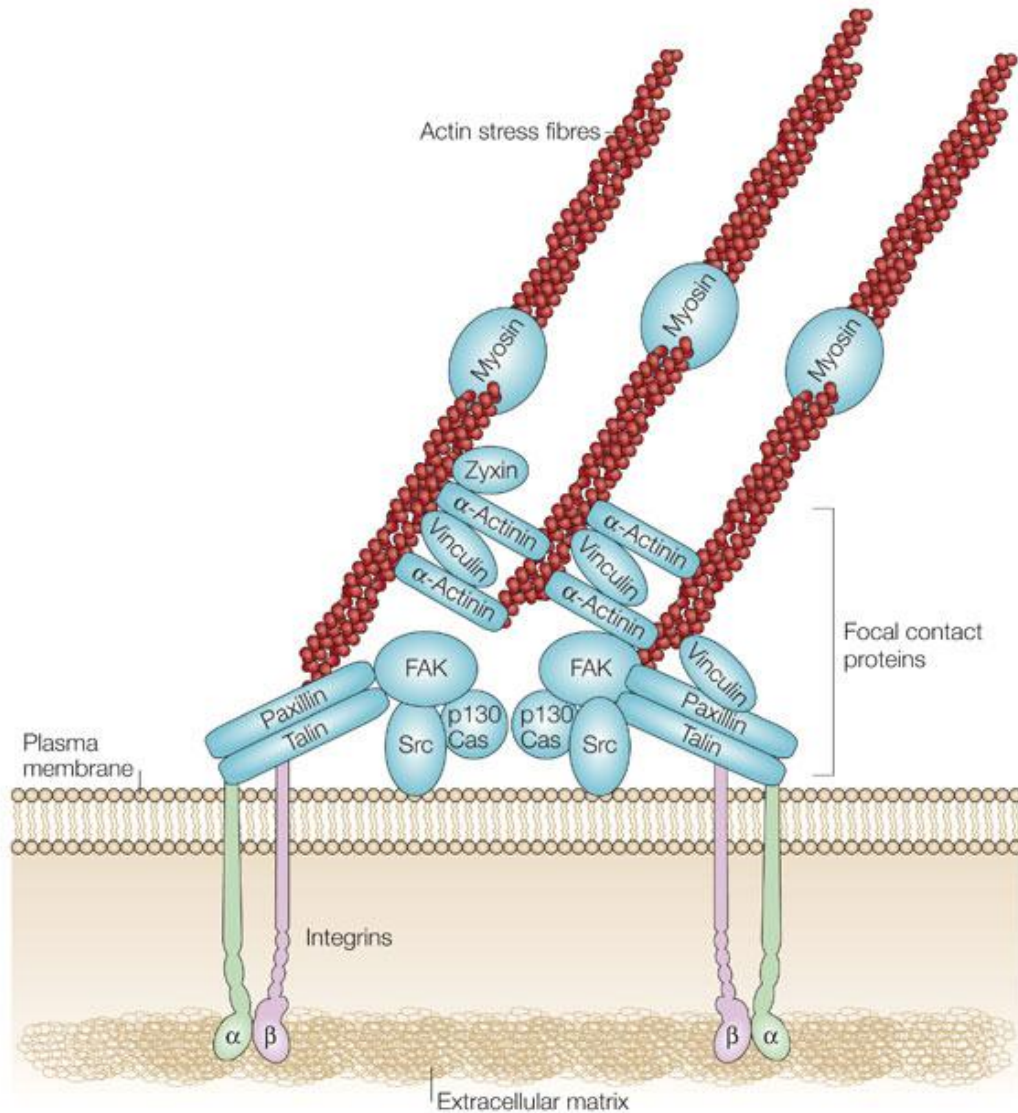
REASSEMBLY OF FILAMENTS AT A NEW SITE

(B)

Axon Movement

Protrusion
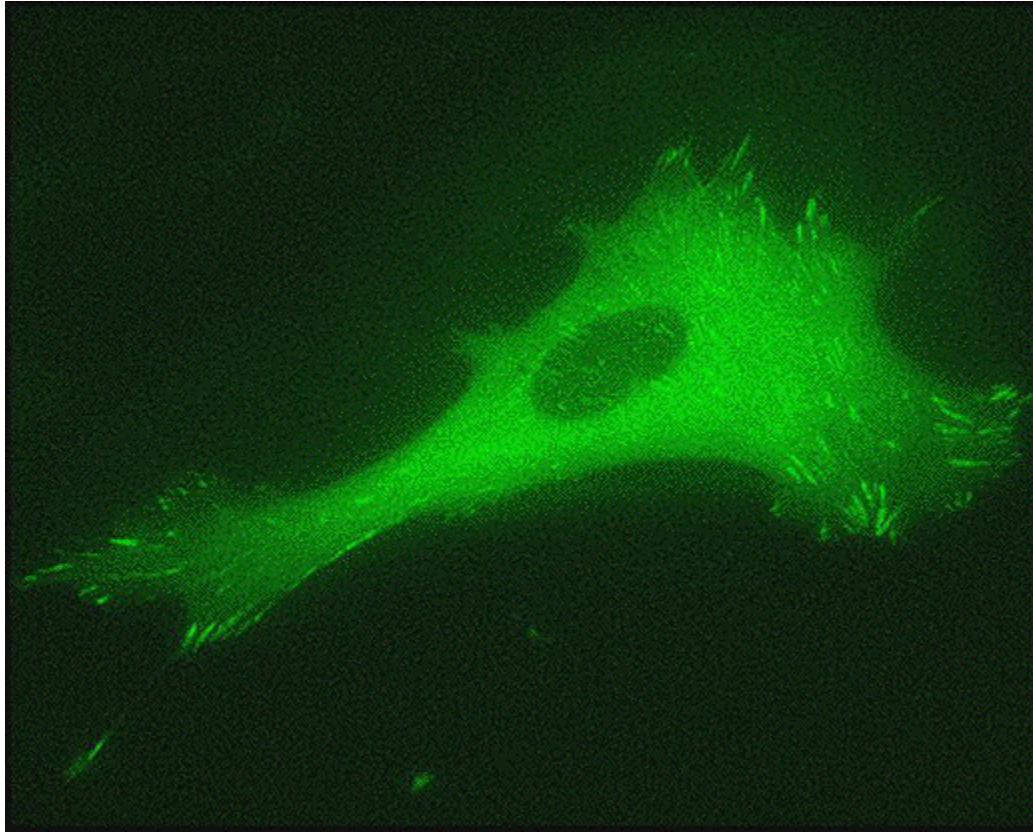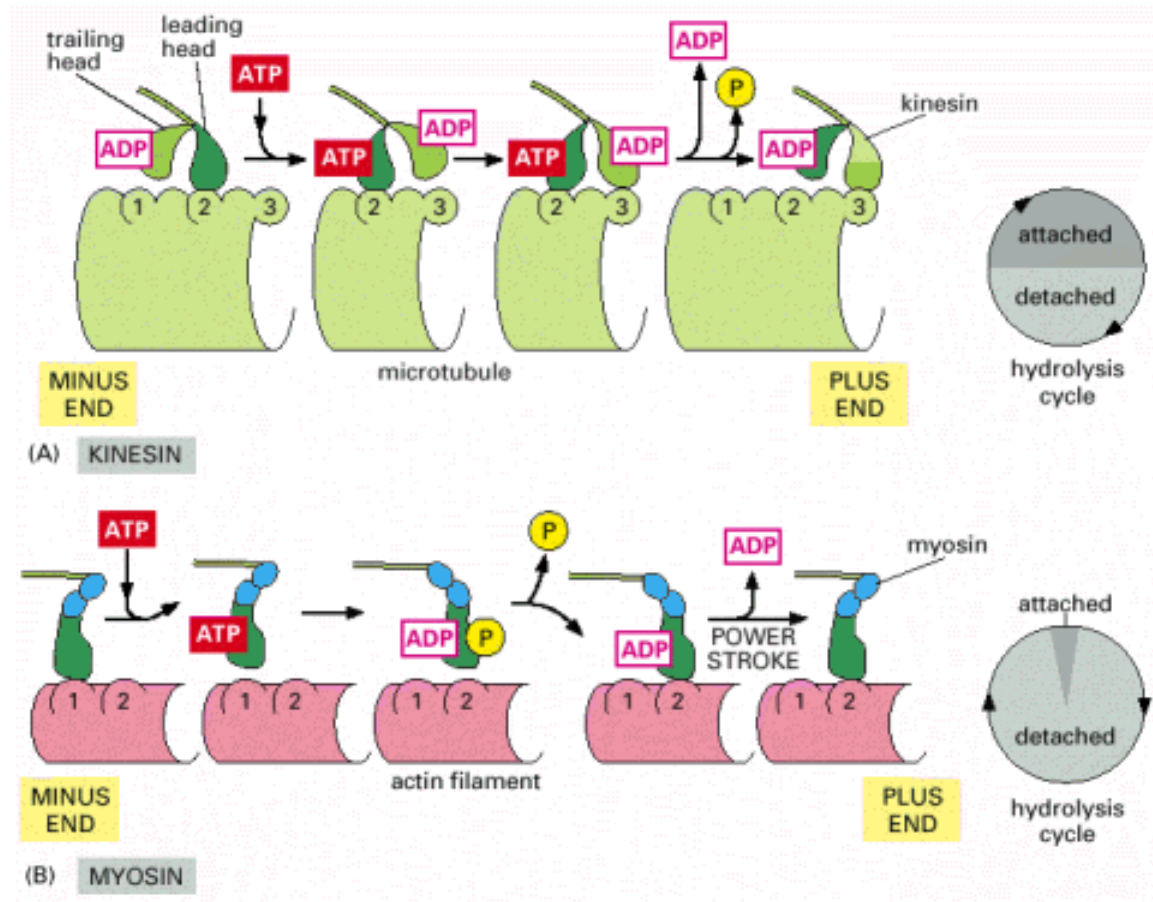
Adhesion

Focal Adhesions

Actin stress fibres

Myosin

Zyxin
α-Actinin
Vinculin
α-Actinin

FAK
Paxillin
Talin
Src p130 Cas p130 Cas Src

α-Actinin
Vinculin
α-Actinin

Vinculin
Paxillin
Talin
FAK

Focal contact proteins

Plasma membrane

Integrins
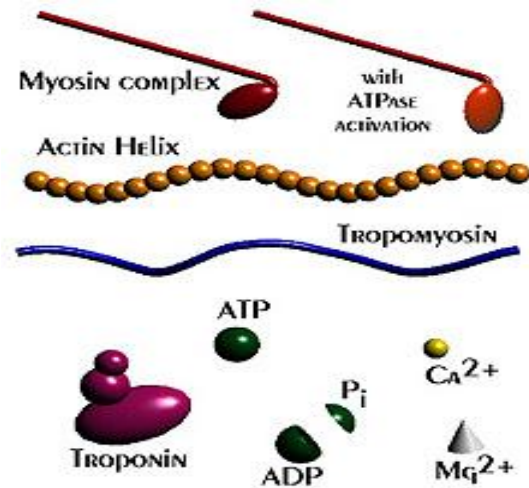
Extracellular matrix

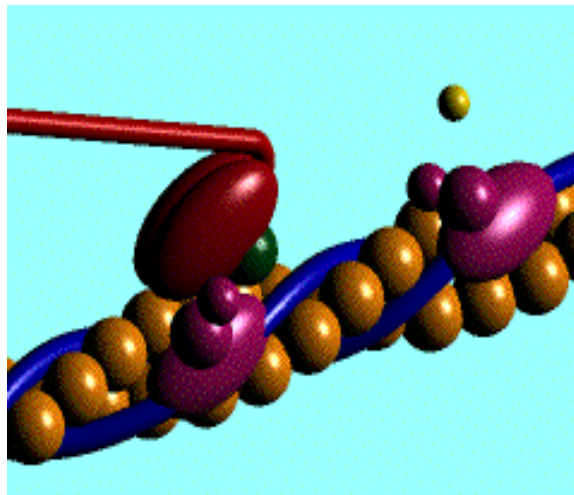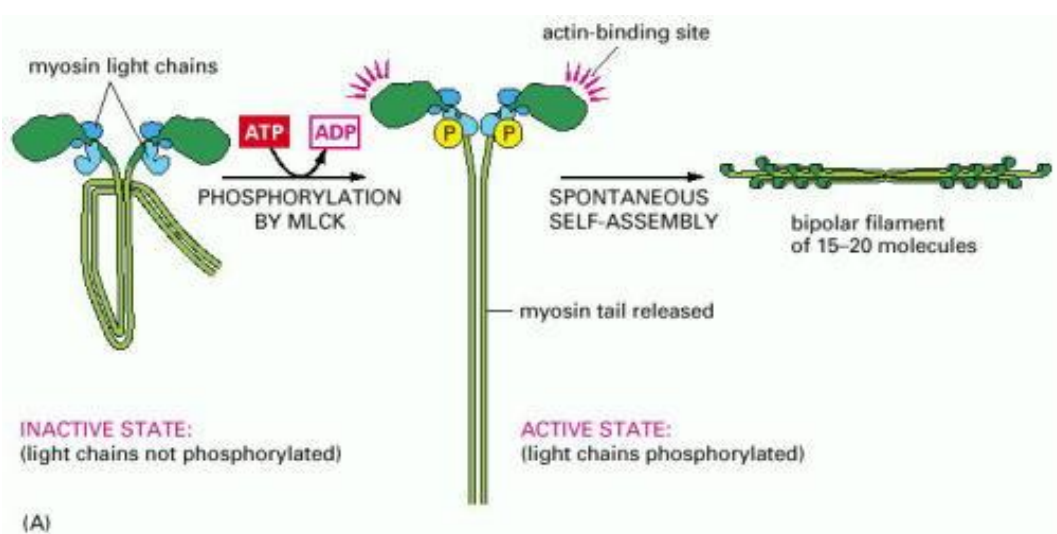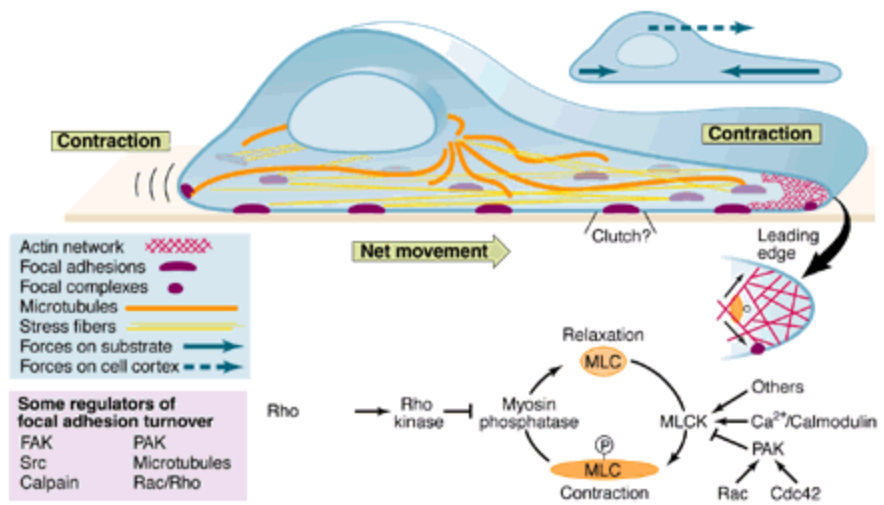α β   β α

Focal Adhesions

Motor Proteins

# Motor Proteins

Activation

Assembly / Disassembly

ON RATES AND OFF RATES

A linear polymer of protein molecules, such as an actin filament or a microtubule, assembles (polymerizes) and disassembles (depolymerizes) by the addition and removal of subunits at the ends of the polymer. The rate of addition of these subunits (called monomers) is given by the rate constant k_{on}, which has units of M^{-1} sec^{-1}. The rate of loss is given by k_{off} (units of sec^{-1}).

polymer (with n subunits)   subunit

+

k_{on} k_{off}

polymer (with $n+1$ subunits)

$M = mol / L$
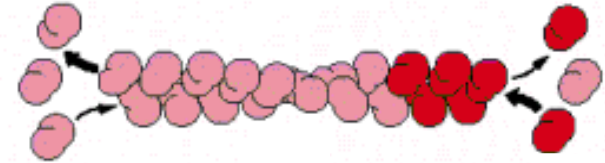
Critical Concentration

C = conc. of free subunits
Added to filament = $k_{on} * C$
Removed to filament = k_{off}

As filament grows, C drops until it reaches a critical value, C_c (critical concentration). At this equilibrium:

$$k_{on} * C = k_{off}$$

→ $C_c = k_{off} / k_{on}$
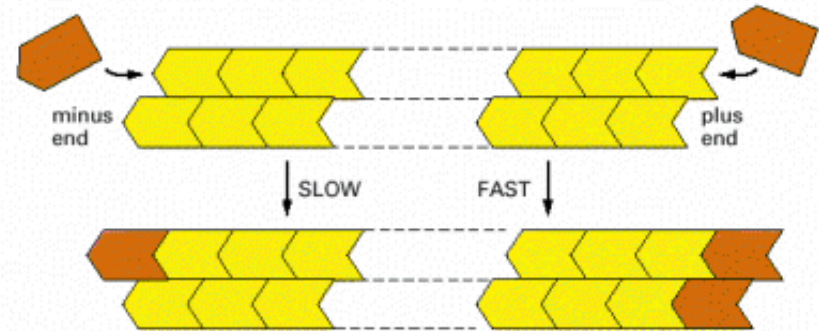
UNIVERSITY OF WASHINGTON

Assembly / Disassembly

PLUS AND MINUS ENDS

The two ends of an actin filament or microtubule polymerize at different rates. The fast-growing end is called the plus end, whereas the slow-growing end is called the minus end. The difference in the rates of growth at the two ends is made possible by changes in the conformation of each subunit as it enters the polymer.

free subunit → subunit in polymer

This conformational change affects the rates at which subunits add to the two ends.

Even though k_{on} and k_{off} will have different values for the plus and minus ends of the polymer, their ratio k_{off}/k_{on}—and hence C_c—must be the same at both ends for a simple polymerization reaction (no ATP or GTP hydrolysis). This is because exactly the same subunit interactions are broken when a subunit is lost at either end, and the final state of the subunit after dissociation is identical. Therefore, the ΔG for subunit loss, which determines the equilibrium constant for its association with the end, is identical at both ends: if the plus end grows four times faster than the minus end, it must also shrink four times faster. Thus, for $C > C_c$, both ends grow; for $C < C_c$, both ends shrink.
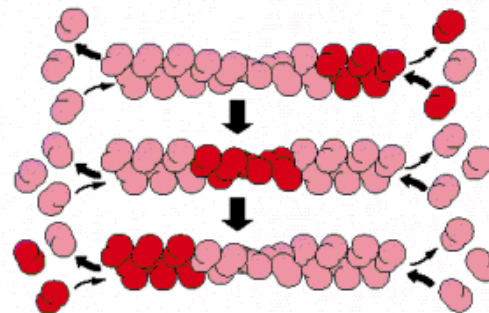
The nucleoside triphosphate hydrolysis that accompanies actin and tubulin polymerization removes this constraint.

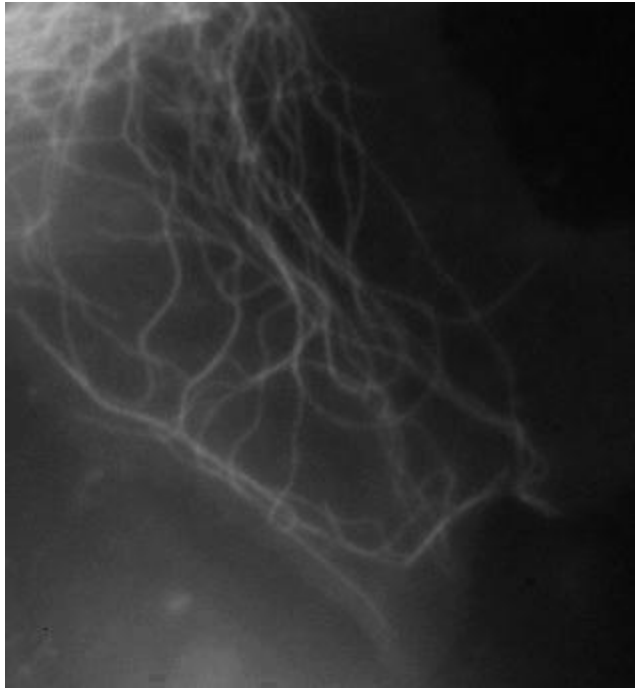minus end   plus end
SLOW   FAST
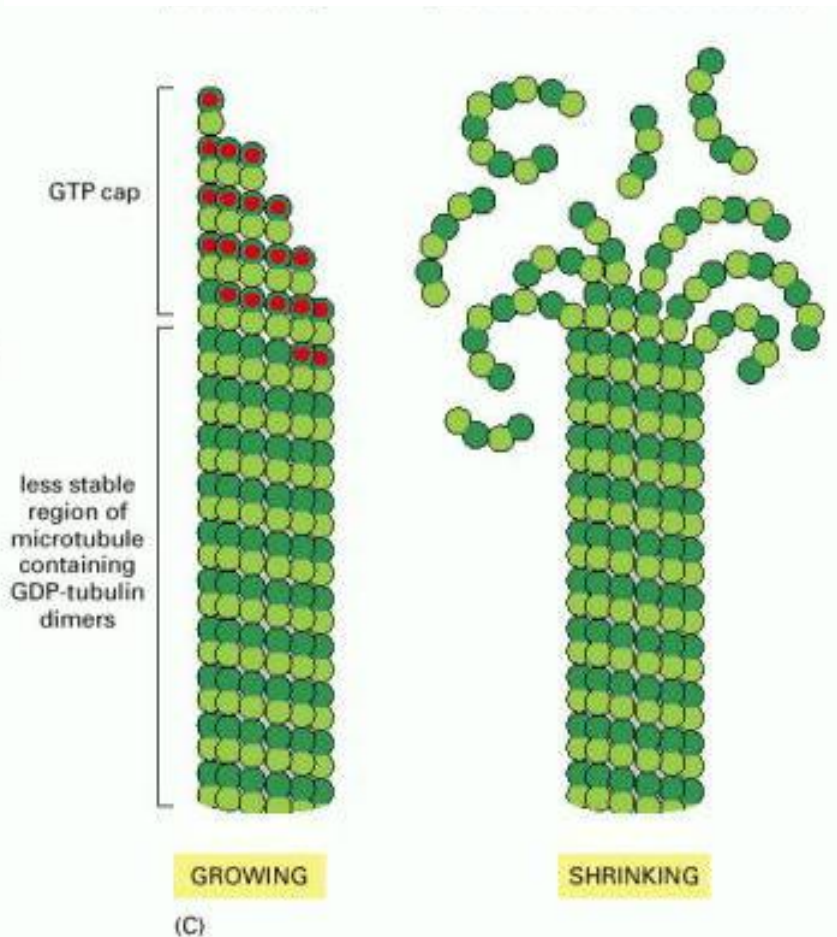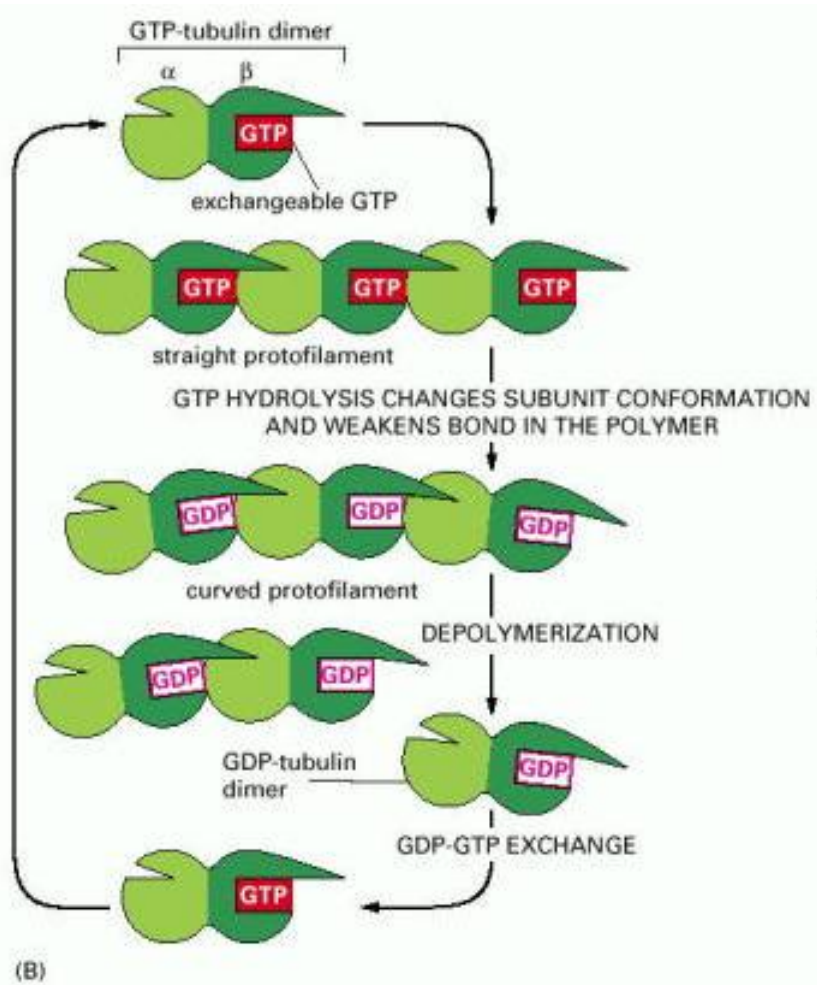
Assembly / Disassembly
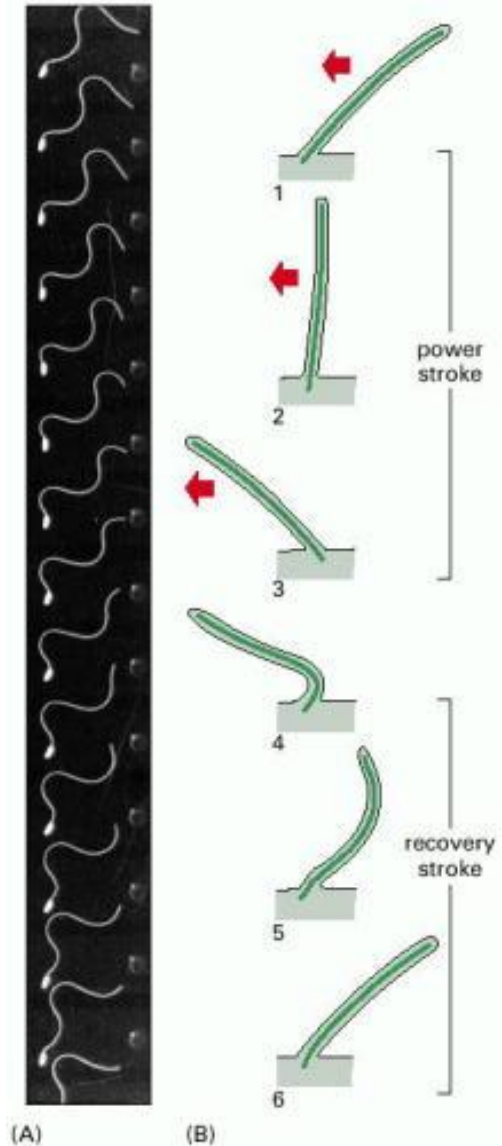
Polymerization
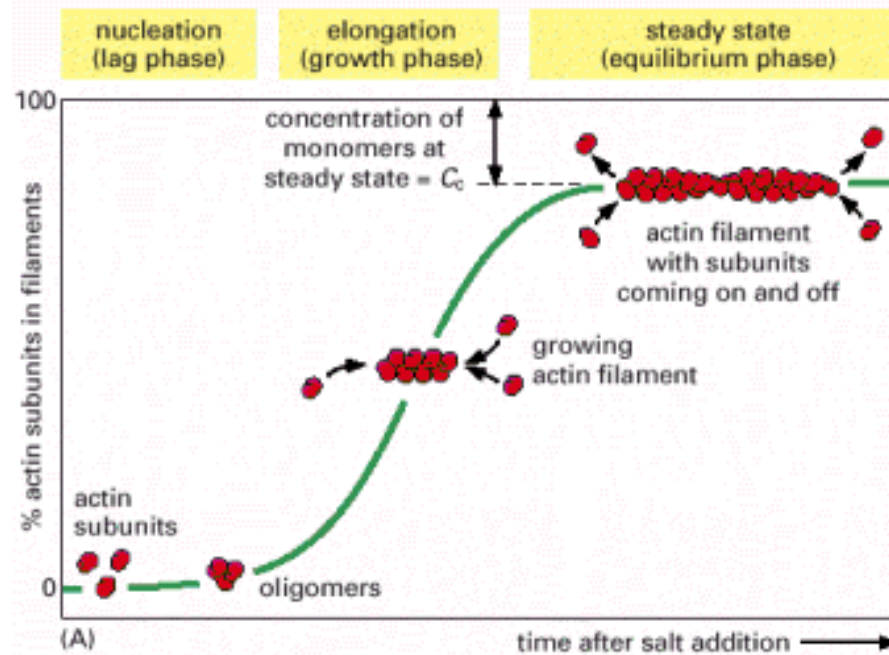
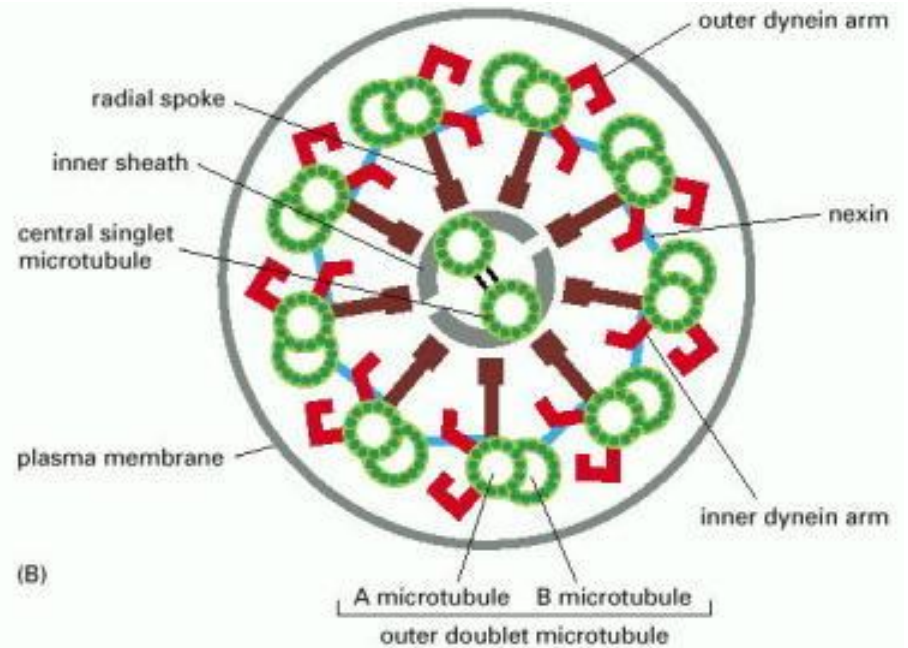Treadmilling

MT Dynamic Instability
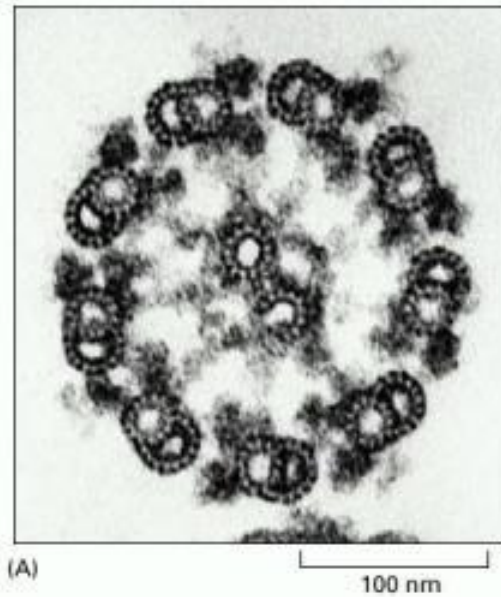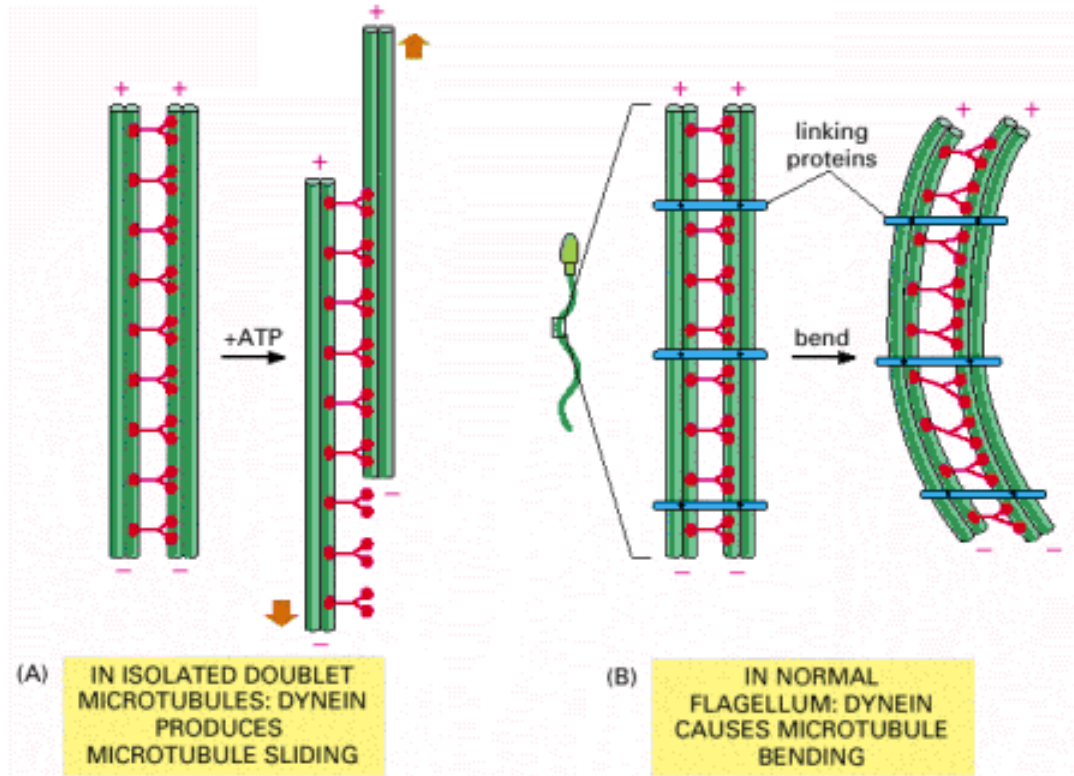

CHO Cytoplast
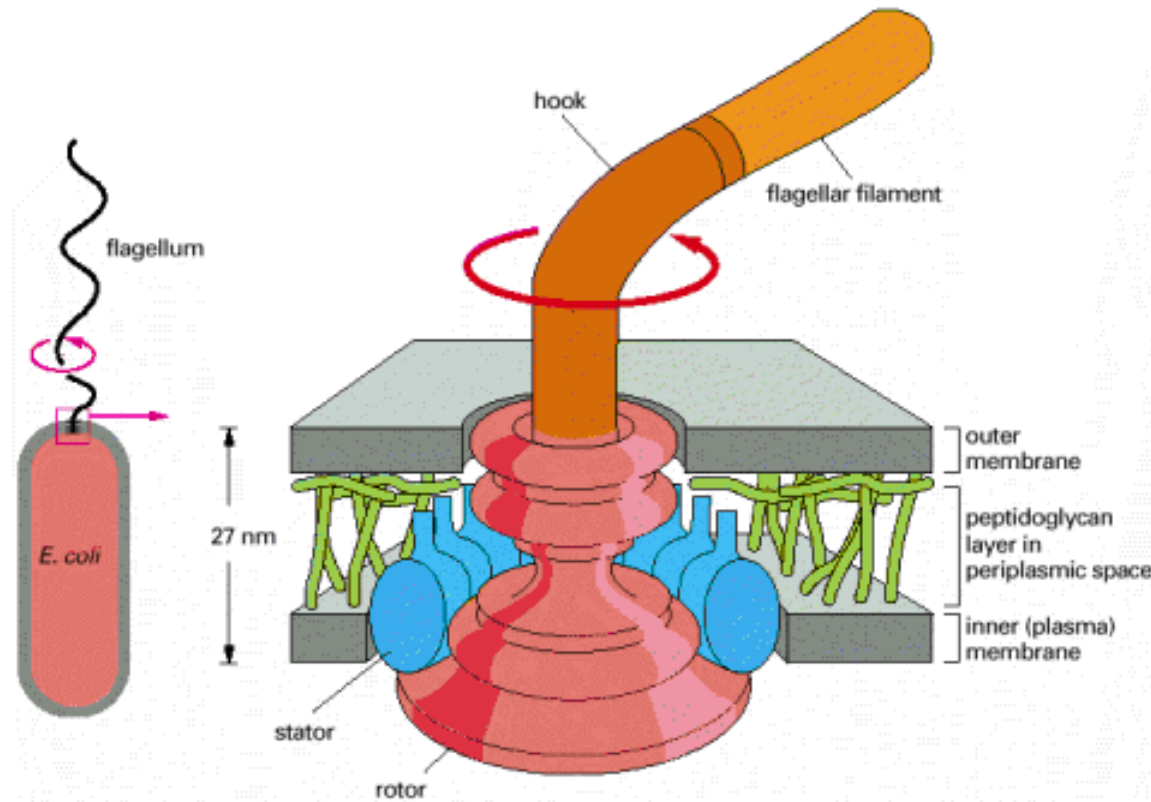with
Centrosome

MT Instability

Flagella & Cilia

Axoneme

Dynein Bending

(A) IN ISOLATED DOUBLET MICROTUBULES: DYNEIN PRODUCES MICROTUBULE SLIDING
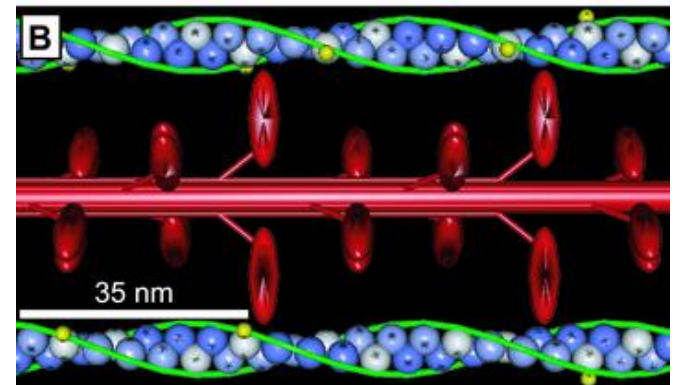
(B) IN NORMAL FLAGELLUM: DYNEIN CAUSES MICROTUBULE BENDING

Bacteria Flagellar

Muscle Cells
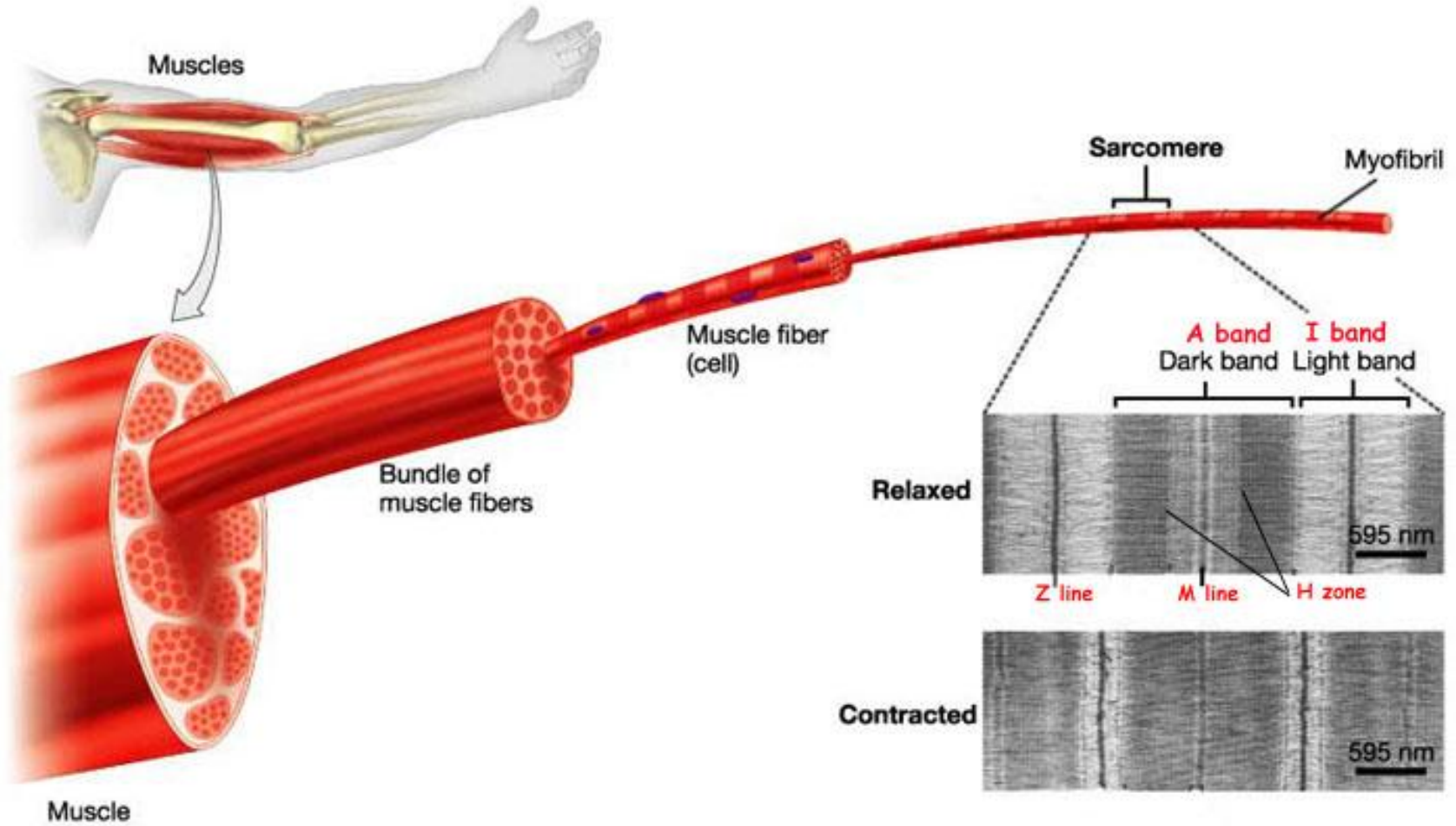
Sarcomere

Cross-Section

thin filament   thick filament

Z disc

35 nm

35 nm

Contraction

Questions?