6. Cytoskeleton and Cell Motility

Undergraduate – Graduate
Histology Lecture Series

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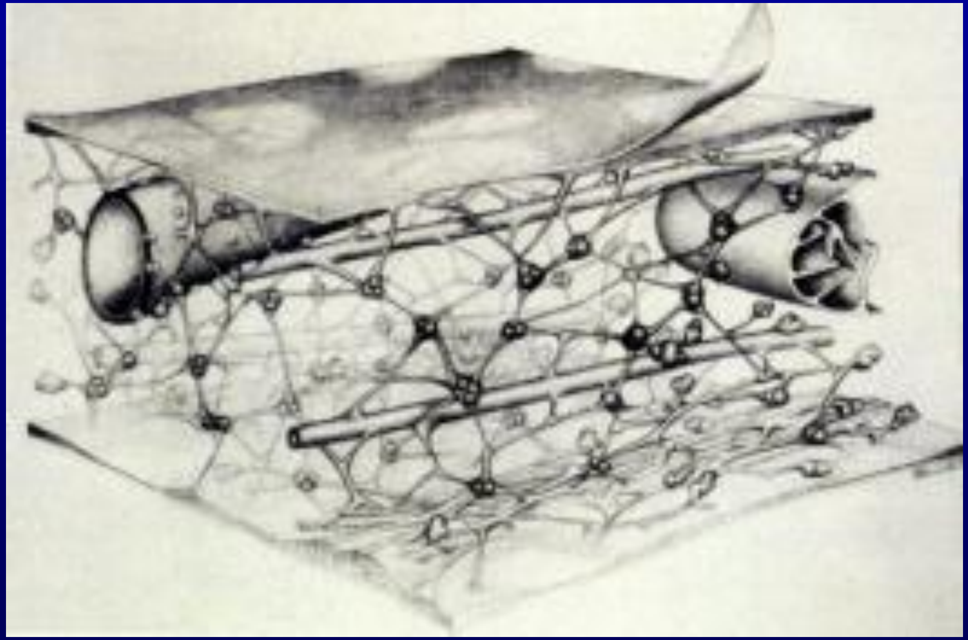
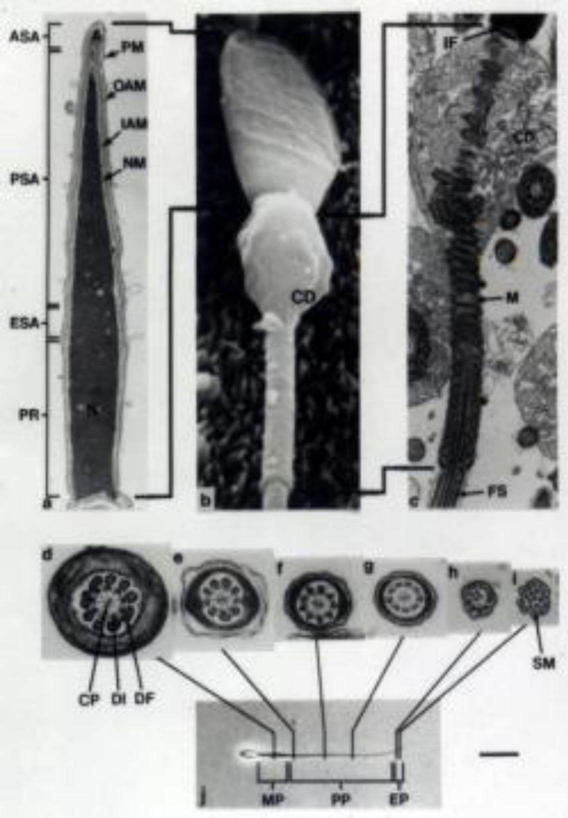
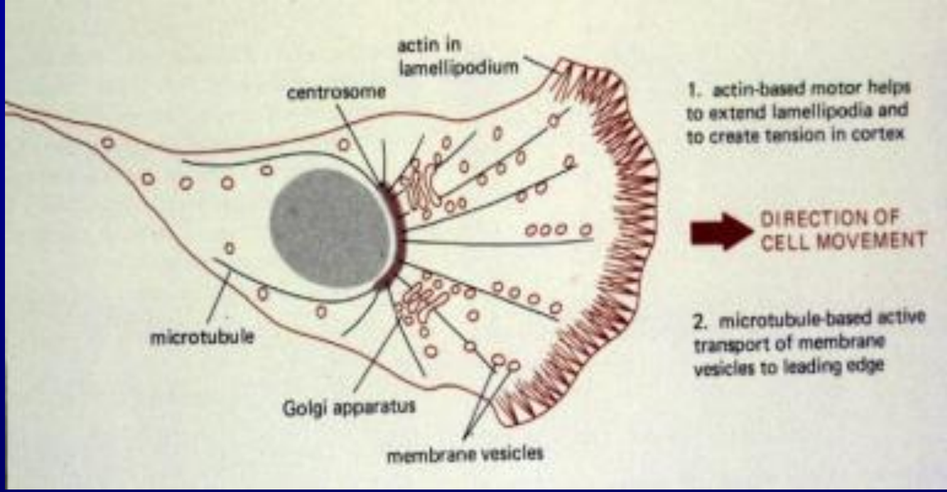
VIBS 443 and VIBS 602







Objective

To survey the structure, protein composition, and functions of a complex network of cytoplasmic filaments known collectively as the cytoskeleton.

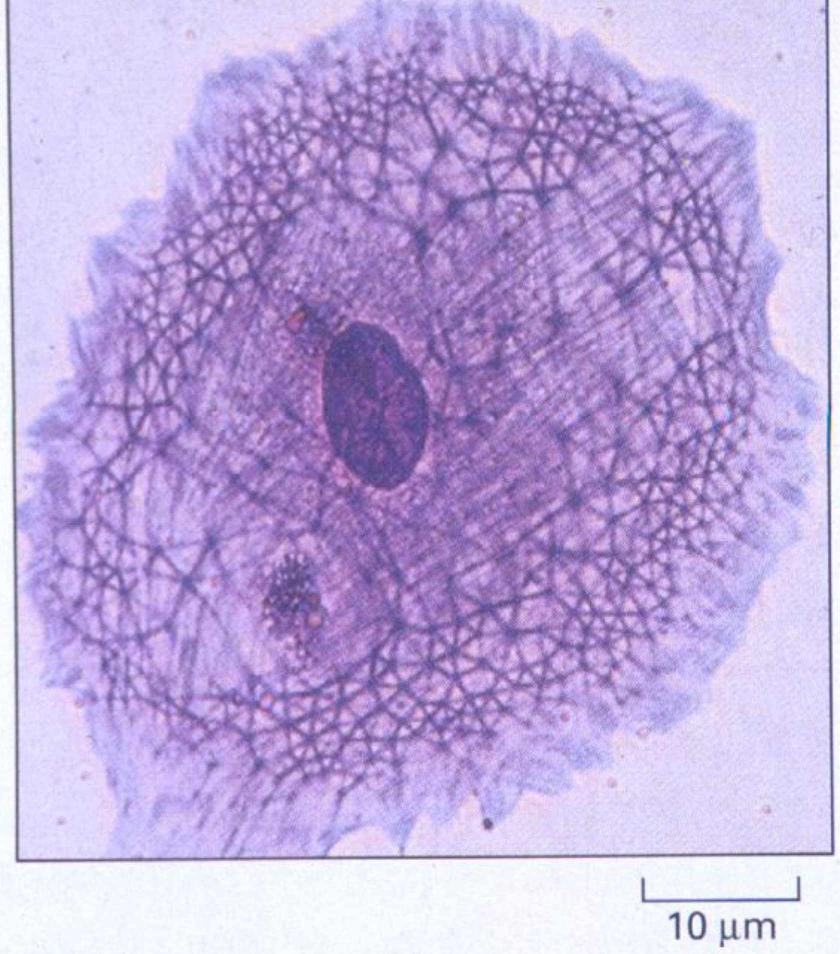
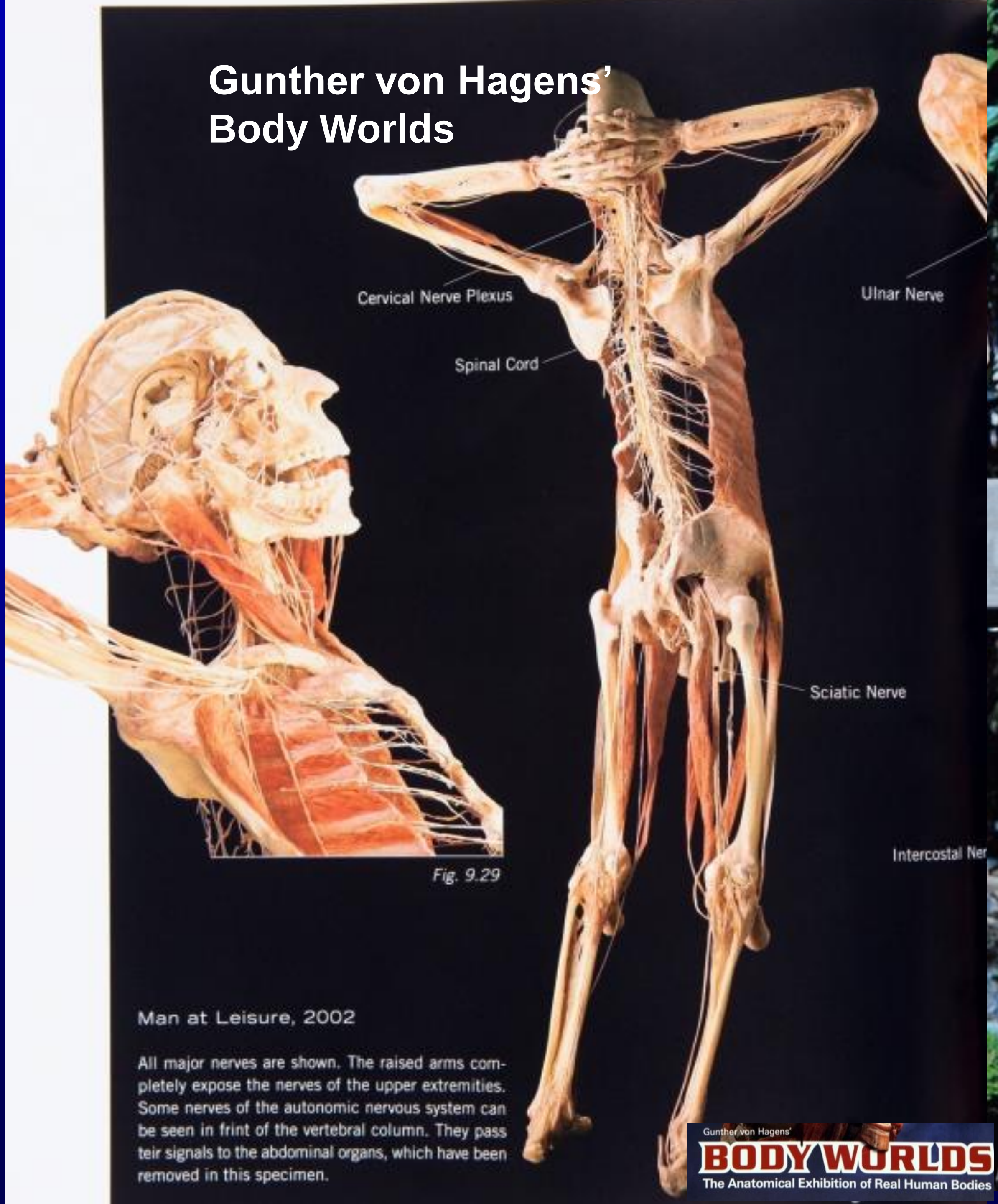


Figure 16–1 The cytoskeleton. A cell in culture has been fixed and stained with Coomassie blue, a general stain for proteins. Note the variety of filamentous structures that extend throughout the cell. (Courtesy of Colin Smith.)

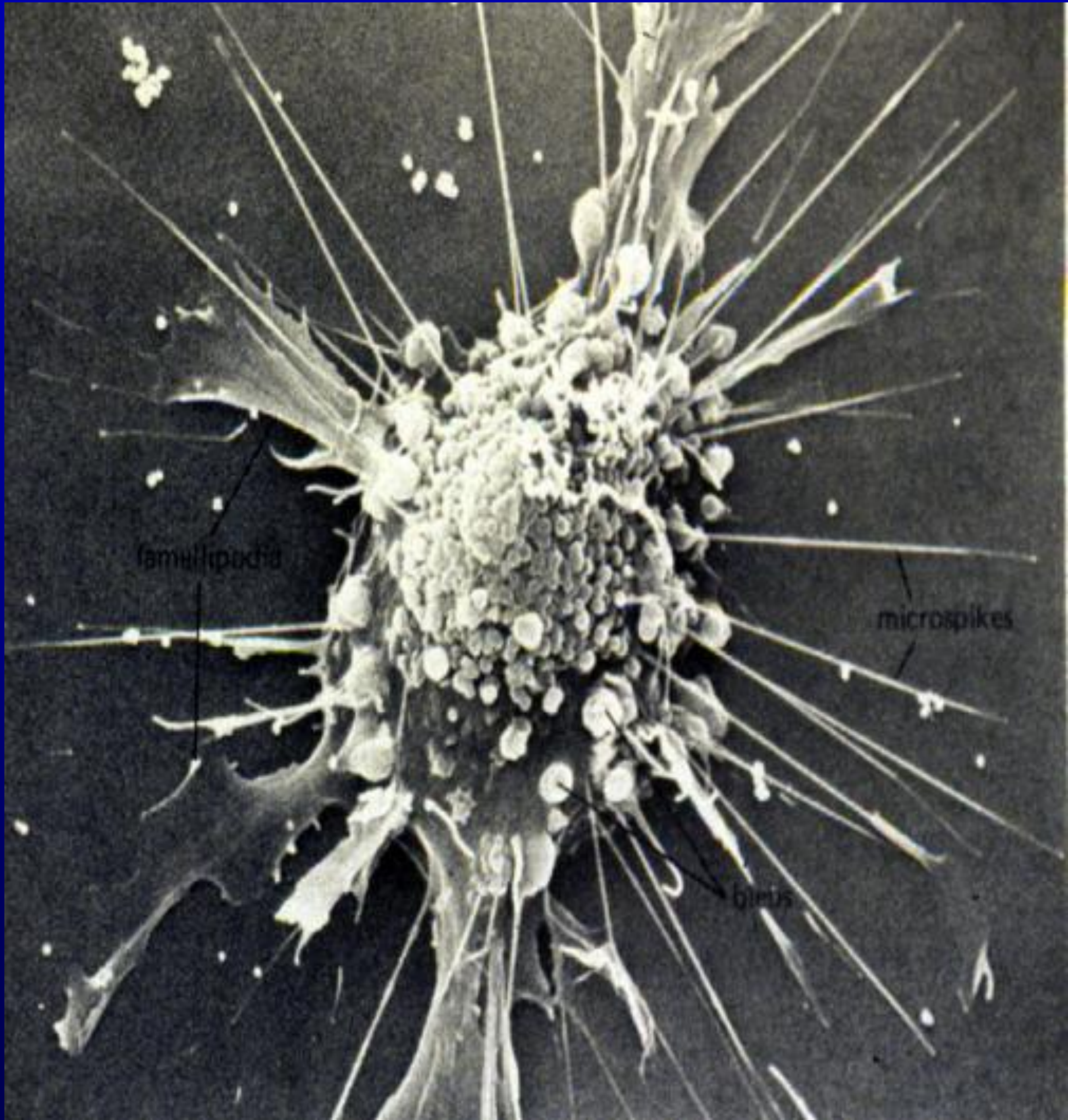
Gunther von Hagens' Body Worlds



Cytoskeleton

Cells must perform tasks requiring **structural framework**

Cell maintains shape
Changes shape
Endocytosis and phagocytosis
Stabilization of cell attachment



Cytoskeleton

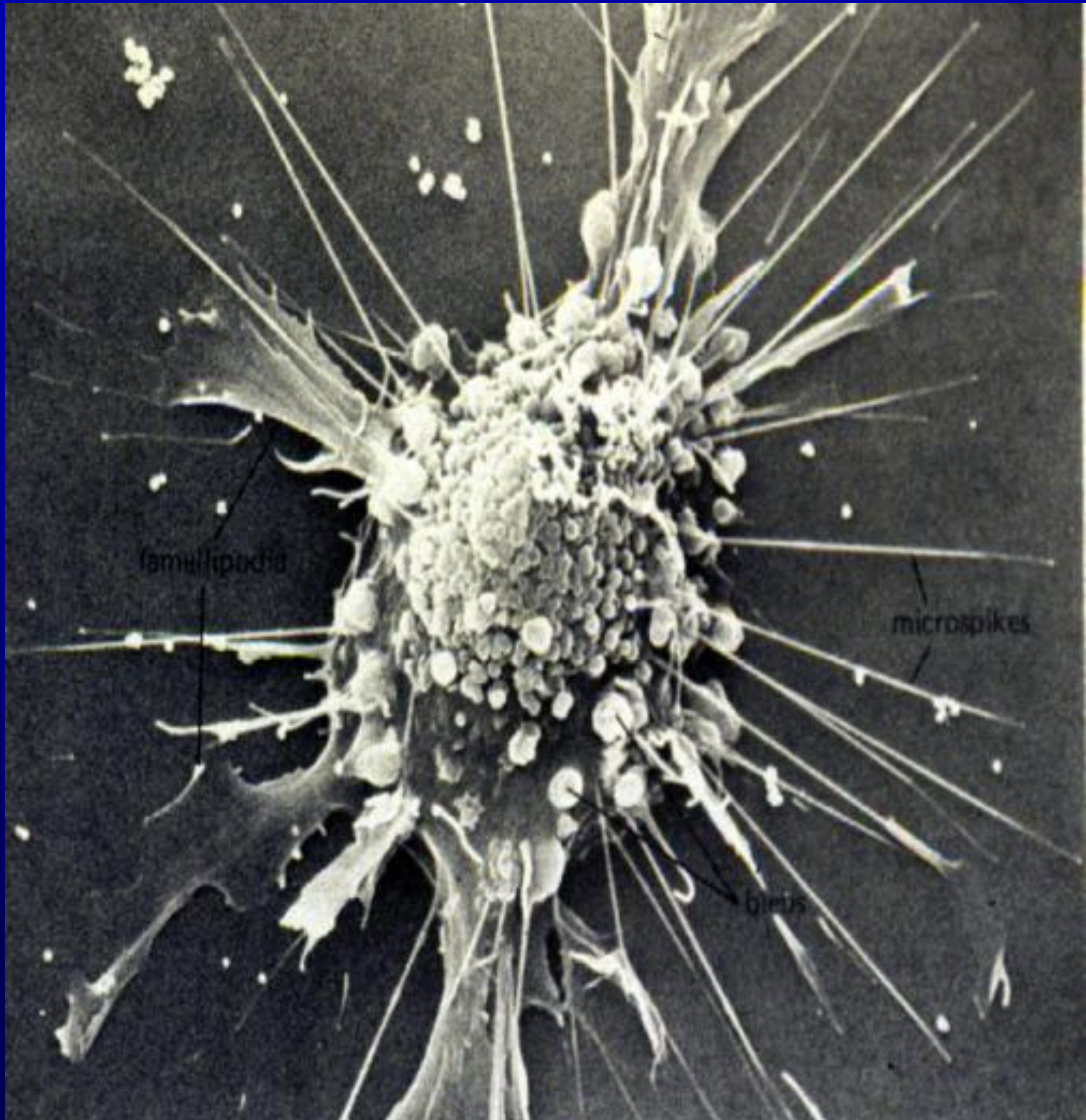
Cells must perform tasks: requiring <u>contractile machinery</u>

Transport vesicles, organelles, and chromosomes

Divide cytoplasm

Specialization of cell surface

Cell motility



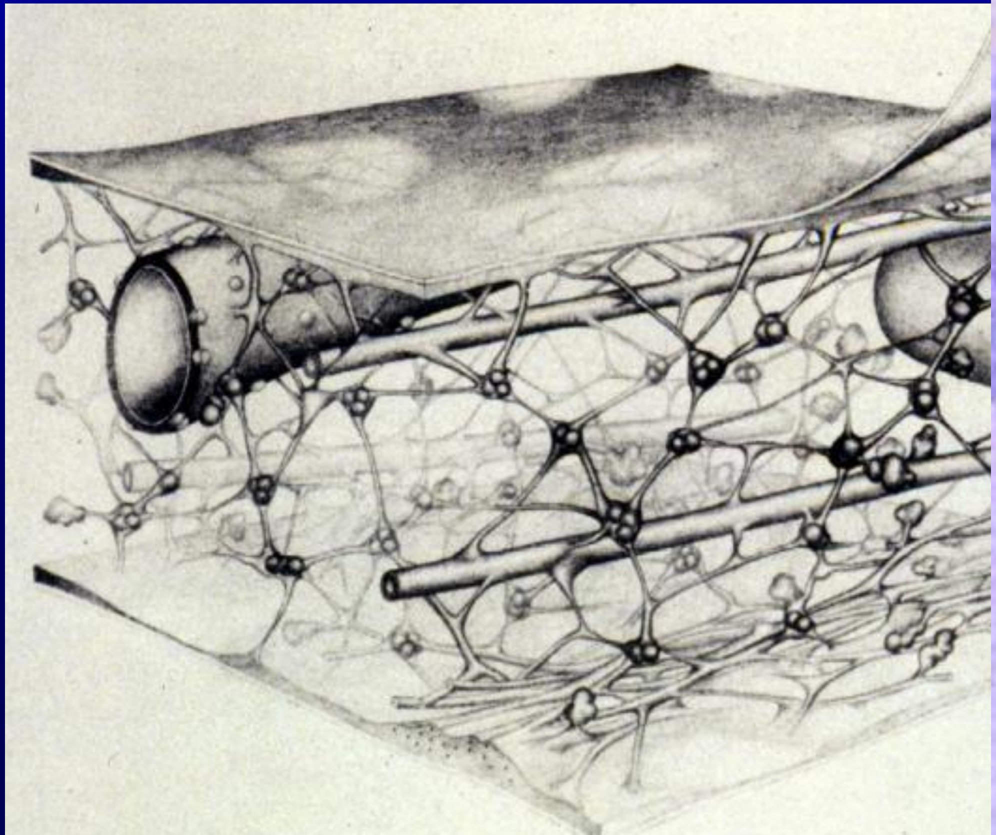
Cytoskeleton

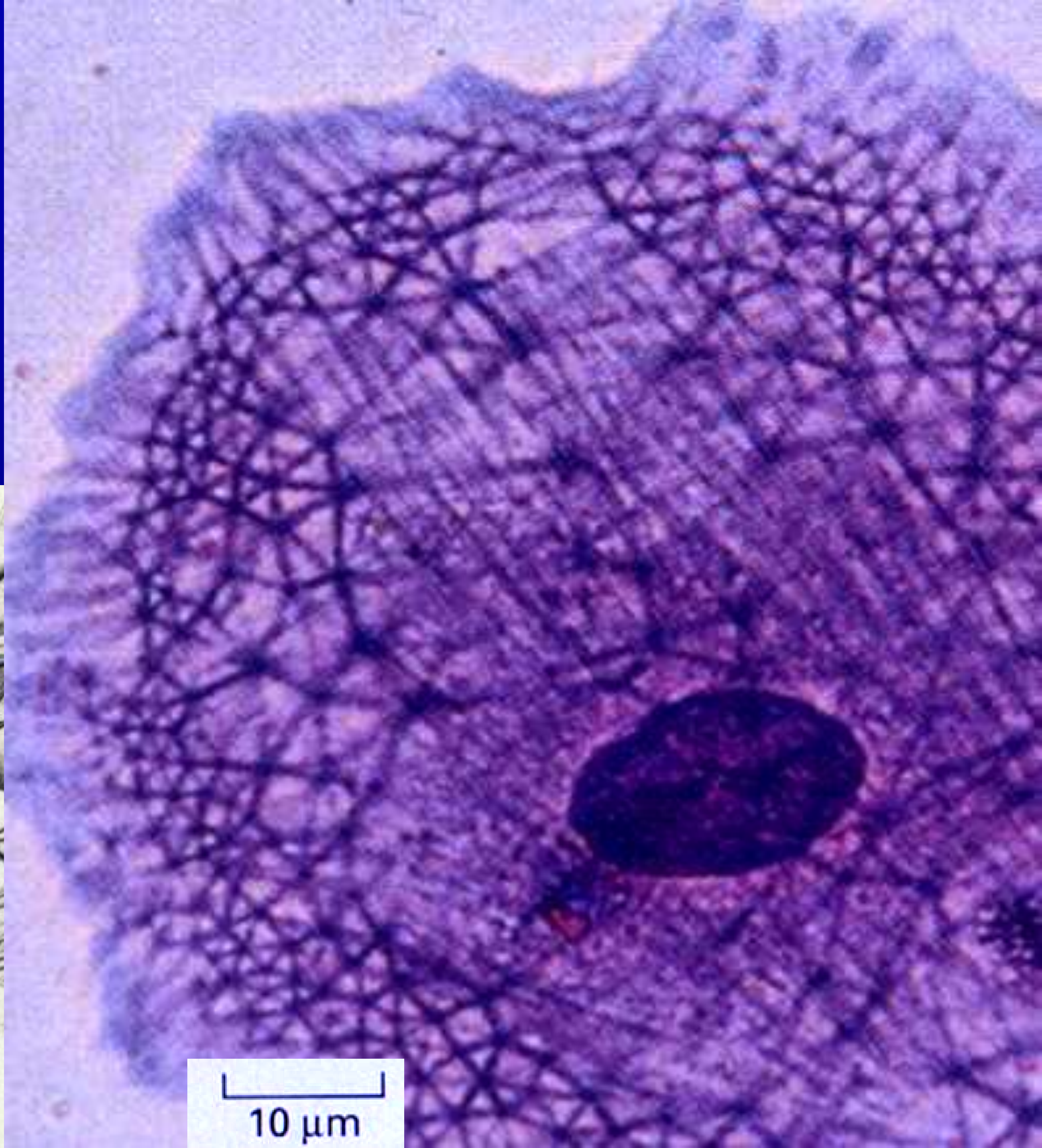
Non-membranous organelles

Microtubules (25 nm)

Microfilament (6 nm)

Intermediate filament (10 nm)





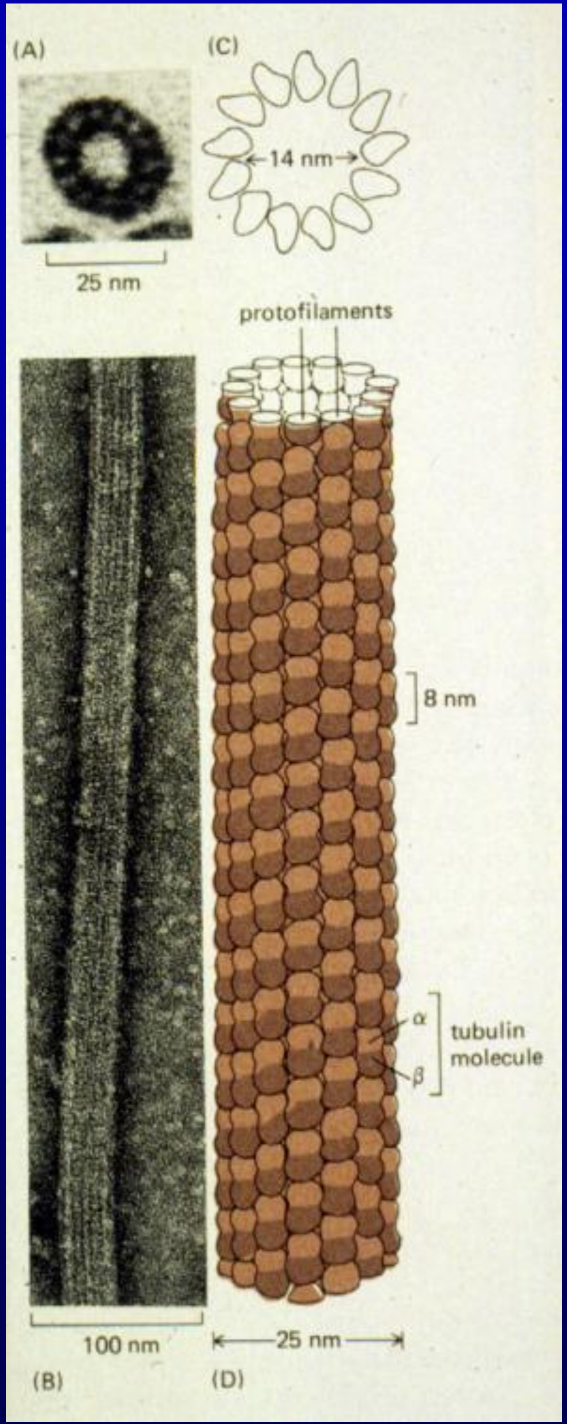
Microtubules

Composed of tubulin - highly conserved protein

Dimer - alpha and beta tubulin protofilament – 13 in a microtubule

Labile - delicate equilibrium of assembled and disassembled

MICROTUBULE ASSOCIATED PROTEINS = MAPs



http://www.youtube.com/watch?v=PvDlilBgoSs&feature=related

- http://www.youtube.com/watch?v=5GATtn4edeU

Microtubule ultrastructure

Cytoplasmic microtubules

Axonemes – cilia and flagella – 9 doublets and centered pair

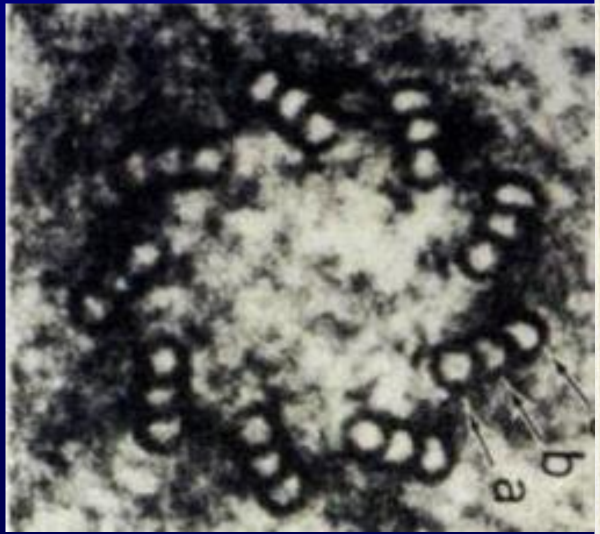
Centrioles –

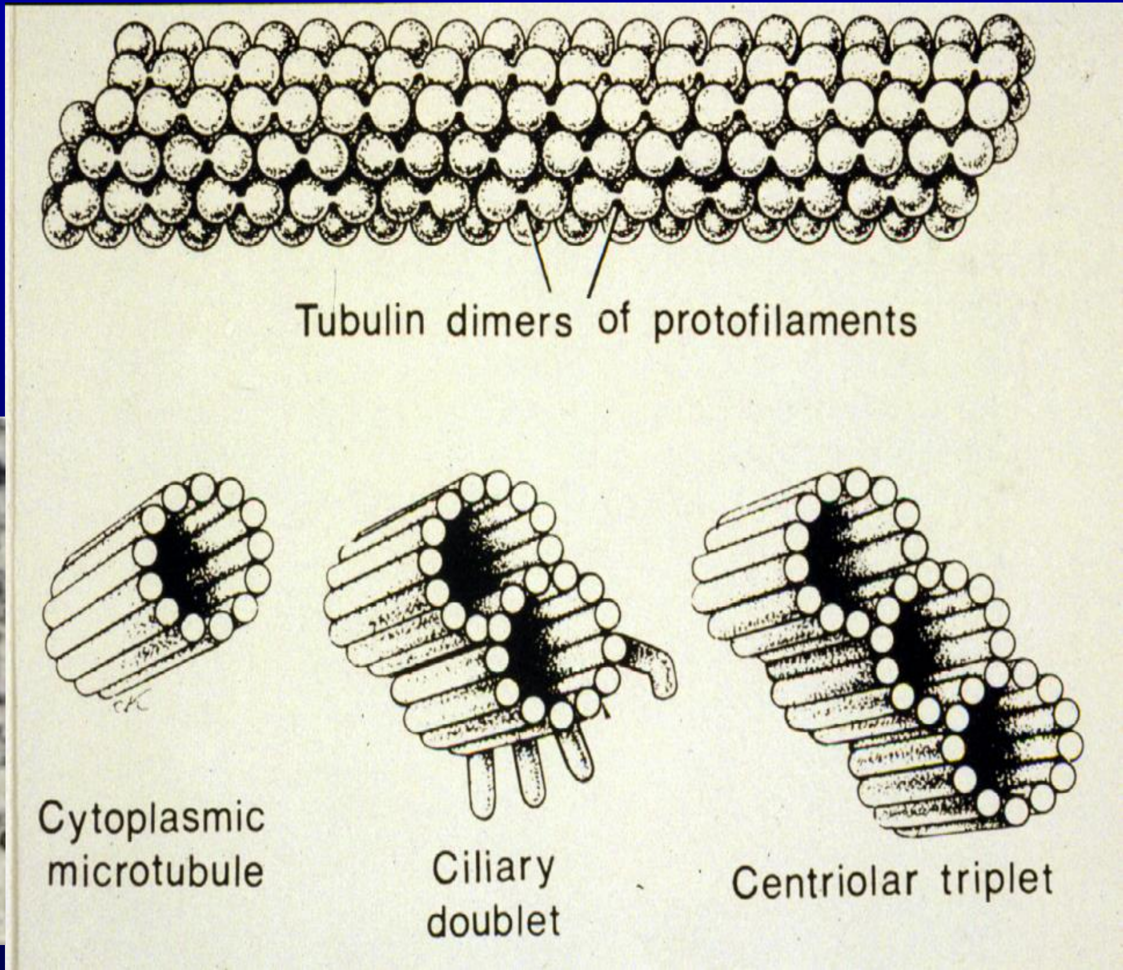
organizing centers of interphase microtubules

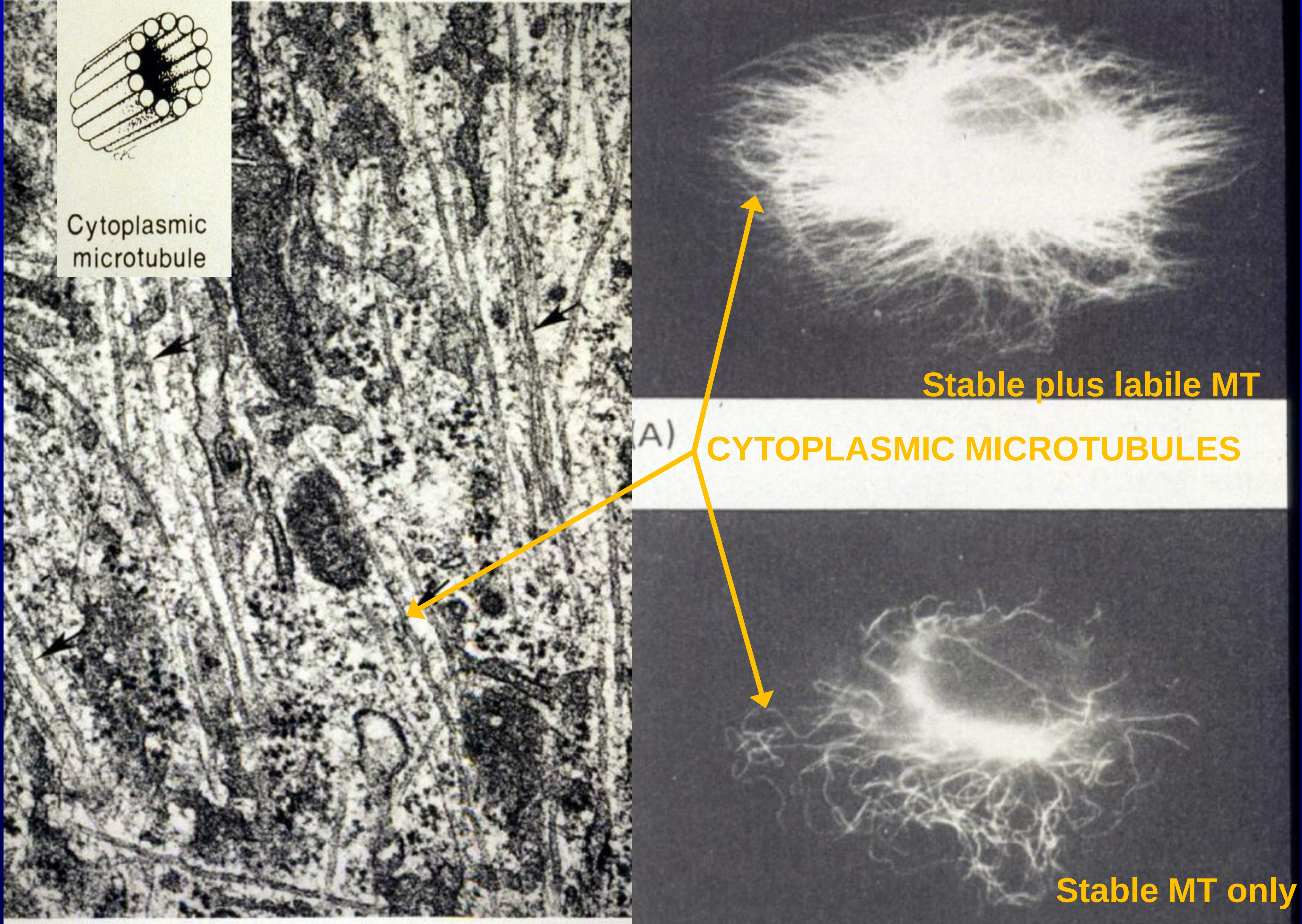
- **9 triplets**

Basal bodies of cilia

- **9 triplets**

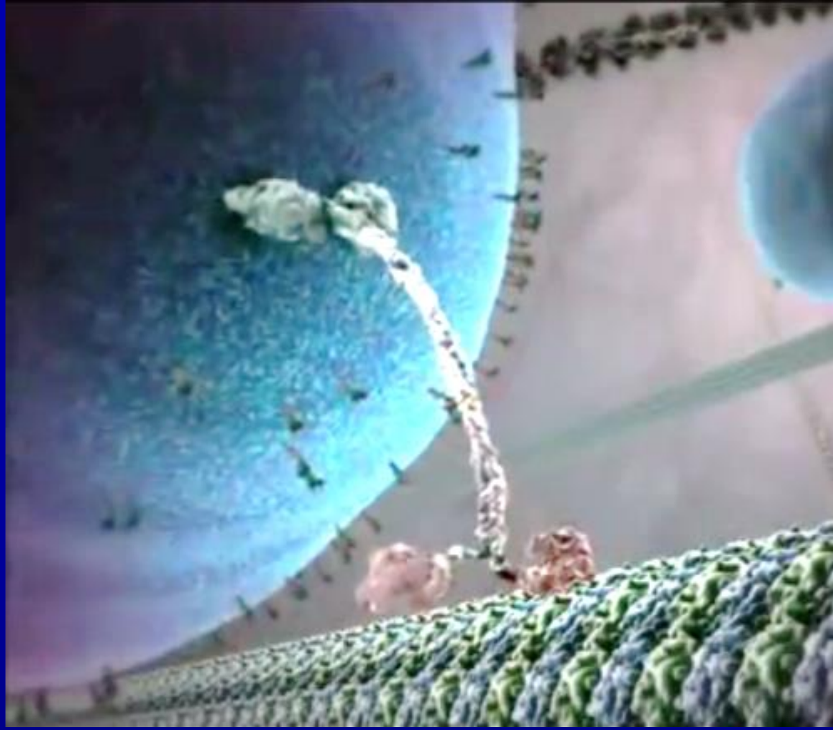






Cytoplasmic
microtubule
Stable plus labile MT
A)
CYTOPLASMIC MICROTUBULES
Stable MT only

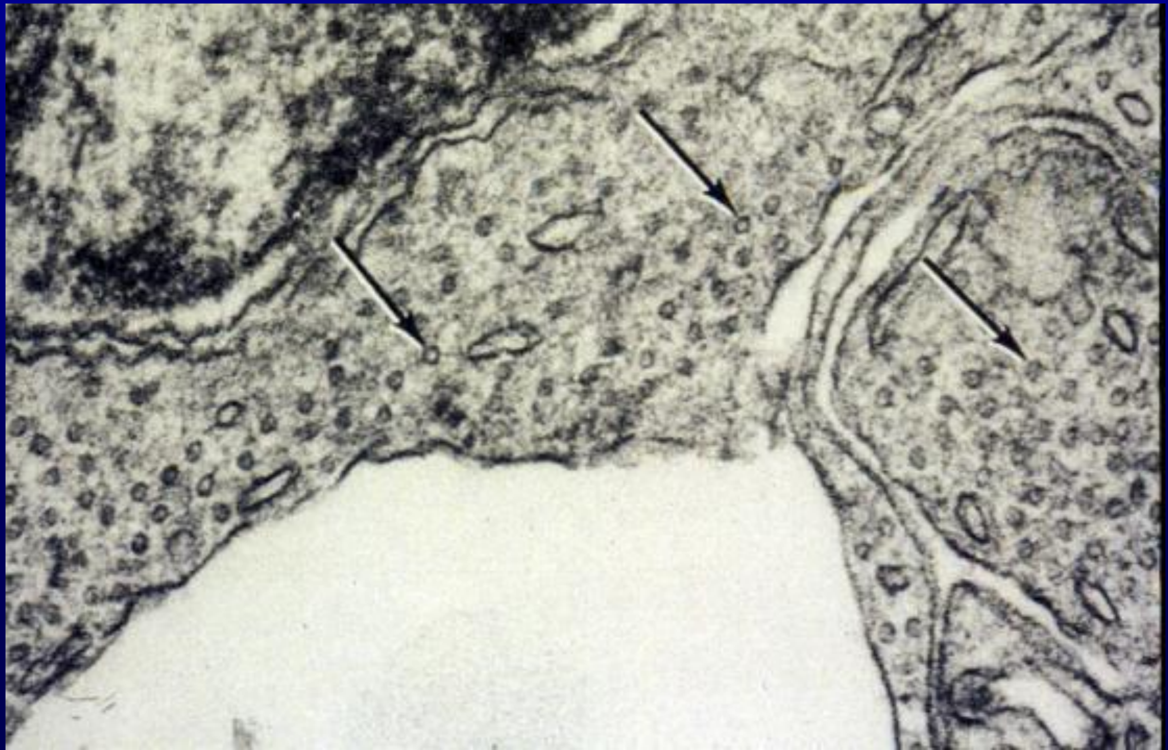
Microtubule function

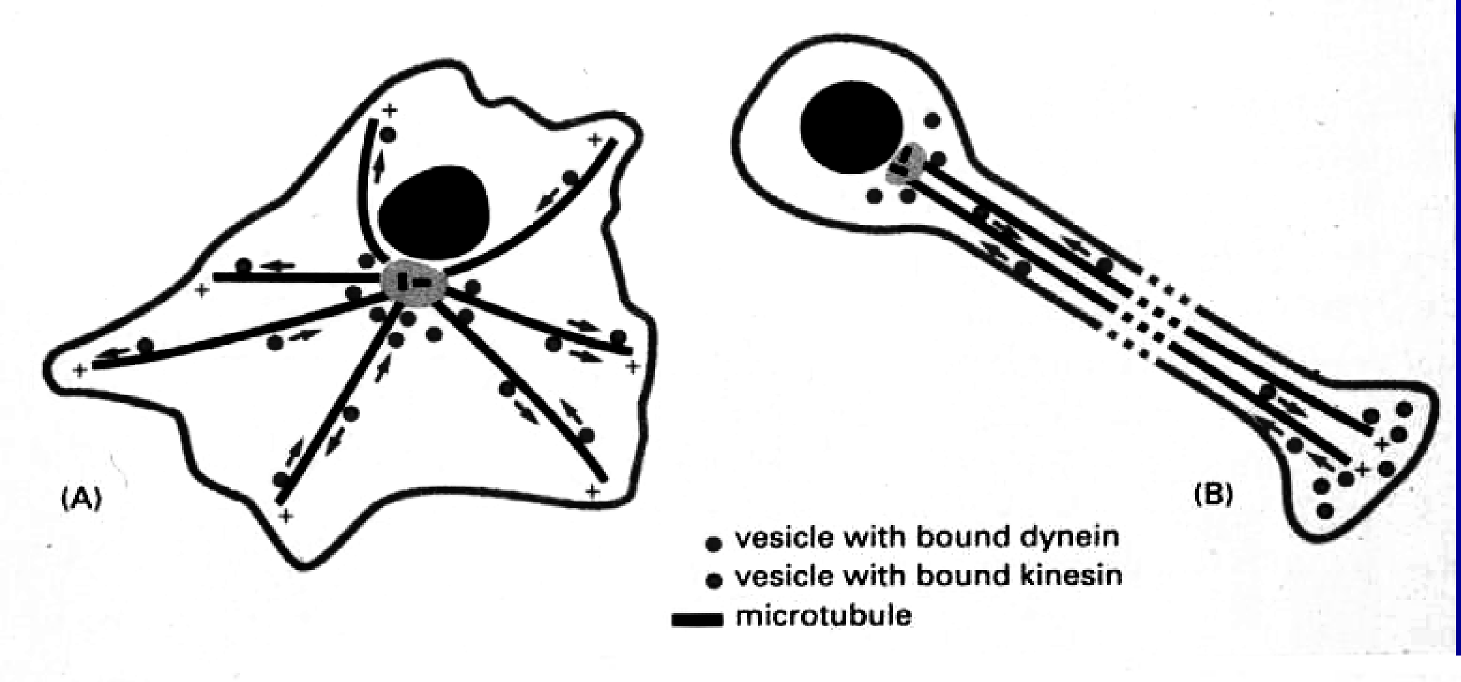


Guide contractile force (actin) to
move the cell organelles within its cytoplasm

Organization of Golgi, ER, and mitochondria

Separate chromosomes during mitosis





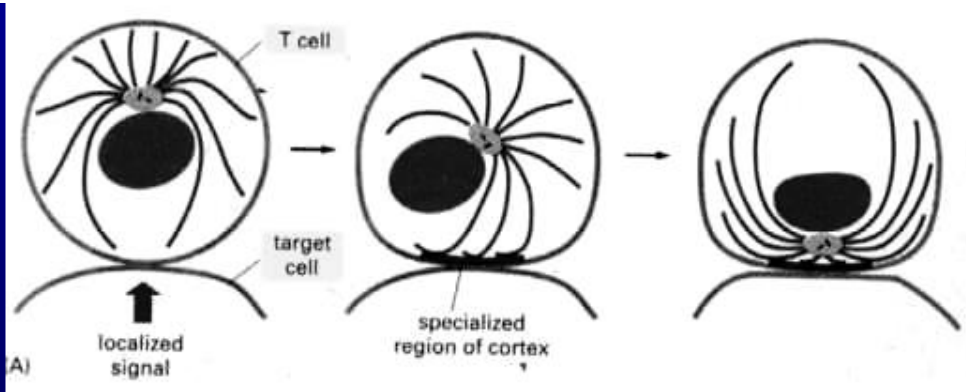
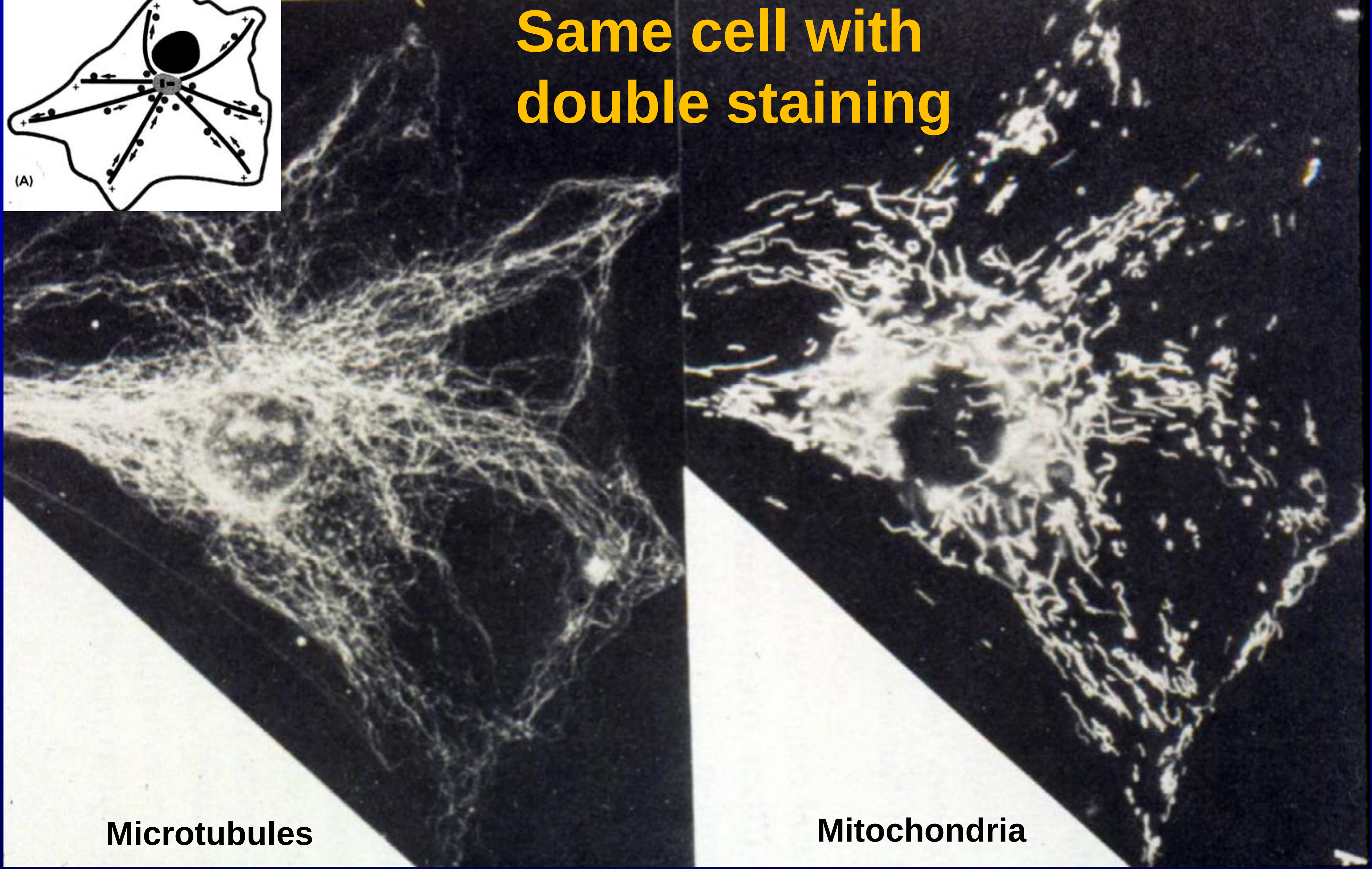
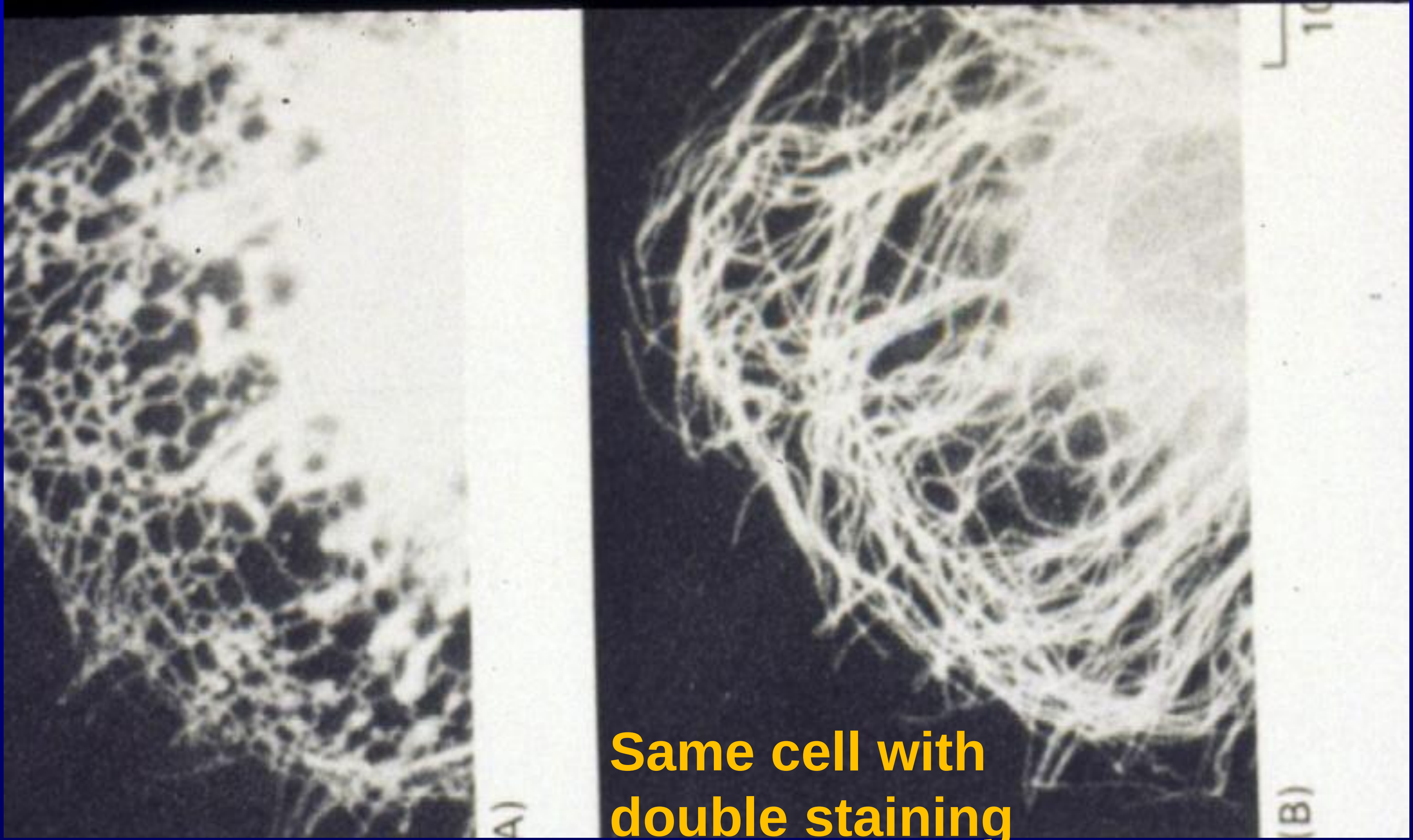


Figure 16–11 The polarization of a cytotoxic T cell after target-cell recognition. (A) Changes in the cytoskeleton of a cytotoxic T cell after it makes contact with a target cell. (B) Immunofluorescence micrograph in which both the T cell (*top*) and its target cell (*bottom*) have been stained with an antibody against microtubules. The centrosome and the microtubules radiating from it in the T cell are oriented toward the point of cell-cell contact. In contrast, the microtubule array in the target cell is not polarized. (B, reproduced from B. Geiger, D. Rosen, and G. Berke, *J. Cell Biol.* 95:137–143, 1982, by copyright permission of the Rockefeller University Press.)

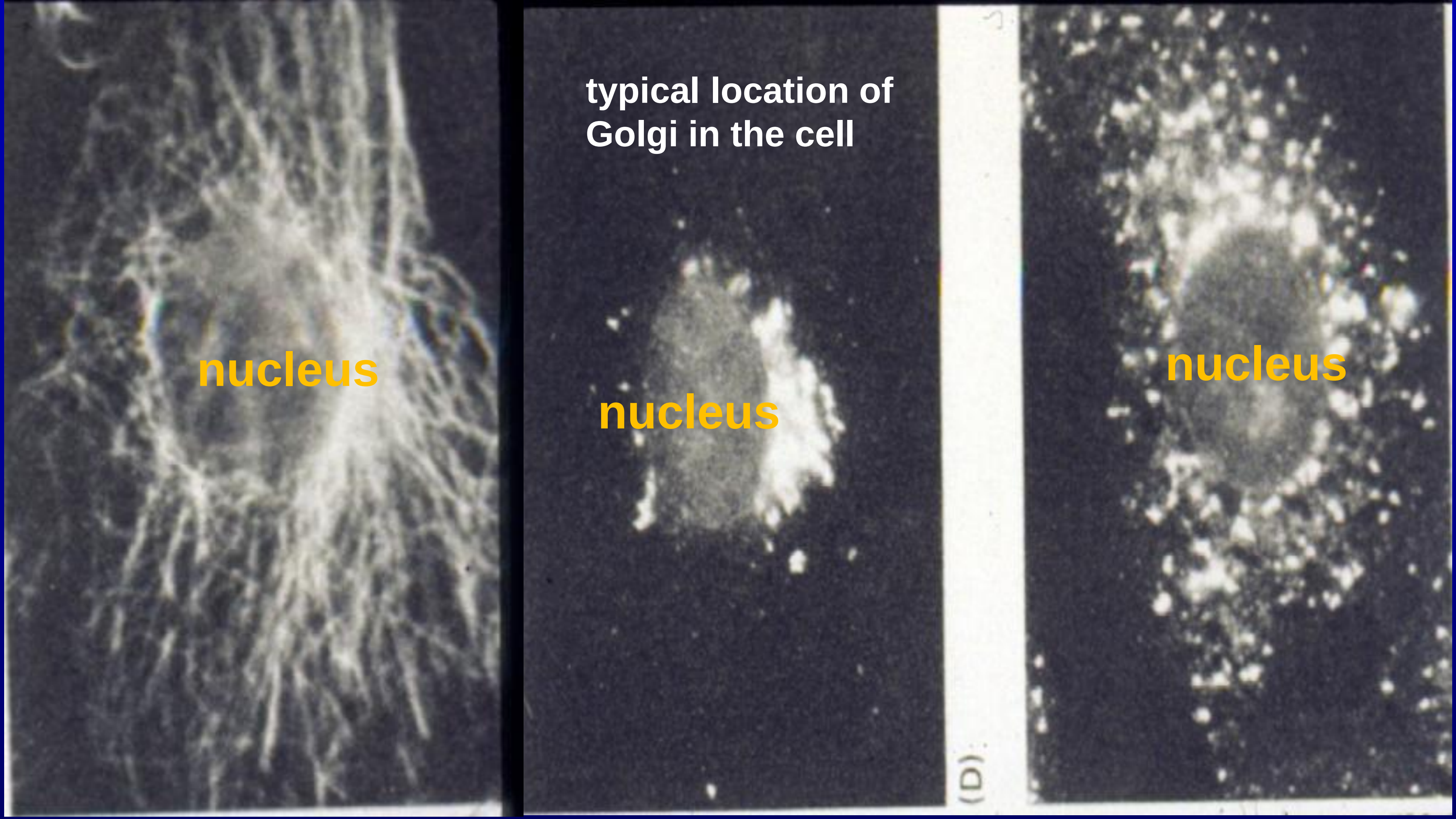


Organization of mitochondria



ER Microtubules

Organization of ER

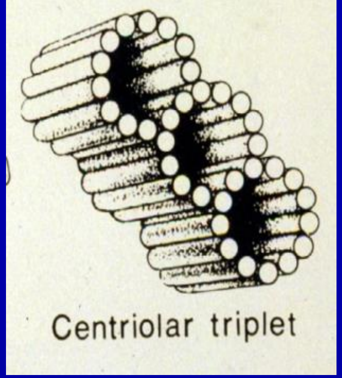


Microtubules shown here

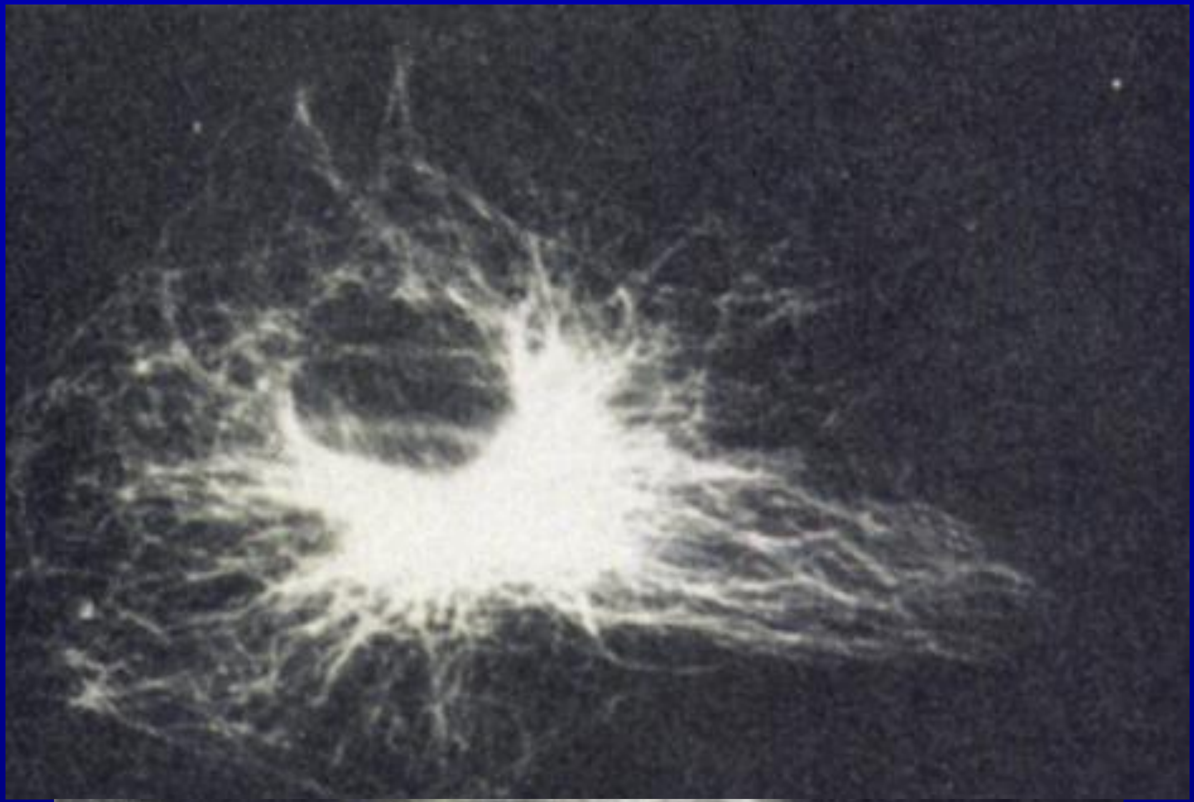
Golgi with microtubules present, but not shown here

Golgi without microtubules present

Organization of Golgi, ER, and mitochondria



Centrioles

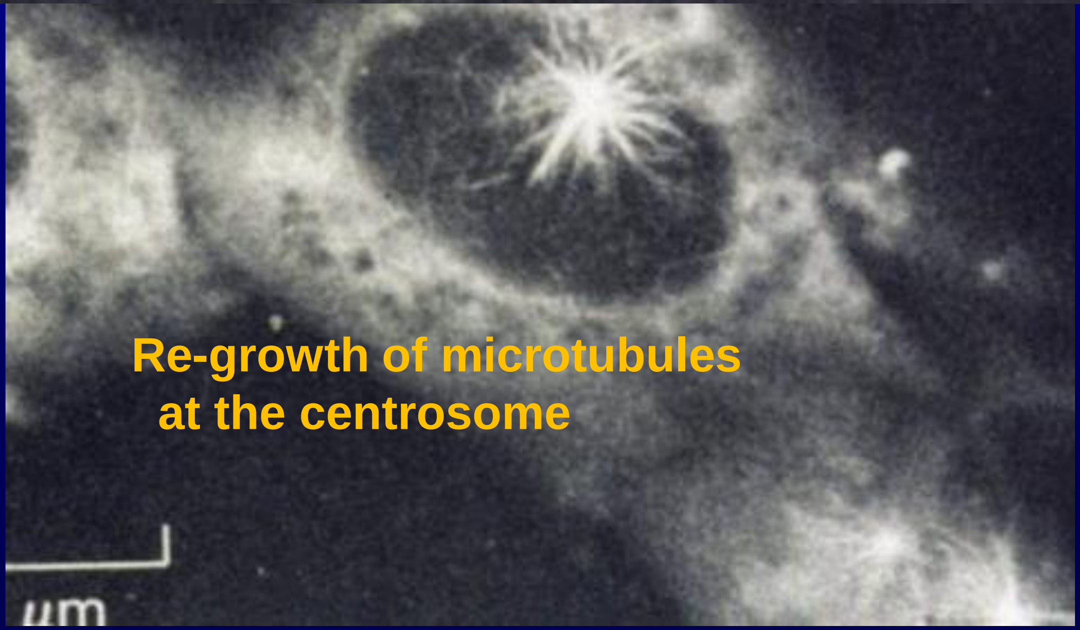


9 triplet microtubules

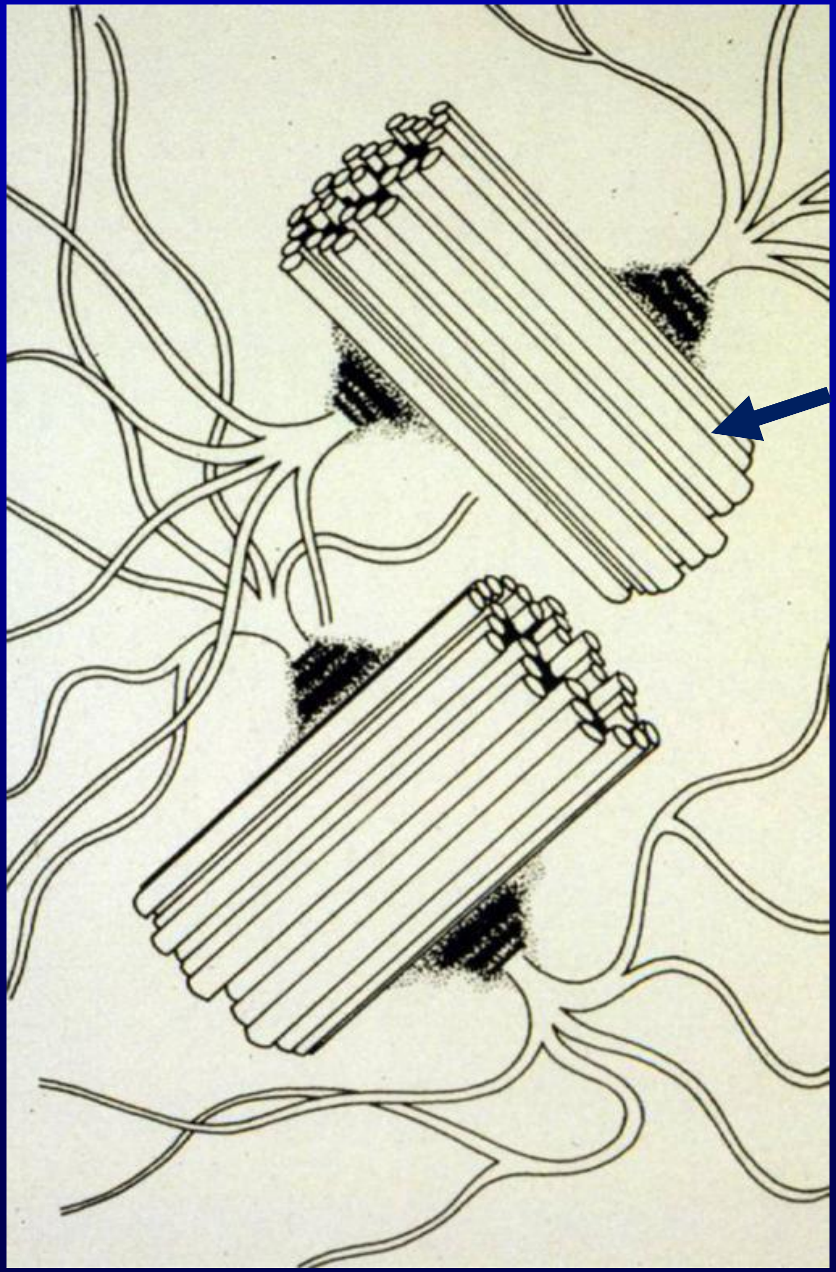
Centrosome - centriolar duplex at the cell's center

Diplosome - pair of centrioles

Self duplicating – develops from pre-existing procentrioles



Diplosome - pair of centrioles



centriole

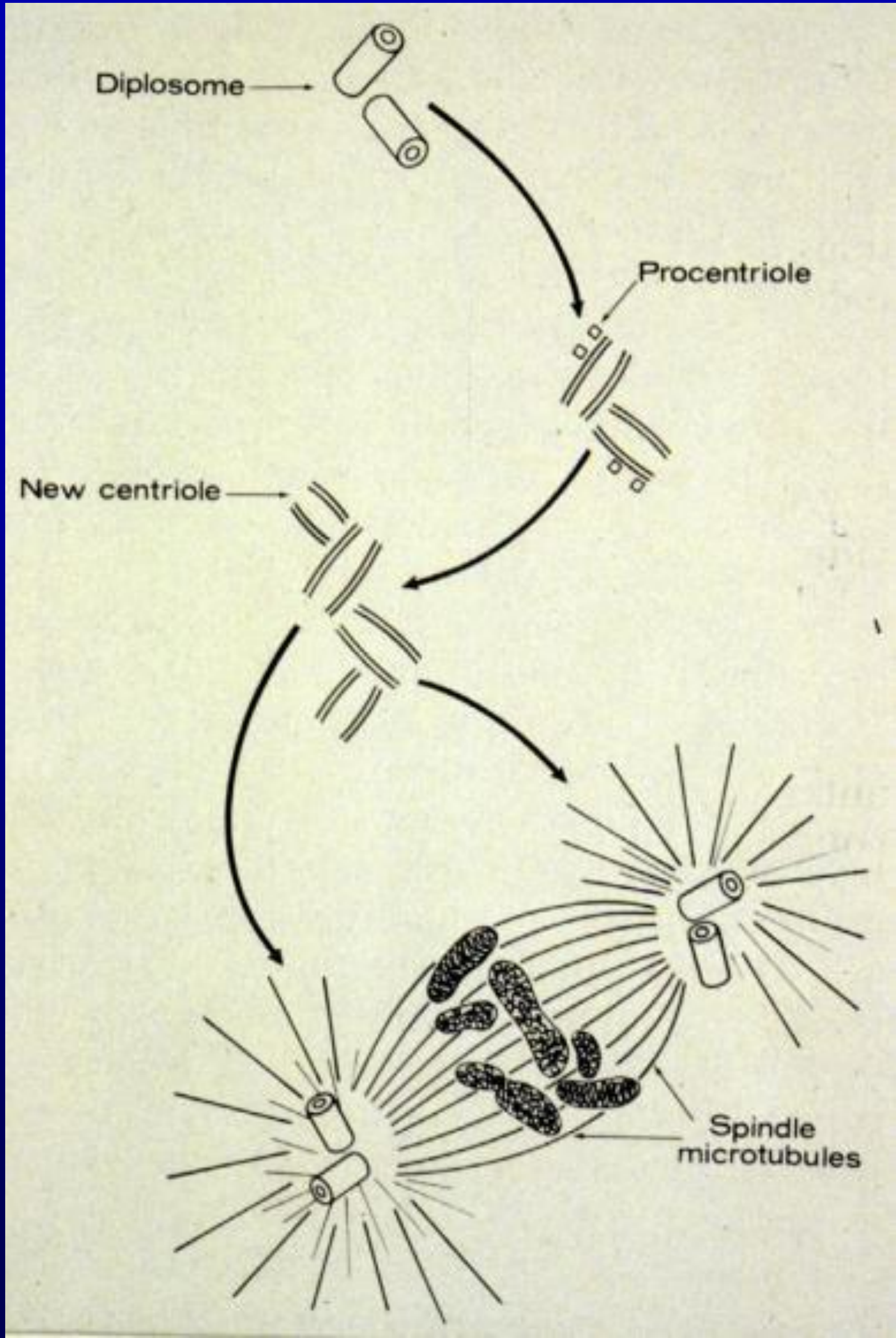
Diplosome

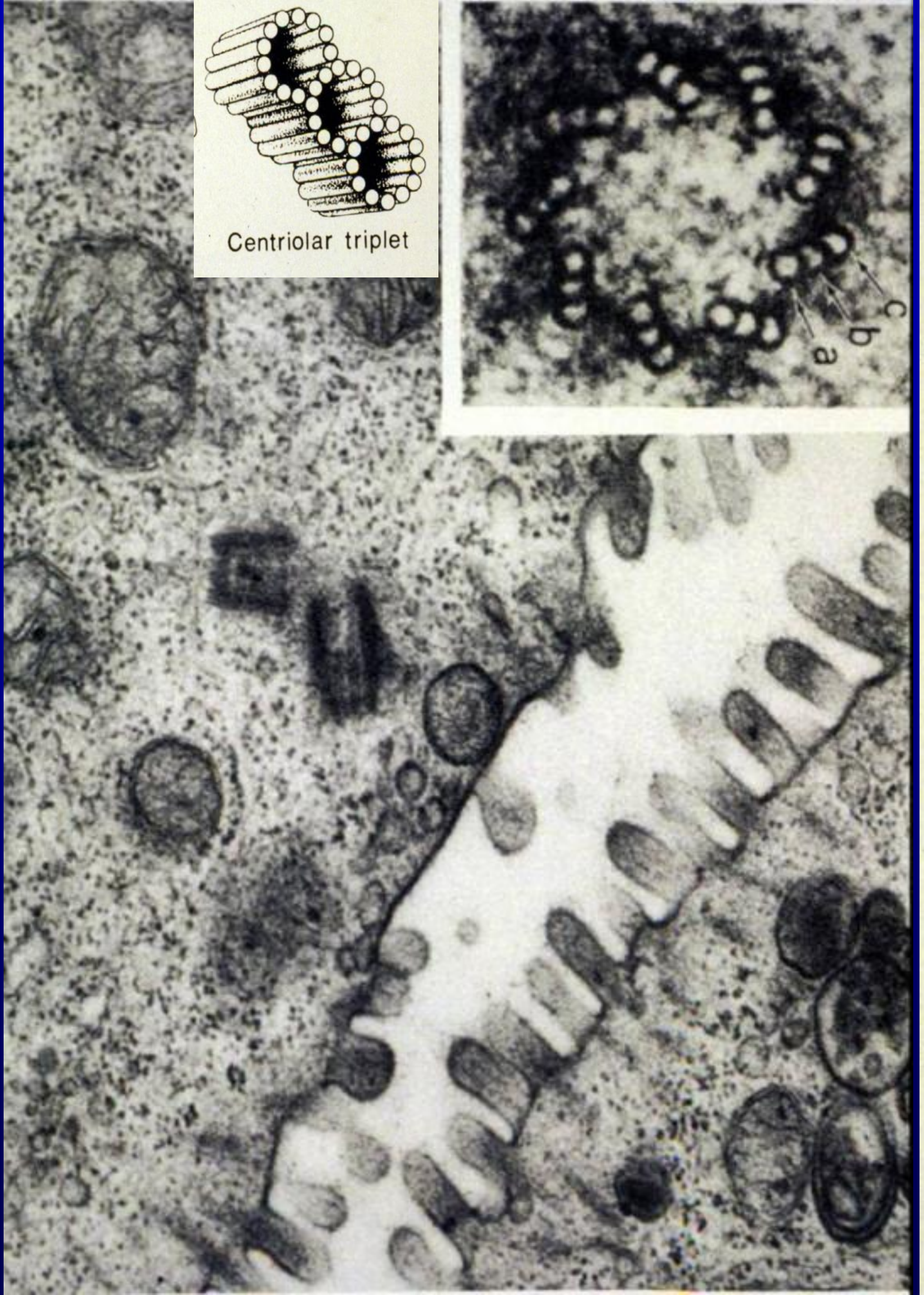
Centrioles

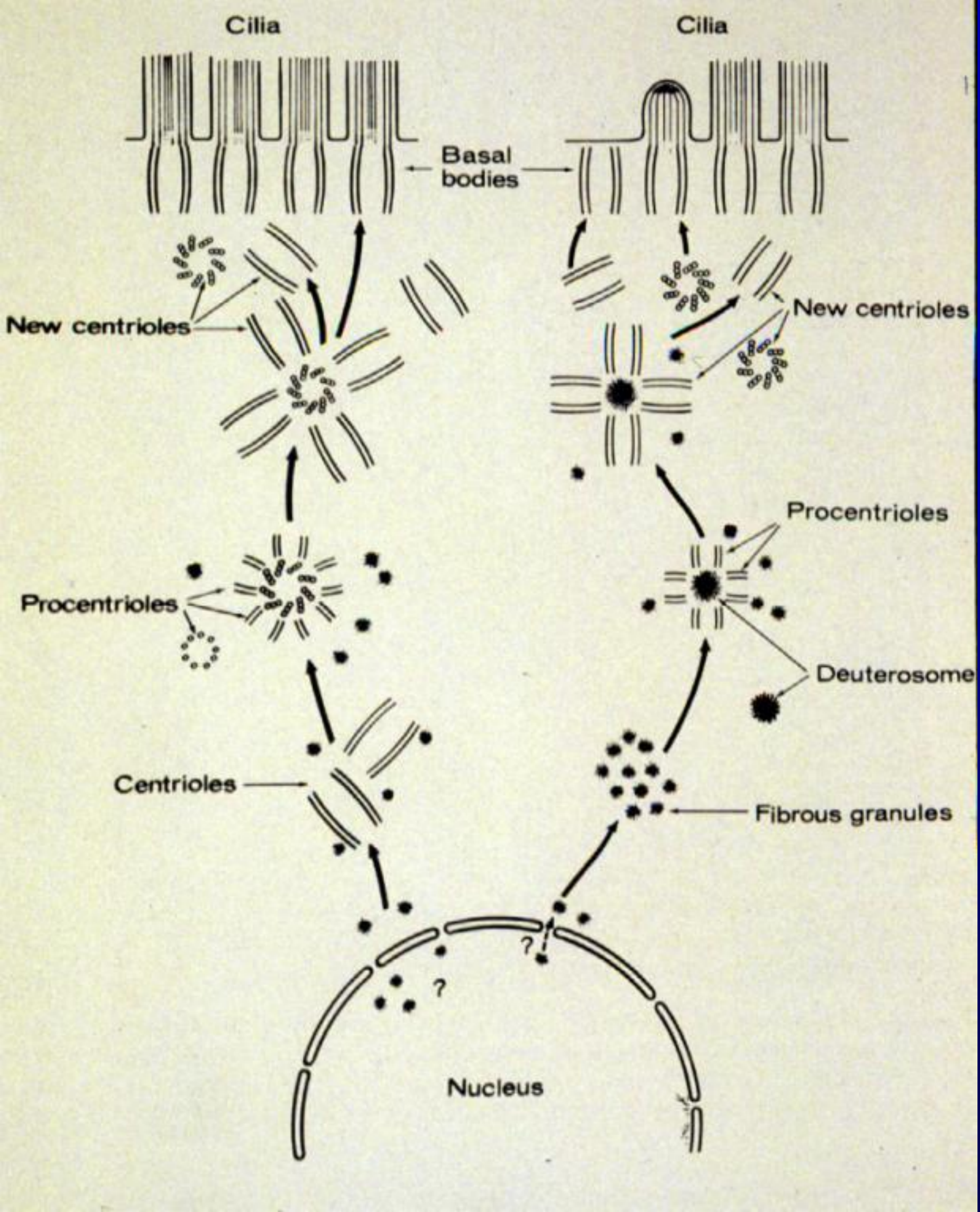
Essential for formation of cilia and flagella

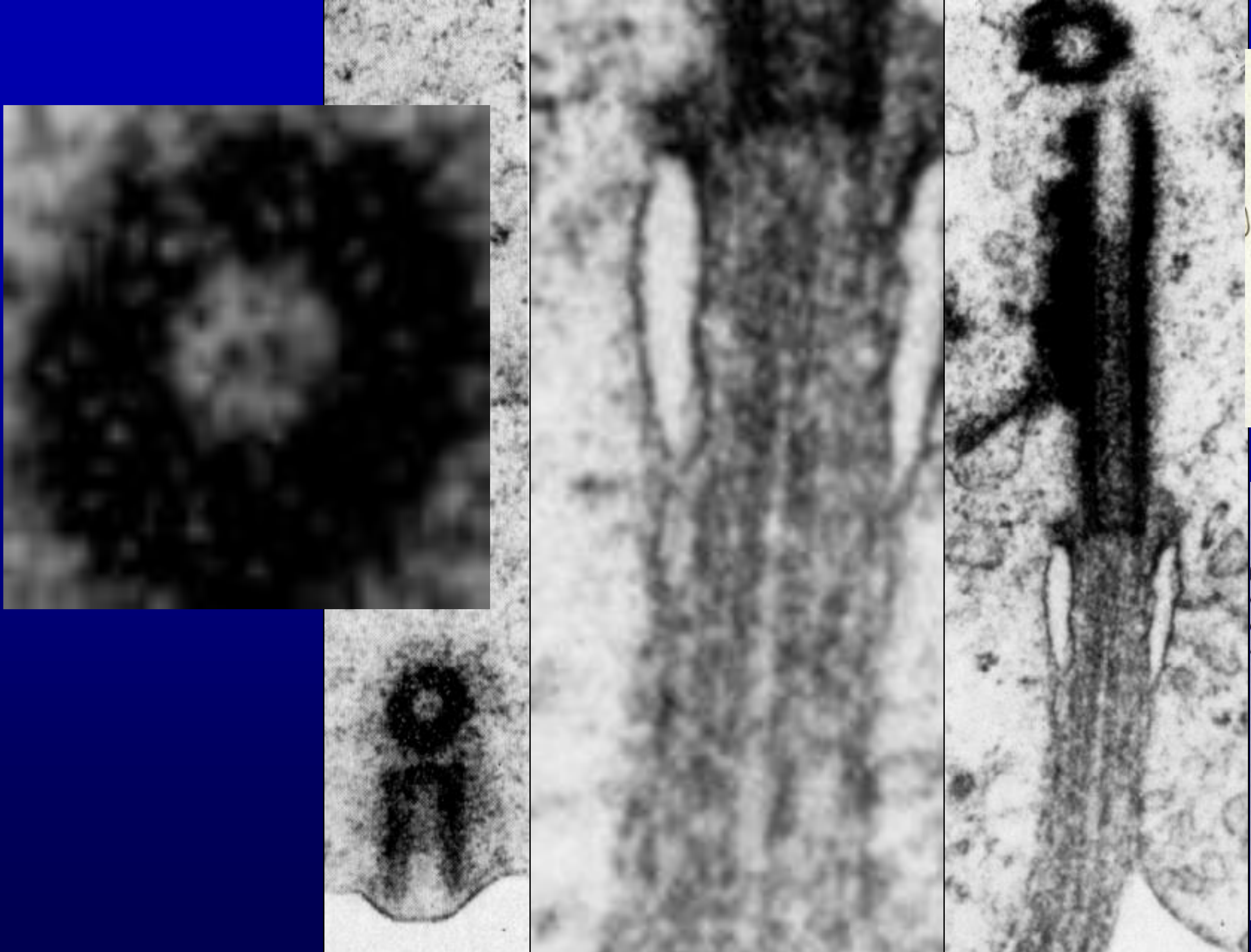
Basal body - root-like anchoring device

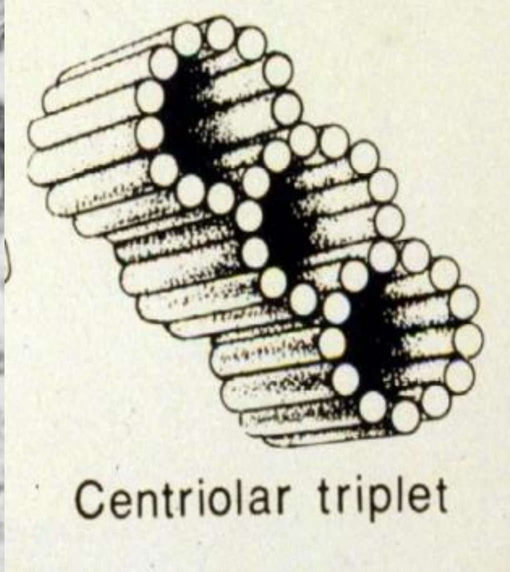
Function in organizing microtubules that pull chromosomes apart in mitosis

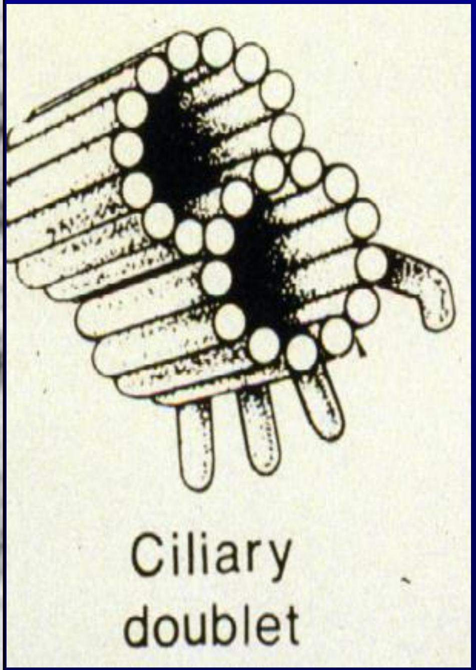


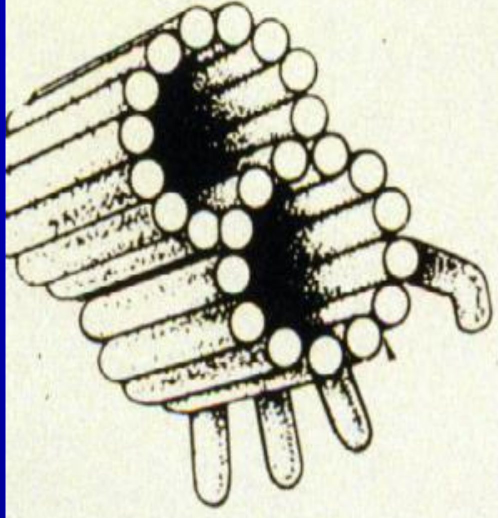

Centriolar triplet
a
b
c


Cilia
Cilia
Basal bodies
New centrioles
New centrioles
Procentrioles
Procentrioles
Deuterosome
Centrioles
Fibrous granules
Nucleus

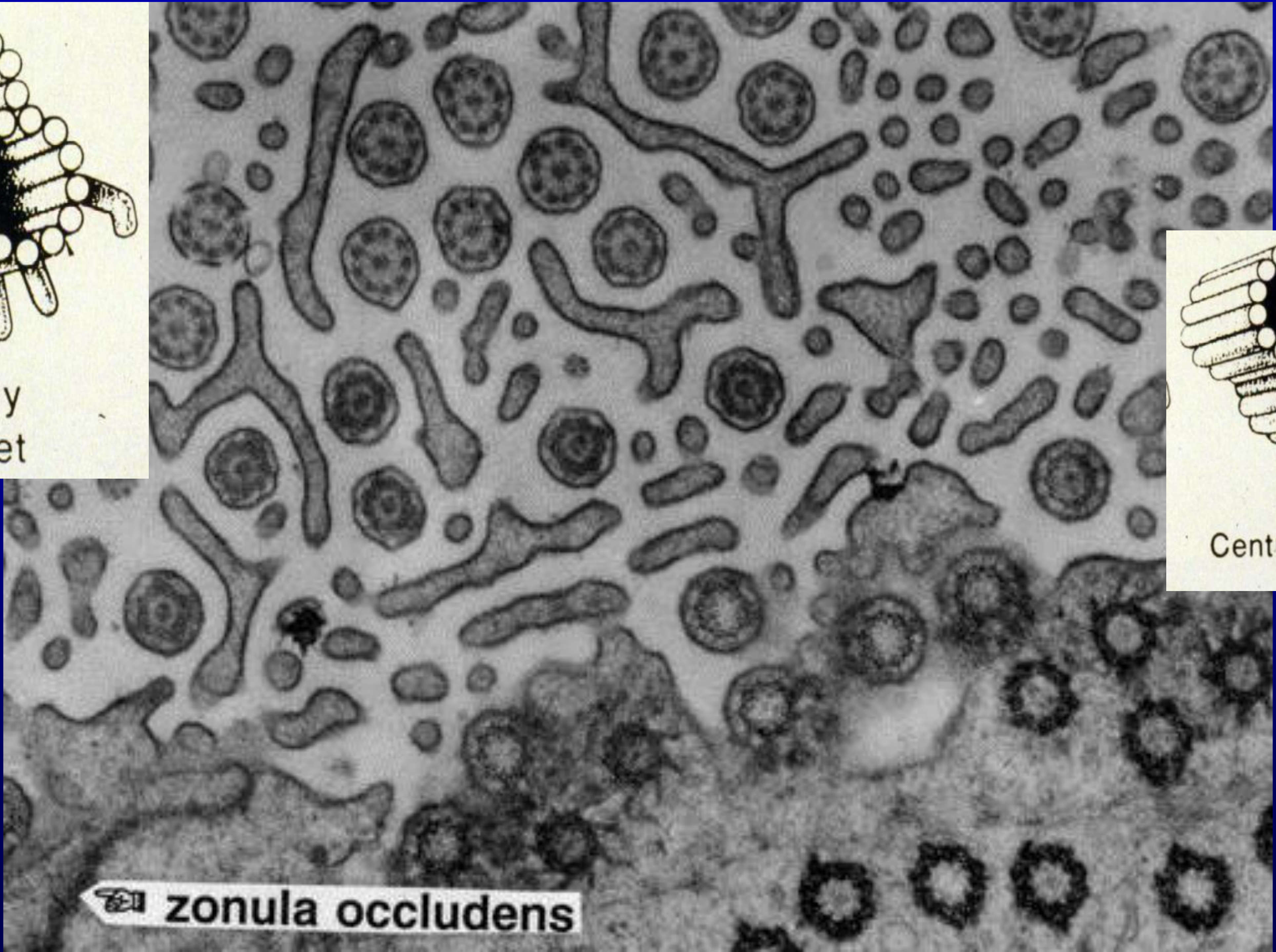


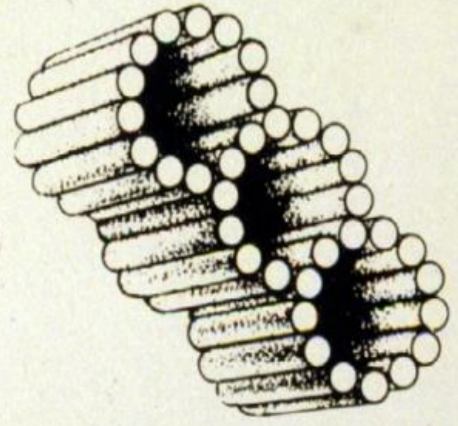

Centriolar triplet


Ciliary
doublet



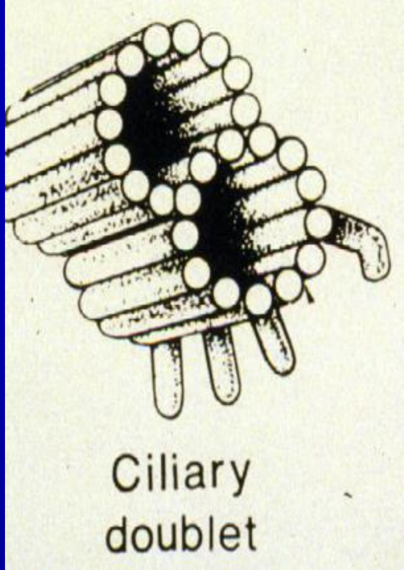
Ciliary doublet



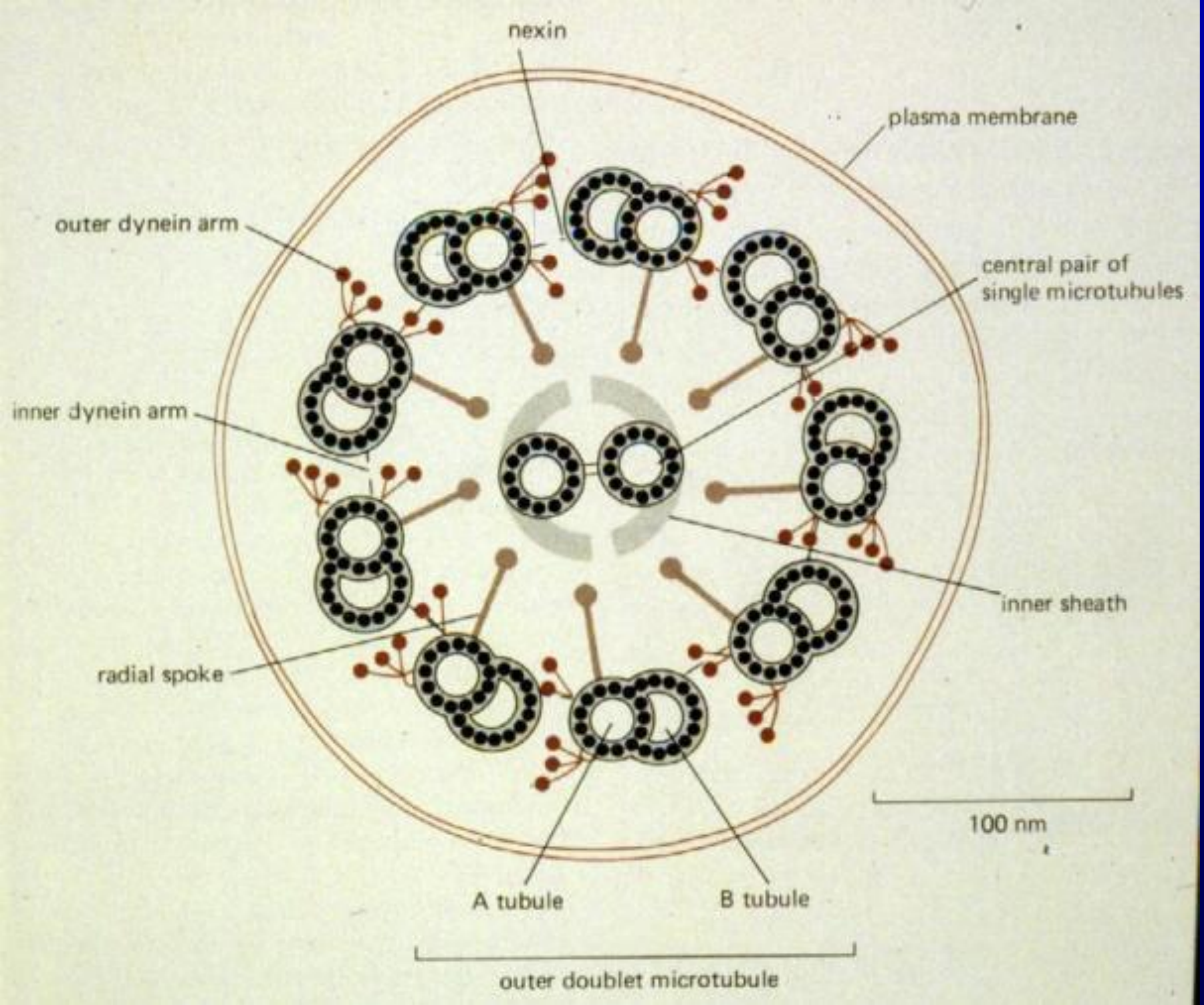


Centriolar triplet

Axoneme of cilia and flagella



- Tubules polymerize to form nine doublets
- Pairs of conjoined microtubules with common wall segment
- Central pair of microtubules

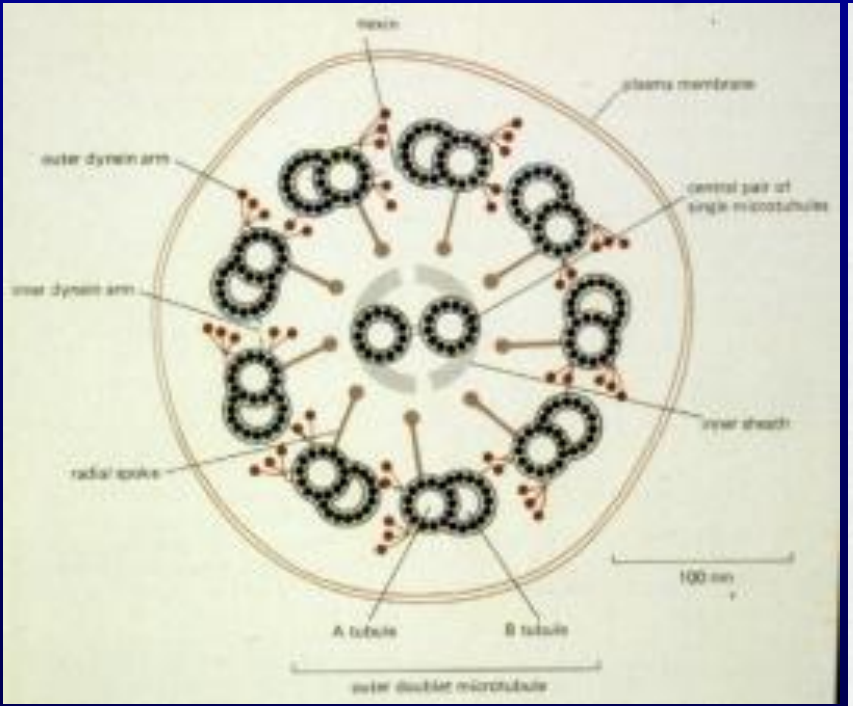


Axoneme of cilia and flagella

Stable

Dynein arms

- Paired lateral appendages
- Protein ATPase activity for ciliary and flagellar motility



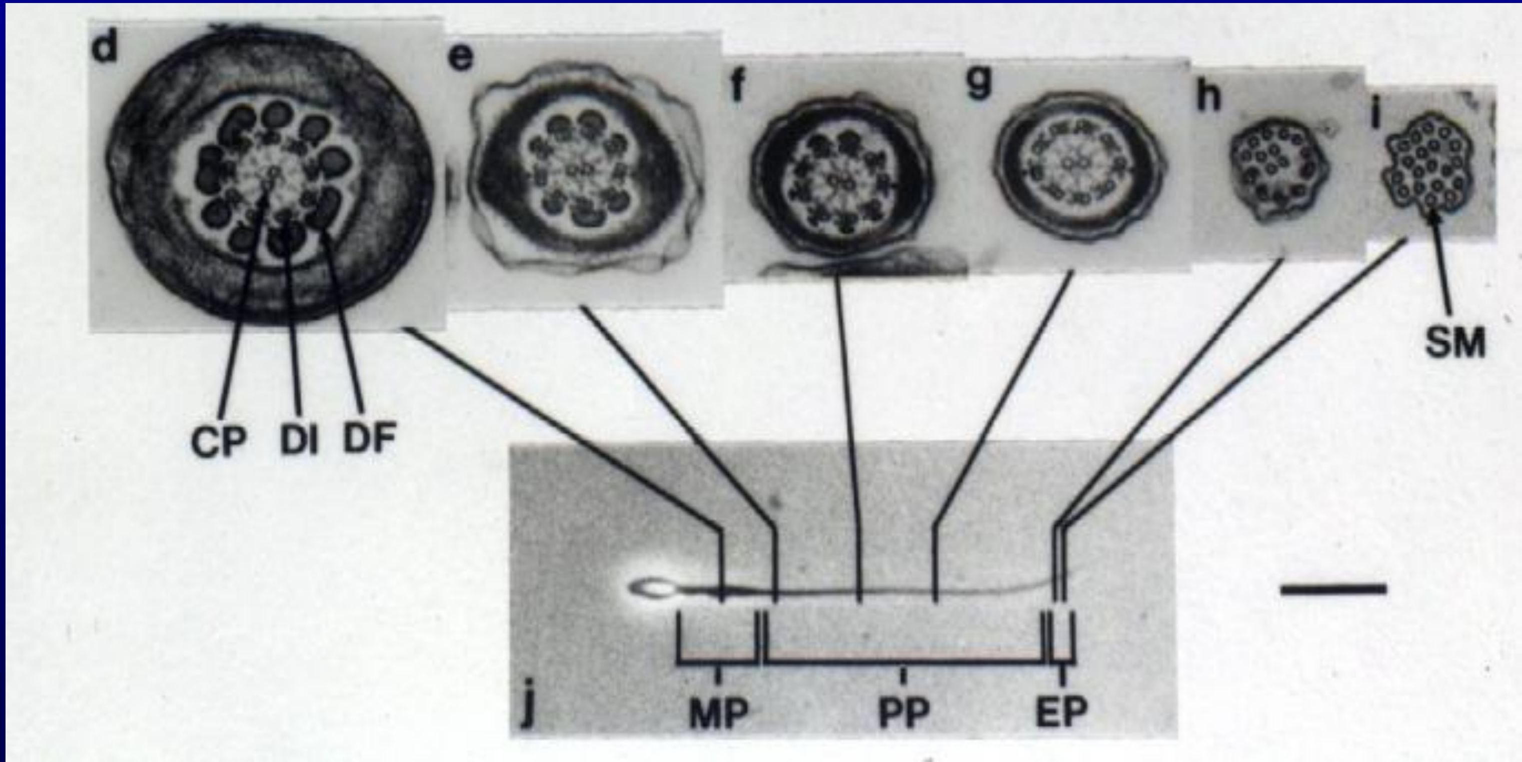
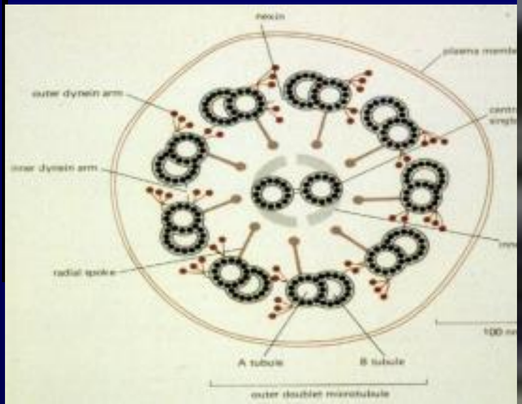
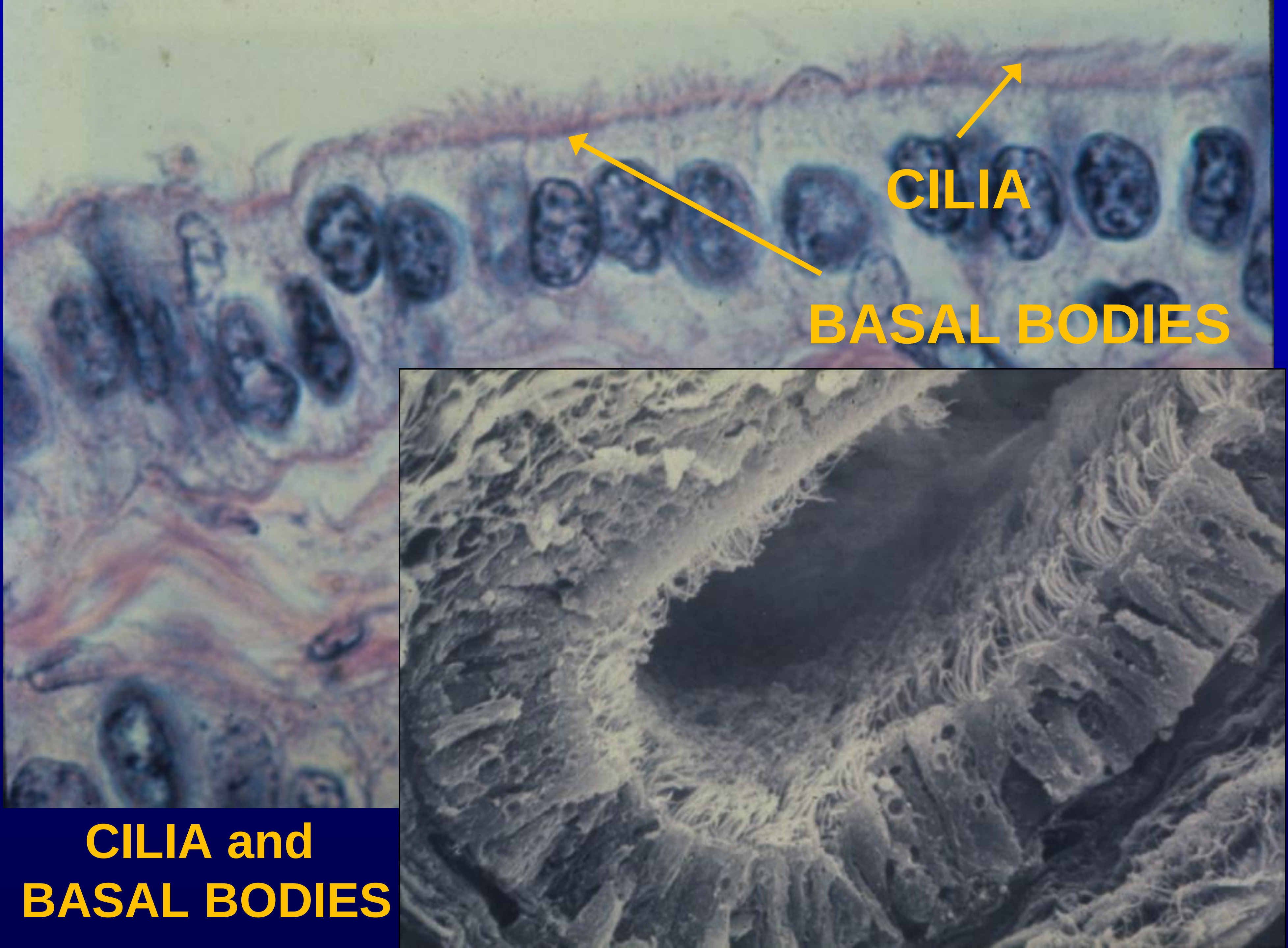
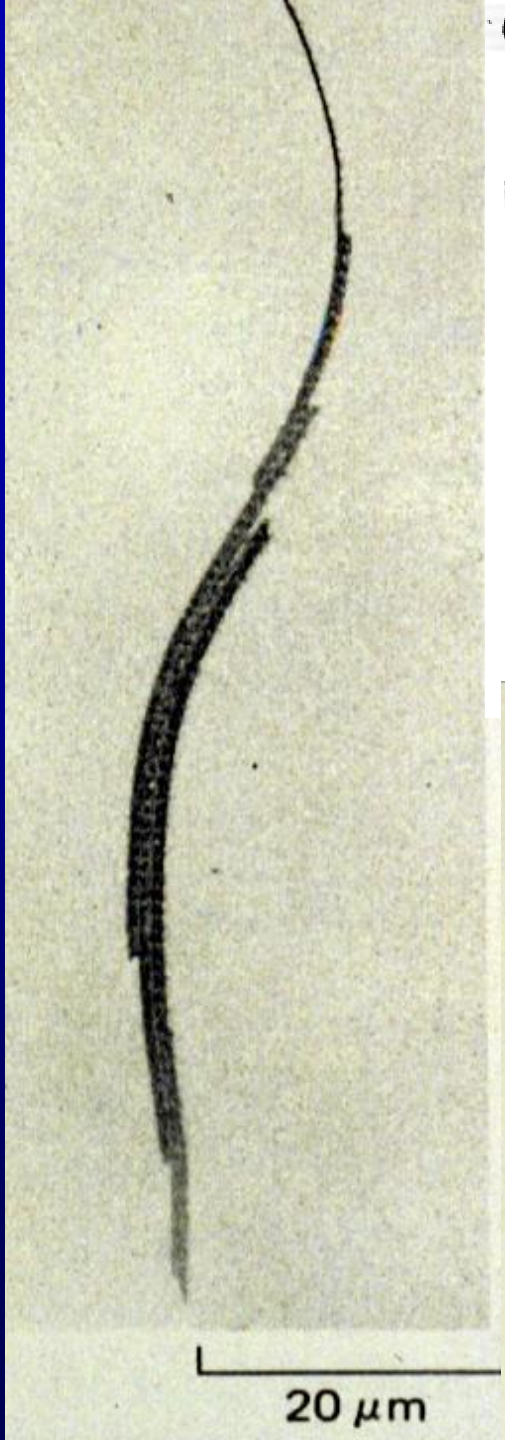


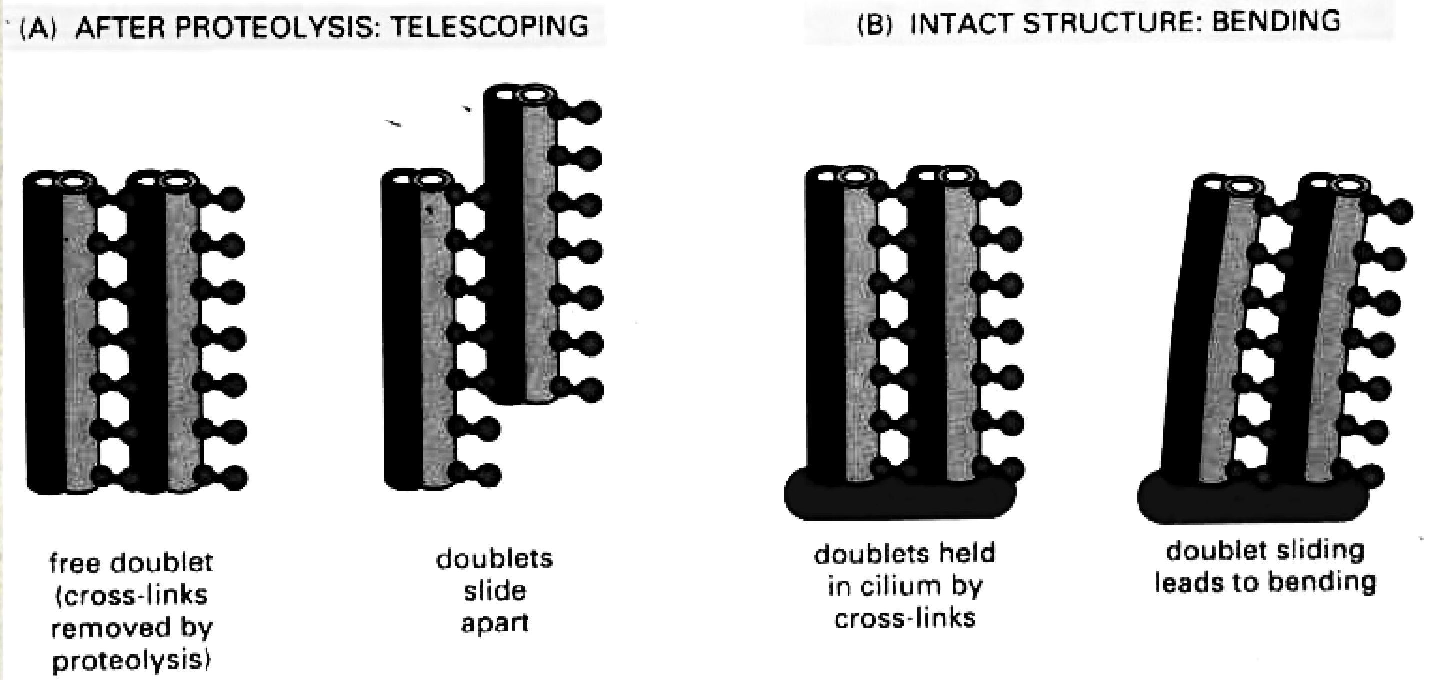
Table 10-3 Major Protein Structures of the Ciliary Axoneme	
Axoneme Component (periodicity along axoneme)	**Function**
Tubulin dimers (8 nm)	principal component of microtubules
Dynein arms (24 nm)	project from microtubule doublets and interact with adjacent doublets to produce bending
Nexin links (86 nm)	hold adjacent microtubule doublets together
Radial spokes (29 nm)	extend from each of the 9 outer doublets inward to the central pair
Sheath projections (14 nm)	project as a series of side arms from the central pair of microtubules; together with the radial spokes these regulate the form of the ciliary beat

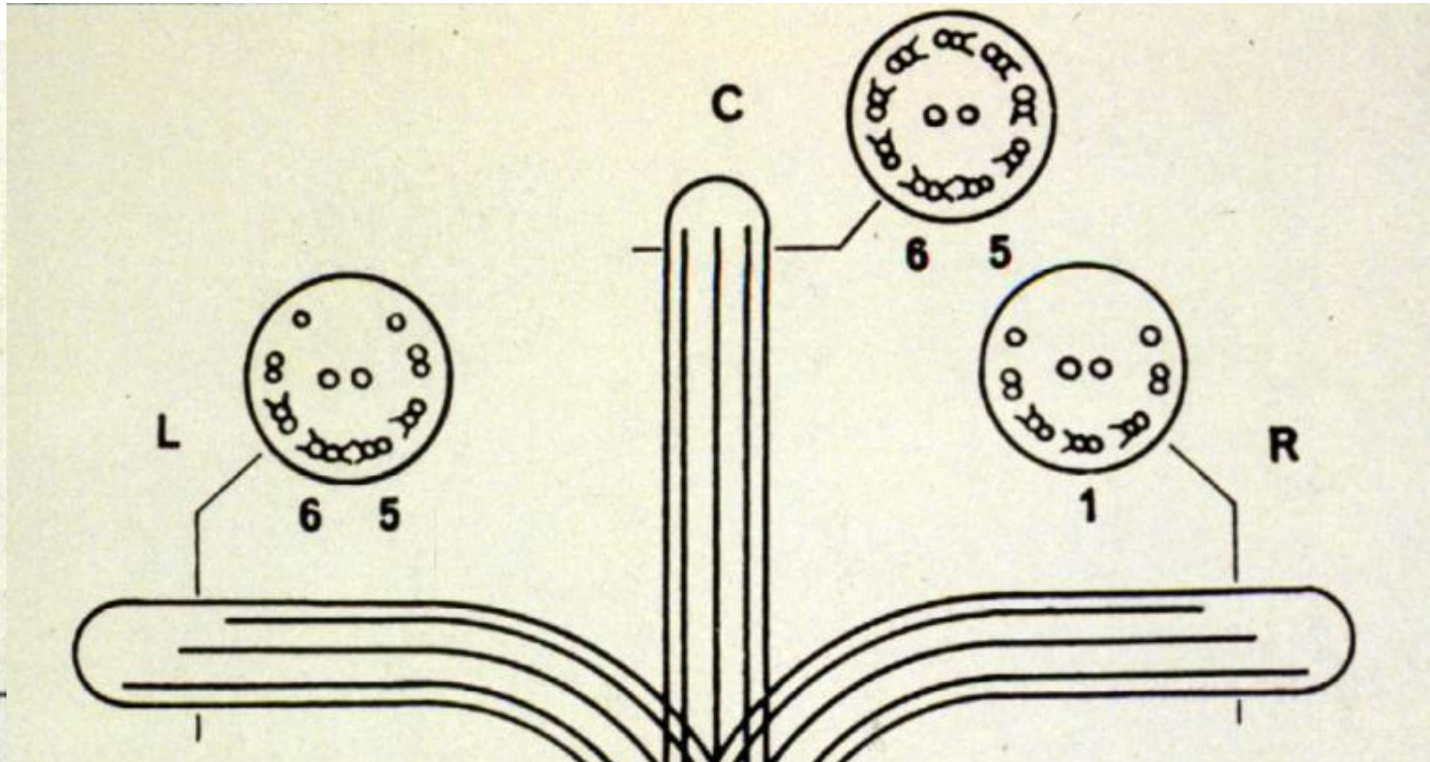


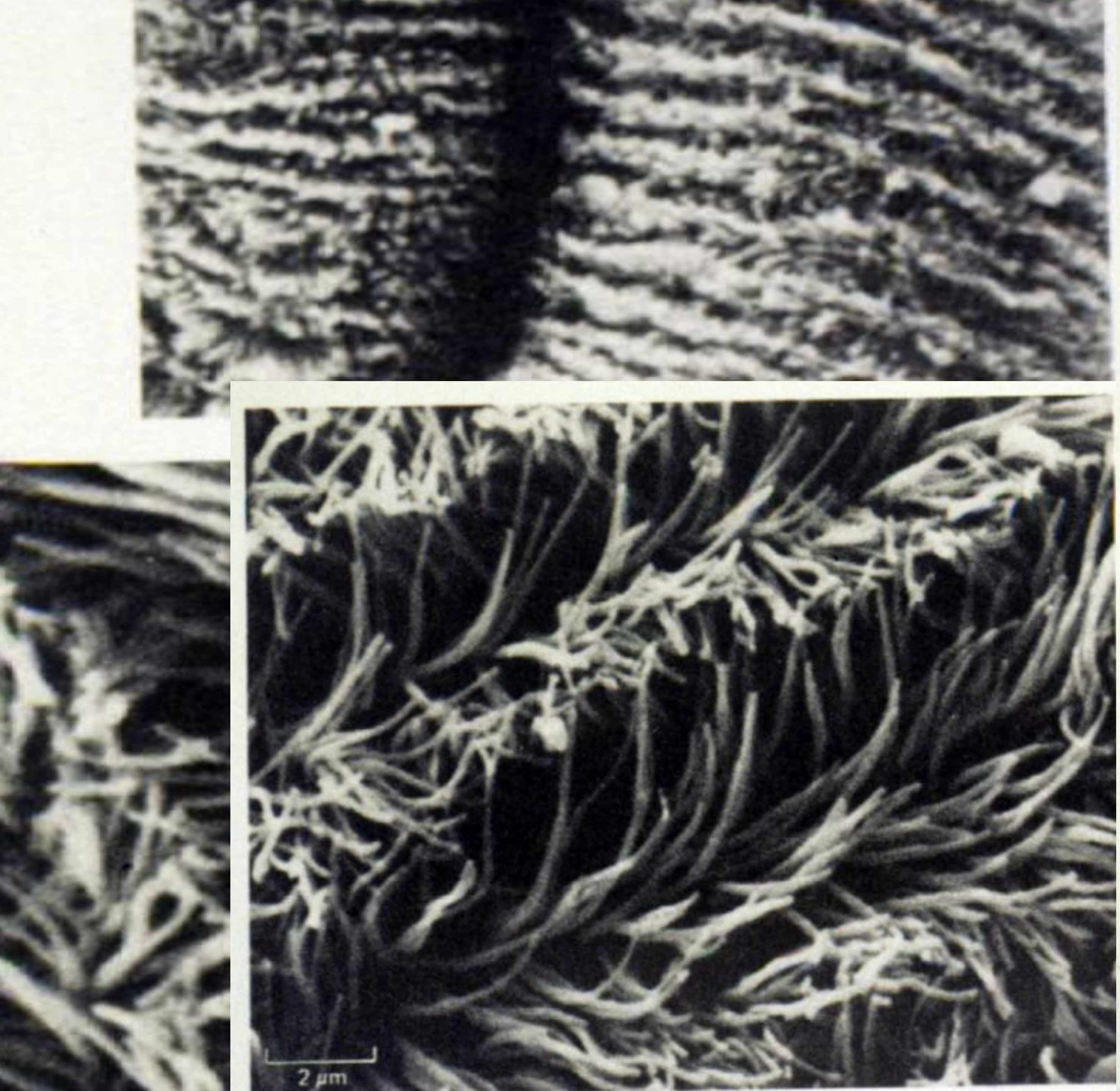


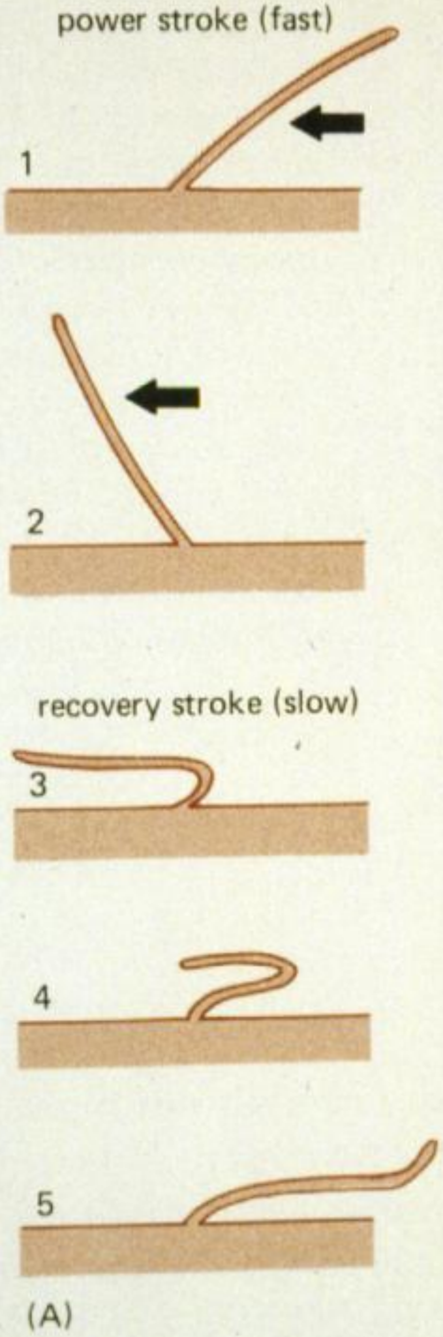
CILIA and
BASAL BODIES

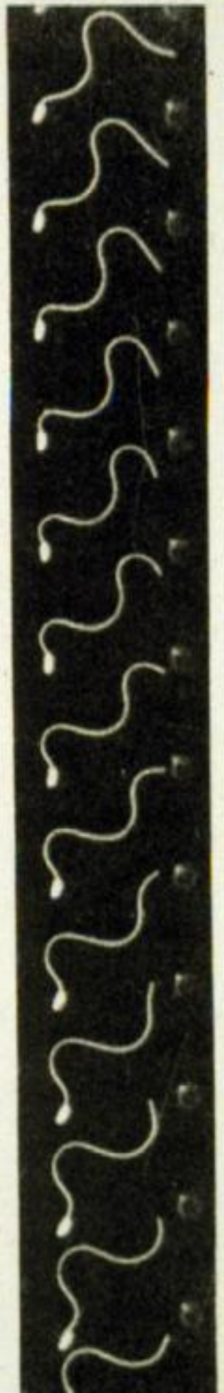

20 μm


(A) AFTER PROTEOLYSIS: TELESCOPING
(B) INTACT STRUCTURE: BENDING
free doublet (cross-links removed by proteolysis)
doublets slide apart
doublets held in cilium by cross-links
doublet sliding leads to bending


C
6
5
L
6
5
R
1


2 µm


power stroke (fast)
1
2
recovery stroke (slow)
3
4
5
(A)



Drugs that influence - microtubules assembly and disassembly

- **Inhibitors:**
  - Colchicine - inhibit assembly <u>in</u> <u>vitro</u>, destroy <u>in</u> <u>vivo</u>
  - Vinblastine - inhibit assembly <u>in</u> <u>vitro</u>, destroy <u>in</u> <u>vivo</u>
- **Stimulator:**
  - Taxol - stimulate assembly <u>in</u> <u>vitro</u>
- Use in cancer therapy?

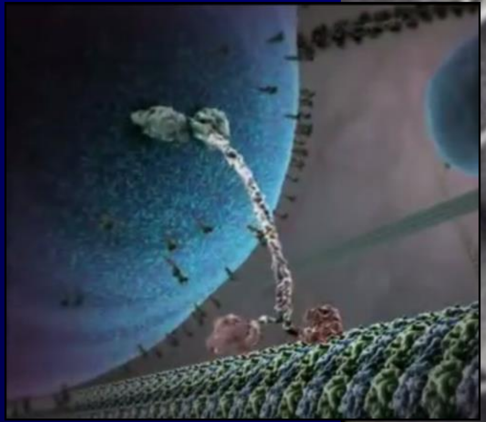
Microtubules - summary

Microtubules - cylindrical walled tubes composed 13 parallel protofilaments

Protofilaments - linear polymers of alpha and beta tubulin

Growth at one end away from nucleation site

Polarity of direction of growth - directs movements of cytoplasmic organelles



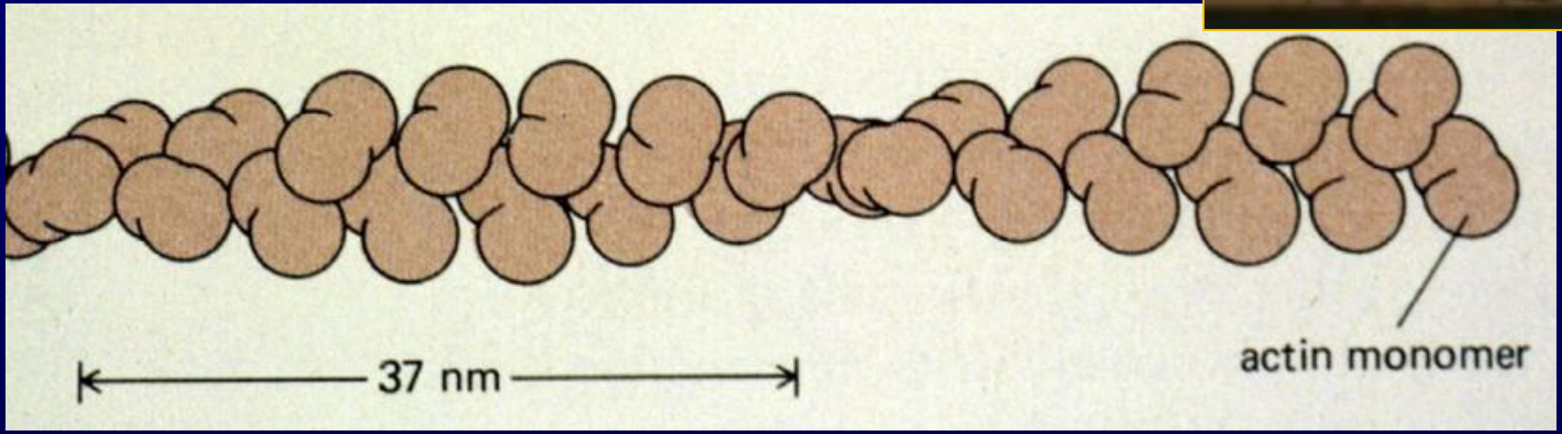
Microfilaments

“actin filaments”

Composition:

- **Actin - highly conserved protein**

http://www.youtube.com/watch?v=YXNVWjAIKC0&feature=related

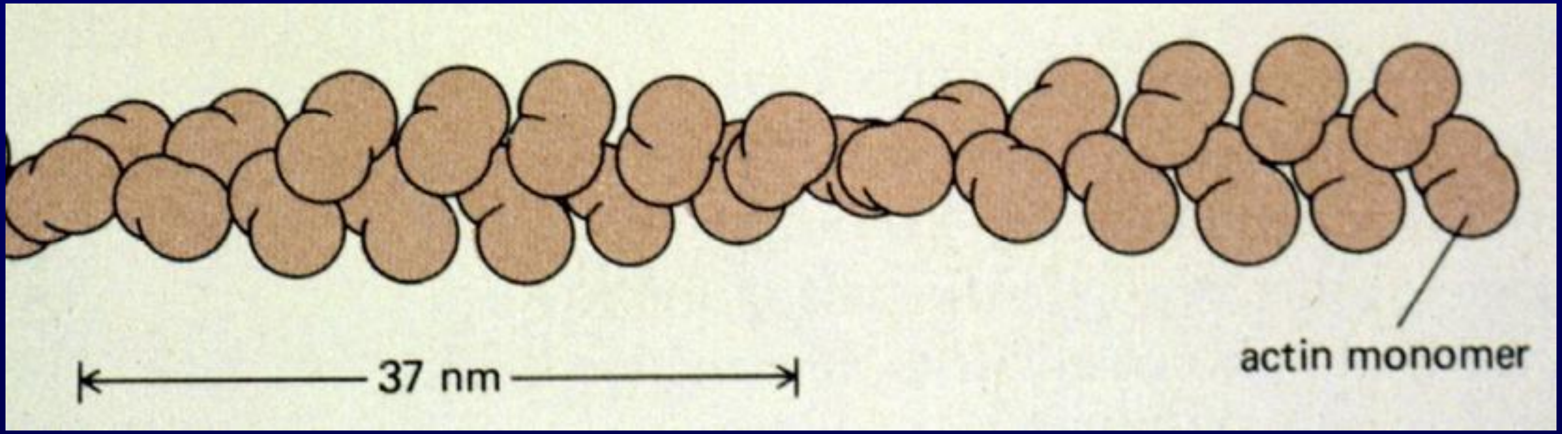


Microfilaments

"actin filaments"

Composition:

- **Actin - highly conserved protein**
- **Actin associated proteins**
  - **MYOSIN - ATPase**
  - **Trophomyosin - rod-like protein**
  - **Filamin - bundles actin filaments**

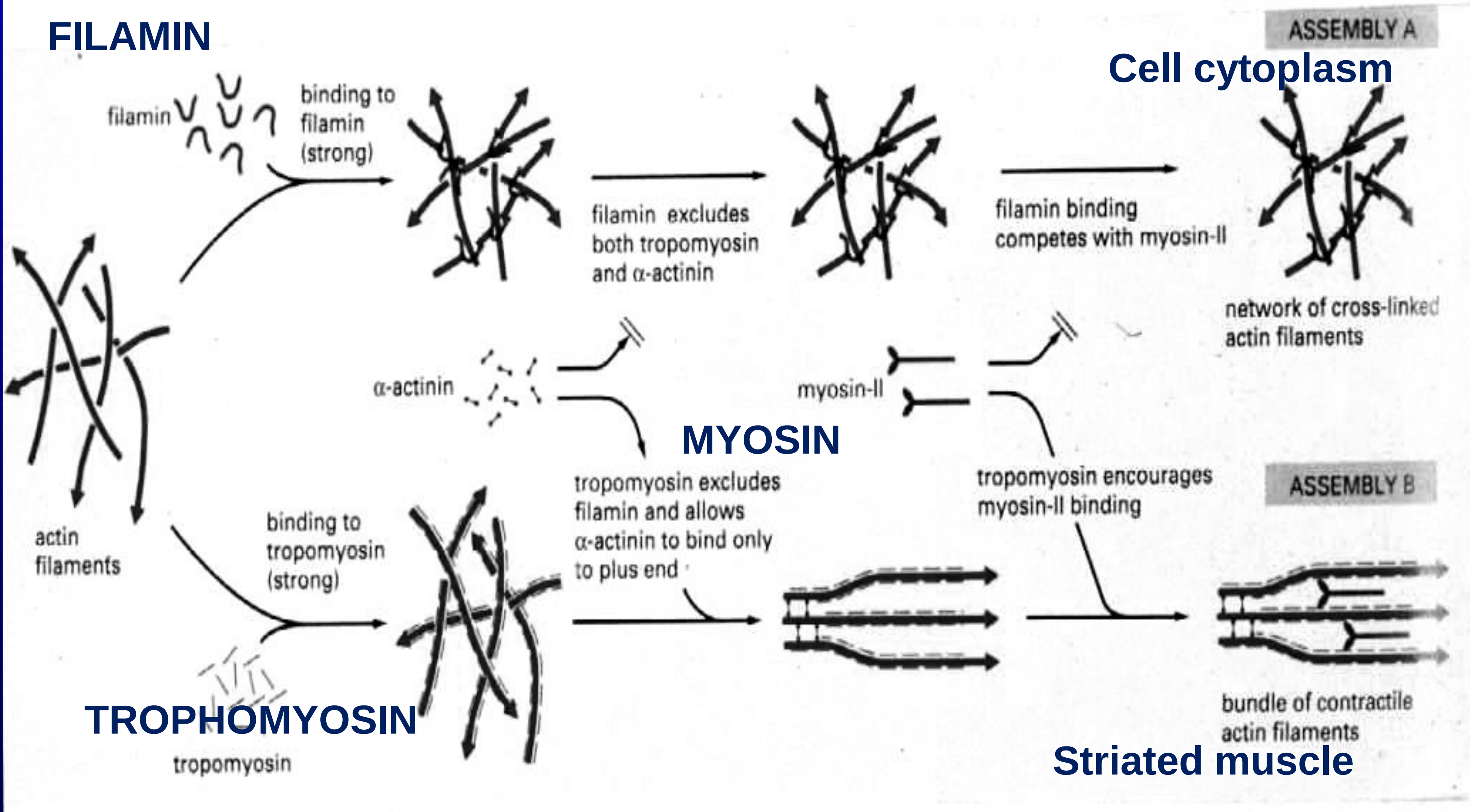


Actin associated proteins

Myosin - ATPase

Trophomyosin - rod-like protein

Filamin - bundles actin filaments



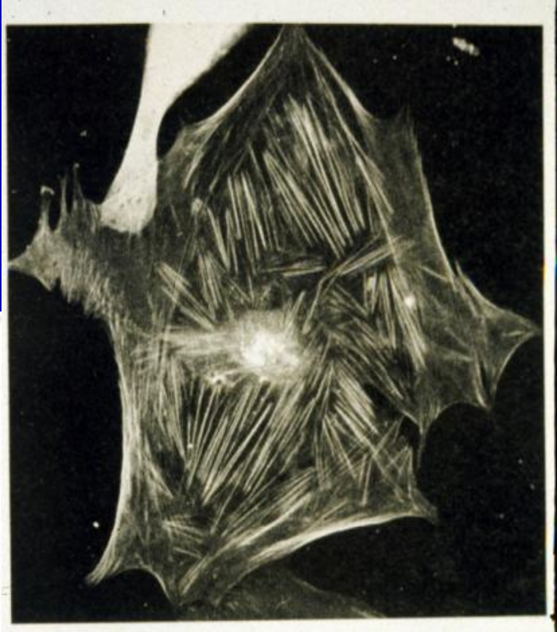
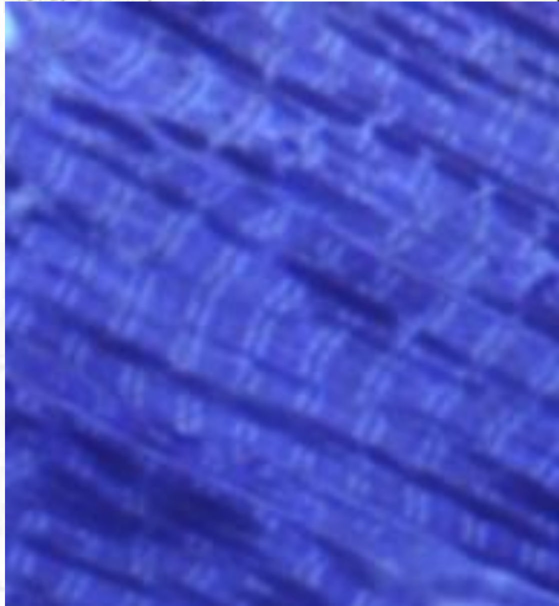
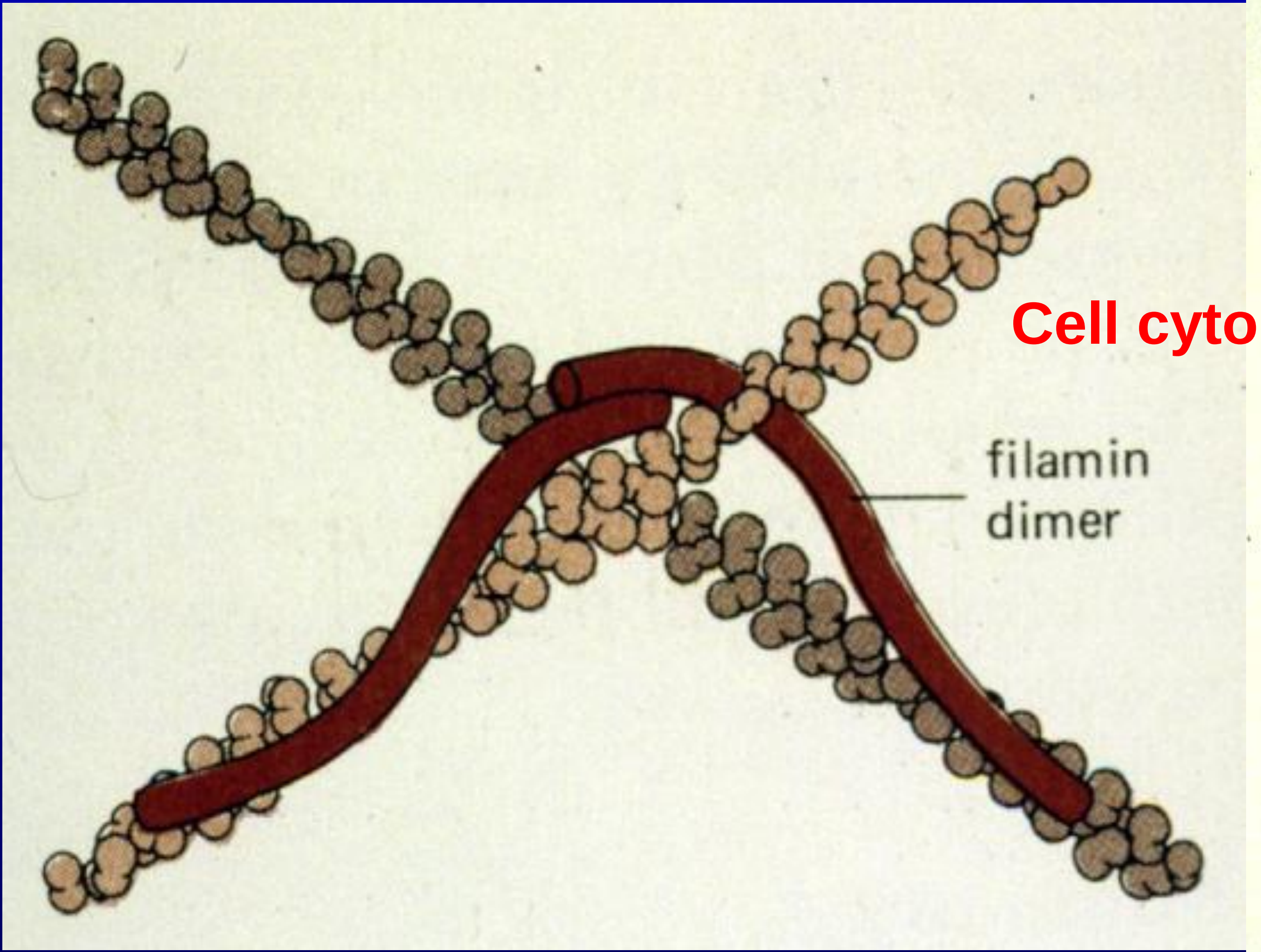
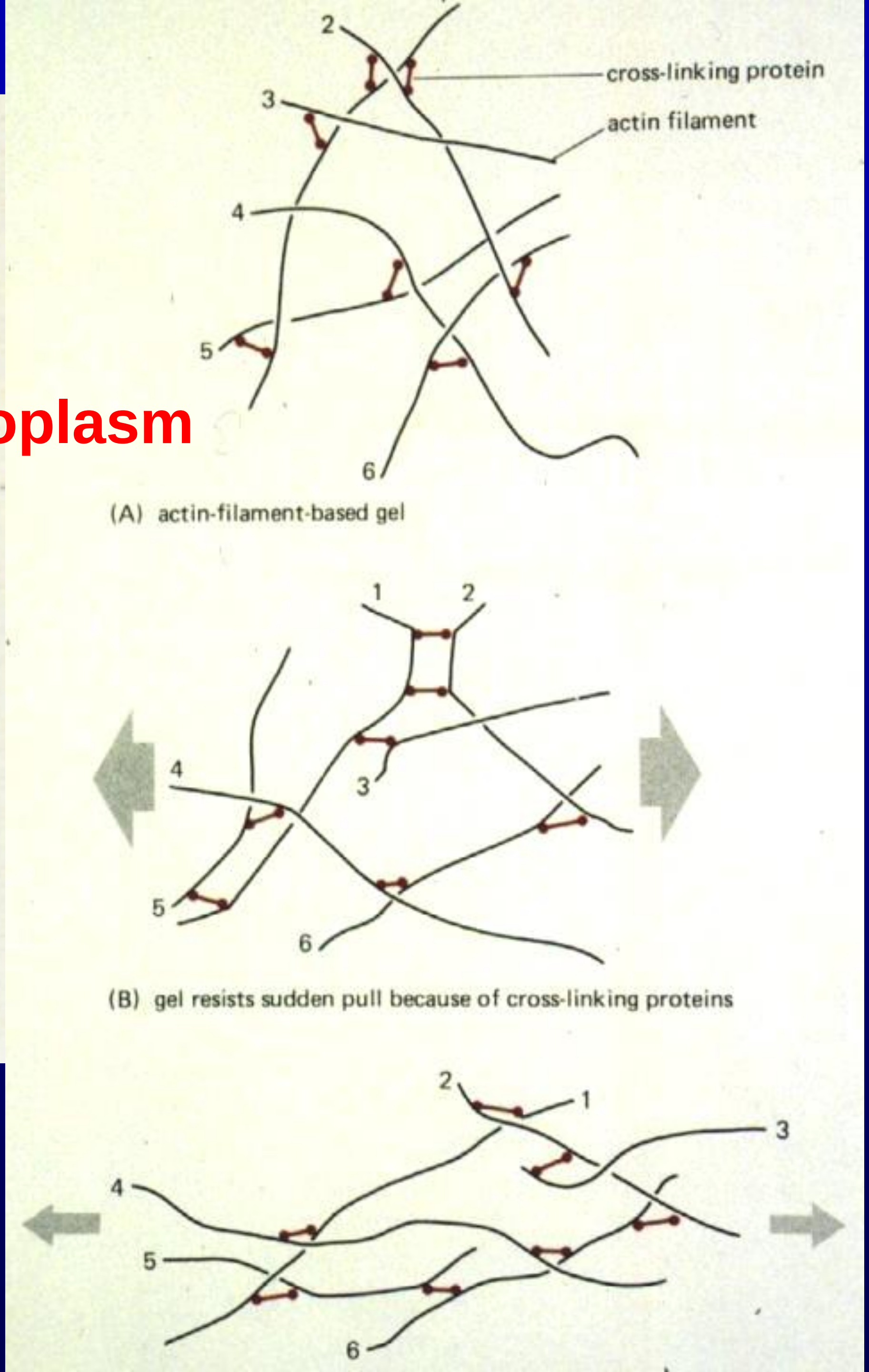


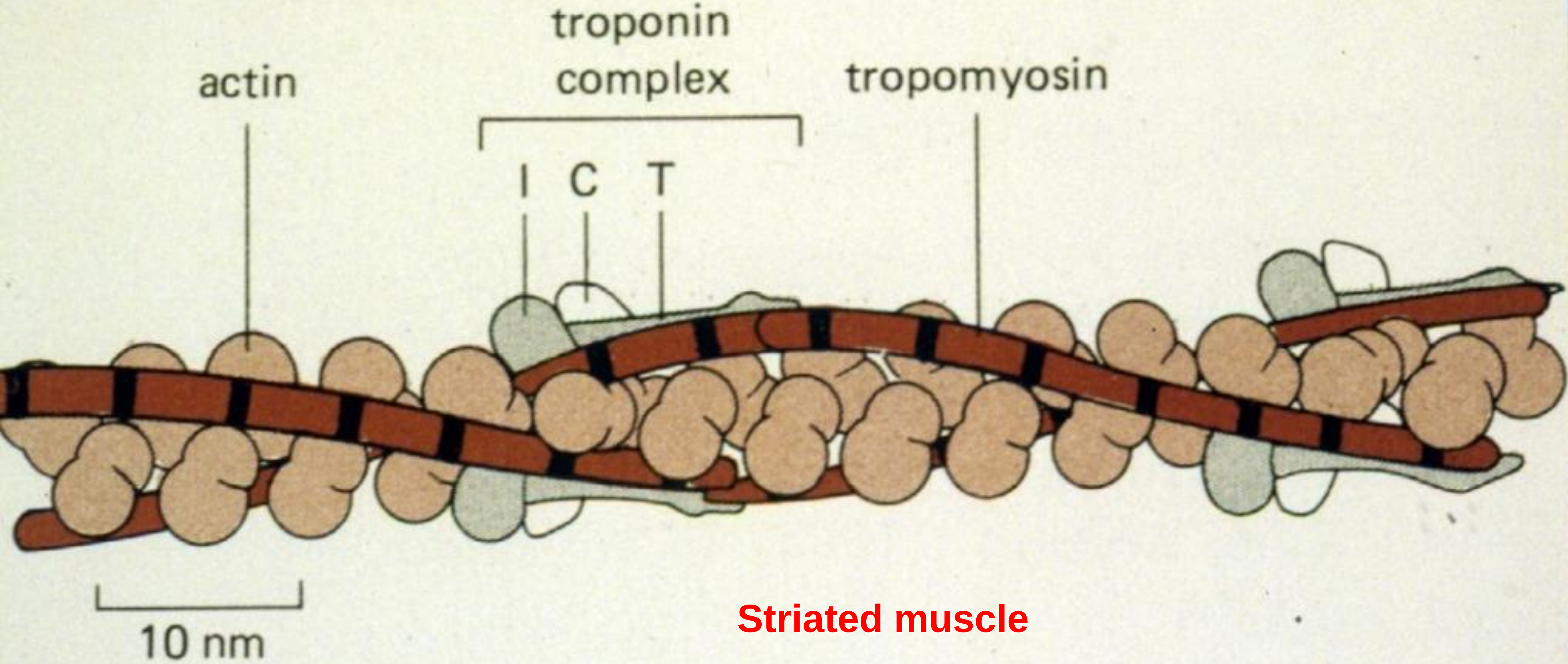
Figure 2–9. Actin fibrils composed of aggregates of actin filaments in the cytoplasm of a cultured human fibroblast preincubated in fluorescent actin antibody. × 1767. (Reproduced, with permission, from E Lazarides: *J Cell Biol* 1975; **65**:549.)



Cell cytoplasm



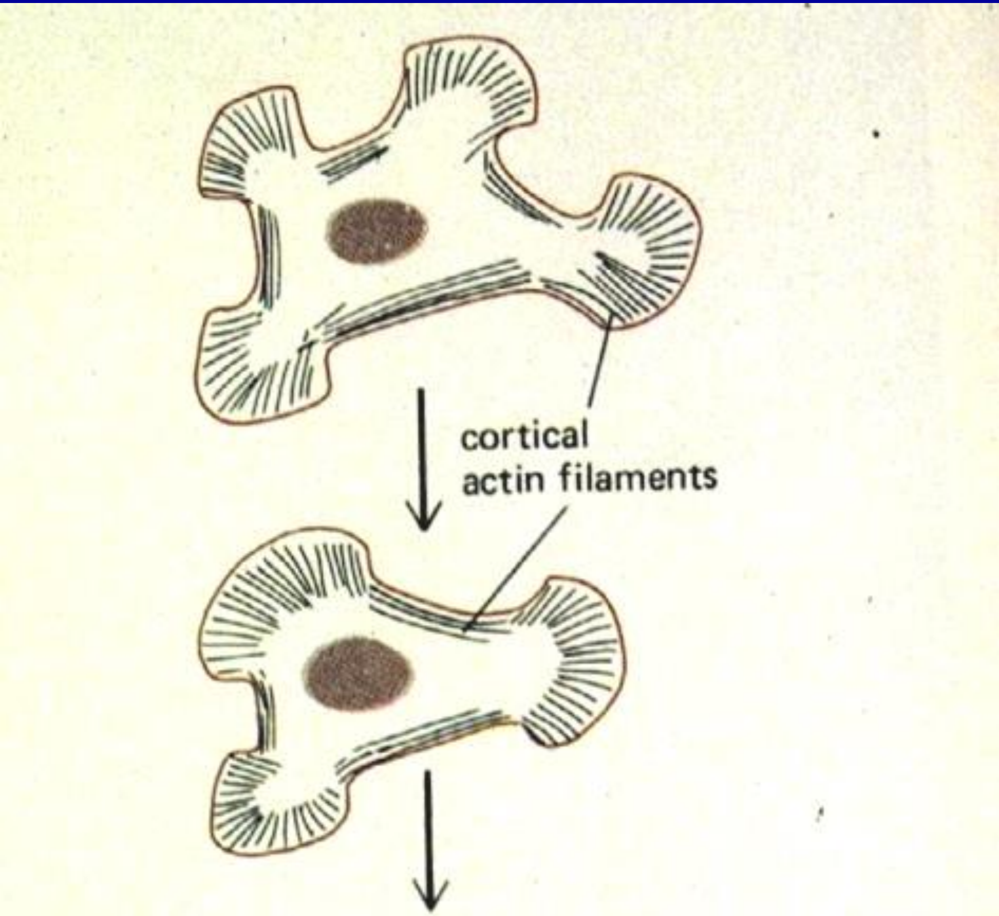


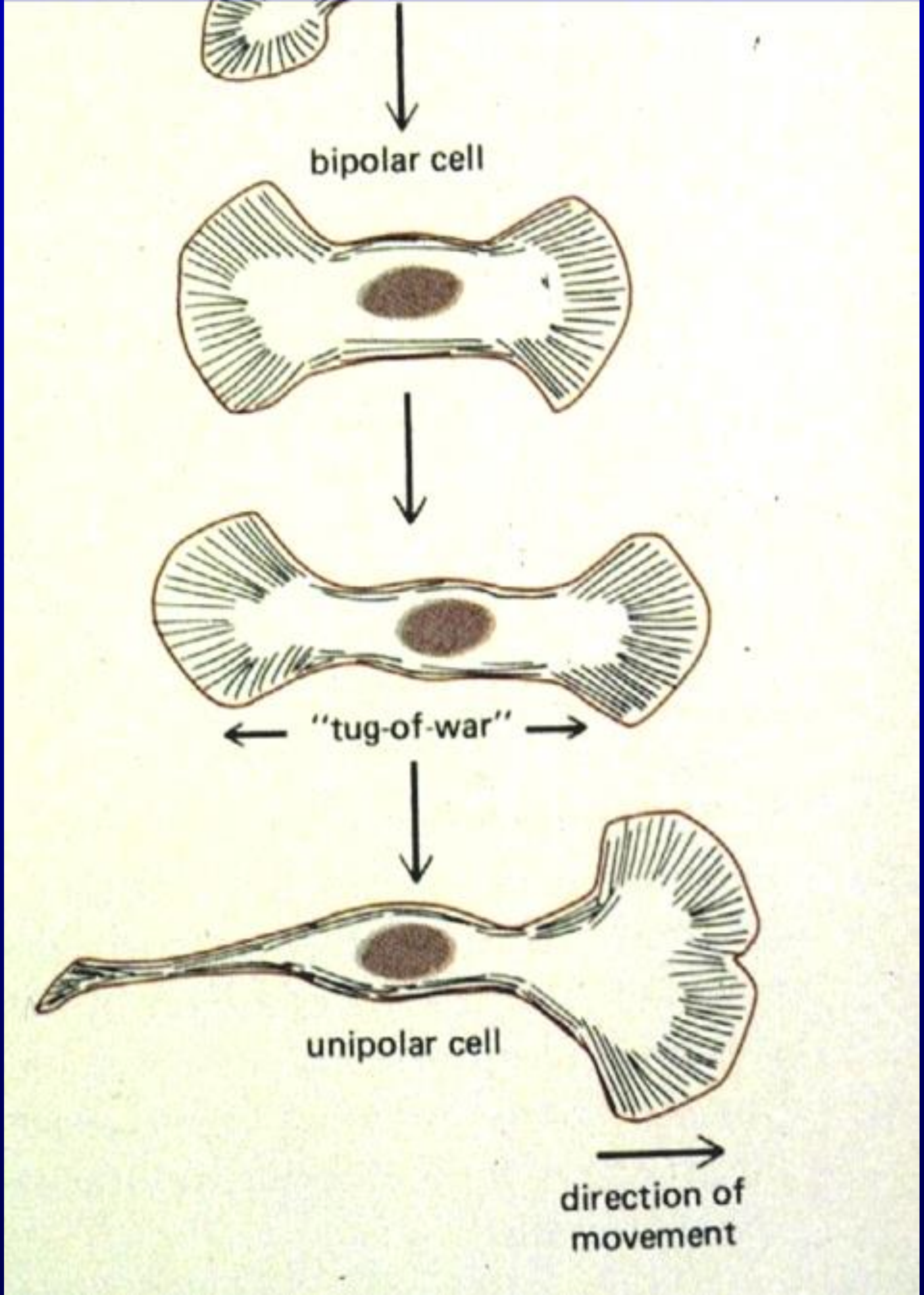


Striated muscle

Microfilaments - function

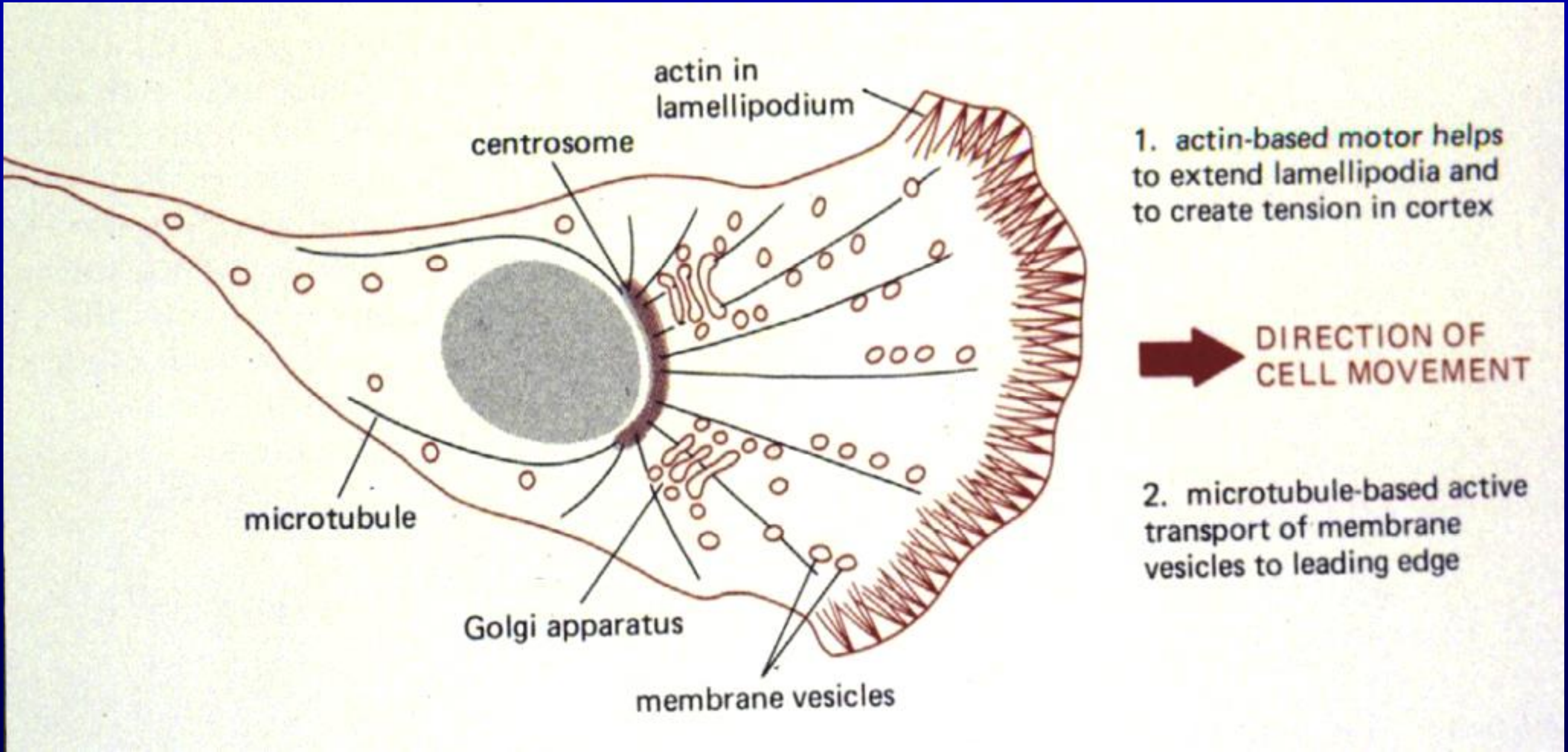
- Cell motility - actin and myosin

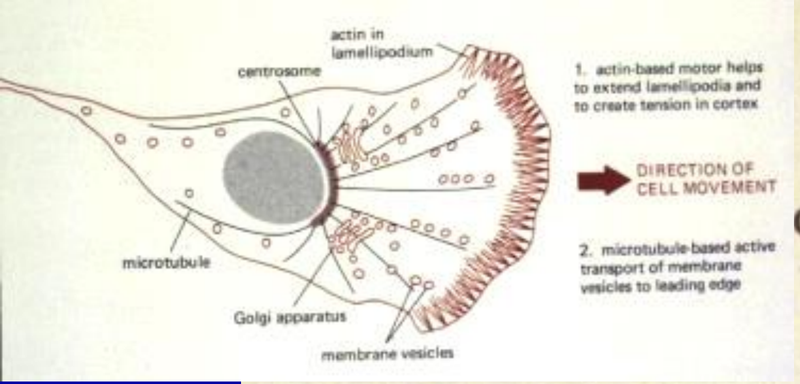


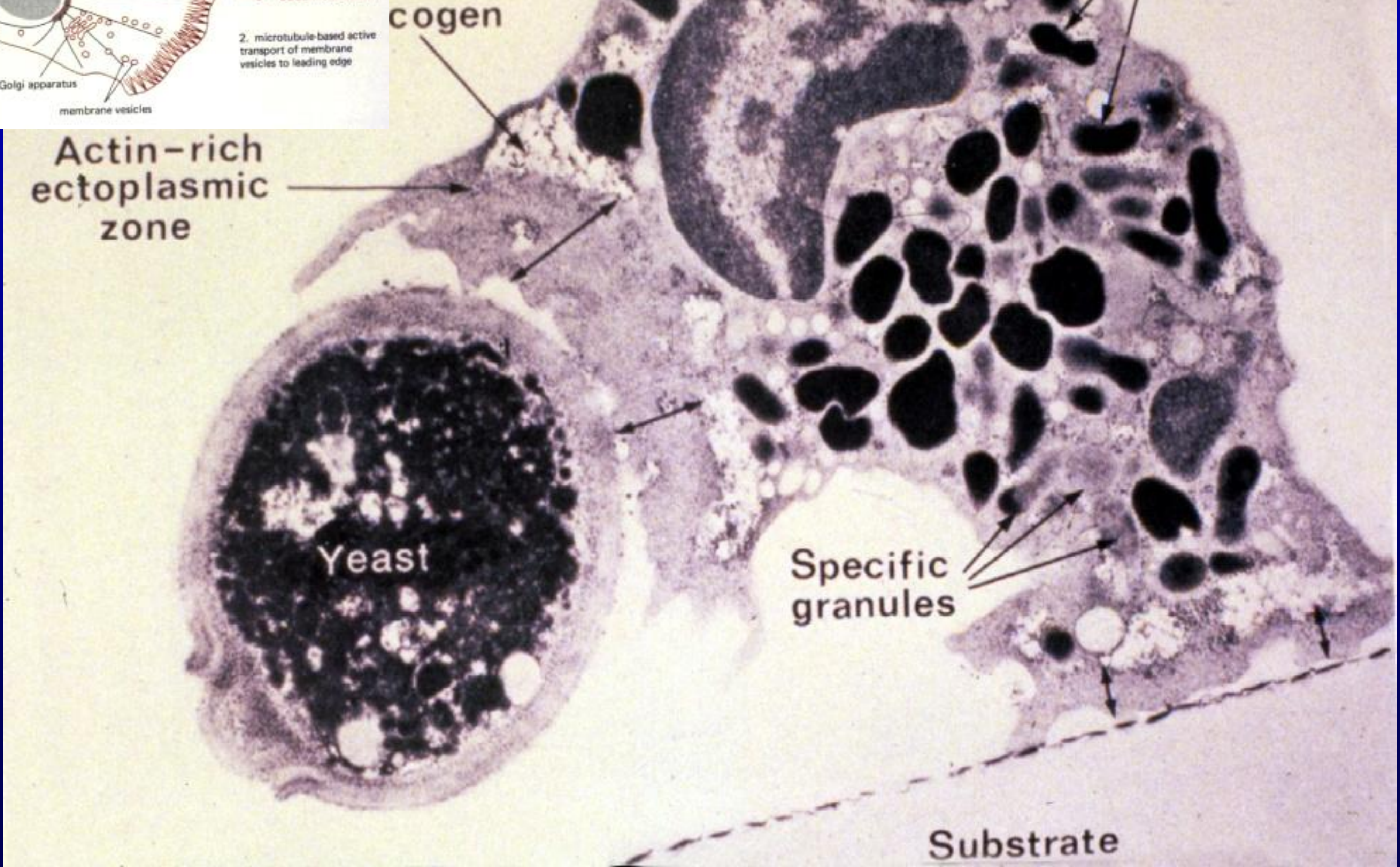


Microfilaments - function

- **Cell motility - actin and myosin**

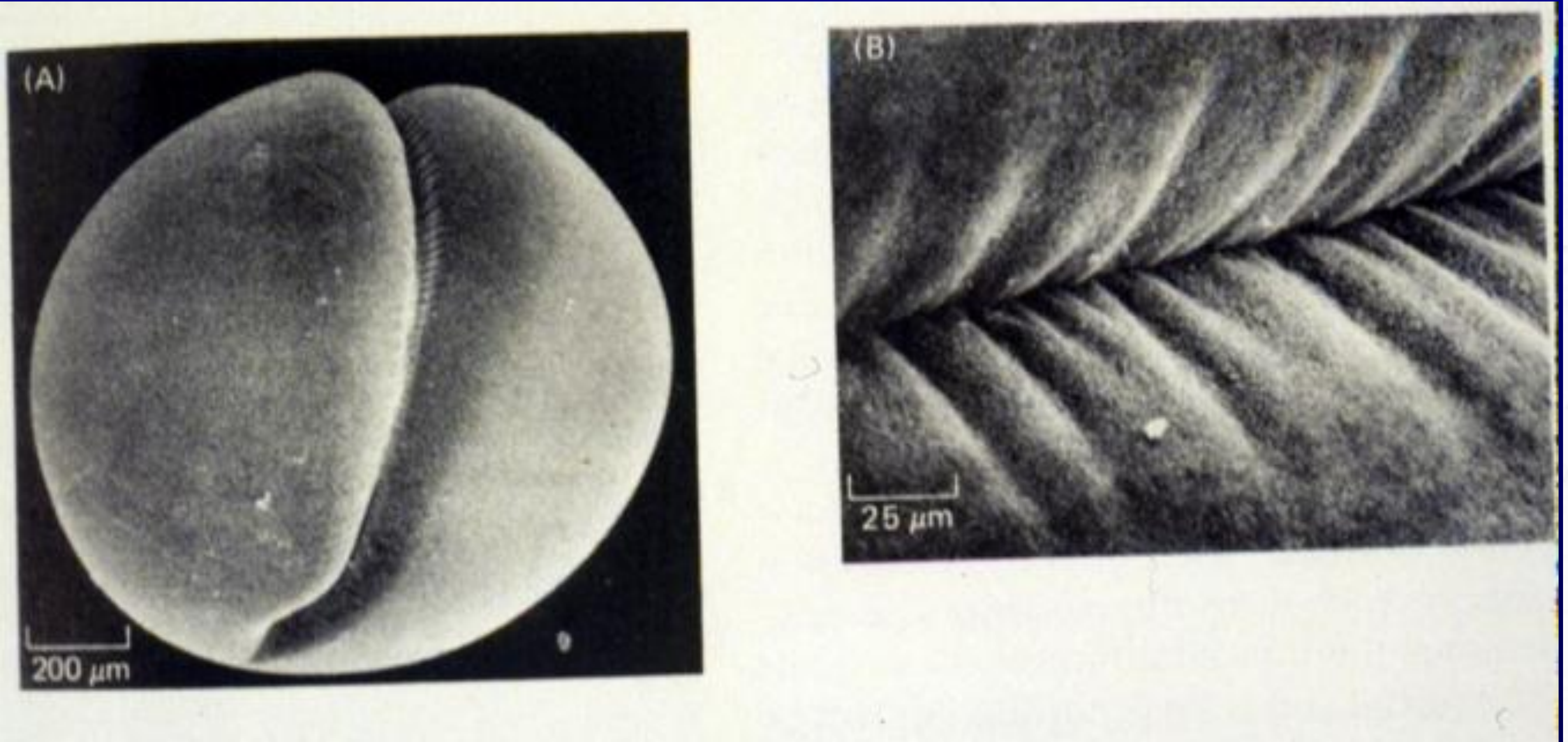


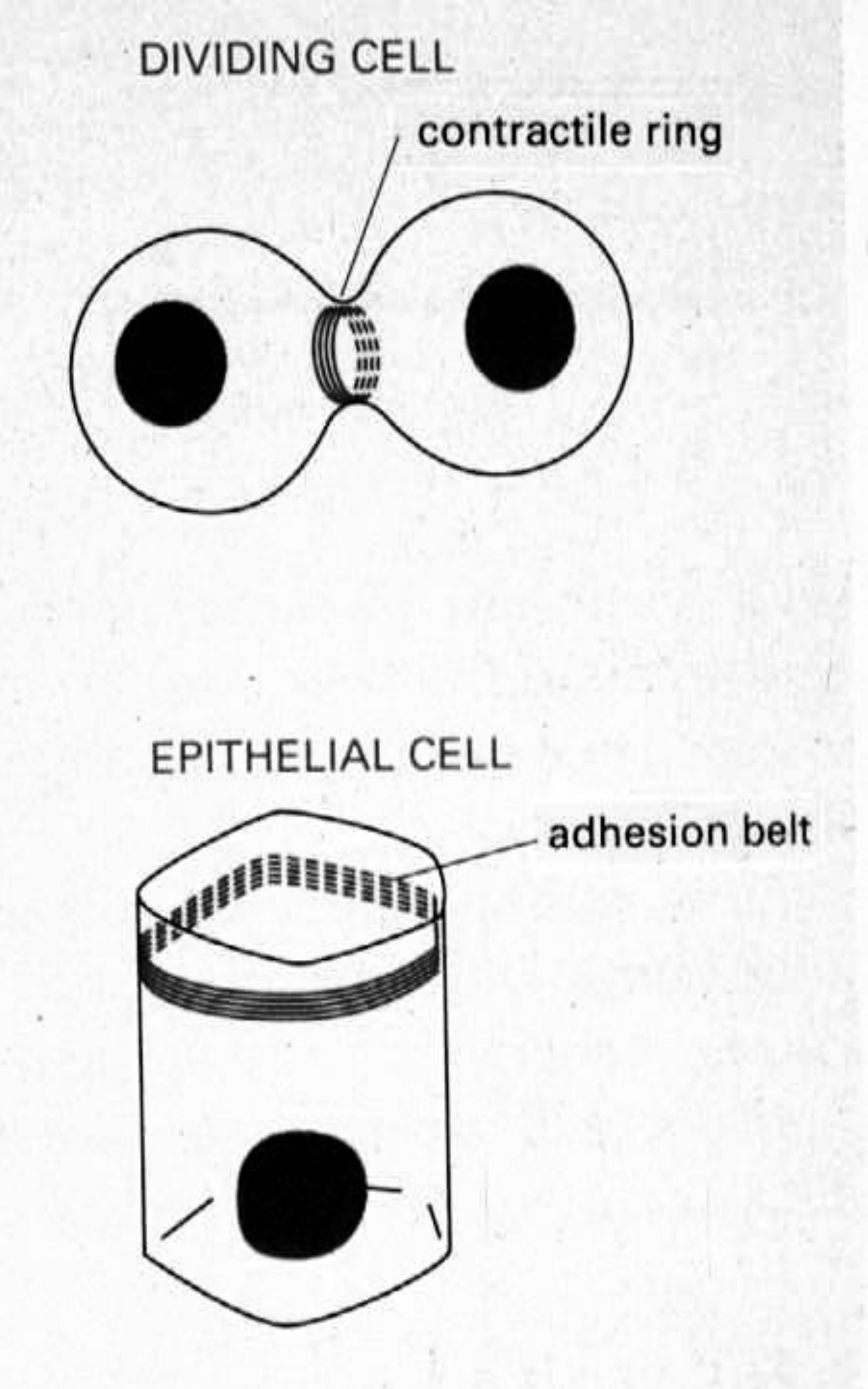

actin in lamellipodium
centrosome
microtubule
Golgi apparatus
membrane vesicles
1. actin-based motor helps to extend lamellipodia and to create tension in cortex
DIRECTION OF CELL MOVEMENT
2. microtubule-based active transport of membrane vesicles to leading edge


Azurophil granules
cogen
Actin-rich ectoplasmic zone
Yeast
Specific granules
Substrate

Microfilaments - function

Cytokinesis - division of cytoplasm

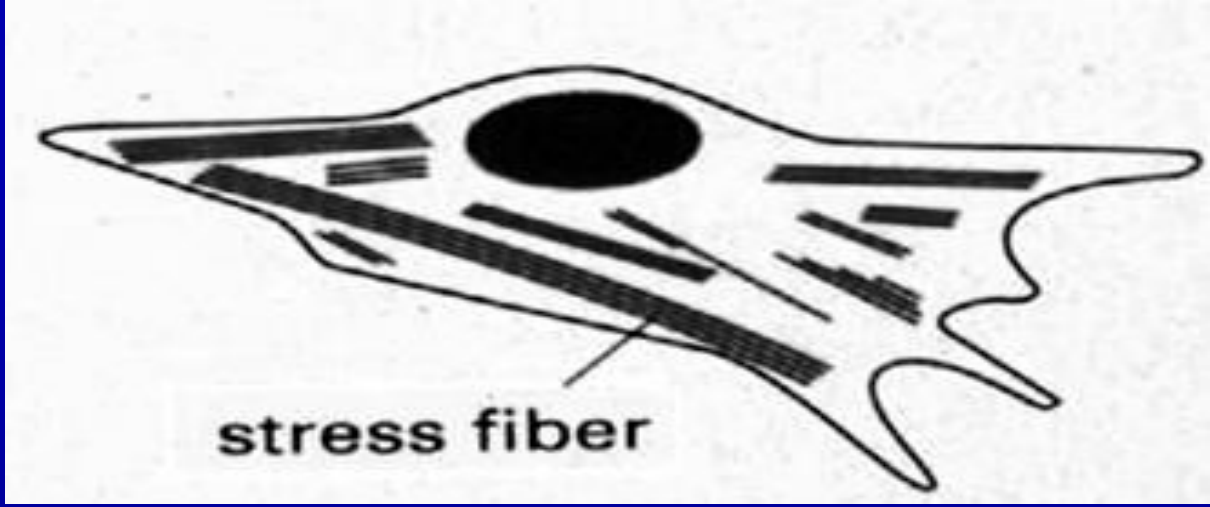


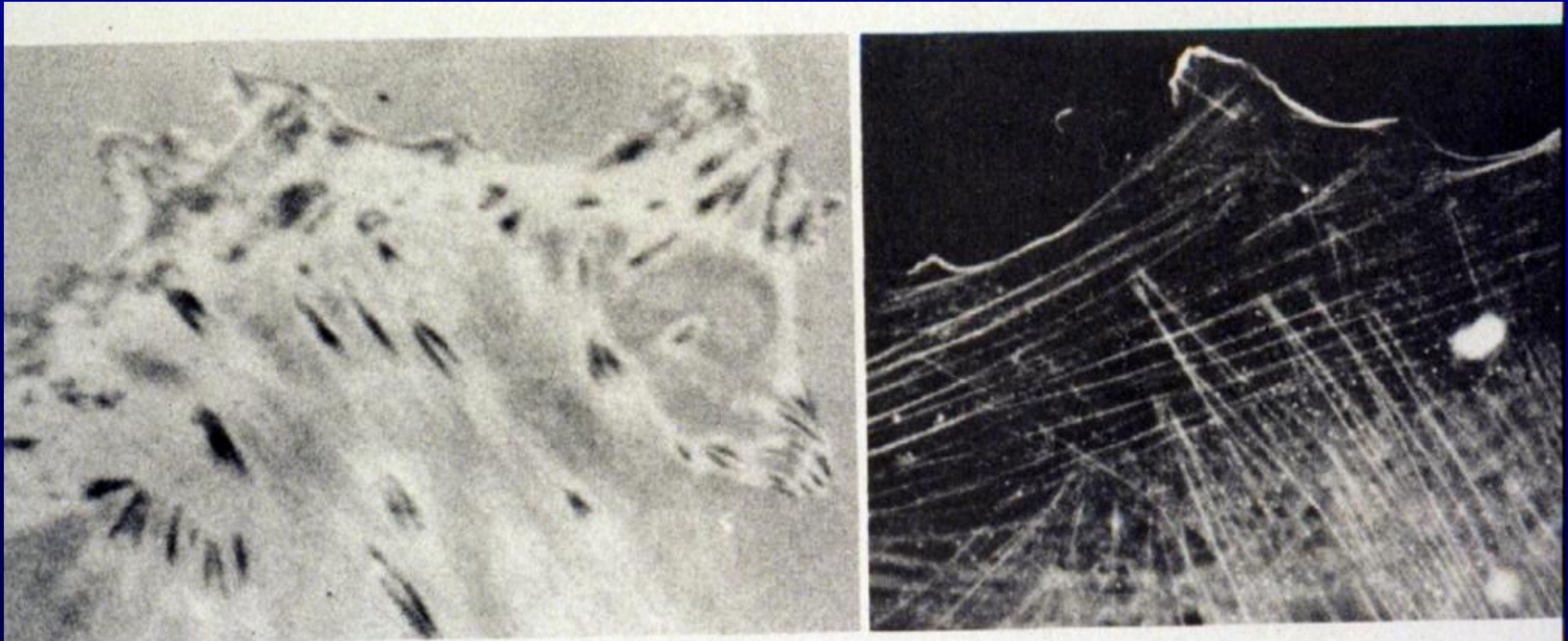


Microfilaments - function

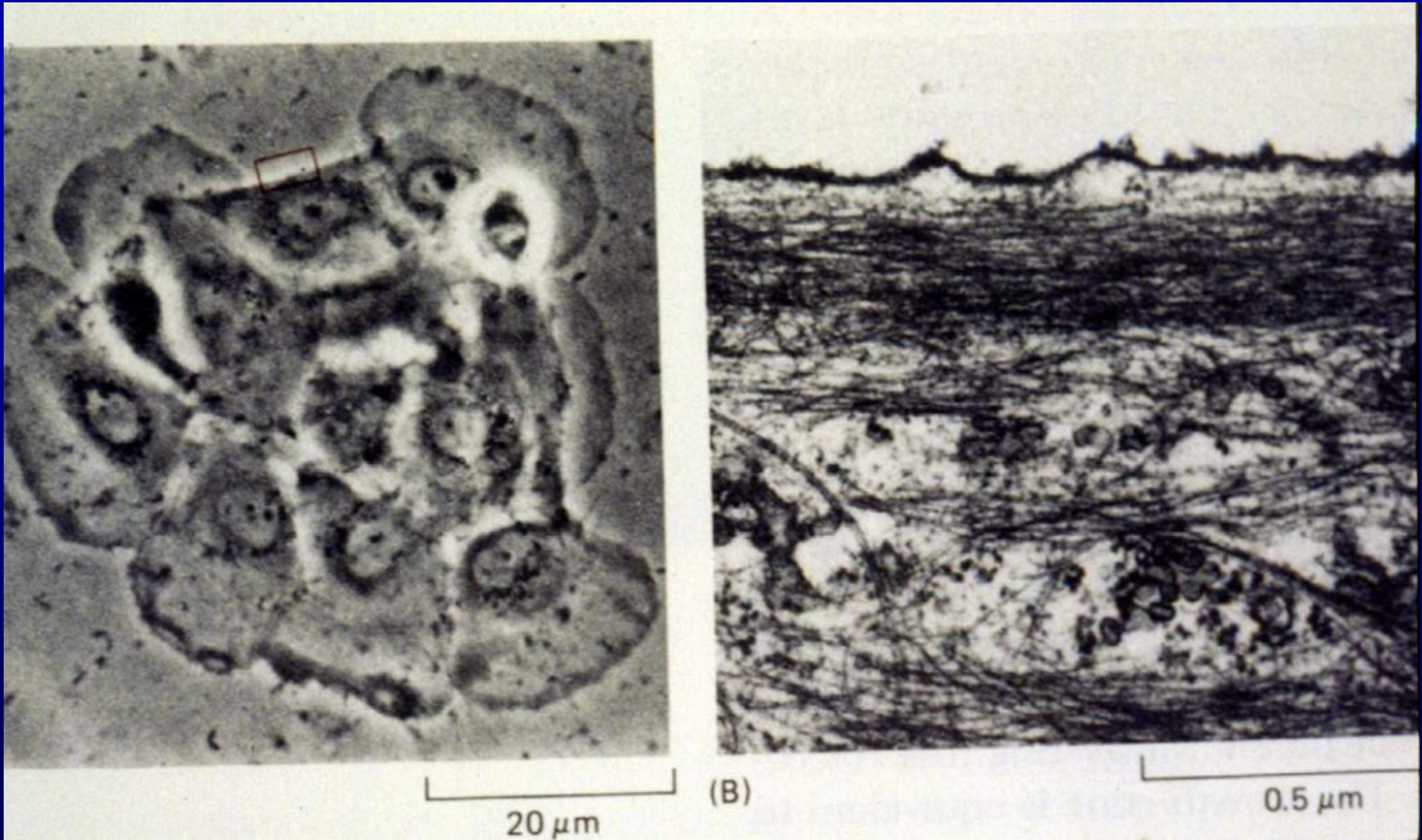
Structural support

– Stress fibers

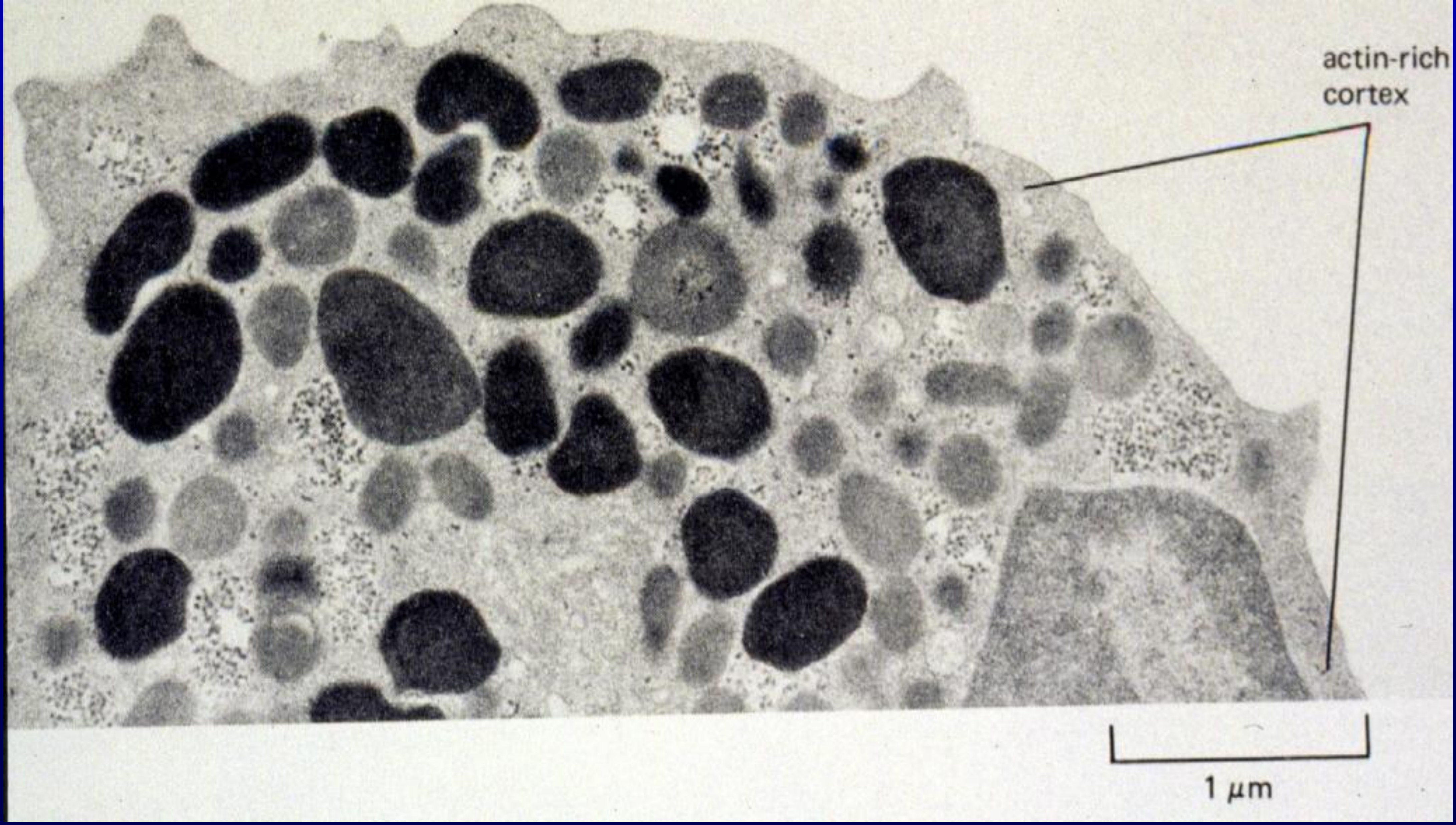




Microfilaments

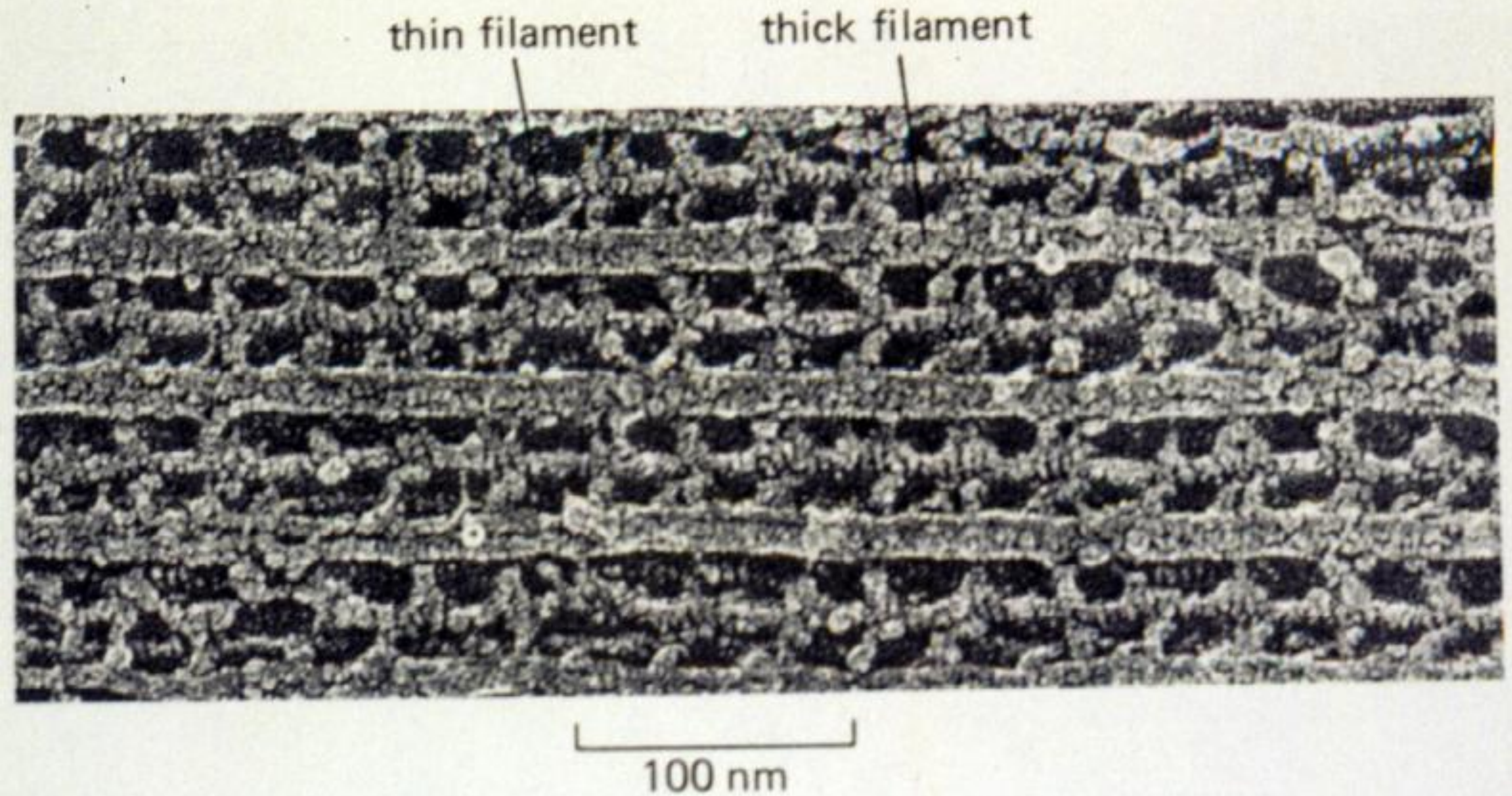


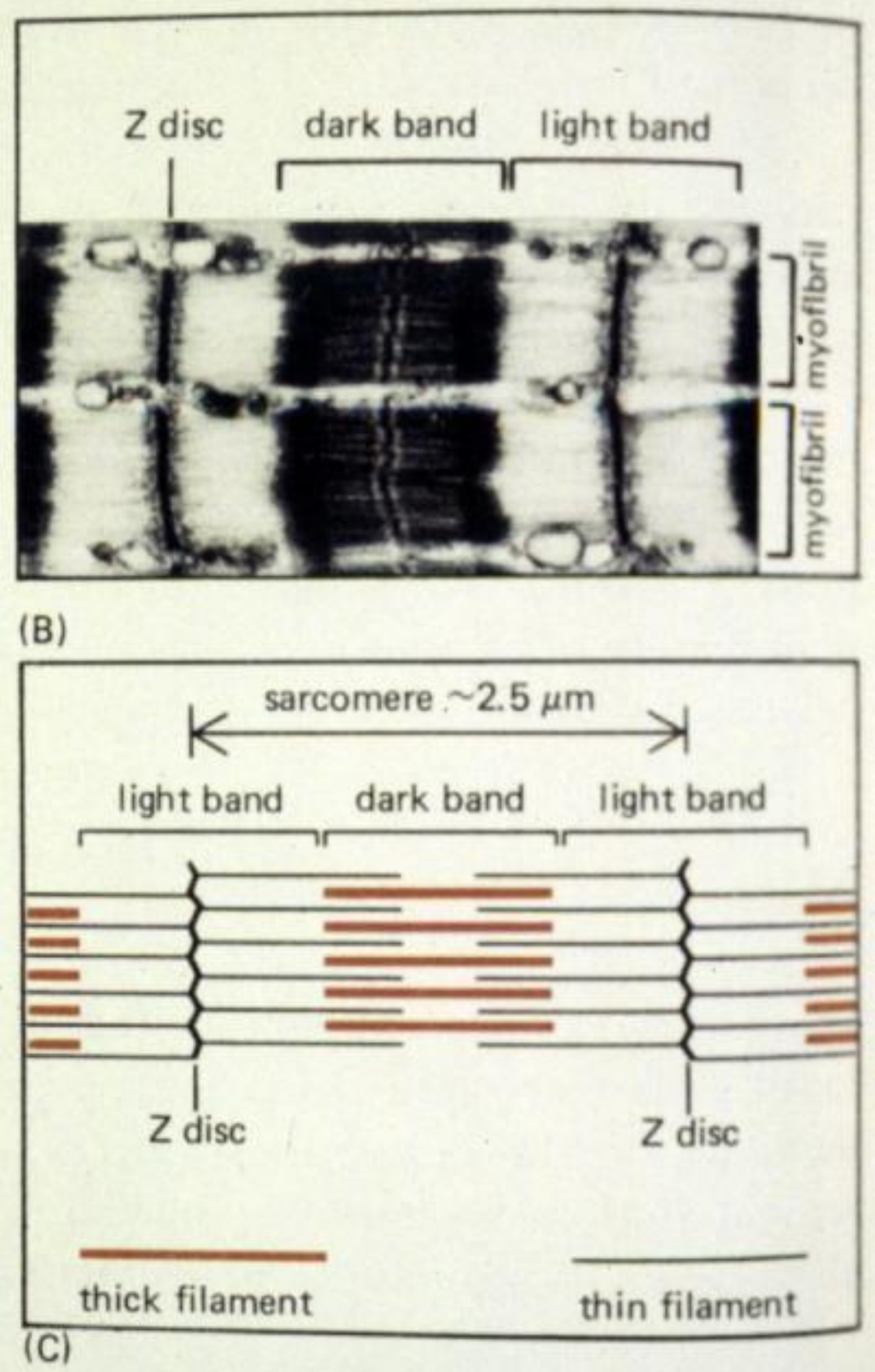
Microfilaments



Microfilaments - function

- Structural support
  - Cell movement



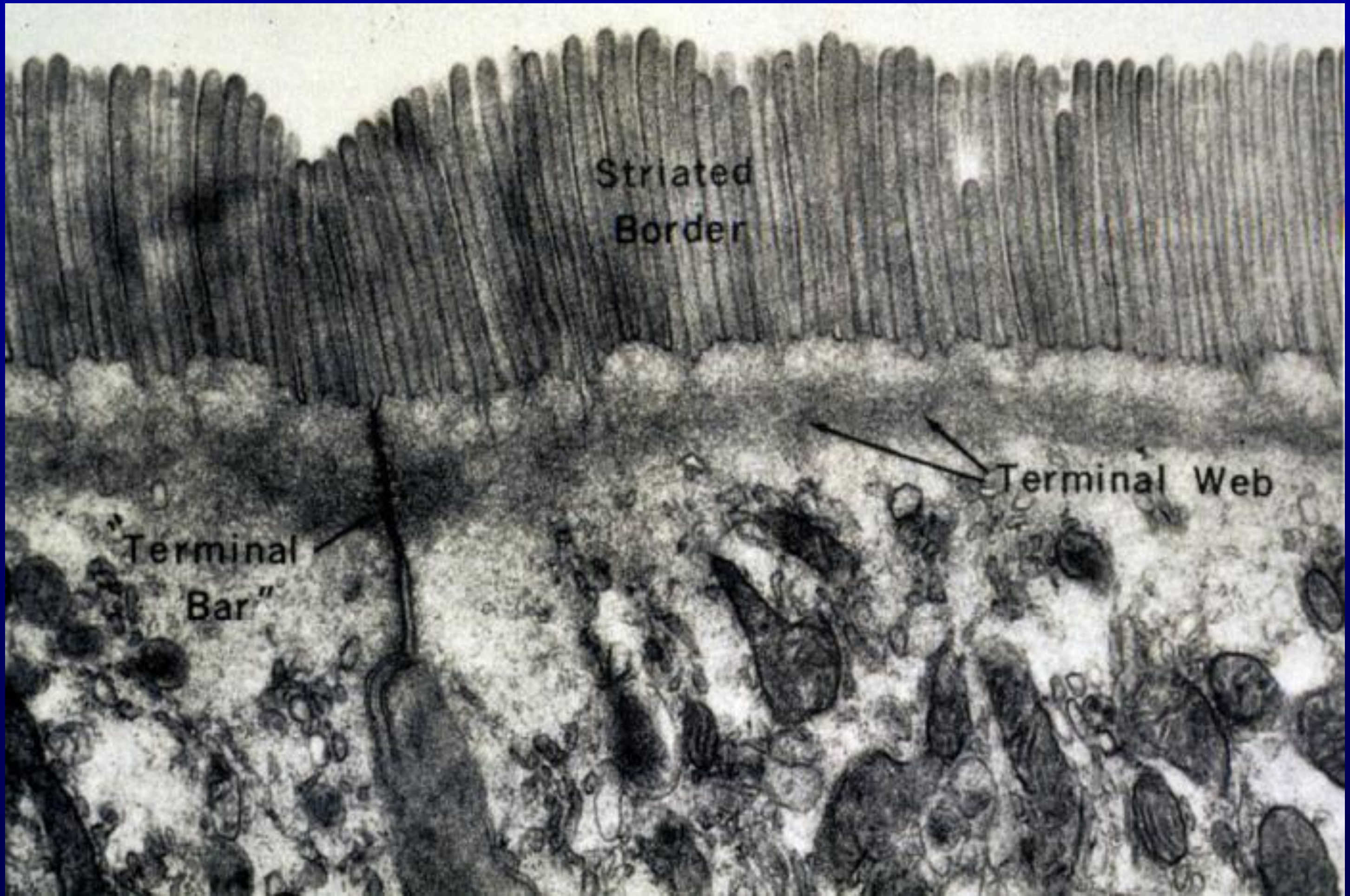


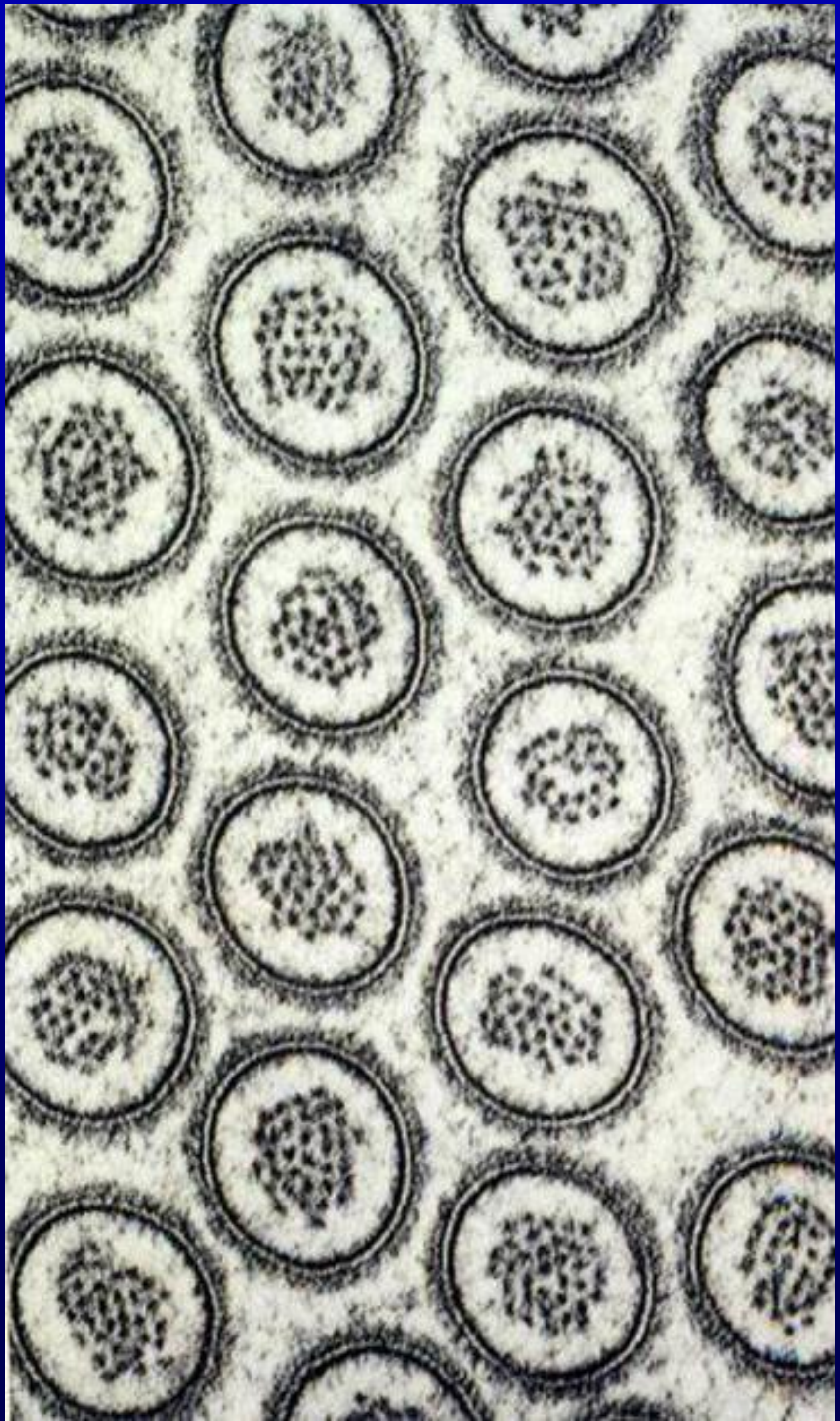
Microfilaments - function

Structural support -

– Microvilli movement and shape

– Pushes membrane out from cell

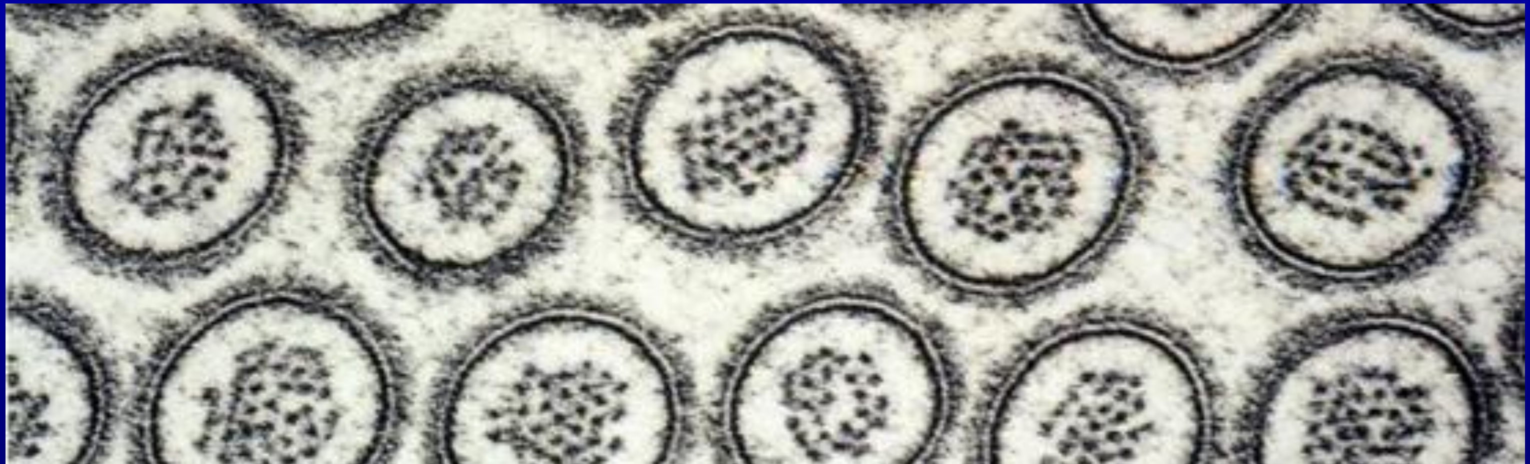


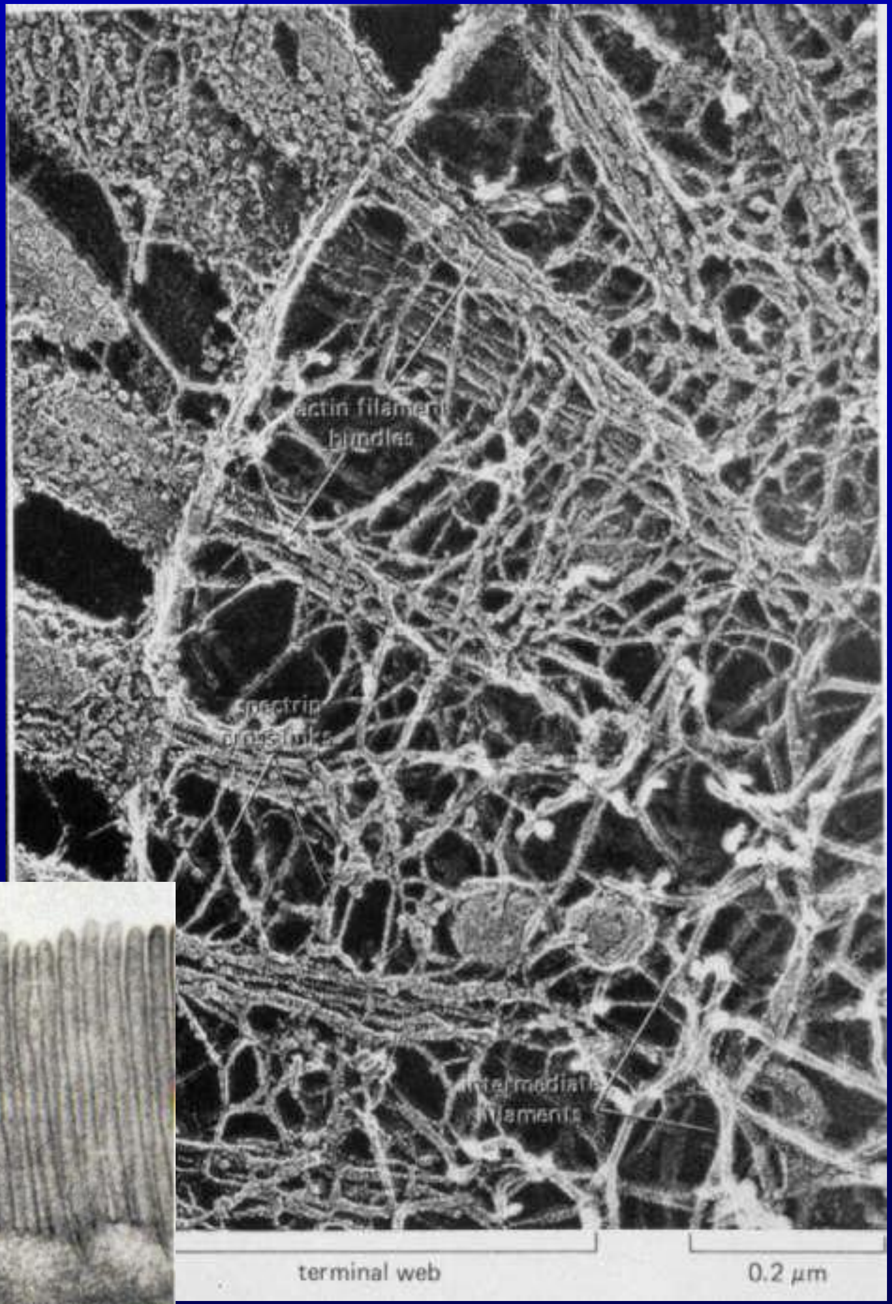


Microfilaments - function

Structural support -

– Microvilli - movement and shape

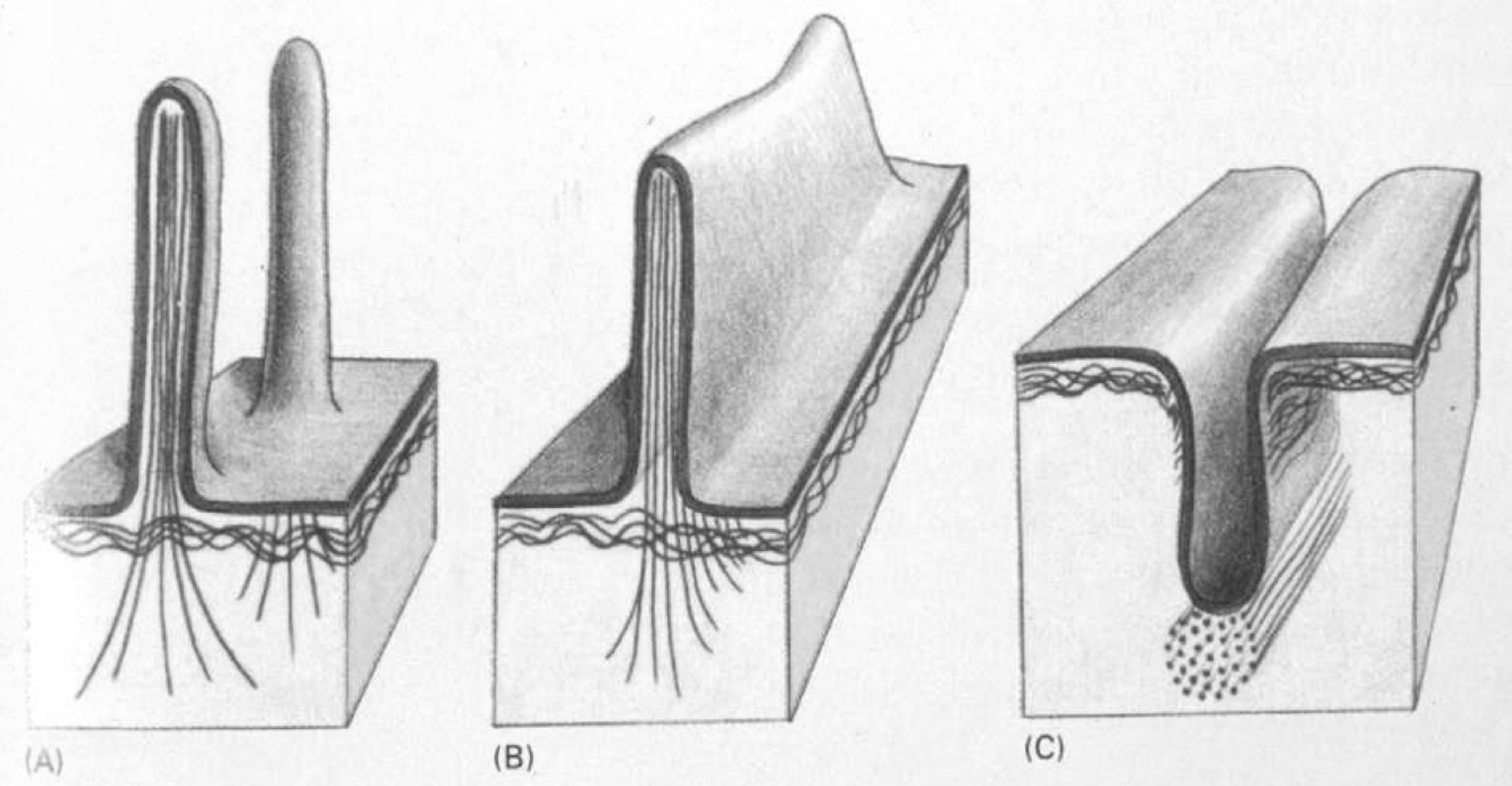




Microfilaments - function

Structural support -

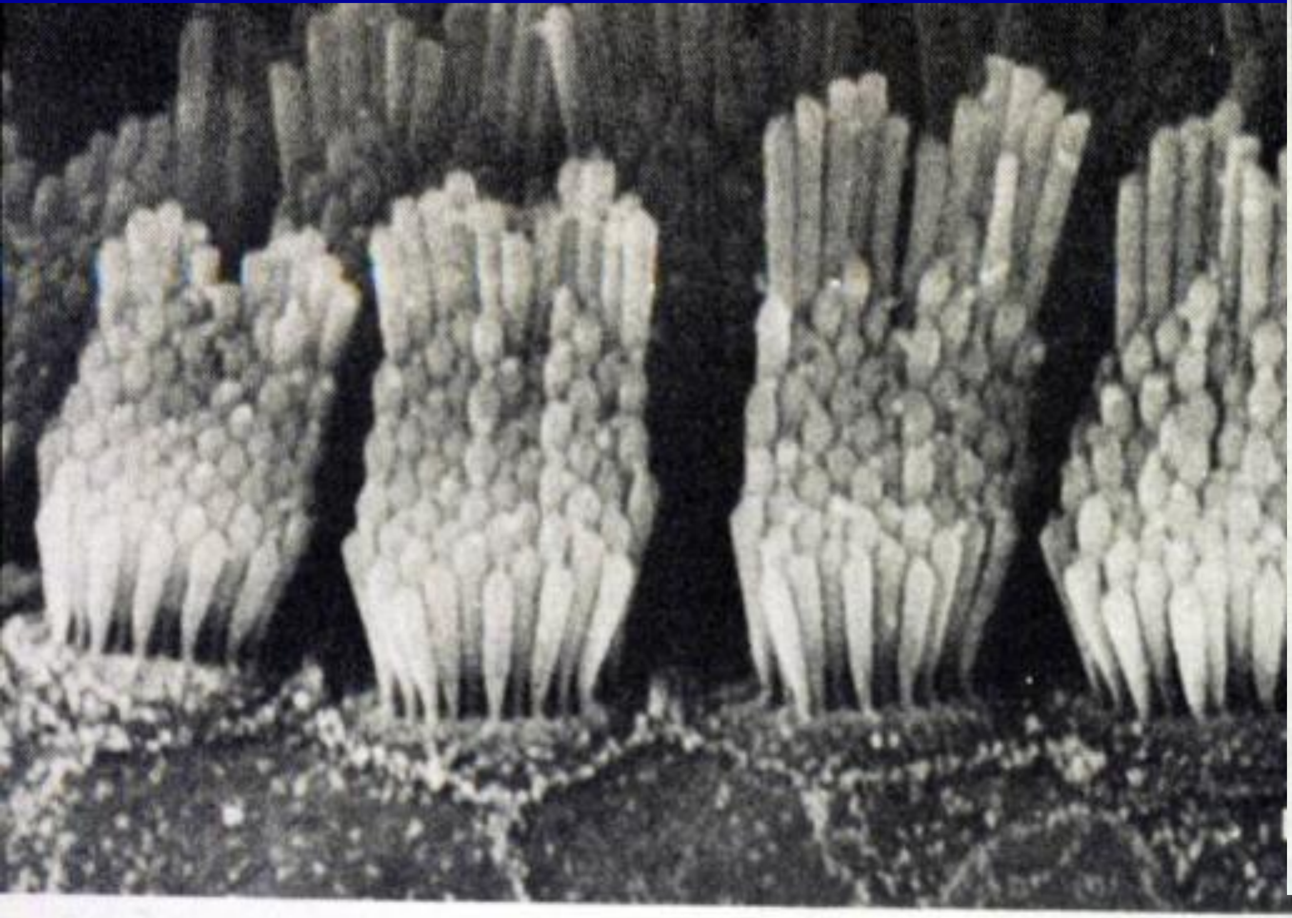
– Microvilli - movement and shape

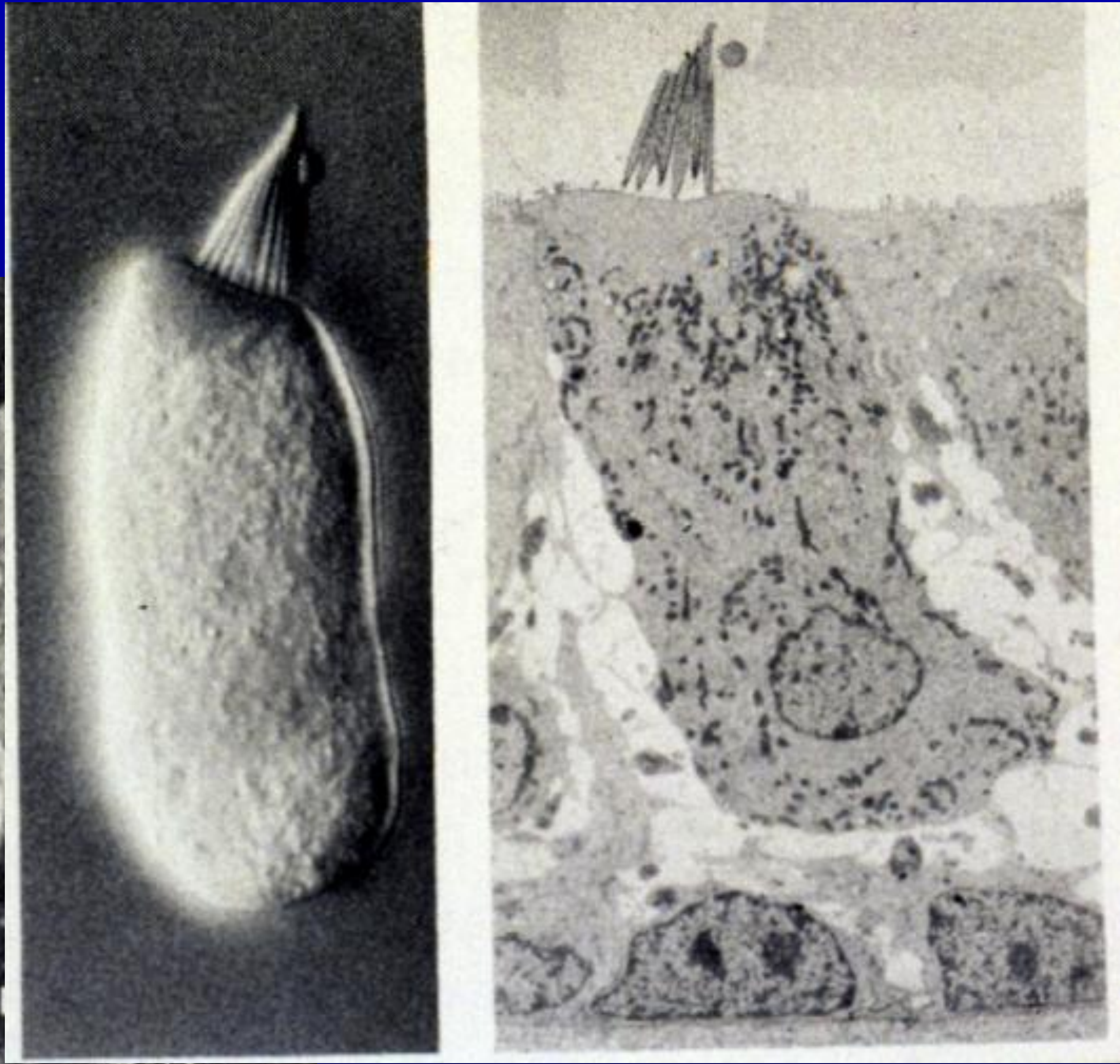


Microfilaments - function

Structural support -

Stereocilia - extension

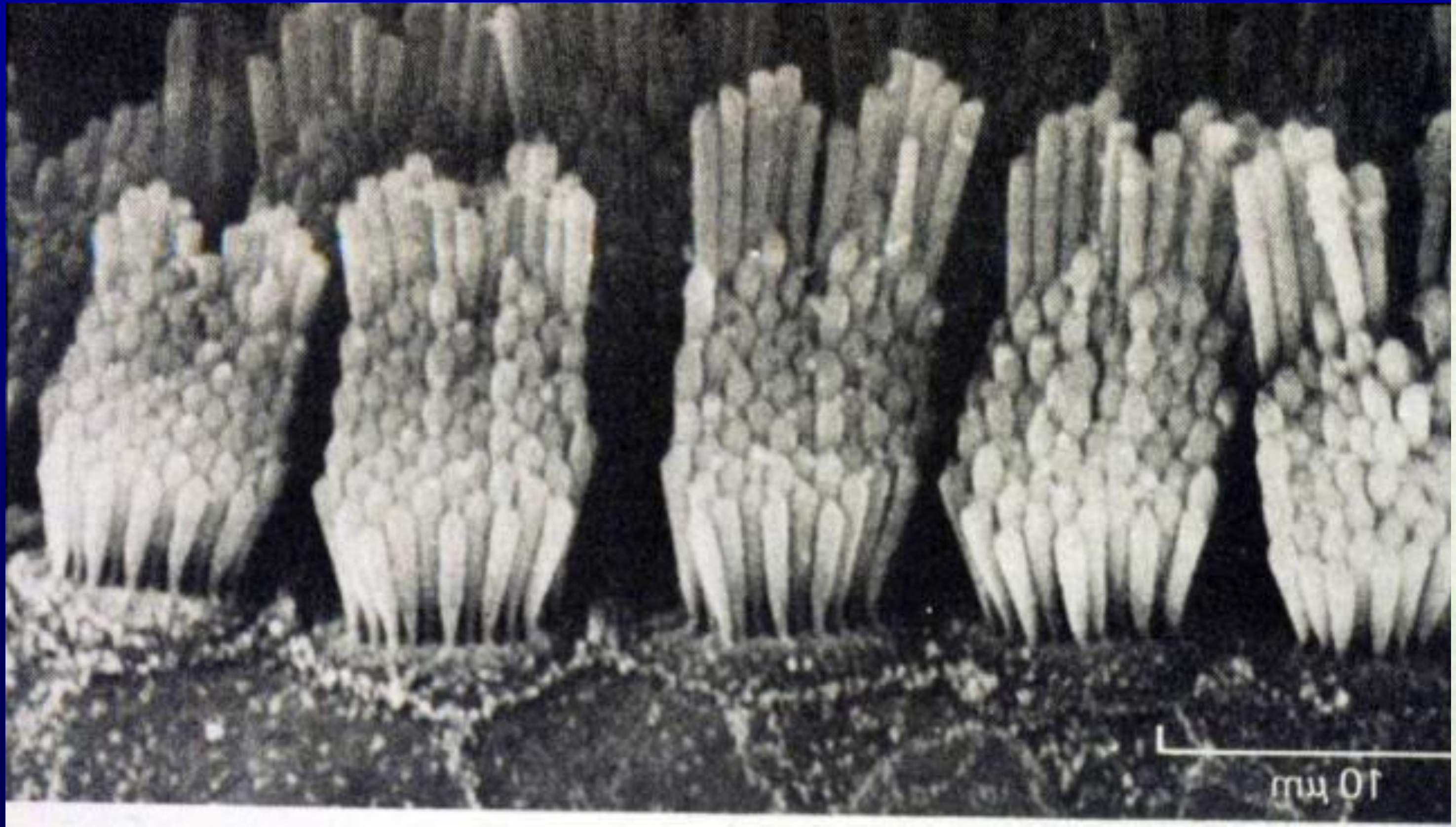


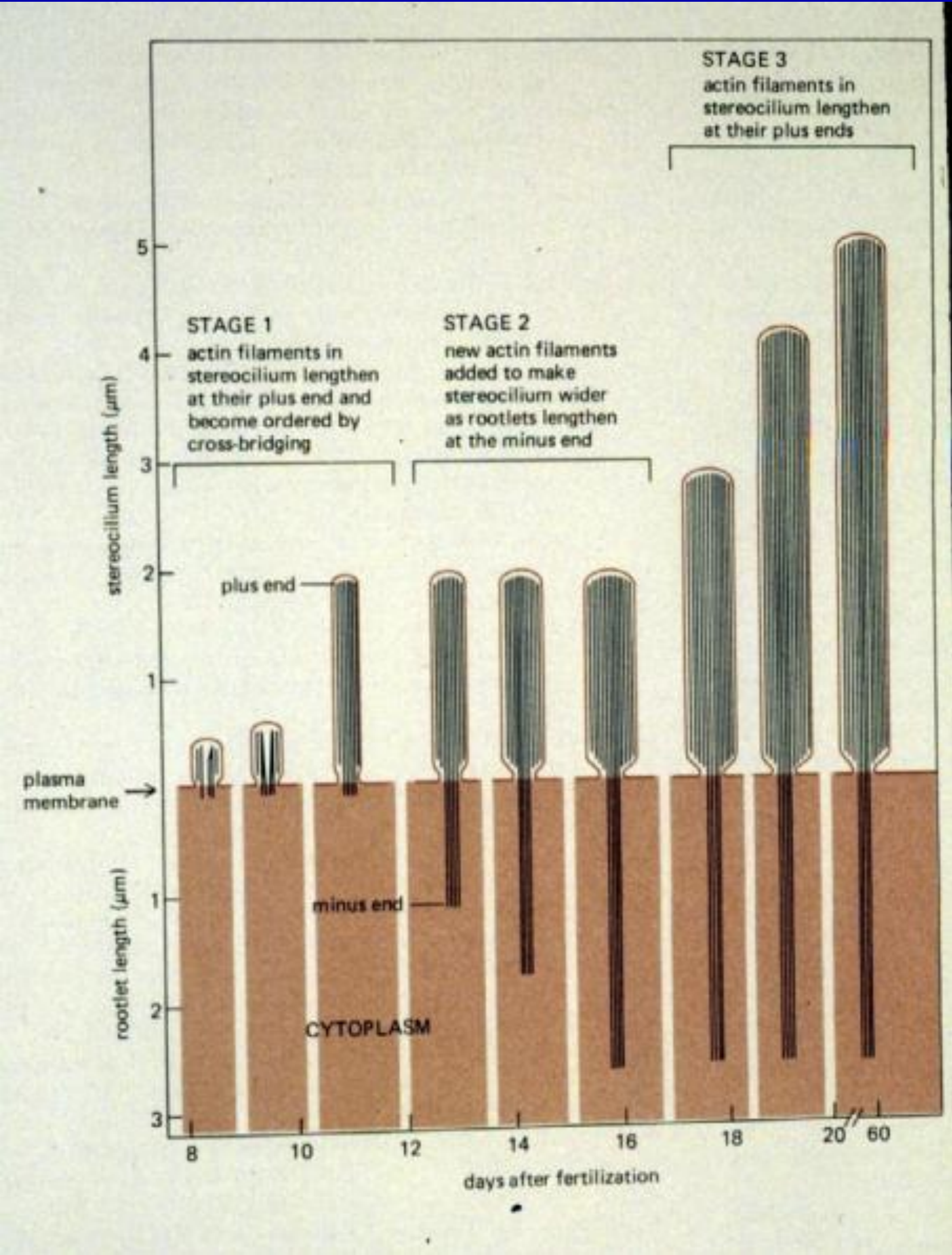


Microfilaments - function

Structural support -

Stereocilia - extension

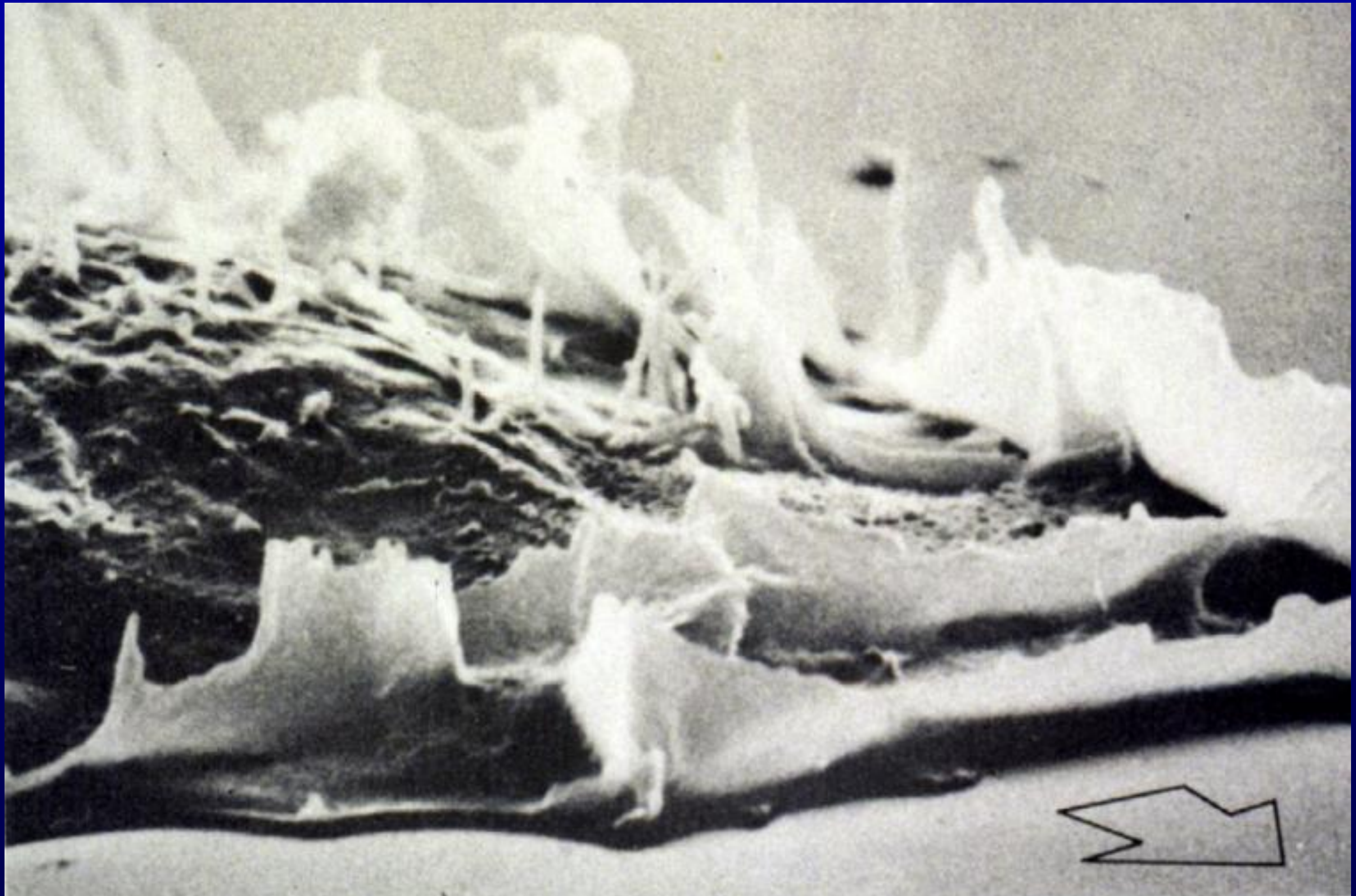


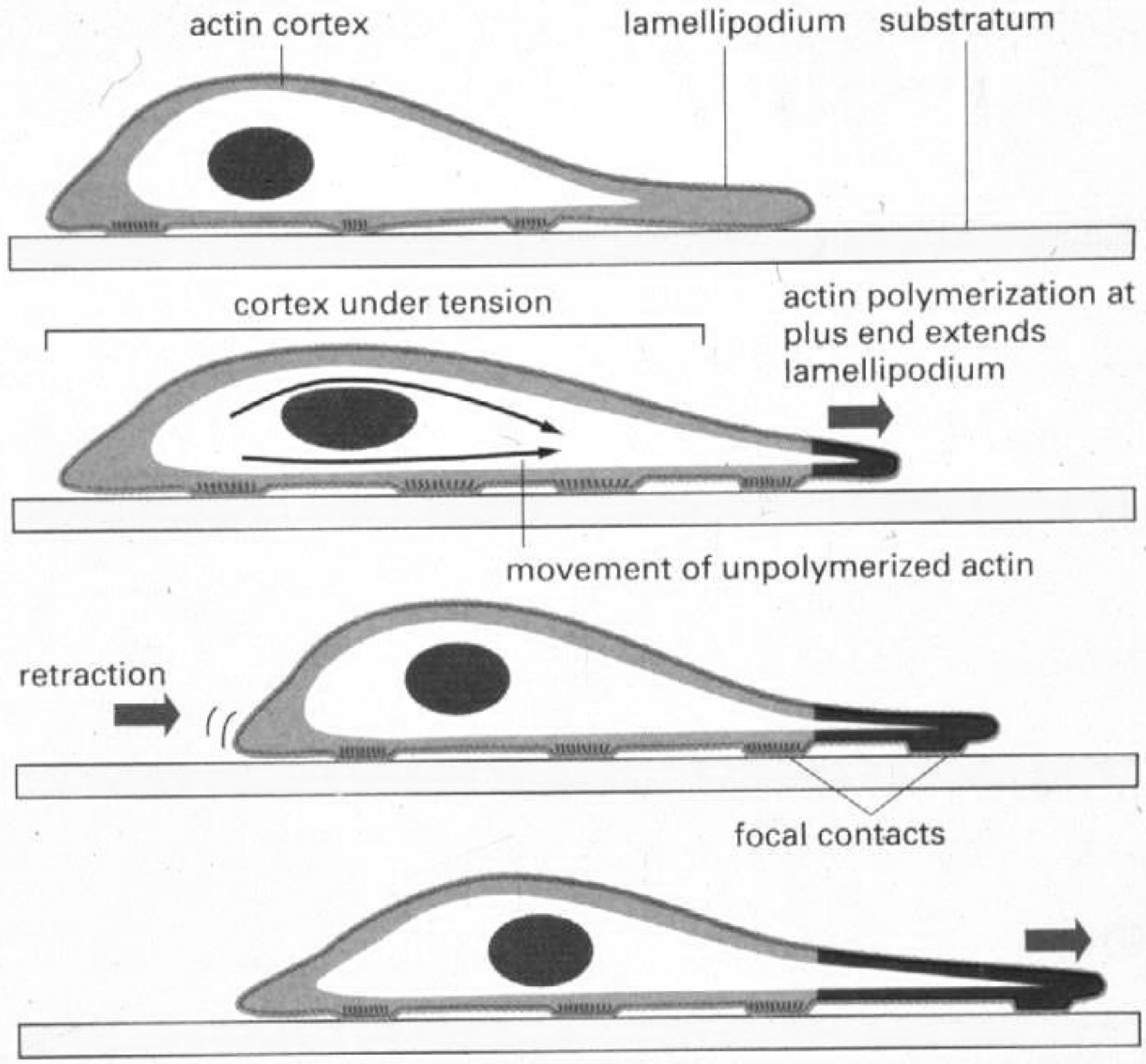


Microfilaments - function

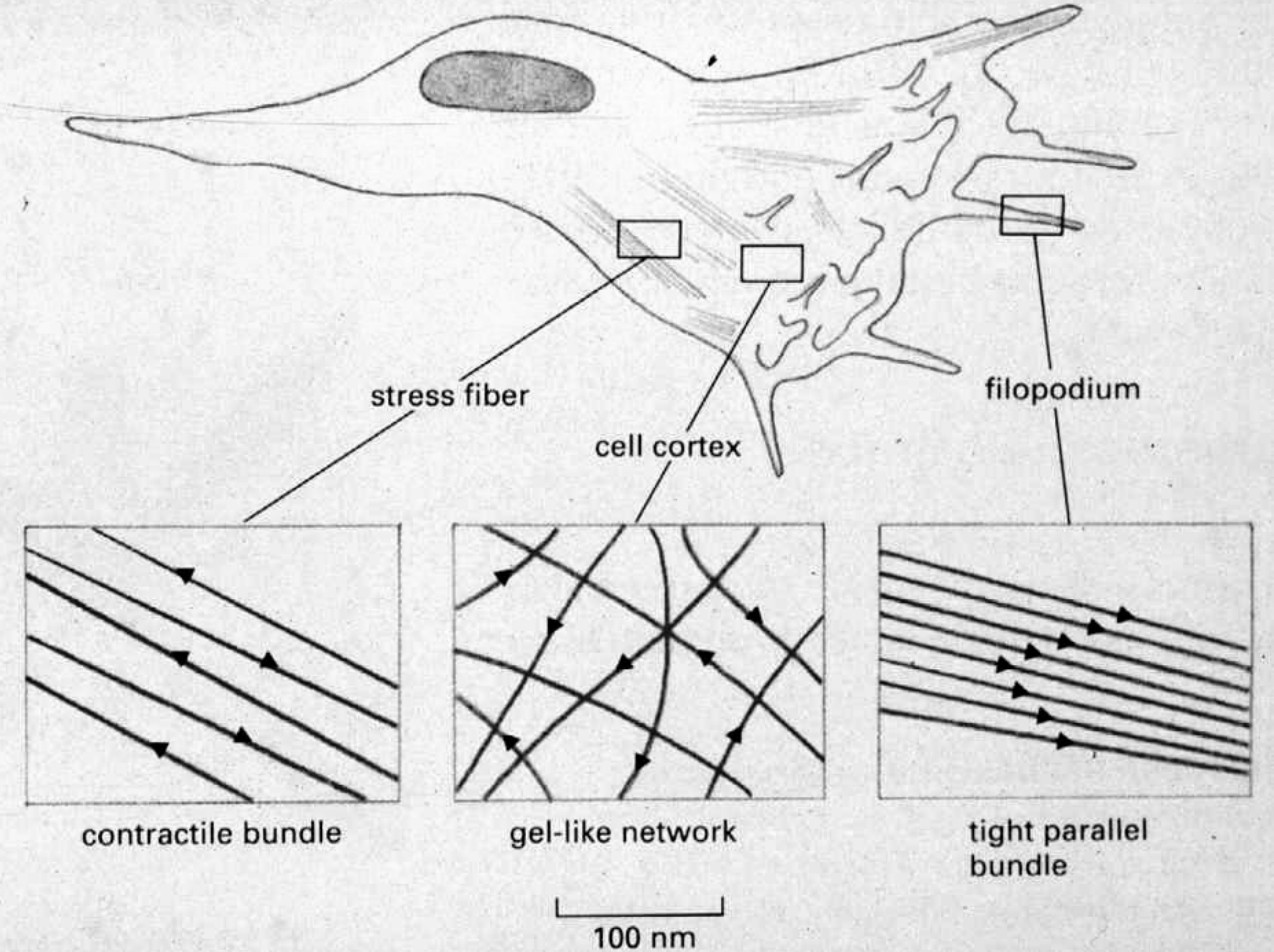
Structural support -

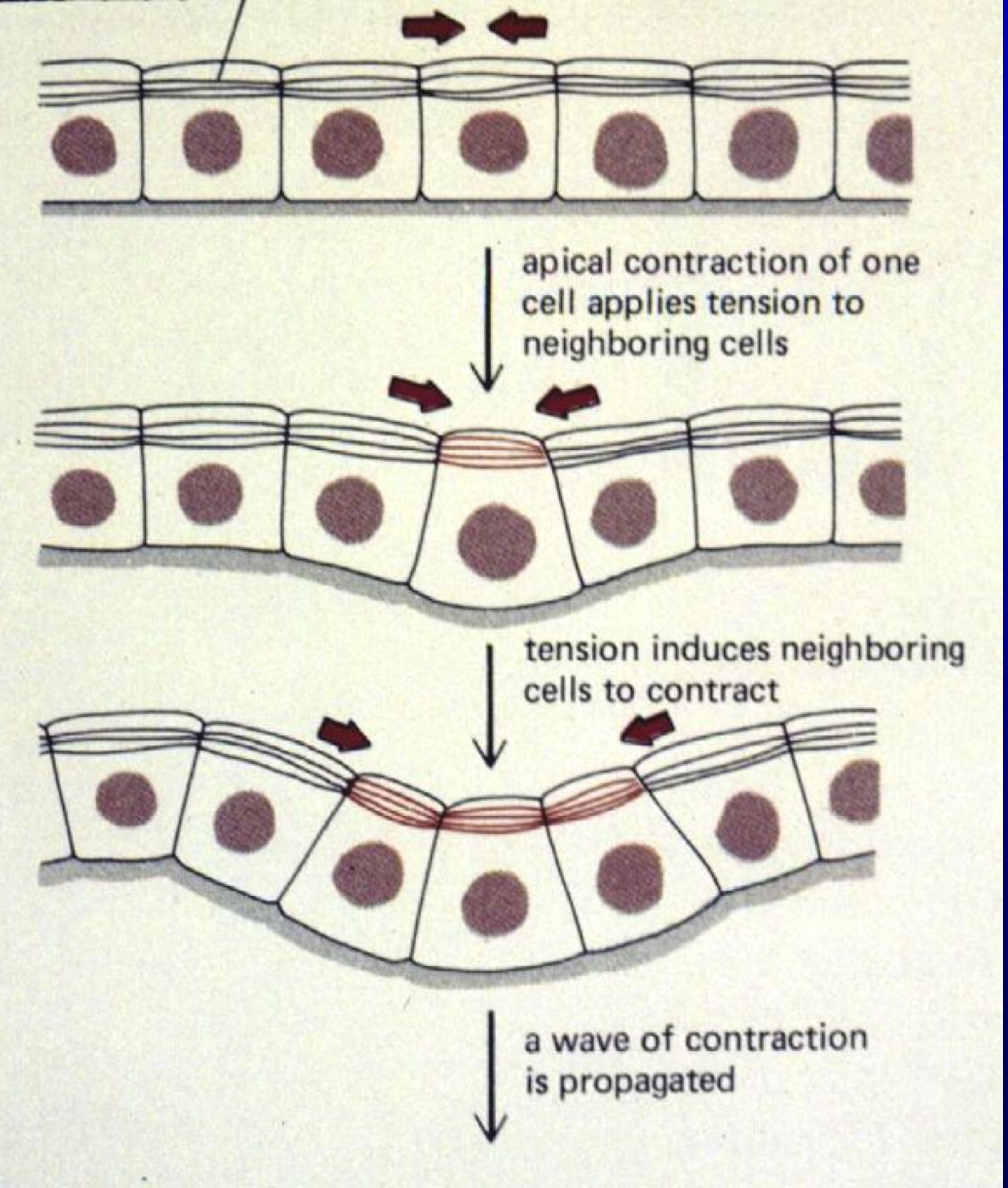
– Microvilli - movement and shape





actin cortex
lamellipodium
substratum
cortex under tension
actin polymerization at plus end extends lamellipodium
movement of unpolymerized actin
retraction
focal contacts


stress fiber
cell cortex
filopodium
contractile bundle
gel-like network
tight parallel
bundle
100 nm



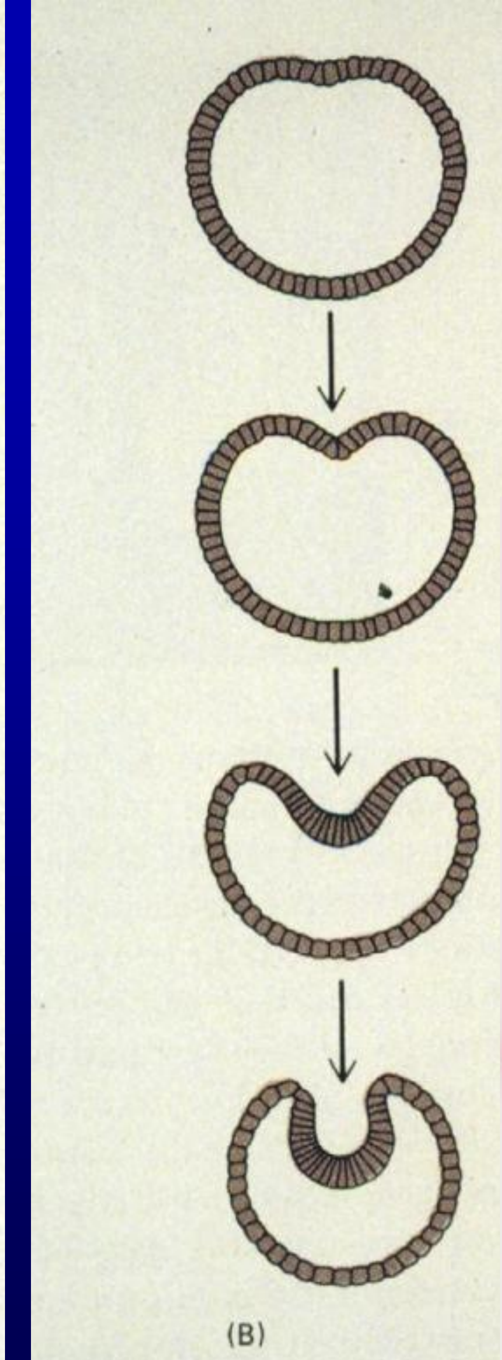
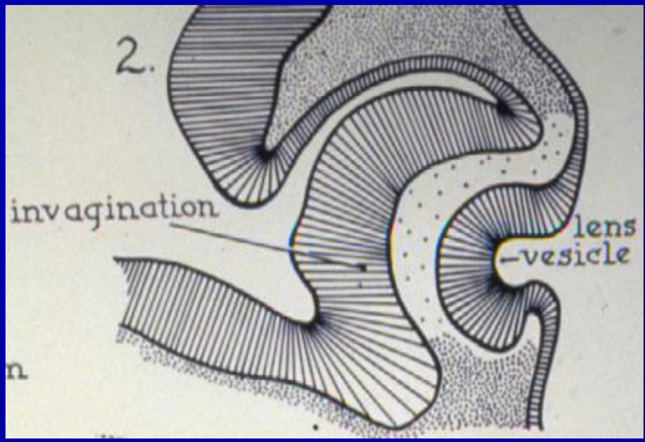
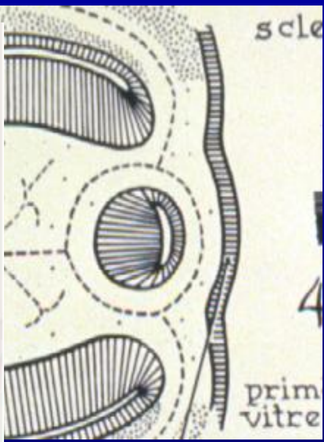


Figure 11–87 Computer m

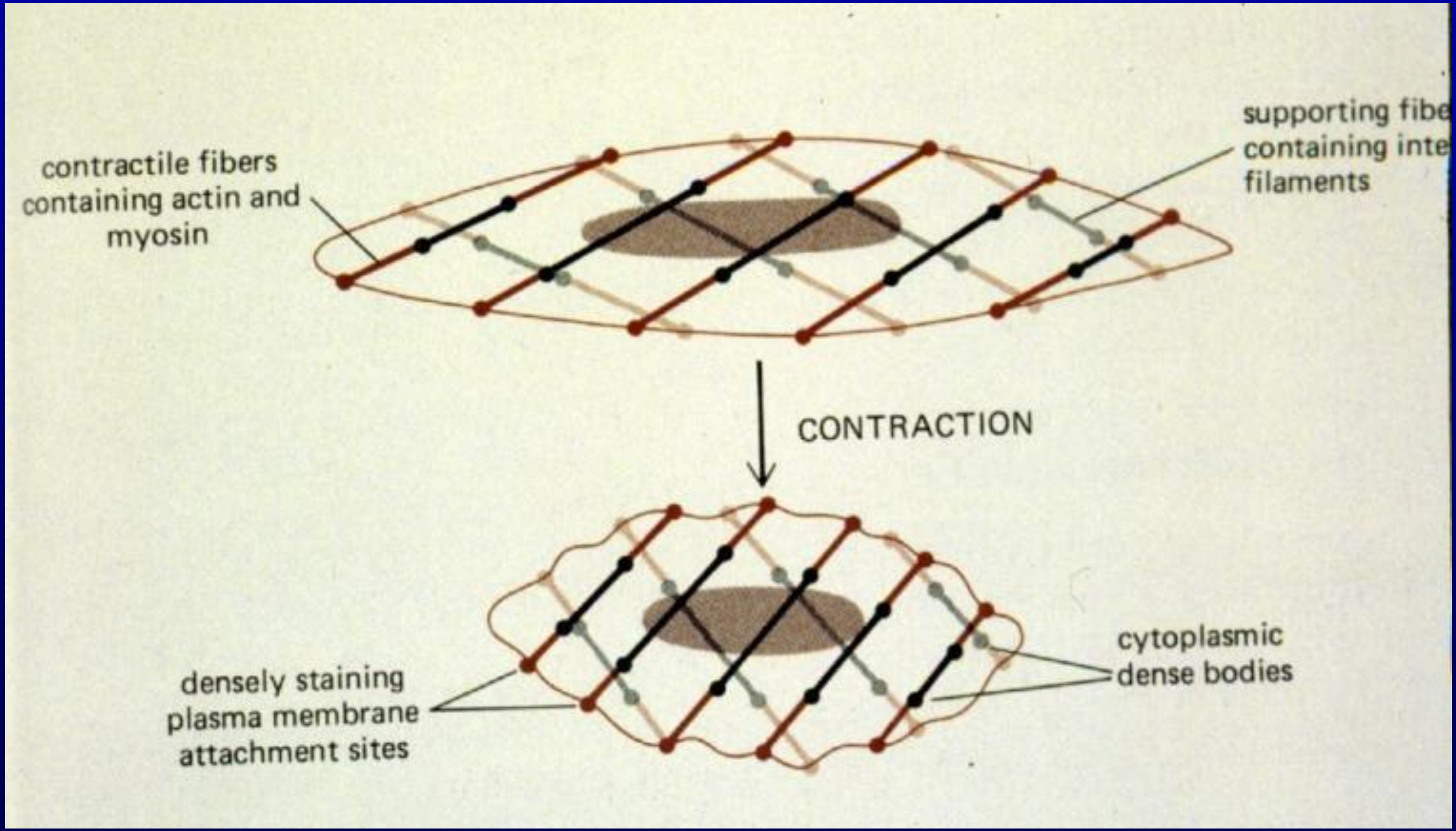




Microfilaments - contractile proteins

Actin and myosin – present in muscle and most all cells

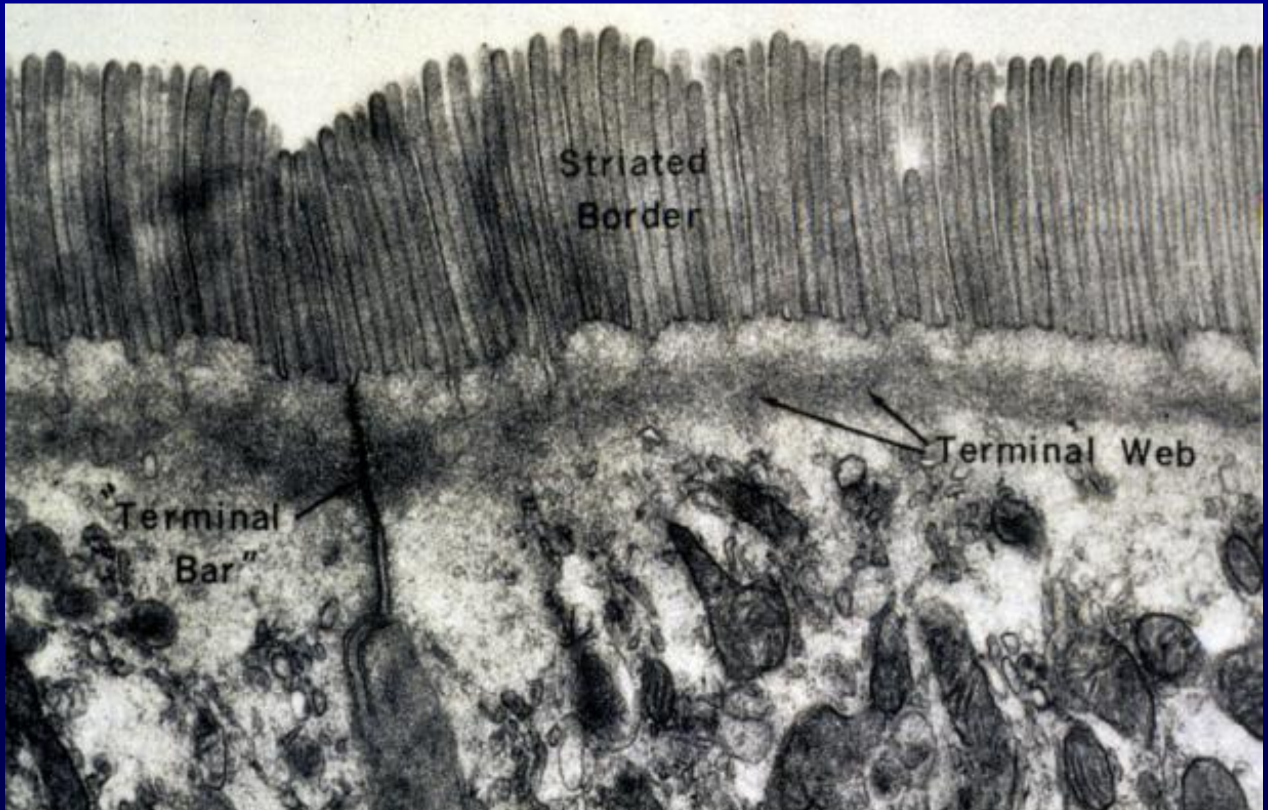
Actin 10% to 15% of cellular protein, widely distributed

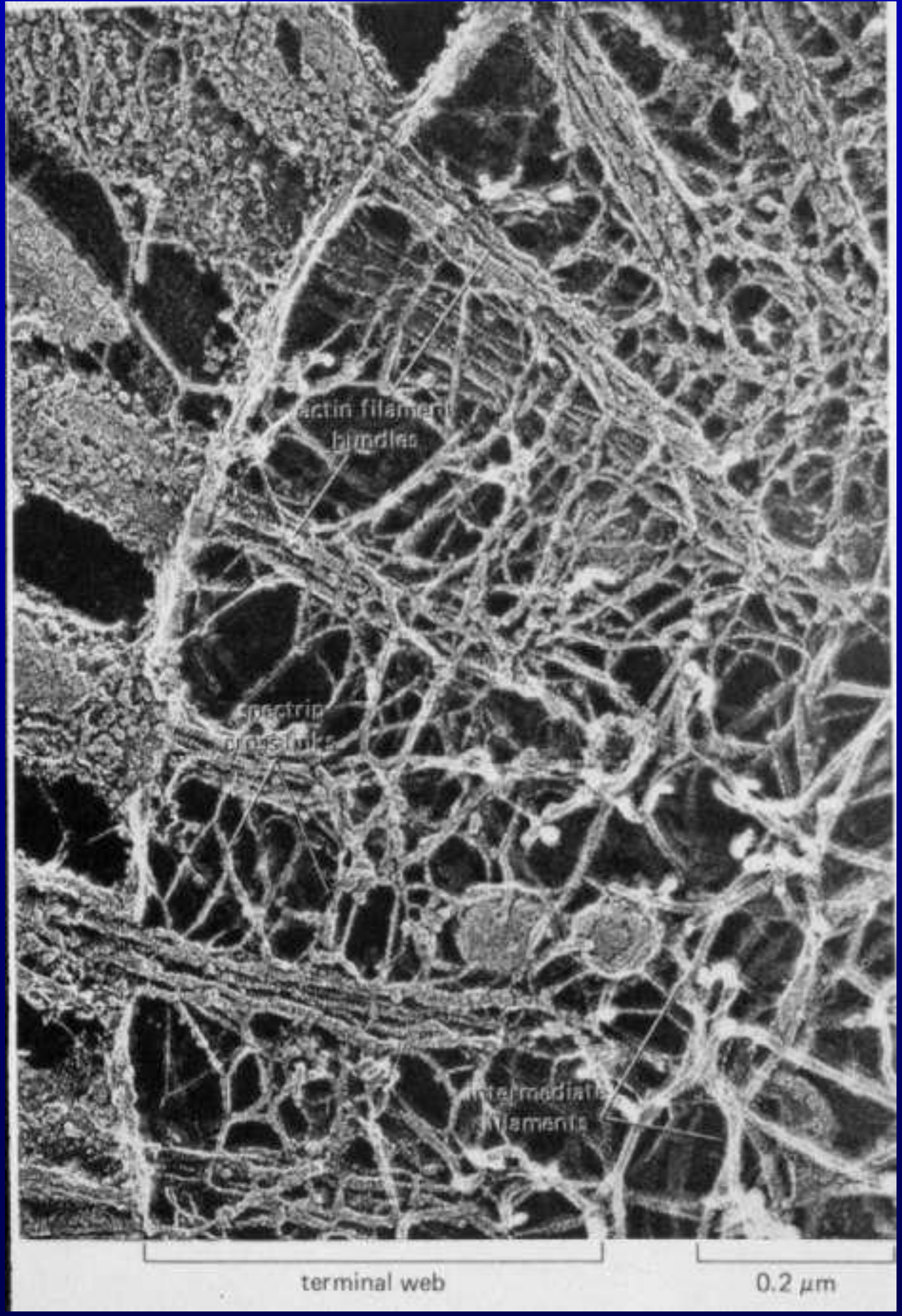


Summary: microfilaments - contractile proteins

Terminal web – anchor actin filaments in microvilli

Below cell surface – its mesh excludes other organelles

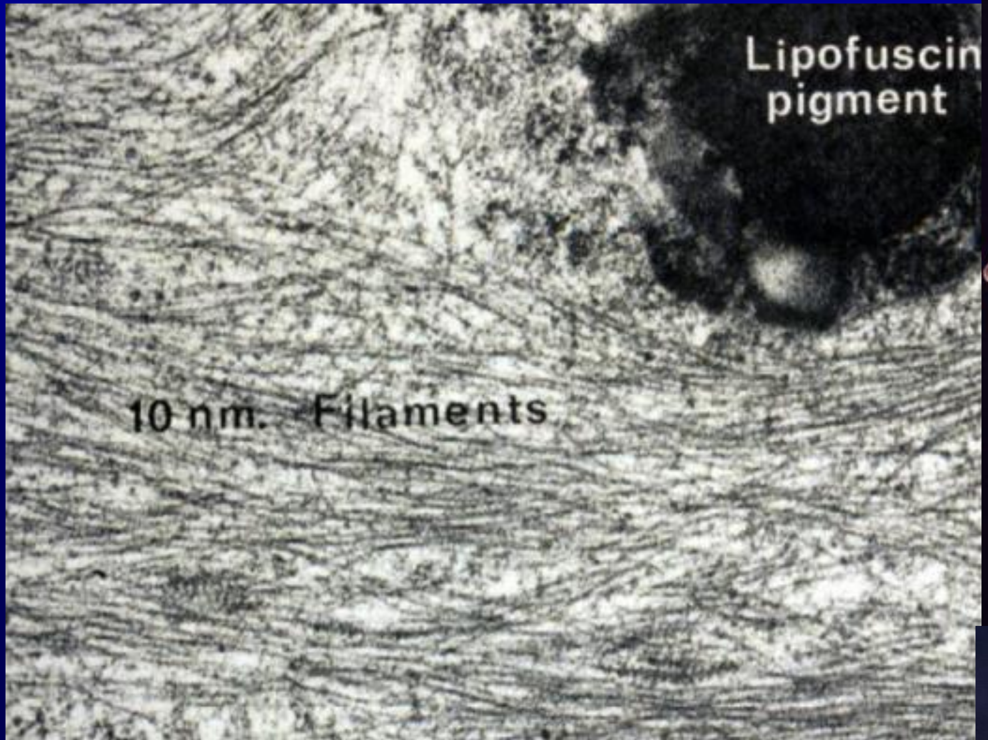


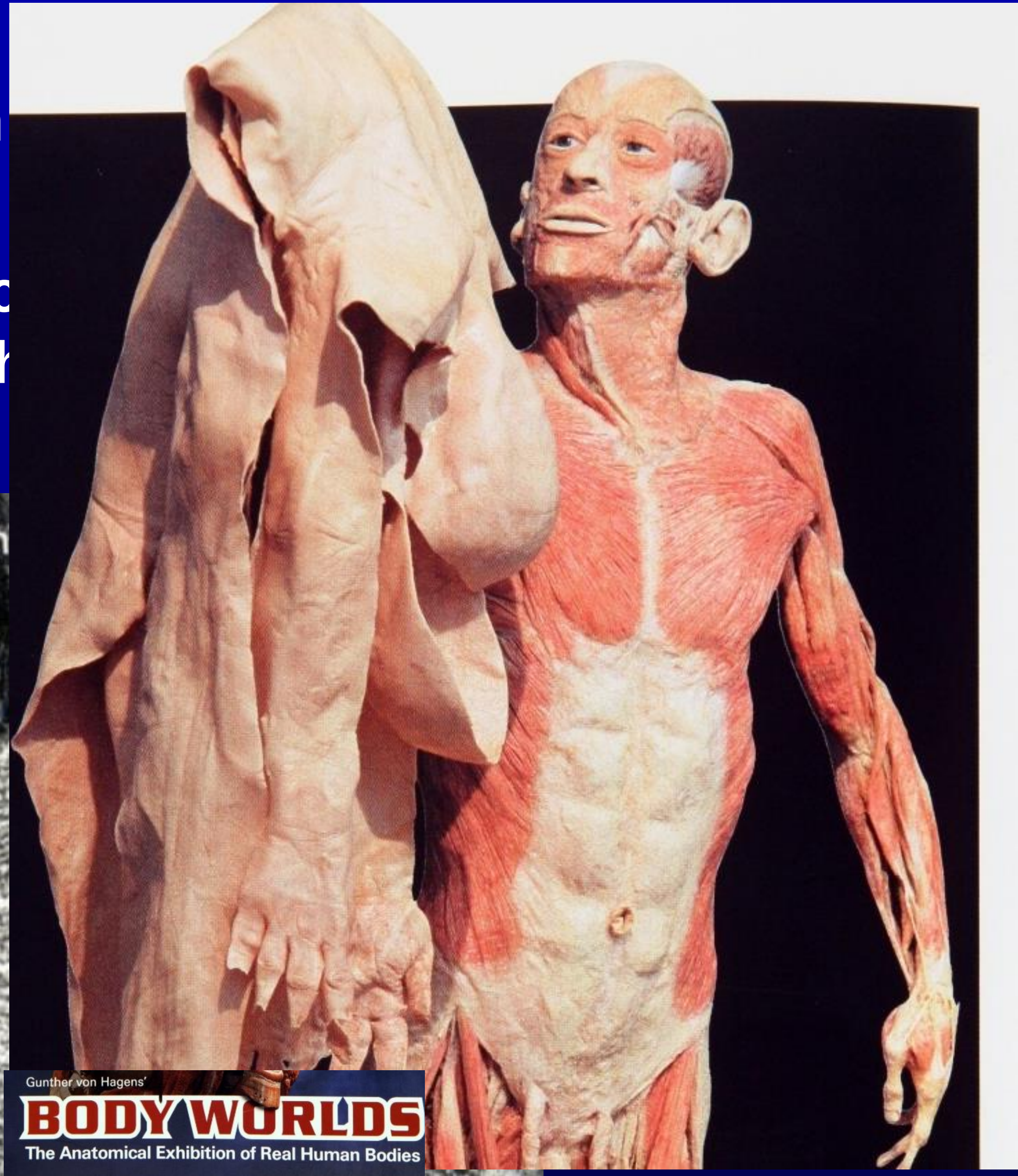


Intermediate filaments

Five classes (not conserved)

1. Keratin – insoluble substance, epithelium
2. Desmin – cytoskeleton in muscle
3. Vimentin – nuclear envelope for mechanic
   and stability of its location in cell, mesench





Intermediate filaments

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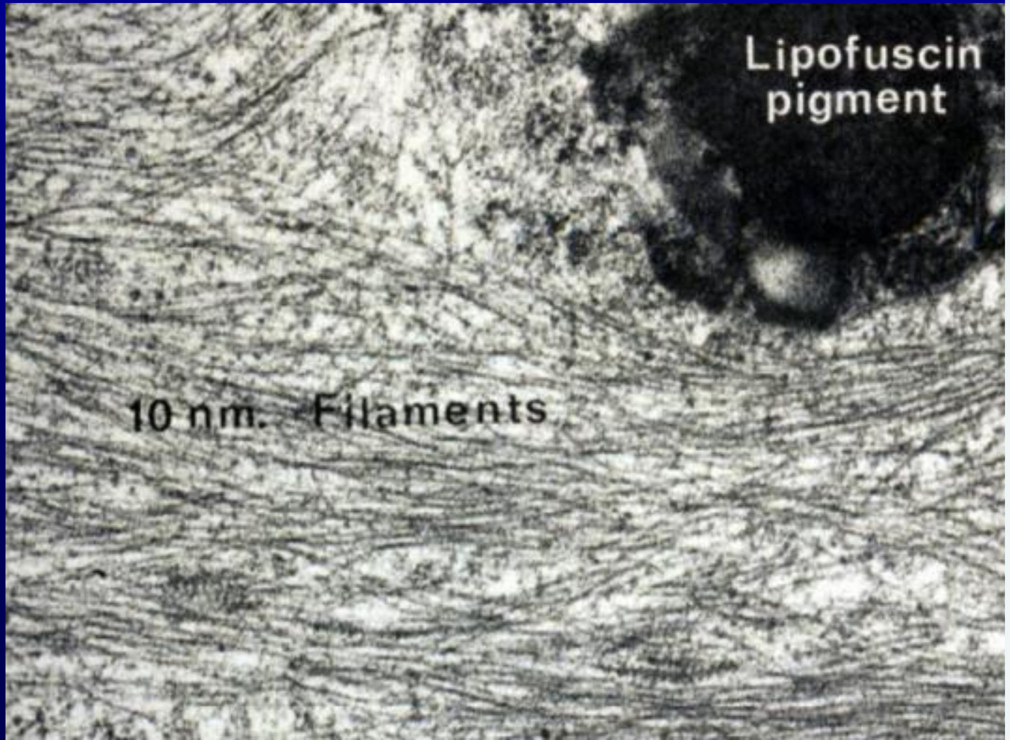
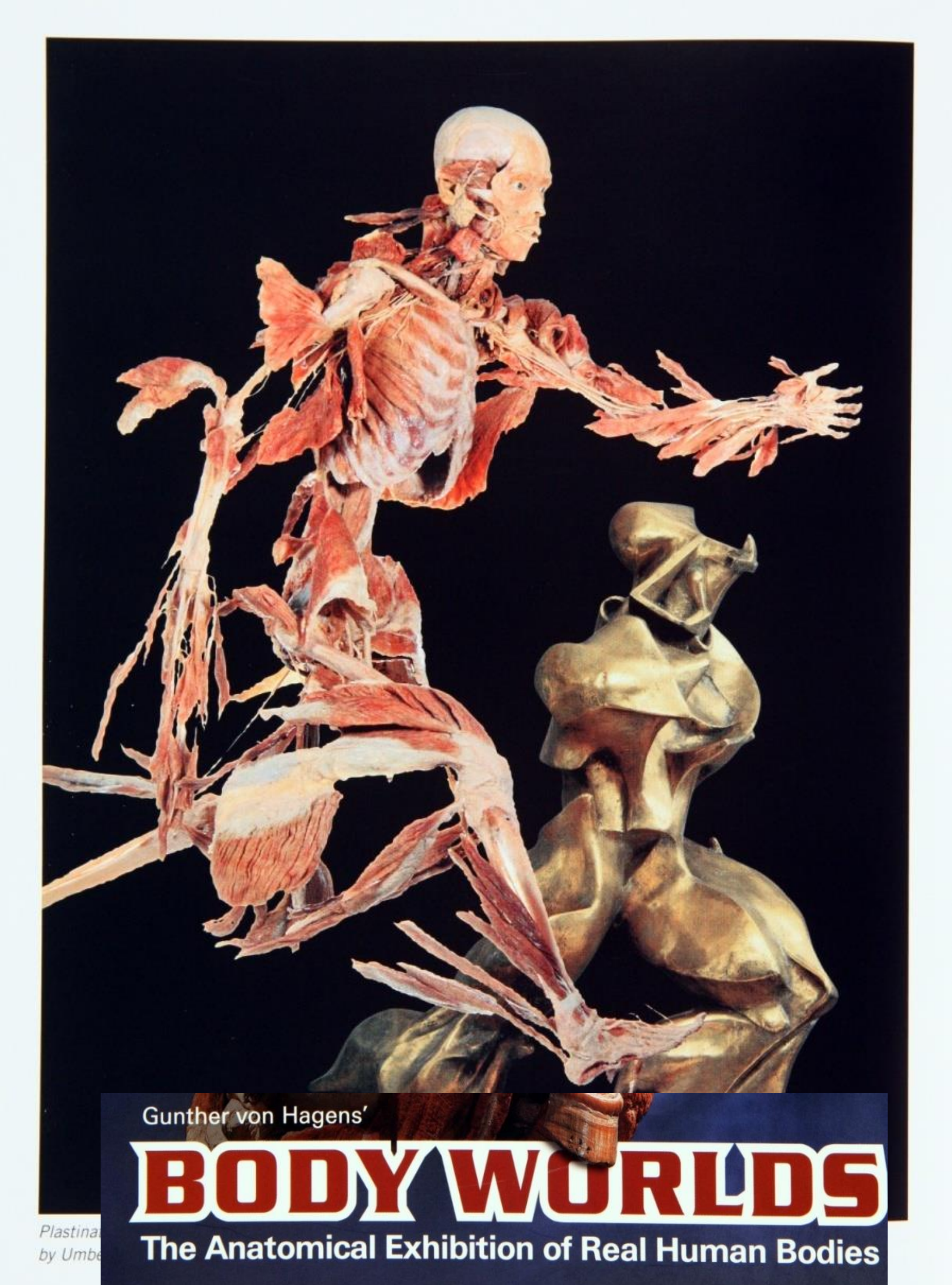
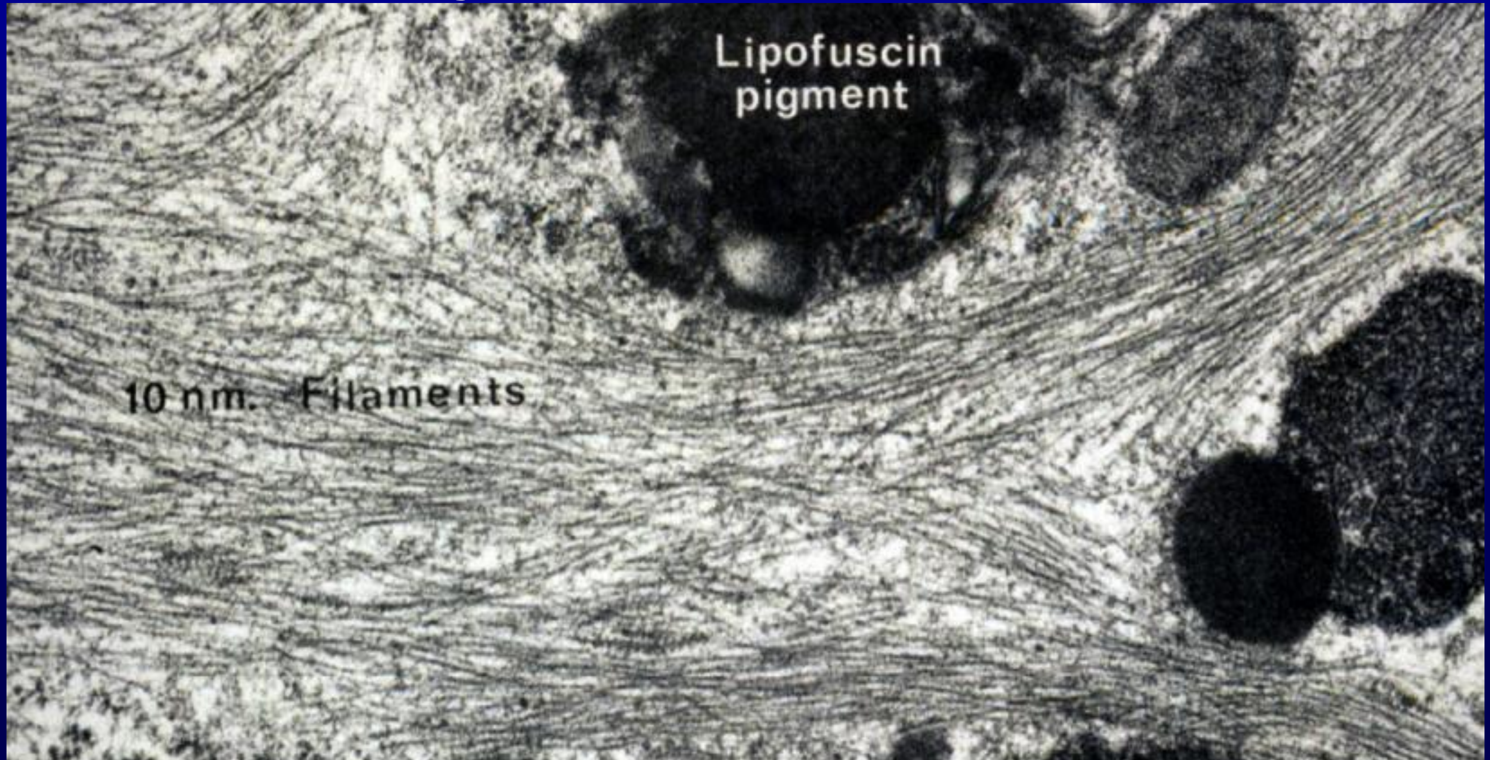


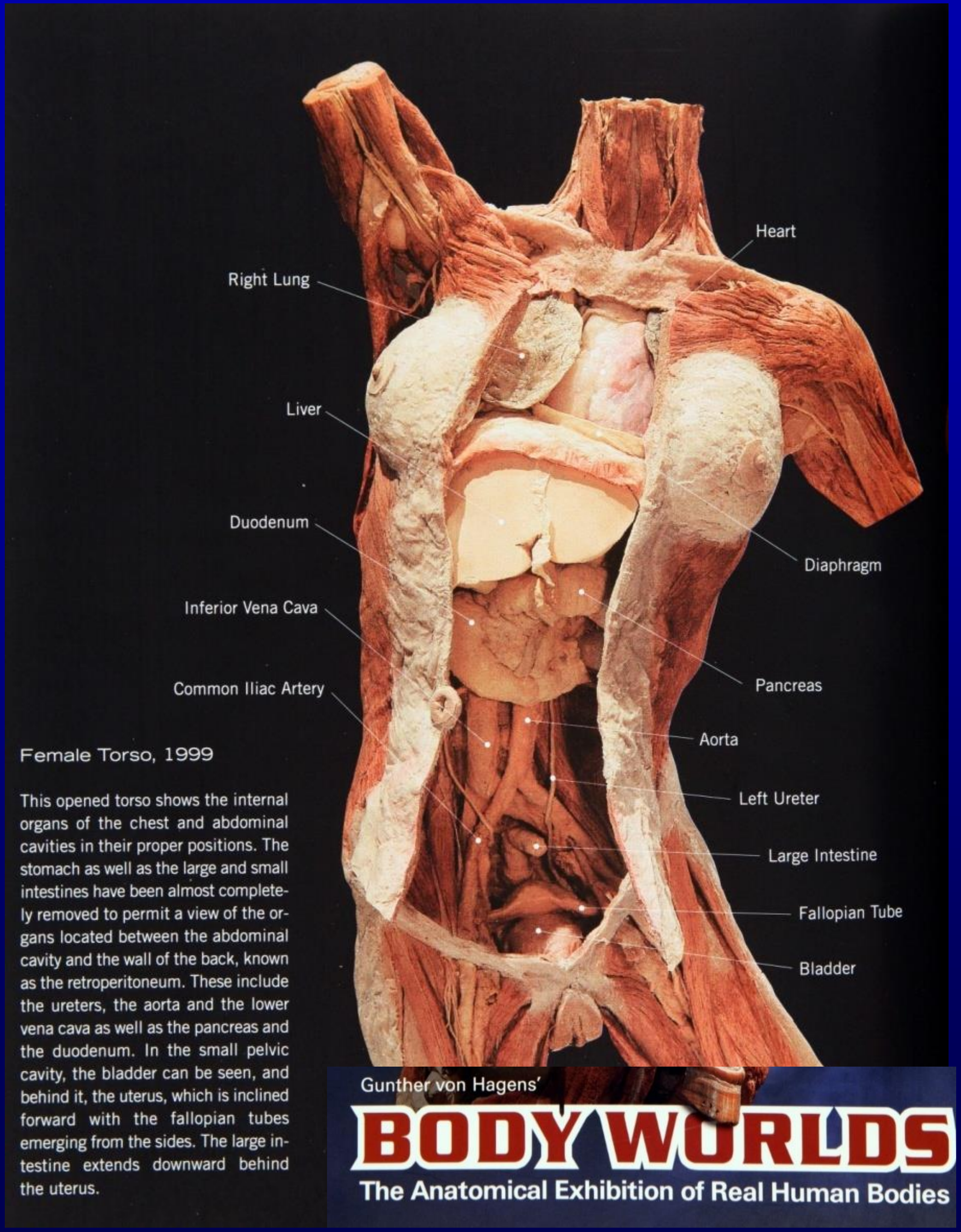


Intermediate filaments

Five classes (not conserved)

1. **Keratin – insoluble substance, epithelium**
2. **Desmin – cytoskeleton in muscle**
3. **Vimentin – nuclear envelope for mechanical support and stability of its location in cell, mesenchymal cell**

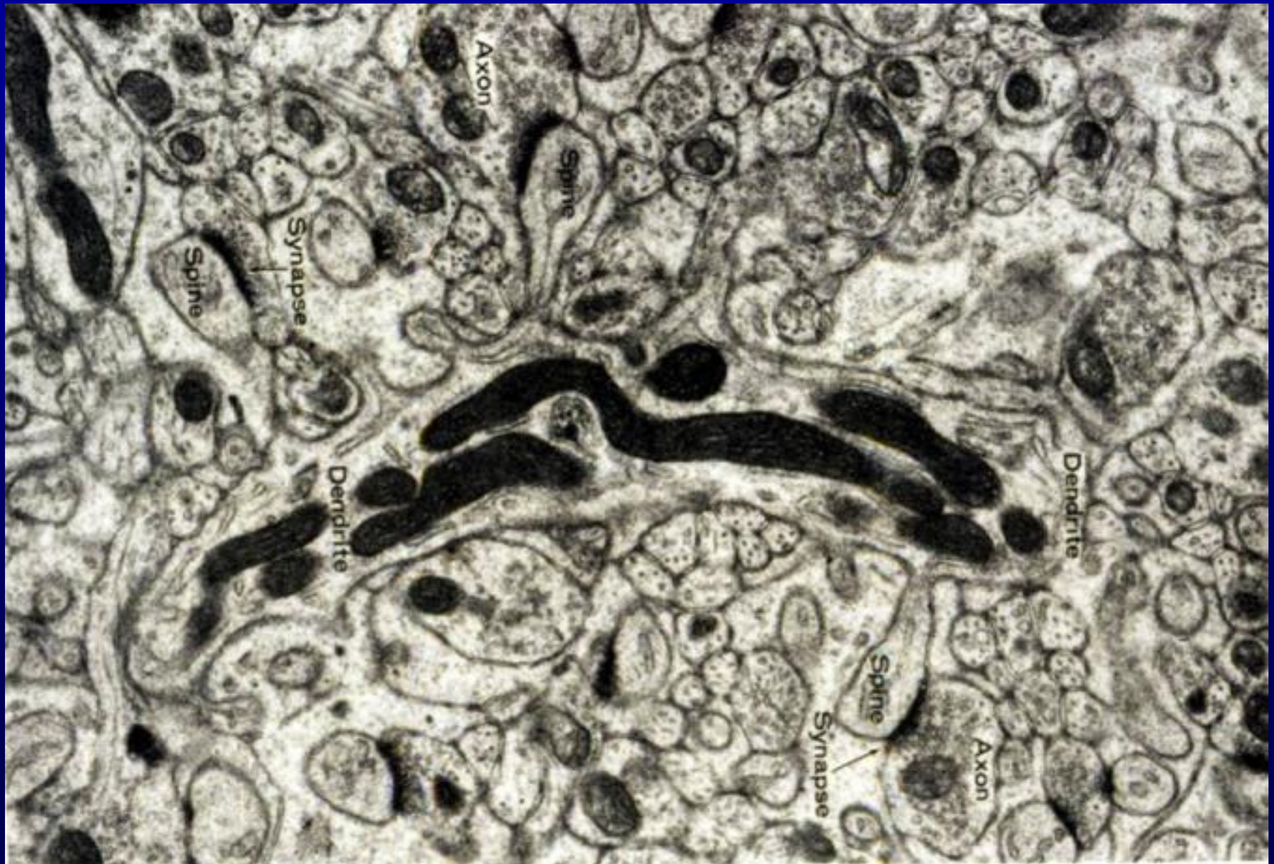


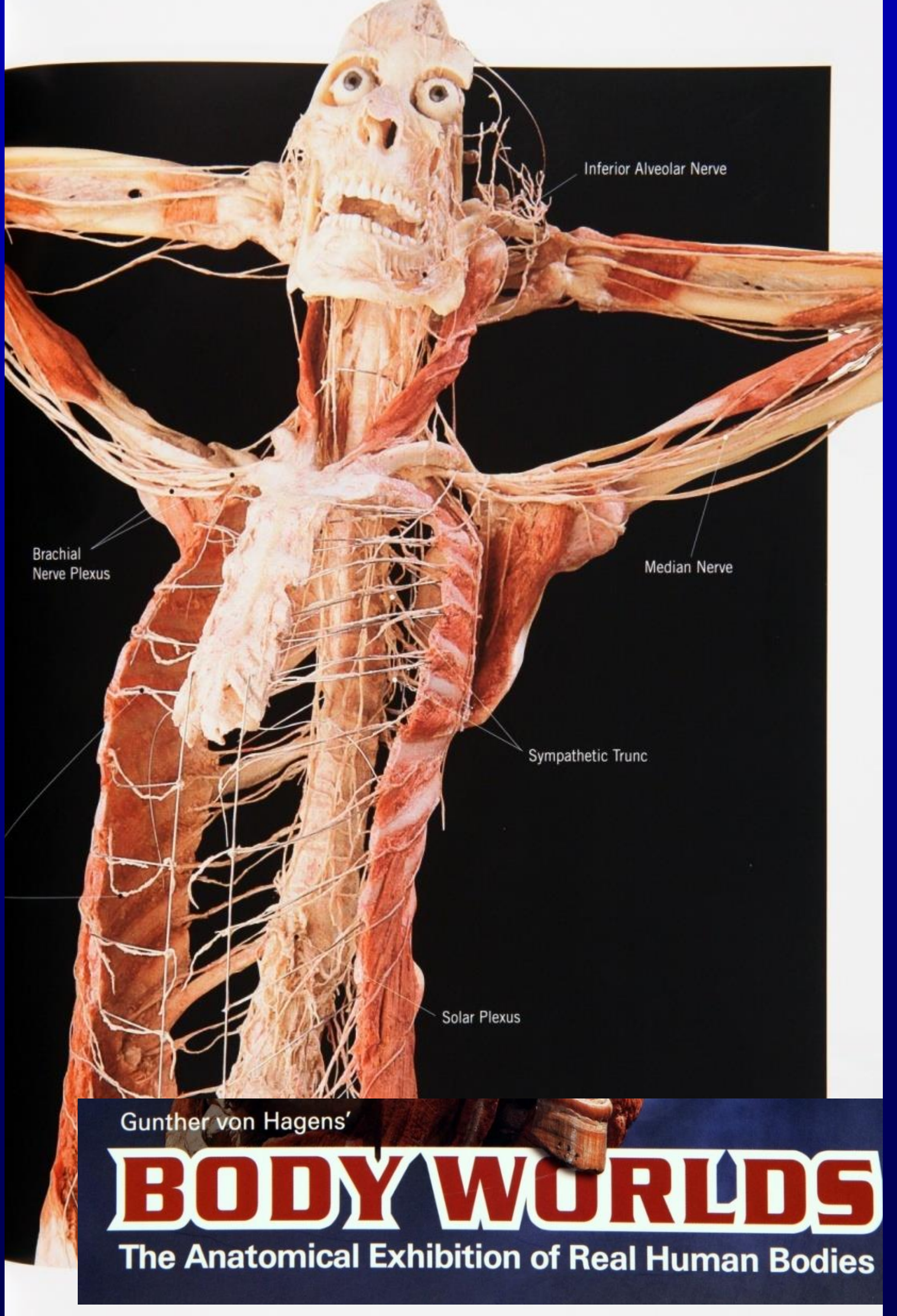


Intermediate filaments

Five classes con't

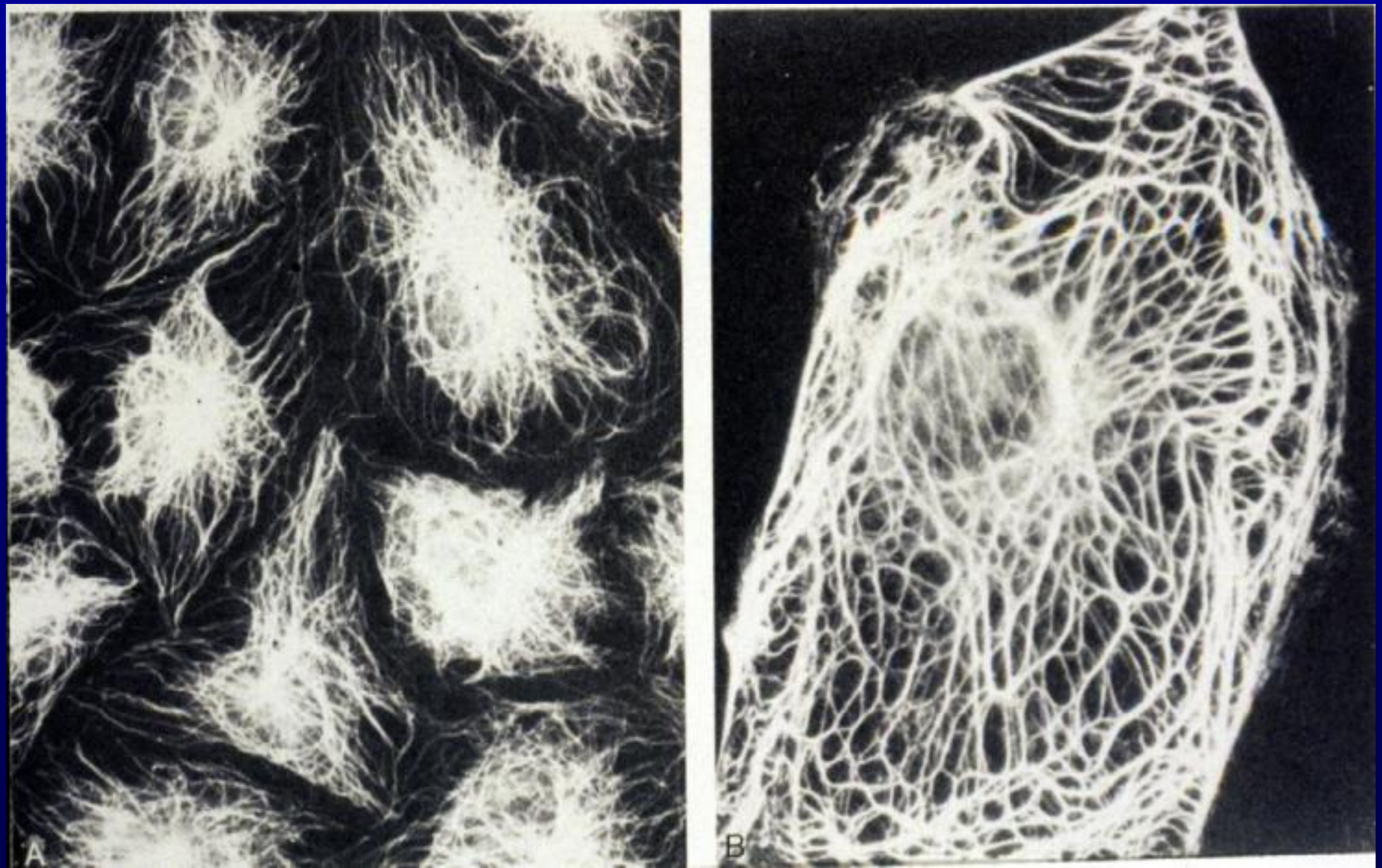
4. Neurofilaments
   - Dendrites and axons of nerve cells
   - Internal support - gelated state of cytoplasm
5. Glial filaments - astrocytes





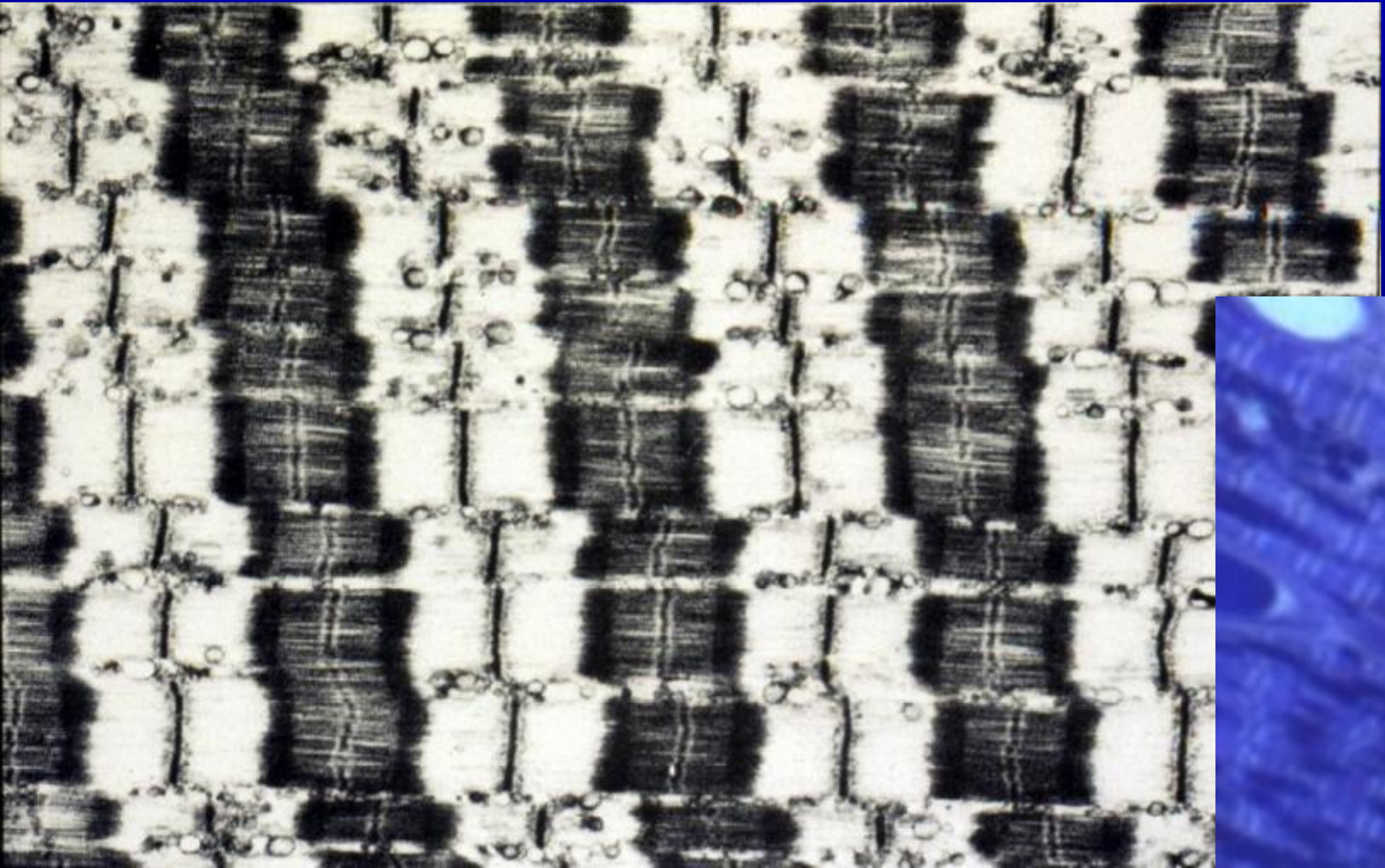
Intermediate filaments

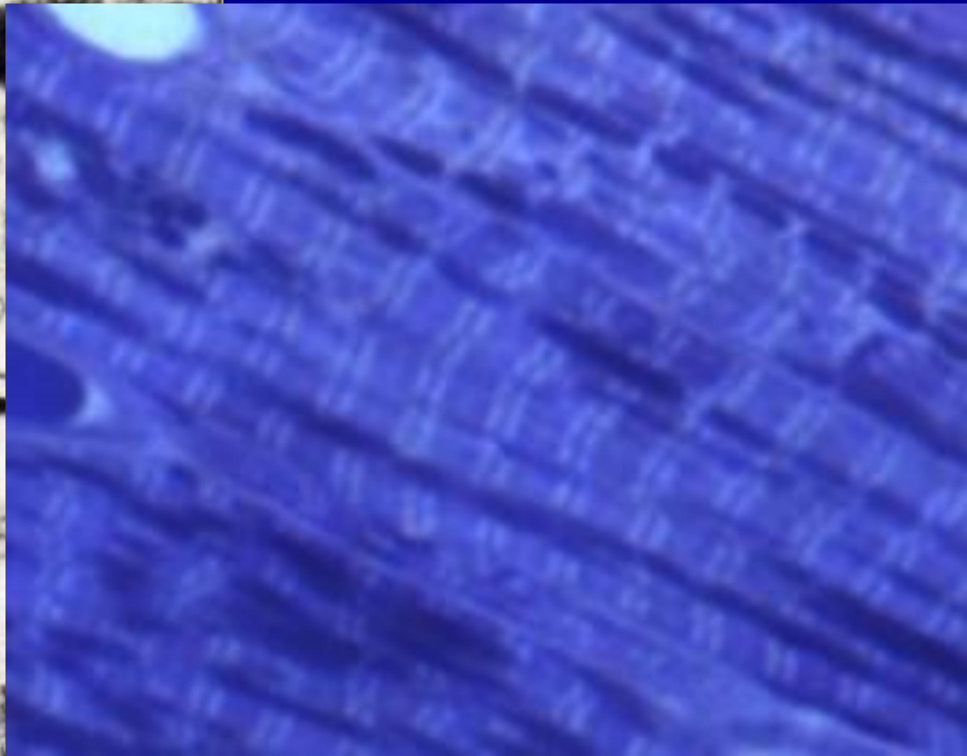
Immunofluorescence detection - tool in distinguishing cell type of origin for malignant tumors



Intermediate filaments - function

Myofibril organization - muscle



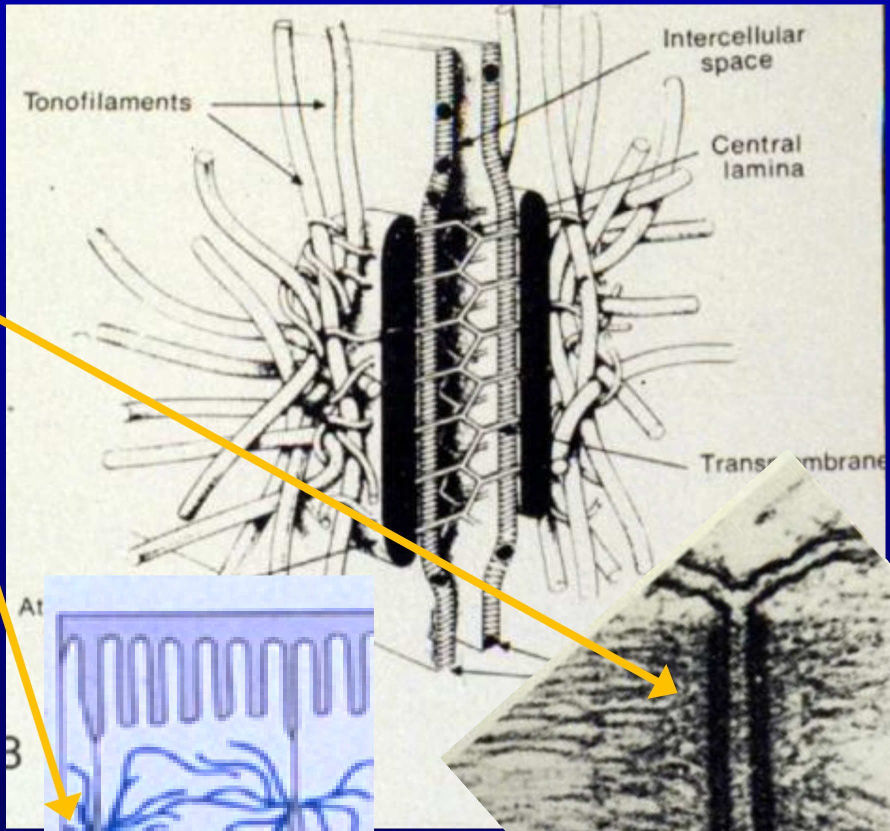


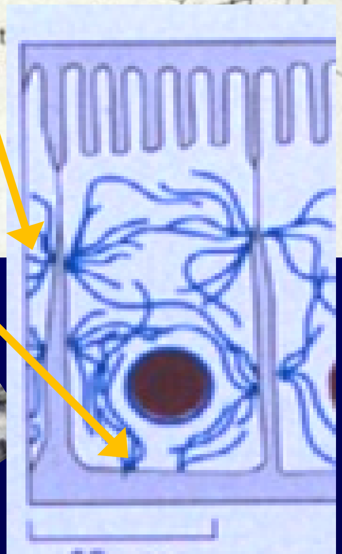
Intermediate filaments - function

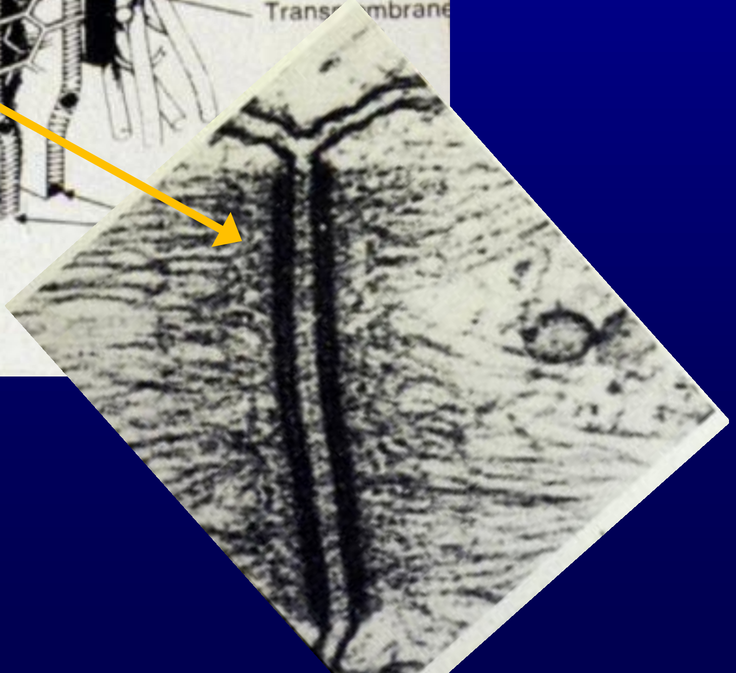
Structural support of epithelial desmosomes

and

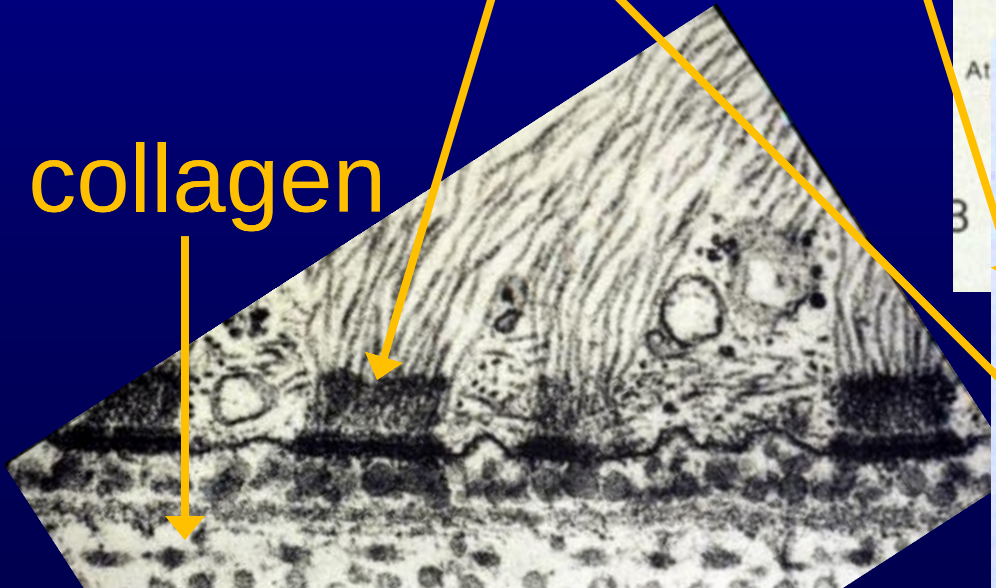
hemidesmosomes





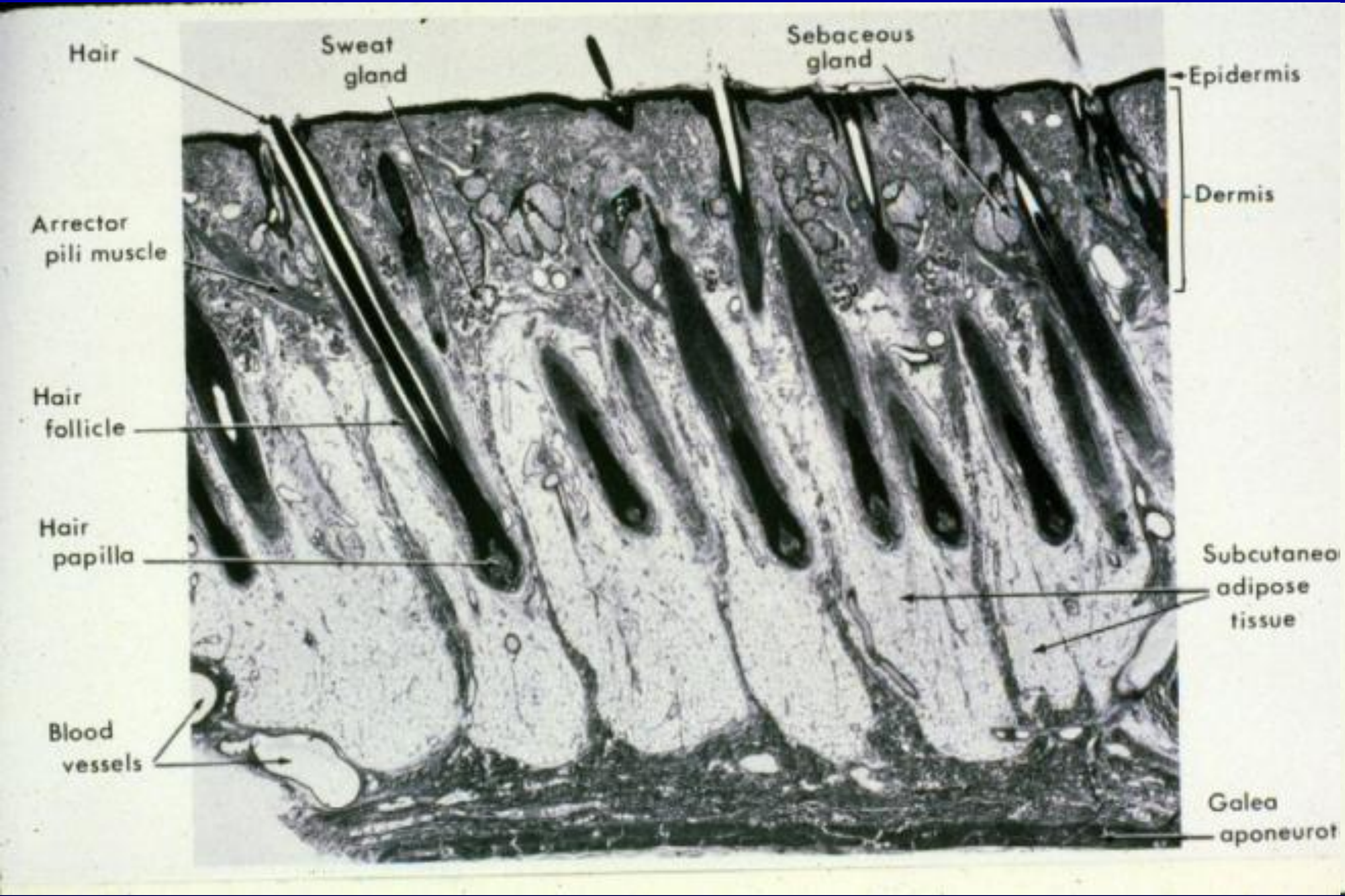


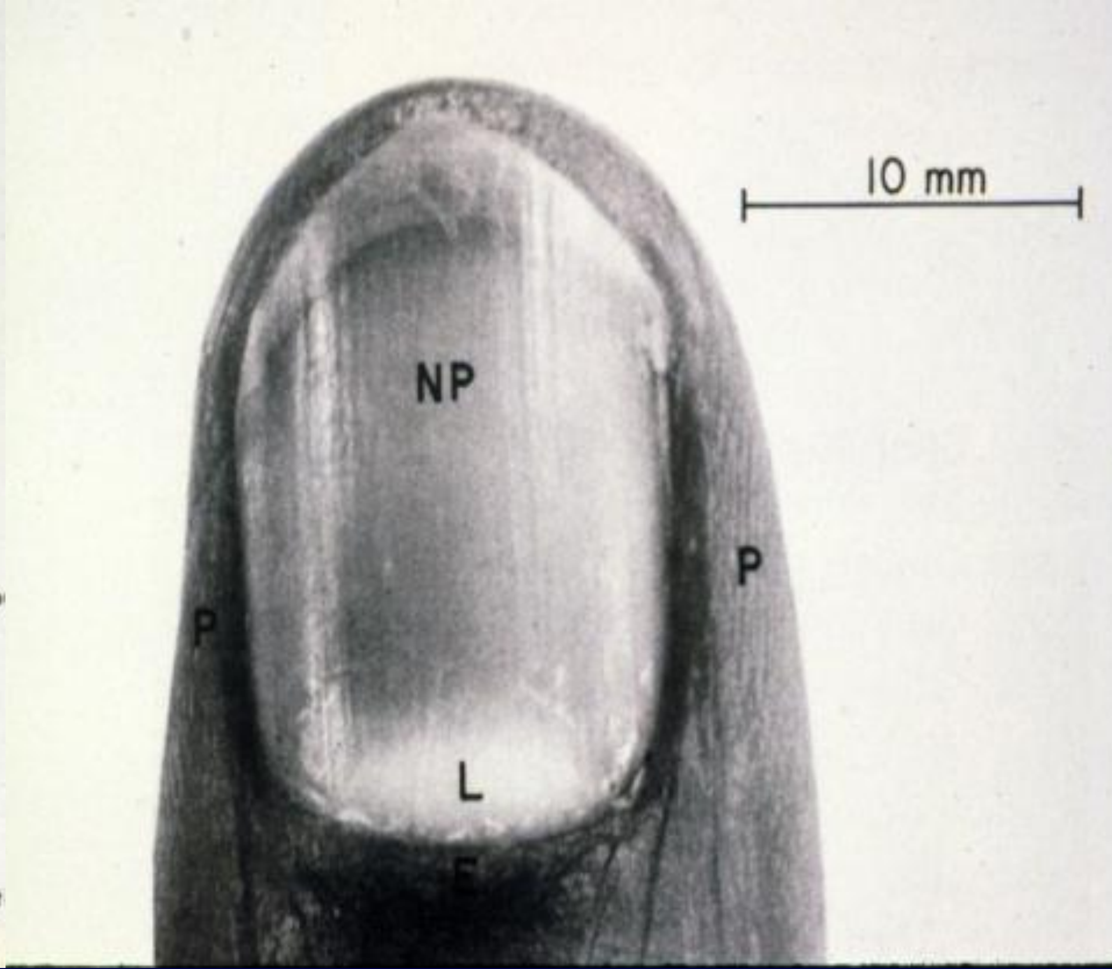
collagen



Intermediate filaments - function

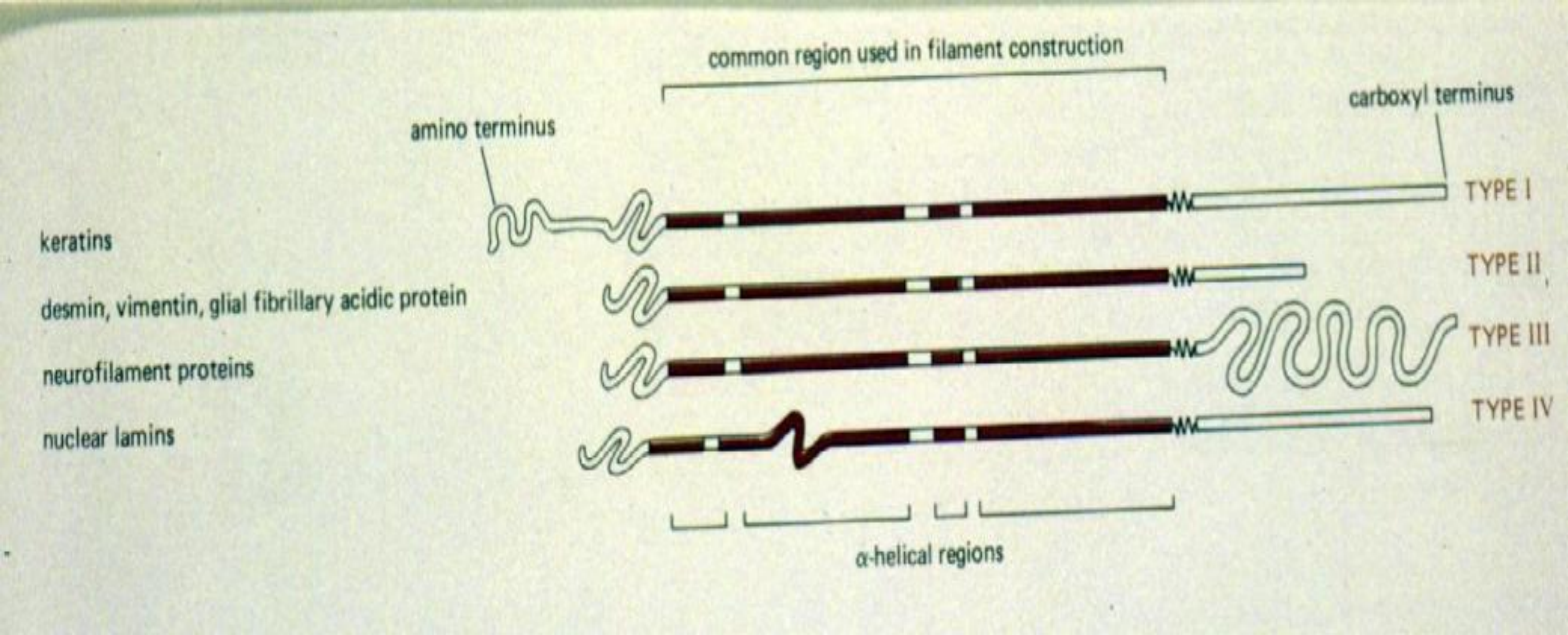
Extracellular - hair, nails, horn, feathers, and scales

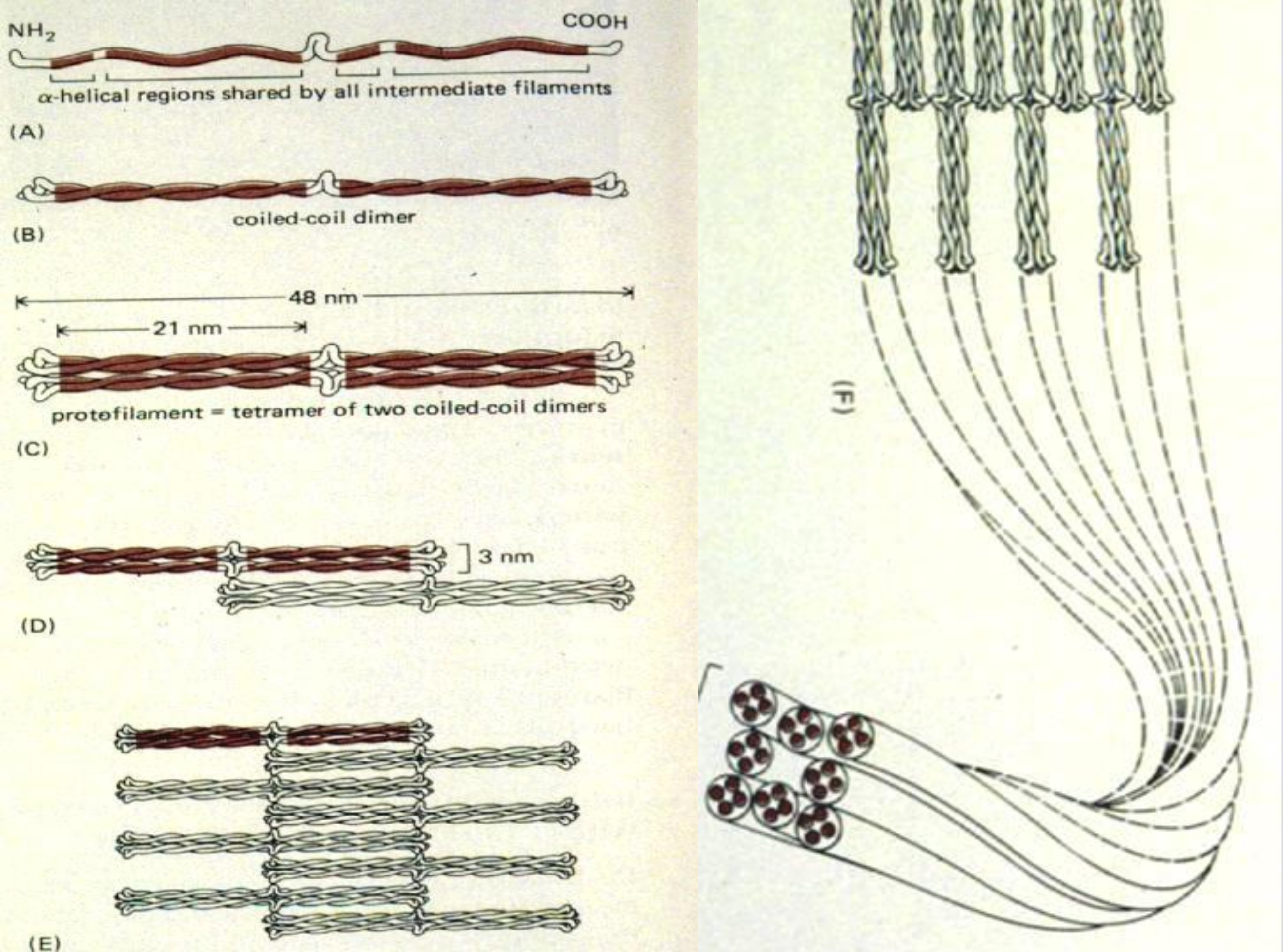




Intermediate filaments

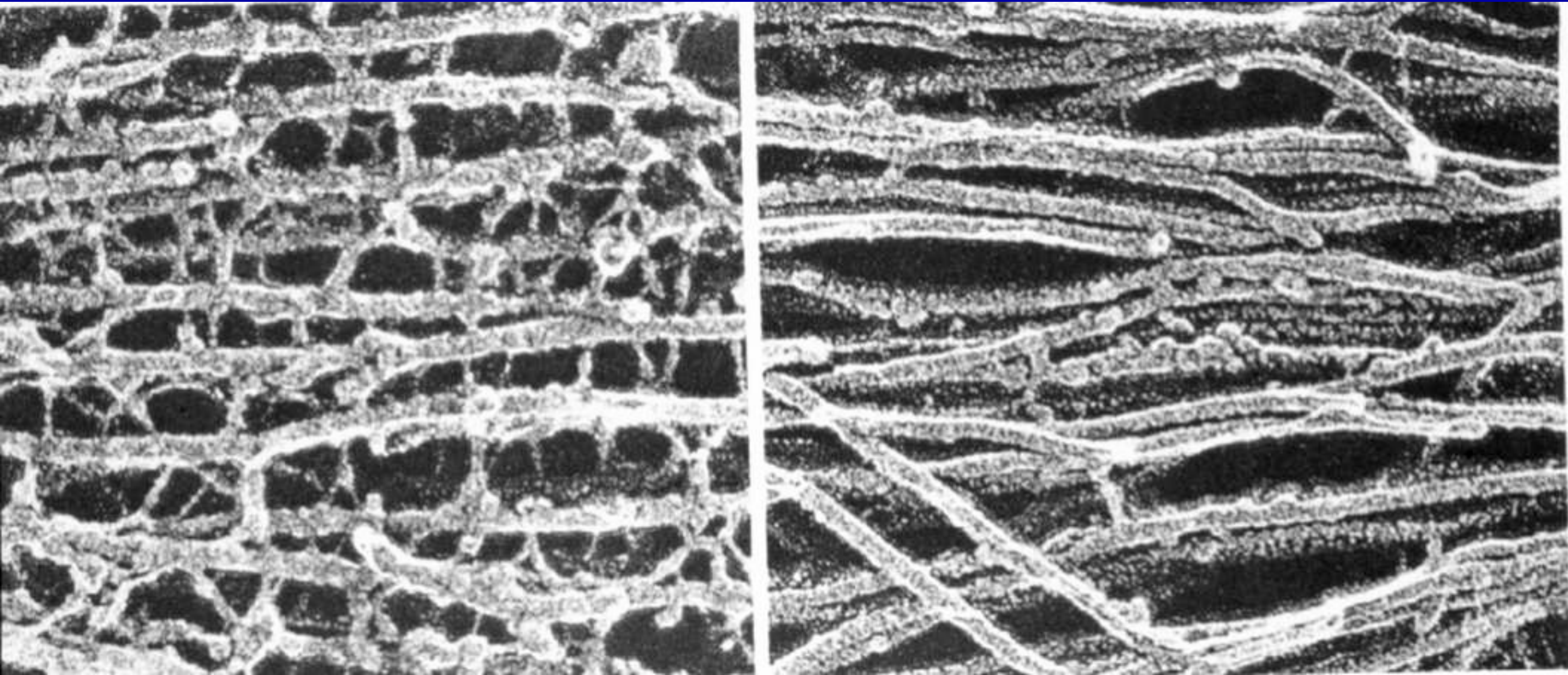
common region in construction



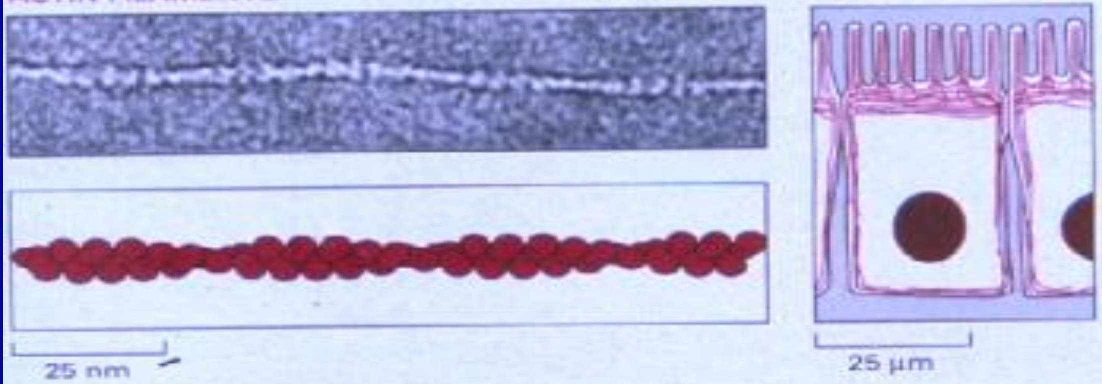


NH2
COOH
α-helical regions shared by all intermediate filaments
(A)
coiled-coil dimer
(B)
48 nm
21 nm
protofilament = tetramer of two coiled-coil dimers
(C)
3 nm
(D)
(E)
(F)

Intermediate filaments

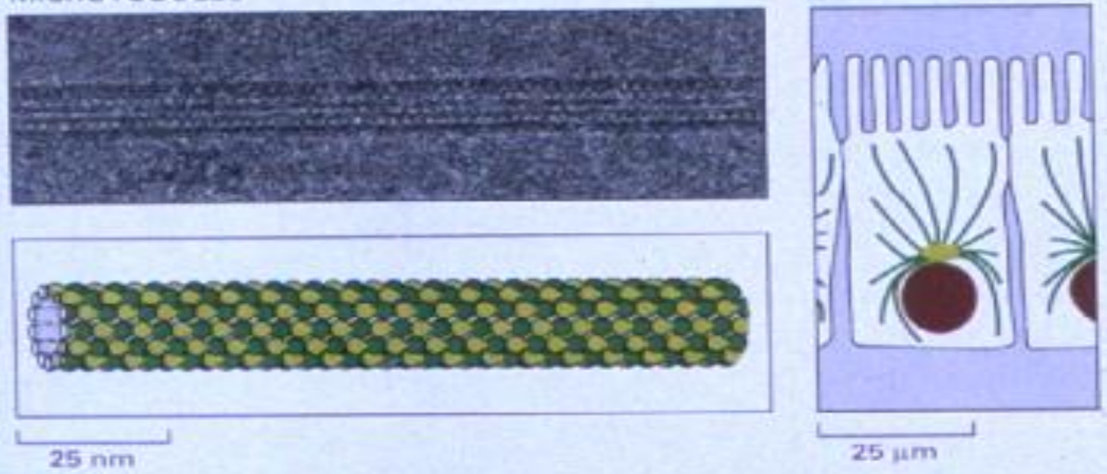


ACTIN FILAMENTS



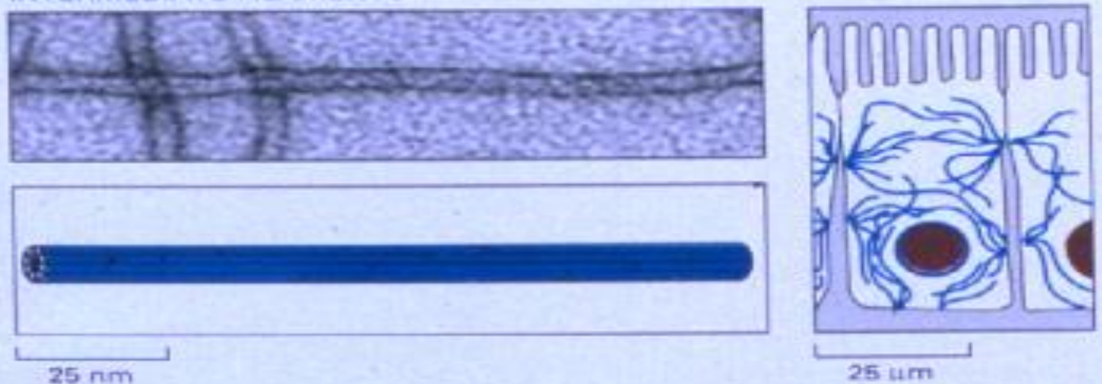
Actin filaments (also known as *microfilaments*) are two-stranded helical polymers of the protein actin. They appear as flexible structures, with a diameter of 5–9 nm, that are organized into a variety of linear bundles, two-dimensional networks, and three-dimensional gels. Although actin filaments are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

MICROTUBULES



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.

INTERMEDIATE FILAMENTS

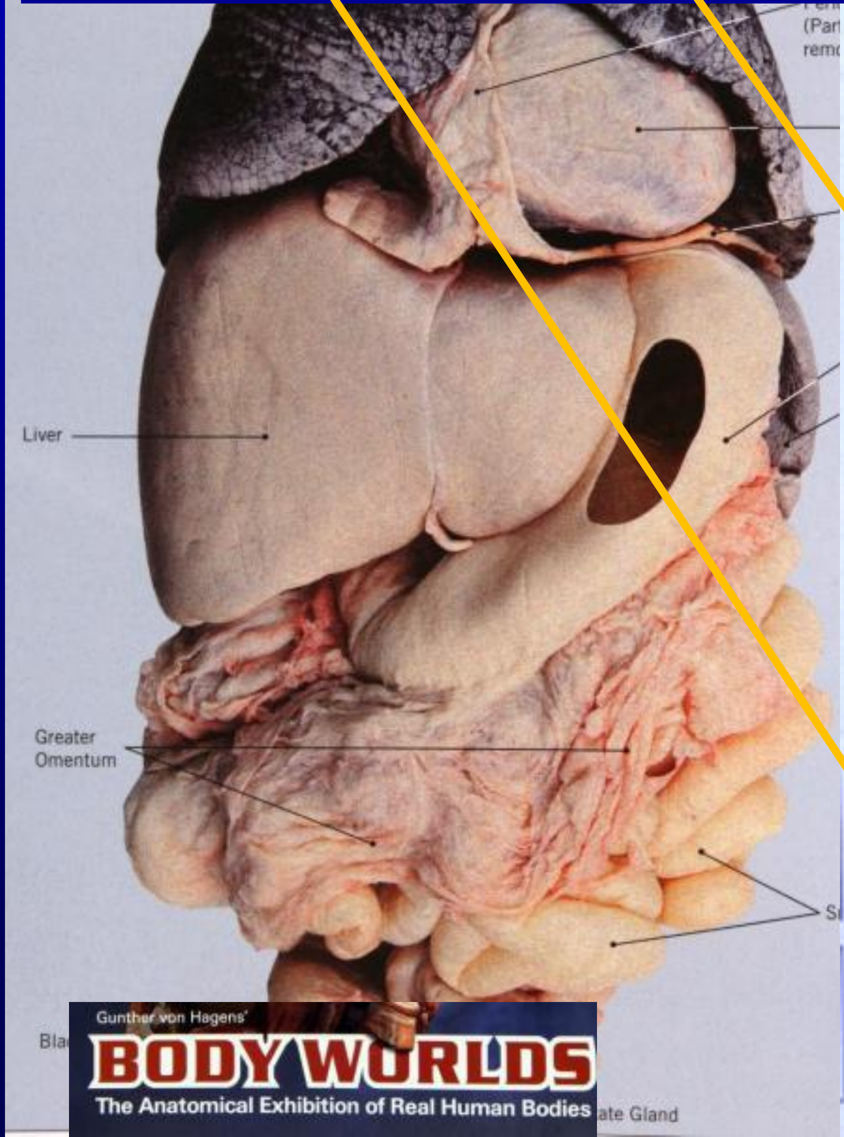


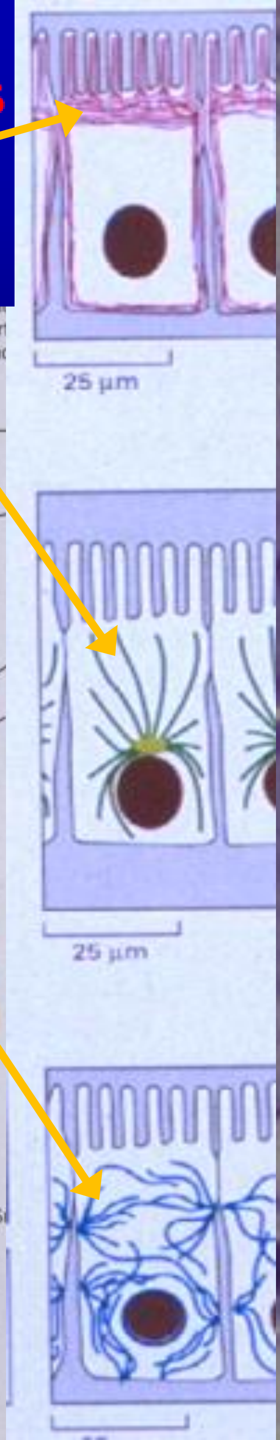
Intermediate filaments are ropelike fibers with a diameter of around 10 nm; they are made of intermediate filament proteins, which constitute a large and heterogeneous family. One type of intermediate filament forms a meshwork called the nuclear lamina just beneath the inner nuclear membrane. Other types extend across the cytoplasm, giving cells mechanical strength and carrying the mechanical stresses in an epithelial tissue by spanning the cytoplasm from one cell-cell junction to another.

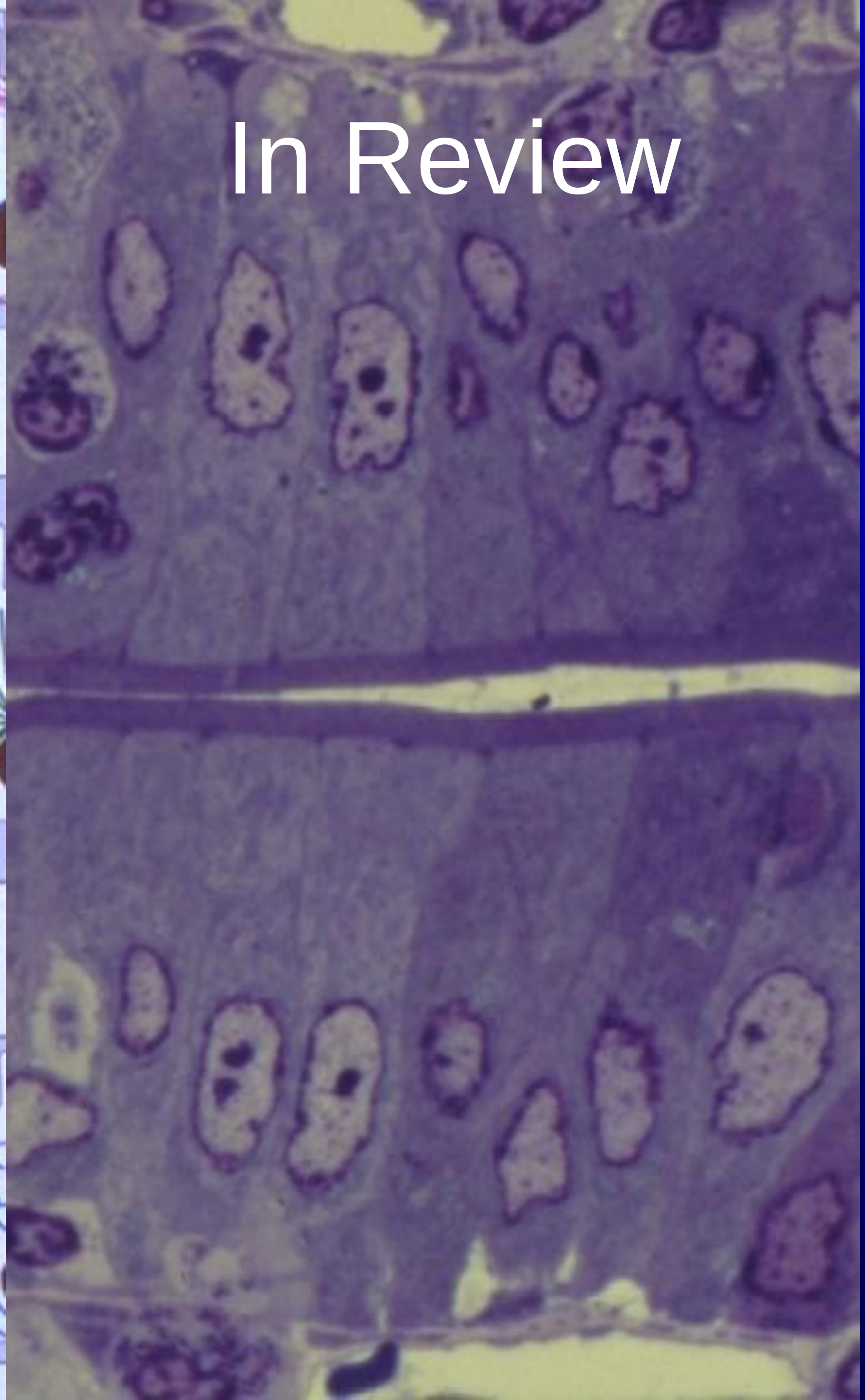
CYTOSKELETON

NON-MEMBRANOUS ORGANELLES

- MICROTUBULES (25 nM)
- MICROFILAMENT (6 nM)
- INTERMEDIATE FILAMENT (10 nM)

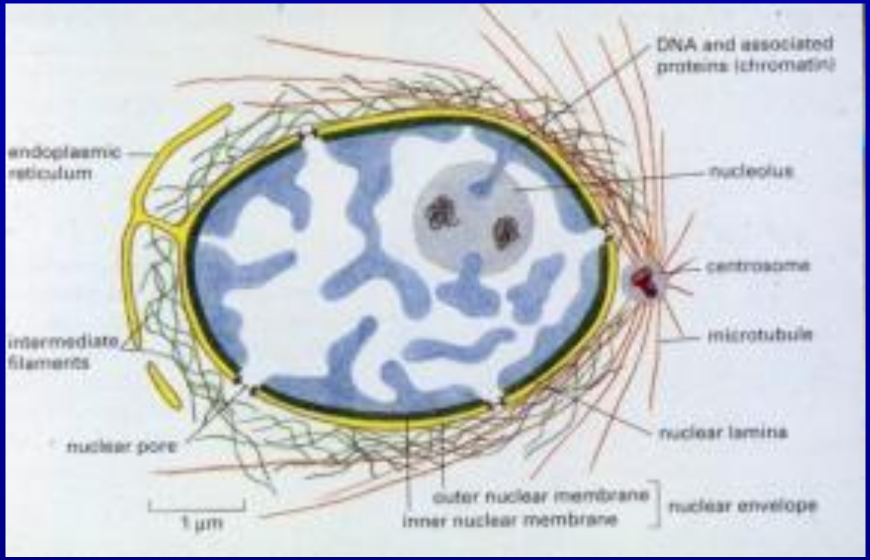


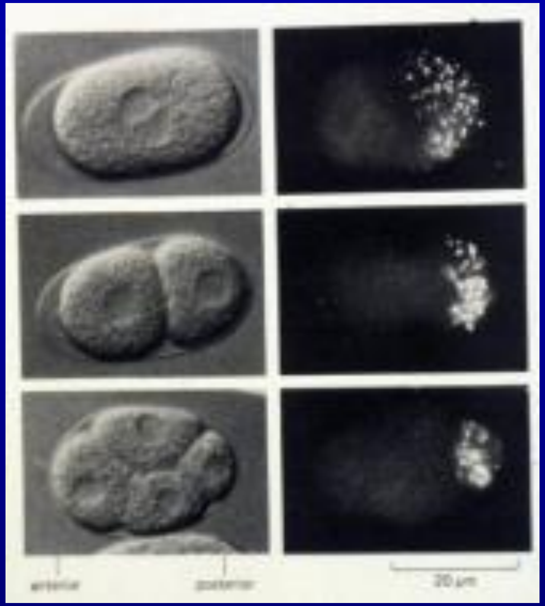


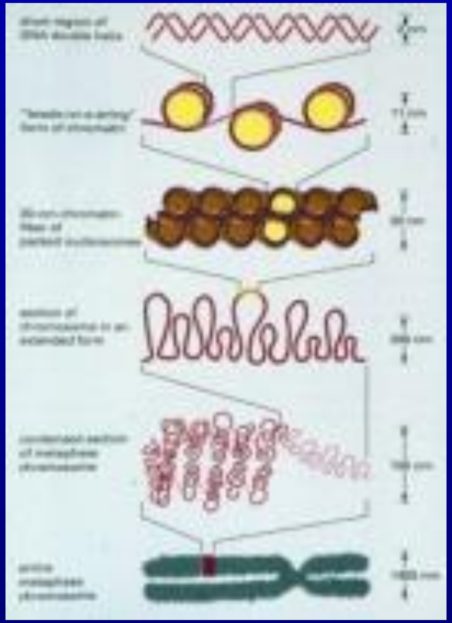


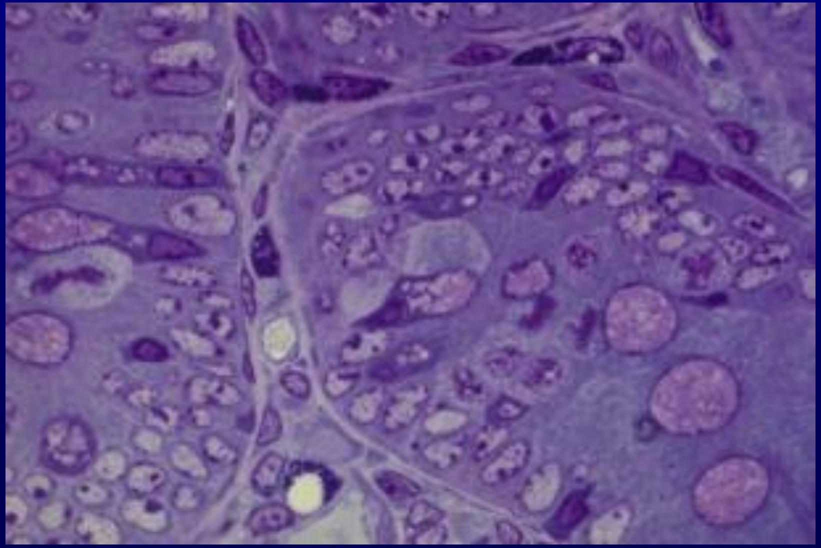
Next time

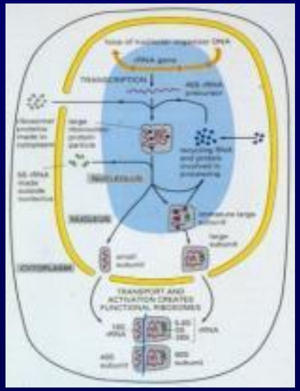
Nucleus and Mitosis

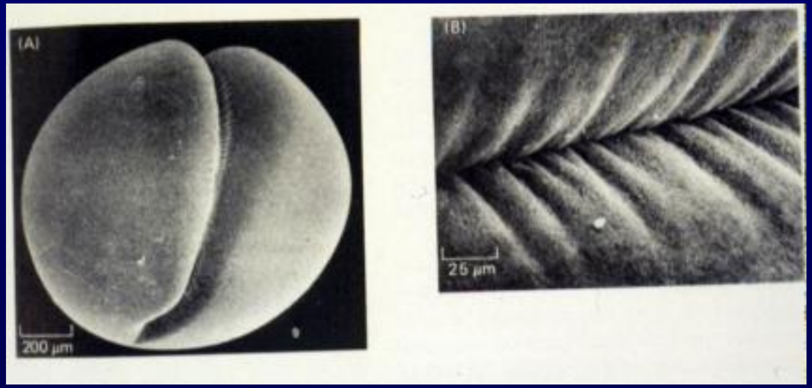












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- Douglas P. Dohrman and TAMHSC Faculty 2012 Structure and Function of Human Organ Systems, Histology Laboratory Manual - Slide selections were largely based on this manual for first year medical students at TAMHSC