6. Cytoskeleton and Cell Motility

VIBS 443 and VIBS 602

Undergraduate – Graduate
Histology Lecture Series

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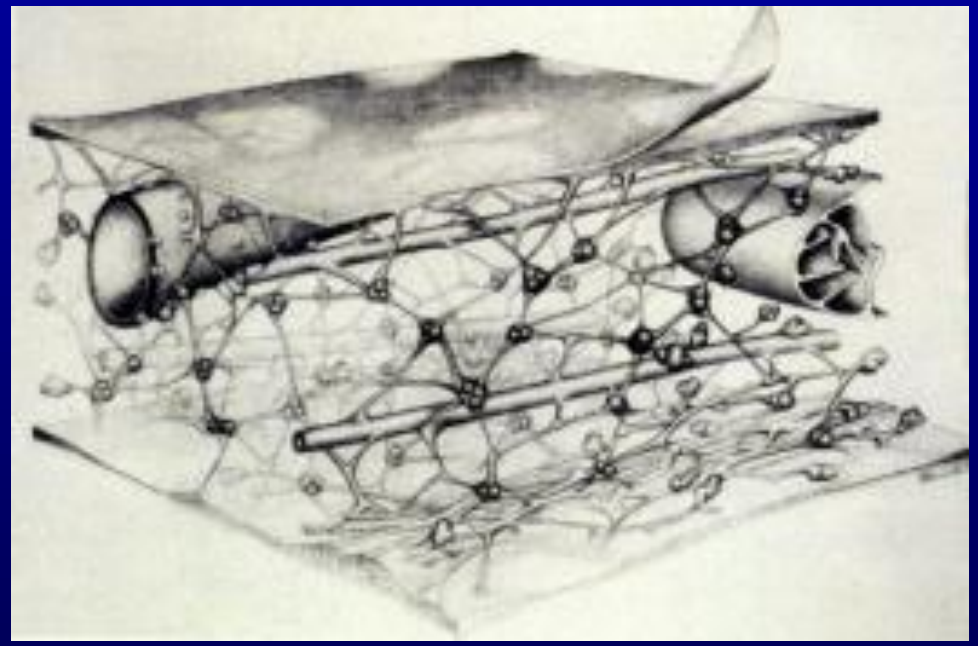
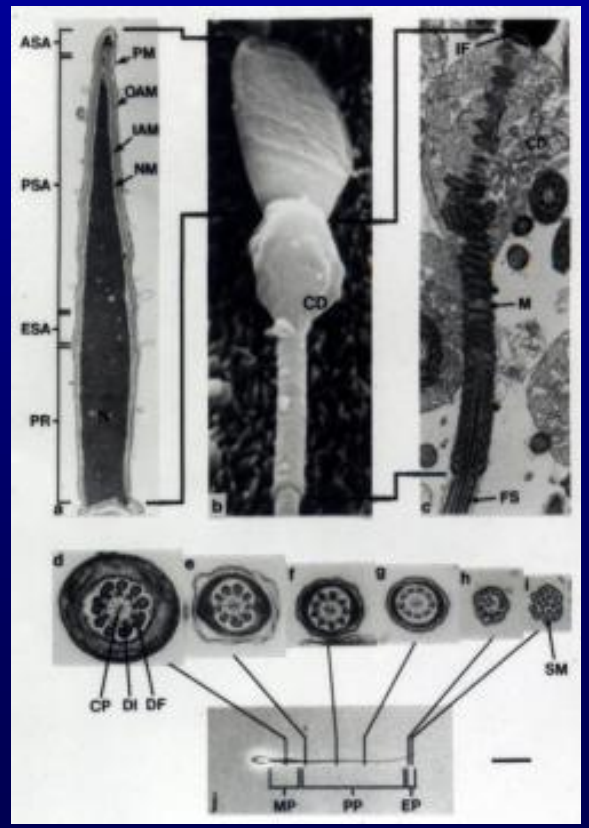
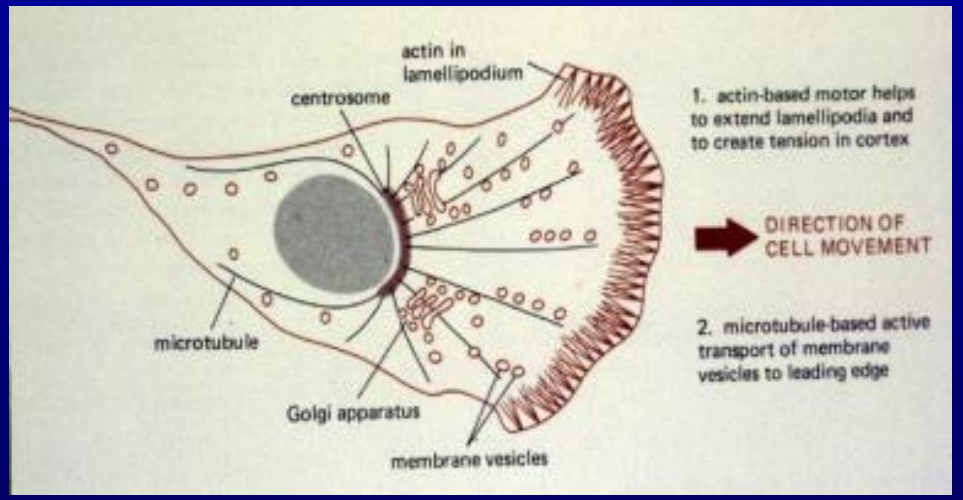






Objective

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

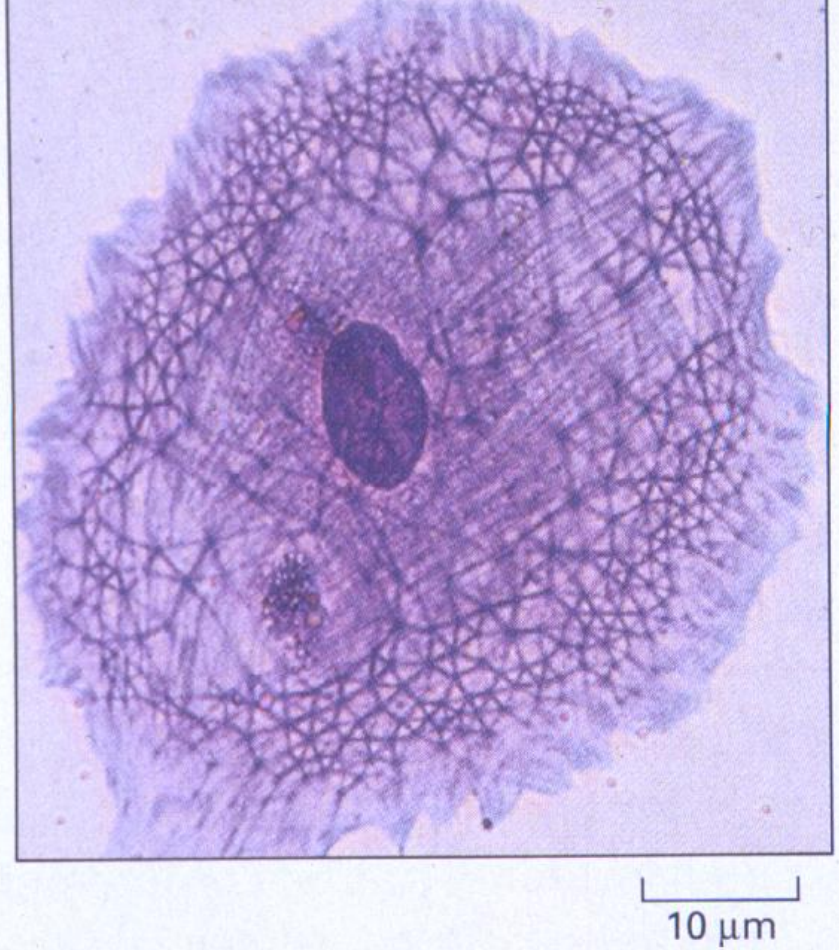


Figure 16–1 The cytoskeleton. A cell in culture has been fixed and stained with Coomassie blue, a general stain for proteins. Note the variety of filamentous structures that extend throughout the cell. (Courtesy of Colin Smith.)

Gunther von Hagens' Body Worlds

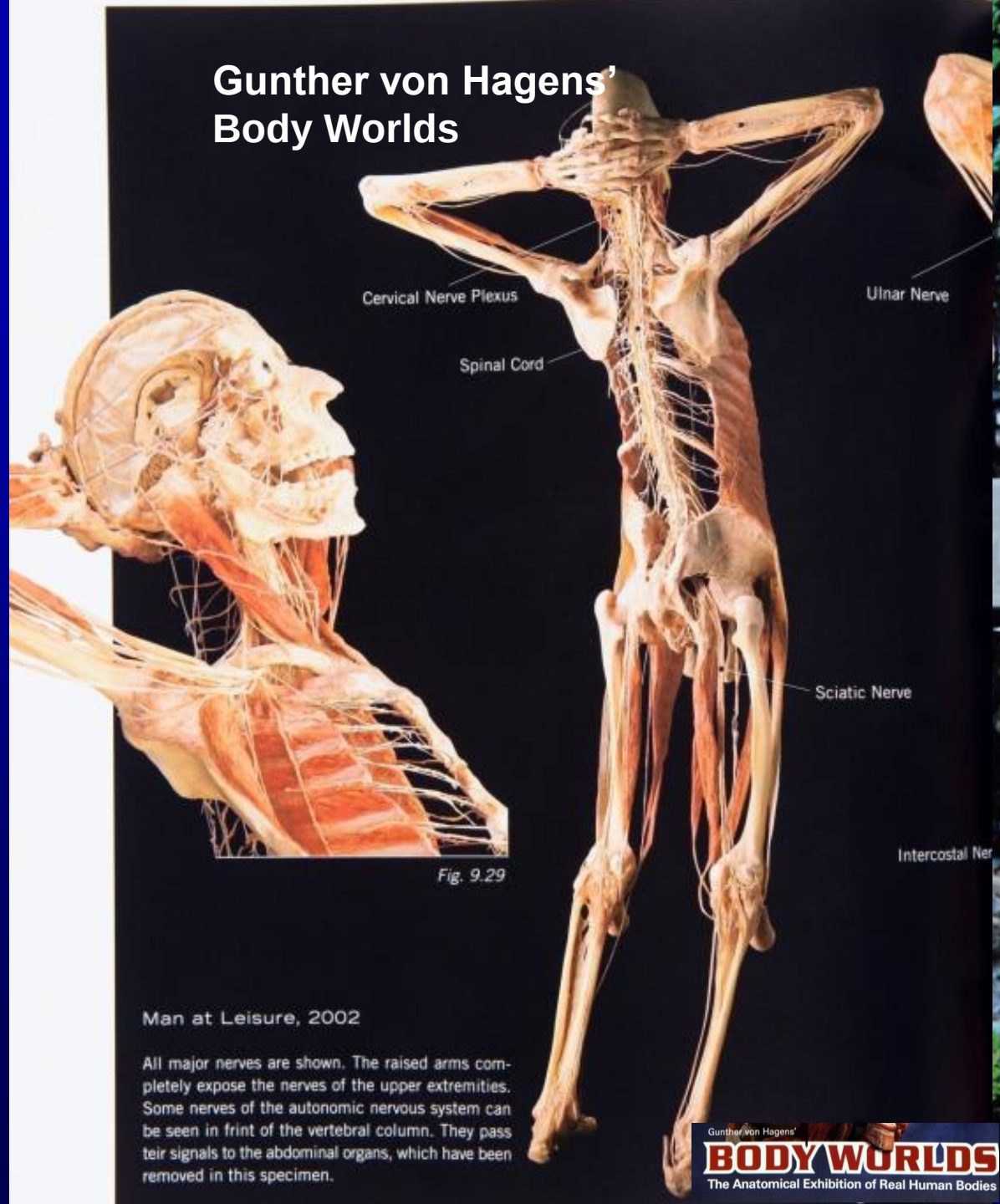


Fig. 9.29

Man at Leisure, 2002

All major nerves are shown. The raised arms completely expose the nerves of the upper extremities. Some nerves of the autonomic nervous system can be seen in frint of the vertebral column. They pass teir signals to the abdominal organs, which have been removed in this specimen.

Gunther von Hagens' BODY WORLDS The Anatomical Exhibition of Real Human Bodies

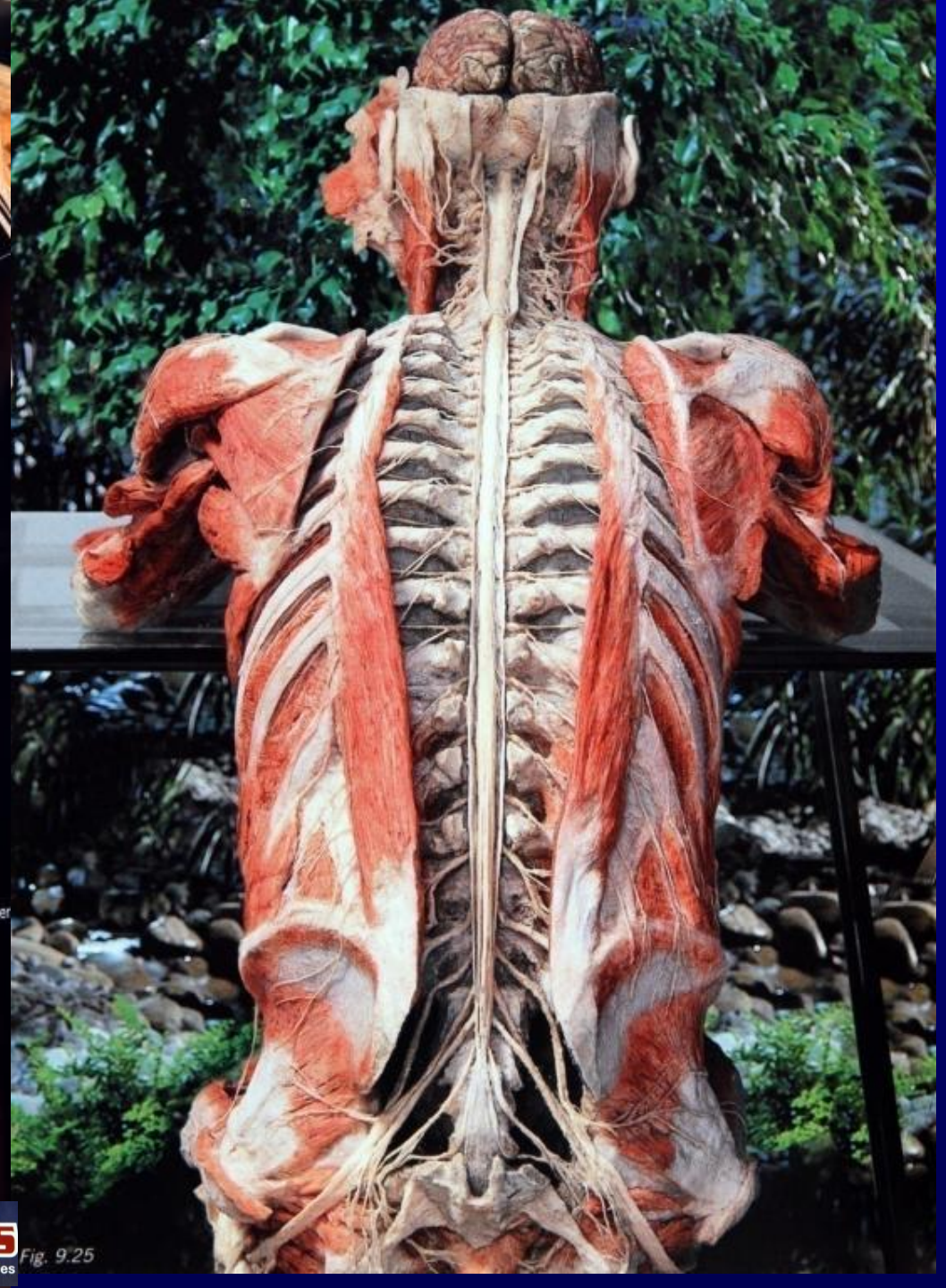
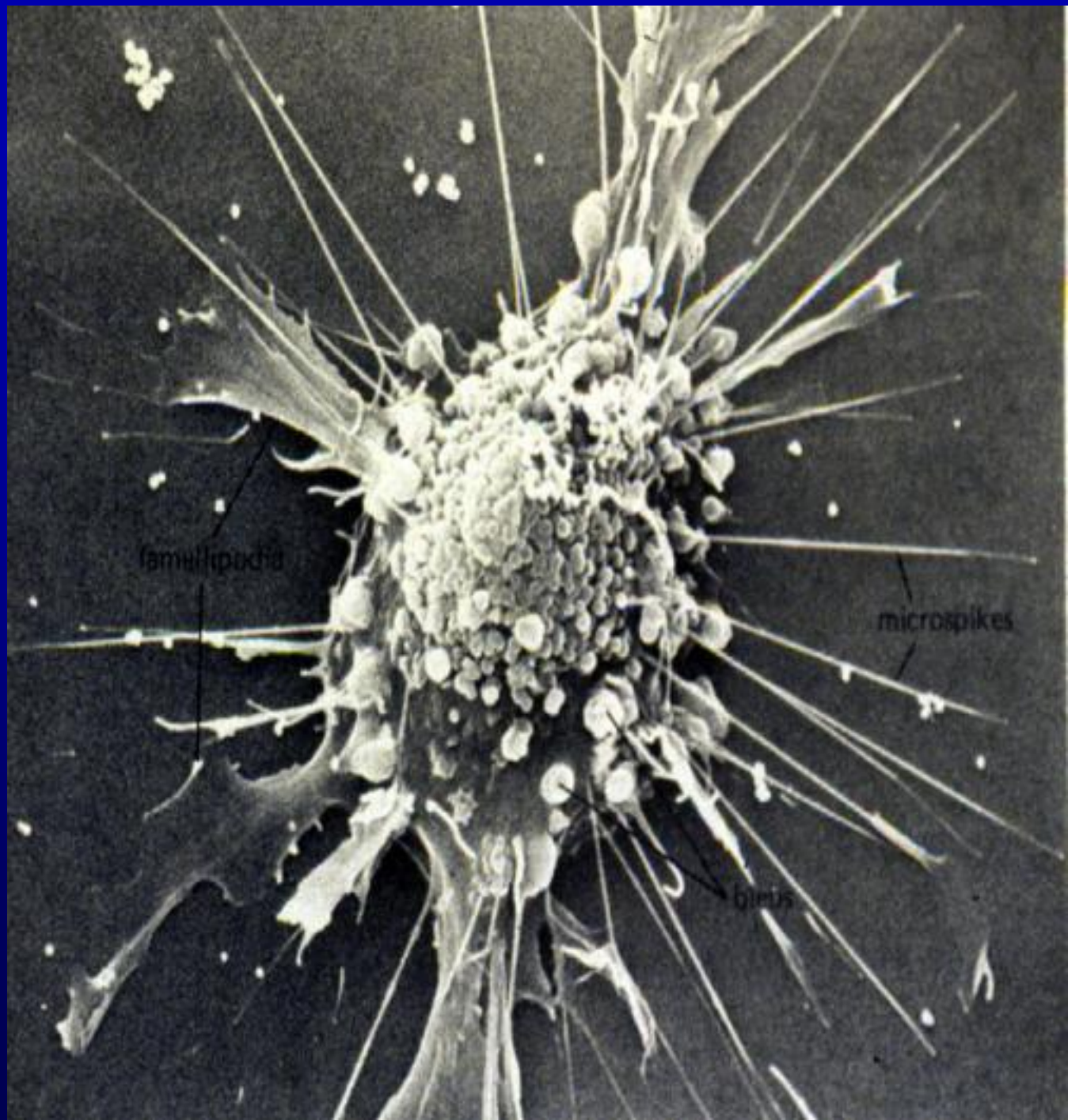


Fig. 9.25

Cytoskeleton

Cells must perform tasks requiring **structural framework**

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



Cytoskeleton

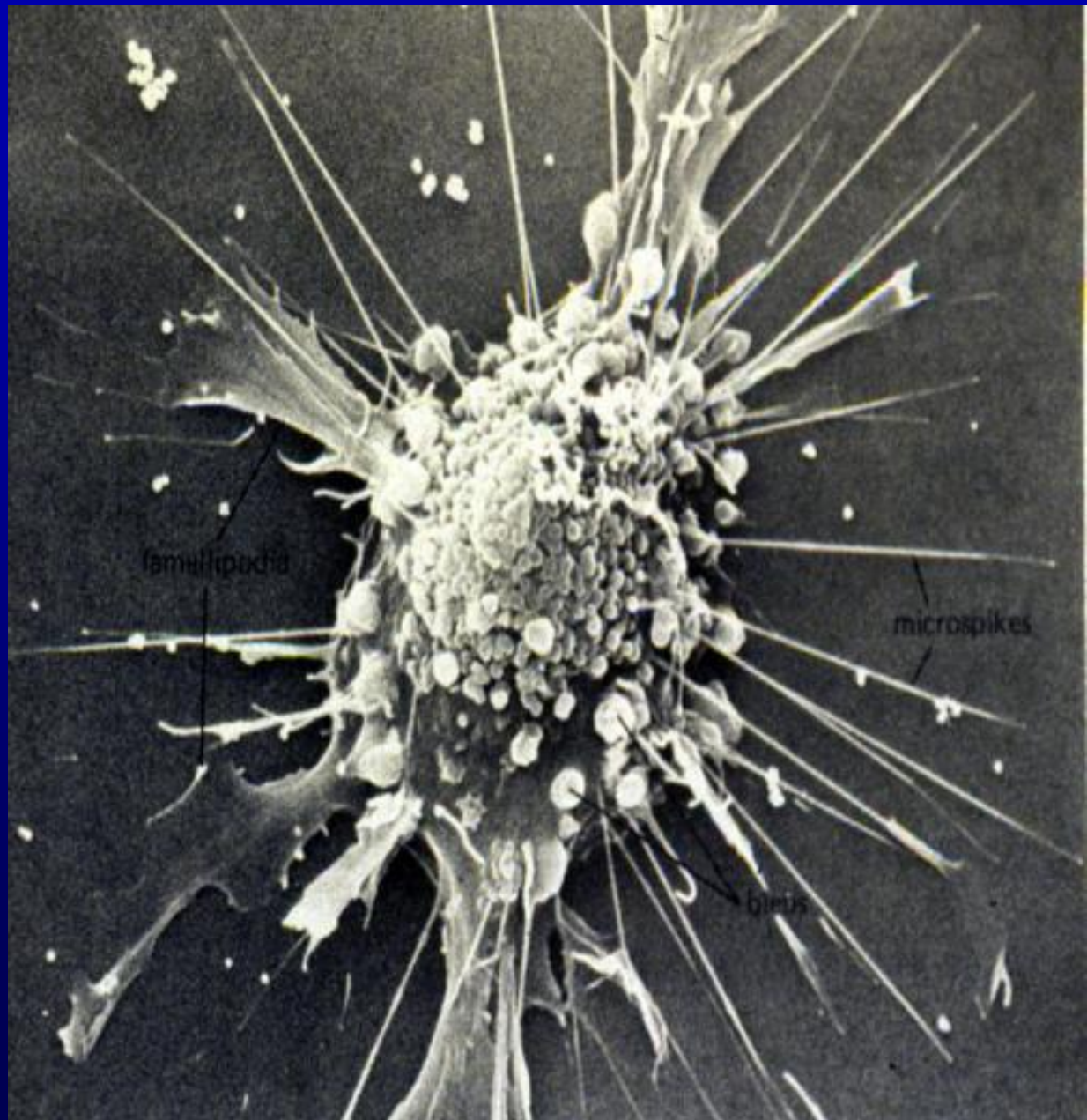
Cells must perform tasks: requiring contractile machinery

Transport vesicles, organelles, and chromosomes

Divide cytoplasm

Specialization of cell surface

Cell motility



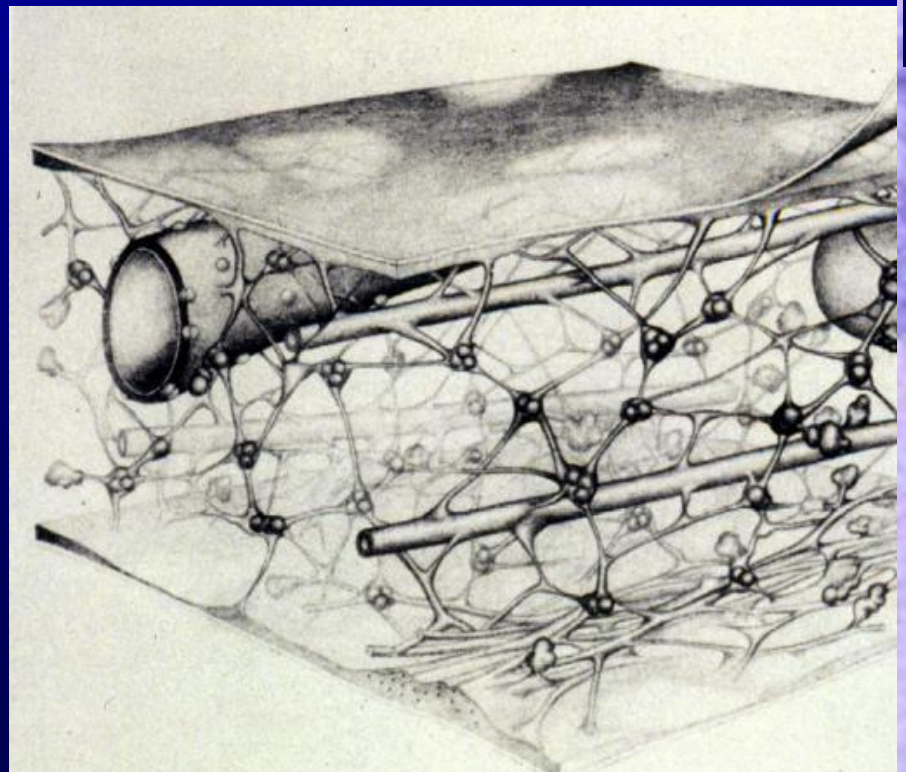
Cytoskeleton

Non-membranous organelles

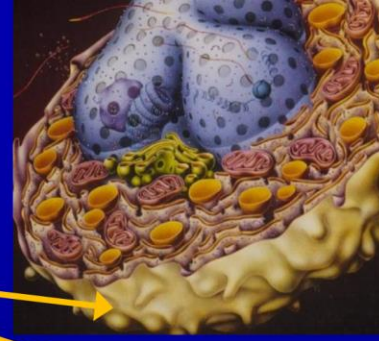
Microtubules (25 nm)

Microfilament (6 nm)

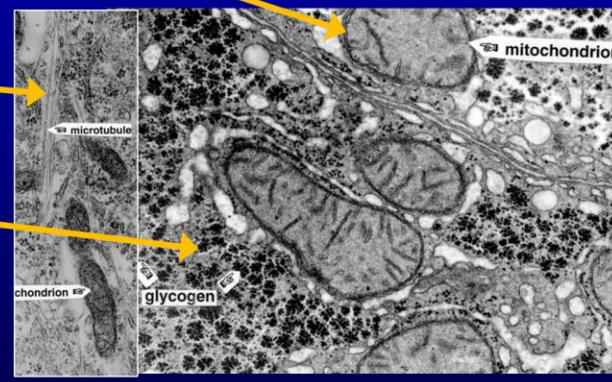
Intermediate filament (10 nm)

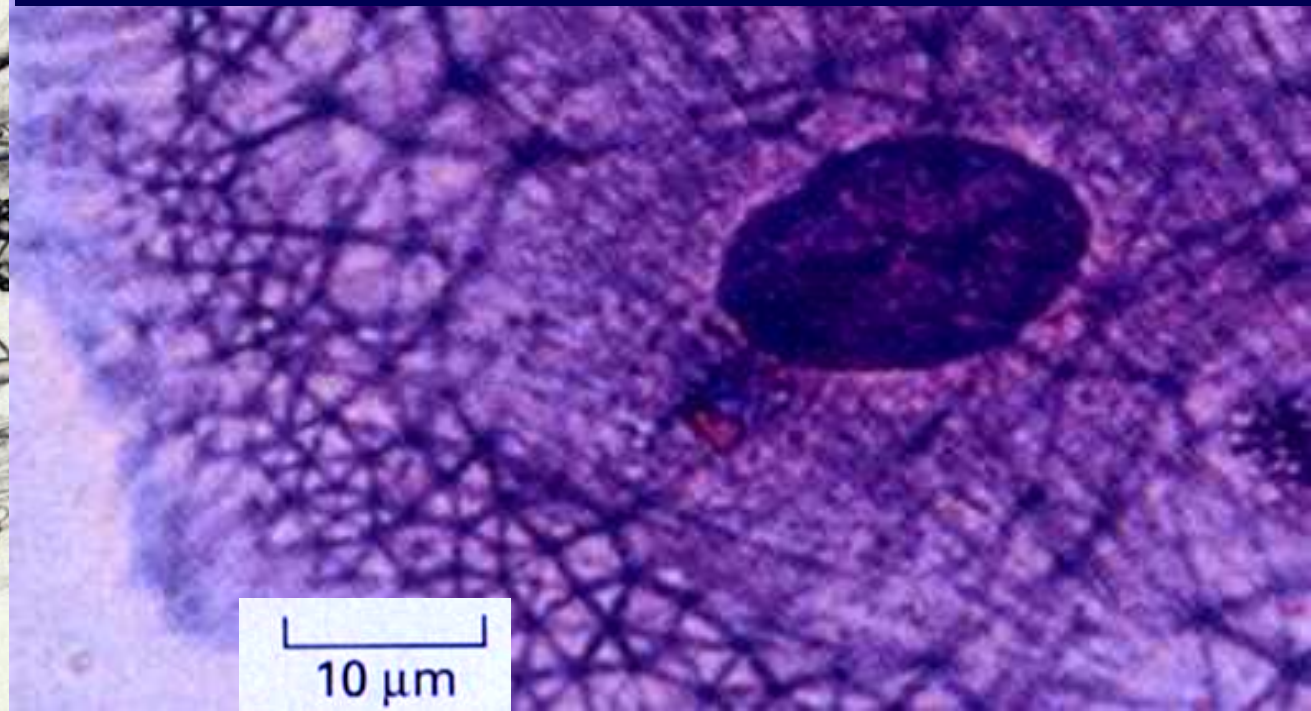


Cell cytoplasm is composition of the cytosol (gel like fluid that holds the contents inside the cell in place) **plus three classes of structures.**



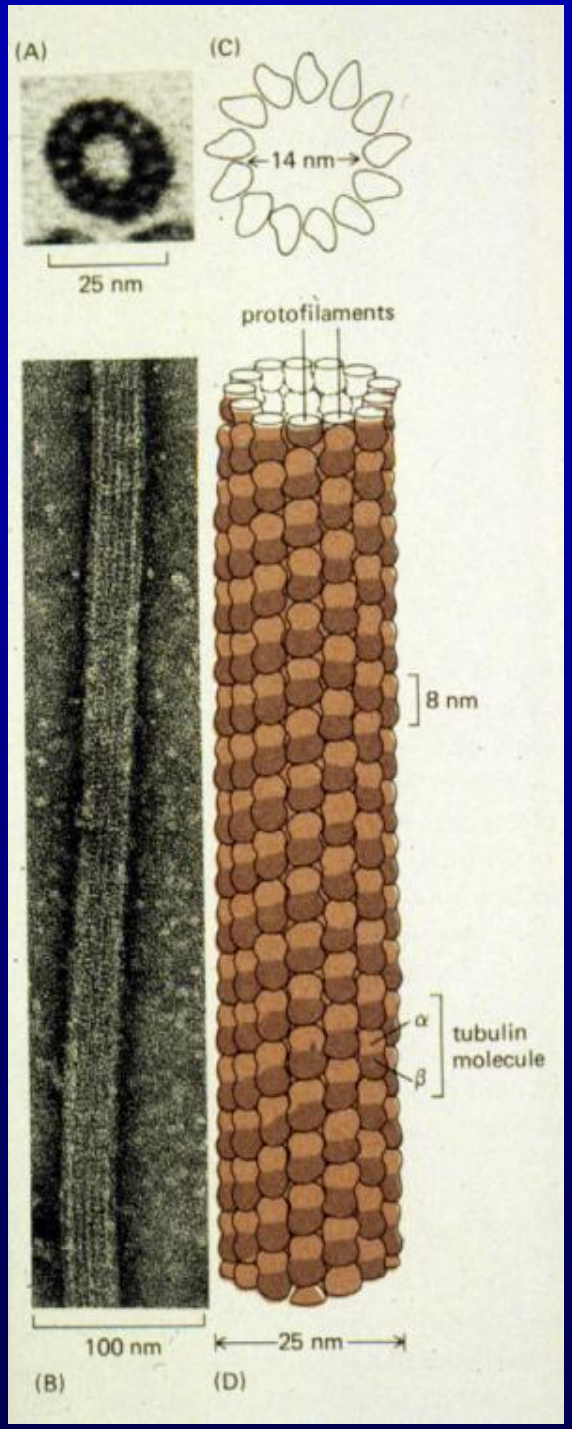
1. **Membranous organelles** - common structures some with metabolic functions: cell membrane, RER, SER, Golgi, mitochondria, lysosomes
2. **Non-membranous organelles** – cytoskeletal components: microtubules, microfilaments, intermediate filaments, free ribosomes
3. **Inclusions** - expendables
   a. nutrients: e.g., glycogen, lipid
   b. pigments: e.g., melanin granules
   c. secretory granules: e.g., zymogen granule of pancreas





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

https://www.youtube.com/watch?v=5rqbmLiSkpk

https://www.youtube.com/watch?v=wJyUtbn0O5Y

Mitochondria

nucleus
https://www.youtube.com/watch?v=7Hk9jct2ozY

https://www.youtube.com/watch?v=LQmTKxI4Wn4

Microtubule ultrastructure

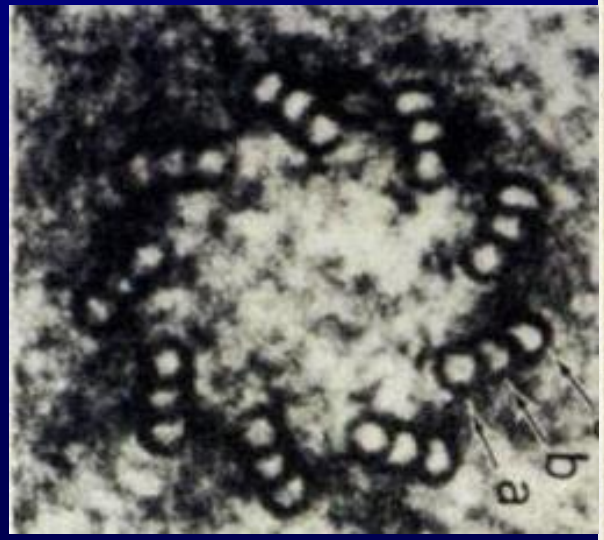
Cytoplasmic microtubules

Axonemes – cilia and flagella – 9 doublets and centered pair

Centrioles –

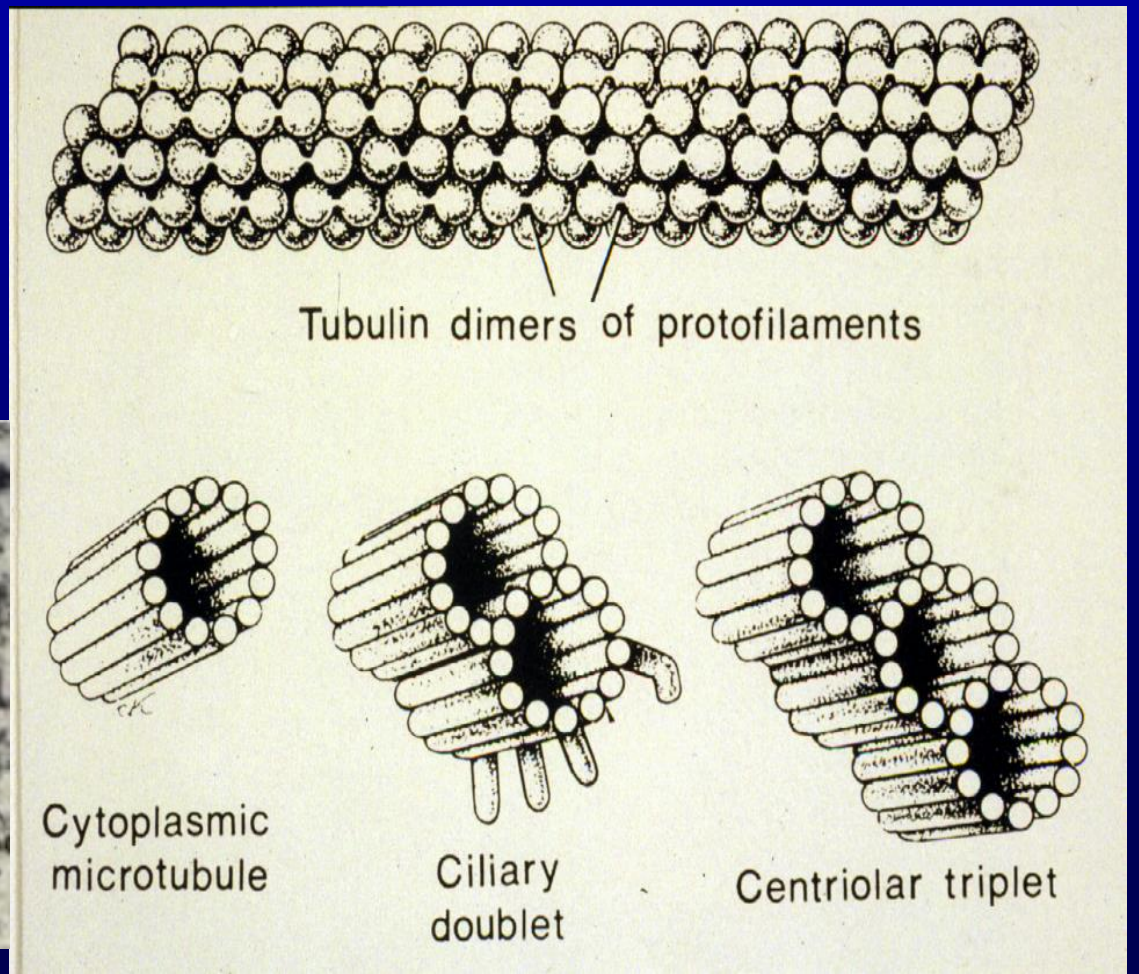
organizing centers of interphase microtubules

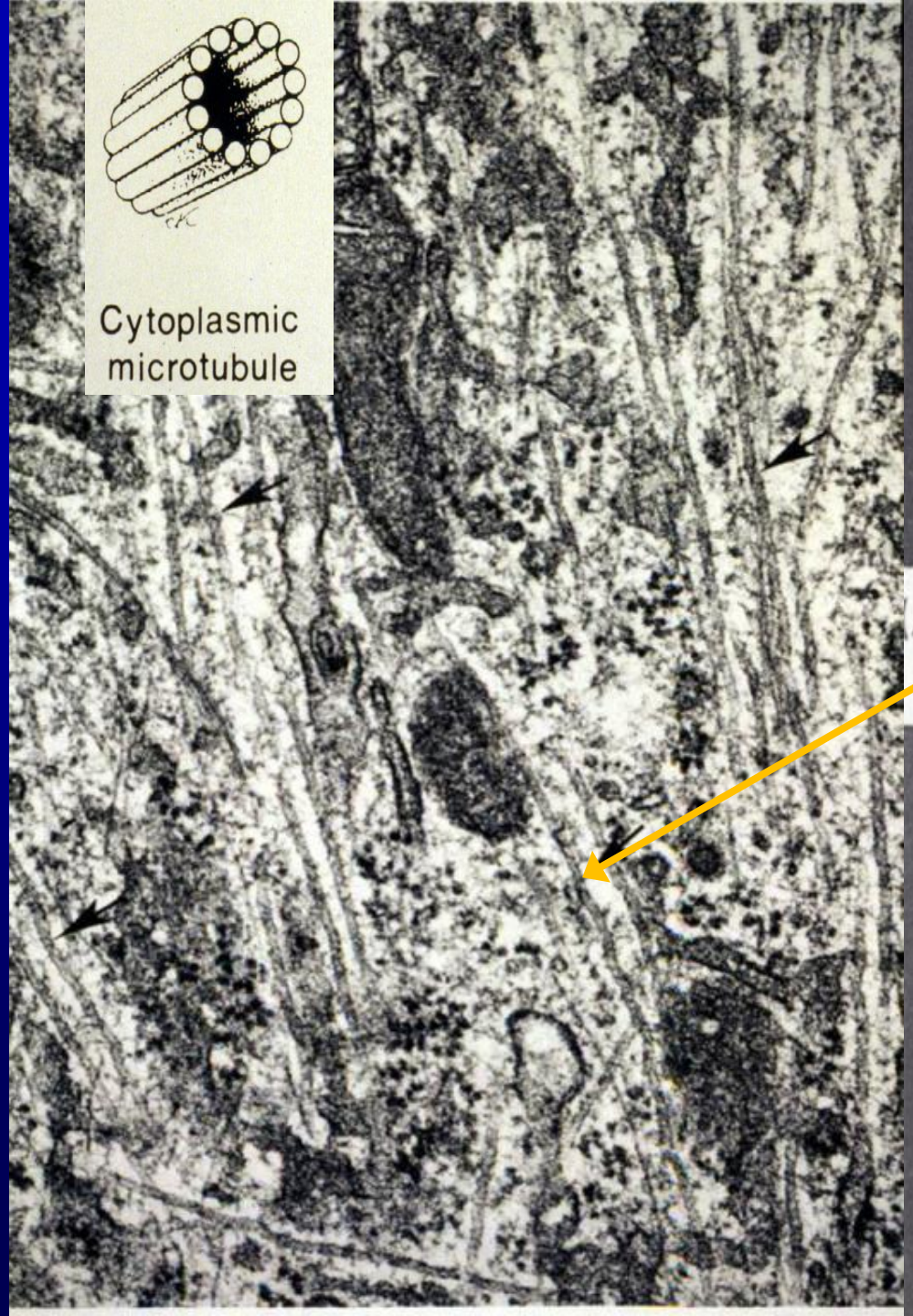
- 9 triplets

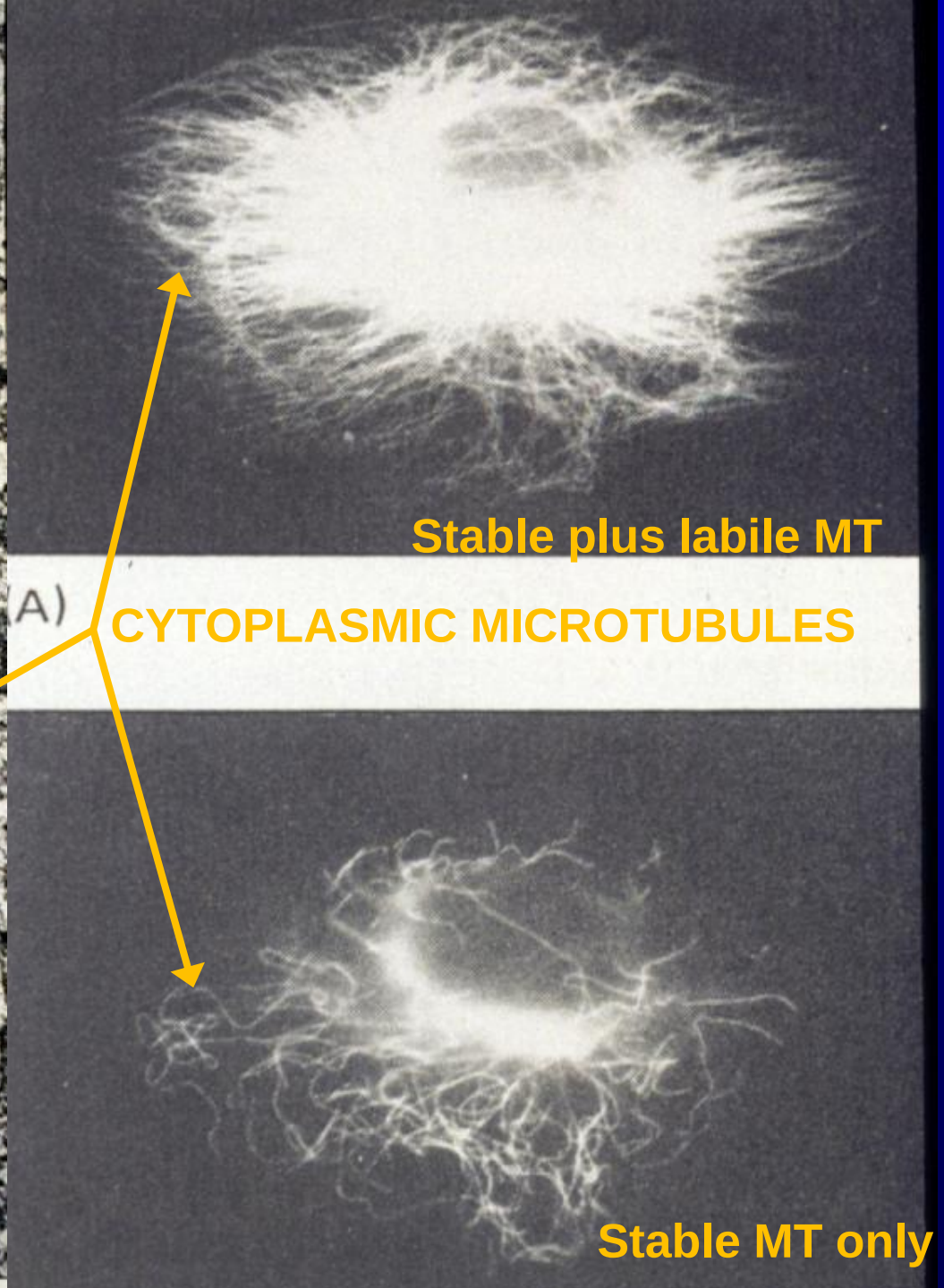


Basal bodies of cilia

- 9 triplets

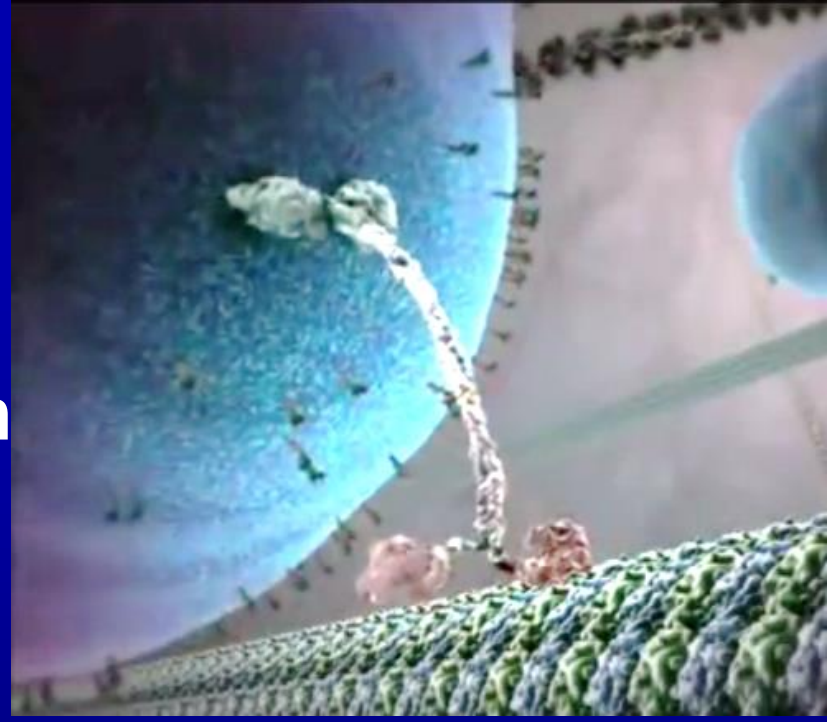


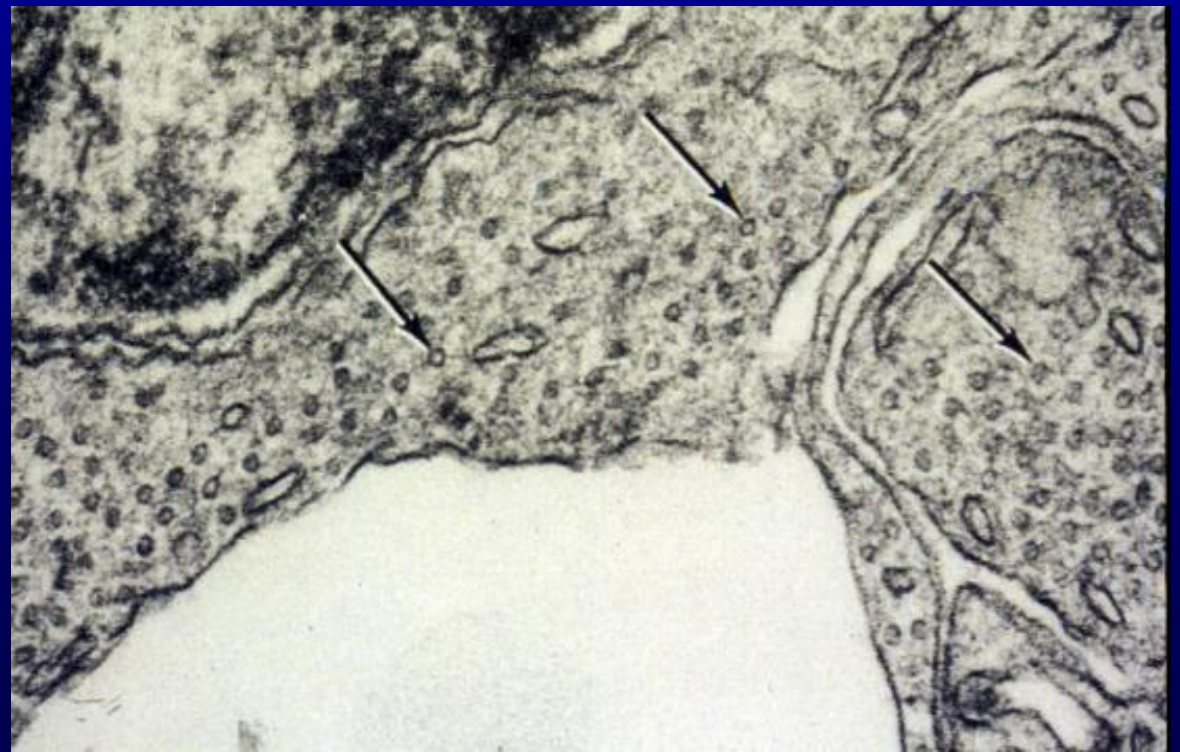

Cytoplasmic
microtubule

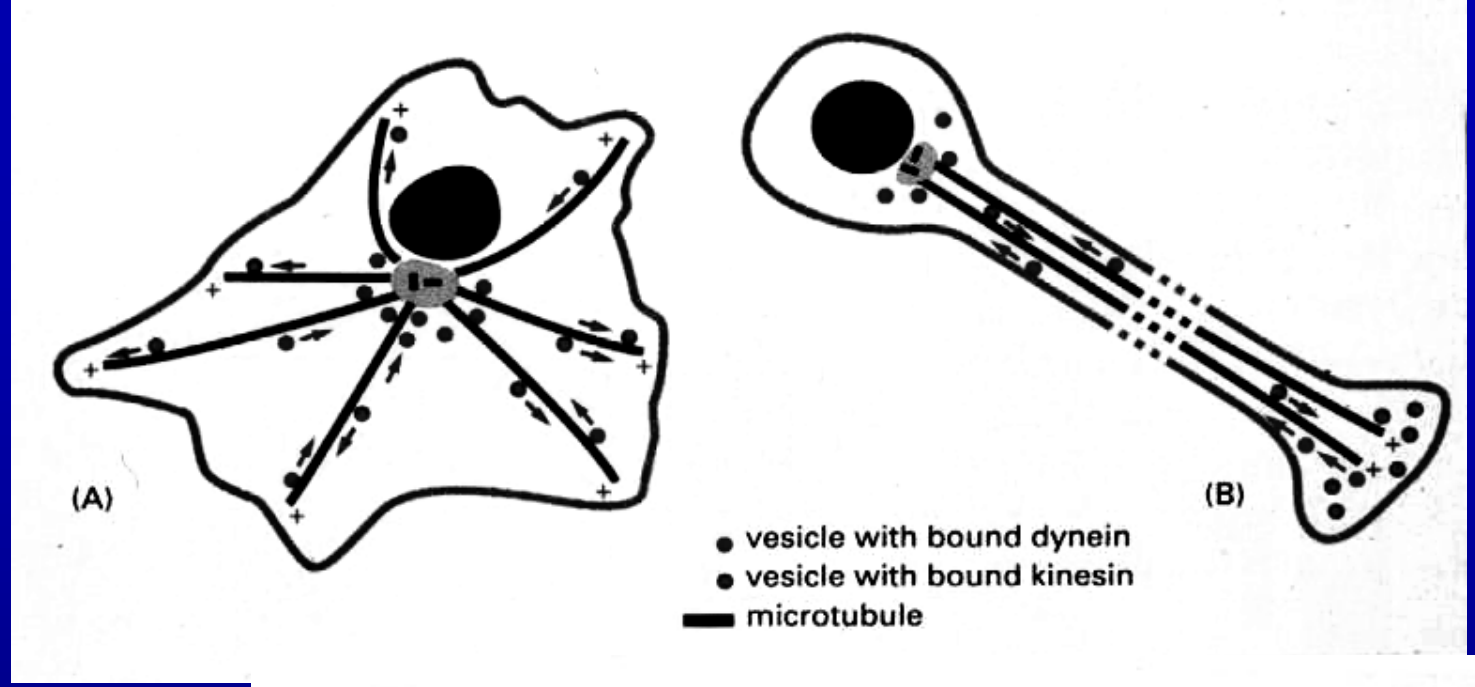

Stable plus labile MT
(A)
CYTOPLASMIC MICROTUBULES
Stable MT only

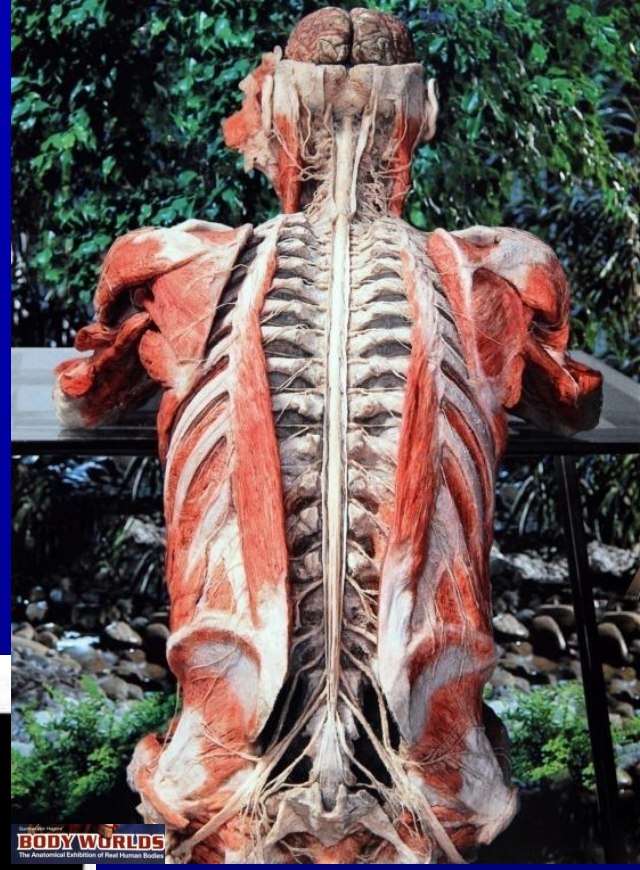
Microtubule function

Guide contractile force (actin) to
move the cell organelles within its cytoplasm
Organization of Golgi, ER, and mitochondria
Separate chromosomes during mitosis









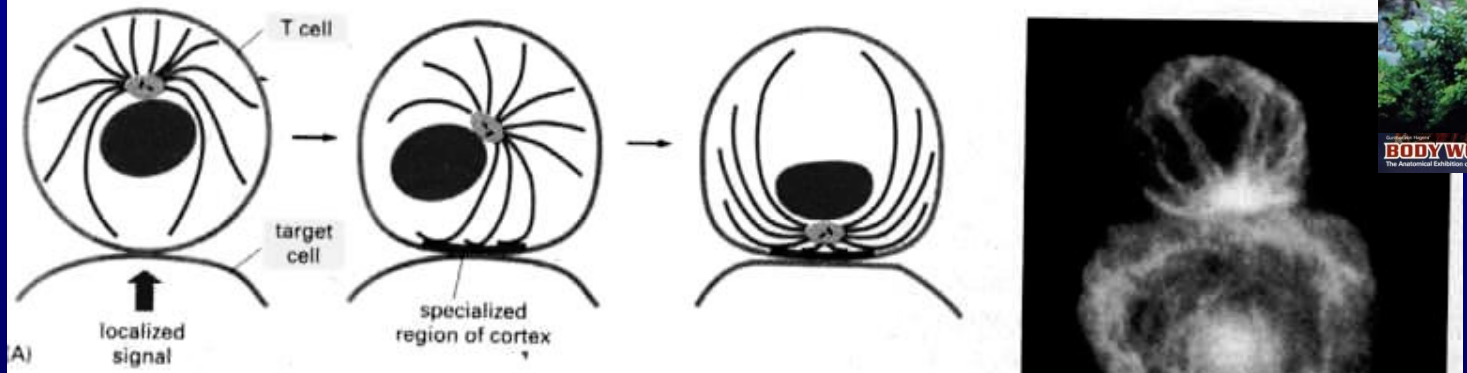


Figure 16–11 The polarization of a cytotoxic T cell after target-cell recognition. (A) Changes in the cytoskeleton of a cytotoxic T cell after it makes contact with a target cell. (B) Immunofluorescence micrograph in which both the T cell (*top*) and its target cell (*bottom*) have been stained with 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.)

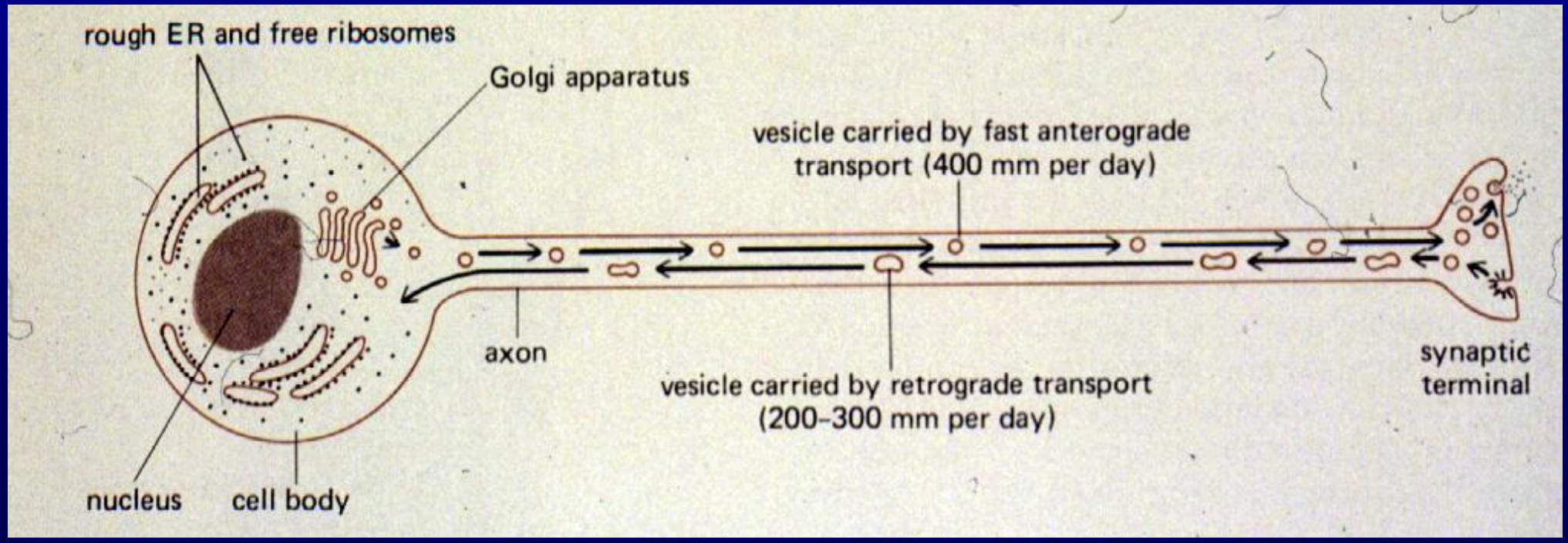
NEURONAL STRUCTURE / FUNCTION

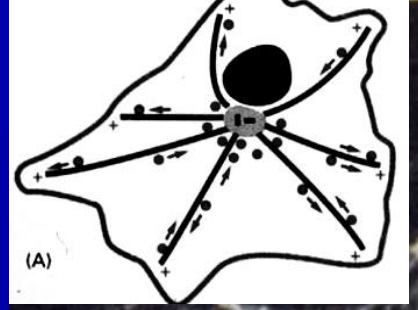
Axonal transport

Anterograde - toward terminal - kinesin

Retrograde - toward cell body - dynein

- **Tetanus toxin**
- **Neurotropic viruses (herpes and rabies) use path to get to cell body in CNS**



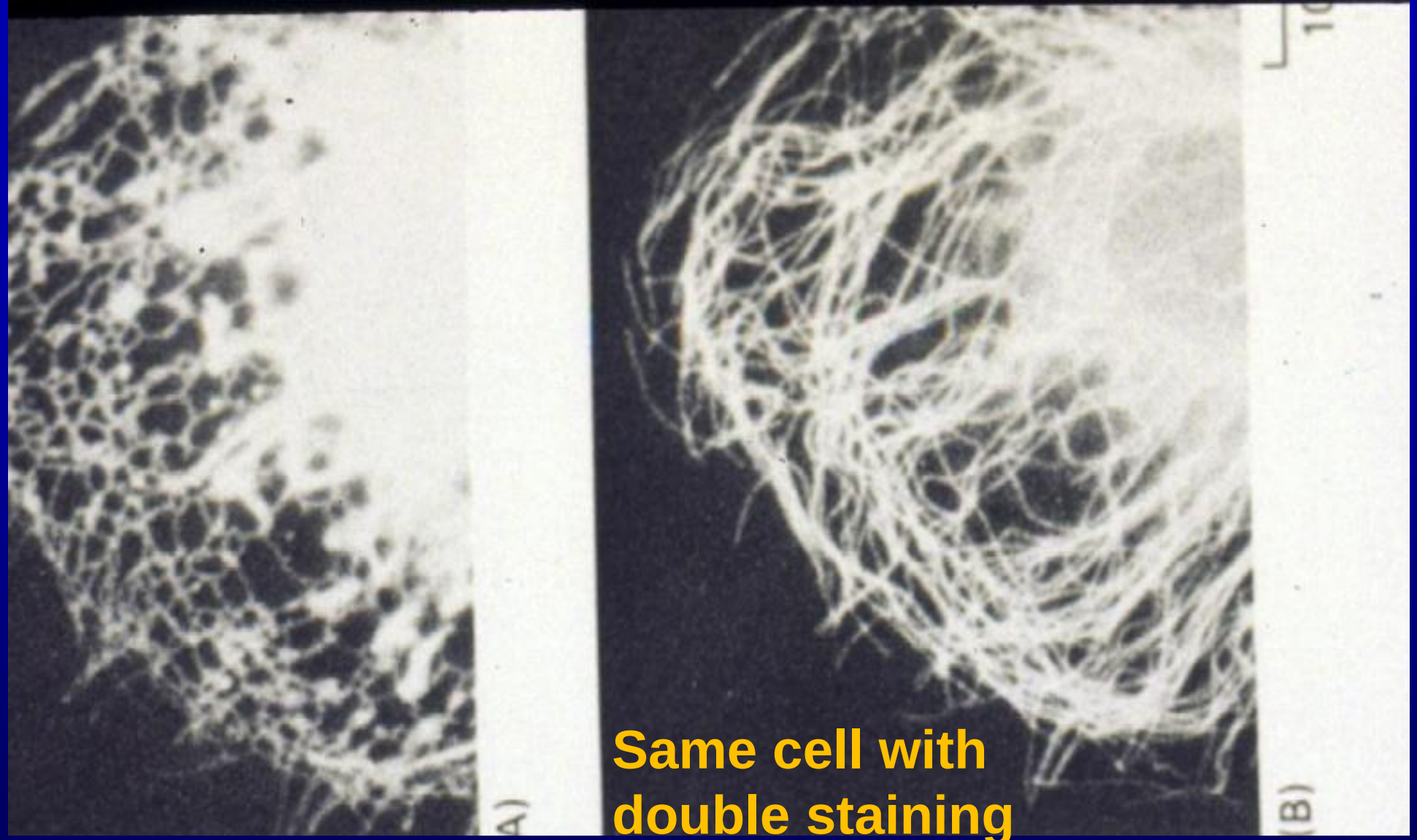


Same cell with double staining

Microtubules

Mitochondria

Organization of mitochondria

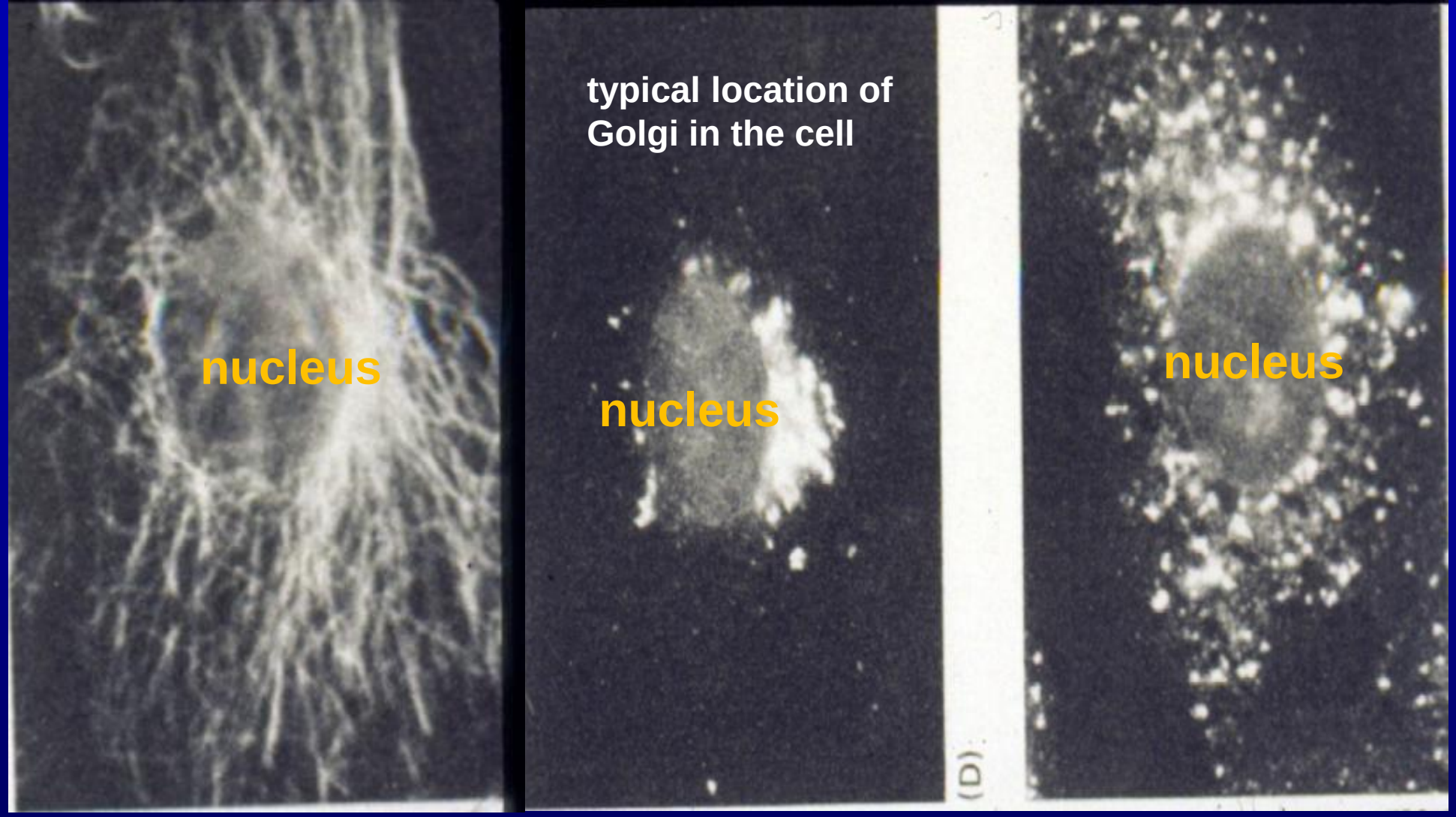


Same cell with double staining

ER

Microtubules

Organization of ER

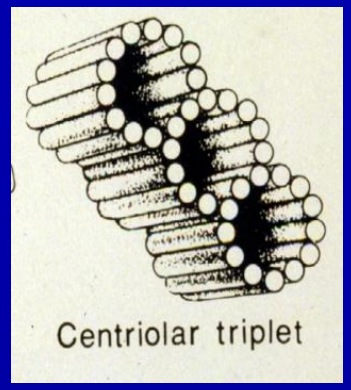


Microtubules shown here

Golgi with microtubules present, but not shown here

Golgi without microtubules present

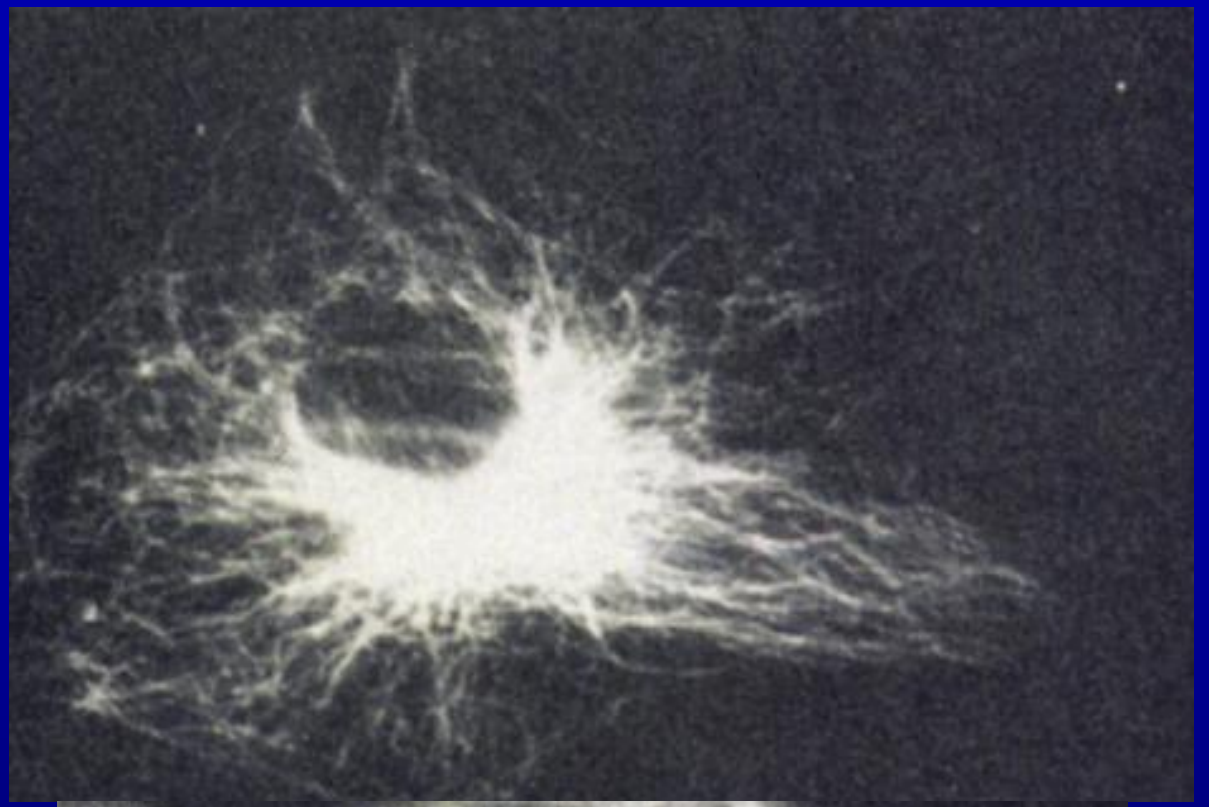
Microtubules are involved in organization of Golgi, ER, and mitochondria.

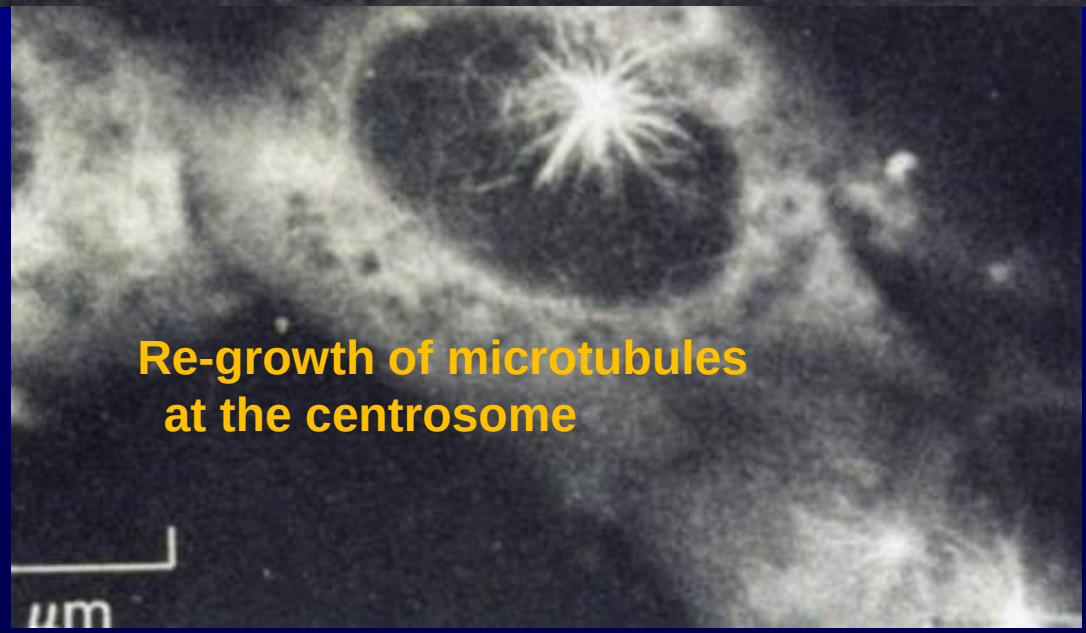


Centrioles

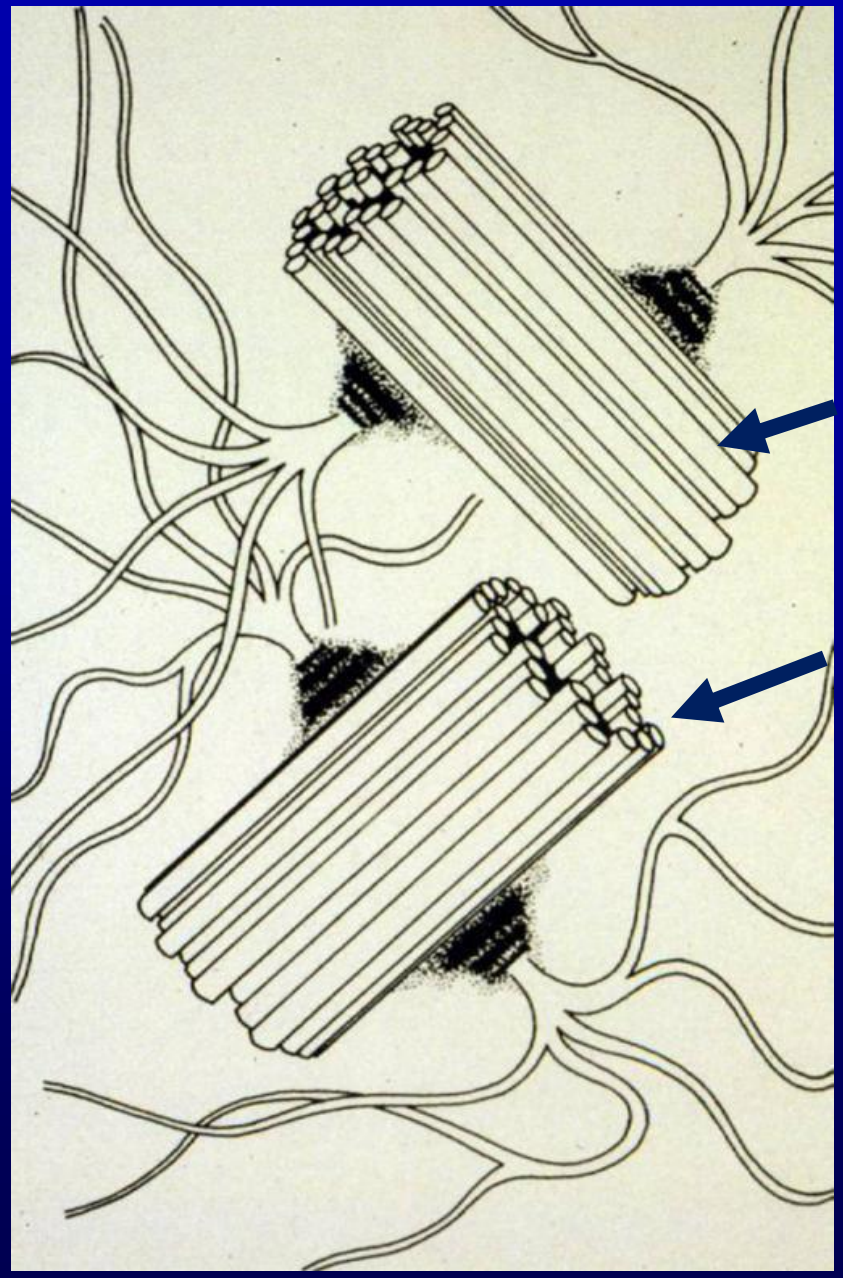
- 9 triplet microtubules
- Centrosome - centriolar duplex at the cell's center

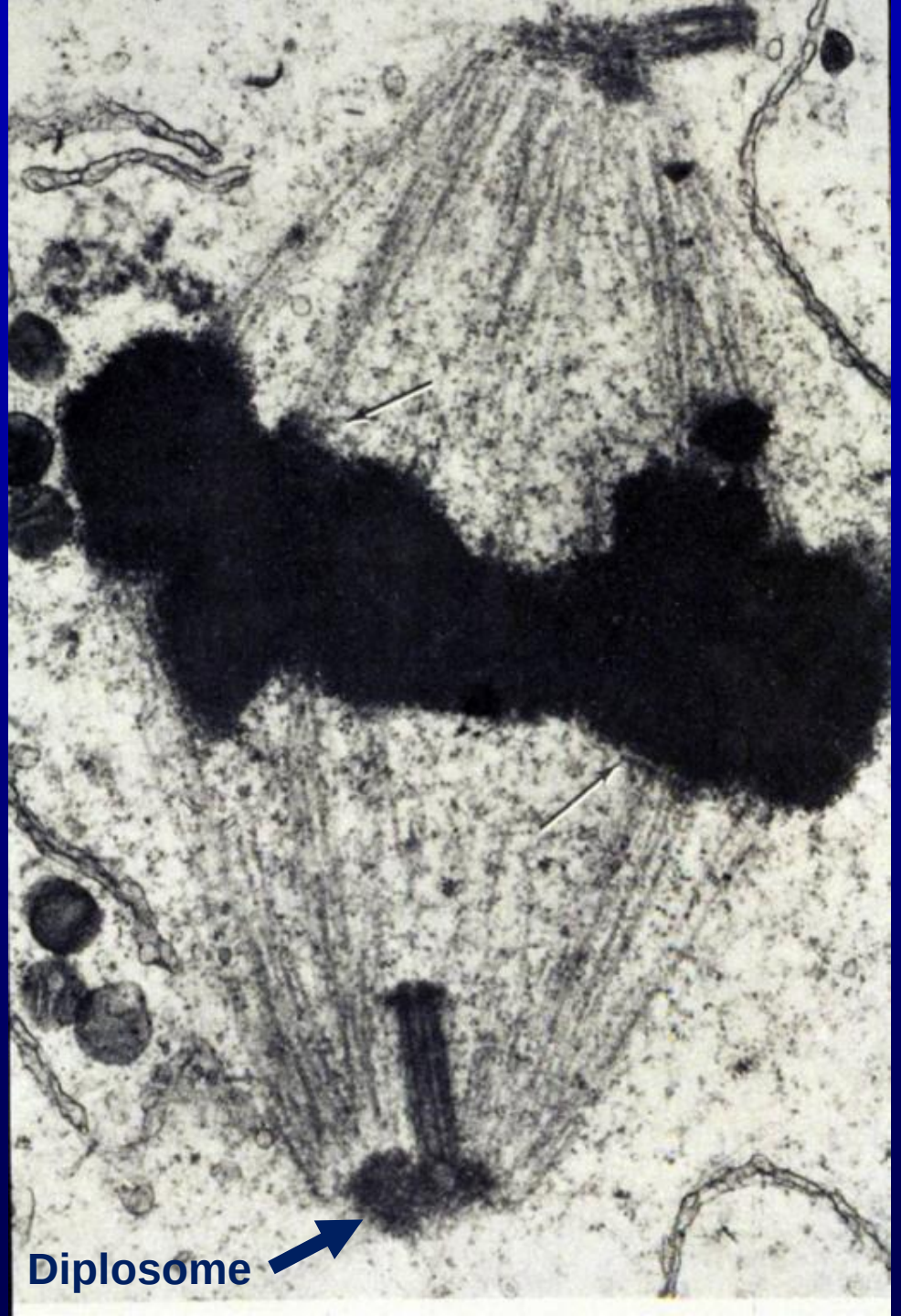
- Diplosome - pair of centrioles
- Self duplicating – develops from pre-existing procentrioles





Diplosome - pair of centrioles



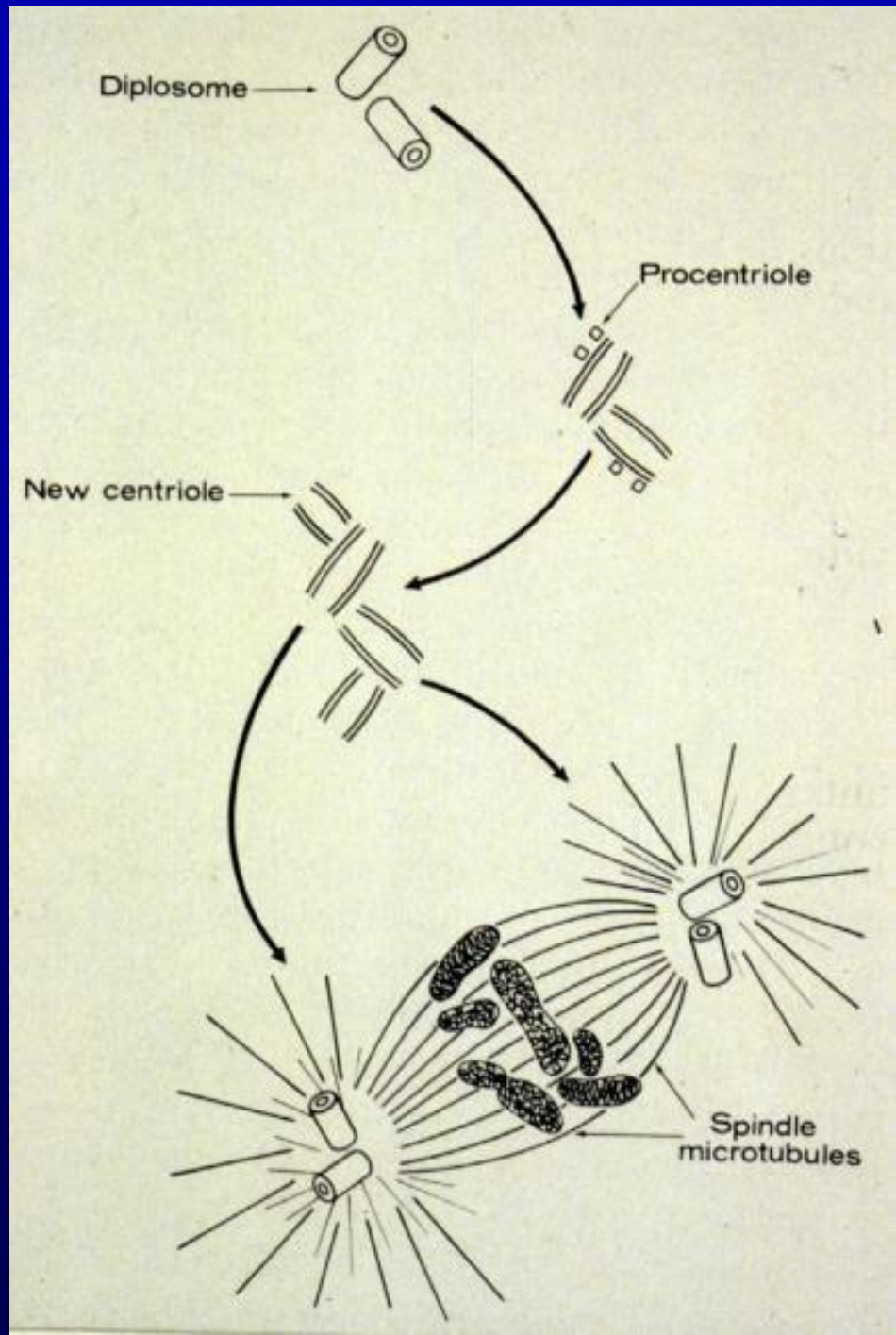


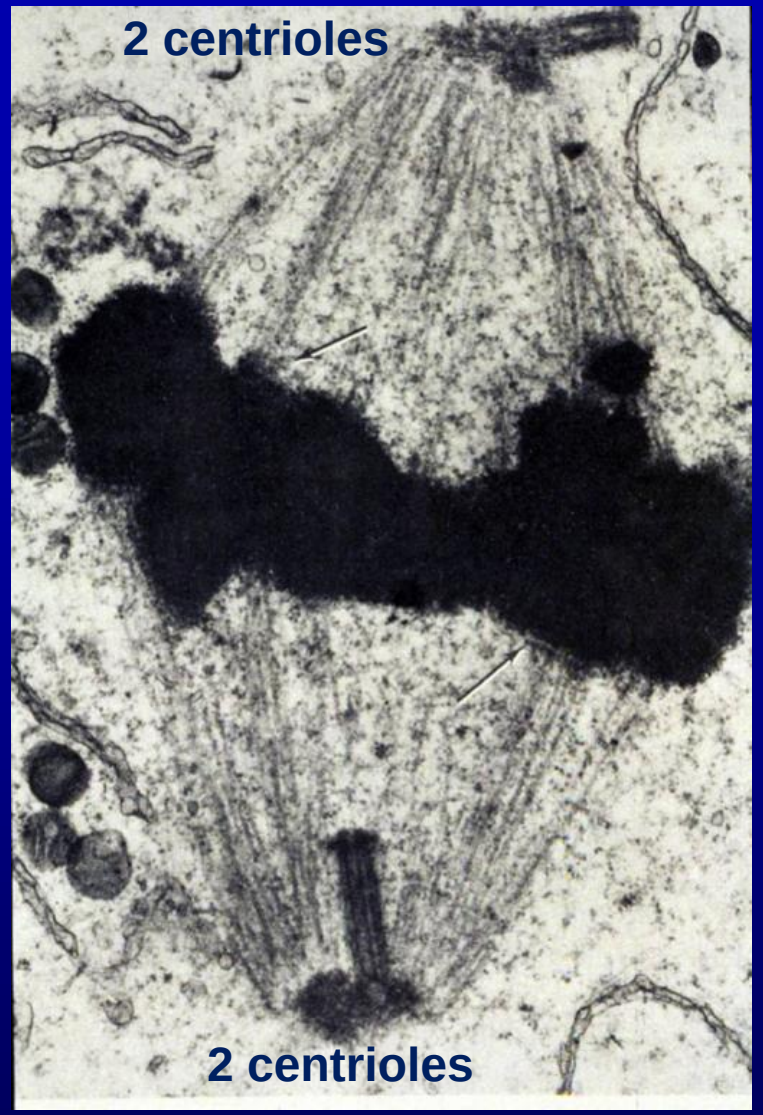
Centrioles

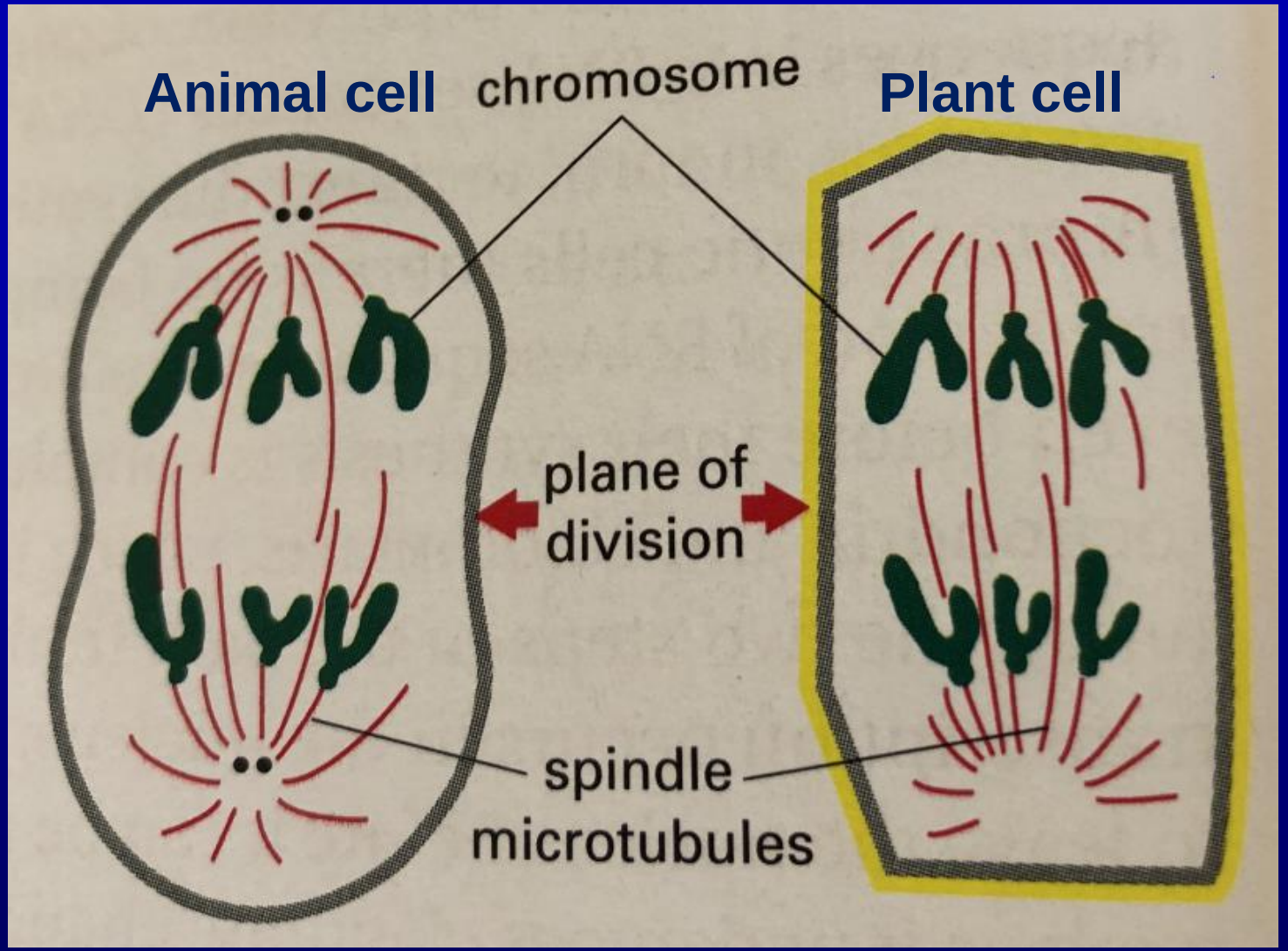
Essential for formation of cilia and flagella

Basal body - root-like anchoring device

Function in organizing microtubules that pull chromosomes apart in mitosis

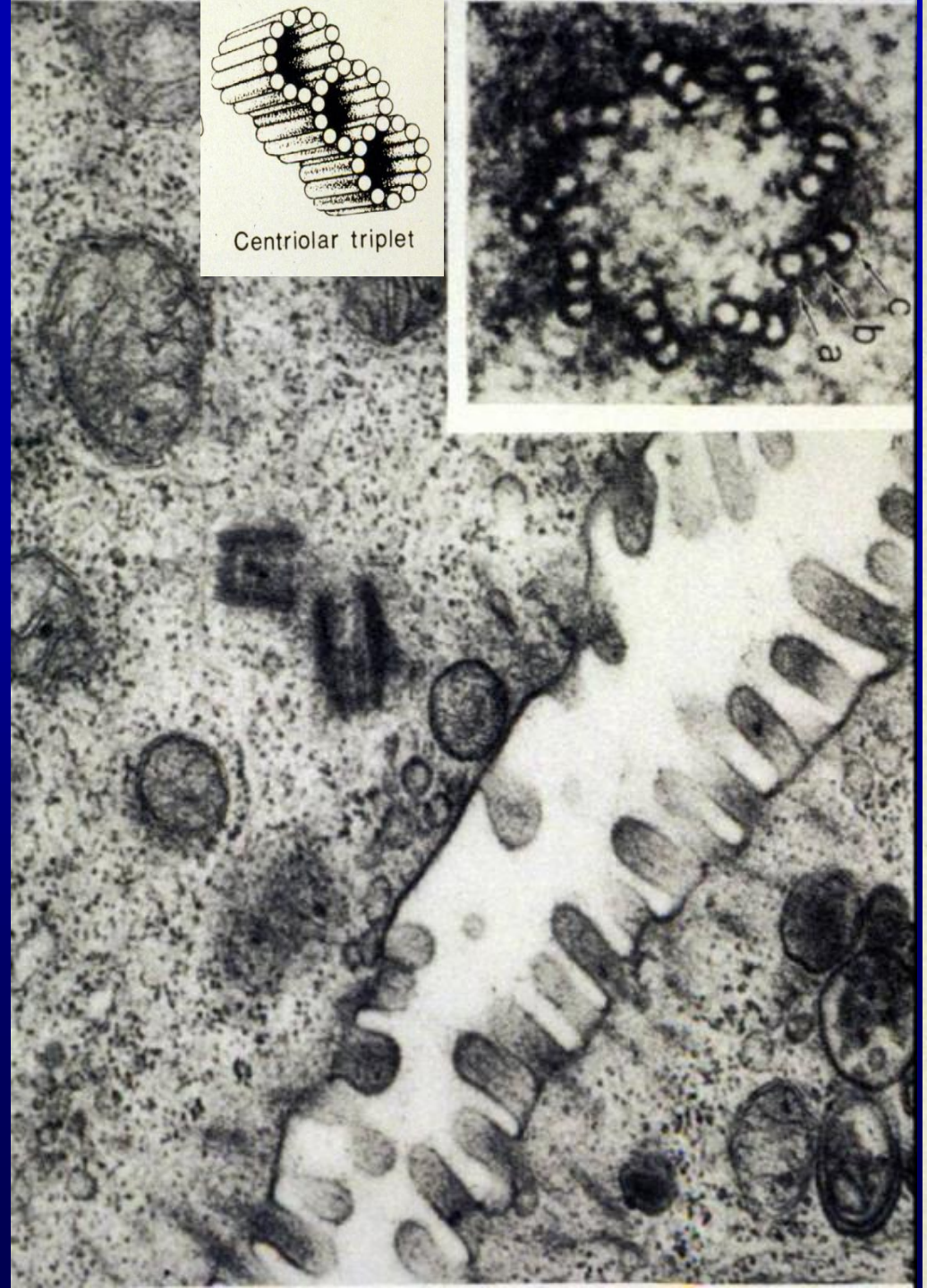


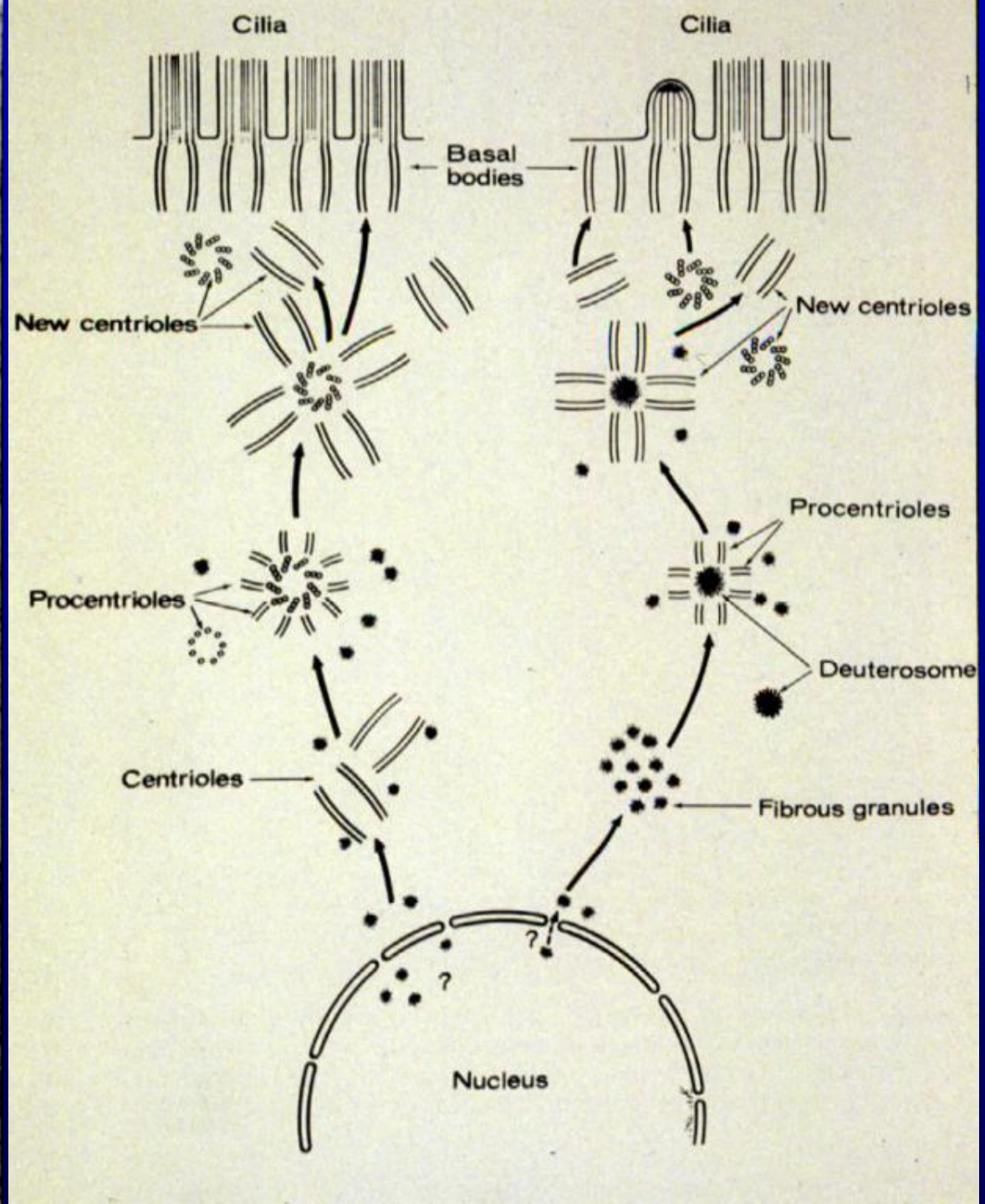


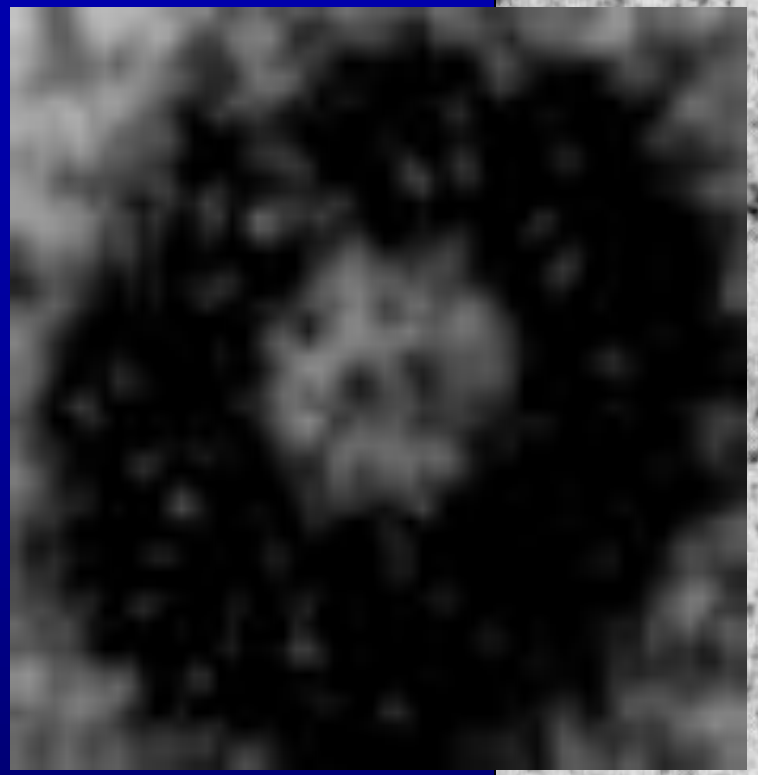


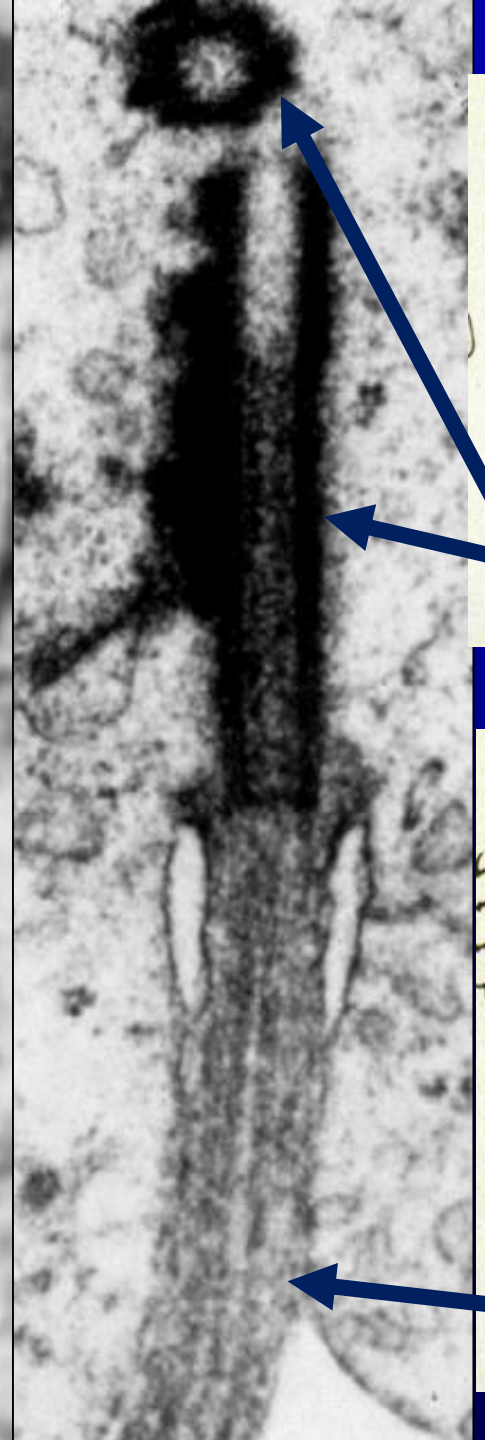
Function in organizing microtubules that pull chromosomes apart in mitosis in animal cells

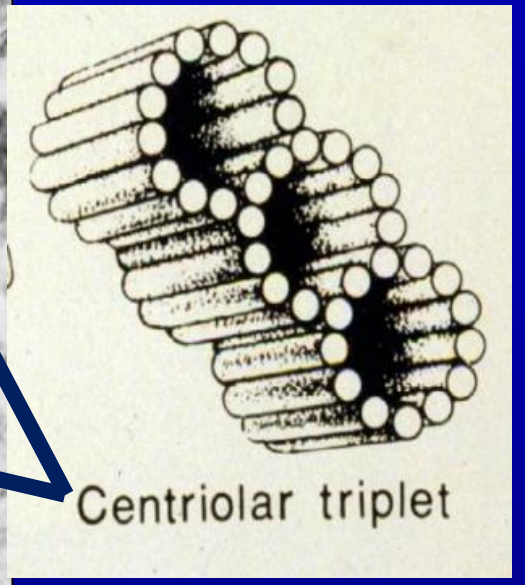
Given that plant cells do not use centrioles in their cell division, what is the essential role of centrioles?

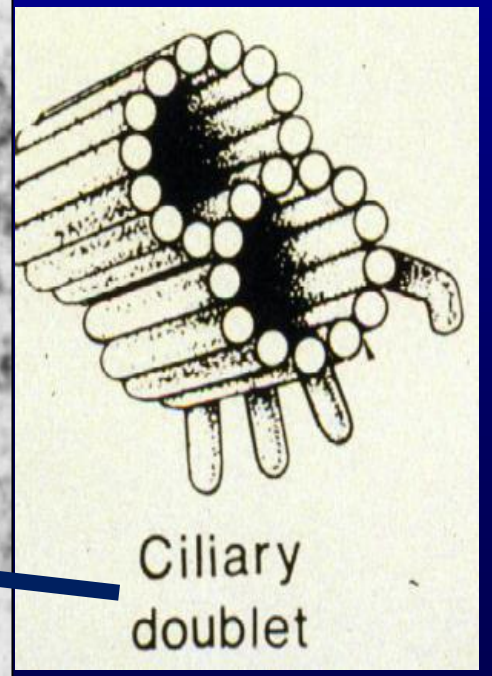

Centriolar triplet
c
b
a

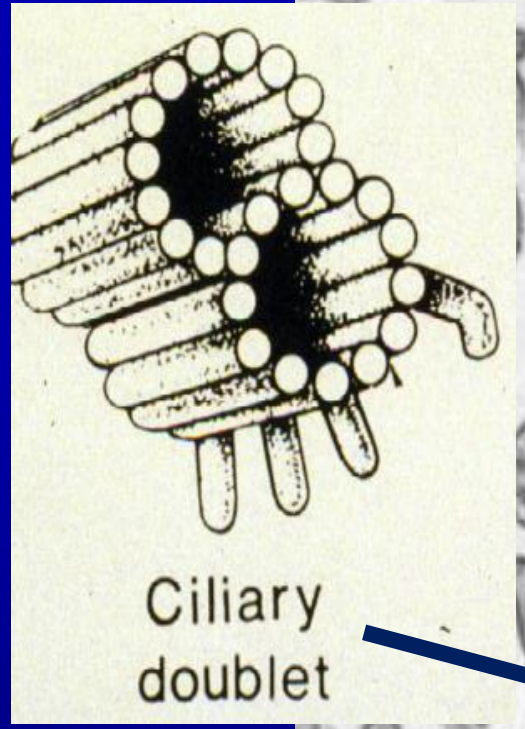

Cilia
Cilia
Basal bodies
New centrioles
New centrioles
Procentrioles
Procentrioles
Deuterosome
Centrioles
Fibrous granules
?
?
Nucleus

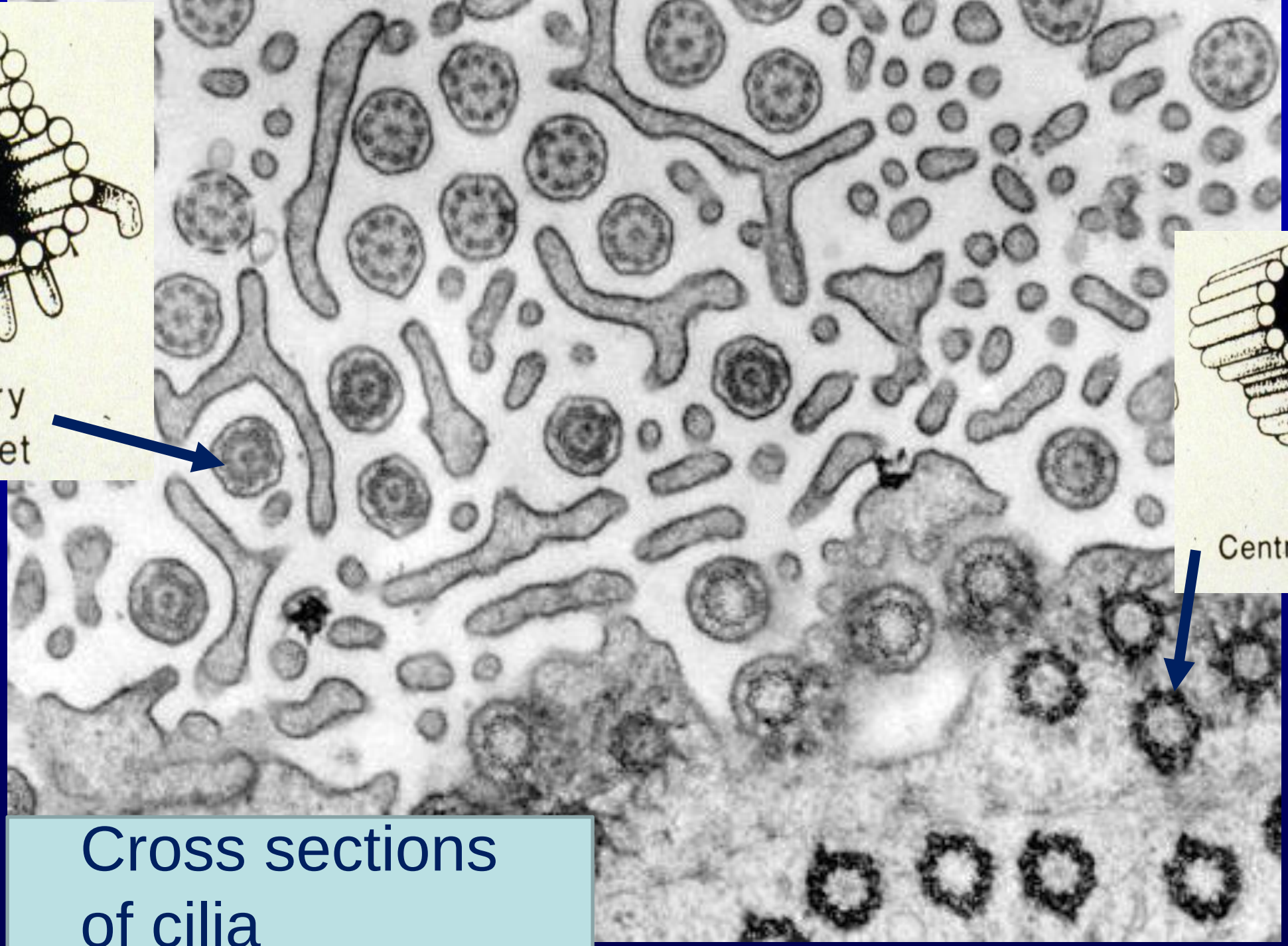


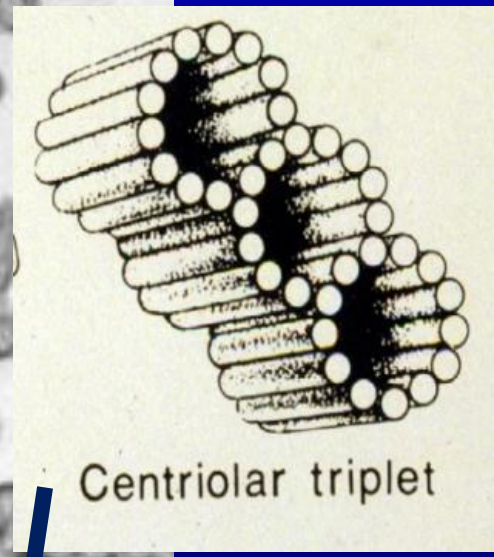



Centriolar triplet

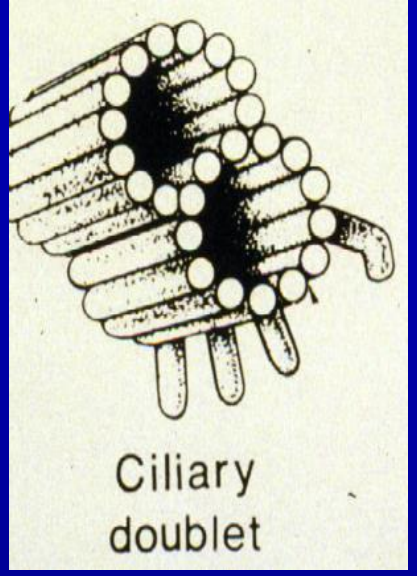

Ciliary
doublet





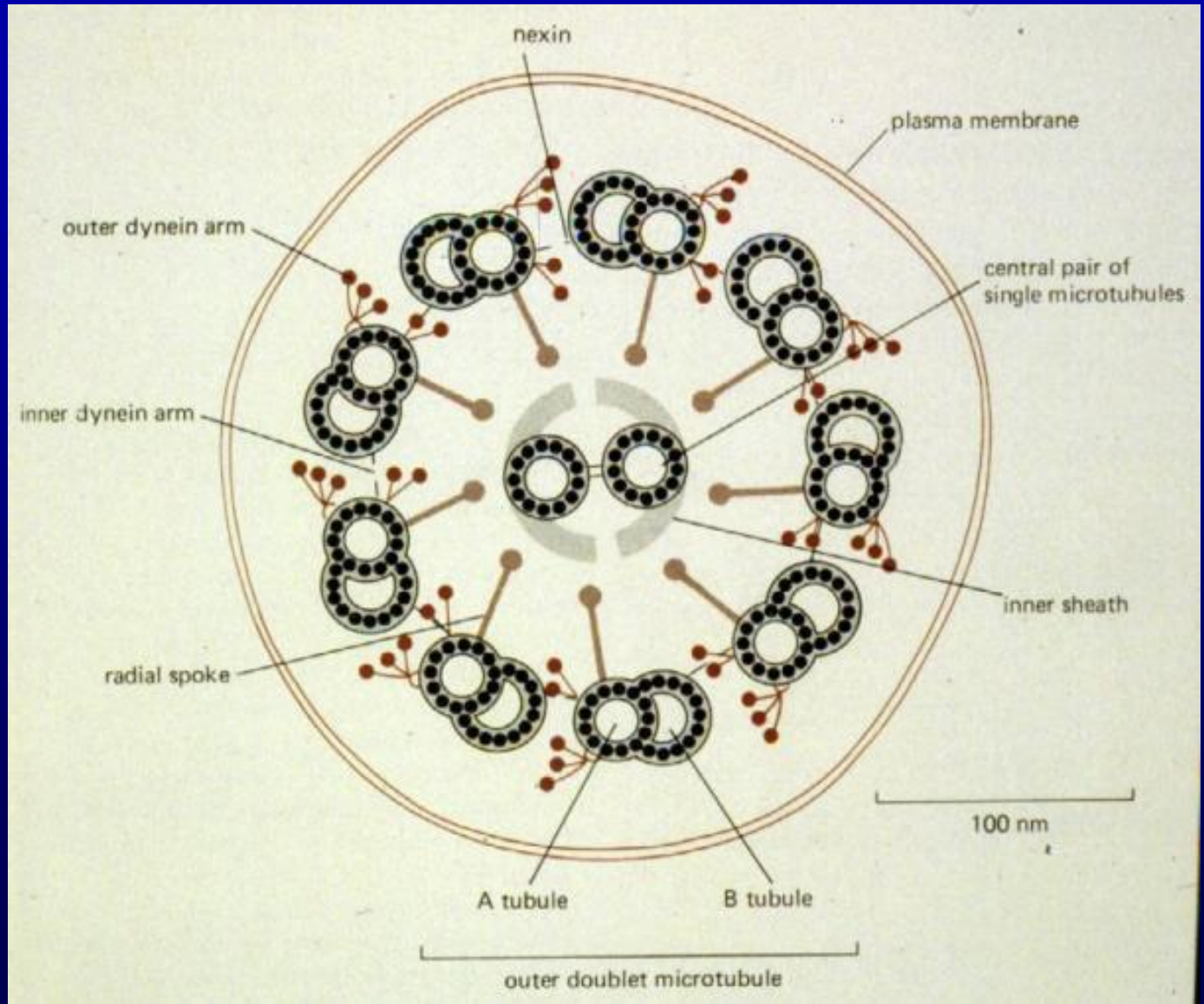


Cross sections of cilia



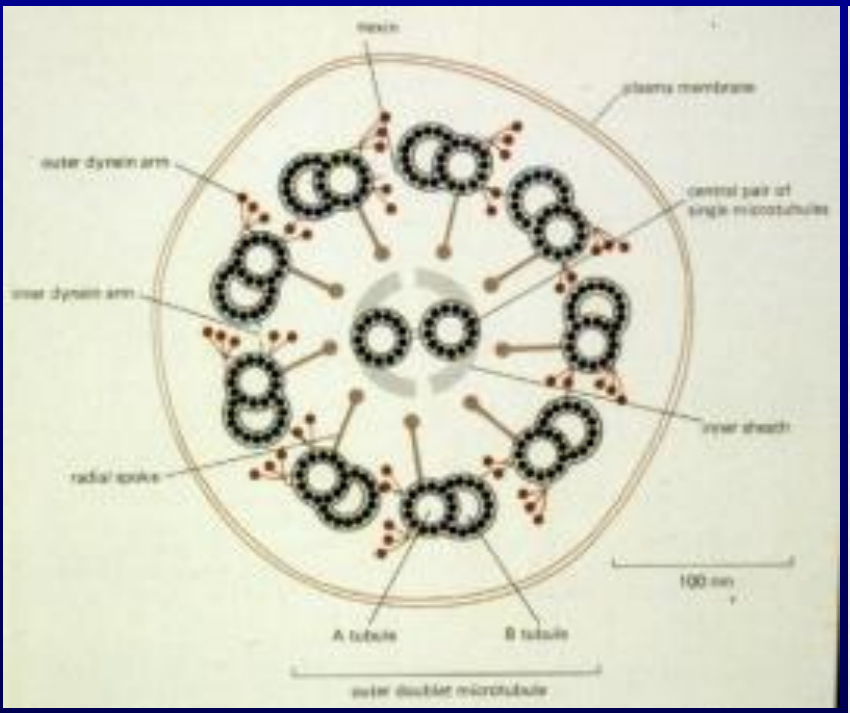
Axoneme of cilia and flagella

- 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



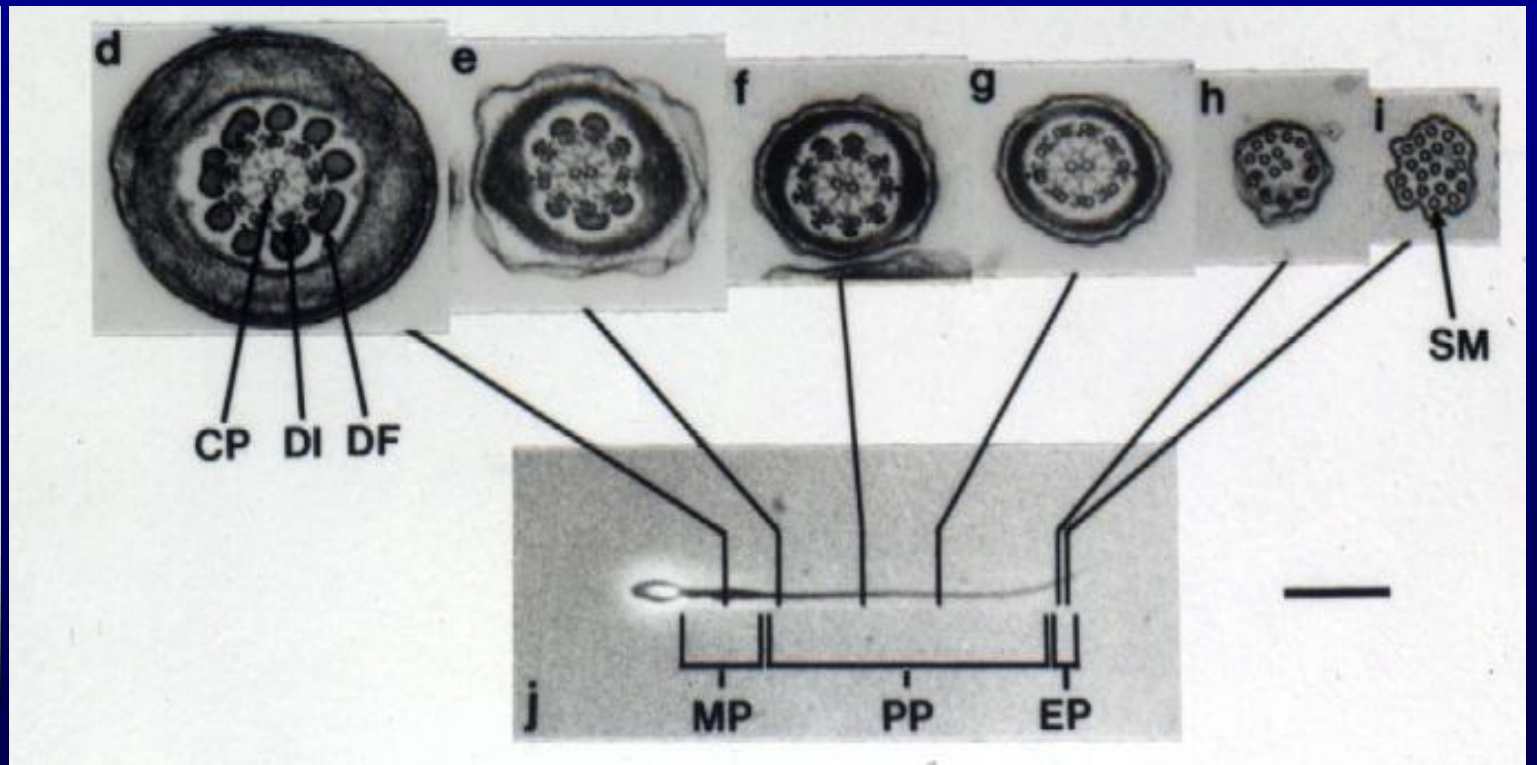
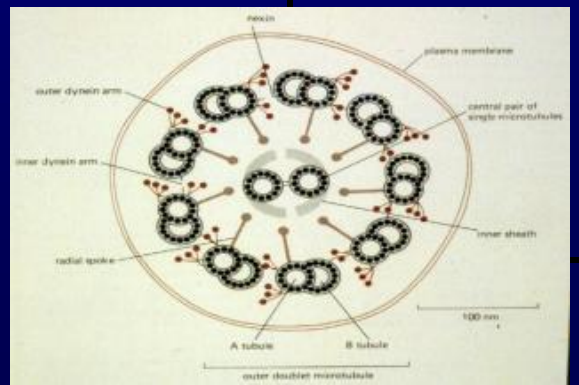
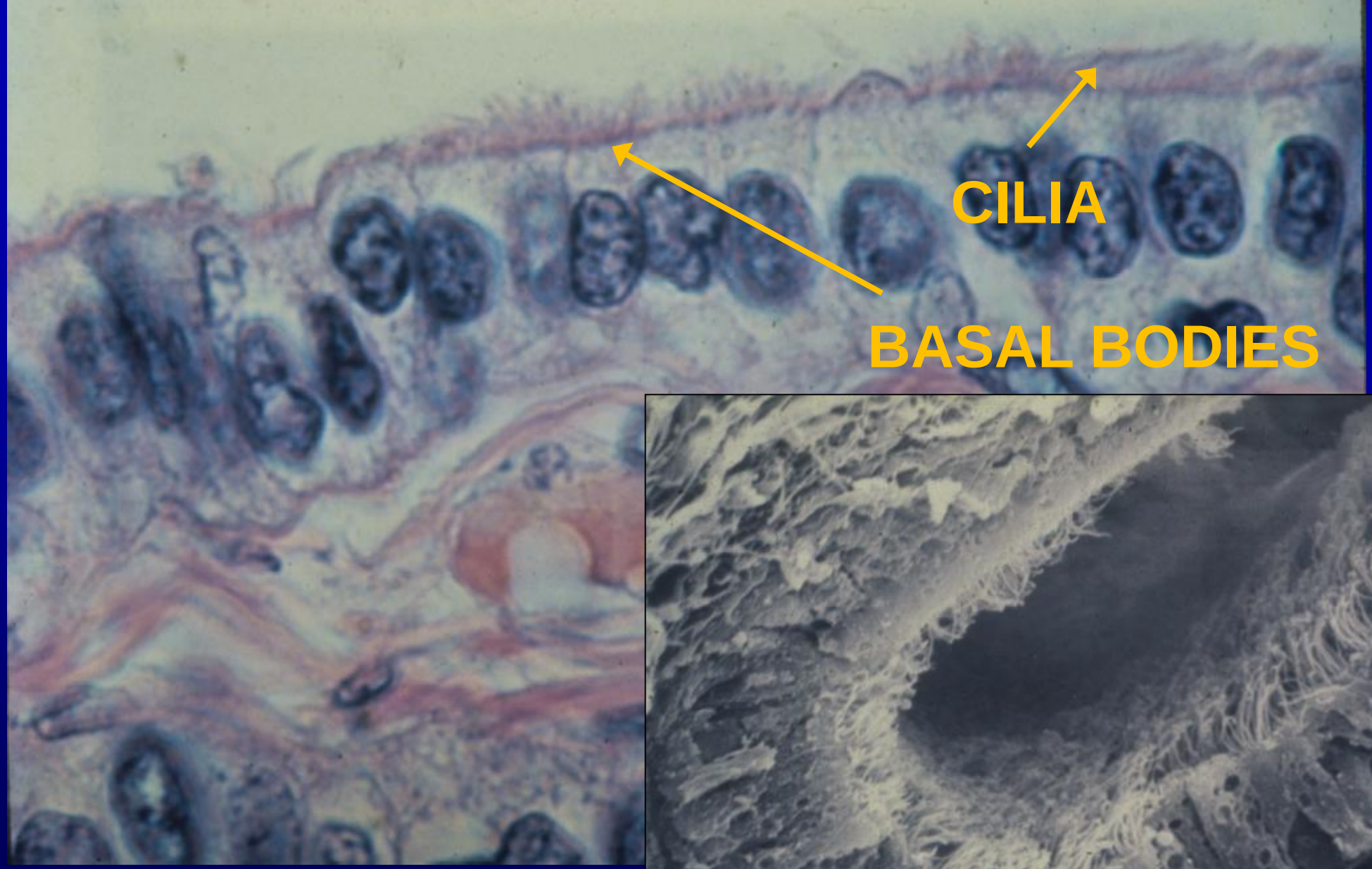
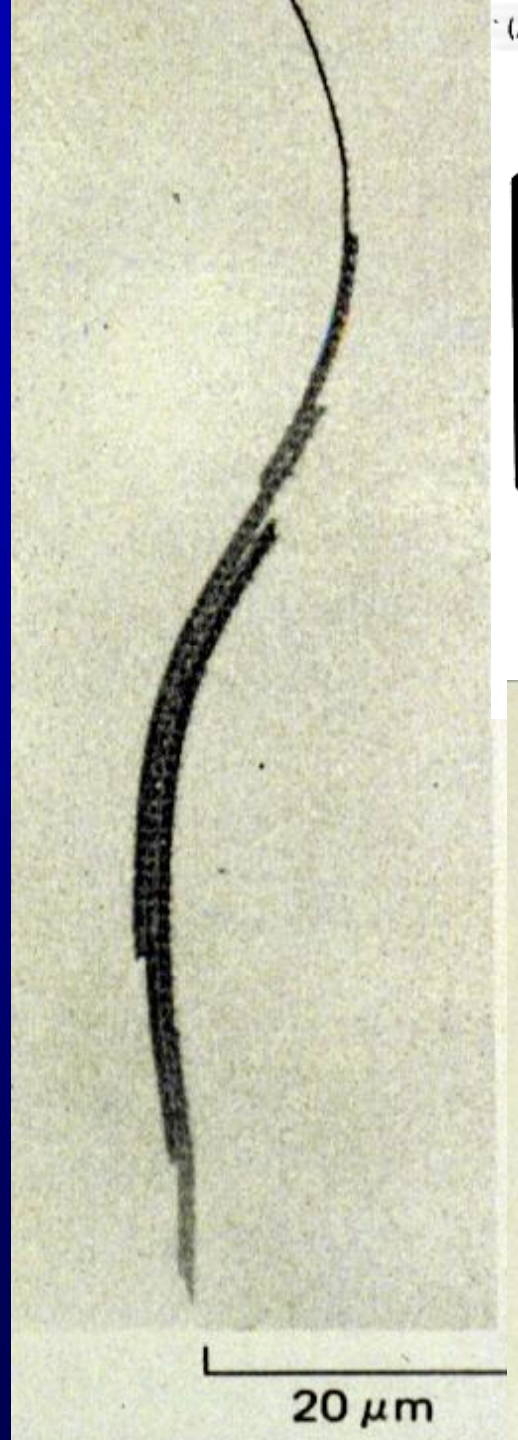


Table 10-3 Major Protein Structures of the Ciliary Axoneme	
Axoneme Component (periodicity along axoneme)	**Function**
Tubulin dimers (8 nm)	**principal component of microtubules**
Dynein arms (24 nm)	**project from microtubule doublets and interact with adjacent doublets to produce bending**
Nexin links (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**



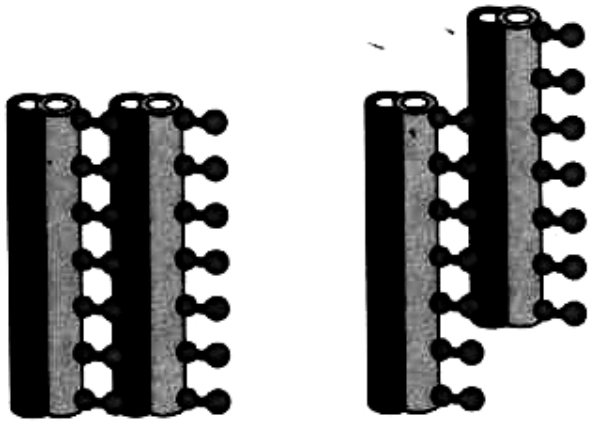


CILIA and BASAL BODIES



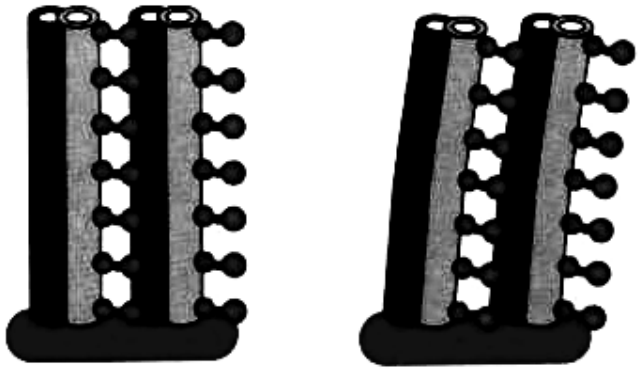
(A) AFTER PROTEOLYSIS: TELESCOPING

(B) INTACT STRUCTURE: BENDING



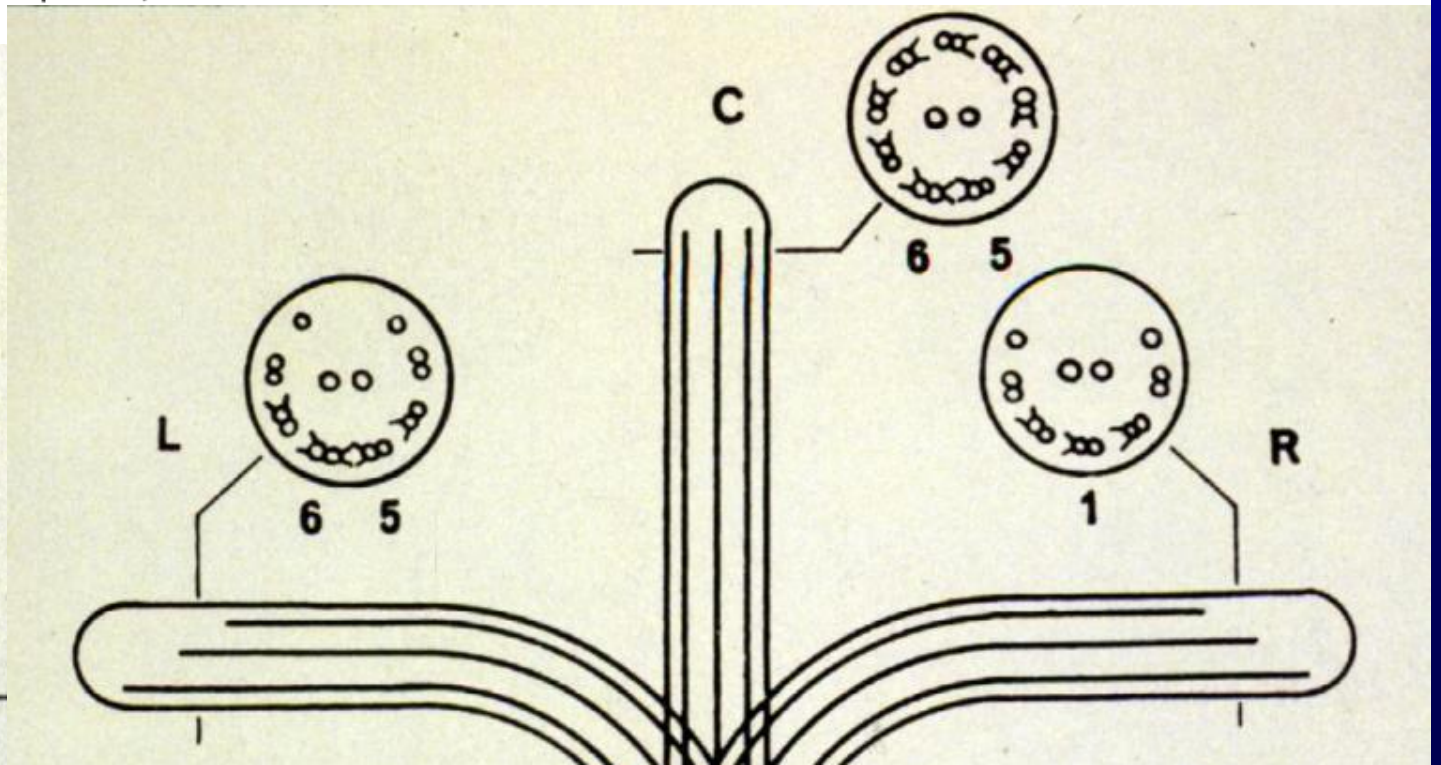
free doublet (cross-links removed by proteolysis)

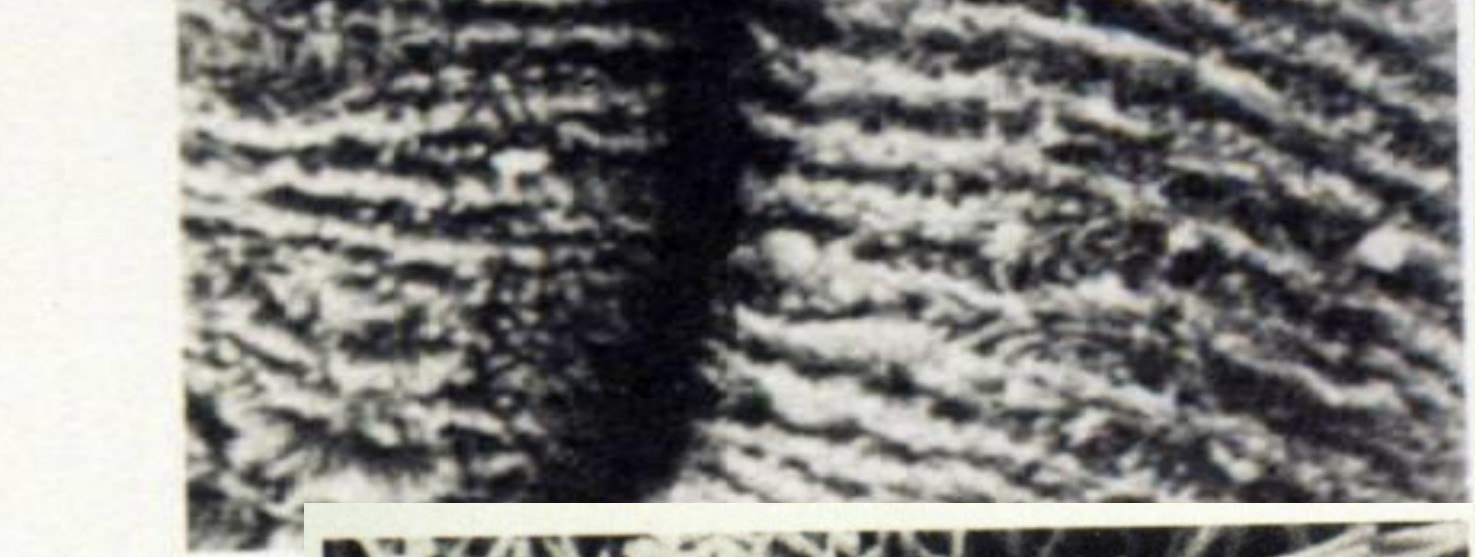
doublets slide apart

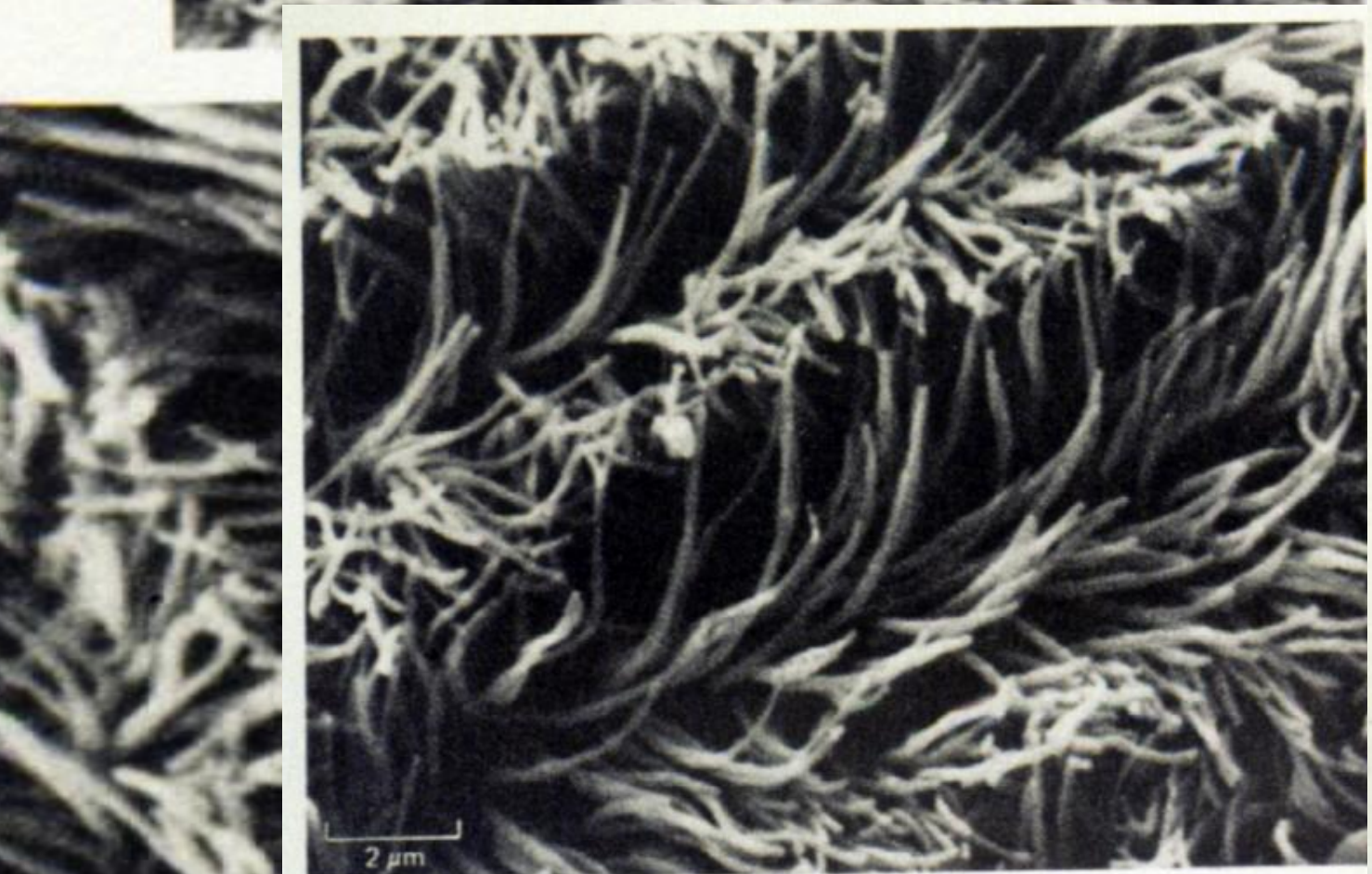


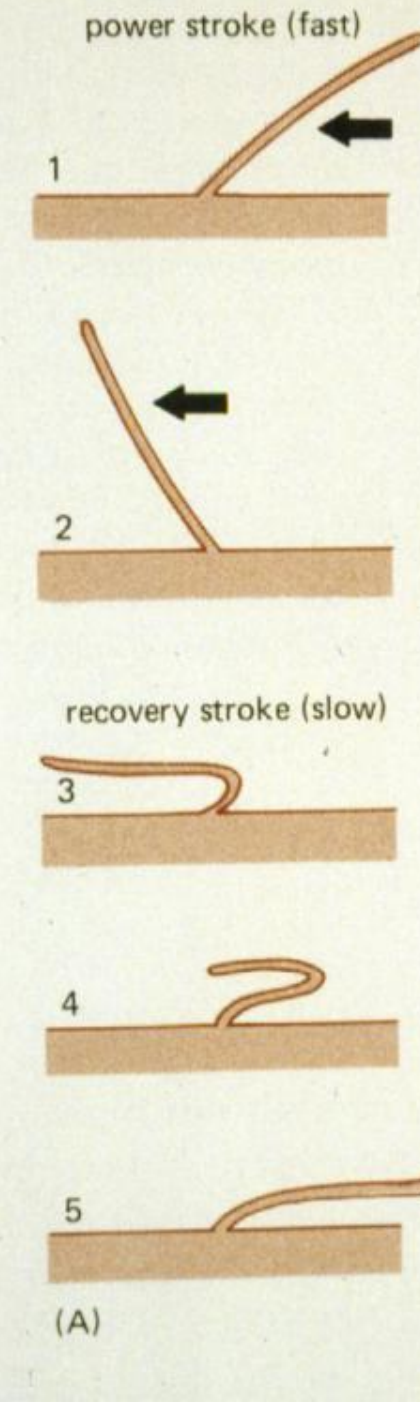
doublets held in cilium by cross-links

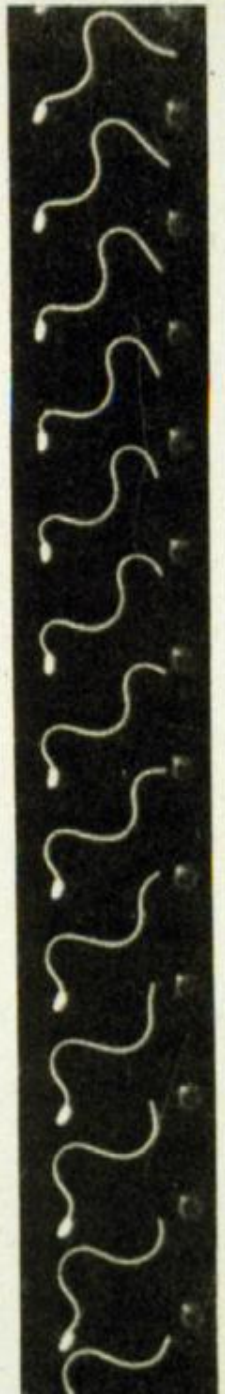
doublet sliding leads to bending






2 μm


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



Drugs that influence - microtubules assembly and disassembly

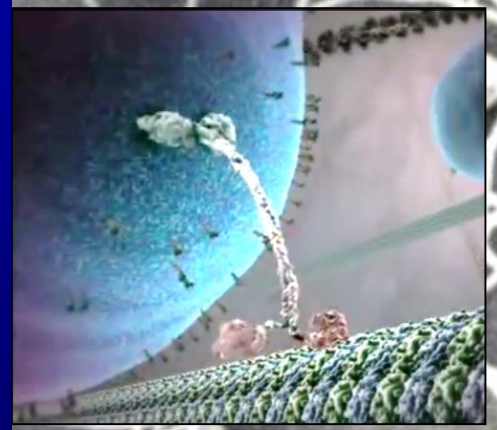
- **Inhibitors:**
  - Colchicine - inhibit assembly in vitro, destroy in vivo
  - Vinblastine - inhibit assembly in vitro, destroy in vivo
- **Stimulator:**
  - Taxol - stimulate assembly in vitro
- Use in cancer therapy?

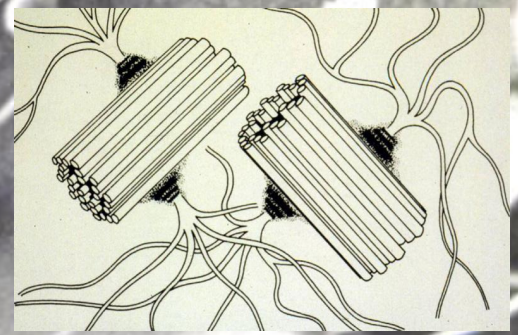
Microtubules - summary

- Protofilaments - linear polymers of alpha and beta tubulin
- Microtubules - cylindrical walled tubes composed 13 parallel protofilaments

- Growth at one end away from nucleation site
- Polarity of direction of growth –
- Directs movements of cytoplasmic organelles

- Microtubule associated proteins - form stabilizing cross links of MT and may be associated with polymerization of microtubules
- Colchicine





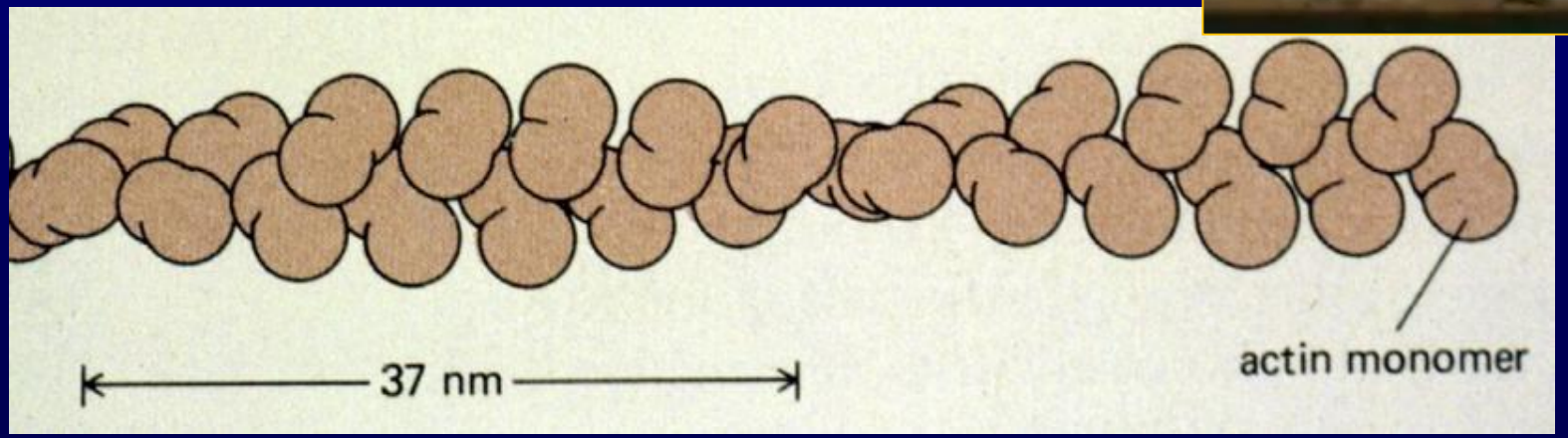
Microfilaments

“actin filaments”

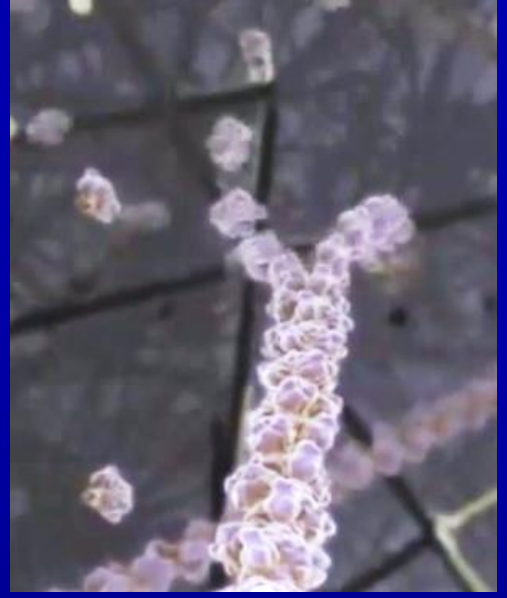
Composition:

- **Actin - highly conserved protein**

https://www.youtube.com/watch?v=7sRZy9PgPvg



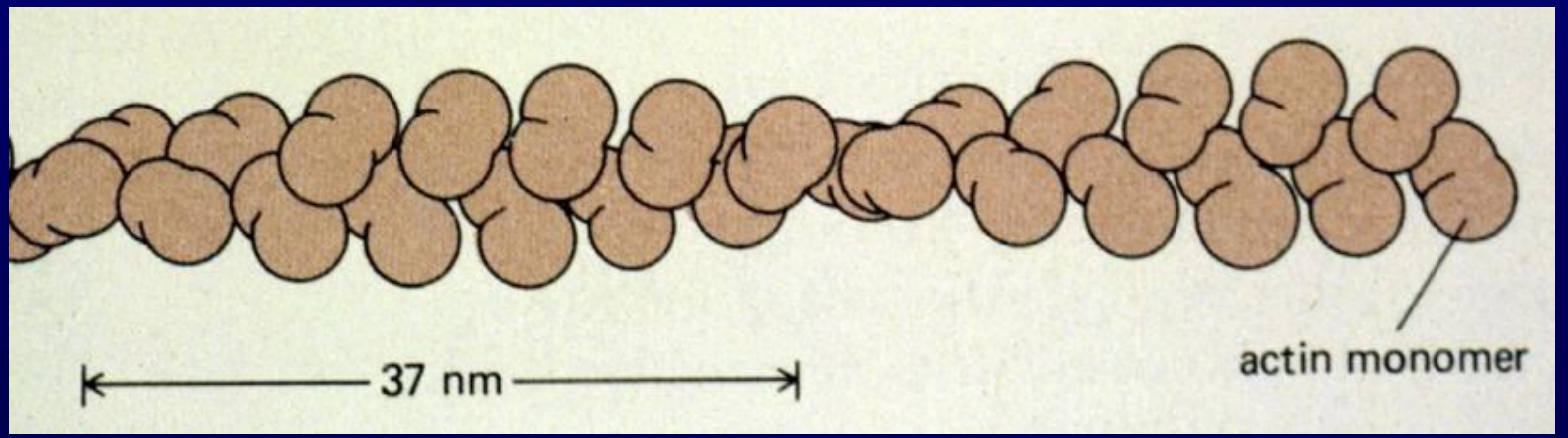
Microfilaments



“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
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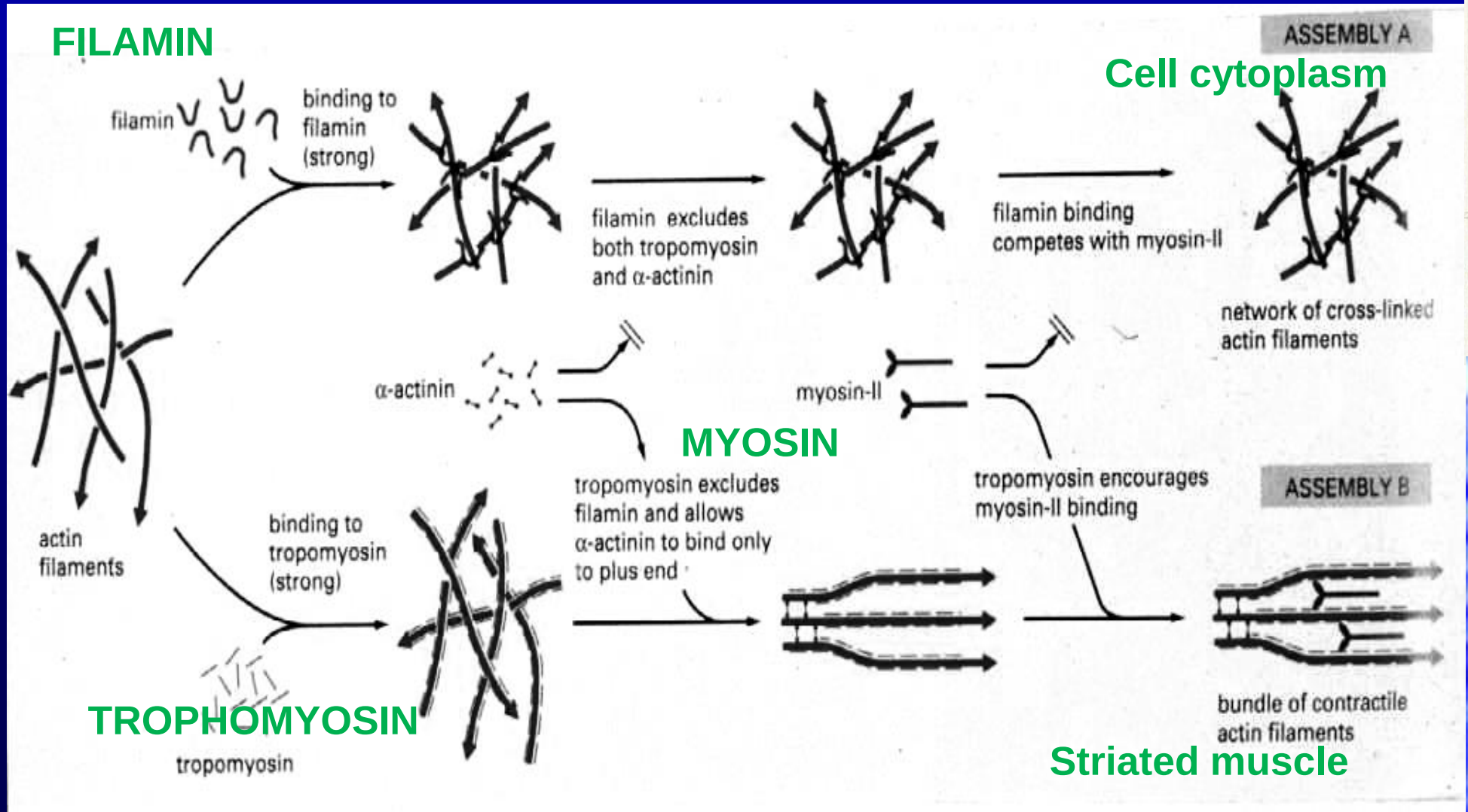


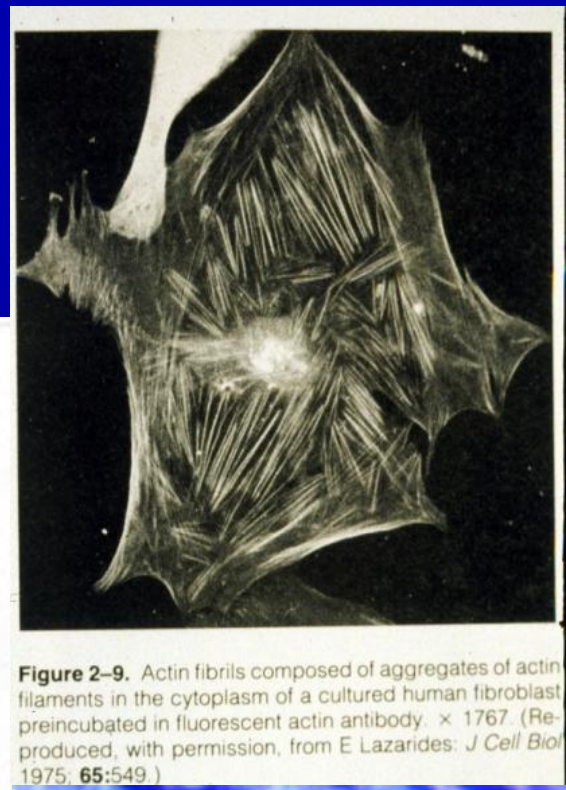
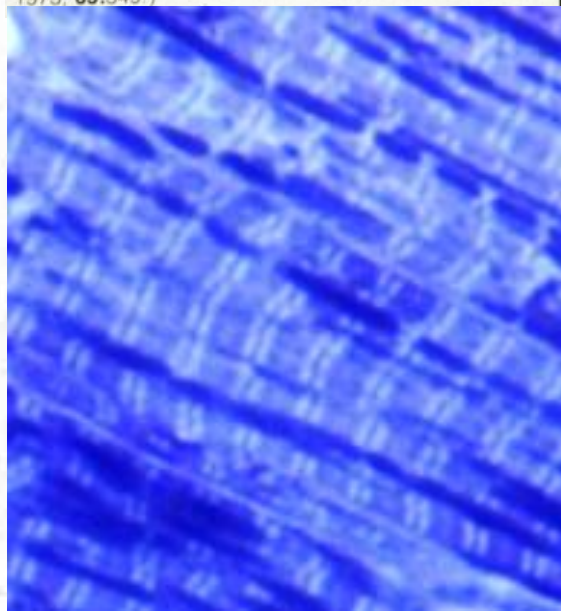
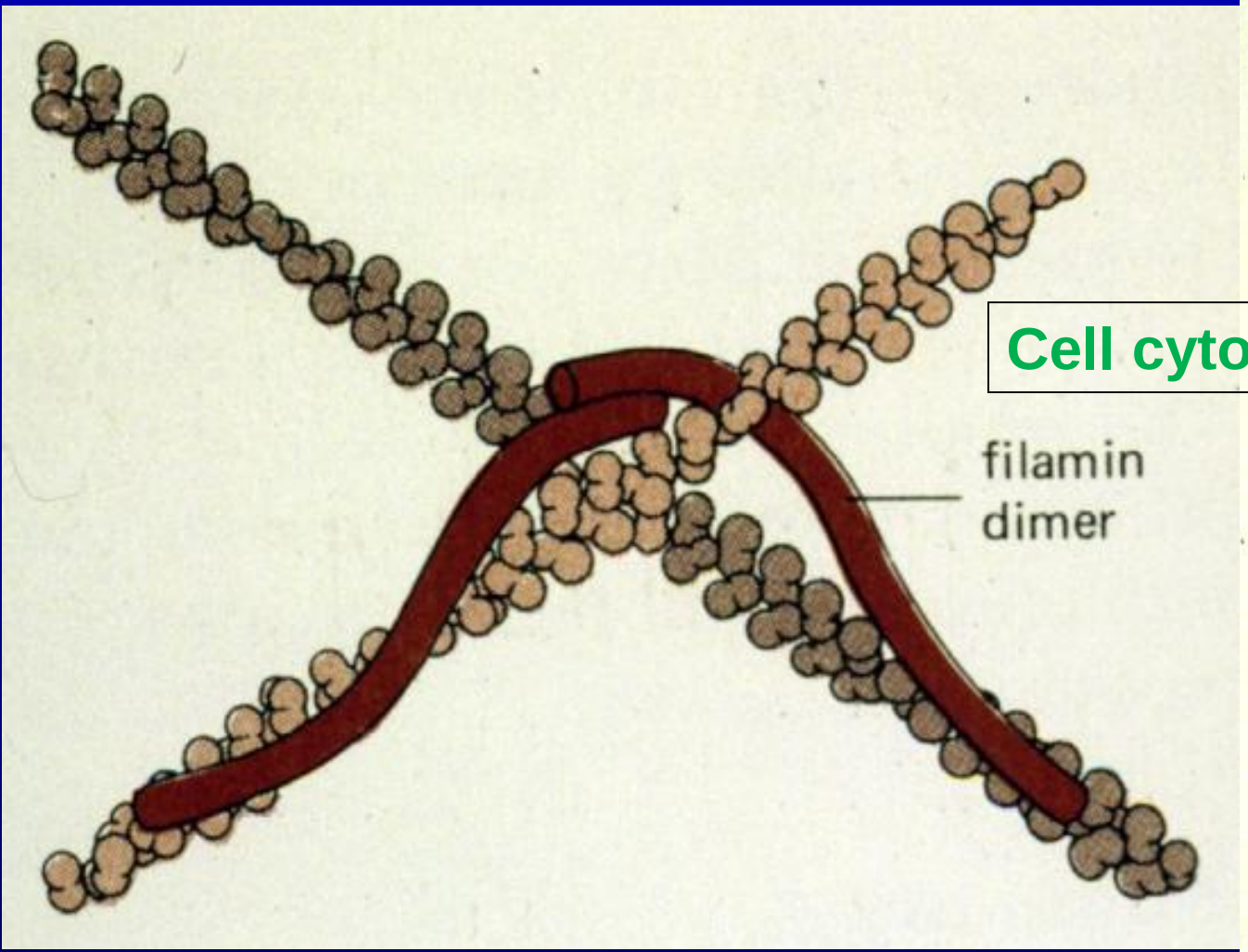
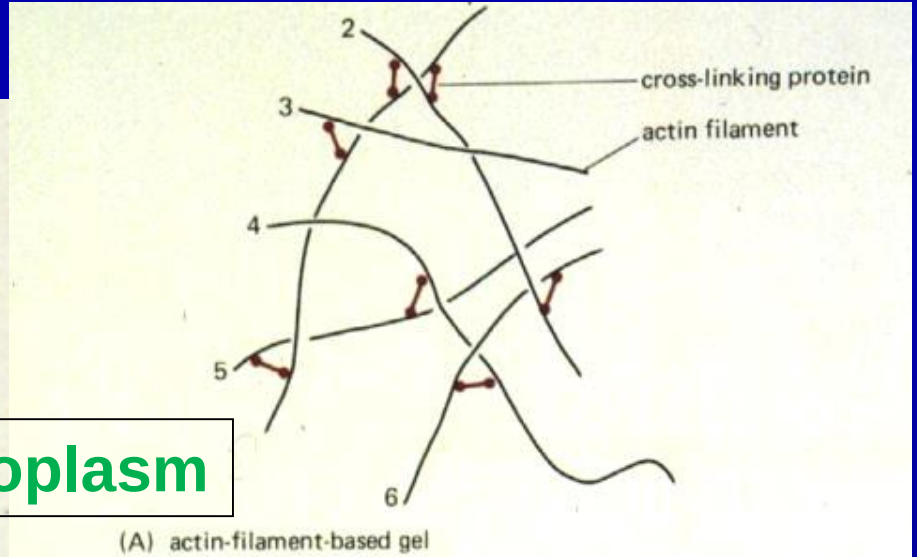


Figure 2–9. Actin fibrils composed of aggregates of actin filaments in the cytoplasm of a cultured human fibroblast preincubated in fluorescent actin antibody. × 1767. (Reproduced, with permission, from E Lazarides: *J Cell Biol* 1975; **65**:549.)

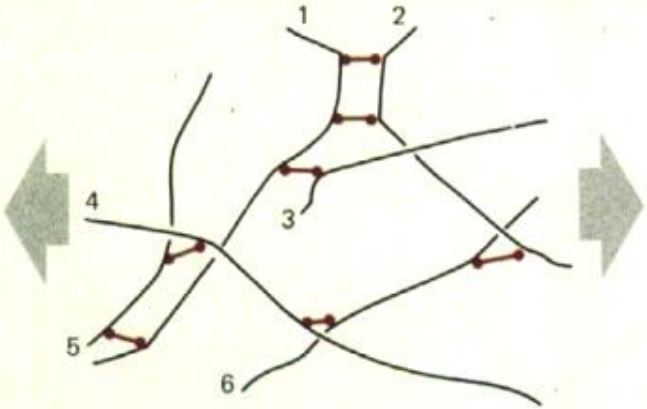




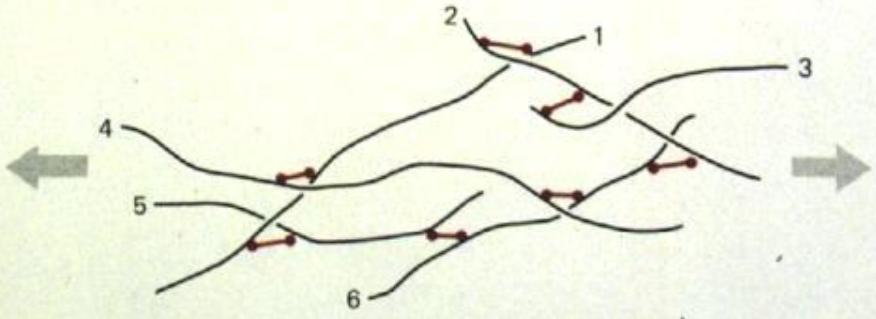
Cell cytoplasm

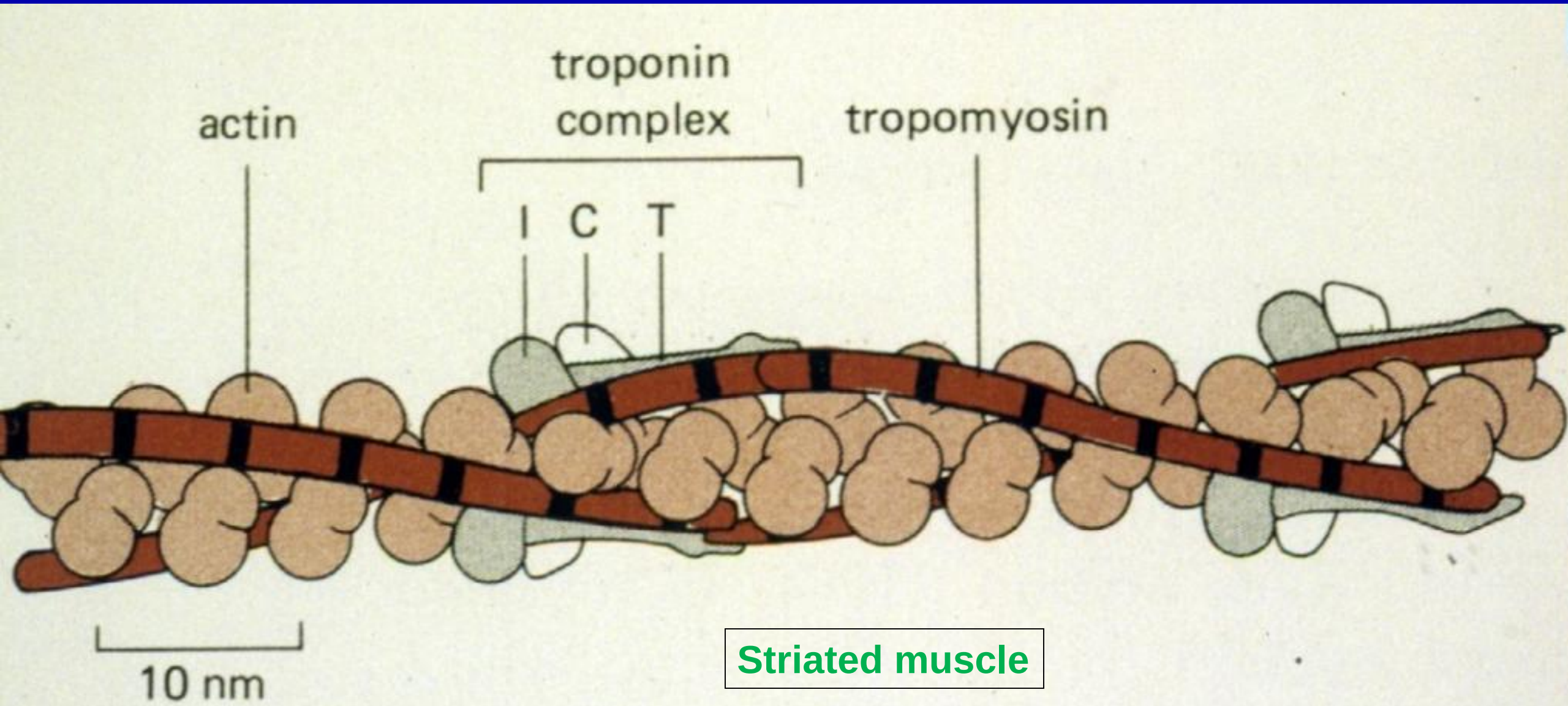


(A) actin-filament-based gel



(B) gel resists sudden pull because of cross-linking proteins

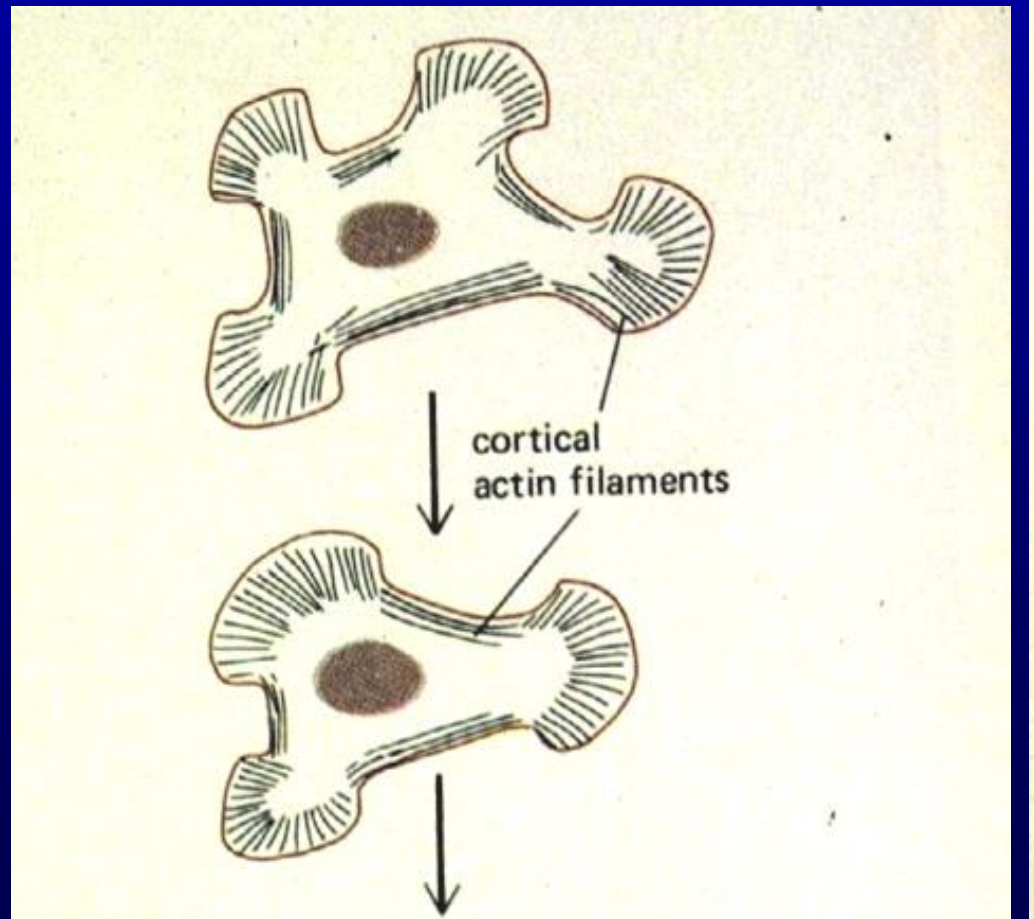


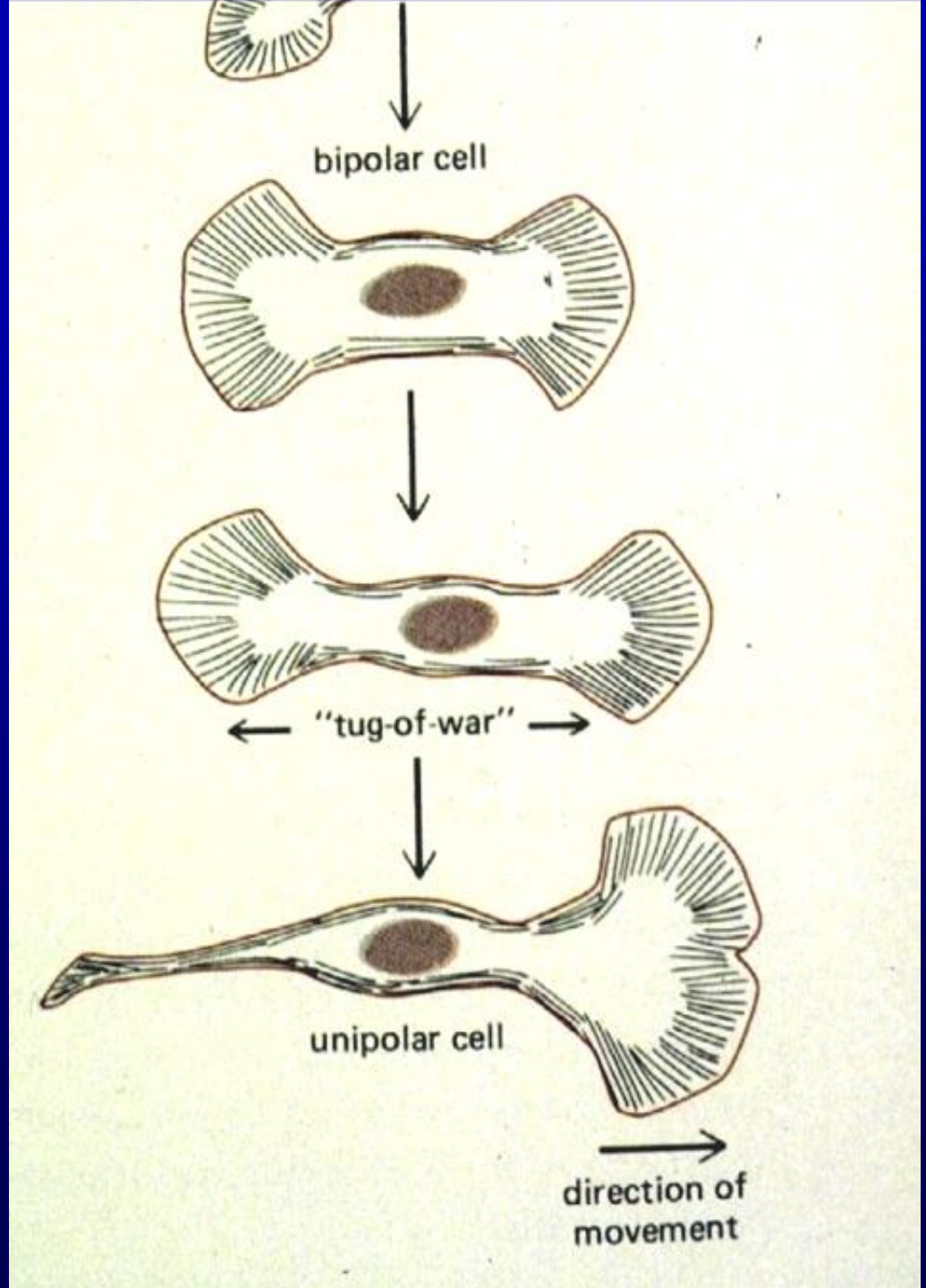


Striated muscle

Microfilaments - function

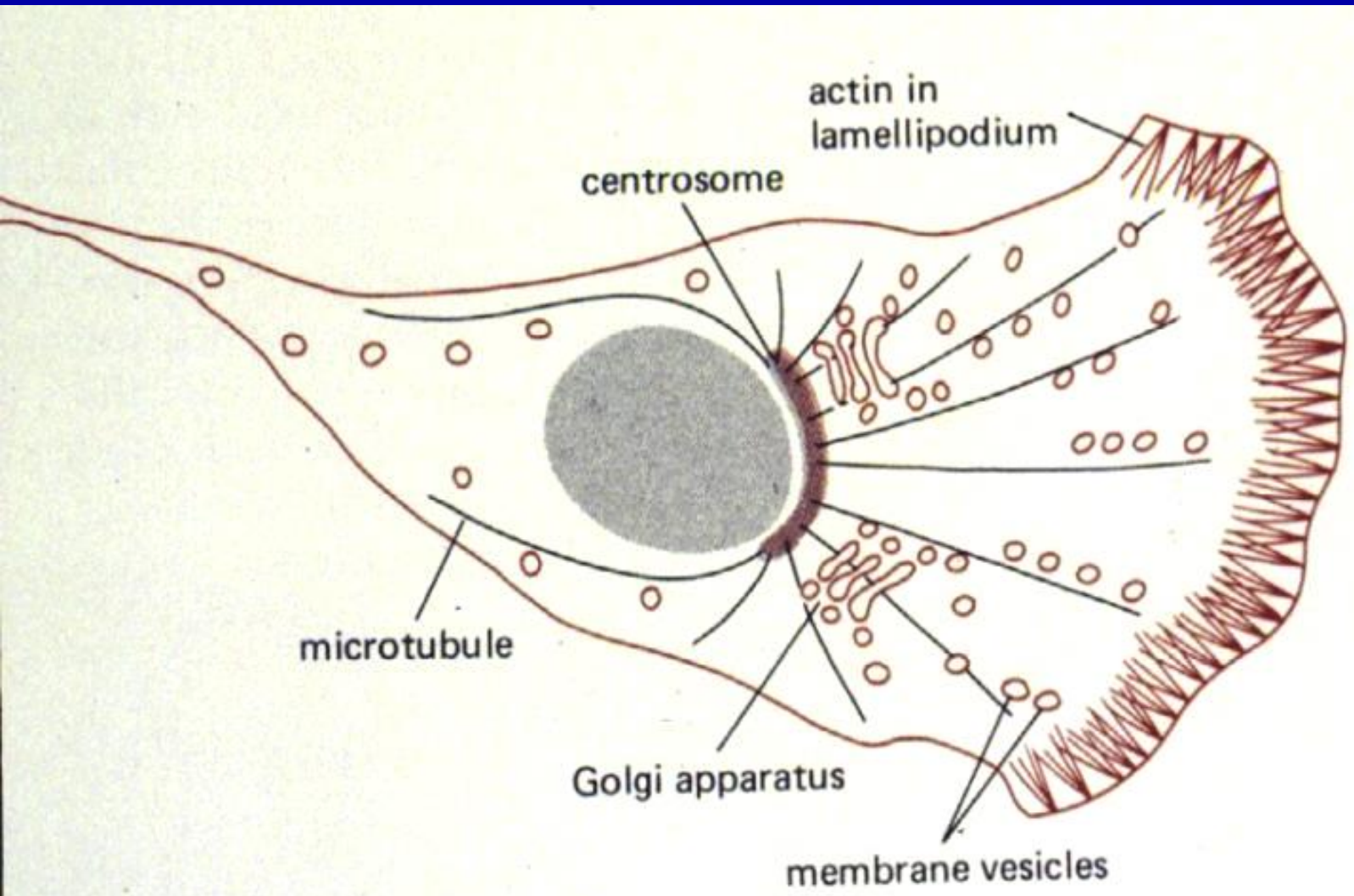
- **Cell motility - actin and myosin**





Microfilaments - function

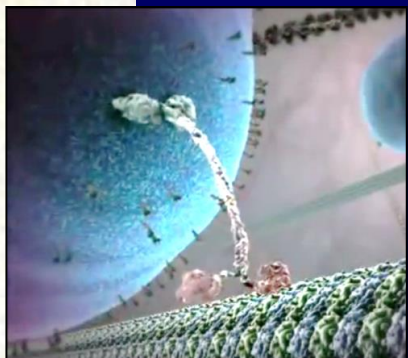
- **Cell motility - actin and myosin**

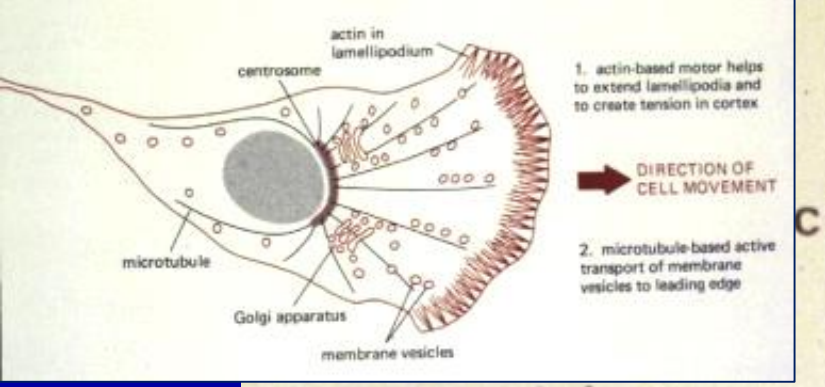


1. actin-based motor helps to extend lamellipodia and to create tension in cortex

DIRECTION OF CELL MOVEMENT

2. microtubule-based active transport of membrane vesicles to leading edge





cogen

Azurophil granules

Actin-rich ectoplasmic zone

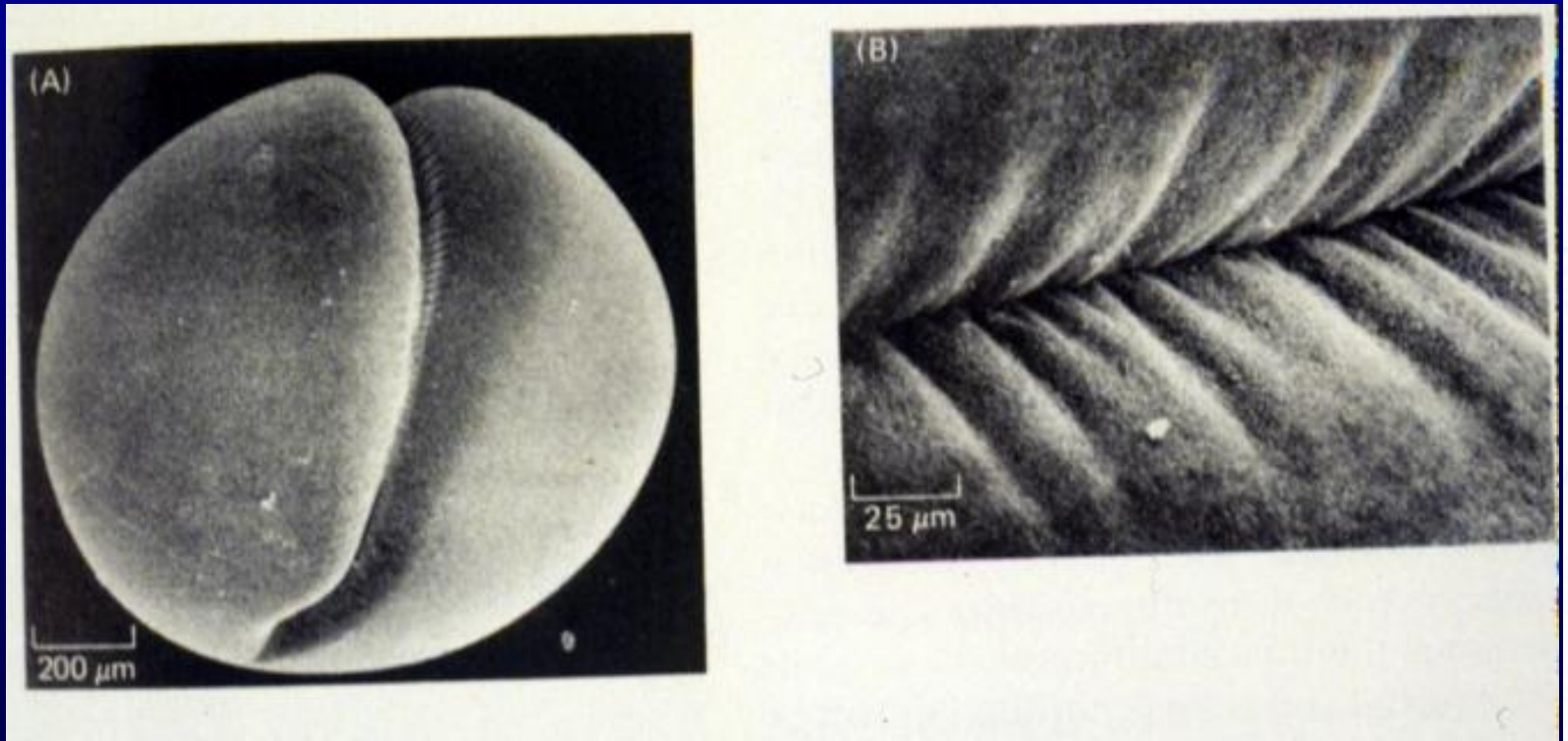
Yeast

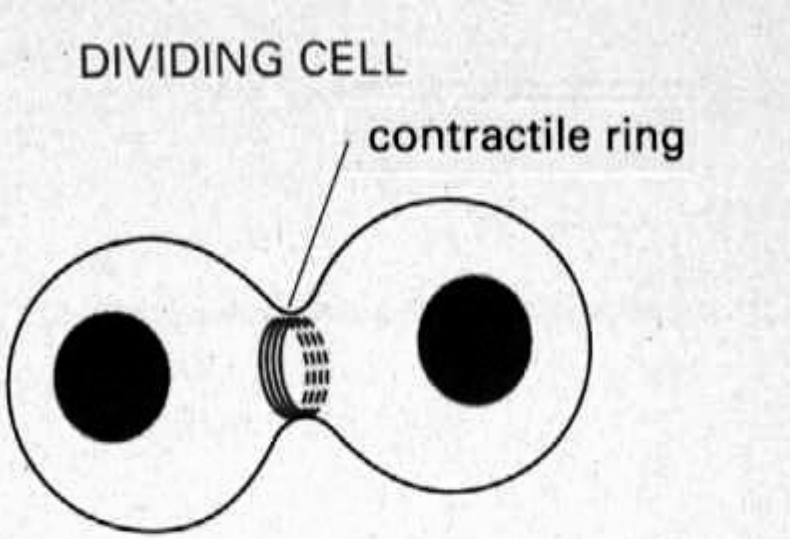
Specific granules

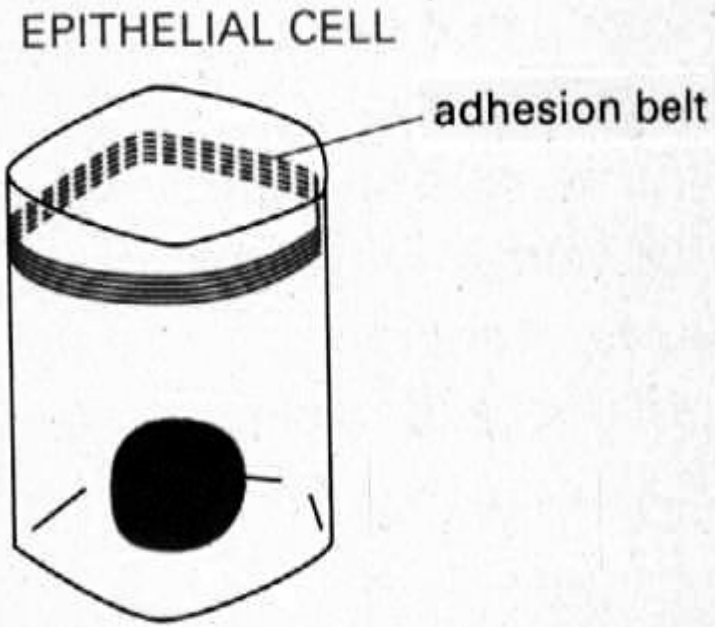
Substrate

Microfilaments - function

Cytokinesis - division of cytoplasm



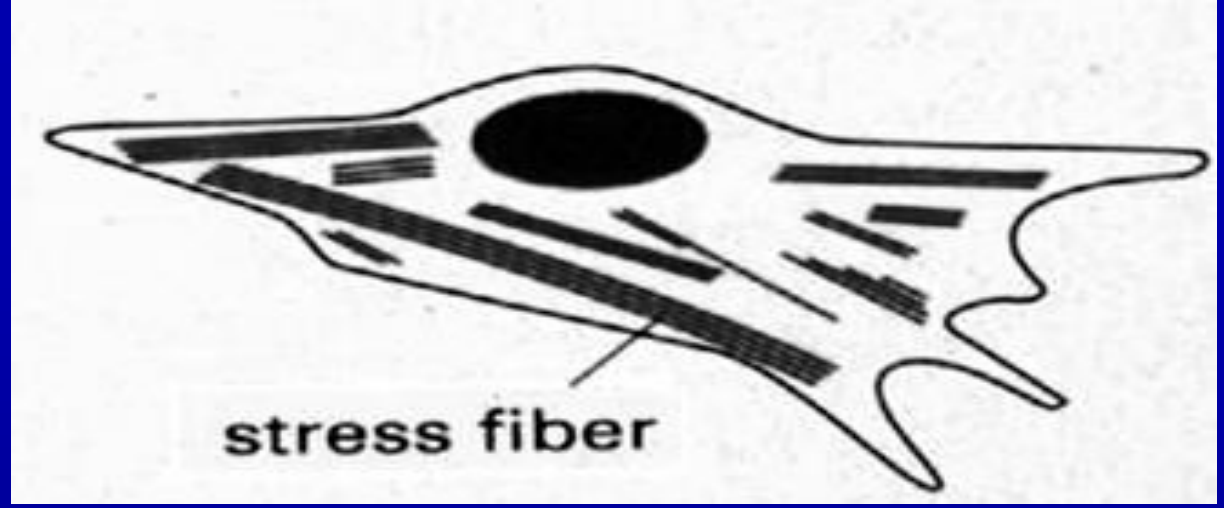


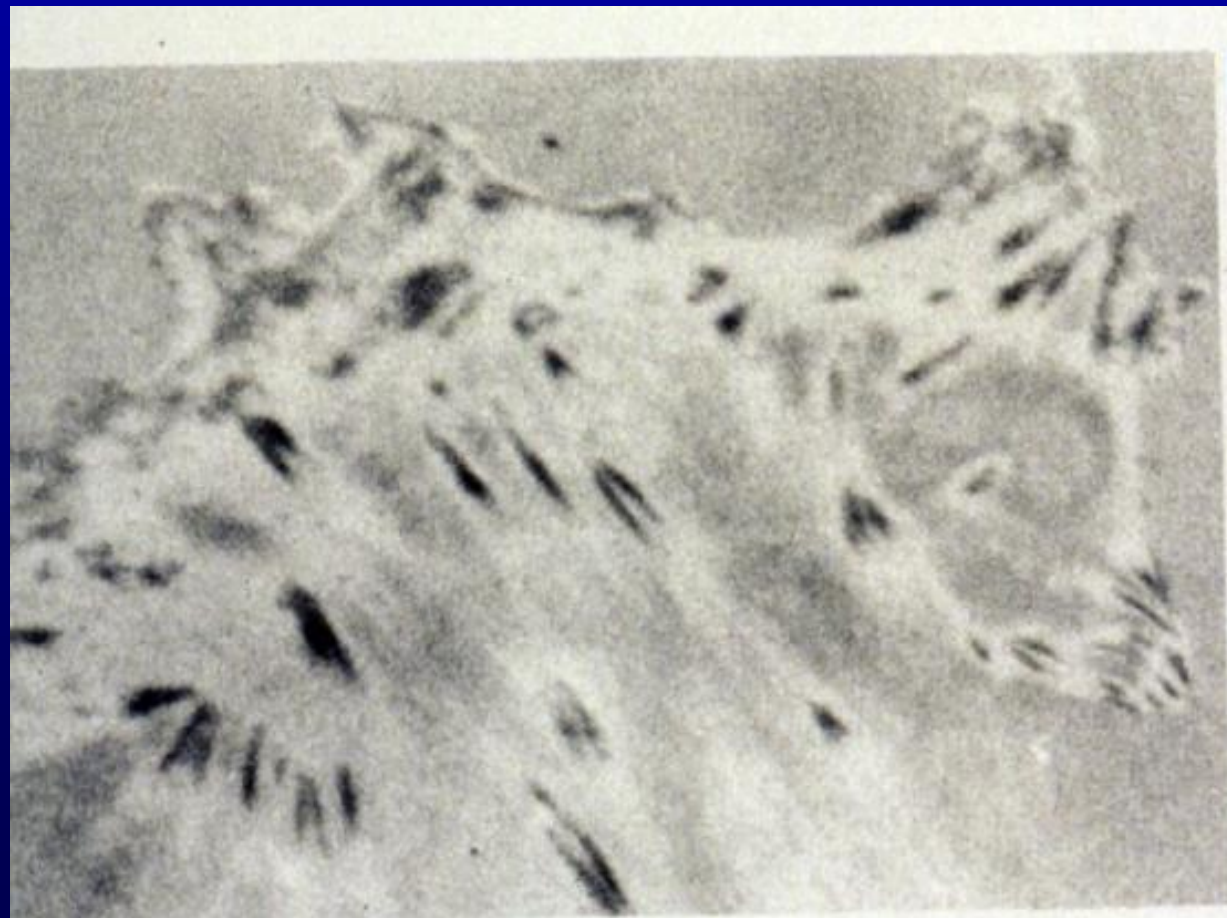


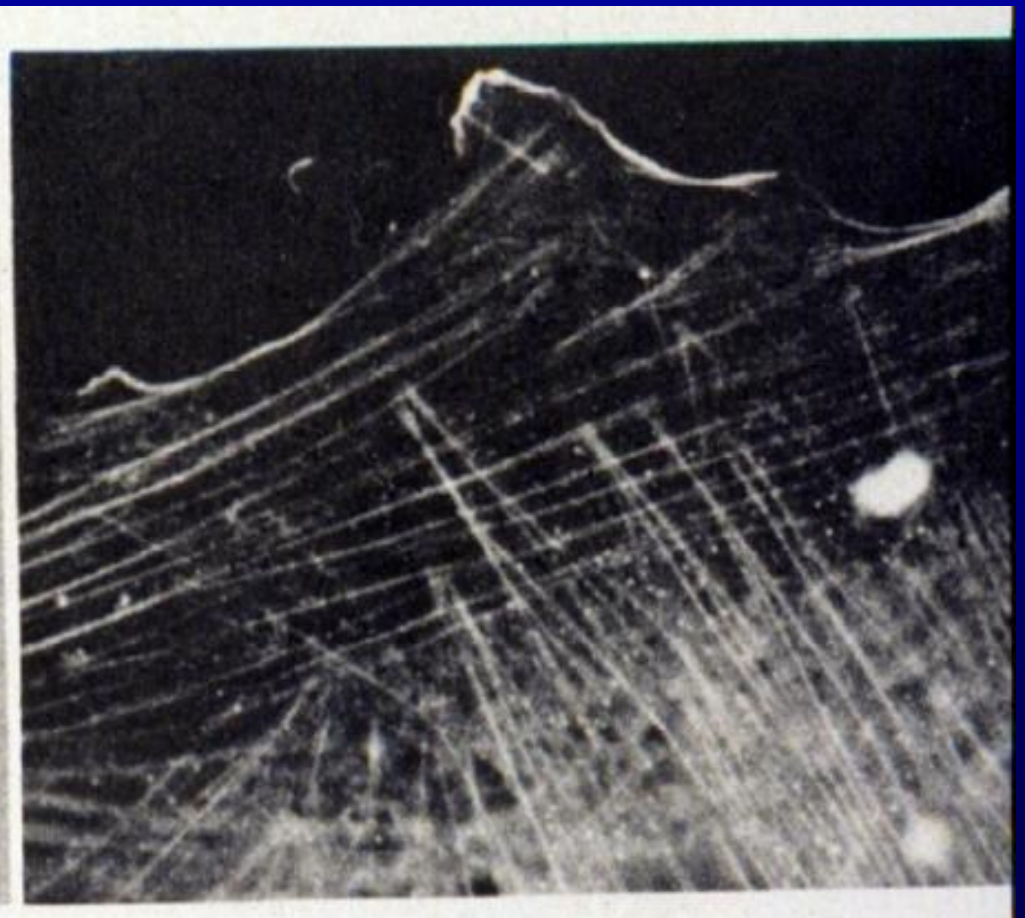
Microfilaments - function

Structural support

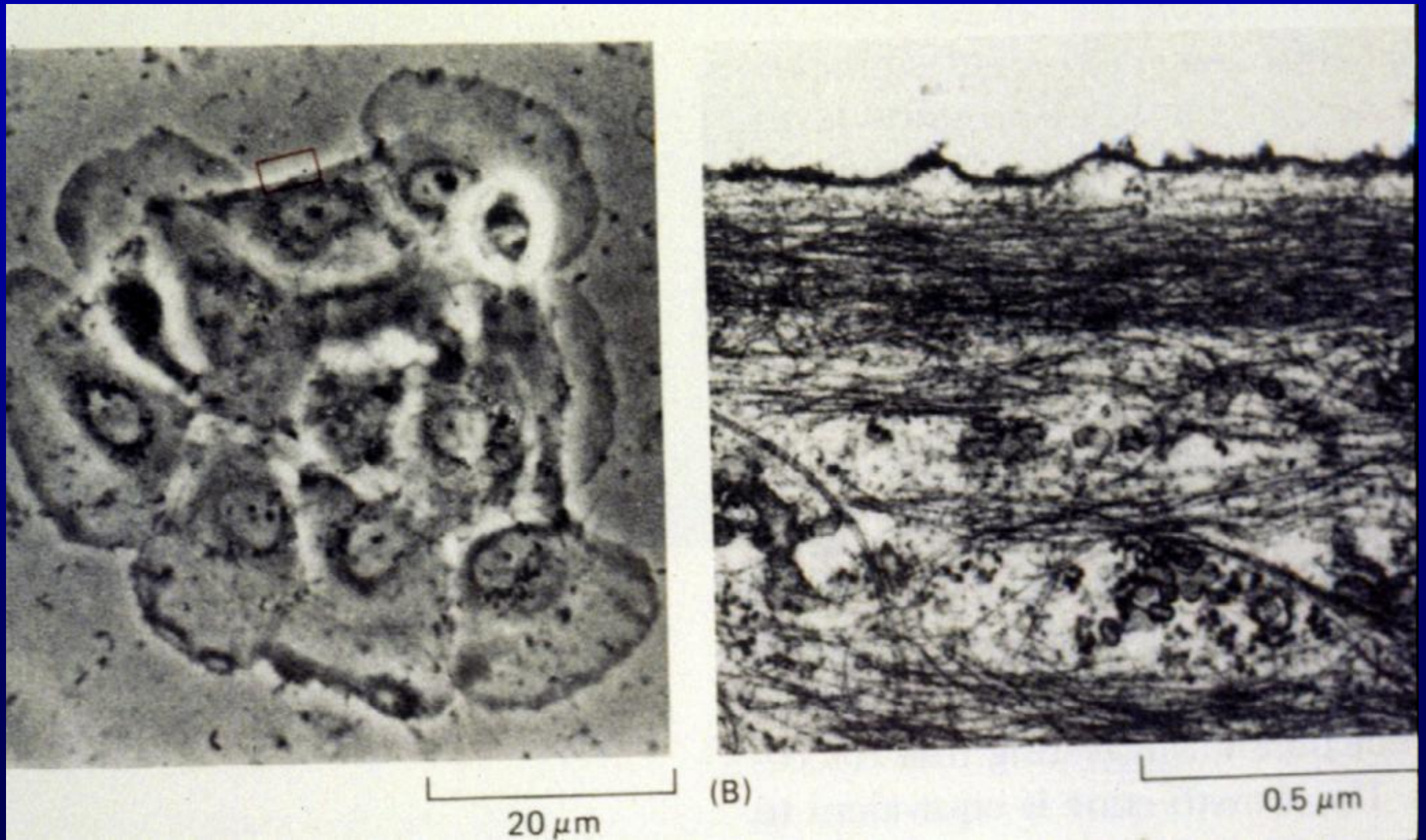
- Stress fibers



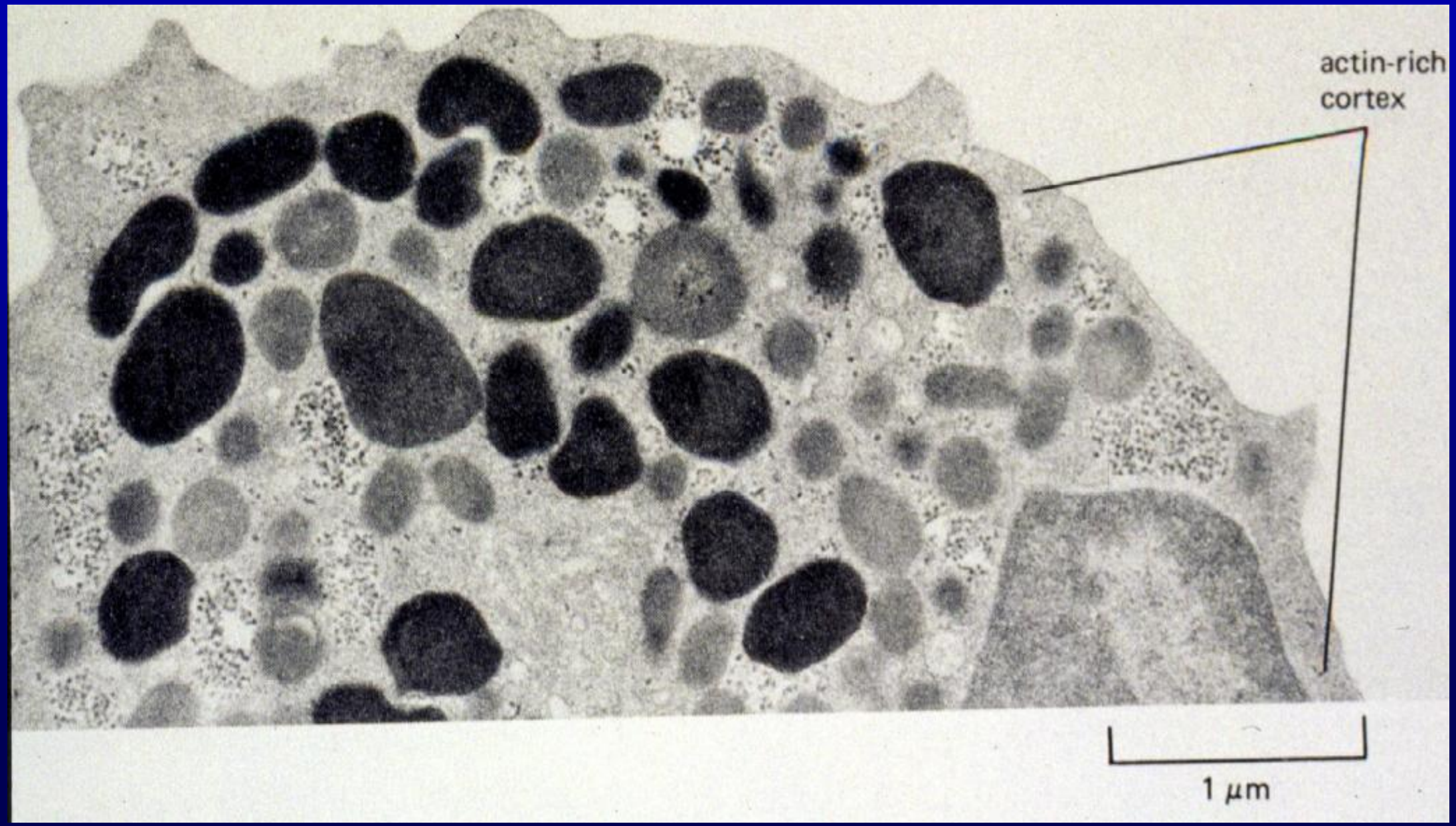




Microfilaments



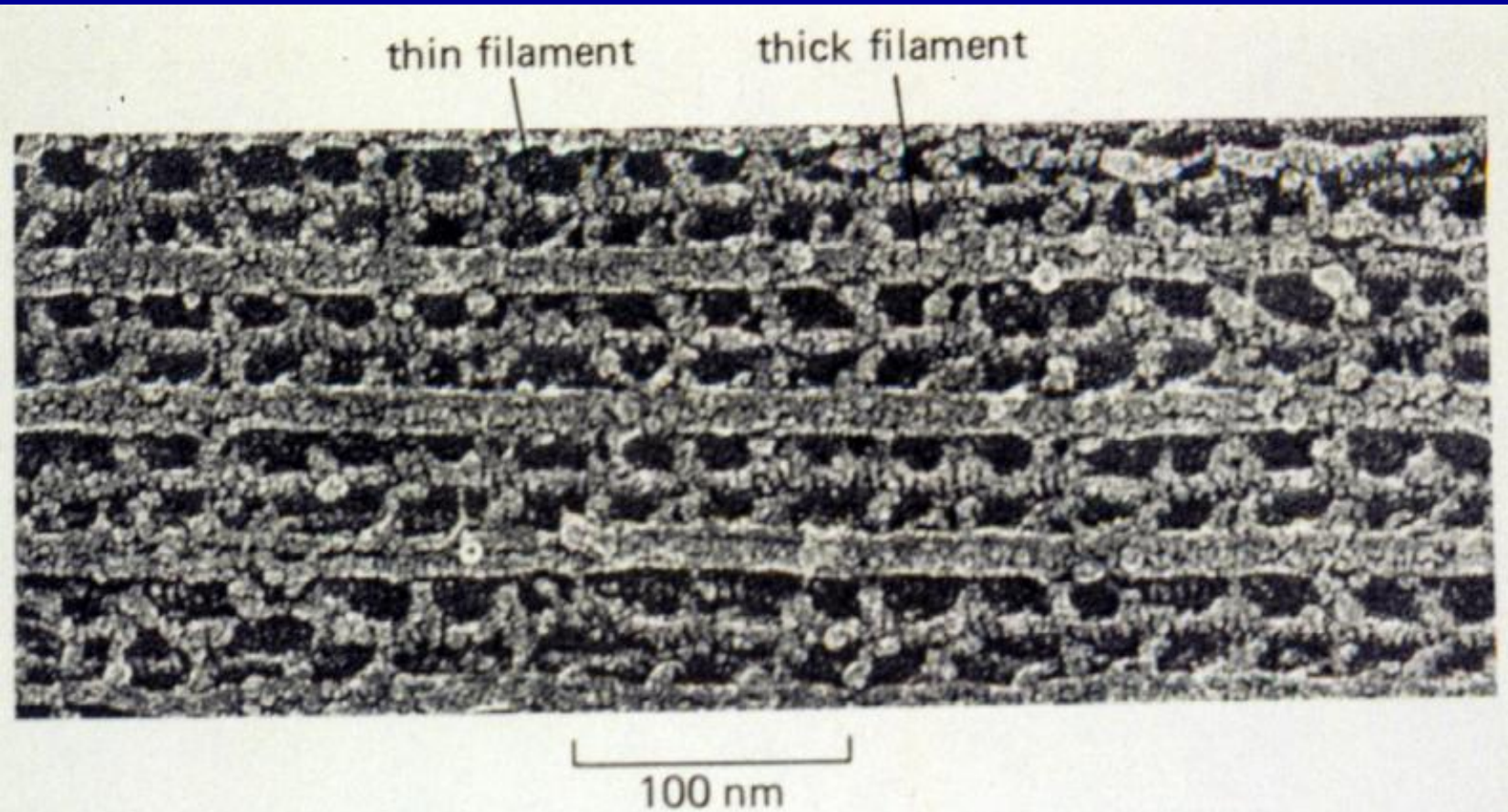
Microfilaments

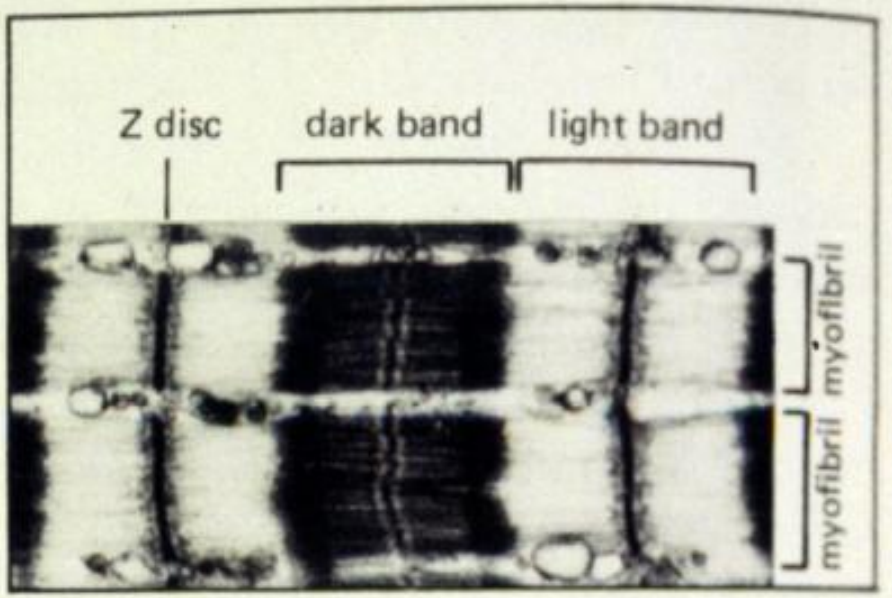


Microfilaments - function

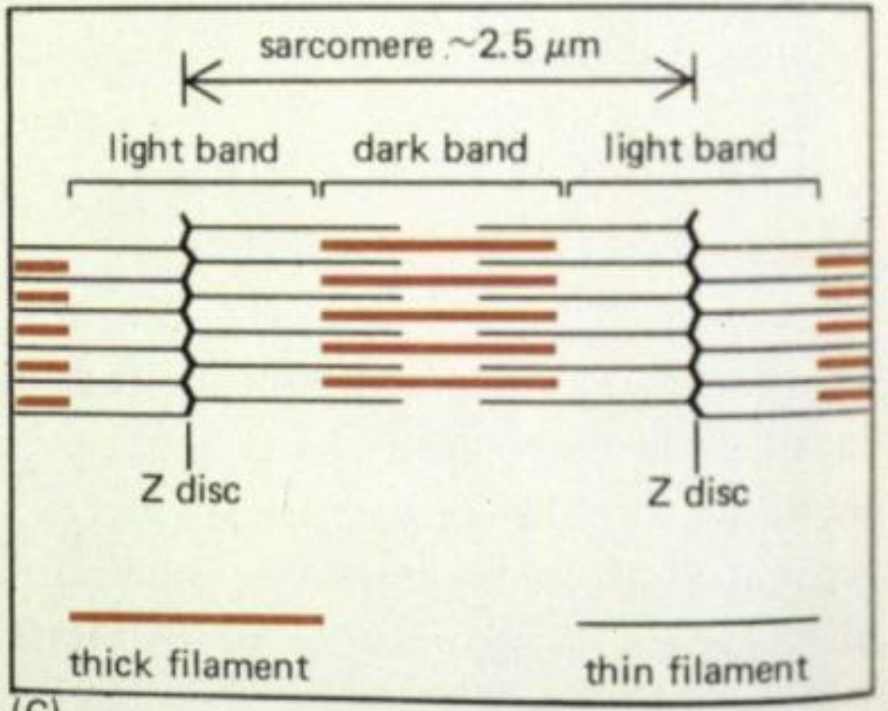
Structural support

– Cell movement





(B)

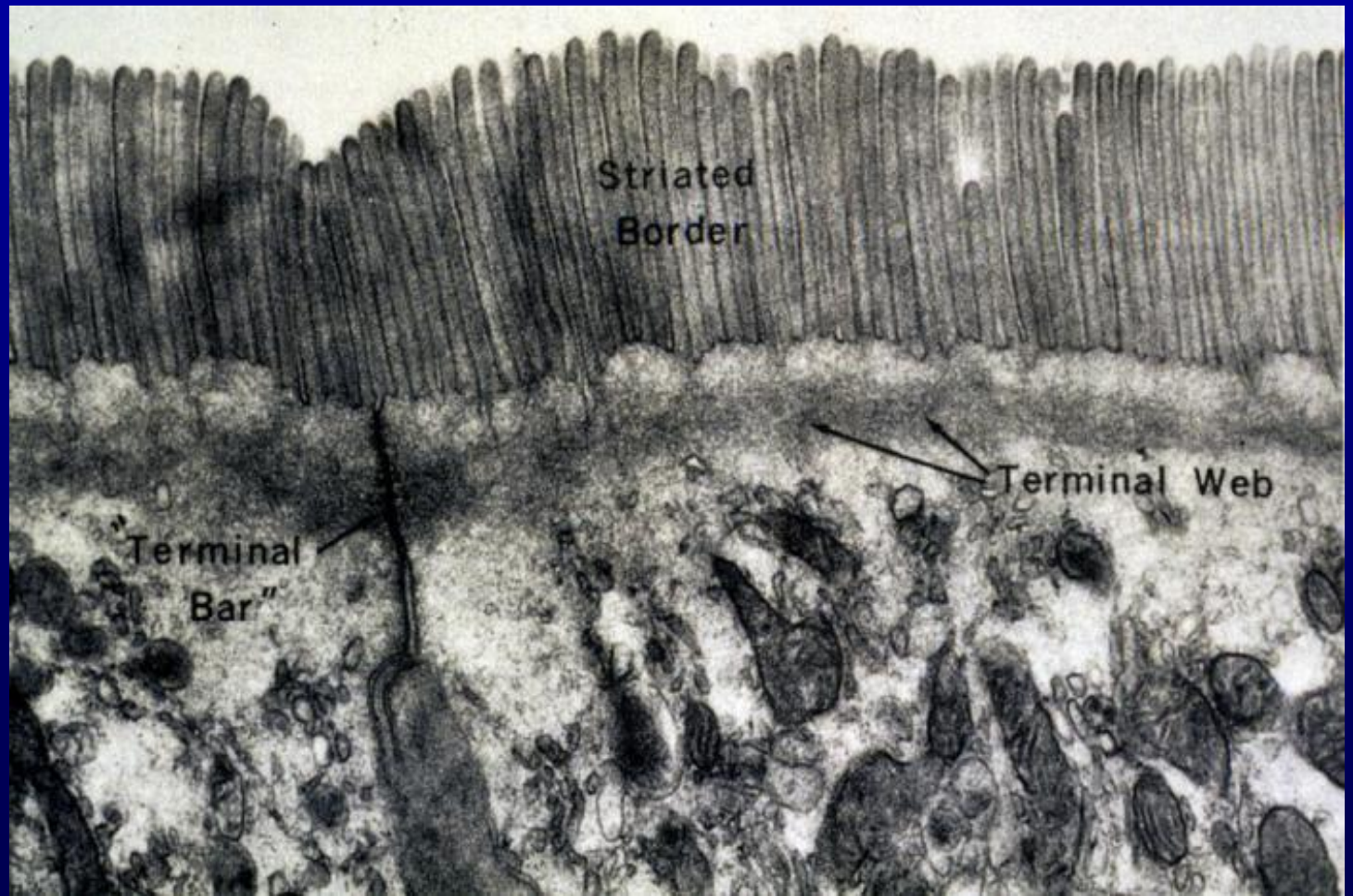


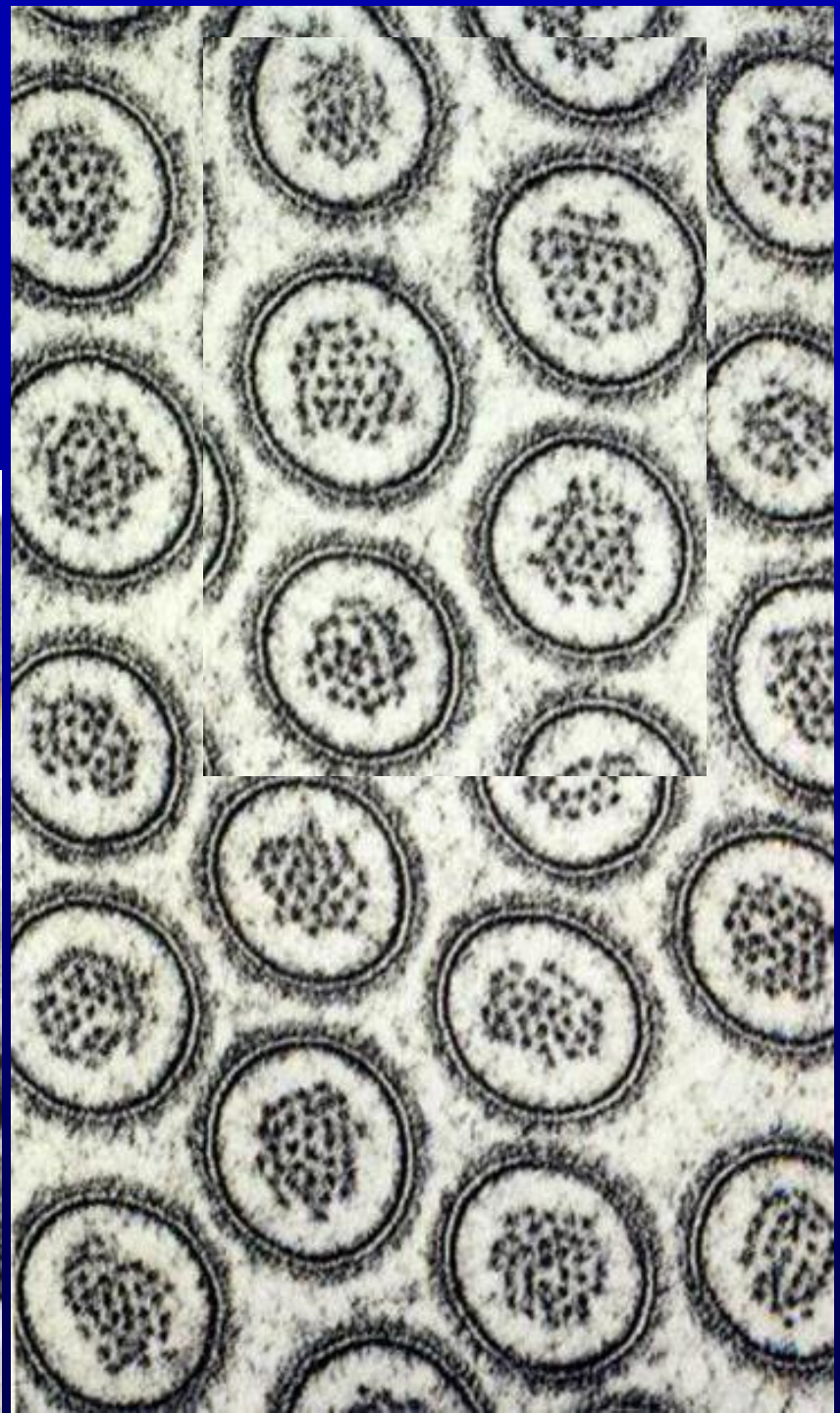
(C)

Microfilaments - function

Structural support -

- Microvilli movement and shape
- Pushes membrane out from cell

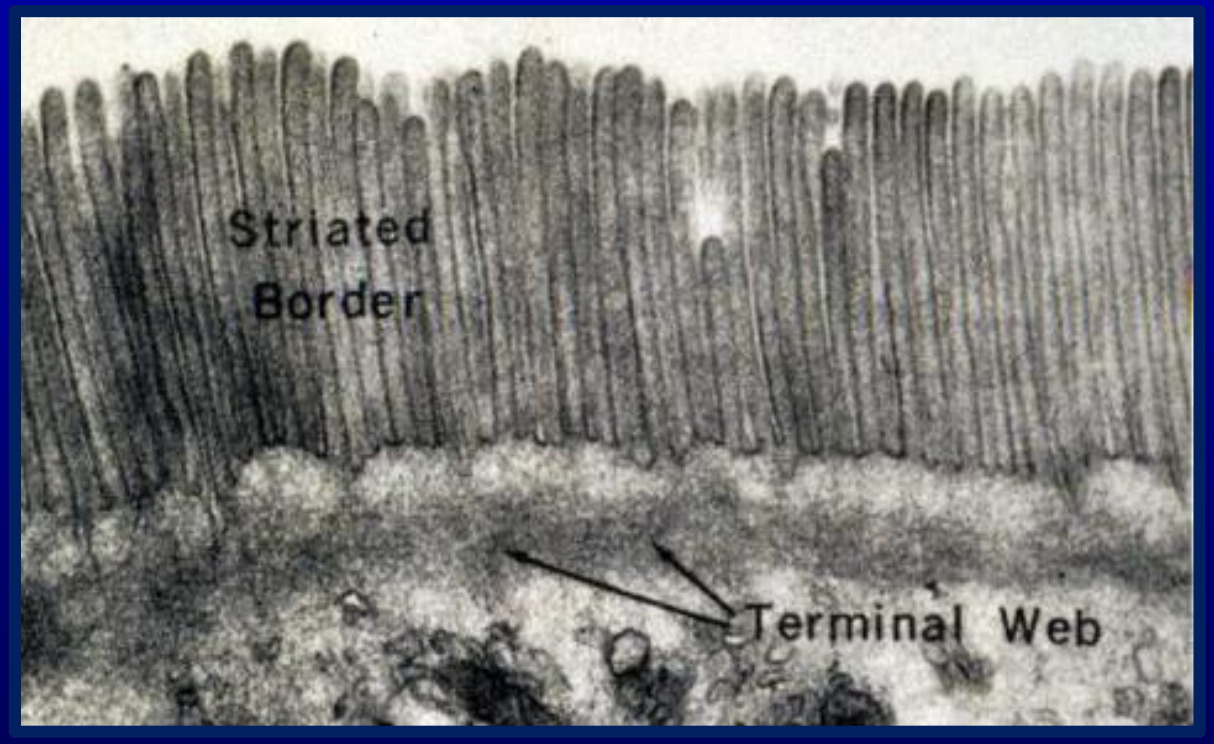




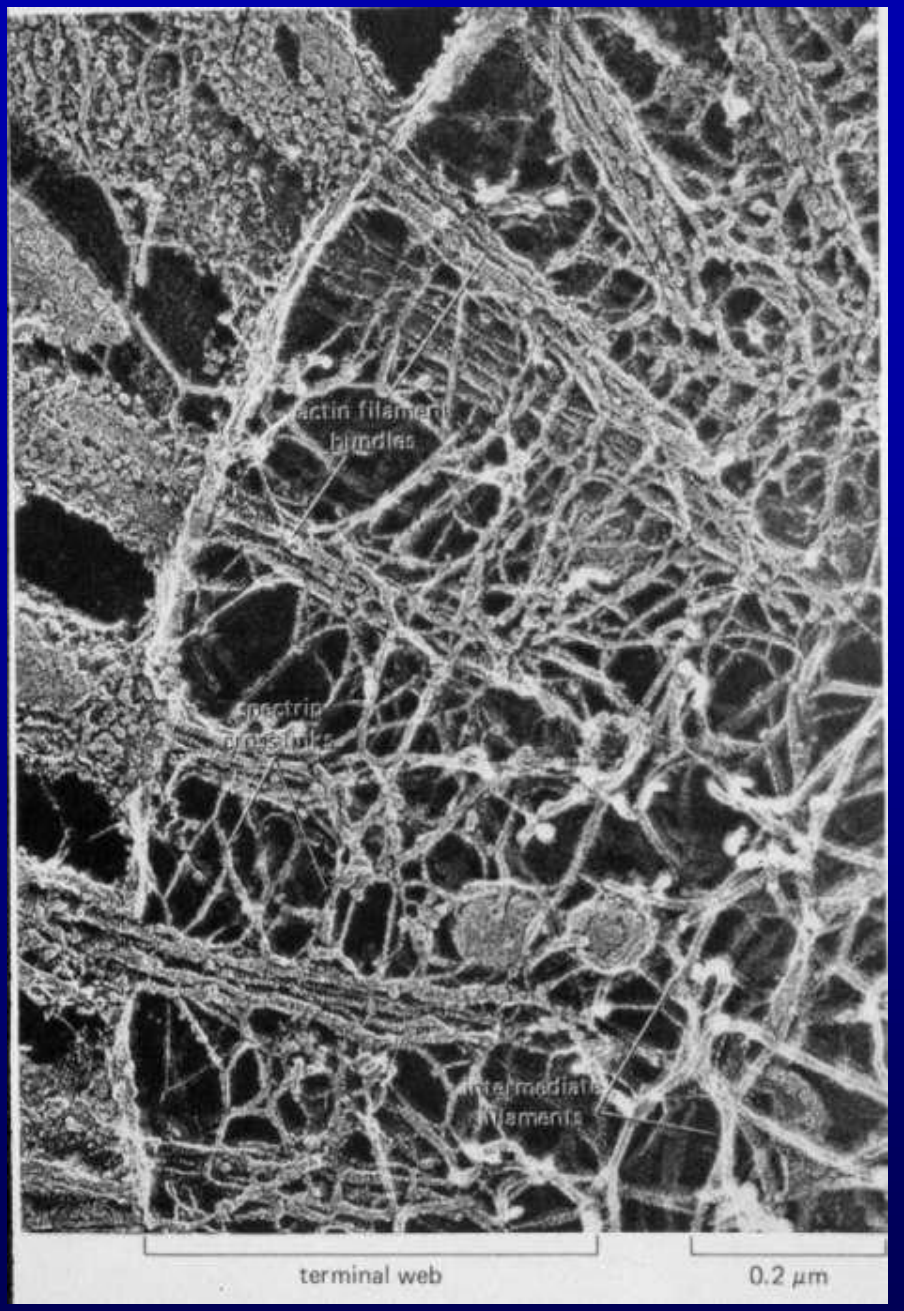
Microfilaments - function

Structural support -

- **Microvilli - movement and shape**



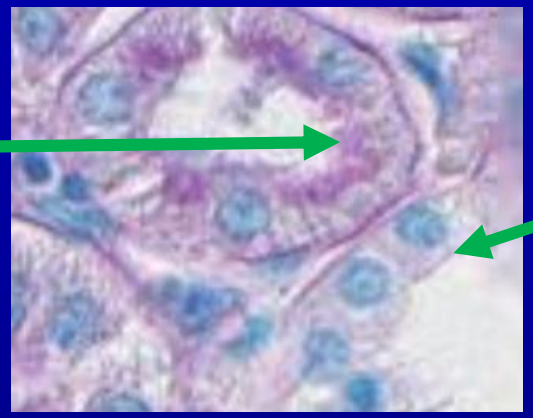
Brush border



Brush border vs typical microvilli in the kidney

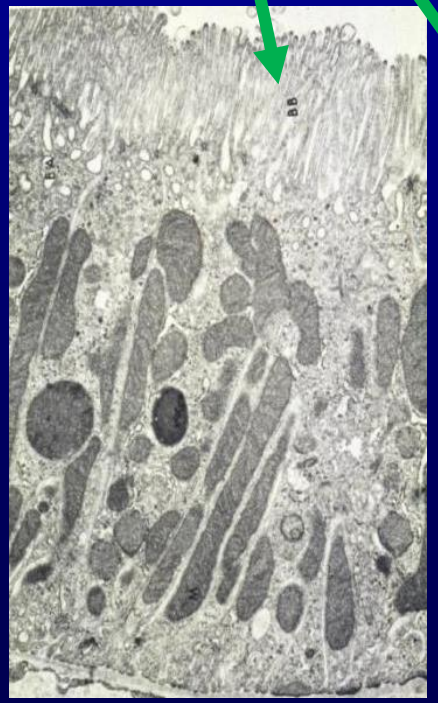
Brush border is composed of a high density of microvilli which are non-branching and uniform in length.

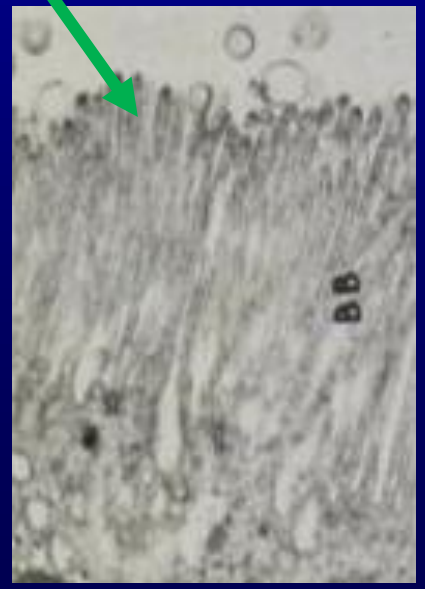
Proximal tubule brush border

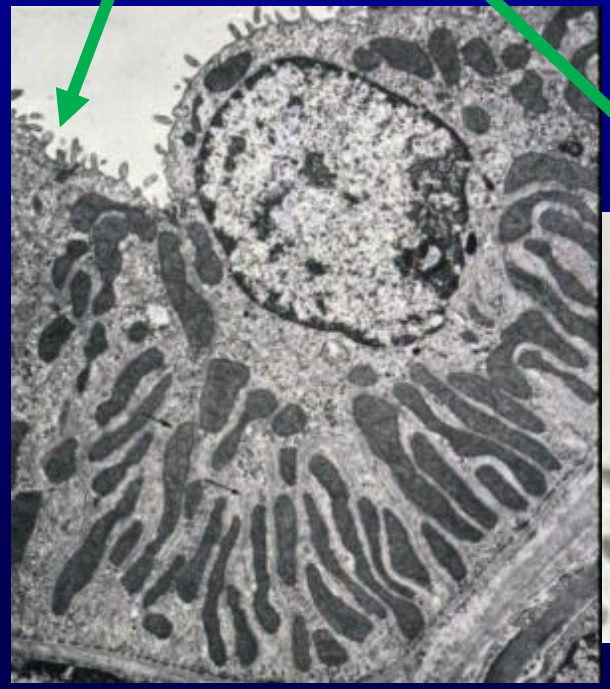


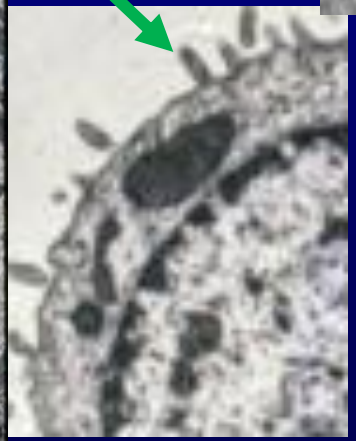
Distal tubule typical microvilli

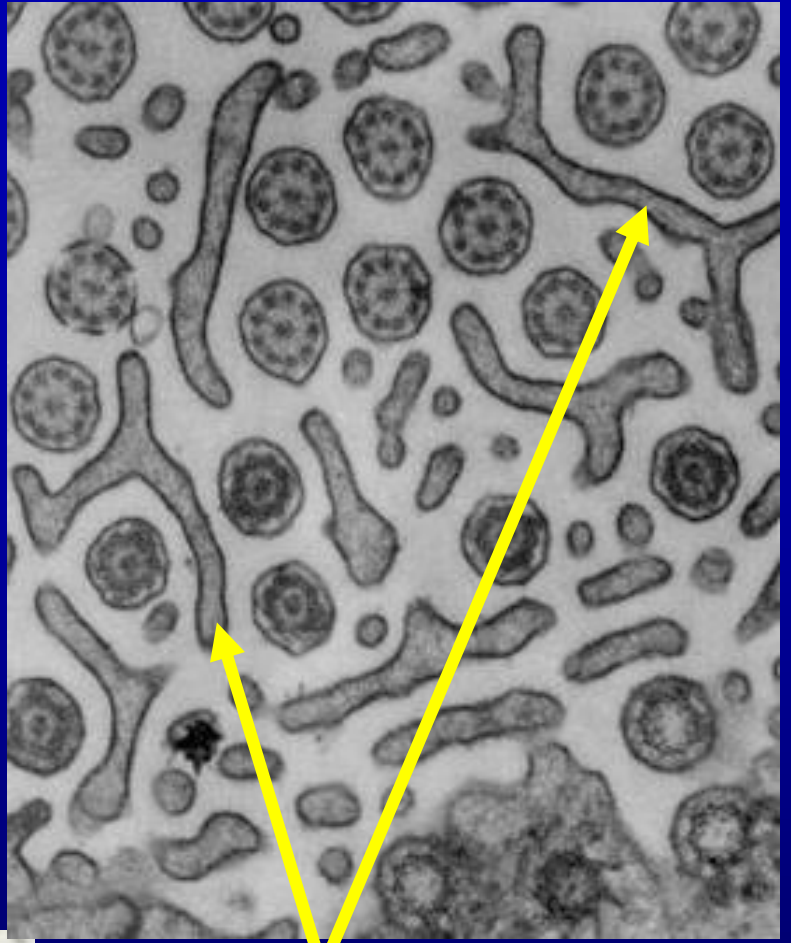
PAS









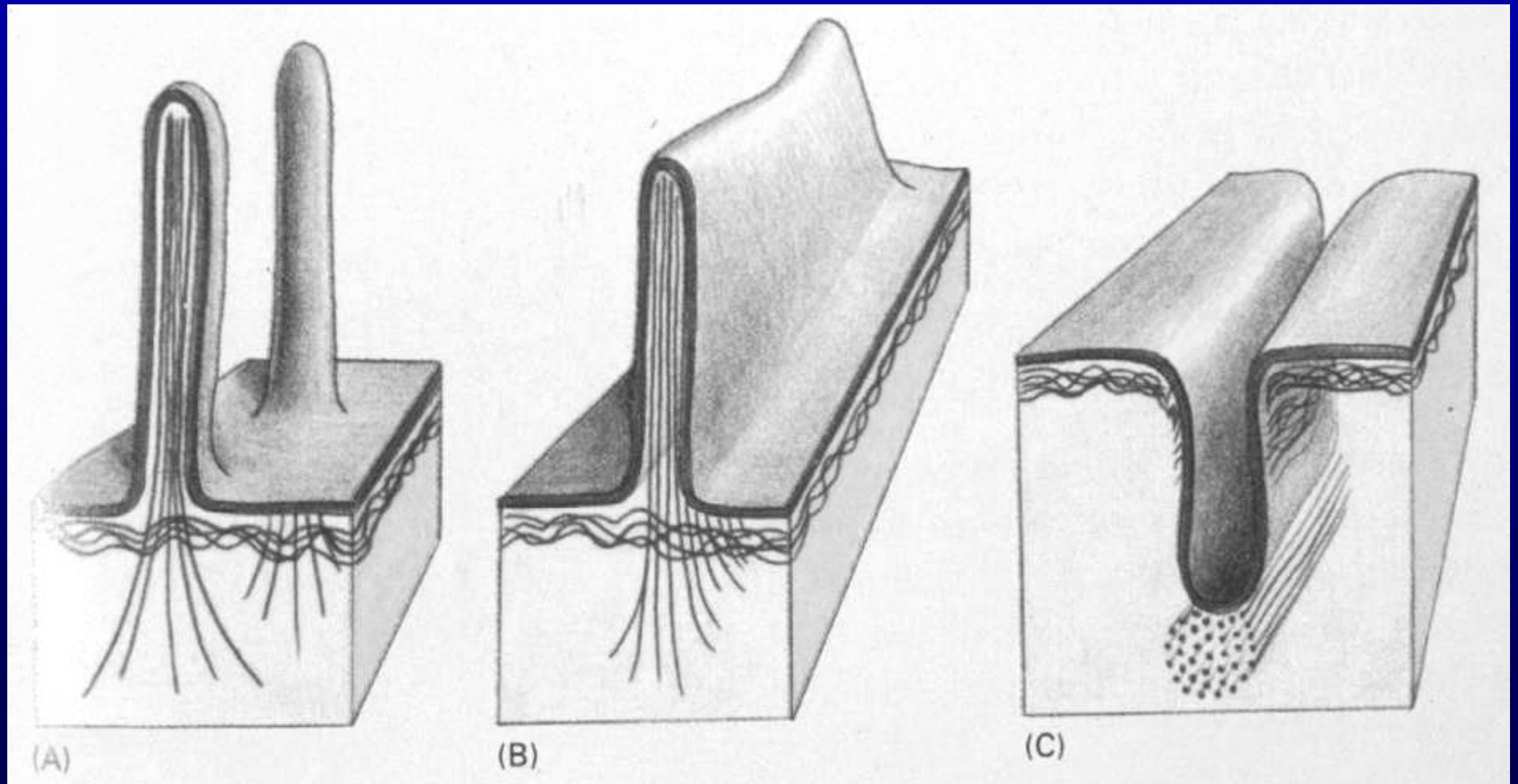


Typical microvilli are branched as seen here on these ciliated cells

Microfilaments - function

Structural support -

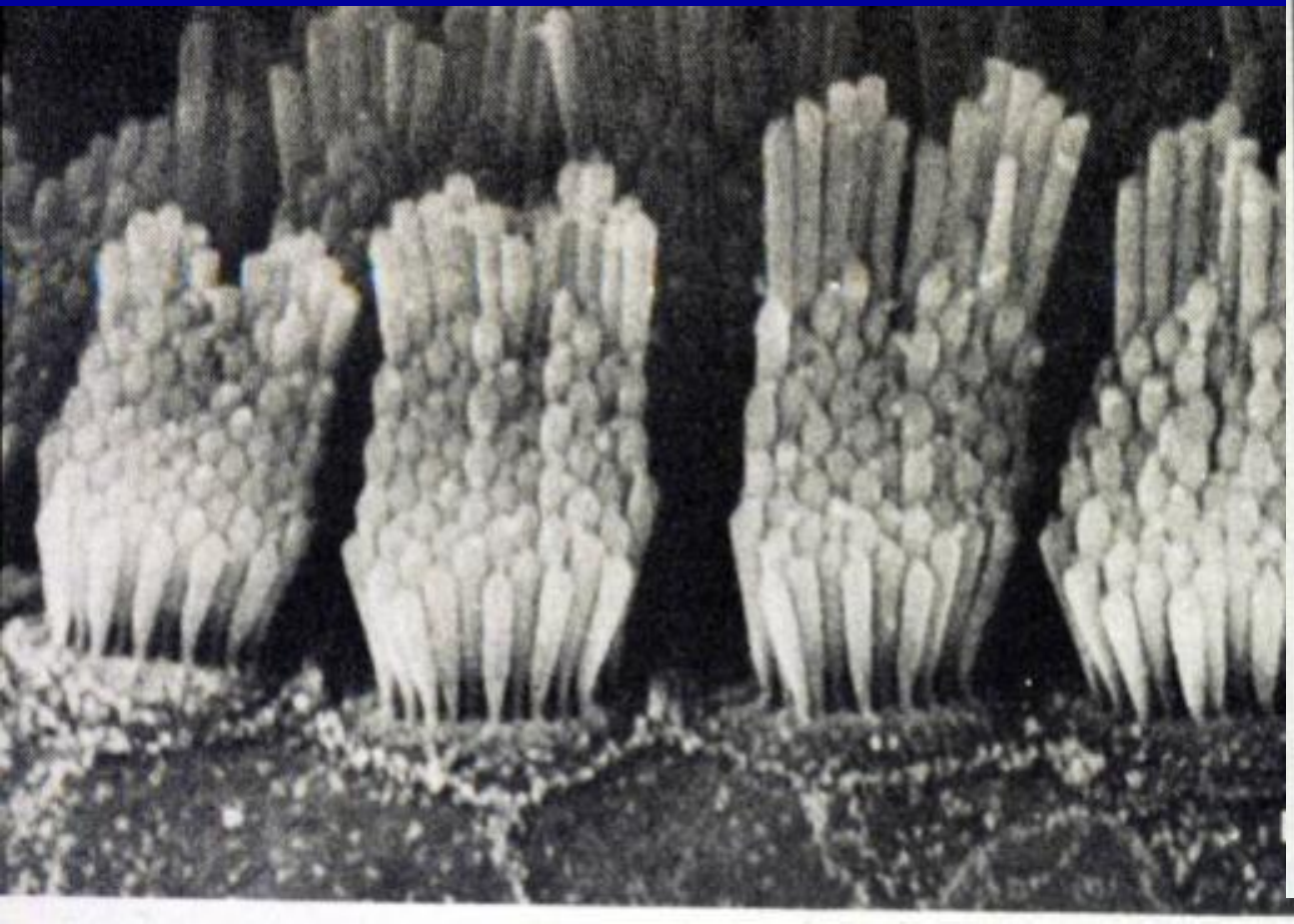
- Microvilli - movement and shape

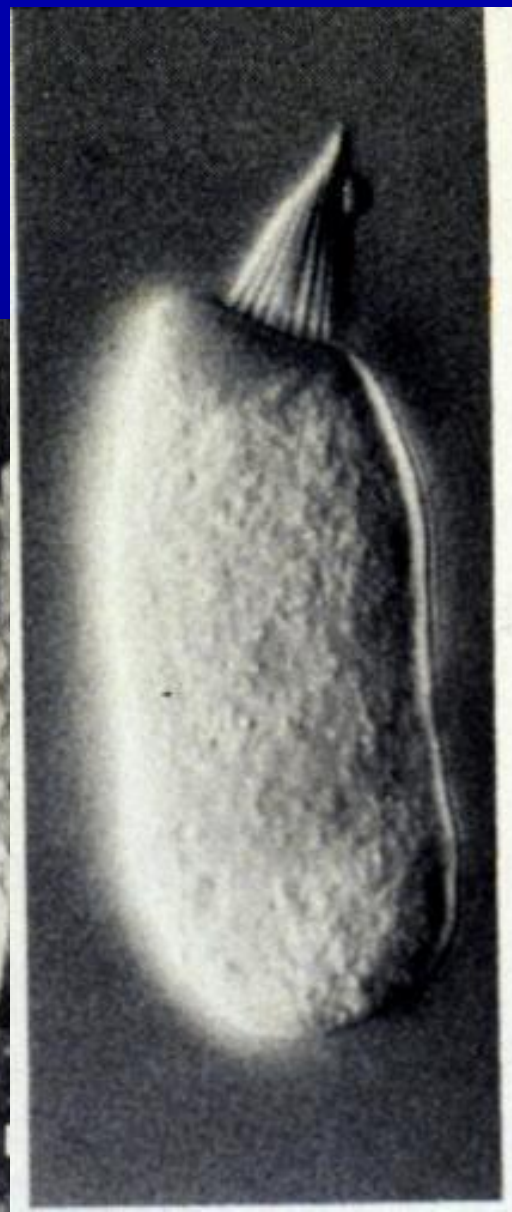


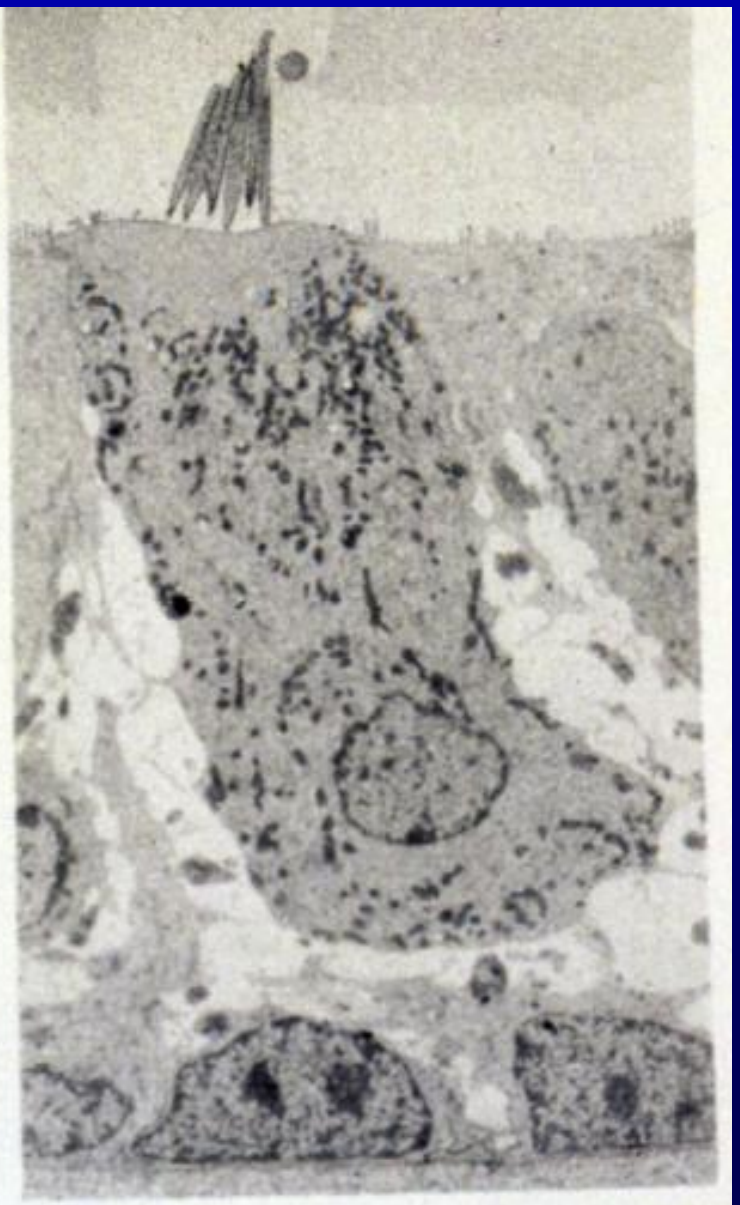
Microfilaments - function

Structural support -

Stereocilia - extension



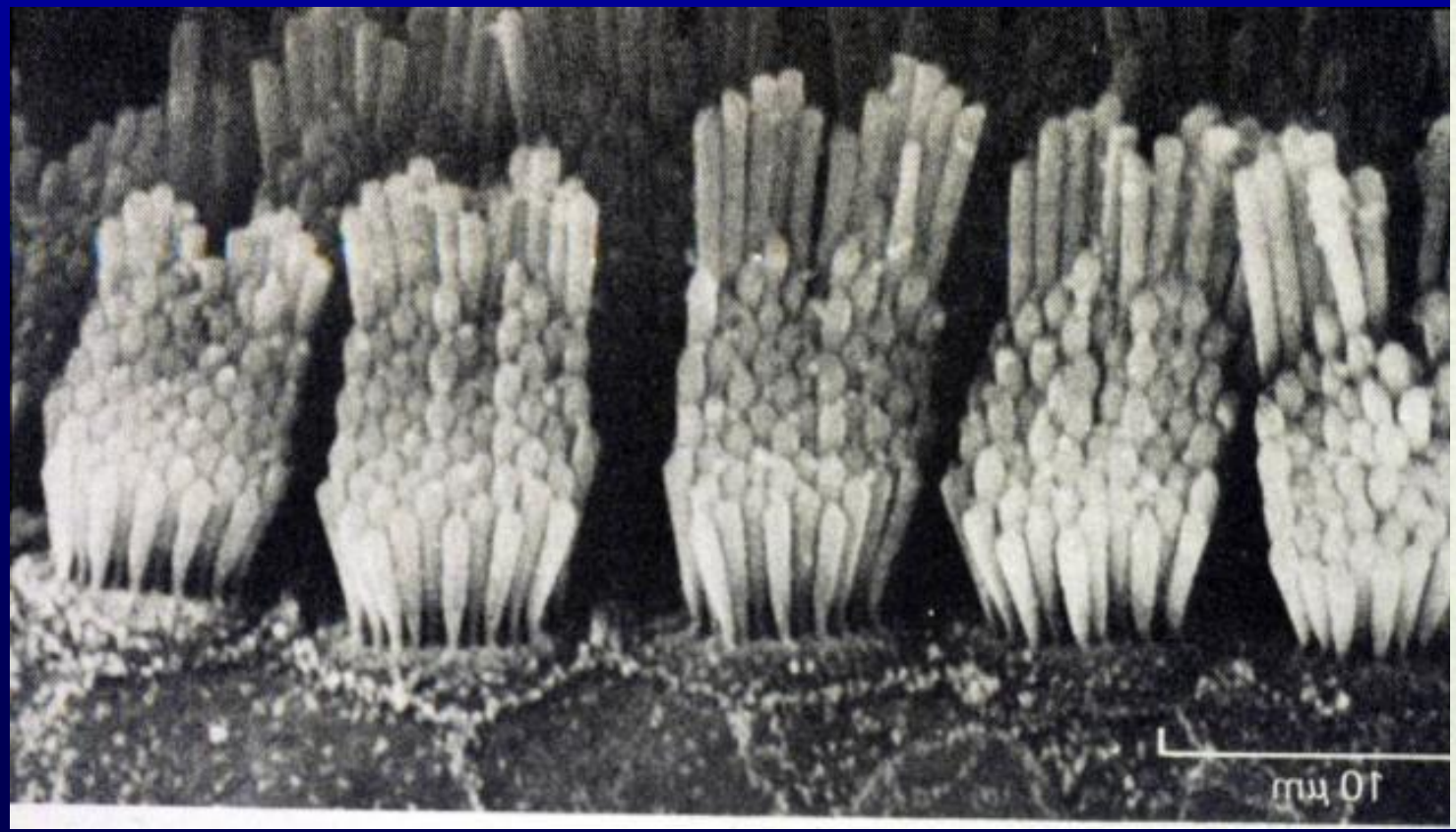


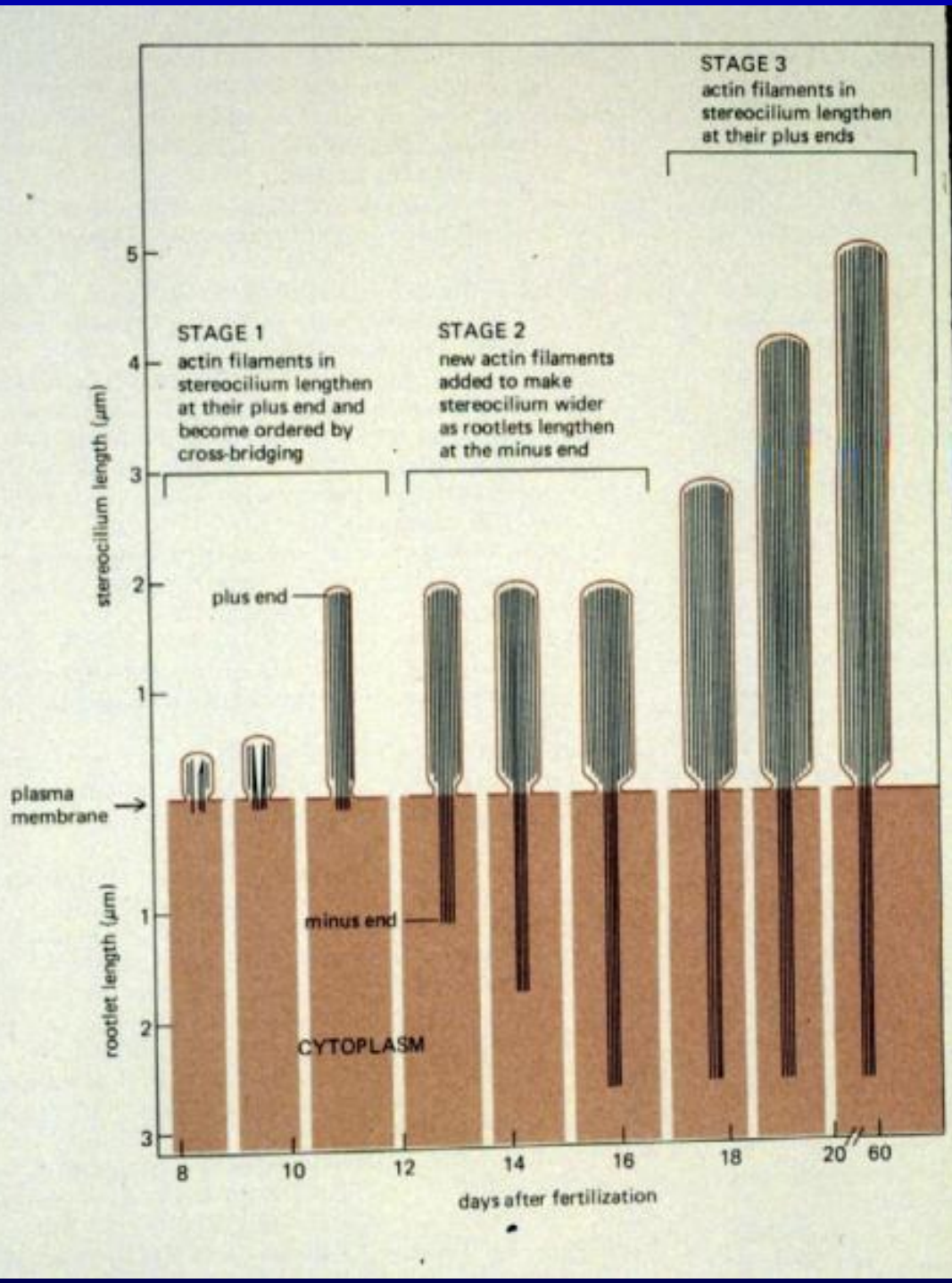


Microfilaments - function

Structural support -

Stereocilia - extension

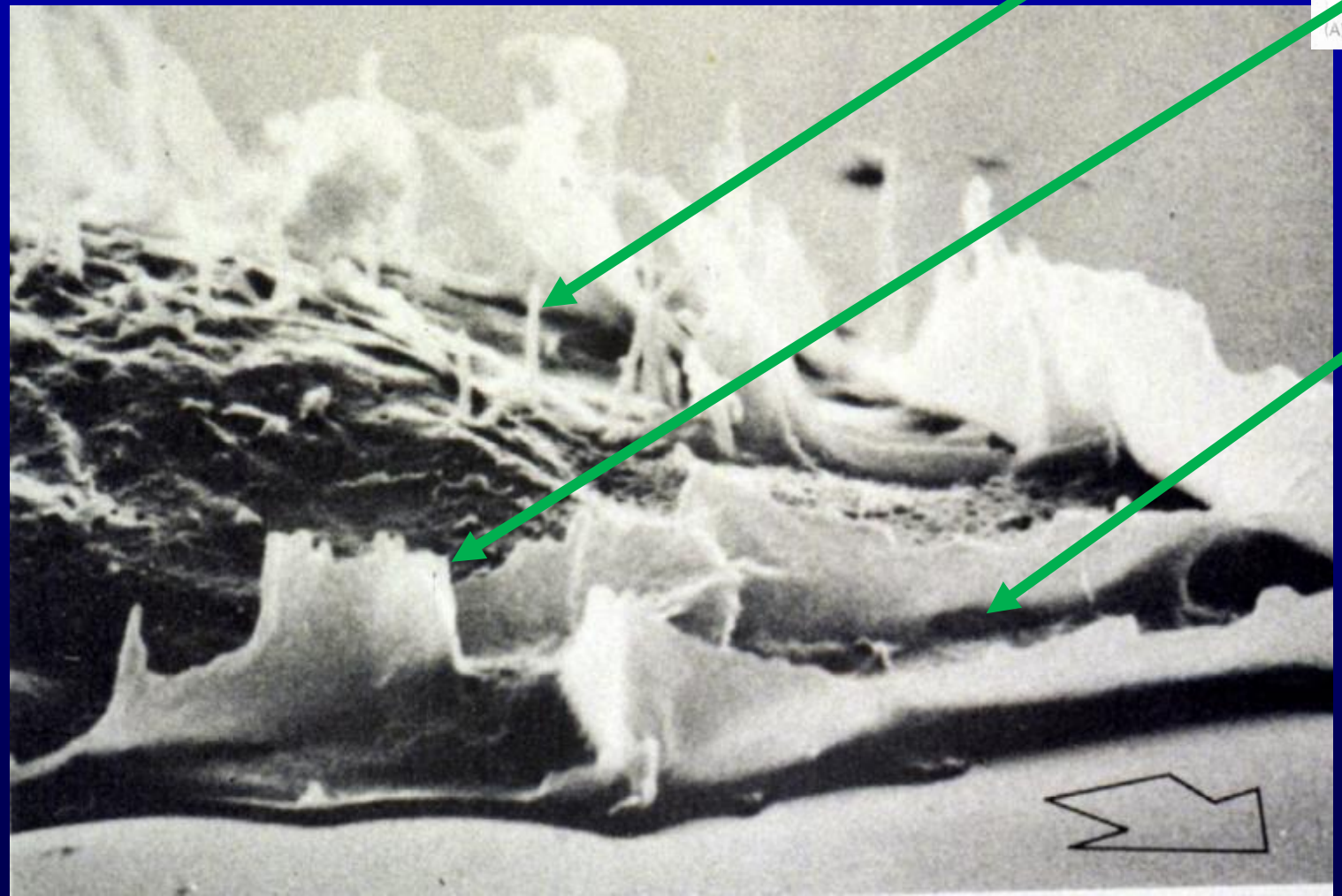


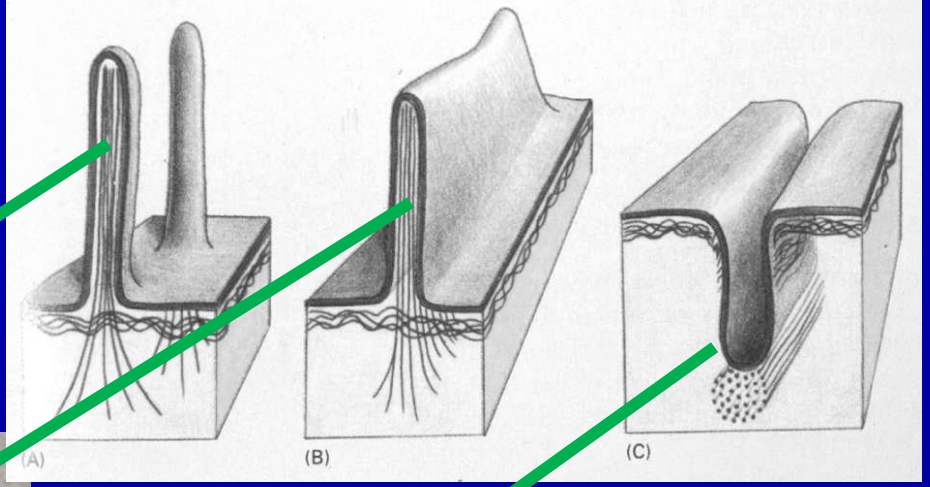


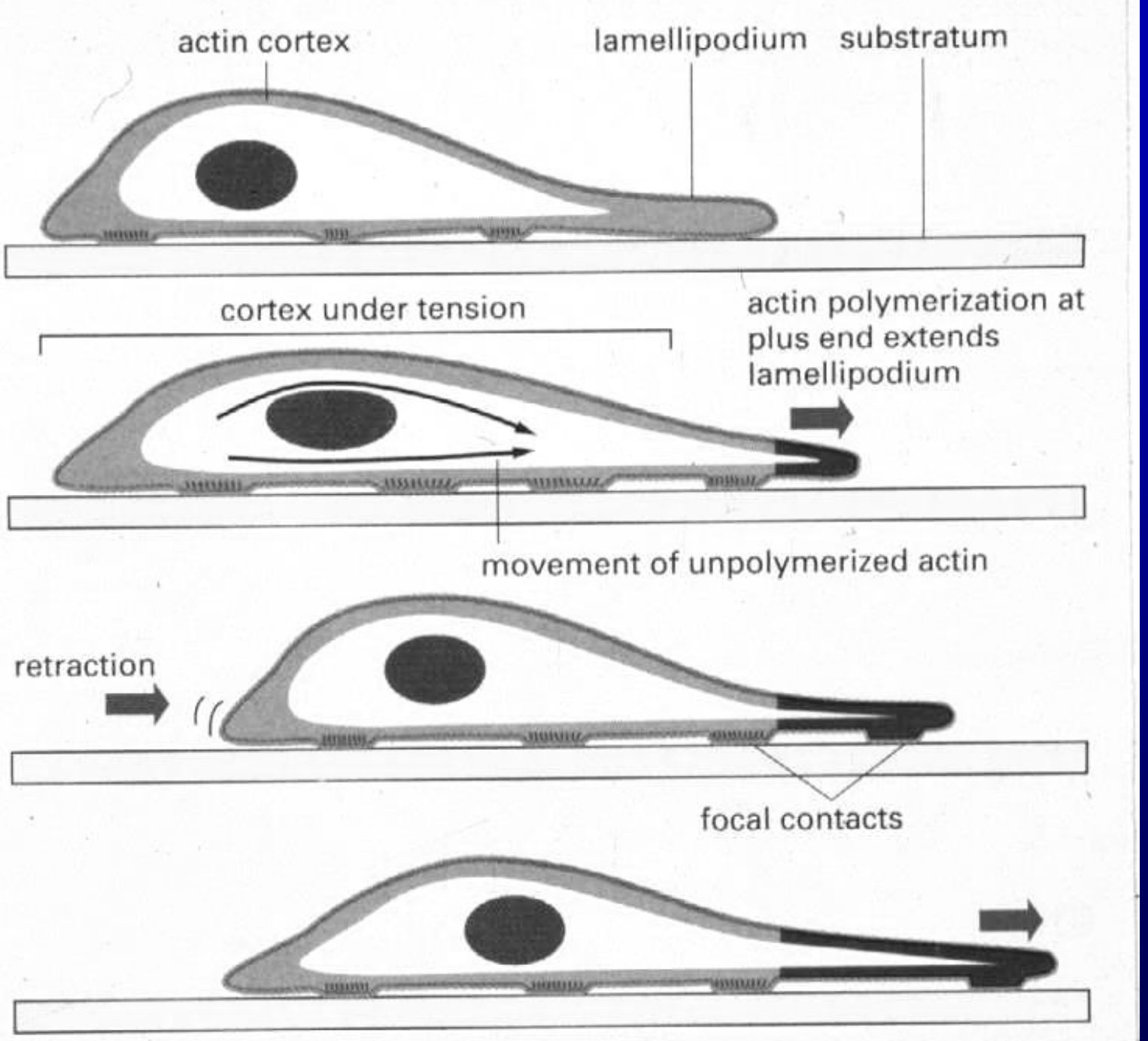
Microfilaments - function

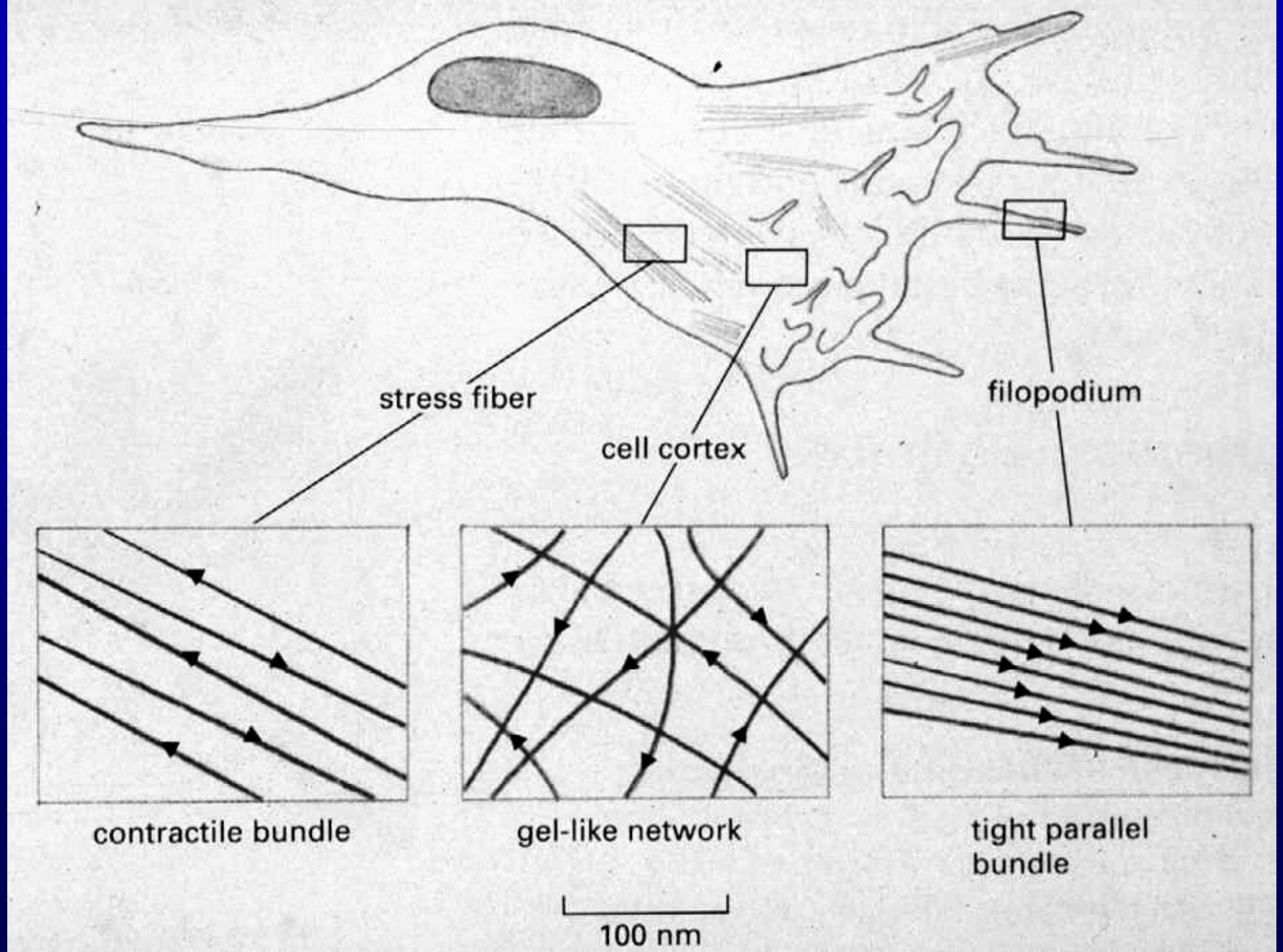
Structural support -

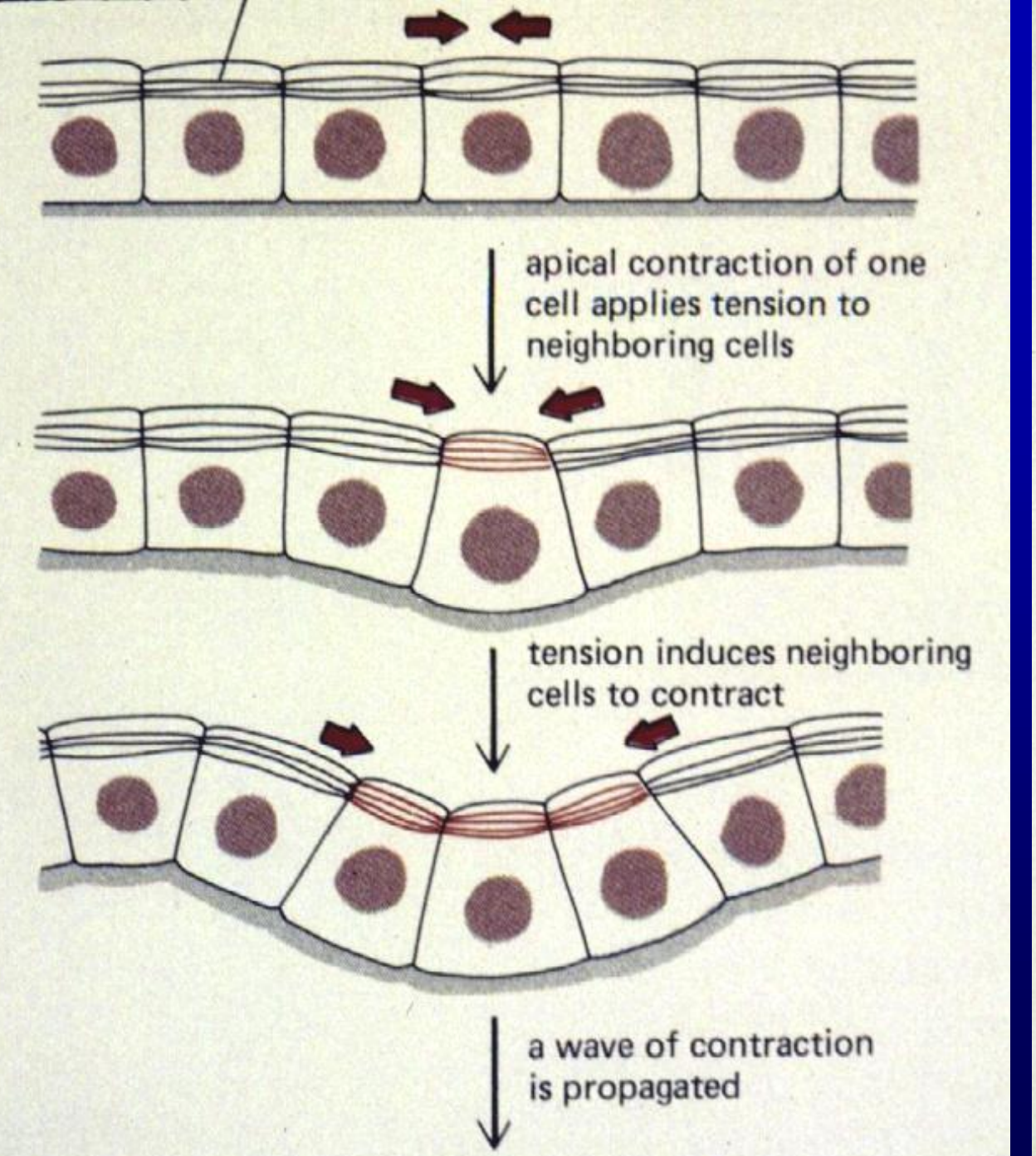
- Microvilli - movement and shape






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



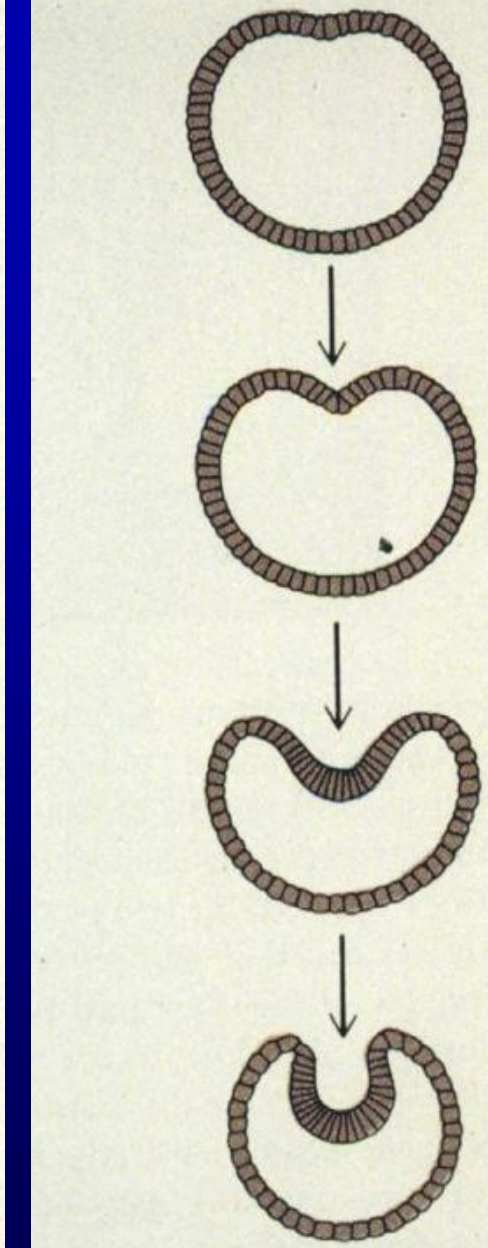
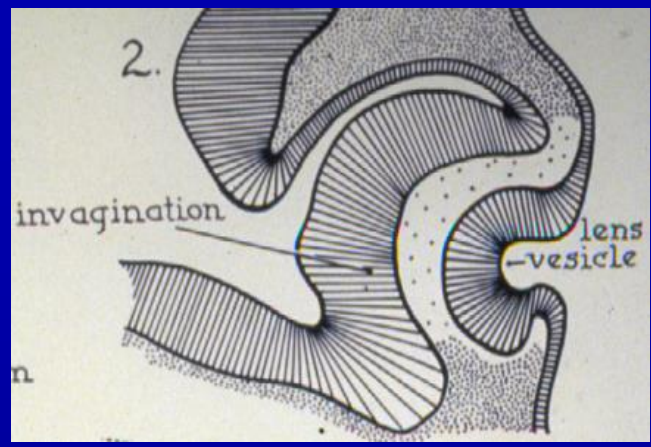
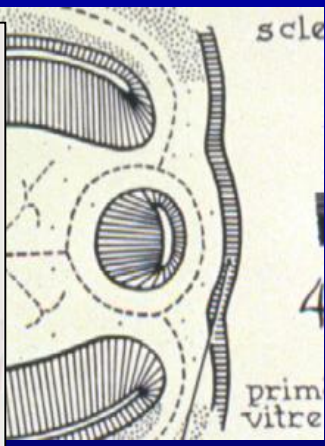


Figure 11–87 Computer r

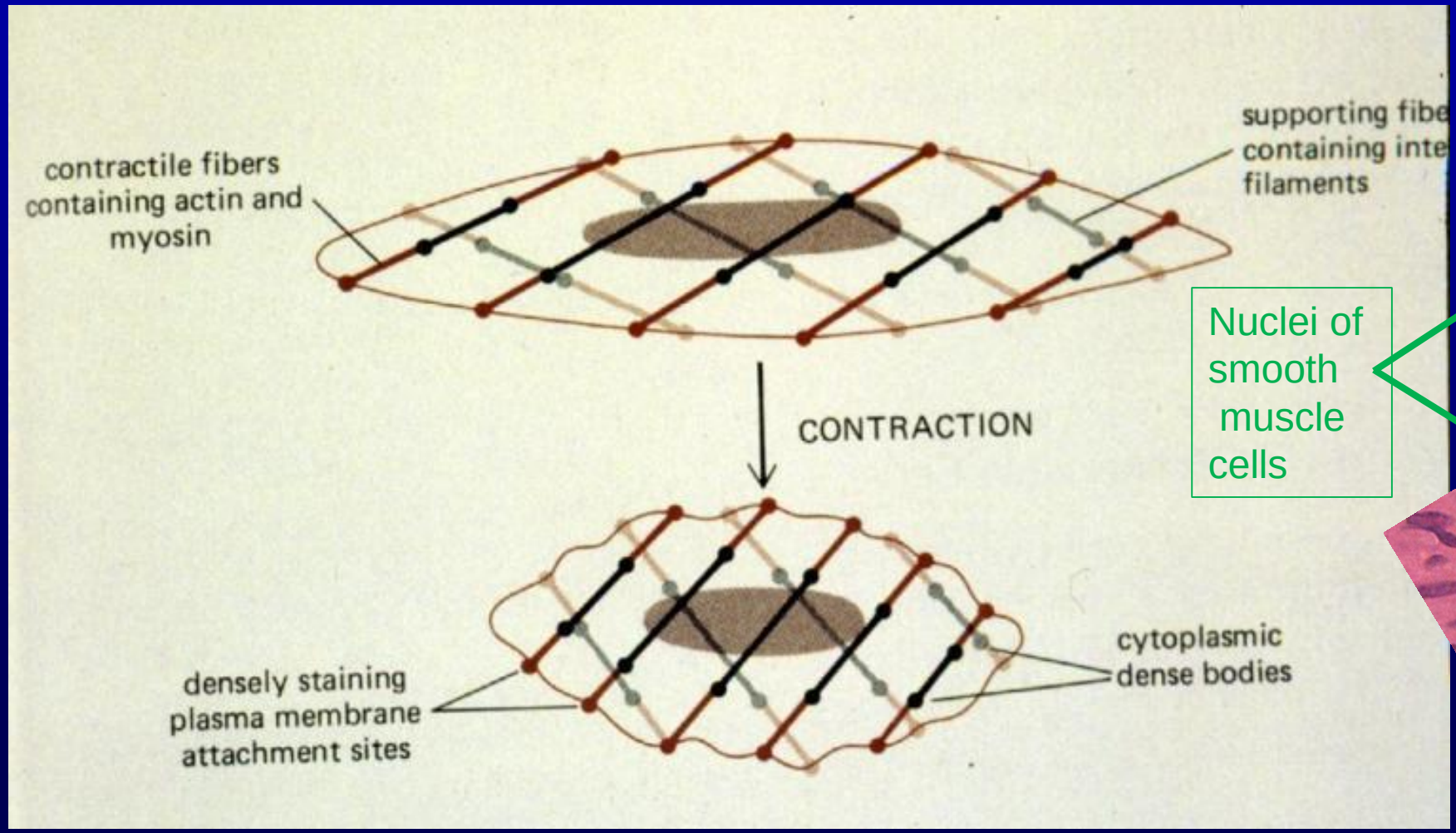




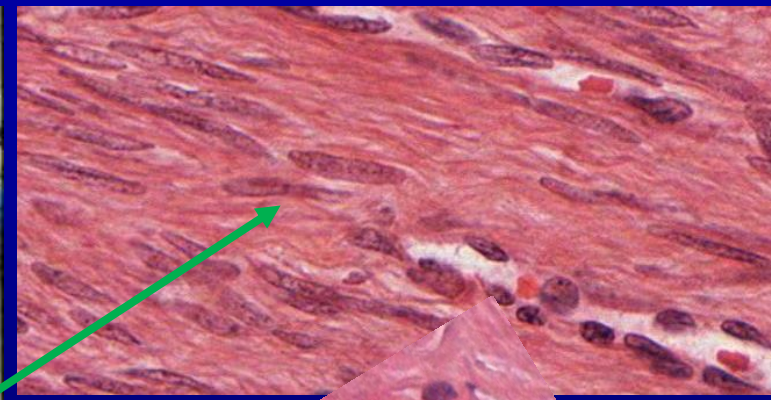
Microfilaments - contractile proteins

Actin and myosin – present in muscle and most all cells

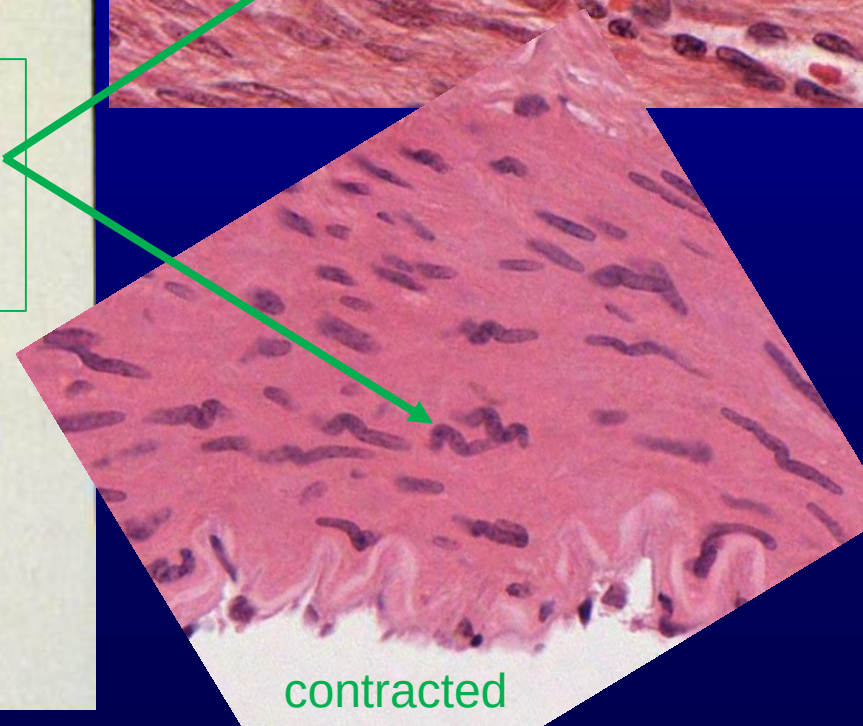
Actin 10% to 15% of cellular protein, widely distributed



relaxed



Nuclei of smooth muscle cells

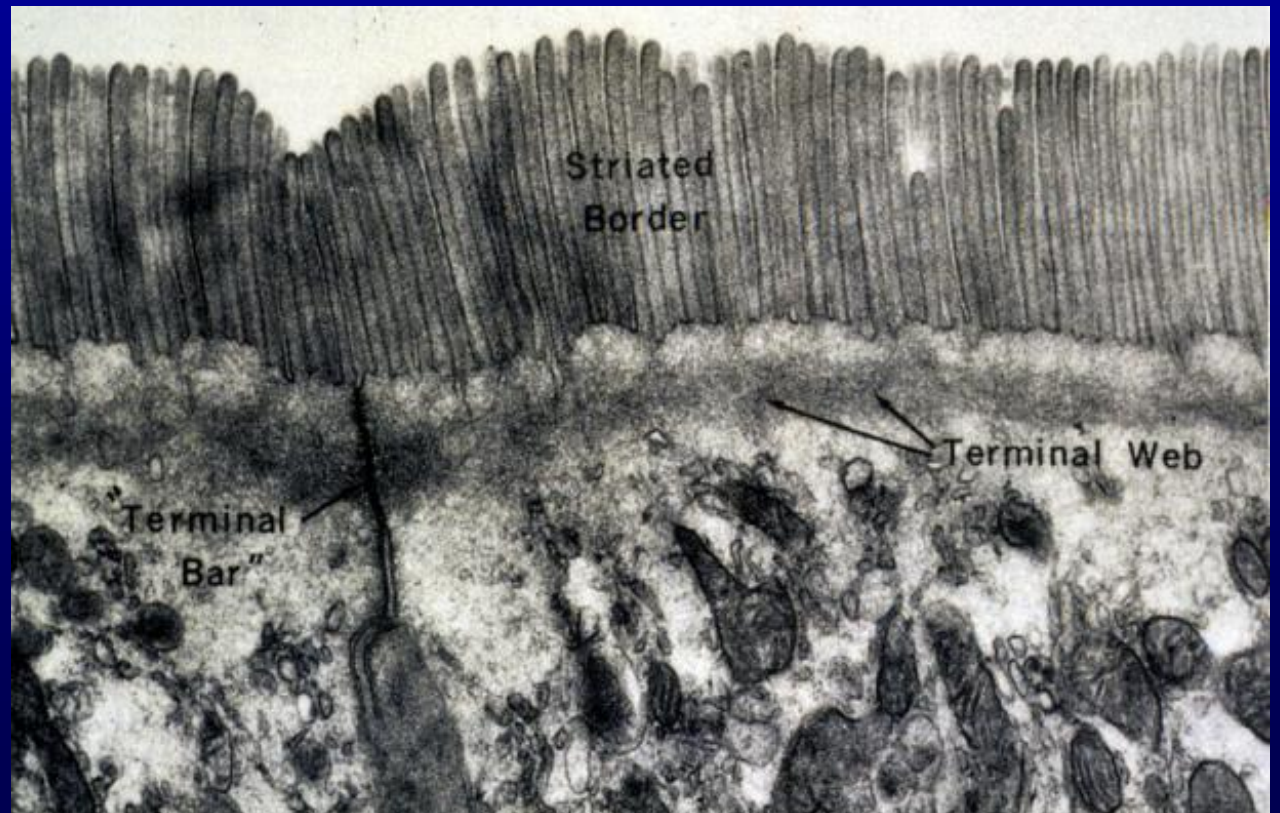


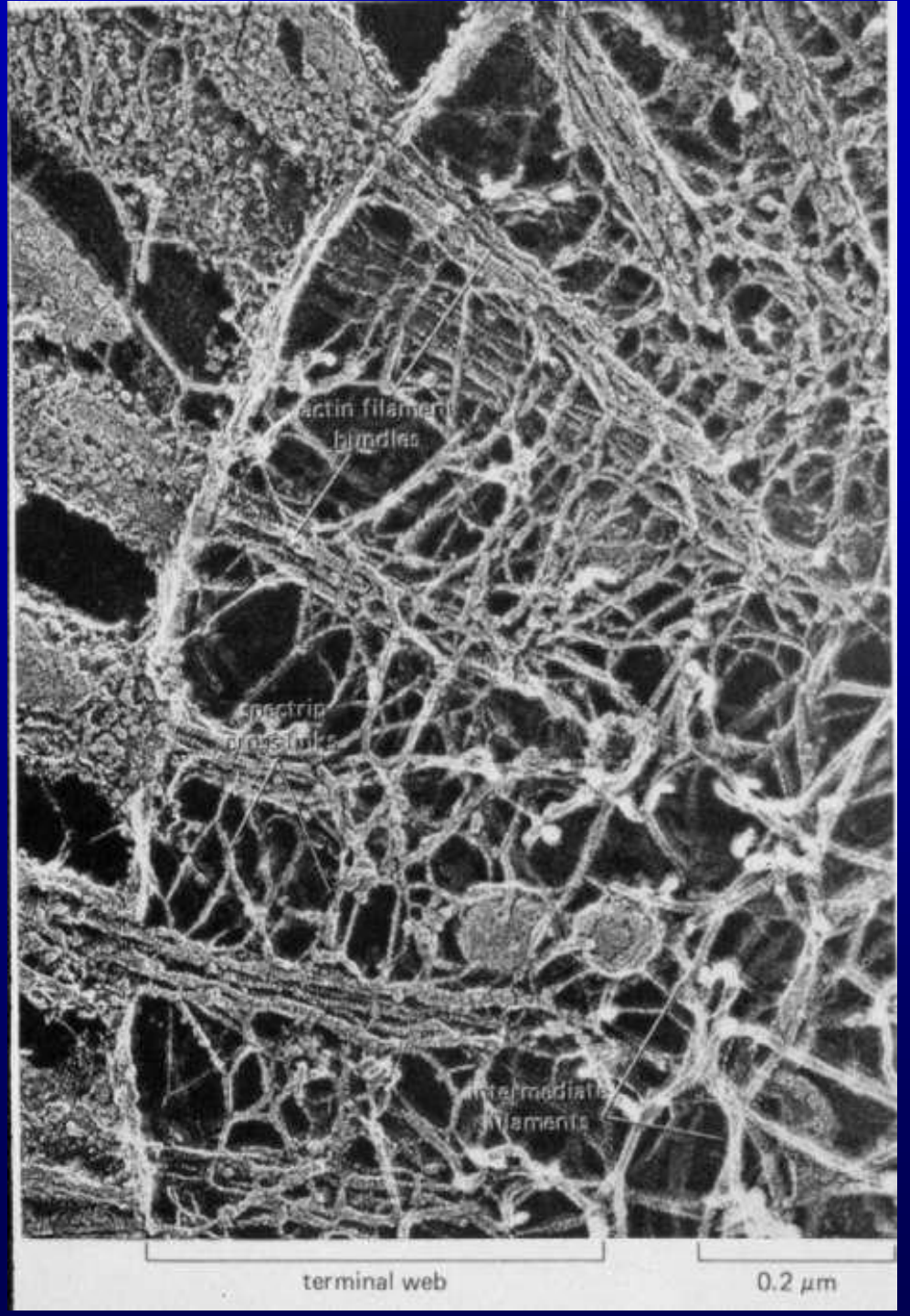
contracted

Summary: microfilaments - contractile proteins

Terminal web – anchor actin filaments in microvilli

Below cell surface – its mesh excludes other organelles

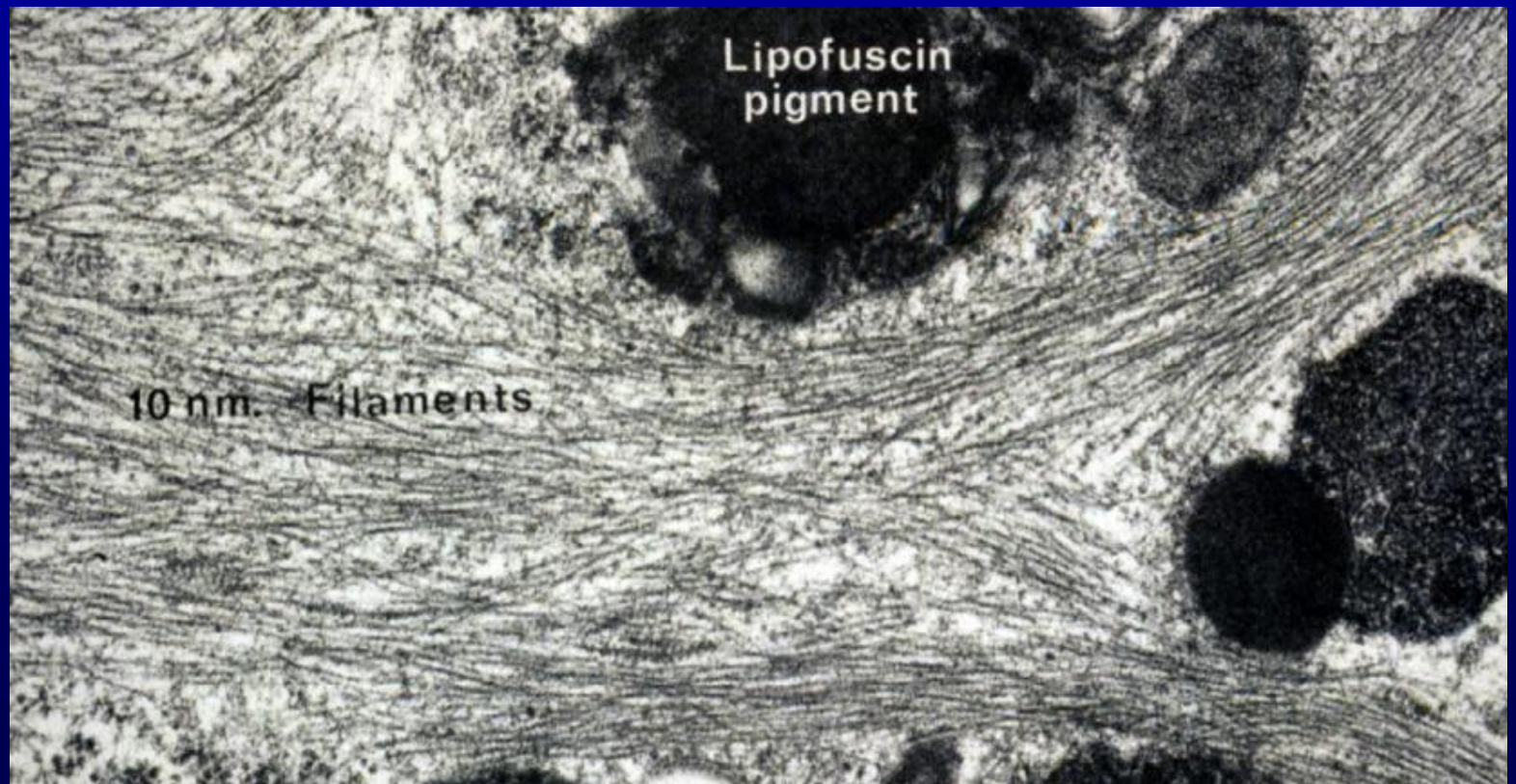


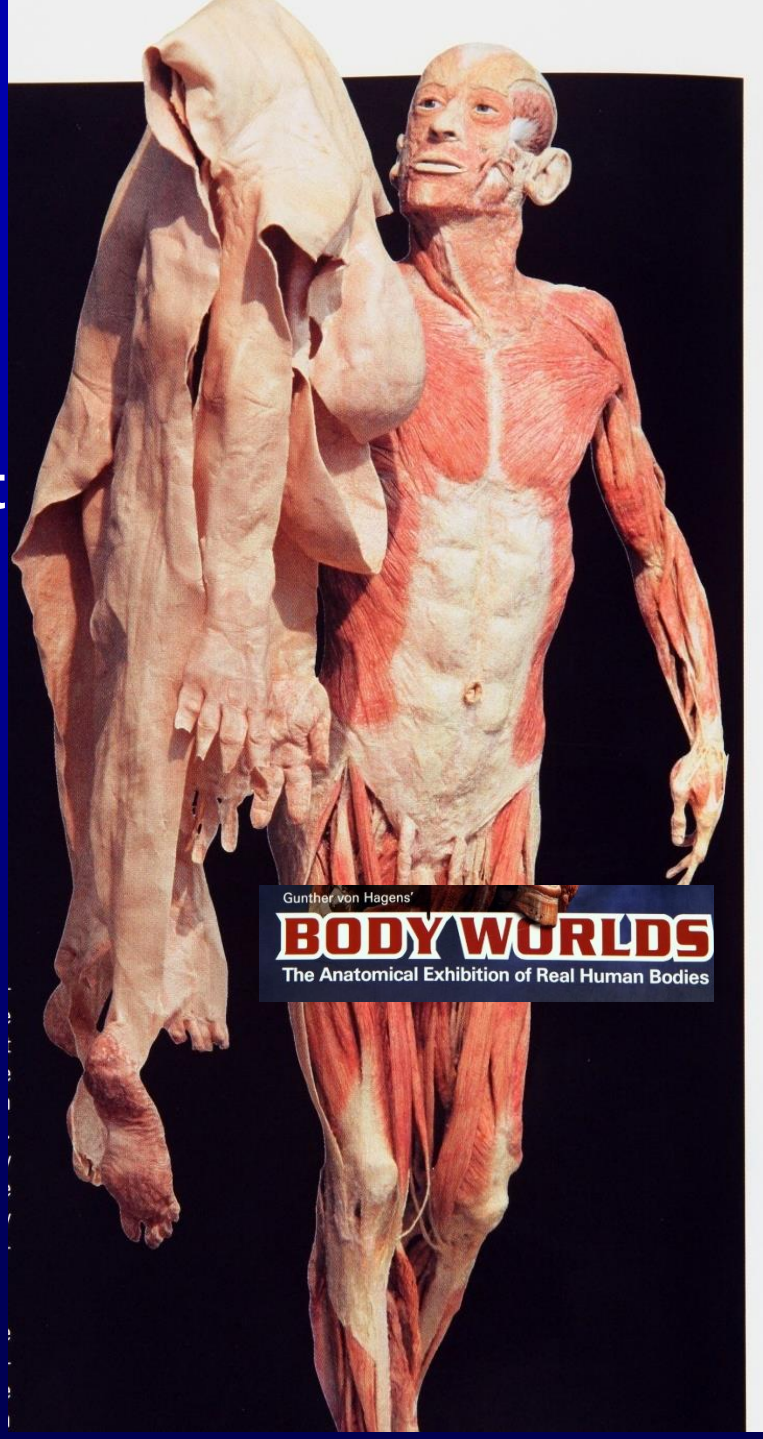


Intermediate filaments

Five classes (not conserved)

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





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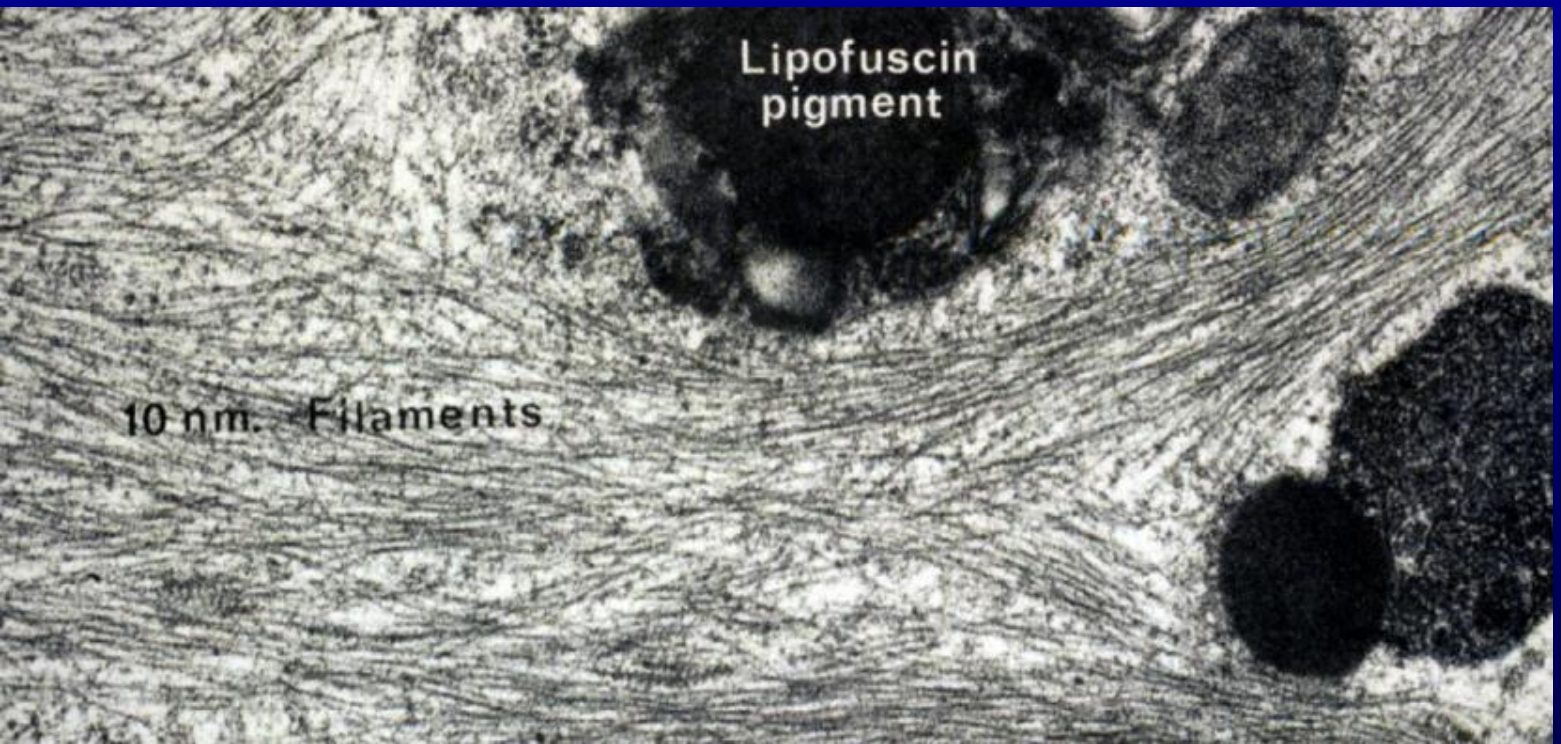

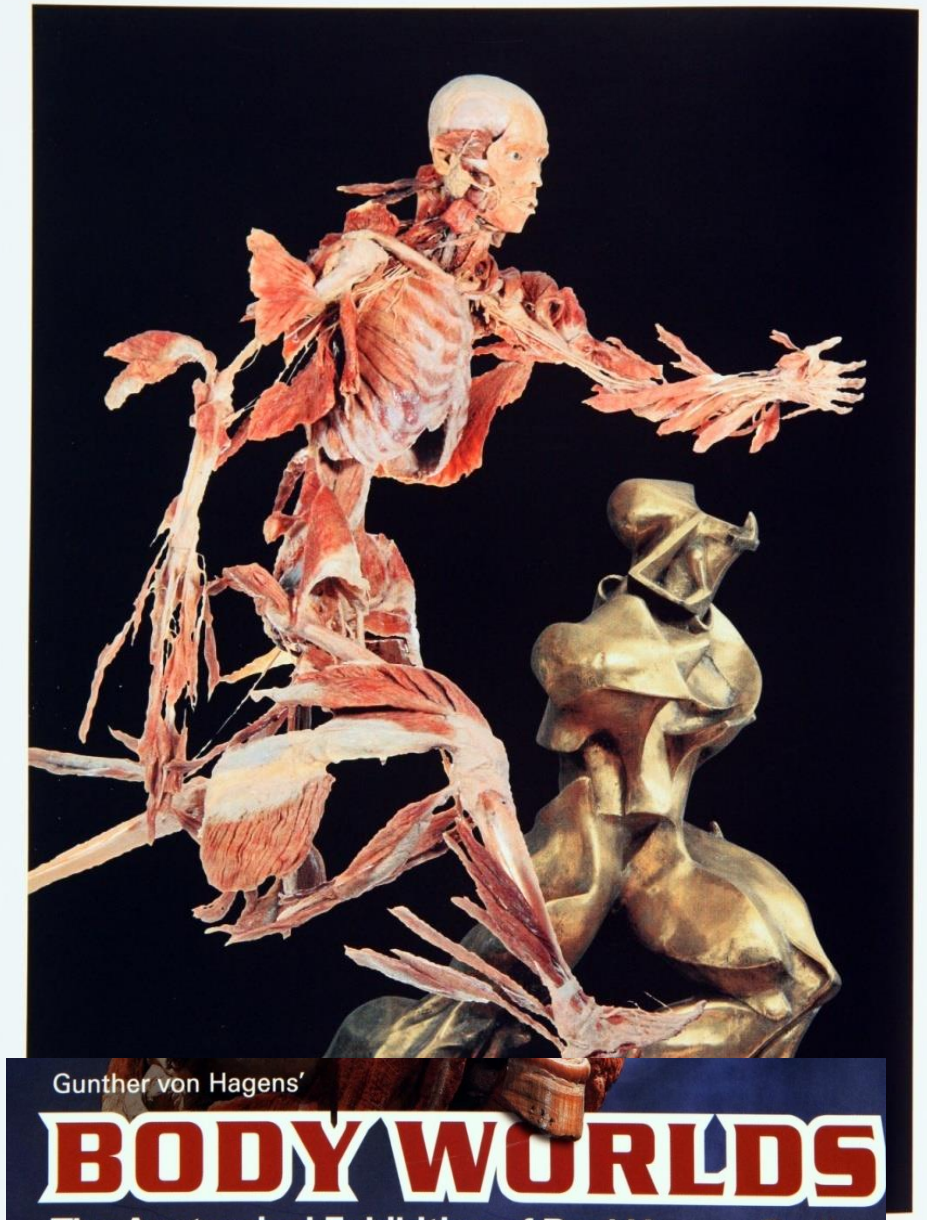

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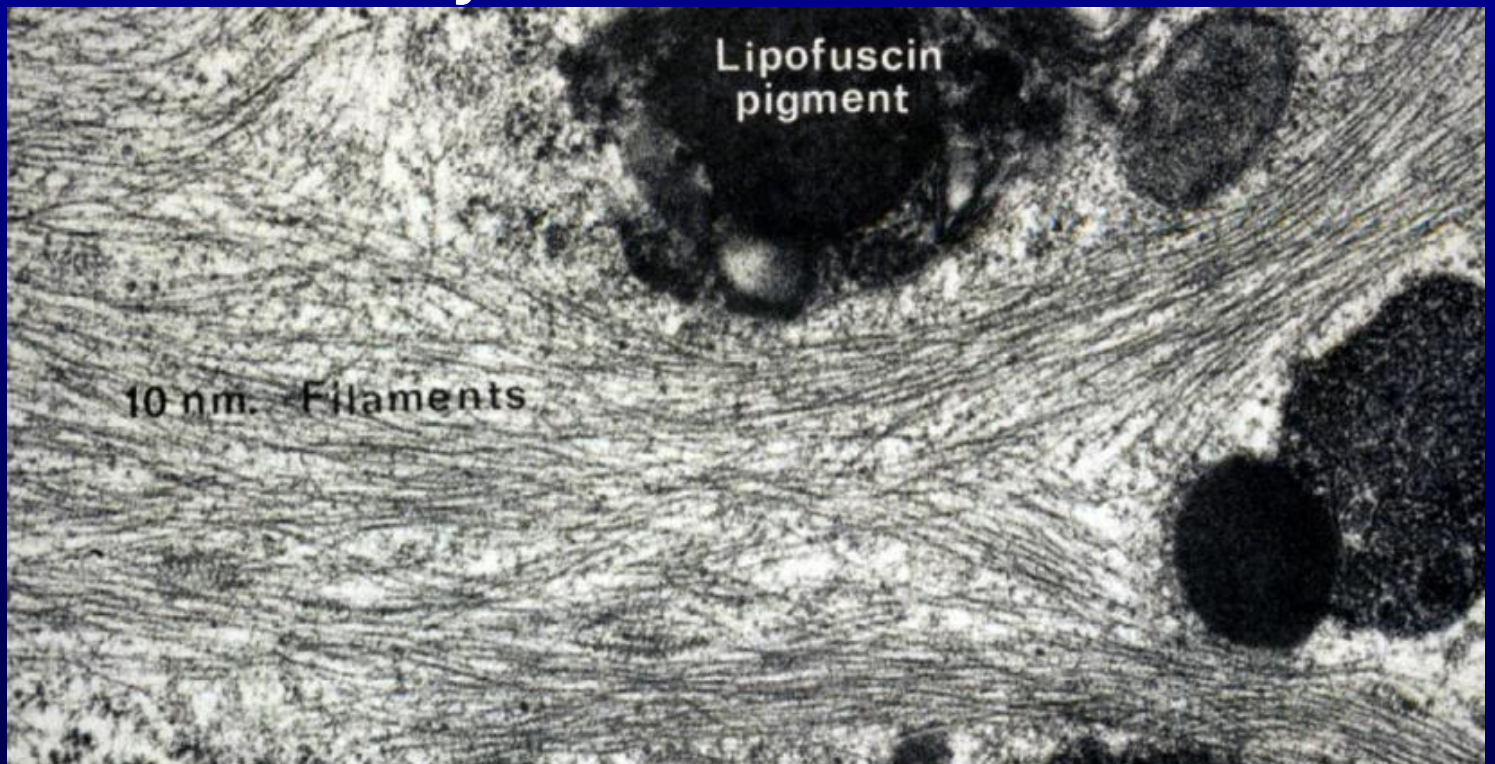
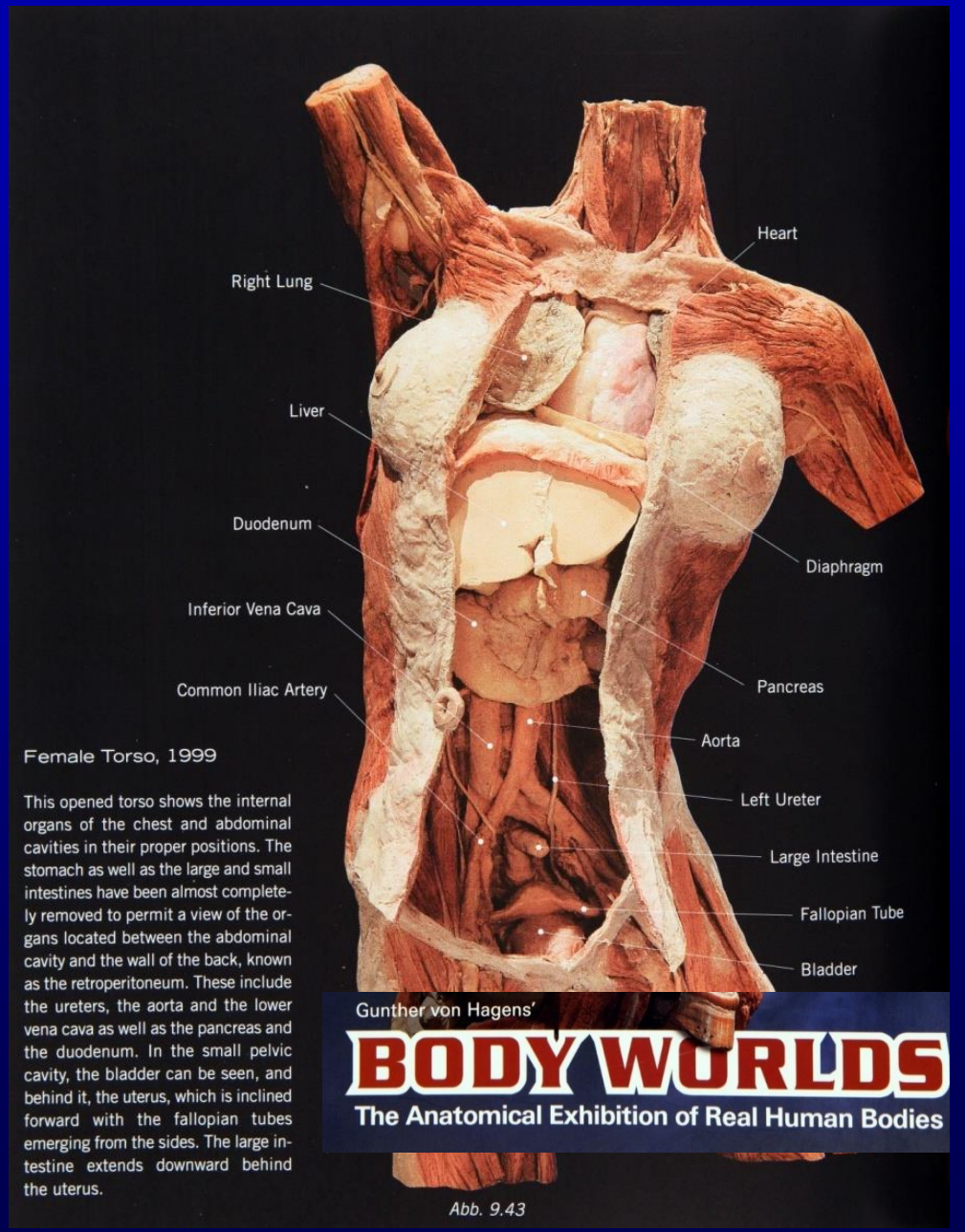
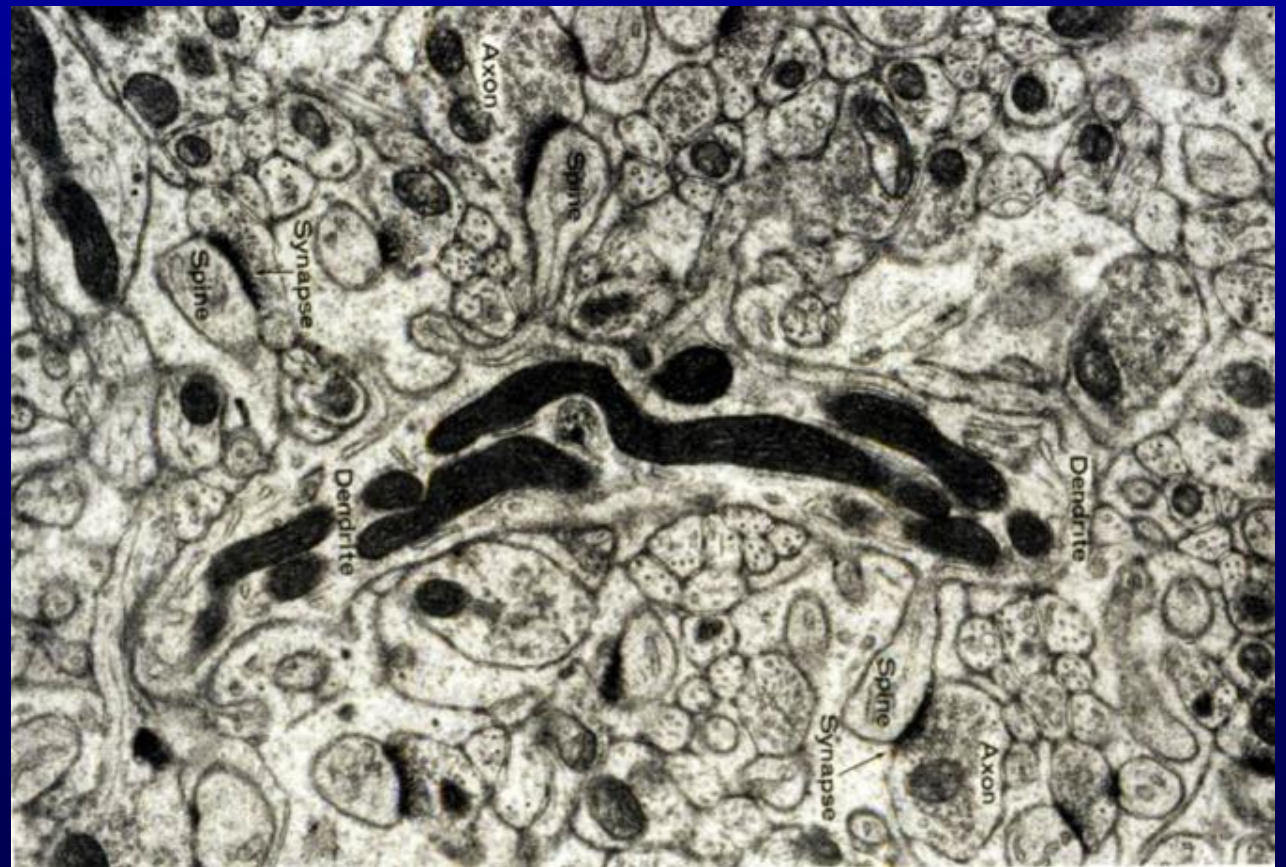


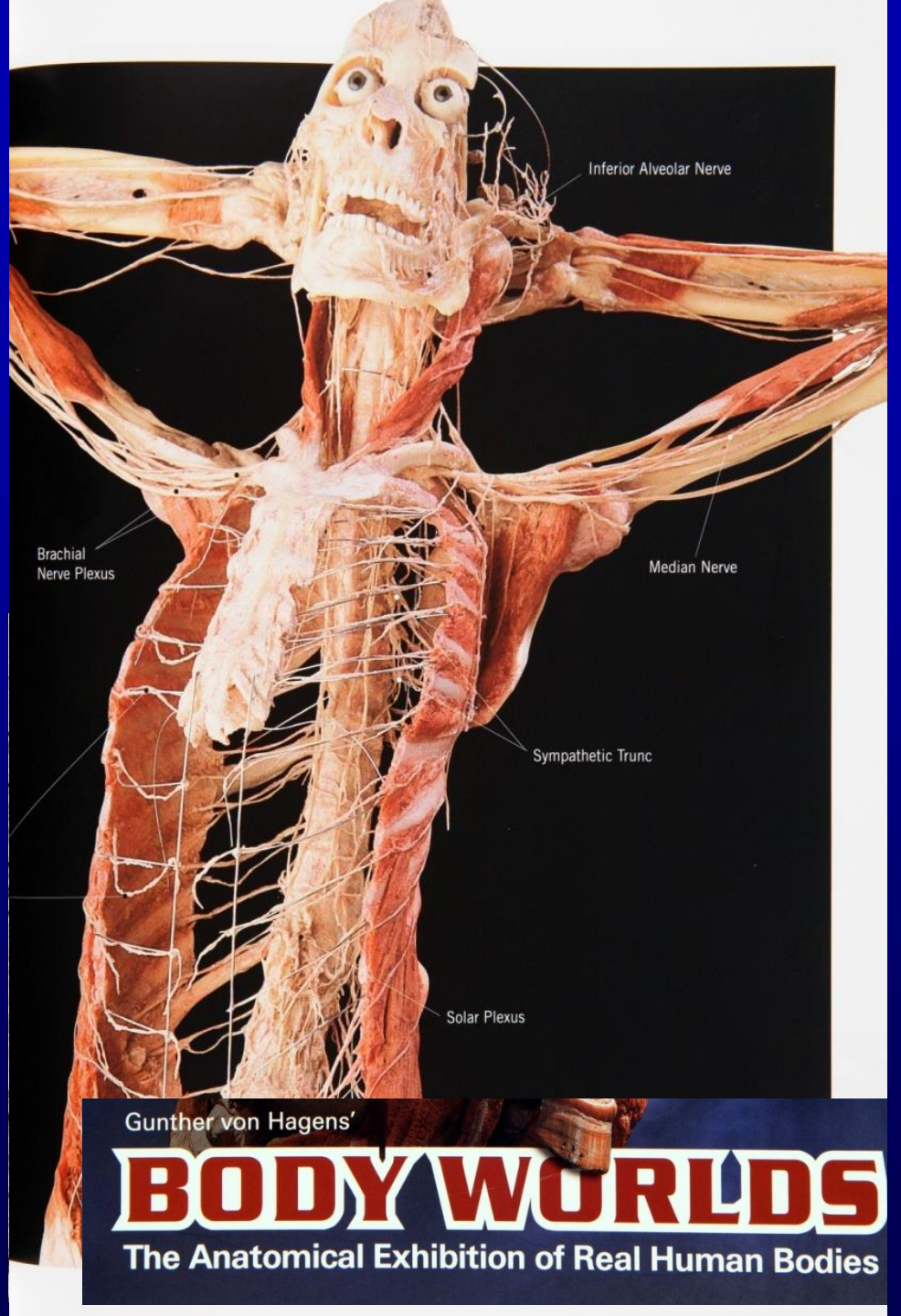


Intermediate filaments

Five classes con't

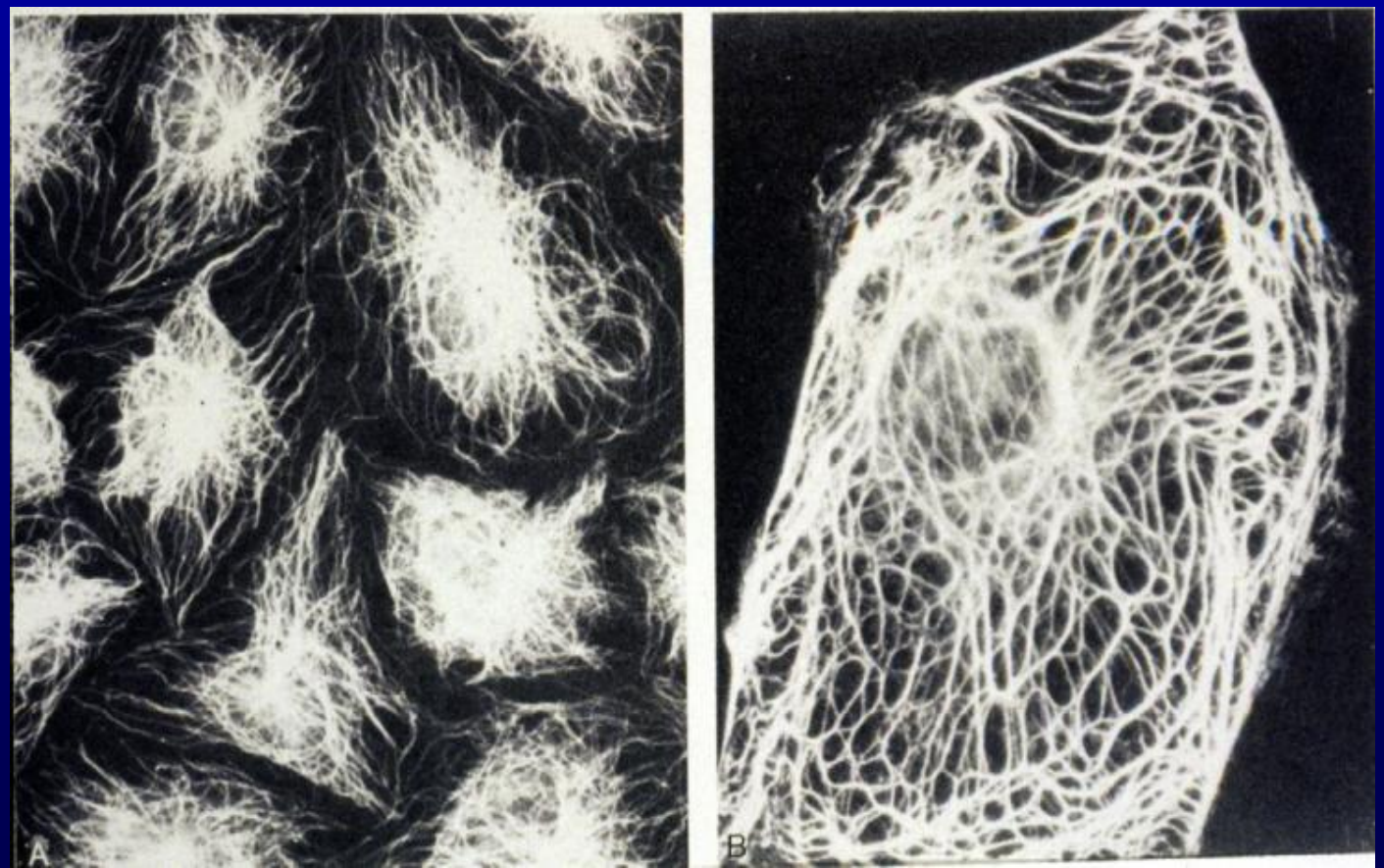
4. Neurofilaments
   - Dendrites and axons of nerve cells
   - Internal support - gelated state of cytoplasm
5. Glial filaments - astrocytes





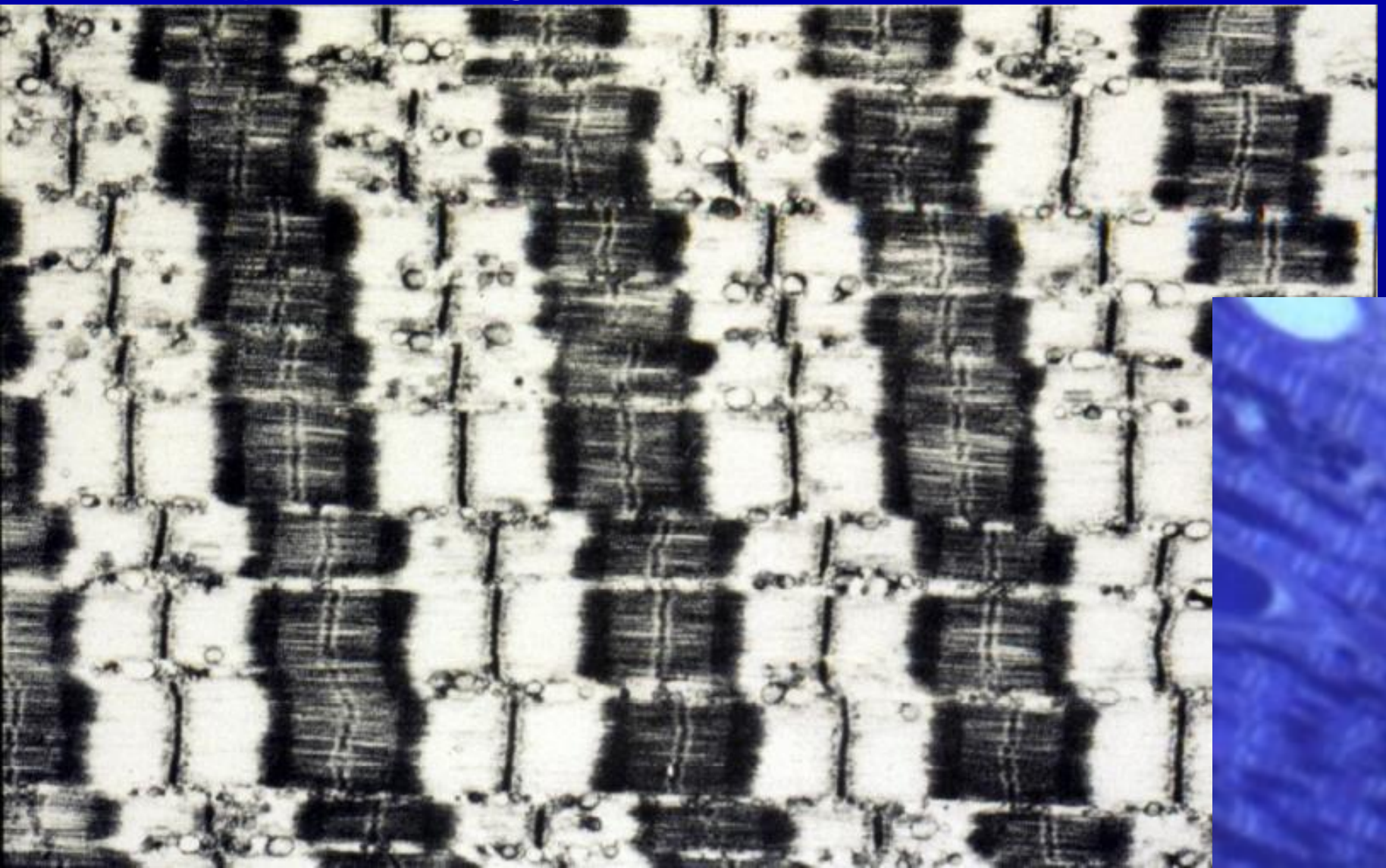
Intermediate filaments

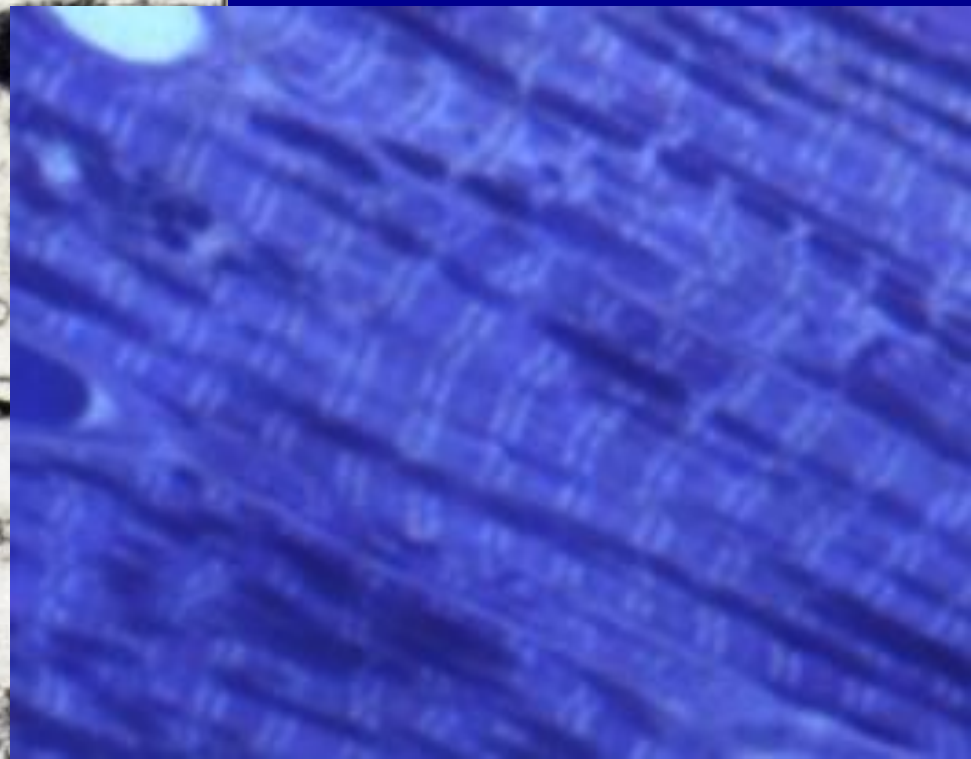
Immunofluorescence detection - tool in distinguishing cell type of origin for malignant tumors



Intermediate filaments - function

Myofibril organization - muscle

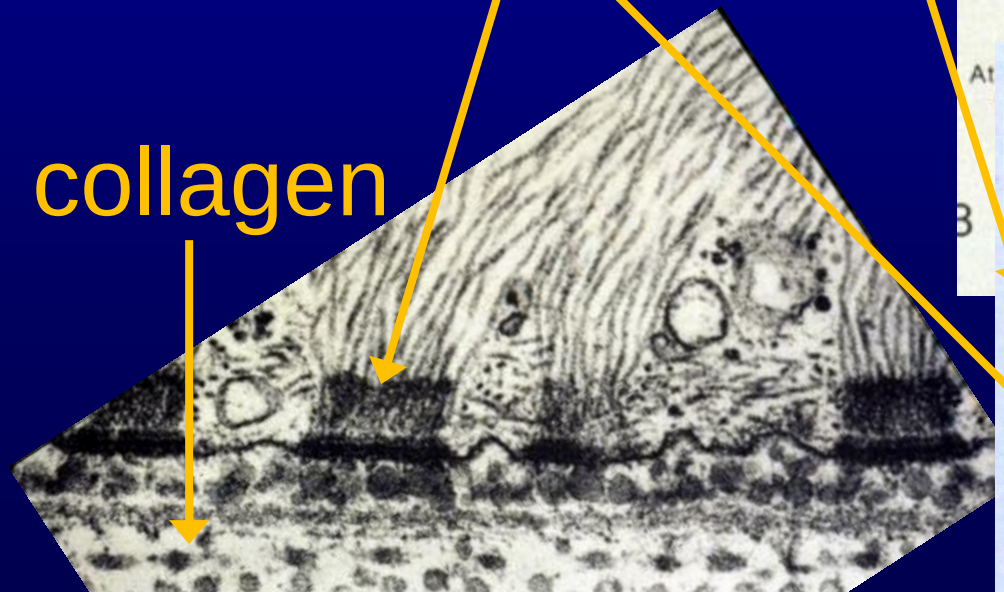


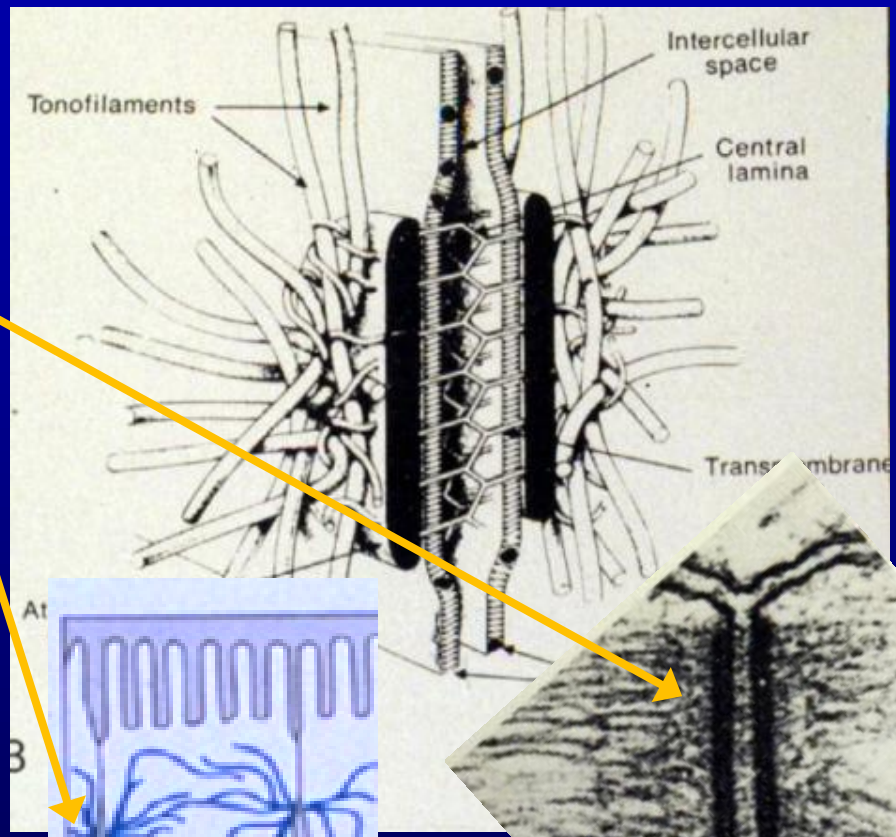


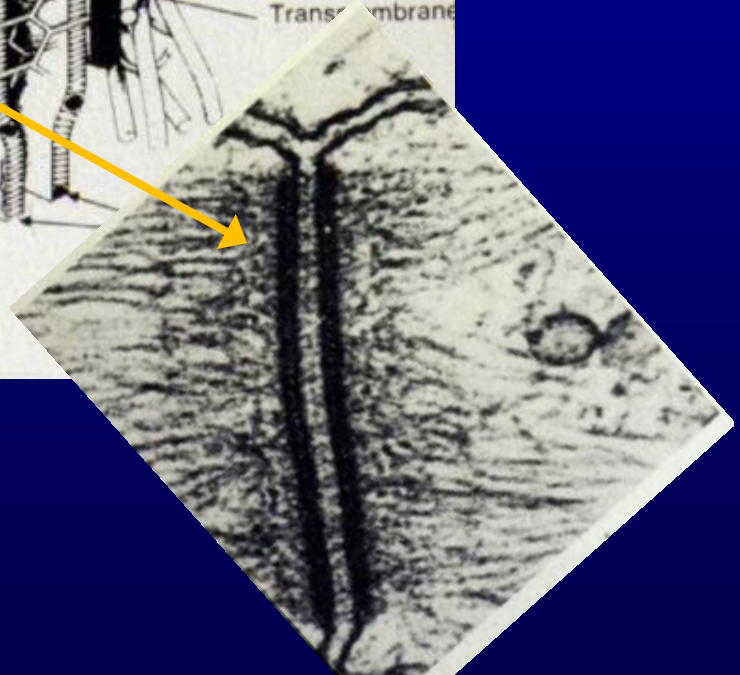
Intermediate filaments - function

Structural support of epithelial desmosomes and hemidesmosomes

collagen

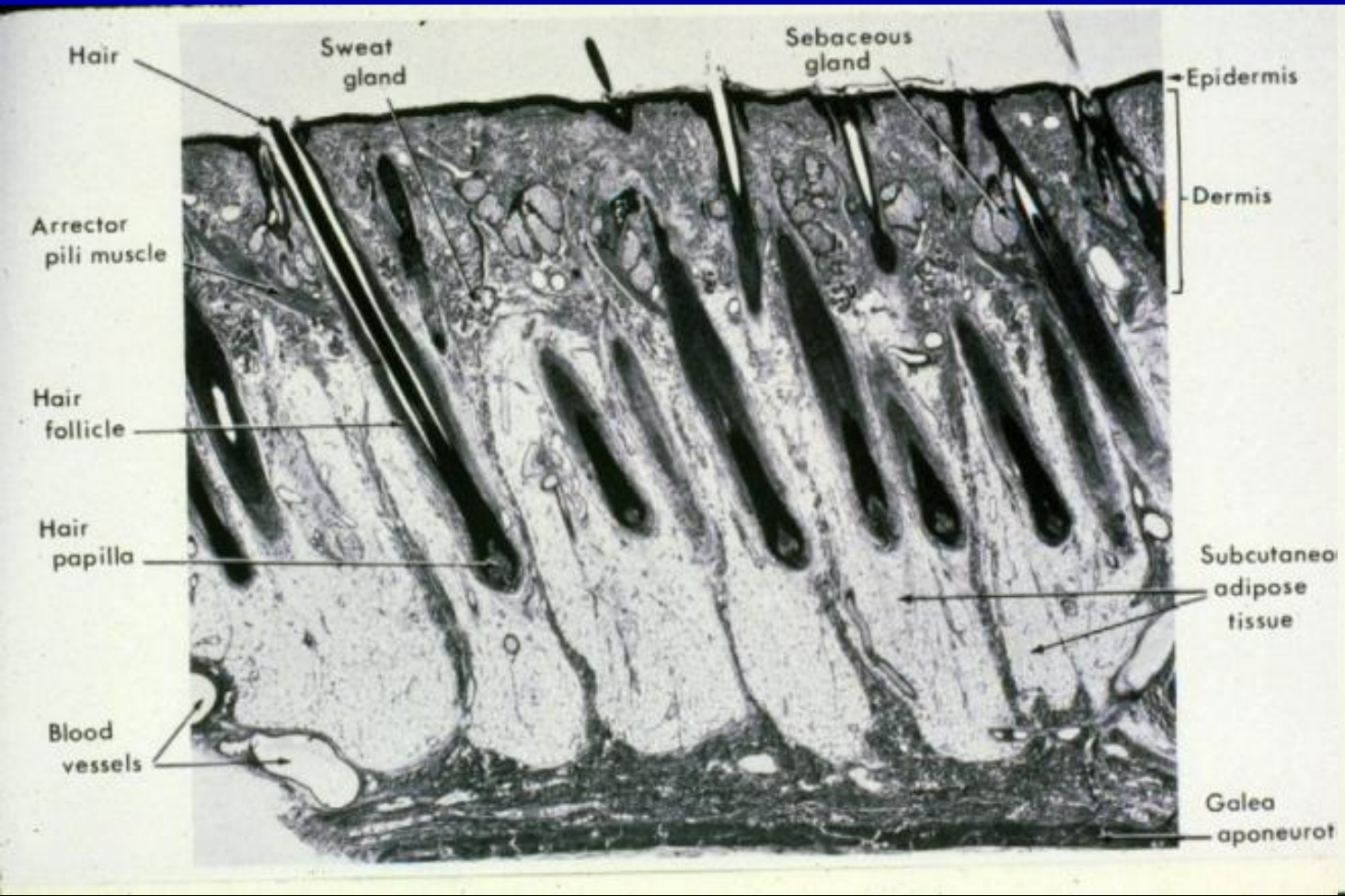


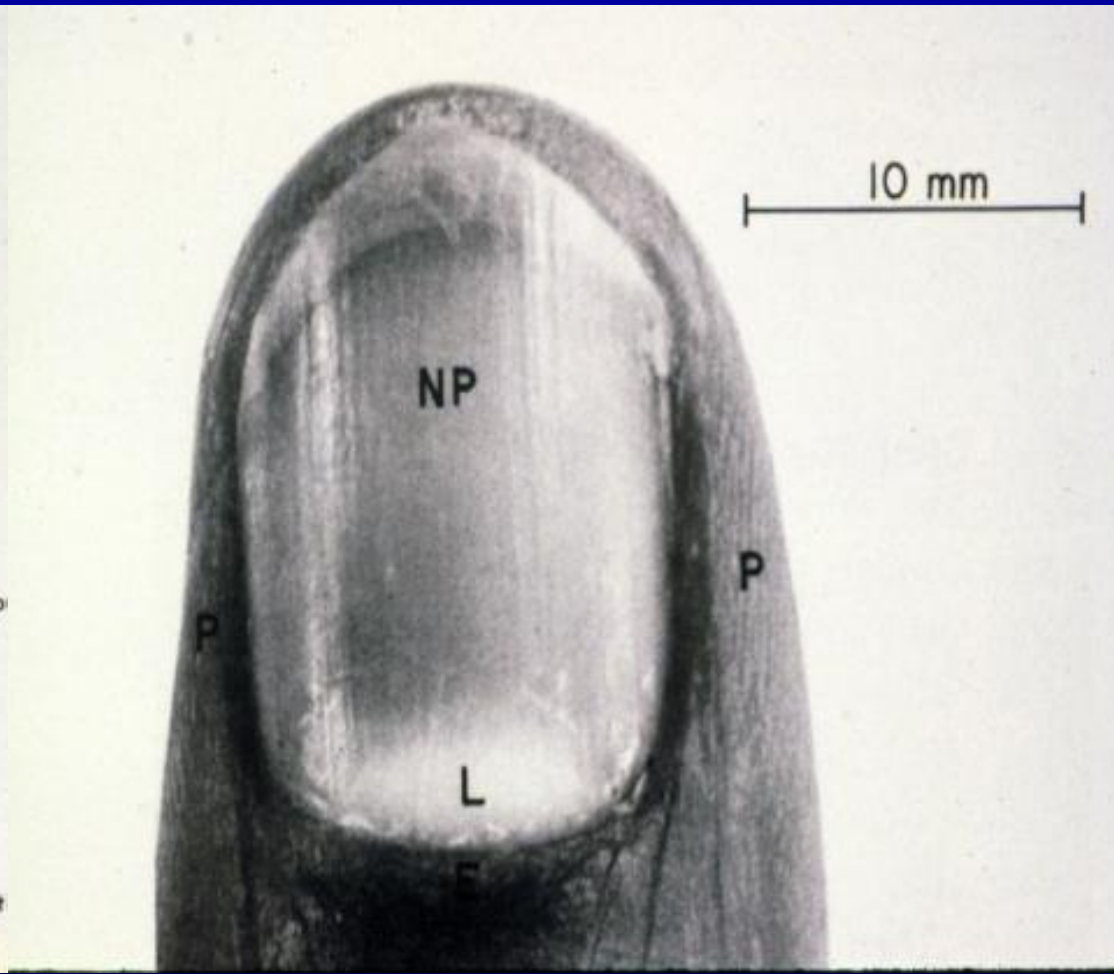




Intermediate filaments - function

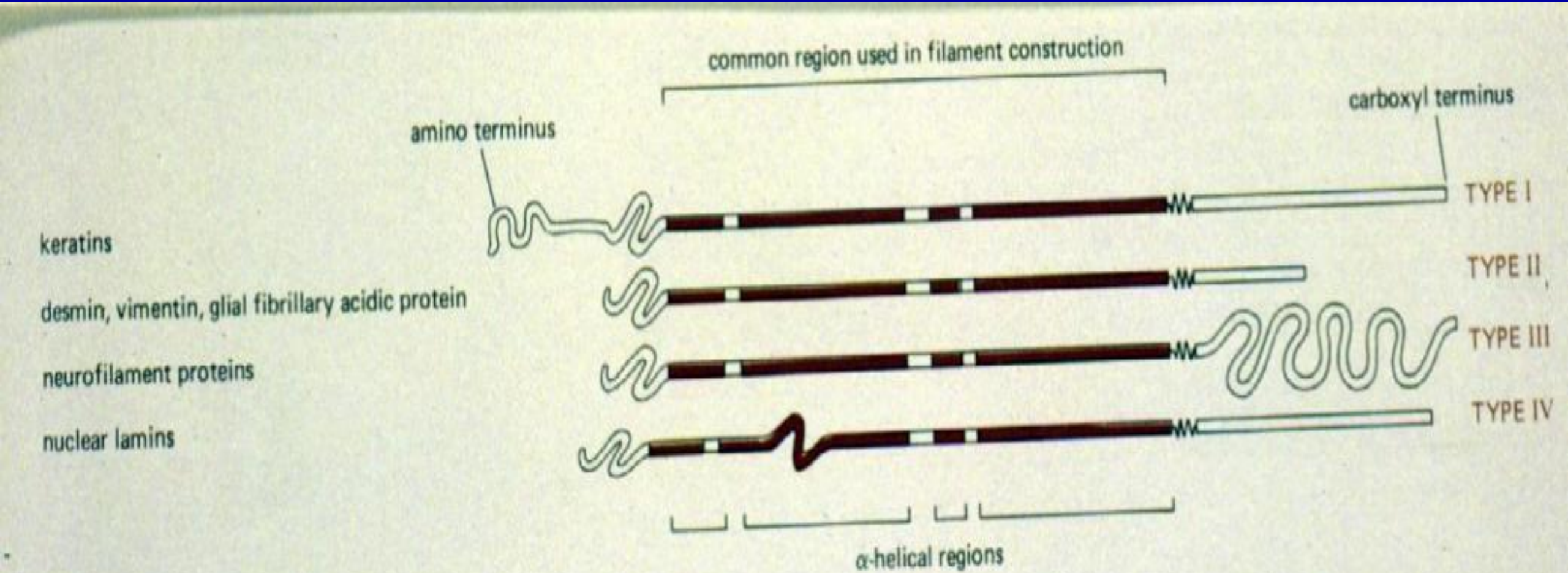
Extracellular - hair, nails, horn, feathers, and scales

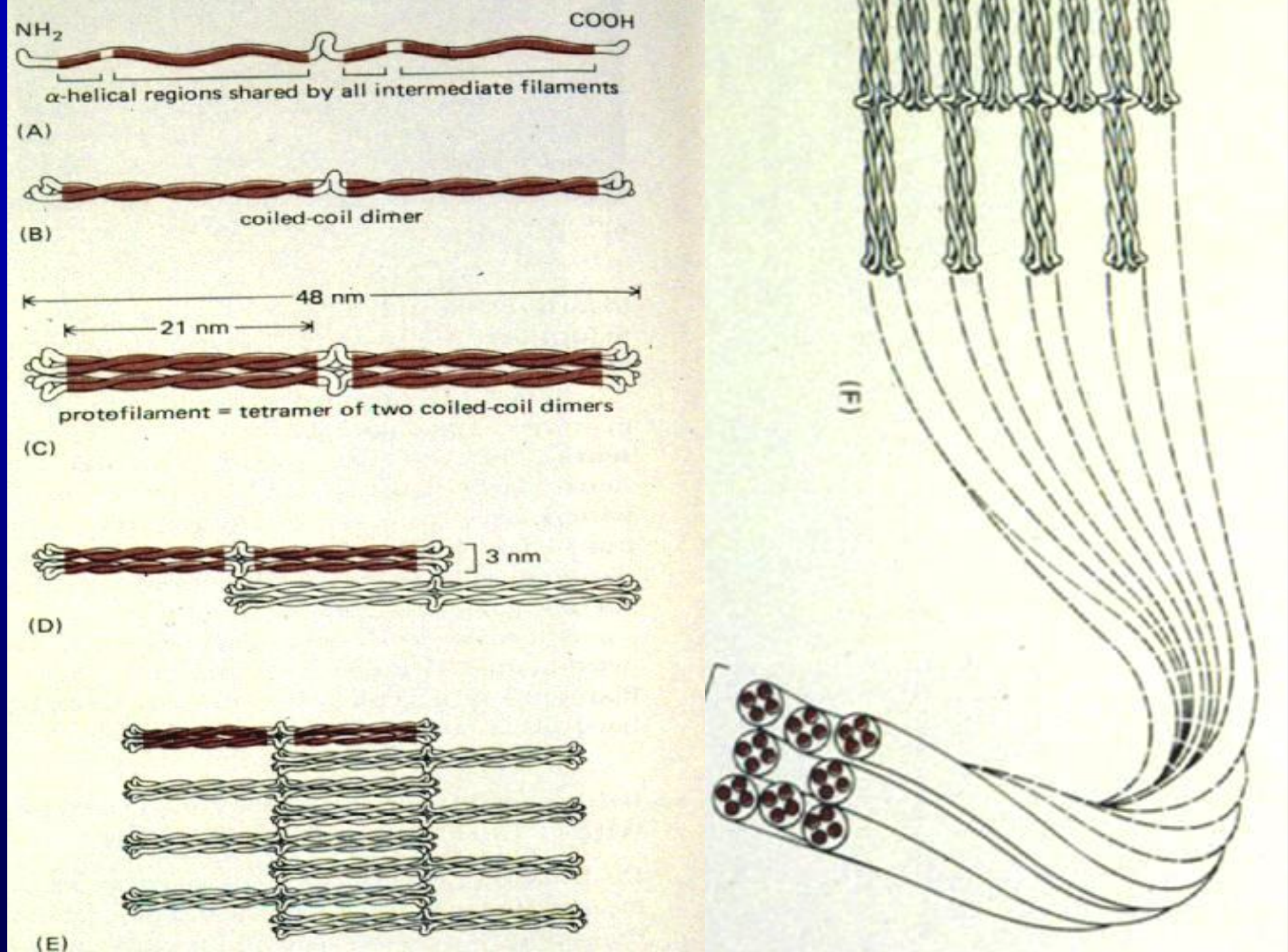




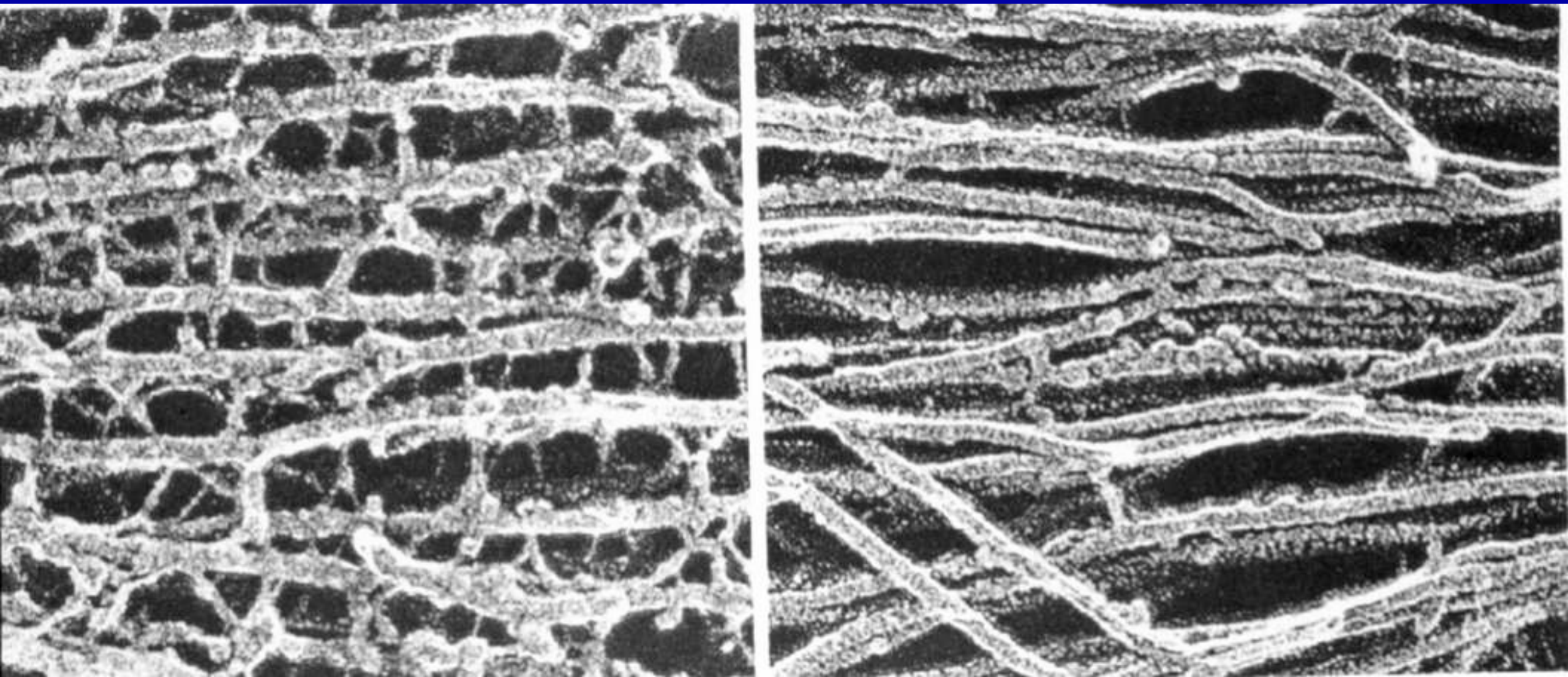
Intermediate filaments

common region in construction

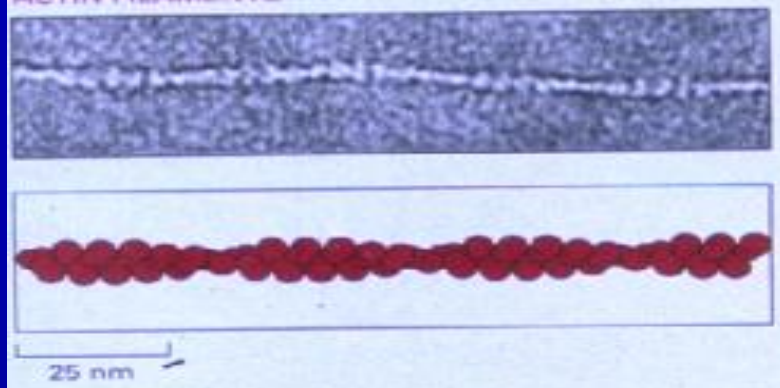


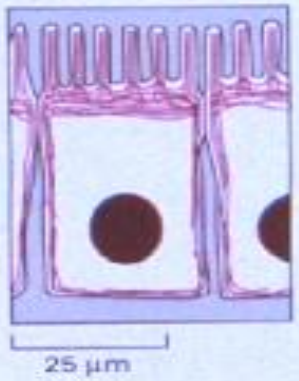

NH_2
COOH
α-helical regions shared by all intermediate filaments
(A)
coiled-coil dimer
(B)
48 nm
21 nm
protofilament = tetramer of two coiled-coil dimers
(C)
3 nm
(D)
(E)
(F)

Intermediate filaments



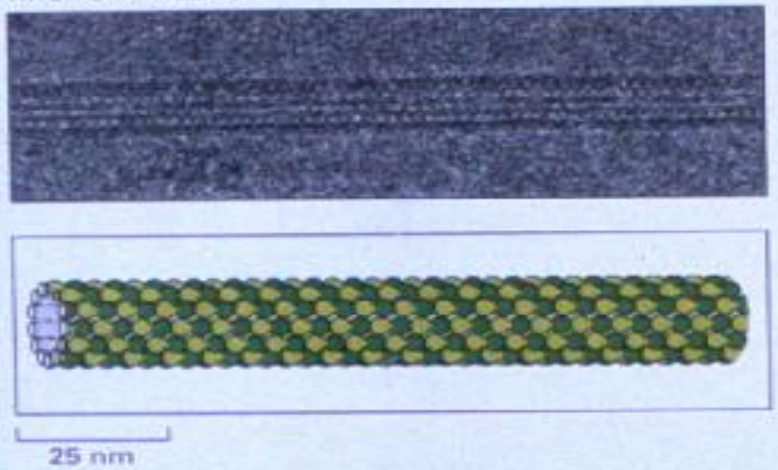
ACTIN FILAMENTS

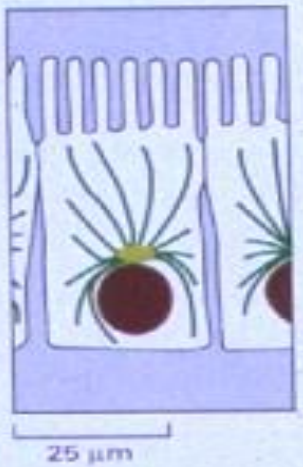




Actin filaments (also known as *microfilaments*) are two-stranded helical polymers of the protein actin. They appear as flexible structures, with a diameter of 5–9 nm, that are organized into a variety of linear bundles, two-dimensional networks, and three-dimensional gels. Although actin filaments are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

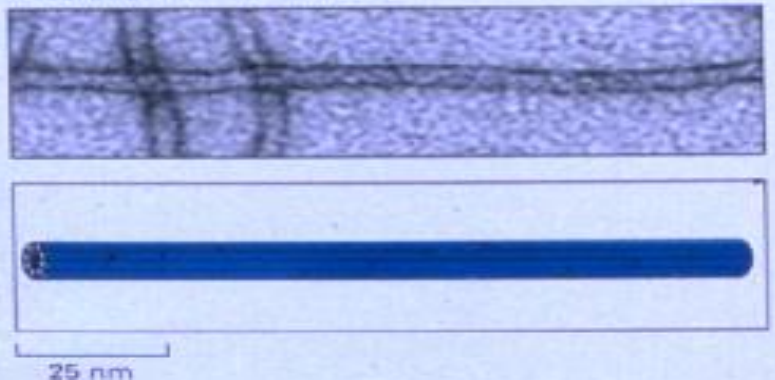
MICROTUBULES





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.

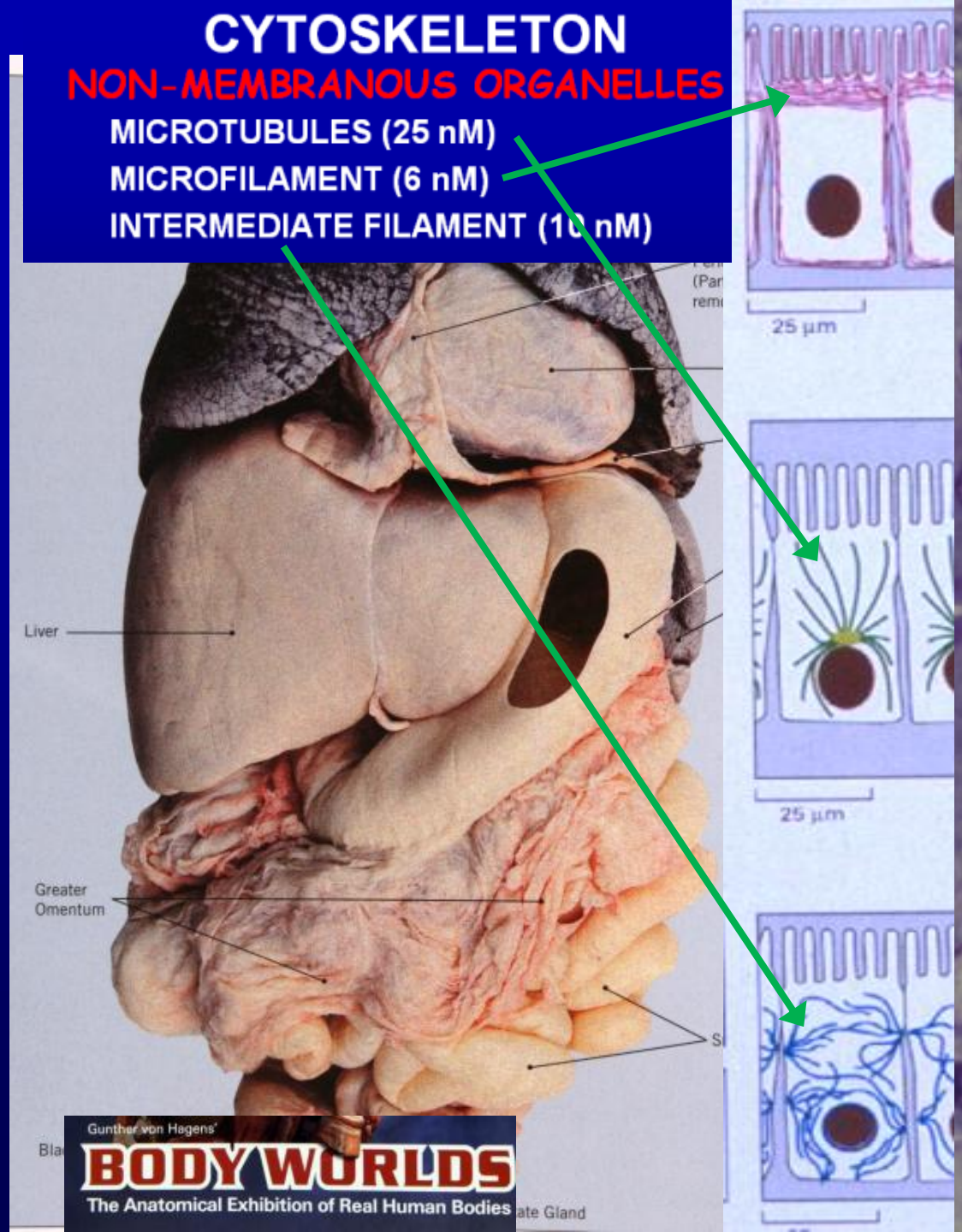
CYTOSKELETON

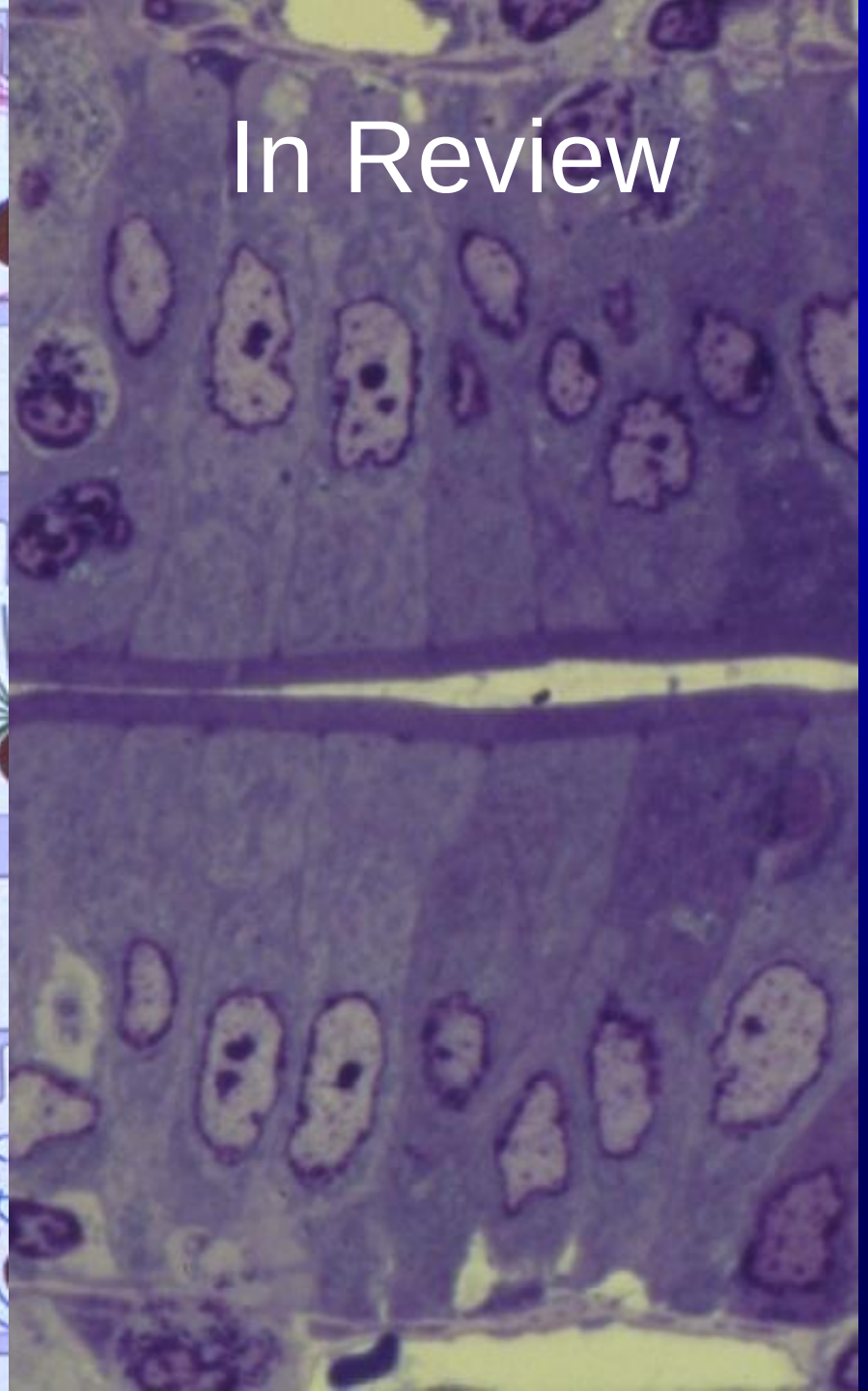
NON-MEMBRANOUS ORGANELLES

MICROTUBULES (25 nM)

MICROFILAMENT (6 nM)

INTERMEDIATE FILAMENT (10 nM)

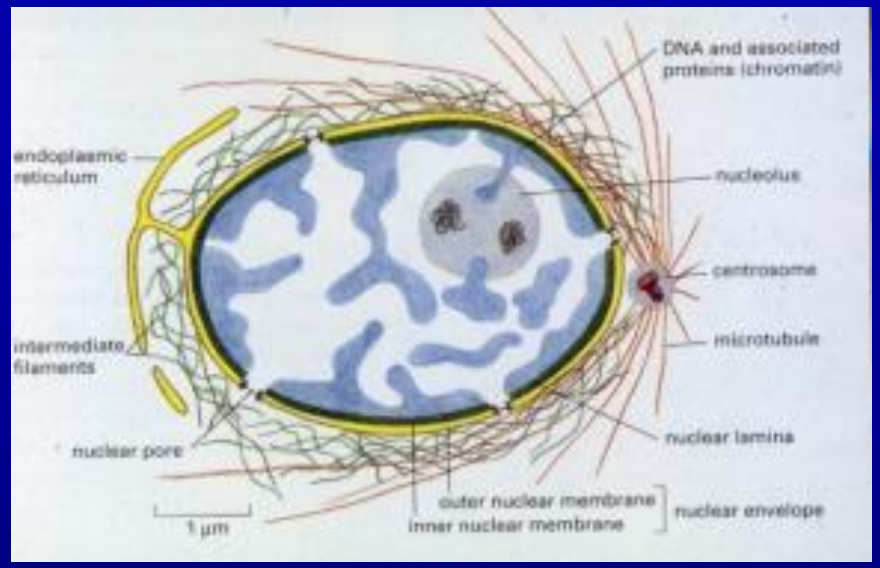


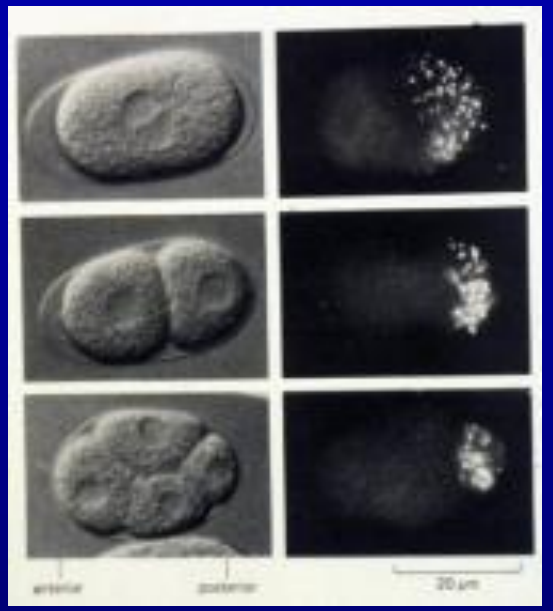


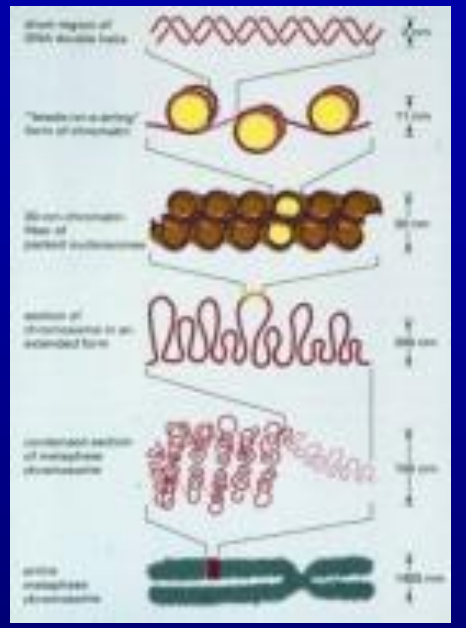
In Review

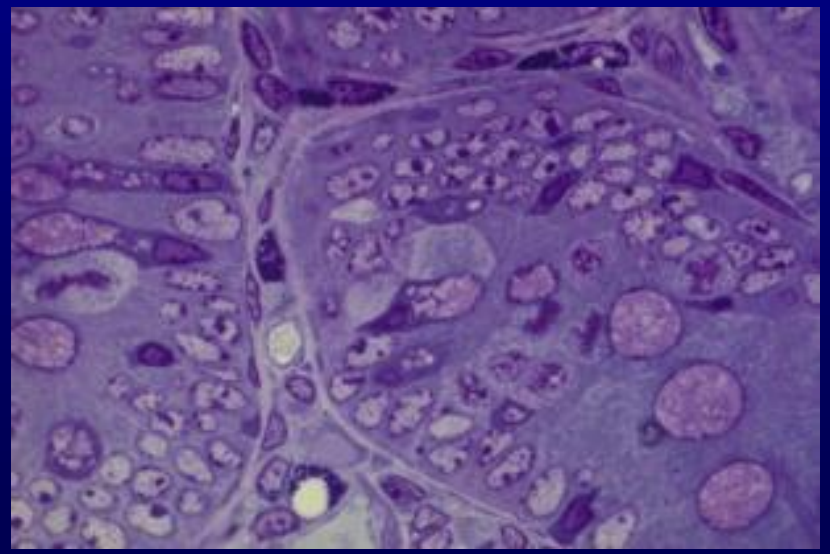
Next time

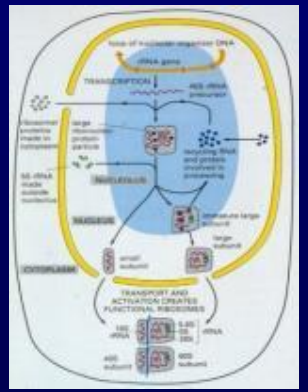
Nucleus and Mitosis

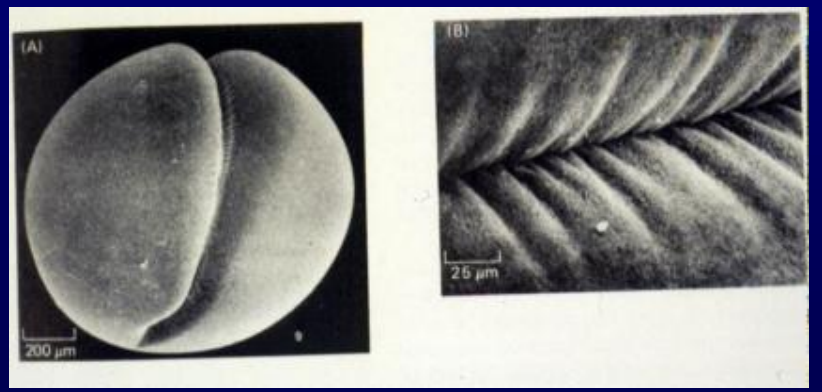












Many illustrations in these VIBS Histology YouTube videos were modified from the following books and sources: Many thanks to original sources!

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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