



Nonmembranous organelles

Cell inclusions

1. Ribosomes

2. The cytoskeleton:

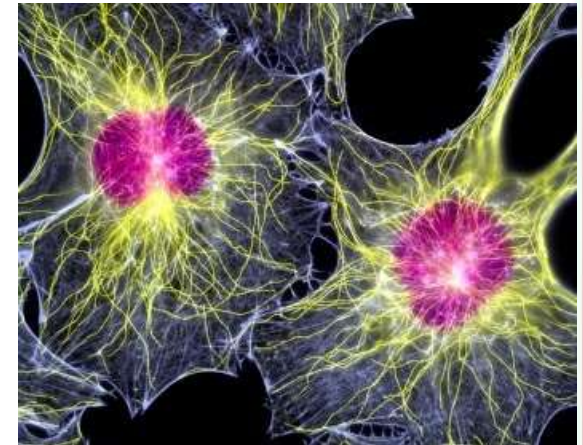
✓ **Microtubules**

➤ **Cilia and flagella**

➤ **Cell center and centrioles**

✓ **Filaments**

3. Cytoplasmic inclusions



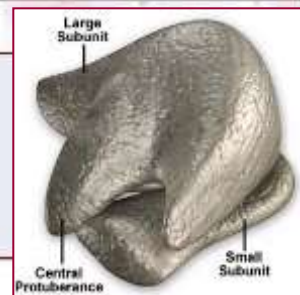


George Emil Palade (1912-2008)

The Nobel Prize in Physiology or Medicine 1974



Ribosomes



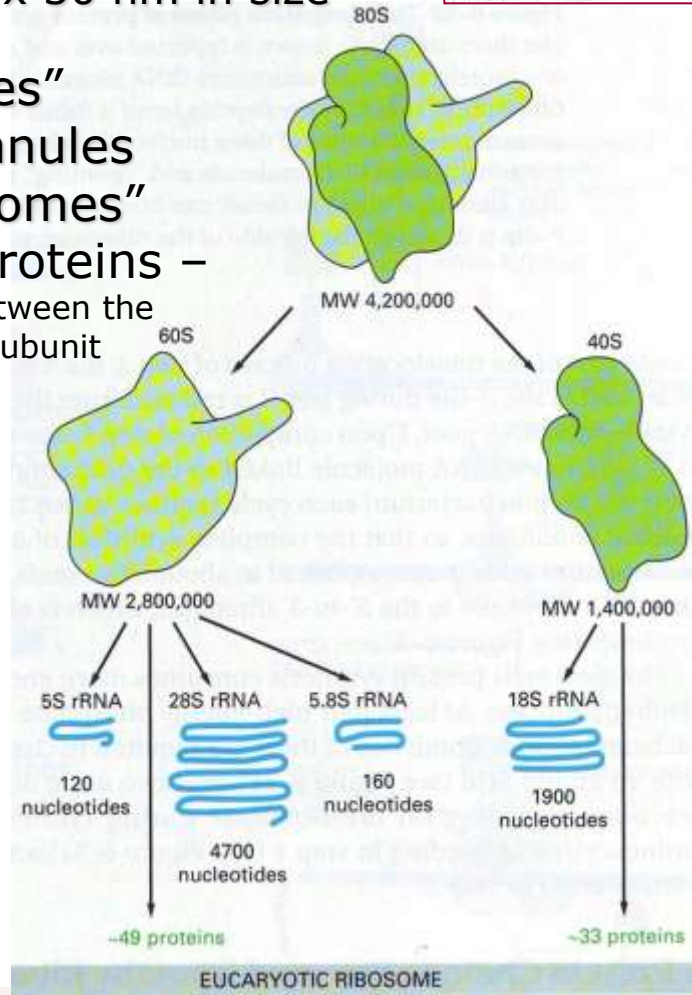
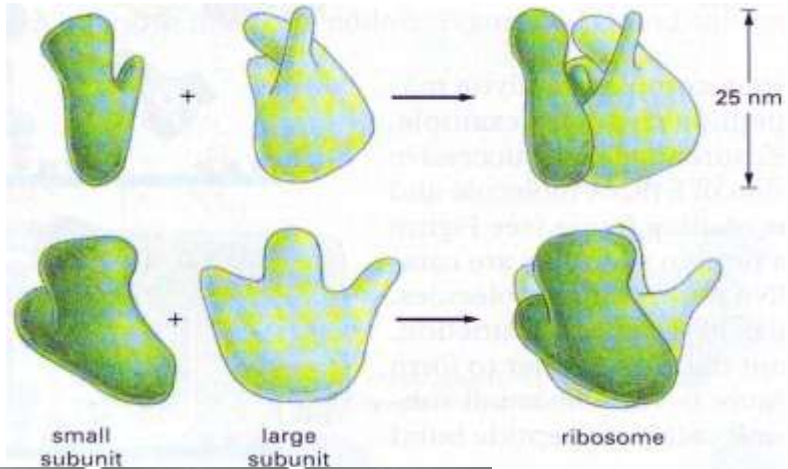
- small electron-dense particles, 20 x 30 nm in size

1943 – Albert Claude ⇒ “microsomes”

1955 – George Palade ⇒ *Palade granules*

1958 – Richard B. Roberts ⇒ “ribosomes”

✓ 65% rRNA and 35% ribonucleoproteins – two subunits linked to each other by interactions between the proteins in one subunit and the rRNAs in the other subunit



Venkatraman Ramakrishnan



Thomas A. Steitz



Ada E. Yonath



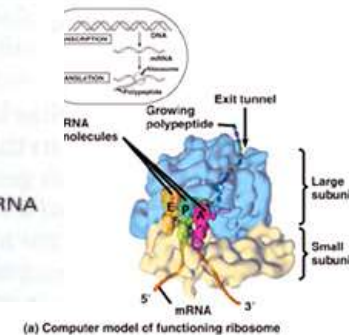
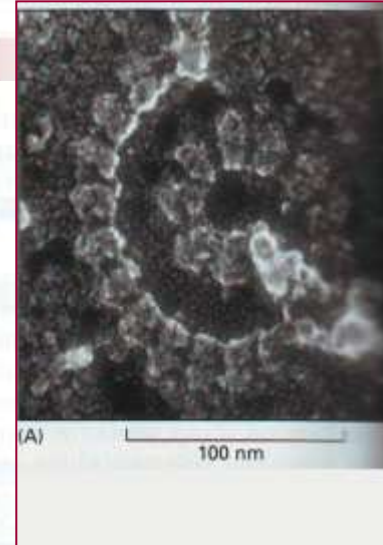
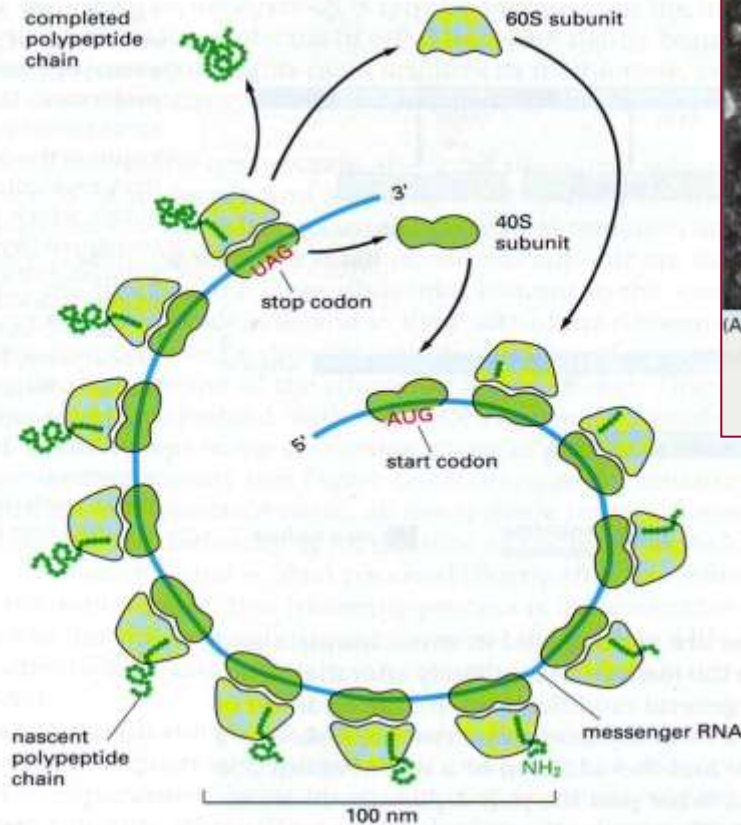
The Nobel Prize in Chemistry 2009

"for studies of the structure and function of the ribosome"

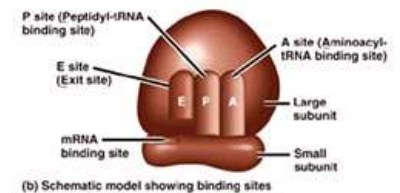
Prof. Dr. Nikolai Lazarov



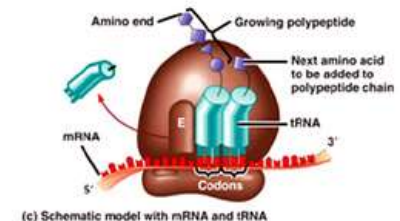
Ribosomes



(a) Computer model of functioning ribosome



(b) Schematic model showing binding sites



(c) Schematic model with mRNA and tRNA

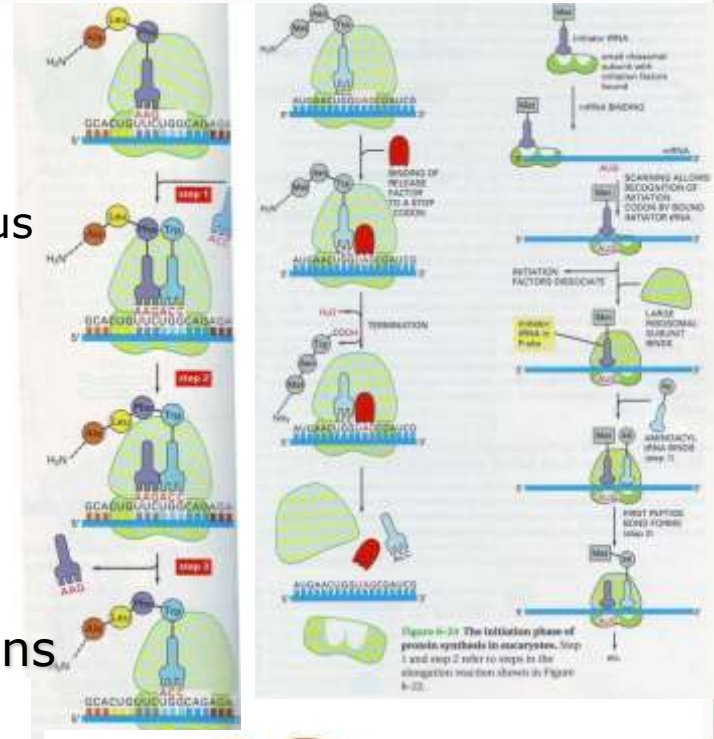
- ✓ free ribosomes ⇒ proteins for use within the cell
 - monosomes and polyribosomes (polysomes)
- ✓ bound ribosomes (ribophorins I and II)
 - ⇒ secretory proteins (Ig, collagen, hormones)



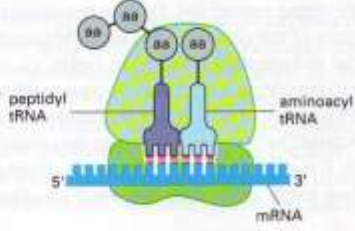
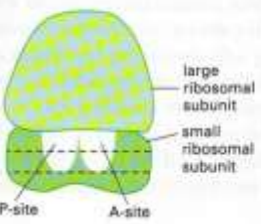
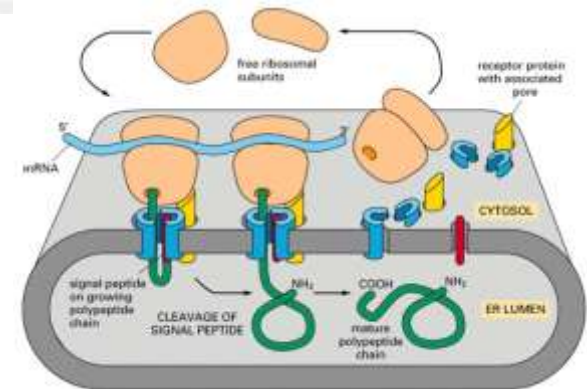
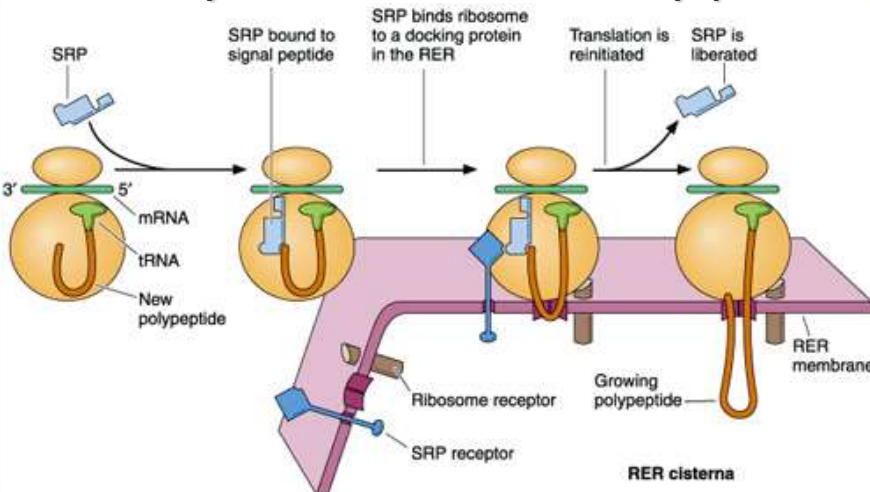
Protein synthesis

2 principal stages:

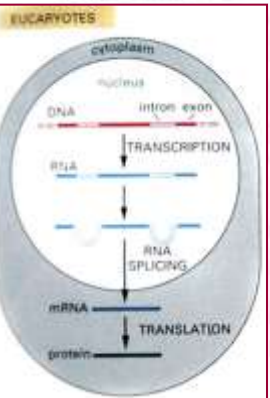
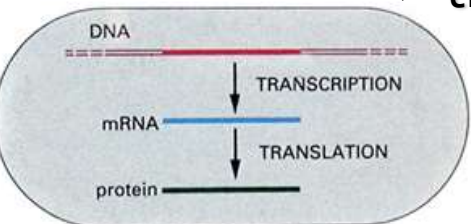
- ✓ transcription - in the cell nucleus
- ✓ translation - in the cytoplasm:
 - initiation
 - elongation
 - termination



Signal hypothesis for the synthesis of secretory proteins

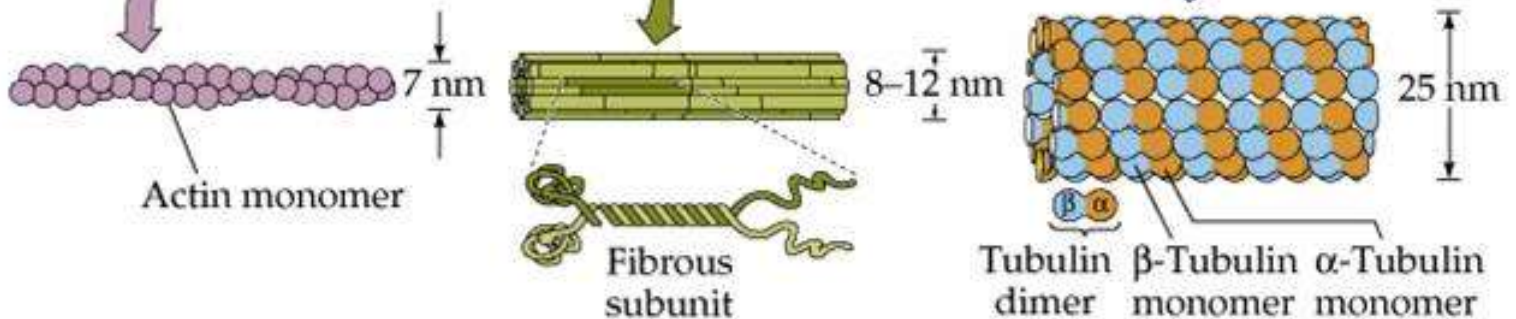
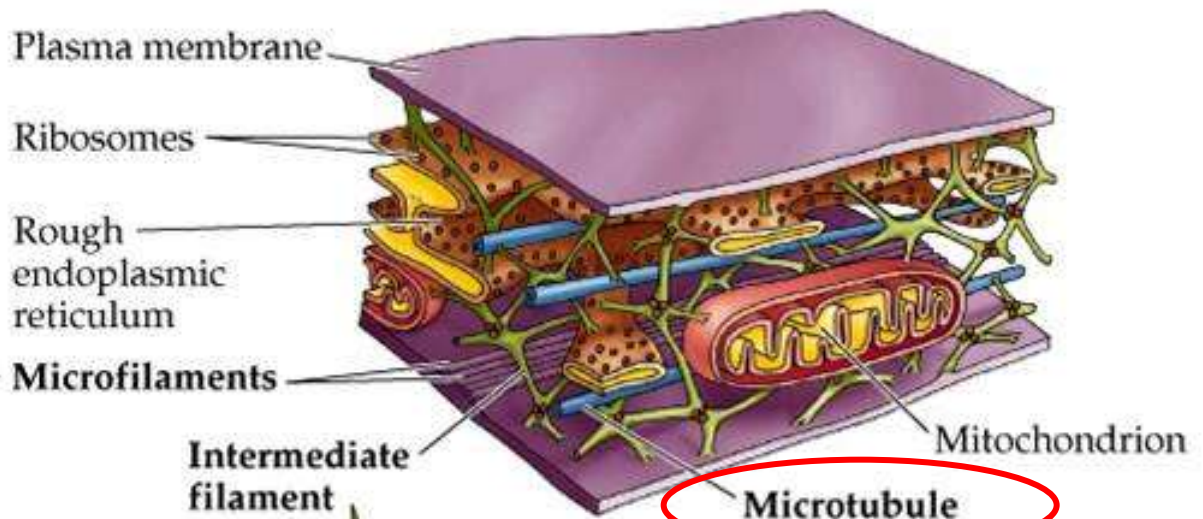


PROKARYOTES



Cytoskeleton

- Gr. *kytos*, cell + *skeleton*, dried body, 'misshapen', amorphous



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CHIFFRE ANNÉE 1931

SOCIÉTÉ DE BIOLOGIE

ET DE MÉDECINE

ANNÉE 1931 - TOME I

(CENT-SIXIÈME TOME DE LA COLLECTION)

LA SOCIÉTÉ ANNONCE LE DÉVELOPPEMENT ET LE

ÉTAT DE LA RECHERCHE EN BIOLOGIE GÉNÉRALE

ET LA SOCIÉTÉ D'ANATOMIE GÉNÉRALE

PAR PAUL WINTREBERT.

On ne peut comprendre le développement et le

fonctionnement des organismes dans les conditions

physiologiques, comme Cœklin (1927) l'a proposé pour

les œufs de *Embryonaria* et de *Cephalopoda*, l'existence d'un squelette

plasma, c'est-à-dire d'une trame protéique et élastique qui croît

dans un milieu et sert en place les divers matériaux circulaires

dans leur développement normal. Il semble, en outre, légitime

de penser que ce squelette, après la section des éléments et

de compartimentage de l'ovule en territoires stricts, est en même

temps la cause de la limitation d'activité à laquelle on a donné le

nom de rigidité et qui, partant du pôle végétal, gagne peu à

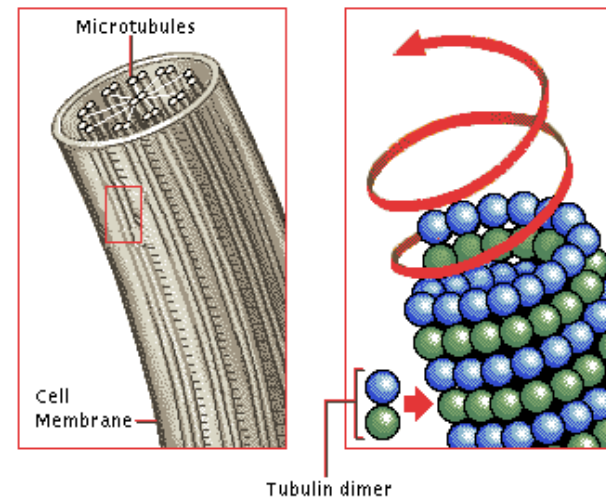
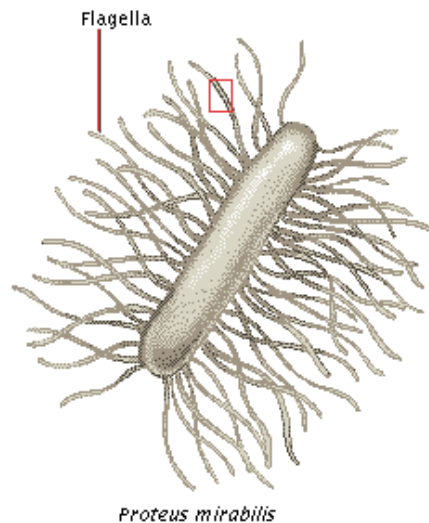
peu le pôle animal.

Paul Wintrebert
1931



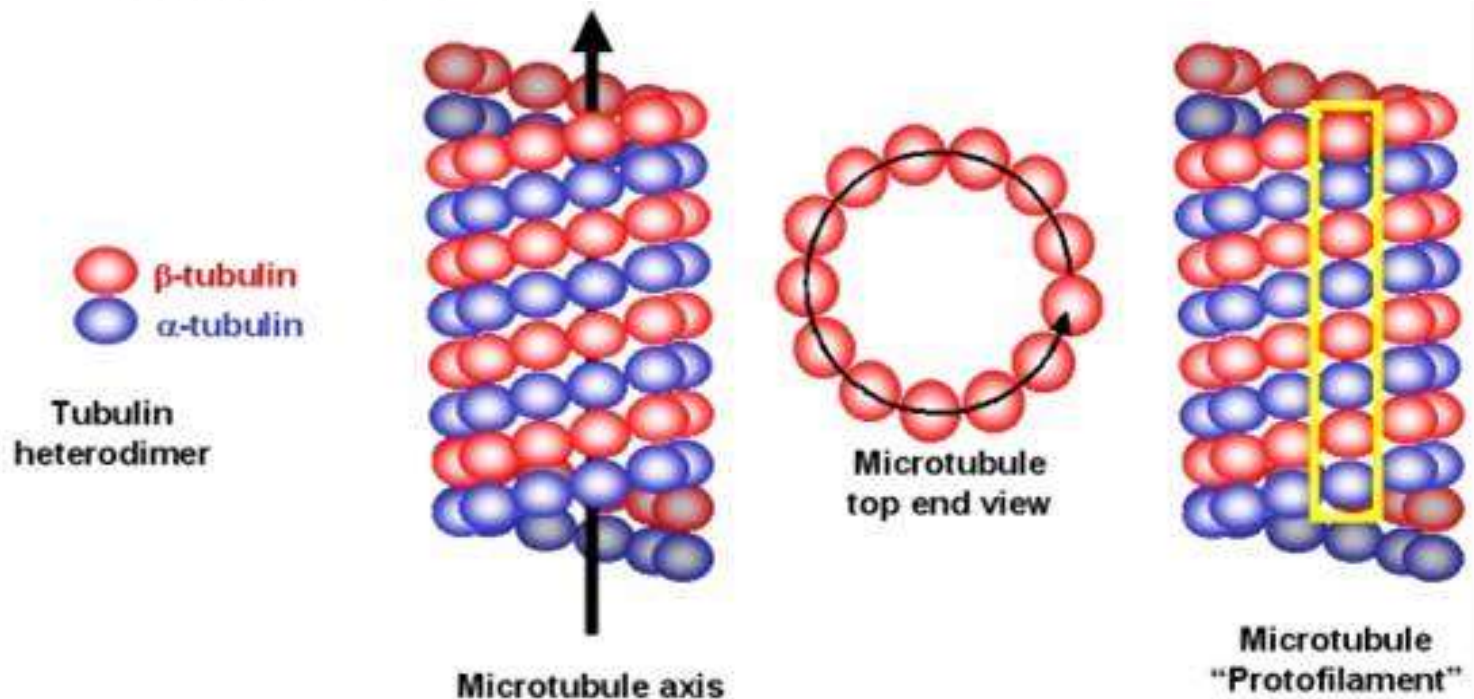
Microtubules

- nonbranching, elongated hollow cylinders, made of protein
- Gr. *micros*, small + *tubulus*, tubule
 - ✓ outer diameter = 24-25 nm
 - ✓ varying length = several μm
- seen only under EM – first described in 1963
- dynamic instability – after fixation:
 - ✓ stabile
 - ✓ labile



Microtubules – structure

- arranged as a ring of 13 protofilaments
- main component – dimeric *tubulin* (alpha&beta)
 - ✓ globular protein d=3.5-5 nm and m.w. 50 kDa
 - ✓ isolated in 1975



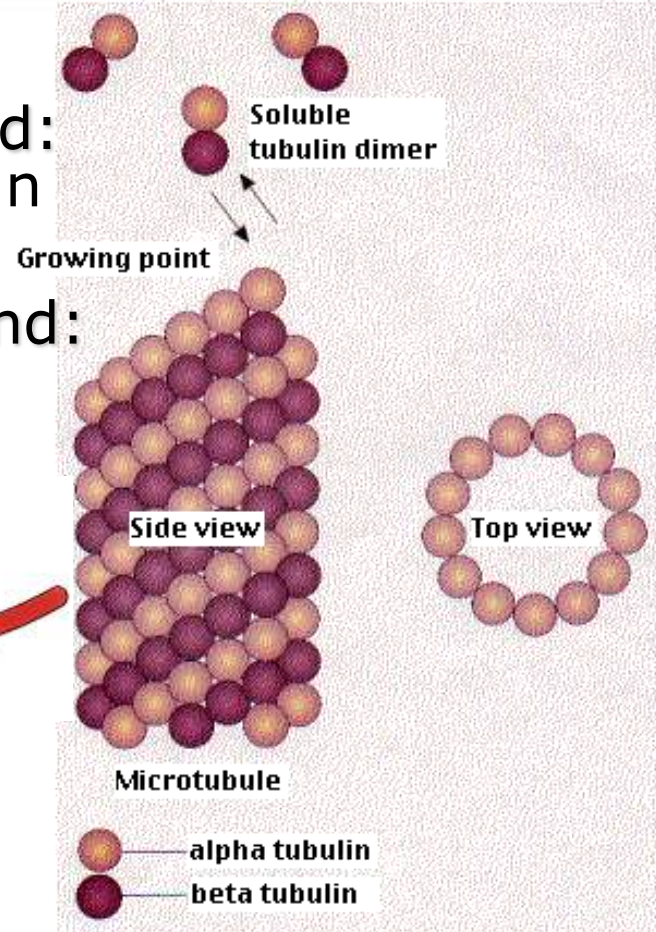
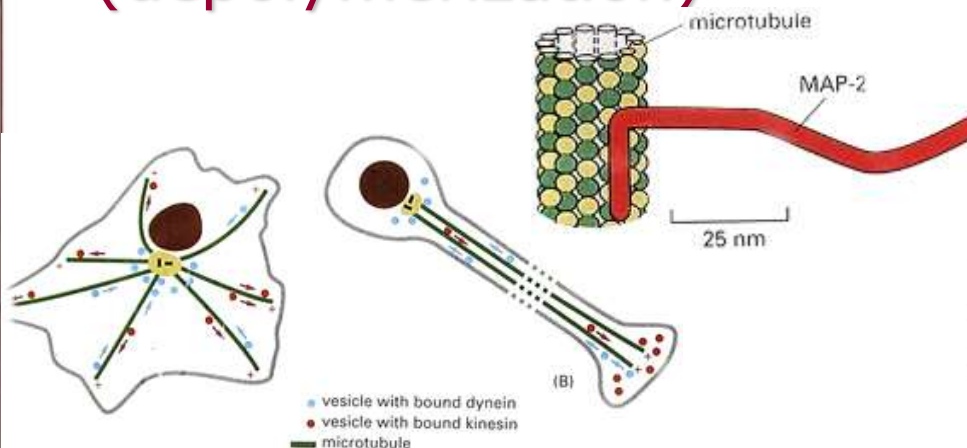
wall – 5 nm thick; hollow core – 14 nm wide



Microtubules – elongation

▪ microtubule organizing centers

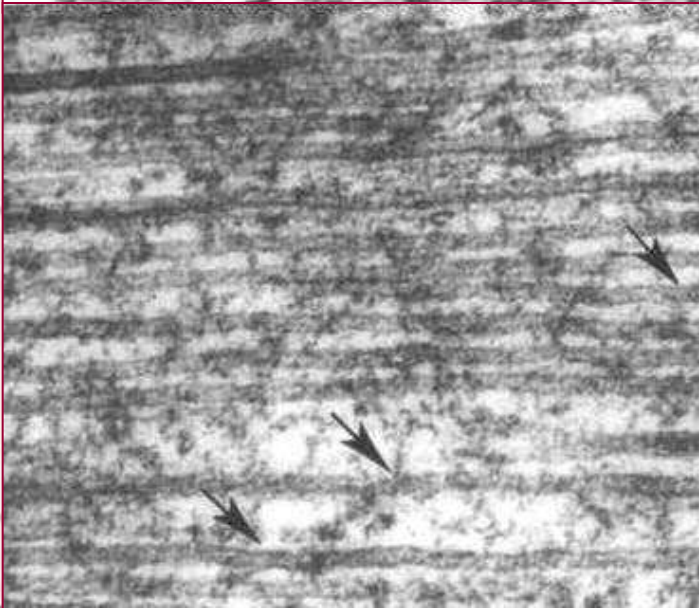
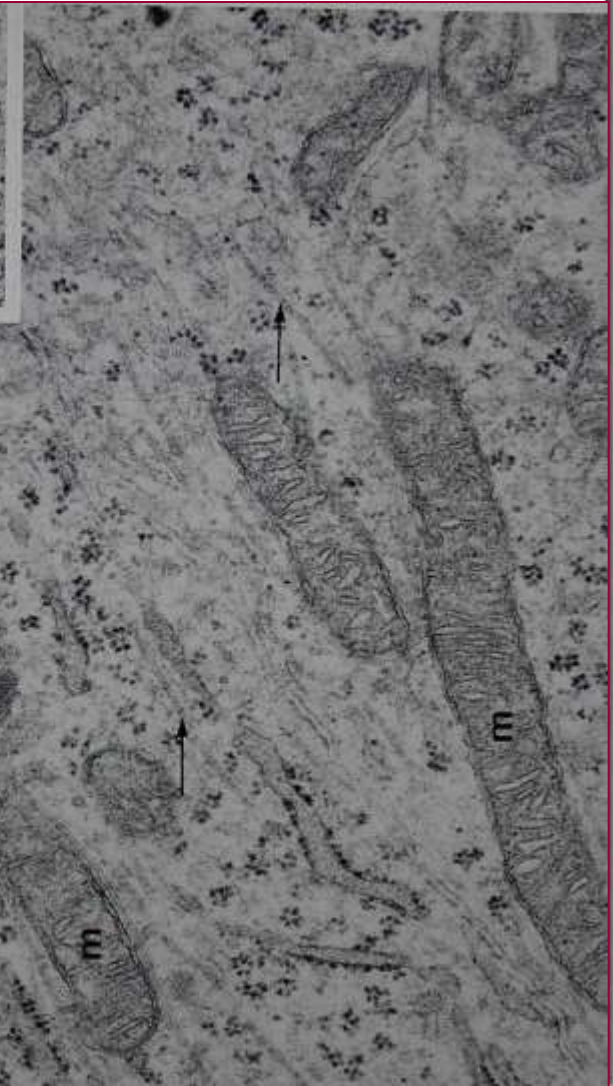
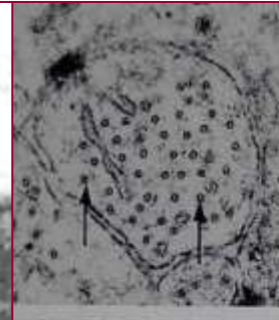
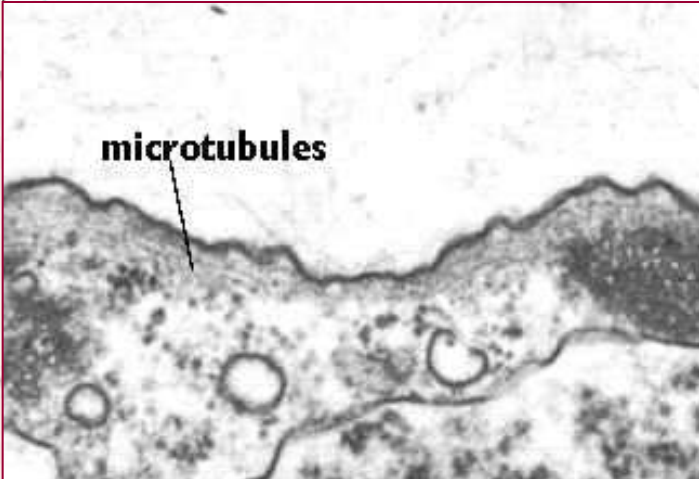
- ✓ positive (+) fast-growing end: growing via adding of tubulin dimers (**polymerization**)
- ✓ negative (-) slow-growing end: removal of tubulin dimers (**depolymerization**)



- ✓ stabilization of the structure: equilibrium of polymerization and depolymerization by means of microtubule-associated proteins (MAP-1 and MAP-2)



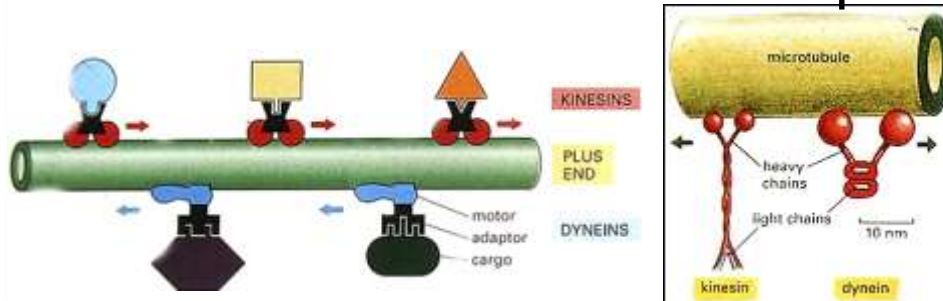
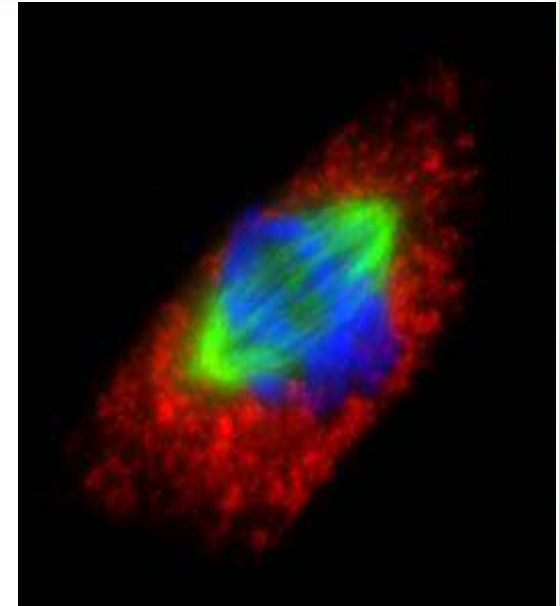
Microtubules - ultrastructure





Microtubules – functions

- component of the cytoskeleton – development and maintenance of cell shape
- intracellular transport of other organelles: motor proteins (kinesins and dyneins)
- formation of the mitotic spindle



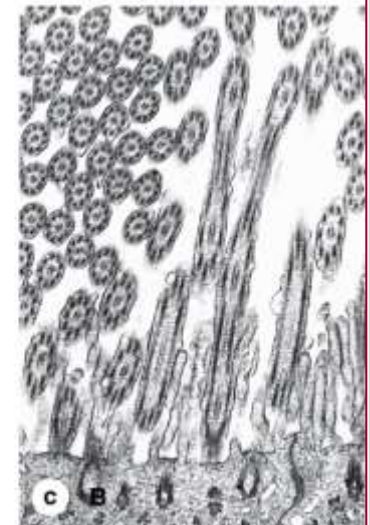
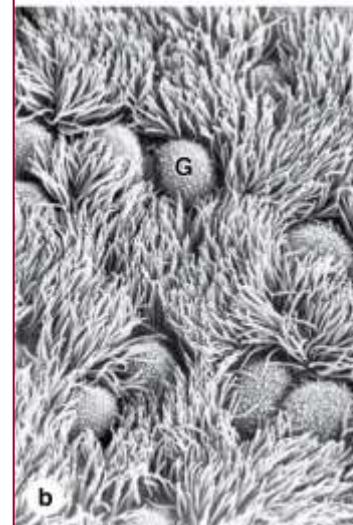
- antimitotic alkaloids – experimental inhibition of mitosis:
 - ✓ colchicine
 - ✓ vinblastine
 - ✓ vincristine➔ cancer treatment (chemotherapy)
- basis for formation of centrioles, basal bodies, 10 cilia and flagella





Cilia

- ✓ cilia = **kinocilia**
Gr. kinesis, movement + cilium, eyelash
 - motile cilia
 - seen on the apical domain of many epithelial cells
- ✓ sensocilia = **monocilia**
 - immotile cilia
- ✓ **stereocilia (stereovilli)**
Gr. stereos = solid, firm
 - resemble microvilli of unusual length
 - much longer but less motile
 - may show branching distally
 - observed in the epididymis, the ductus deferens and the hair cells of the inner ear





Kinocilia

length: 2-10 μm
 diameter: 0.3-0.5 μm

axoneme
 (central core):

9 doublets + 2 singlets
 $9 \times 2 + 2$
 axonemal organization



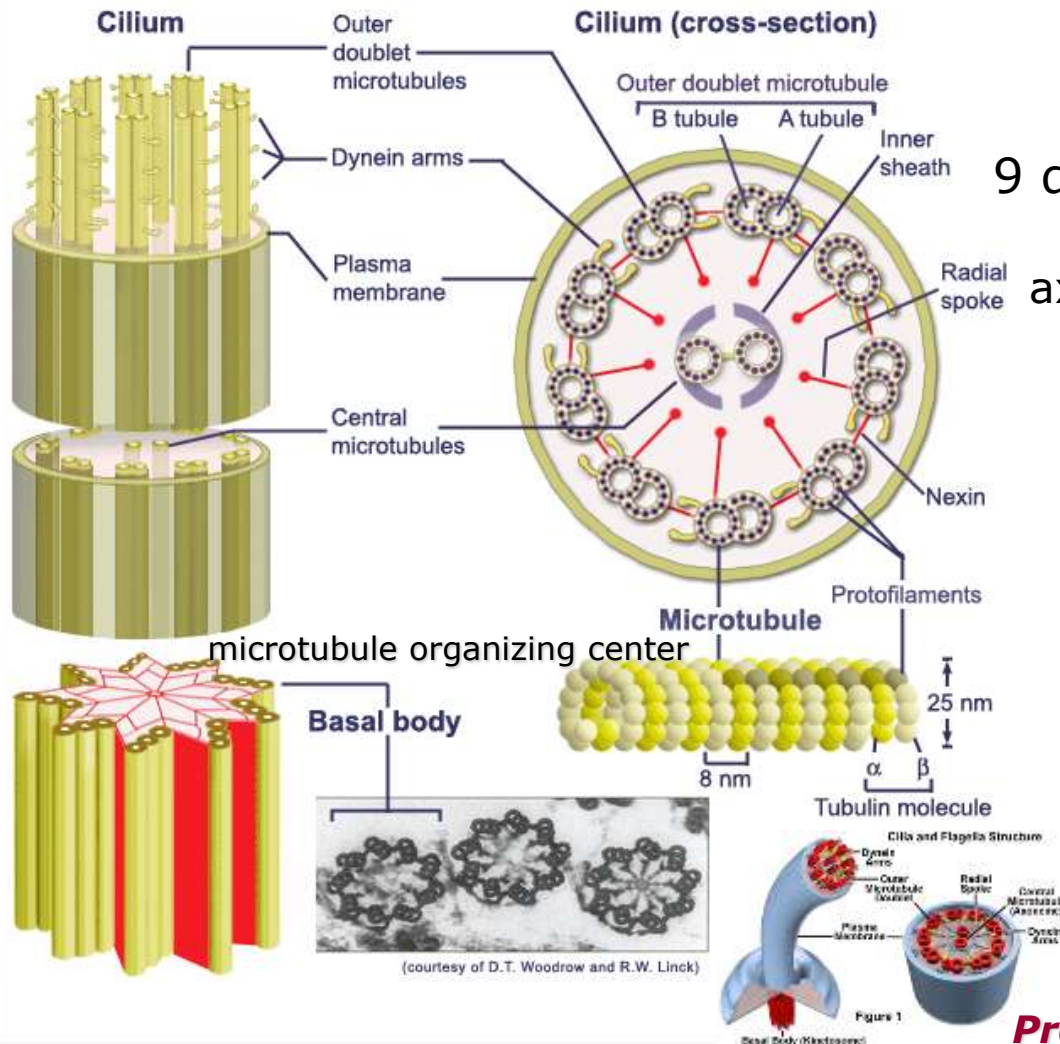
transitory part:



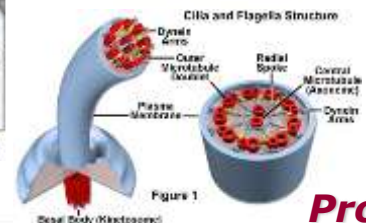
basal bodies
 (kinetosome):

9 triplets
 $9 \times 3 + 0$

12



(courtesy of D.T. Woodrow and R.W. Linck)



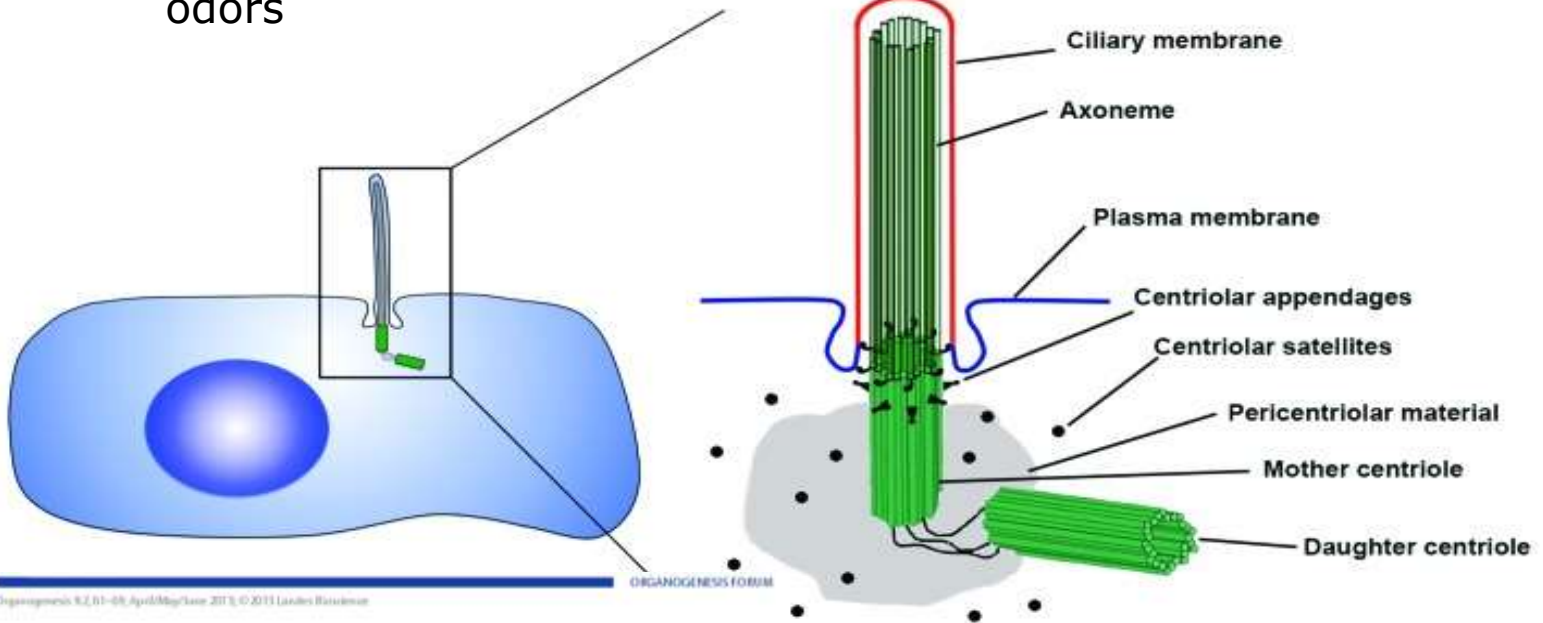


Sensocilia

- Single primary cilia (monocilia)
 - ✓ non motile
 - ✓ enriched with receptors and signal transduction complexes for detection of light, sound or odors

axoneme
(central core):

9 doublets + 0 singlets
 $9 \times 2 + 0$
axonemal organization



Organogenesis 5,2, 01-08 April/May/June 2013, © 2013 Landes Bioscience

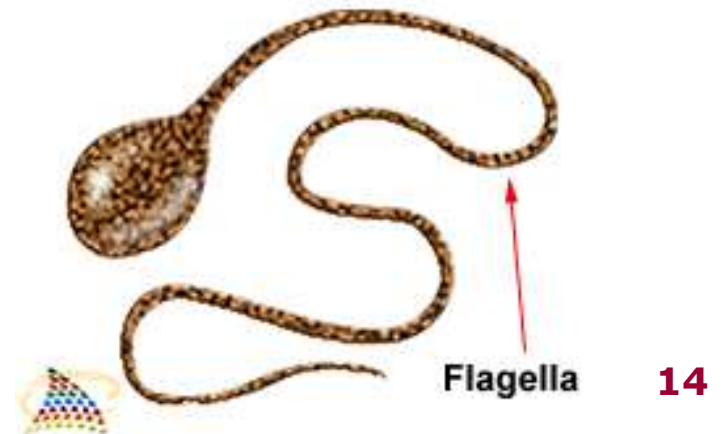
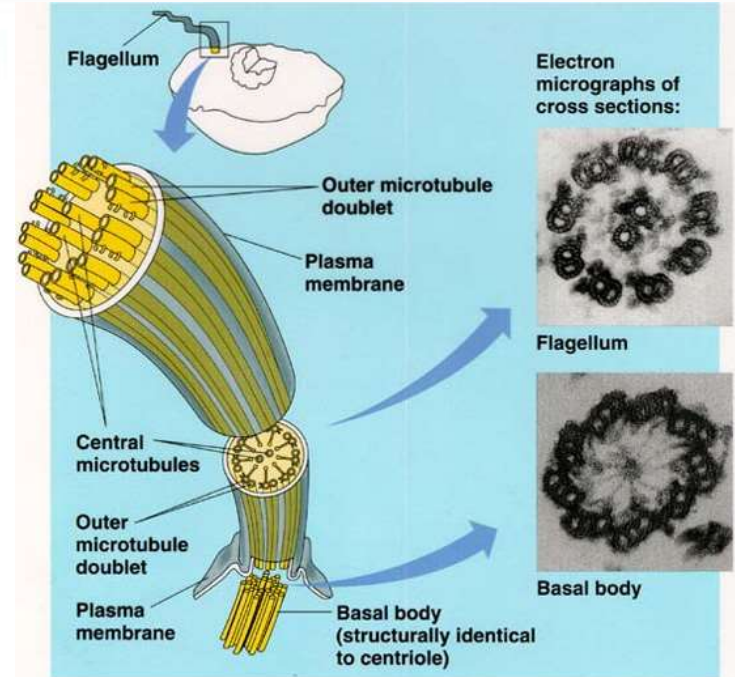
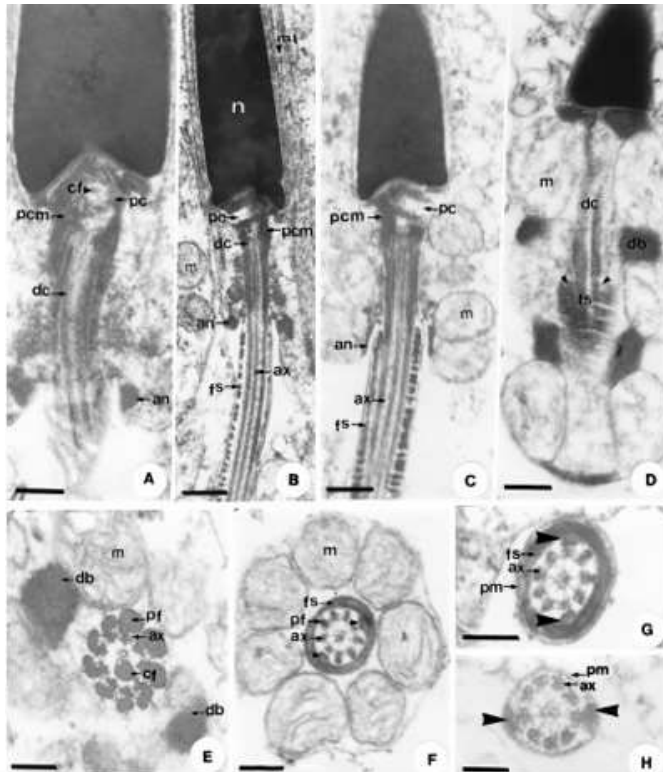


The importance of a single primary cilium

Mira R. Mahjoub
Department of Medicine, Waikato University, St. Louis, MO, USA

Flagellum

- ✓ much longer: 100-200 μm
- ✓ limited to one flagellum per cell
- ✓ in the human body only in spermatozoa

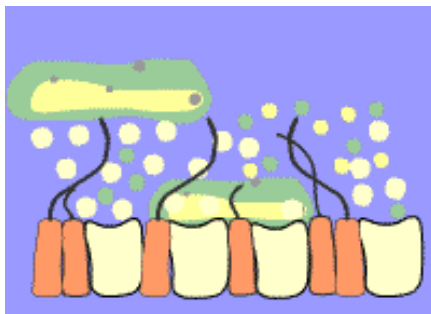
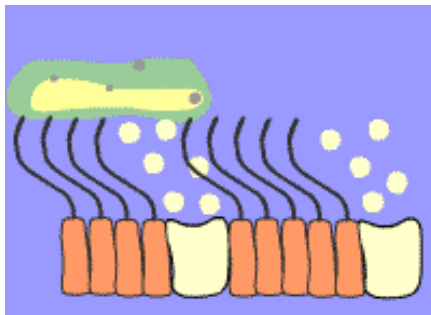
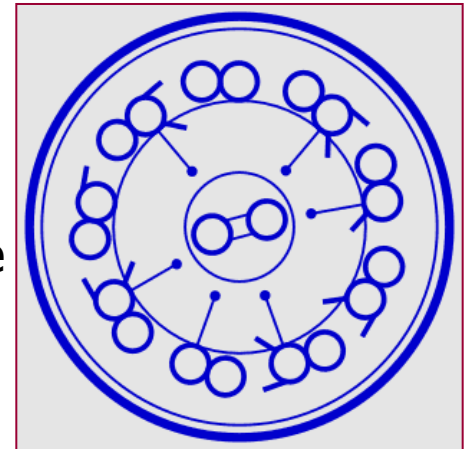


Kartagener's syndrome

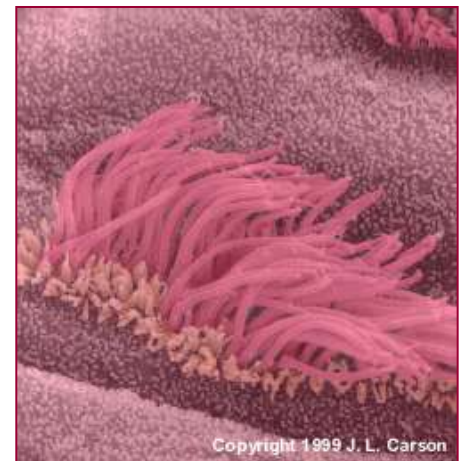


Manes Kartagener
(1897-1975)

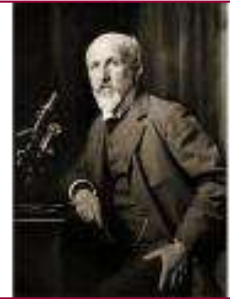
- immotile ciliary syndrome of *Kartagener*
⇒ a defect in the action of the cilia lining the respiratory tract and fallopian tube due to the absence of dynein arms in them



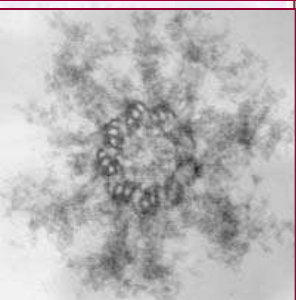
- Chronic respiratory infections and male infertility:
 - ✓ chronic rhinitis
 - ✓ chronic sinusitis
 - ✓ chronic bronchitis
 - ✓ bronchiectasis
 - ✓ sterile males
 - ✓ females may be fertile



Cell center

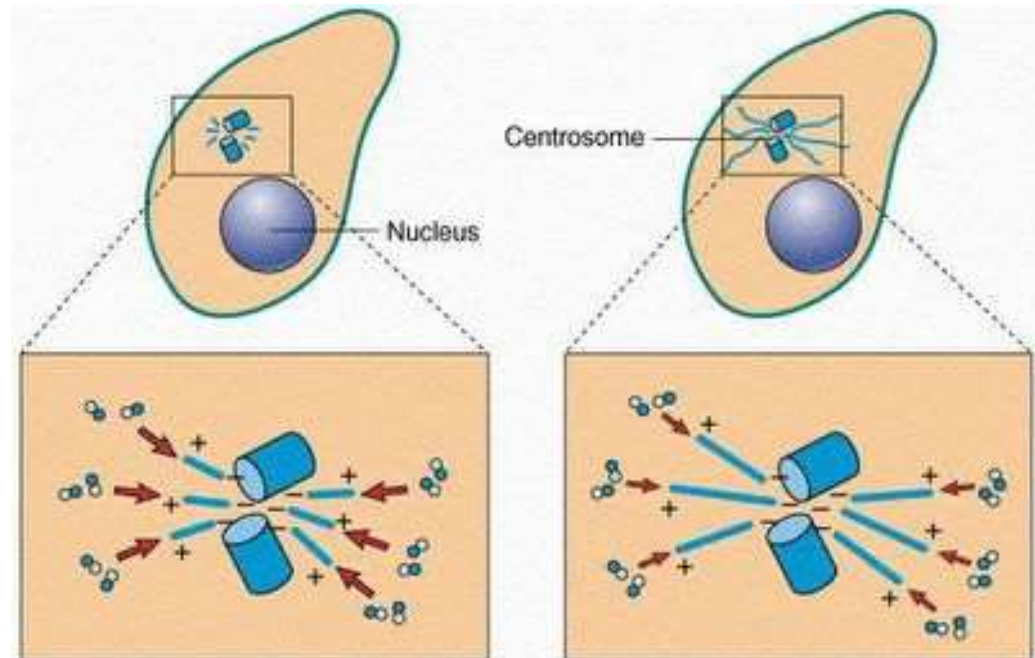


Oscar Hertwig
1849-1922



- synonym: **centrosome**
- first observation: *Oscar Hertwig*, 1875
- EM description: *Bessis*, 1955

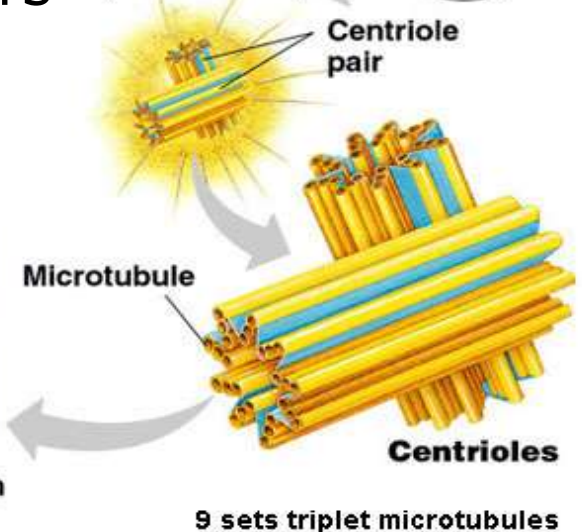
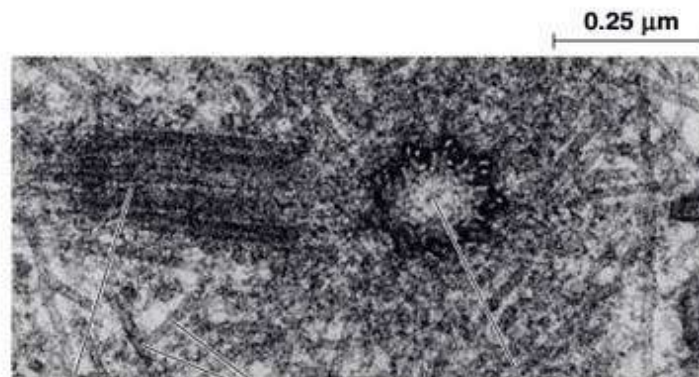
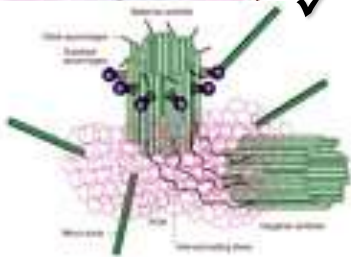
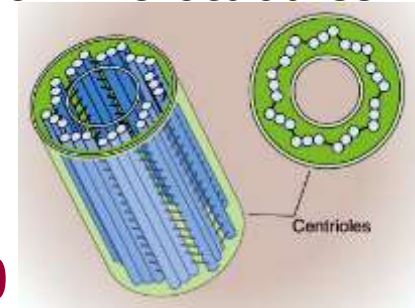
- ✓ diplosome
(a pair of centrioles)
- ✓ centrosphere



Centriole - structure

- barrel-shaped cell structure composed of microtubules

- ✓ diameter: 0.15-0.2 μm
- ✓ length: 0.3-0.7 μm
- ✓ structure: 9 triplets (9 x 3) + 0
- ✓ centriolar satellites: 40-70 nm microtubule organizing centers



Longitudinal section of centriole Microtubules Cross section of centriole

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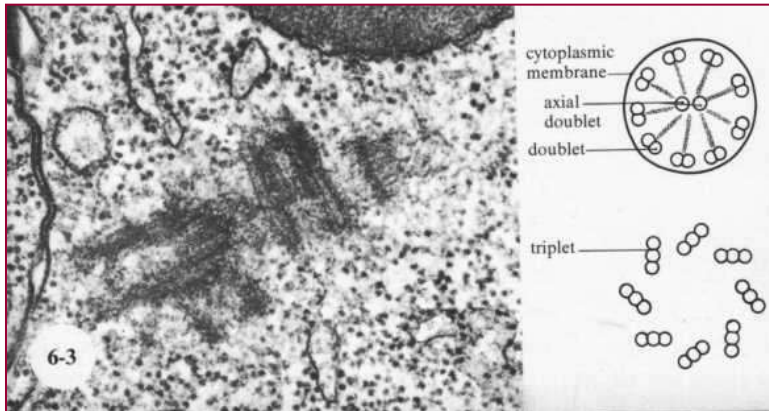
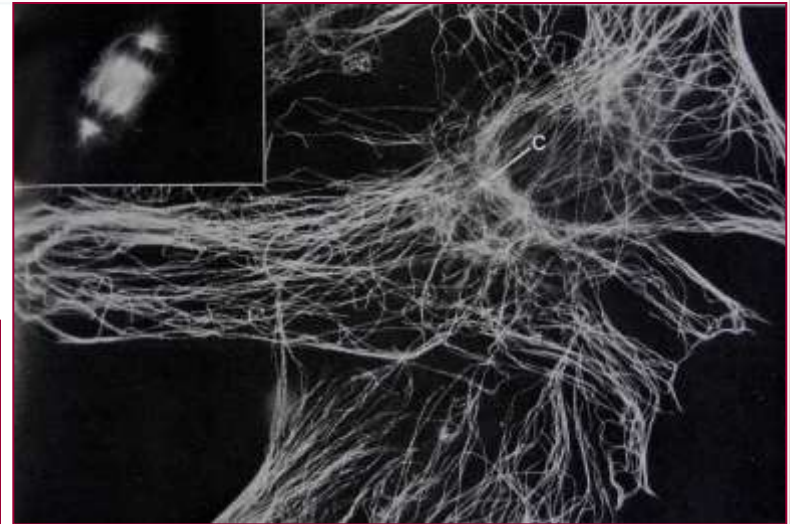




Centriole – functions

✓ role in cell division:

- formation of mitotic spindle

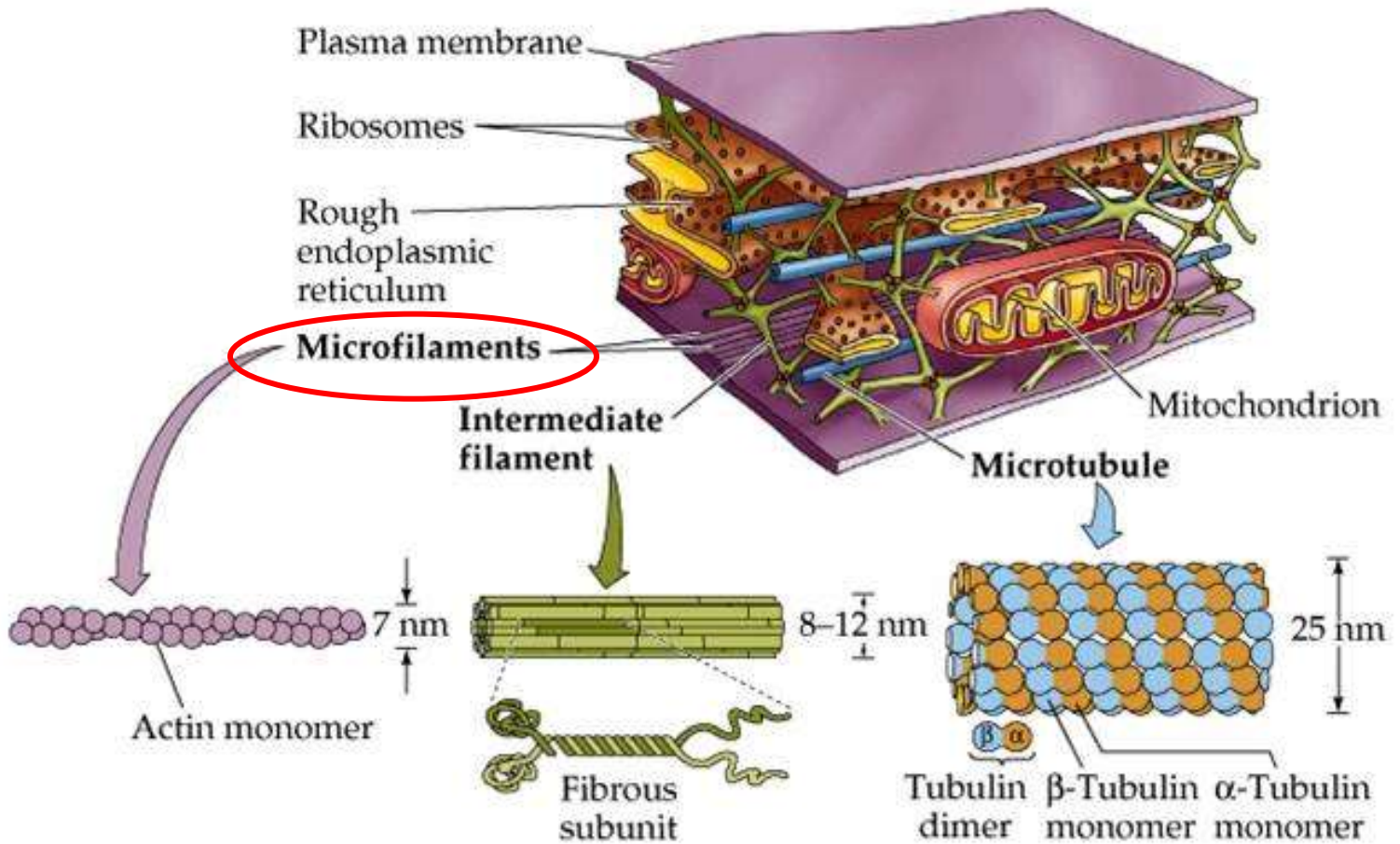


✓ role in generation of the cell's cytoskeleton:

- formation of cilia and flagella
- building of their basal bodies



Cytoskeleton



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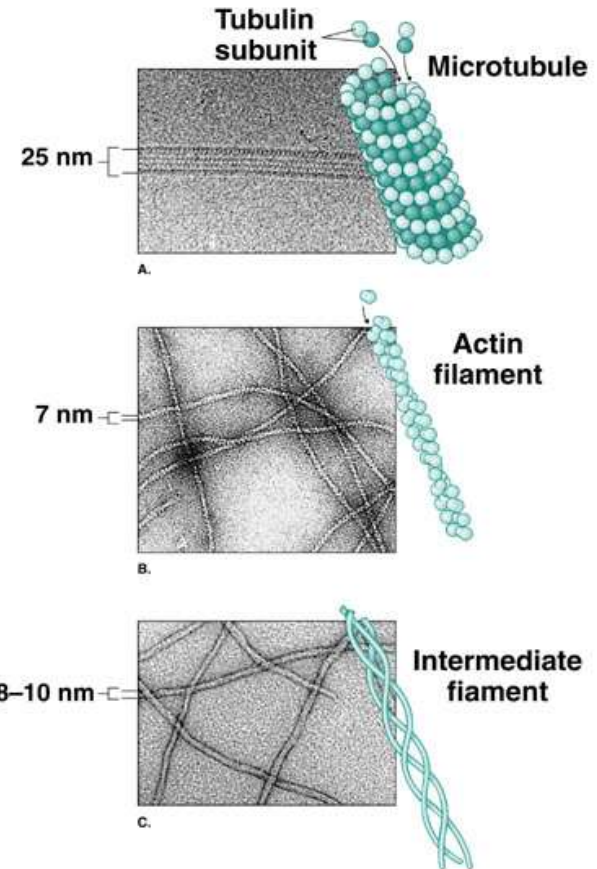




Cytoskeletal filaments

Tobin/Dusheck, Asking About Life, 2/e
Figure 4.16

- ✓ Microfilaments:
actin filaments
- ✓ Intermediate
filaments



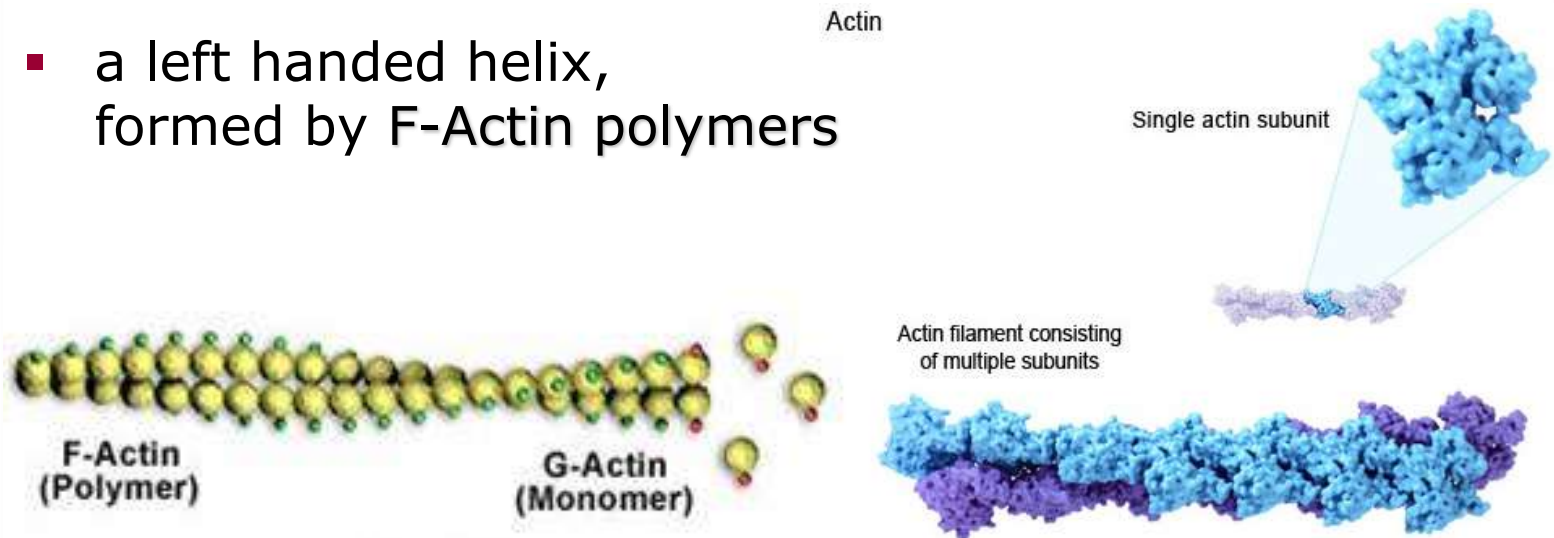
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Microfilaments

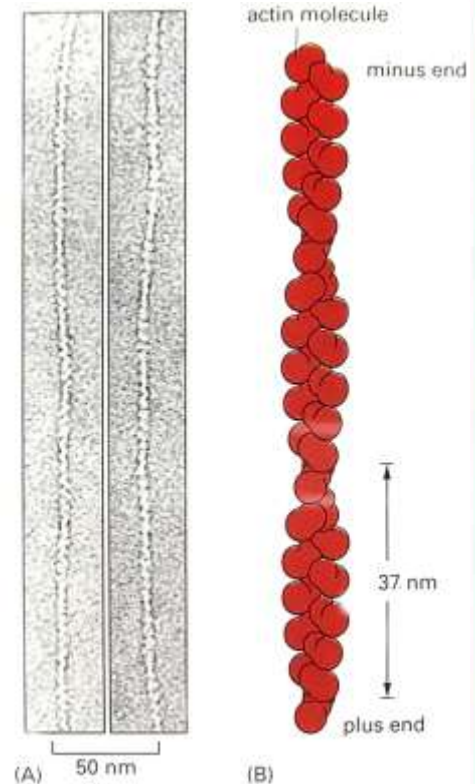
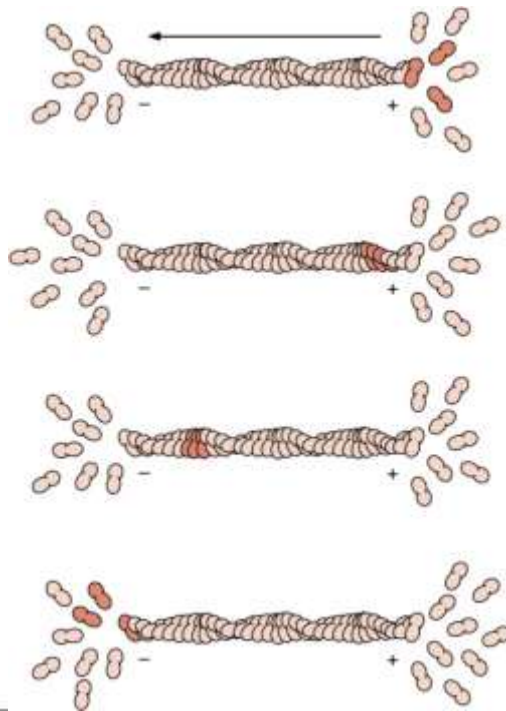
- up to 10% of the total protein of some nonmuscle cells
- Actin filaments – thin filaments:
 - ✓ the thinnest filaments of the cytoskeleton
 - ✓ located close to the cell membrane
 - ✓ grouped as bundles or networks
 - ✓ linear polymers of actin subunits
- a left handed helix,
formed by F-Actin polymers



Microfilaments

Actin filaments – thin filaments:

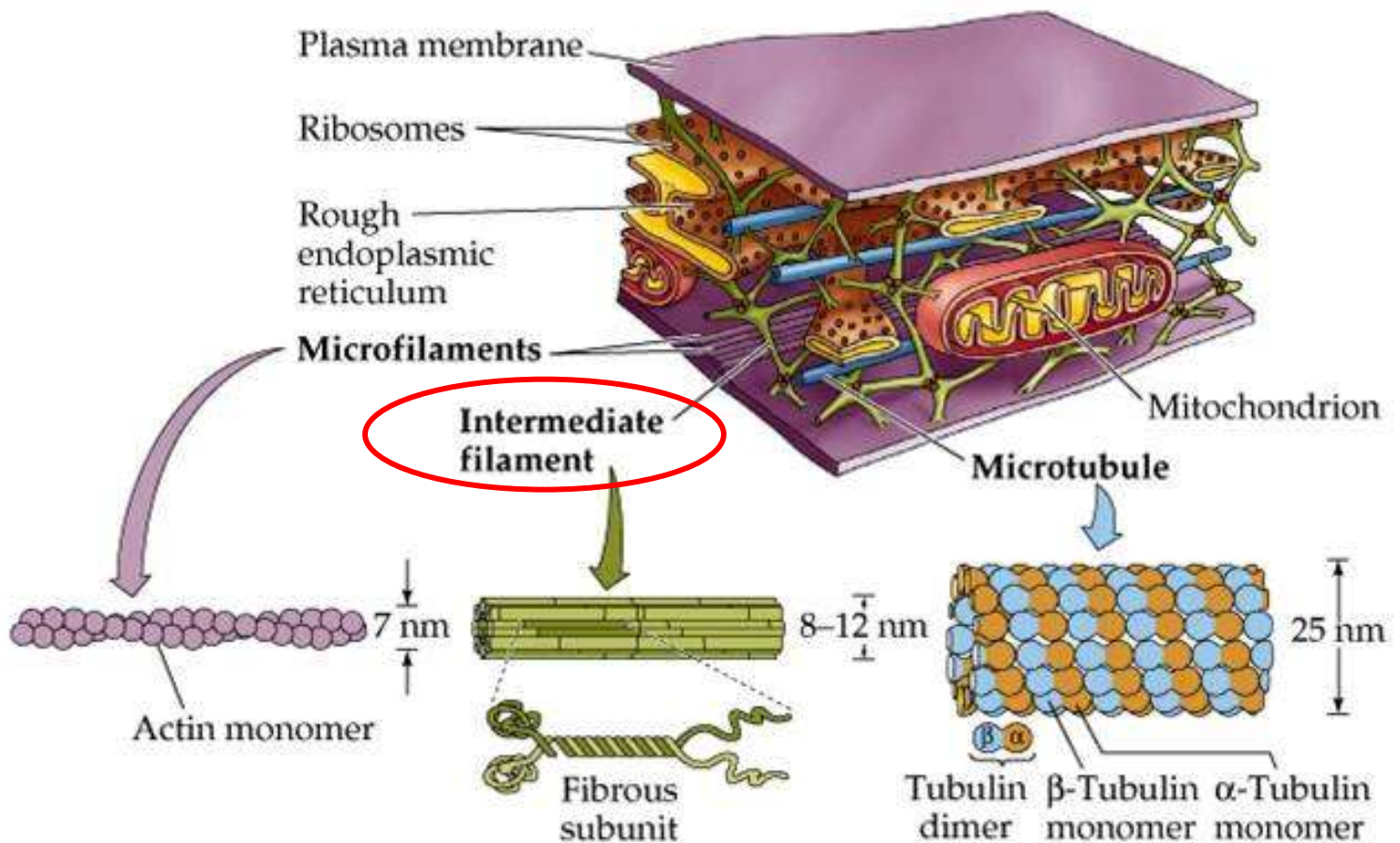
- ✓ linear polymers of actin subunits
- ✓ elongation via polymerization
- ✓ the first step is known as 'nucleation', i.e. the formation of small **actin** oligomers



- ✓ cytochalasin: blocks *actin polymerization*
- ✓ phalloidin: promote *actin polymerization*; stabilize actin polymers **22**



Cytoskeleton



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Prof. Dr. Nikolai Lazarov





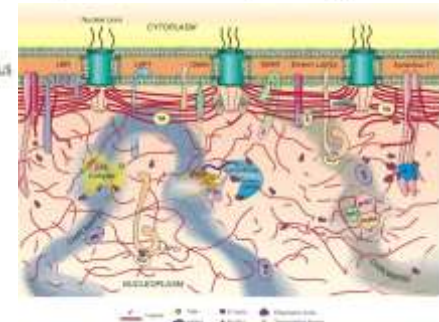
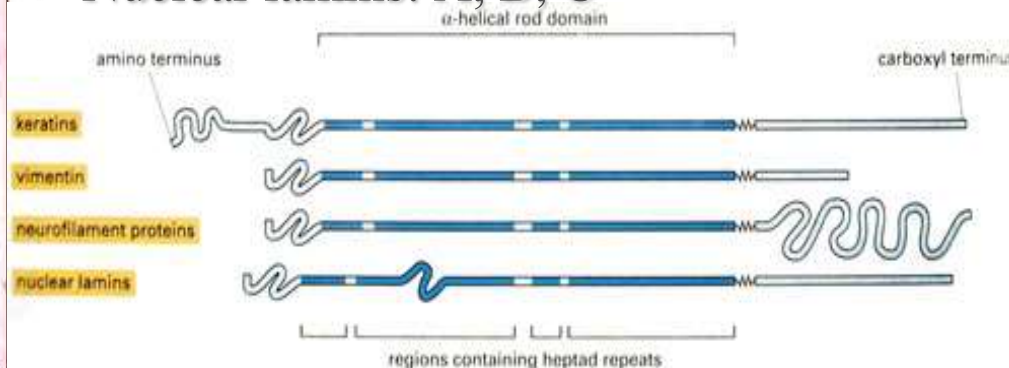
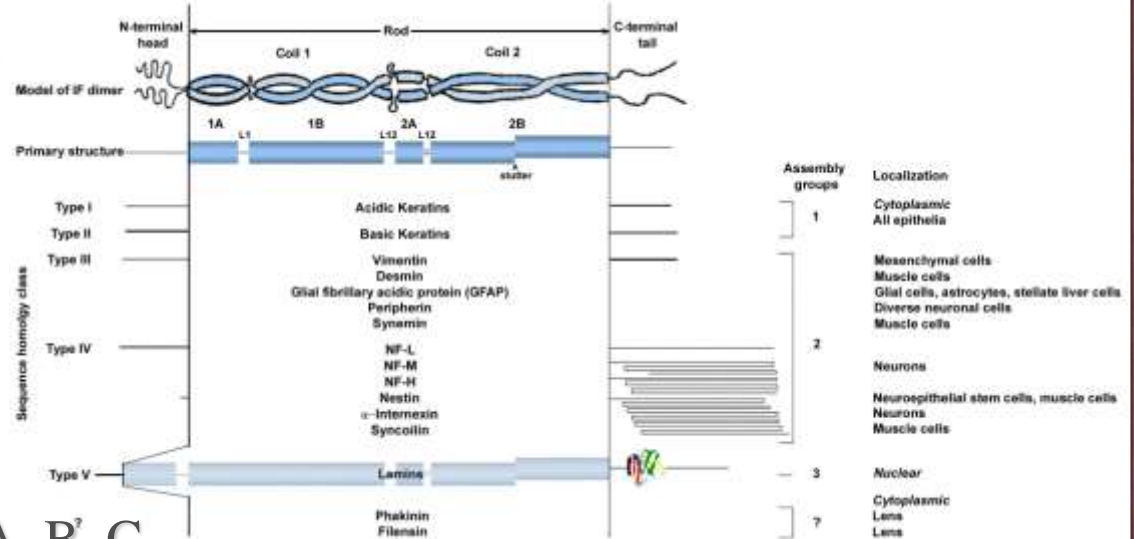
Intermediate filaments

Intermediate Filaments

- Keratin
 - epithelial cells
- Vimentin
 - mesodermal origin
- Desmin
 - muscle cells
- Glial
 - glial cells
- Neurofilament
 - neurons
- Nuclear lamins: A, B₁, B₂, C

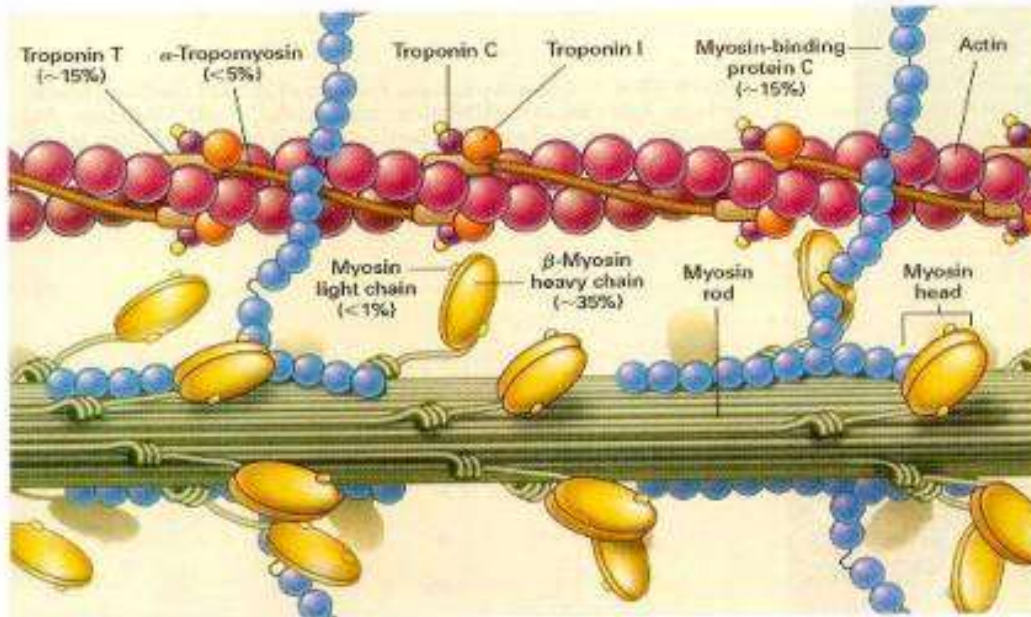
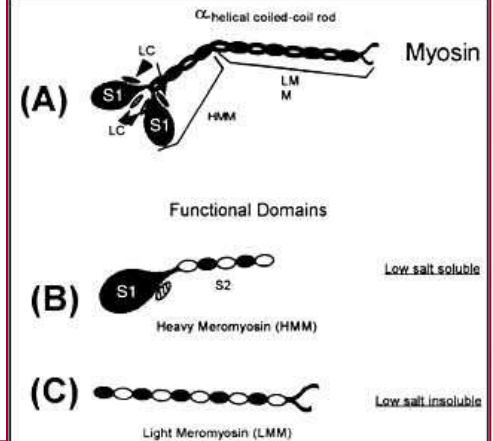
Table 2-4. Examples of Intermediate Filaments Found in Eukaryotic Cells.

Filament Type	Cell Type	Examples
Keratins	Epithelium	Both keratinizing and nonkeratinizing epithelia
Vimentin	Mesenchymal cells	Fibroblasts, chondroblasts, macrophages, endothelial cells, vascular smooth muscle
Desmin	Muscle	Striated and smooth muscle (except vascular smooth muscle)
Glial fibrillary acidic proteins	Glial cells	Astrocytes
Neurofilaments	Neurons	Nerve cell body and processes



Thick filaments

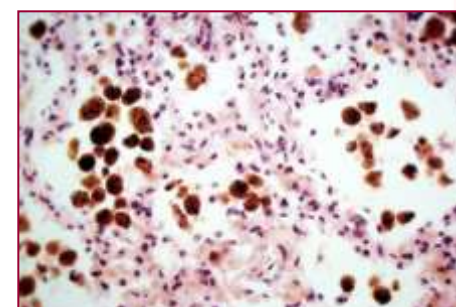
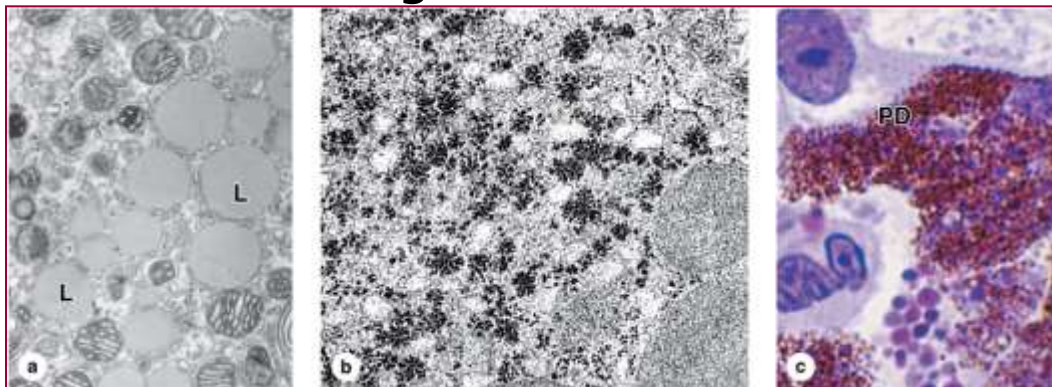
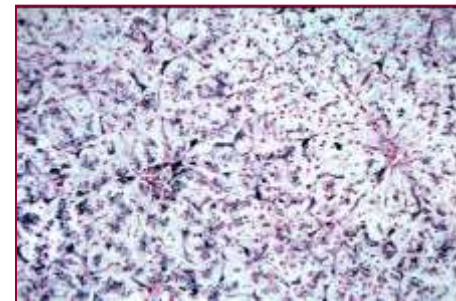
- myosin filaments – 1.6 μm long myosin II dimers:
 - ✓ two heavy chains
 - ✓ four (two pairs) light chains





Cytoplasmic inclusions

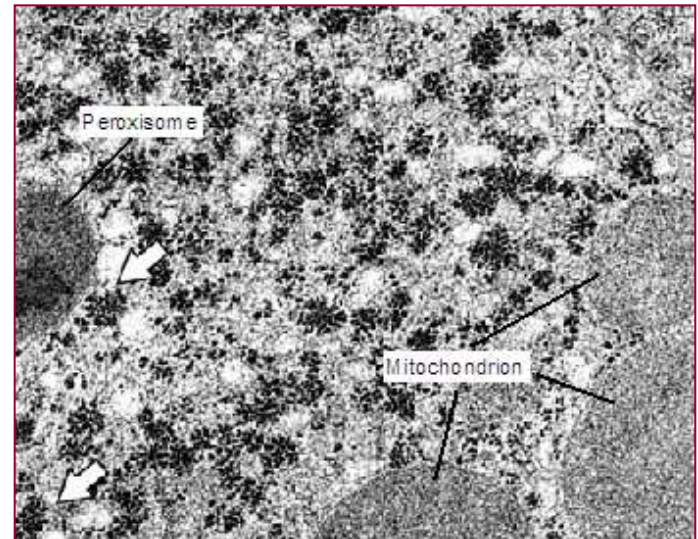
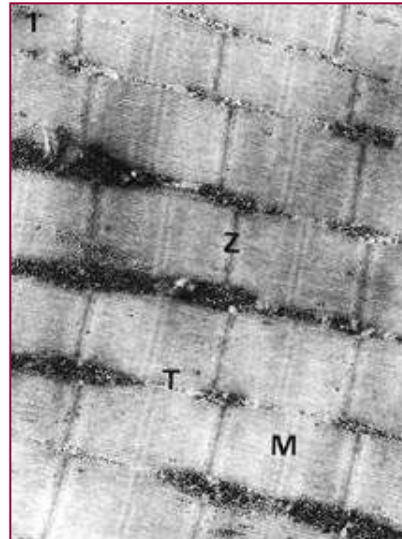
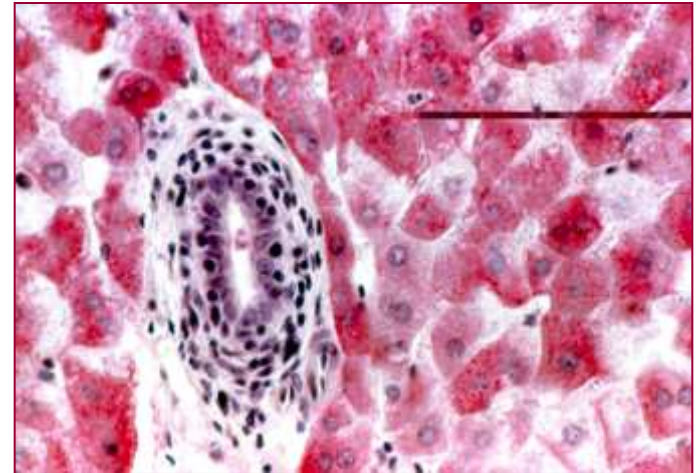
- small particles of insoluble substances suspended in the cytosol
- synonyms: deutoplasm, paraplast
- Cytoplasmic deposits:
 - ✓ proteins: secretory granules
 - ✓ glycogen granules
 - ✓ lipid inclusions (fat droplets)
 - ✓ crystalline inclusions
 - ✓ pigments:
 - exogenous
 - endogenous





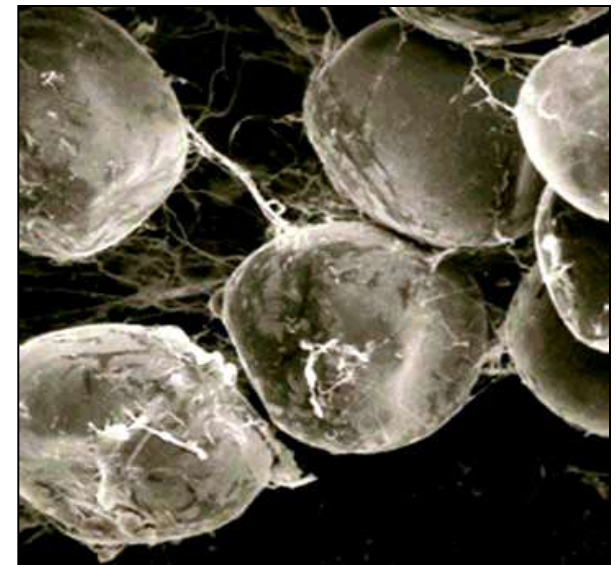
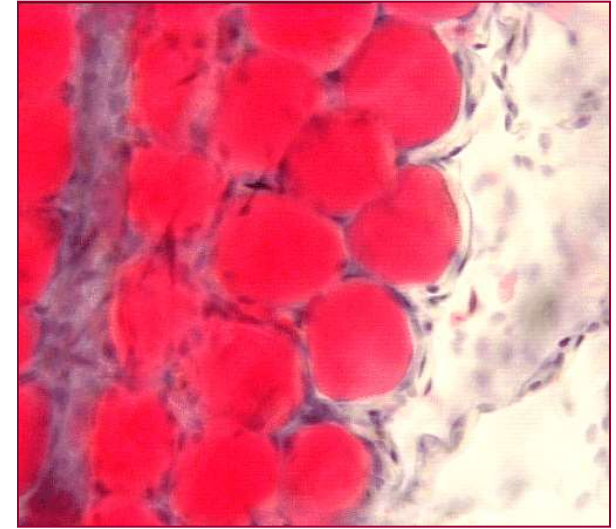
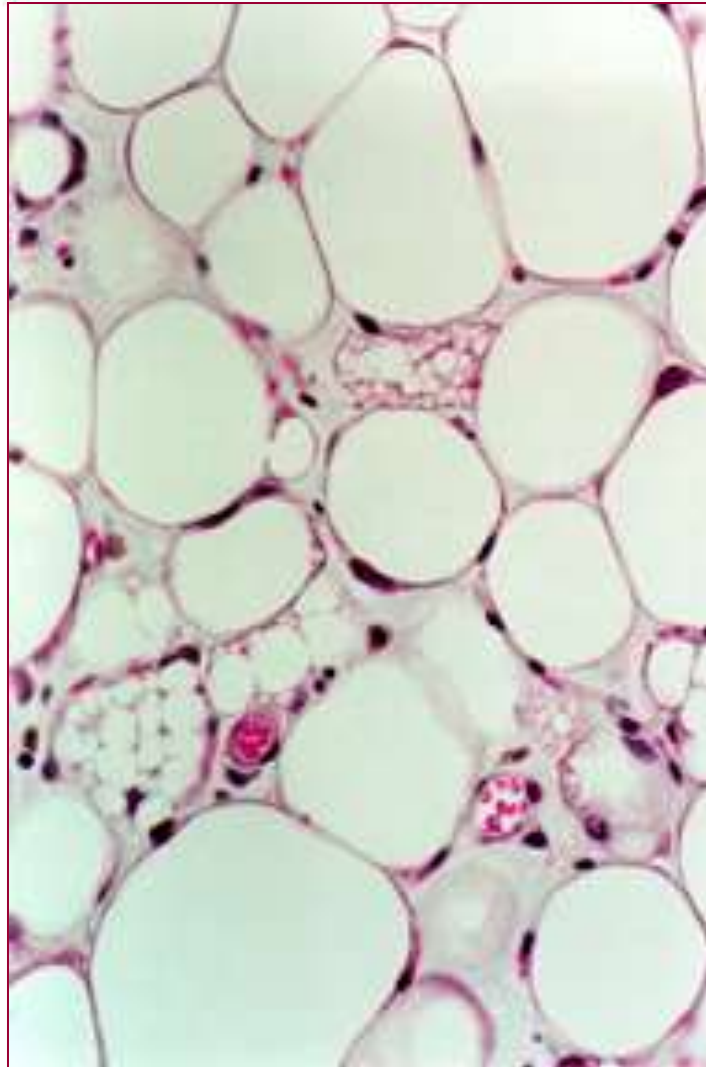
Glycogen granules

- in liver, striated muscle cells, cartilage and nerve cells
- LM: PAS reaction
- EM:
 - ✓ α -granules: 50-200 nm
 - ✓ β -granules: 15-30 nm
 - ✓ γ -granules: 10 nm (thread-like)





Fat droplets



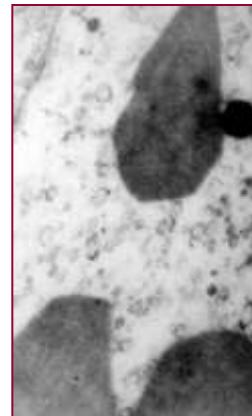
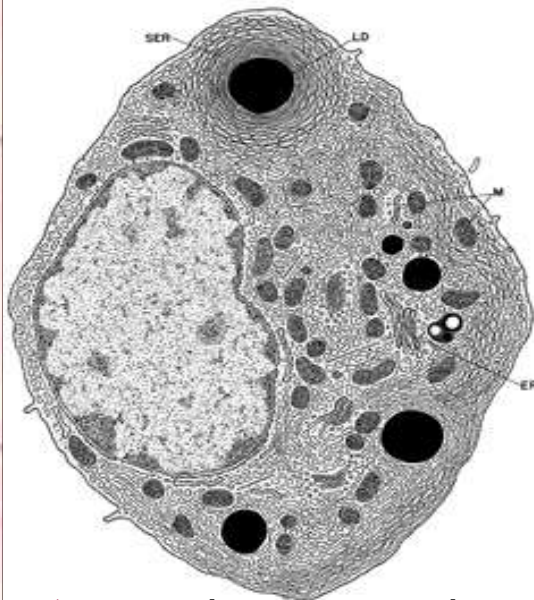
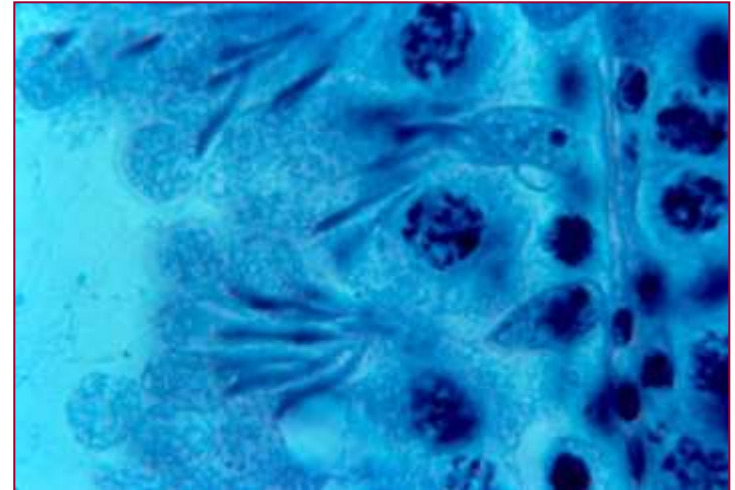
Prof. Dr. Nikolai Lazarov



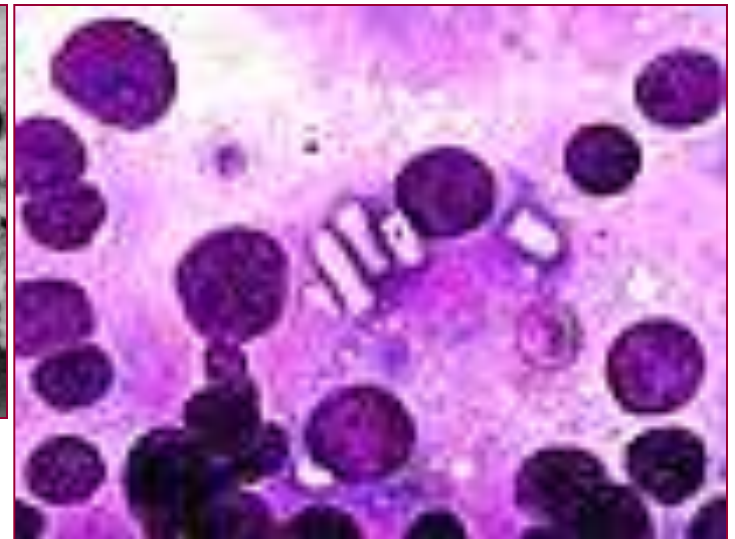


Crystalline inclusions

- Crystalline forms of certain proteins:
- ✓ *Charco-Böttcher* crystals – in Sertoli cells



- ✓ *Reinkes* crystals – in Leydig cells
- ✓ Cholesterol crystals – in macrophages and plasma cells





Pigment deposits

- pigments – naturally colored substances

- Lat. *pigmentum*, from *pingere* – to paint
 - ✓ **endogenous**
(Gr. *endon*, within)
 - ✓ **exogenous**
(Gr. *ex*, outside
+ *genein*, production)





Endogenous pigments

- Porphyrin pigments:
 - ✓ hemoglobin and derived pigments
 - hemosiderin
 - biliverdin
 - bilirubin (formerly hematoidin)
 - ✓ myoglobin
- Iron pigments:
 - ✓ transferrin
 - ✓ ferritin
 - ✓ hemosiderin
- Melanin and melanin-like pigments (*Gr. μέλας, black*):
 - ✓ eumelanin
 - ✓ pheomelanin
 - ✓ neuromelanin
- Lipofuscins:
 - ✓ lipofuscin (wear and tear pigment):
 - neurons
 - cardiomyocytes
 - hepatocytes

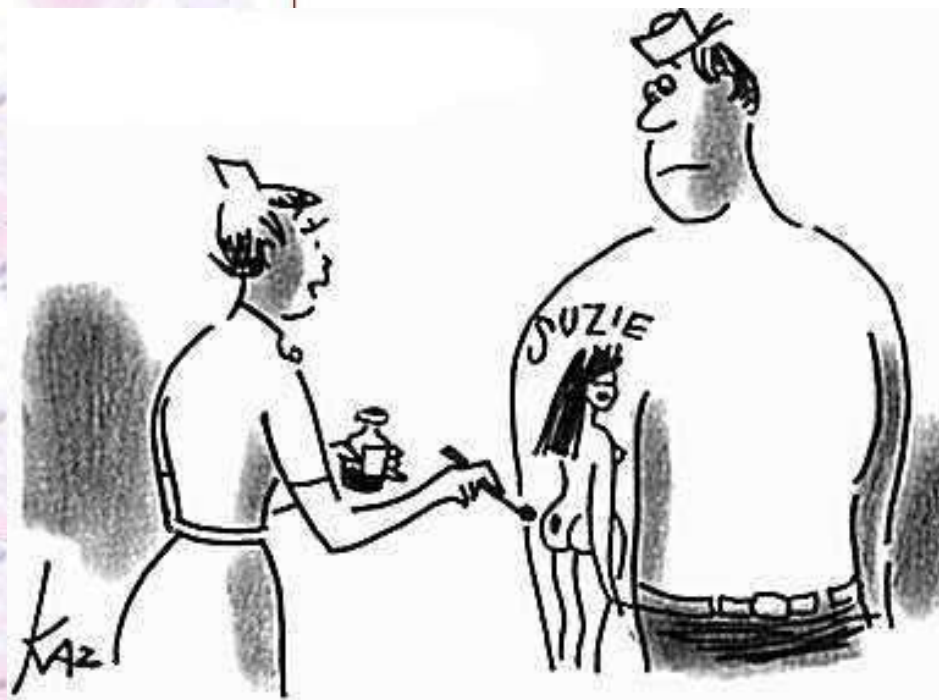




Exogenous pigments

- naturally occurring, fat-soluble pigments:
 - ✓ lipochrome, lipofuscin skin = age spots
 - ✓ carotene – carotenemia
- dusts (carbon) – industrial or environmental exposure by inhalation, ingestion or contact
- mineral pigments – created by combining and heating naturally occurring elements
- tattoos – planned, injected pigments





"You only have a scratch on your arm, but think of poor Suzie."



Thank you...