Histology; Microscopy and Ultrastructure of the Cell

Help

- esc key shows all the slides
- arrows left right advance the slide
- mobile device swipe left right
- slides can go left-right and up-down
- ? gives instant help
- menu bottom left

To save as PDF, see last slide.

How to get the most from the revision slides

- Have a pen & paper ready
- Answer every question
- Attempt to label all slides
- Mark your answer after answering
- Elaborate on each answer
- Add relevant clinical content
- If you have trouble, ask - you know where

Calibration

Community of Truth

What is my answer?

What is the correct answer?

I am am wrong, what was my error?

THUS: Find the truth

Philosophy 1

What is the least amount of work I can do so I can get out of here.

Philosophy 2

Today and Now I will do something for my future self.

Calibration

Assess yourself on each question.
Label all unlabelled slides.

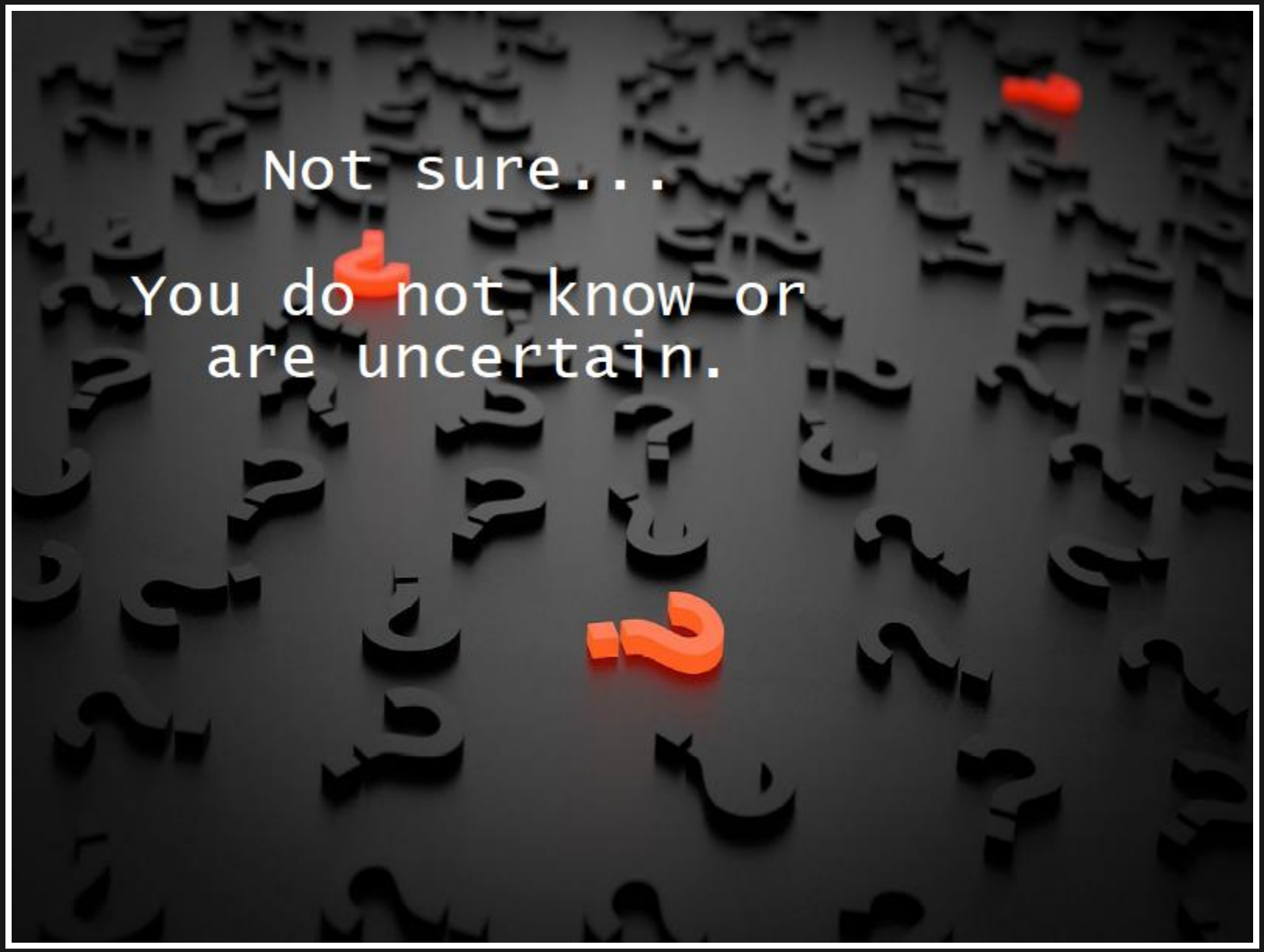
You want incremental improvements over time.

Assess yourself

Nailed it!

Not sure...


Nailed it!
You are confident about your answer.


Not sure...
You do not know or
are uncertain.

Histology

Why Histology?

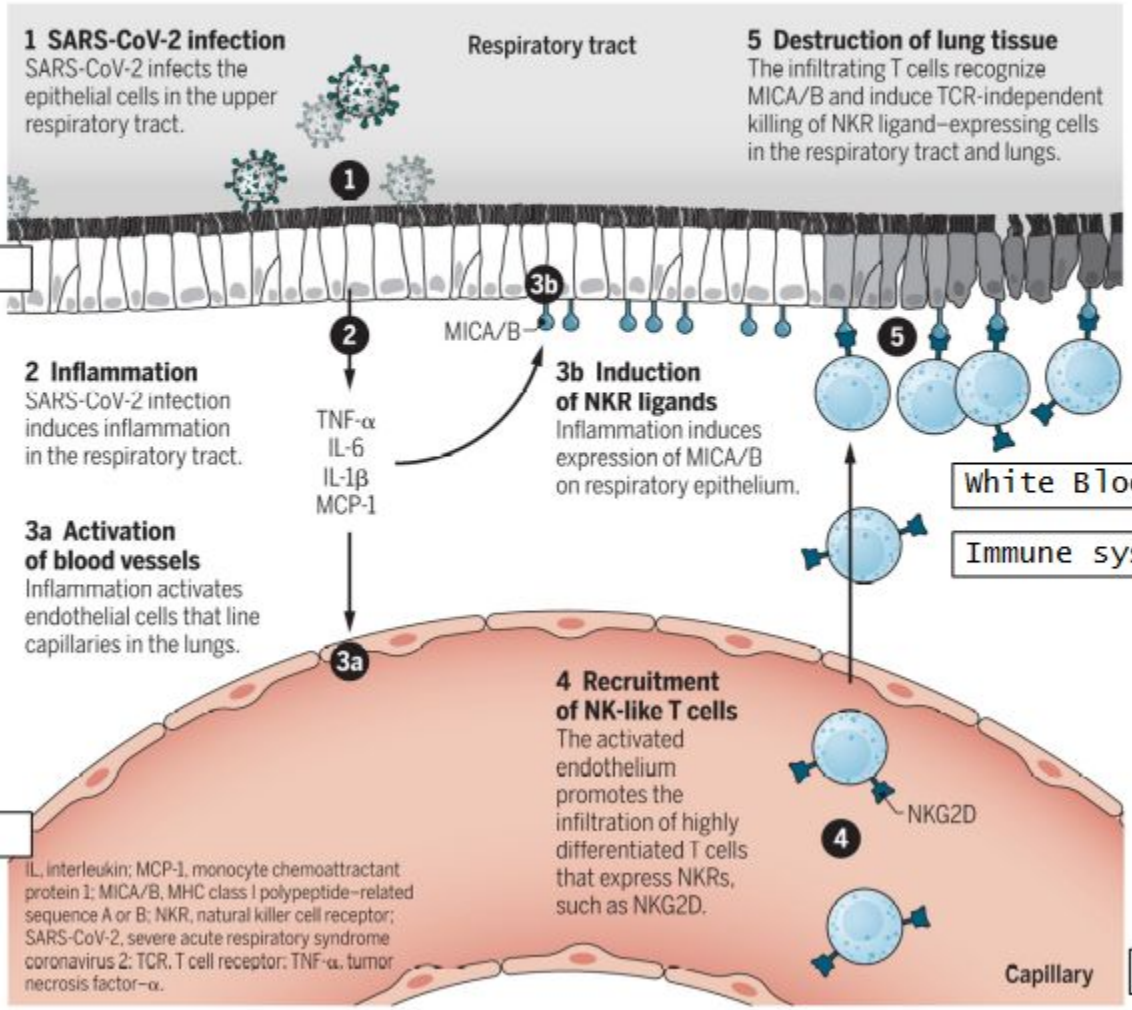
Where does Histology fit?

Endpoint?

- Clinical application
- VERY topical example
- Aging immunity may exacerbate COVID-19
    - Arne N. Akbar, Derek W. Gilroy
    - Science 17 Jul 2020:
    - Vol. 369, Issue 6501, pp. 256-257
    - DOI: 10.1126/science.abb0762

Aged immune responses to SARS-CoV-2 infection

Highly differentiated T cells in older individuals may induce damage in SARS-CoV-2–infected lungs, as hypothesized in the diagram.



Find the Histology:

- The chemistry of cats: Allergies, catnip and urine
- In the infographic, find the histology.
- The image is available on the next slide, but more readible on web version available at the link.

THE CHEMISTRY OF CATS: ALLERGIES, CATNIP, AND URINE

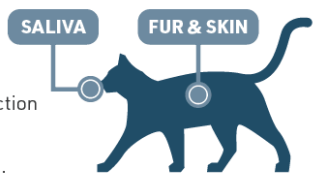
WHAT CAUSES ALLERGIES TO CATS?

10–30% OF PEOPLE ARE ALLERGIC TO CATS

Eight different cat allergens are currently recognised by the World Health Organisation. They're designated as Fel d 1–8. Of these, Fel d 1 is the primary cat allergen.

FEL D 1
MAIN ALLERGEN

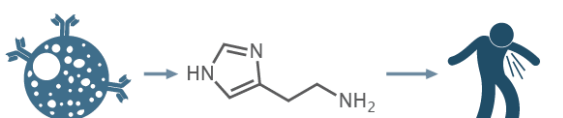
A protein, the biological function of which is still unknown.
Found in over 99% of homes.



♂ FEL D 1 LEVELS > ♀ FEL D 1 LEVELS

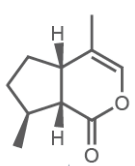
(note: neutered males produce Fel d 1 levels similar to those of females)

Inhalation of Fel d 1 causes an immune response in people who are allergic. As a defence mechanism, the body produces antibodies. The antibodies trigger the release of histamine from mast cells. Histamine causes the symptoms of allergies.



MAST CELLS | HISTAMINE | SYMPTOMS

WHY DO CATS GO CRAZY FOR CATNIP?



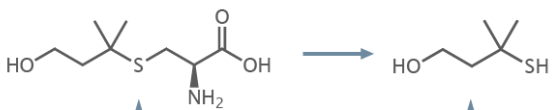
NEPETALACTONE

70% OF CATS ARE AFFECTED

The compound that causes catnip's effect on cats is nepetalactone. It binds to protein receptors in the cat's nasal passages. This triggers responses in the cat's brain that make the cat exhibit behaviour similar to that triggered by cat pheromones, including rolling, rubbing and salivating. The effects last for around ten minutes before wearing off.

WHY DOES CAT URINE SMELL SO BAD?

Fresh cat urine doesn't have a strong odour. However, over time, it develops a strong smell. Felinine, an amino acid in cat urine, gets broken down by enzymes into 3-methyl-3-sulfanylbutan-1-ol (MMB). This, along with the ammonia produced by the breakdown, gives cat urine its pungent smell.



FELININE | MMB

♂ FELININE EXCRETION > ♀ FELININE EXCRETION

(note: neutered males excrete felinine at levels similar to that of females)

CAT KETONE

Cat ketone (4-methyl-4-sulfanylpentan-2-one) is another key cat urine odorant. It also occurs naturally in Sauvignon grapes, and is a key contributor to the odour of blackcurrants.

CAT LITTER COMPOSITION

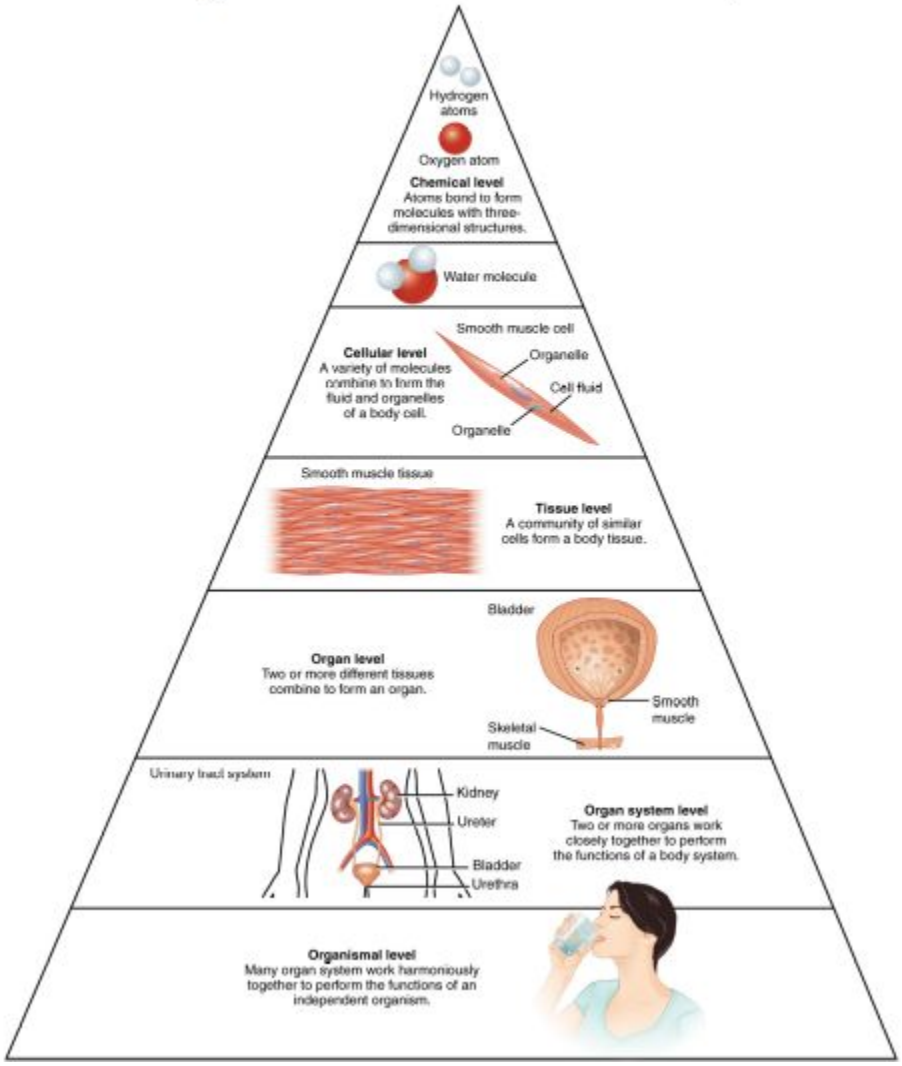
Clay-based, e.g. calcium bentonite; biodegradable and silica gel litters are less commonly used.

Cat litter absorbs urine and odours. In cases where cats urinate elsewhere around your house, enzymatic cleaners should be used. These break down odorous compounds.

Histology: Foundational Knowledge

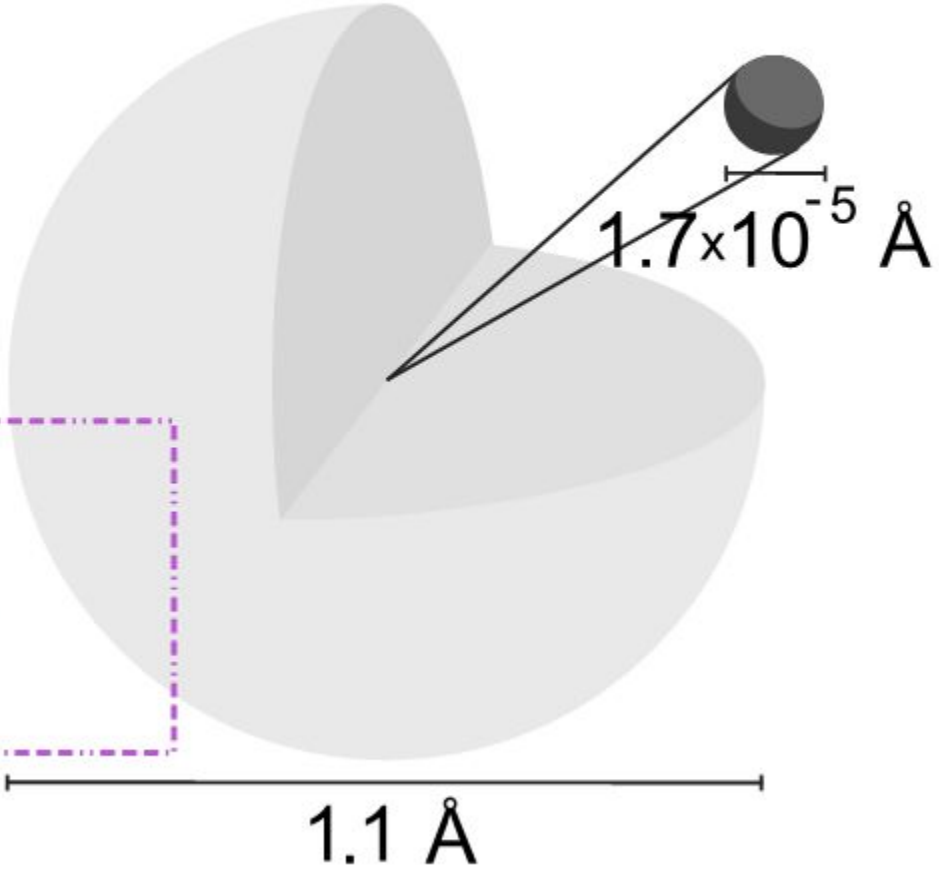
Levels of Organisation

Figure 1.3 Levels of Structural organisation of the Human Body; Anatomy and Physiology 25 April 2013; OpenStax; CC-BY 4.0; https://openstax.org/books/anatomy-and-physiology/pages/1-2-structural-organization-of-the-human-body



Atoms

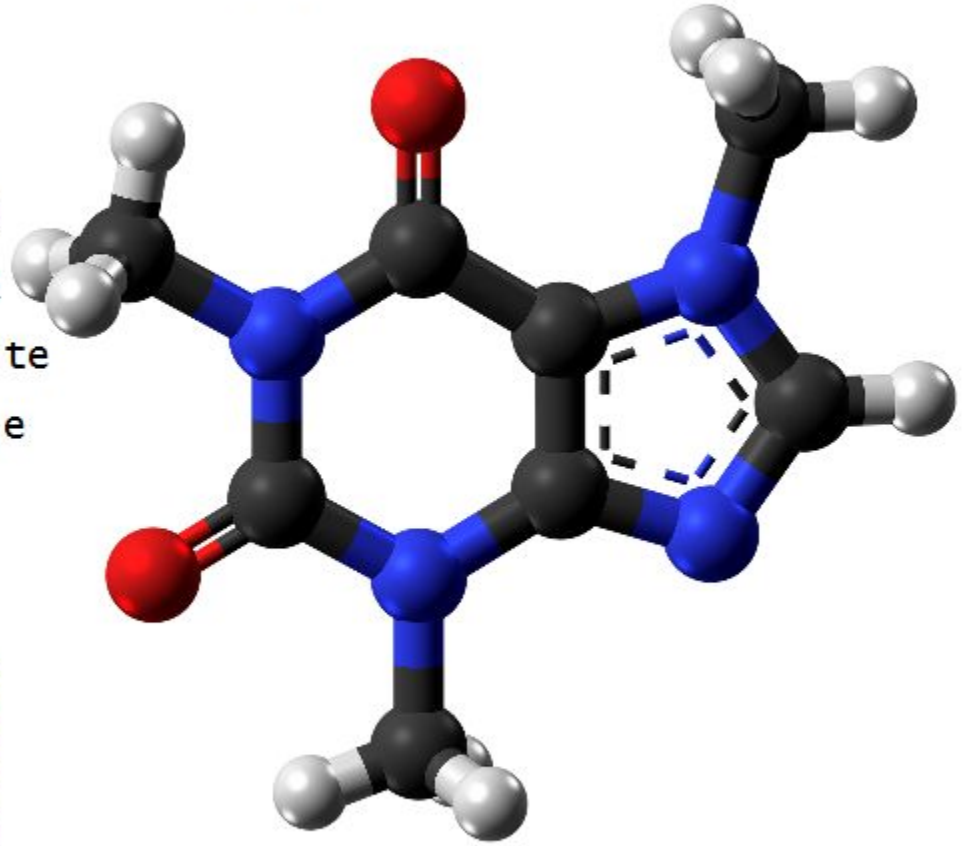
- Hydrogen atom



- Physics
- Chemistry

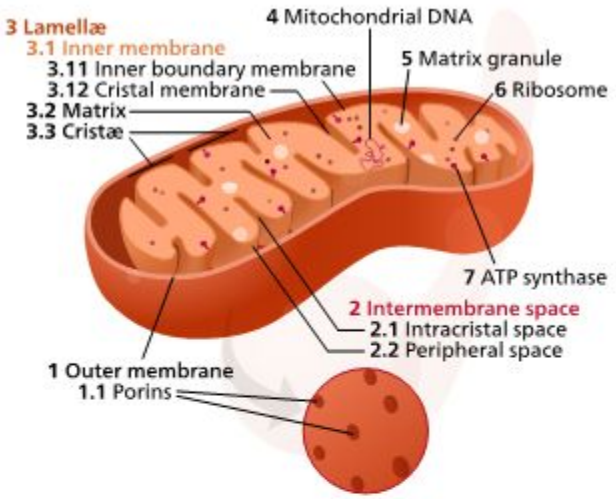
Molecule

- Caffeine molecule
  - Carbon, C: Black
  - Hydrogen, H: White
  - Nitrogen, N: Blue
  - Oxygen, O: Ref



- Chemistry

Organelles

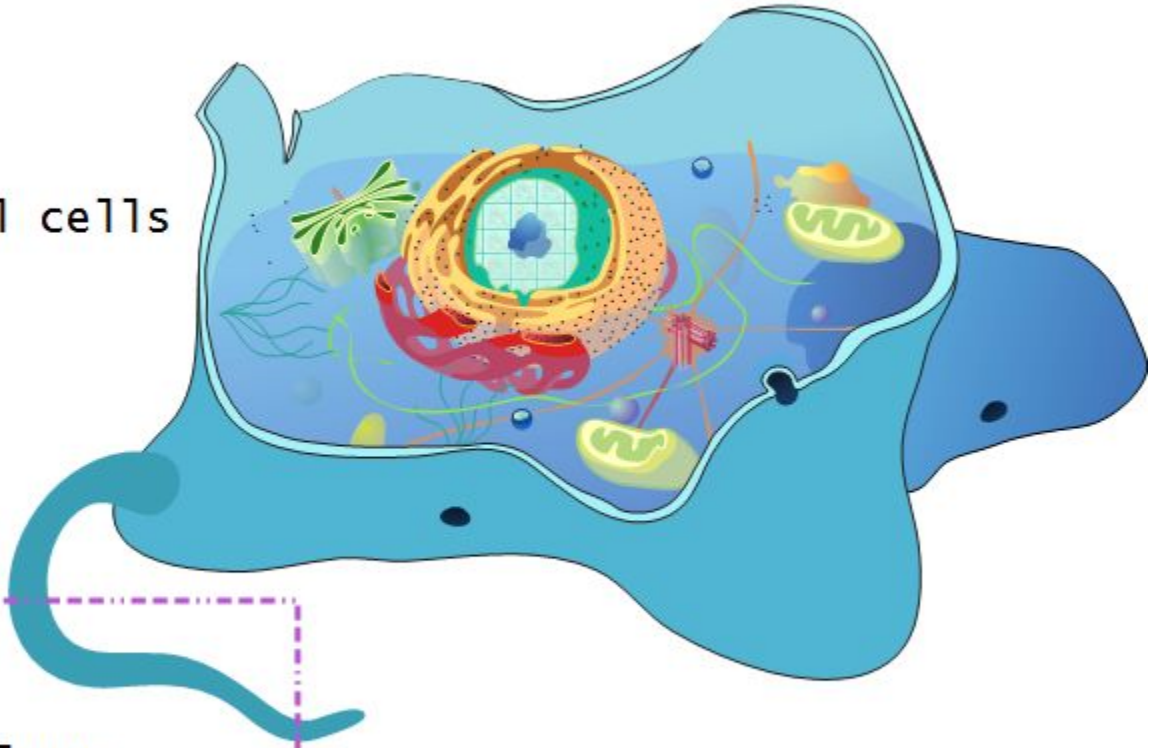


- Mitochondria

- Histology

Cells

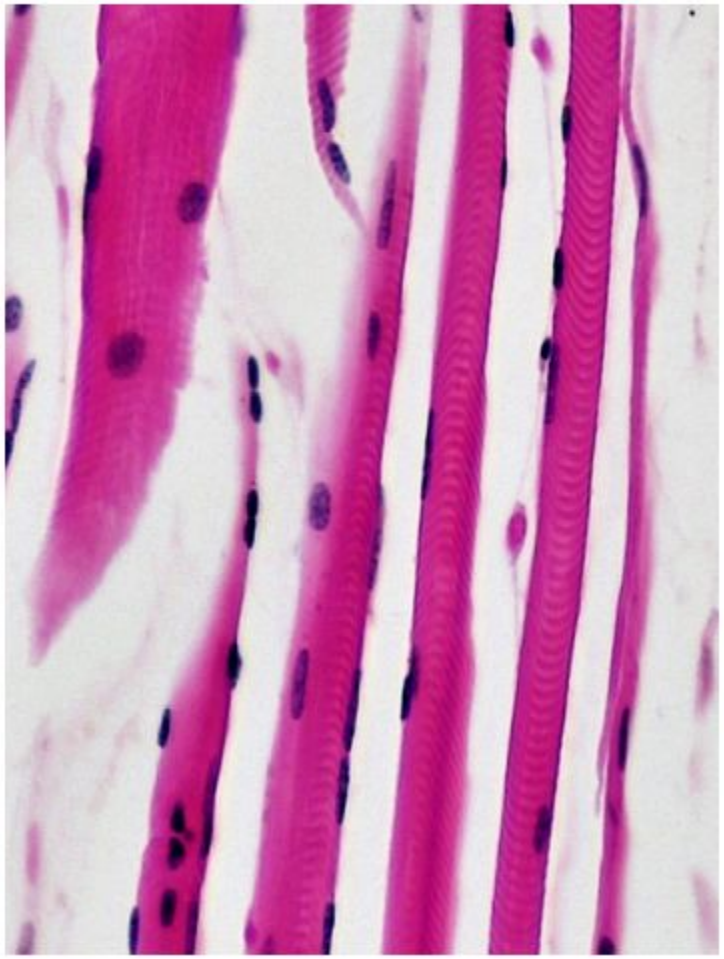
- Animal cells



- Histology

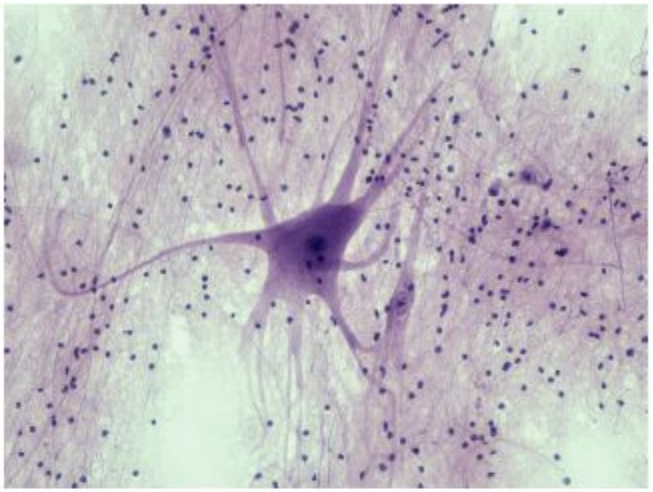
Tissues

- Skeletal muscle



- Histology

Organs



- Brain

- Histology
- Anatomy

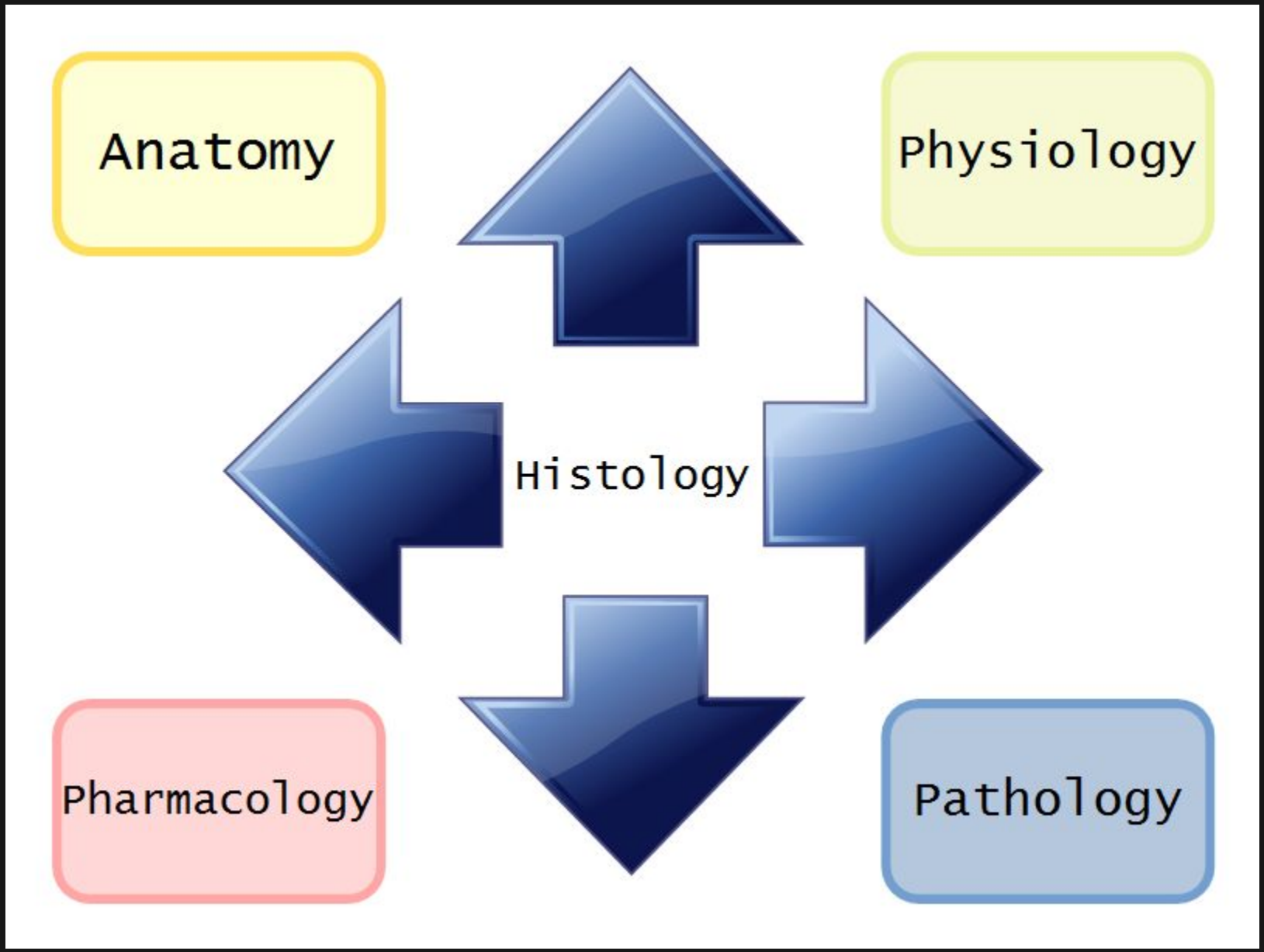
Organism

- Human

- Anatomy
- Physiology

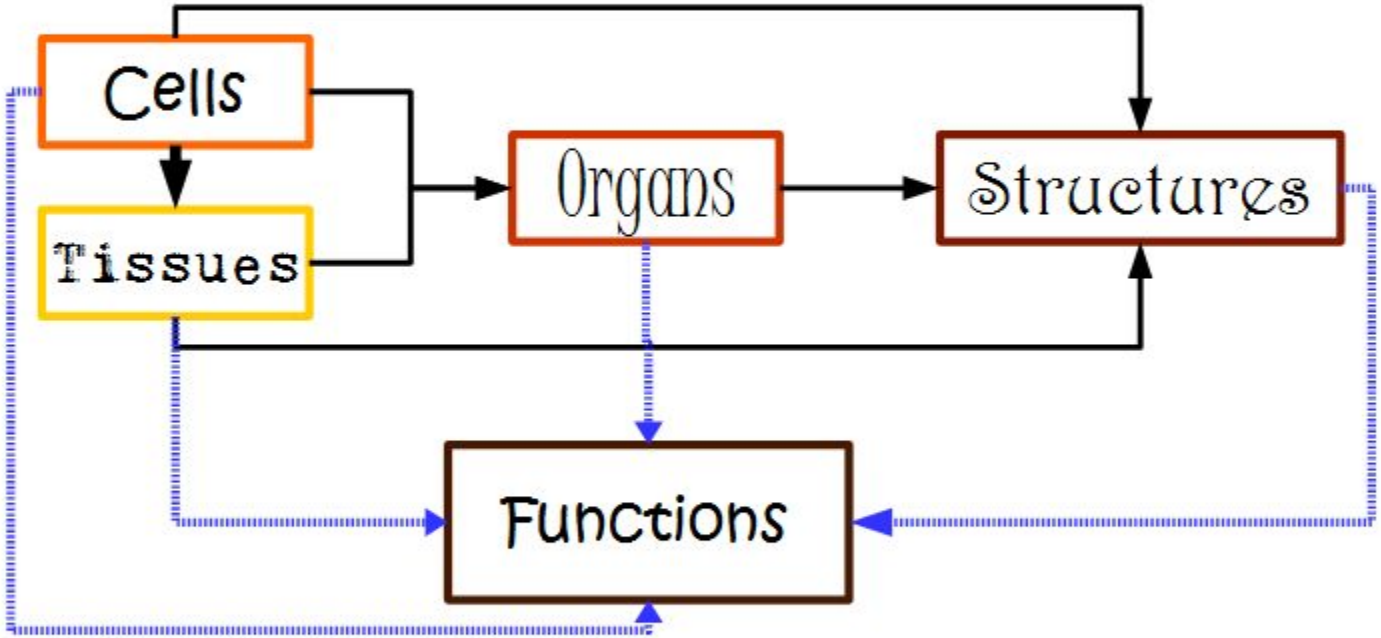
Why histology?

- Knowledge
  - Because all knowledge is worthwhile
  - The more you know, the more you are able to know
- Know the normal to identify the abnormal
  - Pathology
- Functions of many organs
  - Lung, Kidney, Liver
  - Informed by cellular organisation
  - Physiology
- Structure of body informed by cellular organisation
  - Anatomy
- Inflammation, Repair & Treatment dependent on cellular organisation
  - Pharmacology

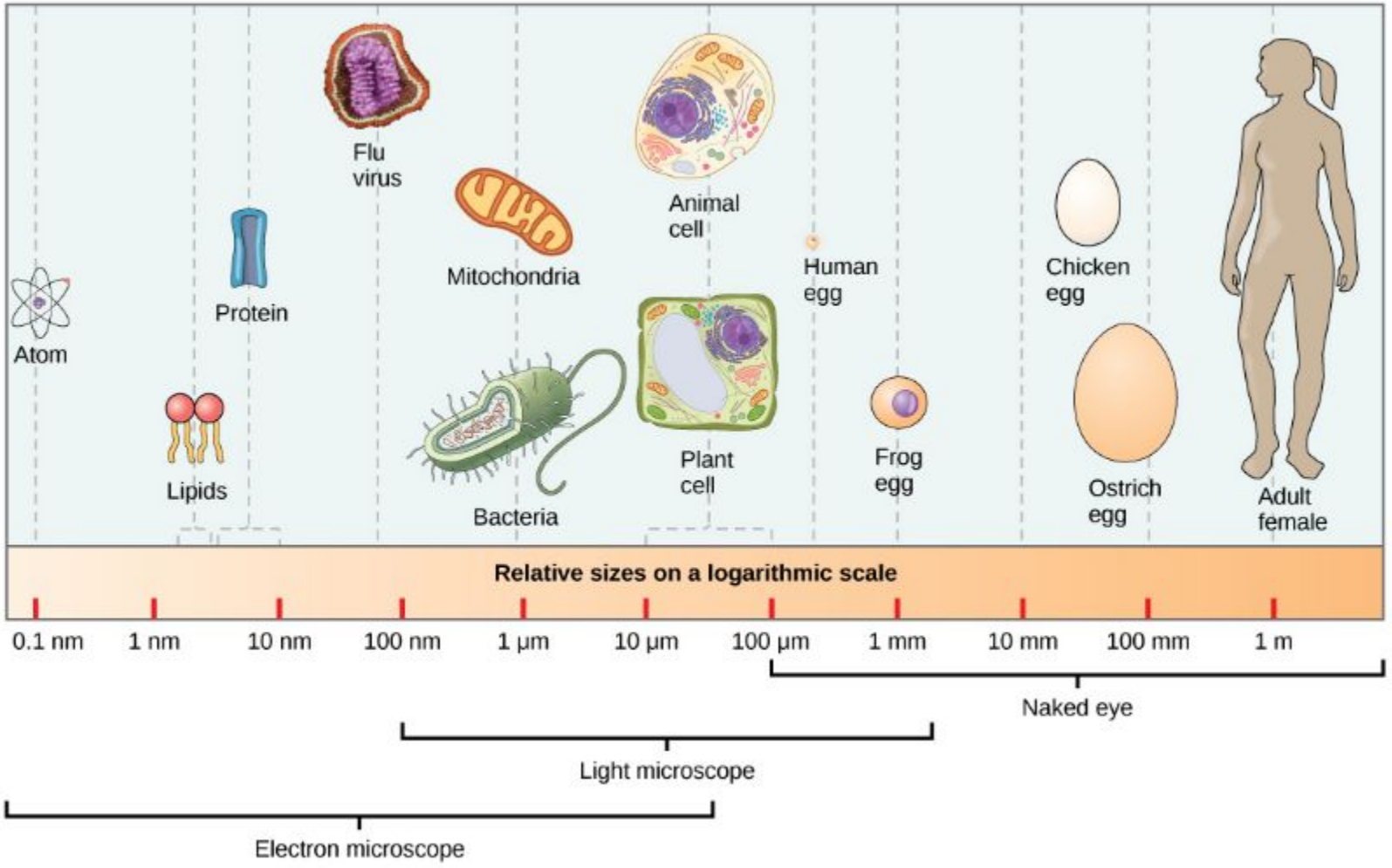

Anatomy
Physiology
Histology
Pharmacology
Pathology

What in Histology

Basic framework to work from


Cells
Tissues
Organs
Structures
Functions

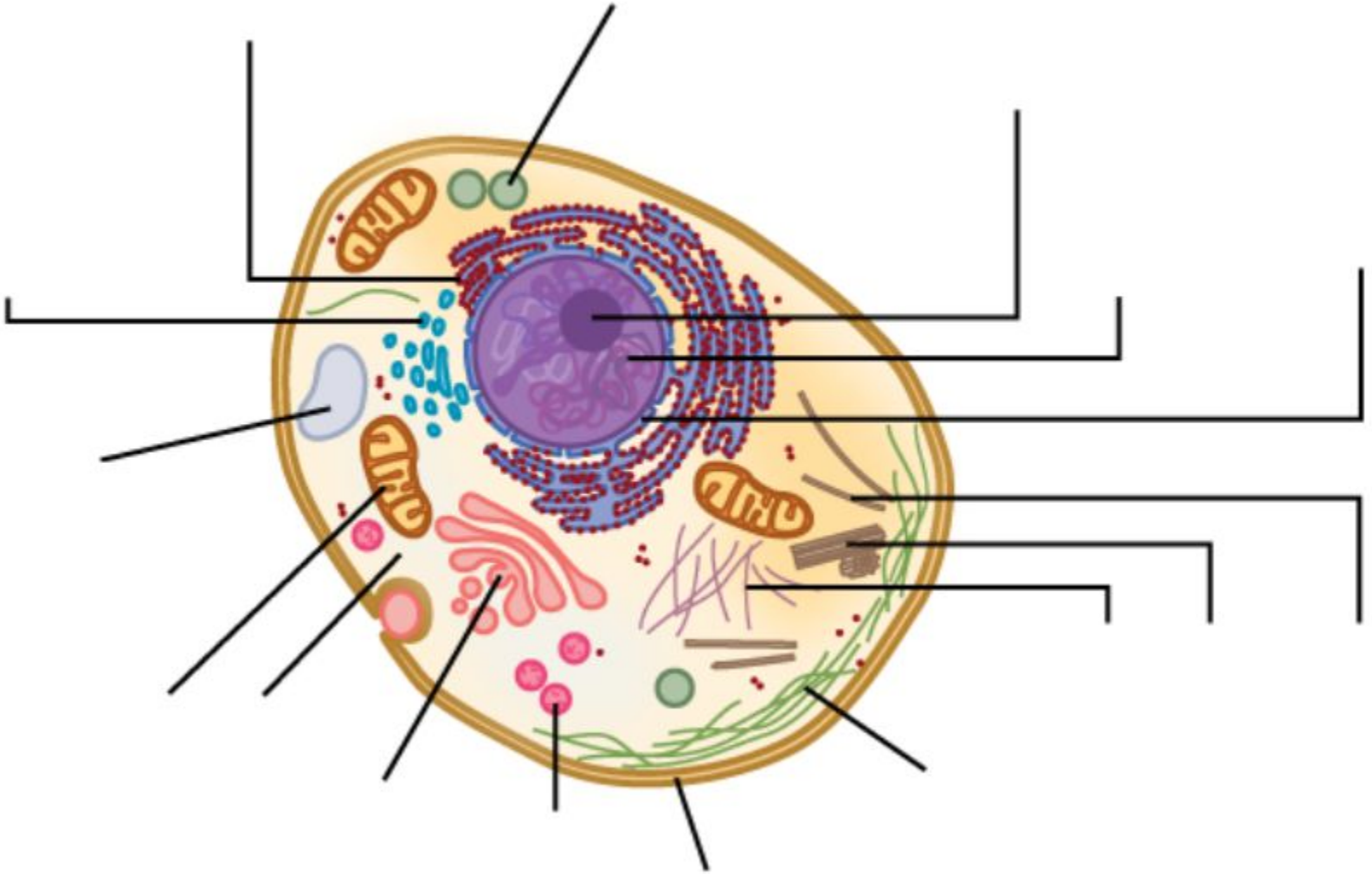
The relative sizes of different kinds of cells and cellular components.

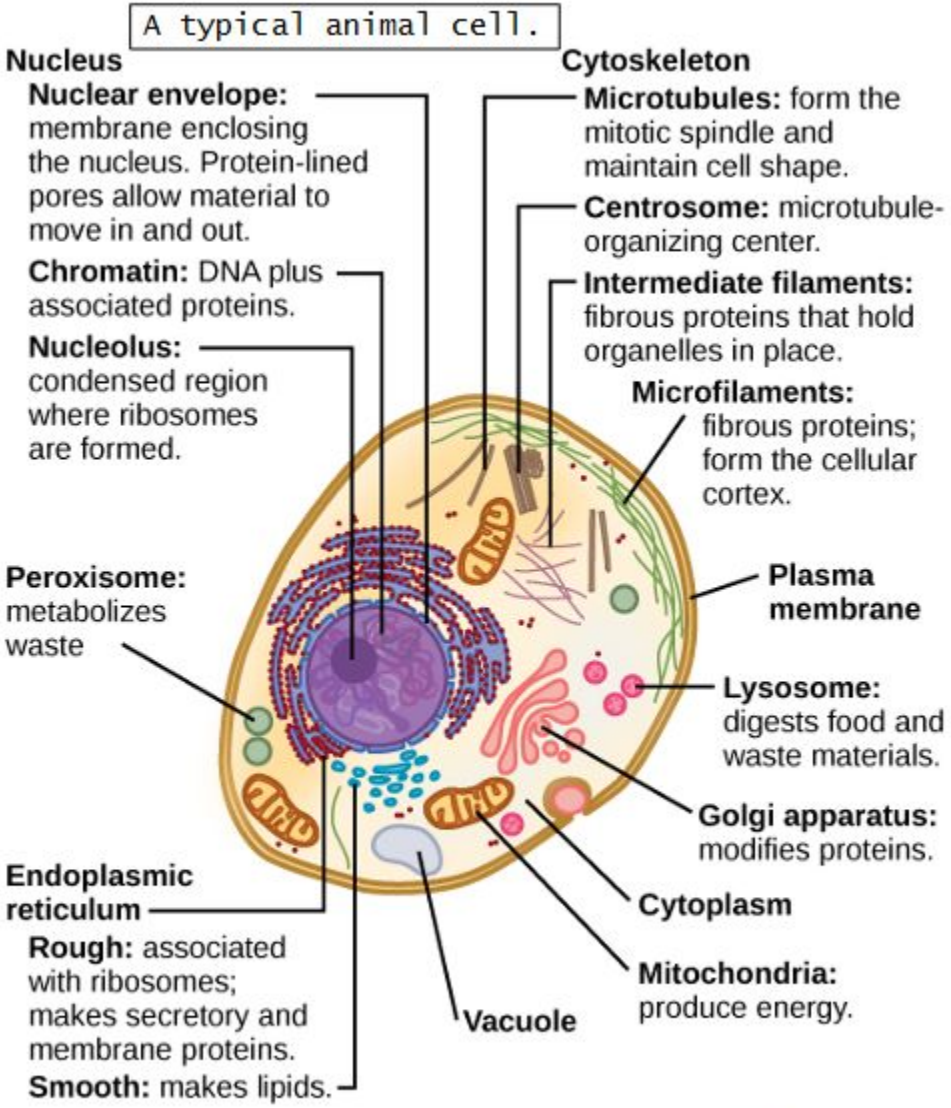


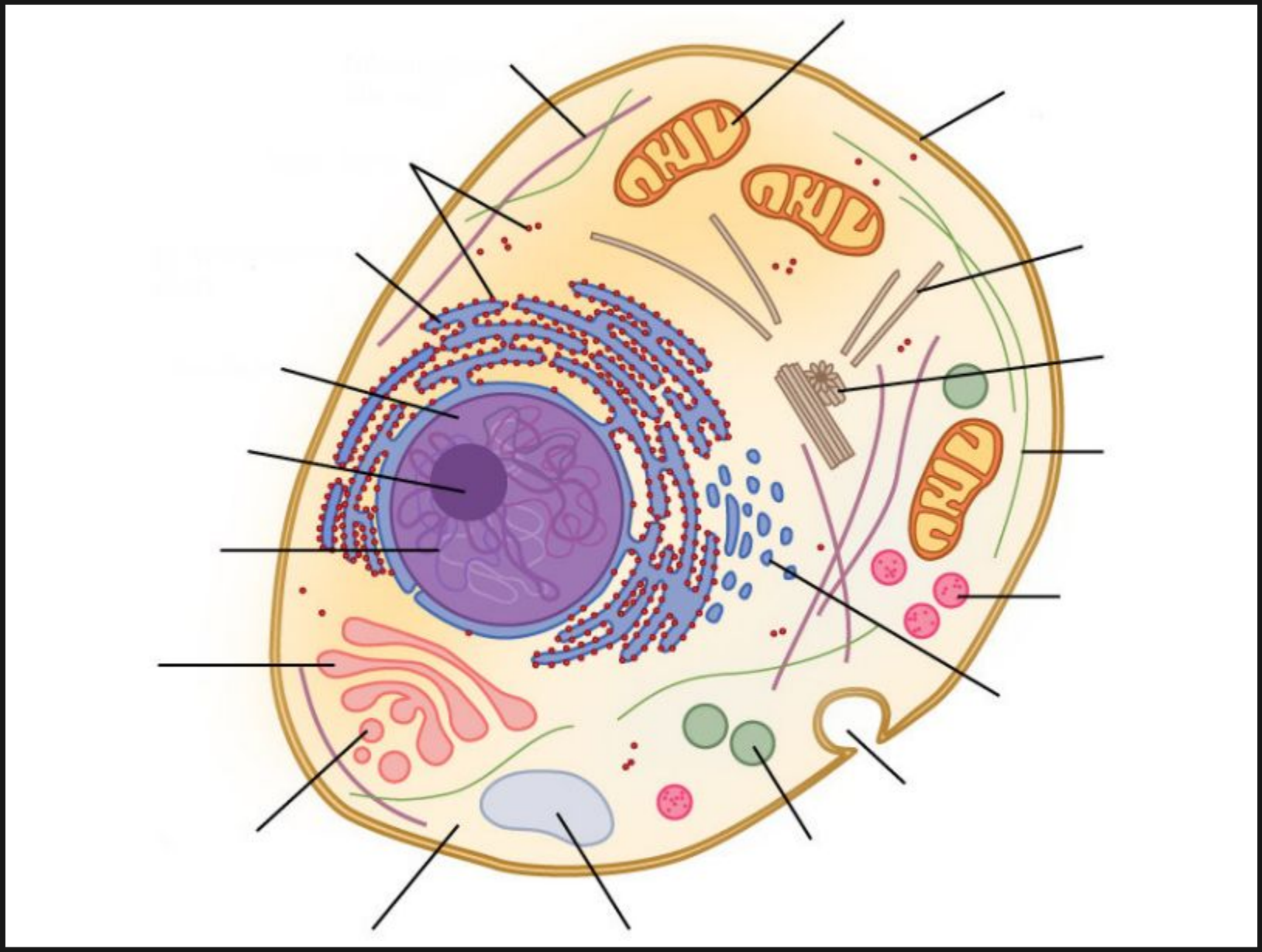
Unlabelled images

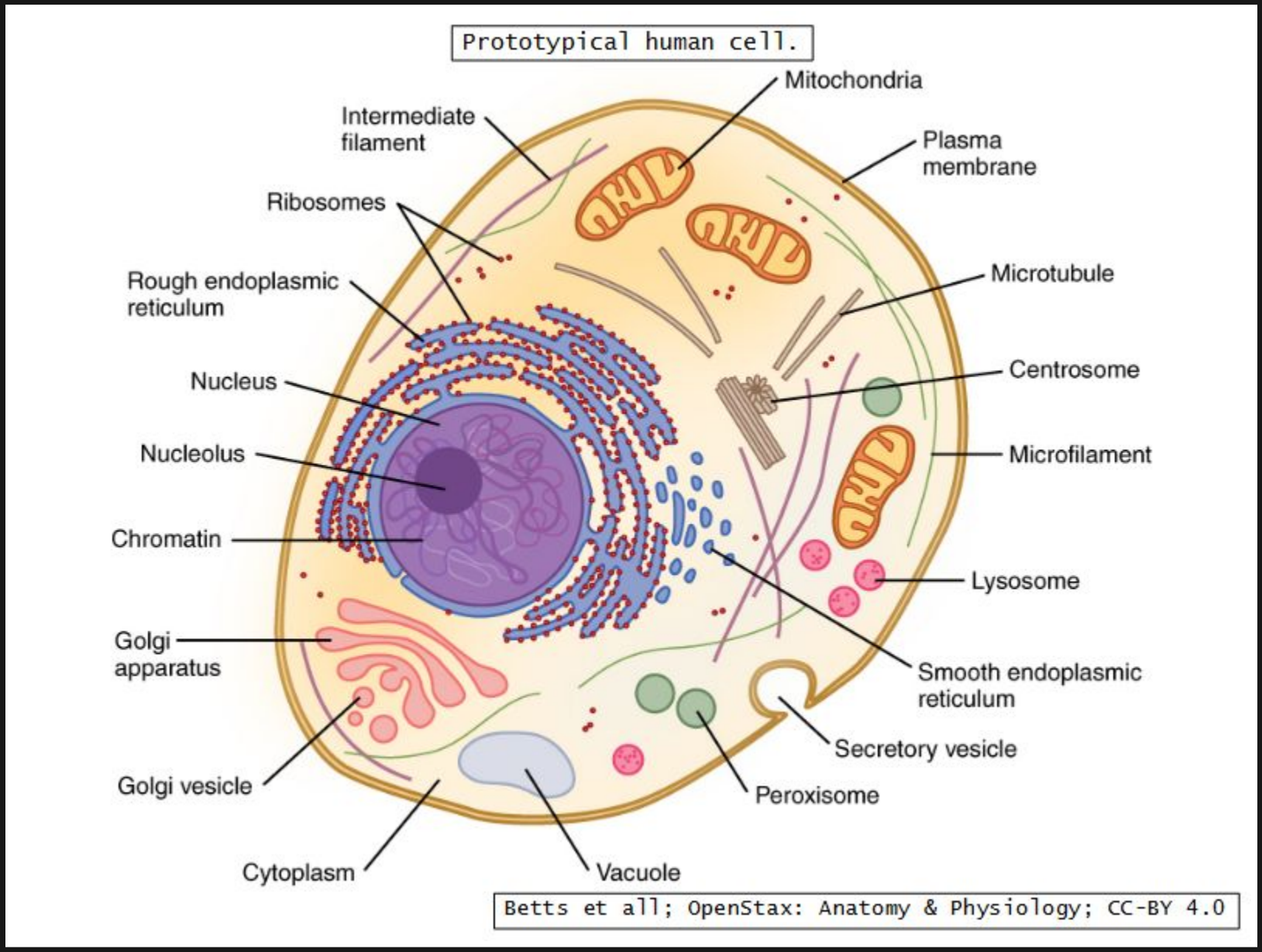
The next slide shows an unlabelled image. Whenever you come across an unlabelled image, attempt to identify as many of the marked structures, BEFORE going to the next slide. Give yourself a score for each attempt, and when you revise, aim for an improvement on your previous score.

Remember - incremental improvements








Prototypical human cell.
Mitochondria
Intermediate filament
Plasma membrane
Ribosomes
Microtubule
Rough endoplasmic reticulum
Centrosome
Nucleus
Microfilament
Nucleolus
Chromatin
Lysosome
Golgi apparatus
Smooth endoplasmic reticulum
Secretory vesicle
Golgi vesicle
Peroxisome
Cytoplasm
Vacuole
Betts et all; OpenStax: Anatomy & Physiology; CC-BY 4.0

Histology How

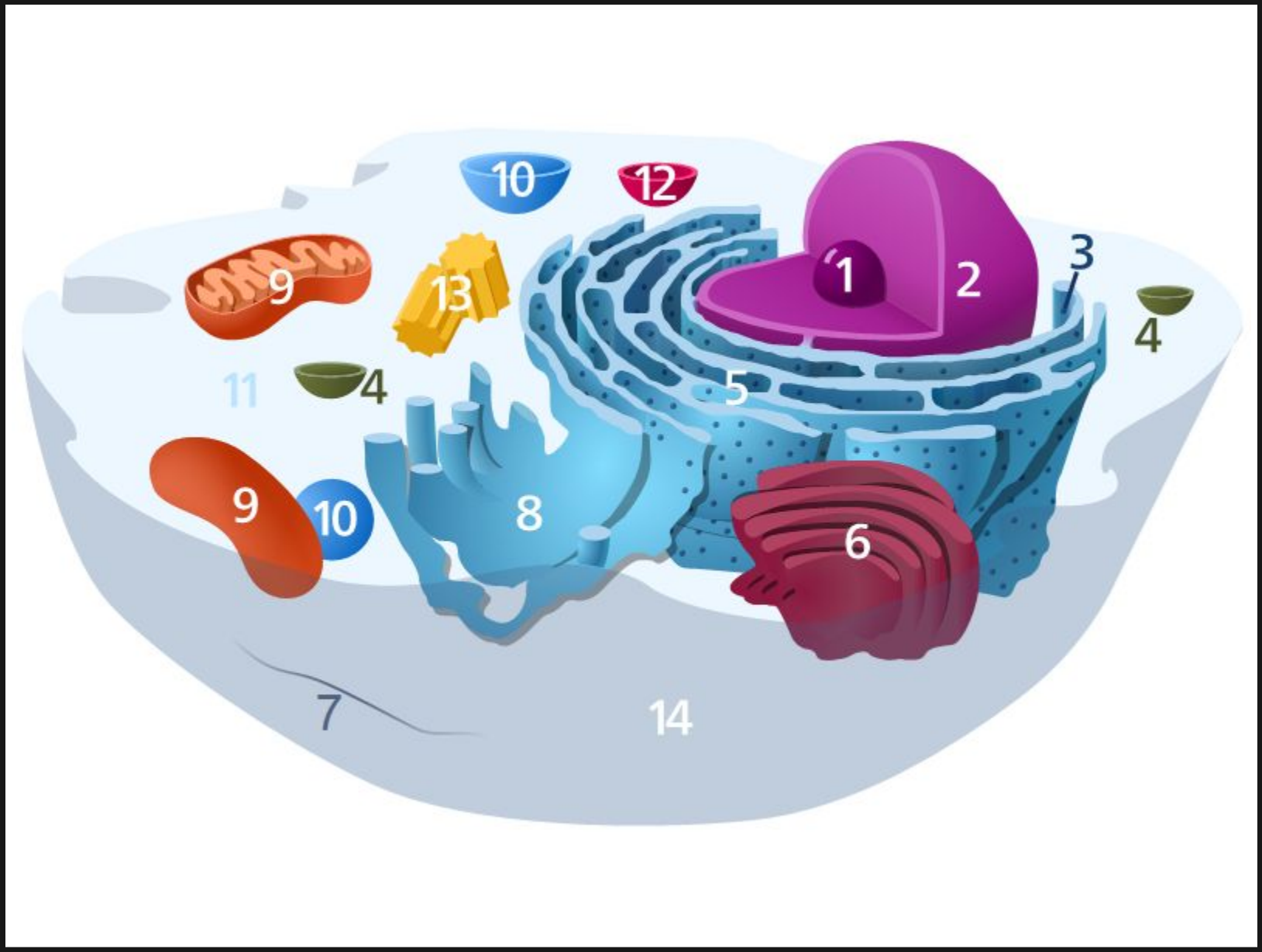
Histology is a visual subject.

You have to look at, identify, draw.

Pictures, illustrations, diagrams.

The Cell

Ultrastructure of the cell


10
12
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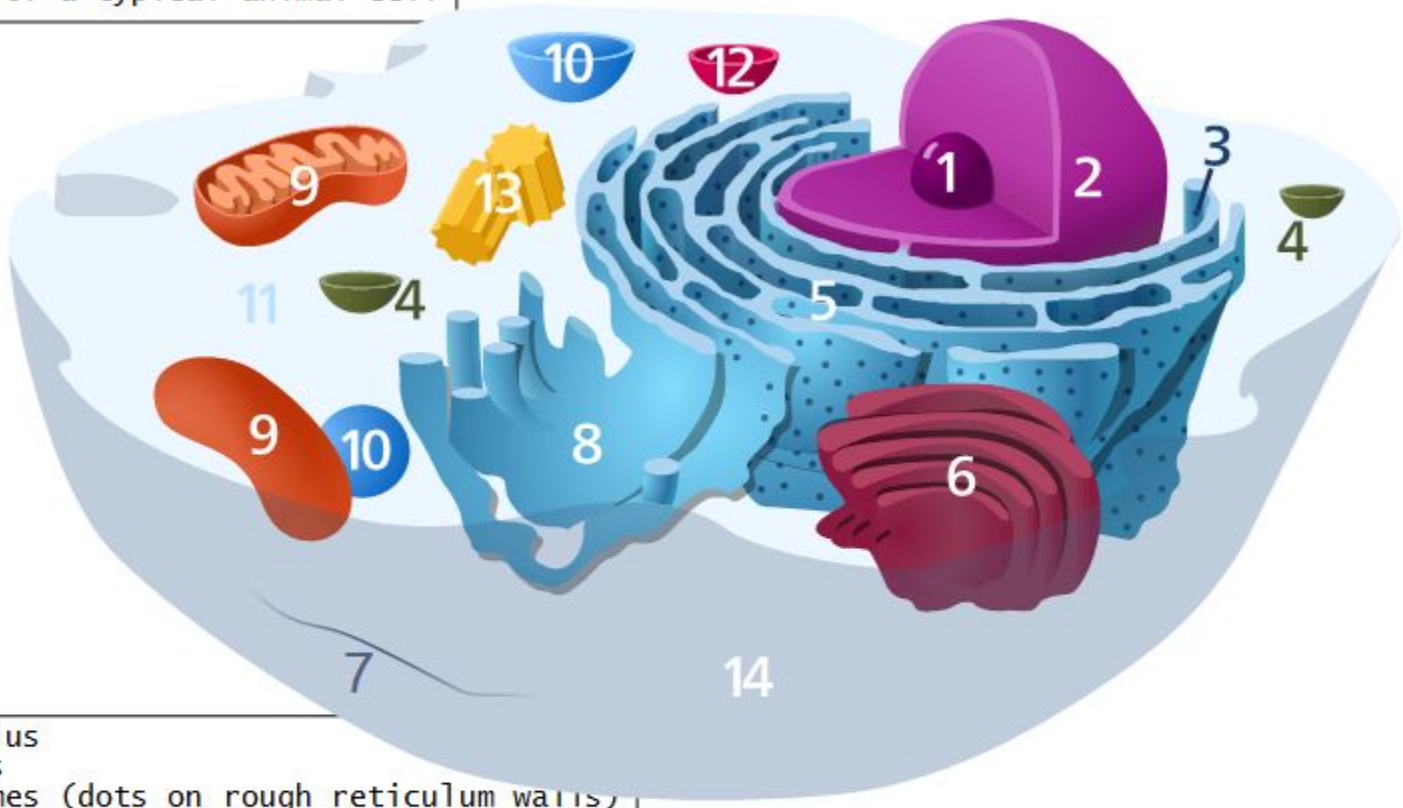
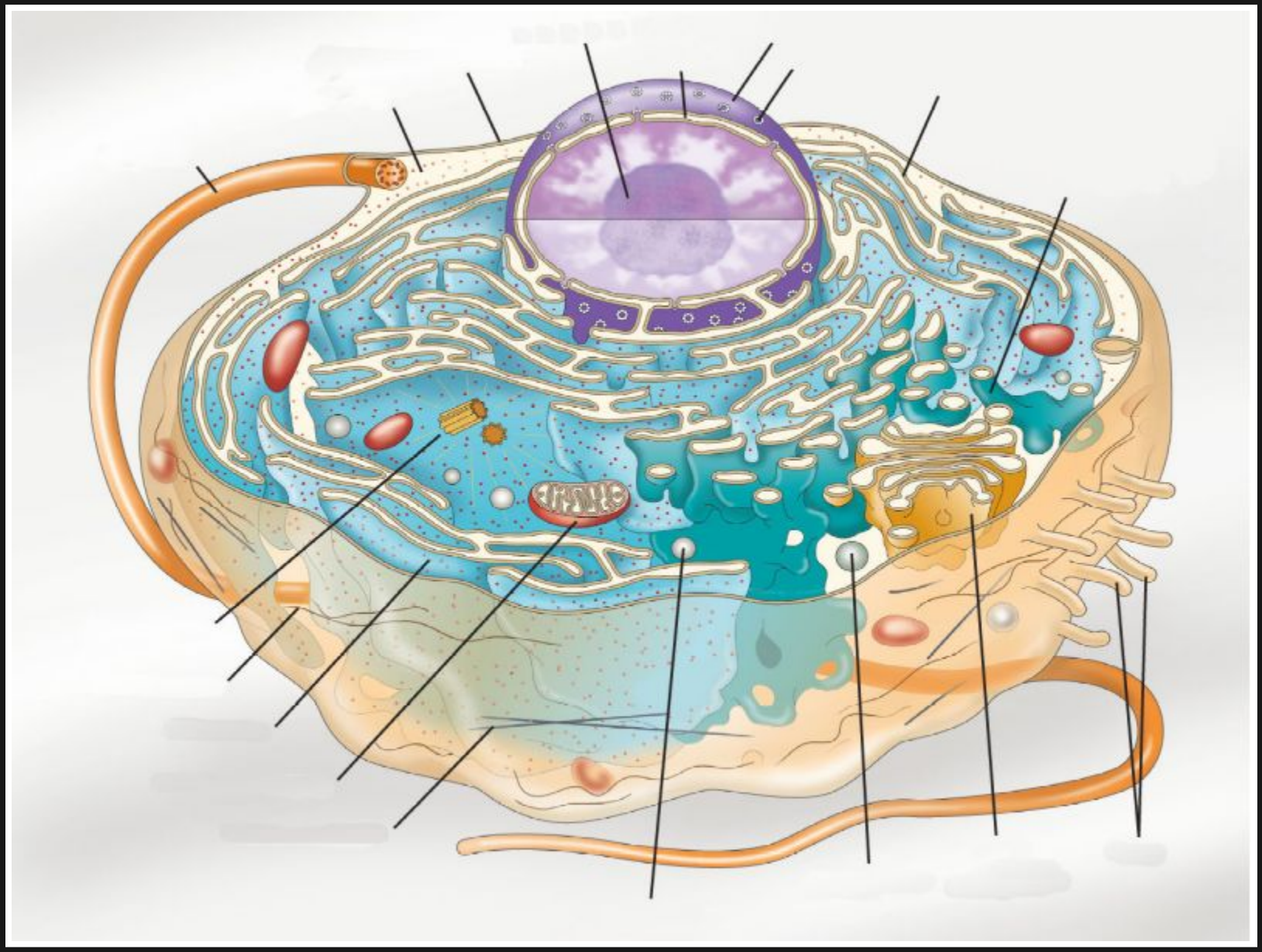
14

Diagram of a typical animal cell

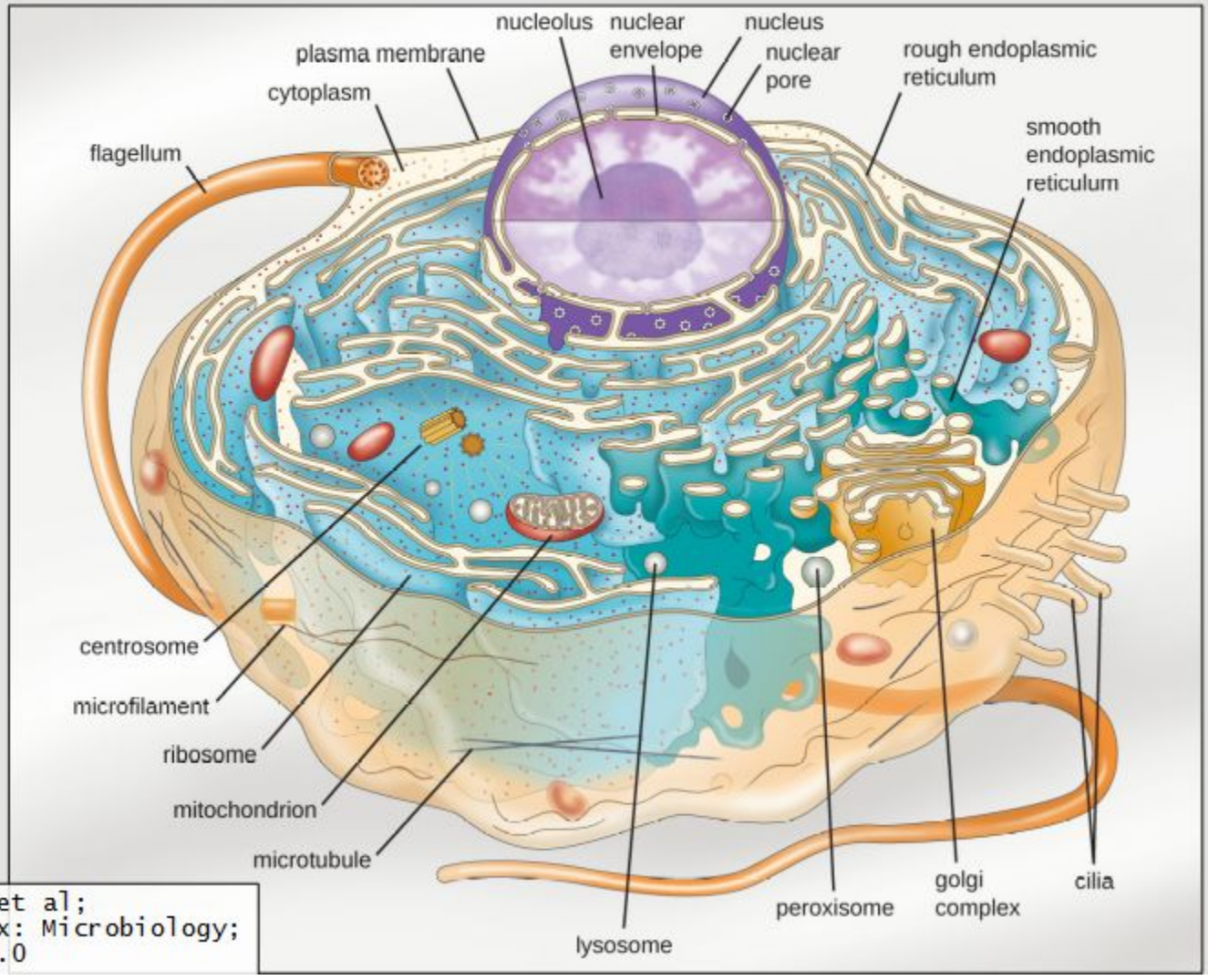


1 Nucleolus
2 Nucleus
3 Ribosomes (dots on rough reticulum walls)
4 Vesicle
5 Rough endoplasmic reticulum
6 Golgi apparatus (or "Golgi body")
7 Cytoskeleton
8 Smooth endoplasmic reticulum
9 Mitochondrion
10 Vacuole
11 Cytosol
12 Lysosome
13 Centriole
14 Cell membrane

Sketch; PD



An illustration of a generalized, single-celled eukaryotic organism. Note that cells of eukaryotic organisms vary greatly in terms of structure & function, & a particular cell may not have all of the structures shown here.



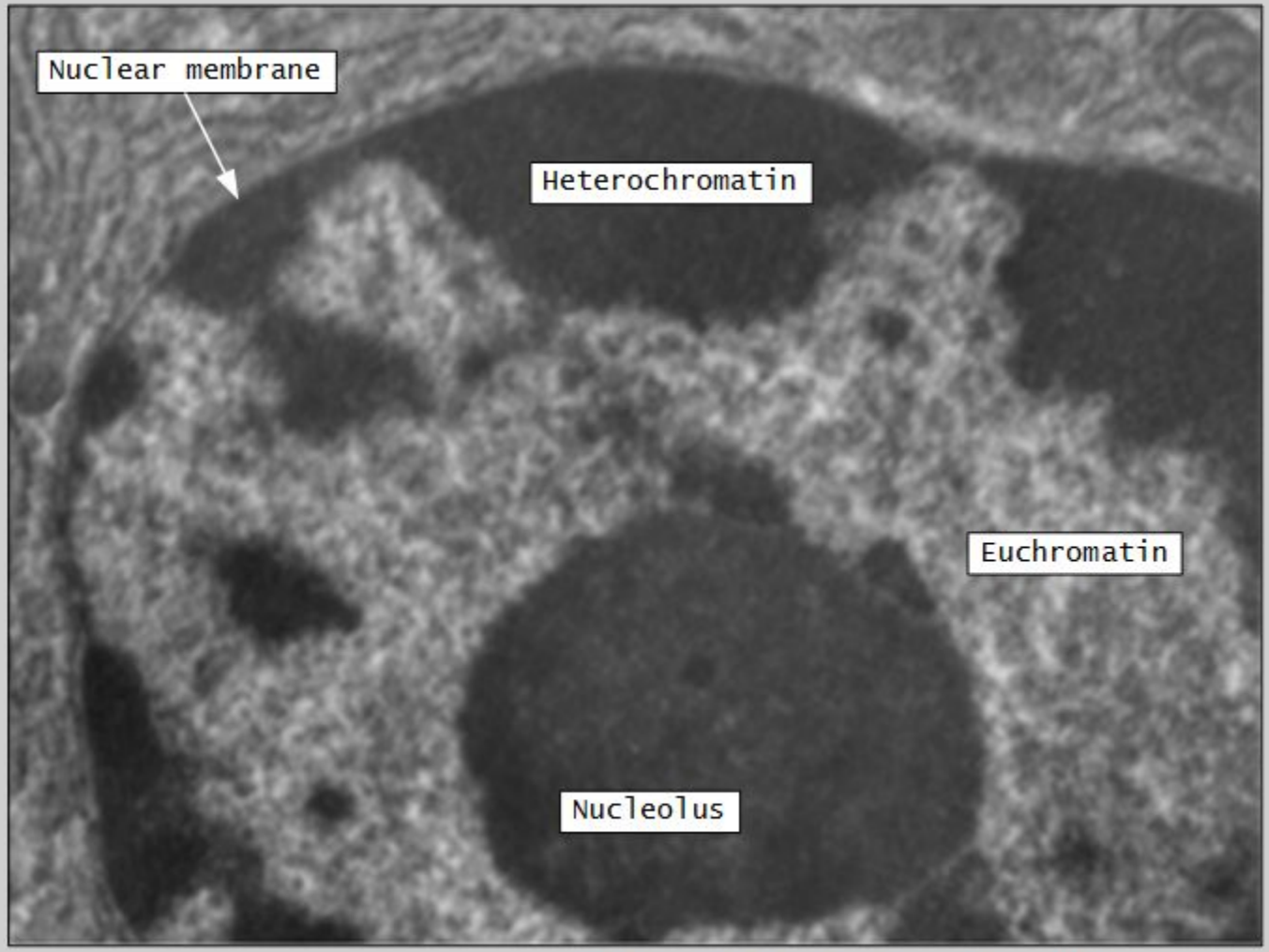
The cell

- Smallest unit living matter
- Two compartments
- Nucleus
    - Contains chromatin -> genetic material
- Cytoplasm
    - Organelles -> metabolically active units
    - Inclusions -> inert accumulations
    - Cytoskeleton

Nucleus

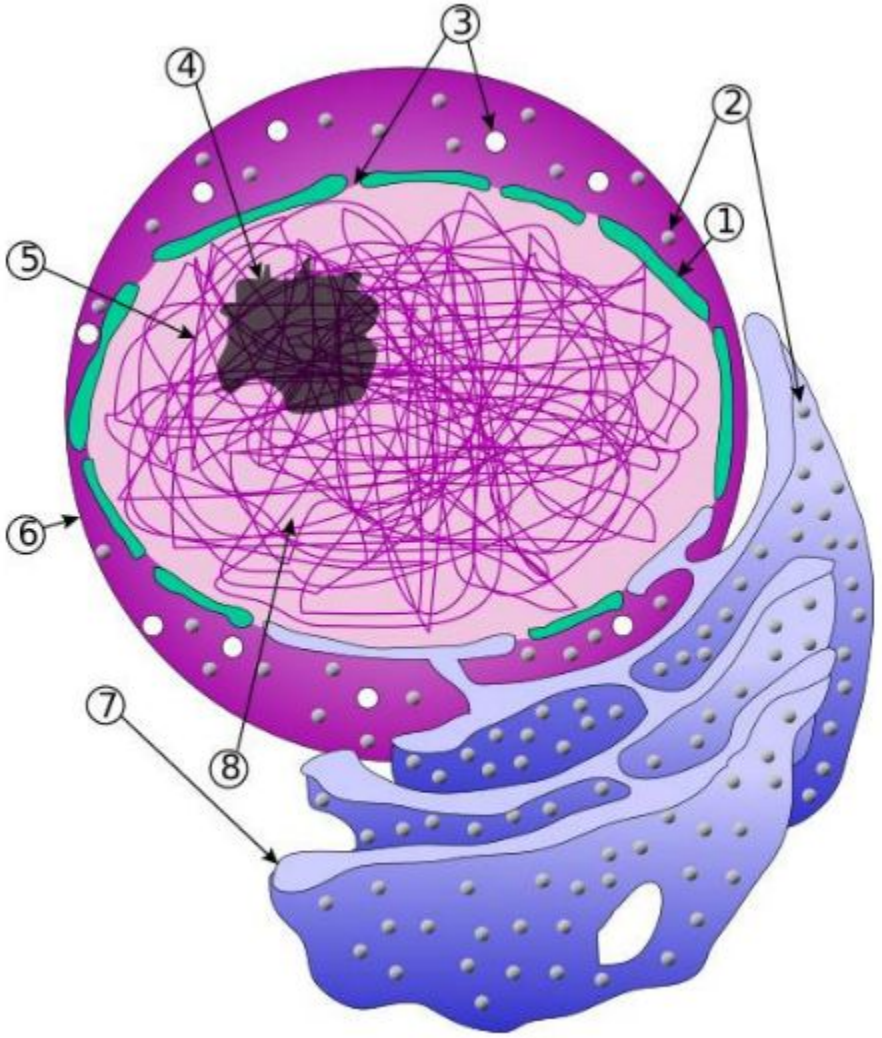
- Contains genetic material
- Encoded in DNA of chromosomes
- Euchromatin
    - lightly stained
    - dispersed chromatin
    - being transcribed
- Heterochromatin
    - densely stained
    - not being transcribed

Eukaryotic cells have a well-defined nucleus surrounded by a nuclear membrane. The large, dark, oval-shaped structure within the nucleolus.



Nuclear envelope

- Two parallel membranes
- Separated by peri-nuclear space
- Inner and outer continuous at nuclear pore
- Nuclear pore interrupt double membrane
- Outer nuclear membrane
- Ribosomes attached
- Continuous with endoplasmic reticulum
- Inner nuclear membrane
- Meshwork interwoven filaments
- Fibrous lamina (nuclear lamina)
- Anchoring site for interphase chromosomes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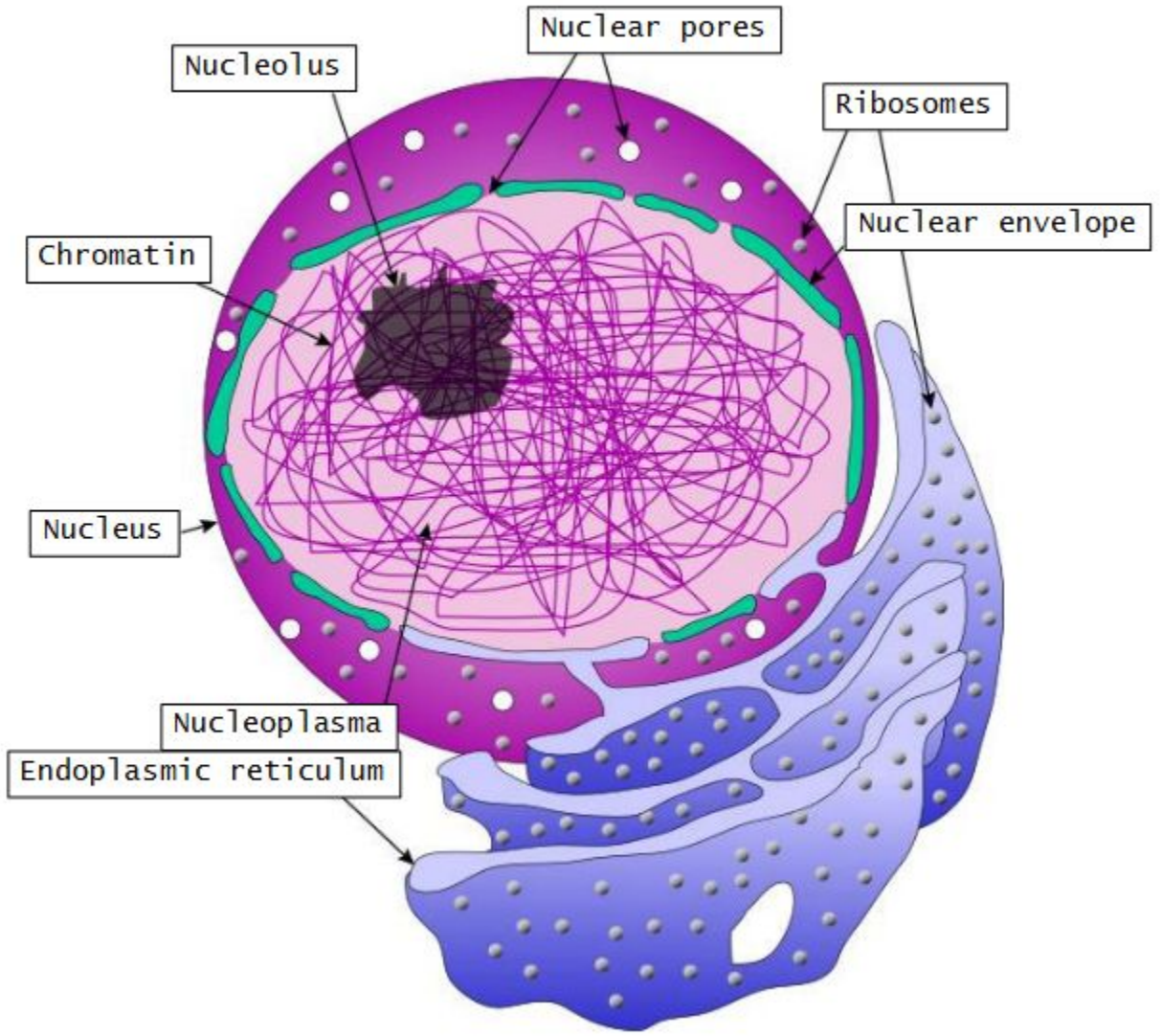
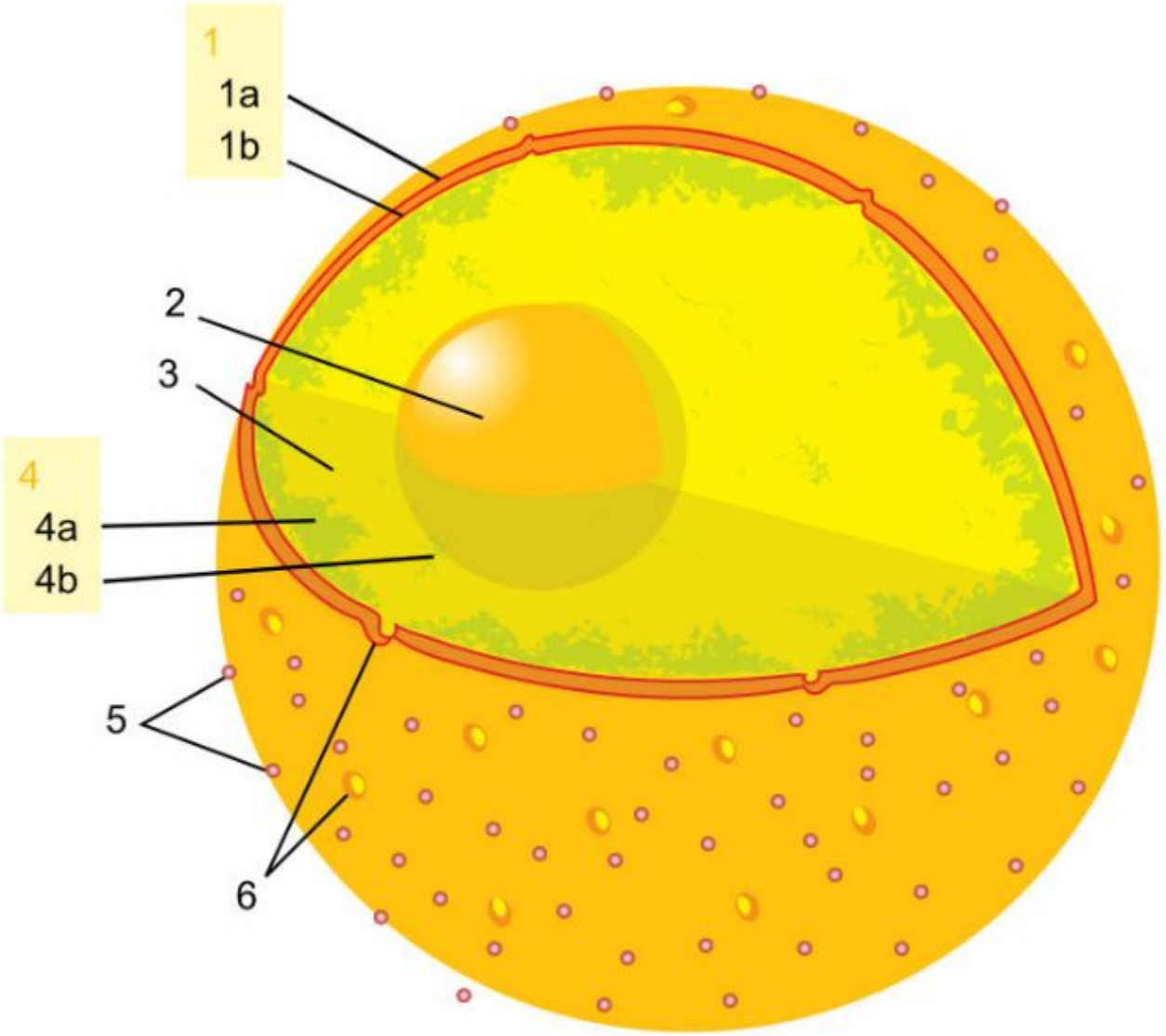
Cell nucleus and endoplasmic reticulum



Nuclear pore

- Membrane-bounded channel between nucleus and cytoplasm
- Outer and inner membrane continuous around pore
- Provide communication between nucleus and cytoplasm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1a
1b
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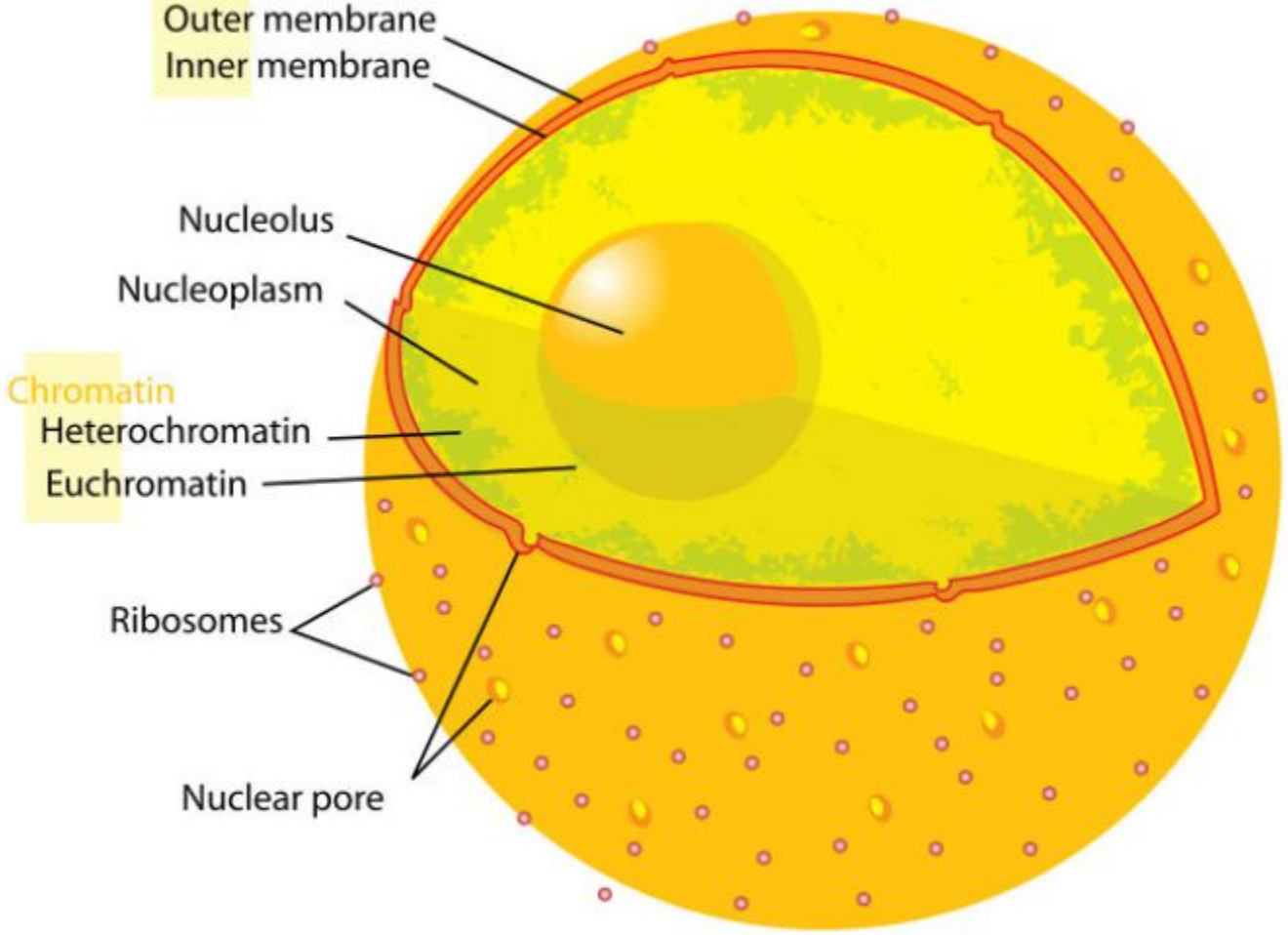
4a
4b
5
6

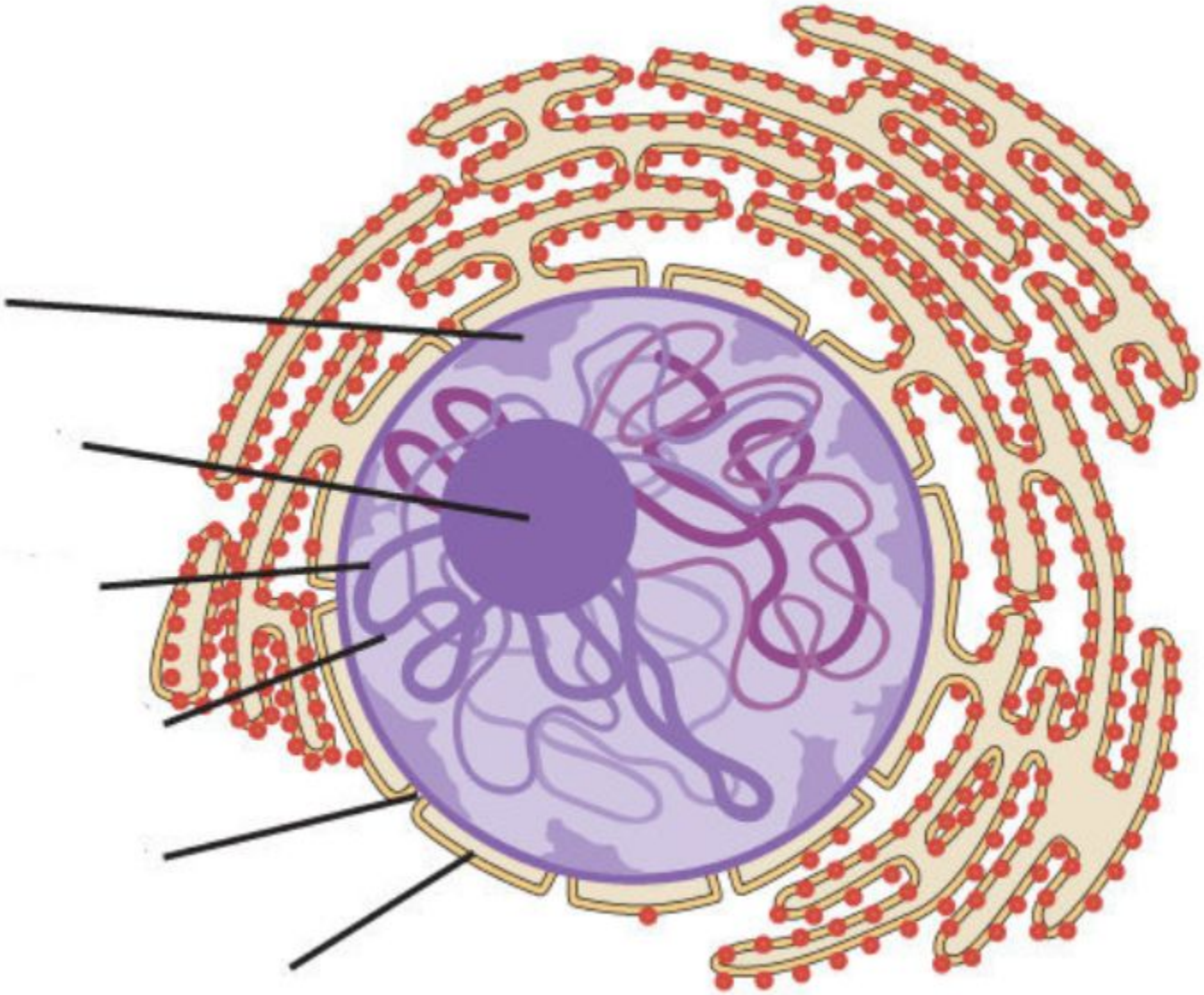
Diagram of cell nucleus



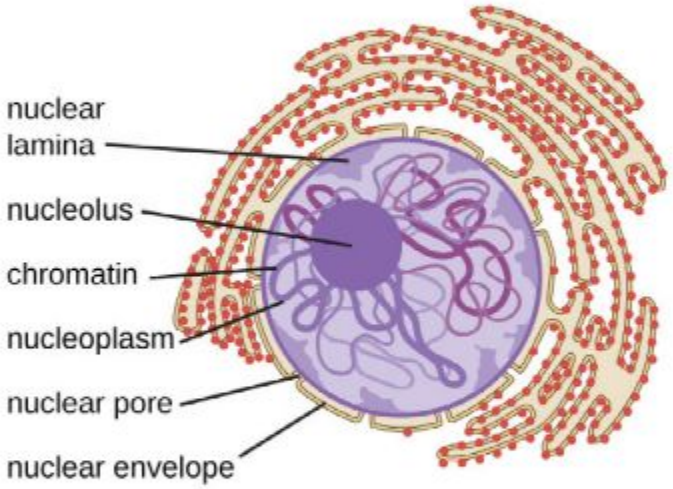
Sketch

Nucleolus

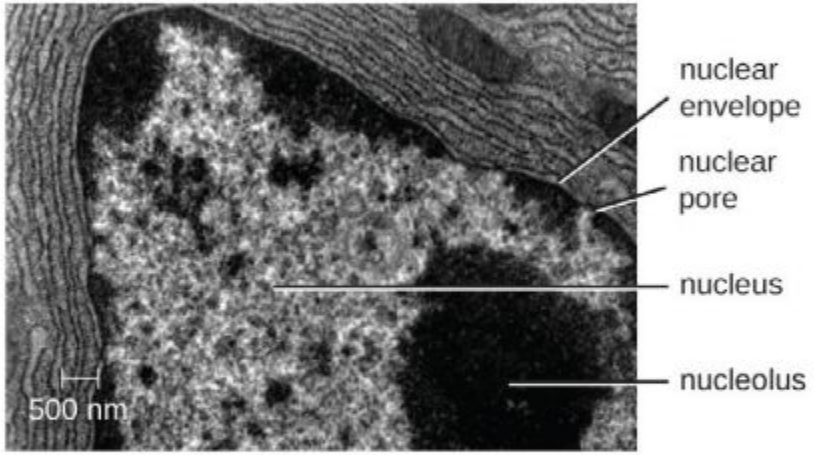
- Well-defined nuclear inclusion
- Seen in cells actively synthesizing protein
- Involved in
    - Synthesis rRNA
    - Packaging rRNA into precursors of ribosomes



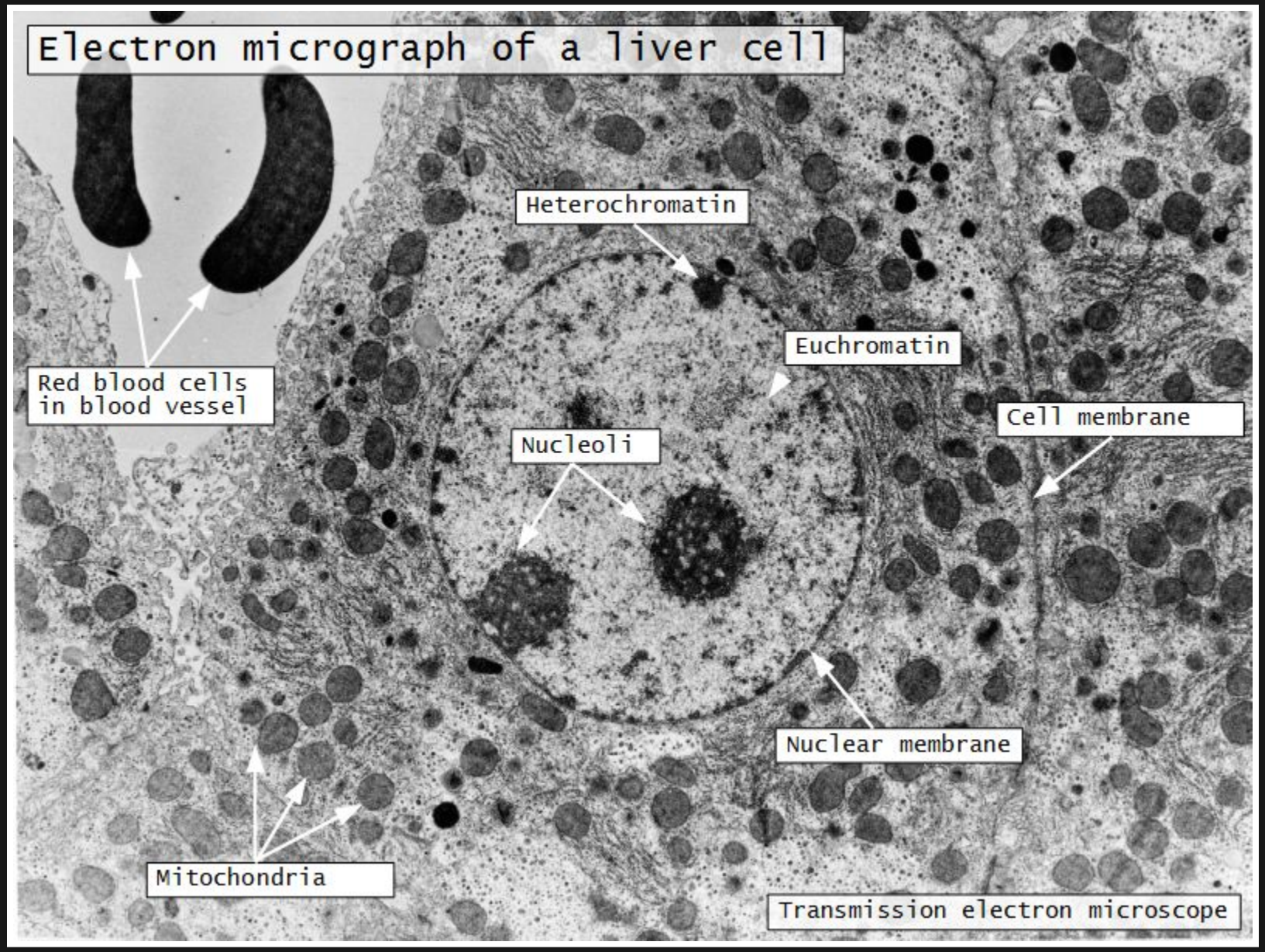
The endomembrane system is a series of membranous intracellular structures, facilitating movement of materials throughout the cell & the cell membrane.

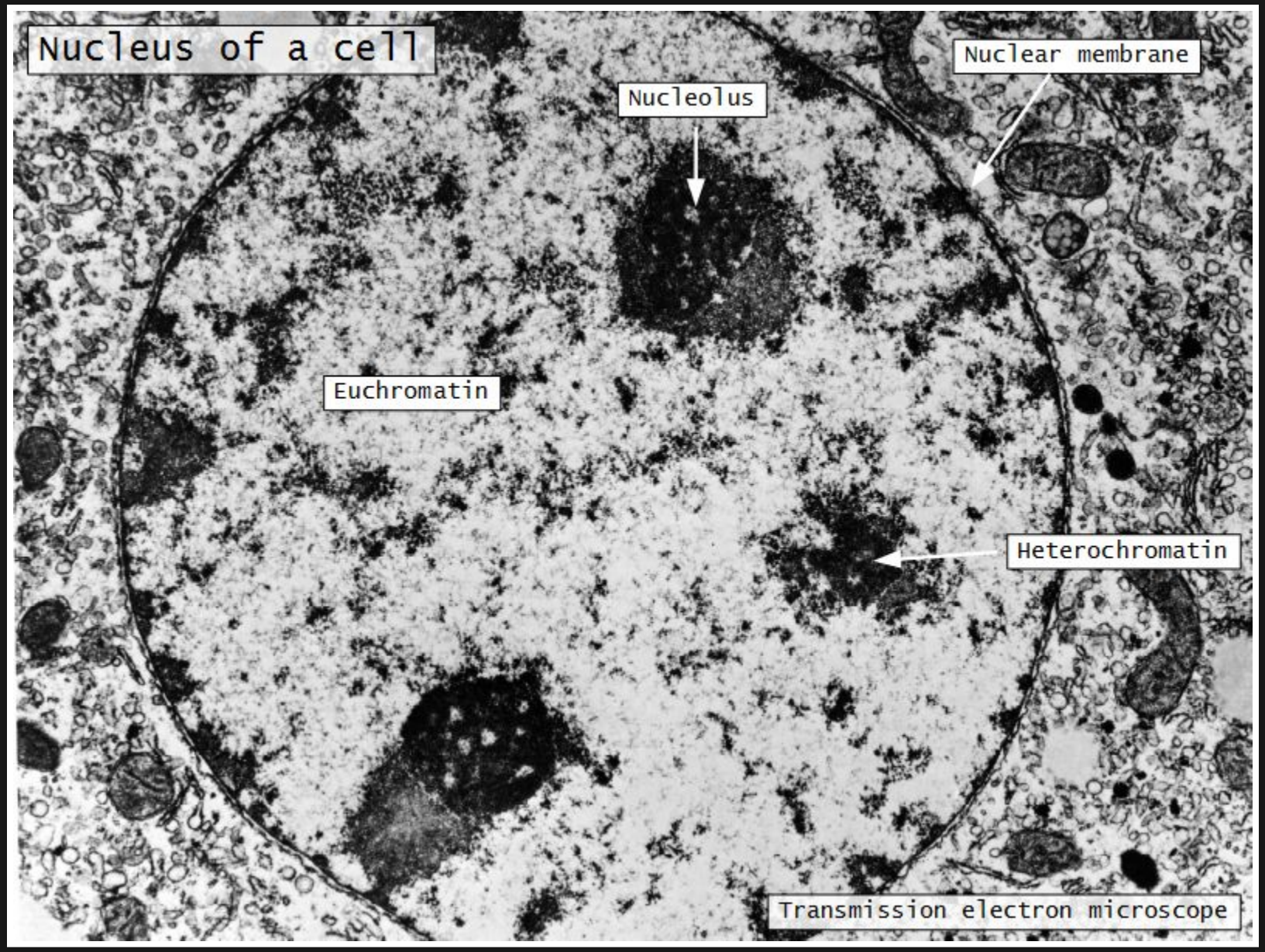


(a)



(b)

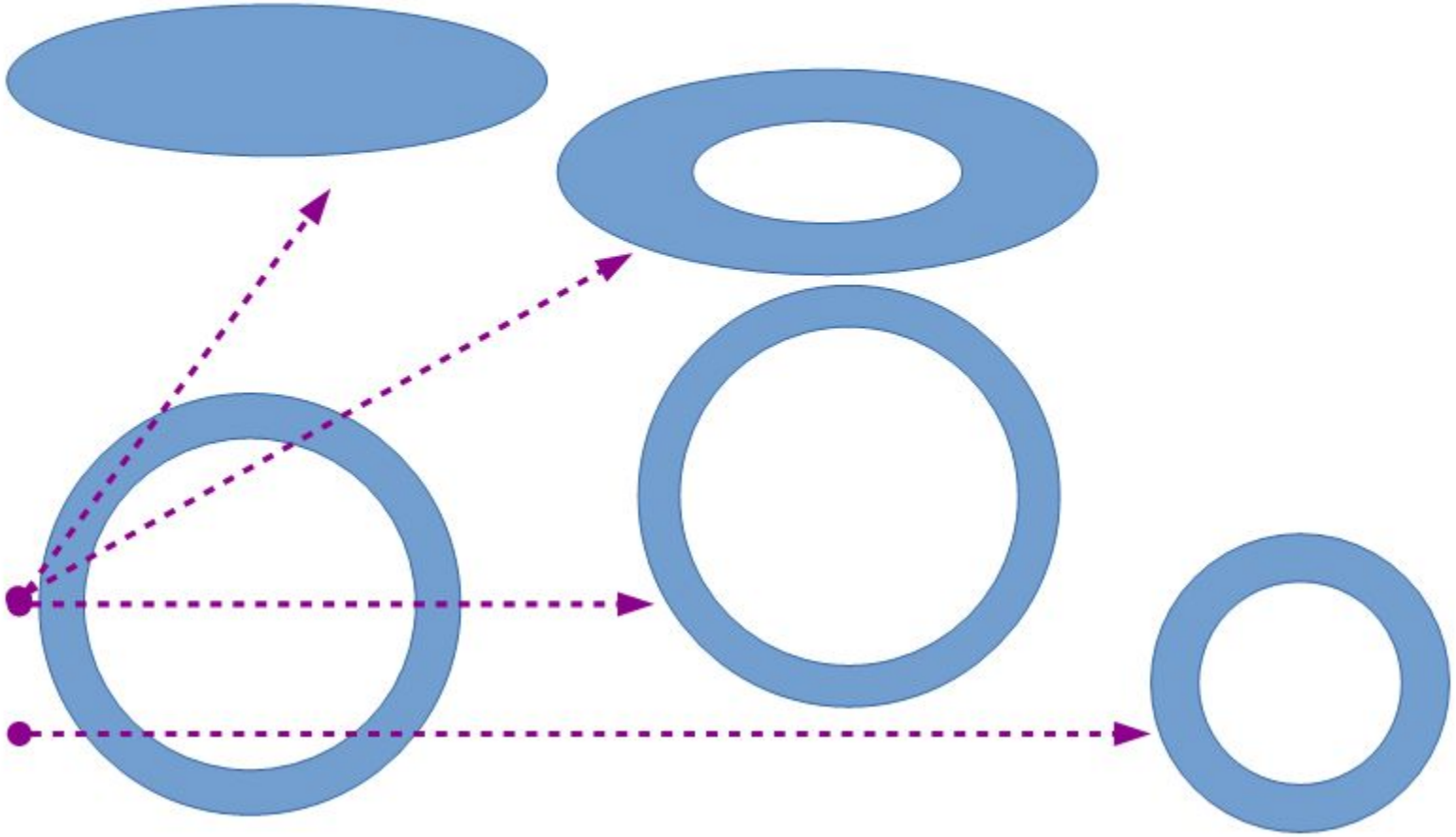

Electron micrograph of a liver cell
Heterochromatin
Euchromatin
Red blood cells in blood vessel
Cell membrane
Nucleoli
Nuclear membrane
Mitochondria
Transmission electron microscope

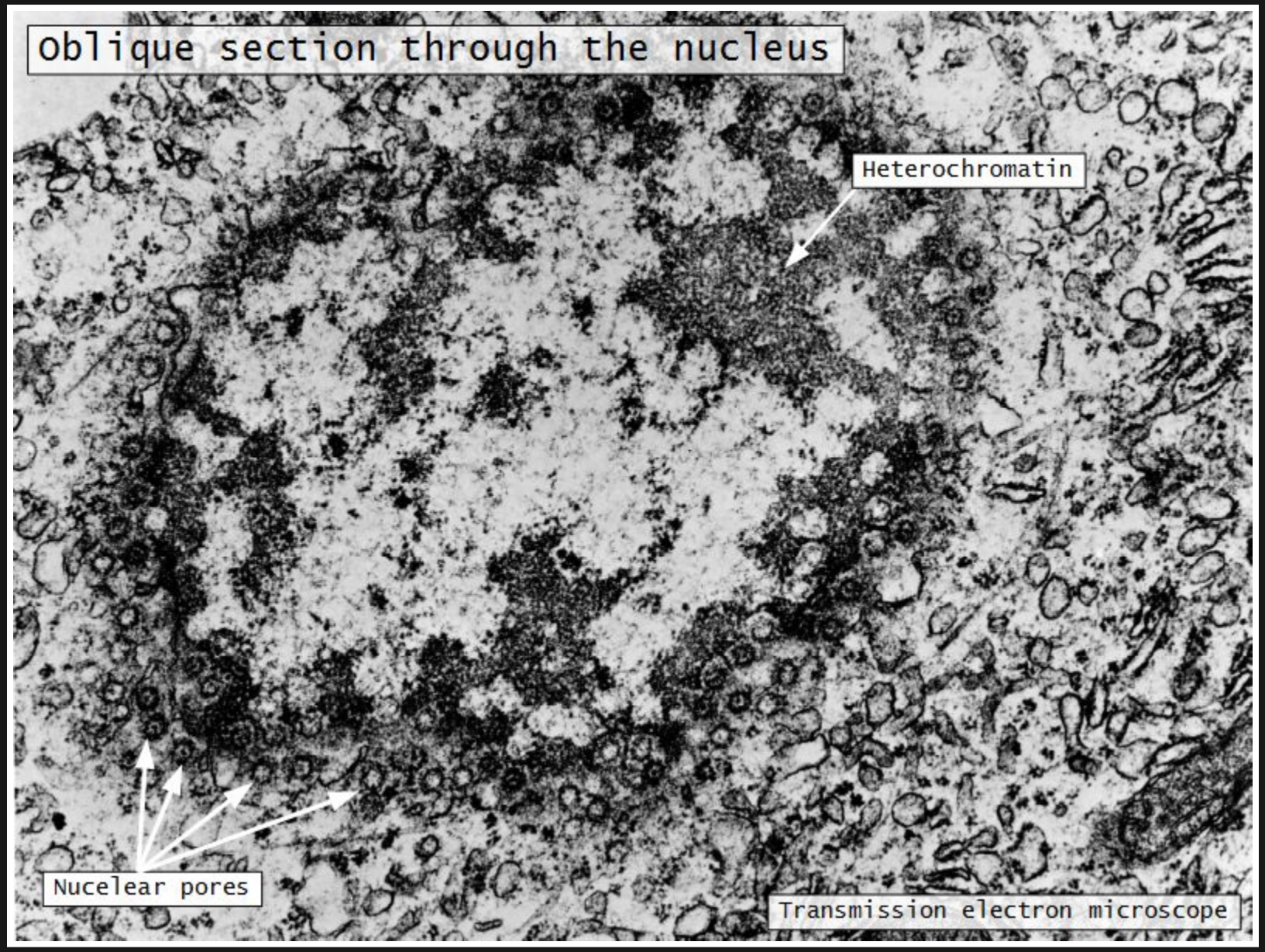

Nucleus of a cell
Nuclear membrane
Nucleolus
Euchromatin
Heterochromatin
Transmission electron microscope

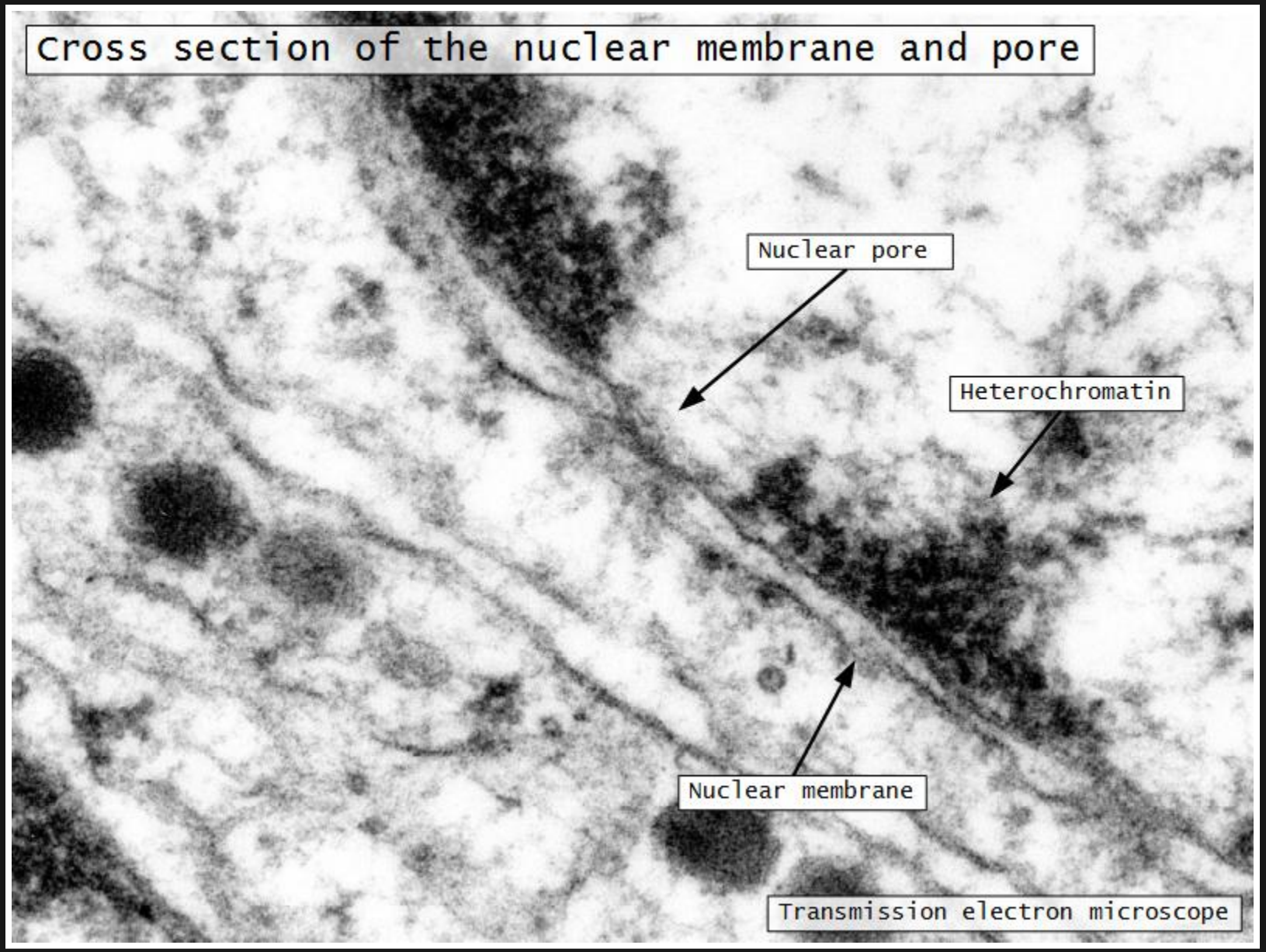
Oblique sections:

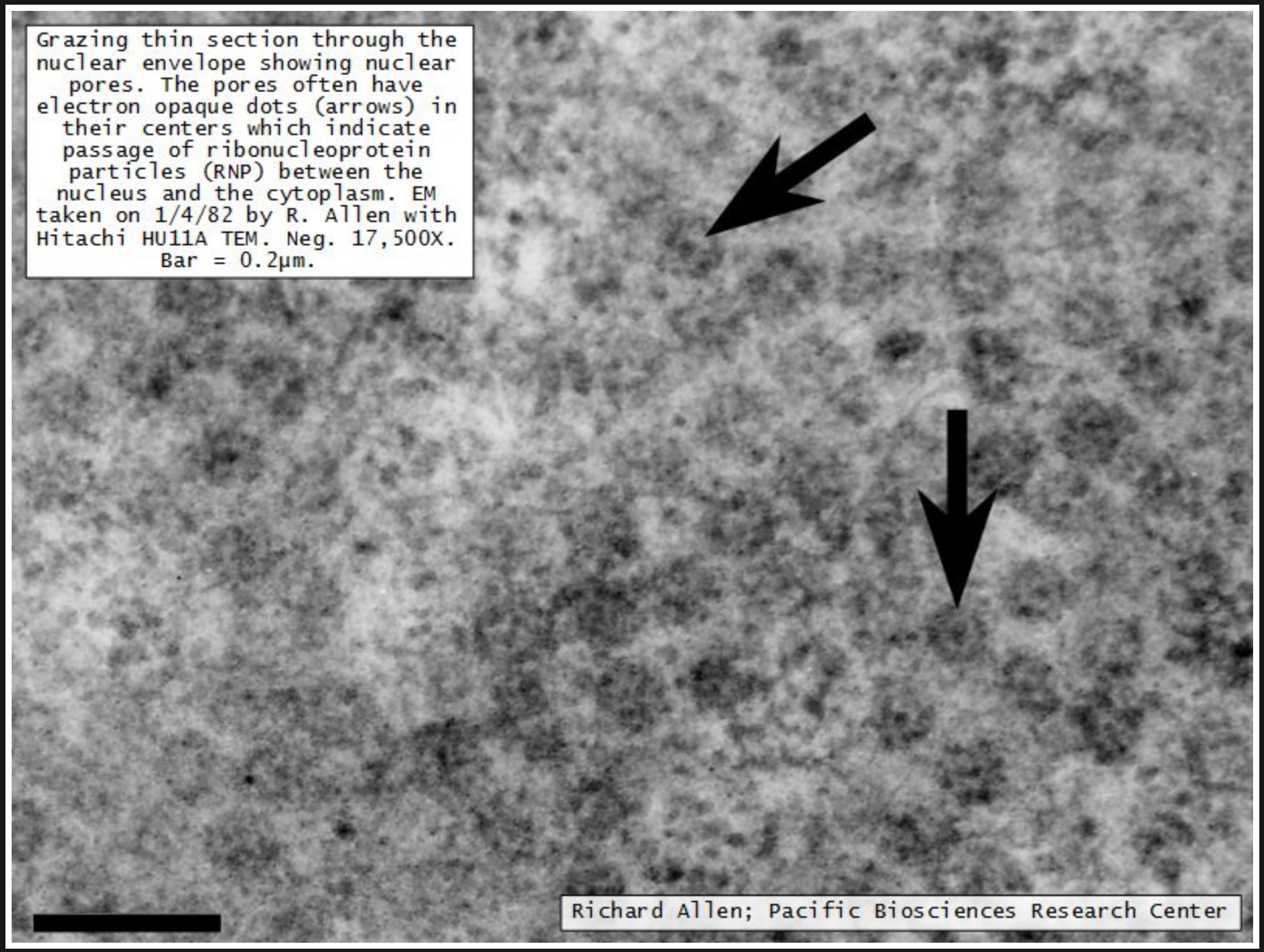
Section does not always cut exactly through the center of a structure. This can reveal additional information about the morphology.

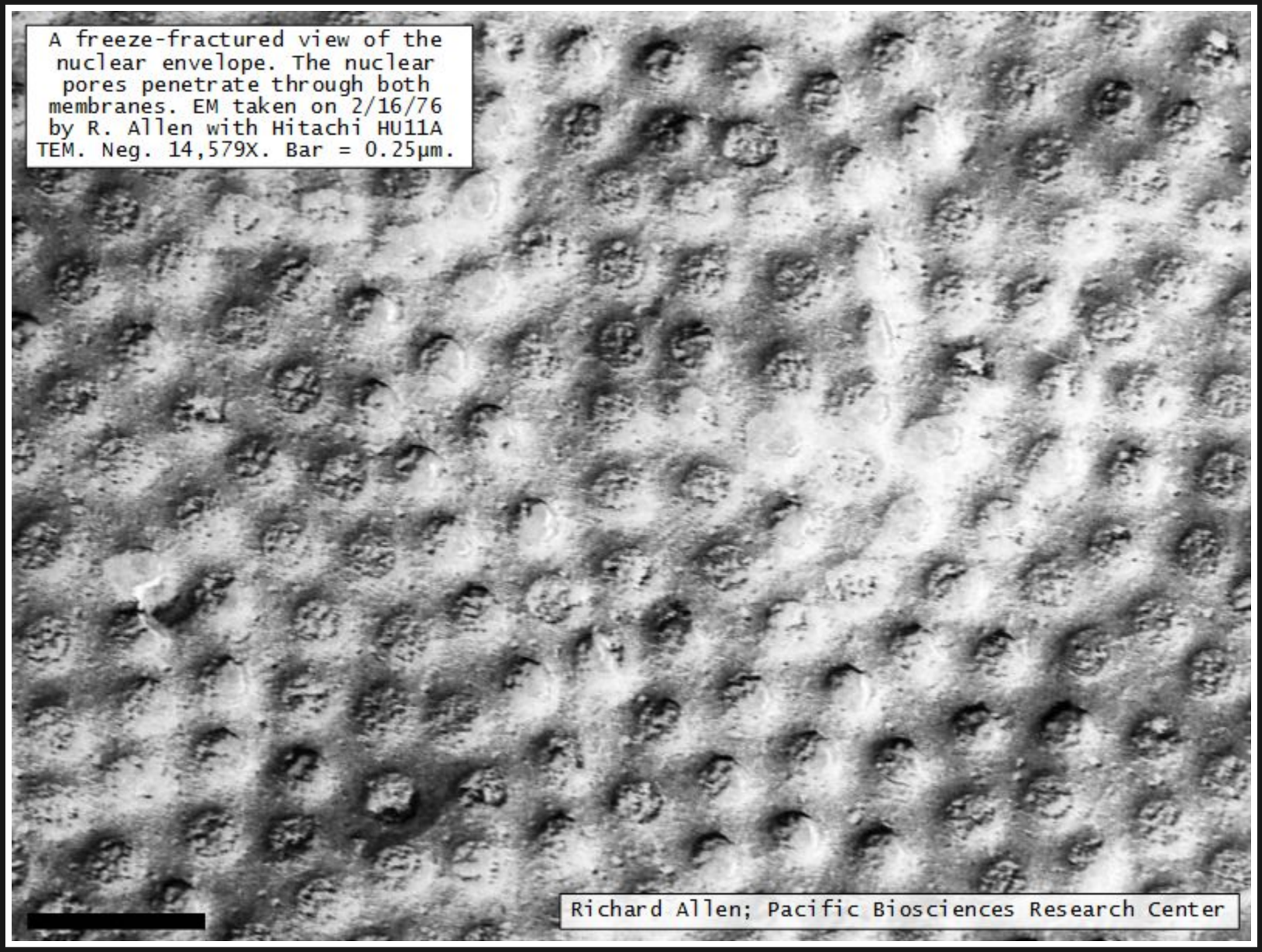
This diagram illustrate 4 sections through a sphere and the corresponding views.




Oblique section through the nucleus
Heterochromatin
Nucelear pores
Transmission electron microscope


Cross section of the nuclear membrane and pore
Nuclear pore
Heterochromatin
Nuclear membrane
Transmission electron microscope


Grazing thin section through the nuclear envelope showing nuclear pores. The pores often have electron opaque dots (arrows) in their centers which indicate passage of ribonucleoprotein particles (RNP) between the nucleus and the cytoplasm. EM taken on 1/4/82 by R. Allen with Hitachi HU11A TEM. Neg. 17,500X. Bar = 0.2µm.
Richard Allen; Pacific Biosciences Research Center


A freeze-fractured view of the nuclear envelope. The nuclear pores penetrate through both membranes. EM taken on 2/16/76 by R. Allen with Hitachi HU11A TEM. Neg. 14,579X. Bar = 0.25µm.
Richard Allen; Pacific Biosciences Research Center

Cytoplasm organelles

- Cell membrane
- Glycocalyx
- Ribosomes
- Rough endoplasmic reticulum
- Smooth endoplasmic reticulum
- Mitochondria
- Golgi apparatus
- Lysosomes
- Residual body
- Peroxisome
- Centrioles

Cytoplasm Cytoskeleton

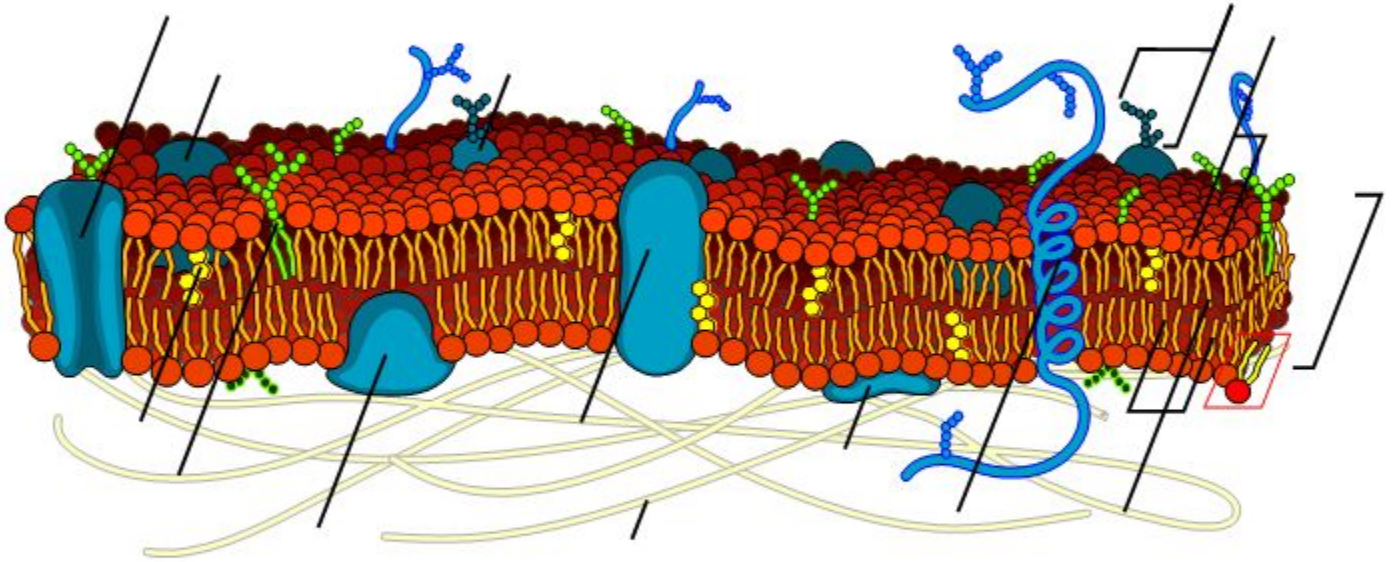
- Microtubules
- Actin microfilaments
- Myosin filaments
- Myosin
- Intermediate filaments
- Keratin filaments
- Desmin filaments
- Vimentin filaments
- Neurofilaments
- Glial filaments
- Microtrabecular lattice

Cytoplasm Inclusions

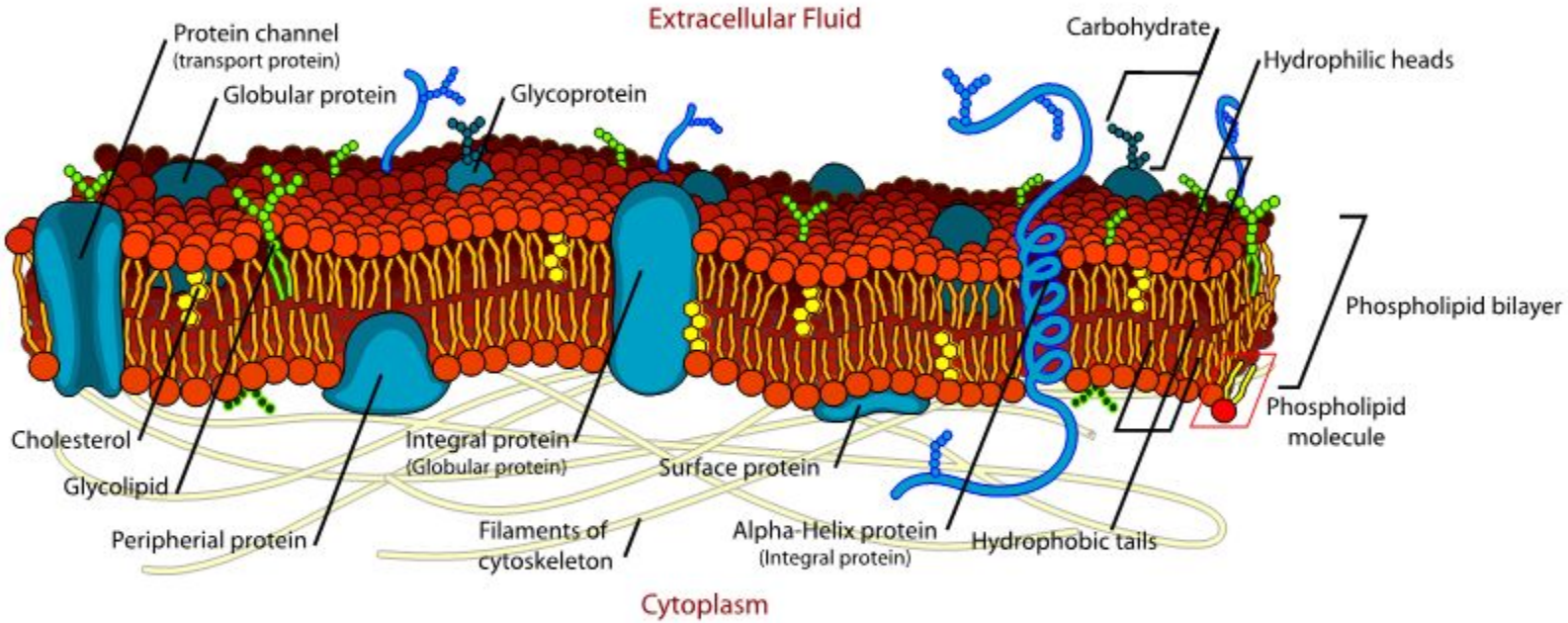
- Glycogen
- Lipid droplets
- Secretion granules

Cell membrane

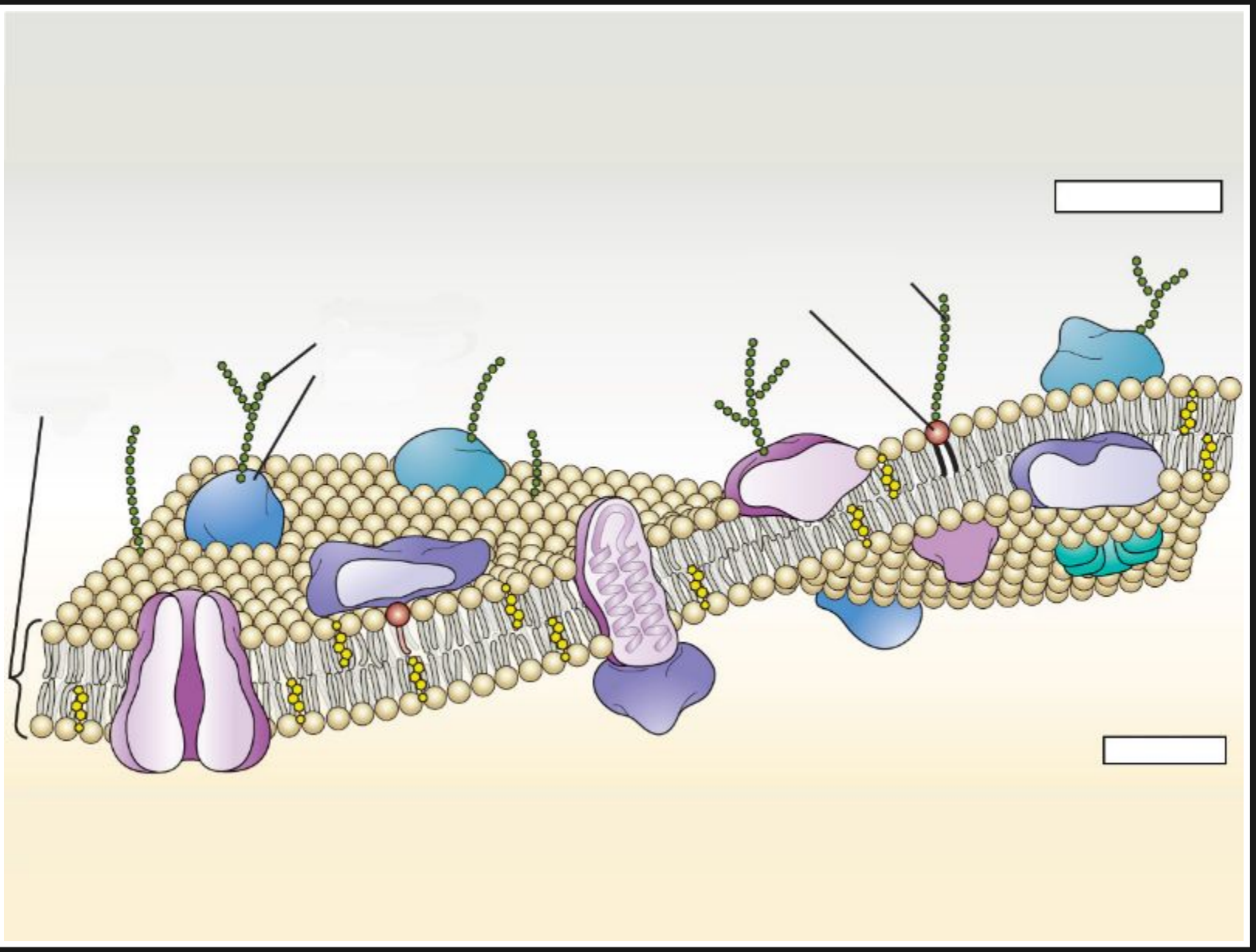
- Surrounds cell
- Boundary between cell & outside world
- Phospholipid bilayer with integral proteins
- Phospholipid
- Hydrophilic ends face outwards
- Hydrophobic chains project inwards
- Protein position varies



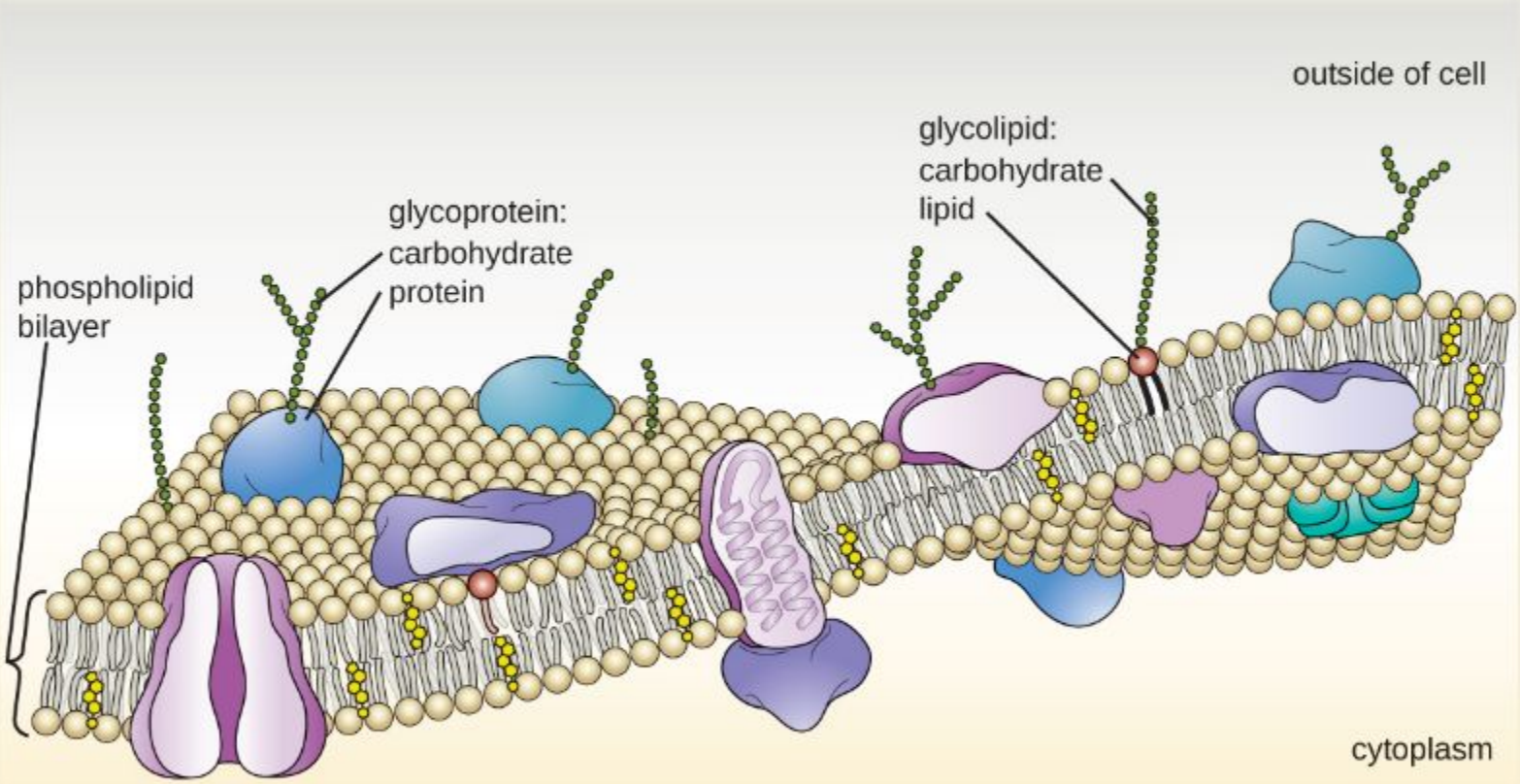
The cell membrane, also called the plasma membrane or plasmalemma, is a semipermeable lipid bilayer common to all living cells. It contains a variety of biological molecules, primarily proteins and lipids, which are involved in a vast array of cellular processes. It also serves as the attachment point for both the intracellular cytoskeleton and, if present, the cell wall.

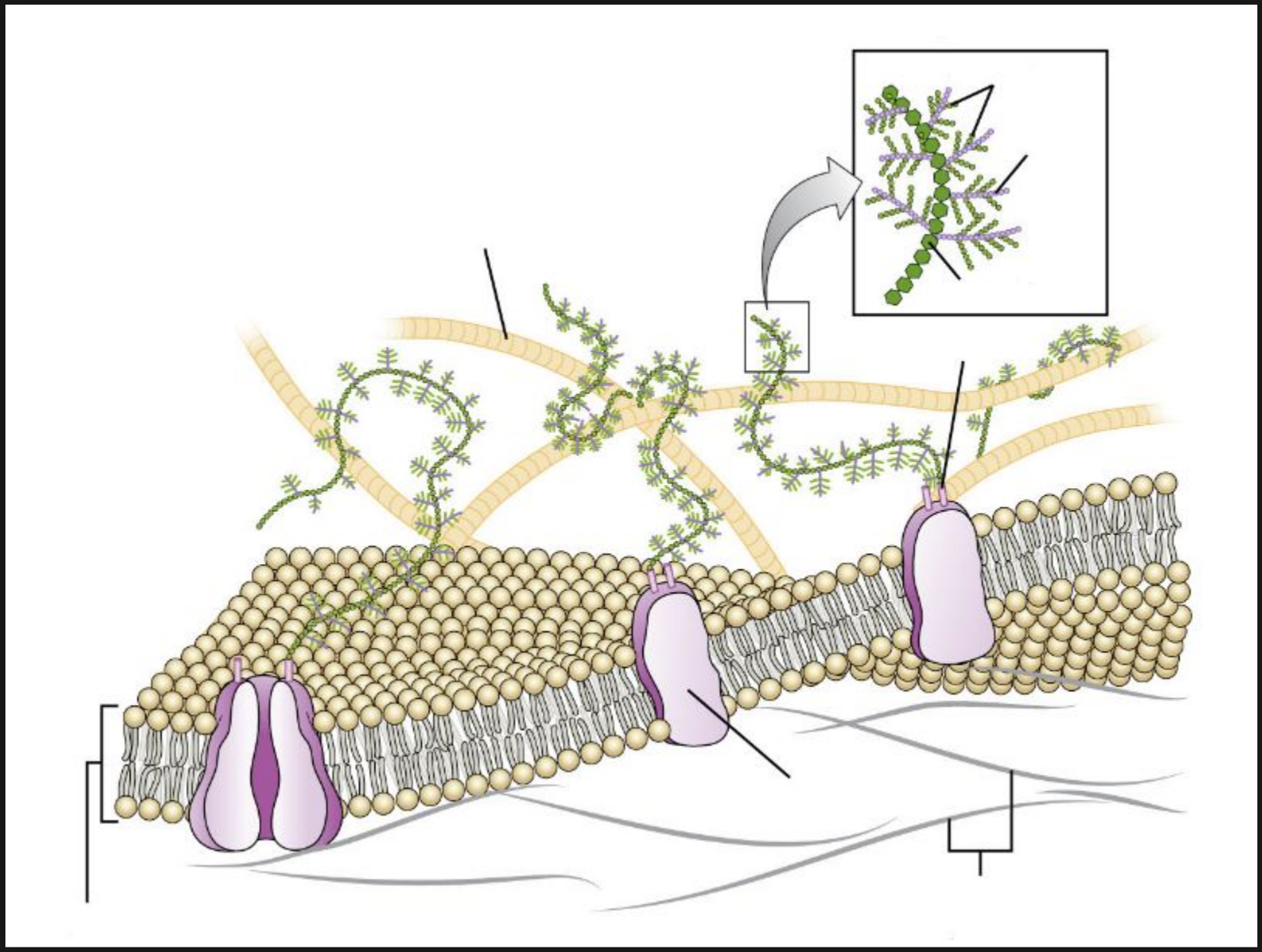


Sketch; LadyofHats; PD

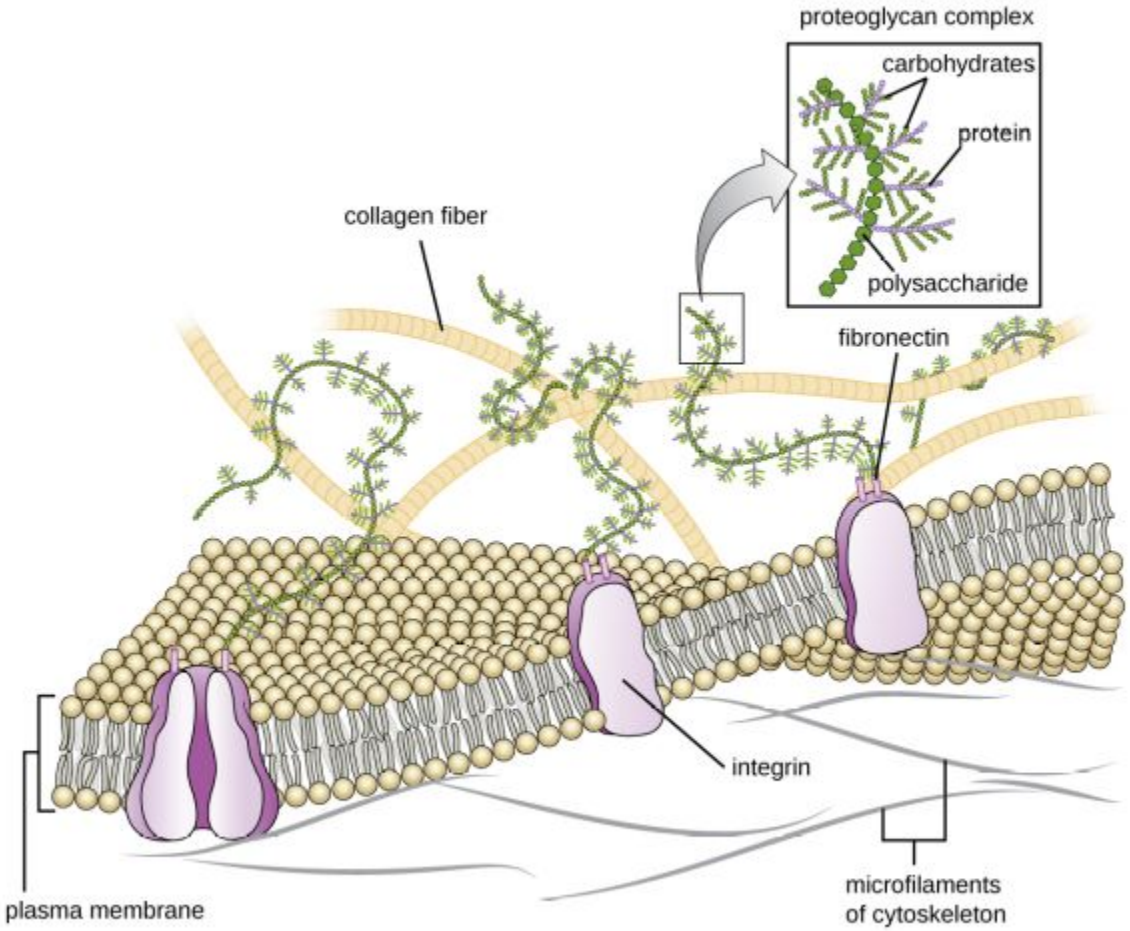


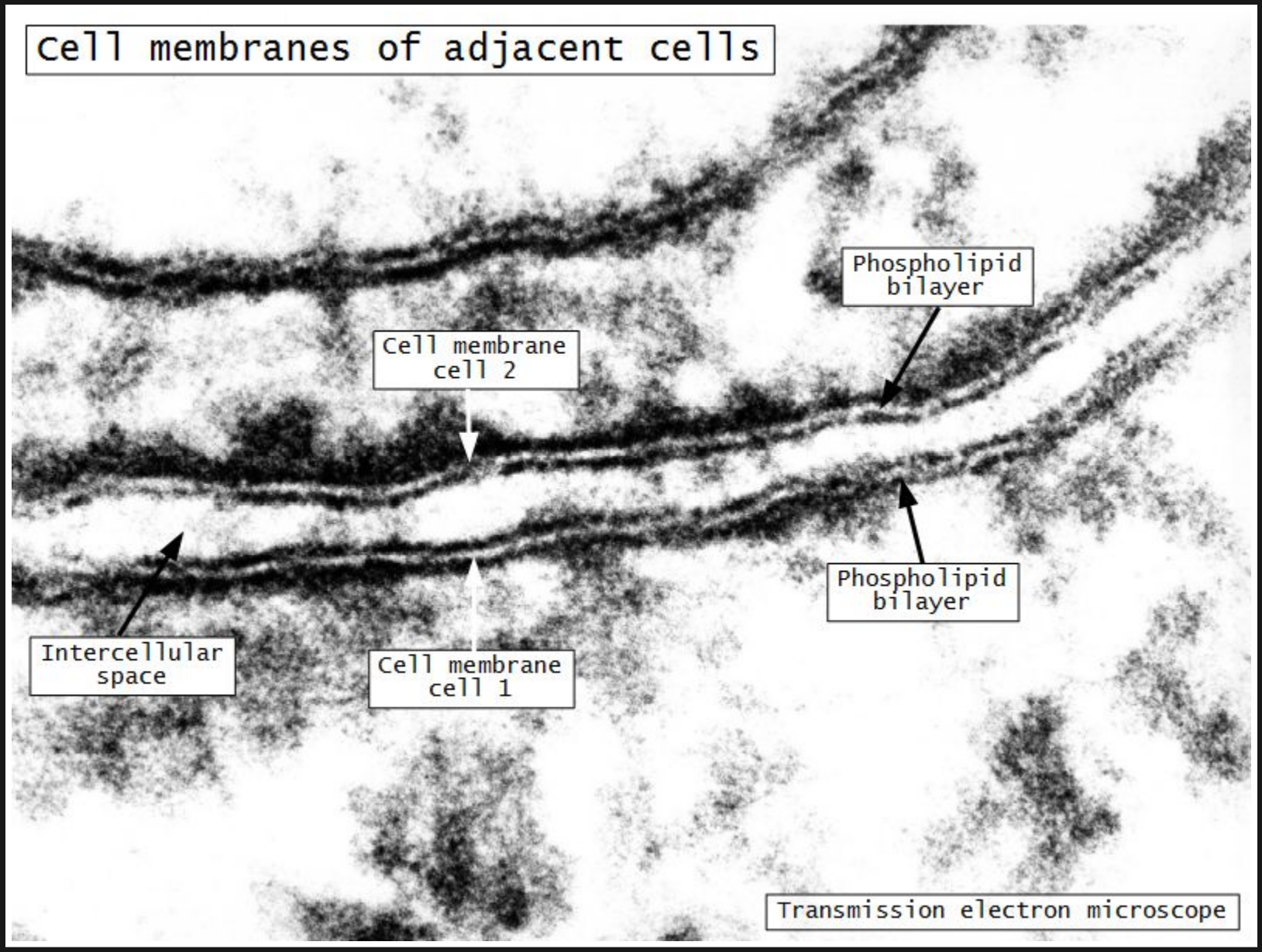
The eukaryotic plasma membrane is composed of a lipid bilayer with many embedded or associated proteins. It contains cholesterol for the maintenance of membrane, as well as glycoproteins and glycolipids that are important in the recognition other cells or pathogens.





The extracellular matrix is composed of protein and carbohydrate components. It protects cells from physical stresses and transmits signals arriving at the outside edges of the tissue to cells deeper within the tissue.



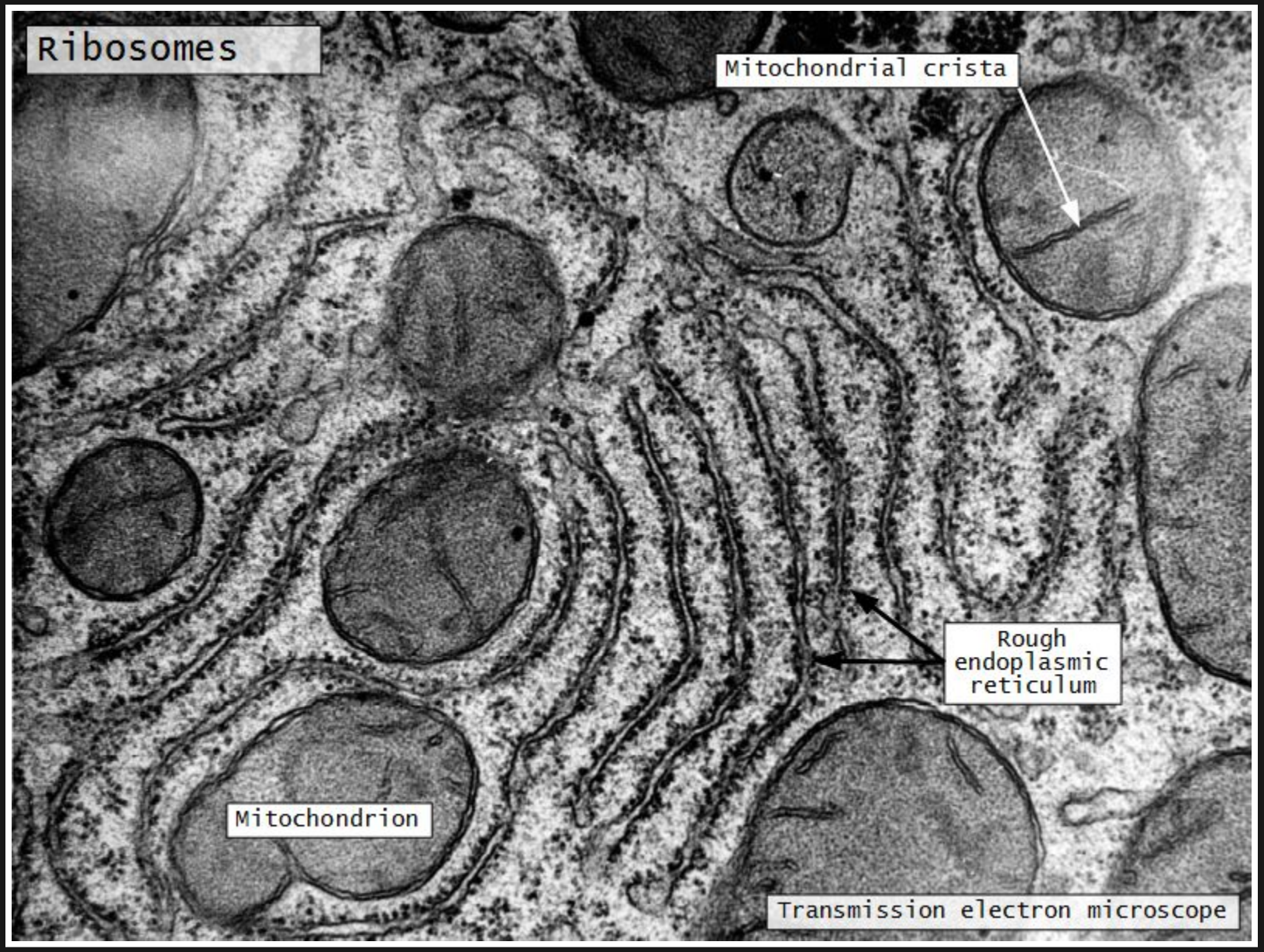

Cell membranes of adjacent cells
Phospholipid bilayer
Cell membrane cell 2
Phospholipid bilayer
Intercellular space
Cell membrane cell 1
Transmission electron microscope

Glycocalyx

- On external surface of plasma membrane
- Plays role in immunological specificity
- Contains blood group antigens
- Has receptor sites
- Protective mechanical barrier
- Can contain enzymes

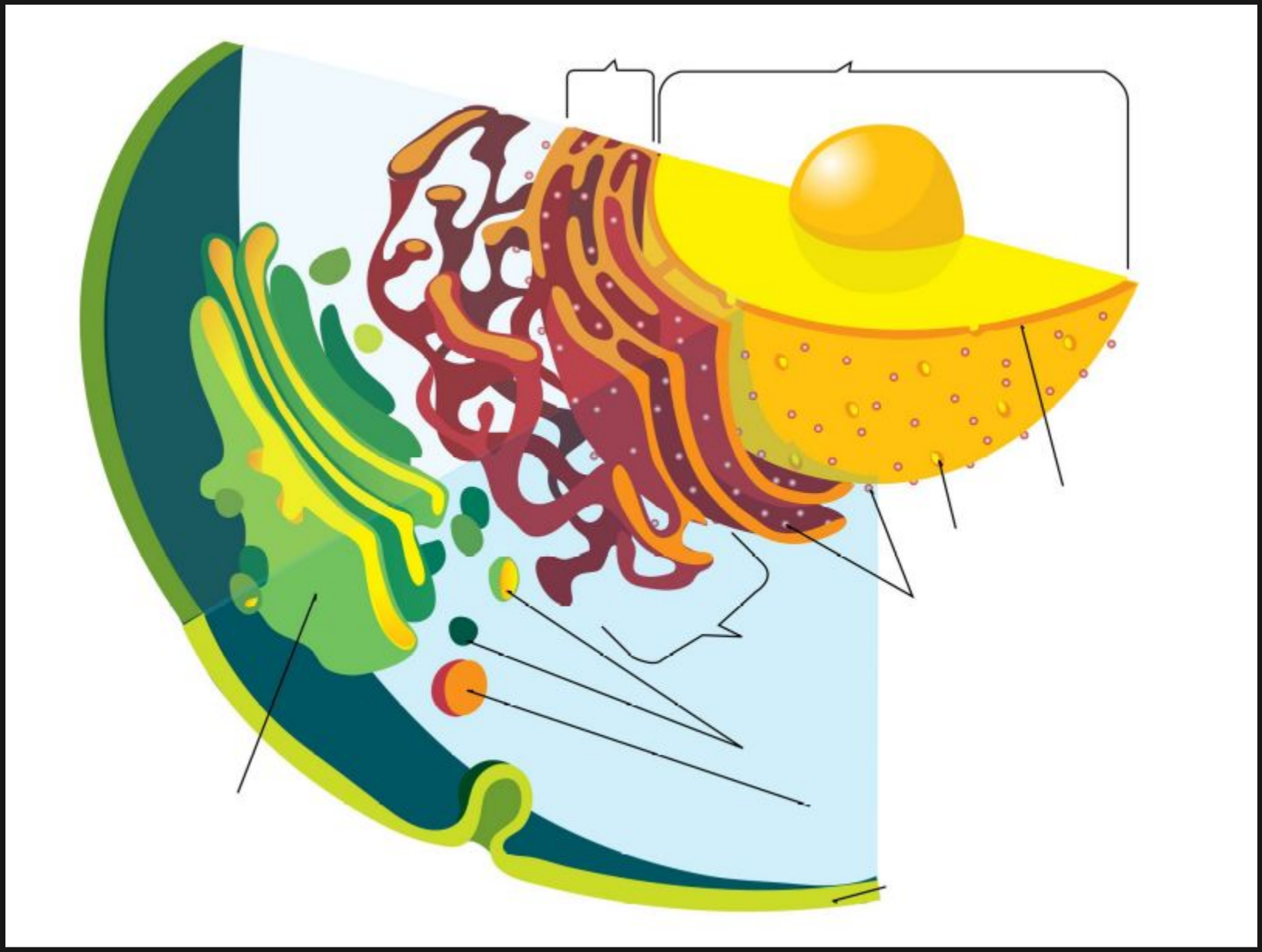
Ribosomes

- Composed of rRNA & proteins
- Cluster in groups along mRNA to form polyribosomes
- Synthesize proteins

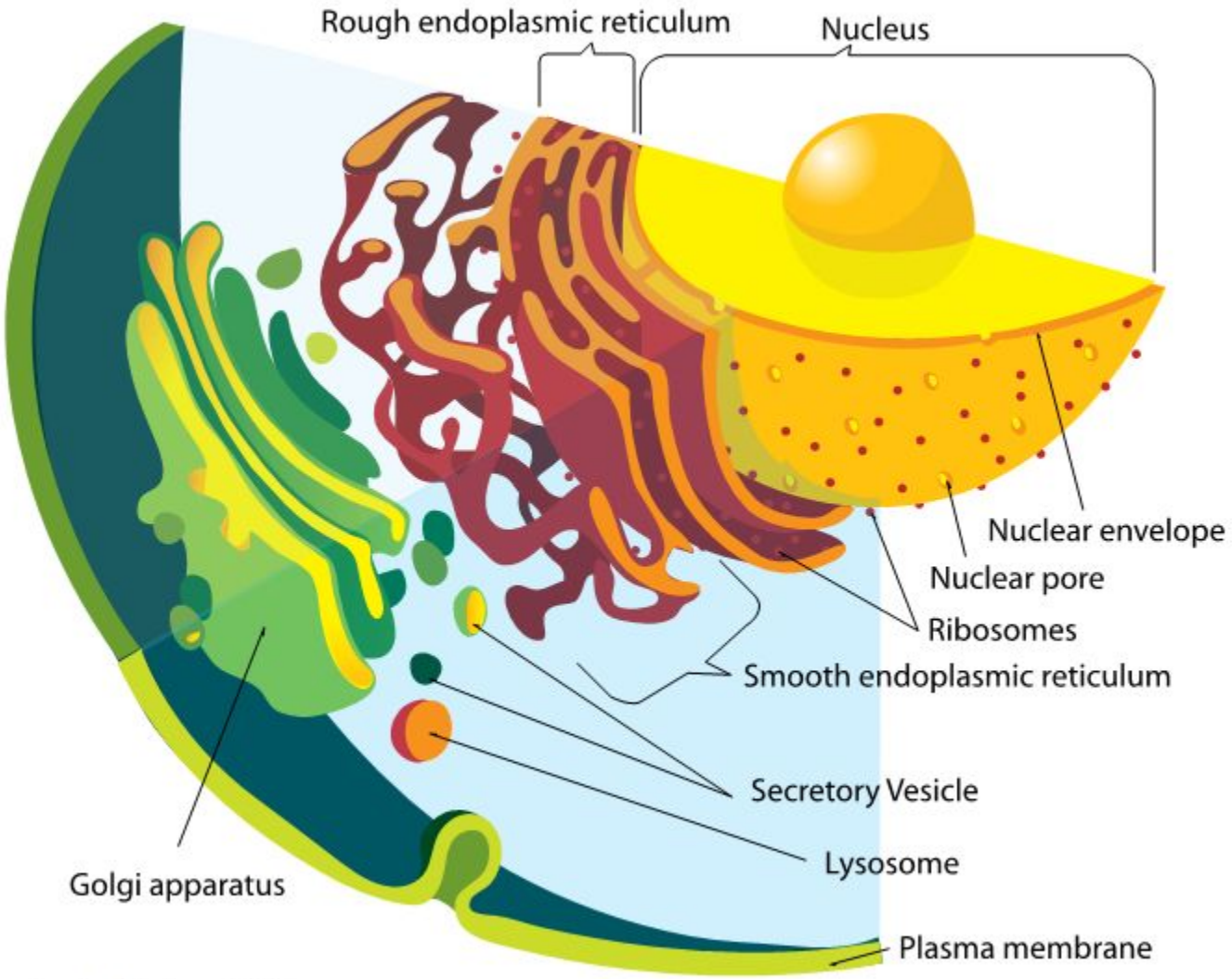

Ribosomes
Mitochondrial crista
Rough endoplasmic reticulum
Mitochondrion
Transmission electron microscope

Rough endoplasmic reticulum

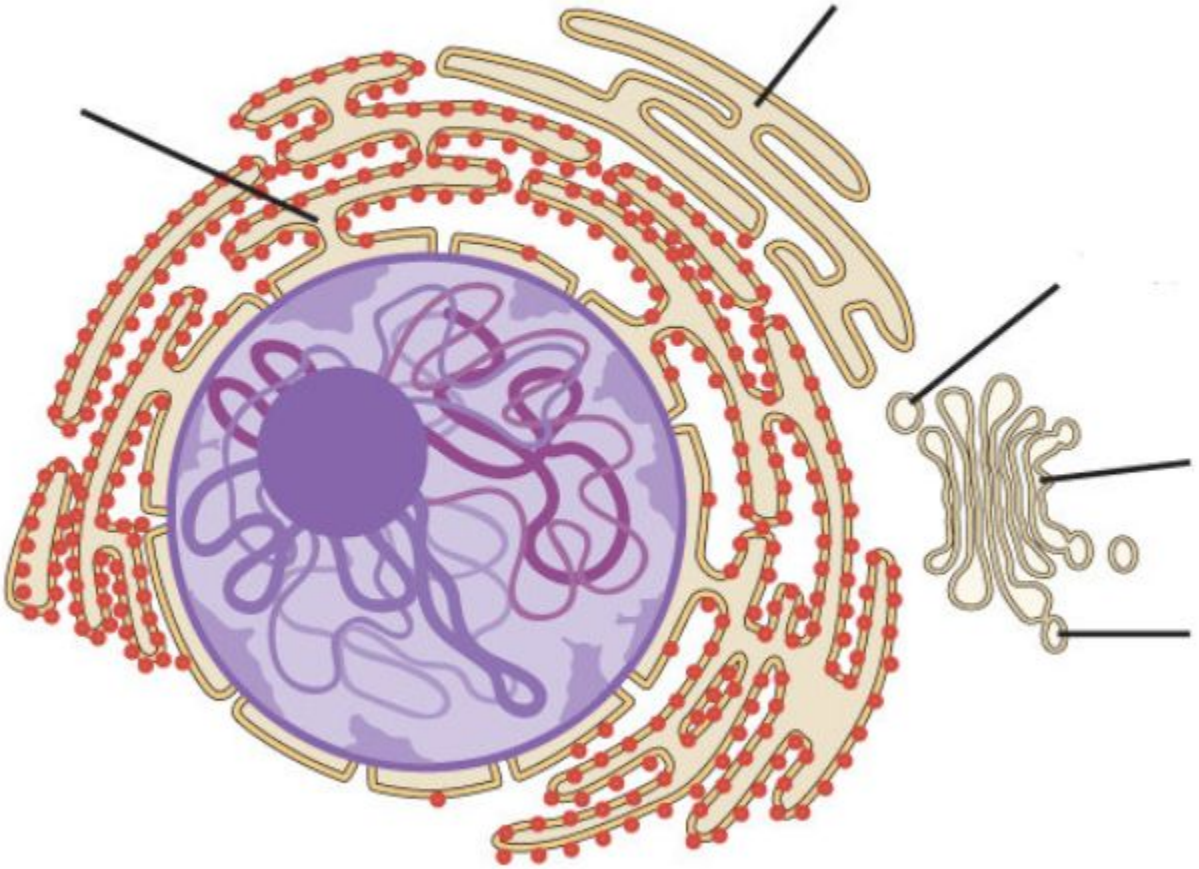
- Sheets & cavities bound by membranes
- Outer surface studded with ribosomes
- Interior region called cisternae
- Has receptors where ribosomes bind
- Common in cells synthesizing proteins for export
    - ie Secretory proteins



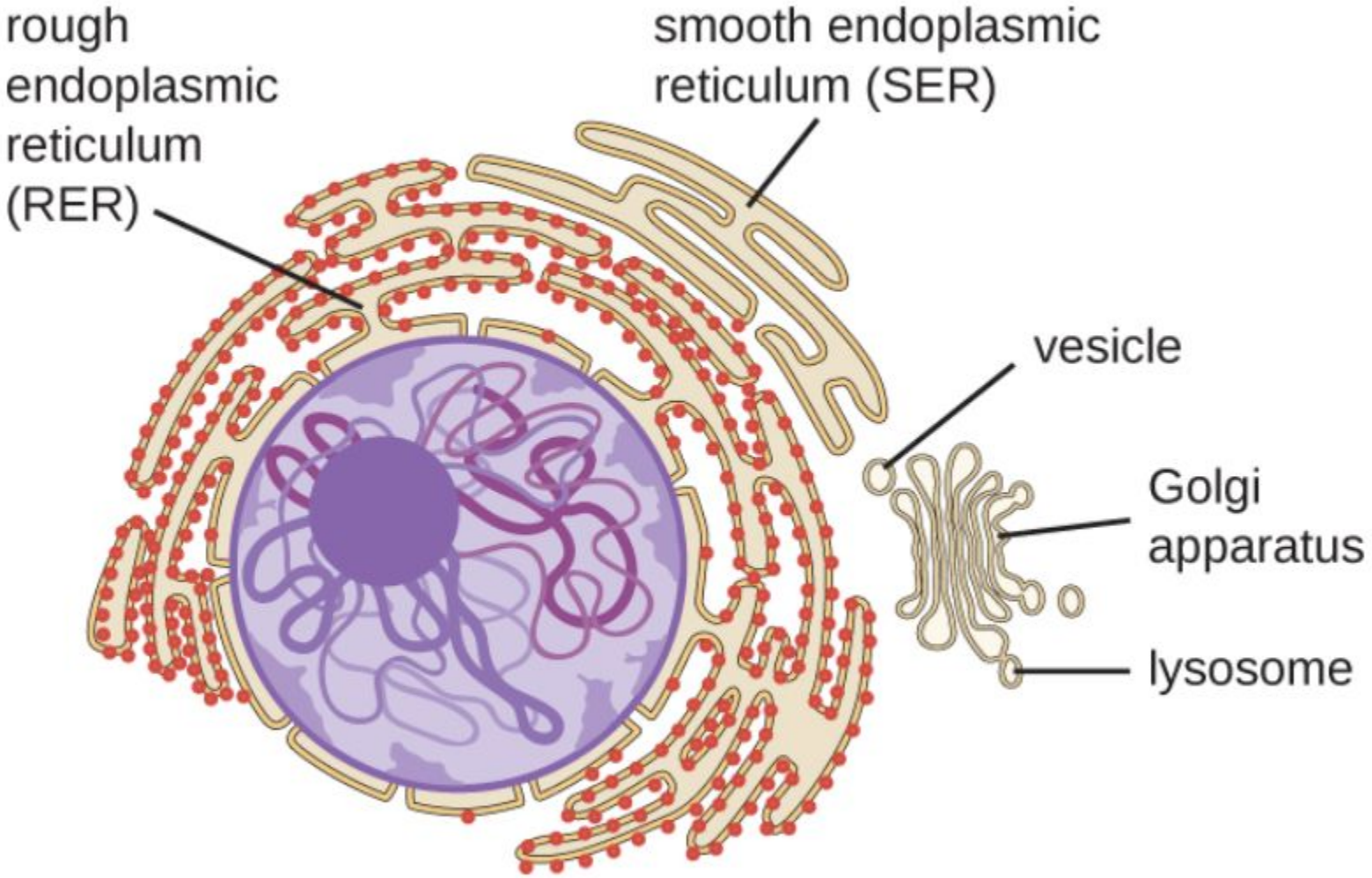
The endomembrane system in an eukaryote cell.



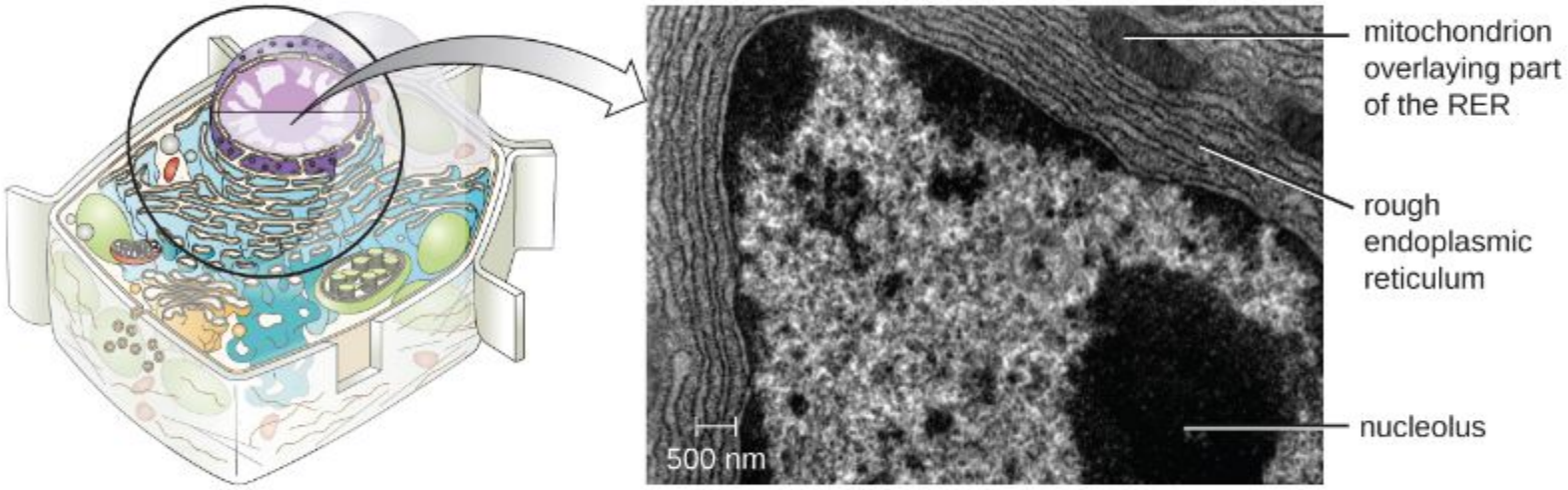
Sketch; LadyofHats; PD



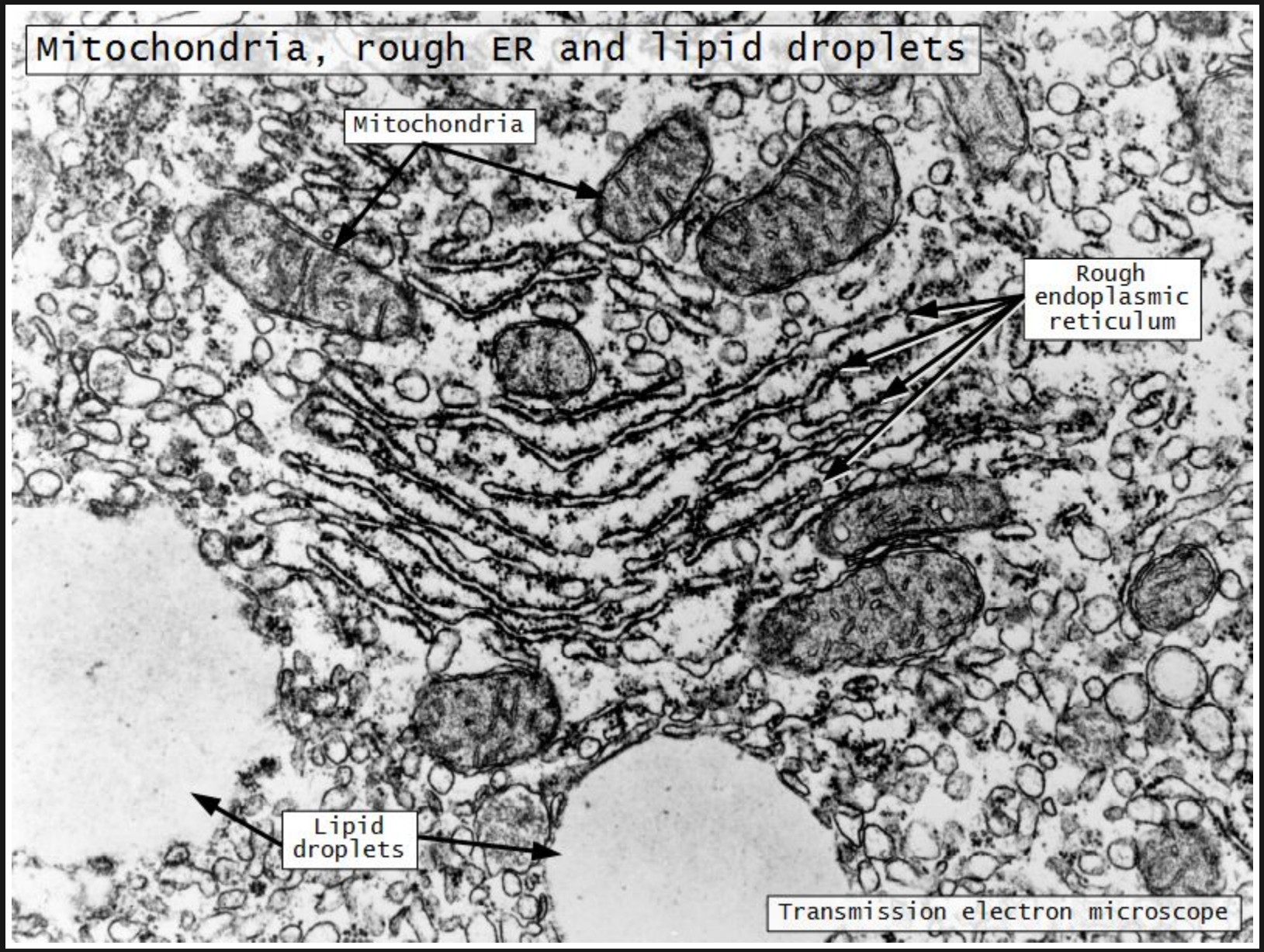
The endomembrane system is a series of membranous intracellular structures, facilitating movement of materials throughout the cell & the cell membrane.



The rough endoplasmic reticulum is studded with ribosomes for the synthesis of membrane proteins (which give it its rough appearance).




A portion of tubular ER showing ribosomes attached to its surfacenascent proteins into the ER lumen. EM taken on 5/12/91 by R. Allen with Zeiss 10A TEM. Neg. 19,800X. Bar = 0.2µm. Published in Int. Rev. Cytol. 198:277-318, 2000.
endoplasmic reticulum
Richard Allen; Pacific Biosciences Research Center


Mitochondria, rough ER and lipid droplets
Mitochondria
Rough endoplasmic reticulum
Lipid droplets
Transmission electron microscope

Smooth endoplasmic reticulum

- Irregular network membrane-bound channels
- Without ribosomes
- Branching & anastomosing tubules & vesicles
- Function depends on cell
    - Steroid hormone synthesis
    - Drug detoxification
    - Metabolism of lipids & cholesterol
    - Calcium ion homeostasis

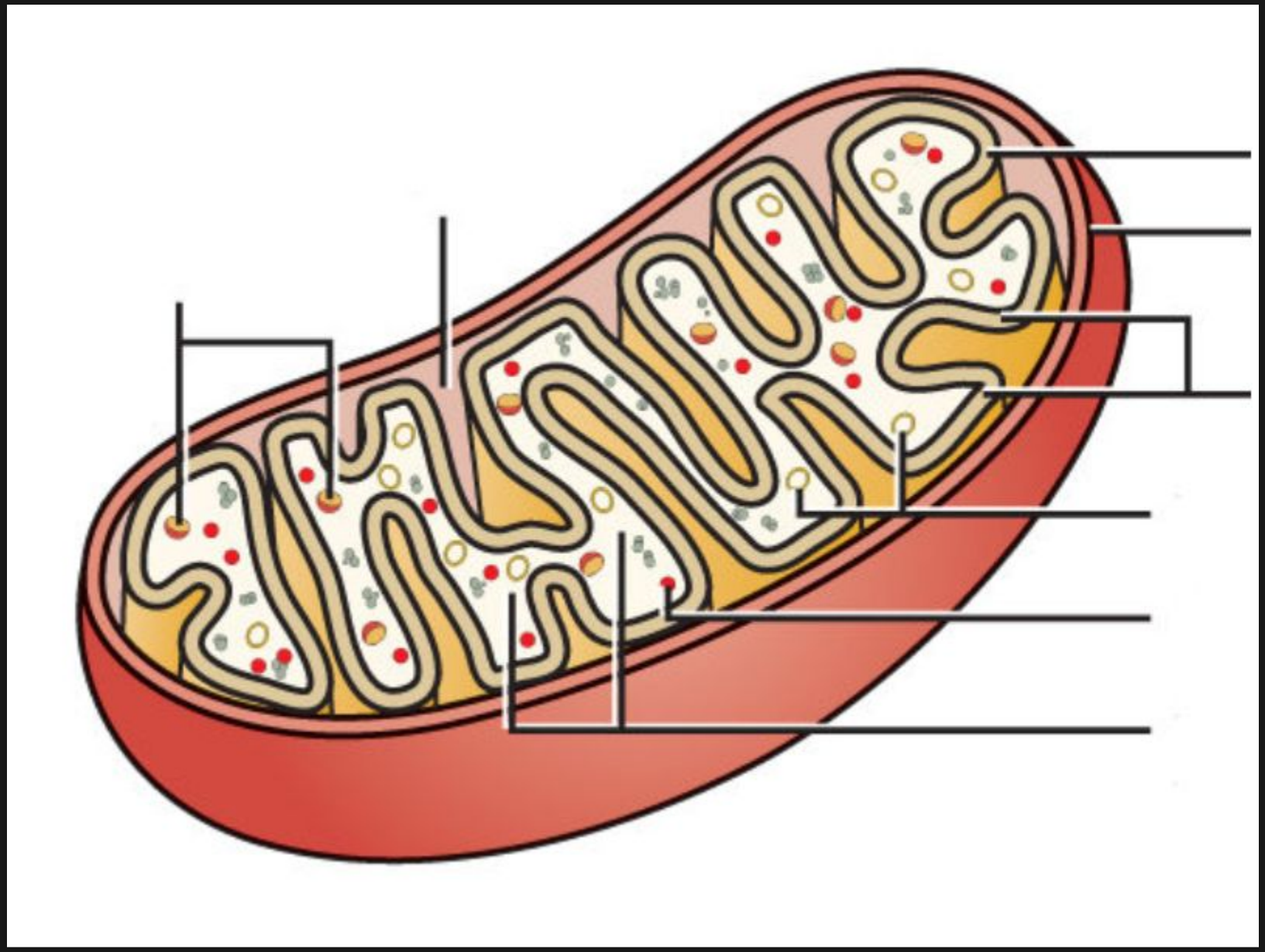
Lysosomes

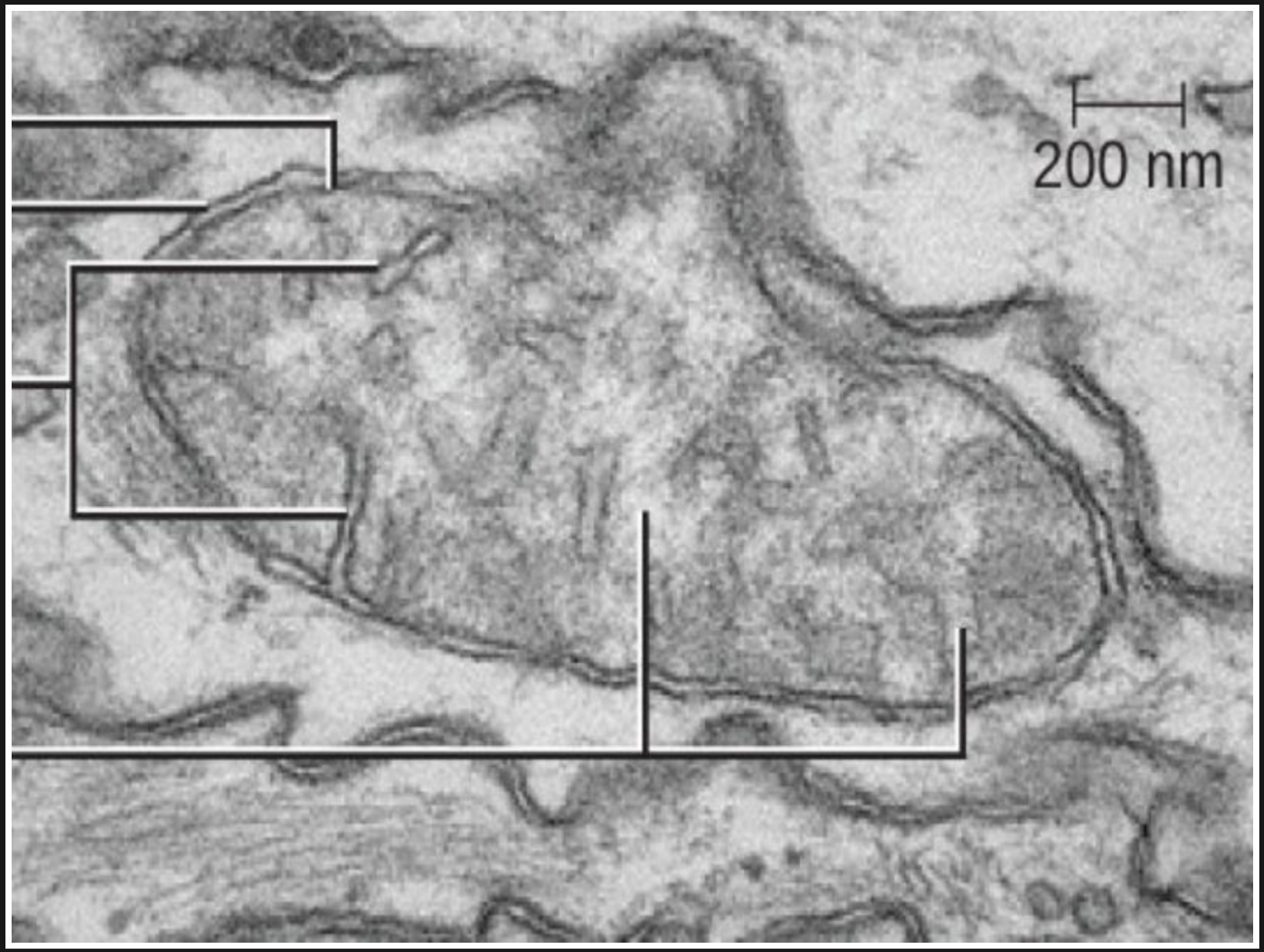
- Membrane-bound dense bodies
- Contains hydrolytic enzymes
- Functions in intracellular digestion


Smooth ER and lysosomes
Lysosomes
Smooth endoplasmic reticulum
Golgi apparatus
Peroxisome
Transmission electron microscope

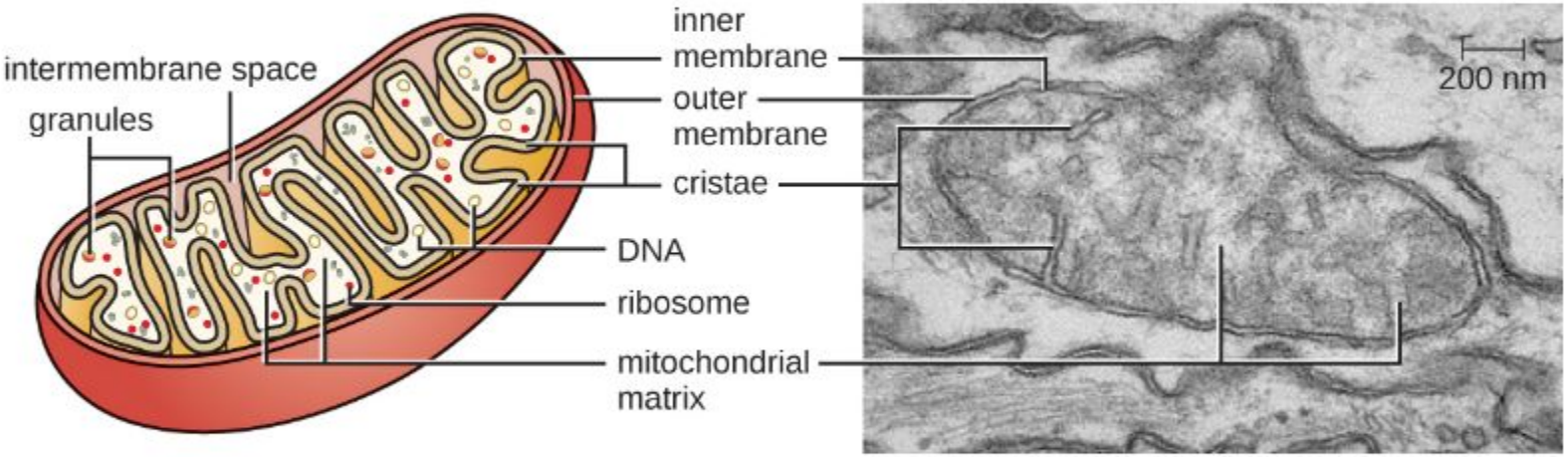
Mitochondria

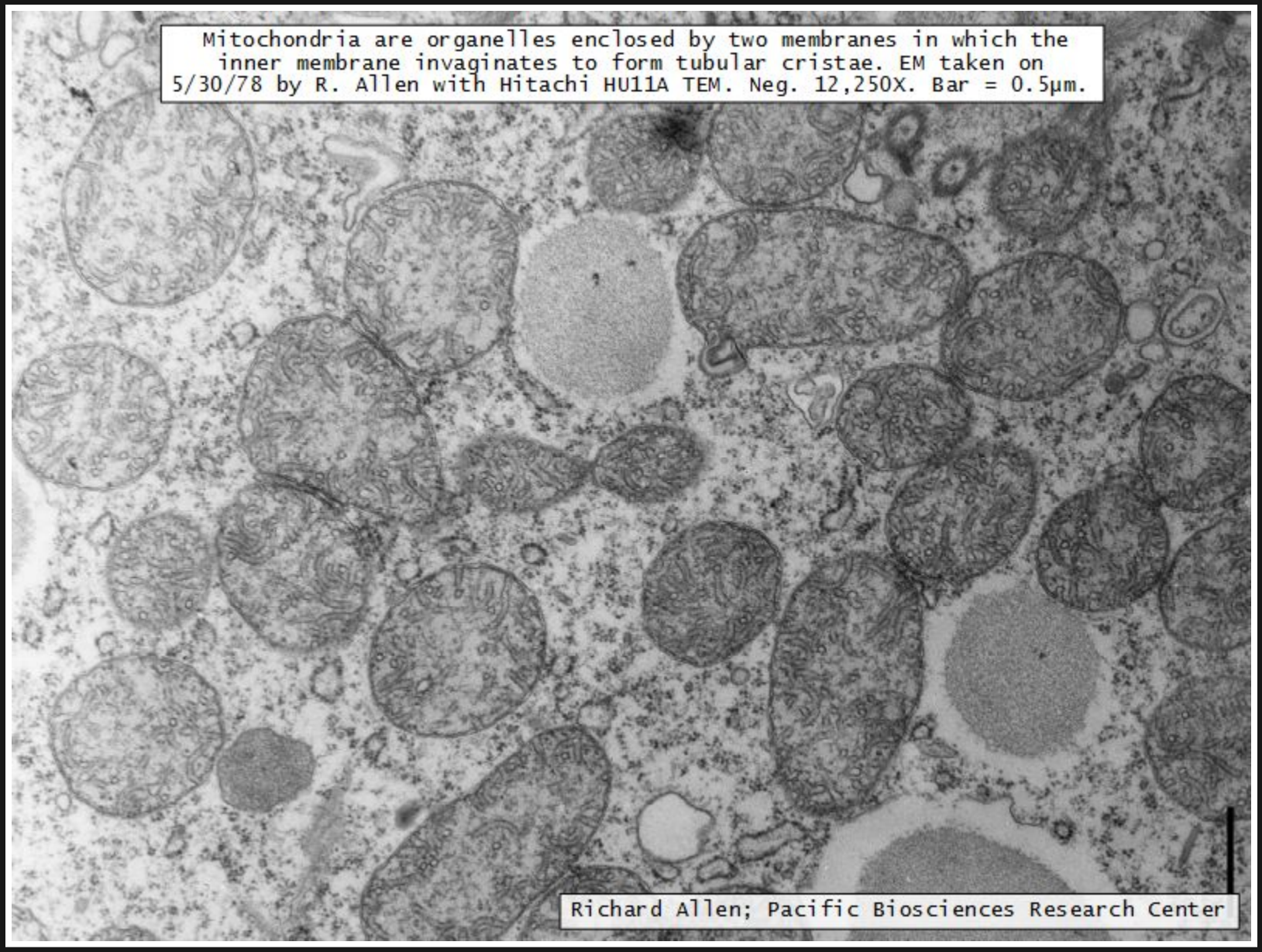
- Rod-shaped organelles
- Double-membrane structure
    - Outer membrane surrounds entire organelle
    - Inner membrane folds into interior
- Inner membrane form cristae
- Have enzymes for Krebs cycle & fatty acid oxidation
- Contain own genetic apparatus
    - DNA, mRNA, tRNA & rRNA
- Produces adenosine triphosphate (ATP)



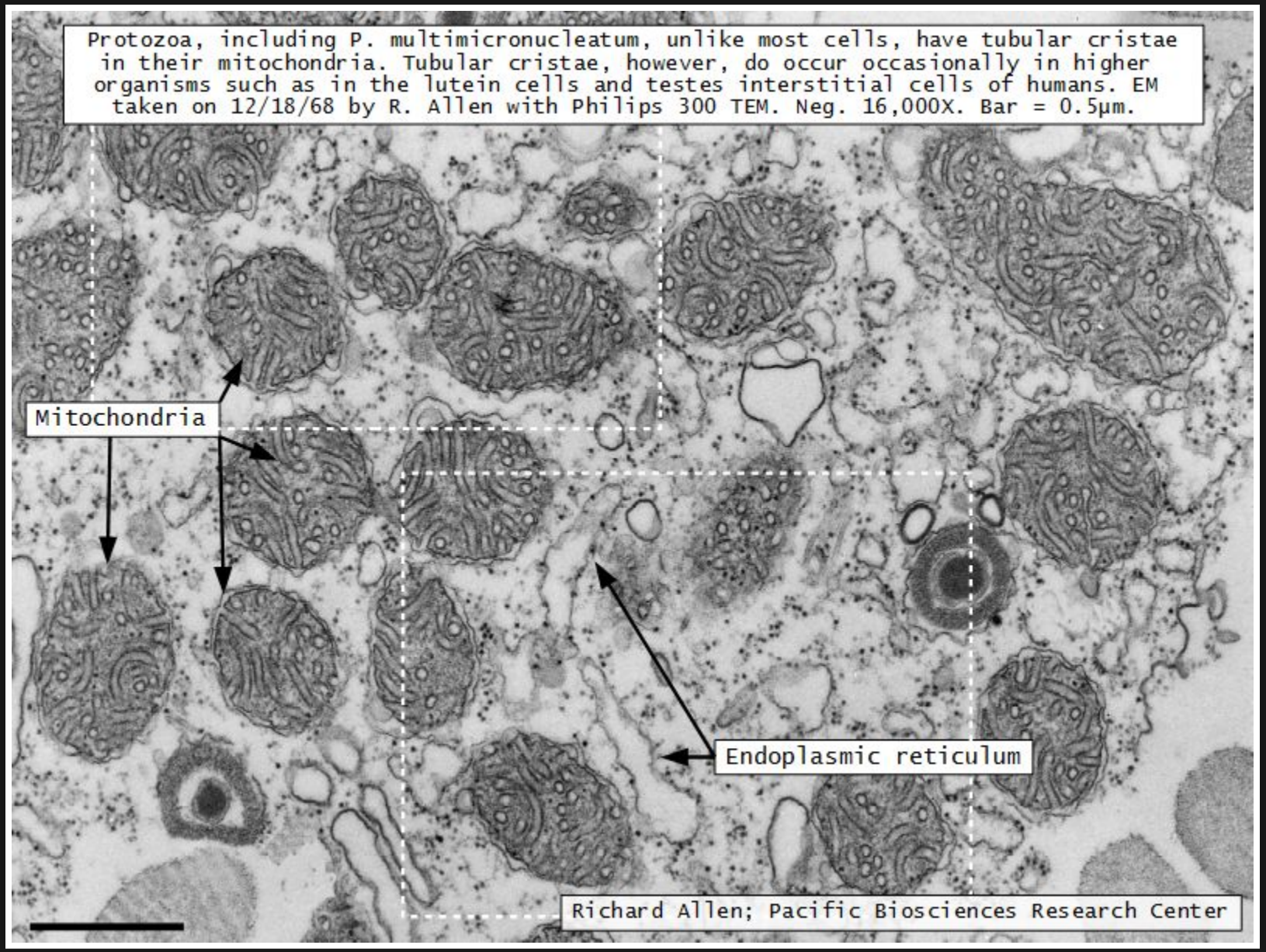

200 nm

Each mitochondrion is surrounded by two membranes, the inner of which is extensively folded into cristae and is the site of the intermembrane space. The mitochondrial matrix contains the mitochondrial DNA, ribosomes, and metabolic enzymes. The transmission electron micrograph of a mitochondrion, on the right, shows both membranes, including cristae and the mitochondrial matrix. (credit "micrograph": modification of work by Matthew Britton; scale-bar data from Matt Russell)

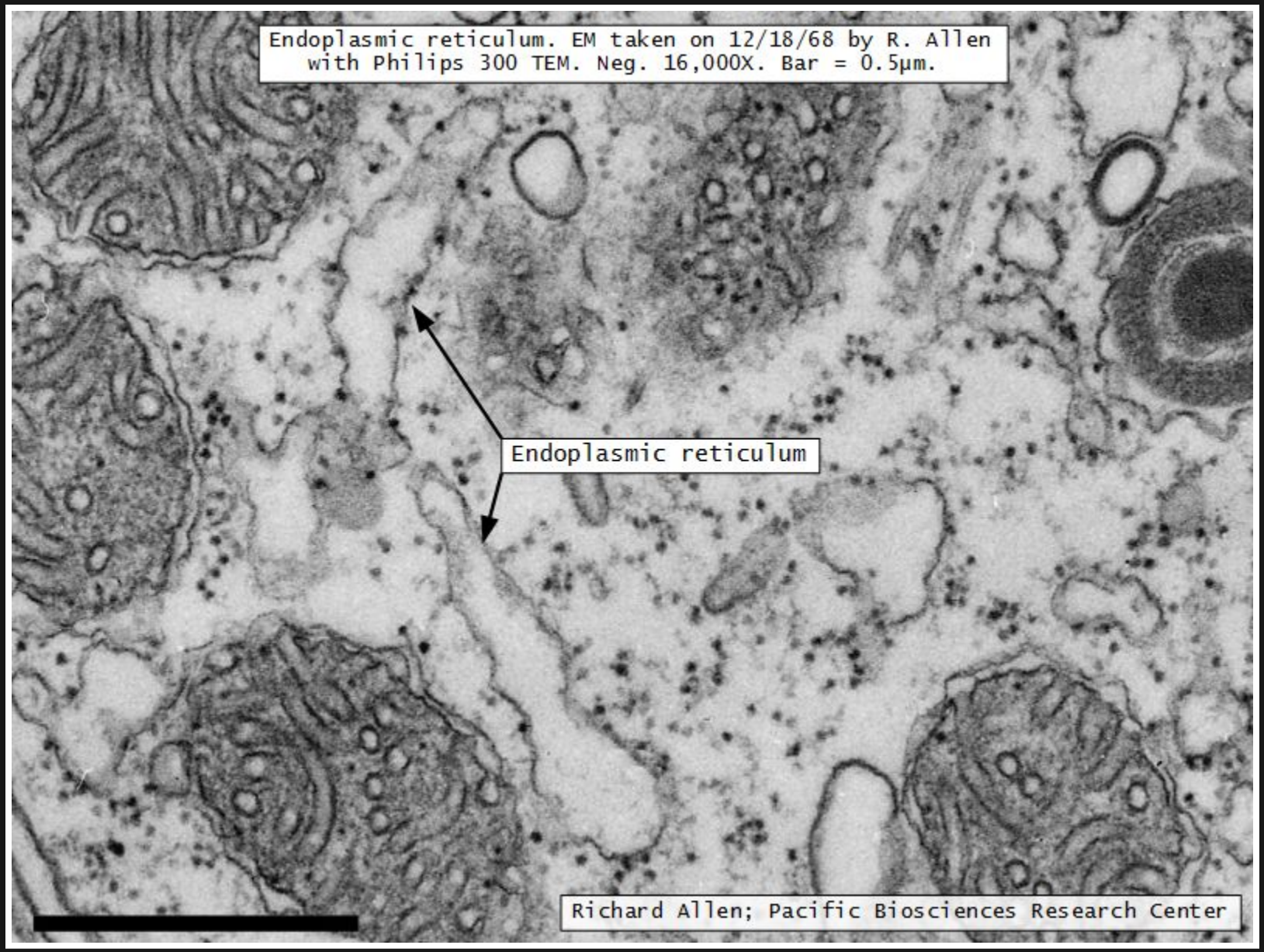


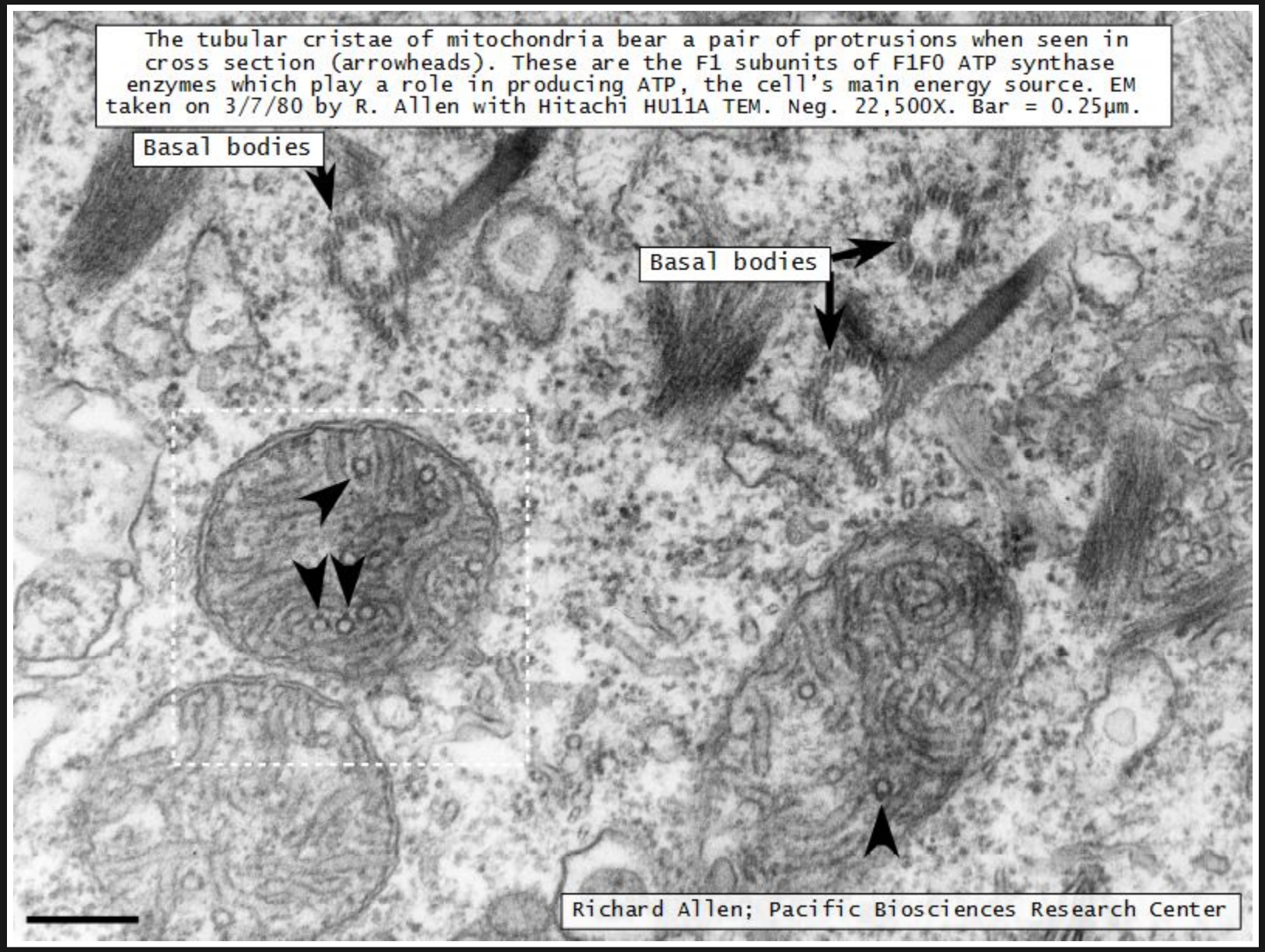

Mitochondria are organelles enclosed by two membranes in which the inner membrane invaginates to form tubular cristae. EM taken on 5/30/78 by R. Allen with Hitachi HU11A TEM. Neg. 12,250X. Bar = 0.5µm.
Richard Allen; Pacific Biosciences Research Center

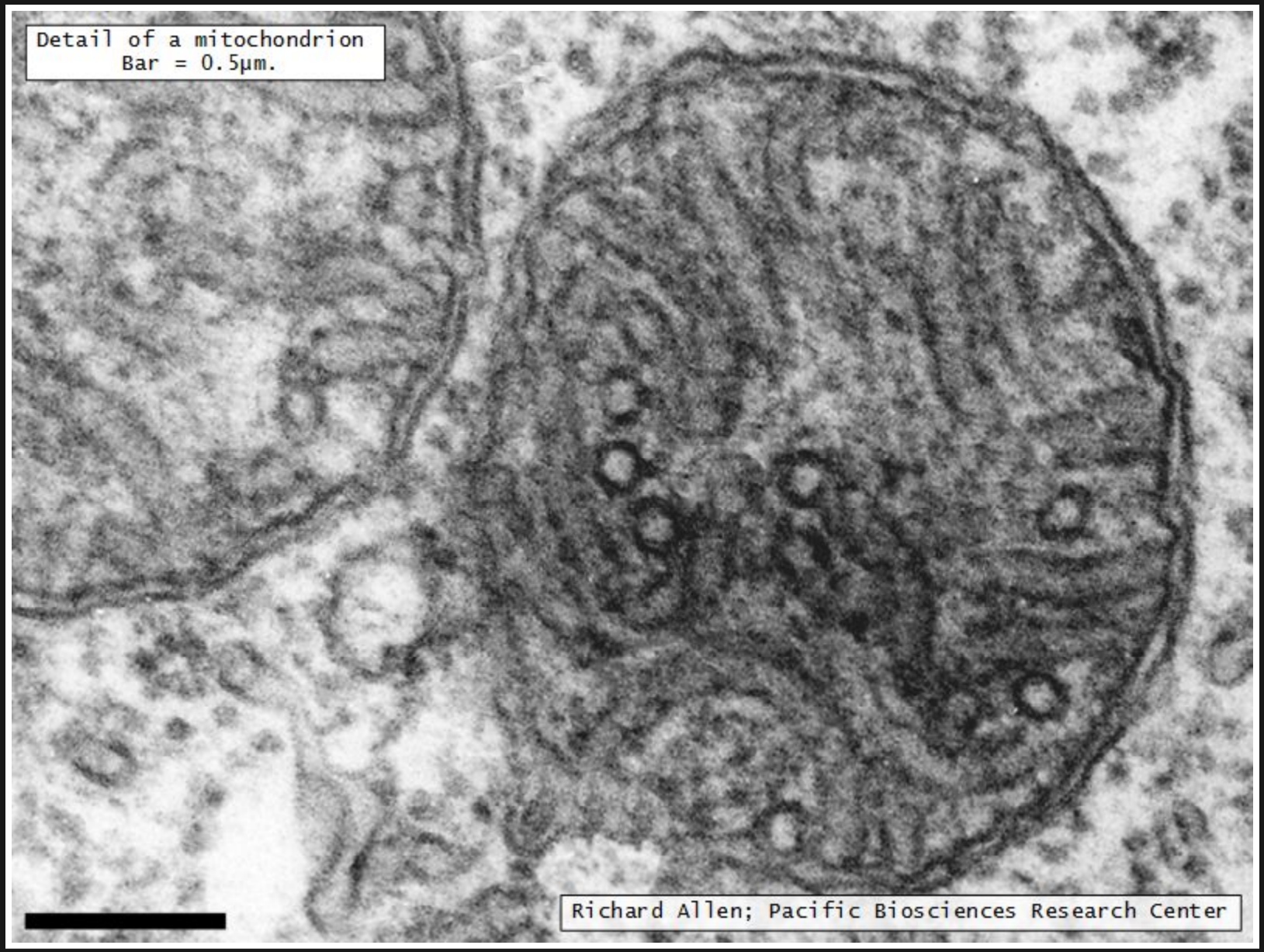

Detail of a mitochondrion
Bar = 0.5µm.
Richard Allen; Pacific Biosciences Research Center

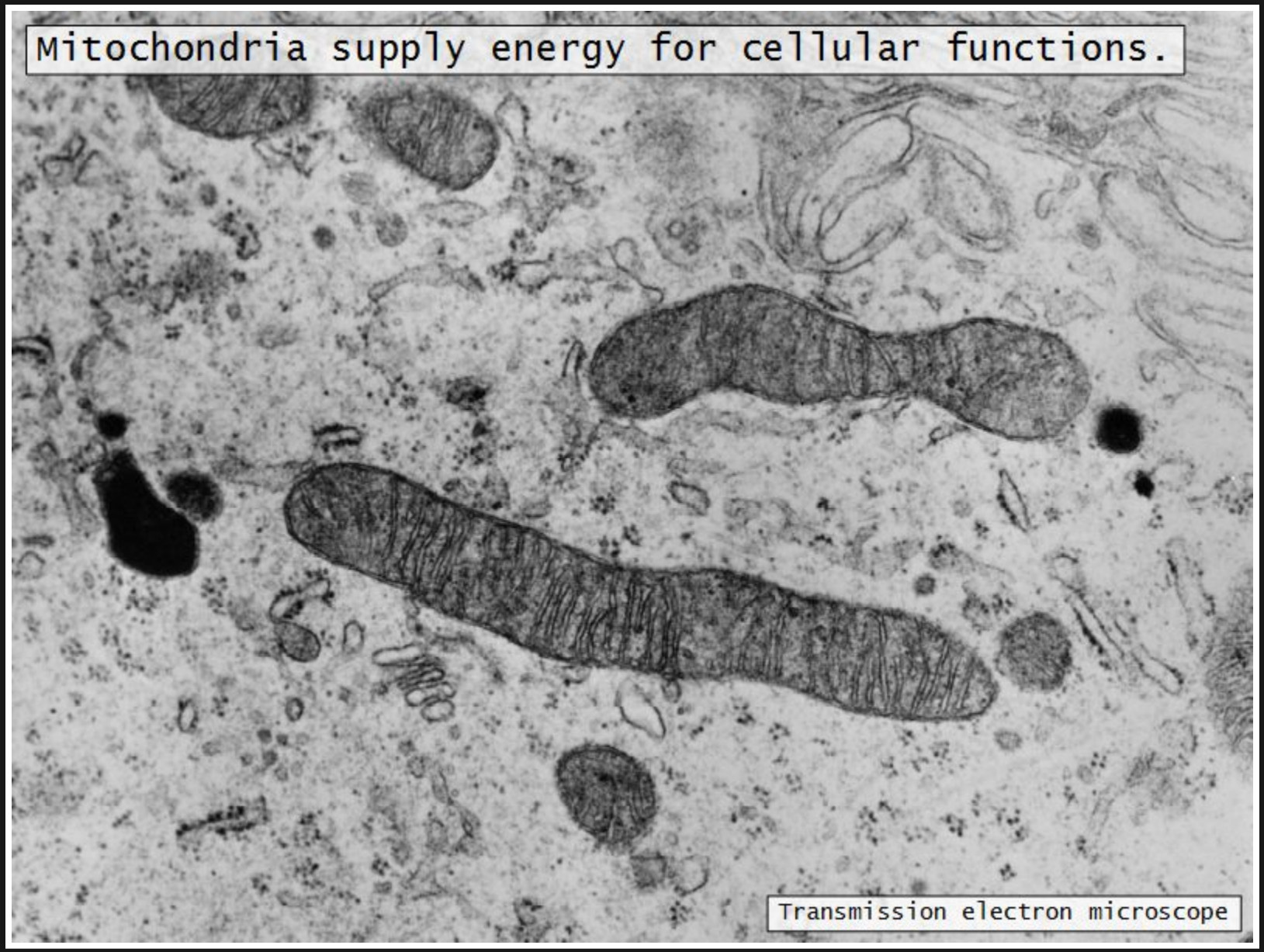

Protozoa, including P. multimicronucleatum, unlike most cells, have tubular cristae in their mitochondria. Tubular cristae, however, do occur occasionally in higher organisms such as in the lutein cells and testes interstitial cells of humans. EM taken on 12/18/68 by R. Allen with Philips 300 TEM. Neg. 16,000X. Bar = 0.5µm.
Mitochondria
Endoplasmic reticulum
Richard Allen; Pacific Biosciences Research Center


Mitochondria with tubular cristae. EM taken on 12/18/68 by R. Allen with Philips 300 TEM. Neg. 16,000X. Bar = 0.5µm.
Tubular crista on cross section
Tubular crista on longitudinal section
Richard Allen; Pacific Biosciences Research Center


Endoplasmic reticulum. EM taken on 12/18/68 by R. Allen
with Philips 300 TEM. Neg. 16,000X. Bar = 0.5µm.
Endoplasmic reticulum
Richard Allen; Pacific Biosciences Research Center

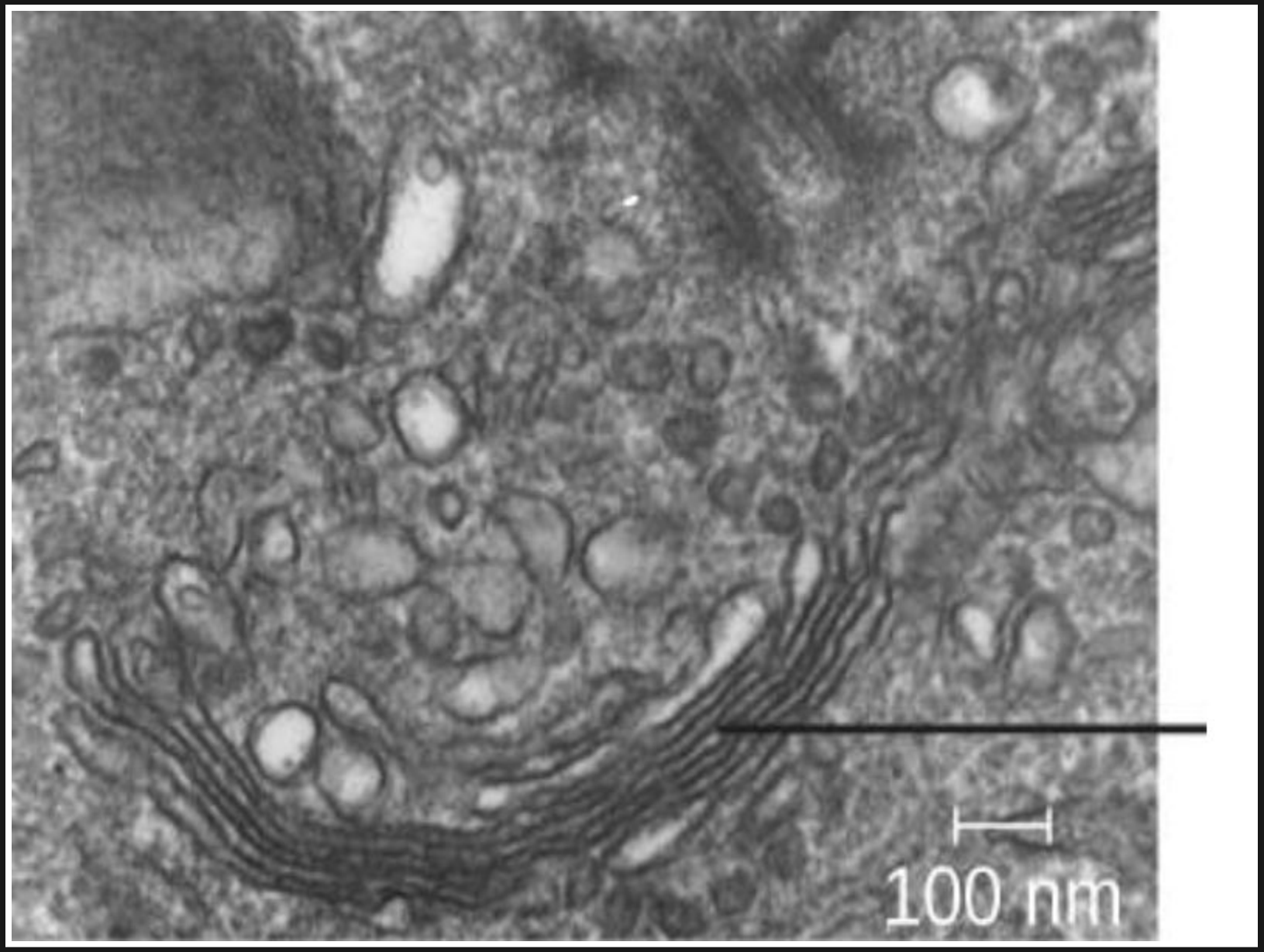

The tubular cristae of mitochondria bear a pair of protrusions when seen in cross section (arrowheads). These are the F1 subunits of F1F0 ATP synthase enzymes which play a role in producing ATP, the cell's main energy source. EM taken on 3/7/80 by R. Allen with Hitachi HU11A TEM. Neg. 22,500X. Bar = 0.25µm.
Basal bodies
Basal bodies
Richard Allen; Pacific Biosciences Research Center

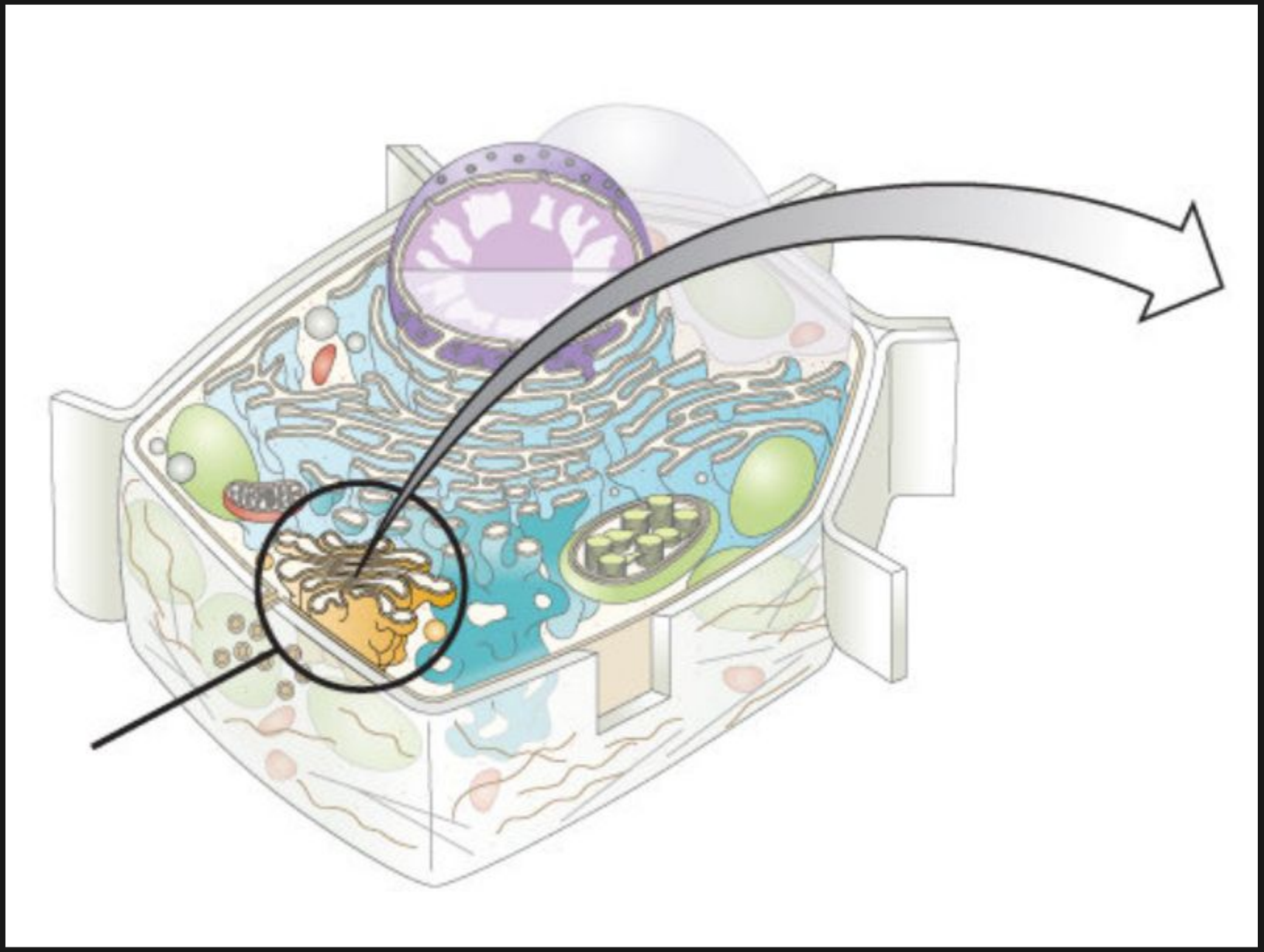

Detail of a mitochondrion
Bar = 0.5µm.
Richard Allen; Pacific Biosciences Research Center

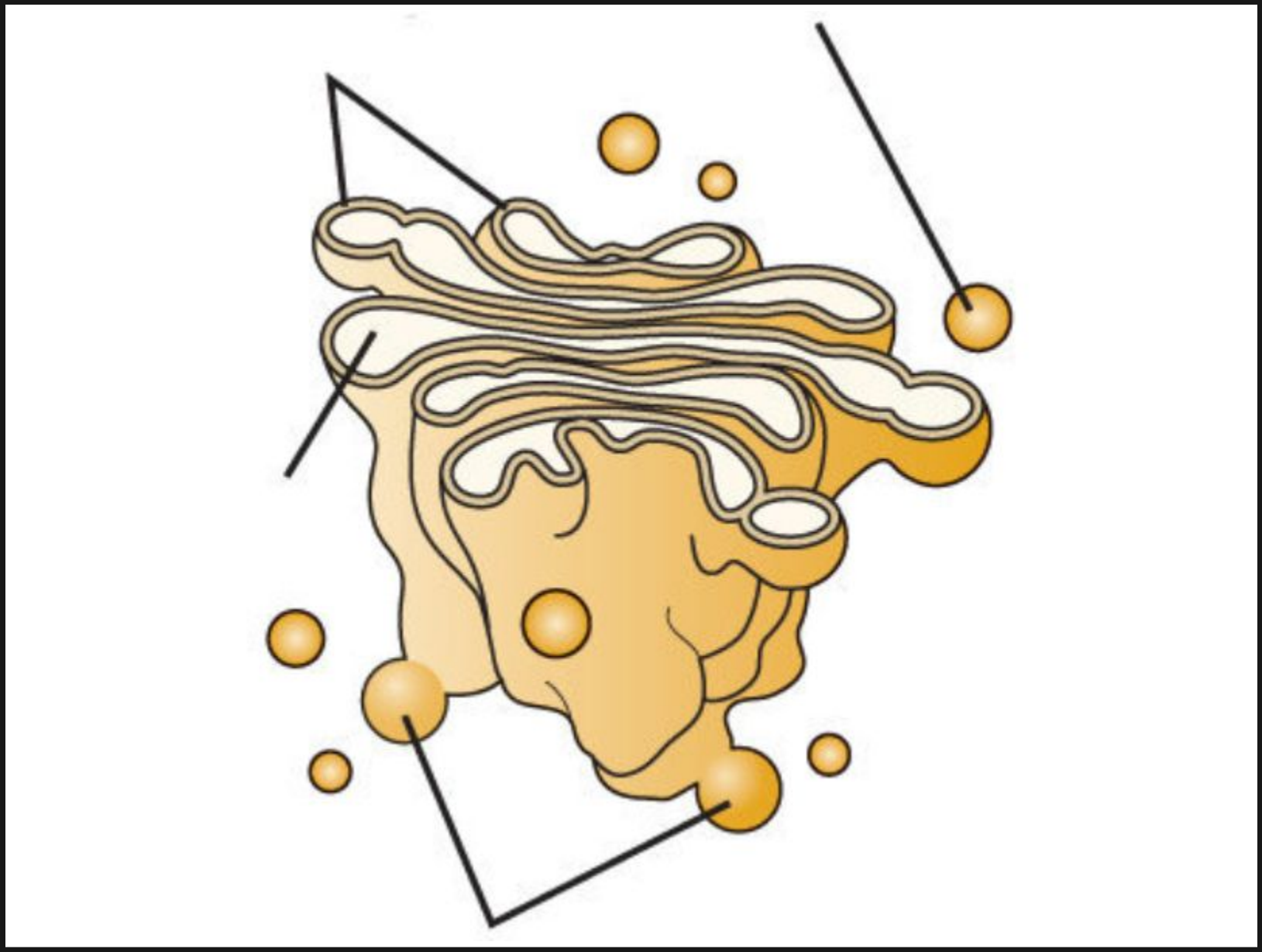

Mitochondria supply energy for cellular functions.
Transmission electron microscope

Golgi apparatus

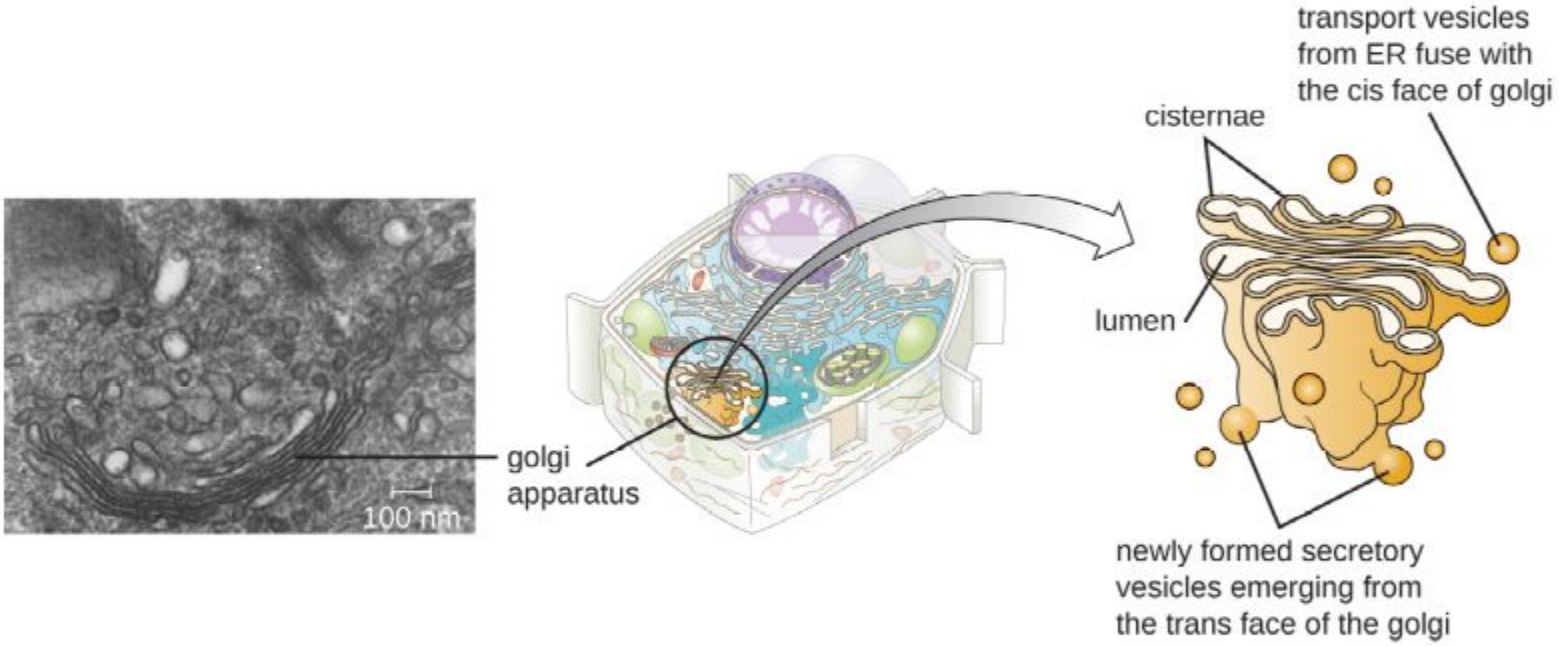
- Several disk-shaped cisternae arranged in a stack
- Two sides on stack
    - Outer convex forming face
        - Associated with small vesicles
        - Usually from rough endoplasmic reticulum
    - Inner concave maturing face
        - Associated with condensing vacuoles
        - Secretory materials condensed into granules
- Functions
    - Membrane recycling & redistribution
    - Synthesis carbohydrates & proteins
    - Modification of cellular products
    - Concentration & packaging of synthesized material into secretory granules


100 nm

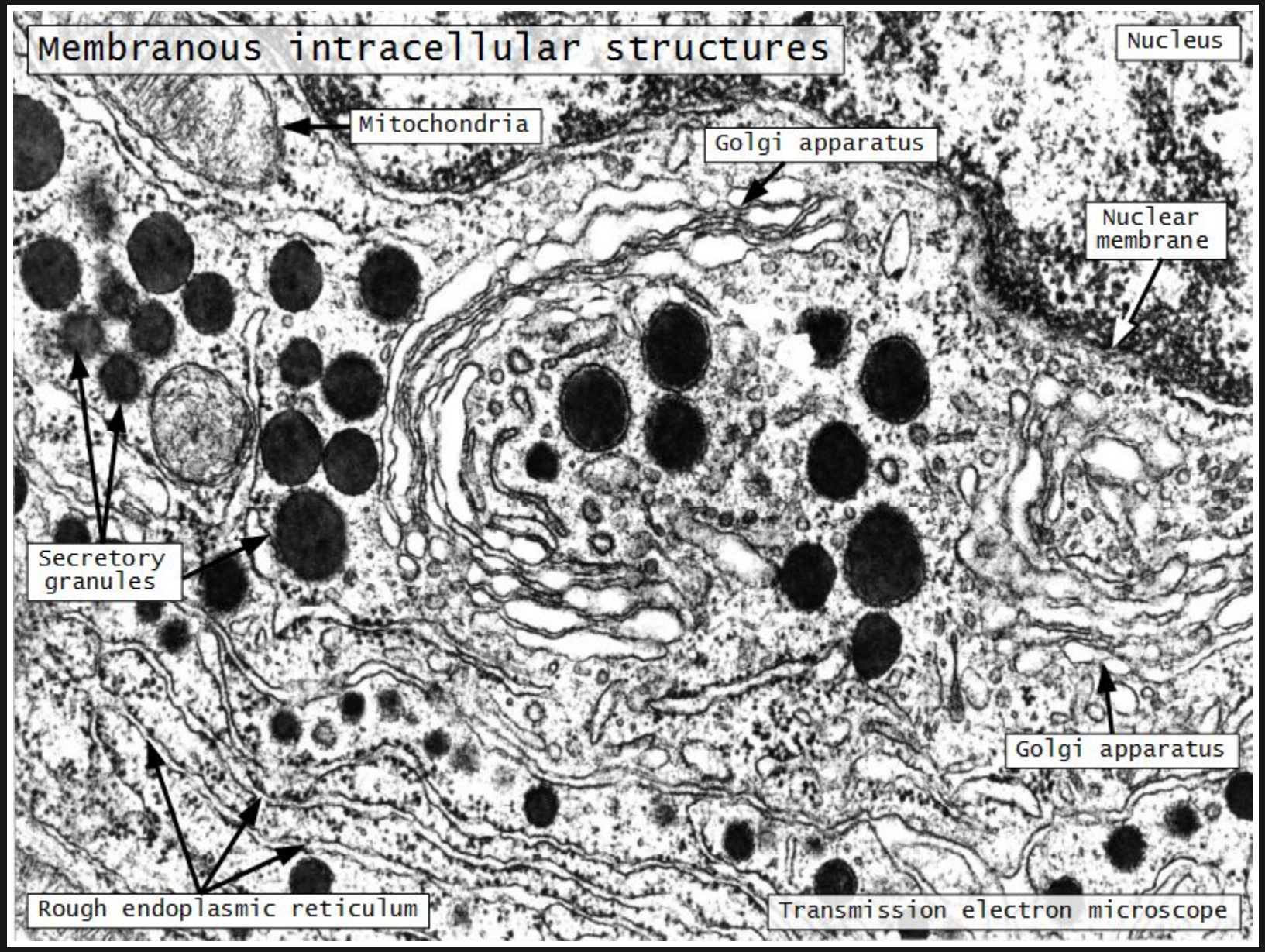




A transmission electron micrograph (left) of a Golgi apparatus. The illustration (right) shows the cup-shaped, stacked disks and several transport vesicles. The Golgi apparatus modifies lipids & proteins, producing glycolipids & glycoproteins, respectively, which are commonly inserted into the plasma membrane.




The Golgi complex of Paramecium multimicronucleatum. EM taken on 9/29/87 by R. Allen with Zeiss 10A TEM. Neg. 19,800X. Bar = 0.2µm. Published in J. Struct. Biol. 110:215-226, 1993.
Richard Allen; Pacific Biosciences Research Center

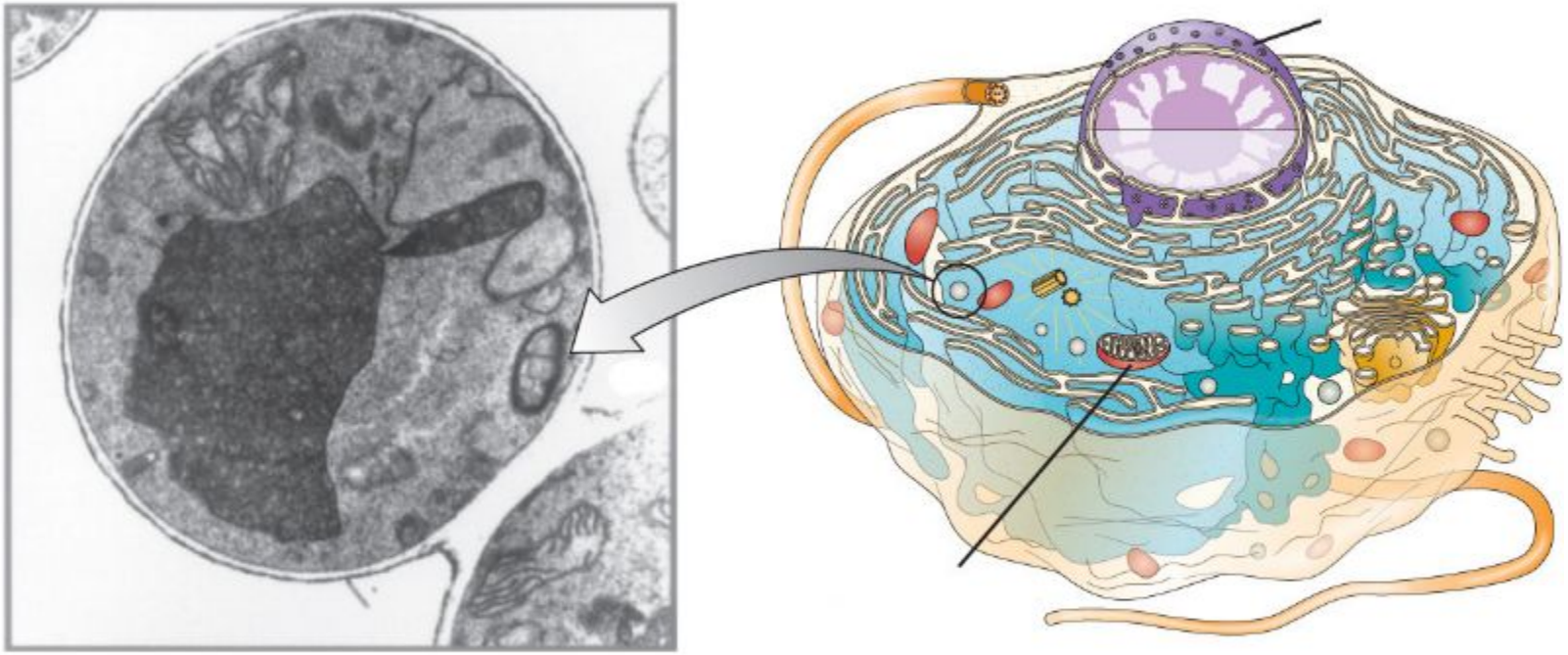

Membranous intracellular structures
Nucleus
Mitochondria
Golgi apparatus
Nuclear membrane
Secretory granules
Golgi apparatus
Rough endoplasmic reticulum
Transmission electron microscope

Residual body

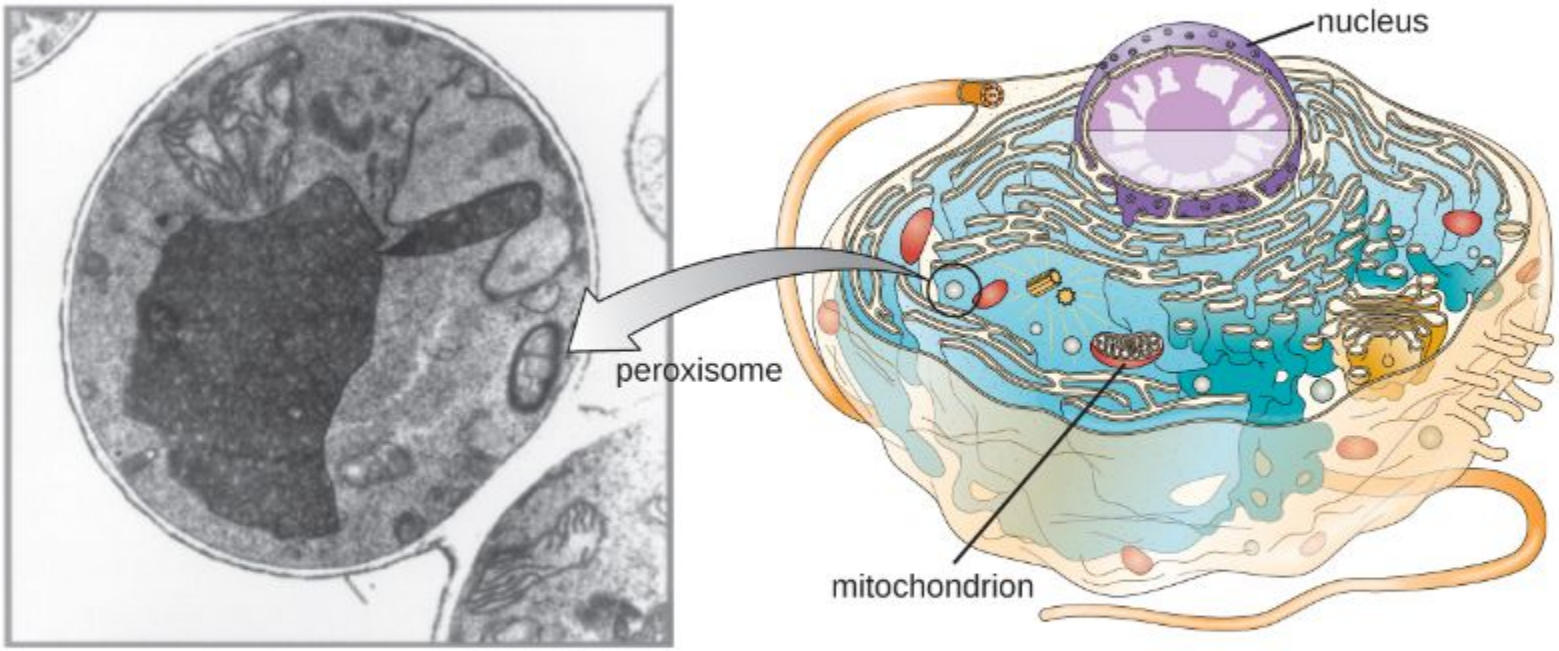
- Cytoplasmic inclusion
- Varies in appearance
- Contains indigestible material

Peroxisome

- Membrane-bound organelle
- Stains cytochemically for catalase
- Catalase synthesizes and destroys hydrogen peroxide
- Often seen in close association with smooth ER
- Function
    - Metabolism of
        - hydrogen peroxide
        - cholesterol
        - lipids
    - Breakdown of
        - purines
        - pyrimidines

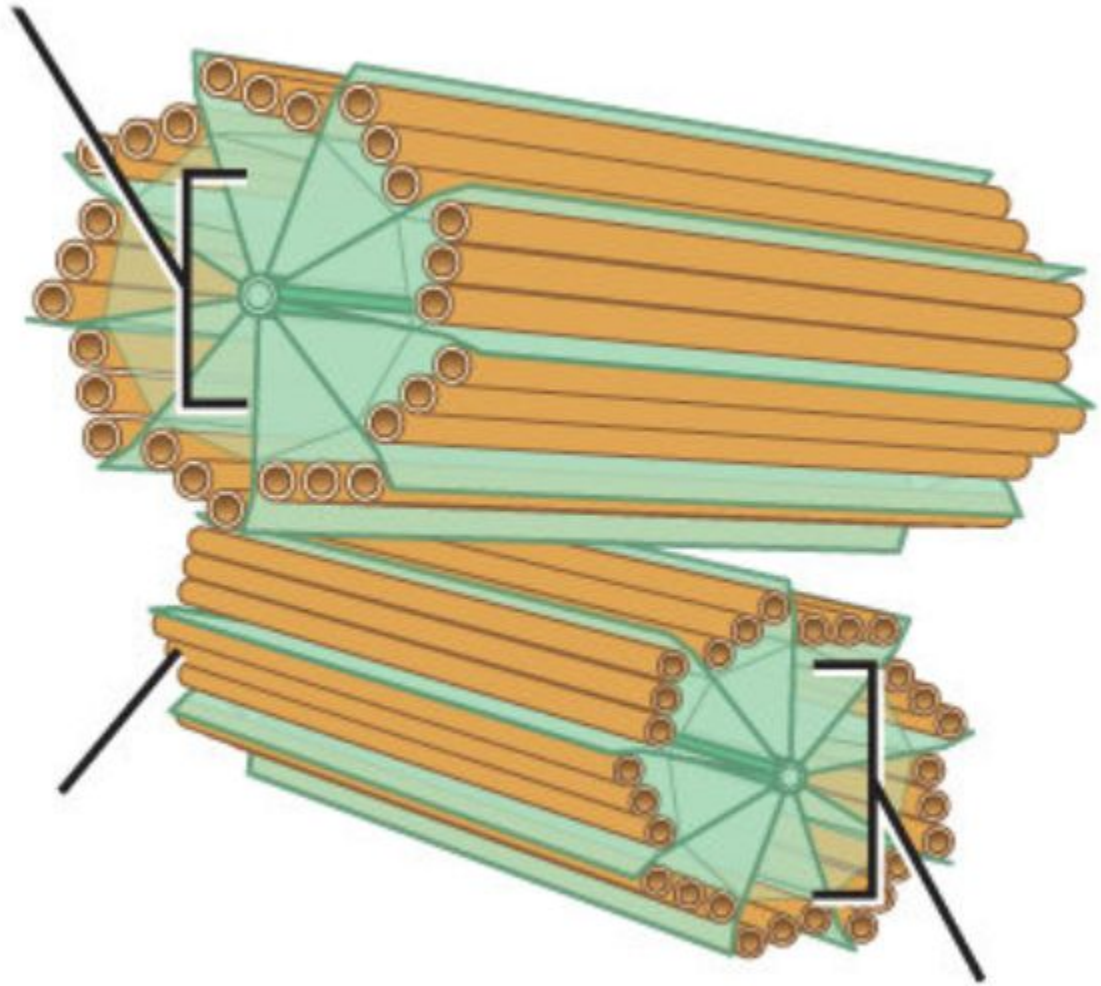


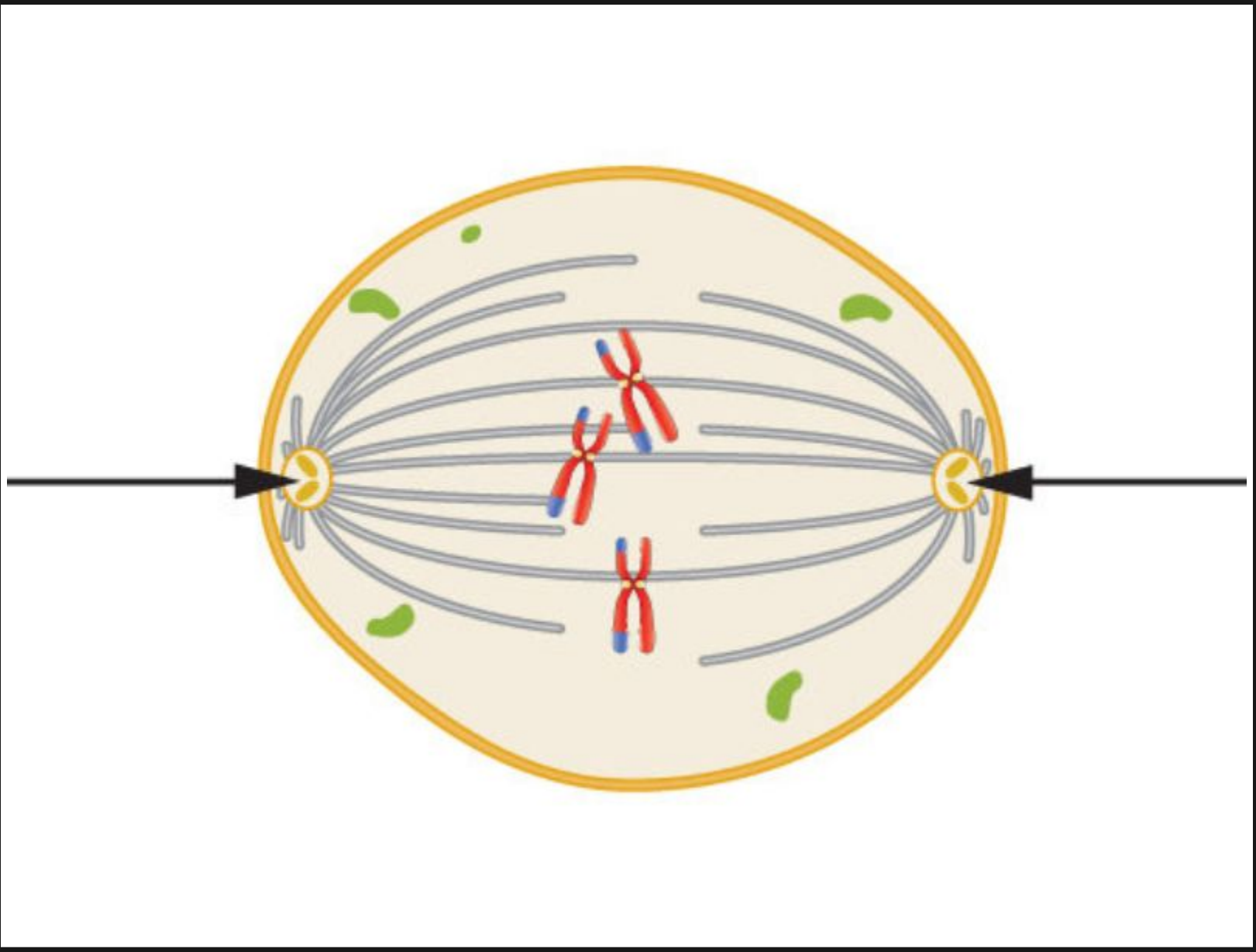
A transmission electron micrograph (left) of a cell containing a peroxisome. The illustration (right) shows the location of peroxisomes in a cell. These eukaryotic structures play a role in lipid biosynthesis and breaking down various molecules. They may also have other specialized functions depending on the cell type. (credit "micrograph": modification of work by American Society for Microbiology)



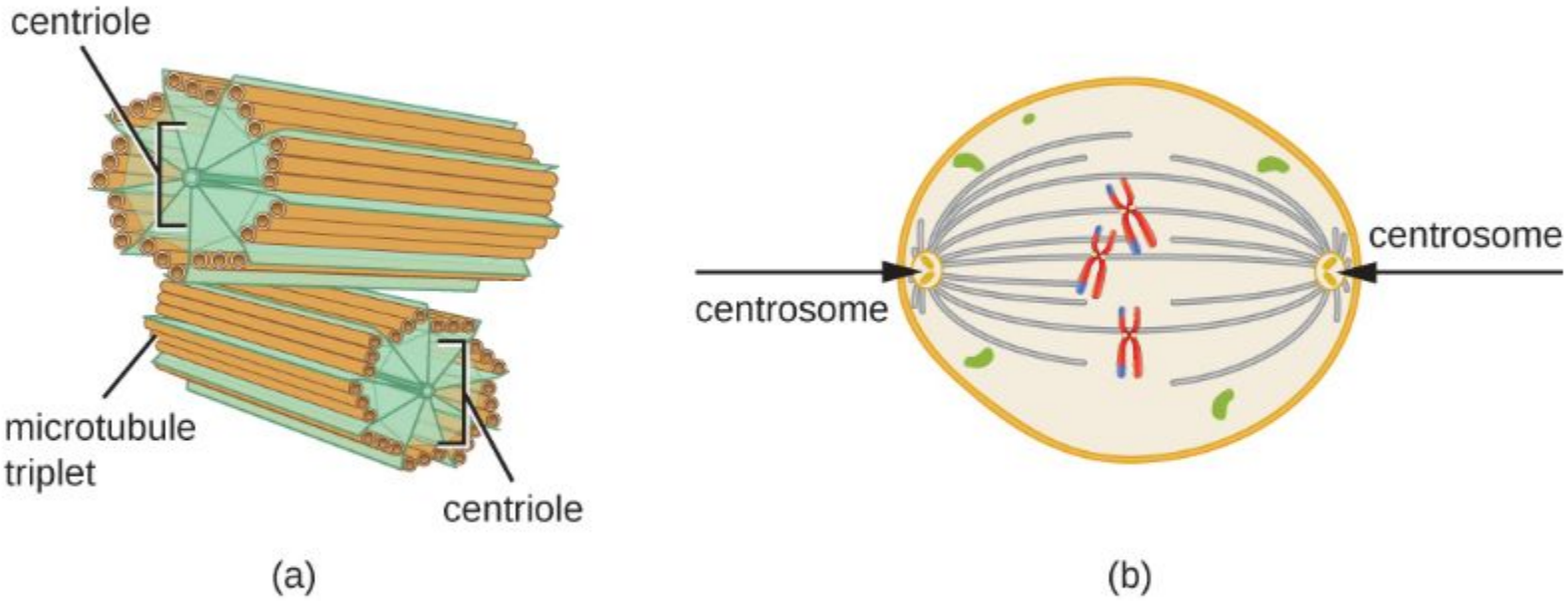
Centrioles

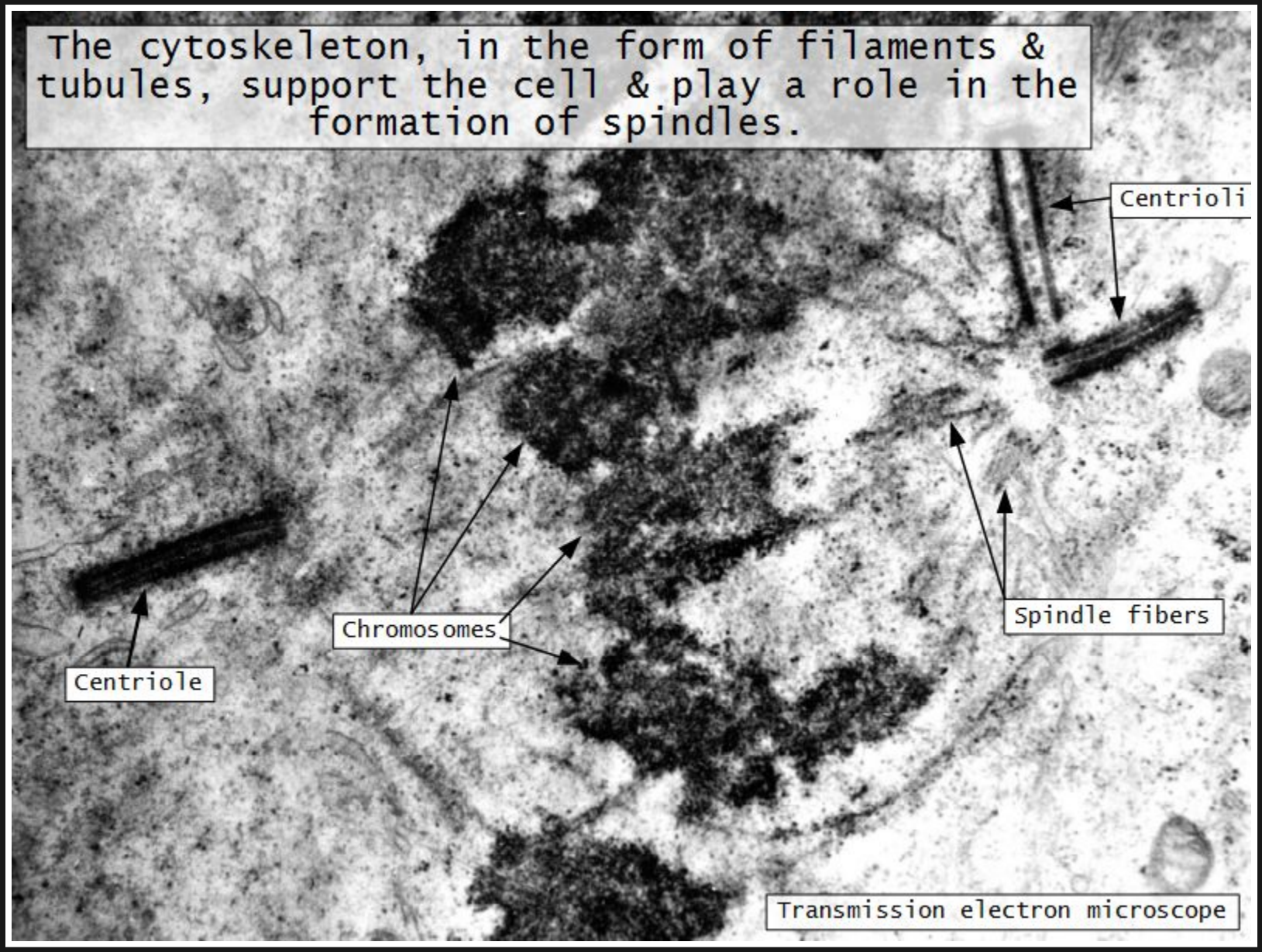
- Involved cell division
- Pair of short rods at right angles to each other
- Self-replicate prior to cell division
- Wall of nine tubular triplets like pinwheel
- Function
    - Form poles of mitotic spindles
    - Form basal bodies for cilia & flagella





Intermediate filaments are composed of multiple strands of polymerized subunits. They are more permanent than other cytoskeletal structures and serve a variety of functions. Intermediate filaments form much of the nuclear lamina.Intermediate filaments form the desmosomes between cells in some animal tissues. (credit c "illustration": modification of work by Mariana Ruiz Villareal)

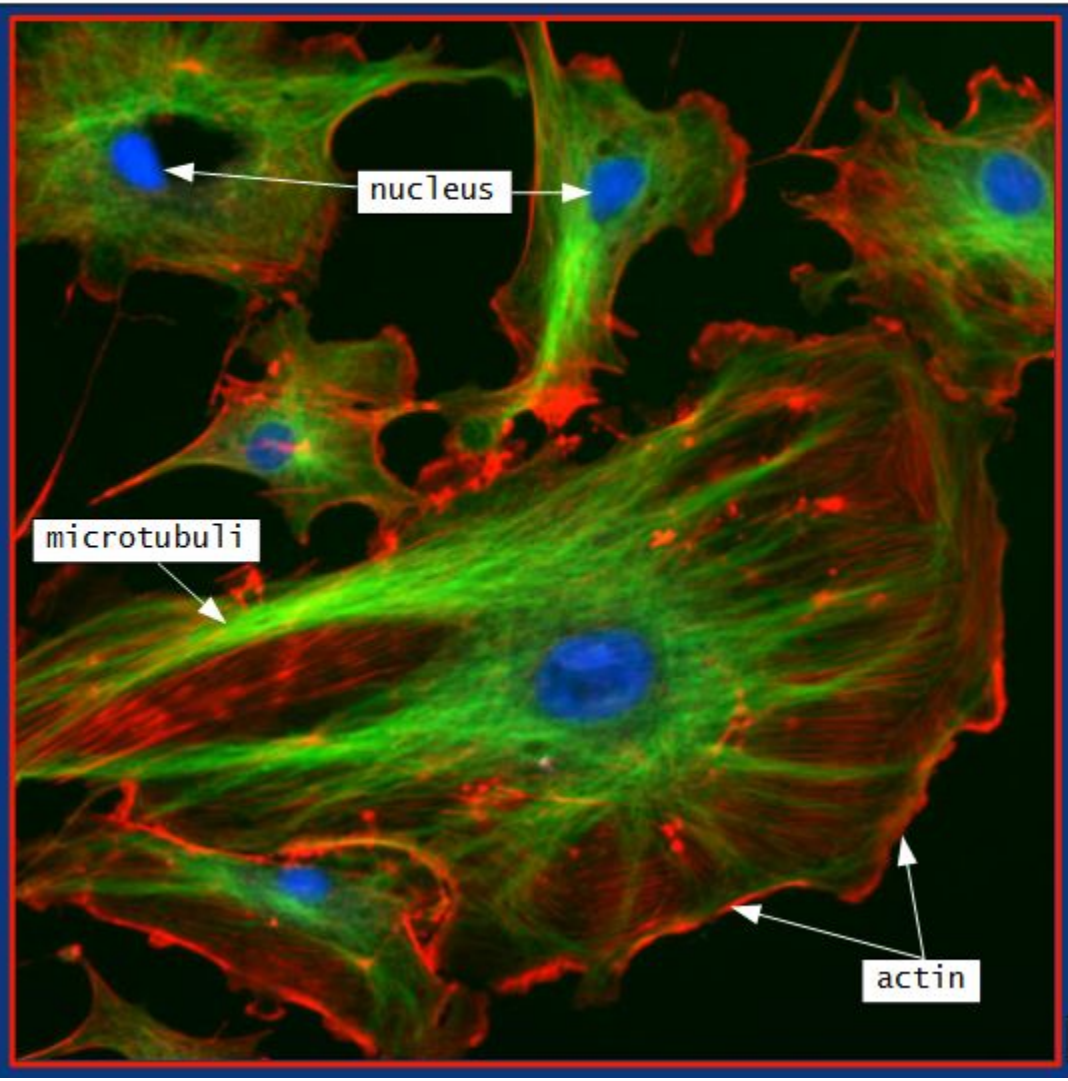



The cytoskeleton, in the form of filaments & tubules, support the cell & play a role in the formation of spindles.
Centrioli
Chromosomes
Spindle fibers
Centriole
Transmission electron microscope

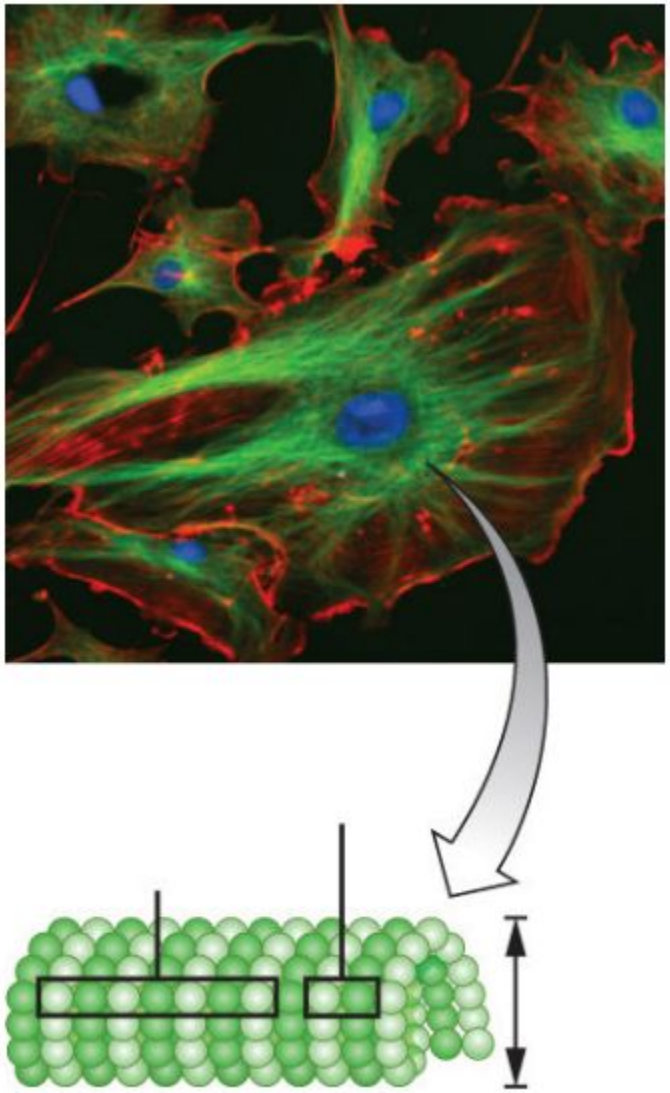
Cytoplasm Cytoskeleton

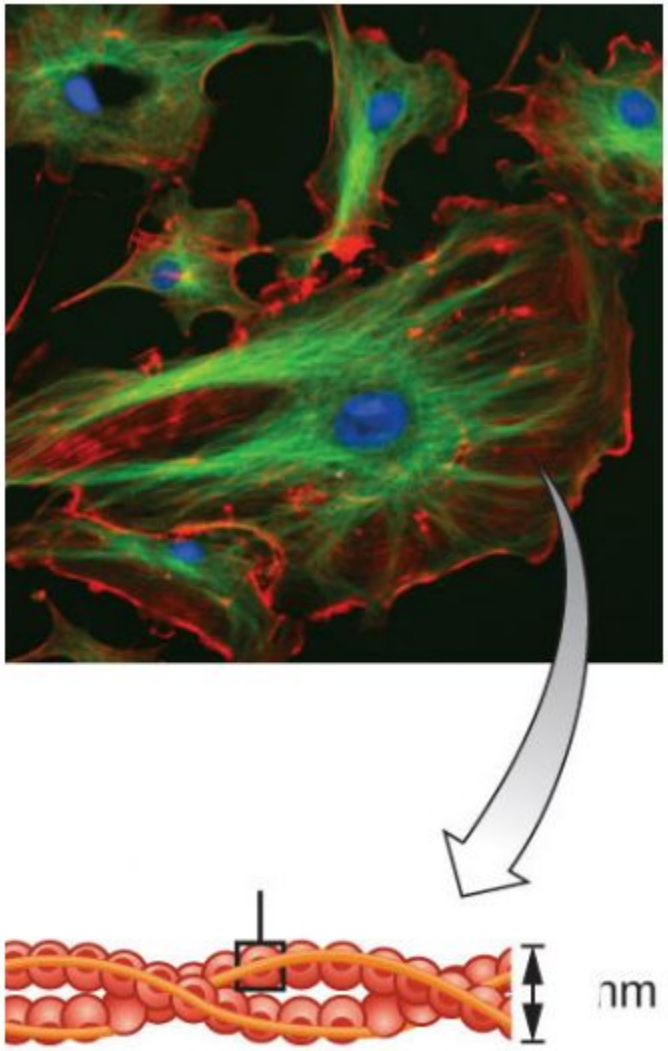
- Microtubules
- Actin microfilaments
- Myosin filaments
- Myosin
- Intermediate filaments
- Keratin filaments
- Desmin filaments
- Vimentin filaments
- Neurofilaments
- Glial filaments
- Microtrabecular lattice

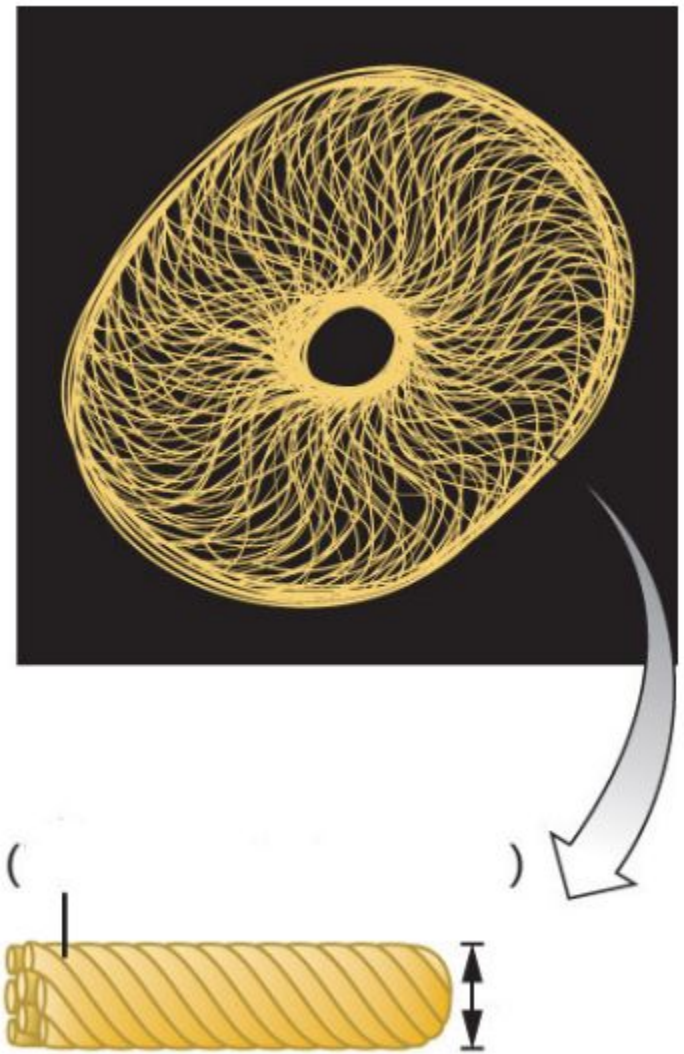
Fluorescent stain of pulmonary arterial endothelial cells to show the cytoskeleton. Blue = nucleus; Green = microtubuli; Red = F-actin



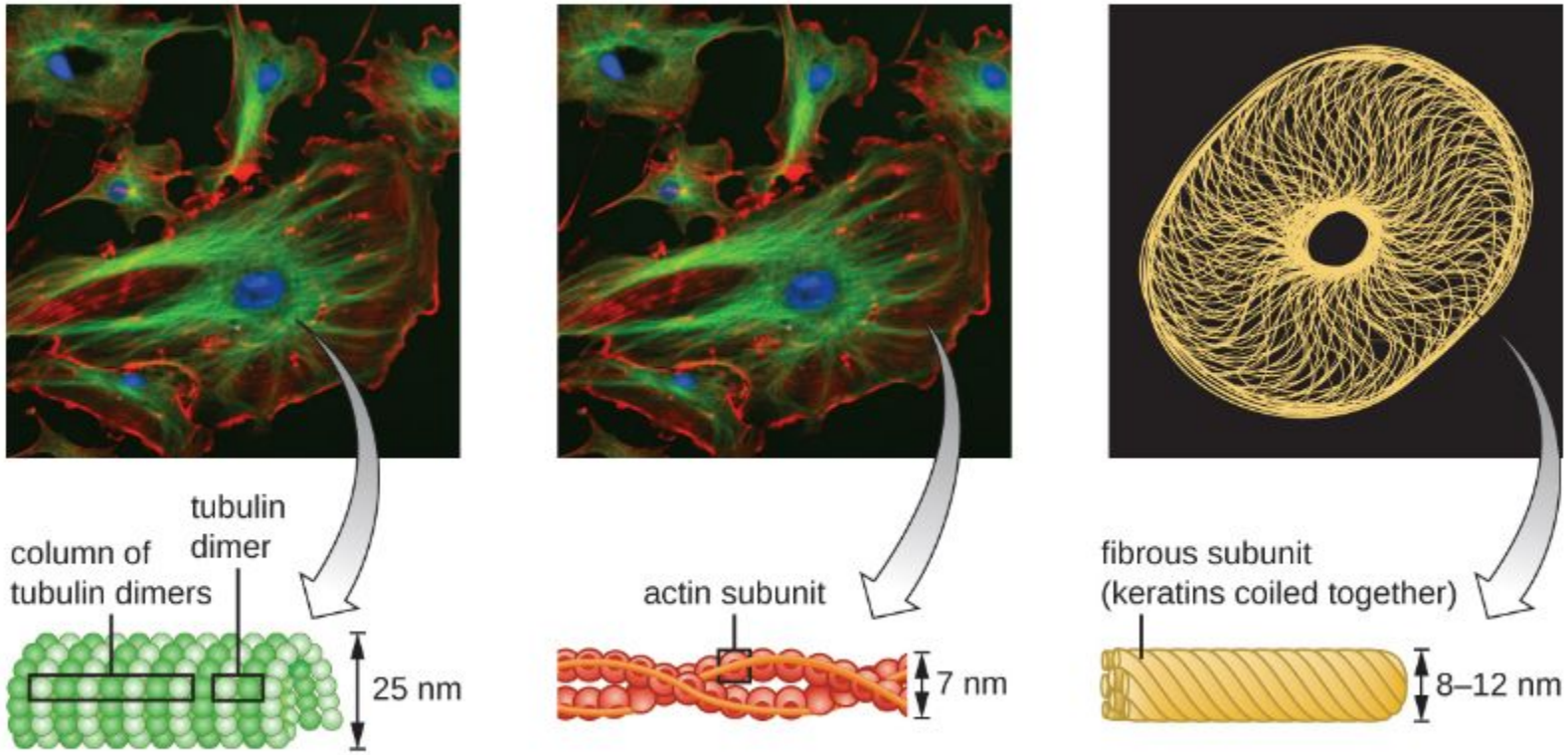
Public domain




nm



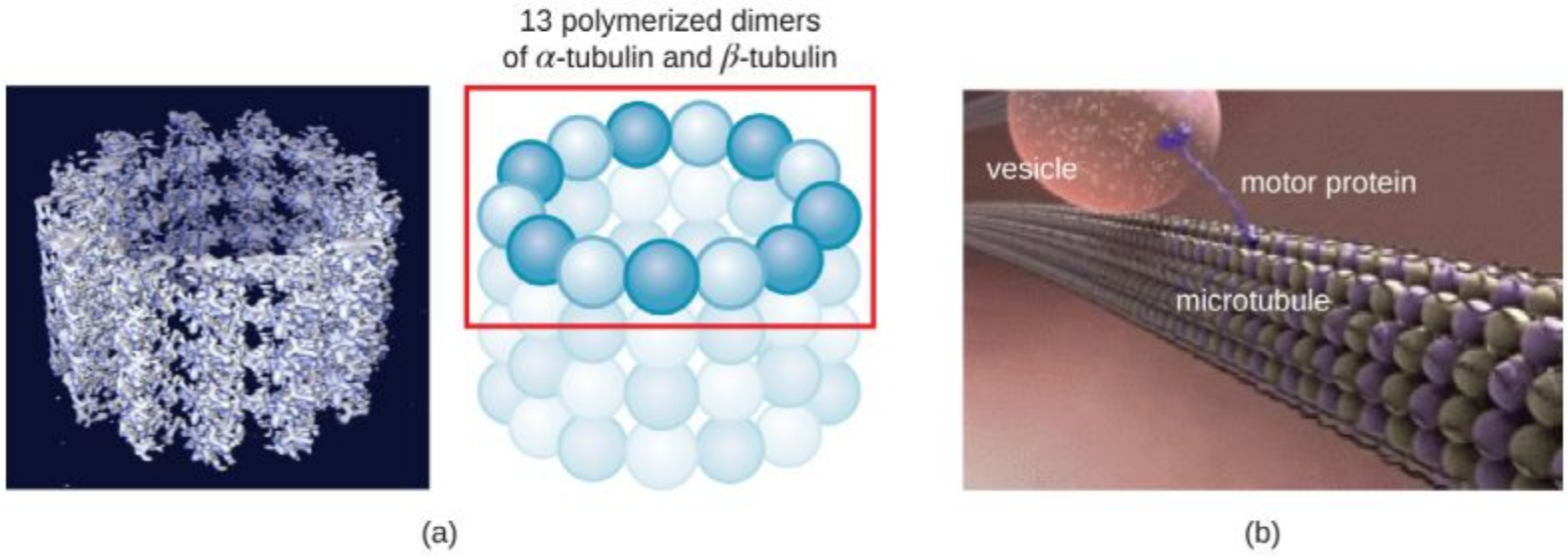
A transmission electron micrograph (left) of a cell containing a peroxisome. The illustration (right) shows the location of peroxisomes in a cell. These eukaryotic structures play a role in lipid biosynthesis and breaking down various molecules. They may also have other specialized functions depending on the cell type. (credit "micrograph": modification of work by American Society for Microbiology)



Microtubules

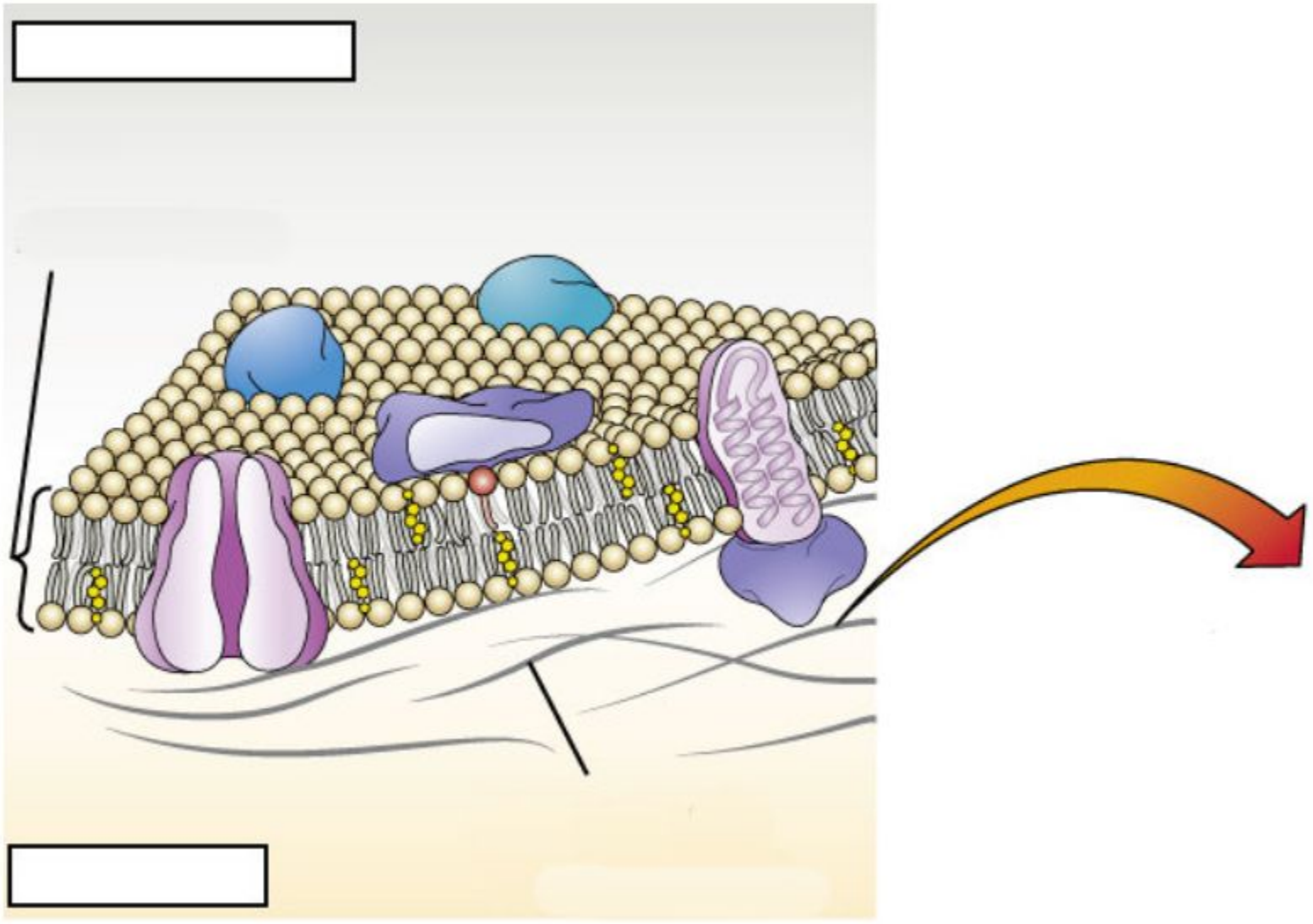
- Straight structures 25 nm x several μm length
- Labile population
    - Free in cytoplasm
    - Polymerize-depolymerize depending on
    - Temperature, pressure, drugs, etc
- Stable population
    - Walls of centrioles
    - Axonemes of cilia & flagella
- Wall 5 nm thick
    - around lumen-like region
    - containing 13 spirally arranged protofilaments
- Associated with intracellular transport
- Maintains cell shape
- Promote movement of cilia, flagella & chromosomes

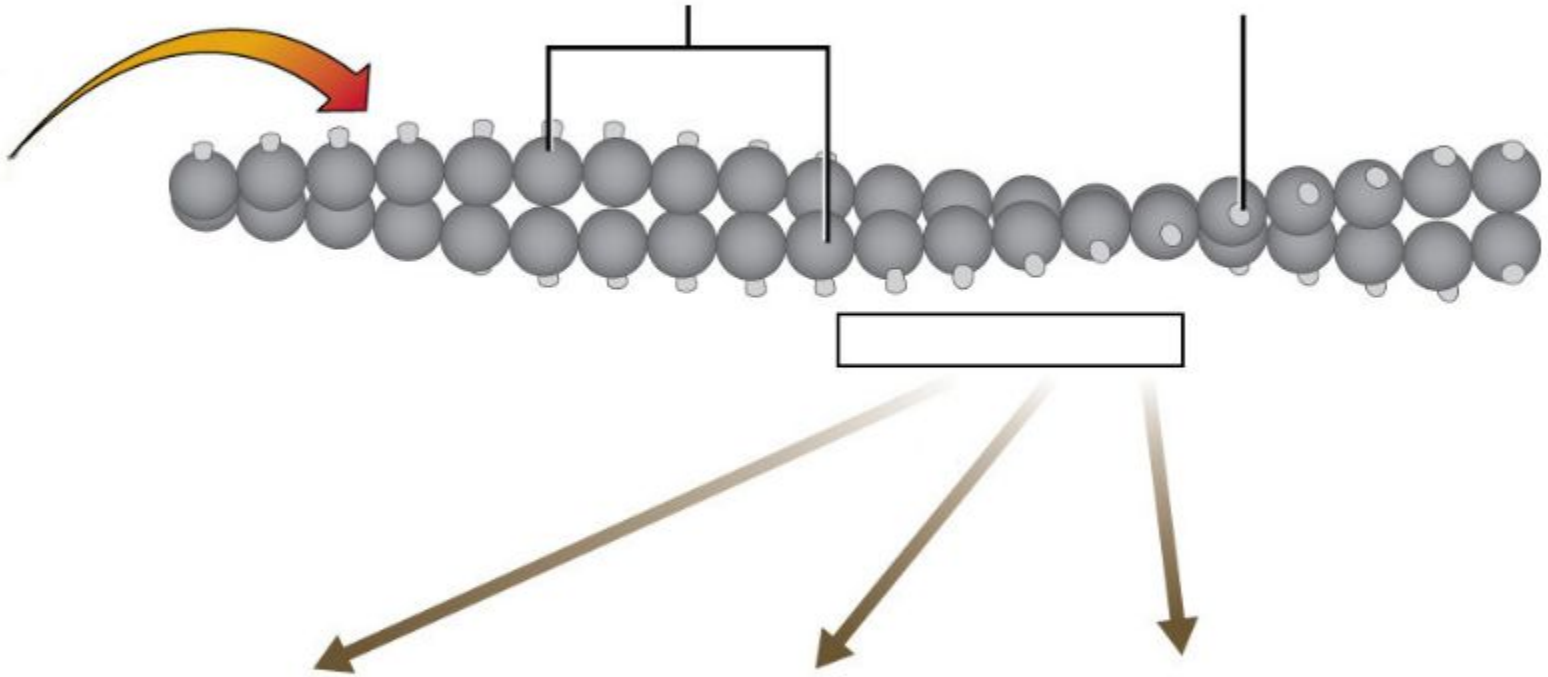
Microtubules are hollow structures composed of polymerized tubulin dimers. They are involved in several cellular processes, including the movement of organelles throughout the cytoplasm. Motor proteins carry organelles along microtubule tracks that crisscross the entire cell. (credit b: modification of work by National Institute on Aging)

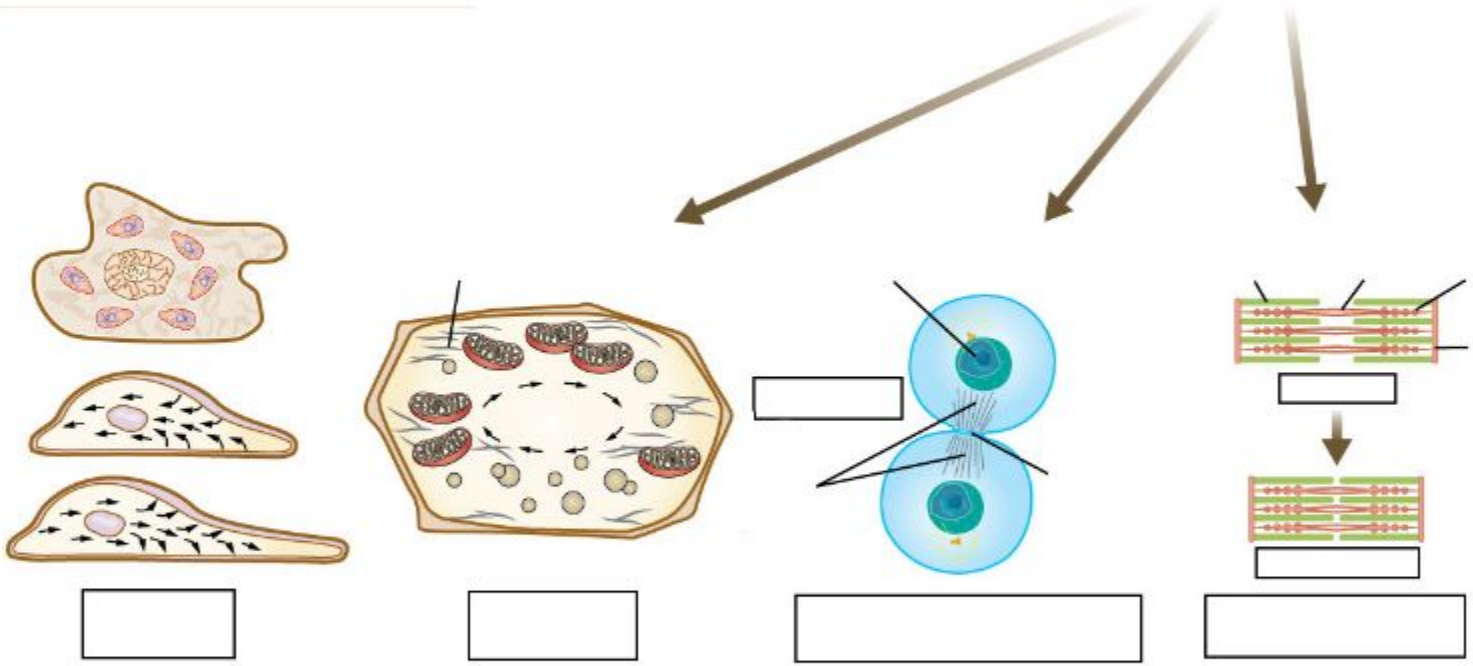


Actin microfilaments

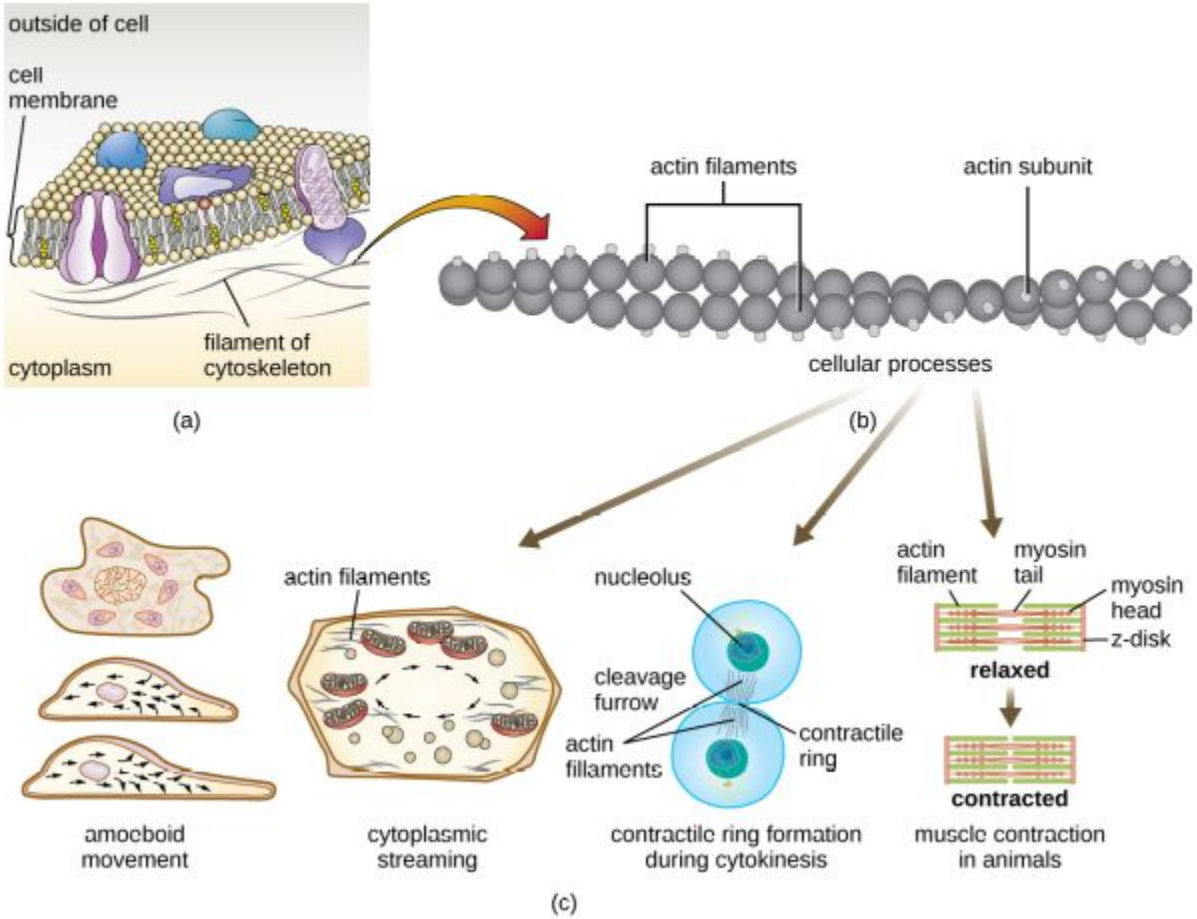
- Thin filaments
- Involved with
    - Ameboid movement
    - Cytoplasmic streaming
    - Contractile ring formation
    - Muscle contraction



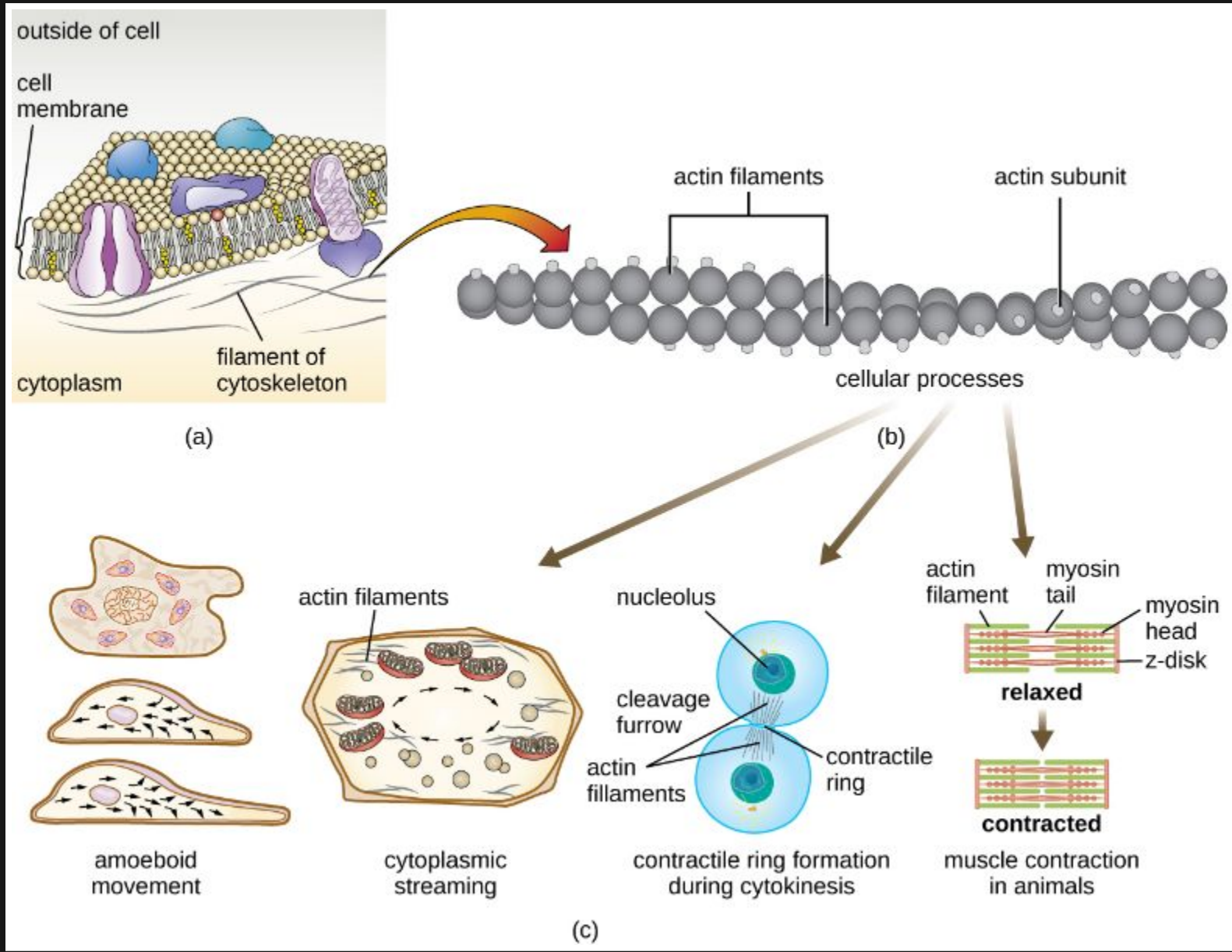




A microfilament is composed of a pair of actin filaments. Each actin filament is a string of polymerized actin monomers.The dynamic nature of actin, due to its polymerization and depolymerization and its association with myosin, allows microfilaments to be involved in a variety of cellular processes, including ameboid movement, cytoplasmic streaming, contractile ring formation during cell division, and muscle contraction in animals.



Parker et al; OpenStax: Microbiology; CC-BY 4.0

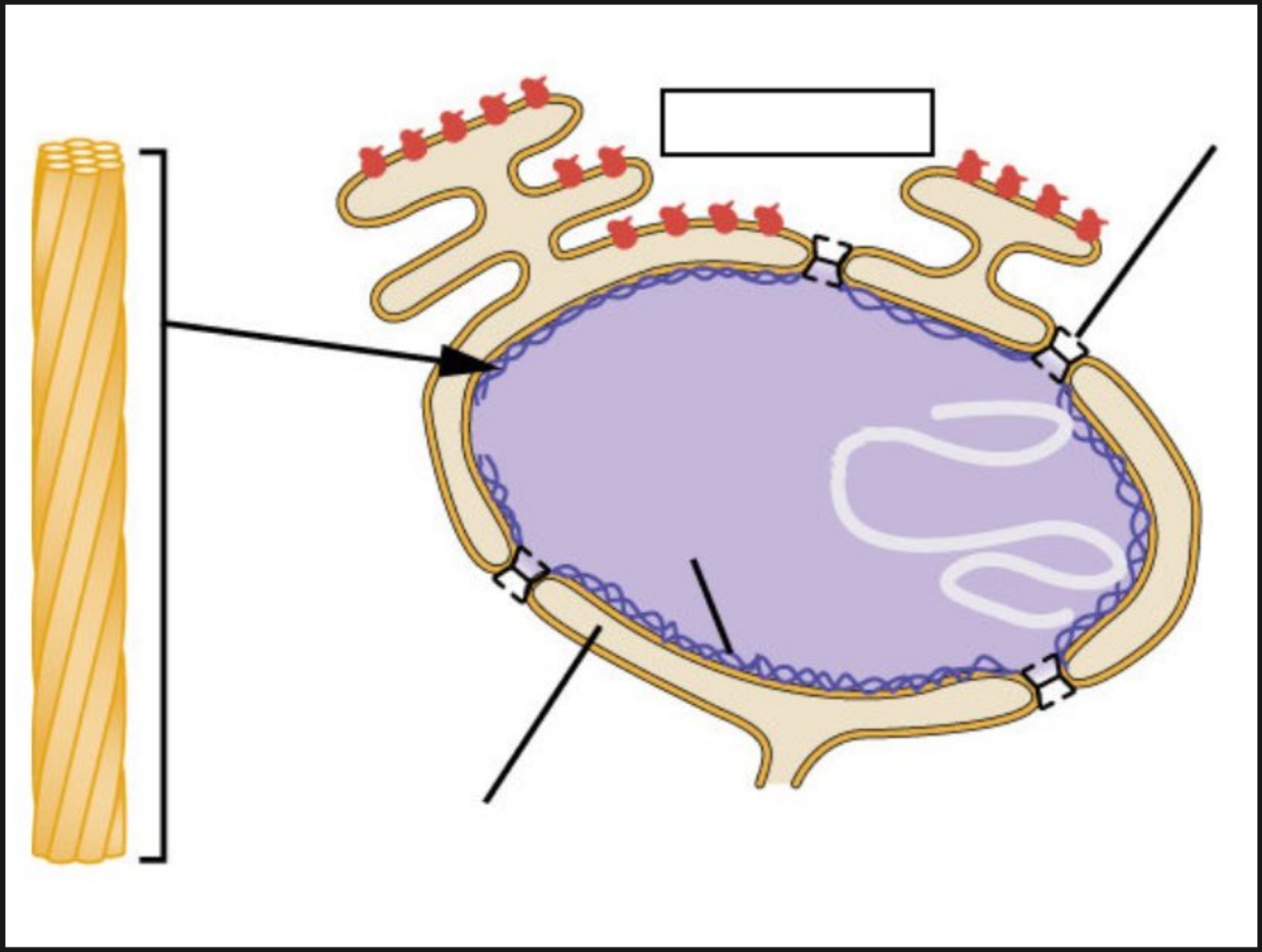

outside of cell
cell membrane
cytoplasm
filament of cytoskeleton
(a)
actin filaments
actin subunit
cellular processes
(b)
amoeboid movement
actin filaments
cytoplasmic streaming
nucleolus
cleavage furrow
actin fillaments
contractile ring
contractile ring formation during cytokinesis
actin filament
myosin tail
myosin head
z-disk
relaxed
contracted
muscle contraction in animals
(c)

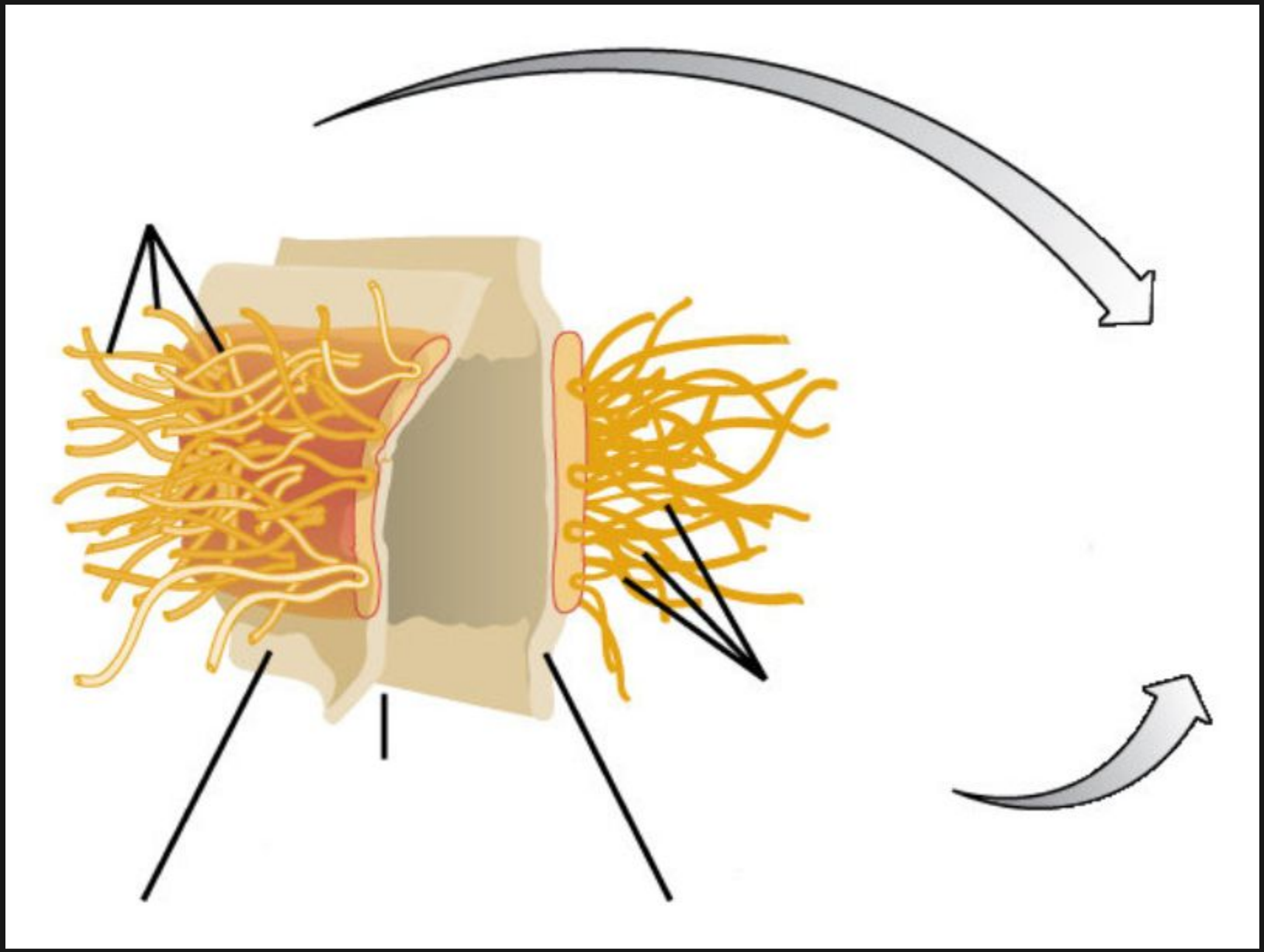
Myosin filaments

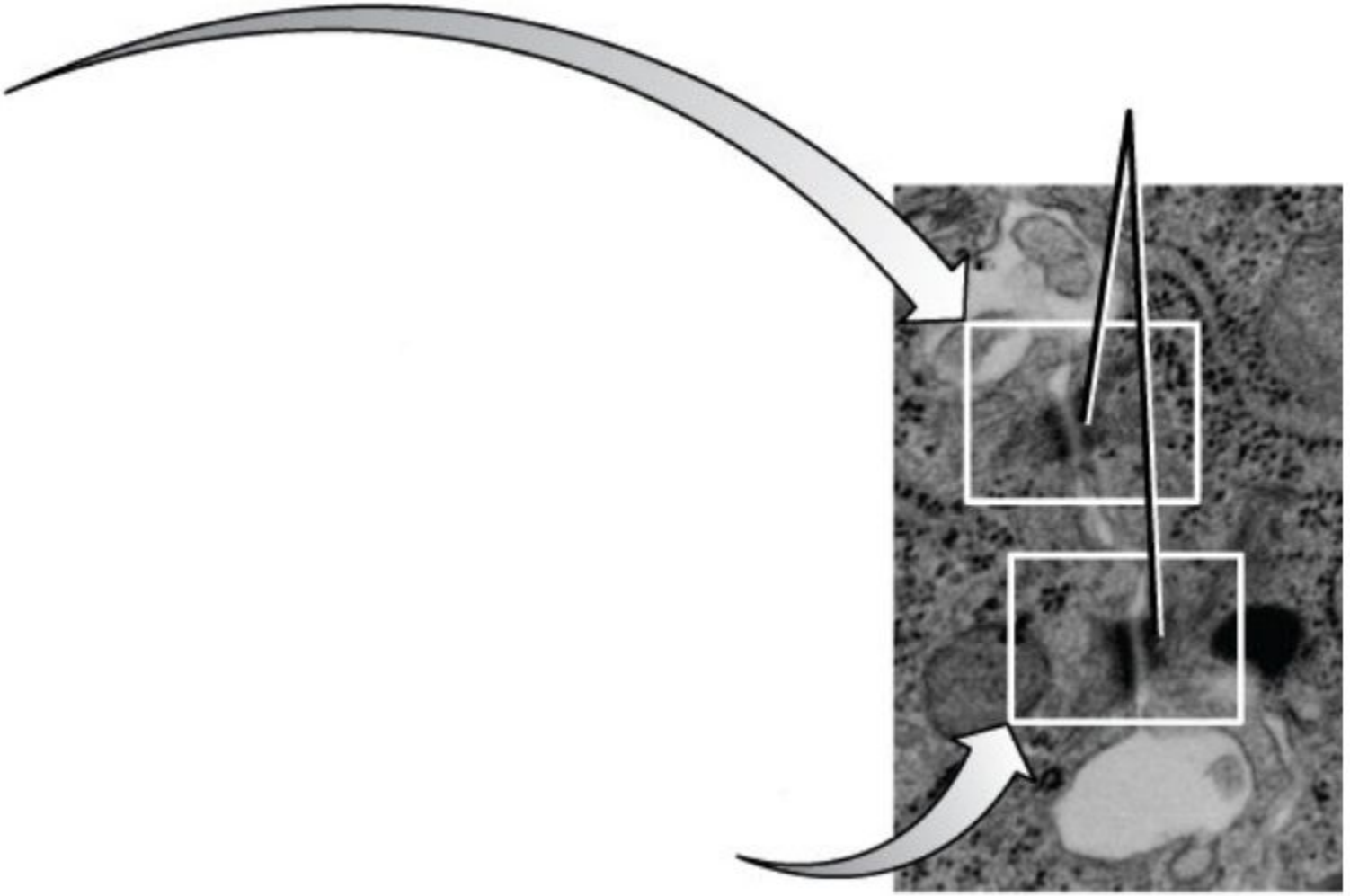
- Thick filaments
- Associated with actin in muscle cells
- Visible as striations in striated muscle

Intermediate filaments

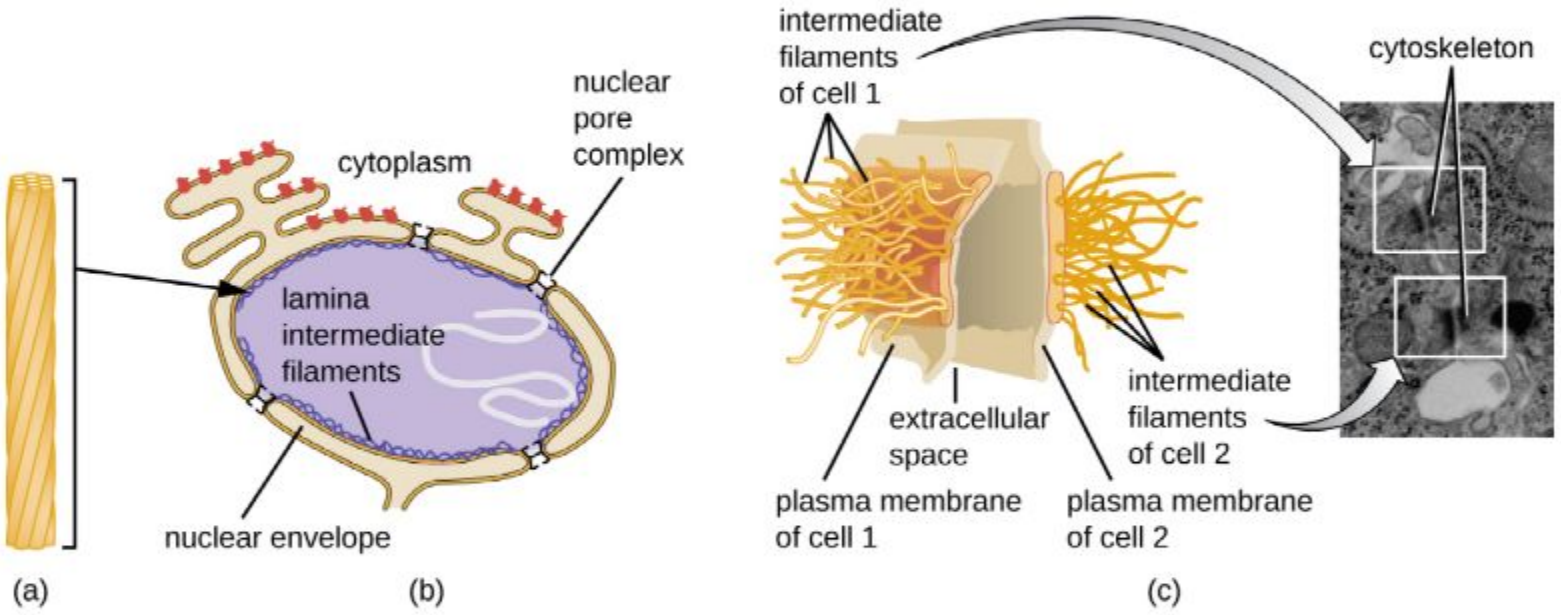
- Heterogenous group
- Includes
- Keratin
    - Found in epithelial cells
    - Associated with desmosomes
- Vimentin
- Desmin
- Neurofilaments
    - Support long processes of nerve cells
- Glial filaments
    - Present in nonneuronal cells of central nervous system
    - Astrocytes, oligodendrocytes, microglia







Intermediate filaments are composed of multiple strands of polymerized subunits. They are more permanent than other cytoskeletal structures and serve a variety of functions. Intermediate filaments form much of the nuclear lamina.Intermediate filaments form the desmosomes between cells in some animal tissues. (credit c "illustration": modification of work by Mariana Ruiz Villareal)



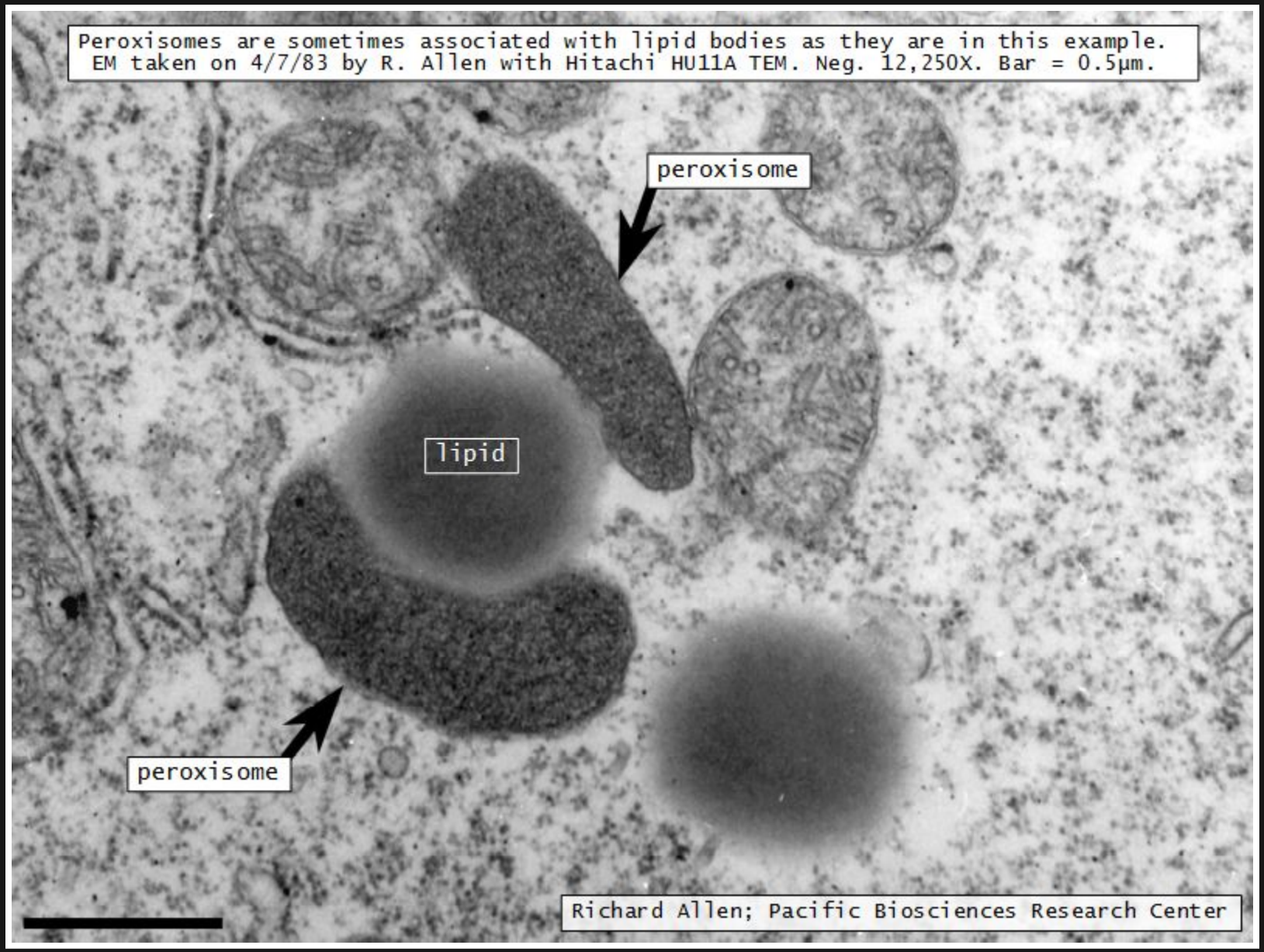
Keratin filaments

Neurofilaments

Glial filaments

Cytoplasm Inclusions

- Glycogen
  - Storage form of carbohydrate
  - Varying appearance depending on stain
- Lipid droplets
  - Varying appearance depending on stain
- Secretion granules
  - Varying appearance
  - Include mucous droplets, hormones, proteins, pigment


Peroxisomes are sometimes associated with lipid bodies as they are in this example.
EM taken on 4/7/83 by R. Allen with Hitachi HU11A TEM. Neg. 12,250X. Bar = 0.5µm.
peroxisome
lipid
peroxisome
Richard Allen; Pacific Biosciences Research Center

Cell surface modifications

- Cell surfaces of epithelia has specific modifications, relating to the function of epithelia
- Three surfaces show modifications
- Lateral surface
    - Junctional complexes
    - Gap junctions
    - Lateral interdigitations
- Basal surface
    - Basal lamina
    - Hemidesmosomes
    - Basal plasma membrane infoldings
- Apical surface
    - Microvilli
    - Stereocilia
    - Cilia

Epithelia

Lines internal -

Covers external -

Surfaces of the body

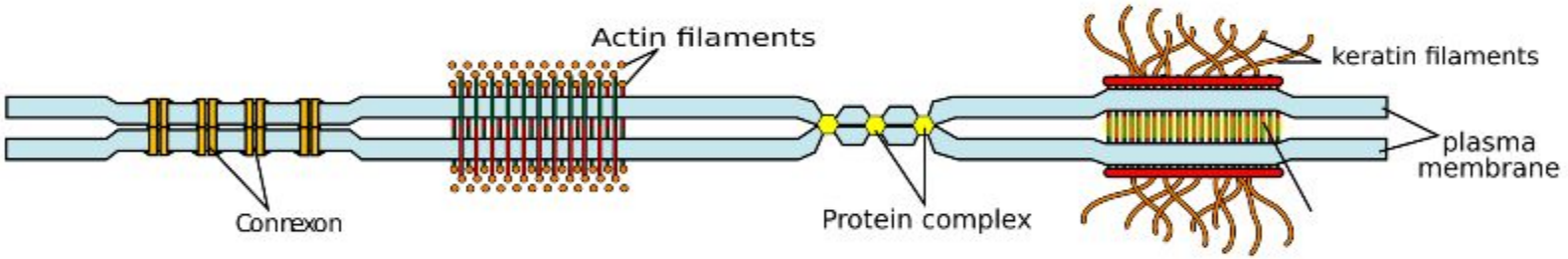
Three surface areas

- Apical surface
- Face the lumen or external environment
- Lateral surface
- Where cells are in contact with each other
- Basal surface
- Bottom edge of cell adjacent to basement membrane

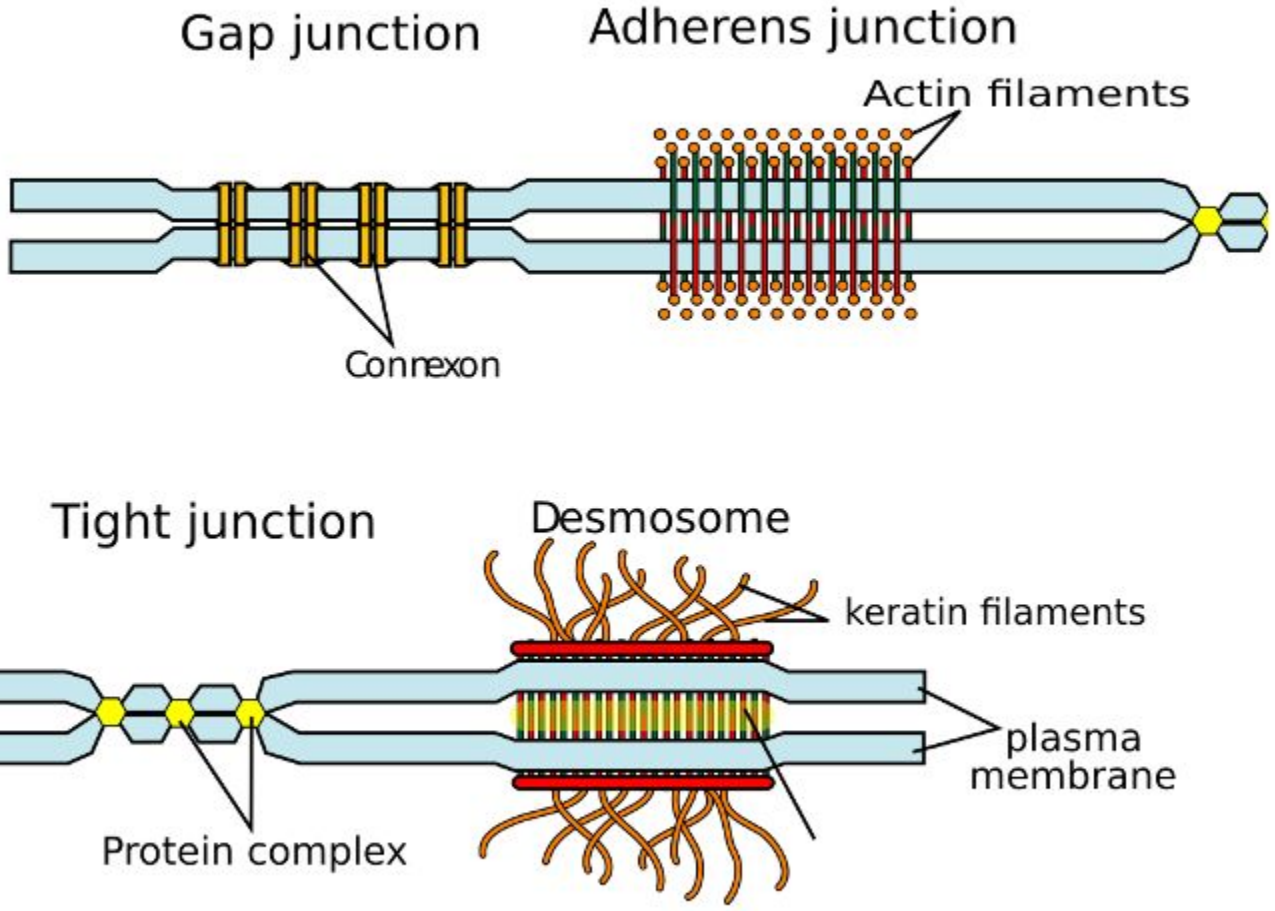
Lateral surface

- Junctional complexes
- Gap junctions
- Lateral interdigitations

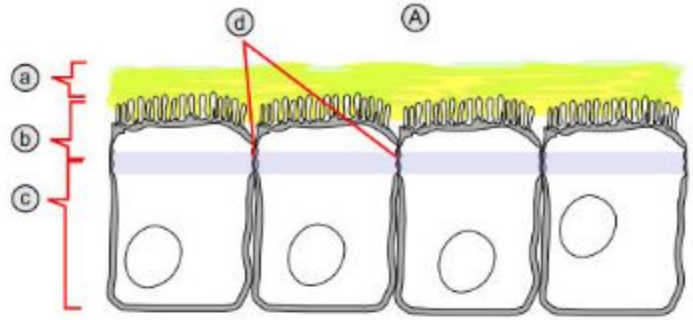
Identify:

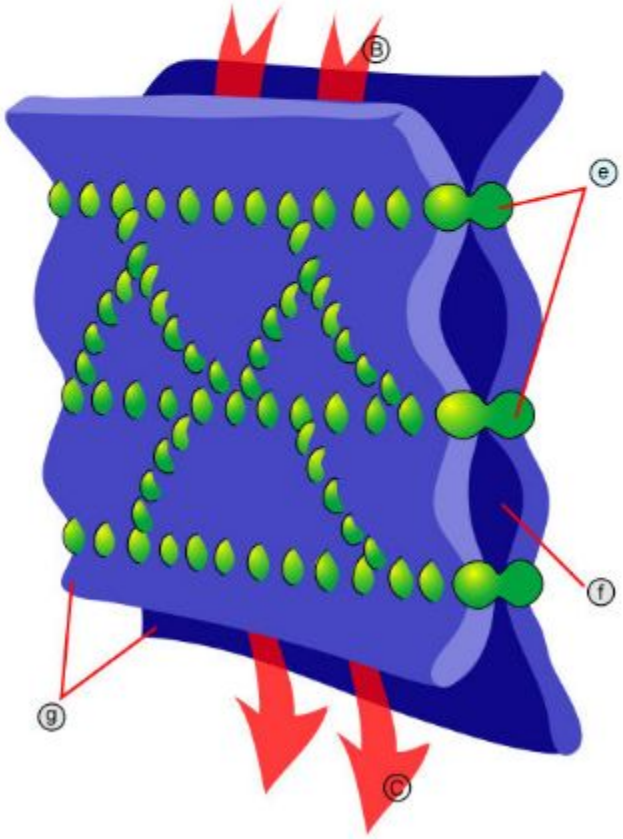

Actin filaments
keratin filaments
plasma membrane
Connexon
Protein complex

Junctional complexes



PD; Mariana Ruiz

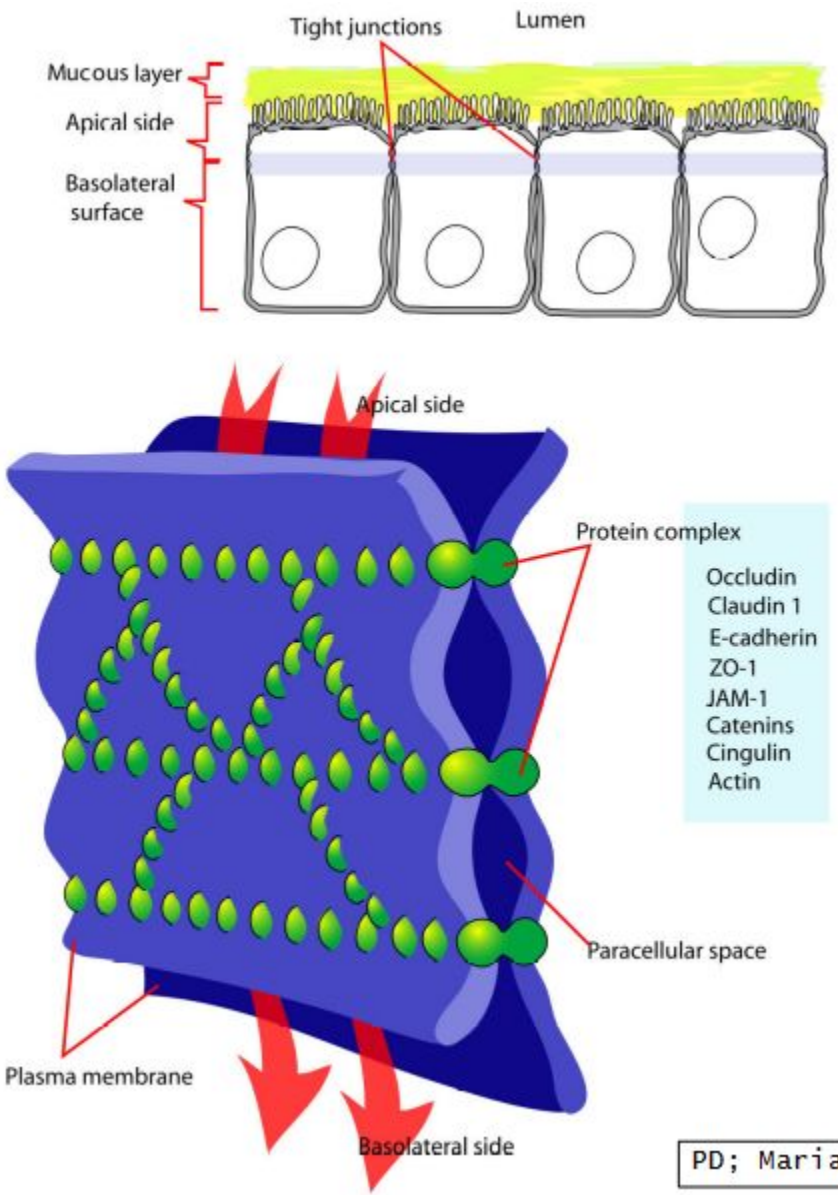

d
A
a
b
c


B
e
f
g
C

Junctional complexes

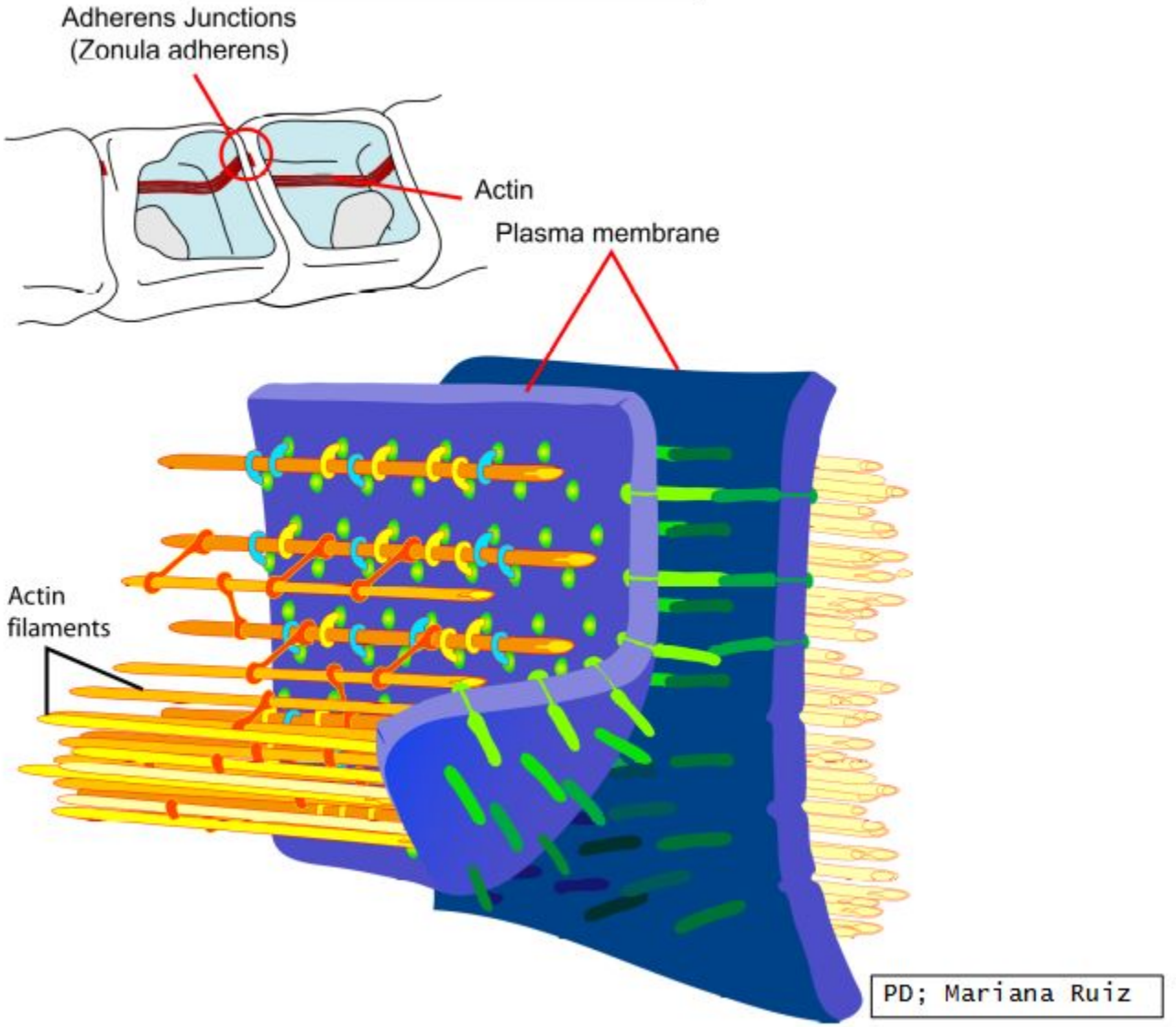
- Three components
- Zonula occludens (tight junction)
    - Outer part of adjacent plasma membranes fuse
    - Around entire apical perimeter of cells
    - Prevents entrance or exit into intercellular space
- Zonula adherens
    - Plasma membranes separated by 10 - 20 nm
    - Reinforced on cytoplasmic surface by actin filaments
    - Adhesive and structurally supportive
- Macula adherens
    - Focal disk shaped adhesive junction
    - Plasma membrane separated by 15 - 30 nm
    - Intermediate filaments loop from cytoplasma
    - Dense material in intercellular space

Diagram of a tight junction. Tight junctions seal adjacent epithelial cells in a narrow band just beneath their apical surface.



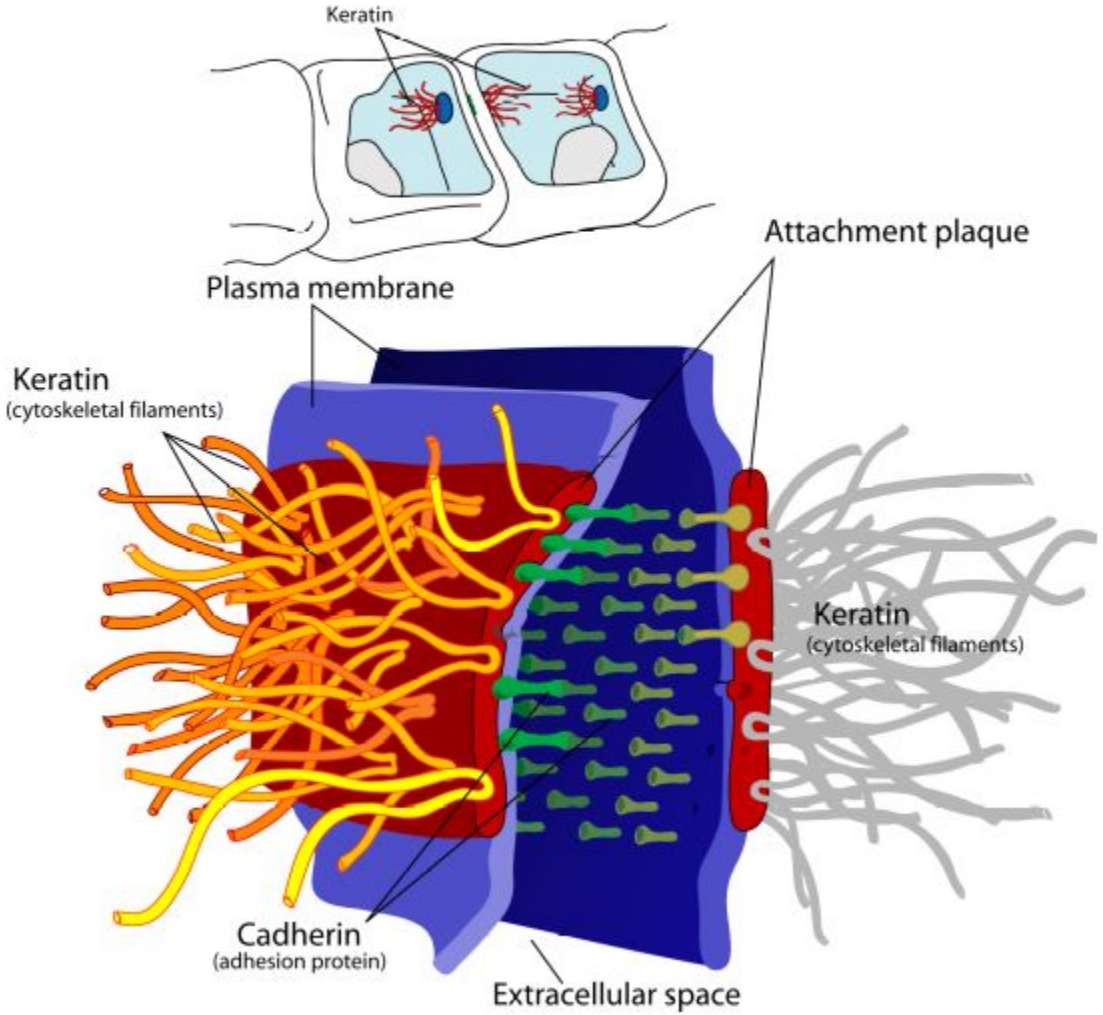
PD; Mariana Ruiz

Diagram of a zonula adherens.



PD; Mariana Ruiz

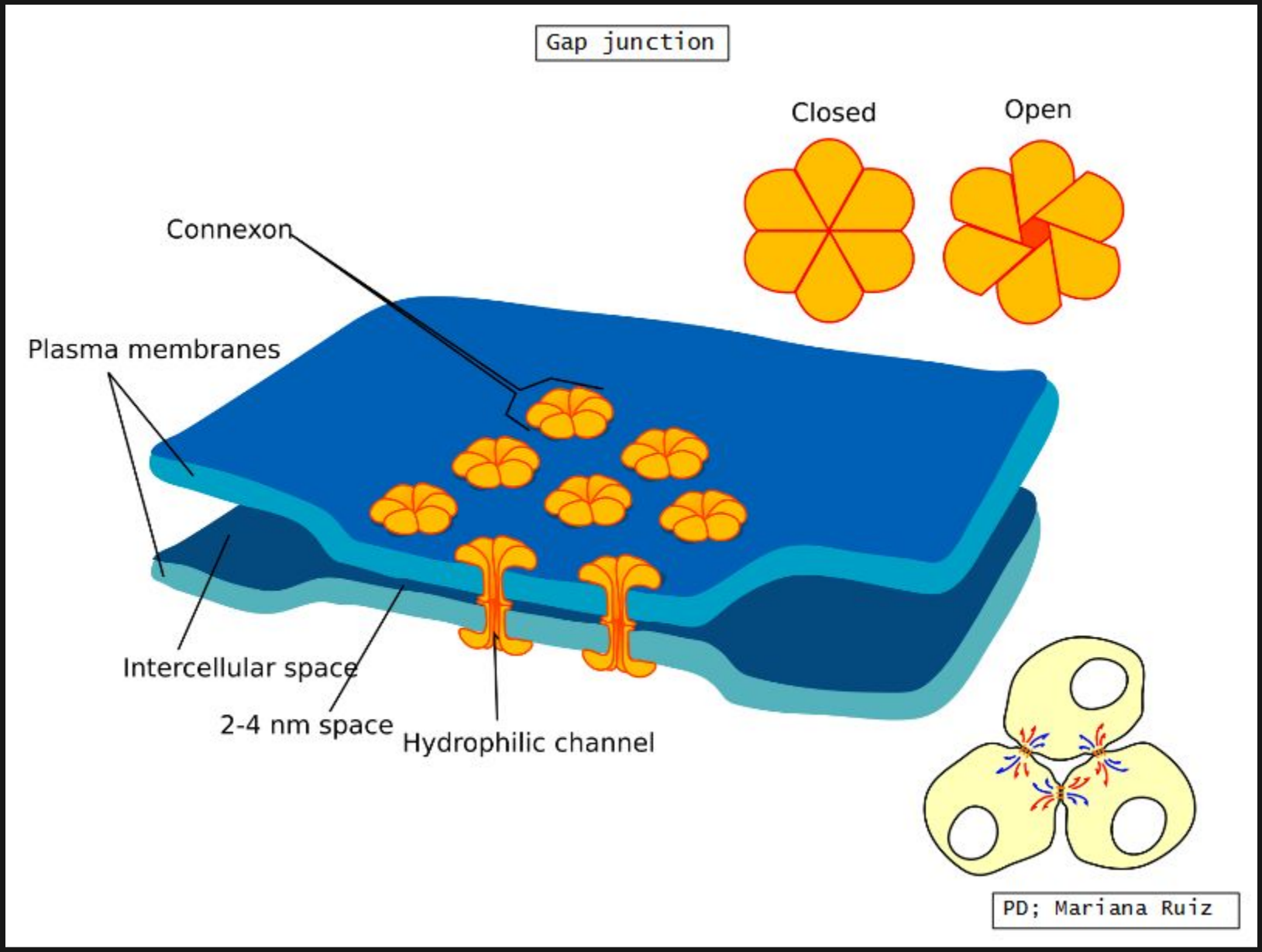
A desmosome, also known as macula adherens (Latin: adhering spot), is a cell structure specialized for cell-to-cell adhesion in animal cells. A type of junctional complex, they are localized spot-like adhesions randomly arranged on the lateral sides of plasma membranes.

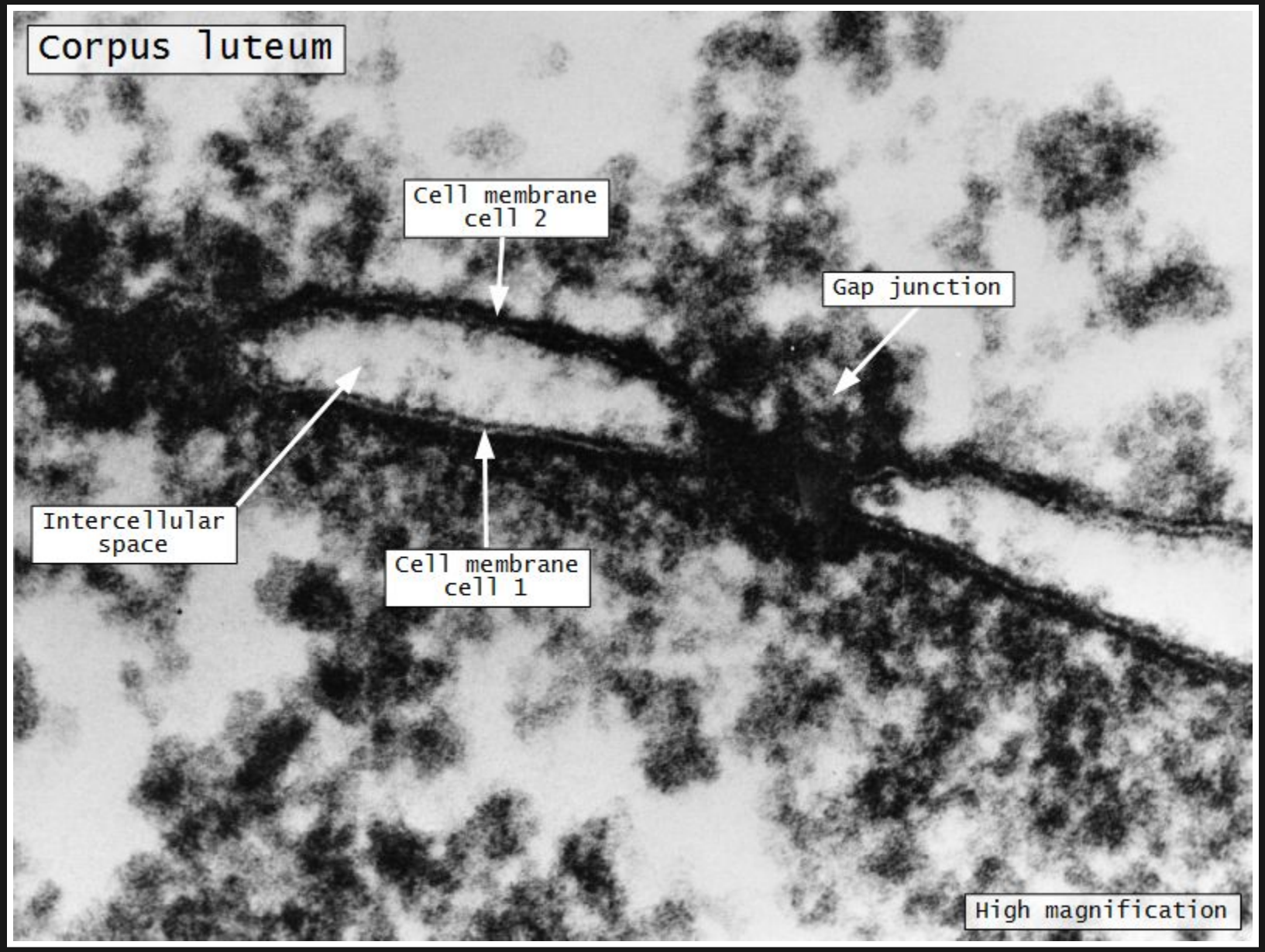


PD; Mariana Ruiz

Gap junctions

- Not limited to epithelial cells
- Also present in CNS, cardiac muscle & smooth muscle
- Opposing plasma membranes separated by 2 nm gap
- Gap is bridged by connexons
- Permit passage of ions & small molecules
- Intercellular communication


Gap junction
Closed
Open
Connexon
Plasma membranes
Intercellular space
2-4 nm space
Hydrophilic channel
PD; Mariana Ruiz


Corpus luteum
Cell membrane cell 2
Gap junction
Intercellular space
Cell membrane cell 1
High magnification

Lateral interdigitations

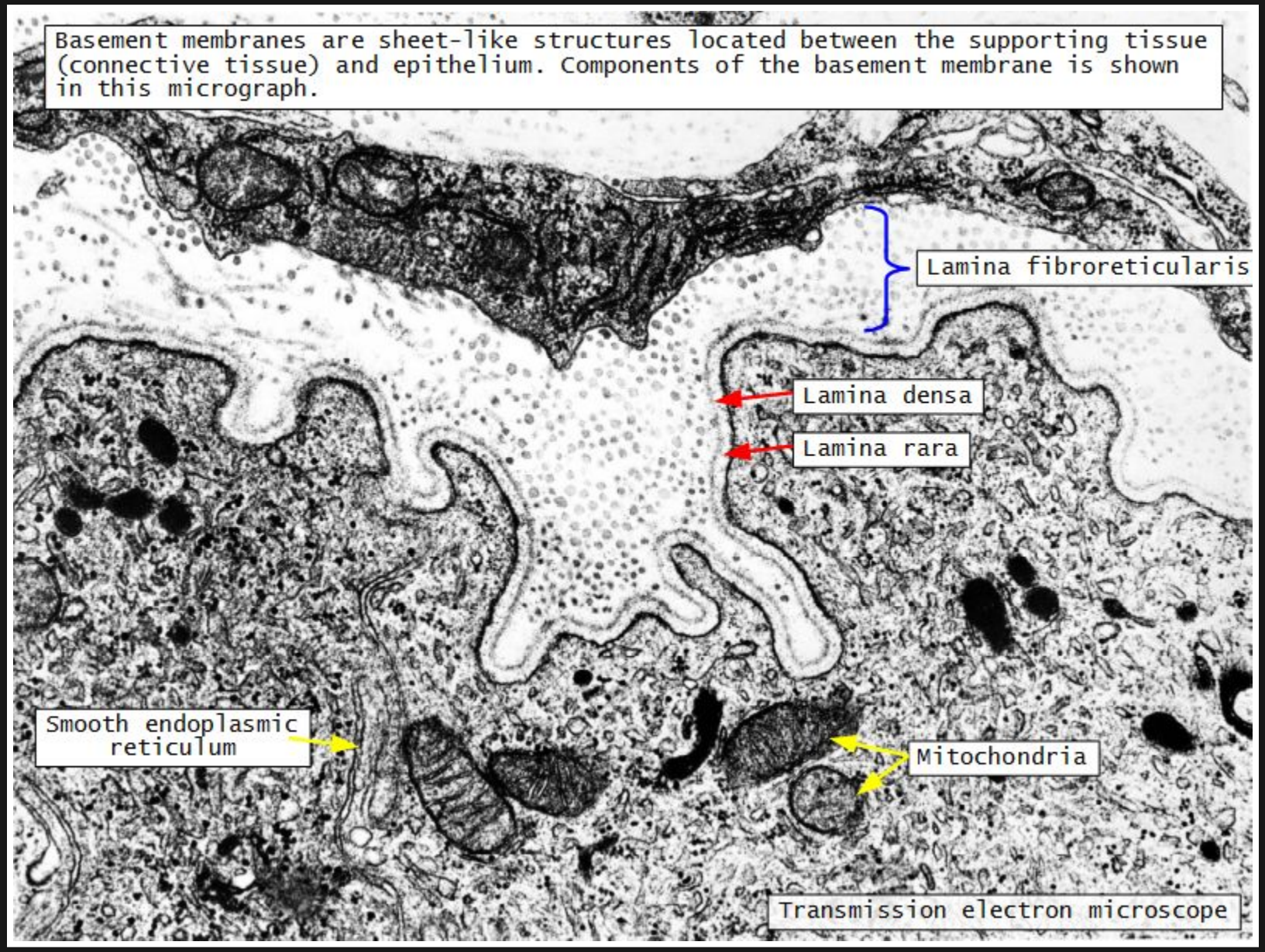
- Finger-like projections interlocking adjacent cells

Basal surface

- Basal lamina
- Hemidesmosomes
- Basal plasma membrane infoldings

Basal lamina

- Acellular support structure
- 20 - 100 nm thick
- Visible by electron microscope
- Produced by epithelium resting on it
- Consists of two zones
    - Lamina rara - low density, next to plasma membrane
    - Lamina dense - dense filament network, next to CT
    - Together = basement membrane of LM


Basement membranes are sheet-like structures located between the supporting tissue (connective tissue) and epithelium. Components of the basement membrane is shown in this micrograph.
Lamina fibroreticularis
Lamina densa
Lamina rara
Smooth endoplasmic reticulum
Mitochondria
Transmission electron microscope

Hemidesmosomes

- Appearance of one-half of desmosome
- Present along basal surface of some cells
- Attaches cell to underlying basal lamina

Basal plasma membrane infoldings

- Seen in ion-transporting epithelia
- Deep invaginations
- Compartmentalize mitochondria
- Ion pumps in plasmalemma in close contact with energy supply (ATP from mitochondria)

Apical surface

- Microvilli
- Stereocilia
- Cilia

Microvilli

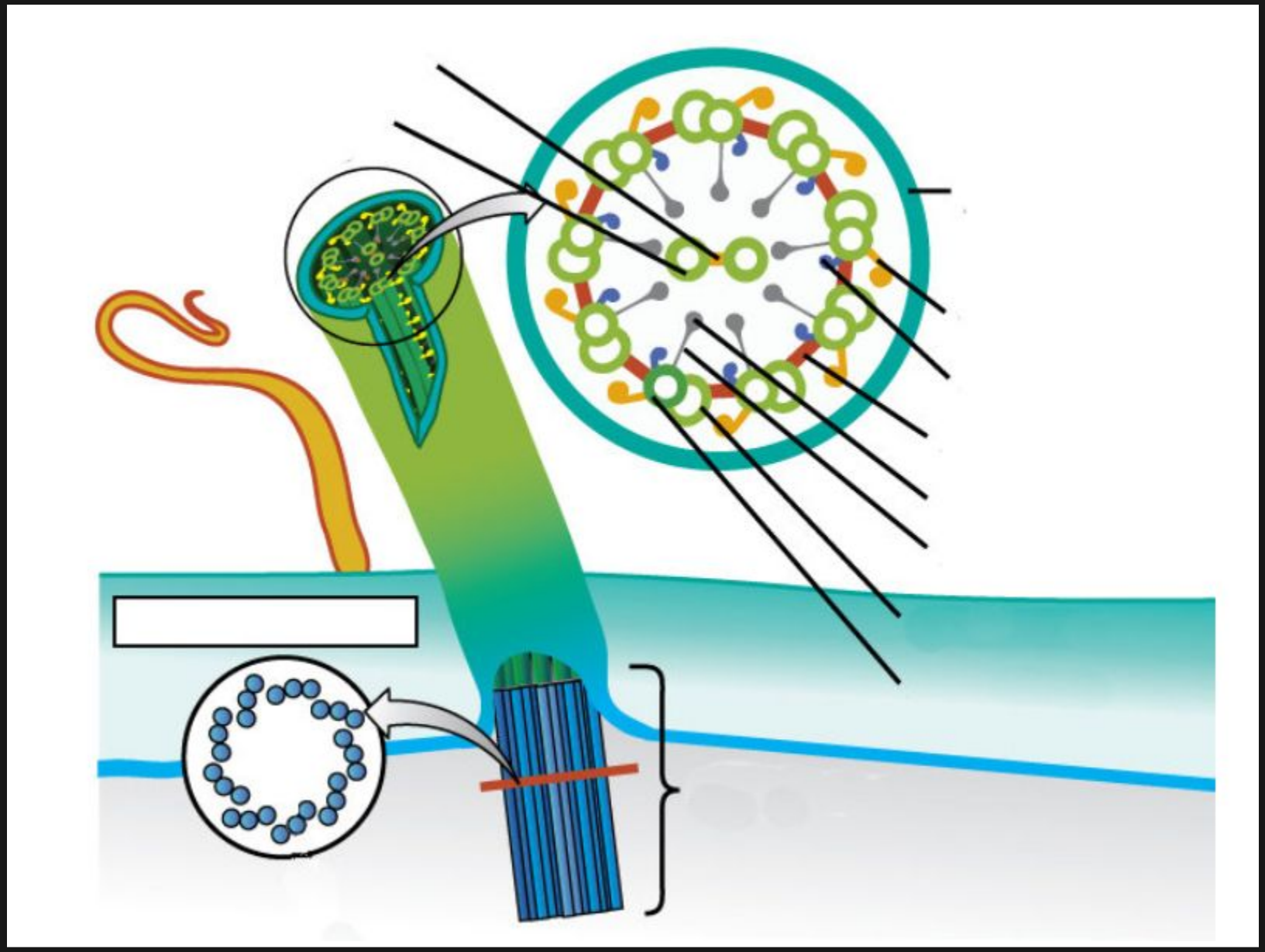
- Finger-like projections of epithelium
- Approximately 1 μm in length
- Increase absorptive surface
- Brush border of kidney proximal tubule cells
- Striated border of intestinal absorptive cells
- Actin filaments in core

Stereocilia

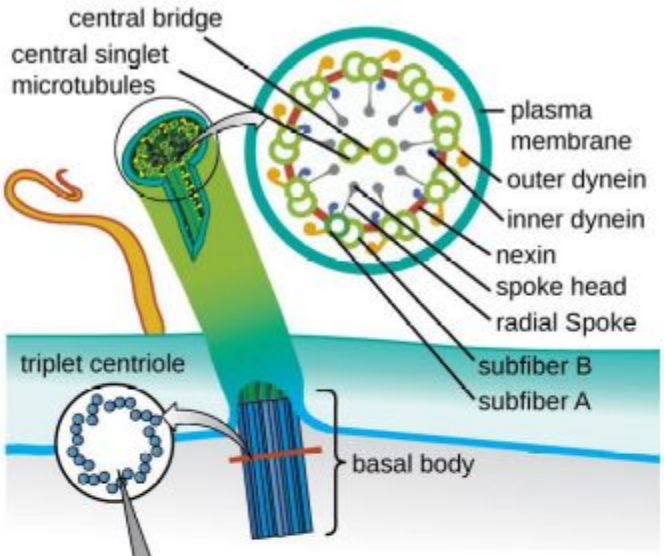
- Very long microvilli
- Not true cilia
- Epididymus & vas deferens

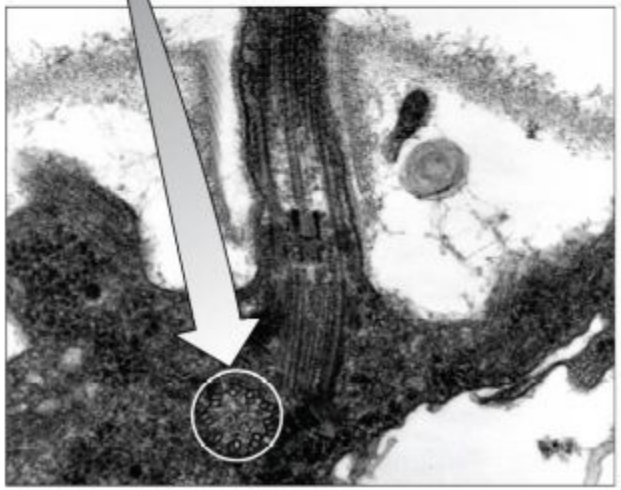
Cilia

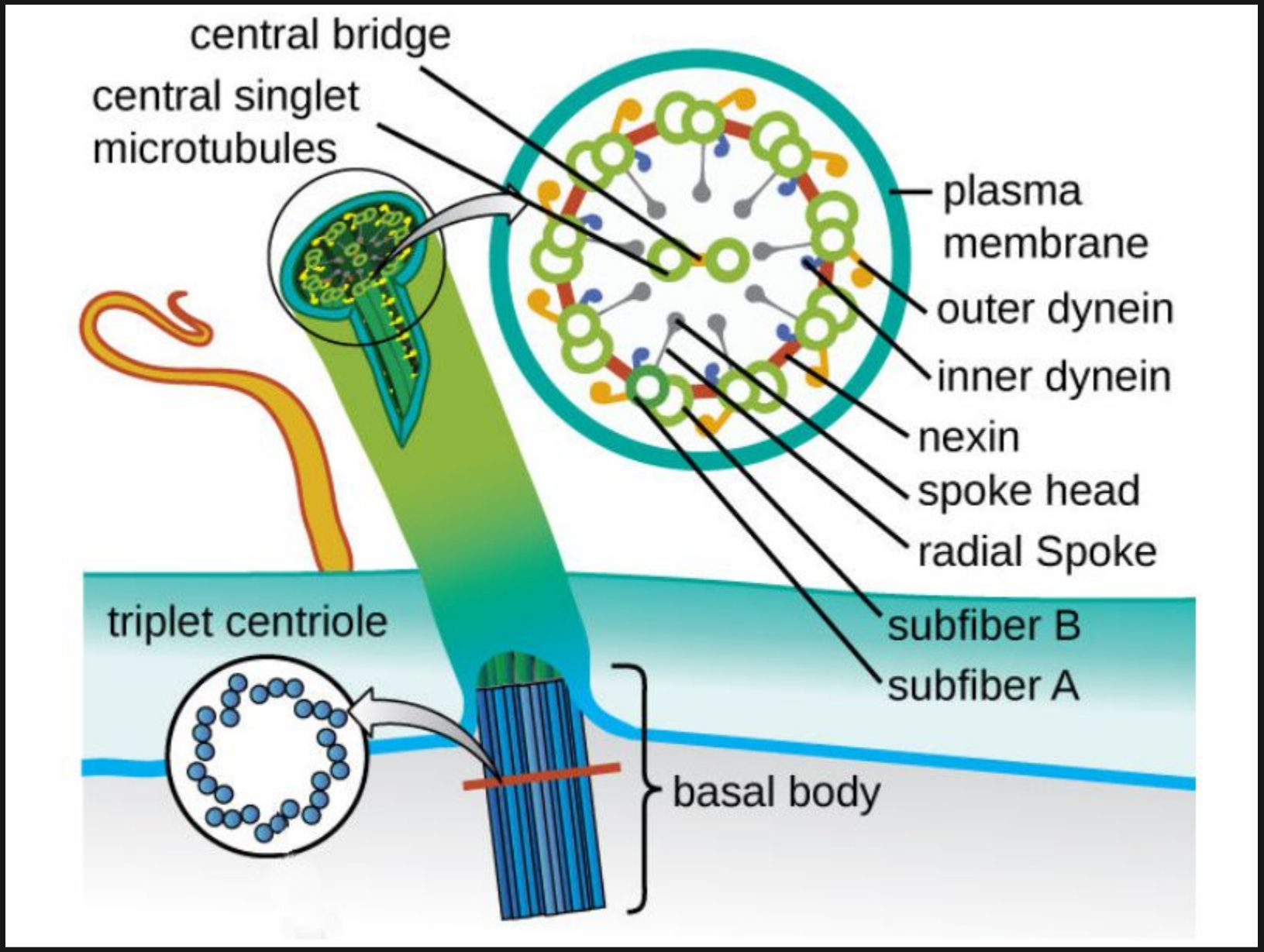
- Active motile specializations of epithelia that transports substances along their surface
- 5 - 10 µm in length
- Covered by plasma membrane
- Contains axoneme
- Nine pairs double tubules around two single microtubules (9+2 pattern)
- At base cylindrical basal body with 9+0 pattern

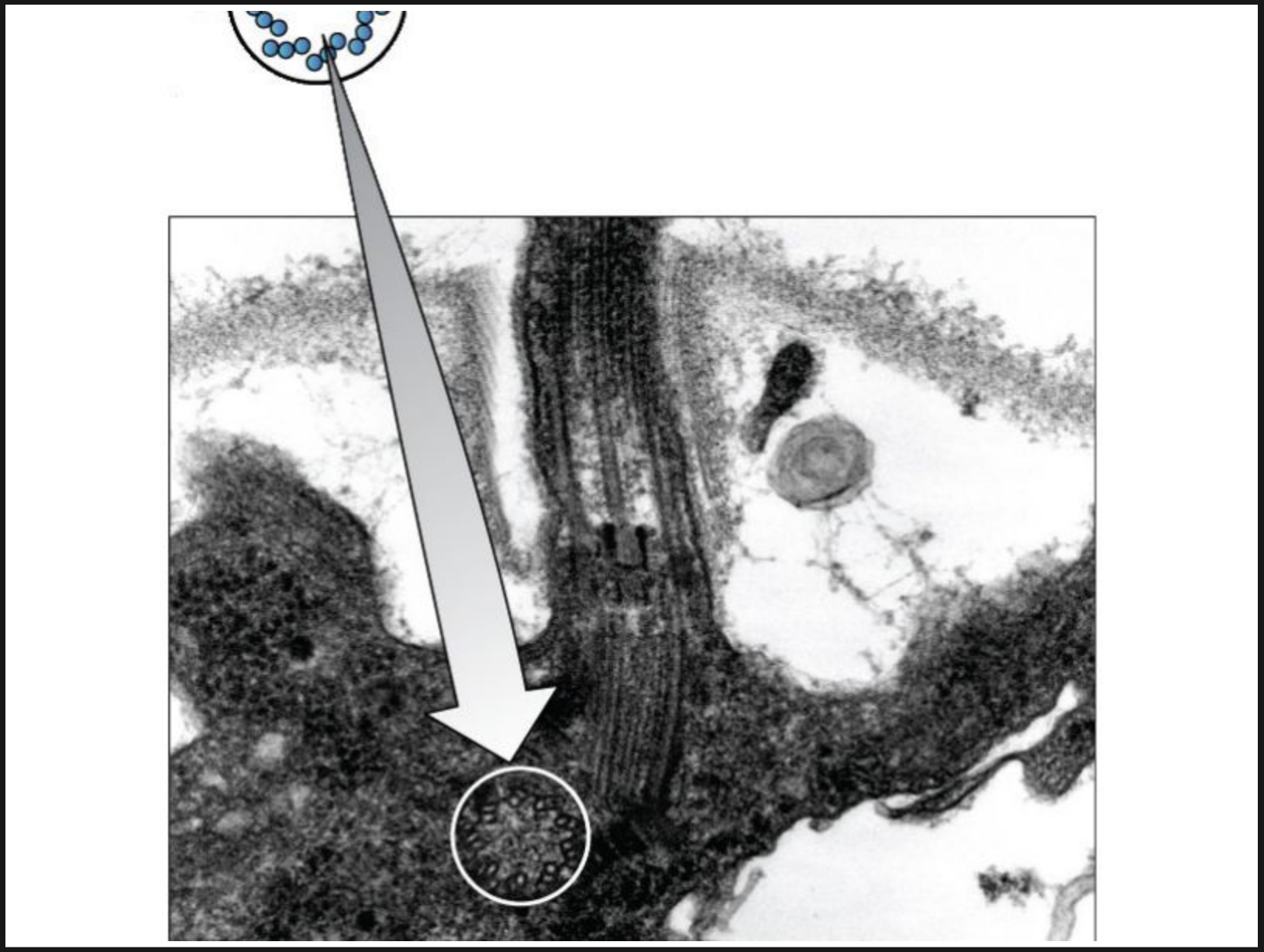


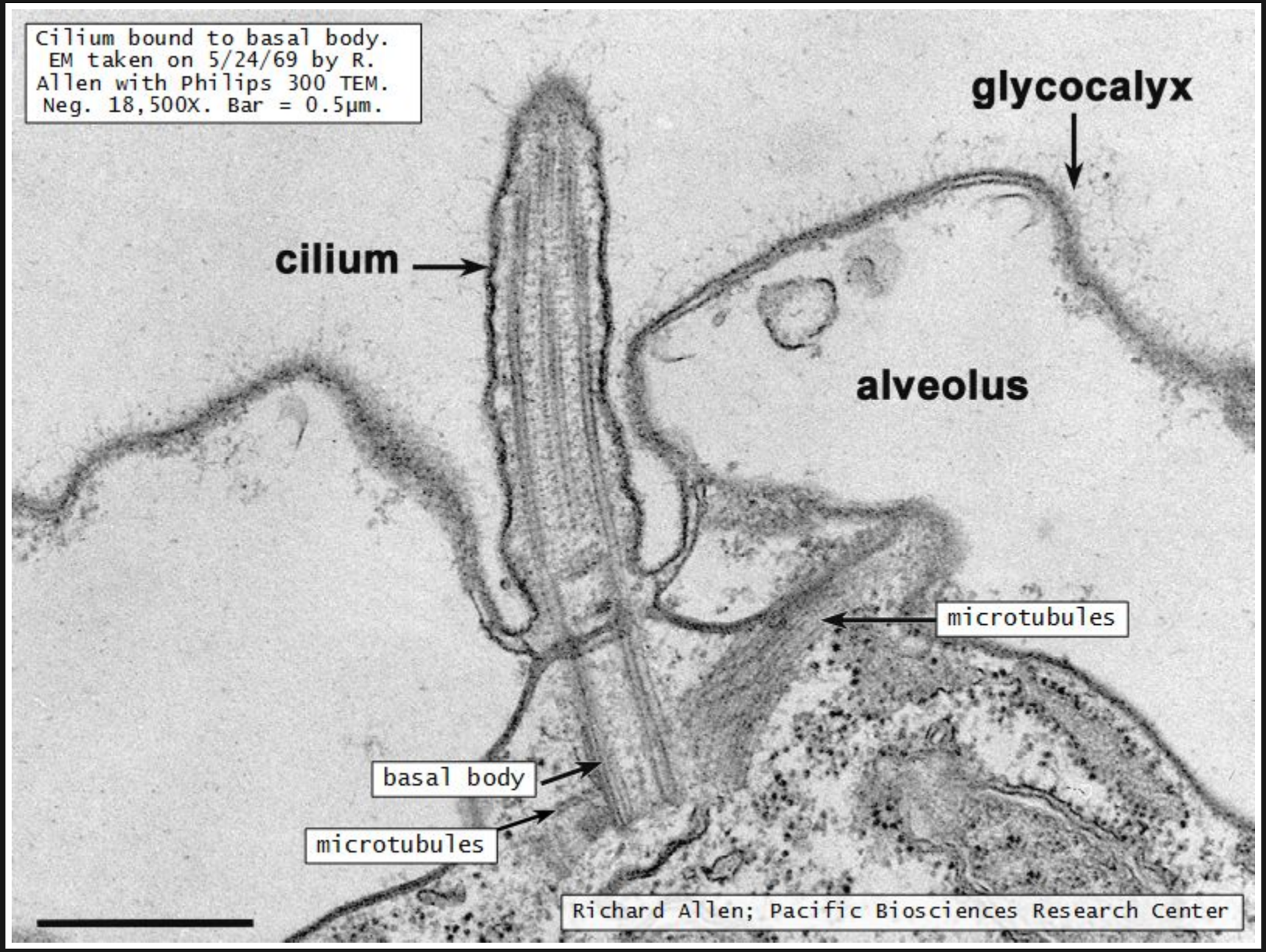
The sliding of these microtubules relative to each other causes a flagellum to bend.

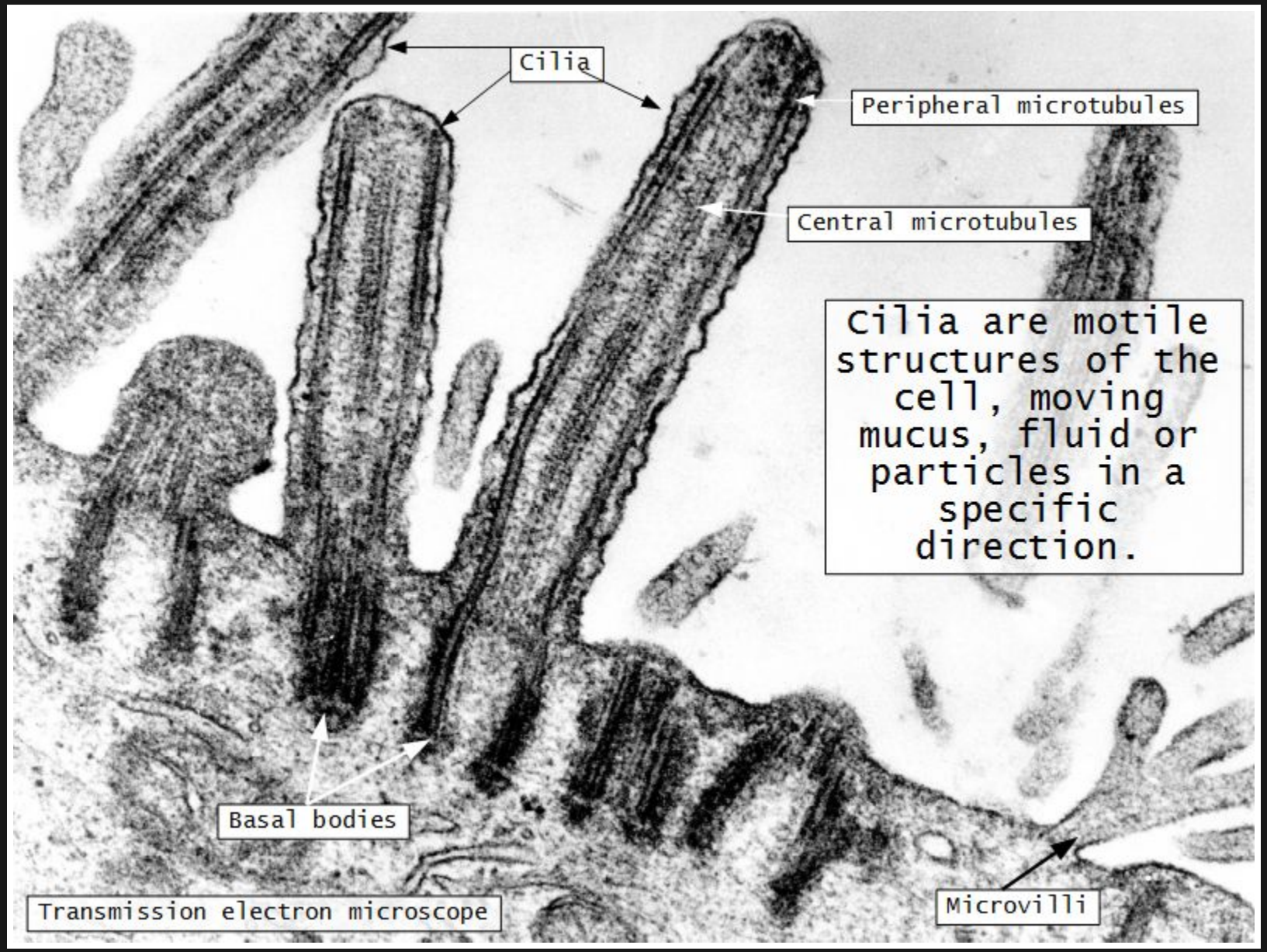




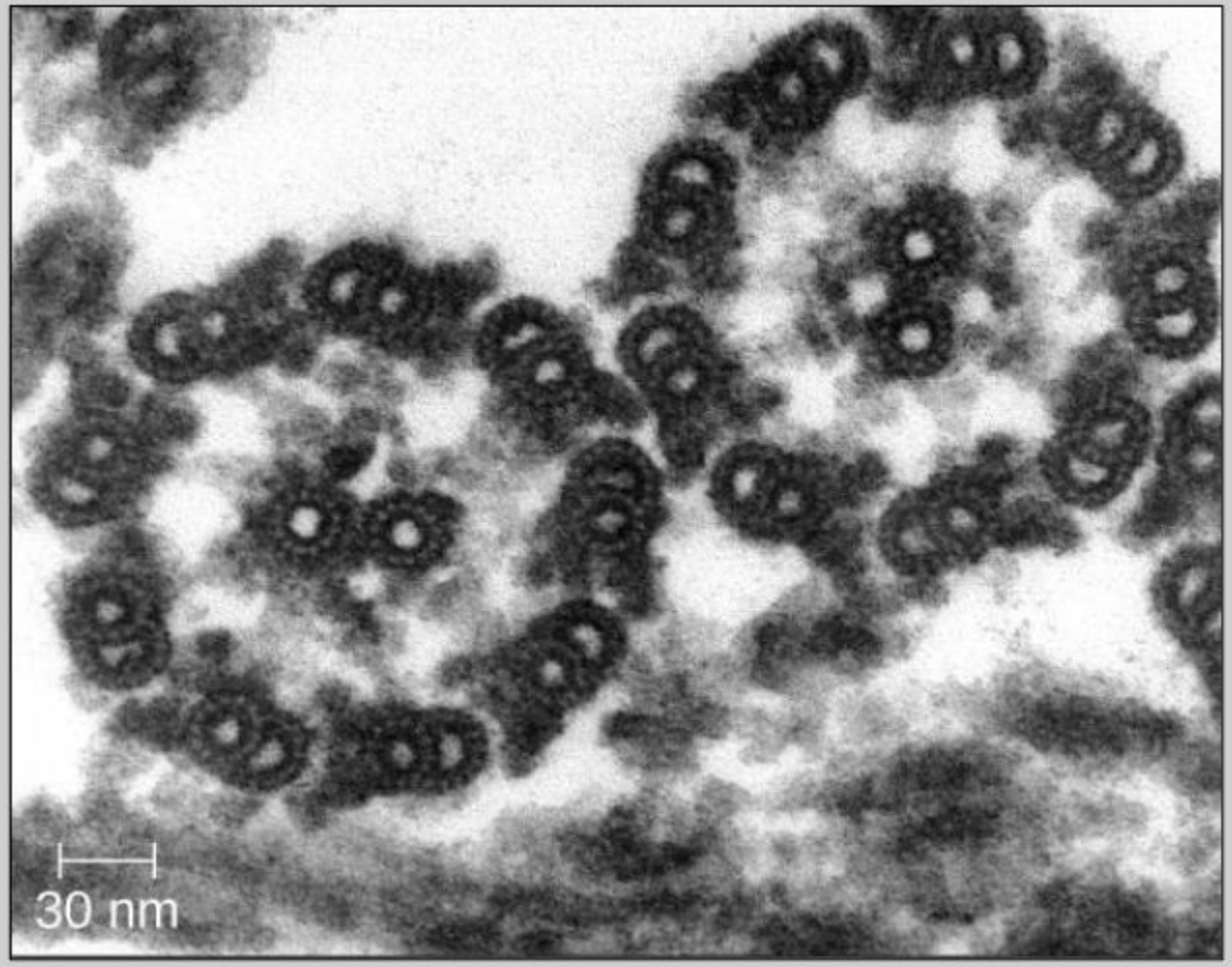

central bridge
central singlet microtubules
plasma membrane
outer dynein
inner dynein
nexin
spoke head
radial Spoke
subfiber B
subfiber A
triplet centriole
basal body

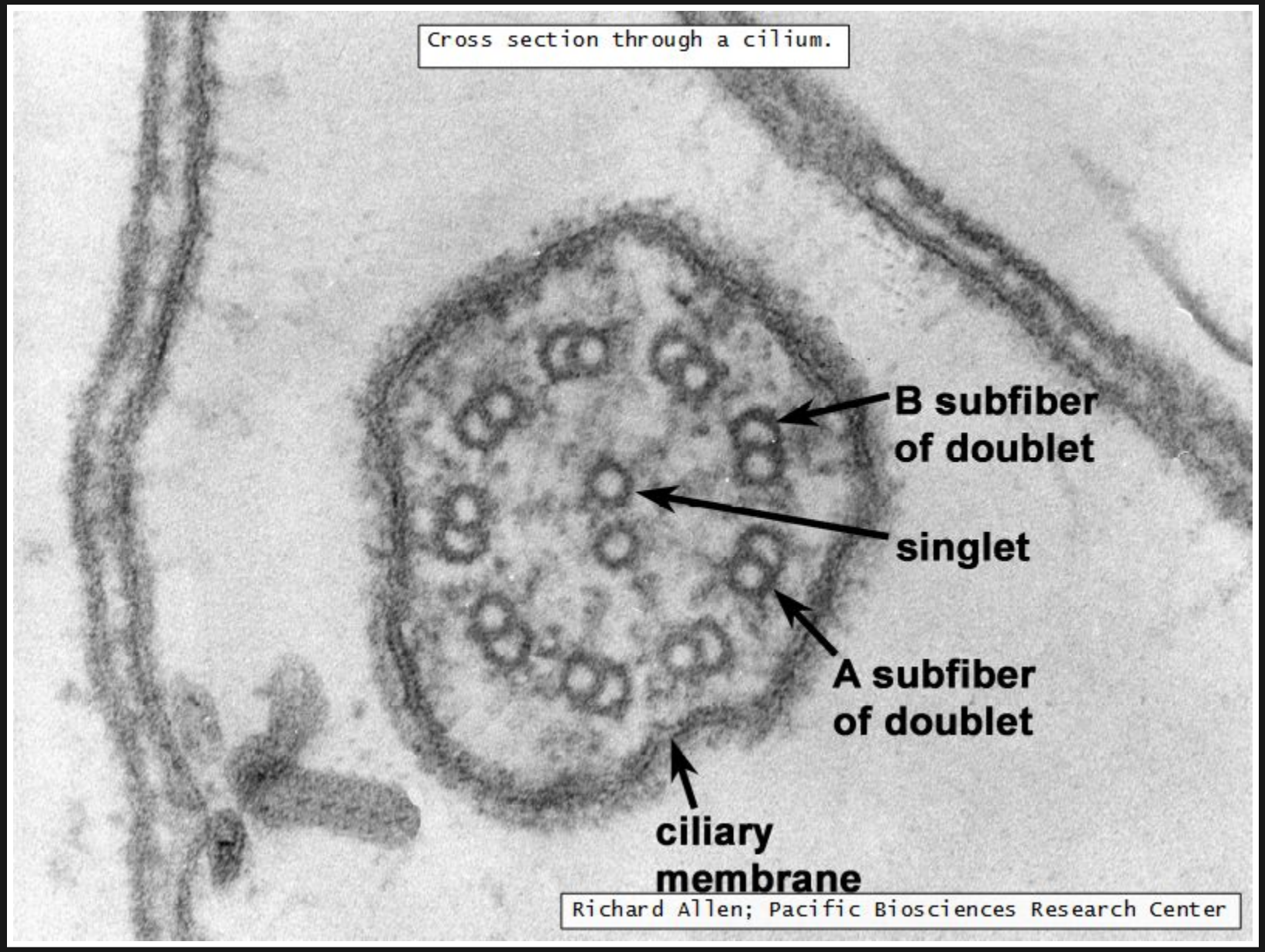



Cilium bound to basal body.
EM taken on 5/24/69 by R.
Allen with Philips 300 TEM.
Neg. 18,500X. Bar = 0.5µm.
glycocalyx
cilium
alveolus
microtubules
basal body
microtubules
Richard Allen; Pacific Biosciences Research Center


Cilia
Peripheral microtubules
Central microtubules
Cilia are motile structures of the cell, moving mucus, fluid or particles in a specific direction.
Basal bodies
Transmission electron microscope
Microvilli

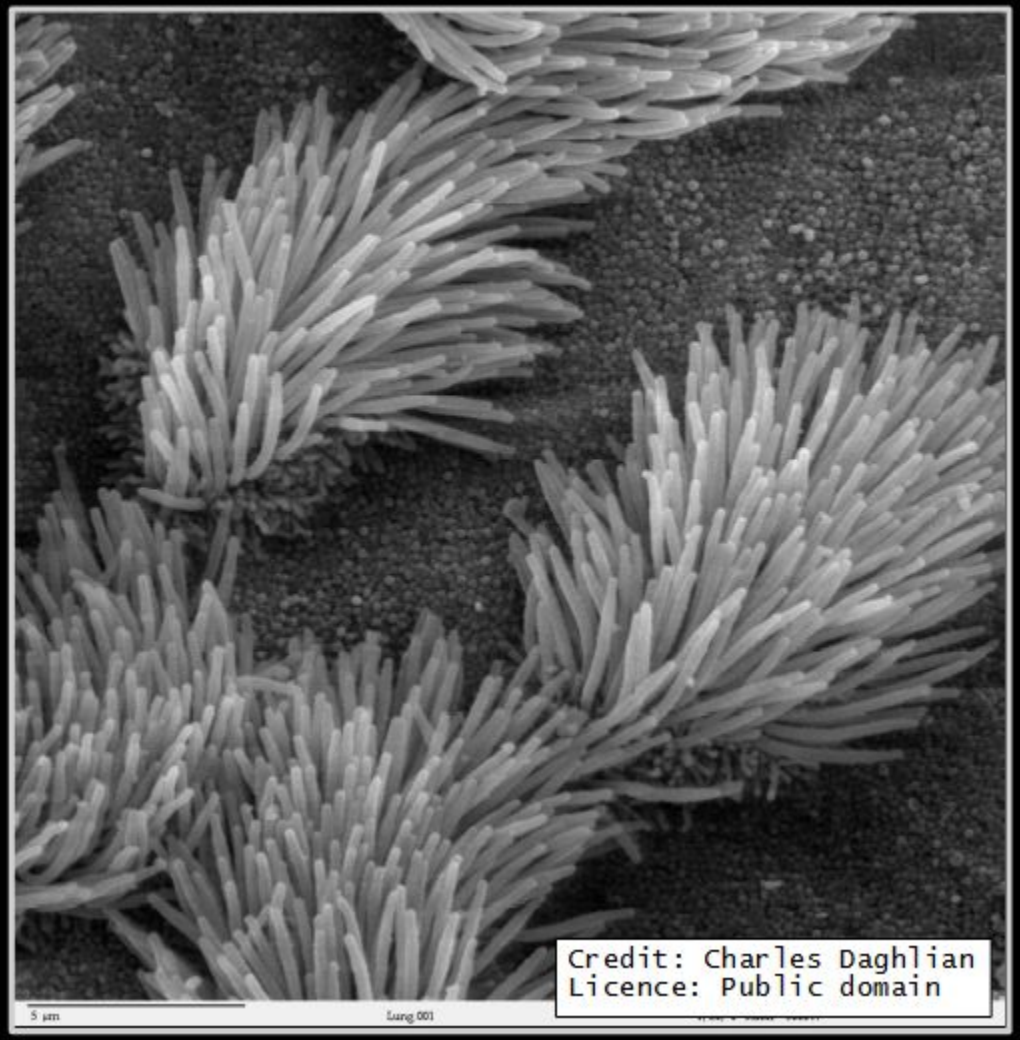
Eukaryotic flagella and cilia are composed of a 9+2 array of microtubules, as seen in this transmission electron micrograph cross-section.



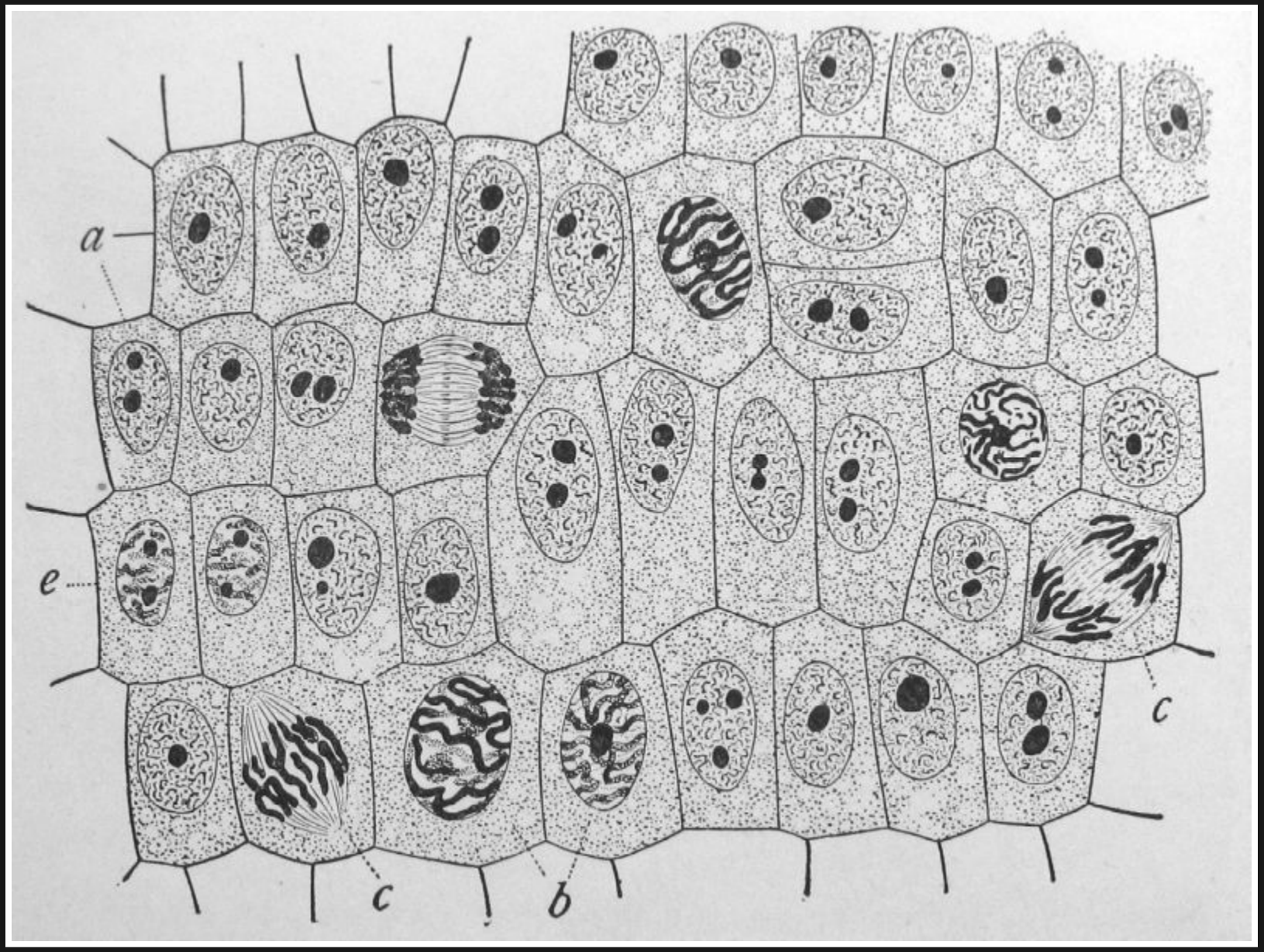

Cross section through a cilium.
B subfiber of doublet
singlet
A subfiber of doublet
ciliary membrane
Richard Allen; Pacific Biosciences Research Center


Cross section through a cilium
Peripheral microtubule doublet
Cilium
Central microtubule pair
Transmission electron microscope

Scanning electron microscope image of lung trachea epithelium.
There are both ciliated & non-ciliated cells in this epithelium. Note the difference in size between the cilia & microvilli (on the non-ciliated cell surface).

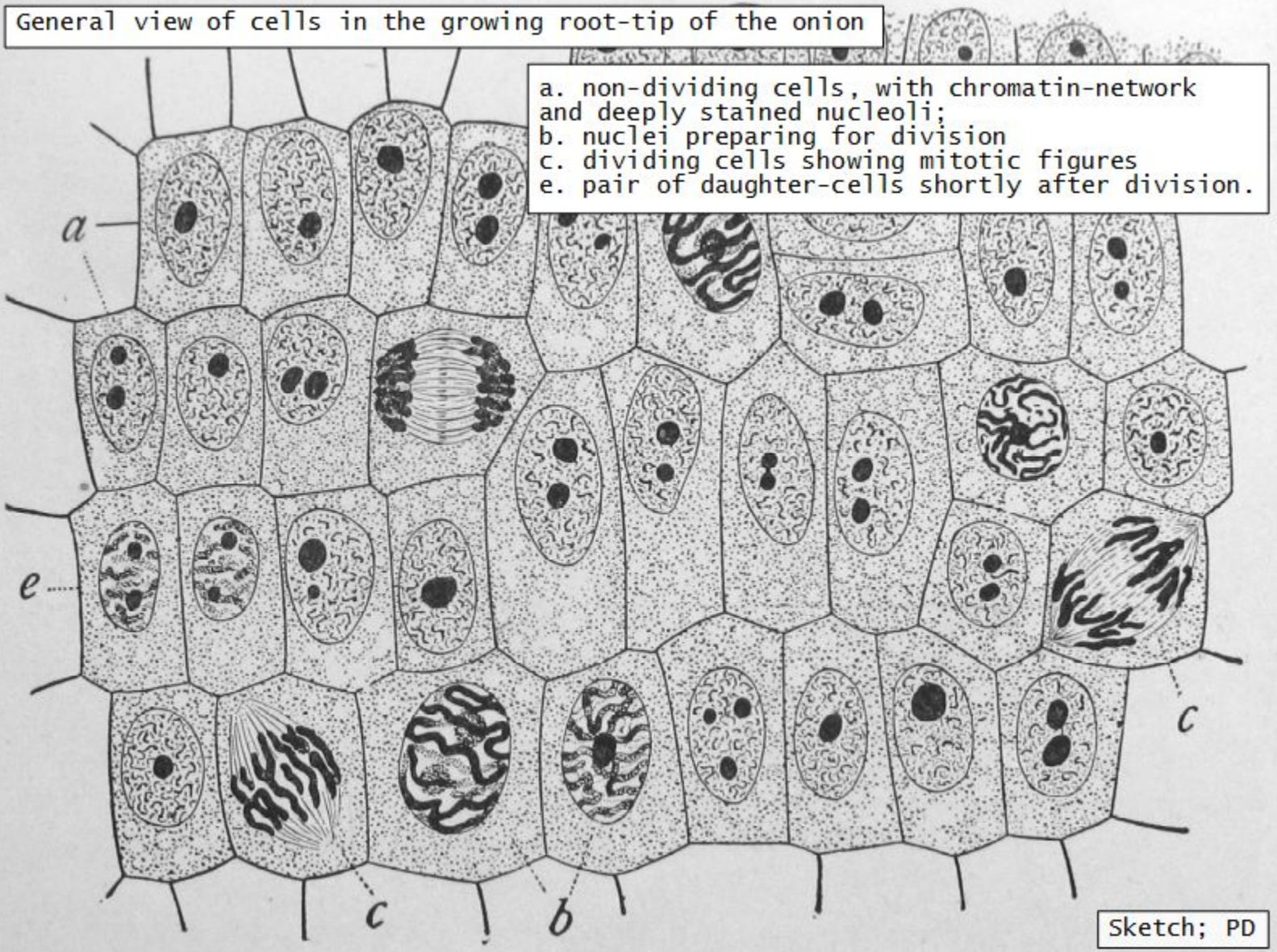


Credit: Charles Daghlian
Licence: Public domain


a
e
c
b
c

General view of cells in the growing root-tip of the onion

a. non-dividing cells, with chromatin-network and deeply stained nucleoli;
b. nuclei preparing for division
c. dividing cells showing mitotic figures
e. pair of daughter-cells shortly after division.

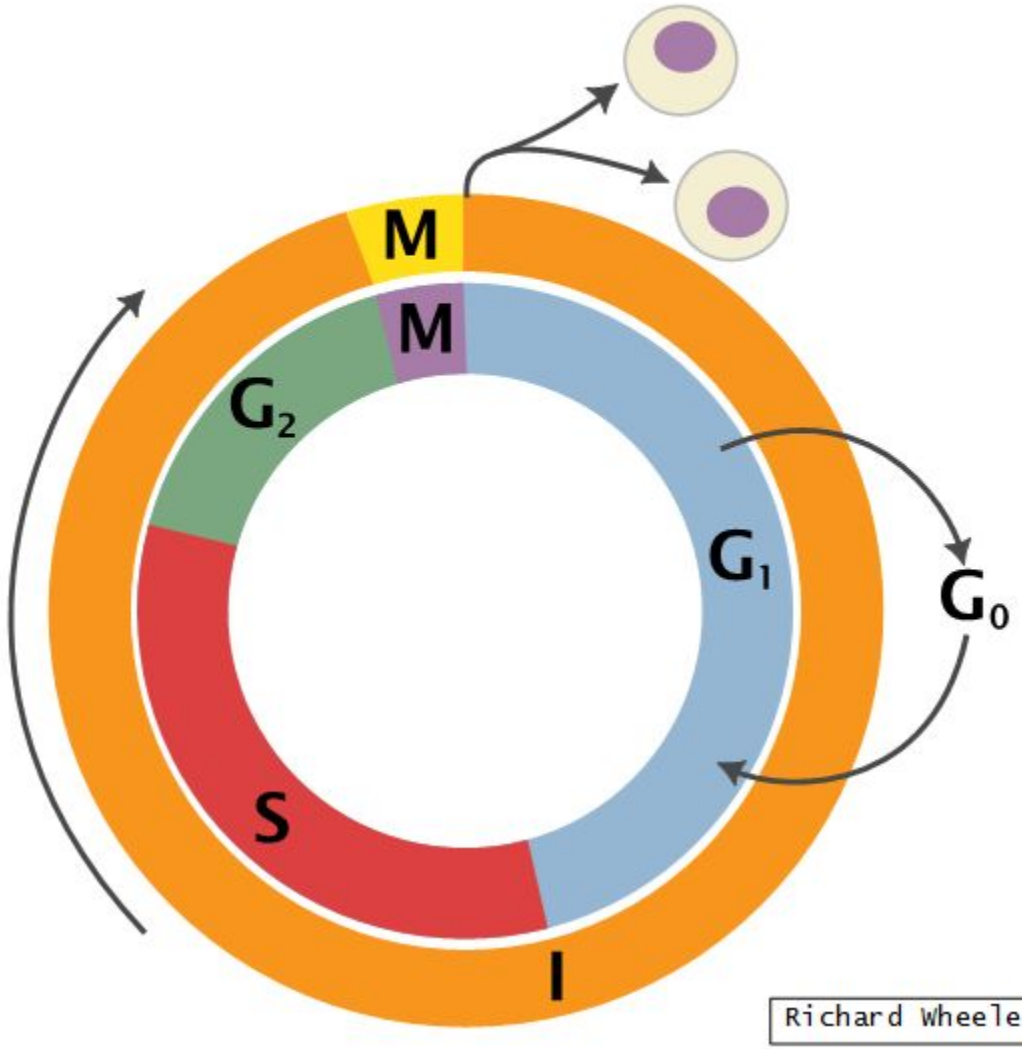


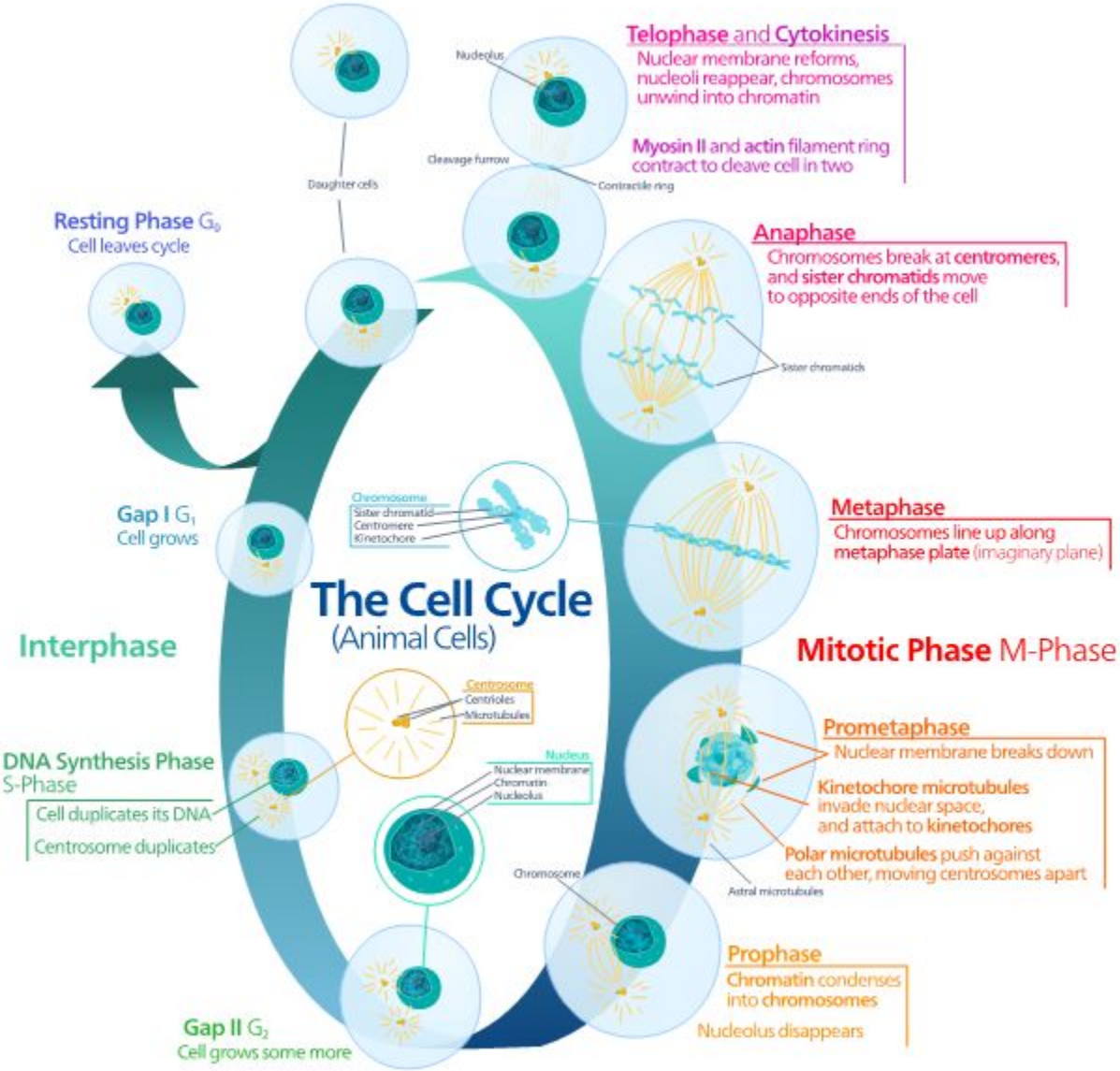
Sketch; PD

Cell cycle

- Consists of two main states and four phases
- Interphase
    - Gap 1: cell increase in size, prepare for DNA synthesis
    - Synthesis: DNA replication
    - Gap 2: continue growth; prepare for division
- Cell division
    - Mitosis: growth stop; division into daughter cells
- Resting = Gap 0
    - Cell left the cycle and stopped dividing

Schematic representation of the cell cycle. Outer ring: I = Interphase, M = Mitosis; inner ring: M = Mitosis, G1 = Gap 1, G2 = Gap 2, S = Synthesis; not in ring: G0 = Gap 0/Resting

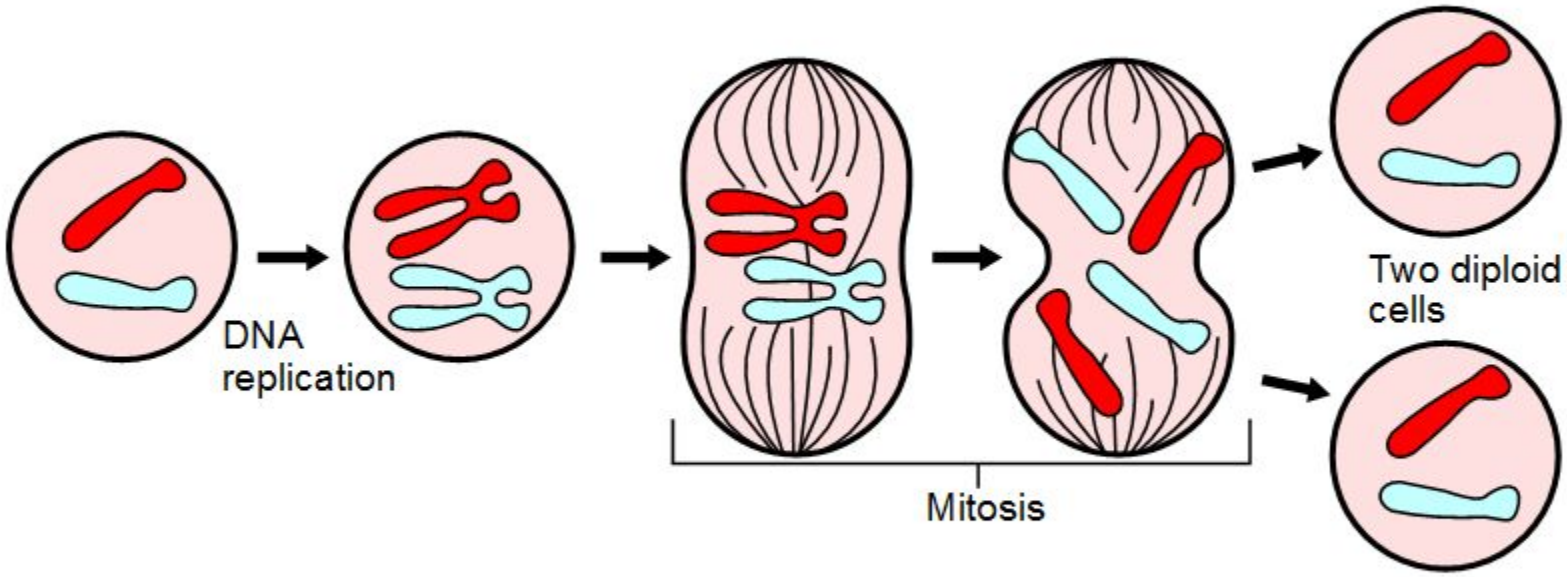



Telophase and Cytokinesis
Nuclear membrane reforms, nucleoli reappear, chromosomes unwind into chromatin
Myosin II and actin filament ring contract to cleave cell in two
Nucleolus
Cleavage furrow
Contractile ring
Daughter cells
Resting Phase G0
Cell leaves cycle
Anaphase
Chromosomes break at centromeres, and sister chromatids move to opposite ends of the cell
Sister chromatids
Chromosome
Sister chromatid
Centromere
Kinetochore
Gap I G1
Cell grows
Metaphase
Chromosomes line up along metaphase plate (imaginary plane)
The Cell Cycle
(Animal Cells)
Interphase
Mitotic Phase M-Phase
Centrosome
Centrioles
Microtubules
Prometaphase
Nuclear membrane breaks down
Kinetochore microtubules invade nuclear space, and attach to kinetochores
Polar microtubules push against each other, moving centrosomes apart
Astral microtubules
DNA Synthesis Phase
S-Phase
Cell duplicates its DNA
Centrosome duplicates
Nucleus
Nuclear membrane
Chromatin
Nucleolus
Chromosome
Prophase
Chromatin condenses into chromosomes
Nucleolus disappears
Gap II G2
Cell grows some more

Cell division

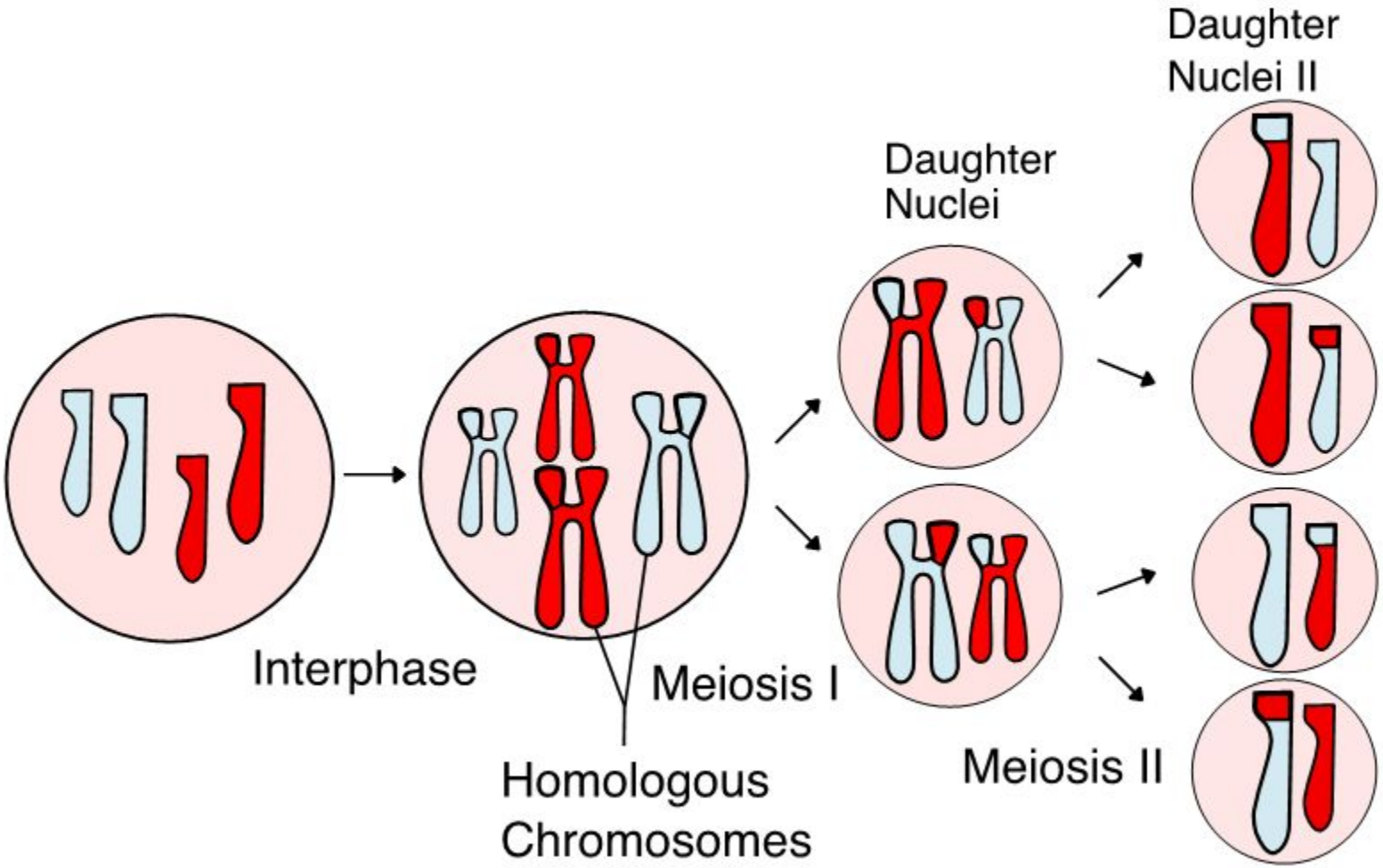
- Mitosis
  - Prophase
  - Metaphase
  - Anaphase
  - Telophase
  - Replicated chromosomes separated into 2 new nuclei
  - 2 identical diploid cells
- Meiosis
  - Cell division used to produce sperm or egg cells
  - Two rounds of division
  - 4 haploid cells

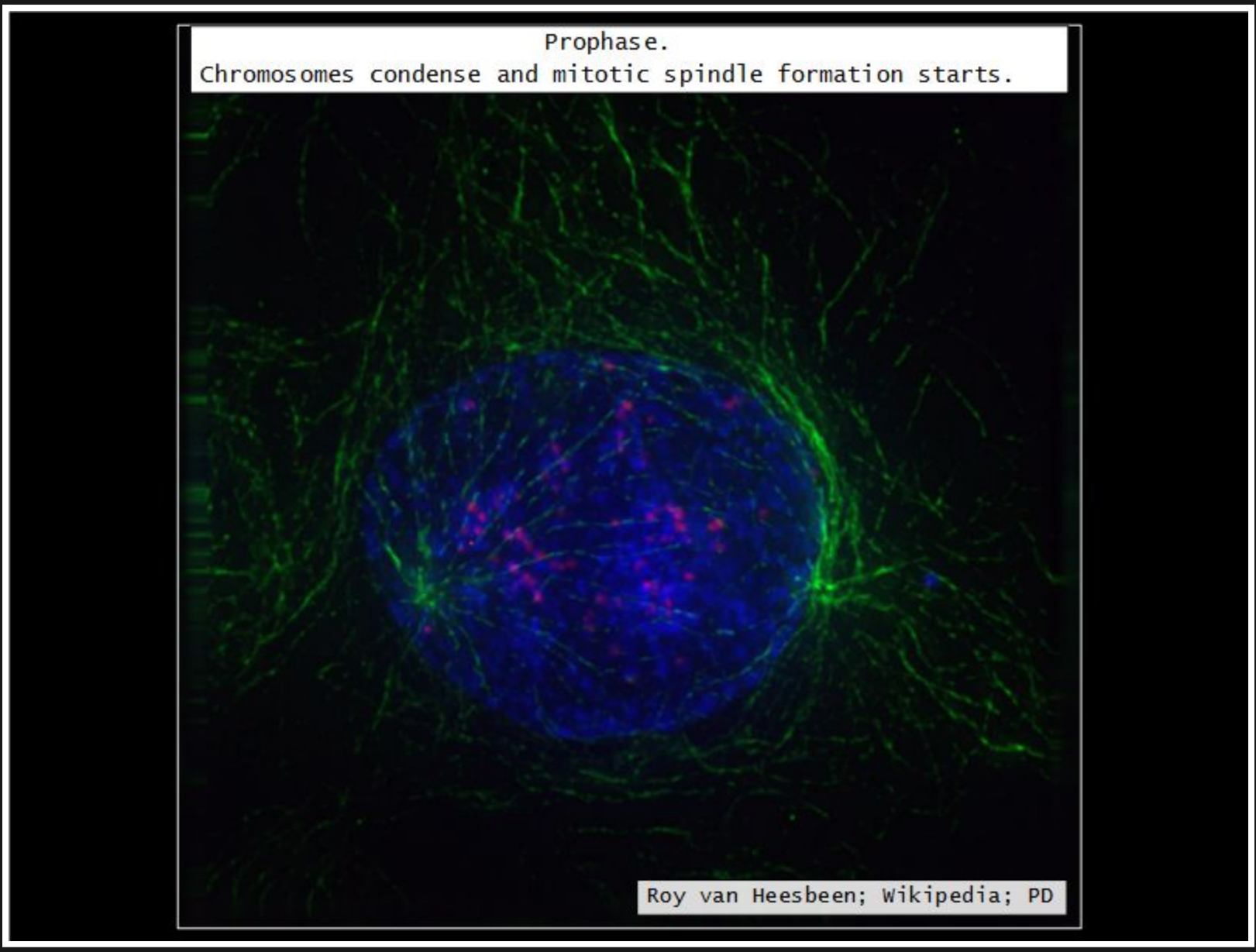
Major events in mitosis.

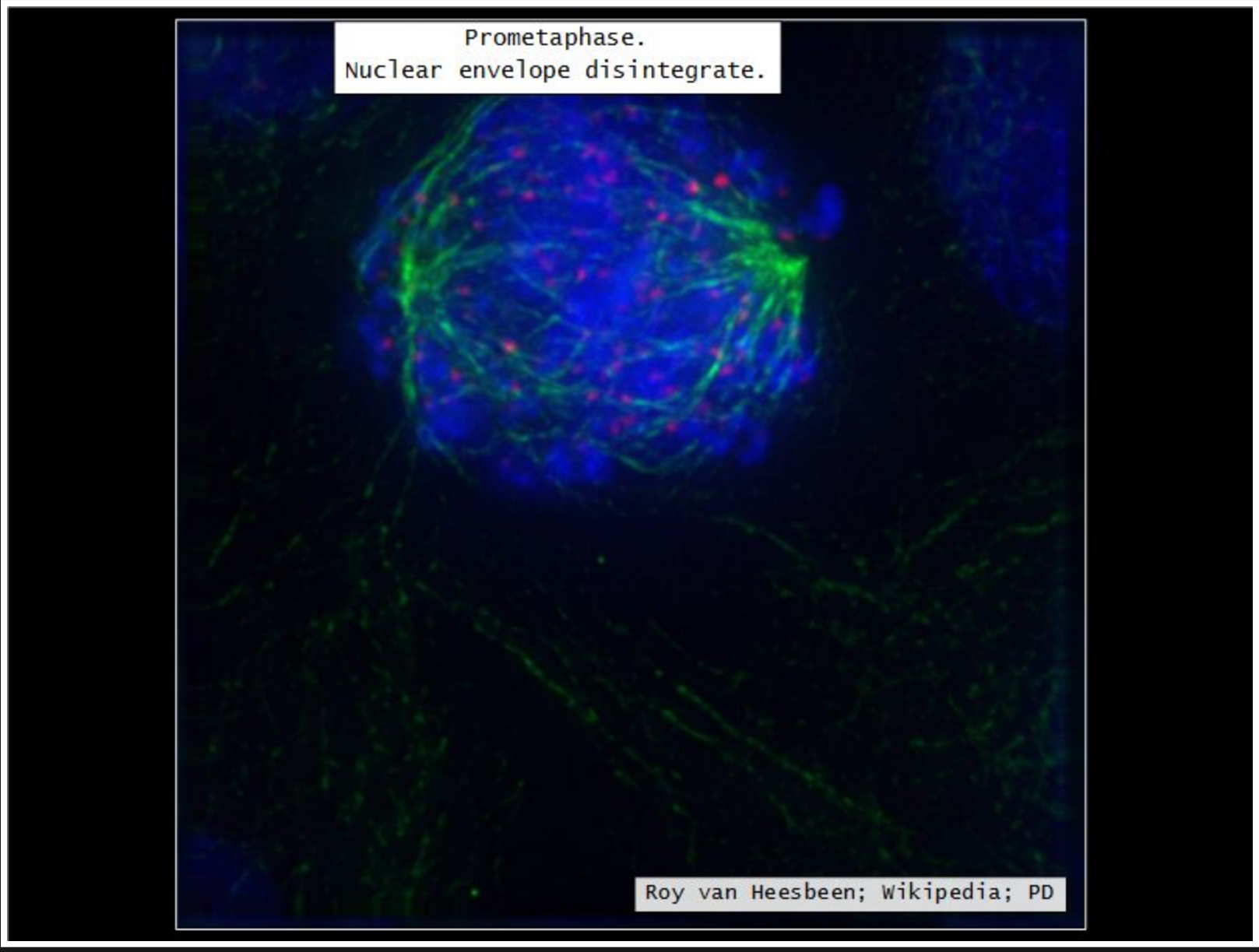


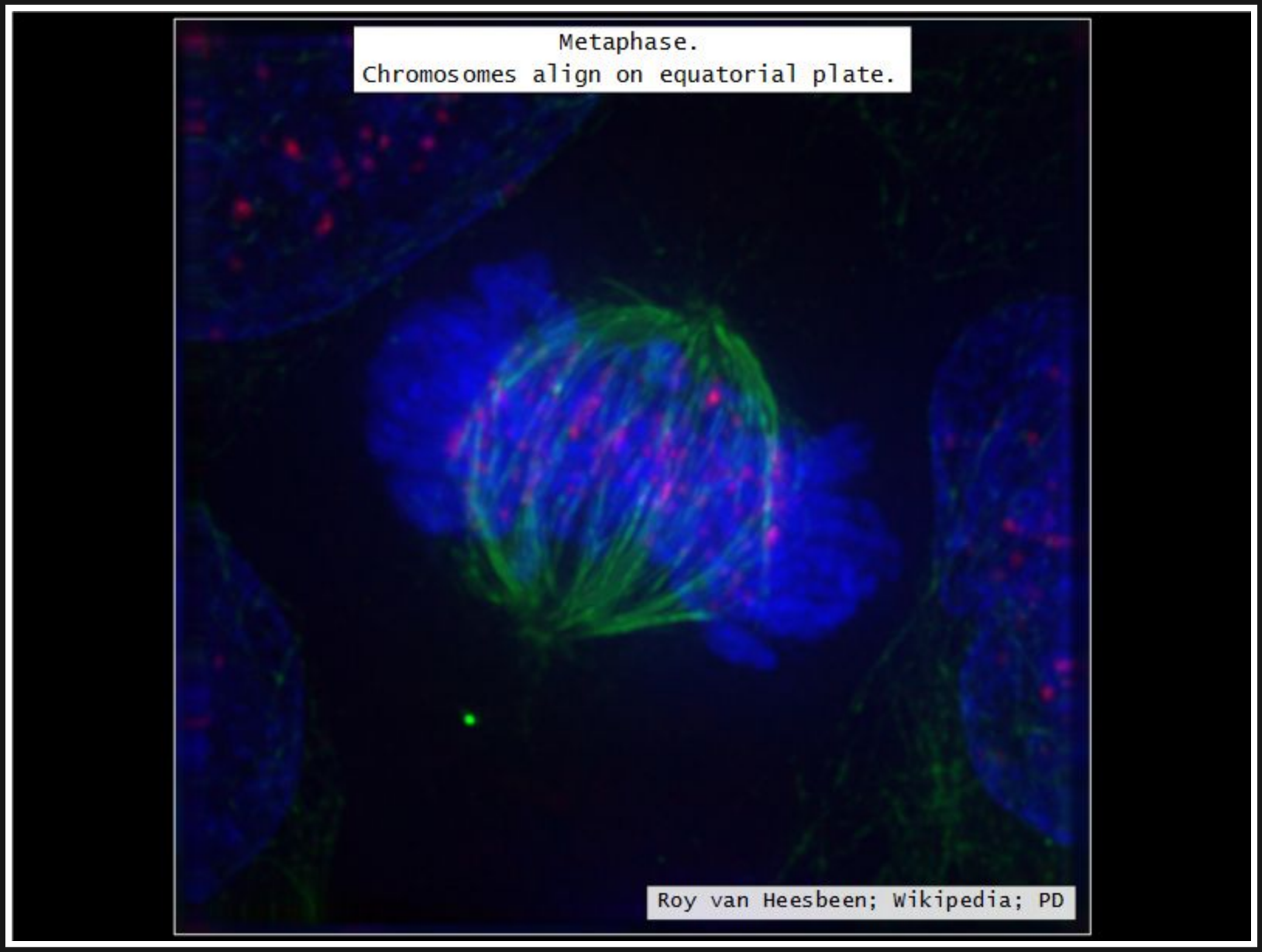
NCBI; PD

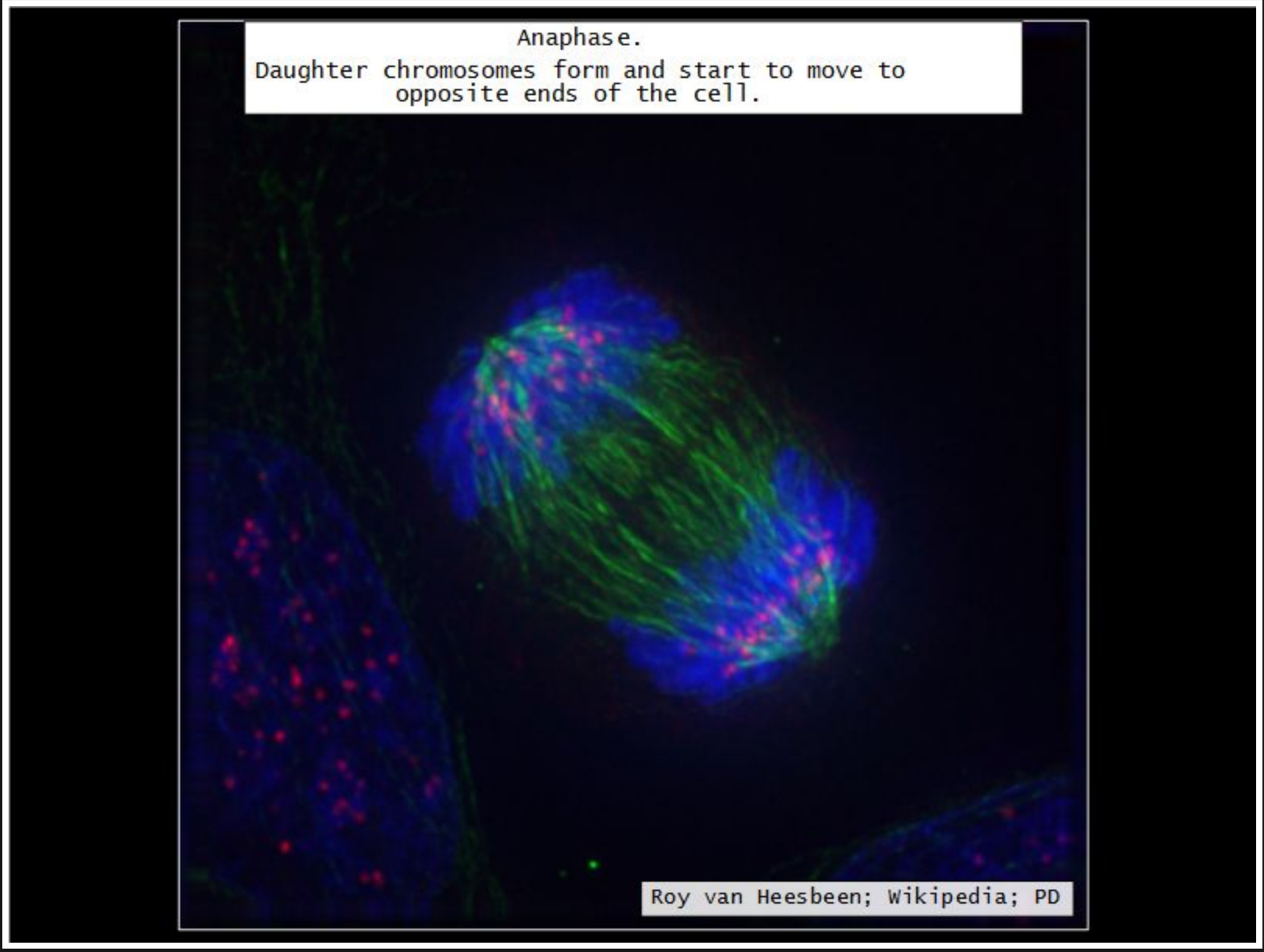
Overview of Meiosis.

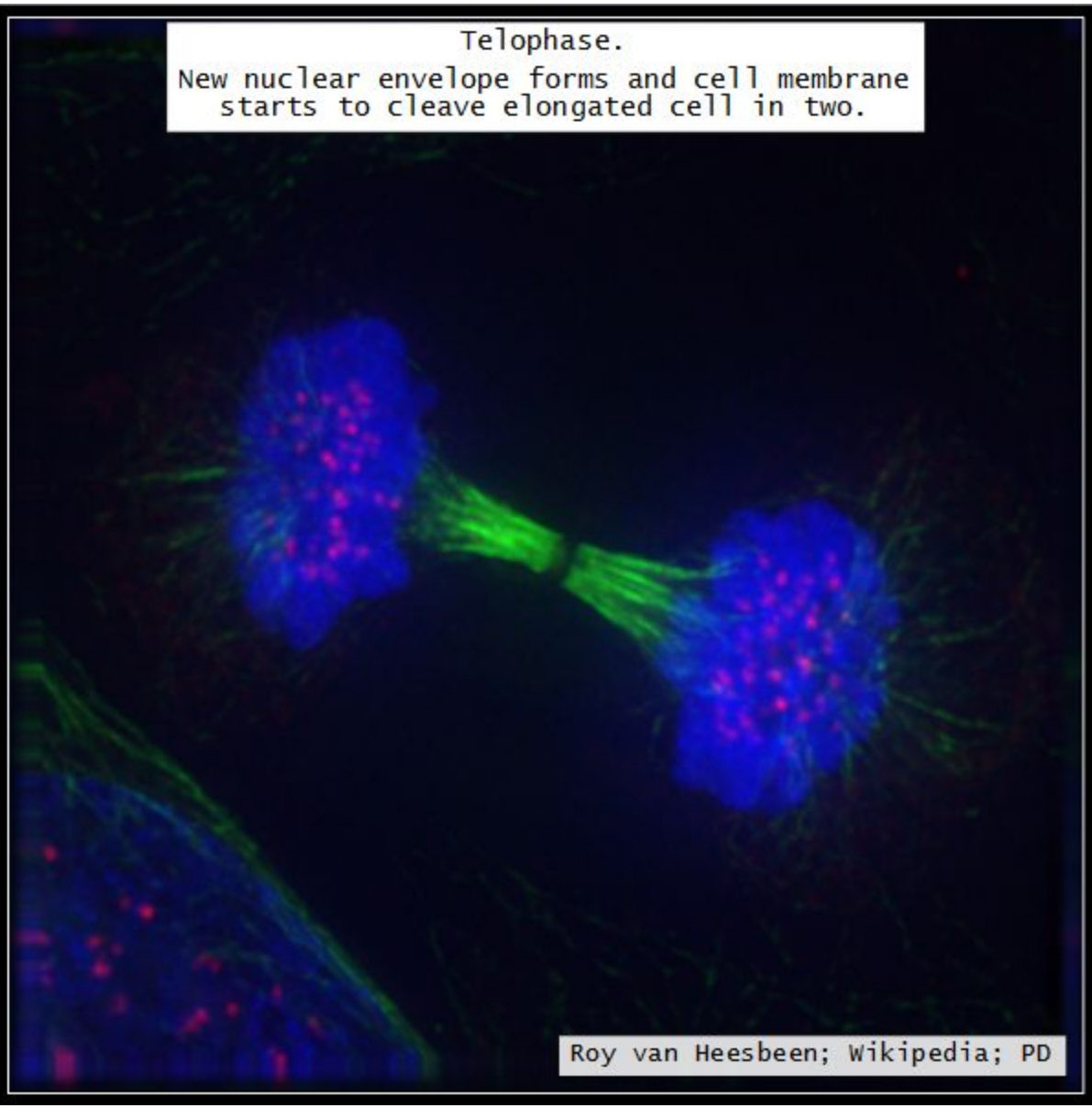



Prophase.
Chromosomes condense and mitotic spindle formation starts.
Roy van Heesbeen; Wikipedia; PD

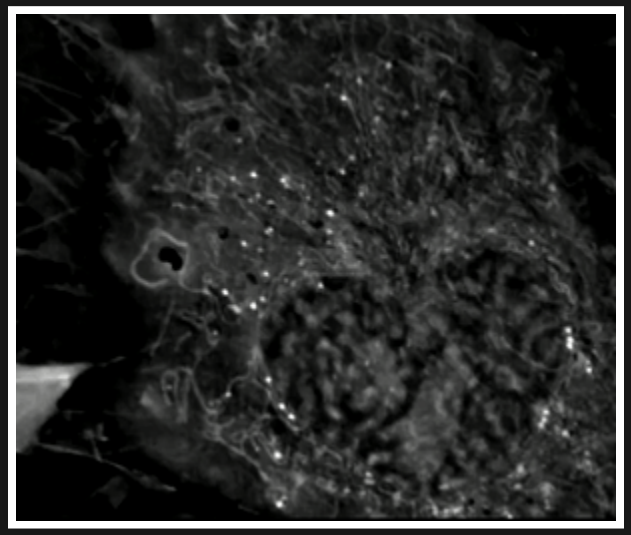

Prometaphase.
Nuclear envelope disintegrate.
Roy van Heesbeen; Wikipedia; PD


Metaphase.
Chromosomes align on equatorial plate.
Roy van Heesbeen; Wikipedia; PD

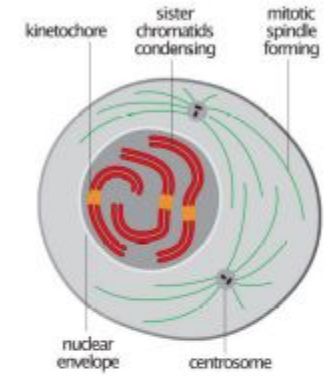

Anaphase.
Daughter chromosomes form and start to move to opposite ends of the cell.
Roy van Heesbeen; Wikipedia; PD

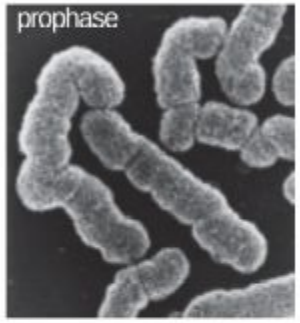

Telophase.
New nuclear envelope forms and cell membrane starts to cleave elongated cell in two.
Roy van Heesbeen; Wikipedia; PD

Mesenchymal stem cells undergoing mitosis.

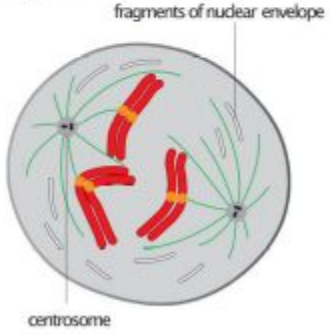


Prophase



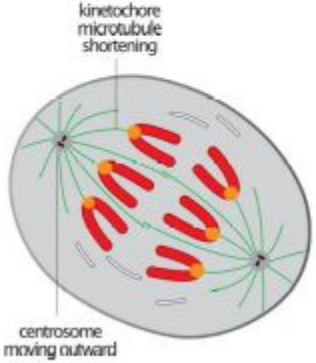


Prometaphase

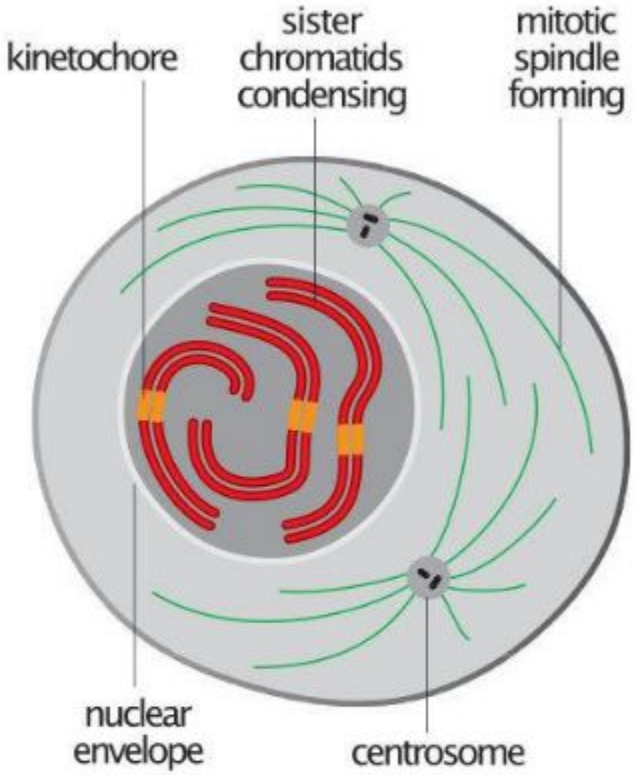


Metaphase

Anaphase

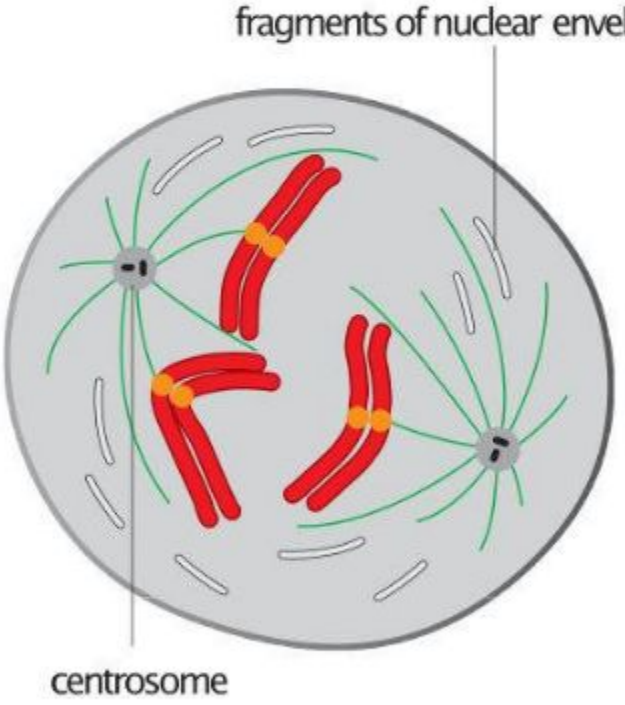


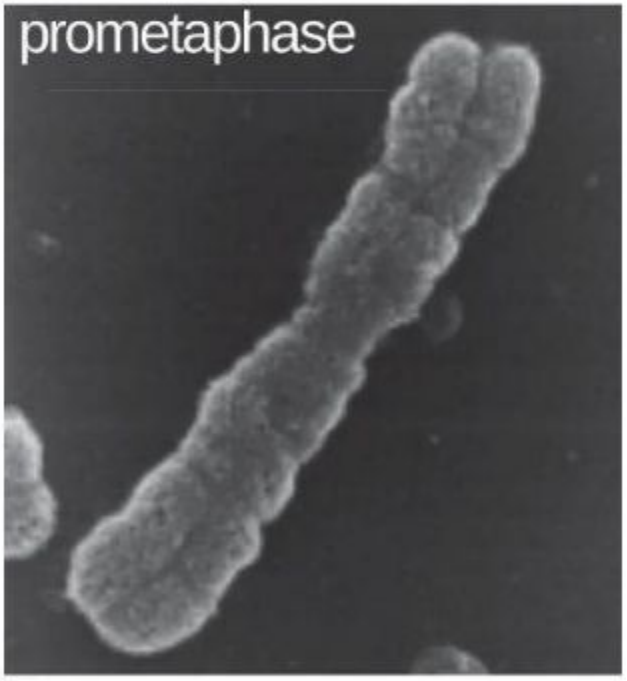
Prophase

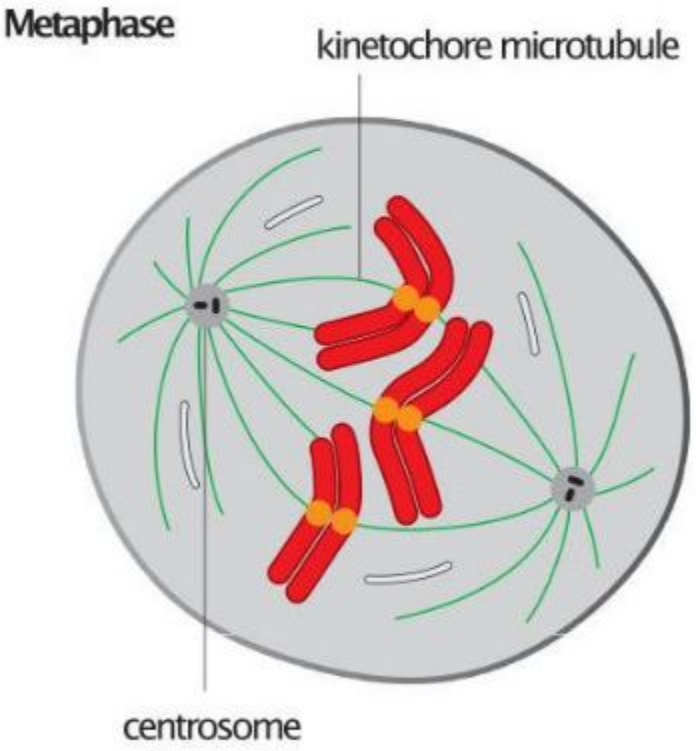

kinetochore
sister chromatids condensing
mitotic spindle forming
nuclear envelope
centrosome

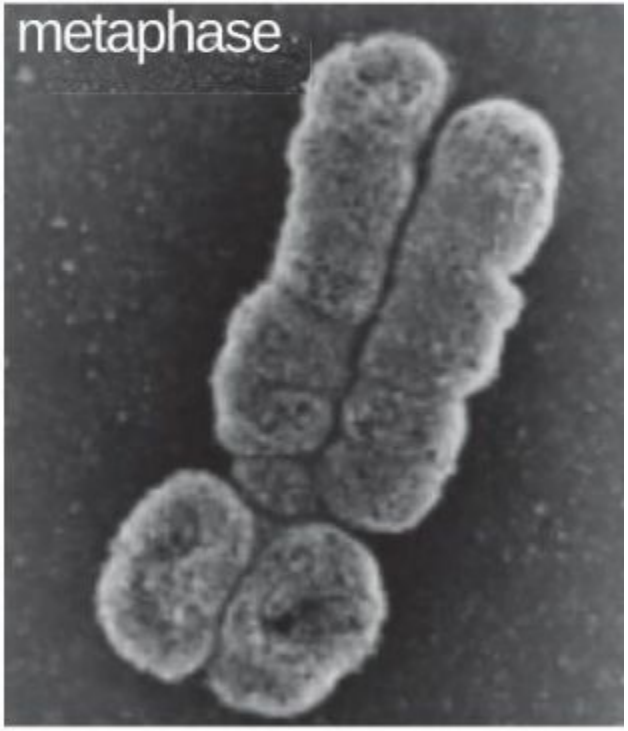

prophase

Prometaphase

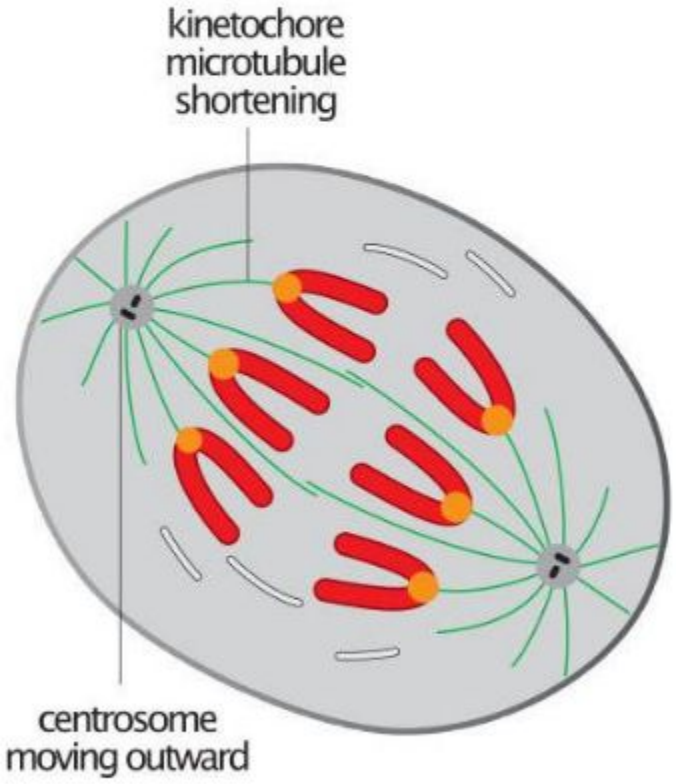


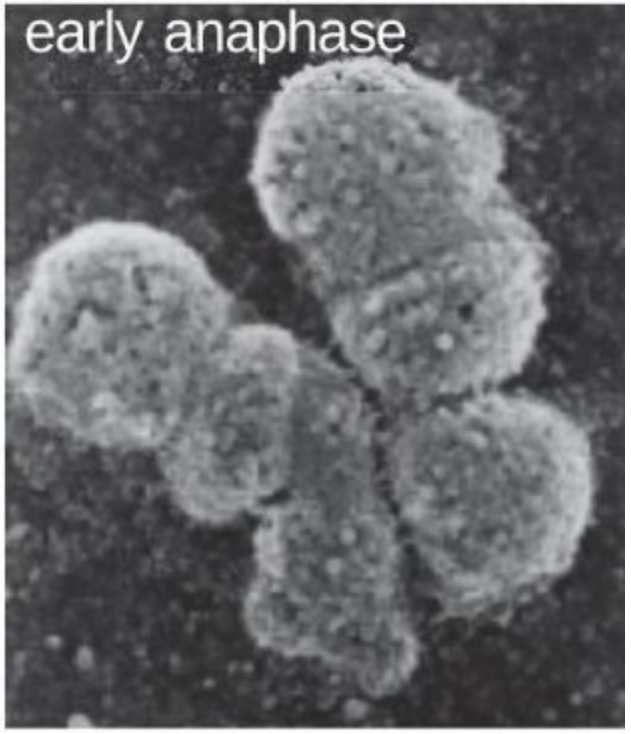


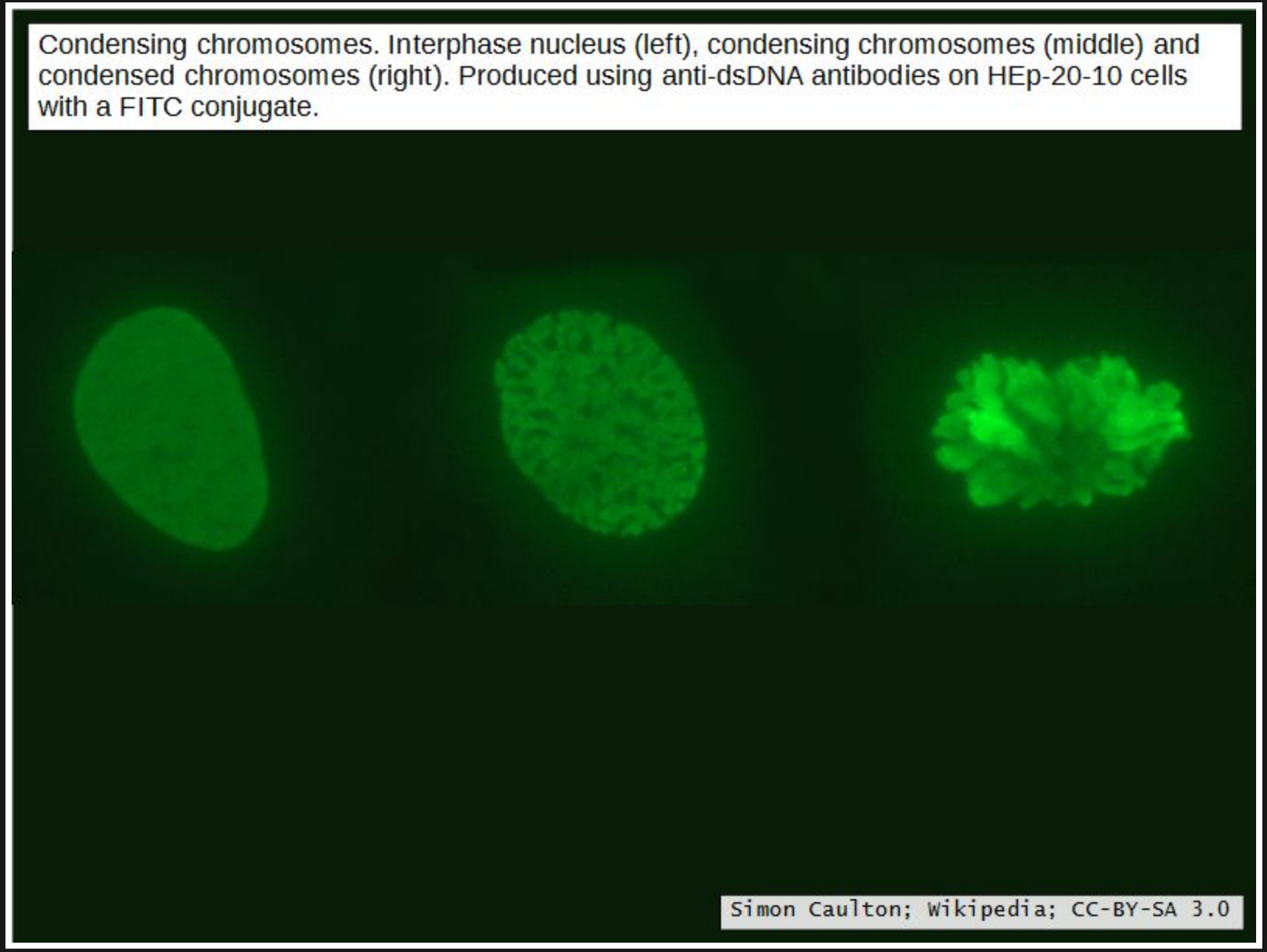

Metaphase
kinetochore microtubule
centrosome


metaphase

Anaphase


kinetochore
microtubule
shortening
centrosome
moving outward


early anaphase


Condensing chromosomes. Interphase nucleus (left), condensing chromosomes (middle) and condensed chromosomes (right). Produced using anti-dsDNA antibodies on HEp-20-10 cells with a FITC conjugate.
Simon Caulton; Wikipedia; CC-BY-SA 3.0

Chromosomes and SARS-CoV-2

- The major genetic risk factor for severe COVID-19 is inherited from Neandertals
  - https://www.biorxiv.org/content/10.1101/2020.07.03.186296v1.fu
- Neanderthals and Covid-19, beyond the hype
  - https://medium.com/@johnhawks/neanderthals-and-covid-19-beyond-the-hype-c258dc8bc2c9

The End

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