Cytophysiology · Lab 1

Organelles under the electron microscope

When	Monday 5 October 2026, 12:00–14:15
Room	A5/018
Teacher	dr hab. prof. UR Sabina Galiniak
Group	Lab group 2
Same day	Lecture 1, 08:00–09:30, A5/4: Membranes, transport, junctions, signalling

What the lab covers

Organelles under the electron microscope. The syllabus lists the cell membrane, mitochondria, SER, RER, lysosome and peroxisome.

How it is graded

- Recognising cell structures on electron micrographs
- Using the light microscope
- A correctly completed exercise book (Wawrzyniak A., Histology Exercise Notebook, University of Rzeszów 2021)
- Attendance
- Activity

The course's final test is 20 single-choice questions, 60 s each.

Bring: the exercise notebook (it is graded) and pencils

In this pack

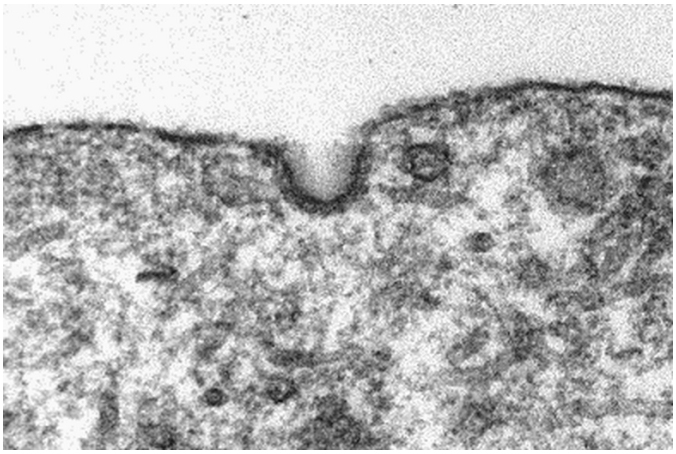
1	Recognising structures on electron micrographs (12)	page 2
2	Practice figures: name each numbered structure (20)	page 9
3	Key points	page 29
4	Light-microscope checklist	page 31
5	Self-test: 20 single-choice questions	page 32
	Answers: practice figures	page 34
	Answers: self-test	page 35

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1 · Recognising structures on electron micrographs

Each structure as the Slide Box shows it: its electron micrographs, how to recognise it, and what not to confuse it with. Test yourself online: medicine.kazimiri.com/semester-1/slides/?lab=9&m=test

Cell membrane · błona komórkowa



The cell membrane at the free (luminal) surface of the embryonic mouse brain (TEM): a thin dark line bounding the cytoplasm, with a pit dipping in where a pinocytotic vesicle forms.

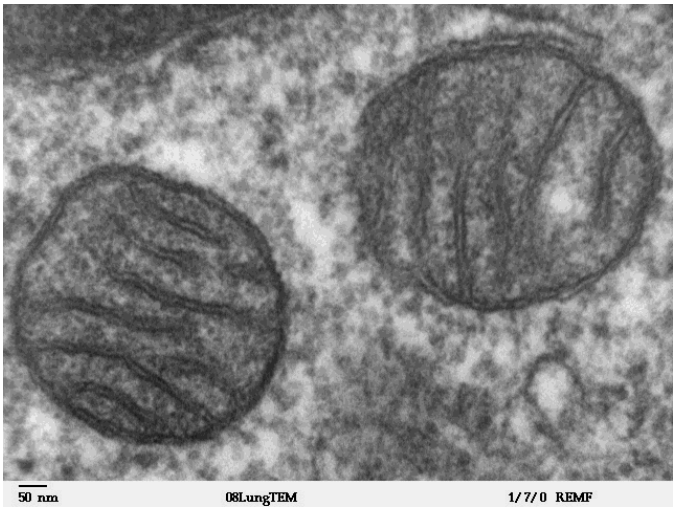
Louisa Howard, Miguel Marin-Padilla (Dartmouth Electron Microscope Facility) · Public domain · commons.wikimedia.org/wiki/File:Junctional_complex_and_pinocytotic_vesicles_-_embryonic_brain-TEM.jpg

How to recognise it

- The cell's outer boundary: at ordinary EM magnifications a thin, dark, continuous line.
- At very high power it is trilaminar, the "unit membrane" about 7.5-10 nm thick: two dark lines with a pale line between.
- Its specialisations show it best: microvilli and pits with pinocytotic vesicles at the free surface, junctions where neighbouring cells meet.

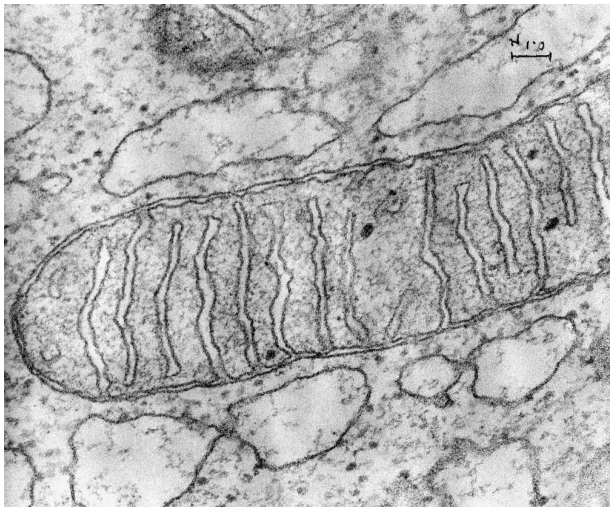
Don't confuse with: The nuclear envelope: two membranes with a perinuclear space and pores. The ER and the Golgi: membranes inside the cell.

Mitochondria · mitochondria



Two mitochondria (TEM, mammalian lung): a double membrane, the inner one folded into shelf-like cristae.

Louisa Howard · Public domain · commons.wikimedia.org/wiki/File:Mitochondria,_mammalian_lung_-_TEM.jpg



A mitochondrion cut along its length (TEM, guinea pig pancreas): the outer membrane, the inner membrane folded into shelf-like cristae, and the matrix between them.

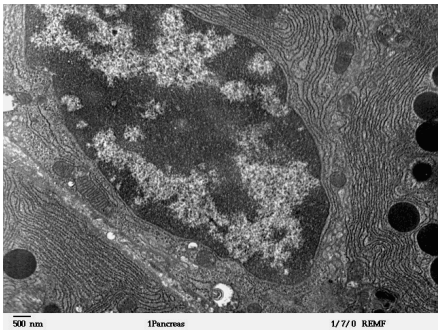
George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37199

How to recognise it

- Oval profiles about 0.5-1 µm across, bounded by two membranes.
- The inner membrane folds into cristae (usually shelf-like), in a dense matrix.
- Plentiful where much ATP is made: muscle, kidney tubules, parietal cells.

Don't confuse with: Lysosomes: a single membrane, dense contents, no cristae.

Rough endoplasmic reticulum · siateczka śródplazmatyczna szorstka



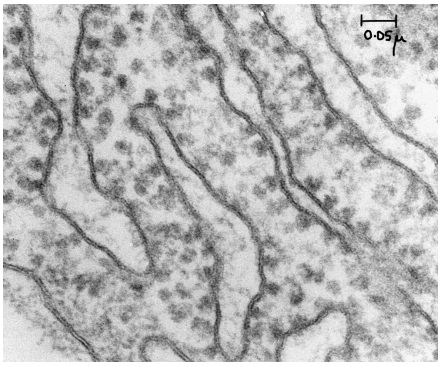
A pancreatic acinar cell (TEM): the nucleus, long parallel rows of rough ER, dark zymogen granules and mitochondria.

Louisa Howard · Public domain · commons.wikimedia.org/wiki/File:Pancreatic_acinar_cells_-_TEM.jpg



A nucleus (TEM, pancreatic acinar cell): the double nuclear envelope with its pores, dark heterochromatin and paler euchromatin, and rough ER outside.

Louisa Howard · Public domain · commons.wikimedia.org/wiki/File:Mammalian_pancreatic_tissue,_nuclear_pores_and_rough_endoplasmic_reticulum.jpg



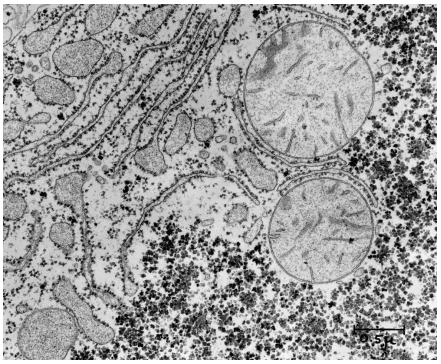
Rough endoplasmic reticulum at very high power (TEM, guinea pig pancreas): the paired membranes of flattened cisternae, studded on their cytoplasmic faces with ribosomes (once called Palade particles).

George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37230



Rough endoplasmic reticulum cut across in a fibroblast (TEM, rat heart): long cisternae lined by membrane-bound polyribosomes.

George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/40996



Rat liver (TEM): parallel cisternae of rough ER, two large mitochondria and dark rosettes of glycogen.

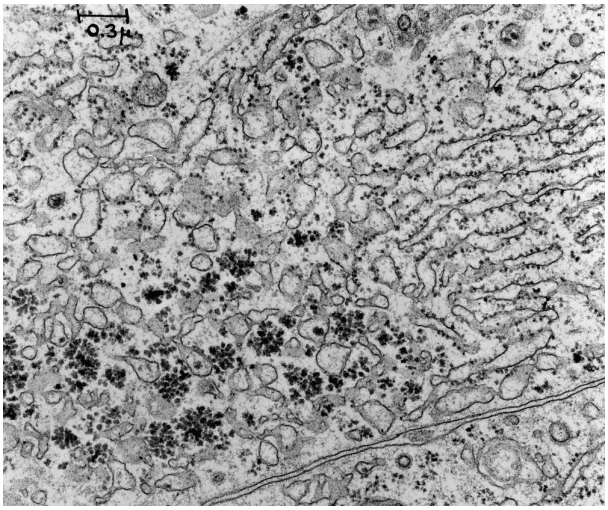
George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37189

How to recognise it

- Long, flattened cisternae in parallel rows.
- The outer surface dotted with ribosomes; continuous with the outer nuclear membrane.
- Abundant in cells that export protein: pancreatic acinar cells, plasma cells.

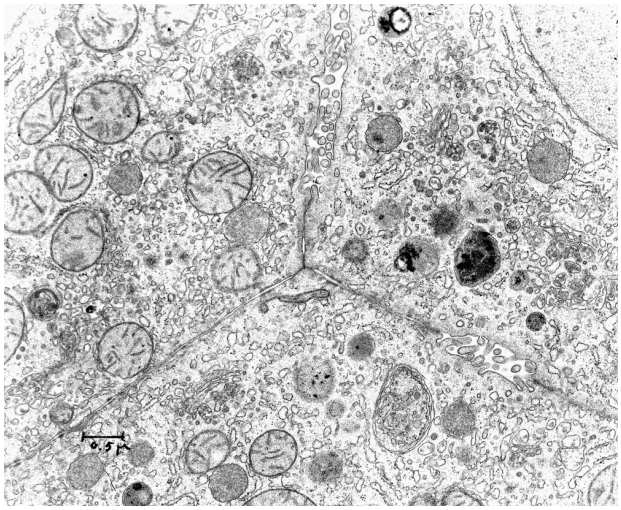
Don't confuse with: The Golgi apparatus: short, curved stacks with no ribosomes and many vesicles.

Smooth endoplasmic reticulum · siateczka śródplazmatyczna gładka



Liver of a 3-day-old rat (TEM): a network of smooth ER tubules among glycogen rosettes, and rough ER studded with ribosomes.

Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37188



Where three liver cells meet (TEM, rat): mitochondria, smooth ER and vesicles, and a bile canaliculus lined with microvilli between the cells.

Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37185

How to recognise it

- A network of branching tubules and small vesicles with no ribosomes on its membranes.
- Abundant where lipids and steroids are made or drugs detoxified: liver, adrenal cortex, Leydig cells; in muscle it is the sarcoplasmic reticulum, the calcium store.
- Often continuous with rough ER.

Don't confuse with: Rough ER: flattened, parallel cisternae with ribosomes on them. Golgi: a curved stack of cisternae with vesicles at its ends.

Golgi apparatus · aparat Golgiego



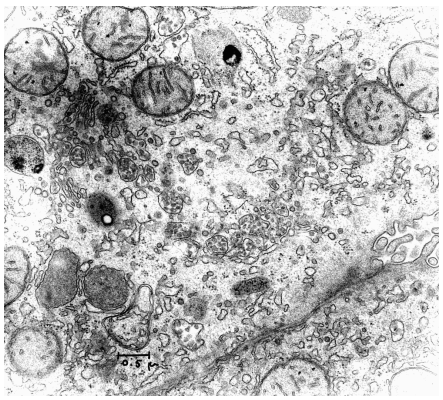
The Golgi apparatus (TEM, human leukocyte): a curved stack of flattened cisternae with small vesicles at its edges.

Louisa Howard · Public domain · commons.wikimedia.org/wiki/File:Human_leukocyte,_showing_golgi_-_TEM.jpg



A pancreatic acinar cell (TEM, guinea pig): rough ER on the left; on the right the Golgi apparatus, a curved stack of smooth cisternae among many small vesicles.

George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37239



Rat liver (TEM): the Golgi apparatus, mitochondria and many smooth ER tubules and vesicles; the junction between two liver cells crosses the lower right.

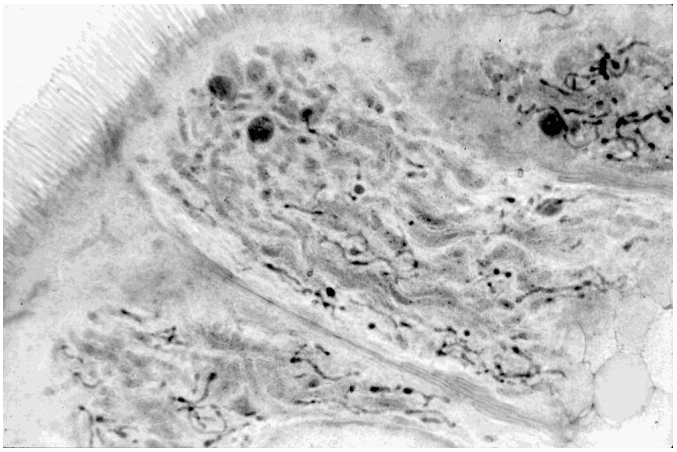
George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37186

How to recognise it

- A curved stack of 4-8 flattened, membrane-bound cisternae with no ribosomes.
- Swarms of small vesicles at the ends and faces of the stack.
- Usually beside the nucleus; cis face towards the ER, trans face towards the cell membrane.

Don't confuse with: Rough ER: longer, straighter, parallel cisternae studded with ribosomes.

Lysosomes · lizosomy



The lining of the human duodenum (EM, peroxisomes stained dark through their catalase with DAB): worm-like peroxisomes, three large round lysosomes and the brush border of microvilli.

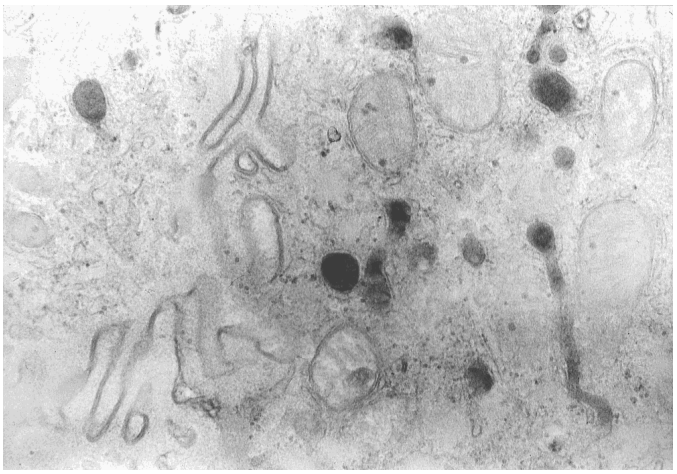
Frank Roels, Marina Pauwels, Peter Van der Spek, via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/47808

How to recognise it

- Round bodies 0.2-0.8 µm across, each bounded by a single membrane.
- Dense, often uneven contents (material being digested); no cristae and no crystalline core.
- Full of acid hydrolases; residual bodies (lipofuscin) build up with age.

Don't confuse with: Peroxisomes: a finely granular matrix, in rodents a crystalline core. Mitochondria: a double membrane with cristae.

Peroxisomes · peroksysomy



Peroxisomes in a human duodenal cell (EM, stained through their catalase with DAB): large rounded ones and thinner elongated ones.

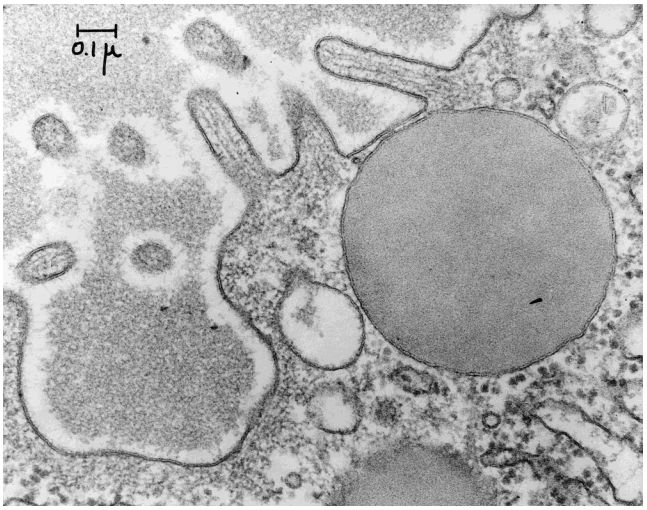
Frank Roels, Marina Pauwels, Peter Van der Spek, via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/47752

How to recognise it

- Small round or elongated bodies (0.2-1 µm) with a single membrane and a finely granular matrix.
- In rodent liver often a dense crystalline core (urate oxidase); human peroxisomes have none.
- Stain dark with DAB through their catalase, which is how they are shown here.

Don't confuse with: Lysosomes: denser, uneven contents. Mitochondria: a double membrane with cristae.

Secretory granules (exocytosis) · ziarnistości wydzielnicze (egzocytoza)



Exocytosis in the rat pancreas (TEM): a zymogen granule beside the apical membrane, and granule contents released into the acinar lumen where a granule has fused with the membrane.

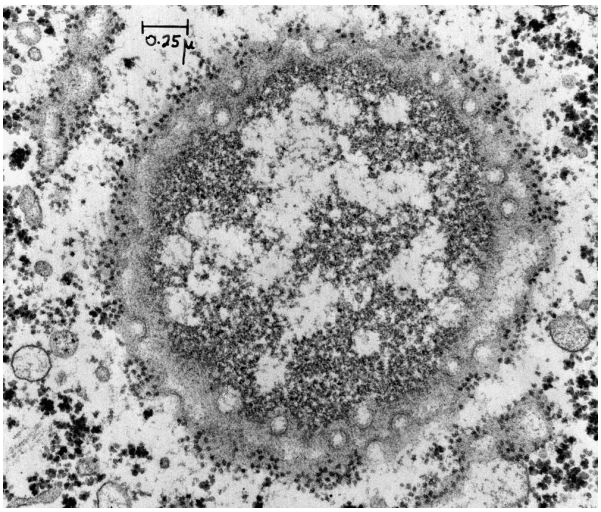
George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37141

How to recognise it

- Large round membrane-bound granules with dense, even contents, gathered towards the free (apical) surface.
- In exocytosis the granule membrane fuses with the cell membrane and opens to the lumen: an omega-shaped profile.
- Typical of pancreatic acinar (zymogen) and other gland cells.

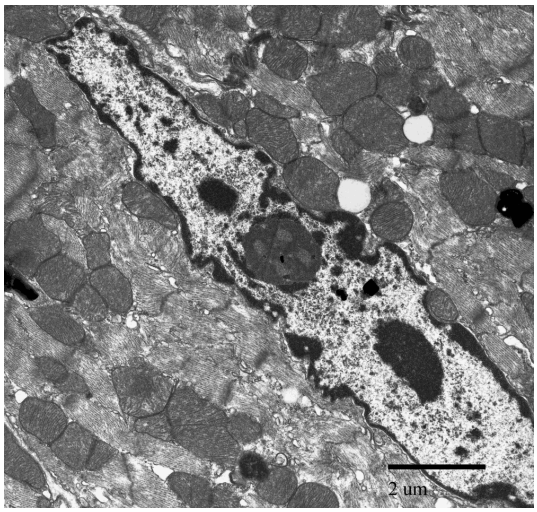
Don't confuse with: Lysosomes: smaller, with uneven contents. Lipid droplets: no membrane, homogeneous.

Nucleus: envelope, pores, nucleolus · jądro komórkowe: otoczka, pory, jąderko



A liver cell nucleus cut tangentially through its envelope (TEM, 1-day-old rat): the nuclear pores seen face-on as pale rings; glycogen rosettes in the cytoplasm around it.

George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37187



A nucleus in mouse heart muscle (TEM): its nucleolus a dense rounded mass with paler areas inside; mitochondria and myofibrils all around.

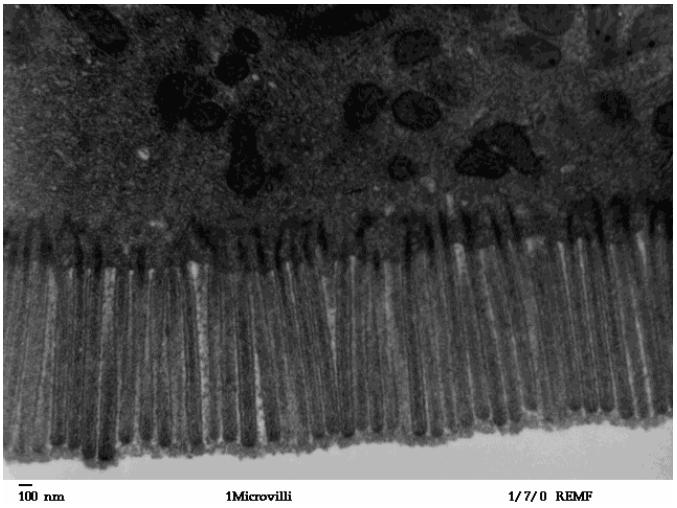
Dee Lauzon, Sue Lancelle, Marian Rice (Mount Holyoke College), via the Cell Image Library · Public domain · cellimagelibrary.org/images/39755

How to recognise it

- The largest organelle, bounded by two membranes (the nuclear envelope) with the perinuclear space between them.
- Nuclear pores break the envelope; seen face-on they are pale rings.
- Heterochromatin dark against the envelope, euchromatin pale; the nucleolus a dense rounded mass.

Don't confuse with: A secretory granule or lipid droplet: homogeneous, with no envelope, pores or nucleolus.

Microvilli (brush border) · mikrokosmki (rąbek szczoteczkowy)



Microvilli of a jejunal absorptive cell (TEM): tightly packed, finger-like projections, each with a core of actin filaments.

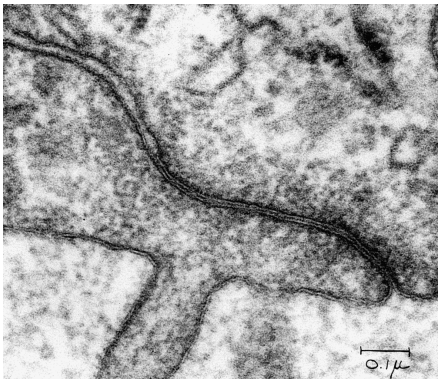
Louisa Howard, Katherine Connollly · Public domain · commons.wikimedia.org/wiki/File:Human_jejunum_microvilli_1_-_TEM.jpg

How to recognise it

- Tightly packed, finger-like projections of the apical cell membrane, all about the same length.
- A core of actin filaments running down into the terminal web.
- On absorptive cells: small intestine, kidney proximal tubule.

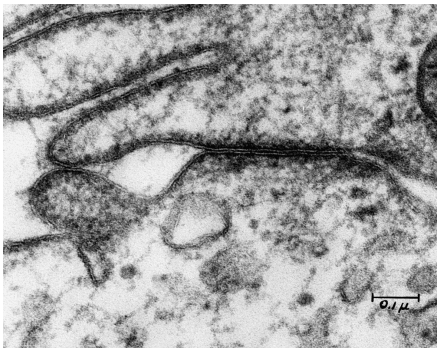
Don't confuse with: Cilia: fewer, longer, with a 9+2 microtubule core.

Tight junction · połączenie zamykające (obwódka zamykająca)



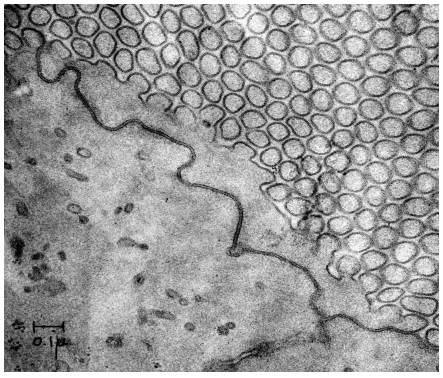
A tight junction (zonula occludens) between two thyroid cells (TEM, rat): the outer leaflets of the two cell membranes fuse, with no plaques.

Marilyn G. Farquhar; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37169



A tight junction in the distal kidney tubule (TEM, rat): the fused membranes of the junctional complex run across the middle.

Marilyn G. Farquhar; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37172



The free surface of rat intestinal cells (TEM): microvilli cut across, and a tight junction running diagonally between two cells; the three layers of the cell membrane show along the microvilli.

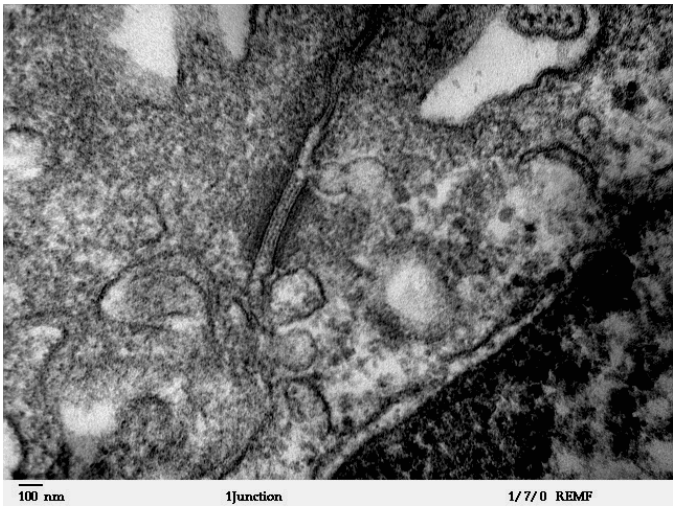
Marilyn G. Farquhar; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37170

How to recognise it

- The outer leaflets of two neighbouring cell membranes fuse at points, closing the space between the cells.
- No dense plaques on either side.
- The most apical part of the junctional complex, just deep to the free surface of an epithelium.

Don't confuse with: Desmosome: dense plaques and a 20-30 nm gap. Gap junction: a 2-4 nm gap and no fusion.

Desmosome · desmosom



A desmosome between two epithelial cells (TEM, mammalian lung): dense plaques on both membranes, a narrow gap with a line of cadherins, and filaments running into the plaques.

Louisa Howard · Public domain · commons.wikimedia.org/wiki/File:Desmosome_-_epithelial_cell_from_mammalian_lung_tissue_-_TEM.jpg



Desmosomes in frog skin (TEM): dense plaques on both membranes with filaments running into them; the upper one is cut obliquely and looks wider.

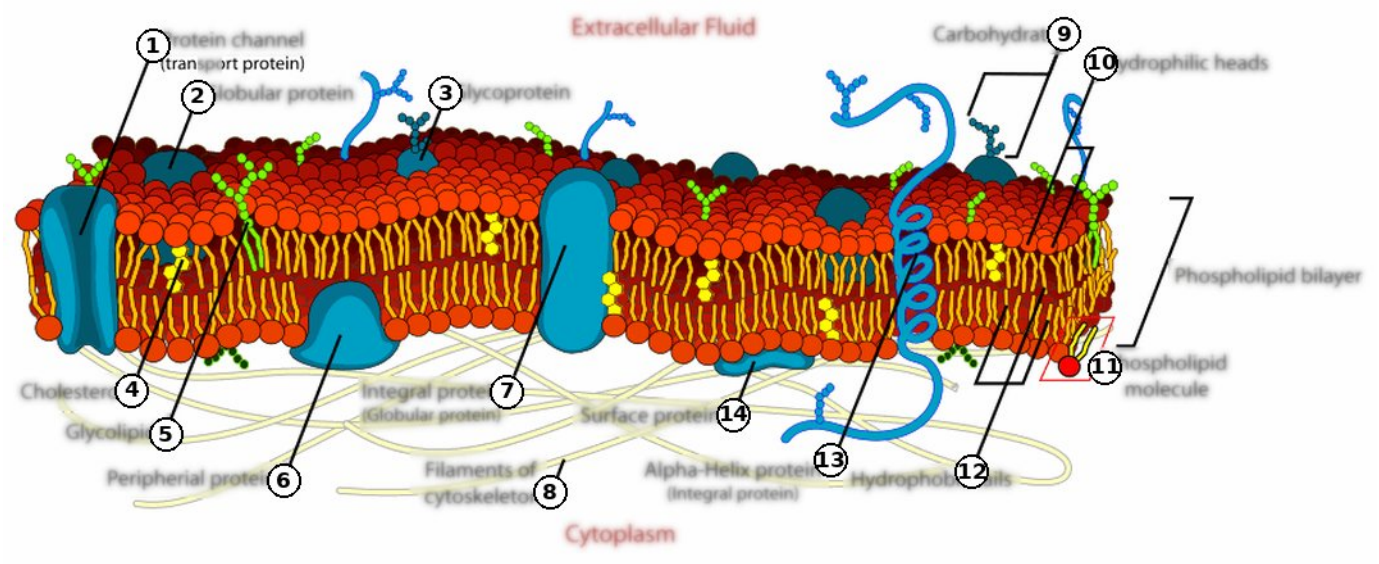
Marilyn G. Farquhar; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · cellimagelibrary.org/images/37171

How to recognise it

- Two dense plaques on the inner faces of neighbouring cell membranes.
- A narrow gap between the membranes, with a faint dense midline (the cadherins).
- Intermediate filaments (keratin in epithelia) loop into the plaques.

Don't confuse with: Tight junction: the outer membrane leaflets fuse, no plaques. Gap junction: a 2-4 nm gap and no plaques.

The cell membrane in detail



1 _____ **2** _____

3 _____ **4** _____

5 _____ **6** _____

7 _____ **8** _____

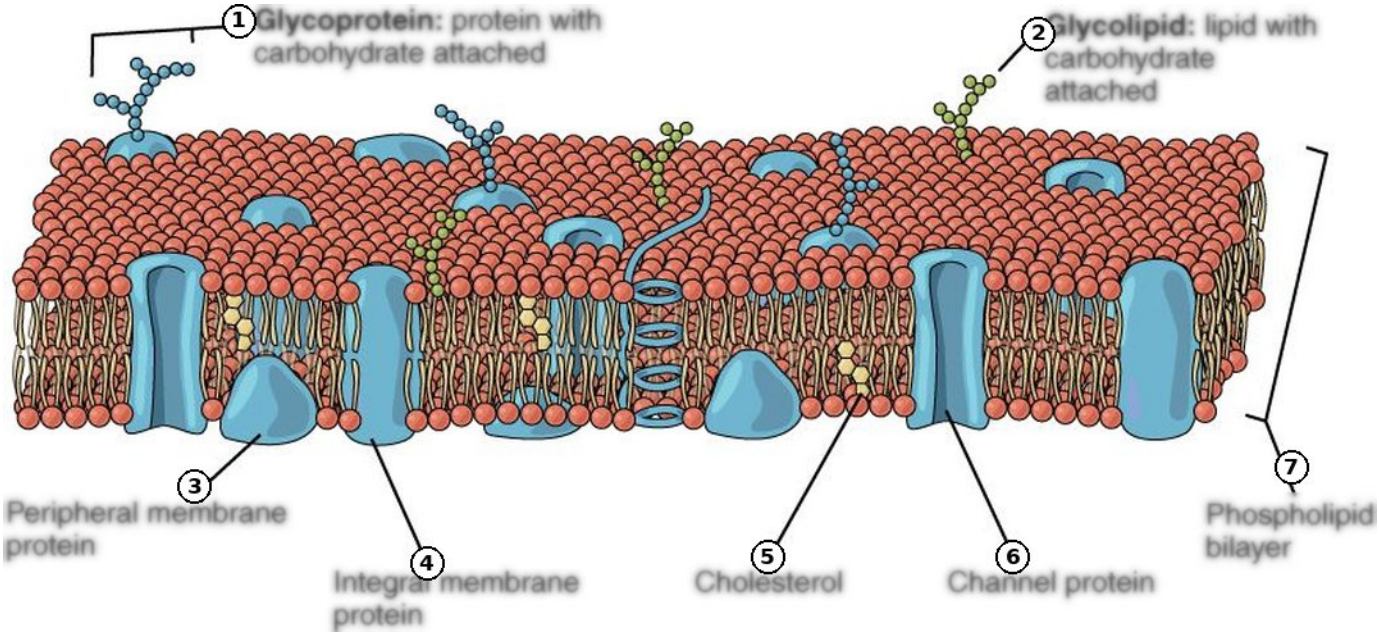
9 _____ **10** _____

11 _____ **12** _____

13 _____ **14** _____

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Credit: Mariana Ruiz · Public domain · commons.wikimedia.org/wiki/File:Cell_membrane_detailed_diagram_en.svg

The fluid mosaic of a cell membrane



1 _____ **2** _____

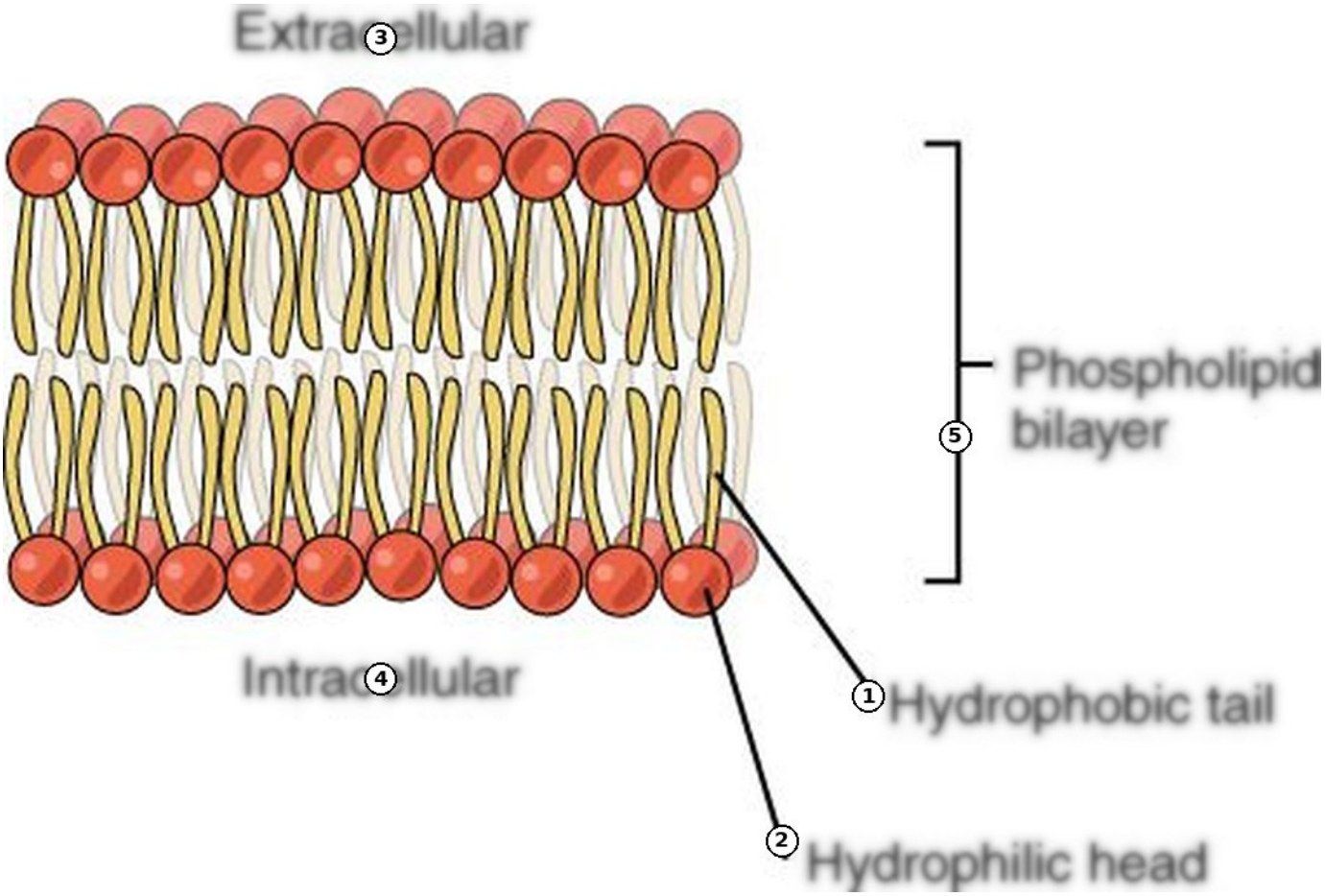
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Credit: OpenStax · CC BY 4.0 · commons.wikimedia.org/wiki/File:0303_Lipid_Bilayer_With_Various_Components.jpg

Two layers of lipid, seen edge on



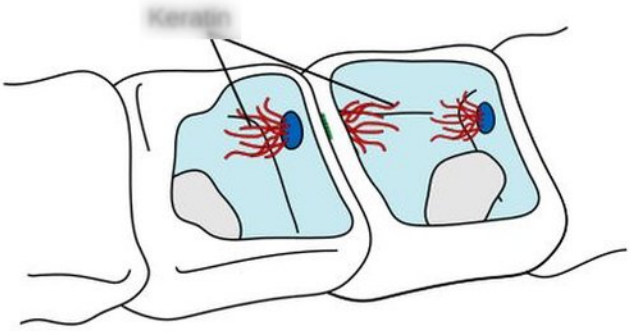
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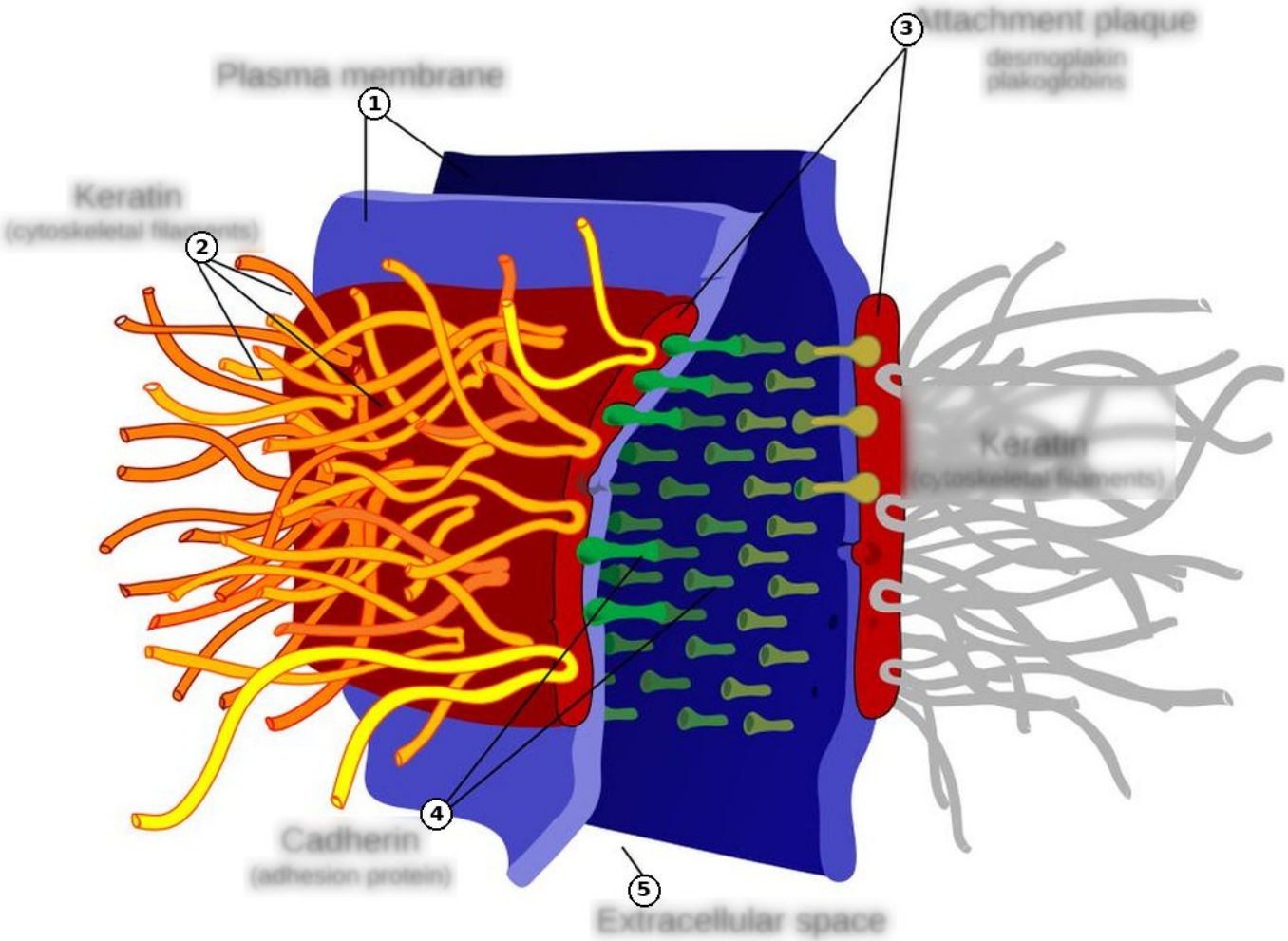
3 _____ **4** _____

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Credit: OpenStax · CC BY 4.0 · commons.wikimedia.org/wiki/File:0302_Phospholipid_Bilayer.jpg

A spot weld between two cells





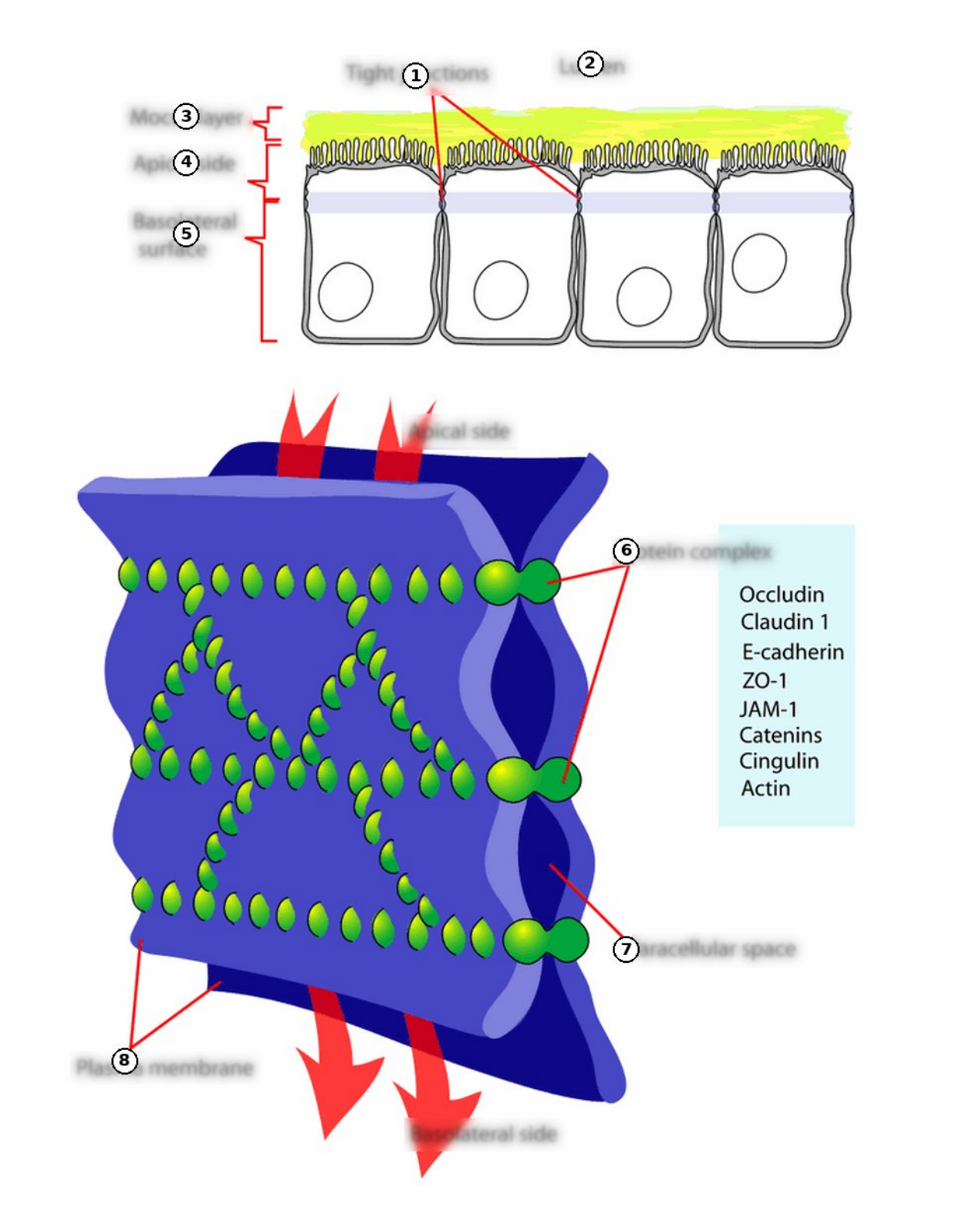
1 _____ **2** _____

3 _____ **4** _____

5 _____

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Credit: Mariana Ruiz LadyofHats · Public domain · commons.wikimedia.org/wiki/File:Desmosome_cell_junction_en.svg

Cells sealed together near their apical surface



1 _____ **2** _____

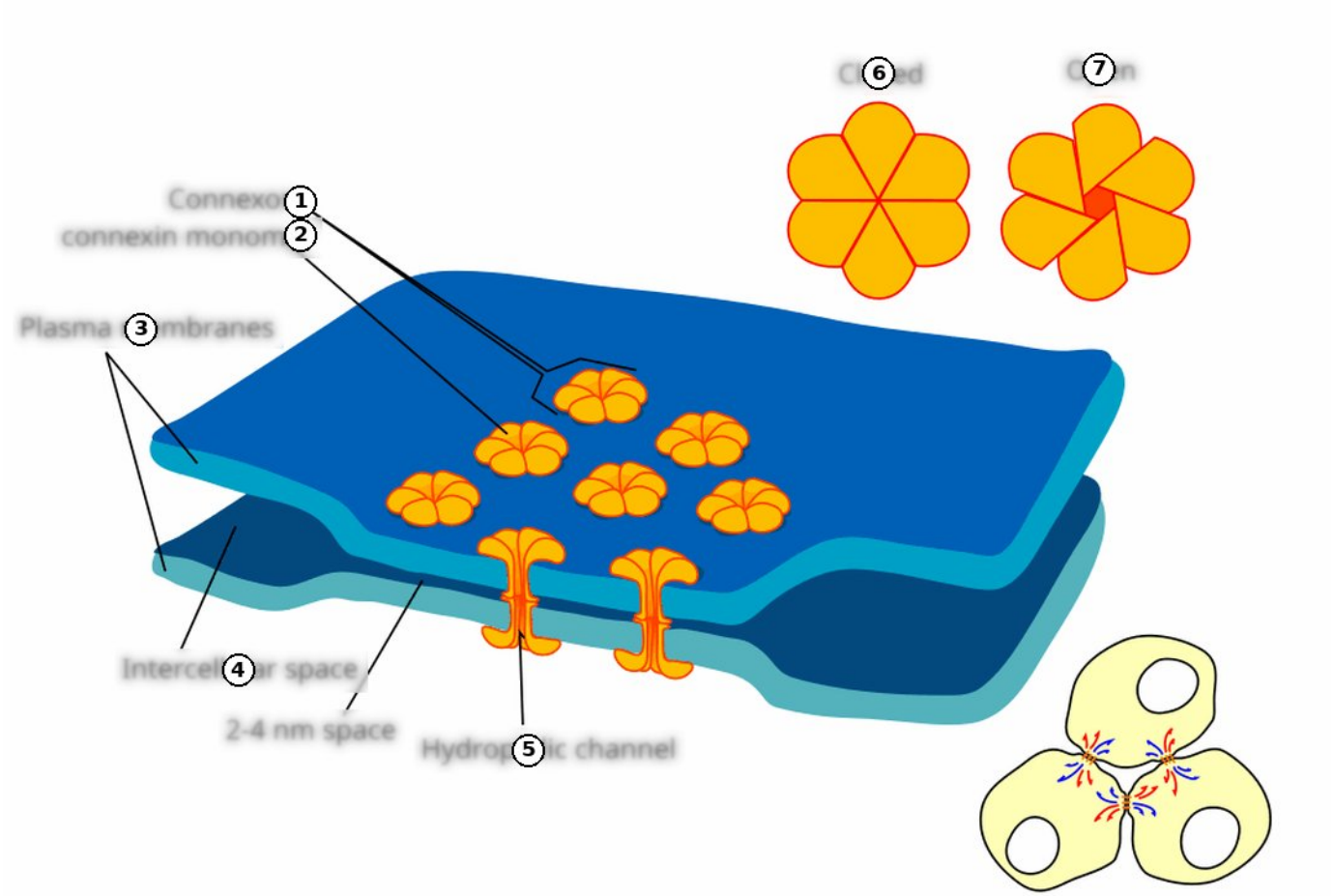
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7 _____ **8** _____

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Credit: Mariana Ruiz LadyofHats · Public domain · commons.wikimedia.org/wiki/File:Cellular_tight_junction-en.svg

Channels joining two cells



1 _____ **2** _____

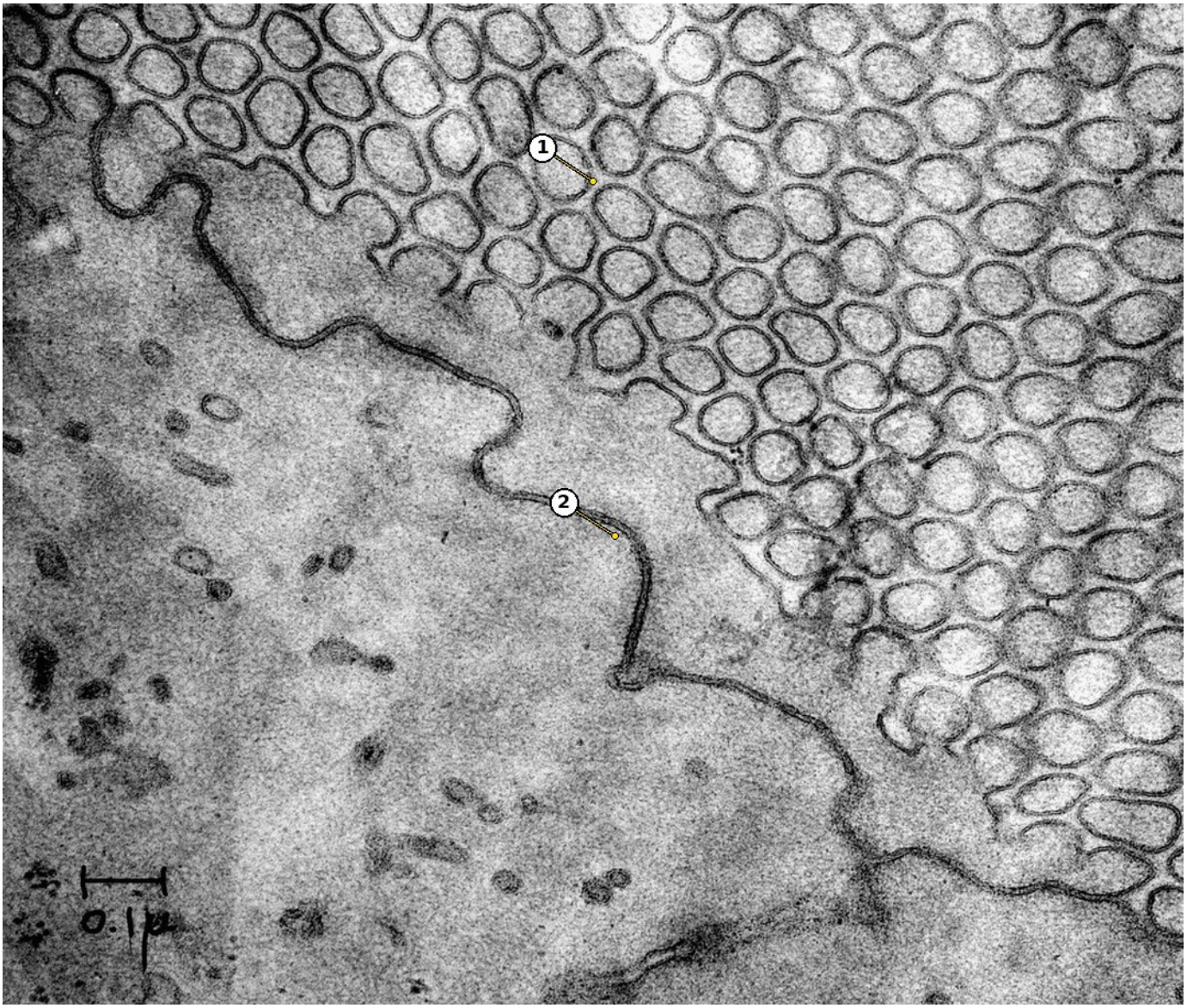
3 _____ **4** _____

5 _____ **6** _____

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Credit: Mariana Ruiz LadyofHats · Public domain · commons.wikimedia.org/wiki/File:Gap_cell_junction-en.svg

The free surface of two gut lining cells (TEM)

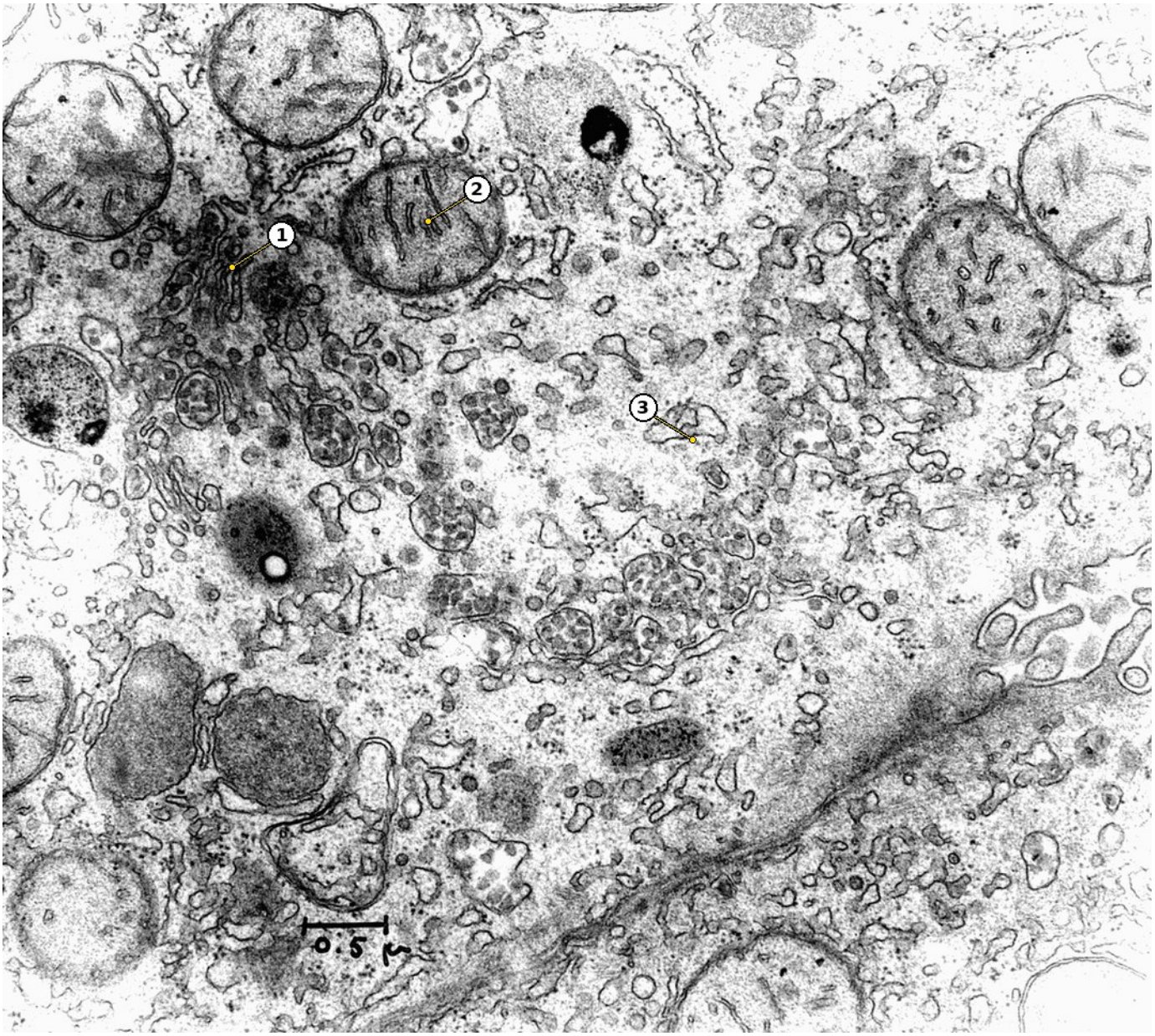


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Credit: Marilyn G. Farquhar; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37170

A liver cell from an ethanol-fed rat (TEM)



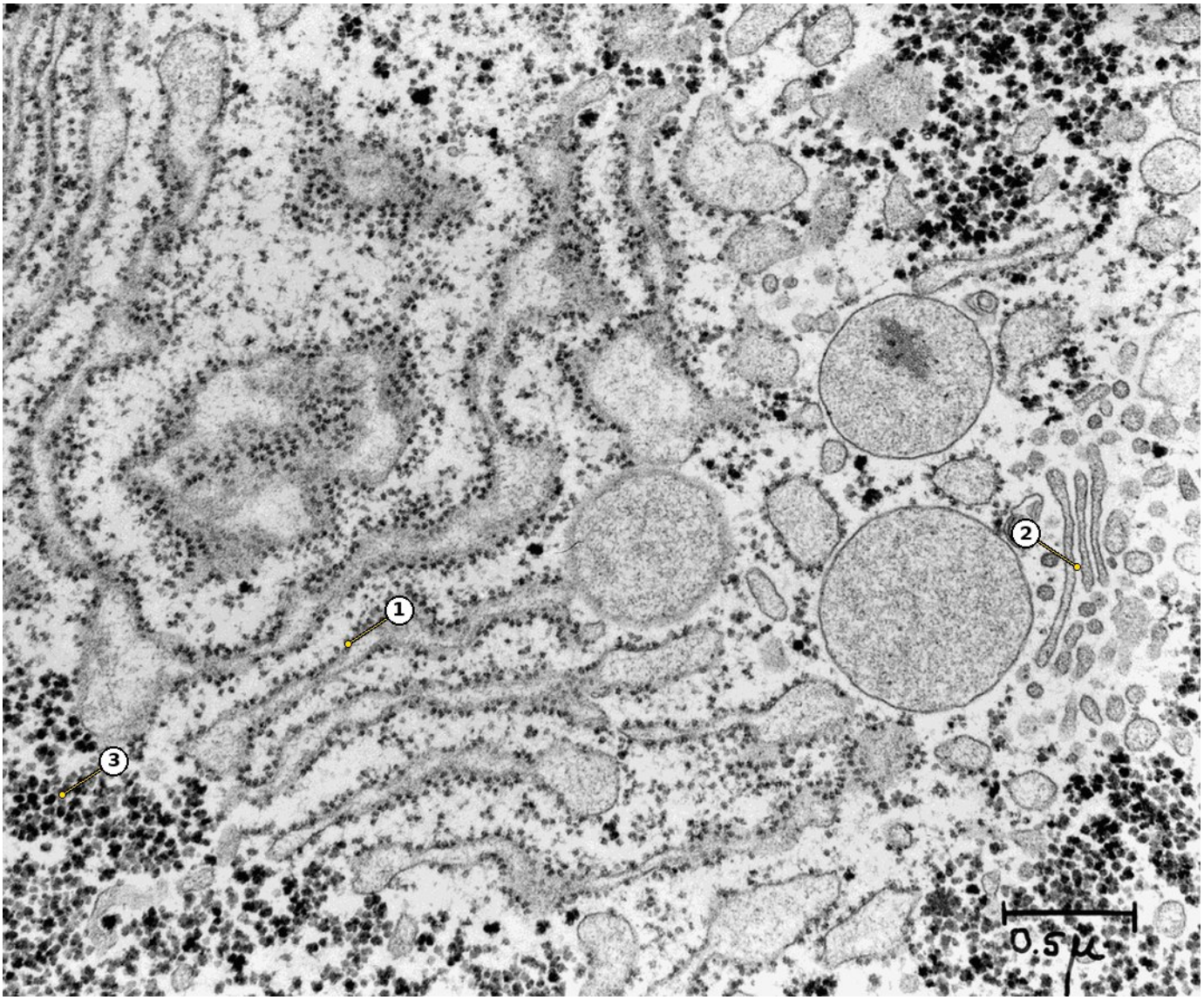
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Credit: George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37186

A newborn rat's liver cell (TEM)



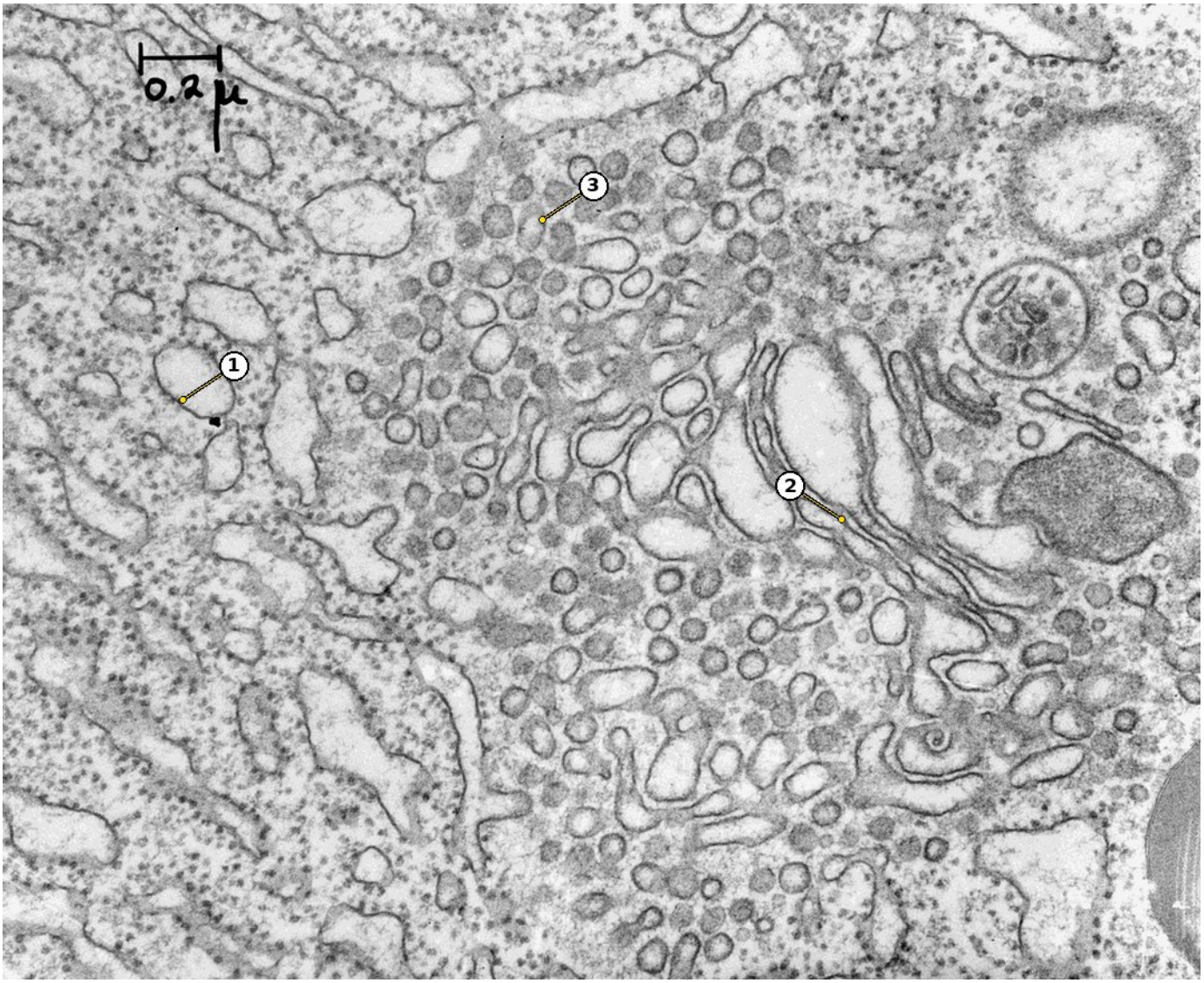
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Credit: George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37190

A pancreatic acinar cell making its export protein (TEM)



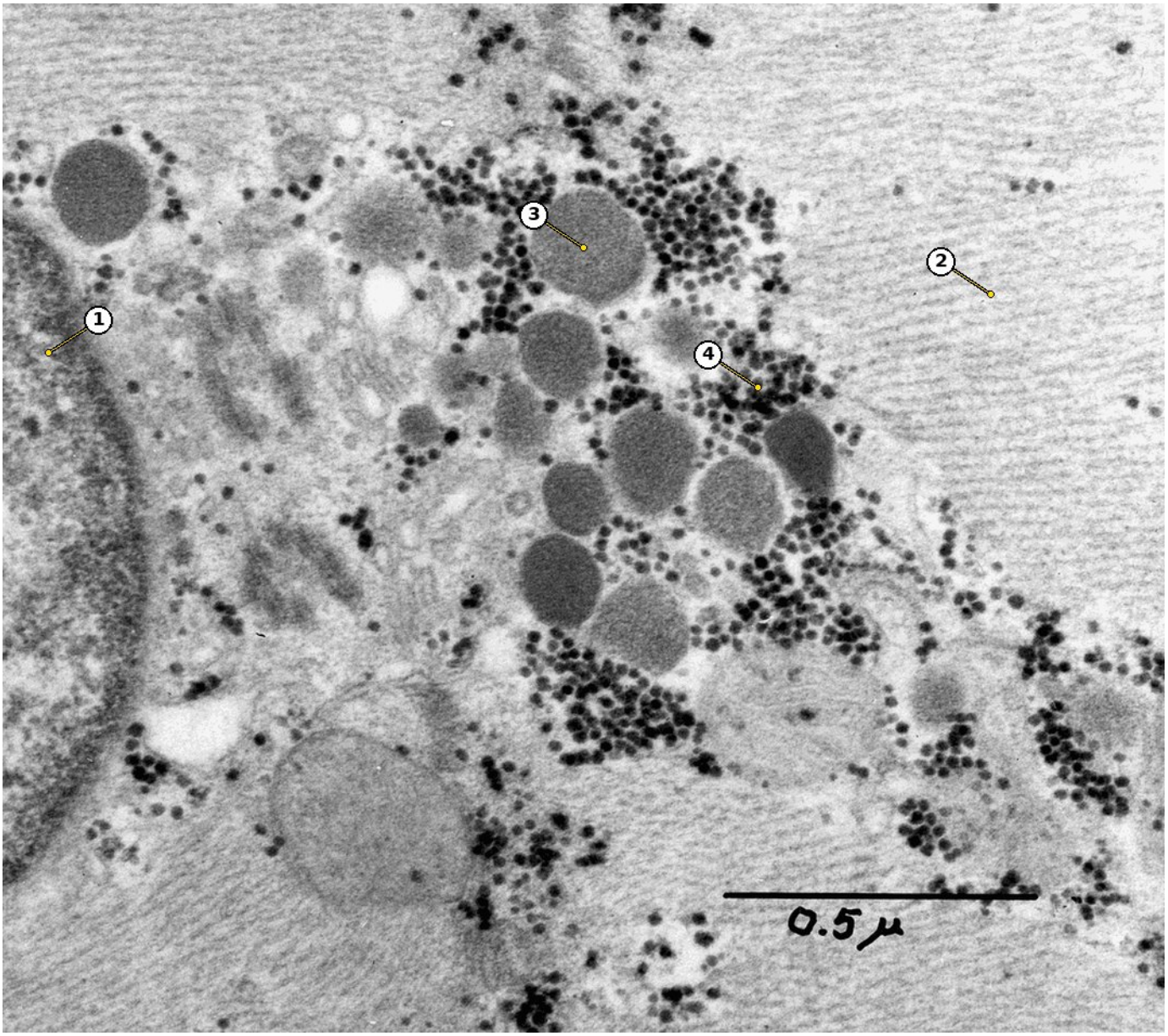
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Credit: George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37239

A second atrial muscle cell from a guinea pig (TEM)



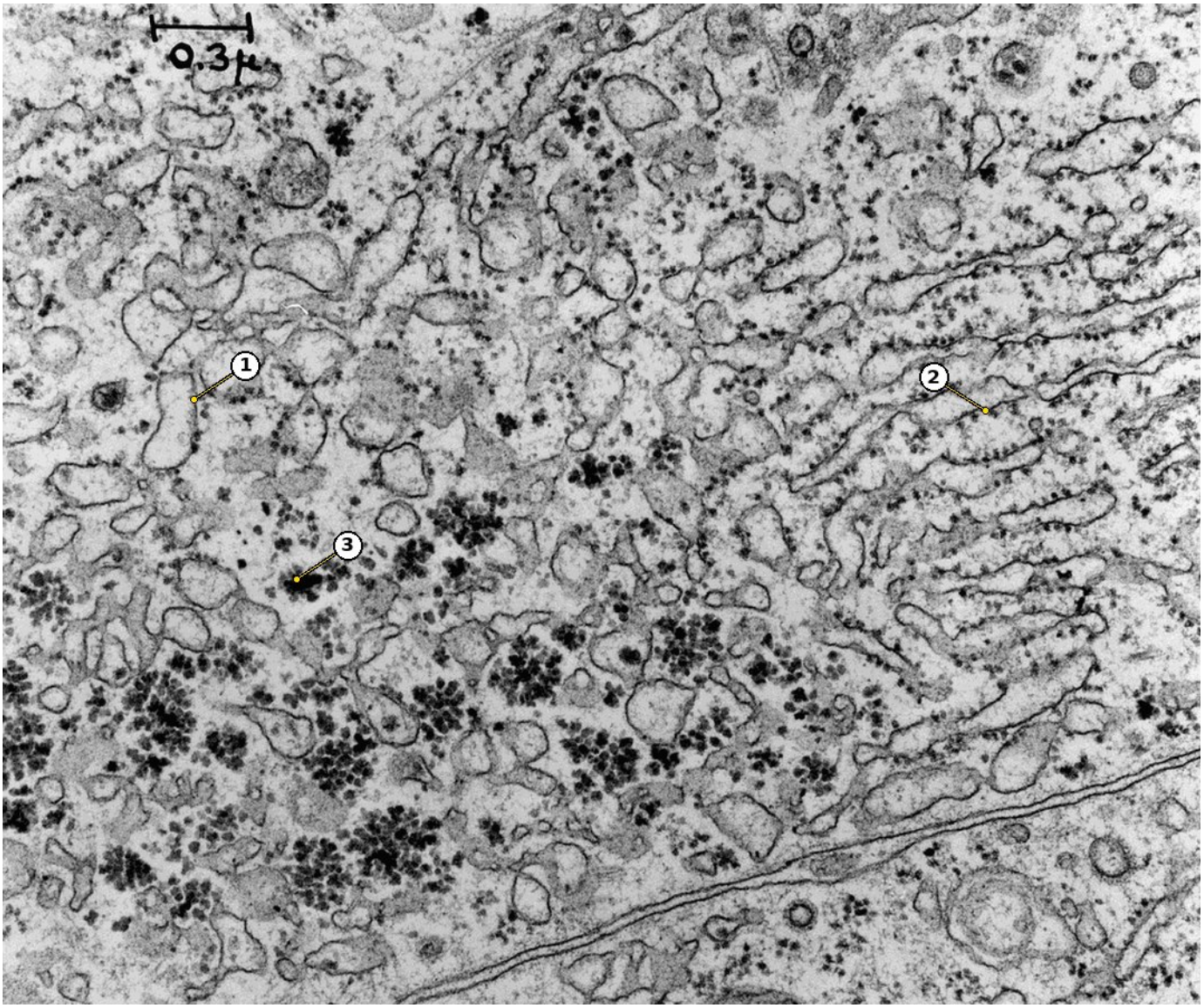
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Credit: George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37202

A young rat's liver cell, two kinds of reticulum (TEM)



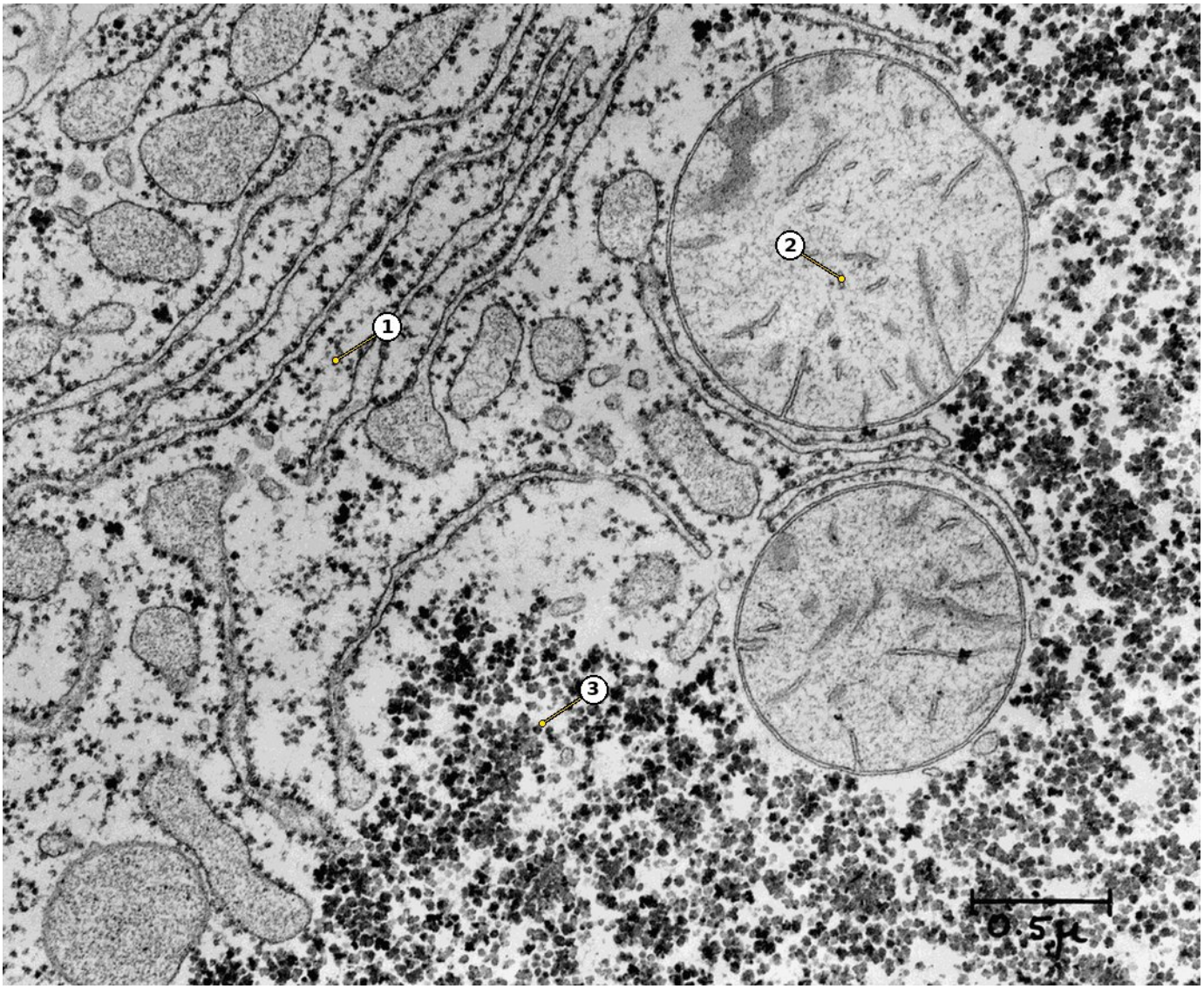
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Credit: Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37188

An adult rat's liver cell (TEM)



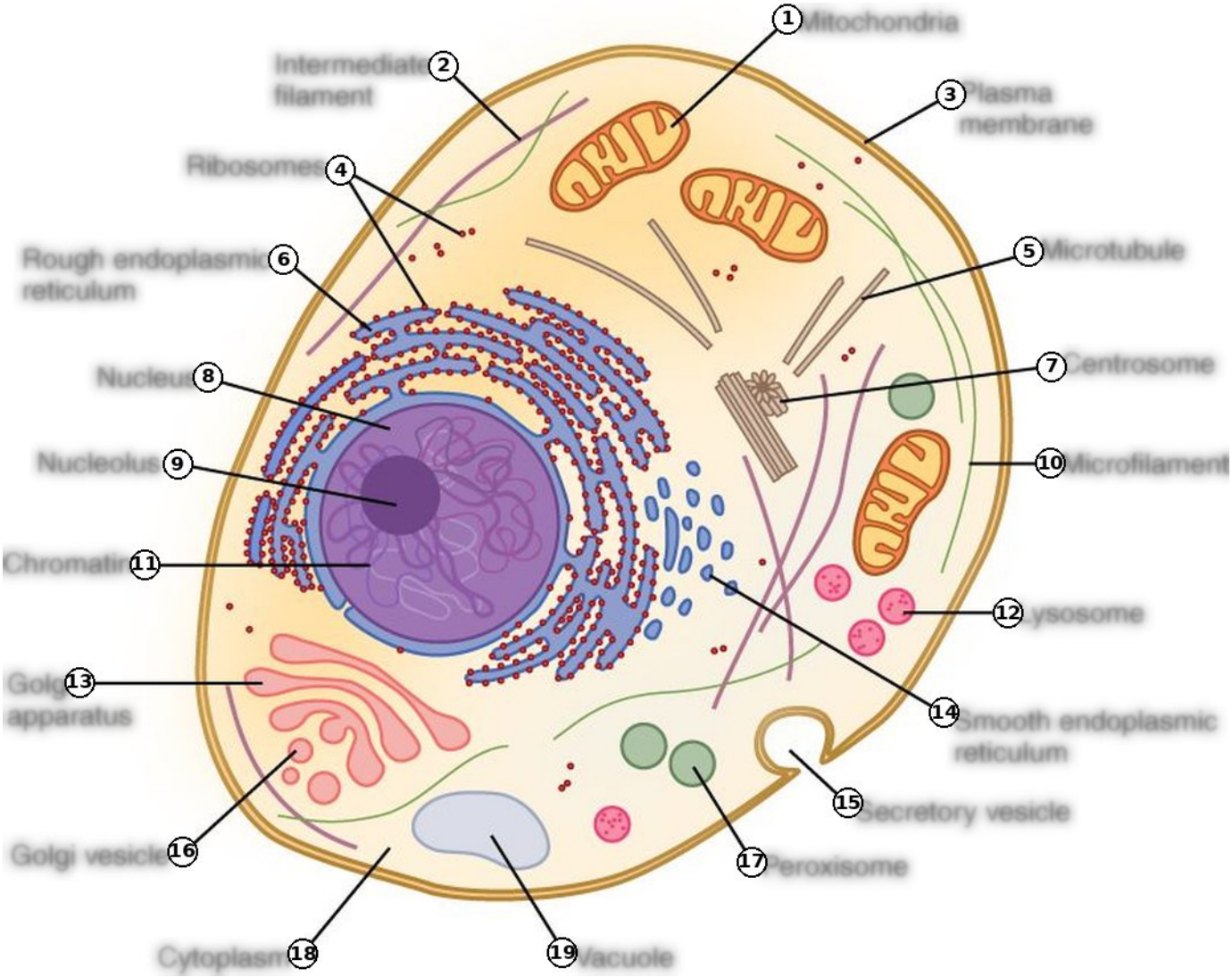
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Credit: George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37189

An animal cell and its parts



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4 _____ **5** _____ **6** _____

7 _____ **8** _____ **9** _____

10 _____ **11** _____ **12** _____

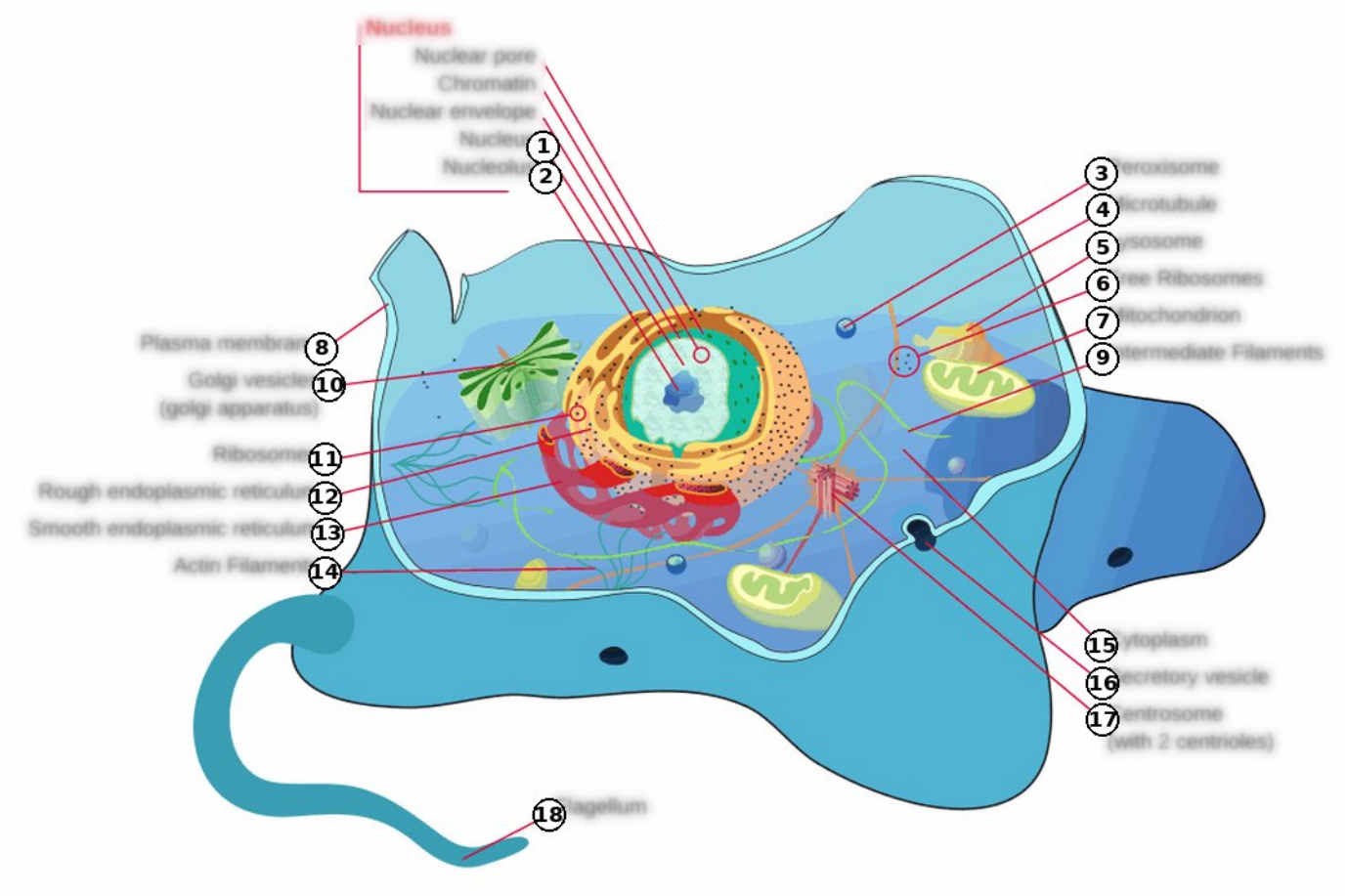
13 _____ **14** _____ **15** _____

16 _____ **17** _____ **18** _____

19 _____

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Credit: OpenStax · CC BY 4.0 · commons.wikimedia.org/wiki/File:0312_Animal_Cell_and_Components.jpg

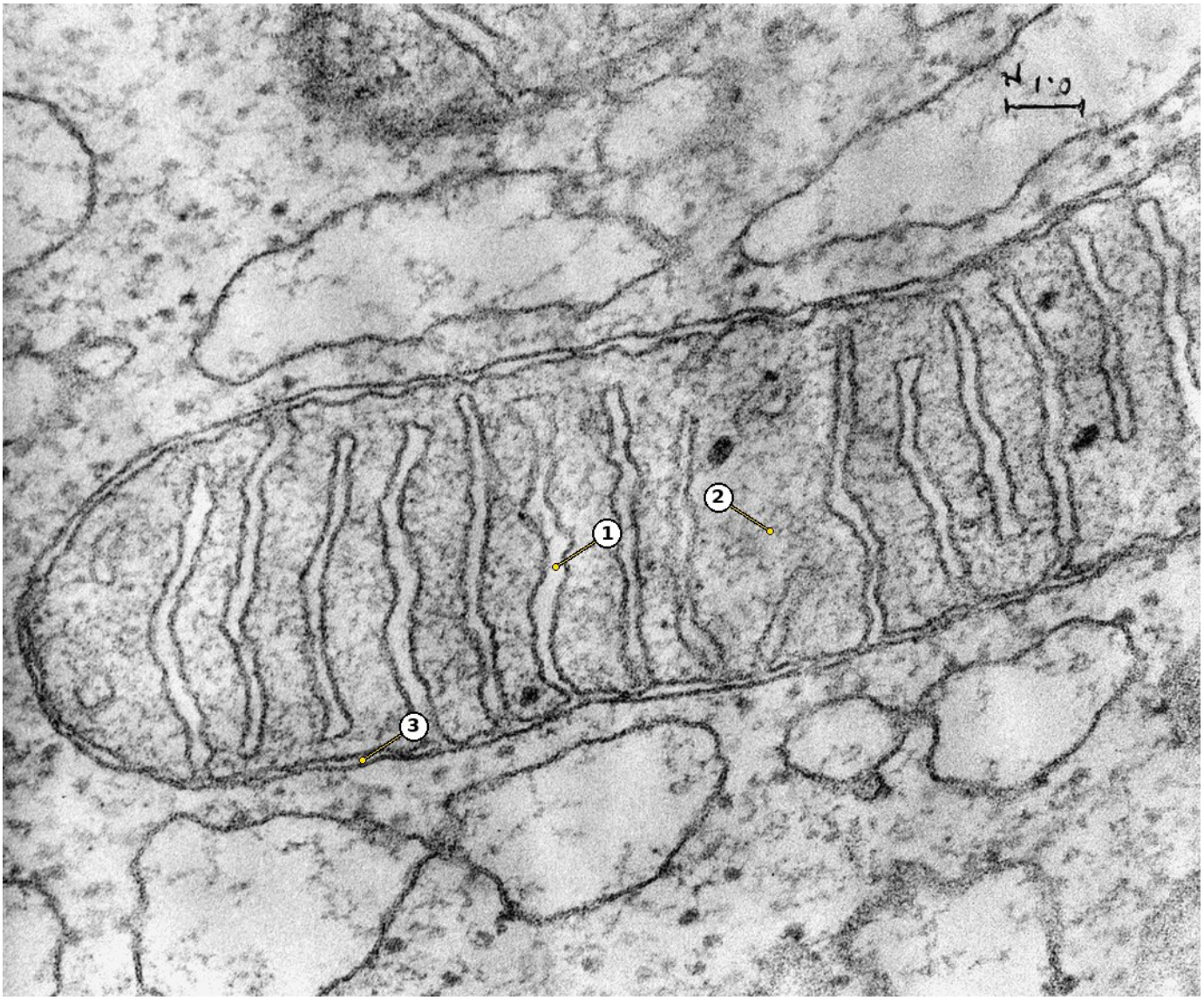
An animal cell, drawn in colour



1 _____	**2** _____	**3** _____
4 _____	**5** _____	**6** _____
7 _____	**8** _____	**9** _____
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Credit: LadyofHats (Mariana Ruiz) · Public domain · commons.wikimedia.org/wiki/File:Animal_cell_structure_en.svg

Inside the cell's power plant (guinea pig pancreas, TEM)



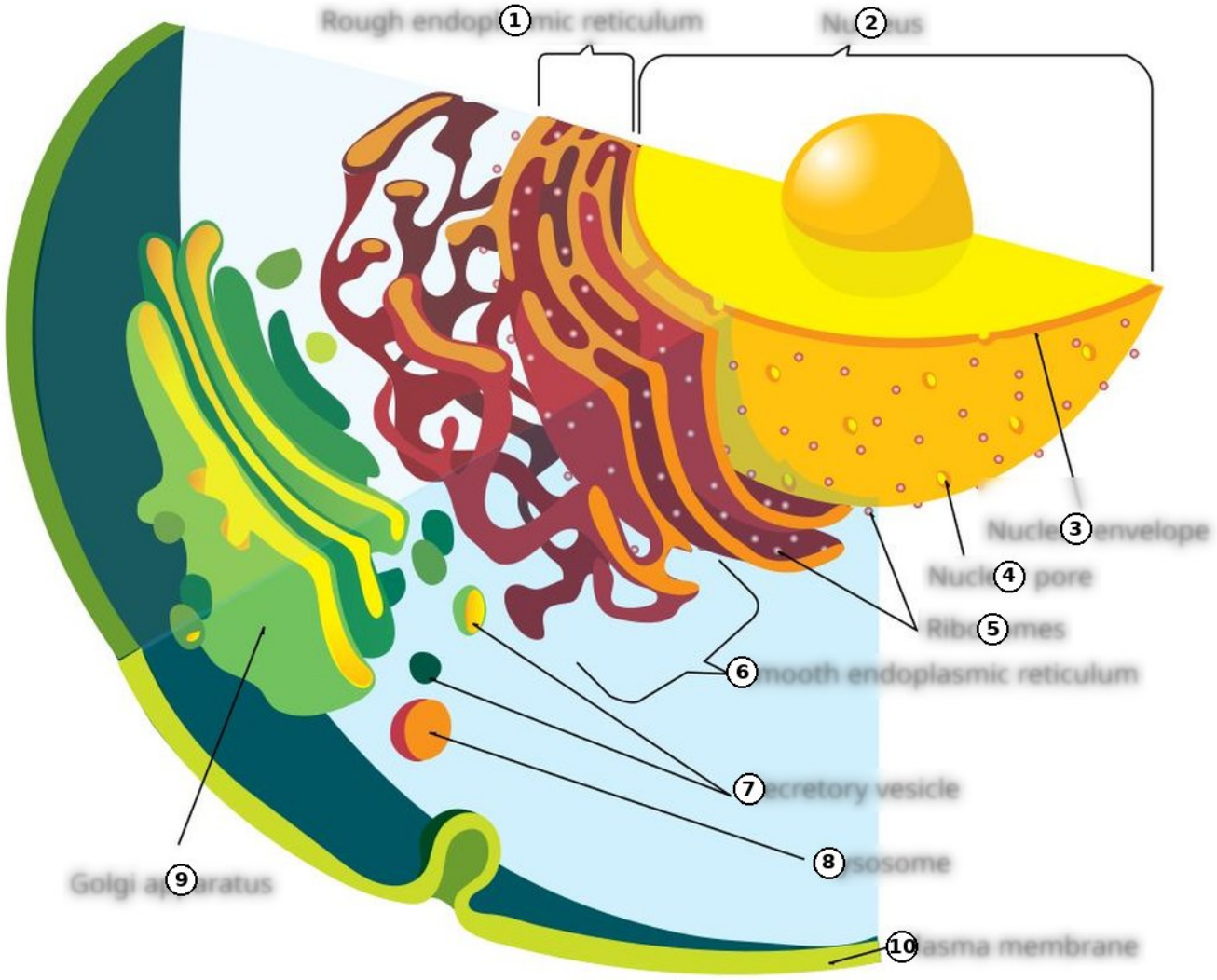
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Credit: George E. Palade; Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37199

Membranes that make and ship proteins



1 _____ **2** _____

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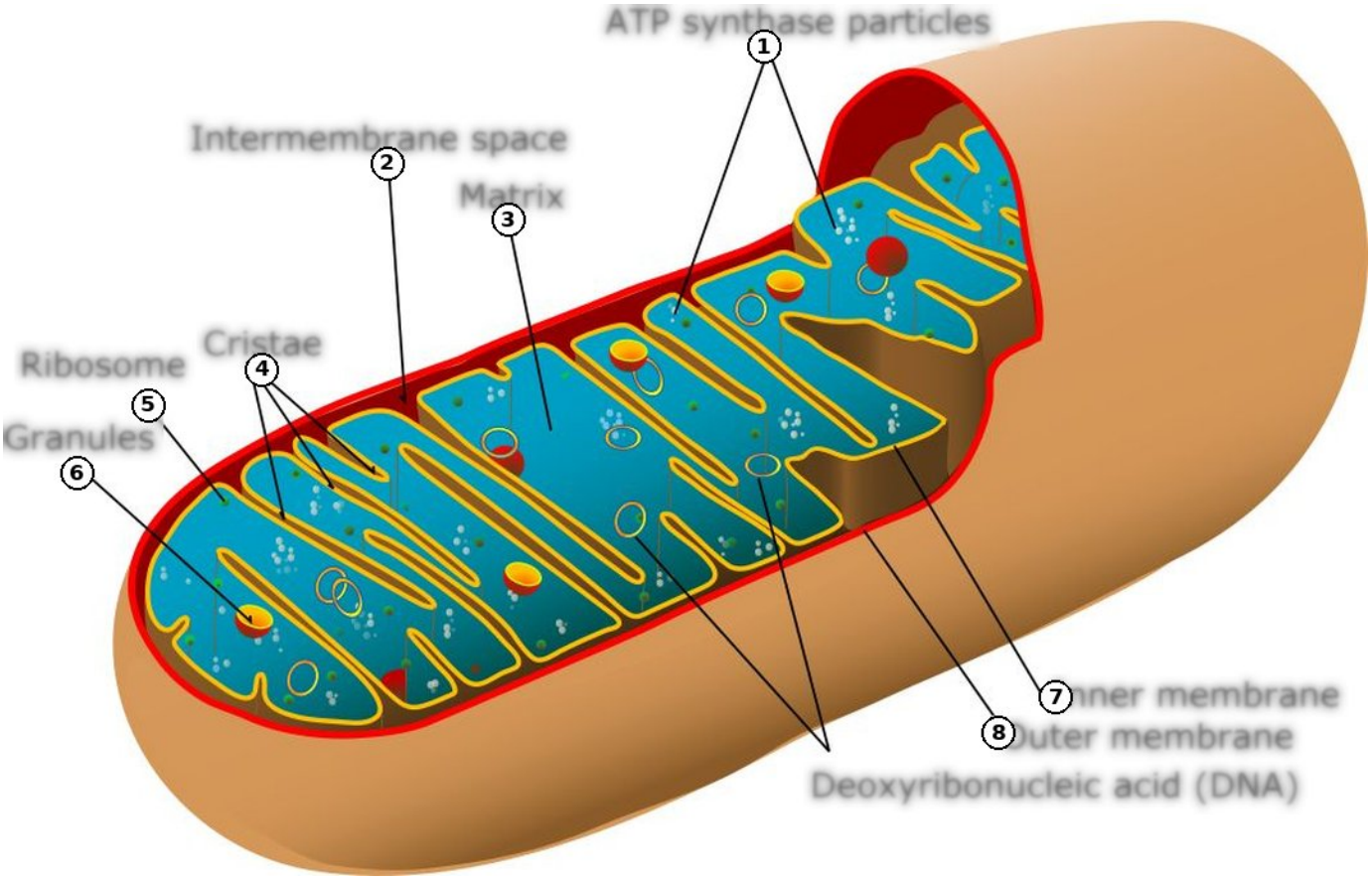
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Credit: Mariana Ruiz LadyofHats · Public domain · commons.wikimedia.org/wiki/File:Endomembrane_system_diagram_en.svg

The cell's power plant, cut open



1 _____ **2** _____

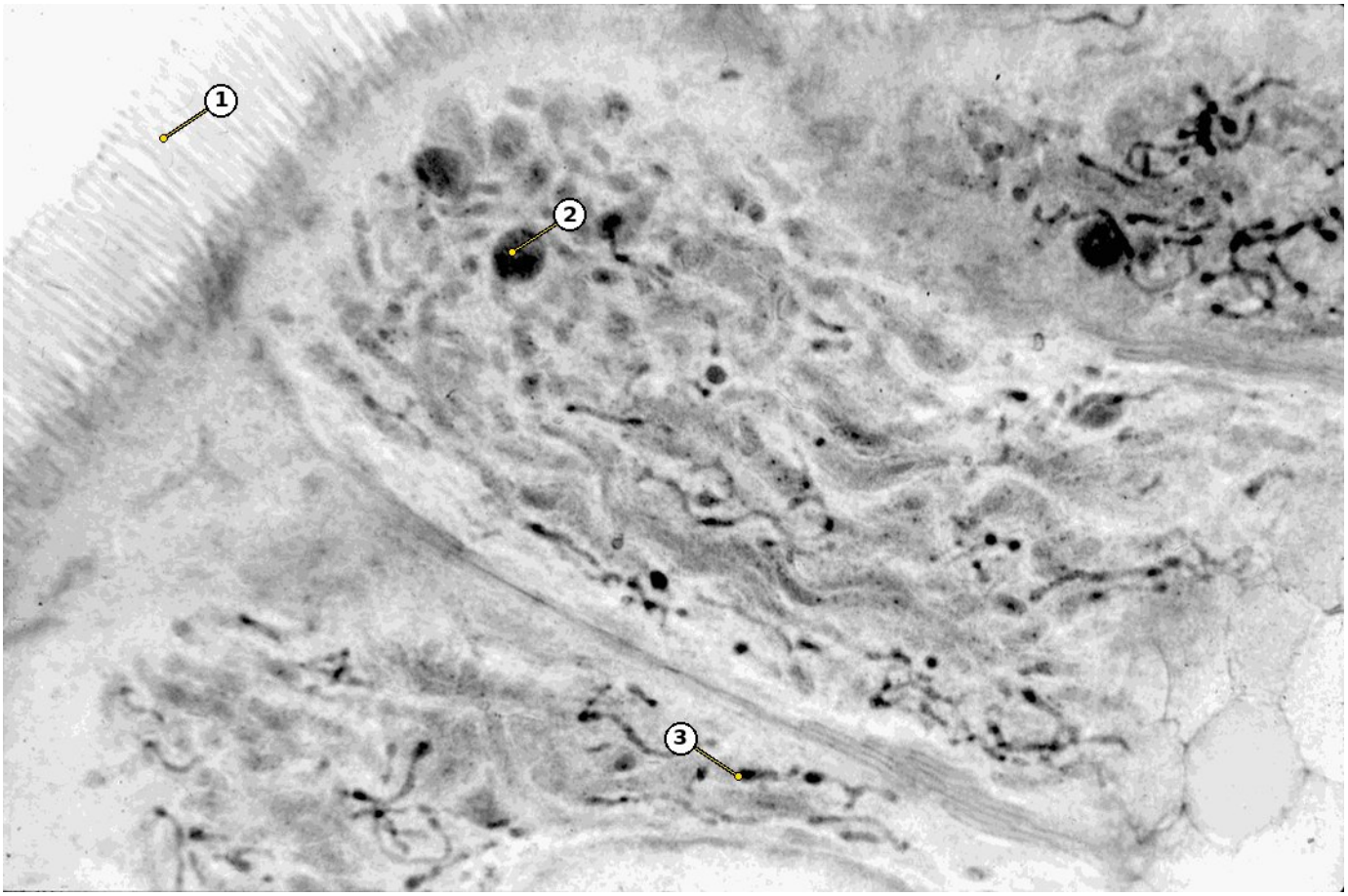
3 _____ **4** _____

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Practise online: medicine.kazimiri.com/semester-1/label/?map=subj-cytophysiology-8125046017
Credit: Mariana Ruiz Villarreal LadyofHats · Public domain · commons.wikimedia.org/wiki/File:Animal_mitochondrion_diagram_en_(edit).svg

The lining of the human duodenum, catalase stained (EM)

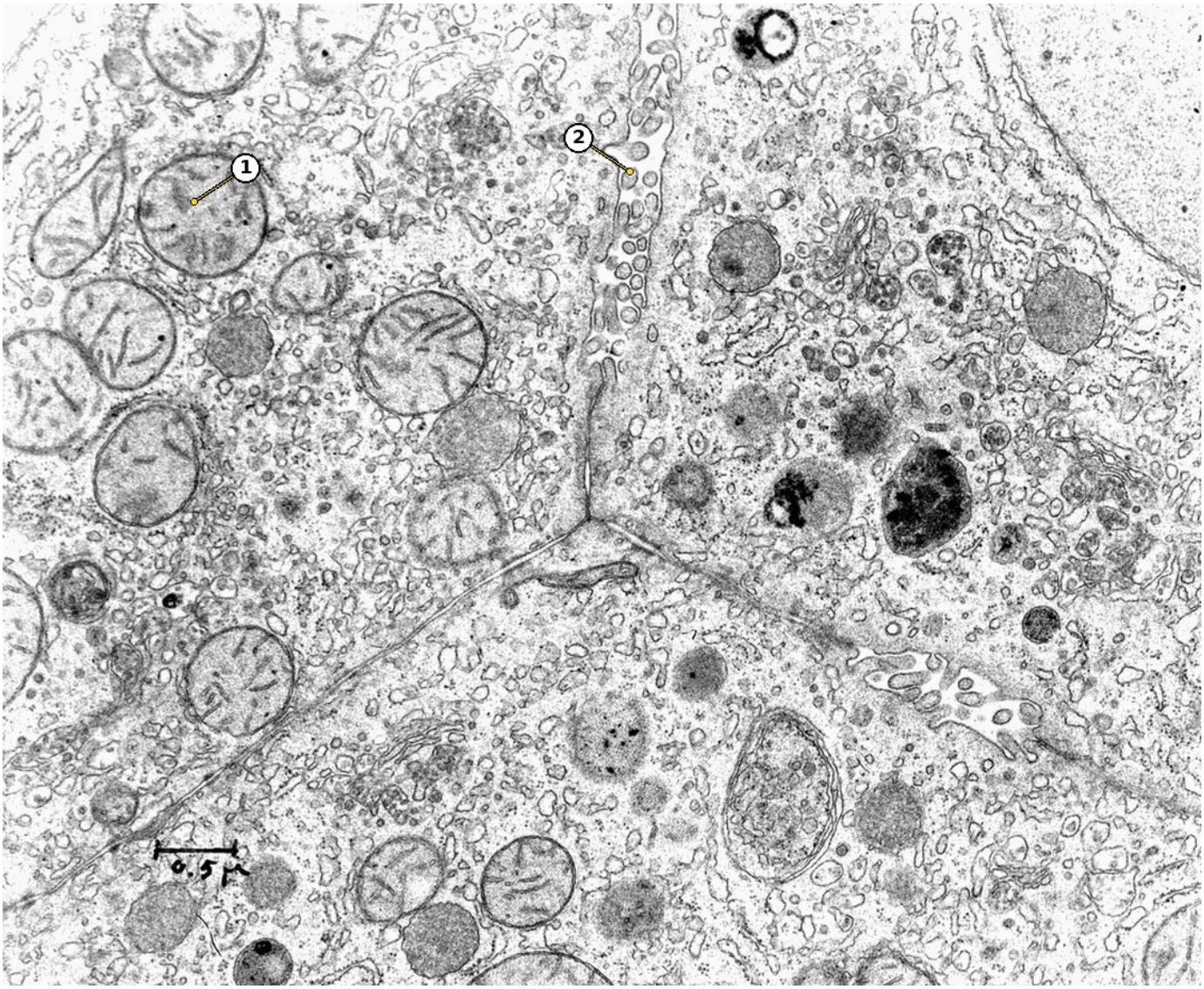


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Practise online: medicine.kazimiri.com/semester-1/label/?map=subj-cytophysiology-d6dcd48b33
Credit: Frank Roels, Marina Pauwels, Peter Van der Spek, via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/47808

Where three liver cells meet (TEM)



1 _____ **2** _____

Practise online: medicine.kazimiri.com/semester-1/label/?map=subj-cytophysiology-c6f660cef9

Credit: Department of Cell Biology, Yale University School of Medicine (J. D. Jamieson), via the Cell Image Library · CC BY-NC-SA 3.0 · www.cellimagelibrary.org/images/37185

3 · Key points

The site's key points for these classes, word for word.

Lecture 1 · Monday 5 October, 08:00–09:30, A5/4 · Membranes, transport, junctions, signalling

The membrane

- Fluid mosaic model (Singer & Nicolson, 1972): a phospholipid bilayer with cholesterol, integral and peripheral proteins, and a glycocalyx.
- Phospholipids are amphipathic: heads face the water, tails the interior. The outer leaflet is rich in phosphatidylcholine and sphingomyelin, the inner in phosphatidylserine and phosphatidylethanolamine.
- Phosphatidylserine appearing on the outer leaflet is an "eat me" signal to phagocytes during apoptosis. Flippases, floppases and scramblases move lipids between leaflets.
- Fluidity rises with shorter and unsaturated (kinked) fatty-acid tails and with temperature; cholesterol buffers it, stiffening the membrane when warm and keeping it fluid when cold.
- Lipid rafts are ordered patches rich in cholesterol and sphingolipids that gather signalling proteins.
- The glycocalyx of glycoproteins and glycolipids carries the ABO blood-group antigens and takes part in recognition and adhesion.
- Membranes are 6-10 nm thick (the plasma membrane about 7.5 nm), asymmetric, fluid and dynamic. Lipids and proteins are about 1:1 by mass, but there are about 50 lipid molecules to each protein. The P face looks into the cytoplasm, the E face outwards; sugars sit only on the E face.
- Membrane models: Danielli and Davson's symmetric protein-lipid "sandwich" (1935); Robertson's "unit membrane" (1959), from the first electron micrograph of a membrane, a red cell's; Singer and Nicolson's fluid mosaic (1972).
- Lipids diffuse laterally (very fast) and rotate; flip-flop between leaflets is rare, so enzymes do it: flippase moves lipids from the outer to the inner leaflet and floppase from the inner to the outer, both using ATP; scramblase moves them both ways without energy. Proteins never flip-flop.
- In the electron microscope a membrane is trilaminar, dark-light-dark: osmium tetroxide binds the polar heads, not the fatty-acid tails.
- Integral proteins cross the bilayer once (single-pass), several times (multipass) or sit in one leaflet (monotopic), and come out only with detergents; peripheral proteins are held by weak bonds and come off with salt or pH changes.
- About 95-98% of a cell's membrane is intracellular. The plasma membrane's marker enzyme is the Na+/K+-ATPase, and only the plasma membrane carries a glycocalyx. Caveolae are flask-shaped pits coated with caveolin (uptake and signalling), common in endothelial and fat cells; lipid rafts are 50-100 nm across.
- New membrane: lipids are made in the smooth ER and proteins in the rough ER, modified in the Golgi and delivered in vesicles. A tear is sealed within seconds: Ca2+ floods in and makes vesicles fuse over the hole.
- The red cell's membrane skeleton: a spectrin web (alpha and beta chains) tied to the anion exchanger band 3 by ankyrin, and to the membrane through the junctional complex (actin, protein 4.1). Red cells burst in a hypotonic solution leave empty "ghosts", the classic model membrane.
- ABO antigens are sugars of the red cell's glycocalyx: group O carries the bare H antigen; the A enzyme adds N-acetylgalactosamine and the B enzyme galactose. The glycosyltransferase is the product of the ABO gene.

Transport

- Passive: simple diffusion (O2, CO2), facilitated diffusion through channels and carriers (GLUT), osmosis (aquaporins).
- Primary active: the Na+/K+-ATPase pumps 3 Na+ out and 2 K+ in per ATP. Secondary active: Na+-glucose symport by SGLT1 in the gut and SGLT2 in the kidney.
- Vesicular: phagocytosis, pinocytosis, receptor-mediated endocytosis (clathrin, e.g. LDL), exocytosis.
- Diffusion is faster with a steeper gradient, a larger area and a thinner membrane (Fick). Small non-polar molecules cross the bilayer easily; ions need channels.
- Carriers are specific and saturate at a maximum rate; channels are far faster and open to a voltage, a ligand or stretch.
- A carrier binds its solute on one side and changes shape to release it on the other (alternating access), a few molecules per cycle, as GLUT1 does with no ATP; a channel opens an aqueous pore through which ions stream; a pump (an ATPase) spends ATP to move ions against their gradient.
- Osmosis: water moves toward the higher solute concentration, so cells swell in a hypotonic solution and shrink in a hypertonic one; 0.9% NaCl is isotonic.
- The resting membrane potential (about −70 mV) comes mainly from K+ leaking out, with the Na+/K+-ATPase keeping the gradients. In cystic fibrosis the CFTR chloride channel is faulty.

- Channels are voltage-gated (nerve and muscle), ligand-gated (neurotransmitters), mechanically gated (inner-ear hair cells: tip links pull them open as the stereocilia bend) or leak channels, always open (K+, Cl-). A channel passes about a million ions a second or more, far faster than a carrier.
- Cystic fibrosis: CFTR mutation classes are I, no protein made; II, the protein misfolds and is destroyed (F508del, the commonest); III, gating, the channel stays shut; IV, conduction; V, too little protein. Classes I and II leave no channel in the membrane, and how ill a patient is depends on how much working channel reaches it.

Cell junctions

- Tight (zonula occludens: claudins, occludin) seal; adherens (cadherins with actin) and desmosomes (cadherins with intermediate filaments) anchor.
- Tight junctions are strands of claudins and occludin with junctional adhesion molecules (JAMs), linked inside the cell through ZO proteins to actin.
- Hemidesmosomes (integrins) anchor cells to the basal lamina; gap junctions (connexons of 6 connexins) pass ions and small molecules.
- The junctional complex of an epithelium, from the apex: tight junction, zonula adherens, desmosome. Tight junctions also keep apical and basolateral membrane proteins apart.
- Disease: in pemphigus vulgaris antibodies against desmoglein split the epidermis; in bullous pemphigoid antibodies against hemidesmosome proteins lift it off the basement membrane.
- Loss of E-cadherin frees cancer cells to leave the epithelium and invade (epithelial-mesenchymal transition).

Cell signalling

- Endocrine, paracrine, autocrine, juxtacrine.
- G-protein-coupled receptors (7 transmembrane helices; cAMP, or IP3/DAG and Ca2+); receptor tyrosine kinases (insulin, growth factors); ligand-gated ion channels; intracellular receptors (steroids, thyroid hormone).
- Gs activates adenylyl cyclase and cAMP activates protein kinase A; Gi inhibits the cyclase. Gq activates phospholipase C: IP3 releases Ca2+ from the ER and DAG activates protein kinase C.
- A receptor tyrosine kinase dimerises and phosphorylates itself when its ligand binds; adaptors pass the signal to Ras and the MAP kinase cascade (Raf, MEK, ERK), which drives proliferation.
- The PI3K-Akt pathway, switched on by insulin and growth factors, promotes survival and growth (through mTOR) and, for insulin, glucose uptake (GLUT4). Nitric oxide activates guanylyl cyclase, and cGMP relaxes smooth muscle.
- Signals are switched off: the G protein hydrolyses its GTP, phosphodiesterases break down cAMP and cGMP, phosphatases remove phosphates, and receptors are taken into the cell.

Lab 1 · Organelles under the electron microscope

Organelles

- Mitochondria: double membrane, cristae, own circular DNA (inherited from the mother), ATP by oxidative phosphorylation; release cytochrome c in apoptosis.
- RER: secretory, membrane and lysosomal proteins. SER: lipids and steroids, detoxification (cytochrome P450), Ca2+ store (sarcoplasmic reticulum).
- Golgi: glycosylation and sorting, cis to trans; mannose-6-phosphate targets enzymes to lysosomes.
- Lysosomes: acid hydrolases at pH 4.5-5. Peroxisomes: catalase, beta-oxidation of very-long-chain fatty acids. Cytosolic ribosomes: 80S (60S + 40S); mitochondrial ones are 55S.
- On electron micrographs: RER, parallel flattened cisternae studded with ribosomes; SER, a tangle of ribosome-free tubules (liver, steroid-making cells); Golgi, a stack of curved smooth cisternae with vesicles at its edges; mitochondria, a double membrane with cristae; peroxisomes, round single-membrane bodies with a fine granular matrix, in rat liver with a dense crystalloid core of urate oxidase (human peroxisomes have none).
- Marker enzymes: acid phosphatase for lysosomes, catalase for peroxisomes, glucose-6-phosphatase for the ER, cytochrome c oxidase for the inner mitochondrial membrane, Na+/K+-ATPase for the plasma membrane.
- Proteins are sorted by signals: a signal peptide sends a new protein into the RER; KDEL returns ER proteins from the Golgi; a nuclear localisation signal takes proteins into the nucleus.
- Lysosomal storage diseases: a missing hydrolase lets its substrate pile up (Tay-Sachs: hexosaminidase A; Gaucher: glucocerebrosidase; Pompe: acid maltase). In I-cell disease the enzymes lack mannose-6-phosphate and leave the cell.
- Proteasomes destroy proteins tagged with a chain of ubiquitins; autophagy delivers worn-out organelles to lysosomes. In Zellweger syndrome proteins are not imported into peroxisomes (PEX genes), which stay empty.

4 · Using the light microscope: checklist

- ☐ Carry the microscope with both hands, one on the arm and one under the base. Lamp at minimum before switching on.
- ☐ Start with the lowest-power objective (4× or 10×) clicked into place. Slide coverslip up, label to the side, held in the mechanical stage.
- ☐ Centre the section over the light with the naked eye first.
- ☐ Watching from the side, raise the stage close to the objective with the coarse focus. Then, looking through the eyepieces, focus by moving the stage AWAY from the objective. Set the eyepiece distance for your eyes.
- ☐ Light: lamp brightness and the condenser's aperture diaphragm. Close the diaphragm for more contrast, open it for more resolution.
- ☐ Higher power: turn the nosepiece; at 40× use the fine focus only.
- ☐ Oil immersion (100×), only when the teacher allows it: a drop of oil on the coverslip, swing in the 100× objective, fine focus only. Never let the 40× objective touch the oil. Wipe oil off the lens and the slide with lens paper afterwards.
- ☐ Total magnification = objective × eyepiece (40 × 10 = 400×). The light microscope resolves about 0.2 µm.
- ☐ At the end: lowest objective in place, stage down, slide out, lamp at minimum and off, dust cover on.

5 · Self-test: 20 single-choice questions

From the site's Cytophysiology quiz (The membrane, Transport, Cell junctions, Cell signalling, Organelles). One answer is right in each; circle it. Give yourself 60 s a question, as in the final test. The answers are on the last page. Questions 19 and 20 adapted from MIT OpenCourseWare, 7.016 Introductory Biology, Fall 2018 (Prof. Barbara Imperiali, Prof. Adam Martin, Dr. Diviya Ray): problem sets and exams. CC BY-NC-SA 4.0.

1. Cholesterol in the membrane:

- **A** only raises fluidity
- **B** only lowers fluidity
- **C** has no effect on fluidity
- **D** buffers fluidity against temperature changes

2. For each ATP, the Na+/K+-ATPase moves:

- **A** 2 Na+ out and 3 K+ in
- **B** 1 Na+ out and 1 K+ in
- **C** 3 Na+ out and 2 K+ in
- **D** 3 Na+ in and 2 K+ out

3. Which junction lets ions pass directly from one cell's cytoplasm into the next?

- **A** tight junction
- **B** gap junction
- **C** desmosome
- **D** hemidesmosome

4. Gq-coupled receptors activate:

- **A** phospholipase C
- **B** adenylyl cyclase
- **C** guanylyl cyclase
- **D** a tyrosine kinase

5. The smooth endoplasmic reticulum:

- **A** makes secretory proteins
- **B** makes lipids and steroids and detoxifies (cytochrome P450)
- **C** glycosylates and sorts proteins
- **D** destroys proteins tagged with ubiquitin

6. In a healthy cell, phosphatidylserine faces the:

- **A** outside (outer leaflet)
- **B** cytosol (inner leaflet)
- **C** nucleus
- **D** lumen of the ER only

7. O_2 and CO_2 cross the plasma membrane by:

- **A** facilitated diffusion through GLUT
- **B** simple diffusion
- **C** primary active transport
- **D** receptor-mediated endocytosis

8. In an epithelium's junctional complex, the junction nearest the apex is the:

- **A** tight junction
- **B** desmosome
- **C** zonula adherens
- **D** hemidesmosome

9. A Gs-coupled receptor raises the level of:

- **A** IP3, through phospholipase C
- **B** cGMP, through guanylyl cyclase
- **C** cAMP, through adenylyl cyclase
- **D** nothing: it inhibits the cyclase

10. The KDEL signal:

- **A** takes proteins into the nucleus
- **B** targets enzymes to lysosomes
- **C** sends a new protein into the RER
- **D** brings ER proteins back from the Golgi

11. Caveolae are coated with:

- **A** clathrin
- **B** spectrin
- **C** caveolin
- **D** COPI

12. The resting membrane potential of about -70 mV comes mainly from:

- **A** K+ leaking out through leak channels
- **B** Na+ leaking in
- **C** Cl- being pumped out
- **D** Ca2+ released from the ER

13. Adherens junctions link cadherins to the cell's:

- **A** intermediate filaments
- **B** microtubules
- **C** basal lamina
- **D** actin filaments

14. cAMP activates:

- **A** protein kinase C
- **B** protein kinase G
- **C** protein kinase A
- **D** the MAP kinase ERK directly

15. On an electron micrograph, parallel flattened cisternae studded with ribosomes are the:

A smooth endoplasmic reticulum
B Golgi apparatus
C rough endoplasmic reticulum
D mitochondrial cristae

16. Which phospholipid lies mainly in the outer leaflet of the plasma membrane?

A phosphatidylcholine
B phosphatidylinositol
C phosphatidylserine
D phosphatidylethanolamine

17. A membrane protein binds glucose on one side and, by changing shape, releases it on the other without using ATP. It is:

A a carrier (transporter)
B a voltage-gated ion channel
C a ligand-gated ion channel
D a proton pump

18. Losing E-cadherin lets carcinoma cells:

A divide more slowly
B make more tight junctions
C stop making keratin
D leave the epithelium and invade

19. Why does circulating adrenaline act only on some cell types?

A only those cells carry the genes for its receptors
B adrenaline cannot leave the capillaries elsewhere
C other cells destroy it at once
D only those cells express its receptors

20. Proteins that help other proteins fold and keep them from aggregating are:

A proteasomes
B chaperones
C cyclins
D ribozymes

Answers · practice figures

Figure 1 · The cell membrane in detail

1 Protein channel
2 Globular protein
3 Glycoprotein
4 Cholesterol
5 Glycolipid
6 Peripheral protein
7 Integral protein
8 Filaments of cytoskeleton
9 Carbohydrate
10 Hydrophilic heads
11 Phospholipid molecule
12 Hydrophobic tails
13 Alpha-helix protein
14 Surface protein

Figure 2 · The fluid mosaic of a cell membrane

1 Glycoprotein
2 Glycolipid
3 Peripheral membrane protein
4 Integral membrane protein
5 Cholesterol
6 Channel protein
7 Phospholipid bilayer

Figure 3 · Two layers of lipid, seen edge on

1 Hydrophobic tail
2 Hydrophilic head
3 Extracellular
4 Intracellular
5 Phospholipid bilayer

Figure 4 · A spot weld between two cells

1 Plasma membrane
2 Keratin filaments
3 Attachment plaque
4 Cadherin
5 Extracellular space

Figure 5 · Cells sealed together near their apical surface

1 Tight junctions
2 Lumen
3 Mucus layer
4 Apical side
5 Basolateral surface
6 Protein complex
7 Paracellular space
8 Plasma membrane

Figure 6 · Channels joining two cells

1 Connexon
2 Connexin monomer
3 Plasma membranes
4 Intercellular space
5 Hydrophilic channel
6 Closed connexon
7 Open connexon

Figure 7 · The free surface of two gut lining cells (TEM)

1 Microvilli
2 Tight junction

Figure 8 · A liver cell from an ethanol-fed rat (TEM)

1 Golgi apparatus
2 Mitochondrion
3 Smooth endoplasmic reticulum

Figure 9 · A newborn rat's liver cell (TEM)

1 Rough endoplasmic reticulum
2 Golgi apparatus
3 Glycogen

Figure 10 · A pancreatic acinar cell making its export protein (TEM)

1 Rough endoplasmic reticulum
2 Golgi apparatus
3 Golgi vesicles

Figure 11 · A second atrial muscle cell from a guinea pig (TEM)

1 Nucleus
2 Myofibrils
3 Atrial granule
4 Glycogen

Figure 12 · A young rat's liver cell, two kinds of reticulum (TEM)

1 Smooth endoplasmic reticulum
2 Rough endoplasmic reticulum
3 Glycogen

Figure 13 · An adult rat's liver cell (TEM)

1 Rough endoplasmic reticulum
2 Mitochondrion
3 Glycogen

Figure 14 · An animal cell and its parts

1 Mitochondria
2 Intermediate filament
3 Plasma membrane
4 Ribosomes
5 Microtubule
6 Rough endoplasmic reticulum
7 Centrosome
8 Nucleus
9 Nucleolus
10 Microfilament
11 Chromatin
12 Lysosome
13 Golgi apparatus
14 Smooth endoplasmic reticulum
15 Secretory vesicle
16 Golgi vesicle
17 Peroxisome
18 Cytoplasm
19 Vacuole

Figure 15 · An animal cell, drawn in colour

1 Nucleus
2 Nucleolus
3 Peroxisome
4 Microtubule
5 Lysosome
6 Free Ribosomes
7 Mitochondrion
8 Plasma membrane
9 Intermediate Filaments
10 Golgi vesicles
11 Ribosomes
12 Rough endoplasmic reticulum
13 Smooth endoplasmic reticulum
14 Actin Filaments
15 Cytoplasm
16 Secretory vesicle
17 Centrosome (with centrioles)
18 Flagellum

Figure 16 · Inside the cell's power plant (guinea pig pancreas, TEM)

1 Cristae
2 Matrix
3 Outer membrane

Figure 17 · Membranes that make and ship proteins

1 Rough endoplasmic reticulum
2 Nucleus
3 Nuclear envelope
4 Nuclear pore
5 Ribosomes
6 Smooth endoplasmic reticulum
7 Secretory vesicle
8 Lysosome
9 Golgi apparatus
10 Plasma membrane

Figure 18 · The cell's power plant, cut open

1 ATP synthase particles
2 Intermembrane space
3 Matrix
4 Cristae
5 Ribosome
6 Granules
7 Inner membrane
8 Outer membrane

Figure 19 · The lining of the human duodenum, catalase stained (EM)

1 Microvilli
2 Lysosome
3 Peroxisome

Figure 20 · Where three liver cells meet (TEM)

1 Mitochondrion
2 Bile canaliculus

Answers · self-test

1 D buffers fluidity against temperature changes — At body temperature cholesterol restrains phospholipid movement; in the cold it keeps the chains from packing tightly, so fluidity stays steady.

2 C 3 Na+ out and 2 K+ in — It keeps the gradients that the resting membrane potential depends on.

3 B gap junction — Connexons of six connexins form the channels.

4 A phospholipase C — Phospholipase C makes IP3 and DAG.

5 B makes lipids and steroids and detoxifies (cytochrome P450) — The rough ER makes secretory and membrane proteins.

6 B cytosol (inner leaflet) — It sits on the inner leaflet; moved to the outer leaflet it becomes the "eat me" signal of apoptosis.

7 B simple diffusion — Small non-polar molecules dissolve in the bilayer and diffuse down their gradient (Fick).

8 A tight junction — Then come the zonula adherens and the desmosome.

9 C cAMP, through adenylyl cyclase — Gs stimulates adenylyl cyclase; Gq activates phospholipase C; Gi inhibits the cyclase.

10 D brings ER proteins back from the Golgi — Proteins that belong in the ER and escape to the Golgi are returned by KDEL receptors.

11 C caveolin — Flask-shaped pits of the plasma membrane, common in endothelial and fat cells; clathrin coats the pits of receptor-mediated endocytosis.

12 A K+ leaking out through leak channels — K+ leaks out down its gradient, leaving the inside negative; the Na+/K+-ATPase keeps the gradients.

13 D actin filaments — The zonula adherens ties cadherins to a belt of actin; desmosomes tie theirs to intermediate filaments.

14 C protein kinase A — cAMP-PKA; DAG and Ca2+ activate PKC; cGMP activates PKG.

15 C rough endoplasmic reticulum — The SER is a tangle of ribosome-free tubules; the Golgi a curved stack of smooth cisternae with vesicles; cristae lie within a double membrane.

16 A phosphatidylcholine — Phosphatidylcholine, with sphingomyelin, faces outward; phosphatidylserine, phosphatidylethanolamine and phosphatidylinositol mostly face the cytosol.

17 A a carrier (transporter) — Alternating access marks a carrier such as GLUT1; channels open a pore, and pumps spend ATP.

18 D leave the epithelium and invade — Cells that let go of their neighbours can migrate: the epithelial-mesenchymal transition.

19 D only those cells express its receptors — Every cell has the same genome but expresses a different set of genes; a cell without the receptor cannot respond.

20 B chaperones — Chaperones such as the heat-shock proteins bind the exposed hydrophobic patches of unfolded chains.