

# Physics of Life

PHYS-468

## **The Structure of Life**



# Biological cells

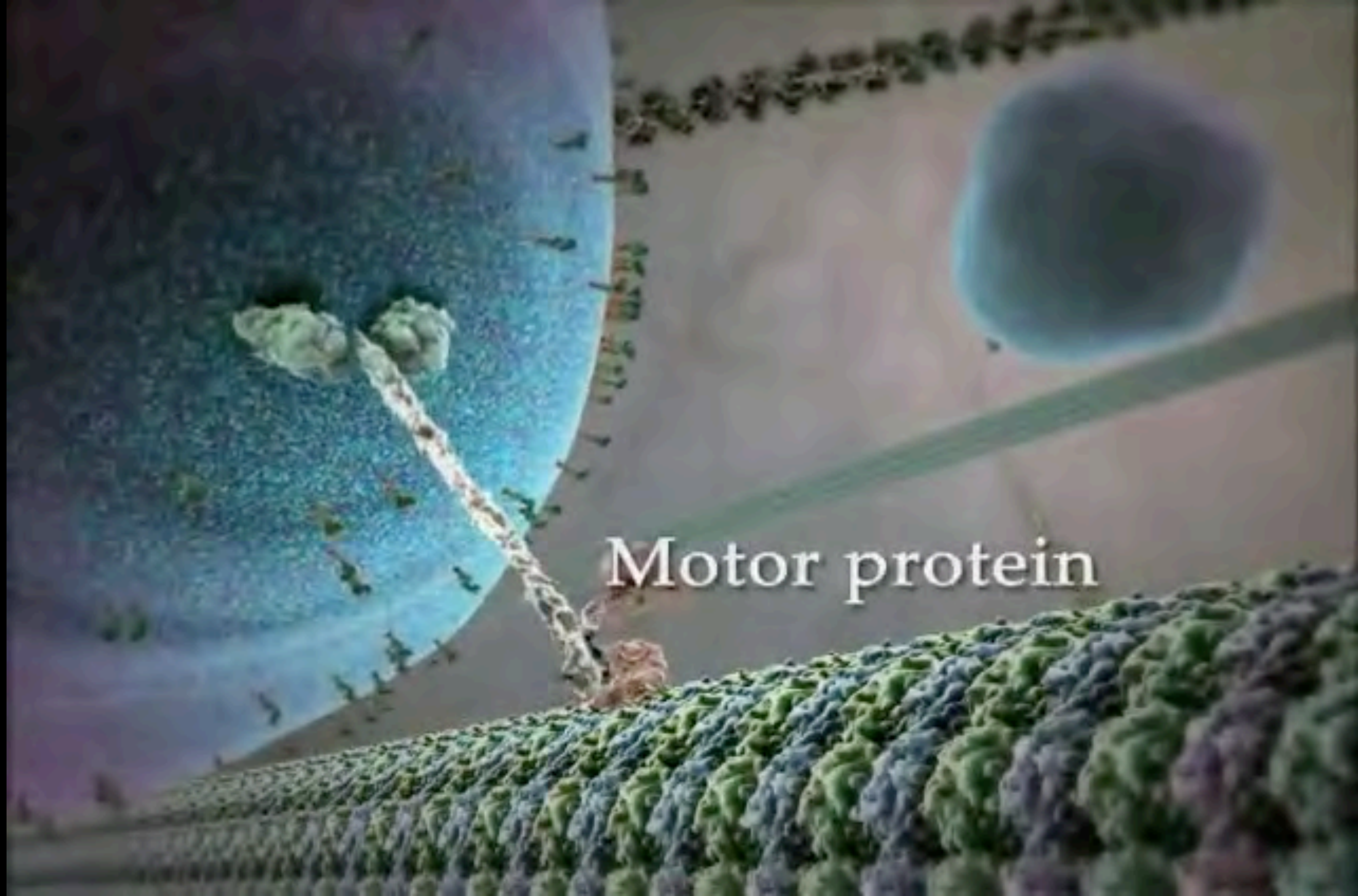
Biological cells are mechanical machines that follow the laws of physics:

- Mechanics
- Thermodynamics
- Electrostatics
- Quantum Dynamics

## Cells feature

- Self-organization
- Communication
- Self-healing
- Self-protection
- Memory
- Regeneration
- Dynamics
- Variation
- Specialization

**We are cells.**



**Motor protein**

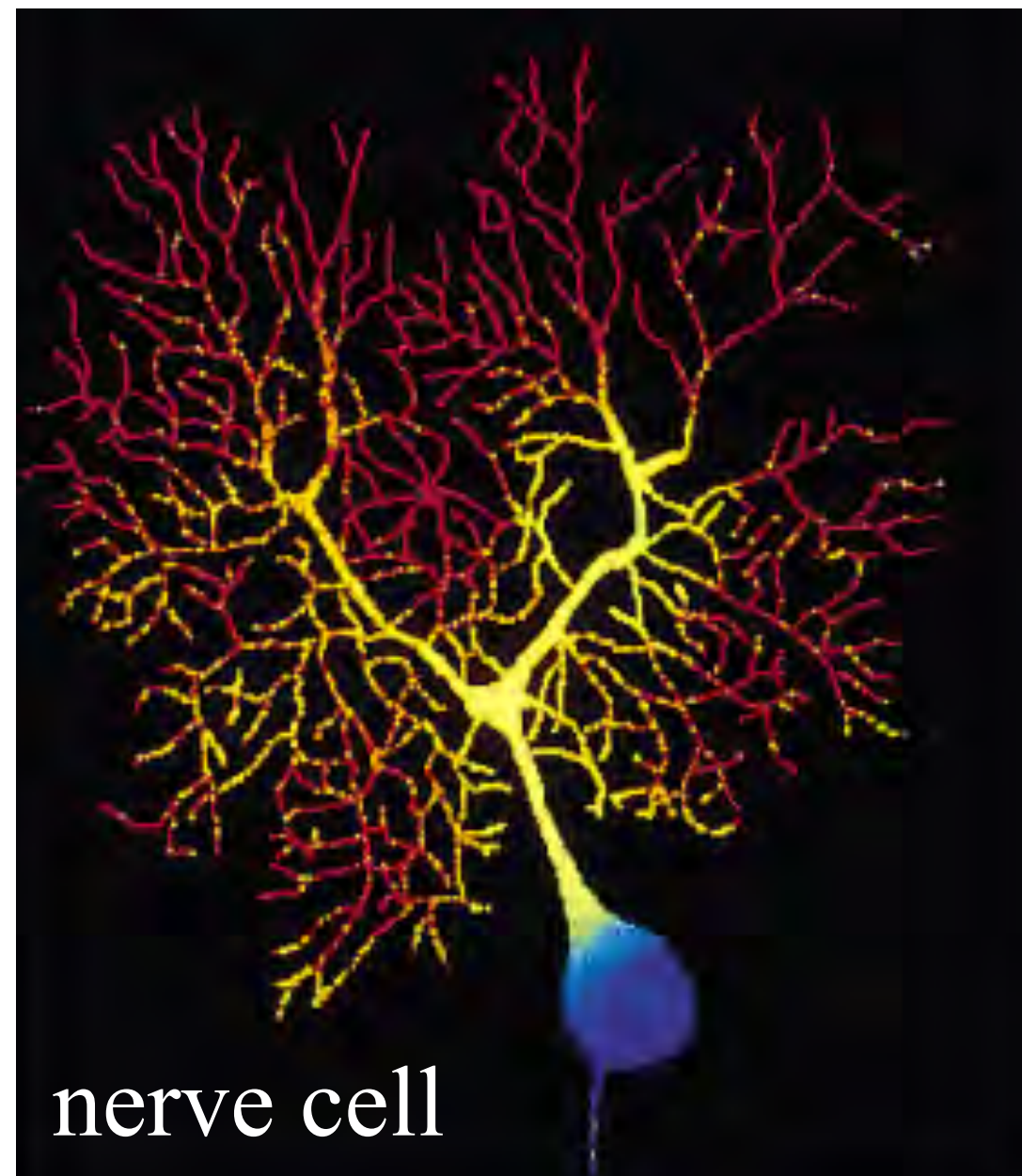


# Cells are Us

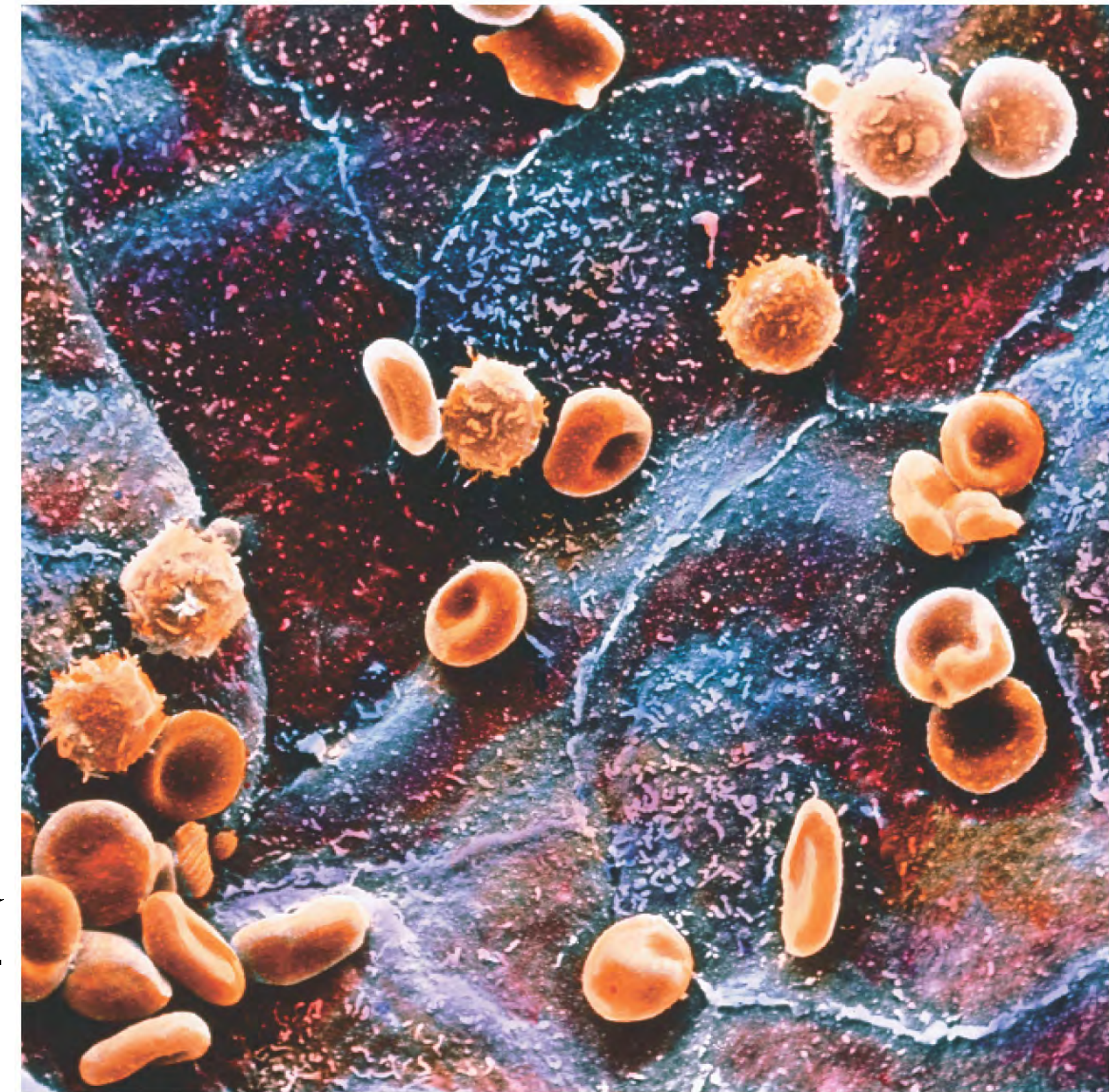
A person contains about 100 trillion ( $10^{14}$ ) cells.

There are about 200 different cell types in one person.

Cells have on average a diameter of  $20\text{ }\mu\text{m}$ .  
There are on average 50 cells per mm.



Red and white blood  
cells above vessel-  
forming cells.





# The Cell Theory

The cell theory (proposed independently by Schleiden in 1838 and Schwann in 1839) is a cornerstone of biology.

All organisms are composed of one or more cells.

Cells are the smallest living things.

Cells arise only by division of previously existing cells.

All organisms living today are possibly the descendants of a single ancestral cell.



Matthias Jakob Schleiden  
1804 – 1881



Theodor Schwann  
1810 – 1882



# Intestinal bacteria

Martin Oeggerli  
*aka.*  
[micronaut.ch](http://micronaut.ch)





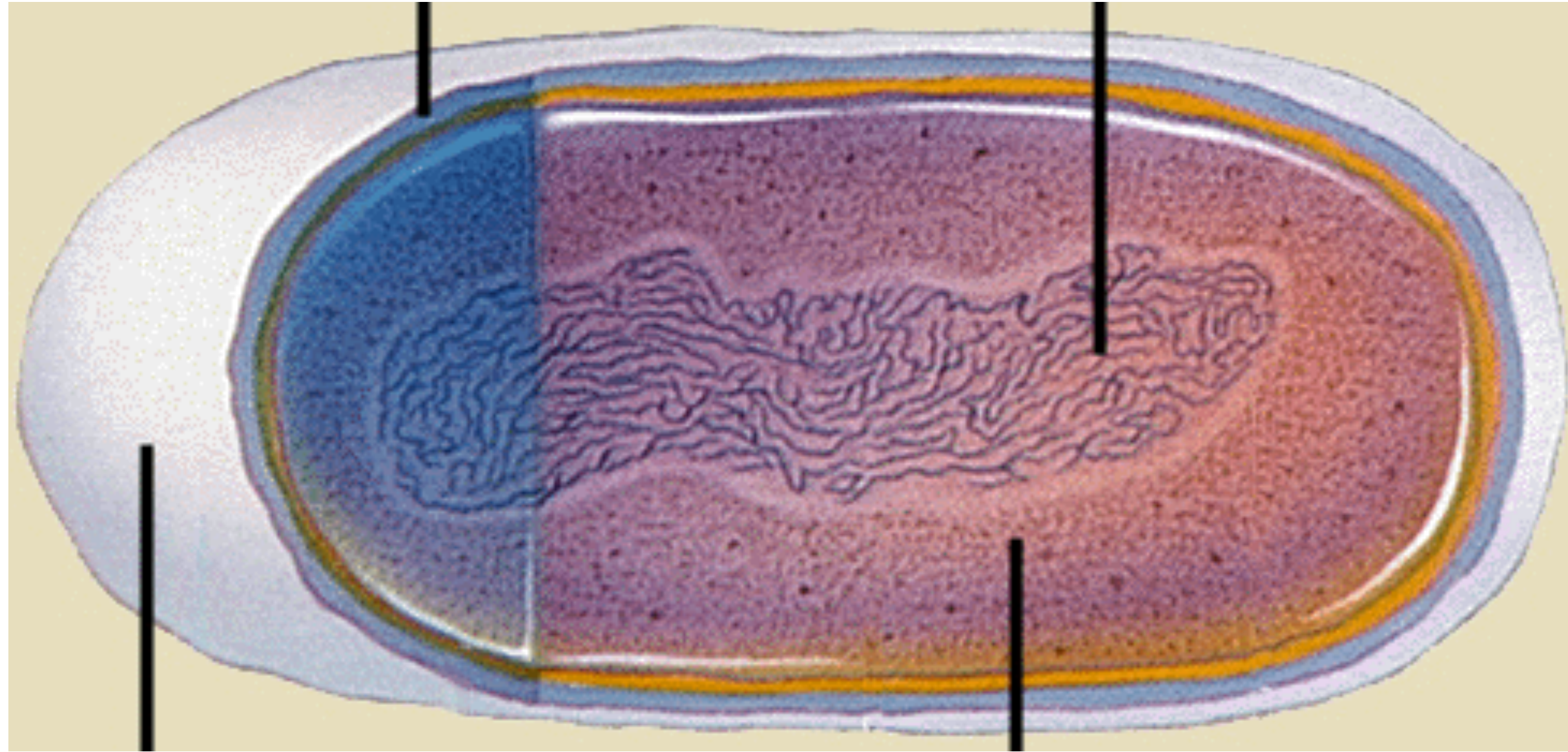
*Helicobacter Pylori*  
bacteria on gut cells



Martin Oeggerli  
*aka.*  
[micronaut.ch](http://micronaut.ch)



# Two Fundamentally Different Types of Cells



A prokaryotic cell

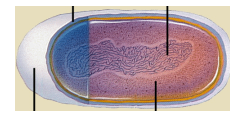


A eukaryotic cell



# Two Fundamentally Different Types of Cells

.... at the same scale



A prokaryotic cell

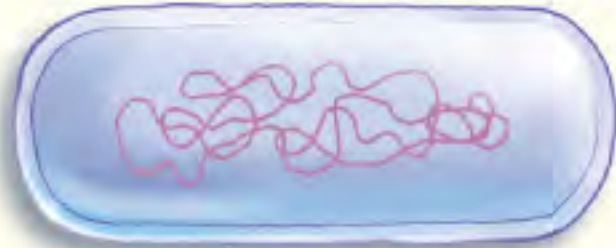




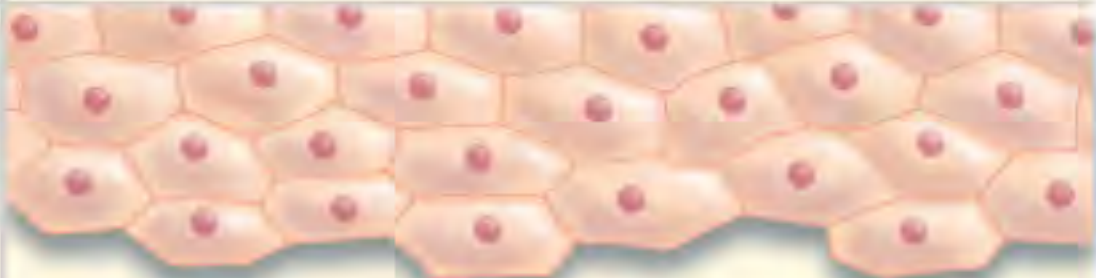






A eukaryotic cell



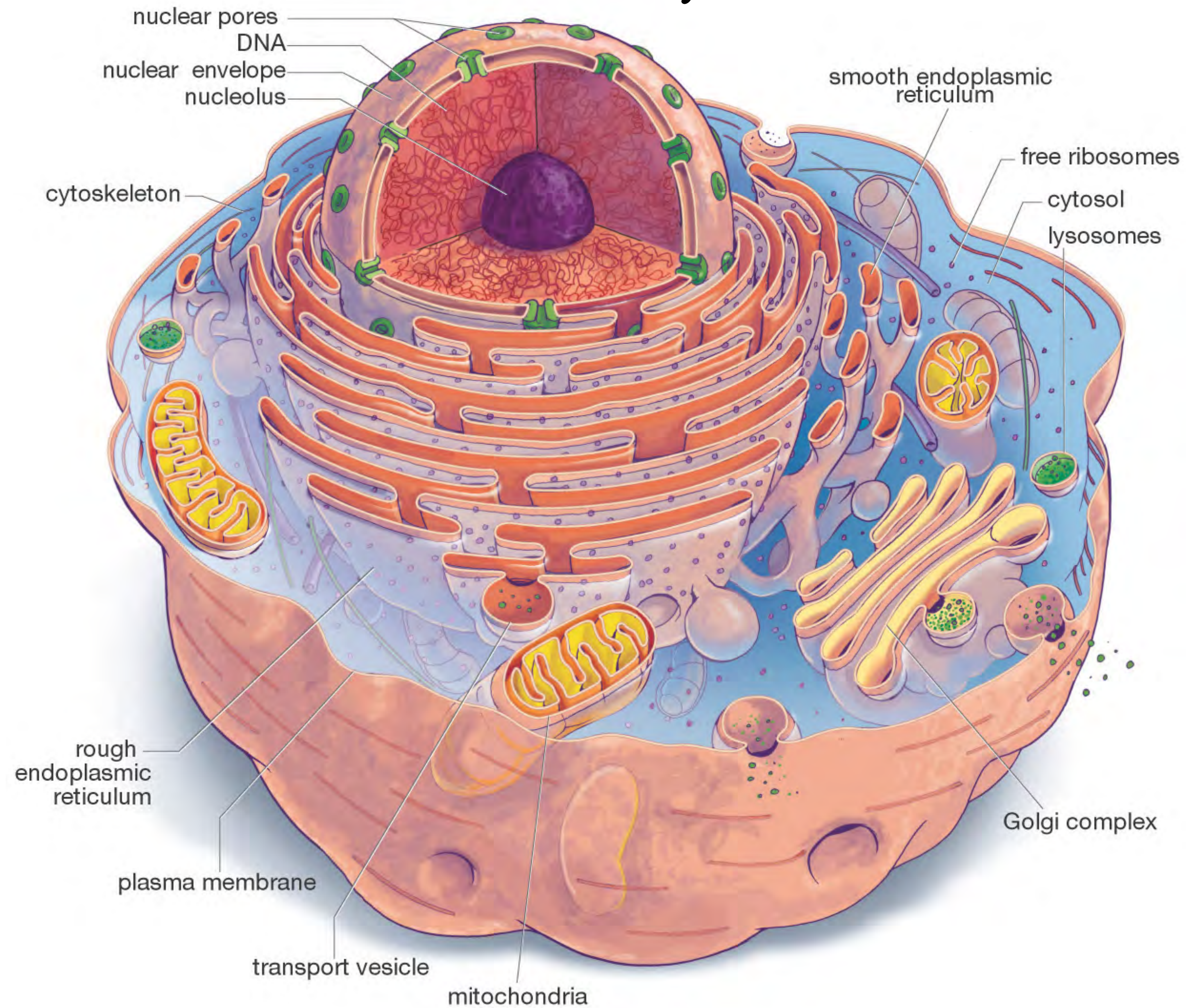
Us *vs.* Them

# Eukaryotes and Prokaryotes

	Prokaryotes	Eukaryotes
DNA	 in “nucleoid” region	 within membrane-bound nucleus
Size	 usually smaller	 usually larger
Organization	 usually single-celled	 often multicellular
Metabolism	 may not need oxygen	 usually need oxygen to exist
Organelles	 no membrane-bound organelles	 membrane-bound organelles

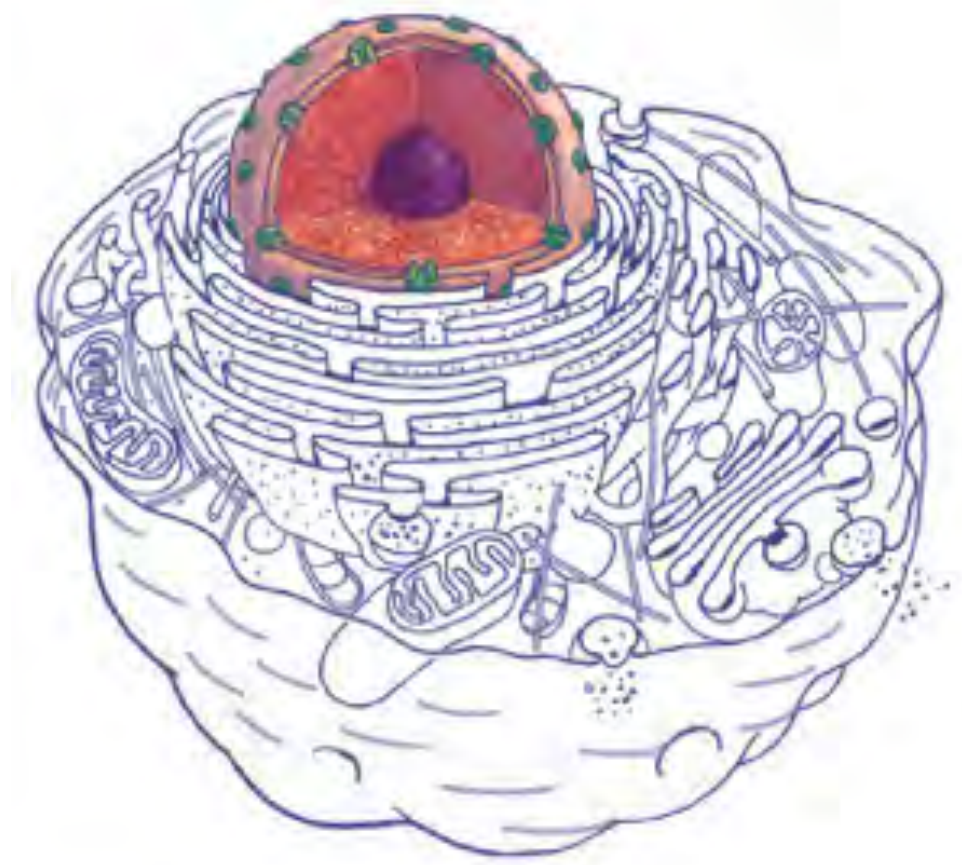


# A Stylized Animal Cell

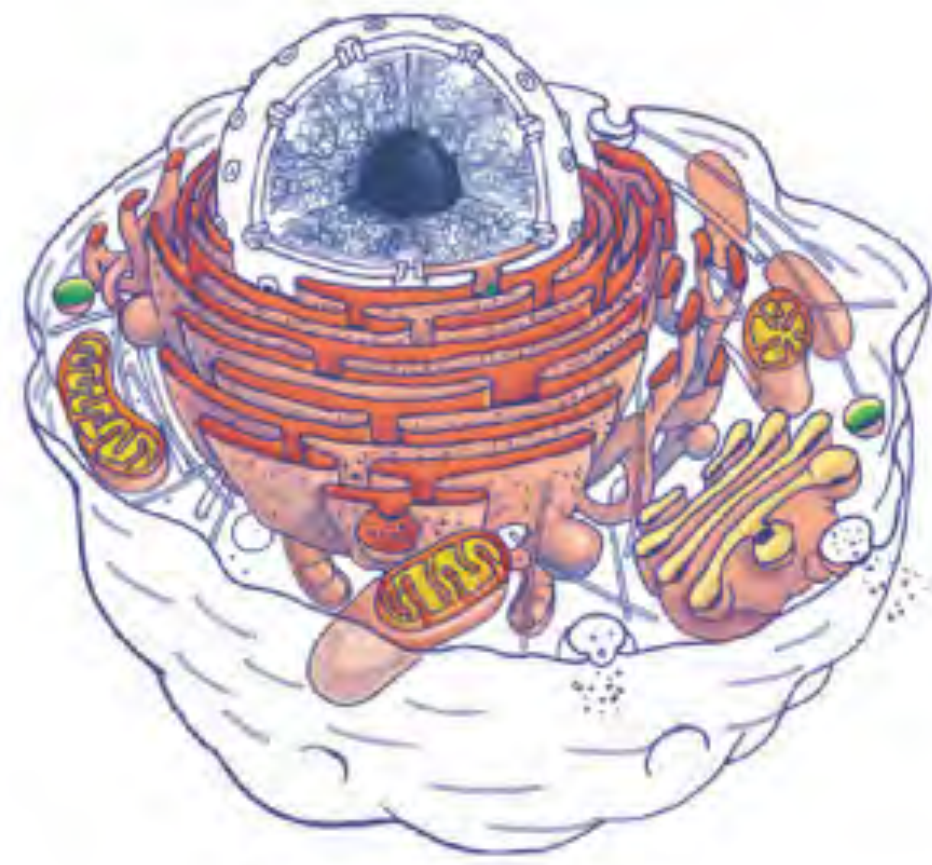




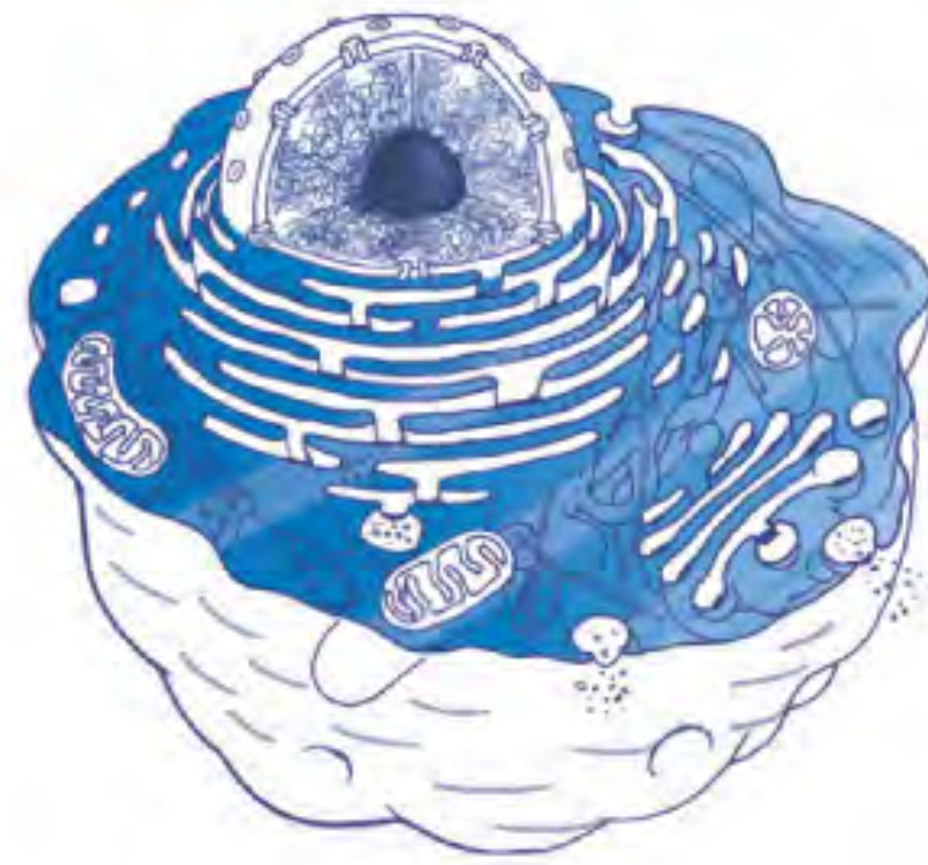
# Major Divisions of the Eukaryotic Cell



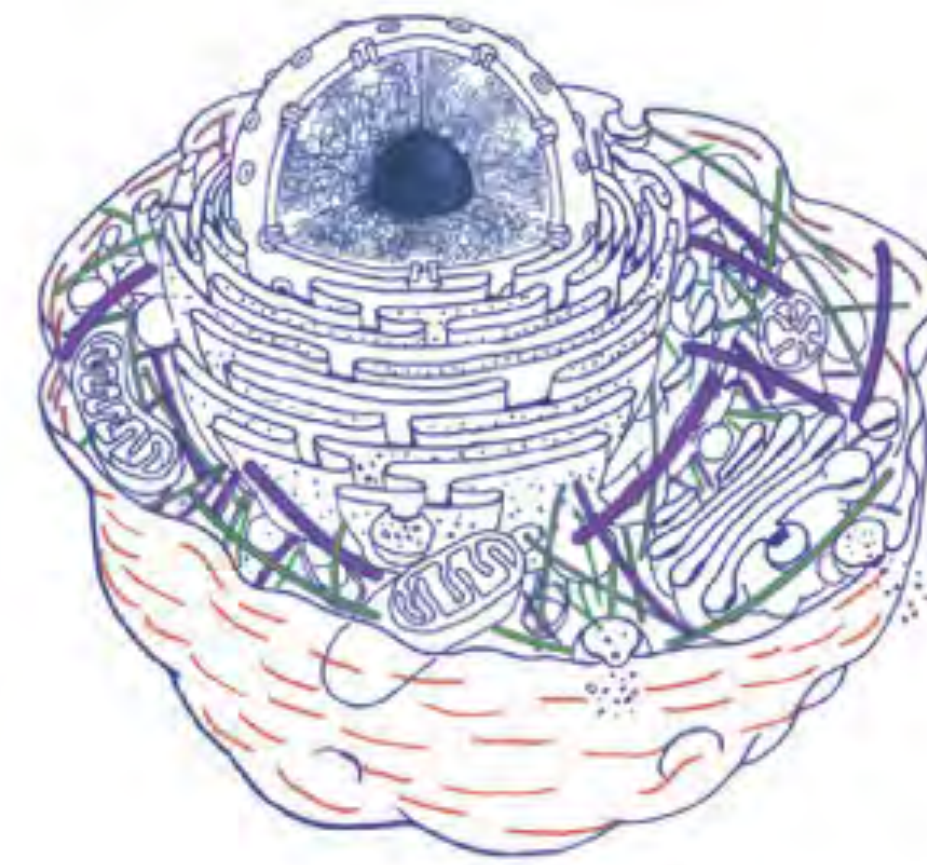
nucleus



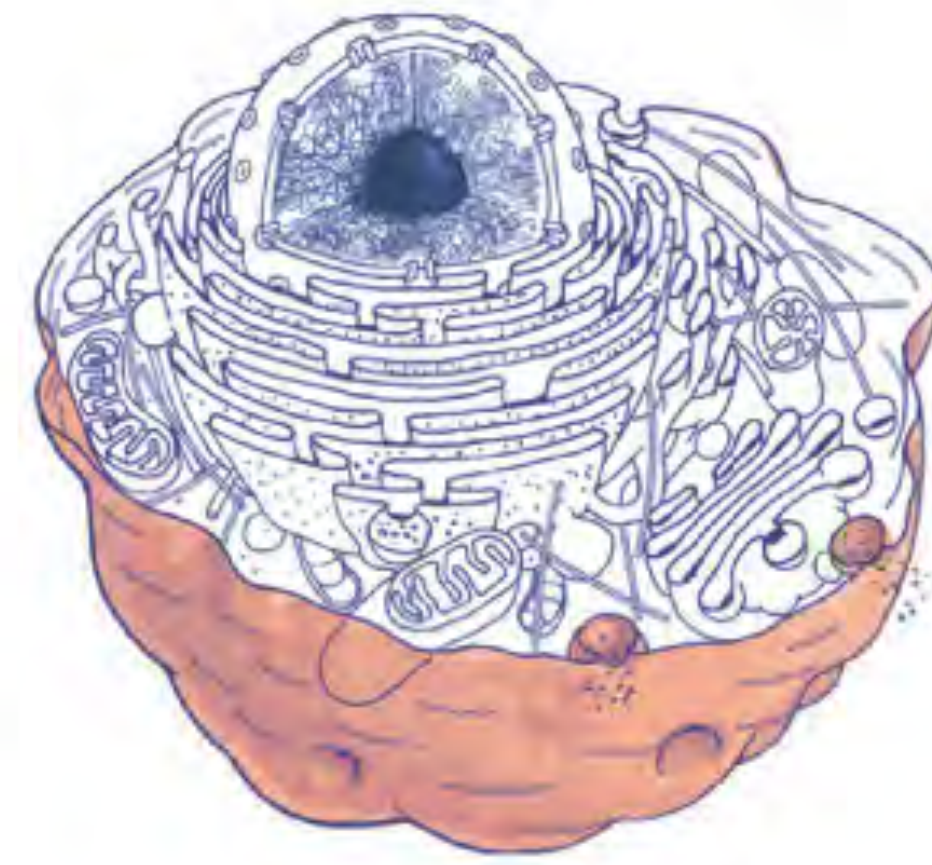
other organelles



cytosol

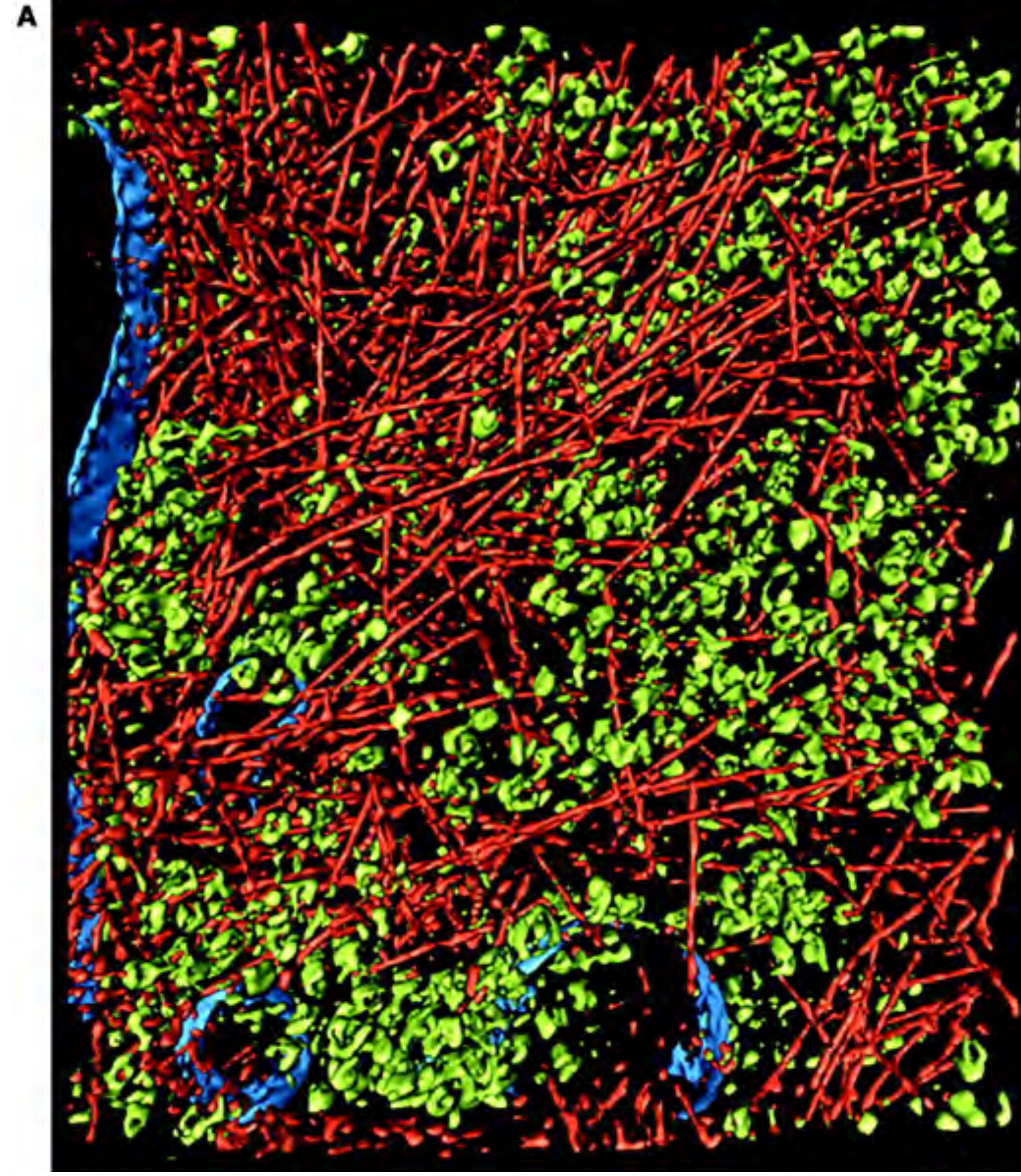
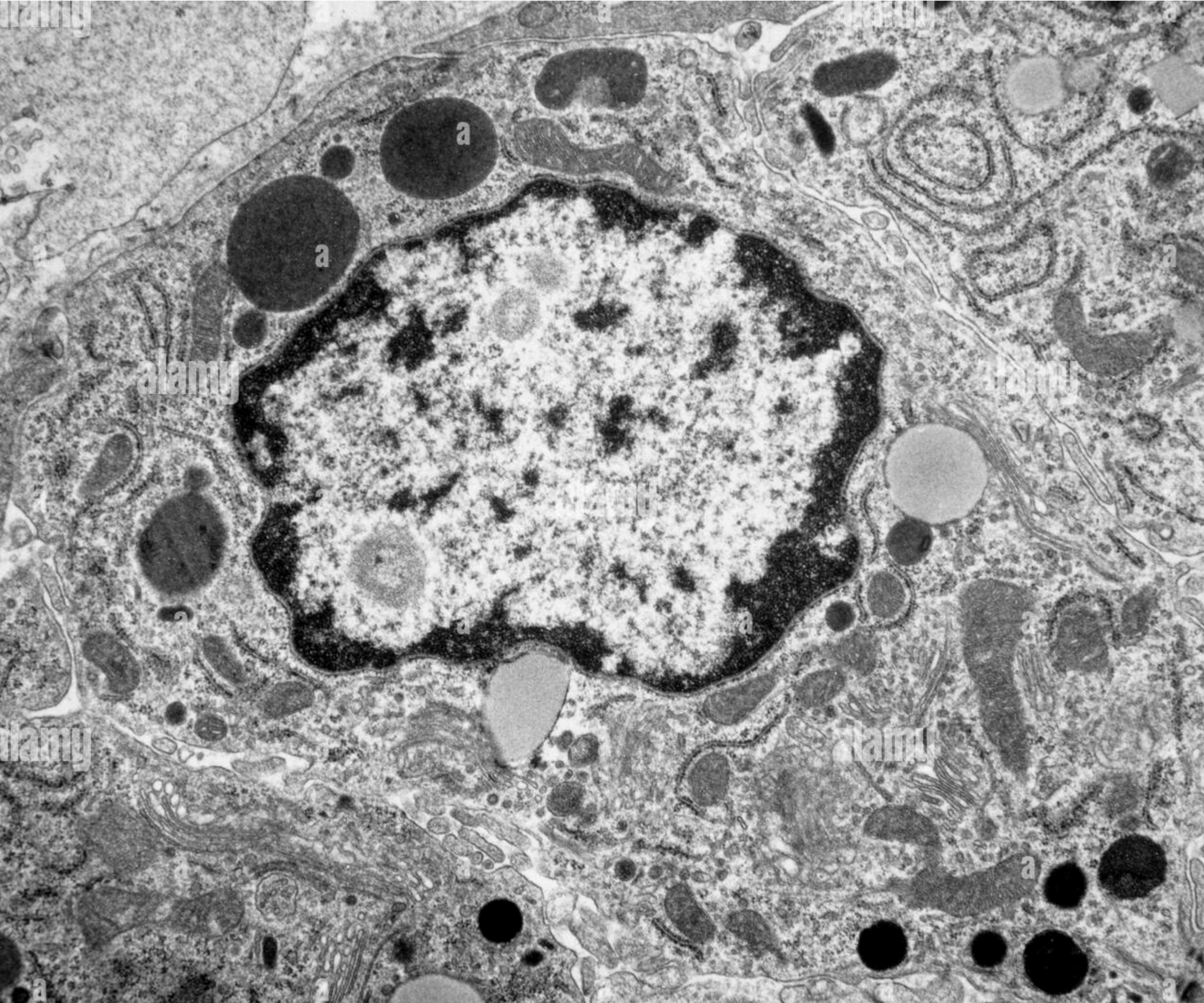


cytoskeleton



plasma membrane



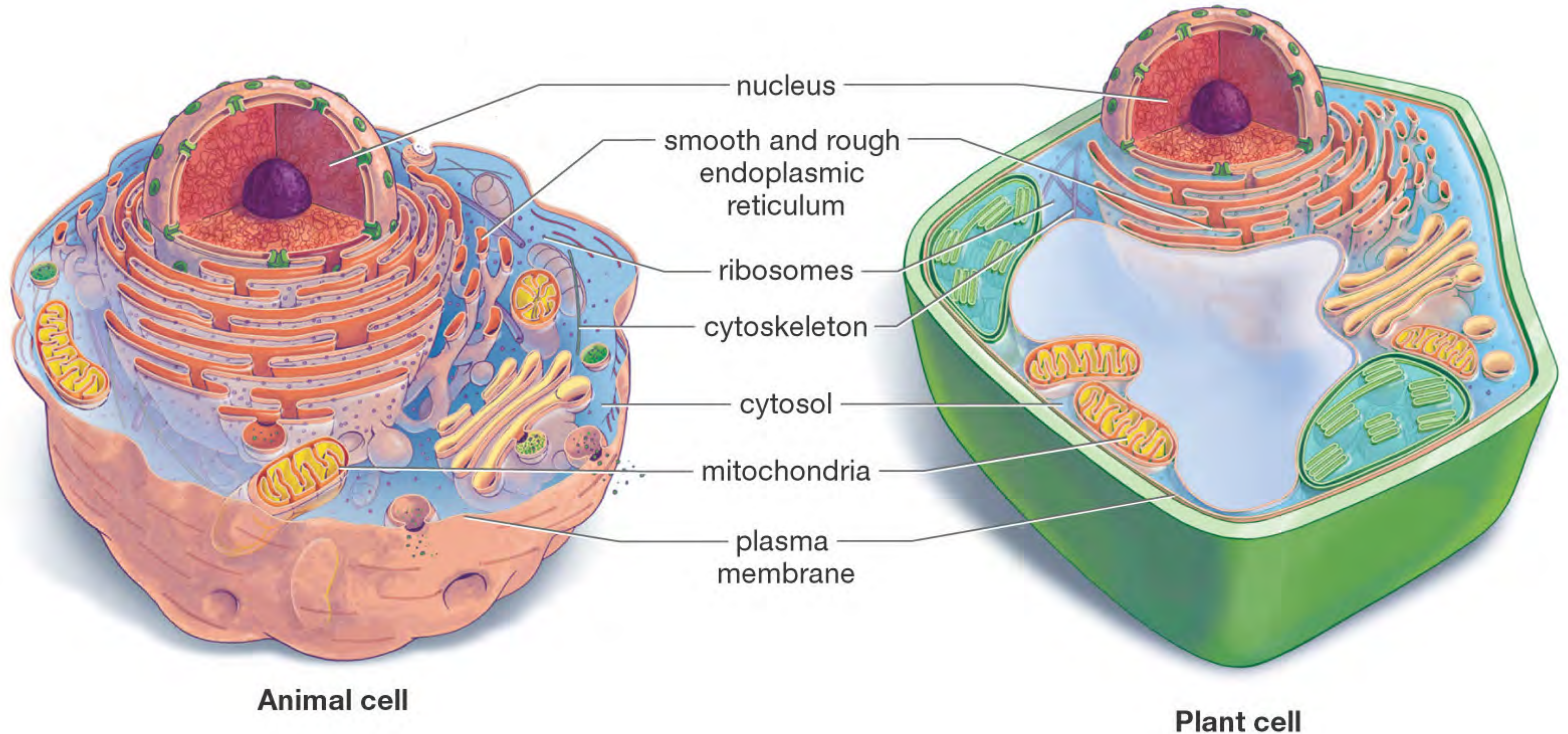


A 3D reconstruction of a cell, showing cytoskeleton (red), ribosomes (green), and membrane (blue)

It's Crowded In There

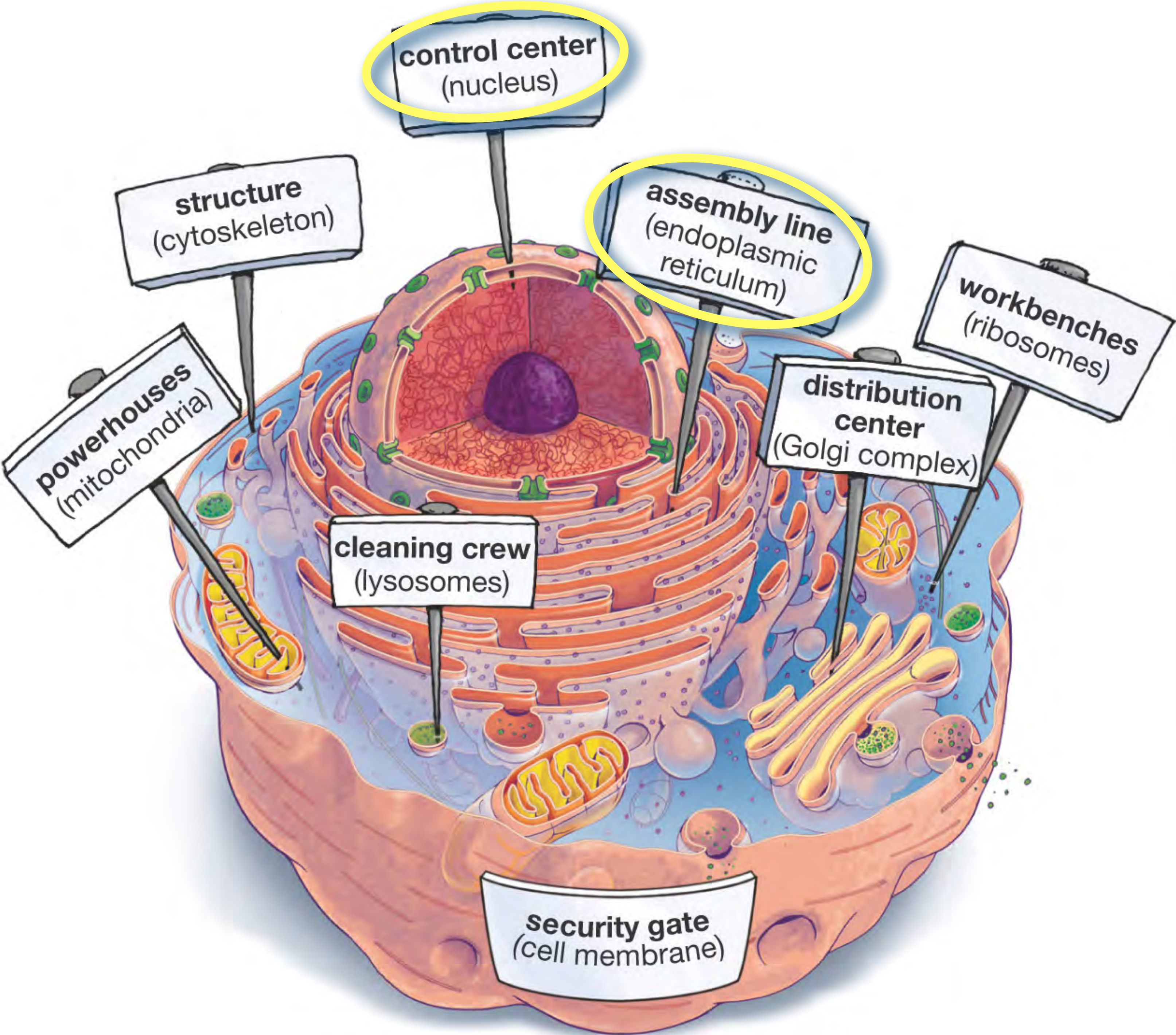


# Animal and Plant Cells Have More Similarities Than Differences



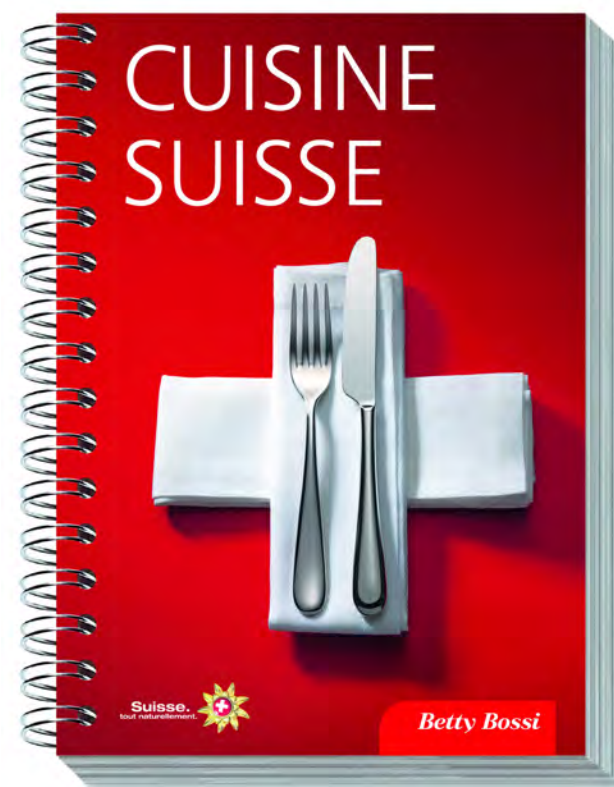
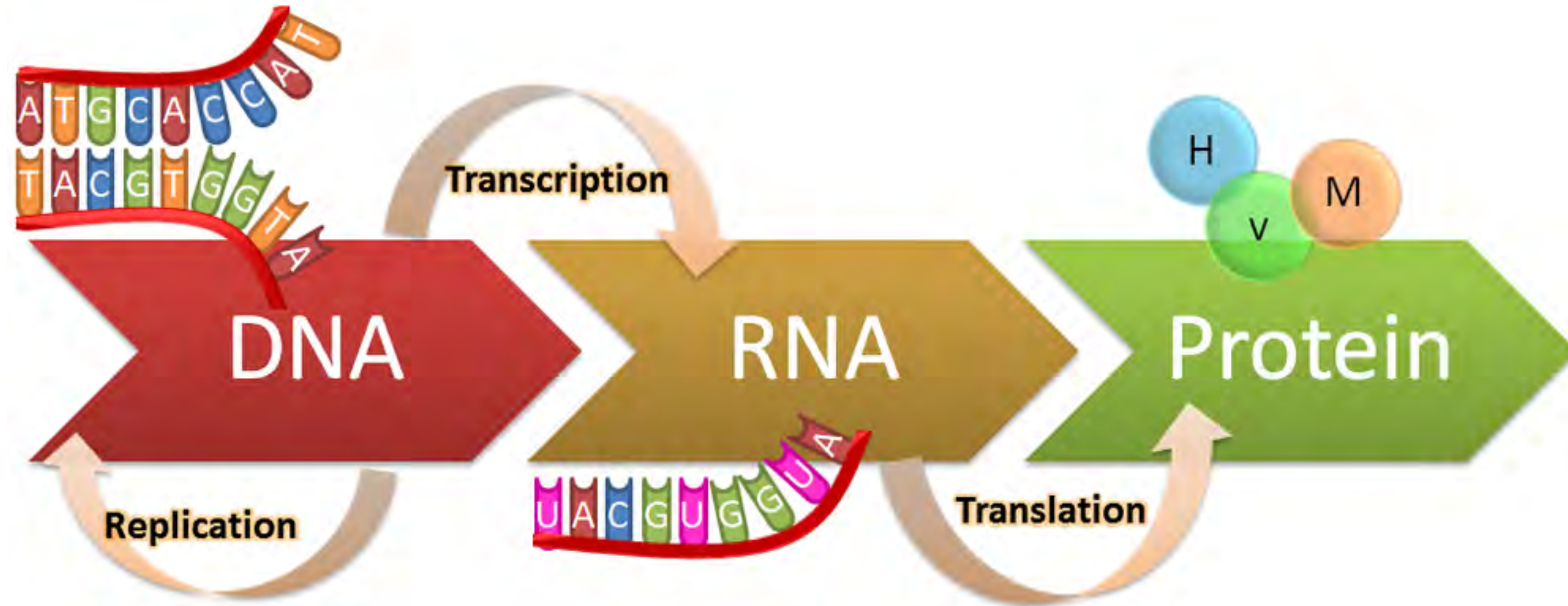


# Cellular Anatomy





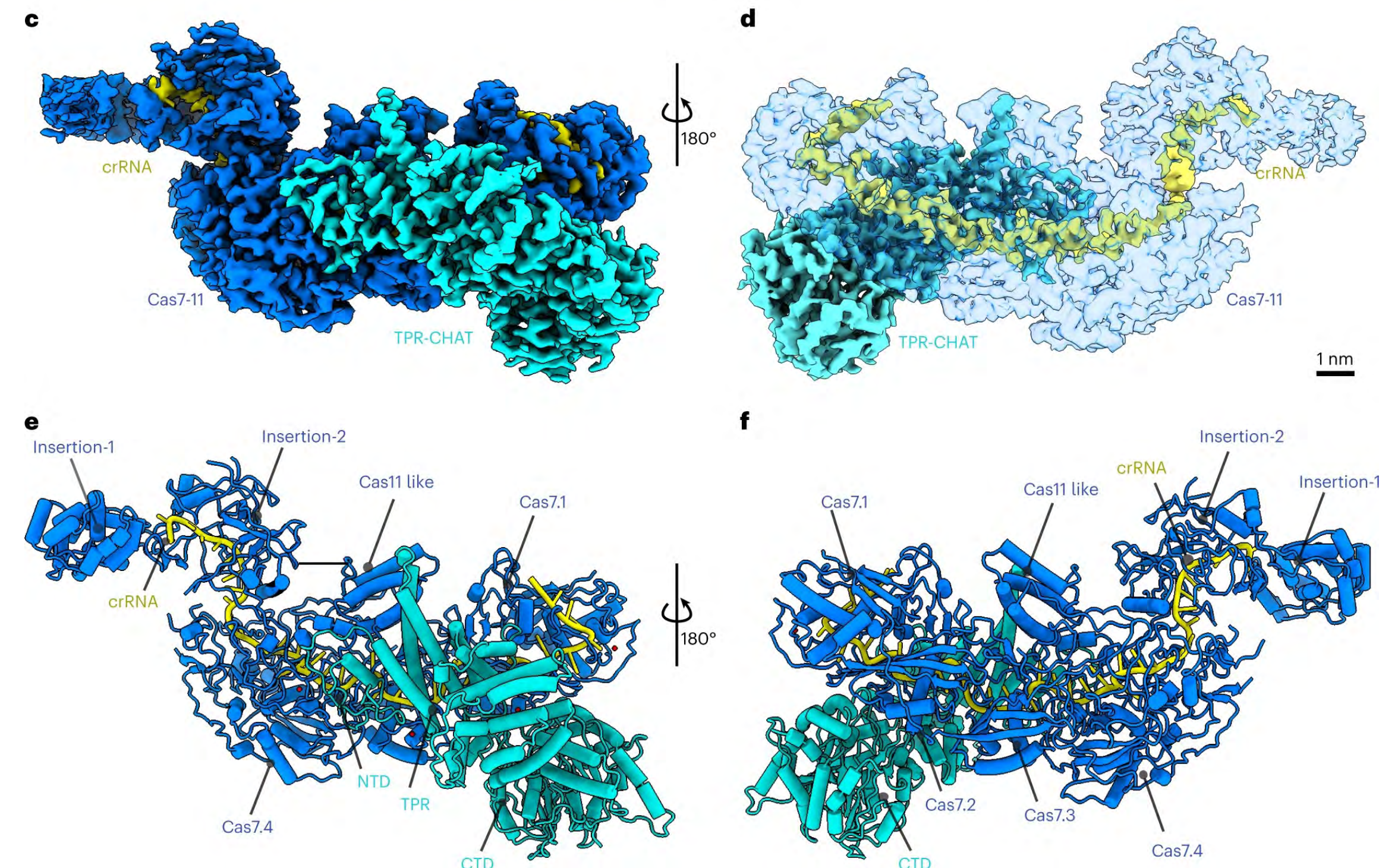
# Central Dogma of Biology





# What are proteins?

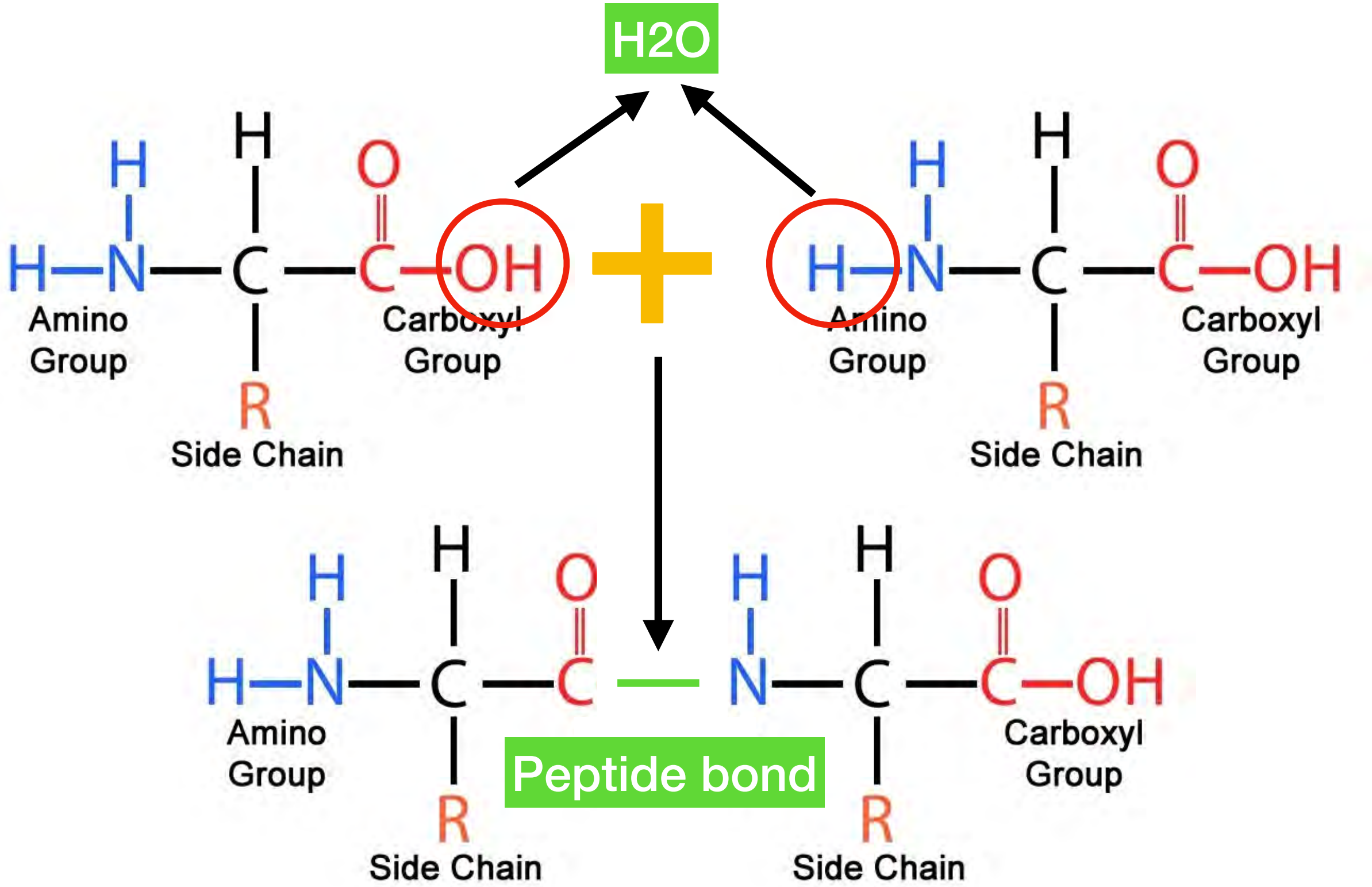
- Proteins are large & complex molecules
- Play many critical roles in the cells
- Made of amino acid
- Examples: antibody, several hormones, contractile proteins  
e.g. myosin, enzymes...



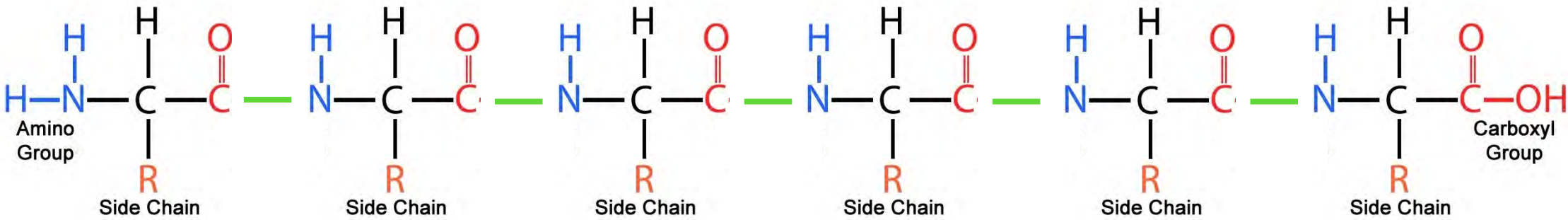


# Amino Acids

R



Protein



Twenty-One Amino Acids

Positive Negative  
Side chain charge at physiological pH 7.4

A. Amino Acids with Electrically Charged Side Chains

Positive

Arginine (Arg) **R**

Histidine (His) **H**

Lysine (Lys) **K**

Negative

Aspartic Acid (Asp) **D**

Glutamic Acid (Glu) **E**

B. Amino Acids with Polar Uncharged Side Chains

Serine (Ser) **S**

Threonine (Thr) **T**

Asparagine (Asn) **N**

Glutamine (Gln) **Q**

C. Special Cases

Cysteine (Cys) **C**

Selenocysteine (Sec) **U**

Glycine (Gly) **G**

Proline (Pro) **P**

D. Amino Acids with Hydrophobic Side Chain

Alanine (Ala) **A**

Isoleucine (Ile) **I**

Leucine (Leu) **L**

Methionine (Met) **M**

Phenylalanine (Phe) **F**

Tryptophan (Trp) **W**

Tyrosine (Tyr) **Y**

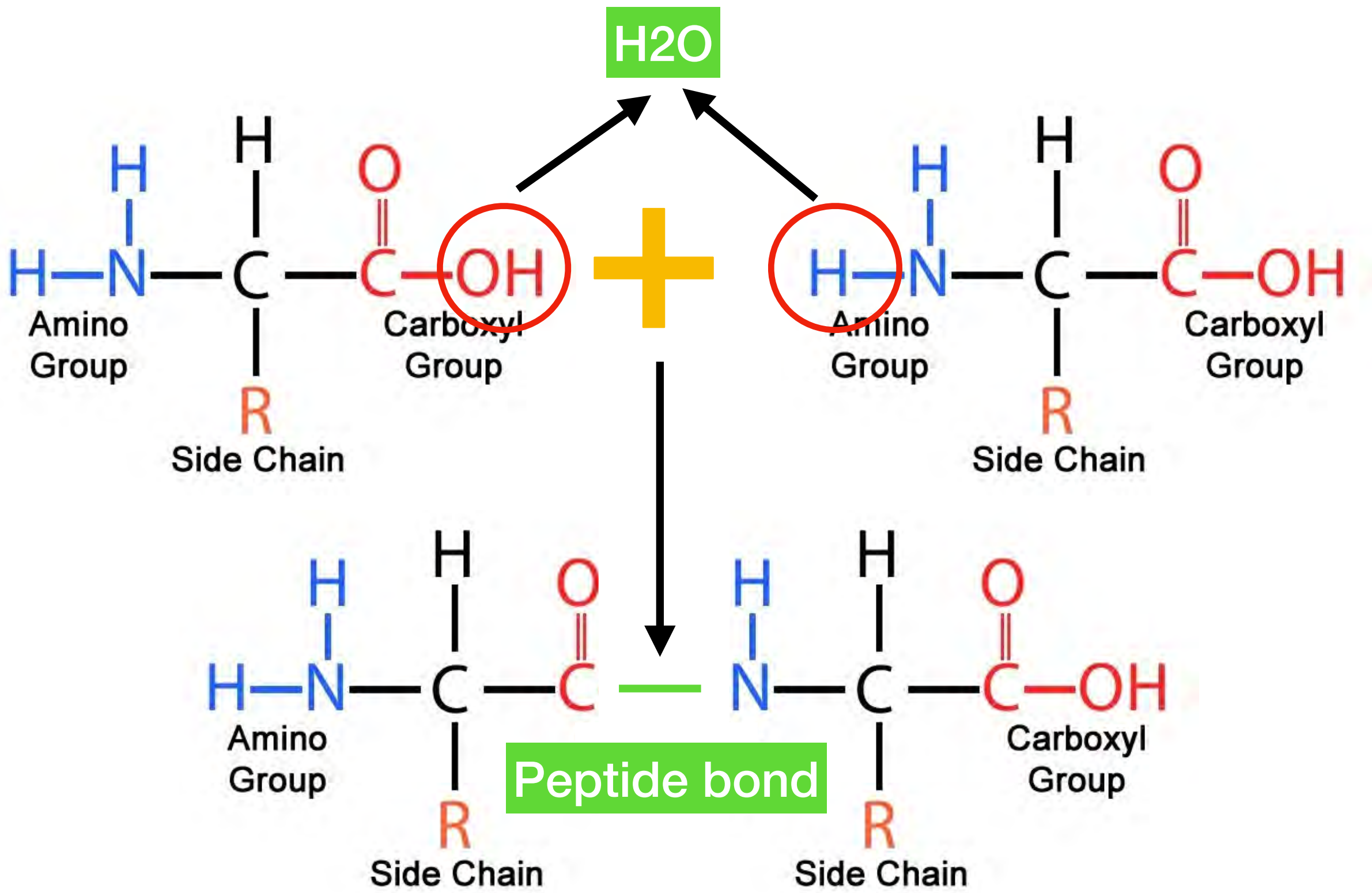
Valine (Val) **V**

pKa Data: CRC Handbook of Chemistry, v.2010

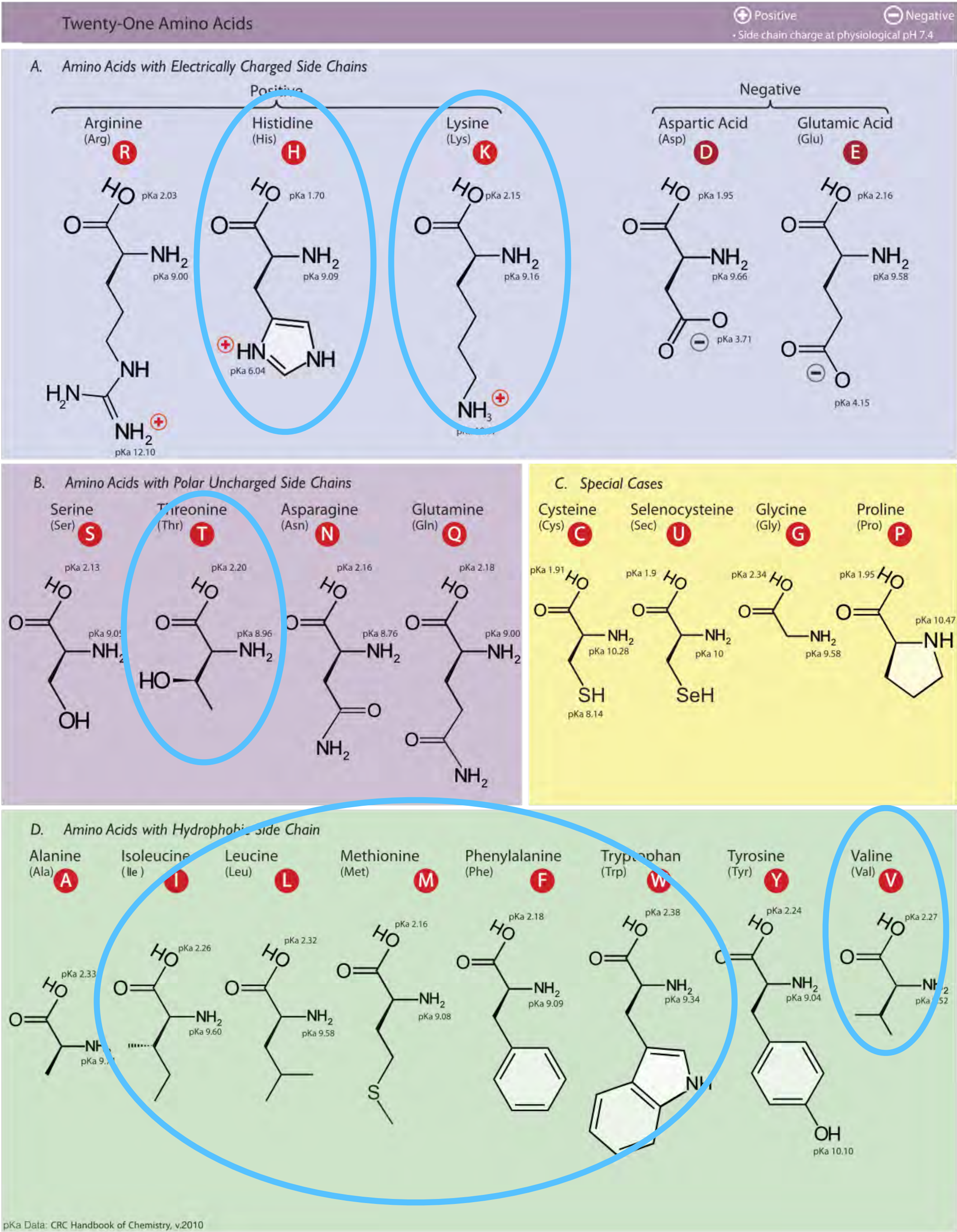
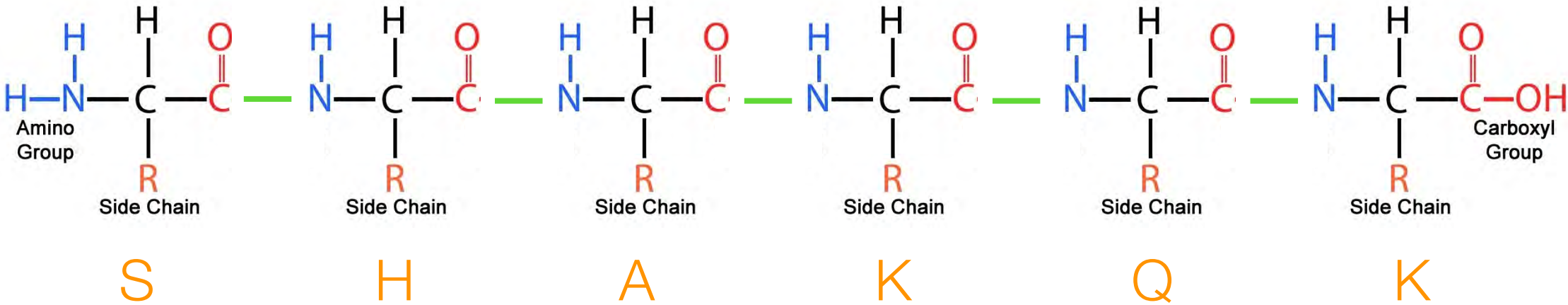


# Amino Acids

R



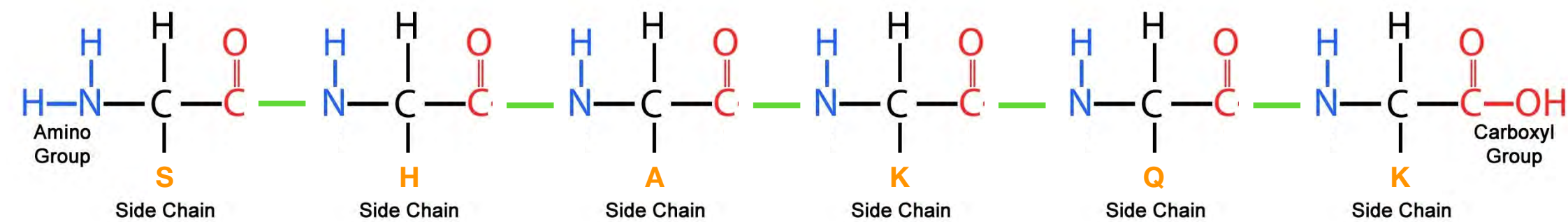
Protein





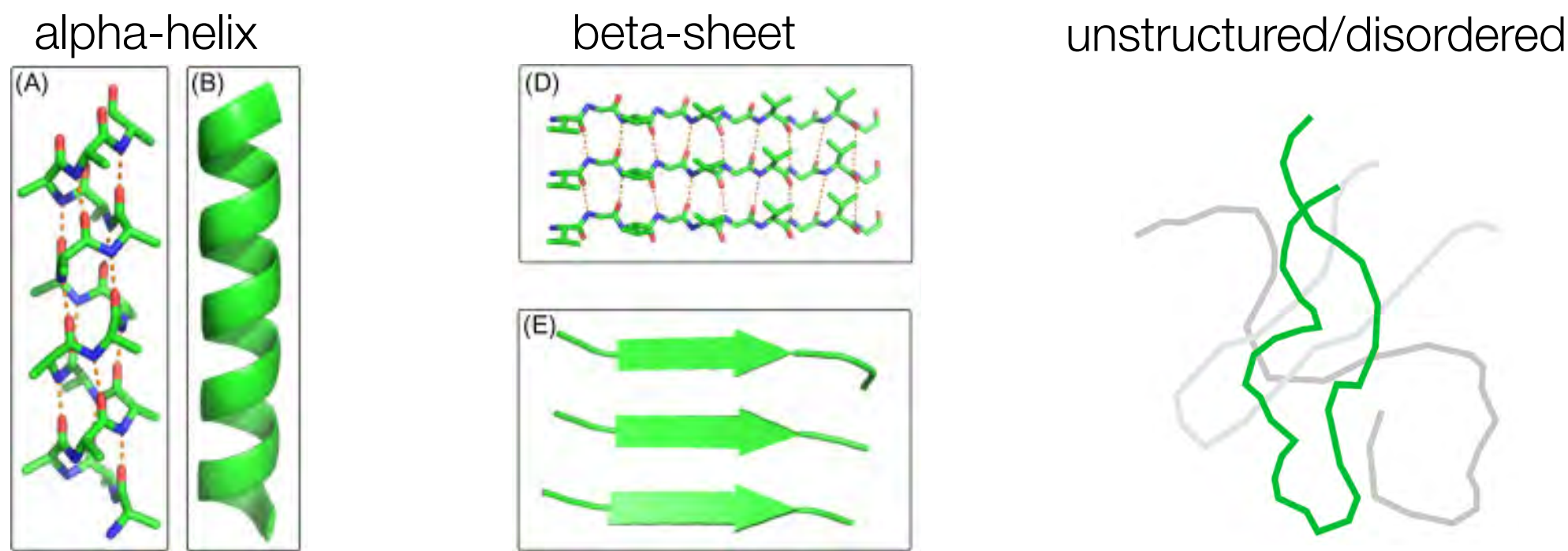
# 4 levels of protein structure

Primary



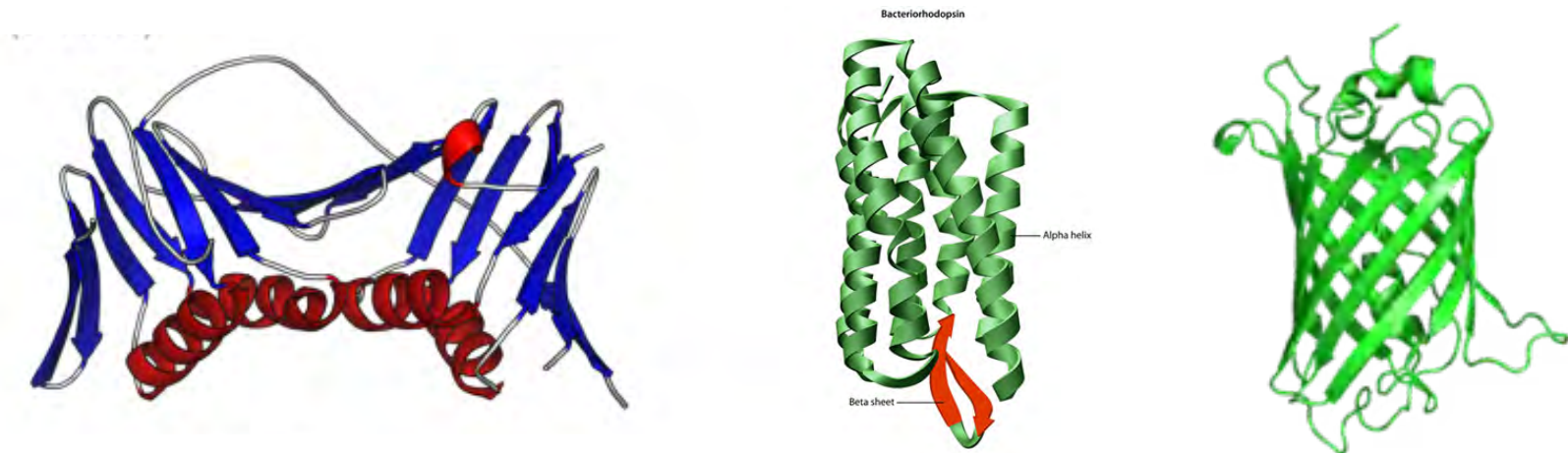
Amino acid sequence  
(up to 27,000 amino acids)

Secondary



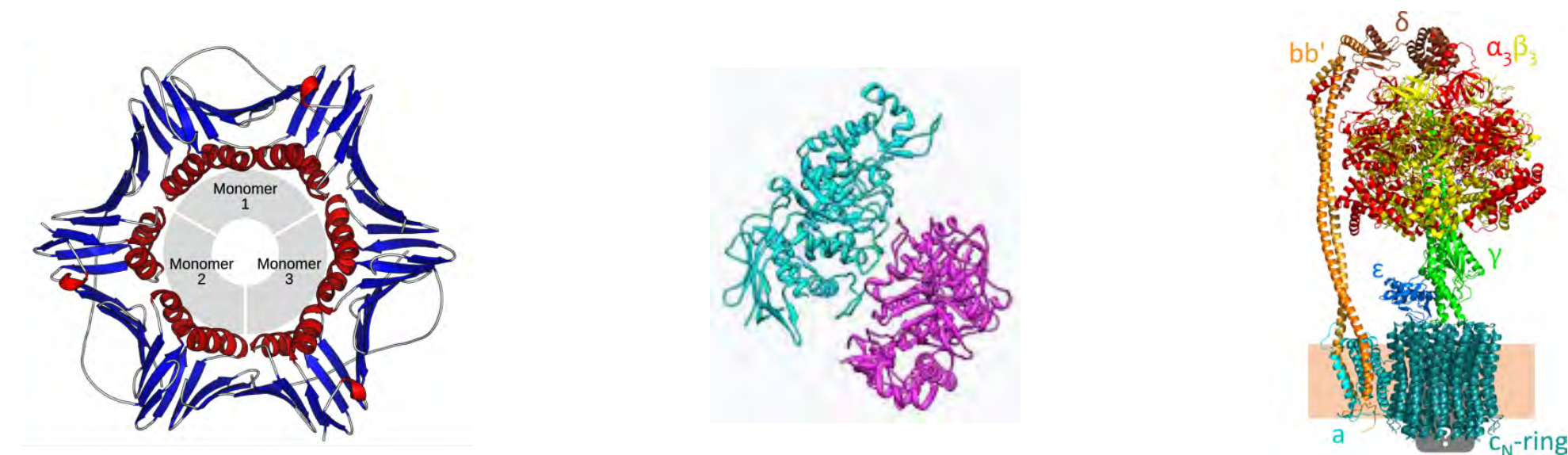
hydrogen bonding of the peptide backbone

Tertiary



interactions of the side chains  
(electrostatic interactions, salt bridges)

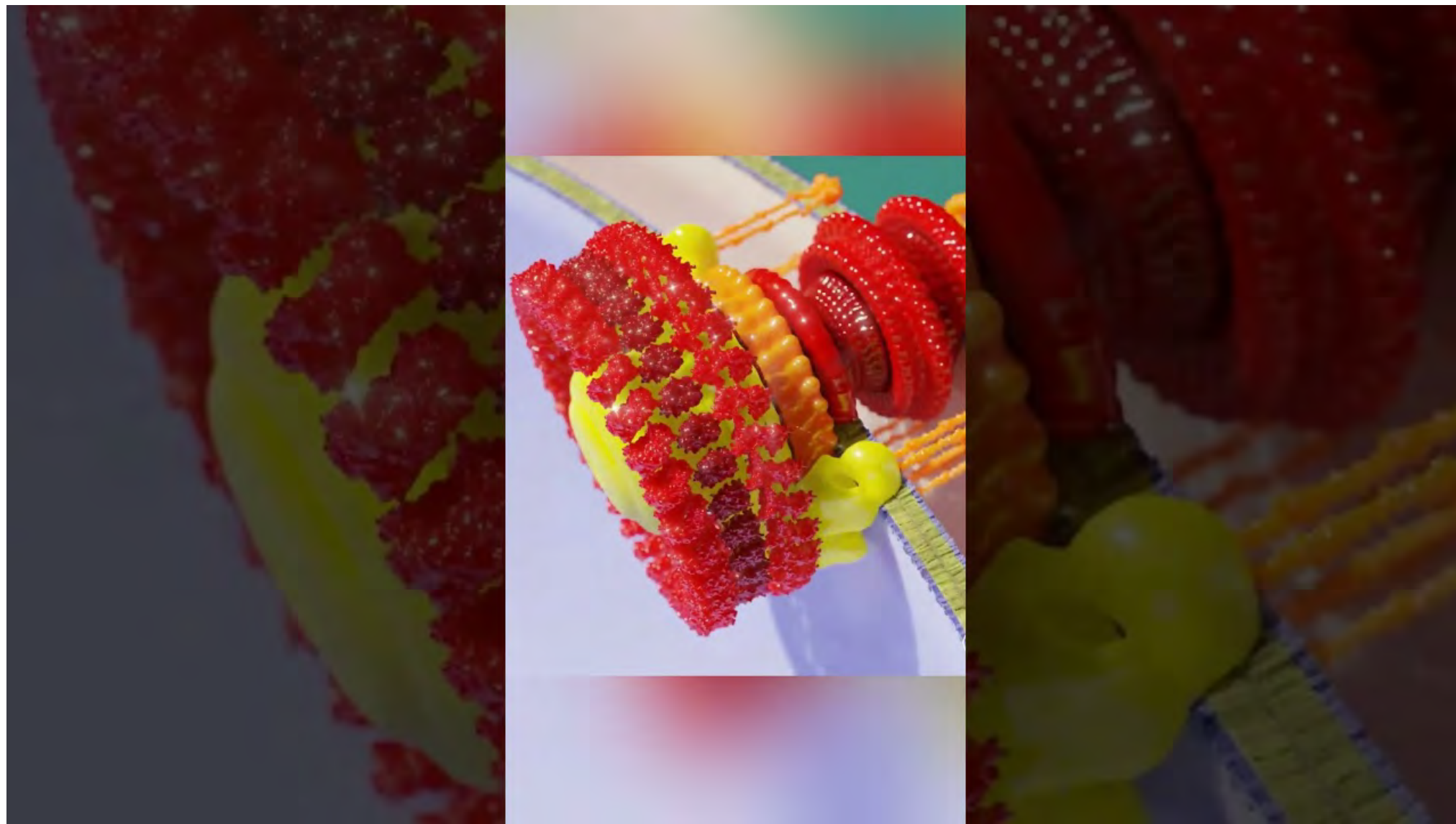
Quaternary



multi-protein complexes



# Molecular machines



pumps  
(Na/K pump)

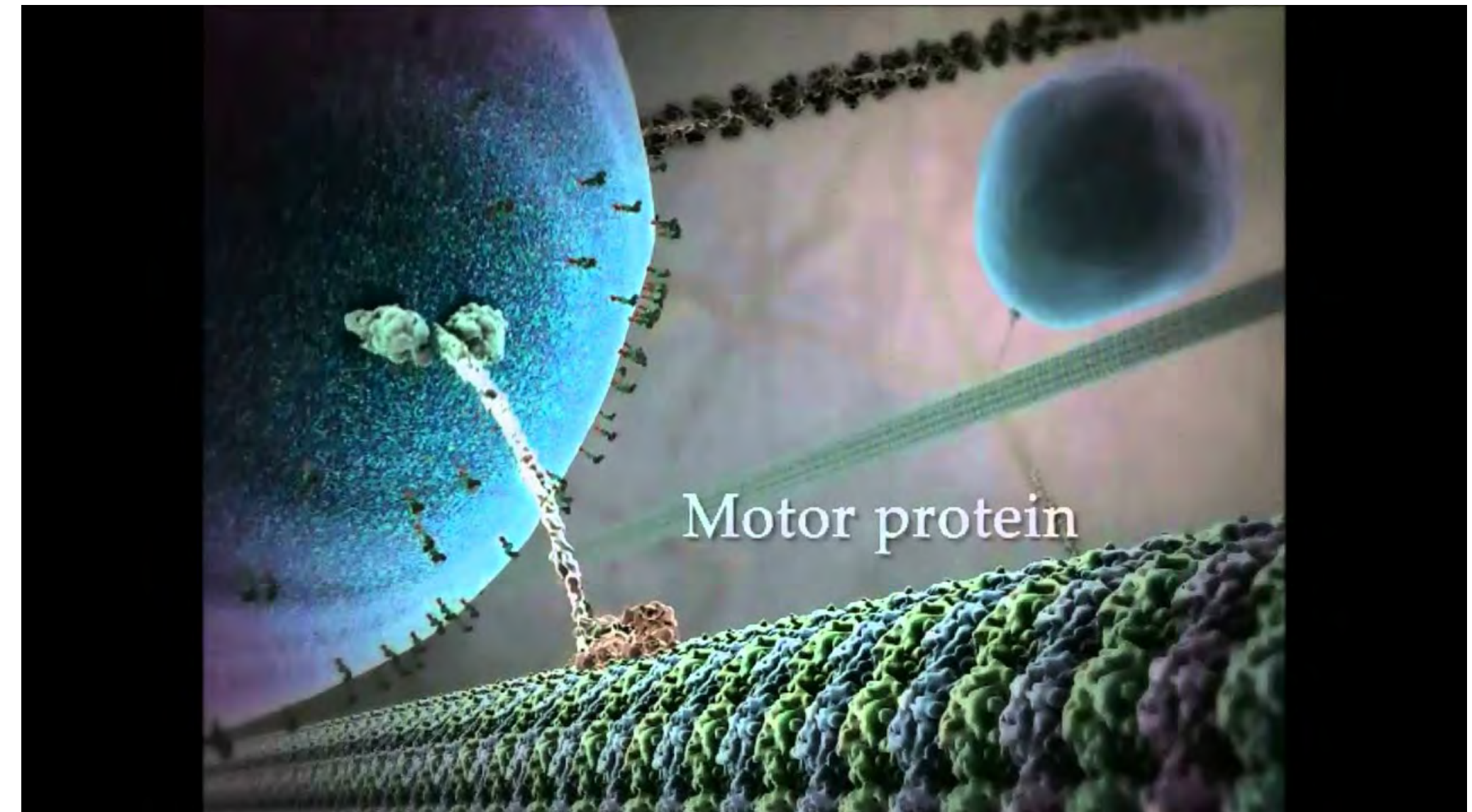
motors  
(ATP Synthase)

printers  
(ribosome)

copiers  
(DNA/RNA polymerase)

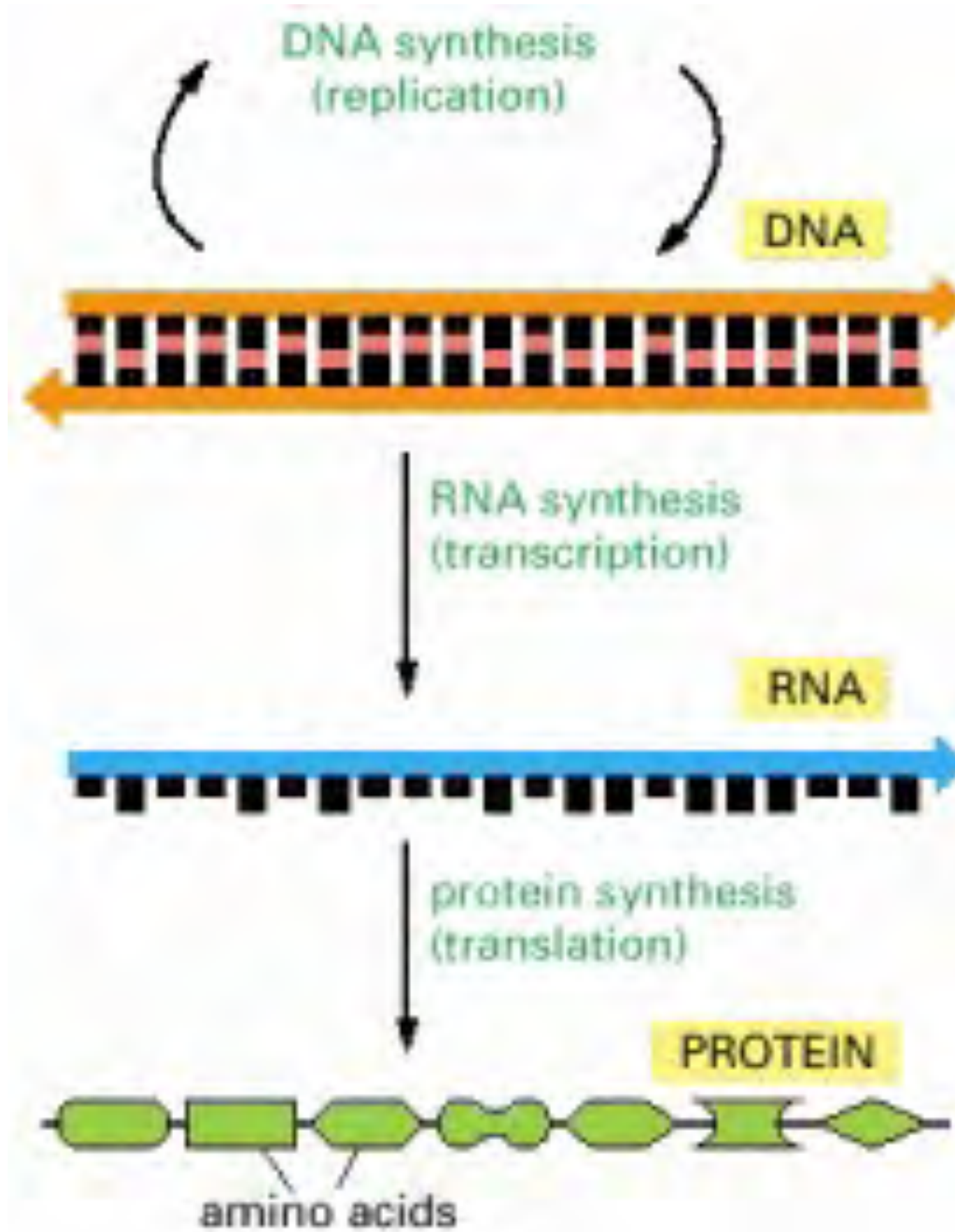
scissors  
(kinases)

and more...

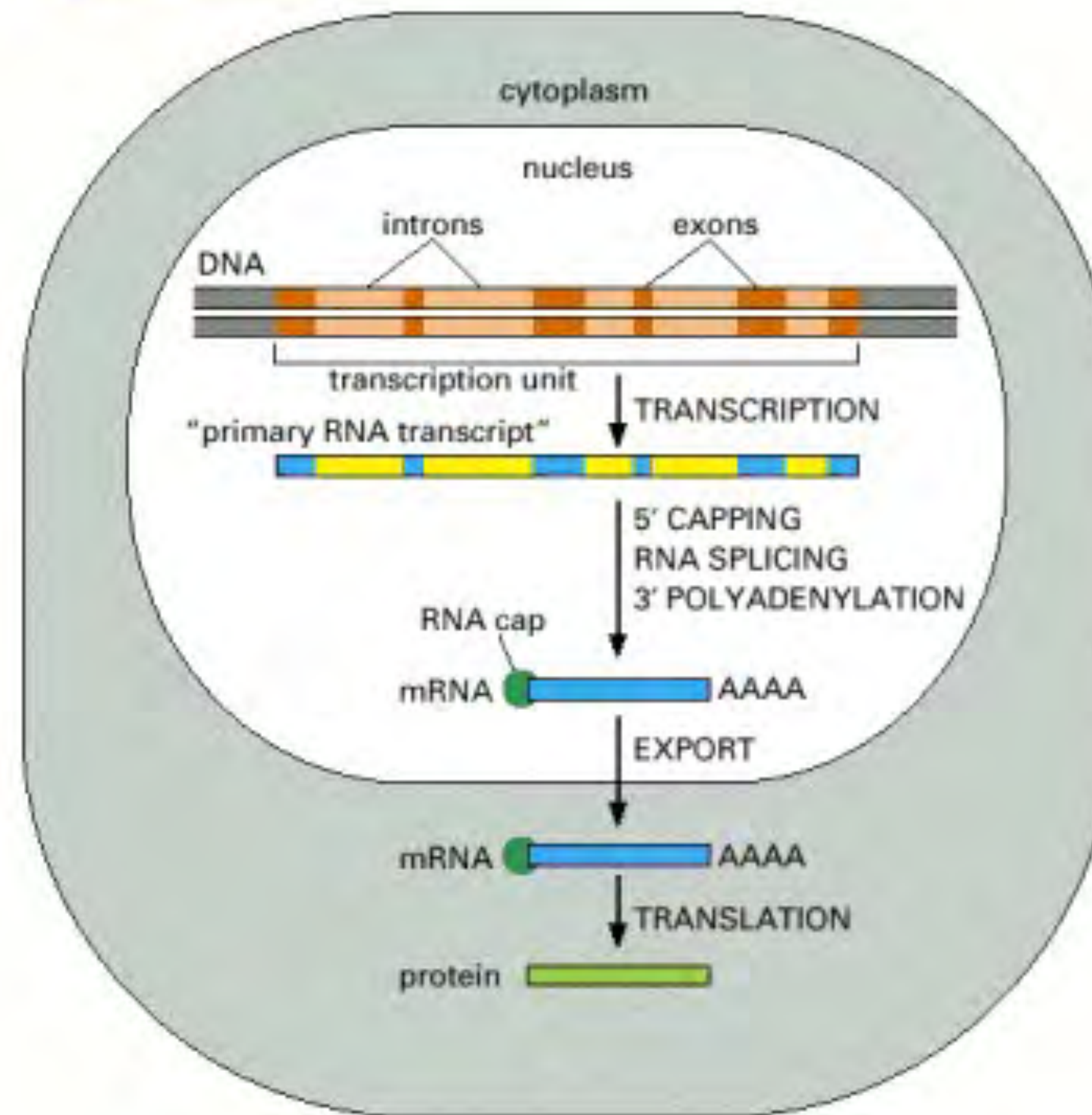




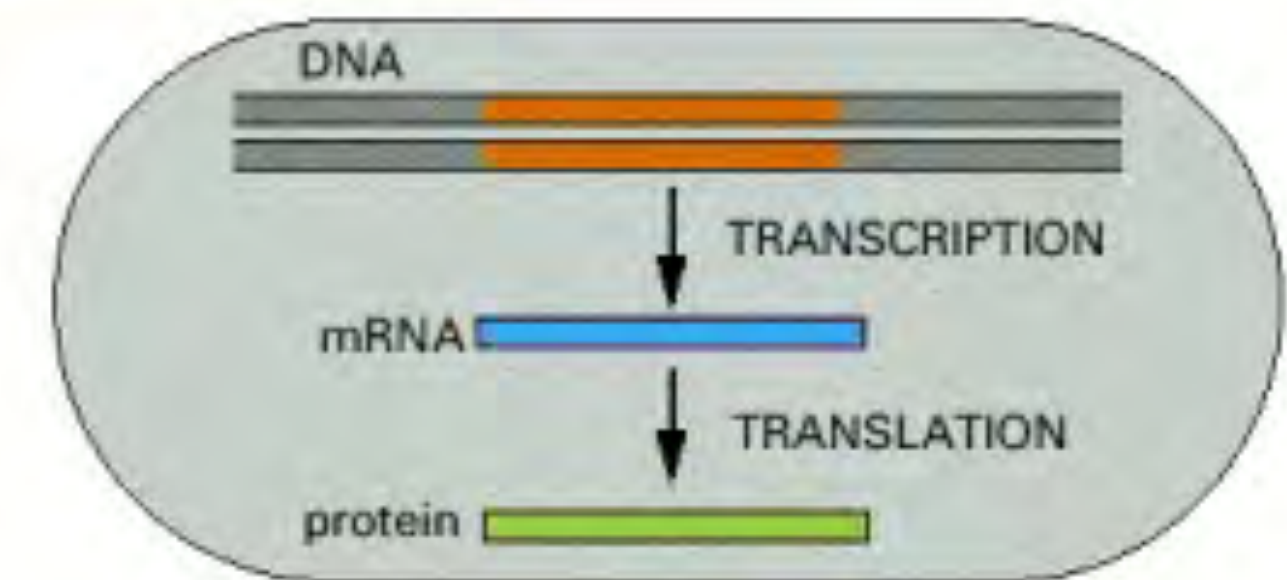
# From DNA to mRNA to protein



(A) EUCARYOTES



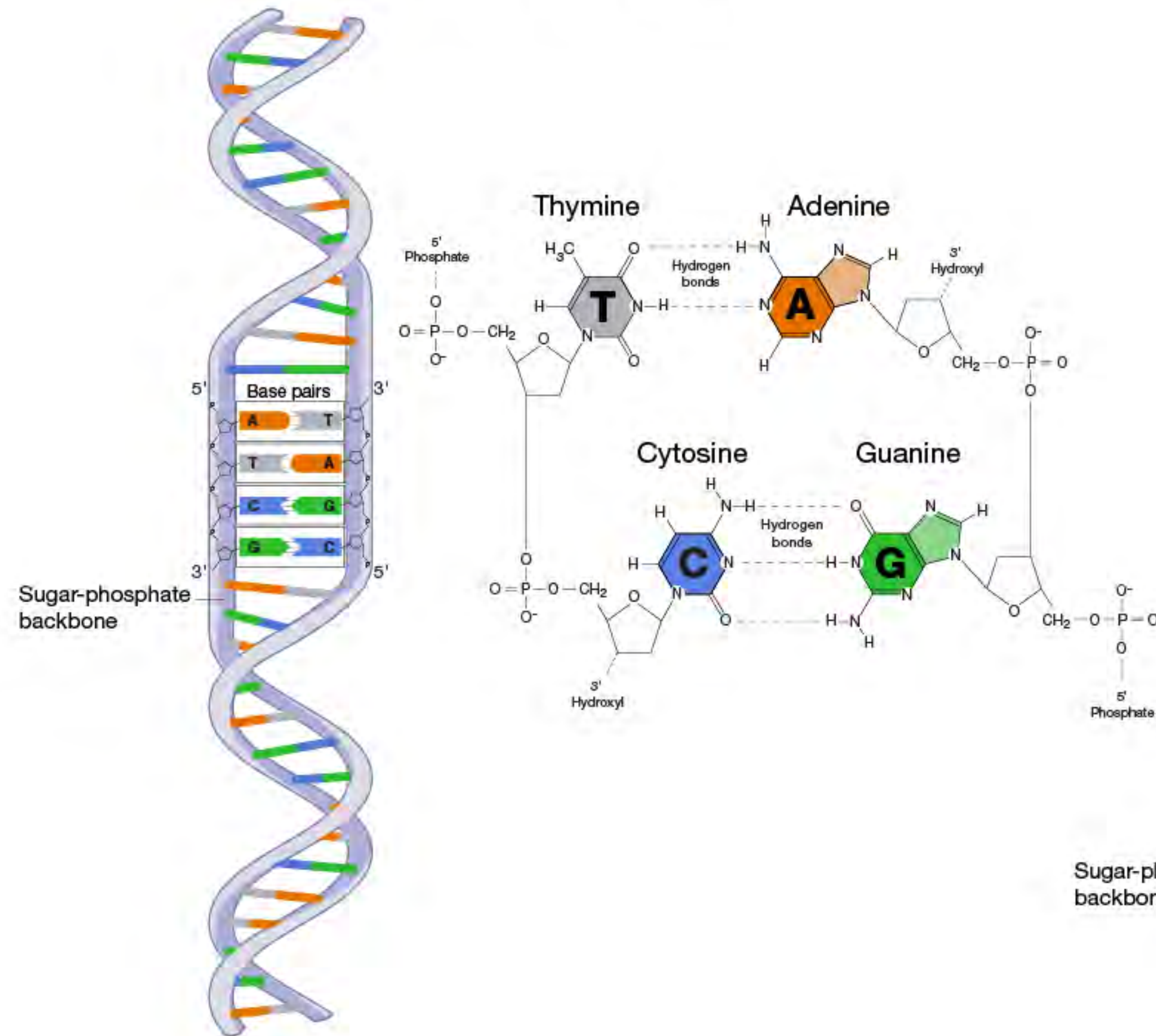
(B) PROCARYOTES



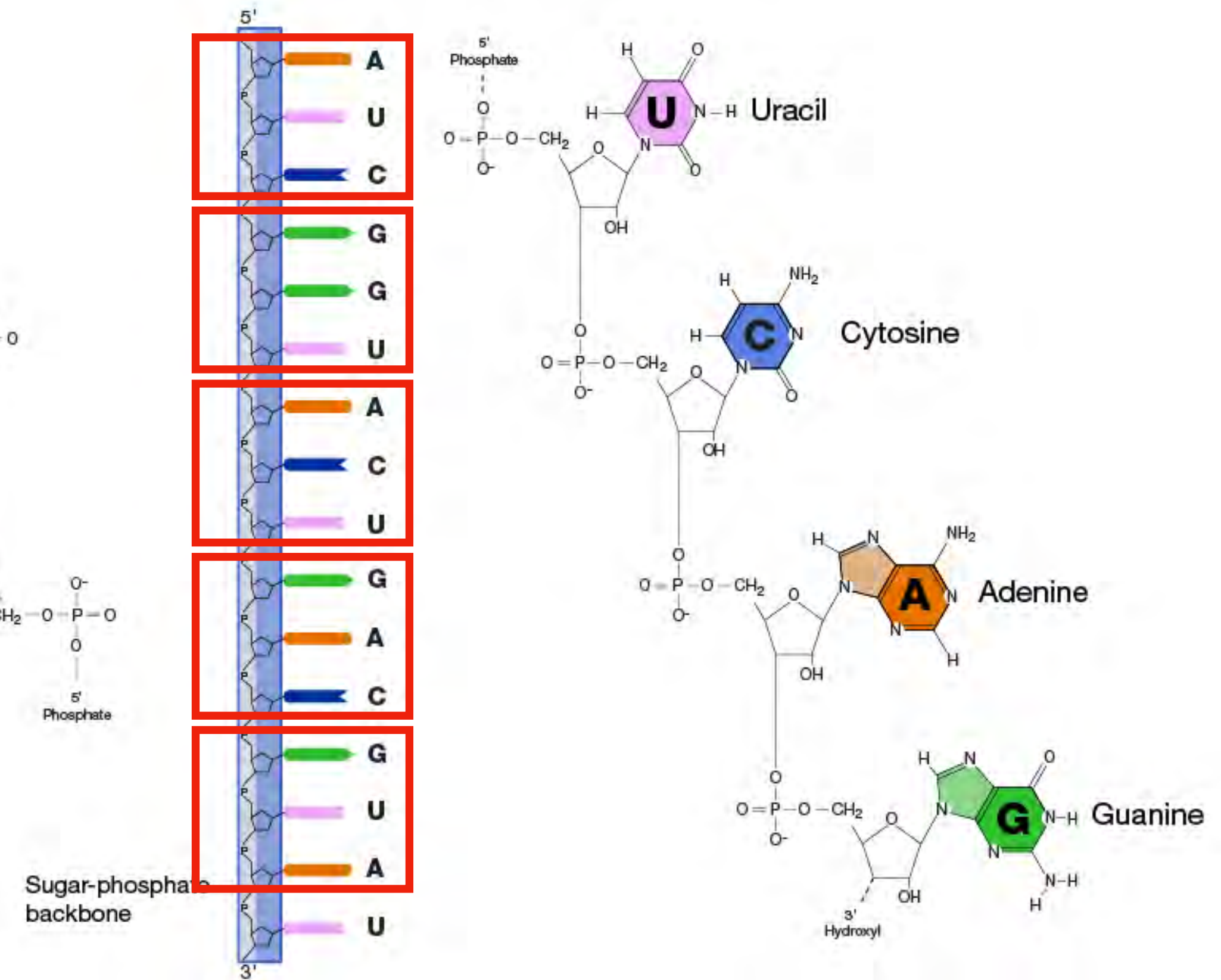


# From DNA to mRNA to protein

## Deoxyribonucleic acid (DNA)



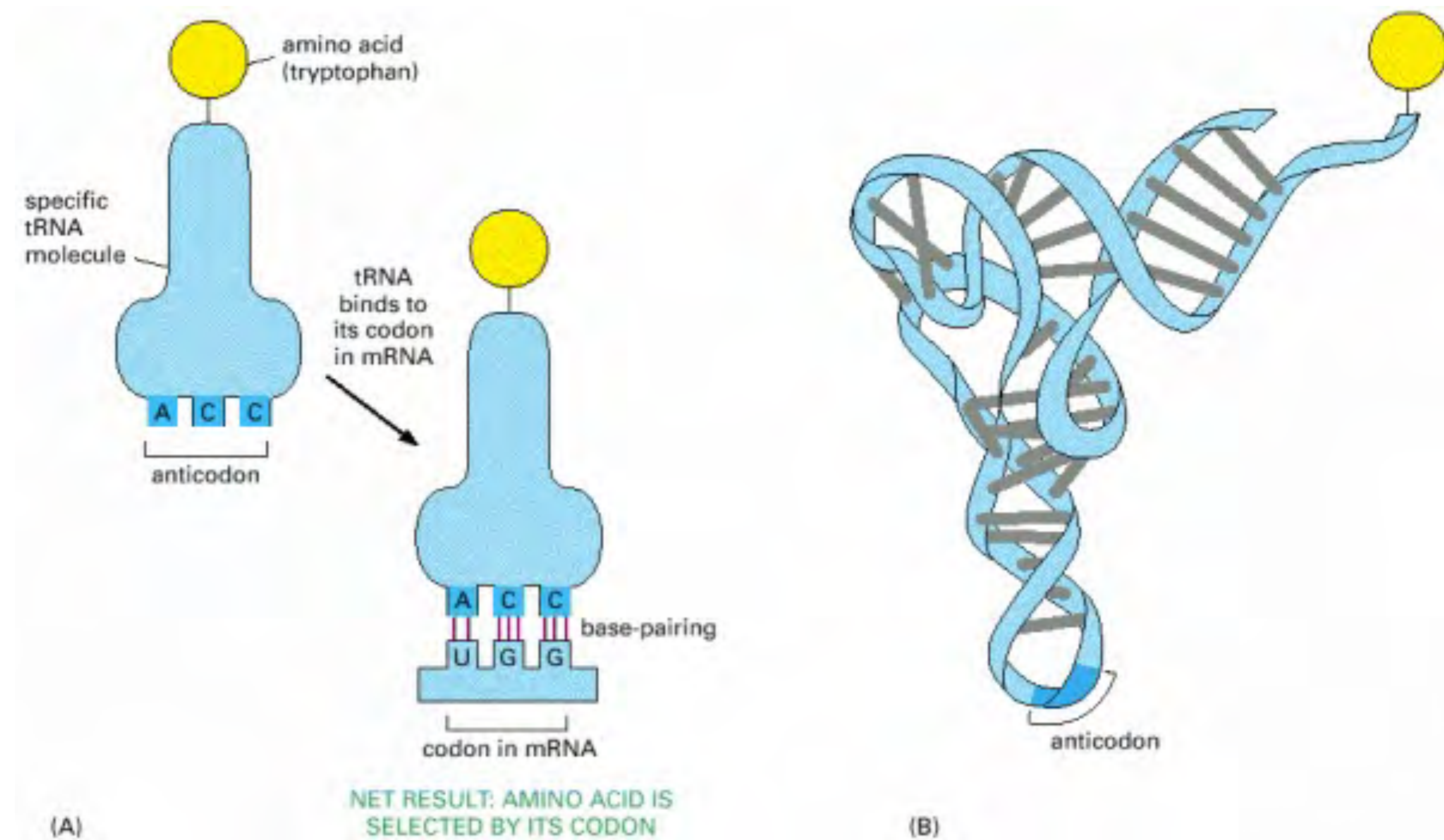
## Ribonucleic acid (RNA)





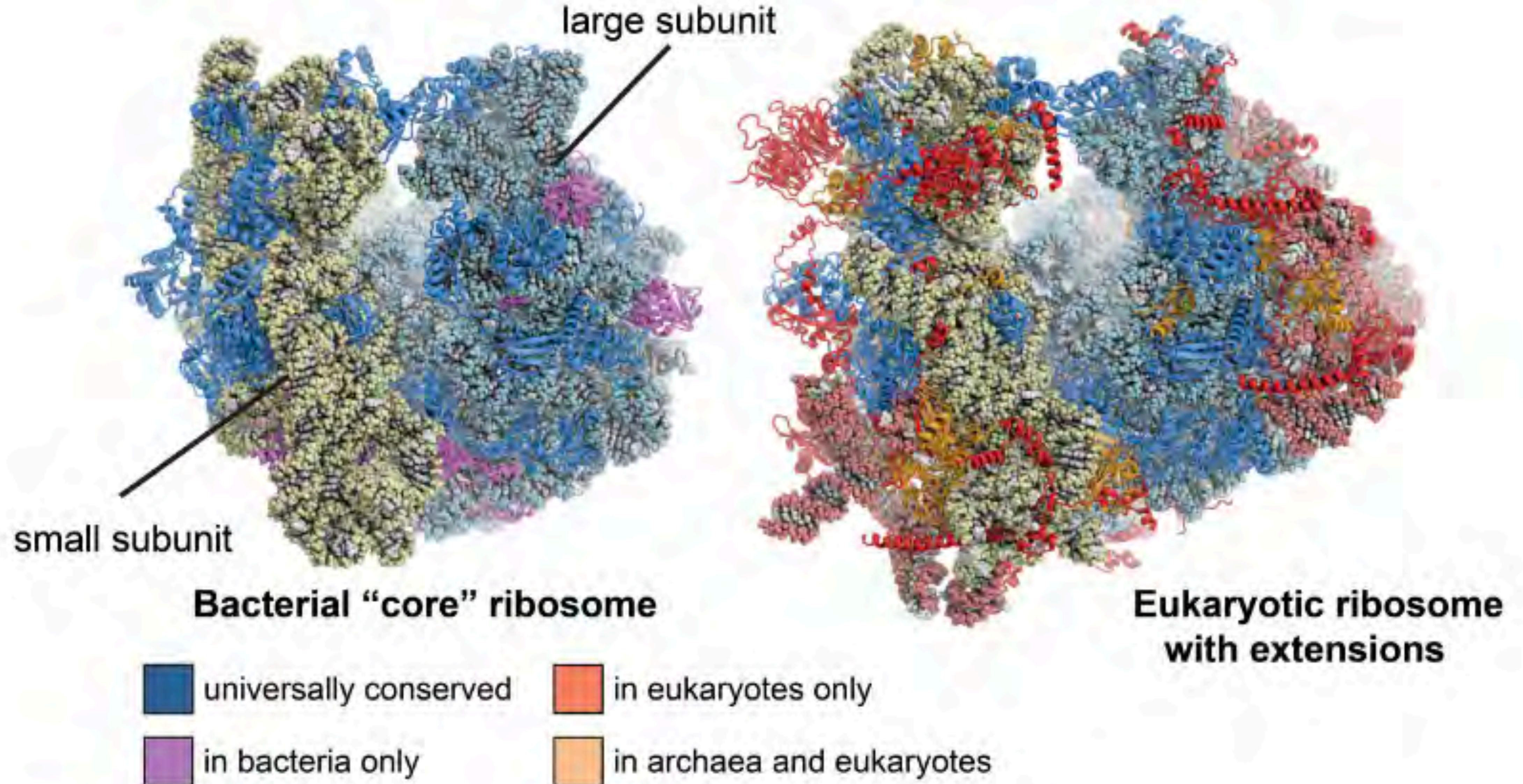
# The genetic code - from 3 nucleotides to 1 amino acid

		Second letter				
		U	C	A	G	
First letter	U	UUU } Phe UUC } UUA } Leu UUG }	UCU } UCC } Ser UCA } UCG }	UAU } Tyr UAC } UAA Stop UAG Stop	UGU } Cys UGC } UGA Stop UGG Trp	U C A G
	C	CUU } CUC } Leu CUA } CUG }	CCU } CCC } Pro CCA } CCG }	CAU } His CAC } CAA } Gln CAG }	CGU } CGC } Arg CGA } CGG }	U C A G
	A	AUU } Ile AUC } AUA } AUG Met	ACU } ACC } Thr ACA } ACG }	AAU } Asn AAC } AAA } Lys AAG }	AGU } Ser AGC } AGA } Arg AGG }	U C A G
	G	GUU } Val GUC } GUA } GUG }	GCU } GCC } Ala GCA } GCG }	GAU } Asp GAC } GAA } Glu GAG }	GGU } GGC } Gly GGA } GGG }	U C A G



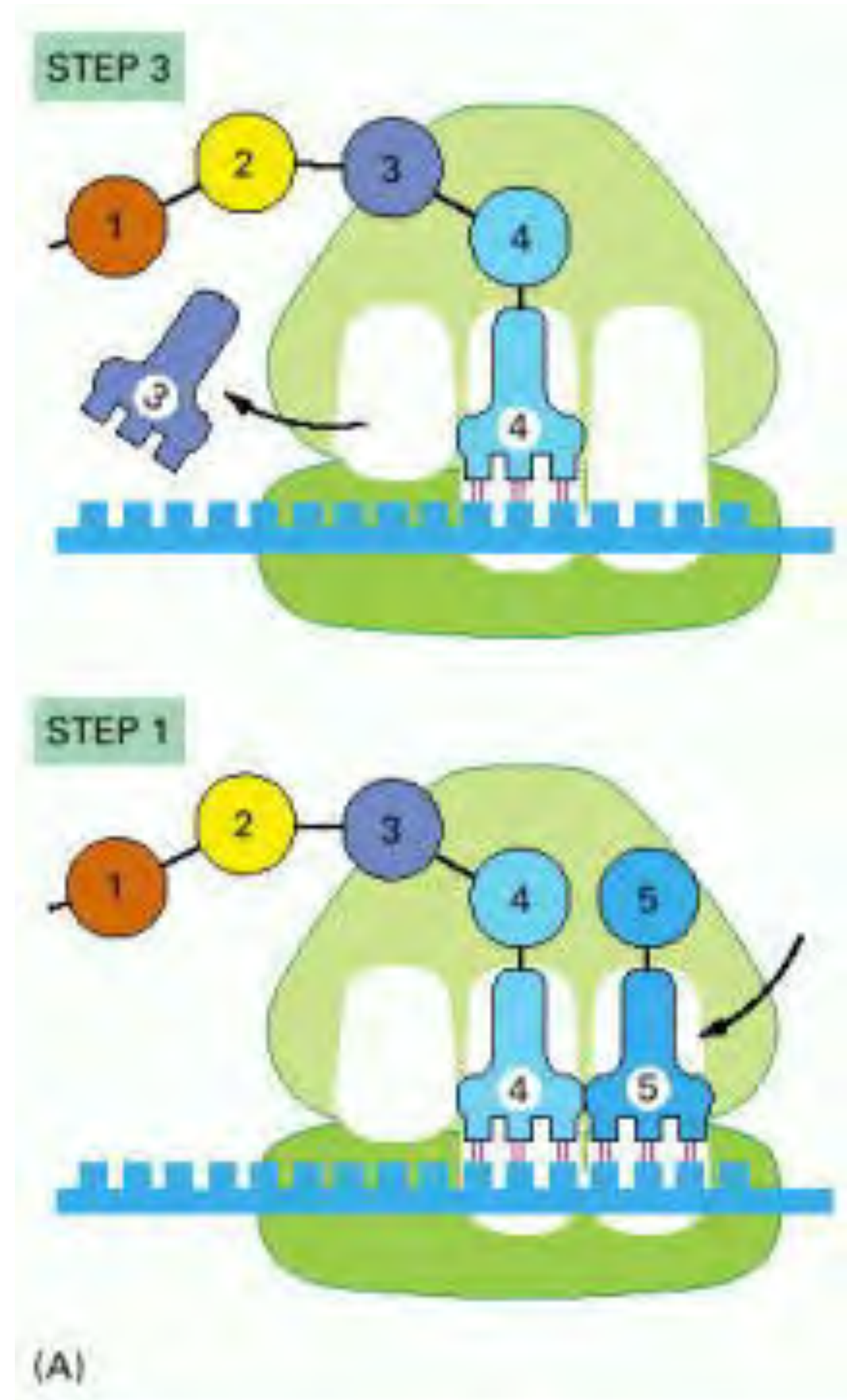
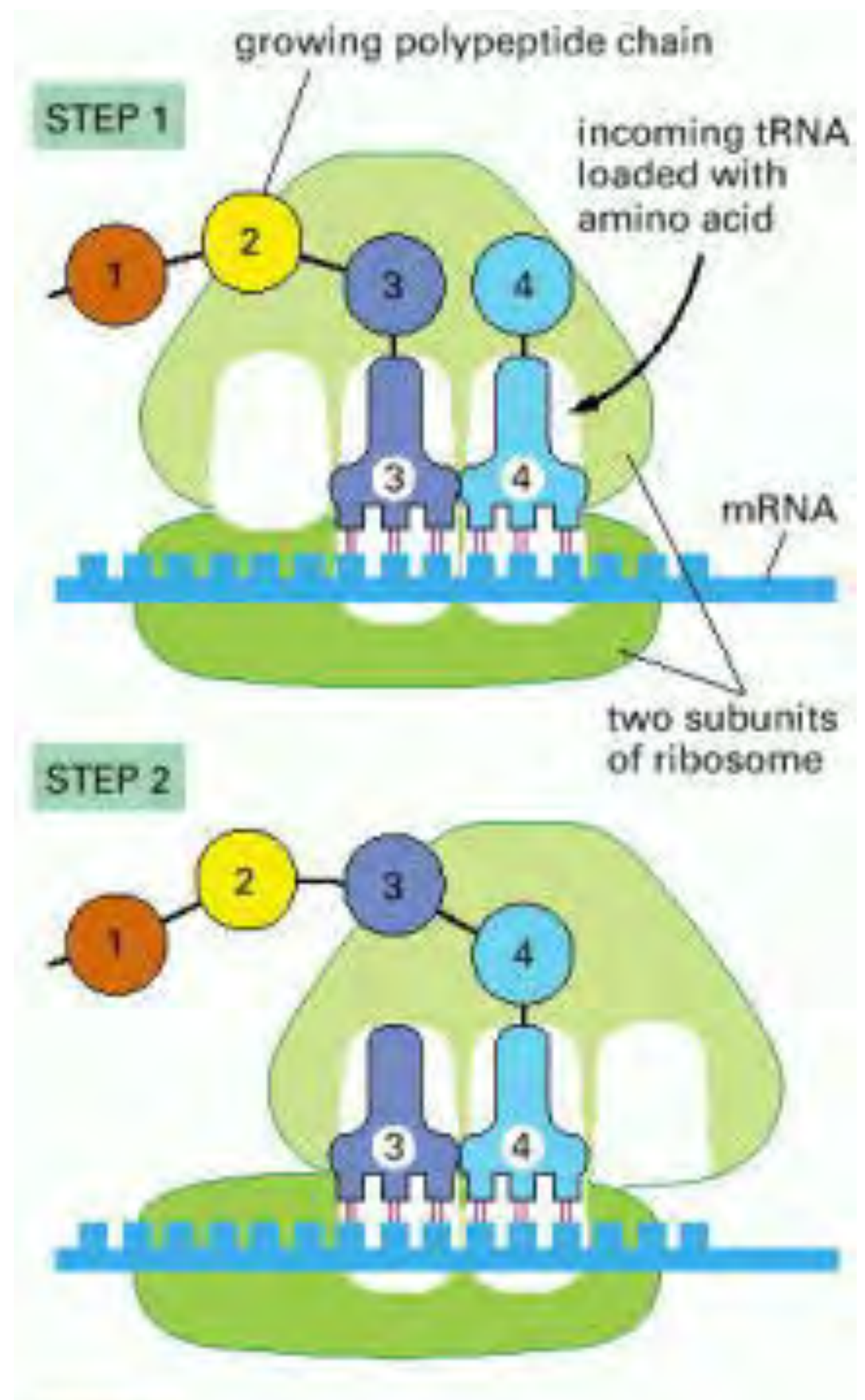
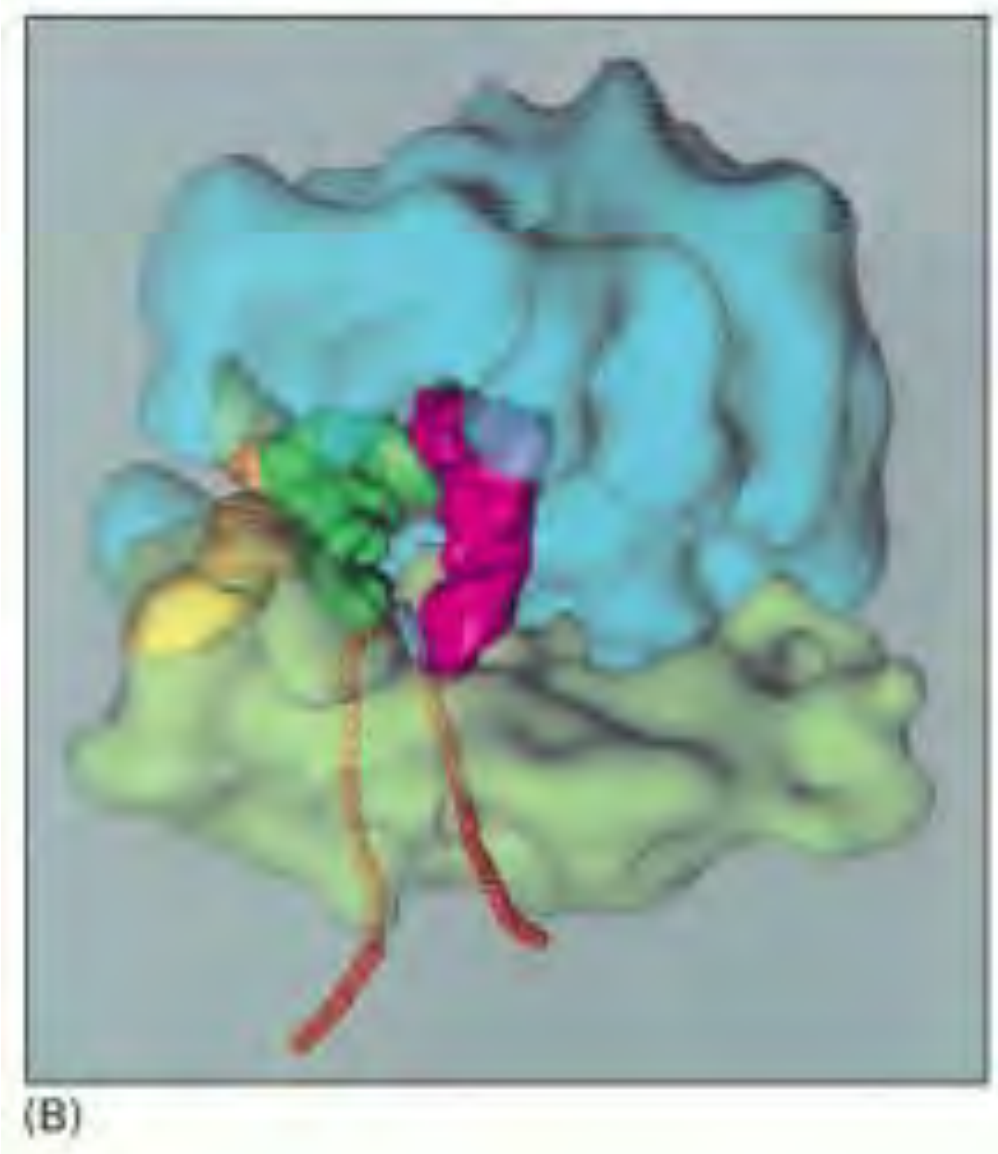
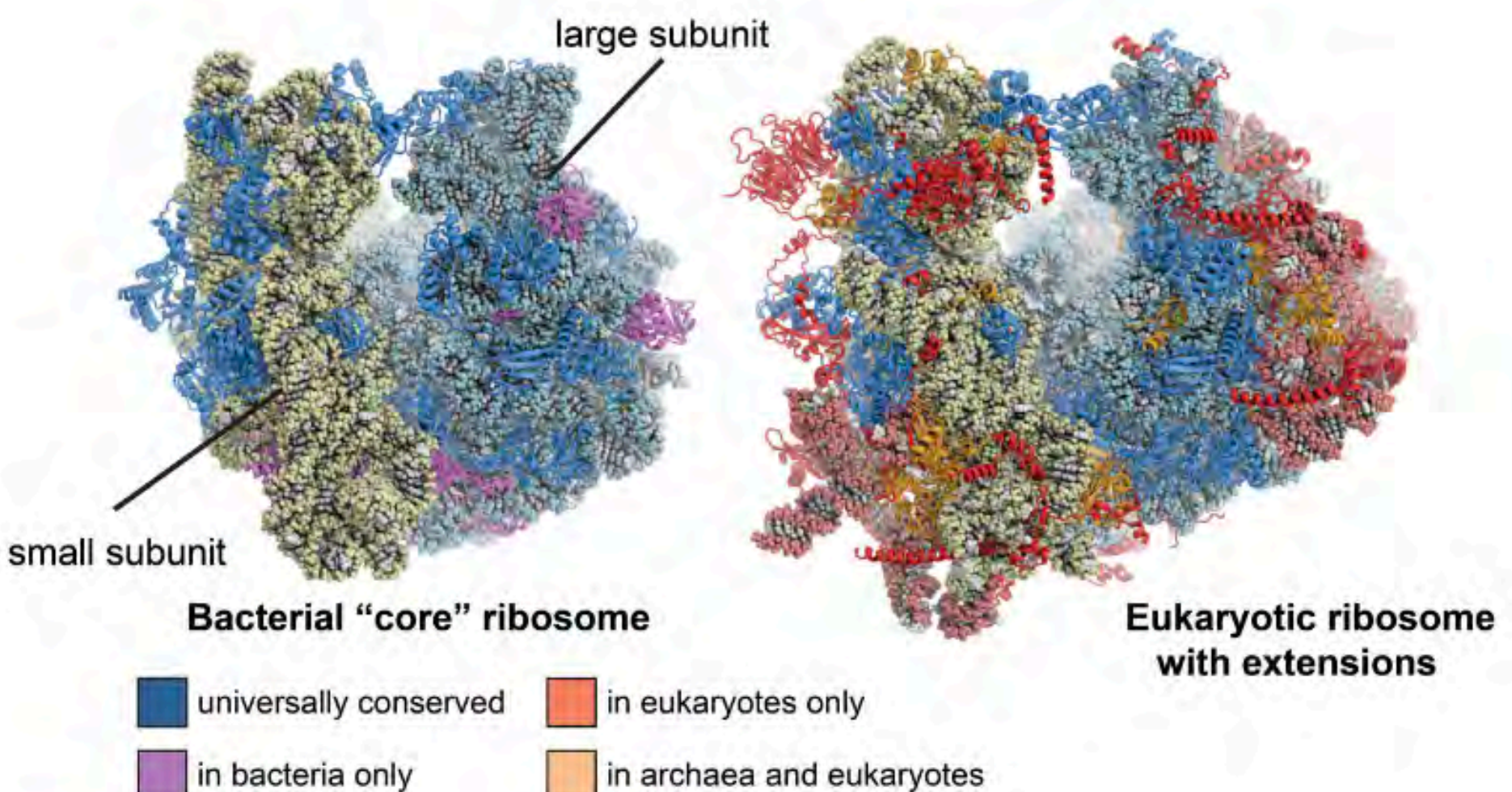


# The role of the ribosome





# The role of the ribosome







[www.dnalc.org](http://www.dnalc.org)



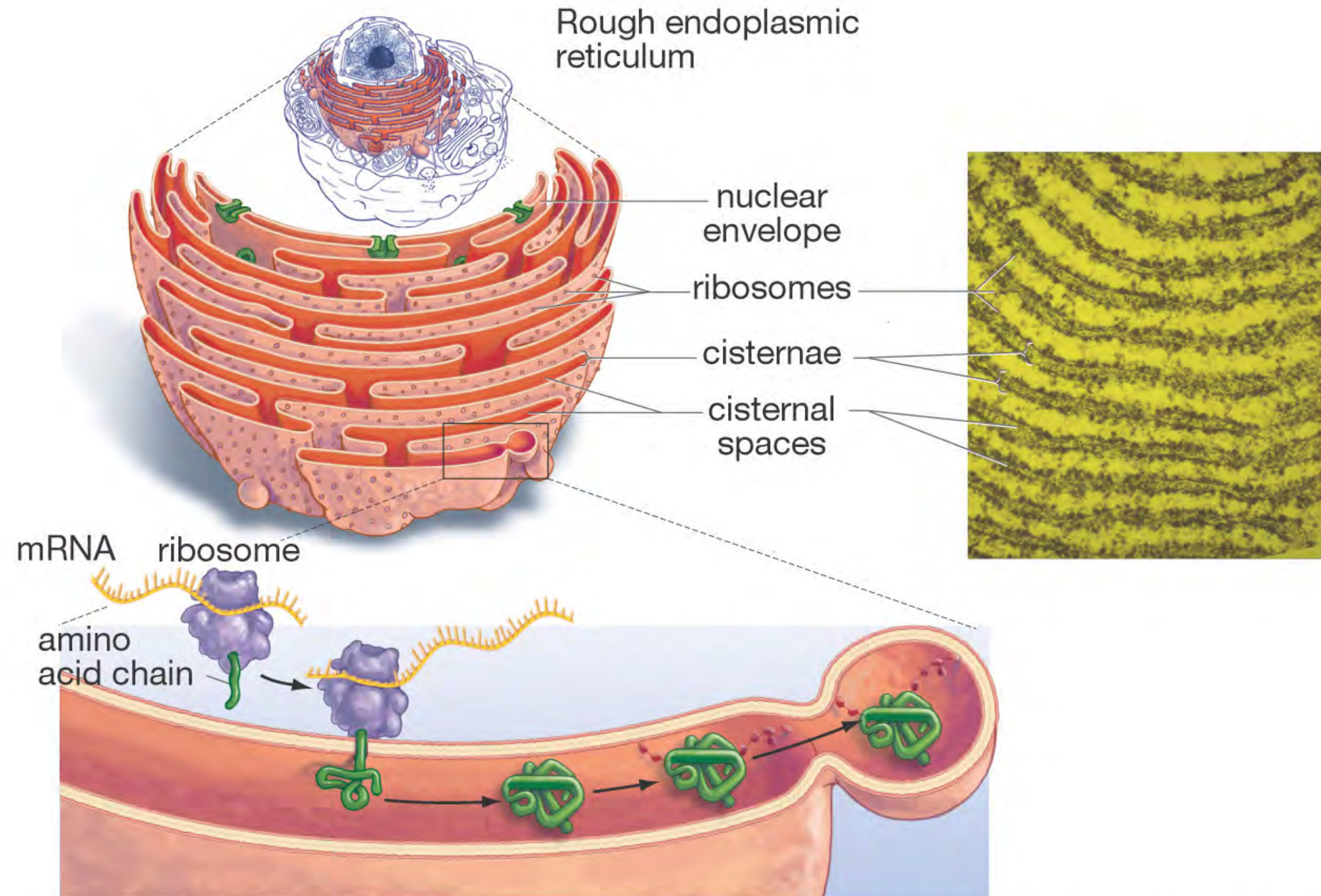
# Ribosomes and the Endoplasmic Reticulum

Functions:

Protein synthesis (about half the cell's proteins are made here).

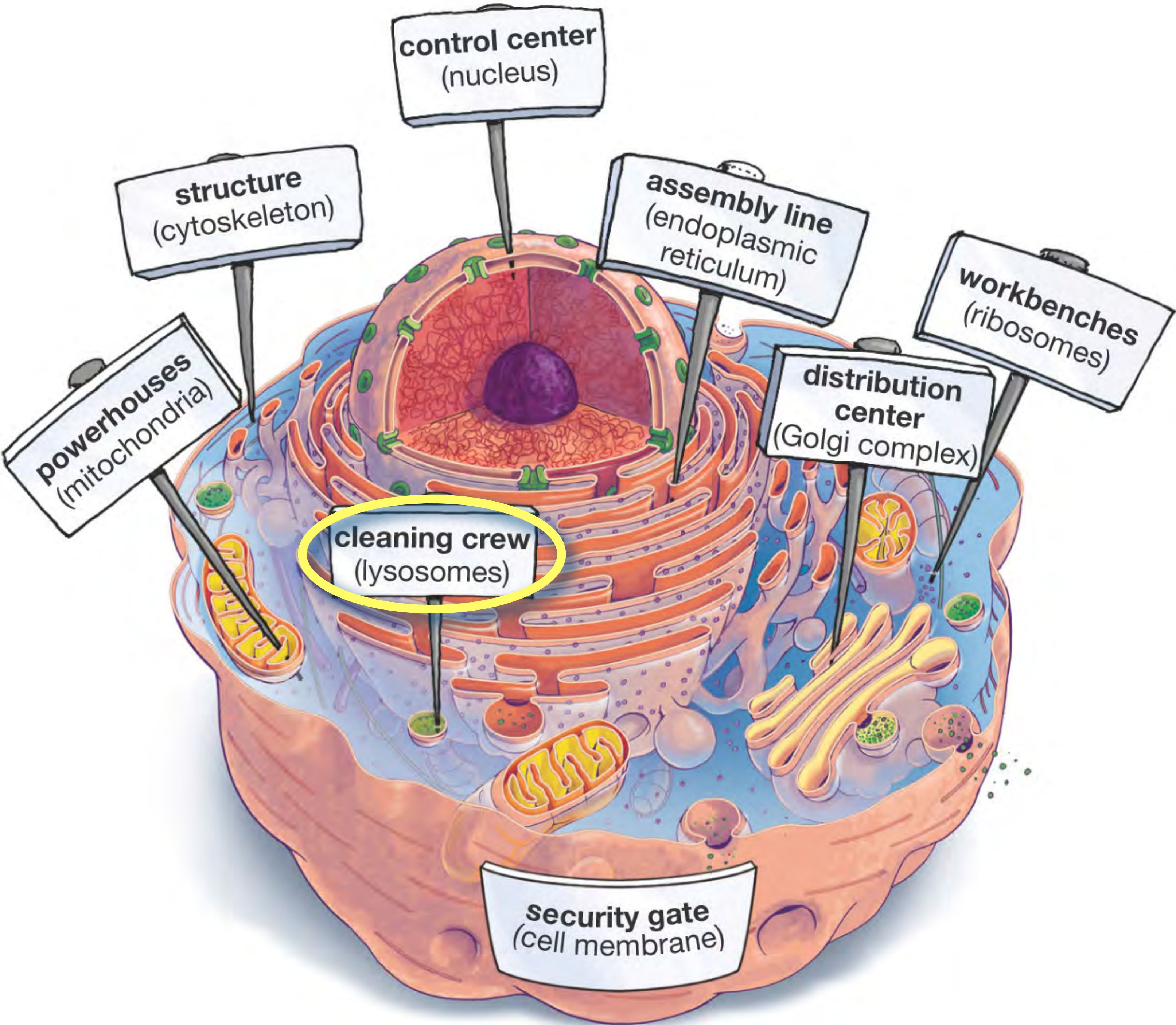
Protein movement (trafficking)

Protein "proofreading"





# Cellular Anatomy





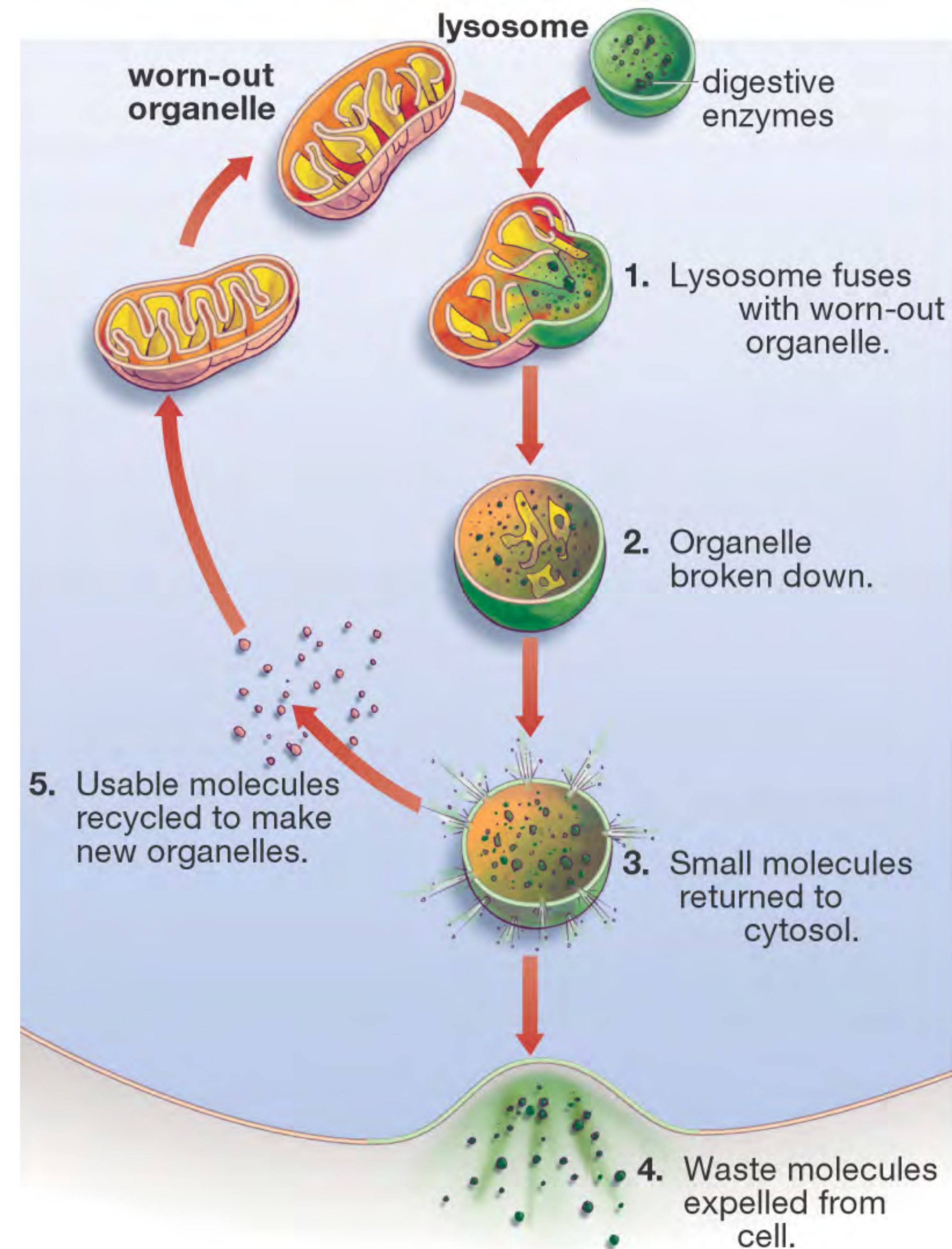
# The Lysosome

Functions:

Digesting food or cellular invaders

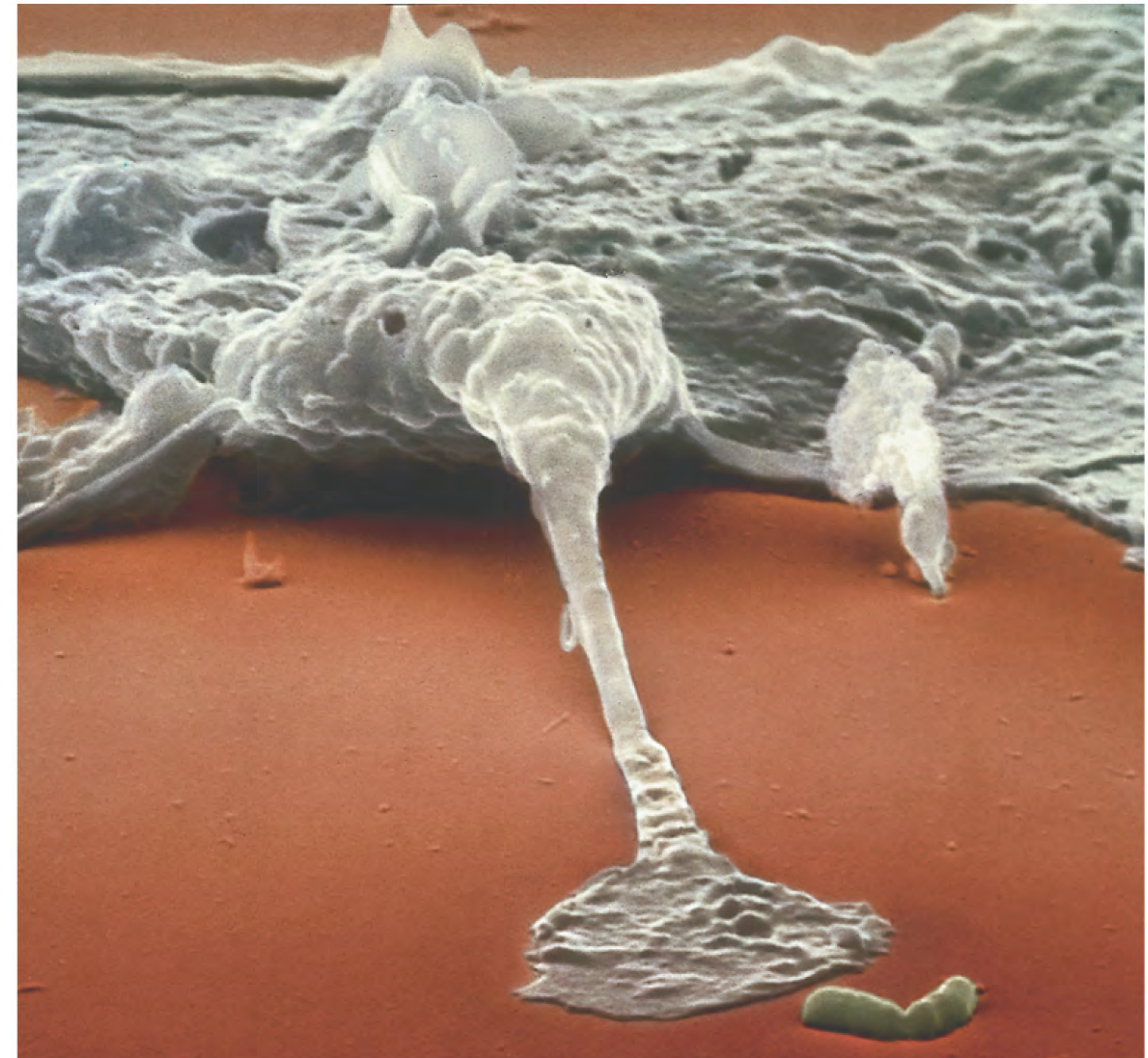
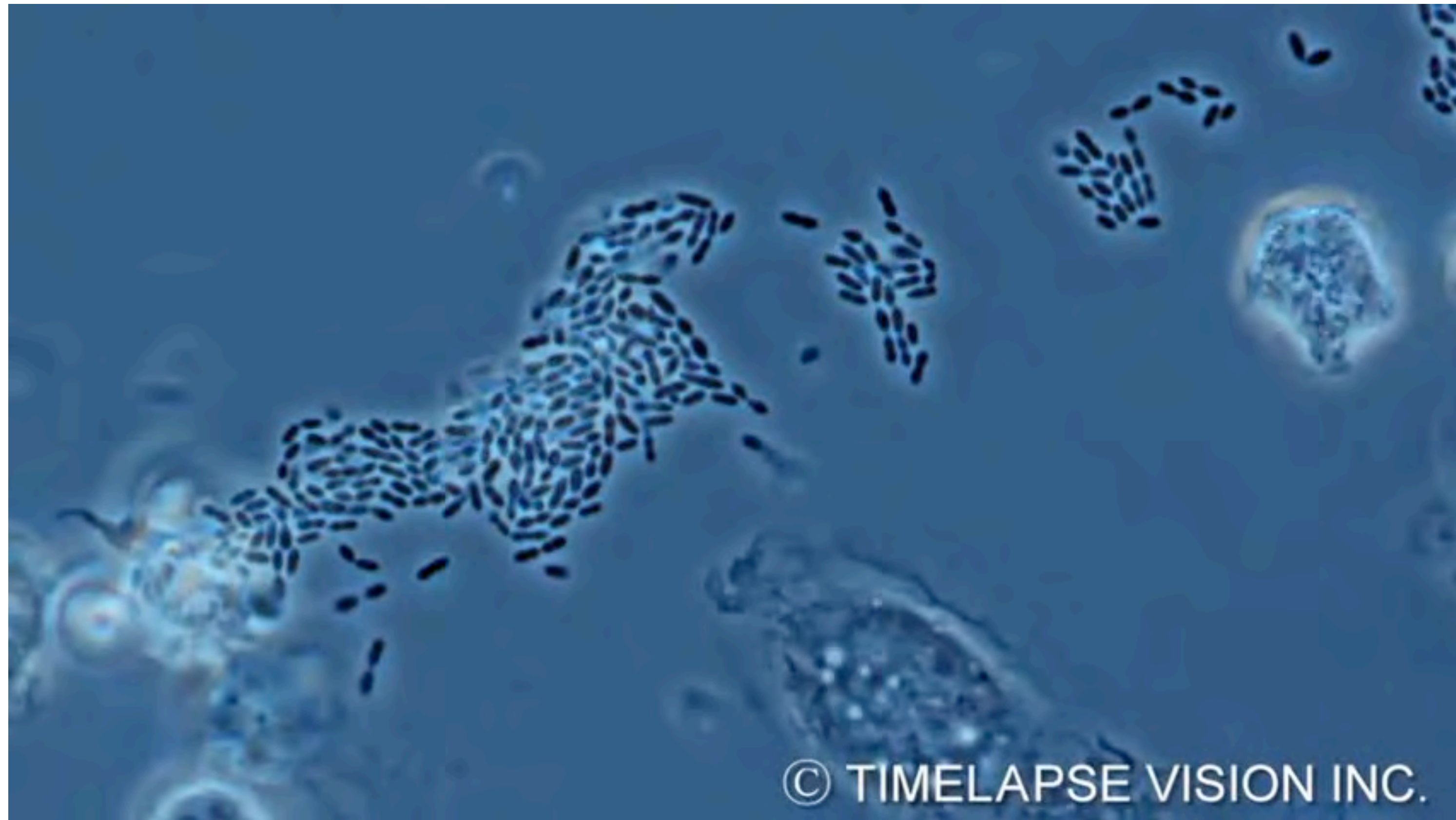
Recycling cellular components

(The lysosome is not found in plant cells)





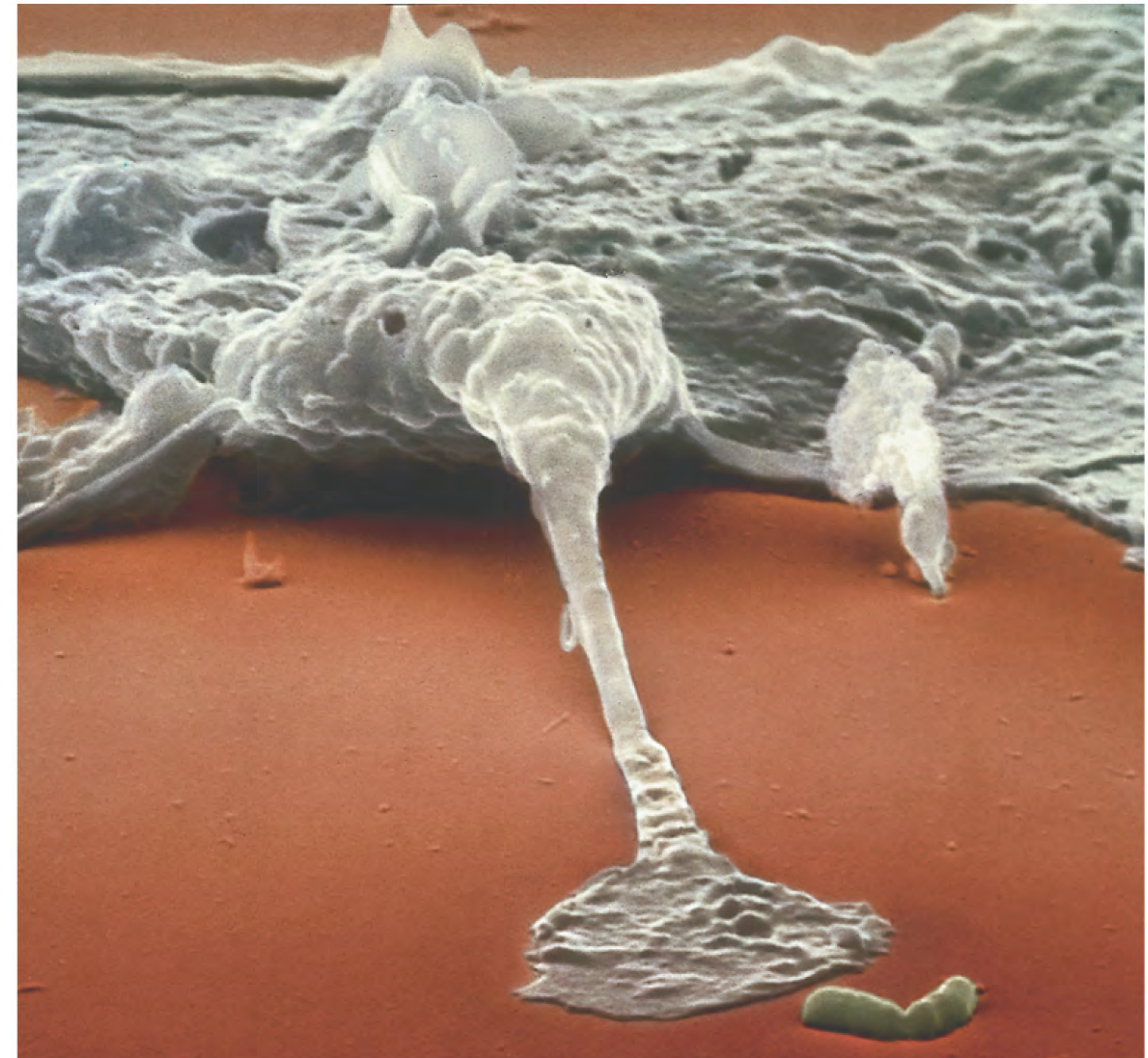
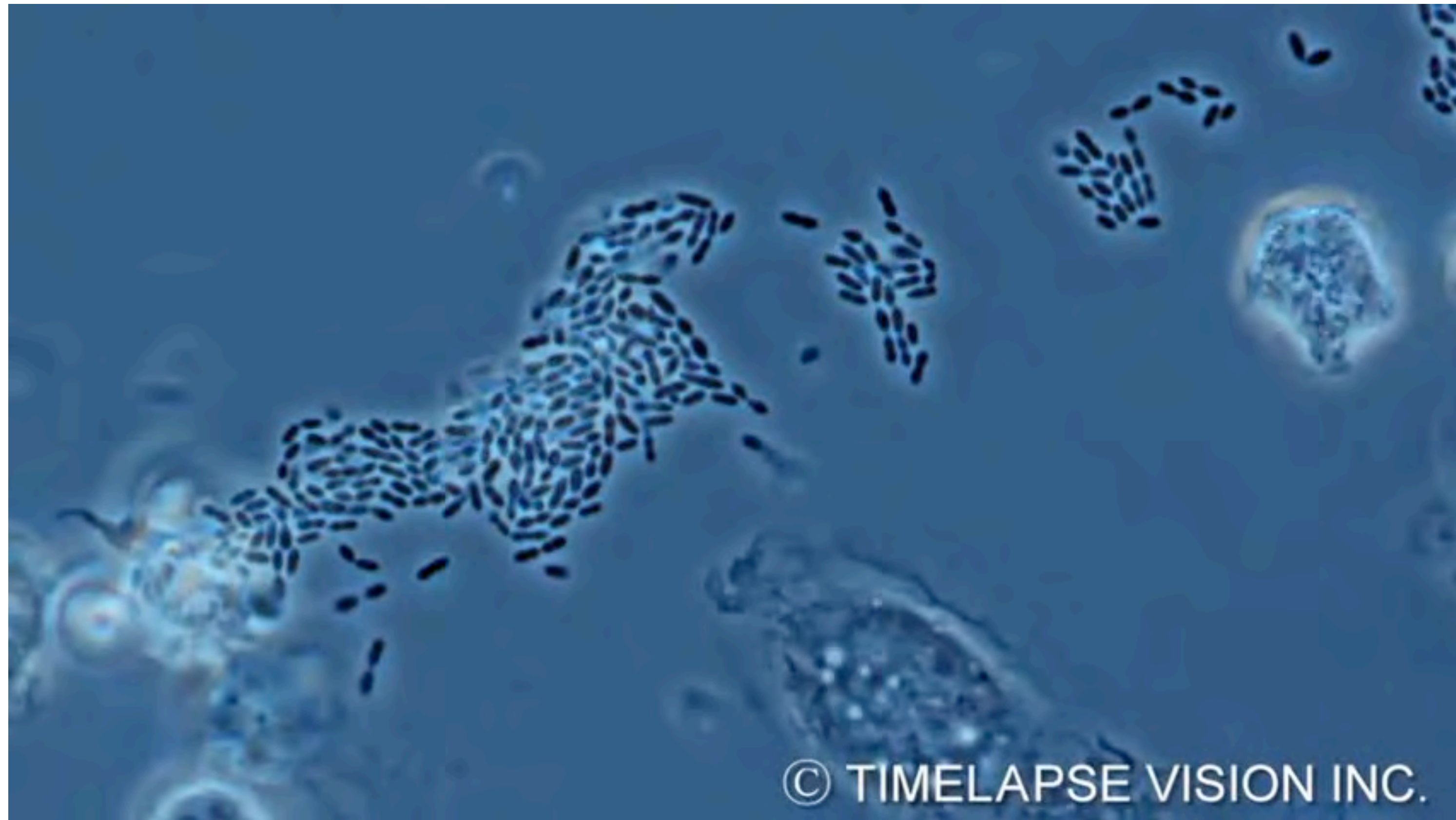
# The Lysosome



This bacterium about to be eaten by an immune system cell will spend the last minutes of its existence within the lysosome of this white blood cell.



# The Lysosome



This bacterium about to be eaten by an immune system cell will spend the last minutes of its existence within the lysosome of this white blood cell.



# Many Diseases are Caused by Lysosome Malfunction



## Conditions we treat

Lysosomal Storage Diseases are genetic disorders caused by enzyme deficiencies in the body. These deficiencies make it difficult for cells to process or break down metabolites. Accumulation of metabolites in the body can lead to organ dysfunction.

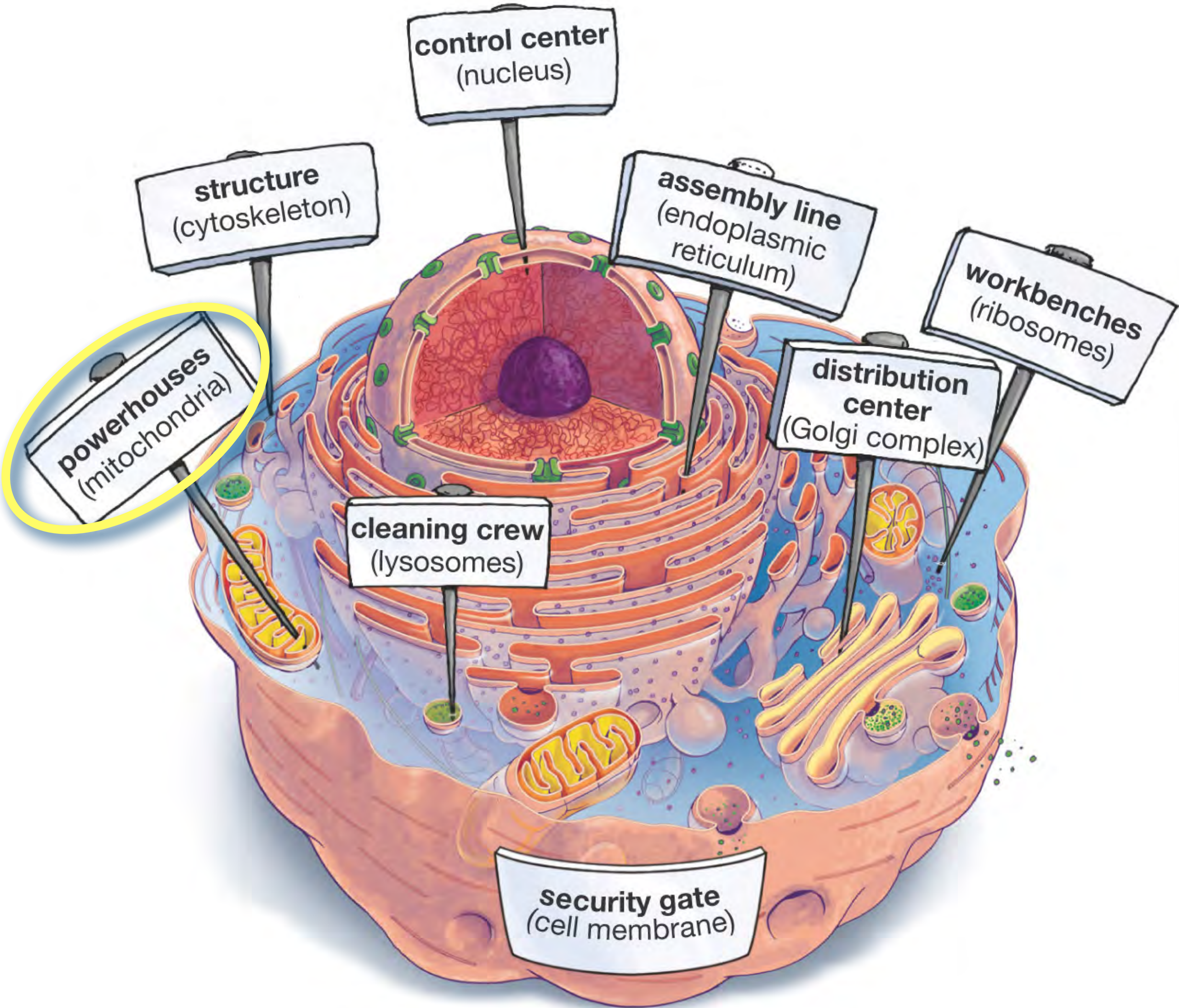
There are more than 50 LSD disorders, all of which are complex, chronic diseases that can involve multiple organs. LSDs can be present at birth or develop later in life. Many cases are difficult to diagnose, which can delay essential treatment and frustrate patients seeking answers.

## LSDs

- Fabry disease  
(causes kidney and heart problems, pain and skin rash)
- Gaucher disease  
(causes the spleen to enlarge, anemia and bone lesions)
- Hurler syndrome  
(causes deformities of the skeleton and facial features, enlargement of the spleen and liver, joint stiffness)
- Mucopolysaccharidosis (MPS)
- Pompe disease (glycogen storage disease type II)
- Multiple sulfatase deficiency
- Mucopolidosis
- Wolman disease (Lysosomal acid lipase deficiency)
- Alpha-mannosidosis
- Gangliosidosis
- Niemann-Pick
- Danon disease
- Metachromatic leukodystrophy



# Cellular Anatomy



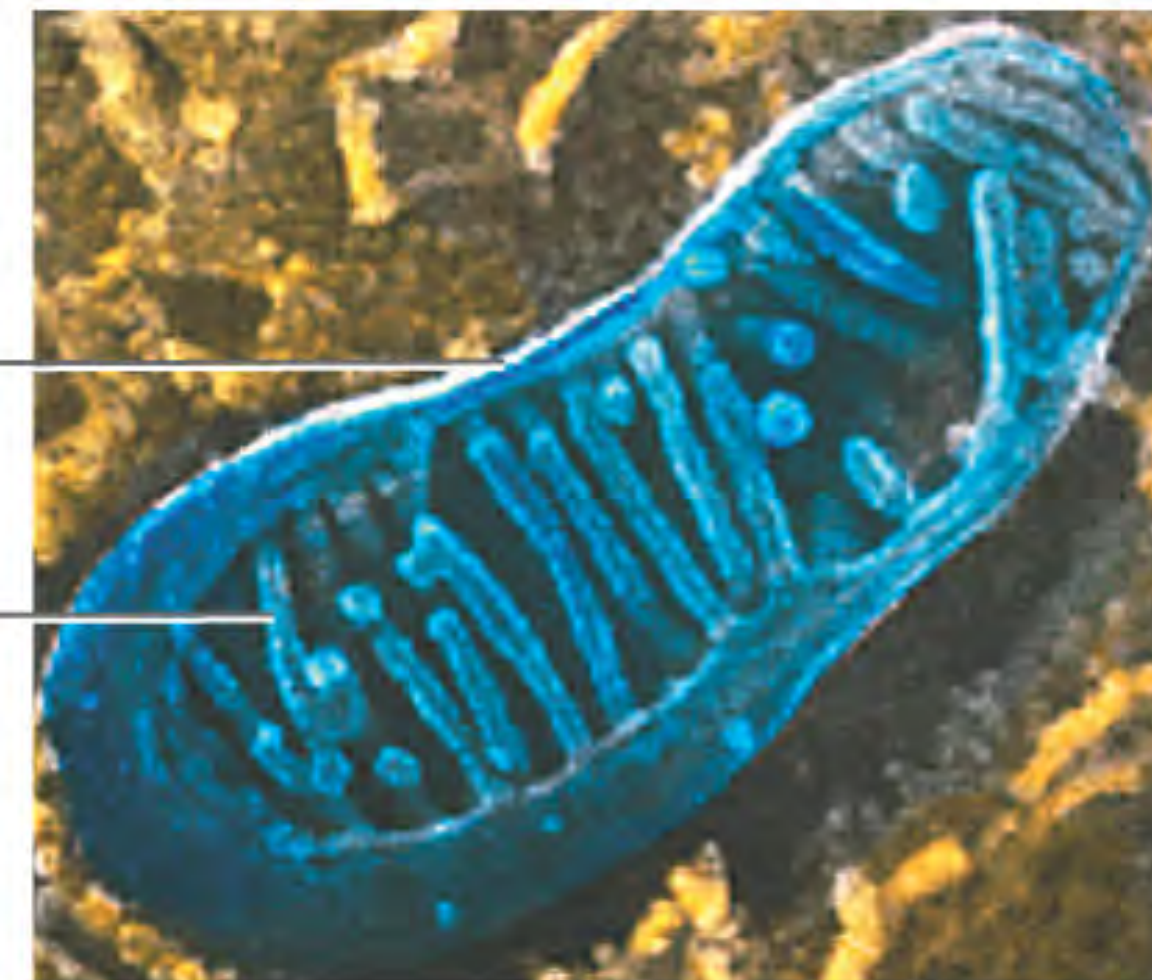
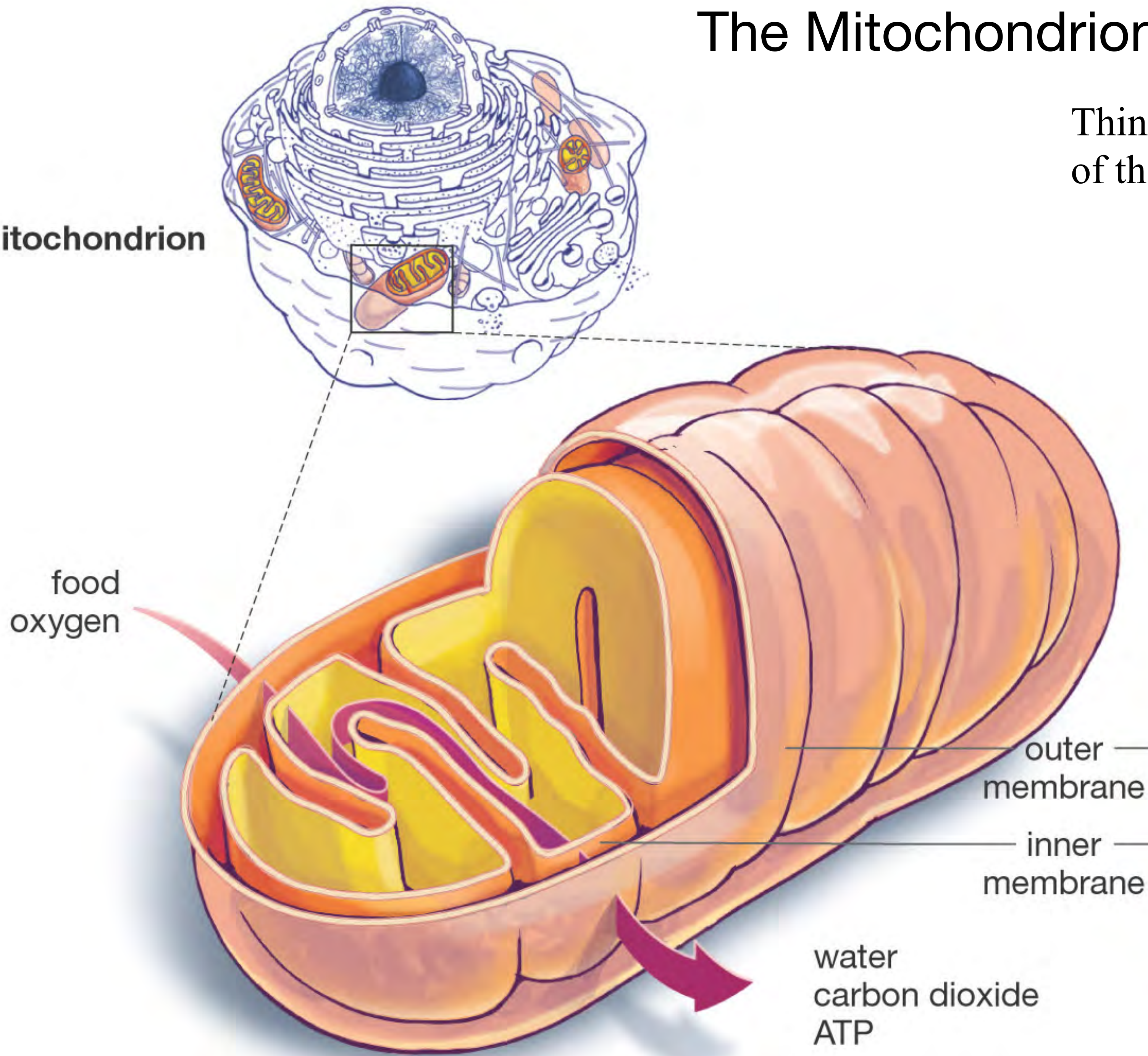


# The Mitochondrion

Think of the mitochondrion as the powerhouse of the cell.

Both plant and animal cells contain many mitochondria.

(Mitochondria is the plural of mitochondrion)





# The Mitochondrion

A class of diseases that causes muscle weakness and neurological disorders are due to malfunctioning mitochondria.



Worn out mitochondria are an important factor in aging.



# Mitochondrial Diseases

## We All Have Mitochondria.

Mitochondria exist in nearly every cell of the human body. It's responsible for creating 90% of the energy you need to sustain life and support organ function.

### What Is Mitochondrial Disease?

When mitochondria cannot convert food and oxygen into life-sustaining energy, cell injury and even cell death follow. When this process is repeated throughout the body, organ systems begin to fail and even stop functioning.











### Why Do Mitochondria Malfunction?

There is still so much to uncover, but this is what we do know. Mitochondrial disease is an inherited condition. Your mitochondria can also be affected by other genetic disorders and environmental factors. You can learn more about the biology behind mitochondrial disease [here](#).



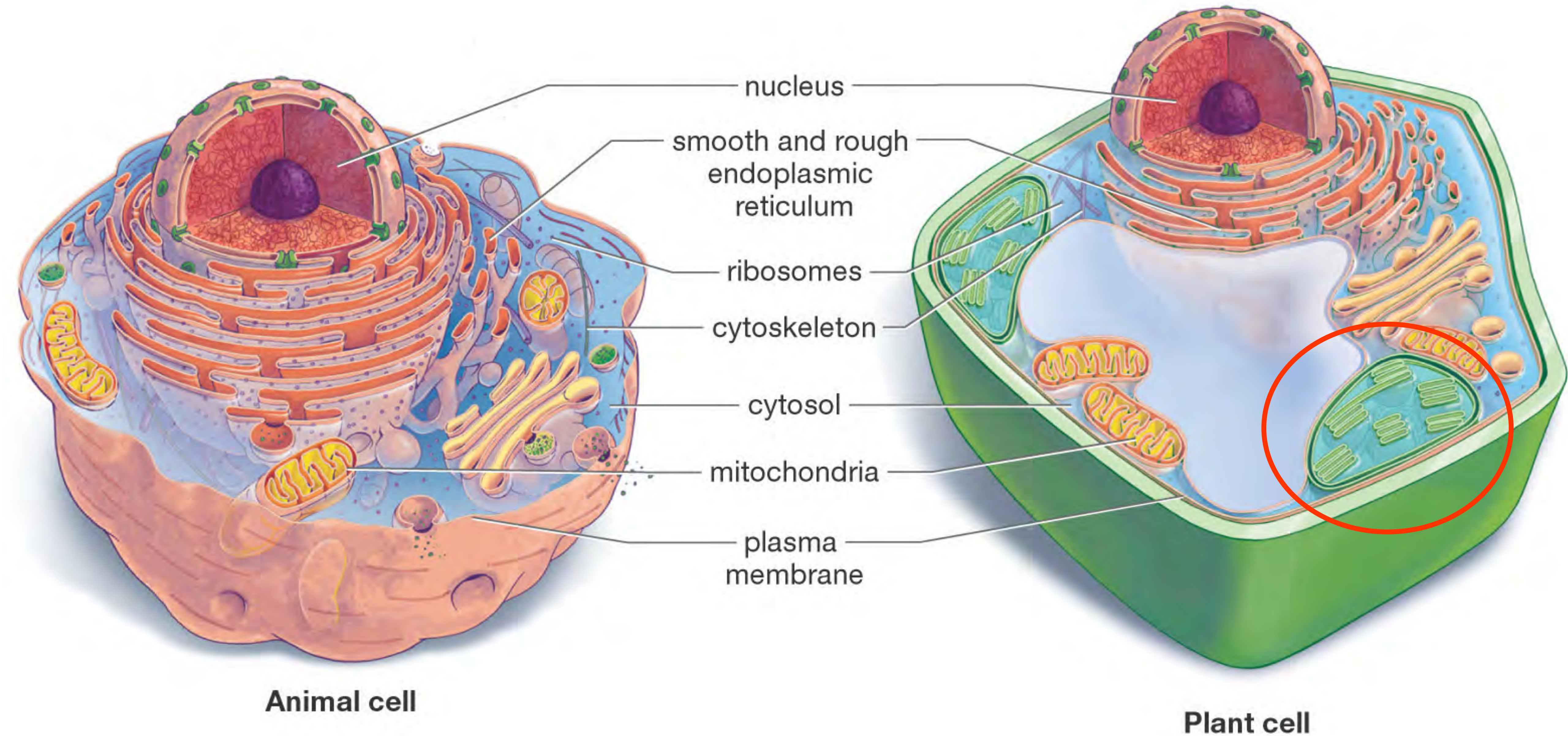
## How Mitochondrial Disease Affects the Body

The parts of your body that need the most energy – heart, brain, muscles – are most affected by mitochondrial disease. An affected individual may exhibit a spectrum of symptoms.

	<b>Brain</b> <i>developmental delays, dementia, migraines, autistic features, seizure, stroke, atypical cerebral palsy, learning disabilities</i>		<b>Muscles</b> <i>weakness/failure, cramping, reflux, vomiting, constipation, diarrhea, hypotonia, dysmotility</i>
	<b>Nerves</b> <i>fainting, zero reflexes, heat/cold intolerance, pain</i>		<b>Pancreas</b> <i>diabetes, pancreatic failure, parathyroid failure</i>
	<b>Kidneys</b> <i>renal tube failure</i>		<b>Heart</b> <i>defects, blockage, cardiomyopathy</i>
	<b>Liver</b> <i>low blood sugar, liver failure</i>		<b>Ears</b> <i>hearing loss</i>
	<b>Eyes</b> <i>vision loss, ptosis, optic atrophy, strabismus, ophthalmoplegia, retinitis pigmentosa</i>		<b>Systemic</b> <i>failure to gain weight, fatigue, short stature, unexplained vomiting, respiratory problems</i>



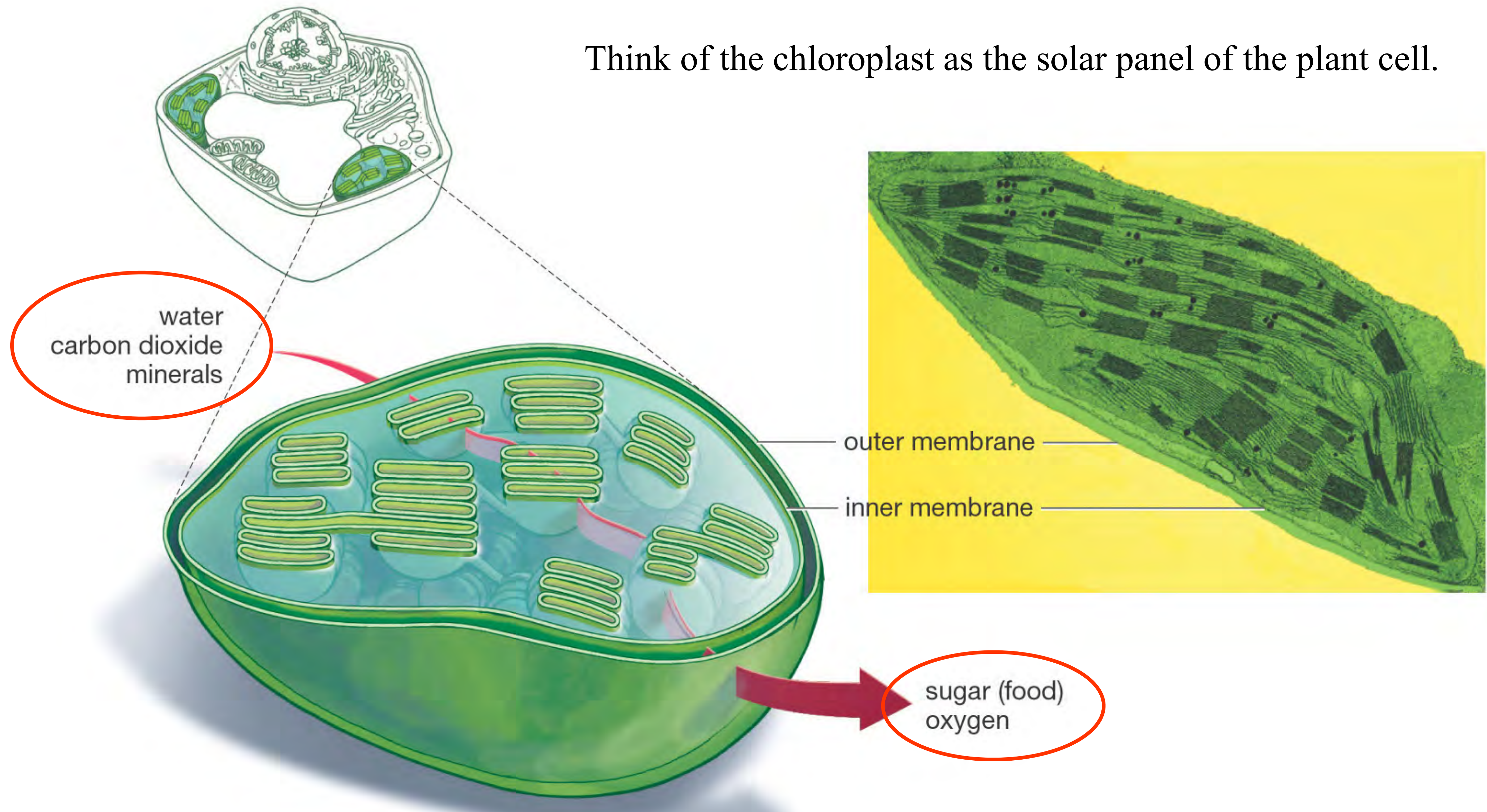
# Animal vs. Plant Cells – Chloroplasts Are a Big Part of the Difference





# The Chloroplast

Think of the chloroplast as the solar panel of the plant cell.



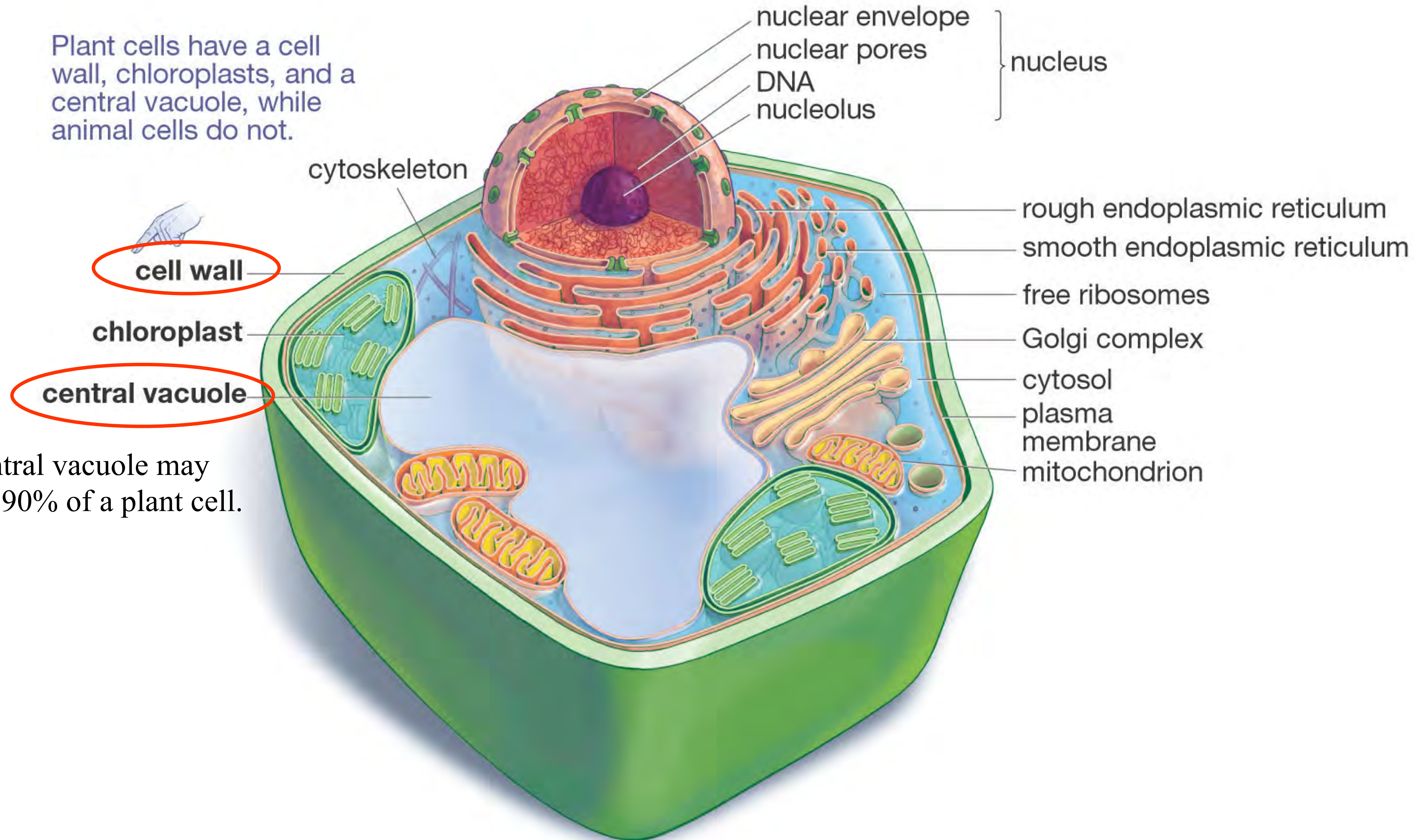
Only plants have chloroplasts, but animals reap the benefits too.



# Two Other Unique Features of Plant Cells

Plant cells have a cell wall, chloroplasts, and a central vacuole, while animal cells do not.

The central vacuole may occupy 90% of a plant cell.





# A Consequence of Cell Walls: the Great Strength of Woody Plants

(a) Wood is mostly cell walls

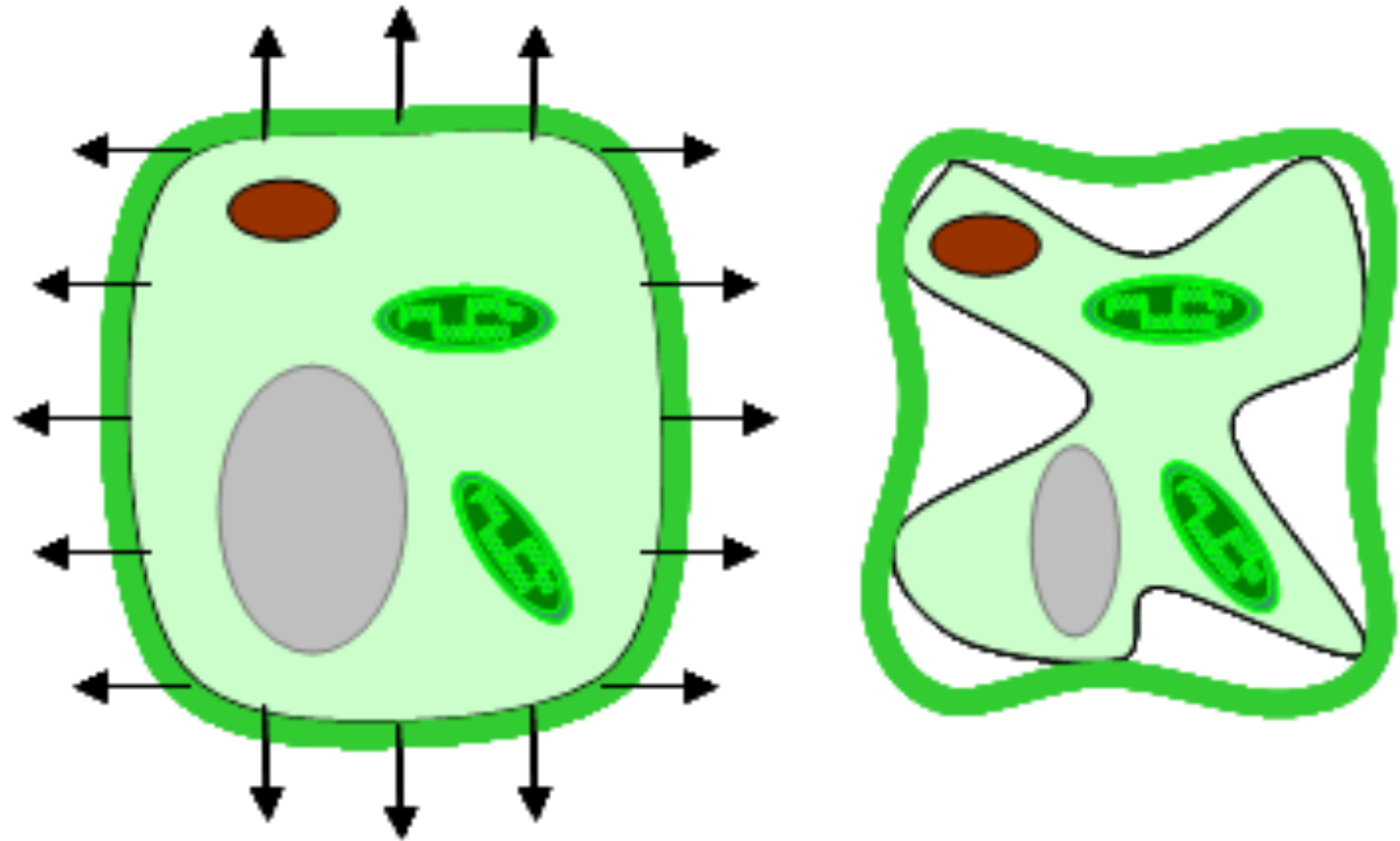


(b) A magnified view of bark





# The Central Vacuole Controls Turgor Pressure



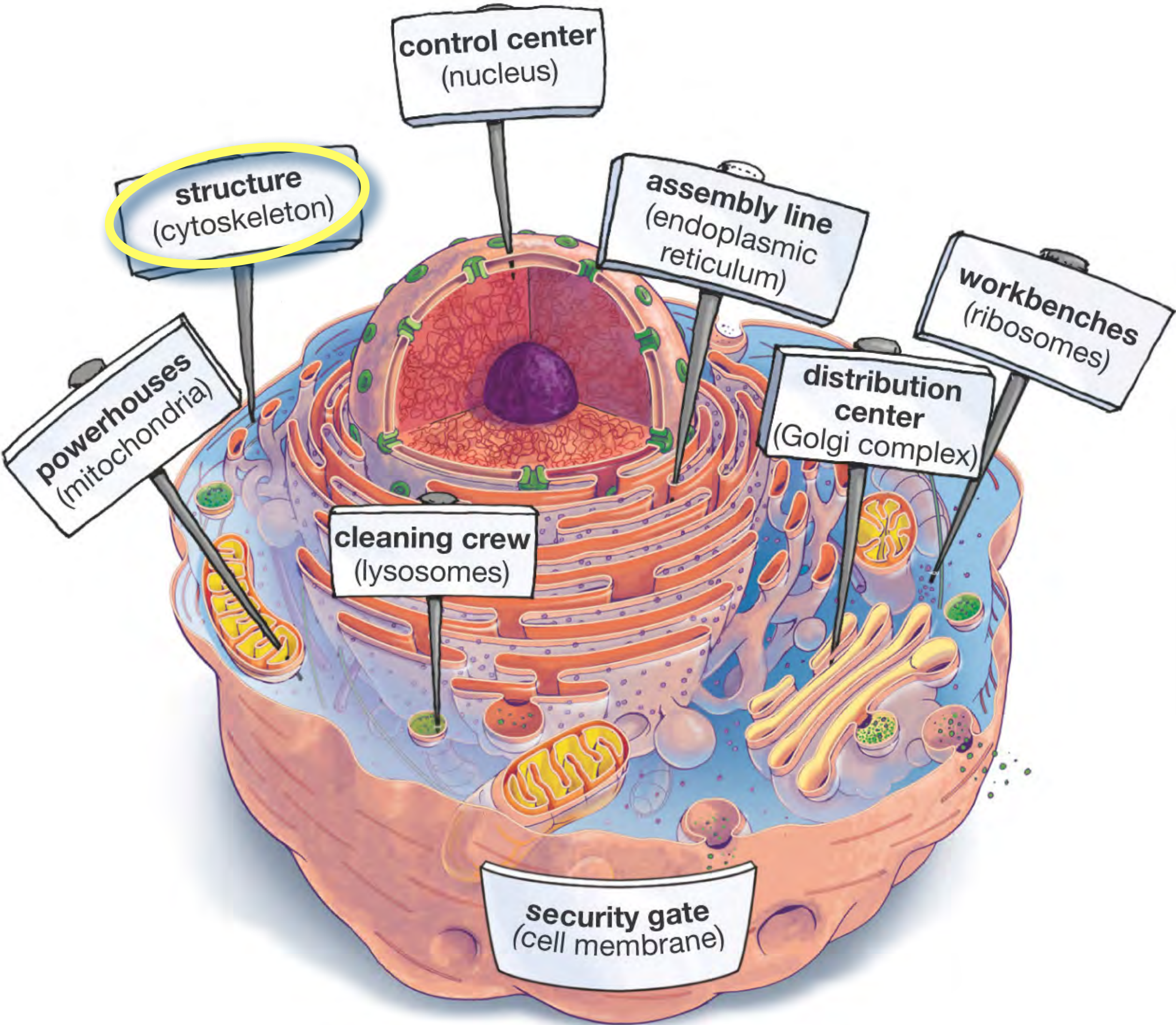
flaccid



turgid



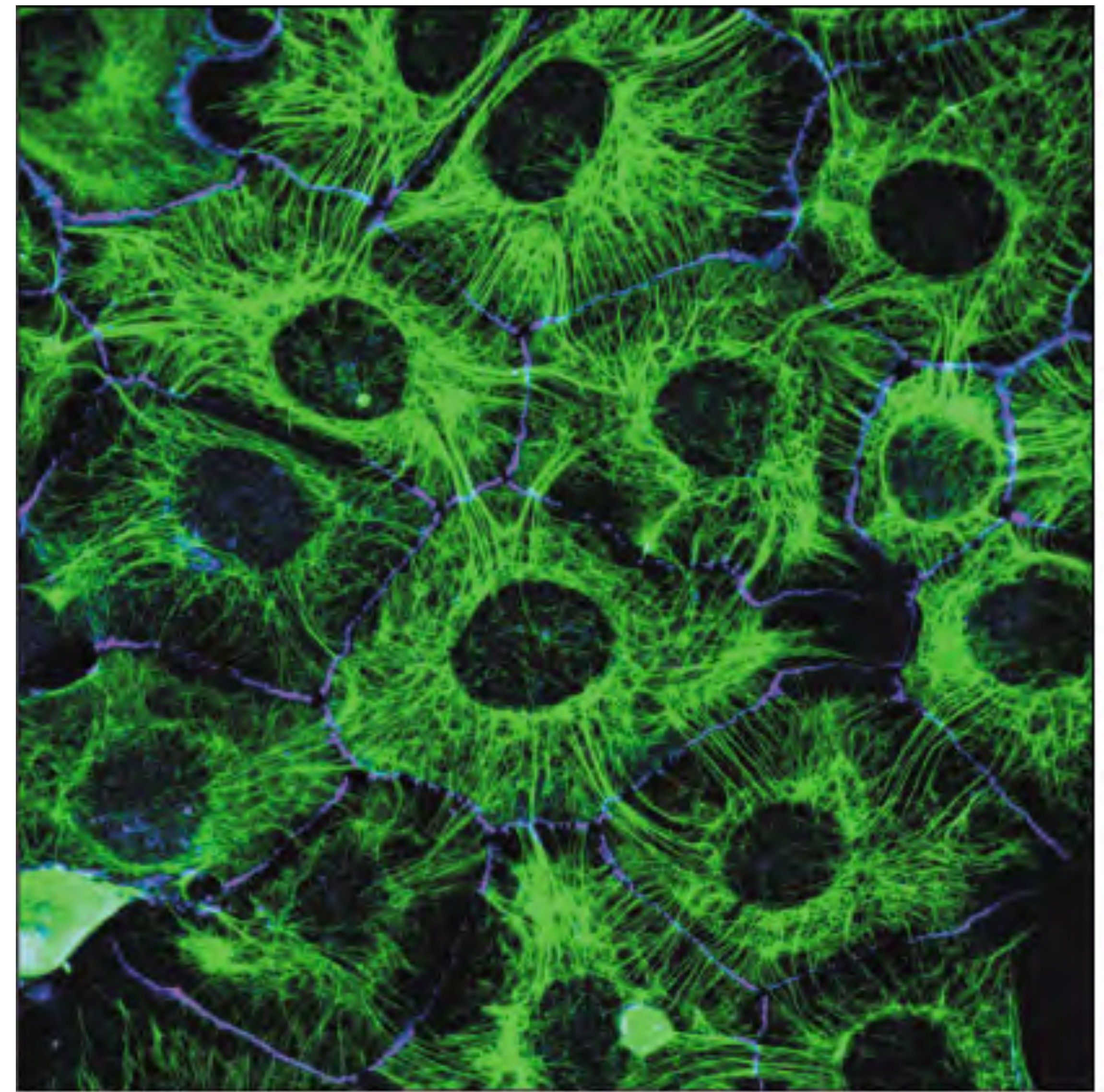
# Cellular Anatomy





# The Cytoskeleton

The name is misleading:  
The cytoskeleton is the skeleton of the cell,  
but it's also like the muscular system,  
able to change the shape of cells in a flash.

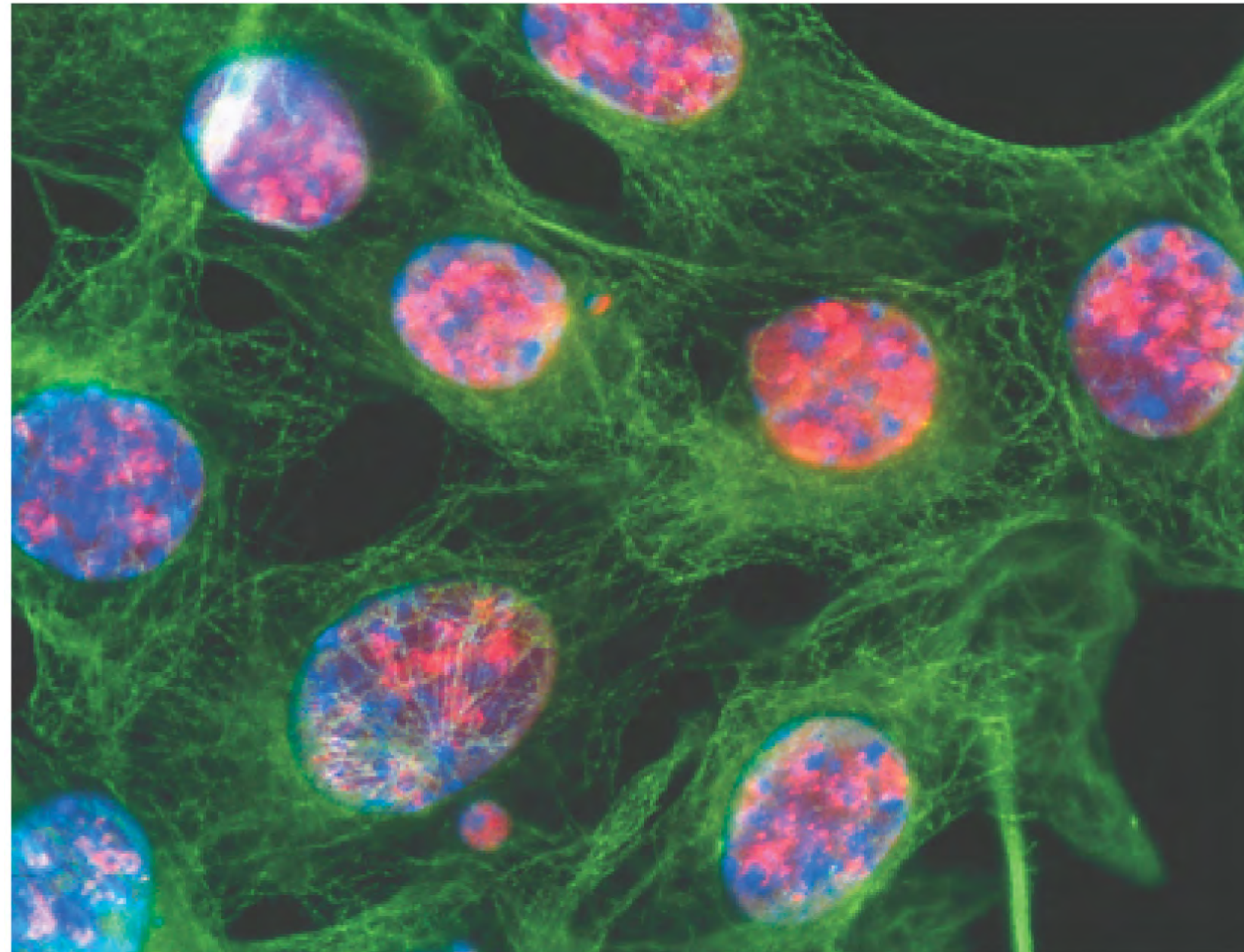
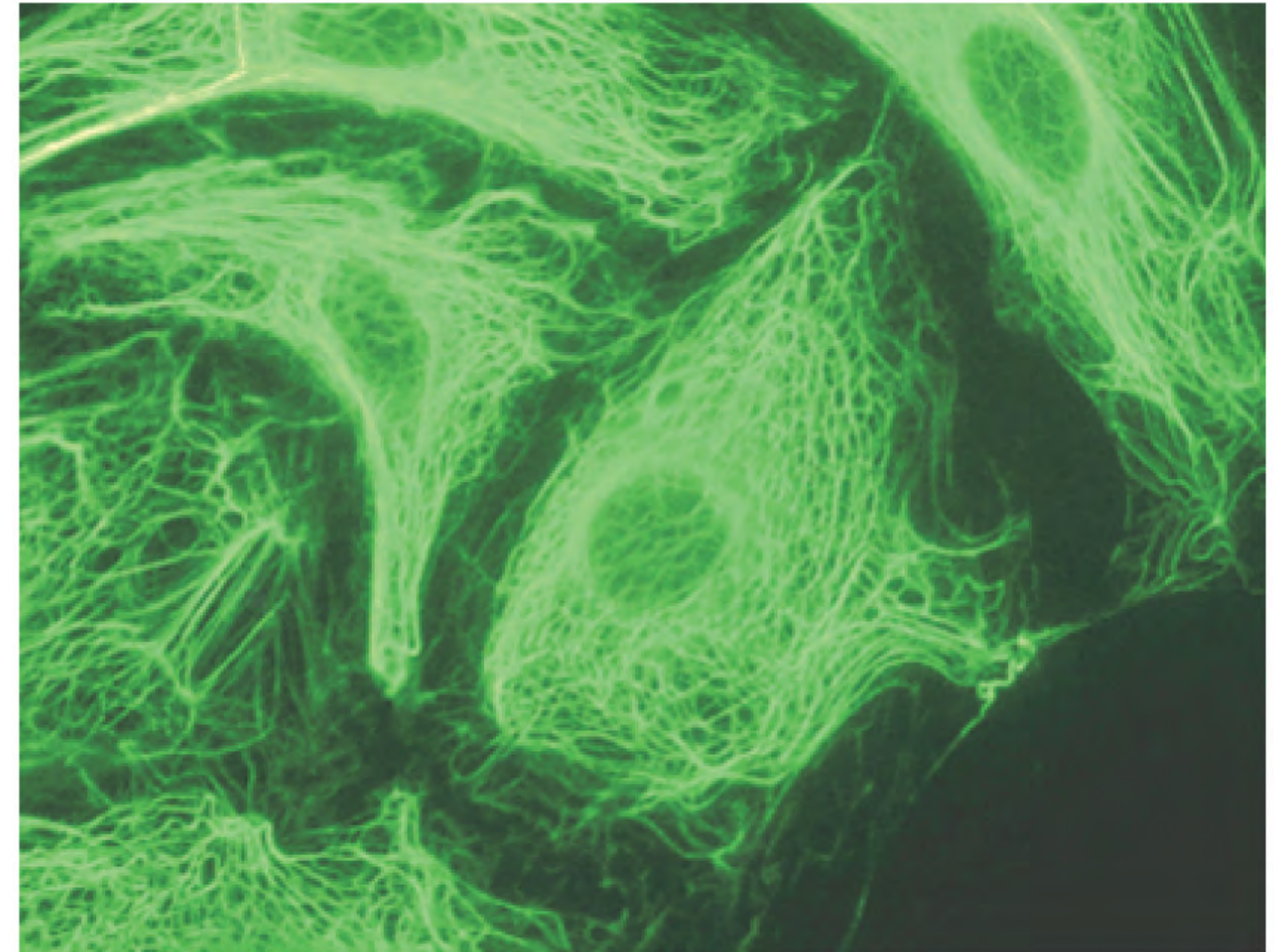
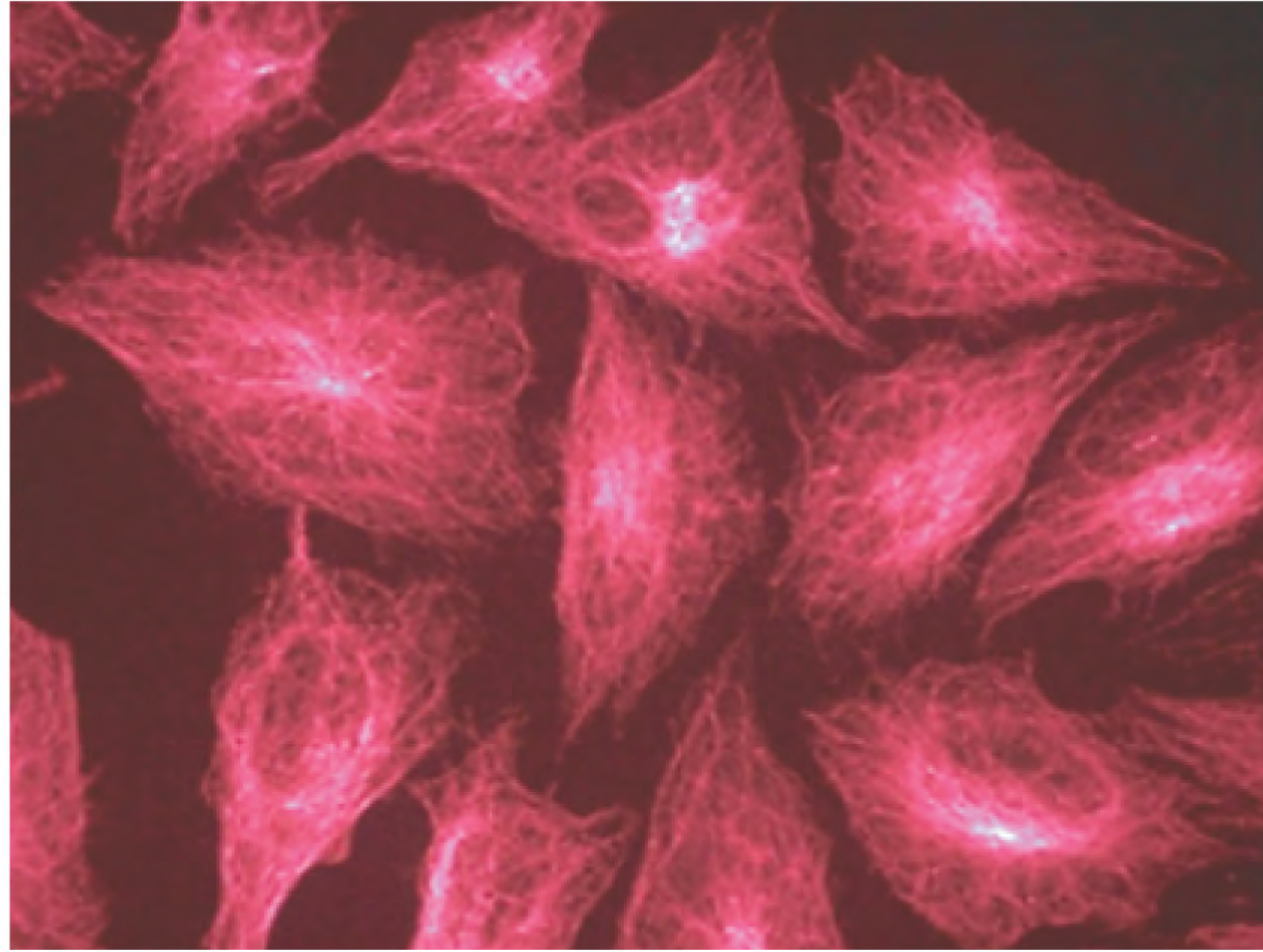


An animal cell cytoskeleton

10  $\mu$ m



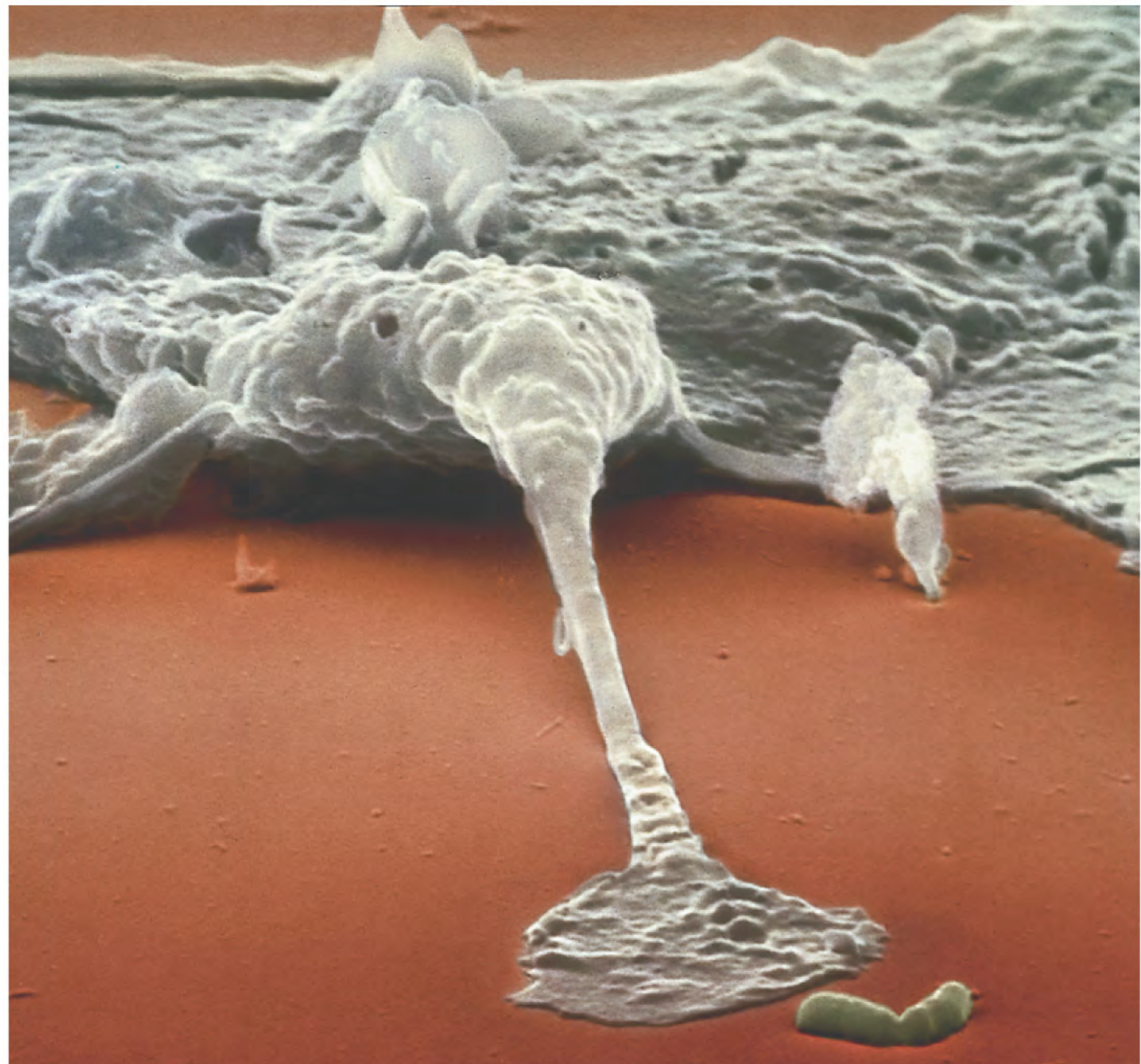
# A Cytoskeleton Gallery





# The Cytoskeleton in Action

A white blood cell using the cytoskeleton to “reach out” for a hapless bacterium.



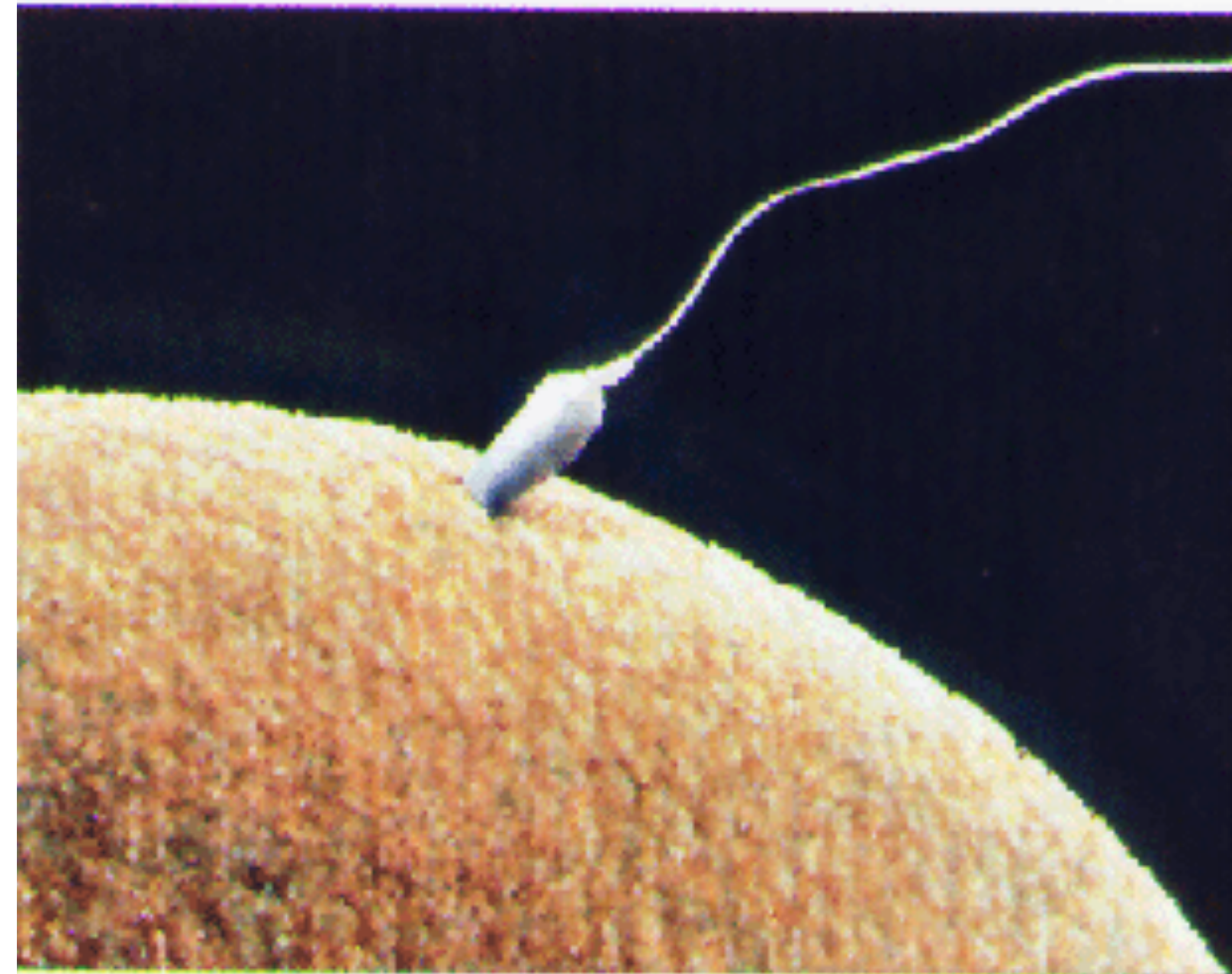


# The Cytoskeleton in Action

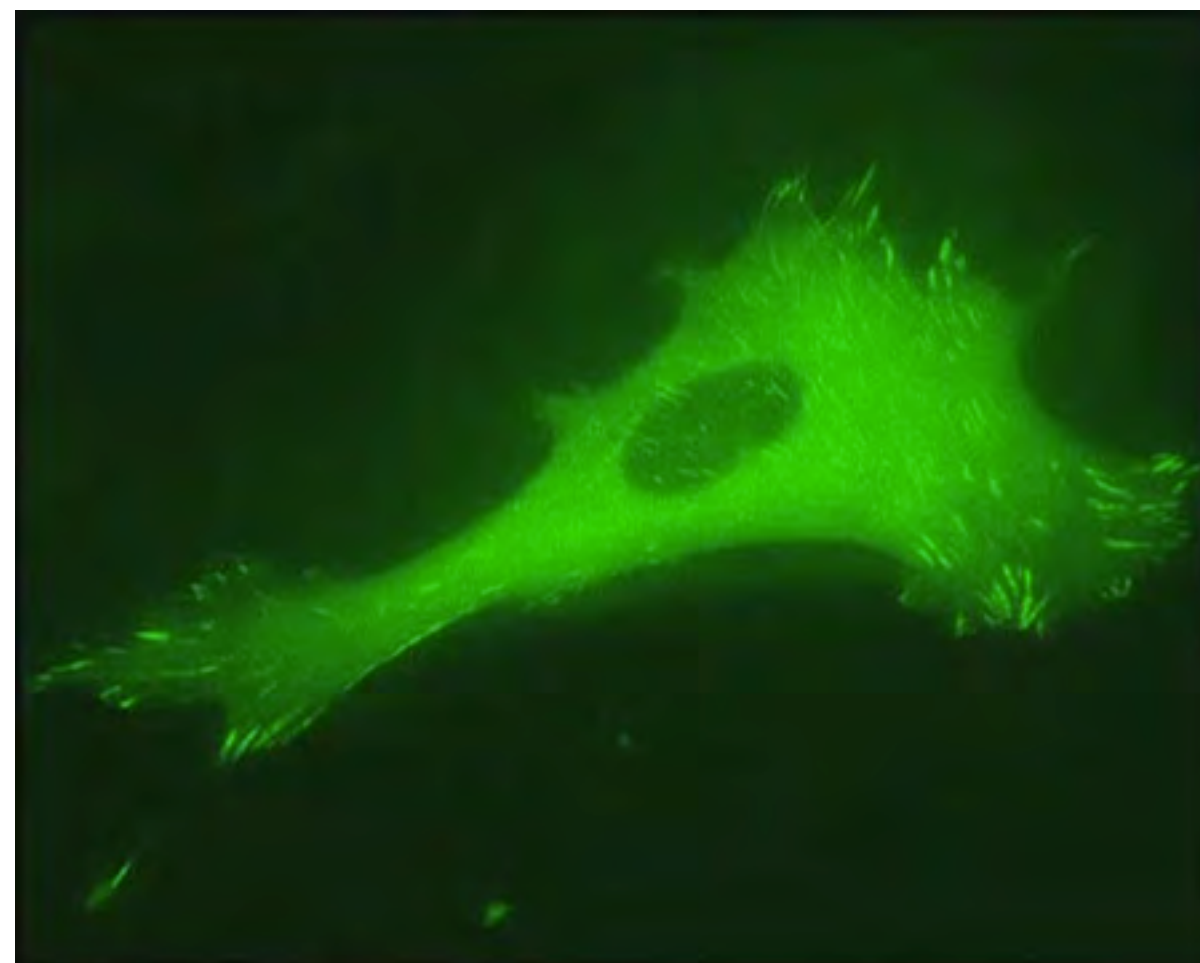
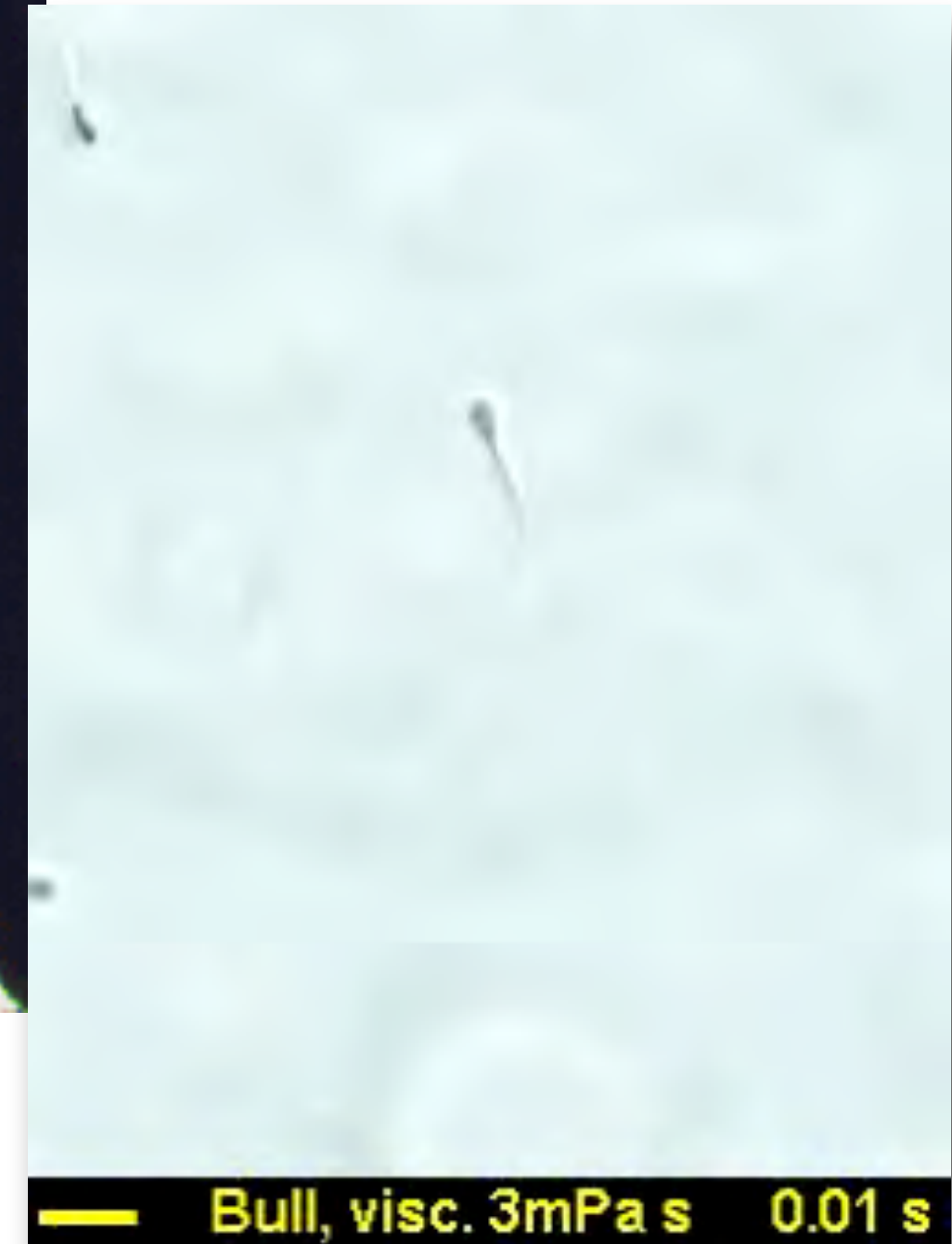


Cilia on a protozoan

Smoker's cough is due to destruction of cilia in the airways.



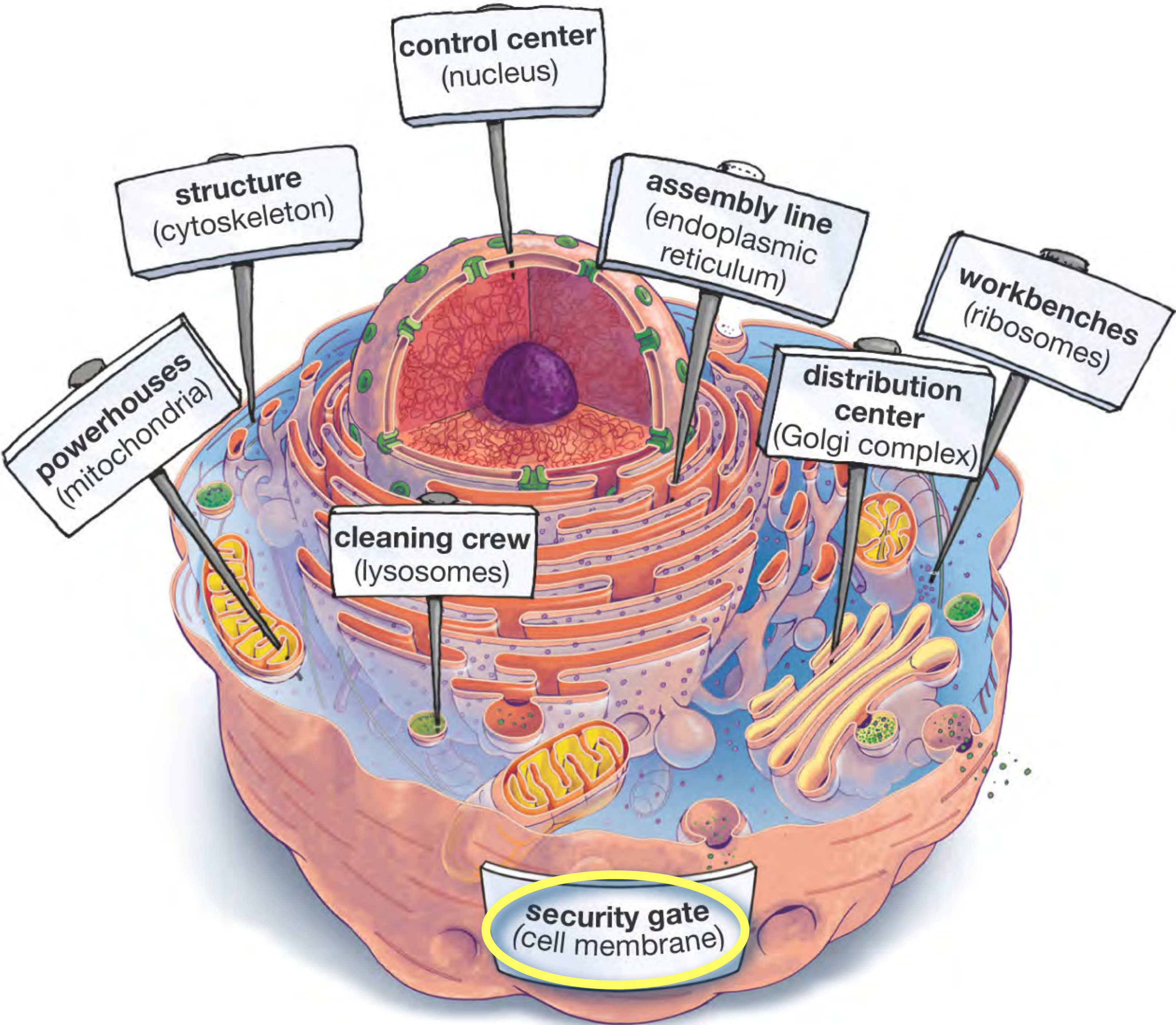
Beating sperm tail at fertilization



The actin cytoskeleton allows a cell to crawl

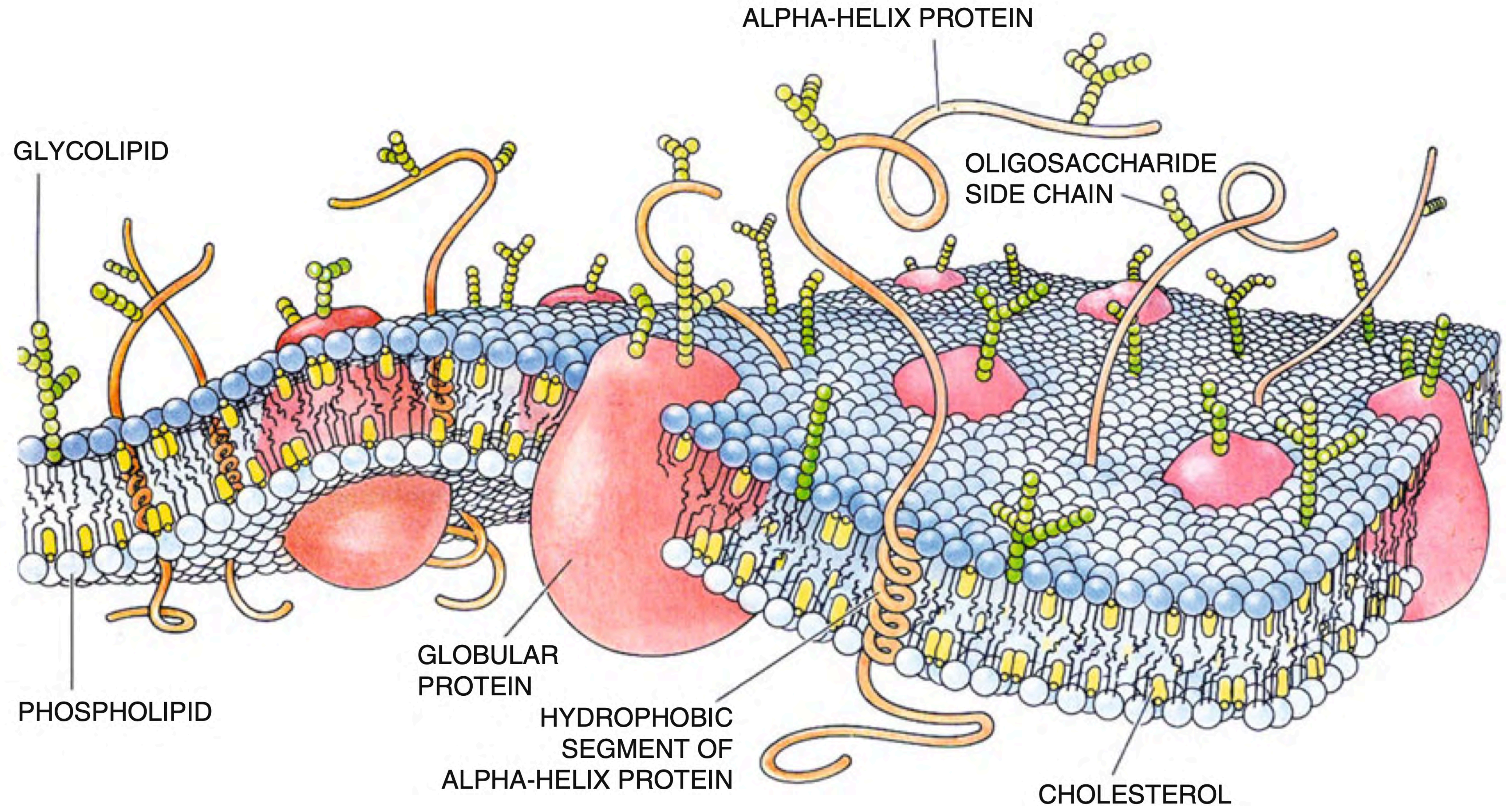


# Cellular Anatomy



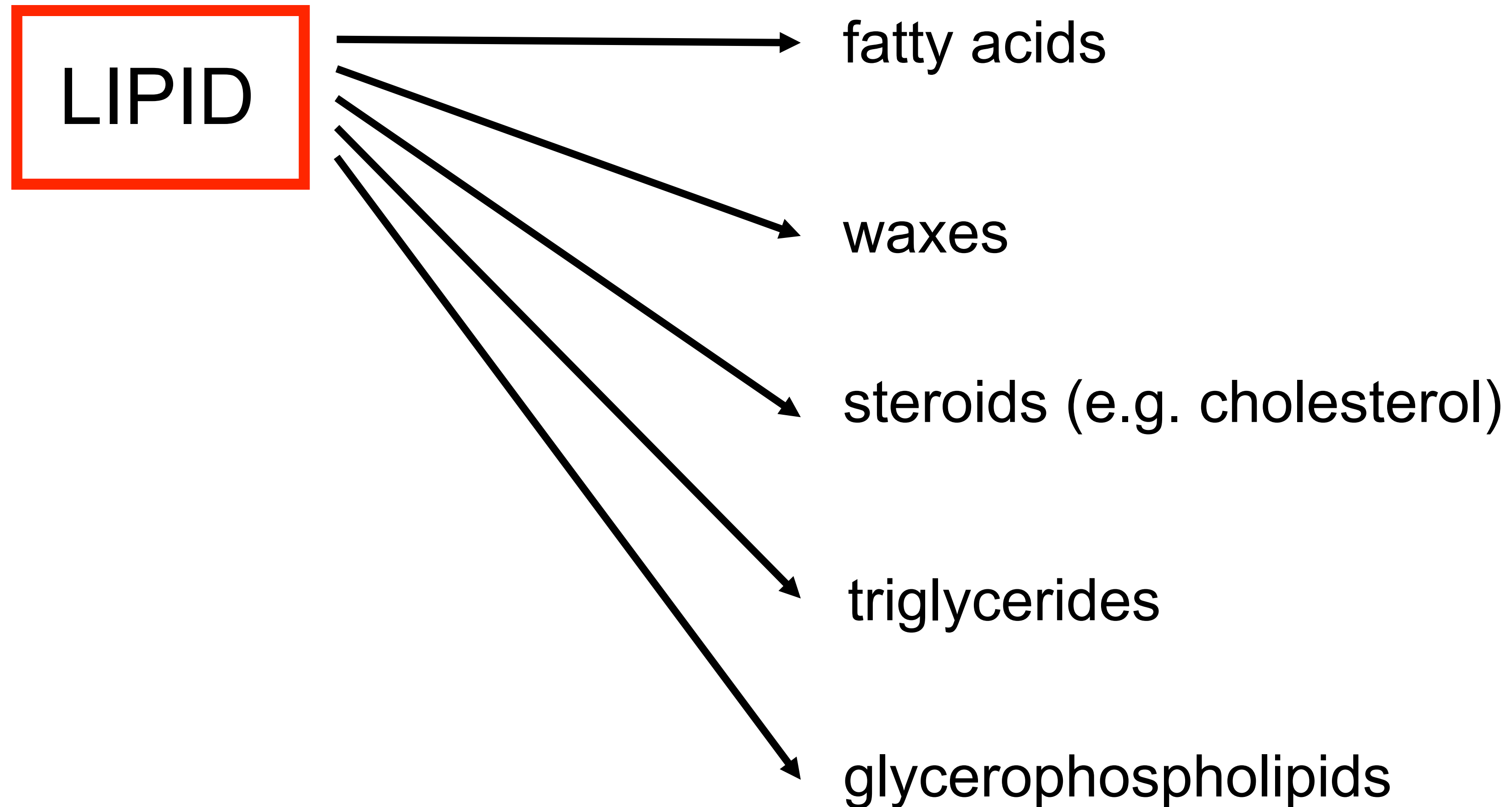


# Biological Membranes



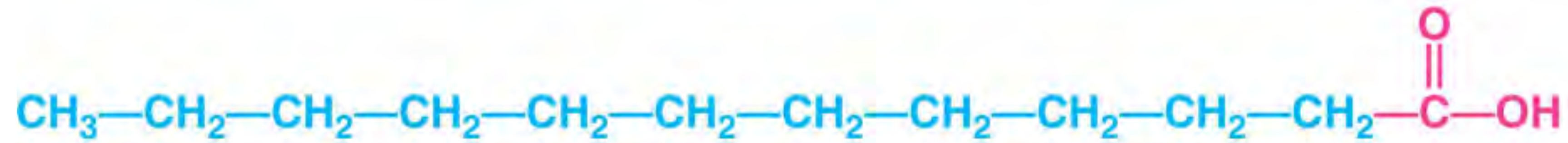


A biological compound that is not soluble in water, but is soluble in nonpolar substances





# FATTY ACIDS



Nonpolar, hydrophobic tail  
(water insoluble)

Polar, hydrophilic head  
(water soluble)

(a)

Nonpolar tail



Polar head

(b)



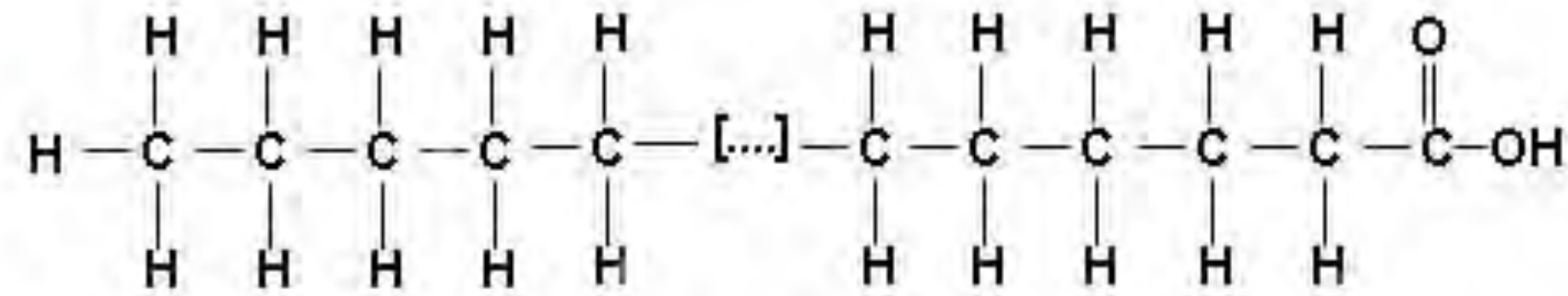
# FATTY ACIDS

- Usually straight chains (no branching)
- Sizes usually range from C<sub>10</sub> to C<sub>20</sub>
- Usually have an even number of carbons
- Can be saturated (no C=C bonds) or unsaturated (has C=C bonds)

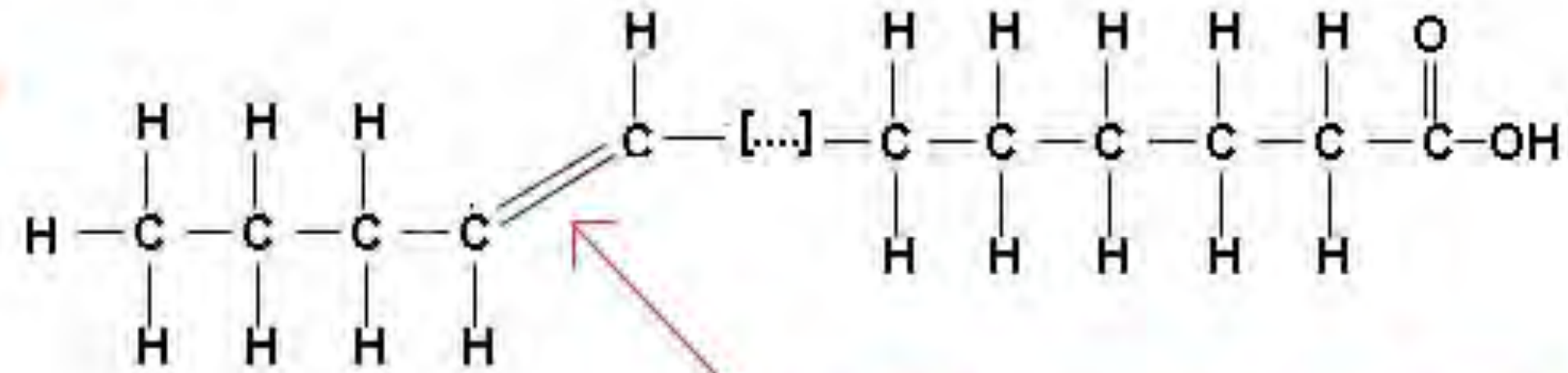


# FATTY ACIDS

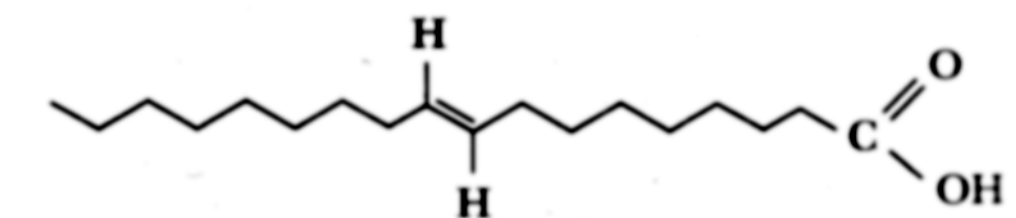
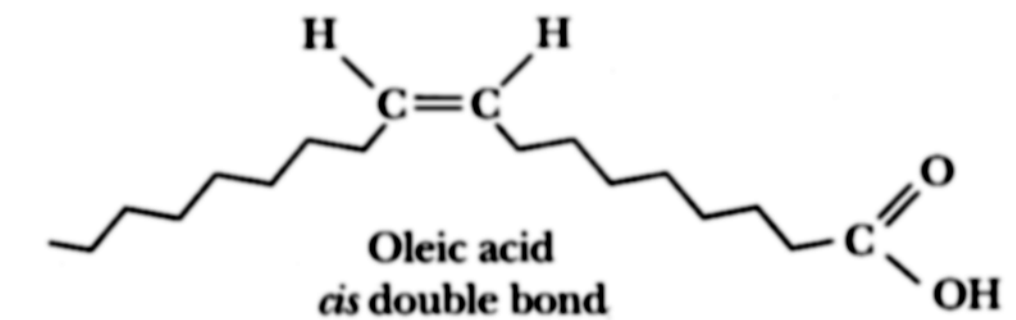
SATURATED  
FATTY ACID



UNSATURATED  
FATTY ACID



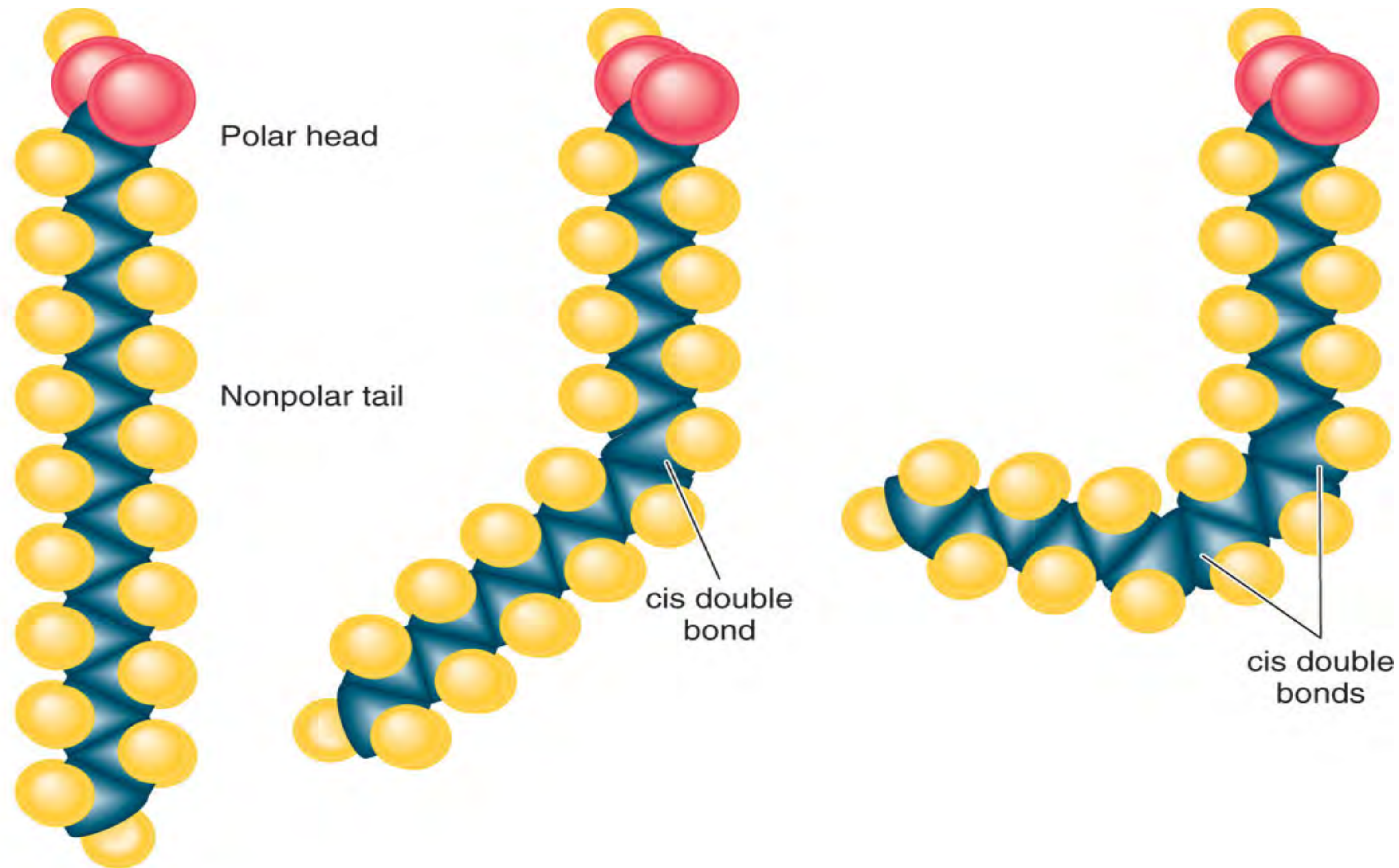
One or more double C=C bonds present  
in the fatty acid.  
This puts a 'kink' in the molecule



Structure of *cis* and *trans* monounsaturated C<sub>18</sub> fatty acids.



# Molecular Shapes

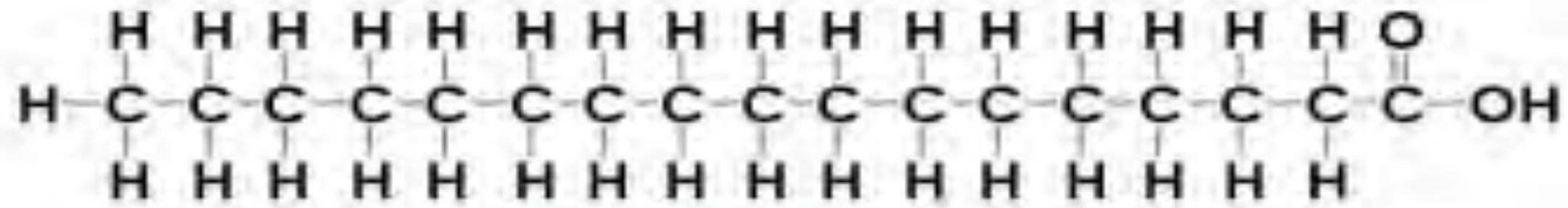


C=C causes “kinking” of the carbon chain

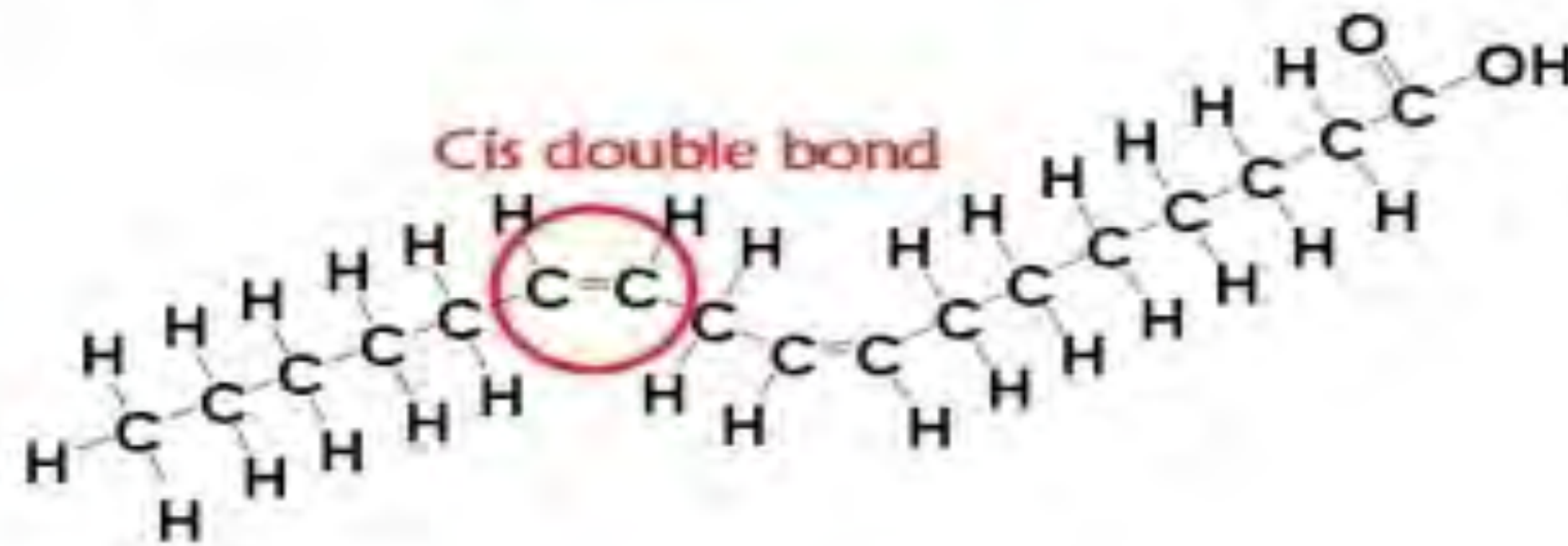


# TRANS FATTY ACIDS

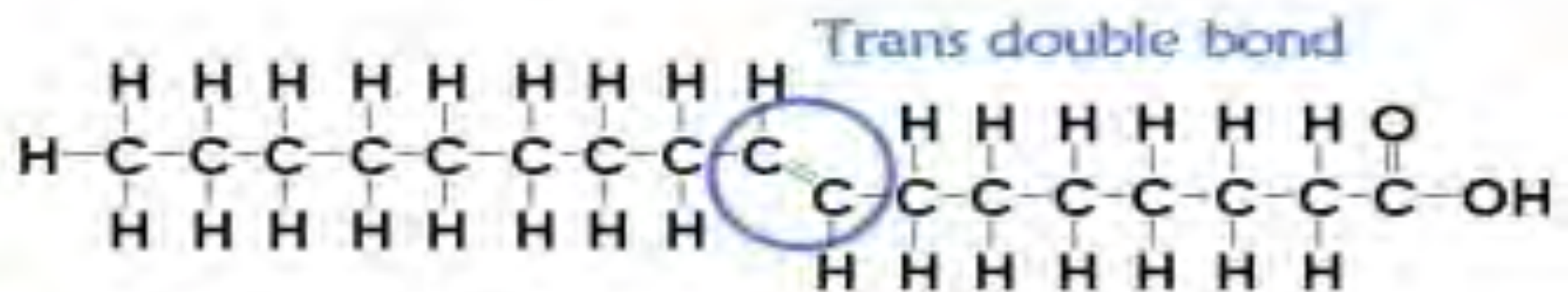
**SATURATED**  
**Stearic acid**  
(found in butter)



**UNSATURATED**  
**Linoleic acid**  
(found in vegetable oil)

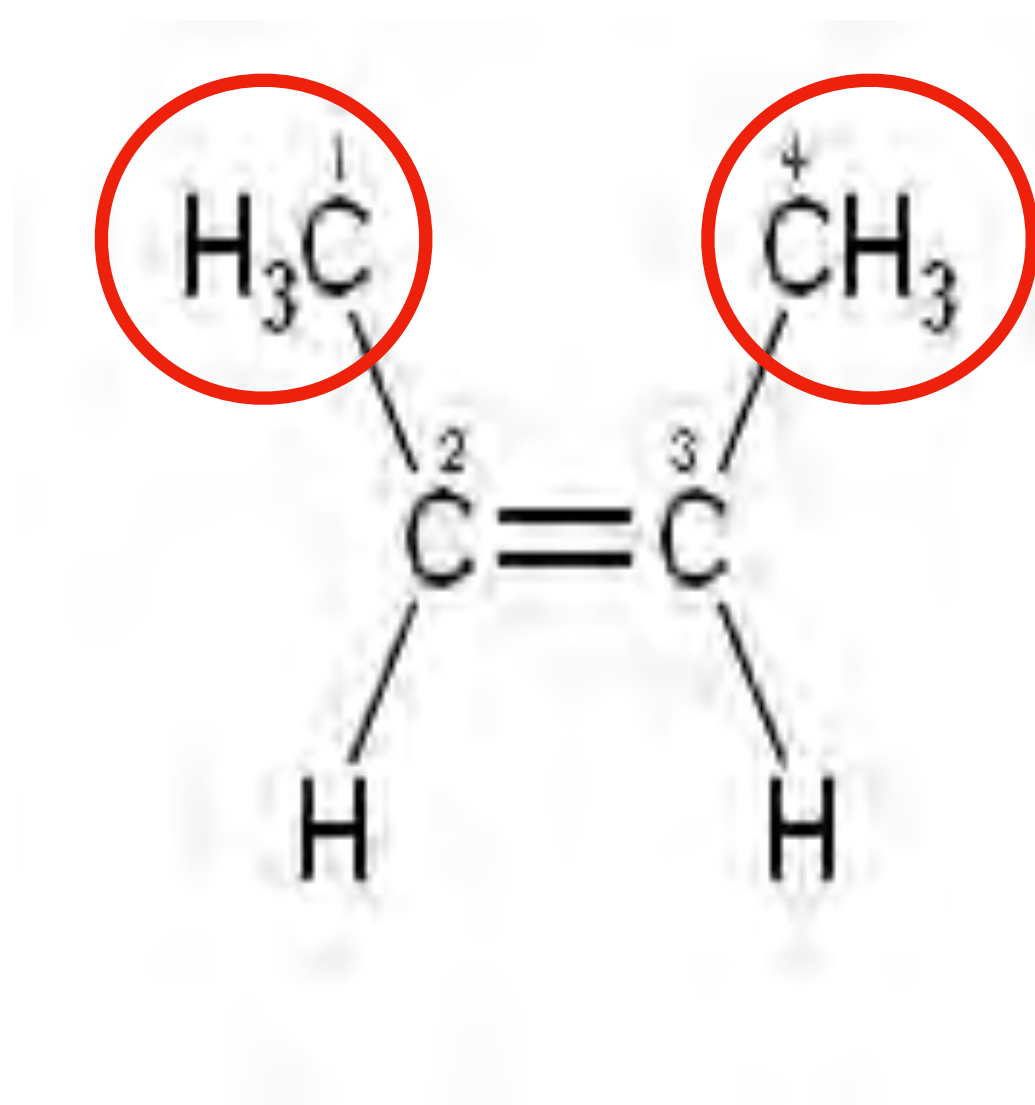


**TRANS**  
**trans-Linoleic acid**  
(found in some  
margarine)

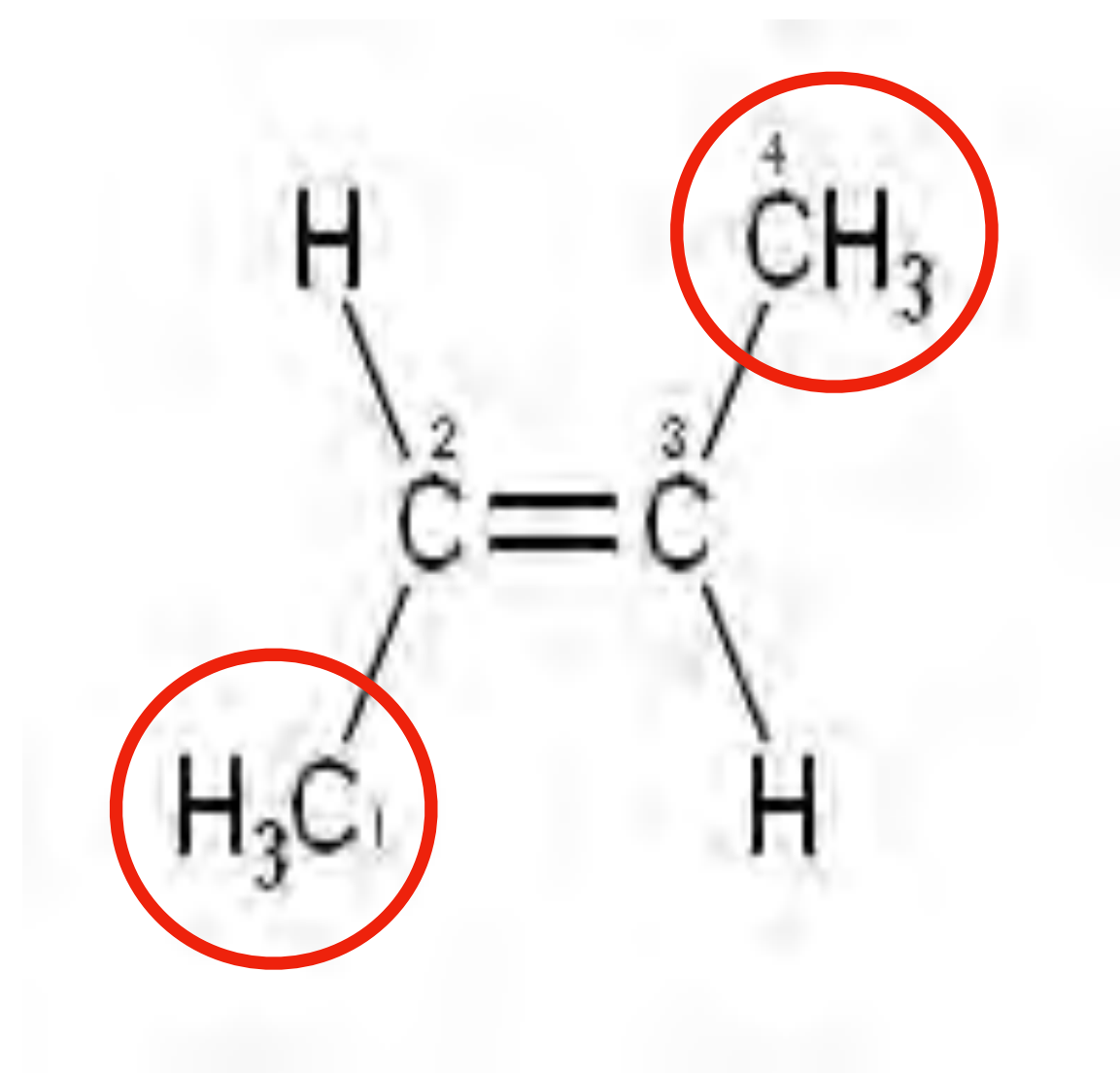




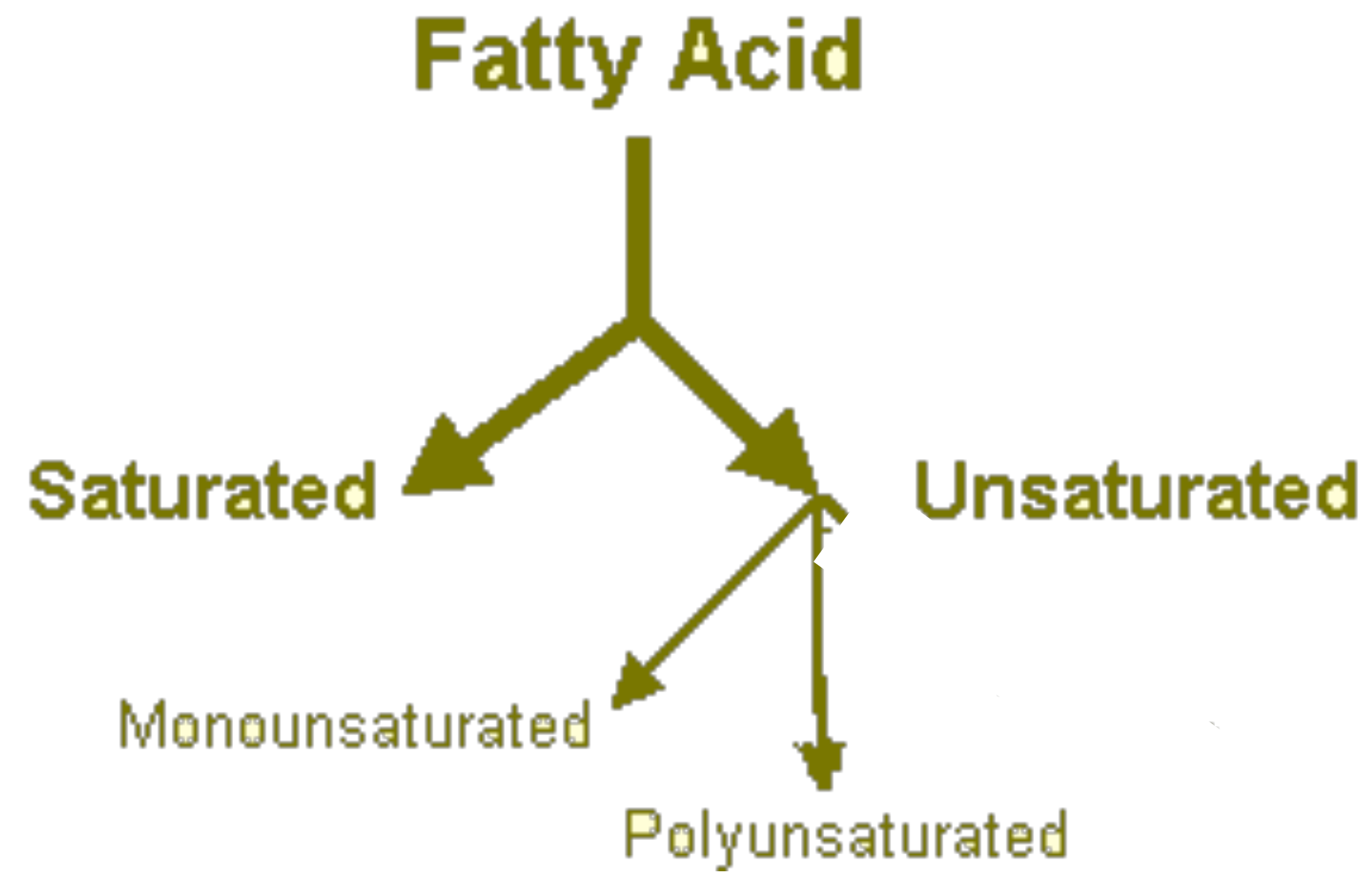
## CIS ISOMER



## TRANS ISOMER





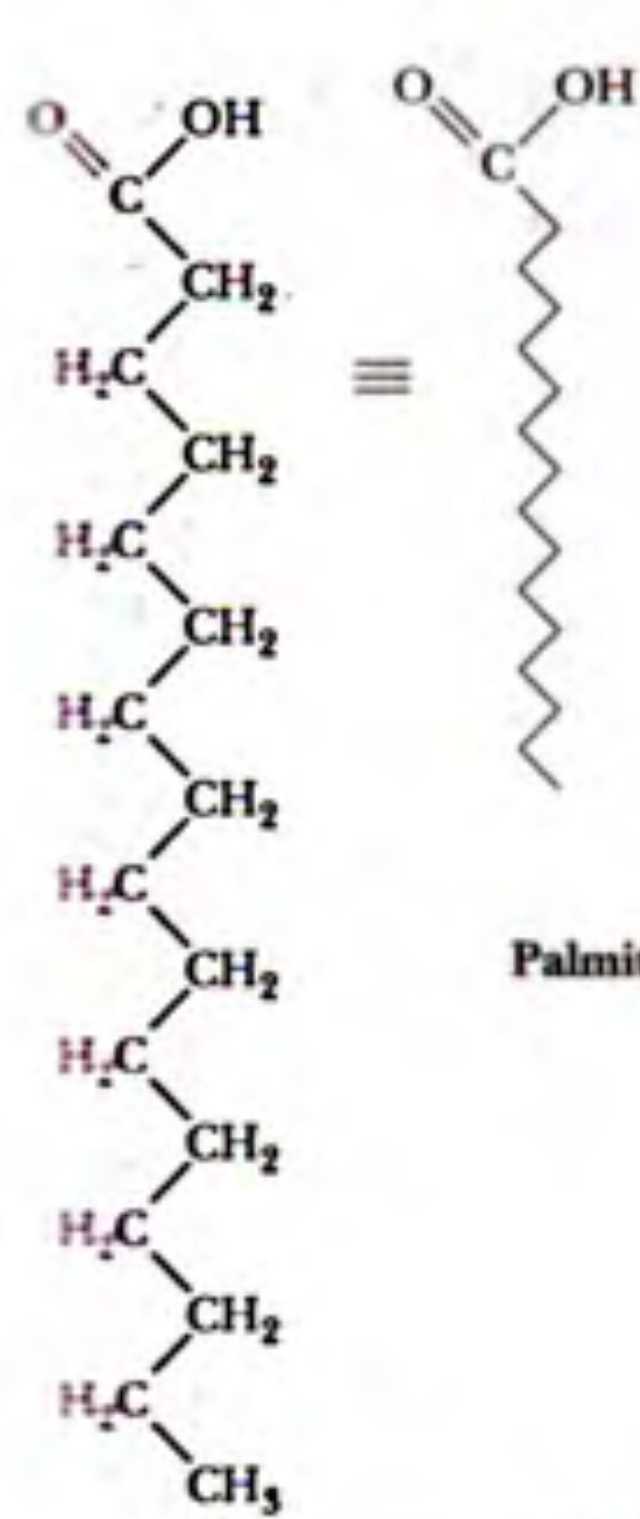


**Mon**ounsaturated – one C=C

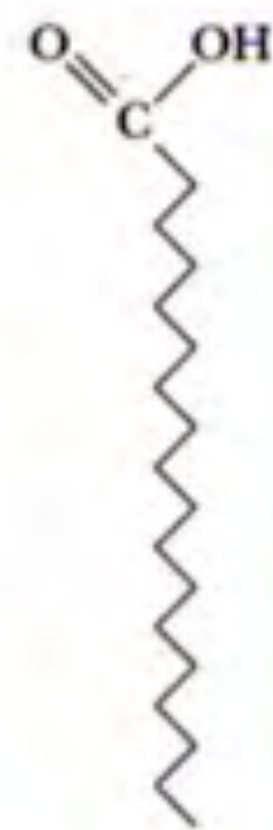
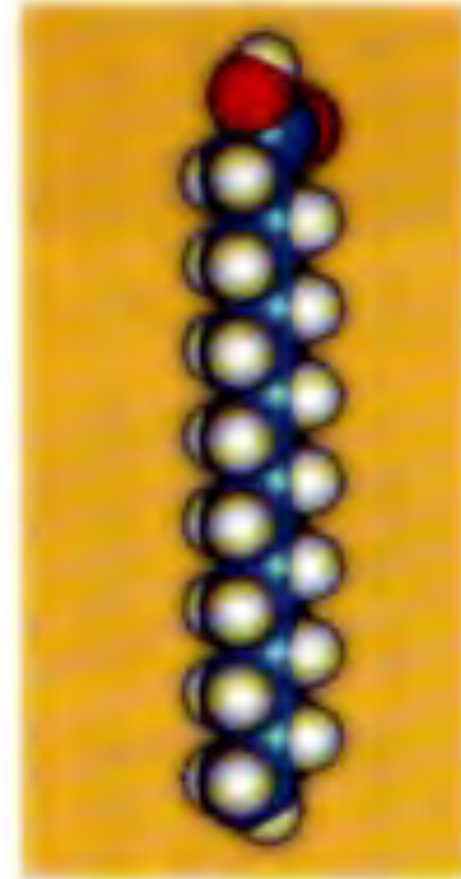
**Poly**unsaturated- more than one C=C



# FATTY ACIDS



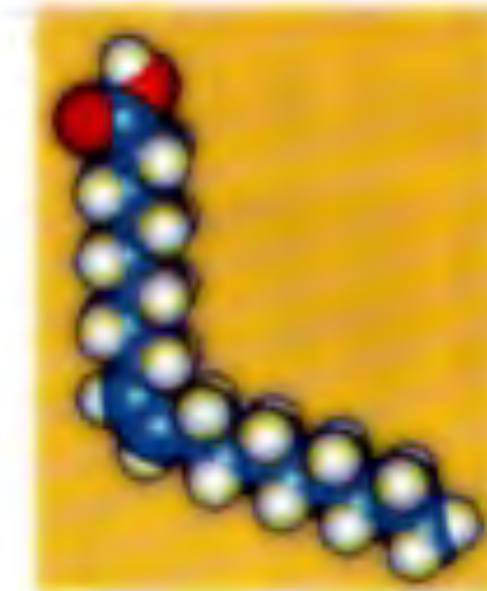
Palmitic acid



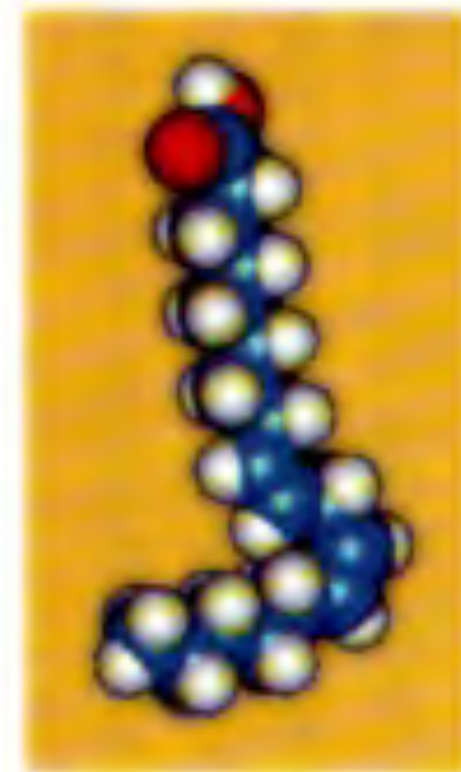
Stearic acid



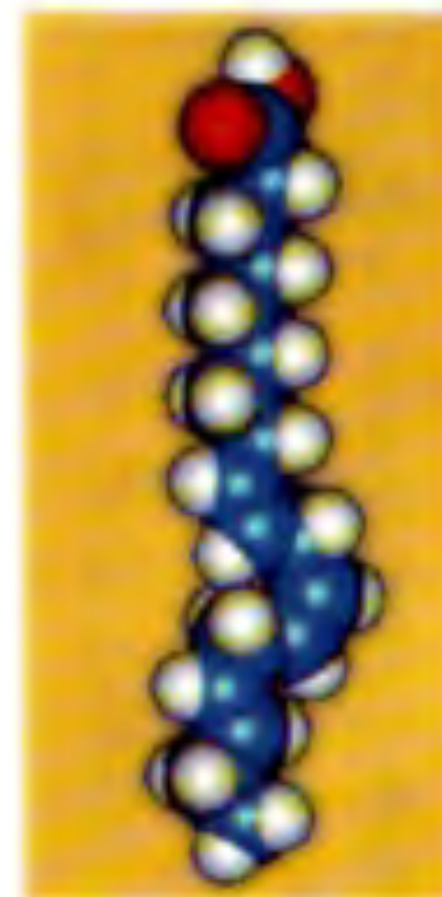
Oleic acid



Linoleic acid



$\alpha$ -Linolenic acid



Arachidonic acid





# FATTY ACIDS

Table 8.1

## Common Biological Fatty Acids

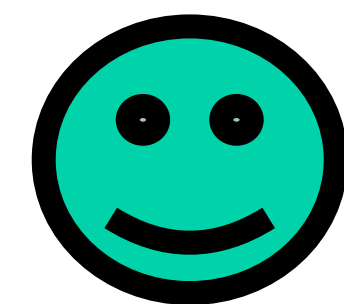
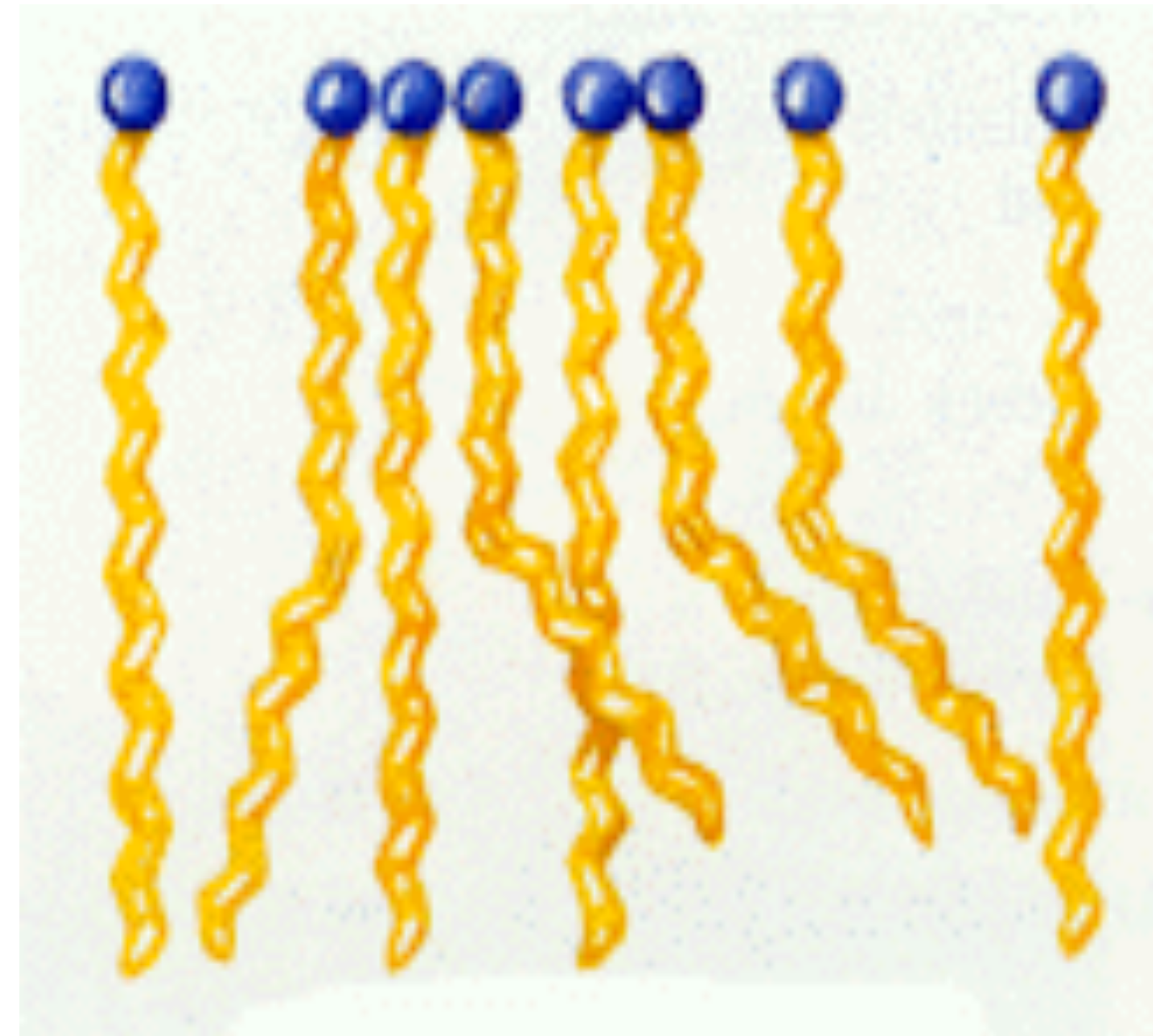
Number of Carbons	Common Name	Systematic Name	Symbol	Structure
Saturated fatty acids				
12	Lauric acid	Dodecanoic acid	12:0	$\text{CH}_3(\text{CH}_2)_{10}\text{COOH}$
14	Myristic acid	Tetradecanoic acid	14:0	$\text{CH}_3(\text{CH}_2)_{12}\text{COOH}$
16	Palmitic acid	Hexadecanoic acid	16:0	$\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$
18	Stearic acid	Octadecanoic acid	18:0	$\text{CH}_3(\text{CH}_2)_{16}\text{COOH}$
20	Arachidic acid	Eicosanoic acid	20:0	$\text{CH}_3(\text{CH}_2)_{18}\text{COOH}$
22	Behenic acid	Docosanoic acid	22:0	$\text{CH}_3(\text{CH}_2)_{20}\text{COOH}$
24	Lignoceric acid	Tetracosanoic acid	24:0	$\text{CH}_3(\text{CH}_2)_{22}\text{COOH}$
Unsaturated fatty acids (all double bonds are cis)				
16	Palmitoleic acid	9-Hexadecenoic acid	16:1	$\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$
18	Oleic acid	9-Octadecenoic acid	18:1	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$
18	Linoleic acid	9,12-Octadecadienoic acid	18:2	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_2(\text{CH}_2)_6\text{COOH}$
18	$\alpha$ -Linolenic acid	9,12,15-Octadecatrienoic acid	18:3	$\text{CH}_3\text{CH}_2(\text{CH}=\text{CHCH}_2)_3(\text{CH}_2)_6\text{COOH}$
18	$\gamma$ -Linolenic acid	6,9,12-Octadecatrienoic acid	18:3	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_3(\text{CH}_2)_3\text{COOH}$
20	Arachidonic acid	5,8,11,14-Eicosatetraenoic acid	20:4	$\text{CH}_3(\text{CH}_2)_4(\text{CH}=\text{CHCH}_2)_4(\text{CH}_2)_2\text{COOH}$
24	Nervonic acid	15-Tetracosenoic acid	24:1	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_{13}\text{COOH}$





## SATURATED

- Can pack closely together
- High Melting point
- Solid
- Animal fat



## UNSATURATED

- Kinks prevent close contact
- Lower Melting point
- Liquid
- Plant and fish oil



# FATTY ACIDS



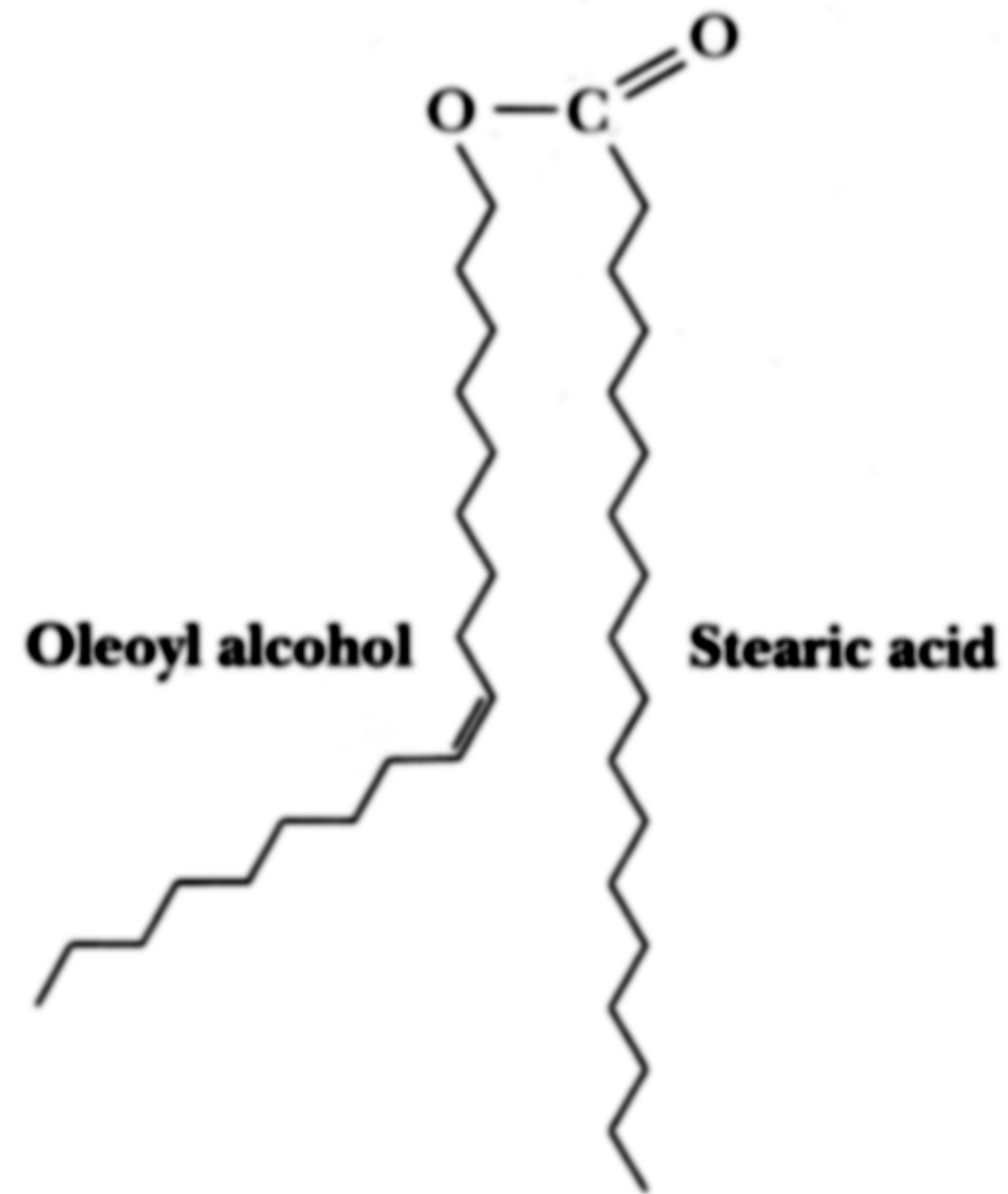
Fatty Acid Compositions of Some Dietary Lipids*					
Source	Lauric and Myristic	Palmitic	Stearic	Oleic	Linoleic
Beef	5	24–32	20–25	37–43	2–3
Milk		25	12	33	3
Coconut	74	10	2	7	
Corn		8–12	3–4	19–49	34–62
Olive		9	2	84	4
Palm		39	4	40	8
Safflower		6	3	13	78
Soybean		9	6	20	52
Sunflower		6	1	21	66

Data from *Merck Index*, 10th ed. Rahway, NJ: Merck and Co.; and Wilson, E. D., et al., 1979, *Principles of Nutrition*, 4th ed. New York: Wiley.

\*Values are percentages of total fatty acids.



# WAXES



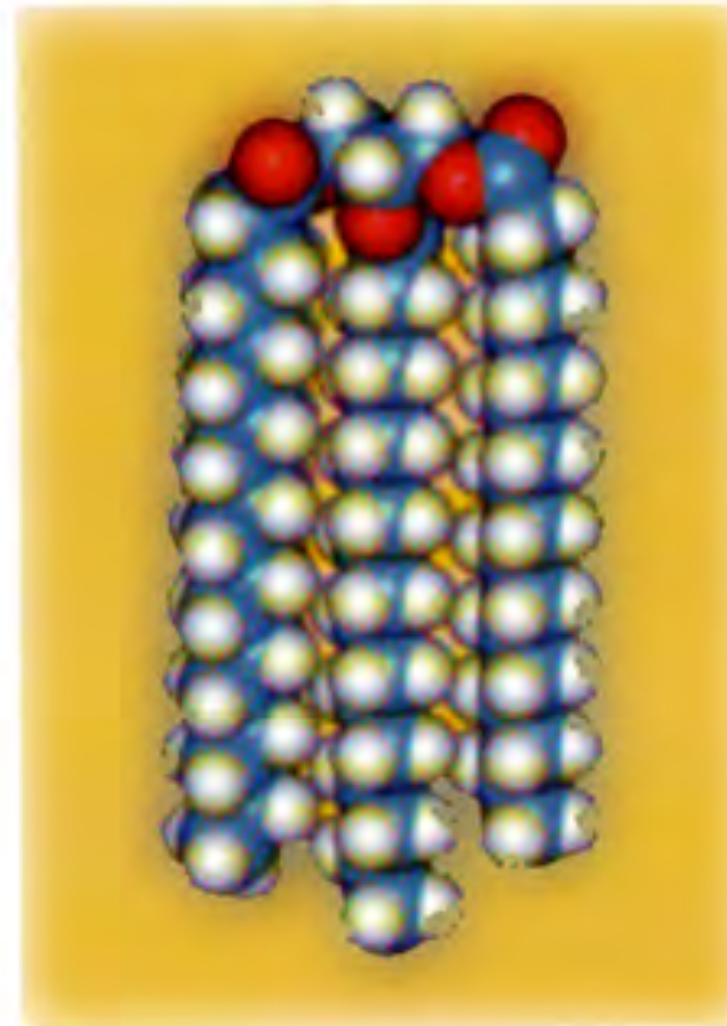
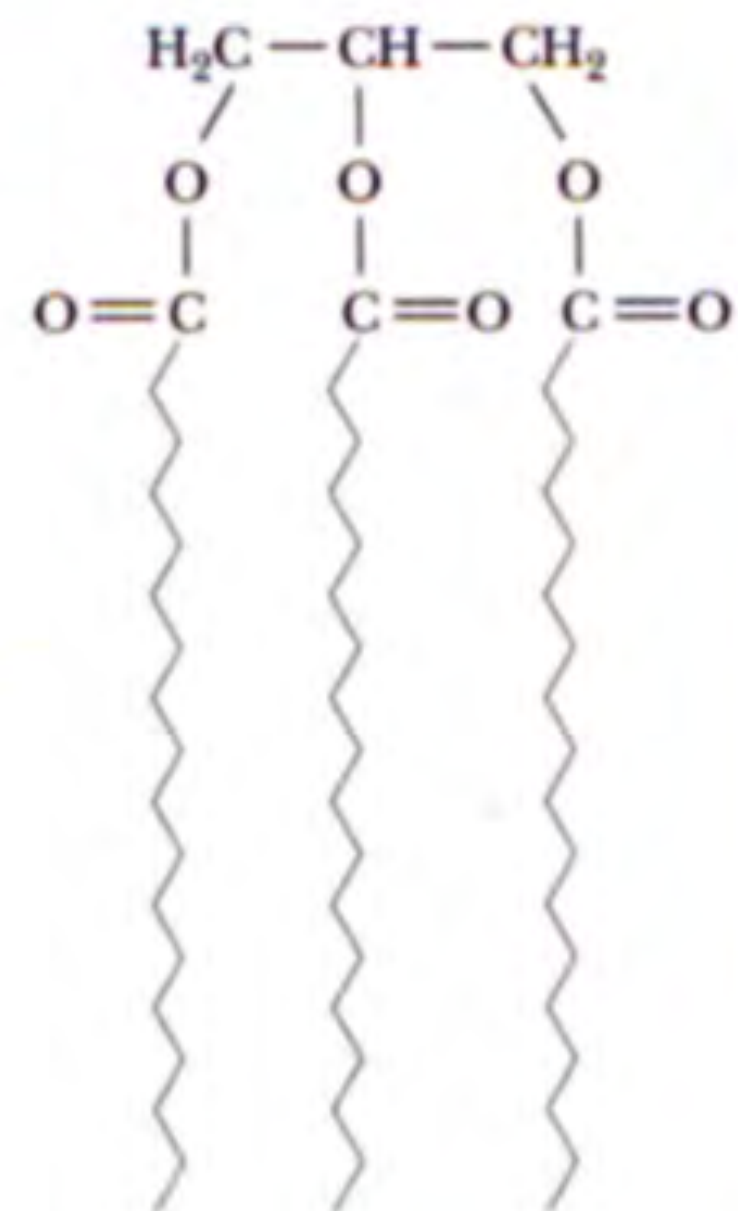
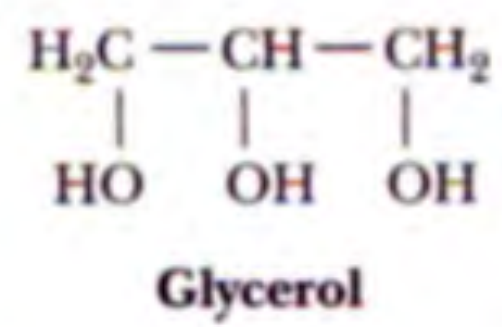
**FIGURE 8.15** An example of a wax. Oleoyl alcohol is esterified to stearic acid in this case.

Primary function in biology is protection

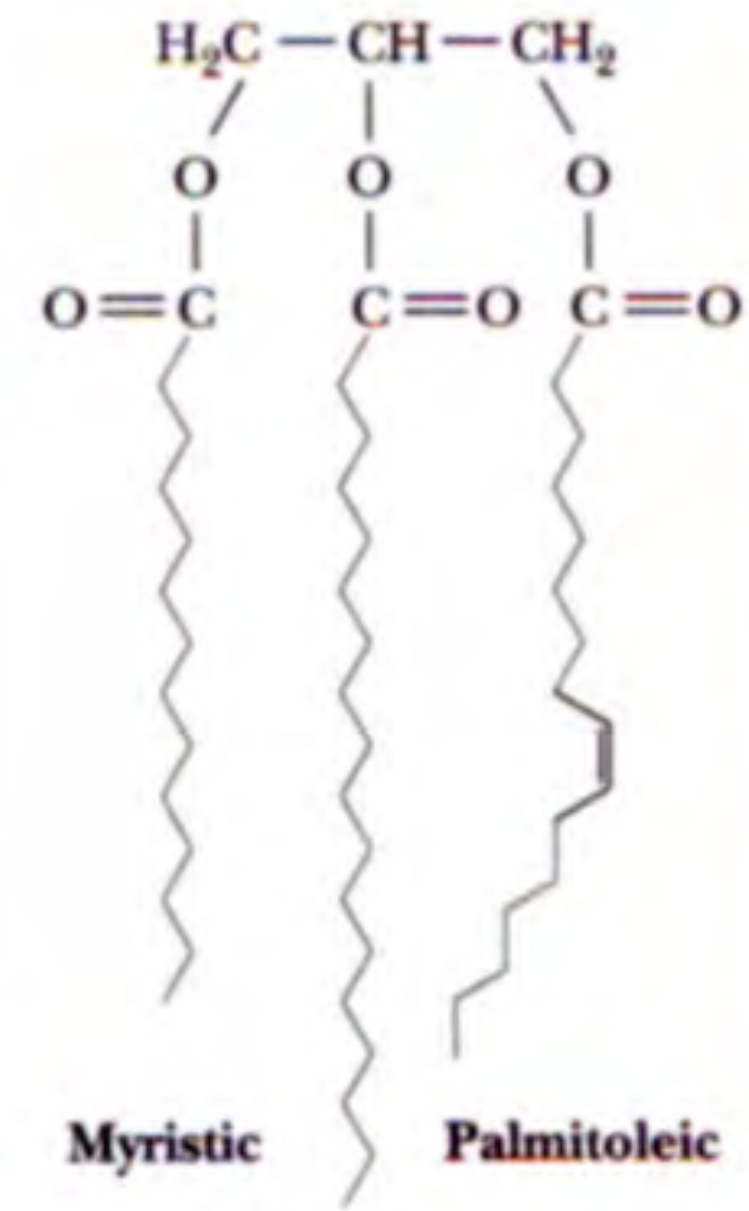




# TRIGLYCERIDES

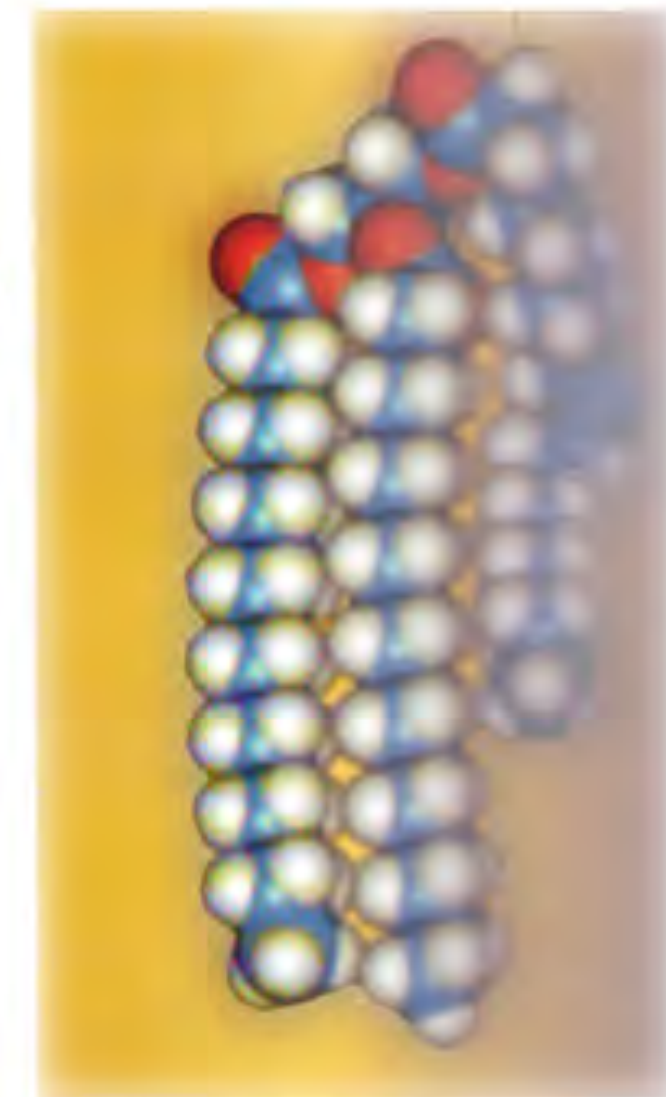


**Tristearin**  
(a simple triacylglycerol)



**Myristic**      **Palmitoleic**  
**Stearic**

A mixed triacylglycerol

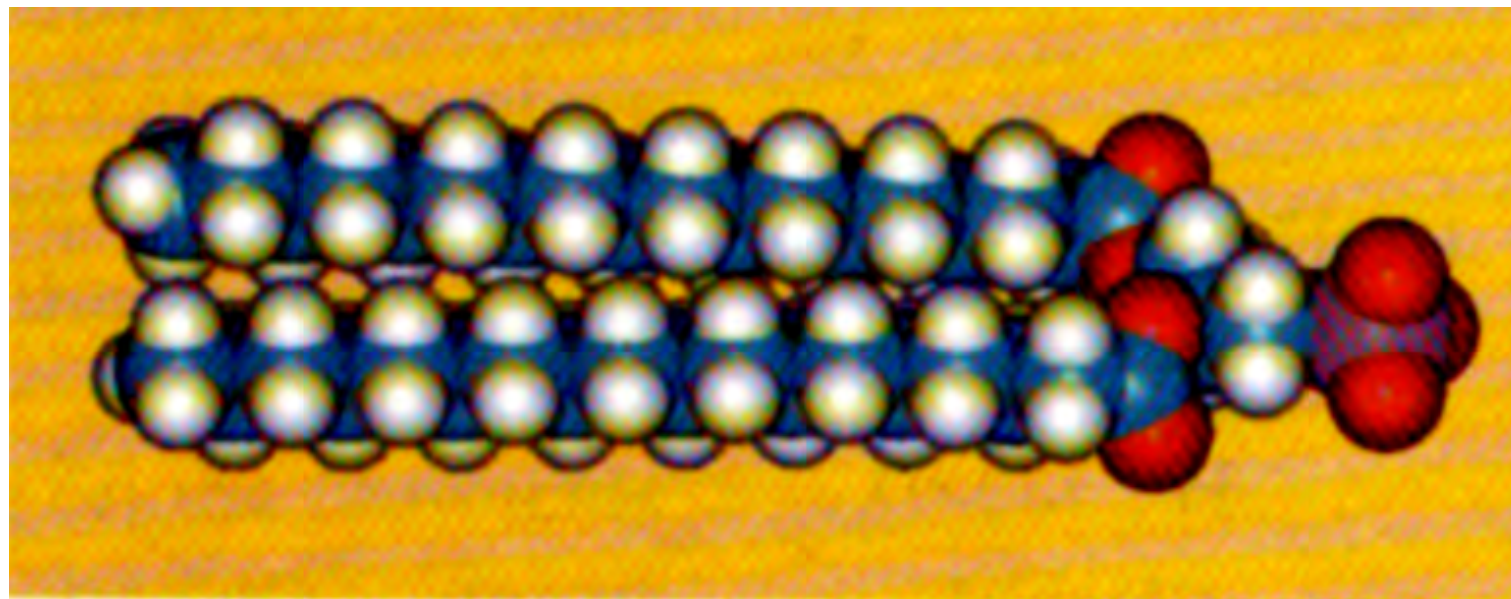
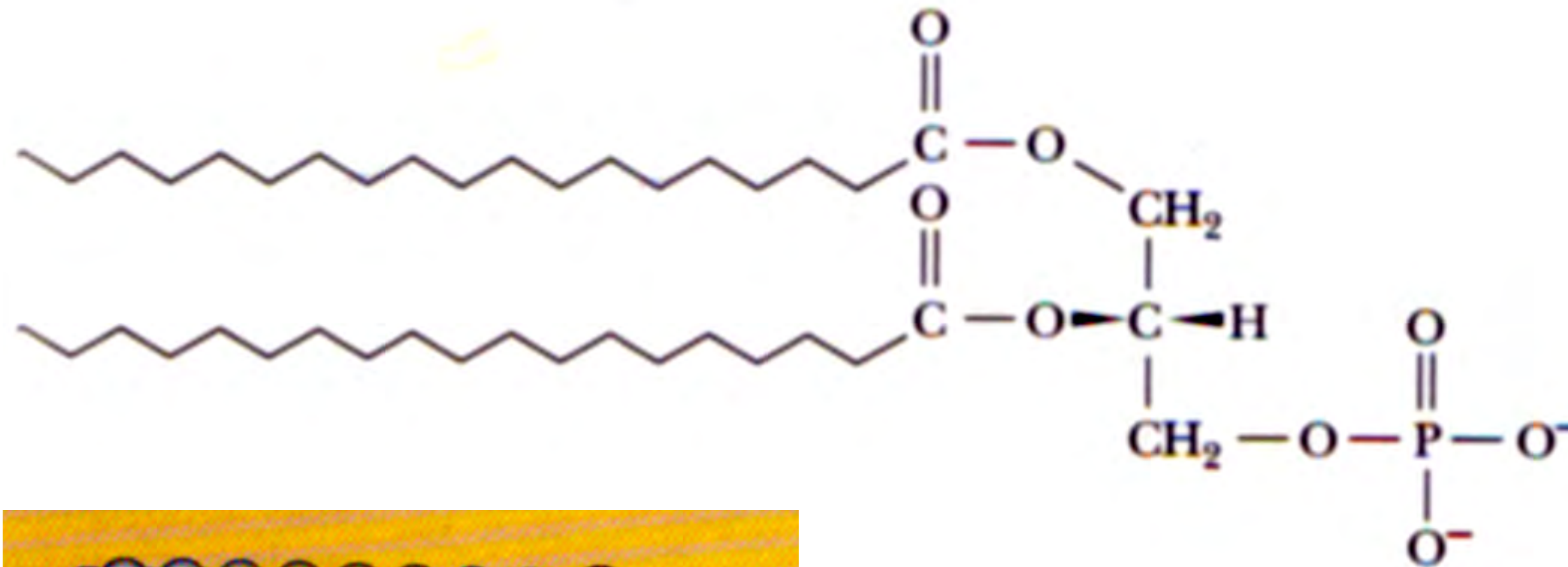


**FIGURE 8.3** Triacylglycerols are formed from glycerol and fatty acids.



# GLYCEROPHOSPHOLIPIDS

(the “membrane” lipids)

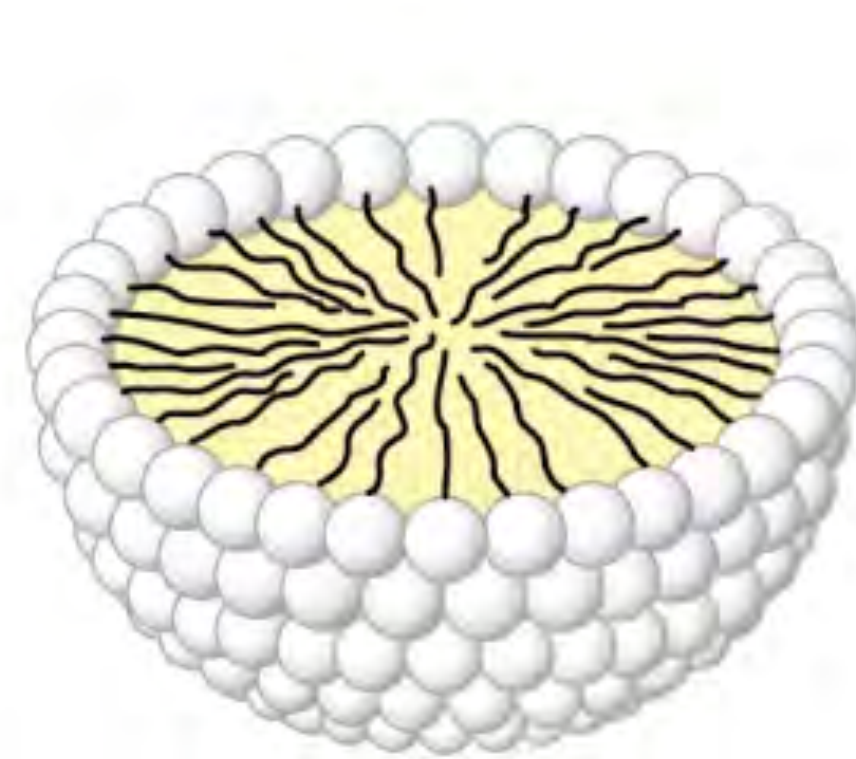


Phosphatidic Acid

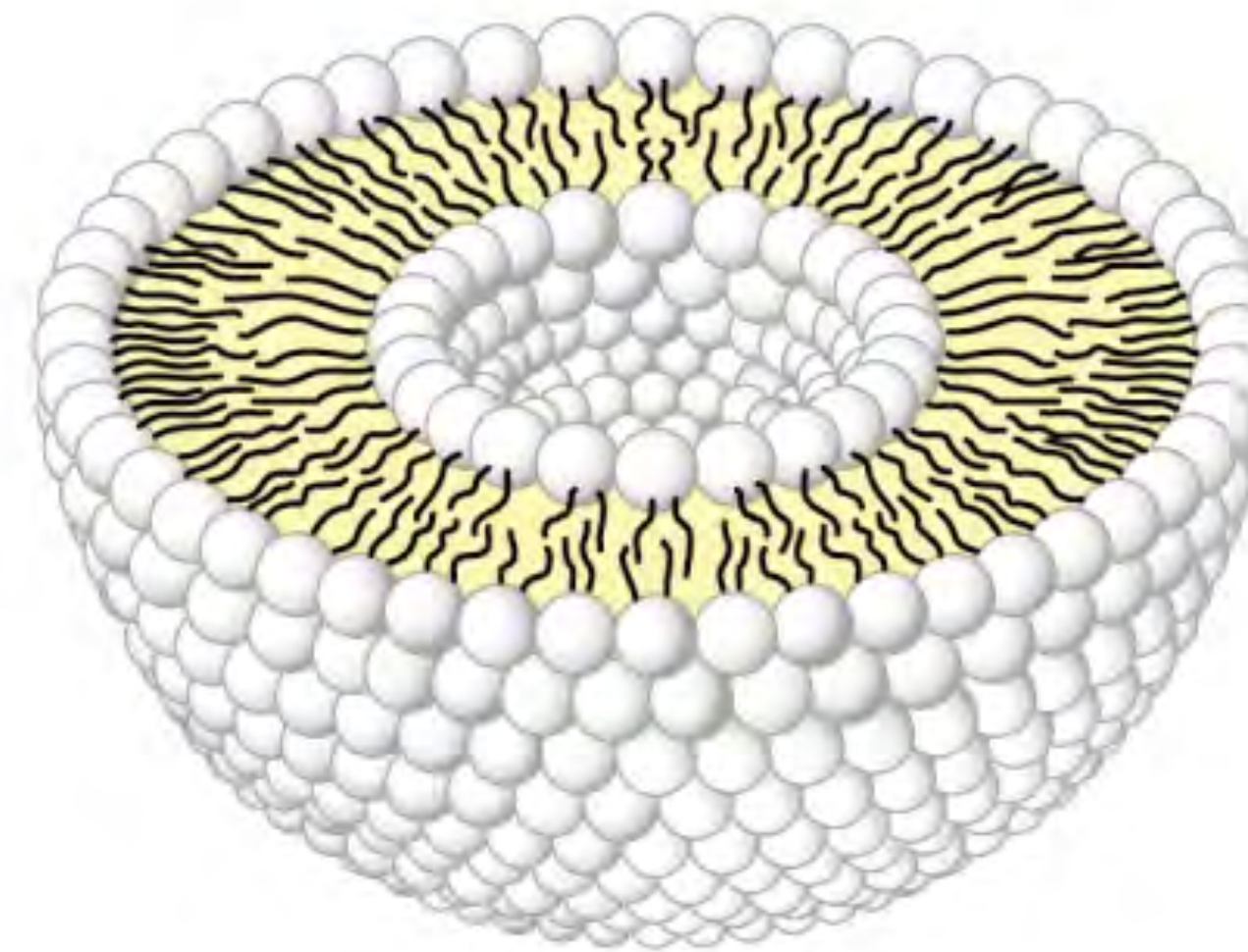
Belong to the class of phospholipids



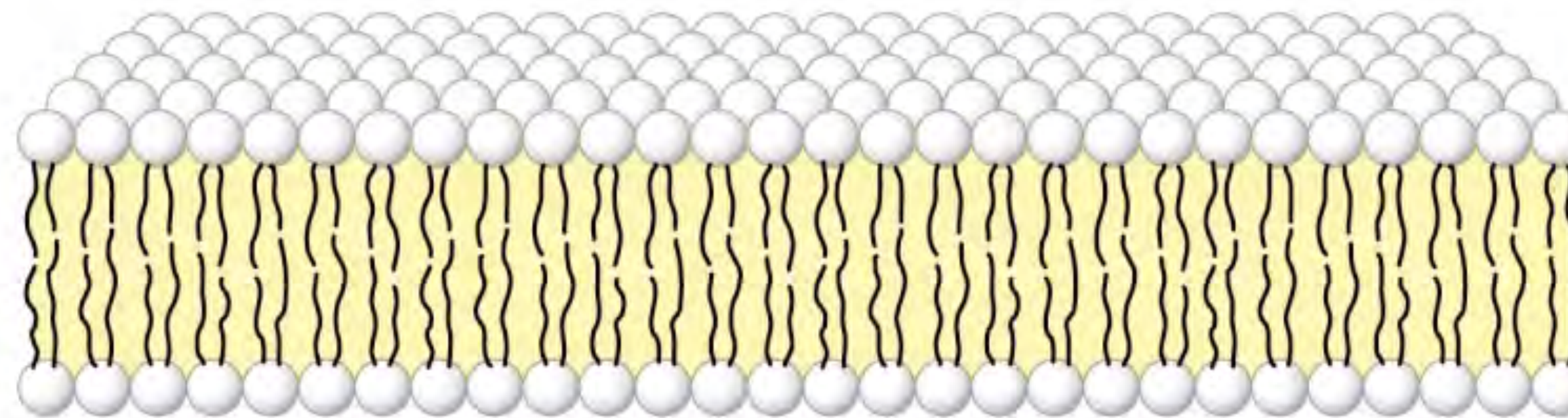
# Interactions between lipids and water can give rise to different structures



Micelle



Liposome



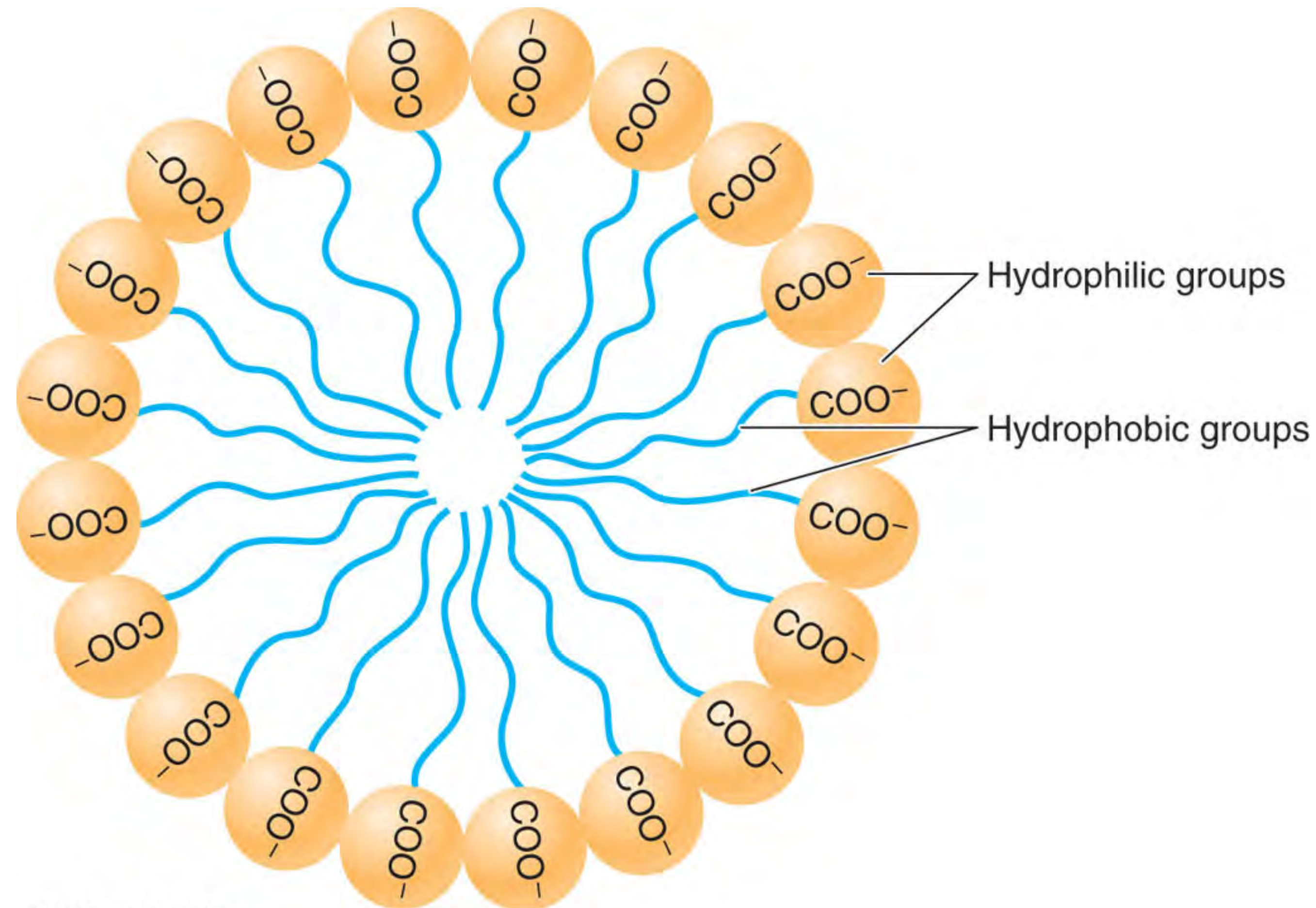
Phospholipid bilayer

Why do lipids form a bilayer and not a micelle?

Two fatty acyl chains are too bulky to fit into the interior of a micelle



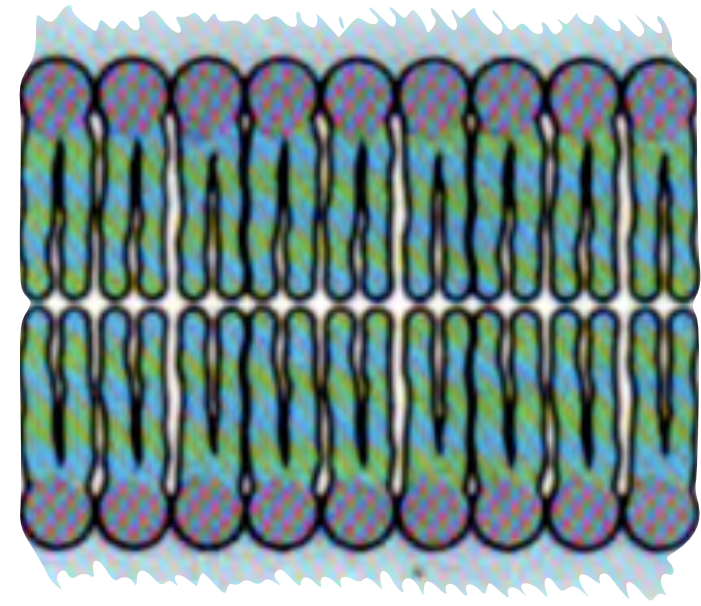
**MICELLE** – spherical cluster of molecules with the nonpolar portion in the middle and the polar portion on the outside



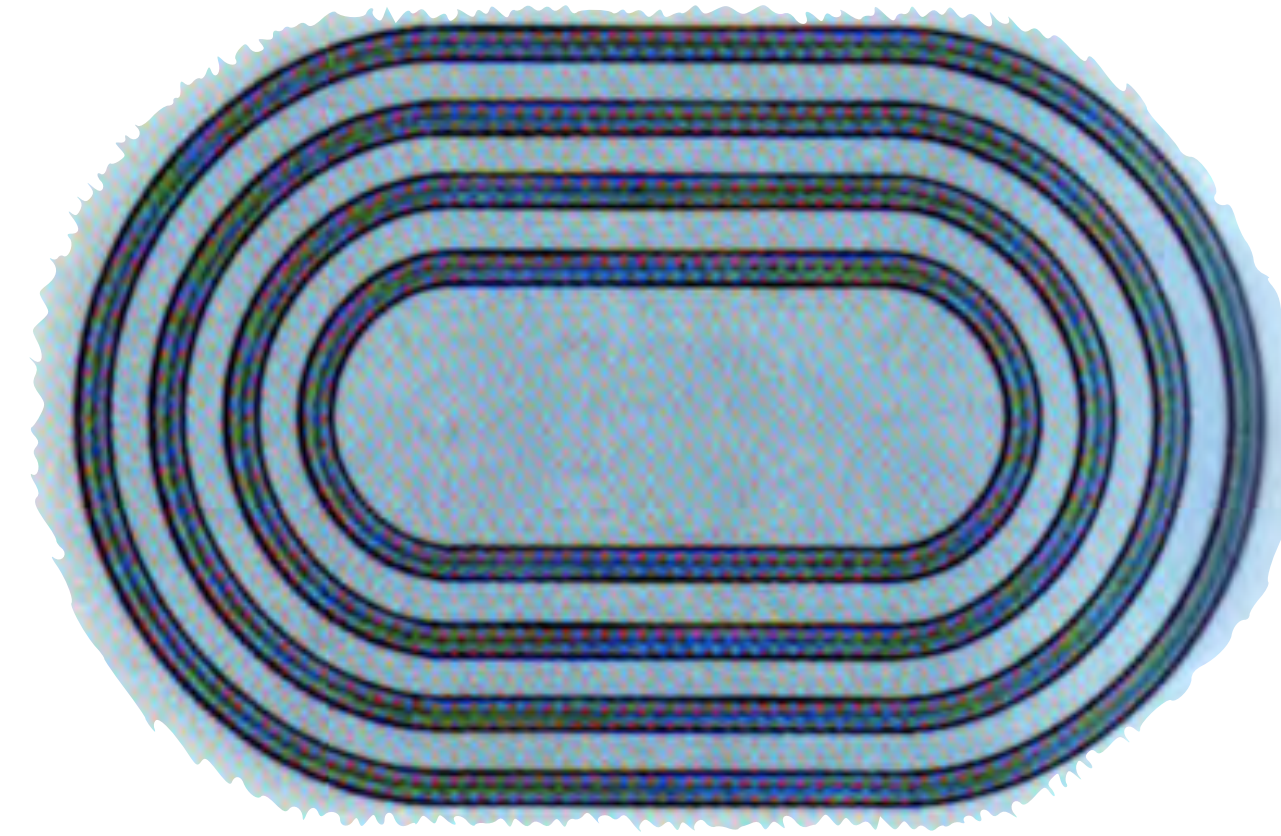


# Vesicles

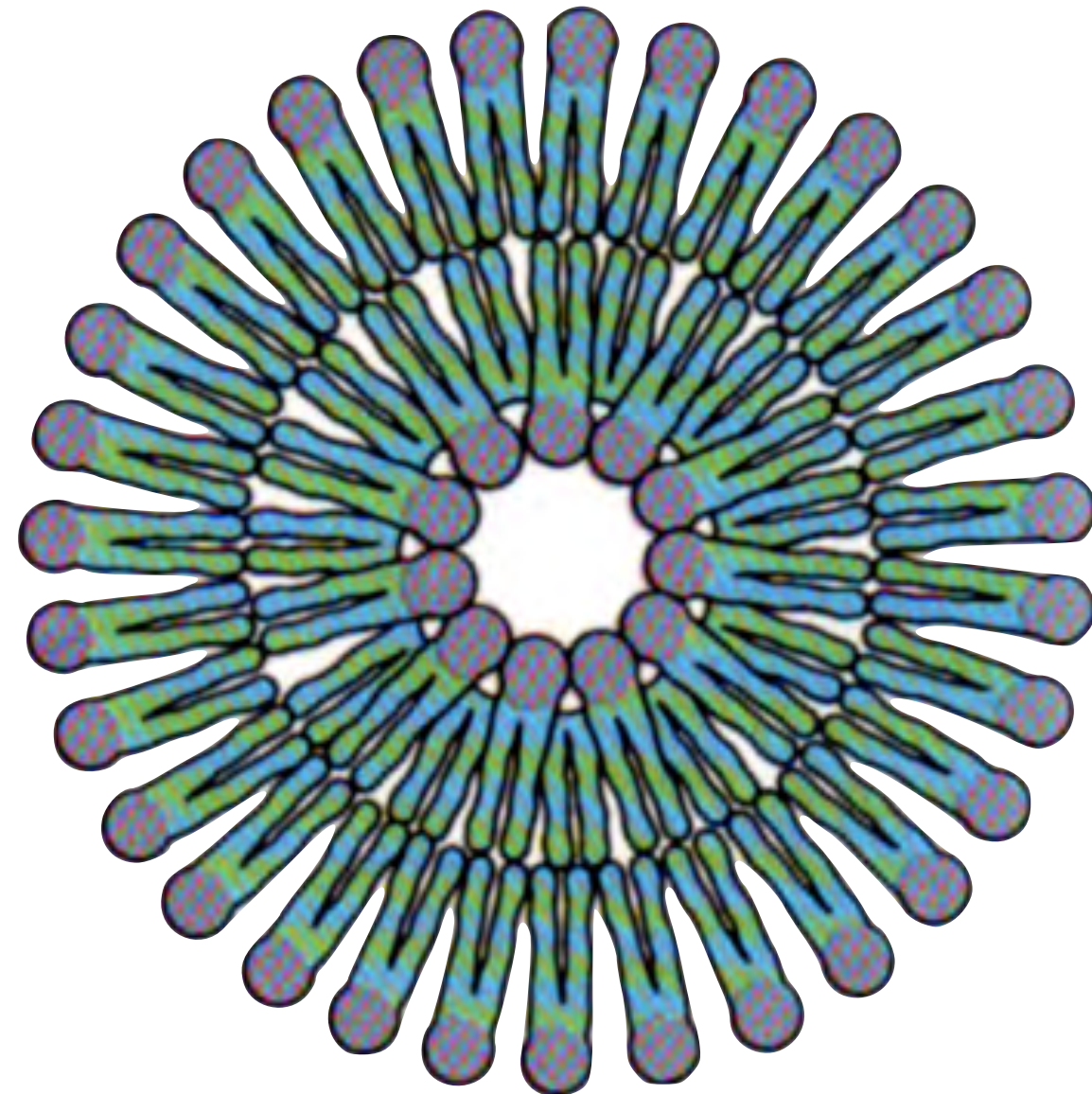
Bilayer



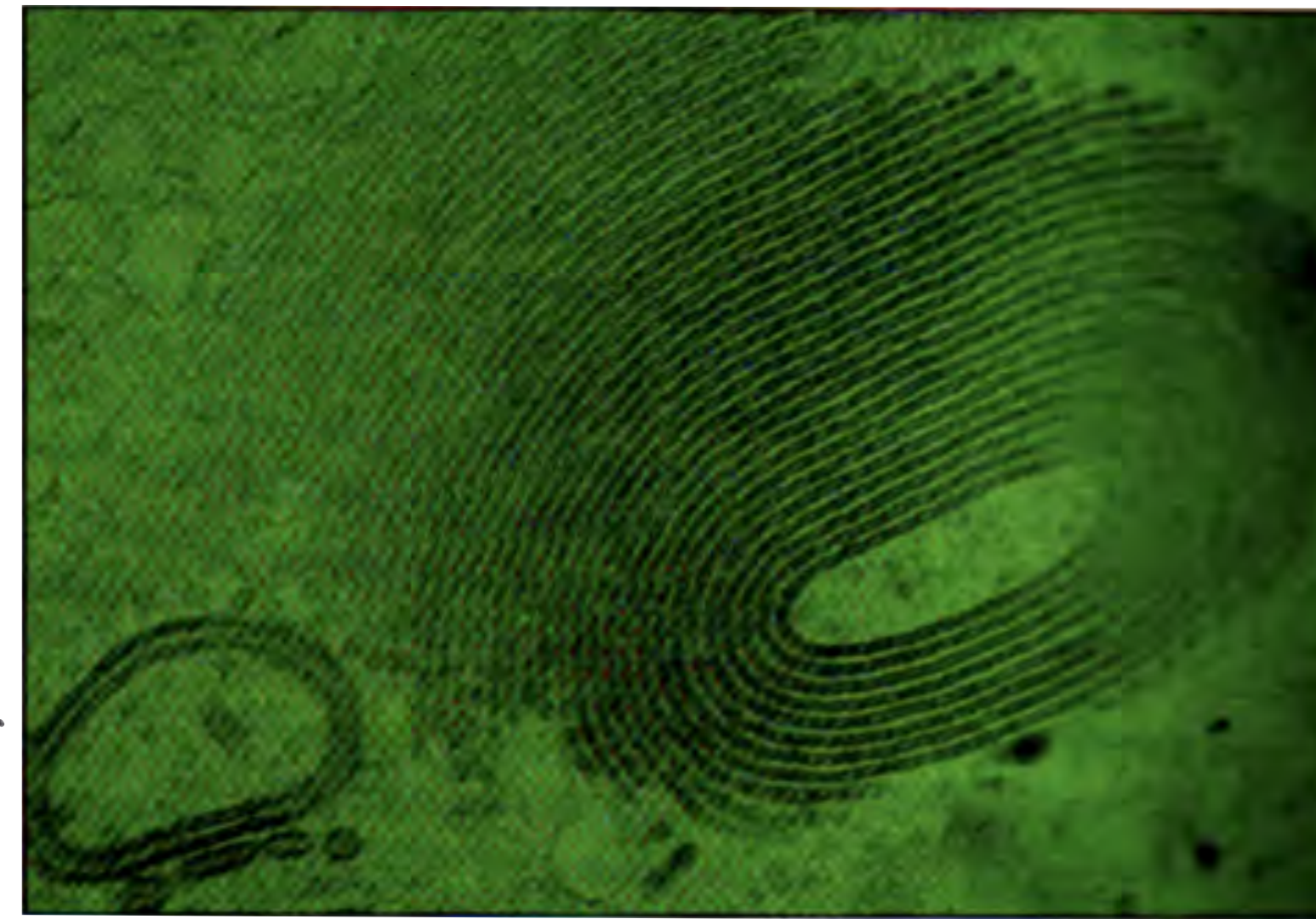
Multilamellar Vesicle



Unilamellar Vesicle

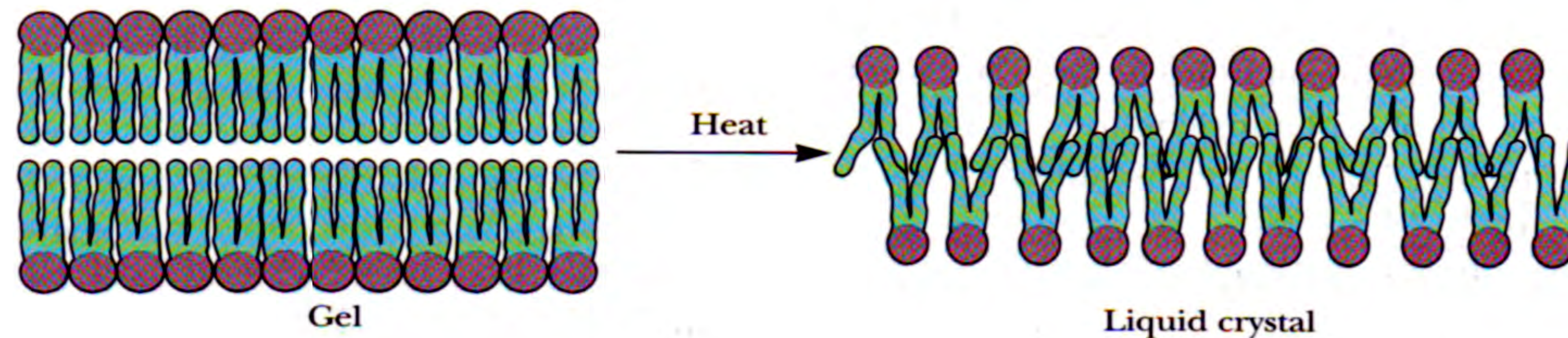
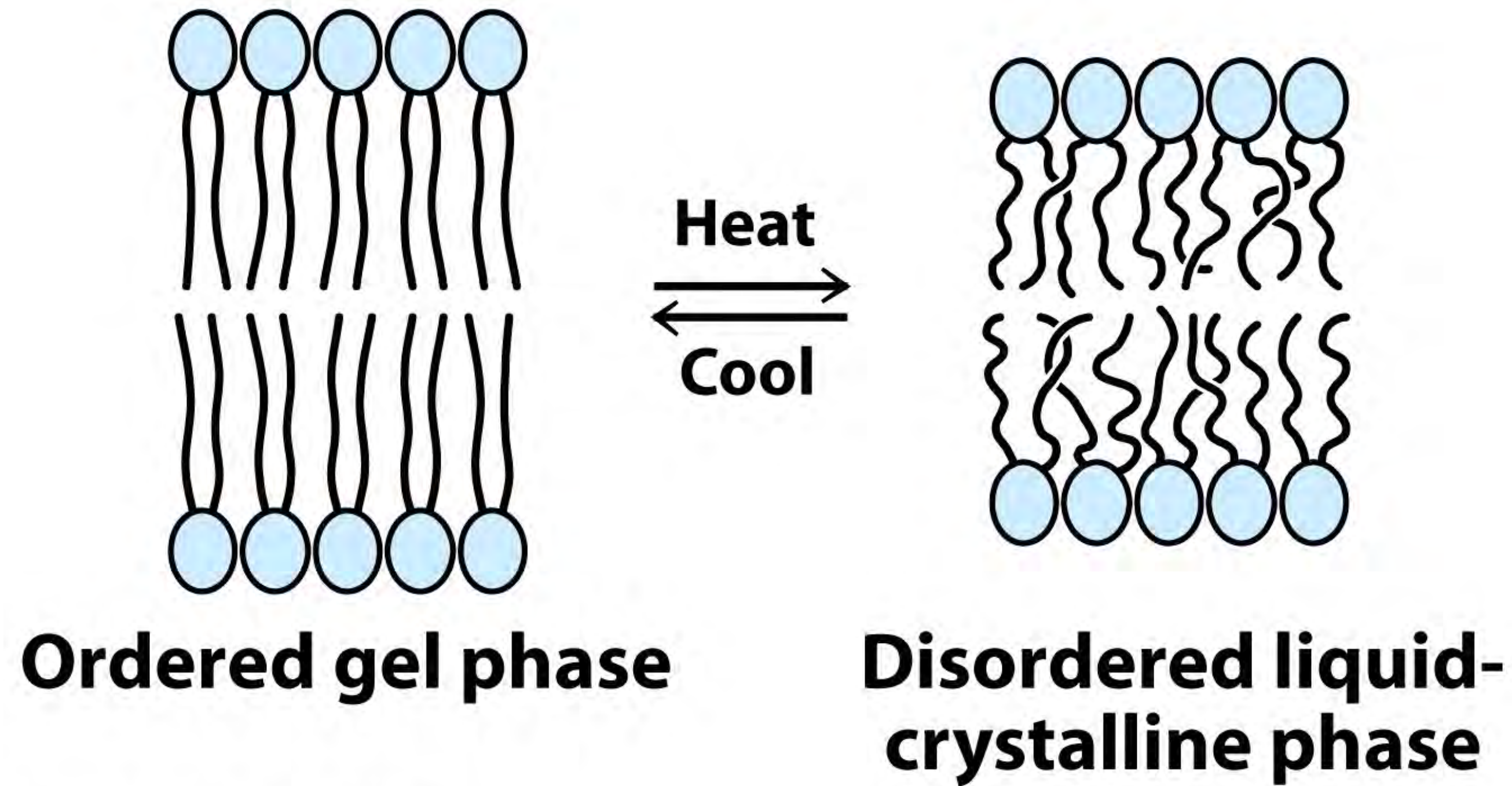


Electron Microscopy image of a multilamellar vesicle



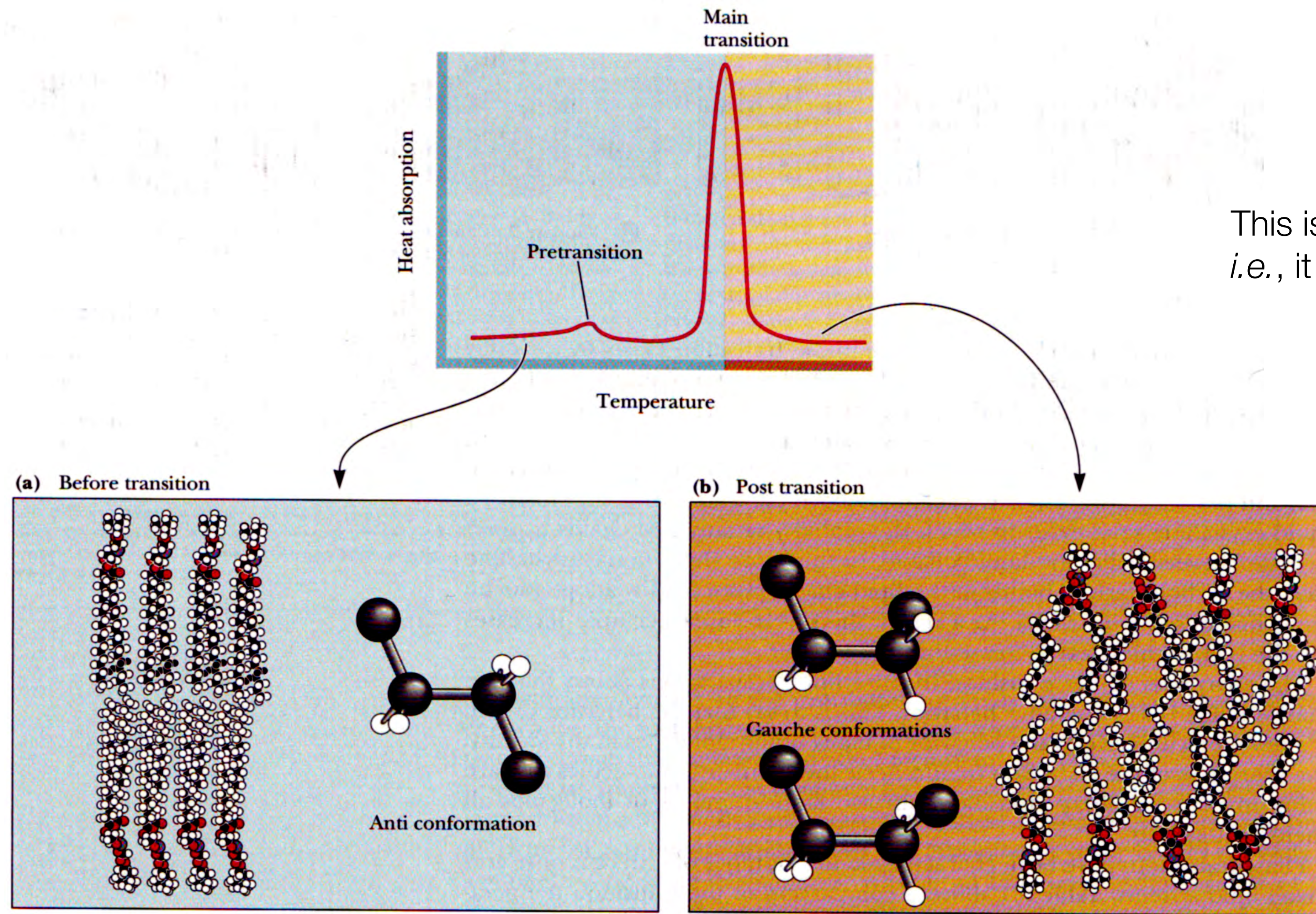


# Membranes are fluid structures





# Membrane Phase Transition



This is a first-order phase transition, *i.e.*, it occurs gradually.

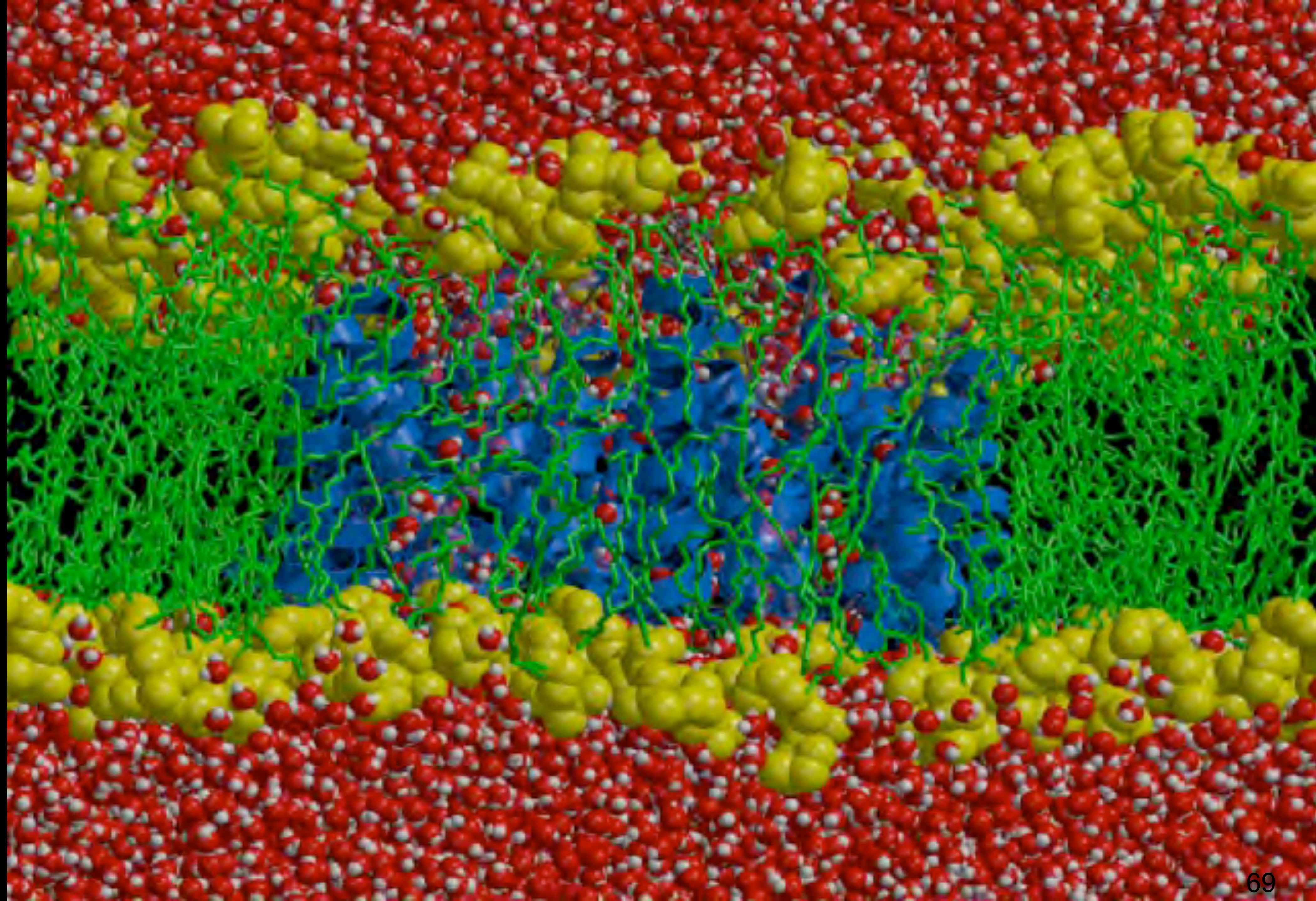


## Phase Transition Temperatures for Phospholipids in Water

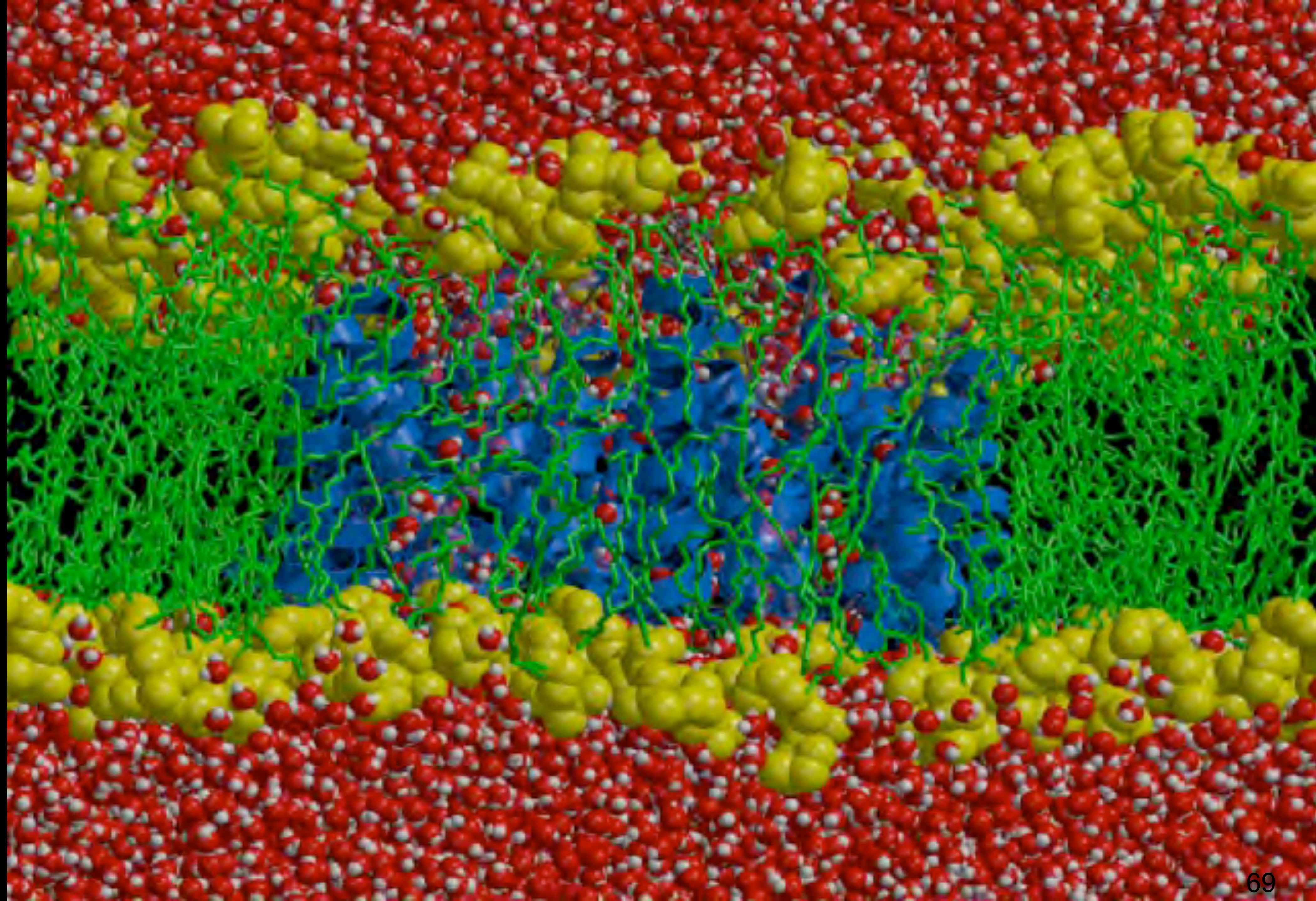
Phospholipid	Transition Temperature ( $T_m$ ), °C
Dipalmitoyl phosphatidic acid (Di 16:0 PA)	67
Dipalmitoyl phosphatidylethanolamine (Di 16:0 PE)	63.8
Dipalmitoyl phosphatidylcholine (Di 16:0 PC)	41.4
Dipalmitoyl phosphatidylglycerol (Di 16:0 PG)	41.0
Dilauroyl phosphatidylcholine (Di 14:0 PC)	23.6
Distearoyl phosphatidylcholine (Di 18:0 PC)	58
Dioleoyl phosphatidylcholine (Di 18:1 PC)	-22
1-Stearoyl-2-oleoyl-phosphatidylcholine (1-18:0, 2-18:1 PC)	3
Egg phosphatidylcholine (Egg PC)	-15

Adapted from Jain, M., and Wagner, R. C., 1980. *Introduction to Biological Membranes*. New York: John Wiley and Sons; and Martonosi, A., ed., 1982. *Membranes and Transport*, Vol. 1. New York: Plenum Press.





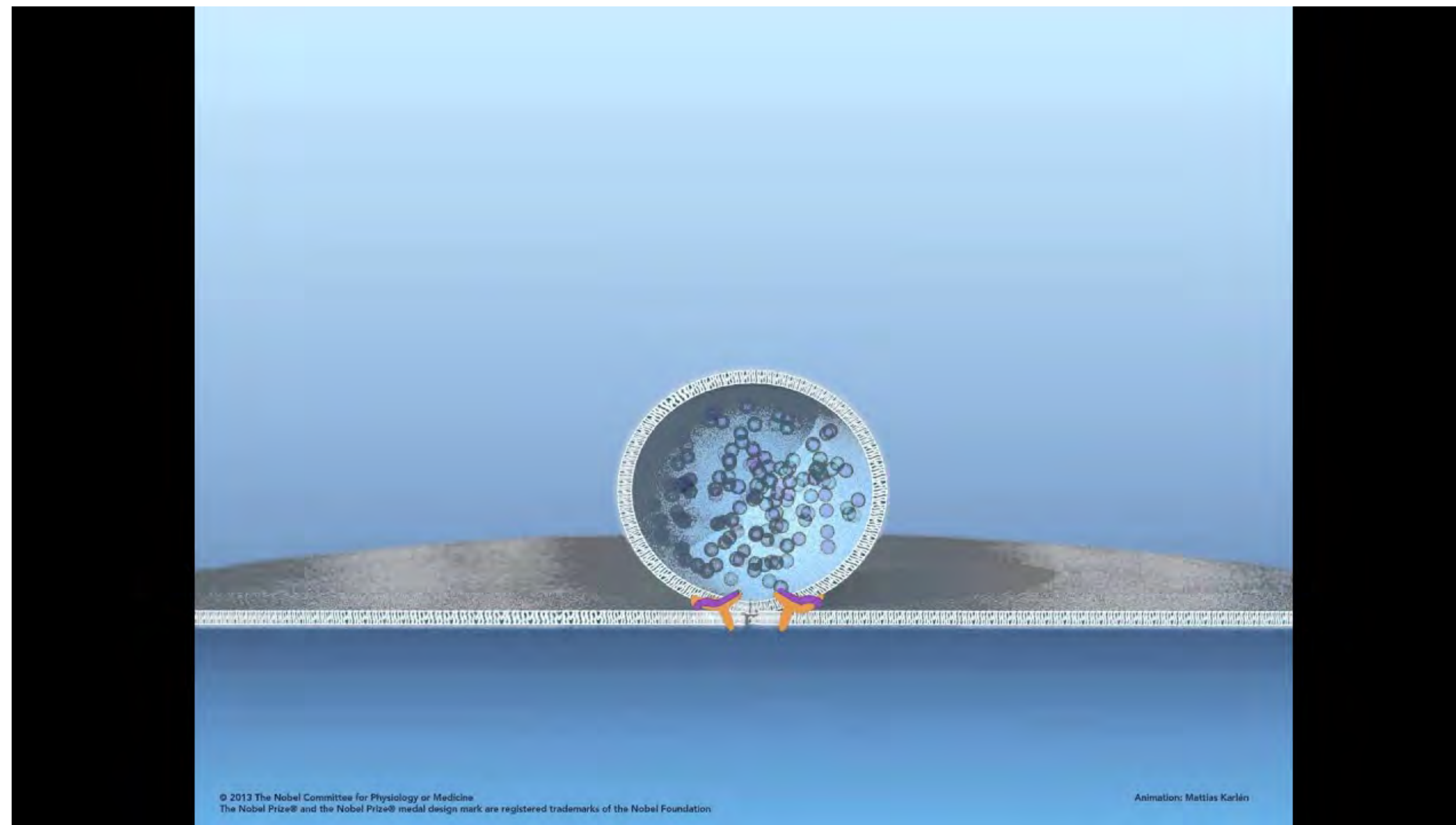






# Membrane fluidity is important for:

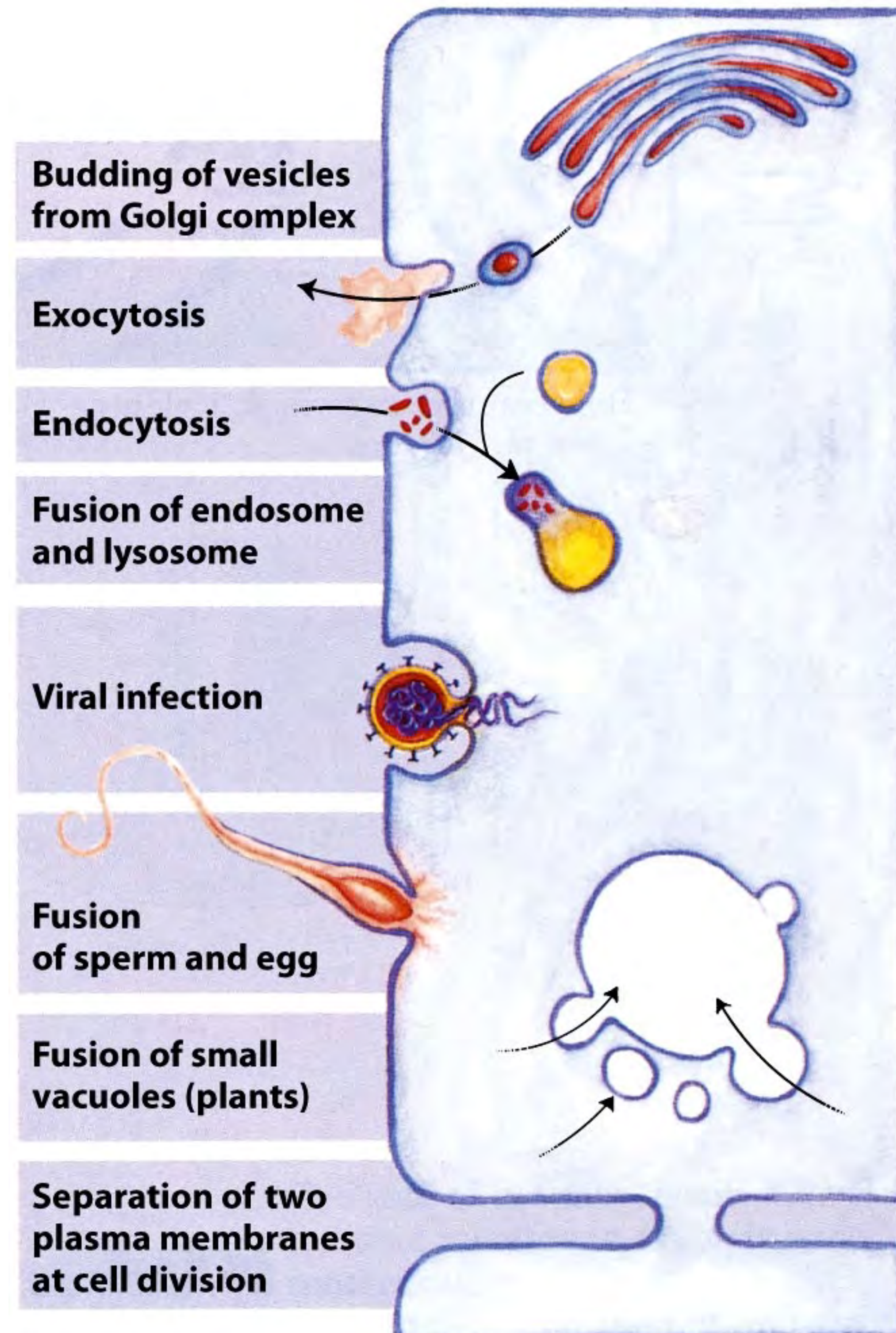
- Fusion of membranes, *e.g.*, fusion of vesicles with organelles or neurotransmitter release.





# Membrane fusion

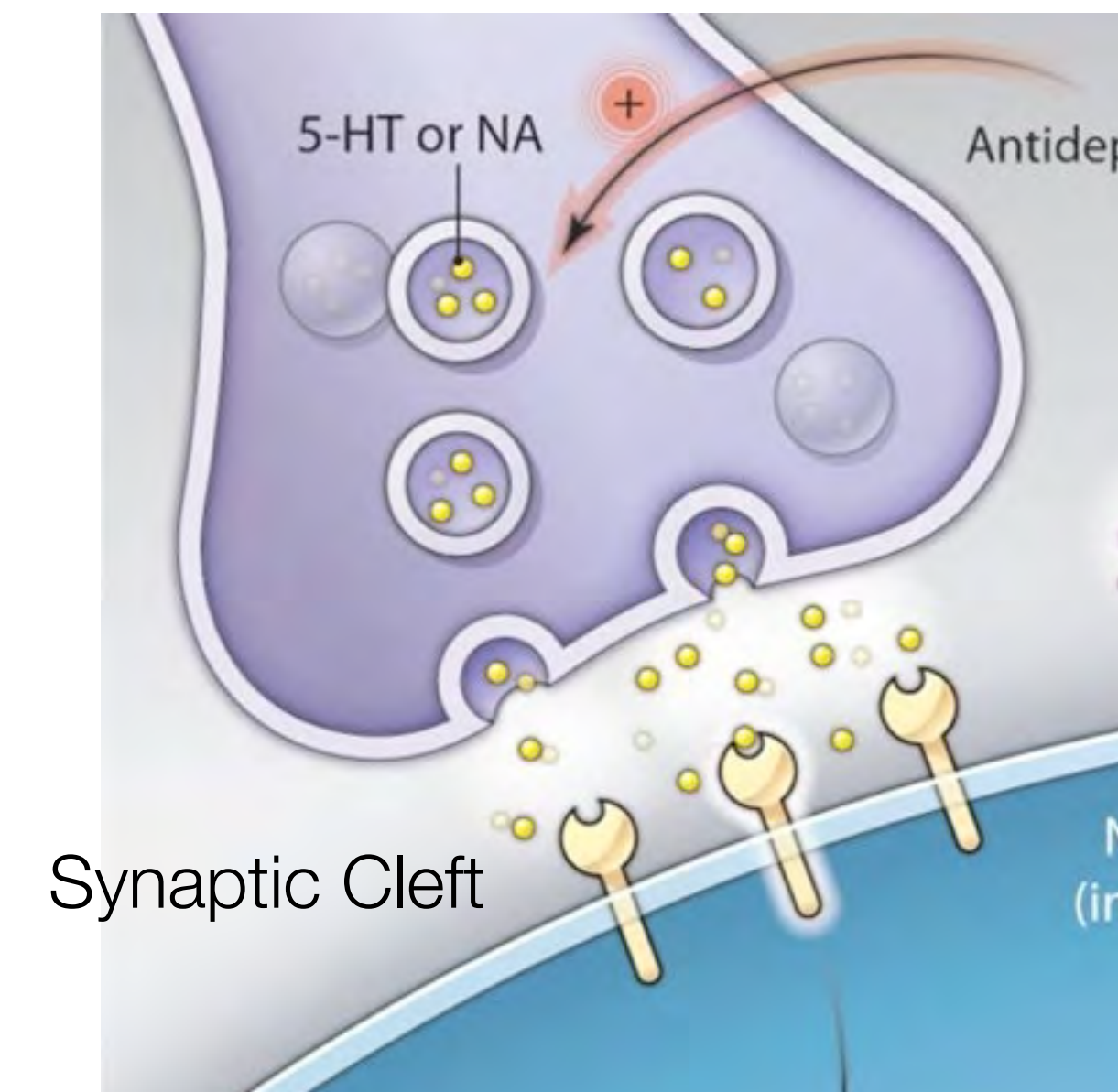
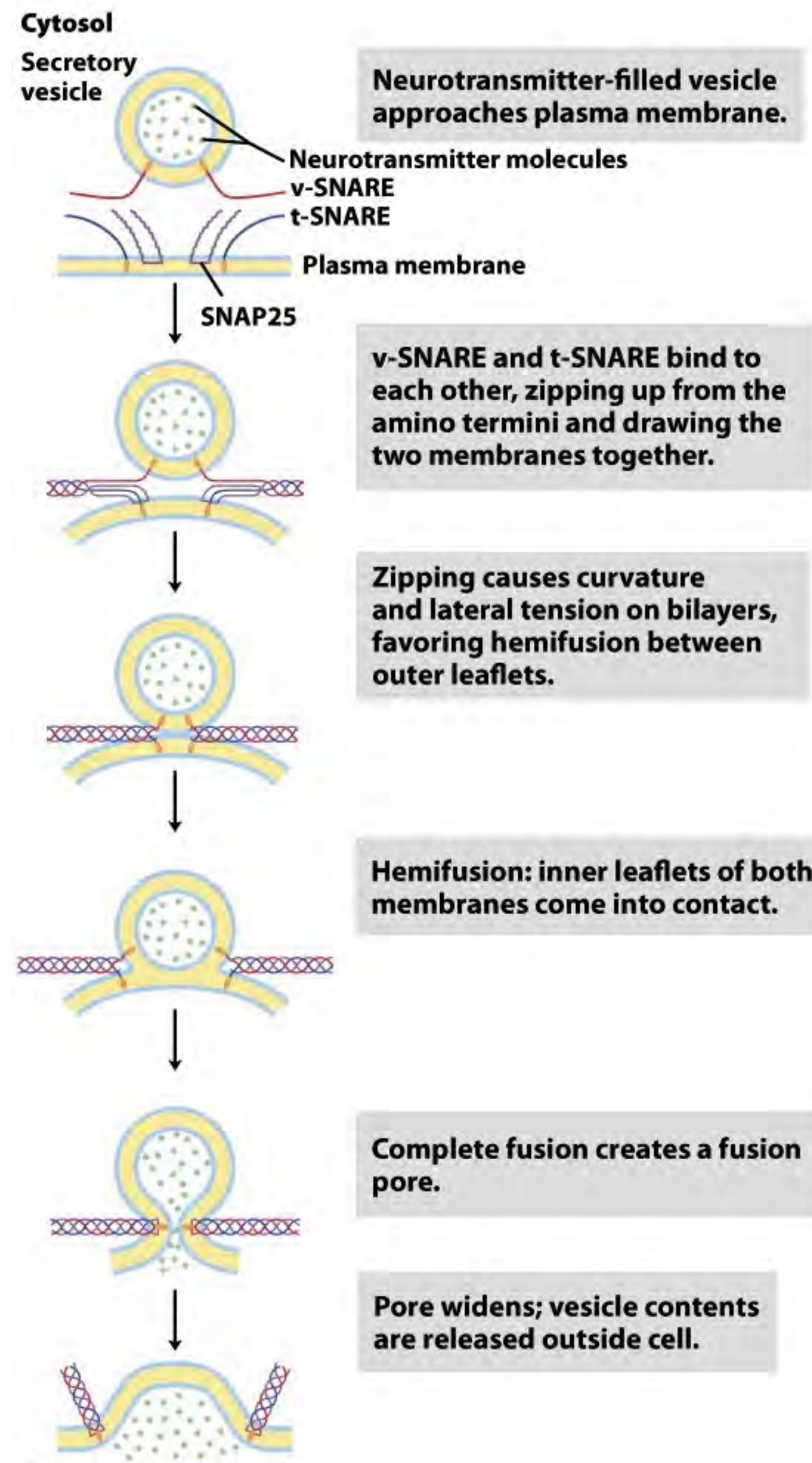
- Membrane budding (separation) and membrane fusion are two sides of the same coin
- Fusion
  1. Recognition
  2. Apposition
  3. Disruption
  4. Bilayer fusion





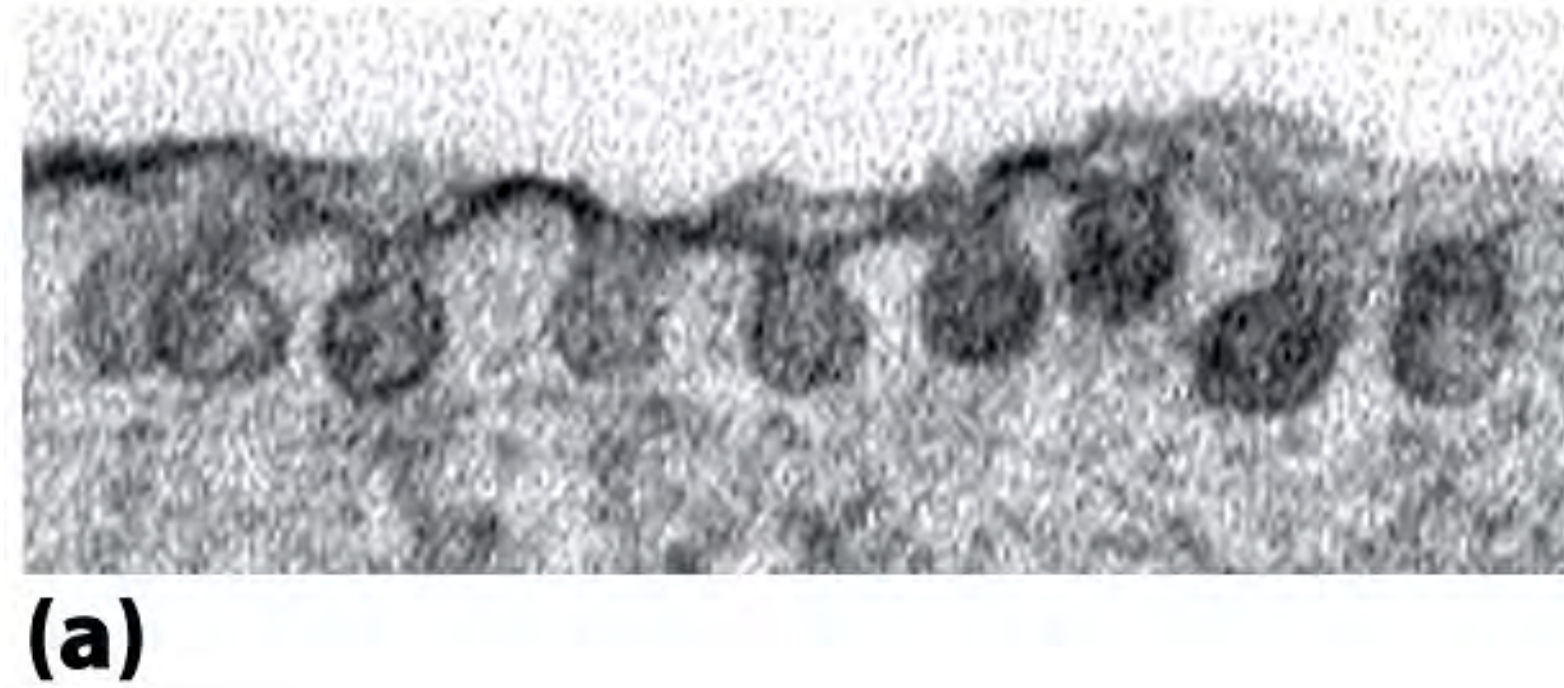
# Neurotransmitter release due to vesicle fusion

- NSF = N-ethylmaleimide-Sensitive Factor
- SNAP = NSF Attachment Protein
- SNARE = Soluble NSF Attachment protein REceptor

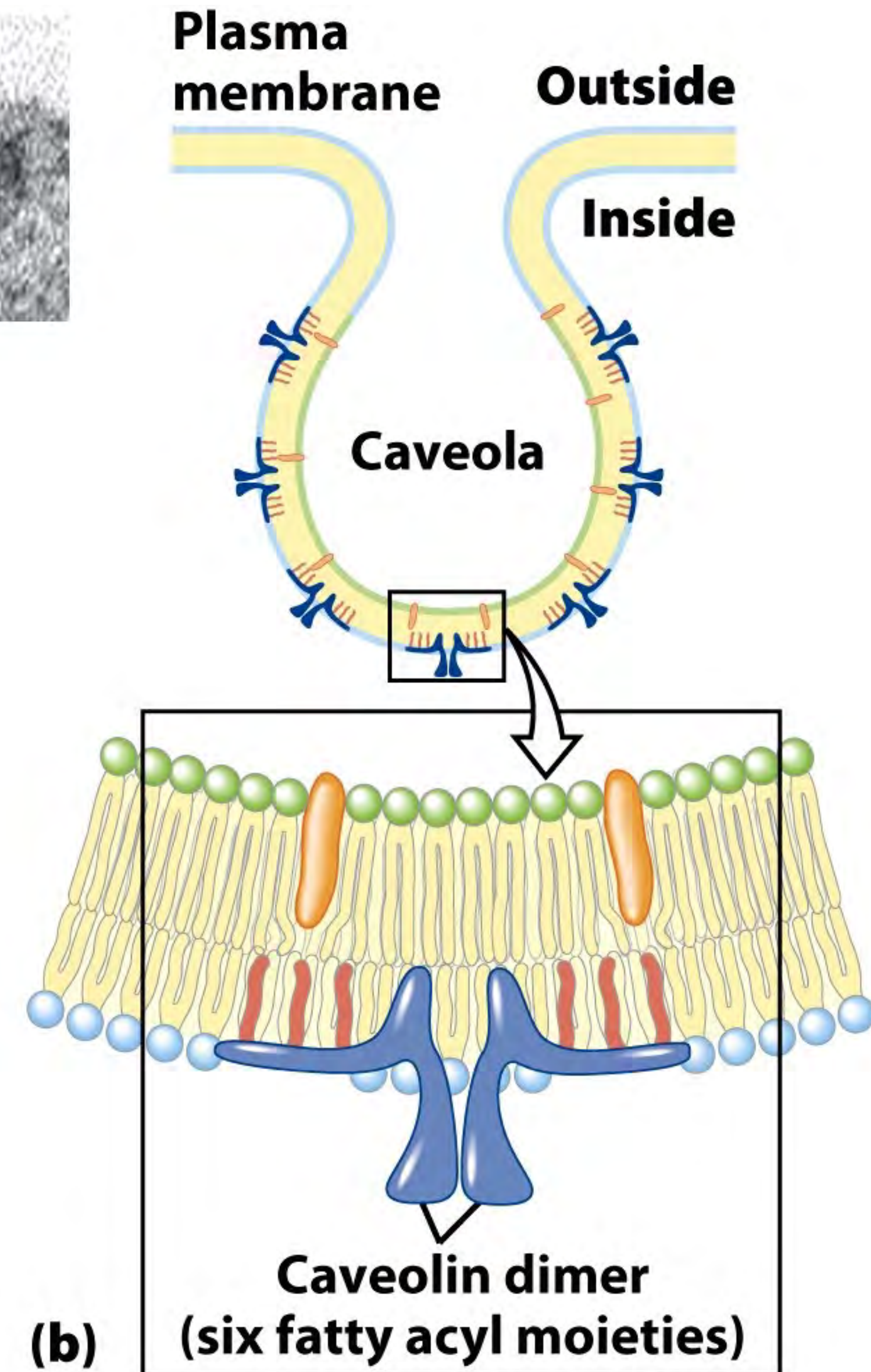




# Caveolae



- Caveolin is an integral membrane protein.
- The dimeric caveolin binds to the inner membrane surface of cells *via* palmitoyl anchors, where it induces membrane curvature.
- Caveolae (as in cave) are formed on the extracellular side of the membrane



**Figure 11-21**  
*Lehninger Principles of Biochemistry, Fifth Edition*  
© 2008 W.H. Freeman and Company



# Membrane fluidity is important for:

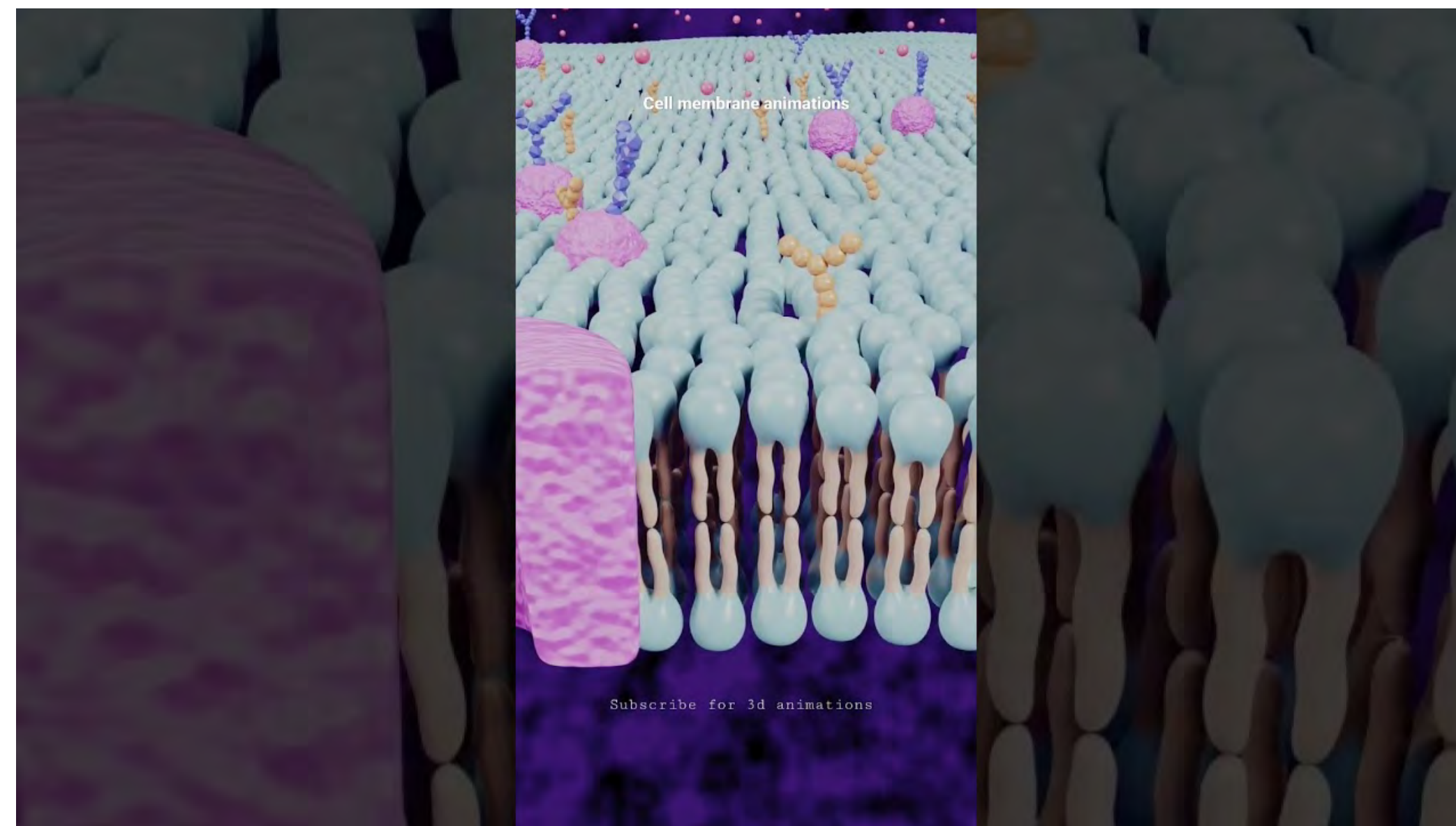
- Fusion of membranes, *e.g.*, fusion of vesicles with organelles.
- Proper separation of membranes during cell division.





# Membrane fluidity is important for:

- Fusion of membranes, *e.g.*, fusion of vesicles with organelles.
- Proper separation of membranes during cell division.
- Lateral diffusion of proteins, lipids and other molecules in the membrane, so they are equally distributed.



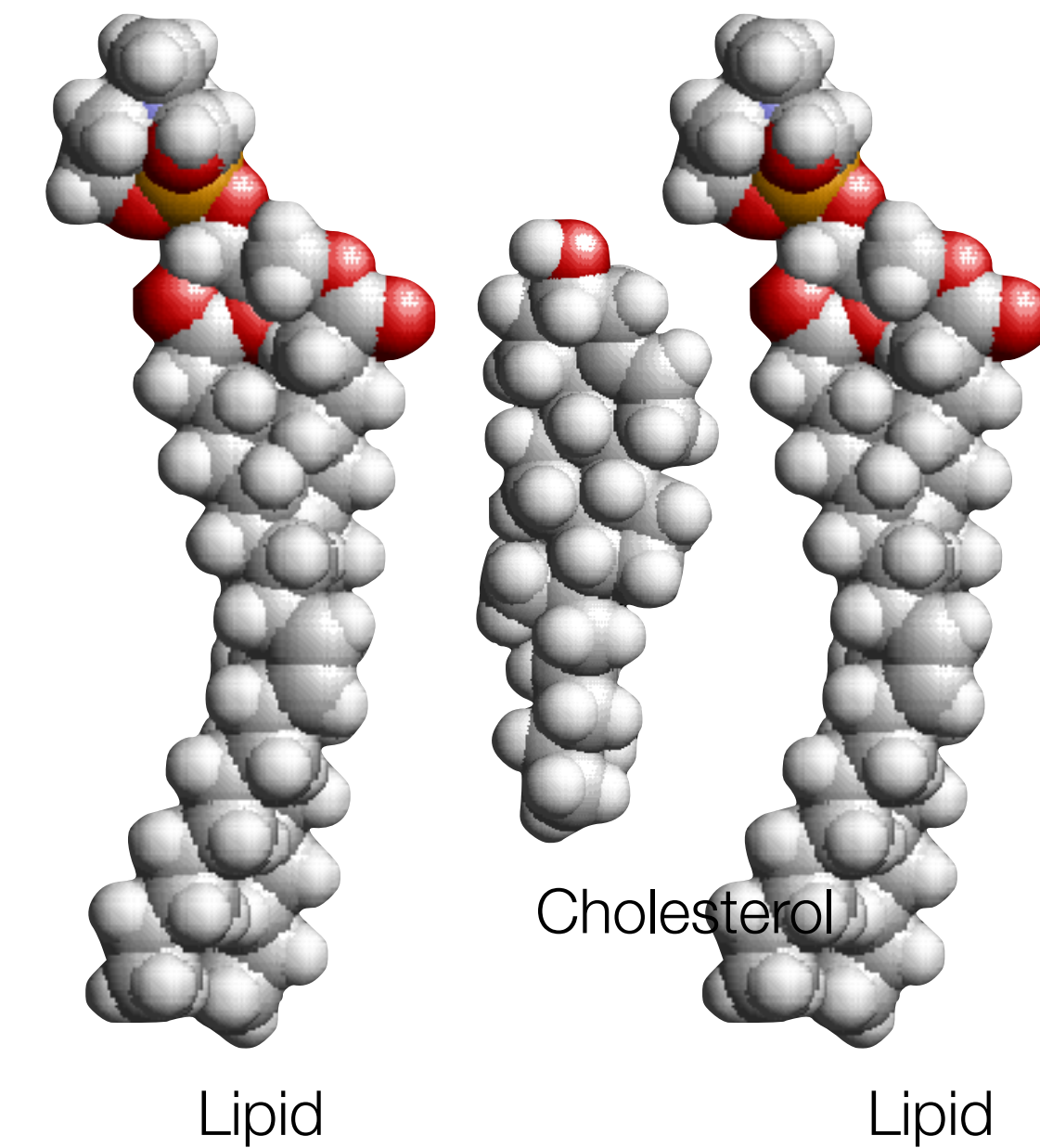
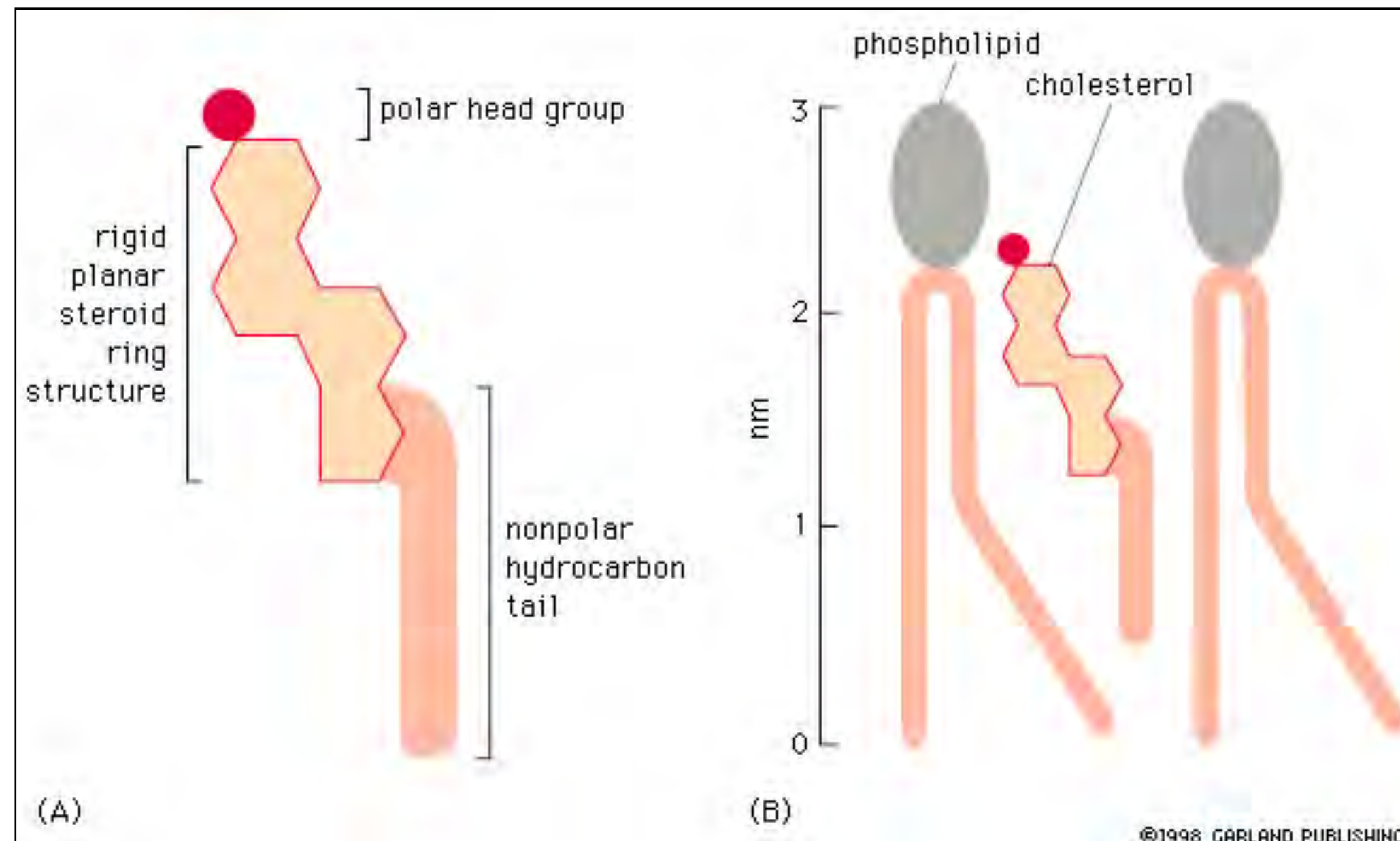


# Membrane fluidity is important for:

- Fusion of membranes, *e.g.*, fusion of vesicles with organelles.
- Proper separation of membranes during cell division.
- Lateral diffusion of proteins, lipids and other molecules in the membrane, so they are equally distributed.
- Providing a flexible environment for membrane proteins to allow conformational changes or shuttling in signaling events.



# Fluidity of the membrane depends on the lipid composition and cholesterol



## Factors that affect membrane fluidity:

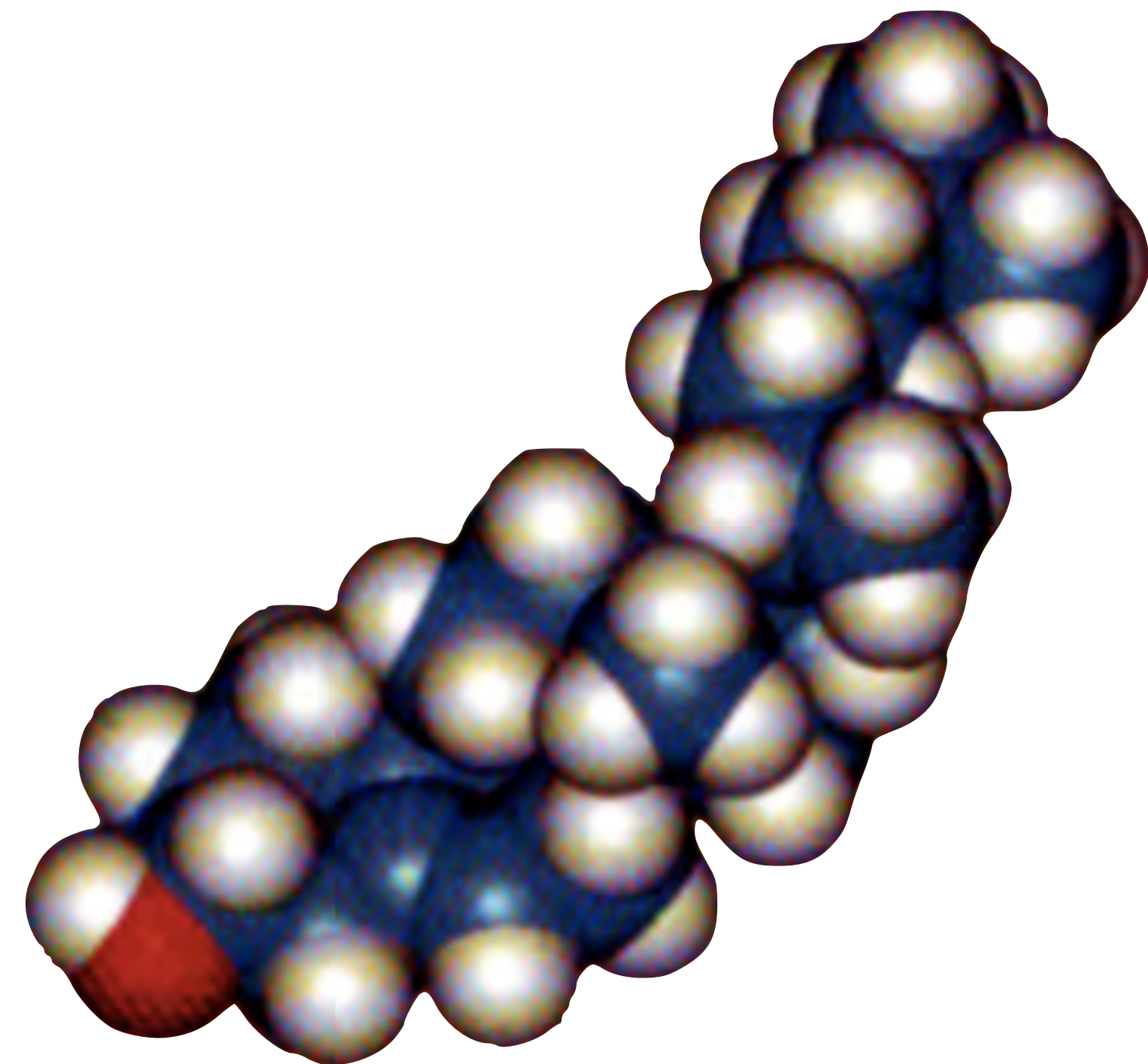
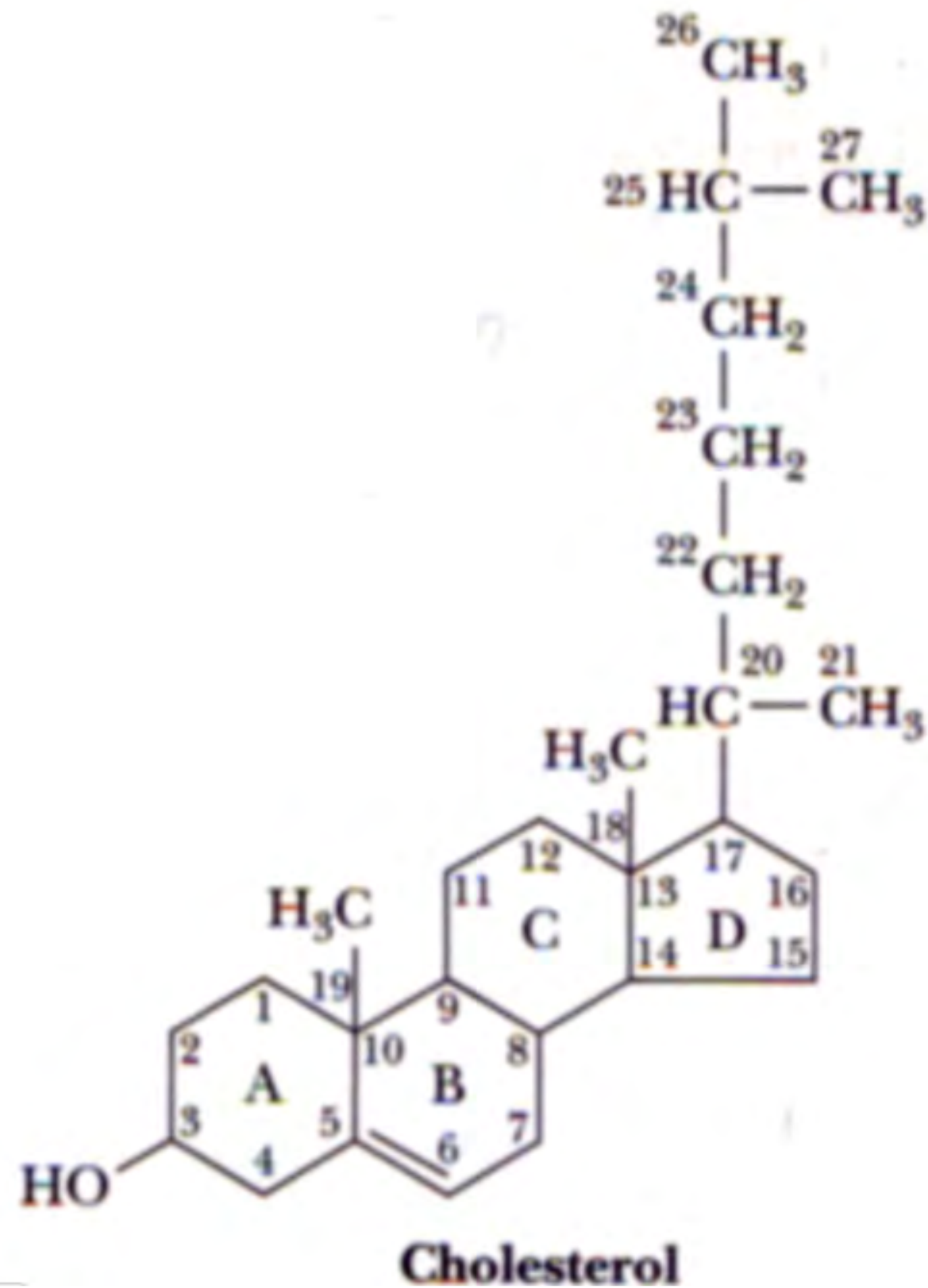
- Length of the fatty acyl chains
- Degree of saturation of the fatty acyl chains
- Presence of cholesterol

The rigid cholesterol ring system interferes with the close packing of phospholipid fatty acid tails and thus inhibits the transition from the liquid-crystal to the crystalline state upon temperature decrease.

At the same time, the rigid cholesterol makes the membrane somewhat less fluid.



# CHOLESTEROL

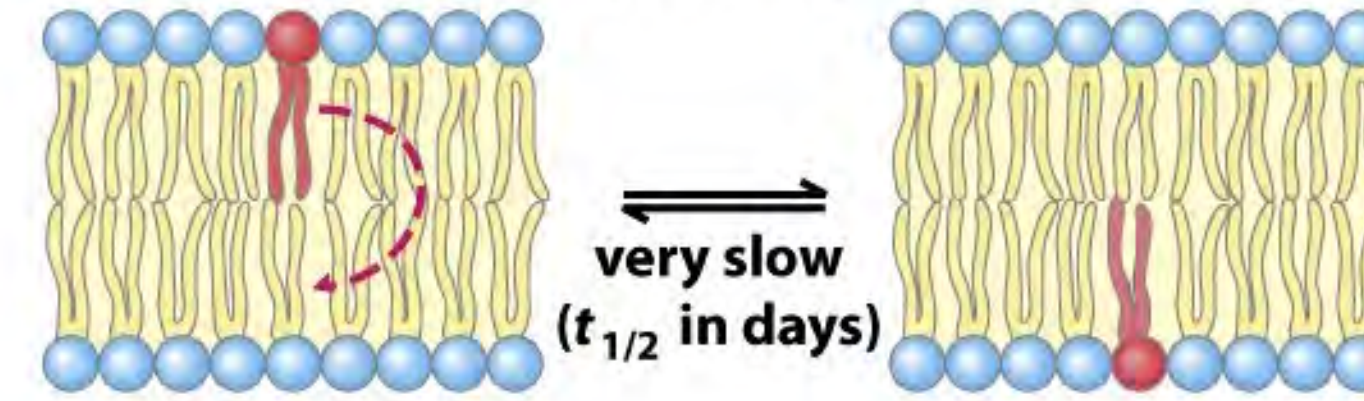




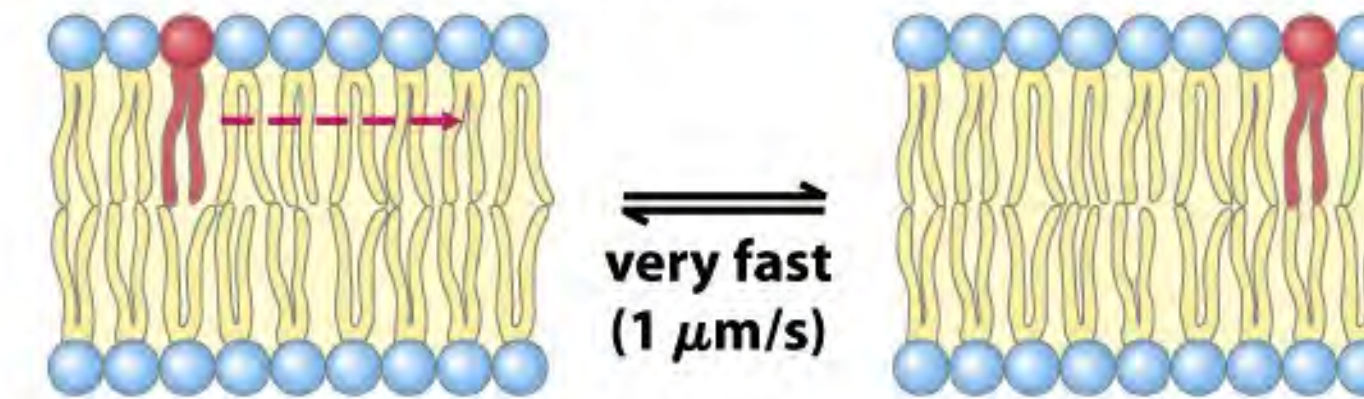
# Transbilayer transport by flippases

- Energetic barriers to transbilayer lipid movement are high
- Lipid biosynthesis on one side of a membrane is coupled to catalyzed transport

(a) Uncatalyzed transbilayer ("flip-flop") diffusion



(b) Uncatalyzed lateral diffusion



(c) Catalyzed transbilayer translocations

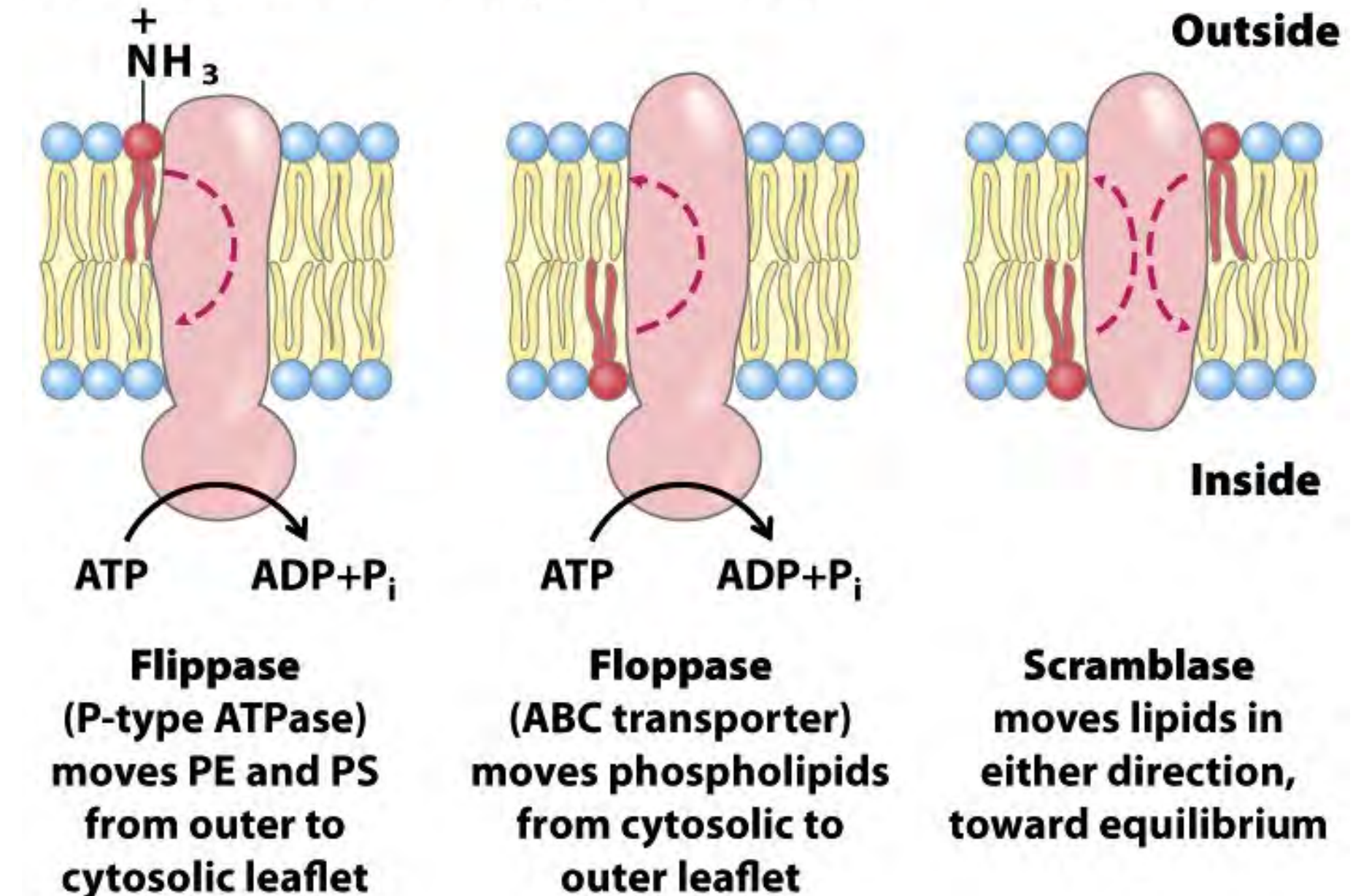


Figure 11-16

*Lehninger Principles of Biochemistry, Fifth Edition*

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# Lateral diffusion

- Lipids and proteins can diffuse in 2D
- Measured by Fluorescence Recovery After Photo-bleaching (FRAP)

**FRAP requires a fluorescent tag on a lipid or protein**

Photobleaching of a small area by intense light pulse makes a dark spot in the membrane

Fluorescence Recovery depends on diffusion of undamaged fluorophores to the bleached spot

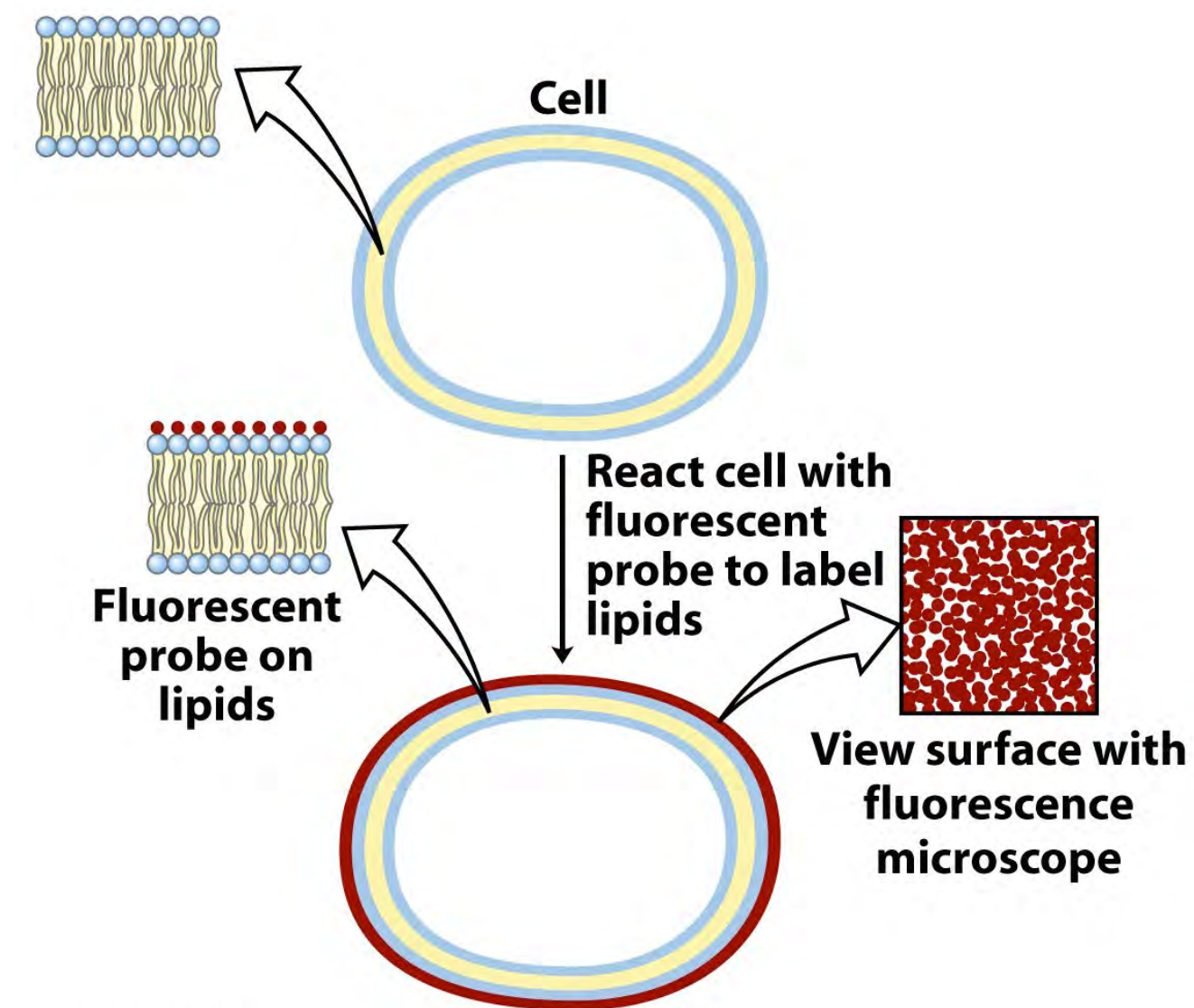
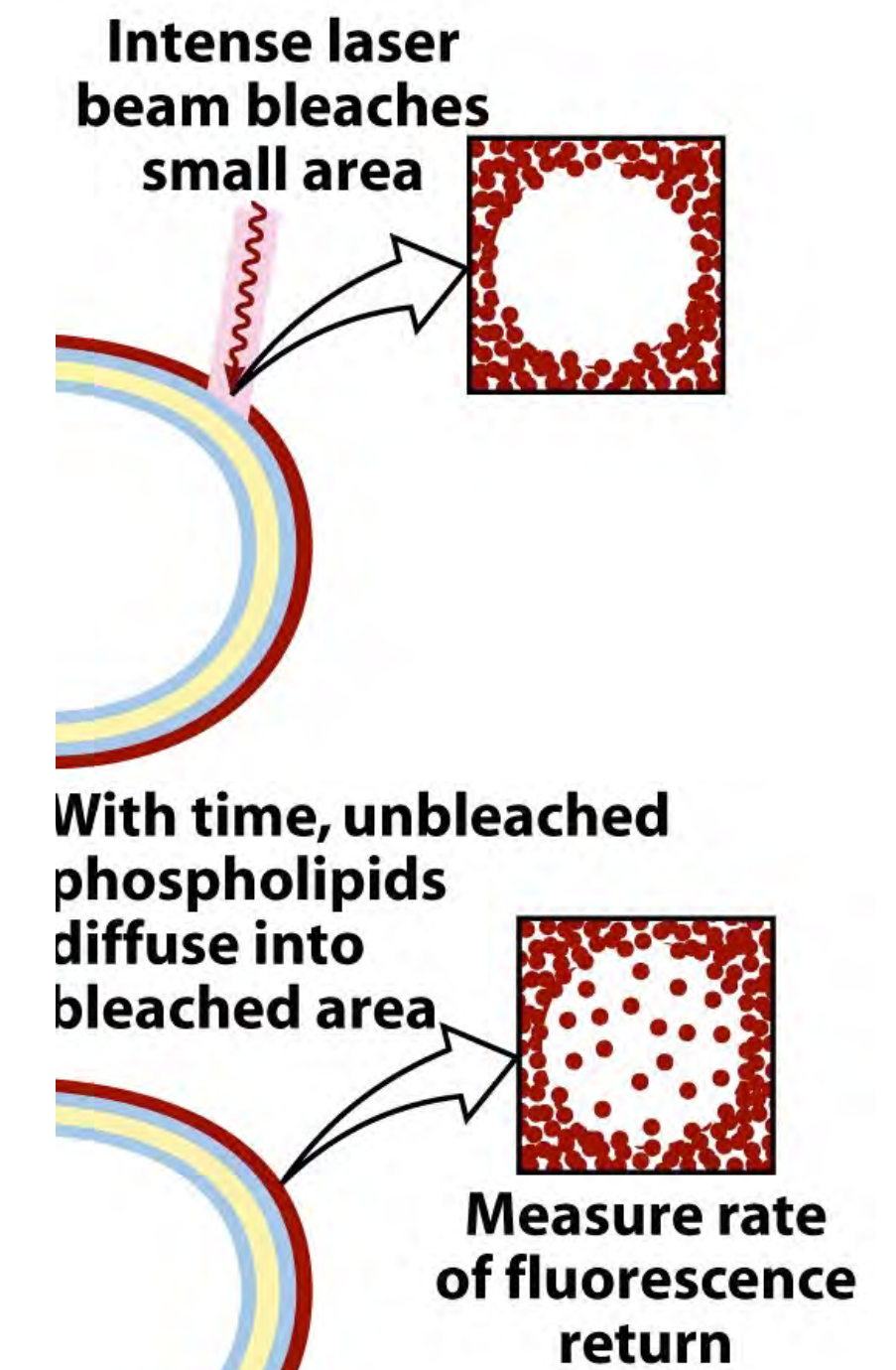


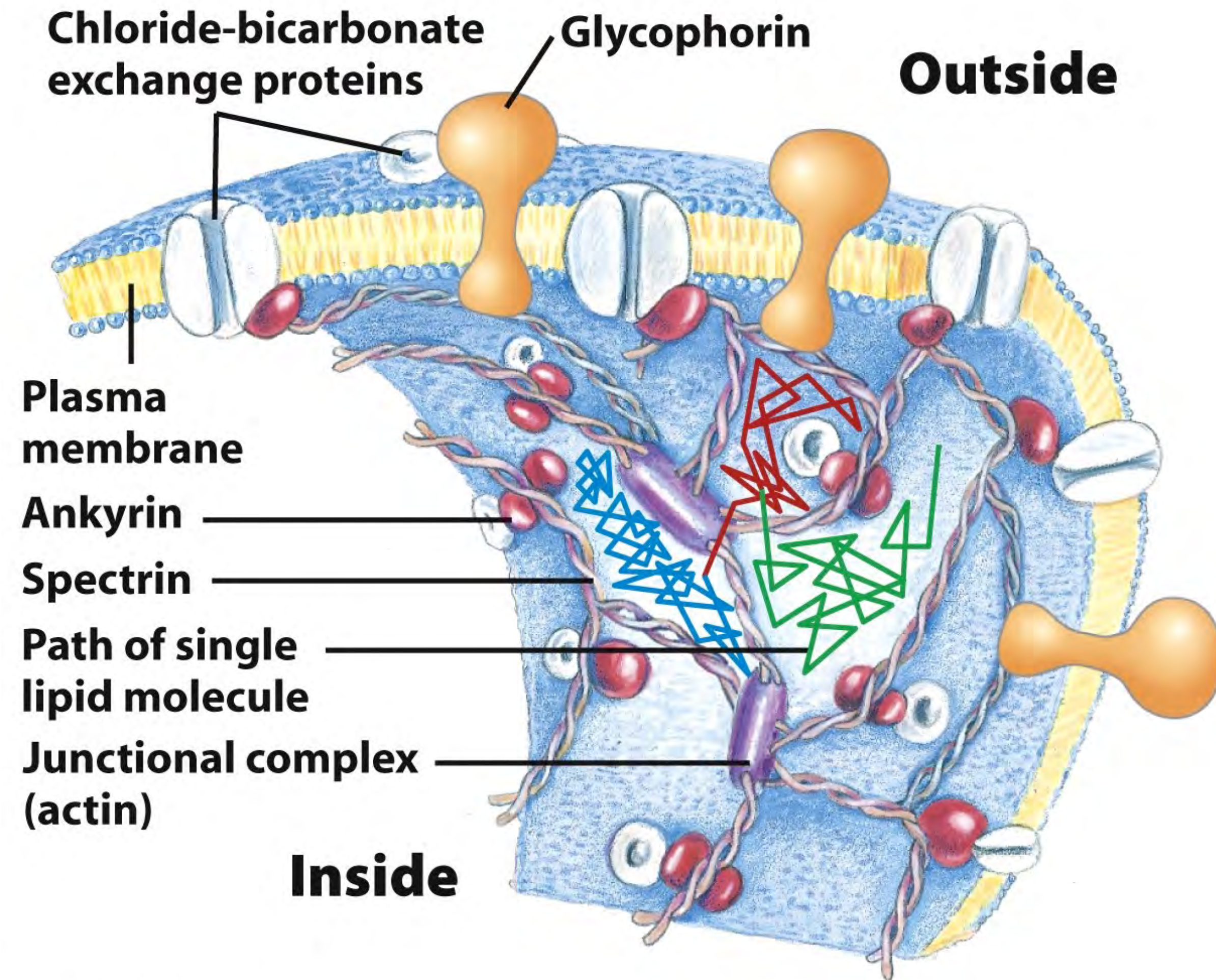
Figure 11-17 part 1  
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# Lateral diffusion may be limited by protein networks

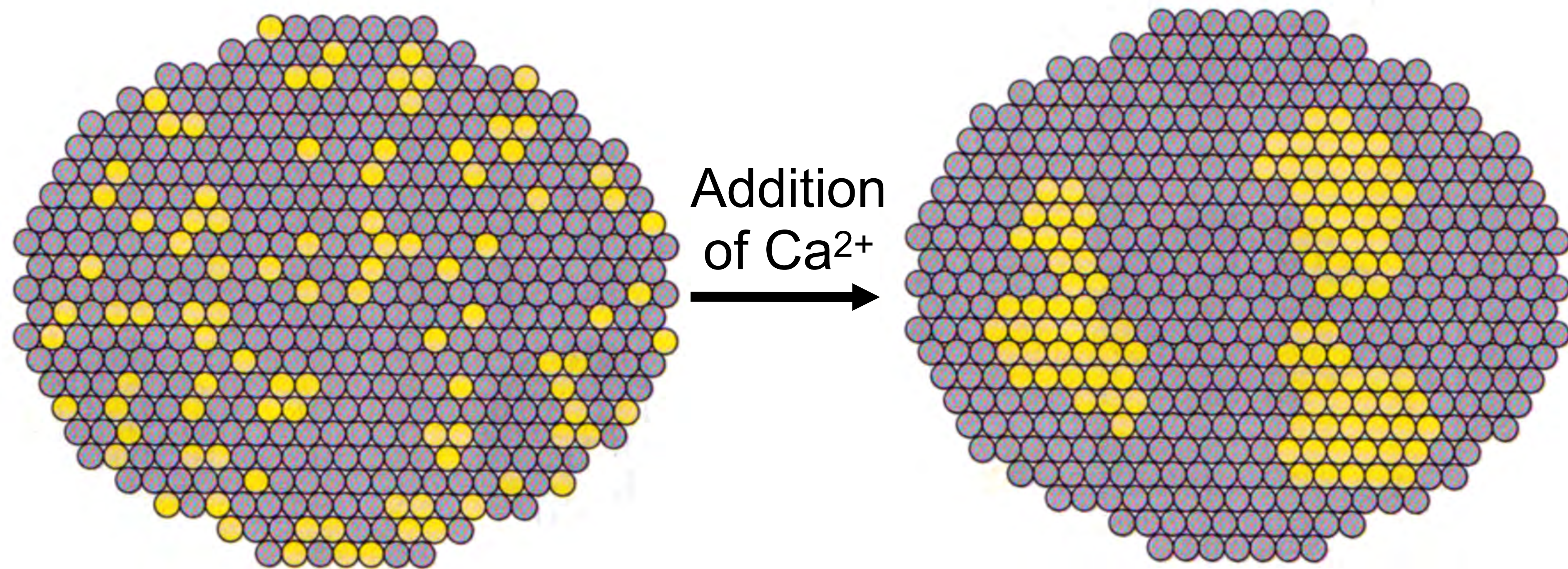
Cytoskeletal connections or membrane patches



**Figure 11-19**  
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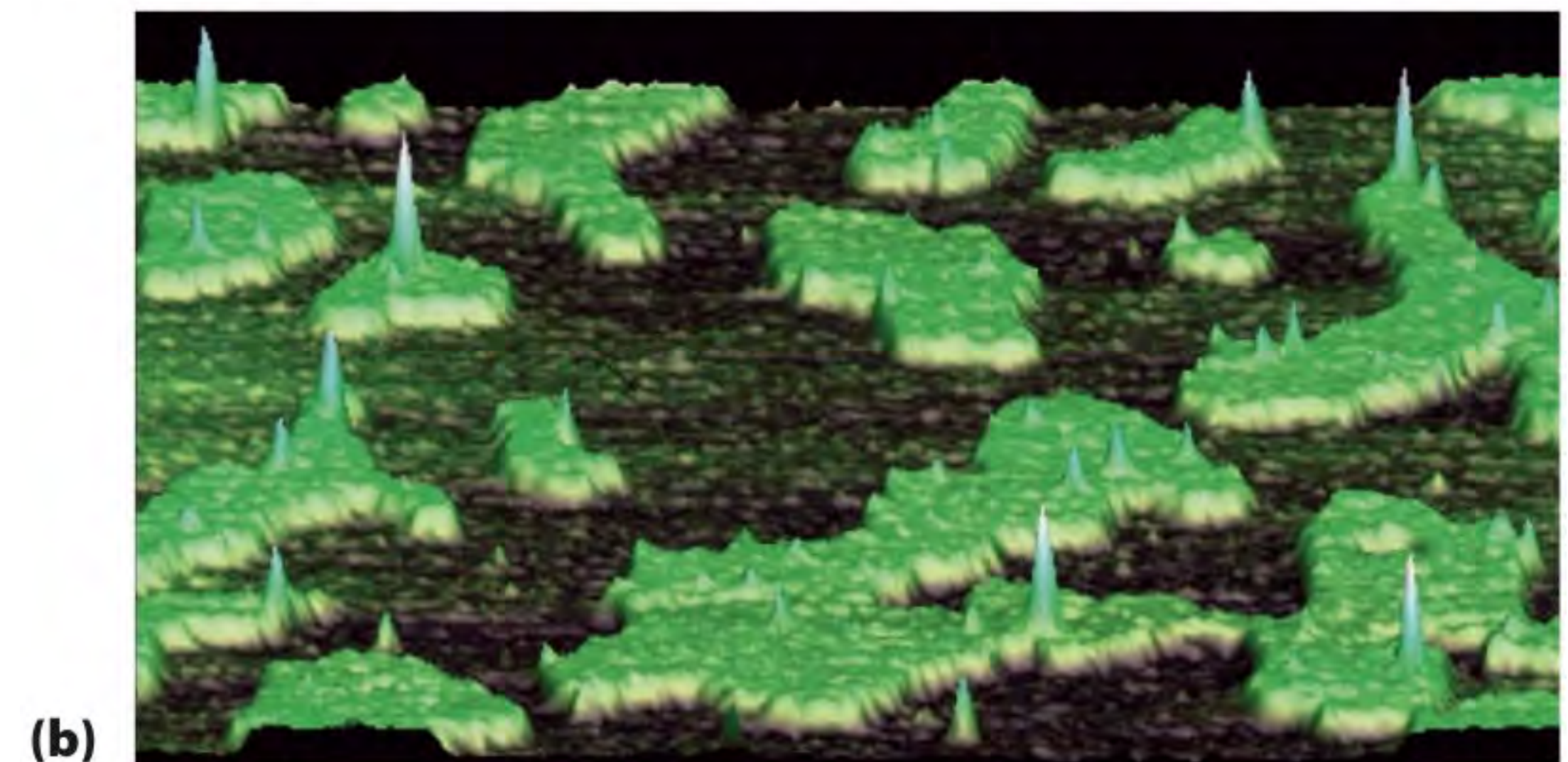
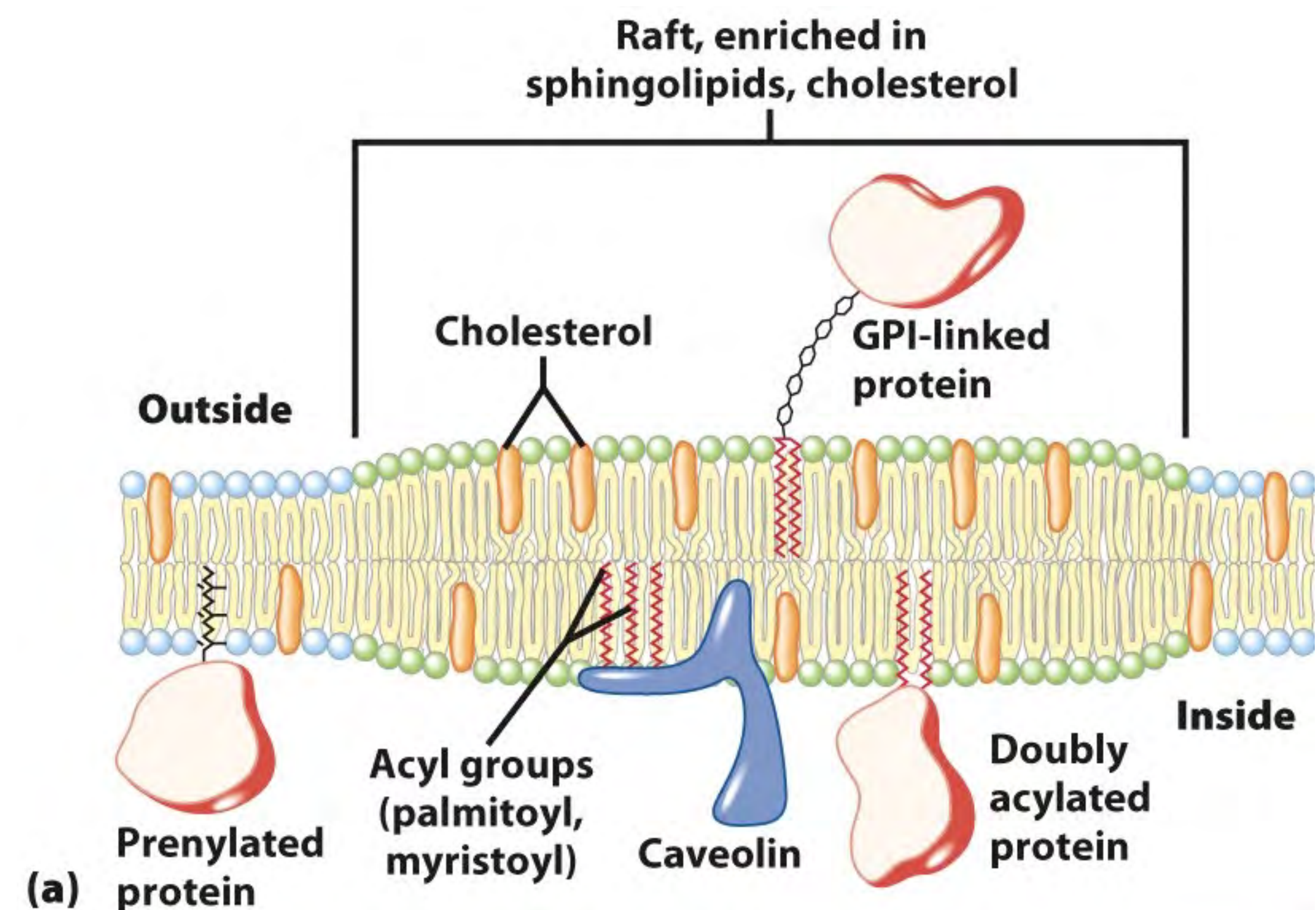
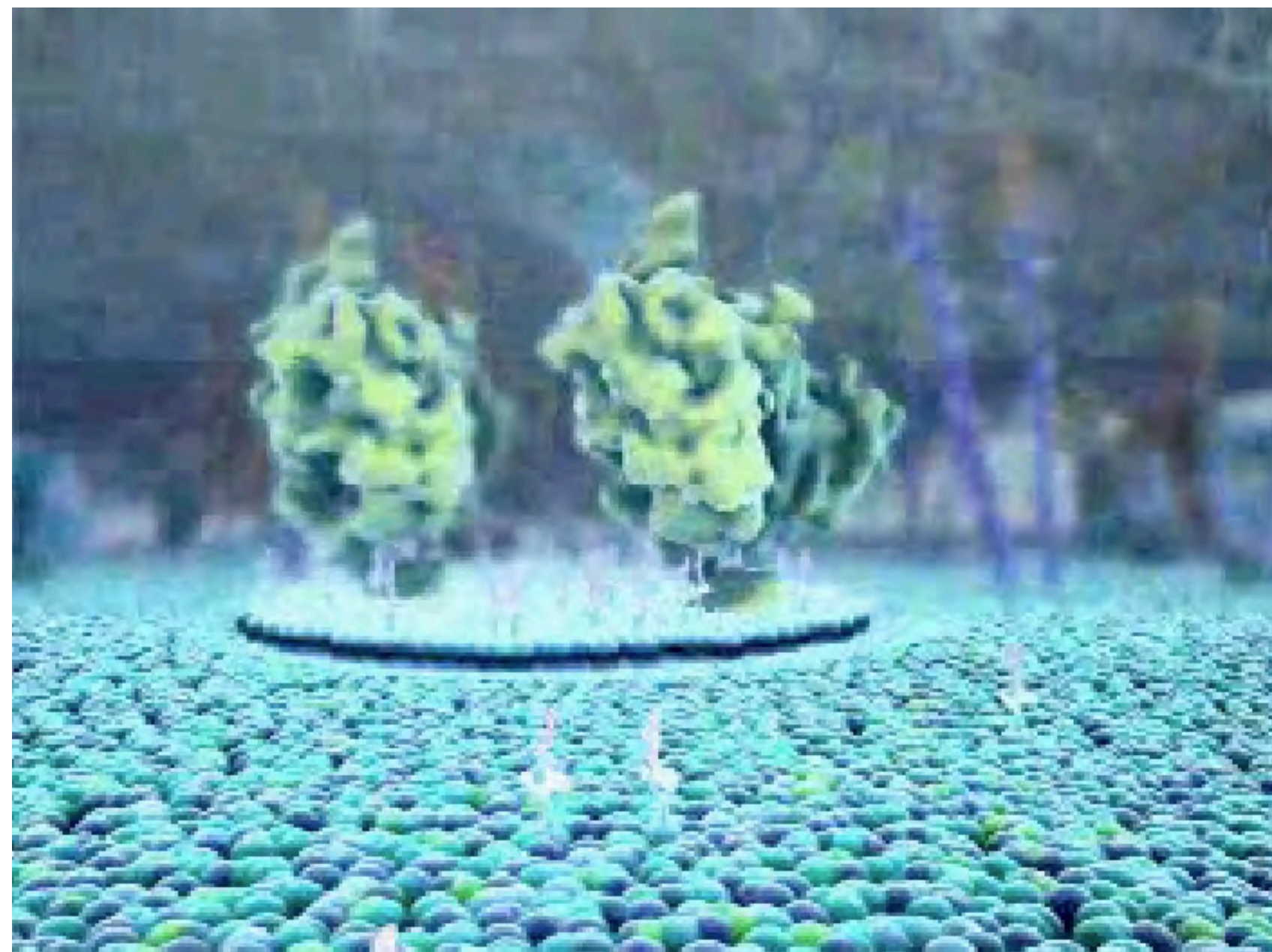
# Lipids can undergo phase separation





# Lipid Rafts

- Lipid Rafts can be formed by glycosphingolipid clusters in the outer membrane
- Cholesterol is also enriched in Lipid Rafts
- Glycosylphosphatidylinositol (GPI), palmitoyl or myristoyl anchors on proteins can anchor them to lipid rafts



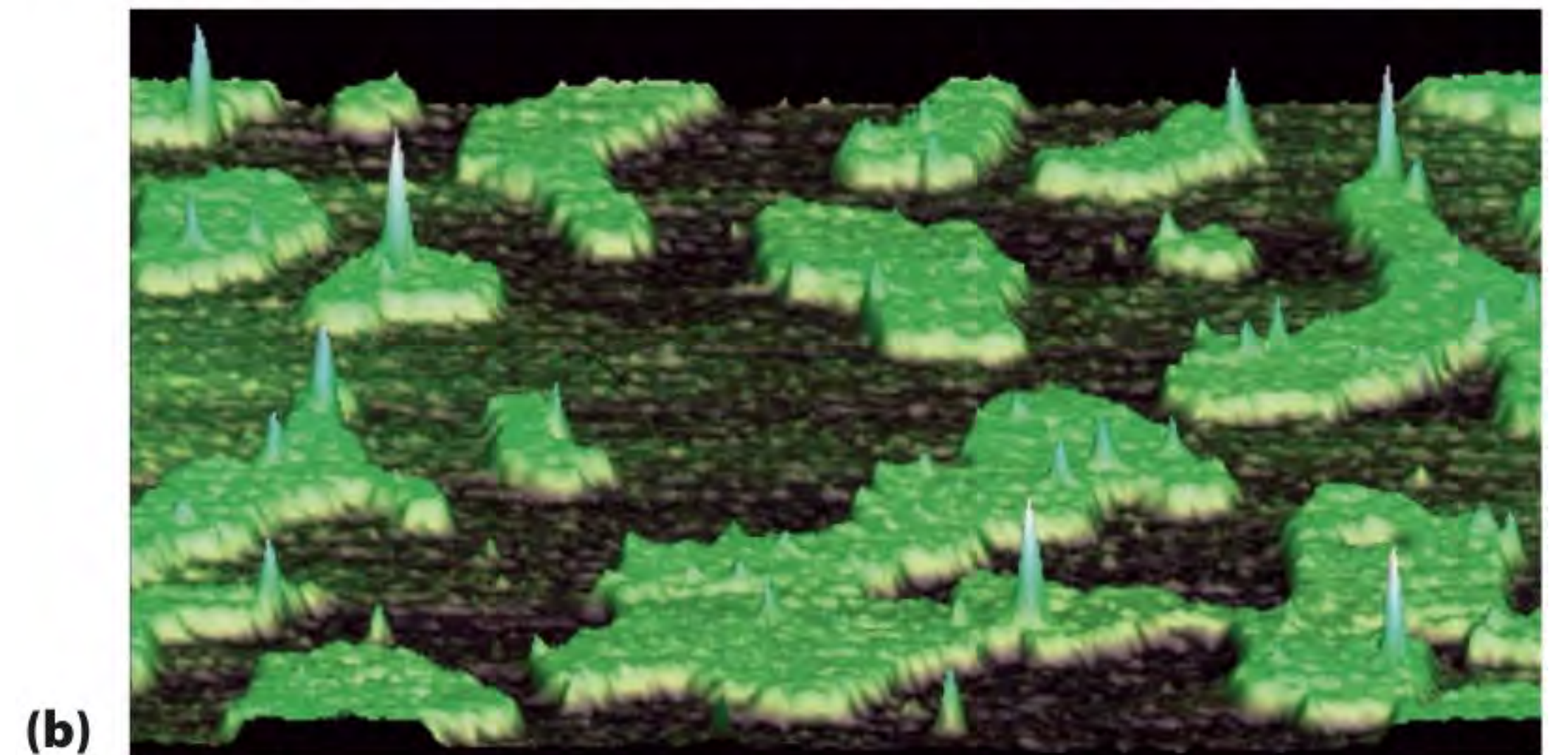
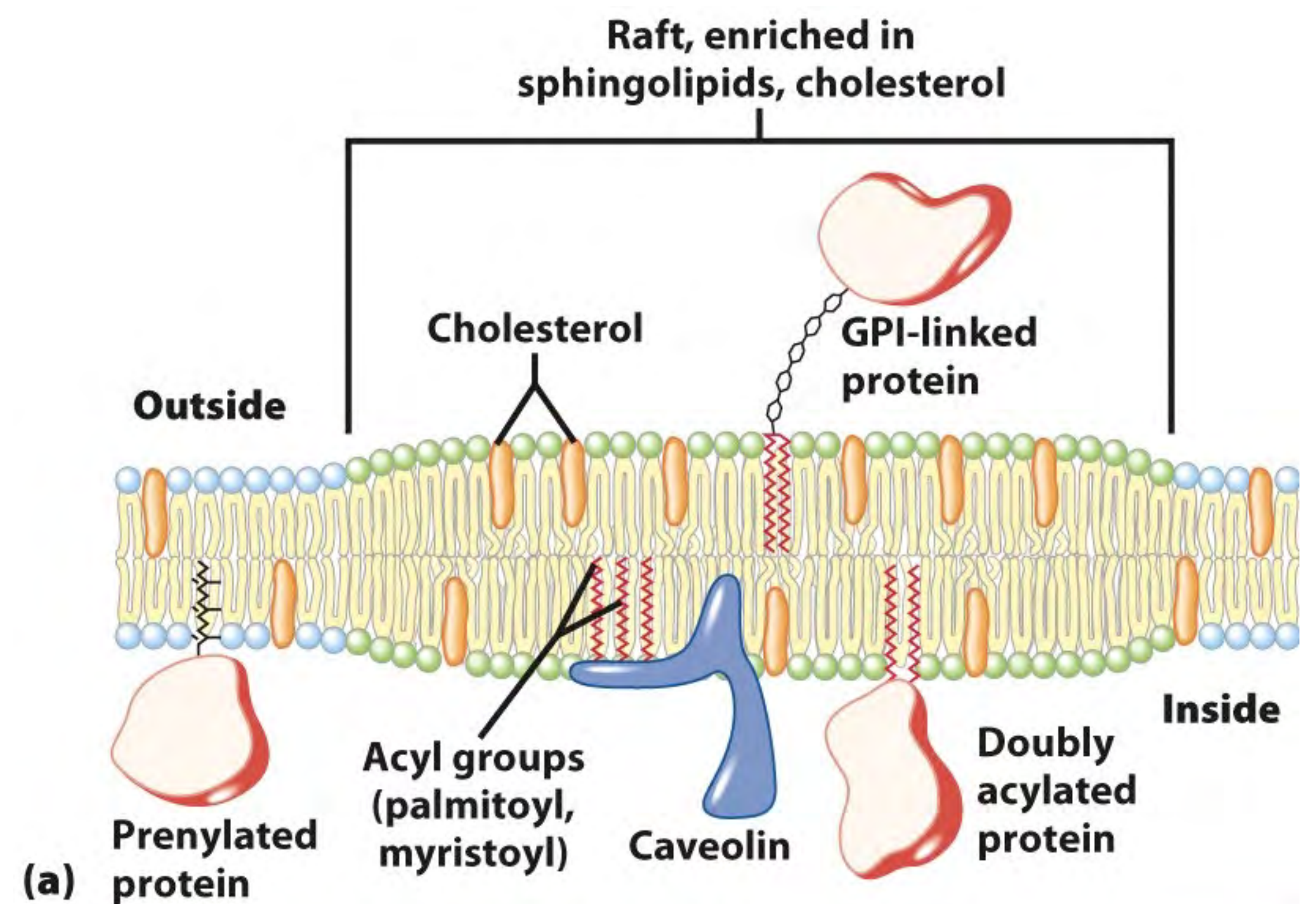
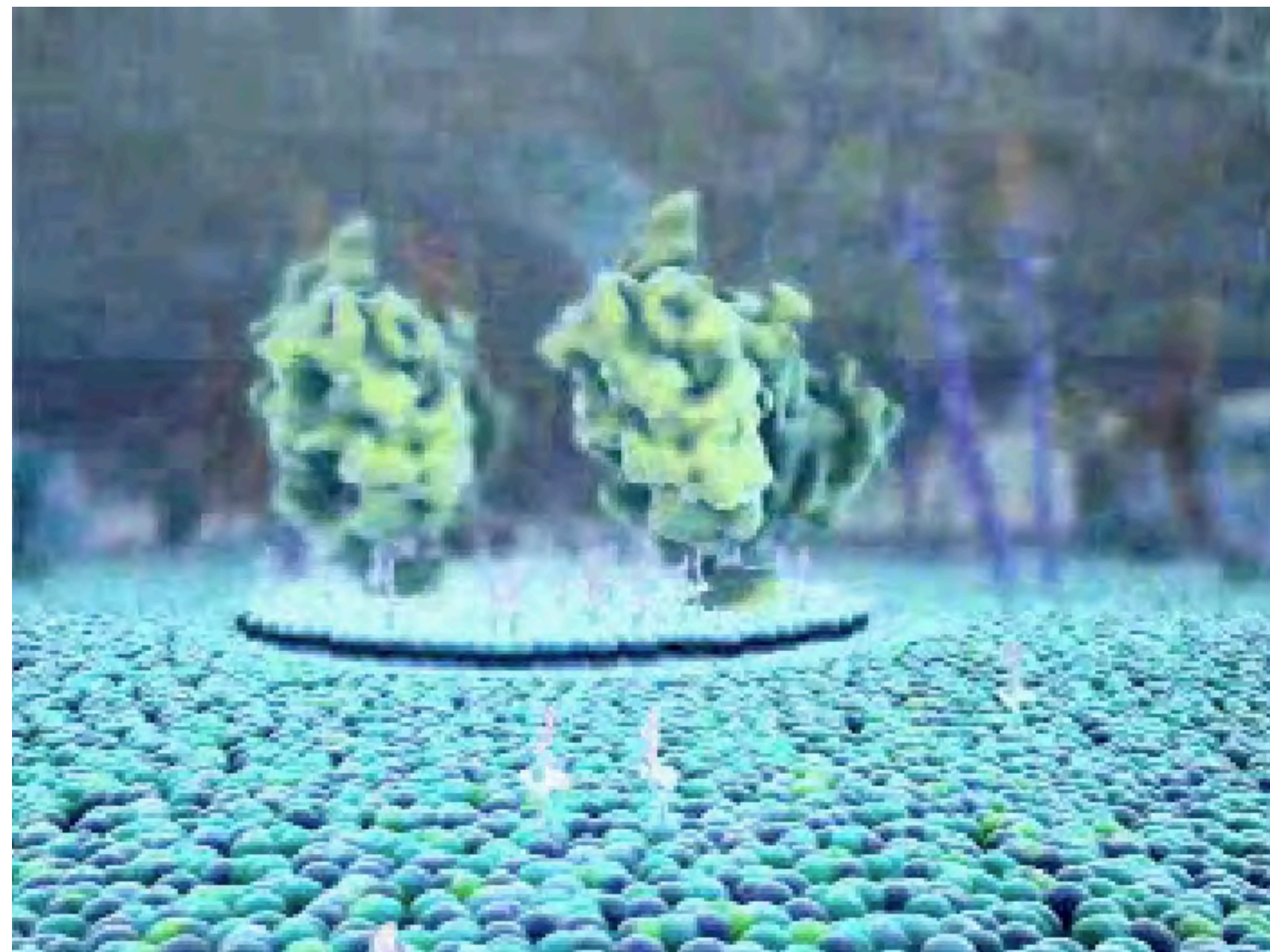
**Figure 11-20**  
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AFM image of a membrane surface



# Lipid Rafts

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- Cholesterol is also enriched in Lipid Rafts
- Glycosylphosphatidylinositol (GPI), palmitoyl or myristoyl anchors on proteins can anchor them to lipid rafts

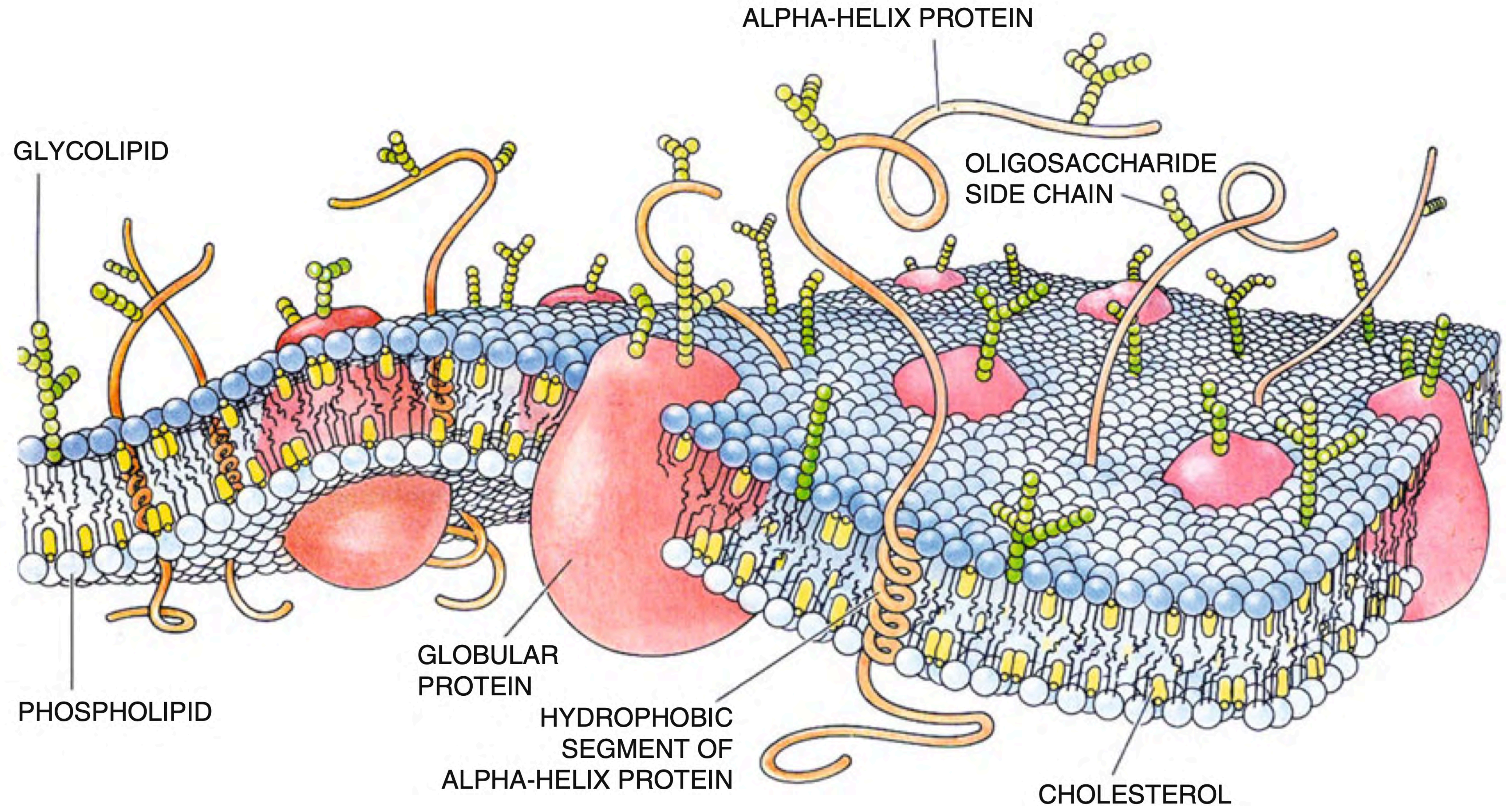


**Figure 11-20**  
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AFM image of a membrane surface



# Biological Membranes



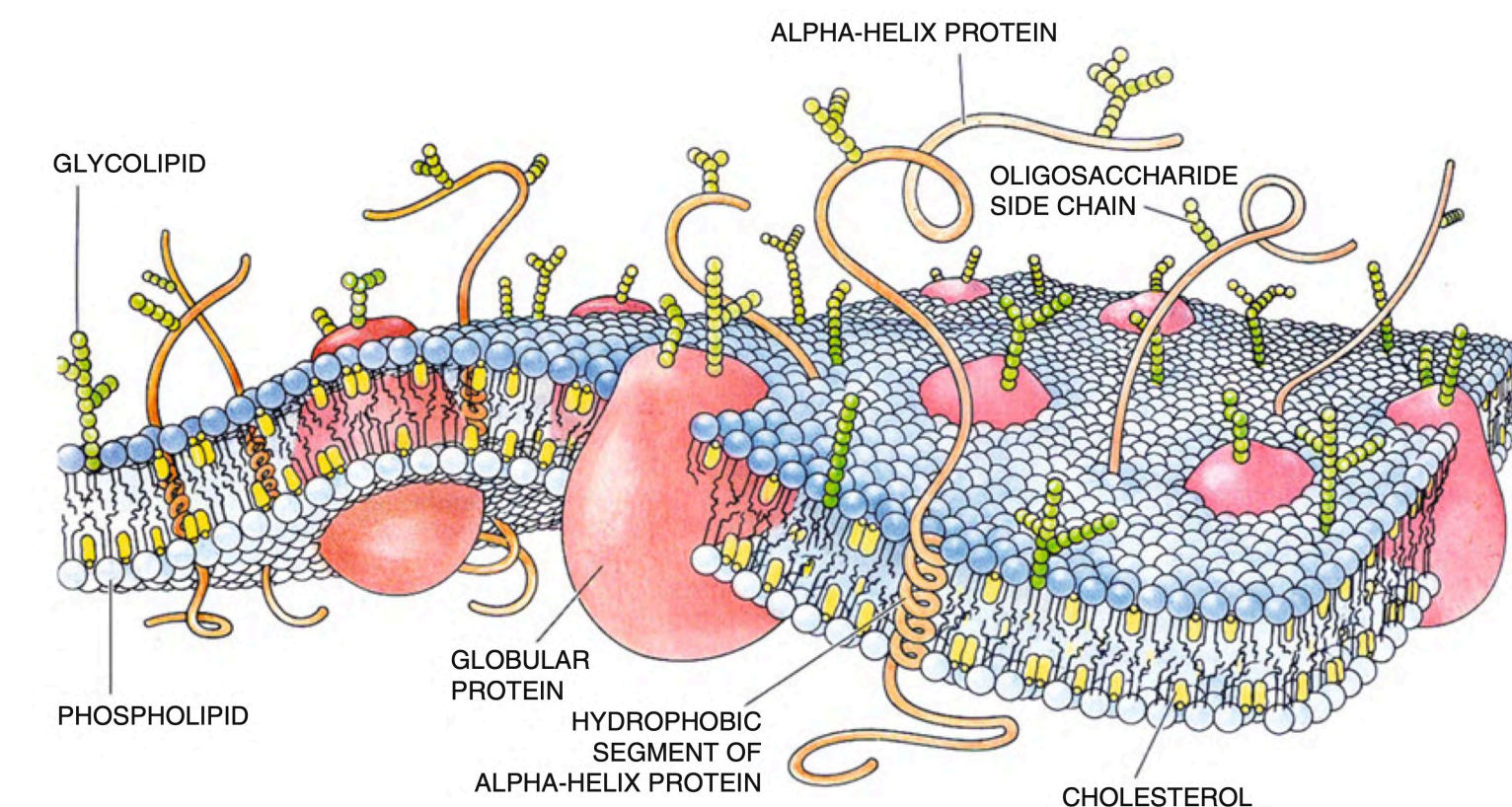


# Fluid Membrane Model (Singer & Nicolson, 1972)

Membranes are two-dimensional arrangements of oriented lipids and proteins.

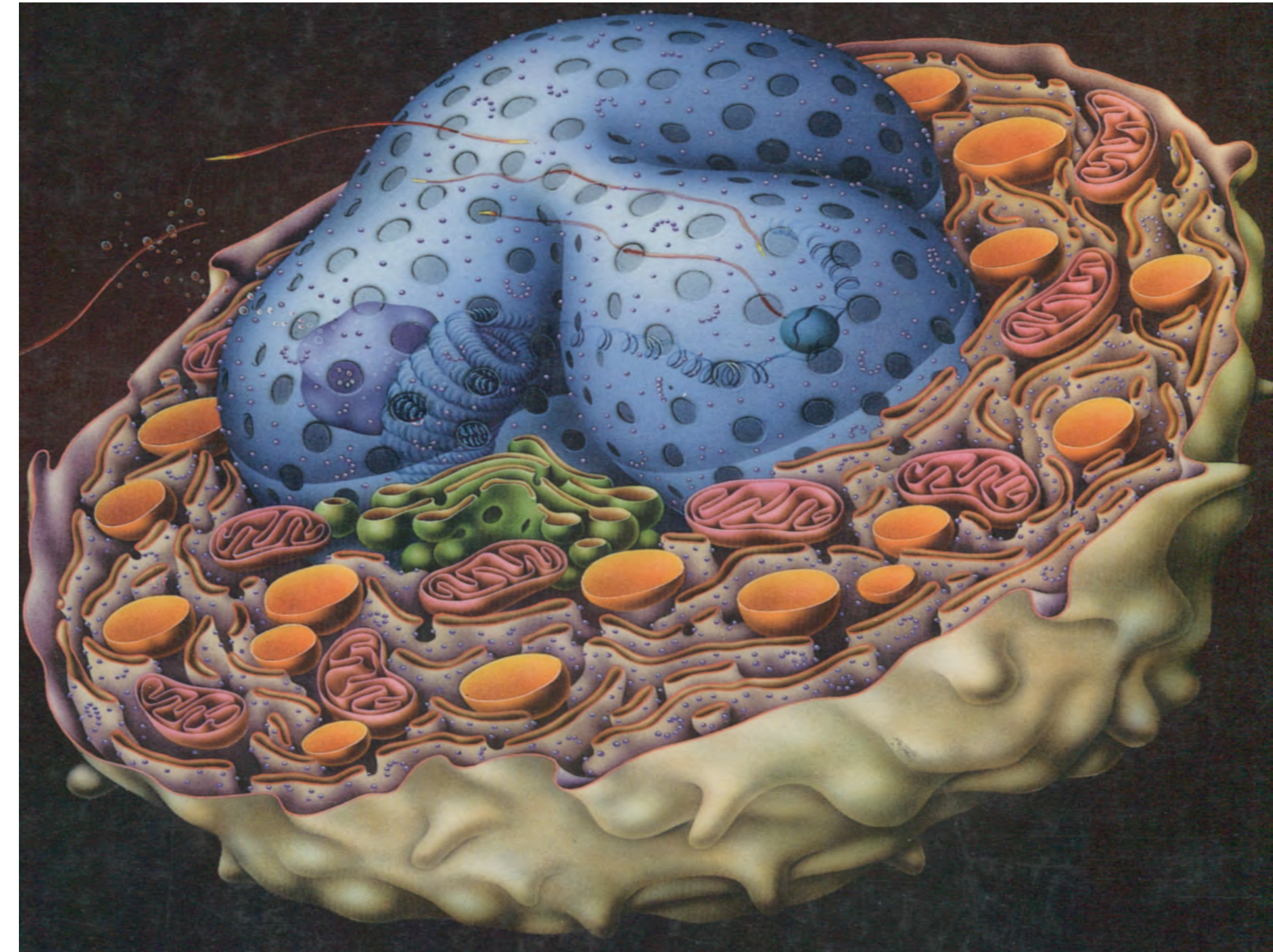
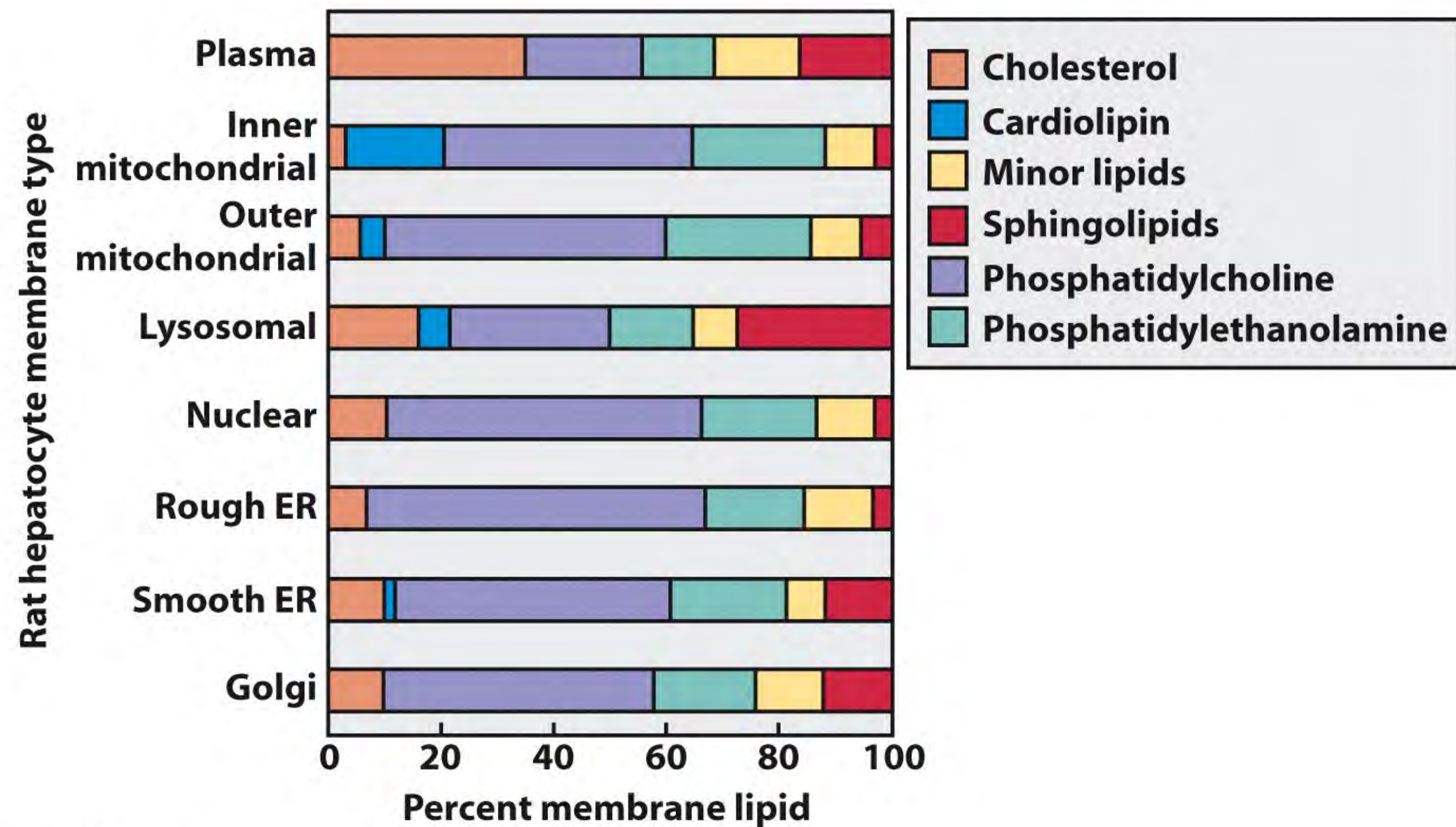
The lipid bilayer has a dual role; it forms a permeability barrier and interacts with proteins keeping them soluble and often regulating the protein activity.

Membrane proteins are free to diffuse laterally, but do not flip from one side of the membrane to the other.





# Membranes contain specialized lipids and proteins



Typical membrane composition:

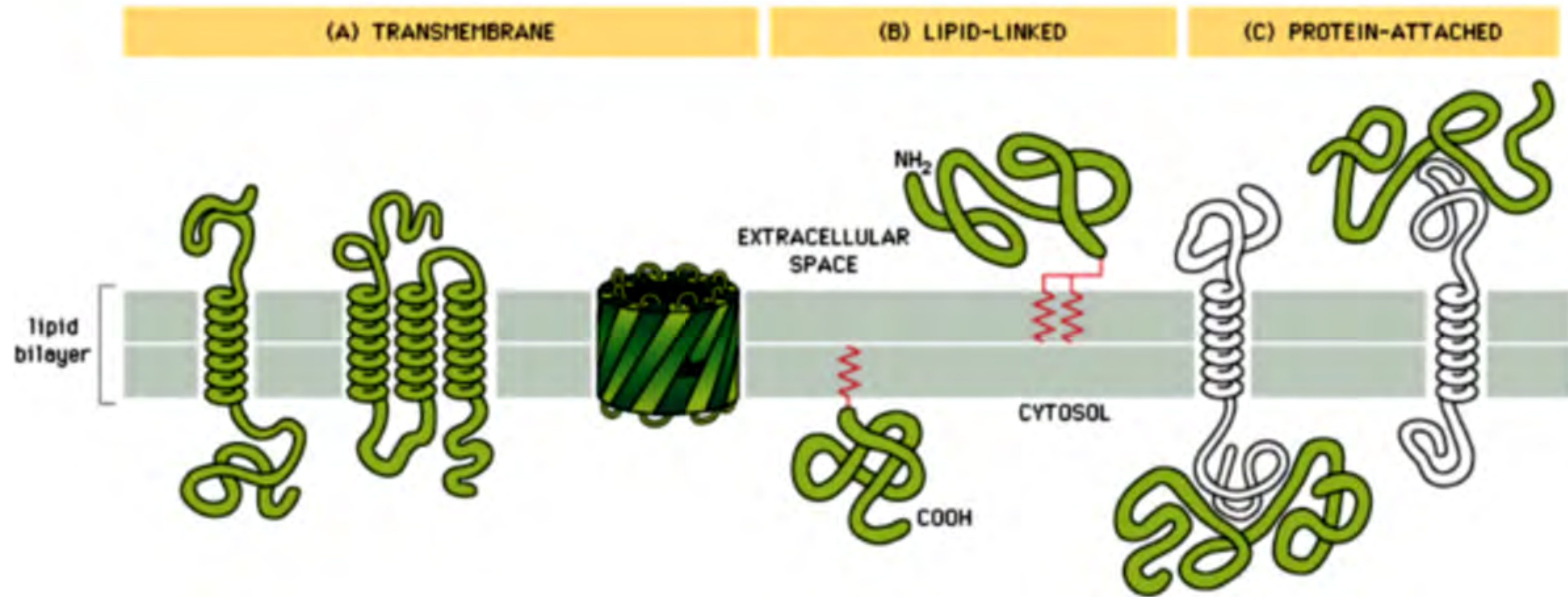
- Proteins 30-70%
- Phospholipids 7-40%
- Sterols 0-25%

Many membranes are specialized:

- Photoreceptor disc membranes have >90% Rhodopsin
- Mitochondrial membranes are very protein rich
- Red Blood Cell membranes are transport optimized (flexible)



# Membrane Proteins

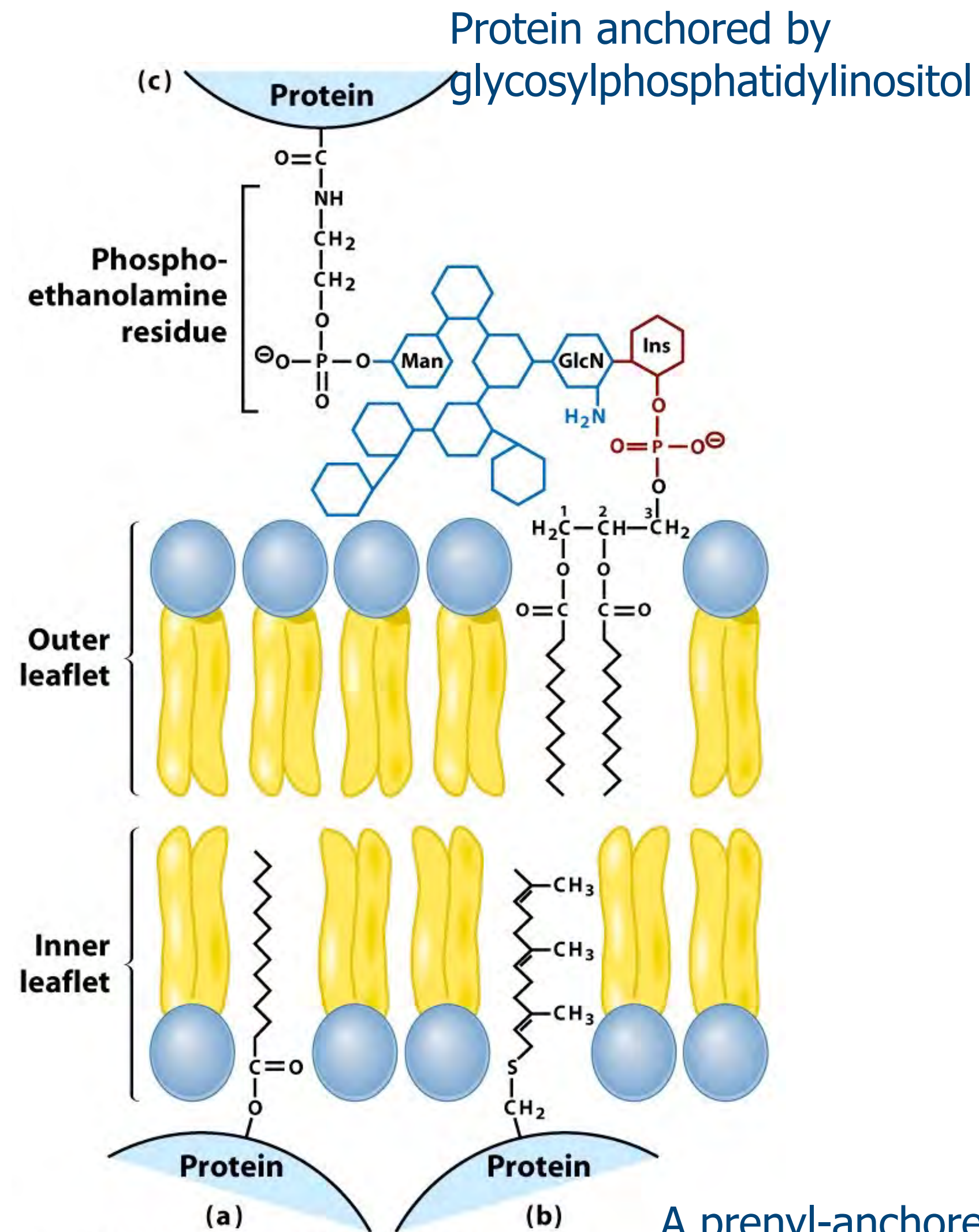


Integral (transmembrane) membrane proteins: span the membrane entirely one or several times and can only be removed from the membrane by detergent.

Peripheral proteins are either covalently linked to lipids or interact tightly with transmembrane proteins. These proteins can be removed from the membrane either by treatment with enzymes or certain reagents without disrupting the membrane integrity.



# Proteins with membrane anchors



A fatty acyl-anchored protein

A prenyl-anchored membrane protein