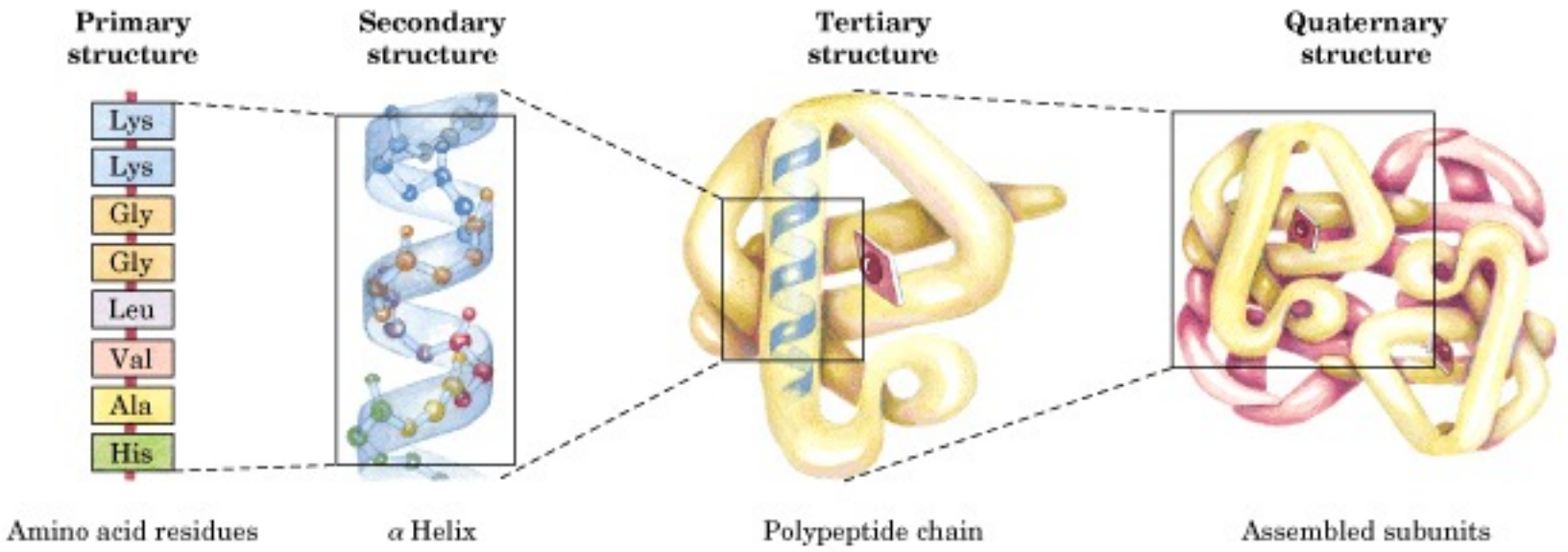
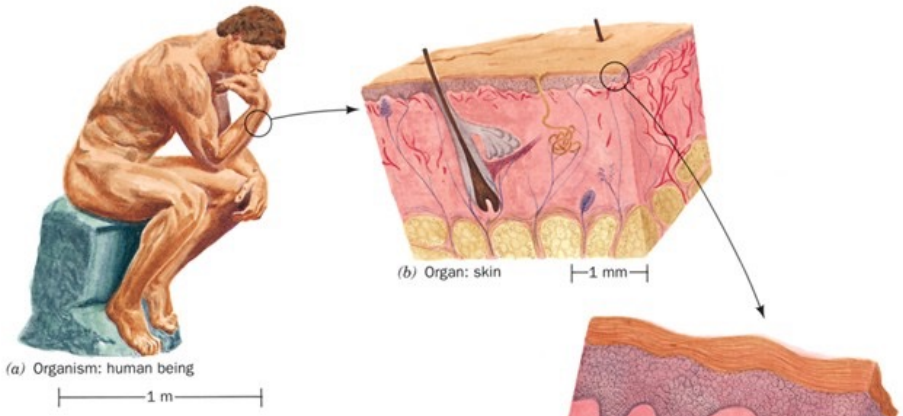
	Maio	
4	Lipídios	PDM
11	Lipídios e membranas - Estrutura / atividade Técnicas de análise de lipídios.	PDM
18	Estrutura e funções de Carboidratos - Estrutura / atividade	PDM
25	Micronutrientes.	PDM

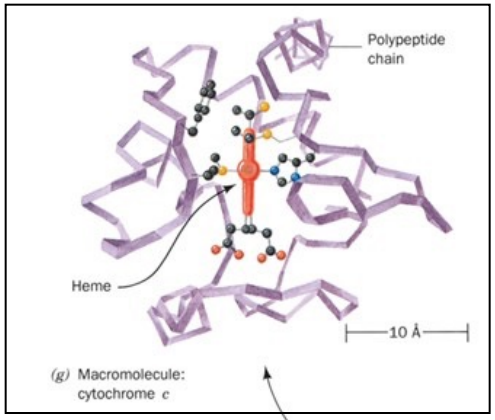
Estrutura das Proteínas pode ser descrita em 4 níveis de organização

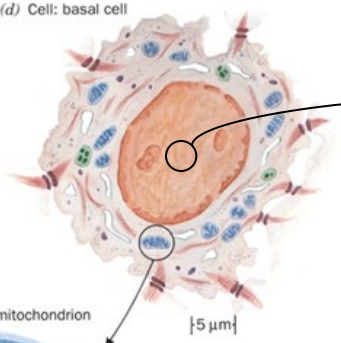


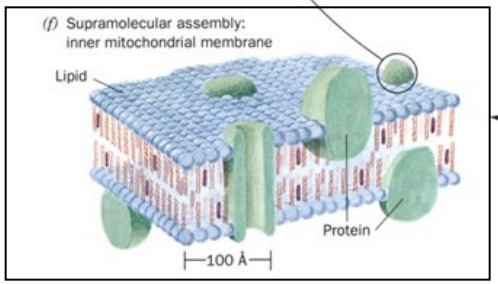


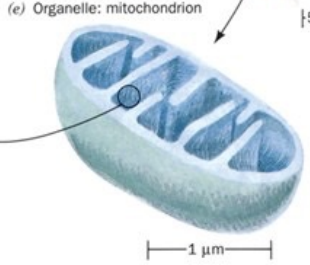
PROTEÍNAS

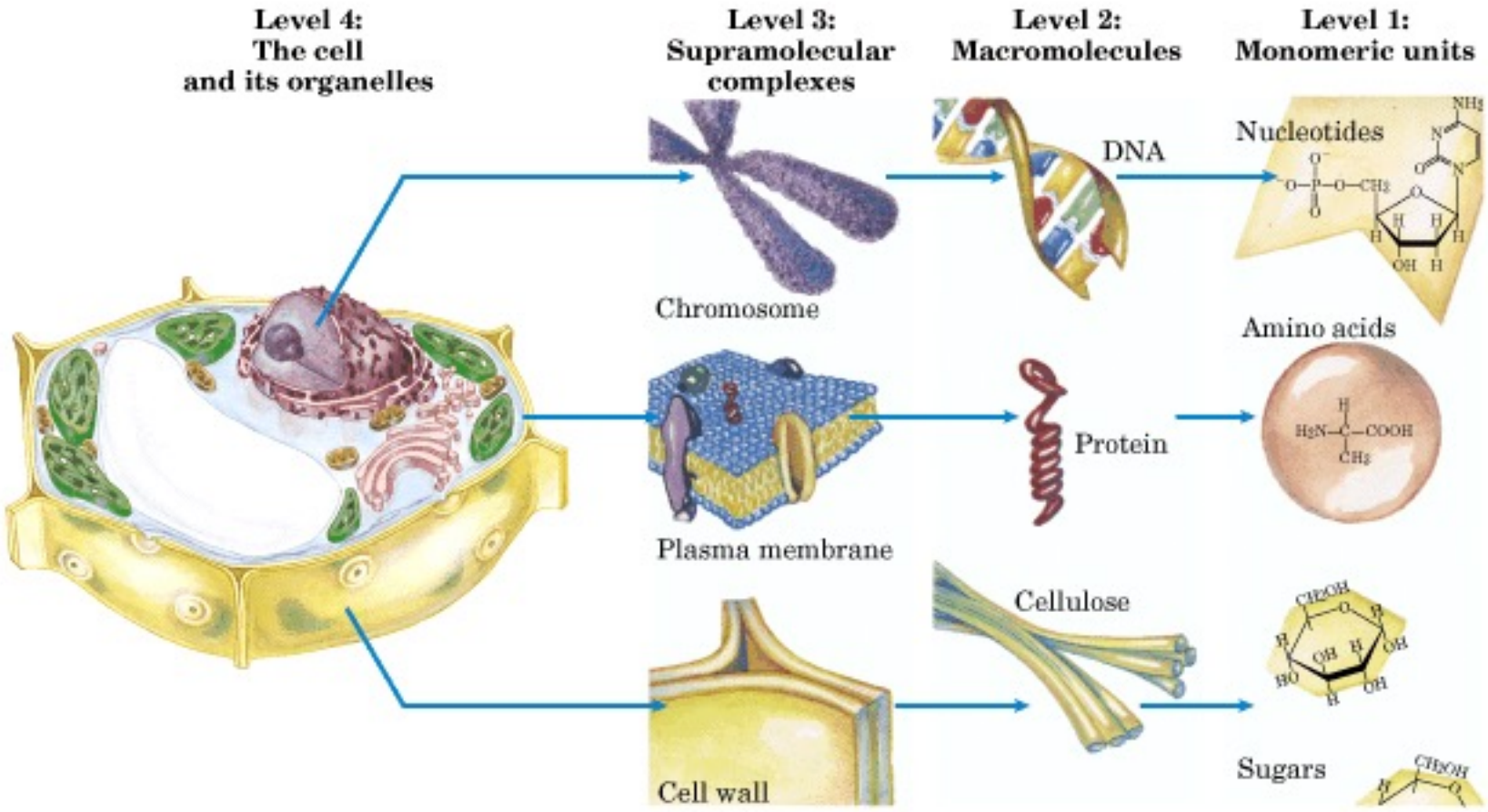
DNA










Level 4:
The cell
and its organelles
Level 3:
Supramolecular
complexes
Level 2:
Macromolecules
Level 1:
Monomeric units
Chromosome
DNA
Nucleotides
Amino acids
Plasma membrane
Protein
Cellulose
Cell wall
Sugars

Os organismos necessitam de um constante fornecimento de energia livre

- Por que?

- Biossíntese de moléculas complexas;

- Transporte ativo de moléculas e íons c através de membranas;

- Realização de Trabalho Mecânico: contração muscular, movimentos celulares...

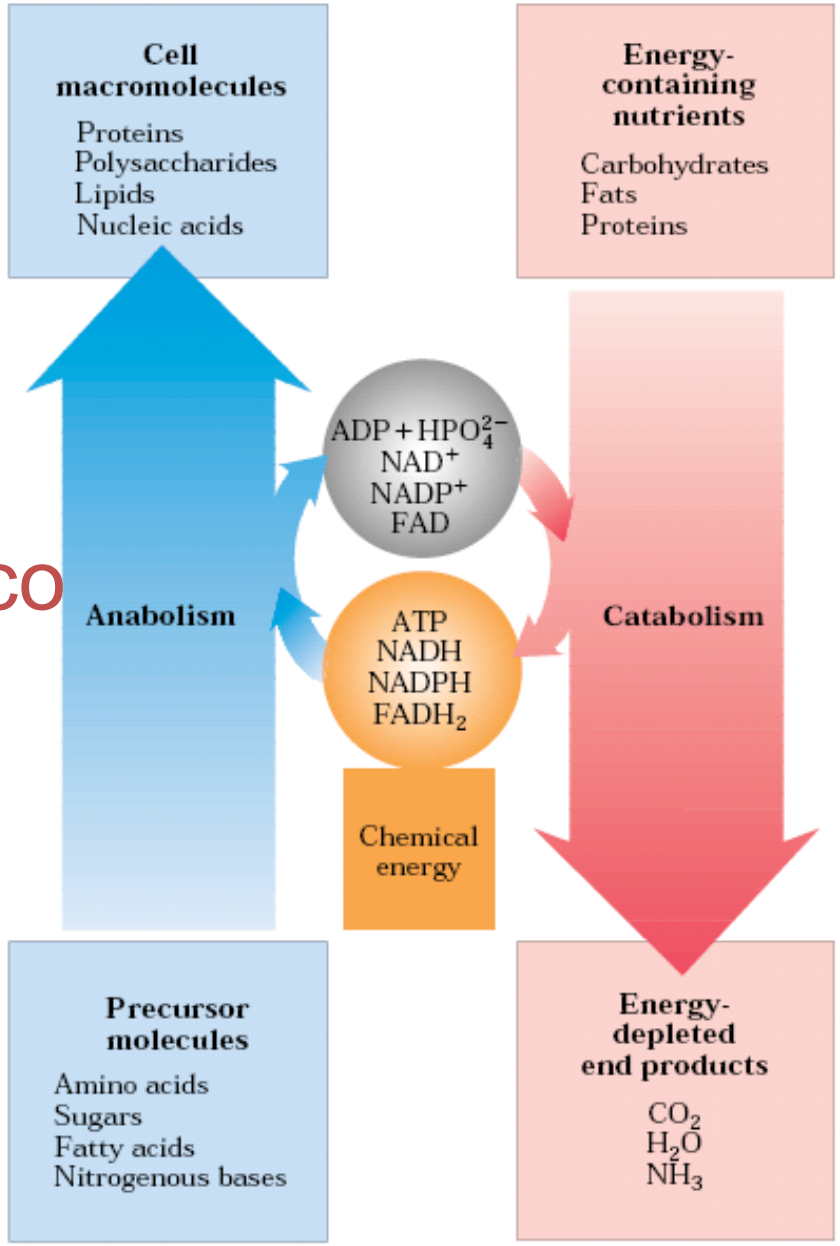
De onde vem essa energia??

Como a célula obtém essa energia??

Energy-containing nutrients

Carbohydrates
Fats
Proteins

Endergônico



Exergônico

Vias Metabólicas

Séries de reações consecutivas catalisadas enzimaticamente, que produzem produtos específicos (metabólitos).

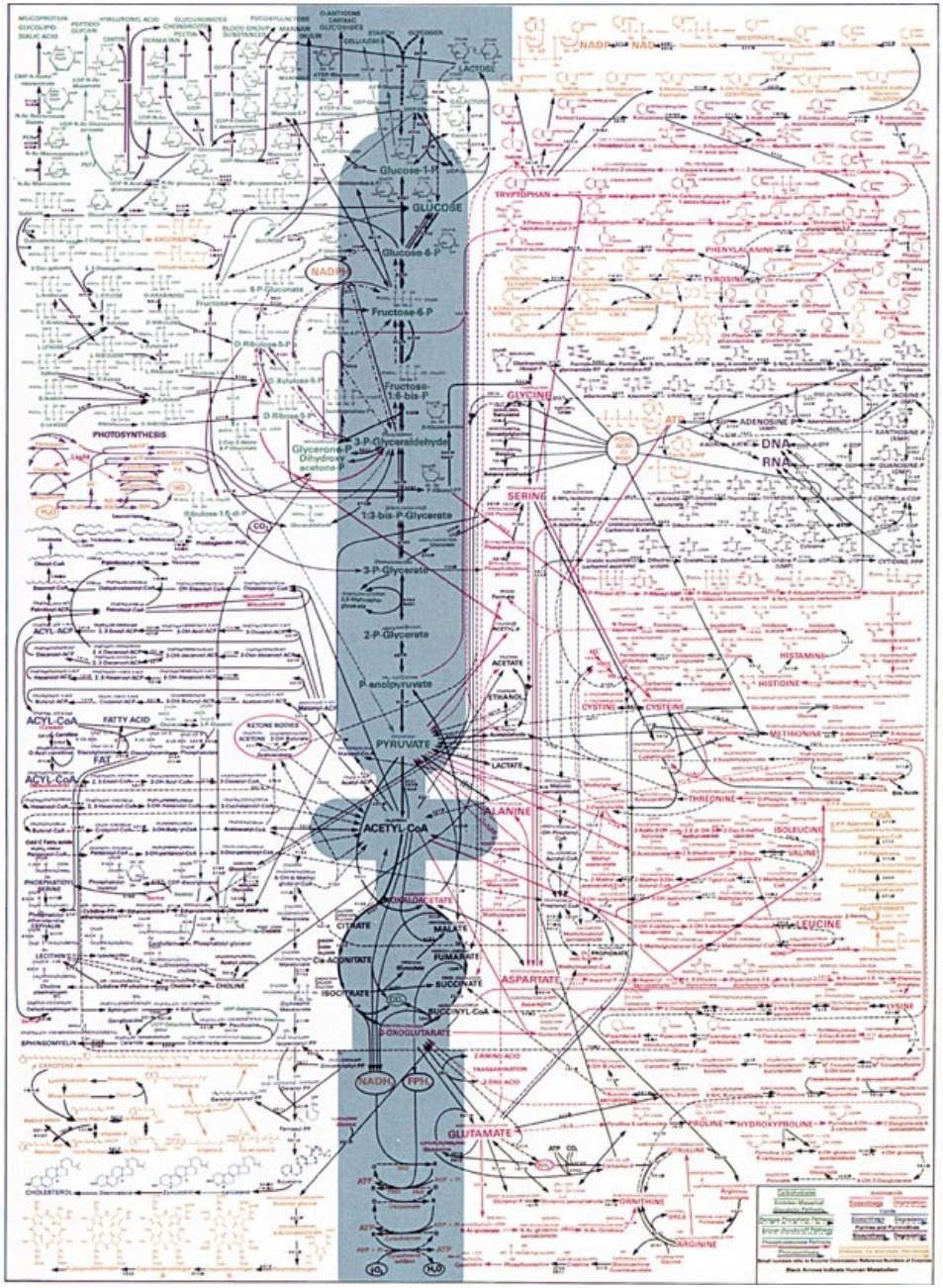
Note que: as vias são interconectadas (pontos de cruzamento).

Pontos importantes:

-conhecer as principais avenidas (vias),

-os cruzamentos mais importantes (intermediários comuns) e

-como o fluxo nessas vias são controladas (regulação)...



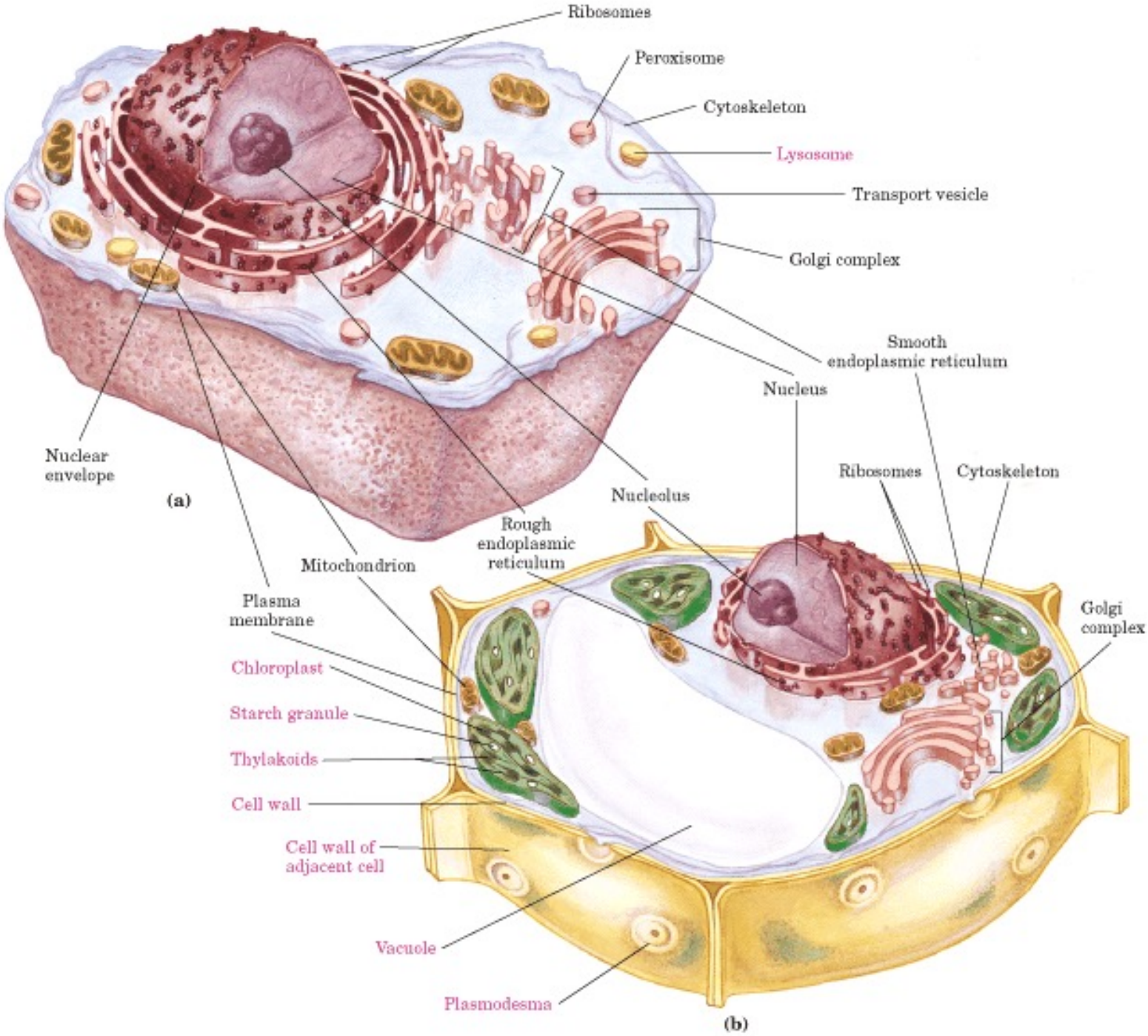
CÉLULAS

- Toda células tem uma membrana celular

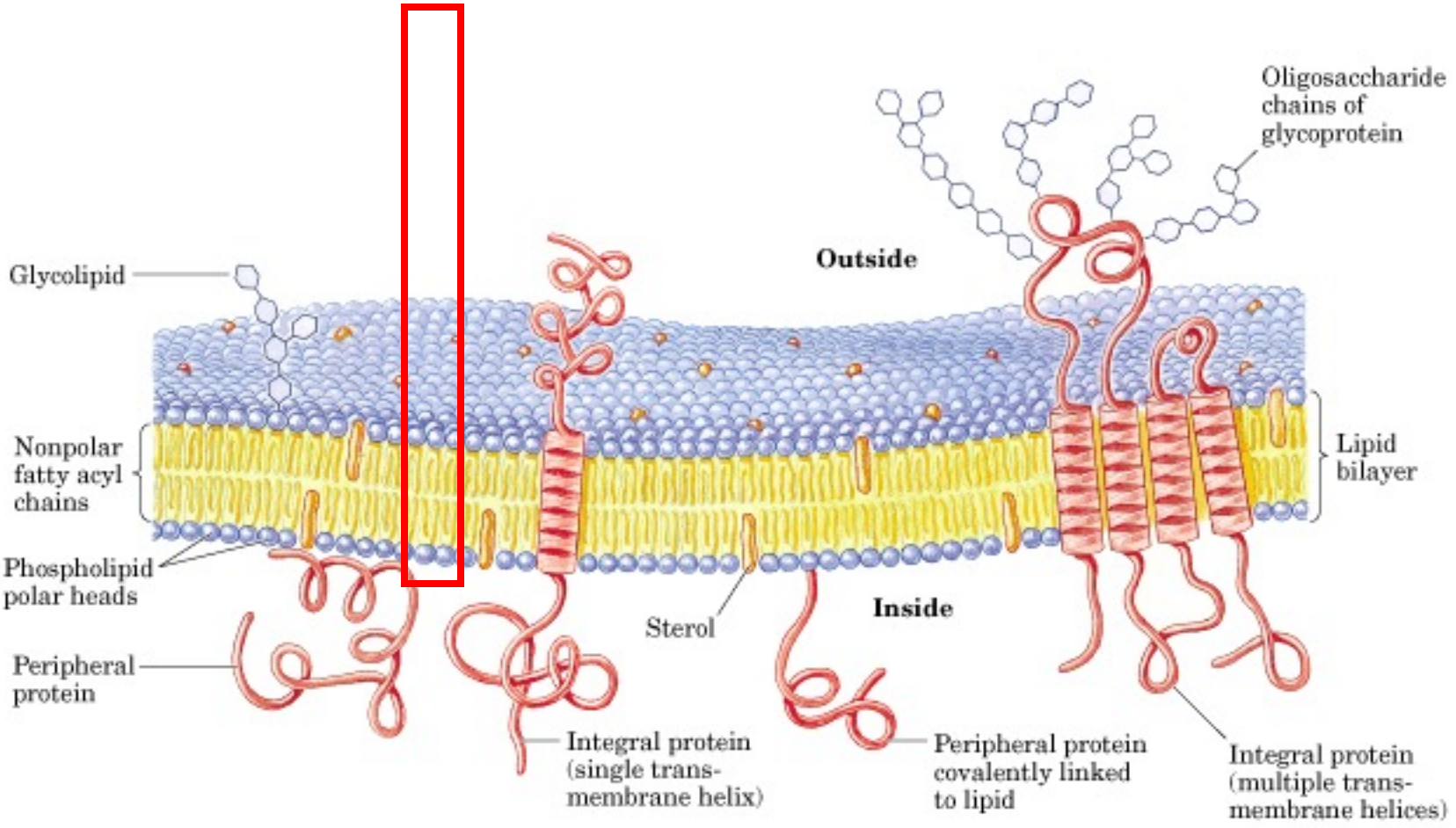
- Células eucarióticas também apresenta organelas separadas por membranas

- As membranas separam as células do meio externo e desempenha um papel importante no transporte e no controle do fluxo de informação entre as células e o meio externo

- Diversas enzimas encontram-se nas membranas e dependem deste ambiente para o desenvolvimento de suas funções


Ribosomes
Peroxisome
Cytoskeleton
Lysosome
Transport vesicle
Golgi complex
Smooth endoplasmic reticulum
Nucleus
Nuclear envelope
(a)
Nucleolus
Ribosomes
Cytoskeleton
Rough endoplasmic reticulum
Mitochondrion
Plasma membrane
Golgi complex
Chloroplast
Starch granule
Thylakoids
Cell wall
Cell wall of adjacent cell
Vacuole
Plasmodesma
(b)

LIPÍDIOS / MEMBRANAS



LIPÍDIOS

- Compostos biológicos "solúveis" somente em solventes apolares
- Ácidos Graxos, são os blocos fundamentais de muitos lipídios
- A cadeia de hidrocarbonetos tem pouca afinidade com a água
- A parte polar associa-se com a água
- As membranas de células animais contém proporções significativas de esfingolipídios e colesterol (hidrofóbico)

Lipídeos

Lipídeos (Estrutura e Classificação)

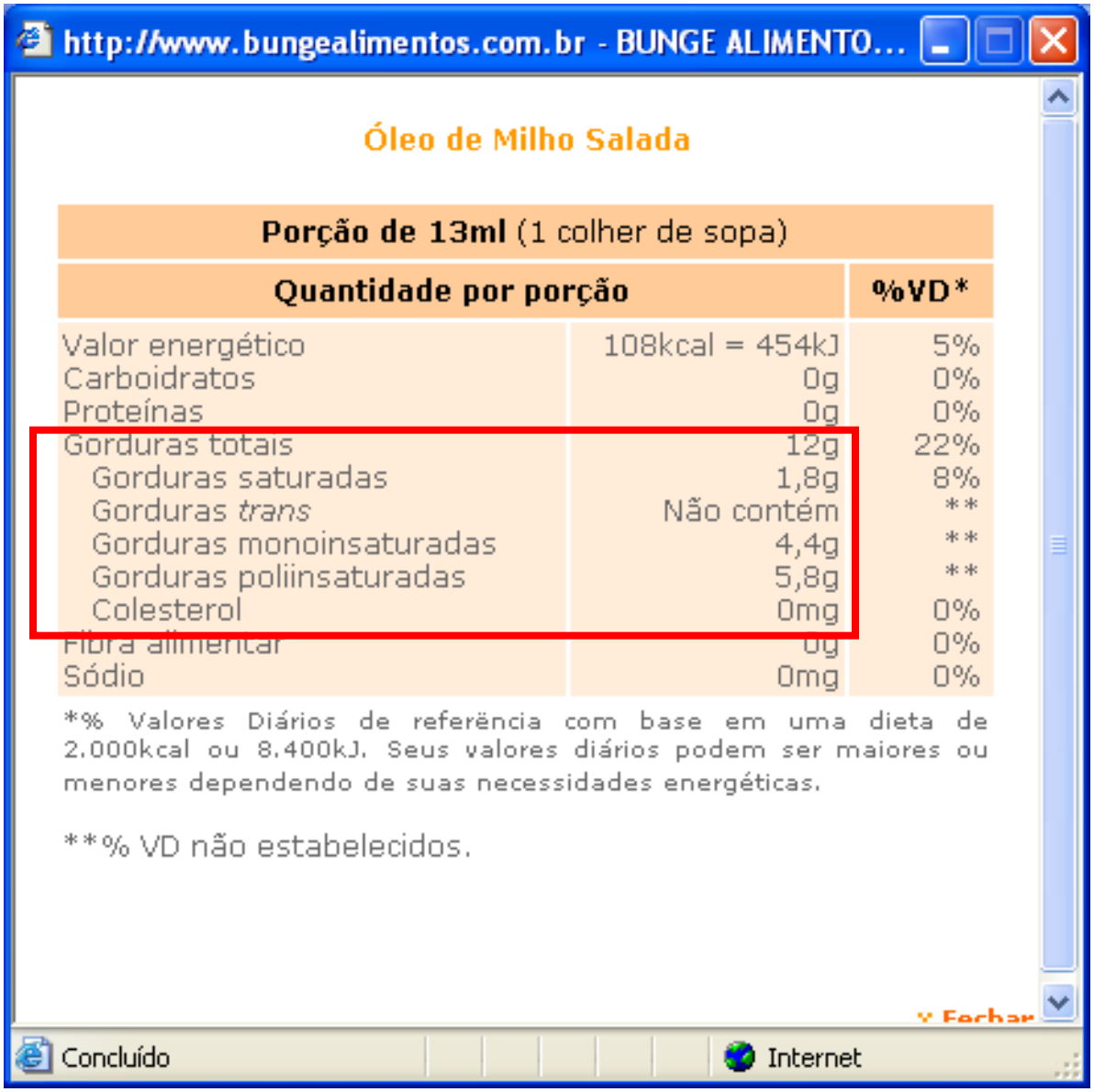
Lipoproteínas (Transporte)

Membranas Biológicas

Onde encontramos os lipídeos??

Óleos e gorduras

Lipídios nos Alimentos



Tecido adiposo

"TG são excelentes reservas de energia"

Vénus de Willendorf

24.000 e 22.000 a.C.

Lipideos

- **Classificados pela solubilidade (não estrutura).**
- **Lipídios (grego “lipos”, gordura): compostos solúveis em solventes orgânicos (metanol, clorofórmio, etc).**
- **São moléculas apolares insolúveis em água. Algumas são anfipáticas.**

Lipídios: Funções Principais

Ácidos Graxos
- Unidades que compõe os triacilgliceróis e fosfolipídios
- Produção de energia
- Precursores de eicosanóides

Triacilgliceróis → Estoque de energia

Fosfolipídios → Principal componente das membranas celulares

Esteróis
(Colesterol/
Esteres de Colesterol)
- Componente de membrana celular
- Precursor de ácidos biliares, vitamina D
- Precursores de hormônios esteroidais

Vitaminas Lipossolúveis

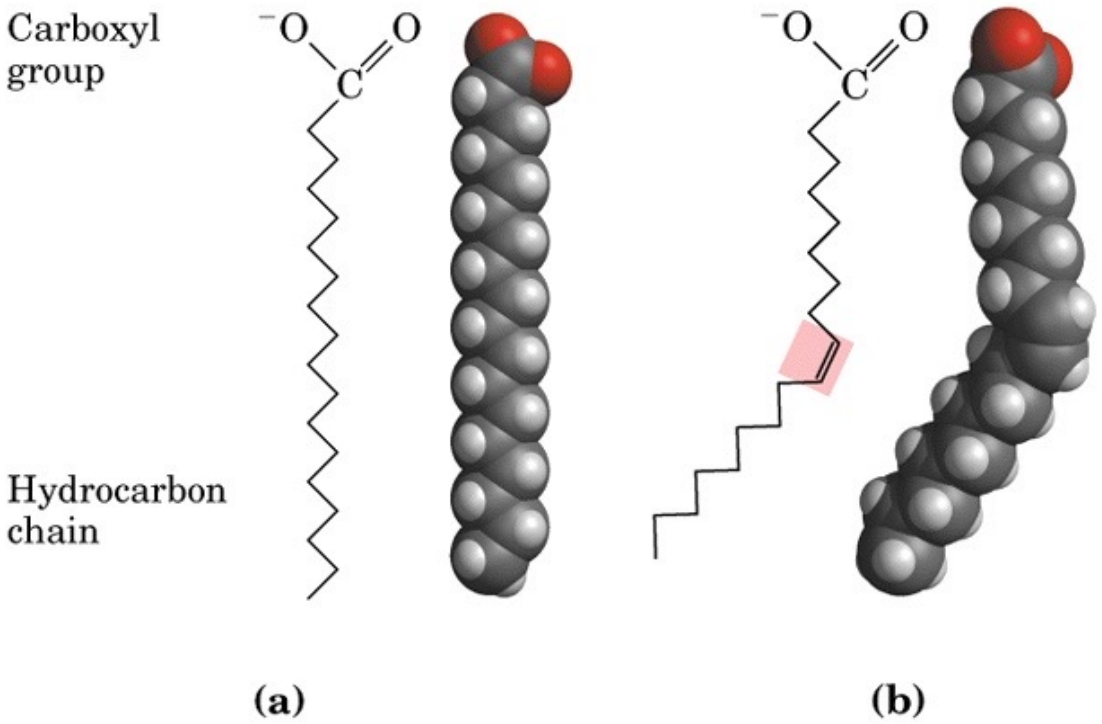
- Vitamina A – visão (retinal + opsin = rhodopsina)
- Vitamina D – metabolismo do cálcio
- Vitamin E – antioxidante que protege as membranas
- Vitamina K – importante para a coagulação.

Ácidos Graxos

Triacilgliceróis

Fosfolipídios

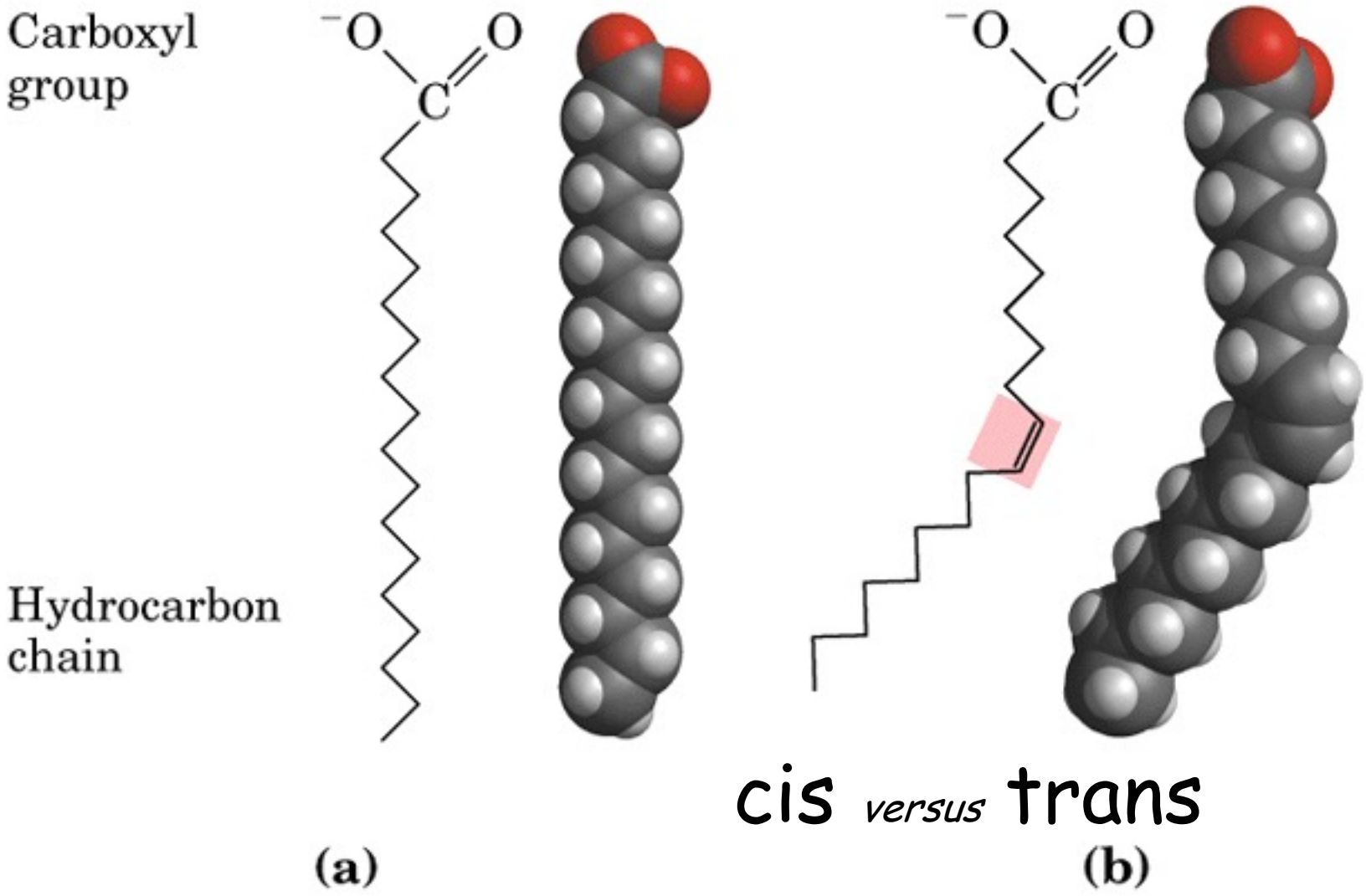
Esteróis
(Colesterol/
Esteres de Colesterol)



✓*São ácidos carboxílicos com grupos laterais de hidrocarbonetos de cadeia longa*

✓*Encontram-se normalmente na forma esterificada*

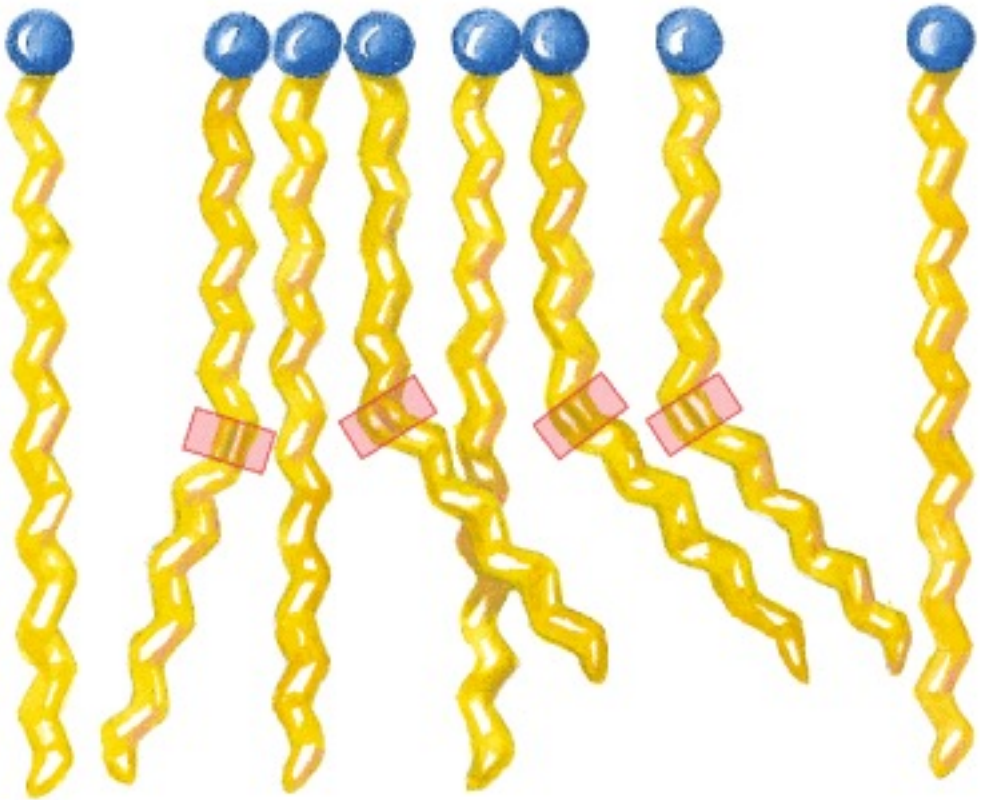
✓*A maioria dos ac.graxos possui número par de carbonos.*



cis *versus* trans

Saturated
fatty acids

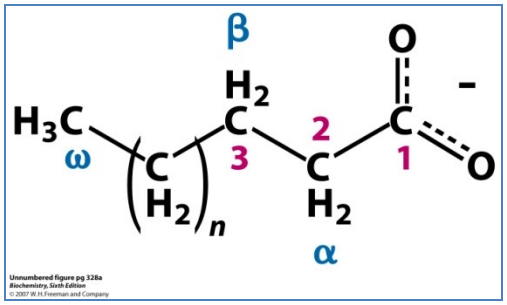
(c)

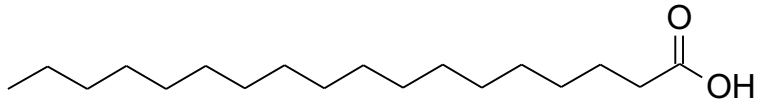


Mixture of saturated and
unsaturated fatty acids

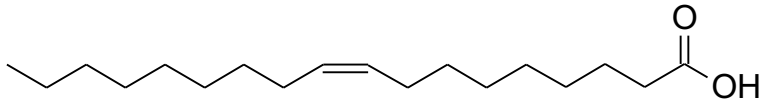
(d)

Ácidos Graxos

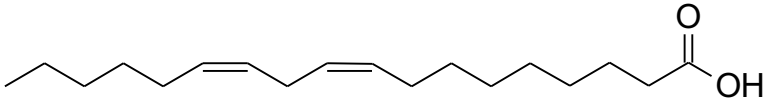




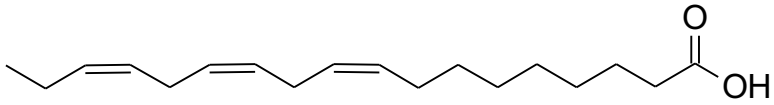
C 16:0



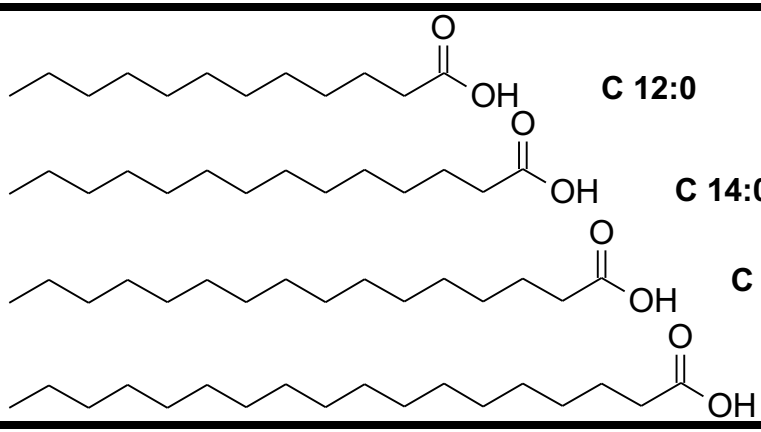
C 18:1 Δ^{9}



C 18:2 $\Delta^{9,12}$



C 18:3 $\Delta^{9,12,15}$



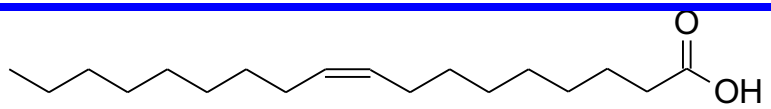
C 12:0 **ácido laurico**

C 14:0 **ácido mirístico**

C 16:0 **ácido palmítico**

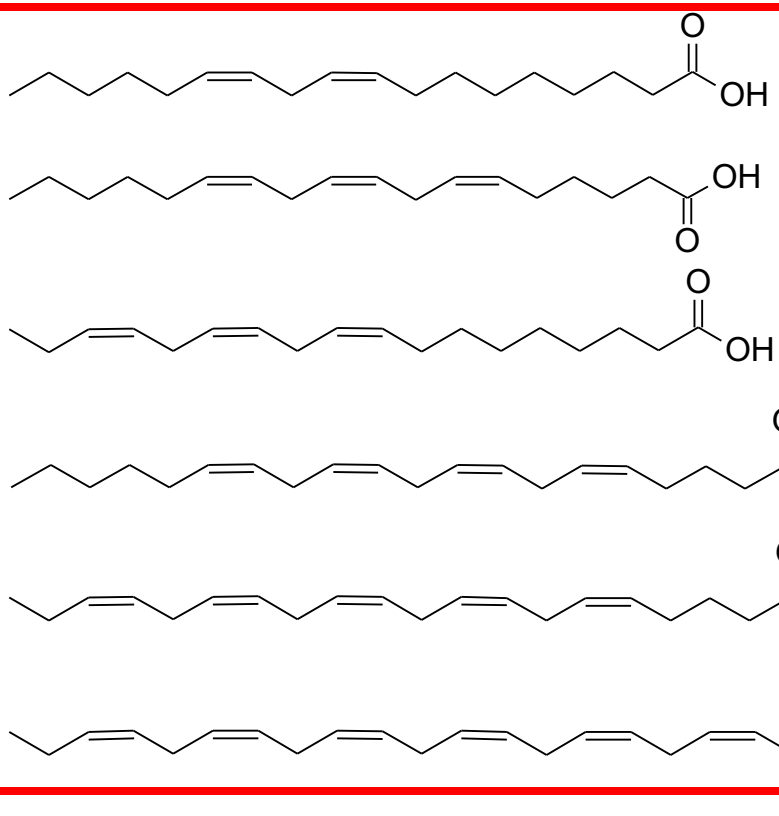
C 18:0 **ácido esteárico**

Saturados



C 18:1 **ácido oleico**

Monoinsaturados



C 18:2 **ácido linoleico**

C 18:3 **ácido γ-linolenico**

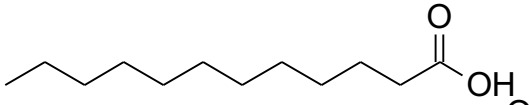
C 18:3 **ácido α-linolenico**

C 20:4 **ácido araquidonico**

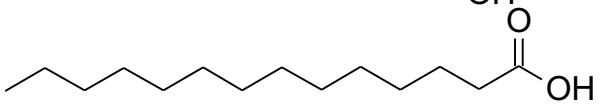
C 20:5 **ácido eicosapentaenóico, EPA**

C 22:6 **ácido docosahexaenóico, DHA**

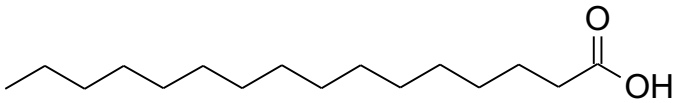
Poliinsaturados



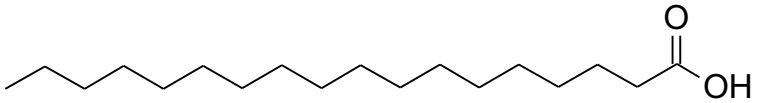
C 12:0 ácido laurico



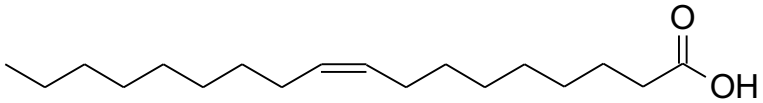
C 14:0 ácido mirístico



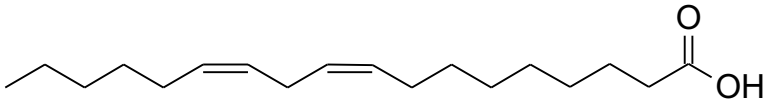
C 16:0 ácido palmítico



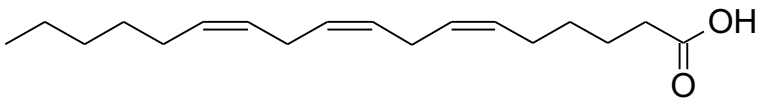
C 18:0 ácido esteárico



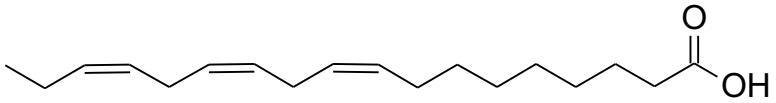
C 18:1 ácido oleico ω-9



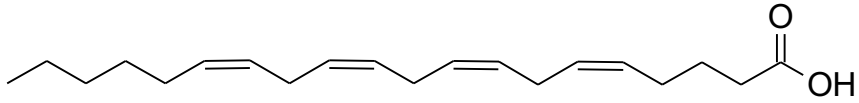
C 18:2 ácido linoleico ω-6



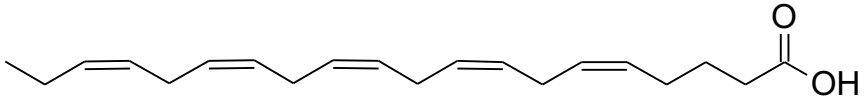
C 18:3 ácido γ-linolenico ω-6



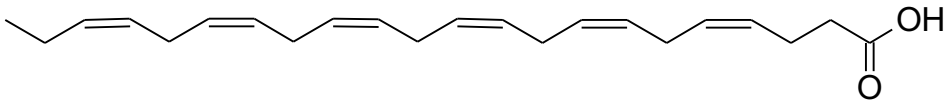
C 18:3 ácido α-linolenico ω-3



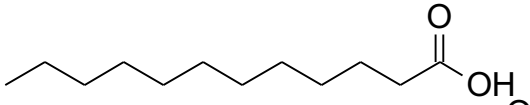
C 20:4 ácido araquidonico ω-6



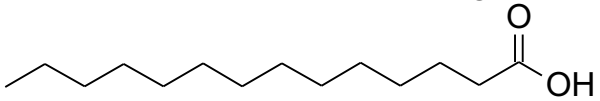
C 20:5 ácido eicosapentaenóico, EPA ω-3



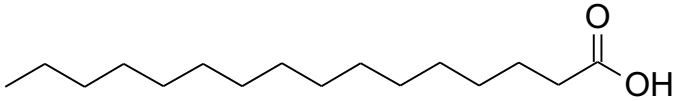
C 22:6 ácido docosahexaenóico, DHA ω-3



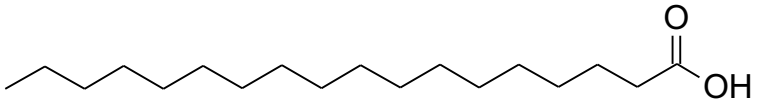
C 12:0 **ácido laurico**



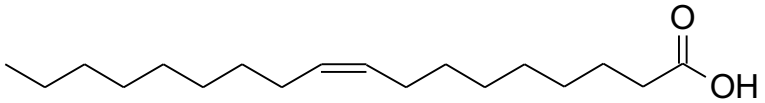
C 14:0 **ácido mirístico**



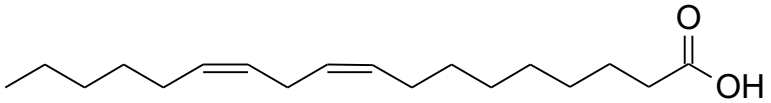
C 16:0 **ácido palmítico**



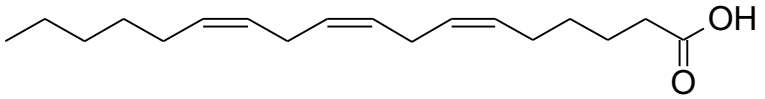
C 18:0 **ácido esteárico**



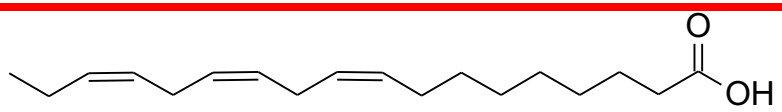
C 18:1 **ácido oleico**



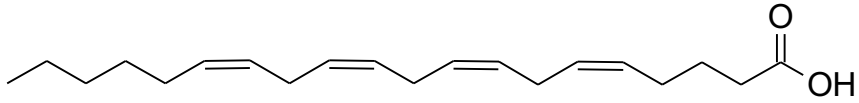
C 18:2 **ácido linoleico**



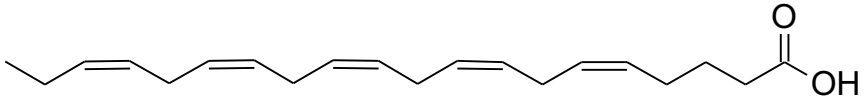
C 18:3 **ácido γ-linolenico**



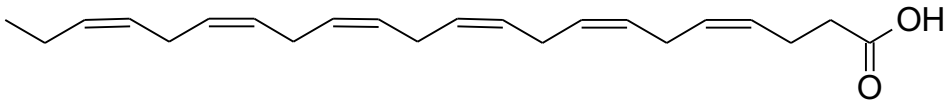
C 18:3 **ácido α-linolenico**



C 20:4 **ácido araquidonico**



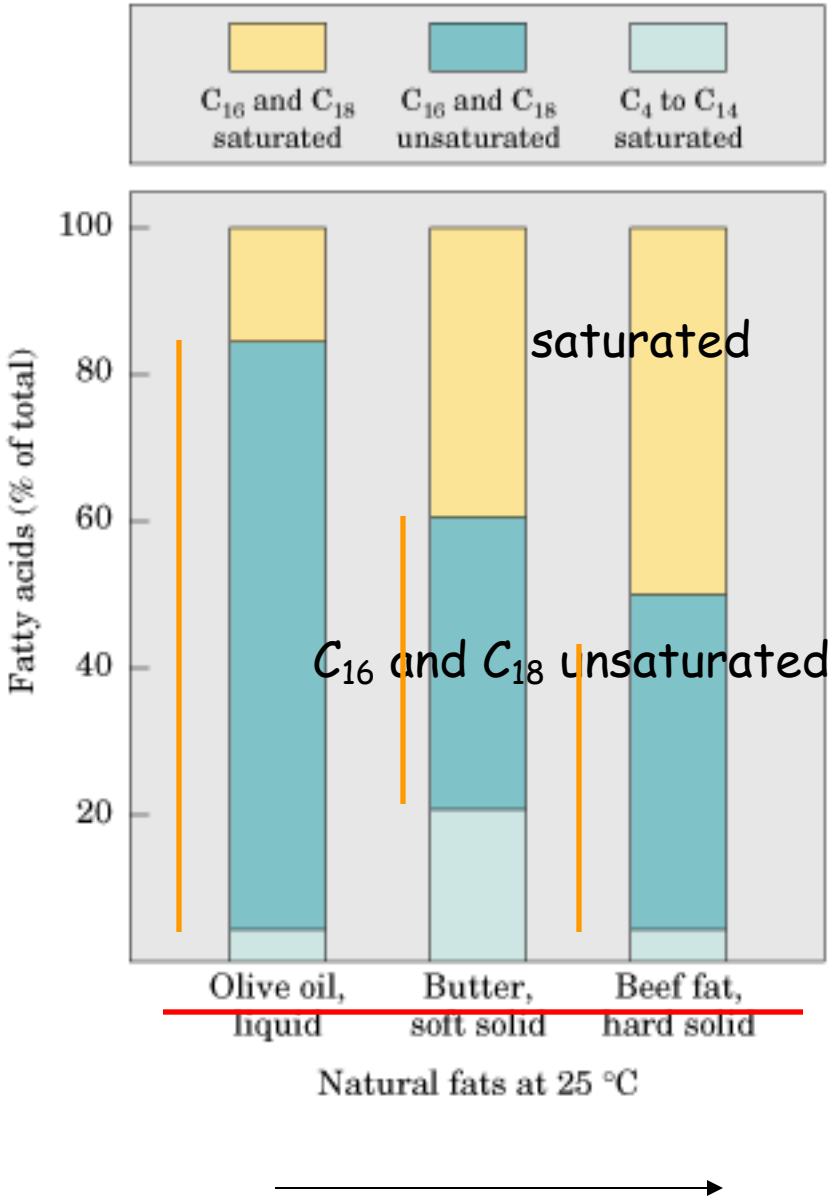
C 20:5 **ácido eicosapentaenóico, EPA**



C 22:6 **ácido docosahexaenóico, DHA**

Ac Graxos Essenciais!!

Fatty acid composition of three food fats



Ácidos Graxos

Triacilgliceróis

Fosfolipídios

Esteróis
(Colesterol/
Esteres de Colesterol)

"TG são excelentes reservas de energia"
-São menos oxidadas do que Carboidratos e Proteínas
-São estocadas de forma "anidra"

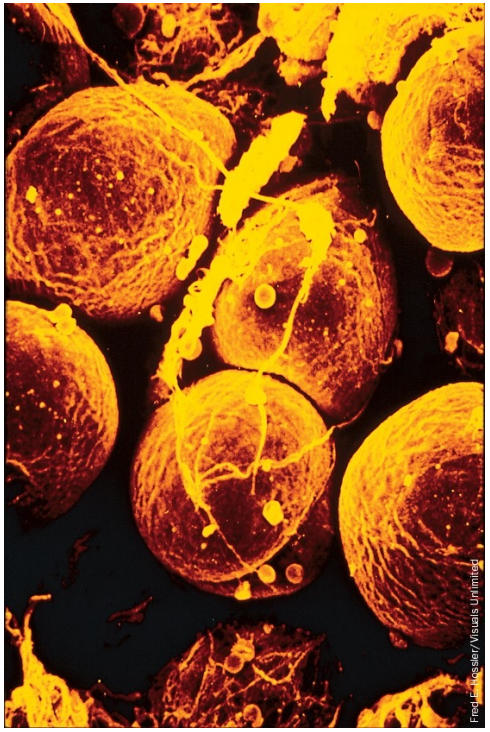


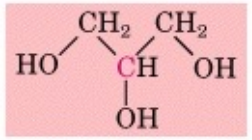
Figura 12-2 (Voet)
Micrografia eletrônica de varredura de adipócitos. Cada célula possui um glóbulo de gordura que ocupa todo o interior da célula.

Ácidos Graxos

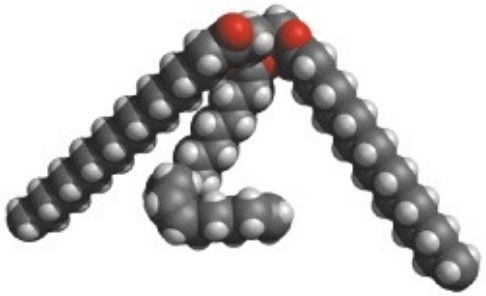
Triacilgliceróis

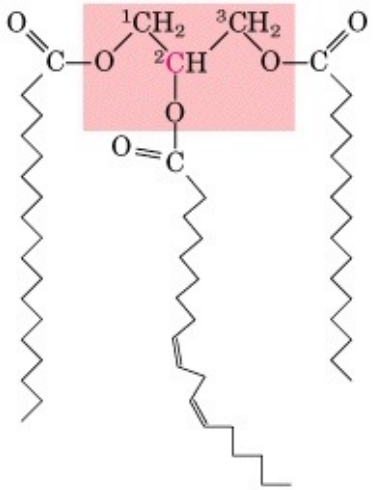
Fosfolipídios

Esteróis
(Colesterol/
Esteres de Colesterol)



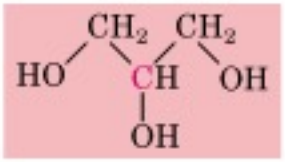
Glycerol





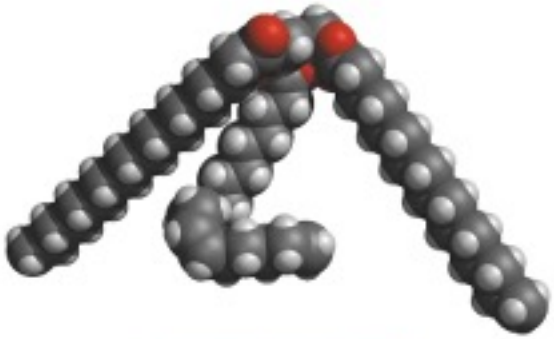
1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol,
a mixed triacylglycerol

Lipídios de armazenamento (neutros)



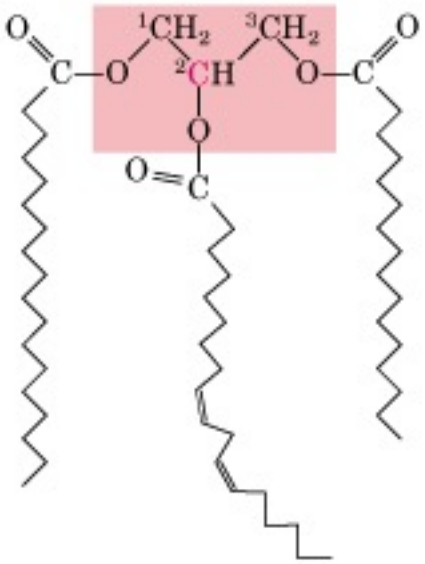
Glycerol

Glicerol



Triacilgliceróis

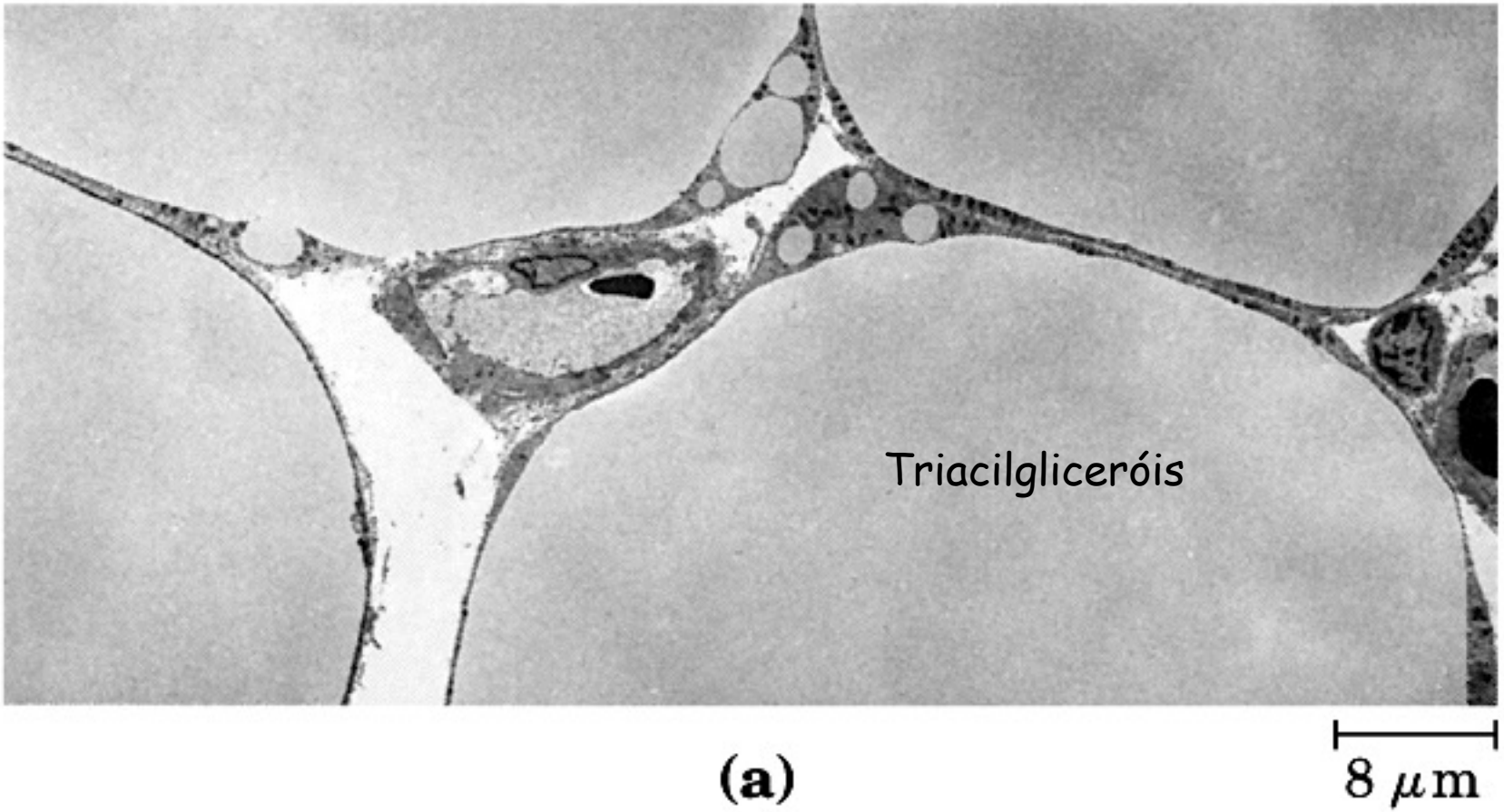
Glicerol esterificado



1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol, a mixed triacylglycerol

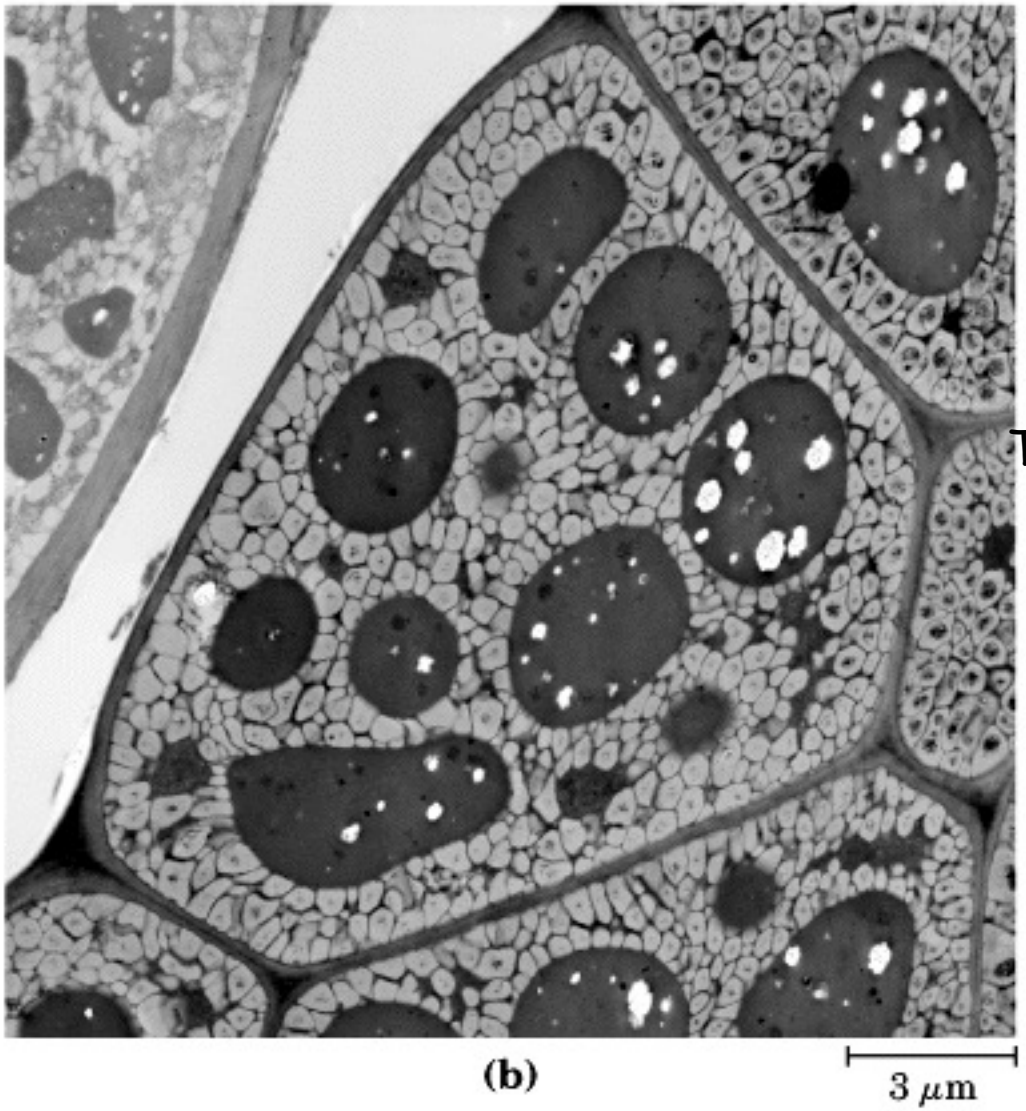
Ácido graxo

Guinea pig adipocyted
Huge fat droplet



(a)

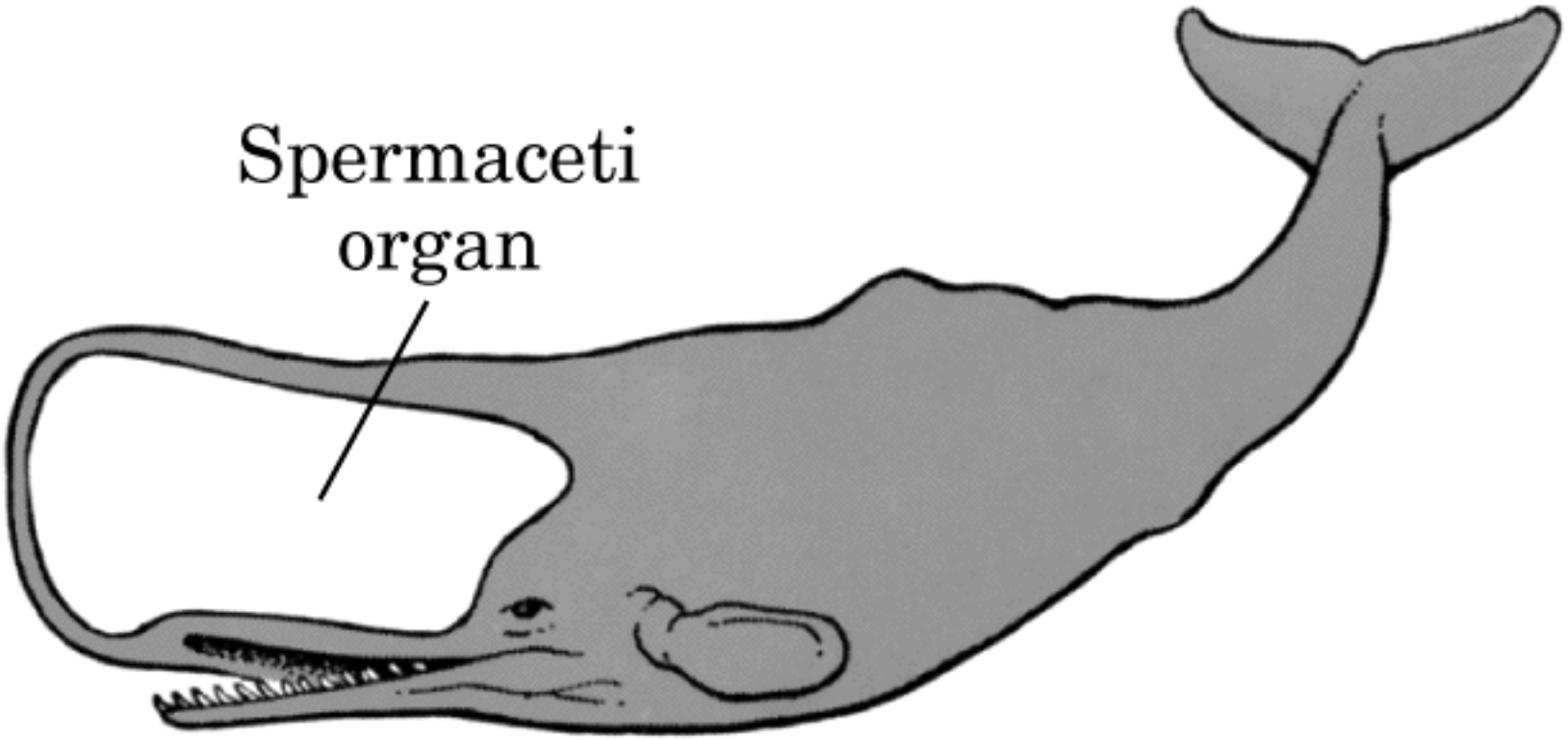
Cotyledon cell from a seed of the plant *Arabidopsis*



Triacilgliceróis

18.000,00 kg, unsaturated fatty acids
37°C, liquid
31°C begins to crystallize

Triacilgliceróis



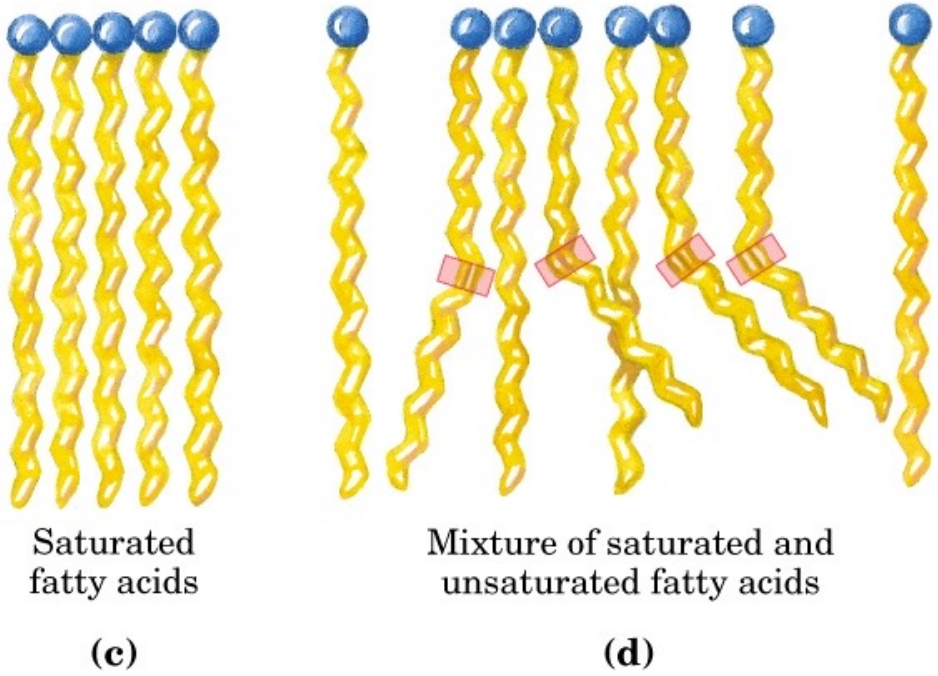
Biochemical adaptation

Óleos e gorduras

O estado líquido ou sólido está relacionado ao ponto de fusão a temperatura ambiente

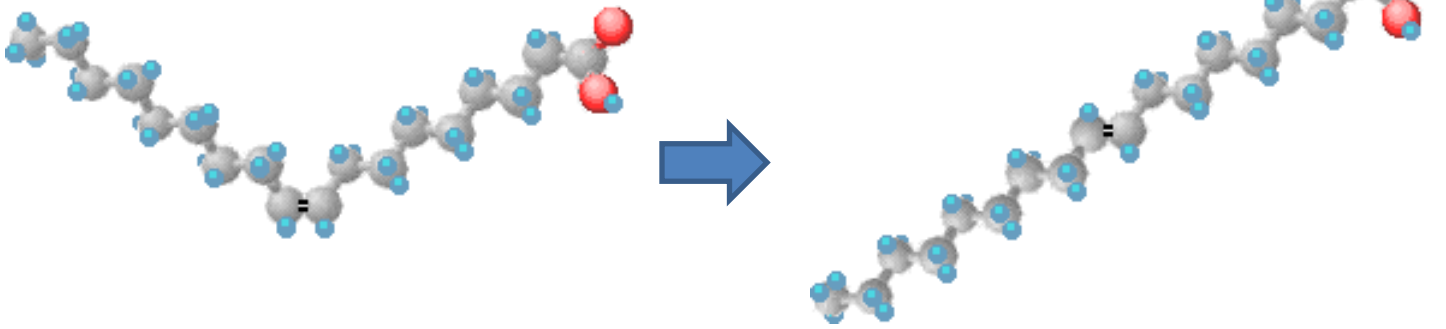
Ácido Graxo	Ponto de Fusão
C4:0	-7.9
C6:0	-1.0
C8:0	16:0
C12:0	48
C14:0	58
C16:0	64
C16:1	0.5
C18:0	69.6
C18:1(cis) (oleic)	14
C18:1(trans) (elaidic)	43.7
C18:2	-5.0
C18:3	-11.0

Saturado x Insaturado



Ácido Graxo	Ponto de Fusão
C4:0	-7.9
C6:0	-1.0
C8:0	16:0
C12:0	48
C14:0	58
C16:0	64
C16:1	0.5
C18:0	69.6
C18:1(cis) (oleic)	14
C18:1(trans) (elaidic)	43.7
C18:2	-5.0
C18:3	-11.0

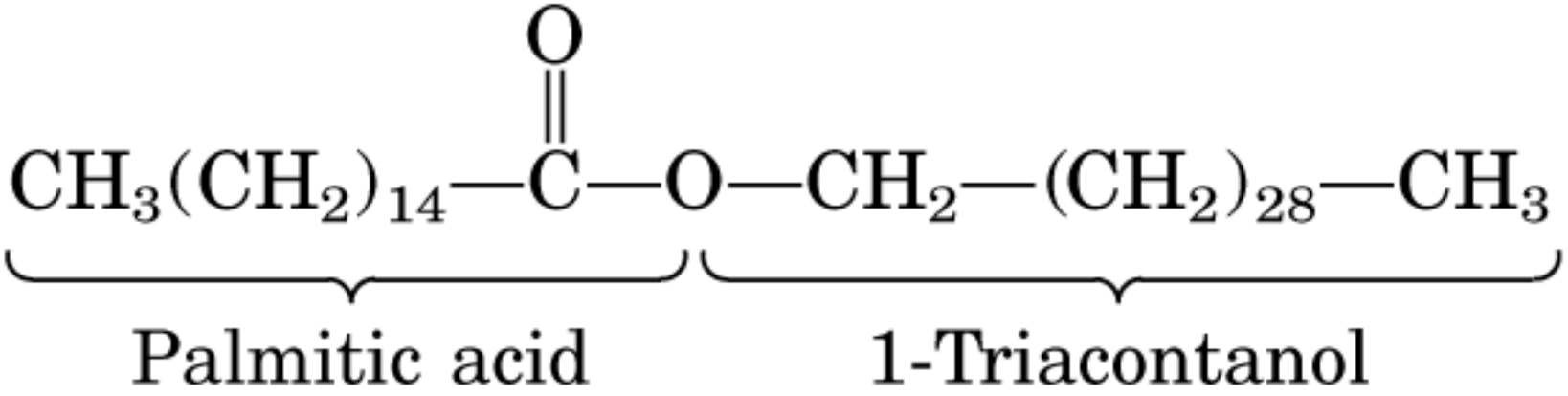
Ácidos Graxos Trans adquire características similares à sua forma saturada....



Cis-9-octadecenoic acid
(Oleic acid)

Trans-9-octadecenoic acid
(Elaidic acid)

Biological wax



Alguns ácidos graxos de ocorrência natural

table 11–1

Some Naturally Occurring Fatty Acids

Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent) Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")	86.0		
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	−0.5		
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")	13.4		
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")	−5		
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	−11		
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	−49.5		

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

†The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

Iterações hidrofóbicas
Arranjos quase cristalinos

R - C = C - R

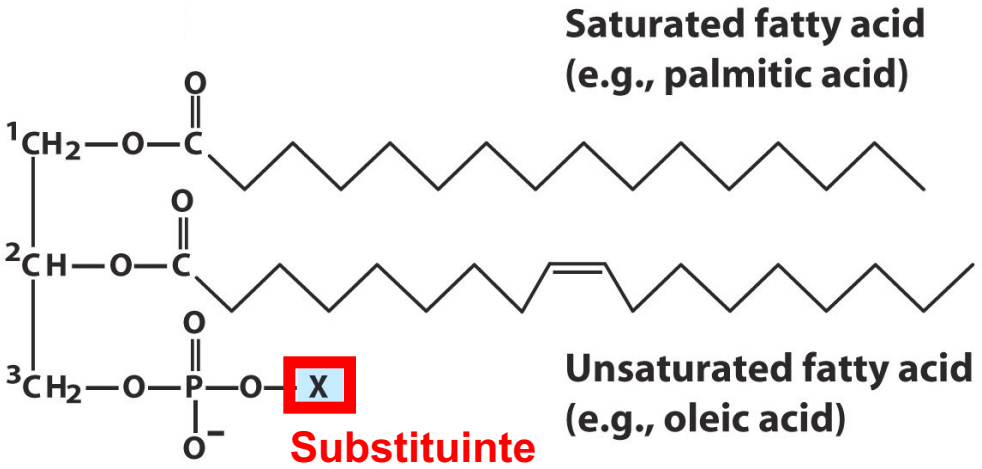
Ácidos Graxos

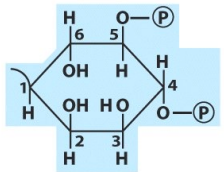
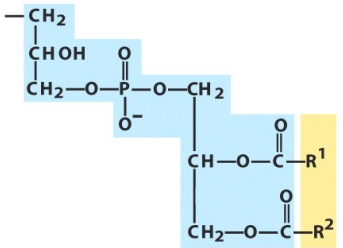
Triacilgliceróis

Fosfolipídeos

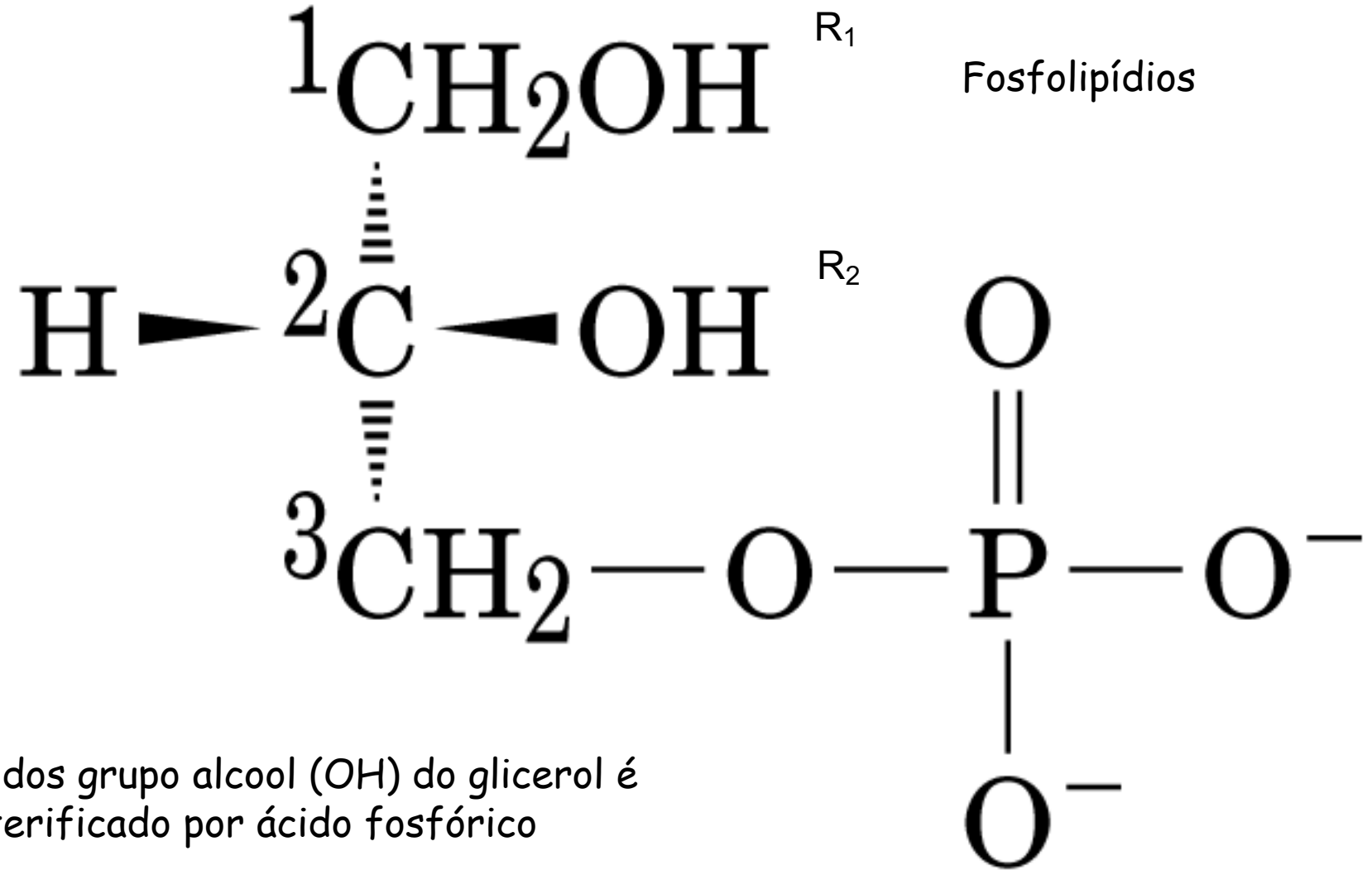
Glicerofosfolipídeos

Esteróis
(Colesterol/
Esteres de Colesterol)



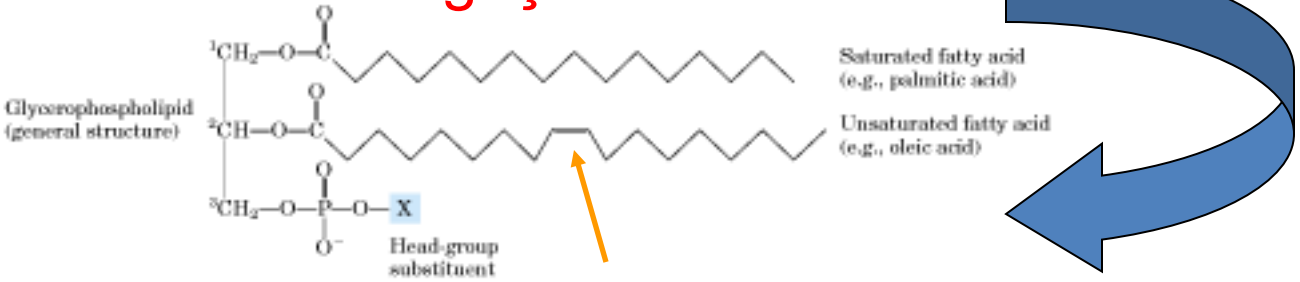
Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-\underset{COO^-}{CH}-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	$-CH_2-\underset{OH}{CH}-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2

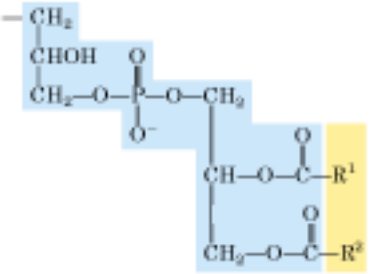
L-Glycerol 3-phosphate, the backbone of phospholipids



Un dos grupo alcool (OH) do glicerol é
Esterificado por ácido fosfórico

Os glicerofosfolipídios são diacilgliceróis unidos a grupos cabeças alcoólicos através de ligação fosfodiéster



Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-\underset{COO^-}{CH}-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	$-CH_2-\underset{OH}{CH}-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2

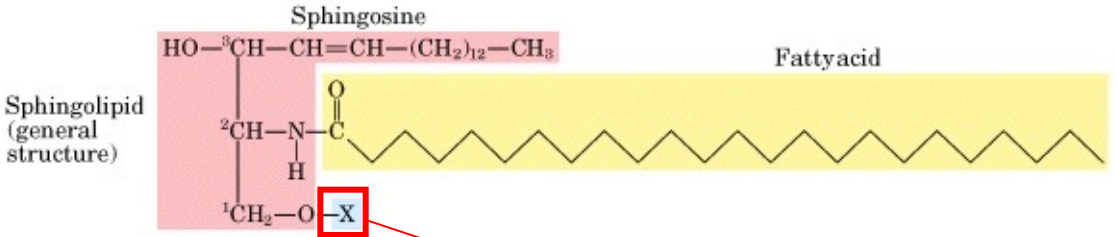
Ácidos Graxos

Triacilgliceróis

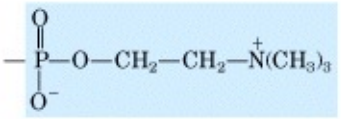
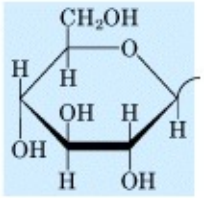
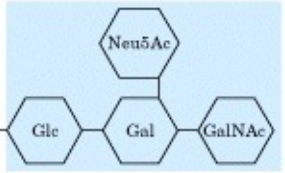
Fosfolipídeos

Esfingolipídeos

Esteróis
(Colesterol/
Esteres de Colesterol)



Glicolipídeos

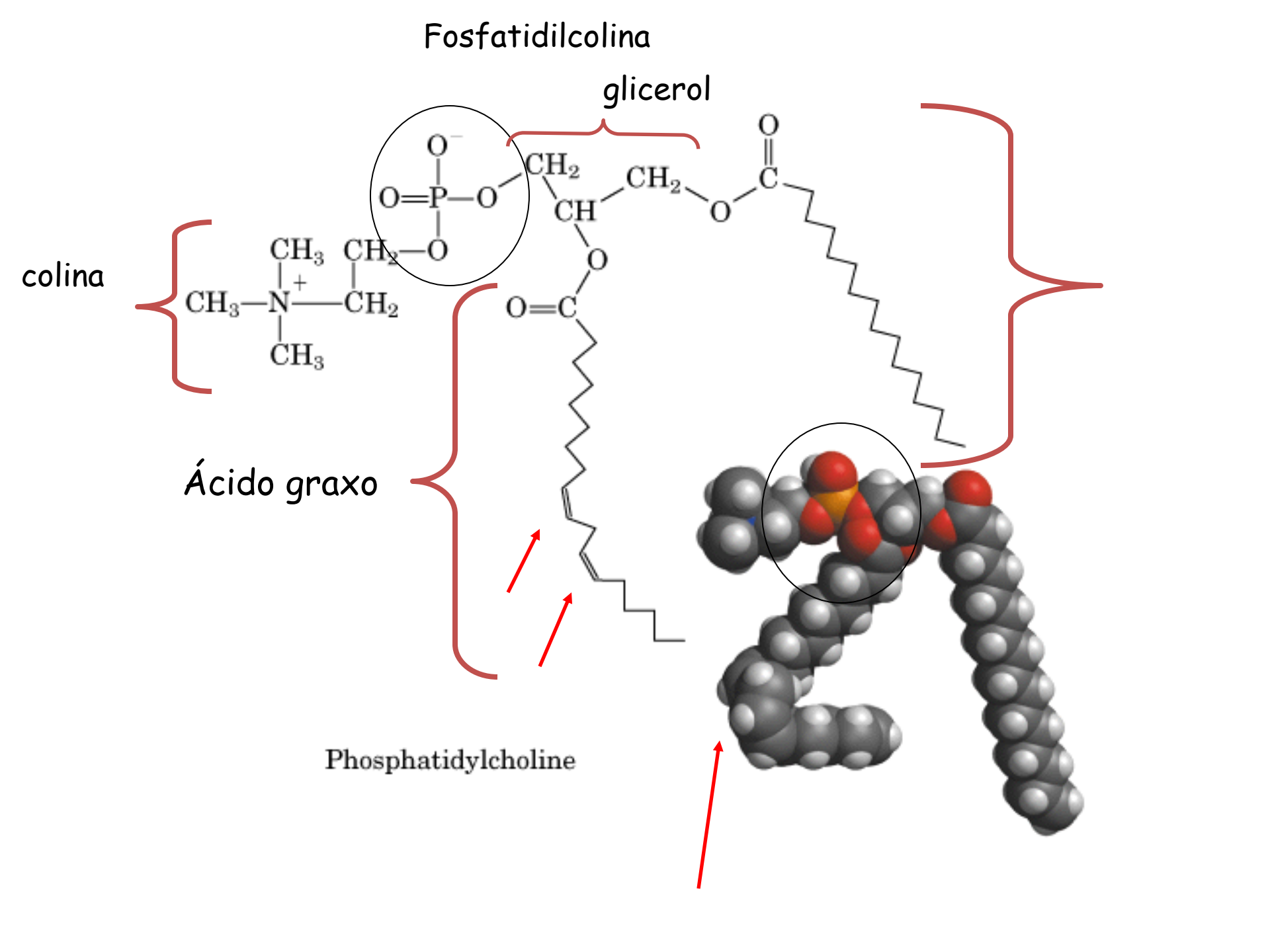
Name of sphingolipid	Name of X	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside Cerebrosídeos	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2 Gangliosídeos	Complex oligosaccharide	

Fosfatidilcolina

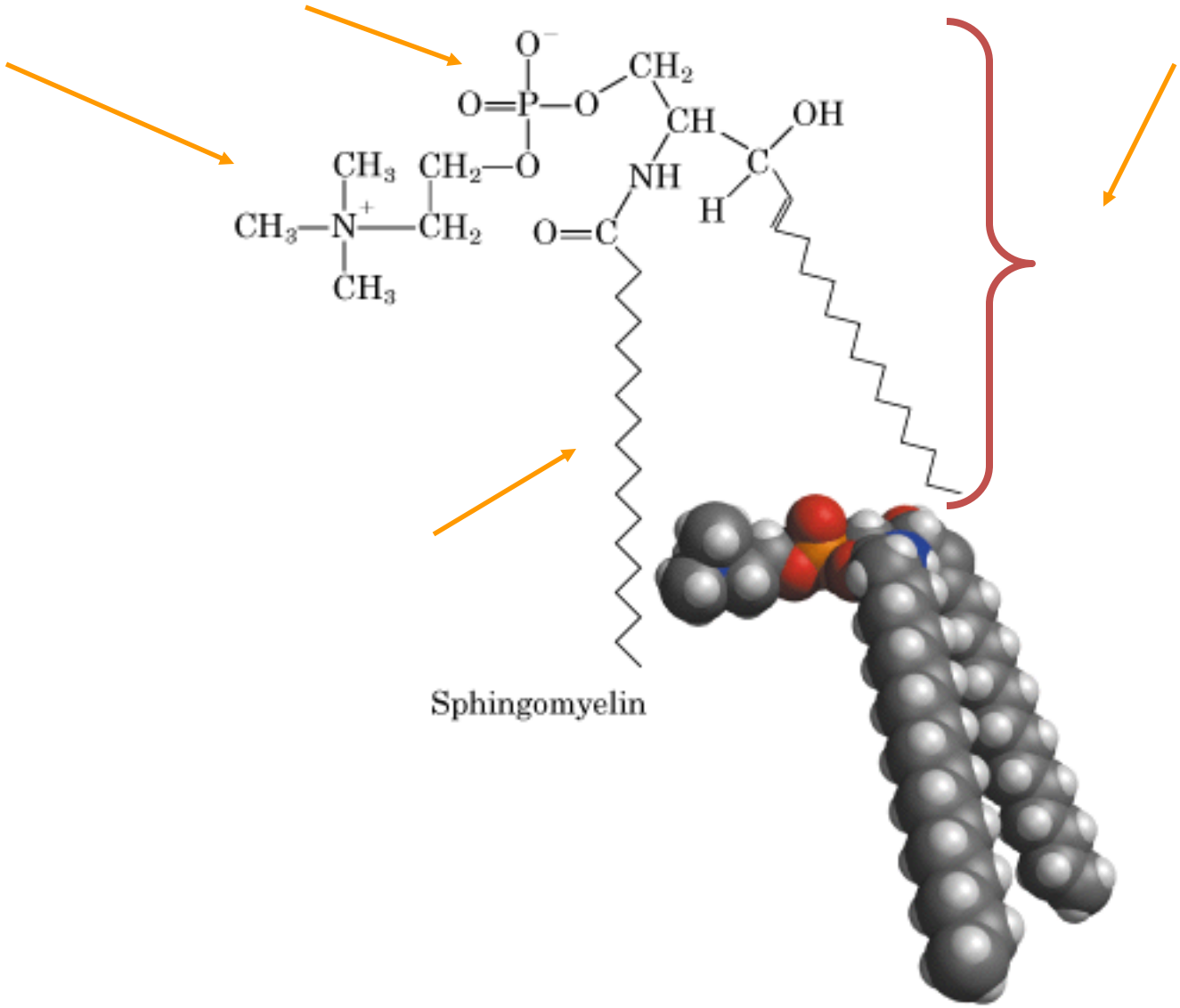
glicerol

colina

Ácido graxo



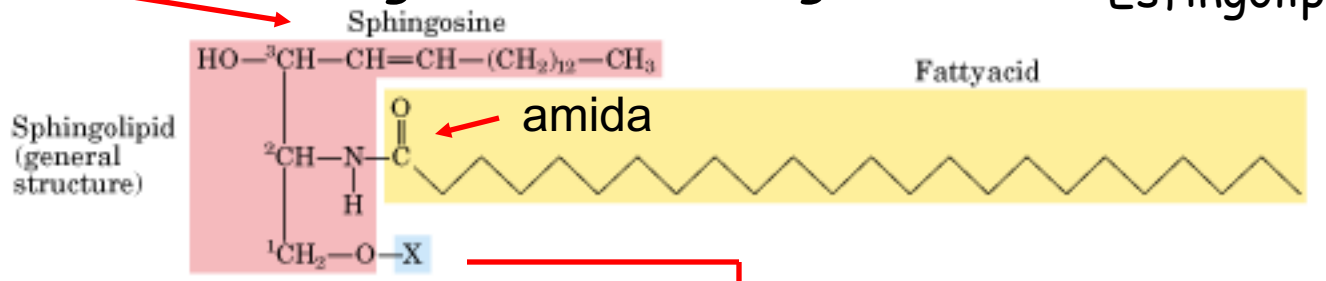
Phosphatidylcholine



Sphingomyelin

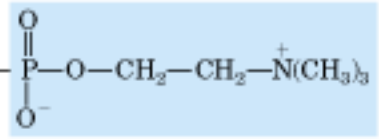
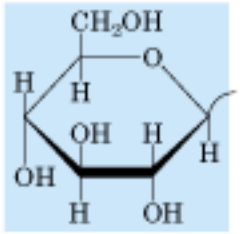
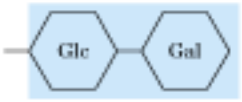
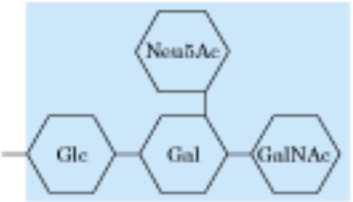
Esfingosina + Ácido graxo

Esfingolipídios



Não contem Glicerol em sua molécula

! Membranas de Celulas nervosas

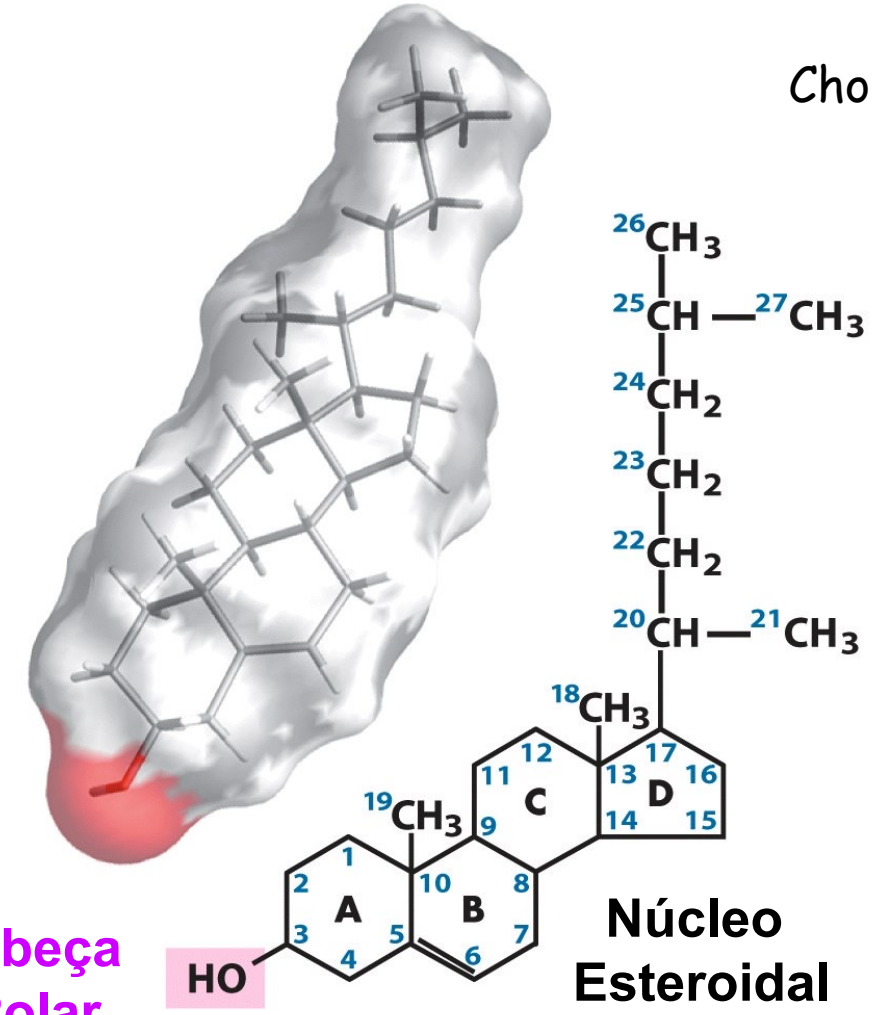
Name of sphingolipid	Name of X	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

Ácidos Graxos

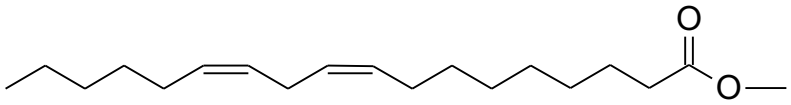
Triacilgliceróis

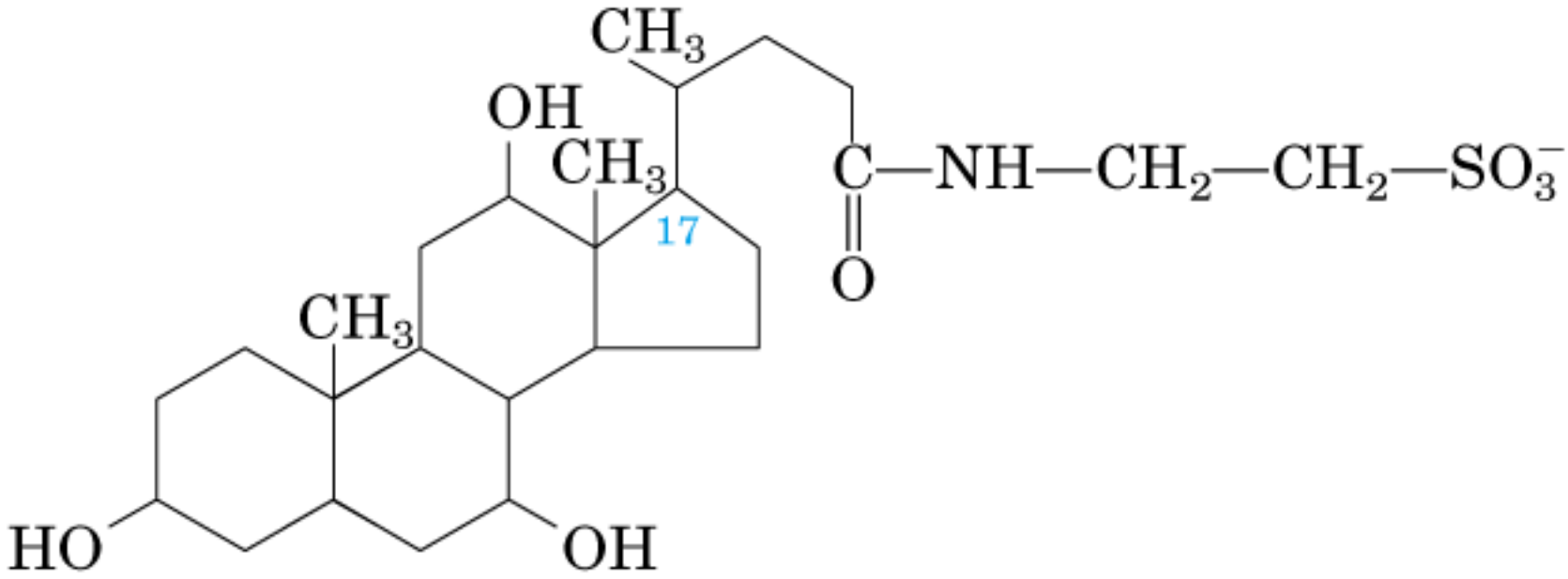
Fosfolipídios

Cholesterol



Esteróis (Colesterol/ Esteres de Colesterol)

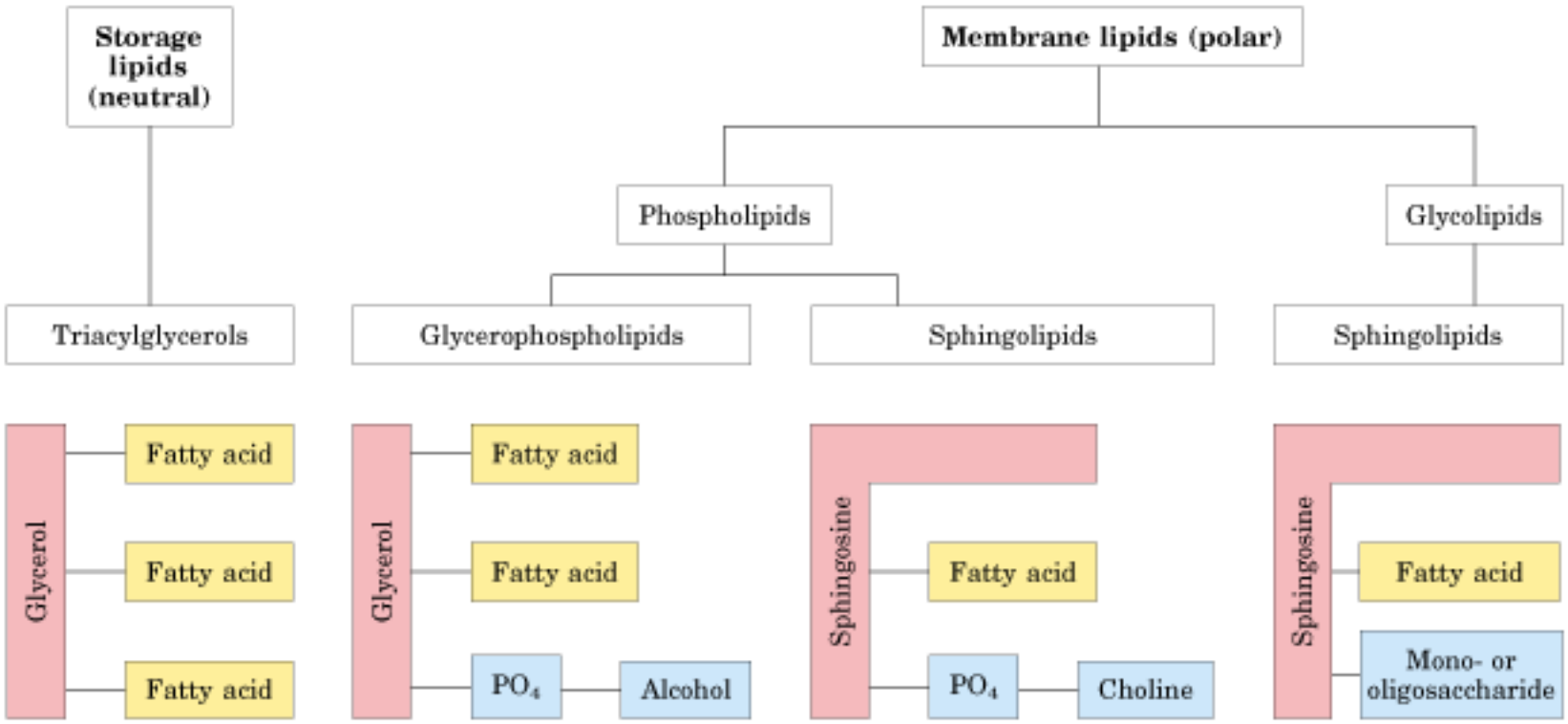




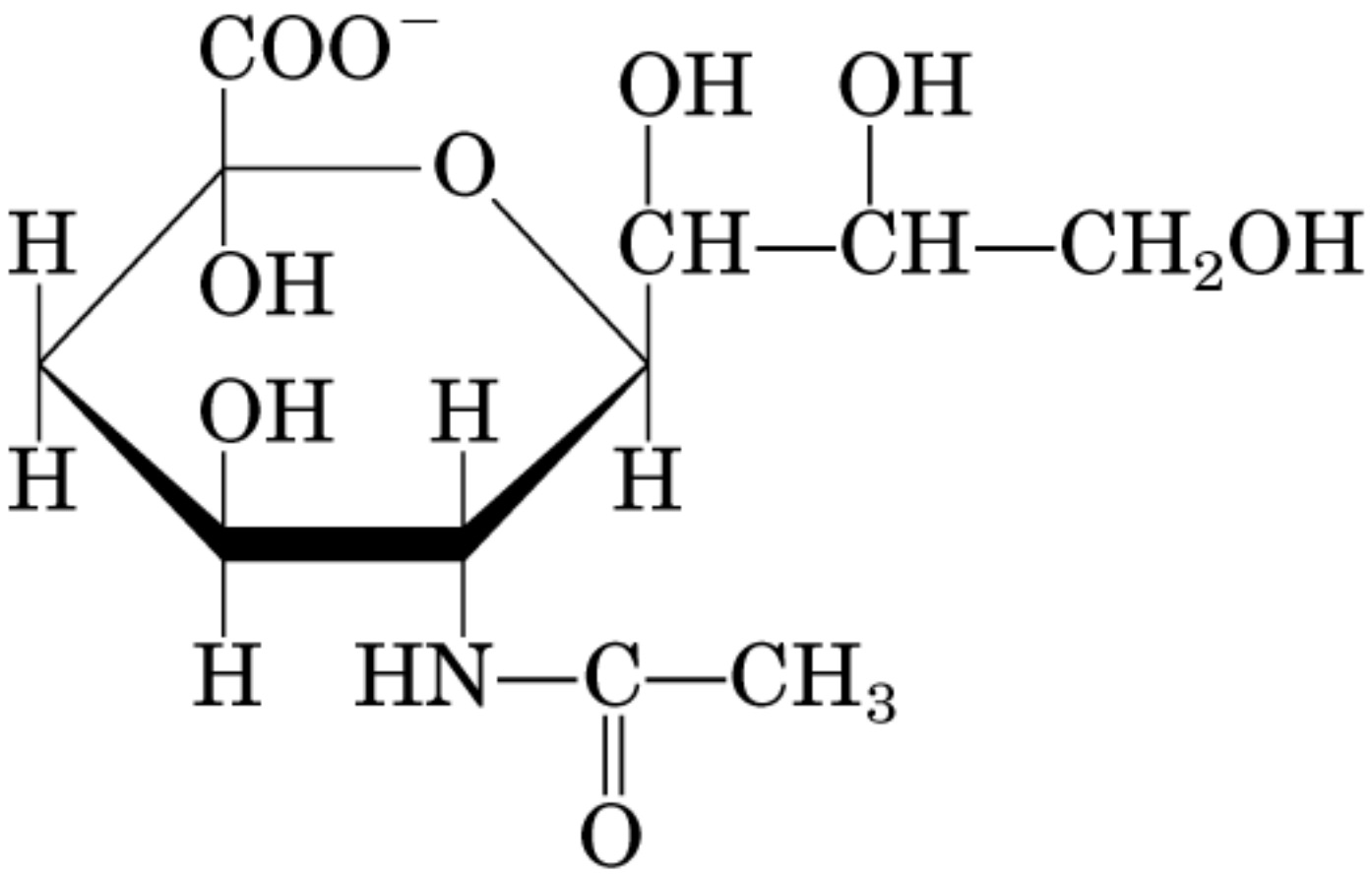
Taurocholic acid
(a bile acid)

Act as detergents in the intestine, emulsifying dietary fats

As classes principais de lipídios de armazenamento e de membrana



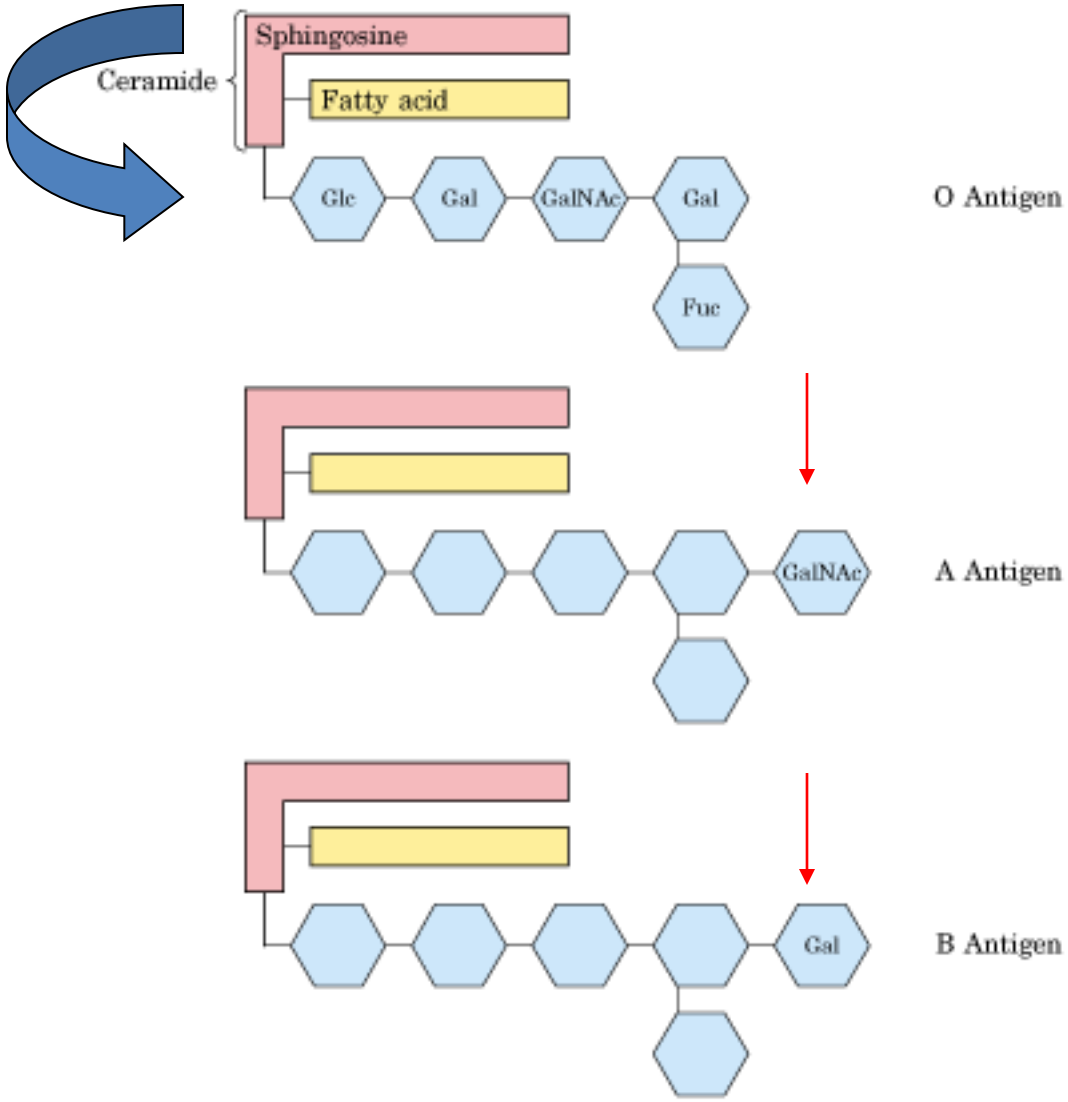
Gangliosides = complex sphingolipids



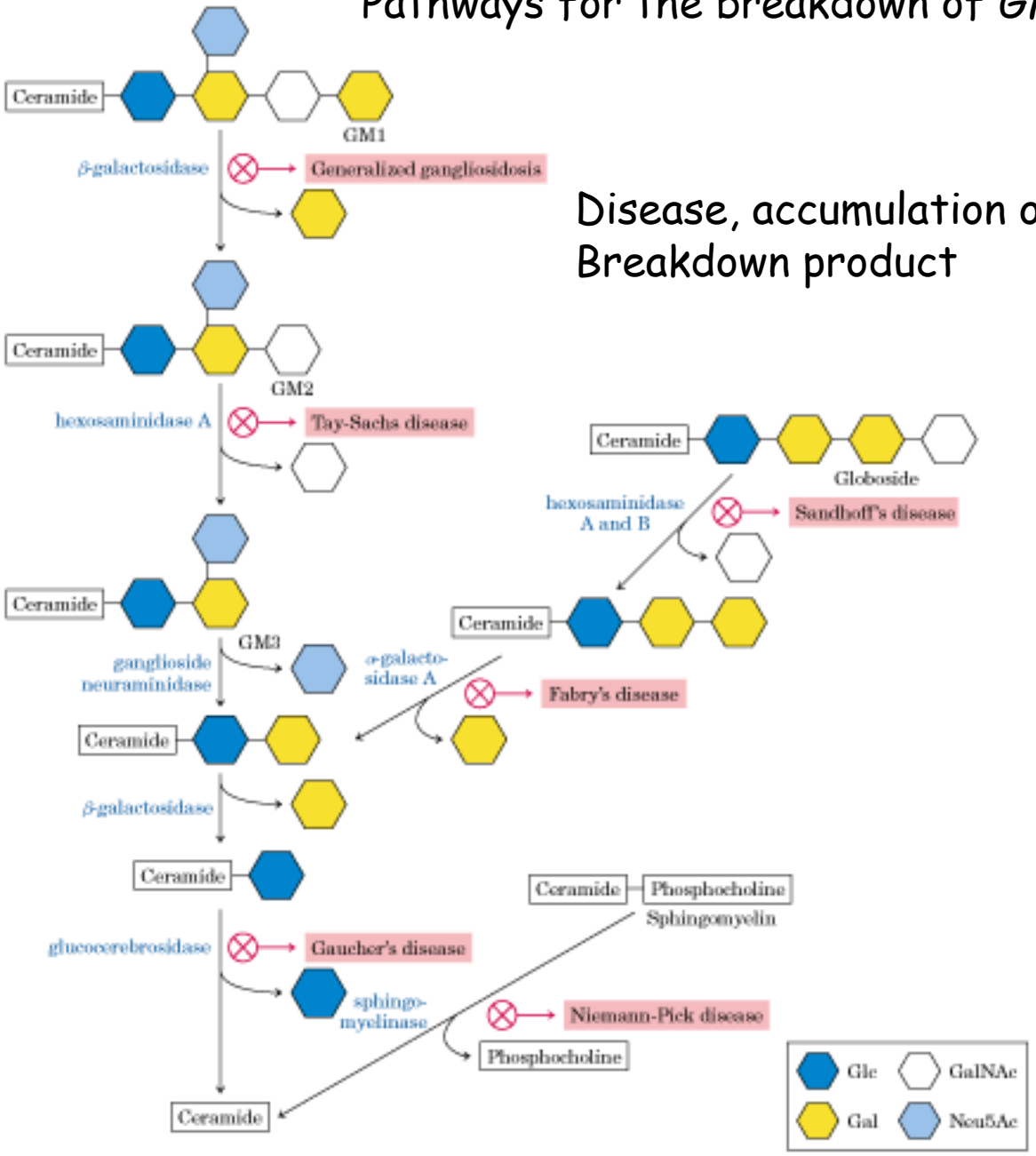
N-Acetylneuraminic acid (sialic acid)
(Neu5Ac)

Glicoesfingoplipídios

Os grupos sangüineos humanos O, A, B são, em parte, determinados
Pela composição em açúcares dos grupos cabeça polares destes Glicoesfingoplipídios

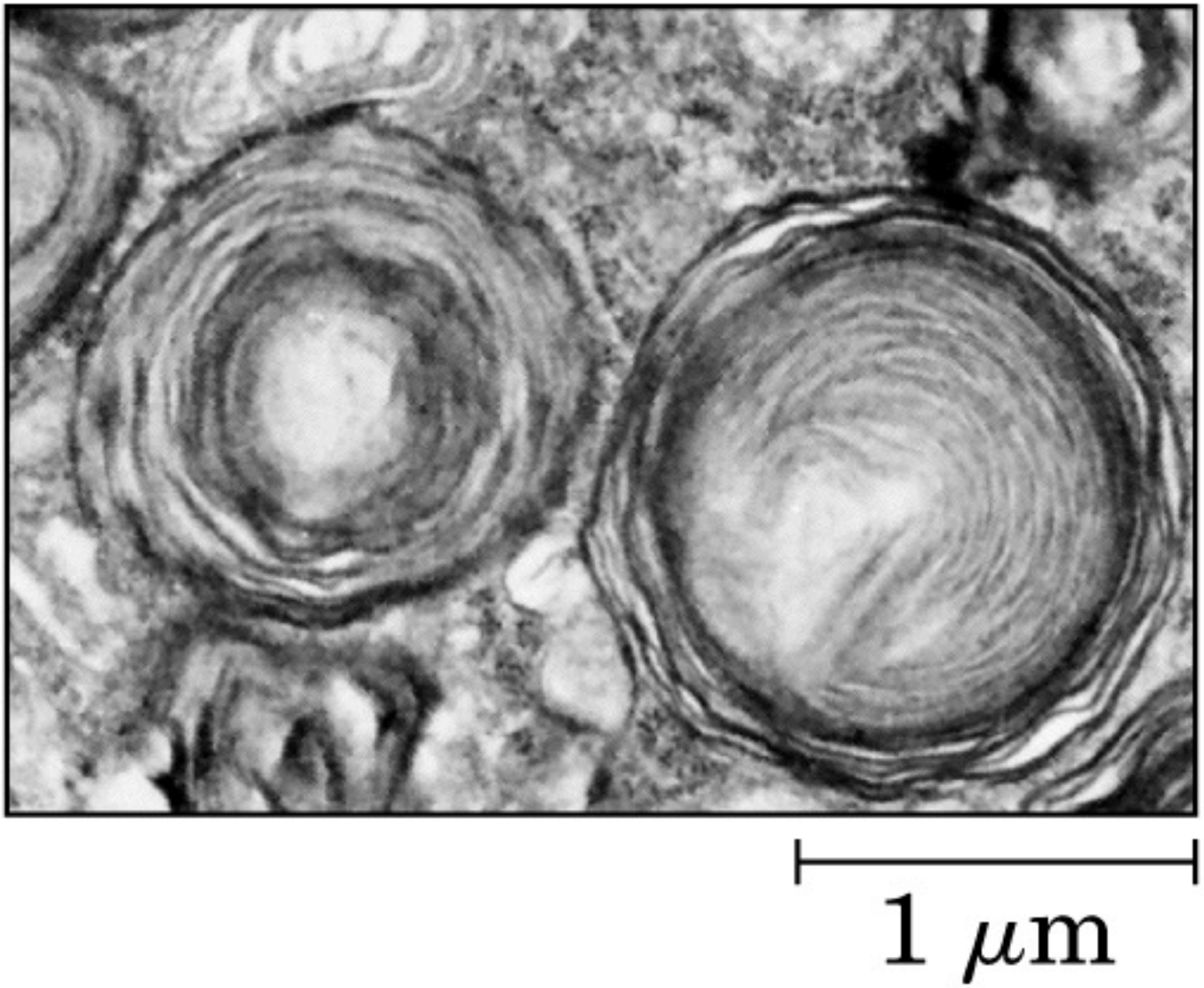


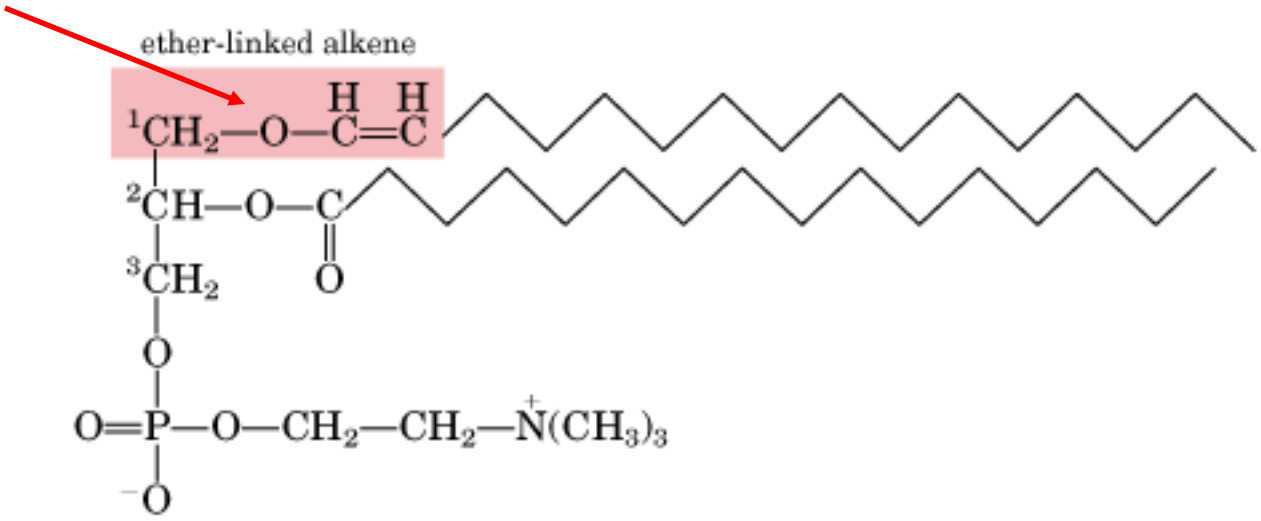
Pathways for the breakdown of GM1



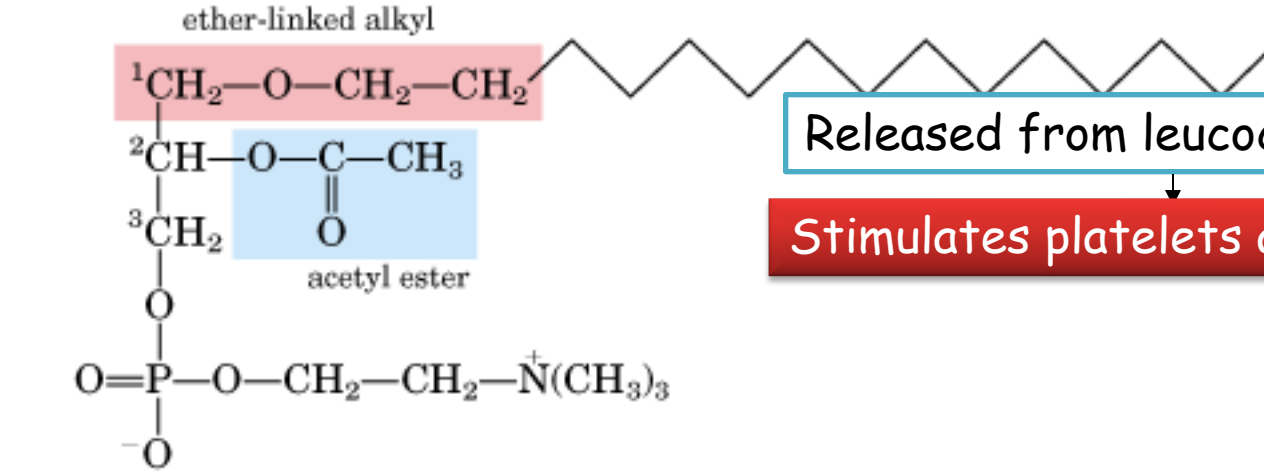
Disease, accumulation of the partial Breakdown product

Electron micrograph of a portion of a brain cell from an infant with Tay-Sachs disease, showing abnormal ganglioside deposits in the lysosomes





Plasmalogen

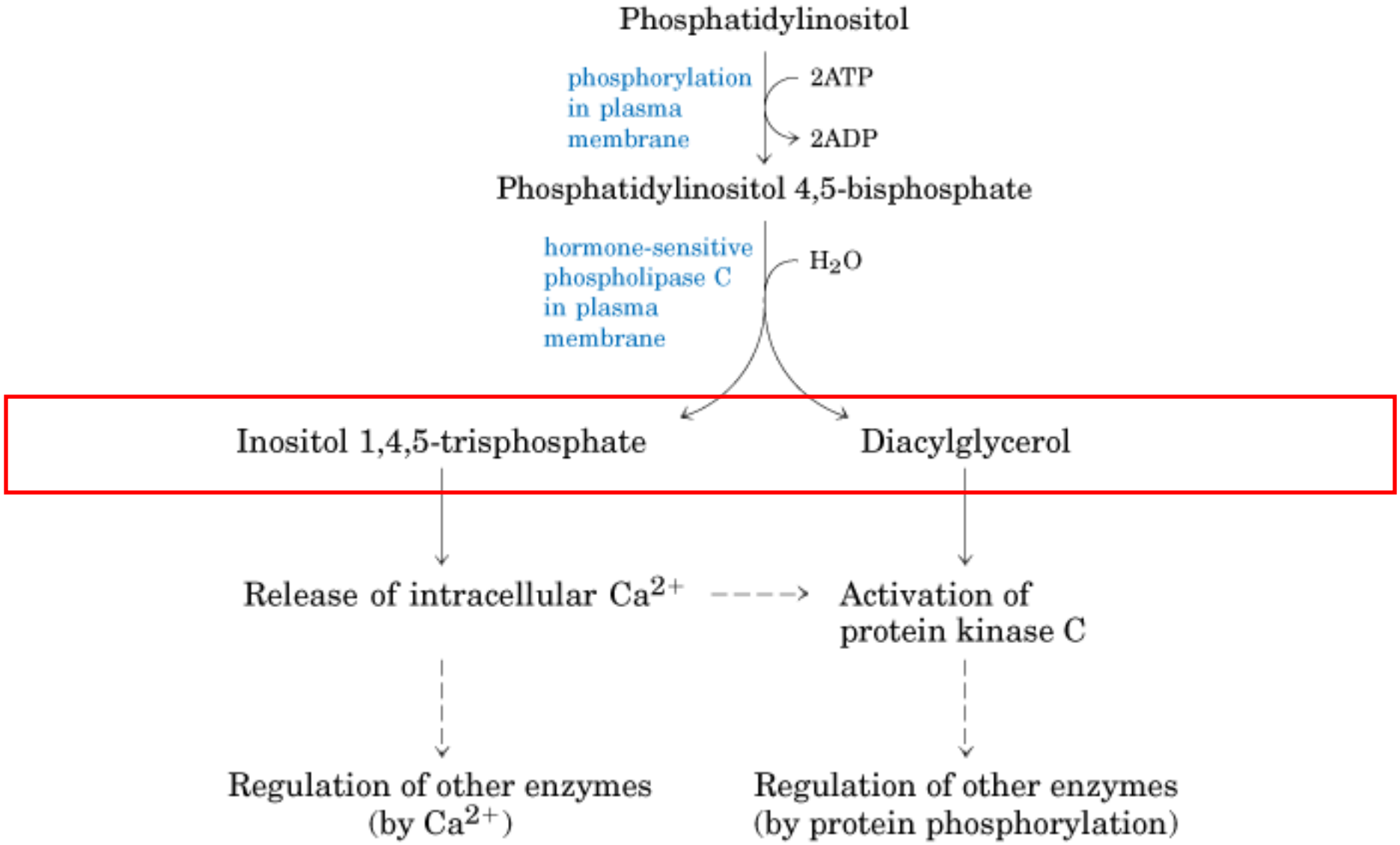


Released from leucocytes (basophils)

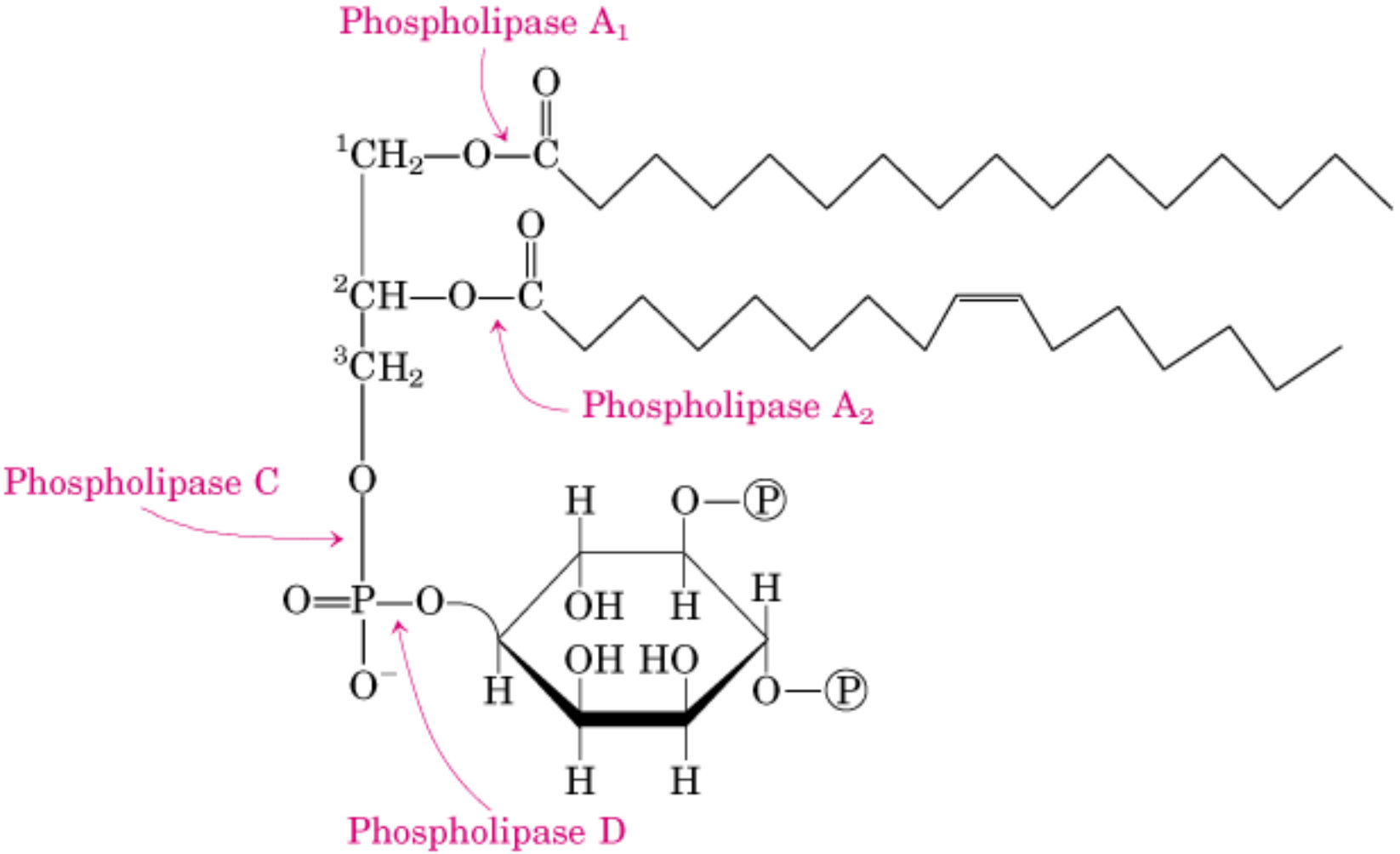
Stimulates platelets aggregation

Platelet-activating factor

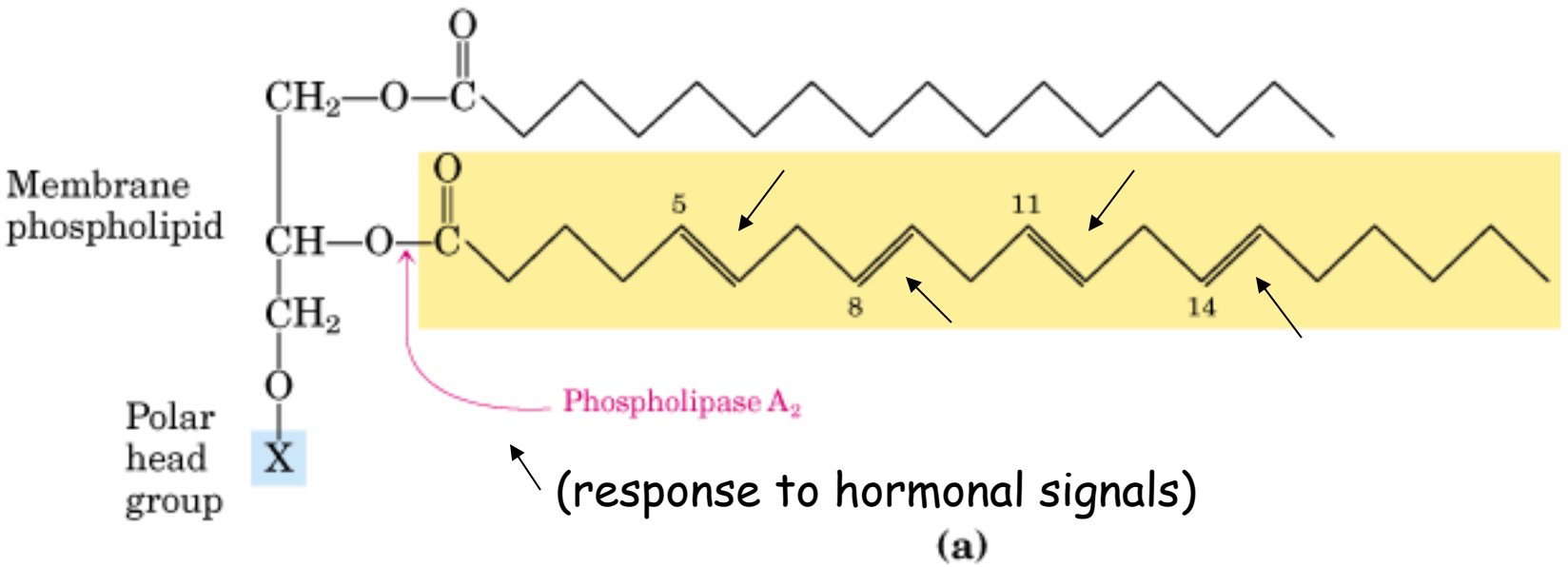
Phosphatidylinositols act as intracellular signals



As especificidades das fosfolipases

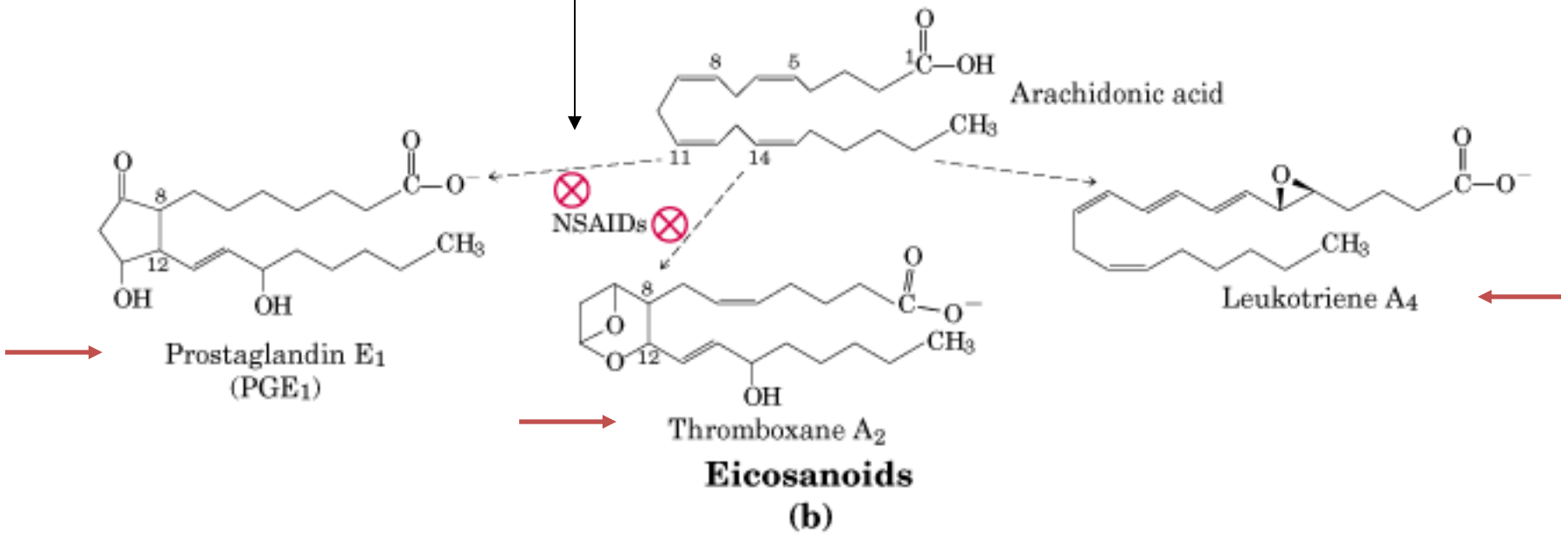


Arachidonic acid an some eicosanoid derivatives



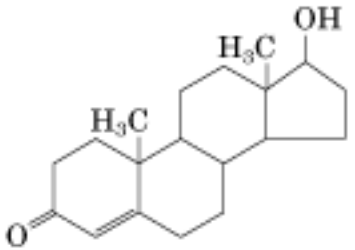
Aspirin, acetaminophen, ...

Inhibiting the enzyme cyclooxygenase

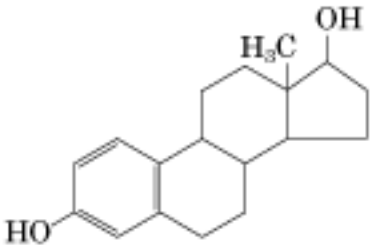


Steroid Hormones carry messages between tissues

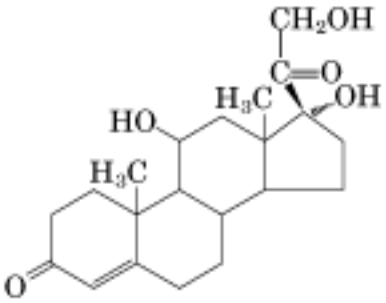
Steroids derived from cholesterol



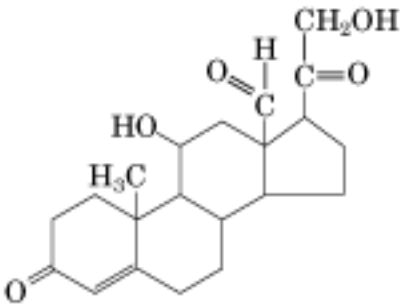
Testosterone



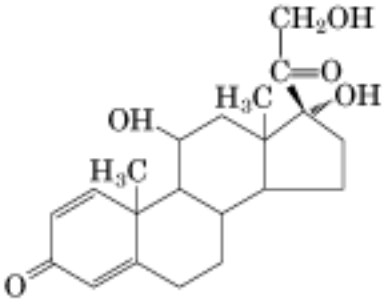
Estradiol



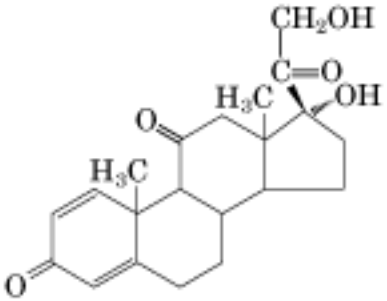
Cortisol



Aldosterone

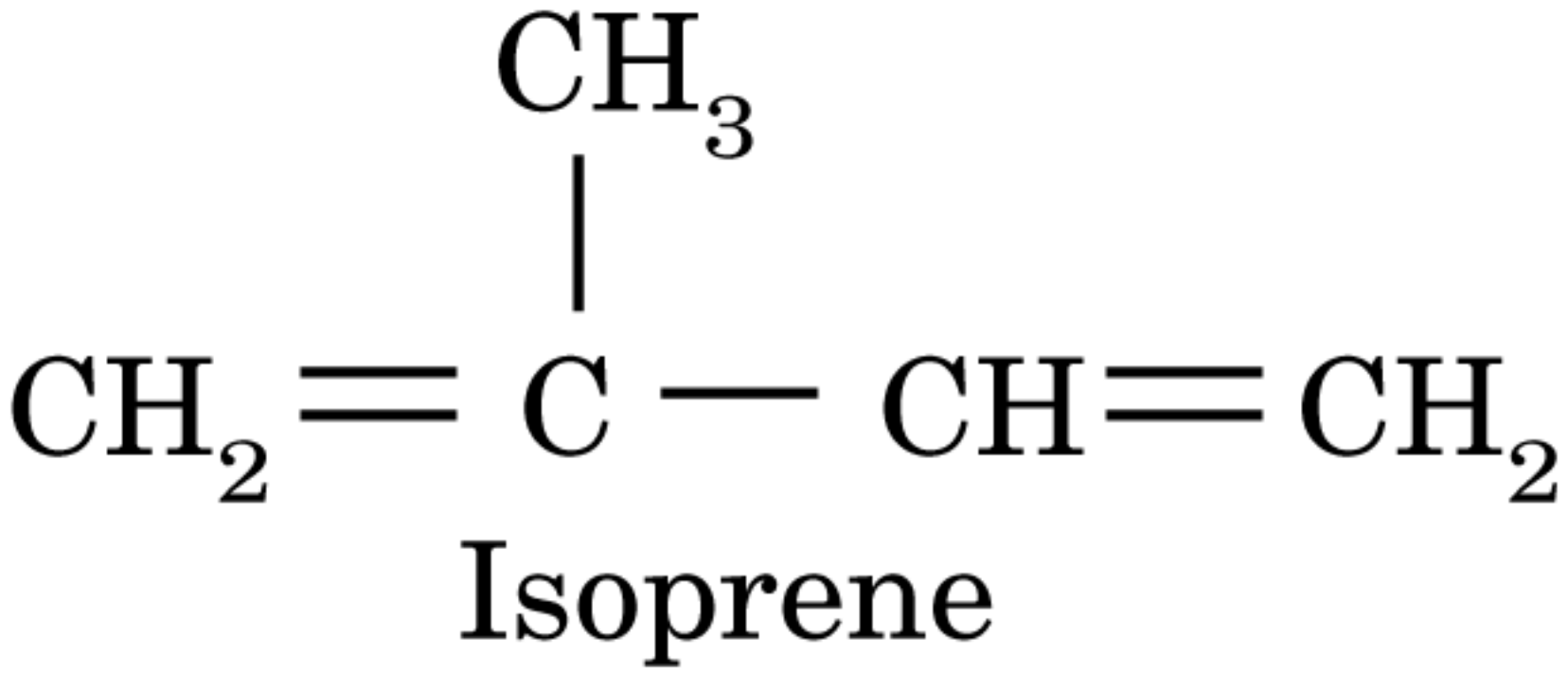


Prednisolone



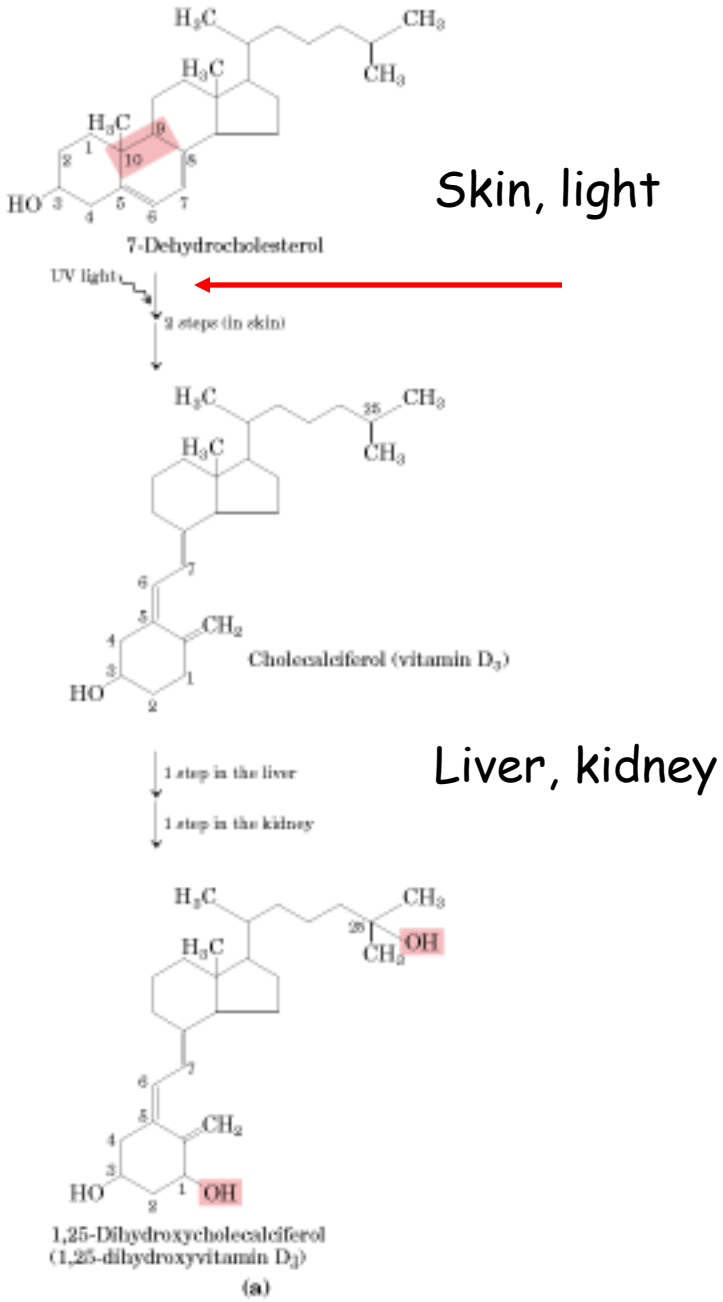
Prednisone

Vitamins D and A are hormone precursors



Isoprene

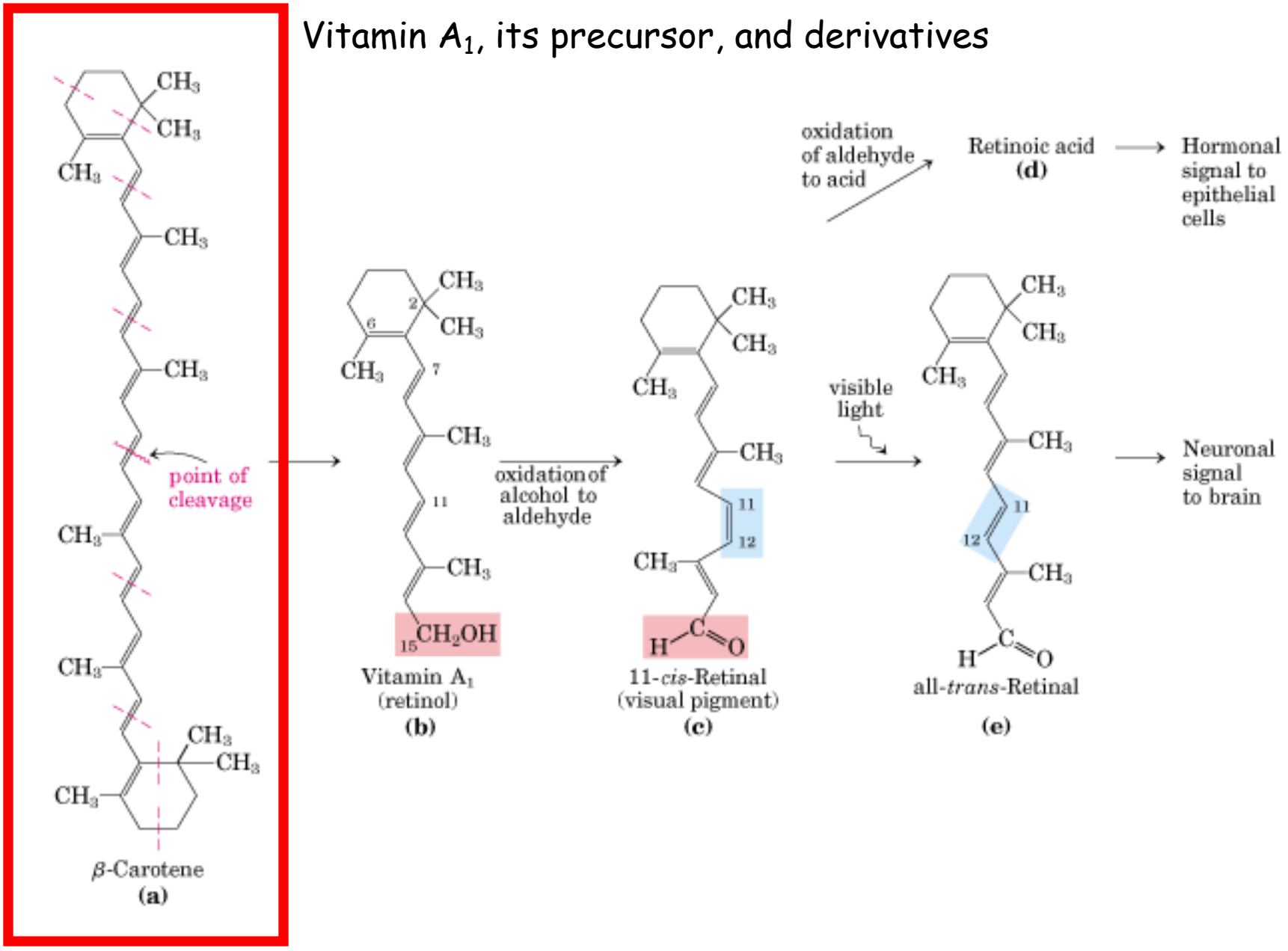
Vitamin D_3 production and metabolism

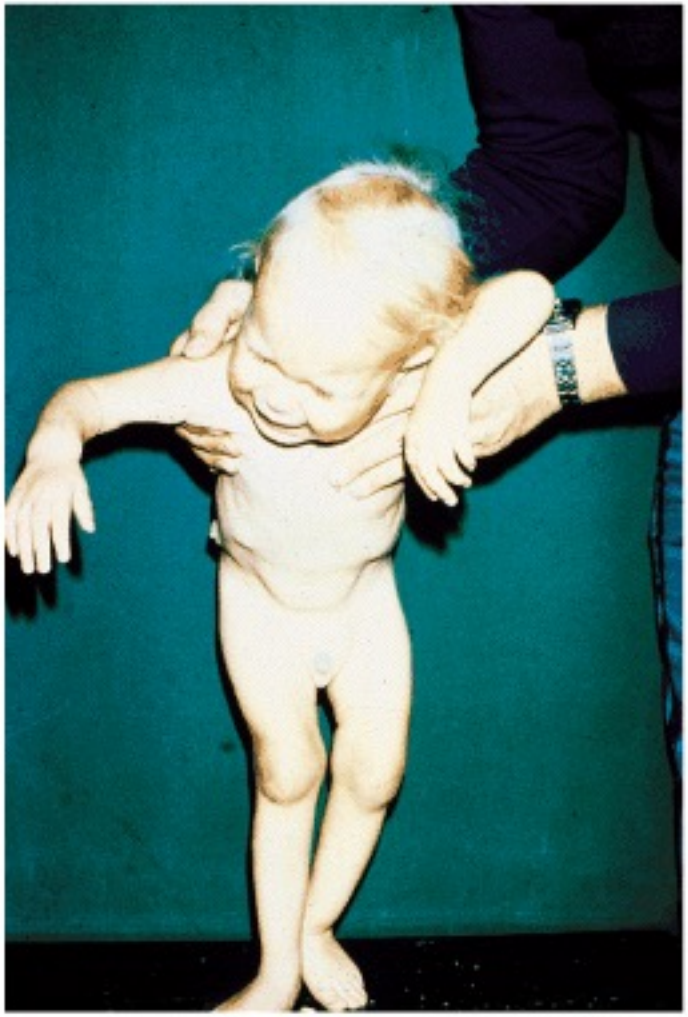


Skin, light

Liver, kidney

Vitamin A_1, its precursor, and derivatives





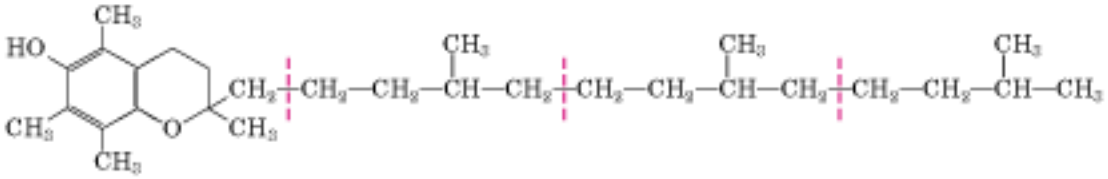
Before vitamin D treatment

After 14 months of vitamin D treatment

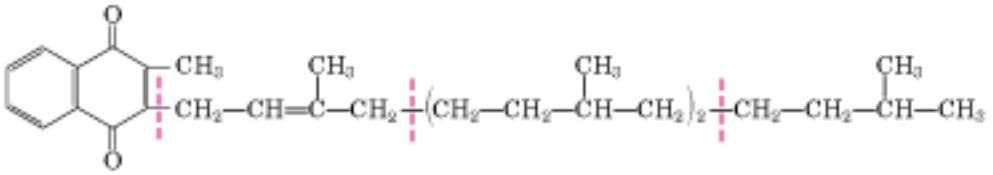
(b)

Vitamins E and K and the lipid Quinones are oxidation-reduction cofactors

(a)
Vitamin E: an antioxidant

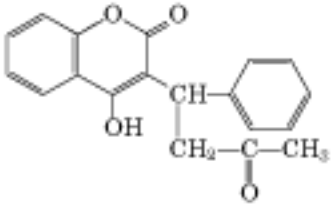


(b)
Vitamin K_1: a blood-clotting cofactor (phylloquinone)

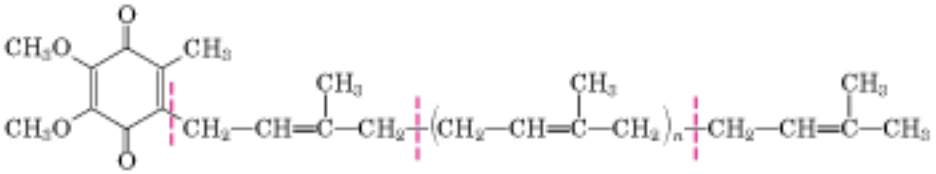


Some other biologically active Isoprenoid compounds or derivatives

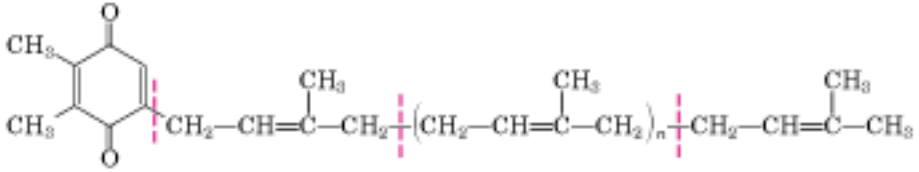
(c)
Warfarin: a blood anticoagulant



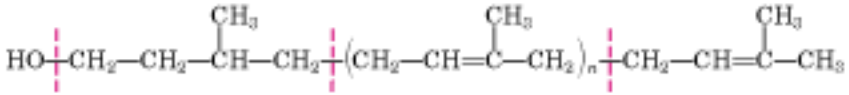
(d)
Ubiquinone: a mitochondrial electron carrier (coenzyme Q) ($n = 4–8$)



(e)
Plastoquinone: a chloroplast electron carrier ($n = 4–8$)



(f)
Dolichol: a sugar carrier ($n = 9–22$)



Análise de Lipídios

- Extração com solventes orgânicos
- Separação dos tipos de lipídios
- Detecção e análise

Análise de Lipídios

- Extração com solventes orgânicos
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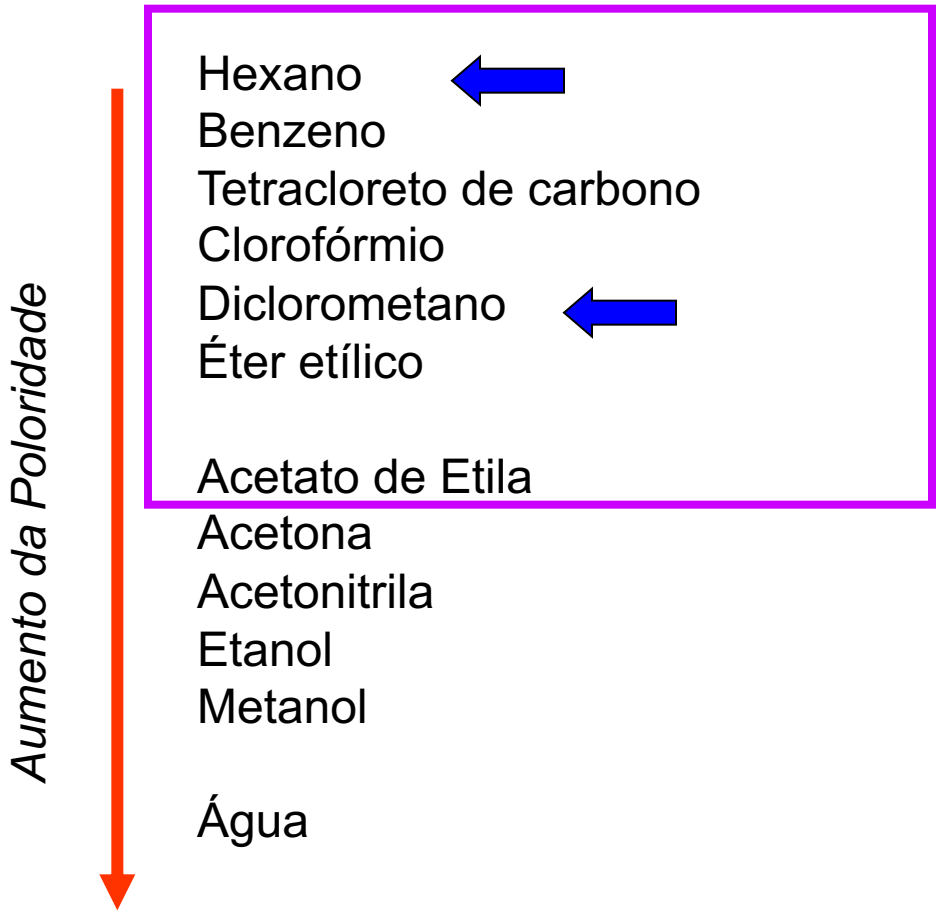
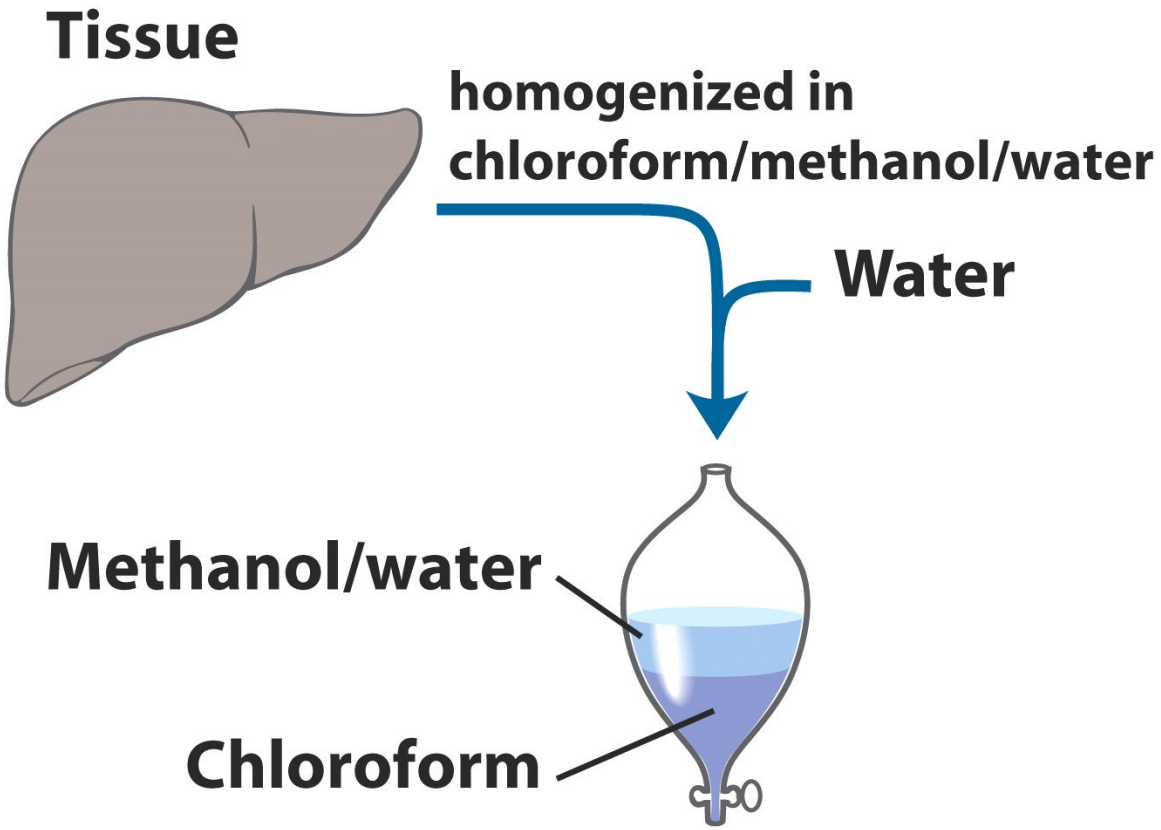
Solventes Orgânicos



++APOLARES

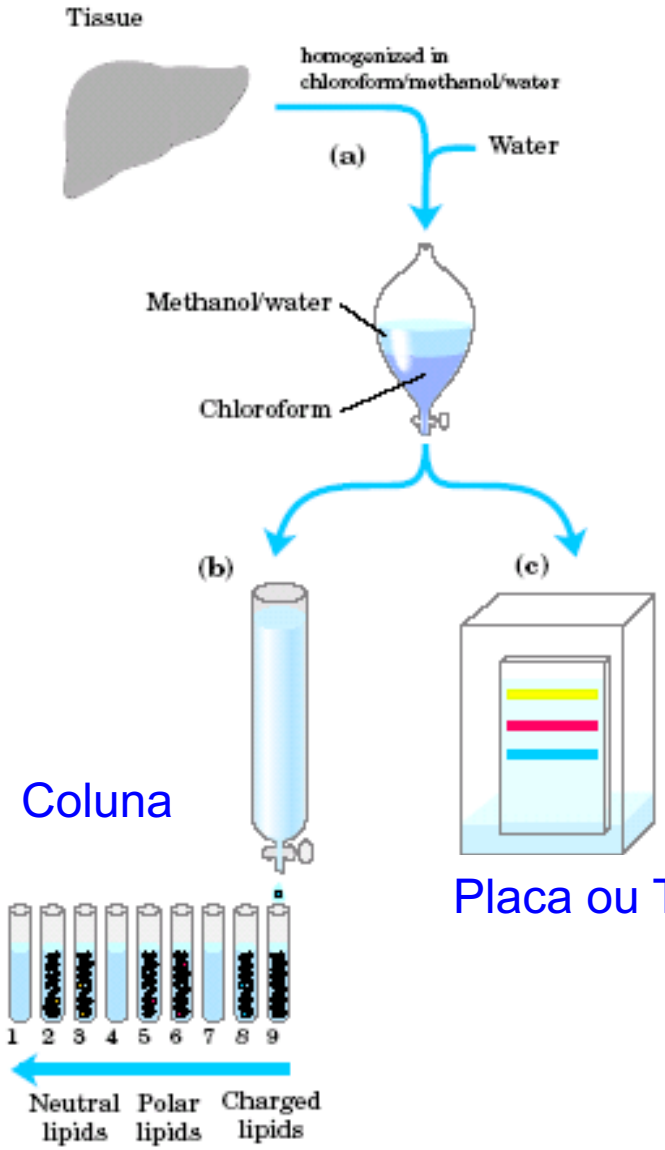
Extração de Lipídios



Análise de Lipídios

- Extração com solventes orgânicos
- Separação dos tipos de lipídios
- Detecção e análise

Separação dos Tipos de Lipídios



Coluna

Placa ou TLC (*Thin Layer Chromatography*)

Cromatografia de Adsorção

Cromatografia de Adsorção

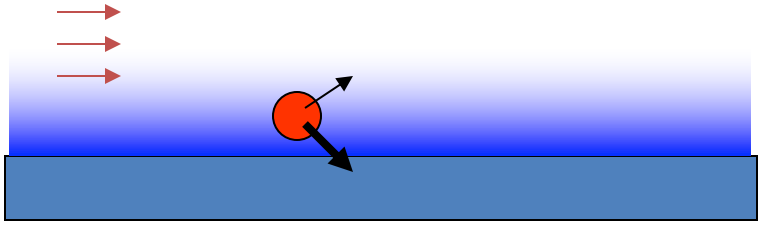
Princípio: Separação de mistura de compostos baseado nas diferenças de afinidade dos vários componentes de uma mistura entre o solvente utilizado (fase móvel) e a substância suporte (fase estacionária)

Cromatografia de Adsorção

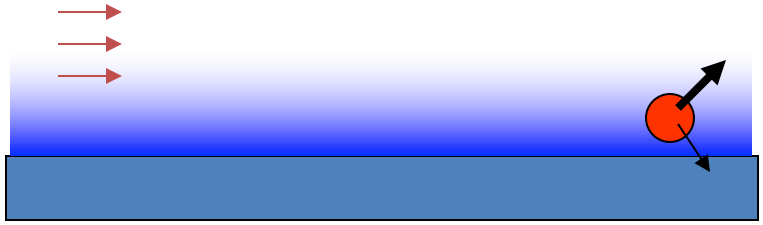
Princípio: Separação de mistura de compostos baseado nas diferenças de afinidade dos vários componentes de uma mistura entre o solvente utilizado (fase móvel) e a substância suporte (fase estacionária)

Fase Móvel

Fase Estacionária



> interação com a fase estacionária



> interação com a fase móvel

Cromatografia de Adsorção

Tipos de cromatografia

Fase Móvel

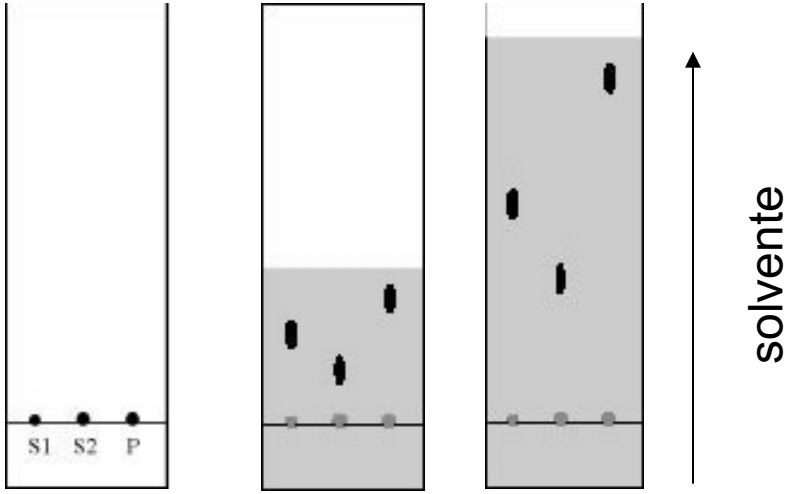
Fase Estacionária

Fase Móvel

- **Líquida** ***(Cromatografia Líquida)***
  - **Placa ou TLC**
  - **Coluna**
- **Gás** ***(Cromatografia Gasosa)***

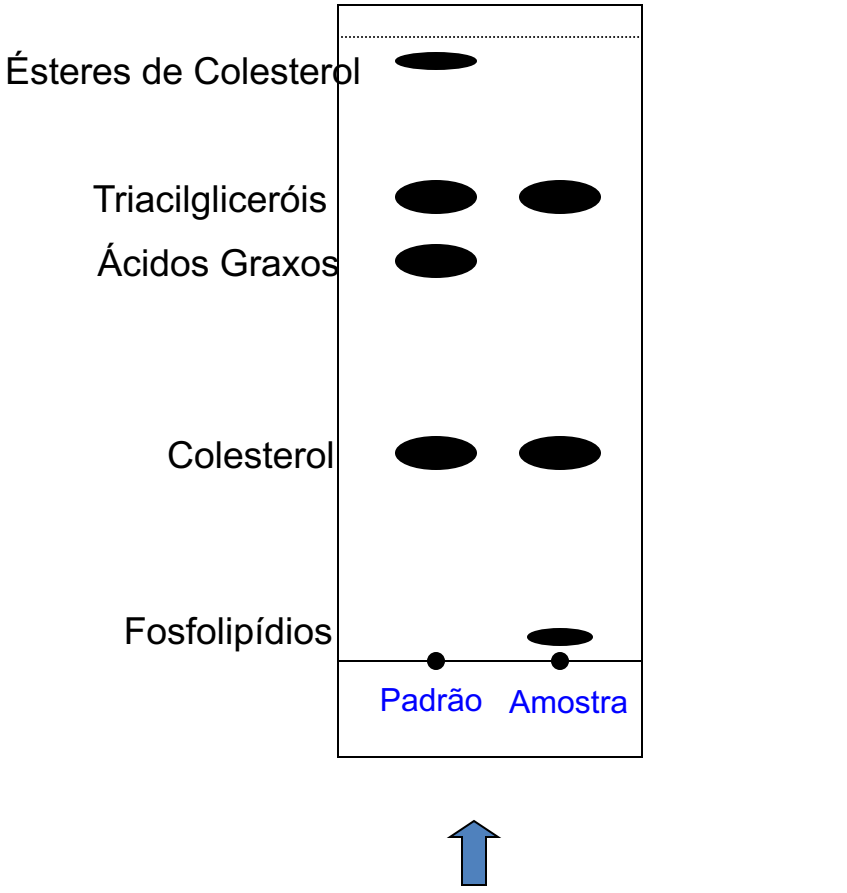
Cromatografia em Placa ou TLC

solvente



Cromatografia em Placa ou TLC

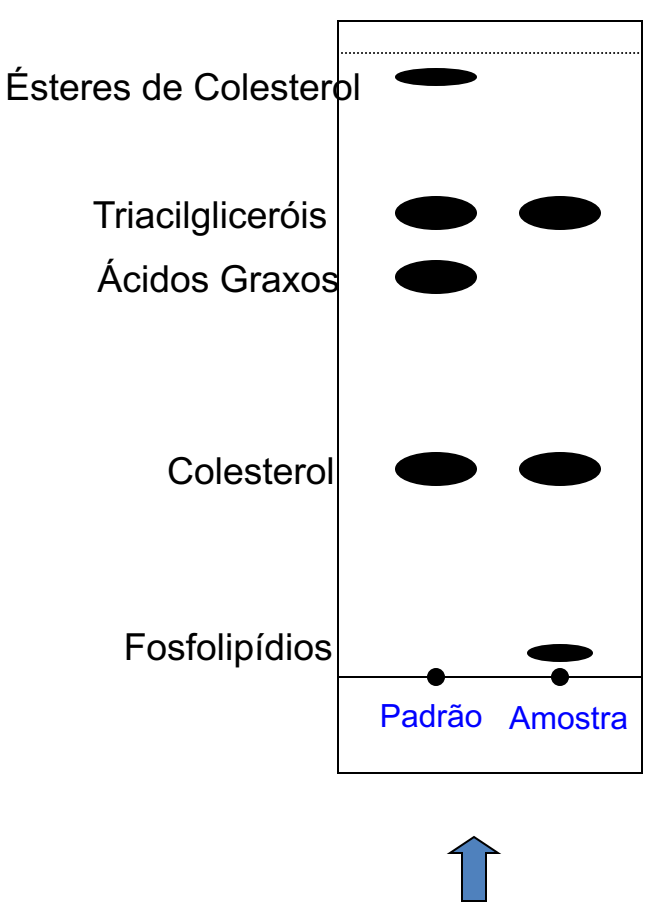
Amostra: Gema de ovo

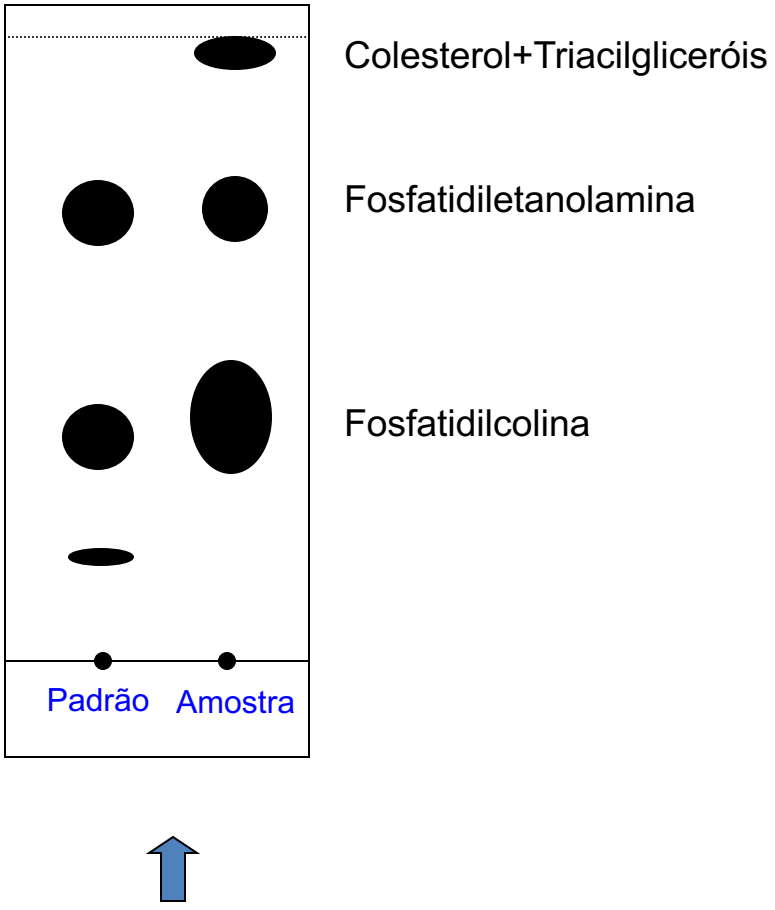


Hexano/Isopropanol/Ácido Acético (90/10/1)

Cromatografia em Placa ou TLC

Amostra: Gema de ovo





Hexano/Isopropanol/Ácido Acético (90/10/1)

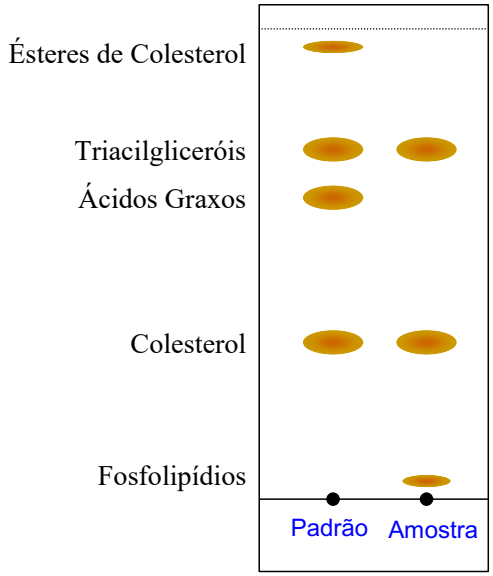
Clorofórmio/Metanol/Água (65/35/5)

Análise de Lipídios

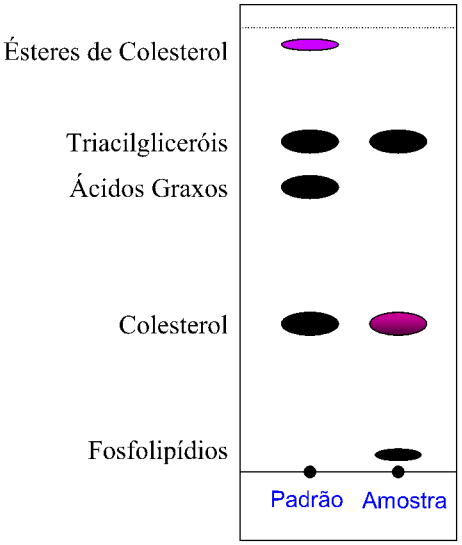
- Extração com solventes orgânicos
- Separação dos tipos de lipídios
- Detecção e análise

Detecção dos lipídios na TLC

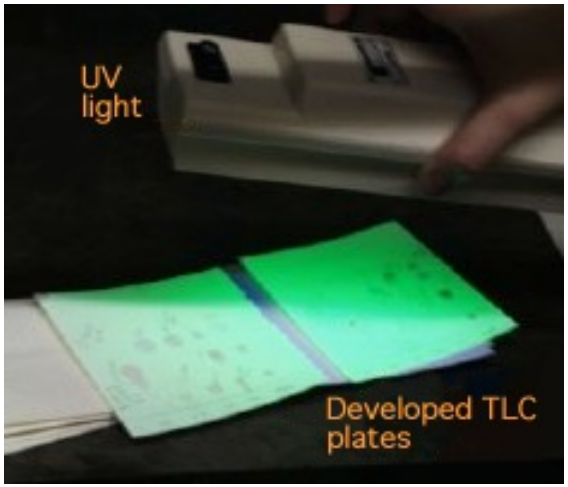
Iodo



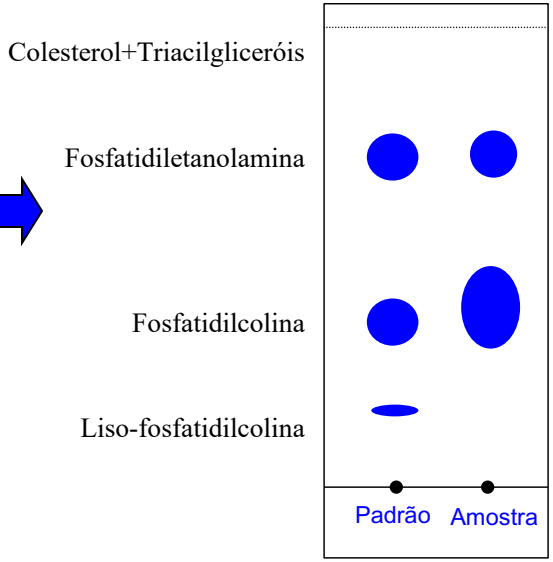
H_2SO_4



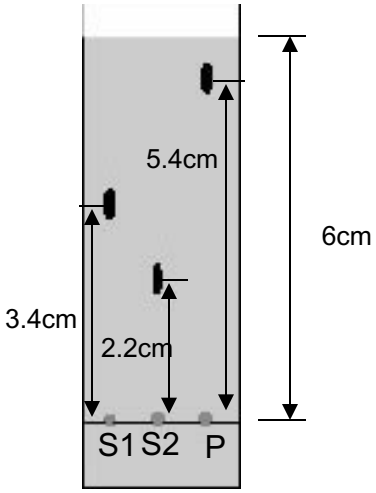
UV



Reagente Dittmer



Medida do Rf



$$R_f = \frac{\text{Distância Amostra}}{\text{Distância Total}}$$

S1 $\quad R_f = \dfrac{2.2\ \text{cm}}{6\ \text{cm}} = 0.37$

S2 $\quad R_f = \dfrac{3.4\ \text{cm}}{6\ \text{cm}} = 0.57$

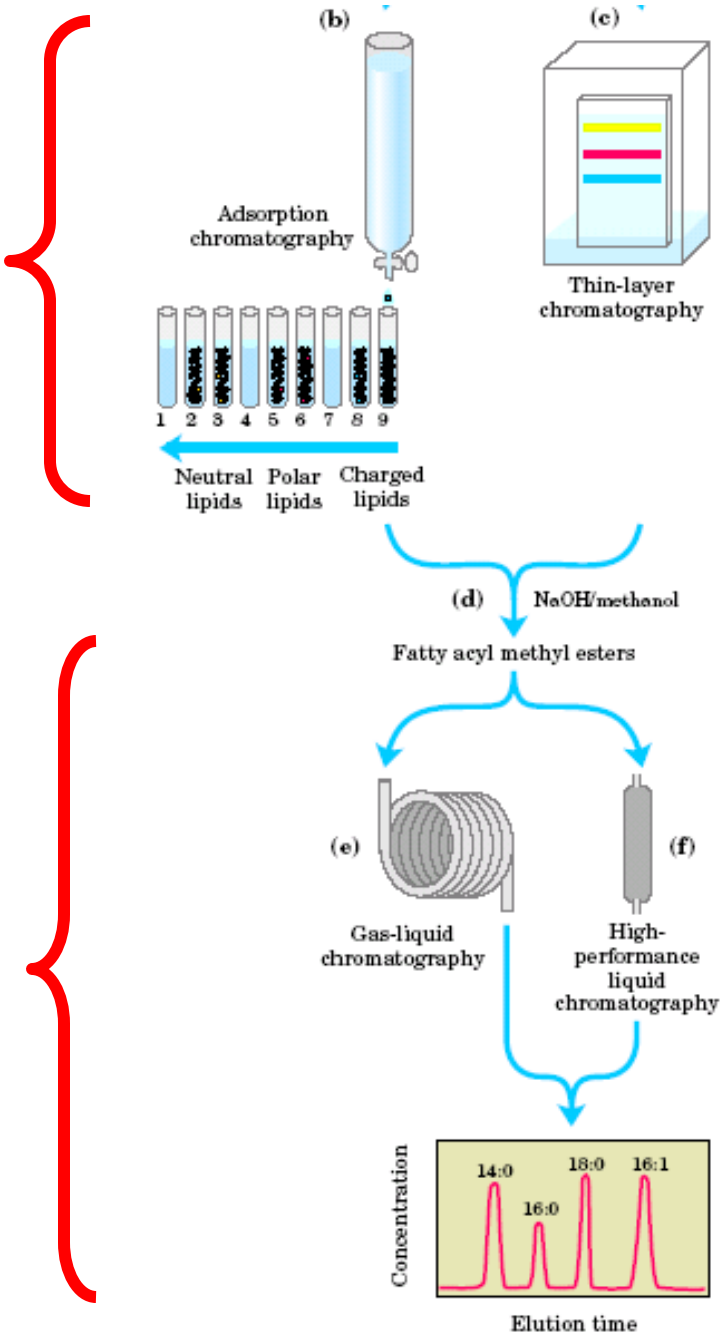
P $\quad R_f = \dfrac{5.4\ \text{cm}}{6\ \text{cm}} = 0.90$

Separação dos Tipos de Lipídios

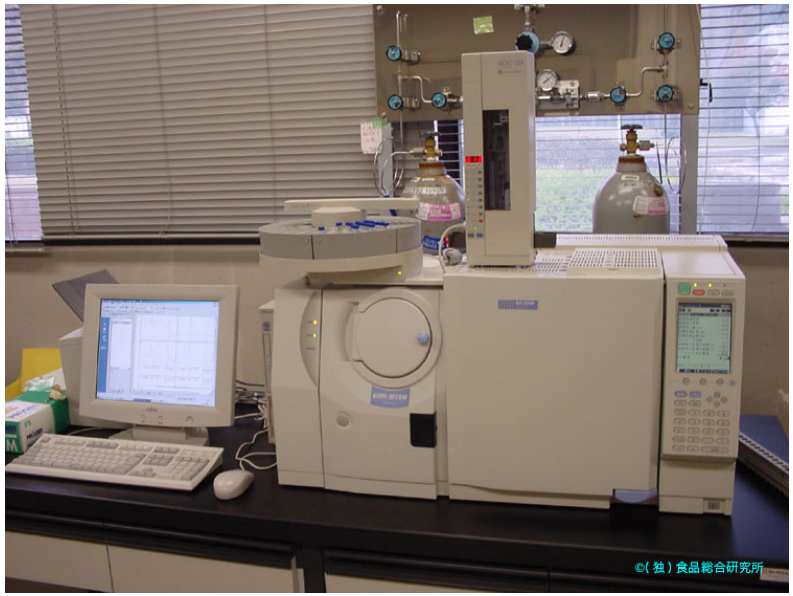
(TG, Colesterol, Fosfolipídio)

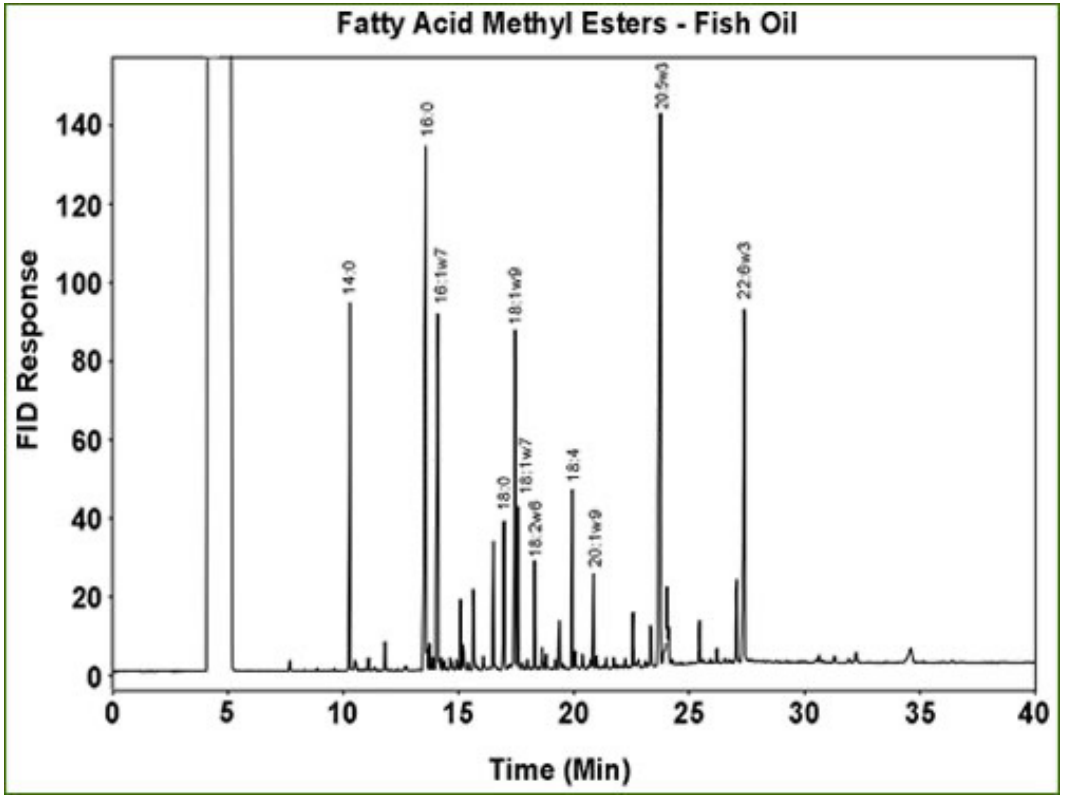
Análise de Ácidos Graxos

(saturados, monoinsaturados, poliinsaturados)



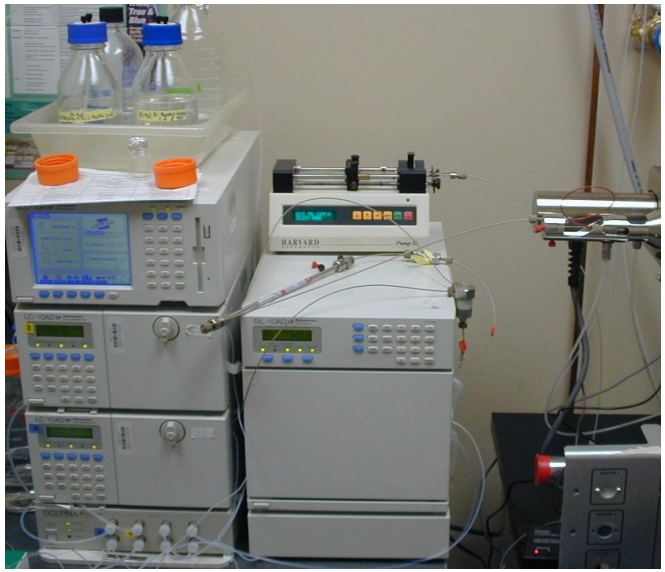
Análise de ácidos graxos metilados por Cromatografia a Gás



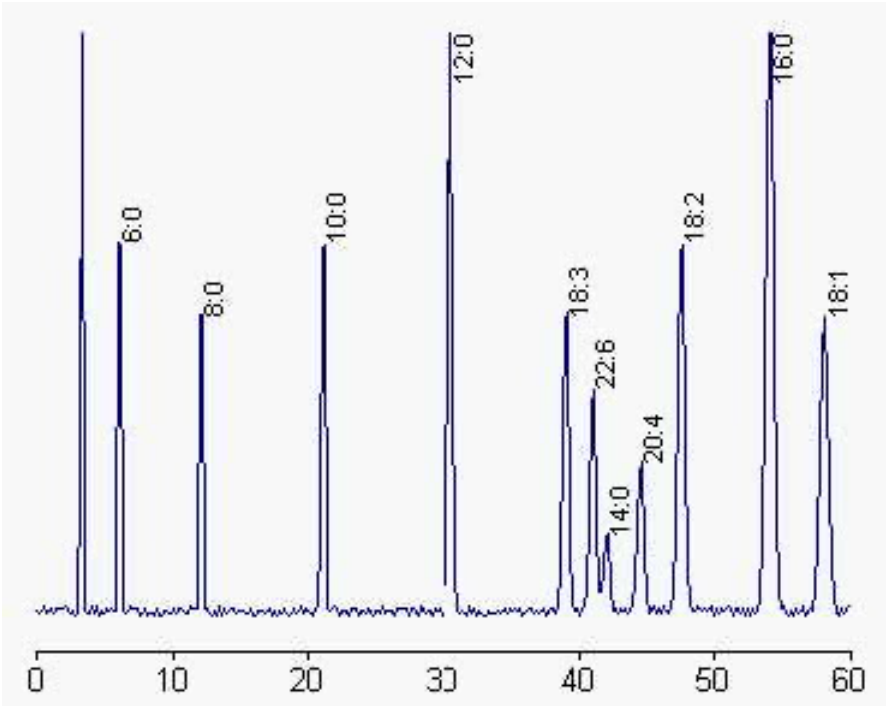


Coluna

Análise de ácidos graxos por HPLC

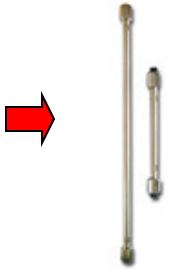


free fatty acids in human plasma

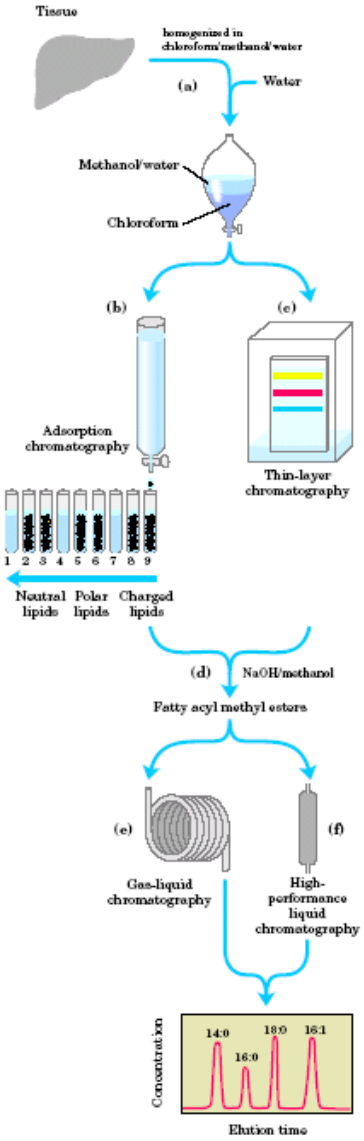


Tempo (min)

Coluna



Análise de Lipídios - Resumo



Extração

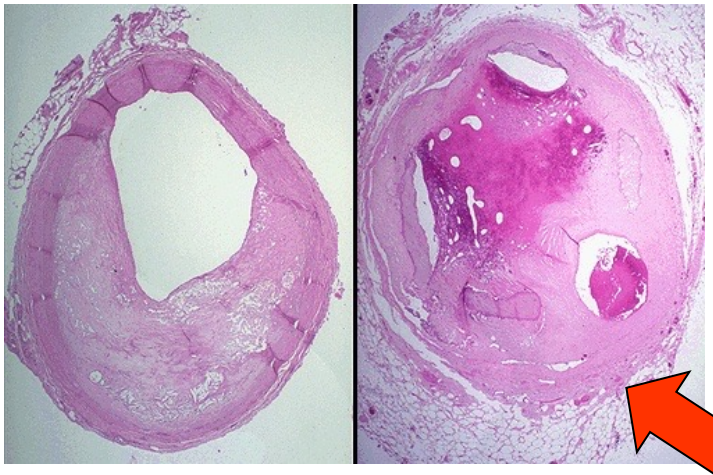
Separação dos tipos de lipídios

Hidrólise

Separação e análise dos ácidos graxos

Por que estudar os lipídios?

Doenças Cardiovasculares



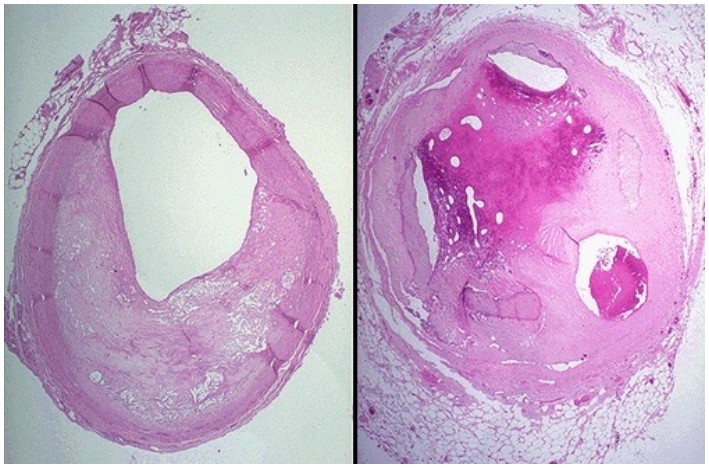
Câncer

Lipídios

Obesidade

Diabetes Tipo II

Doenças Cardiovasculares



Fatores de Risco

Colesterol → LDL

Ácidos Graxos Saturados

Ácidos Graxos Trans

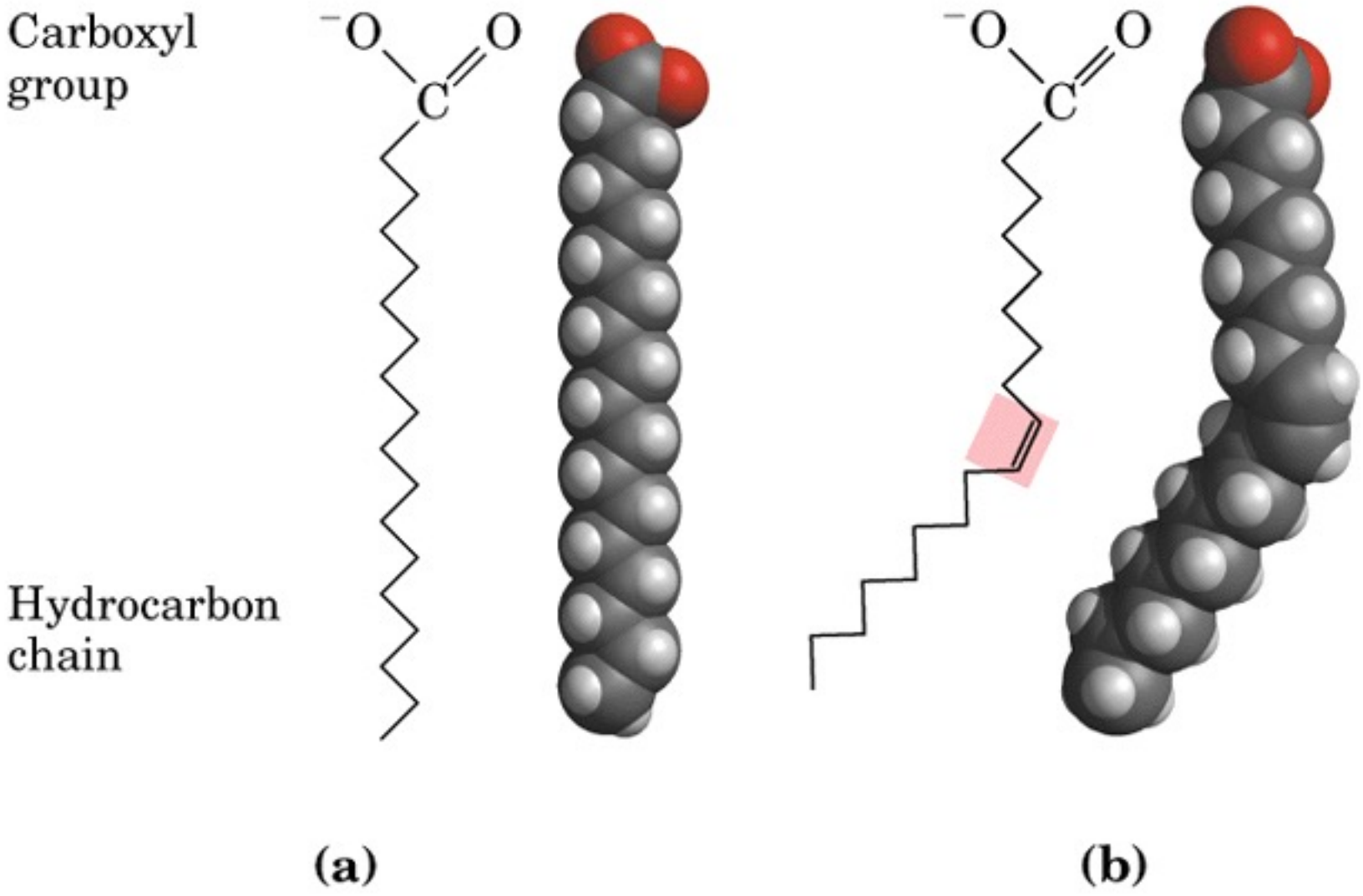
Proteção?

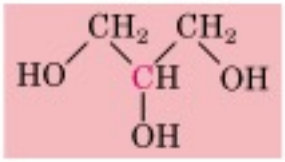
Ácidos Graxos ω-3

Antioxidantes

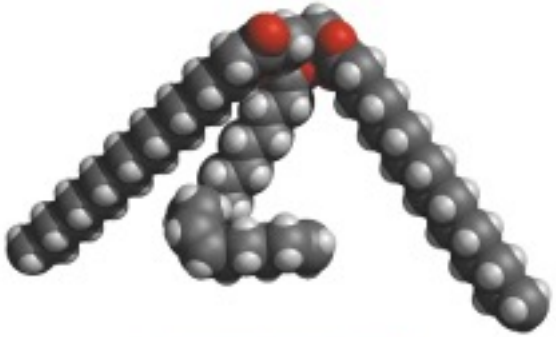
Fontes de Ácidos Graxos

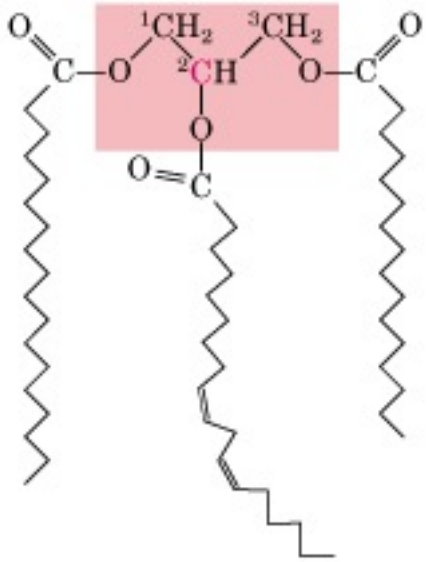
- Dieta
- Estoque de gorduras
- Síntese de outras fontes


Carboxyl group
Hydrocarbon chain
(a)
(b)



Glycerol

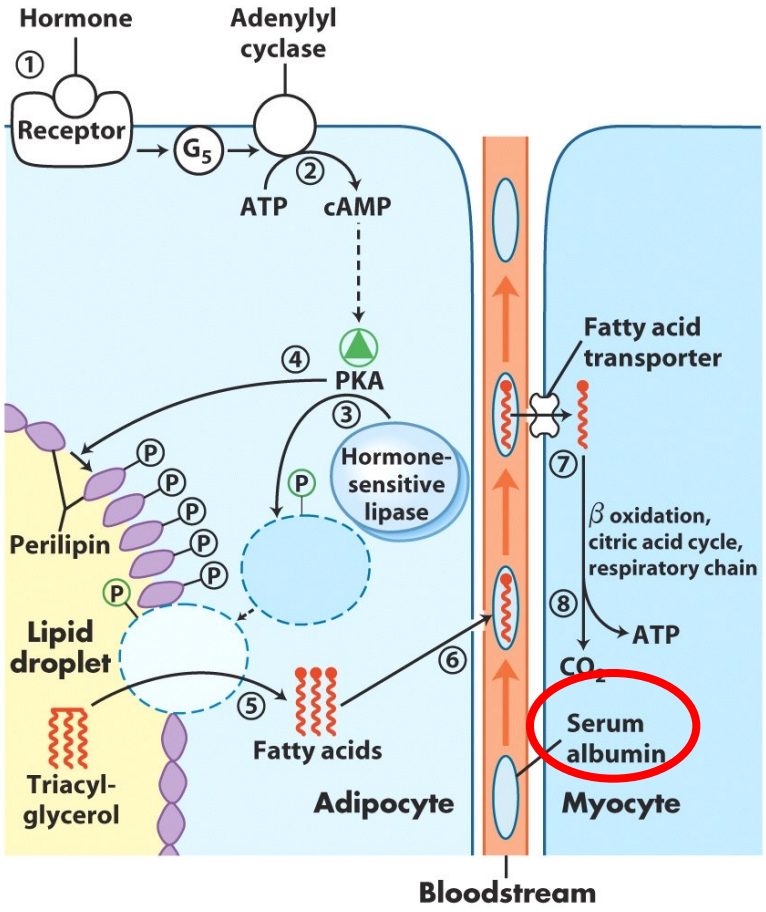




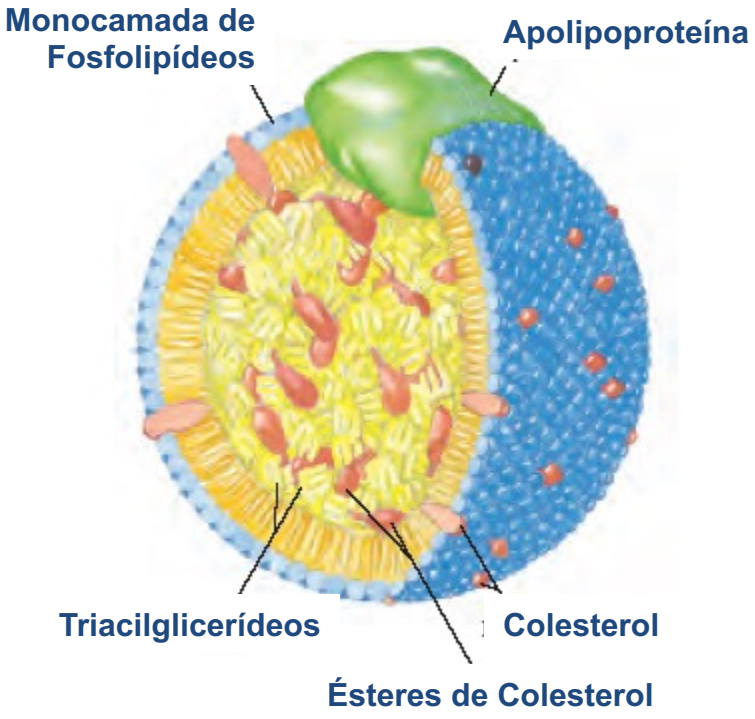
1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol,
a mixed triacylglycerol

Como ocorre o transporte de Lipídeos na Circulação Sanguínea ?

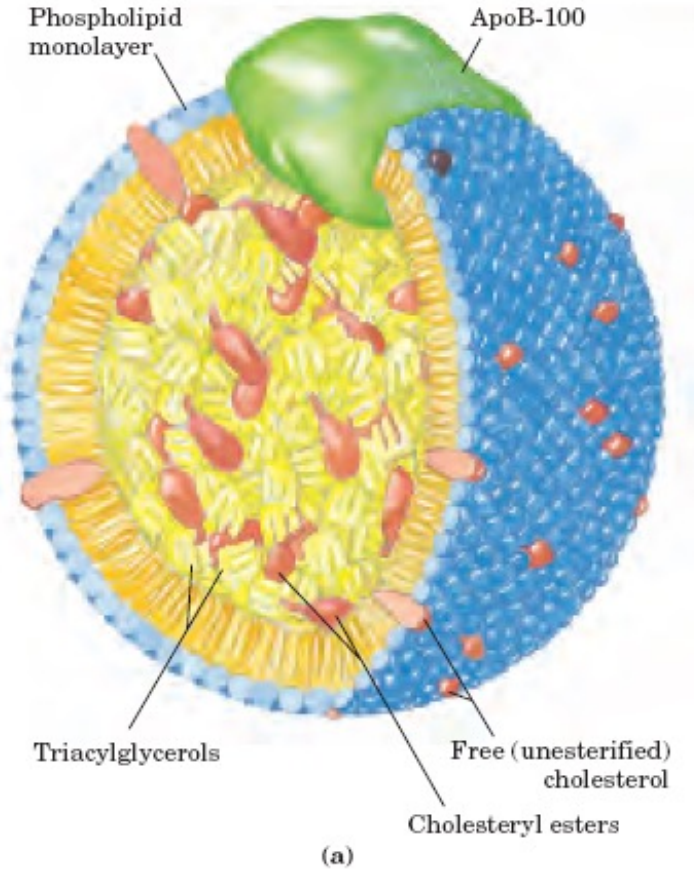
Ácidos graxos livres são transportados no sangue associados a **albumina**



Triacilglicerol, Fosfolipídeos e Colesterol e Ésteres de Colesterol são transportados no sangue incorporados a **lipoproteínas**

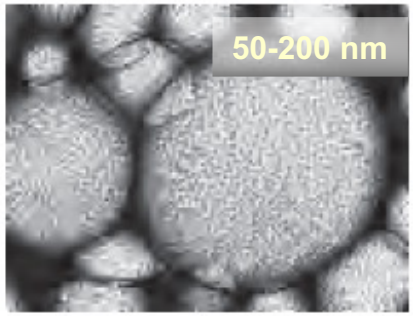


Lipoproteínas

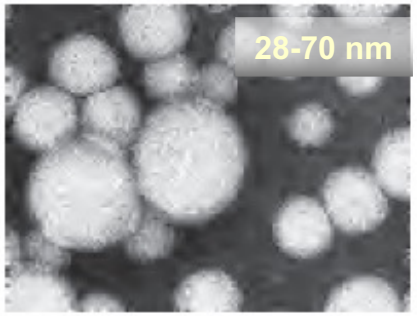


LDL

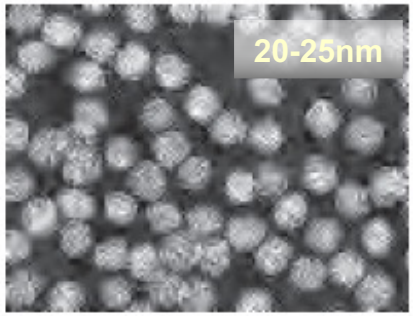
4 tipos principais



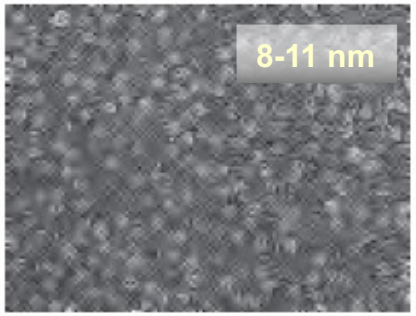
Chylomicrons (×60,000)



VLDL (×180,000)

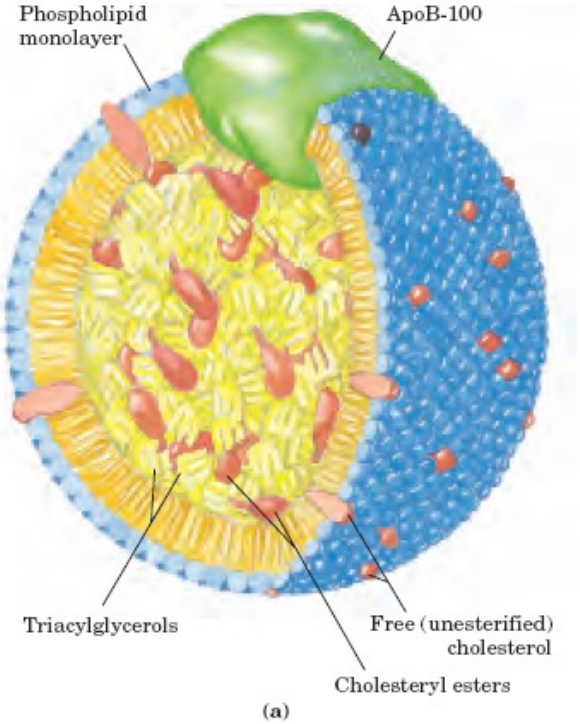


LDL (×180,000)



HDL (×180,000)

Lipoproteínas



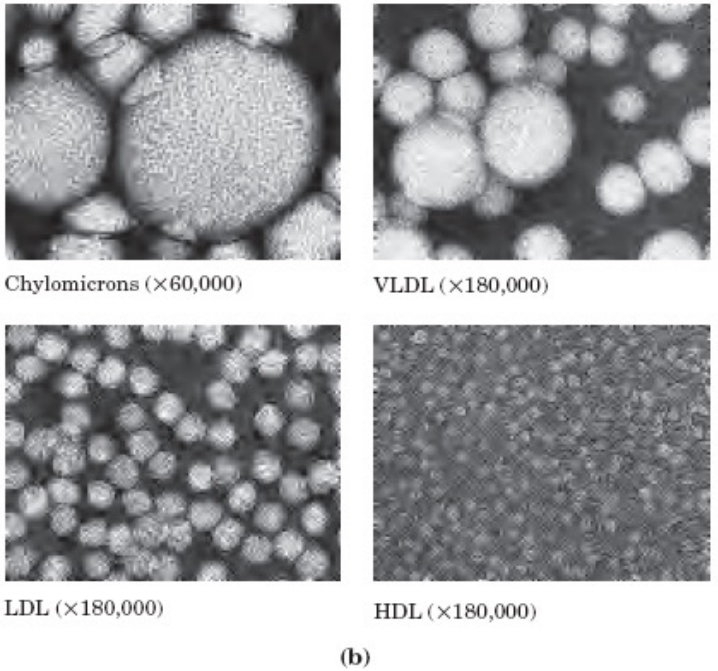


TABLE 21–2 Major Classes of Human Plasma Lipoproteins: Some Properties

		Composition (wt %)				
Lipoprotein	*Density (g/mL)*	*Protein*	*Phospholipids*	*Free cholesterol*	*Cholesteryl esters*	*Triacylglycerols*
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95–1.006	10	18	7	12	50
LDL	1.006–1.063	23	20	8	37	10
HDL	1.063–1.210	55	24	2	15	4

Menos denso

Mais denso

Source: Modified from Kritchevsky, D. (1986) Atherosclerosis and nutrition. *Nutr. int.* **2**, 290–297.

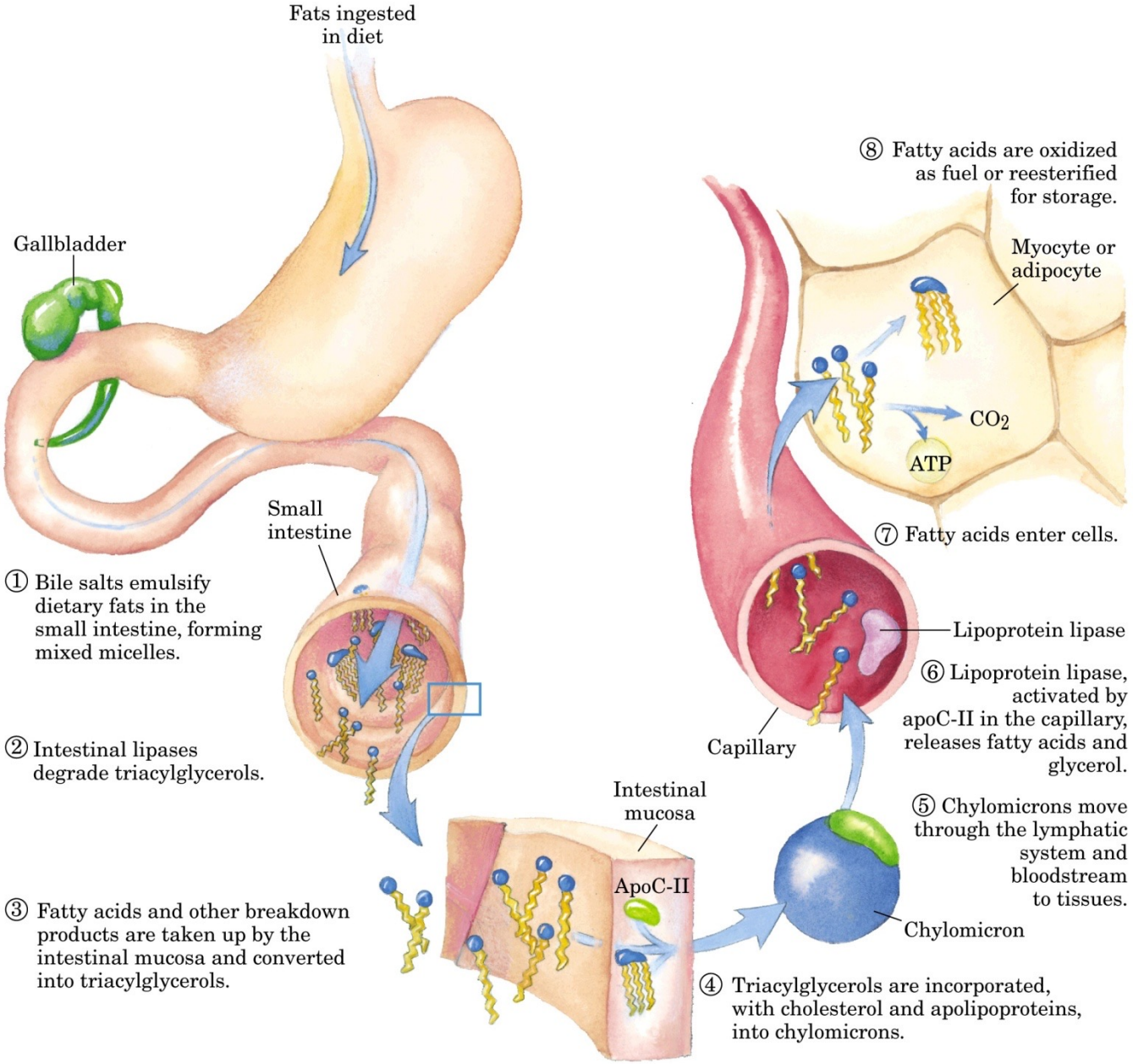
Lipoproteínas

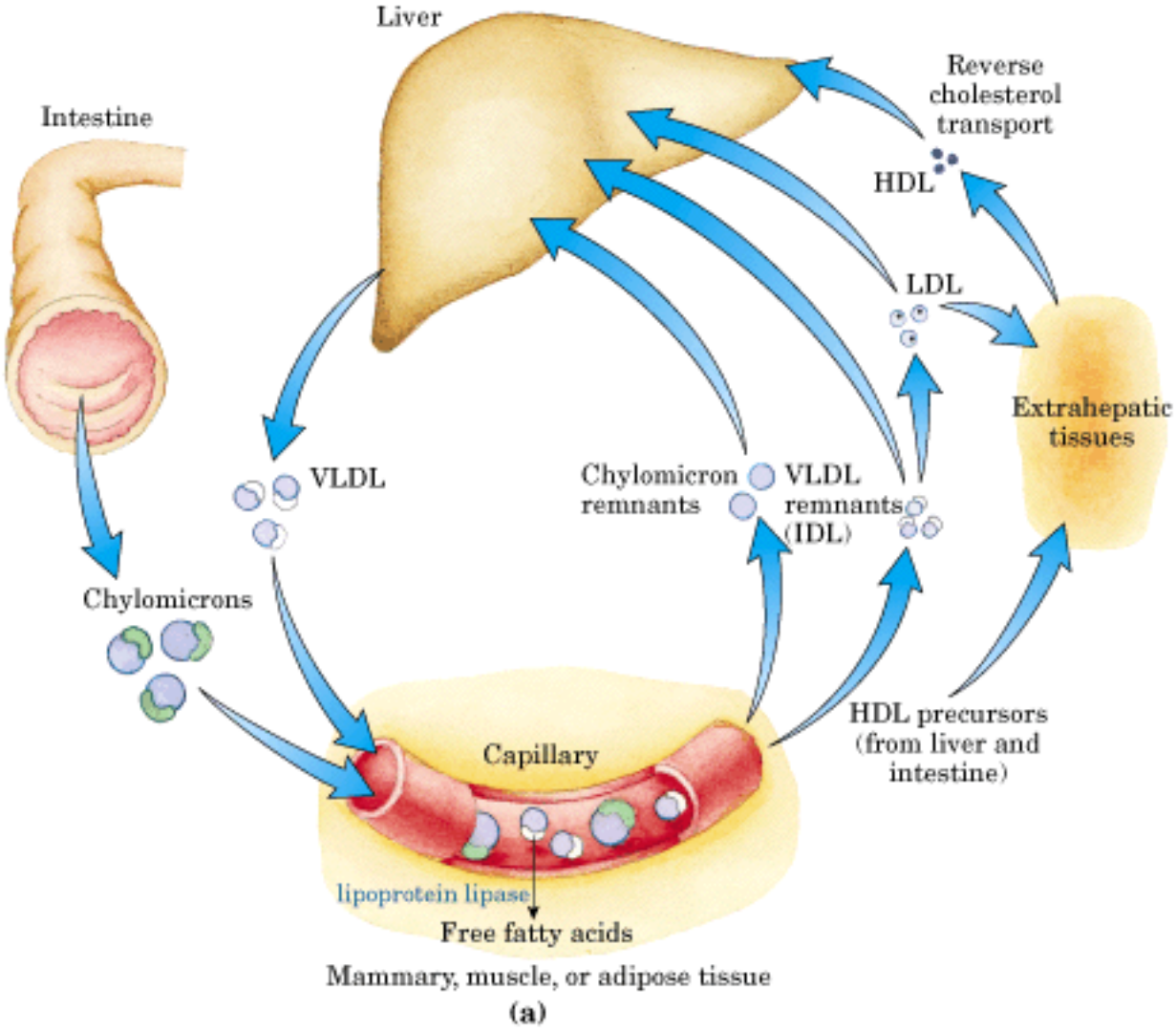
Quilomícrons → Sintetizados na mucosa intestinal. Transporta lipídeos da dieta do intestino para outros tecidos. TG são hidrolisados fornecendo ácidos graxos para os tecidos.

VLDL → Sintetizados no fígado. Transporta TG e colesterol do fígado para outros tecidos. Origina IDL e LDL.

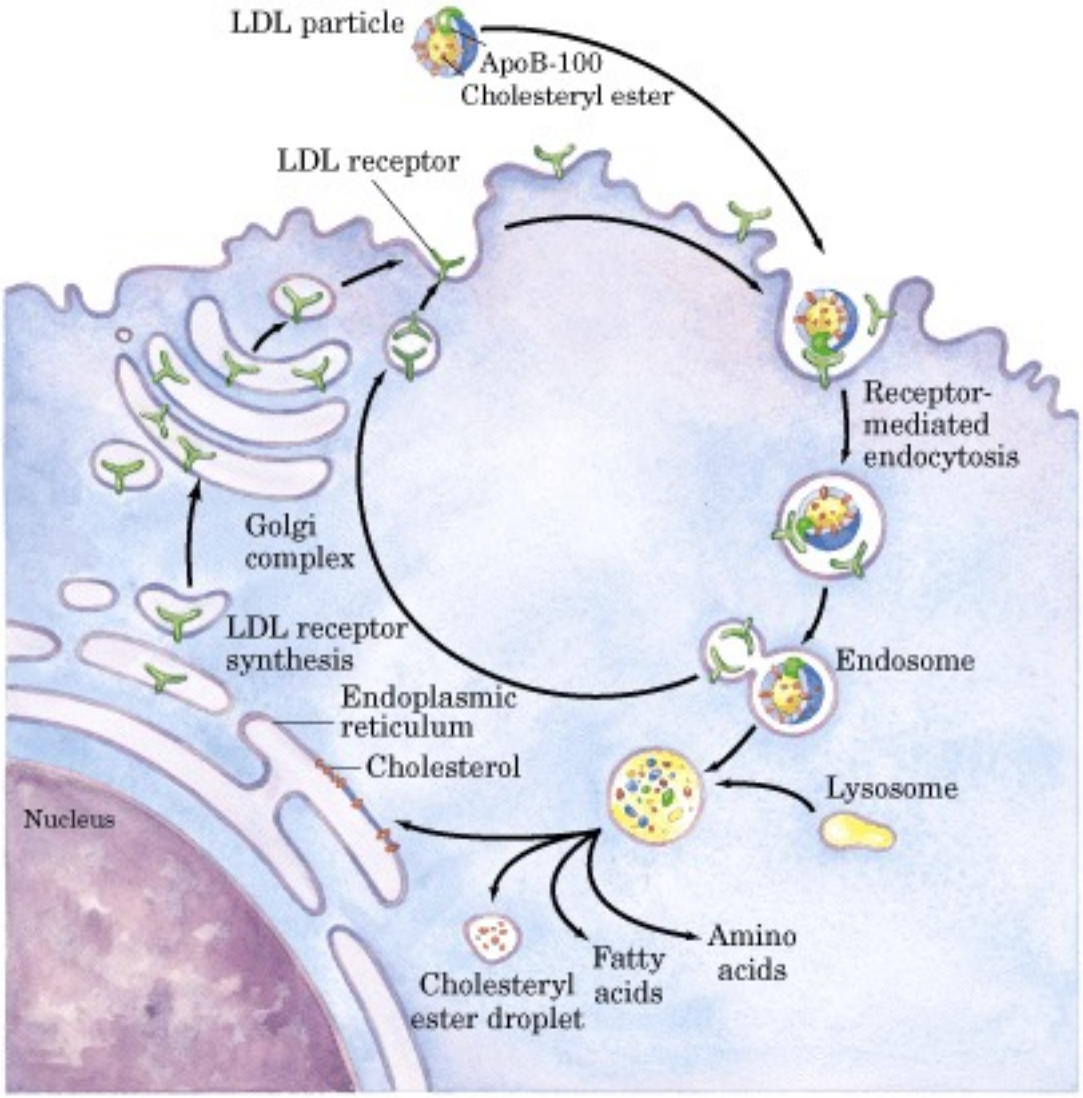
LDL(mau) → Formado a partir da VLDL. Ricas em colesterol. Transporta colesterol para os tecidos extra-hepáticos.

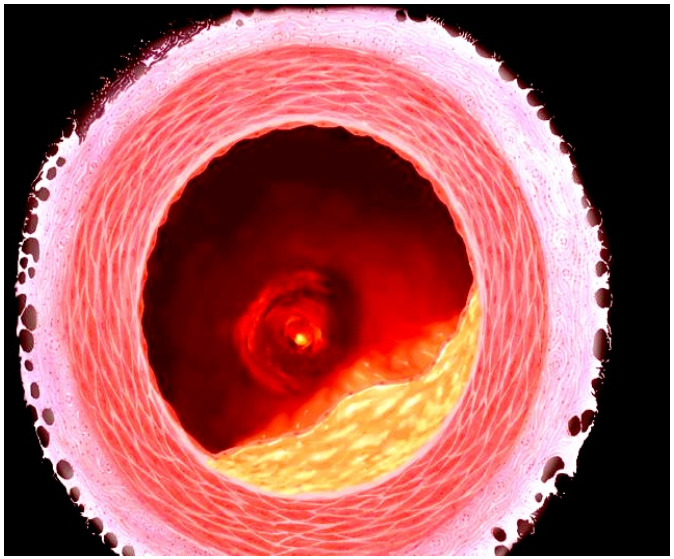
HDL(bom) → Sintetizado no fígado e intestino. Sequestra o colesterol de tecidos extra-hepáticos sob a forma de ésteres de colesterol e leva até o figado.


Fats ingested in diet
Gallbladder
Small intestine
① Bile salts emulsify dietary fats in the small intestine, forming mixed micelles.
② Intestinal lipases degrade triacylglycerols.
③ Fatty acids and other breakdown products are taken up by the intestinal mucosa and converted into triacylglycerols.
Intestinal mucosa
ApoC-II
④ Triacylglycerols are incorporated, with cholesterol and apolipoproteins, into chylomicrons.
⑤ Chylomicrons move through the lymphatic system and bloodstream to tissues.
Chylomicron
⑥ Lipoprotein lipase, activated by apoC-II in the capillary, releases fatty acids and glycerol.
Capillary
Lipoprotein lipase
⑦ Fatty acids enter cells.
⑧ Fatty acids are oxidized as fuel or reesterified for storage.
Myocyte or adipocyte
CO_2
ATP

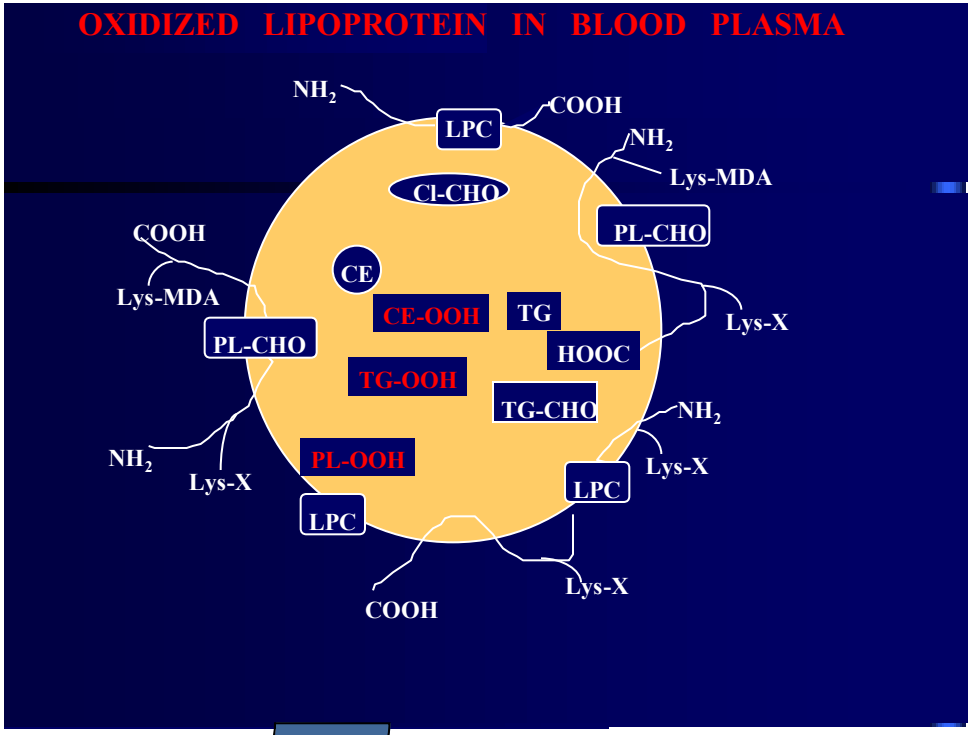

Liver
Intestine
Reverse cholesterol transport
HDL
LDL
Extrahepatic tissues
VLDL
Chylomicron remnants
VLDL remnants (IDL)
Chylomicrons
HDL precursors (from liver and intestine)
Capillary
lipoprotein lipase
Free fatty acids
Mammary, muscle, or adipose tissue
(a)

(b)


LDL particle
ApoB-100
Cholesteryl ester
LDL receptor
Receptor-mediated endocytosis
Golgi complex
LDL receptor synthesis
Endosome
Endoplasmic reticulum
Cholesterol
Lysosome
Nucleus
Amino acids
Fatty acids
Cholesteryl ester droplet



ATHEROSCLEROTIC LESION



Monitoramento da Oxidação de Lipídios

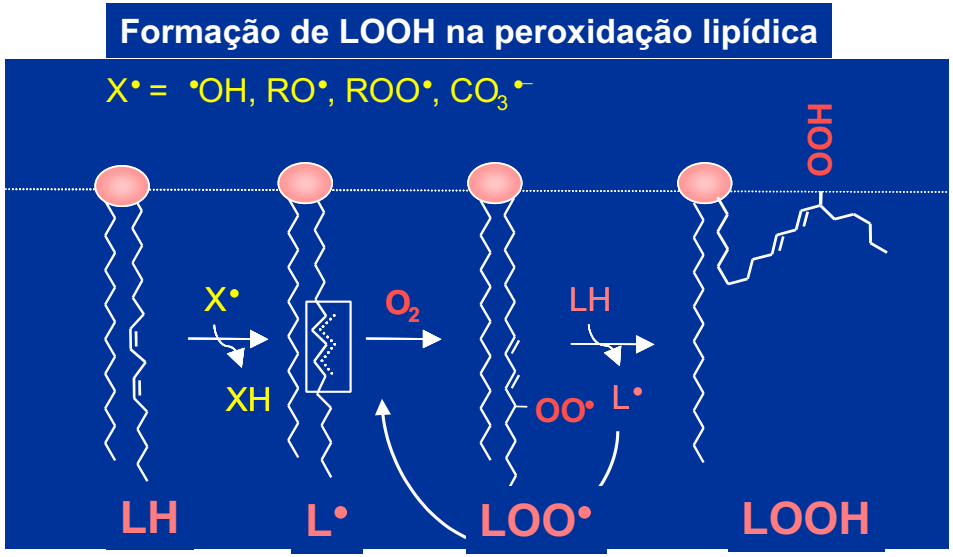
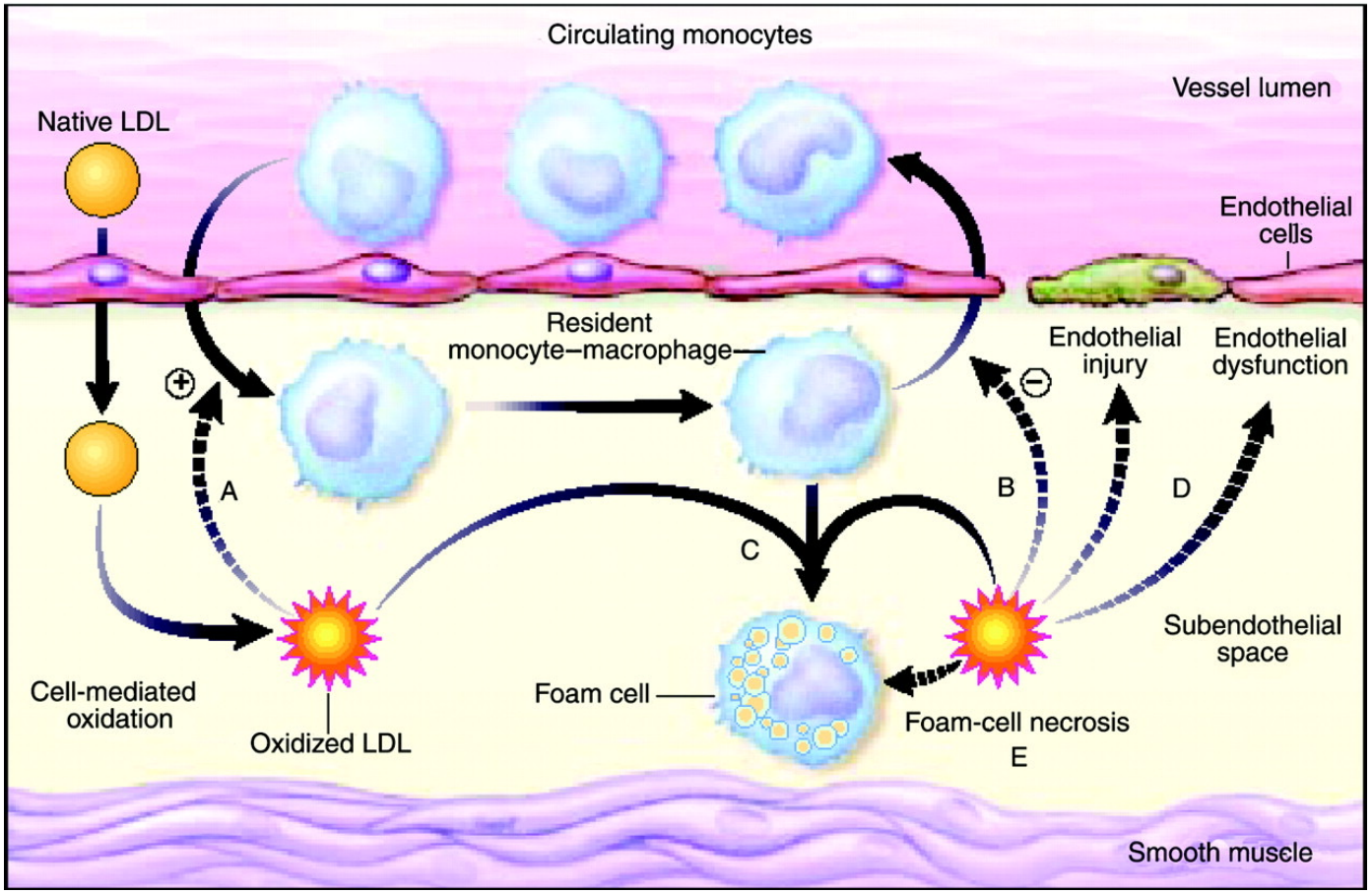
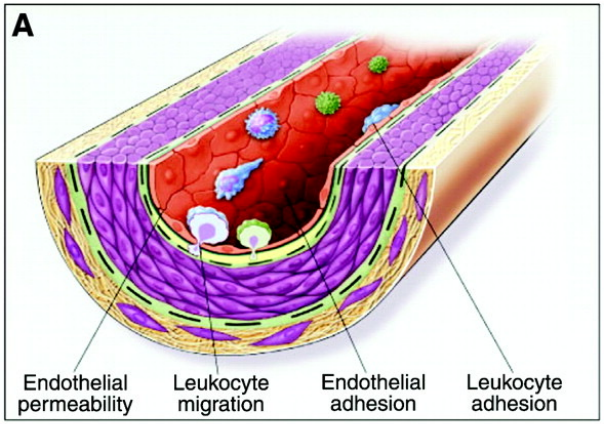


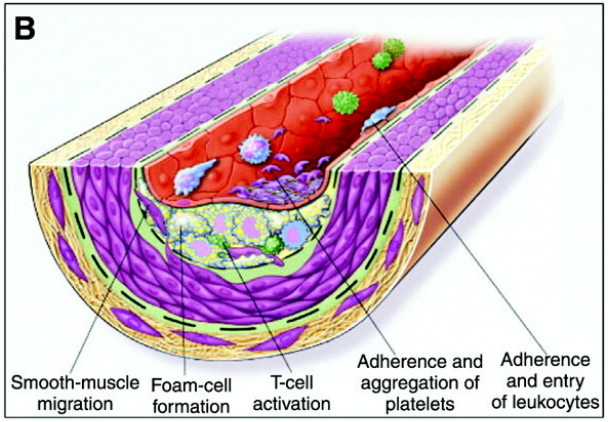
FIG. 5. Oxidative modification hypothesis of atherosclerosis

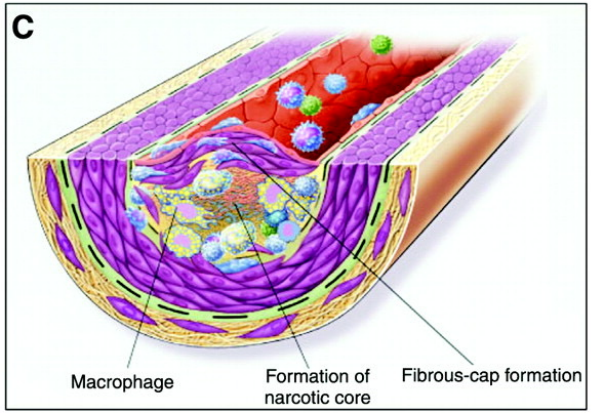


Stocker, R. et al. Physiol. Rev. 84: 1381-1478 2004;
doi:10.1152/physrev.00047.2003

Physiological Reviews

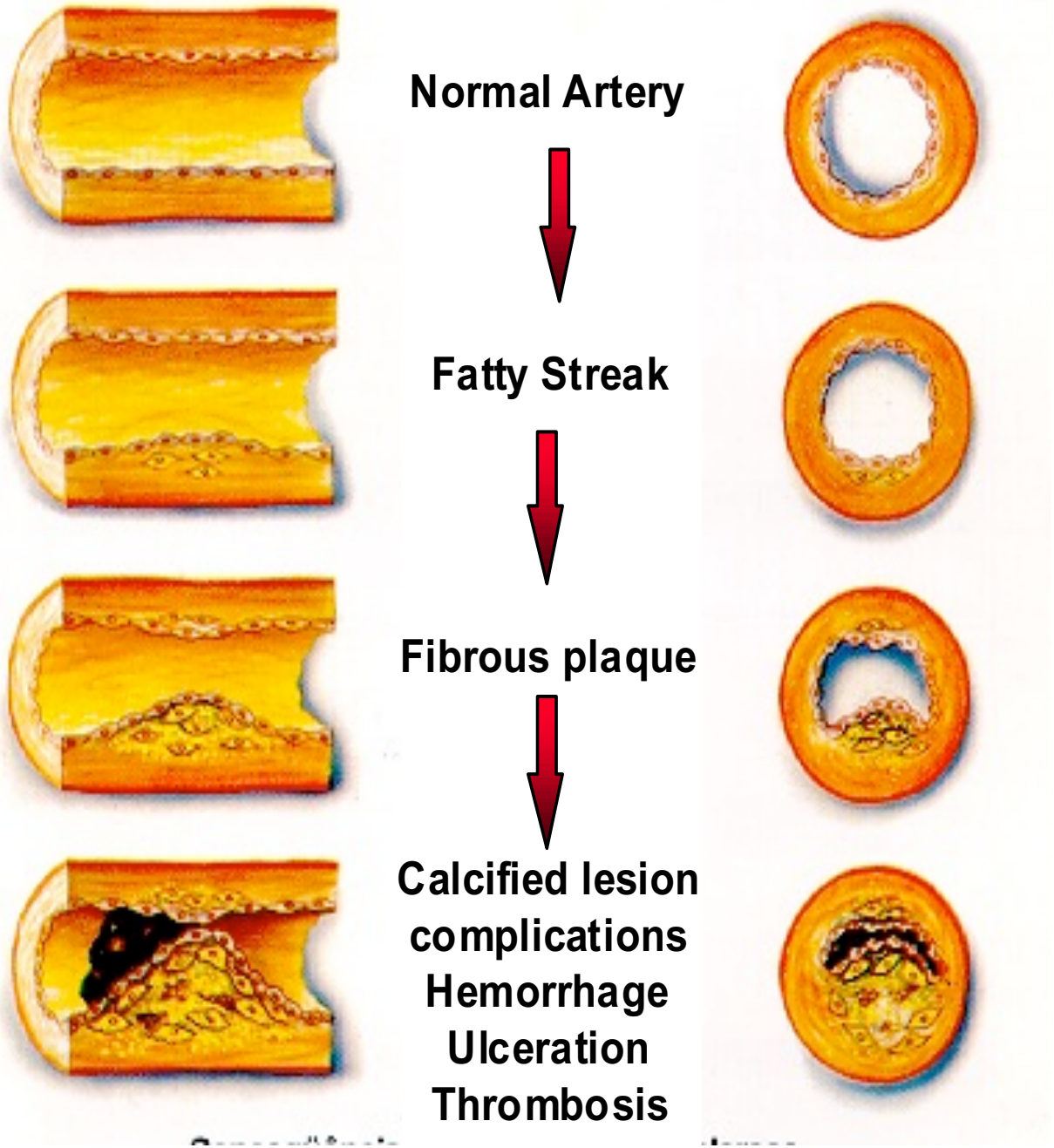

A
Endothelial permeability
Leukocyte migration
Endothelial adhesion
Leukocyte adhesion

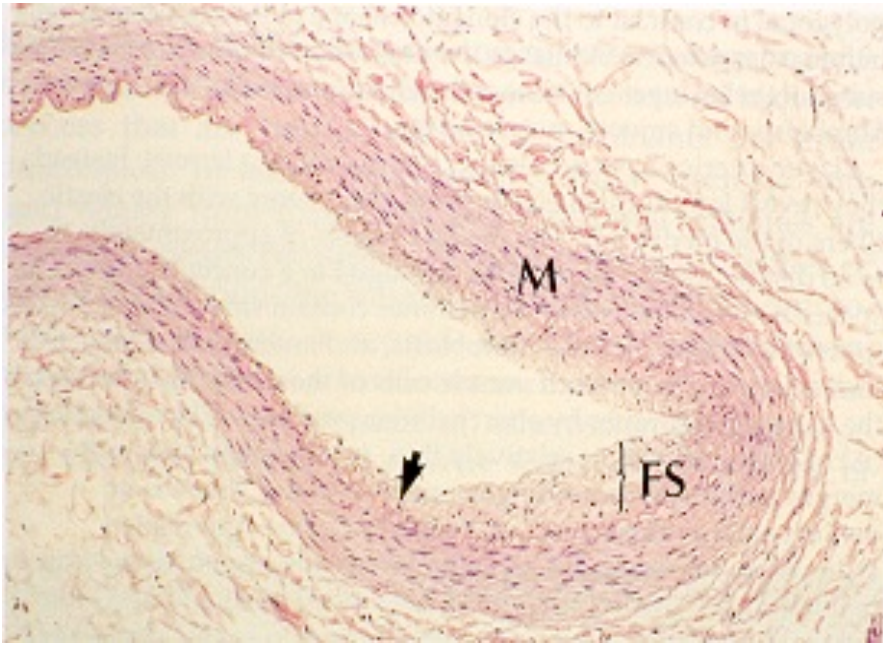

B
Smooth-muscle migration
Foam-cell formation
T-cell activation
Adherence and aggregation of platelets
Adherence and entry of leukocytes

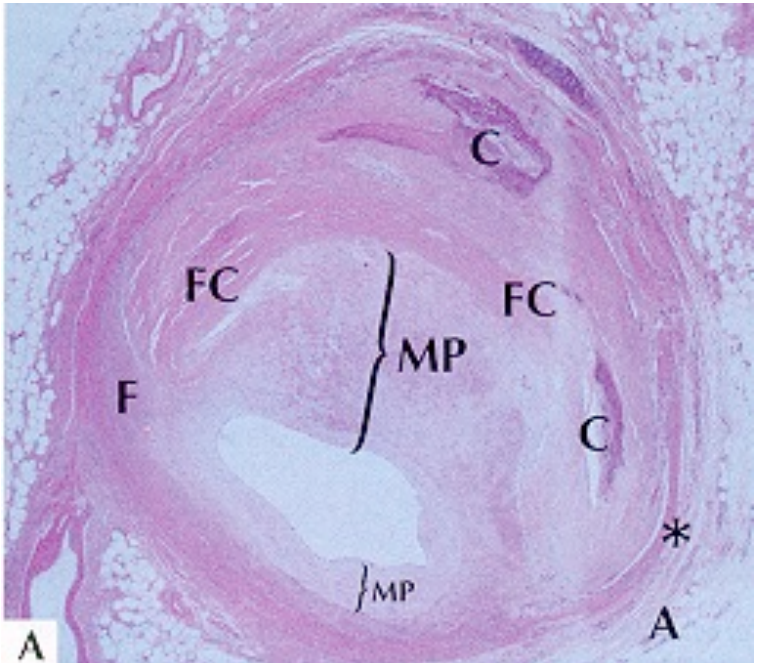

C
Macrophage
Formation of narcotic core
Fibrous-cap formation

ATHEROSCLEROSIS

PROGRESSION




M
FS


C
FC
FC
MP
F
C
*
MP
A
A

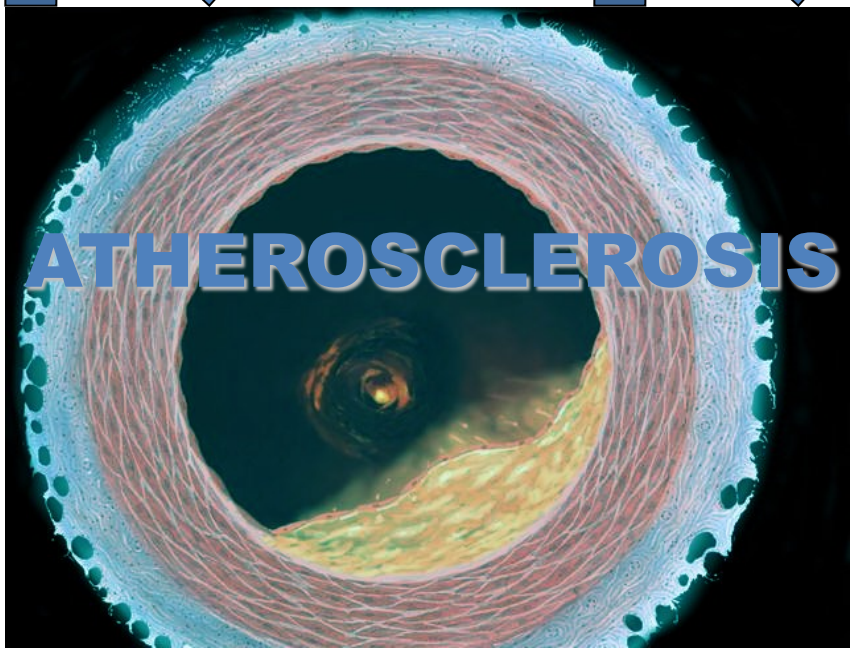
RISK FACTORS

DISLIPIDEMIAS

HYPERTENSION

TABAGISM

DIABETES



OBESITY

DIET

?

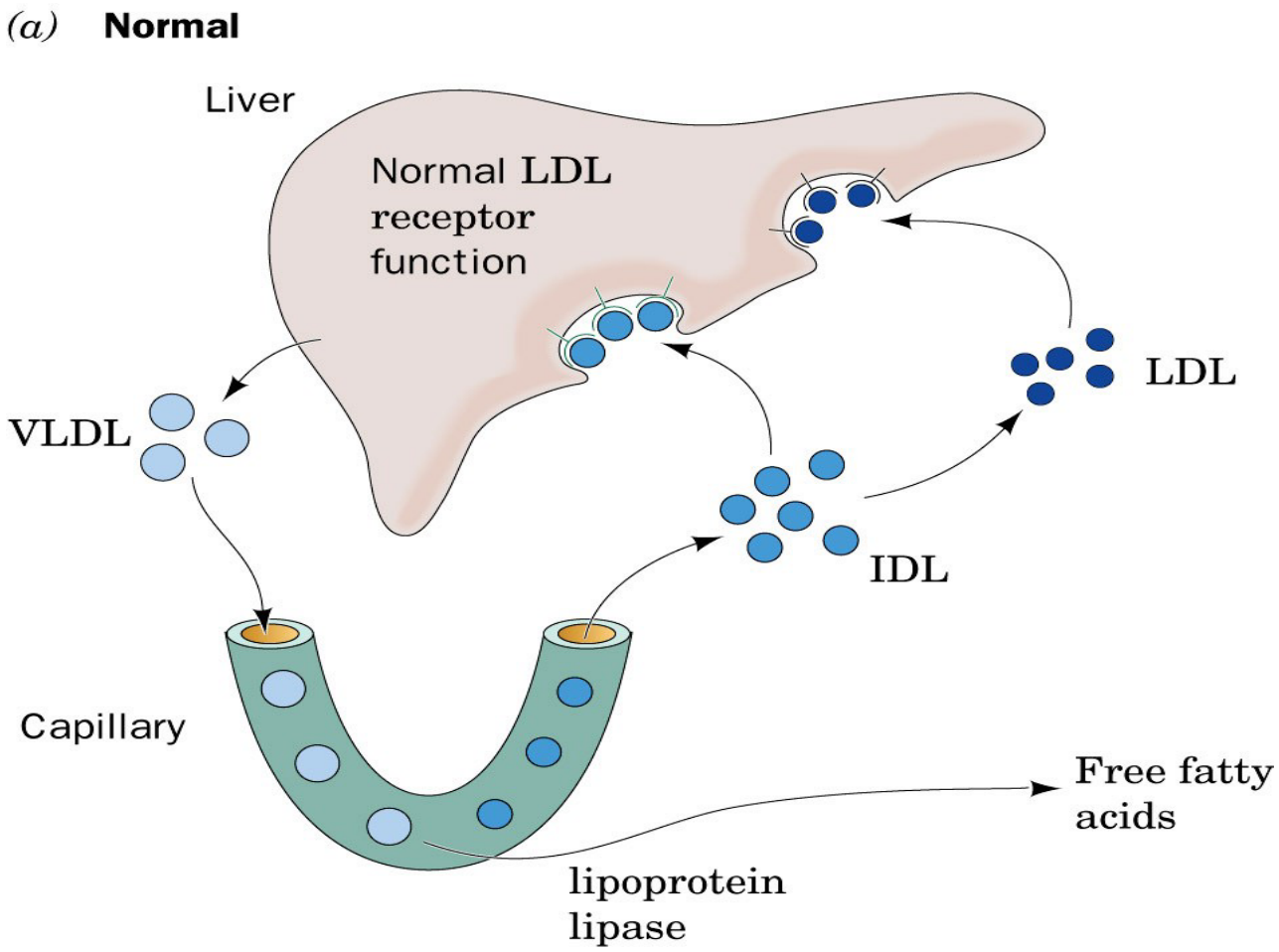
OXIDIZED LIPOPROTEINS

No Fígado o Colesterol é Excretado por meio de sua conversão a Sais Biliares

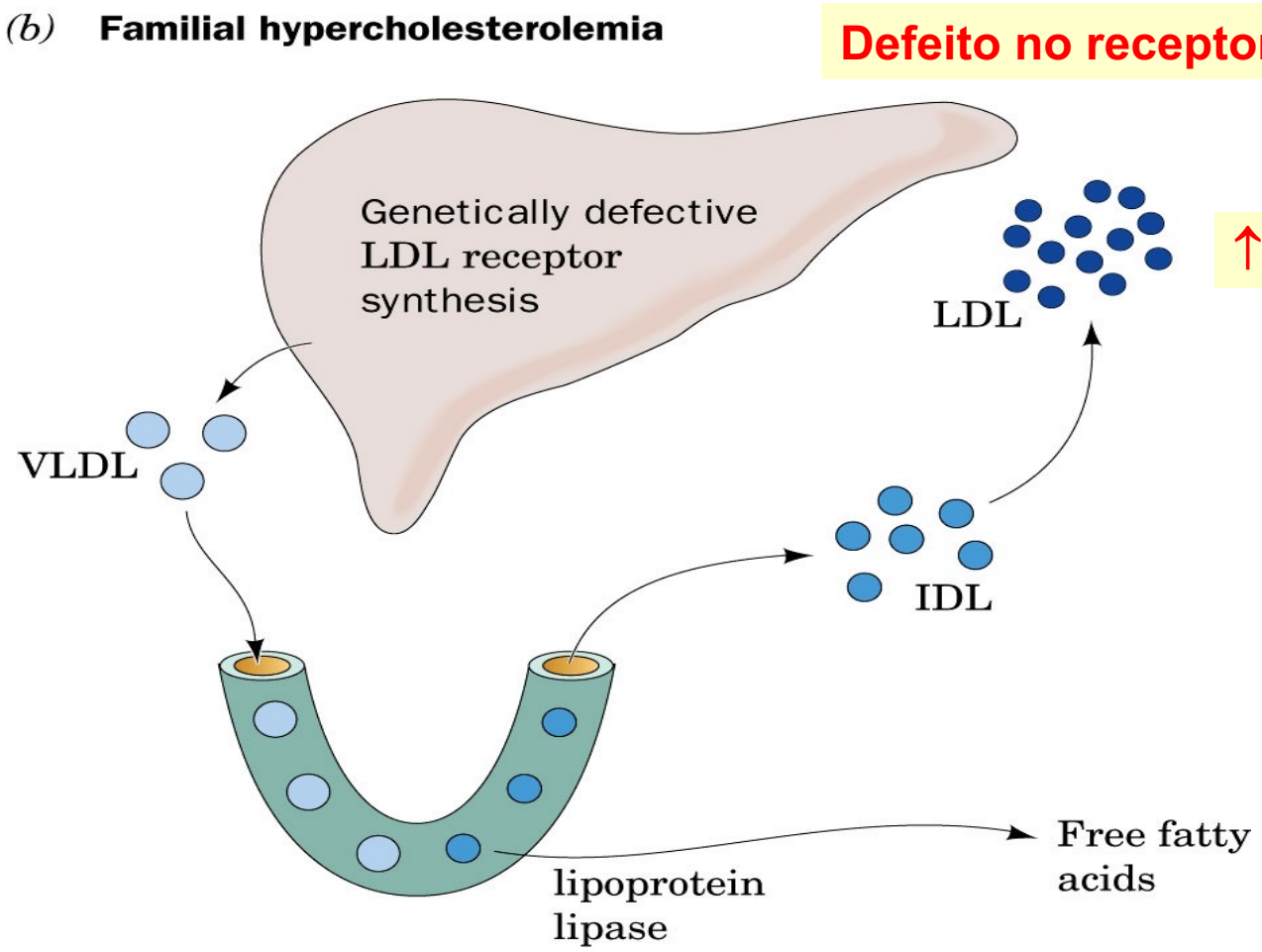
Nos organismos sadios os níveis de colesterol sanguíneo são mantidos pelo controle de sua síntese, excreção/utilização e captação
(o orgão central nesse processo é o fígado)

Defeitos Genéticos que afetam a captação da LDL pelo fígado
e/ou
Condições que aumentam a síntese ou ingestão de Colesterol

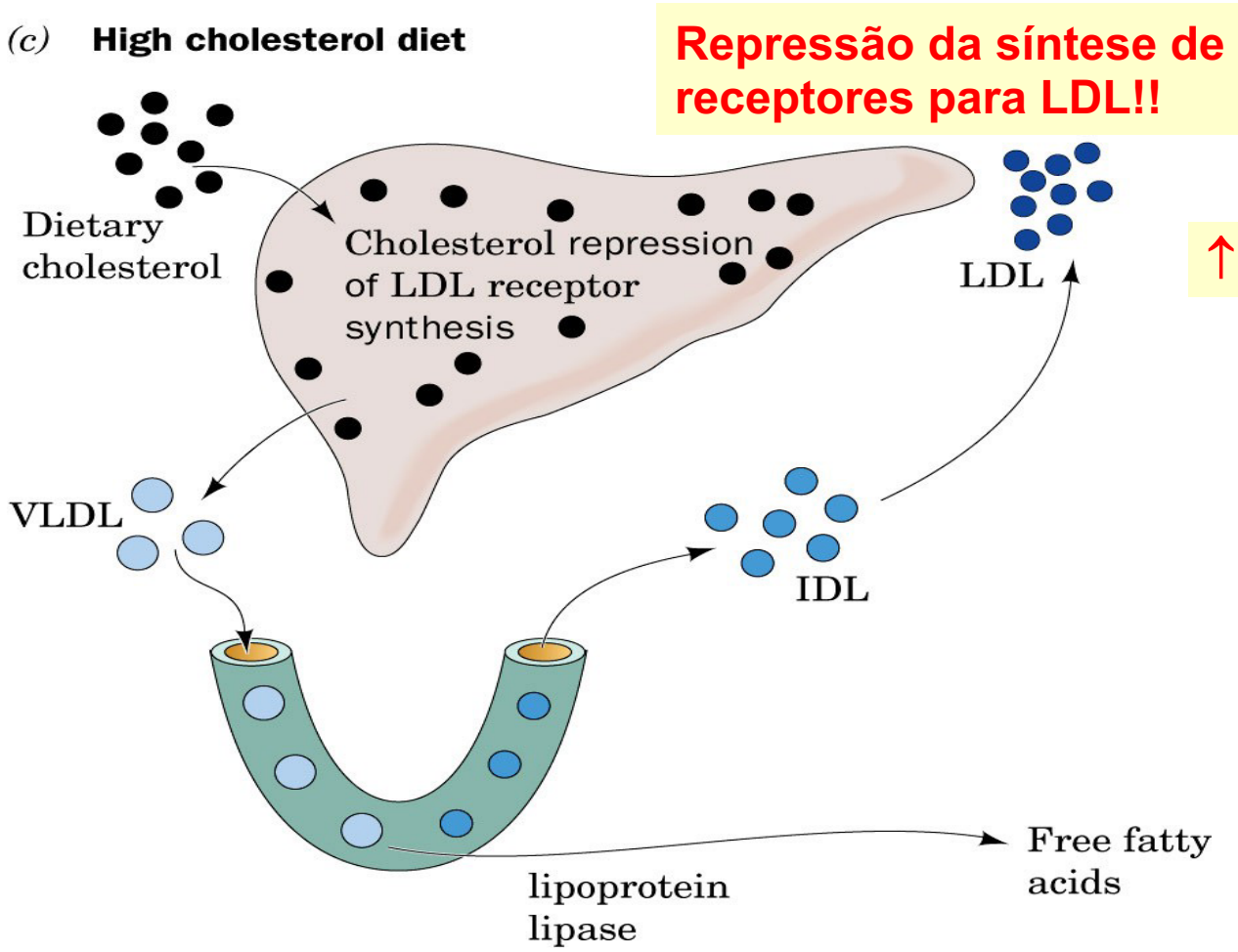
Aumento de LDL (“mau colesterol”)



(*a*) Indivíduos Normais



(*b*) Hipercolesterolemia Familiar

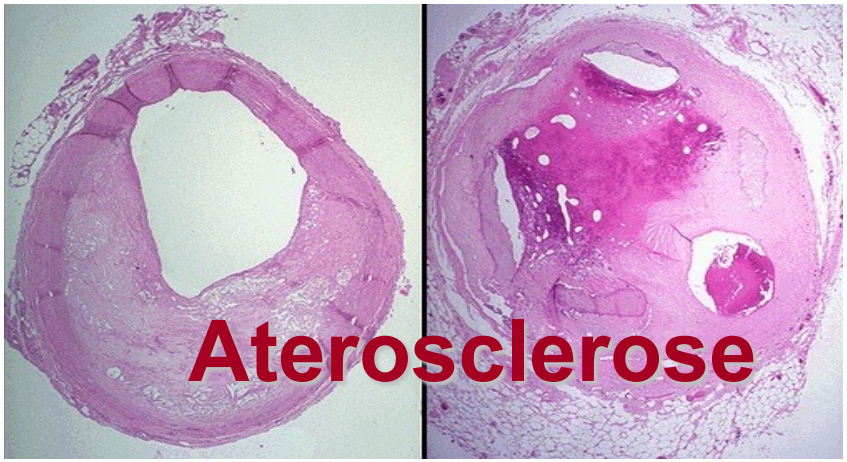


(*c*) Dieta Prolongada Rica em Colesterol

↑LDL

Consequências??

↑LDL



Infarto do Miocárdio
Acidente Vascular Cerebral

↑LDL

Terapias medicamentosas visando redução dos níveis de colesterol

-Redução de síntese de colesterol

-Aumento da excreção na forma de sais biliares

-Diminuição de sua absorção

Membranas

MEMBRANAS

- As membranas tem estruturas tão diversas quanto funções

- Entretanto, várias características são comuns:

  - Formam barreiras entre compartimentos
  - São constituídas principalmente de lipídios e proteínas
  - Contém carboidratos
  - Proteínas específicas desempenham funções distintas em membranas

Membranas celulares

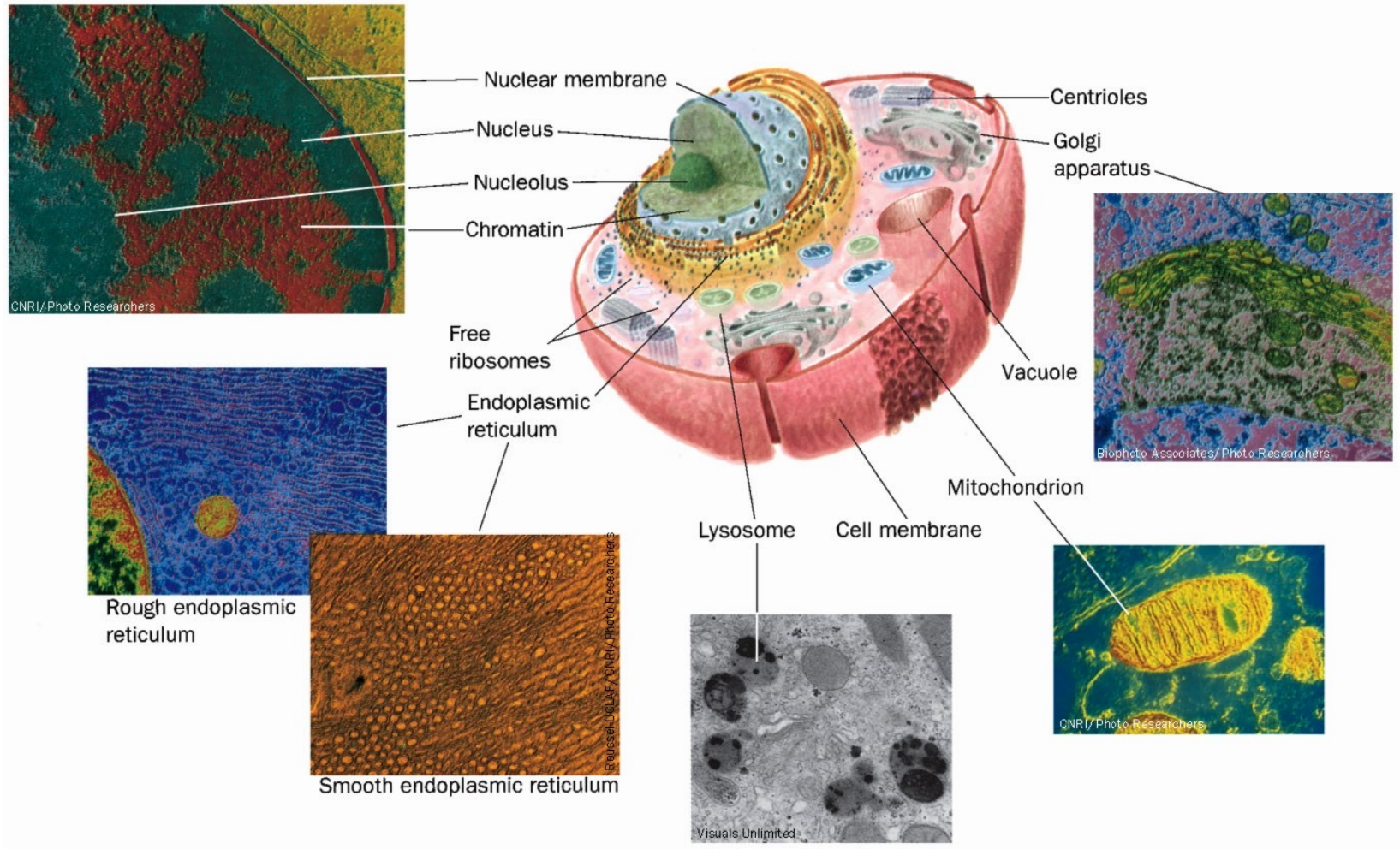
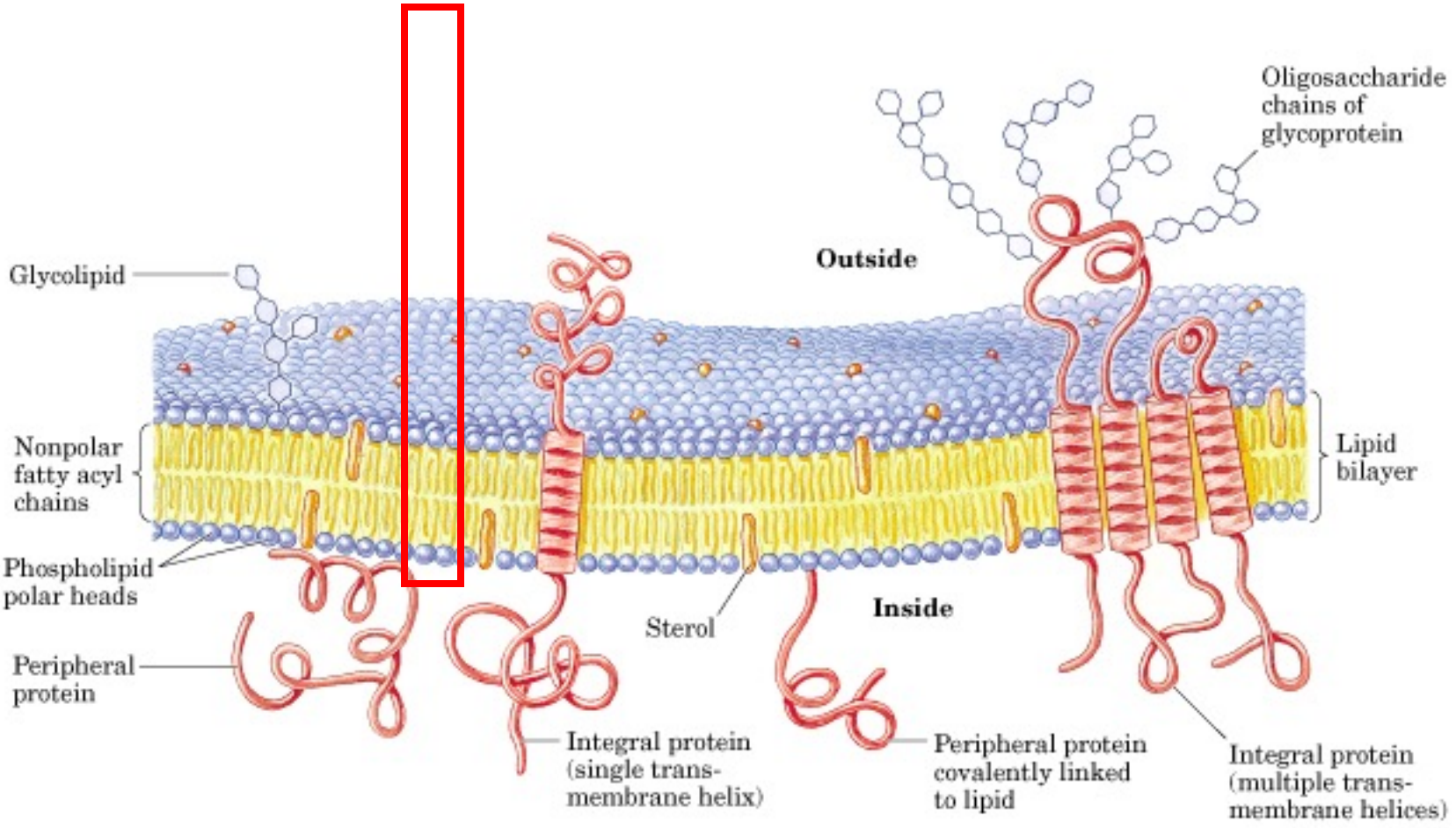
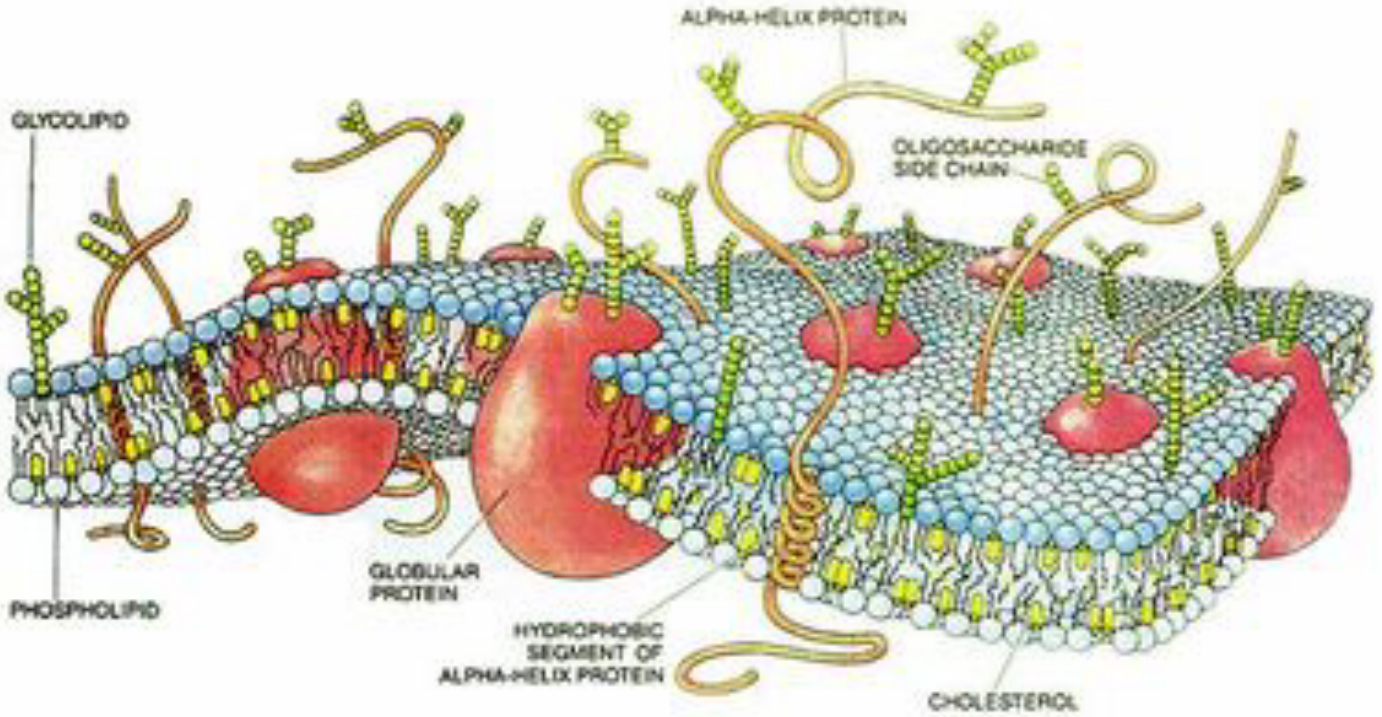


Figure 1-5 Schematic diagram of an animal cell accompanied by electron micrographs of its organelles.

LIPÍDIOS / MEMBRANAS




ALPHA-HELIX PROTEIN
GLYCOLIPID
OLIGOSACCHARIDE SIDE CHAIN
GLOBULAR PROTEIN
PHOSPHOLIPID
HYDROPHOBIC SEGMENT OF ALPHA-HELIX PROTEIN
CHOLESTEROL

Splitting of a membrane bilayer by the freeze-fracture technique

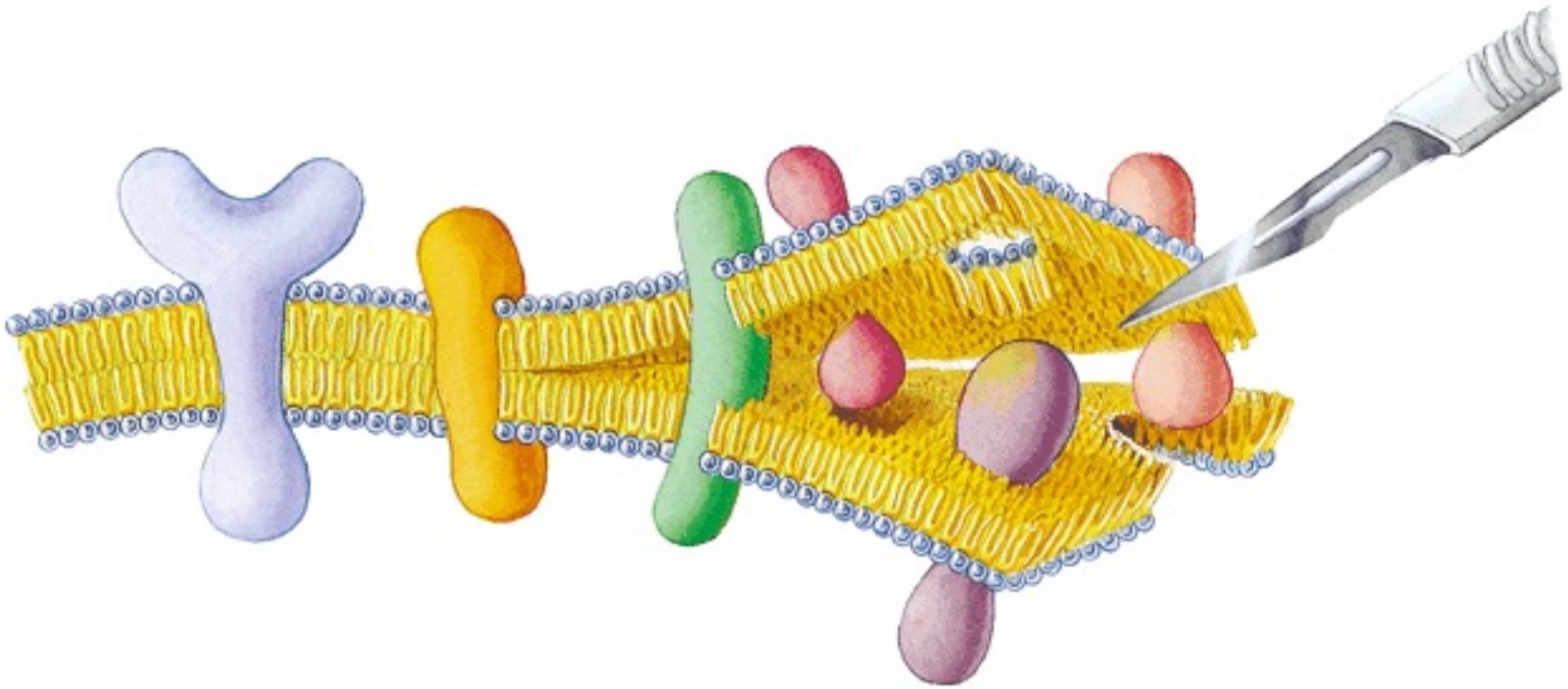
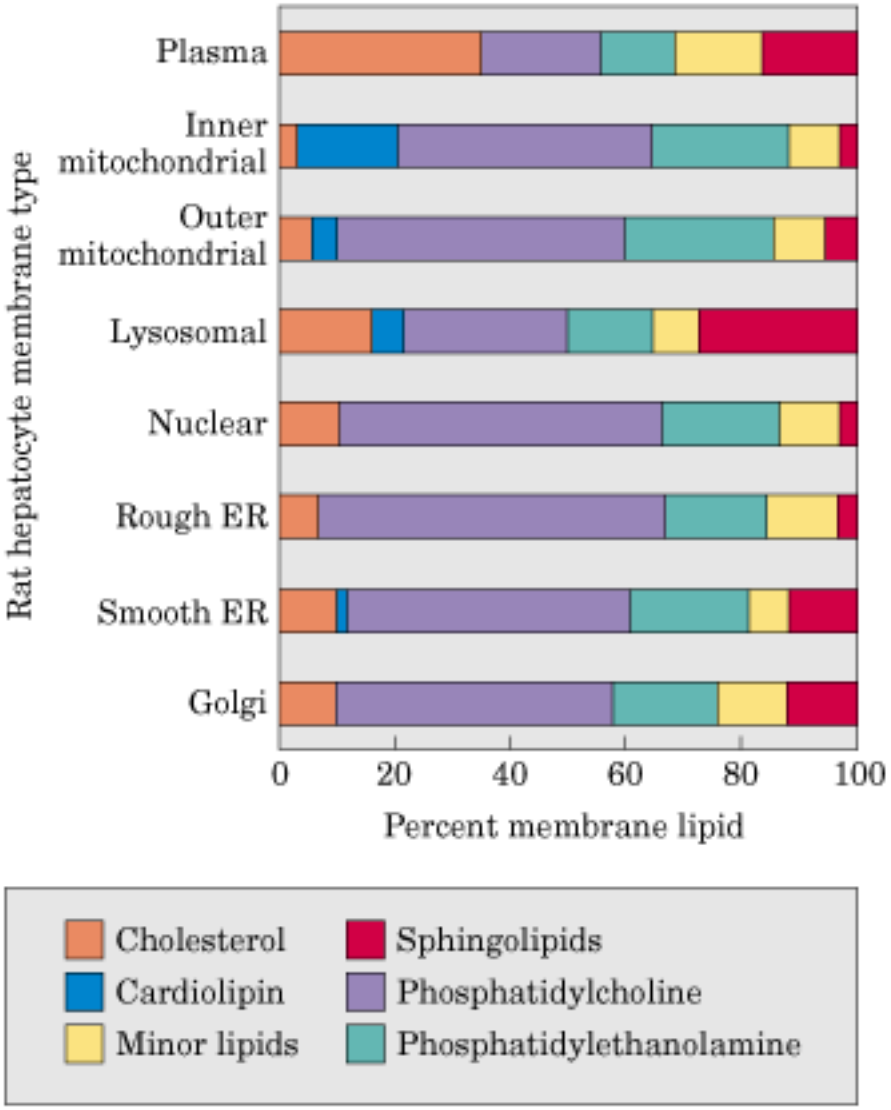


table 12–1

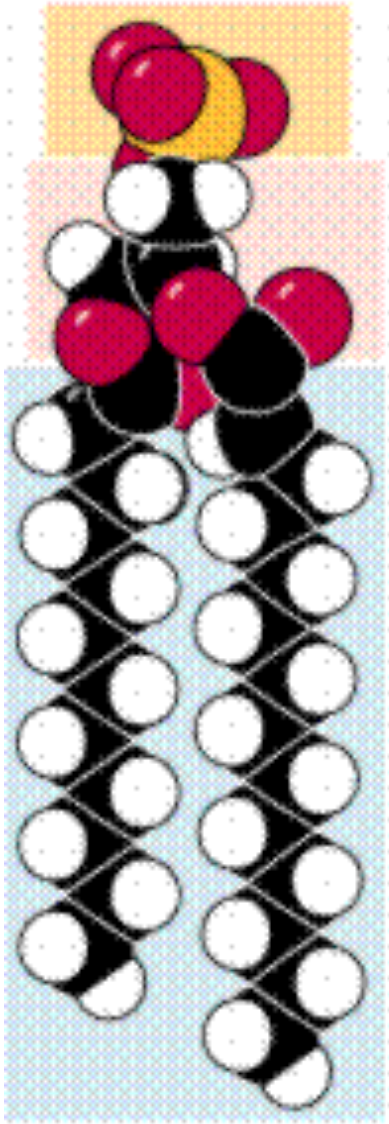
Major Components of Plasma Membranes in Various Organisms

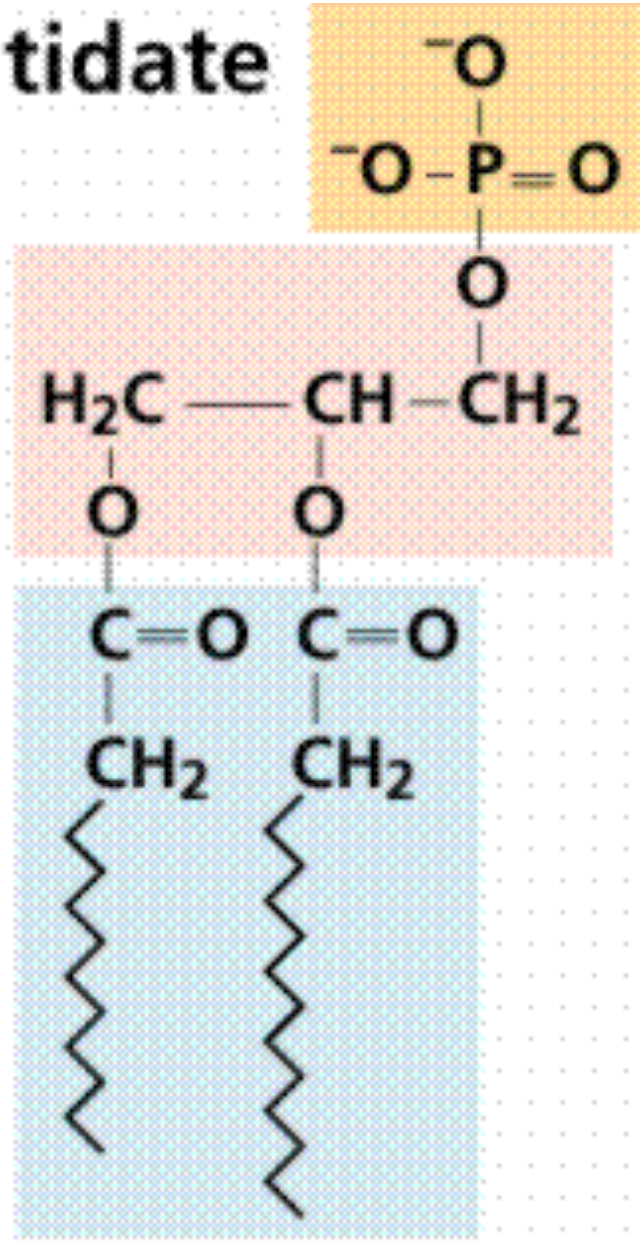
	Components (% by weight)				
	Protein	Phospholipid	Sterol	Sterol type	Other lipids
Human myelin sheath	30	30	19	Cholesterol	Galactolipids, plasmalogens
Mouse liver	45	27	25	Cholesterol	—
Maize leaf	47	26	7	Sitosterol	Galactolipids
Yeast	52	7	4	Ergosterol	Triacylglycerols, steryl esters
Paramecium (ciliated protist)	56	40	4	Stigmasterol	—
E. coli	75	25	0	—	—

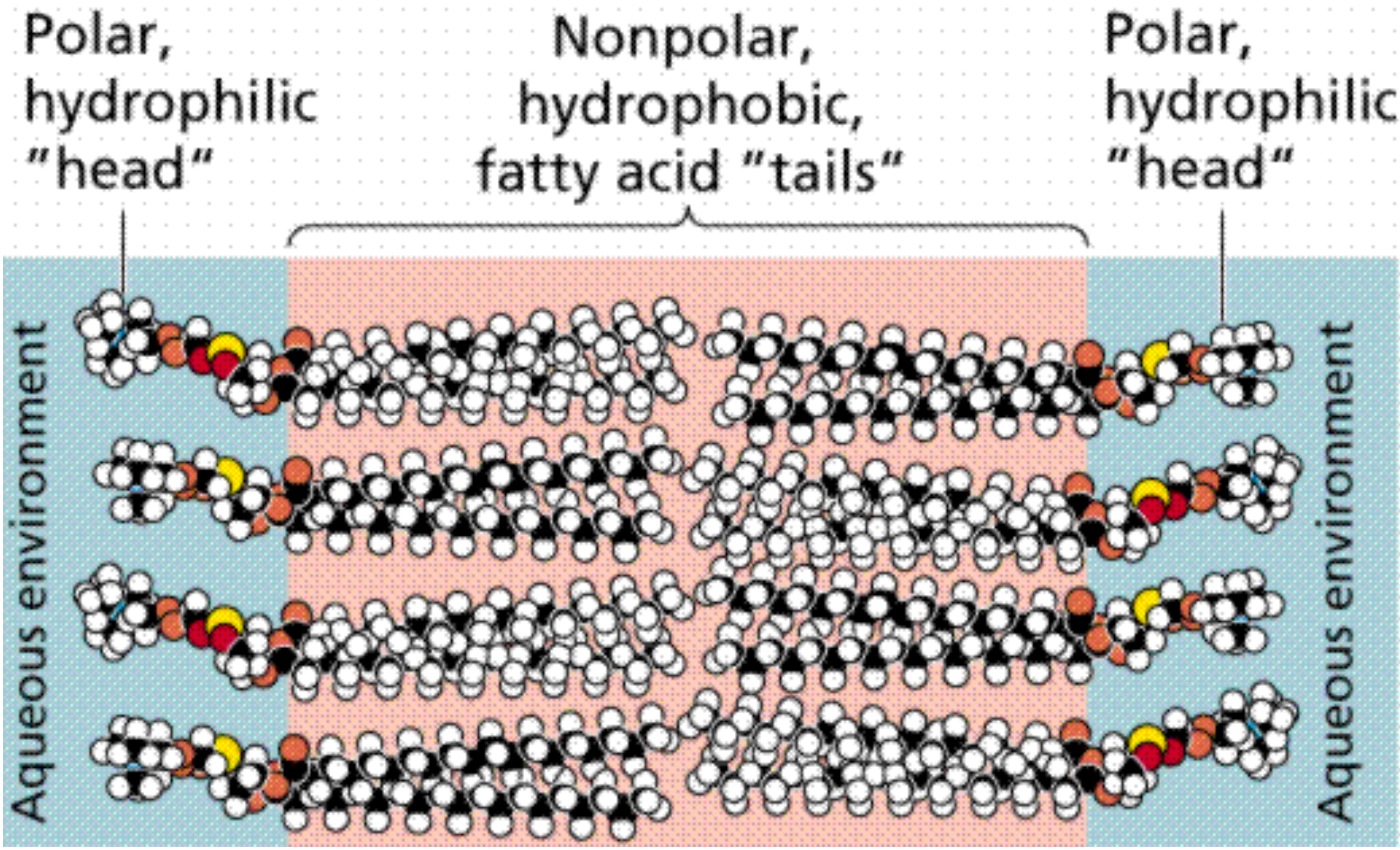
Lipid composition of the plasma membrane and organelle membranes of a rat hepatocyte

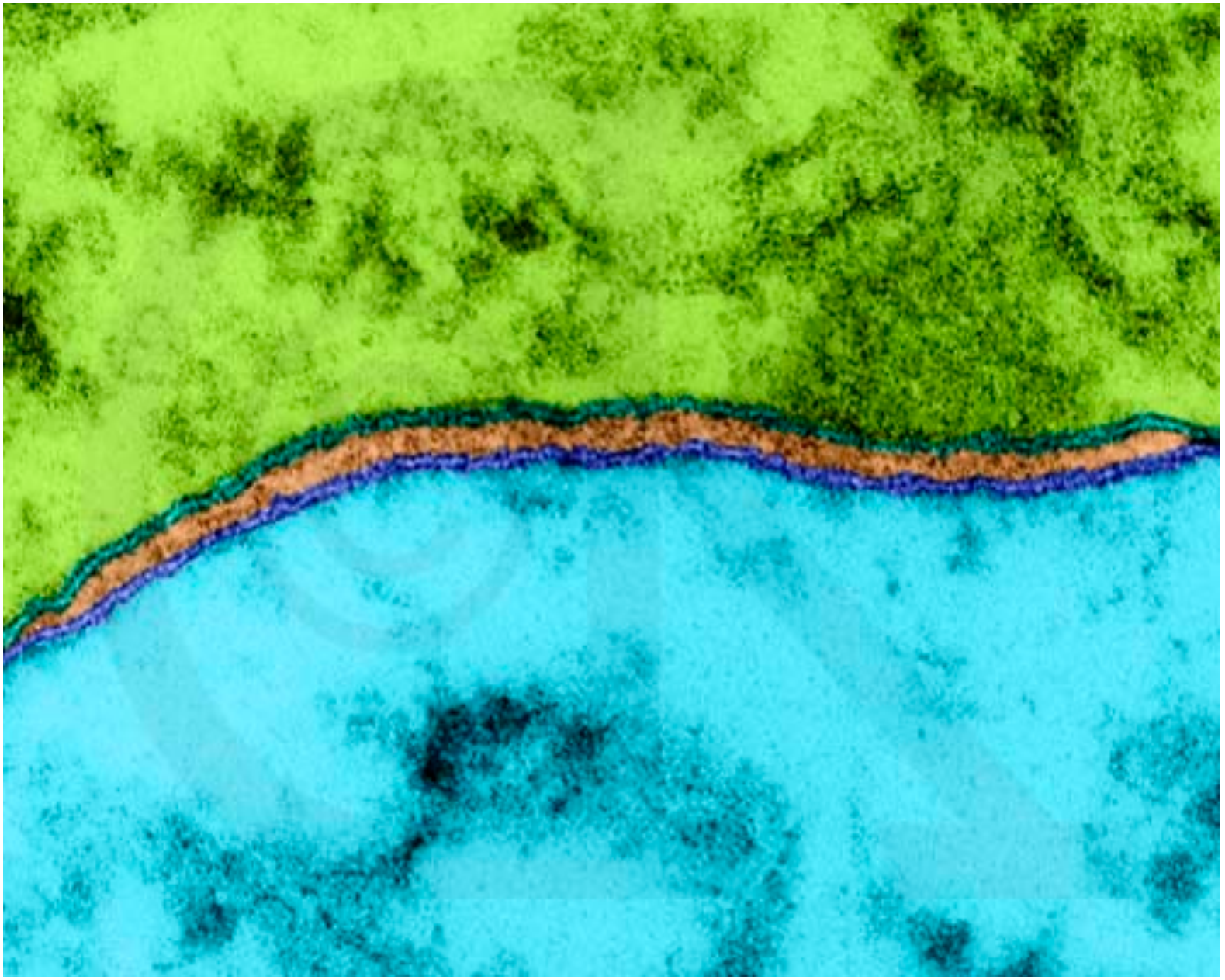


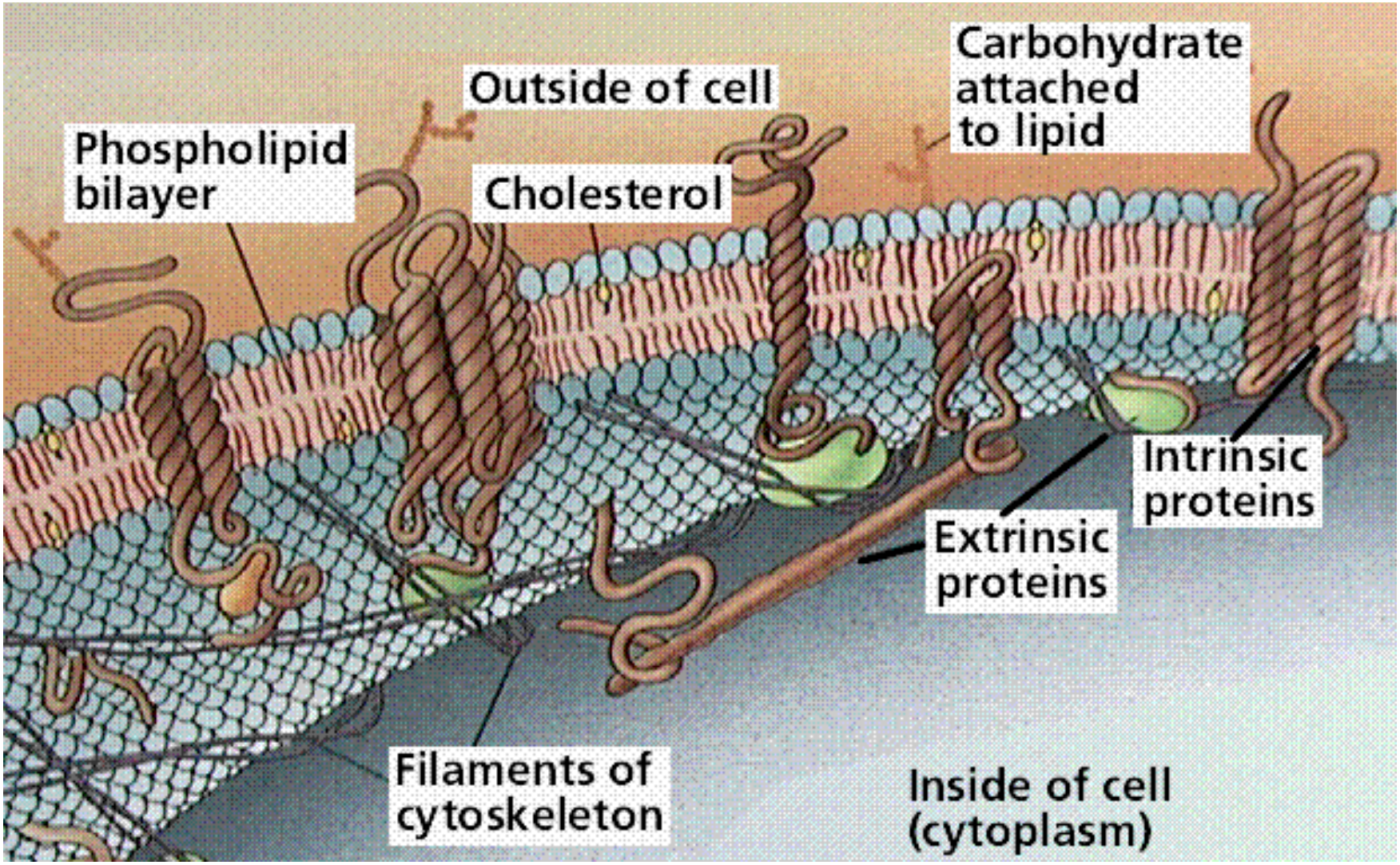
Phosphatidate

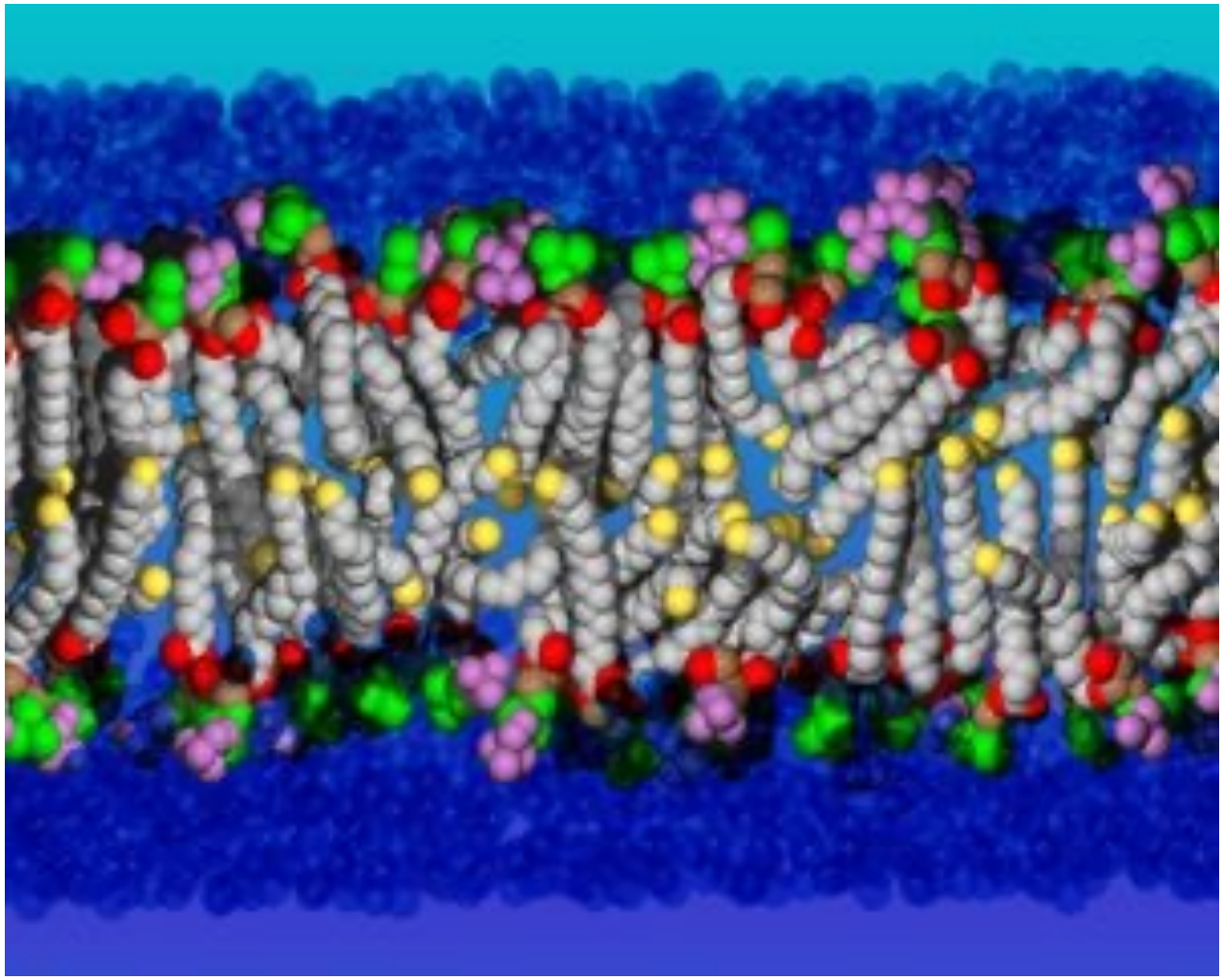





Polar,
hydrophilic
"head"
Nonpolar,
hydrophobic,
fatty acid "tails"
Polar,
hydrophilic
"head"
Aqueous environment
Aqueous environment

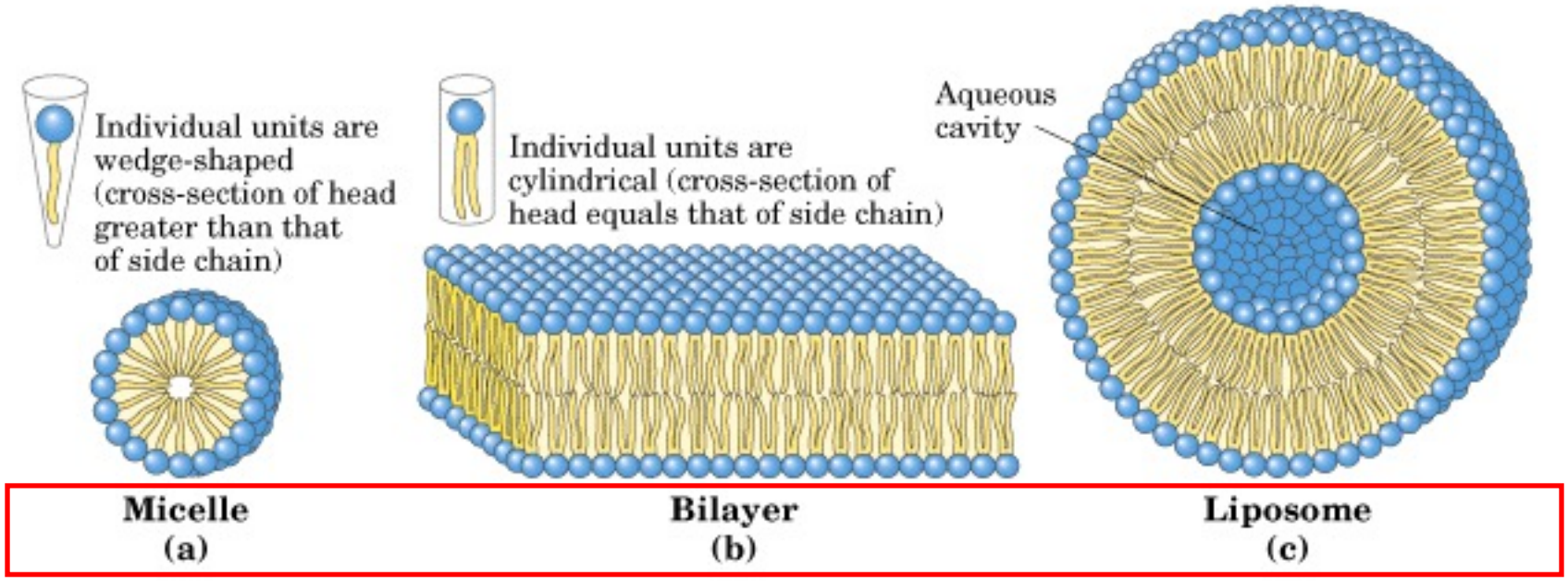



Carbohydrate attached to lipid
Outside of cell
Phospholipid bilayer
Cholesterol
Intrinsic proteins
Extrinsic proteins
Filaments of cytoskeleton
Inside of cell (cytoplasm)

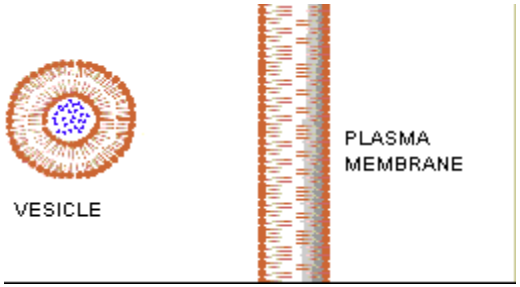


Lipídeos ANFIPÁTICOS podem formar micelas ou bicamadas lipídicas em soluções aquosas

Amphipathic lipid aggregates that form in water

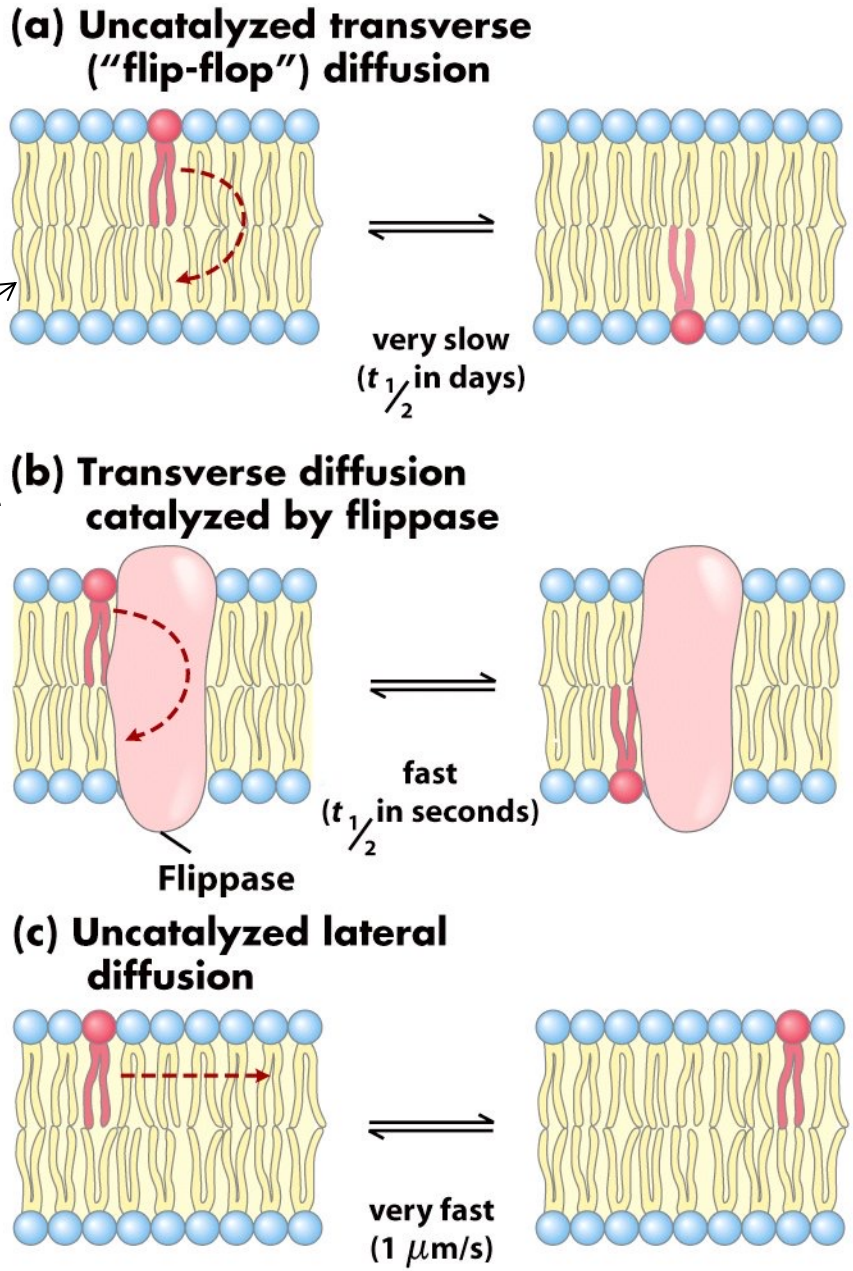


As membranas são fluidas...

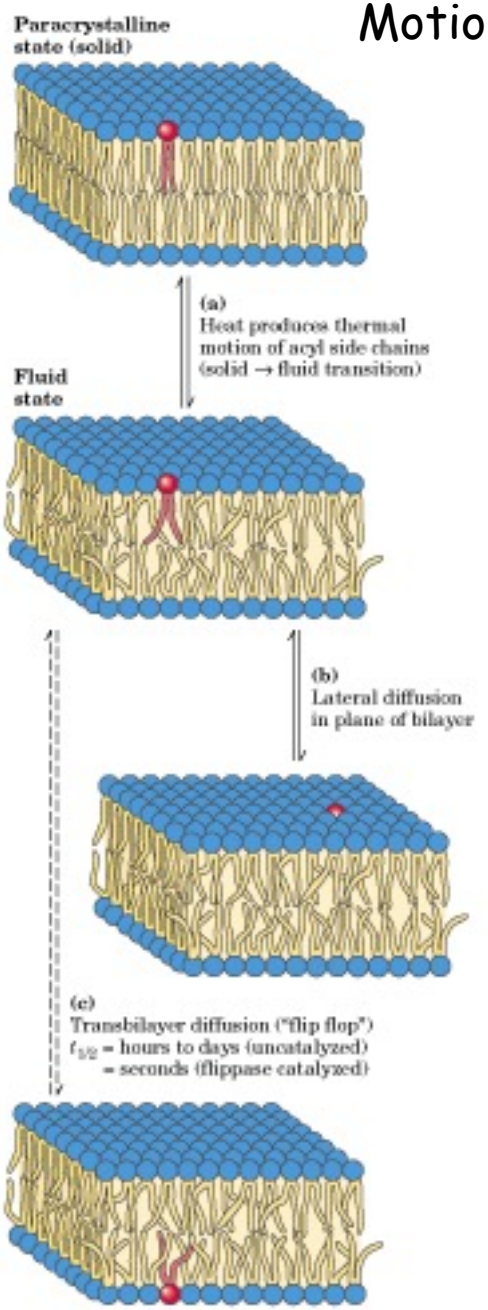

VESICLE
PLASMA
MEMBRANE

Difusão Transversal

Difusão Lateral



Motion of membrane lipids



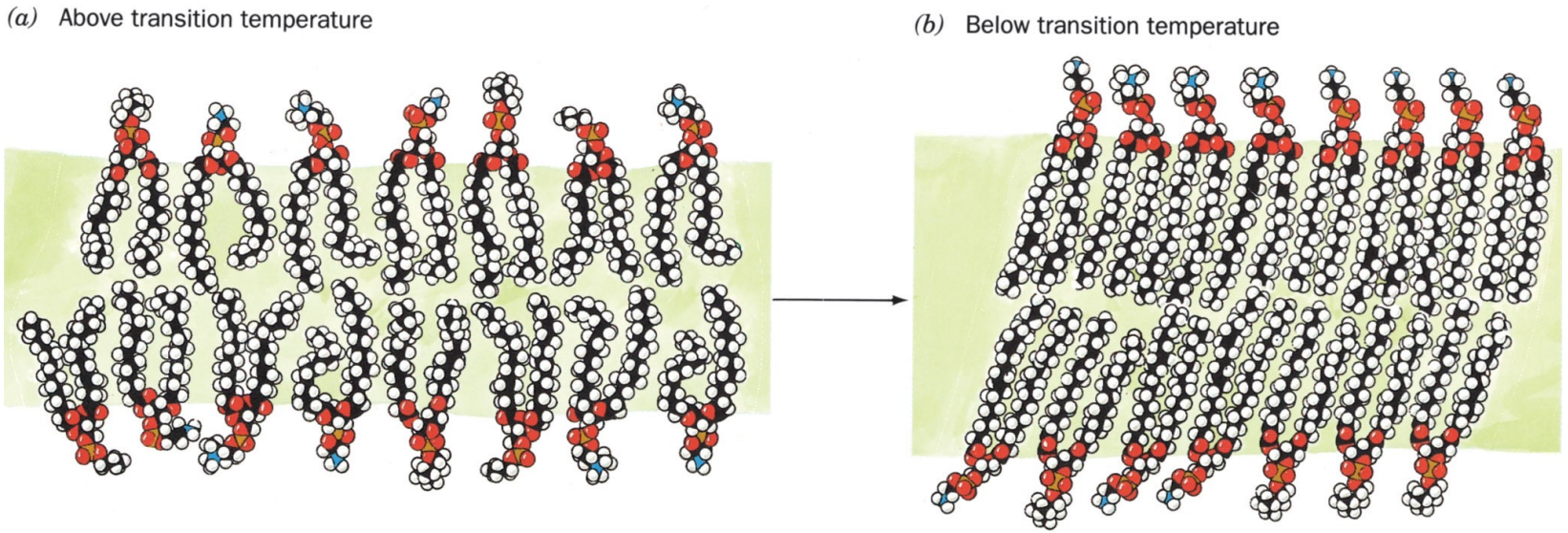
Que fatores que influenciam a fluidez da mb?

Temperatura

Composição de ácidos graxos

Colesterol

Temperatura de Transição



Líquido

Gel “sólido”

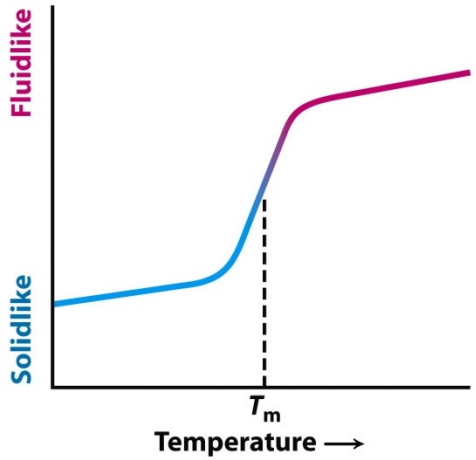


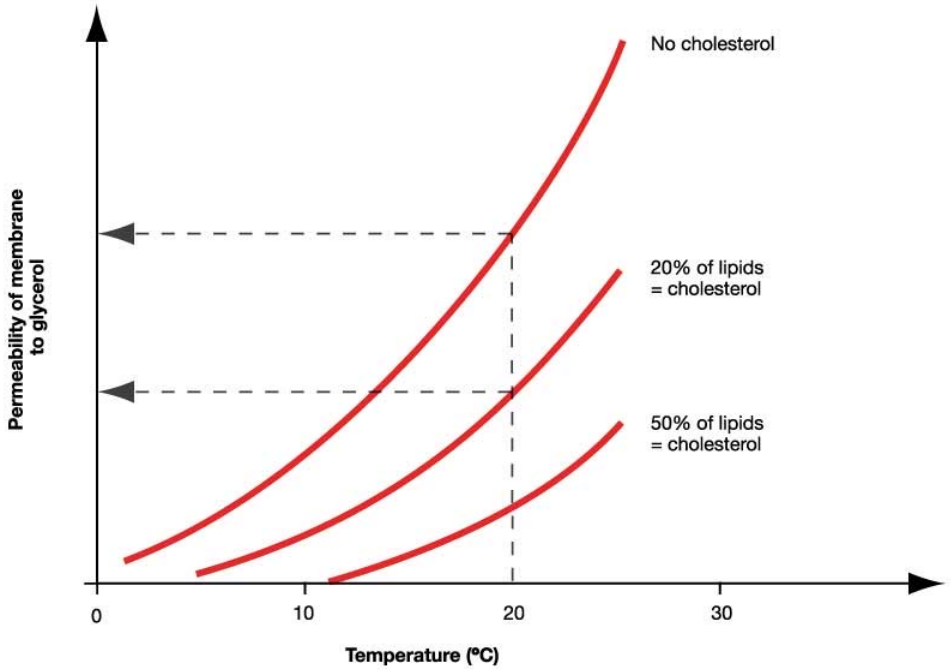
Figure 12-32
Biochemistry, Sixth Edition

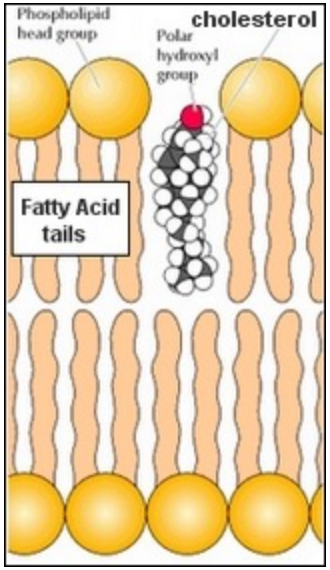
Composição de Ácidos Graxos

TABLE 11–2 Fatty Acid Composition of *E. coli* Cells Cultured at Different Temperatures

	*Percentage of total fatty acids**			
	10 °C	*20 °C*	*30 °C*	*40 °C*
Myristic acid (14:0)	4	4	4	8
Palmitic acid (16:0)	18	25	29	48
Palmitoleic acid (16:1)	26	24	23	9
Oleic acid (18:1)	38	34	30	12
Hydroxymyristic acid	13	10	10	8
Ratio of unsaturated to saturated†	2.9	2.0	1.6	0.38

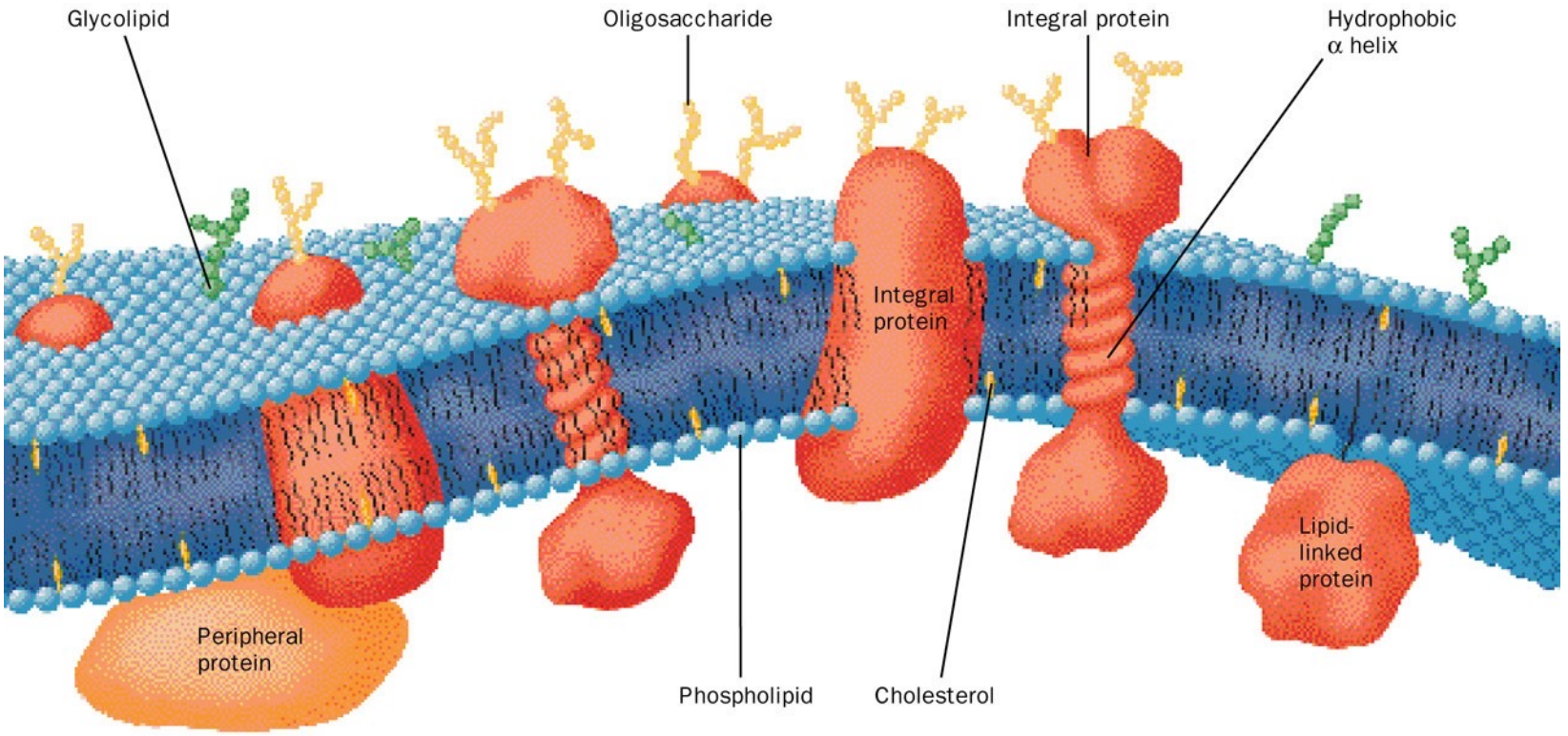
Colesterol


Permeability of membrane to glycerol
No cholesterol
20% of lipids = cholesterol
50% of lipids = cholesterol
0
10
20
30
Temperature (°C)


Phospholipid head group
cholesterol
Polar hydroxyl group
Fatty Acid tails

Membranas Biológicas

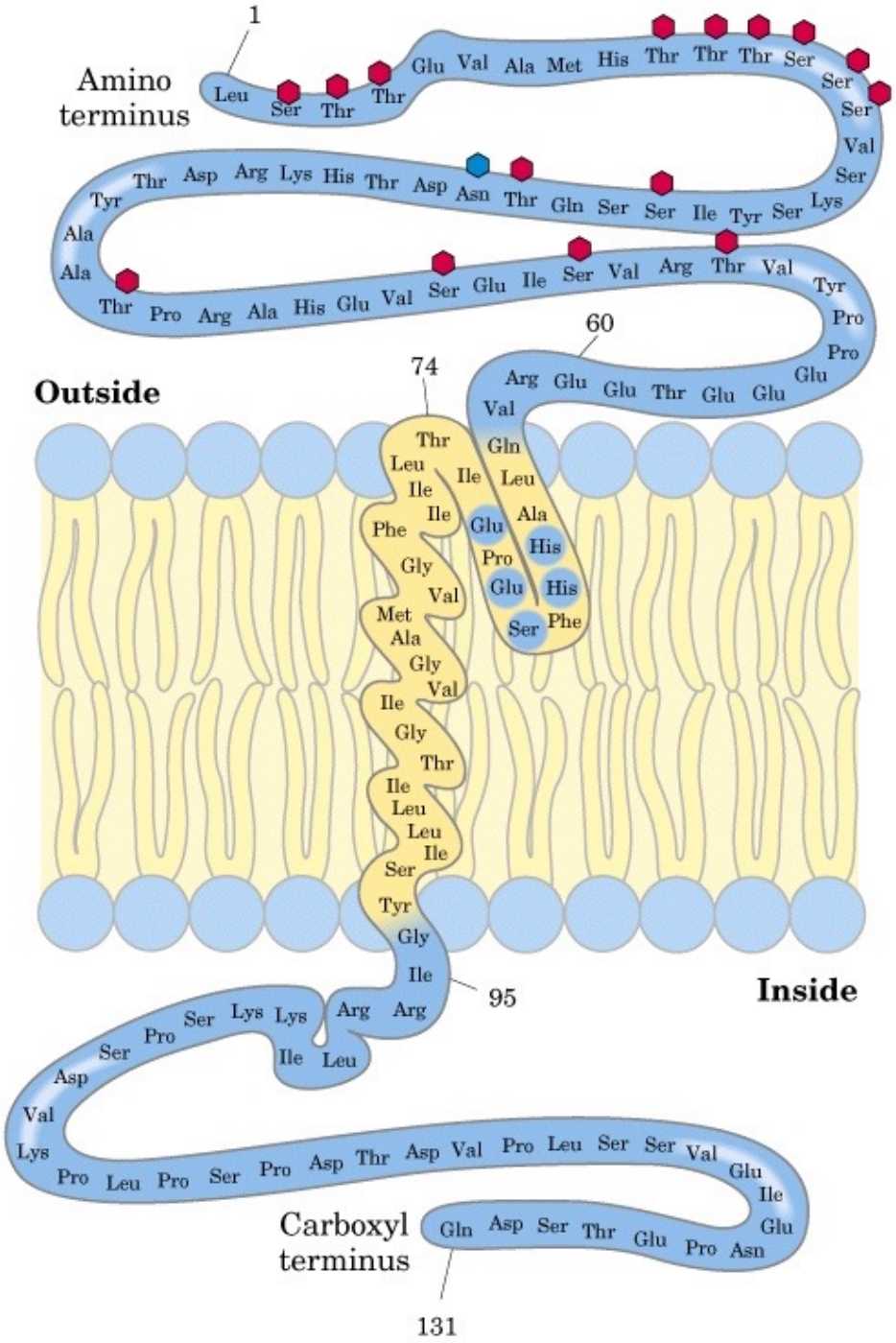
Membranas Biológicas



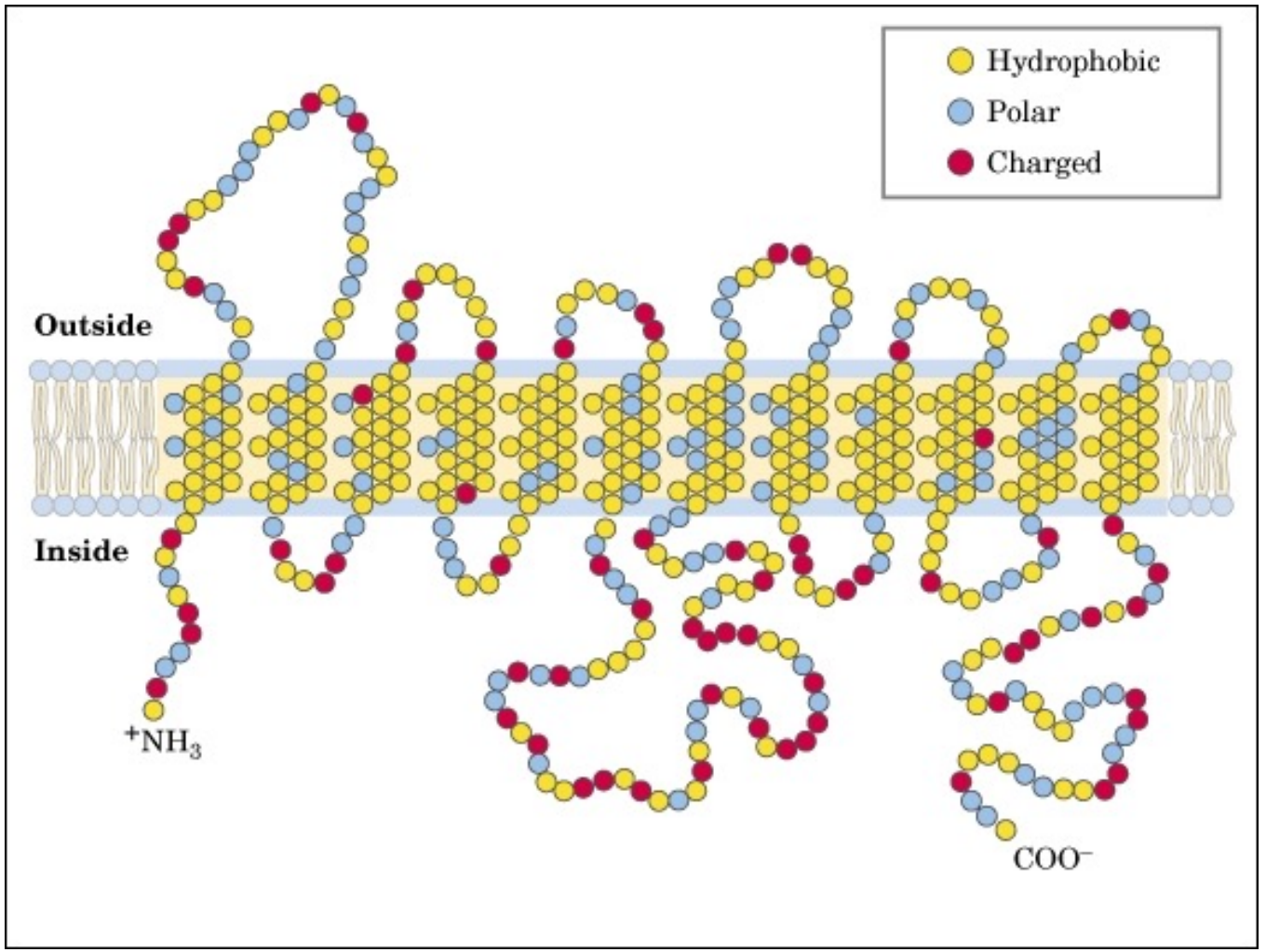
Modelo do Mosaico Fluido (1972, Singer&Nicholson)

A teoria postula que as “Proteínas são icebergs flutuando em um mar de lipídeos”

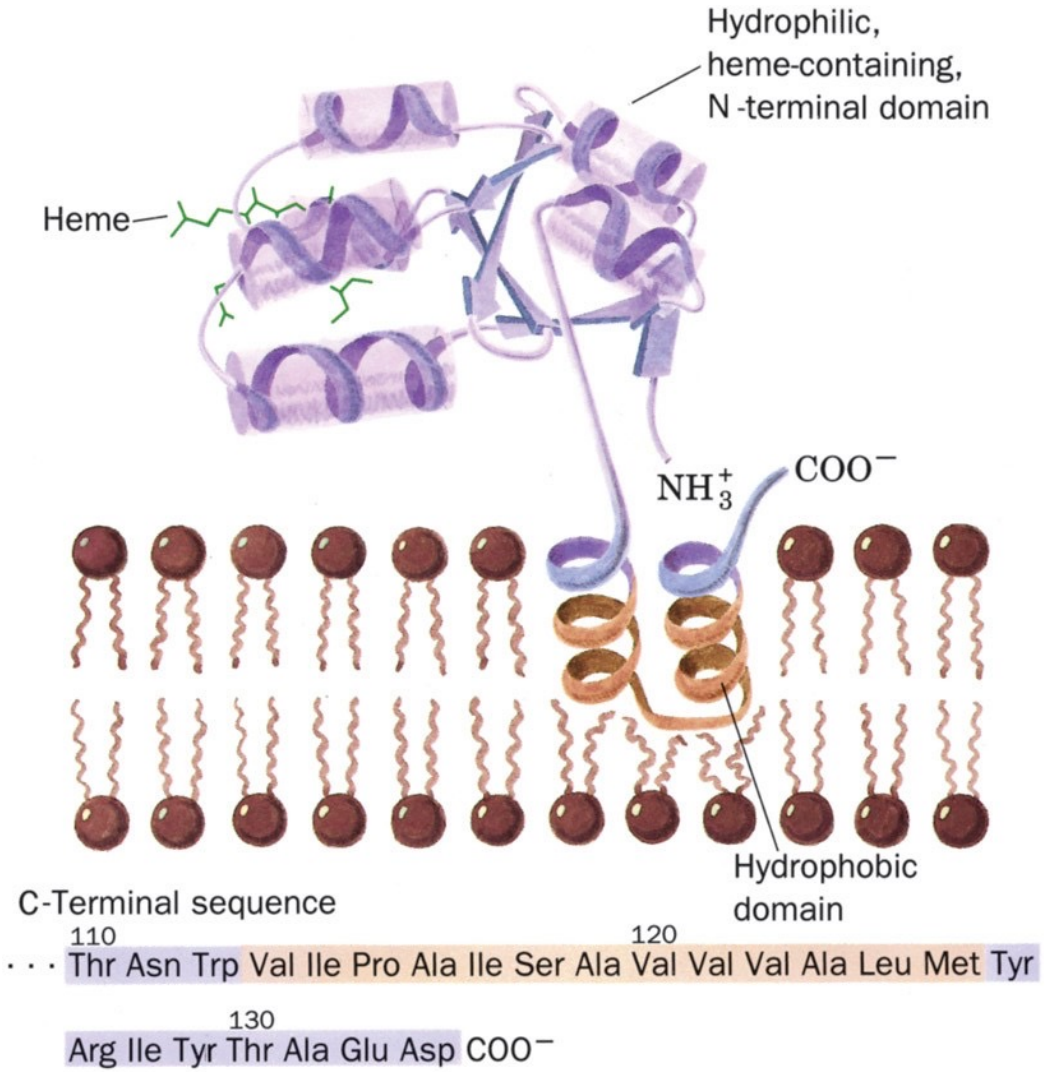
Proteína Integral



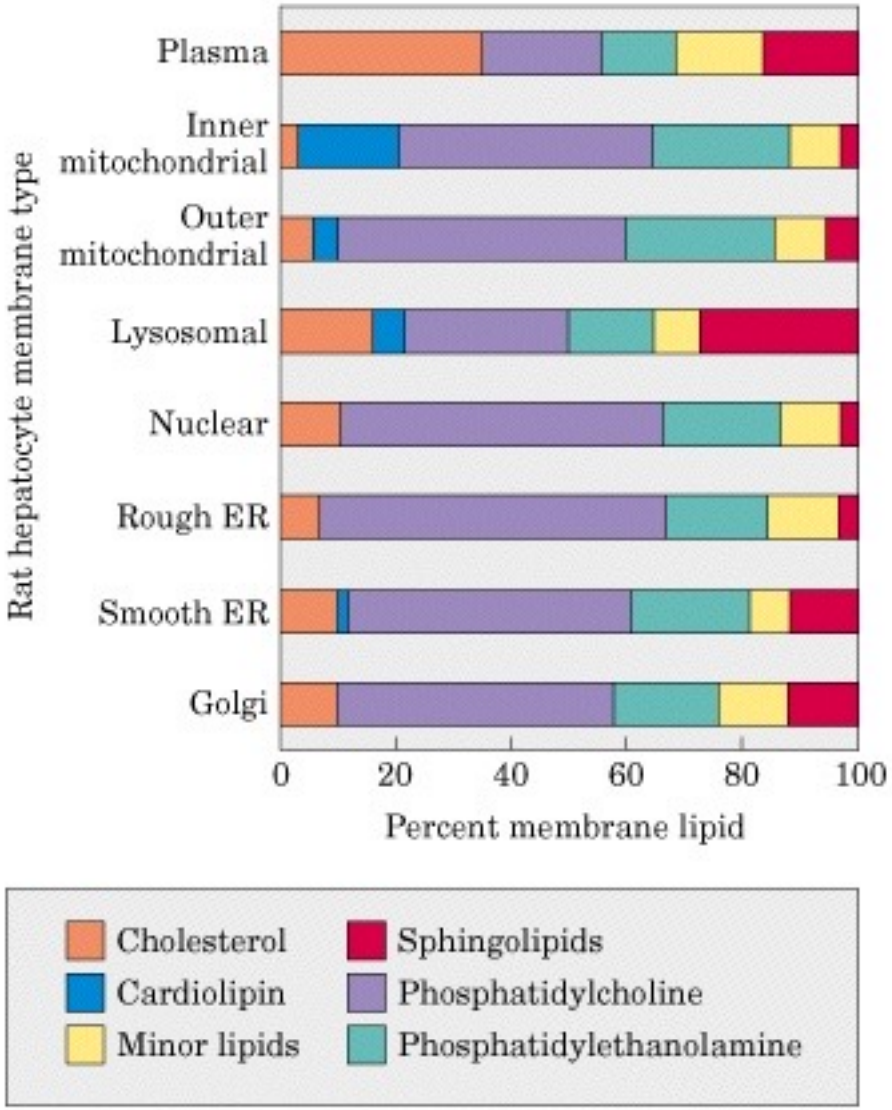
Proteína Integral



Proteína Periférica



Composição de lipídeos de uma membrana varia bastante de acordo com o tipo de organela e o tipo celular

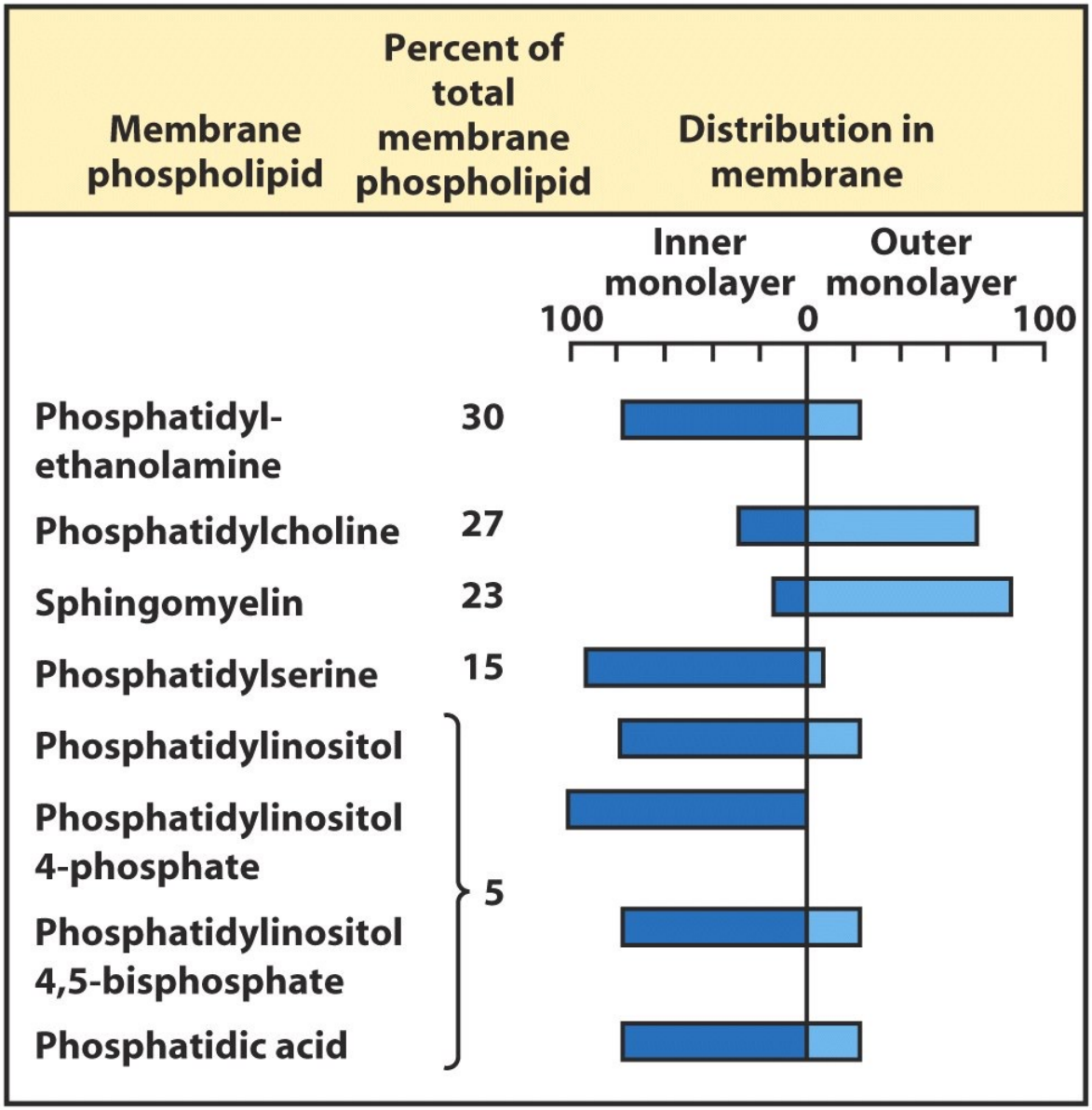

Plasma
Inner mitochondrial
Outer mitochondrial
Lysosomal
Nuclear
Rough ER
Smooth ER
Golgi
Rat hepatocyte membrane type
0
20
40
60
80
100
Percent membrane lipid
Cholesterol
Cardiolipin
Minor lipids
Sphingolipids
Phosphatidylcholine
Phosphatidylethanolamine

Lipid	Human Erythrocyte	Human Myelin	Beef Heart Mitochondria	*E. coli*
Phosphatidic acid	1.5	0.5	0	0
Phosphatidylcholine	19	10	39	0
Phosphatidylethanolamine	18	20	27	65
Phosphatidylglycerol	0	0	0	18
Phosphatidylinositol	1	1	7	0
Phosphatidylserine	8.5	8.5	0.5	0
Cardiolipin	0	0	22.5	12
Sphingomyelin	17.5	8.5	0	0
Glycolipids	10	26	0	0
Cholesterol	25	26	3	0

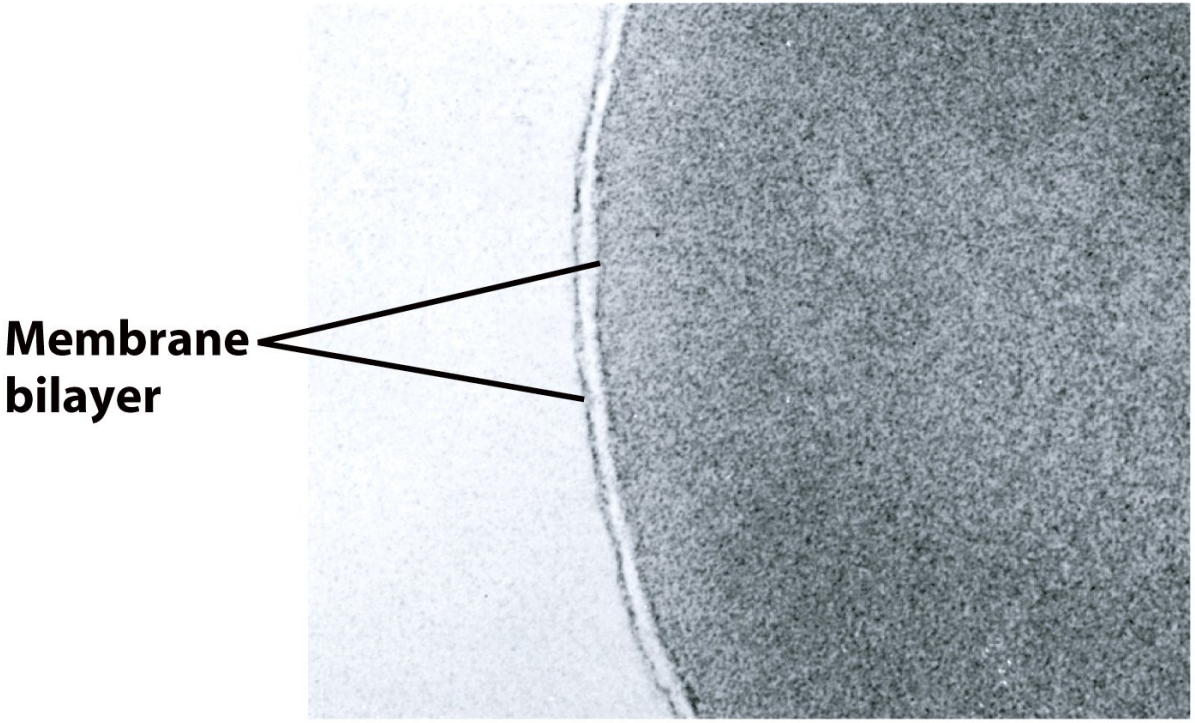
[a]The values given are weight percent of total lipid.

Source: Tanford, C., *The Hydrophobic Effect, p.* 109, Wiley (1980).

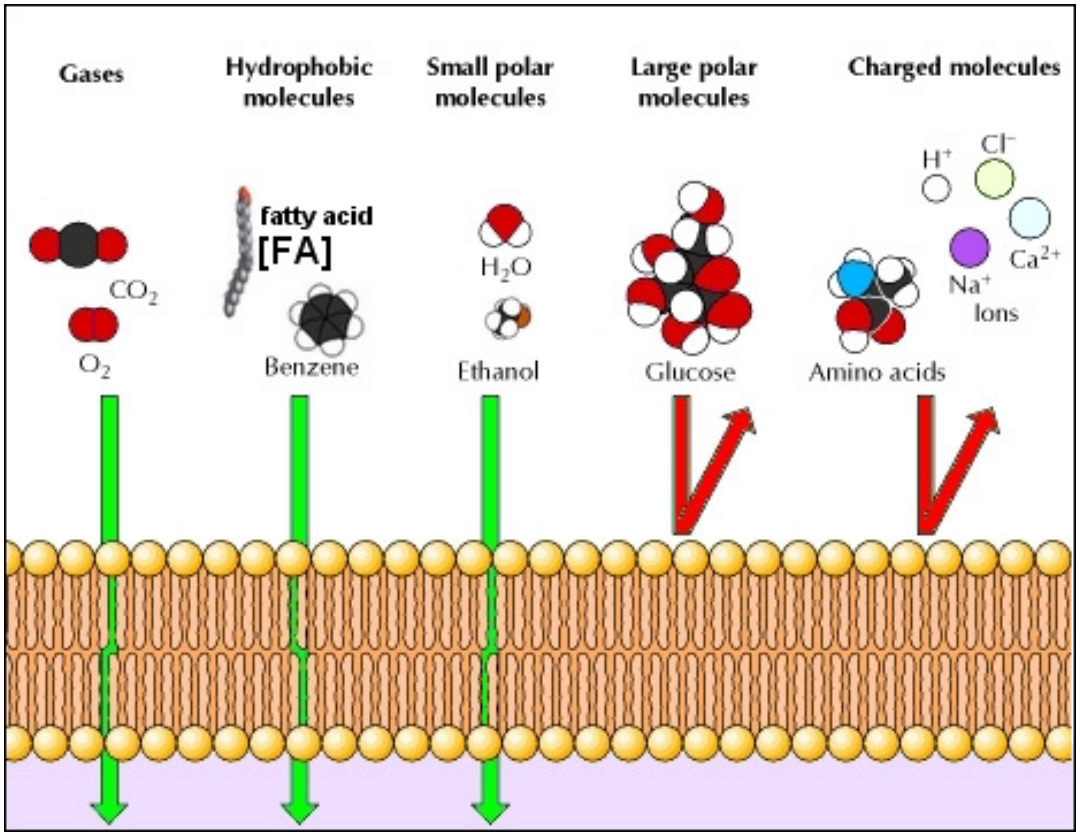
A distribuição de fosfolipídeos na bicamada é assimétrica


Membrane phospholipid
Percent of total membrane phospholipid
Distribution in membrane
Inner monolayer
Outer monolayer
100
0
100
Phosphatidyl-ethanolamine
30
Phosphatidylcholine
27
Sphingomyelin
23
Phosphatidylserine
15
Phosphatidylinositol
Phosphatidylinositol 4-phosphate
Phosphatidylinositol 4,5-bisphosphate
Phosphatidic acid
5

Transporte através das Membranas



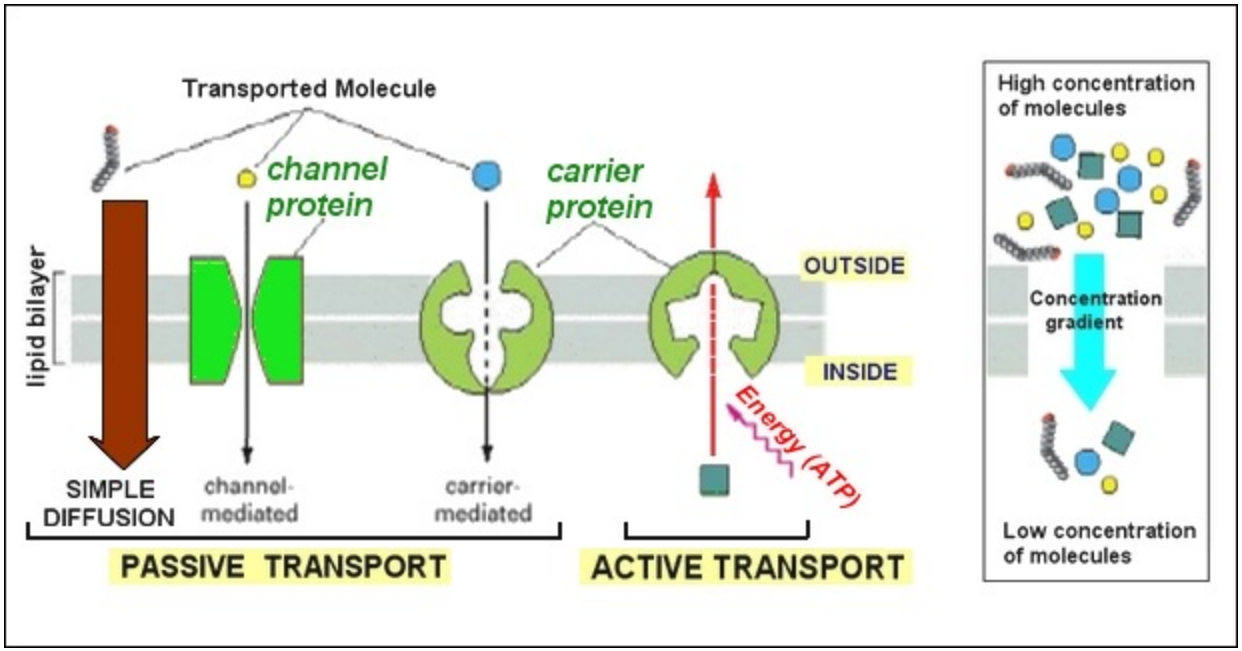
Permeabilidade Seletiva

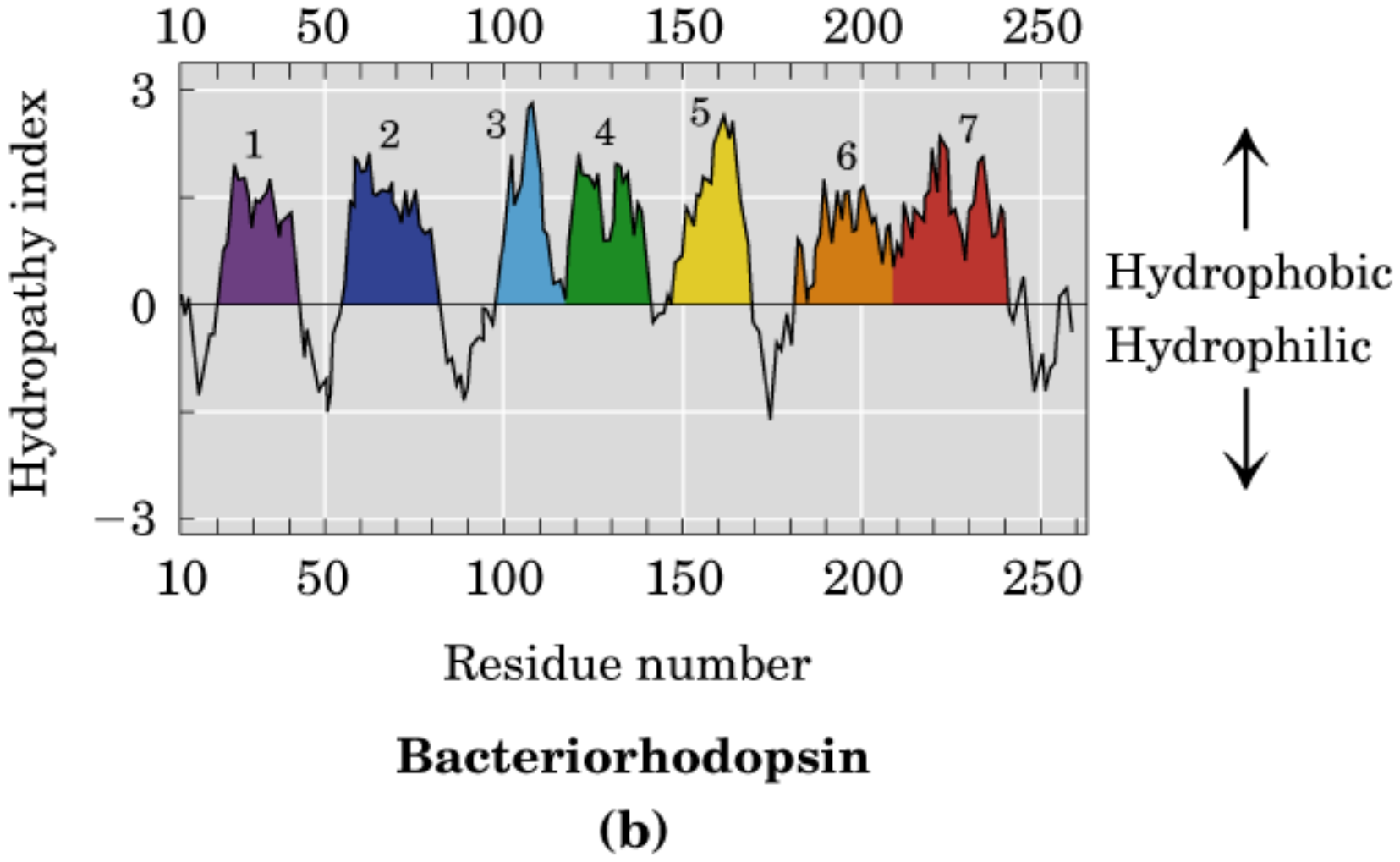


Tamanho =pequenas molécula atravessam, mas grandes não
EX: H_2O, O_2, CO_2, etanol (PM=46), & glicerol (PM=92) atravessa, mas glicose (PM=180) não atravess

Polaridade=Moléculas hidrofóbicas podem se "dissolver" na bicamada, e moléculas polares não.
Etanol é mais apolar que glicerol, e portanto atravessa mais rapidamente.

Carga= Membranas são impermeáveis a íons carregados.

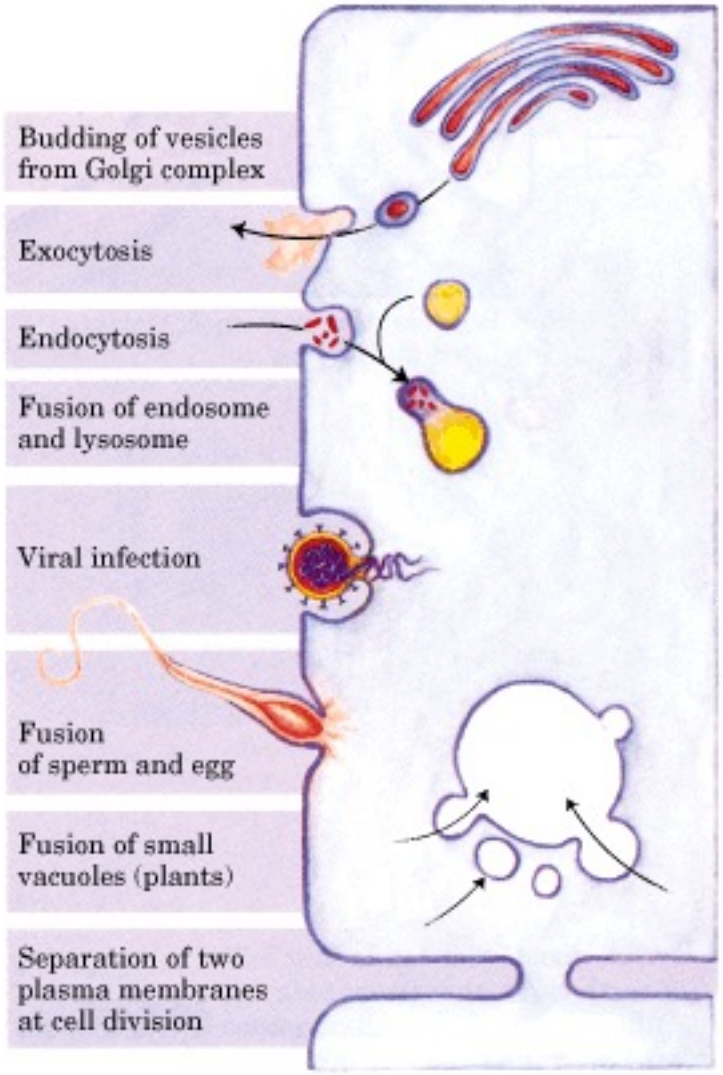

Transported Molecule
channel protein
carrier protein
lipid bilayer
OUTSIDE
INSIDE
Energy (ATP)
SIMPLE DIFFUSION
channel-mediated
carrier-mediated
PASSIVE TRANSPORT
ACTIVE TRANSPORT
High concentration of molecules
Concentration gradient
Low concentration of molecules



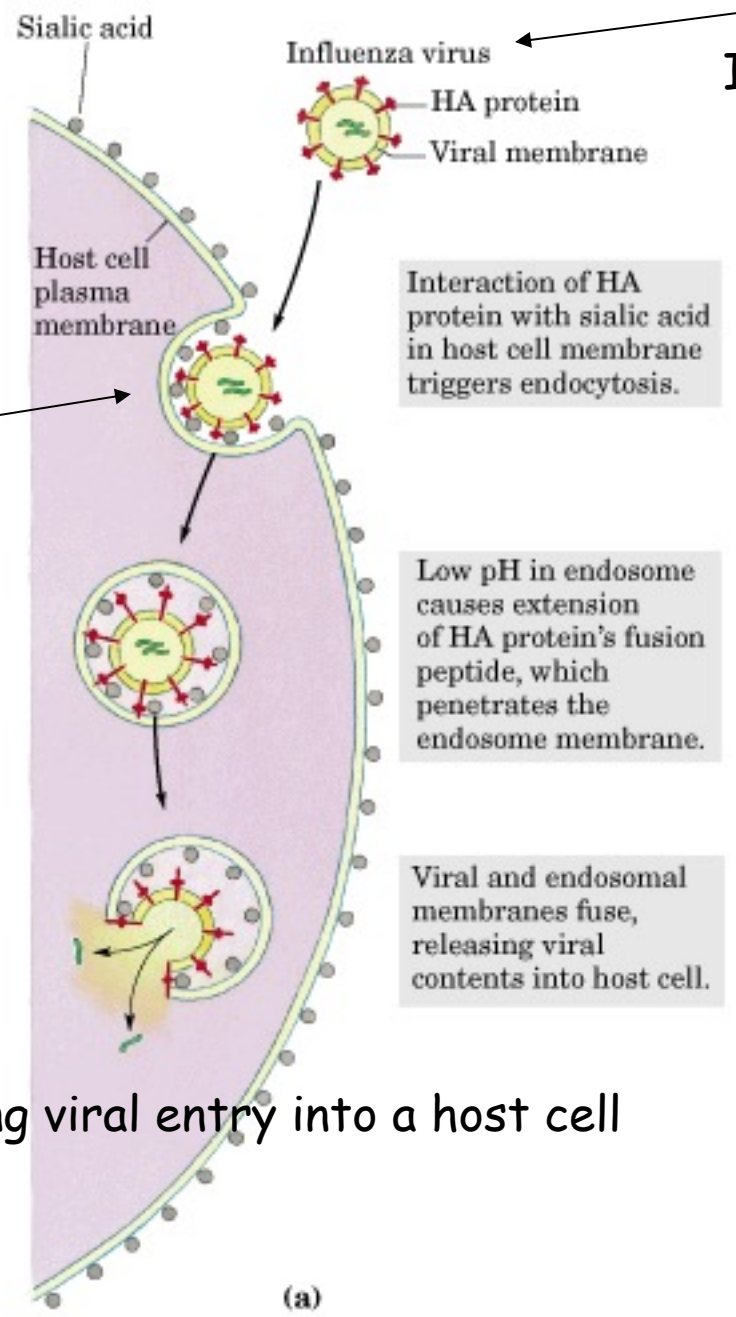
Bacteriorhodopsin

(b)

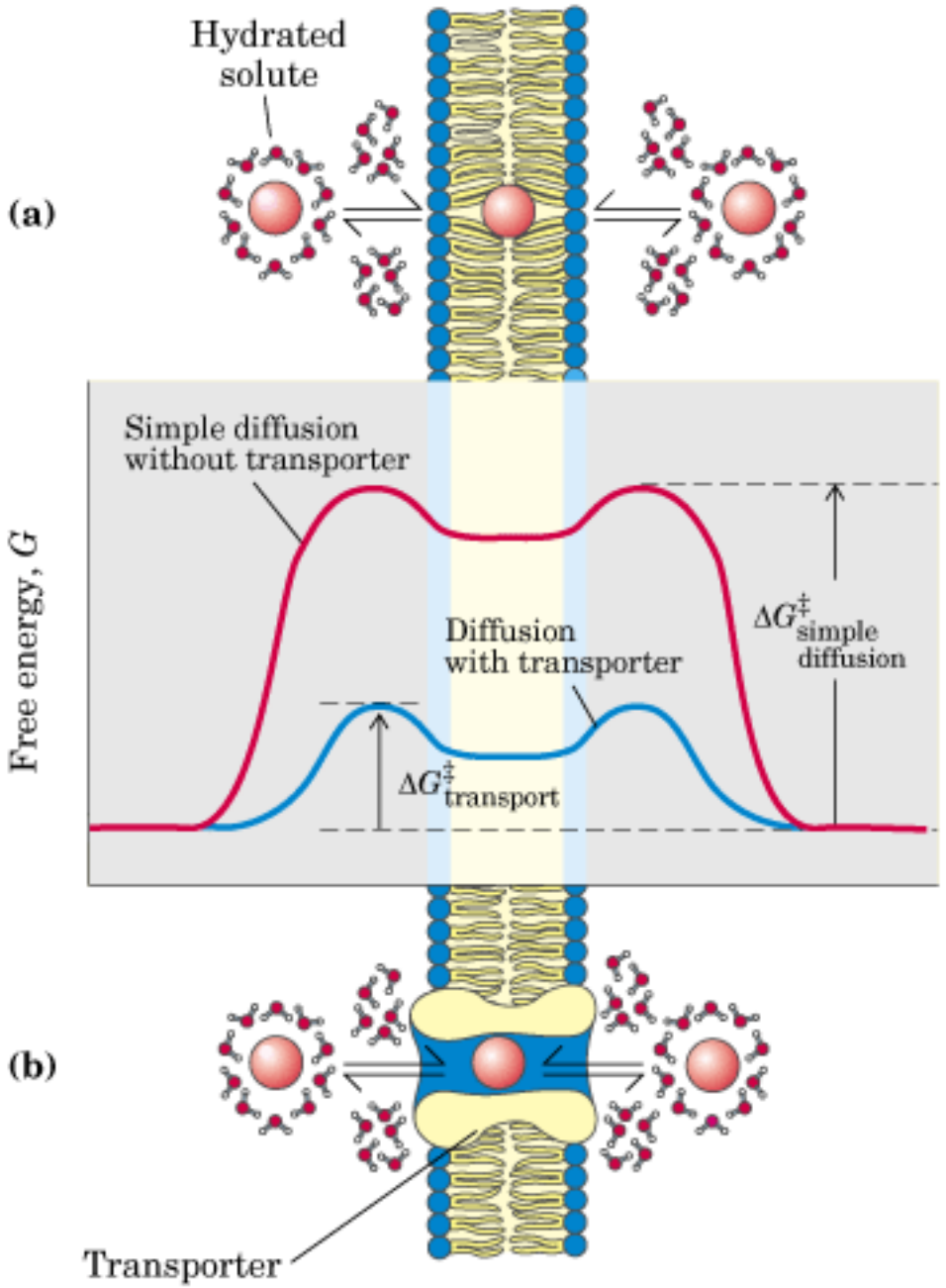
Membrane fusion



Influenza virus



Membrane fusion during viral entry into a host cell


Hydrated solute
(a)
Simple diffusion without transporter
Diffusion with transporter
$\Delta G^{\ddagger}_{\text{simple diffusion}}$
$\Delta G^{\ddagger}_{\text{transport}}$
Free energy, G
(b)
Transporter

Cada tipo de membrana tem lipídeos e proteínas característicos

Certos neurônios tem uma bainha de mielina, uma extensão da membrana plasmática que envolve a célula e funciona como isolante elétrico. Tem grande proporção em peso de lipídeos.

Asymmetric distribution of phospholipids between the inner and outer monolayers of the erythrocyte plasma membrane

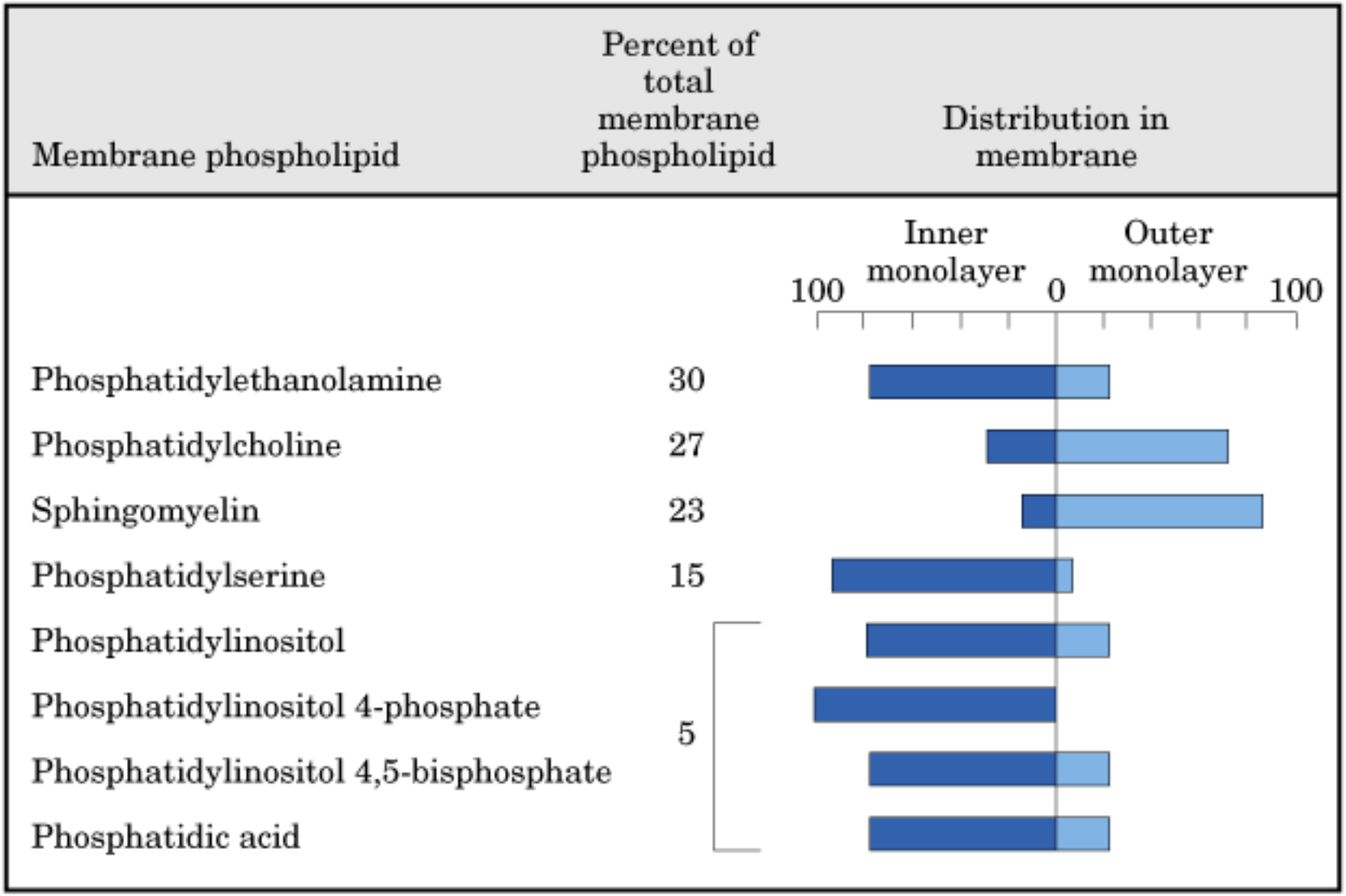


table 12–2

Fatty Acid Composition of *E. coli* Cells Cultured at Different Temperatures

	Percentage of total fatty acids*			
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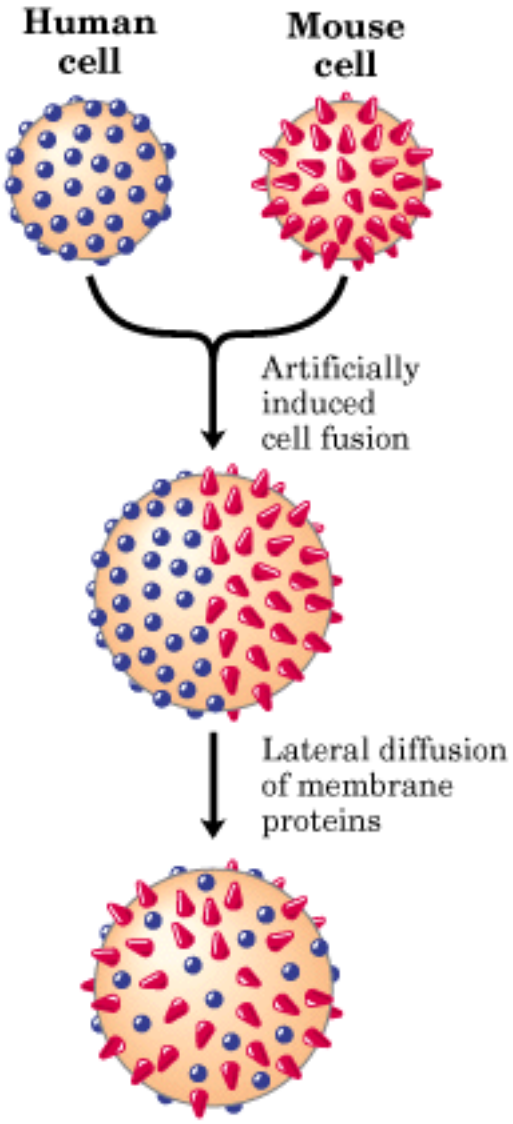
Oleic acid (18:1)	38	34	30	12
Hydroxymyristic acid	13	10	10	8
Ratio of unsaturated to saturated†	2.9	2.0	1.6	0.38

Source: Data from Marr, A.G. & Ingraham, J.L. (1962) Effect of temperature on the composition of fatty acids in *Escherichia coli*. *J. Bacteriol.* **84,** 1260.

*The exact fatty acid composition depends not only on growth temperature but on growth stage and growth medium composition.

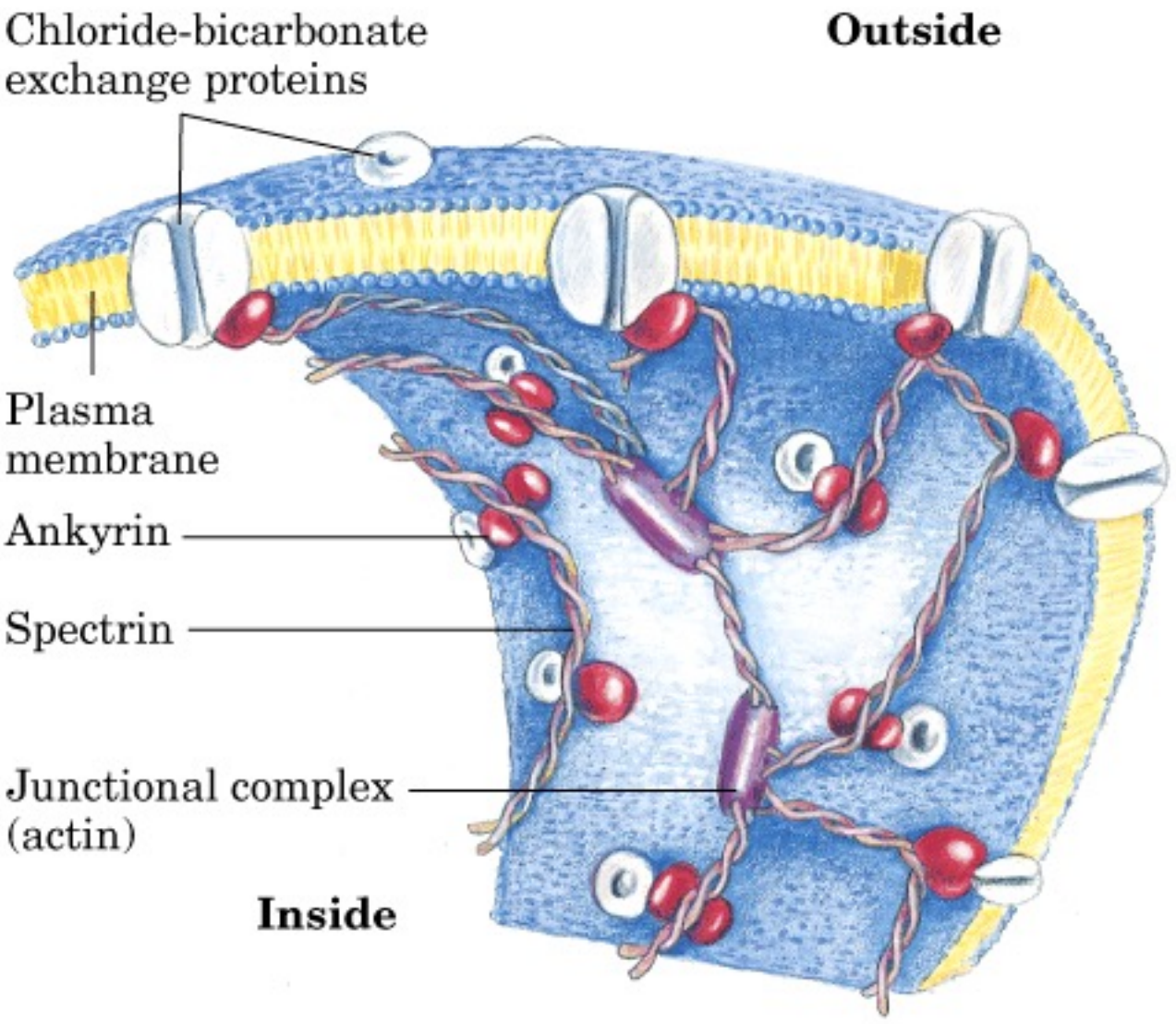
†Calculated as the total percentage of 16:1 plus 18:1 divided by the total percentage of 14:0 plus 16:0. Hydroxymyristic acid was omitted from this calculation.

Demonstration of lateral diffusion of membrane proteins

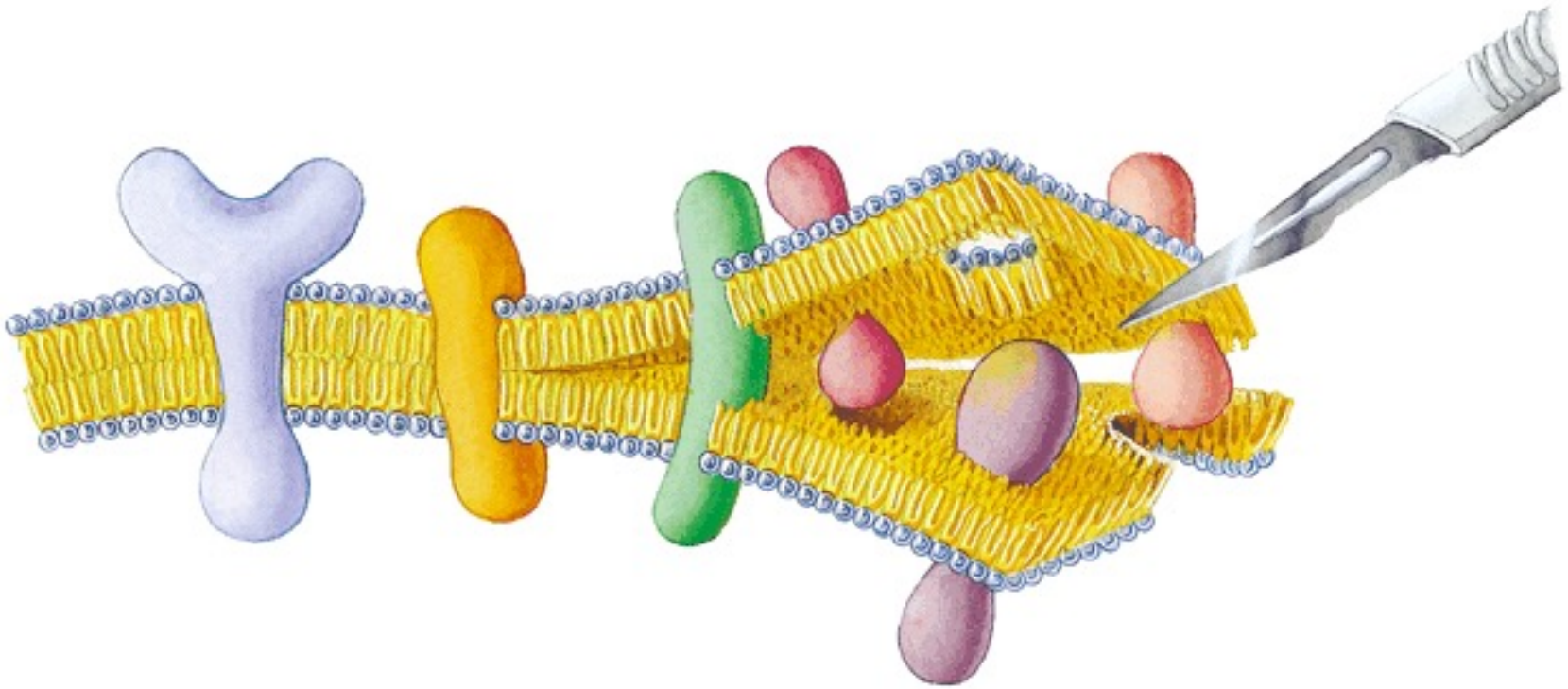


Algumas proteínas de membranas estão associadas formando agregados que só se movem em conjunto. Outras estão ancoradas em estruturas que impedem difusão.

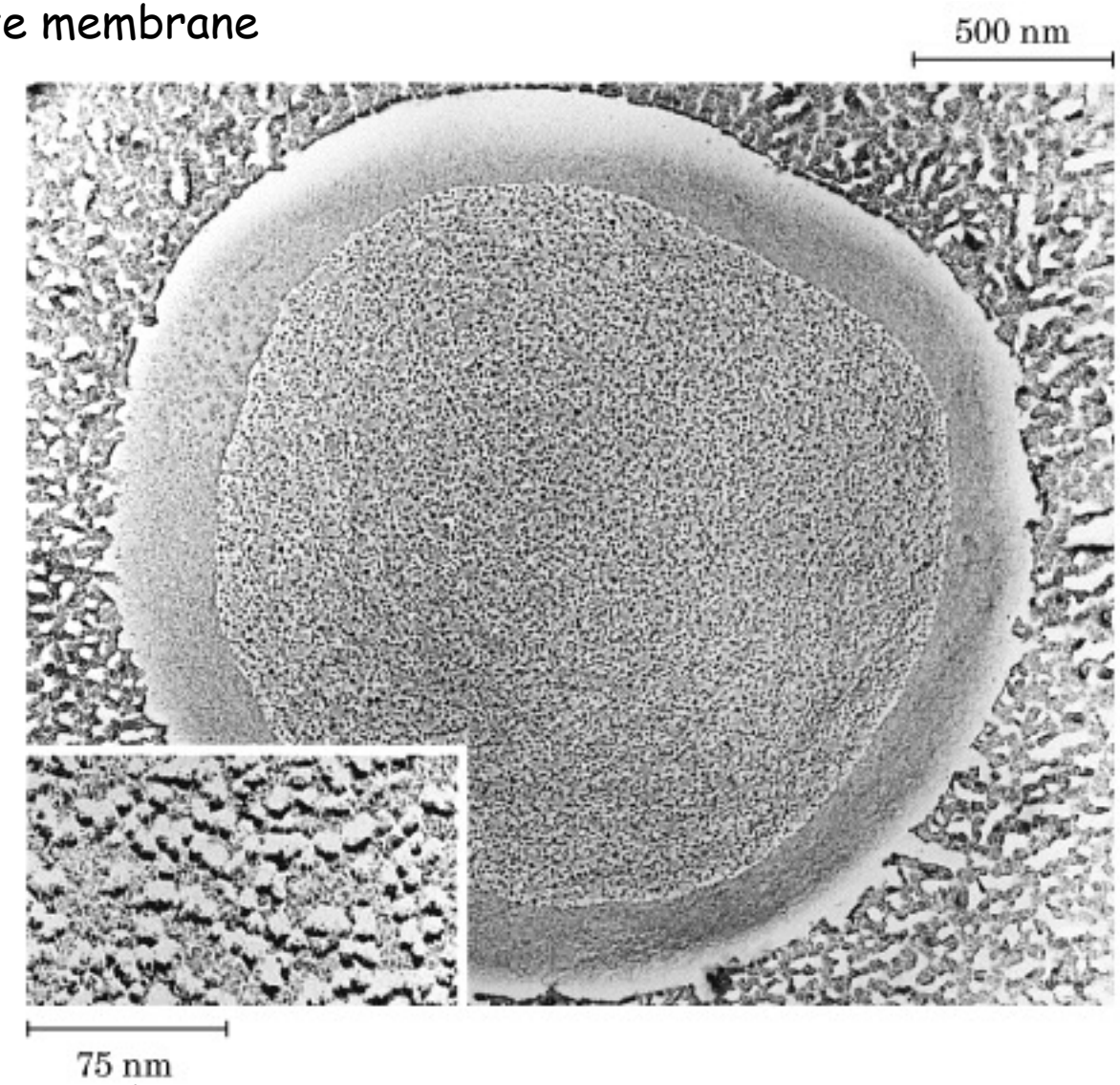
Na membrana do eritrócito algumas proteínas estão ligadas a proteína do citoesqueleto "espectrina". Isso estabiliza a membrana


Chloride-bicarbonate exchange proteins
Outside
Plasma membrane
Ankyrin
Spectrin
Junctional complex (actin)
Inside

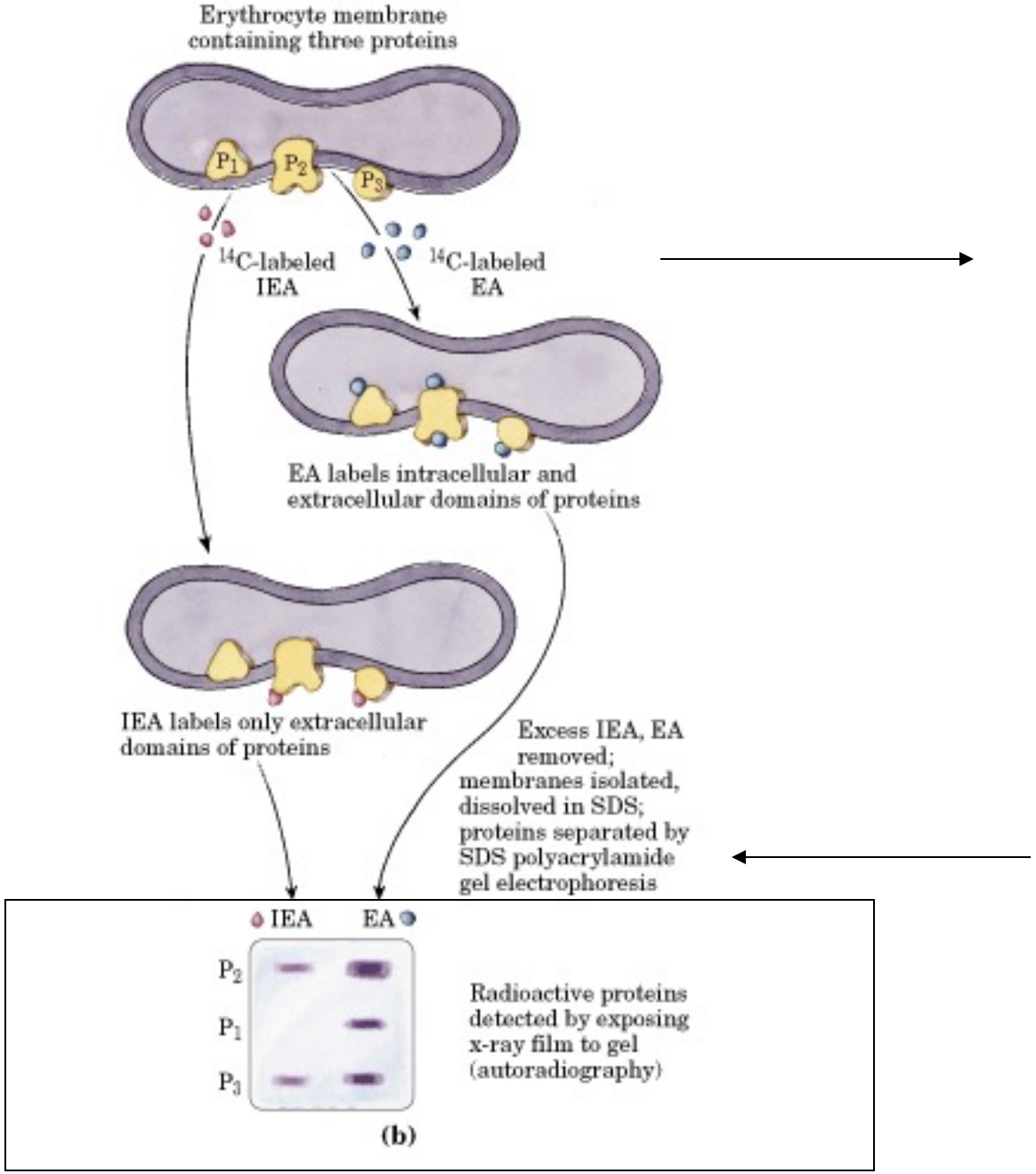
Splitting of a membrane bilayer by the freeze-fracture technique



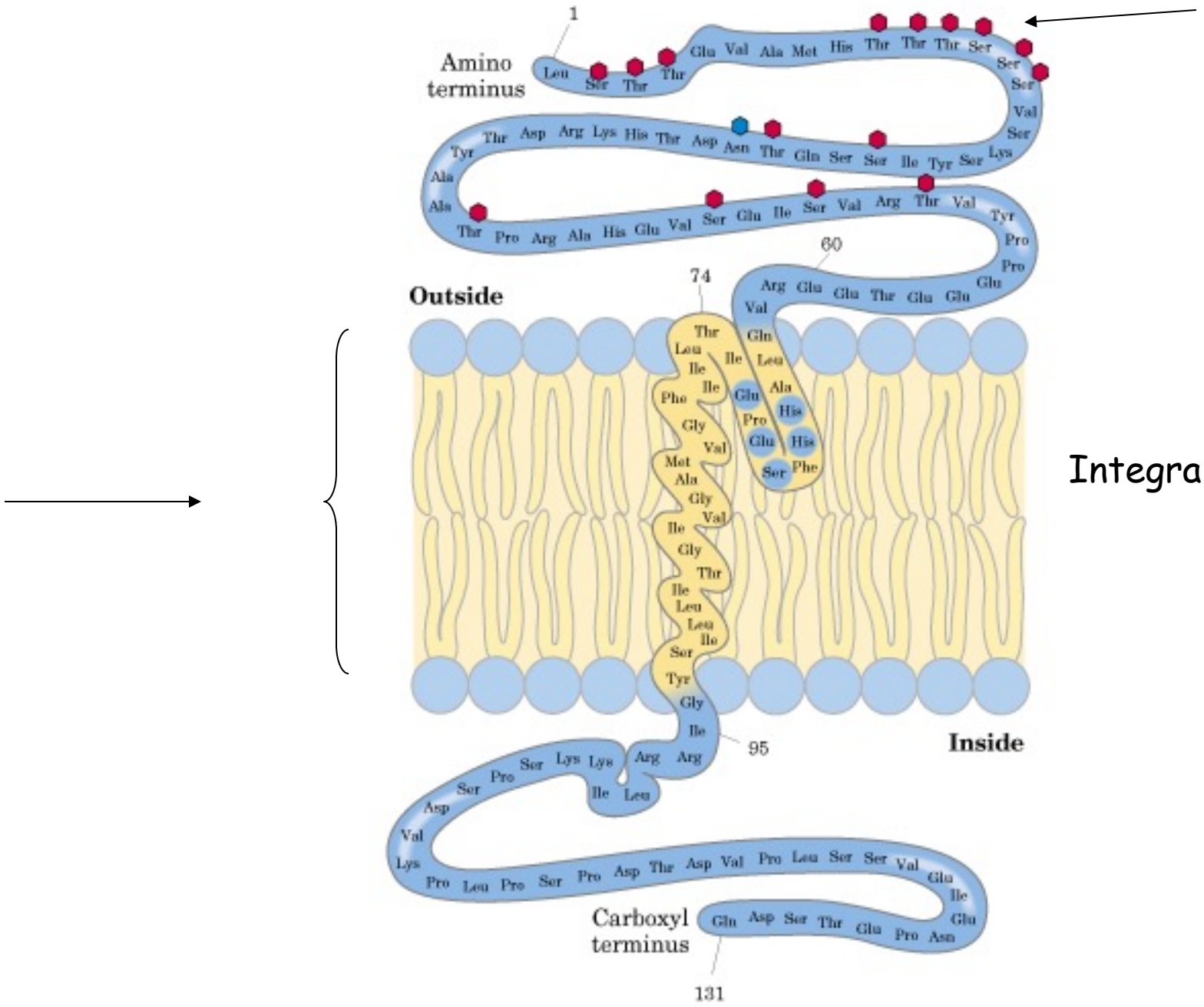
Erythrocyte membrane



Scanning electron microscopy

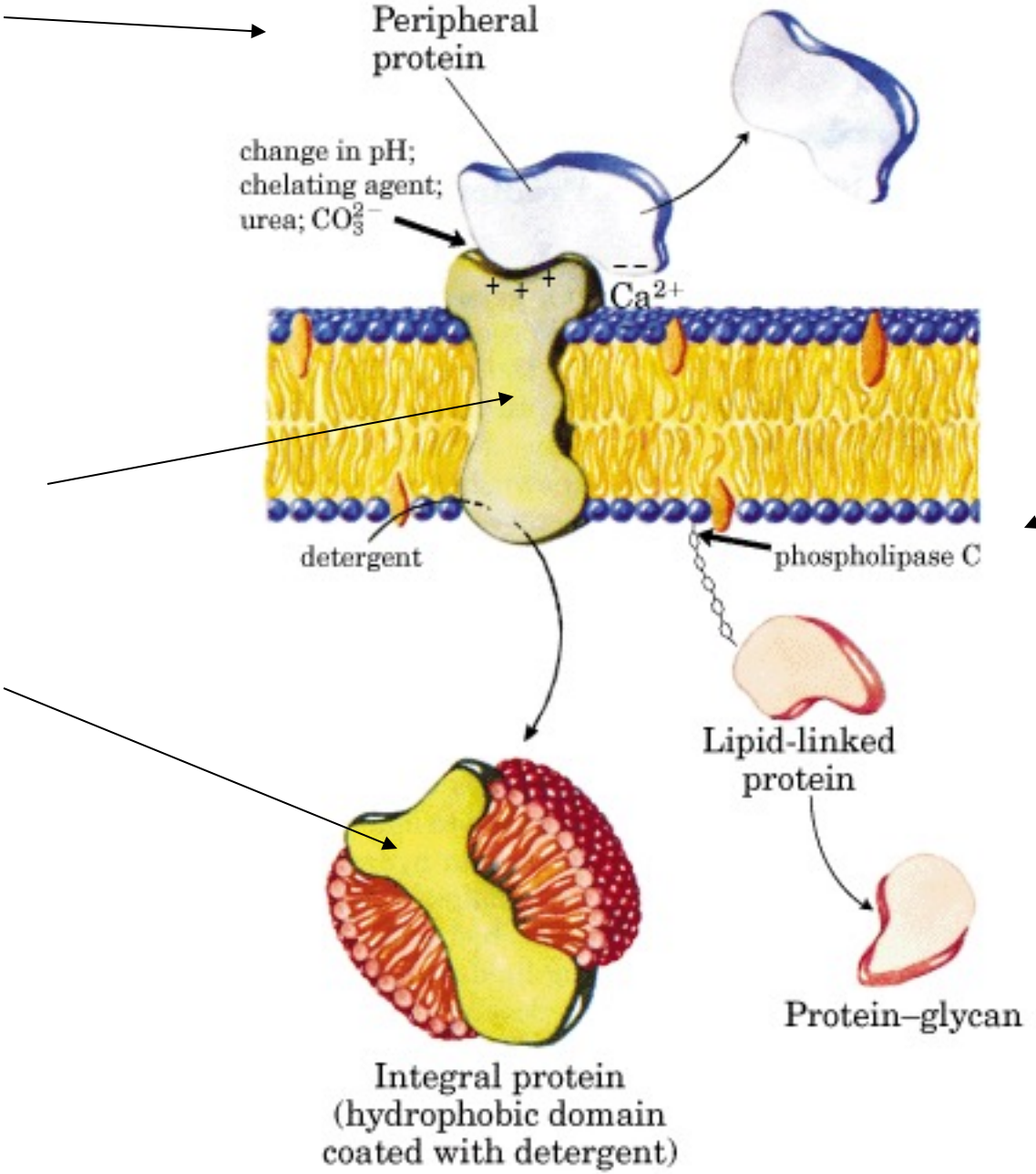

Erythrocyte membrane containing three proteins
P1
P2
P3
14C-labeled IEA
14C-labeled EA
EA labels intracellular and extracellular domains of proteins
IEA labels only extracellular domains of proteins
Excess IEA, EA removed; membranes isolated, dissolved in SDS; proteins separated by SDS polyacrylamide gel electrophoresis
IEA
EA
P2
P1
P3
(b)
Radioactive proteins detected by exposing x-ray film to gel (autoradiography)

A orientação das proteínas na bicamada é assimétrica conferindo lados diferentes na membrana

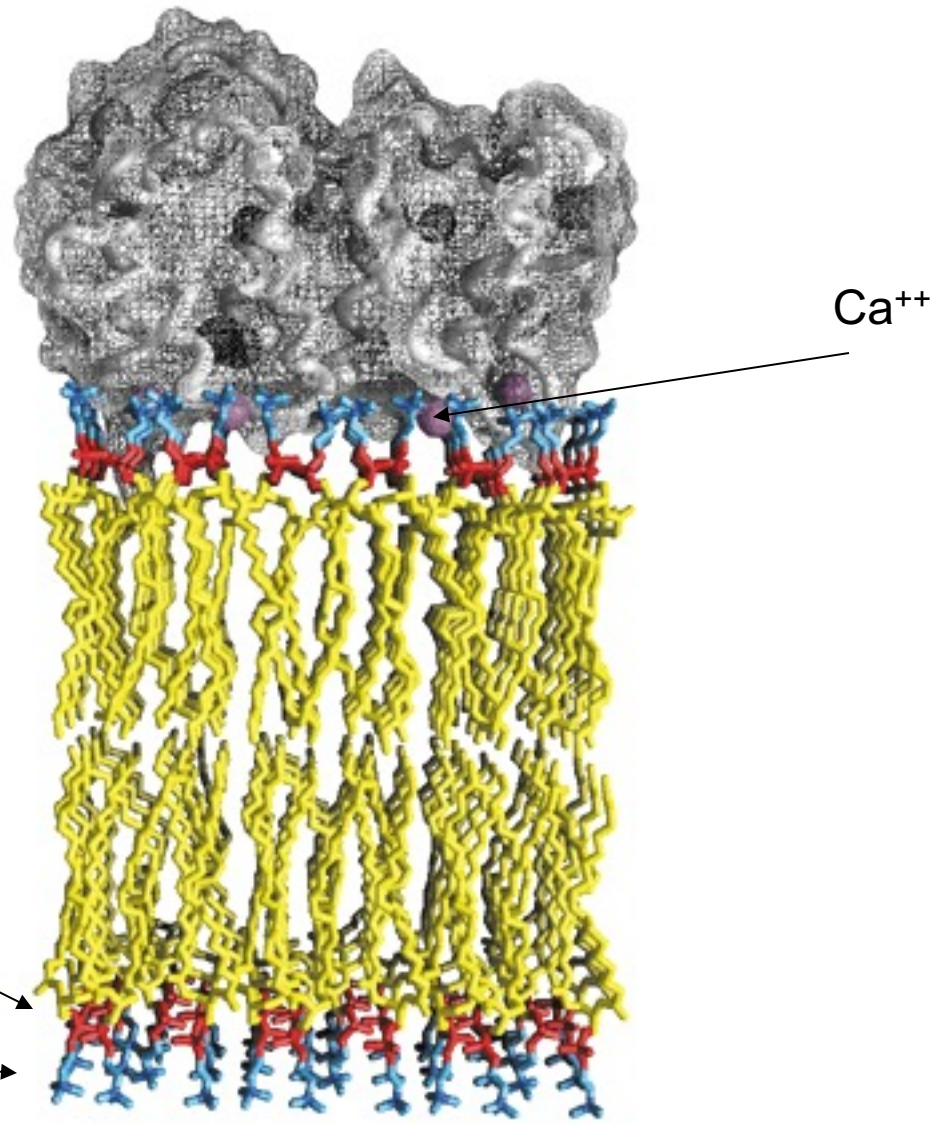


Integral protein

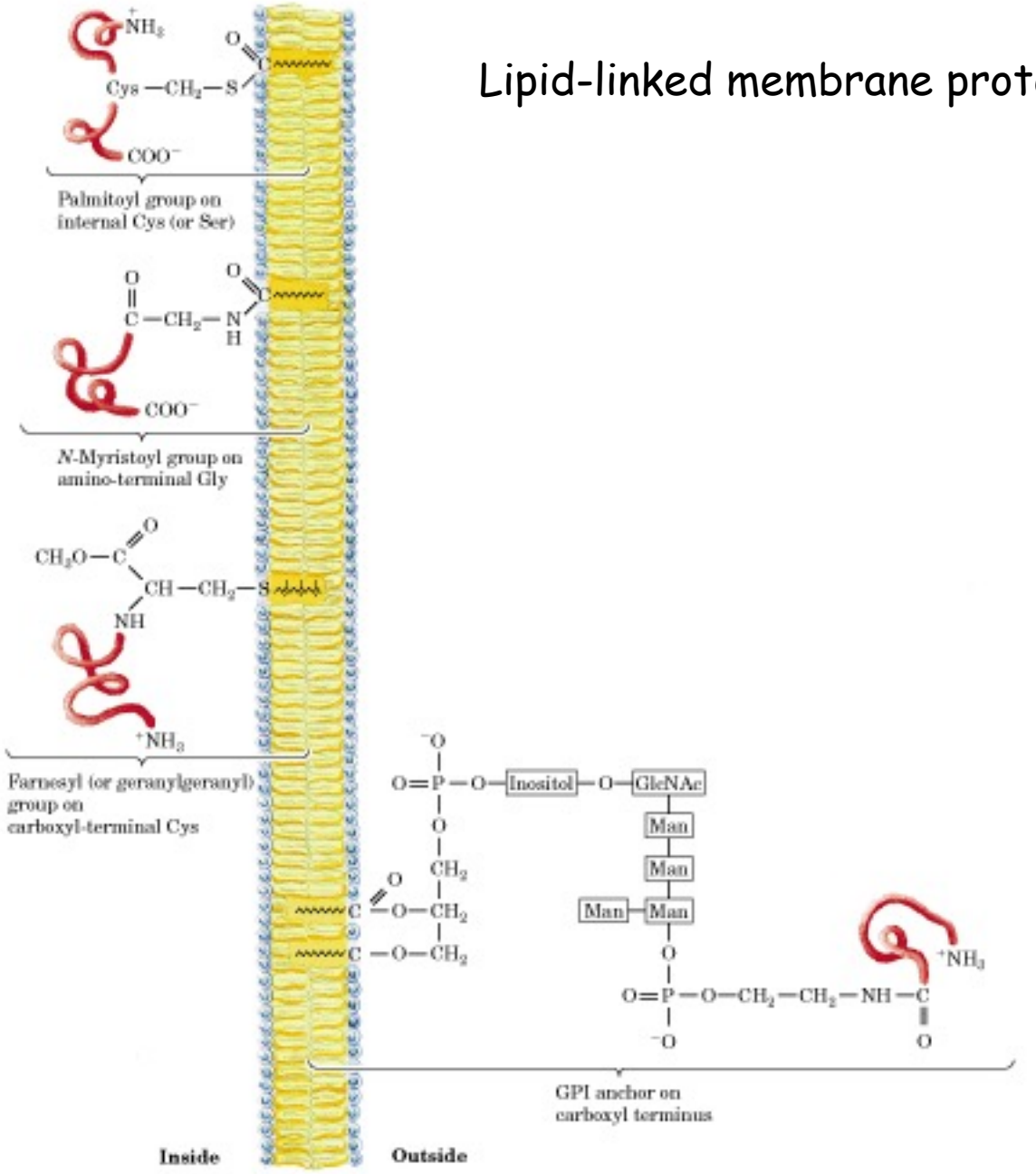
Peripheral and integral proteins



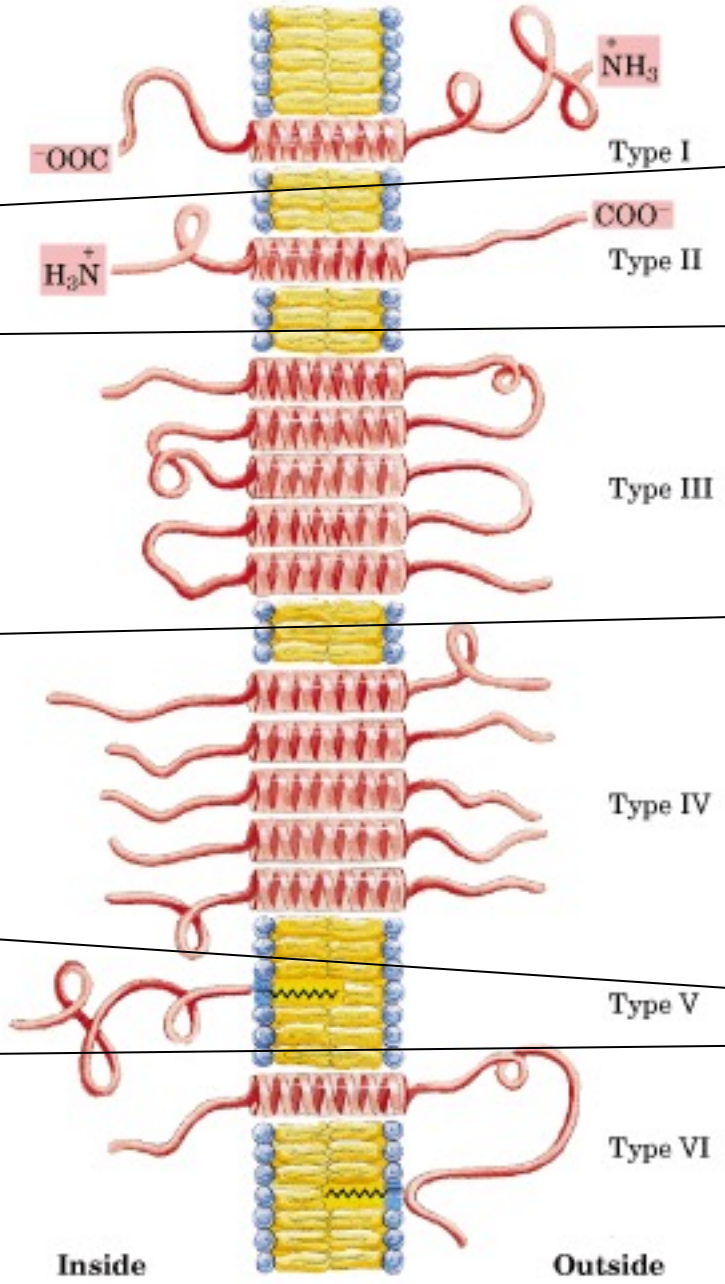
Proposed structure of annexin V in association with the lipid head groups of a membrane



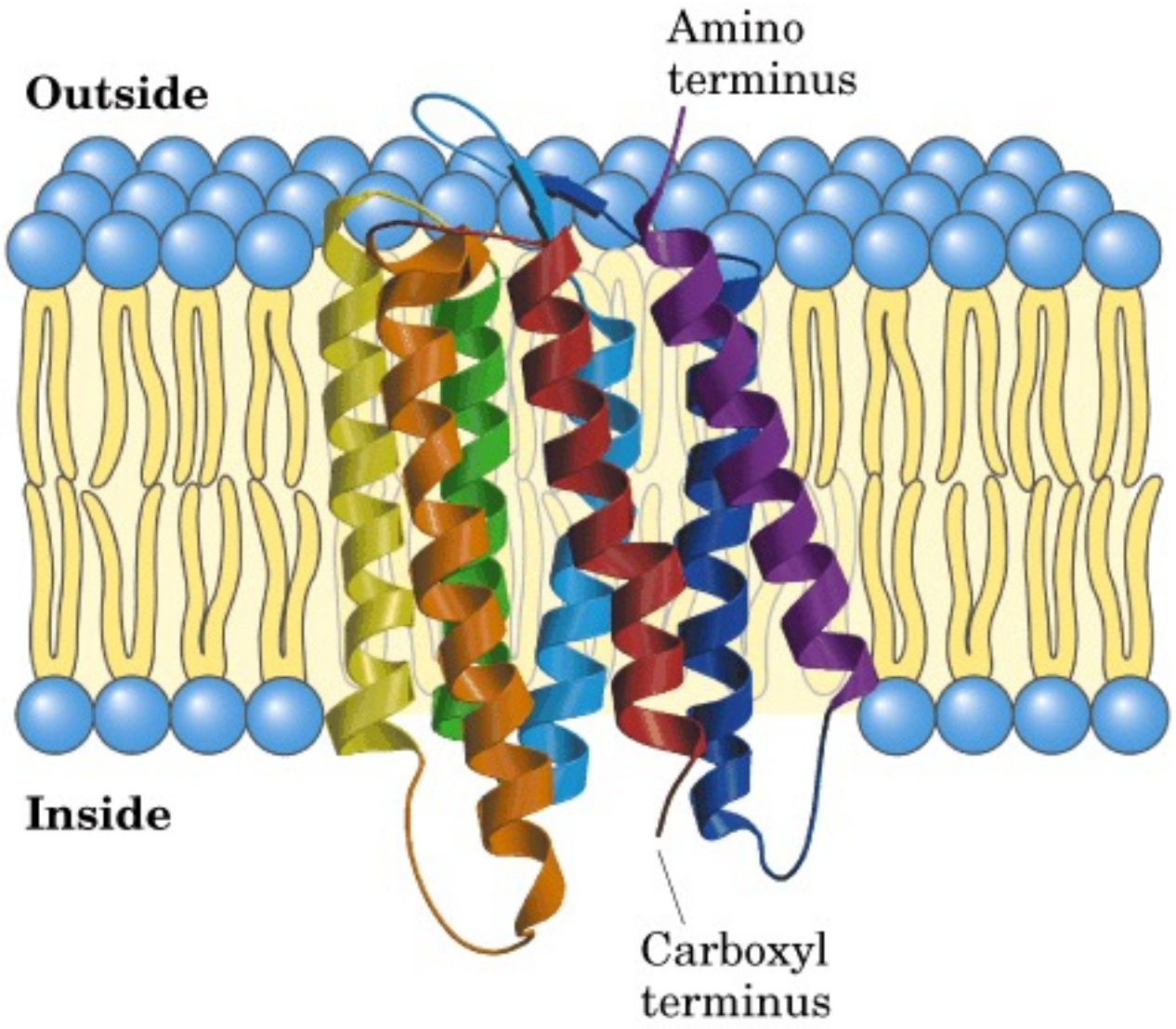
Lipid-linked membrane proteins



Integral membrane proteins



Bacteriorhodopsin, a membrane-spanning protein



Three-dimensional structure of the photosynthetic reaction center of *Rhodoppseudomonas viridis*, a purple bacterium

X-ray