Estrutura e Função de Lipídios

MEMBRANAS

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Definição de Lipídios

- **Definição Operacional**
- Substâncias de origem biológica pouco solúveis em água e solúveis em solventes orgânicos (metanol, clorofórmio, éter, hidrocarbonetos). São compostos de estruturas variadas que contém C, H, O e às vezes N e P.
-
- **Definição "Metabólica"**
- Lipídios são ácidos graxos e seus derivados e substâncias relacionadas biossinteticamente, e/ou funcionalmente, a esses compostos.

- Lipídios são pequenas moléculas hidrofóbicas ou anfipáticas que devem se originar inteiramente ou parcialmente por condensações baseadas em tioésteres (ácidos graxos, policetídeos, etc.) e/ou por condensação baseada em carbocátions de unidades de isopreno (prenóis, esteróis, etc.).

Statistics (4/2/15) Number of lipids per category

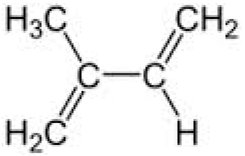
LIPID MAPS Structure Database (LMSD)

Fatty acyls (FA)	6954
Glycerolipids (GL)	7542
Glycerophospholipids (GP)	9387
Sphingolipids (SP)	4352
Sterol lipids (ST)	2833
Prenol lipids (PR)	1257
Saccharolipids (SL)	1293
Polyketides (PK)	6742
TOTAL	40,360 structures

Classificação por Função dos lipídeos

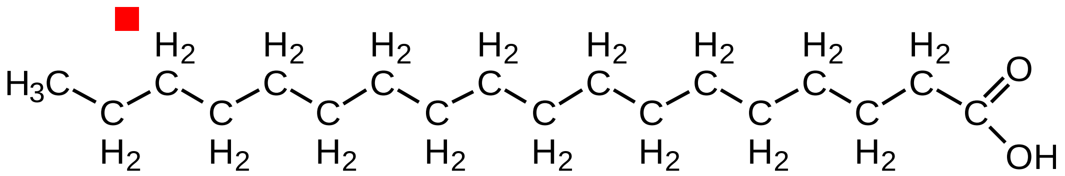
- Lipídios de Armazenamento: Ácidos Graxos
- Triacilgliceróis
- Ceras
- Lipídios Estruturais de Membrana: Fosfolipídios
- Glicerofosfolipídeos
- Esfingolipídeos
- Glicoesfingolipidios
- Esteróis
- Lipidios como Sinalizadores, Cofatores e Pigmentos:
- Fosfatidilinositois e esfingosina
- Eicosanoides, Esteróides, Ubiquinona,
- Vit A (retinol), Vit K, Vit E, prostaglandinas,
- Outros: isoprenóides ou terpenos (borracha)-Farnesol, geraniol, retinol, ubiquinona

Isopreno

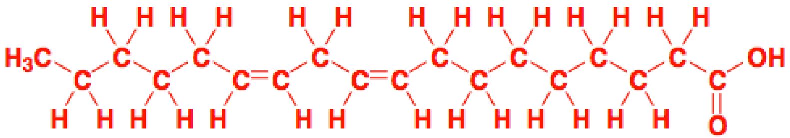


Definição de Ácidos Graxos

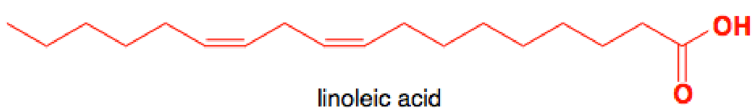
- Ácidos Graxos são ácidos carboxílicos de cadeia longa (C4 a C36). Podem ter anel de 3 C, OH ou ramificações de CH_3)
- Nomeados de acordo com o comprimento da cadeia e duplas ligações a partir da carboxila (C1) e de acordo com o grau de saturação.



C18:0 Ac. n-Octadecanóico
Nome comum- Ácido Esteárico



linoleic acid



linoleic acid

C18:2 ($\Delta^{9,12}$) Ac. cis-cis-9,12-octadecadienóico
Nome comum- Ac. Linoleico

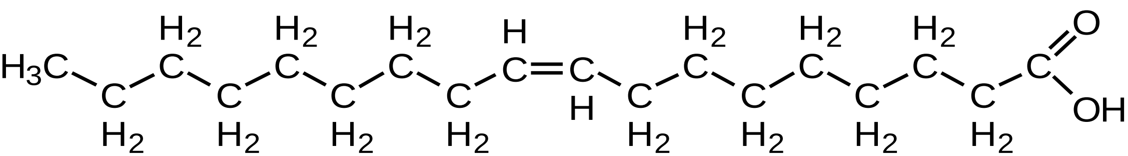
Acidos graxos mais comuns em Di- e Triglicérides

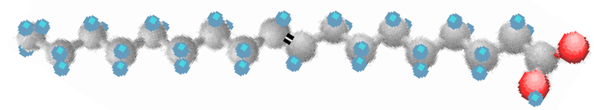
$$CH_3(CH_2)_nCOOH$$

Acido Graxo	Carbono:Dupla ligação	Dupla ligação
Miristico	14:0	
Palmitico	16:0	
Palmitoleico	16:1	*Cis*-9
Esteárico	18:0	
Oleico	18:1	*Cis*-9
Linoleico	18:2	*Cis*-9,12
Linolênico	18:3	*Cis*-9,12,15
Araquidônico	20:4	*Cis*-5,8,11,14
Eicosapentaenóico	20:5	*Cis*-5,8,11,14,17
Docosahexaenóico	22:6	*Cis*-4,7,10,13,16,19

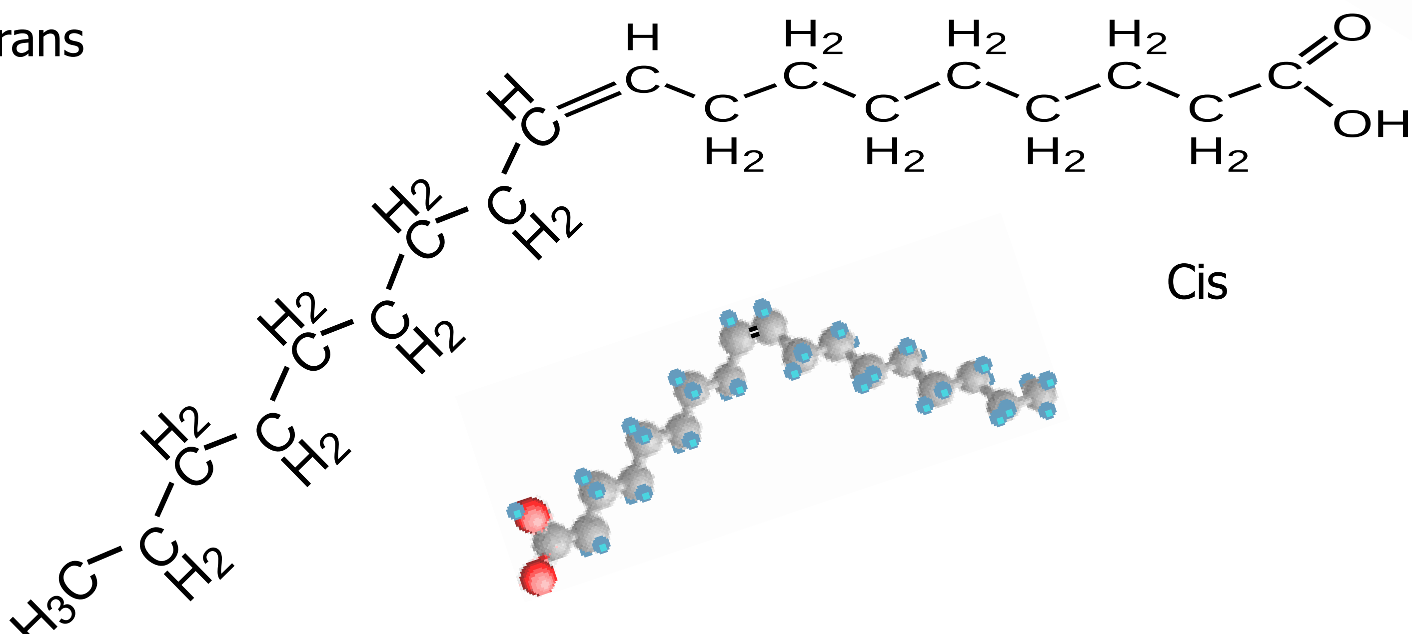
Nomenclatura dos ácidos graxos

Localização dos H's na dupla: *cis* (proximo) ou *trans (através)*





Trans



Cis

Propriedades Físicas:Pontos de Fusão

- Depende do comprimento da cadeia
  - Cadeia maior => maior temperatura de fusão

Ácido graxo:	***C12:0***	***C14:0***	***C16:0***	***C18:0***	***C20:0***
Ponto de fusão:	***44°C***	***58°C***	***63°C***	***72°C***	***77°C***

- PF depende do número de duplas ligações
  - Mais saturado = maior o ponto de fusão

Ácido graxo:	***C18:0***	***C18:1***	***C18:2***	***C18:3***
Ponto de fusão:	***72°C***	***16°C***	***–5°C***	***–11°C***

Estrutura espacial de ácidos graxos com diferentes insaturações.

1 = 2= 3= 4=

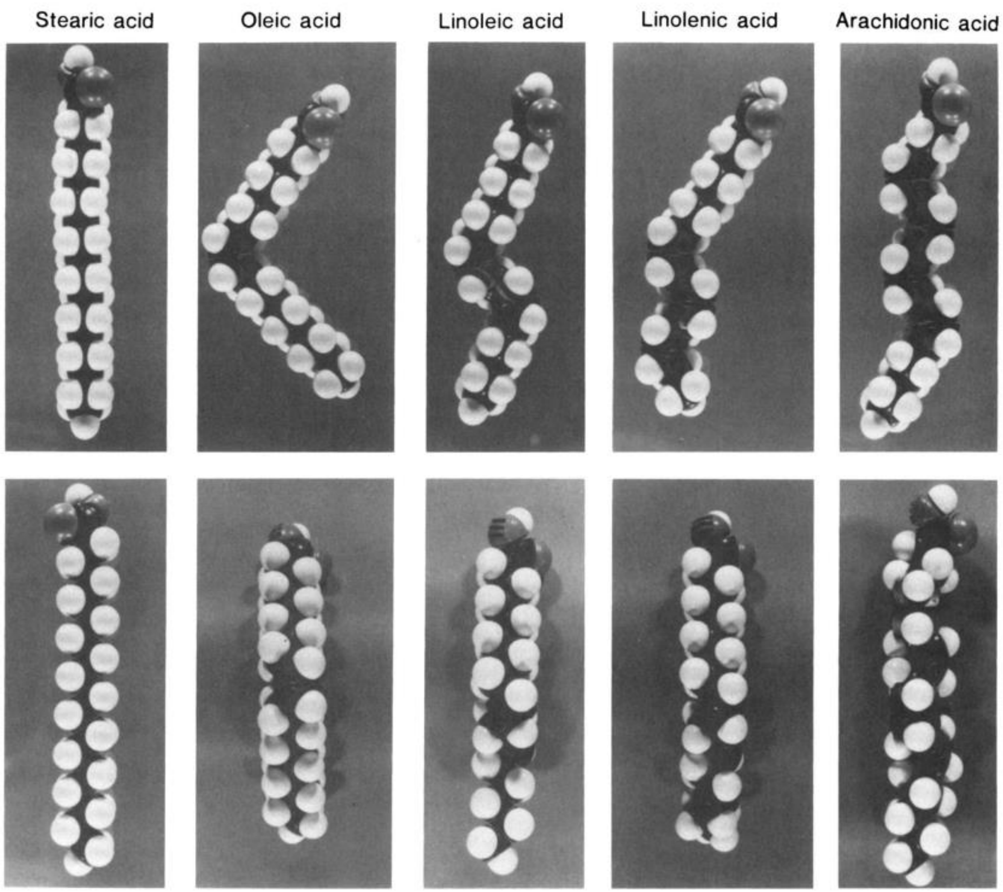
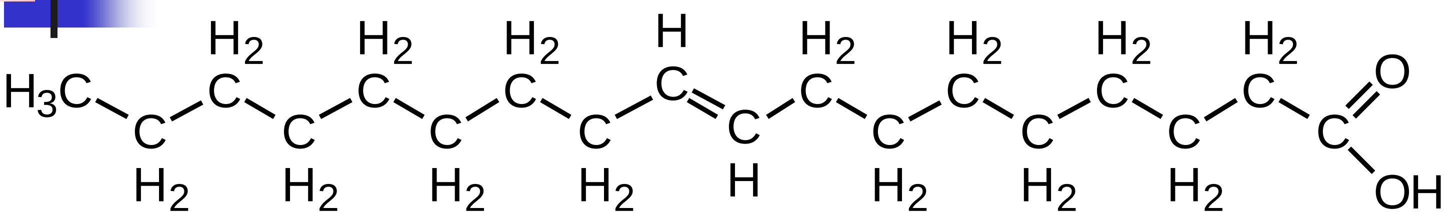


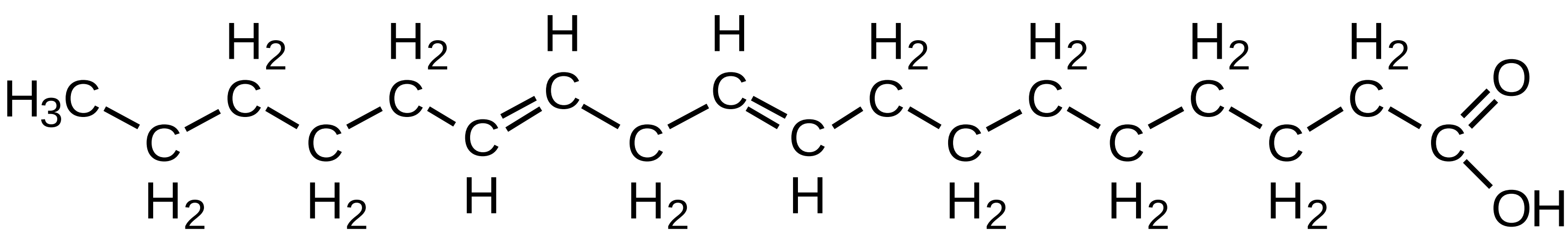
Fig. 1. Space filling models of five fatty acids. The conformation of five fatty acids of increasing unsaturation

D. M. Small, J. Lipid Res. 25 (1984) 1490

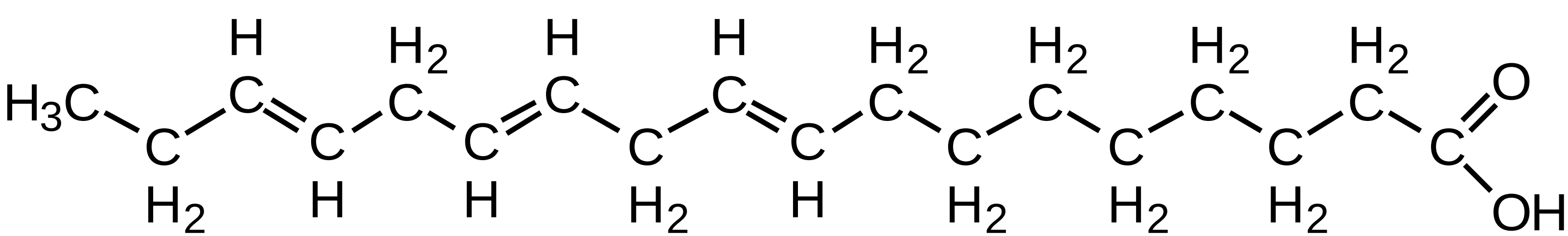
Ácidos graxos ω



Omega 9 ou n–9 ácido graxo



Omega 6 ou n–6 ácido graxo



Omega 3 ou n–3 ácido graxo

Deficiências de ácidos graxos essenciais

- Retardo no crescimento
- Problemas com reprodução
- Lesões de pele
- Problemas no rim e fígado

Nomes Comuns de Ácidos Carboxílicos e Fontes mais Comuns

Ácidos	Carbonos	Duplas	Abrev.	Fontes
Acético	2	0	2:0	Metabolismo Bacteriano
Propiônico	3	0	3:0	Metabolismo Bacteriano
Butírico	4	0	4:0	Manteiga
Capróico	6	0	6:0	Manteiga
Caprílico	8	0	8:0	Óleo de côco
Cáprico	10	0	10:0	Óleo de côco
Láurico	12	0	12:0	Óleo de côco
Mirístico	14	0	14:0	Óleo de semente de palmeira
Palmítico	16	0	16:0	Óleo de palmeira
Palmitolêico	16	1	16:1	Óleo de palmeira
Esteárico	18	0	18:0	Óleo de palmeira
Olêico	18	1	18:1	Azeite de oliva
Linolêico	18	2	18:2	Óleo semente de uva
Linolênico	18	3	18:3	Óleo de linhaça
Araquidônico	20	4	20:4	Óleo amendoim, peixe

Acidos graxos mais comuns em Di- e Triglicérides

$$CH_3(CH_2)_nCOOH$$

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Docosahexaenóico	22:6	*Cis*-4,7,10,13,16,19

Propriedades Físicas dos Ácidos Graxos: Pontos de Fusão

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Ponto de fusão:	***44°C***	***58°C***	***63°C***	***72°C***	***77°C***

- PF depende do número de duplas ligações
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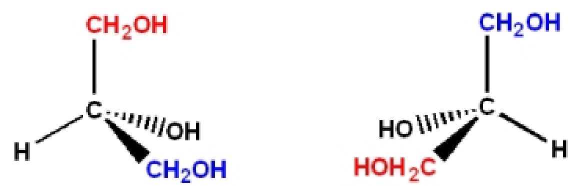
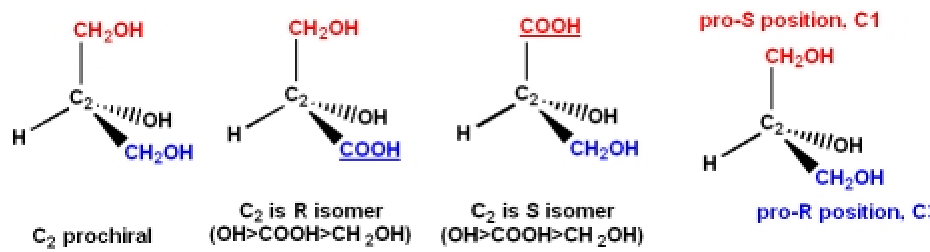
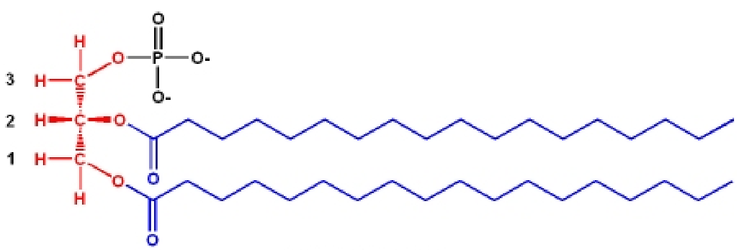
Ácido graxo:	***C18:0***	***C18:1***	***C18:2***	***C18:3***
Ponto de fusão:	***72°C***	***16°C***	***–5°C***	***–11°C***

O Glicerol

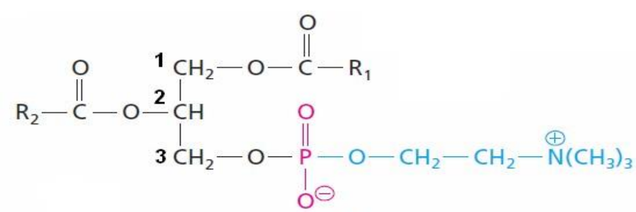


L-glycerol 3-phosphate becomes *sn*-glycerol 3-phosphate to indicate the use of the stereochemical numbering system (sn).





Phosphatidic Acid

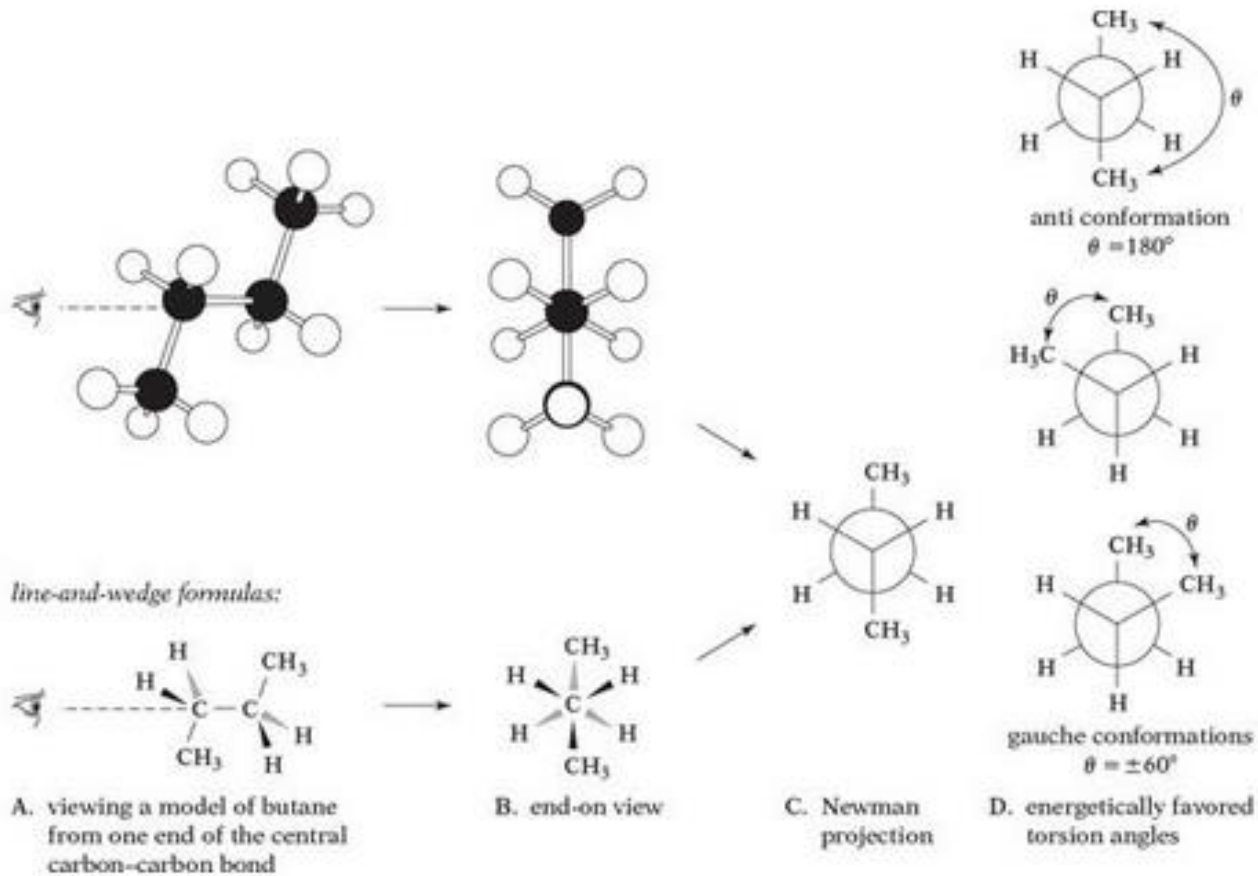


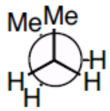
Phosphatidylcholine

1,2-Diacyl-sn-glycero-3-phosphorylcholine

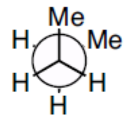
sn-glicerol-3-fosfato (fosfato na posição pro-R, que será chamada C3). E as cadeias alquilicas nas posições 1 e 2.
R –rectus; S= sinister.

Conformações das cadeias alquílicas

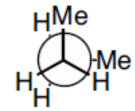




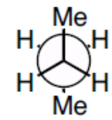
fully eclipsed
(eclipsed)
$\theta_{Me/Me} = 0°$



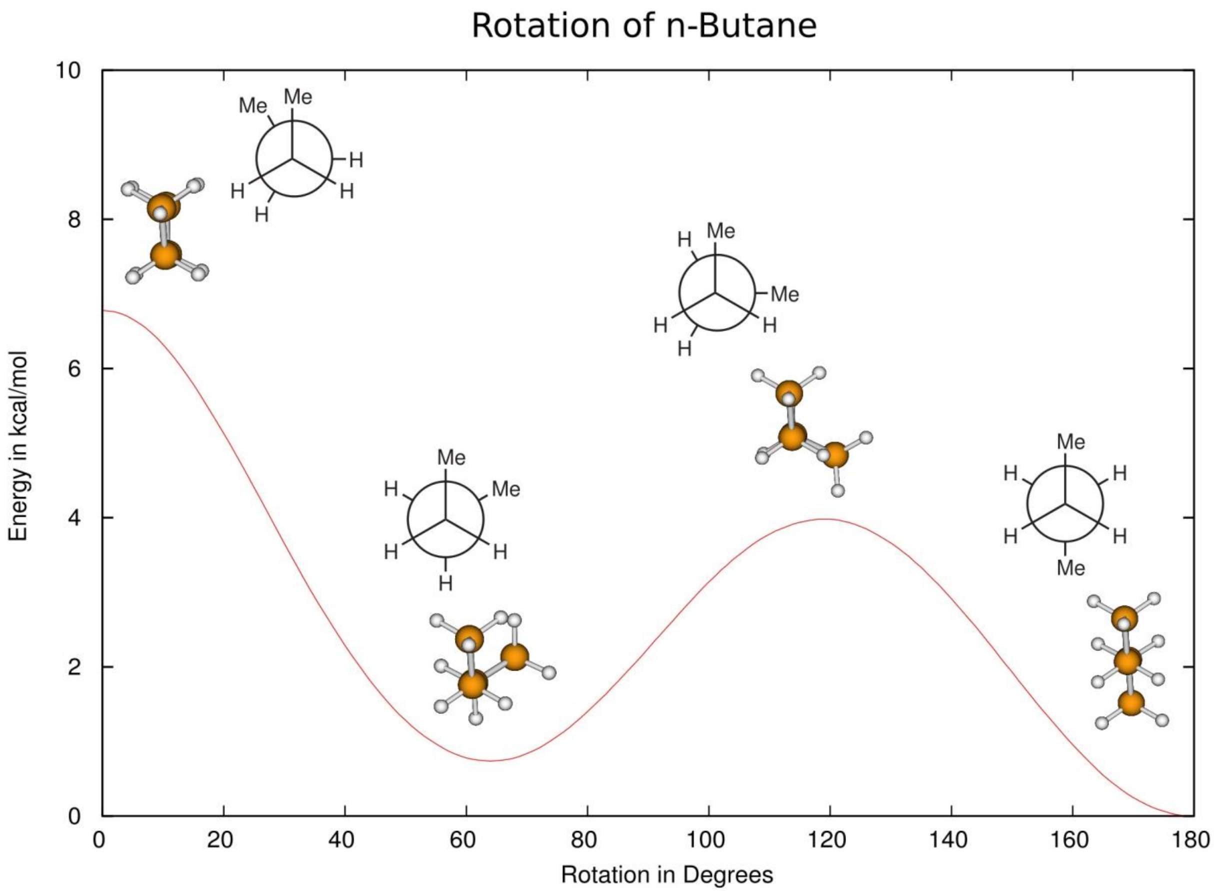
gauche
(staggered)
$\theta_{Me/Me} = 60°$



eclipsed
(eclipsed)
$\theta_{Me/Me} = 120°$

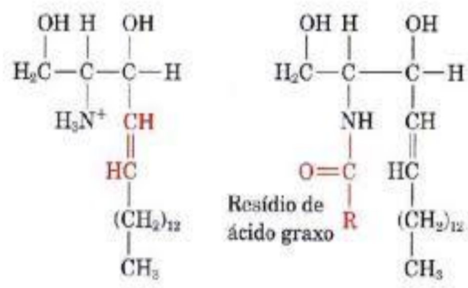


anti
(staggered)
$\theta_{Me/Me} = 180°$

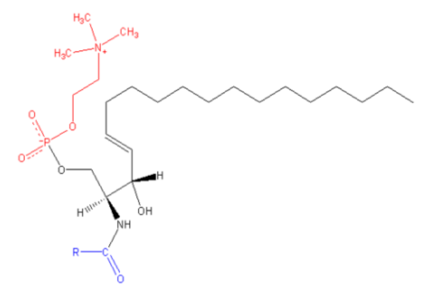


Lipidios Complexos- Fosfolipídios

- Dois tipos primários:
  - Glicerofosfatídeos
    - Estrutura central é o glicerol
    - Parte das membranas das células,
    - quilomicrons. lipoproteinas
  - Esfingofosfatídeos
    - Estrutura central é a esfingosina
    - Parte da esfingomielina



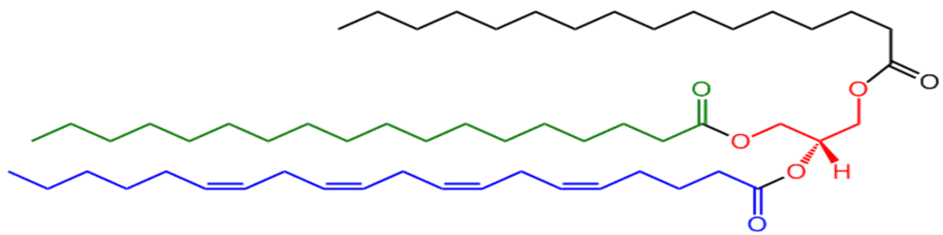
Esfingosina   Uma ceramida



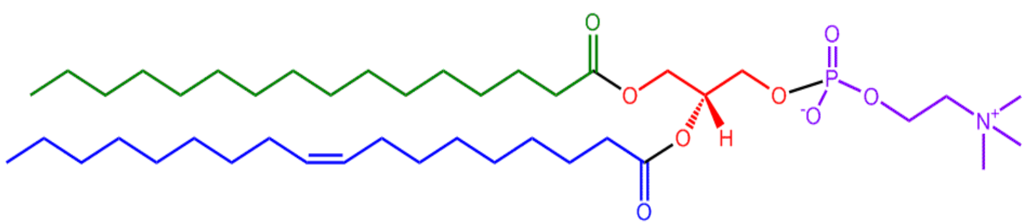
N-acil derivados da esfingosina são as ceramidas
Esfingomielina possui a fosfocolina ou fosfoetanolamina
no OH livre e acido graxo no amino grupo

esfingomielina

Lipidios Complexos- Fosfolipídios

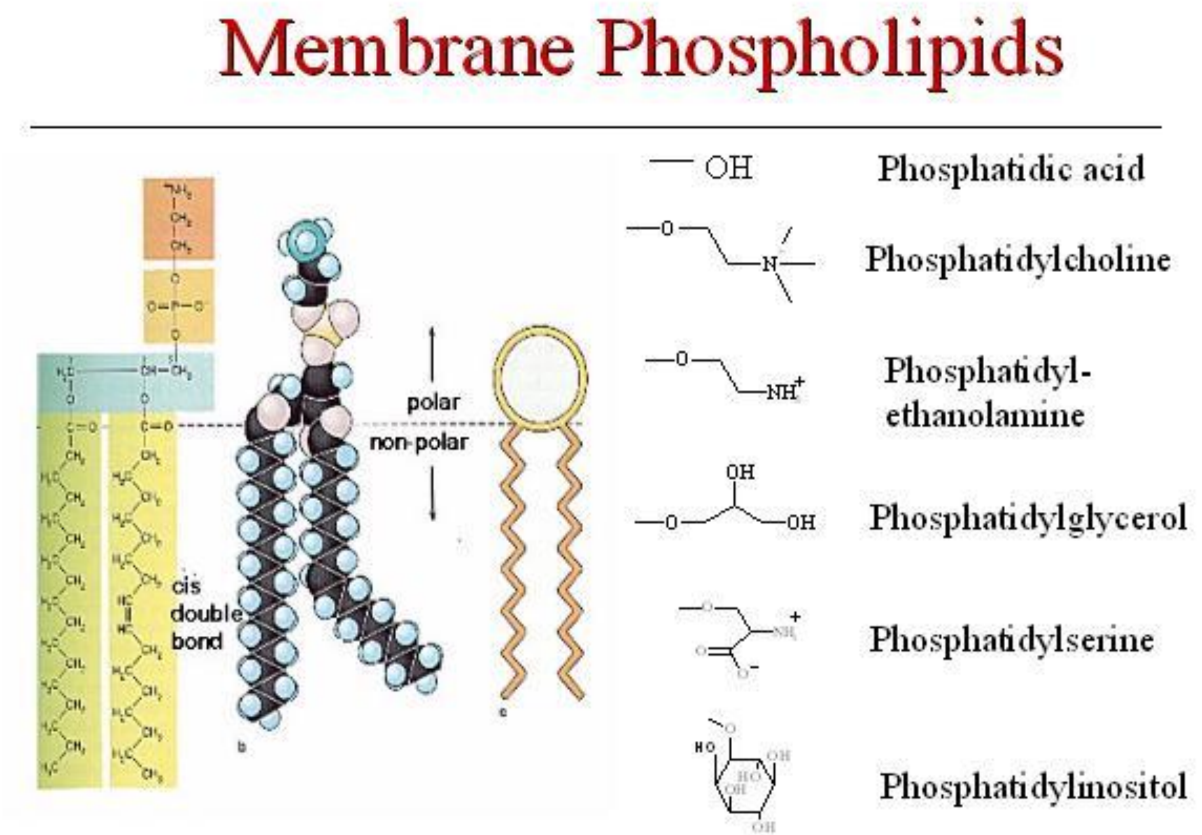


Common name: 1-stearoyl-2-arachidonoyl-3-palmitoyl-triacylglycerol
Systematic name: 1-octadecanoyl-2-(5Z,8Z,11Z,14Z-eicosatetraenoyl)-3-hexadecanoyl-*sn*-glycerol
Abbreviation: TG(18:0/20:4(5Z,8Z,11Z,14Z)/16:0)

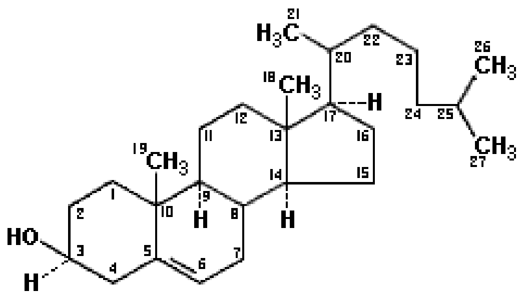


Common name:1-palmitoyl-2-oleoyl-phosphatidylcholine
Systematic name:1-hexadecanoyl-2-(9Z-octadecenoyl)-sn-glycero-3-phosphocholine
Abbreviation: PC(16:0/18:1(9Z))

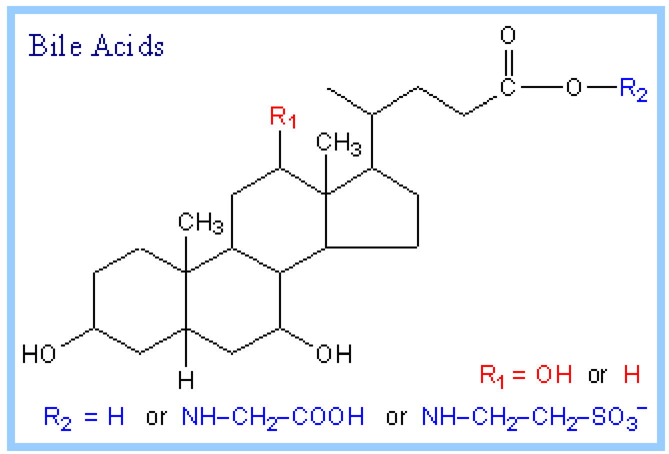
Fosfolipidios de Membranas Biológicas

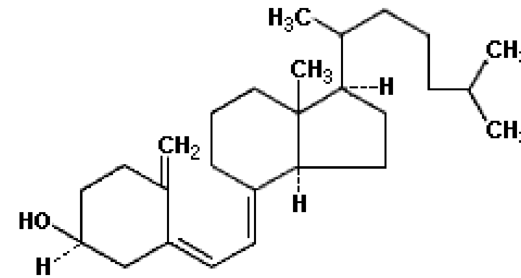


Compostos esteroídicos



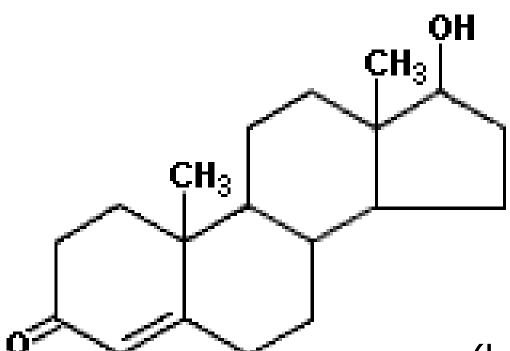
Colesterol



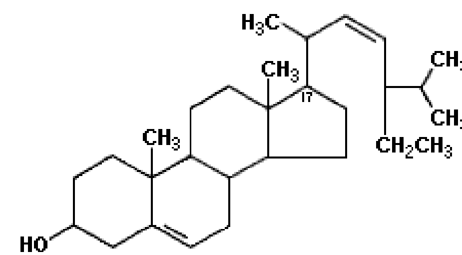


Vitamin D3
(colecalciferol)

Propriedades Emusificantes
Forma micelas

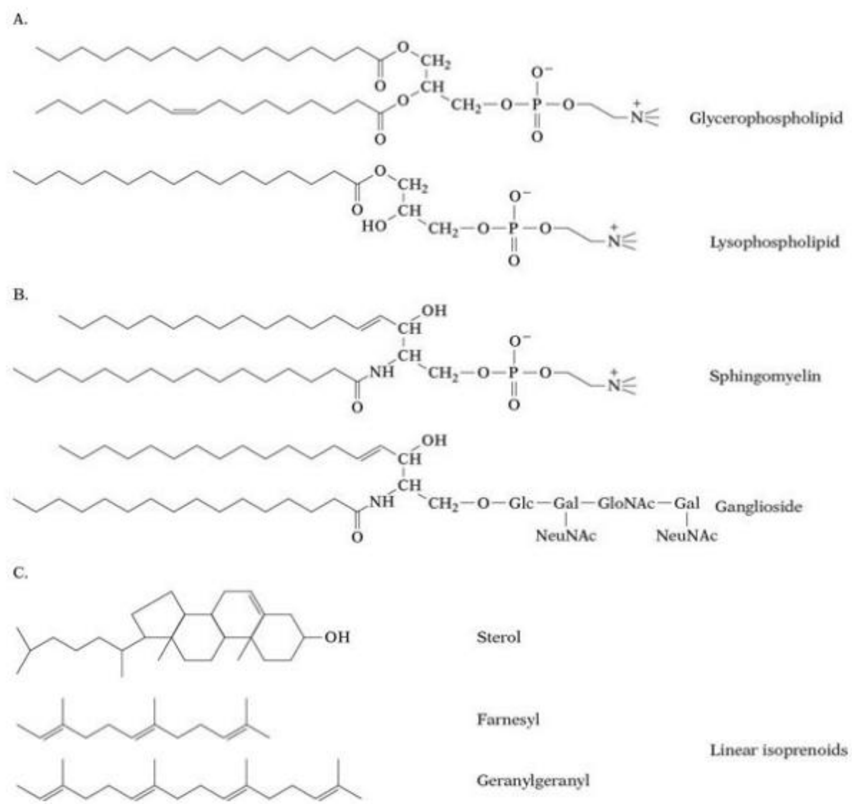


Testosterone
(hormônio esteroídico)



Estigmasterol (um Fitosterol)

2.4. Three major classes of membrane lipids. The structures of representative glycerophospholipids (**A**), sphingolipids (**B**), and sterols and linear isoprenoids (**C**) are shown. An additional class is the glycolipids, which have sugar headgroups typically on a sphingomyelin base. **A** and **B** redrawn from Gennis, R. B., *Biomembranes*, Springer-Verlag, 1989, p. 24; **C** redrawn from Nelson, D. L., and M. M. Cox (eds.), *Lehninger Principles of Biochemistry*, 4th ed., W. H. Freeman, 2005, p. 355.

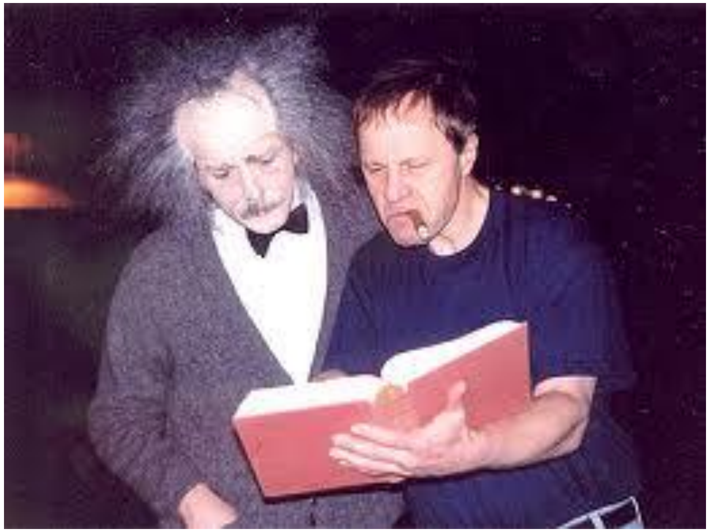


MEMBRANAS

- Lipídios de Membrana
- Organização Supramolecular

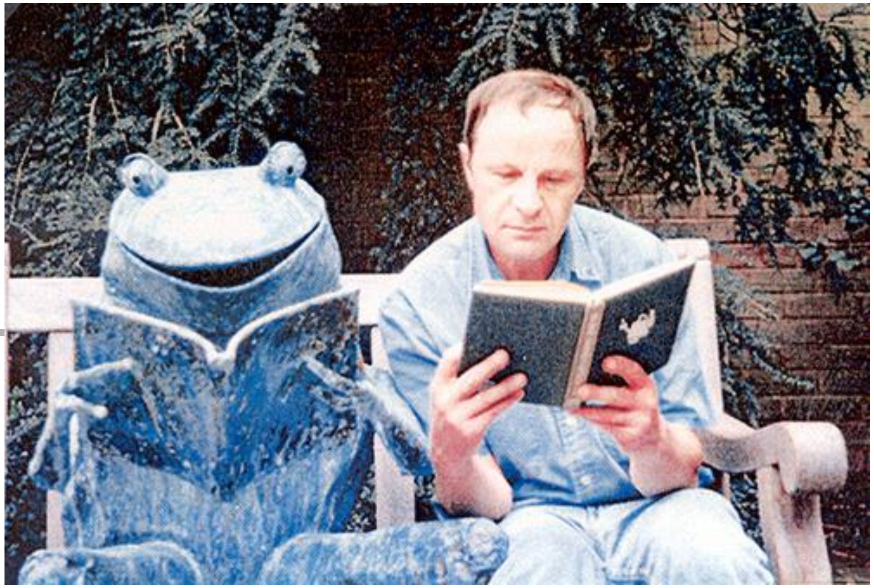
A Tribute to the Phospholipid

Proteins and nucleic acids receive so much attention and hype that a third biological building block, the phospholipid, might well be suffering from an inferiority complex.



Phospholipids have a trivial structure and this has certainly not added to their self-esteem.

Langmuir ***2005, 21, 10336-10341*** Fredric M. Menger et all



Nonetheless, one should feel no pity for the seemingly mundane phospholipid. Living systems could not have evolved until their biochemistries had been enclosed within lipid membranes.

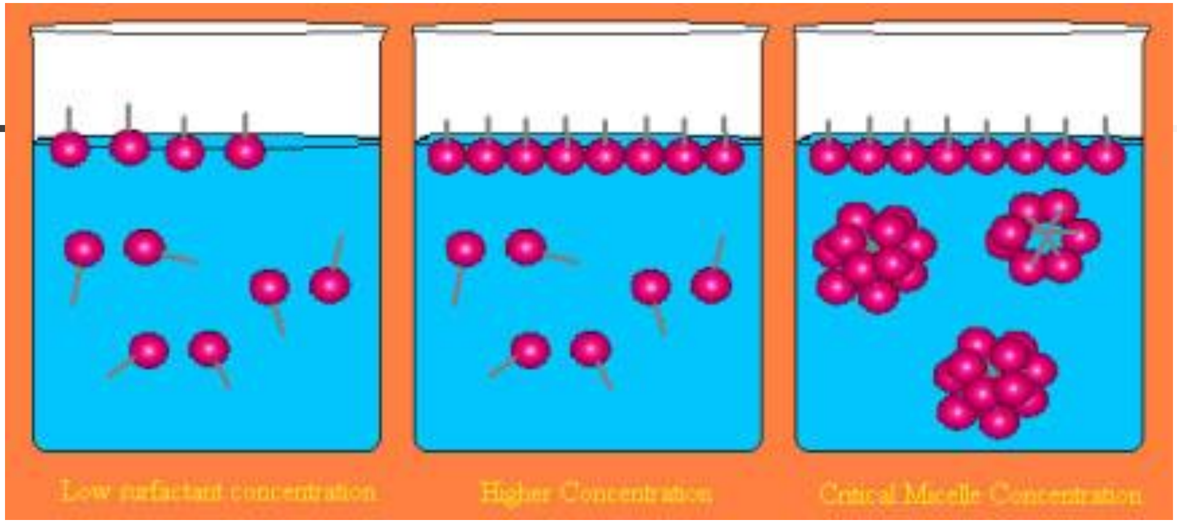
Moreover, phospholipid molecules cannot fold into interesting coils, cannot catalyze reactions, cannot duplicate themselves, and cannot transport oxygen.

Langmuir ***2005, 21, 10336-10341***

Actually, the cell membrane is a remarkable community of molecules, embedded in a structural motif called a bilayer, where multiple types of dynamic events take place. Motions of proteins and nucleic acids might seem rather dull when compared to those within phospholipid self-assemblies.

Menger, F. -Langmuir ***2005, 21, 10336-10341***

McBain -1913



The antipathy of the paraffin chain for water is, however, frequently misunderstood. There is no question of actual repulsion between individual water molecules and paraffin chains, nor is there any very strong attraction of paraffin chains for one another. There is, however, a very strong attraction of water molecules for one another in comparison with which the paraffin-paraffin or paraffin-water attractions are slight."

G. S. Hartley in 1936

Estruturas Supramoleculares formadas por Sais de Ácidos Graxos

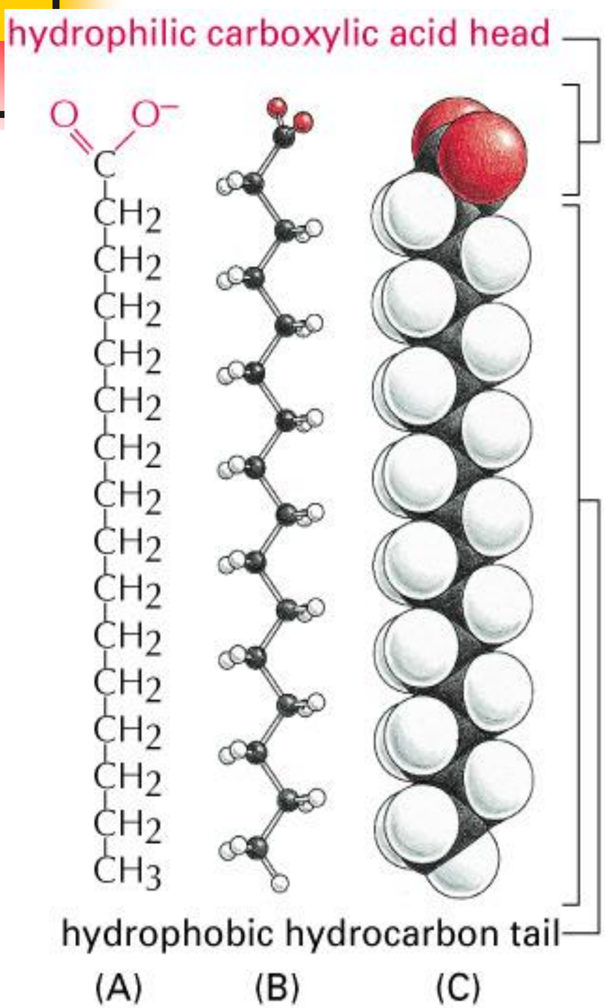


Figure 2–21. Molecular Biology of the Cell, 4th Edition.

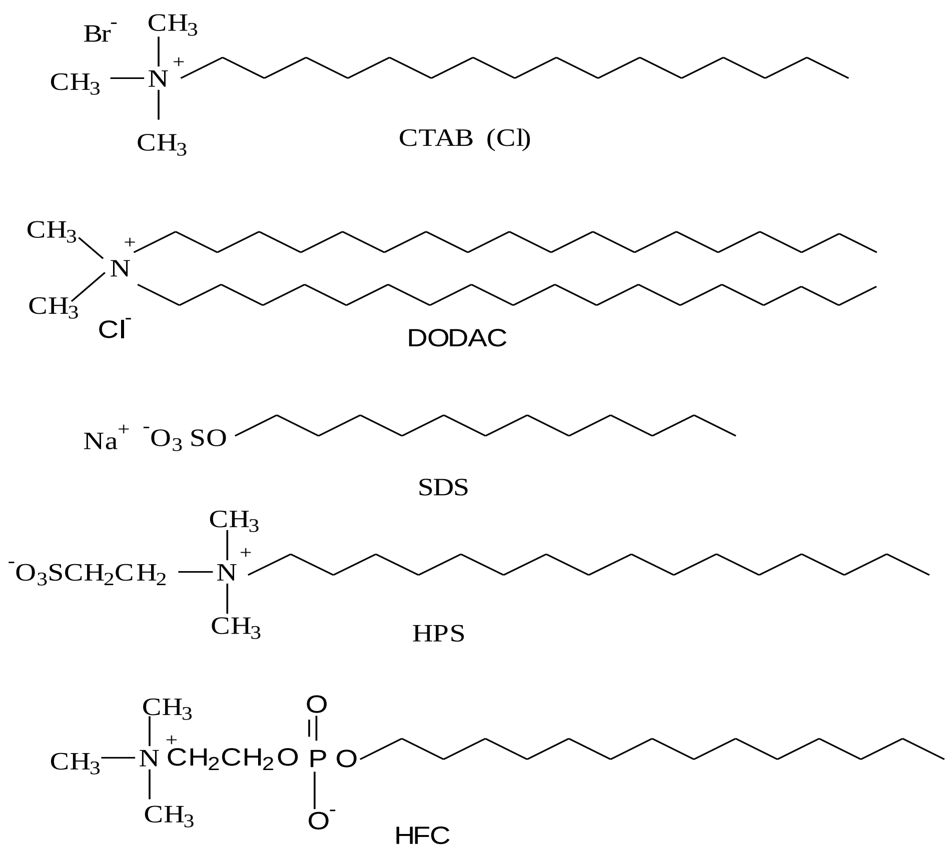
Com algumas exceções os ácidos graxos naturais:

Formam "sabões" com Na & K – solúveis em água.

Sabões com Ca & Mg – Insolúveis em água.

DUPLA PERSONALIDADE!!!

Estruturas de Anfifílicos Sintéticos

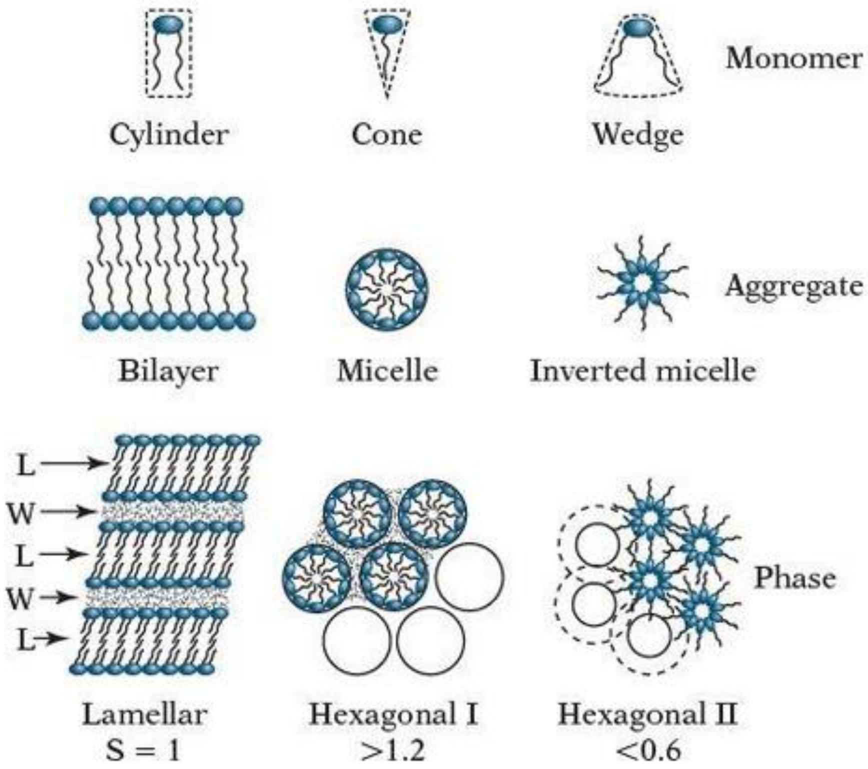


Pc=v/a.l
Pc= Critical Packing Parameter

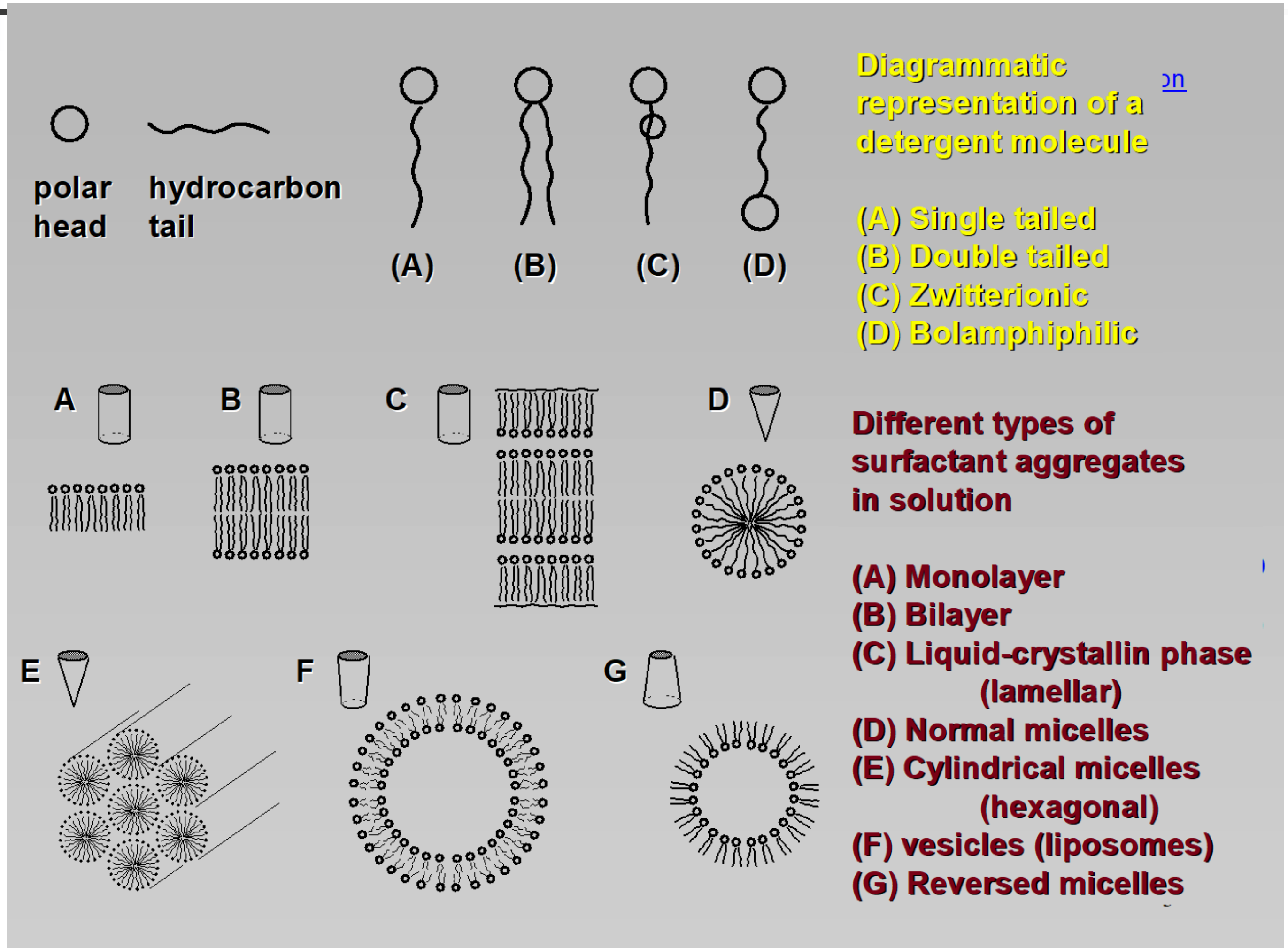
V=volume da cadeia alquilica
a-área da cabeça polar
l-comprimento máximo da cadeia alquilica estendida

P<1/3 micelas
1/3<P>1/2 –cilindro
½<P>1 bicamada

Estruturas Supramoleculares



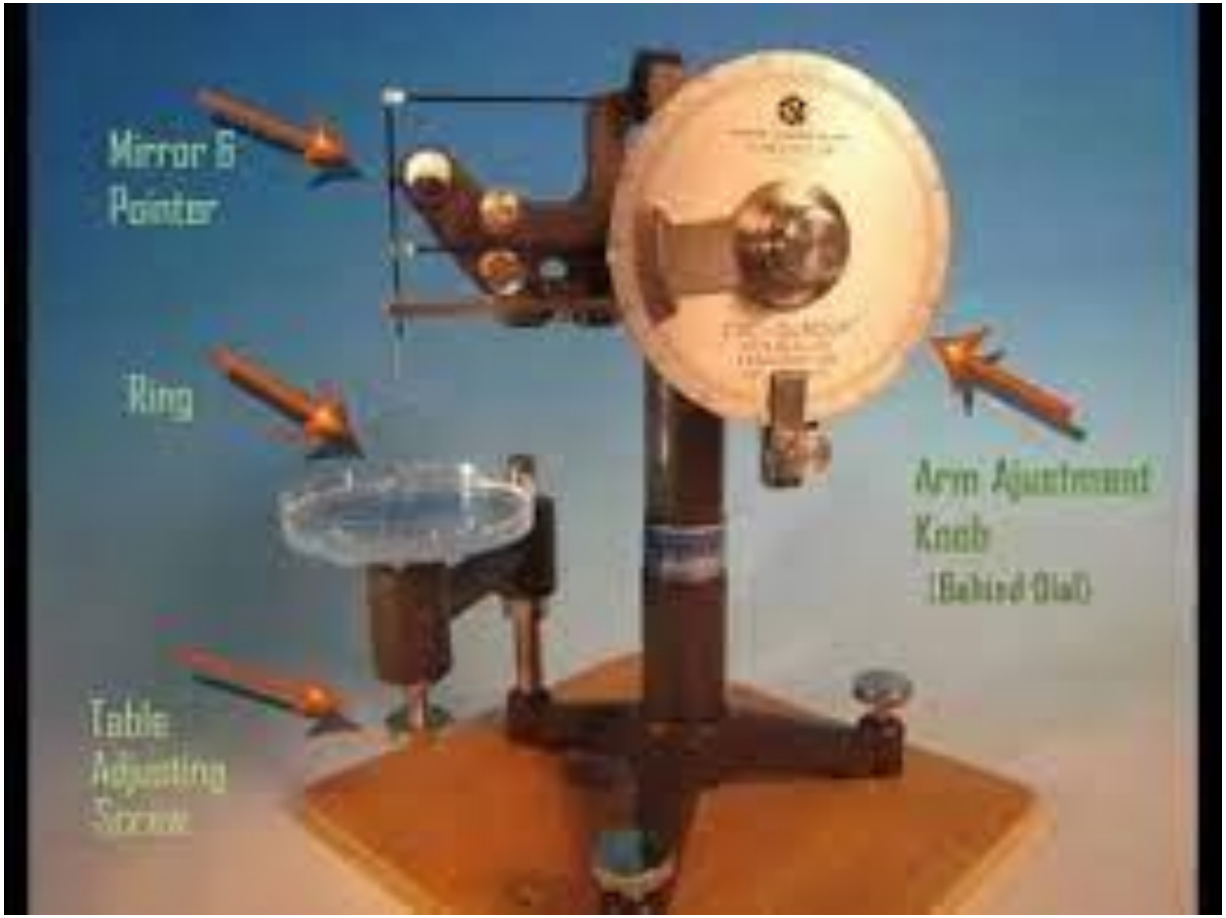
Estruturas Supramoleculares-Efeito Hidrofóbico



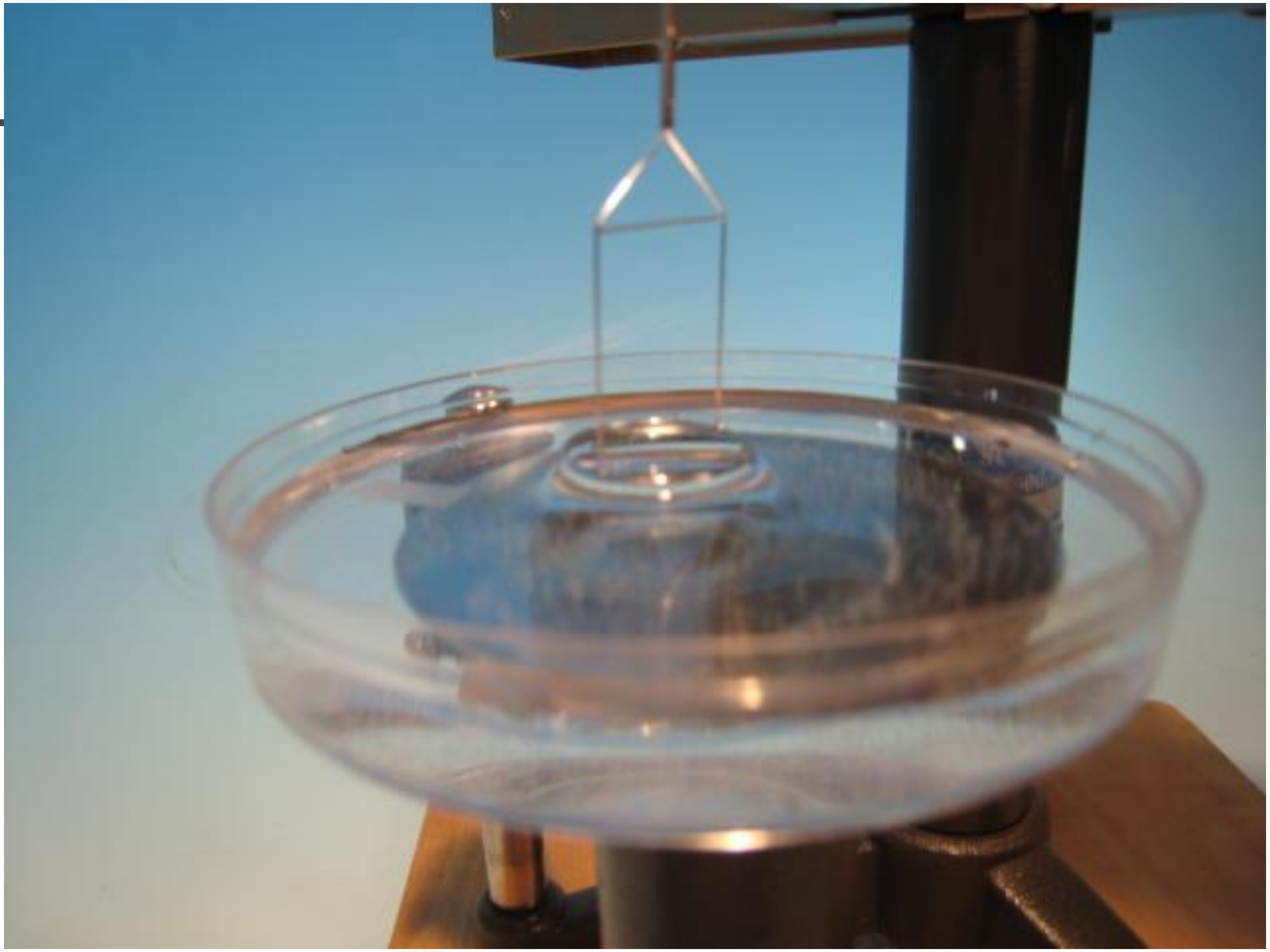
Tensão superficial- andar sobre a água

Tensiômetro

Tensiômetro

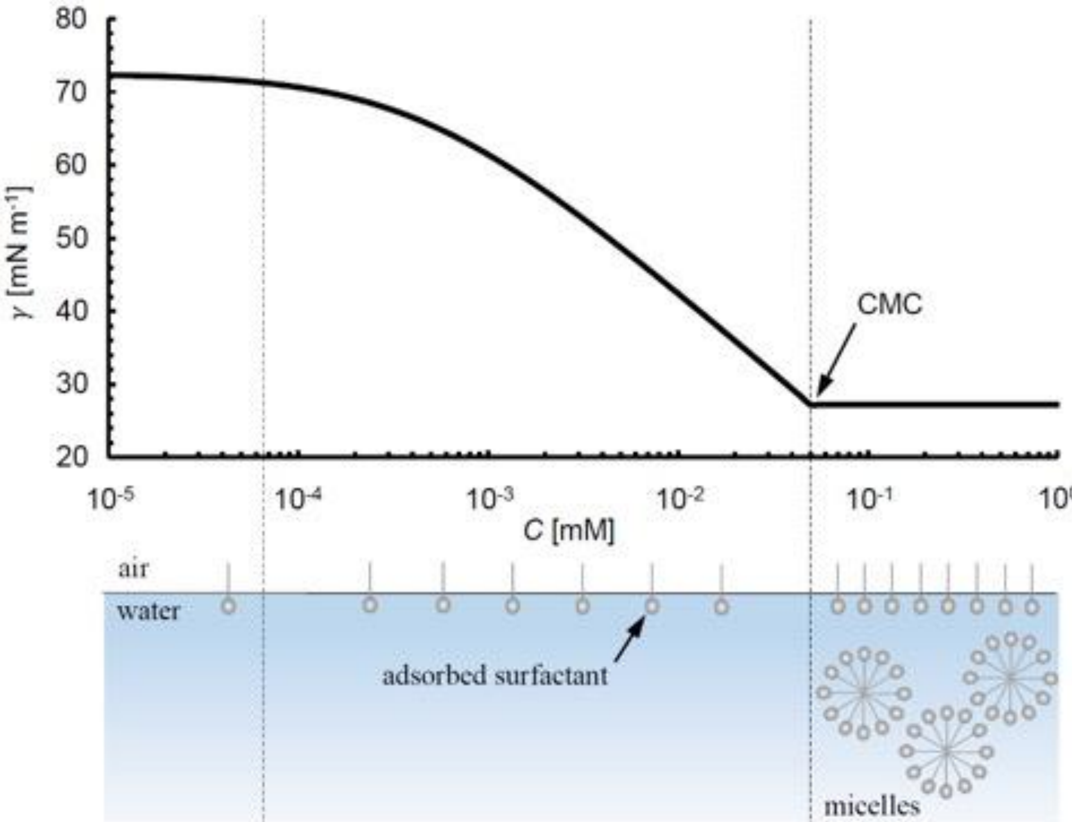


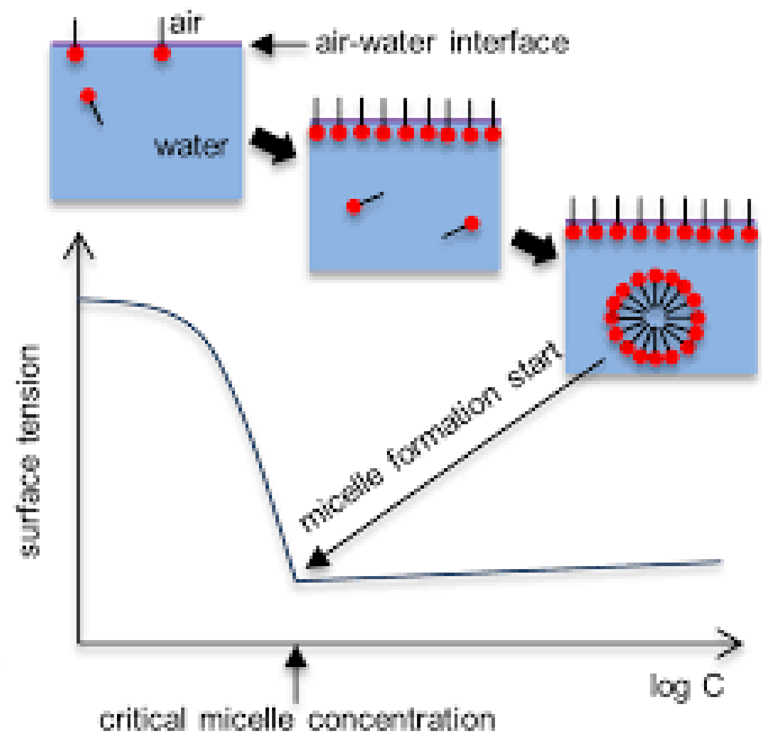
Tensiômetro

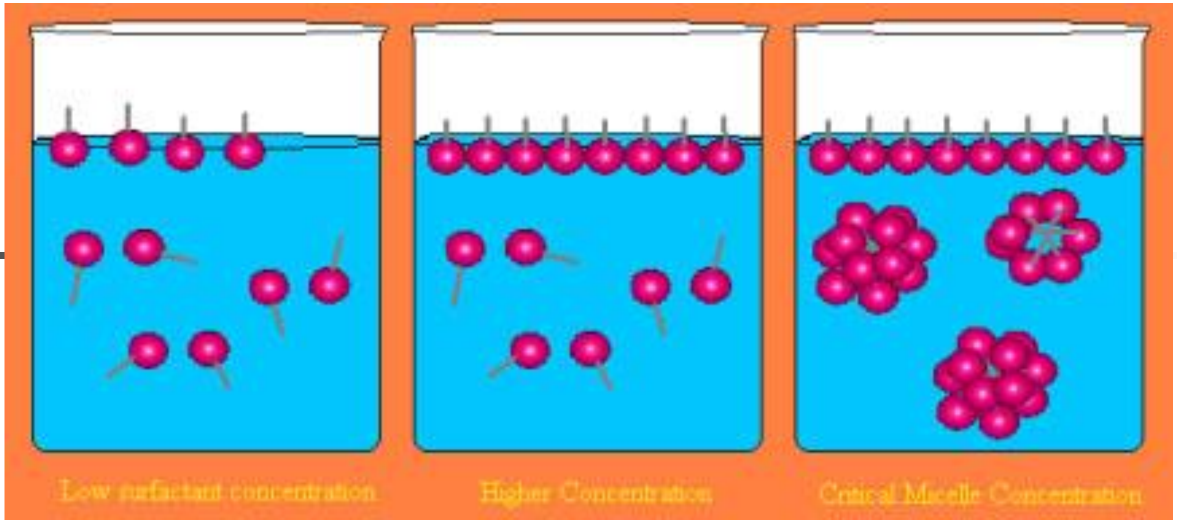


https://www.stevespanglerscience.com/lab/experiments/milk-color-explosion/

Curva de tensão superficial e determinação da CMC de um surfactante



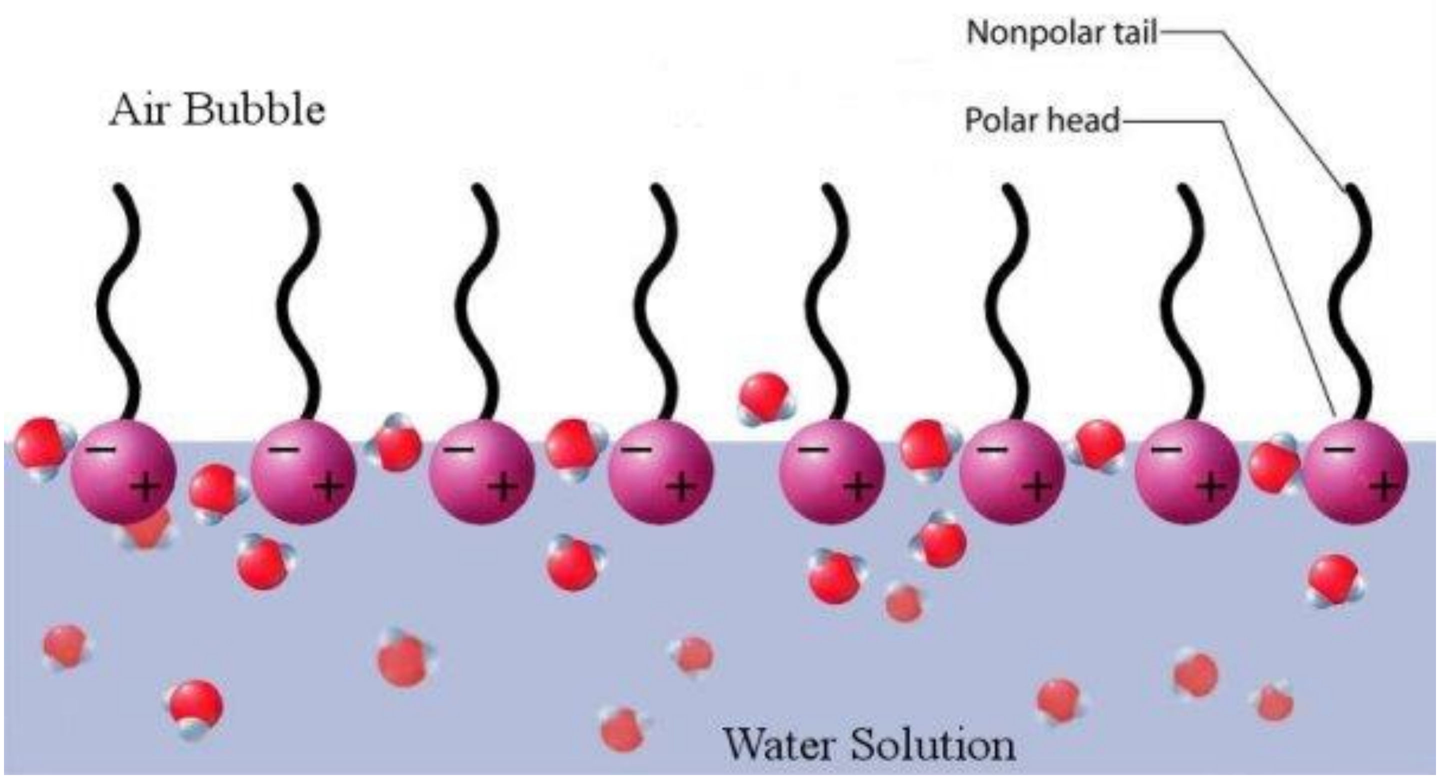




The existence of surfactant molecules in the form of self-assembled aggregates was first suggested by McBain in 1913 based on his studies on how the conductivity of a solution of soap molecules changes with the concentration.

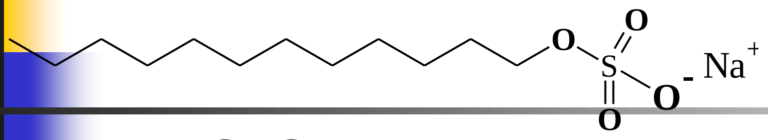
"The antipathy of the paraffin chain for water is, however, frequently misunderstood. There is no question of actual repulsion between individual water molecules and paraffin chains, nor is there any very strong attraction of paraffin chains for one another. There is, however, a very strong attraction of water molecules for one another in comparison with which the paraffin-paraffin or paraffin-water attractions are slight."

G. S. Hartley in 1936

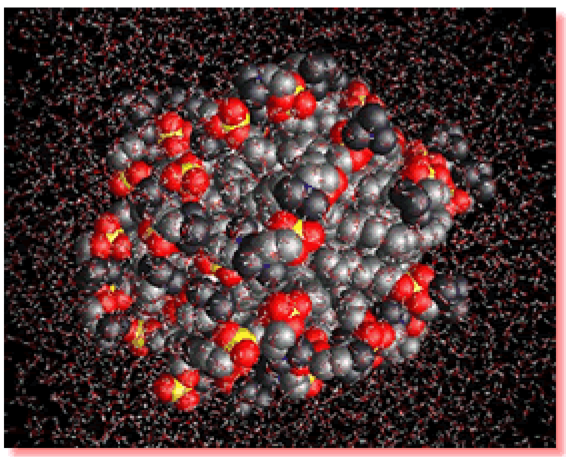


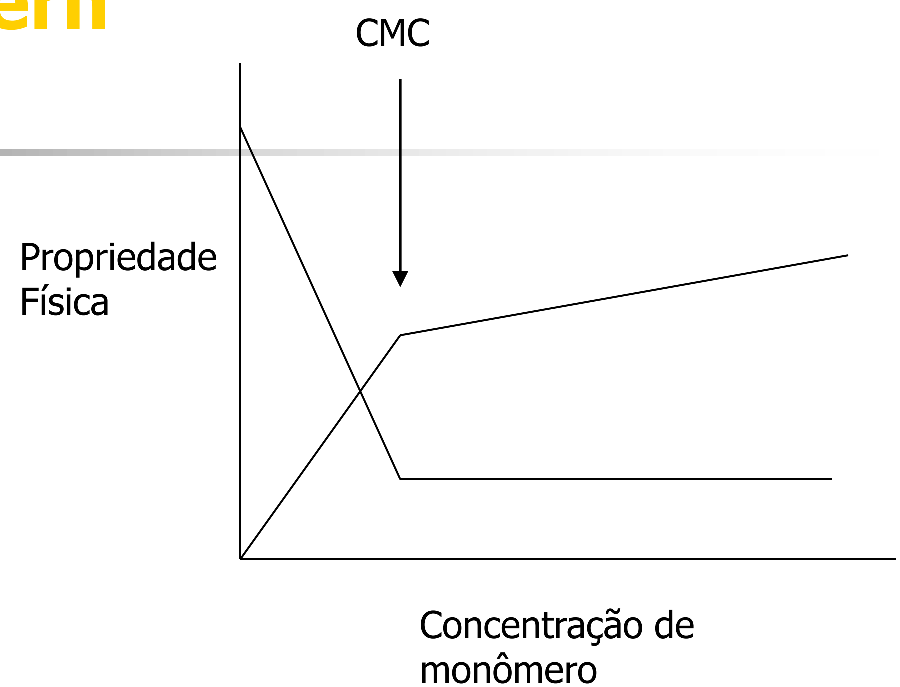
Nonpolar tail
Polar head
Air Bubble
Water Solution

Micelas, Modelos de Micelas e a Camada de Stern

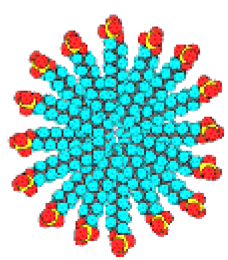


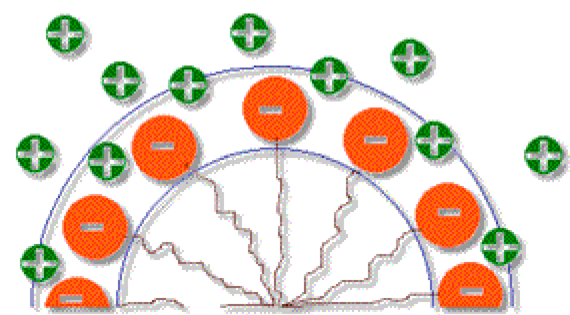
SDS





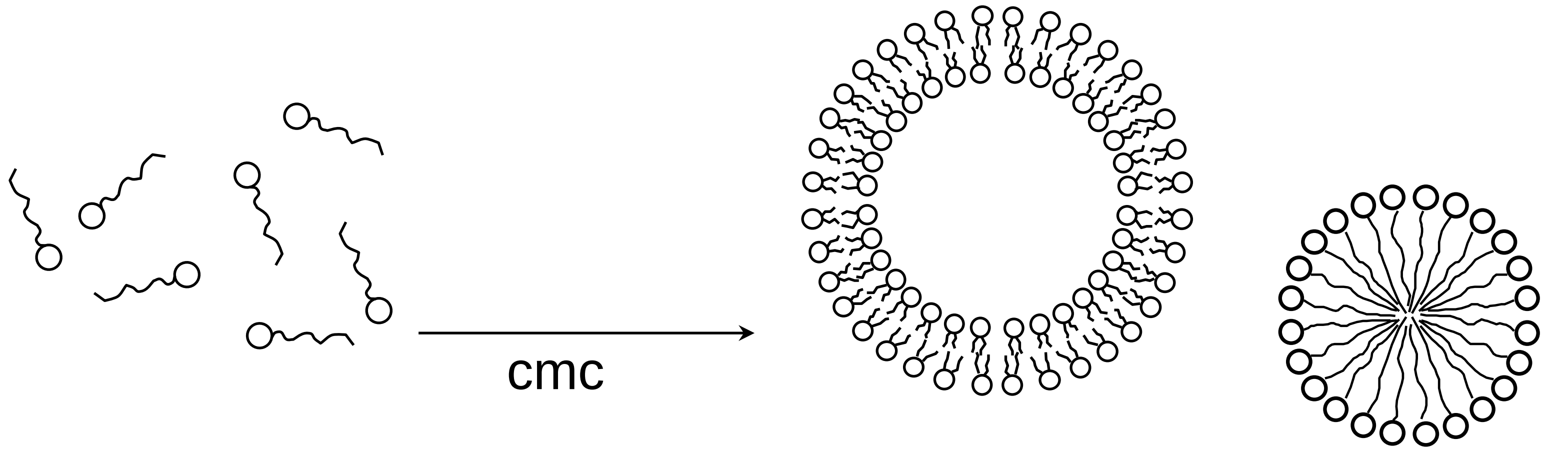
G. S. Hartley in 1936



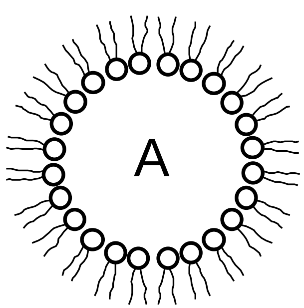


Camada de Stern

1. self-organization: spontaneous formation of ordered structures (…evolution, origin of life…)



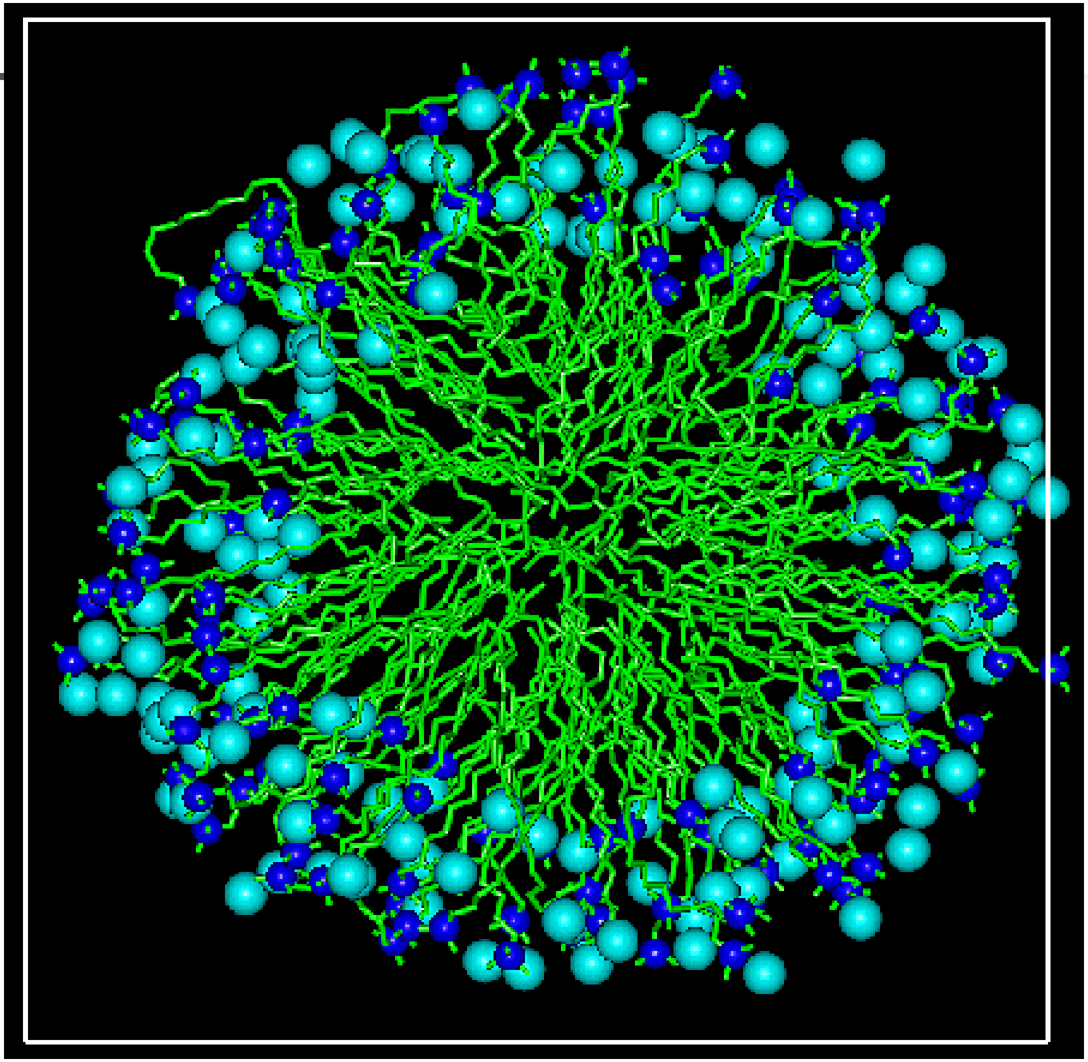
2. compartmentation (microheterogenous reactions...)



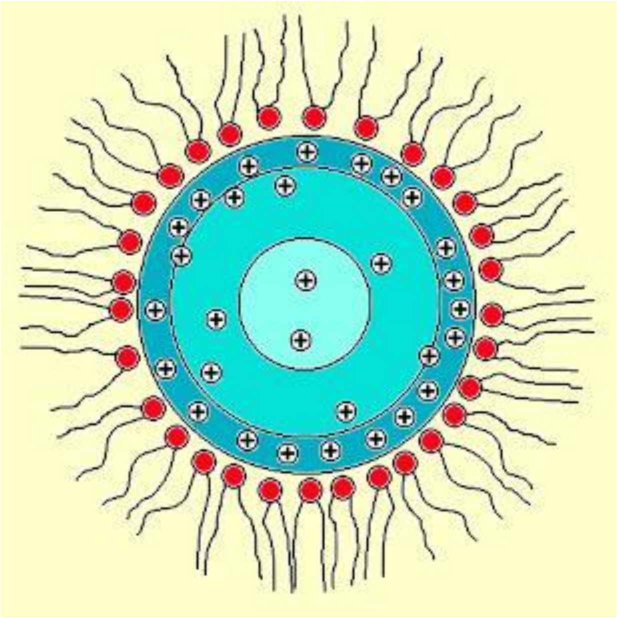
B

$A+B \longrightarrow ?$

Micela

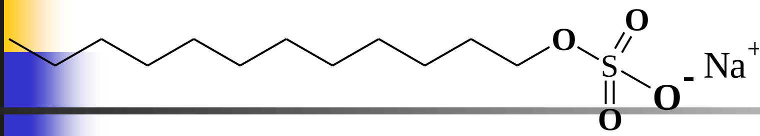


Micela Reversa

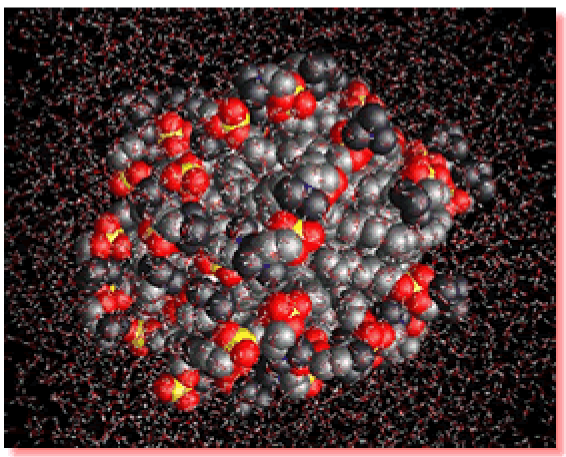


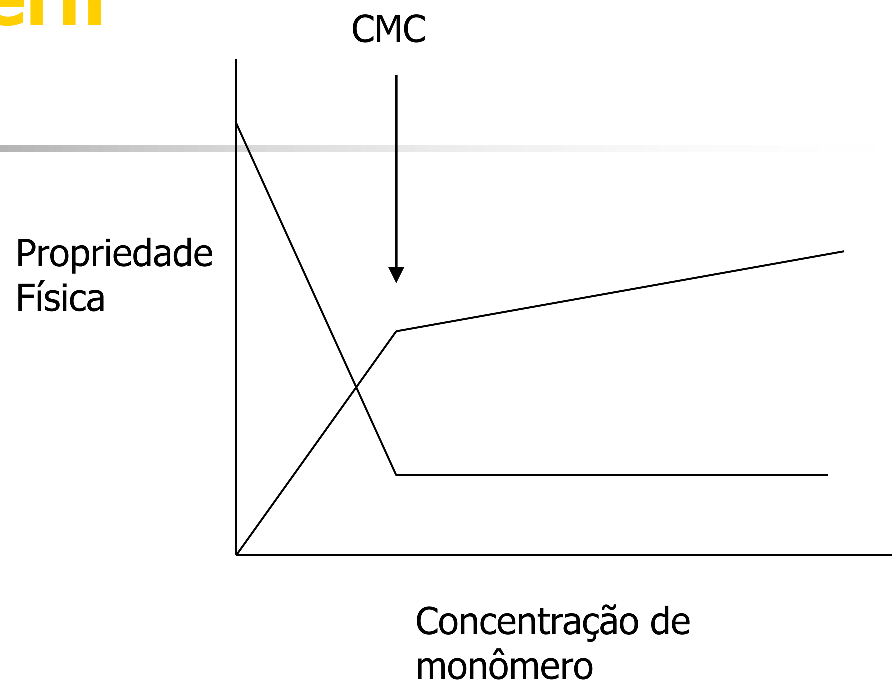
Interior ➔ solvente apolar
Exterior ➔ H_2O

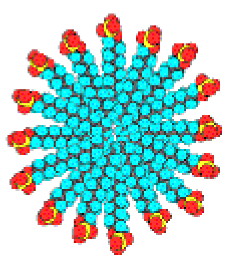
Micelas, Modelos de Micelas e a Camada de Stern

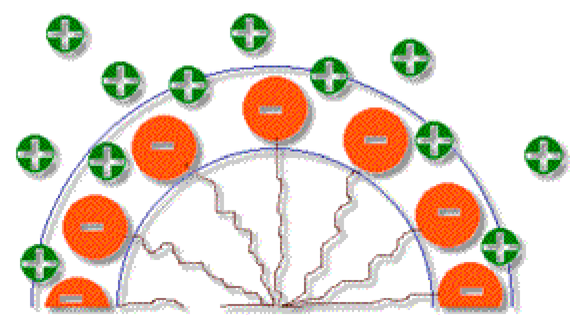


SDS







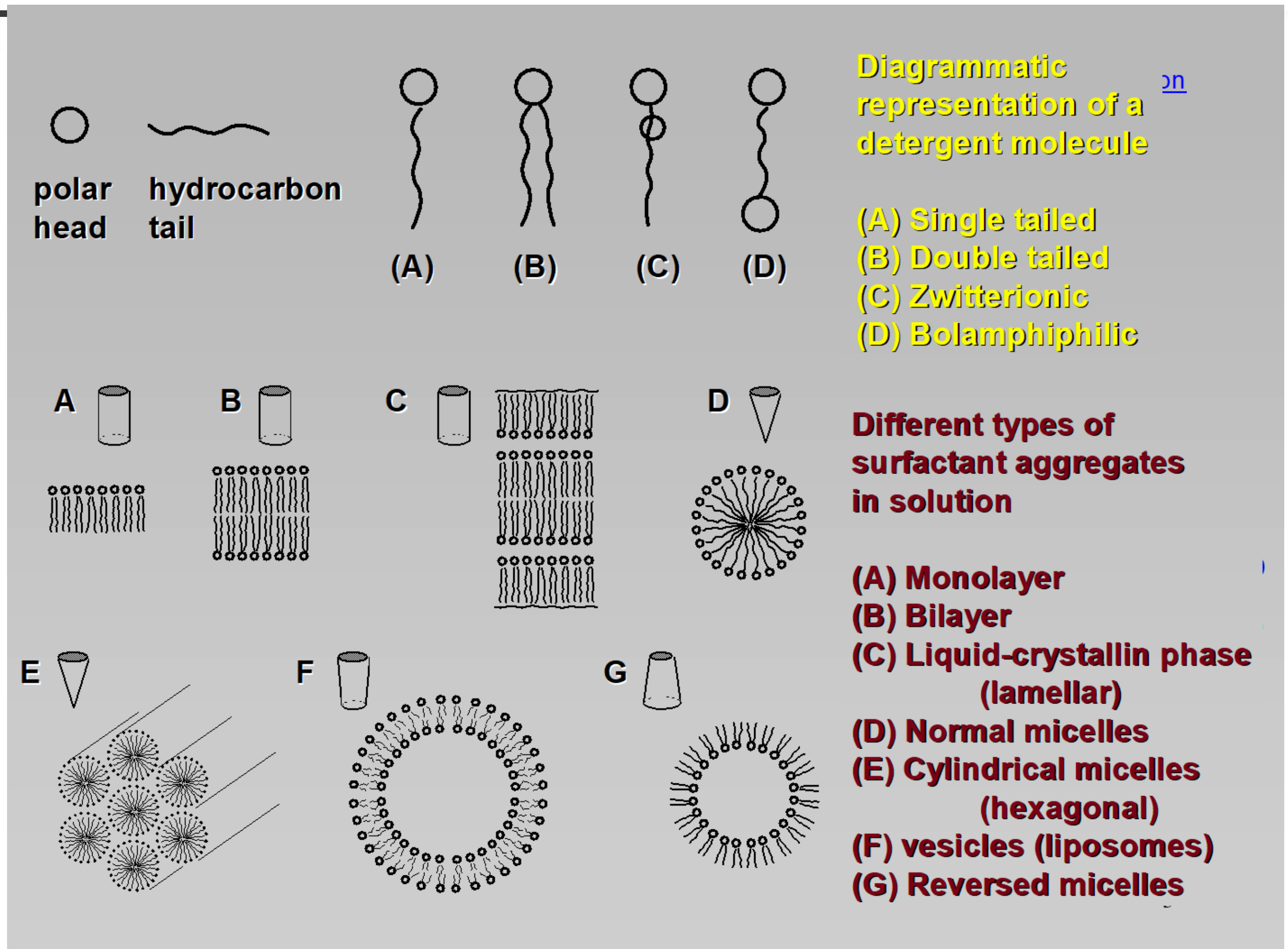


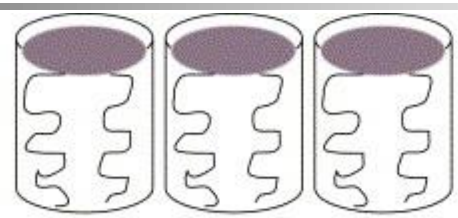
Camada de Stern

Actually, the cell membrane is a remarkable community of molecules, embedded in a structural motif called a bilayer, where multiple types of dynamic events take place. Motions of proteins and nucleic acids might seem rather dull when compared to those within phospholipid self-assemblies.

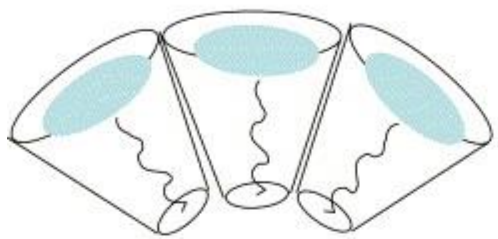
Langmuir ***2005, 21, 10336-10341***

Estruturas Supramoleculares-Efeito Hidrofóbico





Cylindrical shaped lipids (e.g. PC)



Cone shaped lipids

(i.e. micelle forming lipids)

(e.g. OA and CHEMS)

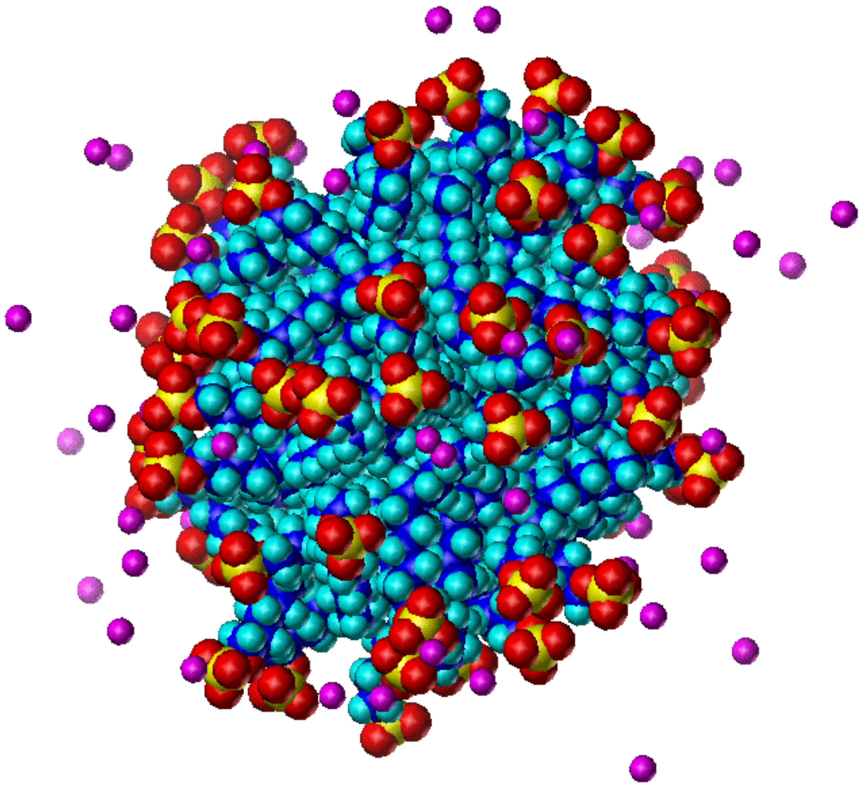
Inverted cone shaped lipids

(e.g. DOPE)

A lamella of a pH-sensitive

liposome

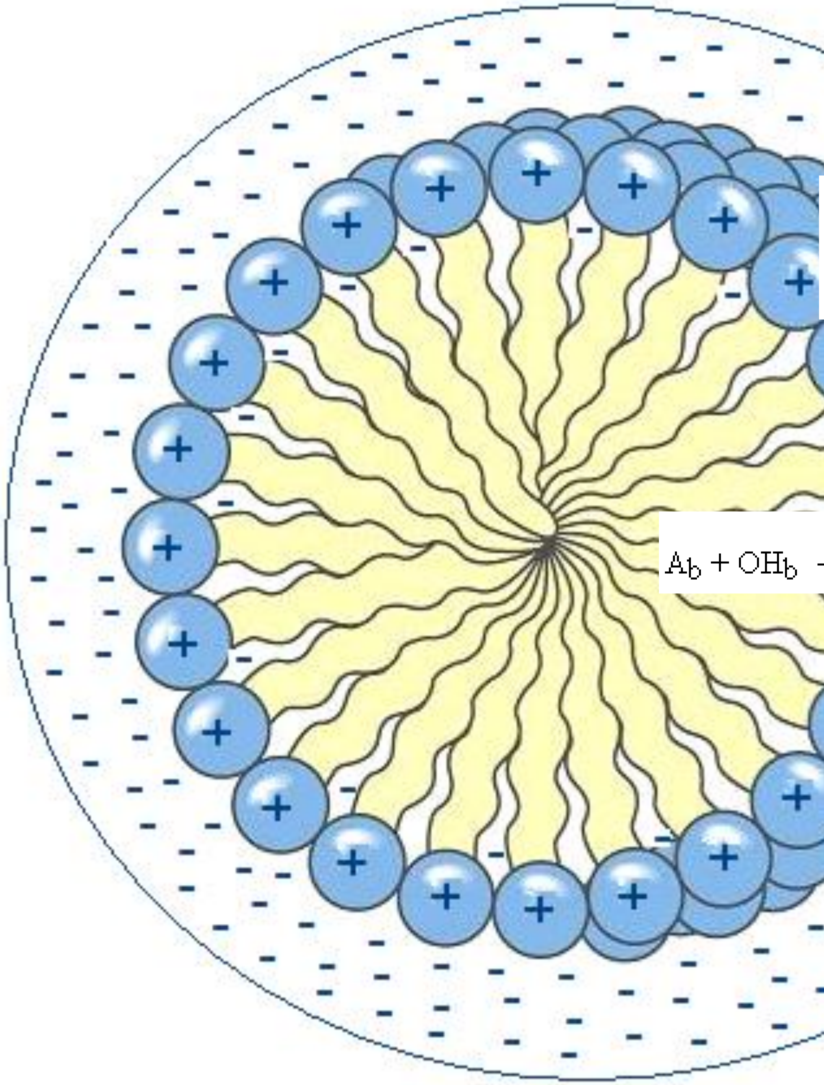
Uma Micela de SDS



Concentração Micelar Crítica- CMC

Grau de Dissociação (alfa)

Cálculo por dinâmica molecular, Mackarel Jr, J Phys Chem. *99*, 1846, 1995



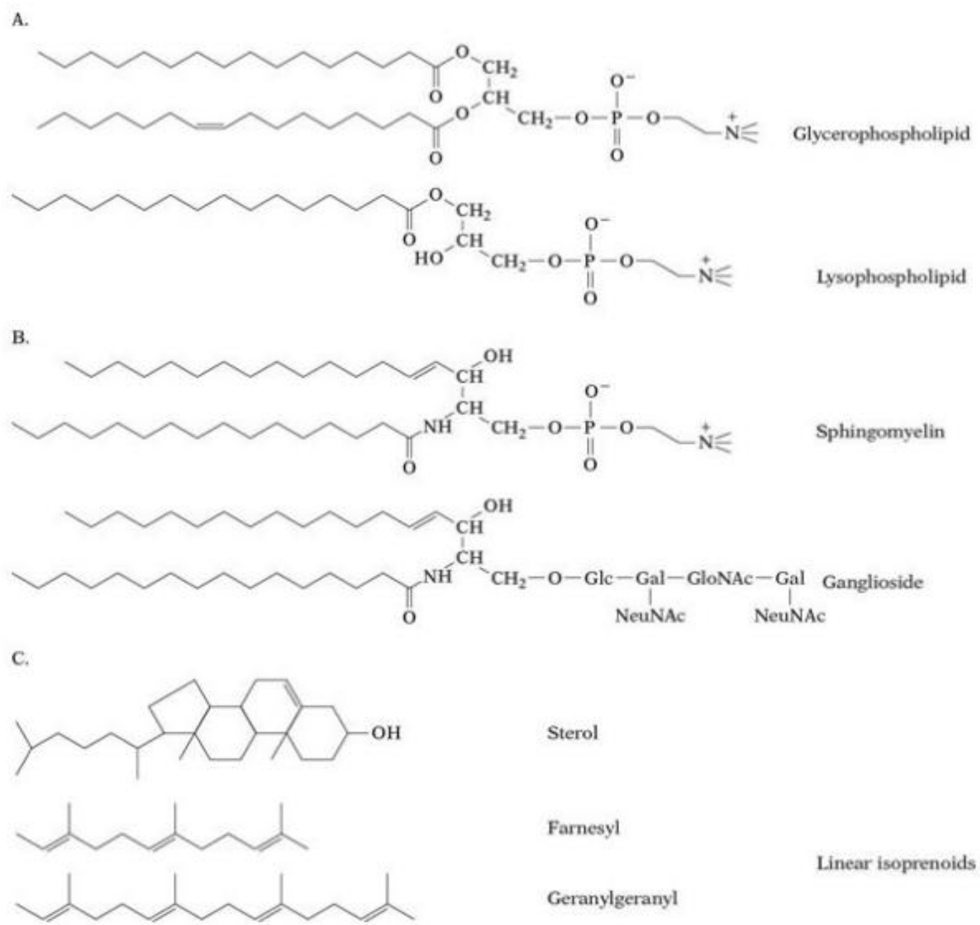
$$OH_f + Y_b \underset{}{\overset{K_{OH/Y}}{\rightleftharpoons}} OH_b + Y_f$$

$$K_{OH/Y} = [OH_b][Y_f]/([OH_f][Y_b])$$

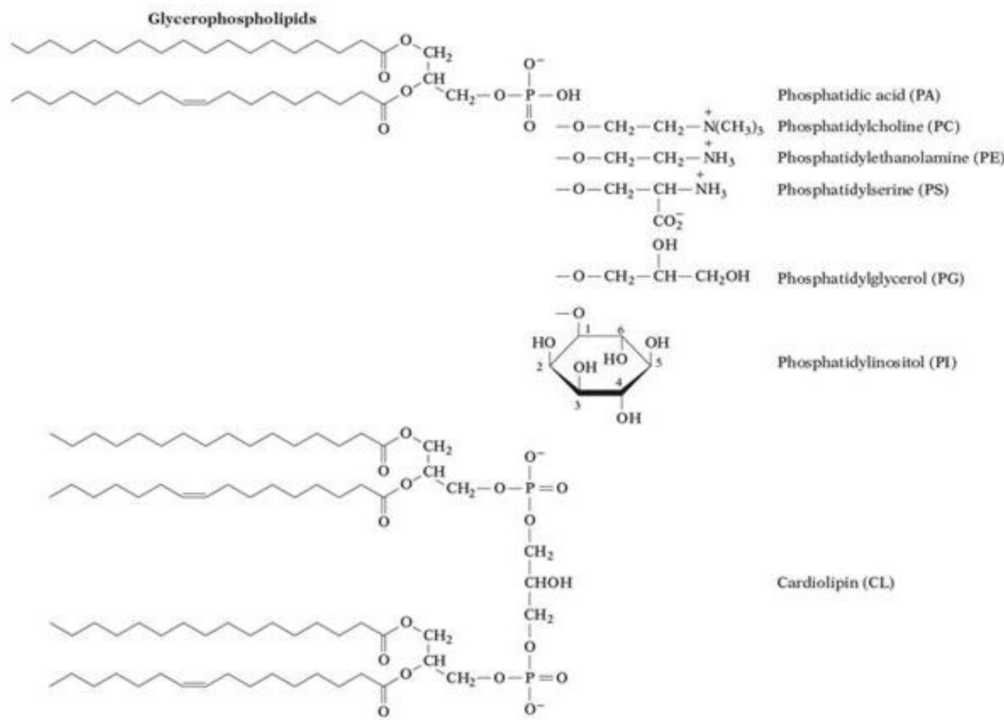
$$A_b + OH_b \xrightarrow{k_m} P$$

$$A_f + OH_f \xrightarrow{k_w} P$$

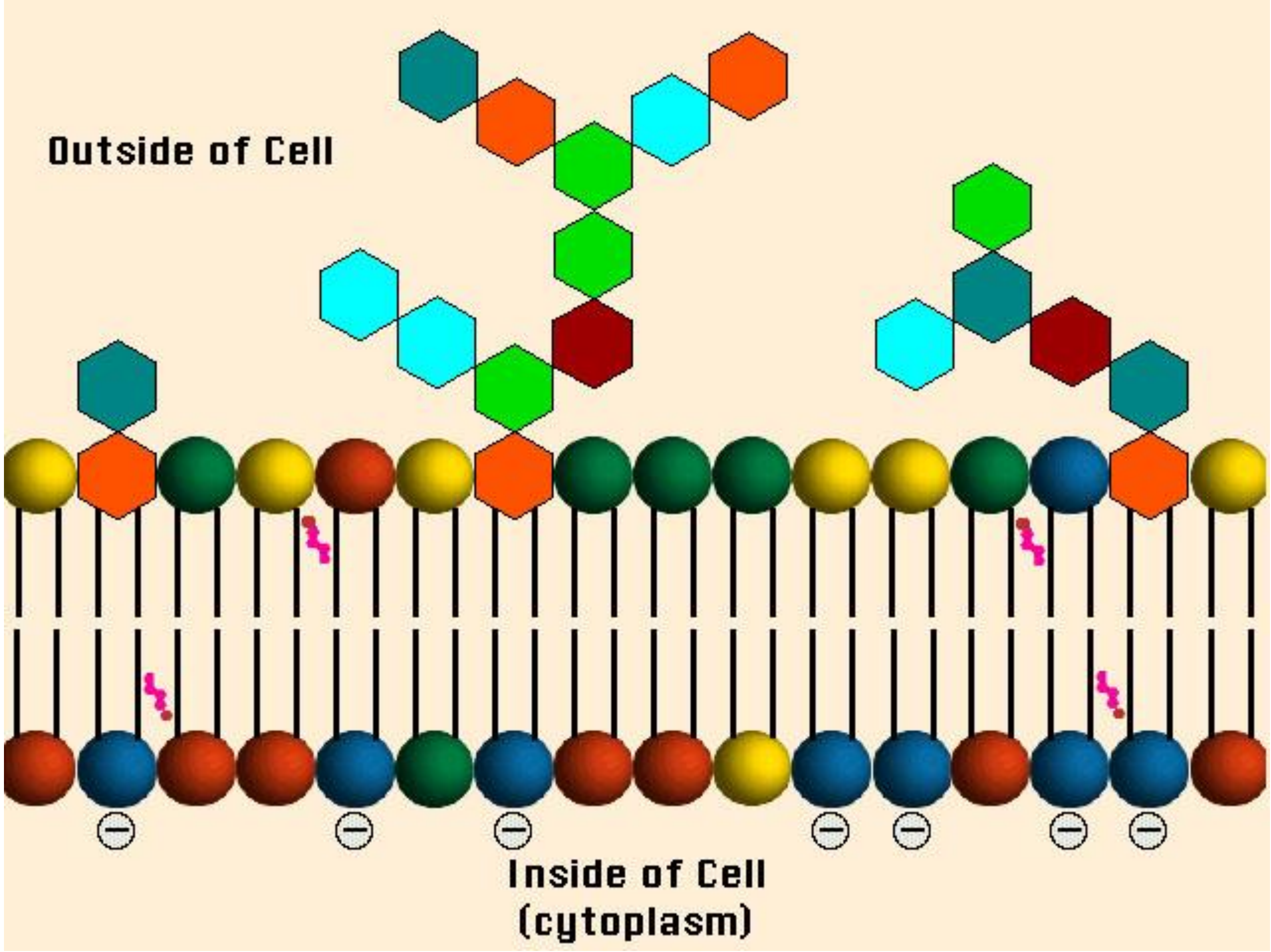
Lipídios de Membranas Biológicas



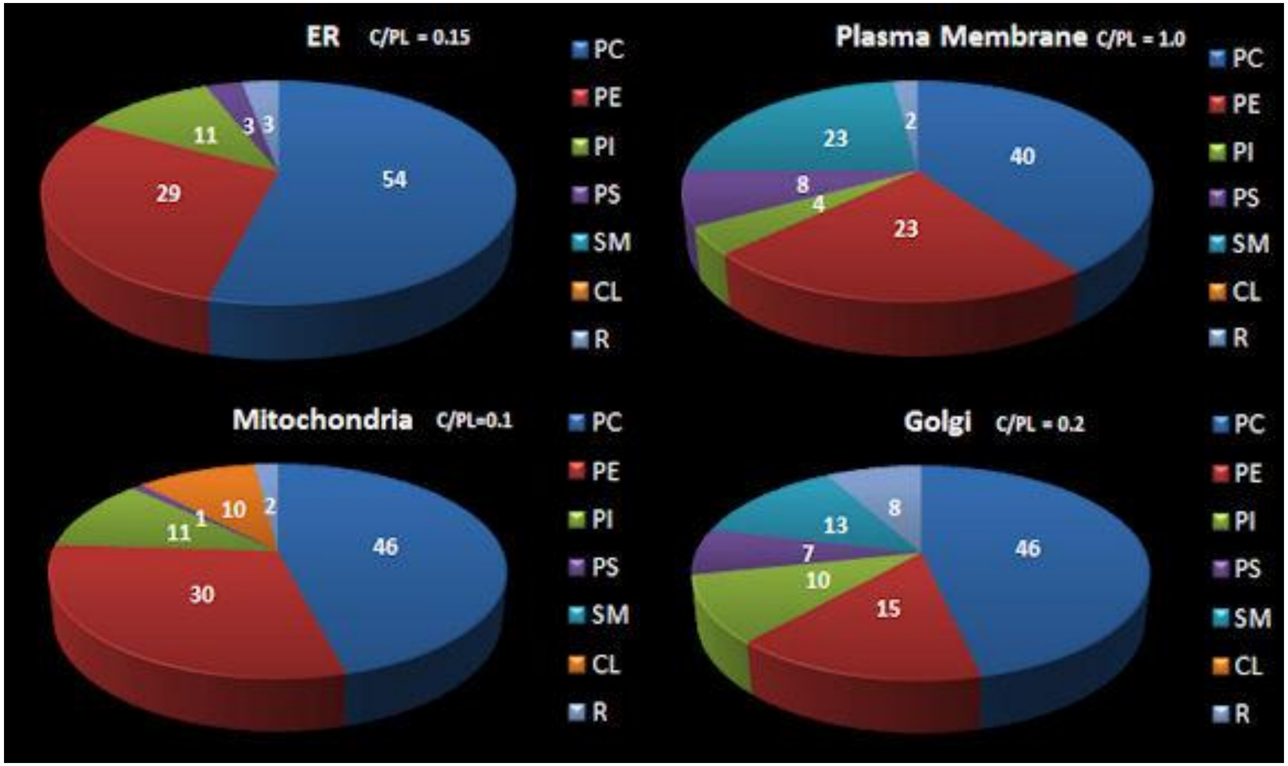
2.5. Structures of glycerophospholipids. The common glycerophospholipids in biological membranes contain one of the polar headgroups shown. In addition, they vary greatly in the length and saturation of their acyl chains, although in general the acyl chain on C1 is saturated and the acyl chain on C2 is unsaturated. Redrawn from Gennis, R. B., *Biomembranes*,



Assimetria dos Fosfolipidios



Composição de Lipidios de Diferentes Membranas



Composição em massa de lipídios/proteína de diferentes membranas

TABLE 1.1. Composition of membrane preparations by percent dry weight[a]

Source	Lipid	Protein	Cholesterol
Rat liver			
Plasma	30–50	50–70	20
Rough ER	15–30	60–80	6
Smooth ER	60	40	10
Inner mitochondria	20–25	70–80	<3
Outer mitochondria	30–40	60–70	<5
Nuclear	15–40	60–80	10
Golgi	60	40	8
Lysosomes	20–25	70–80	14
Rat brain			
Myelin	60–70	20–30	22
Synaptosome	50	50	20
Rat erythrocyte	40	60	24
Rat rod outer segment	50	40	<3
Escherichia coli	20–30	70	0
Bacillus subtilis	20–30	70	0
Chloroplast	35–50	50–65	0

[a] The percentages by weight of membrane preparations from various eukaryotic and prokaryotic sources are given.

ER, endoplasmic reticulum.

Source: Based on Jain, M. K., and R. C. Wagner, *Introduction to Biological Membranes*, 2nd ed. New York: Wiley, 1988, p. 34.

Composição de ácidos graxos de células de *E. coli* crescidas em diferentes temperaturas

TABLE 2.2. Fatty acid composition of *E. coli* cells cultured at different temperatures[a]

	Percentage of total fatty acids[b]			
	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[c]	2.9	2.0	1.6	0.38

[a] The values are given in weight percent of total lipid.
[b] The exact fatty acid composition depends not only on growth temperature but on growth stage and growth medium composition.
[c] Ratios 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.
Source: Data from Marr, A. G., and J. L. Ingraham, Effect of temperature on the composition of fatty acids in *Escherichia coli*. *J Bacteriol.* 1962, 84:1260–1267. Reprinted with permission from Nelson, D. L., and M. M. Cox, *Lehninger Principles of Biochemistry*, 4th ed. New York: W. H. Freeman, 2005.

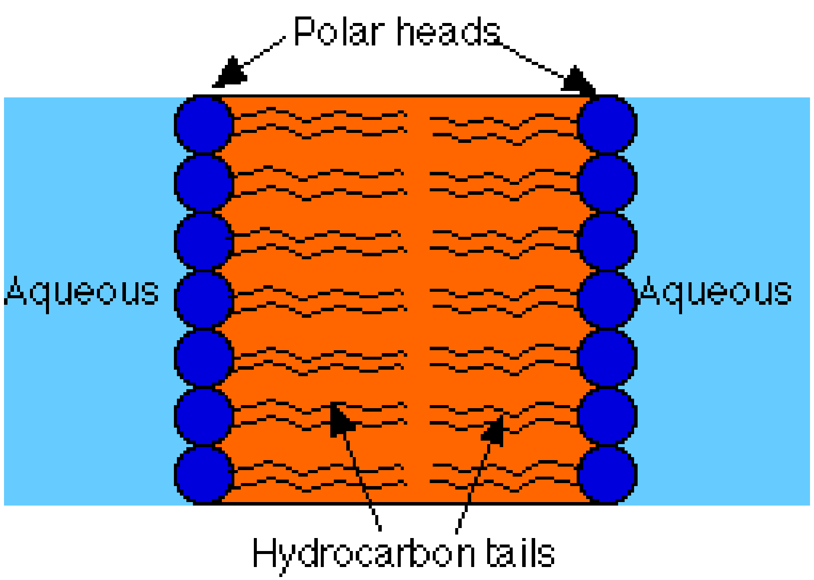
Lipidios de membrana de Archea- Não possuem ácidos graxos

Difitanil tetraéter-ligados a glicerol por ligações eter.
Estáveis em altas temperaturas e pHs baixos.
Possuem cadeias longas (32 carbonos) e portanto, o dobro do comprimento das cadeias dos Fosfolipidios.
Possuem dois glicerois, um em cada extremidade.

Glicerol na configuração R e não S, como nas membranas de bactérias e eucariotos

Propriedades dos Fosfolipídios

- Formam membranas, micelas, lipossomas
  - Orientam-se na interface água:óleo
  - Contém grupos hidrofóbicos e hidrofílicos
  - Formam as bicamadas das membranas



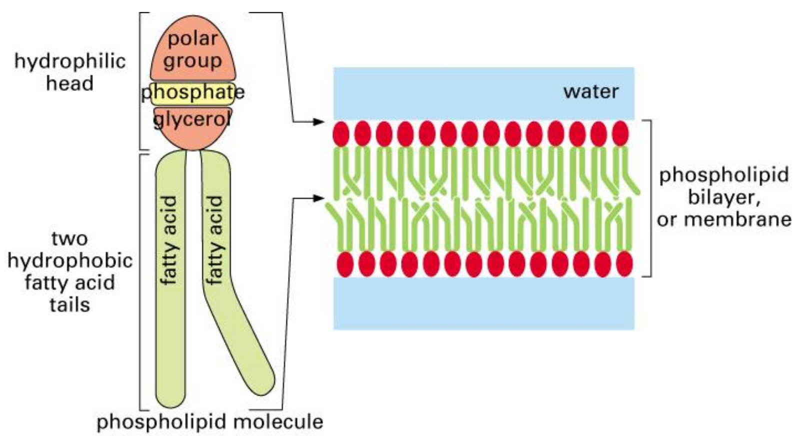
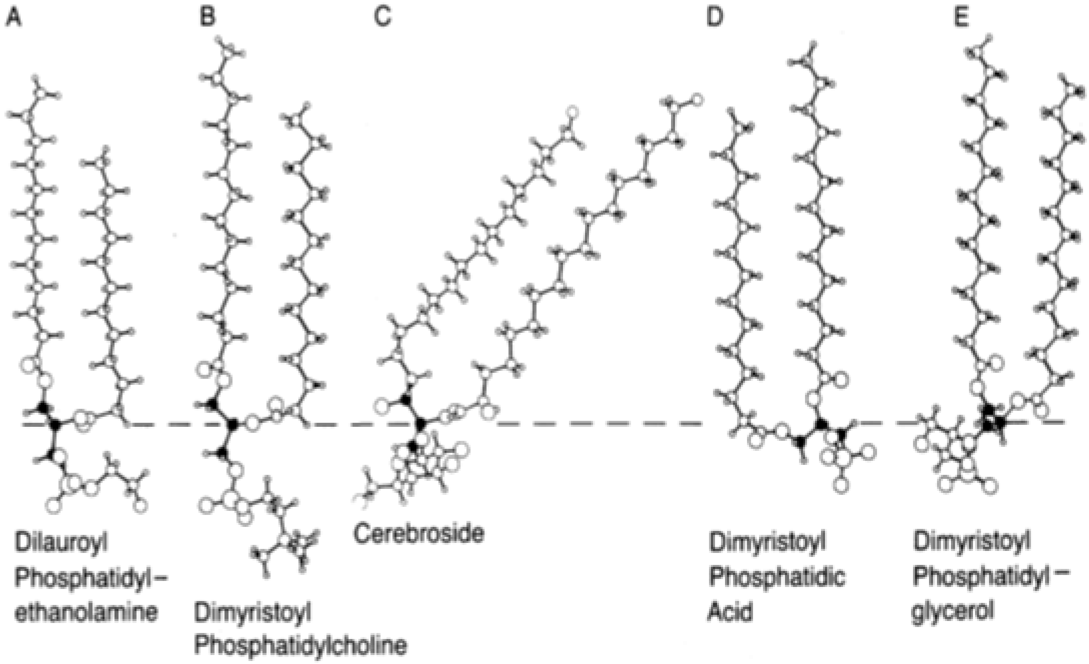
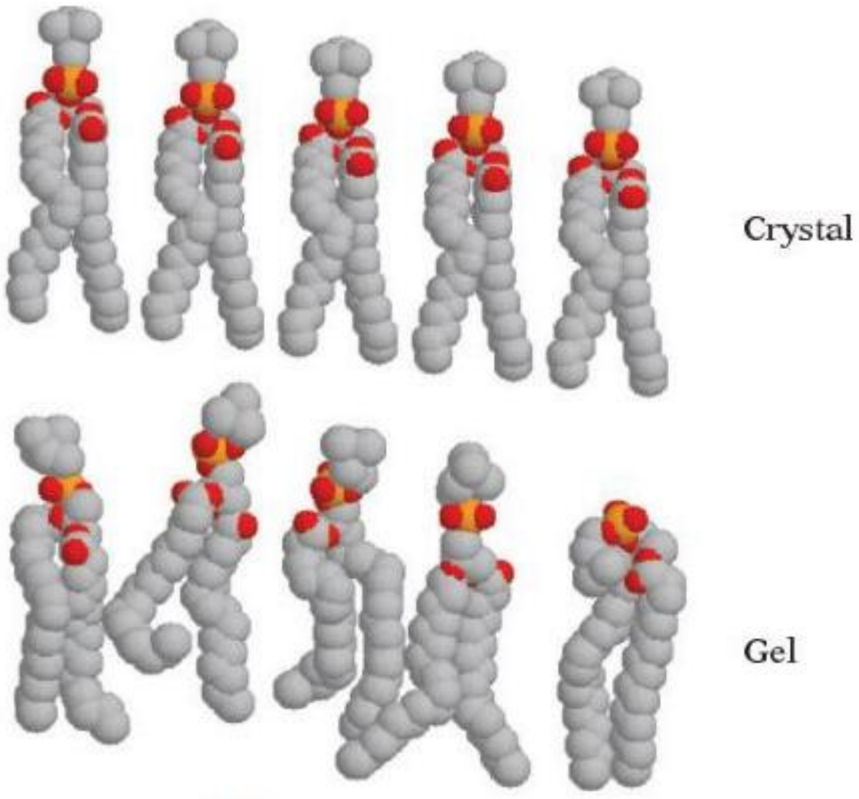


Figure 2–22. Molecular Biology of the Cell, 4th Edition.

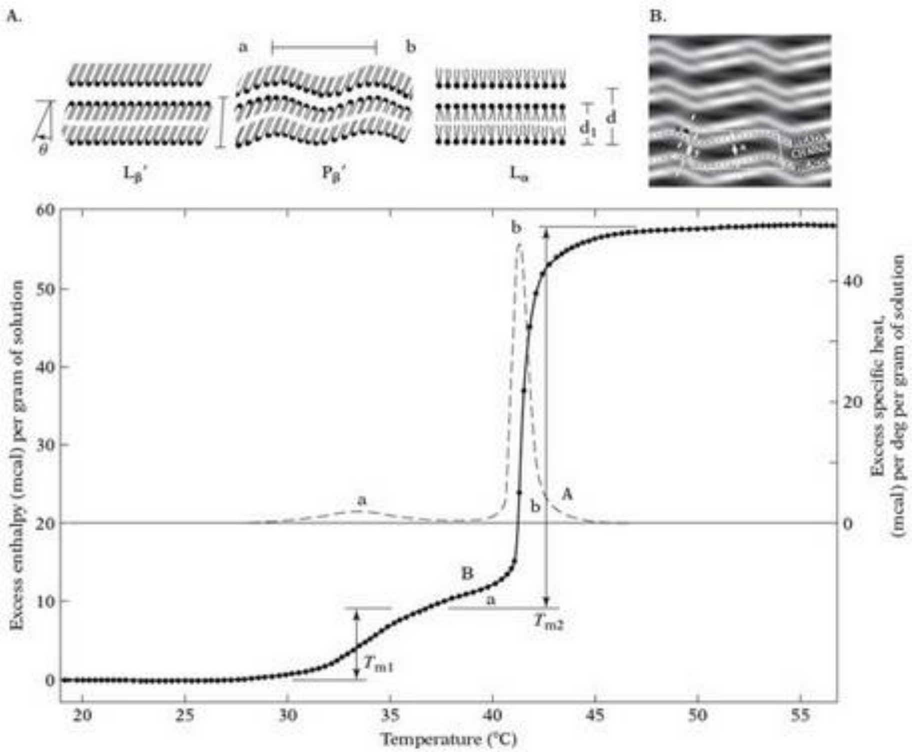
Orientação dos fosfolipídeos na bicamada



Temperatura de Transição



Transição de fase

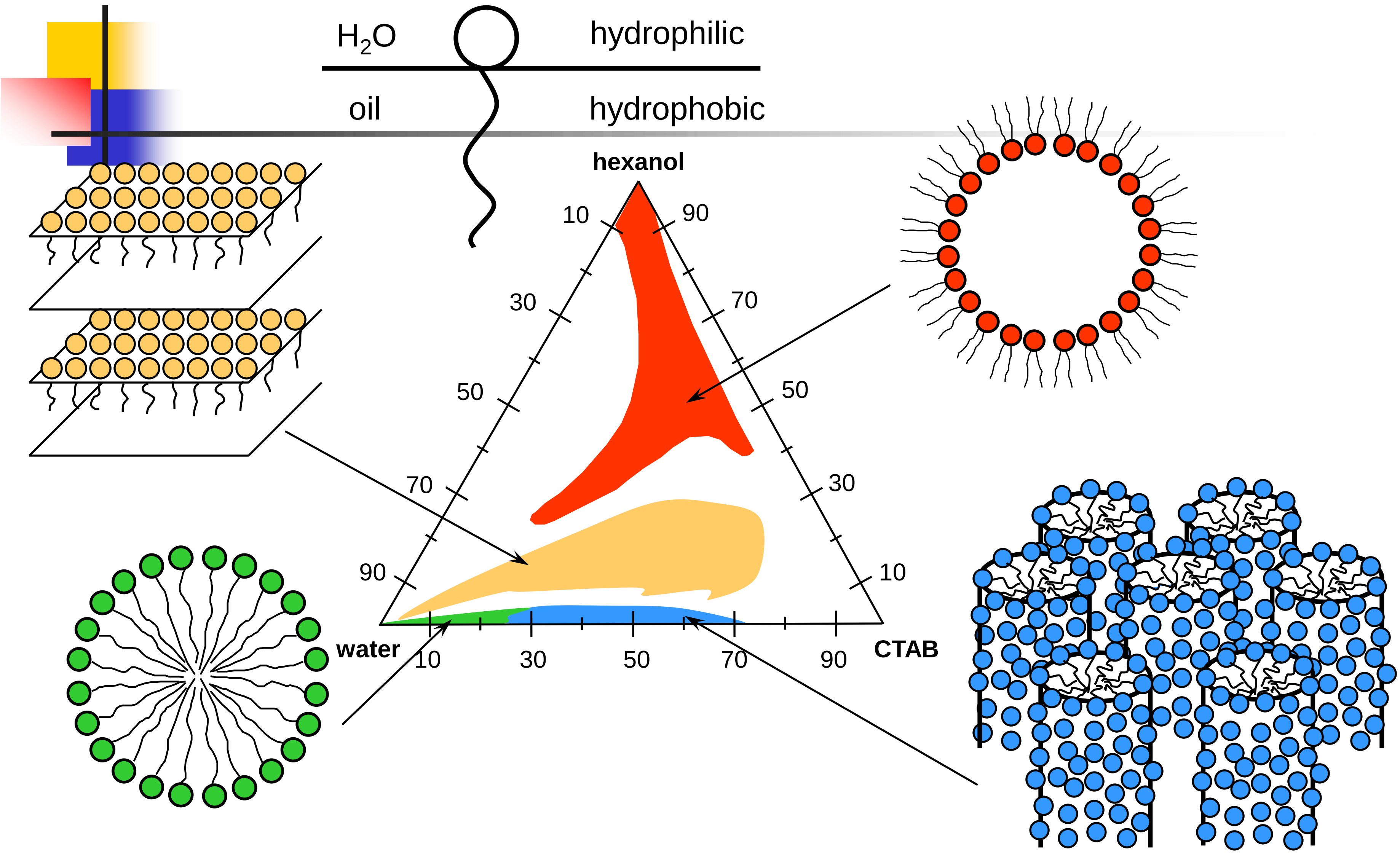


Fase-gel/fase fluida

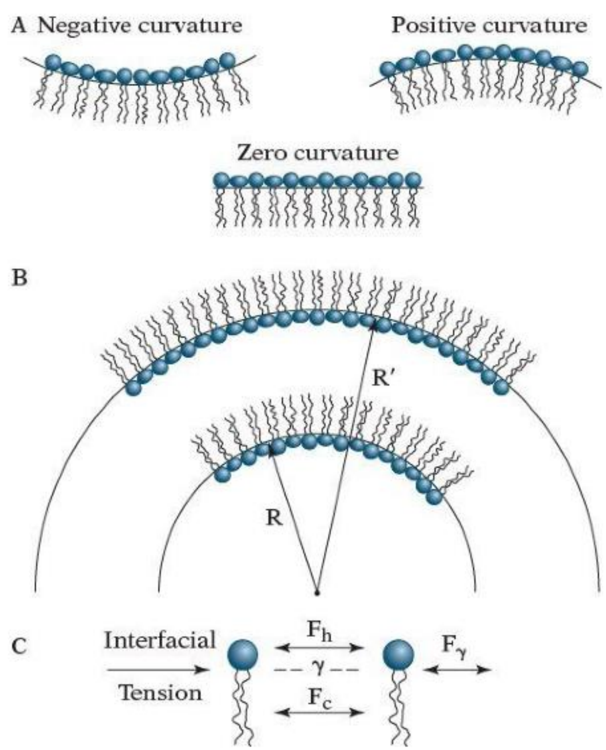
- Transição Trans-Gauche na transição de fase
- Histerese
- Mistura não ideal-clustering

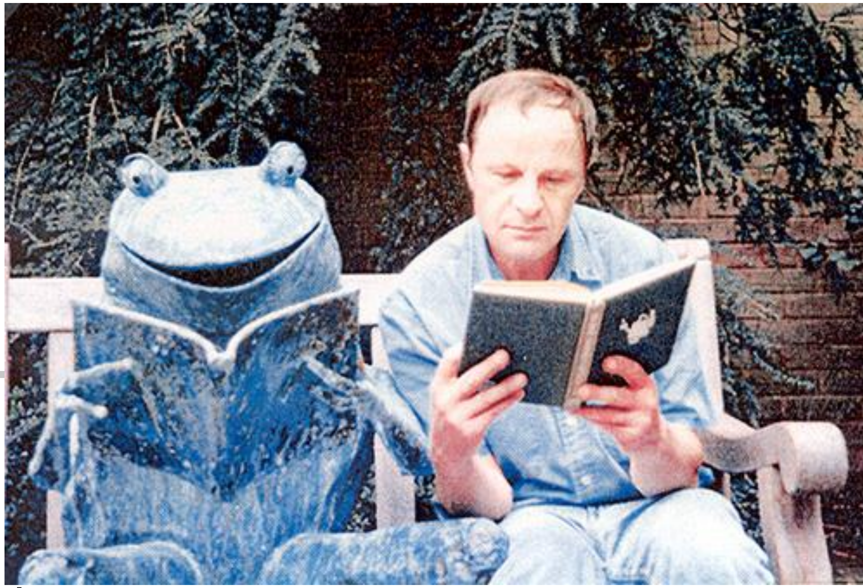
Moléculas Anfifílicas

Diagrama de Fase



2.18. Curvature of a lipid monolayer. **A.** R is the radius of curvature of the lipid/water interface, which is defined as positive for H_I phase (right) and negative for H_{II} phase (left). **B.** A larger value of R produces less curvature than a smaller value of R. **C.** The zero curvature of one leaflet of a lamellar phase is the result of a balance of forces: F_c is the lateral pressure pushing the chains apart due to motions of bond rotation, and F_h is the lateral pressure in the headgroup region that consists of steric, hydrational, and electrostatic effects, in addition to some positive contributions from hydrogen bonds. F_γ is the result of the hydrophobic effect at the interface, where the interfacial tension minimizes the hydrocarbon–water contacts. Redrawn from Lee, A. G., *Biochim Biophys Acta*. 2004, 1666:62–87. © 2004 by Elsevier. Reprinted with permission from Elsevier.





More importantly, lateral mobility within one of the two bilayer “leaflets” allows a lipid molecule to:

(a) drift to a site of action (e.g., to a lipid dependent protein);
(b) accommodate a morphological change (e.g., pseudopod formation or membrane fusion); and
(c) assemble, along with other membrane components, into domains or “rafts”.
(d) Many factors, including cell type, affect lateral diffusion rates, but they are typically quite fast. Thus, lipids can cross an entire cell surface in a few minutes.

Menger, F.-Langmuir ***2005, 21, 10336-10341***

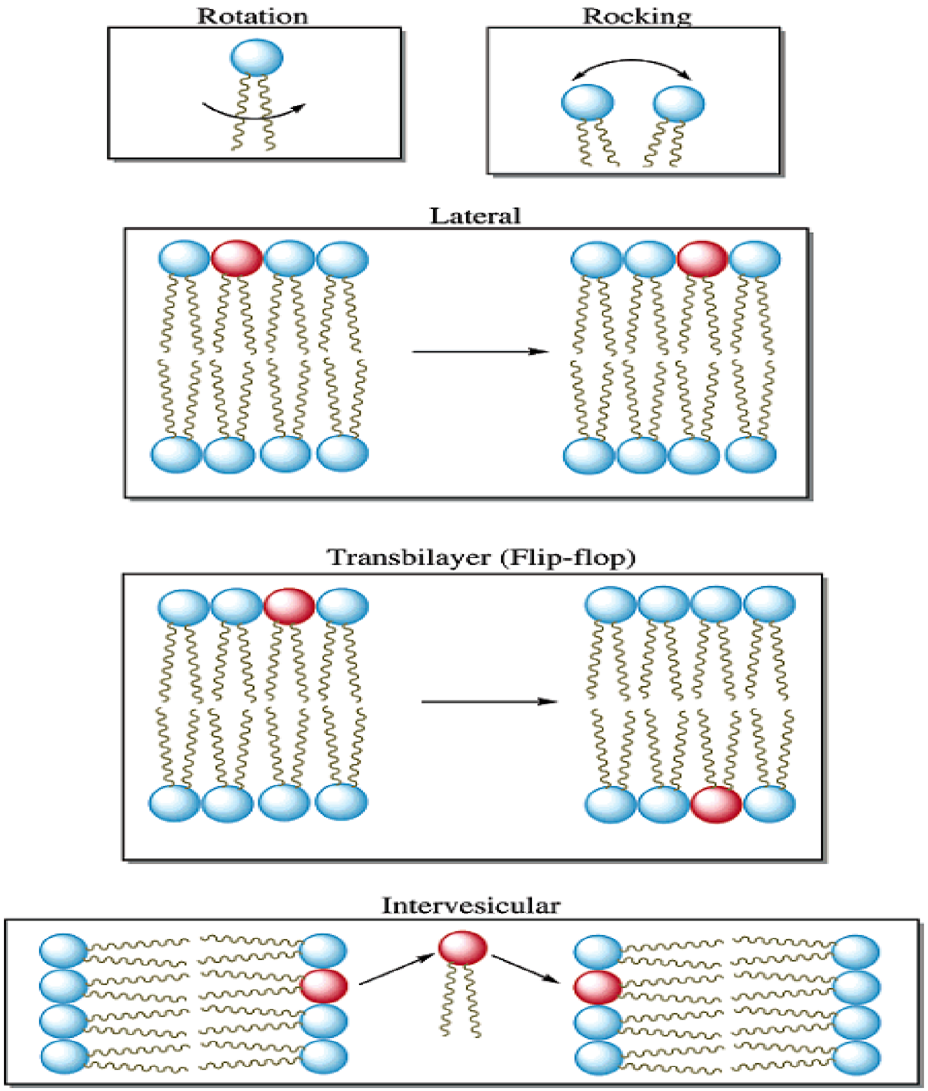


Figure 3. Schematic of various motions possible in a bilayer.

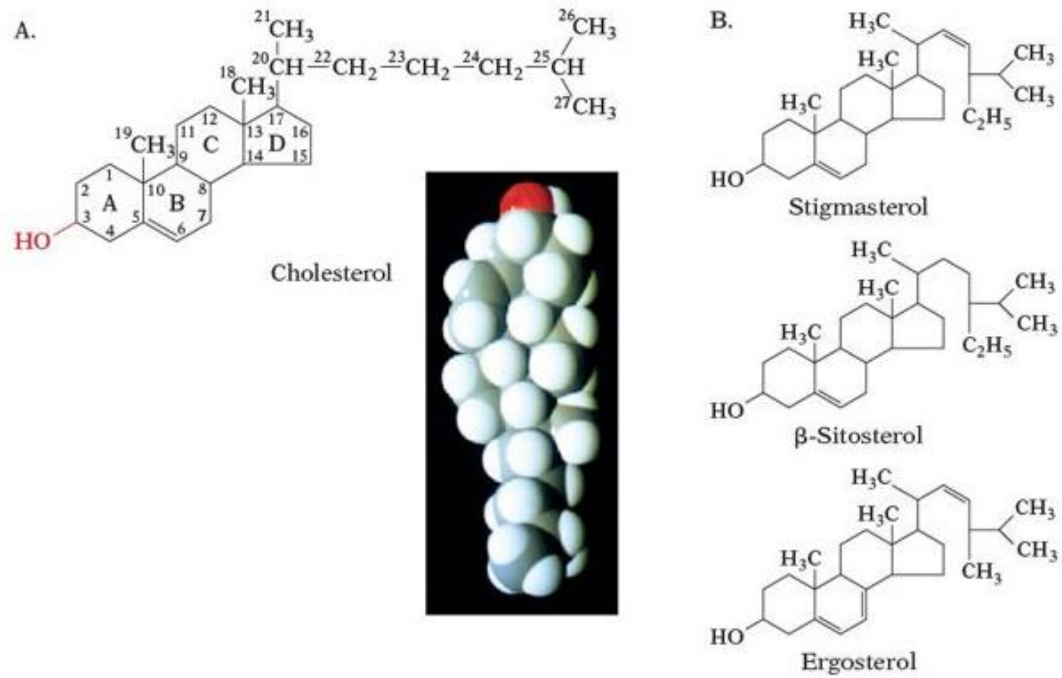
A Tribute to the Phospholipid *Langmuir, Vol. 21, No. 23, 2005* 10337

As a unit, the lipid molecule can rotate, rock, diffuse laterally, flip-flop, and engage in interbilayer migration

Flipases

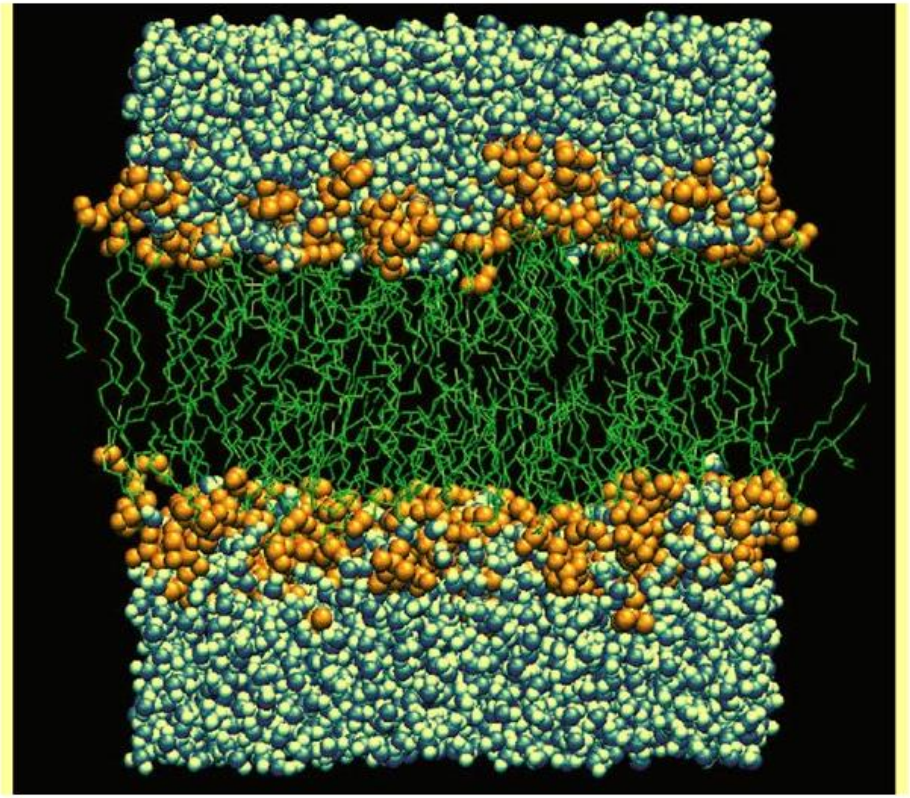
T1/2= horas

T1/2= 2 a 4 h

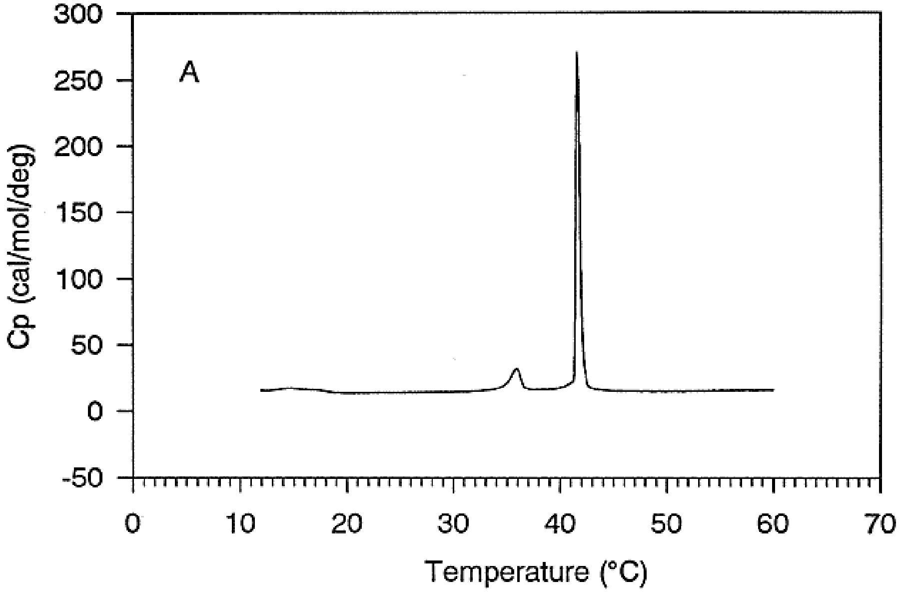


2.8. Sterols found in biological membranes. **A**. The structure and space-filling model of cholesterol, a major component of animal membranes. Redrawn from Voet, D., and J. Voet, *Biochemistry*, 3rd ed., John Wiley, 2004, p. 389. © 2004. Reprinted with permission from John Wiley & Sons, Inc. **B**. Different sterols occur in membranes of other organisms: plants have stigmasterol and β-sitosterol, whereas yeast and fungi have ergosterol.

2.12. A snapshot from a simulated model of a fully hydrated DMPC bilayer. This molecular dynamics simulation shows clearly the disorder among the acyl chains (green). The starting point for the simulation was the lipid configuration from the x-ray crystal structure, which was then "heated" to a constant temperature and pressure. Note the penetration of water molecules (blue and white) into the extensive interfacial regions, while water is absent from the nonpolar center. Phospholipid headgroups are orange, water hydrogens are white, water oxygens are blue, and phospholipid hydrocarbon chains are green. From Chiu, S. W., et al., *Biophys. J.* 1995, 69:1230–1245. © 1995 by the Biophysical Society. Reprinted with permission from the Biophysical Society.

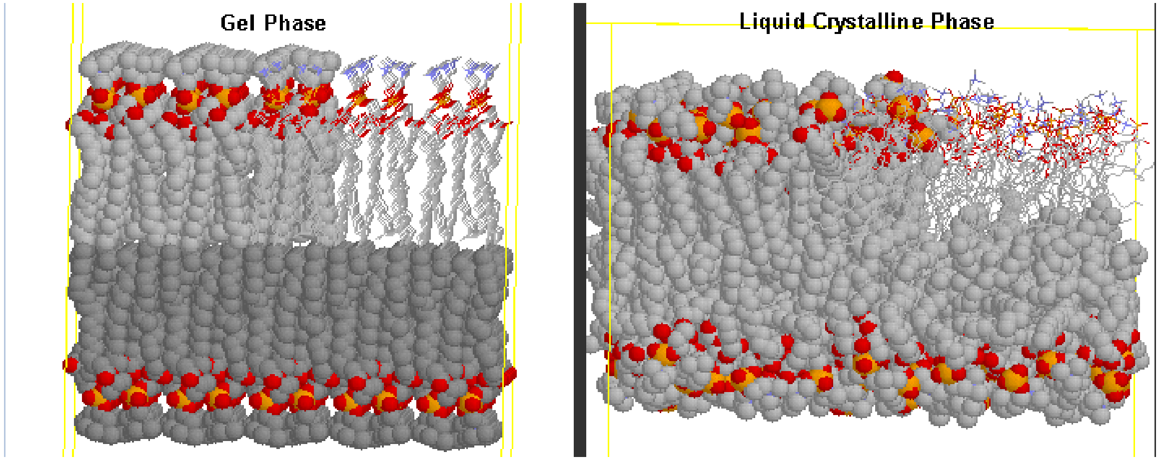


Temperatura de Transição de Lipossomas de DPPC

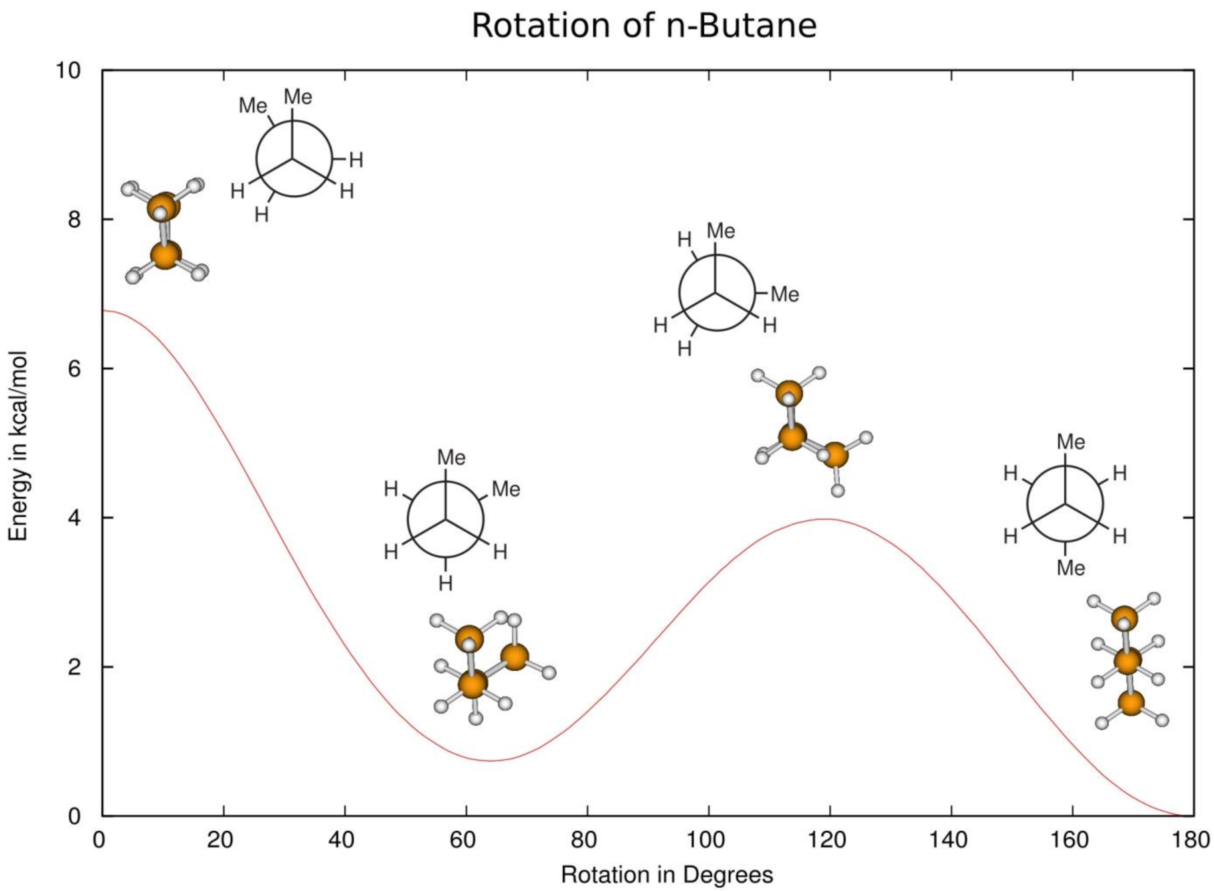


Pre-Transição-
ripple phase or Pβ'

Temperatura de Transição
Fase Gel / Líquido Cristalina
Isomerização Gauche



Lipid bilayer pre-transition as the beginning of the melting process. Riske, K.A.; Barroso, R.P.; Vequi-Suplicy, C.C.; Germano, R.; Henriques, V.B.; Lamy. M.T. Bioch. Biophys. Acta 1788 (2009) 954–963.



Rotation of n-Butane
Energy in kcal/mol
Rotation in Degrees
0
20
40
60
80
100
120
140
160
180
0
2
4
6
8
10
Me
Me
H
H
H
H
Me
H
Me
H
H
H
H
Me
Me
H
H
H
Me
H
H
H
H
Me

Estrutura espacial de ácidos graxos com diferentes insaturações.

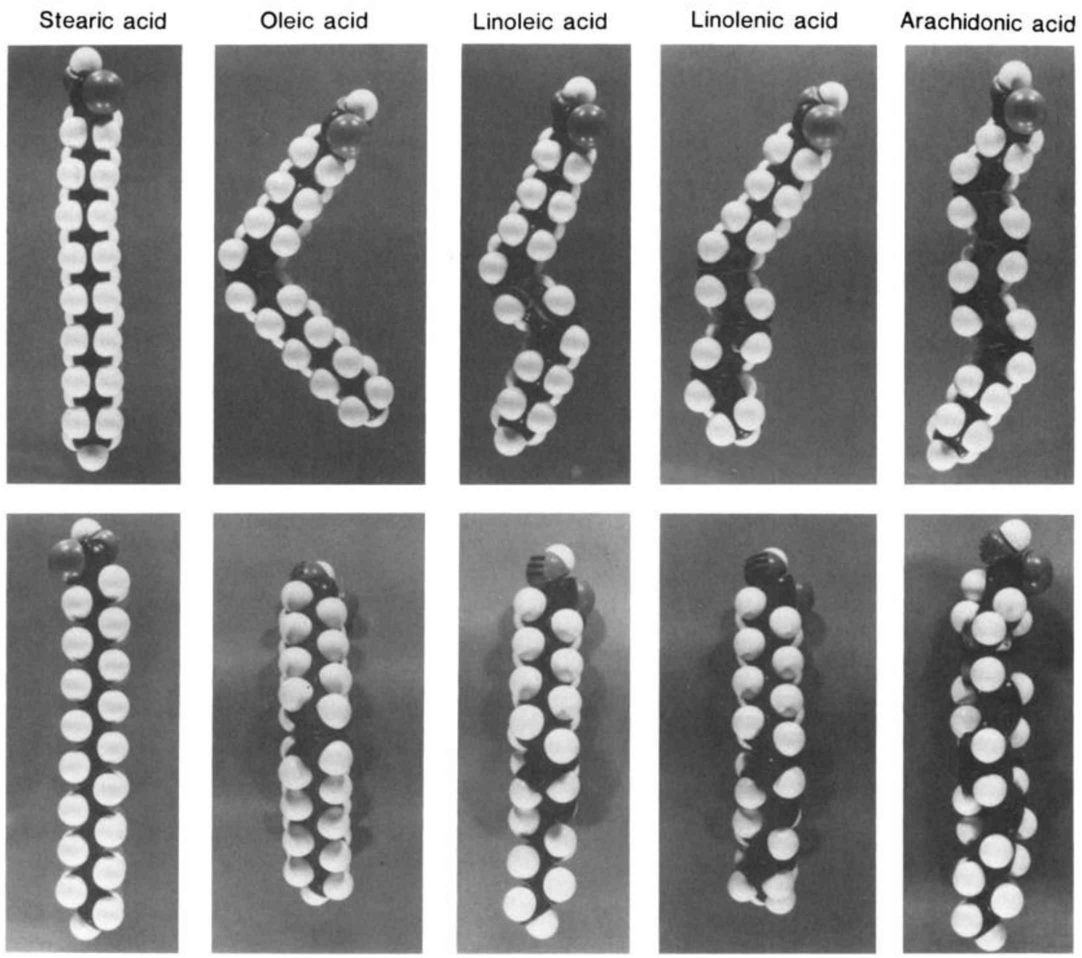
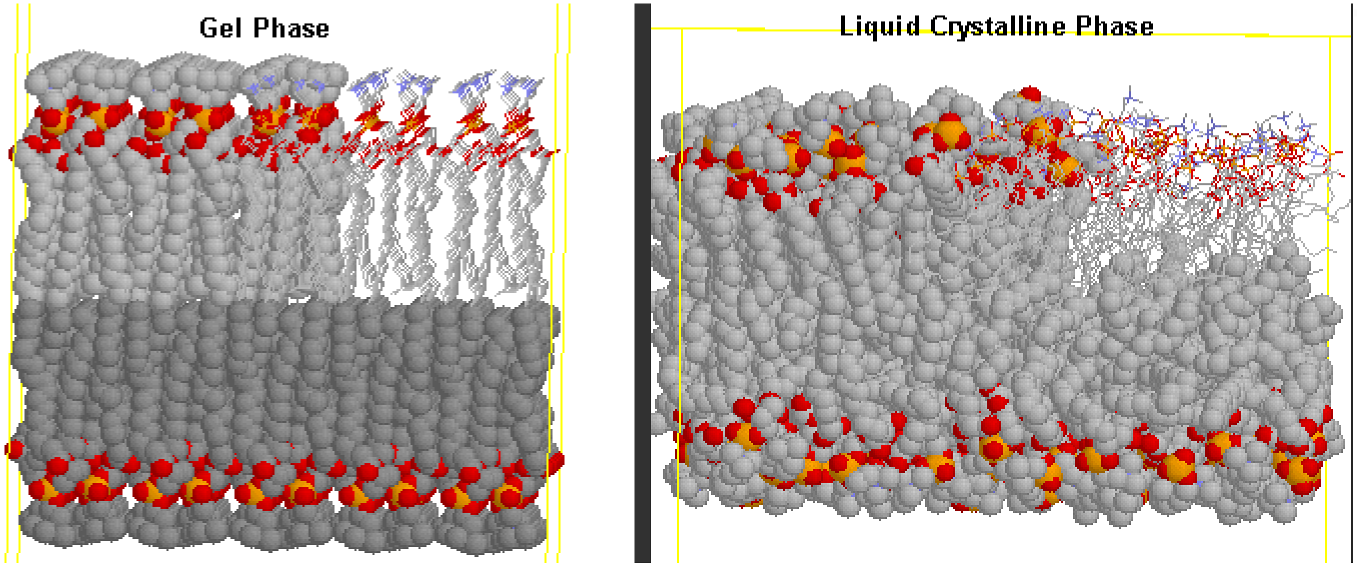


Fig. 1. Space filling models of five fatty acids. The conformation of five fatty acids of increasing unsaturation

D. M. Small, J. Lipid Res. 25 (1984) 1490

Temperatura de Transição



Phospholipid bilayers undergo a melting-like phase transition at a temperature designated Tm. Below Tm, saturated lipids in the bilayer exist in the gel or “solid state” with linear all-trans chains. Above Tm, the bilayer exists in the more disordered liquid crystalline or “liquid state” with several gauche C-C bonds in each carbon chain.

Colesterol- Efeito na Bicamada Lipídica

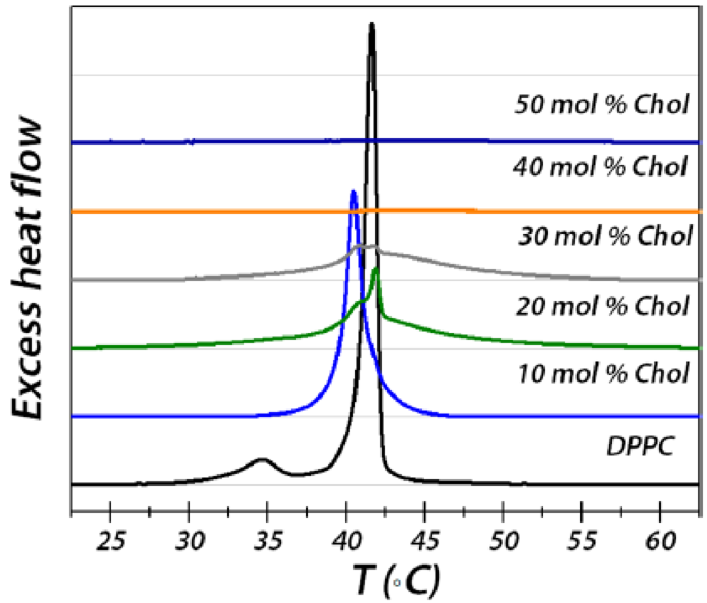


Figure 1. DSC thermograms of DPPC vesicles containing 0, 10, 20, 30, 40, and 50 mol % Chol, suspended in 10 mM HEPES, 20 mM $MgCl_2$, and 150 mM NaCl, pH 7.4.

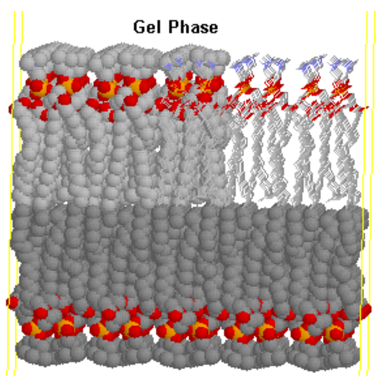
Temperatura de Transição

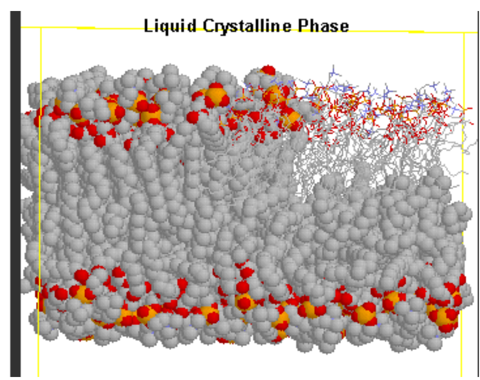
Fase Gel-Fase Fluida ou Líquido Cristalina

Isomerização Gauche

Pre-Transição

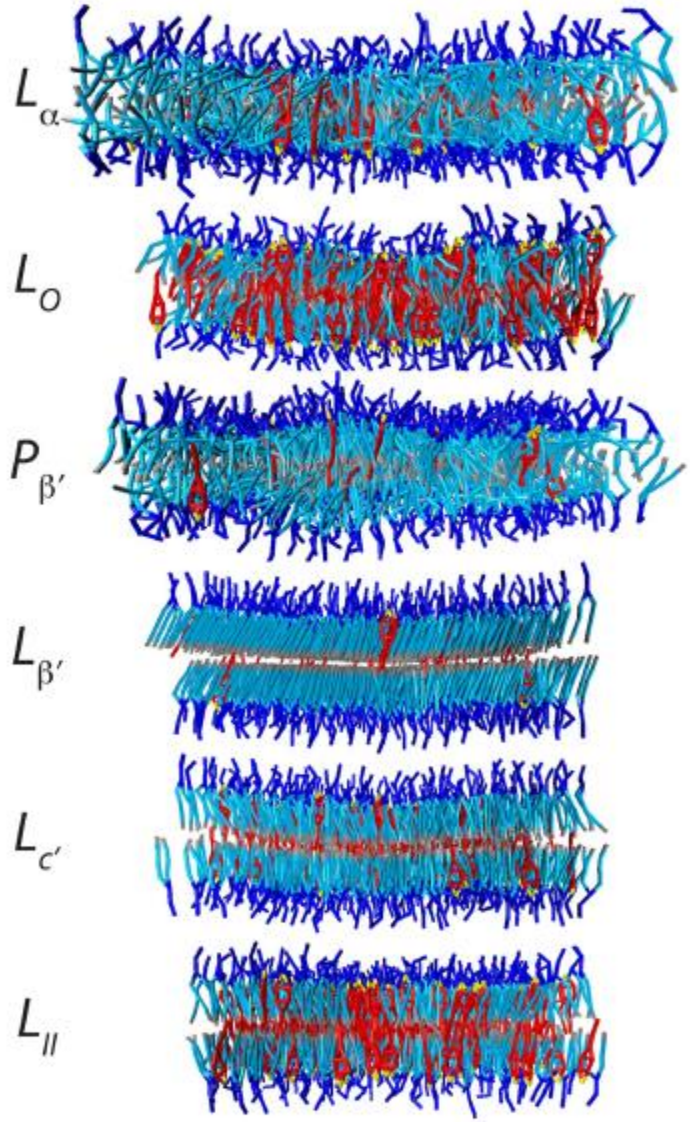
FASE ORDENADA





FASE FLUIDA

Langmuir 2012, 28 12851



A T=37 ^{0}C, Colesterol =10 %

B T=37 ^{0}C, Colesterol =40 %

C T=20 ^{0}C, Colesterol =5 %

D T= 5 ^{0}C, Colesterol = 5 %

E T= 5 ^{0}C, Colesterol = 15 %

F T= 5 ^{0}C, Colesterol = 40 %

Fig. 5. Snapshots of a side view of the bilayer. (A) L_α phase for 10% cholesterol at $T = 37$ °C. (B) L_o phase for 40% cholesterol at $T = 37$ °C. (C) Ripple ($P_{\beta'}$) phase for 5% cholesterol at $T = 20$ °C. (D) $L_{\beta'}$ phase for 5% cholesterol at $T = 5$ °C. (E) L_c' phase for 15% cholesterol at $T = 5$ °C. (F) L_{II} phase for 40% cholesterol at $T = 5$ °C. The hydrophilic and the hydrophobic beads of the phospholipids are depicted in dark blue and in light blue, respectively. The end beads of the lipid tails are depicted in gray. The cholesterol headgroup is depicted in yellow, the cholesterol tetrameric ring and tail beads are depicted in red. For clarity, water beads are not shown. The difference in the width of the bilayers illustrates the condensation effect nicely.

Fase Lα 10% Chol T=37

Effect of cholesterol on the structure of a phospholipid bilayer

Frédérick de Meyer[a,b] and Berend Smit[b,1]

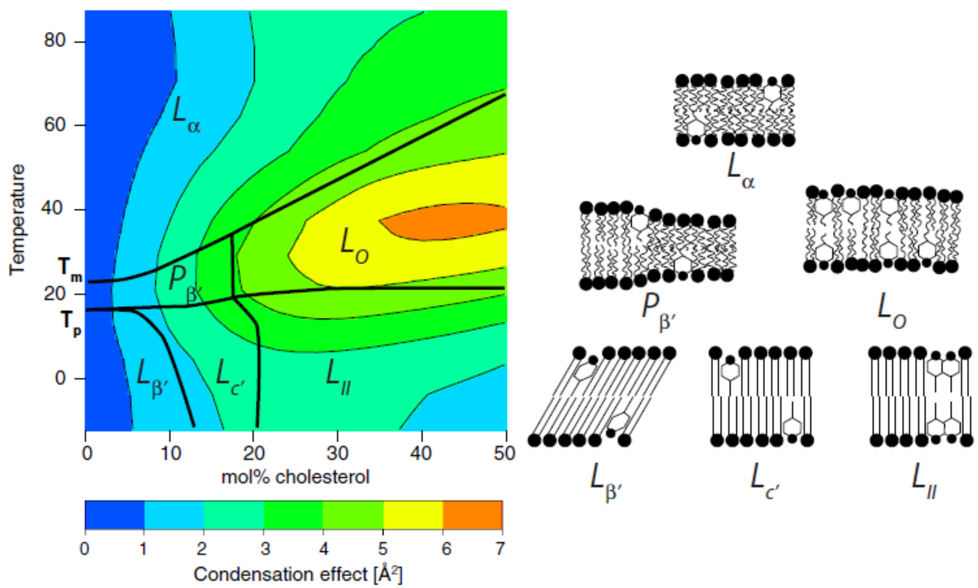


Fig. 2. Phase diagram and the structure of the various phases. (*Left*) Computed-phase diagram as a function of temperature (in degrees centigrade) and cholesterol concentration. The black lines give the phase boundaries. The color coding gives the condensation effect at a given state point, where blue indicates very little condensation and orange a large condensation effect. (*Right*) Schematic drawing of the various phases. L_α, lipids in the liquid phase; P'_β, ripple phase; L'_β, gel phase with tilted lipid chains; L'_c, gel phase with lipid chains not tilted; L_{II}, gel phase, similar to L'_c, containing small cholesterol clusters; L_o, liquid-ordered phase. The condensation effect is defined as the difference, in Å^2, between $A_{M,\ sim}$ and $A_{M,\ ideal}$.

Tm de membranas de mamíferos é menor do que a temperatura corporal.

Bacterias e animais de sangue frio (pecilotérmicos) mudam a composição de acidos graxos dos lipidíos de membrana para manter a mesma fluidez em qualquer temperatura.

A viscosidade da membrana de E. coli em crescimento permanece constante entre 15 e 43 ^{0}C.

1-Temperatura de transição da membrana, Tm, aumenta com o comprimento das cadeias dos ácidos graxos dos fosfolipídios.

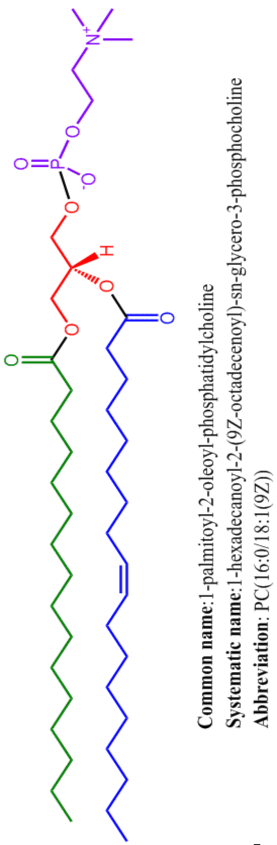
2-Tm diminui com a presença de fosfolipídios contendo ácidos graxos insaturados.

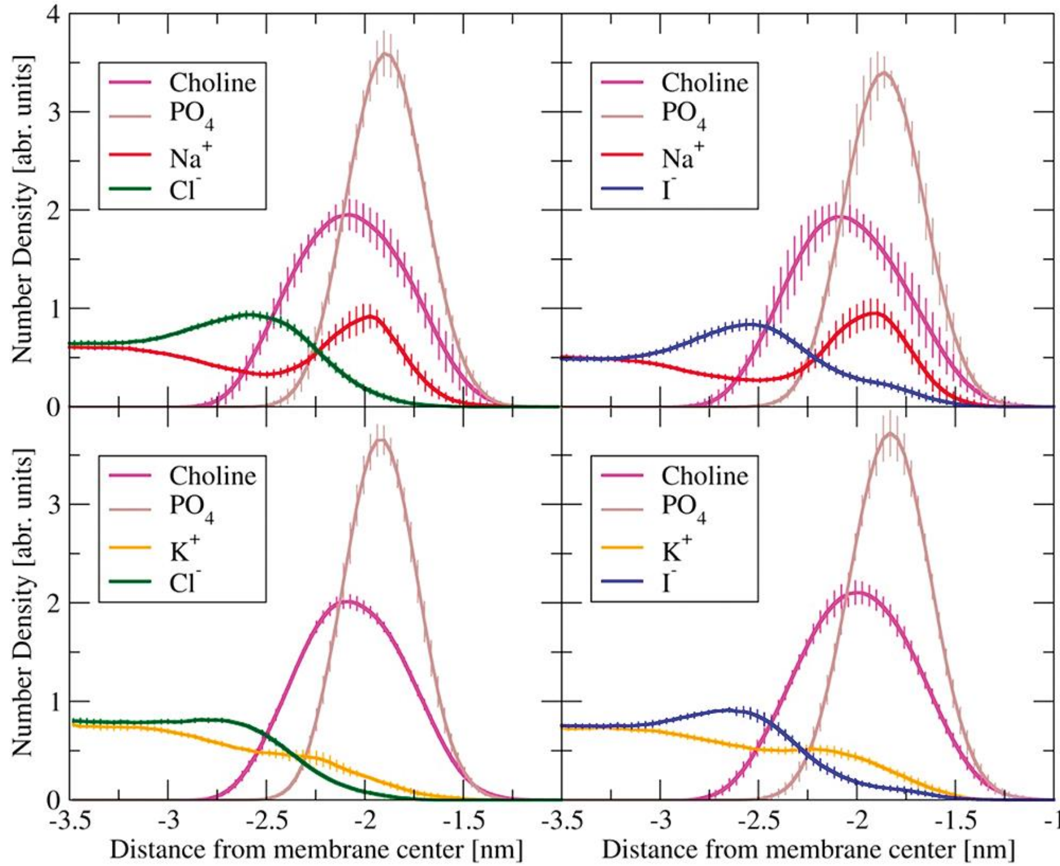
3-Colesterol aumenta a fluidez da membrana abaixo da Tm.

4-Colesterol diminui a fluidez da membrana acima da Tm.

5-Colesterol funciona como um espaçador na bicamada e pode abolir a transição de fase da bicamada dependendo da concentração.

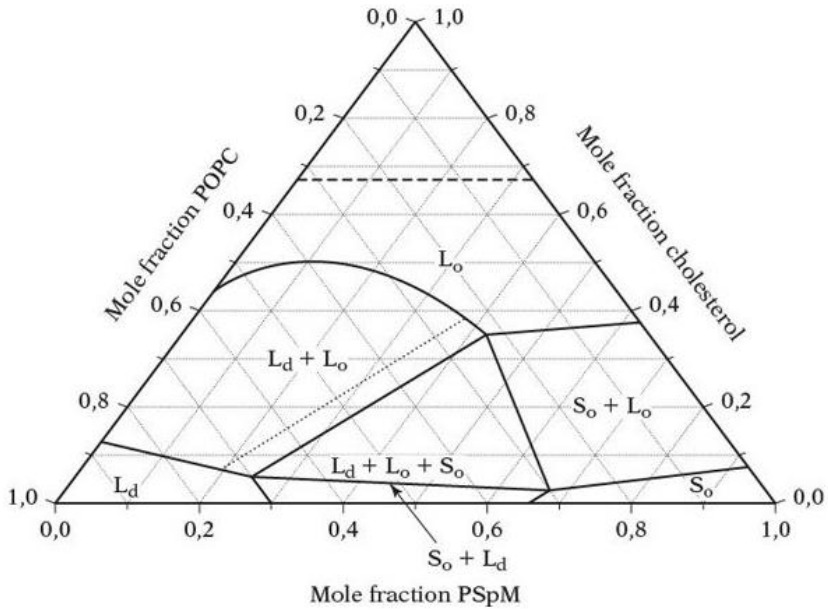
Ligação de Ions à Membrana





M. L. Berkowitz, R. Vachá, Acc. Chem. Res. 44 (2012) 74-82.

Miscibilidade de Lipídios (ou Não)



2.23. Phase diagram for the aqueous ternary mixture of raft lipids at 23°C. The lipids, POPC, palmitoyl-sphingomyelin (PSpM), and cholesterol, are varied in concentration along each of the three axes. The regions of the phase diagram are labeled L_o, L_d, and S_o (solid, ordered)

Modelo do Mosaico Fluido

Biochimica et Biophysica Acta 1838 (2014) 1451–1466

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ELSEVIER

BBA Biomembranes

Review

The Fluid—Mosaic Model of Membrane Structure: Still relevant to understanding the structure, function and dynamics of biological membranes after more than 40 years ☆

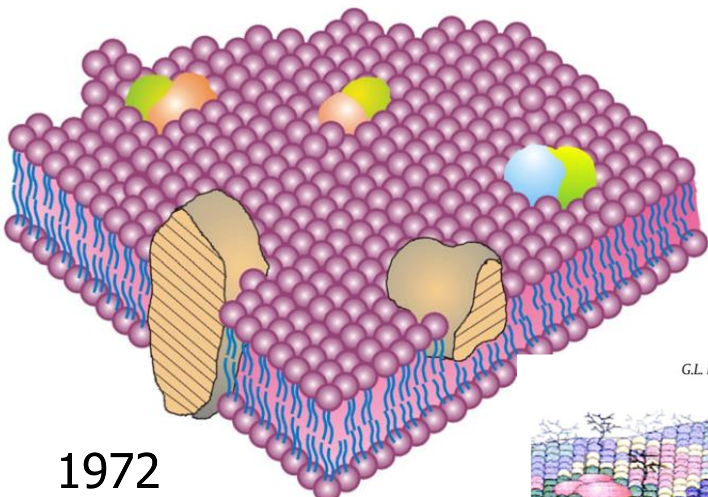
CrossMark

Garth L. Nicolson *

Department of Molecular Pathology, The Institute for Molecular Medicine, Huntington Beach, CA 92649, USA

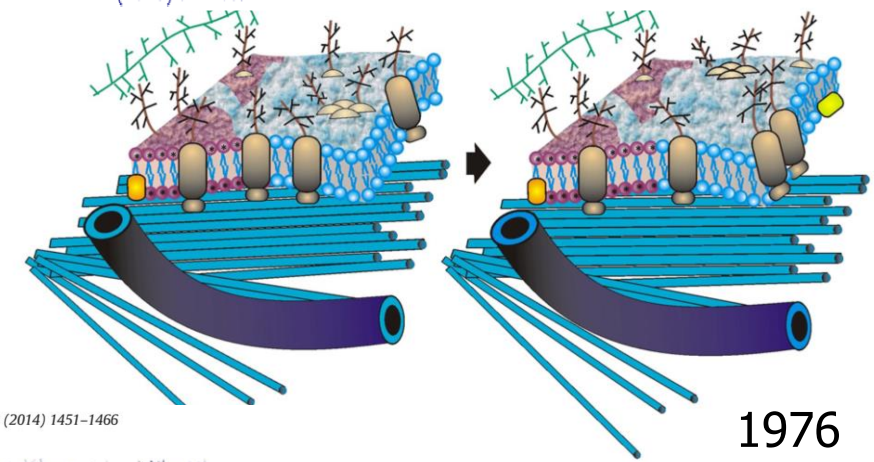
Modelo do Mosaico Fluido

S.J. Singer, G.L. Nicolson, The Fluid Mosaic Model of the structure of cell membranes, Science 175 (1972) 720–731.



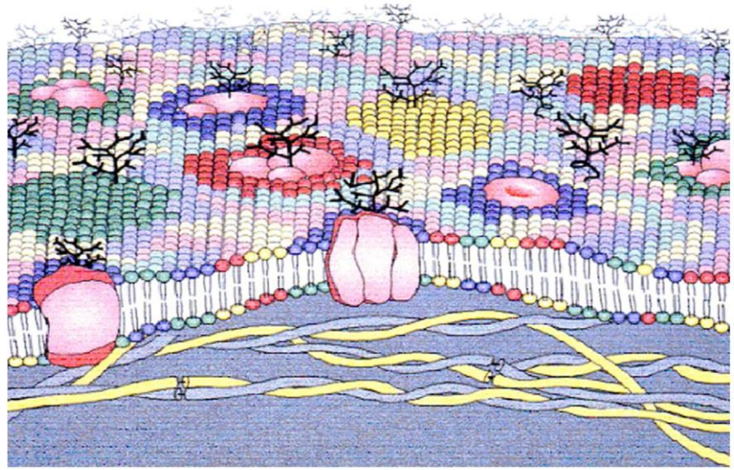
1972

G.L. Nicolson, Transmembrane control of the receptors on normal and tumor cells. I. Cytoplasmic influence over cell surface components, Biochim. Biophys. Acta 457 (1976) 57–108.



1976

G.L. Nicolson / Biochimica et Biophysica Acta 1838 (2014) 1451–1466



2014

Modelo do Mosaico Fluido

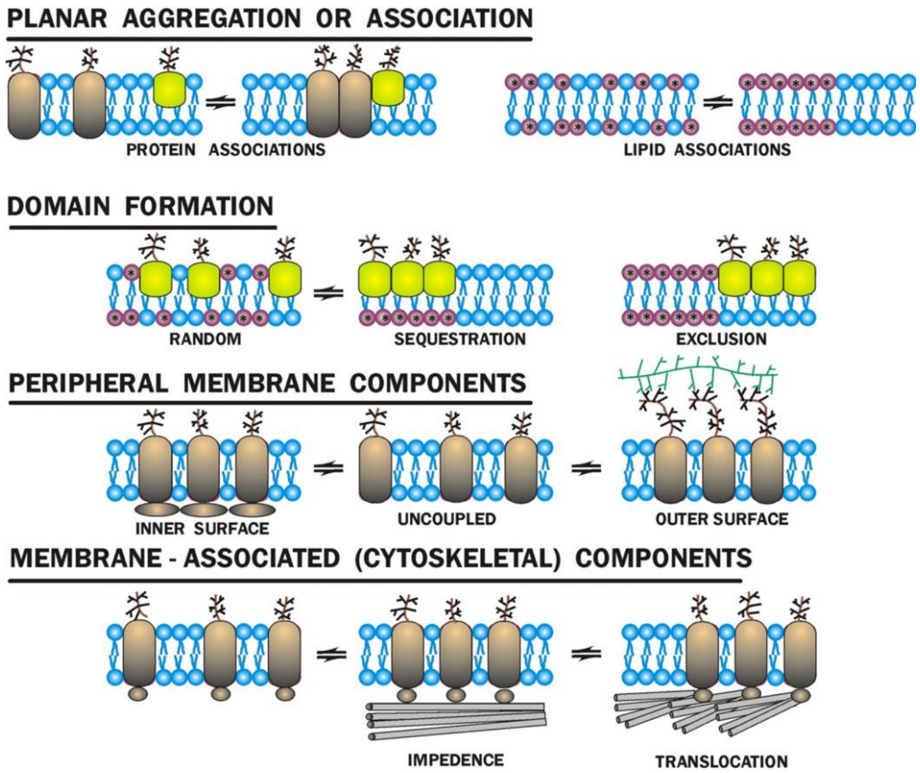


Fig. 2. A modified schematic version of the Fluid–Mosaic Membrane Model of biological membrane structure, as proposed in 1976.

Garth L. Nicolson Biochimica et Biophysica Acta 1838 (2014) 1451–1466

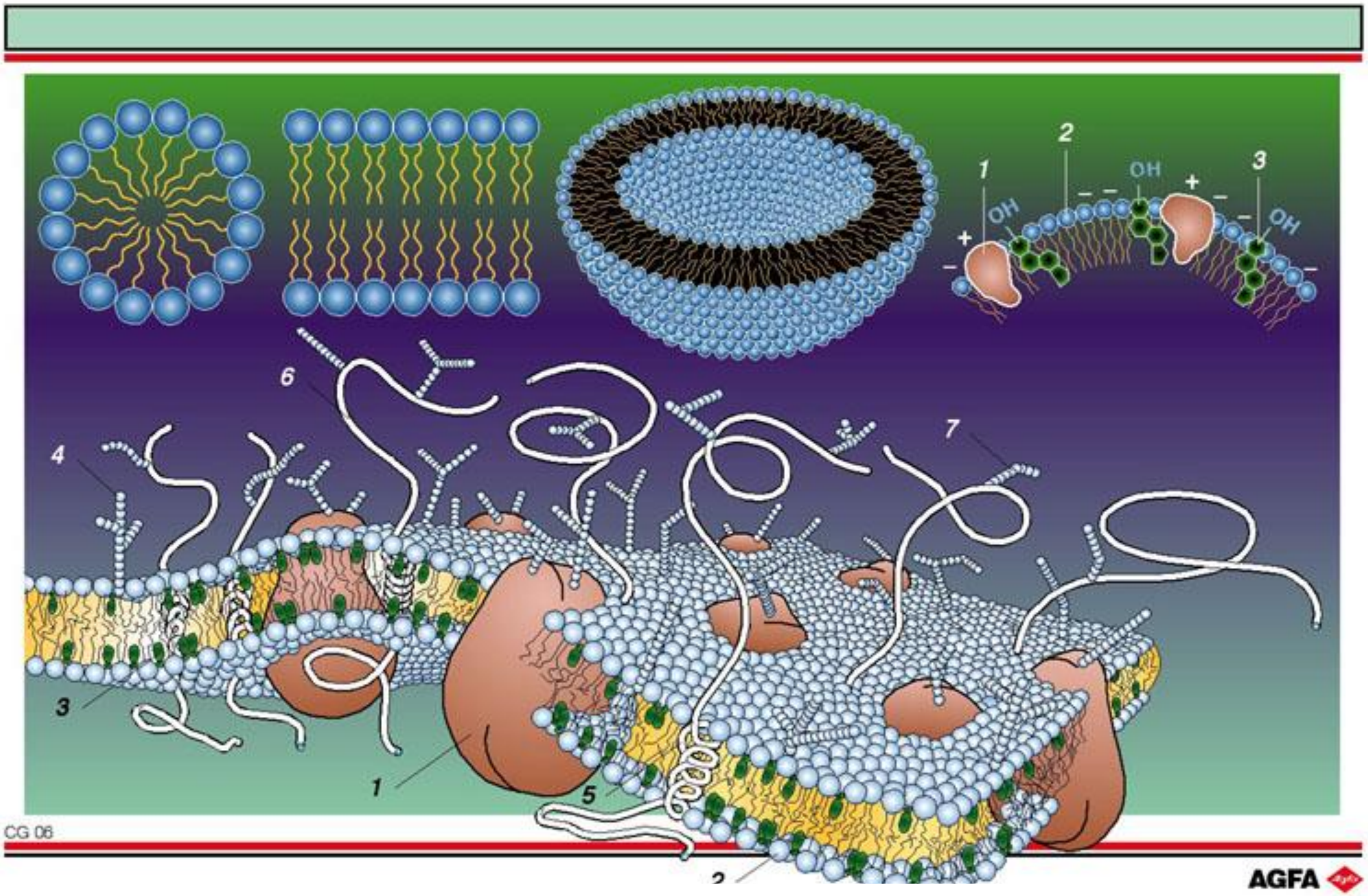
Identificar os componentes da estrutura de uma membrana biológica. Descrever o modelo de mosaico fluido.

Membranas-Modelo do Mosaico Fluido

Mosaico- Palavra de origem grega significa "obra das musas”. É definido como um conjunto de pequenos elementos reunidos por meio de um ligante.

Modelo do Mosaico Fluido:
O componente lipídico da membrana plasmática é fluído e as proteínas se distribuem compondo um mosaico.

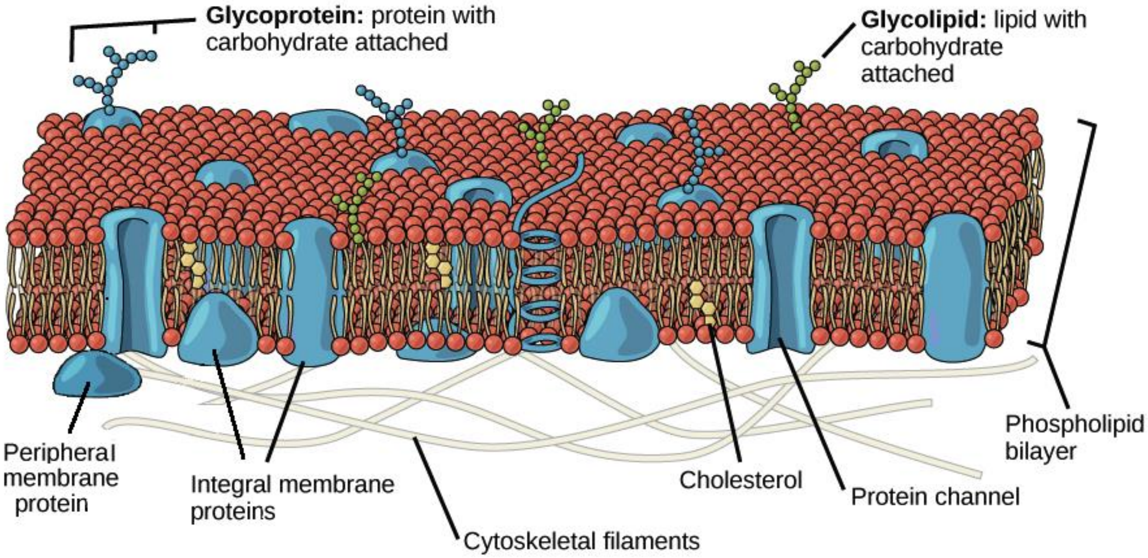
Modelo do Mosaico Fluido



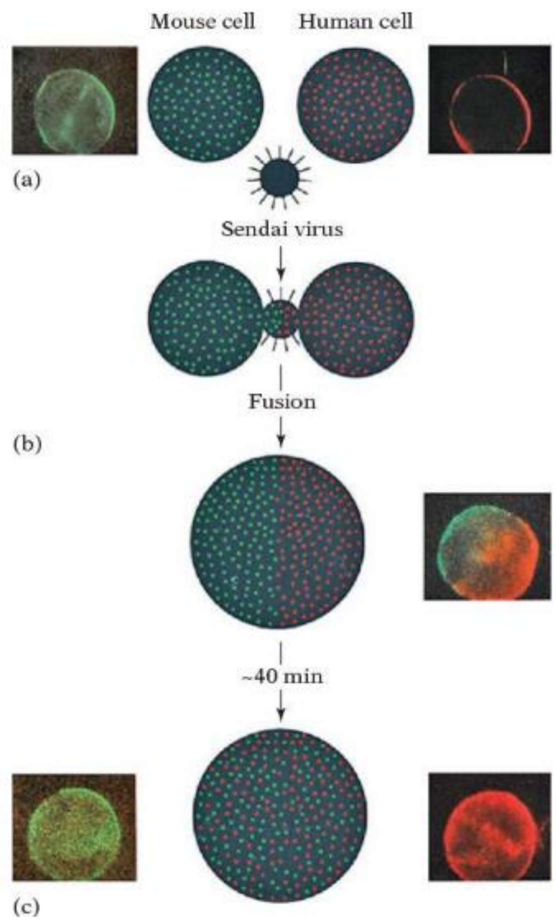
S.J. Singer, G.L. Nicolson, The Fluid Mosaic Model of the structure of cell membranes, Science 175 (1972) 720–731.

old.iupac.org/didac/Slide

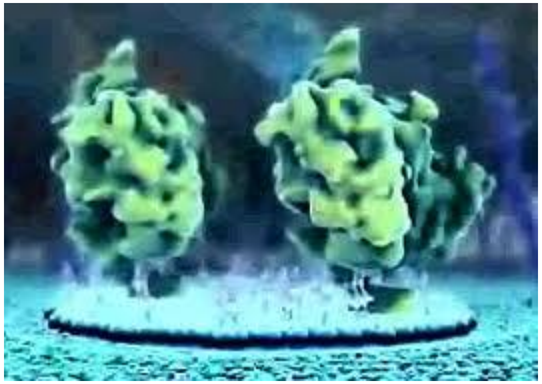
Esquema de uma Membrana
Modelo do Mosaico Fluido

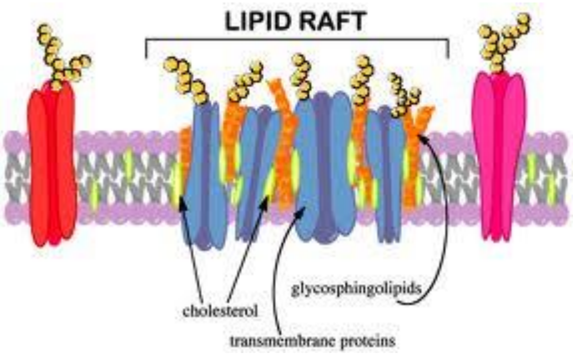


1.8. Diffusion of membrane components after cell fusion. Human and mouse antigens are labeled with red and green fluorescent markers, respectively. Virus-stimulated fusion of the mouse cell and human cell (a) produces a heterokaryon with both types of antigen on its surface (b). After 40 minutes, the red and green markers have fully intermingled (c). From Voet, D., and J. Voet, *Biochemistry*, 3rd ed., John Wiley, 2004, p. 4–5. © 2004. Reprinted with permission from John Wiley & Sons, Inc, and the Company of Biologists.



Lipid Rafts





Lipid Rafts- resistentes a isolamento com detergentes não iônicos (Triton X100). Glicoesfingolipídios (cerebrosídeos e gangliosídeos (ac. graxos saturados e longos) formam agregados transitórios na lamina externa da Membrana que excluem glicerofosfolipídeos) que contem grupo acila insaturados e/ou saturado de cadeia curta.
A esfingomielina forma associações estáveis com colesterol.

TABLE 1.1. Composition of membrane preparations by percent dry weight[a]

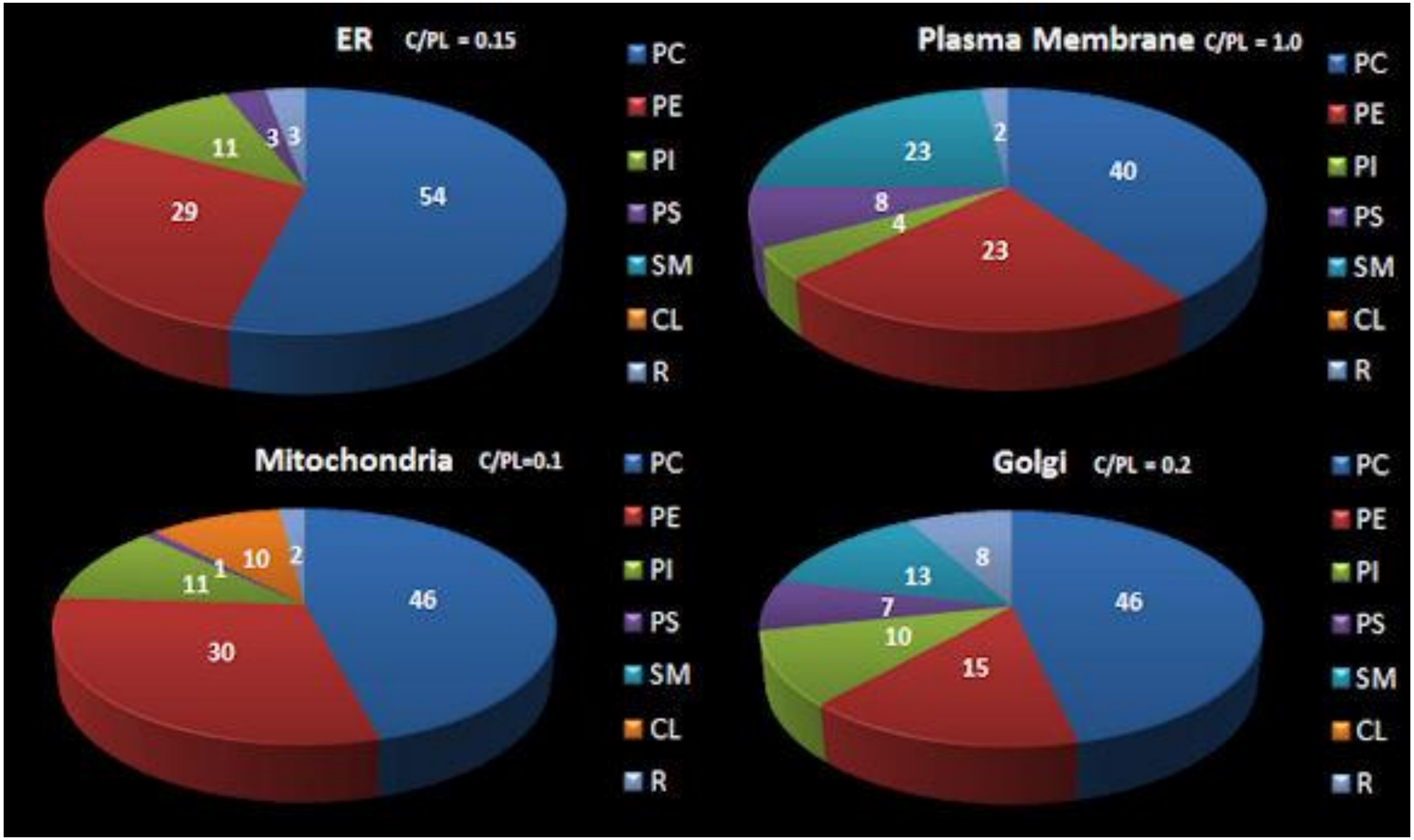
Source	Lipid	Protein	Cholesterol
Rat liver			
Plasma	30–50	50–70	20
Rough ER	15–30	60–80	6
Smooth ER	60	40	10
Inner mitochondria	20–25	70–80	<3
Outer mitochondria	30–40	60–70	<5
Nuclear	15–40	60–80	10
Golgi	60	40	8
Lysosomes	20–25	70–80	14
Rat brain			
Myelin	60–70	20–30	22
Synaptosome	50	50	20
Rat erythrocyte	40	60	24
Rat rod outer segment	50	40	<3
Escherichia coli	20–30	70	0
Bacillus subtilis	20–30	70	0
Chloroplast	35–50	50–65	0

[a] The percentages by weight of membrane preparations from various eukaryotic and prokaryotic sources are given.

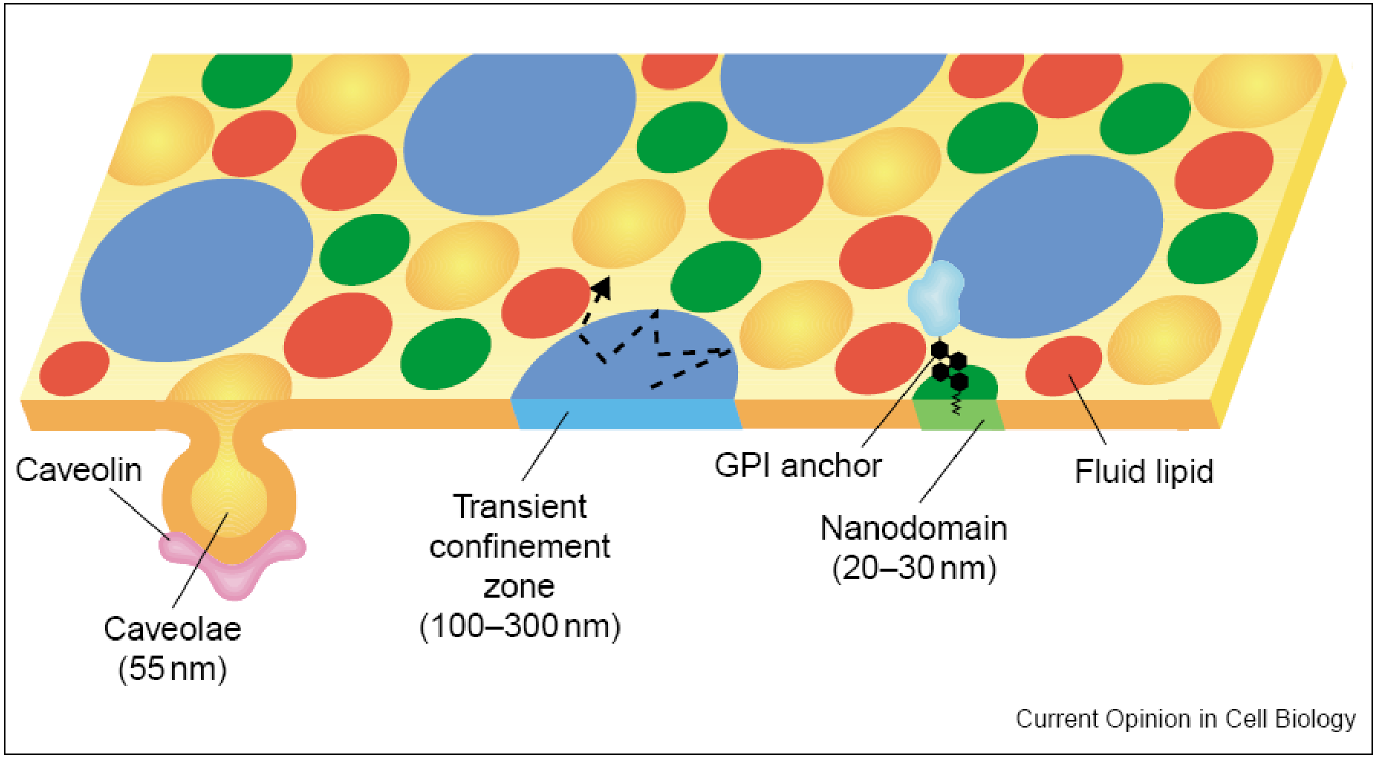
ER, endoplasmic reticulum.

Source: Based on Jain, M. K., and R. C. Wagner, *Introduction to Biological Membranes*, 2nd ed. New York: Wiley, 1988, p. 34.

Distribuição de fosfolipídios em diferentes membranas



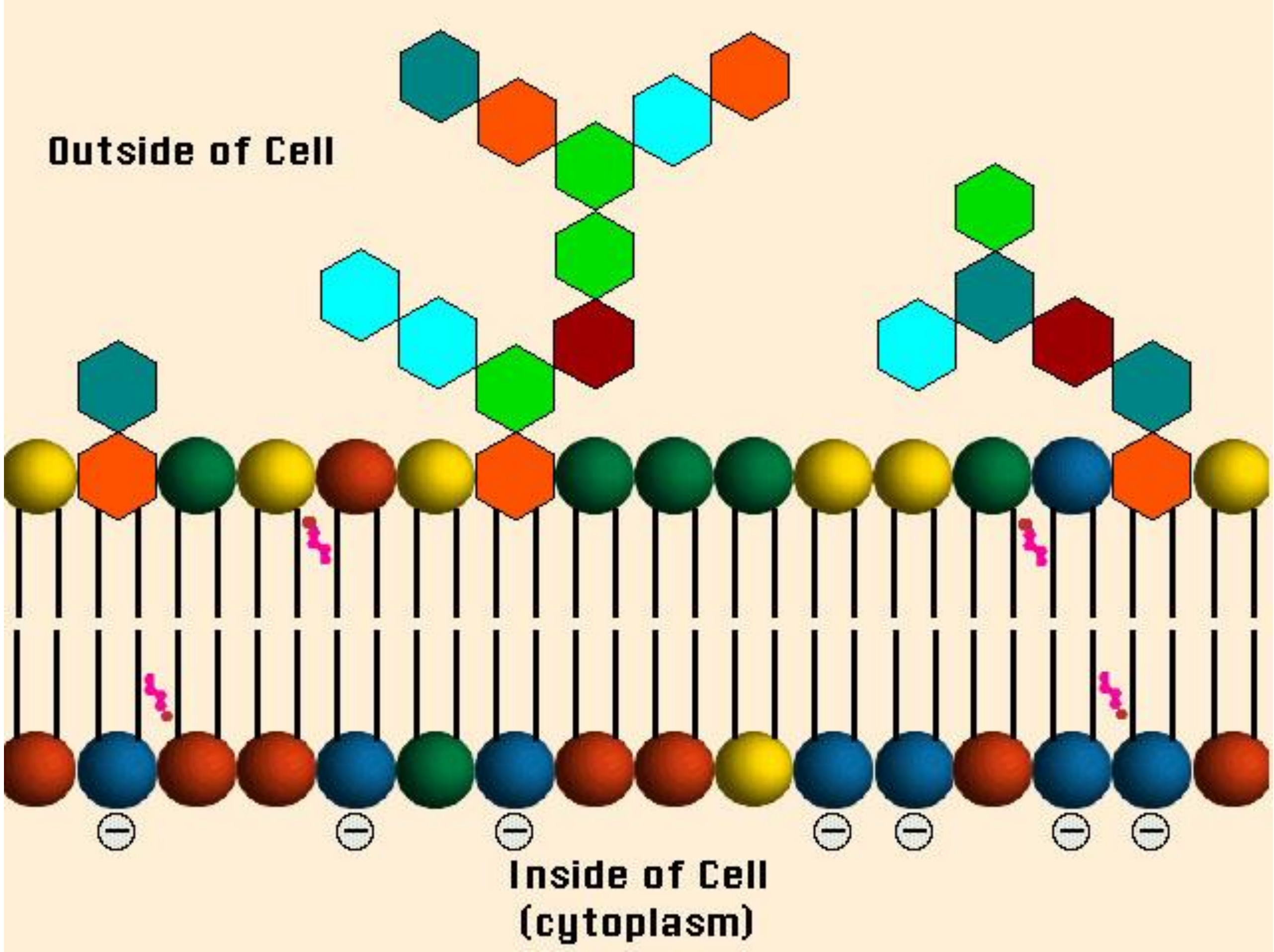
Mosaic Domain Model (Modelo Mosaico de Domínios Lipídicos)



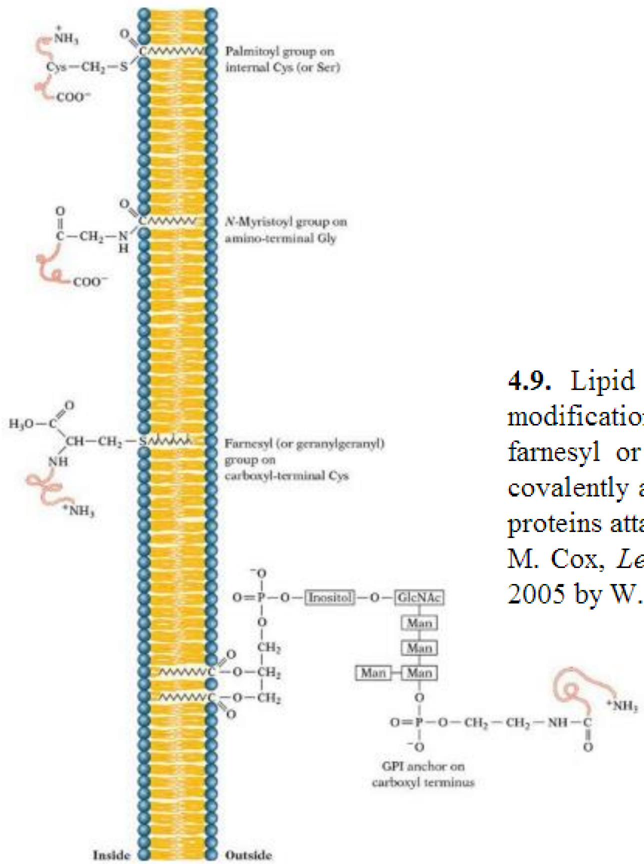
Mosaic Domain Model of the Plasma Membrane.
The Plasma Membrane is modeled as a Mosaic of different lipid domains.

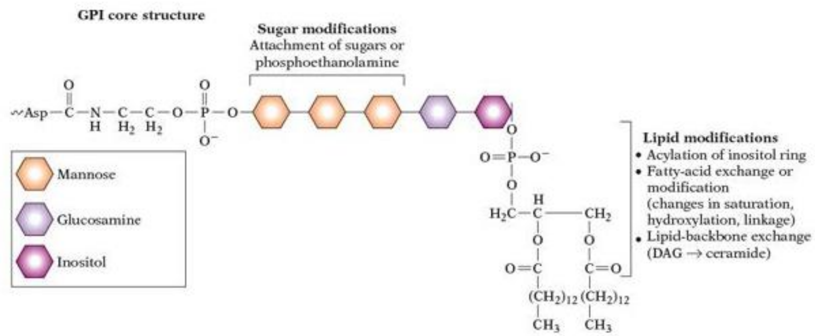
Frederick R. Maxfield, Current Opinion in Cell Biology, 2002, 14, 483-487

Assimetria dos Fosfolipidios



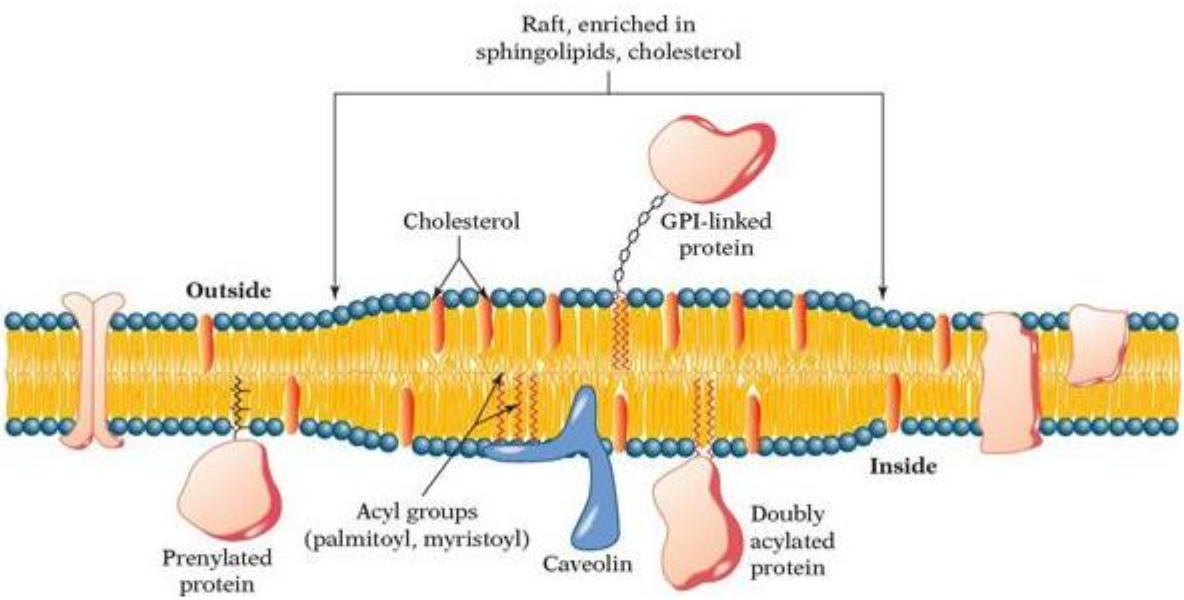
Âncoras de Proteinas

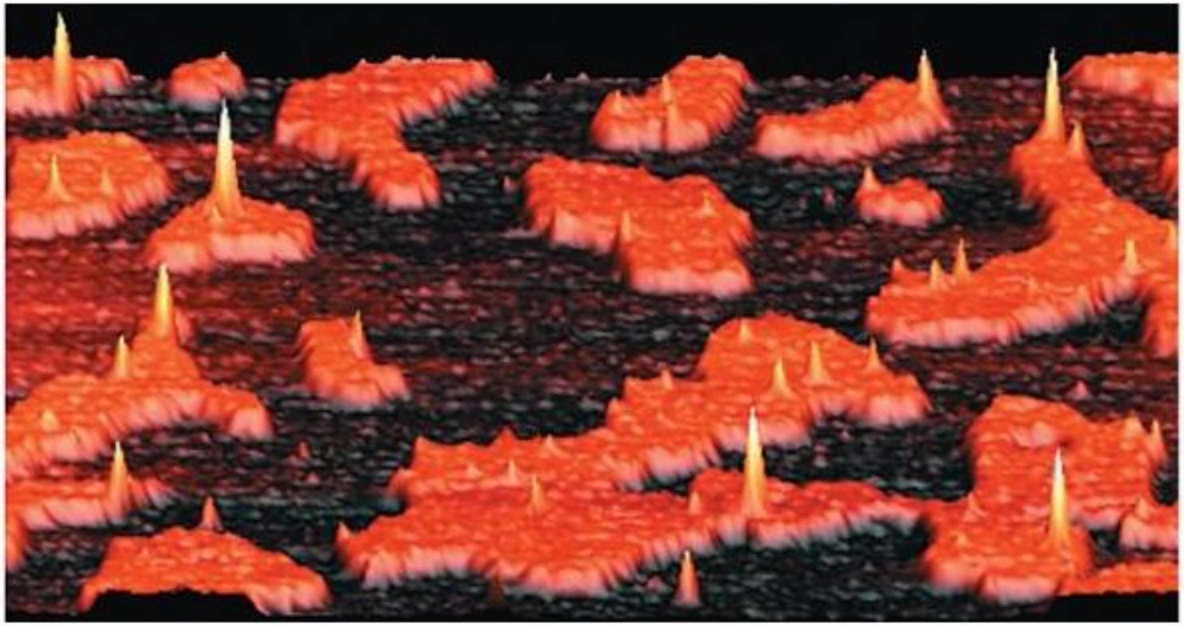




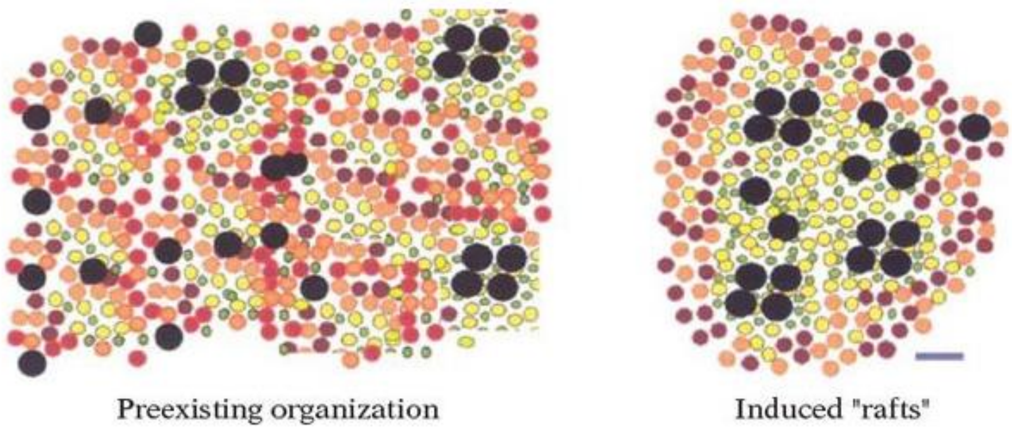
4.9. Lipid anchored proteins. Proteins may be anchored to the bilayer by covalent modification with acyl chains (typically myristate and palmitate), with terpenes (such as farnesyl or geranylgeranyl groups) and with GPI. In the plasma membrane the proteins covalently attached to acyl chains and terpenes are found on the cytoplasmic surface, while proteins attached to GPI are on the extracellular surface. Redrawn from Nelson, D. L., and M. M. Cox, *Lehninger Principles of Biochemistry*, 4th ed., W. H. Freeman, 2005, p. 379. © 2005 by W. H. Freeman and Company. Used with permission.

Lipid Rafts e Proteinas ligadas às âncoras



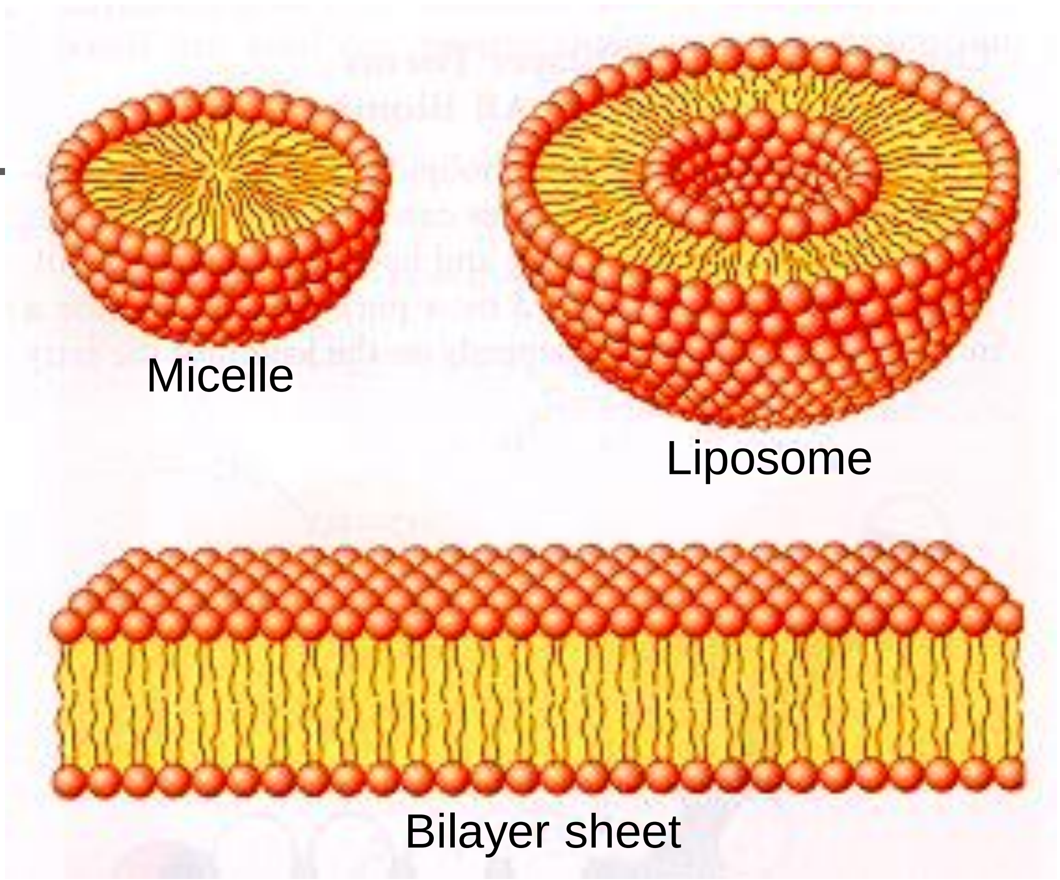


2.22. Observation of rafts by atomic force microscopy, which detects the increased thickness of the L_o domains. From Nelson, D. L., and M. M. Cox (eds.), *Lehninger Principles of Biochemistry*, 4th ed., W. H. Freeman, 2005.



2.24. A model for the clustering of small, preexisting membrane domains into larger rafts. The clustering of small domains into relatively large rafts is actively organized in both space and time. The affinities between some lipids and proteins form preexisting structures (left) that can coalesce into rafts (right). The red and pink circles represent different nonraft lipid species, the yellow circles represent raft lipids, the green circles represent cholesterol, and the larger black circles represent GPI-linked raft proteins. The scale bar is ~5 nm. Redrawn from Mayor, S., *Traffic*. 2004, 5:231–240. © 2004. Reprinted with permission of Blackwell Publishing.

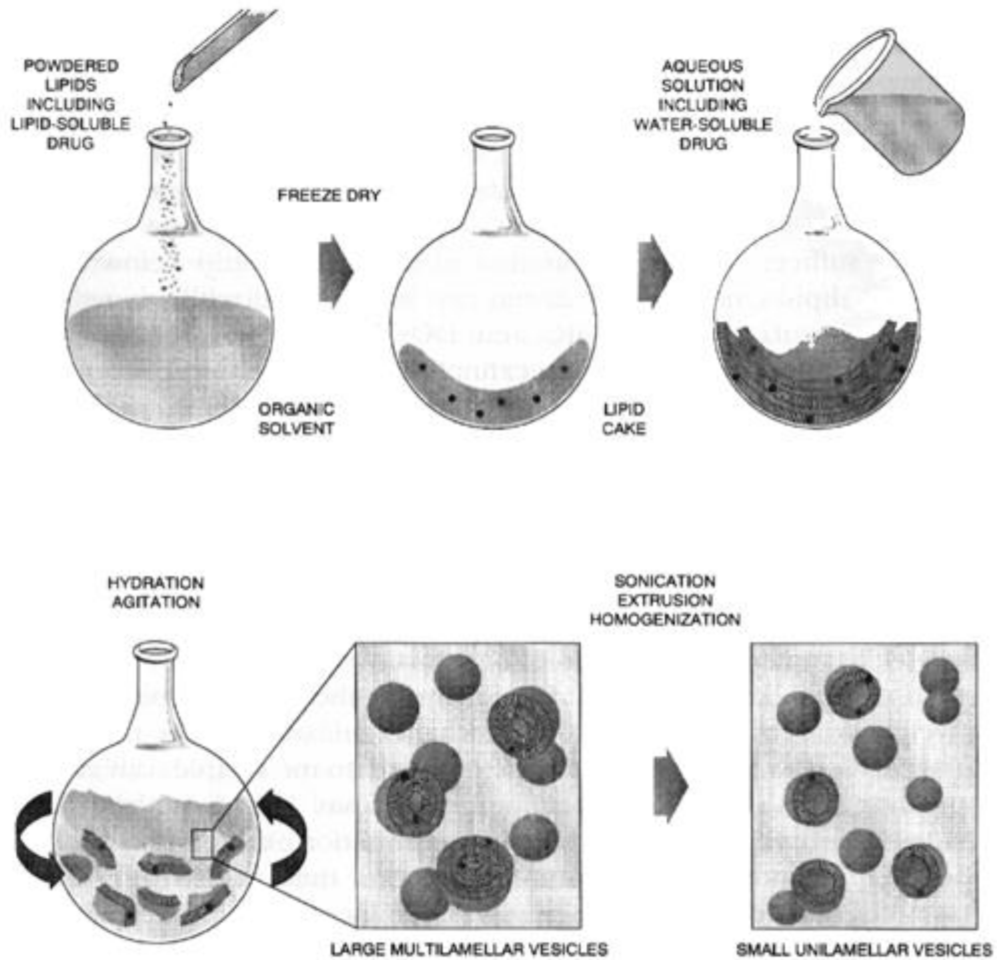
Cross-sectional views of the three structures that can be formed by mechanically dispersing a suspension of phospholipids in aqueous solution

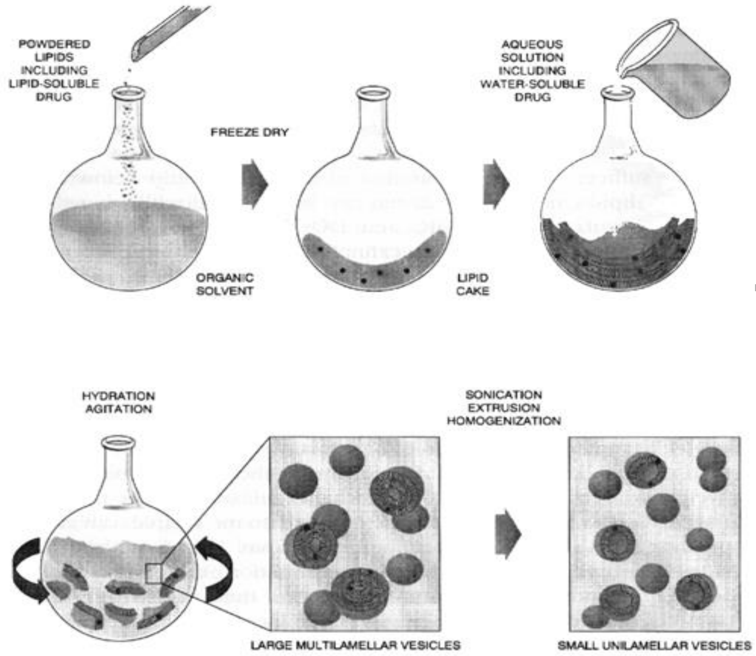


The red circles depict the hydrophilic heads of phospholipids, and the squiggly lines (in the yellow region) the hydrophobic tails.

Metodos de preparação Modelos Biomiméticos

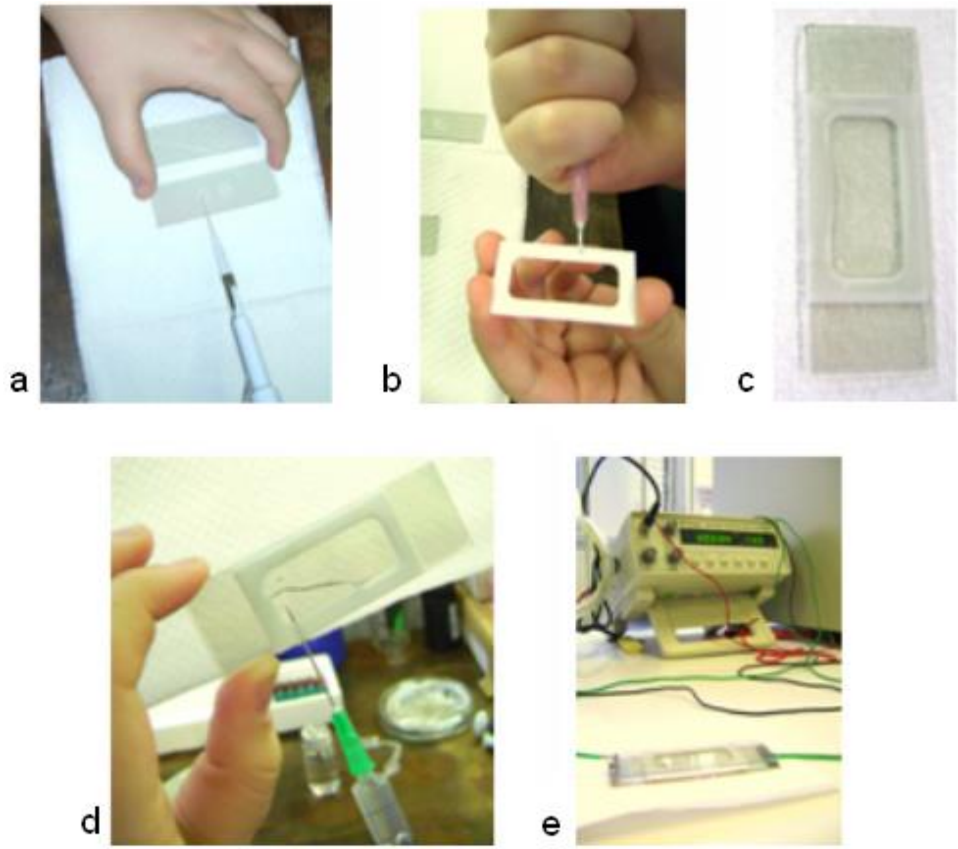
- Micelas
- Lipossomas
- Sonicação
- Injeção etanólica, eterérea, cloroformica
- Extrusão
- Eletroformação


POWDERED
LIPIDS
INCLUDING
LIPID-SOLUBLE
DRUG
FREEZE DRY
ORGANIC
SOLVENT
LIPID
CAKE
AQUEOUS
SOLUTION
INCLUDING
WATER-SOLUBLE
DRUG
HYDRATION
AGITATION
SONICATION
EXTRUSION
HOMOGENIZATION
LARGE MULTILAMELLAR VESICLES
SMALL UNILAMELLAR VESICLES


POWDERED LIPIDS INCLUDING LIPID-SOLUBLE DRUG
FREEZE DRY
AQUEOUS SOLUTION INCLUDING WATER-SOLUBLE DRUG
ORGANIC SOLVENT
LIPID CAKE
HYDRATION AGITATION
SONICATION EXTRUSION HOMOGENIZATION
LARGE MULTILAMELLAR VESICLES
SMALL UNILAMELLAR VESICLES


Avanti Polar Lipids, Inc.

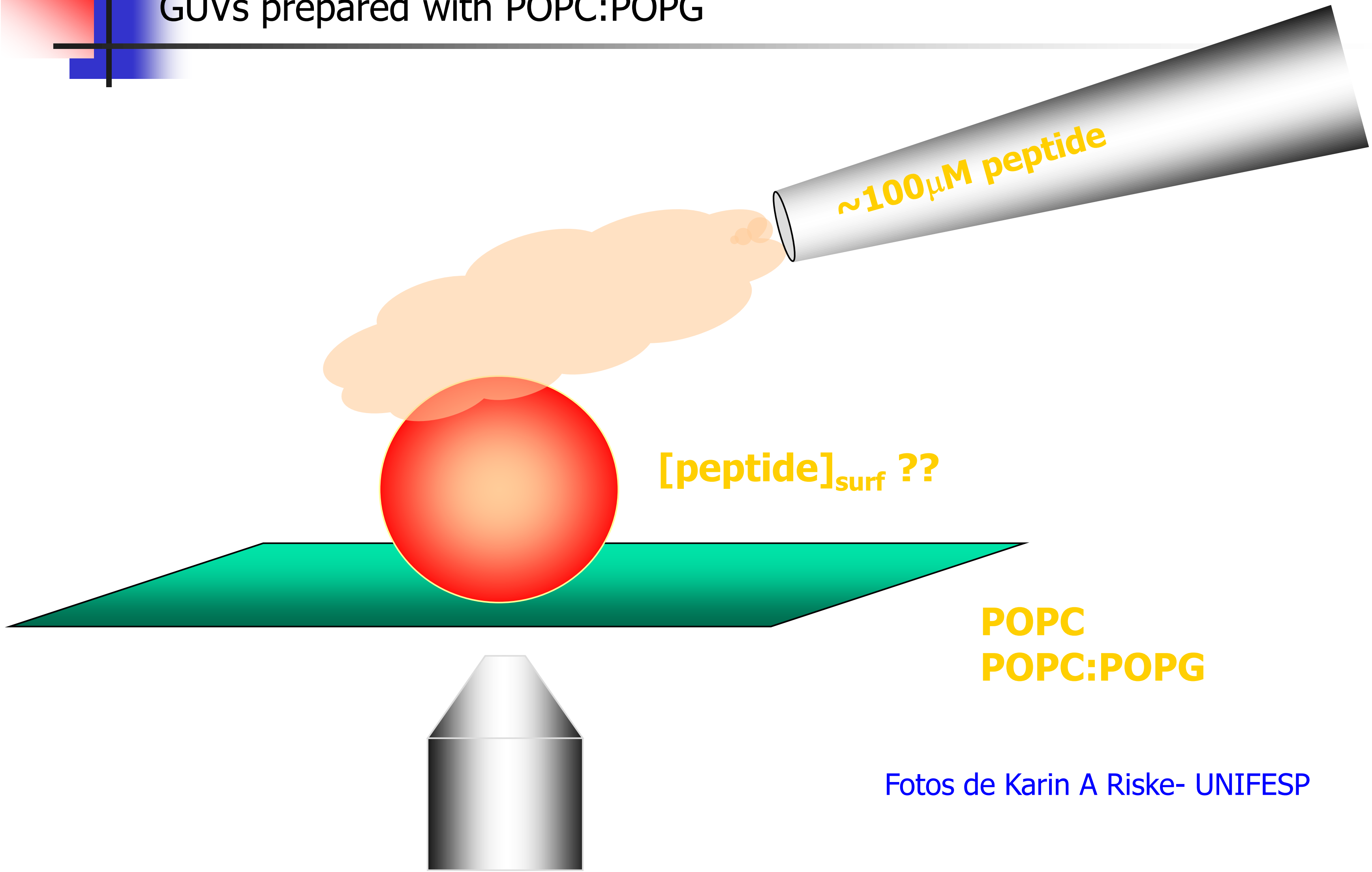
Preparação de Vesículas Gigantes



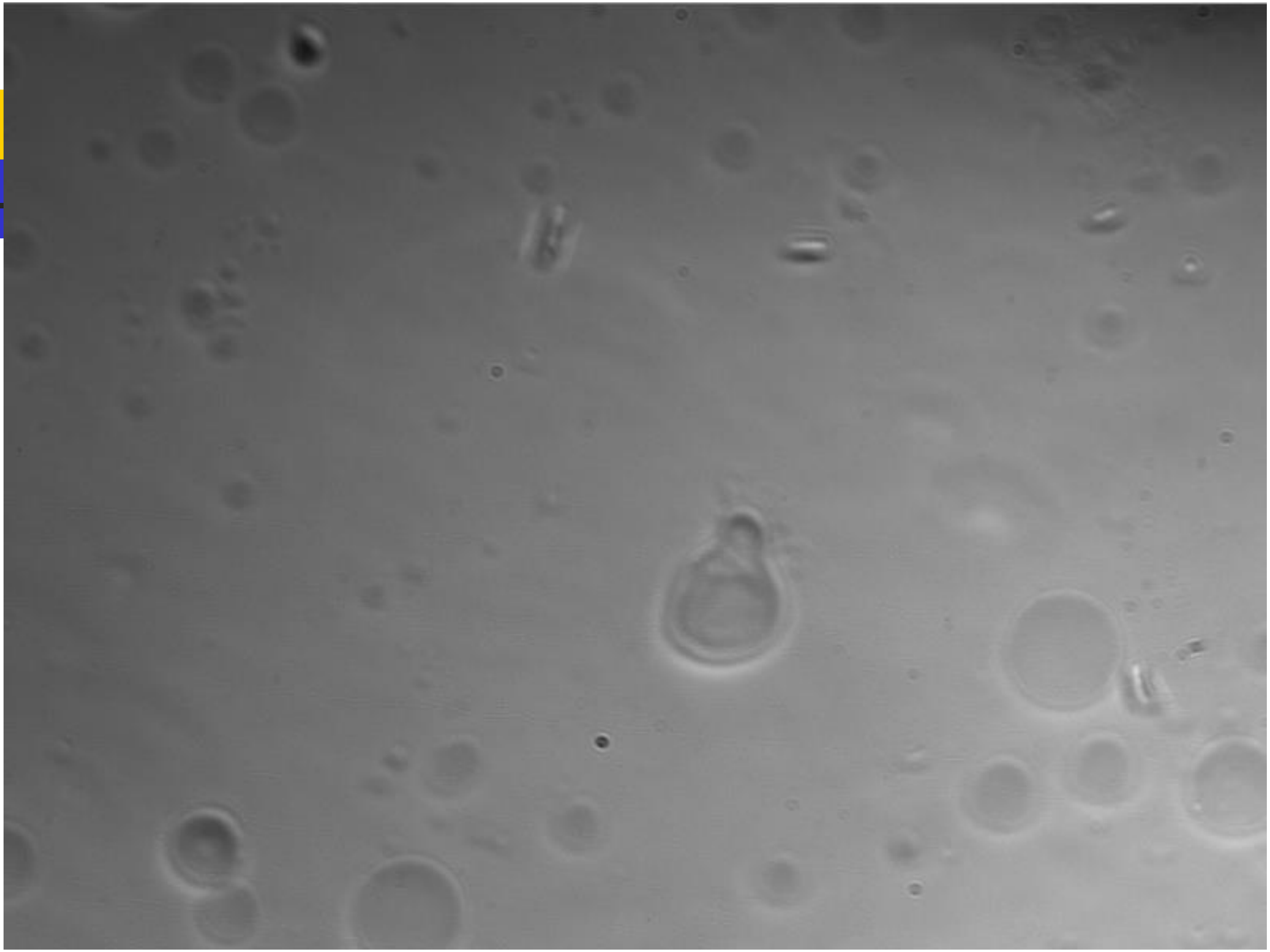
Fotos de Karin A Riske- UNIFESP

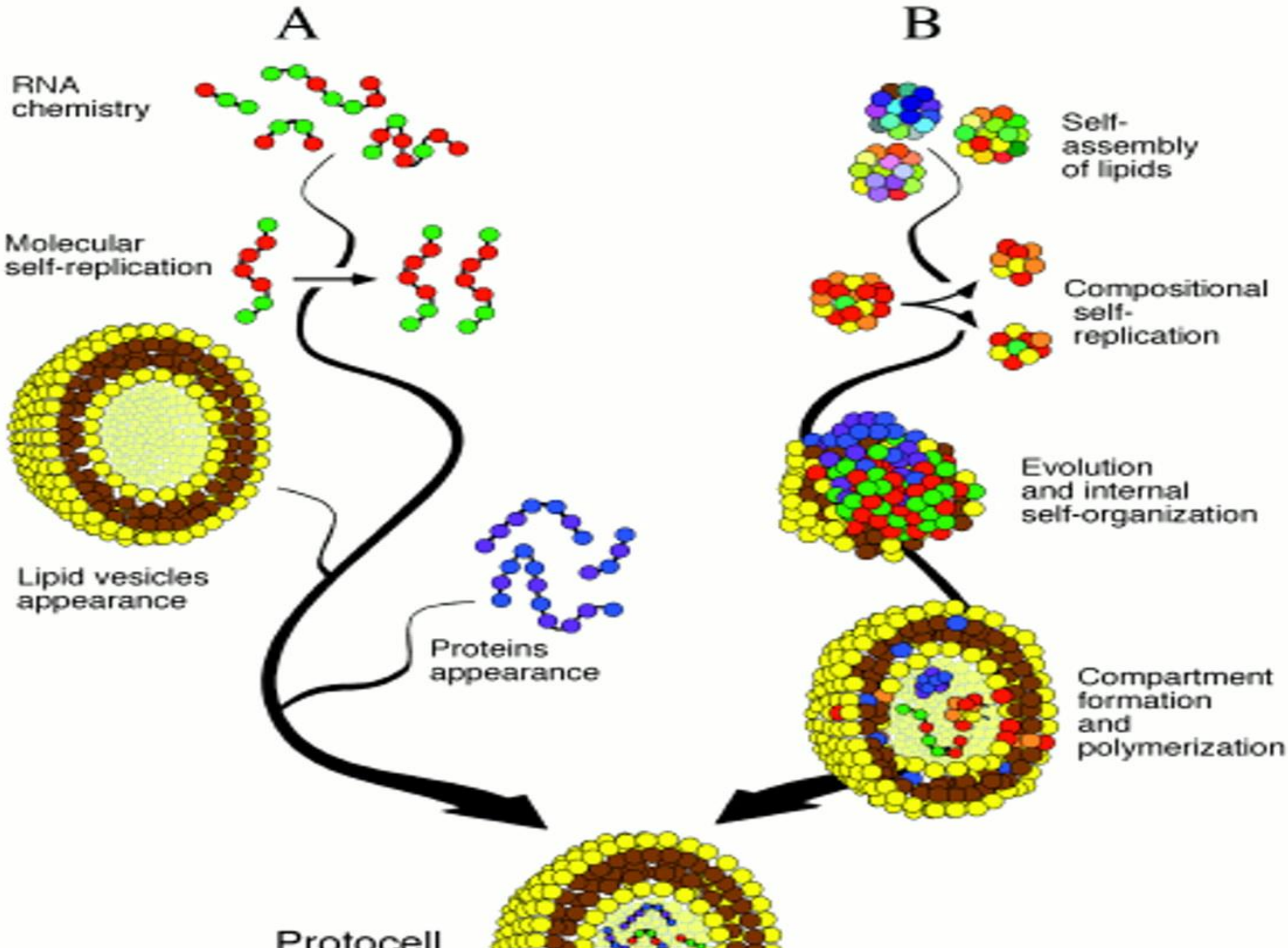
Optical Microscopy of GUVs

GUVs prepared with POPC:POPG



Fotos de Karin A Riske- UNIFESP

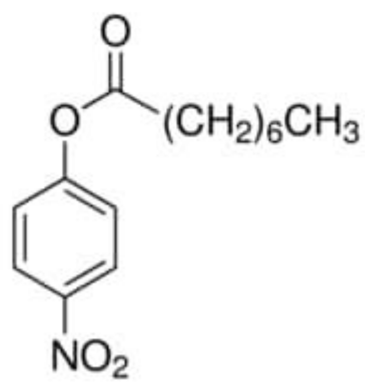




EMBO Reports **vol. 1 | no. 3 | pp 217-222 | 2000**
Daniel Segré and Doron Lancet±

Micelas e Lipossomas
Modelos de Enzimas?

Efeito da estrutura dos agregados e da carga na constante de velocidade relativa da reação de tiólise do éster octanoato de p-nitrofenila.



Tiol	Anfifílico carga,estrutura	$k\psi^{Max} / k\psi^{W}$	k_2^{m} / k_2^{w}
$C_7H_{15}S^-$	SDS micela negativa	0.09	0.27
$C_7H_{15}S^-$	DDPS micela zwitterionice	266	1.0
$C_7H_{15}S^-$	CTAB micela positiva	1.6×10^3	1.2
$C_{15}H_{31}$-NHCys	CTAB micela positiva	1×10^6	15
$C_{15}H_{31}$-NHCys	DODAC vesícula positiva	9×10^6	50