CARBOIDRATOS

1 – ESTRUTURA

CONFIGURAÇÃO
CONFORMAÇÃO
POLIMERIZAÇÃO

2- GLICOPROTEÍNAS E GLICOLIPÍDEOS

3 – GLICOSAMINOGLICANAS E PROTEOGLICANAS

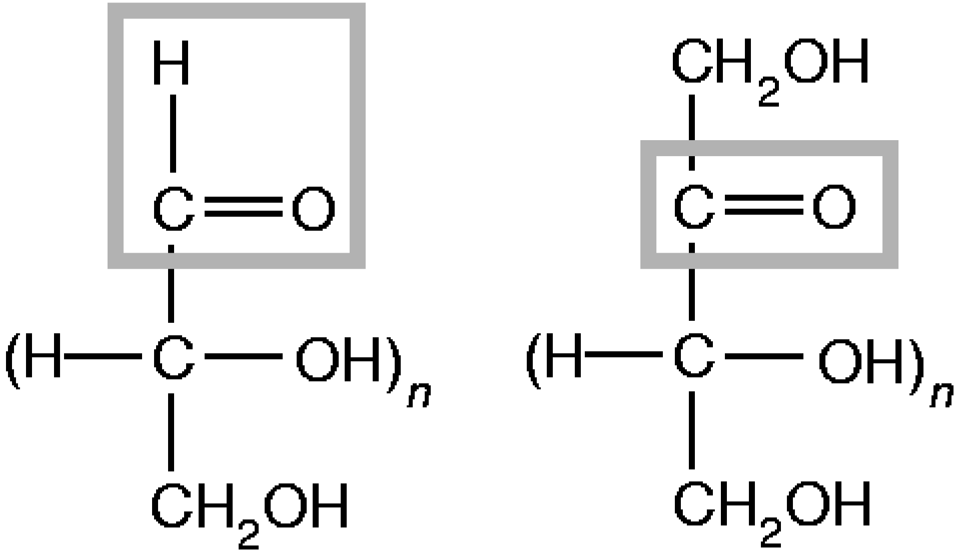
Açúcares
ou
Glicídeos
Oses
Sacarídeos
Carboidratos
Hidratos de carbono → $(CH2O)_n$
$n \geq 3$

Moléculas orgânicas mais abundantes

Diferentes funções: nutrientes
reserva
estrutura

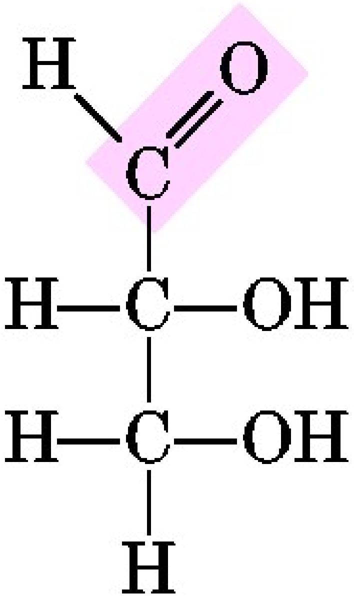
Estrutura química → são poliálcoois $[\,HC - OH\,]_n$

Polihidroxialdeídos ou Polihidroxicetonas

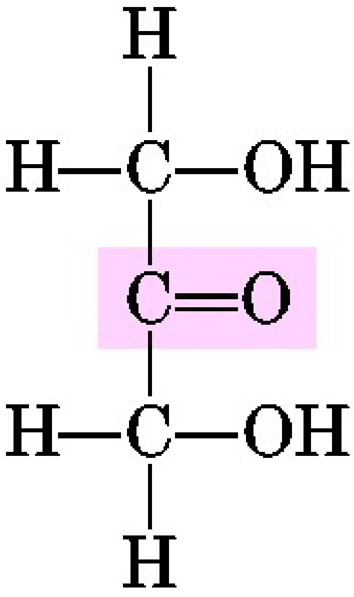


ALDOSE **CETOSE**

Açúcares mais simples :



Gliceraldeído

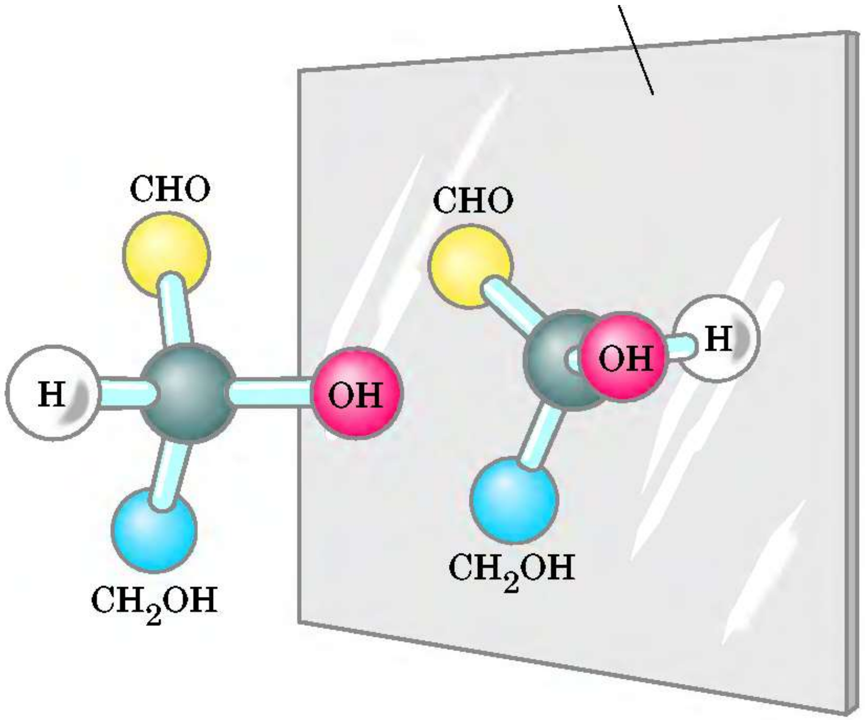


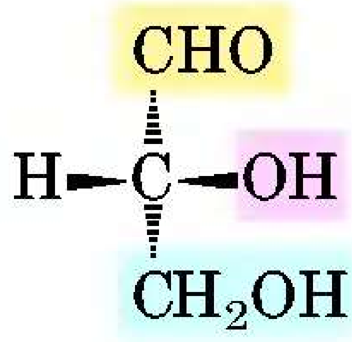
Dihidroxiacetona

Açúcares são **quirais:**

Apresentam centros de assimetria (C*)

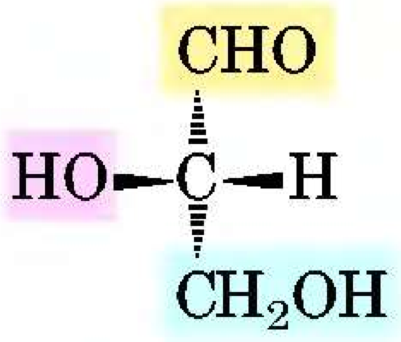
Formam enantiômeros
Isomeria Geométrica L ou D
(e isômeros ópticos)





$$\begin{array}{c} \mathrm{CHO} \\ \mathrm{H{-}C{-}OH} \\ \mathrm{CH_2OH} \end{array}$$

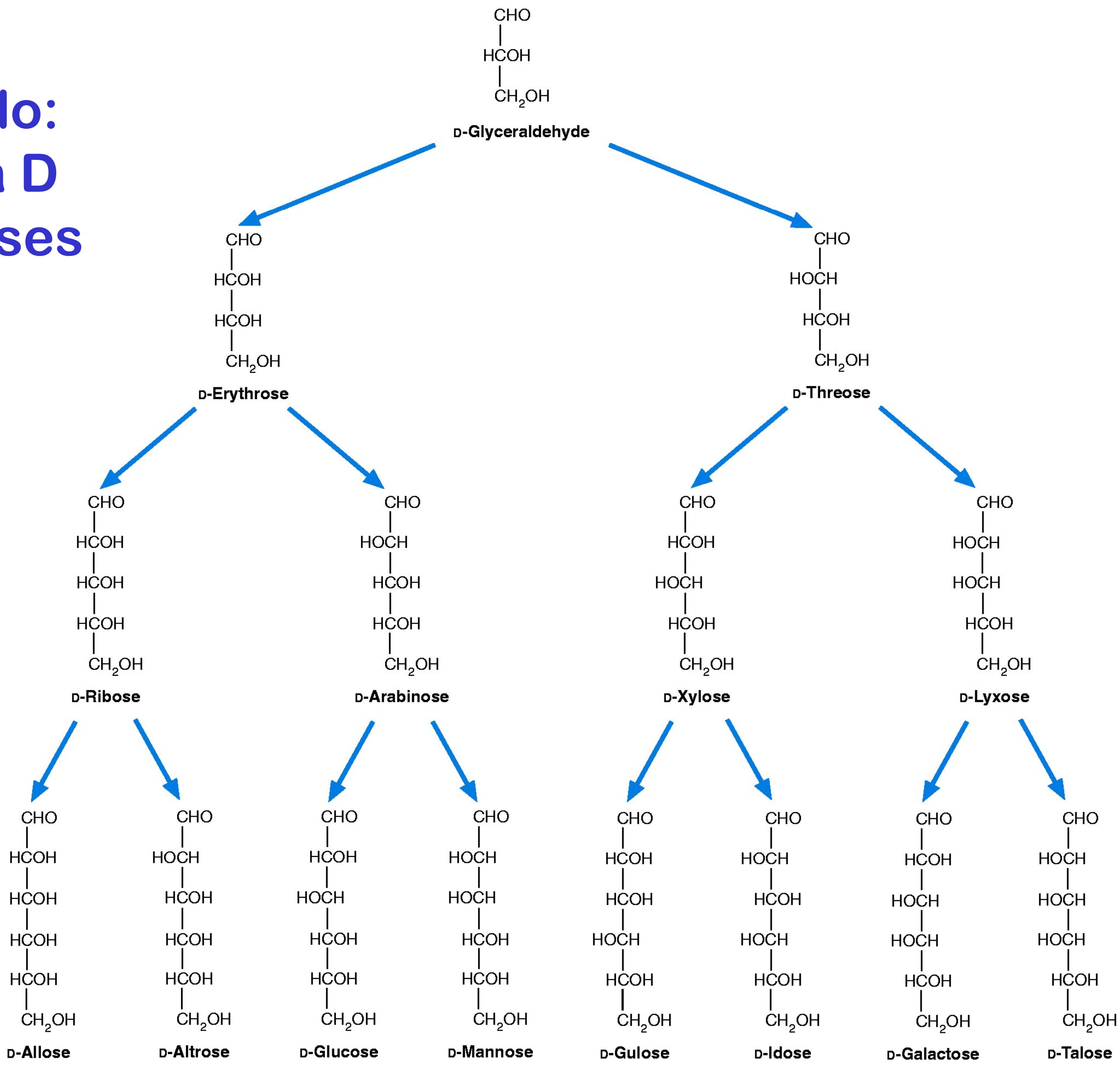
D – Gliceraldeído



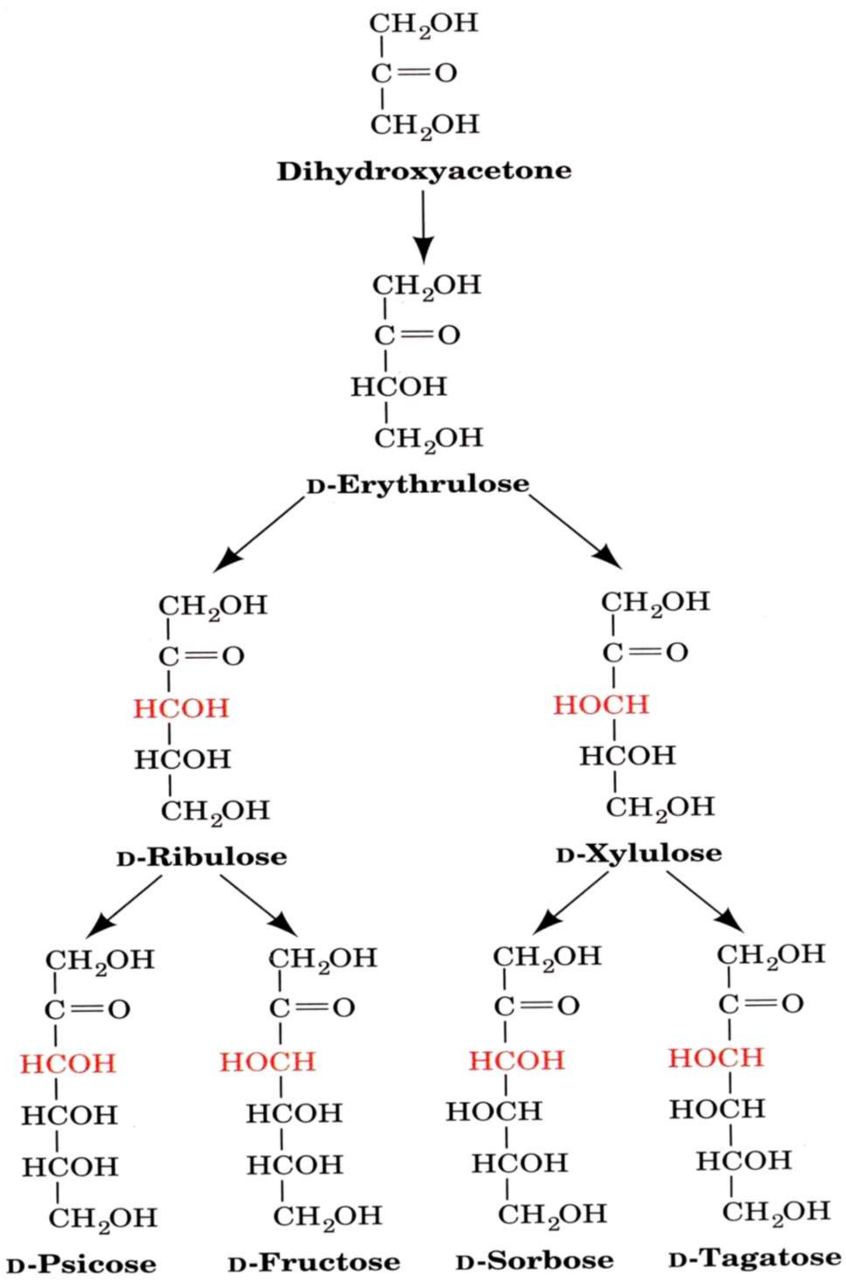
$$\begin{array}{c} \mathrm{CHO} \\ \mathrm{HO{-}C{-}H} \\ \mathrm{CH_2OH} \end{array}$$

L – Gliceraldeído

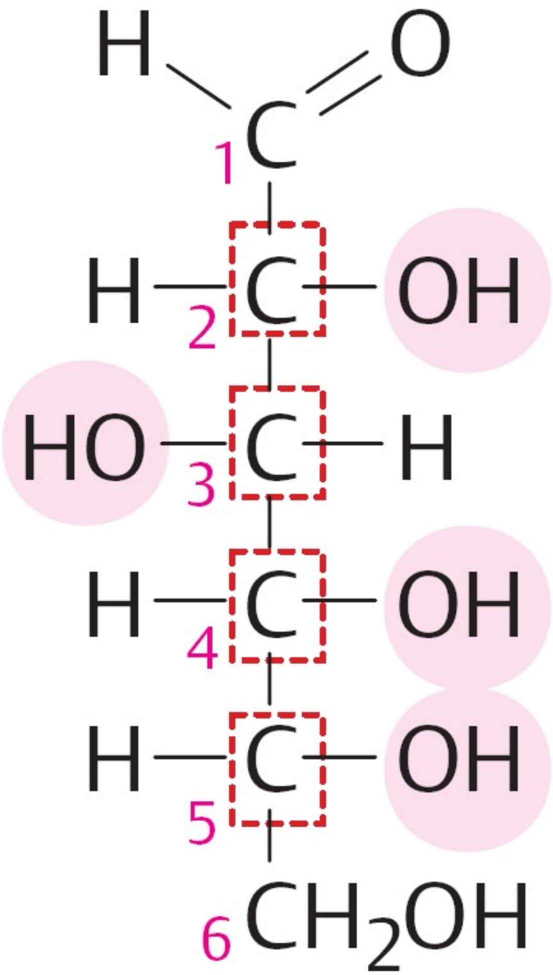
Exemplo: Familia D de Aldoses


CHO
HCOH
CH_2OH
D-Glyceraldehyde
CHO
HCOH
HCOH
CH_2OH
D-Erythrose
CHO
HOCH
HCOH
CH_2OH
D-Threose
CHO
HCOH
HCOH
HCOH
CH_2OH
D-Ribose
CHO
HOCH
HCOH
HCOH
CH_2OH
D-Arabinose
CHO
HCOH
HOCH
HCOH
CH_2OH
D-Xylose
CHO
HOCH
HOCH
HCOH
CH_2OH
D-Lyxose
CHO
HCOH
HCOH
HCOH
HCOH
CH_2OH
D-Allose
CHO
HOCH
HCOH
HCOH
HCOH
CH_2OH
D-Altrose
CHO
HCOH
HOCH
HCOH
HCOH
CH_2OH
D-Glucose
CHO
HOCH
HOCH
HCOH
HCOH
CH_2OH
D-Mannose
CHO
HCOH
HCOH
HOCH
HCOH
CH_2OH
D-Gulose
CHO
HOCH
HCOH
HOCH
HCOH
CH_2OH
D-Idose
CHO
HCOH
HOCH
HOCH
HCOH
CH_2OH
D-Galactose
CHO
HOCH
HOCH
HOCH
HCOH
CH_2OH
D-Talose

Exemplo: Família D de Cetoses


Dihydroxyacetone
D-Erythrulose
D-Ribulose
D-Xylulose
D-Psicose
D-Fructose
D-Sorbose
D-Tagatose

Numeração de Carbonos da D – Glicose

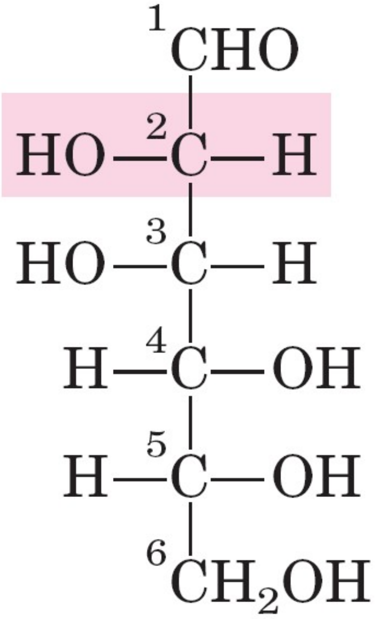

H
O
1 C
H 2 C OH
HO 3 C H
H 4 C OH
H 5 C OH
6 CH_2OH

4 C* (assimétricos) ⬚

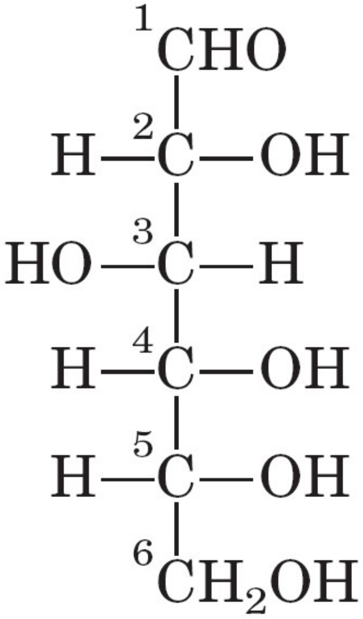
2x2x2x2 (2^4) isômeros

8 isômeros D
(e 8 isômeros L)

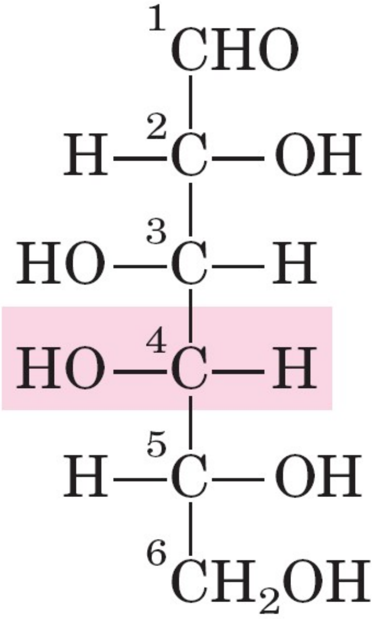
D – Manose



D – Glicose



D – Galactose



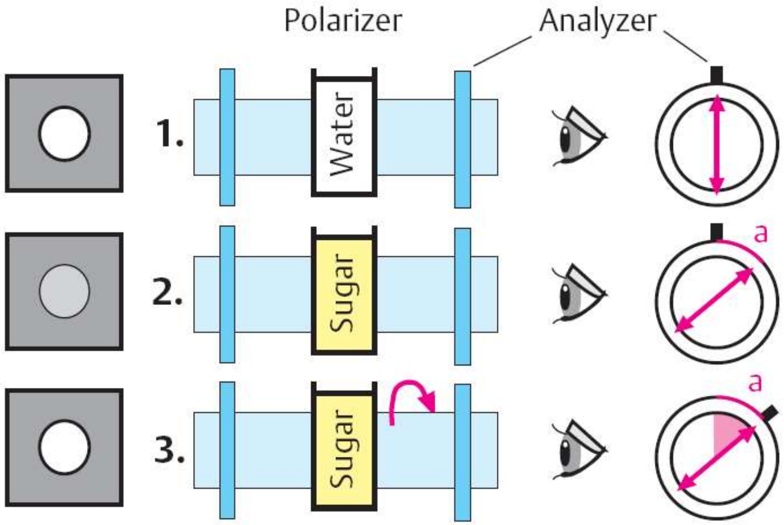
D-Manose e D-Galactose são epímeros da D-Glicose :

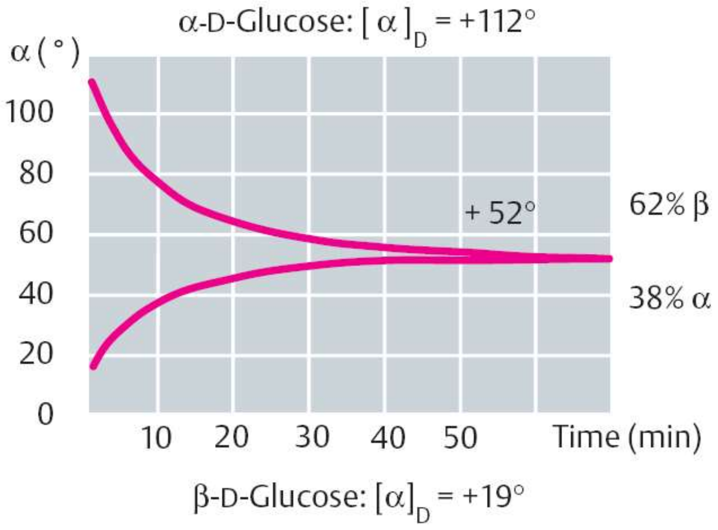
Diferença em apenas 1 dos Carbonos assimétricos

Glicose em água sofre Mutarrotação espontânea

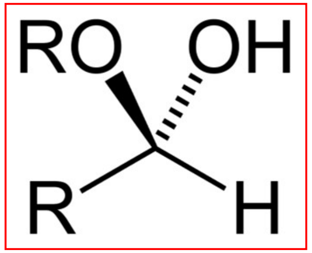
α-D-glicose tem rotação específica de + 112° (dextrógira)

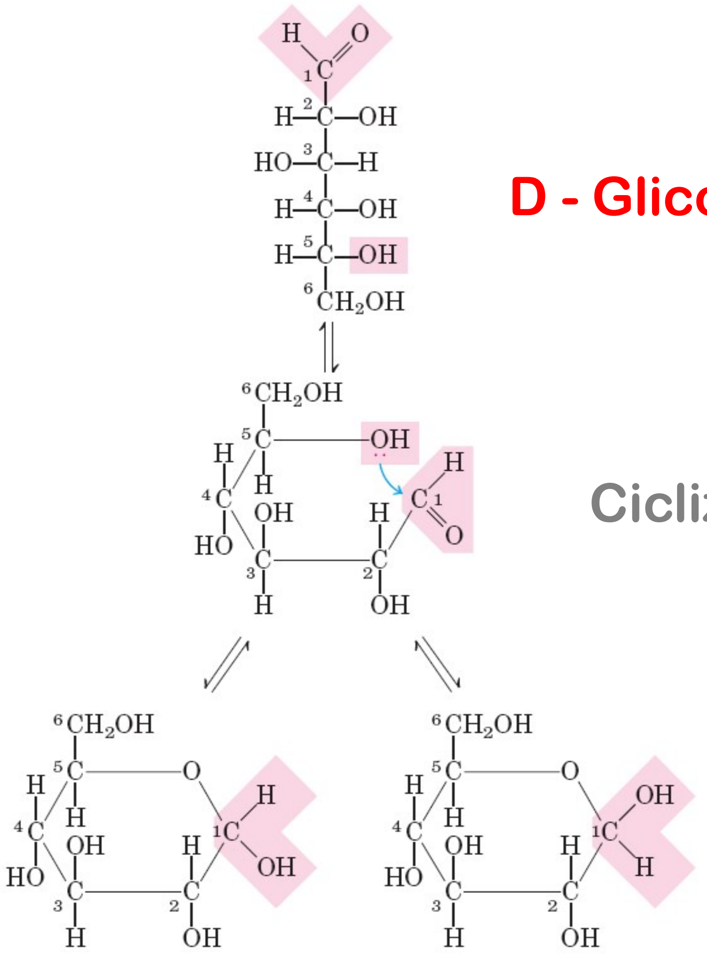
β-D-glicose tem rotação específica de + 19° (dextrógira)


Polarizer
Analyzer
1.
Water
2.
Sugar
a
3.
Sugar
a



Açúcares em solução aquosa
Formam hemiacetais →





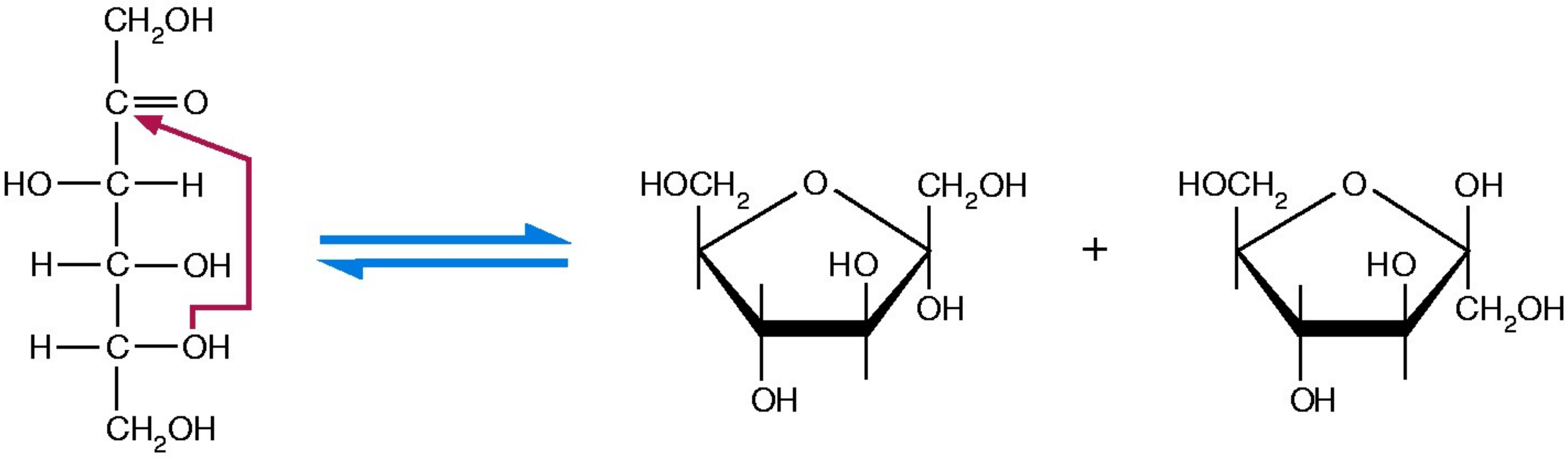
D - Glicose

Ciclização

D – Glicopiranoses (α e β)

Frutose ($C_6H_{12}O_6$) – uma cetose

Também forma hemiacetais em água:

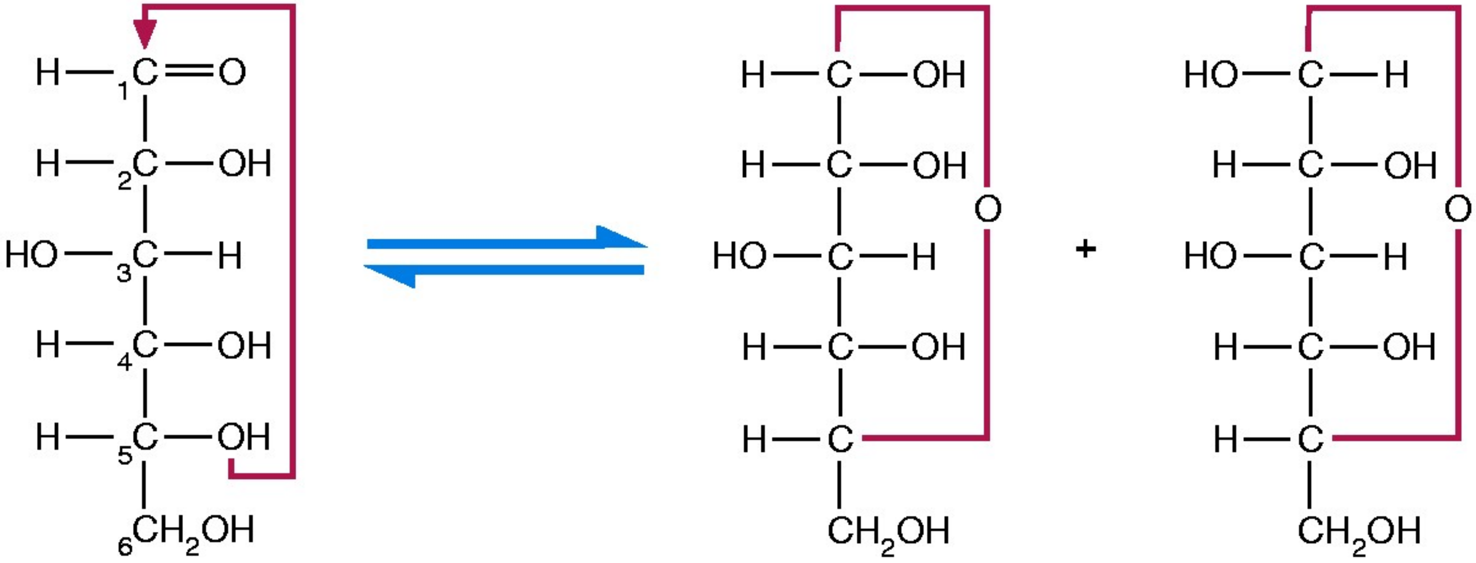


CH_2OH
C=O
HO—C—H
H—C—OH
H—C—OH
CH_2OH
$HOCH_2$
O
CH_2OH
HO
OH
OH
+
$HOCH_2$
O
OH
HO
CH_2OH
OH

α-D-Frutofuranose

β-D-Frutofuranose

Ao formar o Hemiacetal cíclico (anel lactona) é formado um novo C assimétrico (C_1 – carbonila)



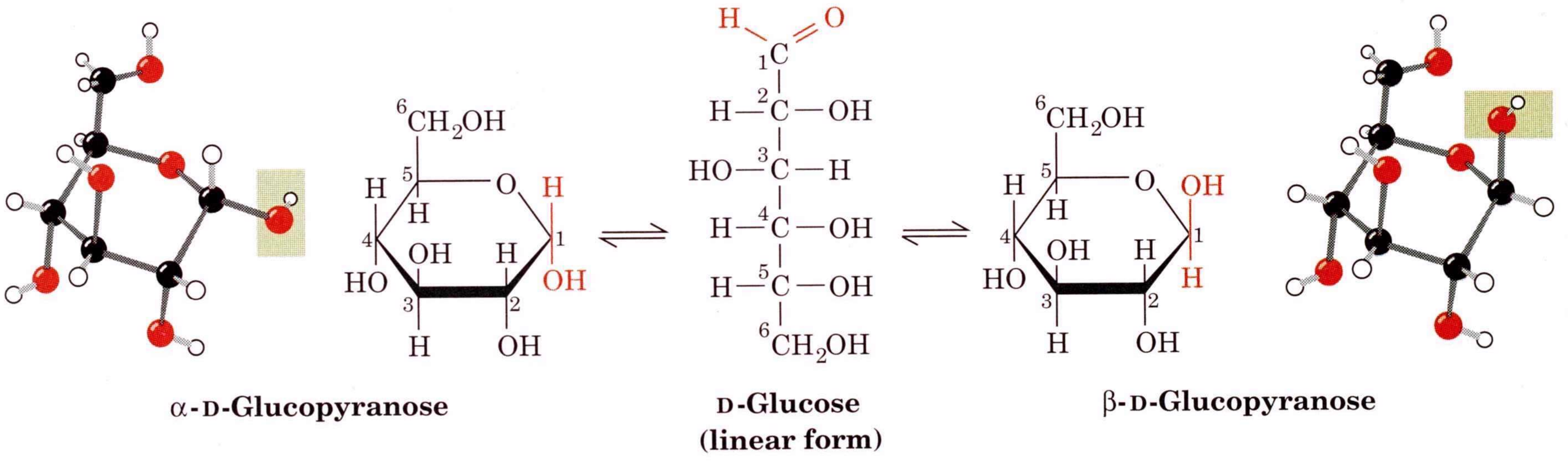
D-glicose

Anômeros

(diferença em apenas 1 C)

Anomeria

Podem ter configuração α (-OH para baixo) ou β (-OH para cima) em relação a CH_2OH.

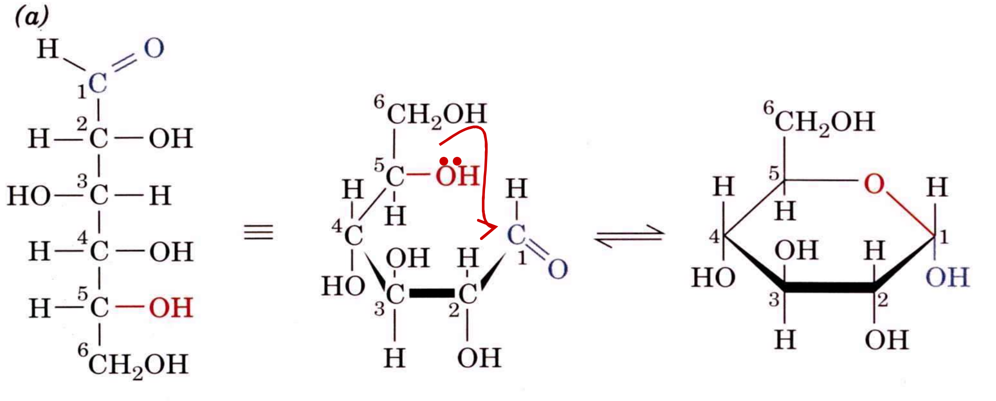


$^6CH_2OH$
H
5
O
H
H
4
OH
H
1
HO
OH
3
2
H
OH
H
O
1 C
H — 2 C — OH
HO — 3 C — H
H — 4 C — OH
H — 5 C — OH
$^6CH_2OH$
$^6CH_2OH$
H
5
O
OH
H
4
OH
H
1
HO
H
3
2
H
OH
α-D-Glucopyranose
D-Glucose
(linear form)
β-D-Glucopyranose

Mutarrotação

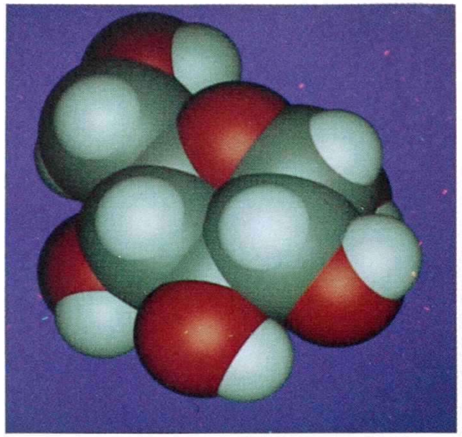
As formas α e β estão em equilíbrio, uma forma pode se converter na outra.

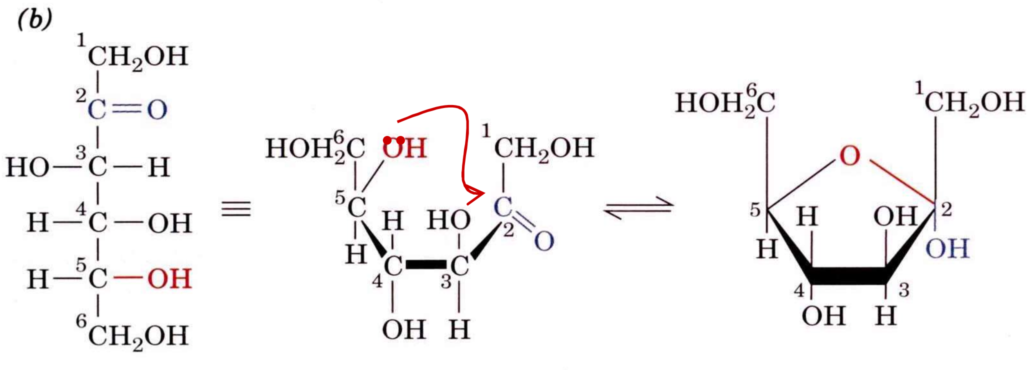
Ciclização Intramolecular


(a)
H
O
C
1
2
3
4
5
6
H—C—OH
HO—C—H
H—C—OH
H—C—OH
CH₂OH
≡
CH₂OH
C—OH
H
OH
HO
C=O
⇌
O

D-Glucose
(linear form)

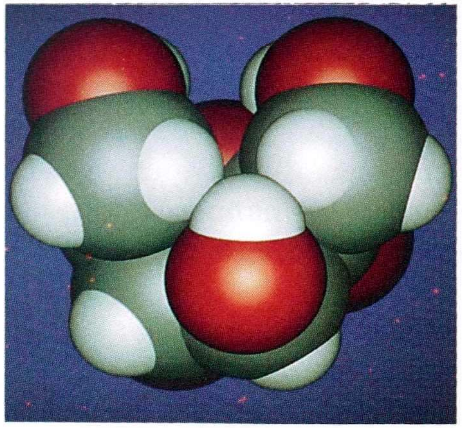
α-D-Glucopyranose
(Haworth projection)




(b)
1
CH₂OH
2
C=O
3
HO—C—H
4
H—C—OH
5
H—C—OH
6
CH₂OH
≡
HOH₂C
OH
CH₂OH
HO
C=O
⇌
O
OH
H

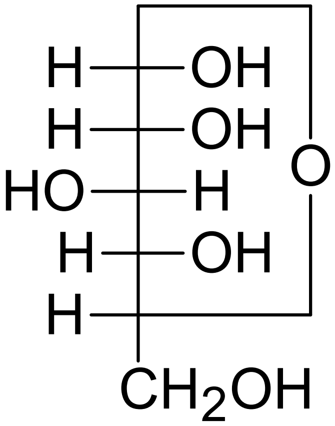
D-Fructose
(linear form)

α-D-Fructofuranose
(Haworth projection)

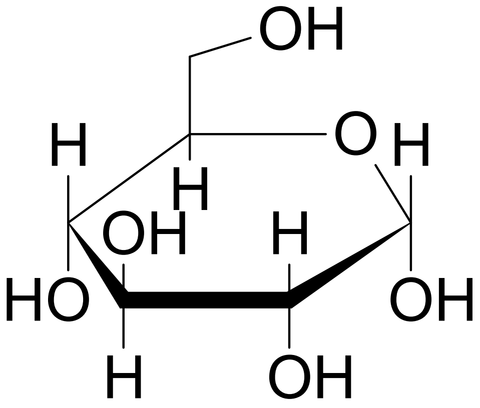


Diferentes formas de representação de α-D-glicopiranose

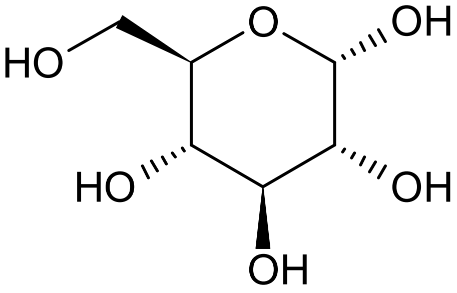
Fisher


H OH
H OH
HO H
H OH
H
O
CH_2OH

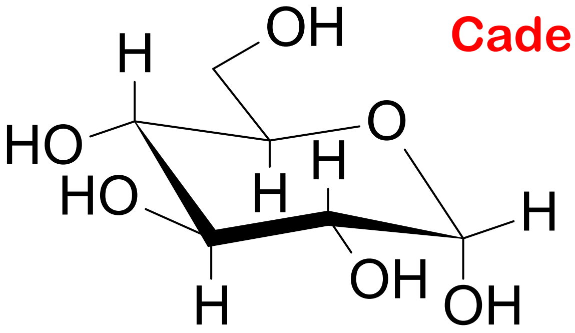
Haworth

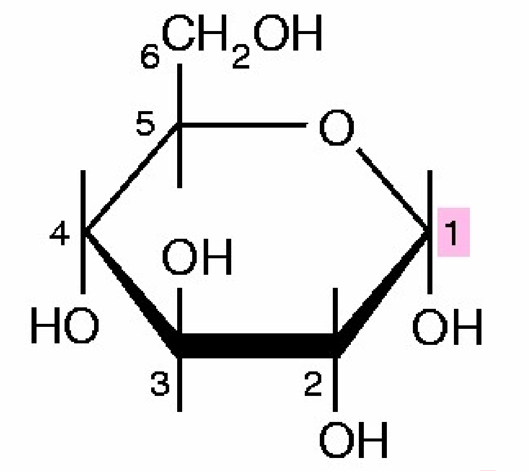

OH
H
O
H
H
OH
H
HO
OH
H
OH

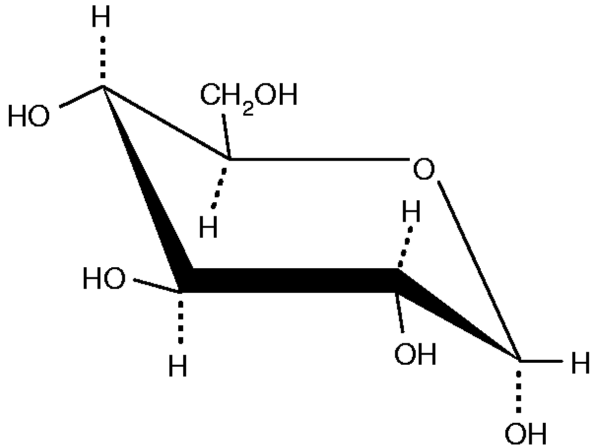
Estereo


HO
O
OH
HO
OH
OH

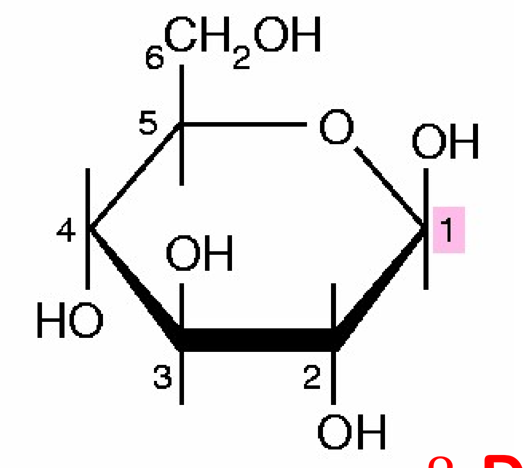
Cadeira-barco

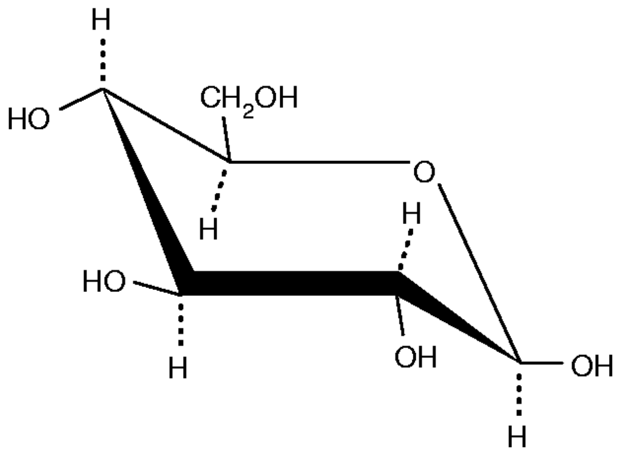

OH
H
O
HO
H
HO
H
H
H
OH
OH


6
CH2OH
5
O
4
1
OH
HO
OH
3
2
OH

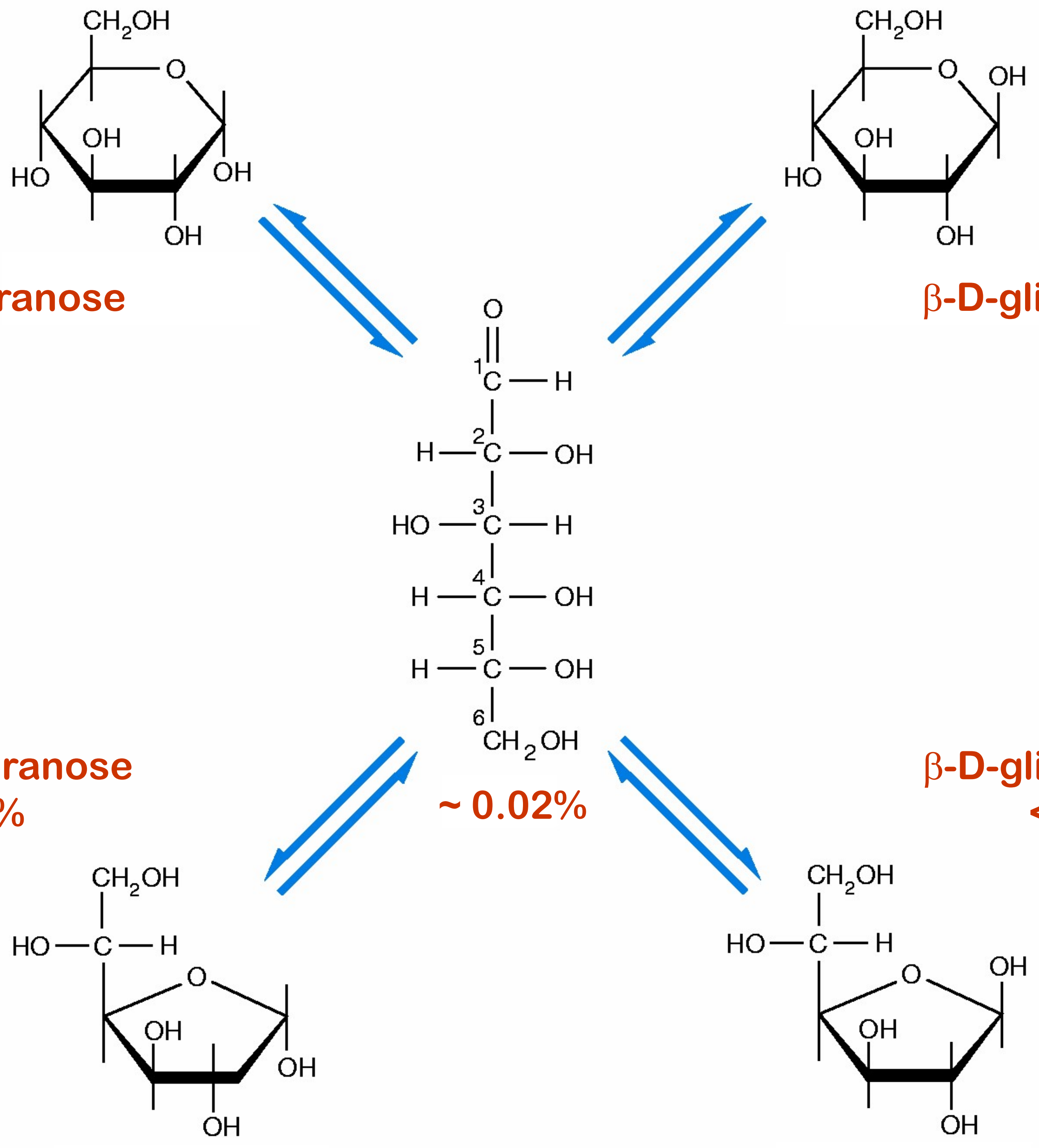

H
HO
CH2OH
O
H
H
HO
H
OH
H
OH

α-D-glicopiranose


6
CH2OH
5
O
OH
4
1
OH
HO
3
2
OH


H
HO
CH2OH
O
H
H
HO
H
OH
OH
H

β-D-glicopiranose


CH₂OH
O
OH
HO
OH
OH
CH₂OH
O
OH
OH
HO
OH
O
1
C
H
H
2
C
OH
HO
3
C
H
H
4
C
OH
H
5
C
OH
6
CH₂OH
CH₂OH
HO
C
H
O
OH
OH
OH
CH₂OH
HO
C
H
O
OH
OH
OH

α-D-glicopiranose
38%

β-D-glicopiranose
62%

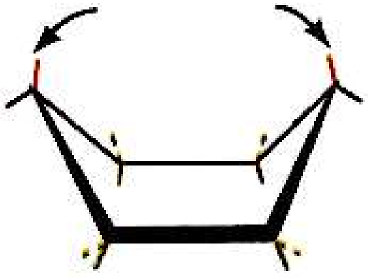
~ 0.02%

α-D-glicofuranose
< 0.5%

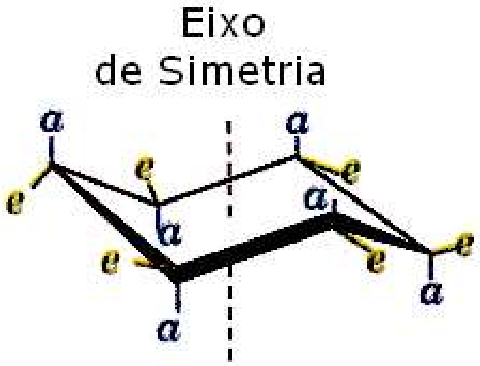
β-D-glicofuranose
< 0.5%

Considerações sobre conformações

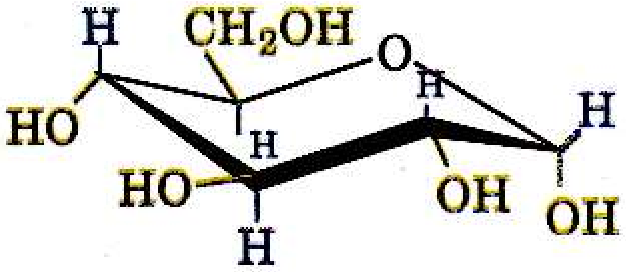
Fórmulas Conformacionais



barco

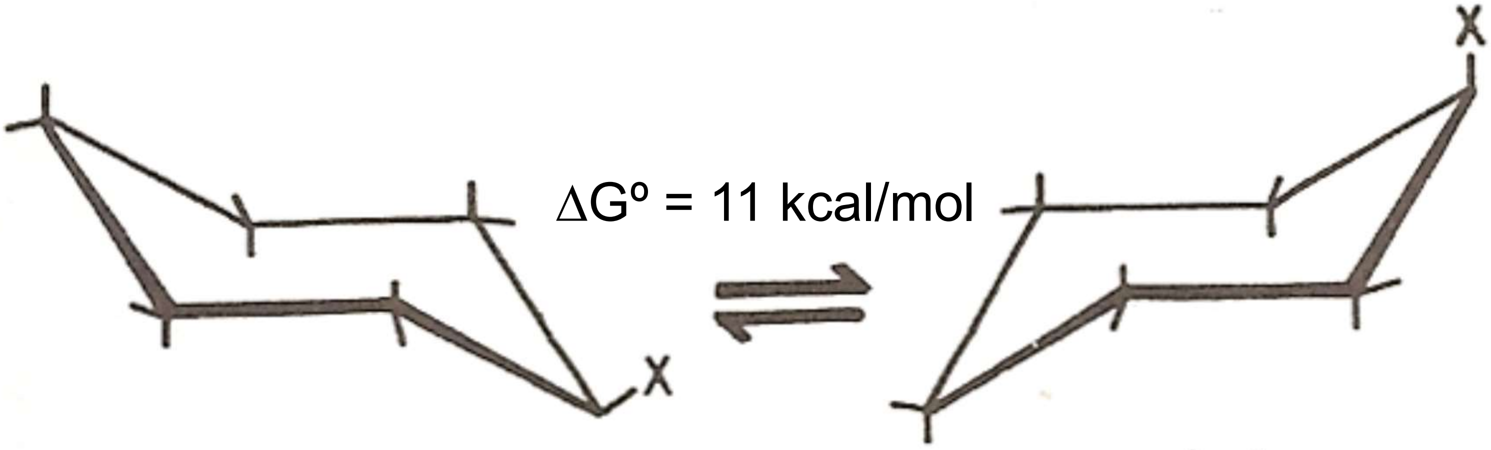

Eixo
de Simetria
a
e
a
e
a
e
a
e
a
e
a
e
a

cadeira


H
CH₂OH
O
HO
H
H
H
HO
OH
OH
H

α-D-Glicopiranose

Interconversão de cadeiras

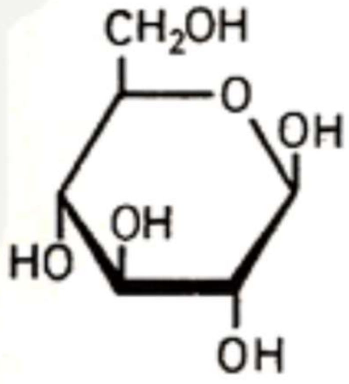


ΔG^o = 11 kcal/mol

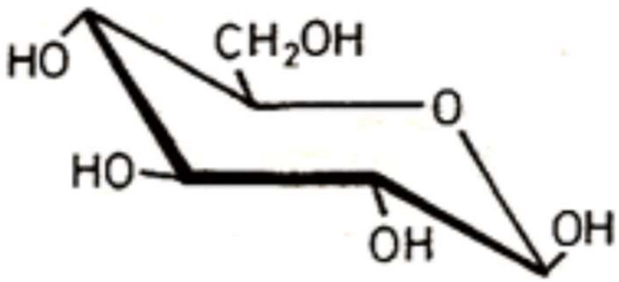
4.3

4.4

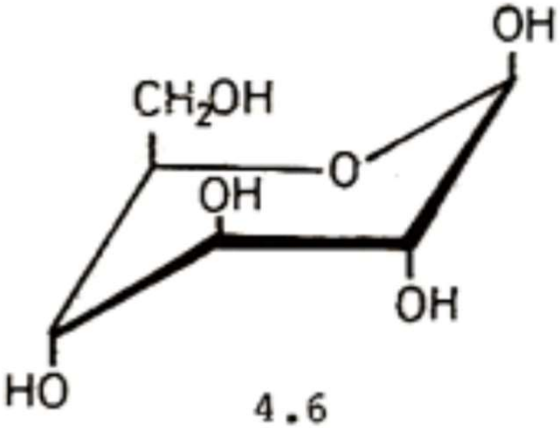
Interconversão com substituintes


CH₂OH
O
OH
OH
HO
OH

β-D-glucopiranosa

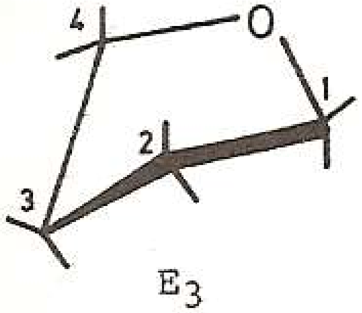

HO
CH₂OH
O
HO
OH
OH

4.5


OH
CH₂OH
O
OH
OH
HO

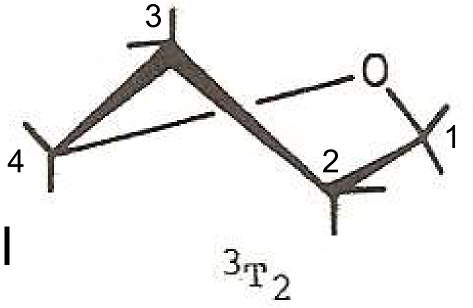
4.6

Confôrmeros furanósicos



Envelope

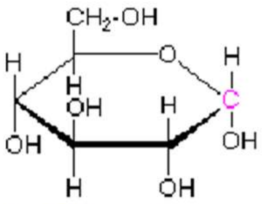
$\Delta G^o \cong$ 3-4 kcal/mol



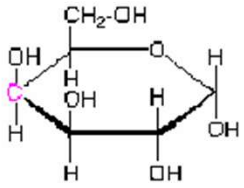
Torcida

ALGUMAS ESTRUTURAS

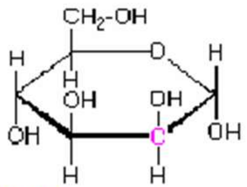
Glicopiranoses mais comuns



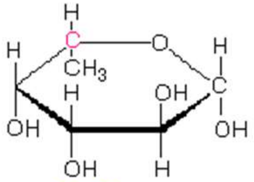
α-D-Glicopiranose
(Glicose)
Glc



α-D-Galactopiranose
(Galactose)
Gal

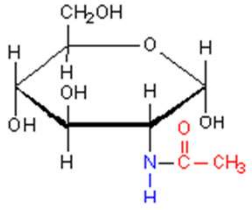


α-D-Manopiranose
(Manose)
Man

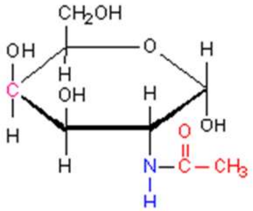


L-Fucose

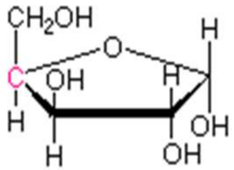
L-Fuc



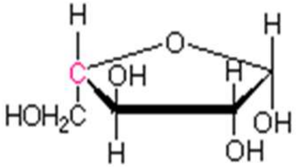
N-Acetil-D-Glicosamina
(GlcNAc)



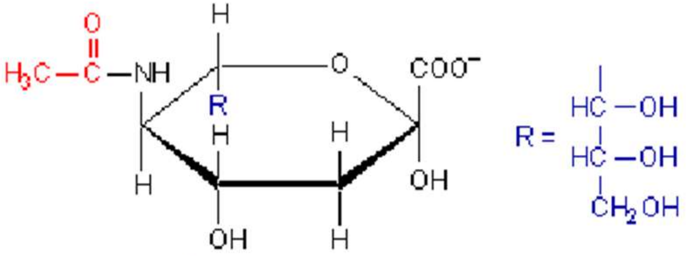
N-Acetil-D-galactosamina
(GalNAc)



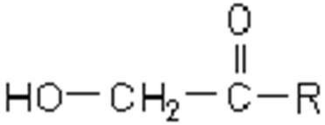
D-Xilose
(Xyl)



L-Arabinose
(L-Ara)



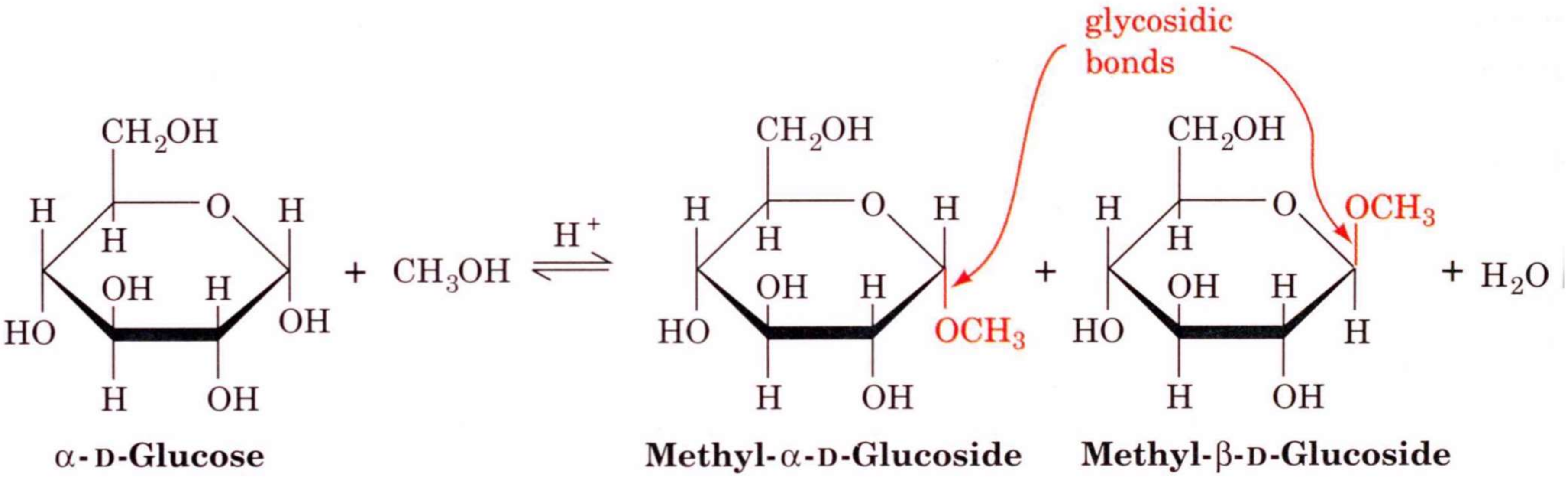
Ácido Siálico
N-Acetil Neuroamínico
(NeuNAc)



$$HO-CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-R$$

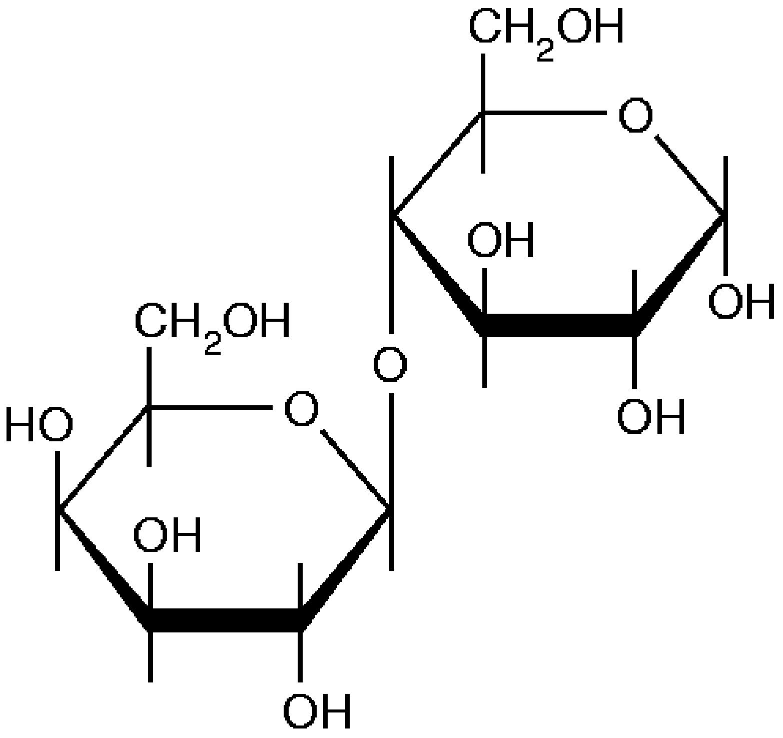
N-Glicolil Neuroamínico

Ligações Glicosídicas ocorrem entre dois açúcares

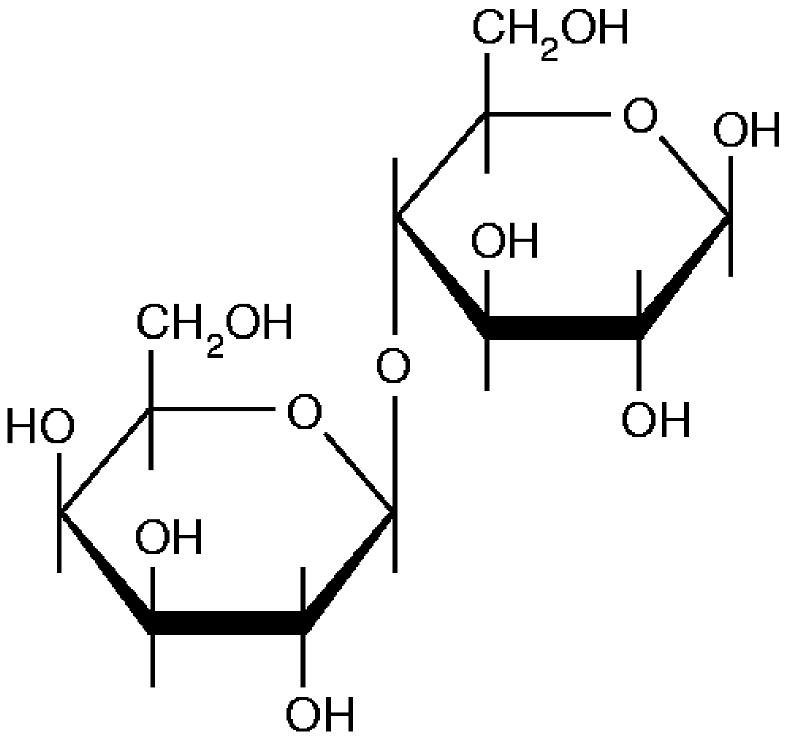

CH2OH
H
O
H
H
OH
H
HO
OH
H
OH
α-D-Glucose
+ CH3OH
H+
glycosidic bonds
OCH3
Methyl-α-D-Glucoside
+
Methyl-β-D-Glucoside
+ H2O

Podem ter configuração α ou β e ligações entre os carbonos 1-2, 1-4 ou 1-6.

Primeiro açúcar que provamos é um Dissacarídeo: 2 monosacarídeos unidos por ligação glicosídica


CH_2OH
O
OH
OH
OH
CH_2OH
HO
O
O
OH
OH

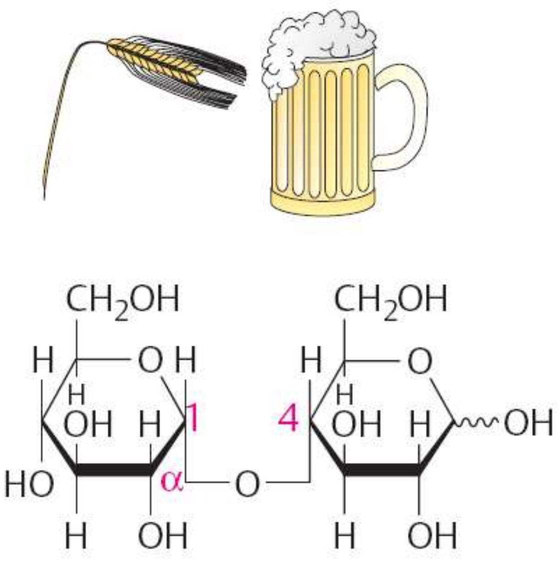
α-Lactose


CH_2OH
O
OH
OH
OH
CH_2OH
HO
O
O
OH
OH

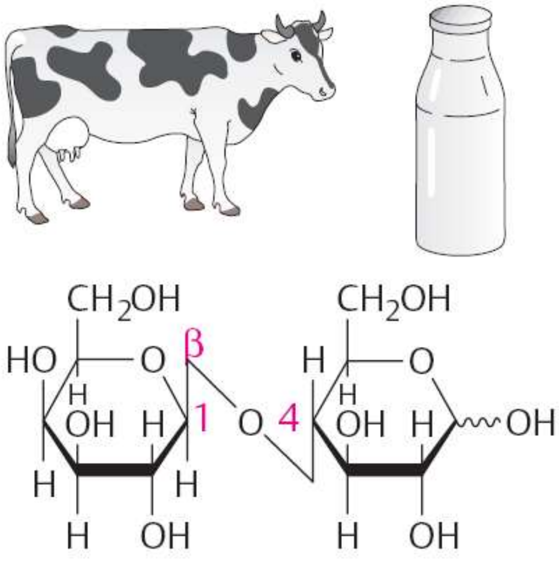
β-Lactose

O-β-D-galactopiranosil (1→4) (α) ou (β)-D-glicopiranose

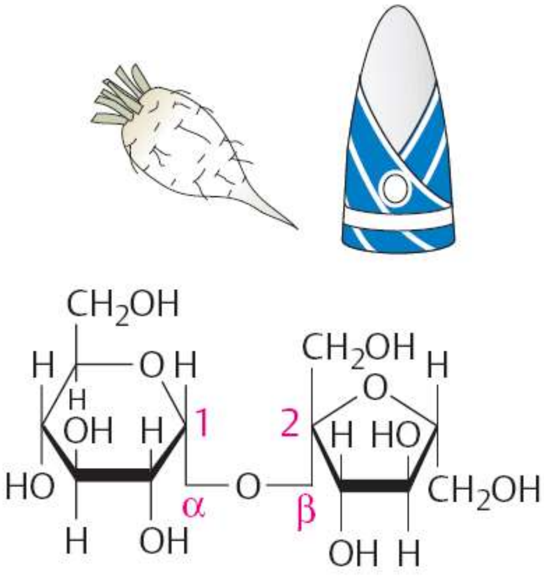
Dissacarídeos importantes


CH₂OH
CH₂OH
H
O
H
H
O
H
H
OH
H
1
4
H
OH
H
OH
HO
α
O
H
OH
H
OH

Maltose


CH₂OH
CH₂OH
HO
O
β
H
O
H
OH
H
1
O
4
H
OH
H
OH
H
H
H
OH
H
OH

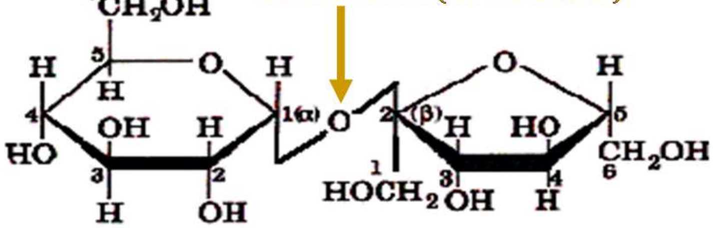
Lactose


CH₂OH
CH₂OH
H
H
O
H
O
H
OH
H
1
2
H
HO
HO
α
O
β
CH₂OH
H
OH
OH
H

Sacarose

Dissacarídeos

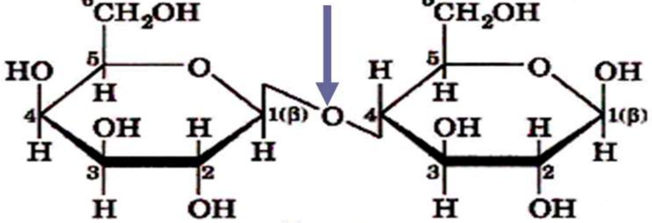
Sacarase (invertase)


6 CH₂OH
H
5
O
H
H
4
OH
H
1(α)
O
2
(β)
H
HO
5
HO
3
2
1
HOCH₂
3
OH
4
H
CH₂OH
6
H
OH

Sacarose

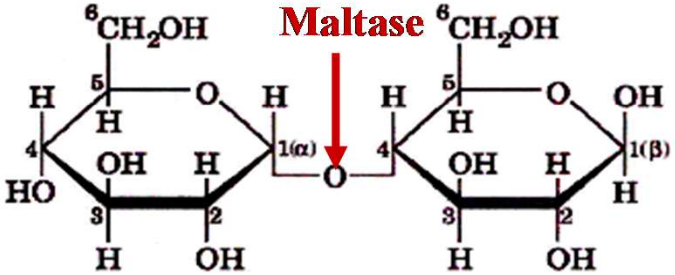
O-α-D-Glicopiranosil-(1→2)-β-D-Frutofuranosídio

Lactase


6 CH₂OH
6 CH₂OH
HO
5
O
H
5
O
OH
H
H
4
OH
H
1(β)
O
4
OH
H
1(β)
H
H
3
2
3
2
H
OH
H
OH

Lactose

O-β-D-Galactopiranosil-(1→4)-β-D-Glicopiranose


6 CH₂OH
6 CH₂OH
H
5
O
H
H
5
O
OH
H
H
4
OH
H
1(α)
O
4
OH
H
1(β)
HO
H
3
2
3
2
H
OH
H
OH

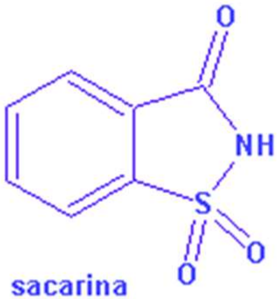
Maltase

Maltose

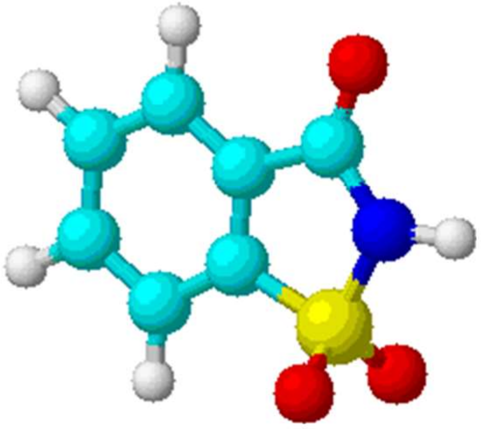
O-α-D-Glicopiranosil-(1→4)-β-D-Glicopiranose

Doçura Relativa

Sacarose	100
Glicose	70
Frutose	170
Maltose	30
Lactose	16
Sacarina	40.000

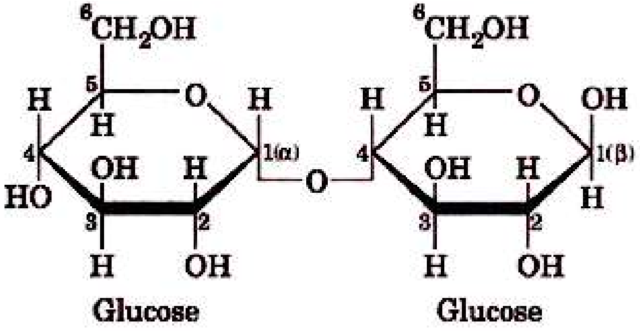


sacarina



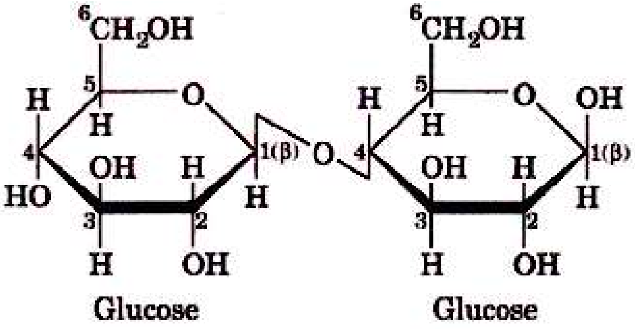
Fontes de Diversidade

Anomeria



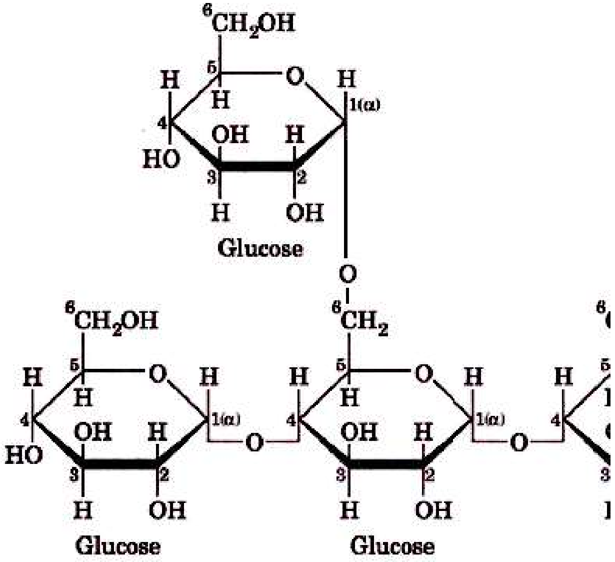
⁶CH₂OH
⁶CH₂OH
H
H
O
H
H
O
OH
HO
OH
H
OH
H
H
1(α)
1(β)
O
H
OH
H
OH
Glucose
Glucose

Maltose



⁶CH₂OH
⁶CH₂OH
H
H
O
H
H
O
OH
HO
OH
H
OH
H
H
H
1(β)
1(β)
O
H
OH
H
OH
Glucose
Glucose

Cellobiose



⁶CH₂OH
H
H
O
H
1(α)
HO
OH
H
H
OH
Glucose
O
⁶CH₂OH
⁶CH₂
H
H
O
H
H
H
O
H
H
HO
OH
H
OH
H
1(α)
1(α)
O
O
H
OH
H
OH
Glucose
Glucose

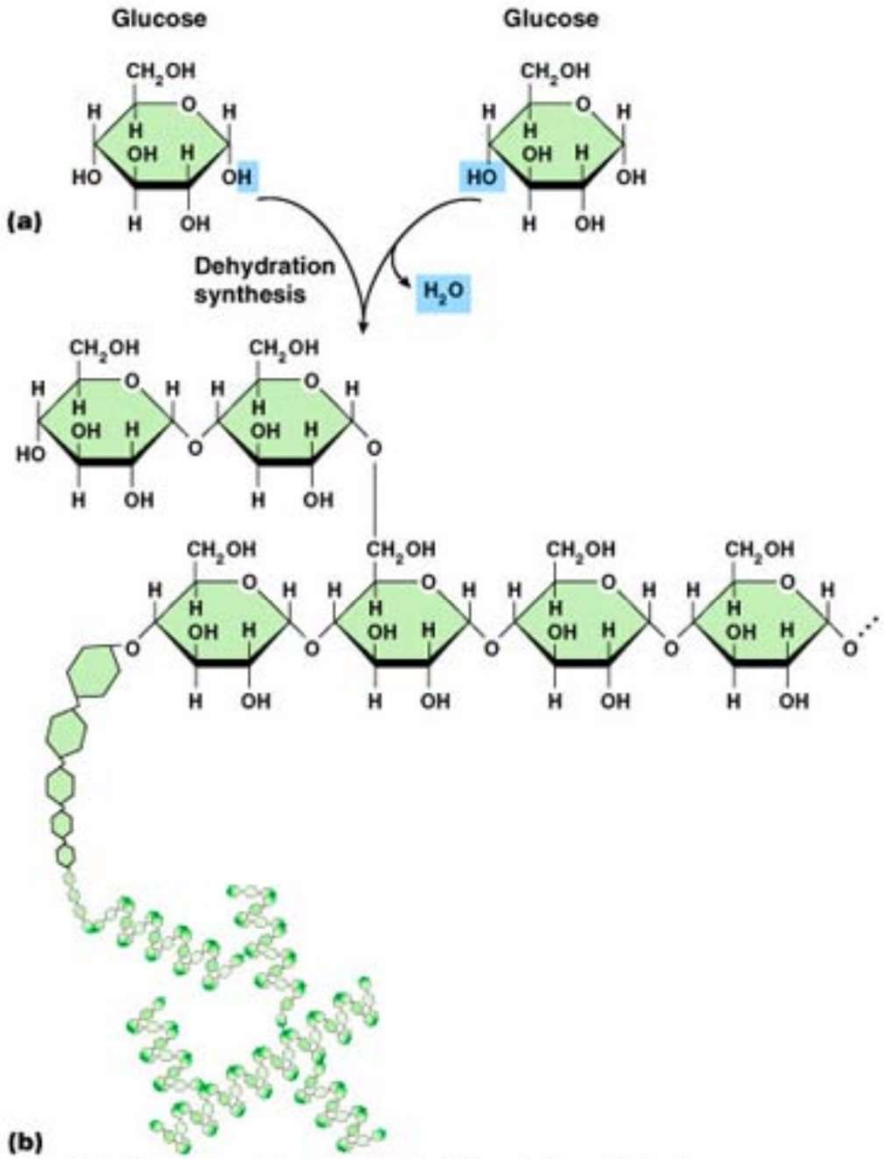
Ramificação

Formas Isoméricas

Composição do Monômero	Produto	Número de Isômeros	
		Peptídeos	Sacarídeos
X2	Dímero	1	11
X3	Trímero	1	176
XYZ	Trímero	6	1056

POLISSACARÍDEOS

Polissacarídeos


Glucose
Glucose
CH2OH
H
O
OH
HO
(a)
Dehydration synthesis
H2O
(b)

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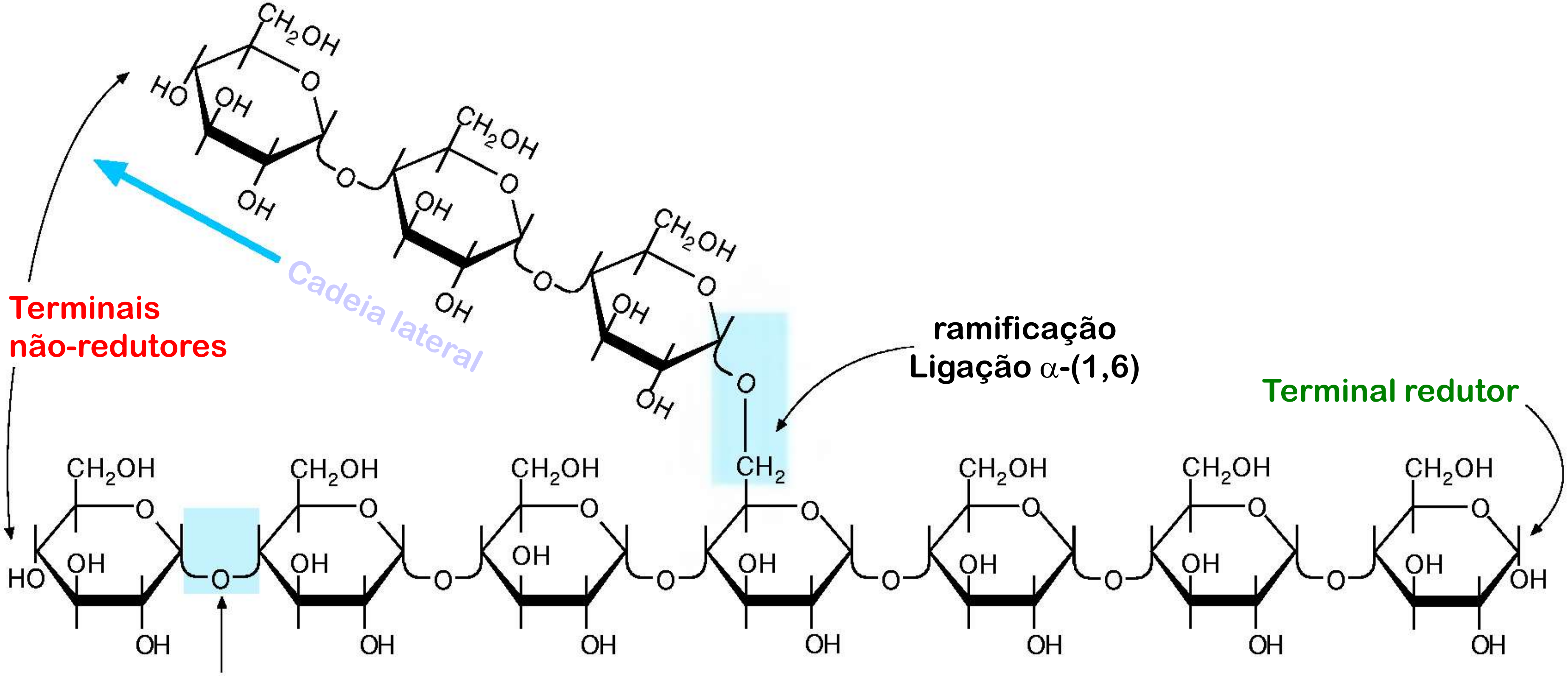
Ramificações das cadeias de glicogênio e amido



Terminais
não-redutores

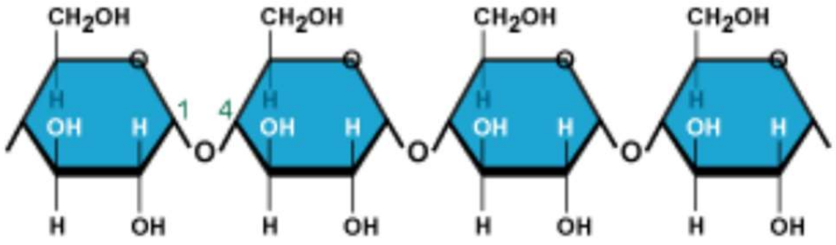
Cadeia lateral

ramificação
Ligação α-(1,6)

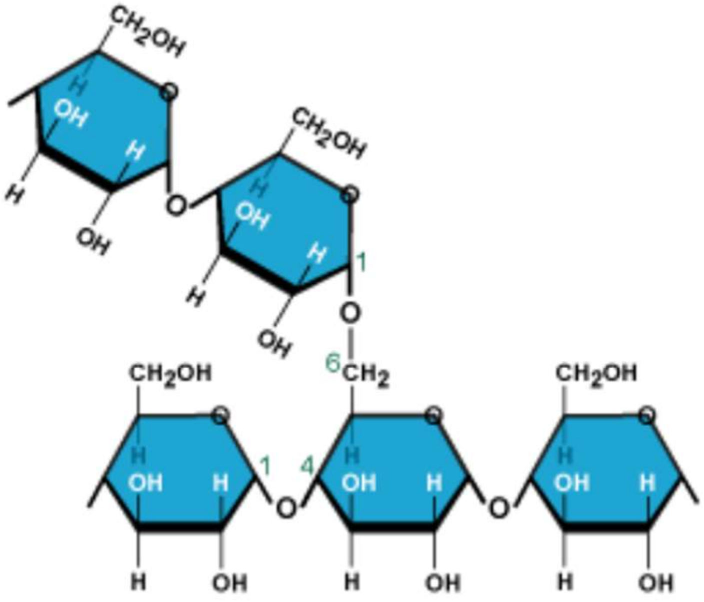
Terminal redutor

Ligação α-(1,4)

α-glucose subunits

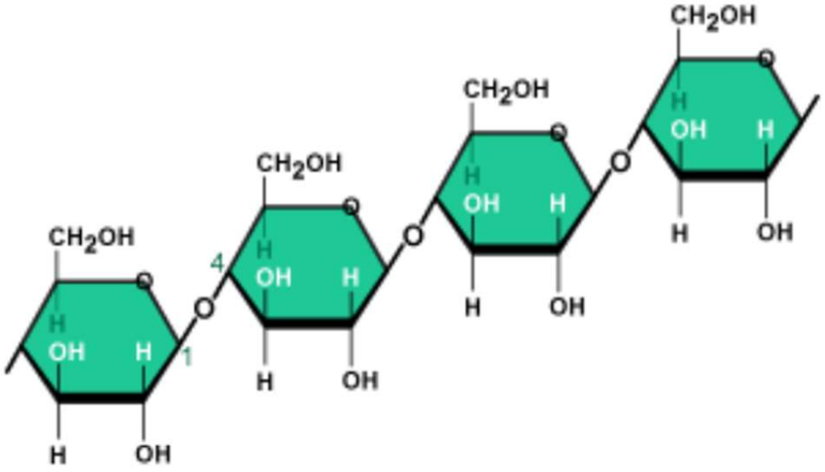

CH₂OH
CH₂OH
CH₂OH
CH₂OH
O
O
O
O
H
OH
H
1
4
H
OH
H
H
OH
H
H
OH
H
O
O
O
H
OH
H
OH
H
OH
H
OH

Starch: Chain of α-glucose subunits


CH₂OH
H
OH
H
O
H
OH
O
CH₂OH
H
OH
H
O
1
H
OH
O
6
CH₂
CH₂OH
CH₂OH
O
O
O
H
OH
H
1
4
H
OH
H
H
OH
H
O
O
H
OH
H
OH
H
OH

Glycogen: Branched chain of α-glucose subunits

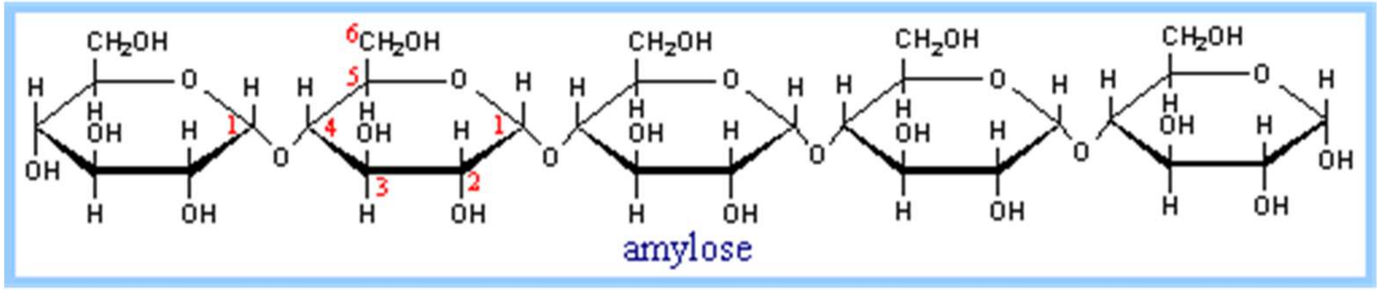
β-glucose subunits


CH₂OH
CH₂OH
CH₂OH
CH₂OH
O
O
O
O
H
OH
H
1
O
4
H
OH
H
O
H
OH
H
O
H
OH
H
H
OH
H
OH
H
OH
H
OH

Cellulose: Chain of β-glucose subunits

Dept. Biol. Penn State ©2002

α-Amilose


CH₂OH
⁶CH₂OH
O
H
OH
1
2
3
4
5
amylose

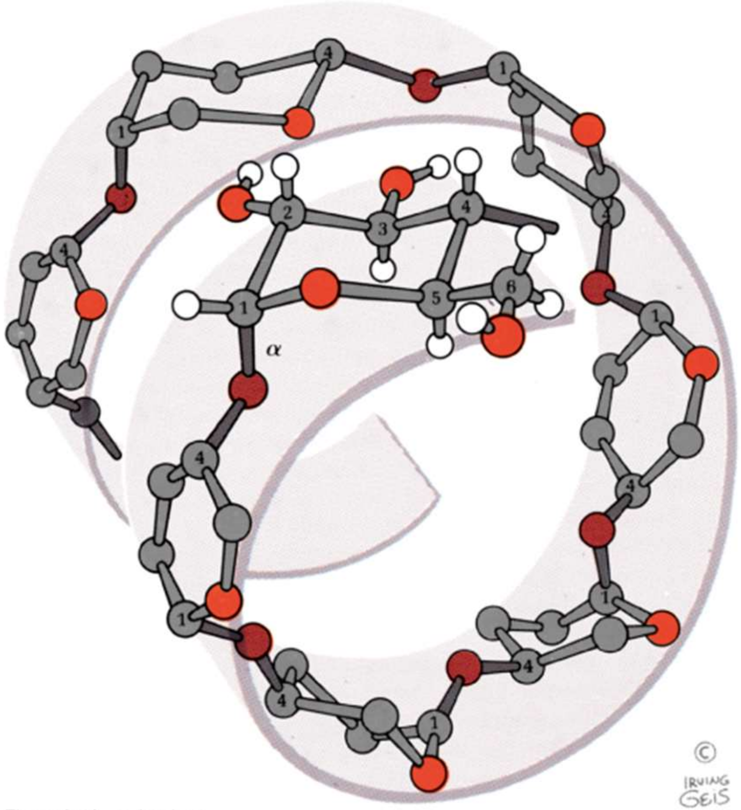

1
2
3
4
5
6
α
©
IRVING GEIS

Figure 8-10. α-Amylose.
[Figure copyrighted © by Irving Geis.]

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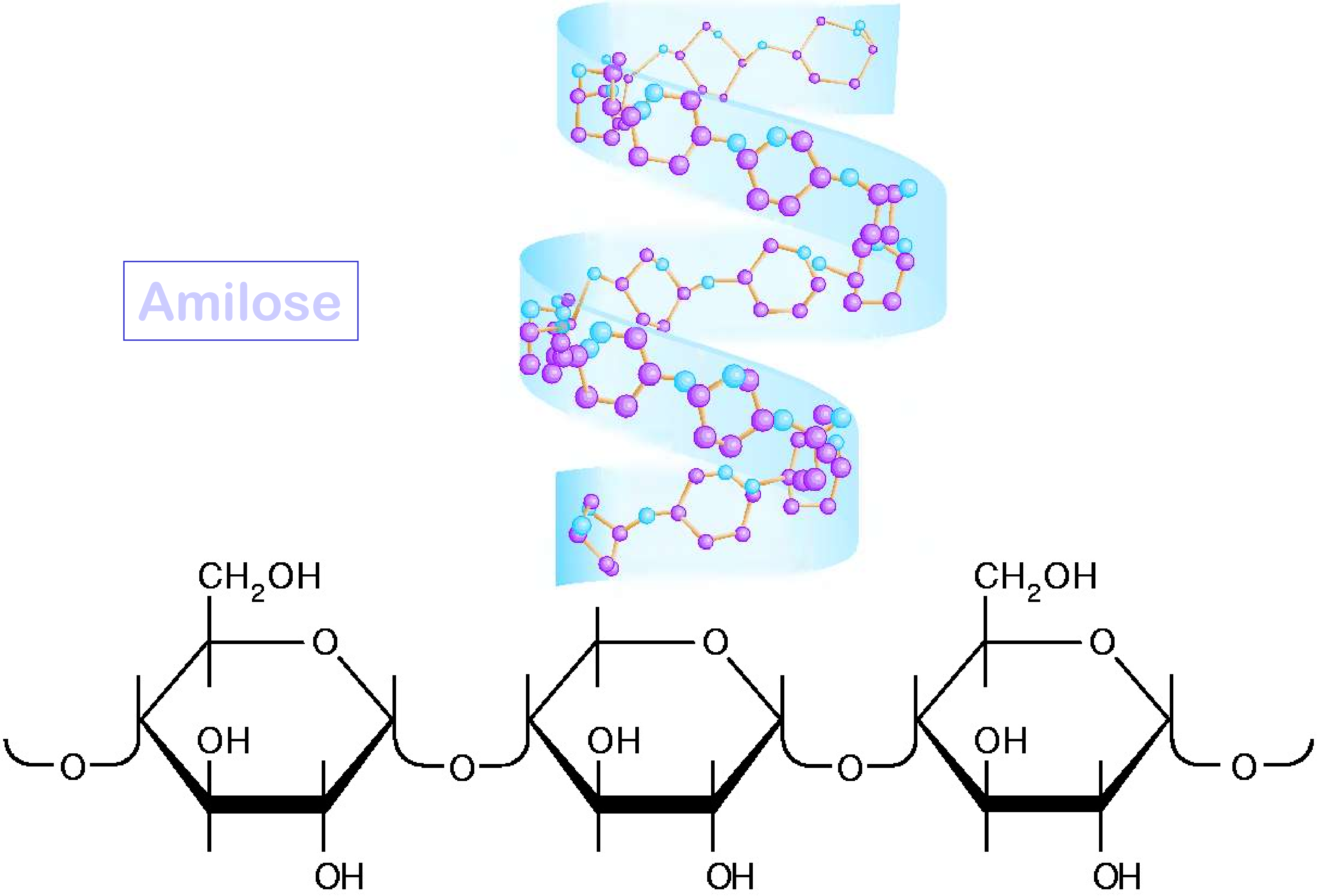
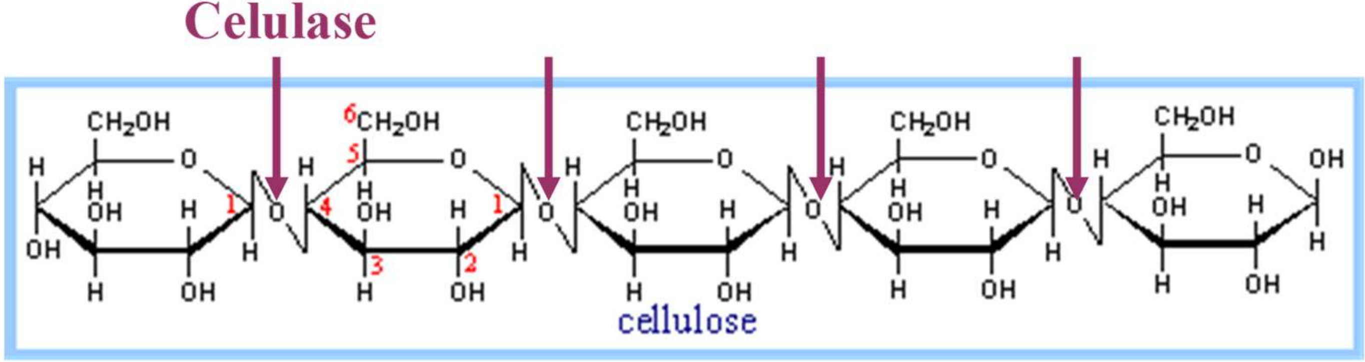
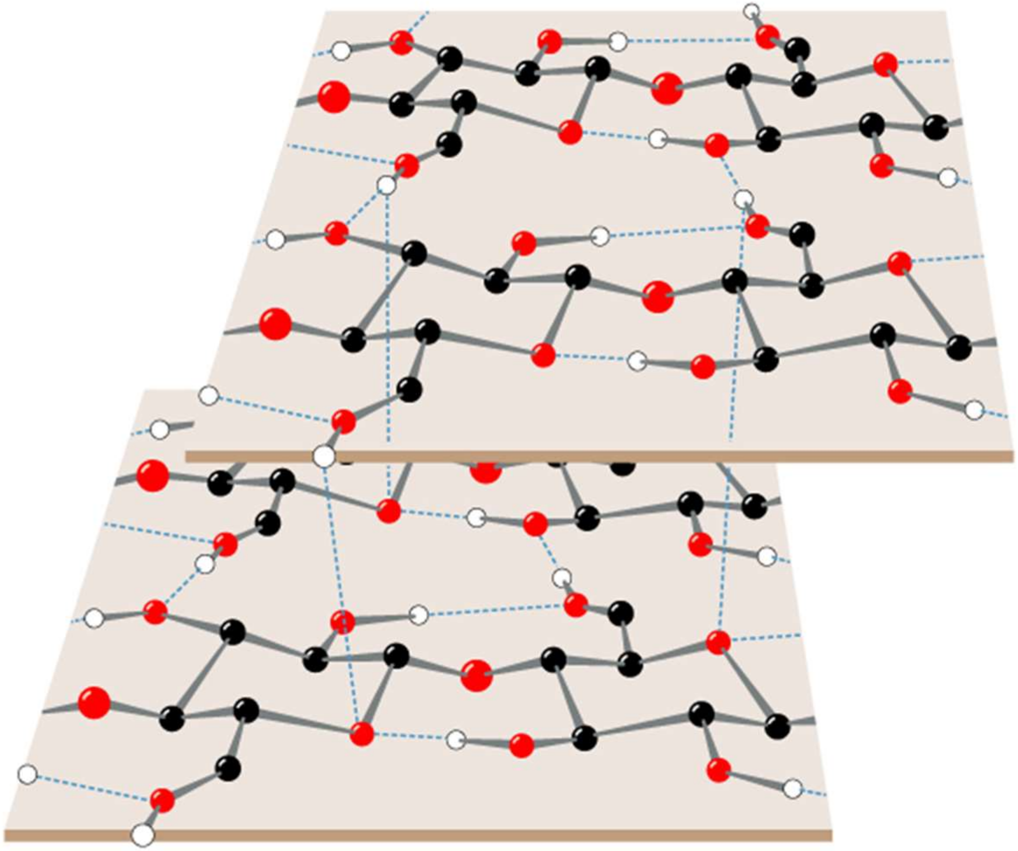
Amilose



CH$_2$OH
O
OH
OH
O
CH$_2$OH
O
OH
OH
O
CH$_2$OH
O
OH
OH
O
O

Celulose (poli-glicose)


Celulase
CH₂OH
O
H
OH
1
2
3
4
5
6
cellulose



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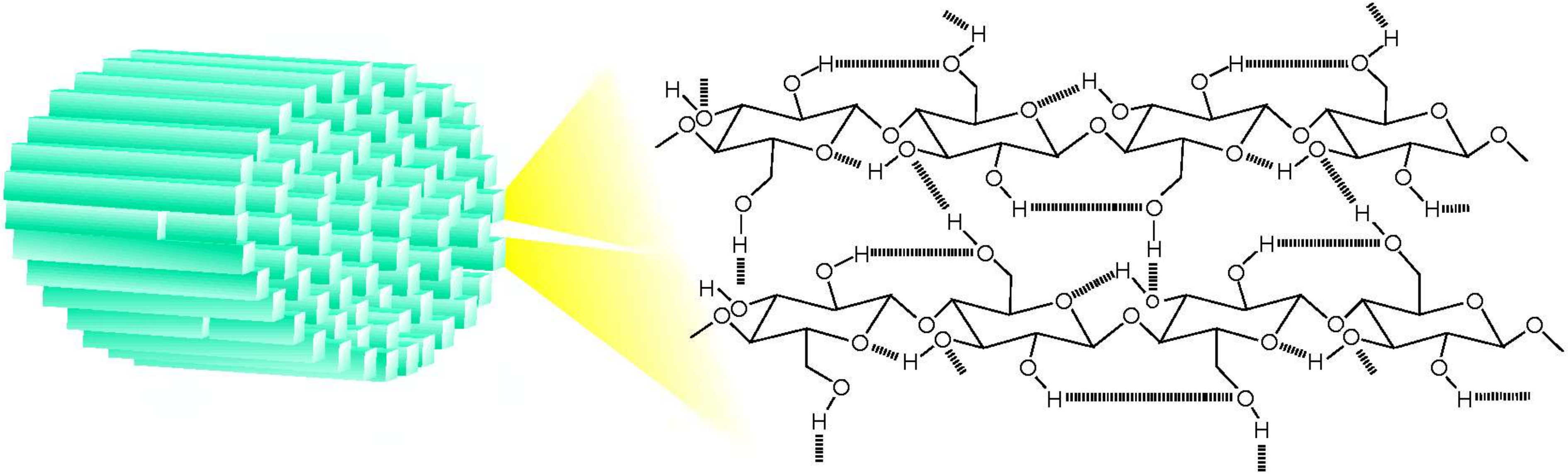
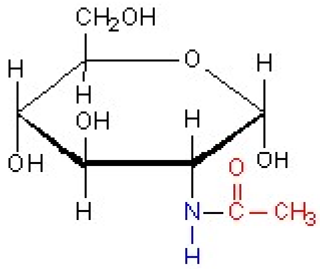
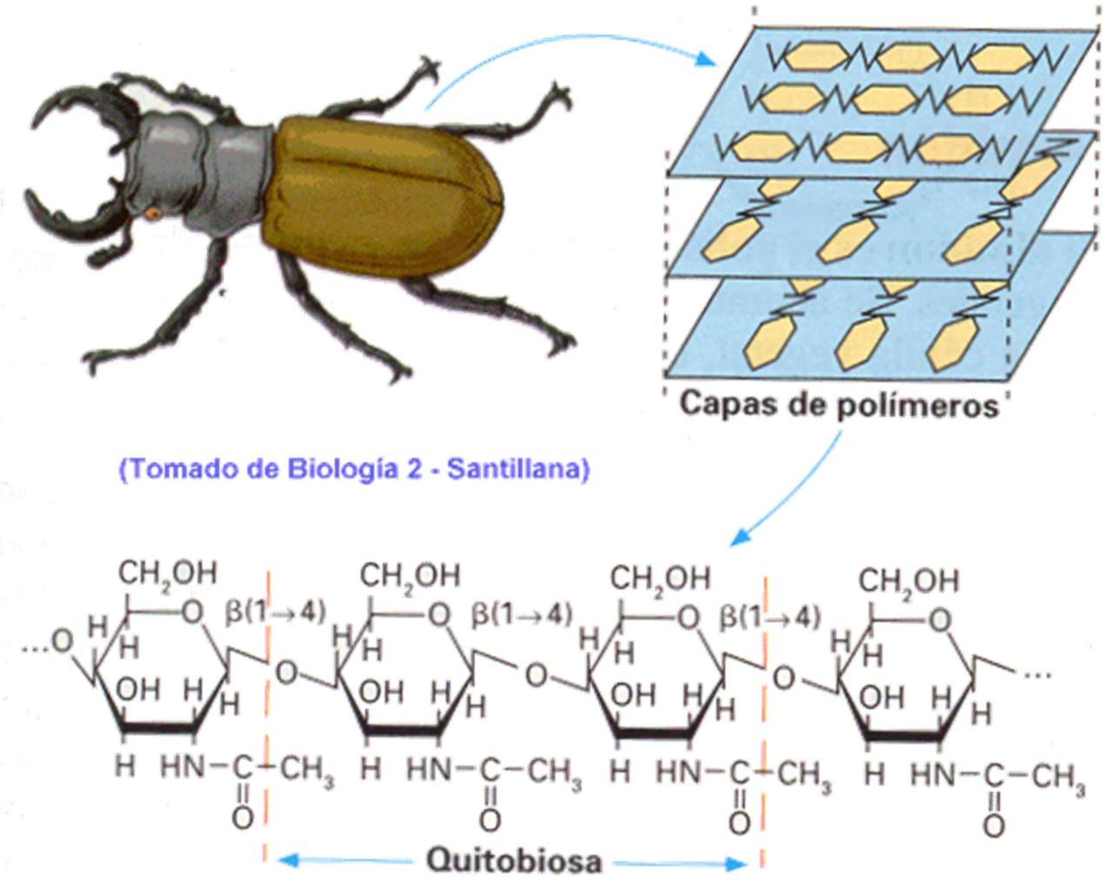
Celulose (função estrutural) →
Estabilizada por pontes de hidrogênio



N-Acetil-D-Glicosamina (polímero em β)

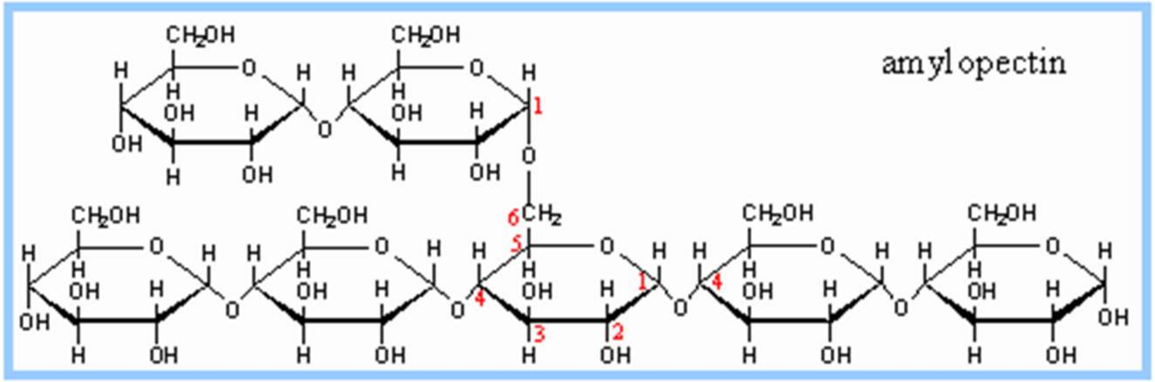

CH2OH
O
H
H
OH
H
OH
OH
H
O
N–C–CH3
H

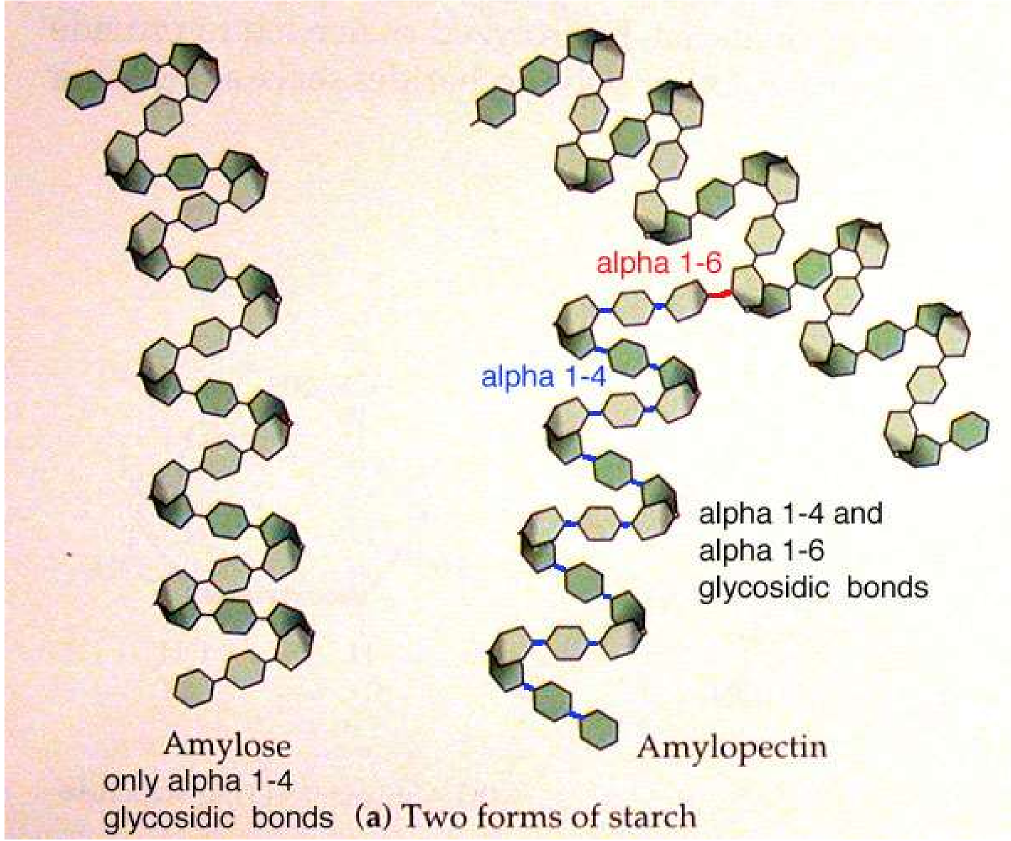
Quitina: insetos, caranguejos, lagosta, camarão


Capas de polímeros
CH2OH
β(1→4)
O
OH
H
HN–C–CH3
Quitobiosa

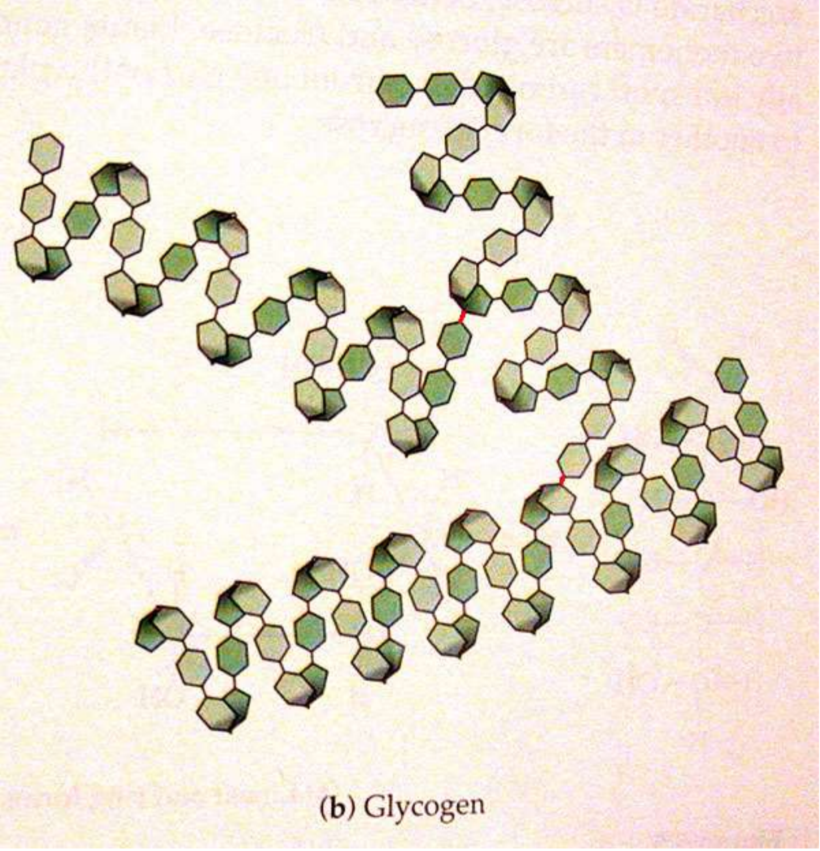
(Tomado de Biología 2 - Santillana)

Amilopectina e Glicogênio


amylopectin
1
6
5
4
3
2
1
4

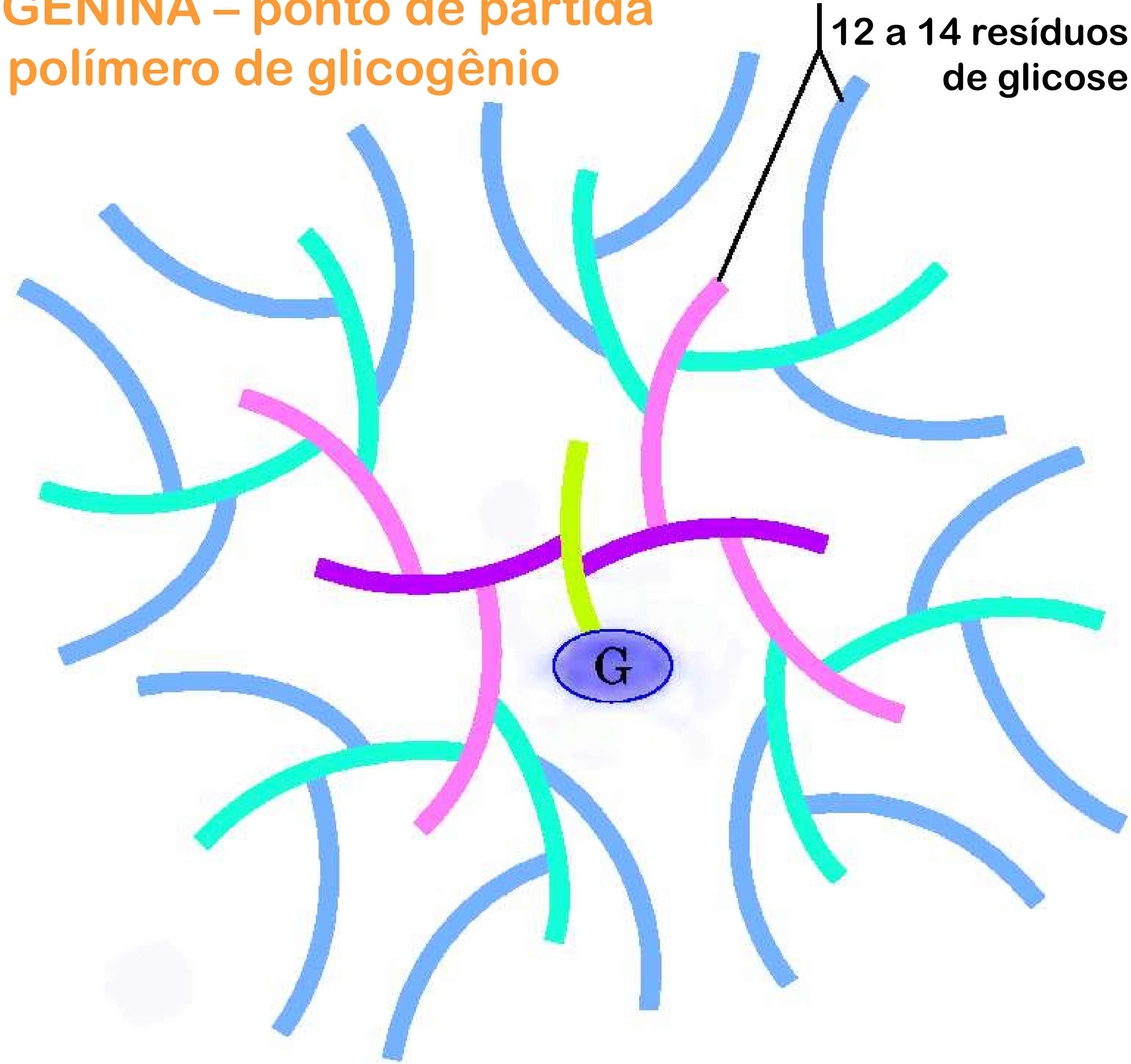

alpha 1-6
alpha 1-4
alpha 1-4 and
alpha 1-6
glycosidic bonds
Amylose
only alpha 1-4
glycosidic bonds
Amylopectin

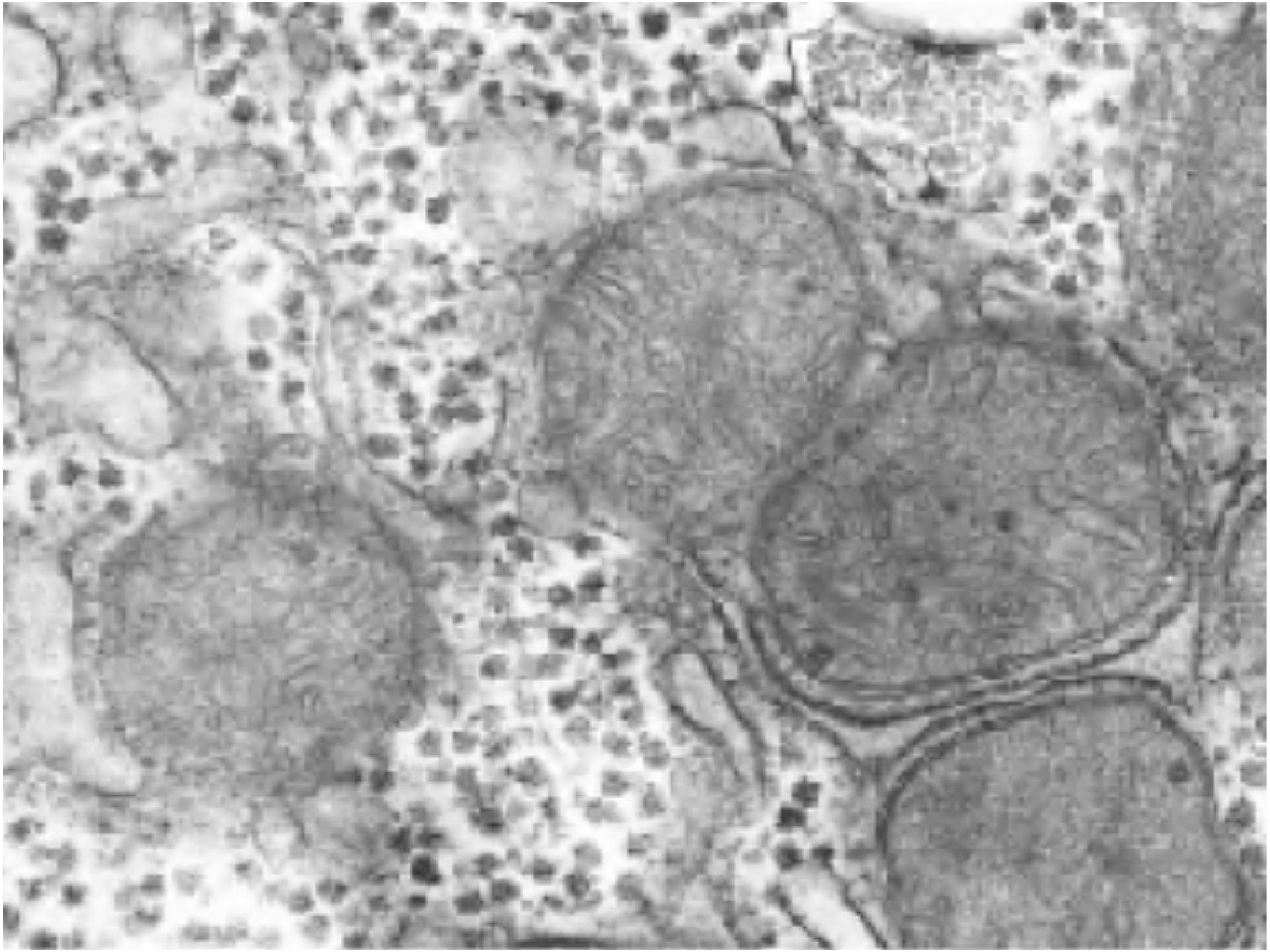
(a) Two forms of starch



(b) Glycogen

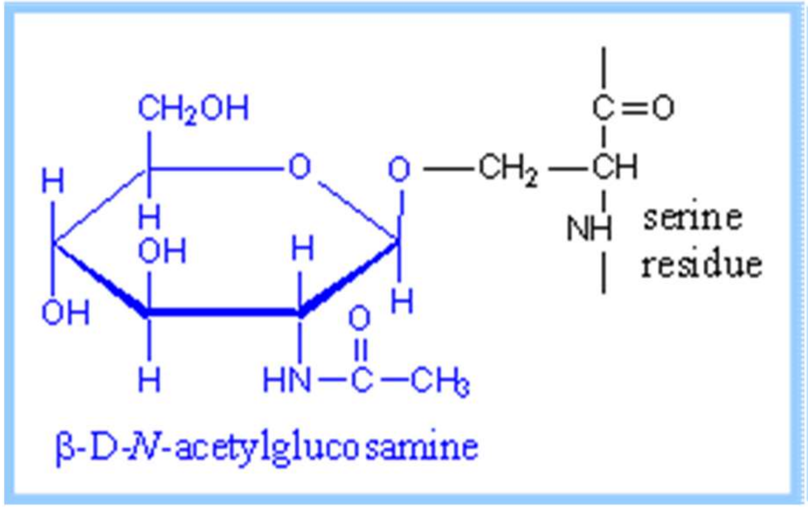
GLICOGENINA – ponto de partida do polímero de glicogênio


12 a 14 resíduos
de glicose
G

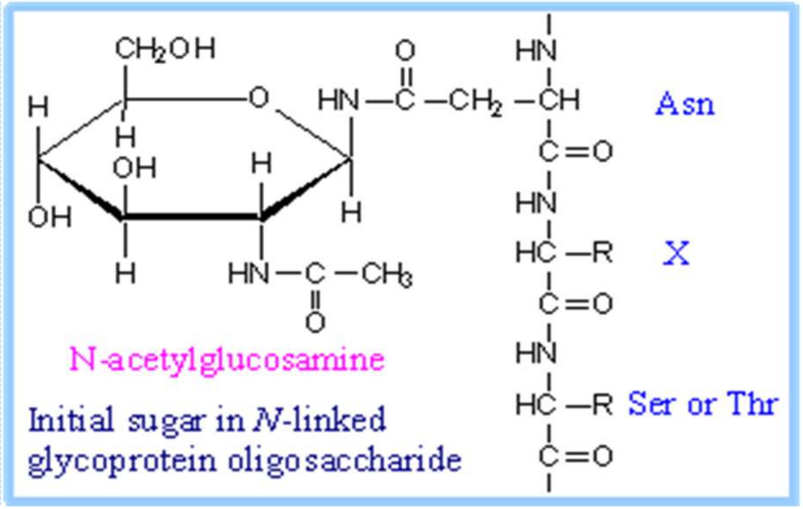


GLICOPROTEÍNAS

Glicoproteínas

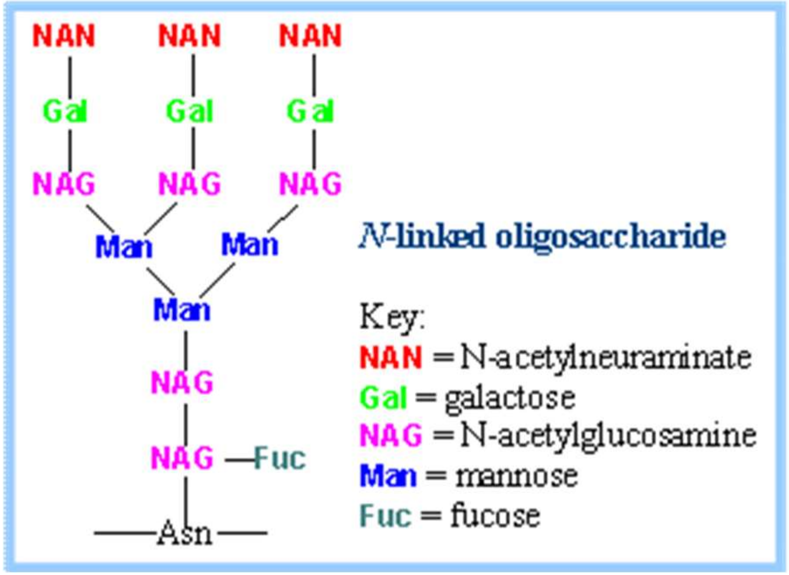

CH2OH
O
H
H
OH
H
OH
H
HN—C—CH3
O
H
O—CH2—CH
C=O
NH
serine
residue

β-D-*N*-acetylglucosamine


CH2OH
O
H
H
OH
H
OH
H
H
HN—C—CH3
O
HN—C—CH2—CH
O
HN
Asn
C=O
HN
HC—R
X
C=O
HN
HC—R
Ser or Thr
C=O

N-acetylglucosamine

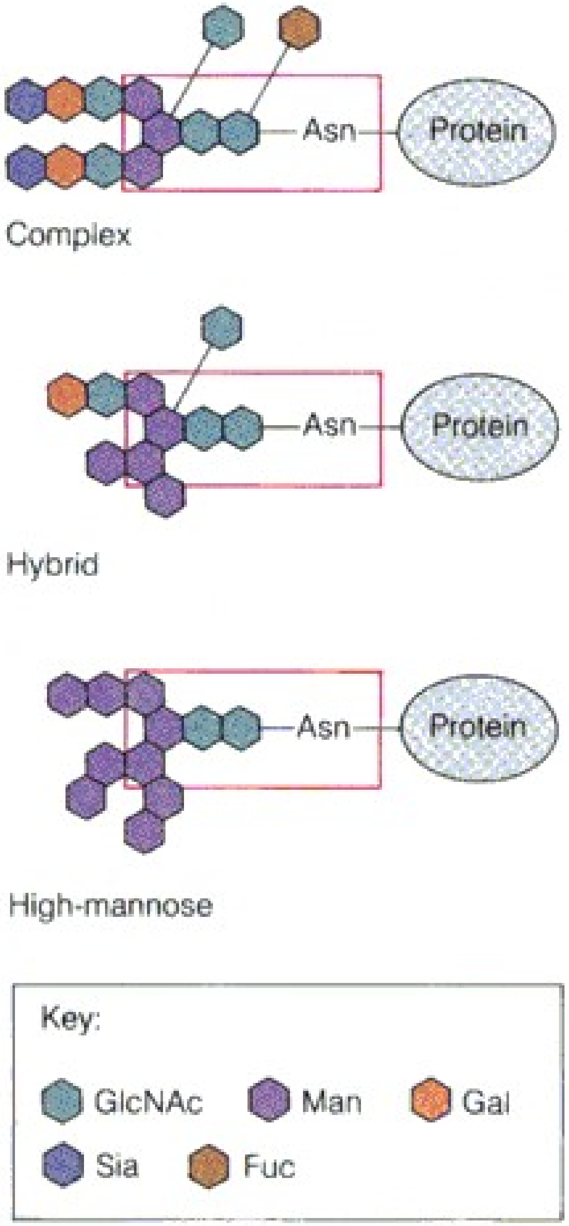
Initial sugar in *N*-linked glycoprotein oligosaccharide


NAN
NAN
NAN
Gal
Gal
Gal
NAG
NAG
NAG
Man
Man
Man
NAG
NAG
Fuc
Asn

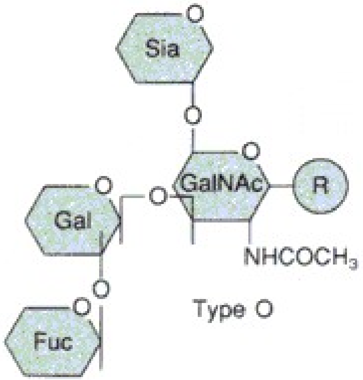
N-linked oligosaccharide

Key:
NAN = N-acetylneuraminate
Gal = galactose
NAG = N-acetylglucosamine
Man = mannose
Fuc = fucose

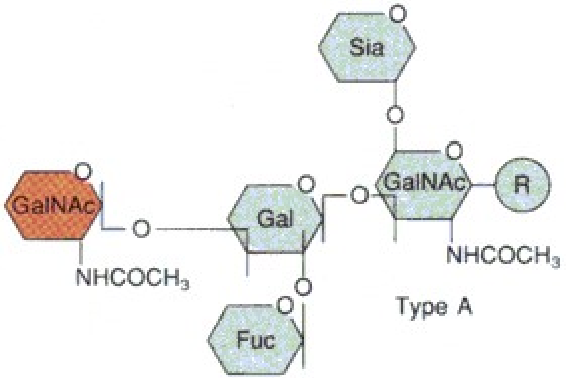
Estruturas dos oligossacarídeos ligados a Asparagina


Asn
Protein
Complex
Asn
Protein
Hybrid
Asn
Protein
High-mannose
Key:
GlcNAc
Man
Gal
Sia
Fuc

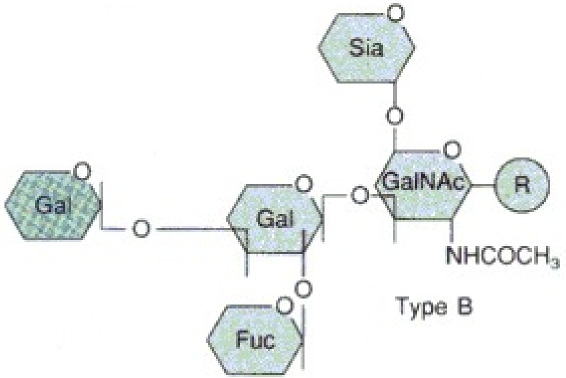
Antígenos dos Grupos Sanguineos ABO


Sia
GalNAc
R
Gal
NHCOCH₃
Fuc

Type O


Sia
GalNAc
R
GalNAc
Gal
NHCOCH₃
NHCOCH₃
Fuc

Type A


Sia
GalNAc
R
Gal
Gal
NHCOCH₃
Fuc

Type B

ENZIMAS QUE LIBERAM OLIGOSSACARÍDEOS DE GLICOPROTEÍNAS

R→GlcNAcβ(1→4)GlcNAc→Asn-Peptídeo

↓ Endo-β-N-glucosaminidases

R→GlcNAc + GlcNAc→Asn-Peptídeo

ENDO D
ENDO H
ENDO CII
ENDO F

ENDO GLUCOSAMINIDASE D

R precisa ser: Manα(1$\rightarrow$3)Manβ(1$\rightarrow$4)GlcNAc

Parte mais importante: resíduo α-manosil do trissacarídeo
Substituição da manose em C4 não inibe a enzima
Substituição da manose em C2 inibe a enzima
Fucα(1$\rightarrow$6)GlcNAc não inibe a enzima
Fucα(1$\rightarrow$6)GlcNAc-peptídeo não inibe a enzima

ENDO GLUCOSAMINIDASE H

R precisa ser: Manα(1$\rightarrow$3)Manα(1$\rightarrow$6)Manβ(1$\rightarrow$4)GlcNAc

- **Parte mais importante: resíduo α-manosil do tetrassacarídeo**
- **Substituição da manose em C2 não inibe a enzima**
- **Fucα(1$\rightarrow$6)GlcNAc não inibe a enzima**
- **Fucα(1$\rightarrow$6)GlcNAc-peptídeo não inibe a enzima**
- **Hidrolisa todas as cadeias "high-mannose" e muitas cadeias híbridas**
- **Não hidrolisa as cadeias complexas porque elas não tem as duas manoses da ponta não redutora**

ENDOGLUCOSAMINIDASE CII

R precisa ser: Manα(1$\rightarrow$3)Manα(1$\rightarrow$6) [Manα(1$\rightarrow$3)] Manβ(1$\rightarrow$4)GlcNAc

Requer pentassacarídeo ramificado

ENDOGLUCOSAMINIDASE F

Mesma especificidade da ENDO H, atuando em cadeias biantenárias, mas não em triantenárias ou tetraantenárias

ENZIMAS QUE LIBERAM OLIGOSSACARÍDEOS DE GLICOPROTEÍNAS

R→GlcNAcβ(1→4)GlcNAc→Asn-Peptídeo

↓

N-glicanase
Glicopeptidase
Peptídeo-N4-(N-acetilβglicosaminil) asparagina amidase

R→GlcNAcβ(1→4)GlcNAc + Asn-Peptídeo

Age com maior velocidade quando o oligassacarídeo está no aa 3 - 40
Não age quando oligossacarídeo está no aa aminoterminal ou carboxiterminal

ENZIMAS QUE LIBERAM OLIGOSSACARÍDEOS DE GLICOPROTEÍNAS

Galβ(1→3)GalNAcα1→Ser/Thr-Peptídeo

↓ O-glicanase
Endo-α-N-acetilgalactosaminidase

Galβ(1→3)GalNAcα1 + Ser/Thr-Peptídeo

Galβ pode estar sialilada em α2→3

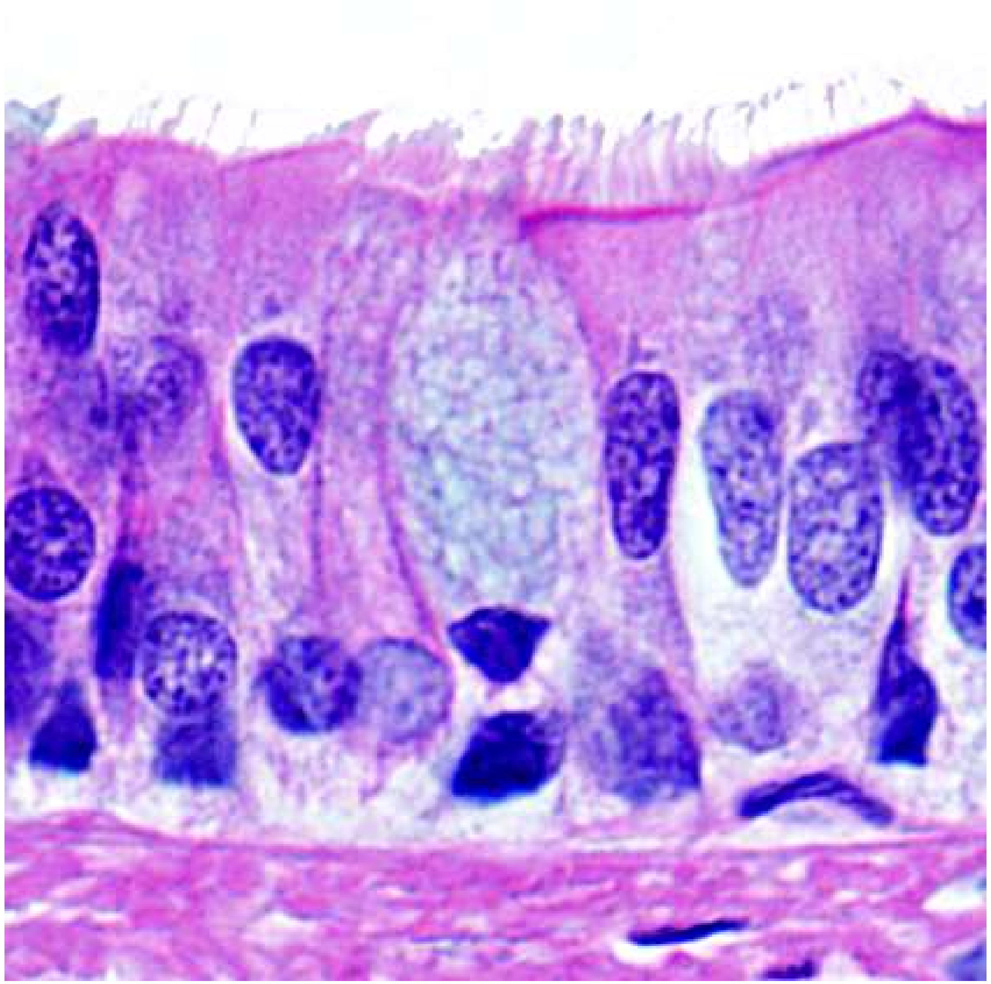
Por isso sempre se trata com neuraminidase antes da O-glicanase

MUCINAS HUMANAS

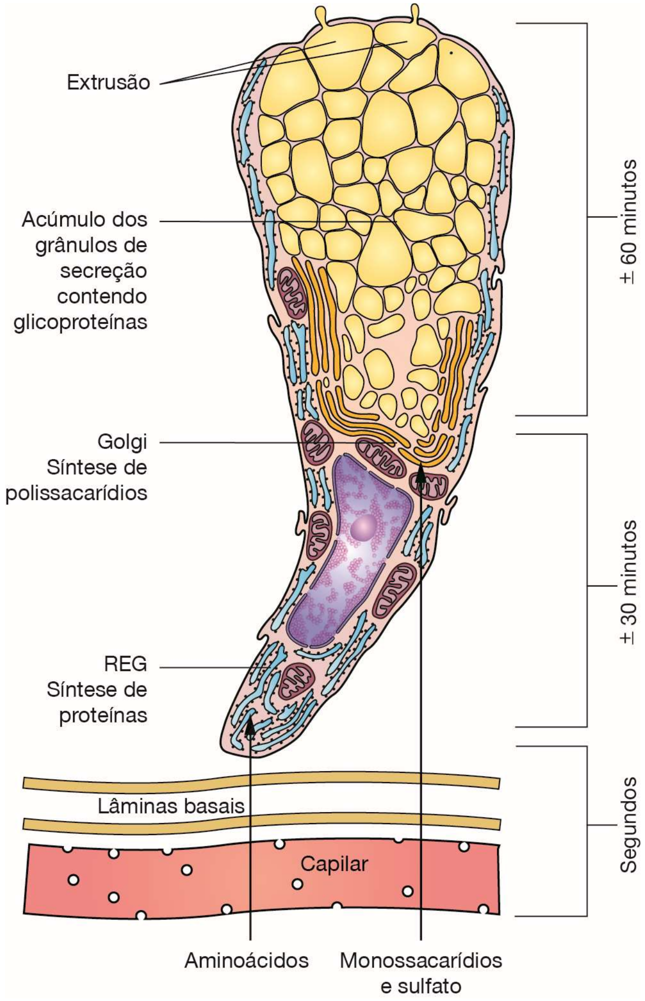
CODIFICADAS POR 22 GENES
MUC 1 A MUC 22

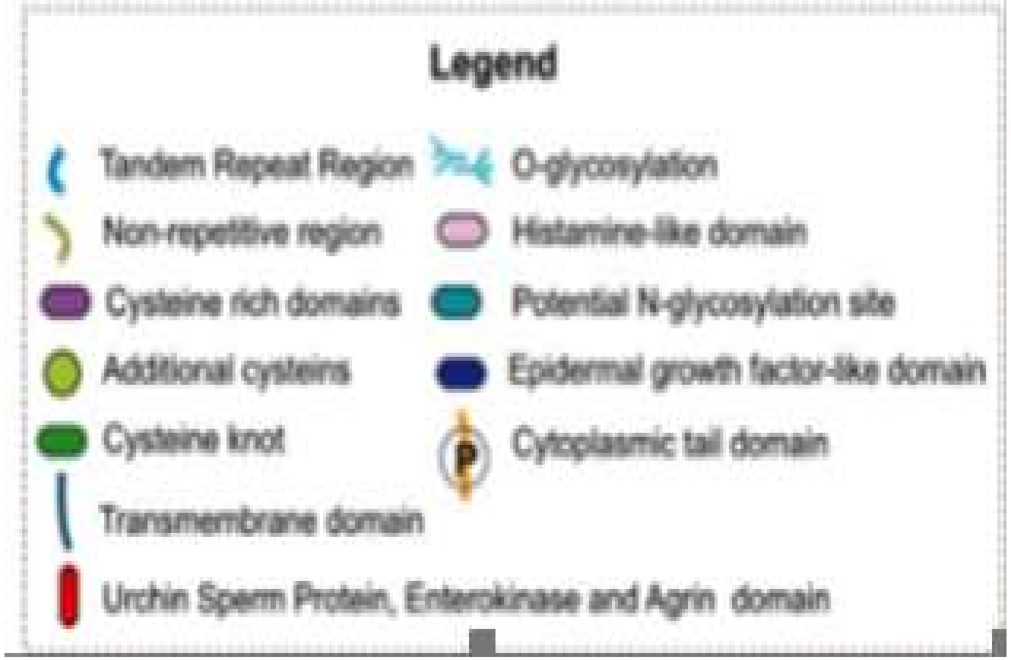
1-TRANSMEMBRÂNICAS
2-SOLÚVEIS FORMADORAS DE GEL
3-SOLÚVEIS QUE NÃO FORMAM GEL

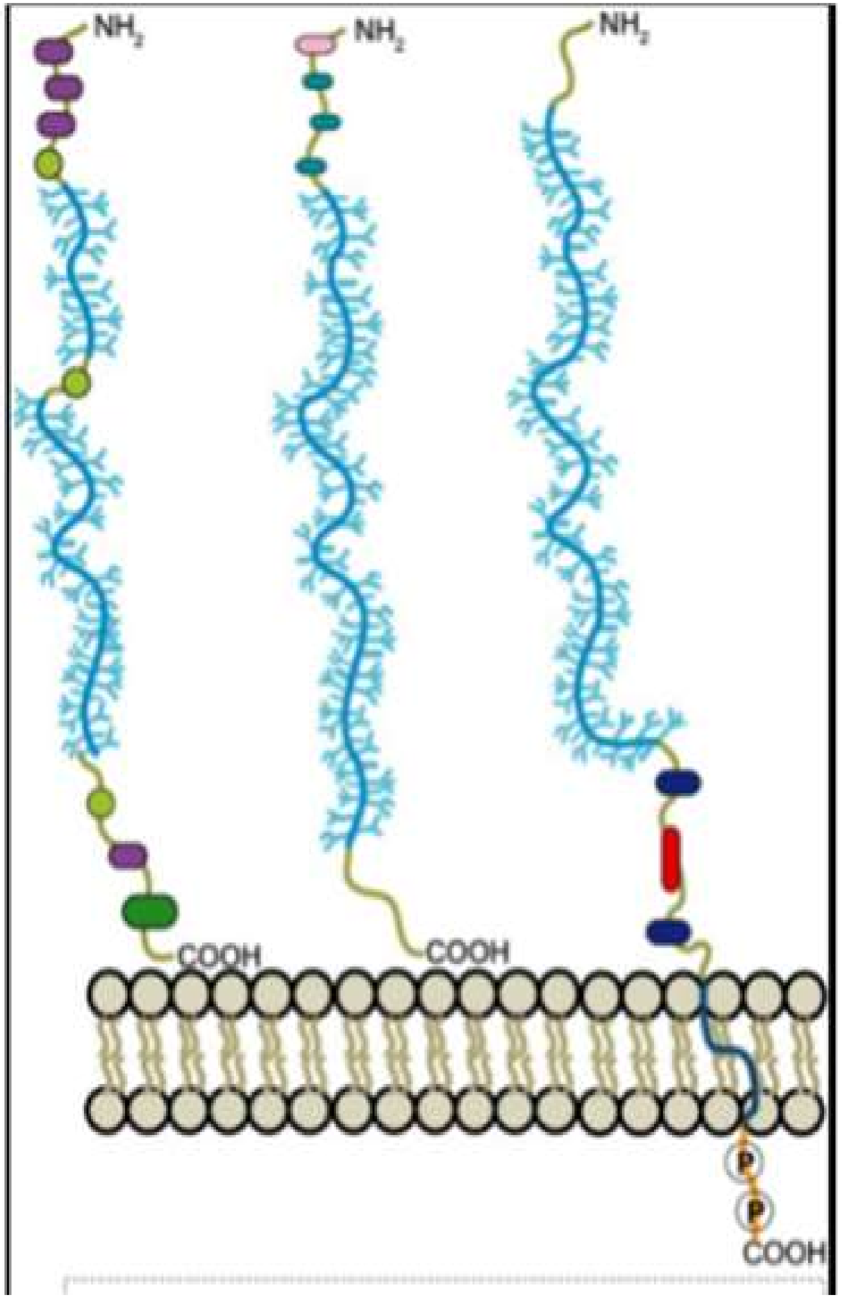
Células Caliciformes/Goblet Cells



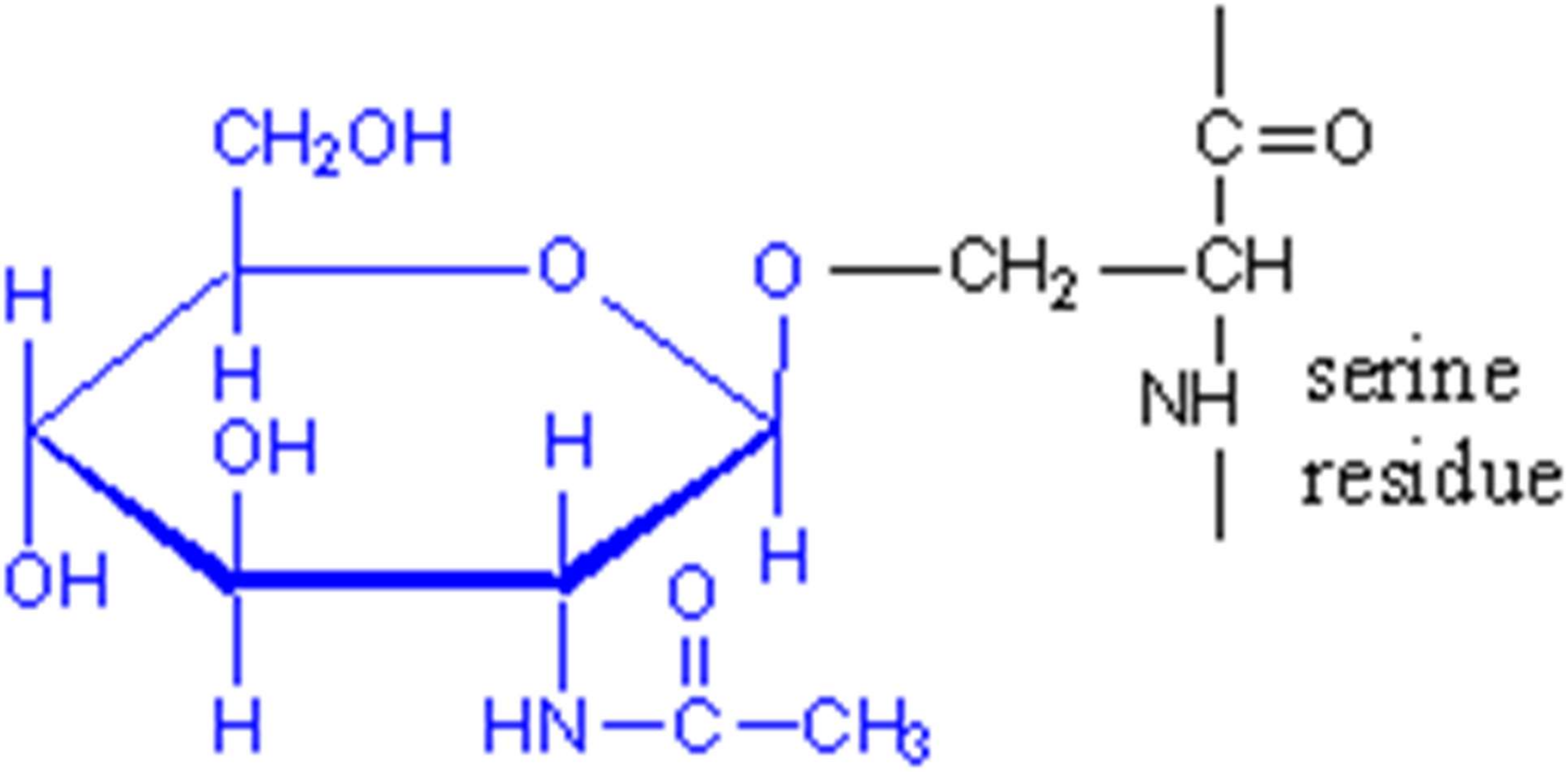
Epitélio de Traqueia


Extrusão
Acúmulo dos grânulos de secreção contendo glicoproteínas
Golgi Síntese de polissacarídios
REG Síntese de proteínas
Lâminas basais
Capilar
Aminoácidos
Monossacarídios e sulfato
± 60 minutos
± 30 minutos
Segundos

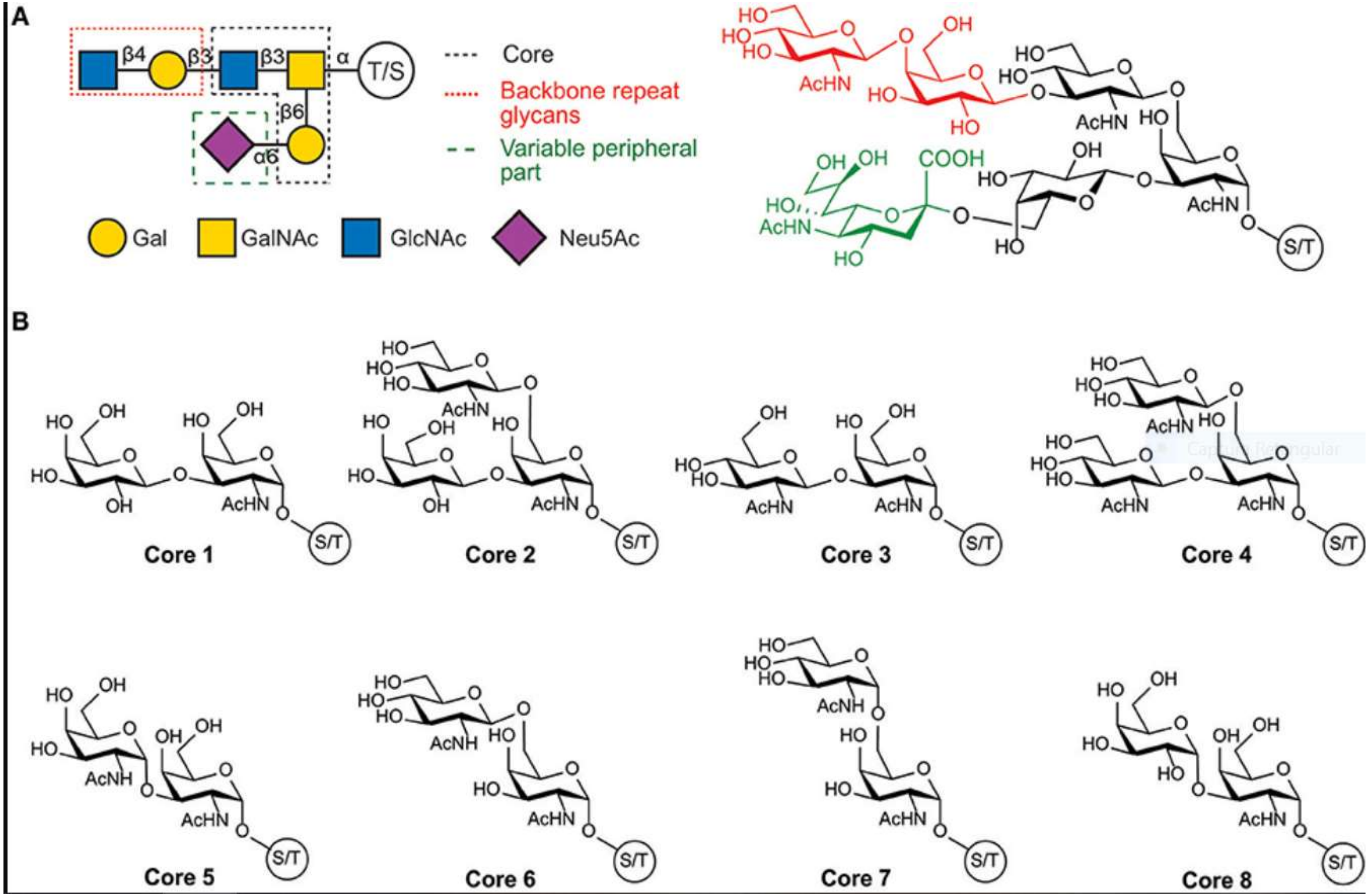

Legend
Tandem Repeat Region
O-glycosylation
Non-repetitive region
Histamine-like domain
Cysteine rich domains
Potential N-glycosylation site
Additional cysteins
Epidermal growth factor-like domain
Cysteine knot
Cytoplasmic tail domain
Transmembrane domain
Urchin Sperm Protein, Enterokinase and Agrin domain


NH2
NH2
NH2
COOH
COOH
P
P
COOH

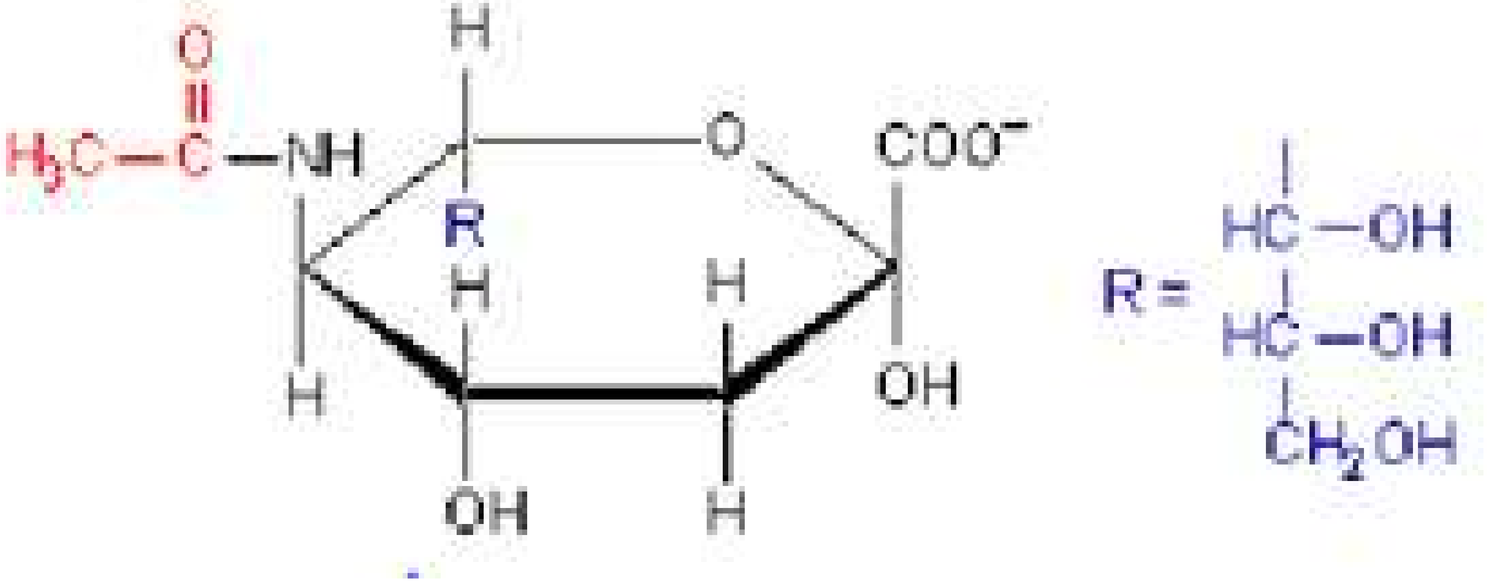
i.org/10.3389/fchem.2019.00710


CH2OH
O
H
H
OH
H
OH
H
H
O
HN
C
CH3
O
CH2
CH
C
O
NH
serine
residue

β-D-*N*-acetylglucosamine


A
β4
β3
β3
α
T/S
β6
α6
Core
Backbone repeat glycans
Variable peripheral part
Gal
GalNAc
GlcNAc
Neu5Ac
COOH
AcHN
S/T
B
Core 1
Core 2
Core 3
Core 4
Core 5
Core 6
Core 7
Core 8

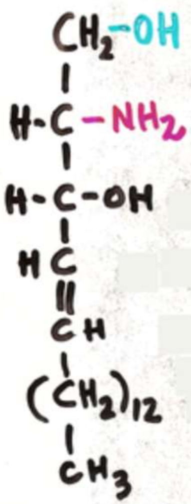
Estrutura das glicanas de mucinas humanas


H
O
H_3C—C—NH
O
COO⁻
R
H
H
H
OH
OH
H
R =
HC—OH
HC—OH
CH_2OH

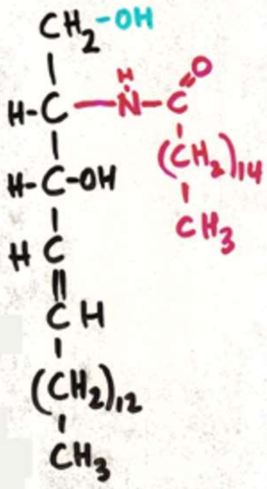
Ácido siálico

Ácido Acetil Neuramínico

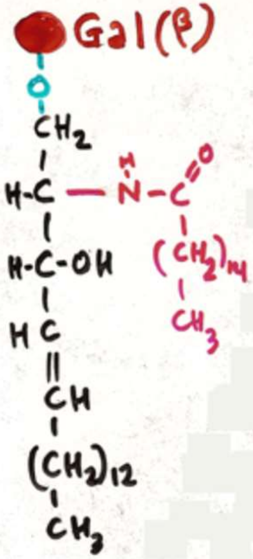
GLICOLIPÍDEOS



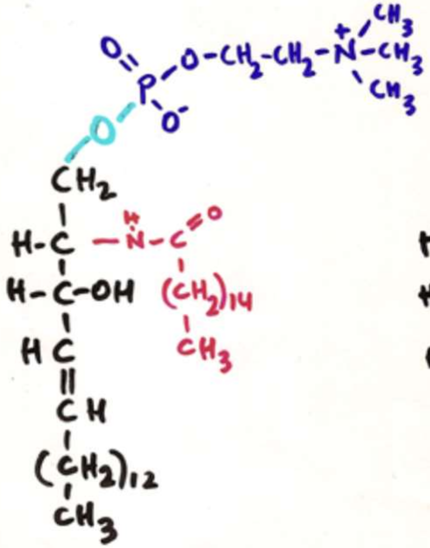
ESFINGOSINA



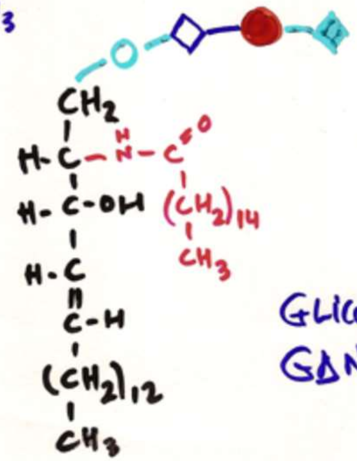
CERAMIDA



GLICOLIPÍDEO
GLICOCERAMIDA
CEREBROSÍDEO
GLICOESFINGOLIPÍDEO



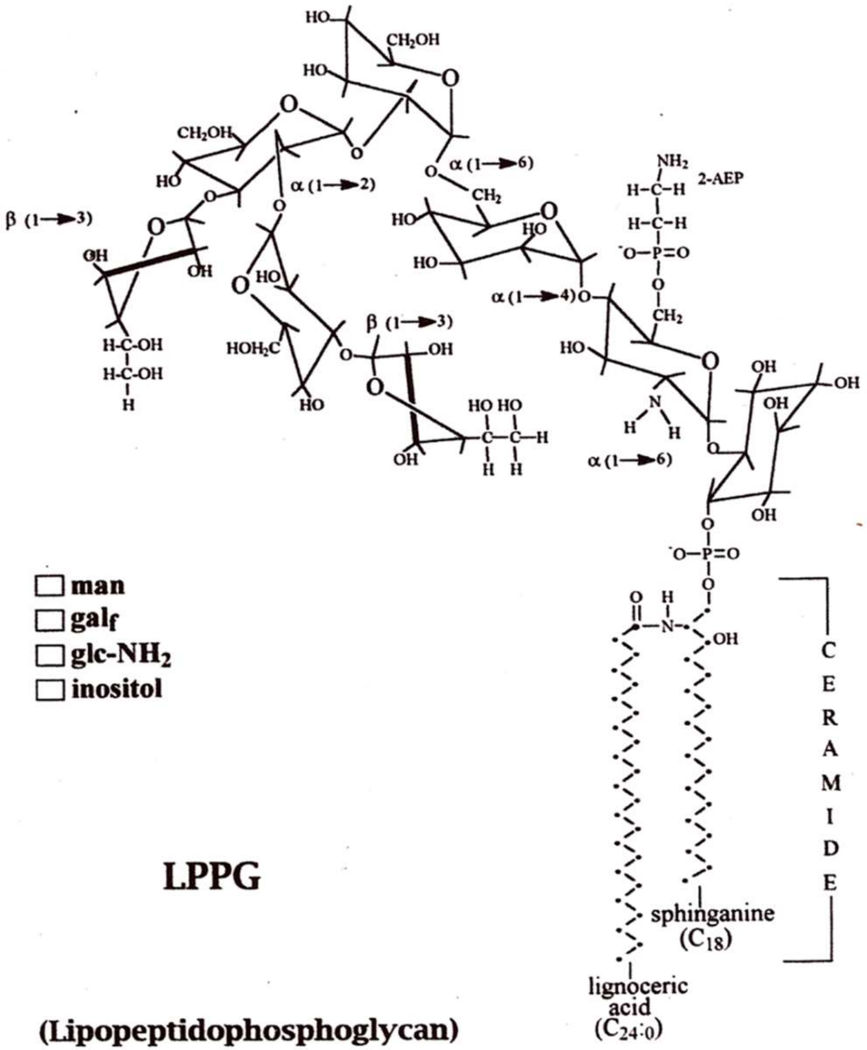
ESFINGOMIELINA



◇ Glc
● Gal
◆ Sia

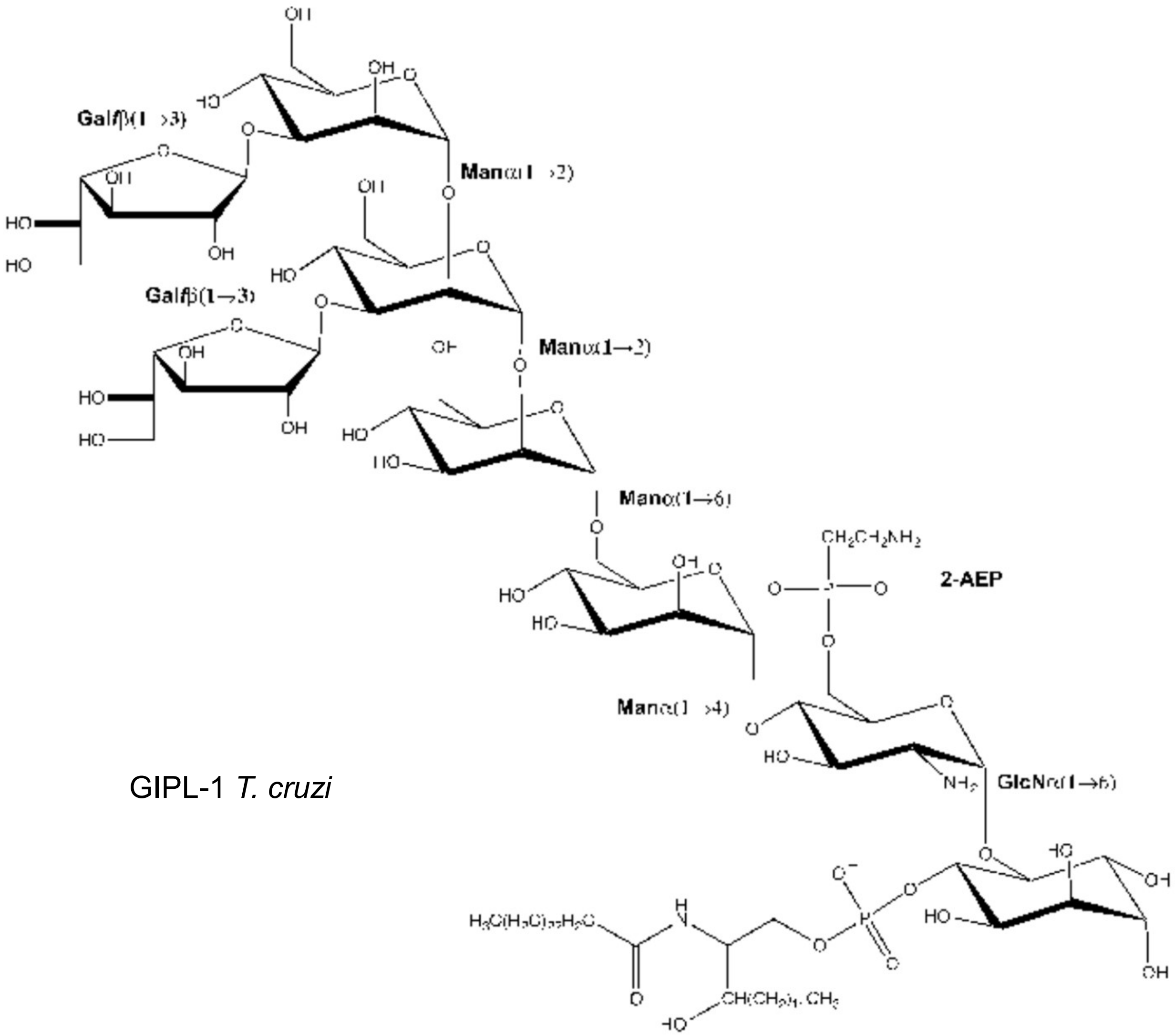
GLICOESFINGOLIPÍDEO
GANGLIOSÍDEO

Trypanosoma cruzi GIPL 1


α (1→2)
β (1→3)
α (1→6)
2-AEP
α (1→4)
β (1→3)
α (1→6)
CERAMIDE
sphinganine (C_{18})
lignoceric acid ($C_{24:0}$)
☐ man
☐ gal_f
☐ glc-NH_2
☐ inositol

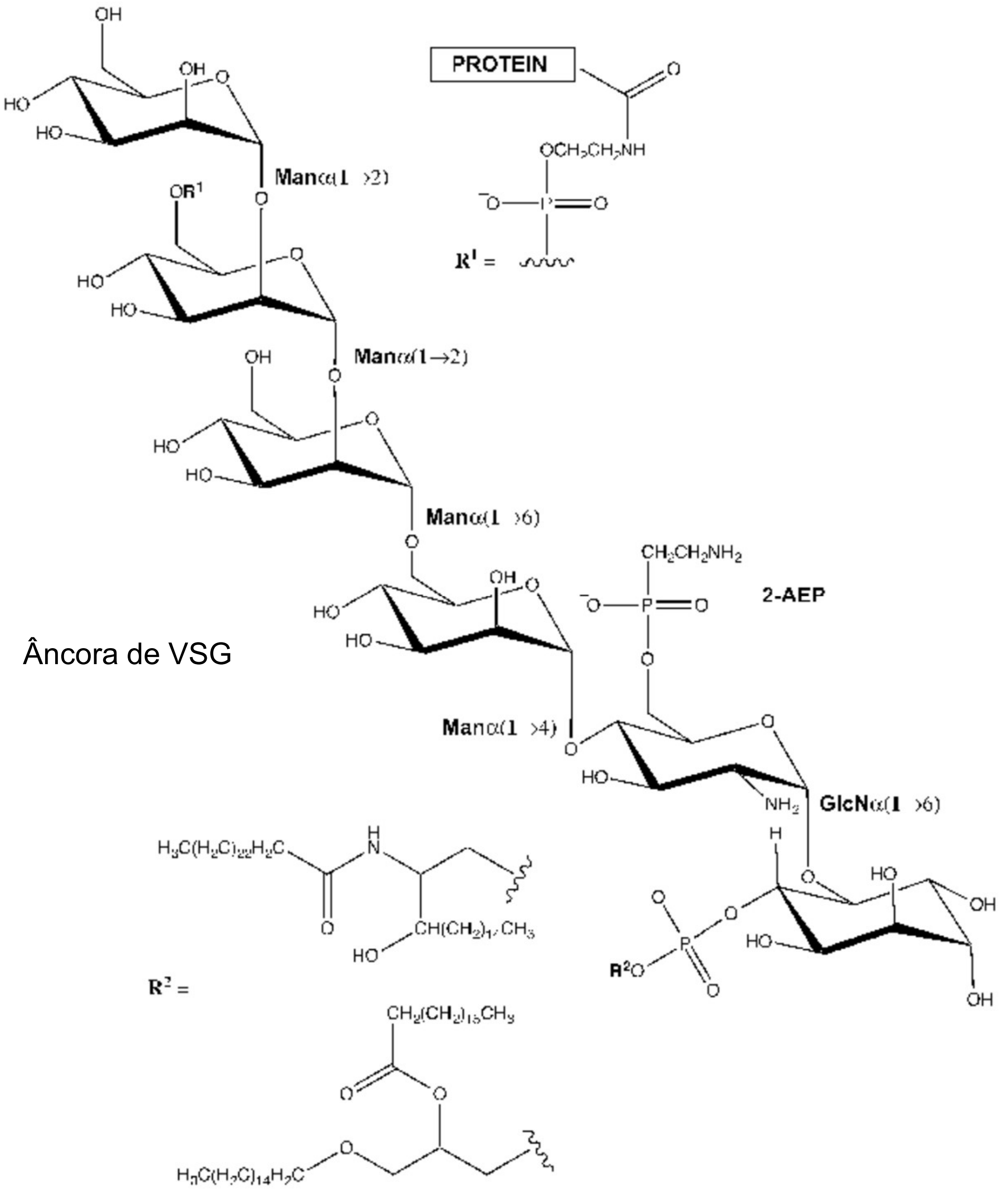
LPPG

(Lipopeptidophosphoglycan)

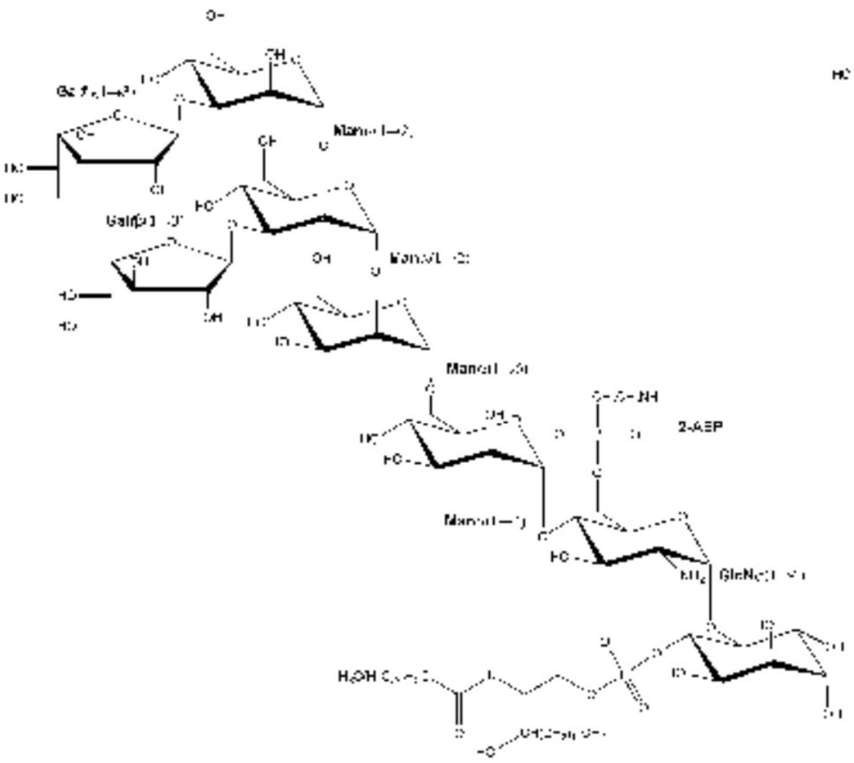

Galfβ(1→3)
Manα(1→2)
Galfβ(1→3)
Manα(1→2)
Manα(1→6)
Manα(1→4)
2-AEP
GlcNα(1→6)
CH2CH2NH2
NH2
H3C(H2C)22H2C
CH(CH2)14CH3

GIPL-1 *T. cruzi*

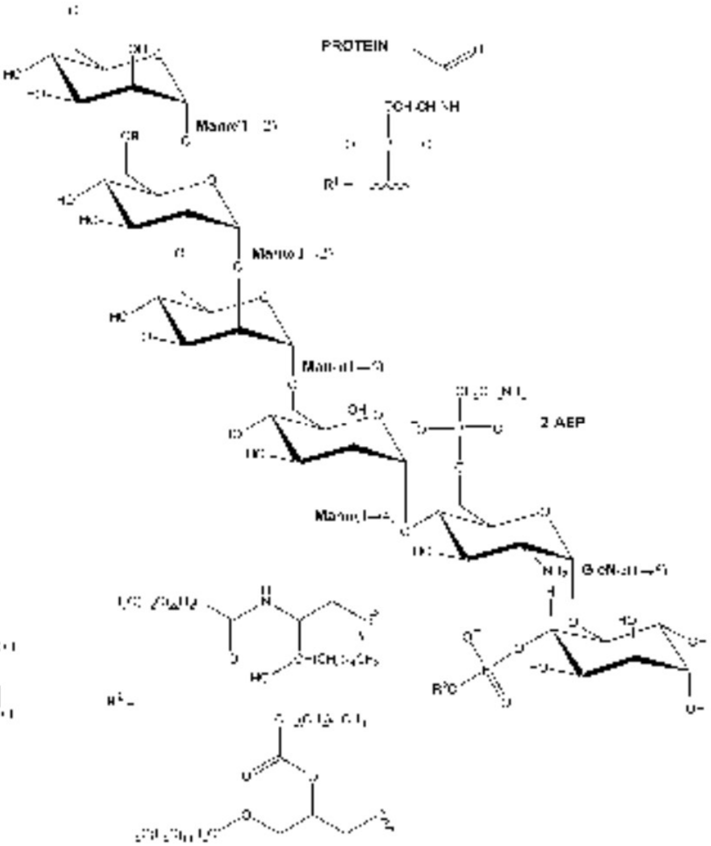
Âncora de VSG

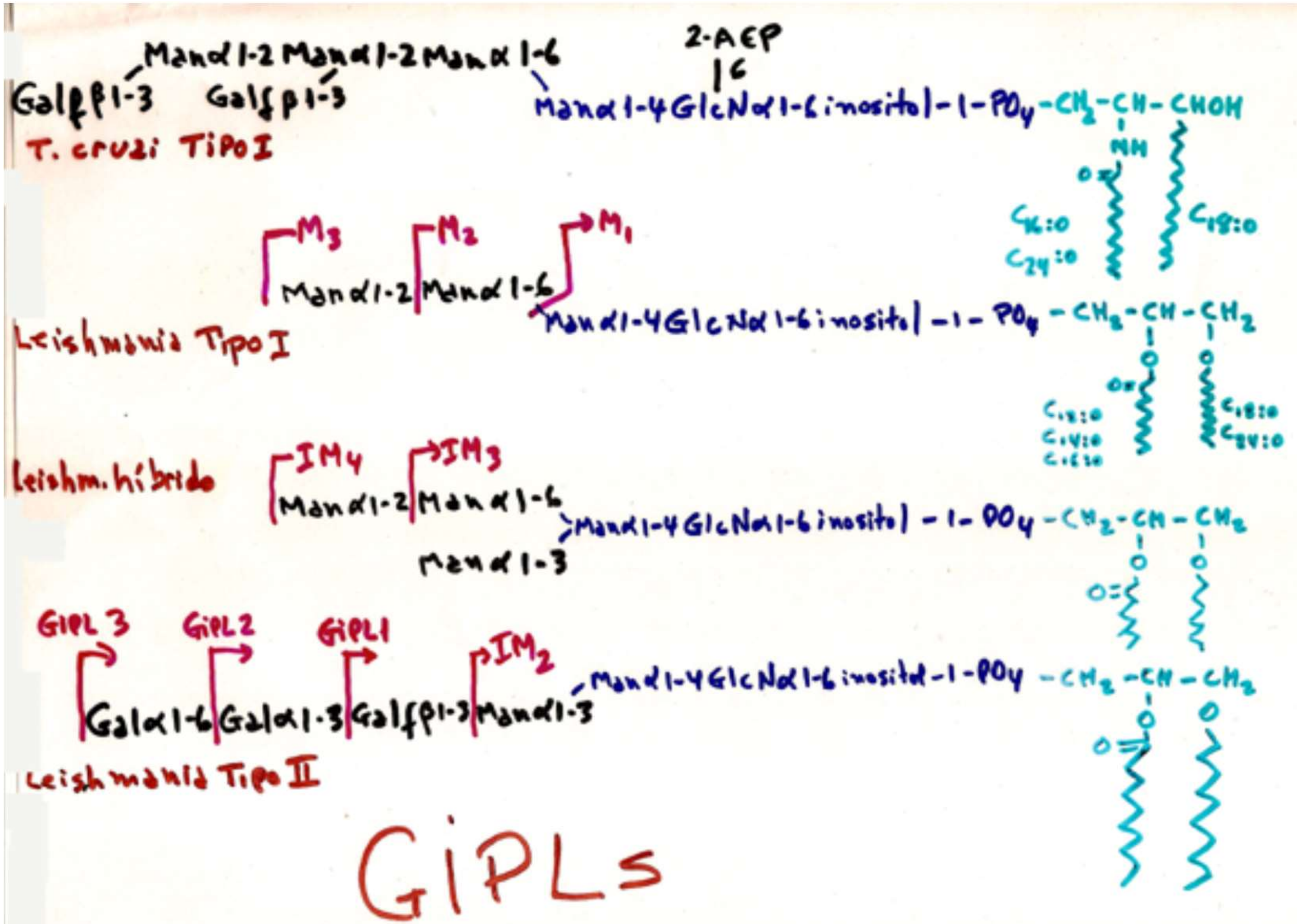

PROTEIN
OCH₂CH₂NH
R¹ =
Manα(1 >2)
OR¹
Manα(1→2)
Manα(1 >6)
CH₂CH₂NH₂
2-AEP
Manα(1 >4)
GlcNα(1 >6)
NH₂
R²O
R² =
H₃C(H₂C)₂₂H₂C
CH(CH₂)₁₇CH₃
CH₂(CH₂)₁₅CH₃
H₃C(H₂C)₁₄H₂C

GIPL-1

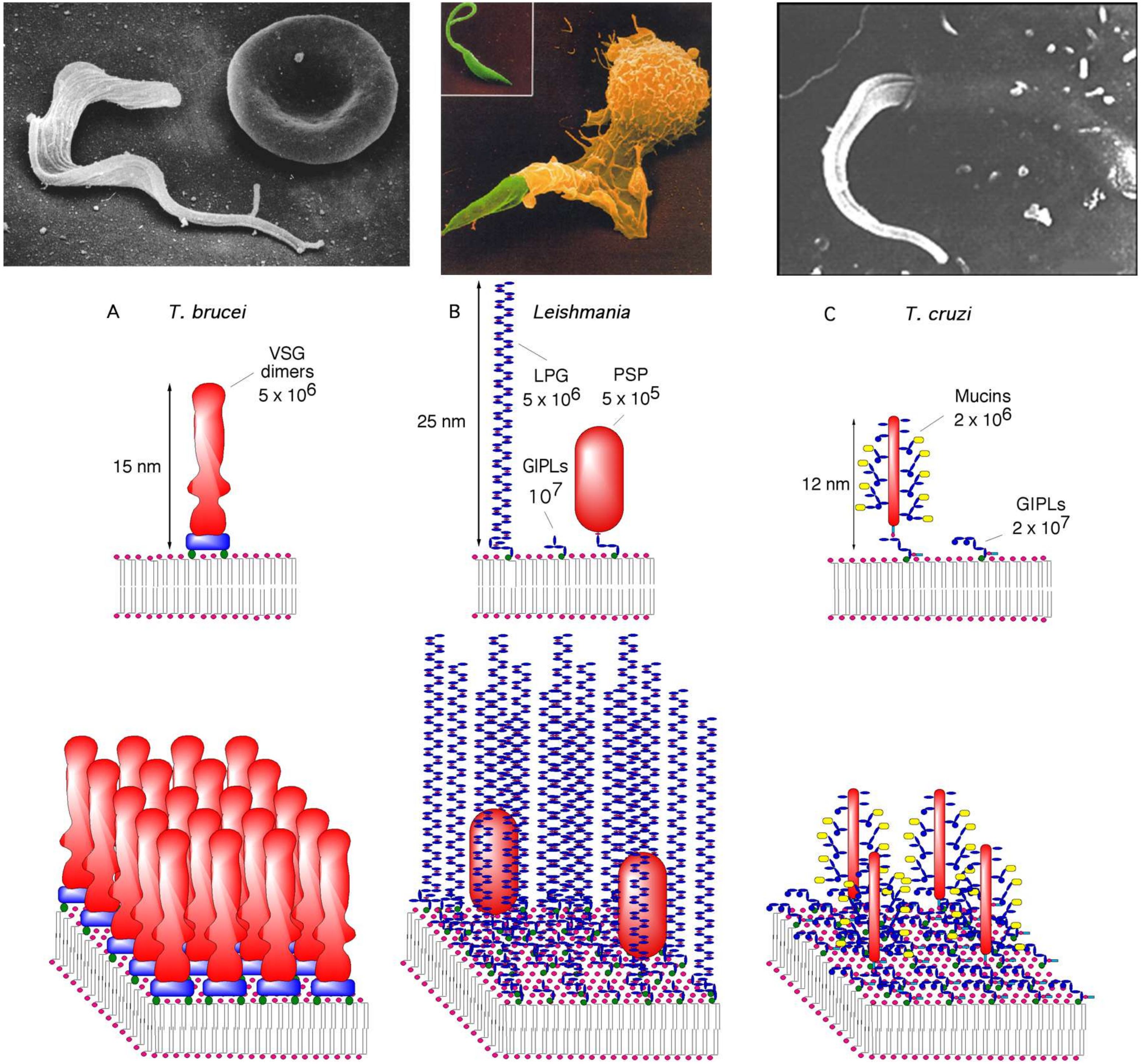

Galf
Galf
Man
Man
Man
Man
GlcN
NH2
2-AEP
OH
HO

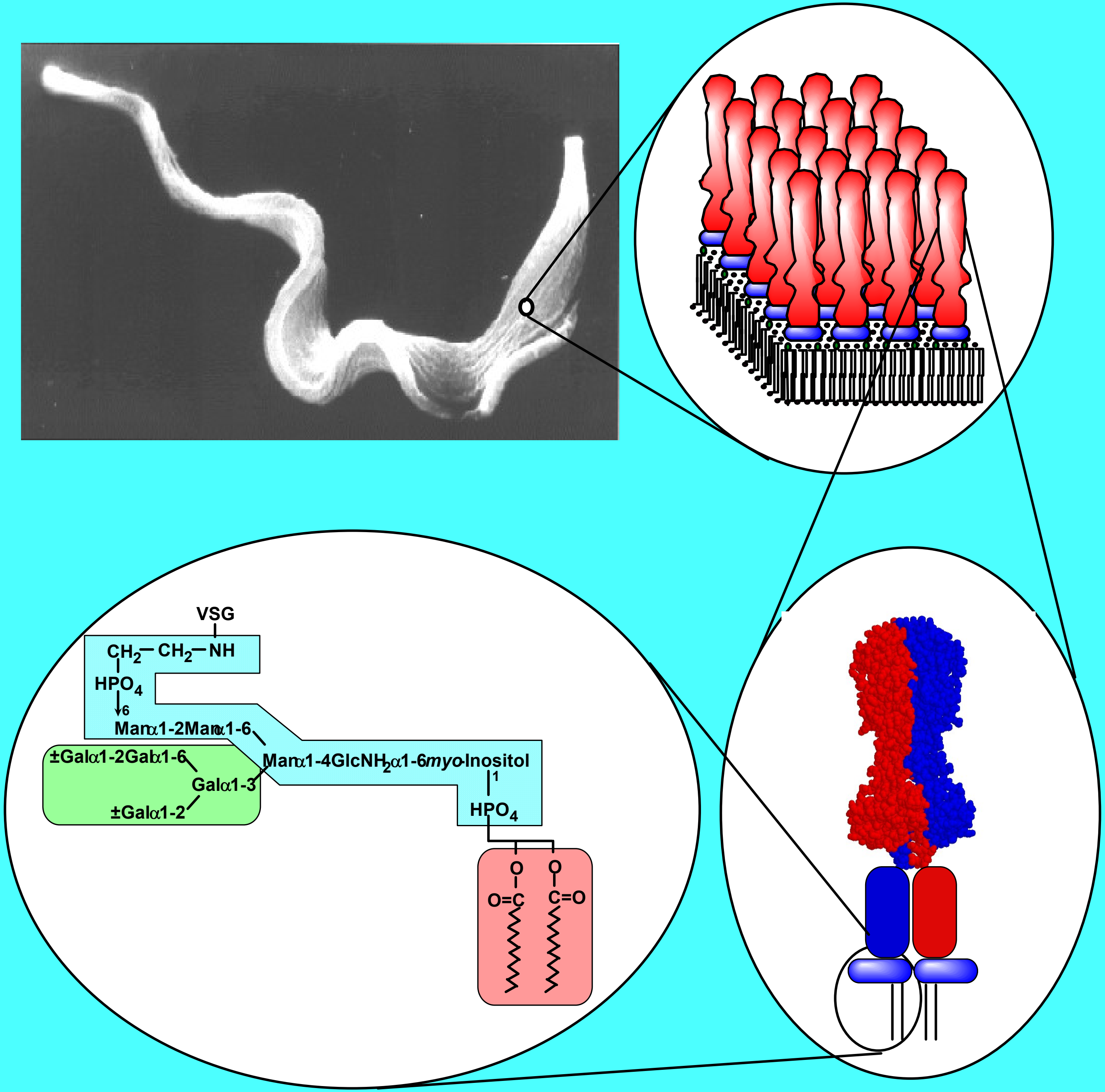
ÂNCORA VSG


PROTEIN
Man
Man
Man
Man
GlcN
NH2
2-AEP
R1 =
R2 =
OH
HO

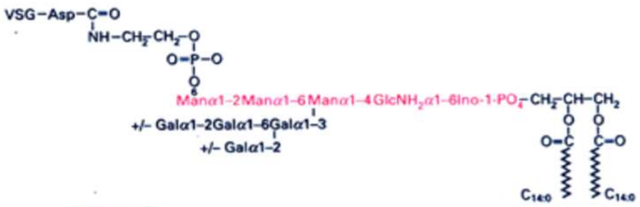

Manα1-2 Manα1-2 Manα1-6
Galfβ1-3 Galfβ1-3
2-AEP
|6
Manα1-4GlcNα1-6inositol-1-PO4-CH2-CH-CHOH
NH
O=
C16:0
C24:0
C18:0
T. cruzi Tipo I
M3
M2
M1
Manα1-2 Manα1-6
Manα1-4GlcNα1-6inositol-1-PO4-CH2-CH-CH2
O
O=
C18:0
C14:0
C16:0
C18:0
C24:0
Leishmania Tipo I
Leishm. híbrido
IM4
IM3
Manα1-2 Manα1-6
Manα1-3
Manα1-4GlcNα1-6inositol-1-PO4-CH2-CH-CH2
O
O=
GIPL 3
GIPL 2
GIPL 1
IM2
Galα1-6 Galα1-3 Galfβ1-3 Manα1-3
Manα1-4GlcNα1-6inositol-1-PO4-CH2-CH-CH2
O
O=
Leishmania Tipo II

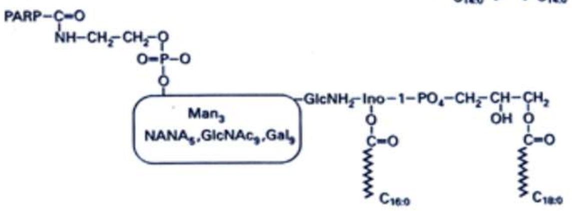
GiPLs


A
T. brucei
VSG dimers
5 x 10^6
15 nm
B
Leishmania
LPG
5 x 10^6
PSP
5 x 10^5
25 nm
GIPLs
10^7
C
T. cruzi
Mucins
2 x 10^6
12 nm
GIPLs
2 x 10^7

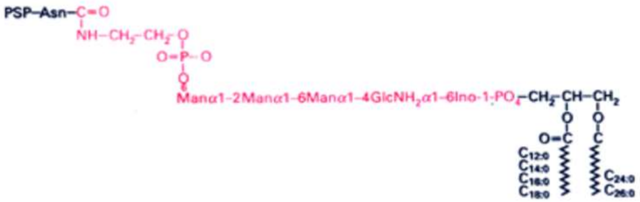

VSG
CH2—CH2—NH
HPO4
6
Manα1-2Manα1-6
±Galα1-2Galα1-6
Manα1-4GlcNH2α1-6myo-Inositol
Galα1-3
1
±Galα1-2
HPO4
O
O
O=C
C=O

Trypanosoma brucei

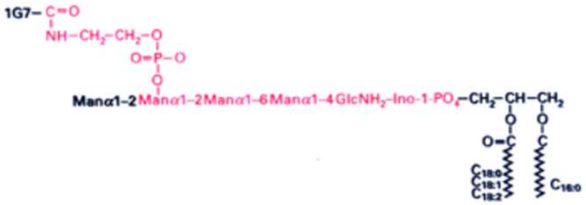

VSG–Asp–C=O
NH–CH₂–CH₂–O
O=P–O
O
Manα1–2Manα1–6Manα1–4GlcNH₂α1–6Ino-1-PO₄–CH₂–CH–CH₂
+/- Galα1–2Galα1–6Galα1–3
+/- Galα1–2
O=C
C=O
C14:0
C14:0


PARP–C=O
NH–CH₂–CH₂–O
O=P–O
O
Man₃
NANA₅,GlcNAc₅,Gal₅
GlcNH₂–Ino–1–PO₄–CH₂–CH–CH₂
OH
C=O
C=O
C16:0
C18:0

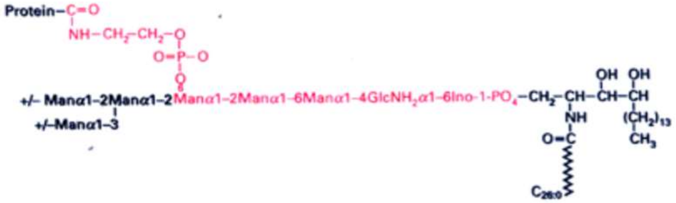
Leishmania major


PSP–Asn–C=O
NH–CH₂–CH₂–O
O=P–O
O
Manα1–2Manα1–6Manα1–4GlcNH₂α1–6Ino-1-PO₄–CH₂–CH–CH₂
O=C
C
C12:0
C14:0
C16:0
C18:0
C24:0
C26:0

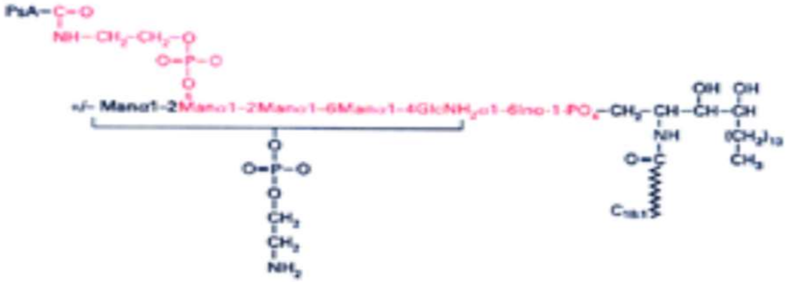
Trypanosoma cruzi


1G7–C=O
NH–CH₂–CH₂–O
O=P–O
O
Manα1–2Manα1–2Manα1–6Manα1–4GlcNH₂–Ino-1-PO₄–CH₂–CH–CH₂
O=C
C
C18:0
C18:1
C18:2
C16:0

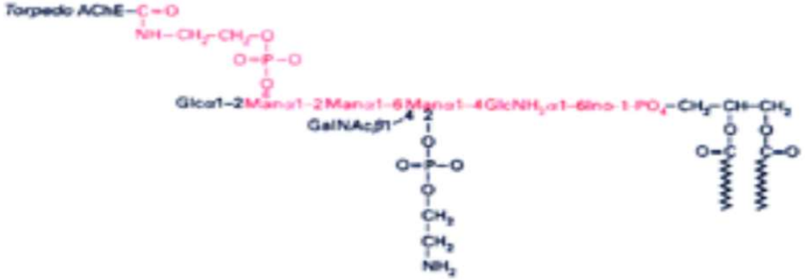
Yeast


Protein–C=O
NH–CH₂–CH₂–O
O=P–O
O
+/- Manα1–2Manα1–2Manα1–2Manα1–6Manα1–4GlcNH₂α1–6Ino-1-PO₄–CH₂–CH–CH–CH
+/-Manα1–3
OH OH
NH
O=C
(CH₂)13
CH₃
C26:0

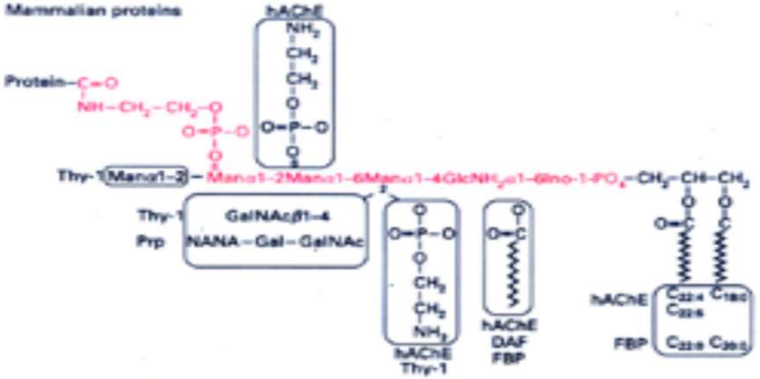
Dictyostelium discoideum


PsA–C=O
NH–CH₂–CH₂–O
O=P–O
+/- Manα1-2Manα1-2Manα1-6Manα1-4GlcNH₂α1-6Ino-1-PO₄–CH₂–CH–CH–CH
OH OH
NH
(CH₂)₁₃
CH₃
O=C
C₁₈:₁
O=P–O
CH₂
CH₂
NH₂

Fish proteins

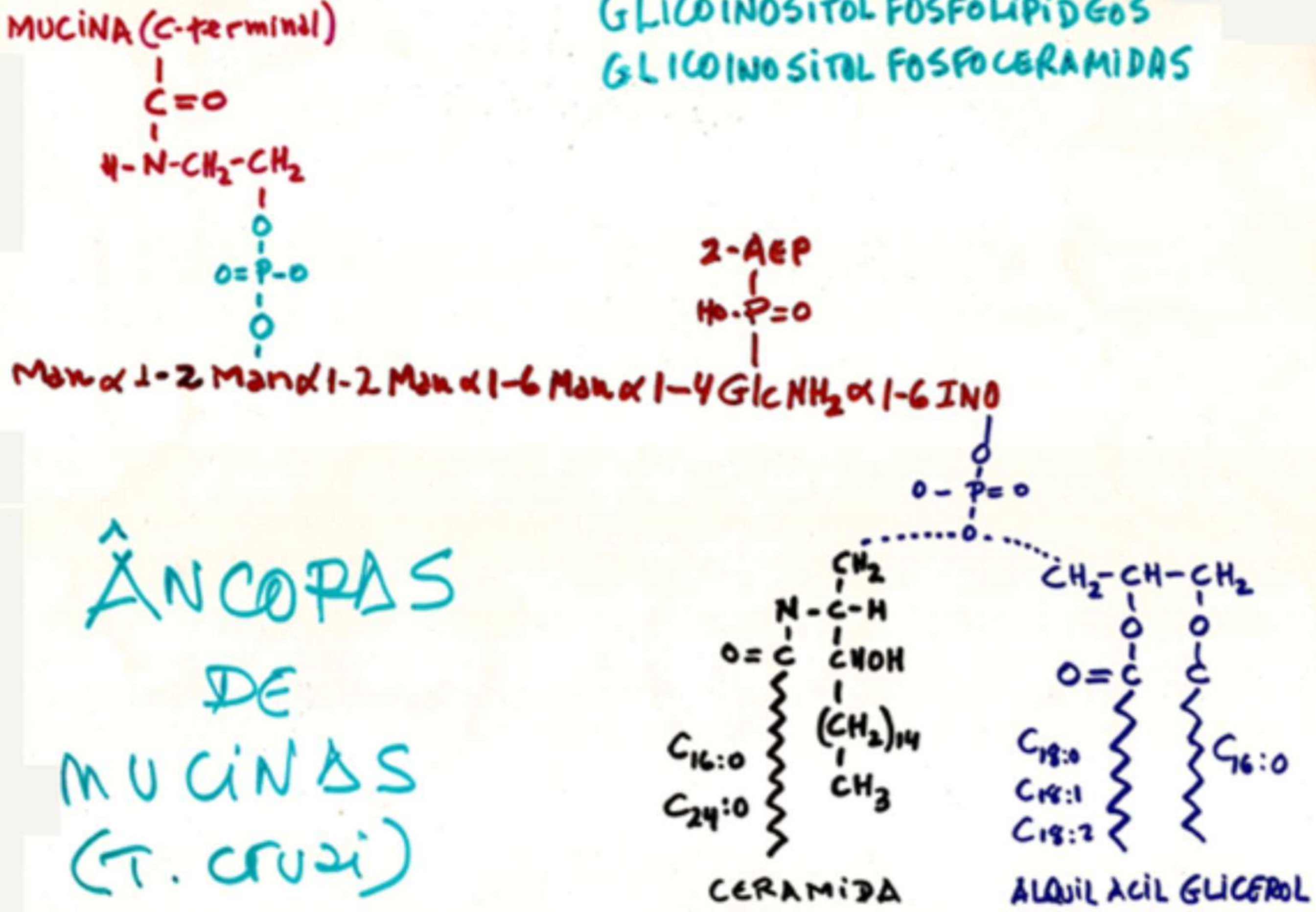

Torpedo AChE–C=O
NH–CH₂–CH₂–O
O=P–O
Glcα1-2Manα1-2Manα1-6Manα1-4GlcNH₂α1-6Ino-1-PO₄–CH₂–CH–CH₂
GalNAcβ1–4
2
O=P–O
CH₂
CH₂
NH₂
O=C
C=O

Mammalian proteins


hAChE
NH₂
CH₂
CH₂
O=P–O
Protein–C=O
NH–CH₂–CH₂–O
O=P–O
Thy-1
Manα1-2
Manα1-2Manα1-6Manα1-4GlcNH₂α1-6Ino-1-PO₄–CH₂–CH–CH₂
Thy-1
GalNAcβ1–4
Prp
NANA–Gal–GalNAc
O=P–O
CH₂
CH₂
NH₂
hAChE
Thy-1
O=C
hAChE
DAF
FBP
hAChE
C₂₂:₄
C₂₂:₆
C₁₈:₀
FBP
C₂₂:₆
C₂₀:₀

GLICOINOSITOL FOSFOLIPÍDEOS
GLICOINOSITOL FOSFOCERAMIDAS

ÂNCORAS DE MUCINAS (T. cruzi)

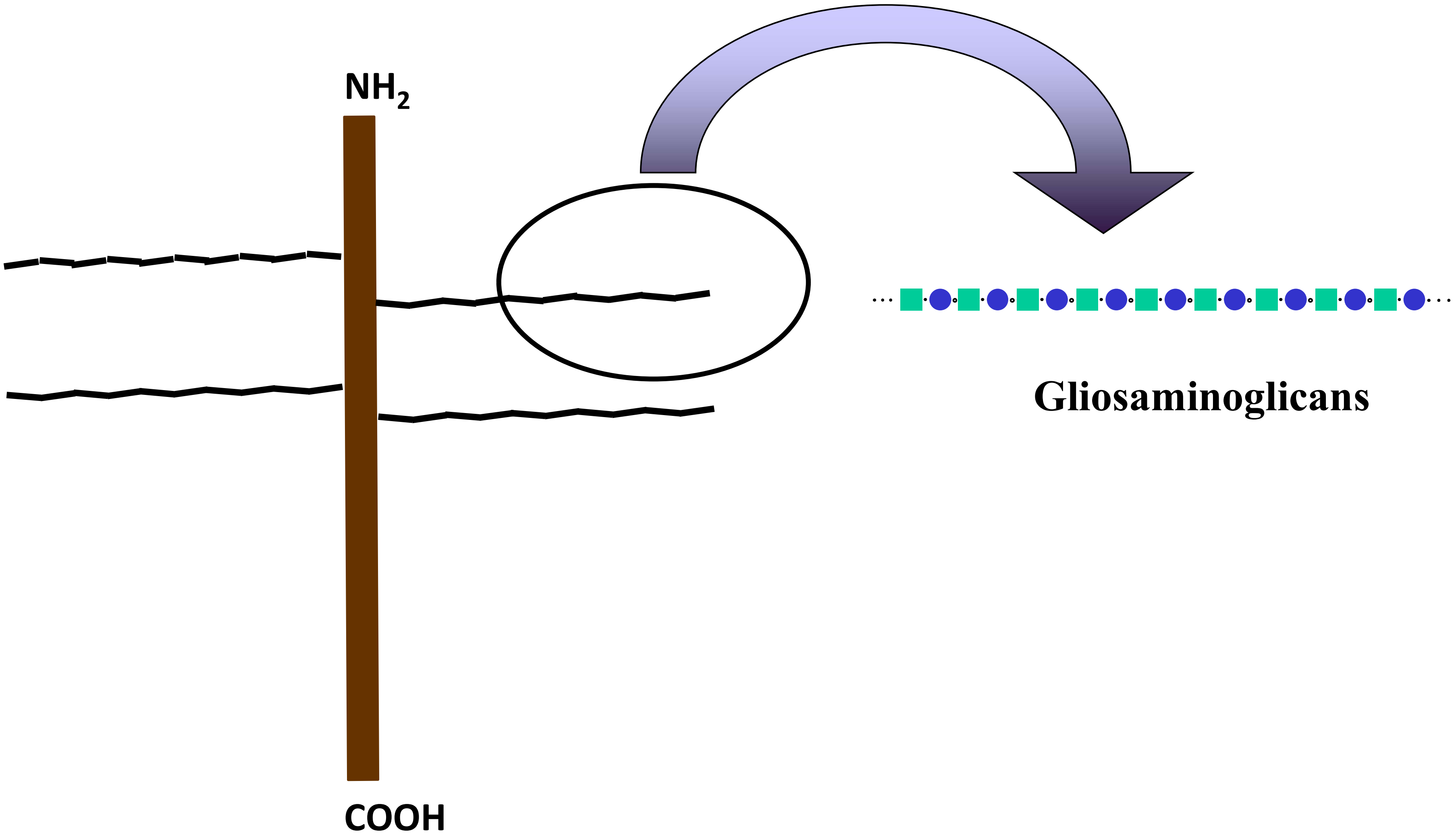

MUCINA (C-terminal)
C=O
H-N-CH₂-CH₂
O
O=P-O
O
2-AEP
HO-P=O
Man α 1-2 Man α 1-2 Man α 1-6 Man α 1-4 GlcNH₂ α 1-6 INO
O
O-P=O
O
CH₂
N-C-H
O=C
CHOH
(CH₂)₁₄
CH₃
C16:0
C24:0
CERAMIDA
CH₂-CH-CH₂
O
O
O=C
C
C18:0
C18:1
C18:2
C16:0
ALQUIL ACIL GLICEROL

SÍTIOS DE CLIVAGEM PARA INSERÇÃO DA ÂNCORA DE GPI

Acetilcolinesterase (Torpedo)	NQFLPKKKNATA**C** **DG**ELSSSGTSSSKGIIFYVLFSILYLIFY
Fosfatase alcalina (placenta)	TACDLAPPAGTT**D** **AA**HPGRSVVPALLPLLAGTLLLLETATAP
Decay Accelerating Factor	HETTPNKGSGTT**S** **GT**TRLLSGHTCFTLTGLLGTLVTMGLLT
Prociclina (*T. brucei* PARP)	EPEPEPEPEPEP**G** **AA**TLKSVALPFAIAAAALVAAF
Prion (hamster)	QKESQAYYDGRR**S** **SA**VLFSSPPVILLISFLIFLMVG
Antígeno Thy-1 (rato)	KTINVIRDKLVK**C** **GG**ISLLVQNTSWLLLLLLSLSFLQATDFISL
VSG (*T. brucei* 117)	ESNCKWENNACK**D** **SS**ILVTKKFALTVVSAAFVALLF
Tc-85 (LBG, *T. cruzi*)	GTAREKGDGGAN**G** **DA**GSAYGRELLPMLLLLGLWALATA

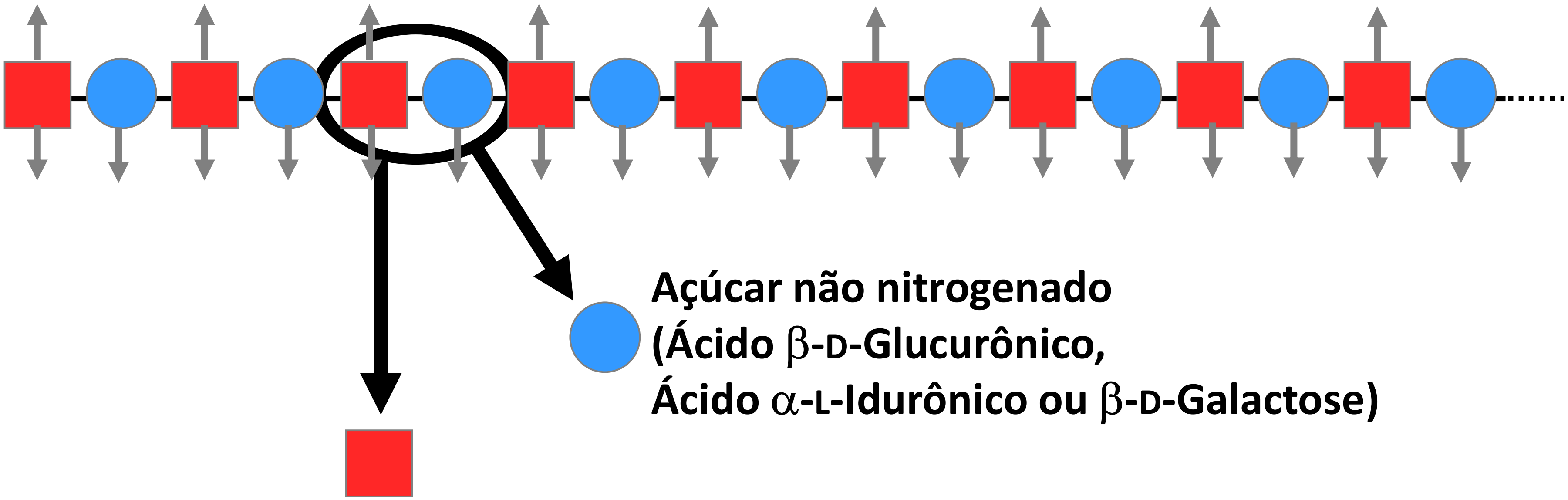
GLICOSAMINOGLICANAS
E
PROTEOGLICANAS

Proteoglicanos



NH$_2$
COOH
Gliosaminoglicans

Glicosaminoglicanos

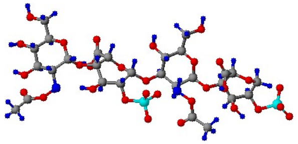


Açúcar não nitrogenado
(Ácido β-D-Glucurônico,
Ácido α-L-Idurônico ou β-D-Galactose)

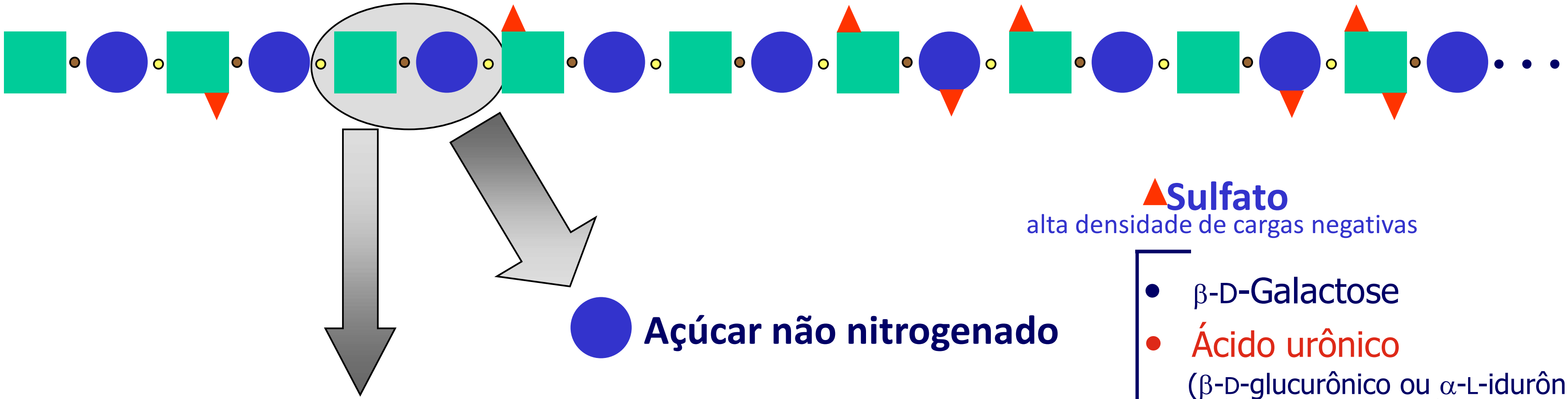
Hexosamina (D-Glucosamina ou D-Galactosamina)

GAGs:
- **Heparina**
- **Heparam Sulfato**
- **Dermatam Sulfato**
- **Condroitim 4-Sulfato**
- **Condroitim 6-Sulfato**
- **Ácido Hialurônico**

Diferenças quanto :
- **Hexosamina;**
- **Açúcar não nitrogenado;**
- **Presença e posição de grupamentos sulfato; e**
- **Tipo de ligação glicosídica.**



Glicosaminoglicanos



● **Açúcar não nitrogenado**

🟩 **Hexosamina**

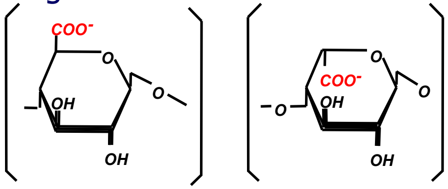
(α-D-Glucosamina ou β-D-Galactosamina)

▲**Sulfato**

alta densidade de cargas negativas

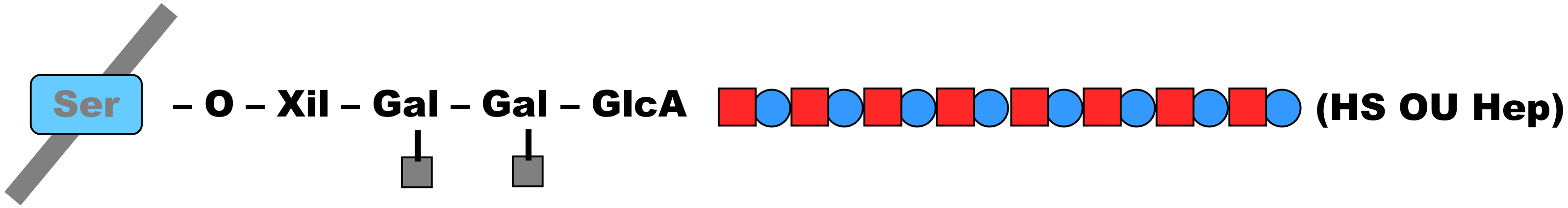
- β-D-Galactose
- Ácido urônico

(β-D-glucurônico ou α-L-idurônico)



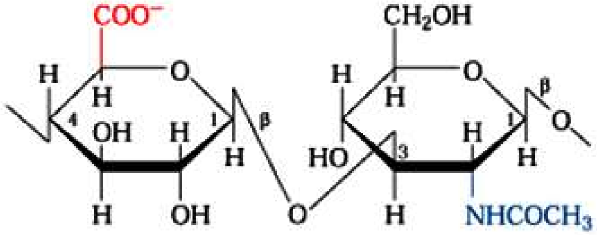
Nos tecidos:

Proteoglicanos = Proteína ("core") + Cadeia linear de GAG



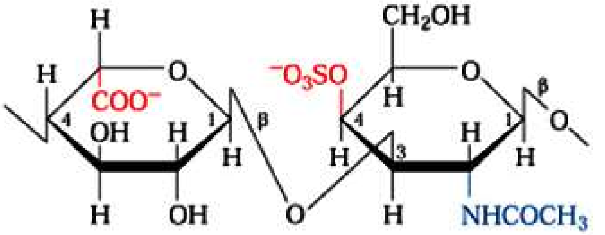
– O – Xil – Gal – Gal – GlcA **(HS OU Hep)**

Glicosaminoglicanos



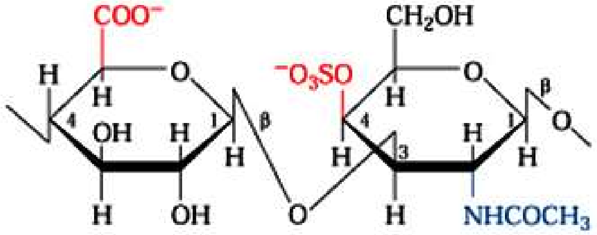
D-Glucuronate N-Acetyl-D-glucosamine

Hyaluronate



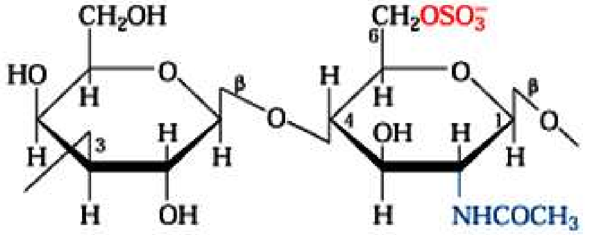
L-Iduronate N-Acetyl-D-galactosamine-4-sulfate

Dermatan sulfate



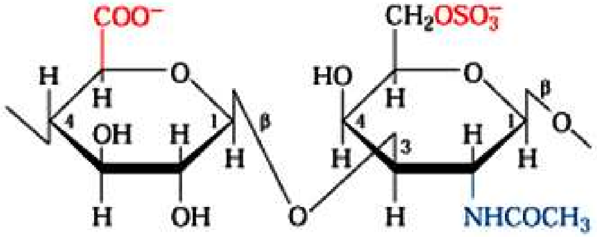
D-Glucuronate N-Acetyl-D-galactosamine-4-sulfate

Chondroitin-4-sulfate



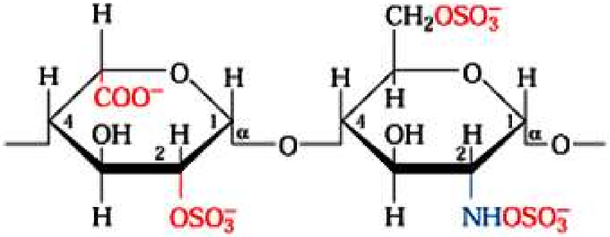
D-Galactose N-Acetyl-D-glucosamine-6-sulfate

Keratan sulfate



D-Glucuronate N-Acetyl-D-galactosamine-6-sulfate

Chondroitin-6-sulfate



D-Iduronate-2-sulfate N-Sulfo-D-glucosamine-6-sulfate

Heparin

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Tabela I

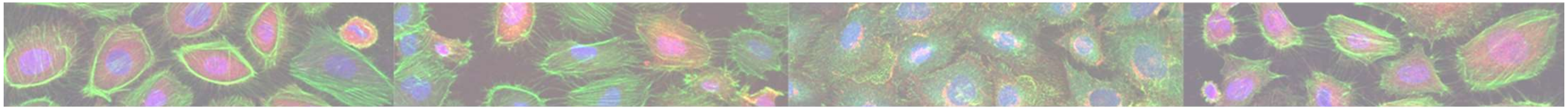
Características estruturais dos glicosaminoglicanos

Glicosaminoglicanos	**Dissacarídeos**			
	Açúcar não nitrogenado	**Ligação intra-dissacarídica**	**Hexosamina**	**Ligação inter-dissacarídica**
Ácido Hialurônico	D-GlcA	β1→3	D-GlcN Ac	β1→4
Condrosam	D-GlcA	β1→3	D-GalN Ac	
Condroitim sulfato	D-GlcA D-GlcA D-GlcA	β1→3 β1→3 β1→3	D-GalN Ac D-GalN Ac (4S) D-GalN Ac (6S)	
Dermatam sulfato	D-GlcA D-GlcA L-IdoA L-IdoA (2S) L-IdoA (2S)	β1→3 β1→3 α1→3 α1→3 α1→3	D-GalN Ac (4S) D-GalN Ac (6S) D-GalN Ac (4S) D-GalN Ac (4S) D-GalN Ac (6S)	
Queratam sulfato	D-Gal (6S)	β1→3	D-GlcN Ac (6S)	
Heparosam	D-GlcA	β1→4	D-GlcN Ac	α1→4
Acaram sulfato	L-IdoA (2S)	α1→4	D-GlcN Ac	
Heparam sulfato	D-GlcA D-GlcA D-GlcA D-GlcA L-IdoA L-IdoA (2S)	β1→4 β1→4 β1→4 β1→4 α1→4 α1→4	D-GlcN Ac D-GlcN Ac (6S) D-GlcN (S) D-GlcN (S, 6S) D-GlcN (S) D-GlcN (S)	
Heparina	D-GlcA D-GlcA L-IdoA (2S) L-IdoA (2S)	β1→4 β1→4 α1→4 α1→4	D-GlcN (S) D-GlcN (S, 6S) D-GlcN (S) D-GlcN (S, 6S)	

D-GlcA: ácido D-glucurônico; L-IdoA: ácido L-idurônico; D-GlcN: D-glucosamina; D-GalN, D-galactosamina; D-Gal, D-galactose.

COMPONENTES DA UNIDADE ESTRUTURAL DOS GLICOSAMINOGLICANOS ÁCIDOS

GLICOSAMINO GLICANO	AÇÚCARES	POSIÇÃO DO SULFATO	LIGAÇÃO INTRA	LIGAÇÃO INTER
Condroitim	GalNAc	-	β 1→3	β 1→4
	GlcUA	-		
Condroitim 4-sulfato	GalNAc	4	β 1→3	β 1→4
	GlcUA	-		
Dermatam sulfato	GalNAc	4	β 1→3	β 1→4
	GlcUA	-	α 1→3	
	IduUA	-		
Condroitim 6-sulfato	GalNAc	6	β 1→3	β 1→4
	GlcUA	-		
Ácido Hialurônico	GlcNAc	-	β 1→3	β 1→4
	Gal	-		
Queratam sulfato	GlcNAc	6	β 1→4	β 1→3
	Gal	-/6		
Heparam sulfato	GlcN	2/6	α 1→4	α 1→4
	GlcNAc	-/6		
	GlcUA	-		
Heparina	GlcN	2/6	α 1→4	α 1→4
	GlcUA	-		
	IduUA	2		



Proteoglicanos

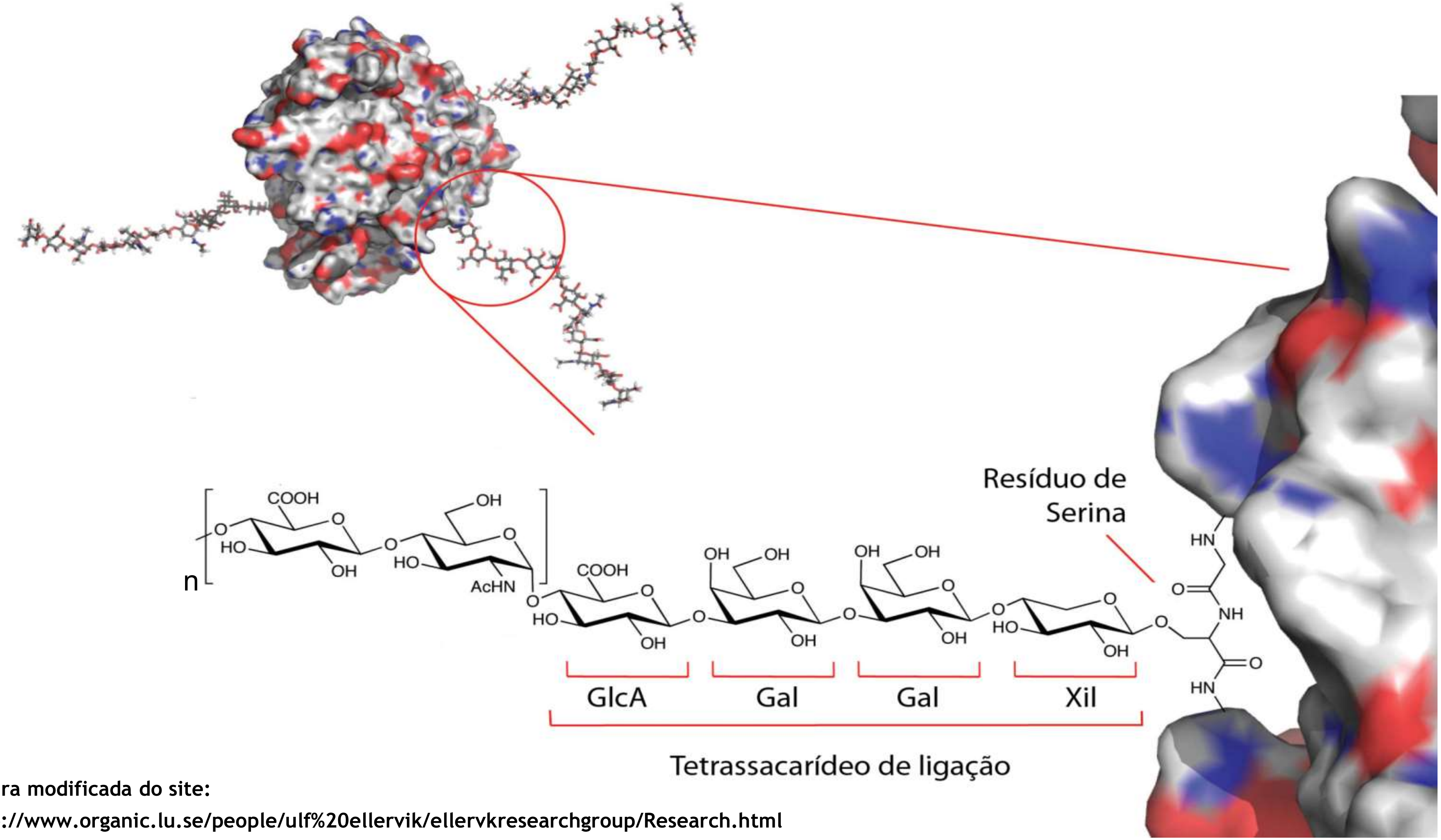
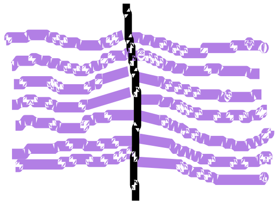

Resíduo de Serina
COOH
OH
HO
O
AcHN
n
HN
NH
GlcA
Gal
Gal
Xil
Tetrassacarídeo de ligação

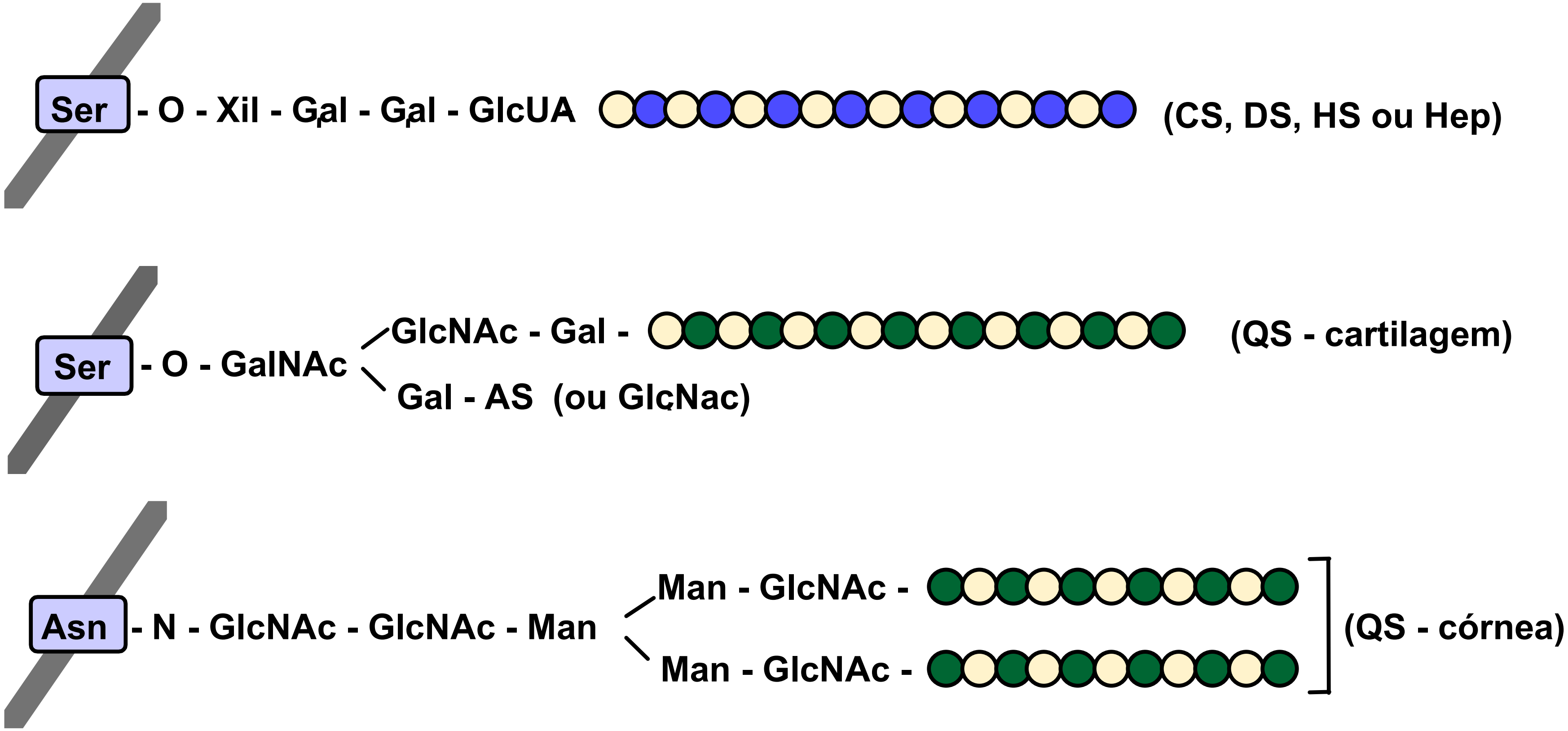
Figura modificada do site:

http://www.organic.lu.se/people/ulf%20ellervik/ellervkresearchgroup/Research.html



Proteoglicanos

Região de Ligação



Ser - O - Xil - Gal - Gal - GlcUA (CS, DS, HS ou Hep)

Ser - O - GalNAc
- GlcNAc - Gal - (QS - cartilagem)
- Gal - AS (ou GlcNac)

Asn - N - GlcNAc - GlcNAc - Man
- Man - GlcNAc -
- Man - GlcNAc -

(QS - córnea)

Proteoglicanos

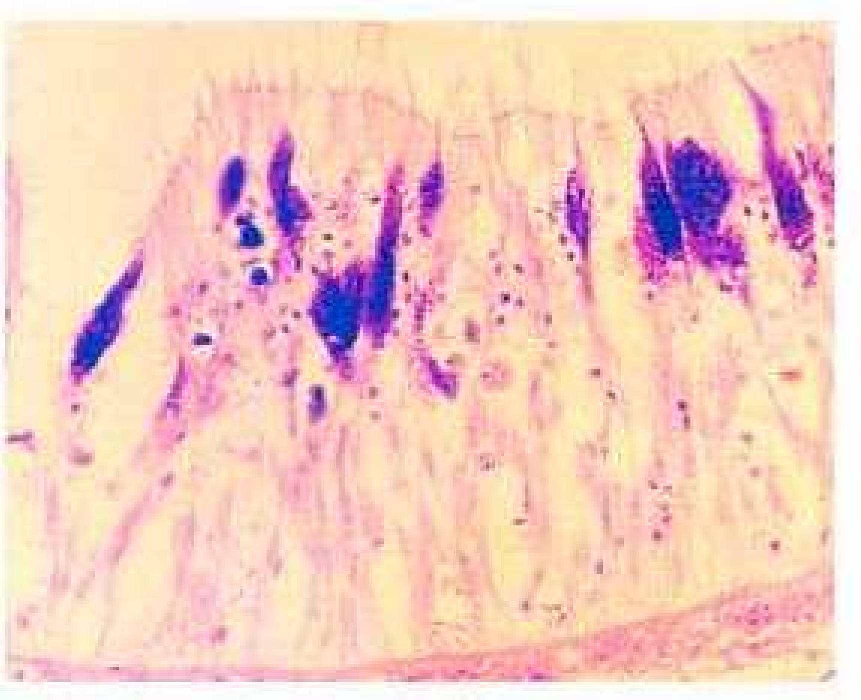
- Células
  - Grânulos citoplasmáticos: serglicim
  - Superfície celular: sindecam, glipicam
- Matriz extracelular
  - Membrana basal: perlecam, bamacam
  - Matriz intersticial:
    - Alto peso molecular, que agregam com ácido hialurônico
    - Baixo peso molecular, da família das proteínas ricas em leucina

Função dos Proteoglicanos

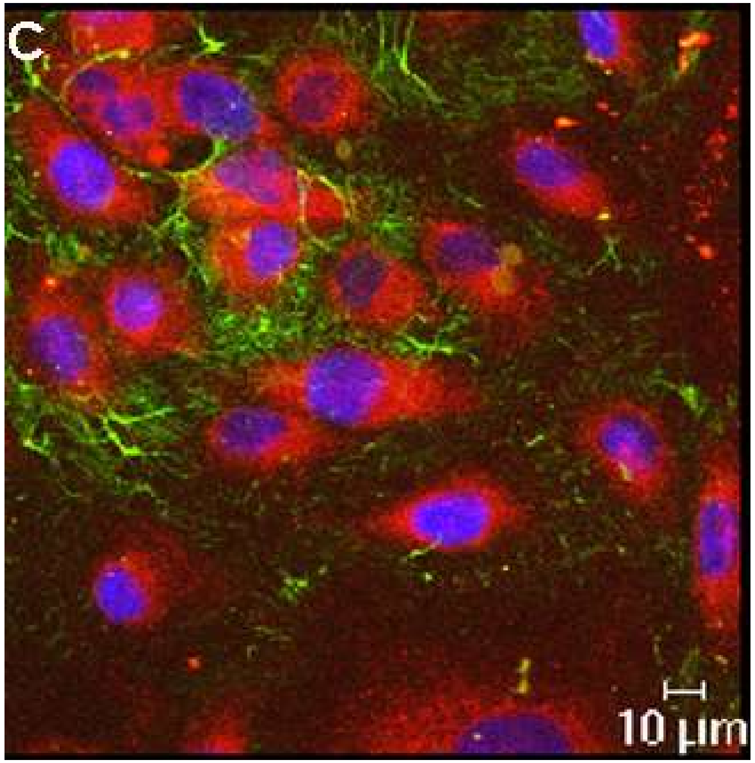
Proteoglicano	Localização	Função
Heparam Sulfato	Em todos os tecidos •Superfície Celular •Matriz Extracelular •Membrana Basal	• Adesão celular • Reconhecimento Celular • Papel importante na divisão celular
Condroitim4- e 6- Sulfato	•Matriz de tecidos conjuntivos, ossos e cartilagens. •Tecidos de proliferação rápida	• Proliferação celular
Dermatam Sulfato	•Tecidos conjuntivos densos (pele e tendão)	• Organização de tecidos ricos em colágenos
Heparina	•Tecidos em contato com o meio externo (pele, pulmão)	• Defesa
Queratam Sulfato	•Estroma da Córnea •Cartilagem óssea	• Transparência a córnea • Crescimento celular

Heparin is found in intracellular granules of mast cells and Heparan Sulfate is located at the cell surface of all animal species with tissue organization

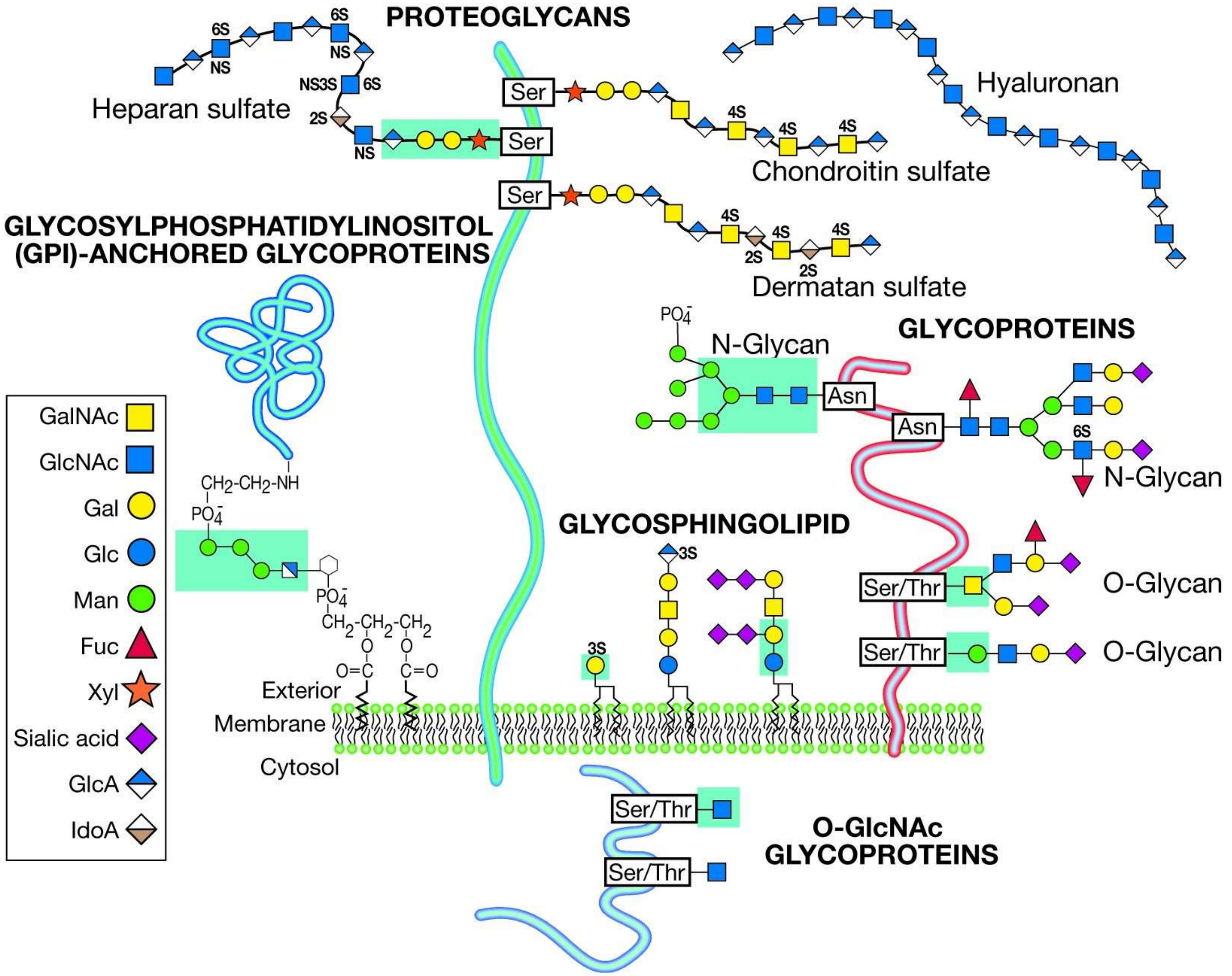
Nucleo azul DAPI, verde fibronectina e vermelho
Proteoglicano de heparam sulfato na superfície,
Visualizados com anticorpos específicos



Heparina corada em roxo com azul de toluidina-metacromasia

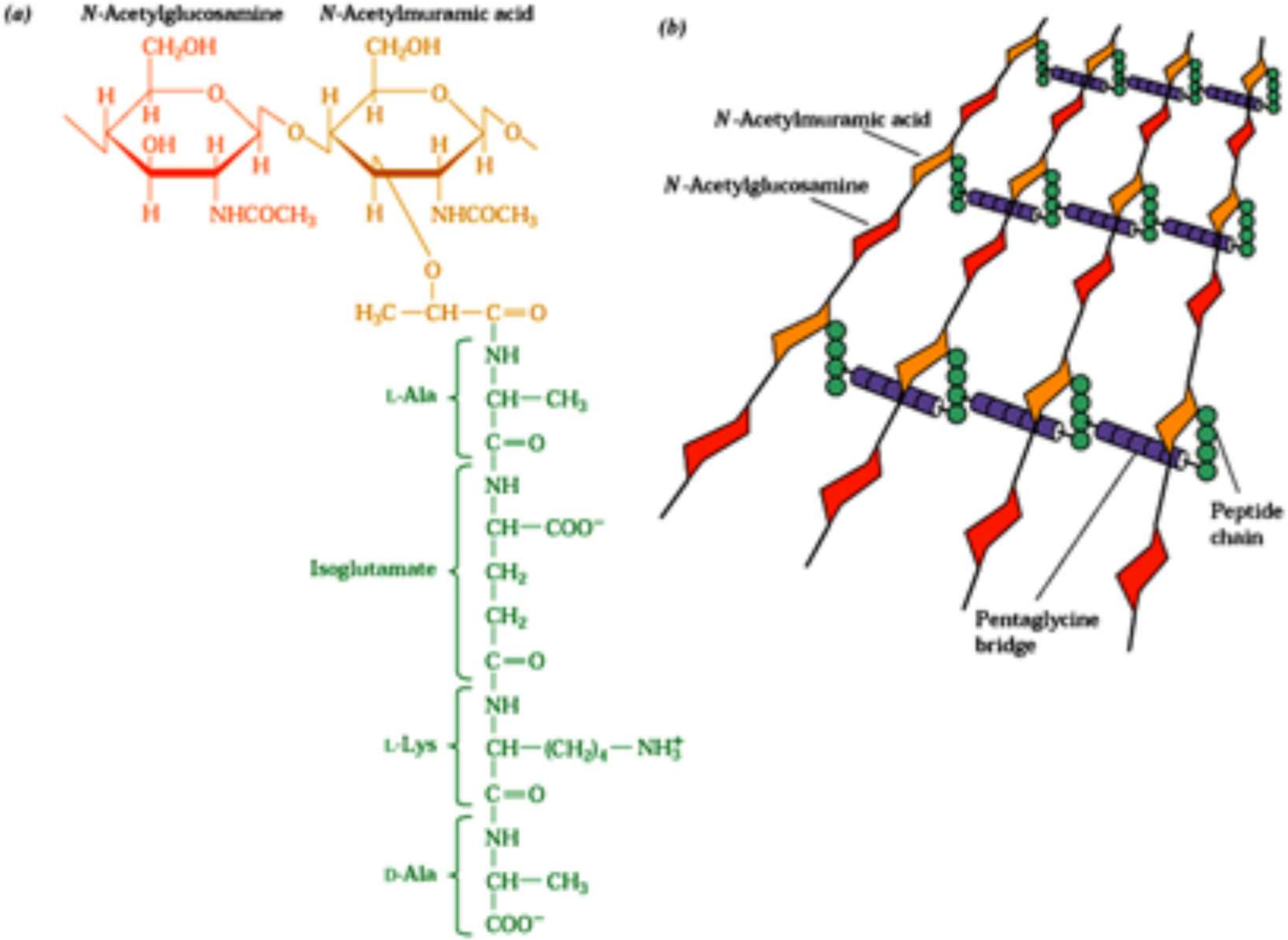


Common Classes of Animal Glycans


PROTEOGLYCANS
6S
NS
6S
NS
NS3S
6S
Heparan sulfate
2S
NS
Ser
Ser
Ser
4S
4S
4S
Chondroitin sulfate
Hyaluronan
4S
4S
4S
2S
2S
Dermatan sulfate
GLYCOSYLPHOSPHATIDYLINOSITOL
(GPI)-ANCHORED GLYCOPROTEINS
PO4-
N-Glycan
GLYCOPROTEINS
Asn
Asn
6S
N-Glycan
GalNAc
GlcNAc
Gal
Glc
Man
Fuc
Xyl
Sialic acid
GlcA
IdoA
CH2-CH2-NH
PO4-
PO4-
CH2-CH2-CH2
O O
O=C C=O
Exterior
Membrane
Cytosol
GLYCOSPHINGOLIPID
3S
3S
Ser/Thr
O-Glycan
Ser/Thr
O-Glycan
Ser/Thr
Ser/Thr
O-GlcNAc
GLYCOPROTEINS

Essentials of Glycobiolog, 2nd Edition, Chpater 1, Figure 6

Peptidioglicano (Parede Celular)


(a)
N-Acetylglucosamine
N-Acetylmuramic acid
CH2OH
H
O
OH
NHCOCH3
H3C—CH—C=O
NH
L-Ala
CH—CH3
C=O
Isoglutamate
CH—COO⁻
CH2
L-Lys
CH—(CH2)4—NH3+
D-Ala
COO⁻
(b)
N-Acetylmuramic acid
N-Acetylglucosamine
Peptide chain
Pentaglycine bridge

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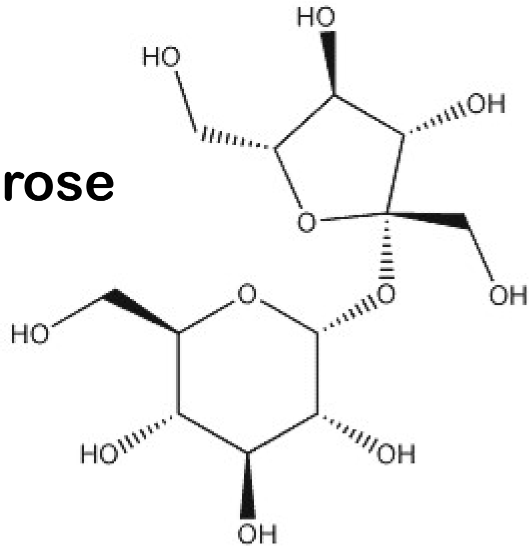
THE END

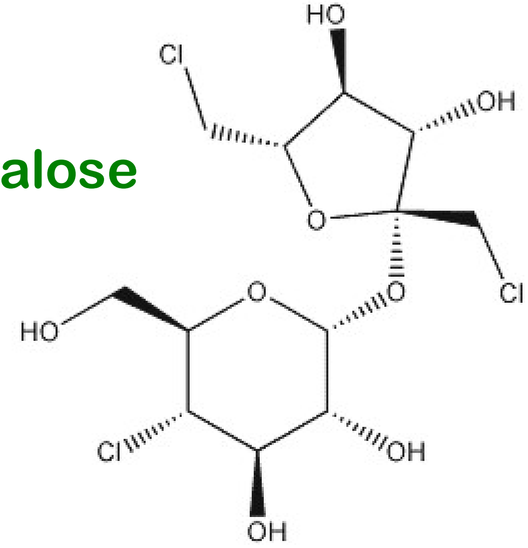
Doçura relativa

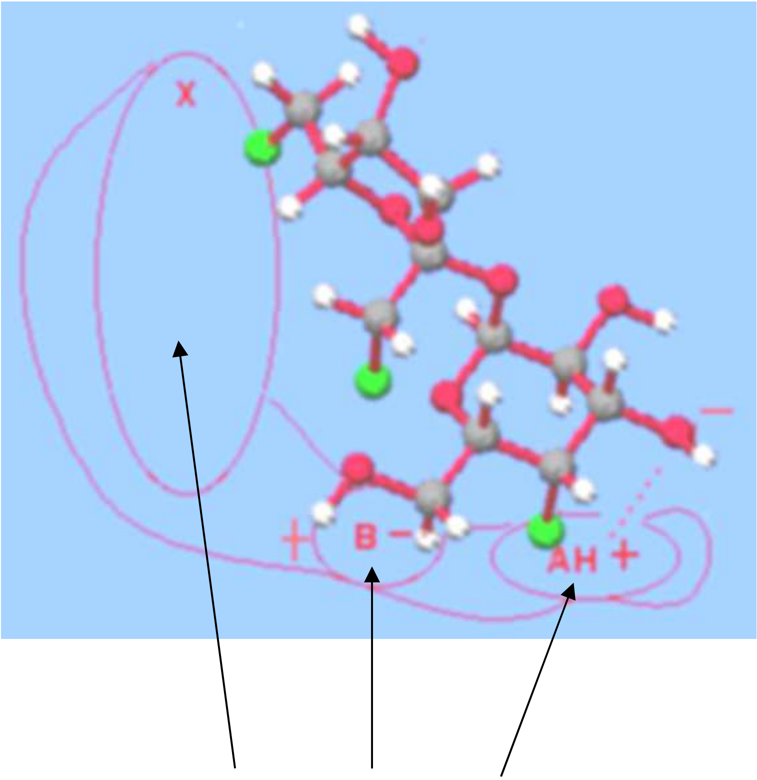
Composto	Escala
Sacarose	100
Frutose	140
Glicose	70 – 80
Galactose	35
Maltose	30 – 50
Lactose	20
Sacarina	300
Ciclamato	30
Aspartame	180
Acesulfame	200
Sucralose	600

Sacarose



Sucralose



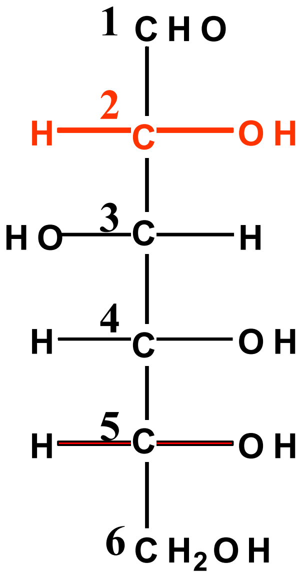


3 regiões de interação

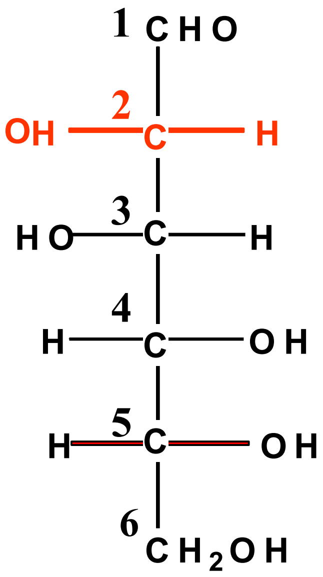
Modelo do receptor da sensação de "doce"

EPÍMEROS (Convenção de Fischer)

Epímeros diferem na configuração de um átomo de carbono

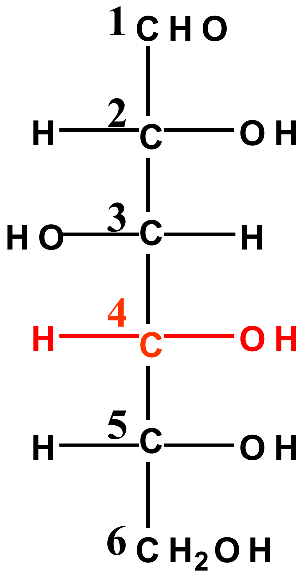

1 CHO
2 H C OH
3 HO C H
4 H C OH
5 H C OH
6 CH2OH

D-Glicose

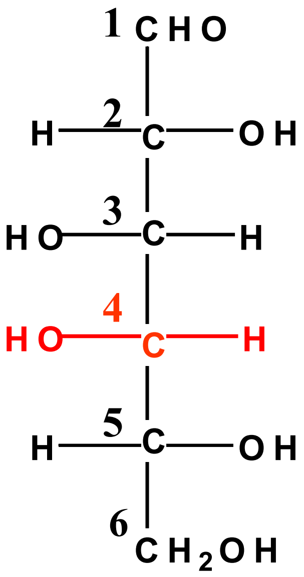

1 CHO
2 OH C H
3 HO C H
4 H C OH
5 H C OH
6 CH2OH

D-Manose

Epímeros do carbono 2


1 CHO
2 H C OH
3 HO C H
4 H C OH
5 H C OH
6 CH2OH

D-Glicose


1 CHO
2 H C OH
3 HO C H
4 HO C H
5 H C OH
6 CH2OH

D-Galactose

Epímeros do carbono 4

Carboidratos são classificados quanto a natureza do grupo carbonila:
cetona = cetoses

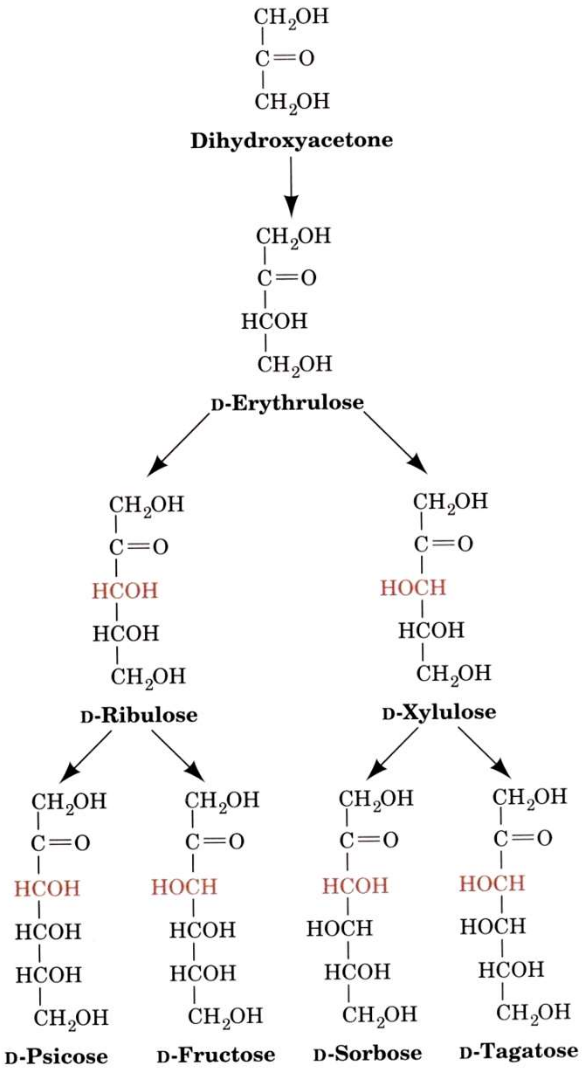
Monossacarídeos (D-cetoses)

Triose

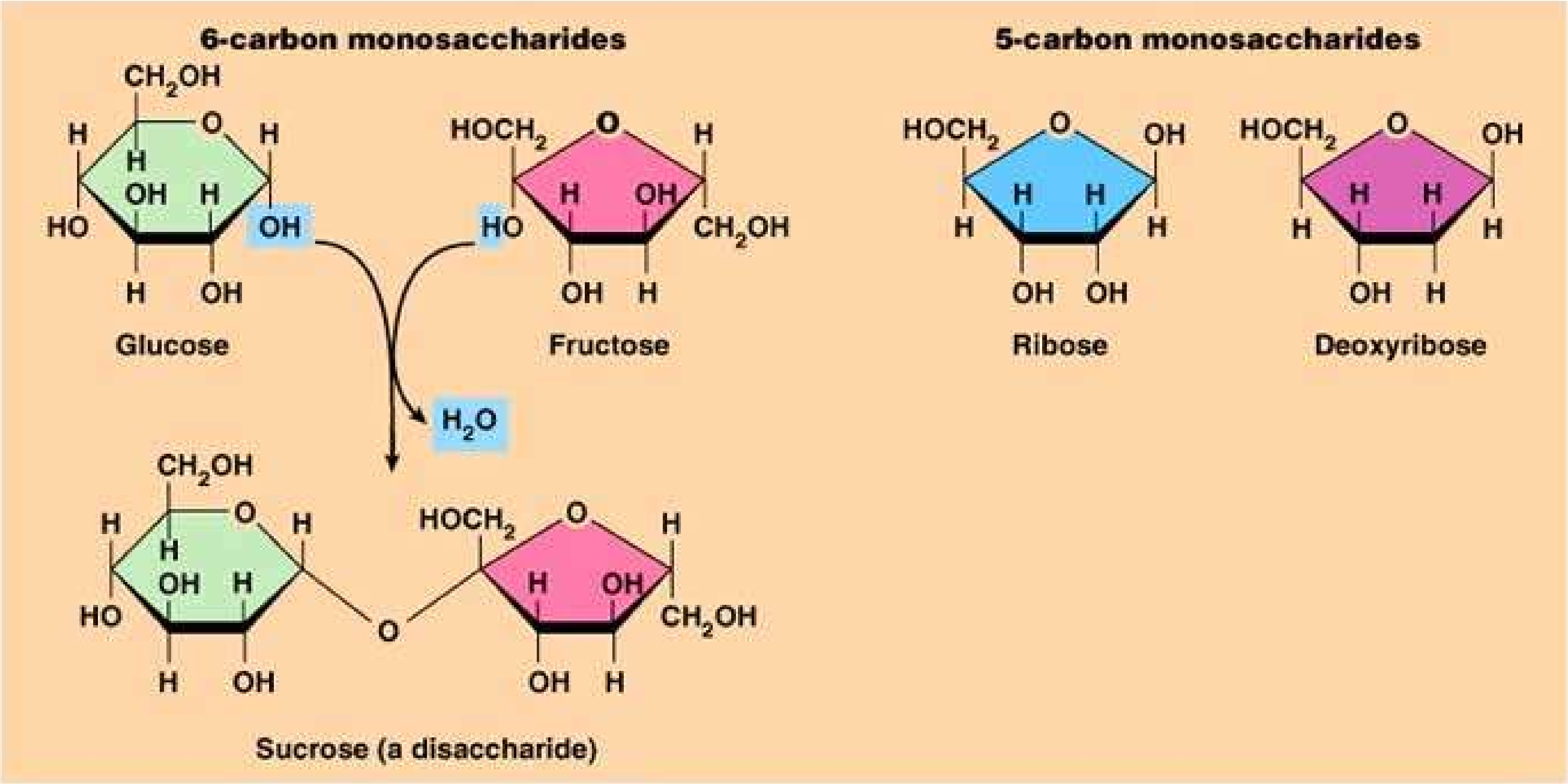
Tetrose

Pentoses

Hexoses


Dihydroxyacetone
D-Erythrulose
D-Ribulose
D-Xylulose
D-Psicose
D-Fructose
D-Sorbose
D-Tagatose

Dissacarídeos


6-carbon monosaccharides
5-carbon monosaccharides
CH_2OH
O
H
OH
HO
HOCH$_2$
CH_2OH
H_2O
Glucose
Fructose
Ribose
Deoxyribose
Sucrose (a disaccharide)

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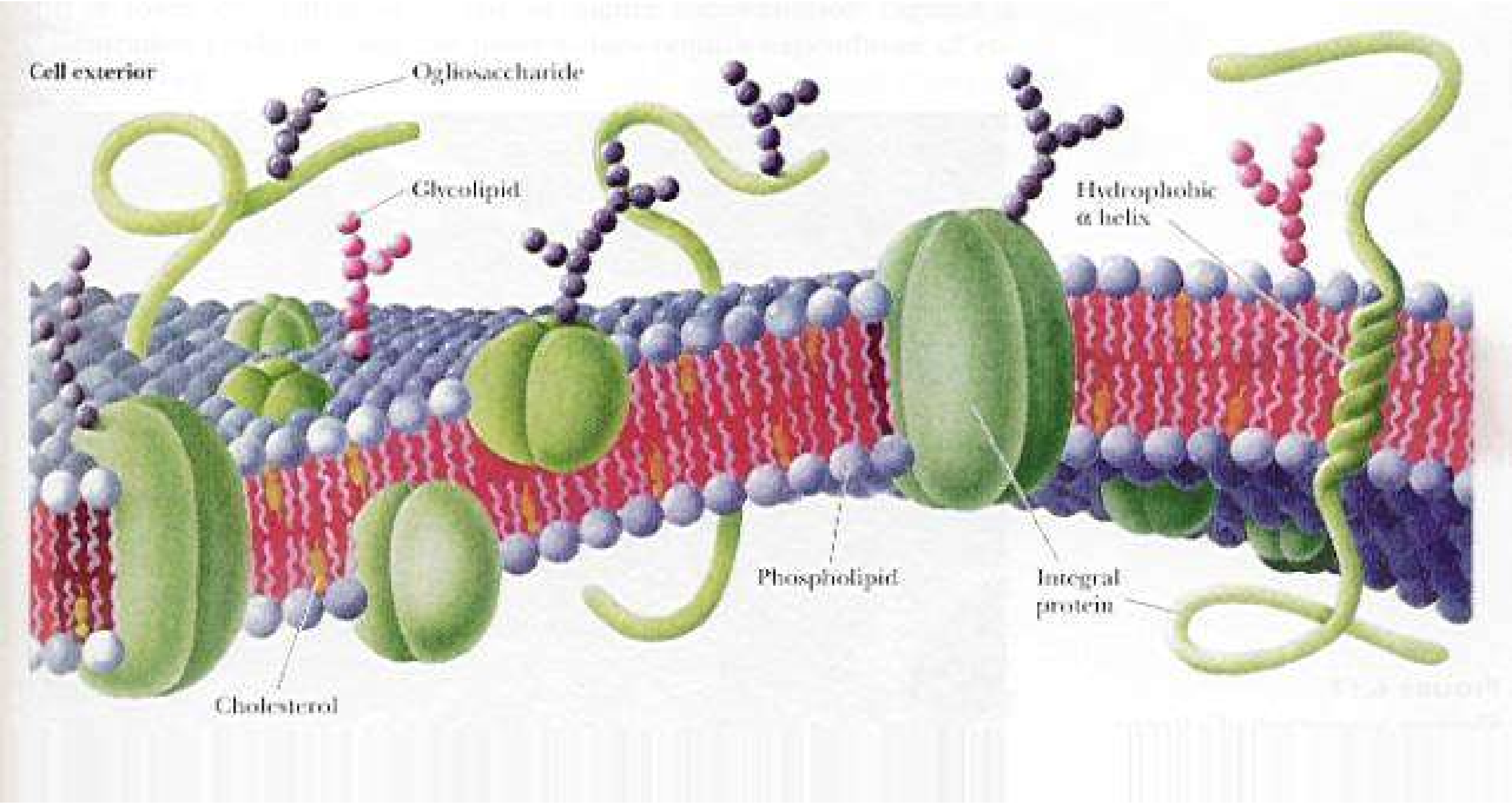
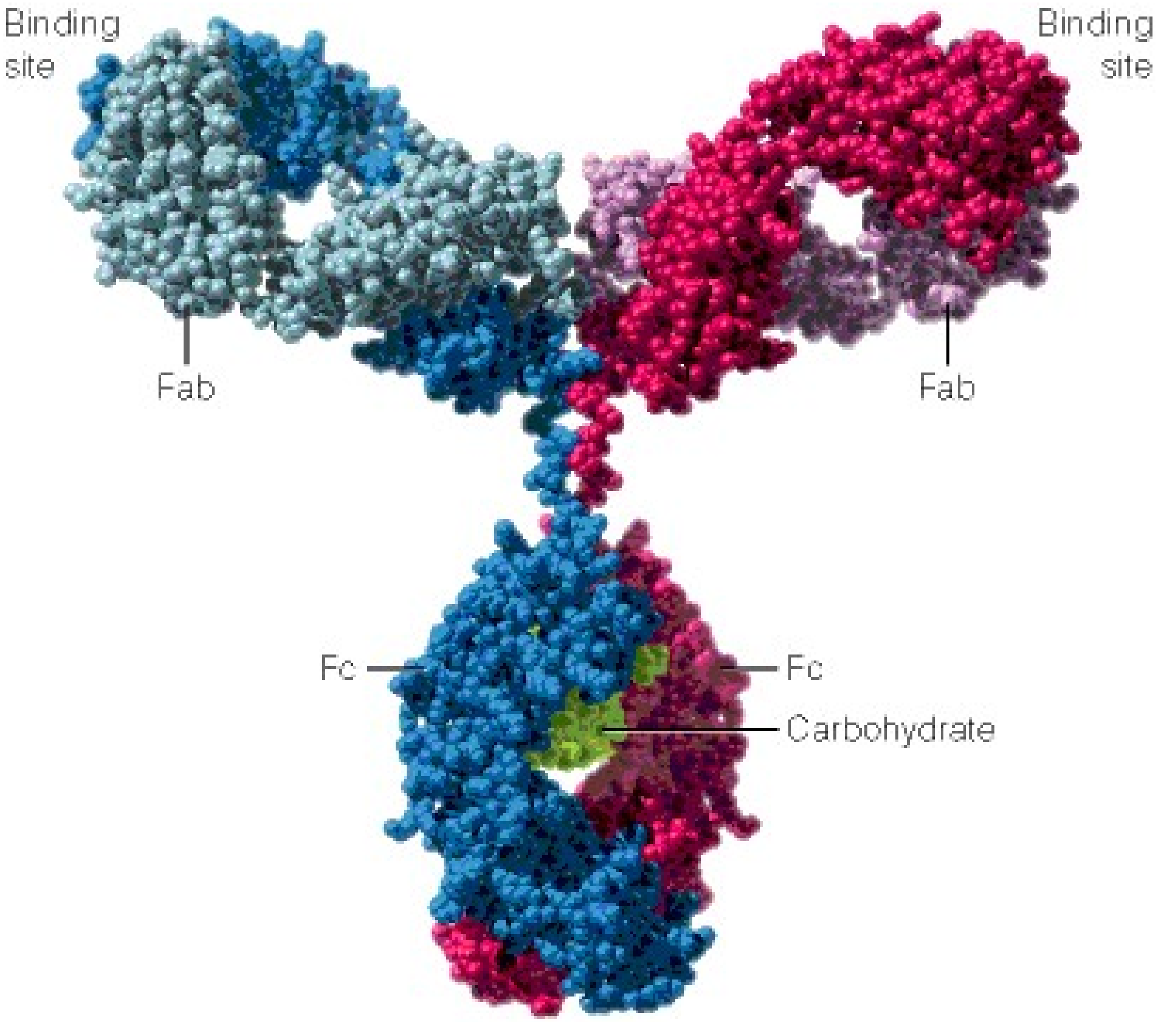
Fatores de Reconhecimento de Superfície Celular


Cell exterior
Ogliosaccharide
Glycolipid
Hydrophobic
α helix
Phospholipid
Integral
protein
Cholesterol

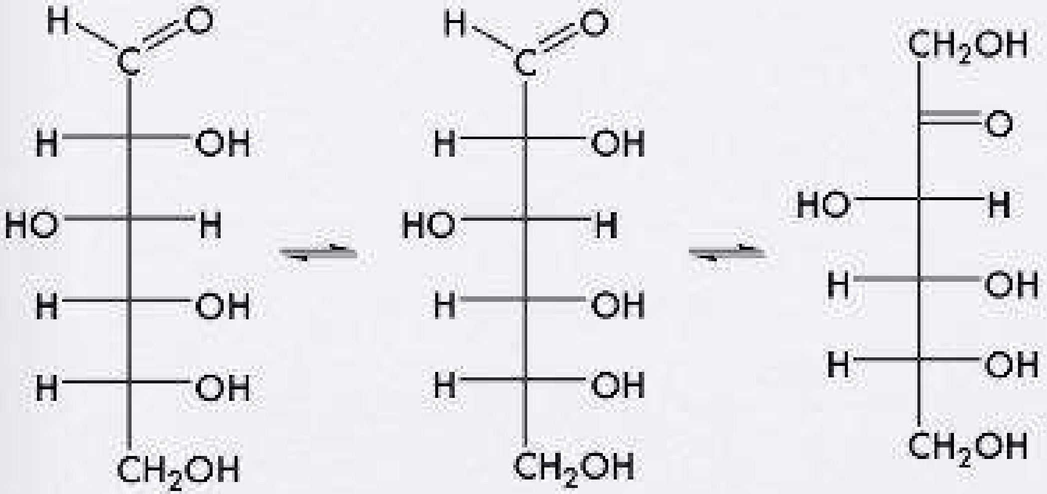
Difração de Raio X – Modelo de IgG


Binding site
Binding site
Fab
Fab
Fc
Fc
Carbohydrate

Ketone sugars

Ketones are not easy to oxidize except ketoses.

Enediol reaction-all monosaccharides are reducing sugars.


H
C
O
H
OH
HO
H
H
OH
H
OH
CH₂OH
H
C
O
H
OH
HO
H
H
OH
H
OH
CH₂OH
CH₂OH
O
HO
H
H
OH
H
OH
CH₂OH

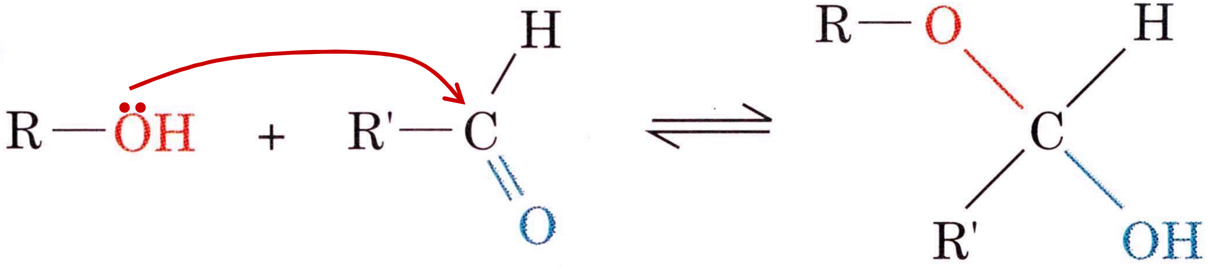
Aldose

***cis*-enediol intermediate**

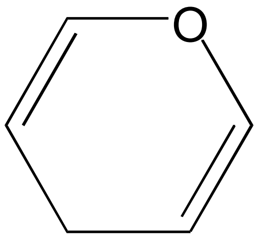
Ketose

Monossacarídeos podem formar estruturas em anel

(a)

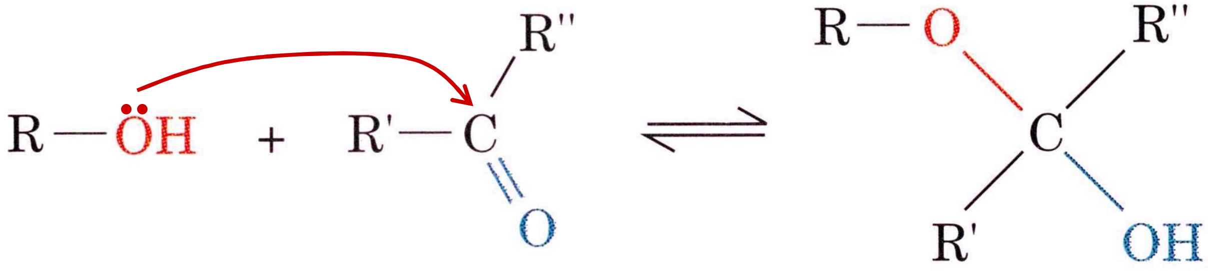


Alcohol Aldehyde Hemiacetal

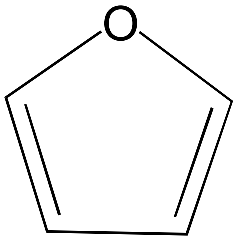


Pirano

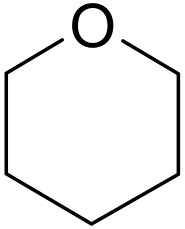
(b)



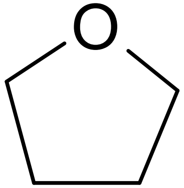
Alcohol Ketone Hemiketal



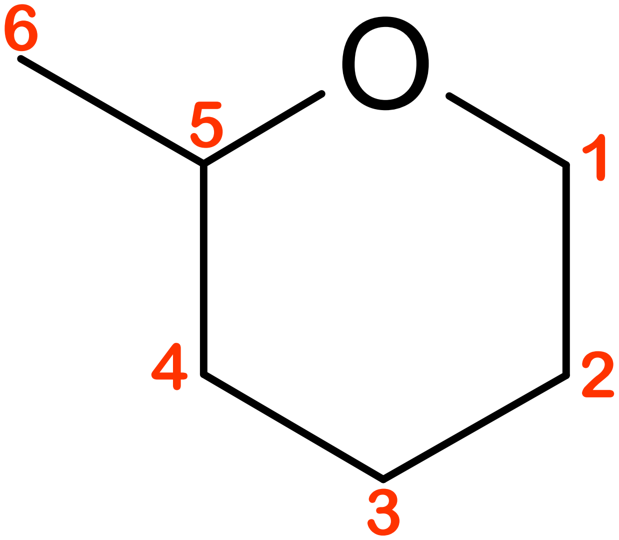
Furano



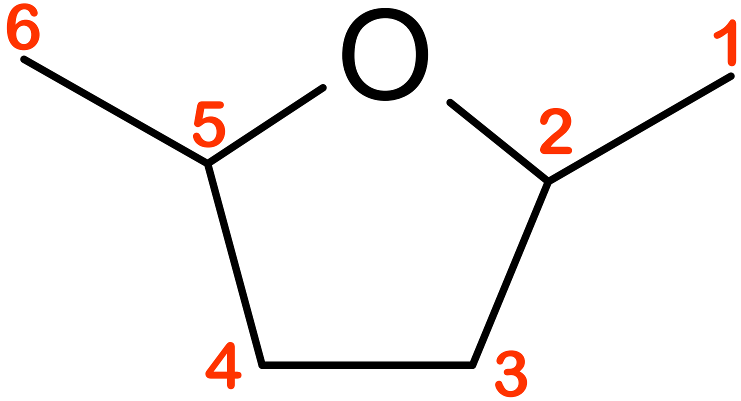
Anel Pirano



Anel Furano



Piranose



Furanose